New monoterpene phenyl ethers from *Illicium micranthum*

Zheng-Ye Guan, a, b Chuan-Fu Dong, a Li Gao, a, b Jia-Ping Wang, a, b Shi-De Luo, a and Yi-Fen Wang a, *b*

a State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming 650201, China

b University of Chinese Academy of Sciences, Beijing 100049, China

Received 24 January 2013; Accepted 10 March 2013

© The Author(s) 2013. This article is published with open access at Springerlink.com

**Abstract:** Seven new monoterpene phenyl ethers, namely micranthunnins A–G (1–7), were isolated from the stem bark of *Illicium micranthum* (Illiciaceae). Their structures were elucidated by comprehensive spectroscopic analyses including MS, IR, 1D and 2D NMR. All compounds were evaluated for their anti-AChE activities.

**Keywords:** *Illicium micranthum*, monoterpene phenyl ethers, micranthunnins, anti-AChE activities

**Introduction**

*Illicium* species, which belong to the only genus of the family Illiciaceae, are mainly distributed in southern and eastern China, and twelve species of *Illicium* L. are found in Yunnan province. ², ³ Phytochemical investigation showed that this genus produced monoterpenoids, ⁴ sesquiterpene lactones, ⁵ diterpenoids, ⁶ triterpenoids, ⁷ lignans and neolignans, ⁸–₁₀ which showed various bioactivities, such as insecticidal activity, ¹¹ cancer chemopreventive activity, ¹² and neurotrophic activity. ¹³-₁⁵ *Illicium micranthum* was a poisonous shrub used as a traditional pesticide. ¹³ Previous studies on this plant have resulted in the isolation of eight secoprezizaane sesquiterpene lactones, ⁵ seven phenylpropanoids ⁹⁻¹⁰ and several other compounds. ²⁰ As an on-going search for neurotrophic active compounds from natural resources, our investigation on *I. micranthum* led to the isolation of seven new monoterpene phenyl ethers (1–7). This paper deals with the isolation, structure characterization, and anti-AChE activity of these compounds.

**Results and Discussion**

A 90% aqueous MeOH extract the stem bark of *I. micranthum* was partitioned between CHCl₃ and H₂O. The CHCl₃ solubes were dried and subjected to silica gel, Sephadex LH-20 and RP-18 gel column chromatography (CC) and semipreparative HPLC to afford seven new compounds.

The molecular formula of micranthumnin A (1) was assigned as C₂₈H₂₁O₂ by on the basis of HREIMS at m/z 348.1931 (calcd for 348.1937, [M]+), indicating 7 degrees of unsaturation.

Its IR spectrum showed the presence of aromatic ring (1602, 1516, 1424 cm⁻¹) and one α,β-conjugated carbonyl (1673 cm⁻¹). The ¹H NMR spectrum of 1 (Table 1) revealed the presence of one 1,3,4-trisubstituted aromatic ring [δH 7.03 (1H, d, J = 1.8 Hz, H-2), 6.91 (1H, d, J = 8.4 Hz, H-5), 6.87 (1H, dd, J = 8.4, 1.8 Hz, H-6)], one methoxy group at δH 3.84 (3H, s, OCH₃), four methyls [δH 1.12 (3H, d, J = 6.6 Hz, H-9), 1.91...
H-9 was disappeared in on (Figure 4) of H-1 + 2

The connected to C-4 of the aromatic ring through an ether bond.

Comparison of the NMR data between (C-9) in with the ROESY correlation from H-1 to H-2 suggested that the monoterpene moiety was -zeometry at C-2.

The similarities of the spectroscopic data (Tables 2 and 3) between 3 and 1 suggested that 3 was identical to 1 except for the methoxy group at C-7, causing a significant downfield chemical shift from δC 77.4 to δC 89.2 due to C-7. HMBC correlation (Figure 2) from OCH3-7 at δH 4.23 to C-7 at δC 89.2 further confirmed the above assignment. Without an isomer as a comparison, as well as the significant difference of C-7 chemical shift between 3 and 1, the relative configuration of 3 was not clarified. Finally, the structure of 3 was established as shown in Figure 1, and named as micranthumin C.

