Guaiane Dimers and Germacranolide from *Artemisia caruifolia*

Chao-mei Ma, Norio Nakamura, Masao Hattori,* Shu Zhu, and Katsuko Komatsu

Institute of Natural Medicine, Toyama Medical and Pharmaceutical University, 2630 Sugitani, Toyama 930-0194, Japan

Received January 7, 2000

One new germacranolide (named caruifolin A) and three new guaiane dimers (caruifolins B−D), together with six known compounds, were isolated from the aerial parts of *Artemisia caruifolia*. The structures were determined by chemical and spectroscopic methods.

The aerial part of *Artemisia caruifolia* Buch.-Ham. ex Roxb. (Asteraceae) is one of the botanical sources of the Chinese herbal drug "Qing Hao". It has been used for the treatment of infectious diseases from ancient time.[1] In the course of a continuing search for inhibitors of human immunodeficiency virus (HIV) and its protease (HIV-PR) from natural sources, we investigated a methanolic extract of this plant. The present paper describes the structural determination of three new guaiane dimers and a new germacranolide from this plant.

Results and Discussion

Repeated column chromatography of a $CHCl_3$-soluble part of the MeOH extract of *A. caruifolia* afforded a guaianolide (**1**), a germacranolide (**2**), and eight guaiane dimers (**3**−**10**). Six of these were known compounds, identified as artabsinolide B (**1**),[2] anabsin (**6**),[3] anabsinthin (**7**),[3] absinthin (**8**),[3,5] absintholide (**9**),[4] and 10′,11′-epi-absinthin (**10**).[5] The compounds named caruifolins A−D (**2**−**5**) are new natural products, and their structures were elucidated as described below.

Caruifolin A (**2**) has a molecular formula of $C_{15}H_{22}O_4$ as established by HREIMS, which indicates five degrees of unsaturation. It exhibits a double doublet signal at δ 5.81, assignable to an oxygenated methylene proton on the lactone ring in the ^{1}H NMR spectrum. Its IR spectrum shows the presence of a γ-lactone group (1770 cm^{-1}). A combination of ^{13}C NMR and DEPT experiments demonstrated the presence of three methyls, three methylenes, six methines, and three quaternary carbons. Two signals at δ 138.8 (C-4) and 124.5 (C-5) suggest the presence of two olefinic carbons. On the basis of ^{1}H−^{1}H COSY and HMQC spectral evidence, two components of the structure for **2** could be established (shown in bold, Figure 1). The two partial structures and the remaining carbons, one carbonyl, two methyl, and one quaternary, could be assembled together by an HMBC experiment (Figure 1), where a methyl proton signal at δ 1.61 (H_3-15) was correlated with the two olefinic carbon signals (C-4 and C-5); methylene proton signals at δ 2.18 and 2.29 (H_2-2) were correlated with the olefinic carbon signal at δ 138.8 (C-4) and a quaternary carbon signal at δ 87.7 (C-10); another methyl proton signal at δ 1.33 (H_3-14) was correlated with a quaternary carbon signal at δ 87.7 (C-10) and a methylene carbon signal at δ 35.5 (C-9); and a methyl proton signal at δ 1.23 (H_3-13) was correlated with a carbonyl carbon signal at δ 180.0. Considering the degrees of unsaturation, the presence of an ether linkage was deduced. The position of the ether bridge was determined by NMR spectral analysis of an acetate of **2**. Acetylation of **2** gave a monoacetate, **2a** (*m*/*z* 308 [M]$^+$), whose HMBC spectrum revealed that an acetyl group was located at C-1. Therefore, the ether linkage was placed at C-3 and C-10.

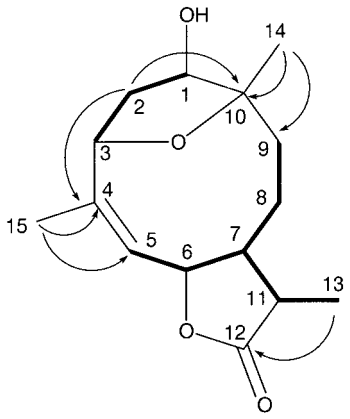


Figure 1. Partial structures (in bold) generated from ^{1}H−^{1}H COSY of **2**. (Solid arrow) HMBC correlations in assembling **2**.

