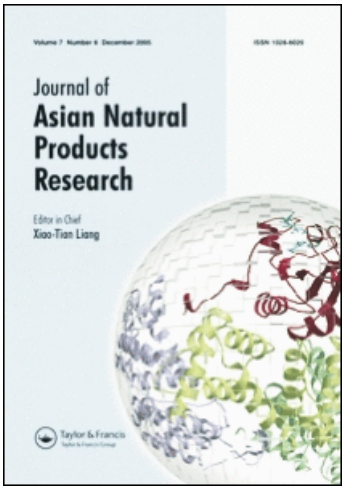

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Seven new meroditerpenoids, from the marine sponge *Strongylophora strongylata*, that inhibited the maturation of starfish oocytes

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Seven new meroditerpenoids, strongylophorines 13–19 (**1**–**7**), have been isolated together with the four known strongylophorines 2 (**8**), 3 (**9**), 4 (**10**), and 8 (**11**) by a screening method using oocytes of the starfish *Asterina pectinifera* from a marine sponge *Strongylophora strongylata* collected at Iriomote Island, Okinawa, Japan. The structures were assigned according to their spectral data. Ten strongylophorines inhibited the maturation of starfish oocytes in the range 1.1–37.6 μM (IC_{50}), while strongylophorine 4 (**10**) was not active at 250 μM.

Keywords: Meroditerpenoid; Strongylophorine; Starfish oocyte assay; Marine sponge; *Strongylophora strongylata*

1. Introduction

Fully-grown oocytes of starfish are arrested at the prophase stage of the first meiotic division, and meiosis is reinitiated by the oocyte maturation-inducing hormone of starfish [1,2]. 1-Methyladenine (1-MeAde) is produced and released by ovarian follicle cells under the influence of a peptide hormone from the radial nerve [3]. On exposure of oocytes to 1-MeAde, the maturation-promoting factor (MPF) is activated in the cytoplasm [3,4]. The MPF has been identified as a complex of cdc2 kinase (cdk1) and cyclin B [5–7], although the signal-transduction pathway from putative 1-MeAde receptors to MPF has not yet been elucidated [8]. Therefore, it has been generally accepted that the oocyte maturation involves the pathways of both signal transduction and cell cycle progression. Breakdown of the germinal vesicle in oocytes is regarded as a marker of such reinitiation. Inhibitors of starfish oocyte maturation were

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sought to provide biologically active substances that might act on either hormonal signal transduction or cell cycle progression, such as cyclinB/cdc2 inhibitors and microtubule assembly inhibitors [9].

As a part of our search for bioactive substances from the sea, a screening method that observed stimulation and inhibition of germinal vesicle breakdown (GVBD) using oocytes of *Asterina pectinifera* was applied to 128 ethanol extracts of marine sponges collected at Iriomote Island, Okinawa, Japan. The extract of *Strongylophora strongylata* showed the strongest inhibitory activity on GVBD. Following bioassay-guided separation, seven new meroditerpenoids, strongylophorines 13 (**1**), 14 (**2**), 15 (**3**), 16 (**4**), 17 (**5**), 18 (**6**), and 19 (**7**), together with four known strongylophorines 2 (**8**), 3 (**9**), 4 (**10**), and 8 (**11**) were separated from this extract. We report here the isolation, structure elucidation, and biological activity of compounds **1**–**11** (figure 1).

2. Results and discussion

The ethanol extract of *S. strongylata* was partitioned between water and $CHCl_3$ to afford a $CHCl_3$-soluble portion as an active fraction. The $CHCl_3$ extract was separated by an ODS column to give 17 fractions. The bioactive fractions 5, 7, 9, and 11 were further purified by reversed-phase HPLC (ODS) to yield strongylophorines 13 (**1**), 14 (**2**), 15 (**3**), 16 (**4**), 17 (**5**), 18 (**6**), 19 (**7**), 2 (**8**), 3 (**9**), 4 (**10**), and 8 (**11**), of which the known strongylophorines 2, 3, 4, and 8 were identified by comparing their NMR spectral data with those reported in the literature [10–14].

