

## Two New Sesquiterpenes from *Salvia roborowskii* MAXIM

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Two new sesquiterpenes, (1 $\beta$ ,3 $\beta$ ,4 $\alpha$ ,5 $\alpha$ ,6 $\alpha$ ,8 $\alpha$ )-guaia-10(14)-ene-3,4,6,8-tetrol 3,6,8-triacetate (**1**) and (3 $\beta$ ,4 $\alpha$ ,6 $\alpha$ ,8 $\beta$ ,9 $\beta$ ,10 $\alpha$ )-8-(acetyloxy)-3,4:9,10-diepoxygermacr-7(11)-eno-12,6-lactone (**2**) were isolated from the EtOH extract of *Salvia roborowskii* MAXIM. Their structures were established by spectroscopic methods, including one- and two-dimensional NMR techniques, and the relative configurations of these compounds were determined on the basis of NOE experiments.

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**Introduction.** – *Salvia roborowskii* is widely distributed in Gansu, Xizang, and Qinhai Province of China. It has been used in the Chinese folk medicine for the treatment of cold and acesodyne [1]. Previously, triterpenoids, germacrane sesquiterpenoids, and other constituents from this species have been reported [2][3]. Many compounds that have closely related structures to these germacrane sesquiterpenoids exhibited biological activities [4]. As a continuing investigation of bioactive metabolites of *S. roborowskii*, a new guaiane (=decahydro-1,4-dimethyl-7-(1-methylethyl)-azulene) sesquiterpene and a new germacrane (=1,7-dimethyl-4-(1-methylethyl)cyclodecane) sesquiterpene were isolated. Herein we described the isolation and structural characterization of these new compounds.

**Results and Discussion.** – Compound **1**<sup>1)</sup> was obtained as a colorless gum with molecular formula C<sub>21</sub>H<sub>32</sub>O<sub>7</sub>, as deduced from the FAB-MS (*m/z* 397.2 ([*M* + H]<sup>+</sup>)) and <sup>13</sup>C-NMR data. Its IR spectrum showed absorption bands for OH (3483 cm<sup>-1</sup>), ester C=O (1726, 1705 cm<sup>-1</sup>), and C=C (1640, 1456 cm<sup>-1</sup>) moieties. Comparison of the <sup>1</sup>H- and <sup>13</sup>C-NMR spectra (*Table*) with those of known sesquiterpenoids [5] suggested that **1** is a sesquiterpene with a guaiane skeleton containing three Ac, an olefinic CH<sub>2</sub>, and an OH group. The <sup>1</sup>H,<sup>1</sup>H-COSY, HMBC (*Fig. 1*), and NOE data established the structure of **1** as (1 $\beta$ ,3 $\beta$ ,4 $\alpha$ ,5 $\alpha$ ,6 $\alpha$ ,8 $\alpha$ )-guaia-10(14)-ene-3,4,6,8-tetrol 3,6,8-triacetate<sup>1)</sup>.

The <sup>1</sup>H- and <sup>13</sup>C-NMR, and DEPT spectra indicated that compound **1** possessed 5 quaternary C-atoms and 7 CH, 3 CH<sub>2</sub>, and 6 Me groups. Furthermore, the <sup>1</sup>H- and <sup>13</sup>C-NMR spectra exhibited characteristic signals for three Ac groups ( $\delta$ (H) 1.96, 2.02, and 1.98 (3s, each 3 H);  $\delta$ (C) 21.0 (*q*) and 170.2 (*s*), 21.4 (*q*) and 170.2 (*s*), and 21.1 (*q*) and 171.1 (*s*)), an *i*-Pr group ( $\delta$ (H) 0.92 and 0.96 (2*d*, *J* = 6.6 Hz,

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<sup>1)</sup> Trivial atom numbering; for systematic names, see *Exper. Part*.

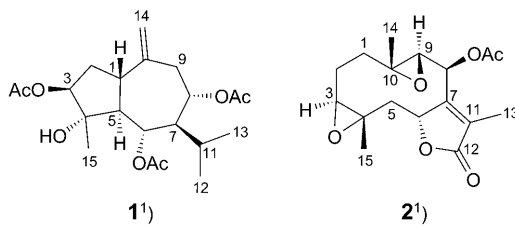


Table.  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR Data (( $\text{D}_6$ )acetone; 400.16 and 100.63 Hz, resp.) of Compounds **1** and **2**<sup>1</sup>.  $\delta$  in ppm rel. to  $\text{Me}_4\text{Si}$ ,  $J$  in Hz.

