New Strongylophorines from the Okinawan Marine Sponge *Petrosia* (*Strongylophora*) *corticata*

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New strongylophorines-22 (**1**), -23 (**2**), -24 (**3**), and -25 (**4**) were isolated from the Okinawan sponge *Petrosia* (*Strongylophora*) *corticata* along with other known strongylophorines. The structures of these strongylophorines were determined on the basis of spectroscopic analysis and chemical conversions. Assessment was also made of the cytotoxicity of strongylophorines-1, -2, -3, -4, -22 (**1**), -23 (**2**), and -24 (**3**) toward HeLa cells.

Strongylophorines are meroditerpenoids, each possessing a hydroquinone situated on an isocopalane-type diterpene skeleton.[1−6] Strongylophorines-1, -2, and -3 were initially isolated from the Papua New Guinean sponge *Strongylophora durissima*, and the absolute configurations of strongylophorines-1 and -3 were determined on the basis of chemical correlation with (+)-manool.[1a] Twenty-one strongylophorines are reported in the literature.[1−6] Most of strongylophorines have been found to possess biological activity, in the form of ichthyotoxic, antimicrobial, antifungal, and cytotoxic activity. While investigating the chemical constituents present in Okinawan marine invertebrates,[7] four new strongylophorines, strongylophorines-22 (**1**), -23 (**2**), -24 (**3**), and -25 (**4**), were isolated from the Okinawan sponge *Petrosia* (*Strongylophora*) *corticata* (Wilson, 1925) along with other known strongylophorines. The isolation and structure determinations are discussed below.

Results and Discussion

Sponge specimens of *Petrosia* (*Strongylophora*) *corticata*, obtained in June 2001 from the coral reef of Hatoma Island (Okinawa, Japan), were extracted with MeOH and then acetone. The combined extracts were partitioned between H_2O and EtOAc. The EtOAc-soluble portion was partitioned between hexane and 80% MeOH. Repeated chromatographic separations of the 80% MeOH-soluble portion gave strongylophorines-22 (**1**), -23 (**2**), -24 (**3**), and -25 (**4**) along with the known strongylophorines-1,[1] -2,[1] -3,[1] -4,[2] -8,[2] -15,[6] and -16.[6]

The molecular formula of strongylophorine-22 (**1**) was found to be $C_{26}H_{38}O_2$ on the basis of the HREIMS spectrum. IR and UV spectra of **1** indicated the presence of a hydroxy group (IR: 3435 cm^{-1}) and aromatic ring (IR: 1496 cm^{-1}, UV: λ_{max} 298, 229, 221 nm). Twenty six carbons of **1** were identified as five methyls, eight sp^3 methylenes, three sp^3 methines, three sp^2 methines, four sp^3 quaternary carbons, and three sp^2 quaternary carbons, from ^{13}C NMR and DEPT spectra. ^1H and ^{13}C NMR correlations were noted in the HMQC spectrum (Table 1). ^1H and ^{13}C NMR indicated a 1,2,4-trisubstituted benzene [δ_H 6.62 (1H, d, J = 8.4 Hz), 6.56 (1H, dd, J = 8.4, 2.9 Hz), 6.55 (1H, br s), δ_C 148.5 (C), 147.2 (C), 123.3 (C), 117.5 (CH), 115.8 (CH), 114.2 (CH)], one oxygenated sp^3 quaternary carbon [δ_C 76.6 (C)], and five methyls [δ_H 1.16 (3H, s), 0.88 (3H, s), 0.86 (3H, s), 0.85 (3H, s), 0.82 (3H, s), δ_C 33.3 (CH_3), 21.4 (CH_3), 20.5 (CH_3), 16.4 (CH_3), 16.0 (CH_3)]. COSY cross-peaks indicated linkages of vicinal protons to give rise to the following carbon sequences: C-1 to C-3, C-5 to C-7, C-9 to C-12, C-14 to C-15, and C-18 to C-19. These partial structures were connected to each other via quaternary carbons, as evident from the following HMBC spectrum correlations: Me-23/C-1, C-5, C-9, C-10; Me-24/C-7, C-8, C-9, C-14; Me-25/C-12, C-13, C-14; Me-26/C-3, C-4, C-5, C-22; H-15/C-16, C-17, C-21; H-18/C-16, C-17, C-20; H-21/C-15, C-17, C-20. A cyclic ether moiety was demonstrated by the degree of unsaturation of **1**. The relative configuration of **1** was deduced from the following NOESY correlations: H-6β (δ_H 1.57)/Me-23, Me-26; H-11β (δ_H 1.32)/Me-23, Me-24, Me-25; H-9/H-5, H-14. The structure of **1** was thus determined to be that shown in **1**.

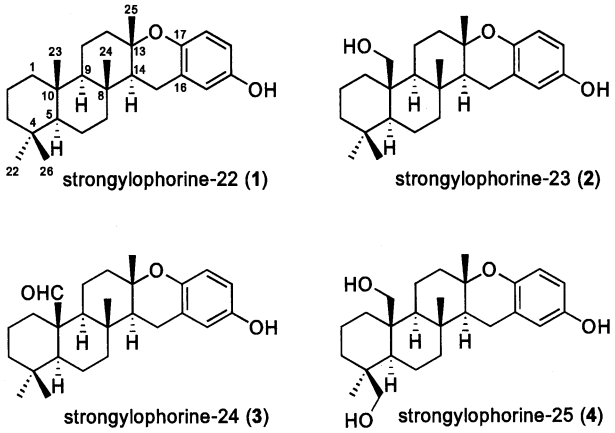

Figure 1.

The molecular formula of strongylophorine-23 (**2**) was $C_{26}H_{38}O_3$ according to the HREIMS spectrum. IR, UV, and NMR spectra of **2** were similar to those of **1**. NMR spectra of **2** suggested that a methyl group of **1** had been replaced with a hydroxymethyl group [δ_H 4.05 (1H, d, J = 11.8 Hz), 3.92 (1H, d, J = 11.8 Hz), δ_C 62.9 (CH_2)] in the case of **2** (Table 1). The position of the hydroxymethyl group of **2** was clearly confirmed by COSY and HMBC spectra as C-10, and the relative configuration of **2** was demonstrated by the NOESY spectrum.