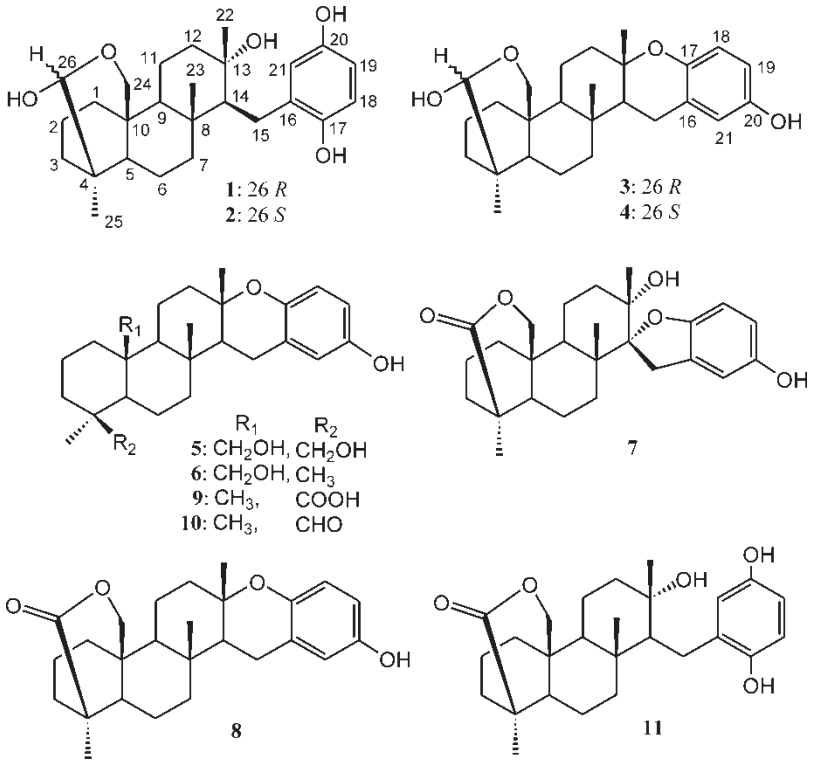

Figure 1. Structures of compounds **1**–**11**.

Strongylophorines 13 (**1**) and 14 (**2**) were obtained as a mixture of interchangeable isomers. Although each compound was separated by HPLC on ODS, both isolates showed similar HPLC chromatograms to that of the original mixture. The ratio of **1** to **2** in the mixture was determined as 3:1 by HPLC. The mixture showed one molecular ion ($[M]^+$) at *m/z* 430 in the FABMS, and the molecular formula was determined as $C_{26}H_{38}O_5$ from HR-FABMS and NMR data. ^1H and ^{13}C NMR spectra of the mixture revealed three methyl groups, nine methylene units (one oxygenated), four methine units (one dioxygenated), four quaternary carbons, and a 1,2,4-trisubstituted benzene ring in the structures of both **1** and **2** (tables 1 and 2). The ^1H and ^{13}C signals of **1** and **2** were clearly distinguished and assigned by $^1H-^1H$ COSY, HMBC, HMQC, and NOESY experiments (tables 1 and 2). A hemiacetal group in both compounds was indicated by the ^1H signals assigned as H-26 [**1**: δ 5.18, **2**: δ 5.06] and 26-OH [**1**: δ 8.02, **2**: δ 7.56], together with two ^{13}C signals ascribed to C-26 [**1**: δ 98.9, **2**: δ 99.1]. The $^1H-^1H$ COSY spectrum shows a four coupling system $^1CH_2—^2CH_2—^3CH_2$, $^5CH—^6CH_2—^7CH_2$, $^9CH—^{11}CH_2—^{12}CH_2$, and $^{14}CH—^{15}CH_2$ for both **1** and **2**. The HMBC spectrum reveals that **1** and **2** are hemiacetal derivatives of strongylophorine 8 (**11**) [11]. The only difference in the structures of **1** and **2** was ascribable to the stereochemistry at the hemiacetal carbons.

The stereochemistry at the hemiacetal carbon of **1** was assigned by the NOESY spectrum of the mixture. Since the NOEs occur between H-26 (δ 5.18) and H-6β (δ 1.60), between H-26 and H-24β (δ 4.17) for **1**, the configuration at C-26 in **1** is as shown in figure 2. The other important NOEs (figure 2) indicate that the stereochemistries of other chiral centers in **1** are the same as those in strongylophorine 8 (**11**) [11].

