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Sesquiterpene lactones from *Carpesium triste* var. *manshuricum*

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Abstract

The whole plants of *Carpesium triste* var. *manshuricum* afforded two known and two new germacranolides, 2α,5-epoxy-5,10-dihydroxy-6α-angeloyloxy-9β-(2-methylbutyloxy)-germacran-8α, 12-olide and 2α,5-epoxy-5,10-dihydroxy-6α-angeloyloxy-9β-(3-methylbutyloxy)-germacran-8α, 12-olide. Their structures were established by physicochemical and spectroscopic methods.

Keywords: *Carpesium triste* var. *manshuricum*; Compositae; Sesquiterpene lactones; Germacranolides

1. Introduction

Carpesium triste var. *manshuricum* K. is a plant which is rare in Korea, and it has long been used as traditional medicinal herb for its antipyretic, analgesic, vermifugic, insecticidal, pain-relief, and antiinflammatory properties (Lee, 1993; Zhu, Wu & Li, 1989). Several sesquiterpene lactones were isolated from the genus *Carpesium*; granilin (Maruyama & Shibata, 1975), carabrone (Maruyama & Omura, 1977), carabrol, ivaxillin, eriolin, 11(13)-dehydroivaxillin (Maruyama, Karube & Sato, 1983), and ivalin from *Carpesium abrotanoides*; divaricin A, B and C (Maruyama, 1990) and the 2β, 5β isomer of divaricin B (Kim, Lee & Zee, 1997) from *Carpesium divaricatum*; ineupatorolide A and B (Maruyama et al., 1995) from *Carpesium glossophyllum*; nepalolide A, B, C and D (Lin, Ou, Kuo, Lin & Lee, 1996) from *Carpesium nepalense*. However there are no reports on the components of *Carpesium triste* var. *manshuricum*.

In the course of our systematic phytochemical investigation of the Korean genus *Carpesium,* four sesquiterpene lactones were isolated from the $CHCl_3$ extract of *Carpesium triste* var. *manshuricum*. This paper reports the isolation of two known (**1** and **2**) sesquiterpene lactones (Maruyama, 1990; Kim et al., 1997) along with the isolation and structural elucidation of two new ones (**3** and **4**).

2. Results and discussion

Repeated column chromatography of the $CHCl_3$ fraction of the MeOH extract of the plant yielded four sesquiterpene lactones. The structures of compounds **1** (Kim et al., 1997) and **2** (Maruyama, 1990) were established by comparison of their mps, UV, IR and NMR spectral data with those reported in the literature.

Compound **3** was assigned the molecular formula $C_{25}H_{37}O_9$ $[M+H]^+$ (m/z 481.2438) by HRFAB-mass spectrometry. Its IR spectrum revealed the presence of an α-methylene-γ-lactone moiety (1773 cm^{-1}) and hydroxyl groups (3502 cm^{-1}) (Baruah, Sharma & Thyagarajan, 1980; Baruah, Baruah, Sharma & Baruah, 1982). The ^1H NMR and ^{13}C NMR spectra (Table 1) were very similar to those of **2** except for the presence of the signals of a 2-methylbutanoyl group. 2-

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Table 1
^{1}H NMR and ^{13}C NMR chemical shifts of compounds **3** and **4** (**3**: CD_3OD, **4**: $CDCl_3$, ^{1}H: 600 MHz, ^{13}C: 150 MHz) (values in parentheses are coupling constants in Hz)

