Acetylenic Strongylodiols from a *Petrosia* (*Strongylophora*) Okinawan Marine Sponge

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Seven new long-chain acetylenic alcohols, strongylodiols D−J, were isolated from an Okinawan marine sponge of the genus *Petrosia* (*Strongylophora*). The structures of these compounds were elucidated on the basis of the results of spectroscopic analysis and chemical reaction. Analysis of the MNA esters of the acetylenic alcohols disclosed that these compounds were each an enantiomeric mixture in a different ratio.

A variety of long-chain acetylenic alcohols possessing significant biological activities have been found in marine sponges.[1,2] Previously, we reported the isolation and structural determination of three new cytotoxic acetylenic alcohols from an Okinawan marine sponge of the genus *Petrosia* (*Strongylophora*).[3] Interestingly, these acetylenic alcohols, strongylodiols A, B, and C, were each found to be an enantiomeric mixture in a different ratio. Further investigation on acetylenic alcohols from the sponge resulted in the isolation of seven new congeners, strongylodiols D−J. Their structures were elucidated on the basis of spectroscopic analysis and chemical reaction. These compounds also were each found to be an enantiomeric mixture in a different ratio. This paper descibes the structural elucidation of these compounds.

Results and Discussion

The isolation and purification were carried out as described in the Experimental Section.

The molecular formula of strongylodiol D (**1**) was found to be $C_{26}H_{42}O_2$ by HREIMS and ^{13}C NMR data (Table 1). The IR spectra showed absorptions at 3287 (OH) and 2148 (C≡C) cm^{-1}. The UV absorptions at 231 (log ϵ 2.59), 244 (2.59), and 257 (2.35) nm indicated the presence of conjugated triple bonds. The ^1H and ^{13}C NMR spectra (Table 1) showed signals due to a primary hydroxyl [δ_H 4.35 (2H, s), δ_C 51.5 (CH_2)], a secondary hydroxyl [δ_H 4.43 (1H, t), δ_C 62.9 (CH)], six sp carbons [δ_C 69.84 (C), 69.85 (C), 77.5 (C), 80.2 (C), 80.3 (C), 80.6 (C)], and an isopropyl moiety [δ_H 0.86 (6H, d)]. The spectral data of **1** were very similar to those of strongylodiol C,[3] except for the lack of the NMR signals due to the double bond at C-16 and the appearance of a new triple bond [δ_C 80.2 (C), 80.3 (C)], indicating that compound **1** was a corresponding acetylenic congener of strongylodiol C at C-16. The position of the new triple bond between C-16 and C-17 was confirmed by collisional activation decomposition in tandem mass spectrometry (MS/MS). In the negative FABMS/MS spectrum of the pseudomolecular ion at $[M - H]^-$ of *m/z* 385, a series of charge remote fragmentation ions was observed as shown in Figure 2 and was consistent with the location of the triple bond between C-16 and C-17.

The absolute configuration of the chiral center at C-6 bearing a secondary hydroxyl group in **1** was examined by applying the modified Mosher's method.[4,5] After protection of the primary hydroxyl group at C-1 by a *tert*-butyldimethylsilyl (TBS) group to give **8**, the secondary hydroxyl group at C-6 was esterified with (*R*)- and (*S*)-methoxy(2-naphthyl)acetic acid (MNA)[5,6] to give (*R*)-MNA ester **9** and (*S*)-MNA ester **10**, respectively. The ^1H NMR spectrum of (*R*)-MNA ester **9** revealed that **9** was accompanied by its diastereomer in a ratio of 95:5. The (*S*)-MNA ester was also found to be a diastereomeric mixture in a similar ratio. These findings indicated that strongylodiol D existed as an enantiomeric mixture in a different ratio. The $\Delta\delta$ values (δR-ester − δS-ester) of the corresponding protons at C-1, C-7, and C-8 between the major diastereomers were calculated from the ^1H NMR spectra of each diastereomeric mixture, indicating the *R* configuration at C-6 for the major enantiomer (see Experimental Section).

The molecular formula of strongylodiol E (**2**) was found to be $C_{31}H_{48}O_2$ by HREIMS and ^{13}C NMR data (Table 1). The IR spectrum showed absorptions at 3310 (OH), 2254 (C≡C), and 2160 (C≡C) cm^{-1}. The UV absorptions at 223 (log ϵ 3.95) and 257 (2.63) nm indicated the presence of conjugated multiple bonds. The ^1H and ^{13}C NMR spectral data of **2** (Table 1) were similar to those of strongylodiol A.[3] However, NMR data of **2** indicated the presence of a pent-3-ene-1-yne system at the terminal position. The presence of the pent-3-en-1-yne system was confirmed by HMBC analysis. The HMBC correlations from the acetylenic proton [δ_H 3.07 (1H, d, J = 2.1 Hz, H-31)] to C-30 [δ_C 80.6 (C)] and C-29 [δ_C 107.9 (CH)], from the olefinic proton [δ_H 5.44 (1H, dd, J = 1.9, 10.8 Hz, H-29)] to C-28, C-30, and C-31, and from another olefinic proton [δ_H 6.00 (1H, dt, J = 7.4, 10.9 Hz, H-28)] to C-27 [δ_C 30.3 (CH_2)] and C-29 were observed. The position of the nonconjugated double bond between C-16 and -17 was determined by the negative FABMS/MS of the pseudomolecular ion $[M - H]^-$ of *m/z* 452. The *Z* configuration of the double bond at C-28 was indicated by the coupling constant (J = 10.9 Hz) between olefinic protons H-28 [δ_H 6.00 (1H, dt, J = 7.4,

