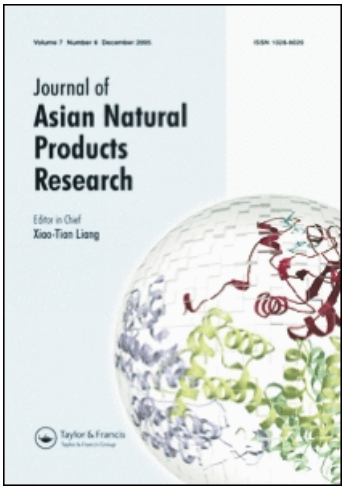

Journal of Asian Natural Products Research
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713454007

Two new monoterpene glycosides and a new (+)-jasmololone glucoside from *Bidens parviflora* Willd.

Nai-Li Wang[a]; Jue Wang[b]; Xin-Sheng Yao[a]; Susumu Kitanaka[b]
[a] Department of Natural Products Chemistry, Shenyang Pharmaceutical University, Shenyang, China [b] College of Pharmacy, Nihon University, Chiba, Japan

Online publication date: 27 July 2010

To cite this Article Wang, Nai-Li , Wang, Jue , Yao, Xin-Sheng and Kitanaka, Susumu(2007) 'Two new monoterpene glycosides and a new (+)-jasmololone glucoside from *Bidens parviflora* Willd.', Journal of Asian Natural Products Research, 9: 5, 449 — 455
To link to this Article: DOI: 10.1080/10286020500532033
URL: http://dx.doi.org/10.1080/10286020500532033

Journal of Asian Natural Products Research, Vol. 9, No. 5, July–August 2007, 449–455

Two new monoterpene glycosides and a new (+)-jasmololone glucoside from *Bidens parviflora* Willd.

NAI-LI WANG†*, JUE WANG‡, XIN-SHENG YAO† and SUSUMU KITANAKA‡*

†Department of Natural Products Chemistry, Shenyang Pharmaceutical University, 103 Wenhua Road. Shenhe District, Shenyang, Shenyang 110015, China
‡College of Pharmacy, Nihon University, 7-7-1 Narashinodai, Funabashi, Chiba 274-8555, Japan

(Received 13 April 2005; revised 7 November 2005; in final form 6 December 2005)

Two new monoterpene glycosides named bidensmenthosides A, B and a new (+)-jasmololone glucoside, were isolated from the air-dried whole plant of *Bidens parviflora* Willd. Their structures were determined as (1*S*, 3*S*, 4*R*)-3-hydroxy-*p*-menth-6-one 3-*O*-β-D-glucopyranoside (**1**), (3*R*, 4*R*)-3-hydroxy-*p*-menth-1 (2)-en-6-one 3-*O*-β-D-glucopyranoside (**2**) and (4*R*)-hydroxy-3-methyl-2-(2 *Z*-pentenyl)-cyclopent-2-enone 4-*O*-β-D-glucopyranoside (**3**) based on spectroscopic analysis and physiochemical properties, respectively. The bidensmenthosides A, B and aglycone of **3** were found to reduce 2, 2-diphenyl-1-picrylhydrazyl (DPPH) radicals.

Keywords: *Bidens parviflora* Willd.; (1*S*, 3*S*, 4*R*)-3-hydroxy-*p*-menth-6-one 3-*O*-β-D-glucopyranoside; (3*R*, 4*R*)-3-hydroxy-*p*-menth-1 (2)-en-6-one 3-*O*-β-D-glucopyranoside; (+)-Jasmololone glucoside; CD analysis; Radical scavenger

1. Introduction

In our screening of bioactivity on Compositae plants, we found the 60% EtOH extract of *Bidens parviflora* that inhibits histamine release from rat mast cells induced by compound 48/80. During our previous studies, the five polyacetylene glucosides [1], three sucrose coumaroylesters and one neolignan have been reported [2]. As a part of our ongoing studies, we report the isolation and structural elucidations of two new monoterpene glycosides named bidensmenthosides A, B and a new (+)-jasmololone glucoside. The 60% EtOH extract from dried whole plant was suspended in water and partitioned with hexane, ethyl acetate and *n*-butanol, respectively. The *n*-butanol fraction was subjected to silica gel, Sephadex LH-20 column chromatography, and further purified by HPLC to give three new compounds **1**, **2** and **3** (figure 1).

