A new acetophenone derivative and other constituents from *Senecio vulgaris*

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A new acetophenone derivative, 5-acetyl-2-(2-hydroxyisopropyl)-7-(3,3-dimethylallyl)-2,3-dihydrobenzofuran, has been isolated from the whole plants of *Senecio vulgaris*. Its structure was established on the basis of spectroscopic methods.

Keywords: *Senecio vulgaris*, acetophenone, benzofuran

The econdary metabolites of *Senecio* species have been extensively investigated and many pyrrolizidine alkaloids and eremophilane-type sesquiterpenoids have been isolated.[1–5] *Senecio vulgaris* is an annual weed of arable and horticultural crops and is a common garden weed. To the best of our knowledge, there are no reports of medicinal applications of this plant. Previous phytochemical studies of *S. vulgaris* have focused on the hepatotoxic pyrrolizidine alkaloids.[6,7] In addition, the flavonoids of this plant have also been reported.[8] In the course of our chemical investigations of *Senecio* species, the lesser polar extracts of *S. vulgaris* were investigated for the first time. As a result, a new prenylated acetophenone derivative, 5-acetyl-2-(2-hydroxyisopropyl)-7-(3,3-dimethylallyl)-2,3-dihydrobenzofuran (**1**), as well as nine known compounds, including eudesm-4(15)-en-1β,6α-diol (**2**),[9] 7*R**)-opposit-4(15)-en-1β,7-diol (**3**),[10] aphanamol (**4**),[11] loliolide (**5**),[12] 3β-hydroxymegastigma-5,7-dien-9-one (**6**),[13] 5α,6α-epoxy-3β-hydroxymegastigma-7-en-9-one (**7**),[14] jacaranone (**8**),[15] 2,6-dimethoxy-*p*-benzoquinone (**9**),[16] methyl 1-hydroxy-2,6-dimethoxy-4-oxocyclohexanacetate (**10**),[15] have been isolated from this plant. The known natural products were identified by comparison of their spectroscopic data with those reported in the literature.

