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SESQUITERPENE LACTONES FROM *CARPESIUM DIVARICATUM*

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Key Word Index—*Carpesium divaricatum*; Compositae; sesquiterpene lactones; germacranolides.

Abstract—The aerial parts of *Carpesium divaricatum* afforded two known and two new germacranolides, 2β,5-epoxy-5,10-dihydroxy-6α-angeloyloxy-9β-isobutyloxy-germacran-8α,12-olide and 2α,5-epoxy-5,10-dihydroxy-6α-angeloyloxy-9β-isobutyloxy-germacran-8α,12-olide. © 1997 Elsevier Science Ltd

INTRODUCTION

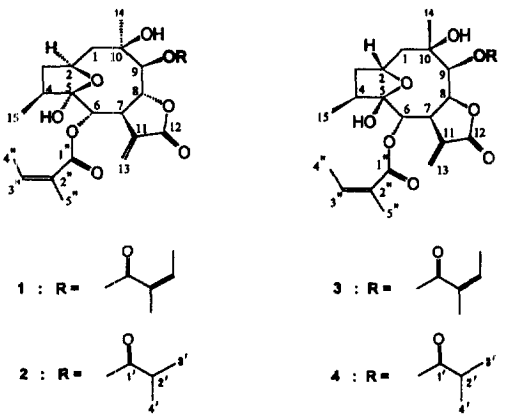
Carpesium divaricatum is a plant which is widely distributed in South Korea, and it has long been used as a Korean traditional medicinal herb for its antipyretic, insectifuge, pain-relief and anti-inflammatory properties [1]. A literature survey revealed that few phytochemical studies had been carried out on the genus *Carpesium*; several sesquiterpene lactones, granilin [2], carpesiolin, carabrone [3], carabrol, ivaxillin [4], ineupatrolide A, B [5] and divaricin A, B, C [6] were reported.

In the course of our systematic phytochemical investigation of Korean genus *Carpesium*, four sesquiterpene lactones were isolated from the methanol extract of *Carpesium divaricatum*. This paper reports the isolation and structural elucidation of two known (**1** and **3**) and two new (**2** and **4**) sesquiterpene lactones.

RESULTS AND DISCUSSION

Repeated column chromatography of the methanol extract yielded four sesquiterpene lactones. The structures of stereoisomers **1** [7, 8] and **3** [6] were established by comparison of their mps, UV, IR and NMR spectral data with those reported in the literature.

Compound **2** was assigned the molecular formula $C_{24}H_{34}O_9$ (*m/z*, 466.2191) by EI- and HR-mass spectrometry. Its IR spectrum revealed the presence of an α-methylene-γ-lactone moiety (1770 cm^{-1}) and hydroxyl groups (3550 cm^{-1}) [9]. The ^1H NMR and ^{13}C NMR spectra (Table 1) were very similar to those of **1** except for the presence of the signals of an isobutyl group. Isobutyric acid appeared at the δ 177.0, 33.9 and 19.0 in the ^{13}C NMR spectrum. 2D NMR ^1H-^1H COSY) and DEPT experiments confirmed the isobutyl group as well as the angelate group. The position of the two groups was confirmed by an HMBC experiment; ^1H-^{13}C long-range correlation between C-9 proton signal (δ 5.15, *d*, J = 5.1 Hz) and C-1′ carbon signals (δ 177.0) of isobutyl group, and the correlation between C-6 proton signal (δ 5.08, *d*, *J* = 7.5 Hz) and the C-1″ carbon signal (δ 165.9) of angelate group were observed (Fig. 1). The stereochemistry of **2** was shown to be identical to that of **1** on the basis of the completely similar coupling constants observed in the ^1H NMR spectrum. Consequently, compound **2** was characterized as 2β,5-epoxy-5,10-dihydroxy-6α-angeloyloxy-9β-isobutyloxy-germacran-8α,12-olide.



The molecular formula of **4** was assigned $C_{24}H_{34}O_9$ (*m/z*, 466.2195) by EI- and HR-mass spectrometry. Its IR spectrum showed the presence of an α-methylene-γ-lactone moiety (1770 cm^{-1}) and hydroxyl groups (3460 cm^{-1}) [8]. Except for the presence of the signals of the isobutyl group (δ 176.4 34.1, 19.0 and 18.9 in the ^{13}C NMR spectrum), the patterns of ^1H NMR and ^{13}C NMR spectra (Table 1) were very similar to **3**. By

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Table 1. ^1H NMR and ^{13}C NMR chemical shifts of Compound **2** and **4** ($CDCl_3$, ^1H: 500 MHz, ^{13}C: 125 MHz)