Micranthumin D (4), yellow gum, had the same molecular formula (C25H28O6) as 1. Analysis of its NMR data (Tables 2 and 3) showed that 4 was similar to 1, except for the signals of one methylene, one oxymethylene, one olefinic methine and one methoxy group at C-7, C-8, and C-9 shifted from δC 77.4, 71.3 and 17.5 to δC 79.2, 72.1 and 18.7, respectively. Moreover, the 1H NMR signals (Table 1) of H-7, H-8 and H-9 shifted from δH 4.43, 3.84 and 1.12 to δH 4.28, 3.77, 0.96. Detailed analysis of 2D NMR spectra revealed that the structure of 2 was also 4-[(2E)-3′,7′-dimethyl-5′-oxo-2′,6′-octadienyl]oxy-3-methoxy-phenylpropane-7,8-diol. The similarity of the NMR spectra between 1 and 2 suggested that they might be erythro and threo isomers. The OH configurations of two stereogenic centers in compounds 1 and 2 were deduced by comparison with the 13C NMR spectra of similar compounds, erythro- and threo-1-phenyl-1,2-dihydroxypropane, for which the structures were confirmed by synthesis.

The relative configurations of 1 and 2 were further confirmed by the derivative reaction. In the reactions, the vienol diol parts in 1 and 2 react with DMP to yield ketal products 1a and 2a, respectively, which makes the carbon-carbon bond between C-7 and C-8 rotate unfreely. The relative configurations of 1 and 2 were determined depending on the two ketal products 1a and 2a whose relative configurations were clarified by ROESY experiments (Figure 3). ROESY correlations of H-7/H-1" and H-8/H-1" were detected while the correlation of H-7/H-9 was disappeared in 1a, which determined the erythro configuration of 1a. The relative configuration of 2a was determined to be threo by ROESY correlations of H-7/H-1", H-8/H-3", and H-7/H-9. Consequently, the relative configurations of 1 and 2 were determined to be erythro and threo, respectively (Figure 1).

Figure 3. Selected ROESY correlations of 1a and 2a

The mass spectrum of compound 3 (HREIMS m/z 362.2098, claed for 362.2093, [M]+) was 14 amu higher than that of 1, indicating that there was probably one more methyl group in 3. The similarities of the spectroscopic data (Tables 2 and 3) between 3 and 1 suggested that 3 was identical to 1 except for the methoxyl group at C-7, causing a significant downfield chemical shift from δC 77.4 to δC 89.2 due to C-7. HMBC correlation (Figure 2) from OCH3-7 at δH 3.23 to C-7 at δC 89.2 further confirmed the above assignment. Without an isomer as a comparison, as well as the significant difference of C-7 chemical shift between 3 and 1, the relative configuration of 3 was not clarified. Finally, the structure of 3 was established as shown in Figure 1, and named as micranthumin C.
Optical rotations were measured on Bruker Avance 500 or AM-400 MHz spectrometers with TMS as internal standard at room temperature. HRESIMS were recorded on a 1H NMR data of compounds 3–7 (δ in ppm, J in Hz)

