

Article

A New Sesquiterpene with a Novel 1β , 8β -Oxygen Bridge from *Heteropappus altaicus* (willd.) Novopokr.

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Abstract: A new guaiane-type sesquiterpene, $4\alpha,7\beta$ -dihydroxy- 10β H-guai-5-en- $1\beta,8\beta$ -endoxide (**1**), was isolated from *Heteropappus altaicus* (Compositae). The structure of compound **1**, which contains exhibited a rare 1,8-oxide bridge, was established on the basis of spectroscopic data.

Keywords: *Heteropappus altaicus* (willd.) Novopokr.; sesquiterpene; oxide bridge

1. Introduction

Heteropappus altaicus (willd.) Novopokr., which belongs to the *Heteropappus* genus (Compositae, tribe Astereae), is used as traditional medicine in Tibet, and especially in Mongolia, against colds and pulmonary diseases [1,2]. The number of diterpenes, triterpenoid saponins and flavone derivatives have been identified in *H. altaicus* collected in Mongolia [3-8]. Investigation of whole plant of *H. altaicus* from Shandong Province of China, in continuation of our project to compare the chemical compositions of the same species collected from different regions, yielded a guaiane-type sesquiterpene **1**, which represents the first sesquiterpenoid of this type isolated from the *H. altaicus*. In this paper we report the isolation and structure elucidation of this compound.

2. Results and Discussion

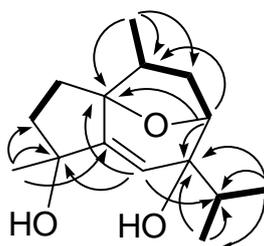
Compound **1** was obtained as a yellow oil. Its molecular formula was determined as C₁₅H₂₄O₃ by HREIMS, which gave a peak at m/z 252.1733 [M]⁺ (calcd. 252.1725) and NMR spectroscopic data (Table 1). The data indicate that the structure of **1** possesses four degrees of unsaturation. Its IR spectrum demonstrated the existence of hydroxyl (3,435 cm⁻¹) and double bond (1,630 cm⁻¹) functions. The ¹³C-NMR and DEPT spectra showed signals for 15 carbons, including four methyls (δ 25.6, 16.5, 16.2 and 16.1 ppm), three sp³ methylenes (δ 39.7, 32.8 and 30.5 ppm), two sp³ methines (δ 42.1 and 30.9 ppm), three sp³ quaternary oxycarbons (δ 88.5, 81.1 and 76.7 ppm), one sp³ tertiary oxycarbon (δ 74.4 ppm) and one double bond (δ 153.8 and 122.7 ppm). The ¹H-NMR spectrum of **1** displayed four methyl groups, including one tertiary methyl (δ 1.36, 3H, s) and three secondary methyls (δ 1.07, 3H, d, J = 6.8 Hz; 0.93, 3H, d, J = 6.8 Hz; 0.92, 3H, d, J = 6.8 Hz), one trisubstituted double bond (δ 5.87, 1H, s) and one oxygen-bearing methine (δ 4.25, 1H, d, J = 8.0 Hz). Thus, the tricyclic structure of **1** was revealed.

Table 1. ¹H- and ¹³C-NMR spectra data of **1** (recorded at 400/100 MHz in CDCl₃; δ in ppm, J in Hz).

No.	¹ H	¹³ C
1	-	88.5 (C)
2	2.25 (1H, m); 1.86 (1H, m)	30.5 (CH ₂)
3	1.94 (1H, m); 1.82 (1H, m)	39.7 (CH ₂)
4	-	76.7 (C)
5	-	153.8 (C)
6	5.87 (1H, s)	122.7 (CH)
7	-	74.4 (C)
8	4.25 (1H, d, J = 8.0 Hz)	81.1 (CH)
9	2.32 (1H, m); 1.26 (1H, m)	32.8 (CH ₂)
10	-	42.1 (C)
11	1.84 (1H, m)	30.9 (CH)
12	0.92 (3H, d, J = 6.8 Hz)	16.2 (CH ₃)
13	1.07 (3H, d, J = 6.8 Hz)	16.5 (CH ₃)
14	0.93 (3H, d, J = 6.8 Hz)	16.1 (CH ₃)
15	1.36 (3H, s)	25.6 (CH ₃)

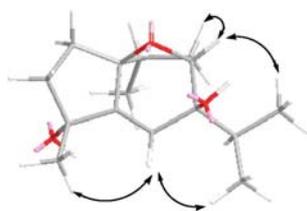
By the analysis of ¹H-¹H COSY correlations (Figure 1), it was possible to establish three partial structures of consecutive proton systems extending from H₂-2 to H₂-3; H₃-14 to H-10, H₂-9 and H-8; H-11 to H₃-12 and H₃-13.

Figure 1. ¹H-¹H COSY correlations (bold lines) and key HMBC correlations (H → C) of **1**.