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Table 1. ^{13}C and ^{1}H NMR Data of for Strongylodiols D (**1**) and E (**2**)[a]

1			**2**		
atom no.	δ_C (mult.)	δ_H (mult., J = Hz)	atom no.	δ_C (mult.)	δ_H (mult., J = Hz)
1	51.5 (CH_2)	4.35 (s)	1	51.5 (CH_2)	4.34 (s)
2	77.5 (C)		2	77.5 (C)	
3	69.84 (C)[b]		3	69.8 (C)	
4	69.85 (C)[b]		4	68.8 (C)	
5	80.6 (C)		5	80.58 (C)[e]	
6	62.9 (CH)	4.43 (t, 6.6)	6	62.9 (CH)	4.43 (t, 6.6)
7	37.5 (CH_2)	1.72 (m)	7	37.5 (CH_2)	1.72 (m)
8	25.0 (CH_2)	1.43 (m)	8	25.0 (CH_2)	1.44 (m)
9−12[c]		1.25−1.29 (m)	9−13[f]		1.27−1.33 (m)
13	28.91 (CH_2)[d]	1.36 (m)	14	29.8 (CH_2)	1.27−1.33 (m)
14	29.2 (CH_2)	1.46 (m)	15	27.2 (CH_2)	2.01 (m)
15	18.8 (CH_2)	2.14 (t, 6.7)	16	129.92 (CH)[g]	5.33 (t, 4.7)
16	80.3 (C)		17	129.87 (CH)[g]	5.33 (t, 4.7)
17	80.2 (C)		18	27.2 (CH_2)	2.01 (m)
18	18.8 (CH_2)	2.14 (t, 6.7)	19	29.8 (CH_2)	1.27−1.33 (m)
19	29.2 (CH_2)	1.46 (m)	20−25[f]		1.27−1.33 (m)
20	28.85 (CH_2)[d]	1.36 (m)	26	28.7 (CH_2)	1.39 (m)
21[c]		1.25−1.29 (m)	27	30.3 (CH_2)	2.32 (q, 7.4)
22	27.3 (CH_2)	1.25−1.29 (m)	28	146.3 (CH)	6.00 (td, 7.4, 10.9)
23	39.0 (CH_2)	1.16 (m)	29	107.9 (CH)	5.44 (dd, 2.1, 10.9)
24	28.0 (CH)	1.49 (m)	30	80.59 (C)[e]	
25	22.7 (CH_3)	0.86 (d, 6.7)	31	81.1 (CH)	3.07 (d, 2.1)
26	22.7 (CH_3)	0.86 (d, 6.7)			

[a] ^{13}C NMR: 125 MHz, ^{1}H NMR: 500 MHz. Assignments of the ^{13}C and ^{1}H signals were made on the basis of HMQC. [b,d,e,g] Values with the same superscript are interchangeable. [c] The unassignable ^{13}C signals [δ_C 29.1 (CH_2), 29.2 (CH_2), 29.4 (CH_2 × 3)] were observed for these carbons. [f] The unassignable ^{13}C signals [δ_C 29.17 (CH_2), 29.19 (CH_2), 29.28 (CH_2), 29.30 (CH_2), 29.43 (CH_2), 29.47 (CH_2), 29.50 (CH_2 × 2), 29.53 (CH_2), 29.56 (CH_2), 29.60 (CH_2)] were observed for these carbons.