	<b>1</b>		<b>2</b>	
	$\delta(\text{H})$	$\delta(\text{C})$	$\delta(\text{H})$	$\delta(\text{C})$
$\text{H}_a\text{-C}(1)$	2.57–2.67 ( <i>m</i> )	40.3 ( <i>d</i> )	1.27 ( <i>d</i> , $J=13.2$ )	38.2 ( <i>t</i> )
$\text{H}_b\text{-C}(1)$			2.15–2.17 ( <i>m</i> )	
$\text{H}_a\text{-C}(2)$	1.54–1.62 ( <i>m</i> )	35.5 ( <i>t</i> )	1.48–1.62 ( <i>m</i> )	25.0 ( <i>t</i> )
$\text{H}_b\text{-C}(2)$	2.50–2.54 ( <i>m</i> )		2.02–2.07 ( <i>m</i> )	
$\text{H-C}(3)$	4.75–4.78 ( <i>m</i> )	78.3 ( <i>d</i> )	2.88 ( <i>dd</i> , $J=1.8, 10.8$ )	67.7 ( <i>d</i> )
$\text{C}(4)$	–	78.7 ( <i>s</i> )	–	58.2 ( <i>s</i> )
$\text{H}_a\text{-C}(5)$	2.09 ( <i>d</i> , $J=1.8$ )	56.4 ( <i>d</i> )	1.31 ( <i>d</i> , $J=12.3$ )	45.3 ( <i>t</i> )
$\text{H}_b\text{-C}(5)$			2.80 ( <i>dd</i> , $J=3.6, 13.2$ )	
$\text{H-C}(6)$	5.50 ( <i>dd</i> , $J=1.8, 4.2$ )	70.5 ( <i>d</i> )	5.22 ( <i>dd</i> , $J=3.9, 11.8$ )	78.6 ( <i>d</i> )
$\text{H-C}(7)$ or $\text{C}(7)$	1.76–1.88 ( <i>m</i> )	49.6 ( <i>d</i> )	–	157.3 ( <i>s</i> )
$\text{H-C}(8)$	5.08–5.13 ( <i>m</i> )	72.9 ( <i>d</i> )	6.36 ( <i>s</i> )	68.1 ( <i>d</i> )
$\text{H}_a\text{-C}(9)$	2.46 ( <i>dd</i> , $J=15.6, 3.7$ )	39.7 ( <i>t</i> )	3.09 ( <i>s</i> )	62.1 ( <i>d</i> )
$\text{H}_b\text{-C}(9)$	2.98 ( <i>dd</i> , $J=15.6, 2.2$ )		–	
$\text{C}(10)$	–	148.7 ( <i>s</i> )	–	63.9 ( <i>s</i> )
$\text{H-C}(11)$ or $\text{C}(11)$	1.76–1.88 ( <i>m</i> )	28.9 ( <i>d</i> )	–	130.2 ( <i>s</i> )
$\text{Me}(12)$ or $\text{C}(12)$	0.96 ( <i>d</i> , $J=6.6$ )	20.9 ( <i>q</i> )	–	172.3 ( <i>s</i> )
$\text{Me}(13)$	0.92 ( <i>d</i> , $J=6.6$ )	20.2 ( <i>q</i> )	1.92 ( <i>s</i> )	9.3 ( <i>q</i> )
$\text{H}_a\text{-C}(14)$ or $\text{Me}(14)$	4.84 ( <i>d</i> , $J=3.0$ )	111.6 ( <i>t</i> )	1.58 ( <i>s</i> )	19.6 ( <i>q</i> )
$\text{H}_b\text{-C}(14)$	4.77 ( <i>d</i> , $J=3.0$ )			
$\text{Me}(15)$	1.20 ( <i>s</i> )	21.4 ( <i>q</i> )	1.58 ( <i>s</i> )	17.4 ( <i>q</i> )
$\text{AcO-C}(3)$	2.02 ( <i>s</i> )	21.4 ( <i>q</i> ), 170.2 ( <i>s</i> )		
$\text{AcO-C}(6)$	1.98 ( <i>s</i> )	21.1 ( <i>q</i> ), 171.1 ( <i>s</i> )	–	–
$\text{AcO-C}(8)$	1.96 ( <i>s</i> )	21.0 ( <i>q</i> ), 170.2 ( <i>s</i> )	2.10 ( <i>s</i> )	20.7 ( <i>q</i> ), 169.6 ( <i>s</i> )

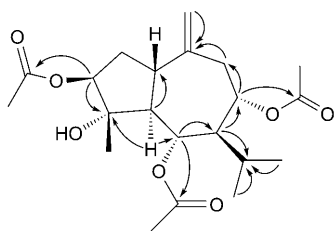


Fig. 1. Key HMBC ( $\text{H} \rightarrow \text{C}$ ) data of **1**

each 3 H), and 1.76–1.88 (*m*, 1 H);  $\delta(\text{C})$  20.2 and 20.9 (*2q*), and 28.9 (*d*), and an olefinic  $\text{CH}_2$  group ( $\delta(\text{H})$  4.84 and 4.77 (*2s*, each 1 H);  $\delta(\text{C})$  111.6 (*t*) and 148.7 (*s*)).

