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Muurolane-*type* sesquiterpenes from marine sponge *Dysidea cinerea*

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Seven new muurolane-*type* sesquiterpenes, (4*R*,5*R*)-muurol-1(6),10(14)-diene-4,5-diol (1), (4*R*,5*R*)-muurol-1(6)-ene-4,5-diol (2), (4*R*,5*R*,10*R*)-10-methoxymuurol-1(6)-ene-4,5-diol (3), (4*S*)-4-hydroxy-1,10-*seco*-muurol-5-ene-1,10-dione (4), (4*R*)-4-hydroxy-1,10-*seco*-muurol-5-ene-1,10-dione (5), (6*S*,10*S*)-6,10-dihydroxy-7,8-*seco*-2,8-*cyclo*-muurol-4(5),7(11)-diene-12-oic acid (6), and (6*R*,10*S*)-6,10-dihydroxy-7,8-*seco*-2,8-*cyclo*-muurol-4(5),7(11)-diene-12-oic acid (7) were isolated from the marine sponge *Dysidea cinerea*. Their structures were determined by the combination of spectroscopic and chemical methods, including 1D-NMR, 2D-NMR, and CD spectra as well as by comparing the NMR data with those reported in the literature. Copyright © 2013 John Wiley & Sons, Ltd.

Keywords: ^{1}H NMR; ^{13}C NMR; circular dichroism; *Dysidea cinerea*; Dysideidae; muurolane; marine sponge

Introduction

The marine sponge *Dysidea cinerea* Keller (Dysideidae) is distributed in Red Sea, Western India, and Zanzibar. Marine sponges had a prolific source of anti-HIV proteins, and study on chemical components of the sponge *D. cinerea* has led to the isolation of avarol and avarone derivatives.[1,2] Several biological activities such as cytotoxic activity[2] and inhibitory activity against HIV type 1 reverse transcriptase[3] also have been reported. In the course of study on chemical constituents from marine sponge *D. cinerea*, seven new compounds were isolated (Fig. 1).

Results and Discussion

Compound **1** was isolated as colorless oil, and its molecular formula was determined to be $C_{15}H_{24}O_2$ by HR-ESI-MS at *m/z* 235.1699 $[M-H]^-$ (Calcd. $C_{15}H_{23}O_2$ for 235.1704). The ^{1}H NMR spectrum of **1** showed the following signals: two olefinic protons at δ_H 4.72 and 4.91, one oxymethine proton at δ_H 3.85, one tertiary methyl group at δ_H 1.18, and two secondary methyls at δ_H 0.78 and 0.97 (Table 1). The ^{13}C NMR and DEPT spectra of **1** revealed 15 carbon signals including four quaternary (δ_C 72.6, 132.0, 139.3, and 146.2), three methine (δ_C 29.8, 42.5, and 74.6), five methylene (δ_C 24.0, 24.7, 31.6, 32.3, and 108.0), and three methyl carbons (δ_C 18.2, 21.8, and 24.4). The ^{1}H NMR and ^{13}C NMR data of **1** were very similar to those of muurolane-*type* sesquiterpenes previously isolated from *Illicium tsangii*.[4] The long-range correlations between H-15 (δ_H 1.18) and C-3 (δ_C 32.3), C-4 (δ_C 72.6), and C-5 (δ_C 74.6); between H-12 (δ_H 0.78) and C-7 (δ_C 42.5), C-11 (δ_C 29.8), and C-13 (δ_C 21.8); between H-13 (δ_H 0.97) and C-7 (δ_C 42.5), C-11 (δ_C 29.8), and C-12 (δ_C 18.2) in the HMBC spectrum (Fig. 2) suggested that the methyl and isopropyl

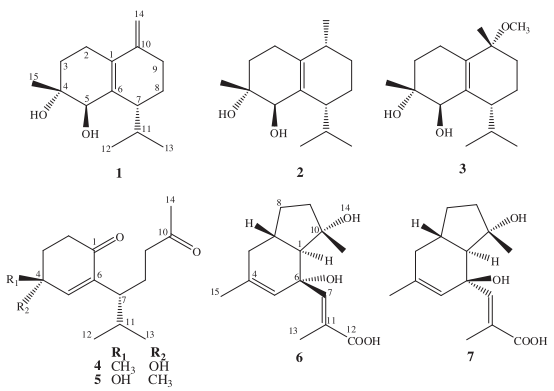

Figure 1. Structures of muurolane-*type* sesquiterpenes **1–7**.

