neo-Clerodane Diterpenoids from the Aerial Part of *Scutellaria barbata*

by **Hanna Lee** and **Sang Hee Shim***

School of Biotechnology, Yeungnam University, 214-1 Dae-dong, Gyeongsan, Gyeongbuk 712-749, South Korea (phone: +82-53-8103028; fax: +82-53-8104769; e-mail: shshim29@ynu.ac.kr)

Three new *neo*-clerodane diterpenoids, barbatellarines C–E (**1**–**3**), were isolated from the $CHCl_3$-soluble fraction of the aerial part of *Scutellaria barbata*. Their chemical structures were elucidated by detailed analysis of NMR and MS data. Compounds **1** and **2** were C(13) epimers, which was confirmed by an NOE difference experiment and the NOESY spectrum. The relative configuration was determined on the basis of the ^{1}H-NMR *J*-value and NOE data, while the absolute configuration of the previously isolated analogue, barbatellarine B (**4**), as a representative member of the group, was assigned by CD analysis.

Introduction. – *Scutellaria barbata* D. DON (Labiatae) is a perennial herb with native distribution throughout Korea and Southern China. This herb is known in traditional Korean medicine as Banjiryun and has been used as an anti-inflammatory and antitumor agent [1–3]. Previous investigations of this plant have revealed the presence of over thirty flavonoids, more than ten *neo*-clerodane-type diterpenoids, triterpenoids, and sterol glucosides, some of which have exhibited interesting biological activities [4–12]. In our previous phytochemical studies of *S. barbata*, we reported on the isolation of two *neo*-clerodane diterpenoid alkaloids, barbatellarines A and B, together with known compounds (*neo*-clerodane = (1*S*,2*R*,4a*S*,5*R*,8a*S*)-decahydro-1,2,4a,5-tetramethyl-1-[(3*R*)-3-methylpentyl]naphthalene) [13].

As part of our ongoing search for new *neo*-clerodane diterpenoids from the aerial part of *S. barbata* distributed in a Korean market, we have further isolated three new *neo*-clerodane type diterpenoids, named barbatellarines C–E[1]) (**1**–**3**; *Fig. 1*). In this report, we describe the isolation and structural elucidation of three new compounds based on 1D- and 2D-NMR data.

Results and Discussion. – Barbatellarine C (**1**) was obtained as a white amorphous powder and gave a quasimolecular-ion peak at *m*/*z* 572.2477 ($[M+H]^+$) in the positive-ion-mode HR-FAB-MS, consistent with the molecular formula $C_{30}H_{37}NO_{10}$ (thirteen unsaturations). The ^{1}H-NMR spectrum of **1** (*Table*) displayed characteristic signals of four Me groups at δ(H) 1.26, 1.21, 1.18, and 1.16 (4*s*), an O-bearing CH_2 group at δ(H) 4.18 and 4.14 (2*d*, $J = 9.0$ Hz each), and an isolated CH_2 group at δ(H) 3.06 and 2.65 (2*d*, $J = 17.4$ Hz each), which indicated that it would be a *neo*-clerodane diterpenoid with a 13-spiro-15,16-γ-lactone moiety. The ^{1}H- and ^{13}C-NMR spectra of **1** were especially similar to those of a previously reported compound, barbatellarine A