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Table 1. NMR Data for **1** and **2**

	1		**2**	
no.	^{13}C NMR[a]	^{1}H NMR[b]	^{13}C NMR[a]	^{1}H NMR[b]
1	39.9 (CH_2)	1.70 (1H, m)	34.4 (CH_2)	2.22 (1H, br d, J = 13.2)
		0.85 (1H, m)		0.77 (1H, m)
2	18.6 (CH_2)	1.67 (1H, m)	18.5 (CH_2)	1.61 (1H, m)
		1.41 (1H, m)		1.48 (1H, m)
3	42.1 (CH_2)	1.34 (1H, m)	41.7 (CH_2)	1.44 (1H, m)
		1.17 (1H, m)		1.19 (1H, m)
4	33.3 (C)		33.0 (C)	
5	56.5 (CH)	0.84 (1H, m)	56.9 (CH)	0.97 (1H, dd, J = 12.5, 2.0)
6	18.2 (CH_2)	1.57 (1H, m)	18.0 (CH_2)	1.54 (1H, m)
		1.38 (1H, m)		1.40 (1H, m)
7	41.0 (CH_2)	1.77 (1H, dt, J = 12.5, 3.2)	41.5 (CH_2)	1.84 (1H, m)
		1.05 (1H,m)		1.11 (1H, m)
8	37.1 (C)		37.3 (C)	
9	60.7 (CH)	0.99 (1H, dd, J = 12.1, 2.0)	61.4 (CH)	1.07 (1H, m)
10	37.5 (C)		42.4 (C)	
11	18.6 (CH_2)	1.71 (1H, m)	21.9 (CH_2)	1.92 (1H, m)
		1.32 (1H, m)		1.74 (1H, m)
12	41.1 (CH_2)	2.02 (1H, dt, J = 12.5, 3.2)	42.3 (CH_2)	2.00 (1H, dt, J = 12.3, 3.1)
		1.65 (1H, m)		1.51 (1H, m)
13	76.6 (C)		76.6 (C)	
14	52.4 (CH)	1.63 (1H, m)	52.8 (CH)	1.63 (1H, m)
15	22.4 (CH_2)	2.56 (2H, d, J = 8.9)	22.5 (CH_2)	2.58 (2H, m)
16	123.3 (C)		123.2 (C)	
17	147.2 (C)		147.0 (C)	
18	117.5 (CH)	6.62 (1H, d, J = 8.4)	117.5 (CH)	6.61 (1H, d, J = 8.5)
19	114.2 (CH)	6.56 (1H, dd, J = 8.4, 2.9)	114.2 (CH)	6.56 (1H, dd, J = 8.5, 2.9)
20	148.5 (C)		148.6 (C)	
21	115.8 (CH)	6.55 (1H, br s)	115.8 (CH)	6.55 (1H, br s)
22	33.3 (CH_3)	0.86 (3H, s)	33.9 (CH_3)	0.87 (3H, s)
23	16.4 (CH_3)	0.85 (3H, s)	62.9 (CH_2)	4.05 (1H, d, J = 11.8)
				3.92 (1H, d, J = 11.8)
24	16.0 (CH_3)	0.88 (3H, s)	15.4 (CH_3)	1.06 (3H, s)
25	20.5 (CH_3)	1.16 (3H, s)	20.1 (CH_3)	1.16 (3H, s)
26	21.4 (CH_3)	0.82 (3H, s)	21.9 (CH_3)	0.78 (3H, s)

[a] 125 MHz, $CDCl_3$. [b] 500 MHz, $CDCl_3$.

Table 2. NMR Data for **3** and **4**

	3		**4**	
no.	^{13}C NMR[a]	^{1}H NMR[b]	^{13}C NMR[a]	^{1}H NMR[b]
1	34.3 (CH_2)	2.61 (1H, m)	35.7 (CH_2)	2.09 (1H, br d, J = 13.2, 4.4)
		0.72 (1H, m)		0.86 (1H, dt, J = 13.2, 4.4)
2	19.3 (CH_2)	1.43 (1H, m)	18.6 (CH_2)	1.61 (1H, m)
		1.26 (1H, m)		1.49 (1H, m)
3	41.6 (CH_2)	1.38 (1H, br d, J = 12.2)	36.3 (CH_2)	1.70 (1H, m)
		1.21 (1H, m)		1.06 (1H, m)
4	33.6 (C)		38.3 (C)	
5	55.0 (CH)	1.25 (1H, m)	56.7 (CH)	1.13 (1H, m)
6	17.6 (CH_2)	1.85 (2H, m)	19.1 (CH_2)	1.67 (2H, m)
7	39.7 (CH_2)	1.93 (1H, m)	42.1 (CH_2)	1.86 (1H, m)
		1.19 (1H, m)		1.04 (1H, m)
8	36.9 (C)		37.1 (C)	
9	60.5 (CH)	1.32 (1H, br d, J = 12.8)	61.8 (CH)	1.11 (1H, m)
10	53.4 (C)		42.0 (C)	
11	19.0 (CH_2)	1.90 (1H, m)	20.9 (CH_2)	1.83 (1H, m)
		1.15 (1H, m)		1.63 (1H, m)
12	40.7 (CH_2)	2.03 (1H, br d, J = 12.8)	41.9 (CH_2)	2.01 (1H, dt, J = 12.2, 2.9)
		1.57 (1H, m)		1.55 (1H, m)
13	76.0 (C)		76.5 (C)	
14	51.4 (CH)	1.68 (1H, dd, J = 12.8, 5.4)	52.7 (CH)	1.64 (1H, m)
15	22.8 (CH_2)	2.57 (2H, m)	22.6 (CH_2)	2.58 (2H, d, J = 9.0)
16	122.7 (C)		123.1 (C)	
17	147.0 (C)		147.1 (C)	
18	117.6 (CH)	6.61 (1H, d, J = 8.4)	117.5 (CH)	6.62 (1H, dd, J = 7.0, 2.5)
19	114.4 (CH)	6.56 (1H, d, J = 8.4)	114.2 (CH)	6.56 (1H, dd, J = 7.0, 2.8)
20	148.6 (C)		148.6 (C)	
21	115.7 (CH)	6.55 (1H, s)	115.7 (CH)	6.55 (1H, s)
22	31.9 (CH_3)	0.94 (3H, s)	27.7 (CH_3)	0.99 (3H, s)
23	206.3 (CHO)	10.11 (1H, s)	63.5 (CH_2)	3.88 (2H, s)
24	16.6 (CH_3)	0.76 (3H, s)	15.0 (CH_3)	1.05 (3H, s)
25	20.3 (CH_3)	1.09 (3H, s)	20.3 (CH_3)	1.17 (3H, s)
26	20.8 (CH_3)	0.80 (3H, s)	67.1 (CH_2)	3.62 (1H, d, J = 11.1)
				3.54 (1H, d, J = 11.1)

