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Taurospongins B and C, new acetylenic fatty acid derivatives possessing a taurine amide residue from a marine sponge of the family Spongiidae†

Takaaki Kubota,[a] Haruna Suzuki,[a] Azusa Takahashi-Nakaguchi,[b] Jane Fromont,[c] Tohru Gonoi[b] and Jun'ichi Kobayashi*[a]

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Two new acetylenic fatty acid derivatives possessing a taurine amide residue, taurospongins B (**1**) and C (**2**), have been isolated from an Okinawan marine sponge of the family Spongiidae. The gross structures of **1** and **2** were elucidated on the basis of their spectral data, especially 2D NMR and FABMS/MS data. The absolute configurations for **1** and **2** were established by chemical means. Taurospongin C (**2**) showed inhibitory activity against *Cryptococcus neoformans*.

Introduction

Marine sponges of the family Spongiidae have been demonstrated to be a rich source of unique bioactive meroterpenoids[1,2] and acetylenic fatty acid derivatives.[3,4] During our search for bioactive metabolites from marine organisms, we investigated the extract of a sponge family Spongiidae (SS-1202), which resulted in the isolation of two new acetylenic fatty acid derivatives possessing a taurine amide residue, taurospongins B (**1**) and C (**2**). Here we describe the isolation and structure elucidation of **1** and **2** (Fig. 1).

Results and discussion

The sponge family Spongiidae collected at Okinawa, was extracted with MeOH. After evaporation, the MeOH extract was partitioned stepwise between organic solvents (EtOAc and *n*-BuOH) and H_2O. A part of *n*-BuOH soluble materials was fractionated by gel filtration (Sephadex LH-20, MeOH). A fraction eluted in a relatively early stage was purified by C_{18} column chromatography (MeOH–H_2O) and SiO_2 column chromatography (CH_3Cl–MeOH) to afford taurospongins B (**1**, 1.7 mg, 0.00048%, wet weight) and C (**2**, 4.2 mg, 0.0012%).

Taurospongin B (**1**) was obtained as an optically active colorless amorphous solid. The molecular formula of **1** was revealed to be $C_{38}H_{69}NO_7S$ by HRESIMS data [*m*/*z* 682.47036 $(M - H)^-$, Δ −1.84 mmu]. IR absorptions indicated the existence of hydroxy (3421 cm^{-1}), ester carbonyl (1732 cm^{-1}), and amide carbonyl (1646 cm^{-1}) functionalities. The inspection of the HMQC and HMBC spectra with ^1H and ^{13}C NMR data disclosed that **1** consists of ester and amide carbonyls, a triple bond, a double bond, three methyls, twenty seven methylenes, an oxymethine, and an oxygenated quaternary carbon (Table 1). Analysis of the ^1H–^1H COSY and TOCSY spectra of **1** revealed connectivities of C-4 to C-10, C-2′ to C-3′, C-6′ to C-10′, C-23′ to C-25′, and C-1″ to C-2″. The geometry of a double bond between C-8′ and C-9′ was assigned as *Z* by the vicinal coupling constant ($^3J_{H\text{-}8'/H\text{-}9'} = 10.3$ Hz). HMBC correlations of H_2-1″/C-1 and H_2-2/C-1 clarified that N-bearing carbon C-1″ (δ_C 37.3) and a carbonyl-bearing carbon C-2 (δ_C 48.6) were connected *via* an amide bond containing a carbonyl carbon C-1 (δ_C 174.6). Linkings of C-2, a methylene carbon C-4, and a methyl carbon C-11 through an oxygenated quaternary carbon C-3 (δ_C 73.4) were inferred from HMBC correlations of H_3-11/C-2, H_2-4/C-3, and H_3-11/C-4. An HMBC correlation of H_2-2′/C-1′ revealed that a carbonyl-bearing carbon C-2′ (δ_C 36.2) was attached to a carbonyl carbon C-1′ (δ_C 174.6). Linkage of C-3′ and C-6′ by a triple bond between acetylenic carbons C-4′ (δ_C 80.2) and C-5′

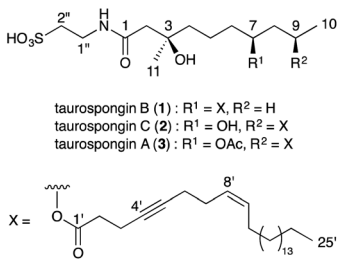

Fig. 1 Taurospongins B (**1**), C (**2**), and A (**3**).

[a]*Graduate School of Pharmaceutical Sciences, Hokkaido University, Sapporo 060-0812, Japan. E-mail: jkobay@pharm.hokudai.ac.jp; Fax: +81 11 706 4989; Tel: +81 11 706 3239*

[b]*Medical Mycology Research Center, Chiba University, Chiba 260-0856, Japan. E-mail: gonoi@faculty.chiba-u.jp; Fax: +81 43 226 2486; Tel: +81 43 226 2492*

[c]*Western Australian Museum, Locked Bag 49, Welshpool DC, WA 6986, Australia. E-mail: Jane.Fromont@museum.wa.gov.au; Fax: +61 8 9212 3882; Tel: +61 8 9212 3745*

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Table 1 ^{1}H and ^{13}C NMR data of taurospongins B (**1**) and C (**2**) in CD_3OD

	1		**2**	
Position	δ_H[a] multi (J in Hz)	δ_C[b]	δ_H[a] multi (J in Hz)	δ_C[b]
1	—	174.6	—	174.5[k]
2	2.40 d (14.0) 2.34 d (14.0)	48.6	2.36[c] m	48.4
3	—	73.4	—	74.2
4	1.59 m[g] 1.53 m[g]	43.8	1.59 m[g] 1.52 m[g]	43.9
5	1.44[c] m[g]	21.6	1.47[c] m[g]	21.8
6	1.61[c] m[g]	36.6	1.64[c] m[g]	36.7
7	4.98 m	76.2	3.67 m[g]	70.1
8	1.59[c] m[g]	38.3	1.85 m[g] 1.64 m[g]	45.3
9	1.43[c] m[g]	20.5[h]	5.15 m	71.3
10	0.96[d] t (7.4)	15.1[i]	1.30[d] d (6.3)	20.7
11	1.25[d] s	27.6	1.27[d] s	27.7
1′	—	174.6	—	174.3[k]
2′	2.51[c] m	36.2	2.50[c] m	36.2
3′	2.48[c] m	16.5	2.48[c] m	16.4
4′	—	80.2	—	80.1
5′	—	82.2	—	82.2
6′	2.18[c] m	20.7[h]	2.18[c] m	20.7
7′	2.23[c] m	28.8[j]	2.23[c] m	28.7[l]
8′	5.44 dt (10.3, 5.6)	130.0	5.44 dt (10.7, 5.4)	130.0
9′	5.45 dt (10.3, 5.6)	132.8	5.46 dt (10.7, 5.4)	132.8
10′	2.09[c] m	29.0[j]	2.09[c] q (6.4)	29.0[l]
11′–22′	1.52–1.15[e] m[g]	31.7–31.1[f]	1.52–1.15[e] m	31.7–31.1[f]
23′	1.33[c] m[g]	33.9	1.38[c] m	33.9
24′	1.38[c] m[g]	24.5	1.33[c] m	24.5
25′	0.94 t (7.1)	15.2[i]	0.94 t (7.0)	15.3
1″	3.66 t (6.5)	37.3	3.67 m[g]	37.3
2″	3.02 t (6.5)	52.2	3.03 t (6.6)	52.2

[a] Recorded at 600 MHz. [b] Recorded at 150 MHz. [c] 2H. [d] 3H. [e] 24H. [f] 12C. [g] J-values were not determined because of overlapping with other signals. [h] These signals might be exchange. [i] These signals might be exchange. [j] These signals might be exchange. [k] These signals might be exchange. [l] These signals might be exchange.

