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Phytochemistry 67 (2006) 2103–2109
PHYTOCHEMISTRY
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α-Pinene-type monoterpenes and other constituents from *Artemisia suksdorfii*

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Received 9 May 2006; received in revised form 7 June 2006
Available online 24 July 2006

Abstract

Two α-pinene-type monoterpenes, 7-hydroxymyrtenol (**1**) and 7-hydroxymyrtenal (**2**), a inositol derivative, (+)-quebrachitol (**3**) and two *p*-menthene triols (**4** and **5**), in addition to two known compounds were isolated from the aerial parts of *Artemisia suksdorfii*. The structures of the isolated compounds were established by analysis of spectroscopic data (IR, HR-MS, ^{1}H and ^{13}C NMR), including high-field 2D NMR techniques (^{1}H–^{1}H COSY, HMQC, HMBC and NOE) and in case of **3** was confirmed by X-ray analysis.

Keywords: *Artemisia suksdorfii*, *Astereacea*; Monoterpenes; α-Pinene; 7-Hydroxymyrtenol; 7-Hydroxymyrtenal; Inositol; (+)-Quebrachitol; *p*-Menthene

1. Introduction

The genus *Artemisia*, of the family Asteraceae, tribe Anthemideae, is a large genus with about 400 species widely distributed in Europe, North America, Asia and South Africa (Heywood and Humphries, 1977; Marco and Barbeŕa, 1990). Species of this genus are important medicinal plants and have been used by many cultures in folk and modern medicine due to their medical interest (Tan et al., 1998). Herbal teas from those species have been used as analgesic, antiplasmodic, anthelminitic, antidiarroheic and a diuretic agent (Benjumea et al., 2005; Tan et al., 1998; Darias et al., 1986), while several extracts and essential oils showed a number of biological activities such as antihyperglycemic (Ribnicky et al., in press), antimicrobial (Setzer et al., 2004) antioxidant (Kordali et al., 2005; Kim et al., 2003; El-Massry et al., 2002) and anti-inflammatory (Guardia et al., 2003; Mĩno et al., 2004). Furthermore, some species of this genus are frequently utilized for the treatment of some diseases such as malaria, hepatitis, cancer and infections by fungi, bacteria, and viruses (Wilairatana and Looareesuwan, 2002; Willcox and Bodeker, 2004; Mueller et al., 2000; Tan et al., 1998; Dhingra et al., 2000; Lee et al., 2002, 2003; Kim et al., 2002; Lee and Lin, 1988; Seo et al., 2003). Chemically, *Artemisia* has been a productive genus in the search for new chemical constituents and biologically active compounds. Therefore, many species of the world have been subjected to extensive phytochemical investigations. The studies showed that this genus is rich in sesquiterpenoids, monoterpenoids, flavonoids and coumarins (Marco and Barbeŕa, 1990; Tang et al., 2000; Tan et al., 1998, 1999; Marco et al., 1998; Ahmed et al., 2004, 1990). In our previous studies on this genus, we reported the isolation and structure elucidation of five new polyol monterpenes, several new sesquiterpene lactones and some known compounds from the aerial parts of *Artemisia suksdorfii* and *Artemisia herba-alba* (Ahmed et al., 2004; Ahmed et al., 1990). In continuation of our studies and searching for new constituents, we have now reinvestigated the extract of the aerial parts of *A. suksdorfii* Piper, a native perennial of the coastal Pacific Northwest area of the United States. The isolation and characterization of