| pos. | 3′ | 4′ | 5′ | 6′ | 7′ |
|------|----|----|----|----|----|
| 2    | 6.79 (s) | 7.01(d, 2.4) | 6.97(d, 1.8) | 7.47(d, 1.8) | 6.96(d, 1.8) |
| 5    | 6.85 (d, 8.3) | 6.96 (d, 8.4) | 6.95 (d, 8.4) | 7.15 (d, 8.4) | 6.84 (d, 8.4) |
| 6    | 6.78 (d, 8.3) | 6.90 (dd, 8.4, 2.4) | 6.86 (dd, 8.4, 1.8) | 7.54 (dd, 8.4, 1.8) | 6.82 (dd, 8.4, 1.8) |
| 7    | 3.77 (d, 8.0) | 4.31 (d, 7.2) | 4.28 (d, 7.2) | 9.83 (s) | 6.32 (dq, 15.6, 1.2) |
| 8    | 3.80 (overlapped) | 3.81 (overlapped) | 3.80 (overlapped) | - | 6.13 (dq, 15.6, 6.6) |
| 9    | 0.96 (d, 5.6) | 0.98 (d, 6.0) | 0.96 (d, 6.6) | - | 1.85 (dd, 6.6, 1.2) |
| 1′   | 4.66 (d, 6.0) | 4.18 (t, 6.6) | 4.16 (t, 6.6) | 4.78 (d, 6.0) | 4.61 (d, 6.0) |
| 2′   | 5.64 (t, 6.0) | 2.65 (t, 6.6) | 3.05 (t, 6.6) | 5.64 (t, 6.0) | 5.60 (dd, 6.0, 1.2) |
| 4′   | 3.14 (s) | 6.25 (d, 1.2) | 6.23 (d, 0.6) | 3.21(s) | 3.14 (s) |
| 6′   | 6.11 (br. s) | 6.17 (br. s) | 6.17 (br. s) | 6.23 (br. s) | 6.18 (br. s) |
| 8′   | 1.88 (s) | 1.94 (d, 1.2) | 2.14 (d, 1.2) | 1.91 (s) | 1.87 (d, 1.2) |
| 9′   | 2.14 (s) | 2.16 (d, 1.2) | 1.91 (d, 1.2) | 2.15 (s) | 2.12 (d, 1.2) |
| 10′  | 1.75 (s) | 2.23 (d, 1.2) | 2.04 (d, 0.6) | 1.79 (s) | 1.71 (s) |
| OCH3-3 | 3.88 (s) | 3.85 (s) | 3.82 (s) | 3.92 (s) | 3.83 (s) |
| OCH3-7 | 3.23 (s) | 3.29 (s) | - | - | - |

*Recorded in CD3OD at 600MHz; †Recorded in CDCl3 at 400MHz.

Figure 4. Selected ROESY correlations of 1, 4 and 5

The molecular formula of 6 was determined as C19H22O5 by HREIMS (m/z 302.1512, calcd for 302.1518, [M]+). Comparison of its NMR data (Tables 2 and 3) with 1 suggested that the 1,2-propanediol group in 1 was replaced by a formyl group at C-1. The HMBC correlations (Figure 2) from H-7 (δH 9.83) to C-1 (δC 131.5), C-2 (δC 110.7), and C-6 (δC 127.7), from H-2 (δH 7.47) and H-6 (δH 7.54) to C-7 (δC 192.9) further confirmed this assignment. Thus, 6 was determined and named as micranthumnin F.

The mass spectrum showed that compound 7 was 34 mass units lower than that of 1, indicating the probable loss of two hydroxyl groups in 7. The NMR data indicated that 7 was similar to 1. Extensive analyses of its 1D and 2D NMR data suggested that the 1,2-propanediol group in 1 was replaced by a propenyl group. The signals corresponding to a propenyl group at δH 6.32 (1H, dq, J = 15.6, 1.2 Hz, H-7), 6.13 (1H, dq, J = 15.6, 6.6 Hz, H-8), and 1.85 (3H, dd, J = 6.6, 1.2 Hz, H-9) were evident in the 1H NMR data (Table 2) of 7. The structure was further confirmed by HMBC correlations (Figure 2) of H-7/C-1, C-2, C-6 and O-8/C-1, C-9. Moreover, the analysis of the ROESY spectrum as well as the coupling constant (J = 15.6 Hz) between H-7 and H-8, indicating an E-geometry double bond. Therefore, the structure of 7 was determined and named as micranthumnin G.

The acetyl cholinesterase (AChE) inhibitory activities of all compounds were assayed using the Ellman method.²⁴ Compound 5 showed weak inhibitory activity (27.4%) at a concentration of 50 μM, using tacrine (0.33 μM) as the positive control (50.56% inhibition). The remaining compounds were inactive at 50 μM.