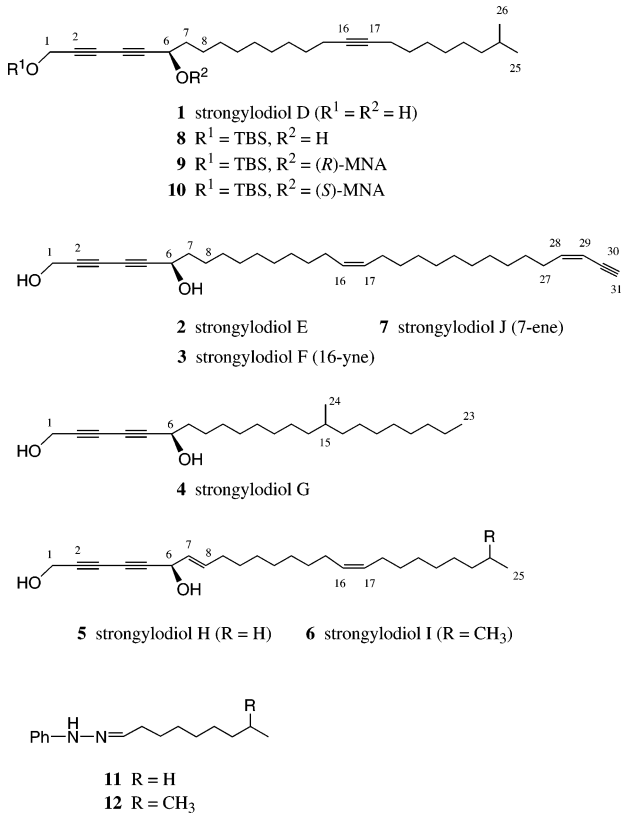

Figure 1. Structures of new acetylenic alcohols and derivatives (the *R* configuration at C-6 for the major enantiomer is depicted in the structures).

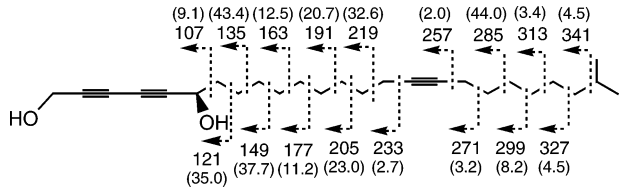

Figure 2. MS/MS data for the $[M - H]^-$ ion (*m/z* 385) of strongylodiol D (**1**) (the numerals in parentheses show relative intensities).

10.9 Hz)] and H-29 [δ_H 5.44 (1H, dd, J = 1.9, 10.9 Hz)]. The *Z* configuration of the double bond at C-16 was elucidated by comparison of the ^{13}C chemical shift (δ_C 27.2) for allylic carbons with those in (*Z*)-2-heptene (δ_C 27.0) and (*E*)-2-heptene (δ_C 32.8).[7]

The (*R*)- and (*S*)-MNA esters were each found to be a diastereomeric mixture in a ratio of 61:39, indicating that natural strongylodiol E (**2**) existed as an enantiomeric mixture in a different ratio. The *R* configuration of the chiral center at C-6 for the major enantiomer was determined by the $\Delta\delta$ values.

The IR, UV, and NMR data of strongylodiol F (**3**) ($C_{31}H_{46}O_2$) were very similar to those of **2**, except for the lack of the NMR signals due to one of the disubstituted double bonds and the appearance of those due to an additional triple bond [δ_C 80.2 (C), 80.3 (C)], indicating that compound **3** was a corresponding acetylenic congener of strongylodiol E (**2**) at C-16. The location of the new triple bond at C-16, the enantiomeric ratio (80:20), and the absolute configuration (*R*) at C-6 of the major enantiomer were determined by the same methods used for **1** and **2**.The IR, UV, and NMR data of strongylodiol G (**4**) ($C_{24}H_{42}O_2$) were very similar to those of strongylodiols A and B, except for the lack of the NMR signals due to the multiple bond at C-16 present in strongylodiols A and B and the appearance of those due to a secondary methyl group [δ_H 0.83 (3H, d, J = 6.5 Hz, H-24)], indicating that compound **4** was a branched acetylenic alcohol. The location of the secondary methyl at C-15 was determined by a similar method used for **1**, **2**, and **3**. The relative configuration at C-15 bearing the secondary methyl was not determined. Interestingly, compound **4** was found to be almost optically pure on the basis of the analysis of the NMR spectra of its (*R*)- and (*S*)-MNA esters. The absolute configuration (*R*) at C-6 was determined by $\Delta\delta$ values.

The IR and NMR data of strongylodiol H (**5**) ($C_{25}H_{40}O_2$) were very similar to those of strongylodiol A, except for

Table 2. ^{13}C and ^{1}H NMR Data for Strongylodiols F (**3**) and G (**4**)[a]