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Table 1. The NMR spectral data of compounds **1 – 3** in CD_3OD

Pos.	1		2		3	
	δ_C[a]	δ_H[b] (mult., *J* in Hz)	δ_C[a]	δ_H[b] (mult., *J* in Hz)	δ_C[a]	δ_H[b] (mult., *J* in Hz)
1	132.0	—	138.8	—	136.4	—
2	24.7	2.11 (m)	27.8	1.92 (m)	24.4	2.12 (m)
		2.41 (m)		2.20 (m)		
3	32.3	1.57 (m)	34.2	1.53 (m)	33.1	1.56 (m, α)
		1.71 (m)		1.62 (m)		1.65 (m, β)
4	72.6	—	73.3	—	72.7	—
5	74.6	3.85 (s)	75.3	3.90 (s)	74.4	3.85 (s)
6	139.3	—	132.9	—	138.3	—
7	42.5	2.42 (m)	40.1	2.35 (m)	40.5	2.31 (m)
8	24.0	1.54 (m)	21.2	1.37 (m)	20.1	1.72 (m, α)
		1.67 (m)		1.64 (m)		1.55 (m, β)
9	31.6	2.18 (m)	31.7	1.15 (m)	31.7	2.06 (m, α)
		2.41 (m)		1.72 (m)		1.28 (m, β)
10	146.2	—	35.3	1.97 (m)	77.5	—
11	29.8	2.19 (m)	29.2	2.25 (m)	29.8	2.25 (m)
12	18.2	0.78 (d, 6.8)	17.2	0.74 (d, 6.8)	18.5	0.85 (d, 6.8)
13	21.8	0.97 (d, 6.8)	21.6	0.94 (d, 6.8)	22.0	0.99 (d, 6.8)
14	108.0	4.72 (s)	20.2	0.97 (d, 6.8)	25.7	1.22 (s)
		4.91 (s)				
15	24.4	1.18 (s)	22.4	1.14 (s)	23.7	1.16 (s)
10-OMe					50.32	3.11 (s)

[a]100 MHz.
[b]400 MHz.
Assignments were performed by HMQC, HMBC, COSY, and ROESY experiments.

groups were at C-4 and C-7, respectively. A double bond at C-10/C-14 was confirmed by the HMBC correlations between H-14 (δ_H 4.72 and 4.91) and C-1 (δ_C 132.0), C-9 (δ_C 31.6), and C-10 (δ_C 146.2). The HMBC correlations from H-5 (δ_H 3.85) to C-3 (δ_C 32.3), C-4 (δ_C 72.6), C-6 (δ_C 139.3), C-7 (δ_C 42.5), and C-1 (δ_C 132.0) indicated the presence of one hydroxyl group at C-5. The constitution of **1** was further confirmed by the COSY correlations between H-2 (δ_H 2.11 and 2.41)/H-3 (δ_H 1.57 and 1.71), between H-12 (δ_H 0.78)/H-11 (δ_H 0.2.19)/H-7 (δ_H 2.42)/H-8 (δ_H 1.54 and 1.67)/H-9 (δ_H 2.18 and 2.41) (Fig. 2). The absolute configuration of **1** was determined by CD spectroscopy combined with the ROESY experiment.[5] The ROESY correlation between H-5 (δ_H 3.85) and H-11 (δ_H 2.19) as well as the absence of the ROESY correlations between H-5 and H-7 (δ_H 2.42) and H-15 (δ_H1.18) were observed (Fig. 3). In addition, the CD spectra of the 4-p-bromo benzoylester (**1a**) showed the positive and negative Cotton effectsat 232 and 253 nm (Fig. 4), respectively, which indicated the configuration at C-5 of **1** to be *R* by the comparison withoxyphyllenodiol B.[5] These confirmed both the configurations at C-4 and C-7 to be *R*. Based on the previously mentioned evidence, compound **1** was elucidated as (4*R*,5*R*)-muurol-1(6),10(14)-diene-4,5-diol.

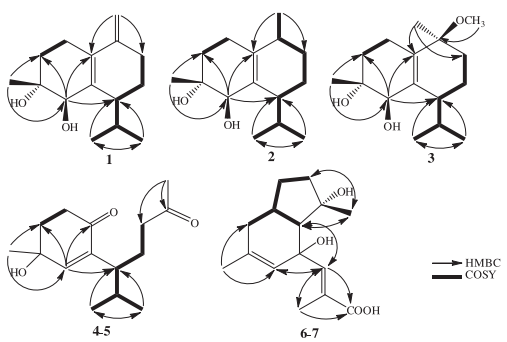

Figure 2. Key HMBC and COSY correlations of muurolane-*type* sesquiterpenes **1–7**.