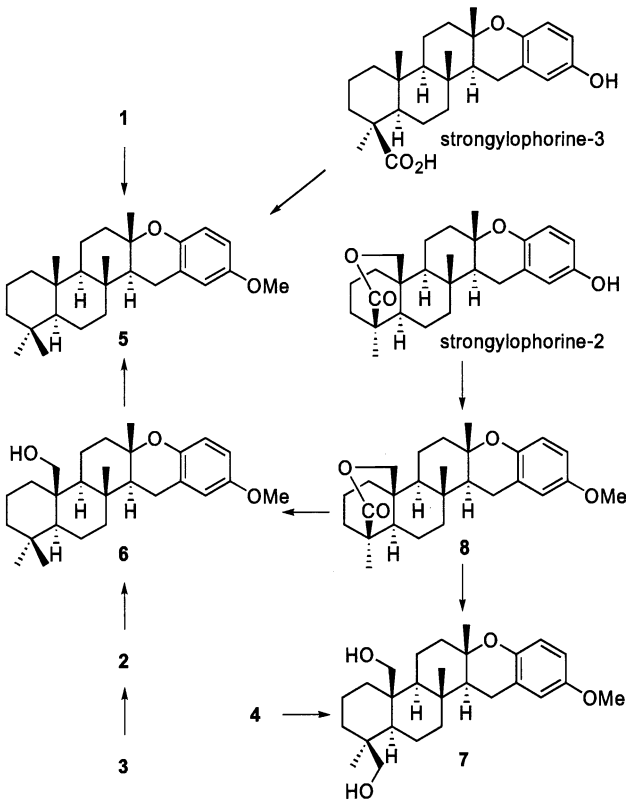
[a] 125 MHz, $CDCl_3$. [b] 500 MHz, $CDCl_3$.

The molecular formula of strongylophorine-24 (**3**) was indicated by the HREIMS spectrum to be $C_{26}H_{36}O_3$. IR, UV, and NMR spectra of **3** were similar to those of **2** except for formyl group [IR: 1704 cm^{-1}, NMR: δ_H 10.11 (1H, s), δ_C 206.3 (C)] (Table 2). The position of the formyl group of **3** was clearly indicated by COSY and HMBC spectra to be C-10, and the relative configuration of **3** was demonstrated by the NOESY spectrum.

The molecular formula of strongylophorine-25 (**4**) was $C_{26}H_{38}O_4$ on the basis of the HRESIMS spectrum. IR, UV, and NMR spectra of **4** were essentially those of **2**. NMR spectra of **4** suggested a methyl group of **2** to have been replaced with a hydroxymethyl group [δ_H 3.62 (1H, d, J = 11.1 Hz), 3.54 (1H, d, J = 11.1 Hz), δ_C 67.1 (CH_2)] in the case of **4** (Table 2). The position of the hydroxymethyl group of **4** was clearly shown by COSY and HMBC spectra to be C-4, and the relative configuration of **4** was found from the NOESY spectrum.

The absolute configurations of strongylophorines-22 (**1**)−25 (**4**) were clarified on the basis of their chemical correlation with strongylophorine-3,[1] whose absolute configuration was already known (Scheme 1). Strongylophorine-22 (**1**) was treated with MeI and K_2CO_3 in acetone to give methyl ether **5**. This methyl ether **5** was also derived from strongylophorine-3 in the following steps: (1) methylation of either carboxy or hydroxy groups, (2) $LiAlH_4$ reduction of ester, (3) PCC oxidation of the primary hydroxy group to give an aldehyde, and (4) Wolff−Kishner reduction of the formyl group. It thus follows that the absolute configuration of **1** could be concluded to be 5*S*, 8*R*, 9*R*, 10*S*, 13*S*, and 14*S*. Strongylophorine-23 (**2**) was converted to the above methyl ether **5** via alcohol **6** by (1) methylation of the phenolic hydroxy group to give **6**, (2) oxidation of the primary hydroxy group, and (3) Wolff−Kishner reduction of the formyl group. Strongylophorine-24 (**3**) was reduced with $LiAlH_4$ to provide strongylophorine-23 (**2**). The absolute configurations of **2** and **3** are thus shown to be 5*S*, 8*R*, 9*S*, 10*R*, 13*S*, and 14*S*. Strongylophorine-25 (**4**) was treated with MeI and K_2CO_3 in acetone to give methyl ether **7**. Methyl ether **7** was obtained from strongylophorine-2[1] via lactone **8** by (1) methylation of the phenolic hydroxy group in strongylophorine-2 to give **8** and (2) $LiAlH_4$ reduction of lactone. Lactone **8** was converted to alcohol **6** by (1) DIBAL-H reduction to give hemiacetal and (2) Wolff−Kishner reduction. The absolute configuration of **4** is clearly shown by these results to be 4*S*, 5*S*, 8*R*, 9*S*, 10*S*, 13*S*, and 14*S*.

Scheme 1



Strongylophorines-1−4 and -22 (**1**)−24 (**3**) displayed antiproliferative activity toward HeLa cells at IC_{50} values of 49.1, >100, 45.2, 50.5, 26.6, 62.0, and >100 μM, respectively.[8,9]

Experimental Section

General Experimental Procedures. Optical rotations were measured with a JASCO DIP-360 polarimeter. IR spectra were recorded with a JASCO FT-IR/620 spectrometer and UV spectra with a JASCO V-550 spectrometer. ^{1}H and ^{13}C NMR spectra were taken with a Bruker DRX-400 or DRX-500 spectrometer. Chemical shifts are given on a δ (ppm) scale with tetramethylsilane (TMS) as the internal standard (s, singlet; d, doublet; t, triplet; m, multiplet; br, broad). EIMS spectra were obtained with a Thermo Quest TSQ 700 spectrometer and high-resolution EIMS (HREIMS) spectra, using a VG Auto Spec E spectrometer. ESIMS and high-resolution ESIMS (HRESIMS) spectra were obtained with a Micromass LCT spectrometer. Flash column chromatography was carried out on Kanto Chemical silica gel 60N (spherical, neutral) 40−50 μm or ODS Wakogel LP-40 C-18. HPLC separations were made using a YMC-Pack R&D ODS (250 × 20 mm) column and UV detector (254 nm).

Animal Material. Sponge specimens (moss-green, hard) were obtained from the coral reef of Hatoma Island, Okinawa, Japan, at a depth of 5 m by hand using scuba, in June 2001. All the sponge specimens belong to the classification *Petrosia* (*Strongylophora*) *corticata* (Wilson, 1925). A voucher specimen has been deposited at University of Amsterdam (ZMA POR 17252) and another at Tokyo University of Pharmacy and Life Science (S-01-1).