3			**4**		
atom no.	δ_C (mult.)	δ_H (mult., J = Hz)	atom no.	δ_C (mult.)	δ_H (mult., J = Hz)
1	51.5 (CH_2)	4.35 (d, 6.1)[e]	1	51.5 (CH_2)	4.34 (s)
2	77.5 (C)		2	77.5 (C)	
3	69.84 (C)		3	69.8 (C)	
4	69.83 (C)		4	68.8 (C)	
5	80.56 (C)		5	80.6 (C)	
6	62.9 (CH)	4.43 (dt, 6.0, 6.3)[e]	6	62.9 (CH)	4.43 (t, 6.6)
7	37.5 (CH_2)	1.72 (m)	7	37.5 (CH_2)	1.72 (m)
8	25.0 (CH_2)	1.45 (m)	8	25.0 (CH_2)	1.44 (m)
9−12[b]		1.25−1.29 (m)	9−13[f]		1.26−1.32 (m)
13	28.86 (CH_2)[c]	1.35 (m)	14	37.1 (CH_2)	1.26−1.32 (m)
14	29.16 (CH_2)	1.48 (m)	15	32.8 (CH)	1.26−1.32 (m)
15	18.8 (CH_2)	2.13 (t, 7.1)	16	37.1 (CH)	1.26−1.32 (m)
16	80.3 (C)[d]		17−20[f]		1.26−1.32 (m)
17	80.2 (C)[d]		21	31.9 (CH_2)	1.26−1.32 (m)
18	18.8 (CH_2)	2.13 (t, 7.1)	22	22.7 (CH_2)	1.26−1.32 (m)
19	29.16 (CH_2)	1.48 (m)	23	14.1 (CH_3)	0.88 (t, 6.9)
20	28.84 (CH_2)[c]	1.35 (m)	24	19.7 (CH_3)	0.83 (d, 6.5)
21−25[b]		1.25−1.29 (m)			
26	28.7 (CH_2)	1.39 (m)			
27	30.3 (CH_2)	2.32 (brq, 7.4)			
28	146.3 (CH)	6.00 (td, 7.4, 10.9)			
29	107.9 (CH)	5.44 (brdd, 2.1, 10.9)			
30	80.60 (C)				
31	81.1 (CH)	3.07 (d, 2.1)			

[a] ^{13}C NMR: 125 MHz, ^{1}H NMR: 500 MHz. Assignments of the ^{13}C and ^{1}H signals were made on the basis of HMQC. [b] The unassignable ^{13}C signals [δ_C 29.10 (CH_2), 29.16 ($CH_2 \times 3$), 29.41 ($CH_2 \times 3$), 29.52 ($CH_2 \times 2$)] were observed for these carbons. [c,d] Values with the same superscript are interchangeable. [e] Each proton couples with the hydroxylic proton. [f] The unassignable ^{13}C signals [δ_C 27.06 (CH_2), 27.08 (CH_2), 29.21 (CH_2), 29.35 (CH_2), 29.49 (CH_2), 29.59 (CH_2), 29.68 (CH_2), 29.97 (CH_2), 30.03 (CH_2)] were observed for these carbons.

the appearance of the signals due to an additional disubstituted double bond. The position of the new double bond at C-7 was deduced from the correlations exhibited by the HMBC from the olefinic proton [δ_H 5.57 (1H, dd, J = 6.2, 15.3 Hz, H-7)] to C-5 [δ_C 78.7 (C)], C-6 [δ_C 63.3 (CH)], and C-9 [δ_C 31.9 (CH_2)] and from another olefinic proton [δ_H 5.89 (1H, td, J = 6.7, 15.3 Hz, H-8)] to C-6 and C-9. The *E* configuration of the double bond at C-7 was determined by the coupling constant (15.3 Hz) between H-7 and H-8. The position of the remaining disubstituted double bond was determined by oxidative cleavage of the double bond. Oxidation of **5** with osmium tetroxide and periodic acid followed by treatment with 2,4-dinitrophenylhydrazine afforded compound **11**. The structure of **11**, 2,4-dinitrophenylhydrazone of nonanal, was identified by MS and ^{13}C NMR data (see Experimental Section). The enantiomeric ratio (94:6) for **5** and the absolute configuration (*R*) at C-6 of the major enantiomer were determined by the same methods used for **1**−**4**.The IR, UV, and NMR data of strongylodiol I (**6**) ($C_{26}H_{42}O_2$) were very similar to those of **5**, except for the appearance of a 6H methyl doublet [δ_H 0.86 (6H, d, J = 6.6 Hz)] coupled to a methine multiplet at δ_H 1.52 (1H, m), indicating that compound **6** was an isopropyl congener of **5**. The location of the double bond at C-16, the enantiomeric ratio (97:3), and the absolute configuration (*R*) at C-6 of the major enantiomer were determined by the same method used for **5**.

The IR, UV, and NMR data of strongylodiol J (**7**) ($C_{31}H_{46}O_2$) were very similar to those of strongylodiol E (**2**), except for the appearance of an additional disubstituted double bond. The position of the new double bond at C-7 was deduced from HMBC correlations. The enantiomeric ratio (96:4) and the absolute configuration (*R*) at C-6 of the major enantiomer were determined by the same methods used for **5** and **6**. The location of the double bond at C-16 is inferred from NMR data comparisons to be the same as that of compound **2**.Optically active natural products isolated as a racemic mixture have been frequently encountered. However, natural products isolated as an enantiomeric mixture in a different ratio are fairly limited.[8−10] This phenomenon is of interest and may be attributed to an artificial change or functions of biosynthetic enzymes. Further investigation on biosynthetic enzymes is expected.

