Sesquiterpenes and Other Metabolites from the Marine Red Alga *Laurencia composita* (Rhodomelaceae)

by **Nai-Yun Ji**[a])[b]), **Xiao-Ming Li**[a]), and **Bin-Gui Wang***[a])

[a]) Key Laboratory of Experimental Marine Biology, Institute of Oceanology, Chinese Academy of Sciences, Qingdao 266071, P. R. China (phone/fax: +86-532-82898553; e-mail: wangbingui@gmail.com)
[b]) Yantai Institute of Coastal Zone Research, Chinese Academy of Sciences, Yantai 264003, P. R. China

Two new halogenated sesquiterpenes, (8*β*)-10-bromo-3-chloro-2,7-epoxychamigr-9-en-8-ol (**1**) and 2-bromo-3-chlorobisabola-7(14),11-diene-6,10-diol (**3**), and one new phytol-derived diterpene, 2,3-epoxyphytyl acetate (**4**), along with *cis*- and *trans*-1-methylcyclohexane-1,4-diol (**5** and **6**) which were isolated from a natural source for the first time but have been previously synthesized, were isolated from the marine red alga *Laurencia composita* and characterized. In addition, a known sesquiterpene, pacifenediol (**2**), and the known furanone derivative **7** were also identified. Their structures were established by NMR and mass spectroscopic methods.

Introduction. – *Laurencia composita* belongs to the marine red algae of the family Rhodomelaceae (order Ceramiales). This species mainly grows on the upper to middle intertidal rocks with a small discoid holdfast. Its thalli are 3–10 cm in height, dark purple in color, and soft in texture. Each thallus possesses a terete, percurrent main axis, which is *ca.* 1 mm in diameter. Previous chemical investigations of *L. composita* revealed the presence of halogenated chamigrane sesquiterpenes and nonhalogenated and nonoxygenated C_{15}-acetogenins [1][2].

As part of our studies on the chemical constituents of Chinese marine red algae of the family Rhodomelaceae [3–19], we examined the chemical constituents of *L. composita* which was collected off the coasts of Nanji Island, Zhejiang Province, P. R. China. These efforts resulted in the identification of ten halogenated chamigrane sesquiterpenes and two nonhalogenated C_{15}-acetogenins [16]. Further investigation of this species allowed the characterization of two new halogenated sesquiterpenes, (8*β*)-10-bromo-3-chloro-2,7-epoxychamigr-9-en-8-ol[1]) (**1**) and 2-bromo-3-chlorobisabola-7(14),11-diene-6,10-diol[1]) (**3**), and one new phytol derivative, 2,3-epoxyphytyl acetate[1]) (**4**). Additionally, two new naturally occurring diols, *cis*-1-methylcyclohexane-1,4-diol (**5**) and *trans*-1-methylcyclohexane-1,4-diol (**6**), which were isolated from a natural resource for the first time but have been previously synthesized [20], together with the known sesquiterpene pacifenediol (**2**) [21] and the known furanone derivative 4-hydroxy-2,3-dimethylnon-2-eno-4-lactone (**7**) [22], were also identified. This article describes the isolation and structure determination of compounds **1**–**7**.

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

Results and Discussion. – The AcOEt-soluble fraction derived from the crude extract of dried and powdered *L. composita* was purified by a combination of silica gel and *Sephadex LH-20* gel column chromatography (CC), prep. TLC, and semi-prep. HPLC to yield compounds **1**–**7** (*Fig. 1*).

