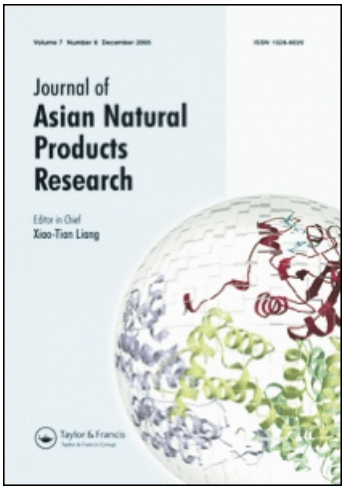

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A new xanthone from *Halenia elliptica* D. Don

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A new xanthone, 1,5-dihydroxy-2,3,4-trimethoxyxanthone (**1**), together with 15 known compounds (**2**–**16**), was isolated from an ethanolic extract of *Halenia elliptica* D. Don. Their structures were elucidated by spectroscopic methods. Among the known compounds, the ^{13}C NMR spectroscopic data of 2,3,4,5-tetramethoxyxanthone-1-O-gentiobioside (**2**) were reported for the first time.

Keywords: *Halenia elliptica*; xanthone; flavonoid; secoiridoid glucoside

1. Introduction

Halenia elliptica D. Don (Gentianaceae) is distributed across the range of the Tibetan plateau and throughout western China. It has been used in Tibetan and Mongolian medicine to cure hepatitis for a long time [1]. Previous phytochemical investigation has led to the isolation of a series of simple oxygenated xanthone aglycones and glycosides [2–7]. These xanthone compounds are believed to contribute to the hepatoprotective effect [8–10], vasorelaxant effect [11–13], and antioxidant activity [14] ascribed to this particular species. During our ongoing search for more bioactive constituents present in this plant, a new xanthone, 1,5-dihydroxy-2,3,4-trimethoxyxanthone (**1**), along with 15 known compounds, including six xanthone glycosides (**2**–**7**), five flavonoids (**8**–**12**), and four secoiridoid glucosides (**13**–**16**), was isolated from an ethanolic extract of *H. elliptica* D. Don (Figure 1). In this paper, we describe the structural elucidation of **1** and report the detailed NMR spectroscopic data of **2**. Compounds **2**, **3**, **9**, **10**, and **12**–**16** are described for the first time in this plant species.

2. Results and discussion

Compound **1** was obtained as a yellow needle and possessed the molecular formula $C_{16}H_{14}O_7$ determined by HR-ESI-MS at *m/z* 319.0817 $[M + H]^+$. The IR spectrum of **1** showed characteristic absorption bands due to conjugated carbonyl (1647 cm^{-1}) and hydroxyl (3491 cm^{-1}) groups. Furthermore, the presence of hydroxyl groups was confirmed by a hydrogen-bonded OH singlet (δ_H 12.68, OH-1) and a broad OH singlet (δ_H 7.57, OH-5) observed in the ^1H NMR spectrum. The ^1H NMR spectrum of **1** in $CDCl_3$ also revealed signals attributed to a 1,2,3-trisubstituted aromatic ring at δ_H 7.34 (H-6, dd, $J = 7.9$, 1.6 Hz), 7.26 (H-7, t, $J = 7.9$ Hz), and 7.75 (H-8, dd, $J = 7.9$, 1.6 Hz), along with three aromatic methoxyl groups at δ_H 4.16, 3.96, and 3.95 (Table 1). Sixteen carbons were shown in

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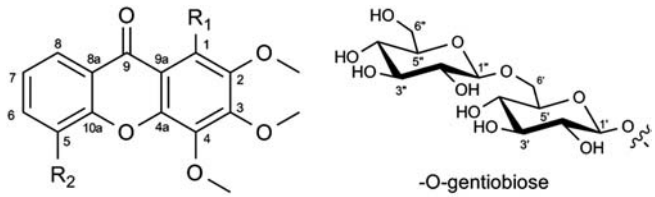