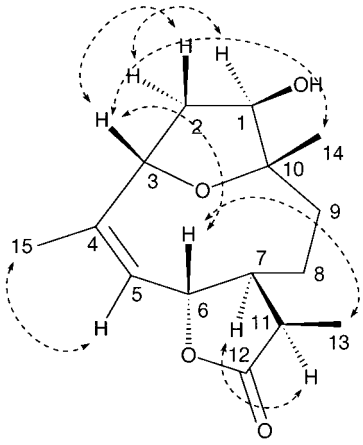
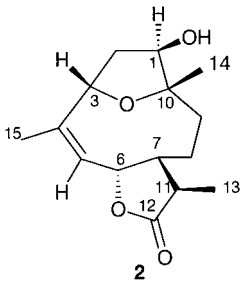


Figure 2. NOE interactions defining the relative configuration at stereogenic centers in **2**.

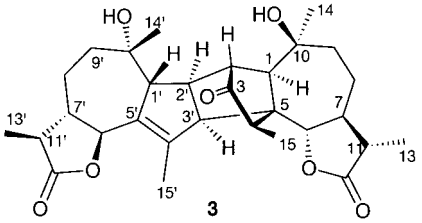
The relative stereochemistry of **2** was established by NOESY (Figure 2). A strong NOE between H-15 and H-5 indicated that methyl and vinyl protons are cis. Because the configuration of the 7,11-bond in all well-characterized sesquiterpene lactones is β,[6] H-7 was projected toward the α-face. H-7 showed a significant NOE correlation with H-11, indicating that H-11 is α-orientated and a geminal methyl group (H_3-13) is β-orientated. Correlations observed

* To whom correspondence should be addressed. Tel.: +81-76-434-7630. Fax: +81-76-434-5060. E-mail: saibo421@ms.toyama-mpu.ac.jp.

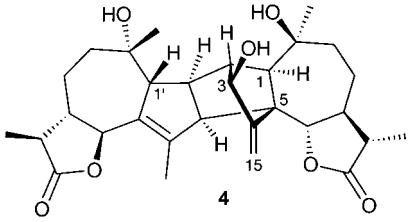
10.1021/np000005+ CCC: $19.00
Published on Web 11/02/2000



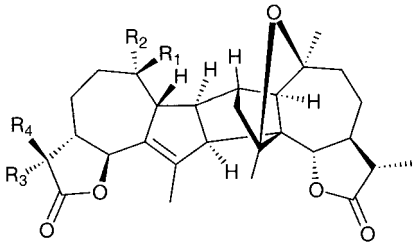
2



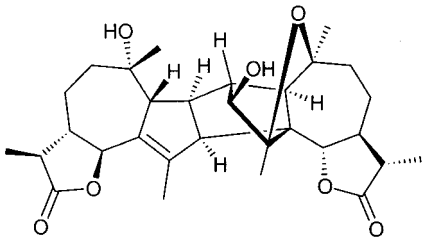
3



4



5 R_1 = OH; R_2 = CH_3; R_3 = CH_3; R_4 = H
7 R_1 = CH_3; R_2 = OH; R_3 = H; R_4 = CH_3



6 anabsin

between H-13 and H-6, H-6 and H-3, and H-3 and H_3-14 revealed that they are all oriented toward the β-face. In addition, a large coupling constant between H-6 and H-7 ($J_{6,7}$ = 9.5 Hz) confirmed their trans configuration. The β-orientated H-3 correlated more significantly to the H-2 proton at δ 2.29 than to the H-2 proton at δ 2.18, indicating the former to be H-2β and the latter to be H-2α. H-2α showed a much stronger NOE correlation with H-1 than H-2β, indicating that H-1 is α-orientated. The stereochemistry determined by NOESY was further supported by a molecular modeling study. A coupling constant value of ca. 0 Hz between H-1 and H-2β indicated a dihedral angle close to 90° between these two protons. Furthermore, in the Chem3D modeling studies of **2**, it was possible to fix the dihedral angle between H-1 and H-2β to ca. 90°, and all the protons experiencing NOEs simultaneously were within

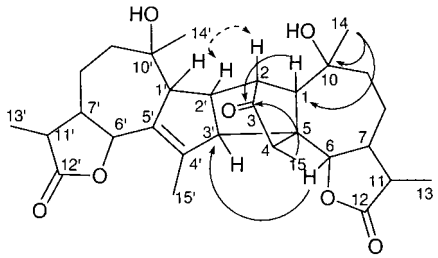


Figure 3. HMBC (solid arrow) and $^1H-^1H$ COSY (dashed arrow) correlations in assignment of the carbonyl at C-3, hydroxyl at C-10 and in confirming the location of the two sesquiterpene monomers in **3**.