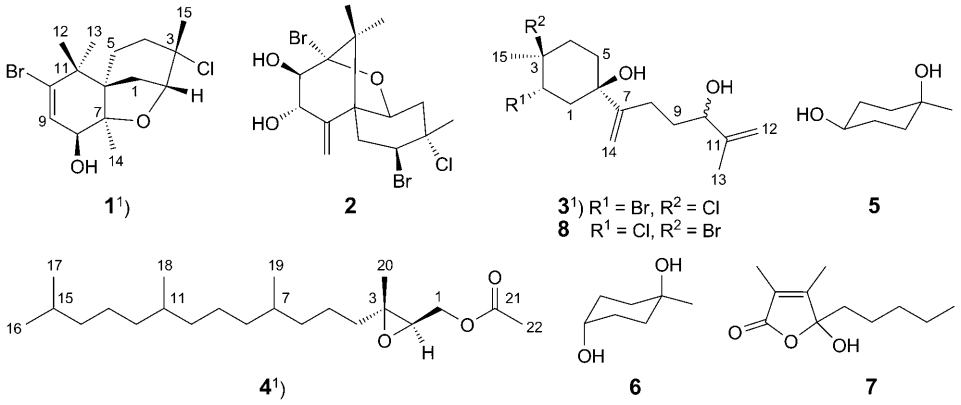

Fig. 1. *Compounds isolated from* L. composita

Compound **1** was obtained as colorless crystals. The EI-MS exhibited a characteristic molecular-ion cluster at *m/z* 352, 350, and 348 (1 : 4 : 3; M^+), indicating the presence of one Br- and one Cl-atom in **1**. The molecular formula was determined as $C_{15}H_{22}BrClO_2$ on the basis of high-resolution ESI-MS (*m/z* 373.0372 ($[M+Na]^+$, $C_{15}H_{22}{}^{81}Br^{35}ClNaO_2^+$)), suggesting four degrees of unsaturation. The ^{1}H-NMR spectrum (*Table*) displayed four Me *s*s at δ(H) 1.15 (Me(12) and Me(13)), 1.26 (Me(14)), and 1.62 (Me(15)), two CH−O groups with one broad *d* at δ(H) 4.33 ($J = 7.5$ Hz, H−C(2)) and one broad *dd* at δ(H) 4.20 ($J = 5.9, 3.1$ Hz, H−C(8)), one olefinic proton with a *d* at δ(H) 6.22 ($J = 5.9$ Hz, H−C(9)), and one OH group with a broad *d* at δ(H) 2.98 ($J = 3.1$ Hz, OH−C(8)). The ^{13}C-NMR (DEPT) spectrum (*Table*) exhibited the presence of four Me, three CH_2, and three CH groups, and five quaternary C-atoms. By analysis of the ^{1}H- and ^{13}C-NMR data, compound **1** was deduced to possess a chamigrane skeleton related to (8α)-10-bromo-3-chloro-2,7-epoxychamigr-9-en-8-ol, which was recently reported from *L. saitoi* [17]. The ^{1}H,^{1}H-COSY cross-peaks indicated the presence of three spin systems, including $-CH_2-CH-$ (C(1) to C(2)), $-CH_2-CH_2-$ (C(4) to C(5)), and $-CHOH-CH=$ (C(8) to C(9)). In the HMBC spectrum, the observed correlations (*Fig. 2*) from Me(15) to C(2), C(3), and C(4), from Me(14) to C(6), C(7), and C(8), from Me(13) to C(6), C(10), C(11), and C(12), from Me(12) to C(6), C(10), C(11), and C(13), and from CH_2(1) and CH_2(5) to C(6) established the connections of the above three spin systems. The epoxy linkage between C(2) and C(7) was established by the observed HMBC cross-peak between H−C(2) and C(7). The Cl-atom was assigned to be at C(3) by comparison with a similar structure [17]. So, the Br-atom indicated by the molecular formula was bonded to C(10). The above spectral evidence established the constitutional formula for **1**. The relative configuration of **1** was determined by a ROESY experiment. The observed ROESY correlation between Me(14) and H−C(8) indicated their *cis*-orientation,

Table. *^{1}H- and ^{13}C-NMR Data* (500 and 125 MHz, resp.; $CDCl_3$) *of* **1**[1]) *and* **3**[1]). Assignments were corroborated by ^{1}H,^{1}H-COSY, HSQC, and HMBC experiments.

