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Dibenzocyclooctadiene lignans from *Schisandra neglecta* and their anti-HIV-1 activities

Yuan-Xing Duan^{abc}, Jing-Li Cao^{bc}, Rong-Rong Wen^{bc}, Guang-Yu Yang^{abc}, Jian-Xin Pu^a, Han-Dong Sun^a, Wei-Lie Xiao^{a*} and Gan-Peng Li^{ab*}

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Two new dibenzocyclooctadiene lignans, schinegllignans A and B (**1** and **2**), together with 11 known (**3**–**13**) were isolated from the fruit of *Schisandra neglecta*. Their structures and stereochemistries were elucidated by spectroscopic methods, including 1D, 2D NMR, and HR-ESI-MS techniques. Compounds **1** and **2** were evaluated for their anti-HIV activities, and they showed moderate anti-HIV-1 activities with therapeutic index values of 18.5 and 24.6.

Keywords: *Schisandra neglecta*; dibenzocyclooctadiene lignans; schinegllignans A and B; anti-HIV-1 activities

1. Introduction

The family Schisandraceae, consisting of *Schisandra* and *Kadsura* genera, is medicinally important. The stems or fruits of *Schisandraceae* plant are commonly used in Traditional Chinese Medicine for their diverse beneficial bioactivities [1,2]. Previous studies have shown that the plants of the *Schisandraceae* family are rich in lignans, especially dibenzocyclooctadiene lignans, which have been found to possess some beneficial pharmacological effects, including anti-HIV, antitumor, cytotoxic, antioxidant, and antihepatotoxic effects [3–12].

Schisandra neglecta, one of species of this genus, is a climbing plant mainly distributed in the southwest of China. In a previous study, some new dibenzocyclooctadiene lignans from *S. neglecta* were reported [11,12]. In our continuing efforts to identify bioactive natural pro-

ducts from the *Schisandraceae* medicinal plants, a chemical investigation on the fruit of *S. neglecta* (Schisandraceae), indigenous to the Dali Prefecture of Yunnan Province of China, was carried out, and two new dibenzocyclooctadiene lignans, together with 11 known were separated from this plant. In addition, the anti-HIV-1 activities of compounds **1** and **2** were evaluated. In this paper, their structure elucidation and biological activities are described.

2. Results and discussion

Column chromatography on silica gel, Sephadex LH-20, RP-18, and preparative HPLC separation of the Et₂O-soluble fraction of the methanol extract of the fruit of *S. neglecta* yielded two new dibenzocyclooctadiene lignans, named schinegllignans A and B (**1** and **2**), together with 11 known lignans, which

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were identified as rubrisandrin A (**3**) [13], gomisin O (**4**) [14], epigomisin O (**5**) [14], benzoylgomisin O (**6**) [15], schisanwilsonin A (**7**) [16], schisanwilsonin C (**8**) [17], gomisin T (**9**) [18], schizandrin (**10**) [19], acetylgomisin K (**11**) [17], gomisin D (**12**) [20], and gomisin E (**13**) [14]. The structures of the compounds **1–13** were shown in Figure 1, and the ^1H and ^{13}C NMR spectroscopic data of **1** and **2** are listed in Table 1.

Compound **1** was obtained as a yellow gum. Its molecular formula was determined as $\text{C}_{22}\text{H}_{28}\text{O}_6$ by HR-ESI-MS at m/z 389.1959 $[\text{M} + \text{H}]^+$. Its ^1H and ^{13}C NMR spectra showed signals of 26 hydrogens and 22 carbons, respectively, corresponding to two aromatic rings with two aromatic protons (δ_{H} 6.78 s and 6.41 s), two methylene carbons (δ_{C} 40.2 t and 36.2 t), two methine carbons (δ_{C} 35.3 d and 42.7 d), two methyl groups (δ_{C} 13.0 q and 22.2 q; δ_{H} 0.71, d, $J = 7.2$ Hz; δ_{H} 0.98, d, $J = 7.2$ Hz), and four methoxy groups (δ_{C} 56.5 q, 60.8 q, 61.1 q, and 61.2 q; δ_{H} 3.54 s, 3.57 s, 3.81 s, 3.84 s), suggesting the presence of a biphenyl moiety [21]. UV absorption maxima at 216 and 249 nm, along with NMR spectra as discussed below, indicated that **1** was a dibenzocyclooctadiene lignan. The ^1H and ^{13}C NMR spectra of **1** are similar to those of rubrisandrin A [13]. The obvious chemical shift differences resulted from the different substituent groups in the aromatic rings.