	2		**4**	
	^1H	^{13}C	^1H	^{13}C
1a	obsc.*	47.9	1.84 *m*	44.0
1b	obsc.		1.74 *m*	
2	4.35 *m*	71.9	4.71 *m*	74.0
3a	2.58 *m*	40.8	2.03 *m*	37.5
3b	obsc.		1.76 *m*	
4	2.34 *m*	44.8	2.56 *m*	36.7
5		106.0		106.2
6	5.08 *d*(7.5)	74.0	5.26 *d*(10.9)	75.7
7	3.89 *m*	45.6	3.11 *m*	45.1
8	4.73 *dd*(6.5, 5.1)	77.2	5.26 *dd*(10.0, 1.4)	77.4
9	5.15 *d*(5.1)	80.3	4.62 *d*(10.0)	77.9
10		73.1		72.2
11		134.1		133.2
12		169.3		168.3
13a	6.21 *d*(3.1)	125.6	6.33 *d*(1.6)	127.2
13b	5.57 *d*(3.1)		5.66 *d*(1.6)	
14	1.38 *s*	25.4	1.26 *s*	30.8
15	1.02 *d*(6.5)	13.2	1.16 *d*(6.5)	14.5
1′		177.0		176.4
2′	2.69 *sep*	33.9	2.68 *sep*	34.1
3′	1.22 *d*(7.0)	19.0	1.24 *d*(7.1)	19.0
4′	1.22 *d*(7.0)	19.0	1.21 *d*(7.1)	18.9
1″		165.9		166.6
2″		126.7		126.4
3″	6.19 *q*(7.0)	141.2	6.14 *q*(7.0)	141.5
4″	1.99 *d*(7.0)	15.9	1.97 *d*(7.0)	15.9
5″	1.93 *s*	20.4	1.92 *s*	20.4

* Obscured.
Values in parentheses are coupling constants in Hz.

2D NMR (^1H-^1H COSY), DEPT and HMBC experiments the positions of the isobutyl and angelate groups were confirmed; ^1H-^{13}C long-range correlation between C-9 proton signal (δ 4.62, *d*, J = 10.0 Hz) and C-1′ carbon signals (δ 176.4) of isobutyl group, and the correlation between C-6 proton signal (δ 5.26, *d*, J = 10.9 Hz) and the C-1′ carbon signal (δ 166.6) of angelate group were observed in the HMBC spectrum. The stereochemistry of **4** was also determined to be identical to that of **3** on the basis of the very similar coupling constants observed in the ^1H NMR spectrum. Thus, the structure of **4** was established as 2α,5-epoxy-5,10-dihydroxy-6α-angeloyloxy-9β-isobutyloxy-germacran-8α,12-olide.

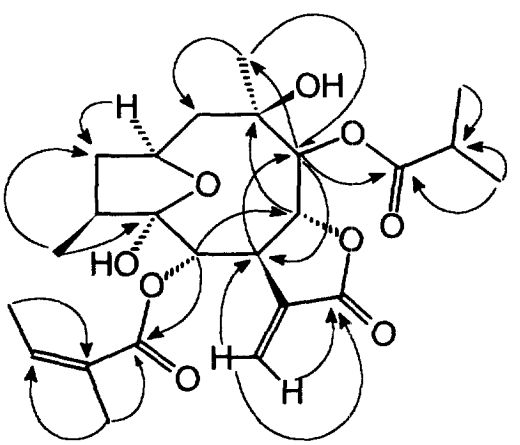

Fig. 1. HMBC correlations of **2**

EXPERIMENTAL

General. Mps: uncorr. NMR: 500, 400 MHz (^1H) and 125 MHz (^{13}C). EI-MS: 70 eV; IR: Nujol. CC: silica gel (SDS: 40–63 μm). LPLC: Merck Lichroprep silica 60 (240 × 10 mm), Merck Lichroprep RP-18 (240 × 10 mm).

Plant material. Carpesium divaricatum was collected in August 1994 on the Samyeongsan, Kangwondo, Korea. A voucher specimen is deposited in the herbarium of College of Pharmacy, Sung Kyun Kwan University (SKKU-94-005).

Extraction and isolation. The air-dried plant material (3.5 kg) was finely ground and extracted at room temp. with MeOH. The resultant MeOH extract (110 g) followed by the successive solvent partition to give CH_2Cl_2 (30 g), *n*-BuOH (22 g) and H_2O (50 g) soluble frs.

The CH_2Cl_2 soluble fr. was chromatographed over

silica gel using a gradient solvent system of hexane–EtOAc(5:1 → 0:1) as eluent to give five sub-frs, whose fourth one was chromatographed on silica gel eluting with $CHCl_3$–EtOAc(15:1), followed by hexane–CH_2Cl_2–EtOAc(1:1:1) to give five frs. Fr. 2 was rechromatographed on LPLC (MeOH–H_2O, 3:2) to yield 20 mg **1**, and fr. 4 and 5 afforded 15 mg **2**, 10 mg **3** and 15 mg **4** by LPLC (CH_2Cl_2–EtOAc, 3:1).

2*β*,5-*Epoxy*-5,10-*dihydroxy*-6*α*-*angeloyloxy*-9-*isobutyloxy-germacran*-8*α*,12-*olide* (**2**). Needles; mp 180–182°; $[\alpha]_D^{24}$ −41.6° (MeOH, *c* 1.1); EI-MS *m/z* 466.2191 calcd for $C_{24}H_{34}O_9$ 466.2022; IR ν_{max}^{Nujol} cm^{-1}: 3550, 3380, 1770, 1690, 1650; ^1H and ^{13}C NMR: Table 1.

2*α*,5-*Epoxy*-5,10-*dihydroxy*-6*α*-*angeloyloxy*-9-*isobutyloxy-germacran*-8*α*,12-*olide* (**4**). Needles; mp 174–177°; $[\alpha]_D^{24}$ −5.2° (MeOH, *c* 1.2); EI-MS *m/z* 466.2195 calcd for $C_{24}H_{34}O_9$ 466.2202; IR ν_{max}^{Nujol} cm^{-1}: 3460, 1770, 1720, 1650; ^1H and ^{13}C NMR: Table 1.

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