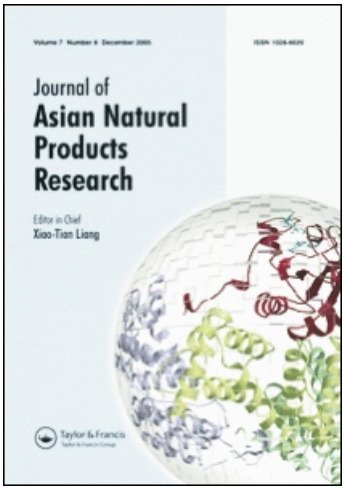

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Norisoprenoids from *Ulva lactuca*

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Norisoprenoids from *Ulva lactuca*

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Five norisoprenoids were isolated from the green marine alga *Ulva lactuca*. Two new compounds were assigned to (3*R*,5*R*,6*R*,7*E*)3,5,6-trihydroxy-7-megastigmen-9-one (**1**) and (3*S*,5*R*,6*S*,7*E*)3,5,6-trihydroxy-7-megastigmen-9-one (**2**). The structures and absolute configurations of the five compounds were determined by analyses of NMR, MS and circular dichroism (CD).

Keywords: Green alga; *Ulva lactuca*; Norisoprenoids; Circular dichroism

1. Introduction

The green alga *Ulva lactuca* is distributed widely on the coast of the BoHai, China. It has been reported that *Ulva lactuca* contains simple bromophenols and bromoperoxidases measured by GC-MS spectrometry, but only a few compounds have been isolated from *Ulva lactuca* [1]. In the subsequent chemical studies on *Ulva lactuca*, we obtained five apocarotenoids including two new C_{13} norisoprenoids (3*R*,5*R*,6*R*,7*E*)3,5,6-trihydroxy-7-megastigmen-9-one (**1**) and (3*S*,5*R*,6*S*,7*E*)3,5,6-trihydroxy-7-megastigmen-9-one (**2**), and three known norisoprenoids grasshopper ketone (**3**), (3*S*,6*R*)3,6-dihydroxy-4,7-megastigmadien-9-one (**4**) and isololiolide (**5**) (figure 1). Many norisoprenoids showed phytotoxic effect on the germination and growth of plants [2–5].

2. Results and discussion

Compound **1** was obtained as colourless oil. Its molecular formula was determined as $C_{13}H_{22}O_4$ by HRFAB-MS [*m/z* 243.2667 $(M + H)^+$].The ^1H NMR spectrum (table 1) showed the presence of four methyl singlets at δ 1.16, 1.51, 1.68 and 2.29, four aliphatic protons as four multiplets ranging from δ 1.94 to 2.44, a methine proton to hydroxyl as a multiplet at δ 4.54 ($J = 3.4$ Hz) and two conjugated olefinic proton doublets at δ 6.92

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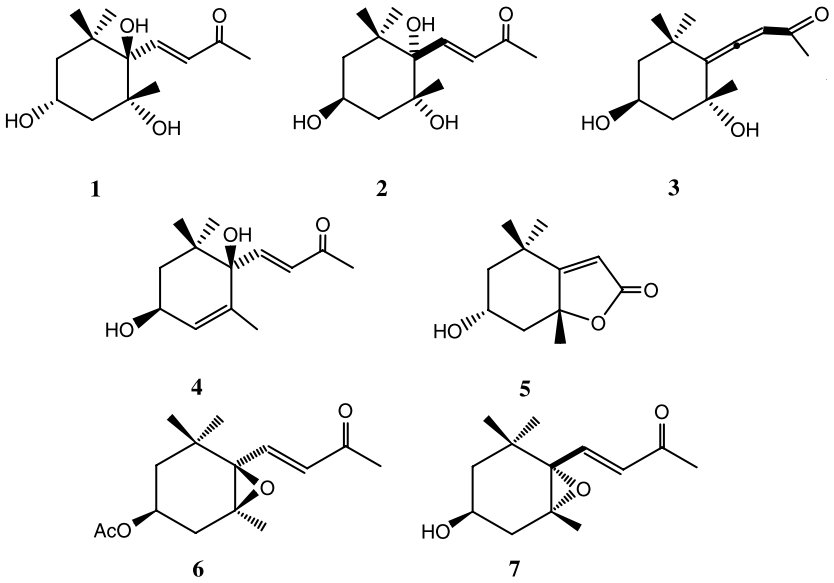

Figure 1. Norisoprenoids **1**–**5** from *Ulva lactuca*.