Experimental Section

General Experimental Procedures. Optical rotations were measured on a JASCO P-1020 polarimeter. IR and UV spectra were recorded on a Bruker Tensor 27 FT-IR spectrometer and a Shimadzu UV2401PC spectrometer, respectively. 1D and 2D NMR spectra were recorded on Bruker Avance III-600, DRX-500 or AM-400 MHz spectrometers with TMS as internal standard at room temperature. HRESIMS were recorded on a
Table 3. $^{13}$C NMR data of compounds 1–7 (δ in ppm)

| Pos. | 1$^a$ | 2$^a$ | 3$^a$ | 4$^a$ | 5$^a$ | 6$^a$ | 7$^a$ |
|------|-------|-------|-------|-------|-------|-------|-------|
| 1    | 133.2 s | 133.9 s | 131.0 s | 136.9 s | 136.4 s | 131.5 s | 131.3 s |
| 2    | 109.9 d | 109.9 d | 110.0 d | 112.4 d | 112.1 d | 110.7 d | 108.7 d |
| 3    | 149.4 s | 149.4 s | 149.5 s | 151.0 s | 150.8 s | 151.3 s | 149.4 s |
| 4    | 147.6 s | 147.7 s | 148.0 s | 149.2 s | 149.3 s | 155.3 s | 147.0 s |
| 5    | 112.9 d | 112.9 d | 112.6 d | 115.0 d | 114.3 d | 113.5 d | 113.2 d |
| 6    | 118.9 d | 119.1 d | 120.3 d | 120.9 d | 120.9 d | 127.7 d | 118.5 d |
| 7    | 77.4 d  | 79.2 d  | 89.2 d  | 80.1 d  | 80.2 d  | 192.9 d | 130.5 d |
| 8    | 71.3 d  | 72.1 d  | 71.3 d  | 73.0 d  | 73.0 d  | 123.8 d | 123.8 d |
| 9    | 17.5 q  | 18.7 q  | 18.0 q  | 19.4 q  | 19.4 q  | 18.3 q  | 18.3 q  |
| 1'   | 65.6 t  | 65.6 t  | 65.6 t  | 68.4 t  | 69.1 t  | 66.6 t  | 65.6 t  |
| 2'   | 124.5 d | 124.5 d | 124.5 d | 41.6 t  | 34.9 t  | 125.1 d | 124.7 d |
| 3'   | 134.7 s | 134.7 s | 134.8 s | 155.9 s | 157.1 s | 137.0 s | 134.6 s |
| 4'   | 55.0 t  | 54.9 t  | 55.0 t  | 128.4 d | 128.6 d | 55.6 t  | 55.1 t  |
| 5'   | 198.2 s | 198.3 s | 198.2 s | 193.8 s | 193.0 s | 200.5 s | 198.3 s |
| 6'   | 122.7 d | 122.7 d | 122.7 d | 127.3 d | 127.1 d | 123.8 d | 122.7 d |
| 7'   | 156.5 s | 156.6 s | 156.4 s | 156.8 s | 156.9 s | 158.4 s | 156.5 s |
| 8'   | 27.7 q  | 27.7 q  | 27.7 q  | 27.9 q  | 27.9 q  | 27.7 q  | 27.7 q  |
| 9'   | 20.7 q  | 20.7 q  | 20.7 q  | 20.9 q  | 20.9 q  | 20.9 q  | 20.9 q  |
| 10'  | 16.9 q  | 16.9 q  | 16.9 q  | 19.6 q  | 26.9 q  | 17.1 q  | 16.9 q  |
| OCH$_3$ | 55.8 q | 55.8 q | 55.8 q | 55.9 q | 56.6 q | 56.5 q | 56.4 q |
| OCH$_2$ | 56.5 q |

*aRecorded in CD$_3$OD at 150MHz; *bRecorded in CDCl$_3$ at 100MHz.

Plant Material. Stem bark of *I. micranthum* were collected in Dongschuan of Yunnan province, China, in May 2011. The plant material was identified by Dr. Rong Li of Kunming Institute of Botany, Chinese Academy of Sciences. A sample was deposited in our laboratory. A voucher specimen of *I. micranthum* (Li Rong 560) is deposited in State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences.