[1]) Arbitrary atom numbering; for systematic names, see *Exper. Part.*

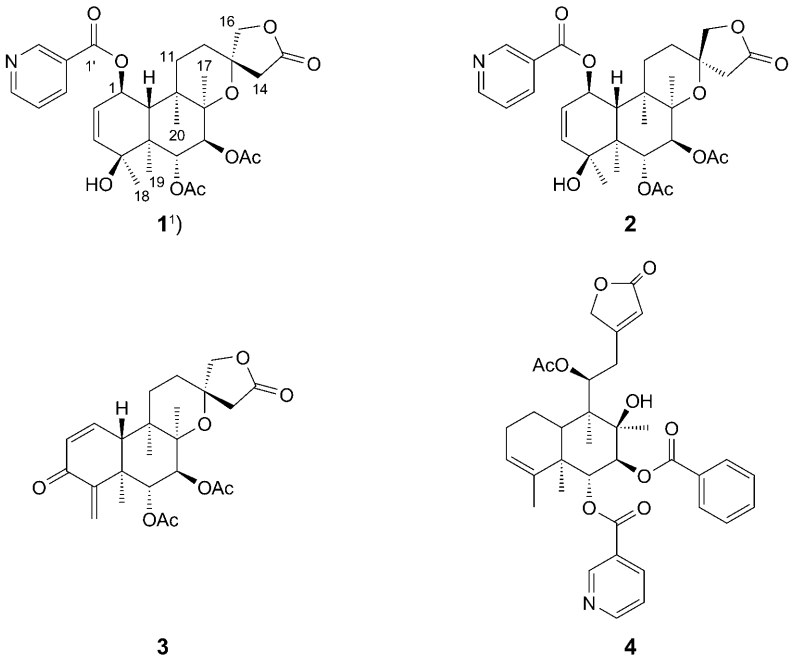

Fig. 1. *Compounds* **1**–**4**, *isolated from* S. barbata

[13], and differed in the existence of a nicotinic acid ester group at δ(H) 9.20 (*s*), 8.85 (*d*, $J = 5.0$ Hz), 8.33 (*d*, $J = 7.8$ Hz), and 7.56 (*d*, $J = 7.8$ Hz) in **1**, instead of a Bz group in barbatellarine A. Through detailed examination of ^{1}H,^{1}H-COSY, HMQC, and HMBC data, all of the NMR data for a partial structure C(10)–C(1)–C(2)–C(3) were assigned. A HMBC cross-peak of H–C(1) (δ(H) 5.92) (br. *d*, $J = 10$ Hz) with a nicotinic acid ester C-atom (δ(C) 163.9) indicated attachment of the nicotinic acid ester group at C(1), as shown in *Fig. 2*. In addition, HMBCs of two vicinally coupled H-atoms at δ(H) 5.92 (*d*, $J = 10$ Hz, H–C(6)) and 5.28 (*d*, $J = 10$ Hz, H–C(7)) with two Ac C=O groups at δ(C) 171.6 and 170.7, respectively, indicated attachment of two Ac groups to C(6) and C(7). The relative configuration of **1** was established by the NOESY data, as well as coupling constants. Strong NOESY correlations H–C(1)/Me(19) and H–C(1)/Me(20) indicated that the nicotinic acid ester group at C(1) was on the face opposite to the Me groups, as shown in *Fig. 3*. The coupling constant (10.8 Hz) between H–C(6) and H–C(7) indicated that both of the H-atoms were in axial positions. A strong NOESY correlation H–C(7)/Me(17) indicated that the Ac group at C(7) was on the face opposite to the Me groups, and, thus, Ac–C(6) was presumed to be on the same face as the Me groups. In addition, a strong NOESY correlation CH_2(16)/Me(17) indicated that CH_2(16) was on the same face as the Me groups. On the basis of the above data, the structure of barbatellarine C (**1**) was elucidated as (3*S*,4′a*R*,5′*S*,6′*R*,6′a*S*,7′*S*,10′*R*,10′a*R*,10′b*R*)-5′,6′-bis(acetyloxy)-1′,2′,4′a,5′,6′,6′a,7′,10′,10′a,10′b-decahydro-7′-hydroxy-10′-(nicotinoyloxy)-4′a,6′a,7′,10′b-tetramethylspiro[furan-3(2*H*),3′-[3*H*]naphtho[2,1-*b*]pyran]-5(4*H*)-one[1].

