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Eudesmane-type sesquiterpenes from *Senecio ambraceus*

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Investigation of the aerial parts of *Senecio ambraceus* afforded four eudesmane-type sesquiterpenes (**1**–**4**), of which **1** was isolated from a natural source for the first time. Its structure was established on the basis of spectroscopic methods, including IR, EI–MS, HR–ESI–MS, 1D and 2D NMR spectroscopy.

Keywords: Compositae, *Senecio ambraceus*, sesquiterpene, eudesmane

The genus *Senecio* belongs to the Senecioneae tribe of the Compositae family with more than 200 species occuring in China.[1] Several species have been used in Chinese folk medicine for the treatment of inflammation, malaria, burns and heatstroke.[2] Phytochemical research has shown that *Senecio* species are a rich source of eremophilane-type sesquiterpenoids.[3] Apart from eremophilanes, other types of sesquiterpenoid, skeleta such as bisabolane,[4] eudesmane,[5] oplopane,[6] bakkenolane,[7] and germacrane[8] have also been isolated from some species. Earlier phytochemical investigation of *Senecio ambraceus* was limited to the isolation and characterisation of several pyrrolizidine alkaloids.[9] In the course of our search for antibacterial sesquiterpenoids from *Senecio* species growing in Shandong Province, China, four eudesmanes (**1**–**4**) (Fig. 1) were isolated from the aerial parts of *Senecio ambraceus*. In this paper, we report the isolation and identification of the new natural compound **1**.

By comparing the spectral data (EI-MS, ^{1}H and ^{13}C NMR) with those reported in the literature, the known compound **2**–**4** were identified, respectively, as 4(15)-eudesmene-1β,5α-diol,[10]4(15)-eudesmene-1β,7α-diol,[11]4α,15-epoxyeudesmene-1β,6α-diol.[10]

Compound **1** was obtained as colourless crystals. Its IR spectrum indicated the presence of hydroxyl group at 3404 cm^{-1}, carbonyl group at 1702 cm^{-1} and a double bond at 1646 cm^{-1}. Its EI–MS spectrum exhibited a molecular ion at *m/z* 236 [M]$^+$. Combined with the ^{1}H and ^{13}C NMR (DEPT) data (1), the molecular formula was deduced to be $C_{15}H_{24}O_2$, and this was further confirmed by the quasi molecular ion peak at *m/z* 254.2120 ([M + NH$_4$]$^+$, $C_{15}H_{28}NO_2$, calcd. 254.2115) in HR–ESI–MS spectrum. The ^{1}H NMR spectrum of **1** indicated the presence of an isopropyl group in agreement with signals for two secondary methyl groups at δ_H 0.91 (d, *J* = 6.6 Hz, 3H) and 0.92 (d, *J* = 6.6 Hz, 3H) and a methine proton at δ_H 1.53 (m, 1H) (1). In addition, a tertiary methyl group at δ_H 1.04 (s, 3H) and an exocyclic methylene group at δ_H 5.07 (s, 1H) and 4.98 (s, 1H) were observed. The ^{13}C NMR (DEPT) spectrum of **1** showed the presence of 15 carbons, including a carbonyl carbon at δ_C 214.3 (s), two olefinic carbons at δ_C 148.4 (s) and 110.6 (t), and an oxygenated quaternary carbon at δ_C 77.9 (Table 1). On the basis of these findings and comparison of the ^{1}H and ^{13}C NMR spectroscopic data with those of 4(15)-eudesmene-1β,5α-diol (**2**),[10] compound **1** was shown to be a eudesmane-type sesquiterpene with an exocyclic double bond between C-4 and C-15, a carbonyl group at C-1, and a hydroxyl group at C-5.

The structure of compound **1** was further confirmed by the HMBC spectrum (Fig. 2). The HMBC correlations of δ_H 1.04 (H-14)/δ_C 214.3 (C-1) and δ_H 2.47 (H-3)/δ_C 214.3 (C-1) indicated that the carbonyl group was located at C-1. The HMBC correlations of δ_H 2.47 (H-3)/δ_C 148.4 (C-4), δ_H 2.47 (H-3)/δ_C 110.6 (C-15), δ_H 5.07 (H-15)/δ_C 148.4 (C-4), δ_H 4.98 (H-15)/δ_C 148.4 (C-4), δ_H 5.07 (H-15)/δ_C 77.9 (C-5), δ_H 4.98 (H-15)/δ_C 77.9 (C-5) suggested the placement of a double bond between C-4 and C-15, and a hydroxyl group at C-5. The isopropyl group at C-7 was assigned the β-relative stereochemistry according to literature,[12] and this was used as the starting point for determining the relative stereochemistry of the molecule. In the NOESY spectrum (Fig. 2), the correlations between CH$_3$-14 and CH$_3$-12, and between CH$_3$-14 and H-8β suggested that the CH$_3$-14 had the β-orientation, and the hydroxyl group at C-5 had an α-orientation.[10] Thus, the structure of **1** was assigned as 5α-hydroxy-4(15)-eudesmene-1-one (Fig. 1).

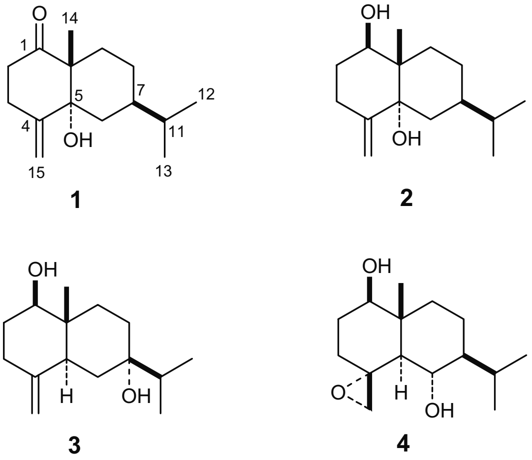

Fig. 1 The structures of compounds **1**–**4**.