2. Results and discussion

Bidensmenthoside A (**1**) was obtained as a yellow oil, $[\alpha]_D^{23} + 61.9$. The HRFABMS indicated the molecular ion peak at *m/z* 333.1762, which corresponded to the molecular

*Corresponding authors. Email: wangnl@sz.tsinghua.edu.cn; kitanaka@pha.nihon-u.ac.jp

Journal of Asian Natural Products Research
ISSN 1028-6020 print/ISSN 1477-2213 online © 2007 Taylor & Francis
http://www.tandf.co.uk/journals
DOI: 10.1080/10286020500532033

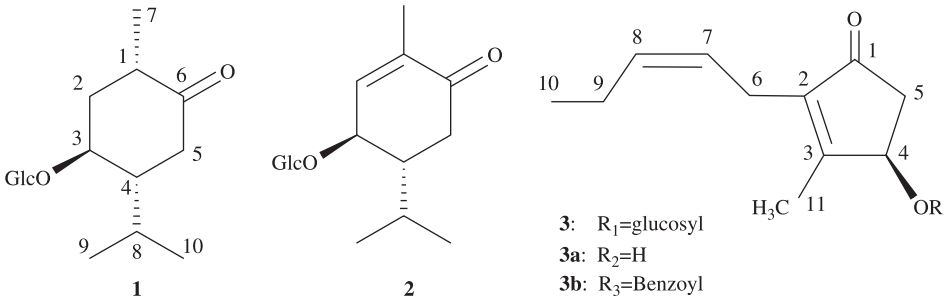

Figure 1. Structures of compounds **1**, **2** and **3**.

formula $C_{16}H_{28}O_7$. In the IR spectrum, absorptions at 3649, 3423 and 1740 cm^{-1} indicated the presence of hydroxyls and carbonyl groups. The ^{1}H-NMR and ^{13}C-NMR spectra (table 1) revealed the presence of a β-glucopyranosyl moiety at δ_H 4.42 (1H, *d*, $J = 7.6$ Hz, glc-H-1′), δc 105.8 (C-1′), 78.3 (C-5′), 78.0 (C-3′), 75.5 (C-2′), 71.7(C-4′) and 62.9 (C-6′). In its ^{13}C NMR spectrum, except for the signals due to the glucose, the remaining ten carbon signals, consisted of one carbonyl group (δc 216.6), one oxygen-bearing methine (δc 77.3), three methyls (δc14.4, 20.8, 21.3), two methylenes (δc 42.0, 42.4) and three methines (δc 29.8, 40.1, 52.7). The molecular formula revealed the presence of three unsaturation. Therefore, the aglycone must be monocyclic since there is only one ketone. From the ^{1}H–^{1}H COSY and HMQC spectra of **1**, the presence of a partial structure CH_3—CH—CH_2—CH(O)—CH[—CH_2—]CH—$(CH_3)_2$ was suggested. In the HMBC experiment, the proton signals at δ_H0.95 (Me-7), 2.98 (H-1), 2.60 (H-2), 2.54 (H-4) and 1.44 (H-4) were correlated with the carbonyl signal at δc 216.6 (C-6). These facts clearly revealed the structure of

Table 1. ^{13}C-NMR and ^{1}H-NMR spectral data for compounds **1** and **2**.

	1		*2*	
	δC	*δH*	*δC*	*δH*
Aglycone				
1	40.1	2.98 *qdd* (6.8, 4.9, 4.2)	136.7	
2	42.0	ax 2.60 *dd* (16.5, 4.9)	146.7	7.03 *dd* (5.8, 1.5)
		eq 1.42 *dd* (16.5, 4.2)		
3	77.3	4.15 *m*	74.2	4.38 *dd* (7.1, 5.8)
4	52.7	1.44 *ddm* (6.6, 5.2)	47.8	1.76 *ddm* (7.1, 4.8,)
5	42.4	ax 2.54 *dd* (16.4, 6.6)	38.5	ax 2.53 *dd* (16.5, 7.1)
		eq 2.32 *dd* (16.4, 5.2)		eq 2.46 *dd* (16.5, 4.8)
6	216.6		202.9	
7	14.2	0.95 *d* (6.8)	15.6	1.74 *d* (1.5)
8	29.8	1.98 *m*	28.7	2.04 *m*
9	20.8	0.89 *d* (6.8)	21.1	0.93 *d* (6.8)
10	21.3	1.01 *d* (6.8)	21.6	1.03 *d* (6.8)
Glucosyl				
1′	105.8	4.42 *d* (7.6)	105.6	4.41 *d* (7.6)
2′	75.5		75.4	
3′	78.0		77.8	
4′	71.7		71.6	
5′	78.3		78.1	
6′	62.9		62.9	