Table. *NMR Data of Barbatellarines C–E* (**1**–**3**)[a]). δ in ppm, J in Hz

	1		**2**		**3**	
	δ(H)	δ(C)	δ(H)	δ(C)	δ(H)	δ(C)
H–C(1)	5.92 (br. *d*, $J=10.0$)	72.4	5.92 (br. *d*, $J=10.0$)	72.4	6.76 (br. *d*, $J=9.6$)	146.6
H–C(2)	5.65 (br. *d*, $J=10.2$)	127.2	5.65 (br. *d*, $J=10.2$)	127.2	6.29 (*d*, $J=9.6$)	131.2
H–C(3) or C(3)	5.57 (*d*, $J=10.2$)	135.6	5.57 (*d*, $J=10.2$)	135.6		189.3
C(4)		72.8		72.8		151.5
C(5)		47.3		47.3		48.1
H–C(6)	5.92 (*d*, $J=10.0$)	70.9	5.92 (*d*, $J=10.0$)	70.9	5.71 (*d*, $J=10.0$)	71.9
H–C(7)	5.28 (*d*, $J=10.0$)	73.2	5.28 (*d*, $J=10.0$)	73.2	5.32 (*d*, $J=10.0$)	73.7
C(8)		80.7		80.8		80.4
C(9)		38.4		38.3		37.7
H–C(10)	3.37 (*d*, $J=10.0$)	36.8	3.34 (*d*, $J=10.0$)	36.8	3.25 (br. *s*)	43.0
CH_2(11)	1.89–1.87, 1.63–1.58 (2*m*)	29.4	1.89–1.87, 1.63–1.58 (2*m*)	29.3	1.81–1.76[b]), 1.73–1.67 (2*m*)	28.4
CH_2(12)	2.31–2.28, 1.77–1.74 (2*m*)	28.8	2.31–2.28, 1.66–1.63 (2*m*)	29.1	1.88–1.85, 1.81–1.76 (2*m*)[b])	27.4
C(13)		79.6		76.1		76.5
CH_2(14)	3.06, 2.65 (2*d*, $J=17.4$)	43.9	2.76, 2.50 (2*d*, $J=16.8$)	42.5	3.10, 2.49 (2*d*, $J=17.0$)	44.1
C(15)		173.8		174.9		173.8
CH_2(16)	4.18, 4.14 (2*d*, $J=9.0$)	76.7	4.40, 4.26 (2*d*, $J=9.0$)	76.6	4.25, 4.17 (2*d*, $J=9.0$)	76.1
Me(17)	1.18 (*s*)	19.7	1.24 (*s*)	19.8	1.20 (*s*)	19.6
Me(18) or CH_2(18)	1.21 (*s*)	25.5	1.21 (*s*)	25.5	5.77, 5.20 (2*s*)	115.7
Me(19)	1.26 (*s*)	13.5	1.26 (*s*)	13.5	1.33 (*s*)	16.5
Me(20)	1.16 (*s*)	21.6	1.16 (*s*)	21.4	1.07 (*s*)	21.5
C(1′)		163.9		163.9		
C(2′)		126.6		126.6		
H–C(3′)	9.20 (br. *s*)	149.5	9.19 (br. *s*)	149.4		
H–C(5′)	8.85 (br. *d*, $J=5.4$)	152.4	8.85 (br. *d*, $J=5.0$)	152.4		
H–C(6′)	7.56 (*dd*, $J=5.4, 7.8$)	124.3	7.56 (*dd*, $J=5.0, 7.8$)	124.3		
H–C(7′)	8.33 (br. *d*, $J=7.8$)	138.3	8.34 (br. *d*, $J=7.8$)	138.4		
*Ac*O–C(6)	2.05 (*s*)	171.6, 21.6	2.05 (*s*)	171.7, 21.6	2.00 (*s*)	170.1, 20.9
*Ac*O–C(7)	2.12 (*s*)	170.7, 20.8	2.11 (*s*)	170.7, 20.8	2.12 (*s*)	170.8, 20.8

[a]) Data were recorded in $CDCl_3$ at 600 (^{1}H, COSY, HMQC, HMBC) and 150 MHz (^{13}C). [b]) Overlapped.