	1		**3**	
	δ(H)	δ(C)	δ(H)	δ(C)
CH_2(1)	1.69 (*d*, *J* = 12.2), 2.24 (*ddd*, *J* = 12.2, 7.5, 4.0)	33.6 (*t*)	2.12–2.17, 2.30–2.35 (2*m*)	45.6 (*t*)
H–C(2)	4.33 (br. *d*, *J* = 7.5)	84.5 (*d*)	4.78 (*dd*, *J* = 12.5, 4.4)	60.1 (*d*)
C(3)		74.5 (*s*)		71.1 (*s*)
CH_2(4)	1.88 (br. *dd*, *J* = 13.5, 6.9), 2.91 (*ddd*, *J* = 13.5, 12.9, 7.4)	38.3 (*t*)	2.20–2.25, 2.54–2.58 (2*m*)	38.1 (*t*)
CH_2(5)	1.57 (*ddd*, *J* = 13.8, 12.9, 6.9), 2.06 (*ddd*, *J* = 13.8, 7.4, 4.0)	31.5 (*t*)	1.60–1.64, 1.78–1.82 (2*m*)	33.7 (*t*)
C(6)		48.7 (*s*)		75.2 (*s*)
C(7)		85.0 (*s*)		153.6 (*s*)
H–C(8) or CH_2(8)	4.20 (br. *dd*, *J* = 5.9, 3.1)	73.1 (*d*)	2.10–2.20 (*m*)	26.7 (*t*)
H–C(9) or CH_2(9)	6.22 (*d*, *J* = 5.9)	128.8 (*d*)	1.68–1.78 (*m*)	34.3 (*t*)
C(10) or H–C(10)		139.5 (*s*)	4.08–4.12 (*m*)	75.4 (*d*)
C(11)		45.4 (*s*)		147.4 (*s*)
Me(12) or CH_2(12)	1.15 (*s*)	22.7 (*q*)	4.87, 4.96 (2 br. *s*)	111.1 (*t*)
Me(13)	1.15 (*s*)	29.3 (*q*)	1.74 (br. *s*)	17.8 (*q*)
Me(14) or CH_2(14)	1.26 (*s*)	29.4 (*q*)	4.91, 5.13 (2 br. *s*)	109.4 (*t*)
Me(15)	1.62 (*s*)	28.4 (*q*)	1.69 (*s*)	23.4 (*q*)
OH	2.98 (br. *d*, *J* = 3.1)			

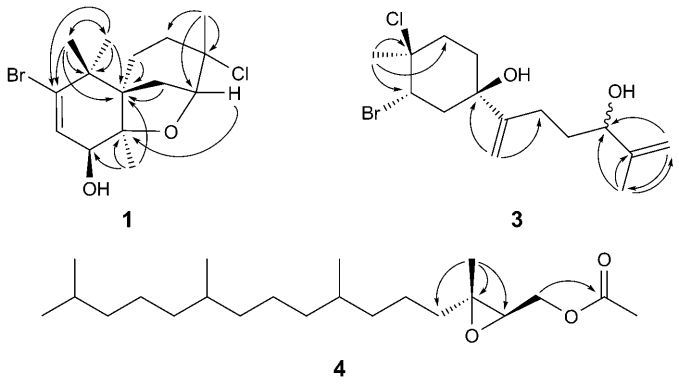

Fig. 2. *Selected HMBCs for* **1**, **3**, *and* **4**

while the correlation between H–C(2) and Me(15) also indicated their *cis*-orientation. In contrast, no ROESY correlation could be observed between H–C(2) and Me(14) indicating the *trans*-orientation for them. The above spectral evidence established the relative configuration and resulted in the assignment of the structure of **1** as (8β)-10-bromo-3-chloro-2,7-epoxychamigr-9-en-8-ol[1]).

Compound **3** was obtained as a colorless oily mixture with **2** in a 1:2 ratio. They displayed one spot on TLC and a single peak on HPLC analysis. Attempts to separate them by CC, preparative TLC, and semi-preparative HPLC with different solvent