Table 1. ^{13}C NMR data for strongylophorines 13–19 (**1**–**7**), 2 (**8**), 3 (**9**), 4 (**10**), and 8 (**11**)[a].

C#	*1*[b]	*2*[b]	*3*[b]	*4*[b]	*5*[b]	*6*[b]	*7*[b]	*8*[b]	*9*[b]	*10*[b]	*11*[c]
1	40.4	40.4	40.5	40.5	35.6	35.0	39.9	40.0	40.5	39.2	39.2
2	22.8	22.9	22.9	22.7	19.2	19.0	20.1	21.0	20.3	18.9	20.5
3	35.3	40.9	35.1	40.7	36.4	42.1	40.3	40.2	38.7	34.5	39.5
4	37.3	37.1	37.4	37.1	39.1	33.2	43.2	43.3	43.9	48.3	42.4
5	51.1	48.7	51.5	49.1	57.3	57.0	49.7	50.1	57.0	56.4	48.9
6	19.8	20.0	21.0	20.4	18.9	18.4	21.2	20.5	19.8	18.9	19.6
7	40.1	40.6	38.9	39.3	42.9	41.9	31.9	38.1	41.0	40.6	38.9
8	39.4	39.7	36.4	36.6	37.5	37.5	43.5	36.7	37.2	37.0	38.1
9	56.9	57.5	56.9	57.6	62.4	62.1	46.3	55.3	60.2	59.5	54.7
10	37.8	37.6	37.9	37.7	42.4	42.8	36.7	36.5	38.2	37.7	35.9
11	17.6	17.6	19.0	18.0	22.1	22.5	19.1	18.7	19.0	18.0	18.7
12	44.7	44.7	42.1	42.1	43.0	43.1	39.9	41.9	41.8	41.6	43.7
13	73.8	73.8	76.3	76.3	76.7	76.7	74.0	76.0	76.4	78.2	72.3
14	63.0	63.0	53.0	53.0	53.4	53.4	99.6	52.9	53.0	52.8	62.3
15	27.6	27.6	22.9	22.9	23.1	23.0	31.9	22.7	22.8	22.8	24.3
16	131.9	131.9	123.5	123.5	123.5	123.5	130.1	123.5	123.5	123.5	130.8
17	149.9	149.9	146.8	146.8	146.9	146.8	154.0	146.5	146.8	146.7	147.2
18	117.7	117.7	118.0	118.0	118.0	118.0	108.7	118.0	118.0	118.0	115.8
19	114.6	114.6	115.3	115.3	115.3	115.3	114.4	116.5	115.3	115.3	112.8
20	151.3	151.3	152.2	152.2	152.0	152.0	152.6	152.3	152.1	152.1	149.4
21	119.4	119.4	116.9	116.9	116.9	116.8	112.4	115.4	116.9	116.6	117.1
22	24.7	24.7	21.0	21.0	20.5	20.5	24.9	21.0	20.8	20.7	24.2
23	16.4	16.5	15.7	15.7	15.5	15.6	17.5	15.8	15.7	15.7	15.8
24	67.9	62.0	67.9	62.0	62.2	61.5	73.8	73.5	14.7	15.1	72.8
25	24.3	24.1	24.0	24.2	28.6	34.2	23.5	23.5	29.3	24.0	22.8
26	98.9	99.1	98.9	99.1	64.9	22.0	176.1	176.0	180.1	205.6	175.0

[a] Signals assigned based on HMQC and HMBC experiments.
[b] Measured in pyridine-d_5 (125 MHz).
[c] Measured in DMSO-d_6 (75 MHz).

Table 2. ^{1}H NMR data for strongylophorines 13–21 (**1**–**7**)[a].