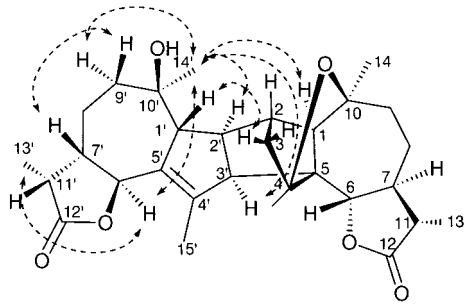


Figure 4. NOE interactions defining the relative configuration at stereogenic centers of the left half part in **5**.

3.8 Å after the energy was minimized by MM2. Therefore, the structure and the relative stereochemistry of **2** were determined as (3*S*,10*S*-epoxy-1β-hydroxy-(4*Z*)-germacren-12,6α-olide.

Caruifolin B (**3**) has a molecular formula of $C_{30}H_{40}O_7$, as determined by HREIMS. Its IR spectrum shows the presence of hydroxyl (3470 cm^{-1}) and lactone (1760 cm^{-1}) groups. The ^1H NMR spectrum of **3** exhibits two sets of oxygenated methylene protons on the lactone rings at δ 4.65 and 4.82, as well as three secondary and three tertiary methyl protons. The ^{13}C NMR spectrum of **3** contains 30 resonance peaks, including a pair of signals for olefinic carbons at δ 140.4 and 144.3, a ketone carbon at δ 221.8, and two lactone carbonyl carbons at δ 181.5 and 181.0. These spectral features were similar to those of a known guaiane dimer, anabsin (**6**). In comparison with **6**, compound **3** has one more carbonyl carbon signal at δ 221.8 but lacks one oxygenated carbon signal at δ 90.9 (C-4) in the ^{13}C NMR spectrum. Because the degree of unsaturation is the same in **3** and **6**, it could be deduced that **3** has a hydroxyl group in place of the ether bridge in **6**. A detailed comparison of the NMR spectra of **3** with those of **6**, as well as the analyses of the 2D NMR spectra of **3** established the left half of the structure of **3** to be the same as that of **6**. The positions of the hydroxyl and ketone groups were established by HMBC (Figure 3). The hydroxyl-bearing carbon (C-10) signal at δ 71.5 was correlated with a singlet methyl signal at δ 1.17, while the latter was confirmed to be H_3-14, because it also correlated with the C-1 signal at δ 65.2. A ketonic carbon signal at δ 221.8 was correlated with H-1 and H-15 signals at δ 2.13 and 1.28, respectively. The location of the two sesquiterpene lactones could be established by HMBC and $^1H-^1H$ COSY experiments, where the H-6 signal correlated with C-3′ in the HMBC spectrum and the H-2 signal correlated with the H-2′ signal in the $^1H-^1H$ COSY spectrum.

The relative stereochemistry of **3** was determined on the basis of the NOESY spectrum. NOE interactions found between H-1′ and H-7′, H-7′ and H-13′, and H-1′ and H-14′, indicated that all these protons are oriented to the β-face.

On the other hand, H-11′ and H-6′, which showed an NOE correlation, are consequently oriented to the α-face. Therefore, the stereochemistry of the left half of the molecule was confirmed to be the same as that of **6**.

Turning to the right half of the molecule, NOE interactions found between H-14 and H-1, H-1 and H-2′, H-1 and H-3′, H-3′ and H-7, and H-7 and H-13 indicated that all these protons are oriented to the α-face. A sole bridge-proton, H-4, had an NOE interaction with H-1′, indicating the bridge carbons C-3 and C-4 are oriented to the *β*-face. H-15 showed an NOE interaction with H-6, indicating that a methyl group at C-4 is located to the H-6 side (*R*-configuration at C-4). The stereochemistry determined by NOESY was further supported by a Chem3D molecular modeling study, which revealed that the distances between all the protons of **3** that show NOEs are all within 2.2−3.2 Å. From the above evidence, the structure of **3** was determined as shown. Interestingly, the orientation of the methyl group at C-4 in **3** is opposite that of the 4-*O*-10-bridged compounds **5**−**7**.