systems all failed. Fortunately, compound **3** could be distinguished from **2** due to their different amounts in the ^{1}H- and ^{13}C-NMR spectra, aided by 2D-NMR experiments including ^{1}H,^{1}H-COSY, HSQC, and HMBC. The structure of compound **2** was readily identified as pacifenediol by detailed NMR spectral data analysis and comparison with literature data [21]. The ESI-MS data of **3** exhibited a characteristic *quasi*-molecular ion cluster at *m*/*z* 377, 375, and 373 (1:4:3; $[M+Na]^+$), indicating the presence of one Br- and one Cl-atom in **3**. The molecular formula was determined to be $C_{15}H_{24}BrClO_2$ based on high-resolution ESI-MS (*m*/*z* 375.0511 ($[M+Na]^+$, $C_{15}H_{24}{}^{79}Br^{37}ClNaO_2^+$)), suggesting three degrees of unsaturation. The ^{1}H-NMR spectrum (*Table*) displayed two methyl *s*s at δ(H) 1.69 (Me(15)) and 1.74 (Me(13)), one *m* at δ(H) 4.08–4.12 (H–C(10)), and one *dd* at δ(H) 4.78 (J = 12.5, 4.4 Hz, H–C(2)) attributed to two CH–O groups, and two *AB* systems at δ(H) 4.87 and 4.96 (CH_2(12)) and δ(H) 4.91 and 5.13 (CH_2(14)) characteristic for exocyclic CH_2= groups. The ^{13}C-NMR (DEPT) spectrum (*Table*) revealed the presence of two Me, seven CH_2, and two CH groups, and four quaternary C-atoms. Comparing **3** with 3-bromo-2-chloro-2,3-dihydro-6,10-dihydroxy-β-bisabolene (= 3-bromo-2-chlorobisabola-7(14),11-diene-6,10-diol; **8**), which was isolated from *L. scoparia* [23], revealed that **3** differed from **8** mainly at C(2) and C(3). The chlorinated CH at δ(C) 67.4 (C(2)) and brominated quaternary C-atom at δ(C) 68.2 (C(3)) of **8** were replaced by a CH at δ(C) 60.1 (C(2)) and a quaternary C-atom at δ(C) 71.1 (C(3)) in **3**, respectively. However, the NMR data of C(2) and C(3) of **3** were identical with those of 2,10-dibromo-3-chloro-β-chamigrene (C(2) at δ(C) 60.3 and C(3) at δ(C) 70.7) [24], indicating that C(2) and C(3) of **3** were bonded, respectively, to Br- and Cl-atoms. The ^{1}H,^{1}H-COSY cross-peaks CH_2(1)/H–C(2), CH_2(4)/CH_2(5), and CH_2(9)/CH_2(8) and H–C(10), as well as the observed HMBCs (*Fig. 2*) CH_2(12)/C(10) and C(13), Me(13)/C(10), C(11), and C(12), CH_2(14)/C(6) and C(8), and Me(15)/C(2), C(3), and C(4) further confirmed the planar structure for **3**. The relative configurations at C(2), C(3), and C(6) of **3** were established to be the same as that of **8** by the observed correlation Me(15)/CH_2(14) and no correlation between Me(15) and H–C(2) in the ROESY plot. However, the configuration at C(10) remained unknown. The above spectral evidence established **3** to be 2-bromo-3-chlorobisabola-7(14),11-diene-6,10-diol[1]).

Compound **4** was obtained as a colorless oil. Its molecular formula was deduced as $C_{22}H_{42}O_3$ by high-resolution ESI-MS (*m*/*z* 377.3032 ($[M+Na]^+$, $C_{22}H_{42}NaO_3^+$)), suggesting two degrees of unsaturation. The ^{1}H-NMR spectrum displayed four Me *d*s at δ(H) 0.86 (J = 6.4 Hz, Me(16) and Me(17)), 0.84 (J = 6.5 Hz, Me(18)), and 0.85 (J = 6.3 Hz, Me(19)), two Me *s*s at δ(H) 1.30 (Me(20)) and 2.11 (Me(22)), one epoxy CH group *dd* at δ(H) 2.98 (J = 6.9, 4.3 Hz, H–C(2)), and two *dd* at δ(H) 4.32 (J = 12.1, 4.3 Hz, H_a–C(1)) and 4.04 (J = 12.1, 6.9 Hz, H_b–C(1)) assignable to a CH_2–O group. The ^{13}C-NMR (DEPT) spectrum revealed the presence of six Me, ten CH_2, and four CH groups, and two quaternary C-atoms. A detailed NMR comparison with those reported for phytyl acetate revealed that **4** differed from phytyl acetate mainly at C(2) and C(3) [25]. The olefinic ^{13}C-NMR signals at δ(C) 117.9 (*d*, C(2)) and 142.8 (*s*, C(3)) of phytyl acetate were replaced by epoxy signals at δ(C) 59.6 (*d*, C(2)) and 60.8 (*s*, C(3)) in **4**. The olefinic ^{1}H-NMR signal at δ(H) 5.34 (*t*, J = 7.3 Hz, H–C(2)) of phytyl acetate [25] was replaced by an epoxy signal at δ(H) 2.98 (*dd*, J = 6.9, 4.3 Hz, H–C(2)) in **4**. So, compound **4** was deduced to be a 2,3-epoxy derivative of phytyl acetate. The

