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OPLOPANE SESQUITERPENES FROM *PETASITES PALMATUS*

KOJI HAYASHI

Faculty of Pharmaceutical Sciences, Hokkaido University, Sapporo, 060, Japan

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Key Word Index—*Petasites palmatus*; Compositae; sesquiterpenes; petasipaline A and B; oplopane skeleton; 2D-NMR; manganese dioxide oxidation.

Abstract—Chemical investigation of *Petasites palmatus* afforded two new sesquiterpenes, designated as petasipaline A and B, together with known bakkenolide A. The structures of the new sesquiterpenes each with an oplopane skeleton were elucidated by chemical and spectroscopic methods.

INTRODUCTION

Petasites species (tribe Senecioneae) are mainly distributed in the northern parts of the Eurasian and North American continents. The *Petasites* plants so far examined contain eremophilane and bakkenane type sesquiterpenoids [1]. In the author's chemotaxonomic approach of this species, the chemical composition of *P. palmatus*, which is distributed in the North Pacific area from Sakhalin (introduced) to California, was investigated to yield two new sesquiterpenes (**1** and **2**) each with an oplopane skeleton. In this decade, Bohlmann and his co-workers have shown that various Senecioneae plants contain oplopane sesquiterpenoids [2].

RESULT AND DISCUSSION

The dried aerial parts of *P. palmatus* yielded bakkenolide A (**3**) and the two new sesquiterpenes petasipaline A (**1**) and B (**2**).

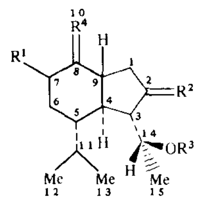
Bakkenolide A (**3**) was identified by mmp and comparison of its spectral data with authentic samples [3]. Petasipaline A (**1**) has the molecular formula $C_{19}H_{28}O_5$ by EIMS (m/z 336 $[M]^+$) and elemental analysis. The EIMS showed fragment peaks at m/z 293 $[M-43]^+$, 249 $[M-87]^+$, 276 $[M-60]^+$, and 216 $[M-2\times 60]^+$. These peaks suggested the presence of isopropyl, 1-acetoxy ethyl, and another acetoxy group, respectively. Furthermore, two peaks at m/z 234 and 174 suggested that elimination of ketene (42 amu) might occur from the ions of m/z 276 and 216, respectively. These have an α,β-unsaturated ketone structure due to the easier elimination of acetic acid from the β-keto-acetate.

In the ^{1}H NMR spectrum of **1** (Table 1), the following signals were observed, three doublet methyls at δ0.79, 0.99 and 1.22, two acetoxy methyls at δ2.07 and 2.13, exomethylene protons at δ4.80 and 5.13, and two acetoxy methines at δ5.12 (*dq*, $J=3$, 7 Hz), and 5.55 (*t*, $J=3$ Hz). These assignments were supported by its ^{13}C NMR spectrum, which in addition showed a carbonyl carbon signal at δ213.8. Thus, it was deduced that **1** has two carbocycles but not a spirostructure because no quaternary sp^3 carbon signal was observed. The IR spectrum of **1** showed the presence of an acetate group (1740 and 1240 cm^{-1}), an exomethylene group (1665 and 910 cm^{-1}), and a five-membered ketone (1730 cm^{-1}). Therefore, **1** was inferred to be a perhydroindan-2-one with an α-(1-acetoxy)-ethyl substituent as well as other substituents (isopropyl, exomethylene, and acetoxy groups) in the six-membered ring. When **1** was treated with 5% methanolic potassium hydroxide solution, a bisdeacetyl compound (**4**) which contained a mono-methoxy methyl group at C-14 was obtained*. This suggested that β-elimination of the acetic acid to the ketone formed an α,β-unsaturated ketone, and then Michael addition of a methanol molecule occurred to the β-position.