a) Assigned by the ^{1}H–^{1}H COSY, HMQC, and HMBC spectra.
b) 125 MHz for δ^{13}C, 500 MHz for δ^1H, TMS as internal standard, (ppm, in MeOH-d_4).

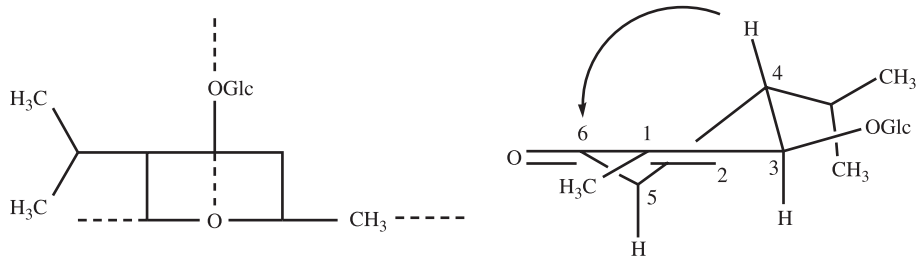

Figure 2. CD analysis of **1** and **2**.

3-hydroxy-*p*-menth-6-one. Additionally, the HMBC correlations between the H-1′(δ_H 4.42) and C-3 (δc 77.3) as well as between the H-3 (δ_H 4.15) and C-1′(δc 105.8) suggested that the glucospyranosyl moiety was attached at the C-3. In the NOESY spectra, we observed H-3 (δ_H 4.15) showed marked correlation with H-1 (δ_H2.98) and H-5$_{ax}$ (δ_H 2.54).The H-4 (δ_H 1.44) signal showed NOE correlation with H-2$_{ax}$ (δ_H 2.60) which indicated the relative configuration of H-1/ H-4 and H-4/H-3 were both *trans*. Finally, the CD spectrum of **1** exhibited a positive Cotton effect for the n $\rightarrow \pi^*$ band, $\Delta\varepsilon_{294} = +0.25$ (figure 2). According to the octant rule [4,5] the isopropyl substitute should be equatorial, in view of the fact that CH_3-7 and 3-glucopyranosyl have no contribution to the Cotton effects. Thus the absolute structure of **1** was suggested as (1*S*, 3*S*, 4*R*)-3-hydroxy-*p*-menth-6-one 3-*O*-β-D-glucoside.