Compound **2** was also isolated as colorless oil, and its molecular was determined to be $C_{15}H_{26}O_2$ by HR-ESI-MS at *m/z* 273.1625 $[M+Cl]^-$ (Calcd. $C_{15}H_{26}O_2Cl$ for 273.1627). The ^1H NMR and ^{13}C NMR spectra revealed that **2** were an analogue of compound **1** except for the disappearance of a double bond at C-10/C14 and the addition of one methyl group (Table 1). The position of the new methyl group was confirmed by the HMBC correlations between H-14 (δ_H 0.97) and C-1 (δ_C 138.8), C-9 (δ_C 31.7), and C-10 (δ_C 35.3) (Fig. 2). Compound **2** was supposed to have the same configuration at C-7 as its biogenetic derivative, compound **1**. In addition, the ROESY correlation between H-5 (δ_H 3.90) and H-11 (δ_H 2.25) and the absence of the ROESY correlation between H-5 and H-7 (δ_H 2.35) and H-15 (δ_H 1.14) indicated both the configurations at C-4 and C-7 to be *R* (Fig. 3). Thus, the structure of **2** was elucidated as (4*R*,5*R*)-muurol-1(6)-ene-4,5-diol.

The molecular of **3** was determined to be $C_{16}H_{28}O_3$ by HR-ESI-MS at *m/z* 267.1948 $[M-H]^-$ (Calcd $C_{16}H_{27}O_3$ for 267.1966). The ^1H NMR and ^{13}C NMR data of **3** were very similar to those of compound **2** except for the addition of a methoxy group at C-10. The HMBC correlations between H-14 (δ_H 1.22) and C-1 (δ_C 136.4), C-9 (δ_C 31.7), and C-10 (δ_C 77.5); between 10-OMe (δ_H 3.11) and C-10 (δ_C 77.5) were observed (Fig. 2), suggesting

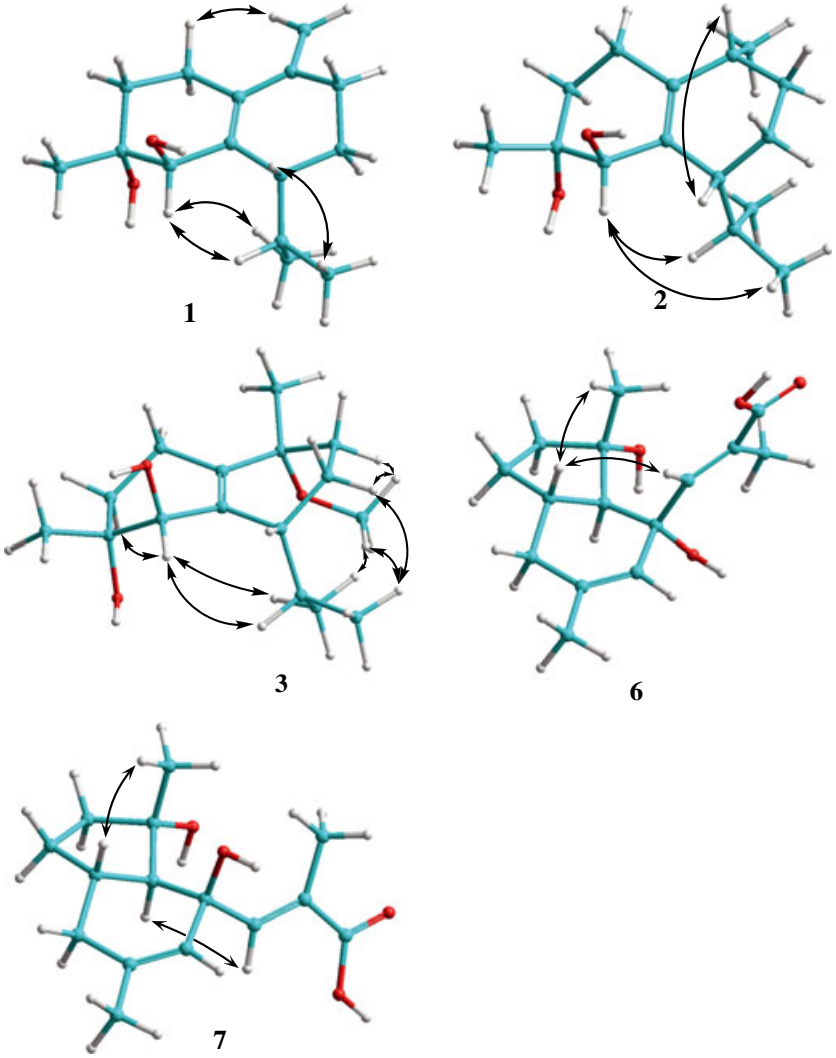

Figure 3. Major ROESY correlations for muurolane-*type* sesquiterpenes **1–3**, **6**, and **7**.

that both methyl and methoxy groups at C-10. The COSY correlations were shown in Fig. 2. The ROESY correlations between H-5 (δ_H 3.85) and H-11 (δ_H 2.25), H-12 (δ_H 0.85), and H-13 (δ_H 0.99); between 10-OMe (δ_H 3.11) and H-11 (δ_H 2.25), H-12 (δ_H 0.85), and H-13 (δ_H 0.99) confirmed that position of hydroxyl at C-5 and methoxy at C-10 were at β and α configurations, respectively. The detail ROESY correlation was also shown in Fig. 3. Consequently, compound **3** was defined as (4*R*,5*R*,10*R*)-10-methoxymuurol-1(6)-ene-4,5-diol.