Barbatellarine D (**2**), which was obtained as a white amorphous powder, was almost identical to compound **1**, showing a pseudomolecular-ion peak at *m*/*z* 572.2477 ($[M+H]^+$) in the positive-ion-mode HR-FAB-MS and similar ^{1}H- and ^{13}C-NMR spectra, except for the 13-spiro-15,16-γ-lactone moiety. The most remarkable difference from the spectra of compound **1** was a considerable upfield shift of C(13) in the ^{13}C-NMR spectrum from δ(C) 79.6 in **1** to 76.1 in **2**. Additionally, the δ(H) of CH_2(14) were

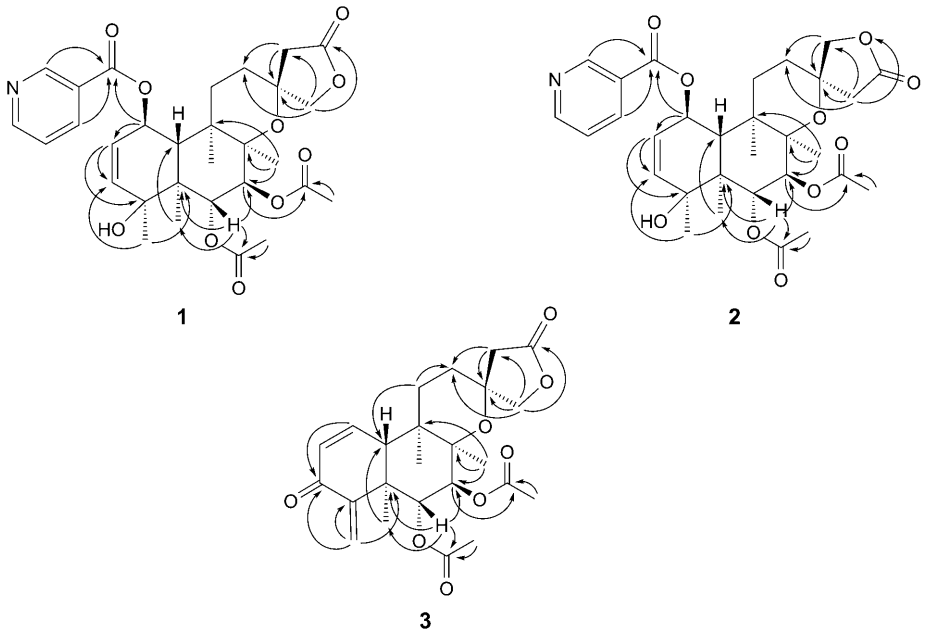

Fig. 2. *Key HMBCs* (H → C) *of compounds* **1**–**3**

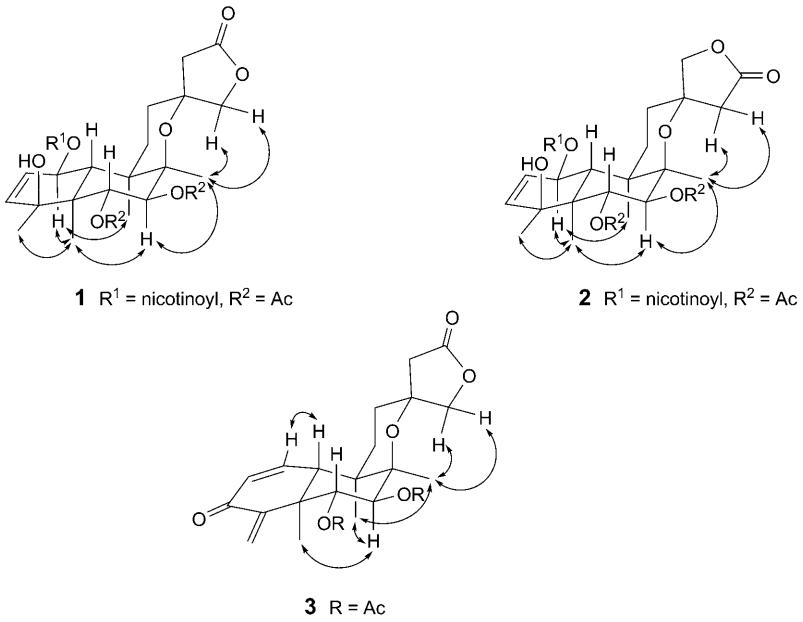

Fig. 3. *Key NOESY correlations* (H ↔ H) *of compounds* **1**–**3**

upfield shifted from δ(H) 3.06 and 2.65 (2*d*, $J = 17.4$ Hz each) in **1** to 2.76 and 2.50 (2*d*, $J = 17.0$ Hz each) in **2**, whereas those of CH_2(16) showed a downfield shift from δ(H) 4.18 and 4.14 (2*d*, $J = 9.0$ Hz each) in **1** to 4.40 and 4.26 (2*d*, $J = 9.0$ Hz each) in **2**. Most likely, the chemical-shift differences for only a few resonances was due to a change in the relative configuration of the two compounds, which was confirmed by analysis of NOE difference data, as well as the NOESY spectrum. Irradiation of CH_2(14) at δ(H) 2.76 and 2.50 resulted in NOE enhancement of the signal corresponding to Me(17) at δ(H) 1.24 (*s*), indicating that CH_2(14) was in the α-orientation. In addition, NOESY correlation between Me(17) and CH_2(14) was observed in the NOESY plot (*Fig. 3*), which suggested that **2** was a C(13) epimer of **1**. Therefore, the structure of **2** was determined to be (3*R*,4′a*R*,5′*S*,6′*R*,6′a*S*,7′*S*,10′*R*,10′a*R*,10′b*R*)-5′,6′-bis(acetyloxy)-1′,2′,4′a,5′,6′,6′a,7′,10′,10′a,10′b-decahydro-7′-hydroxy-10′-(nicotinoyloxy)-4′a,6′a,7′,10′b-tetramethylspiro[furan-3(2*H*),3′-[3*H*]naphtho[2,1-*b*]pyran]-5(4*H*)-one[1]).

