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Chemical components of *Dysoxylum densiflorum*

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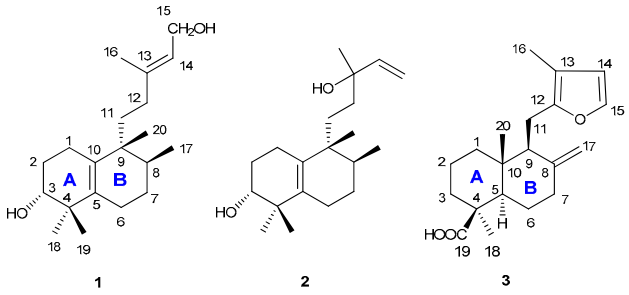
Abstract: Three new diterpenoids, including two halimanes, 5(10),13*E*-halimadiene-3*α*,15-diol (**1**), and 5(10),14-halimadiene-3*α*,13*ξ*-diol (**2**), one labdane, 12-(3-methyl-furan)-labd-8(17)-en-19-oic acid (**3**), together with sixteen known compounds were isolated from the barks of *Dysoxylum densiflorum.* All compounds were elucidated by extensive spectroscopic analysis.

Keywords: halimane, labdane, *Dysoxylum densiflorum*

Introduction

The plants of genus *Dysoxylum*, with about 200 species, is distributed naturally in India and south-east Asia. About 10 species of this genus have been found in Yunnan province.[1] According to the literatures, this genus have provided sorts of compounds, such as limonoids,[1,2] steroids,[3] sesquiterpenoids,[4] diterpenes,[5] triterpenes,[6] triterpene glycosides,[6d] and alkaloids.[7] Many plants of this genus have been used as traditional medicine by the indigenous.[8] *D. densiflorum,* is mainly distributed in southern China, Malaysia, and Philippines. Phytochemical research on *D. densiflorum* led to the isolation of terpenoids, steroids and flavonoids.[9] In the course of our ongoing investigation of genus *Dysoxylum* provided a series of bioactive chemical constituents by our lab,[1,2c,6b,10] including nineteen compounds from the EtOAc extracts of *D. densiflorum*. In the present research, three new diterpenoids including two new halimanes, 5(10),13*E*-halimadiene-3*α*,15-diol (**1**) and 5(10),14-halimadiene-3*α*,13*ξ*-diol (**2**), one new labdane, 12-(3-methyl-furan)-labd-8(17)-en-19-oic acid (**3**), were isolated and characterized by extensive spectroscopic analysis. Compounds **1** and **2** possessed 5(10)-halimane skeleton were rare in nature since the 20-methyl rearranged labdane skeleton does not conform to the biogenetic 'isoprene rule'.[11] The known compounds were determined as piscidinol A,[12] 3-oxotirucalla-7,24-dien-23-ol,[13] 3*β*-acetoxy-betulin,[14] isocupressic acid,[15] 12-oxo-15-hydroxylabda-8(17),13*E*-dien-19-oic acid,[16] 14(*R*),15-dihydroxy-8(17),12(*E*)-labdadien-19-oic acid,[17] 15-nor-14-oxolabda-8(17),12*E*-dien-19-oic acid,[18] cryptotrienolic acid,[19] 7-hydroxy-cupressic acid,[20] (+)-labda-8(17),13(Z)-dien-15,16-diol,[21] 4*β*-hydroxy-15-(3-methyl-2-butenyl)-aromadendr-$\Delta^{10(12)}$-en,[22] 4(15)-eudesmene-1*β*,7*α*-diol,[23] *β*-sitosterol, 7*α*-hydroxysitosterol,[24] 3,4,5-trihydroxycinnamate,[25] and 5,6-dihydroxy-6-methyl-3-en-2-one.[26] Herein, we report the isolation and structural elucidation of the isolated compounds.