Bidensmenthoside B (**2**) was obtained as a yellow oil, $[\alpha]_D^{23} + 91.2$. The molecular formula of **2** was determined as $C_{16}H_{26}O_7$ by HRFABMS analysis. The IR spectrum exhibited absorption due to a conjugated C═C (1620 cm^{-1}), a conjugated carbonyl (1664 cm^{-1}) and hydroxyls (3616, 3490 cm^{-1}). The ^{1}H-NMR and ^{13}C-NMR spectra (table 1) of **2** indicated the presence of a β-glucopyranosyl moiety at δ 4.41 (1H, *d*, $J = 7.6$ Hz, glc-H-1′), δc 105.6 (C-1′), 78.1 (C-5′), 77.8 (C-3′), 75.4 (C-2′), 71.6 (C-4′), and 62.9 (C-6′). Except for the signals due to the glucosyl moiety in the ^{13}C-NMR, the remaining ten carbon signals, which consisted of one carbonyl group (δc 202.9), two olefinic carbons (δc 136.7, 146.7), one oxygen-bearing methine (δc 74.2), three methyls (δc 15.6, 21.1, 21.6), one methylene (δc 38.5) and two methines (δc 28.7, 47.8), suggested the aglycone as a mono cyclic monoterpene having a carbonyl and a double bond. Partial structure of CH_2-CH [CH—$(CH_3)_2$]CH (O)—CH— was determined by detailed analysis of ^{1}H-^{1}H COSY and HMQC experiments. HMBC correlations between H-9 (δ_H 0.93) and H-10 (1.03) and C-4 (δc 47.8) of the two isopropyl methyls, between H-7 (δ_H 1.74) and C-1 (δc 136.7), C-2 (δc 146.7) and C-6 (δc 202.9) of the double bond methyl, and between H-1′ (δ_H 4.41) and C-3 (δc 74.2) established the plane structure of **2**. It is a 1, 2-dehydrogenated derivative of **1**. The Cotton effect of the CD spectrum was $\Delta\varepsilon_{311} = -5.77$. The observed Cotton led to the 3*R*, 4*R* absolute configuration based on the helicity rule for α,β-unsaturated ketone [3,4] (figure 2). In terms of all these data, the structure of **2** was finally elucidated as (3*R*, 4*R*)-3-hydroxy-*p*-menth-1 (2)-en-6-one 3-*O*-β-D-glucopyranoside. We subsequently learned that the aglycone moiety of **2** is identical to a known (−)-2-oxo-T-cadinol [4,5].

(+)-Jasmololone glycoside (**3**) was obtained as colorless crystals, mp 173–174°C, $[\alpha]_D^{23} + 11.8$. The molecular formula of **3** was determined as $C_{17}H_{26}O_7$ by HRFABMS

analysis. The IR spectrum exhibited characteristic absorption of hydroxyl at 3519 and 3357 cm^{-1}, a conjugated carbonyl at 1681 cm^{-1}, and C=C absorption at 1650 cm^{-1}. The ^{1}H-NMR spectrum of **3a** showed signals of three sets of methylene protons at δ_H 2.17 (1H, dd, $J = 15.9$, 2.1 Hz, H-5), 2.75 (1H, *dd*, $J = 15.9$, 6.3 Hz, H-5), 2.95 (1H, *d*, $J = 7.3$ Hz, H-6), 2.16 (1H, *q*, $J = 7.5$ Hz, H-9), two sets of methyl protons at δ_H 2.13 (3H, *s*, H-11), 0.96 (3H, *t*, $J = 7.5$ Hz, H-10), a methine proton at δ_H 4.63 (1H, *dd*, $J = 6.2$, 2.1 Hz, H-4), two olefinic protons at δ_H 5.21 (1H, *dm*, $J = 12.5$ Hz, H-7), 5.38 (1H, *dm*, $J = 12.5$ Hz, H-8)], and a glucosyl-anomeric proton at δ_H 4.46 (1H, *d*, $J = 8.0$ Hz, H-1′). On hydrolysis by β-D-glucosidase[1], **3** gave the aglycone (**3a**) and glucose. The sugar moiety was suggested to β-D-glucose. From ^{1}H–^{1}H COSY and HMQC experiments, two partial structures from the signals of the methyl at δ_H 0.96 (H-10) to the methylene at δ_H 2.95 (H-6), the oxy-bearing methine at δ_H 4.70 (1H, *dd*, $J = 5.5$, 1.9 Hz, H-4), the nonequivalent methylene at olefine at δ_H 2.51 (1H, *dd*, $J = 18.9$, 1.9 Hz, H-5), and 2.75 (1H, *dd*, $J = 18.9$, 6.3 Hz) were assigned. The HMBC correlations of H-6 and H-7 with C-2 (δc 142.2) as well as the H-11 with C-3 (δc 170.1), C-2 (δc 142.2) and C-4 (δc 80.9), and the H-5 at δ_H 2.51 with C-1 (δc 207.8), C-2 (δc 142.2), C-4 (δc 80.9), C-3 (δc 170.1) gave the plane structure of 4-hydroxy-3-methyl-2-(pent-2-enyl)-cyclopent-2-enone. The isomer of $\Delta^{7,8}$ was *Z*, which was deduced from the NOE correlations between the two protons and their coupling constants ($J = 12.5$ Hz). On the other hand, the stereochemistry of C-4 was resolved by the excition chirality method. The aglycone (**3a**) was reacted with benzoyl chloride affording the benzoate (**3b**). The Cotton effects of **3b**: $\Delta\varepsilon_{282} = +2.16$, $\Delta\varepsilon_{228} = -1.74$ were observed.