Barbatellarine E (**3**) was obtained as a white amorphous powder, and its molecular formula, $C_{24}H_{30}O_8$, was established by HR-ESI-MS and NMR data. Analysis of the ^{1}H- and ^{13}C-NMR data of **3** (*Table*) revealed structural similarities to barbatellarines C (**1**) and D (**2**), which facilitated the structure elucidation of this compound. The characteristic resonances for *neo*-clerodane diterpenoids found in **1**, including the 13-spiro-15,16-γ-lactone moiety, were observed. ^{1}H-, ^{13}C-, and DEPT-NMR data indicated that **3** had three tertiary Me groups at δ(H) 1.20 corresponding to δ(C) 19.6, at δ(H) 1.33 corresponding to δ(C) 16.5, and at δ(H) 1.07 corresponding to δ(C) 21.5, rather than four as in **1** and **2**. In addition, the spectral data suggested that **3** had an α,β-unsaturated C=O group at δ(H) 6.76 and 6.29 (2*d*, $J = 9.6$ Hz each), an exocyclic methylene group at δ(H) 5.77 and 5.20 (2*s*), and two Ac groups at δ(H) 2.00 and 2.12 (2*s*). The HMBCs from the exocyclic CH_2(18) to the C=O group at δ(C) 189.3 indicated conjugation of this exocyclic methylene group with the α,β-unsaturated C=O group (*Fig. 2*). The above described groups corresponded to C(1)–C(2)–C(3)–C(4)–C(18) in the *neo*-clerodane skeleton based on the HMBCs H–C(10)/C(1), C(5), and C(9), and Me(19)/C(4), C(5), and C(10). In addition, the HMBCs H–C(6)/ester C=O at δ(C) 170.1 and H–C(7)/ester C=O at δ(C) 170.8 indicated attachment of two Ac groups to C(6) and C(7), respectively. The relative configuration of **3** was established by the NOESY data. The strong NOESY correlations H–C(7)/Me(19) and Me(20) indicated that Ac–C(7) was on the face opposite to the Me groups, as shown in *Fig. 3*. In addition, based on the coupling constant (10 Hz) of H–C(6) and H–C(7), Ac–C(6) was presumed to be on the same face as the Me groups, as with compounds **1** and **2**. The strong NOESY correlations CH_2(16)/Me(17) indicated that CH_2(16) was in the α-orientation, as in compound **1**. Therefore, the structure of **3** was determined to be (3*S*,4′a*R*,5′*S*,6′*R*,6′a*R*,10′a*S*,10′b*R*)-5′,6′-bis(acetyloxy)-1′,2′,4′a,5′,6′a,7′a,10′a,10′b-octahydro-4′a,6′a,10′b-trimethyl-7′-methylenespiro[furan-3(2*H*),3′-[3*H*]naphtho[2,1-*b*]pyran]-5,8′(4*H*,6′*H*)-dione.

