Two Eudesmane Sesquiterpenes from *Laggera pterodonta*


***Note: This version of the document is not the copy of record. Made available courtesy of Taylor & Francis. Link to Article: [http://www.tandfonline.com/doi/abs/10.1080/10286020500034964](http://www.tandfonline.com/doi/abs/10.1080/10286020500034964)***

**Abstract:**
The phytochemical study of the aerial parts of *Laggera pterodonta* afforded two new eudesmane sesquiterpenes, 3α,4β,11-trihydroxyenantioeudesmane (pterodontriol E) (1) and 4β,8β,11-trihydroxyenantioeudesmane (pterodontriol F) (2), along with seven known compounds. Their structures were elucidated on the basis of spectroscopic data.

**Article:**

**INTRODUCTION**

*Laggera pterodonta* (DC.) Benth is widely distributed in southwestern China, mainly in Yunnan province. The aerial part of *L. pterodonta* has been used as folk medicine dating from ancient times. Pharmacological research indicated that extract of *L. pterodonta* has anti-leukaemia, antibacterial, anti-inflammatory and anti-malarial activities [1-3]. Many eudesmane sesquiterpenes and related glucosides, as well as flavonoids, have been reported from *L. pterodonta* [3-13]. In our search for pharmacologically active compounds from crude drugs of plant origin, the chemical constituents of *L. pterodonta* were studied. This paper deals with the isolation and structural elucidation of two new and seven known compounds (1–9) from the aerial parts of *L. pterodonta*.

**RESULTS AND DISCUSSION**
The ethyl acetate-soluble fraction from *Lagger pterodonta* was separated by repeated silica-gel column chromatography, HPLC and gel permeation chromatography (GPC), to give two new sesquiterpenes, named pterodontriol E (1) and pterodontriol F (2), as well as seven known compounds (3–9).

Pterodontriol E (1) was obtained as an amorphous powder, exhibiting a molecular ion peak at m/z 279.1939 [M+ Na]+ (HR FTMS), indicating a molecular formula of C_{15}H_{28}O_{3} for 1. The IR spectrum showed the presence of hydroxyl group (3321 cm$^{-1}$). The $^1$H NMR spectral data of 1 revealed the presence of four methyl groups [$\delta_H$ 1.29, 1.28, 1.05, and 0.91 (each 3H, s)] and one oxygenated methine proton signal [$\delta_H$ 3.45 (1H, dd, $J = 4.5, 11.9$ Hz)]. Its $^{13}$C NMR spectral data showed 15 carbons, including four methyls, five methylenes, one oxygenated methine, two oxygenated quaternary carbons and other three carbon signals. Based on the above facts,
compound 1 was proposed to be a eudesmane sesquiterpene, the same as pterodontriols A–D isolated from the same plant [3-5]. The $^{13}$C NMR spectral data of 1 were similar to those of pterodondiol [5], except for C–2 and C–3. In the HMBC spectrum of 1, the proton signal at $\delta_H$ 0.91 (H-14) was correlated with the carbon signals at $\delta_C$ 47.2 (C-5), 41.3 (C-9), 39.7 (C-1) and 34.3 (C-10), the signal at $\delta_H$ 1.05 (H-15) was correlated with the signals at $\delta_C$ 79.9 (C-3), 76.5 (C-4), and 47.2 (C-5), while the signal at $\delta_H$ 3.45 (H-3) was correlated with the signals at $\delta_C$ 76.5 (C-4), 27.5 (C-2), and 15.7 (C-15). Therefore, the hydroxyl group was located at the C-3 position. Thus, compound 1 should be a 3-hydroxy pterodondiol.

In the NOESY spectrum, the proton signal at $\delta_H$ 3.45 (H-3) was correlated with the signals at $\delta_H$ 1.68 (H-5) and 1.42 (H-1β); the methyl signal at $\delta_H$ 0.91 (H-14) was correlated with the signal at $\delta_H$ 1.05 (H-15). Furthermore, the coupling constant of H-3 ($J = 4.5, 11.9$ Hz) indicated that it has axial orientation. Thus, the relative configurations of two hydroxyl groups were determined as 3α and 4β. According to the literature [3-5,11,12], all the pterodontriols isolated from L. pterodonta (including known compounds 3–7, see section 3) have positive $[\alpha]_D$ values and their structures were determined as enantio-eudesmantriol by comparing with $[\alpha]_D$ values to those of eudesmantriols. Therefore, the positive $[\alpha]_D$ value (+78.6) of 1 indicated pterodontriol E (1) was apparently also an enantio-eudesmantriol. The structure of pterodontriol E was thus determined as shown in figure 1.