(δ_C 82.2) was uncovered by HMBC correlations of H_2-3′/C-4′ and H_2-6′/C-5′. The chemical shift of a proton H-7 (δ_C 4.98) of an oxygenated carbon C-7 (δ_C 76.2) implied that C-7 was esterified to C-1′. These data and the molecular formula of **1** indicated an attachment of a sulfo group to C-2″ and the connection of C-10′ and C-23′ by a methylene chain (Fig. 2).

The structure of **1** elucidated from the NMR data was also confirmed by a charge-remote fragmentation pattern induced by a sulfo group observed in the FABMS/MS spectrum of **1** (Fig. 3). Thus, the gross structure of taurospongin B (**1**) was elucidated as shown.

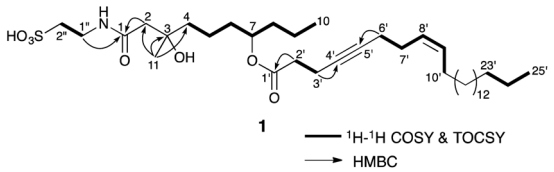


Fig. 2 Selected 2D NMR correlations for taurospongins B (**1**).

The relative stereochemistry of taurospongin B (**1**) was established by comparison of the NMR data of taurineamide part (**4**) of **1** with its two possible diastereomers (**6a** and **6b**). The taurineamide part (**4**) was obtained by methanolysis of an ester linkage of **1** with an acetylenic fatty acid part (**5**) of **1** (Scheme 1).[4]

The taurine amides **6a** and **6b** were synthesized from D-mevalonolactone as follows (Schemes 2 and 3). A hydroxy group of D-mevalonolactone was protected by a TES group and then treated with DIBAL to give lactol (**8**), which was coupled with phosphorane by Wittig reaction. After protection of hydroxy group by a BOM group, the resulting chloro-olefin (**10**) was subjected to a coupling reaction with *n*-butylaldehyde to afford a mixture of acetylenic alcohols (**11a** and **11b**), which was converted into an acetylenic ketone (**12**) by oxidation using AZADO.[5]

The acetylenic ketone (**12**) was derived to chiral acetylenic alcohol (**11a**) by a Noyori asymmetric transfer hydrogenation using Ru[(*S*,*S*)-Tsdpen](*p*-cymene).[6] The absolute stereochemistry at C-7 of **11a** was verified by modified Mosher's method[7] to be *R*-configuration. After the hydroxy group of the **11a** was protected by TBS group, deprotection of BOM group and reduction of the triple bond were accomplished by using Pearlman's catalyst.[8] The resulting primary alcohol (**14a**) was oxidized to carboxylic acid (**15a**) by combination of Parikh–Doering oxidation[9] and Lindgren–Kraus oxidation.[10] Finally, the carboxylic acid was coupled with taurine by amidation using DMT-MM[11] to obtain 3*S*,7*R*-isomer (**6a**). The 3*S*,7*S*-isomer (**6b**) was prepared from the acetylenic ketone (**12**) in a similar manner using Ru[(*R*,*R*)-Tsdpen](*p*-cymene).[6] Since the ^{1}H NMR

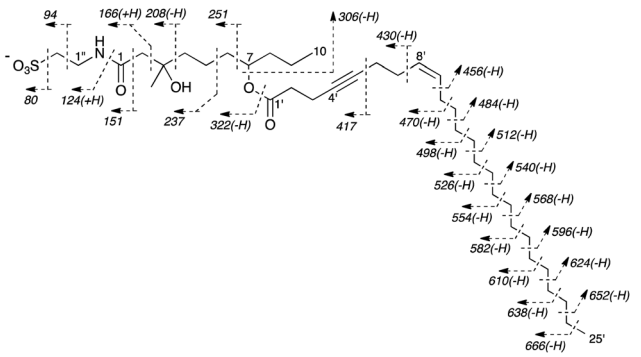
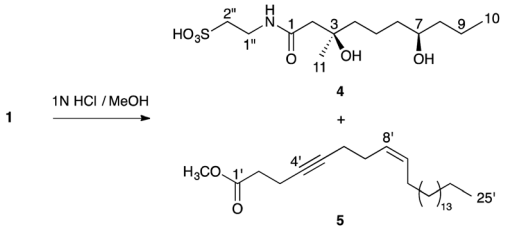
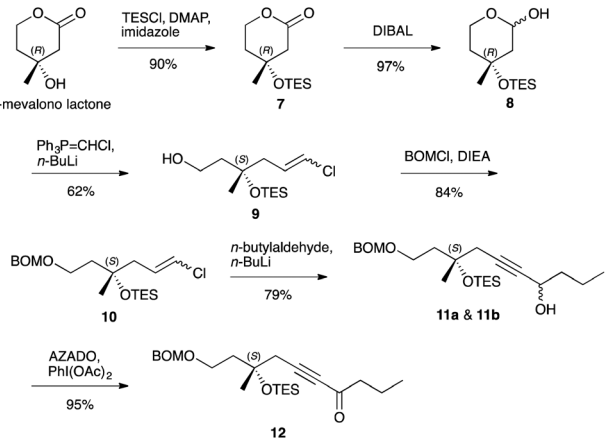


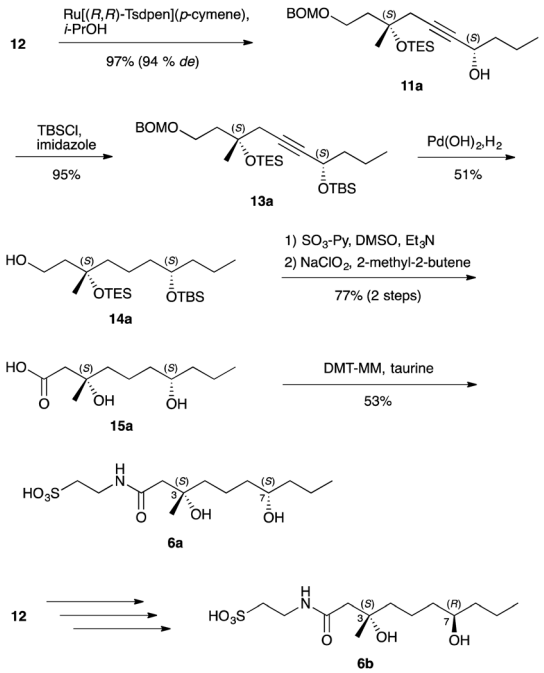
Fig. 3 Fragmentation patterns observed in FABMS/MS spectrum of taurospongin B (**1**) [precursor ion, m/z 682 $(M - H)^-$]. The m/z values were indicated in italics.



Scheme 1 Methanolysis of taurospongin B (**1**).