As described in the Introduction, Bohlmann's group has reported that a lot of oplopane sesquiterpenes, which differ mainly in the ester substituents are found in the Senecioneae. Some of their ^{1}H NMR data are very close to those of **1**. Cross peaks in the 2D ^{1}H–^{1}H COSY spectrum of **1** suggested that **1** has the same skeleton with the substituents as that of the oplopanes isolated by Bohlmann. Heteronuclear C–H COSY and HMBC (heteronuclear multiple bond correlation) spectra [4] of **1** allowed complete assignment of all the ^{1}H and ^{13}C NMR signals. Thus the structure of petasipaline A is deduced to be **1**.

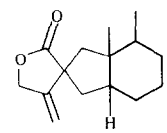
Reduction of **1** with lithium aluminium hydride afforded a triol (**5**) which gave a triacetate (**6**). In order to confirm the allylic alcohol in the molecule, **5** was oxidized with manganese dioxide. However, this gave the unexpected five-membered ketone **7**, which was converted to **1** by usual acetylation. It has been reported that some allylic alcohols with axial oriented hydroxyl groups are resistant to manganese dioxide oxidation [5]. This observation is in agreement with the supposed structure of **1**. On the other hand, ozonolysis of **1** followed by reduction with zinc/acetic acid yielded two compounds, both of which lacked exomethylene proton signals in the ^{1}H NMR spectra. The less polar compound (**8**) has the molecular formula $C_{16}H_{22}O_3$ and showed only one acetoxyl signals at δ2.10 and 5.10 in its ^{1}H NMR spectrum. Its IR spectrum showed a six-membered ketone

*Numbering as Bohlmann *et al.* [2].



	R[1]	R[2]	R[3]	R[4]
1	OAc	O	Ac	CH_2
2	H	O	Ac	CH_2
4	OH	O	Me	CH_2
5	OH	H, OH	H	CH_2
6	OAc	H, OAc	Ac	CH_2
7	OH	O	H	CH_2
8	H	O	Ac	O
9	OAc	O	Ac	O
11	3-Me-2-pen	O	Ac	CH_2

(3-Me-2-pen = 3-methyl-2-pentenoyl)



3

Table 1. ^{1}H (400 MHz) and ^{13}C (22.5 MHz) NMR chemical shifts of compound **1** (pyridine-d_5)

C	^{1}H	^{13}C
1	2.55α *ddd*; 2.38β *ddd*	42.6
2		213.8
3	2,66β *dd*	57.4
4	1.52α *q*	49.1
5	2.02β *m*	44.1
6	1.35β *ddd*; 2.00α *ddd*	31.4
7	5.72α *t*	74.2
8		146.6
9	2.70β *m*	42.5
10	4.83 *br s*; 5.19 *br s*	110.3
11	2.43 *m*	27.7
12	0.70 *d*	15.6
13	0.90 *d*	21.6
14	5.28 *qd*	69.8
15	1.30 *d*	15.4
Ac × 2	2.04, 2.10	21.3, 21.2
		170.4 × 2

J (Hz): 1α, 1β = 16; 1α, 9β = 13.5; 1β, 9β = 6; 3β, 4α = 11; 3β, 14 = 3; 4α, 9β = 11; 4α, 5β = 11; 6α, 7α = 6β, 7α = 3; 11, 12 = 11, 13 = 7; 14, 15 = 7. The multiplicities of the carbon signals were determined by INEPT measurements.

absorption band at 1715 cm^{-1} in addition to absorption bands at 1740 and 1260 cm^{-1} (five-membered ketone and acetate). The other compound (**9**) from its spectral data corresponded to one formed by oxidative removal of the exomethylene of **1**. The formation of **7** accounted for the presence of an acetoxy group next to the exomethylene due to reductive removal of the acetoxy group during the work-up after ozonolysis.

