Rubupungenosides A and B, Two Novel Triterpenoid Saponin Dimers from the Aerial Parts of *Rubus pungens*

Bin-Gui Wang,[†,‡] Wei-Ming Zhu,[‡] Xiao-Ming Li,[‡] Zhong-Jian Jia,*[,†] and Xiao-Jiang Hao*[,‡]

Department of Chemistry, Institute of Organic Chemistry, National Laboratory of Applied Organic Chemistry, Lanzhou University, Lanzhou 730000, People's Republic of China, and Laboratory of Phytochemistry, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming 650204, People's Republic of China

Received September 27, 1999

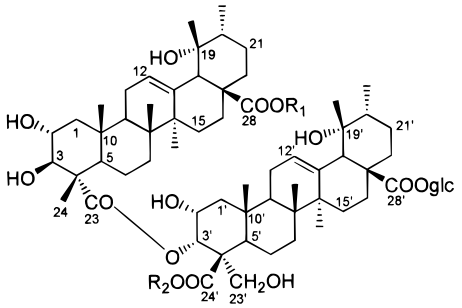
Two new triterpenoid saponin dimers, rubupungenosides A (**1**) and B (**2**), were isolated in their methylated forms **1a** and **2a**, respectively, from an ethanol extract of the aerial parts of *Rubus pungens*. The structures of **1a** and **2a** were established on the basis of spectroscopic and chemical methods.

Species of the genus *Rubus* (Rosaceae) are widely distributed in the People's Republic of China, and many of them have been used in traditional Chinese medicine as antibacterial, antiinflammatory, and antitumor agents, and for the treatment of various diseases such as arthritis, dysentery, enteritis, and rheumatism.[1,2] During previous chemical investigation of *Rubus* species, we have reported several pentacyclic triterpenoids and their glucosides and methylglucosides, with a highly oxygenated ring A.[3−6] Previous studies on bioactivity revealed that these types of pentacyclic triterpenoids and their glycosides from *Rubus* species possess antibacterial and antinociceptive activities.[7,8] We describe herein the isolation and structure determination of two novel triterpenoid glycoside dimers, namely, rubupungenosides A (**1**) and B (**2**), from the aerial parts of *R. pungens* Camb. var. *oldhamii* Maxim.

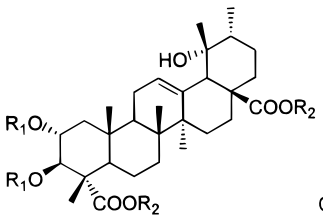
The ethanolic extract of the aerial part of *R. pungens* Camb. var. *oldhamii* was fractionated to afford a triterpenoid glycoside fraction. This fraction was treated with diazomethane in methanol because of difficulties encountered in the separation of the natural products **1** and **2**. The methylated fraction was separated by repeated column chromatography on Si gel and Sephadex LH-20 and finally purified by reversed-phase HPLC to afford compounds **1a** and **2a**.

Compound **1a**, obtained as amorphous powder, gave positive colorations in the Liebermann-Burchard and Molish tests, suggesting that it was a triterpenoid glycoside. Its IR spectrum revealed the presence of hydroxyl (3435 cm^{-1}), ester carbonyl (1727 cm^{-1}), and double-bond (1646 cm^{-1}) functionalities in the molecule. The molecular formula of **1a** was determined by negative HRFABMS as $C_{74}H_{114}O_{24}$. The ^{13}C NMR spectrum exhibited most signals in pairs having close chemical shifts, which suggested that **1a** might be a triterpenoid dimer.