Compound **4** was obtained as colorless oil, and it was determined to be $C_{15}H_{24}O_3$ by HR-ESI-MS at *m/z* 287.1417 $[M+Cl]^-$ (Calcd $C_{15}H_{24}O_3Cl$ for 287.1419). One olefinic proton at δ_H 6.44, two tertiary methyl protons at δ_H 1.38 and 2.05, and two secondary methyl groups at δ_H 0.76 and 0.88 were observed in the ^1H NMR spectrum (Table 2). Two carbonyls at δ_C 200.9 and 211.8, two olefinic at δ_C 139.9 and 153.0, and one oxygenated carbons at δ_C 69.3 were shown in the ^{13}C NMR spectrum. Although the ^1H NMR and ^{13}C NMR data of **4** were very similar to those of 1,10-seco-4ξ-hydroxy-muurol-5-ene-1,10-dione, the stereochemistry centers of the reference compound have not been fully determined yet. The HMBC correlations between H-15 (δ_H 1.38) and C-3 (δ_C 38.0), C-4 (δ_C 69.3), and C-5 (δ_C 153.0); between H-5 (δ_H 6.44) and C-1 (δ_C 200.9), C-3 (δ_C 38.0), C-4 (δ_C 69.3), C-6 (δ_C 139.9), and C-7 (δ_C 45.1) were observed (Fig. 2). These suggested that the presence of a methyl group at C-4 and α,β-unsaturated carbonyl moiety in compound **4**. Furthermore, the long-range correlations from H-12 (δ_H 0.88) and H-13 (δ_H 0.76) to C-7 (δ_C 45.1) and C-11 (δ_C 32.7); from H-14 (δ_H 2.05) to C-9 (δ_C 42.4) and C-10 (δ_C 211.8) suggested that the isopropyl and acetyl groups were at C-7 and C-9, respectively. In addition, the COSY correlations of H-2/H-3, H-7/H-8, H-8/H-9, H-7/H-11, H-11/H-12, H-11/H-13 gave important clues to the constitution of **4** (Fig. 2). The configuration at C-4 of cyclohexenone was determined by measuring CD spectrum based on the octant rule for the $n_{OH}\pi_{CO}$ transition.[6] The positive and negative Cotton effects at 213 and 243 nm, respectively (Fig. 4), suggested the configuration at C-4 of cyclohexenone **4** to be *S*, similar to those of abieseconordine A (positive and negative effects at 210 and 239 nm, respectively).[7] From the evidence described previously, the structure of compound **4** was elucidated as (4*S*)-4-hydroxy-1,10-*seco*-muurol-5-ene-1,10-dione.

Compound **5** was also obtained as colorless oil. HRESIMS experiments resulted as the same molecular formula as that of **4** (Experimental Section). The ^1H NMR and ^{13}C NMR data of **5** were almost the same as those of **4**, suggesting the possibilities of different configuration at the chiral carbon C-4 (Table 2). In line

