Neolignans and Caffeoyl Derivatives from *Selaginella moellendorffii*

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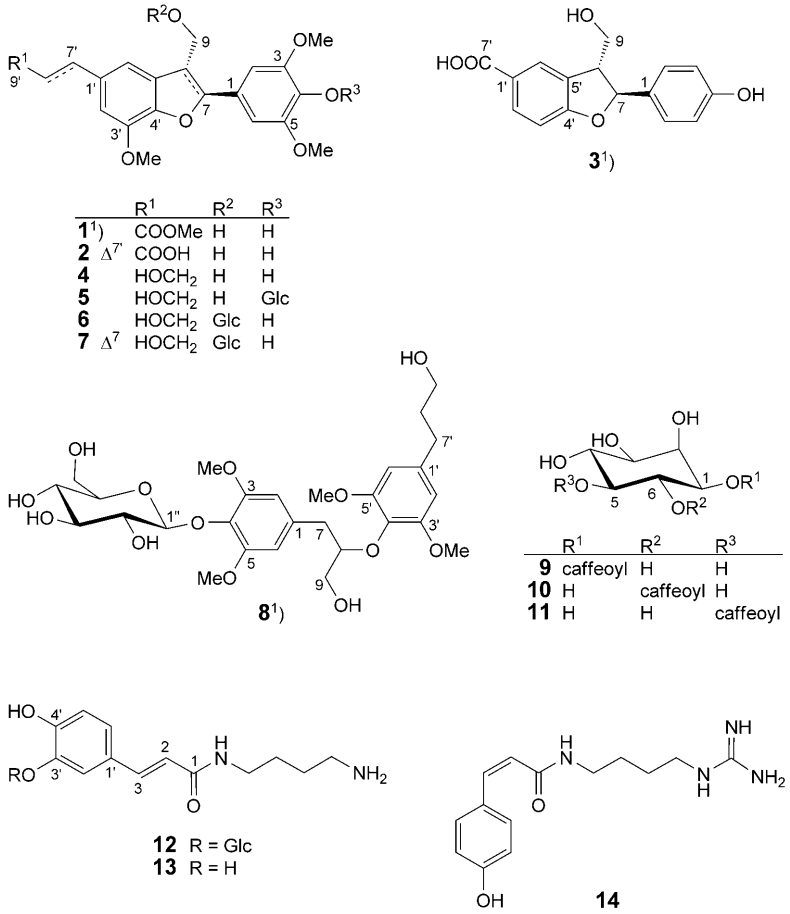
Ten new phenolic compounds including the six neolignans **1**–**3** and **6**–**8** and four caffeoyl derivatives, *i.e.*, *myo*-inositol 1-caffeate (**9**), *myo*-inositol 6-caffeate (**10**), *myo*-inositol 5-caffeate (**11**), and paucine 3′-β-D-glucopyranoside (**12**) were isolated from the whole plants of *Selaginella moellendorffii* (caffeic acid = 3-(3,4-dihydroxyphenyl)prop-2-enoic acid). Their structures were established by spectroscopic and chemical methods.

Introduction. – *Selaginella moellendorffii* HIERON. (Selaginellaceae), a perennial herb, is mainly distributed in the southern area of the Changjiang River in China and has been used to treat jaundice, gonorrhea, bleeding, acute hepatitis, and idiopathic thrombocytopenic purpura (ITP) in traditional Chinese folk medicine. Earlier studies found a coumarin, fatty acids [1], a lignan glucoside [2], flavone glycosides [3], and cytotoxic [4] and antioxidative [5] biflavones in this plant. In our recent research, a series of pyrrolidinoindoline alkaloids were found from this plant [6]. In continuation of the studies on this plant, ten new phenolic derivatives, **1**–**3** and **6**–**12**, and four known ones, compounds **4** and **5**, paucine (=(2*E*)-*N*-(4-aminobutyl)-3-(3,4-dihydroxyphenyl)prop-2-enamide **13**) [7], and N^1-*cis*-*p*-coumaroylagmatine (=(2*Z*)-*N*-{4-[(aminoiminomethyl)amino]butyl}-3-(4-hydroxyphenyl)prop-2-enamide **14**) [8], were isolated from the whole plants of *S. moellendorffii*. The structure elucidation of these new compounds is reported.

Results and Discussion. – Compound **1**[1]) was obtained as an amorphous solid with an *m*/*z* of 441.1518 ($[M+Na]^+$) by HR-ESI-MS, leading us to assign it a molecular formula $C_{22}H_{26}O_8$. The IR spectrum of **1** showed absorptions for hydroxy (3441 cm^{-1}), carbonyl (1731 cm^{-1}), and aromatic groups (1616, 1519, and 1500 cm^{-1}). In the ^{13}C-NMR spectrum of **1** (*Table 1*), 22 signals for 4 MeO groups (δ(C) 56.1 (2*q*), 55.8 (*q*), and 51.5 (*q*)), 12 aromatic (δ(C) 147.1 (2*s*), 146.4 (*s*), 143.9 (*s*), 134.5 (*s*), 133.7 (*s*),

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



132.2 (*s*), 128.2 (*s*), 116.1 (*d*), 112.1 (*d*), and 103.0 (2*d*)), 1 ester carbonyl (δ(C) 173.7 (*s*)), and 5 alphatic C-atoms (δ(C) 88.0 (*d*), 63.5 (*t*), 53.7 (*d*), 36.0 (*t*), and 30.6 (*t*)) suggested that this compound might be a lignan. Careful comparison of the NMR data of **1** (*Table 1*) with those of known neolignans revealed that compound **1** is a dihydrobenzofuran neolignan with oxidation of C(9′) and methoxy substituentes at C(3), C(3′), C(5), and C(9′) [9][10], which was confirmed by the HMBCs of *Me*O–C(3,5)/C(3,5), *Me*O-C(3′)/C(3′), and *Me*O-C(9′)/C(9′) (*Fig.*). The relative

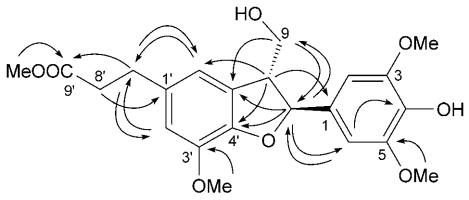


Figure. *Key HMBCs* (H → C) *of* **1**

Table 1. *^{1}H- and ^{13}C-NMR Data of* **1**–**4**. δ in ppm, J in Hz. Asterisks (*) mark overlapping signals.