C#	***1***	***2***	***3***	***4***	***5***	***6***	***7***
1	1.00, m	1.00, m	1.00, m	1.00, m	0.77, m	0.67, m	0.86, m
	2.17, m	2. 17, m	2.17, m	2.17, m	2.51, m	2.53, m	1.95, m
2	1.55, m	1.56, m	1.56, m	1.56, m	1.45, m	1.43, m	1.15, m
	2.84, m	2.50, m	2.83, m	2.56, m	1.88, m	1.74, m	1.50, m
3	1.22, m	1.34, m	1.20, m	1.34, m	1.09, m	1.16, m	1.30, m
	2.50, m	1.56, m	2.52, m	1.56, m	2.14, m	1.37, m	1.74, m
5	0.88, m	0.80, m	1.12, m	1.04, m	1.13, m	0.90, m	1.15, m
6	1.25, m	1.50, m	1.06, m	1.72, m	1.73, 2H, m	1.44, 2H, m	1.15, m
	1.60, m	2.50, m	1.65, m	2.60, m			1.50, m
7	0.88, m	0.88, m	0.88, m	0.88, m	0.95, m	1.00, m	1.25, m
	2.06, m	2.06, m	1.65, m	1.65, m	1.76, m	1.72, m	1.58, m
9	0.85, m	0.85, m	0.94, m	0.94, m	1.10, m	1.03, d (11.0)[b]	2.05, d (12.5)
11	1. 28, m	1.28, m	1.12, m	1.55, m	2.03, m	2.05, m	1.17, m
	1.55, m	1.55, m	1.74, m	1.72, m	2.16, m	2.20, m	1.70, m
12	1.75, m	1.75, m	1.74, m	1.74, m	1.76, m	1.74, m	1.93, m
	2.03, m	2.03, m	2.08, m	2.08, m	2.14, m	2.12, m	2.22, m
14	1.95, m	1.95, m	1.65, m	1.65, m	1.74, m	1.72, m	
15	2.65, m	2.65, m	2.60, 2H, m	2.60, 2H, m	2.66, 2H, d, (9.0)	2.68, 2H, m	3.02, d (15.0)
	3.24, m	3.24, m					3.51, d (15.0)
18	7.18, m	7.18, m	6.98, m	6.98, m	6.99, d (9.0)	6.99, d (9.0)	6.80, d (9.0)
19	7.10, m	7.10, m	7.04, m	7.04, m	7.04, dd (3.0, 9.0)	7.04, dd (3.0, 9.0)	6.94, d (9.0)
21	7.34, m	7.34, m	7.05, m	7.05, m	7.09, d (3.0)	7.09, d (3.0)	7.12, br. s
22	1.36, 3H, s	1.36, 3H, s	1.17, 3H, s	1.16, 3H, s	1.25, 3H, s	1.25, 3H, s	1.38, 3H, s
23	0.87, 3H, s	0.96, 3H, s	0.75, 3H, s	0.86, 3H, s	1.15, 3H, s	1.17, 3H, s	0.96, 3H, s
24	3.65, d (12.5)	3.40, d (12.5)	3.67, d (11.0)	3.42, d (11.0)	4.09, dd (5.5, 12.0)	4.03, dd (5.5, 12.0)	4.01, d (12.5)
	4.17, d (12.5)	4.57, d (12.5)	4.20, d (11.0)	4.61, d (11.0)	4.23, dd (5.5, 12.0)	4.20, dd (5.5, 12.0)	4.76, d (12.5)
25	1.01, 3H, s	1.08, 3H, s	1.03, 3H, s	1.11, 3H, s	1.25, 3H, s	0.87, 3H, s	1.18, 3H, s
26	5.18, br. S	5.06, d (3.3)	5.20, br. S	5.08, d (3.3)	3.75, d (10.0)	0.80, 3H, s	
					3.99, d (10.0)		
OH	8.02, br. S	7.56, d (3.3)	8.10, br. S	7.65, d (3.3)			

[a] Measured in pyridine-d_5 (500 MHz). Signals assigned by ^{1}H–^{1}H COSY, HMQC and HMBC experiments.
[b] *J* in Hz.

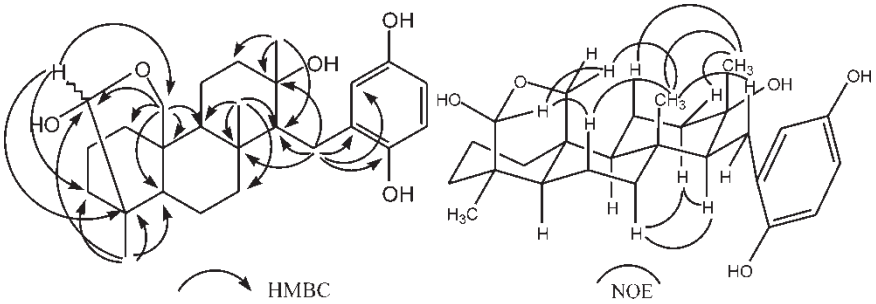

Figure 2. Key HMBC correlations and NOE correlations for **1**.