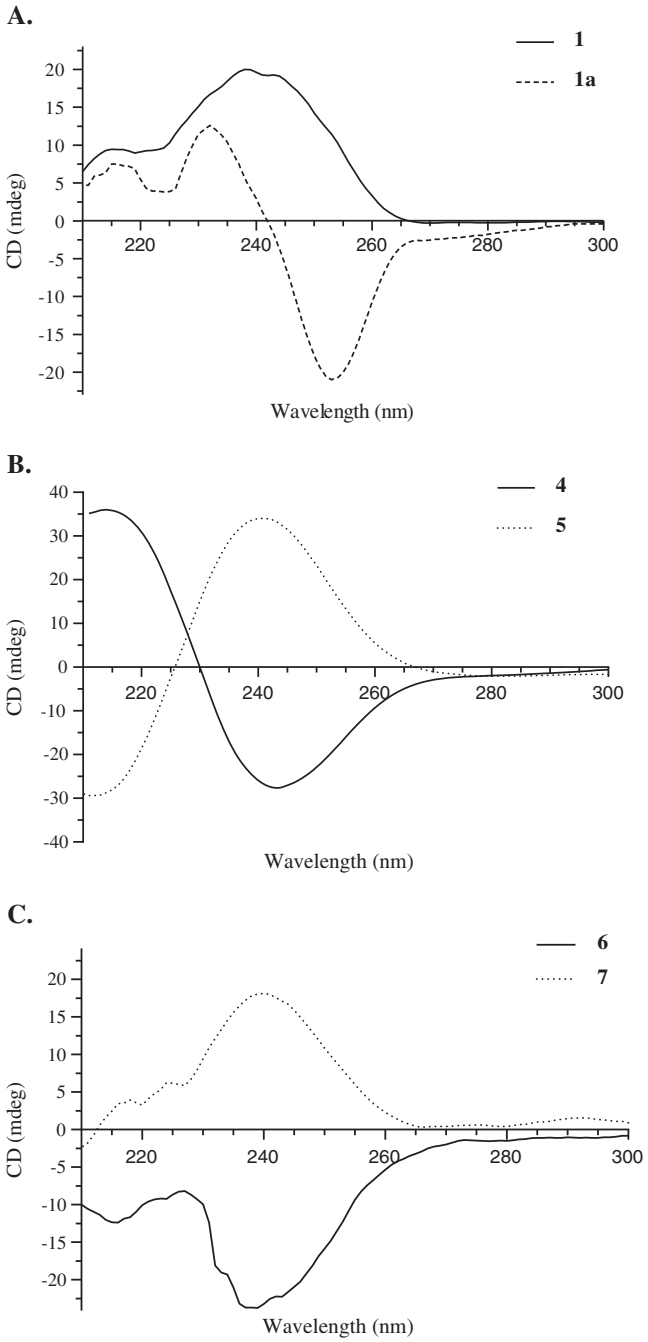

Figure 4. Circular dichroism spectra of muurolane-*type* sesquiterpenes. A. Compounds **1** and **1a**; B. Compounds **4** and **5**; and C. Compounds **6** and **7**.

with this, ^{1}H, ^{13}C, HSQC, HMBC, and COSY spectral analyses also confirmed that **5** had the same constitution as **4**. The CD spectra of **4** and **5** were opposite at the wavelength from 205 to 300 nm, indicating the absolute configuration at C-4 of cylohexenone in **5** to be *R*. Taken together, the structure of **5** was defined as (4*R*)-4-hydroxy-1,10-*seco*-muurol-5-ene-1,10-dione.

Compound **6** was isolated as colorless oil, and its molecular formula was determined to be $C_{15}H_{22}O_4$ by HR-ESI-MS at *m/z* 265.1455 $[M–H]^-$ (Calcd $C_{15}H_{21}O_4$ for 265.1445). The ^{1}H NMR spectrum of **6** showed two olefinic protons at δ_H 5.25 and 7.29, three tertiary methyl group at δ_H 1.00, 1.70, and 1.86 (Table 2). The ^{13}C NMR and DEPT spectra of **6** revealed 15 carbon signals including one carboxylic carbonyl (δ_C 176.2), four olefinic (δ_C 118.2, 129.6, 138.5, and 155.1), two oxygenated (δ_C 78.7 and 87.4), and three methyl (δ_C 10.4, 20.3, and 25.5) carbons. The HMBC correlations between H-15 (δ_H 1.70) and C-3 (δ_C 40.5), C-4 (δ_C 138.5), and C-5 (δ_C 118.2); between H-5 (δ_H 5.25) and C-1 (δ_C 57.8), C-3 (δ_C 40.5), C-4 (δ_C 138.5), C-6 (δ_C 87.4), and C-7 (δ_C 155.1); between H-14 (δ_H 1.00) and C-1 (δ_C 57.8), C-9 (δ_C 42.7), and C-10 (δ_C 78.7) were observed (Fig. 2). These suggested the presence of two methyl groups at C-4 and C-10 and one double bond at C-4/C-5. The HMBC correlations between H-13 (δ_H 1.86) and C-7 (δ_C 155.1), C-11 (δ_C 129.6), and C-12 (δ_C 176.2); between H-7 (δ_H 7.29) and C-1 (δ_C 57.8), C-5 (δ_C 118.2), C-6 (δ_C 87.4), C-12 (δ_C 176.2), and C-13 (δ_C 10.4) suggested that both methyl and carboxylic groups were at C-11, and this branch was at C-6 (Fig. 2). Moreover, the constitution of **6** could be determined using the COSY correlations between H-1/H-2, H-2/H-3, H-2/H-8, and H-8/H-9. Compound **6** has a novel structure isolated from nature for the first time, and it seems to be resulted from the broken bond between C-7 and C-8 and the formation of new bond between C-2 and C-8. The absolute configuration of C-6 was deduced to be *S* by measuring CD spectrum (a negative effect at 239 nm), similar to those of (1′*S*,6′*R*)-8′-hydroxyabscisic acid β-D-glucopyranoside (positive and negative effects at 233 and 266 nm).[8] The ROESY correlations between H-2 (δ_H 2.48) and H-7 (δ_H 7.29) and H-14 (δ_H 1.00) suggested that these groups are on the same side (Fig. 3). Furthermore, the coupling constant of two proton H-1 and H-2 ($J_{H-1/H-2}$ = 12.8 Hz) confirmed the opposite position of these two protons. Based on the previously mentioned evidence, compound **6** was elucidated as (6*S*,10*S*)-6,10-dihydroxy-7,8-*seco*-2,8-*cyclo*-muurol-4(5),7(11)-diene-12-oic acid.