Results and Discussion

Compound **1**, as an optically active white amorphous powder {$[\alpha]_D^{19}$ + 68.3 (*c* 0.172, Me_2CO)}, possessed the molecular formula $C_{20}H_{34}O_2$ by HREIMS at *m/z* 306.2566 $[M]^+$, indicating four degrees of unsaturation. The IR spectrum revealed absorption bands for hydroxyl (3430 cm^{-1}) and olefinic bond (1631 cm^{-1}). The ^1H, ^{13}C NMR and DEPT spectra of **1** exhibited 20 carbon resonances, assigned to one tetrasubstituted double bond [δ_C 132.4 (s), 138.0 (s)]; one trisubstituted double bond [δ_C 125.5 (d), 138.4 (s)] with a corresponding proton at δ_H 5.33 (t, J = 6.2 Hz, H-14); five methyls with corresponding four tertiary methyl protons at δ_H 1.62 (Me-16), 1.04 (Me-18), 0.94 (Me-19), and 0.82 (Me-20), and a secondary methyl protons at δ_H 0.85 (d, J = 6.9 Hz, Me-17); seven methylenes (one oxygenated); two methines (one oxygenated); and two quaternary carbons. Besides a

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Table 1. ^{1}H NMR data of 1–3[a] (δ in ppm and J in Hz)

no.	1	2	3
1a	2.15, m	2.06, overlap	1.89, m
1b	1.95, overlap	1.99, overlap	1.25, m
2a	1.71, m	1.67, m	1.92, overlap
2b	1.59, m	1.56, m	1.49, overlap
3a	3.40, dd (7.5, 4.1)	3.36, m	2.14, m
3b			1.11, td (13.2, 3.9)
5			1.46, m overlap
6a	2.05, overlap	2.04, overlap	2.00, m
6b	2.00, overlap	1.96, overlap	1.91, overlap
7a	1.46, overlap	1.43, overlap	2.33, overlap
7b	1.36, m	1.34, m	1.93, overlap
8	1.63, overlap	1.61, overlap	
9			2.31, overlap
10			
11a	1.48, overlap	1.42, overlap	2.75, dd (15.4, 2.9)
11b	1.44, overlap	1.39, overlap	2.67, d (10.4)
12a	1.92, overlap	1.42, overlap	
12b	1.63, overlap	1.13, m	
14	5.33, t (6.2)	5.90, dd (17.3, 10.7)	6.12, d (1.6)
15a	4.04, t (5.7)	5.18, dd (17.3, 1.8)	7.22, d (1.6)
15b		4.94, dd (10.7, 1.8)	
16	1.62, s	1.20, s	1.94, s
17a	0.85, d (6.9)	0.82, d (7.2)	4.75, s
17b			4.60, s
18	1.04, s	1.01, s	1.22, s
19	0.94, s	0.92, s	
20	0.82, s	0.81, s	0.72, s

[a]Compounds **1**–**3** were measured in acetone-d_6.

tetrasubstituted double bond and a trisubstituted double bond, the degrees of unsaturation required two rings for the structure. Similarities of the chemical shifts and coupling constants of **1** with known compound 3ξ-hydroxy-5(10),13*E*-halimadien-15-al[11b] revealed that **1** possesses a halimane-type diterpenoid skeleton (Tables 1 and 2). The difference was the presence of an oxygenated methylene in **1** with the chemical shift of δ_C 59.1 (t), instead of an aldehyde group in 3ξ-hydroxy-5(10),13*E*-halimadien-15-al [δ_C 189.8 (d)] at C-15. This was further confirmed by the HMBC correlation from δ_H 5.33 (t, J = 6.2 Hz, H-14) and 3.47 (15-OH) to δ_C 59.1 (t, C-15), and from δ_H 4.04 (t, J = 5.7 Hz, H-15) to δ_C 138.4 (s, C-13).