Compound **1** was isolated as a colourless oil. The IR spectrum exhibited absorption bands of hydroxy group at 3428 cm^{-1}, a conjugated carbonyl group at 1671 cm^{-1}, and a phenyl group at 1600 and 1436 cm^{-1}. Its HR-ESI-MS showed a quasi molecular ion peak at *m/z* 289.1792 ([M+H]$^+$, $C_{18}H_{25}O_3^+$; Calcd 289.1804), suggesting the molecular formula $C_{18}H_{24}O_3$. The ^{1}H NMR signals at δ_H 7.58 (1H, brs) and δ_H 7.55 (1H, brs), and the complicated signals in the downfield region of ^{13}C NMR spectrum of **1** (Table 1) indicated the presence of a tetra-substituted aromatic ring. Furthermore, the ^{1}H, ^{13}C NMR and DEPT spectra of **1** (Table 1), obtained with the aid of the HMBC spectrum, also showed signals due to an acetyl group attached to an aromatic ring [δ_H 2.45 (3H, s, Me-2‴); δ_C 196.9 (C-1‴), 26.4 (C-1‴)], an isopentenyl group [δ_H 1.66 (6H, s, Me-4″ and Me-5″), 5.21 (1H, dd, *J* = 7.6, 7.1 Hz, H-2″), 3.27 (1H, dd, *J* = 15.3, 7.6 Hz, H_a-1″), 3.20 (1H, dd, *J* = 15.3, 7.1 Hz, H_b-1″); δ_C 17.8 (Me-5″), 25.8 (Me-4″), 133.2 (C-3″), 121.3 (C-2″), 28.4 (C-1″)], another two tertiary methyl groups [δ_H 1.14 (3H, s, Me-2′), 1.27 (3H, s, Me-3′); δ_C 24.0 (C-2′), 25.7 (C-3′)], an oxygenated quaternary carbon atom [δ_C 71.8 (C-1′)], an oxygenated methine [δ_H 4.63 (1H, t, *J* = 8.9 Hz, H-2); δ_C 90.1 (C-2)], and a methylene [δ_H 3.12 (2H, d, *J* = 8.9 Hz, H-3); δ_C 30.2 (C-3)]. Comparison of the above data with those reported in the literature,[17,18] indicated that the structure of compound **1** was very similar to 5-acetyl-2-(2-hydroxyisopropyl)-7-(3,3-dimethylallyl)-benzofuran, except for the absence of a double bond in the furan ring. Hence, the structure of **1** was 5-acetyl-2-(2-hydroxyisopropyl)-7-(3,3-dimethylallyl)-2,3-dihydrobenzofuran. The HMBC spectrum (Fig. 2) further confirmed the structure of **1**. The HMBC correlation of H-2‴ (δ_H 2.45)/C-1‴ (δ_C 196.9) suggested the presence of the acetyl group, and the correlations of H-4 (δ_H 7.58)/C-1‴ (δ_C 196.9) and H-6 (δ_H 7.55)/C-1‴ (δ_C 196.9) indicated the acetyl group was *ortho* to the two aromatic hydrogen atoms. In the furan ring moiety, the HMBC correlations between H-2 (δ_H 4.63)/C-7a (δ_C 161.8), C-3a (δ_C 127.1), and H-3 (δ_H 3.12)/C-7a (δ_C 161.8) and C-3a (δ_C 127.1) were also observed. The HMBC correlations of H-2′ (δ_H 1.14)/C-1′ (δ_C 71.8) and C-2 (δ_C 90.1), and H-3′ (δ_H 1.27)/C-1′ (δ_C 71.8) and C-2 (δ_C 90.1) indicated that a 2-hydroxyisopropyl group was attached at C-2. The isopentenyl group was shown to be at C-7 by the HMBC correlations between H-1″ (δ_H 3.27, 3.20)/C-7a (δ_C 161.8), and H-6 (δ_C 7.55)/C-1″ (δ_C 28.4). Consequently, the structure of **1** was firmly established as 5-acetyl-2-(2-hydroxyisopropyl)-7-(3,3-dimethylallyl)-2,3-dihydrobenzofurane (Fig. 1). The stereochemistry at C-2 was not determined.

Table 1 ^{1}H, ^{13}C and DEPT data for compound **1** ($CDCl_3$, δ in ppm, TMS)[a]

No.	δ_H	δ_C
2	4.63 (1H, t, 8.9)	90.1 d
3	3.12 (2H, d, 8.9)	30.2 t
3a	–	127.1 s
4	7.58 (1H, brs)	123.3 d
5	–	130.9 s
6	7.55 (1H, brs)	129.8 d
7	–	122.9 s
7a	–	161.8 s
1′	–	71.8 s
2′	1.14 (3H, s)	24.0 q
3′	1.27 (3H, s)	25.7 q
1″	3.27 (1H, dd, 15.3, 7.6) 3.20 (1H, dd, 15.3, 7.1)	28.4 t
2″	5.21 (1H, dd, 7.6, 7.1)	121.3 d
3″	–	133.2 s
4″	1.66 (3H, brs)	25.8 q
5″	1.66 (3H, brs)	17.8 q
1‴	–	196.9 s
2‴	2.45 (3H, s)	26.4 q

[a] Measured at 500 MHz for ^{1}H NMR and 125 MHz for ^{13}C NMR.

Experimental

Optical rotation was measured on a Perkin-Elmer 341 polarimeter. IR spectra were taken on Vertex 70 FT-IR spectrometer. ^{1}H, ^{13}C NMR (DEPT) and 2D NMR spectra were recorded on a Bruker AVANCE 500 spectrometer. The HR-ESI-MS spectra were measured on Bruker APEX II spectrometers. Silica gel (200–300 and 300–400 mesh) used for column chromatography (CC) and silica GF_{254} for TLC were supplied by Qingdao Marine Chemical Factory in China.