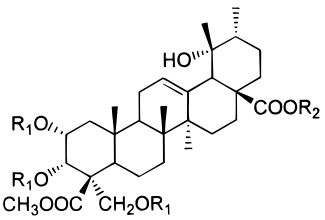
Hydrolysis of **1a** with 3% NaOH aqueous solution afforded two triterpenoids, **3** and **4**, indicating that **1a** was a triterpenoid dimer composed of **3** and **4**. The ^1H and ^{13}C NMR, DEPT, and EIMS data of **3** were identical with those of 2α,3*β*,19α-trihydroxyurs-12-ene-23,28-dioic acid, the aglycon of suavissimoside R1 previously obtained from two *Rubus* species.[4,9] Treatment of **3** with diazomethane in CH_3OH afforded dimethyl ester **3a**, which was further acetylated with Ac_2O/pyridine at room temperature to yield the corresponding diacetylated product **3b**. These chemical transformations confirmed the structure of **3**. The NMR spectral data of **4** and those of 2α,3α,19α,23-tetrahydroxyurs-12-ene-24,28-dioic acid[10] were found to be similar. A difference of 14 mass units in the EIMS of **4** suggested an additional methyl group was present, compared with 2α,3α,19α,23-tetrahydroxyurs-12-ene-24,28-dioic acid,[10] consistent with the methyl signal observed at *δ* 3.65 (3H, s) in the ^1H NMR spectrum and the ester methyl carbon signal at *δ* 51.8 in the ^{13}C NMR spectrum. In the EIMS, the fragment ion peak at *m*/*z* 264 derived from a typical retro-Diels−Alder rearrangement of ring C of a Δ^{12}-ursene triterpene suggested that the additional ester methyl group was located in rings A/B (C-24 position).[11] Similarly, treatment of **4** with diazomethane in CH_3OH yielded dimethyl ester **4a**, which was then acetylated with Ac_2O/pyridine at room temperature to afford the corresponding tri-acetylated product **4b**.



1 R_1 = 6′-*O*-methyl-β-D-glucopyranosyl, R_2 = H
1a R_1 = 6′-*O*-methyl-β-D-glucopyranosyl, R_2 = CH_3
2 R_1 = 3′-*O*-methyl-β-D-glucopyranosyl, R_2 = H
2a R_1 = 3′-*O*-methyl-β-D-glucopyranosyl, R_2 = CH_3



3 R_1 = R_2 = H
3a R_1 = H, R_2 = CH_3
3b R_1 = Ac, R_2 = CH_3



4 R_1 = R_2 = H
4a R_1 = H, R_2 = CH_3
4b R_1 = Ac, R_2 = CH_3

* To whom correspondence should be addressed. Tel.: 0086-931-8912408. Fax: 0086-931-8912586. E-mail: zhengrl@lzu.edu.cn (Z.-J.J.). Tel.: 0086-871-5219684. Fax: 0086-871-5150227. E-mail: xjhao@mail.kib.ac.cn (X.-J.H.).
† Lanzhou University.
‡ Kunming Institute of Botany.

10.1021/np990473n CCC: $19.00
Published on Web 05/10/2000

Table 1. ^{13}C NMR Data for Compounds **1a** and **2a**[a]