The Cotton effect with positive excitation chirality proved the absolute configuration of C-4 to be *R* (figure 3) [6]. Therefore, this result elucidated the absolute structure of **3** as (4*R*)-hydroxy-3-methyl-2-(2 *Z*-pentenyl)-cyclopent-2-enone 4-*O*-β-D-glucopyranoside, i.e. (+)-Jasmololone glucoside. (*4S*) Form of **3** was reported by Yamamura *et al.* [7]. However, the isomer of the 7, 8-double bond seems to be wrong, because it should possess a *E*-configuration, rather than *Z*, judging by the large coupling constant ($J_{7,8} = 17.8$ Hz).

We examined the DPPH scavenging activity of **1**, **2**, **3** and **3a**., among which **1** (IC_{50} 15.1 μM), **2** (IC_{50} 16.3 μM), **3** (187.3 μM) and **3a** (IC_{50} 17.2 μM) exhibit higher activity than the potent antioxidant agent Ascorbic acid (IC_{50} 14.3 μM). However, the IC_{50} concentration (187.3 μM) of **3** is ten times lower than those of **1** and **2**. These results suggested that the moiety of α, β-unsaturated ketone in the structure can transform to enol. The presence of sugar moiety in the structure would bring down its radical scavenging activity.

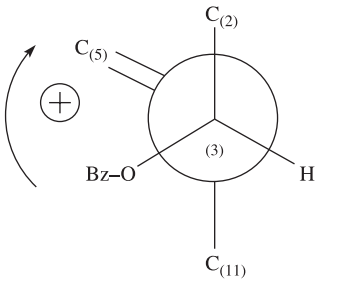

Figure 3. The positive excitor chirality of **3b**.

This is the first report on the free radical scarvenging activity of α,β-unsaturated ketone derivatives.

3. Experimental

3.1 General experimental procedure

Melting points were determined on a Yanagimoto micro-melting-point apparatus, and are uncorrected. The UV spectrum was obtained in MeOH on a Hitachi 200-10 spectrophotometer, and the IR spectrum was recorded on a JASCO IR A-2 spectrophotometer. Optical rotations were taken in MeOH on a JASCO DIP-360 polarimeter. The CD spectra were obtained in MeOH with a JASCO J-600 spectrophotometer. The NMR spectra were taken on a JEOL GL-500 spectrometer with TMS as an internal standard. The MS spectra were obtained on a Hitachi M-80B mate. Sephadex LH-20 (Pharmacia Fine Chemical Industry Ltd.). HPLC was performed on a JASCO PU-2089 HPLC equipped with a JASCO UV-2075 detector. Senshu Pak PEGASIL Silica 60-5 (10 mm i.d. × 250 mm) and Senshu pak PWGASIL ODS (10 mm i.d. × 250 mm) columns were used for preparative purpose. DPPH α-tocopherol was purchased from Wako Chemical Co., Ltd. (Osaka, Japan).

3.2 Plant materials

The whole plant of *Bidens parviflora* Willd. was collected from Da-Hei-Shan of Liaoning province, China, in July 1999 and was identified by Prof. Weichun Wu (Department of Medical Plants, Shenyang Pharmaceutical University, China). A voucher specimen (99-DHS-953) is deposited at the College of Pharmacy, Nihon University and the Department of Natural Products Chemistry of Shenyang Pharmaceutical University.

3.3 Extraction and isolation

The dried whole plant (5.5 kg) was extracted twice with 60% ethanol under reflux. Evaporation of the solvent under reduced pressure gave the extract (672 g). The extract was dissolved, suspended in water and partitioned with hexane, ethyl acetate and *n*-butanol in the same volume for three times, respectively, the butanol phase was concentrated under vacuum to give the extract (176 g), which was subjected to silica gel column chromatography (SiO_2, 500 g), eluted with $CHCl_3$ and MeOH in increasing polarity to obtain 12 fractions. The fraction 8 (6.5 g) was applied to a Sephadex LH-20 column eluted with 50% MeOH to obtain fractions 3–6 and was purified by HPLC (INW 125 Fluofix, 10 mm i.d. × 250 mm, UV detector, 254 nm) eluted with 18% CH_3CN in water to give **1** (12.2 mg), **2** (13.1 mg) and **3** (40.8 mg).