The relative stereochemistry of **1** was deduced by analyses of the ^{1}H–^{1}H coupling constants except for that at C-14. The quartet signal with $J = 11$ Hz assignable to H-4 establishes that the H-4 proton is oriented in an *anti-trans*-axial direction with respect to the neighbour three protons, H-3, H-5, and H-9. The hydroxy group at C-7 is β-axial judging from the triplet signal with $J = 3$ Hz of H-7 and a typical result of manganese dioxide oxidation mentioned above. The stereochemistry at C-14 was determined by analysis of the NOE difference spectra of the acetonide (**10**) of **5**. On reduction of **1**, the reagent attacked the ketone from the less hindered upper side of the molecule to give an α-oriented hydroxyl group. Therefore, the acetonide (**10**) is as illustrated. According to a Dreiding model, the acetonide ring adopts the twist boat form rather than chair because of the severe steric hindrance between the isopropyl methyls, acetonide methyl and C-15 methyl groups. The assignment of the proton signals was completed by the ^{1}H–^{1}H COSY spectrum of **10**. When the H-3β signal at δ2.29 was irradiated, an NOE was observed with the H-2α and H-14 proton signals at δ4.41 and 4.13, respectively, and irradiation at δ1.46 of the 15-methyl group signal gave an effect with the H-14 proton signal. These facts suggested that the H-3β proton is directed anti *trans* to the H-15 methyl. The absolute stereo structure was estimated by optical rotatory dispersion measurement which gave a relatively large negative Cotton effect ($a = -160$). Klyne *et al.* reported that (−)-*trans* hydroindan-2-one gave a negative Cotton effect ($a = -222$) [6]. The α-1-acetoxy ethyl substituent to the ketone seemed to contribute negatively. Thus, the structure of petasipaline A is determined as **1**. This structure was analogous to the oplopane derivatives isolated by Bohlmann's group. Chinese chemists isolated tussilagone (**11**) which has a (3-methyl)-pent-2-enoyl group at C-7 instead of an acetyl group as in **1** from *Tussilago farfara* and determined by X-ray analysis [7]. The *R* stereochemistry at C-14 in **11** coincided with that of **1**.

Petasipaline B (**2**) has the molecular formula $C_{17}H_{26}O_3$ by EIMS(M^+ m/z 278) and elemental analysis. The ^{1}H and ^{13}C NMR spectra showed the absence of a C-7 acetoxy group from **1**. The C-8 and C-10 carbon signals of the exomethylene were shifted to lower (+2.8 ppm) and higher (−5.8 ppm) field, respectively. Ozonolysis of **2** yielded **7** identified by comparison with spectral data and mmp.

EXPERIMENTAL

Mps: uncorr. Optical rotations were measured in $CHCl_3$ at room temp. ^{1}H NMR: 270 and 400 MHz with TMS as the int. standard in $CDCl_3$ or pyridine-d_5 soln; ^{13}C NMR: 22.5 and 67.5 MHz in $CDCl_3$ or pyridine-d_5; IR: $CHCl_3$ or Nujol; EIMS spectra were carried out with a JEOL LMS-D-303 mass spectrometer; ORD curve was obtained with a JASCO ORD/UV-5; CC: Wakogel C-200, and C-300; TLC: precoated plates, Kiesel gel $60F_{254}$ (Merck) or silica gel $70F_{254}$ (Wako).

Plant material. Petasites palmatus was originally introduced from Sahkalin before 1940 to Hokkaido Island, Japan, as a vegetable. The material used in this study was a sample which was cultivated in the Botanical Garden of the Experimental Station of medicinal plants of Hokkaido University. The specimen has been cultivated in this garden.

Extraction and isolation. Dried and powdered aerial parts of *P. palmatus* (640 g) were extracted with MeOH in a Soxleht apparatus. The concd extract under red. pres. was partitioned between EtOAc (1.5 l) and H_2O (1.5 l). The organic layer gave 15.3 g of dark brown tar, which was submitted to silica gel (250 g) CC eluted with C_6H_6–Me_2CO (C_6H_6 increasing polarity). The first C_6H_6 eluate gave 2.14 g of bakkenolide A (**3**). The second C_6H_6 eluated gave 0.46 g of petasipaline B (**2**). Then the 5% Me_2CO–C_6H_6 eluate gave 0.22 g of petasipaline A (**1**).