carbon	**1a**	**2a**	carbon	**1a**	**2a**	carbon	**1a**	**2a**
1	48.7 t	48.7 t	1′	42.8 t	43.0 t	C-28 sugar		
2	69.5 d	69.9 d	2′	65.8 d	66.1 d	1	95.6 d	95.7 d
3	80.8 d	81.0 d	3′	73.9 d	73.4 d	2	73.8 d	73.8 d
4	55.5 s	55.5 s	4′	55.5 s	55.5 s	3	77.8 d	78.3 d
5	52.2 d	52.4 d	5′	54.4 d	54.5 d	4	71.0 d	71.1 d
6	21.2 t	21.4 t	6′	20.7 t	20.7 t	5	78.7 d	79.2 d
7	32.8 t	33.1 t	7′	33.3 t	33.6 t	6	72.5 t	62.2 t
8	40.4 s	40.7 s	8′	40.4 s	40.4 s	MeO-3		60.9 q
9	48.5 d	48.9 d	9′	48.5 d	47.3 d	MeO-6	59.1 q	
10	38.7 s	39.0 s	10′	38.3 s	38.6 s	C-28′ sugar		
11	24.1 t	24.3 t	11′	24.2 t	24.2 t	1	95.9 d	95.7 d
12	128.2 d	128.4 d	12′	127.8 d	128.1 d	2	74.1 d	74.1 d
13	139.2 s	139.4 s	13′	139.1 s	139.3 s	3	88.8 d	79.3 d
14	42.8 s	42.3 s	14′	40.4 s	40.7 s	4	70.9 d	71.4 d
15	29.0 t	29.1 t	15′	29.0 t	29.3 t	5	79.0 d	79.0 d
16	25.9 t	26.2 t	16′	26.0 t	26.2 t	6	62.2 t	62.5 t
17	48.1 s	48.9 s	17′	48.1 s	48.9 s			
18	54.3 d	54.6 d	18′	54.3 d	54.5 d			
19	72.4 s	72.8 s	19′	72.4 s	72.8 s			
20	42.0 d	42.3 d	20′	42.0 d	42.2 d			
21	26.8 t	26.8 t	21′	26.6 t	26.8 t			
22	37.5 t	37.7 t	22′	37.5 t	37.7 t			
23	177.6 s	177.6 s	23′	68.7 t	68.9 t			
24	12.8 q	12.9 q	24′	175.1 s	175.3 s			
25	17.3 q	17.5 q	25′	17.3 q	17.5 q			
26	16.5 q	17.5 q	26′	16.5 q	16.8 q			
27	24.4 q	24.7 q	27′	24.1 q	24.6 q			
28	176.7 s	177.1 s	28′	176.7 s	177.1 s			
29	26.8 q	27.1 q	29′	26.8 q	27.1 q			
30	16.5 q	16.8 q	30′	14.4 q	14.6 q			
CO_2Me-24				51.5 q	51.6 q			

[a] Spectral data were obtained at 100 MHz and recorded in C_5D_5N.

A careful comparison of the ^1H and ^{13}C NMR spectral data of **1a** with those of coreanoside F1, a triterpenoid glucosyl ester dimer isolated from leaves of *Rubus coreanus*,[10] showed that the structures of these two compounds were similar, except that **1a** had two additional methoxyl groups, with one being the C-24′ ester methyl at δ 51.5 and the other attached at the C-6 position of the glucosyl moiety. Furthermore, the seven carbon signals of the 6-*O*-methyl-β-D-glucopyranosyl moiety observed in the ^{13}C NMR spectrum of **1a** (Table 1) corresponded almost exactly to those reported for 6-*O*-methyl-β-D-glucopyranose.[12] The anomeric proton signals at δ 6.25 (1H, d, J = 8.2 Hz) and 6.18 (1H, d, J = 8.2 Hz) in the ^1H NMR spectrum of **1a** indicated the β-configuration for both of the glucosyl and methylglucosyl moieties.

The only remaining problem in the structure determination of **1a** was the placement of the glucosyl and 6-*O*-methylglucosyl moieties. The fragment ion peaks at *m*/*z* 677.3927 ($C_{37}H_{57}O_{11}$) and 501.3252 ($C_{30}H_{45}O_6$) (*m*/*z* 677-methylglucosyl) in the HRFABMS suggested that a 6-*O*-methyl-β-D-glucopyranosyl moiety was attached to the C-28 position rather than the C-28′ position, and therefore the β-D-glucopyranosyl moiety must be attached to the C-28′ position.

From all the above-mentioned information, the structure of compound **1a** was assigned as shown. The naturally occurring compound corresponds to **1** and has been named rubupungenoside A. This is only the second example of a triterpenoid dimer from the genus *Rubus*.[10]

Compound **2a** also gave positive colorations in the Liebermann-Burchard and Molish tests, indicating that it was a further triterpenoid glycoside. The presence of hydroxyl, ester carbonyl, and double-bond functionalities in the molecule was suggested by the absorption bands at 3440, 1727, and 1648 cm^{-1} in the IR spectrum. The negative FABMS showed almost the exactly same molecular and fragment ion peaks as those in **1a**, indicating that **2a** has the same molecular formula as **1a** ($C_{74}H_{114}O_{24}$). This was confirmed by the similar NMR spectral data of these two compounds (Table 1).