Compound **7** was also obtained as colorless oil. HRESIMS experiments resulted in the same molecular formula as that of **6**. ^{1}H NMR and ^{13}C NMR data of **7** were almost the same as those of **6**. In line with this, ^{1}H, ^{13}C, HSQC, HMBC, and COSY spectral analyses showed that **7** had the same constitution as **6**. The CD spectra of **6** and **7** were opposite at the wavelength from 205 to 300 nm (Fig. 4), suggesting that the absolute configuration at C-6 of **7** was *R*. Moreover, ROESY correlation between H-1 (δ_H 1.58) and H-7 (δ_H 7.27) was observed, confirming protons H-1 and H-7 on the same side. Moreover, the coupling constant of two proton H-1 and H-2, J_{1-2} = 12.8 Hz, suggesting two these protons on the different side. In addition, the ROESY correlation between H-2 (δ_H 2.92) and H-14 (δ_H 1.22) suggested the methyl group at C-10 to be β. Consequently, compound **7** was elucidated as (6*R*,10*S*)-6,10-dihydroxy-7,8-*seco*-2,8-*cyclo*-muurol-4(5),7(11)-diene-12-oic acid.

Experimental

General experimental procedures

All NMR spectra were recorded on an Agilent 400-MR spectrometer (Agilent Technologies, Santa Clara, CA) operated at 400 and 100 MHz for hydrogen and carbon, respectively. NMR measurements, including ^{1}H, ^{13}C, HSQC, HMBC, ROESY, and COSY experiments, were carried out using 5-mm probe tubes at temperature of 39.0°C in CD_3OD solutions, with TMS as the internal standard. Chemical shifts are reported in parts per million (ppm) from TMS. Signals are reported as follows: chemical shift (ppm), coupling constants (Hz), and assignment. The pulse conditions were as follows: for the ^{1}H spectrum, spectrometer frequency = 399.88 MHz, acquisition time (AQ) = 2.1837 s, relaxation delay (RD) = 4 s,

Table 2. The NMR spectral data of compounds **4–7** in CD_3OD

Pos.	4		5		6		7	
	δ_C[a]	δ_H[b] (mult., *J* in Hz)	δ_C[a]	δ_H[b] (mult., *J* in Hz)	δ_C[a]	δ_H[b] (mult., *J* in Hz)	δ_C[a]	δ_H[b] (mult., *J* in Hz)
1	200.9	—	200.9	—	57.8	1.97 (d, 12.8)	56.6	1.58 (d, 12.8)
2	36.2	2.42 (ddd, 5.6, 9.2, 16.0) 2.55 (ddd, 5.6, 5.6, 16.0)	36.3	2.44 (ddd, 5.6, 9.2, 16.0) 2.55 (ddd, 5.6, 5.6, 16.0)	42.2	2.48 (m)	43.0	2.92 (m)
3	38.0	2.04 (m)	38.0	2.05 (m)	40.5	1.77 (d, 17.6) 2.58 (d, 17.6)	40.1	1.77 (d, 18.0) 2.58 (d, 18.0)
4	69.3	—	69.4	—	138.5	—	138.8	—
5	153.0	6.44 (s)	152.5	6.43 (s)	118.2	5.25 (s)	118.4	5.24 (s)
6	139.9	—	140.0	—	87.4	—	87.7	—
7	45.1	2.26 (m)	44.0	2.34 (m)	155.1	7.29 (s)	153.5	7.27 (d, 1.2)
8	25.9	1.58 (m) 1.88 (m)	25.7	1.54 (m) 1.87 (m)	26.5	1.38 (m) 1.91 (m)	27.0	1.17 (m) 1.98 (m)
9	42.4	2.25 (m)	42.3	2.28 (m)	42.7	1.72* 1.80*	43.5	1.74* 1.89*
10	211.8	—	211.9	—	78.7	—	78.9	—
11	32.7	1.68 (m)	33.0	1.64 (m)	129.6	—	130.3	—
12	20.8	0.88 (d, 6.8)	20.6	0.85 (d, 6.8)	176.2	—	176.3	—
13	21.2	0.76 (d, 6.8)	21.0	0.75 (d, 6.8)	10.4	1.86 (s)	10.5	1.86 (d, 1.2)
14	29.9	2.05 (s)	29.9	2.06 (s)	25.5	1.00 (s)	28.8	1.22 (s)
15	27.4	1.38 (s)	27.5	1.40 (s)	20.3	1.70 (s)	20.7	1.75 (s)