Scheme 2 Synthesis of **6a** and **6b** (part 1).



Scheme 3 Synthesis of **6a** and **6b** (part 2).

spectra of taurineamide part (**4**) of taurospongin B (**1**) was coincident with that of **6a**, relative relasionship for two hydroxy groups of **4** were uncoverd to be *syn* relationship.

The absolute configuration at C-7 of taurospongin B (**1**) was established by modified Mosher's method.[7] Treatment of taurineamide part (**4**) with (*R*)-(−)- and (*S*)-(+)-MTPACl gave (*S*)- and (*R*)-MTPA esters of **4**, respectively. $\Delta\delta$ values obtained from ^{1}H NMR data of MTPA esters of **4** (Fig. 4) indicated that **4** was an enantiomer of **6a** and the absolute configuration at C-7 of **4** was *R*. Therefore, the absolute configurations at C-3 and C-7 of taurospongin B (**1**) were assigned as both *R*.

Taurospongin C (**2**) was obtained as an optically active colorless amorphous solid. The molecular formula of **2** was elucidated as $C_{38}H_{69}NO_8S$ by HRESIMS data [*m*/*z* 698.46739 $(M - H)^-$, Δ +0.28 mmu]. IR absorptions suggested that **2**

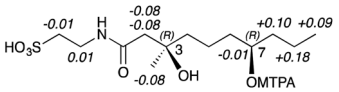


Fig. 4 $\Delta\delta$ values [$\Delta\delta$ (in ppm) = $\delta_S - \delta_R$] obtained for the (*S*)- and (*R*)-MTPA esters of taurineamide part (**4**) of taurospongin B (**1**). $\Delta\delta$ values were indicated in italic.

possesses hydroxy (3369 cm^{-1}), ester carbonyl (1730 cm^{-1}), and amide carbonyl (1636 cm^{-1}) functionalitiess. The ^{1}H and ^{13}C NMR data of **2** were almost superimposable to those of taurospongin A (**3**),[4,12,13] except for disappearance of signals derived from an acetyl group. In addition, the difference of the molecular formula between **2** and **3** implied that **2** was a 9-*O*-desacetyl form of **3**. To verify the prediction, **2** was derived to 9-*O*-acetyl form by treatment of **2** with acetic anhydride and pyridine. Since the spectral data of 9-*O*-acetyl form of **2** was identical with those of **3**, **2** was assigned as 9-*O*-desacetyl taurospongin A (**3**).

Antimicrobial assay[14] of taurospongins B (**1**), C (**2**), and A (**3**) revealed that **2** and **3** exhibited mild and good antifungal activity, respectively, against *Cryptococcus neoformans* (MIC, 32 and 1 μg mL^{-1}), while **1** did not show such activity (MIC > 32.0 μg mL^{-1}). Taurospongins B (**1**), C (**2**), and A (**3**) were not active against other fungi *Aspergillis niger*, *Trichophyton mentagrophytes*, and *Candida albicans* (MIC > 32 μg mL^{-1}), and bacteria *Escherichia coli*, *Staphylococcus aureus*, *Bacillus subtilis*, and *Micrococcus luteus* (IC_{50} > 32 μg mL^{-1}). Taurospongins B (**1**), C (**2**), and A (**3**) did not show cytotoxicity (IC_{50} > 10 μg mL^{-1}) against murine lymphoma L1210 and human epidermoid carcinoma KB cells *in vitro*.

Conclusions

Taurospongins B (**1**) and C (**2**), two new acetylenic fatty acid derivatives possessing a taurine amide residue, have been isolated from an Okinawan marine sponge of the family Spongiidae. The absolute structures of **1** and **2** were established by combination of spectroscopic analysis and synthetic chemistry. Taurospongins C (**2**) and A (**3**) showed mild and good antifungal activity, respectively, against *Cryptococcus neoformans* (MIC, 32 and 1 μg mL^{-1}).

Experimental section

General experimental procedures

Optical rotations were recorded on a JASCO P-1030 polarimeter. IR spectra were recorded on JASCO FT/IR-230 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on JEOL ECA400 and JEOL ECA500 spectrometers using 5 mm cell and a Bruker AMX-600 spectrometer using 2.5 mm micro cell. The 7.20 and 77.0 ppm resonances of residual $CHCl_3$ and $CDCl_3$, and 3.35 and 49.8 ppm resonances of residual CD_2HOD and CD_3OD were used as internal references for ^{1}H and ^{13}C NMR spectra, respectively. EIMS spectra were recorded on a JEOL JMS-700TZ mass spectrometer. ESIMS spectra were recorded on JEOL JMS-700TZ and Thermo Scientific Exactive mass spectrometers.

Sponge description

The sponge (SS-1202, family Spongiidae) was collected at Unten Port, Okinawa, and kept frozen until used. The sponge was medium brown mound with a spiky, conulose surface, hispid with a fine adherent membrane, and alcohol brown stains. Dermis was unarmored. The sponge has a reticulate fibre skeleton with some pithing of fibres centrally. The reticulation is irregular and all fibres are uncored. Primary fibres are ~50 μm wide. Secondary fibres are ~40 μm wide with finer fibres between as a tertiary skeleton, 10 μm wide. The voucher specimen was deposited at Graduate School of Pharmaceutical Sciences, Hokkaido University.

Extraction and isolation

The sponge of the family Spongiidae (SS-1202, 1.25 kg, wet weight) collected at Okinawa, was extracted with MeOH (2L × 2) to afford the extract (73.3 g), which was partitioned stepwise between organic solvents [EtOAc (500 mL × 3) and *n*-BuOH (500 mL × 3)] and H_2O (500 mL) to give EtOAc-soluble materials (11.8 g) and *n*-BuOH-soluble materials (3.6 g). A part (1.0 g) of *n*-BuOH soluble materials was fractionated by gel filtration (Sephadex LH-20, GE Healthcare; eluent, MeOH). A fraction was purified by C_{18} column chromatography (Cosmosil 140 C_{18} PREP, Nakarai Tesque Inc.; eluent, MeOH–H_2O, 70 : 30 to 100 : 0) and SiO_2 column chromatography (Wakosil C-300, Wako Pure Chemical Industries, Ltd.; eluent, CH_3Cl–MeOH, 95 : 5 to 0 : 100) to afford taurospongins B (**1**, 1.7 mg, 0.00048%, wet weight) and C (**2**, 4.2 mg, 0.0012%).

Taurospongin B (1). Colorless amorphous solid; $[\alpha]_D^{25}$ + 3.4 (*c* 1.0, MeOH); IR (film) ν_{max} 3421, 1732, 1646, 1456, 1172, 1046 cm^{-1}; ^1H and ^{13}C NMR data see Table 1; HRESIMS (neg.) *m*/*z* 682.47036 [calcd for $C_{38}H_{68}NO_7S$ $(M - H)^-$, Δ −1.84 mmu].

Taurospongin C (2). Colorless amorphous solid; $[\alpha]_D^{25}$ + 0.5 (*c* 1.0, MeOH); IR (film) ν_{max} 3369, 1730, 1636, 1465, 1171, 1044 cm^{-1}; ^1H and ^{13}C NMR data see Table 1; HRESIMS (neg.) *m*/*z* 698.46739 [calcd for $C_{38}H_{68}NO_8S$ $(M - H)^-$, Δ +0.28 mmu].