3.3.1 Bidensmenthoside A (1). Yellow oil, $[\alpha]_D^{23} + 61.9$ ($c = 0.46$, MeOH). FAB-MS *m/z*: 331 $[M - H]^-$, HRFABMS (negative mode) *m/z*: 331.1762$[M - 1]^-$ (calcd for $C_{16}H_{27}O_7$, 331.1762); UV λ_{max}^{MeOH} nm (logε): 206 (3.51); IR ν_{max}^{KBr} cm^{-1}: 3838, 3734, 3649, 3423, 2920, 2852, 1740, 1669; CD ($c = 2.32 \times 10^{-5}$, MeOH): $\Delta\varepsilon_{208} = -7.72$, $\Delta\varepsilon_{263} = +1.74$, $\Delta\varepsilon_{294} = +0.25$; ^{1}H-NMR and ^{13}C-NMR spectral data (in CD_3 OD; 500 MH_Z and 125 MH_Z; see table 1).

3.3.2 Bidensmenthoside B (2). Yellow oil, $[\alpha]_D^{23} + 91.2$ ($c = 0.52$, MeOH). FABMS *m/z*: 329 $[M - H]^-$, HRFABMS(negative mode) *m/z*: 329.1614 $[M - 1]^-$ (calcd for $C_{16}H_{25}O_7$, 329.1700); UV λ_{max}^{MeOH} nm (log ε): 229 (3.72); IR ν_{max}^{KBr} cm^{-1}: 3616, 3490, 3363, 3084, 2902, 1664, 1620, 1560; CD ($c = 4.17 \times 10^{-5}$, MeOH): $\Delta\varepsilon_{221} = +40.05$, $\Delta\varepsilon_{239} = +53.52$, $\Delta\varepsilon_{311} = -5.57$; ^{1}H-NMR and ^{13}C-NMR spectral data (in CD_3 OD; 500 MH_Z and 125 MH_Z; see table 1).

3.3.3 (+)-Jasmololone glucoside (3). Colorless crystals, mp 173–174°C, $[\alpha]_D^{23} + 11.8$ ($c = 0.41$, MeOH). FAB-MS *m/z*: 343 $[M + H]^+$, HRFABMS (positive mode) *m/z*: 343.1765 $[M + 1]^+$ (calcd for $C_{17}H_{27}O_7$, 343.1757); UV λ_{max}^{MeOH} nm (logε): 233 (4.61); IR ν_{max}^{KBr} cm^{-1}: 3519, 3357, 2964, 2883, 1681, 1650, 1344, 1201, 1076, 1033; ^{1}H and ^{13}C NMR spectral data (in CD_3 OD; 500 MH_Z and 125 MH_Z; see table 2).

3.3.4 (+)-Jasmololone (3a). Colorless powder, $[\alpha]_D^{23} + 4.8$($c = 0.38$, MeOH). EI-MS *m/z*: 180, HREIMS *m/z*: 180.1641 [M] + (calcd for $C_{11}H_{16}O_2$, 180.1642); UV λ_{max}^{MeOH} nm (logε): 233(4.51); ^{1}H and ^{13}C NMR spectral data (in CD_3OD; 500 MH_Z and 125 MH_Z; see table 2).

3.4 Preparation of benzoate (3b)

The aglycone **3a** (2.1 mg) was dissolved in pyridine (0.2 ml) and benzoyl chloride (10 μl), and then kept at 37°C for 20 h. The reaction mixture was added MeOH (1 ml) and kept for 3 h. The solution was evaporated to give benzoate (**3b**, *ca.* 0.8 mg), which was purified by HPLC (column: Capcell Pack C-18, solvent: 18% $CHCN_3$: 82% H_2O) likewise.

Table 2. ^{13}C-NMR and ^{1}H-NMR spectral data for compounds **3** and **3a**.

