Lignanamides and Sesquiterpenoids from Stems of *Mitrephora thorelii*

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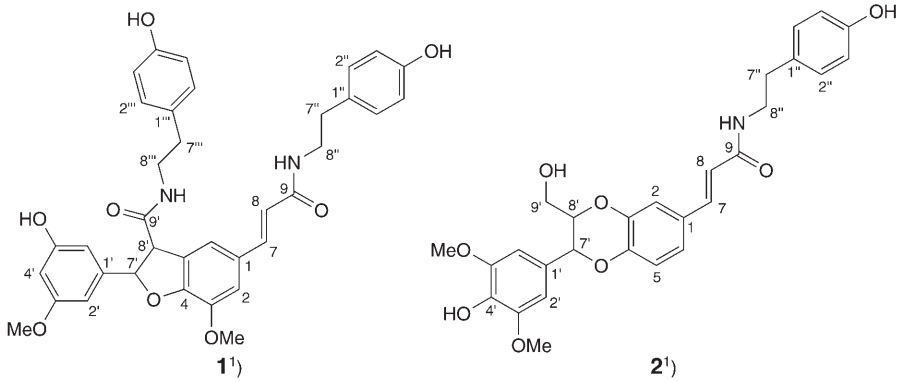
The first phytochemical investigation on stems of *Mitrephora thorelii* led to the isolation of three new lignanamides, thoreliamides A–C (**1**–**3**), and a new sesquiterpenoid, thorelinin (**4**), together with ten known compounds. The structures of the new compounds were established on the basis of extensive spectroscopic analyses. Thoreliamide C is the first trimer derived from cinnamic acid amide units.

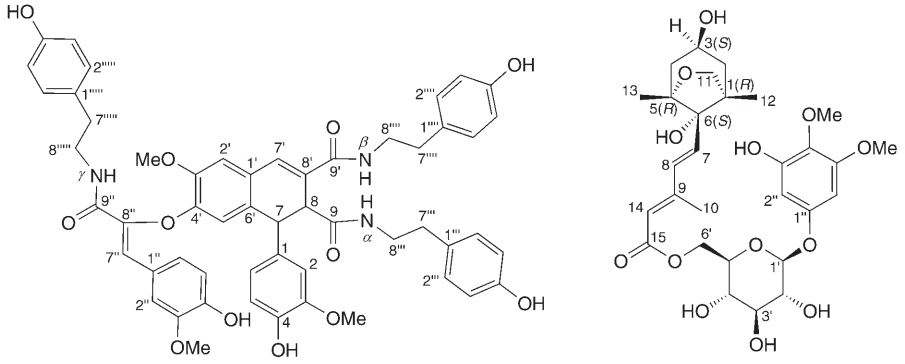
Introduction. – The genus *Mitrephora* (Annonaceae), including *ca.* 40 species, is distributed widely throughout tropical areas in Asia. Some plants of this genus have been used as a tonic traditional medicine in Thailand [1]. So far, five species, *i.e.*, *M. celebica* [2], *M. maingayi* [3], *M. tomentosa* [4], *M. glabra* [5], and *M. zippeliana* [6] have been investigated. Alkaloids from *M. maingayi* possessing an unprecedented skeleton and diterpenoids from *M. glabra* bearing a novel skeleton have been successively reported. The potent and broad anticancer activity of the diterpenoids attracted us to further investigate another species of this genus, *Mitrephora thorelii* PIERRE, distributed in southwest China.

Our first phytochemical study reported here led to the isolation and characterization of three new lignanamides, thoreliamides A–C (**1**–**3**, resp.), and a new sesquiterpene, thorelinin (**4**), along with ten known compounds, liriodenine, oxoputerine, *N-trans*-sinapoyltyramine, *N-trans*-feruloyltyramine, *N-trans*-caffeoyltyramine [7], *N-trans*-feruloyldopamine, *N-trans*-feruloyl-3-methyldopamine [8], *N-p*-coumaroyltyramine [9], cannabisin G, and cannabisin F [10] from stems of *M. thorelii*. Thoreliamide C (**3**) is the first cinnamic acid amide trimer reported from the plant kingdom. The structure elucidation of **1**–**4** was accomplished on the basis of spectroscopic data, especially 2D-NMR.

Results and Discussion. – Thoreliamide A (**1**) was obtained as an optically inactive, colorless amorphous powder. The IR spectrum showed absorptions for OH (3345 cm^{-1}) and conjugated C=O (1654 cm^{-1}) groups. The molecular ion $[M+Na]^+$ at *m/z* 647.2397 in the HR-ESI-MS suggested a molecular formula of $C_{36}H_{36}N_2O_8$, which is consistent with that of an *N-trans*-feruloyltyramine dimer. Compound **1** was found to be closely related to a known compound, grossamide, by comparing their NMR data [11][12]. The ^{13}C-NMR data of **1** and grossamide strongly resembled each other. The ^{1}H-NMR spectrum of **1** (see *Table 1*), combined with the ^{1}H,^{1}H-COSY spectrum, displayed signals for two tyramine moieties (two $N-CH_2CH_2$ groups:



1[1]) **2**[1])



3[1]) **4**[1])