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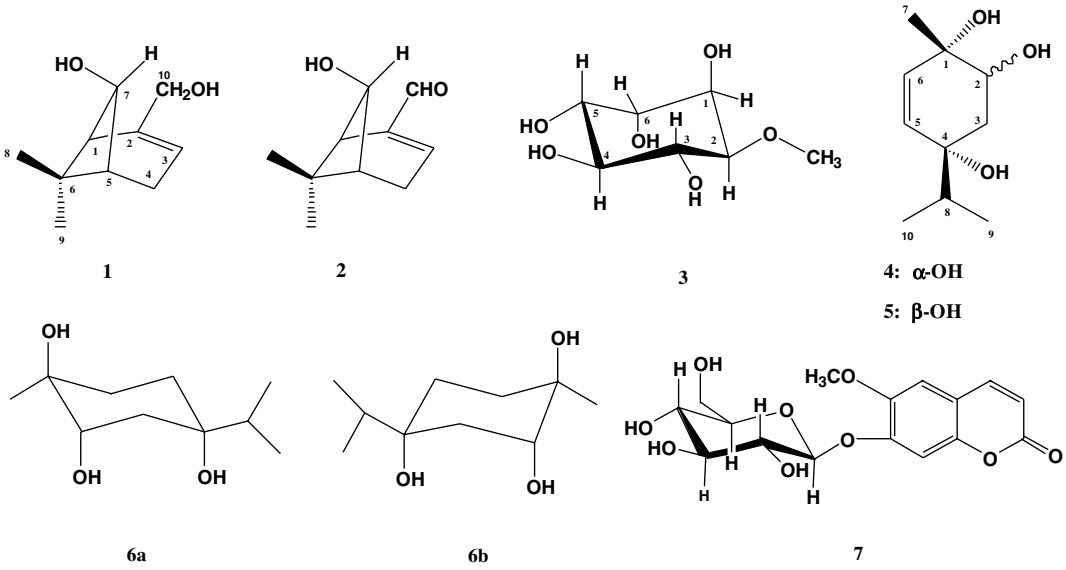
doi:10.1016/j.phytochem.2006.06.013



two new α-pinene-type monoterpenes, 7-hydroxymyrtenol (**1**) and 7-hydroxymyrtenal (**2**), a new inositol derivative, (+)-quebrachitol (**3**) and two *p*-menthene triols, (+) (1*S**, 2*R**, 4*R**)-trihydroxy-*p*-menth-5-ene (**4**) and (−) (1*S**, 2*S**, 4*R**)-trihydroxy-*p*-menth-5-ene (**5**), in addition to the known compounds (+) (1*R**, 2*R**, 4*R**)-trihydroxy-*p*-menth-3-ene (**6a**) (Cristea et al., 2002) and scopolin (**7**) have been reported.

2. Results and discussion

Repetitive chromatographic steps of the methanol–dichloromethane (1:1) extract of the aerial parts of *A. suksdorfii* yielded compounds **1**–**7**. The structural characterization of these compounds utilized spectroscopic techniques (high-resolution 2D NMR measurements, HMQC, HMBC, COSY, NOE and HRMS), and X-ray crystallography for **3**.

7-Hydroxymyrtenol (**1**) was isolated as colorless oil (0.002%). The molecular formula was established as $C_{10}H_{16}O_2$ by high resolution positive-ion CI-MS, which showed a $[M+H]^+$ peak at *m*/*z* 169.1238; Calc. 169.1228. This formula was confirmed by ^{13}C NMR and DEPT spectroscopic analysis suggesting the presence of a monoterpene derivative. The fragmentation pattern of the mass spectrum exhibited two ion peaks at *m*/*z* 151 $[M-18+H]^+$ (100%) and 133 $[M-36+H]^+$ (95%), corresponding to the loss of one and two water molecules, respectively. This suggested that the two oxygen-containing functionalities were hydroxyl groups. The IR spectrum supported this result by a strong absorption at $\nu = 3400\ cm^{-1}$ (OH). The ^{13}C NMR spectrum of **1** (Table 1), together with the information from the DEPT spectrum, showed the presence of 10 carbon signals assigned to two CH_3 groups (δ 23.1 and 26.9), two CH_2 groups including one bearing oxygen (δ 65.1 and 31.9), four CH groups including one olefinic and one bearing oxygen (δ 119.4, 78.2, 49.5 and 46.3) and two quaternary carbons including one olefinic (δ 145.7 and 36.9). The ^1H NMR spectrum of **1** showed the presence of two tertiary methyl groups [δ 0.80 (*s*) and 1.49 (*s*)], an olefinic proton (δ 5.38), a hydroxymethylene group (δ 3.84, 2H), a proton geminal to a hydroxyl group (δ 3.84), while the remaining signals were assigned to an aliphatic methylene group (δ 2.24, 2H, *m*) and two aliphatic methine protons (δ 2.09 and 1.93). The assignments of all these protons in **1** and their connectivities to adjacent protons and carbons were determined from the results of the 2D ^1H–^1H COSY and HMQC experiments. In the ^1H–^1H COSY spectrum, the olefinic proton at δ 5.38 (*br s*, H-3) was coupled to the allylic oxymethylene protons at δ 3.84 (*m*, H-10) and the aliphatic methylene protons at δ 2.24 (*m*, H-4). The H-4 was coupled to the proton at δ 1.93 (*m*, H-5) which was coupled to the aliphatic proton at δ 2.09 (*d*, $J = 7.0$ Hz, H-1), which was in turn coupled to the oxymethine proton at δ 3.84 (*br s*, H-7). These data revealed the presence of two segments, (A) —CH_2(O)—C(R)=CH—CH_2—CH(R)— and (B) —CH(O)—CH(R)—. The connection between these segments (A) and (B) through the methyl groups and the quaternary carbon (C-6) was established from the HMBC experiments. The two methyl groups at δ_H 1.49 (CH_3-8) and 0.80 (CH_3-9), showed HMBC correlations with their corresponding carbons at δ 26.9 (C-8) and 23.1 (C-9), in addition to a similar set of correlations with the quaternary carbon at δ 36.9 (C-6) and the methine carbons at δ 49.5 (C-1) and 46.3 (C-5). Furthermore, the two aliphatic methine protons H-1 (δ 2.09) and H-5 (δ 1.93) showed HMBC correlations with the quaternary carbon C-6 at δ 36.9. Attaching the quaternary carbon (C-6) to C-1 and C-5 and the methyl carbons (CH_3-8 and CH_3-9) to C-6 indicated that the monoterpene structure was α-pinene. Among 16 protons in the molecular formula ($C_{10}H_{16}O_2$), 14 protons were fitted to their carbons