observed key ^{1}H,^{1}H-COSY cross-peak CH_2(1)/H–C(2) and the HMBCs (*Fig. 2*) Me(20)/C(2), C(3), and C(4), and CH_2(1)/C(21) further confirmed the planar structure of **4**. The relative configuration of **4** was determined by a ROESY experiment establishing the *cis* position of H–C(2) and CH_2(4). Based on the above evidence, the structure of compound **4** was deduced to be 2,3-epoxyphytyl acetate[1]).

Chamigrane sesquiterpenes are representative metabolites of *L. composita*. Compound **1** with a unique 2,7-epoxychamigrane skeleton is a new addition to the molecular diversity of chamigrane sesquiterpenes from this species [16]. In addition, compound **3** is the first bisabolane sesquiterpene isolated from *L. composita*, which allows to distinguish this species from *L. okamurai* [16].

This work was financially supported by the *National High-Tech R & D Project* (2007AA09Z403), the *National Natural Science Foundation of China* (30530080), the *Department of Science and Technology of Shandong Province* (2006GG2205023), and the *Chinese Academy of Sciences for Key Topics in Innovation Engineering* (KZCX2-YW-QN209).

Experimental Part

General. Column chromatography (CC): commercial silica gel (SiO_2; 200–300 mesh; *Qingdao Haiyang Chemical Group Co.*) and *Sephadex LH-20* (*Pharmacia*). TLC: precoated SiO_2 plates (*GF-254*; *Qingdao Haiyang Chemical Group Co.*). HPLC: *Dionex* HPLC system (*P680* HPLC pump, *UVD-340U* UV/VIS photodiode-array detector, *C_{18}* column (5 μm, 8.0 × 250 mm)). M.p.: *SGW-X-4* micro melting-point apparatus; uncorrected. Optical rotation: *Atago-Polax-L* polarimeter. NMR Spectra: *Bruker-Avance-500* spectrometer; at 500 (^{1}H) and 125 MHz (^{13}C); δ in ppm, *J* in Hz. Low- and high-resolution MS: *VG-Autospec-3000* spectrometer; in *m*/*z* (rel. %).

Algal Material. The marine red alga *Laurencia composita* YAMADA was collected off the coasts of Nanji Island, Zhejiang Province, P. R. China, in May 2007. A voucher specimen (HZ0705a) has been deposited with the Key Laboratory of Experimental Marine Biology of the Institute of Oceanology, Chinese Academy of Sciences.

Extraction and Isolation. The dried and powdered alga *L. composita* (1.5 kg) was extracted exhaustively with $CHCl_3$/MeOH 1:1. The concentrated extract was partitioned between H_2O and AcOEt. The AcOEt-soluble fraction was subjected to CC (SiO_2, petroleum ether/AcOEt gradient): *Frs. I–VI*. *Fr. II* (eluted with petroleum ether/AcOEt 100:1) was further purified by CC (*Sephadex LH-20*, $CHCl_3$/MeOH 1:1) and prep. TLC ($CHCl_3$): **4** (7.4 mg). *Fr. V* (eluted with petroleum ether/AcOEt 3:1) was also purified by CC (1. *Sephadex LH-20*, $CHCl_3$/MeOH 1:1; 2. SiO_2, petroleum ether/AcOEt 4:1), prep. TLC, and semi-prep. HPLC: **1** (11.6 mg), **2**/**3** (13.5 mg, 2:1), and **7** (5.6 mg). *Fr. VI* (eluted with AcOEt) was also separated by CC (1. *Sephadex LH-20*, $CHCl_3$/MeOH 1:1; 2. SiO_2, petroleum ether/acetone 3:1) and prep. TLC (AcOEt; $CHCl_3$/MeOH 10:1; $CHCl_3$/AcOEt 1:1): **5** (5.5 mg) and **6** (2.5 mg).