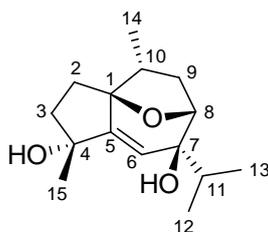
By further analysis of the HMBC correlations (Figure 1), the guaiane-type skeleton of **1** was established. The hydroxyl groups should be positioned at a methyl-bearing carbon C-4 and an isopropyl-bearing carbon C-7, as designated by the HMBC correlations observed from the tertiary methyl (δ 1.36, 3H, s) to the quaternary carbons at δ 76.7 (C-4) and 153.8 (C-5) and the secondary methyls (δ 1.07, 3H, d, J = 6.8 Hz; 0.92, 3H, d, J = 6.8 Hz) to the quaternary carbon at δ 74.4 (C-7), respectively. Therefore, the last one additional oxygen atom should be used to form an oxide bridge in the cycloheptene moiety of the molecule. The HMBC correlations found from the H-8 (δ 4.25, d, J = 8.0 Hz) to C-1 (δ 88.5, C) further confirmed the 1,8-endoxide linkage.

Figure 2. Selective NOESY correlations of **1**.



In the $^1\text{H-NMR}$ spectrum, the chemical shift value of H-9 α at δ 2.32 was typical for guaiane-type sesquiterpenoid having α -methyl group at C-10 [9,10]. It was found that H₃-15 (δ 1.36, 3H, s) showed a NOE interaction with H-6 (δ 5.87, 1H, s), suggesting the H₃-15 should be positioned on the β -face which leads to a lack of NOE connectivity between H₃-15 and H₃-14 α . The above observations together with the NOE correlations observed in the NOESY spectrum (Figure 2) supported the relative structure of **1** as 4 α ,7 β -dihydroxy-10 β H-guai-5-en-1 β ,8 β -endoxide (Figure 3).

Figure 3. Structure of compound **1**.



3. Experimental

3.1. General

Optical rotations were measured on a Perkin-Elmer Model 341 polarimeter. IR spectra were recorded on a Nicolet NEXUS 670 FT-IR instrument, using KBr discs, over the range 400–4,000 cm^{-1} . NMR spectra were measured on a Bruker AM-400 NMR spectrometer with TMS as an internal standard. High-resolution mass spectrometry experiments were obtained on a Bruker Daltonics Apex III spectrometer. Column chromatography was carried out on Si gel (200–300 mesh) and TLC on Si gel (GF254 10–40 μm), both supplied by Qingdao Marine Chemical Co.

3.2. Plant Material

The whole plant of *H. altaicus* (willd.) Novopokr. was collected from Taian (Shandong Province, P.R. China) and was identified by Prof. Xiaochuan Liu (School of Life Science, Zhejiang Sci-Tech University). A voucher specimen (No. 080901) has been deposited in the Department of Chemistry, Zhejiang Sci-Tech University, China.

3.3. Extraction and Isolation

The air-dried plant of *H. altaicus* (10 kg) was pulverized and extracted with MeOH (24.0 L) at room temperature for 7 days. The extracts were filtered and the filtrate was concentrated under reduced pressure to yield a crude methanol extract (500 g), which was suspended in H₂O (1.0 L) and extracted with petroleum ether (boiling point 60–90 °C, 0.5 L), ethyl acetate (0.5 L) and *n*-butanol (0.5 L). The EtOAc extract (200 g) was subjected to repeated chromatography, eluting with a gradient of petroleum ether-EtOAc (20:1–0:1, v/v) and seven crude fractions (A–G) were obtained. Fraction C (2 g) was chromatographed on a silica gel column, eluting with petroleum ether-EtOAc (10:1–1:1) to give seven subfractions (C-1—C-7), of which subfraction C-4 was separated by preparative TLC developed by petroleum ether-EtOAc 7:1 to yield **1** (20 mg).

4α,7β-Dihydroxy-10βH-guai-5-en-1β,8β-endoxide (1). Yellow oil; $[\alpha]_D^{25} +39$ (*c* 0.14 CHCl₃); HREIMS *m/z* 252.1733 [M]⁺ (calcd. for C₁₅H₂₄O₃, 252.1725); IR (KBr) ν_{\max} : 3435, 2983, 1630, 1065 cm⁻¹; ¹H- and ¹³C-NMR(CDCl₃) data, see Table 1.

4. Conclusions

A new guaiane-type sesquiterpene, *4α,7β-dihydroxy-10βH-guai-5-en-1β,8β-endoxide (1)*, was isolated from the whole plant of *Heteropappus altaicus* (willd.) Novopokr. Compound **1** contains a rare 1,8-oxide bridge. Its structure was established on the basis of spectroscopic data. As far as we know, this is the first report of guaiane-type sesquiterpenoid isolated from the *H. altaicus* and compound **1** is also the first guaiane-type sesquiterpenoid having a 1,8-endoxide bridge.

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Sample Availability: Samples of the compound 4 α ,7 β -dihydroxy-10 β H-guai-5-en-1 β ,8 β -endoxide are available from the authors.

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