Table 1
^{1}H, ^{13}C and HMBC spectral data of compounds **1**–**3** ($CDCl_3$, 500 MHz, δ ppm)[a]

Position	δ_C	DEPT	δ_H (mult., J in Hz)	HMBC
*7-Hydroxymyrtenol (**1**)*				
1	49.5	CH	2.09 (1H, *d*, $J = 7.0$ Hz)	C-2, C-3, C-5, C-6, C-7, C-8, C-10
2	145.7	C	–	
3	119.4	CH	5.38 (1H, *br s*)	C-1, C-5, C-10
4	31.9	CH_2	2.24 (2H, *m*)	C-2, C-3, C-5 C-6, C-7
5	46.3	CH	1.93 (1H, *m*)	C-1, C-3, C-7, C-9
6	36.9	C	–	–
7	78.2	CH	3.84 (1H, *br s*)	C-2, C-4, C-6
8	26.9	CH_3	1.49 (3H, *s*)	C-1, C-5, C-6, C-9
9	23.1	CH_3	0.80 (3H, *s*)	C-1, C-5, C-6, C-8
10	65.1	CH_2	3.84 (2H, *m*)	C-1, C-2, C-3
*7-Hydroxymyrtenal (**2**)*				
1	44.3	CH	2.84 (1H, *d*, $J = 7.0$ Hz)	C-2, C-3, C-5, C-6, C-7, C-8, C-10
2	149.5	C	–	–
3	149.3	CH	6.76 (1H, *br s*)	C-1, C-5, C-10
4	33.6	CH_2	2.64 (2H, *m*)	C-2, C-3, C-5 C-6, C-7
5	48.5	CH	2.11 (1H, *m*)	C-1, C-3, C-9
6	36.6	C	–	–
7	77.5	CH	3.78 (1H, *br s*)	C-2, C-4, C-6
8	26.4	CH_3	1.63 (3H, *s*)	C-1, C-5, C-6, C-9
9	22.9	CH_3	0.80 (3H, *s*)	C-1, C-5, C-6, C-8
10	191.0	CH	9.38 (1H, *s*)	C-1, C-2, C-3
*(+)-Quebrachitol (**3**)*[b]				
1	69.2	CH	4.12 (1H, *t*, $J = 3.5$)	C-2, C-3, C-5, C-6
2	82.4	CH	3.33 (1H, *dd*, $J = 9.5, 3.5$)	C-1, C-3, C-4, O-Me
3	73.7	CH	3.60 (1H, *t*, $J = 9.5$)	C-2, C-4, C-5
4	74.6	CH	3.56 (1H, *t*, $J = 9.5$)	C-2, C-3, C-5
5	72.3	CH	3.68 (1H, *dd*, $J = 9.5, 3.6$)	C-3, C-4
6	73.2	CH	3.94 (*t*, $J = 3.6$)	C-1, C-2, C-4, C-5
–OMe	57.8	CH_3	3.45 (3H, *s*)	C-2

[a] Assignments of all protons and carbons were deduced from ^{1}H–^{1}H COSY, HMQC and HMBC experiments. Carbon multiplicities were determined by DEPT experiments.
[b] $CDCl_3$, 600 MHz.