	R_1	R_2
1	OH	OH
2	-O-gentiobiose	OCH_3

Figure 1. Structures of compounds **1** and **2**.

the ^{13}C NMR spectrum, including three methoxyl carbons, three sp^2 methines, nine quaternary sp^2 carbons, and one carbonyl carbon (δ_C 181.7) (Table 1). A comparison of ^{13}C NMR spectroscopic data and UV spectrum with those of the reported polyoxygenated xanthones [15–17] suggested a penta-oxygenated xanthone skeleton of **1**. The assignments of H-8, H-7, and H-6 were supported by the long-range C-H correlations of H-8/C-9, C-10a, and C-6; H-7/C-5 and C-8a; and H6/C-8 and C-10a in the HMBC experiment (see Figure 2).

Table 1. ^1H NMR and ^{13}C NMR spectral data of compound **1**.

Position	δ_C	δ_H (multiplicity, J in Hz)
1	151.5	–
2	135.7	–
3	154.1	–
4	132.0	–
4a	144.6	–
10a	144.8	–
5	145.1	–
6	121.2	7.34 (dd, $J = 7.9$, 1.6 Hz)
7	124.4	7.26 (t, $J = 7.9$ Hz)
8	116.5	7.75 (dd, $J = 7.9$, 1.6 Hz)
8a	120.6	–
9a	104.8	–
9	181.7	
OCH_3-2	61.2	3.95 (s)
OCH_3-3	61.7	4.16 (s)
OCH_3-4	62.3	3.96 (s)
OH-1	–	12.68 (s)
OH-5	–	7.57 (br)

Notes: NMR data were measured in $CDCl_3$ at 400 MHz for ^1H or 100 MHz for ^{13}C, respectively. The assignments were based on HSQC and HMBC experiments.

Another important HMBC correlations observed between the hydrogen-bonded OH-1 and C-1 (δ_C 151.5), C-9a and a methoxyl-bearing carbon (δ_C 135.7, based on the HMBC correlation from the methoxyl proton at δ_H 3.95 to this carbon) (see Figure 2) indicated an adjacent methoxyl group at C-2, which was then confirmed by the NOE correlation between OH-1 and OCH_3-2 in the 1D-NOESY experiment. The other two methoxyl groups were assigned to OCH_3-3 and OCH_3-4, respectively, due to the fact that the irradiation of OCH_3-3 (δ_H 4.16) enhanced the signal intensity of both OCH_3-2 (δ_H 3.95) and OCH_3-4 (δ_H 3.96). In consideration of the molecular formula and the downfield chemical shift of C-5 (δ_C 145.1), there should be a hydroxyl group at C-5. Therefore, the structure of **1** was established as 1,5-dihydroxy-2,3,4-trimethoxyxanthone (see Figure 1).

Fifteen known compounds were characterized as 2,3,4,5-tetramethoxyxanthone-1-O-gentiobioside (**2**) [18], 2,3,5-trimethoxyxanthone-1-O-gentiobioside (**3**) [19], 2,3,4,5-tetramethoxy-

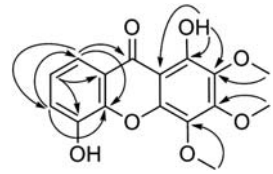

Figure 2. Key HMBC correlations of **1** (H → C).

xanthone-1-O-primeveroside (**4**) [6,7,18], 2,3,4,7-tetramethoxyxanthone-1-O-primeveroside (**5**) [7,18], 2,3,5-trimethoxyxanthone-1-O-primeveroside (**6**) [6,7], 2,3,7-trimethoxyxanthone-1-O-primeveroside (**7**) [7,18], luteolin (**8**) [20], apigenin (**9**) [20], luteolin-7-O-gentiobioside (**10**), luteolin-7-O-glucoside (**11**) [21], apigenin-7-O-gentiobioside (**12**), sweroside (**13**) [22], gentiopicroside (**14**) [23], vogeloside (**15**) [19], and epi-vogeloside (**16**) [19]. Compound **2** was once identified by LC-thermospray (TSP)-MS from *Halenia corniculata* [18] without further confirmation. We reported herein the detailed ^{13}C NMR spectroscopic data of **2** for the first time (Table 2). Compounds **8** and **11** have previously been detected in this plant using a capillary zone electrophoretic method [24]. To our knowledge, this is the first report of compounds **2**, **3**, **9**, **10**, and **12**–**16** from *H. elliptica*.