According to literatures,[11c,11h,11j] the Me-20 of **1** was positioned at axial bond for reducing steric hindrance of C-9 side chain, and assigned as β-orientation temporarily. In the ROESY spectrum of **1**, ROESY correlations of δ_H 0.82 (Me-20)/2.15 (H-1a) assigned the β-position of H-1a. Furthermore, cross-peaks of 1.95 (H-1b)/3.59 (3-OH), 3.59 (3-OH)/1.04 (Me-18), 1.04 (Me-18)/2.00 (H-6b), 2.00 (H-6b)/1.63 (H-8) suggested they were all located on the same face and assigned as α-position. Accordingly, the Me-17 and Me-19 were elucidated to be β-oriented. In addition, ROESY correlation of δ_H 4.04 (H-15)/1.62 (Me-16) indicated an *E*-configuration of $\Delta^{13/14}$. Thus, compound **1** was elucidated to be 5(10),13*E*-halimadiene-3α,15-diol as shown in Figure 1.

Compound **2** had an identical molecular formula $C_{20}H_{34}O_2$ as **1** according to its HREIMS at *m/z* 306.2550 $[M]^+$. The ^{1}H and ^{13}C NMR spectra of **2** (Tables 1 and 2) were close similarities to those of **1**, except that the allylic alcohol moiety (R_2C=$CHCH_2OH$, C-13–C-16) in **1** was changed to be an oxygenated quaternary carbon (δ_C 72.8) at C-13 and a terminal double bond [δ_C 147.2 (d), 111.1 (t)] at $\Delta^{14/15}$ in **2**. The assumption was further supported by the HMBC correlations of δ_H 5.18 (dd, J = 17.3, 1.8 Hz, H-15a) and 4.94 (dd, J = 10.7, 1.8 Hz, H-15b) with δ_C 72.8 (s, C-13), of δ_H 1.13 (m, H-12b) and 1.20 (s, Me-16) with δ_C 147.2 (d, C-14). Other parts of **2**

Table 2. ^{13}C NMR data of 1–3[a] (δ in ppm and J in Hz)

no.	1	2	3
1	25.3 CH_2	25.1 CH_2	39.8 CH_2
2	28.6 CH_2	28.6 CH_2	20.8 CH_2
3	75.9 CH	75.9 CH	38.9 CH_2
4	40.7 C	40.6 C	44.5 C
5	138.0 C	137.5 C	56.6 CH
6	26.5 CH_2	26.6 CH_2	26.9 CH_2
7	28.1 CH_2	28.1 CH_2	39.2 CH_2
8	34.2 CH	34.2 CH	149.0 C
9	41.2 C	40.8 C	54.6 CH
10	132.4 C	132.7 C	41.0 C
11	35.2 CH_2	30.4 CH_2	22.2 CH_2
12	34.8 CH_2	37.4 CH_2	151.4 C
13	138.4 C	72.8 C	114.0 C
14	125.5 CH	147.2 CH	113.6 CH
15	59.1 CH_2	111.1 CH_2	140.2 CH
16	16.3 CH_3	28.1 CH_3	10.1 CH_3
17	16.4 CH_3	16.3 CH_3	107.3 CH_2
18	25.5 CH_3	25.4 CH_3	29.3 CH_3
19	20.4 CH_3	20.4 CH_3	178.7 C
20	21.3 CH_3	21.6 CH_3	13.0 CH_3

[a]Compounds **1**–**3** were measured in acetone-d_6.

were identical to those of **1**, as supported by HSQC, HMBC, and ROESY spectra. Thus, **2** was deduced as 5(10),14-halimadiene-3α,13ξ-diol.