by the HMQC spectrum. The remaining two protons were assignable to two hydroxyl groups based on the MS and IR spectroscopic data in addition to the ^{1}H and ^{13}C chemical shifts of the signals at δ_H 3.84/δ_C 78.2 and δ_H 3.84/δ_C 65.1. The presence of a hydroxylmethyl group on C-10 was elucidated from the hydroxymethylene protons at δ 3.84 (H-10), which correlated in the HMQC spectrum with a hydroxymethylene carbon signal at δ 65.1, while in the HMBC spectrum showed long-range correlations with the methine carbon C-1 (δ 49.5) and with the olefinic signals C-2 (δ 145.7) and C-3 (δ 119.4). The second hydroxyl group was located at C-7 based on the methine proton signal at δ 3.84 (H-7), which correlated in the HMQC spectrum with a methine carbon signal at δ 78.2, while in the HMBC spectrum it showed connections to C-2 (δ 145.7), C-4 (δ 31.9) and C-6 (δ 36.9). The relative stereochemistry of **1** was determined from the NOE measurements (Fig. 1) with inspection of the Dreiding model, H-7/H-3, H-7/H-4β, H-1/H-8β, H-5/H-8β and H-4α/H-9 showed correlation with each other. In addition, the *J*-value of 7.0 Hz for the coupling between H-1 and H-5 supported also the β orientation of these protons (Van Dyk et al., 1998; Saad et al., 2000). Therefore, **1** was identified as 2-hydroxymethyl-6,6-dimethyl-bicyclo[3.1.1]hept-2-en-7-ol, and was named 7-hydroxymyrtenol.

7-Hydroxymyrtenal (**2**) was isolated as colorless gum (0.0015%). The molecular formula was determined as $C_{10}H_{14}O_2$ by high resolution positive-ion CI-MS, which showed a $[M+H]^+$ peak at *m*/*z* 167.1070; Calc. 167.1072. The fragmentation pattern of the mass spectrum exhibited $[M-H_2O+H]^+$ ion peak at *m*/*z* 149 (70%) and $[M-H_2O-CHO+H]^+$ ion peak at *m*/*z* 121 (30%), which suggested the presence of a hydroxyl group and an aldehydic function. The IR spectrum supported this result and showed characteristic bands for a hydroxyl group (3390 cm^{-1}) and an α,β-unsaturated aldehydic carbonyl group (1682 cm^{-1}). The structure of **2** was established from the ^{1}H and ^{13}C NMR spectra (Table 1) which were quite similar to those of 7-hydroxymyrtenol (**1**), except for the signals attributable to the hydroxylmethylene group, which in the case of

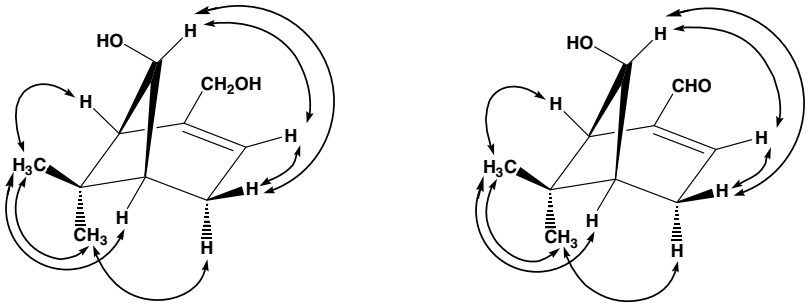


Fig. 1. NOE correlations of compounds **1** and **2**.

compound **2** indicated the presence of aldehyde (^{1}H; 9.38, *s*, ^{13}C; 191.0). The assignments of all protons in **2** and their connectivity to adjacent protons and carbons were determined by the 2D ^{1}H–^{1}H COSY, HMQC, while the complete structure was confirmed by HMBC experiments (Table 1). The relative stereochemistry of **2** was determined to be the same as that of **1** from the NOE measurements (Fig. 1) and the coupling constants. Therefore, **2** was identified as 7-hydroxy-6,6-dimethyl-bicyclo[3.1.1]hept-2-ene-2-carbaldehyde, and was named 7-hydroxymyrtenal.