The locations of the three Ac, the olefinic  $\text{CH}_2$ , and the OH group were assigned by HMBC experiments; the correlations between the three ester  $\text{C}=\text{O}$  C-atoms with H–C(3), H–C(6), and H–C(8) indicating that the OH group was located at C(4) and the three Ac groups at C(3), C(6), and C(8) (Fig. 1). The entire sequence of H-atoms at the C-skeleton was established by  $^1\text{H},^1\text{H}$ -COSY and HMBC. In the difference NOE experiment, irradiation of the H–C(6) signal caused NOE enhancements of the signals of H–C(11), Me(12), Me(13), and Me(15), irradiation of the H–C(8) signal caused NOE enhancements of the signals of  $\text{H}_b$ -C(2),  $\text{H}_b$ -C(9), H–C(11), Me(12), and Me(13), and irradiation of the Me(15) signal caused NOE enhancements of the signals of H–C(1) and H–C(6).

Compound **2**<sup>1</sup> was obtained as a colorless gum. The molecular formula of **2** was deduced as  $\text{C}_{17}\text{H}_{22}\text{O}_6$  from the quasi-molecular-ion peak at  $m/z$  323.0 ( $[\text{M} + \text{H}]^+$ ) in its FAB-MS and from the  $^{13}\text{C}$ -NMR and DEPT data. Its IR spectrum showed absorption bands for an ester  $\text{C}=\text{O}$  group ( $1755\text{cm}^{-1}$ ). Comparison of the  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR spectra of **2** (Table) with those of germacrane sesquiterpenoids reported in [3][4][6] indicated closely related structures for these compounds, both displaying two epoxy groups. The  $^1\text{H},^1\text{H}$ -COSY, HMBC (Fig. 2), and NOE data allowed to deduce the structure of **2** as ( $3\beta,4\alpha,6\alpha,8\beta,9\beta,10\alpha$ )-8-(acetyloxy)-3,4:9,10-diepoxygermacr-7(11)-eno-12,6-lactone<sup>1</sup>.

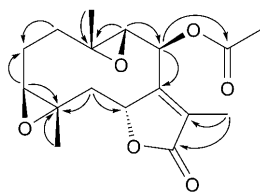


Fig. 2. Key HMBC (H  $\rightarrow$  C) data of **2**

The  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR, and DEPT spectra indicated that **2** possessed 6 quaternary C-atoms and 4 CH, 3  $\text{CH}_2$ , and 4 Me groups and showed characteristic signals for an  $\alpha,\beta$ -unsaturated lactone ( $\delta(\text{C})$  157.3 (*s*), 130.2 (*s*), and 172.3 (*s*)), an Ac group ( $\delta(\text{H})$  2.10 (*s*, 3 H);  $\delta(\text{C})$  20.7 (*q*), and 169.6 (*s*)), four CH–O groups ( $\delta(\text{H})$  2.88 (*dd*,  $J=10.8, 1.8$ ), 5.22 (*dd*,  $J=11.8, 3.9$ ), 6.36 (*s*), and 3.09 (*s*);  $\delta(\text{C})$  67.7 (*d*), 78.6 (*d*), 68.1 (*d*), and 62.1 (*d*)), and two quaternary C–O moieties ( $\delta(\text{C})$  58.2 (*s*) and 63.9 (*s*)). In the gHMBC spectrum, the cross-peaks H–C(3)/C(4) and H–C(9)/C(10) indicated that the two epoxy groups were located at C(3) and C(4), and C(9) and C(10); the cross-peaks  $\text{C}=\text{O}(\text{Ac})/\text{H}-\text{C}(8)$  indicated that the Ac group was linked to C(8) (Fig. 2). The entire sequence of H-atoms at the C-skeleton was established by  $^1\text{H},^1\text{H}$ -COSY and HMBC experiments. In the difference NOE experiment, irradiation of the H–C(8) signal caused NOE enhancements of the signals of H–C(9) and Me(13), irradiation of the H–C(6) signal caused NOE enhancements of the signals of  $\text{H}_b$ -C(5), Me(14), and Me(15), and irradiation of the H–C(9) signal caused NOE enhancements of the signals of  $\text{H}_a$ -C(1),  $\text{H}_a$ -C(2), H–C(3), and  $\text{H}_a$ -C(5).