Extraction and Isolation. Wet specimens (8.0 kg) were cut into small pieces and extracted with MeOH (12.0 L × 3) and then acetone (12.0 L × 3). The combined extracts were concentrated and partitioned between EtOAc (4.0 L × 4) and water (2.0 L) to give an EtOAc-soluble portion (210 g). The EtOAc-soluble portion was partitioned between hexane (1.0 L × 4) and 80% MeOH (2.0 L) to give a hexane-soluble portion (59.1 g) and an 80% MeOH-soluble portion (148 g). The 80% MeOH-soluble portion was chromatographed on silica gel using a hexane−EtOAc (2:1, 1:1, 1:2) gradient and MeOH as eluent to produce fractions 1 (15.3 g), 2 (55.0 g), 3 (21.8 g), 4 (23.2 g), and 5 (33.3 g). Fraction 1 was subjected to flash silica gel column chromatography (elution with hexane−EtOAc (5:2)) to give fractions 1-1 (2.49 g), 1-2 (1.96 g), 1-3 (1.68 g), and 1-4 (9.10 g). Fraction 1-1 was subjected to flash silica gel column chromatography (elution with hexane−EtOAc (5:1)) to give strongylophorine-22 (**1**) (1.31 g). Fraction 1-2 was chromatographed on flash silica gel with hexane−EtOAc (4:1) as eluent to give strongylophorine-1[1] (1.03 g). Fraction 1-3 was chromatographed on flash silica gel with hexane−EtOAc (3:1), giving fractions 1-3-1 (468 mg), 1-3-2 (75.0 mg), and 1-3-3 (1.15 g). Fraction 1-3-2 was subjected to silica gel HPLC (elution with hexane−acetone (7:1)) and ODS-HPLC (elution with MeOH−H_2O (19:1)) to give strongylophorine-24 (**3**) (14.4 mg). By the recrystallization of fraction 1-3-3 from MeOH strongylophorine-4[2] (1.06 g) was obtained. Fraction 1-4 was chromatographed on flash silica gel with hexane−EtOAc (3:1) as eluent to give strongylophorine-23 (**2**) (148 mg). Fraction 2 was subjected to flash silica gel column chromatography (elution with hexane−EtOAc (2:1)) to give strongylophorine-3[1] (54.2 g). Fraction 3 was recrystallized from $CHCl_3$−MeOH−Et_2O to give strongylophorines-15[6] and -16[6] (9.32 g). Fraction 4 was subjected to flash silica gel column chromatography (elution with $CHCl_3$−MeOH (19:1)) to give strongylophorine-2[1] (15.2 g). Fraction 5 was chromatographed on flash silica gel using hexane−EtOAc (2:3), EtOAc, and MeOH as eluent to give strongylophorine-8[2] (13.1 g) and strongylophorine-25 (**4**) (362 mg).

Strongylophorine-22 (1): colorless needles (MeOH); mp 190−191 °C; $[\alpha]^{25}_D$ −75.2° (*c* 1.1, $CHCl_3$); UV (EtOH) λ_{max} (ϵ) 298 (4432), 229 (5932), 221 (6684) nm; IR (KBr) ν_{max} 3435, 1496, 1232 cm^{-1}; ^{1}H and ^{13}C NMR, see Table 1; COSY correlations (H/H) H-2α (δ_H 1.67)/H-1α (δ_H 0.85), H-3α (δ_H 1.34), H-3β (δ_H 1.17); H-2β (δ_H 1.41)/H-1α (δ_H 0.85), H-1β (δ_H 1.70), H-3β (δ_H 1.17); H-6α (δ_H 1.38)/H-5, H-7β (δ_H 1.77); H-6β (δ_H 1.57)/H-5, H-7α (δ_H 1.05), H-7β (δ_H 1.77); H-11α (δ_H 1.71)/H-12β (δ_H 2.02); H-11β (δ_H 1.32)/H-9, H-12α (δ_H 1.65), H-12β (δ_H 2.02); H-14/H-15; H-18/H-19; HMBC correlations (H/C) H-3/C-4, C-22; H-5/C-3, C-4, C-22; H-7/C-5; H-9/C-23, C-24; H-12/C-9, C-11, C-13, C-25; H-14/C-7, C-8, C-9, C-12, C-13, C-15, C-24, C-25; H-15/C-13, C-14, C-16, C-17, C-21; H-18/C-16, C-17, C-20; H-19/C-17, C-20; H-21/C-15, C-17, C-20; Me-22/C-3, C-4, C-5, C-26; Me-23/C-1, C-5, C-9, C-10; Me-24/C-7, C-8, C-9, C-14; Me-25/C-12, C-13, C-14; Me-26/C-3, C-4, C-5, C-22; NOE correlations (H/H) H-5/H-3α (δ_H 1.34), H-9; H-6β (δ_H 1.57)/Me-23, Me-26; H-9/H-1α (δ_H 0.85), H-14; H-11β (δ_H 1.32)/Me-23, Me-24, Me-25; H-14/H-7α (δ_H 1.05); H-15/H-7β (δ_H 1.77), H-21, Me-24, Me-25; Me-22/H-6α (δ_H 1.38); Me-25/H-12β (δ_H 2.02); Me-26/H-2β (δ_H 1.41), H-3β (δ_H 1.17); EIMS *m*/*z* 382 [M$^+$] (100), 367 (5), 297 (20), 259 (24), 123 (31); HREIMS *m*/*z* 382.2878 (calcd for $C_{26}H_{38}O_2$, 382.2872).

Strongylopholine-23 (2): colorless, amorphous; $[\alpha]^{23}_D$ −52.2° (*c* 1.2, $CHCl_3$); UV (MeOH) λ_{max} (ϵ) 298 (3822), 229 (5066), 220 (5950) nm; IR (KBr) ν_{max} 3409, 1494, 1232 cm^{-1}; ^{1}H and ^{13}C NMR, see Table 1; COSY correlations (H/H) H-2α (δ_H 1.48)/H-1α (δ_H 0.77), H-1β (δ_H 2.22), H-3α (δ_H 1.19); H-2β (δ_H 1.61)/H-1α (δ_H 0.77), H-1β (δ_H 2.22), H-3α (δ_H 1.19); H-6α (δ_H 1.54)/H-5, H-7β (δ_H 1.11); H-6β (δ_H 1.40)/H-5, H-7α (δ_H 1.84), H-7β (δ_H 1.11); H-11α (δ_H 1.92)/H-9, H-12α (δ_H 1.51), H-12β (δ_H 2.00); H-11β (δ_H 1.74)/H-9, H-12α (δ_H 1.51), H-12β (δ_H 2.00); H-14/H-15; H-18/H-19; HMBC correlations (H/C) H-1/C-2, C-3, C-5, C-9, C-10, C-23; H-2/C-1, C-3, C-4; H-3/C-1, C-2, C-4, C-5, C-22, C-26; H-5/C-4, C-6, C-9, C-10, C-22, C-23, C-26; H-6/C-5, C-7, C-8; H-7/C-5, C-6, C-8, C-9, C-14, C-24; H-9/C-10, C-11, C-12, C-24; H-11/C-8, C-9, C-10, C-12, C-13; H-12/C-9, C-11, C-13, C-14, C-25; H-14/C-7, C-8, C-9, C-13, C-15, C-24, C-25; H-15/C-8, C-13, C-14, C-16, C-17, C-21; H-18/C-16, C-17, C-20; H-19/C-17, C-20, C-21; H-21/C-15, C-17, C-19, C-20; Me-22/C-3, C-4, C-5; H-23/C-1, C-9, C-10; Me-24/C-7, C-8, C-9, C-14; Me-25/C-12, C-13, C-14; Me-26/C-3, C-4, C-5, C-22; NOE correlations (H/H) H-1β (δ_H 2.22)/H-11α (δ_H 1.92); H-5/H-1α (δ_H 0.77), H-3α (δ_H 1.19), H-9, Me-22; H-6β (δ_H 1.40)/H-23a (δ_H 3.92), Me-24, Me-26; H-9/H-1α (δ_H 0.77), H-7α (δ_H