Table 2. ^{1}H NMR and ^{13}C NMR spectral data of compound **2**.

Position	δ_C	δ_H (multiplicity, J in Hz)
1	144.4	–
2	137.6	–
3	152.4	–
4	142.7	–
4a	147.2	–
10a	144.7	–
5	148.2	–
6	116.2	7.48 (dd, $J = 8.0$ Hz, 1.1 Hz)
7	124.0	7.36 (t, $J = 8.0$ Hz)
8	116.6	7.67 (dd, $J = 8.0$ Hz, 1.1 Hz)
8a	122.2	–
9a	111.2	–
9	175.5	–
OCH_3-2	61.6[a]	4.01 (s)
OCH_3-3	61.4	4.06 (s)
OCH_3-4	61.6[a]	3.84 (s)
OCH_3-5	56.6	3.99 (s)
1′	104.3	4.91 (d, $J = 7.8$ Hz)
2′	74.0[b]	2.84–4.01 (m)
3′	76.7[c]	
4′	69.9[e]	
5′	76.4[d]	
6′	68.3	
1″	102.9	4.00 (o)
2″	73.4[b]	2.84–4.01 (m)
3″	76.6[c]	
4″	69.8[e]	
5″	76.3[d]	
6″	60.8	

Notes: NMR spectral data were measured in DMSO-d_6 at 600 MHz for ^{1}H or 150 MHz for ^{13}C, respectively. The assignments were based on the HMBC experiment. [a–e] Assignments may be interchanged. (o) means signals overlapped with others.

3. Experimental

3.1 General experimental procedures

Melting point was determined on an X_4 micromelting point apparatus. UV spectra were recorded on Hitachi's U-2900 double beam spectrophotometer. IR spectra (KBr) were obtained on an Avatar 360 ESP FT-IR spectrometer (ν in cm^{-1}). NMR spectra were recorded at 400 MHz for ^{1}H and 100 MHz for ^{13}C on a Varian Mercury Plus-400 spectrometer and a Bruker AV-400 spectrometer, or at 600 MHz for ^{1}H and 150 MHz for ^{13}C on a Varian Inova-600 spectrometer, in $CDCl_3$ or DMSO-d_6, using tetramethylsilane as an internal standard. The chemical shifts (δ) were given in ppm and the coupling constants (J) in Hz. ESI-MS data were measured with an Agilent 1100 chromatography system coupled with an Agilent G1946D mass detector. HR-ESI-MS data were measured with a YA019 Q-Tof micro mass spectrometer. Column chromatography was performed with commercial silica gel (200–300 mesh, Qingdao Marine Chemical Co., Qingdao, China), silica gel H (10–40 μm, Qingdao Marine Chemical Co.), Diaion HP-20 (Mitsubishi Chemical Co., Tokyo, Japan), MCI gel CHP 20P (75–150 μm, Mitsubishi Chemicals Co.), Sephadex LH-20 (Amersham Pharmacia Biotech, Inc., Piscataway, NJ, USA), and OUYA-RP18 silica gel (15–35 μm, Unicorn, Switzerland).

3.2 Plant material

H. elliptica D. Don was collected during April 2005 in Dali, Yunnan Province,

China. The plant was identified by Prof. Xiaokuang Ma, Department of Pharmacognosy, School of Pharmacy, Dali University, China. A voucher specimen (No.HE0505) has been deposited at the Department of Natural Products Chemistry, School of Pharmacy, Fudan University, Shanghai, China.