	[3]		[4]	
	^{1}H	^{13}C	^{1}H	^{13}C
1a	2.09 *dd* (15.7, 12.2)	45.3	1.83 *m*	43.8
1b	1.65 *dd* (15.7, 4.1)		1.73 *m*	
2	4.59 *m*	75.2	4.71 *m*	73.9
3a	1.95 *m*	38.7	2.02 *m*	37.4
3b	1.80 *m*		1.76 *m*	
4	2.75 *m*	37.3	2.56 *m*	36.6
5	–	107.2	–	106.1
6	5.19 *d* (10.8)	77.2	5.25 *d* (10.6)	75.6
7	3.36 *dd* (10.8, 1.1)	46.5	3.09 *d* (10.6)	45.0
8	5.28 *dd* (9.9, 1.1)	79.4	5.23 *d* (10.1)	77.4
9	4.62 *d* (10.0)	79.6	4.62 *d* (10.1)	77.9
10	–	72.7	–	72.0
11	–	136.1	–	133.1
12	–	171.4	–	168.4
13a	6.13 *d* (1.5)	126.9	6.32 *d* (1.6)	127.2
13b	5.70 *d* (1.5)	–	5.66 *d* (1.6)	
14	1.23 *s*	30.8	1.24 *s*	30.8
15	1.16 *d* (7.0)	15.1	1.16 *d* (6.5)	14.4
1′	–	178.1	–	172.5
2′	2.49 *m*	42.6	2.37 *dd* (15.2, 7.2)	43.0
	–	–	2.27 *dd* (15.2, 7.2)	–
3′	1.78 *m*	27.7	2.15 *m*	25.3
	1.50 *m*	–	–	
4′	0.98 *t*	12.1	0.99 *d* (6.7)	22.3
5′	1.16 *d* (6.5)	17.2	0.97 *d* (6.7)	22.3
1″	–	167.8	–	166.4
2″	–	128.6	–	126.2
3″	6.13 *q*	140.9	6.13 *q*	141.5
4″	1.93 *d* (7.3)	16.0	1.95 *d* (7.2)	15.8
5″	1.91 *s*	20.7	1.91 *s*	20.3

methylbutanoate appeared at δ 178.1, 42.6, 27.7, 17.2 and 12.1 in the ^{13}C NMR spectrum. HMBC, HMQC and DEPT experiments confirmed the 2-methylbutanoyl group as well as the angelate group. The position of the two groups was confirmed by an HMBC experiment; ^{1}H-^{13}C long-range correlation between the C-9 proton signal (δ 4.62, *d*, J = 10.0 Hz) and the C-1′ carbon signal (δ 178.1) of the 2-methylbutanoyl group, and the correlation between C-6 proton signal (δ 5.19, *d*, J = 10.8 Hz) and the C-1″ carbon signal (δ 167.8) of angelate group were observed. The stereochemistry of **3** was shown to be identical to that of **2** on the basis of similar coupling constants observed in the ^{1}H NMR spectrum. Thus, the structure of **3** was established as 2α, 5-epoxy-5,10-dihydroxy-6α-angeloyloxy-9β-(2-methylbutyloxy)-germacran-8α,12-olide.

The molecular formula of **4** was assigned $C_{25}H_{36}O_9$ (m/z 480.2353) by HREI-mass spectrometry. Its IR spectrum showed the presence of an α-methylene-γ-lactone moiety (1758 cm^{-1}) and hydroxyl groups (3460 cm^{-1}) (Maruyama, 1990). Except for the presence of the signals of the 3-methylbutanoyl group (δ 172.5, 43.0, 25.3 and 22.3), the patterns of the ^{1}H NMR and ^{13}C NMR spectra (Table 1) were very similar to **1**. By DEPT and HMBC experiments the positions of the 3-methylbutanoate and angelate groups were confirmed; ^{1}H-^{13}C long-range correlation between the C-9 proton signal (δ 4.62, *d*, J = 10.1 Hz) and the C-1′ carbon signal (δ 172.5) of the 3-methylbutanoate group, and the correlation between the C-6 proton signal (δ 5.25, *d*, J = 10.6 Hz) and the C-1″ carbon signal (δ 166.4) of the angelate group were observed in the HMBC spectrum (Fig. 1). The stereochemistry of **4** was also determined to be identical to that of **1** on the basis of the very similar coupling constants observed in the ^{1}H NMR spectrum. Thus, the structure of **4** was established as 2α,5-epoxy-5,10-dihydroxy-6α-angeloyloxy-9β-(3-methylbutyloxy)-germacran-8α,12-olide.