In the ^{13}C NMR spectrum, the most significant differences of **2a** from **1a** were the changes in chemical shifts apparent for C-3 and C-6 in the C-28 methylglucosyl moiety. The C-3 signal of the C-28 methylglucosyl unit in **2a** resonated at δ 88.8, 11.0 ppm downfield shifted compared to that of the same position in **1a**, confirming that the methylation occurred at C-3 of the methylglucosyl moiety, and this was also supported by the upfield shift observed at the C-6 position of this residue. The seven carbon signals of 3-*O*-methylglucopyranosyl moiety of **2a** were observed at almost the same positions as reported for 3-*O*-methyl-β-D-glucopyranose.[12] The other carbons of **2a** resonated in the same positions as in **1a** (Table 1). From the above evidence the structure of compound **2a** was established as shown. The structure of the corresponding natural compound should as be **2**.

Experimental Section

General Experimental Procedures. Melting points were determined using a Kofler micromelting point apparatus and are uncorrected. Optical rotations were determined on a Horiba SEPA-300 polarimeter. IR spectra were obtained as KBr pellets using a Bio-Rad FTS-135 spectrometer. NMR spectra were recorded on a Bruker AM-400 spectrometer using TMS as internal standard. EIMS and HRFABMS measurements were carried out on a VG Auto Spec-3000 spectrometer. TLC was performed on plates precoated with Si gel F_{254} (Qingdao Marine Chemical Ltd., Qingdao, People's Republic of China). Solvents were double-distilled prior to use.

Plant Material. The aerial parts of *R. pungens* Camb. var. *oldhamii* were collected in Zhang County, Gansu Province, People's Republic of China, in September 1994. The plant was identified by Professor Ze-Xiang Peng, Department of Biology,

Lanzhou University. A voucher specimen (no. 9409011R) has been deposited in the Institute of Organic Chemistry, Lanzhou University.

Extraction and Isolation. The aerial parts of *R. pungens* Camb. var. *oldhamii* (5.0 kg) were air-dried, ground, and extracted three times with 95% EtOH (12 L each time) at room temperature. The EtOH extract was evaporated in vacuo to yield a residue (350 g). To this residue, 1200 mL of hot water were added, and the solution was successively extracted with petroleum ether, EtOAc, and *n*-BuOH. The *n*-BuOH extract was concentrated to yield the crude glycoside residue (40 g), which was chromatographed on a highly porous resin (SIP 1400; manufactured by Shanghai Resin Factory, Shanghai, People's Republic of China) eluted successively with H_2O-EtOH (1:0 to 0:1). Because TLC indicated that this refined glycoside fraction was of complex composition, it was treated with diazomethane in methanol and then passed over a column containing Sephadex LH-20. Further purification was carried out by repeated Si gel (200−300 mesh) column chromatography. The fractions that eluted with $CHCl_3$−CH_3OH−H_2O (30:10:1) were combined and concentrated under vacuum to afford a mixture of **1a** and **2a**. The mixture was then separated by preparative reversed-phase HPLC (ODS column, 10 × 250 mm, eluted with CH_3OH−H_2O, 60:40) to yield compounds **1a** (63 mg, R_f 0.28, $CHCl_3$−CH_3OH−H_2O, 30:10:1) and **2a** (30 mg, R_f 0.25, $CHCl_3$−CH_3OH−H_2O, 30:10:1).