The absolute configuration of **1**–**3** was established by analogy with that of barbatellarine B (**4**), a *neo*-clerodane which was reported by us in a previous paper [13]. Since **4** has aromatic groups at C(6) and C(7) which could be applied to the exciton chirality rule by means of a circular dichroism (CD) spectrum, we here describe the determination of the absolute configuration of barbatellarine B (**4**). The CD spectrum of **4** was recorded in MeOH, and a clear bisignate *Cotton* effect was observed

at λ_{max} 236 nm. On the basis of the exciton chirality rule [14], compound **4** is thus proposed to have (6*R*,7*R*) absolute configuration. The presumption of the presence of the same configuration at C(6) and C(7), suggests that barbatellarines C – E (**1** – **3**) have the absolute configurations shown.

Previous phytochemical investigations of *S. barbata* have led to the discovery of many compounds, especially *neo*-clerodane diterpenoids [4 – 13]. However, no studies have been reported on the existence of an exocyclic methylene group at C(4) conjugated with an α,β-unsaturated C=O group at C(1)–C(2)–C(3) in the *A* ring of the *neo*-clerodane skeleton.

Experimental Part

General. TLC: normal-phase silica gel *60 F_{254}* (SiO_2, *Merck*); visualization by spraying with 20% aq. H_2SO_4 soln., followed by heating. Column chromatography (CC): SiO_2 (70 – 230 mesh; *Merck*). Prep. reversed-phase HPLC: *Agilent-1200* high-performance liquid chromatograph equipped with a *G1322A* vacuum degasser, *G1311A* quaternary pump, *G1315D* DAD detector, *G1328B* manual injector, and *G1316A* thermostatted column compartment connected to a computer with *Agilent* ChemStation software; *Agilent-Eclipse-XDB-C_{18}* column (5 μm, 9.4 × 250 mm); t_R in min. CD Spectrum: *Jasco J-175*; λ ($\Delta\varepsilon$) in nm. ^{1}H-, ^{13}C-, and 2D-NMR Spectra: *Varian-VNS-600* spectrometer; at 600 (^{1}H) and 150 MHz (^{13}C); in $CDCl_3$; δ in ppm rel. to solvent peak used for referencing, *J* in Hz. HR-ESI-MS: *Jeol-JMS-700* mass spectrometer; in *m*/*z*.

Plant Material. Aerial parts of *Scutellaria barbata* D. DON (Lamiaceae) were obtained from the Kim Tae Kyun oriental medicine clinic. A voucher specimen (No. YN-BT-002) is deposited with the Natural Products Chemistry Laboratory of the School of Biotechnology, Yeungnam University.