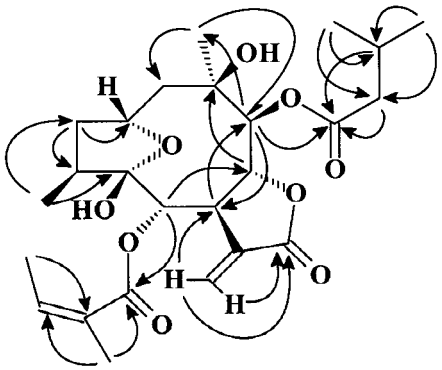

Fig. 1. HMBC correlations of compound **4**

3. Experimental

3.1. General

Mps: uncorr. NMR: 600 MHz (^{1}H) and 150 MHz (^{13}C). EI-MS: 70 eV. FAB-MS: Double focusing MS. FT-IR: KBr. CC: silica gel (40–63 μm). semi-preparative HPLC: Hichrom RPB (250 × 10 mm). Polarimeter: AUTOPOL® III.

3.2. Plant material

Carpesium triste var. *manshuricum* was collected in August 1995 in the Sobaeksan, Chungbuk, South Korea. A voucher specimen is deposited in the herbarium of College of Pharmacy, Chungbuk National University, Cheongju, South Korea (CBNU-95-008).

3.3. Extraction and isolation

The air-dried whole plant material (950 g) was finely ground and extracted at room temperature with 90%

aqueous MeOH. The resultant MeOH extract (98 g) was successively partitioned to give *n*-hexane (12 g), $CHCl_3$ (10.7 g), EtOAc (6.3 g), *n*-BuOH (23 g) and H_2O (43 g) soluble frs.

The $CHCl_3$ soluble fr. was chromatographed over silica gel using a step-wise solvent system of $CHCl_3$ and MeOH as eluent to give six sub-frs. The first one was rechromatographed on silica gel using a gradient solvent system of hexane–EtOAc (3:1 → 1:2, v/v) and $CHCl_3$–MeOH (19:1 → 0:1, v/v) to give ten sub-frs. Fr. 9 was rechromatographed on silica gel eluting with $CHCl_3$–MeOH (40:1 → 1:1, v/v) to give four frs. The sub-fr. 9-3 was rechromatographed on semi-preparative HPLC (CH_3CN-H_2O, 50:50, v/v) to yield 19 mg **1**, and the sub-fr. 9-2 afforded 19 mg **2**, 30 mg **3** and 50 mg **4** by semi-preparative HPLC (MeOH–H_2O, 57:43, v/v).

*3.4. 2α,5-epoxy-5,10-dihydroxy-6α-angeloyloxy-9β-(2-methylbutyloxy)-germacran-8α,12-olide (**3**)*

White crystals; mp 160–164°; $[\alpha]_D^{25} + 1.13°$ (MeOH, *c* 1.0); HRFAB-MS *m/z* 481.2438; FT-IR V_{max}(KBr) cm^{-1}: 3502, 1773, 1723, 1647; ^1H and ^{13}C NMR spectra: Table 1.

*3.5. 2α,5-epoxy-5,10-dihydroxy-6α-angeloyloxy-9β-(3-methylbutyloxy)-germacran-8α,12-olide (**4**)*

White crystals; mp 190–193°; $[\alpha]_D^{25} -4.3°$ (MeOH, *c* 1.0); HREI-MS *m/z* 480.2353 calcd for $C_{25}H_{36}O_9$ 480.2360; FT-IR V_{max}(KBr) cm^{-1}: 3460, 1758, 1723, 1650; ^1H and ^{13}C NMR spectra: Table 1

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