(8β)-10-Bromo-3-chloro-2,7-epoxychamigr-9-en-8-ol (= rel-*(2*R*,3*S*,5a*R*,9*S*,9a*R*)-7-Bromo-3-chloro-2,3,4,5,9,9a-hexahydro-3,6,6,9a-tetramethyl-6*H*-2,5a-methano-1-benzoxepin-9-ol*; **1**): Colorless crystals. M.p. 191–193°. $[\alpha]_D^{25} = -100.8$ (*c* = 0.27, $CHCl_3$). ^{1}H- and ^{13}C-NMR: *Table*. EI-MS: 352 (0.3), 350 (1.2), 348 (0.9, M^+), 321 (4), 319 (16), 317 (11), 271 (15), 269 (32), 215 (33), 201 (44), 172 (58), 157 (55), 137 (100), 121 (88), 93 (56). HR-ESI-MS: 373.0372 ($[M+Na]^+$, $C_{15}H_{22}{}^{81}Br^{35}ClNaO_2^+$; calc. 373.0369).

2-Bromo-3-chlorobisabola-7(14),11-diene-6,10-diol (= rel-*(α,1*R*,3*S*,4*S*)-3-Bromo-4-chloro-1-hydroxy-4-methyl-δ-methylene-α-(1-methylethenyl)cyclohexanebutanol*; **3**): Colorless oil. ^{1}H- and ^{13}C-NMR: *Table*. ESI-MS: 377, 375, 373 (1:4:3, $[M+Na]^+$). HR-ESI-MS: 375.0511 ($[M+Na]^+$, $C_{15}H_{24}{}^{79}Br^{37}ClNaO_2^+$; calc. 375.0516).

2,3-Epoxyphytyl Acetate (= rel-*(2*R*,3*R*)-3-Methyl-3-(4,8,12-trimethyltridecyl)oxirane-2-methanol Acetate*; **4**): Colorless oil. $[\alpha]_D^{25} = +2.3$ (*c* = 0.27, $CHCl_3$). ^{1}H-NMR: 4.32 (*dd*, *J* = 12.1, 4.3, H_a–C(1)); 4.04 (*dd*, *J* = 12.1, 6.9, H_b–C(1)); 2.98 (*dd*, *J* = 6.9, 4.3, H–C(2)); 2.11 (*s*, Me(22)); 1.30 (*s*, Me(20)); 0.86

(*d*, *J* = 6.4, Me(16), Me(17)); 0.85 (*d*, *J* = 6.3, Me(19)); 0.84 (*d*, *J* = 6.5, Me(18)). ^{13}C-NMR: 170.8 (*s*, C(21)); 63.4 (*t*, C(1)); 60.8 (*s*, C(3)); 59.6 (*d*, C(2)); 39.4 (*t*, C(14)); 38.5 (*t*, C(4)); 37.4 (*t*, C(10)); 37.3 (*t*, C(12)); 37.3 (*t*, C(8)); 36.9 (*t*, C(6)); 32.8 (*d*, C(11)); 32.8 (*d*, C(7)); 28.0 (*d*, C(15)); 24.8 (*t*, C(13)); 24.5 (*t*, C(9)); 22.7 (*q*, C(17)); 22.6 (*q*, C(16)); 22.5 (*t*, C(5)); 20.7 (*q*, C(22)); 19.7 (*q*, C(18)); 19.6 (*q*, C(19)); 16.9 (*q*, C(20)). ESI-MS: 377 ($[M+Na]^+$). HR-ESI-MS: 377.3032 ($[M+Na]^+$, $C_{22}H_{42}NaO_3^+$; calc. 377.3031).