	3		***3a***	
	δC	*δH*	*δC*	*δH*
Aglycon				
1	207.8		207.8	
2	142.2		141.2	
3	170.1		172.4	
4	80.9	4.70 *dd* (5.5, 1.9)	72.0	4.63 *dd* (6.3, 2.1)
5	44.3	2.51 *dd* (16.9, 1.9)	44.3	2.17 *dd* (15.9, 2.1)
		2.75 *dd* (16.9, 6.3)		2.75 *dd* (15.9, 6.3)
6	21.7	2.95 *d* (6.3)	21.8	2.95 *d* (7.4)
7	125.4	5.21 *dt* (12.5)	125.6	5.21 *dt* (12.5)
8	133.7	5.38 *dt* (12.5)	133.7	5.38 *dt* (12.5)
9	21.5	2.16 *q* (7.5)	21.5	2.15 *q* (7.5)
10	14.5	0.98 *t* (7.5)	13.9	0.96 *t* (7.5)
11	14.4	2.16 *s*	14.5	2.13 *s*
Glucosyl				
1′	105.4	4.46 *d* (8.0)		
2′	75.8			
3′	78.4			
4′	71.4			
5′	77.9			
6′	62.9			

a) Assigned by the ^{1}H–^{1}H COSY, HMQC, and HMBC spectra.
b) 125 MHz for δ^{13}C, 500 MHz for δ^1H, TMS as internal standard, (ppm, in MeOH-d_4).

3.4.1 4-benzoyoxyl-3-methyl-2-(*Z*-pent-2-enyl)-cyclopent-2-enone (3b). Yellow oil, FAB-MS *m/z*: 285 $[M + H]^+$, HRFABMS (positive mode) *m/z*: 285.1765$[M + 1]^+$ (calcd for $C_{18}H_{20}O_3$, 284.1757); UV λ_{max}^{MeOH} nm (log ε): 228 (4.58), 210 (2.82), 202 (3.49).

3.5 Scavenging activity of DPPH radical

Radical was determined according to Cavin *et al.* [8,9]. The assay mixture contained 1.0 mM DPPH redical solution (0.3 ml), 99% ethanol (2.4 ml) and sample solution (0.3 ml). The solution was rapidly mixed and the scavenging capacity was measured erectrophotometrically by monitoring the decrease in absorbance at 517 nm determined after 10 min and the scavenging activity calculated as a percentage of the radical reduction. Ascorbic acid was used as a positive control.

Acknowledgements

This study was financially supported by a Grant-in-Aid for Research on Eye and Ear Science, Allergy and Organ Transplantation from the Health Science Research Grants, for the Ministry of Health, Labour and Welfare, by Technology of Japan and for the promotion and mutual aid corporation for private school of Japan to Nihon University and by a Grant from the Ministry of Education, Culture, Sports, Science and Technology of Japan to promote multidisciplinary research projects.

References

[1] N.L. Wang, X.S. Yao, R. Ishii, S. Kitanaka. *Chem. Pharm. Bull.*, **49**, 938 (2001).
[2] N.L. Wang, X.S. Yao, R. Ishii, S. Kitanaka. *Phytochemistry*, **62**, 741 (2003).
[3] C. Djerassi, W. Klyne, T. Norin, G. Ohloff, E. Kein. *Tetrahedron*, **21**, 163 (1965).
[4] J. DE Pascual-T, I.S. Bellido, C. Torres, B.A. Sastre, M. Grande. *Phytochemistry*, **20**, 163 (1981).
[5] F. Bohlmann, W. Kramp, R.K. Gupta, R.M. King, H. Robinson. *Phytochemistry*, **20**, 2375 (1981).
[6] S. Nozoe, K. Hirai. *Tetrahedron*, **30**, 2773 (1996).
[7] S. Yamamura, K. Ozawa, K. Ohtani, R. Kasai, K. Yamasaki. *Phytochemistry*, **48**, 131 (1998).
[8] A. Cavin, K. Hostettmann, W. Dyatmyko, O. Potter. *Planta Med.*, **64**, 393 (1998).
[9] Y. Okada, M. Okada. *J. A Food Chem.*, **46**, 147 (1998).