Meanwhile, an NOE was found between the signals at δ 5.06 (H-26) and at δ 1.56 for **2** in the NOESY spectrum of the mixture. Although the multiplets at δ 1.56 consist of H-2α and H-3β, the NOE is ascribed to be between H-26 and H-3β since the H-26 and H-2α are not close enough to show an NOE. Therefore, the stereochemistry of C-26 in **2** is assigned as *S*∗ (figure 3). Consequently, the structures of **1** and **2** were assigned as shown in figure 1.

Strongylophorines 15 (**3**) and 16 (**4**) were also obtained as a mixture (3:1) of interchangeable isomers, which showed a single molecular ion peak ($[M]^+$) at *m/z* 412 in the FAB mass spectrum. The molecular formula was determined as $C_{26}H_{36}O_4$ for both **3** and **4** by HR-FABMS and NMR data. The ^{1}H and ^{13}C NMR spectra of the mixture of **3** and **4** is similar to those of the mixture of **1** and **2**, and the signals of **3** and **4** were clearly distinguished and assigned by ^{1}H–^{1}H COSY, HMBC, HMQC, and NOESY spectra (tables 1 and 2). A hemiacetal group is suggested by the ^{1}H signals due to H-26 [**3**: δ 5.20, **4**: δ 5.08] and 26-OH [**3**: δ 8.10, **4**: δ 7.65], together with the corresponding ^{13}C signals assigned to C-26 [**3**: δ 98.9, **4**: δ 99.1]. The ^{13}C spectrum of **3** and **4** are very similar to those of strongylophorine 2 (**8**), except for the signals of C-3, 4, 24, and 26 [10–12] (table I). The differences in ^{13}C NMR data between **3** or **4** and **8** are ascribable to the hemiacetal groups at the C-26 in **3** and **4** instead of the lactone carbonyl in **8**. Therefore, **3** and **4** are suggested to be hemiacetal derivatives of **8**, which was confirmed by the HMBC spectrum of the mixture of **3** and **4**.

The relative stereochemistries of **3** and **4** were assigned by the NOESY spectrum, which revealed that the configurations of chiral centers in **3** and **4** were the same as those in **1** and **2**. In the NOESY spectrum of the mixture, NOEs occur between H-26 (δ 5.20) and H-6β (δ 1.65), between H-26 and H-24β (δ 4.20) for **3**. Similarly, an NOE is seen between H-26

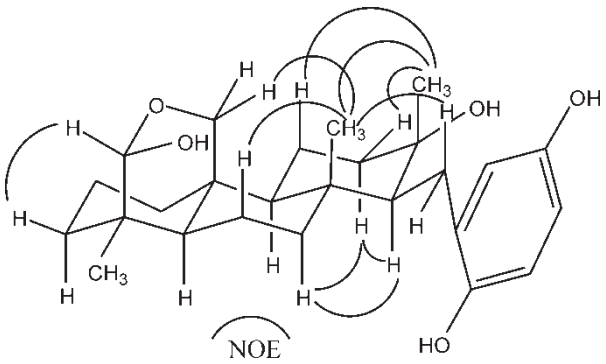

Figure 3. Key NOE correlations for **2**.

(δ 5.08) and H-3β (δ 1.56) for **4**. Thus, the configurations at C-26 in **3** and **4** are assigned as *R** and *S**, and the structures of **3** and **4** were assigned (figure 1).

Compound **5** shows a molecular ion ($[M]^+$) at *m/z* 414 in the FAB mass spectrum, and the molecular formula ($C_{26}H_{38}O_4$) was deduced from HR-FABMS and NMR data. ^1H and ^{13}C signals were assigned by $^1H-^1H$ COSY, HMBC, HMQC, and NOESY spectra (tables 1 and 2). The NMR spectra of **5** revealed two CH_2OH groups at δ_C 62.2 [δ_H 4.09 (1H, dd, $J = 5.5, 12.0$ Hz) and 4.23 (1H, dd, $J = 5.5, 12.0$ Hz)], δ_C 64.9 [δ_H 3.75 (1H, d, $J = 10.0$ Hz) and 3.99 (1H, $J = 10.0$ Hz)] and a 1,2,4-trisubstituted benzene ring. The ^{13}C data of **5** are similar to the reported values of strongylophorine 5, except for the signal assigned to be CH_2—OH at δ_c 62.2 of **5**, which replaced the methyl group at C-10 of strongylophorine 5 [11]. The position of the CH_2OH groups was confirmed by the HMBC data (figure 4). The NOESY spectrum of **5** (figure 4) revealed that **5** has the same stereochemistry as that of strongylophorine 5; compound **5** is named strongylophorine 17.