Caruifolin C (**4**) was assigned the molecular formula $C_{30}H_{40}O_7$, the same as **3**, based on the HREIMS. In the ^{1}H NMR spectrum, however, **4** shows only five methyl signals. A pair of broad singlets at *δ* 5.13 and 5.18 clearly indicate there is an *exo*-olefinic function in the structure of **4**. In the ^{13}C NMR spectrum, **4** shows no ketone signal. Instead, a hydroxyl carbon signal at *δ* 72.5 is observed and correlates with a proton signal at *δ* 4.14 in the HMQC spectrum. The position of the *exo*-olefin was assigned to C-4 and C-15 by HMBC, in which H-15 at *δ* 5.18 and 5.13 were correlated with C-5 at *δ* 60.5 and C-3 at *δ* 72.5. The hydroxy group was located at C-3 based on observed long-range correlations between H-3 at *δ* 4.14 and C-5 at *δ* 60.5, and between H-3 and C-1 at *δ* 63.9 in the HMBC spectrum.

In the NOESY spectrum of **4**, H-3 was found to have an NOE interaction with H-1′, indicating that H-3 faces H-1′. The stereochemistry of the other parts of compound **4** was confirmed to be the same as that of **3** by NOESY.

Caruifolin D (**5**) has a molecular formula of $C_{30}H_{40}O_6$ as determined by HREIMS. It displays four singlet and two doublet methyl signals in the ^{1}H NMR spectrum, and a pair of olefinic carbons in the ^{13}C NMR spectrum. The planar structure of **5** was established to be the same as that of known compound anabsinthin (**7**) by analyses of its 2D NMR spectra. However, a shielded methyl signal at *δ* 0.90 in the ^{1}H NMR spectrum of **5** was obviously different from that of **7**. The NOESY spectrum of **5** (Figure 4) revealed that the stereochemistry was the same as that of **7** except for positions 10′ and 11′. The stereochemistry of positions C-10′ and -11′ of compound **5** were determined by NOESY as follows: H-1′ has an NOE interaction with one of the H-3 protons (*δ* 1.51), indicating that H-1′ and C-3 are *β*-oriented. H-14′ has an NOE interaction with the α-oriented H-1; therefore, the methyl group at C-10′ is oriented to the α-face (different from that of **7**). By observation of NOE correlations with H-14′, protons H-2′, H-3′, H-6′, and H-9′α (*δ* 1.94) were assigned to the α-face of the molecule. H-13′ was also determined to be α-oriented, due to its correlation with H-6′. H-7′ was determined to be *β*-oriented, because it shows an NOE correlation with H-9′*β* (*δ* 1.65). From these findings, **5** was determined to be a stereoisomer of **7**, the configurations of C-10′ and C-11′ being opposite in these two compounds. The stereochemical difference between **5** and **7** is the same as that observed for the known guaiane dimers 10′,11′-epiabsinthin and absinthin. The changes in the chemical shifts of these isomers were also similar to those observed for the known compounds,[5] which further confirmed the structure of **5**.

All of the isolated compounds were tested for their inhibitory activity on HIV-1 protease; compounds **2**−**9** showed 22−46% of inhibition at a concentration of 100 *μ*g/mL, and **3** showed concentration-dependent inhibition of the enzyme with an IC_{50} value of 150 *μ*g/mL. In addition, **3** and **8** showed weak anti-HIV activity, completely inhibiting an HIV-1-induced cytopathic effect in MT cells at 500 and 250 *μ*g/mL, respectively.

Experimental Section

General Experimental Procedures. Melting points were measured on a Yanagimoto hot-stage micromelting point apparatus without correction. Optical rotations were measured with a JASCO DIP-360 automatic polarimeter. IR spectra were measured with a JASCO FT/IR-230 infrared spectrometer. ^{1}H and ^{13}C NMR spectra were measured with a Varian GEMINI 300 (^{1}H, 300 MHz; ^{13}C, 75 MHz) or Varian UNITY 500 (^{1}H, 500 MHz; ^{13}C, 125 MHz), or JEOL JNA-LA 400WB-FT (^{1}H, 400 MHz; ^{13}C, 100 MHz) spectrometer, the chemical shifts being represented as parts per million (ppm), with TMS as an internal standard. EIMS were measured with a JEOL JMS-AX 505 HAD mass spectrometer at an ionization voltage of 70 eV.