Experimental Section

General Experimental Procedures. Optical rotations were measured with a JASCO DIP-370 automatic polarimeter. IR spectra were recorded with a Perkin-Elmer FT-IR 1600 spectro-photometer and UV spectra with a JASCO V-520 spectrophotometer. All NMR spectra were recorded with a Bruker DRX-500 (^{1}H, 500 MHz; ^{13}C, 125 MHz) spectrometer in $CDCl_3$. $^{1}H-^{1}H$ COSY, NOESY, HMQC, and HMBC spectra were measured using standard Bruker pulse sequences. Chemical shifts are given on a δ (ppm) scale with $CHCl_3$ (^{1}H, 7.26 ppm) and $CDCl_3$ (^{13}C, 77.0 ppm) as the internal standard. Mass spectra were taken with a Micromass Auto Spec spectrometer. Tandem mass spectra (MS/MS) were taken with a JEOL HX110A spectrometer.

Animal and Material. The sponge of the genus *Petrosia* (*Strongylophora*) (class Demospongiae, order Haplosclerida, family Petrosidae) was collected from a coral reef off Ishigaki Island, Okinawa Prefecture, Japan, in June 1998 and June 2002, at a depth of 13−15 m. The sponge formed a lumpy branched cylindrical body of 2−3 cm in diameter. The oscules were studded on the upper part of the body. The texture was hard. The colors of the surface and inside were greenish-gray and pale yellowish-brown, respectively. One of the authors, R.W.M.V.S., identified the sponge as belonging to the genus *Strongylophora*. Recently, he proposed that the genus *Strongylophora* should be combined with the genus *Petrosia*.[11] Therefore, we expressed the present sponge as the genus *Petrosia* (*Strongylophora*) in this paper. A voucher specimen is presently on deposit in the Zoological Museum at the University of Amsterdam under the registration number ZMA POR. 14879.

Extraction and Isolation. Wet specimens (1.93 kg) of the sponge collected in 1998 were extracted with MeOH. The MeOH extract was partitioned between EtOAc and H_2O to obtain an EtOAc-soluble portion (37.2 g). A part (25.6 g) of the EtOAc-soluble portion was chromatographed on a silica

Table 3. ^{13}C and ^{1}H NMR Data for Strongylodiols H (**5**) and I (**6**)[a]

5			**6**		
atom no.	δ_C (mult.)	δ_H (mult., J = Hz)	atom no.	δ_C (mult.)	δ_H (mult., J = Hz)
1	51.5 (CH_2)	4.36 (d, 6.3)	1	51.5 (CH_2)	4.35 (d, 5.8)
2	77.9 (C)		2	77.9 (C)	
3	69.8 (C)		3	69.80 (C)[g]	
4	69.8 (C)		4	68.83 (C)[g]	
5	78.7 (C)		5	78.7 (C)	
6	63.3 (CH)	4.89 (brt, 6.2)	6	63.3 (CH)	4.89 (brt, 6.0)
7	127.7 (CH)	5.57 (dd, 6.2, 15.3)	7	127.7 (CH)	5.51 (brdd, 6.0, 15.3)
8	135.2 (CH)	5.89 (td, 6.7, 15.3)	8	135.2 (CH)	5.90 (td, 6.8, 15.3)
9	31.9 (CH_2)[b]	2.06 (q, 6.7)[d]	9	32.0 (CH_2)	2.06 (q, 6.8)
10	28.8 (CH_2)	1.39 (m)	10	28.8 (CH_2)	1.39 (m)
11−13[c]		1.24−1.31 (m)	11−13[h]		1.24−1.30 (m)
14	28.7 (CH_2)[d]	1.34 (m)	14	29.74 (CH_2)[i]	1.34 (m)
15	27.18 (CH_2)[e]	2.01 (q, 6.1)	15	27.19 (CH_2)[j]	2.02 (q, 6.0)
16	129.8 (CH)[f]	5.35 (m)	16	129.8 (CH)[k]	5.34 (m)
17	130.0 (CH)[f]	5.35 (m)	17	130.0 (CH)[k]	5.34 (m)
18	27.21 (CH_2)[e]	2.01 (q, 6.1)	18	27.22 (CH_2)[j]	2.02 (q, 6.0)
19	29.8 (CH_2)[d]	2.14 (t, 6.7)	19	29.77 (CH_2)[i]	1.34 (m)
20−22[c]		1.24−1.31 (m)	20−21[h]		1.24−1.30 (m)
23	32.0 (CH_2)[b]	1.24−1.31 (m)	22	27.4 (CH_2)	1.24−1.30 (m)
24	22.7 (CH_2)	1.24−1.31 (m)	23	39.0 (CH_2)	1.15 (m)
25	14.1 (CH_3)	0.88 (t, 6.7)	24	28.0 (CH)	1.52 (m)
23	39.0 (CH_2)	1.16 (m)	25	22.7 (CH_3)	0.86 (d, 6.6)
24	28.0 (CH)	1.49 (m)	26	22.7 (CH_3)	0.86 (d, 6.6)
25	22.7 (CH_3)	0.86 (d, 6.7)	CH_2OH		1.60 (brt, 5.8)
			CHO*H*		1.83 (d, 6.0)