Solvolysis of taurospongin B (1). Taurospongin B (1, 1.0 mg, 1.46 μmol) was dissolved in MeOH–1 M HCl (10 : 1, 500 μl). After stirring for 12 h at 80 °C, the mixture was concentrated by Ar blowing. The residue was extracted with $CHCl_3$, which was concentrated by Ar blowing to afford acetylenic fatty acid part (5, 0.5 mg, 1.28 μmol, 88%). The remaining $CHCl_3$ insoluble material was taurineamide part (4, 0.4 mg, 1.23 μmol, 84%).

Taurineamide part (4). ^1H NMR (600 MHz, CD_3OD) δ 3.67 (t, J = 6.6 Hz, 2H), 3.58 (m, 1H), 3.03 (t, J = 6.6 Hz, 2H), 2.43 (d, J = 14.0 Hz, 1H), 2.36 (d, J = 14.0 Hz, 1H), 1.66–1.32 (m, 10H), 1.27 (s, 3H), 0.97 (t, J = 7.1 Hz, 9H); HRESIMS (neg.) *m*/*z* 324.14876 [calcd for $C_{13}H_{26}NO_6S$ $(M - H)^-$, Δ +0.13 mmu].

(*S*)-MTPA ester of 4. (*R*)-(−)-MTPACl (1.23 μl) was added to a solution of 4 (0.4 mg, 1.23 μmol) in pyridine (50 μl). After stirring for 1 h at rt, (*R*)-(−)-MTPACl (1.23 μl) was added to the mixture additionally. After stirring for 1 h at rt, the reaction mixture was concentrated *in vacuo*. The residue was dissolved with MeOH and passed through an ion-exchange column (Amberlite IR-120 H^+ form, eluent, MeOH) and concentrated *in vacuo*. Then, the residue was purified by C18 HPLC (Mightysil RP-18 GP, Kanto Chemical Co., Inc., 4.6 × 250 mm; eluent, CH_3CN–H_2O, 70–100%; flow rate, 1.0 mL min^{-1}; UV detection at 230 nm) to afford (*S*)-MTPA ester of 4 (0.4 mg, 0.74 mmol, 60%); ^1H NMR (600 MHz, CD_3OD) δ 7.57 (m, 1H), 7.48 (m, 1H), 5.16 (m, 1H), 3.65 (t, J = 6.6 Hz, 2H), 3.59 (s, 3H), 3.02 (t, J = 6.6 Hz, 2H), 2.30 (d, J = 14.3 Hz, 1H), 2.24 (d, J = 14.3 Hz, 1H), 1.59 (m, 2H), 1.24 (m, 2H), 1.80–1.10 (m, 6H), 1.14 (s, 3H), 0.99 (t, J = 7.3 Hz, 3H); HRESIMS (neg.) *m*/*z* 540.18929 [calcd for $C_{23}H_{33}NO_8F_3S$ $(M - H)^-$, Δ +0.84 mmu].

(*R*)-MTPA ester of 4. The (*R*)-MTPA ester of 4 (0.4 mg, 0.74 mmol) was obtained from 4 (0.4 mg, 1.23 μmol) in 60% by using (*S*)-(+)-MTPACl through the same procedure as described for preparation of the (*S*)-MTPA ester of **4**.; ^1H NMR (600 MHz, CD_3OD) δ 7.57 (m, 1H), 7.47 (m, 4H), 5.17 (m, 1H), 3.66 (t, J = 6.6 Hz, 2H), 3.60 (s, 3H), 3.02 (t, J = 6.6 Hz, 2H), 2.38 (d, J = 14.3 Hz, 1H), 2.32 (d, J = 14.3 Hz, 1H), 1.69 (m, 2H), 1.42 (m, 2H), 1.80–1.10 (m, 6H), 1.22 (s, 3H), 0.90 (t, J = 7.3 Hz, 3H); HRESIMS (neg.) *m*/*z* 540.18851 [calcd for $C_{23}H_{33}NO_8F_3S$ $(M - H)^-$, Δ +0.06 mmu].

(*R*)-4-Methyl-4-((triethylsilyl)oxy)tetrahydro-2*H*-pyran-2-one (7). Imidazole (1.12 g, 16.45 mmol), DMAP (100.4 mg, 0.82 mmol), and TESCl (2.06 mL, 12.27 mmol) were added to a solution of D-mevalonolactone (1.07 g, 8.22 mmol) in DMF (20 mL) at 0 °C. After stirring for 24 h at rt, H_2O was added to the mixture, which was extracted with EtOAc. The organic layer was washed with saturated aqueous $CuSO_4$, H_2O, and brine, dried with $MgSO_4$, and concentrated *in vacuo*. The residue was purified by a SiO_2 column (*n*-hexane–EtOAc, 100 : 0 to 85 : 15) to afford 7 (1.81 g, 7.41 mmol, 90%); yellow oil; $[\alpha]_D^{21}$ − 28 (*c* 1.6, $CHCl_3$); IR (neat) ν_{max} 2957, 2877, 1738, 1458, 1223, 1005, 725 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.58 (m, 1H), 4.34 (m, 1H), 2.67 (brd, J = 17.2 Hz, 1H), 2.43 (d, J = 17.2 Hz, 1H), 1.84 (m, 2H), 1.39 (s, 3H), 0.94 (t, J = 8.0 Hz, 9H), 0.60 (q, J = 8.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 70.4, 66.1, 45.6, 36.9, 29.0, 6.8, 6.3; HRESIMS (pos.) *m*/*z* 267.13881 [calcd for $C_{12}H_{24}O_3NaSi$ $(M + Na)^+$, Δ +0.12 mmu].

(4*R*)-4-Methyl-4-((triethylsilyl)oxy)tetrahydro-2*H*-pyran-2-ol (8). DIBAL (1.04 M in hexane, 8.76 mL, 9.11 mmol) was added to a solution of 7 (1.85 g, 7.57 mmol) in CH_2Cl_2 (20 mL) at −78 °C. After stirring for 1 h at −78 °C, MeOH and saturated aqueous potassium sodium tartrate were added to the mixture, which was allowed to warm to rt with vigorous stirring for 1 h and extracted with EtOAc. The organic layer was washed with H_2O and brine, dried with $MgSO_4$, and concentrated *in vacuo*. The residue was purified by a SiO_2 column (*n*-hexane–EtOAc, 100 : 0 to 85 : 15) to afford 8 (1.81 g, 7.35 mmol, 97%), which was directly used in the next step; yellow oil; HRESIMS (pos.) *m*/*z* 269.15447 [calcd for $C_{12}H_{26}O_3NaSi$ $(M + Na)^+$, Δ +0.13 mmu].

(*S*)-6-Chloro-3-methyl-3-((triethylsilyl)oxy)hex-5-en-1-ol (9). *n*-BuLi (1.60 M in hexane, 18.6 mL, 29.76 mmol) was added dropwise to a solution of (chloromethyl)triphenylphosphonium chloride (10.33 g, 29.76 mmol) in THF (40 mL) at −78 °C. After stirring for 30 min at −78 °C, a solution of 8 (1.83 g, 7.43 mmol) in THF (3 mL) was added dropwise to the mixture at −78 °C. After stirring for 39 h at −78 °C, saturated aqueous NH_4Cl was added to the mixture, which was extracted with EtOAc. The organic layer was washed with H_2O and brine, dried with

$MgSO_4$, and concentrated *in vacuo*. The residue was purified by a SiO_2 column (*n*-hexane–EtOAc, 100 : 0 to 90 : 10) to afford 9 (1.29 g, 4.63 mmol, 62%), which was directly used in the next step; pale yellow oil; HRESIMS (pos.) *m*/*z* 301.13601 [calcd for $C_{13}H_{27}O_2ClNaSi$ (M + Na) $^+$, Δ −0.10 mmu].