On the basis of the HSQC spectrum, the protons at δ_{H} 2.58 and 2.44 were attached at C-6 (δ_{C} 40.2 t) and the protons at δ_{H} 2.20 and 1.96 were attached at C-9 (δ_{C} 36.2 t). HMBC correlations of the proton at δ_{H} 2.58 with the carbons at δ_{C} 13.0 (CH_3 -18) and 35.3 (C-7), and of the proton at δ_{H} 2.20 with the carbons at δ_{C} 22.2 (CH_3 -17) and 42.7 (C-8) indicated the resonances at δ_{H} 2.58 and 2.44 corresponded with H_2 -6, and the resonances at δ_{H} 2.20 and 1.96 corresponded with H_2 -9. The cyclooctadiene moiety structure was confirmed by ^1H – ^1H COSY correlations

of H-6/H-7/H-8/H-9, H-7/H-18, and H-8/H-17 (Figure 2).

HMBC correlations of H-4 (δ_{H} 6.78 s) with C-5 (δ_{C} 136.3 s), C-6 (δ_{C} 40.2 t), C-16 (δ_{C} 121.9 s), and of H-11 (δ_{H} 6.41) with C-9 (δ_{C} 36.2 t), C-10 (δ_{C} 135.6 s), C-15 (δ_{C} 119.1 s) suggested that two aromatic proton resonances corresponded with H-4 and H-11, respectively. Their corresponding carbon signals resonated at δ_{C} 112.3 and 107.9, respectively, by HSQC techniques. On the basis of HMBC correlations of H-4 with the aromatic carbons at δ_{C} 150.1 and 141.4 and of H-11 with the carbons at δ_{C} 152.5 and 139.7, these four carbons were assigned as C-3, C-2, C-12, and C-13, respectively.

The HMBC correlations of four *O*-methyls (δ_{H} 3.57 s, 3.54 s, 3.81 s, 3.84 s) with carbons at δ_{C} 151.3, 141.4, 152.5, and 152.3, respectively, revealed that these four substitutions were located at C-1, C-2, C-12, and C-14, respectively. The positions of the two hydroxyls were located at C-3 and C-13. These assignments were supported by the ^{13}C NMR chemical shifts of the four *O*-methyl groups (δ_{C} 60.8, 61.1, 56.5, and 61.2) [13,22], and the presence of the ROESY correlation between 12-OMe at δ_{H} 3.84 and H-11 at δ_{H} 6.41. Moreover, the difference between **1** and rubrisandrin A were substituents on C-13 and C-14, which was confirmed by the aromatic carbon signals at δ_{C} 152.3 (C-14) in **1** shifting downfield about 6 ppm compared with that in rubrisandrin A [13]. Thus, the planar structure of **1** was established.