	1		**2**		**3**		**4**	
	δ(H)[a])	δ(C)[b])	δ(H)[c])	δ(C)[d])	δ(H)[c])	δ(C)[d])	δ(H)[a])	δ(C)[b])
C(1)		132.2		133.3		133.6		132.2
H–C(2,6)	6.65 (*s*, 2 H)	103.0	6.67 (*s*)	104.1	7.18 (*d*, *J* = 8.5)	128.3	6.65 (*s*)	103.1
H–C(3,5)		147.1		149.4	6.76 (*d*, *J* = 8.5)	116.4		147.1
C(4)		134.5		136.5		158.6		134.6
H–C(7)	5.52 (*d*, *J* = 6.5)	88.0	5.58 (*d*, *J* = 6.5)	89.9	5.57 (*d*, *J* = 6.1)	89.6	5.49 (*d*, *J* = 6.3)	88.1
H–C(8)	3.55 (*dd*, *J* = 12.5, 6.5)	53.7	3.53 (*dd*, *J* = 11.5, 6.5)	55.0	3.51 (*dd*, *J* = 12.2, 6.1)	54.1	3.46 (*dd*, *J* = 11.7, 6.3)	53.8
CH_2(9)	3.87*	63.5	3.80–3.88 (*m*)	64.6	3.79–3.84 (*m*)	64.7	3.81–3.87, 3.73–3.78 (2*m*)	63.7
C(1′)		133.7		129.8		124.4		135.5
H–C(2′)	6.65 (*s*)	112.1	7.15 (*s*)	113.6	7.91 (*dd*, *J* = 8.5, 1.5)	133.0	6.72 (*s*)	112.4
C(3′) or H–C(3′)		143.9		145.8	6.84 (*d*, *J* = 8.5)	109.9		144.2
C(4′)		146.4		151.8		165.4		146.5
C(5′)		128.2		130.8		129.7		127.7
H–C(6′)	6.68 (*s*)	116.1	7.18 (*s*)	119.0	7.94 (br. *s*)	128.1	6.71 (*s*)	115.9
CH_2(7′), H–C(7′), or C(7′)	2.88 (*t*, *J* = 7.5)	30.6	7.62 (*d*, *J* = 16.0)	146.8		170.0	2.61 (*t*, *J* = 7.7)	32.0
CH_2(8′) or H–C(8′)	2.63 (*t*, *J* = 7.5)	36.0	6.33 (*d*, *J* = 16.0)	116.4			1.77–1.84 (*m*)	34.6
C(9′) or CH_2(9′)		173.7		170.9			3.56 (*t*, *J* = 6.5)	62.2
*Me*O–C(3,5)	3.86 (*s*)	56.1	3.81 (*s*)	56.7			3.80 (*s*)	56.3
*Me*O–C(3′)	3.89 (*s*)	55.8	3.90 (*s*)	56.7			3.85 (*s*)	56.0
*Me*O–C(9′)	3.67 (*s*)	51.5						

[a]) In $CDCl_3$ at 500 MHz. [b]) In $CDCl_3$ at 125 MHz. [c]) In CD_3OD at 500 MHz. [d]) In CD_3OD at 100 MHz.

configuration of H–C(7) and H–C(8) was assigned as *trans* by the ROESY correlations of H–C(7)/CH_2(9); *J* values are useless to distinguish *cis*/*trans* diastereoisomers of the dihydrobenzofuran neolignans [9]. On the other hand, a significant difference in chemical shifts of C(8) in 9-hydroxydihydrobenzofuran neolignans, appearing at δ *ca.* 54 in the *trans* isomers and at δ *ca.* 49 in the *cis* ones [9][11], is a reliable criterion to distinguish both diastereoisomers. The chemical shift of C(8) (δ 53.7) in **1** also suggested the relative *trans*-configuration of H–C(7) and H–C(8).

The absolute configurations of dihydrobenzofuran neolignans are usually determined by the signs of the band ^1L_b (270–300 nm) or ^1L_a (220–240 nm) in the circular-dichroism (CD) spectrum. The positive signs of the ^1L_b band predict the absolute configuration of 7,8-*trans*-3-methoxydihydrobenzofuran neolignans to be (7*S*,8*R*) [12][13]. The CD spectrum of **1** showed a positive *Cotton* effect at 282 nm ($\Delta\varepsilon$ +0.13), indicating that the absolute configuration of **1** was the (7*S*,8*R*)-configuration. Therefore, compound **1** was elucidated as (7*S*,8*R*)-4,9-dihydroxy-3,3′,5-trimethoxy-4′,7-epoxy-8,5′-neolignan-9′-oic acid methyl ester[1]).

Compound **2**[1]) was obtained as colorless amorphous solid. The HR-ESI-MS of **2** had a molecular-ion peak at *m*/*z* 401.1236 ($[M-H]^-$), consistent with the molecular formula $C_{21}H_{22}O_8$. The ^{13}C-NMR spectra of **2** (*Table 1*) were very similar to those of **1**, except for the signals of the side chain at **1** at δ(C) 30.6 (*t*, C(7′)), 36.0 (*t*, C(8′)), 173.7 (*s*, C(9′)), and 51.5 (*q*, *Me*O–C(9′)) which were replaced by those of **2** at δ(C) 146.8 (*d*, C(7′)), 116.4 (*d*, C(8′)), and 170.9 (*s*, C(9′)), implying that C(7′) and C(8′) were dehydrogenated and the carboxyl group (C(9′)) was not esterified in **2**. The C(7′)=C(8′) bond had (*E*)-configuration according to the coupling constant (J(7′,8′) = 16.0 Hz, *Table 1*), and the relative configuration of **2** was determined as *trans* by the chemical shift of C(8) (δ(C) 55.0). The structure of **2** was thus confirmed to be *rel*-(7*R*,7′*E*,8*S*)-4,9-dihydroxy-3,3′,5-trimethoxy-4′,7-epoxy-8,5′-neolign-7′-en-9′-oic acid[1]).