Extraction and Isolation. Aerial parts of *Scutellaria barbata* D. DON (1 kg) were finely cut and extracted in MeOH under refluxing to give 150 g of crude extract. The extract was suspended in H_2O and then partitioned with hexane, $CHCl_3$, AcOEt, and BuOH. The $CHCl_3$-soluble extract was separated by CC (SiO_2, gradient MeOH/CH_2Cl_2): *Frs. I – VI*. *Fr. V* (626.6 mg) was further separated by CC (SiO_2, cyclohexane/acetone 80 : 20 → 50 : 50): *Frs. V.1 – V.13*. *Fr. V.12* (15.8 mg) was further subjected to semi-prep. reversed-phase HPLC (*Agilent Eclipse XDB-C_{18}*, flow rate 2 ml/min, 60 → 80% MeOH/H_2O for 30 min, UV detection at 254 nm): **1** and **2** (each 2.0 mg, t_R 20.1 and 21.2, resp.). *Fr. V.13* (145.5 mg) was also subjected to CC (SiO_2, $CHCl_3$/acetone 90 : 10 → 50 : 50): *Frs. V.13.1 – V.13.28*. *Fr. V.13.22* (19.5 mg) was further subjected to semi-prep. reversed-phase HPLC (*Agilent Eclipse XDB-C_{18}*, flow rate 2 ml/min; 60 → 80% MeOH/H_2O for 30 min; UV detection at 254 nm): **3** (3.4 mg, t_R 10.2).

Barbatellarine C (=*(3*S*,4′a*R*,5′*S*,6′*R*,6′a*S*,7′*S*,10′*R*,10′a*R*,10′b*R*)-5′,6′-Bis(acetyloxy)-1′,2′,4′a,5′,6′,6′a,7′,10′,10′a,10′b-decahydro-7′-hydroxy-10′-(nicotinoyloxy)-4′a,6′a,7′,10′b-tetramethylspiro[furan-3(2*H*),3′-[3*H*]naphtho[2,1-*b*]pyran]-5(4*H*)-one = Pyridine-3-carboxylic Acid (3*S*,4′a*R*,5′*S*,6′*R*,6′a*S*,7′*S*,10′*R*,10′a*R*,10′b*R*)-5′,6′-Bis(acetyloxy)-1′,2′4,4′a,5,5′,6,6′a,7′,10′,10′a,10′b-dodecahydro-7′-hydroxy-4′a,6′a,7′,10′b-tetramethyl-5-oxospiro[furan-3(2*H*),3′-[3*H*]naphtho[2,1-*b*]pyran]-10′-yl Ester*; **1**): White amorphous powder. $[\alpha]_D = +34.1$ ($c = 1.0 \cdot 10^{-3}$ g/ml, MeOH). ^{1}H- and ^{13}C-NMR: *Table*. HR-ESI-MS (pos.): 572.2477 ($[M+H]^+$, $C_{30}H_{38}NO_{10}^+$; calc. 572.2496).

Barbatellarine D (=*(3*R*,4′a*R*,5′*S*,6′*R*,6′a*S*,7′*S*,10′*R*,10′a*R*,10′b*R*)-5′,6′-Bis(acetyloxy)-1′,2′,4′a,5′,6′,6′a,7′,10′,10′a,10′b-decahydro-7′-hydroxy-10′-(nicotinoyloxy)-4′a,6′a,7′,10′b-tetramethylspiro[furan-3(2*H*),3′-[3*H*]naphtho[2,1-*b*]pyran]-5(4*H*)-one = Pyridine-3-carboxylic Acid (3*R*,4′a*R*,5′*S*,6′*R*,6′a*S*,7′*S*,10′*R*,10′a*R*,10′b*R*)-5′,6′-Bis(acetyloxy)-1′,2′4,4′a,5,5′,6,6′a,7′,10′,10′a,10′b-dodecahydro-7′-hydroxy-4′a,6′a,7′,10′b-tetramethyl-5-oxospiro[furan-3(2*H*),3′-[3*H*]naphtho[2,1-*b*]pyran]-10′-yl Ester*; **2**): White amorphous powder. $[\alpha]_D = -15.7$ ($c = 1.0 \cdot 10^{-3}$ g/ml, MeOH). ^{1}H- and ^{13}C-NMR: *Table*. HR-ESI-MS (pos.): 572.2477 ($[M+H]^+$, $C_{30}H_{38}NO_{10}^+$; calc. 572.2496).