The CD spectrum of **1** had a negative Cotton effect at 250 nm and a positive Cotton effect at 220 nm, indicating that **1** has an *S*-biphenyl configuration [21]. The ROESY correlations (Figure 3) between H-4/ CH_3 -18 and H-11/H-9 in **1** suggested a twist-boat–chair conformation for the cyclooctadiene ring [23]. The substituent positions and stereochemical assignments in the cyclooctadiene ring of **1** were supported by the ROESY correlations of

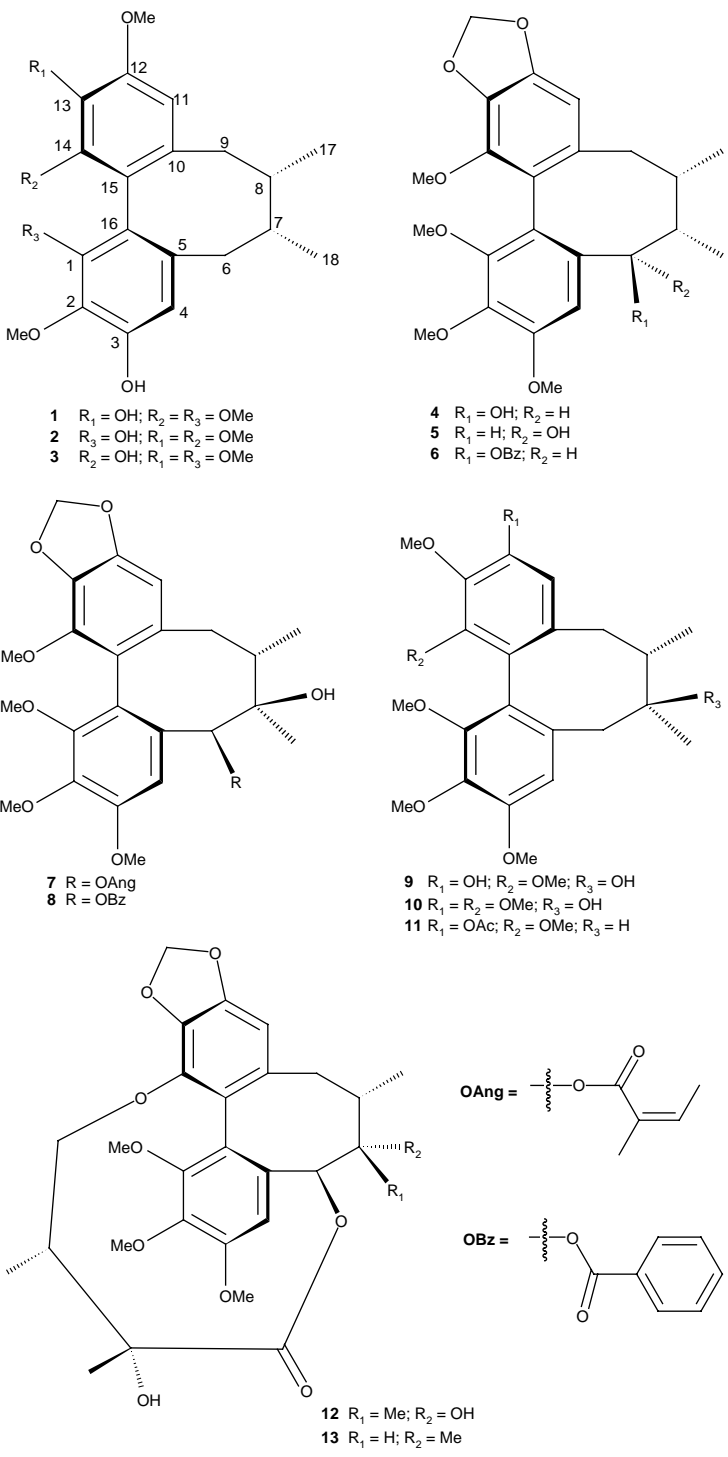
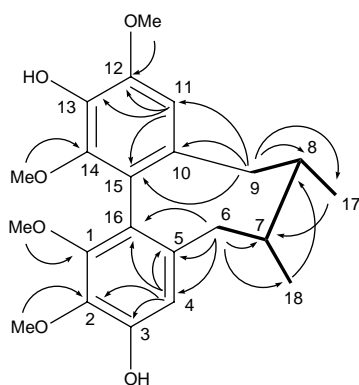


Figure 1. Structures of compounds 1–13.