1.84), H-14; H-14/H-12α (δ_H 1.51); H-15/H-7α (δ_H 1.84), H-21, Me-24, Me-25; Me-22/H-6α (δ_H 1.54), Me-26; H-23b (δ_H 4.05)/H-2β (δ_H 1.61), Me-26; Me-24/H-11β (δ_H 1.74), H-23a (δ_H 3.92), Me-25; Me-25/H-11β (δ_H 1.74), H-12β (δ_H 2.00); EIMS *m/z* 398 [M^+] (100), 367 (10), 275 (8); HREIMS *m/z* 398.2807 (calcd for $C_{26}H_{38}O_3$, 398.2821).

Strongylopholine-24 (3): colorless needles (MeOH−H_2O); mp 214−216 °C; $[\alpha]^{26}_D$ −25.5° (*c* 1.0, $CHCl_3$); UV (EtOH) λ_{max} (ϵ) 297 (3803), 228 (5296), 220 (6273) nm; IR (KBr) ν_{max} 3428, 1704, 1495, 1231 cm^{-1}; ^1H and ^{13}C NMR, see Table 2; COSY correlations (H/H) H-2α (δ_H 1.43)/H-1α (δ_H 0.72), H-1β (δ_H 2.61), H-3β (δ_H 1.38); H-2β (δ_H 1.26)/H-1α (δ_H 0.72), H-1β (δ_H 2.61), H-3β (δ_H 1.38); H-6/H-5, H-7α (δ_H 1.19); H-11α (δ_H 1.15)/H-9, H-12α (δ_H 1.57), H-12β (δ_H 2.03); H-11β (δ_H 1.90)/H-9, H-12α (δ_H 1.57); H-14/H-15; H-18/H-19; HMBC correlations (H/C) H-1/C-3, C-5, C-10, C-23; H-2/C-3, C-4, C-10; H-3/C-1, C-5; H-5/C-4, C-6, C-7, C-10, C-23; H-6/C-5, C-7, C-8, C-10; H-7/C-5, C-6, C-9, C-24; H-9/C-8, C-10, C-11, C-12, C-14, C-23, C-24; H-11/C-8, C-9, C-12, C-13; H-12/C-9, C-11, C-13, C-14, C-25; H-15/C-13, C-14, C-16, C-17, C-21; H-18/C-16, C-20; H-19/C-17, C-21; H-21/C-15, C-17, C-19, C-20; Me-22/C-3, C-4, C-5, C-26; CHO-23/C-1, C-10; Me-24/C-7, C-8, C-9, C-14; Me-25/C-12, C-13, C-14; Me-26/C-3, C-4, C-5, C-22; NOE correlations (H/H) H-9/H-1α (δ_H 0.72), H-5, H-12α (δ_H 1.57), H-14; H-14/H-7α (δ_H 1.19), H-12α (δ_H 1.57); H-15/H-21, Me-24, Me-25; Me-22/H-3α (δ_H 1.21), H-6, Me-26; CHO-23/H-6, H-11β (δ_H 1.90), Me-24, Me-26; Me-24/H-11β (δ_H 1.90), Me-25; Me-25/H-12β (δ_H 2.03); Me-26/H-3β (δ_H 1.38); EIMS *m/z* 396 [M^+] (100), 367 (5), 297 (3), 278 (28), 245 (20), 91 (32); HREIMS *m/z* 396.2677 (calcd for $C_{26}H_{36}O_3$, 396.2664).

Strongylopholine-25 (4): colorless needles (MeOH); mp 262−263 °C; $[\alpha]^{22}_D$ −60.0° (*c* 0.1, $CHCl_3$); UV (EtOH) λ_{max} (ϵ) 298 (3993), 228 (5405), 221 (6299) nm; IR (KBr) ν_{max} 3410, 1474, 1229 cm^{-1}; ^1H and ^{13}C NMR, see Table 2; COSY correlations (H/H) H-2α (δ_H 1.49)/H-1α (δ_H 0.86), H-1β (δ_H 2.09), H-3α (δ_H 1.06), H-3β (δ_H 1.70); H-2β (δ_H 1.61)/H-1α (δ_H 0.86), H-1β (δ_H 2.09), H-3α (δ_H 1.06), H-3β (δ_H 1.70); H-6/H-5, H7-α (δ_H 1.04), H-7β (δ_H 1.86); H-11α (δ_H 1.83)/H-9, H-12α (δ_H 1.55), H-12β (δ_H 2.01); H-11β (δ_H 1.63)/H-9, H-12β (δ_H 2.01); H-14/H-15; H-18/H-19; HMBC correlations (H/C) H-1/C-2, C-3, C-5, C-9, C-10, C-23; H-3/C-1, C-2, C-4, C-22, C-26; H-5/C-4, C-6, C-9, C-22; H-6/C-5; H-7/C-5, C-6, C-8, C-10, C-24; H-9/C-5, C-7, C-8, C-10, C-11, C-14, C-23, C-24; H-11/C-8, C-12, C-13; H-12/C-9, C-11, C-13, C-14, C-25; H-14/C-7, C-8, C-9, C-15, C-24, C-25; H-15/C-8, C-13, C-14, C-16, C-21; H-18/C-16, C-17, C-20; H-19/C-17, C-20, C-21; H-21/C-15, C-19; Me-22/C-3, C-4, C-5, C-26; H-23/C-1, C-5, C-9, C-10; Me-24/C-7, C-8, C-9, C-14; Me-25/C-12, C-13, C-14; H-26/C-3, C-4, C-5, C-22; NOE correlations (H/H) H-1β (δ_H 2.09)/H-11α (δ_H 1.83); H-5/H-1α (δ_H 0.86), H-3α (δ_H 1.06), H-7α (δ_H 1.04), Me-22; H-9/H-1α (δ_H 0.86), H-12α (δ_H 1.55), H-14; H-11β (δ_H 1.63)/Me-24, Me-25; H-14/H-7α (δ_H 1.04); H-15/H-7β (δ_H 1.86), H-21, Me-24, Me-25; Me-22/H-6, H-26a (δ_H 3.62), H-26b (δ_H 3.54); H-23/H-1β (δ_H 2.09), H-2β (δ_H 1.61), H-6, Me-24, H-26a (δ_H 3.62), H-26b (δ_H 3.54); Me-25/H-12β (δ_H 2.01), Me-24; H-26a (δ_H 3.62)/H-2β (δ_H 1.61); H-26b (δ_H 3.54)/H-6; ESIMS *m/z* 415 [$M^+ + H$] (50), 397 (100), 379 (33), 301 (90), 273 (28); HRESIMS *m/z* 415.2818 (calcd for $C_{26}H_{38}O_4$, $M^+ + H$, 415.2848).