[a] ^{13}C NMR: 125 MHz, ^{1}H NMR: 500 MHz. Assignments of the ^{13}C and ^{1}H signals were made on the basis of HMQC. [b,d,e,f,g,i,j,k] Values with the same superscript are interchangeable. [c]The unassignable ^{13}C signals [δ_C 29.1 (CH_2), 29.2 (CH_2), 29.31 (CH_2 × 2), 29.33 (CH_2), 29.5 (CH_2)] were observed for these carbons. [h]The unassignable ^{13}C signals [δ_C 29.1 (CH_2), 29.2 (CH_2), 29.3 (CH_2 × 2), 29.81 (CH_2)] were observed for these carbons.

Table 4. ^{13}C and ^{1}H NMR Data for Strongylodiol J (**7**)[a]

atom no.	δ_C (mult.)	δ_H (mult., J = Hz)
1	51.5 (CH_2)	4.35 (brs)
2	78.0 (C)	
3	69.8 (C)	
4	69.8 (C)	
5	78.7 (C)	
6	63.3 (CH)	4.88 (brs)
7	127.7 (CH)	5.57 (tdd, 1.4, 6.2, 15.3)
8	135.2 (CH)	5.89 (dtd, 1.0, 6.8, 15.3)
9	32.0 (CH_2)	2.06 (q, 6.8)
10	28.7 (CH_2)[b]	1.40 (m)
11−13[c]		1.25−1.35 (m)
14	29.73 (CH_2)[d]	1.25−1.35 (m)
15	27.18 (CH_2)[e]	2.01 (q, 6.4)
16	129.8 (CH)[f]	5.35 (m)
17	130.0 (CH)[f]	5.35 (m)
18	27.20 (CH_2)[e]	2.01 (q, 6.4)
19	29.75 (CH_2)[d]	1.25−1.35 (m)
20−25[c]		1.25−1.35 (m)
26	28.8 (CH_2)[b]	1.40 (m)
27	30.3 (CH_2)	2.32 (brq, 7.5)
28	146.3 (CH)	6.00 (td, 7.5, 10.8)
29	107.9 (CH)	5.44 (brd, 10.8)
30	80.6 (C)	
31	81.1 (CH)	3.07 (d, 2.0)
CH_2OH		1.70 (brs)
CHO*H*		1.91 (brd, 5.3)

[a] ^{13}C NMR: 125 MHz, ^{1}H NMR: 500 MHz. Assignments of the ^{13}C and ^{1}H signals were made on the basis of HMQC. [b,d,e,f] Values with the same superscript are interchangeable. [c] The unassignable ^{13}C signals [δ_C 29.16 (CH_2 × 2), 29.19 (CH_2), 29.30 (CH_2), 29.33 (CH_2), 29.4 (CH_2), 29.53 (CH_2), 29.55 (CH_2), 29.60 (CH_2)] were observed for these carbons.

gel column. Stepwise elution with hexane (1500 mL), hexane−EtOAc (4:1, 2000 mL), hexane−EtOAc (1:1, 1500 mL), EtOAc (1500 mL), and MeOH (1000 mL) afforded five fractions. The second fraction [8.51 g, eluted with hexane−EtOAc (4:1)] was further subjected to flash column chromatography. Stepwise elution with hexane−EtOAc (29:1 and 19:1) and EtOAc afforded three fractions. HPLC separation (reversed-phase, acetonitrile) of the third fraction (4.94 g, eluted with EtOAc) afforded six fractions (A−F). Purification of fraction B using HPLC (reversed-phase, acetonitrile, equipped with a recycle loop) afforded strongylodiols B[3] (229 mg) and H (**5**, 2.4 mg). Similar purification of the other fractions afforded strongylodiols F (**3**, 34 mg) and I (**6**, 2.7 mg) from fraction C, strongylodiols A[3] (227 mg), D (**1**, 16 mg), and E (**2**, 50 mg) from fraction E, and strongylodiols C[3] (127 mg), G (**4**, 26 mg), and J (**7**, 3.3 mg) from fraction F.

Strongylodiol D (1): amorphous solid; $[\alpha]^{25}_D$ −8.0° (*c* 0.56, $CHCl_3$); UV (EtOH) λ_{max} (log ϵ) 231 (2.59), 244 (2.56), 257 (2.35) nm; IR ν_{max} (film) 3387, 2928, 2849, 2148 cm^{-1}; ^{13}C and ^{1}H NMR, see Table 1; HREIMS *m/z* 387.3258 $[M + H]^+$ (calcd for $C_{26}H_{43}O_2$, 387.3263).