HIV Protease Assay. HIV protease assay kit (3700 Horizon Drive, King of Prussia, PA 19406, kit lot no. 1) was used. The assay was performed, and inhibitory activity was calculated, as described previously.[7] Acetyl pepstatin was used as a positive control and shows an IC_{50} value of 0.07 *μ*M.

Anti-HIV-1 Assay. The inhibitory activity on HIV-1-induced cytopathic effect in MT-4 cells was measured by the method reported previously.[8] AZT and dextran sulfate (DS) 8000 were used as positive controls which showed IC_{100} values of 0.031 and 3.9 *μ*g/mL, respectively (CC_0 of >1 and >1000 *μ*g/mL, respectively).

Plant Material. The aerial part of *A. caruifolia* was purchased from Yaocaigongyingzhan of Huhhot, Inner Mongolia, People's Republic of China, in September 1998. A voucher specimen (TMPW19154) is stored at the Museum of Materia Medica, Toyama Medical and Pharmaceutical University, Japan.

Extraction and Isolation. The plant (3.0 kg) was extracted with MeOH under reflux (20 L × 3, each 2 h). After being evaporated, the MeOH extract (190 g) was partitioned with $CHCl_3$ and H_2O. The $CHCl_3$-soluble part (96 g) was chromatographed on Si gel eluted with hexane−EtOAc 7:3−0:1 (fractions 1−4) and finally EtOAc−EtOH−H_2O 6:2:1 (fraction 5) to give 56.3, 9.6, 3.1, 5.5, and 18 g of the fractions, respectively.

Fraction 2 was chromatographed on ODS with 30−60% MeOH. Fractions from this column were further purified by SiO_2 column chromatography eluted with C_6H_6−Me_2CO 9:1 to obtain compounds **2** (23 mg), **7** (100 mg), and **8** (30 mg). Fraction 3 was chromatographed on ODS with 50−60% MeOH to give compounds **1** (30 mg) and **6** (200 mg). Fraction 4 was chromatographed on ODS with 50% MeOH. Fractions from this column were further chromatographed on a SiO_2 column eluted with C_6H_6−Me_2CO 8:2 and finally purified by HPLC (TSK gel ODS-80TM with 50−80% MeOH) to obtain compounds **3**−**5**, **9**, and **10** (20, 8, 5, 15, and 2 mg, respectively).

Caruifolin A (2): amorphous powder; $[\alpha]^{24}_D$ −27.4° (*c* 1.22, $CHCl_3$); IR (KBr) ν_{max} 3440 (OH), 2975, 2950, 2880, 1770 (C=O, *γ*-lactone), 1680 (C=C), 1460, 1380, 1320, 1220, 980 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 1.23 (3H, d, *J* = 8.0 Hz, H-13), 1.33 (3H, s, H-14), 1.46 (1H, dd, *J* = 9.0, 14.5 Hz, H-9a), 1.57 (1H, br dd, *J* = 9.5, 14.5 Hz, H-9b), 1.61 (3H, s, H-15), 1.77 (1H, m, H-8a), 1.84 (1H, m, H-8b), 2.18 (1H, overlapped signal, H-2α), 2.23 (1H, overlapped signal, H-7), 2.29 (1H, dd, *J* = 8.5, 14.0 Hz, H-2*β*), 2.68 (1H, quin, *J* = 8.0 Hz, H-11), 3.89 (1H, d, *J* = 5.0 Hz, H-1), 4.77 (1H, t, *J* = 8.5 Hz, H-3), 5.16 (1H, br d, *J* = 6.0 Hz, H-5), 5.81 (1H, dd, *J* = 6.0, 9.5 Hz, H-6); ^{13}C NMR (75 MHz) *δ* 77.3 (C-1), 41.2 (C-2), 79.7 (C-3), 138.8

Table 1. ^{1}H NMR Spectral Data of **3**−**5** in $CDCl_3$ (except for **3** in CD_3OD)