![Figure 1: Structures of compounds 1–9.](image)

Pterodontriol F (2) had the molecular formula C$_{15}$H$_{28}$O$_3$, the same as 1. The $^1$H NMR spectral data of 2 showed the presence of four methyl groups [$\delta_H$ 1.65, 1.58, 1.35, and 0.99 (each3H, s)], and one oxygenated methine proton signal [$\delta_H$ 4.66 (1H, ddd, $J = 8.1, 8.1, 5.3$ Hz)]. Comparing the $^{13}$C NMR spectral data of 2 with those of 1, compound 2 also appeared to be a eudesmane sesquiterpene with three hydroxyl groups (table 1). In the HMBC spectrum of 2, the methyl proton signal at $\delta_H$ 0.99 (H-14) was correlated with the carbon signals at $\delta_C$ 49.0 (C-5), 43.4 (C-
1), and 52.6 (C-9), the signal at δH 1.81 (H-9a) was correlated with the signals at δC 21.2 (C-14), 69.8 (C-8), 47.1 (C-7), while the signal at δH 2.66 (H-6a) was correlated with the signals at δC 35.4 (C-10) and 69.8 (C-8). In turn, the methine signal at δH 4.66 (H-8) was correlated with the signal at δC 74.9 (C-11). Thus, the secondary hydroxyl group was located at the C-8 position. In the NOESY spectrum, the methyl proton signal at δH 0.99 (H3-14) was correlated with the signals at δH 1.35 (H-15) and 4.66 (H-8). Thus, the two hydroxyl groups have 4β and 8β orientations. Therefore, pterodontriol F (2) was determined as 4β,8β,11-trihydroxyenantiouesmane (figure 1).

Table 1: 1H NMR and 13C NMR spectral data of 1 and 2.

<table>
<thead>
<tr>
<th>No.</th>
<th>13C</th>
<th>1 (CDCl3)</th>
<th>2(C5D5N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>39.7</td>
<td>1.42,1.22 (m)</td>
<td>43.4</td>
</tr>
<tr>
<td>2</td>
<td>27.5</td>
<td>1.71,1.51 (m)</td>
<td>21.4</td>
</tr>
<tr>
<td>3</td>
<td>79.9</td>
<td>3.45 (dd, 4.5, 11.9)</td>
<td>44.8</td>
</tr>
<tr>
<td>4</td>
<td>76.5</td>
<td>–</td>
<td>71.7</td>
</tr>
<tr>
<td>5</td>
<td>47.2</td>
<td>1.68 (m)</td>
<td>49</td>
</tr>
<tr>
<td>6</td>
<td>20.4</td>
<td>2.09 (brd, 13.6), 1.49 (m)</td>
<td>21.5</td>
</tr>
<tr>
<td>7</td>
<td>41.3</td>
<td>1.67 (m)</td>
<td>47.1</td>
</tr>
<tr>
<td>8</td>
<td>21.3</td>
<td>1.75,1.65 (m)</td>
<td>69.8</td>
</tr>
<tr>
<td>9</td>
<td>41.3</td>
<td>1.47,1.19 (m)</td>
<td>52.6</td>
</tr>
<tr>
<td>10</td>
<td>34.3</td>
<td>–</td>
<td>35.4</td>
</tr>
<tr>
<td>11</td>
<td>74.9</td>
<td>–</td>
<td>74.9</td>
</tr>
<tr>
<td>12</td>
<td>29.6</td>
<td>1.29 (s)</td>
<td>30.2</td>
</tr>
<tr>
<td>13</td>
<td>30</td>
<td>1.28 (s)</td>
<td>31.9</td>
</tr>
<tr>
<td>14</td>
<td>18.8</td>
<td>0.91 (s)</td>
<td>21.2</td>
</tr>
<tr>
<td>15</td>
<td>15.7</td>
<td>1.05 (s)</td>
<td>23.3</td>
</tr>
</tbody>
</table>

* The chemical shift of proton signals was read by HSQC spectrum.

Several known compounds were identified by their spectroscopic data in comparison with literature values as follows: pterodontriol A (3) [5], pterodontriol B (4) [5], pterodontriol C (5) [3], laggerone A (6) [3], pterodondiol (7) [5], pendultin (8) [13], chrysosptertin (9) [13].

EXPERIMENTAL

General experimental procedures

NMR analysis of samples were performed with a Bruker AVANCE 300 instrument (1H 300 MHz, 13C 75 MHz), both with teramethylsilane as an internal standard. HR FTMS data and EIMS data were obtained on Bruker Apex 7.0 Tesla and VG ZAB-HS (70 eV) instruments, respectively. Column chromatography was performed on silica-gel (Qingdao Haiyang Chemical Co. Ltd), Sephadex LH-20 (Amersham Pharmacia Biotech) and Toyopearl HW-40 (TOSOH). HPLC was a JASCO Gulliver Series with PU-1580 (pump), RI-1530 and UV-1575 (detector). Preparative HPLC column was used as follows: ODS (YMC-Pack ODS-A, SH-343-5), GPC (Shodex, Asahipak GS-310, 20 G, MeOH), Si-HPLC (Hibar RT 250-25, Lichrosorb, Si60 7 μm). IR spectra were recorded on a FTS3000 Infrared Fourier Transform spectrometer (Bio-Rad). Optical rotation was measured with a MC 241 digital polarimeter (Perkin-Elmer).

