A Novel Norditerpene from *Eupatorium adenophorum*

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A novel norditerpene was isolated from the flower of *Eupatorium adenophorum*, named (4aR,7R,8S,8aR)-1,2,4a,5,6,7,8,8a-octahydro-8-[3-methylenecyclo-4-allyl]-4,4a,7,8-tetramethylnaphthalene-2(1H)-one (1). Its structure was established by extensive NMR experiments. Based on the diversity of the side chains, a possible biodegradation pathway for the compound from the clerodane skeleton is proposed.

*Key words:* (4aR,7R,8S,8aR)-1,2,4a,5,6,7,8,8a-Octahydro-8-[3-methylenecyclo-4-allyl]-4,4a,7,8-tetramethylnaphthalene-2(1H)-one, *Eupatorium adenophorum*, Biodegradation, Clerodane

**Introduction**

*Eupatorium adenophorum* Spreng, originating from Mexico, has invaded into the Yunnan Province of China from Burma since 1950s. It has resulted in much balefulness to agriculture and environment [1]. Many cadinene derivatives had been extracted by Ding et al. from the flowers of *E. adenophorum* [1]. This time a new compound named (4aR,7R,8S,8aR)-1,2,4a,5,6,7,8,8a-octahydro-8-[3-methylenecyclo-4-allyl]-4,4a,7,8-tetramethylnaphthalene-2(1H)-one (1) and two known compounds 2–3 were isolated from it [2, 3]. In this paper we mainly report the isolation and the structure elucidation of compound 1. Its structure was established by extensive NMR spectroscopic experiments including HMQC, HMBC and NOESY techniques.

**Results and Discussion**

Compound 1 showed a quasimolecular ion peak at *m/z* = 288 in its EI mass spectrum. The molecular formula of 1 was revealed as C_{19}H_{28}O_{2} by HRESIMS data [M+H]^+ (found 289.2164, calc. 289.2167). The $^1$H and $^{13}$C NMR (Table 1) spectra showed the signals of six quaternary, four CH, five CH$_2$, and four methyl carbon atoms. Two C=O moieties are evident from the $^1$H and $^{13}$C NMR signals [δ$_H$ = 9.51 (s, H-14), δ$_C$ = 200.2 (s, C-2), δ$_C$ = 194.6 (d, C-14)]. The signals δ$_H$ = 1.95 (d, 2.4, H-10), δ$_H$ = 1.59 (br, H-8), δ$_C$ = 45.4 (d C-10), 35.9 (d, C-8), 39.7 (s, C-5), 38.7 (s, C-9) suggest that 1 has a clerodane-type skeleton [4, 5]. The data also indicated that 1 is partially similar to 2 and 3, except for the side chain at C-11 [6, 7], (Fig. 1).

![Fig. 1. Structures of 1–3.](image)

Based on HMBC, the correlations between H-12 [δ$_H$ = 1.96 (br), 2.25 (m)] and C-13, C-14, C-16 [δ$_C$ = 150.2 (s, C-13), 194.6 (d, C-14), 133.8 (t, C-16)], between H-16 [δ$_H$ = 6.24 (s), 5.97 (s)] and C-12, C-13, C-14, [δ$_C$ = 20.9 (t, C-12), 150.2 (s, C-13), 194.6 (d, C-14)], and between H-14 [δ$_H$ = 9.51 (s)]
Table 1. NMR spectral data of 1, 2, and 3 in CDCl₃ (500 MHz for ^1^H and 125 MHz for ^1^C, J in Hz).

<table>
<thead>
<tr>
<th>1</th>
<th>δ_H (s)</th>
<th>δ_C</th>
<th>2</th>
<th>δ_H (s)</th>
<th>δ_C</th>
<th>3</th>
<th>δ_H (s)</th>
<th>δ_C</th>
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<tr>
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<td>34.8 (t)</td>
<td>2</td>
<td>2.29 (s)</td>
<td>34.8 (t)</td>
<td>3</td>
<td>2.29 (s)</td>
<td>34.9 (t)</td>
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<tr>
<td>2</td>
<td>2.38 (d, 2.4)</td>
<td>2.36 (d, 3.6)</td>
<td>2</td>
<td>200.2 (s)</td>
<td>200.1 (s)</td>
<td>200.5 (s)</td>
<td>2</td>
<td>125.5 (d)</td>
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<tr>
<td>3</td>
<td>172.5 (s)</td>
<td>39.7 (s)</td>
<td>5</td>
<td>1.40 (br)</td>
<td>35.4 (s)</td>
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</tr>
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<td>2.68 (t)</td>
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<td>1.59 (br)</td>
<td>35.9 (d)</td>
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<td>38.7 (s)</td>
</tr>
<tr>
<td>5</td>
<td>1.59 (br)</td>
<td>36.1 (d)</td>
<td>9</td>
<td>1.40 (br)</td>
<td>35.4 (t)</td>
<td>1.52 (br)</td>
<td>10</td>
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<tr>
<td>6</td>
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<td>37.0 (t)</td>
<td>11</td>
<td>2.25 (m)</td>
<td>20.9 (t)</td>
<td>2.23 (m)</td>
<td>13</td>
<td>150.2 (s)</td>
</tr>
<tr>
<td>7</td>
<td>9.51 (s)</td>
<td>194.6 (d)</td>
<td>14</td>
<td>2.11 (s)</td>
<td>30.1 (q)</td>
<td>5.34 (d, 6.4)</td>
<td>15</td>
<td>4.09 (d, 6.8)</td>
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<td>8</td>
<td>6.24 (s)</td>
<td>133.8 (t)</td>
<td>16</td>
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<td>18.3 (q)</td>
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<td>20</td>
<td>0.80 (s)</td>
<td>17.7 (q)</td>
<td>0.78 (s)</td>
<td>17.7 (q)</td>
<td>0.80 (s)</td>
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</table>