Experimental

The melting points were determined on a Kofler melting point apparatus and are uncorrected. IR spectra were recorded with a Bruker Vertex 70 FT-IR spectrometer in KBr. Optical rotation was measured on a Perkin-Elmer 341 polarimeter. ^{1}H, ^{13}C NMR (DEPT) and 2D NMR were recorded on Bruker Avance 600 spectrometer with TMS as the internal reference. EI–MS and HR–ESI–MS spectra were obtained respectively on HP-5988A GC/MS and Bruker APEX II instruments using a direct insertion probe. Silica gel (200–300 and 300–400 mesh) used for column chromatography (CC), were supplied by Qingdao Marine Chemical Factory in China. The purity

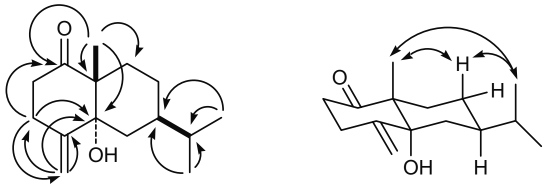

Fig. 2 The key HMBC and NOESY correlations for compound **1**.

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

No.	δ_H	δ_C	DEPT
1	–	214.3	C
2α	2.39 (ddd, 15.6, 12.0, 8.4, 1H)	36.5	CH_2
2β	2.67 (ddd, 15.6, 7.2, 1.2, 1H)		
3α	2.99 (ddd, 13.8, 12.0, 7.2, 1H)	29.9	CH_2
3β	2.47 (ddd, 13.8, 8.4, 1.2, 1H)		
4	–	148.4	C
5	–	77.9	C
6	1.65 (m, 2H)	33.6	CH_2
7	1.68 (m, 1H)	38.0	CH
8α	1.48 (m, 1H)	23.3	CH_2
8β	1.13 (m, 1H)		
9α	1.99 (ddd, 14.3, 13.8, 4.2, 1H)	26.7	CH_2
9β	2.47 (ddd, 14.3, 3.6, 3.0, 1H)		
10	–	51.6	C
11	1.53 (m, 1H)	32.6	CH
12	0.91, (d, 6.6, 3H)	19.6	CH_3
13	0.92, (d, 6.6, 3H)	20.2	CH_3
14	1.04 (s, 3H)	19.9	CH_3
15	5.07 (s, 1H), 4.98 (s, 1H)	110.6	CH_2
5-OH	1.36 (brs, 1H)	–	–

[a]Measured at 600 MHz for ^{1}H NMR and 150 MHz for ^{13}C NMR.
[b]Assigned by ^{1}H-^{1}H COSY and HMBC spectrum.

of the samples were checked on TLC (silica gel, GF_{254} and RP-18) under UV light at 254 nm or by heating after spraying with 5% H_2SO_4 in C_2H_5OH.

Plant material

The aerial parts of *Senecio ambraceus* were collected from the Kunyu Mountains, Weihai, P. R. China in September 2007, and identified by Associate Prof. Hong Zhao, Marine College, Shandong University at Weihai. A voucher specimen (No. KY2007006) is deposited in the Laboratory of Botany, Marine College, Shandong University at Weihai.

Extraction and isolation

The air-dried aerial parts of *Senecio ambraceus* (1.2 kg) were pulverised and extracted with CH_3OH three times (6 days each time) at room temperature. The extract was concentrated under reduced pressure to afford a residue (112 g). This residue (112 g) was suspended in water (650 ml), and the suspension was extracted successively with hexane and $CHCl_3$. The $CHCl_3$ soluble fraction was concentrated under reduced pressure to yield a residue (17 g). This residue was subjected to a silica gel column chromatography (200–300 mesh, 200 g) with a gradient of hexane–acetone (10 : 1, 5 : 1) as eluent. Three fractions were collected according to TLC analysis. Fraction 1 (hexane–acetone 10 : 1, 1.6 g) was isolated by silica-gel column chromatography with hexane–acetone (15 : 1) as eluent and preparative TLC to afford **1** (4 mg). Fraction 2 (hexane–acetone 10: 1, 3.6 g) was subject to a silica-gel column with petroleum ether (b.p. 60–90 °C) – acetone (10 : 1) as eluent to yield compound **4** (16 mg) and a mixture (180 mg), this mixture was further purified by a low-pressure reverse-phased C-18 silica gel column chromatography eluted with 40% H_2O in CH_3OH to yield compound **2** (5 mg) and **3** (3 mg). There is no significant spot found in the fraction 3 (hexane–acetone 5: 1, 3.8 g).

5α-Hydroxy-4(15)-eudesmene-1-one (**1**): $C_{15}H_{24}O_2$, Colourless crystal m.p. 133–134 °C. $[\alpha]_D^{18}$ + 104 (*c* 0.2, $CHCl_3$). IR (KBr) ν_{max}/cm^{-1}: 3404, 3088, 2956, 2909, 2867, 1702, 1646, 1467, 1354, 1080, 1009. EI-MS *m/z* (rel. int.): 236 (34, $[M]^+$), 218 (5), 221 (4), 203 (5), 193 (18), 175 (19), 165 (12), 151 (10), 147 (14), 139 (19), 133 (21), 125 (48), 109 (32), 95 (32), 91 (29), 69 (54), 55 (75), 53 (33), 43 (88), 41 (100). HR-ESI-MS: *m/z*: 254.2120 ($[M + NH_4]^+$, $C_{15}H_{28}NO_2^+$; calcd. 254.2115). ^{1}H, ^{13}C NMR and DEPT data see Table 1.

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