Compound 1a: obtained as an amorphous powder; mp 231−233 °C; $[\alpha]^{21}$ +12.3° (*c* 0.35, CH_3OH); IR (KBr) ν_{max} 3435 (OH), 1727, 1646, 1456, 1382, 1229, 1139, 1072 cm^{-1}; ^1H NMR (pyridine-d_5, 400 MHz) δ 6.25 (1H, d, J = 8.2 Hz, anomeric proton of methylglucosyl moiety), 6.18 (1H, d, J = 8.2 Hz, anomeric proton of glucosyl moiety), 5.47 (1H, br s, H-12 or H-12′), 5.42 (1H, br s, H-12′ or H-12), 5.13 (1H, br s, H-3′), 4.86 (2H, d, J = 7.0 Hz, H-23′), 4.38 (1H, d, J = 10.5 Hz, H-3), 3.75 (3H, s, $COOCH_3$-24′), 3.50 (3H, s, methyl proton of methylglucosyl group), 3.03 (1H, brs, H-18 or H-18′), 2.86 (1H, br s, H-18′ or H-18), 1.60 (3H, s, H-27), 1.55 (3H, s, H-27′), 1.47 (3H, s, H-24), 1.33 (3H, d, J = 6.8 Hz, H-30 or H-30′), 1.17 (3H, d, J = 8.3 Hz, H-30′ or H-30), 1.07 (3H, s, H-29), 1.05 (3H, s, H-29′), 1.03 (3H, s, H-25), 1.01 (3H, s, H-25′), 0.99 (3H, s, H-26), 0.97 (3H, s, H-26′); ^{13}C NMR data, Table 1; HRFABMS (negative) *m/z* 1385.7638 (calcd for $C_{74}H_{113}O_{24}$, 1385.7622, [M − 1]$^-$), 1223.7162 (calcd for $C_{68}H_{103}O_{19}$, 1223.7094, [M − glc − 1]$^-$), 1209.6889 (calcd for $C_{67}H_{101}O_{19}$, 1209.6937, [M − methylglc − 1]$^-$), 1047.6491 (calcd for $C_{61}H_{91}O_{14}$, 1047.6409, [M − methylglc − glc − 1]$^-$), 1001.6425 (calcd for $C_{60}H_{89}O_{12}$, 1001.6354, [M − methylglc − COOH − 1]$^-$), 677.3927 (calcd for $C_{37}H_{57}O_{11}$, 677.3901), 501.3252 (calcd for $C_{30}H_{45}O_6$, 501.3216).

Hydrolysis of Compound 1a. Aqueous NaOH (3%, 3 mL) was added to a solution of **1a** (25 mg) and kept at 85 °C for 4 h. The reaction mixture was neutralized with 5% HCl and then extracted with *n*-BuOH. The *n*-BuOH extract was separated by column chromatography on Si gel eluting with $CHCl_3$−CH_3OH−H_2O (40:10:1) to afford compounds **3** (5 mg) and **4** (6 mg).

Compound 3: ^1H NMR (CD_3OD, 400 MHz) δ 5.28 (1H, br s, H-12), 3.73 (1H, d, J = 8.5 Hz, H-3), 3.66 (1H, m, H-2), 2.49 (1H, br s, H-18), 1.34 (3H, s, H-27), 1.19 (3H, s, H-29), 1.10 (3H, s, H-24), 1.02 (3H, s, H-25), 0.93 (3H, d, J = 6.4 Hz, H-30), 0.77 (3H, s, H-26); ^{13}C NMR (CD_3OD, 100 MHz) 181.0 (C-23, s), 181.0 (C-28, s), 140.1 (C-13, s), 129.1 (C-12, d), 81.1 (C-3, d), 73.6 (C-19, s), 69.4 (C-2, d), 55.1 (C-4, s), 55.1 (C-18, d), 52.7 (C-5, d), 48.8 (C-9, d), 48.8 (C-17, s), 48.4 (C-1, t), 43.1 (C-20, d), 42.7 (C-14, s), 41.1 (C-8, s), 39.2 (C-10, s), 39.0 (C-22, t), 33.7 (C-7, t), 29.6 (C-15, t), 27.3 (C-21, t), 27.1 (C-29, q), 26.6 (C-16, t), 24.7 (C-11, t), 24.7 (C-27, q), 21.8 (C-6, t), 17.4 (C-25, q), 17.4 (C-26, q), 16.6 (C-30, q), 13.1 (C-24, q); EIMS (70 eV) *m/z* 518 [M]$^+$ (5), 500 [M − H_2O]$^+$ (4), 472 [M − COOH − 1]$^+$ (42), 454 (10), 400 (22), 264 (21), 246 (36), 201 (55), 187 (35), 146 (100).