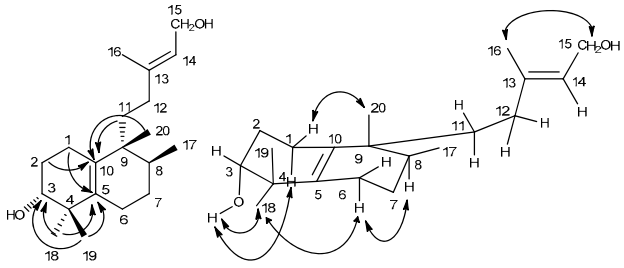

Figure 1. Selected HMBC ( ) and ROESY ( ) correlations of **1**

Compound **3**, as a white amorphous powder, exhibited the molecular formula $C_{20}H_{28}O_3$ by HREIMS at *m/z* 316.2039 $[M]^+$, indicating seven degrees of unsaturation. The ^{1}H, ^{13}C NMR and DEPT spectra of **3** (Tables 1 and 2) exhibited 20 carbon signals, ascribed to one carbonyl group [δ_C 178.7 (s)]; one exocylic double bond [δ_C 149.0 (s), 107.3 (t)], with corresponding protons at δ_H 4.75, 4.60 (s, H-17); four olefinic carbons [δ_C 113.6 (d), 114.0 (s), 140.2 (d), 151.4 (s)], with corresponding protons at δ_H 6.12 (d, J = 1.6 Hz, H-14) and 7.22 (d, J = 1.6 Hz, H-15); three tertiary methyls with corresponding methyl protons at δ_H 1.94 (Me-16), 1.22 (Me-18), and 0.72 (Me-20); six methylenes, two methines, and two quaternary carbons. As four degrees of unsaturation were accounted by one carbonyl group and three C-C double bonds, the remaining three degrees of unsaturation were attributed to three rings for **3**. Comparison of the ^{1}H and ^{13}C NMR data of **3** with those of 12-oxo-15-hydroxylabda-8(17),13*E*-dien-19-oic acid[16] suggested that **3** possesses a labdane skeleton. A furan moiety was suggested on the basis of four olefinic carbons at δ_C 113.6 (d), 114.0 (s), 140.2 (d), 151.4 (s), and the corresponding protons at δ_H 6.12 (d, J = 1.6 Hz, H-14) and 7.22 (d, J = 1.6 Hz, H-15). The HMBC correlations of δ_H 2.31 (overlap, H-9), 1.94 (s, Me-16), 6.12 (d, J = 1.6Hz, H-14) and 7.22 (d, J = 1.6Hz, H-15) with δ_C 151.4 (s, C-12), of δ_H 2.75

(dd, J = 15.4, 2.9 Hz, H-11a), 2.67 (d, J = 10.4 Hz, H-11b) with δ_C 114.0 (s, C-13), and of δ_H 1.94 (s, Me-16) with δ_C 113.6 (d, C-14) further permitted the assignment of a 3-methyl-furan moiety at C-12.

In the ROESY spectrum of **3**, ROESY correlations of δ_H 1.46 (H-5)/1.25 (H-1b), 2.31 (H-9) suggested that they all located on the same side. Me-20 (δ_H 0.72) did not show ROESY correlation to any of above protons, but showed correlations with the proton signals at δ_H 2.75, 2.67 (2H, H-11) and 1.89 (H-1a), which placed them at another side. The A/B ring was deduced to be *trans*-fused, which was consistent with labdane-type diterpenoids reported.[15,16,18,27] According to the literatures, H-5 was assigned at α-position, which further assigned the H-9 to be α-oriented and Me-20 to be β-oriented. Moreover, ROESY cross-peak of δ_H 1.46 (H-5)/1.22 (Me-18) suggested the α-orientation of Me-18. Hence, compound **3** was established as 12-(3-methyl-furan)-labd-8(17)-en-19-oic acid (Figure 2).

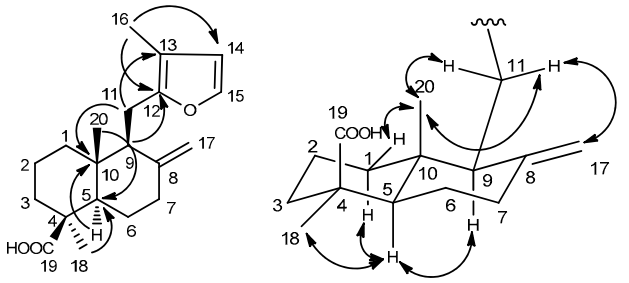

Figure 2. Selected HMBC ( ) and ROESY ( )