Strongylodiol E (2): amorphous solid; $[\alpha]^{25}_D$ −1.8° (*c* 0.51, $CHCl_3$); UV (EtOH) λ_{max} (log ϵ) 223 (3.95), 257 (2.63) nm; IR ν_{max} (film) 3310, 2921, 2852, 2254, 2160 cm^{-1}; ^{13}C and ^{1}H NMR, see Table 1; HREIMS *m/z* 453.3713 $[M + H]^+$ (calcd for $C_{31}H_{49}O_2$, 453.3733).

Strongylodiol F (3): amorphous solid; $[\alpha]^{25}_D$ −5.3° (*c* 0.36, $CHCl_3$); UV (EtOH) λ_{max} (log ϵ) 221 (4.00), 256 (2.88) nm; IR ν_{max} (film) 3296, 2926, 2849, 2251, 2168 cm^{-1}; ^{13}C and ^{1}H NMR, see Table 2; HREIMS *m/z* 473.3333 $[M + Na]^+$ (calcd for $C_{31}H_{46}O_2Na$, 473.3400).

Strongylodiol G (4): amorphous solid; $[\alpha]^{22}_D$ −3.9° (*c* 0.55, $CHCl_3$); UV (EtOH) λ_{max} (log ϵ) 229 (2.78), 243 (2.72), 257 (2.52) nm; IR ν_{max} (film) 3331, 2923, 2853, 2162 cm^{-1}; ^{13}C and ^{1}H NMR, see Table 2; HREIMS *m/z* 385.3094 $[M + Na]^+$ (calcd for $C_{24}H_{40}O_2Na$, 385.3083).

Strongylodiol H (5): colorless oil; $[\alpha]^{22}_D$ −43.8° (*c* 0.35, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 208 (3.79) nm; IR ν_{max} (film) 3330, 2920, 2255, 2164, 1667 cm^{-1}; ^{13}C and ^{1}H NMR, see Table 3; HRESIMS *m/z* 379.3213 $[M + Li]^+$ (calcd for $C_{25}H_{40}O_2Li$, 379.3188).

Strongylodiol I (6): colorless oil; $[\alpha]^{22}_D$ −33.4° (*c* 0.13, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 208 (3.76) nm; IR ν_{max} (film) 3332, 2921, 2854, 2255, 2164, 1667 cm^{-1}; ^{13}C and ^{1}H NMR, see Table 3; HRESIMS *m/z* 393.3310 $[M + Li]^+$ (calcd for $C_{26}H_{42}O_2Li$, 393.3345).

Strongylodiol J (7): colorless oil; $[\alpha]^{22}_D$ −32.6° (*c* 0.44, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 208 (3.79) nm; IR ν_{max} (film)

3311, 2921, 2852, 2256, 2164, 1667 cm^{-1}; ^{13}C and ^{1}H NMR, see Table 4; HRESIMS *m/z* 457.3689 $[M + Li]^+$ (calcd for $C_{31}H_{46}O_2Li$, 457.3658).

Preparation of MNA Esters of 1. To a solution of **1** (1.0 mg) in dry CH_2Cl_2 (0.2 mL) were added successively *tert*-butyldimethylsilyl chloride (0.3 mg), DMAP (1.9 mg), and NEt_3 (10 μL). The mixture was stirred for 1 h at 0 °C under an argon atmosphere. After addition of an excess of ether the reaction mixture was washed with aqueous $NaHCO_3$, aqueous NH_4Cl, and saturated aqueous NaCl, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to afford compound **8** (1.2 mg).

To a solution of **8** (0.5 mg) in dry CH_2Cl_2 (0.2 mg) were added successively (*R*)-MNA (1.5 mg), DMAP (0.9 mg), and EDC hydrochloride (8.7 mg). The mixture was stirred for 2 h at room temperature under an argon atmosphere. Excess ether was added to the reaction mixture, and the mixture was washed with 10% aqueous tartaric acid, aqueous $NaHCO_3$, and saturated aqueous NaCl, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography and HPLC to afford (*R*)-MNA ester **9** (0.9 mg). (*S*)-MNA ester **10** (1.0 mg) was similarly prepared from **1**.

(*R*)-MNA ester 9: colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm) 0.090 (6H, s), 0.86 (6H, d, J = 6.6 Hz), 0.89 (9H, s), 1.21−1.39 (24H, m), 1.49 (1H, m), 1.77 (2H, m, H-7), 2.13 (4H, m), 3.47 (3H, s), 4.33 (2H, s, H-1), 4.96 (1H, s), 5.45 (1H, t, J = 6.7 Hz, H-6), 7.47−7.56 (3H, m), 7.82−7.92 (4H, m); HRFABMS *m/z* 705.4884 $[M + Li]^+$ (calcd for $C_{45}H_{66}O_4SiLi$, 705.4890).