Extraction and Isolation. The air-dried stem bark of *I. micranthum* (14 kg) was powdered and extracted with MeOH (3 × 25 L) at room temperature, and concentrated in vacuo to give a crude extract. The extract was successively fractionated with CHCl$_3$ and EtOAc. A portion of the CHCl$_3$ extract (310 g) was separated by silica gel column chromatography, using CHCl$_3$/MeOH (20:1 to 2:1) as a gradient solvent system to afford fractions I–VI.

Fraction II was isolated by silica gel eluting with a gradient of petroleum ether/EtOAc (40:1, 20:1, 10:1, 5:1, to 2:1) to afford four subfractions (A1–A4). Fraction A2 was chromatographed over Sephadex LH-20 with MeOH to yield 7 (31 mg). Fraction III was subjected to RP-18 column chromatography (MeOH/H$_2$O, 30:70 to 80:20) to afford three fractions. The first fraction was chromatographed over Sephadex LH-20 with MeOH and applied to silica gel CC (eluted with CHCl$_3$/Me$_2$CO, 40:1), and then purified by semipreparative HPLC to give 1 (15 mg, t$_R$ 21.5 min, MeCN/H$_2$O 39:61), and 2 (40 mg, t$_R$ 25.0 min, MeCN/H$_2$O 39:61), respectively. The second fraction was subjected to silica gel CC using CHCl$_3$/Me$_2$CO (40:1), with final purification by semipreparative HPLC (MeCN/H$_2$O 45:55), to give 4 (3.5 mg, t$_R$ 17.0 min) and 5 (42 mg, t$_R$ 23.0 min). Compound 3 (3.2 mg) was obtained from the last fraction after repeated silica gel CC and Sephadex LH-20 CC, followed by semipreparative HPLC (t$_R$ 38.0 min, MeOH/H$_2$O 70:30). Fraction IV was subjected to repeated silica gel CC (petroleum ether/Me$_2$CO, 95:5 to 1:1), to afford seven subfractions (B1–B7). Fraction B4, eluted with MeOH over Sephadex LH-20, was further separated on semipreparative HPLC to yield 6 (4.5 mg, t$_R$ 18.5 min, CH$_3$OH/H$_2$O 70:30).

Micanthumin A (1): yellow gum; [α]$_D^25$ = 7.9 (c 0.13, MeOH); UV (MeOH) $\lambda_{max}$ (log ε) 233 (2.31), 204 (2.55) nm; IR $\nu_{max}$ (KBr) 3443, 2965, 2900, 1673, 1602, 1516, 1424, 1262, 1228, 1137, 994, 854, 621 cm$^{-1}$; $^1$H (600 MHz, CD$_3$OD) and $^{13}$C NMR (100 MHz, CDCl$_3$) data, see Tables 1 and 3; HREIMS: m/z 348.1931 [M]+, (calcd for C$_{22}$H$_{20}$O$_5$, 348.1937).

Micanthumin B (2): yellow gum; [α]$_D^25$ = 7.6 (c 0.17, MeOH); UV (MeOH) $\lambda_{max}$ (log ε) 233 (2.27), 204 (2.52) nm; IR $\nu_{max}$ (KBr) 3424, 2973, 2933, 2912, 1685, 1617, 1513, 1448, 1262, 1225, 1138, 1035, 809, 624 cm$^{-1}$; $^1$H (600 MHz, CD$_3$OD) and $^{13}$C NMR (100 MHz, CDCl$_3$) data, see Tables 1 and 3; HREIMS: m/z 348.1925 [M]+, (calcd for C$_{22}$H$_{20}$O$_5$, 348.1937).
Miconthumunin C (3): yellow gum; [α]_D^20 = –20.2 (c 0.08, MeOH); UV (MeOH) λ max (log ε) 233 (2.21), 204 (2.47) nm; IR ν max (KBr) 3441, 2968, 2932, 1687, 1620, 1513, 1449, 1261, 1138, 1034, 975 cm⁻¹; ¹H (600 MHz, CD₃OD) and ¹³C NMR (100 MHz, CDCl₃) data, see Tables 2 and 3; HREIMS: m/z 362.2098 [M] (found for C₂₃H₂₃O₈, 362.2093). 