($J = 16.4$ Hz) and δ 7.98 ($J = 16.4$ Hz).The ^{13}C NMR spectrum showed 13 carbon signals, identified by DEPT experiments, as four methyls (δ 27.0, 27.1, 28.5 and 28.9), two methylenes (δ 40.8 and 43.7), one oxymethine (δ 68.1), two olefinic carbons (δ 131.4, 151.9), three quaternary carbons (δ 38.9, 76.6 and 80.5), and one carbonyl carbon (δ 197.9). All the carbons were correlated to the corresponding protons on the results of HMQC. In the HMBC experiment of **1** (figure 2), the bisnorsesquiterpene skeleton and locations of the functional groups were established. The HMBC experiment showed correlations of the carbons bearing oxygen C-5 (δ 76.6) with H-3, H-4α, H_3-13, and C-3 (δ 68.1) with H-2α, H-2β, H-4α, and H-4β. Meanwhile, the tertiary hydroxyl group was positioned at C-6 (δ 80.5) on the basis of the HMBC that showed correlations between C-6 and H-4α, H-7, H-8, H_3-11, H_3-12, H_3-13 protons, which demonstrated C-6 was the connective position of the six-membered ring and

Table 1. ^{1}H NMR (600 MH_Z), ^{13}C NMR (150 MH_Z) data of compounds **1** (C_5D_5N) and **2** (CD_3OD).

No.	***1***		***2***	
	δ_C	δ_H (*J*, *Hz*)	δ_C	δ_H (*J*, *Hz*)
1	38.9		35.0	
2	43.7	1.94 (m)	46.4	1.58 (m)
		2.20 (dd, 15.0, 3.4)		1.28 (dd, 14.3, 10.8)
3	68.1	4.54 (tt, 3.4, 3.4)	63.2	3.76 (tt, 10.8, 4.2)
4	40.8	2.14 (m)	40.2	2.29 (m)
		2.44 (dd, 14.8, 3.4)		1.65 (dd, 14.5, 10.5)
5	76.6		67.6	
6	80.5		69.7	
7	151.9	6.92 (d, 16.4)	144.2	6.18 (d, 16.2)
8	131.4	7.98 (d, 16.4)	132.7	7.16 (d, 16.2)
9	197.9		199.1	
10	27.0	2.29 (s)	24.0	2.28 (s)
11	28.9	1.16 (s)	28.6	1.17 (s)
12	28.5	1.68 (s)	26.2	0.95 (s)
13	27.1	1.51 (s)	18.9	1.18 (s)

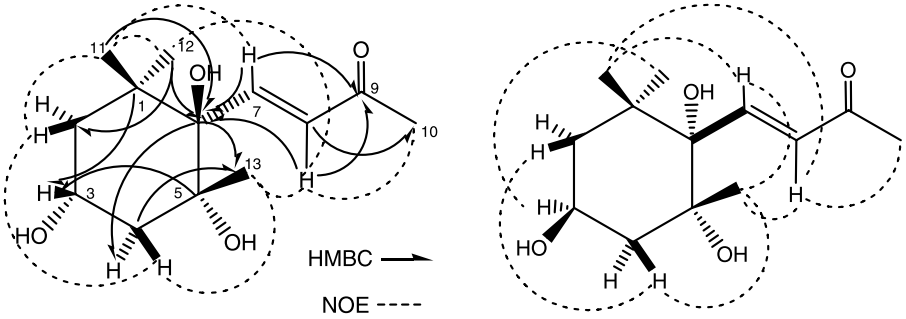

Figure 2. Key HMBC and NOE correlations of compound **1** and **2**.

the side chain. In addition, the olefinic protons at δ 6.92 (H-7) and 7.98 (H-8) were correlated to the hydroxyl carbon (C-6), as well as the carbonyl carbon (C-9), indicating the conjugated olefinic carbons connected to the six-membered ring and the carbonyl carbon, respectively. Therefore, **1** possessed the basic structure of C_{13} nor-isoprenoid. The stereochemistry of **1** was determined on the basis of the coupling constants, NOESY and circular dichroism**.** In the NOESY (figure 2), correlations of H-2β with CH_3-11, H-4β with CH_3-13 indicated that the two methyls at C-1 and C-5 were in the equatorial position. The H-3 appeared to be triple triplets of $J = 3.4$ Hz in the ^{1}H NMR spectrum, which indicated the axial position for the hydroxyl group. In addition, correlations in the NOESY spectrum of H-7 with CH_3-11, H-8 with CH_3-12 and CH_3-13 demonstrated that OH-6 was also in the axial position. The CD spectrum of **1** showed a positive cotton effect, $\Delta\varepsilon_{238.6\,\mathrm{nm}}$ +9.926, suggesting C-6 of **1** to have the same configuration as C-6 of **6** [6,7]. Therefore, the structure of **1** was identified as (3*R*,5*R*,6*R*,7*E*)3,5,6-trihydroxy-7-megastigmen-9-one.