REFERENCES

[1] M. Masuda, T. Abe, T. Suzuki, M. Suzuki, *Phycologia* **1996**, *35*, 550.
[2] M. Masuda, S. Kawaguchi, T. Abe, T. Kawamoto, M. Suzuki, *Phycol. Res.* **2002**, *50*, 135.
[3] N.-Y. Ji, X.-M. Li, L.-P. Ding, B.-G. Wang, *Helv. Chim. Acta* **2007**, *90*, 385.
[4] N.-Y. Ji, X.-M. Li, C.-M. Cui, B.-G. Wang, *Helv. Chim. Acta* **2007**, *90*, 1731.
[5] N.-Y. Ji, X.-M. Li, K. Li, B.-G. Wang, *J. Nat. Prod.* **2007**, *70*, 1499.
[6] N.-Y. Ji, X.-M. Li, K. Li, L.-P. Ding, J. B. Gloer, B.-G. Wang, *J. Nat. Prod.* **2007**, *70*, 1901.
[7] N.-Y. Ji, X.-M. Li, Y. Zhang, B.-G. Wang, *Biochem. Syst. Ecol.* **2007**, *35*, 627.
[8] K. Li, X.-M. Li, N.-Y. Ji, B.-G. Wang, *Bioorg. Med. Chem.* **2007**, *15*, 6627.
[9] K. Li, X.-M. Li, N.-Y. Ji, B.-G. Wang, *J. Nat. Prod.* **2008**, *71*, 28.
[10] X.-J. Duan, W.-W. Zhang, X.-M. Li, B.-G. Wang, *Food Chem.* **2006**, *95*, 37.
[11] X.-J. Duan, X.-M. Li, B.-G. Wang, *J. Nat. Prod.* **2007**, *70*, 1210.
[12] K. Li, X.-M. Li, N.-Y. Ji, J. B. Gloer, B.-G. Wang, *Org. Lett.* **2008**, *10*, 1429.
[13] N.-Y. Ji, X.-M. Li, H. Xie, J. Ding, K. Li, L.-P. Ding, B.-G. Wang, *Helv. Chim. Acta* **2008**, *91*, 1940.
[14] N.-Y. Ji, X.-M. Li, K. Li, L.-P. Ding, B.-G. Wang, *Nat. Prod. Res.* **2008**, *22*, 715.
[15] N.-Y. Ji, X.-M. Li, B.-G. Wang, *Molecules* **2008**, *13*, 2894.
[16] N.-Y. Ji, X.-M. Li, K. Li, J. B. Gloer, B.-G. Wang, *Biochem. Syst. Ecol.* **2008**, *36*, 938.
[17] N.-Y. Ji, X.-M. Li, K. Li, B.-G. Wang, *Helv. Chim. Acta* **2009**, *92*, 1873.
[18] B.-G. Wang, W.-W. Zhang, X.-J. Duan, X.-M. Li, *Food Chem.* **2009**, *113*, 1101.
[19] Y. Liang, X.-M. Li, C.-M. Cui, C.-S. Li, B.-G. Wang, *Chin. Chem. Lett.* **2009**, *20*, 190.
[20] J. H. Bushweller, L. Anzalone, T. A. Spencer, *Synth. Commun.* **1989**, *19*, 745.
[21] C. R. Kaiser, L. F. Pitombo, A. C. Pinto, *Magn. Reson. Chem.* **2001**, *39*, 147.
[22] L. Chen, S. Izumi, D. I. Ito, T. Iwaeda, R. Utsumi, T. Hirata, *Chem. Lett.* **1996**, *25*, 205.
[23] D. Davyt, R. Fernandez, L. Suescun, A. W. Mombrú, J. Saldaña, L. Domínguez, M. T. Fujii, E. Manta, *J. Nat. Prod.* **2006**, *69*, 1113.
[24] M. Suzuki, M. Segawa, T. Suzuki, E. Kurosawa, *Bull. Chem. Soc. Jpn.* **1983**, *56*, 3824.
[25] D. Itoh, K. Kawano, K. Nabeta, *J. Nat. Prod.* **2003**, *66*, 332.

Received April 15, 2010