Plant material

Laggera pterodonta (DC.) Benth was purchased from Kunming, Yunnan province of China in August 2002 and identified by Professor Wen-Yuan Gao. A voucher specimen (D20020818) is deposited at the College of Pharmaceutical Science and Biotechnology, Tianjin University, China.
Extraction and isolation

The dried aerial parts (0.85 kg) of *L. pterodonta* were crushed and extracted three times with EtOH (95%, 10 L each) at 60°C for 6 h. The EtOH extract was concentrated under reduced pressure to give a residue (110 g), which was suspended in H₂O, and then partitioned with petroleum ether, EtOAc and n-BuOH, respectively. The EtOAc layer was concentrated to afford a residue (12 g), which was subjected to column chromatography with silica gel, and was eluted with solvents of increasing polarity [(CHCl₃/MeOH (95:5, 9:1, 8:2, MeOH)] to yield eight fractions. Fraction 7 (439 mg) was chromatographed on Sephadex LH-20 (MeOH) to give four fractions (fr. 7.1–7.4). Fraction 7.2 (298 mg) was purified by HPLC (ODS, MeOH/H₂O 8:2, and then 7:3) to give 1 (13.8 mg) and 4 (11 mg). Fraction 5 (643 mg) was chromatographed on Toyopearl HW-40 (CHCl₃/MeOH, 2:1) to give three fractions (fr. 5.1-5.3). Fraction 5.2 (349 mg) was chromatographed on ODS column (MeOH/H₂O 8:2) to give four fractions (fr. 5.2.1–5.2.7). Fraction 5.2.4 (22 mg) was purified by HPLC (GPC, MeOH) to give 2 (8.5 mg).

Fraction 5.2.3 (35 mg) was separated by Si-HPLC (CHCl₃/MeOH, 95:5) to give 5 (4.5 mg) and 6 (4 mg). Fraction 4 (1.5 g) was chromatographed on Sephadex LH-20 (MeOH) to give four fractions (fr. 4.1–4.4). Fraction 4.3 was further chromatographed on a silica-gel column [(CHCl₃/MeOH (95:5, 9:1)] to give three fractions (fr. 4.3.1–4.3.3). Fraction 4.3.2 (346 mg) was separated by HPLC (ODS, MeOH/H₂O 8:2) to give 7 (55 mg). Fraction 8 (513 mg) was chromatographed on LH-20 (MeOH) to give four fractions (fr. 8.1–8.4). Fraction 8.3 (110 mg) was separated by HPLC (ODS, MeOH/H₂O 8:2, and then Si-60, CHCl₃/MeOH, 85:15) to give 3 (18.6 mg). Fraction 3 (1.2 g) was chromatographed on silica-gel column [(CHCl₃/MeOH (99:1, 98:2, 95:5, 9:1)] to give five fractions (fr. 3.1–3.5). Fraction 3.4 (463 mg) was chromatographed on Toyopearl HW-40 (CHCl₃–MeOH, 2:1) to give four fractions (fr. 3.4.1–3.4.4). Fraction 3.4.3 (110 mg) was separated by Si-HPLC (CHCl₃/MeOH, 97:3) to give 8 (6.7 mg) and 9 (13.6 mg).

Pterodontriol E (1) was isolated as an amorphous powder, [α]D²⁵ +78.6 (c 1.5, CHCl₃). IR (KBr) ν max cm⁻¹: 3321, 2945, 1459, 1406, 1387, 1265, 1220, 1186, 1150, 1089, 1067, 1035, 984, 907, 859. EI-MS: m/z [M]+(1), 238 (10), 220 (8), 205 (9), 179 (31), 147 (21), 123 (31), 95 (30), 59 (55), 43 (100), 27 (9). HR-FTMS m/z 279.1939 [M+ Na]+ (calcd for C₁₅H₂₈O₃Na 279.1931). ¹H NMR and ¹³C NMR (CDCl₃) data are listed in table 1.

Pterodontriol F (2) was isolated as an amorphous powder, [α]D²⁵ +45.2 (c 0.8, CHCl₃). IR (KBr) ν max cm⁻¹: 3369, 2930, 1459, 1384, 1173, 1101, 1050, 942, 914, 756. EI-MS: m/z 256 [M]+(1), 238 (2), 220 (10), 205 (12), 177 (53), 162 (49), 109 (29), 95 (45), 59 (54), 43 (100), 27 (11). HR-FTMS m/z 279.1944 [M+Na]+ (calcd for C₁₅H₂₈O₃Na 279.1931). ¹H NMR and ¹³C NMR (C₅D₅N) data are listed in table 1.

[α]D values of 3–7: 3, [α]D²⁵ 22.7 (c 0.22, MeOH); 4, [α]D²⁵ 31.8 (c 0.26, MeOH); 5, [α]D²⁵ 88.6 (c 0.7, MeOH); 6, [α]D²⁵ 42.4 (c 0.67, MeOH); 7, [α]D²⁵ 27.3 (c 2.2, CHCl₃).

REFERENCES