Compound **3**[1]) was assigned the molecular formula $C_{16}H_{14}O_5$ by HR-ESI-MS analysis (*m*/*z* 285.0754 ($[M-H]^-$, $C_{16}H_{13}O_5^-$)). The IR spectrum showed absorption bands at 3397, 1674, 1611, 1600, and 1518 cm^{-1} due to hydroxy, carbonyl, and phenyl groups. The ^{1}H-NMR spectrum (*Table 1*) of **3** indicated the presence of a *p*-disubstituted (δ(H) 7.18 (*d*, J = 8.5 Hz, 2 H) and 6.76 (*d*, J = 8.5 Hz, 2 H)) and a 1,2,4-trisubstituted (δ(H) 7.94 (br. *s*), 7.91 (*dd*, J = 8.5, 1.5 Hz), and 6.84 (*d*, J = 8.5 Hz)) benzene ring in **3**. Its ^{13}C-NMR spectrum (*Table 1*) showed 16 signals, including the characteristic ones for dihydrobenzofuran neolignans (δ(C) 89.6 (*d*), 64.7 (*t*), and 54.1 (*d*)), 12 ones for two benzene rings (δ(C) 165.4, 158.6, 133.6, 133.0, 129.7, 128.3 (2 C), 128.1, 124.4, 116.4 (2 C), and 109.9), and one for a carboxy group (δ(C) 170.0), which implied that this compound might be a 8′,9′-dinor-dihydrobenzofuran neolignan. This was confirmed by the HMBC spectrum of **3**. The relative configuration of **3** was also determined as *trans* by the chemical shift of C(8) (δ(C) 54.1), and the absolute configuration of **3** was assigned as (7*S*,8*R*) by comparing its CD data with those of the known (+)-conocarpan [14–16]. Therefore, compound **3** was determined as (7*S*,8*R*)-4,9-dihydroxy-4′,7-epoxy-8′,9′-dinor-8,5′-neolignan-7′-oic acid[1]).

Compound **4**[1]) showed the $[M+Cl]^-$ ion peak at *m*/*z* 425.1370 in the negative-ion-mode HR-ESI-MS, indicating the molecular formula $C_{21}H_{26}O_7$. The NMR spectra of **4** (*Table 1*) were very similar to those of (+)-(7*R*,8*S*)-5-methoxydihydrodehydroconi-

feryl alcohol [10]. However, the optical rotation value of **4** was negative rather than positive, implying the absolute configuration of **4** to be (7*S*,8*R*), which is consistent with those of **1** and **3**. Consequently, **4** is (7*S*,8*R*)-3,3′,5-trimethoxy-4′,7-epoxy-8,5′-neolignan-4,9,9′-triol[1]). An analog without optical activity was also reported in two other references [17][18].

The molecular formula of **5**[1]) was determined as $C_{27}H_{36}O_{12}$ by the $[M+Cl]^-$ ion peak at *m*/*z* 587.1883 in the HR-ESI-MS. The NMR data of **5** (*Table 2*) were very similar to those of a known neolignan glucoside [19]. The relative configuration of H−C(7) and H−C(8) in the known compound was suggested to be *cis* according to the *J* value between the two protons by the authors. It should be revised as *trans* based on the chemical shift of C(8) (δ(C) 55.8) [9][11]. Because the optical value of this compound has not been reported, it was difficult to determine if compound **5** is identical to this known one. Acidic hydrolysis of **5** provided a D-glucose. Thus, **5** was deduced as *rel*-(7*R*,8*S*)-3,3′,5-trimethoxy-4′,7-epoxy-8,5′-neolignan-4,9,9′-triol 4-β-D-glucopyranoside[1]).

Compound **6**[1]) had the molecular formula $C_{27}H_{36}O_{12}$ as deduced from an HR negative-ion-mode ESI-MS. Its NMR data (*Table 2*) showed signals for a neolignan moiety identical to that of **4** and a β-glucose moiety (δ(H) 4.36 (*d*, $J=7.9$ Hz, H−C(1″))). The glucosyloxy group was located at C(9) by the long-range correlations between H−C(9) (δ(H) 4.10 (*t*, $J=8.5$ Hz)) and C(1″) (δ(C) 104.1), and H−C(1″) to C(9) (δ(C) 72.3) in the HMBC spectrum of **6**. Therefore, **6** is *rel*-(7*R*,8*S*)-3,3′,5-trimethoxy-4′,7-epoxy-8,5′-neolignan-4,9,9′-triol 9-β-D-glucopyranoside[1]).

Compound **7**[1]) was found to have the formula $C_{27}H_{34}O_{12}$, two H-atoms less than that of **6**, from the HR-ESI-MS (neg.). Comparison of the NMR spectra (*Table 2*) and the formula of **7** with those of **6** indicated that **7** is a 7,8-didehydro derivative of **6**, namely 3,3′,5-trimethoxy-4′,7-epoxy-8,5′-neolign-7-ene-4,9,9′-triol 9-β-D-glucopyranoside[1]), which was further confirmed by the HMBC spectrum of **7**.

Compound **8**[1]) was shown to have a molecular formula of $C_{28}H_{40}O_{13}$ by HR-ESI-MS (neg.). Signals for two 1,2,3,5-tetrasubstituted benzene moieties (δ(H) 6.60 (*s*, H−C(2,6)) and 6.50 (*s*, H−C(2′,6′))) and an anomeric proton (δ(H) 4.80 (*d*, $J=$ 7.9 Hz)) of a β-glucosyl group were observed in the ^{1}H-NMR spectrum of **8** (*Table 2*). In the ^{13}C-NMR spectrum of **8** (*Table 2*), 28 signals for 4 MeO (δ(C) 57.5 (2*q*) and 57.0 (2*q*)), two aromatic (δ(C) 154.5 (2*s*), 153.8 (2*s*), 139.8 (*s*), 136.9 (*s*), 134.8 (*s*), 134.6 (*s*), 108.4 (2*d*), and 106.7 (2*d*)), and a glucosyl group (δ(C) 105.6 (*d*), 78.3 (*d*), 77.8 (*d*), 75.7 (*d*), 71.2 (*d*), and 63.6 (*t*)), and 6 other alphatic C-atoms (δ(C) 84.9 (*d*), 63.6 (*t*), 62.1 (*t*), 39.0 (*t*), 35.4 (*t*), and 33.4 (*t*)) implied that this compound might be a lignan glucoside, which was further determined as a 8,4′-oxyneolignan 4-glucoside by the HMBC cross-peaks H−C(8)/C(4′) and H−C(1″)/C(4). Accordingly, compound **8** was elucidated as 3,3′,5,5′-tetramethoxy-8,4′-oxyneolignane-4,9,9′-triol 4-β-D-glucopyranoside[1]).