Petasipaline A (**1**). Fine needles from hexane; mp 101–103°, $[\alpha]_D$ −51.6° ($CHCl_3$ *c* 0.38). (Found: C, 67.85; H, 8.39. $C_{19}H_{28}O_5$ requires C, 67.83; H, 8.39%). MS *m/z*: 336 $[M]^+$, 293 $[M-(Me)_2CH]^+$, 276 $[M-OHAc]^+$, 249 $[M-MeCH(OAc)]^+$, 234 $[276-CH_2=C=O]^+$, 216 $[M-2\times HOAc]^+$, 173 $[216-CH_2=C=O]^+$; IR ν_{max}^{Nujol} cm^{-1}: 1740, 1730, 1665, 910; ORD (MeOH; *c* 0.55) $[\phi]$: $trough_{319}$ −7414°, $peak_{279}$ +9930°, molecular amplitude −160.71. ^1H and ^{13}C NMR: see Tables 1 and 2.

Petasipaline B (**2**). Plates from MeOH; mp 88–90.5°, $[\alpha]_D$ −56.3°($CHCl_3$; *c* 0.46). (Found: C, 73.23; H. 9.40. $C_{17}H_{26}O_3$ requires C, 73.34; H, 9.41%). MS *m/z*: 278 $[M]^+$, 235 $[M-(Me)_2CH]^+$, 218 $[M-OHAc]^+$, 191 $[M-MeCH(OAc)]^+$, 176 $[218-CH_2=C=O]^+$. IR ν_{max}^{Nujol} cm^{-1}: 1740, 1730, 1655, 885. ORD (MeOH; *c* 0.44) $[\phi]$: $trough_{319}$ −7056°, $peak_{279}$ +9015°, molecular amplitude −173.44; ^1H NMR (270 MHz): δ0.77 and 0.99 (each 3H, *d*, *J* = 7 Hz, H-12, 13), 1.20 (3H, *d*, *J* = 7 Hz, H-15), 2.08 (3H, *s*, −OAc), 4.53 and 4.75 (each 1H, *br s*, H-10), 5.10 (1H, *qd*, *J* = 7, 3 Hz, H-14). ^{13}C NMR: see Table 2.

Bakkenolide A (**3**). Plates from MeOH; mp 76.5–81.5°, (Found: C, 76.59; H, 9.41, $C_{15}H_{22}O_2$ requires C, 76.88; H, 9.46%). MS *m/z*: 234 $[M]^+$, 124, 123, 111, 109; IR ν_{max}^{Nujol} cm^{-1}: 1765, 1670, 880; ^1H NMR; δ0.83 (3H, *d*, *J* = 6 Hz), 1.00 (3H, *s*), 4.76 (2H, *m*), 5.03 (1H, *br s*), 5.10 (1H, *br s*).

Alkali treatment of **1**. 30 mg of **1** was dissolved in 5 ml of 5% methanolic KOH soln and the mixture refluxed for 14 hr. After evapn of the MeOH, the residual material was extracted with 30 ml of Et_2O. The Et_2O phase was washed with 2 m HCl and satd NaCl soln, dried over $MgSO_4$, and the solvent removed under red. pres. The residue was recrystallized from hexane to give 12.2 mg of prisms (**4**); mp 129–130.5°, $[\alpha]_D$ −158° ($CHCl_3$; *c* 0.725). MS *m/z*: 266.1887 $[M]^+$ ($C_{16}H_{26}O_3$ requires 266.1892), 248 $[M-H_2O]^+$, 234 $[M-MeOH]^+$, 223 $[M-(Me)_2CH]^+$, 205 $[248-(Me)_2CH]^+$, 191 $[223-MeOH]^+$: IR ν_{max}^{Nujol} cm^{-1}: 3480, 1730, 1655, 900; ^1H NMR (270 MHz) δ: 0.81 and 0.98 (each 3H, *d*, *J* = 7 Hz, H-12, 13), 1.39 (3H, *d*, *J* = 7 Hz, H-15), 2.29 (1H, *s*, OH), 2.69 (1H, *br q* *J* = 10 Hz, H-3β), 3.27 (3H, *s*, OMe), 3.53 (1H, *dq*, *J* = 1.5, 7 Hz, H-14), 4.50 (1H, *t*, *J* = 3 Hz, H-7α), 4.67, and 4.96 (each 1H, *br s*, H-10). ^{13}C NMR: see Table 2.