Compounds **1** and **2** were diastereomers of each other. Compound **2** was also obtained as colourless oil. The molecular formula of **2** was also established as $C_{13}H_{22}O_4$ by HRFAB-MS. The ^{1}H NMR and ^{13}C NMR spectra were similar to **1** (table 1). The ^{1}H NMR and ^{13}C NMR spectra also presented two conjugated olefinic protons, three carbons bearing hydroxyl and one carbonyl carbon. The H-3 appeared to be triple triplets of $J = 10.8$ Hz and 4.2 Hz in the ^{1}H NMR spectrum, which indicated the equatorial position for the hydroxyl group. Correlations in the NOESY spectrum between CH_3-13 and H-4β, as well as between H-3 and CH_3-12 demonstrated that CH_3-13 was in the equatorial position of C-5 and CH_3-12 was in the axial position of C-1. NOE correlations of both H-7 and H-8 with CH_3-11 and CH_3-13 indicated the equatorial position for OH-6. The CD spectrum of **2** showed a negative cotton effect, $\Delta\varepsilon_{231.8\,\mathrm{nm}}$ − 68.75, suggesting C-6 of **2** to have the same configuration as C-6 of **7** [6,7]. Therefore, the structure of **2** was deduced to be (3*S*,5*R*,6*S*,7*E*)3,5,6-trihydroxy-7-megastigmen-9-one.

Compounds **3**–**5** were determined by comparison of physical data, spectroscopic and CD evidences with literature values [6–9].

3. Experimental

3.1 General experimental procedures

UV spectra were measured on a Shimadzu UV-1601. All the NMR spectra were recorded by using a Bruker-ARX-600 spectrometer (^{1}H at 600 MHz and ^{13}C at 150 MHz). HRFAB-MS

spectra were measured by MAT-95 mass spectrometer. CD spectra were recorded on Jasco J-810 CD spectro-polarimeter. Column chromatography was performed on silica gel G (200–300 mesh, Qingdao Haiyang Chemical Factory) and reversed-Phase silica gel (Chromatorex C_{18}).

3.2 Plant material

The green alga *Ulva lactuca* was collected on the coast of the BoHai, China, in April 2003, and identified by Professor Xiao Fan, Institute of Oceanology, Chinese Academy of Sciences. A voucher specimen is deposited at Shenyang Pharmaceutical University.

3.3 Extraction and isolation

Ulva lactuca (4.50 kg) was extracted with EtOH at room temperature for 4 × 72 h. The solvent was evaporated under reduced pressure to give the residue, which was suspended in H_2O and then partitioned with petro-ether, EtOAc and n-BuOH. The EtOAc fraction (20.6 g) was chromatographed over silica gel, eluting with a gradient of increasing MeOH (0–100%) in $CHCl_3$, and separated into 11 fractions by TLC analyses. Fraction 4–6 were chromatographed over ODS flash column eluting with a gradient of increasing MeOH (0–100%) in H_2O to give corresponding subfractions. Subfraction 3 was further purified on reversed-phase preparative HPLC using MeOH/H_2O (30:70) to yield compounds **1** (3 mg), **2** (4 mg), **3** (4 mg), **4** (2 mg), **5** (5 mg), respectively.

3.3.1 Compound 1. Colourless oil (MeOH); UV (MeOH) λ_{max} nm 229, 203; ^{1}H NMR and ^{13}C NMR data: see table 1; HRFAB-MS: $[M + H]^+$ ion peak at *m/z* 243.2667 (calcd for $C_{13}H_{22}O_4$, *m/z* 243.2652).CD (MeOH) $\Delta\varepsilon_{238.6\,nm}$ +9.926, $\Delta\varepsilon_{217.7\,nm}$ −1.426.

3.3.2 Compound 2. Colourless oil (MeOH); UV (MeOH) λ_{max} nm 229, 203; ^{1}H NMR and ^{13}C NMR data: see table 1; HRFAB-MS: $[M + H]^+$ ion peak at *m/z* 243.2649 (calcd for $C_{13}H_{22}O_4$, *m/z* 243.2652). CD (MeOH) $\Delta\varepsilon_{231.8\,nm}$ −68.75, $\Delta\varepsilon_{202.6\,nm}$ +6.869.

3.3.3 Compound 3. Colourless oil (MeOH); UV (MeOH) λ_{max} nm 231, 203; IR (KBr) ν_{max} (cm^{-1}). 3388, 2965, 1936, 1735, 1675, 1456, 1364, 1238, 1157, 1026. ESI-MS 224 [M^+]. CD (MeOH) $\Delta\varepsilon_{258.3\,nm}$ −7.663, $\Delta\varepsilon_{229.9\,nm}$ +12.041, $\Delta\varepsilon_{206.6\,nm}$ −10.047.

3.3.4 Compound 4. Colourless oil (MeOH); ESI-MS 224 [M^+]. CD (MeOH) $\Delta\varepsilon_{234.9\,nm}$ +37.713, $\Delta\varepsilon_{203.6\,nm}$ +6.604.

3.3.5 Compound 5. Colourless oil (MeOH); ESI-MS 196 [M^+]. CD (MeOH) $\Delta\varepsilon_{297.7\,nm}$ −1.324, $\Delta\varepsilon_{247.7\,nm}$ +6.280, $\Delta\varepsilon_{217.2\,nm}$ −27.814.

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