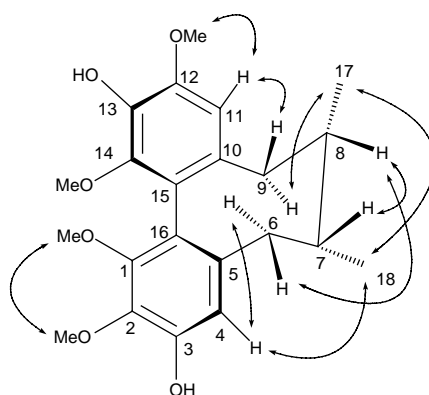
Table 1. ^1H and ^{13}C NMR spectral data of compounds **1** and **2** in CD_3OD medium (δ in ppm).

No.	Compound 1		Compound 2	
	^{13}C (mult)	^1H (mult, J in Hz)	^{13}C (mult)	^1H (mult, J in Hz)
1	151.3 s		148.8 s	
2	141.4 s		139.6 s	
3	150.1 s		150.0 s	
4	112.3 d	6.78 s	115.7 d	6.54 s
5	136.3 s		135.2 s	
6	40.2 t	2.44, dd, $J = 13.5, 1.4$ 2.58, dd, $J = 13.5, 7.5$	39.8 t	2.40, dd, $J = 13.4, 2.0$ 2.49, dd, $J = 13.4, 7.6$
7	35.3 d	1.88 m	35.2 d	1.85 m
8	42.7 d	1.74 m	42.4 d	1.76 m
9	36.2 t	2.20, dd, $J = 13.0, 9.4$ 1.96, d, $J = 13.0$	36.5 t	2.23, dd, $J = 12.8, 9.6$ 2.02, d, $J = 12.8$
10	135.6 s		135.9 s	
11	107.9 d	6.41 s	104.3 d	6.40 s
12	152.5 s		152.6 s	
13	139.7 s		140.9 s	
14	152.3 s		153.6 s	
15	119.1 s		118.1 s	
16	121.9 s		123.0 s	
17	22.2 q	0.71, d, $J = 7.2$	22.2 q	0.71, d, $J = 7.2$
18	13.0 q	0.98, d, $J = 7.2$	13.0 q	0.98, d, $J = 7.2$
1-OMe	60.8 q	3.54 s		
2-OMe	61.1 q	3.81 s	60.9 q	3.75 s
3-OMe				
12-OMe	56.5 q	3.84 s	56.2 q	3.85 s
13-OMe			61.1 q	3.83 s
14-OMe	61.2 q	3.57 s	61.2 q	3.53 s

H-4/H-6 α , H-4/CH₃-18, H-6 β /H-8, H-7/H-8, CH₃-18/CH₃-17, H-9 α /CH₃-17, H-9 β /H-11, and H-11/OMe-12. Thus, the structure of **1** was determined as shown in Figure 1, and given the name as schineg-lignan A.

Figure 2. Selected HMBC (→) and ^1H - ^1H COSY (→) correlations of **1**.

Compound **2** was obtained as yellow gums, and showed a *quasi*-molecular ion peak at m/z 389.1954 $[\text{M} + \text{H}]^+$ in its HR-ESI-MS, corresponding to the molecular formula of $\text{C}_{22}\text{H}_{28}\text{O}_6$. The ^1H and ^{13}C

Figure 3. Key ROESY correlations of compound **1**.

NMR spectra of **2** were very similar to those of **1** and rubrisandrin A. The obvious chemical shift differences resulted from the substituent group variations in the aromatic rings. Analysis of the HSQC, HMBC, and ROESY spectra of **2** showed that the methoxy groups were located at C-2, C-12, C-13, and C-14, and the phenolic hydroxy groups at C-1 and C-3, which were confirmed by HMBC correlations of H-11 (δ_{H} 6.40) with the aromatic carbons at C-13 (δ_{C} 140.9) and of 13-OMe (δ_{H} 3.83) with C-13 (δ_{C} 140.9), and the aromatic carbon signals at δ_{C} 148.8 (C-1) in **2** was shifted upfield about 2.5 ppm compared with that in **1**. Compound **2** showed a similar negative Cotton effect at 251 nm and a positive Cotton effect at 220 nm. Thus, the structure of **2** was established, and it has been accorded the trivial name of schinegglignan B.