Synthesis of Methyl Ether 5 from Strongylopholine-22 (1). To a solution of strongylopholine-22 (**1**) (11.0 mg, 28.8 μmol) in acetone (300 μL) were added K_2CO_3 (16.0 mg, 115 μmol) and iodomethane (5.4 μL, 84.6 μmol). The mixture was stirred at 40 °C for 24 h. The reaction mixture was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (elution with hexane−EtOAc (24:1)) to give methyl ether **5** (11.4 mg, 100% yield): colorless, amorphous; $[\alpha]^{26}_D$ −71.9° (*c* 1.1, $CHCl_3$); UV (EtOH) λ_{max} (ϵ) 295 (3614), 230 (6463), 221 (6406) nm; IR (KBr) ν_{max} 1495, 1234 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 6.67 (2H, m), 6.61 (1H, br s), 3.74 (3H, s), 2.59 (2H, d, J = 9.1 Hz), 2.03 (1H, dt, J = 12.3, 3.1 Hz), 1.78 (1H, dt, J = 12.6, 3.1 Hz), 1.77−1.56 (7H, m), 1.44−1.26 (5H, m), 1.16 (3H, s), 1.19−0.98 (3H, m), 0.89 (3H, s), 0.85 (6H, s), 0.82 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 152.9, 147.2, 123.0, 117.4, 114.3, 113.0, 76.5, 60.7, 56.5, 55.7, 52.4, 42.1, 41.1, 41.0, 39.9, 37.4, 37.1, 33.3, 33.3, 22.6, 21.4, 20.5, 18.6, 18.6, 18.2, 16.4, 16.0; EIMS *m/z* 396 [M^+] (100), 381 (5), 259 (16), 137 (30); HREIMS *m/z* 396.3023 (calcd for $C_{27}H_{40}O_2$, 396.3028).

Synthesis of Methyl Ether 5 from Strongylopholine-3. To a solution of strongylopholine-3[1] (100 mg, 240 μmol) in acetone (2.40 mL) were added K_2CO_3 (134 mg, 970 μmol) and iodomethane (45.4 μL, 730 μmol). The mixture was stirred at 40 °C for 53 h. The reaction mixture was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (elution with hexane−EtOAc (10:1)) to give methyl ether (77.9 mg, 73% yield): colorless, amorphous; $[\alpha]^{26}_D$ −22.4° (*c* 1.0, $CHCl_3$); UV (EtOH) λ_{max} (ϵ) 295 (3670), 229 (6639), 220 (6644) nm; IR (KBr) ν_{max} 1727, 1497, 1230 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 6.67 (2H, m), 6.62 (1H, br s), 3.74 (3H, s), 3.65 (3H, s), 2.61 (2H, d, J = 9.1 Hz), 2.16 (1H, br d, J = 13.5 Hz), 2.03 (1H, br d, J = 12.5 Hz), 1.97−1.25 (10H, m), 1.18 (3H, s), 1.16 (3H, s), 1.08−0.90 (5H, m), 0.90 (3H, s), 0.68 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 177.9, 152.9, 147.1, 122.9, 117.4, 114.3, 113.0, 76.4, 60.0, 57.0, 55.7, 52.3, 51.2, 43.8, 41.1, 40.8, 40.1, 38.0, 37.7, 36.9, 28.6, 22.6, 20.6, 19.6, 19.1, 18.8, 15.5, 14.0; EIMS *m/z* 440 [M^+] (100), 304 (26), 120 (58), 93 (35); HREIMS *m/z* 440.2909 (calcd for $C_{28}H_{40}O_4$, 440.2927).

To a solution of the above methyl ether (71.6 mg, 160 μmol) in THF (28.3 mL) was added $LiAlH_4$ (94.4 mg, 2.49 mmol) followed by refluxing for 1.5 h. To the reaction mixture diluted with Et_2O was added Na_2SO_4−$10H_2O$. The mixture was stirred at room temperature for 2 h, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (elution with hexane−EtOAc (3:1)) to give an alcohol (66.1 mg, 98% yield): colorless, amorphous; $[\alpha]^{26}_D$ −68.3° (*c* 1.0, $CHCl_3$); UV (EtOH) λ_{max} (ϵ) 295 (3668), 229 (6532), 220 (6446) nm; IR (KBr) ν_{max} 3316, 1496, 1232 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 6.67 (2H, m), 6.61 (1H, br s), 3.74 (3H, s), 2.58 (2H, d, J = 8.9 Hz), 2.03 (1H, dt, J = 12.3, 3.0 Hz), 1.80−1.28 (11H, m), 1.16 (3H, s), 1.12−0.80 (7H, m), 0.96 (3H, s), 0.87 (3H, s), 0.84 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 152.9, 147.1, 122.9, 117.4, 114.3, 113.0, 76.4, 65.4, 60.8, 57.1, 55.7, 52.3, 41.3, 41.0, 40.0, 38.6, 37.3, 37.1, 35.6, 26.8, 22.6, 20.5, 18.7, 18.4, 18.2, 16.8, 15.9; EIMS *m/z* 412 [M^+] (100), 381 (5), 275 (8), 137 (54); HREIMS *m/z* 412.2963 (calcd for $C_{27}H_{40}O_3$, 412.2977).