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### Experimental Part

*General.* Column chromatography (CC): silica gel (SiO<sub>2</sub>, 200–300 mesh; *Qindao Marine Chemical Factory*, P. R. China). TLC: Visualization under UV or by heating at 110° and spraying with 98% H<sub>2</sub>SO<sub>4</sub>/EtOH 5:95. Optical rotations: *Rudolph-Research Autopol-III* automatic polarimeter. IR Spectra: *Nicolet-170SX* FT-IR spectrometer (USA); KBr pellets;  $\tilde{\nu}$  in cm<sup>-1</sup>. <sup>1</sup>H- (400.13 Hz) and <sup>13</sup>C-NMR (100.62 Hz): *Varian Inova-400* FT-NMR spectrometer (USA); in (D<sub>6</sub>)acetone with Me<sub>4</sub>Si as internal standard;  $\delta$  in ppm, *J* in Hz. MS: *VQZAB-2F* or *Autospec-UltimaETOF* mass spectrometer; in *m/z*.

*Plant Material.* The plant material, *Salvia roborowskii* MAXIM, was collected from Zhang County, Gansu Province, P. R. China, in August 2000. The identification was verified by Prof. *Guo-Liang Zhang* (Lanzhou University, P. R. China). A voucher specimen is deposited with the Herbariums of the Institute of Materia Medica, Chinese Academy of Medical Science and Peking Union Medical College.

*Extraction and Isolation.* Air-dried powdered whole plants (10 kg) were extracted with 95% EtOH. The EtOH extract was concentrated to give a residue (300 g) which was subjected to CC (SiO<sub>2</sub>, petroleum ether/AcOEt). The fraction eluted with petroleum ether/AcOEt 9:6 was resubjected for several times to CC (SiO<sub>2</sub>, CHCl<sub>3</sub>/MeOH 7:1): **1** (18 mg) and **2** (20 mg).

(1 $\beta$ ,3 $\beta$ ,4 $\alpha$ ,5 $\alpha$ ,6 $\alpha$ ,8 $\alpha$ )-*Guai-10(14)-ene-3,4,6,8-tetrol 3,6,8-Triacetate* (=rel-(1R,2R,3aR,6R,7S,8-R,8aR)-*Decahydro-1-methyl-4-methylene-7-(1-methylethyl)azulene-1,2,6,8-tetrol 2,6,8-Triacetate*; **1**): Colorless gum.  $[\alpha]_D^{20} = +46$  (*c* = 0.2, CHCl<sub>3</sub>). IR (film): 3483, 2974, 2933, 1726, 1705, 1456, 1377, 1238, 1207, 1055, 1117, 1028, 951, 904, 742, 688, 625, 494. <sup>1</sup>H- and <sup>13</sup>C-NMR: *Table*. FAB-MS: 397.2 ([*M* + H]<sup>+</sup>).

(3 $\beta$ ,4 $\alpha$ ,6 $\alpha$ ,8 $\beta$ ,9 $\beta$ ,10 $\alpha$ )-8-(*Acetyloxy*)-3,4:9,10-diepoxygermacr-7(11)-eno-12,6-lactone (=rel-(1aR,2aS,6R,7aS,9aR)-6-(*Acetyloxy*)-2,2a,6,6a,7a,8,9,9a-octahydro-1a-5,7a-trimethylbisoxireno[4,5:8,9]-cyclodeca[1,2-b]furan-4(1aH)-one; **2**): Colorless gum.  $[\alpha]_D^{20} = +50$  (*c* = 0.12, CHCl<sub>3</sub>). IR (film): 2933, 2871, 1755, 1390, 1388, 1227, 1107, 1003, 918, 891, 795, 754, 737. <sup>1</sup>H- and <sup>13</sup>C-NMR: *Table*. FAB-MS: 323.0 ([*M* + H]<sup>+</sup>).

### REFERENCES

- [1] The Edition Commission of Chinese Herbal, 'The Herbal of China', Science and Technology Press of Shanghai, Shanghai, 1999, p. 6197.
- [2] S. F. Wang, S. Li, Z. G. Li, *Pharmazie* **2001**, *56*, 420.
- [3] Y. Li, Y. Q. Wu, X. Du, Y. P. Shi, *Planta Med.* **2003**, *69*, 782.
- [4] A. F. Barrero, M. M. Herrador, J. F. Quilez, R. A. Manzaneda, D. Portal, J. A. Gavin, D. G. Gravalos, M. S. J. Simmonds, W. M. Blaney, *Phytochemistry* **1999**, *51*, 529.
- [5] A. Giovanni, P. Tettamanzi, P. Gariboldi, *J. Chem. Soc., Perkin Trans. 1* **1990**, *7*, 2139.
- [6] B. Ferdinand, J. Jakupovic, M. Ahmed, A. Schuster, *Phytochemistry* **1983**, *22*, 1623.

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