Plant material

The whole plants of *S. vulgaris* were collected in the Changbai Mountains, Jilin Province, P. R. China in September 2008, and identified by Prof. Jun Lin Yu, Department of Pharmaceutical and Food Science,

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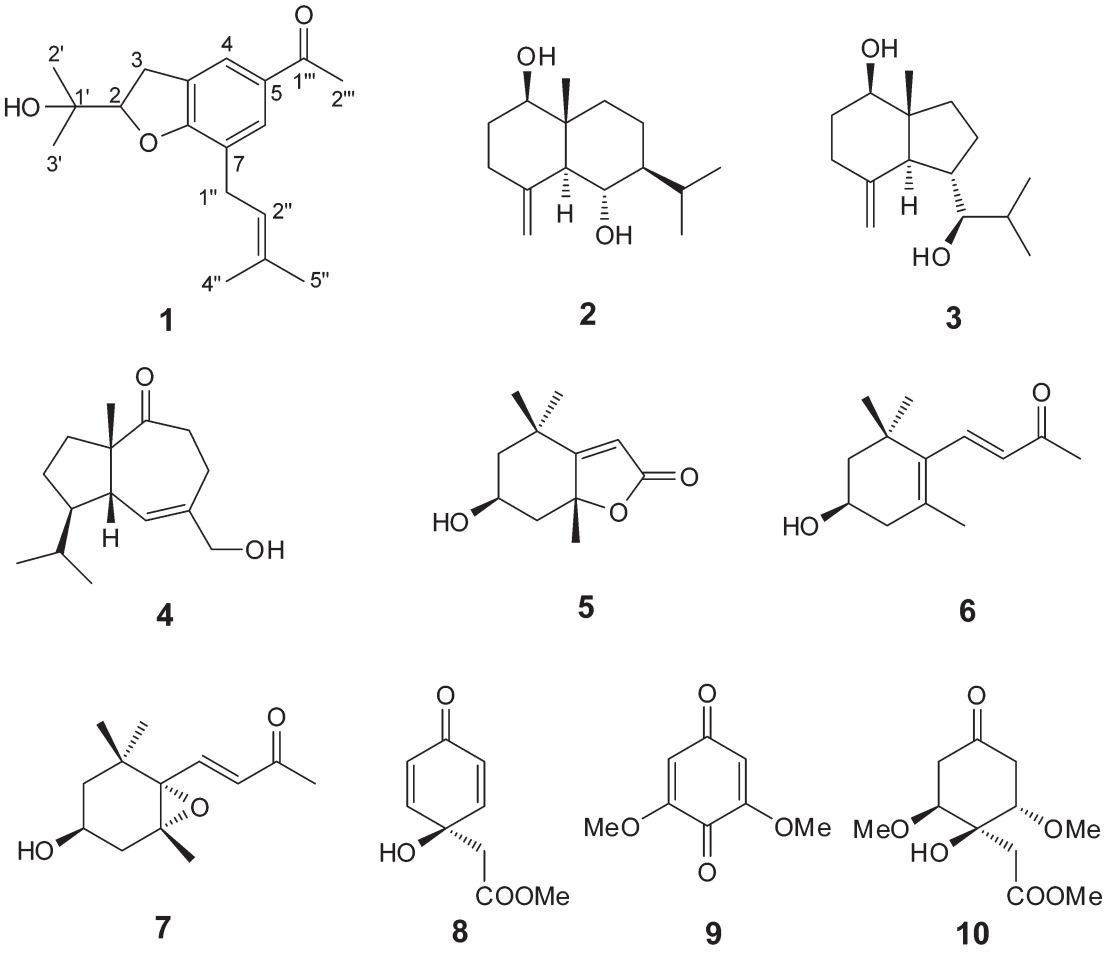

Fig. 1 The structures of compounds **1–10**.