Compound **3** was isolated as colorless crystals (0.005%) with $[\alpha]_D^{25} + 20.0$ (*c* 2.0, MeOH). The molecular formula was established as $C_7H_{14}O_6$ on the basis of CIMS, ^{13}C and DEPT NMR analysis (Table 1). The CI-MS exhibited an ion peak $[M+H]^+$ at *m/z* 195 (100%). The ^{13}C NMR spectrum showed seven carbon signals, while their multiplicities were assigned by DEPT analysis as six oxygenated CH groups (δ 82.4–69.2) and one OCH_3 group (δ 57.8). The ^{1}H NMR spectrum showed the presence of a methoxyl group at δ 3.45 (3H, *s*) and six oxymethine protons at δ 4.12 (1H, *t*, $J = 3.5$ Hz), 3.94 (1H, *t*, $J = 3.6$ Hz), 3.68 (1H, *dd*, $J = 9.6$, 3.6 Hz), 3.60 (1H, *t*, $J = 9.5$ Hz), 3.56 (1H, *t*, $J = 9.5$ Hz) and 3.33 (1H, *dd*, $J = 9.5$, 3.5 Hz). These ^{1}H and ^{13}C NMR spectral data were similar to those reported for 2-*O*-methyl-*chiro*-inositol [(−)-quebrachitol] (Abraham et al., 2005; Sureshan et al., 2004; Clark, 1936). The major difference between **3** and (−)-quebrachitol [−81.2°, *c* (10, H_2O)] was the sign of the optical rotation. The positive sign [+20.4 (*c* 2.0, MeOH)] for **3** clearly indicated that it was the (+) enantiomer of (−)-quebrachitol. Finally, the complete structure and the relative stereochemistry were confirmed by solving its single crystal X-ray structure (Fig. 2). Therefore, **3** was identified as (+)-2-*O*-methyl-*chiro*-inositol [(+)-quebrachitol)] which has not been previously isolated.

Compound **4** was isolated as colorless oil (0.0017%) with $[\alpha]_D^{25} + 37.0$ (*c* 0.4, MeOH). The molecular formula was established as $C_{10}H_{18}O_3$ on the basis of HRCI-MS, ^{13}C and DEPT NMR analysis (Table 2). The CIMS exhibited an ion peak $[M-H_2O+H]^+$ at *m/z* 169 ($C_{10}H_{16}O_2$), followed by a fragment at *m/z* 151 $[M-2H_2O+H]^+$. The ^{13}C and DEPT spectra exhibited 10 carbons as: three CH_3 groups, one aliphatic CH_2 group, two olefinic CH groups,

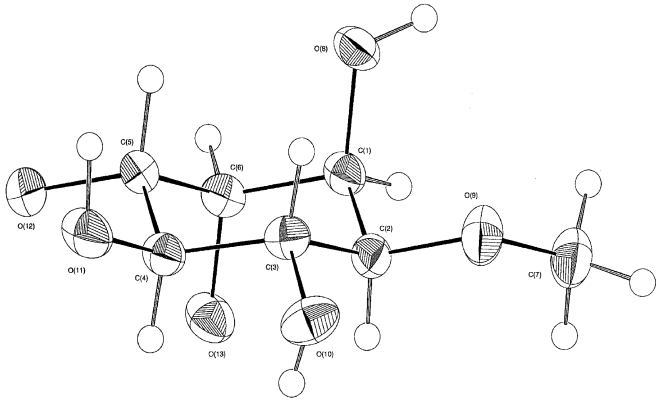


Fig. 2. ORTEP diagram of the crystal structure of **3**.

Table 2
^{1}H NMR spectral data of compounds **4**–**6a** ($CDCl_3$, 500 MHz, δ ppm)[a]

Protons	δ_H (mult., *J* in Hz)		
	4	**5**	**6a**
H-2	3.64 (*dd*, $J = 1.5$, 1.5 Hz)	3.96 (*dd*, $J = 13.0$, 4.0 Hz)	3.52 *br s*
H-3α	2.01 (*dd*, $J = 14.0$, 1.5 Hz)	1.72 (*ddd*, $J = 13.0$, 4.0, 1.5 Hz)	1.69 (*ddd*, $J = 14.5$, 3.0, 3.0 Hz)
H-3β	1.58 (*dd*, $J = 14.0$, 1.5 Hz)	1.59 (*dd*, $J = 13.0$, 13.0 Hz)	1.95 (*ddd*, $J = 14.5$, 14.0, 5.4 Hz)
H-5α	5.54 (*d*, $J = 11.5$ Hz)	5.40 (*dd*, $J = 10.0$, 1.5 Hz)	1.93 (*m*)
H-5β			1.78 (*ddd*, $J = 14.5$, 14.0, 4.0 Hz)
H-6	5.46 (*d*, $J = 11.5$ Hz)	5.62 (*d*, $J = 10$ Hz)	1.44 (*m*)
H-7	1.18 (*s*)	1.13 (*s*)	1.28 (*s*)
H-8	1.58 (*qq*, $J = 7.0$, 7.0 Hz)	1.67 (*m*)	1.59 (*m*)
H-9	0.81 (*d*, $J = 7.0$ Hz)	0.90 (*d*,$J = 7.0$ Hz)	0.91 (*d*, $J = 7.5$ Hz)
H-10	0.76 (*d*, $J = 7.0$ Hz)	0.81 (*d*, $J = 7.0$ Hz)	0.91 (*d*, $J = 7.5$ Hz)