Experimental Section

General Experimental Procedures. Optical rotations were obtained with a Jasco P-1020 Automatic Digital Polariscope. UV spectrua was measured with a Shimadzu UV2401PC in MeOH solution. IR spectra (KBr) were obtained on a Bruker tensor-27 infrared spectrophotometer. ^{1}H, ^{13}C, and 2D NMR spectra were recorded on a Bruker AM-400, a DRX-500 NMR and an Avance Ⅲ 600 spectrometer with TMS as internal standard. MS data were obtained on a Waters Autospec Premier P776 for HREI. Column chromatography (CC) was performed on Silica gel (200–300 mesh, Qingdao Marine Chemical Co., Ltd., Qingdao, China) and RP-18 gel (20–45 μm, Fuji Silysia Chemical Co., Ltd., Tokyo, Japan). Fractions were monitored by TLC (GF 254, Qingdao Marine Chemical Co., Ltd., Qingdao, China), and spots were visualized by 10% H_2SO_4-ethanol reagent.

Plant Material. The barks of *Dysoxylum densiflorum* was collected from Xishuangbanna Autonomous Prefecture, Yunnan Province, China, and identified by Jingyun Cui of Xishuangbanna Botanic Garden. A voucher specimen (Cui200811-18) has been deposited at Herbarium of Kunming Institute of Botany, Chinese Academy of Sciences.

Extraction and Isolation. The air-dried barks (5.0 kg) of *Dysoxylum densiflorum* was extracted with MeOH three times under normal temperature. After removal of the solvent, the extract suspended in H_2O and extracted with ethyl acetate four times. The EtOAc fraction (129.0 g) was subjected to CC on Si gel, eluted with gradient mixtures of $CHCl_3$-Me_2CO (1:0–0:1). According to differences in composition monitored by TLC, five fractions were obtained. Fraction III (15.6 g) was separated to MPLC with RP-18 CC (MeOH-H_2O, 3:7–8:2), then followed by Si gel CC (petroleum ether-EtOAc, 5:1–1:1) to afford **3** (5.0 mg), 3,4,5-trihydroxycinnamate (12.0 mg), and two subfractions IIIa and IIIb. Subfraction IIIa was chromatographed on a Si gel CC ($CHCl_3$-Me_2CO, 12:1–8:1) to yield 7-hydroxy-cupressic acid (9.0 mg) and 5,6-dihydroxy-6-methyl-3-en-2-one (6.0 mg). Subfraction IIIb was separated with a Si gel CC (petroleum ether-Me_2CO, 8:1–5:1) to get piscidinol A (47.0 mg), 4(15)-eudesmene-1β,7α-diol (13.0 mg), and a mixture. The mixture was further chromatographed on a Si gel CC ($CHCl_3$-Me_2CO, 10:1–6:1) to yield isocupressic acid (20.0 mg). Fraction IV (5.3 g) was subjected to MPLC with RP-18 CC (MeOH-H_2O, 3:7–7:3) to afford a mixture. The mixture was lately separated by Si gel CC (petroleum ether-Me_2CO, 4:1–2:1) to yield 15-nor-14-oxolabda-8(17),12*E*-dien-19-oic acid (4.0 mg) and 3β-acetoxy-betulin (26.0 mg). Fraction V (24.0 g) was isolated with MPLC RP-18 CC (MeOH-H_2O, 2:8–7:3) to obtained different subfractions Va–c. Subfraction Va was chromatographed on a Si gel CC ($CHCl_3$-Me_2CO, 8:1–5:1) to yield **2** (33.0 mg) and 3-oxotirucalla-7,24-dien-23-ol (22.0 mg). Then, subfraction Vb was purified by a Si gel CC (petroleum ether-EtOAc, 3:1–2:1) to the isolation of **1** (18.0 mg), (+)-labda-8(17),13(Z)-dien-15,16-diol (7.0 mg), and cryptotrienolic acid (2.0 mg). With MeOH-H_2O (4:6–6:4) as elution solvent, subfraction Vc was separated with RP-18 CC into two mixtures, one of which was further purified by a Si gel CC (petroleum ether-EtOAc, 1:1) to give the separation of 12-oxo-15-hydroxylabda-8(17),13*E*-dien-19-oic acid (14.0 mg), 7α-hydroxysitosterol (24.0 mg), and β-sitosterol (425.0 mg). The other one was subjected through a Si gel CC (petroleum ether-Me_2CO, 3:1–2:1) to afford 4β-hydroxy-15-(3-methyl-2-butenyl)-aromadendr-$\Delta^{10(12)}$-en (14.0 mg) and 14(*R*),15-dihydroxy-8(17),12(*E*)-labdadien-19-oic-acid (26.0 mg).