position	3	4	5
1′	2.27 br s	2.70 br s	2.63 br s
2′	3.01 dt (10.0,6.0)	2.71 dt (10.0,4.5)	2.75 br dt (10.0,2.0)
3′	3.18 br d (10.0)	3.07 br d (10.0)	3.42 br d (10.0)
6′	4.82 br d (11.0)	4.61 br d (11.0)	4.79 d (11.0)
7′	1.75 m	1.82 m	2.43 dt (11.0,8.0)
11′	2.31 dq (12.0,7.0)	2.23 quin (6.5)	2.66 quin (7.0)
13′	1.15 d (7.0)	1.22 d (6.5)	1.20 d (7.0)
14′	1.21 s	1.30 s	0.90 s
15′	1.78 br s	1.80 s	1.91br s
1	2.13 br s	1.98 br s	2.36 br s
2	2.64 br d (5.5)	2.43 br d (4.5)	2.26[a]
3		4.14 br s	1.68 dd (6.0,14.0)
			1.51 br d (14.0)
4	2.15 d (7.0)		
6	4.65 d (10.5)	4.66 d (10.0)	4.16 br d (10.5)
7	2.19 m	1.94 m	1.80 m
11	2.39 dq (7.0,11.5)	2.26 quin (7.0)	2.25[a] dq (12.0,7.0)
13	1.24 d (7.0)	1.25 d (6.5)	1.23 d (7.0)
14	1.17 s	1.35 s	1.26 s
15	1.28 d (7.0)	5.13 br s	1.19 s
		5.18 br s	

[a] Overlapped signals.

(C-4), 124.5 (C-5), 82.5 (C-6), 45.9 (C-7), 23.1 (C-8), 35.5 (C-9), 87.7 (C-10), 40.1 (C-11), 180.0 (C-12), 12.7 (C-13), 19.3 (C-14), 20.6 (C-15); EIMS *m*/*z* 266 $[M]^+$ (20), 248 $[M - H_2O]^+$ (60), 230 $[M - 2 \times H_2O]^+$ (45), 177 (100); HREIMS *m*/*z* 266.1498 (calcd for $C_{15}H_{22}O_4$, 266.1519).

Acetylation of 2. To a solution of **2** (5 mg) in pyridine (0.5 mL) was added acetic anhydride (0.5 mL). The solution was allowed to stand at room temperature overnight and then added into 5 mL of ice−H_2O. The mixture was extracted three times with $CHCl_3$ (5 mL), and the $CHCl_3$ solution was concentrated to dryness and purified by a SiO_2 column with C_6H_6−Me_2CO 95:5 to obtain **2a** (3.4 mg): amorphous powder; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.23 (3H, d, J = 8.8 Hz, H-13), 1.25 (3H, s, H-14), 1.52 (1H, m, H-9a), 1.67 (1H, m, H-9b), 1.60 (3H, s, H-15), 1.80 (2H, m, H-8), 2.11 (3H, s, CH_3CO−), 2.20 (1H, overlapped signal, H-7), 2.29 (2H, overlapped signals, H-2), 2.69 (1H, dd, J = 7.7, 7.7 Hz, H-11), 4.75 (1H, t, J = 8.0 Hz H-3), 5.01 (1H, d, J = 5.0 Hz, H-1), 5.19 (1H, br d, J = 6.0 Hz, H-5), 5.78 (1H, dd, J = 6.6, 9.3 Hz, H-6); ^{13}C NMR (75 MHz) δ 78.9 (C-1), 39.0 (C-2), 80.0 (C-3), 138.3 (C-4), 125.1 (C-5), 82.5 (C-6), 46.2 (C-7), 23.3 (C-8), 35.8 (C-9), 86.6 (C-10), 40.4 (C-11), 180.0 (C-12), 12.7 (C-13), 19.5 (C-14), 20.6 (C-15), 21.4 (*C*H_3CO−), 170.4 (CH_3*C*O−); EIMS *m*/*z* 308 $[M]^+$ (5), 293 $[M - CH_3]^+$ (2), 248 $[M - HOAc]^+$ (100), 230 (65), 215 (65).

Caruifolin B (3): colorless needles (from C_6H_6), mp 276−280 °C; $[\alpha]^{24}_D$ +91.4° (*c* 0.95, $CHCl_3$); IR (KBr) ν_{max} 3470 (OH), 2970, 2930, 2875, 1760 (C═O, γ-lactone + five-membered ketone), 1665 (C═C), 1460, 1380, 1320, 1240, 1180 cm^{-1}; ^{1}H NMR, see Table 1; ^{13}C NMR, see Table 2; EIMS *m*/*z* 512 $[M]^+$ (30), 494 $[M - H_2O]^+$ (25), 421 (20), 264 [right half]$^+$ (100), 249 (40), 231 (80); HREIMS *m*/*z* $[M]^+$ 512.2770 (calcd for $C_{30}H_{40}O_7$ 512.2775).