Strongylophorine 18 (**6**) gave the molecular ion ($[M]^+$) at *m/z* 398 in the FAB mass spectrum, and the molecular formula ($C_{26}H_{38}O_3$), as determined from HR-FABMS and NMR data. ^1H and ^{13}C NMR spectra of **6** resemble those of **5**, except for the absence of one CH_2OH group and the presence of one more methyl group at δ_C 22.0 [δ_H 0.80 (3H, s)]. The ^1H and ^{13}C signals were assigned by $^1H-^1H$ COSY, HMBC, HMQC, and NOESY spectra (tables 1 and 2). Differences in ^{13}C NMR data ($\Delta\delta$ 5.6–5.9) occur between **6** and **5** at C-3, 4, and 25. These data and the HMBC spectrum of **6** reveal the position of the CH_2OH group to be at C-10. The relative stereochemistry of **6** was assigned to be identical to strongylophorine 5 by means of NOESY data. Therefore, **6** is an isomer of strongylophorine 5, and named strongylophorine 18.

Compound **7** shows an $[M + H]^+$ion at *m/z* 427 in its FAB mass spectrum, and the molecular formula was deduced as $C_{26}H_{34}O_5$ from HR-FABMS and NMR data. A lactone moiety is suggested by signals at δ_C 176.1 and 73.8, δ_H 4.01 (1H, d, $J = 12.5$ Hz) and 4.76 (1H, d, $J = 12.5$ Hz) in the NMR spectrum. Three aromatic protons at δ 6.80 (1H, d, $J = 9.0$ Hz), 6.94 (1H, d, $J = 9.0$ Hz), and 7.12 (1H, br s) and six aromatic carbon signals (table 1) reveal a 1,2,4-trisubstituted benzene ring. The ^1H and ^{13}C signals were assigned by $^1H-^1H$ COSY, HMBC, HMQC, and NOESY spectra (tables 1 and 2). The ^{13}C NMR spectrum of **7** resembles that of strongylophorine 2 (**8**) [10–12]. Compounds **7** and **8** differ, remarkably, in that the quaternary carbon at δ_C 99.6 for **7** is replaced by the methine at δ_C 52.9 in the ^{13}C NMR spectrum of **8**. This quaternary carbon is assigned as C-14 by HMBC correlations from this carbon to H_3-22 (δ 1.38), H_3-23 (δ 0.96), and H_2-15 (δ 3.02 and 3.51). The great downfield shift of the ^{13}C signal of C-14 is very similar to that of stypodiol

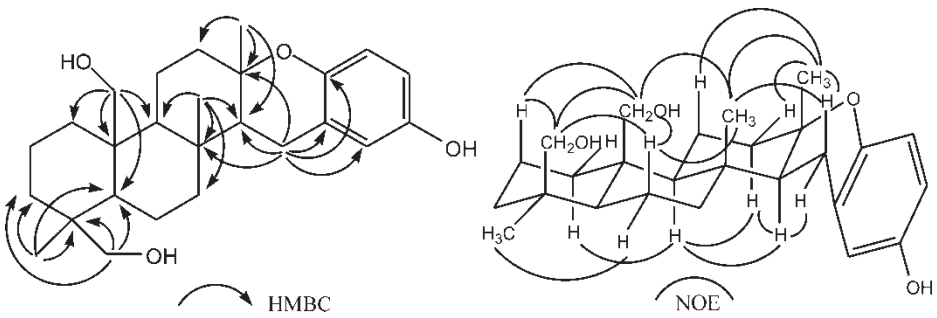

Figure 4. Key HMBC and NOE correlations for **5**.