(*S*)-7-(3-Chloroallyl)-9,9-diethyl-7-methyl-1-phenyl-2,4,8-trioxa-9-silaundecane (10). *N*,*N*-Diisopropylethylamine (3.15 mL, 18.56 mmol) and benzylchloromethyl ether (1.91 mL, 13.92 mmol) were added to a solution of 9 (1.29 g, 4.63 mmol) in CH_2Cl_2 (32 mL) at 0 °C. After stirring for 12 h at 0 °C, saturated aqueous NH_4Cl was added to the mixture, which was extracted with EtOAc. The organic layer was washed with H_2O and brine, dried with $MgSO_4$, and concentrated *in vacuo*. The residue was purified by a SiO_2 column (*n*-hexane–EtOAc, 100 : 0 to 90 : 10) to afford 10 (1.56 g, 3.91 mmol, 84%), which was directly used in the next step; pale yellow oil; HRESIMS (pos.) *m*/*z* 421.19366 [calcd for $C_{21}H_{35}O_3ClNaSi$ (M + Na)$^+$, Δ +0.04 mmu].

(8*S*)-10-((Benzyloxy)methoxy)-8-methyl-8-((triethylsilyl)oxy)-dec-5-yn-4-ol (11a and 11b). *n*-BuLi (1.60 M in hexane, 6.64 mL, 10.63 mmol) was added dropwise to a solution of 10 (1.41 g, 3.53 mmol) in THF (15 mL) at −78 °C. After stirring for 2 h at −78 °C, *n*-BuLi (1.60 M in hexane, 2.21 mL, 3.54 mmol) was added dropwise at −78 °C additionally. Then a solution of butyraldehyde (0.80 mL, 8.86 mmol) in THF (15 mL) was added dropwise to the mixture. After stirring for 1 h at −78 °C, saturated aqueous NH_4Cl was added to the mixture, which was extracted with EtOAc. The organic layer was washed with H_2O and brine, dried with $MgSO_4$, and concentrated *in vacuo*. The residue was purified by a SiO_2 column (*n*-hexane–EtOAc, 100 : 0 to 90 : 10) to afford mixture of **11a** and **11b** (1.21 g, 2.78 mmol, 79%), which was directly used in the next step; pale yellow oil; HRESIMS (pos.) *m*/*z* 457.27449 [calcd for $C_{25}H_{42}O_4NaSi$ (M + Na)$^+$, Δ +0.03 mmu].

(*S*)-10-((Benzyloxy)methoxy)-8-methyl-8-((triethylsilyl)oxy)-dec-5-yn-4-one (12). Iodobenzene diacetate (1.36 g, 4.23 mmol) and AZADO (42.9 mg, 0.28 mmol) were added to a solution of **11a** and **11b** (1.24 g, 2.82 mmol) in CH_2Cl_2 (4 mL). After stirring for 4 h at rt, CH_2Cl_2 (35 mL) and a mixture of saturated aqueous $NaHCO_3$ and saturated aqueous Na_2SO_4 (1 : 1, 30 mL) were added to the mixture, which was extracted with CH_2Cl_2. The organic layer was washed with brine, dried with $MgSO_4$, and concentrated *in vacuo*. The residue was purified by a SiO_2 column (*n*-hexane–EtOAc, 100 : 0 to 90 : 10) to afford 12 (1.16 g, 2.68 mmol, 95%); pale yellow oil; $[\alpha]_D^{22}$ + 5.0 (*c* 1.25, $CHCl_3$); IR (neat) ν_{max} 3019, 2876, 2211, 1673, 1455, 1377, 1240, 1171, 1114, 1045, 742, 698 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.26 (m, 5H), 4.75 (s, 2H), 4.60 (s, 2H), 3.72 (m, 2H), 2.61 (d, J = 17.1 Hz, 1H), 2.54 (d, J = 17.1 Hz, 1H), 2.50 (t, J = 7.3 Hz, 1H), 1.96 (ddd, J = 13.9, 7.3, 6.8 Hz, 1H), 1.89 (ddd, J = 13.9, 7.5, 6.4 Hz, 1H), 1.69 (qt, J = 7.3, 7.3 Hz, 2H), 1.37 (s, 3H), 0.95 (qt, J = 7.8 Hz, 9H), 0.93 (t, J = 7.3 Hz, 3H), 0.60 (q, J = 7.8 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 188.1, 138.0, 128.4, 127.8, 127.7, 94.7, 91.1, 82.6, 73.9, 69.4, 64.1, 47.4, 41.6, 33.8, 28.1, 17.6, 13.5, 7.0, 6.7; HRESIMS (pos.) *m*/*z* 455.25877 [calcd for $C_{25}H_{40}O_4NaSi$ (M + Na)$^+$, Δ −0.04 mmu].

(4*S*,8*S*)-10-((Benzyloxy)methoxy)-8-methyl-8-((triethylsilyl)oxy)-dec-5-yn-4-ol (11a). A solution of 12 (580 mg, 1.34 mmol) in i-PrOH (11.6 mL) was added to a solution of [(1*S*,2*S*)-*N*-(*p*-toluenesulfonyl)-1,2-duphenylethanediamine]-(*p*-cymene)ruthenium(II) (68.4 mg, 0.11 mmol) in i-PrOH (8.29 mL). After stirring for 3 h at rt, the reaction mixture was concentrated *in vacuo*. The residue was purified by a SiO_2 column (*n*-hexane–EtOAc, 100 : 0 to 80 : 20) to afford 11a (563 mg, 1.30 mmol, 97%, 97 : 3 dr); pale brown oil; $[\alpha]_D^{23}$ + 4.8 (*c* 1.23, $CHCl_3$); IR (neat) ν_{max} 3441, 2956, 2875, 1455, 1376, 1150, 1111, 1041, 733 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.26 (m, 5H), 4.76 (s, 2H), 4.61 (s, 2H), 4.33 (brt, J = 6.5 Hz, 1H), 3.74 (t, J = 7.4 Hz, 2H), 2.44 (dd, J = 16.4 and 1.5 Hz, 1H), 2.36 (dd, J = 16.4 and 1.8 Hz, 1H), 2.03–1.75 (m, 3H), 1.63 (m, 2H), 1.46 (m, 2H), 1.33 (s, 3H), 0.94 (t, J = 7.9 Hz, 9H), 0.93 (t, J = 7.3 Hz, 3H), 0.59 (q, J = 7.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.8, 128.4, 127.9, 127.7, 94.5, 83.4, 82.3, 74.0, 69.3, 64.4, 62.4, 41.2, 40.1, 33.4, 28.0, 18.4, 13.7, 7.0, 6.7; HRESIMS (pos.) *m*/*z* 457.27512 [calcd for $C_{25}H_{42}O_4NaSi$ (M + Na)$^+$, Δ +0.66 mmu].