5(10),13*E*-halimadiene-3*α*,15-diol (1): a white amorphous powder; $[\alpha]_D^{19}$ + 68.3 (c 0.172, Me_2CO); IR (KBr) ν_{max} 3430, 2965, 2931, 1631, 1467, 1381, 1050, 1006 cm^{1}; ^{1}H (400 MHz) and ^{13}C NMR (150 MHz) data (Me_2CO), see Tables 1 and 2, respectively; HREIMS m/z 306.2566 (calcd for $C_{20}H_{34}O_2$ [M]$^+$, 306.2559).

5(10),14-halimadiene-3*α*,13*ξ*-diol (2): a white amorphous powder; $[\alpha]_D^{20}$ + 61.0 (c 0.120, Me_2CO); IR (KBr) ν_{max} 3431, 2965, 2925, 1634, 1457, 1380, 1049 cm^{-1}; ^{1}H (400 MHz) and ^{13}C NMR (150 MHz) data (Me_2CO), see Tables 1 and 2, respectively; HREIMS m/z 306.2550 (calcd for $C_{20}H_{34}O_2$ [M]$^+$, 306.2559).

12-(3-methyl-furan)-labd-8(17)-en-19-oic acid (3): a white amorphous powder; $[\alpha]_D^{19}$ – 4.7 (c 0.114, Me_2CO); UV (MeOH) λ_{max} (log ε) 218 (3.03), 202 (3.16) nm; IR (KBr) ν_{max} 3440, 2958, 2934, 1693, 1632, 1449, 1266, 1181, 1151 cm^{-1};

^{1}H (500 MHz) and ^{13}C NMR (150 MHz) data (Me_2CO), see Tables 1 and 2, respectively; HREIMS *m/z* 316.2039 (calcd for $C_{20}H_{28}O_3$ $[M]^+$, 316.2038).

Electronic Supplementary Material

Supplementary material is available in the online version of this article at http://dx.doi.org/ 10.1007/s13659-013-0025-8 and is accessible for authorized users.

Acknowledgments

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References

[1] Luo, X. D.; Wu, S. H.; Wu, D. G.; Ma, Y. B.; Qi, S. H., *Tetrahedron* **2002**, *58*, 7797–7804.

[2] (a) Qi, S. H.; Wu, D. G.; Zhang, S.; Luo, X. D., *Z. Naturforsch. B: Chem. Sci.* **2003**, *58*, 1128–1132; (b) Nagakura, Y.; Yamanaka, R.; Hirasawa, Y.; Hosoya, T.; Rahman, A.; Kusumawati, I.; Zaini, N. C.; Morita, H., *Heterocycles* **2010**, *80*, 1471–1477; (c) Tan, Q. G.; Luo, X. D. *Chem. Rev.* **2011**, *111*, 7437–7522; (d) Liu, W. X.; Tang, G. H.; He, H. P.; Zhang, Y.; Li, S. L.; Hao, X. J. *Nat. Prod. Bioprospect.* **2012**, *2*, 29–34.

[3] (a) Govindachari, T. R.; Kumari, G. N. K.; Suresh, G. *Phytochemistry* **1996**, *44*, 153–155; (b) Wah, L. K.; Abas, F.; Cordell, G. A.; Ito, H.; Ismail, I. S. *Steroids* **2012**, *78*, 210–219.

[4] Mulholland, D. A.; Iourine, S.; Taylor, D. A. H. *Phytochemistry* **1998**, *47*, 1421–1422.