(a strongylophorines-like meroditerpenoid with a dihydrofuran ring at C-14), suggesting the formation of a furan ring at C-14 in **7** [15,16]. The form of dihydrofuran ring at C-14 was finally confirmed by the NOEs between H_3-23 (δ 0.96) and H-15a (δ 3.02) and between H_3-22 (δ 1.38) and H-15b (δ 3.51). The skeletal structure of **7** was assigned on the basis of the HMBC data (figure 5), and the relative stereochemistry revealed by the NOESY spectrum (figure 5). Consequently, the structure of **7** was established and the compound is named strongylophorine 19.

A few bioactivities have been reported for meroditerpenoids [11,12,15–17], such as ichthyotoxicity, insecticidal activity on larvae of *Spodoptera littoralis*, antibacterial activity to *Micrococcus luteus* and *Salmonella typhii*, antifungal activity to phytopathogenic fungus *Cladosporium cucumerinum*, and lethal toxicity to brine shrimp. In our assay against the maturation of starfish oocytes, strongylophorines 13 and 14 (**1** and **2**), 15 and 16 (**3** and **4**), 17 (**5**), 18 (**6**), 19 (**7**), 2 (**8**), 3 (**9**), and 8 (**11**) showed inhibitory activities on the maturation of starfish oocytes with IC_{50}s of 35.0, 36.4, 1.2, 37.6, 35.2, 36.6, 36.4, and 1.1 μM, respectively.

3. Experimental section

3.1 General experimental procedures

NMR spectra were measured on either a JEOL JNM A-500 NMR spectrometer or a Varian Unity Inova-500 spectrometer. Mass spectra were obtained by a JEOL HX-110 mass spectrometer (FAB mode, with *m*-nitrobenzylalcohol as matrix). UV spectra were recorded on an Hitachi U-3000 spectrometer. Optical rotations were obtained on a JASCO DIP-130 polarimeter.

3.2 Marine sponge

Strongylophora strongylata was collected by scuba diving in April 1999 at Iriomote Island, Okinawa, Japan. The sponge was kept in a freezer at − 20°C until extraction. It was identified by comparison with the published data in the book of Tropical Pacific Invertebrates [18]. A voucher specimen has been deposited at the Department of Ocean Sciences, Tokyo University of Fisheries as TUF number 99-04-06 = 1-2.

3.3 Bioassay

Asterina pectinifera was collected from the coastal waters off Japan during the breeding season and kept in artificial seawater. Immature oocytes were prepared and adjusted to 100 cells mL^{-1} according to a previously reported method [9]. The oocyte suspension (1 mL) and 10 μL of each test sample were added into a 24-cell plate and incubated on ice for 10 min followed by the addition of 10 μL of 1-MeAde (1.25 μM). After incubation at 20°C for 60 min, the state of germinal vesicles was observed under an inverted microscope. The 50% inhibitory concentration for a test sample was defined as the concentration at which 50% inhibition of GVBD was achieved. DMSO was used to dissolve the samples and the final concentration was less than 1%. D-α-Tocopheryl acid succinate (1 mM) was used as a positive control.

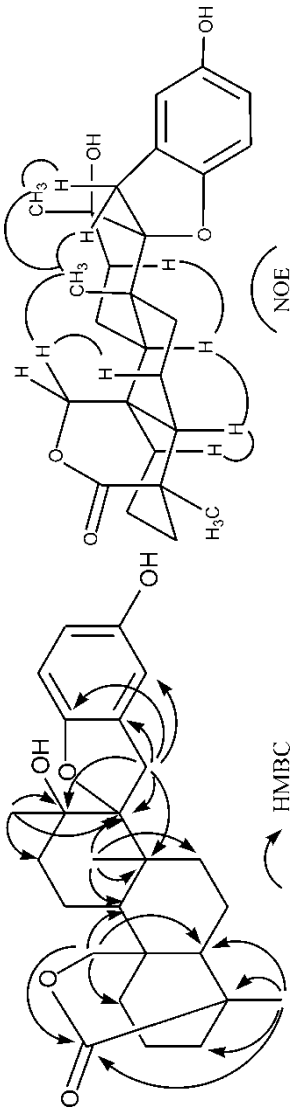

Figure 5. Key HMBC and NOE correlations for **7**.