Compound **9** was obtained as a colorless amorphous solid. The negative-ion-mode HR-ESI-MS exhibited an accurate ion peak at *m*/*z* 341.0878 ($[M-H]^-$), in accordance with the molecular formula $C_{15}H_{18}O_9$. The IR spectrum showed absorption bands due to hydroxy (3407 cm^{-1}), conjugated carbonyl (1688 and 1631 cm^{-1}), and phenyl (1604, 1523, and 1445 cm^{-1}) groups. A caffeoyl (δ(H) 7.02 (*s*), 6.98 (*d*, $J=8.0$ Hz), 6.75 (*d*, $J=$ 8.0 Hz), 7.49 (*d*, $J=16.0$ Hz), and 6.24 (*d*, $J=16.0$ Hz); δ(C) 166.5 (*s*, C(9′))) and a

Table 2. *^{1}H- and ^{13}C- NMR Data* (500 and 100 MHz, resp.; CD_3OD) *of* **5**–**8**. δ in ppm, J in Hz. Asterisks (*) mark overlapping signals.

	5		**6**		**7**		**8**	
	δ(H)	δ(C)	δ(H)	δ(C)	δ(H)	δ(C)	δ(H)	δ(C)
C(1)		140.3		133.9		122.2		136.9
H–C(2,6)	6.73 (*s*)	104.4	6.71 (*s*)	104.2	7.23 (*s*)	105.9	6.60 (*s*)	108.4
C(3,5)		154.4		149.2		149.5		153.8
C(4)		135.6		136.1		137.8		134.6
H–C(7), C(7), or CH_2(7)	5.55 (*d*, *J* = 5.5)	88.5	5.59 (*d*, *J* = 6.1)	89.4		157.0	2.98 (*d*, *J* = 6.1)	39.0
H–C(8) or C(8)	3.41–3.48 (*m*)	55.8	3.62–3.66 (*m*)	53.0		111.7	4.20–4.25 (*m*)	84.9
CH_2(9)	3.83–3.89, 3.72–3.77 (2*m*)	65.0	4.10 (*t*, *J* = 8.5), 3.85–3.91 (*m*)	72.3	5.08 (*d*, *J* = 11.0), 4.90*	61.8	3.55–3.59, 3.48–3.55 (2*m*)	63.6
C(1′)		137.2		137.0		139.4		139.8
H–C(2′)	6.73 (*s*)	114.1	6.72 (*s*)	114.1	6.75 (*s*)	108.6	6.50 (*s*)	106.7
C(3′)		145.2		145.2		146.1		154.5
C(4′)		147.4		147.4		142.5		134.8
C(5′)		129.4		129.5		133.3		154.5
H–C(6′)	6.70 (*s*)	117.9	6.78 (*s*)	118.1	7.18 (*s*)	112.1	6.50 (*s*)	106.7
CH_2(7′)	2.61 (*t*, *J* = 7.5)	32.9	2.62 (*t*, *J* = 7.8)	32.9	2.77 (*t*, *J* = 7.3)	33.4	2.62 (*t*, *J* = 7.9)	33.4
CH_2(8′)	1.77–1.83 (*m*)	35.8	1.77–1.84 (*m*)	35.8	1.87–1.93 (*m*)	36.0	1.78–1.85 (*m*)	35.4
CH_2(9′)	3.55 (*t*, *J* = 6.5)	62.2	3.52–3.57 (*m*)	62.2	3.60 (*t*, *J* = 6.5)	62.2	3.51–3.59 (*m*)	62.1
H–C(1″)	4.85 (*d*, *J* = 7.3)	105.2	4.36 (*d*, *J* = 7.9)	104.1	4.48 (*d*, J = 7.9)	102.9	4.80 (*d*, *J* = 7.9)	105.6
H–C(2″)	3.43–3.48 (*m*)	75.6	3.22 (*t*, *J* = 7.9)	75.2	3.23 (*t*, J = 7.9)	75.2	3.43–3.49 (*m*)	75.7
H–C(3″)	3.38–3.42 (*m*)	77.8	3.36 (*t*, *J* = 7.9)	78.2	3.30*	78.3	3.38–3.43 (*m*)	77.8
H–C(4″)	3.38–3.42 (*m*)	71.2	3.25–3.31 (*m*)	71.6	3.29*	71.7	3.38–3.43 (*m*)	71.2
H–C(5″)	3.17–3.21 (*m*)	78.3	3.25–3.30 (*m*)	78.0	3.26*	78.2	3.16–3.22 (*m*)	78.3
CH_2(6″)	3.74–3.79 (*m*), 3.62–3.68 (*dd*, *J* = 11.6, 5.0)	62.5	3.84–3.88, 3.62–3.70 (2*m*)	62.7	3.91 (*d*, *J* = 11.6), 3.70 (*dd*, *J* = 11.6, 5.5)	62.8	3.75*, 3.66 (*dd*, *J* = 11.6, 4.9)	63.6
*Me*O–C(3,5)	3.80 (*s*)	57.0	3.81 (*s*)	56.8	3.94 (*s*)	57.1	3.81 (*s*)	57.0
*Me*O–C(3′)	3.86 (*s*)	56.8	3.86 (*s*)	56.7	3.99 (*s*)	56.4	3.76 (*s*)	57.5
*Me*O–C(5′)							3.76 (*s*)	57.5

myo-inositol group (δ(H) 4.50 (br. *d*, $J = 9.6$ Hz, H−C(1)), 3.84 (br. *s*, H−C(2)), 3.21 (br. *d*, $J = 9.6$ Hz, H−C(3)), 3.40 (*t*, $J = 9.6$ Hz, H−C(4)), 3.00 (*t*, $J = 9.6$ Hz, H−C(5)), and 3.64 (*t*, $J = 9.6$ Hz, H−C(6)) were easily deduced from its NMR spectra (*Table 3*). The two moieties were linked through the bonds C(1)−O−C(9′) by the long-range correlation H−C(1)/C(9′) in the HMBC spectrum of **9**. Therefore, compound **9** was elucidated as *myo*-inositol 1-caffeate. Its absolute configuration was not determined.