Compound 4: ^1H NMR (CD_3OD, 400 MHz) δ 5.28 (1H, br s, H-12), 4.15 (1H, m, H-2), 3.99, 3.81 (1H each, d, J = 10.2 Hz, H-23a, 23b), 3.65 (3H, s, $COOCH_3$-24), 3.40 (1H, br s, H-3), 2.49 (1H, br s, H-18), 1.34 (3H, s, H-27), 1.18 (3H, s, H-29), 0.91 (3H, d, J = 7.3 Hz, H-30), 0.80 (3H, s, H-25), 0.78 (3H, s, H-26); ^{13}C NMR (CD_3OD, 100 MHz) 181.2 (C-28, s), 177.1 (C-24, s), 140.1 (C-13, s), 129.4 (C-12, d), 73.6 (C-19, s), 70.3 (C-3, d), 67.1 (C-2, d), 67.1 (C-23, t), 55.5 (C-4, s), 55.2 (C-18, d), 51.8 (C-24 methoxyl carbon, q), 48.8 (C-17, s), 47.7 (C-5, d), 46.8 (C-9, d), 43.1 (C-20, d), 42.8 (C-1, t), 42.8 (C-14, s), 40.9 (C-8, s), 39.5 (C-22, t), 39.0 (C-10, s), 34.1 (C-7, t), 28.9 (C-15, t), 27.3 (C-21, t), 27.1 (C-29, q), 26.7 (C-16, t), 24.8 (C-11, t), 24.7 (C-27, q), 20.9 (C-6, t), 17.4 (C-30, q), 16.6 (C-26, q), 14.8 (C-25, q); EIMS (70 eV) *m/z* 548 [M]$^+$ (4), 530 [M − H_2O]$^+$ (3), 502 [M − COOH − 1]$^+$ (16), 486 (9), 264 (29), 246 (39), 201 (57), 189(23), 187 (30), 146 (87).

Methylation of Compounds 3 and 4. Compound **3** (5 mg) was dissolved in 0.5 mL of CH_3OH, 0.5 mL of diazomethane in Et_2O was added, and the reaction mixture was stored at 5 °C overnight. Removal of the solvents afforded a residue that was purified by flash column chromatography over Si gel to give 4 mg of **3a**. Compound **4** was also treated with diazomethane in the manner described for **3** to yield **4a** (4 mg).

Compound 3a: EIMS (70 eV) *m/z* 546 [M]$^+$ (5), 528 [M − H_2O]$^+$ (3), 486 [M − $COOCH_3$ − 1]$^+$ (16), 454 (12), 279 (8), 278 (21), 260 (22), 219 (19), 201 (54), 179 (68), 146 (45).

Compound 4a: EIMS (70 eV) *m/z* 562 [M]$^+$ (22), 544 [M − H_2O]$^+$ (9), 502 [M − $COOCH_3$-1]$^+$ (34), 464 (17), 279 (25), 278 (63), 260 (54), 219 (45), 201 (93), 179 (100), 146 (70).

Acetylation of Compounds 3a and 4a. A solution of **3a** (4 mg) in Ac_2O (0.5 mL) and pyridine (0.5 mL) was kept at room-temperature overnight. The acetylated product was purified by flash column chromatography over Si gel to give diacetate **3b** (2 mg). Compound **4a** was also acetylated in the same manner as that for **3a** to afford triacetate **4b** (2 mg).

Compound 3b: EIMS (70 eV) *m/z* 630 [M]$^+$ (5), 570 [M − $COOCH_3$ − 1]$^+$ (16), 279 (6), 278 (15), 260 (14), 219 (15), 201 (33), 179 (44), 146 (39).

Compound 4b: EIMS (70 eV) *m/z* 688 [M]$^+$ (20), 670 [M − H_2O]$^+$ (10), 628 [M − $COOCH_3$ − 1]$^+$ (35), 279 (12), 278 (42), 260 (32), 218 (23), 201 (58), 179 (64), 146 (32), 143 (100).