As certain of dibenzocyclooctadiene lignans from *Schisandra* genus species exhibit potential anti-HIV activities, the new compounds **1** and **2** were tested for their potencies in preventing the cytopathic effects of HIV-1 in C8166 cells. Cytotoxicity was measured in parallel with the determination of antiviral activity, using AZT as a positive control (0.0043 $\mu\text{g/ml}$ and $\text{CC}_{50} > 200 \mu\text{g/ml}$) [24]. The results indicated that compounds **1** and **2** showed moderate anti-HIV-1 activities with EC_{50} of 1.8 and 2.2 $\mu\text{g/ml}$, and therapeutic index values of 18.5 and 24.6, respectively.

3. Experimental

3.1 General experimental procedures

Optical rotations were measured with a Horiba SEPA-300 polarimeter. UV spectra were obtained using a Shimadzu UV-2401A spectrophotometer. CD spectra were measured on a JASCO J-810 spectropolarimeter. A Tenor 27 spectrophotometer was used for scanning IR spectrometry. 1D and 2D NMR spectra were recorded on a DRX-500 NMR spectrometer with TMS as an internal standard. Unless otherwise speci-

fied, chemical shifts (δ) are expressed in ppm with reference to the solvent signals. HR-ESI-MS was performed on a VG Autospec-3000 spectrometer. Semi-preparative HPLC was performed on a Shimadzu LC-8A preparative liquid chromatography with Zorbax PrepHT GF (21.2 mm \times 250 mm) or Venusil MP C_{18} (20 mm \times 250 mm) columns. Column chromatography was performed using silica gel (200–300 mesh, Qing-dao Marine Chemical, Inc., Qingdao, China), Lichroprep RP-18 gel (40–63 μm , Merck, Darmstadt, Germany), and MCI gel (75–150 μm , Mitsubishi Chemical Corporation, Tokyo, Japan). The fractions were monitored by TLC, and spots were visualized by heating silica gel plates sprayed with 5% H_2SO_4 in EtOH.

3.2 Plant material

The fruits of *S. neglecta* were collected in Dali Prefecture, Yunnan Province, China, in July 2007. The identification of the plant material was verified by Prof. Xi-Wen Li of Kunming Institute of Botany, Chinese Academy of Sciences. A voucher specimen (KIB 07-9-18) has been deposited in the State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences.

3.3 Extraction and isolation

The air-dried and powdered fruits of *S. neglecta* (2.6 kg) were extracted four times with 70% aqueous MeOH (4 \times 5 l) at room temperature and filtered, with the filtrate evaporated under reduced pressure and partitioned with EtOAc (3 \times 2 l). The EtOAc partition (262 g) was applied to silica gel (200–300 mesh) column chromatography, eluting with a CHCl_3 – Me_2CO gradient system (20:1, 9:1, 8:2, 7:3, 6:4, 5:5), to give five fractions A–E. The further separation of fraction B (32.6 g) by silica gel column chromatography, eluted with petroleum ether–acetone (20:1–1:2), yielded

mixtures B1–B6. Fraction B2 (4.65 g) was subjected to silica gel column chromatography using petroleum ether–acetone and semi-preparative HPLC (75% MeOH–H₂O, flow rate 12 ml/min) to give **6** (22.6 mg), **10** (22.4 mg), **11** (8.8 mg), and **13** (86.2 mg). Fraction B3 (2.8 g) was subjected to silica gel column chromatography using petroleum ether–acetone (10:1–3:1) and semi-preparative HPLC (65% MeOH–H₂O, flow rate 12 ml/min) to give **4** (42.1 mg), **5** (16.4 mg), **7** (16.3 mg), **8** (13.4 mg), **9** (14.6 mg), and **12** (43.5 mg). Fraction B4 (2.7 g) was subjected to silica gel column chromatography using petroleum ether–acetone (5:1–1:1) and semi-preparative HPLC (60% MeOH–H₂O, flow rate 12 ml/min) to afford **1** (11.5 mg), **2** (13.4 mg), and **3** (15.4 mg).