3.4 Isolation of meroditerpenoids

The sponge (284 g, wet wt.) was thawed, cut into pieces and extracted with ethanol (3 × 500 mL). The ethanol extract was then evaporated and the residue partitioned between water (200 mL) and chloroform (2 × 200 mL). The $CHCl_3$ extract (1.2 g) was applied to an ODS column (3 × 30 cm) and eluted with a methanol–water gradient (from 60% to 100%) to afford 17 fractions. The bioactive fraction 5 (0.3 g) was separated by HPLC with an ODS column (10 mm × 25 cm; mobile phase, 65% $CH_3OH—H_2O$; flow rate, 2.0 mL min^{-1}) to give strongylophorines 13 and 14 (**1** and **2**, 5.6 mg), 19 (**7**, 1.0 mg), and 8 (**11**, 12.0 mg). Strongylophorines 17 (**5**, 7.0 mg) and 2 (**8**, 10.0 mg) were obtained from fraction 7 (85 mg) by HPLC on ODS (73% $CH_3OH—H_2O$). Fraction 9 (0.1 g) was further purified by HPLC on ODS (78% $CH_3OH—H_2O$) to afford strongylophorines 15 and 16 (**3** and **4**, 18.3 mg). Strongylophorines 18 (**6**, 4.0 mg), 3 (**9**, 1.5 mg) and 4 (**10**, 8.0 mg) were isolated from fraction 11 (0.16 g) by HPLC on ODS (80% $CH_3OH— H_2O$) Strongylophorines 13 (**1**) and 14 (**2**): white powder; UV (MeOH) λ_{max} (nm) (ε): 203 (8500), 293 (3300); HR-FABMS, *m/z* 430.2706 $[M]^{\dagger}$ (calcd for $C_{26}H_{38}O_5$, 430.2719); ^{13}C and ^{1}H NMR data see tables 1 and 2, respectively. The ratio of **1** and **2** in the mixture was determined as 3:1 from the peak areas by HPLC analysis (10 mm × 25 cm; mobile phase, 65% $CH_3OH—H_2O$; flow rate, 2.0 mL min^{-1}; t_R = 18 and 33 min, respectively).

Strongylophorines 15 (**3**) and 16 (**4**): white powder; UV (MeOH) λ_{max} (nm) (ε): 204 (13000), 220 (sh, 4100), 230 (sh, 3100), 296 (2100); HR-FABMS, *m/z* 412.2595 $[M]^{+}$ (calcd for $C_{26}H_{36}O_4$, 412.2614); ^{13}C and ^{1}H NMR data see tables 1 and 2, respectively. The ratio of **3** and **4** in the mixture was determined as 3:1 from the peak areas by HPLC analysis (10 mm × 25 cm; mobile phase, 65% $CH_3OH—H_2O$; flow rate, 2.0 mL min^{-1}; t_R = 15 and 25 min, respectively).

Strongylophorine 17 (**5**): white powder; $[\alpha]_D$ −47.9 (*c* 0.6, pyridine); UV (MeOH) λ_{max} (nm) (ε): 208 (11000), 220 (sh, 6600), 228 (sh, 5800), 250 (1600), 257 (1600), 263 (sh, 1300), 296 (3400); HR-FABMS, *m/z* 414.2774 $[M]^{+}$ (calcd for $C_{26}H_{38}O_4$, 414.2770); ^{13}C and ^{1}H NMR data see tables 1 and 2, respectively.

Strongylophorine 18 (**6**): white powder; $[\alpha]_D$ −36.5 (*c* 0.26, pyridine); UV (MeOH) λ_{max} nm (ε): 206 (9300), 220 (sh, 4700), 229 (sh, 4000), 295 (2100); HR-FABMS, *m/z* 398.2792 $[M]^{\dagger}$ (calcd for $C_{26}H_{38}O_3$, 398.2821); ^{13}C and ^{1}H NMR data see tables 1 and 2, respectively.

Strongylophorine 19 (**7**): white powder; $[\alpha]_D$ −3.6 (*c* 0.15, pyridine); UV (MeOH) λ_{max} (nm) (ε): 207 (22000), 229 (sh, 5400), 257 (2500), 297 (1600); HR-FABMS, *m/z* 427.2465 $[M + H]^{\dagger}$ (calcd for $C_{26}H_{35}O_5$, 427.2484); ^{13}C and ^{1}H NMR data see tables 1 and 2, respectively.

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