Table 3. *^{1}H- and ^{13}C- NMR Data* (400 and 100 MHz, resp.; (D_6)DMSO) *of* **9**–**11**. δ in ppm, J in Hz.

	9		**10**		**11**[a])	
	δ(H)	δ(C)	δ(H)	δ(C)	δ(H)	δ(C)
H−C(1)	4.50 (br. *d*, $J = 9.6$)	74.6	3.40 (*dd*, $J = 9.6, 2.4$)	69.8	3.20–3.27 (*m*)	71.8
H−C(2)	3.84 (br. *s*)	70.1	3.74 (*t*, $J = 2.4$)	73.0	3.69–3.75 (*m*)	72.6
H−C(3)	3.21 (br. *d*, $J = 9.6$)	71.4	3.19 (*dd*, $J = 9.6, 2.4$)	71.6	3.20–3.27 (*m*)	71.8
H−C(4)	3.40 (*t*, $J = 9.6$)	72.4	3.43 (*t*, $J = 9.6$)	72.8	3.55 (*ddd*, $J = 10.0, 10.0, 5.5$)	70.7
H−C(5)	3.00 (*t*, $J = 9.6$)	75.2	3.13 (*t*, $J = 9.6$)	75.3	4.64 (*t*, $J = 10.0$)	76.7
H−C(6)	3.64 (*t*, $J = 9.6$)	70.1	5.03 (*t*, $J = 9.6$)	75.3	3.55 (*ddd*, $J = 10.0, 10.0, 5.5$)	70.7
C(1′)		125.5		125.8		125.8
H−C(2′)	7.02 (*s*)	114.6	7.03 (*d*, $J = 1.7$)	115.3	7.03 (*s*)	114.7
C(3′)		145.7		145.6		145.6
C(4′)		148.6		148.2		148.2
H−C(5′)	6.75 (*d*, $J = 8.0$)	115.8	6.74 (*d*, $J = 8.2$)	115.8	6.73 (*d*, $J = 8.0$)	115.8
H−C(6′)	6.98 (*d*, $J = 8.0$)	121.3	6.97 (*dd*, $J = 8.2, 1.7$)	121.2	6.97 (*d*, $J = 8.0$)	121.2
H−C(7′)	7.49 (*d*, $J = 16.0$)	144.9	7.49 (*d*, $J = 15.8$)	144.3	7.40 (*d*, $J = 16.0$)	144.3
H−C(8′)	6.24 (*d*, $J = 16.0$)	114.5	6.23 (*d*, $J = 15.8$)	114.6	6.24 (*d*, $J = 16.0$)	115.3
C(9′)		166.5		166.4		166.2

[a]) ^{1}H-NMR Signals of the OH groups: 9.56 (*s*, OH−C(4′)); 9.18 (*s*, OH−C(3′)); 4.76 (*d*, $J = 5.5$, OH−C(4), OH−C(6)); 4.66 (overlapped, OH−C(2)); 4.60 (*d*, $J = 5.5$, OH−C(1), OH−C(3)).

Compounds **10** and **11** had the same molecular formula $C_{15}H_{18}O_9$ as compound **9**, as determined by HR-ESI-MS (neg.). Based on the MS and NMR spectra (*Table 3*), **10** and **11** also comprised a caffeoyl and a *myo*-inositol moiety. The differences concerned the linkage positions of the two fragments. The caffeoyl group was located at O−C(6) in **10** and at O−C(5) in **11** as shown by the HMBC spectra. Thus, compounds **10** and **11** were deduced as *myo*-inositol 6-caffeate and *myo*-inositol 5-caffeate, respectively.

Generally, hydroxy cinnamic acids including caffeic acid are esters bound to various alcohols, most frequently sugars [20]. However, only a few inositol hydroxycinnamates were reported. As far as known, *myo*-inositol *trans*- and *cis*-*p*-coumarates were isolated from two *Taxus* plants [21][22] and several *myo*-insitol ferulate derivatives were synthesized [23]. Compounds **10** and **11** represent the first examples of inositol caffeate derivatives.

Compound **12** was obtained as a colorless amorphous solid having the molecular formula $C_{19}H_{28}N_2O_8$ as determined by HR-ESI-MS ($[M+H]^+$ at m/z 413.1933). The IR spectrum of **12** showed absorptions for hydroxy (3439 cm^{-1}), carbonyl (1639 cm^{-1}), and aromatic (1630, 1547, and 1511 cm^{-1}) groups. The NMR spectra of **12** indicated the

presence of a β-glucopyranose, a caffeoyl, and a putrescine (= butane-1,4-diamine). Comparison of the NMR data of **12** with those of paucine (**13**) revealed that compound **12** is a glucoside of paucine [7]. The glucose was located at C(3′) according to the HMBC cross-peak H–C(1″)/C(3′). Therefore, compound **12** was elucidated as paucine 3′-β-D-glucopyranoside.

Compounds **7** and **11**, and N^1-*cis*-*p*-coumaroylagmatine (**14**) were tested for biological activity against the leukemia K562 cell line, and compound **12** and paucine against acetylcholinesterase (AChE). However, none of these compounds showed inhibitory effects up to the 200 μg/ml dose used.