3.3.1 *Schinegllignan A (1)*

C₂₂H₂₈O₆, a yellow gum; $[\alpha]_D^{22.8} + 17.3$ (c 0.22, MeOH); UV (MeOH) λ_{\max} (log ϵ) 216 (4.97), 249 (3.47), 322 (1.22) nm; CD (c 0.028, MeOH) $\Delta\epsilon_{250\text{ nm}} - 18.5$, $\Delta\epsilon_{232\text{ nm}} - 6.32$, $\Delta\epsilon_{220\text{ nm}} + 9.18$, $\Delta\epsilon_{210\text{ nm}} - 4.62$; IR (KBr): ν_{\max} 3425, 2955, 2933, 2871, 1612, 1583, 1489, 1456, 1124, 1080, 1004, 850 cm⁻¹; ¹H (CD₃OD, 500 MHz) and ¹³C (CD₃OD, 125 MHz) NMR spectral data see Table 1; positive ESI-MS: m/z 389 [M + H]⁺; HR-ESI-MS: m/z 389.1959 [M + H]⁺ (calcd for C₂₂H₂₉O₆, 389.1964).

3.3.2 *Schinegllignan B (2)*

C₂₂H₂₈O₆, a yellow gum; $[\alpha]_D^{23.2} - 26.7$ (c 0.26, MeOH); UV (MeOH) λ_{\max} (log ϵ) 215 (5.08), 248 (3.68), 329 (0.97), 348 (0.69) nm; CD (c 0.06, MeOH), $\Delta\epsilon_{251\text{ nm}} - 55.6$, $\Delta\epsilon_{240\text{ nm}} - 36.5$, $\Delta\epsilon_{220\text{ nm}} + 26.4$, $\Delta\epsilon_{210\text{ nm}} + 3.4$; IR (KBr): ν_{\max} 3427, 2955, 2934, 2871, 2840, 1612, 1584, 1489, 1456, 1420, 1123, 1078, 1003, 944, 848, 802 cm⁻¹; ¹H (CD₃OD, 500 MHz) and ¹³C (CD₃OD, 125 MHz) NMR spectral data see Table 1; positive ESI-MS m/z 389 [M + H]⁺; HR-ESI-MS m/z 389.

1954 [M + H]⁺ (calcd for C₂₂H₂₉O₆, 389.1964).

3.4 Anti-HIV-1 assay

The cytotoxicity assay against C8166 cells (CC₅₀) was assessed using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium (MTT) method and anti-HIV-1 activity was evaluated by the inhibition assay for the cytopathic effects of HIV-1 (EC₅₀) [24].

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Supporting information available

¹H and ¹³C NMR, HSQC, HMBC COSY, ROESY, and HR-ESI-MS spectra of **1**, ¹H and ¹³C NMR, HSQC, HMBC, and HR-ESI-MS spectra of **2**.