3.3 Extraction and isolation

The aerial parts of *H. elliptica* (5 kg) were extracted consecutively with 95% EtOH (50 liters) at room temperature for 120 h. After evaporation of the EtOH under reduced pressure, the residue (140 g) was suspended in H_2O and partitioned sequentially with petroleum ether and EtOAc. The EtOAc part was evaporated *in vacuo* to give a residue (39.5 g) and the aqueous phase was lyophilized to give 45.2 g of powder. The EtOAc part was then chromatographed on a silica gel (200–300 mesh) column eluting with gradient mixtures of petroleum ether/EtOAc (10:1 → 1:1) to give 11 fractions (Fr_e. A–K). Fr_e. C (805 mg, eluted by petroleum ether/EtOAc; 8:1) was subjected to a silica gel (200–300 mesh, petroleum ether/EtOAc; 9:1) column and then a silica gel H (10–40 μm, petroleum ether/$CHCl_3$; 1:1) column to afford **1** (20 mg). Forty grams of powder of the water-soluble part were dissolved in water and subjected to a Diaion HP 20 resin with gradient mixtures of H_2O/EtOH (100:0 → 5:95) to give five fractions (Fr_w. A–E). Fr_w. E (1005 mg, eluted by 95% EtOH) was subjected to Sephadex LH-20 column with gradient mixtures of H_2O/MeOH (100:0 → 0:100) to give three subfractions: Fr_w. E-1–E-3. Fr_w. E-1 (120 mg) was then separated repeatedly by C_{18} reversed-phase silica gel column, using a mobile phase of H_2O/MeOH (55:45) to afford compounds **2** (1.2 mg), **3** (1.0 mg), **4** (12.8 mg), **5** (3.2 mg), **6** (5.6 mg), and **7** (4.4 mg). Fr_w. E-3 (20 mg) was also separated repeatedly by C_{18} reversed-phase silica gel column, using a mobile phase of H_2O/MeOH (45:55) to afford compounds **8** (7.0 mg) and **9** (4.0 mg). Fr_w. D (1480 mg, eluted by 50% EtOH) was subjected to MCI-gel CHP 20P column, eluting with 40% MeOH to afford compounds **10** (5.0 mg), **11** (6.1 mg), and **12** (24 mg). Fr_w. C (2550 mg, eluted by 20% EtOH) was subjected to Sephadex LH-20 to give four subfractions: Fr_w. C-1–C-4. Fr_w.C-2 (720 mg) was then purified repeatedly by C_{18} reversed-phase silica gel column, using the mobile phase of H_2O/MeOH (70:30) to yield compounds **13** (48.6 mg), **14** (6.5 mg), **15** (18.6 mg), and **16** (12.6 mg), respectively.

3.3.1 Compound *1*

A yellow needle crystal ($CHCl_3$), 20 mg, mp 152–154°C; UV (CH_3OH) λ_{max} (log ϵ): 381 (3.54), 316 (4.02), 260 (4.45), 245 (4.37), 201 (4.36) nm; IR (KBr) ν_{max}: 3491, 3177, 2944, 1647, 1600, 1498, 1461, 1424, 1359,1272, 1222, 1127, 1082, 1046, 1012, 928, 776, 758, 722 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz) spectral data, see Table 1; ESI-MS (positive mode): *m/z* 319.1 $[M + H]^+$(100), 659.0 $[2M + Na]^+$(33); HR-ESI-MS (positive mode): *m/z* 319.0817 $[M + H]^+$ (calcd for $C_{16}H_{15}O_7$, 319.0818)

3.3.2 Compound *2*

A pale yellow amorphous powder, 1.2 mg; ^1H NMR (DMSO-d_6, 600 MHz) and ^{13}C NMR (DMSO-d_6, 150 MHz) spectral data see Table 2; ESI-MS (positive mode): *m/z* 679.2 $[M + Na]^+$(100), 695.2 $[M + K]^+$(35); HR-ESI-MS (positive mode): *m/z* 679.1856 $[M + Na]^+$ (calcd for $C_{29}H_{36}O_{17}Na$, 679.1850).

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