[5] (a) Fujioka, T.; Yamamoto, M.; Kashiwada, Y.; Fujii, H.; Mihashi, K.; Ikeshiro, Y.; Chen, I. S.; Lee, K. H., *Bioorg. Med. Chem. Lett.* **1998**, *8*, 3479–3482; (b) Duh, C. Y.; Wang, S. K.; Chen, I. S. *J. Nat. Prod.* **2000**, *63*, 1546–1547.

[6] (a) Mohamad, K.; Martin, M. T.; Litaudon, M.; Gaspard, C.; Sevenet, T.; Pais, M. *Phytochemistry* **1999**, *52*, 1461–1468; (b) Luo, X. D.; Wu, S. H.; Ma, Y. B.; Wu, D. G. *Phytochemistry* **2000**, *54*, 801–805; (c) Liu, H.; Heilmann, J.; Rali, T.; Sticher, O. *J. Nat. Prod.* **2001**, *64*, 159–163; (d) Kurimoto, S. I.; Kashiwada, Y.; Lee, K. H.; Takaishi, Y. *Phytochemistry* **2011**, *72*, 2205–2211; (e)Wang, F.; Guan, Y. *Fitoterapia* **2012**, *83*, 13–17.

[7] Yang, D. H.; Cai, S. Q.; Zhao, Y. Y.; Liang, H. *J. Asian Nat. Prod. Res.* **2004**, *6*, 233–236.

[8] Aalbersberg, W.; Singh, Y. *Phytochemistry* **1991**, *30*, 921–926.

[9] (a) Xie, B. J.; Yang, S. P.; Yue, J. M. *Phytochemistry* **2008**, *69*, 2993–2997; (b) Li, C. S.; Yu, H. W.; Li, G. Y.; Zhang, G. L., *Zhongguo Tianran Yaowu* **2010**, *8*, 270–273.

[10] (a) Luo, X.; Wu, S.; Ma, Y.; Wu, D. *Yunnan Zhiwu Yanjiu* **2001**, *23*, 368–372; (b) Luo, X. D.; Wu, S. H.; Ma, Y. B.; Wu, D. G., *Phytochemistry* **2001**, *57*, 131–134; (c) Zhang, X. Y.; Li, Y.; Wang, Y. Y.; Cai, X. H.; Feng, T.; Luo, X. D. *J. Nat. Prod.* **2010**, *73*, 1385–1388.

[11] (a) Hara, N.; Asaki, H.; Fujimoto, Y.; Gupta, Y. K.; Singh, A. K.; Sahai, M. *Phytochemistry* **1995**, *38*, 189–194; (b) Nagashima, F.; Tanaka, H.; Kan, Y.; Huneck, S.; Asakawa, Y. *Phytochemistry* **1995**, *40*, 209–212; (c) Ono, M.; Ito, Y.; Nohara, T. *Chem. Pharm. Bull.* **2001**, *49*, 1220–1222; (d) Nagashima, F.; Suzuki, M.; Takaoka, S.; Asakawa, Y. *J. Nat. Prod.* **2001**, *64*, 1309–1317; (e) Appendino, G.; Borrelli, F.; Capasso, R.; Campagnuolo, C.; Fattorusso, E.; Petrucci, F.; Taglialatela-Scafati, O. *J. Agric. Food Chem.* **2003**, *51*, 6970–6974; (f) Meragelman, T. L.; Pedrosa, D. S.; Gil, R. R. *Biochem. Syst. Ecol.* **2004**, *32*, 45–53; (g) Kanlayavattanakul, M.; Ruangrungsi, N.; Watanabe, T.; Kawahata, M.; Therrien, B.; Yamaguchi, K.; Ishikawa, T. *J. Nat. Prod.* **2005**, *68*, 7–10; (h) Ono, M.; Yamasaki, T.; Konoshita, M.; Ikeda, T.; Okawa, M.; Kinjo, J.; Yoshimitsu, H.; Nohara, T. *Chem. Pharm. Bull.* **2008**, *56*, 1621–1624; (i) Ono, M.; Eguchi, K.; Konoshita, M.; Furusawa, C.; Sakamoto, J.; Yasuda, S.; Ikeda, T.; Okawa, M.; Kinjo, J.; Yoshimitsu, H.; Nohara, T. *Chem. Pharm. Bull.* **2011**, *59*, 392–396; (j) Kubota, T.; Iwai, T.; Takahashi-Nakaguchi, A.; Fromont, J.; Gonoi, T.; Kobayashi, J. *Tetrahedron* **2012**, *68*, 9738–9744.