Compound 2a: obtained as an amorphous powder; mp 216−218 °C; $[\alpha]^{21}_D$ +15.81° (*c* 0.25, CH_3OH); IR (KBr) ν_{max} 3440 (OH), 1727, 1648, 1457, 1382, 1229, 1137, 1074 cm^{-1}; ^1H NMR (pyridine-d_5, 400 MHz) δ 6.28 (1H, d, J = 8.0 Hz, anomeric proton of methylglucosyl group), 6.23 (1H, d, J = 8.2 Hz, anomeric proton of glucosyl moiety), 5.50 (1H, br s, H-12 or H-12′), 5.45 (1H, br s, H-12′ or H-12), 5.21 (1H, br s, H-3′), 4.88 (2H, d, J = 9.5 Hz, H-23′), 4.34 (1H, d, J = 8.9 Hz, H-3), 3.89 (3H, s, $COOCH_3$-24′), 3.75 (3H, s, methyl proton of methylglucosyl group), 3.06 (1H, br s, H-18 or H-18′), 2.89 (1H, br s, H-18′ or H-18), 1.68 (3H, s, H-27), 1.64 (3H, s, H-27′), 1.63 (3H, s, H-29), 1.50 (3H, s, H-29′), 1.37 (3H, d, J = 7.1 Hz, H-30 or H-30′), 1.19 (3H, s, H-24), 1.11 (3H, s, H-25), 1.09 (3H, s, H-25′), 1.05 (3H, d, J = 6.0 Hz, H-30′ or H-30), 0.99 (3H, s, H-26), 0.98 (3H, s, H-26′); ^{13}C NMR data, Table 1; FABMS *m/z* 1386 (10), 1224 (81), 1210 (55), 1048 (27), 1002 (16), 677 (8), 501 (15), 471 (100).

Acknowledgment. Financial support by a grant from the National Natural Science Foundation of the People's Republic of China is gratefully acknowledged. B.-G.W. wishes to thank the K. C. Wong Education Foundation (Hong Kong) for partial financial support.

References and Notes

(1) Jiangsu New Medical College. *Zhongyao Dacidian* (*A Dictionary of Traditional Chinese Medicine*); Shanghai Science and Technology Publishing House: Shanghai, 1977.
(2) Xie Z. W. *Quanguo Zhongcaoyao Huibian* (*A Collection of Chinese National Herbal Drugs*), 2nd ed.; People's Health Publishing House: Beijing, 1996; Vols. I and II.
(3) Wang, B. G.; Jia, Z. J. *Zhongcaoyao* **1999**, *30*, 83−87.
(4) Wang, B. G.; Jia, Z. J. *Phytochemistry* **1998**, *49*, 185−188.
(5) Li, B. Z.; Wang, B. G.; Jia, Z. J. *Phytochemistry* **1998**, *49*, 2477−2481.
(6) Wang, B. G.; Shen, X. M.; Yang, L.; Jia, Z. J. *Phytochemistry* **1997**, *46*, 559−563.
(7) Zhu, Z. H.; Zhang, H. Q.; Yuan, M. J. *Zhongguo Zhongyao Zazhi* **1990**, *15*, 427−429.

(8) Niero, R.; Filko, V. C.; Souza, M. M.; Montanari, J. L.; Yunes, R. A.; Monache, F. D. *J. Nat. Prod.* **1999**, *62*, 1145−1146.
(9) Gao, F.; Chen, F. H.; Tanaka, T.; Kasai, R.; Seto, T.; Tanaka, O. *Chem. Pharm. Bull.* **1985**, *33*, 37−40.
(10) Ohtani, K.; Miyajima, C.; Takahasi, T.; Kasai, R.; Tanaka, O.; Hahn, D. G.; Naruhashi, N. *Phytochemistry* **1990**, *29*, 3275−3280.
(11) Budzikiewicz, H.; Wilson, J. M.; Djerassi, C. *J. Am. Chem. Soc.* **1963**, *85*, 3688−3699.
(12) Usui, T.; Yamaoka, N.; Matsuda, K.; Tuzimura, K. *J. Chem. Soc., Perkin Trans. 1* **1973**, 2425−2432.
(13) Abe, F.; Yamauchi, T. *Chem. Pharm. Bull.* **1987**, *35*, 1748−1754.
(14) Zhou, J. J.; Le, X. F.; Han, J. X.; Yang, W. Y. *Zhongguo Yiyao Gongye Zazhi* **1993**, *24*, 455−457.

NP990473N