(*S*)-MTPA ester of 11a. DMAP (0.2 mg), Et_3N (0.65 μl), and (*R*)-(−)-MTPACl (0.33 μl) were added to a solution of **11a** (0.5 mg, 1.15 mmol) in CH_2Cl_2 (30 μl). After stirring for 3 h at rt, *N*,*N*-dimethyl 1,3-propanediamine (0.64 μl) was added to the mixture. After stirring for 15 min at rt, the reaction mixture was concentrated *in vacuo*. The residue was purified by SiO_2 (hexane–EtOAc, 1 : 0 to 2 : 1) to afford (*S*)-MTPA ester of 11a (0.7 mg, 1.08 mmol, 94%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.71–7.29 (m, 10H), 5.56 (t, J = 6.7 Hz, 1H), 4.73 (s, 2H), 4.59 (s, 2H), 3.71 (t, J = 7.3 Hz, 2H), 3.58 (s, 3H), 2.46 (d, J = 16.4 Hz, 1H), 2.38 (d, J = 16.4 Hz, 1H), 1.93 (m, 1H), 1.86 (m, 1H), 1.73 (m, 2H), 1.35 (m, 2H), 1.31 (s, 3H), 0.93 (t, J = 7.9 Hz, 9H), 0.87 (t, J = 7.3 Hz, 3H), 0.57 (q, J = 7.9 Hz, 6H); HRESIMS (pos.) *m*/*z* 673.31519 [calcd for $C_{35}H_{49}O_6F_3NaSi$ (M + Na)$^+$, Δ +0.92 mmu].

(*R*)-MTPA ester of 11a. The (*R*)-MTPA ester (0.7 mg, 1.08 mmol) of **11a** was obtained from **11a** (0.5 mg, 1.15 mmol) in 94% by using (*S*)-(−)-MTPACl through the same procedure as described for preparation of the (*S*)-MTPA ester of **11a**; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.70–7.29 (m, 10H), 5.53 (t, J = 6.7 Hz, 1H), 4.73 (s, 2H), 4.59 (s, 2H), 3.70 (t, J = 7.1 Hz, 2H), 3.54 (s, 3H), 2.42 (d, J = 16.4 Hz, 1H), 2.35 (d, J = 16.4 Hz, 1H), 1.91 (m, 1H), 1.84 (m, 1H), 1.80 (m, 2H), 1.46 (m, 2H), 1.29 (s, 3H), 0.93 (t, J = 7.4 Hz, 3H), 0.92 (t, J = 7.8 Hz, 9H), 0.56 (q, J = 7.9 Hz, 6H); HRESIMS (pos.) *m*/*z* 673.31528 [calcd for $C_{35}H_{49}O_6F_3NaSi$ (M + Na)$^+$, Δ +1.01 mmu].

(4*R*,8*S*)-10-((Benzyloxy)methoxy)-8-methyl-8-((triethylsilyl)-oxy)dec-5-yn-4-ol (11b). 11b (555 mg, 1.28 mmol) was obtained from 12 (580 mg, 1.34 mmol) in 96% (97 : 3 dr) by using [(1*R*,2*R*)-*N*-(*p*-toluenesulfonyl)-1,2-duphenylethanediamine]-(*p*-cymene)ruthenium(II) through the same procedure as described for preparation of 11a; pale brown oil; $[\alpha]_D^{23}$ + 8.4 (*c* 1.77, $CHCl_3$); IR (neat) ν_{max} 3447, 2956, 2875, 1455, 1376, 1150, 1112, 1041, 741 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.26 (m, 5H), 4.76 (s, 2H), 4.61 (s, 2H), 4.33 (brs, 1H), 3.74 (t, J = 7.3 Hz, 2H), 2.44 (dd, J = 16.4 and 1.8 Hz, 1H), 2.36 (dd, J = 16.4 and 1.8 Hz, 1H), 1.98 (m, 1H), 1.87 (m, 2H), 1.63 (m, 2H), 1.46 (m, 2H), 1.33 (s, 3H), 0.94 (t, J = 7.8 Hz, 9H), 0.93 (t, J = 7.4 Hz, 3H), 0.59 (q, J = 7.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.8, 128.4, 127.9, 127.7, 94.5, 83.4, 82.3, 74.0, 69.2, 64.4, 62.4, 41.2, 40.1, 33.4,

28.0, 18.5, 13.7, 7.1 6.6; HRESIMS (pos.) *m*/*z* 457.27408 [calcd for $C_{25}H_{42}O_4NaSi$ $(M + Na)^+$, Δ −0.38 mmu].

(*S*)-MTPA ester of 11b. The (*S*)-MTPA ester (0.7 mg, 1.08 mmol) of **11b** was obtained from **11b** (0.5 mg, 1.15 mmol) in 94% through the same procedure as described for preparation of the (*S*)-MTPA ester of **11a**; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.71–7.29 (m, 10H), 5.53 (t, J = 6.4 Hz, 1H), 4.72 (s, 2H), 4.58 (s, 2H), 3.69 (t, J = 7.3 Hz, 2H), 3.54 (s, 3H), 2.43 (d, J = 16.4 Hz, 1H), 2.35 (d, J = 16.4 Hz, 1H), 1.89 (m, 1H), 1.83 (m, 1H), 1.81 (m, 2H), 1.46 (m, 2H), 1.29 (s, 3H), 0.93 (t, J = 7.8 Hz, 9H), 0.88 (t, J = 7.5 Hz, 3H), 0.57 (q, J = 7.8 Hz, 6H); HRESIMS (pos.) *m*/*z* 673.31405 [calcd for $C_{35}H_{49}O_6F_3NaSi$ $(M + Na)^+$, Δ −0.22 mmu].

(*R*)-MTPA ester of 11b. The (*R*)-MTPA ester (0.7 mg, 1.08 mmol) of **11b** was obtained from **11b** (0.5 mg, 1.15 mmol) in 94% by using (*S*)-(−)-MTPACl through the same procedure as described for preparation of the (*S*)-MTPA ester of **11a**; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.71–7.29 (m, 10H), 5.56 (t, J = 6.6 Hz, 1H), 4.73 (s, 2H), 4.58 (s, 2H), 3.71 (t, J = 7.3 Hz, 2H), 3.58 (s, 3H), 2.46 (d, J = 16.4 Hz, 1H), 2.39 (d, J = 16.4 Hz, 1H), 1.92 (m, 1H), 1.85 (m, 1H), 1.73 (m, 2H), 1.36 (m, 2H), 1.32 (s, 3H), 0.93 (t, J = 7.9 Hz, 9H), 0.87 (t, J = 7.3 Hz, 3H), 0.58 (q, J = 7.9 Hz, 6H); HRESIMS (pos.) *m*/*z* 673.31402 [calcd for $C_{35}H_{49}O_6F_3NaSi$ $(M + Na)^+$, Δ −0.25 mmu].