Miconthumunin D (4): yellow gum; [α]_D^20 = 7.6 (c 0.10, MeOH); UV (MeOH) λ max (log ε) 288 (2.23), 203 (2.40) nm; IR ν max (KBr) 3431, 2970, 2931, 1668, 1627, 1514, 1263, 1138, 1034, 871, 764 cm⁻¹; ¹H (600 MHz) and ¹³C NMR (150 MHz) data (CD₃OD), see Tables 2 and 3; HREIMS: m/z 348.1937 [M] (found for C₂⁴H₂₃O₈, 348.1937). 

Miconthumunin E (5): yellow gum; [α]_D^20 = –13.6 (c 0.09, MeOH); UV (MeOH) λ max (log ε) 239 (2.37), 205 (2.32) nm; IR ν max (KBr) 3425, 2971, 2933, 1669, 1626, 1515, 1263, 1138, 1033, 872, 769 cm⁻¹; ¹H (600 MHz) and ¹³C NMR (150 MHz) data (CD₃OD), see Tables 2 and 3; HREIMS: m/z 348.1932 [M] (found for C₂₃H₂₃O₈, 348.1937). 

Miconthumunin F (6): colorless gum; [α]_D^20 = –7.4 (c 0.20, MeOH); UV (MeOH) λ max (log ε) 230 (2.37), 205 (2.32) nm; IR ν max (KBr) 3426, 2936, 1684, 1586, 1508, 1424, 1267, 1136, 991, 731 cm⁻¹; ¹H (600 MHz, CD₃OD) and ¹³C NMR (150 MHz, CDCl₃) data, see Tables 2 and 3; HREIMS: m/z 302.1512 [M] (found for C₂₃H₂₃O₈, 302.1518). 

Miconthumunin G (7): colorless gum; [α]_D^20 = –3.9 (c 0.31, MeOH); UV (MeOH) λ max (log ε) 253 (2.32), 210 (2.47) nm; IR ν max (KBr) 2933, 2913, 1686, 1618, 1511, 1446, 1262, 1225, 1137, 964 cm⁻¹; ¹H (400 MHz) and ¹³C NMR (100 MHz) data (CDCl₃), see Tables 2 and 3; HREIMS: m/z 314.1887 [M] (found for C₂₃H₂₃O₈, 314.1882). 

Derivative Reaction. 1 [9 mg, 0.026 mmol in DMP (1 mL)] and 2 [10 mg, 0.029 mmol in DMP (1 mL)] were stirred with PPTs (1 ng), respectively, and protected with argon at room temperature for 24 hours. 

Anti-AChE Assay. AChE inhibitory activities of the compounds isolated were assayed by the spectrophotometric method developed by Ellman et al. ¹⁷ Acetylthiocholine iodide (Sigma) was used as substrate in the assay. Compounds were dissolved in DMSO. The mixture contained 110 μL phosphate buffer (pH 8.0), 10 μL of test compound solution (50 μM), and 40 μL AChE solution (0.04 U/100 μL), and the mixture was incubated for 20 min (30 °C). The reaction was initiated by the addition of 20 μL of DTNB (6.25 mM) and 20 μL of acetylthiocholine iodide (6.25 mM). The hydrolysis of acetylthiocholine was monitored at 405 nm after 30 min. Taccrine was used as positive control. All the reactions were performed in triplicate. The percentage inhibition was calculated as follows: % inhibition = (E – S)/E × 100 (E is the activity of the enzyme without test compound and S is the activity of enzyme with test compound). 

Electronic Supplementary Material

Supplementary material is available in the online version of this article at http://dx.doi.org/10.1007/s13659-013-0007-x and is accessible for authorized users.

Acknowledgments

This work was supported by the National Natural Science Foundation (20872148). The authors are grateful to the analytical group of the Laboratory of Phytochemistry, Kunming Institute of Botany, Chinese Academy of Sciences for measuring NMR, MS, and IR data.