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Experimental Part

General. Optical rotations: *Jasco-DIP-370* automatic digital polarimeter. UV Spectra: *Shimadzu-210A* double-beam spectrometer; λ_{max} (log ε) in nm. CD Spectra: *Jasco-J-715* spectropolarimeter; λ ($\Delta\varepsilon$) in nm. IR Spectra: *Bio-Rad-FTS-135* spectrophotometer; KBr pellets; in cm^{-1}. NMR Spectra: *Bruker-AM-400* and *-DRX-500* spectrometers; δ in ppm rel. to Me_4Si, *J* in Hz. FAB-MS: *VG-Autospec-3000* magnetic-sector instrument; glycerol as matrix in the negative-ion mode and 3-nitrobenzyl alcohol in the positive-ion mode; in *m*/*z*. ESI-MS and HR-ESI-MS: *API-Qstar-Pulsar-1* instrument; in *m*/*z*. Anal. TLC: precoated silica-gel-F_{254} plates (*Qingdao Meigao Chemical Co.*, Qingdao, P. R. China); detection by spraying with 5% H_2SO_4 in EtOH, followed by heating. Prep. TLC: silica gel F_{254} (*Qingdao Meigao Chemical Co.*). Column chromatography (CC): silica gel (200–300 mesh; *Qingdao Meigao Chemical Co.*), *C-18* silica gel (40–75 μm; *Fuji Silysia Chemical Ltd.*), D_{101} resin (*Qingdao Meigao Chemical Co.*), *Sephadex LH-20* (40–70 μm; *Amersham Pharmacia Biotech AB*, Uppsala, Sweden). HPLC: *Agilent-1200* chromatograph; semi-prep. column *Zorbax SB-C*$_{18}$ (9.4 × 250 mm, 5 μm).

Plant Material. *Selaginella moellendorffii* was collected from the Jingxi County of the Guangxi Zhuang Autonomous Region, P. R. China, in June 2008. The plant was identified by Dr. *Guang-Wan Hu* (Kunming Institute of Botany, Chinese Academy of Sciences), and a voucher specimen (No. JX0801) was deposited with the Laboratory of Ethnobotany, Kunming Institute of Botany.

Extraction and Isolation. The air-dried whole plants of *S. moellendorffii* (6 kg) were exhaustively extracted with MeOH (6 l; 4, 3, and 3 h, resp.) at 70°. The solvent was evaporated, and the remaining residue (780 g) was partitioned by CC (silica gel) into three fractions, with $CHCl_3$ (*A*, 32 g), Me_2CO (*B*, 154 g), and MeOH (*C*, 350 g). *Fraction C* was separated by CC (D_{101} resin) into *Fr. C*$_1$ with H_2O (270 g) and *Fr. C*$_2$ with MeOH (71 g). *Fr. C*$_2$ was fractionated by CC (*C18*, MeOH/H_2O 5:95 → 95:5): *Fr. C*$_{21}$ with 5% MeOH (18 g), *Fr. C*$_{22}$ with 10% MeOH (18 g), *Fr. C*$_{23}$ with 20% MeOH (11 g), *Fr. C*$_{24}$ with 30% MeOH (14 g), and *Fr. C*$_{25}$ with 50% MeOH (13 g). *Fr. C*$_{21}$ was subjected to CC (silica gel, $CHCl_3$/MeOH/HCOOH 90:30:1) and semi-prep. HPLC (MeOH/H_2O (containing 0.05% CF_3COOH) 10:90): **11** (29.0 mg; t_R 10.3 min), **10** (16.0 mg; t_R 12.4 min), and **9** (12.0 mg; t_R 18.3 min). *Fr. C*$_{22}$ was subjected to CC (silica gel, $CHCl_3$/MeOH/HCOOH 50:10:1, and $CHCl_3$/MeOH 1:1) and semi-prep. HPLC (MeOH/H_2O (containing 0.05% CF_3COOH) 20:80): **12** (17.4 mg; t_R 12.8 min) and **14** (11.0 mg; t_R 14.0 min). *Fr. C*$_{23}$ was subjected to CC (silica gel, $CHCl_3$/MeOH 1:1; *Sephadex LH-20*, MeOH: **13** (16.0 mg). *Fr. C*$_{24}$ was subjected to CC (silica gel, $CHCl_3$/MeOH/HCOOH 40:10:1; *Sephadex LH-20*, MeOH): **8** (7.0 mg; R_f 0.6) and **6** (6.2 mg; R_f 0.4), purified by prep. TLC ($CHCl_3$/MeOH/HCOOH, 40:10:1), and **5** (13.4 mg; R_f 0.6) and **7** (5.3 mg; R_f 0.7), purified by prep. TLC (AcOEt/MeOH 3: 1). *Fr. C*$_{25}$ was subjected to CC (silica gel, $CHCl_3$/MeOH 50:1, 20:1, 10:1, and 5:1; *Sephadex LH-20*, MeOH): **1** (23.0 mg), **4** (28.0 mg), **2** (3.5 mg), and **3** (9.0 mg).

(7S,8R)-4,9-Dihydroxy-3,3′,5-trimethoxy-4′,7-epoxy-8,5′-neolignan-9′-oic Acid Methyl Ester (= *(2S,3R)-2,3-Dihydro-2-(4-hydroxy-3,5-dimethoxyphenyl)-3-(hydroxymethyl)-7-methoxybenzofuran-5-propanoic Acid Methyl Ester*; **1**): Colorless amorphous solid. $[\alpha]_D^{26} = -4.4$ ($c = 0.36$, MeOH). UV (MeOH): 379 (3.07), 290 (3.52), 209 (4.45). CD ($c = 0.03$, MeOH): 282 (+0.13), 204 (+1.22). IR: 3441, 1731, 1616, 1519, 1500, 1462, 1213, 1143, 1113, 1033. ^{1}H- and ^{13}C-NMR: *Table 1*. FAB-MS (pos.): 419 ($[M+H]^+$). HR-ESI-MS (pos.): 441.1518 ($[M+Na]^+$, $C_{22}H_{26}NaO_8^+$; calc. 441.1525).

rel-*(7R,7′E,8S)-4,9-Dihydroxy-3,3′,5-trimethoxy-4′,7-epoxy-8,5′-neolign-7′-en-9′-oic Acid* (= rel-*(2E)-3-[(2R,3S)-2,3-Dihydro-2-(4-hydroxy-3,5-dimethoxyphenyl)-3-(hydroxymethyl)-7-methoxybenzofuran-5-yl]prop-2-enoic Acid*; **2**): Colorless amorphous solid. $[\alpha]_D^{25} = -48.0$ ($c = 0.083$, MeOH). UV (MeOH): 391 (3.03), 294 (3.63), 207 (4.21). CD ($c = 0.05$, MeOH): 302 (−0.52), 238 (+0.87), 217 (−1.26), 203 (+2.26). ^{1}H- and ^{13}C-NMR: *Table 1*. ESI-MS (neg.): 401 ($[M-H]^-$). HR-ESI-MS (neg.): 401.1236 ($[M-H]^-$, $C_{21}H_{21}O_8^-$; calc. 401.1236).