(7*S*,11*S*)-7,13,13,14,14-Pentamethyl-1-phenyl-11-propyl-7-((triethylsilyl)oxy)-2,4,12-trioxa-13-silapentadec-9-yne (13a). Imidazole (175.4 mg, 2.58 mmol) and TBSCl (290.3 mg, 1.94 mmol) were added to a solution of **11a** (560 mg, 1.29 mmol) in CH_2Cl_2 (11 mL). After stirring for 3 h at rt, saturated aqueous NH_4Cl was added to the mixture, which was extracted with CH_2Cl_2. The organic layer was washed with H_2O and brine, dried with $MgSO_4$, and concentrated *in vacuo*. The residue was purified by a SiO_2 column (*n*-hexane–EtOAc, 100 : 0 to 90 : 10) to afford 13a (675 mg, 1.23 mmol, 95%); colorless oil; $[\alpha]_D^{24}$ − 14.6 (*c* 1.17, $CHCl_3$); IR (neat) ν_{max} 2956, 2876, 1456, 1251, 1111, 1041, 836, 776, 731 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.26 (m, 5H), 4.75 (s, 2H), 4.60 (s, 2H), 4.33 (brt, J = 6.3, 1H), 3.73 (t, J = 7.4 Hz, 2H), 2.43 (dd, J = 16.4 and 1.5 Hz, 1H), 2.34 (dd, J = 16.4 and 1.9 Hz, 1H), 1.98 (m, 1H), 1.86 (m, 1H), 1.61 (m, 2H), 1.42 (m, 2H), 1.33 (s, 3H), 0.94 (t, J = 7.9 Hz, 9H), 0.91 (t, J = 7.3 Hz, 3H), 0.90 (s, 9H), 0.58 (q, J = 7.9 Hz, 6H), 0.11 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.9, 128.4, 127.9, 127.6, 94.6, 84.0, 81.1, 74.1, 69.2, 64.4, 62.9, 41.1, 41.1, 33.5, 28.0, 25.8, 18.6, 18.2, 13.8, 7.1, 6.7, −4.5, −5.1; HRESIMS (pos.) *m*/*z* 571.36206 [calcd for $C_{31}H_{56}O_4NaSi_2$ $(M + Na)^+$, Δ +1.13 mmu].

(7*S*,11*R*)-7,13,13,14,14-Pentamethyl-1-phenyl-11-propyl-7-((triethylsilyl)oxy)-2,4,12-trioxa-13-silapentadec-9-yne (13b). 13b (674 mg, 1.23 mmol) was obtained from **11b** (554 mg, 1.27 mmol) in 97% through the same procedure as described for preparation of **13a**; colorless oil; $[\alpha]_D^{23}$ + 16.5 (*c* 1.52, $CHCl_3$); IR (neat) ν_{max} 2958, 2876, 1456, 1251, 1111, 1041, 836, 776, 731 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.26 (m, 5H), 4.75 (s, 2H), 4.60 (s, 2H), 4.33 (brt, J = 6.5 Hz, 1H), 3.73 (t, J = 7.4 Hz, 2H), 2.43 (dd, J = 16.3 and 1.8 Hz, 1H), 2.35 (dd, J = 16.3 and 1.8 Hz, 1H), 1.98 (m, 1H), 1.86 (m, 1H), 1.62 (m, 2H), 1.42 (m, 2H), 1.33 (s, 3H), 0.94 (t, J = 7.8 Hz, 9H), 0.91 (t, J = 7.1 Hz, 3H), 0.90 (s, 9H), 0.59 (q, J = 7.8 Hz, 6H), 0.12 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.9, 128.4, 127.9, 127.6, 94.6, 84.0, 81.1, 74.1, 69.2, 64.3, 62.9, 41.1, 41.1, 33.5, 28.0, 25.8, 18.6, 18.2, 13.8, 7.1, 6.7, −4.5, −5.1; HRESIMS (pos.) *m*/*z* 571.36052 [calcd for $C_{31}H_{56}O_4NaSi_2$ $(M + Na)^+$, Δ −0.41 mmu].

(3*S*,7*S*)-7-((*tert*-Butyldimethylsilyl)oxy)-3-methyl-3-((triethylsilyl)oxy)decan-1-ol (14a). 20% $Pd(OH)_2$/C (13.5 mg) was added to a solution of **13a** (27 mg, 0.049 mmol) in EtOAc (2.5 mL) and the mixture was stirred under H_2 at rt. Additional 20% $Pd(OH)_2$/C (13.5 mg) and EtOAc (2.5 mL) were added to the mixture every 1 h. After stirring under H_2 for 5 h at rt, the mixture was filtered through a cotton plug, and the filtrate was concentrated *in vacuo*. The residue was purified by a SiO_2 column ($CHCl_3$) to afford 14a (10.9 mg, 0.025 mmol, 51%); colorless oil; $[\alpha]_D^{24}$ + 4.2 (*c* 1.87, $CHCl_3$); IR (neat) ν_{max} 3363, 2956, 2932, 2875, 1455, 1253, 1040, 773 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.78 (brq, 5.2 Hz, 2H), 3.63 (brquin, J = 5.6 Hz, 1H), 3.18 (brt, J = 4.5 Hz, 1H), 1.75 (dt, J = 14.5, 5.6 Hz, 1H), 1.70–1.56 (m, 2H), 1.53–1.15 (m, 12H), 0.95 (t, J = 7.9 Hz, 9H), 0.89 (t, J = 7.2 Hz, 3H), 0.87 (s, 9H), 0.60 (q, J = 7.9 Hz, 6H), 0.03 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 77.8, 72.0, 60.0, 43.2, 42.0, 39.4, 37.6, 27.7, 25.9, 20.6, 18.5, 18.1, 14.3, 7.0, 6.7, −4.5; HRESIMS (pos.) *m*/*z* 455.33454 [calcd for $C_{23}H_{52}O_3NaSi_2$ $(M + Na)^+$, Δ −0.18 mmu].

(3*S*,7*R*)-7-((*tert*-Butyldimethylsilyl)oxy)-3-methyl-3-((triethylsilyl)oxy)decan-1-ol (14b). 14b (8.4 mg, 0.019 mmol) was obtained from **13b** (15 mg, 0.027 mmol) in 70% through the same procedure as described for preparation of **14a**; colorless oil; $[\alpha]_D^{24}$ + 2.2 (*c* 1.39, $CHCl_3$); IR (neat) ν_{max} 3368, 2955, 2931, 2876, 1461, 1251, 1041, 773 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.79 (2H, brt, J = 5.0 Hz), 3.63 (brquin, J = 5.6 Hz), 3.18 (brs, 1H), 1.75 (dt, J = 14.4, 5.5 Hz, 1H),1.70–1.17 (m, 12H), 0.96 (9H, t, J = 7.9 Hz, TES-Me), 0.89 (t, J = 7.1 Hz, 3H), 0.88 (s, 9H), 0.61 (q, J = 7.9 Hz, 6H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 77.9, 71.9, 60.0, 43.1, 41.9, 39.4, 37.7, 27.7, 25.9, 20.5, 18.6, 18.1, 14.3, 7.0, 6.8, −4.5; HRESIMS (pos.) *m*/*z* 455.33408 [calcd for $C_{23}H_{52}O_3NaSi_2$ $(M + Na)^+$, Δ −0.64 mmu].