[a] Assignments of all protons were deduced from ^{1}H–^{1}H COSY, HMQC, HMBC and NOE experiments.

two CH groups (one bearing oxygen), and two quaternary carbons bearing oxygen. The ^{1}H NMR spectrum of **4** exhibited two olefinic protons at δ 5.54, and 5.46 (each *d*, $J = 11.5$ Hz, H-5 and H-6). The narrow double doublet oxymethine signal at δ 3.64 (1H, $J = 1.5$, 1.5 Hz, H-2) showed correlations in the ^{1}H–^{1}H COSY spectrum with two signals at δ 2.01 (*dd*, $J = 14.0$, 1.5 Hz, H-3α) and 1.58 (*dd*, $J = 14.0$, 1.5 Hz, H-3β). The small couplings of H-2 (1.5 and 1.5 Hz) with H-3α and H-3β were in accord with equatorial–equatorial and equatorial–axial orientation, respectively. The isopropyl group was detected as two methyl doublet at δ 0.81 (H-9) and 0.76 (H-10), which showed couplings in the ^{1}H–^{1}H COSY spectrum with a methine proton at δ 1.58 (H-8). In the HMBC spectrum, the isopropyl protons (H-8, H-9 and H-10) correlated with the carbon signal at δ 72.4 (C-4), and H-7 correlated with the carbon signal at δ 69.7 (C-1) and 73.3 (C-2), while H-8 correlated with the olefinic carbon at δ 133.1 (C-5). Finally, the relative stereochemistry of **1** was determined by NOE experiments, H-7/H-2, H-2/H-3β and H-3β/H-8 correlated with each other, which suggested the β-orientation of the protons. Therefore, **4** was identified as (1*S**, 2*R**, 4*R**)-trihydroxy-*p*-menth-5-ene.

Compound **5** was isolated as colorless oil (0.0015%) with $[\alpha]_D^{25} - 24.0$ (*c* 0.5, MeOH). The ^{13}C, DEPT and CIMS data suggested the same monoterpene skeleton as **4**. However, the pronounced difference in the coupling constant of H-2 (13.0 and 4.0 Hz), in **4**, compared to **3** (1.5 and 1.5 Hz) supported the epimeric stereochemistry at C-2. This difference in hydroxyl position resulted in observable changes in the chemical shifts of the carbon signals (Table 3). The two oxygenated quaternary carbons (C-1 and C-2) and the two olefinic carbons (C-5 and C-6) were distinguished from each other by HMBC experiments, H-7/C-6, H-3/C-5, H-3/C-4 and H-9, H-10/C-4 showed correlation with each other. Additionally, the relative stereochemistry of the chiral centers were established from NOE experiments, H-7/H-3β, H-3β/H-9, H-10 showed correlation with each other which indicated the β-orientation of the protons. Therefore, **5** was identified as (1*S**, 2*S**, 4*R**)-trihydroxy-*p*-menth-5-ene.

Compounds **4** and **5** have been identified in literature by names from the essential oil of *Chenopodium multifidum* (De Pascual et al., 1981). However, NMR data were not provided and as such, we report both compounds as new natural products. Some monoterpene glucosides with closely related structures to **4** and **5** were isolated from cumin (Ishikawa et al., 2002).

Compound **6** was isolated as white powder (0.0018%) with $[\alpha]_D^{25} + 20.0$ (*c* 0.5, MeOH). The molecular formula was found to be $C_{10}H_{20}O_3$ on the basis of HRCI-MS which gave ion peak $[M+H]^+$ at *m*/*z* 189.1484. Its IR, MS and ^{1}H, ^{13}C NMR spectral data (Table 2 and 3) were found to be consistent with those reported for (1*R**, 2*R**, 4*R**)-trihydroxy-*p*-menthane (Harkenthal et al., 2000; Garg et al., 1989; Kitajima et al., 1998). Two enantiomers, **6a** and **6b**, could be suggested for **6**, however the positive sign of the optical rotation agreed with the **6a** structure (Cristea et al., 2002).