(7S,8R)-4,9-Dihydroxy-4′,7-epoxy-8′,9′-dinor-8,5′-neolignan-7′-oic Acid (= *(2S,3R)-2,3-Dihydro-3-(hydroxymethyl)-2-(4-hydroxyphenyl)benzofuran-5-carboxylic Acid*; **3**): Colorless amorphous solid. $[\alpha]_D^{26} = +96.3$ ($c = 0.52$, MeOH). UV (MeOH): 373 (2.96), 258 (3.82), 204 (4.27). CD ($c = 0.04$, MeOH): 260 (+7.54), 229 (−6.06), 203 (+6.76). IR: 3397, 1674, 1611, 1600, 1518, 1490, 1250, 1172, 1118, 833, 775. ^{1}H- and ^{13}C-NMR: *Table 1*. FAB-MS (neg.): 285 ($[M-H]^-$). HR-ESI-MS (neg.): 285.0754 ($[M-H]^-$, $C_{16}H_{13}O_5^-$; calc. 285.0762).

(7S,8R)-3,3′,5-Trimethoxy-4′,7-epoxy-8,5′-neolignan-4,9,9′-triol (= *(2S,3R)-2,3-Dihydro-2-(4-hydroxy-3,5-dimethoxyphenyl)-3-(hydroxymethyl)-7-methoxybenzofuran-5-propanol*; **4**): Colorless amorphous solid. $[\alpha]_D^{16} = -3.9$ ($c = 0.80$, MeOH). UV (MeOH): 284 (3.44), 208 (4.39). IR: 3425, 1613, 1518, 1499, 1462, 1214, 1142, 1115. ^{1}H- and ^{13}C-NMR: *Table 1*. ESI-MS (neg.): 425 ($[M+Cl]^-$). HR-ESI-MS (neg.): 425.1370 ($[M+Cl]^-$, $C_{21}H_{26}ClO_7^-$; calc. 425.1367).

rel-*(7R,8S)-3,3′,5-Trimethoxy-4′,7-epoxy-8,5′-neolignan-4,9,9′-triol 4-β-D-Glucopyranoside* (= *4-[(2S,3R)-2,3-Dihydro-3-(hydroxymethyl)-5-(3-hydroxypropyl)-7-methoxybenzofuran-2-yl]-2,6-dimethoxyphenyl β-D-Glucopyranoside*; **5**): Colorless amorphous solid. $[\alpha]_D^{16} = -33.0$ ($c = 0.67$, MeOH). UV (MeOH): 281 (3.39), 208 (4.60). CD ($c = 0.03$, MeCN): 206 (−1.89). IR: 3424, 1599, 1501, 1463, 1422, 1124, 1069. ^{1}H- and ^{13}C-NMR: *Table 2*. ESI-MS (neg.): 587 ($[M+Cl]^-$). HR-ESI-MS (neg.): 587.1883 ($[M+Cl]^-$, $C_{27}H_{36}ClO_{12}^-$; calc. 587.1895).

rel-*(7R,8S)-3,3′,5-Trimethoxy-4′,7-epoxy-8,5′-neolignan-4,9,9′-triol 9-β-D-Glucopyranoside* (= rel-*[(2R,3S)-2,3-Dihydro-2-(4-hydroxy-3,5-dimethoxyphenyl)-5-(3-hydroxypropyl)-7-methoxybenzofuran-3-yl]methyl β-D-Glucopyranoside*; **6**): Colorless amorphous solid. $[\alpha]_D^{26} = -19.3$ ($c = 0.20$, MeOH). UV (MeOH): 377 (3.00), 291 (3.52), 208 (4.26). CD ($c = 0.075$, MeOH): 310 (−0.28), 272 (−0.10), 246 (+0.30), 229 (−0.18), 206 (−0.75). IR: 3423, 2930, 1603, 1516, 1501, 1463, 1116, 1075, 1043. ^{1}H- and ^{13}C-NMR: *Table 2*. ESI-MS (neg.): 587 ($[M+Cl]^-$). HR-ESI-MS (neg.): 587.1881 ($[M+Cl]^-$, $C_{27}H_{36}ClO_{12}^-$; calc. 587.1895).

3,3′,5-Trimethoxy-4′,7-epoxy-8,5′-neolign-7-ene-4,9,9′-triol 9-β-D-Glucopyranoside (= *[2-(4-Hydroxy-3,5-dimethoxyphenyl)-5-(3-hydroxypropyl)-7-methoxybenzofuran-3-yl]methyl β-D-Glucopyranoside*; **7**): Colorless amorphous solid. $[\alpha]_D^{28} = -46.6$ ($c = 0.27$, MeOH). UV (MeOH): 307 (4.04), 219 (4.21), 204 (4.21). IR: 3421, 1614, 1516.6, 1462, 1219, 1110. ^{1}H- and ^{13}C-NMR: *Table 2*. FAB-MS (neg.): 549 ($[M-H]^-$). HR-ESI-MS (neg.): 549.1956 ($[M-H]^-$, $C_{27}H_{33}O_{12}^-$; calc. 549.1972).