[12] McChesney, J. D.; Dou, J.; Sindelar, R. D.; Goins, D. K.; Walker, L. A.; Rogers, R. D. *J. Chem. Crystallogr.* **1997**, *27*, 283–290.

[13] Kumar, V.; Niyaz, N. M. M.; Wickramaratne, D. B. M.; Balasubramaniam, S. *Phytochemistry* **1991**, *30*, 1231–1233.

[14] Kim, D. S. H. L.; Chen, Z.; Van, T. N.; Pezzuto, J. M.; Qiu, S.; Lu, Z. Z. *Synth. Commun.* **1997**, *27*, 1607–1612.

[15] Fang, J. M.; Chen, Y. C.; Wang, B. W.; Cheng, Y. S. *Phytochemistry* **1996**, *41*, 1361–1365.

[16] Li, C. J.; Zhang, D. M.; Luo, Y. M.; Yu, S. S.; Li, Y.; Lu, Y. *Phytochemistry* **2008**, *69*, 2867–2874.

[17] Ren, X. Y.; Ye, Y. *J. Asian Nat. Prod. Res.* **2006**, *8*, 677–682.

[18] Hsieh, Y. L.; Fang, J. M.; Cheng, Y. S. *Phytochemistry* **1998**, *47*, 845–850.

[19] Muhammad, I.; Mossa, J. S.; El-Feraly, F. S. *Phytother. Res.* **1996**, *10*, 604–607.

[20] Rodrigues-Filho, E.; Magnani, R. F.; Xie, W.; Mirocha, C. J.; Pathre, S. V. *J. Braz. Chem. Soc.* **2002**, *13*, 266–269.

[21] Villamizar, J.; Pittelaud, J. P.; Rodrigues, J. R.; Gamboa, N.; Canudas, N.; Tropper, E.; Salazar, F.; Fuentes, J. *Nat. Prod. Res.* **2009**, *23*, 891–902.

[22] Anjaneyulu, A. S. R.; Krishnamurthy, M. V. R.; Rao, G. V. *Tetrahedron* **1997**, *53*, 9301–9312.

[23] Sun, Z.; Chen, B.; Zhang, S.; Hu, C. *J. Nat. Prod.* **2004**, *67*, 1975–1979.

[24] Cui, E. J.; Park, J. H.; Park, H. J.; Chung, I. S.; Kim, J. Y.; Yeon, S. W.; Baek, N. I. *J. Korean Soc. Appl. Biol. Chem.* **2011**, *54*, 362–366.

[25] Venkateswarlu, S.; Ramachandra, M. S.; Krishnaraju, A. V.; Trimurtulu, G.; Subbaraju, G. V. *Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem.* **2006**, *45*, 252–257.

[26] Liang, X. T.; Yu, D. Q.; Wu, W. L.; Deng, H. C. *Hua Hsueh Hsueh Pao* **1979**, *37*, 215–230.

[27] (a) Lin, S. J.; Rosazza, J. P. N. *J. Nat. Prod.* **1998**, *61*, 922–926; (b) Iwamoto, M.; Ohtsu, H.; Matsunaga, S.; Tanaka, R. *J. Nat. Prod.* **2000**, *63*, 1381–1383; (c) Li, Y. C.; Kuo, Y. H., *Chem. Pharm. Bull.* **2002**, *50*, 498–500; (d) Minami, T.; Wada, S. I.; Tokuda, H.; Tanabe, G.; Muraoka, O.; Tanaka, R. *J. Nat. Prod.* **2002**, *65*, 1921–1923; (e) Wang, Y. Z.; Tang, C. P.; Ke, C. Q.; Weiss, H. C.; Gesing, E. R.; Ye, Y. *Phytochemistry* **2007**, *69*, 518–526.