3. Experimental

3.1. General experimental procedures

The ^{1}H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$), and 2D spectra were measured with a Varian 500 spectrometer, with TMS as internal standard. The IR spectra (oily film, $CHCl_3$) were taken on a Perkin–Elmer FT-IR spectrophotometer. Mass spectra were recorded with a TSQ-70-Triple Stage Quadrupole mass spectrometer 70 eV). TLC: precoated silica gel $60F_{254}$ plate (Merck); preparative TLC: silica gel PF_{254} (Merck, $200 \times 200 \times 0.25$ mm); CC: silica gel type 60 (Merck). Optical rotation was determined with a JASCO-20C automatic recording spectropolarimeter.

3.2. Plant material

The aerial parts of *A. suksdorfii* were collected by Mr. George Sturtz during the flowering stage, July 2003, in Linn County, OR, USA. A voucher specimen (192499) has been deposited at Department of Forest, Oregon State University Herbarium, USA.

3.3. Extraction and separation

The air-dried aerial parts (600 g) were powdered and extracted with CH_2Cl_2–MeOH (1:1) (5 L) at room temperature, and the extract was concentrated to obtain 35 g of residue. The extract was prefractionated by column chromatography (6×100 cm) on silica gel (600 g) eluting with *n*-hexane and a gradient of *n*-hexane–CH_2Cl_2 up to 100% CH_2Cl_2 and CH_2Cl_2–MeOH (2 L of each solvent mixture) resulting in five fractions: fr. 1 (*n*-hexane–CH_2Cl_2 3:1), fr. 2 (*n*-hexane–CH_2Cl_2 1:1), fr. 3 (*n*-hexane–CH_2Cl_2 3:1), fr. 4 (Et_2O 100%), fr. 5 (Et_2O–MeOH 9:1). Fractions 3 and 4 were collected and separated on silica gel column (600 g, 5×100 cm) eluted with *n*-hexane–CH_2Cl_2 (1:1) (ca. 500 mL × 2) to give fractions 1-A and 1-B. Fraction 1-A was further purified on a Sephadex LH-20 column (250 g, 4×90 cm) eluted with *n*-hexane–CH_2Cl_2–MeOH (5:7:0.5) to afford **1** (12 mg), and **2** (9 mg). Fr. 5 was separated on silica gel column (600 g, 5×100 cm) eluted with *n*-hexane–CH_2Cl_2–MeOH (1:2:0.5) (ca. 500 mL × 3) to give three fractions (5A–5C). Fraction 5A was further purified on a sephadex LH-20 column (250 g, 4×90 cm) eluted with *n*-hexane–CH_2Cl_2–MeOH (4:7:1) followed by preparative TLC (silica gel PF_{254}) eluted with petroleum ether–Et_2O–MeOH (1:4:0.5) gave **4** (10 mg), **5** (9 mg) and **6b** (11 mg). Fraction 5C was further purified on a sephadex LH-20 column (250 g, 4×90 cm) eluted with *n*-hexane–CH_2Cl_2–MeOH (4:7:2) to give **3** (30 mg) and **7** (14 mg).

3.4. 2-Hydroxymethyl-6,6-dimethyl-bicyclo[3.1.1]hept-2-en-7-ol (7-hydroxymyrtenol) (**1**)

Colorless oil; $[\alpha]_D^{25} + 15.6$ (*c* 2.0, MeOH); IR ν_{max} (CH_3Cl, film) 3400 (OH), 2930, 1378, 1030 cm^{-1}; HRCI-MS *m/z* 169.1238 (Calc. for $C_{10}H_{17}O_2$, 169.1228); CI-MS *m/z* (rel. int.) 169 $[M+H]^+$ (12), 151 $[M-H_2O+H]^+$ (100), 133 $[M-2H_2O+H]^+$ (95), 123 (50), 121 (35), 107 (35), 95 (35); ^1H, ^{13}C NMR and HMBC, see Table 1.

3.5. 7-Hydroxy-6,6-dimethyl-bicyclo[3.1.1]hept-2-ene-2-carboaldehyde (7-hydroxymyrtenal) (**2**)

Colorless oil; $[\alpha]_D^{25} - 5.1$ (*c* 2.0, $CHCl_3$); IR ν_{max} (CH_3Cl, film) 3390 (OH), 2928, 1682 (α,β-unsaturated CHO), 1456, 1059 cm^{-1}; HRCI-MS *m/z* 167.1070 (Calc. for $C_{10}H_{15}O_2$, 167.1072); CI-MS *m/z* (rel. int.) 167 $[M+H]^+$ (100), 149 $[M-H_2O+H]^+$ (70), 121 $[M-H_2O-CHO+H]^+$ (30), 107 (10); ^1H, ^{13}C NMR and HMBC, see Table 1.