Table 2. ^{13}C NMR chemical shifts of compounds **1**, **2**, **4**, **5**, **7** and **8** ($CDCl_3$)

C	1	2	4	5	7	8
1	42.3	43.2	42.9	38.3	42.0	40.5
2	214.9	215.8	217.0	75.6	218.8	213.7
3	57.3	57.3	58.5	52.2	60.0	57.6
4	49.1	49.5	48.2	50.3	50.0	49.0
5	44.0	46.6	42.8	44.0	43.6	49.0
6	31.2	34.9	33.2	34.8	34.3	25.8
7	74.1	43.2	72.7	72.2	70.7	39.5
8	146.0	149.4	154.6	154.6	152.9	208.8
9	42.3	49.6	41.2	42.8	42.8	52.3
10	110.6	104.5	107.4	104.2	104.4	—
11	27.6	28.1	27.9	28.5	28.5	27.9
12	21.5	21.8	21.7	22.0	21.7	22.4
13	15.2	15.2	15.6	16.0	15.9	15.1
14	69.6	69.8	77.8	70.1	67.0	69.2
15	15.4	15.8	16.7	20.8	19.5	15.7
	2 × Ac	Ac	MeO			Ac
	21.6 × 2	21.4	56.7			21.4
	170.3	171.1				171.2
	171.6					

Chemical shifts with asterisks in each column may be interchangeable. The order of 12-, 13-Me signals is tentative. The multiplicities of the signals were determined by INEPT measurements.

$LiAlH_4$ *reduction of* **1**. To a soln of 62 mg of **1** in 6 ml of dry Et_2O was added 44 mg of $LiAlH_4$ gradually and the mixt. stirred for 2.5 hr at room temp. Excess reagent was destroyed by dropwise addition of 2 ml MeOH. The reaction mixture was poured into 30 ml water and extracted with Et_2O (20 ml × 3). The Et_2O phases were combined and washed successively with 2 M HCl, satd $NaHCO_3$ soln and satd NaCl soln, and dried over $MgSO_4$. Evaporation of the solvent and recrystallization from EtOAc–hexane gave 35 mg of colourless prisms of triol (**5**); mp 166–169°. $[\alpha]_D$ +18° ($CHCl_3$; *c* 0.36). IR ν_{max}^{Nujol} cm^{-1}: 3600, 1640, 900; MS *m/z*: 236.1789 $[M-H_2O]^+$ ($C_{15}H_{24}O_2$ requires 236.1776), 218 $[M-2\times H_2O]^+$, 193 $[236-(Me)_2CH]^+$; ^1H NMR (270 MHz) δ; 0.70, and 0.95 (each 3H, *d*, *J* = 7 Hz, H-12 and 13), 1.47 (3H, *d*, *J* = 7 Hz, H-15), 4.07 (1H, *qd*, *J* = 7, 3 Hz, H-14), 4.40 (1H, *t*, *J* = 3 Hz, H-7α), 4.61 (1H, *ddd*, *J* = 10, 10, 6 Hz, H-2β), 4.69 and 4.88 (each 1H, *br s*, H-10). ^{13}C NMR; see Table 2.

Acetylation of **5**. To a soln of 3.2 mg **5** in 0.3 ml pyridine was added 0.2 ml Ac_2O and the mixture left to stand overnight at room temp. The reaction mixture was diluted with 30 ml MeOH and evapd under red. pres. to dryness. This process was repeated × 4 until the smell of pyridine and HOAc disappeared. The residual substance (**6**) showed the following ^1H NMR spectrum, (270 MHz) δ0.74 and 0.94 (each 3H, *d*, *J* = 7 Hz, H-12, 13), 1.42 (3H, *d*, *J* = 7 Hz, H-15), 1.99, 2.03 and 2.09 (each 3H, *s*, −OAc × 3), 2.26 (1H, *br dt*, *J* = 4, 11 Hz, H-9β), 2.51 (1H, *dt*, *J* = 4, 10 Hz, H-3β), 4.80 and 5.03 (each 1H, *s*, H-10), 5.04 (1H, *qd*, *J* = 7, 4 Hz, H-14), 5.42 (1H, *ddd*, *J* = 10, 10, 6.6 Hz, H-2α), 5.45 (1H, *t*, *J* = 3 Hz, H-7α).

