

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, 2 β ,5-epoxy-5,10-dihydroxy-6 α -angeloyloxy-9 β -isobutyloxy-germacran-8 α ,12-olide and 2 α ,5-epoxy-5,10-dihydroxy-6 α -angeloyloxy-9 β -isobutyloxy-germacran-8 α ,12-olide. © 1997 Elsevier Science Ltd

INTRODUCTION

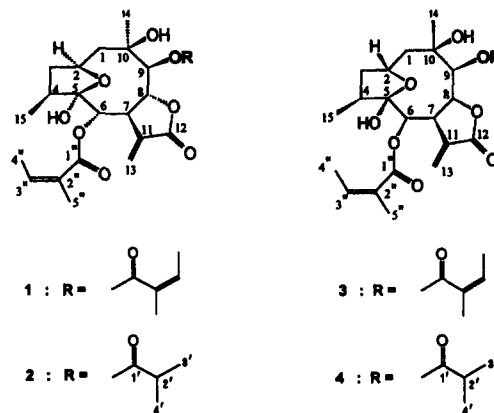
Carpesium divaricatum is a plant which is widely distributed in South Korea, and it has long been used as a Korean traditional medicinal herb for its antipyretic, insectifuge, pain-relief and anti-inflammatory properties [1]. A literature survey revealed that few phytochemical studies had been carried 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 C₂₄H₃₄O₉ (*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 ¹³C 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 ¹³C 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-¹³C 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 2 β ,5-epoxy-5,10-dihydroxy-6 α -angeloyloxy-9 β -isobutyloxy-germacran-8 α ,12-olide.

The molecular formula of 4 was assigned C₂₄H₃₄O₉ (*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 ¹³C NMR spectrum), the patterns of ¹H NMR and ¹³C 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)

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

mined 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 2 α ,5-epoxy-5,10-dihydroxy-6 α -angeloyloxy-9 β -isobutyloxy-germacran-8 α ,12-olide.

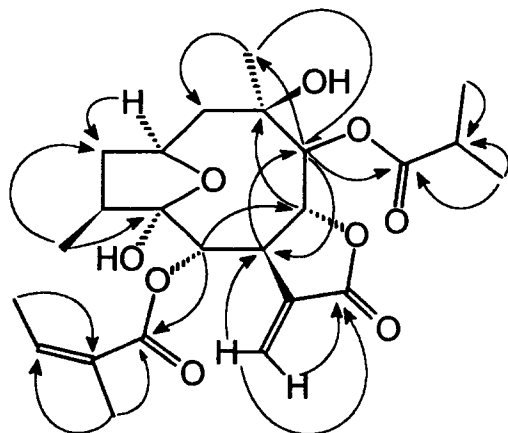
EXPERIMENTAL

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 \times 10 mm), Merck Lichroprep RP-18 (240 \times 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

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

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 CHCl₃–EtOAc(15:1), followed by hexane–CH₂Cl₂–EtOAc(1:1:1) to give five frs. Fr. 2 was rechromatographed on LPLC (MeOH–H₂O, 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 (CH₂Cl₂–EtOAc, 3:1).

2β,5-Epoxy-5,10-dihydroxy-6α-angeloyloxy-9-isobutyloxy-germacran-8α,12-olide (2). Needles; mp 180–182°; $[\alpha]_D^{24}$ –41.6° (MeOH, *c* 1.1); EI-MS *m/z* 466.2191 calcd for C₂₄H₃₄O₉, 466.2022; IR $\nu_{\max}^{\text{Nujol}}$ cm⁻¹: 3550, 3380, 1770, 1690, 1650; ¹H and ¹³C NMR: Table 1.

2α,5-Epoxy-5,10-dihydroxy-6α-angeloyloxy-9-isobutyloxy-germacran-8α,12-olide (4). Needles; mp 174–177°; $[\alpha]_D^{24}$ –5.2° (MeOH, *c* 1.2); EI-MS *m/z* 466.2195 calcd for C₂₄H₃₄O₉, 466.2202; IR $\nu_{\max}^{\text{Nujol}}$ cm⁻¹: 3460, 1770, 1720, 1650; ¹H and ¹³C NMR: Table 1.

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