Barbatellarine E (=*(3*S*,4′a*R*,5′*S*,6′*R*,6′a*R*,10′a*S*,10′b*R*)-5′,6′-Bis(acetyloxy)-1′,2′,4′a,5′,6′a,7′a,10′a,10′b-octahydro-4′a,6′a,10′b-trimethyl-7′-methylenespiro[furan-3(2*H*),3′-[3*H*]naphtho[2,1-*b*]pyran]-

*5,8′(4*H,*6′*H*)-dione*; **3**): White amorphous powder. $[\alpha]_D = +32.7$ ($c = 1.0 \cdot 10^{-3}$ g/ml, MeOH). ^{1}H- and ^{13}C-NMR: *Table*. HR-ESI-MS (pos.): 447.2014 ($[M+H]^+$, $C_{24}H_{31}O_8^+$; calc. 447.2019).

Barbatellarine B (**4**). CD: 221 ($\Delta\varepsilon$ −0.592), 236 ($\Delta\varepsilon$ +0.609).

REFERENCES

[1] B. Y. Y. Wong, B. H. S. Lau, T. Yamasaki, R. W. Teel, *Cancer Lett.* **1993**, *68*, 75.
[2] H. Rugo, E. Shtivelman, A. Perez, C. Vogel, S. Franco, E. T. Chiu, M. Melisko, M. Tagliaferri, I. Cohen, M. Shoemaker, Z. Tran, D. Tripathy, *Breast Cancer Res. Treat.* **2007**, *105*, 17.
[3] S.-J. Suh, J.-W. Yoon, T.-K. Lee, U.-H. Jin, S.-L. Kim, M.-S. Kim, D. Y. Kwon, Y.-C. Lee, C.-H. Kim, *Phytother. Res.* **2007**, *21*, 135.
[4] S.-J. Dai, D.-D. Liang, Y. Ren, K. Liu, L. Shen, *Chem. Pharm. Bull.* **2008**, *56*, 207.
[5] S.-J. Dai, J.-Y. Tao, K. Liu, Y.-T. Jiang, L. Shen, *Phytochemistry* **2006**, *67*, 1326.
[6] S.-J. Dai, G.-F. Wang, M. Chen, K. Liu, L. Shen, *Chem. Pharm. Bull.* **2007**, *55*, 1218.
[7] S.-J. Dai, M. Chen, K. Liu, Y.-T. Jiang, L. Shen, *Chem. Pharm. Bull.* **2006**, *54*, 869.
[8] J. Yu, J. Lei, H. Yu, X. Cai, G. Zou, *Phytochemistry* **2004**, *65*, 881.
[9] Y. Wang, X. Xue, Y. Xiao, F. Zhang, Q. Xu, X. Liang, *J. Sep. Sci.* **2008**, *31*, 1669.
[10] M. Bruno, F. Piozzi, S. Rosselli, *Nat. Prod. Rep.* **2002**, *19*, 357.
[11] S.-J. Dai, W.-B. Peng, L. Shen, D.-W. Zhang, Y. Ren, *J. Asian Nat. Prod. Res.* **2009**, *11*, 451.
[12] H. Kizu, N. Sugita, T. Tomimori, *Chem. Pharm. Bull.* **1998**, *46*, 988.
[13] H. Lee, Y. Kim, I. Choi, B. S. Min, S. H. Shim, *Bioorg. Med. Chem. Lett.* **2010**, *20*, 288.
[14] G. Cai, N. Bozhkova, J. Odingo, N. Berova, K. Nakanishi, *J. Am. Chem. Soc.* **1993**, *115*, 7192.

Received July 19, 2010