MnO_2 *oxidation of* **5**. A soln of 30 mg of **5** in 6 ml of CH_2Cl_2 was stirred with MnO_2 prepared by Morton's procedure [8] for 2.5 hr. Then the MnO_2 was filtered off, and washed with *ca* 10 ml CH_2Cl_2. The washing and the filtrate were combined and evapd to dryness to give a crystalline mass (25.3 mg). Recrystallization of the mass from hexane yielded 18.4 mg of colourless needles (**7**). Mp 172–174°, $[\alpha]_D$ − 107° ($CHCl_3$; *c* 1.08). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3610, 1720, 1650, 915; MS *m/z*: 252.1727 $[M]^+$ ($C_{15}H_{24}O_3$ requires 252.1728), 234 $[M-H_2O]^+$, 216 $[M-2\times H_2O]^+$, 209 $[M-(Me)_2CH]^+$, 173 $[209-2\times H_2O]^+$; ^1H NMR (400 MHz) δ: 0.73 and 0.98 (each 3H, *d*, *J* = 7 Hz, H-12, 13), 1.18 (3H, *d*, *J* = 7 Hz, H-15), 1.37 (1H, *q*, *J* = 11 Hz, H-4), 1.40 (1H, *m*, H-6α), 1.98 (2H, *m*, H-6β and 11), 2.04 (1H, *m*, H-5β), 2.15 (1H, *dd*, *J* = 16, 13.5, H-1α), 2.42 (1H, *dd*, *J* = 16, 6, H-1β), 2.51 (1H, *dd*, *J* = 11, 3, H-3β), 2.80 (1H, *m*, H-9β), 4.04 (1H, *qd*, *J* = 7, 3 Hz, H-14), 4.50 (1H, *t*, *J* = 3 Hz, H-7α), 4.68 and 4.99 (each 1H, *br s*, H-10). ^{13}C NMR: see Table 2.

Acetylation of **7**. A 0.6 ml pyridine soln of 5 mg **7** was kept for 16 hr with 0.3 ml Ac_2O. Then the mixture was diluted with 20 ml H_2O and extracted with Et_2O (20 ml × 3). The organic soln was washed with 20 ml 2 m HCl, 20 ml satd $NaHCO_3$ soln and 20 ml satd NaCl soln, and dried over $MgSO_4$. After evapn of the solvent, the residue was recrystallized from hexane to give 2.5 mg of colourless needles, mp 100–101.5°. Its ^1H NMR spectrum was identical with that of **1**. Mmp showed no depression; mp 99.5–101.5°.

Ozonolysis of **1**. To a soln of 107 mg **1** in 6 ml CH_2Cl_2, O_2 containing 0.3% O_3 was bubbled for two hr on a dry ice Me_2CO bath. After the starting material had disappeared (by TLC), the reaction mixture was warmed-up to room temp and the solvent was flashed out with a N_2 stream. Then the residue was dissolved into 6 ml HOAc and stirred with 1 g Zn dust for 5 hr. The reaction mixture was diluted with 100 ml Et_2O. After removal of the Zn by filtration, the Zn was washed with about 20 ml Et_2O. The filtrate and the washing were combined, washed with satd $NaHCO_3$ soln several times, and water (40 ml × 3), and dried over $MgSO_4$. After evapn of the solvent, the oily residue (64.4 mg) was chromatographed over silica gel eluted with 30% Me_2CO –hexane to give a less polar substance (27.3 mg) and a polar substance 7.6 mg). The former was recrystallized from Me_2CO/hexane to give 21.7 mg of prisms (**8**): mp 172–174°. $[\alpha]_D$ −107.4° ($CHCl_3$; *c* 1.08). MS *m/z*: 220.1484 $[M-HOAc]^+$ ($C_{14}H_{20}O_2$ requires 220.1463), 177 $[M-HOAc-(Me)_2CH]^+$; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1740, 1715, 1260. ^{1}H NMR (270 MHz) δ:0.82 and 1.07 (each 3H, *d*, $J=7$ Hz, H-12, 13), 1.20 (3H, *d*, $J=7$ Hz, H-15), 2.10 (3H, *s*, −OAc), 2.56 (1H, *dd*, $J=11$, 3 Hz, H-3β), 2.70 (1H, *ddd*, $J=11$, 11, 8 Hz, H-9β), 5.10 (1H, *qd*, $J=7$, 3 Hz, H-14). ^{13}C NMR; see Table 2.