To a solution of the above alcohol (46.2 mg, 110 μmol) in CH_2Cl_2 (1.10 mL) were added 4A MS (58.0 mg) and PCC (58.0 mg, 260 μmol) followed by stirring at room temperature for 4 h. The reaction mixture was diluted with EtOAc and filtered through a silica gel column. The filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (elution with hexane−acetone (9:1)) to give an aldehyde (36.7 mg, 80% yield): colorless, amorphous; $[\alpha]^{24}_D$ −66.0° (*c* 1.0, $CHCl_3$); UV (EtOH) λ_{max} (ϵ) 295 (3604), 230 (6390), 221 (6347) nm; IR (KBr) ν_{max} 1709, 1497, 1234 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 9.80 (1H, s), 6.67 (2H, m), 6.62 (1H, br s), 3.75 (3H, s), 2.61 (2H, d, J = 9.0 Hz), 2.12 (1H, br d, J = 13.5 Hz), 2.04 (1H, dt, J = 12.5, 3.2 Hz), 1.90−1.47 (10H, m), 1.33 (1H, dq, J = 13.5, 3.1 Hz), 1.20 (1H, dd, J = 12.5, 2.3 Hz), 1.16 (3H, s), 1.08−0.88 (3H, m), 1.01 (3H, s), 0.91 (3H, s), 0.73 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 205.8, 152.9, 147.1, 122.7, 117.4, 114.3, 113.1, 76.3, 59.5, 56.7, 55.7, 52.3, 48.4, 41.0, 40.7, 39.2, 37.7, 36.9, 34.4, 24.1, 22.6, 20.5, 18.8, 18.3, 17.8, 15.8, 15.2; EIMS *m/z* 410 [M^+] (100), 381 (2), 273 (6); HREIMS *m/z* 410.2810 (calcd for $C_{27}H_{38}O_3$, 410.2821).

To a solution of the above aldehyde (32.6 mg, 79.4 μmol) in diethylene glycol (1.60 mL) were added KOH (40.1 mg, 710 μmol) and H_2NNH_2−H_2O (48.6 μL, 950 μmol), and refluxing was conducted for 4.5 h. The reaction mixture was diluted with Et_2O and EtOAc, washed with saturated aqueous NH_4Cl, H_2O, and saturated aqueous NaCl, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (elution with hexane−EtOAc (20:1)) to give methyl ether **5** (24.4 mg, 77% yield): colorless, amorphous; $[\alpha]^{19}_D$ −74.0° (*c* 1.0, $CHCl_3$). The spectral data were

identical with those of methyl ether **5** prepared from strongylopholine-22 (**1**).

Synthesis of Methyl Ether 6 from Strongylopholine-23 (2). To a solution of strongylopholine-23 (**2**) (28.7 mg, 72.0 μmol) in acetone (700 μL) were added K_2CO_3 (39.8 mg, 230 μmol) and iodomethane (13.4 μL, 220 μmol). The mixture was stirred at 40 °C for 21 h, diluted with Et_2O and EtOAc, washed with H_2O and saturated aqueous NaCl, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (elution with hexane−EtOAc (4:1)) to give methyl ether **6** (25.1 mg, 84% yield): colorless, amorphous; $[\alpha]^{26}_D$ −59.3° (*c* 0.5, $CHCl_3$); UV (EtOH) λ_{max} (ϵ) 296 (3842), 229 (6936), 221 (6941) nm; IR (KBr) ν_{max} 3436, 1496, 1229 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 6.67 (2H, m), 6.61 (1H, d, J = 2.0 Hz), 4.05 (1H, br d, J = 11.7 Hz), 3.92 (1H, m), 3.74 (3H, s), 2.63 (2H, m), 2.23 (1H, br d, J = 13.1 Hz), 2.00 (1H, dt, J = 12.3, 3.2 Hz), 1.93−1.37 (9H, m), 1.26−0.96 (5H, m), 1.17 (3H, s), 1.07 (3H, s), 0.88 (3H, s), 0.79 (3H, s), 0.78 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 152.9, 147.2, 122.9, 117.4, 114.4, 113.0, 76.5, 62.9, 61.5, 56.9, 55.7, 52.9, 42.4, 42.4, 41.8, 41.6, 37.3, 34.5, 33.9, 33.0, 22.7, 21.9, 21.9, 20.2, 18.5, 18.0, 15.5; EIMS *m*/*z* 412 [M$^+$] (100), 381 (7), 257 (15); HRESIMS *m*/*z* 413.3071 (calcd for $C_{27}H_{40}O_3$, M$^+$ + H, 413.3056).

Synthesis of Methyl Ether 5 from Methyl Ether 6. To a solution of methyl ether **5** (20.9 mg, 50.7 μmol) in CH_2Cl_2 (500 μL) were added 4A MS (13.1 mg) and PCC (13.1 mg, 60.8 μmol), followed by stirring at room temperature for 2.5 h. The reaction mixture was diluted with EtOAc and filtered through a silica gel column. The filtrate was concentrated under reduced pressure. The residue was recrystallized from $CHCl_3$−acetone to give an aldehyde (20.5 mg, 99% yield): colorless, amorphous; $[\alpha]^{26}_D$ −25.0° (*c* 0.5, $CHCl_3$); UV (EtOH) λ_{max} (ϵ) 295 (3888), 230 (6724), 220 (6993) nm; IR (KBr) ν_{max} 1690, 1498, 1236 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 10.11 (1H, d, J = 1.0 Hz), 6.66 (2H, m), 6.61 (1H, br s), 3.74 (3H, s), 2.60 (3H, m), 2.02 (1H, dt, J = 12.7, 3.3 Hz), 1.96−1.78 (4H, m), 1.69 (1H, dd, J = 12.6, 5.6 Hz), 1.56 (1H, m), 1.47−1.10 (8H, m), 1.10 (3H, s), 0.94 (3H, s), 0.81 (3H, s), 0.77 (3H, s), 0.75 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 206.1, 153.0, 147.1, 122.5, 117.5, 114.3, 113.2, 76.0, 60.6, 55.7, 55.0, 53.4, 51.5, 41.6, 40.8, 39.8, 36.9, 34.4, 33.7, 31.9, 23.0, 20.8, 20.3, 19.3, 19.0, 17.6, 16.6; ESIMS *m*/*z* 410 [M$^+$ + H] (100), 393 (19), 219 (30); HRESIMS *m*/*z* 411.2873 (calcd for $C_{27}H_{38}O_3$, M$^+$ + H, 411.2899).

To a solution of the above aldehyde (12.7 mg, 30.9 μmol) in diethylene glycol (600 μL) were added H_2NNH_2−H_2O (79.1 μL, 1.55 mmol) and concentrated HCl (15.7 μL, 150 μmol), followed by refluxing for 12 h. The mixture was then treated with KOH (69.9 mg, 1.24 mmol) and refluxed for 2 h. The reaction mixture was diluted with Et_2O and washed with saturated aqueous NH_4Cl, H_2O, and saturated aqueous NaCl. The aqueous layer was extracted with $CHCl_3$. The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel TLC (development with hexane−EtOAc (8:1)) to give methyl ether **5** (1.2 mg, 10% yield): colorless, amorphous; $[\alpha]^{26}_D$ −72.7° (*c* 0.1, $CHCl_3$). The spectral data were identical with those of methyl ether **5** prepared from strongylopholine-3.