(*S*)-MNA ester 10: colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm) 0.12 (6H, s), 0.86 (6H, d, J = 6.7 Hz), 0.90 (9H, s), 0.88−1.52 (25H, m), 1.59 (2H, m, H-7), 2.13 (2H×2, q, J = 6.7 Hz), 3.47 (3H, s), 4.37 (2H, s, H-1), 4.95 (1H, s), 5.46 (1H, t, J = 6.5 Hz, H-6), 7.47−7.54 (3H, m), 7.81−7.91 (4H, m); HRFABMS *m/z* 705.4902 $[M + Li]^+$ (calcd for $C_{45}H_{66}O_4SiLi$, 705.4890).

$\Delta\delta$ values ($\delta_{R\text{-ester}} - \delta_{S\text{-ester}}$) between (*R*)-MNA ester 9 and (*S*)-MNA ester 10 for 1: −0.04 ppm for H-1 and +0.18 ppm for H-7. These data indicated an *R* configuration at C-6 for the major enantiomer of **1**.

Preparation of MNA Esters of 2−7. (*R*)- and (*S*)-MNA esters of strongylodiols E (**2**)−J (**7**) were prepared by a method similar to that for strongylodiol D (**1**).

$\Delta\delta$ values ($\delta_{R\text{-ester}} - \delta_{S\text{-ester}}$) (ppm): −0.04 (H-1) and +0.18 (H-7) for **2**; −0.04 (H-1) and +0.17 (H-7) for **3** and **4**; −0.05 (H-1), +0.20 (H-7), +0.19 (H-8), and +0.15 (H-9) for **5**, **6**, and **7**. These data indicated each *R* configuration at C-6 of the major enantiomer for **2**−**7**.

Oxidative Degradation of 5. To a solution of **5** (5.0 mg) in *t*-BuOH−H_2O (1:1, 0.34 mL) were added successively OsO_4 (0.68 mg), H_5IO_4 (18.4 mg), and one drop of 30% aqueous AcOH. The mixture was stirred for 80 min at room temperature. After neutralization with 0.05 M aqueous NaOH to pH 7, a solution of 2,4-dinitrophenylhydrazine (21.4 mg) in 5% H_3PO_4−*t*-BuOH (1:1, 0.8 mL) was added. The mixture was stirred for 30 min at room temperature. Excess EtOAc was added to the reaction mixture, and the mixture was washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by HPLC [normal-phase, hexane−EtOAc (85:15)] to afford 2,4-dinitrophenylhydrazone **11** (1.5 mg). Similar degradation of **6** afforded the corresponding 2,4-dinitrophenylhydrazone **12**.

Compound 11: yellow powder; ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm) 0.89 (3H, t, J = 5.4 Hz), 1.26−1.34 (10H, m), 1.62 (2H, quint, J = 7.4 Hz), 2.43 (2H, dt, J = 5.4, 7.4 Hz), 7.53 (1H, t, J = 5.4 Hz), 7.93 (1H, d, J = 9.6 Hz), 8.30 (1H, dd, J = 2.9, 9.6 Hz), 9.12 (1H, d, J = 2.9 Hz), 11.01 (1H, s, NH); ^{13}C NMR (125 MHz, $CDCl_3$, δ ppm) 14.1 (CH_3), 22.6 (CH_2), 26.3 (CH_2), 29.16 (CH_2), 29.17 (CH_2), 29.3 (CH_2), 31.8 (CH_2), 32.5 (CH_2), 116.5 (CH), 123.5 (CH), 128.8 (C), 130.0 (CH), 137.8 (C), 145.2 (C), 152.6 (C); HREIMS *m/z* 323.1713 $[M + H]^+$ (calcd for $C_{15}H_{23}N_4O_4$, 323.1719).

Compound 12: yellow powder; ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm) 0.87 (6H, t, J = 6.6 Hz), 1.18 (2H, quint, J = 7.1 Hz), 1.32 (4H, m), 1.40 (2H, quint, J = 7.2 Hz), 1.57 (1H, m), 1.62 (2H, quint, J = 7.5 Hz), 2.43 (2H, dt, J = 5.5, 7.4 Hz), 7.53 (1H, t, J = 5.4 Hz), 7.93 (1H, d, J = 9.6 Hz), 8.30 (1H, dd, J = 2.8, 9.6 Hz), 9.12 (1H, d, J = 2.8 Hz), 11.01 (1H, s, NH); HREIMS *m/z* 337.1829 $[M + H]^+$ (calcd for $C_{16}H_{25}N_4O_4$, 337.1876).

Supporting Information Available: Copies of ^{1}H and ^{13}C NMR spectra of strongylodiols D−J (**1**−**7**). These materials are available free of charge via the Internet at http://pubs.acs.org.

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