Fig. 2. Key HMBC correlations (left) and key NOESY (right) correlations of 1.

and C-12, C-13, C-16 [δ_C = 20.9 (t, C-12), 150.2 (s, C-13), 133.8 (t, C-16)] indicated that the side chain at C-11 is a D group (Fig. 2). The NOESY spectra, with correlations between H-10 [δ_H = 1.95 (d, 2.4, H-10)] and H-8 [δ_H = 1.59 (br, H-8)], and between H-19 [δ_H = 1.11 (s, H-19)] and H-20 [δ_H = 0.80 (s, H-20)], together with the resonances of C-5 [δ_C = 39.7 (s)] and C-10 [δ_C = 45.4 (d)] bear out that 1 has an AB/AA junction and that H-10 is in a β orientation.

Fig. 3. Possible biodegradation pathway from 3 to 1.
A possible biosynthesis pathway is proposed in Fig. 3.

**Experimental Section**

**General**

NMR spectra were run on a BRUKER DRX-500 (500 MHz for $^1$H NMR and 2D NMR, 125 MHz for $^{13}$C NMR) instrument with TMS as internal standard; IR spectra were measured on a Bio-Rad FTS-135 spectrometer with KBr pellets; EI-MS spectra were recorded on a VG Auto Spec-3000 spectrometer; UV spectra were obtained on a Shimadzu double-beam 210A spectrophotometer. EI-MS: 70 eV; Silica gel (200 – 300 mesh).

**Plant material**

The whole flower of *E. adenophorum* was collected and identified by Prof. Xiao-Dong Luo in June 2005 in Kunming Yunnan Province, P. R. China. A Voucher specimen has been deposited in the herbarium of the Department of Taxonomy, Kunming Institute of Botany, Chinese Academy of Science.

**Extraction and isolation**

The air-dried and powdered flowers (10 kg) were extracted with methanol (4 × 25 L) at r.t. and the solution concentrated in vacuum to give a crude extract (800 g), which was partitioned in H$_2$O and extracted with petroleum ether and EtOAc three times each. The petroleum ether layer (170 g) was chromatographed over silica gel using petroleum ether/acetone (10 : 0–0 : 10) as an eluent to give 7 fractions; the EtOAc layer (178 g) was partitioned into 9 fractions in the same way. Fraction 6 of the petroleum ether layer and fraction 2 of the EtOAc layer are similar according to the TLC detection. They were mixed to give a total of 27 g. The mixture was repeatedly chromatographed over silica gel using petroleum ether/Me$_2$CO (20 : 1–0 : 20) as an eluent to give 5 fractions. Fraction 1 (5.8 g) was subjected to RP-18 (MeOH/H$_2$O, 50 : 50–100 : 0), then repeatedly subjected to silica gel using petroleum ether/EtOAc (30 : 1) as an eluent to yield 1 (3 mg) and 3 (100 mg). Fraction 3 (4.0 g) was subjected to the same procedure as above to yield 2 (53 mg).

**Physical and spectroscopic data: compound 1**, colorless oil. $[a]_{D}^{25} = -14.2 \ (c = 0.5, \ CHCl_3)$. UV (CHCl$_3$): $\lambda_{max}(\text{nm})$ = 241 (4.21). IR (film): $\nu$ = 2871, 2698, 1687, 1622, 1873, 947, 1668 cm$^{-1}$. EI-MS (70 eV): $m/z$ (%): 288 (3) [M]+, 273 (10), 245 (18), 205 (26), 189 (35), 135 (49), 121 (100), 109 (86), 95 (45). – HRESIMS: $m/z = 289.2164$ [M+H]$^+$ (found 289.2164, calcld. 289.2167). – $^1$H and $^{13}$C NMR spectral data: see Table 1.

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