[a]100 MHz.
[b]400 MHz.
* Overlapped signal.
Assignments were performed by HMQC, HMBC, COSY, and ROESY experiments.

pulse 90° width = 5.2 μs, spectral width (SW) = 7503 Hz, and digital resolution = 0.4580 Hz; for the ^{13}C spectrum, spectrometer frequency = 100.56 MHz, AQ = 1.3107 s, RD = 1 s, pulse 90° width = 3.2 μs, SW = 31407 Hz, and digital resolution = 0.96 Hz; for the COSY spectrum, AQ = 0.15 s, RD = 1.0 s, SW = 4499.6 Hz, number of points (NP) = 1280, and number of increments (NI) = 132; for the ROESY spectrum, AQ = 0.216 s, RD = 1.5 s, SW = 4749 Hz, NP = 1024, NI = 512, and mixing time 0.5 s; for the HSQC spectrum, observation frequency = 399.88 MHz, a delay for optimized one-bond coupling constant = 140 Hz, AQ = 0.1501 s, RD = 1.0 s, SW = 4501 (^1H) and 15087 (^{13}C) Hz, NP = 1024, NI = 256; for the HMBC spectrum, observation frequency = 399.88 MHz, an evolution delay for long range coupling = 8 Hz, AQ = 0.501 s, RD = 1.0 s, SW = 6410 (^1H) and 24132 (^{13}C) Hz, NP = 2048, NI = 256. Data processing was carried out with MestReNova v6.0.2 program. The HR-ESI-mass spectra were obtained using an Agilent 6550 iFunnel Q-TOF LC/MS system. The ESI-MS was obtained on an Agilent 1200 SERIES LC-MSD Trap spectrometer. Optical rotations were determined on a Jasco DIP-370 automatic polarimeter. Circular dichroism spectra were determined on a Chirascan™ CD spectrometer. Preparative HPLC was carried out using an Agilent 1200 HPLC system. Column chromatography was performed using a silica-gel (Kieselgel 60, 70–230 mesh and 230–400 mesh, Merck) or YMC RP-18 resins (30–50 μm, Fujisilisa Chemical Ltd.), thin layer chromatography using a pre-coated silica-gel 60 F254 (0.25 mm, Merck) and RP-18 F254S plates (0.25 mm, Merck).

Plant material

The sponge *D. cinerea* was collected in Lang Co beach, Thua Thien Hue, Vietnam during August 2011 and identified by the author, Dr Do Cong Thung. A voucher specimen (DC1108) was deposited at the Herbarium of Institute of Marine Biochemistry, Vietnam Academy of Science and Technology, 18 Hoang Quoc Viet, Caugiay, Hanoi, Vietnam.

Extraction and isolation

The freeze tissue of *D. cinerea* (1.0 kg) was cleaned to remove sodium chloride and then extracted with MeOH three times under reflux for 15 h to yield 60 g of a dark solid extract. This extract was suspended in water and successively partitioned with chloroform ($CHCl_3$) to obtain $CHCl_3$ (DC1, 20.0 g) and water (DC2, 40 g) layers after removal of the solvents *in vacuo*. The layer DC1 (20.0 g) was chromatographed on a silica gel column and eluting with gradient elution of *n*-hexane – acetone (40 : 1 → 0 : 1, v/v) to obtain five sub-fractions, DC1A (3.2 g), DC1B (4.5 g), DC1C (3.3 g), DC1D (3.1 g), and DC1E (5.0 g). The sub-fraction DC1B (4.5 g) was chromatographed on a silica gel column eluting with *n*-hexane – EtOAc (10 : 1, v/v) to give three smaller fractions, DC1B1 (1.0 g), DC1B2 (1.5 g), and DC1B3 (1.7 g). The fraction DC1B1 was chromatographed on an YMC RP-18 column eluting with MeOH – water (5 : 1, v/v) to give three fractions, DC1B1A (150 mg), DC1B1B (180 mg), and DC1B1C (200 mg). The fraction DC1B1A was chromatographed on HPLC using J'sphere ODS H-80 250 mm × 20 mm with solvent condition of 35% acetonitrile in water at a flow rate of 3 ml/min to yield **4** (9.0 mg), **5** (4.0 mg), and **6** (5.6 mg). The fraction DC1B1B was chromatographed on HPLC using J'sphere ODS H-80 250 mm × 20 mm with solvent condition of 45% acetonitrile in water at a flow rate of 3 ml/min to yield **1** (3.9 mg), **3** (3.2 mg), and **7** (4.9 mg). The fraction DC1B1C was chromatographed on HPLC using J'sphere ODS