The second compound (**9**) remained amorphous $[\alpha]_D$ +10.6° ($CHCl_3$; *c* 0.56). MS *m/z*: 278.1496 $[M-HOAc]^+$ ($C_{16}H_{22}O_4$ requires 278.1518), 218 $[M-2\times HOAc]^+$. IR $\nu_{max}^{CHCl_3}$ cm−1: 1740, 1715, 1260; MS *m/z*: 278 $[M-OHAc]^+$, 218 $[M-2\times HOAc]^+$; ^{1}H NMR (270 MHz) δ:1.14 (6H, *d*, $J=7$ Hz, H-12, 13), 1.30 (3H, *d*, $J=7$ Hz, H-15), 2.02 (3H, *s*, −OAc), 2.15 (3H, *s*, −OAc), 2.94 (1H, *m*), 3.09 (1H, *d*, $J=18$ Hz), 3.23 (1H, *dd*, $J=8$, 6 Hz), 5.11 (1H, *qd*, $J=7$, 3 Hz, H-14), 5.33 (1H, *dd*, $J=13$, 6 Hz, H-7α).

Acetonide of **5**. A soln of 10.5 mg **5** in 6 ml dry Me_2CO was stirred with 5 mg *p*-toluene sulphonic acid for one day. Then the mixture was neutralized with K_2CO_3 and filtered. The filtrate was concd to give a syrup, which was chromatographed over a short silica gel column with $CHCl_3$ to give 7.3 mg of oily material (**10**), $[\alpha]_D$ −70° ($CHCl_3$; *c* 0.11),. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600, 1650, 900. MS *m/z*: 279.1970 $[M-Me]^+$ ($C_{17}H_{27}O_3$ requires 279.1969), 219, 201 $[219-H_2O]^+$; ^{1}H NMR (400 MHz) δ:0.71 and 0.94 (each 3H, *d*, $J=7$ Hz, H-12, 13), 1.39 and 1.43 (each 3H, *s*, acetonide Me), 1.46 (3H, *d*, $J=7$ Hz, H-15). 1.25 (1H, *m*, H-4α), 1.30 (1H, *m*, H-6β), 1.61 (1H, *ddd*, $J=13$, 11, 9.5 Hz, H-1α), 1.74 (1H, *m*, H-5β), 1.77 (1H, *m*, H-11), 1.89 (1H, *dt*, $J=14$, 3 Hz, H-6α), 2.22 (1H, *ddd*, $J=11$, 7, 4.5 Hz, H-1β), 2.29 (1H, *ddd*, $J=10$, 9, 7 Hz, H-3β), 2.38 (1H, *m*, H-9β), 4.13 (1H, *quintet*, $J=7$ Hz, H-14), 4.41 (1H, *ddd*, $J=10$, 10, 7 Hz, H-2β), 4.42 (1H, *t*, $J=3$ Hz, H-7α), 4.71 (1H, *t*, $J=1.6$ Hz, H-10), 4.90 (1H, *t*, $J=1.4$ Hz, H-10).

Ozonolysis of **2**. To a soln of 30.3 mg **2** in 6 ml CH_2Cl_2, O_2 containing 0.3% O_3 was bubbled for 2 hr on a dry ice–Me_2CO bath. The reaction mixture was worked-up by the same manner as in the case of **1** to give 12.2 mg of prisms which were identified with **8**; mp 176–177°, mmp, mp 175.5–177°.

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