References

- [1] Committee of Pharmacopoeia of China, *Pharmacopoeia of the People's Republic of China (Part 1)* (Pharmacopoeia Commission of the Ministry of Public Health of PRC, Beijing, 1990), p. 454.
- [2] G. Hao, M.L. Chye, and R.M.K. Saunders, *Bot. J. Linn. Soc.* **135**, 401 (2001).
- [3] J.B. Chang, J. Reiner, and J.X. Xie, *Chem. Rev.* **105**, 4581 (2005).
- [4] L. Li, Q. Pan, M. Sun, Q. Lu, and X. Hu, *Life Sci.* **80**, 741 (2007).
- [5] H.Y. Min, E.J. Park, J.Y. Hong, Y.J. Kang, S.J. Kim, H.J. Chung, E.R. Woo, and Y.S. Kim, *Bioorg. Med. Chem. Lett.* **18**, 523 (2008).
- [6] Y.C. Shen, Y.C. Lin, Y.B. Cheng, M.Y. Chiang, S.S. Liou, and A.T. Khalil, *Phytochemistry* **70**, 114 (2009).

- [7] G.Y. Yang, P. Fan, R.R. Wang, J.L. Cao, W.L. Xiao, L.M. Yang, J.X. Pu, and H.D. Sun, *Chem. Pharm. Bull.* **58**, 734 (2010).
- [8] J.X. Pu, L.M. Yang, W.L. Xiao, R.T. Li, C. Lei, X.M. Gao, S.X. Huang, and H.D. Sun, *Phytochemistry* **69**, 1266 (2008).
- [9] J. Zhang, L.L. Shi, and Y.N. Zheng, *Nat. Prod. Commun.* **5**, 231 (2010).
- [10] G.Y. Yang, Y.K. Li, R.R. Wang, X.N. Li, W.L. Xiao, J.X. Pu, and H.D. Sun, *J. Nat. Prod.* **73**, 915 (2010).
- [11] M. Chen, X.M. Xu, Z.H. Liao, L. Dong, L. Li, and C.Z. Huang, *Molecules* **13**, 548 (2008).
- [12] M. Chen, Z.Z. Liao, X.M. Xu, Y. Wen, M. Sun, H.X. Zhang, and W.X. Ma, *Molecules* **13**, 1148 (2008).
- [13] M. Chen, N. Kilgore, K.H. Lee, and D.F. Chen, *J. Nat. Prod.* **69**, 1697 (2006).
- [14] Y. Ikeya, H. Taguchi, I. Yosioka, and H. Kobayashi, *Chem. Pharm. Bull.* **27**, 2695 (1979).
- [15] C.C. Chen, C.C. Shen, Y.Z. Shin, and T.M. Pan, *J. Nat. Prod.* **57**, 1164 (1994).
- [16] W.H. Ma, Y. Lu, H. Huang, P. Zhou, and D.F. Chen, *Bioorg. Med. Chem. Lett.* **19**, 4958 (2009).
- [17] Y. Ikeya, H. Taguchi, and I. Yosioka, *Chem. Pharm. Bull.* **28**, 2422 (1980).
- [18] Y. Ikeya, H. Kanatani, M. Hakozaiki, H. Taguchi, and H. Mitsuhashi, *Chem. Pharm. Bull.* **36**, 3974 (1988).
- [19] Y. Ikeya, H. Taguchi, and I. Yosioka, *Chem. Pharm. Bull.* **26**, 328 (1978).
- [20] Y. Ikeya, H. Taguchi, I. Yosioka, Y. Iitaka, and H. Kobayashi, *Chem. Pharm. Bull.* **27**, 1395 (1979).
- [21] Y. Ikeya, H. Taguchi, I. Yoshioka, and H. Kobayashi, *Chem. Pharm. Bull.* **27**, 1383 (1979).
- [22] Y.B. Cheng, M.T. Chang, Y.W. Lo, C.J. Ho, Y.C. Kou, C.T. Chien, S.Y. Chen, S.S. Liou, Y.H. Kuo, and Y.C. Shen, *J. Nat. Prod.* **72**, 1663 (2009).
- [23] J.S. Liu and L. Li, *Phytochemistry* **32**, 1293 (1993).
- [24] J.H. Wang, S.C. Tam, H. Huang, D.Y. Ouyang, Y.Y. Wang, and Y.T. Zheng, *Biochem. Biophys. Res. Commun.* **317**, 965 (2004).