Synthesis of Strongylopholine-23 (2) from Strongylopholine-24 (3). To a solution of strongylopholine-24 (**3**) (4.5 mg, 11.3 μmol) in THF (300 μL) was added $LiAlH_4$ (0.9 mg, 22.6 μmol), followed by stirring at room temperature for 30 min. The reaction mixture was diluted with Et_2O, treated with Na_2SO_4−$10H_2O$, stirred at room temperature for 2 h, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (elution with hexane−EtOAc (2:1)) to give strongylopholine-23 (**2**) (4.5 mg, 99% yield): colorless, amorphous; $[\alpha]^{25}_D$ −56.2° (*c* 0.5, $CHCl_3$). The spectral data were identical with those of strongylopholine-23 (**2**).

Synthesis of Diol 7 from Strongylopholine-25 (4). To a solution of strongylopholine-25 (**4**) (5.0 mg, 12.1 μmol) in DMF (100 μL) were added Cs_2CO_3 (19.6 mg, 60.3 μmol) and iodomethane (3.8 μL, 60.3 μmol). The mixture was stirred at 40 °C for 30 min, diluted with $CHCl_3$, washed with H_2O and saturated aqueous NaCl, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (elution with $CHCl_3$−MeOH (9:1)) to give diol **7** (3.5 mg, 68% yield): colorless, amorphous; $[\alpha]^{20}_D$ −54.3° (*c* 0.4, $CHCl_3$); UV (EtOH) λ_{max} (ϵ) 296 (3767), 230 (6628), 221 (6569) nm; IR (KBr) ν_{max} 3423, 1496, 1231 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 6.66 (2H, m), 6.61 (1H, s), 3.88 (2H, s), 3.74 (3H, s), 3.58 (2H, q, J = 10.5 Hz), 2.62 (2H, d, J = 9.1 Hz), 2.02 (1H, br d, J = 11.9 Hz), 1.87 (1H, br d, J = 12.6 Hz), 1.85 (2H, m), 1.73−1.47 (8H, m), 1.17−0.99 (4H, m), 1.17 (3H, s), 1.05 (3H, s), 0.99 (3H, s), 0.86 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 152.9, 147.2, 122.9, 117.4, 114.3, 113.1, 76.5, 67.0, 63.5, 61.8, 56.7, 55.7, 52.7, 42.1, 42.0, 42.0, 38.3, 37.1, 36.2, 35.6, 27.7, 22.8, 21.0, 20.3, 19.0, 18.6, 15.0; ESIMS *m*/*z* 429 [M$^+$ + H] (58), 411 (100), 393 (84); HRESIMS *m*/*z* 429.3041 (calcd for $C_{27}H_{40}O_4$, M$^+$ + H, 429.3005).

Synthesis of Methyl Ether 8 from Strongylopholine-2. To a solution of strongylopholine-2[1] (10.0 mg, 24.4 μmol) in acetone (300 μL) were added K_2CO_3 (13.5 mg, 97.6 μmol) and iodomethane (4.5 μL, 73.2 μmol), followed by stirring at 40 °C for 51 h. The reaction mixture was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (elution with $CHCl_3$−acetone (49:1)) to give methyl ether **8** (10.0 mg, 97% yield): colorless, amorphous; $[\alpha]^{24}_D$ −61.5° (*c* 0.1, $CHCl_3$); UV (MeOH) λ_{max} (ϵ) 296 (3288), 229 (5873), 221 (5939) nm; IR (KBr) ν_{max} 1719, 1496, 1233 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 6.67 (2H, m), 6.61 (1H, br s), 4.78 (1H, dd, J = 12.3, 2.2 Hz), 4.03 (1H, d, J = 12.3 Hz), 3.74 (3H, s), 2.62 (2H, m), 2.18 (1H, br d, J = 12.9 Hz), 2.09 (1H, dt, J = 12.9, 3.1 Hz), 1.91−1.63 (7H, m), 1.52 (1H, m), 1.36−1.02 (7H, m), 1.21 (3H, s), 1.18 (3H, s), 1.01 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 176.6, 153.1, 146.9, 122.3, 117.5, 114.3, 113.3, 76.0, 73.4, 55.7, 55.3, 52.5, 50.4, 43.2, 41.3, 40.2, 38.1, 36.7, 36.6, 36.5, 23.2, 22.5, 20.9, 20.7, 20.4, 18.6, 15.8; EIMS *m*/*z* 424 [M$^+$] (100), 287 (18), 229 (32), 137 (36); HREIMS *m*/*z* 424.2593 (calcd for $C_{27}H_{36}O_4$, 424.2614).

Synthesis of Diol 7 from Lactone 8. To a solution of lactone **8** (104 mg, 244 μmol) in THF (5.00 mL) was added $LiAlH_4$ (30.0 mg, 731 μmol). The mixture was refluxed for 1 h, treated with 1 N HCl, and extracted with $CHCl_3$. The $CHCl_3$-soluble portion was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (elution with $CHCl_3$−MeOH (9:1)) to give diol **7** (105 mg, 100% yield): colorless, amorphous; $[\alpha]^{20}_D$ −54.3° (*c* 0.4, $CHCl_3$). The spectral data were identical with those of diol **7** prepared from strongylopholine-25 (**4**).

Synthesis of Alcohol 6 from Lactone 8. To a solution of lactone **8** (104 mg, 244 μmol) in CH_2Cl_2 (2.50 mL) was added DIBAL-H (290 μL, 268 μmol, 0.93 M in hexane) at −78 °C followed by stirring for 1 h. The reaction mixture was treated with 1 N HCl and extracted with $CHCl_3$. The $CHCl_3$-soluble portion was dried over Na_2SO_4 and concentrated under reduced pressure to give a crude hemiacetal. The crude hemiacetal was used in the next reaction without purification.

To a solution of the above crude hemiacetal in diethylene glycol (2.50 mL) were added H_2NNH_2−H_2O (500 μL, 16.1 mmol) and concentrated HCl (500 μL, 30.0 mmol). The mixture was refluxed for 12 h, treated with KOH (400 mg, 7.13 mmol), and refluxed for 10 h. After 1 N HCl addition, the mixture was extracted with $CHCl_3$, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (elution with hexane−EtOAc (4:1)) to give alcohol **6** (19.8 mg, 20% yield (two steps)): colorless, amorphous; $[\alpha]^{23}_D$ −60.0° (*c* 1.5, $CHCl_3$). The spectral data were identical with those of alcohol **6** prepared from strongylopholine-23 (**2**).

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Supporting Information Available: ^{1}H NMR, ^{13}C NMR, ^{1}H−^{1}H COSY, HMQC, HMBC, and NOESY spectra of **1** and ^{1}H NMR and ^{13}C NMR spectra of **2**−**4**. This material is available free of charge via the Internet at http://pubs.acs.org.

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