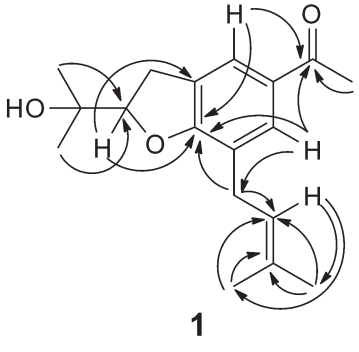

Fig. 2 The key HMBC correlations for compound **1**.

Tonghua Normal University. A voucher specimen (No. CB 2008003) is deposited in the Laboratory of Botany, Marine College, Shandong University at Weihai.

Extraction and isolation

The air-dried whole plants of *S. vulgaris* (7.6 kg) were extracted with CH_3OH three times (7 days each time) at room temperature. The combined extracts were evaporated under reduced pressure to yield a residue (636 g). This residue was suspended in water (2500 mL) and successiveliy extracted with petroleum ether (b.p. 60–90 ºC) and $CHCl_3$ to give a dry petroleum ether extract (142 g) and $CHCl_3$ extract (126 g), respectively. The $CHCl_3$ extract was separated into four fractions (Fr.1–Fr.4) by silica gel CC (200– 300 mesh, 1300 g) with a gradient of hexane/acetone (10:1, 5:1, 3:1 and 1:1) as eluent. Fr.1 (hexane/acetone 10:1; 20.7 g) was further purified by silica gel CC (200–300 mesh, 220 g) with a hexane/EtOAc (20:1–0:1) gradient to give four subfractions (Fr.1a–Fr.1d). The main components of Fr.1a (hexane/EtOAc 20:1, 3.6 g) are essential oil and *β*-sitosterol identified by TLC comparison with an authentic sample. Fr.1b (hexane/EtOAc 10:1, 2.7 g) was isolated by silica gel CC (300–400 mesh) with hexane–acetone (15:1) as eluent, and further purified by low pressure C-18 CC eluting with H_2O/MeOH (1:1 and 3:1) to yield **2** (22 mg) and **4** (7 mg), respectively. Fr.1c (hexane/EtOAc 5:1, 2.4 g) was purified by repeated silica gel CC with hexane-acetone (10:1) as eluent to yield **8** (12 mg) and **1** (5 mg). Fr.1d (hexane/EtOAc 3:1, 2.7 g) was subjected to a silica gel CC with hexane/EtOAc (3:1) as eluent to afford **10** (14 mg) and a mixture. This mixture was purified by low pressure C-18 CC eluting with H_2O/MeOH (1:1 and 2:1) to yield **6** (6 mg) and **7** (9 mg), respectively. Fr.2 (hexane/acetone 5:1; 9.1 g) was isolated by repeated silica gel CC with a gradient of hexane/EtOAc (10:1–2:1), and further purified by low pressure C-18 CC eluting with H_2O/MeOH (1:8) elution to yield **5** (4 mg) and **3** (10 mg). Fr.3 (hexane/acetone 3:1; 32.1 g) was purified by repeated silica gel CC (300–400 mesh) with $CHCl_3$/acetone (10:1) as eluent to yield **9** (8 mg).

5-Acetyl-2-(2-hydroxyisopropyl)-7-(3,3-dimethylallyl)-2,3-dihydrobenzofuran (**1**): Colourless oil; $[\alpha]_D^{20}$ = –245 (c 0.3, $CHCl_3$). IR (KBr) ν_{max}/cm^{-1}: 3428, 2979, 2921, 2859, 1671, 1600, 1480, 1436, 1369, 1311, 1182. HR-ESI-MS *m/z*: 289.1792 ([M+H]$^+$, Calcd for $C_{18}H_{25}O_3^+$: 289.1804). ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (DEPT) (125 MHz, $CDCl_3$) spectroscopic data see Table 1.

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