3,3′,5,5′-Tetramethoxy-8,4′-oxyneolignan-4,9,9-triol 4-β-D-Glucopyranoside (= *4-{3-Hydroxy-2-[4-(3-hydroxypropyl)-2,6-dimethoxyphenoxy]propyl}-2,6-dimethoxyphenyl β-D-Glucopyranoside*; **8**): Colorless amorphous solid. $[\alpha]_D^{26} = -25.0$ ($c = 0.35$, MeOH). UV (MeOH): 269 (3.56), 207 (4.57). IR: 3419, 1594, 1504, 1462, 1422, 1243, 1226, 1125, 1067. ^{1}H- and ^{13}C-NMR: *Table 2*. FAB-MS (neg.): 583 ($[M-H]^-$). HR-ESI-MS (neg.): 619.2145 ($[M+Cl]^-$, $C_{28}H_{40}ClO_{13}^-$; calc. 619.2157).

myo-*Inositol 1-Caffeate* (= myo-*Inositol 1-[(2E)-3-(3,4-Dihydroxyphenyl)prop-2-enoate]*; **9**): Colorless amorphous solid. $[\alpha]_D^{26} = -6.4$ ($c = 0.14$, MeOH). UV (MeOH): 329 (3.96), 244 (3.78), 234 (3.78), 218 (3.94). IR: 3407, 1688, 1631, 1604, 1523, 1445, 1281, 1182, 1116, 1034. ^{1}H- and ^{13}C-NMR: *Table 3*. FAB-MS (neg.): 341 ($[M-H]^-$). HR-ESI-MS (neg.): 341.0878 ($[M-H]^-$, $C_{15}H_{17}O_9^-$; calc. 341.0872).

myo-*Inositol 6-Caffeate* (= myo-*Inositol 6-[(2E)-3-(3,4-Dihydroxyphenyl)prop-2-enoate]*; **10**): Colorless amorphous solid. $[\alpha]_D^{27} = -7.9$ ($c = 0.24$, MeOH). UV (MeOH): 327 (3.68), 297 (3.61), 206 (3.83).

IR: 3345, 1690, 1633, 1607, 1519, 1460, 1401, 1380, 1260, 1180, 1112, 1040. ^{1}H- and ^{13}C-NMR: *Table 3*. ESI-MS (neg.): 341 ($[M-H]^-$). HR-ESI-MS (neg.): 341.0874 ($[M-H]^-$, $C_{15}H_{17}O_9^-$; calc. 341.0872).

myo-*Inositol 5-Caffeate* (= myo-*Inositol 5-[(2*E*)-3-(3,4-Dihydroxyphenyl)prop-2-enoate]*; **11**): Colorless amorphous solid. UV (MeOH): 327 (3.75), 300 (3.66), 216 (3.79). IR: 3372, 1688, 1632, 1598, 1528, 1445, 1116, 1042, 718. ^{1}H- and ^{13}C-NMR: *Table 3*. ESI-MS (neg.): 341 ($[M-H]^-$). HR-ESI-MS (neg.): 341.0879 ($[M-H]^-$, $C_{15}H_{17}O_9^-$; calc. 341.0872).

*Paucine 3′-β-*D*-Glucopyranoside* (= N-*(4-Aminobutyl)caffeamide 3′-β-*D*-Glucopyranoside* = *(2*E*)*-N-*(4-Aminobutyl)-3-[3-(β-*D*-glucopyranosyloxy)-4-hydroxyphenyl]prop-2-enamide*; **12**): Colorless amorphous solid. $[\alpha]_D^{26} = -23.3$ ($c = 0.35$, MeOH). UV (MeOH): 387 (2.18), 373 (2.30), 312 (3.64), 293 (3.61), 230 (3.60), 216 (3.62). IR: 3439, 1639, 1630, 1547, 1511, 1250, 1173, 1033. ^{1}H-NMR (CD_3OD, 500 MHz): 3.33 (*t*, $J = 7.1$, $CH_2CH_2CH_2CH_2NCO$), 1.66 – 1.73 (*m*, $CH_2CH_2CH_2CH_2NCO$), 1.60 – 1.66 (*m*, $CH_2CH_2CH_2CH_2NCO$), 2.96 (*t*, $J = 6.6$, $CH_2CH_2CH_2CH_2NCO$), 7.46 (*s*, H–C(2′)); 6.84 (*d*, $J = 8.0$, H–C(5′)); 7.12 (*d*, $J = 8.0$, H–C(6′)); 7.43 (*d*, $J = 16.0$, H–C(3)); 6.41 (*d*, $J = 16.0$, H–C(2)); 4.80 (*d*, $J = 7.7$, H–C(1″)); 3.47 – 3.54 (*m*, H–(2″)); 3.46 – 3.52 (*m*, H–C(3″)); 3.38 (*t*, $J = 9.0$, H–C(4″)); 3.43 – 3.50 (*m*, H–C(5″)); 3.94 (*d*, $J = 11.5$, H_a–C(6″)); 3.71 (*dd*, $J = 11.5$, 6.0, H_b–C(6″)). ^{13}C-NMR (CD_3OD, 125 MHz): 39.6 (*t*, C(1) (Bu)); 25.9 (*t*, C(2) (Bu)); 27.6 (*t*, C(3) (Bu)); 40.4 (*t*, C(4) (Bu)); 128.4 (*s*, C(1′)); 117.4 (*d*, C(2′)); 147.1 (*s*, C(3′)); 150.4 (*s*, C(4′)); 117.4 (*d*, C(5′)); 125.7 (*d*, C(6′)); 141.9 (*d*, C(3)); 119.0 (*d*, C(2)); 169.3 (*s*, C(1)); 104.2 (*d*, C(1″)); 74.9 (*d*, C(2″)); 77.6 (*d*, C(3″)); 71.5 (*d*, C(4″)); 78.5 (*d*, C(5″)); 62.6 (*t*, C(6″)). ESI-MS (pos.): 413 ($[M+H]^+$). HR-ESI-MS (pos.): 413.1933 ($[M+H]^+$, $C_{19}H_{29}N_2O_8^+$; calc. 413.1923).

Acid Hydrolysis of **5**. Compound **5** (5 mg) was dissolved in 2N HCl (2 ml) and hydrolyzed (4 h) at 90°. The acidic soln. was concentrated, and the residue separated by CC (silica gel, $CHCl_3$/MeOH/H_2O 40 : 10 : 0.5): 0.8 mg of D-glucose, detected by TLC and optical rotation. $[\alpha]_D^{22} = +28.2$ ($c = 0.08$, H_2O).

Biological Testing. The activity of compounds **7** and **11**, and *N*^{1}-*cis-p*-coumaroylagmatine (**14**) against K562 cells were measured by the MTT method with adriamycin as pos. control ($IC_{50} = 0.32$ μM) [24], and that of compound **12** and paucine (**13**) against AChE was assessed by *Ellman*'s method with tacrine as pos. control ($IC_{50} = 0.20$ μM) [25], resp.

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