3.6. (+)-2-O-methyl-chiro-inositol [(+)-quebrachitol] (**3**)

Colorless crystal; $[\alpha]_D^{25} + 20$ (*c* 2.0, MeOH); CI-MS *m/z* (rel. int.) 195 $[M+H]^+$ (100), 177 $[M-H_2O+H]^+$ (18), 159 $[M-2H_2O+H]^+$ (45), 127 (85), 109 (44), 87 (28); ^1H, ^{13}C NMR and HMBC, see Table 1.

3.6.1. X-ray crystallography data of **3**

Crystal data: $C_7H_{14}O_6$, mol. wt. = 194.1825, monoclinic space group $P2_1$, $a = 6.6920(5)$ Å, $b = 7.1990(5)$ Å, $c = 8.7350(8)$ Å, $\alpha = 90.00°$, $\beta = 90.202$ (3)°, $\gamma = 90.00°$, $V = 420.81(6)$ Å^3, $Z = 2$, $D_c = 1.533$ Mg m^{-3}, $M_r = 194.183$. All diagrams and calculations were performed using maXus (Bruker Nonius, Delft & Mac Science, Japan). The intensity data of all unique reflections within the $\theta_{max} = 25.69°$ were collected at 293 K, using graphite monochromated Mo Kα ($\lambda = 0.71073$ Å) radiation. A total of 2525 independent reflections were measured, and 1519 were considered to be observed. The structures were refined by full-matrix least-squares on F^2 using method SHELXL-97 (Sheldrick, 1997). Crystallographic data for the structural analysis have been deposited at the Cambridge crystallographic data center (CCDC) (Deposition No. CCDC 251558). These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving/html (or from the CCDC, 12 union Road; Cambridge CB2 1EZ, UK; fax: +44 1223 336 033; e-mail: deposit@ccdc.cam.ac.uk).

3.7. (+) (1S*, 2R*, 4R*)-trihydroxy-p-menth-5-ene (**4**)

Colorless oil; $[\alpha]_D^{25} + 37$ (*c* 0.4, MeOH); IR ν_{max} (KBr, film) 3360, 2961, 1371, 1059 cm^{-1}; HRCI-MS *m/z* (rel. int.) 169.12318 (Calc. for $C_{10}H_{17}O_2$, 169.12285); CI-MS *m/z* (rel. int.) 169 $[M-H_2O+H]^+$ (68), 151 $[M-2H_2O+H]^+$ (100); ^1H and ^{13}C NMR, see Tables 2 and 3.

Table 3
^{13}C NMR spectral data and DEPT analysis of compounds **4**–**6a** ($CDCl_3$, 125 MHz, δ-values)

Carbons[a]	4	5	6a	(DEPT)
1	69.7	73.2	71.6	C
2	73.3	71.9	75.3	CH
3	32.6	35.8	35.0	CH_2
4	72.4	74.6	75.0	C
5	133.1 CH	130.2 CH	30.6 CH_2	
6	132.0 CH	135.9 CH	30.5 CH_2	
7	24.4	19.6	27.8	CH_3
8	36.9	37.5	39.0	CH
9	17.0	17.3	17.5	CH_3
10	16.1	15.9	17.4	CH_3

[a] All assignments were based on 1D and 2D NMR.

3.8. (−) (1S*, 2S*, 4R*)-trihydroxy-p-menth-5-ene (**5**)

Colorless oil; $[\alpha]_D^{25} - 24$ (*c* 0.5, MeOH); IR; CI-MS and HRCI-MS; the same as **4**; ^1H and ^{13}C NMR, see Tables 2 and 3.

3.9. (+) (1R*, 2R*, 4R*)-trihydroxy-p-menth-3-ene (**6a**)

White powder; $[\alpha]_D^{25} + 20$ (*c* 0.5, MeOH); IR ν_{max} (KBr, film) 3345, 2910, 2400 cm^{-1}; HRCI-MS *m/z* (rel. int.) 189.1484 (Calc. for $C_{10}H_{21}O_3$, 189.1490); CIMS *m/z* (rel. int.) 189 $[M+H]^+$ (16), 171 $[M-H_2O+H]^+$ (100), 153 $[M+2H_2O+H]^+$ (78); ^1H and ^{13}C NMR, see Tables 2 and 3.

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