(3*S*,7*S*)-3,7-Dihydroxy-3-methyldecanoic acid (15a). DMSO (70.0 μl) and Et_3N (24.0 μl) were added to a solution of **14a** (5.0 mg, 0.012 mmol) in CH_2Cl_2 (212.0 μl). After stirring for 5 min at 0 °C, SO_3–pyr. 19.2 mg was added to the mixture. After stirring for 1 h at rt, additional SO_3–pyr. (19.2 mg) was added to the reaction mixture. After stirring for 1 h at rt, the mixture was extracted with diethyl ether. The organic layer was washed with H_2O and brine, dried with $MgSO_4$, and concentrated *in vacuo* to afford crude aldehyde. Then *t*-BuOH (0.73 mL), NaH_2PO_4 (8.2 mg in 182.0 μl of H_2O), and 2-methyl-2-butene (2 M in THF, 50.4 μl) were added to the crude aldehyde. After stirring for 5 min at rt, $NaClO_2$ (7.3 mg) was added to the mixture. After stirring for 15 min at 0 °C, saturated aqueous $NaHSO_4$ was added to the mixture, which was extracted with EtOAc. The organic layer was washed with H_2O and brine, dried with $MgSO_4$, and concentrated *in vacuo*. The residue was purified by a SiO_2 column (*n*-hexane–EtOAc, 100 : 0 to 90 : 10) to afford **15a** (2.0 mg, 0.0092 mmol, 77%); colorless oil; $[\alpha]_D^{18}$ − 5.9 (*c* 2.02, $CHCl_3$); IR (neat) ν_{max} 3410, 2923, 2853, 1717, 1562, 1456, 1240, 1129, 774 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.05 (brs, 1H), 3.64 (m, 1H), 2.56 (d, J = 15.6 Hz, 1H), 2.47 (d, J = 15.6 Hz, 1H), 1.61–1.29 (m, 10H), 1.28 (s, 3H), 0.92 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8, 71.5, 71.4, 44.6, 41.6, 39.6, 37.2, 26.7, 19.9, 18.8, 14.1; HRESIMS (pos.) *m*/*z* 241.14118 [calcd for $C_{11}H_{22}O_4Na$ $(M + Na)^+$, Δ +0.15 mmu].

(3*S*,7*R*)-3,7-Dihydroxy-3-methyldecanoic acid (15b). **15b** (1.4 mg, 0.0064 mmol) was obtained from **14b** (4.0 mg, 0.0092 mmol) in 70% through the same procedure as described for preparation of **15a**; colorless oil; $[\alpha]_D^{20}$ − 4.87 (*c* 1.72, $CHCl_3$); IR (neat) ν_{max} 3362, 2920, 2850, 1717, 1575, 1456, 1219, 1123, 772 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.20 (brs, 1H), 3.64 (m, 1H), 2.56 (d, J = 15.6 Hz, 1H), 2.48 (d, J = 15.6 Hz, 1H), 1.62–1.29 (m, 10H), 1.28 (s, 3H), 0.92 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9, 71.6, 71.5, 44.8, 41.6, 39.6, 37.2, 26.6, 19.9, 18.8, 14.1; HRESIMS (pos.) *m*/*z* 241.14116 [calcd for $C_{11}H_{22}O_4Na$ $(M + Na)^+$, Δ +0.13 mmu].

2-((3*S*,7*S*)-3,7-Dihydroxy-3-methyldecanamido)ethanesulfonic acid (6a). DMT-MM (95 mg) and Et_3N (400 μl) were added to a solution of **15a** (25.0 mg, 0.11 mmol) in DMF (5 mL). After stirring for 10 min at rt, taurine (190 mg) was added to the mixture. After stirring for 10 h at rt, the mixture was concentrated *in vacuo*. The residue was dissolved with MeOH and passed through an ion-exchange column (Amberlite IR-120 H^+ form, eluent, MeOH) and concentrated *in vacuo*. The residue was purified by a SiO_2 column ($CHCl_3$–MeOH, 100 : 0 to 50 : 50) to afford 6a (19.0 mg, 0.058 mmol, 53%); colorless oil; $[\alpha]_D^{20}$ + 3.5 (*c* 1.14, MeOH); IR (neat) ν_{max} 3366, 2955, 2871, 2280, 1638, 1555, 1284, 1144, 1059, 938 cm^{-1}; ^1H NMR (600 MHz, CD_3OD) δ 3.67 (brt, J = 6.7 Hz, 2H), 3.58 (m, 1H), 3.03 (t, J = 6.6 Hz, 2H), 2.43 (d, J = 14.0 Hz, 1H), 2.36 (d, J = 14.0 Hz, 1H), 1.66–1.32 (m, 10H), 1.27 (s, 3H), 0.97 (t, J = 7.1 Hz, 9H); ^{13}C NMR (100 MHz, CD_3OD) δ 175.2, 73.9, 72.8, 52.3, 48.3, 44.2, 41.6, 39.6, 37.2, 27.8, 22.1, 20.8, 15.3; HRESIMS (neg.) *m*/*z* 324.14903 [calcd for $C_{13}H_{26}NO_6S$ $(M - H)^-$, Δ +0.40 mmu].

2-((3S,7*R*)-3,7-Dihydroxy-3-methyldecanamido)ethanesulfonic acid (6b). **6b** (20.5 mg, 0.063 mmol) was obtained from **15b** (24 mg, 0.11 mmol) in 57% through the same procedure as described for preparation of **6a**; colorless oil; $[\alpha]_D^{20}$ − 0.4 (*c* 1.28, MeOH); IR (neat) ν_{max} 3439, 2957, 2857, 2279, 1644, 1565, 1282, 1147, 1069, 921 cm^{-1}; ^1H NMR (600 MHz, CD_3OD) δ 3.68 (brt, J = 6.6 Hz, 2H), 3.58 (m, 1H), 3.03 (t, J = 6.6 Hz, 2H), 2.44 (d, J = 14.0 Hz, 1H), 2.38 (d, J = 14.0 Hz, 1H), 1.66–1.32 (m, 10H), 1.29 (s, 3H), 0.97 (t, J = 7.1 Hz, 9H); ^{13}C NMR (100 MHz, CD_3OD) δ 175.4, 74.0, 72.8, 52.3, 48.2, 44.2, 41.6, 39.6, 37.2, 27.8, 22.1, 20.8, 15.3; HRESIMS (neg.) *m*/*z* 324.14892 [calcd for $C_{13}H_{26}NO_6S$ $(M - H)^-$, Δ +0.29 mmu].

Antimicrobial assay

Antimicrobial assay of **1–3** against *Escherichia coli*, *Staphylococcus aureus*, *Bacillus subtilis*, *Micrococcus luteus*, *Aspergillus niger*, *Candida albicans*, *Cryptococcus neoformans*, and *Trichophyton mentagrophytes* was carried out as previously described.[14] Amphotericin B, micafungin, hygromycin B, and kanamycin showed antifungal activity against *Cryptococcus neoformans* (MIC, <0.05, <0.1, 4.0, and 8.0 μg mL^{-1}, respectively).

Cytotoxic assays

Human epidermoid carcinoma (KB) and murine leukemia L1210 cells were cultured in an incubator at 37 °C for 48 h in 100 μl of medium containing various concentrations of test compounds dissolved in 1% DMSO. The IC_{50} values were obtained by plotting the logarithm of the concentration of the test compound *versus* the growth rate of the treated cells. Paclitaxel was used as positive control (IC_{50}, <0.005 and <0.1 μg mL^{-1}, respectively).

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