Open Access This article is distributed under the terms of the Creative Commons Attribution License which permits any use, distribution, and reproduction in any medium, provided the original author(s) and source are credited.

References

[1] Wu C. Flora of China; Sciences Press: Beijing, 1997; Vol. 8, pp 199–203. 
[2] Wu C. The Families and Genera of Angiosperms in China; Sciences Press: Beijing, 2003; p 81. 
[3] Wu C. Flora Yunnanica; Sciences Press: Beijing, 2000; Vol. 11, pp 1–12. 
[4] Ngo, K. S.; Brown, G. D. Tetrahedron 1996, 55, 759–770. 
[5] Dong, X. J.; Zhu, X. D.; Wang, Y. F.; Wang, Q.; Ju, P.; Luo, S. D. Helv. Chim. Acta. 2006, 89, 983–987. 
[6] Huang, J. M.; Yang, C. S.; Zhao, R.; Takahashi, H.; Fukuyama, Y. Chem. Pharm. Bull. 2004, 52, 104–107. 
[7] Yokoyama, R.; Huang, J. M.; Hosoda, A.; Kino, Y.; Yang, C. S.; Fukuyama, Y. J. Nat. Prod. 2003, 66, 799–803. 
[8] Schmidt, T. J.; Schmidt, H. M.; Müller, E.; Peters, W.; Froneczek, F. R.; Truesdale, A.; Fischer, N. H. J. Nat. Prod. 1998, 61, 230–236. 
[9] Sy, L. K.; Brown, G. D. J. Nat. Prod. 1998, 61, 907–912. 
[10] Takahashi, K.; Takani, M. Chem. Pharm. Bull. 1975, 23, 538–542. 
[11] Dong, C. F.; Liu, L.; Luo, H. R.; Li, X. N.; Guan, Z. Y.; Wang, Y. F. Nat. Prod. Bioprospect. 2012, 2, 133–137. 
[12] Sy, L. K.; Brown, G. D. J. Nat. Prod. 1998, 61, 987–992. 
[13] Morimoto, S.; Tanabe, H.; Nanaka, G. I.; Nishio, I. Phytochemistry 1988, 27, 907–910. 
[14] Park, I. K.; Shin, S. C. Agric. Food Chem. 2005, 53, 4388–4392. 
[15] Itoigawa, M.; Ito, C.; Tokuda, H.; Enjo, F.; Nishio, H.; Furukawa, H. Cancer Lett. 2004, 214, 165–169. 
[16] Yokoyama, R.; Huang, J. M.; Yang, C. S.; Fukuyama, Y. J. Nat. Prod. 2002, 65, 527–531. 
[17] Kubo, M.; Okada, C.; Huang, J. M.; Harada, K.; Hioki, H.; Fukuyama, Y. Org. Lett. 2009, 11, 5190–5193. 
[18] Trzoss, L.; Xu, J.; Lacoske, M. H.; Moby, W. C.; Theodorakis, E. A. Org. Lett. 2011, 13, 4554–4557. 
[19] Zheng, S. Q.; Chen, Y.; Li, Q.; Hu, Z. Y. Chinese Traditional Patent Medicine 2009, 31, 1724–1726. 
[20] Li, H. L.; Wang, G. L. Nat. Prod. Res. Dev. 1994, 6, 18–22. 
[21] Perry, N. B.; Foster, L. M.; Lorimer, S. D.; May, B. C. H.; Weavers, R. T.; Toyota M.; Nakaishi E.; Asakawa Y. J. Nat. Prod. 1996, 59, 729–733. 
[22] Shen, C. C.; Ni, C. L.; Shen, Y. C.; Huang, Y. L.; Kuo, C. H.; Wu, T. S.; Chen, C. C. J. Nat. Prod. 2009, 72, 168–171. 
[23] Pelter, A.; Peeverall, S.; Pitchford, A. Tetrahedron 1996, 52, 1085–1094. 
[24] Ellman, G. L.; Courtney, K. D.; Andres, V. J.; Featherstone, R. M. Biochem. Pharmacol. 1961, 7, 88–95.