Caruifolin C (4): amorphous powder; $[\alpha]^{24}_D$ +137.0° (*c* 0.51, $CHCl_3$); IR (KBr) ν_{max} 3420 (OH), 2970, 2930, 2880, 1760 (C═O, γ-lactone), 1650 (C═C), 1460, 1380, 1320, 1240, 1175, 1040 cm^{-1}; ^{1}H NMR, see Table 1; ^{13}C NMR, see Table 2; EIMS *m*/*z* 512 $[M]^+$ (3), 494 $[M - H_2O]^+$ (40), 421 (20), 264 [right half]$^+$ (70), 249 (70), 231 (100); HREIMS *m*/*z* $[M]^+$ 512.2798 (calcd for $C_{30}H_{40}O_7$ 512.2775).

Table 2. ^{13}C NMR Data of Compounds **3**−**5** in $CDCl_3$ (except for **3** in CD_3OD)

position	3	4	5
1′	58.1	54.8	57.9
2′	44.5	42.7	43.1
3′	61.5	56.0	52.8
4′	140.4	131.8	132.8
5′	144.3	150.4	146.8
6′	84.1	80.6	80.4
7′	50.8	49.2	44.5
8′	25.3	23.2	22.6
9′	44.8	43.5	45.8
10′	75.2	74.3	75.6
11′	43.2	42.5	40.3
12′	181.5	179.3	179.9
13′	12.6	12.3	9.5
14′	30.1	29.0	23.0
15′	19.1	17.1	16.6
1	65.2	63.6	63.0
2	56.9	47.9	41.7
3	221.8	72.5	34.9
4	43.9	155.7	88.5
5	56.9	60.5	62.2
6	84.3	84.6	82.7
7	45.4	47.5	49.4
8	28.9	27.6	25.8
9	44.6	43.8	39.4
10	71.5	71.9	78.0
11	43.7	41.9	43.0
12	181.0	178.7	178.8
13	13.5	13.0	12.8
14	31.0	31.6	27.3
15	10.8	107.9	17.2

Caruifolin D (5): amorphous powder; $[\alpha]^{24}_D$ +108.0° (*c* 0.29, $CHCl_3$); IR (KBr) ν_{max} 3480 (OH), 2970, 2930, 2880, 1775 (C═O, γ-lactone), 1650 (C═C), 1460, 1380, 1320, 1220, 1185, 1040, 985 cm^{-1}; ^{1}H NMR, see Table 1; ^{13}C NMR, see Table 2; EIMS *m*/*z* 496 $[M]^+$ (100), 478 $[M - H_2O]^+$ (30), 423 (40), 247 (20); HREIMS *m*/*z* $[M]^+$ 496.2808 (calcd for $C_{30}H_{40}O_6$ 496.2826).

Acknowledgment. We are grateful to Dr. Takuya Kawahada and Dr. Toru Otake of Osaka Prefectural Institute of Public Health, Japan, for the anti-HIV assay.

References and Notes

(1) Ling, Y.; Ling, Y.-R. *Flora Republicae Popularis Sinicae*; Science Press: Beijing, China, 1991; pp 60−61.
(2) Beauhaire, J.; Fourrey, J.-L. *J. Chem. Soc., Perkin Trans. 1* **1982**, 861−864.
(3) Kasymov, Sh. Z.; Abdullaev, G. P.; Sidyakin, G. P.; Yagudaev, M. R. *Chem. Nat. Compd.* (Engl. transl.) **1979**, 430−435.
(4) Beauhaire, J.; Fourrey, J.-L.; Guittet, E. *Tetrahedron Lett.* **1984**, *25*, 2751−2754.
(5) Bohlmann, F.; Ang, W.; Trinks, C.; Jakupovic, J.; Huneck, S. *Phytochemistry* **1985**, *24*, 1009−1015.
(6) Matsunaga, K.; Saitoh, M.; Ohizumi, Y. *Tetrahedron Lett.* **1996**, *37*, 1455−1456.
(7) Ma, C.-M.; Nakamura, N.; Miyashiro, H.; Hattori, M.; Shimotohono, K. *Chem. Pharm. Bull.* **1999**, *47*, 141−145.
(8) Kawahata, T.; Otake, T.; Mori, H.; Morimoto, M.; Ueba, N.; Kusumoto, I. T.; El-mekkawy, S.; Hattori, M.; Namba, T. *J. Trad. Med.* **1996**, *13*, 59−65.

NP000005+