H-80 250 mm × 20 mm with solvent condition of 55% acetonitrile in water at a flow rate of 3 ml/min to yield **2** (2.7 mg).

(4*R*,5*R*)-Muurol-1(6),10(14)-diene-4,5-diol (**1**): Colorless oil, $[\alpha]_D^{25}$: +60.3 ($c = 0.1$, MeOH); CD spectrum (MeOH) (Fig. 4); $C_{15}H_{24}O_2$, HR-ESI-MS found *m/z*: 235.1699 $[M-H]^-$ (Calcd. $C_{15}H_{23}O_2$ for 235.1704); ^{1}H NMR and ^{13}C NMR (Table 1).

(4*R*,5*R*)-Muurol-1(6)-ene-4,5-diol (**2**): Colorless oil, $[\alpha]_D^{25}$: +43.6 ($c = 0.1$, MeOH); $C_{15}H_{26}O_2$, HR-ESI-MS found *m/z*: 237.1831 $[M-H]^-$ (Calcd. $C_{15}H_{25}O_2$ for 237.1860); ^{1}H NMR and ^{13}C NMR (Table 1).

(4*R*,5*R*,10*R*)-10-Methoxymuurol-1(6)-ene-4,5-diol (**3**): Colorless oil, $[\alpha]_D^{25}$: −39.6 ($c = 0.1$, MeOH); $C_{16}H_{28}O_3$, HR-ESI-MS found *m/z*: 267.1948 $[M-H]^-$ (Calcd. $C_{16}H_{27}O_3$ for 267.1966); ^{1}H NMR and ^{13}C NMR (Table 1).

(4*S*)-4-Hydroxy-1,10-*seco*-muurol-5-ene-1,10-dione (**4**): Colorless oil, $[\alpha]_D^{25}$: −113.5 ($c = 0.1$, MeOH); CD spectrum (MeOH) (Fig. 4); $C_{15}H_{24}O_3$, HR-ESI-MS found *m/z*: 287.1417 $[M+Cl]^-$ (Calcd. $C_{15}H_{24}O_3Cl$ for 287.1419); ^{1}H-NMR and ^{13}C-NMR (Table 2).

(4*R*)-4-Hydroxy-1,10-*seco*-muurol-5-ene-1,10-dione (**5**): Colorless oil, $[\alpha]_D^{25}$: +185.2 ($c = 0.1$, MeOH); CD spectrum (MeOH) (Fig. 4); $C_{15}H_{24}O_3$, HR-ESI-MS found *m/z*: 287.1416 $[M+Cl]^-$ (Calcd. $C_{15}H_{24}O_3Cl$ for 287.1419); CD spectrum (MeOH) (Fig. 4); ^{1}H NMR and ^{13}C NMR (Table 2).

(6*S*,10*S*)-6,10-Dihydroxy-7,8-*seco*-2,8-*cyclo*-muurol-4(5),7(11)-diene-12-oic acid (**6**): Colorless oil, $[\alpha]_D^{25}$: −94.5 ($c = 0.1$, MeOH); CD: ($\Delta\varepsilon_{239}$, −23.22, MeOH); $C_{28}H_{38}O_{13}$, HR-ESI-MS found *m/z*: 265.1455 $[M-H]^-$ (Calcd. $C_{15}H_{21}O_4$ for 265.1445); CD spectrum (MeOH) (Fig. 4); ^{1}H NMR and ^{13}C NMR (Table 2).

(6*R*,10*S*)-6,10-Dihydroxy-7,8-*seco*-2,8-*cyclo*-muurol-4(5),7(11)-diene-12-oic acid (**7**): Colorless oil, $[\alpha]_D^{25}$: +73.7 ($c = 0.1$, MeOH); CD spectrum (MeOH) (Fig. 4); $C_{28}H_{38}O_{13}$, HR-ESI-MS found *m/z*: 265.1448 $[M-H]^-$ (Calcd. $C_{15}H_{21}O_4$ for 265.1445); CD spectrum (Fig. 4); ^{1}H NMR and ^{13}C NMR (Table 2).

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