2.75 (*t*, *J* = 7.3), 3.56 (*t*, *J* = 7.3), 2.68–2.73 (*m*), 2.77–2.83 (*m*), 3.33–3.39 (*m*), 3.62–3.68 (*m*); two *para*-substituted Ph groups (7.05 (*d*, *J* = 8.3, 2 H), 6.78 (*d*, *J* = 8.3, 2 H), 7.03 (*d*, *J* = 8.3, 2 H), 6.74 (*d*, *J* = 8.3, 2 H)), two MeO groups (3.82, 3.78), one *trans* C=C bond (7.42 (*d*, *J* = 15.6), 6.48 (*d*, *J* = 15.6)), and characteristic signals of a benzofuran-type lignan (6.01 (*d*, *J* = 8.4), 4.18 (*d*, *J* = 8.4)). All these data were similar to the corresponding values of grossamide. The major differences were found in the aromatic region. Five *singlet*s (δ(H) 7.08, 6.98, 6.80, 6.80, and 6.58) instead of the *ABX* system and two *singlet*s of grossamide were observed, suggesting the presence of a 1,3,5-trisubstituted and a 1,3,4,5-tetrasubstituted Ph group each in the molecule of **1**. HMBC Correlations of CH_2(8″)/C(9)[1]) and CH_2(8‴)/C(9′) suggested the attachment of the two tyramine moieties to C(9) and C(9′) *via* amide bonds, respectively. Accordingly, the structure of **1** was constructed and further confirmed by the combined analyses of ROESY, HSQC, and HMBC data (*Fig.*). The optical inactivity of **1** suggested that it was racemic. The relative configuration at C(7′) and C(8′) was established as *cis*

[1]) Arbitrary numbering. For systematic names, see *Exper. Part*.

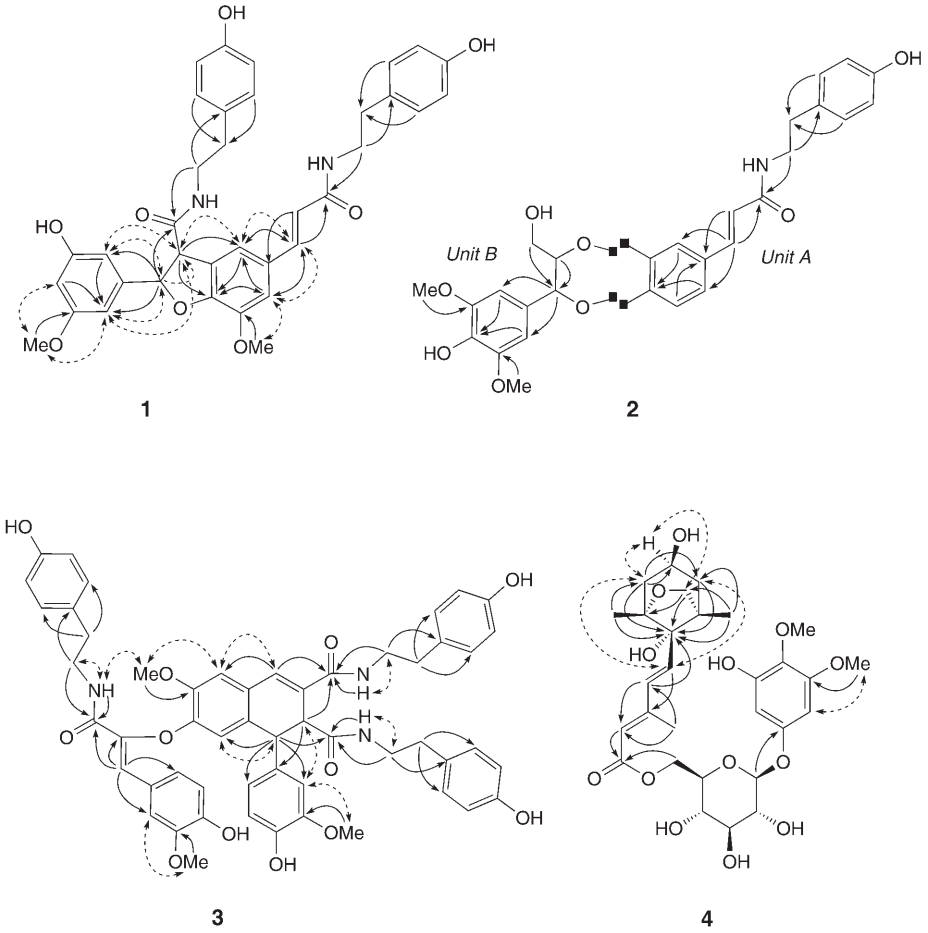


Figure. *Key HMBC* (→) *and ROESY* (←- - -→) *correlations for* **1**–**4**

(racemate) on the basis of the coupling constant (8.4 Hz) for H–C(7′) and H–C(8′) [13].

Thoreliamide B (**2**) was obtained as an optically inactive, colorless amorphous powder. On the basis of HR-ESI-MS analysis (*m*/*z* 508.1989 $[M + H]^+$; calc. 508.1971), its molecular formula was established as $C_{28}H_{29}NO_8$ with 15 degrees of unsaturation. The IR absorptions at 3386, 1656, 1612, and 1515 cm^{-1} showed the existence of OH, conjugated C=O, and olefinic functional groups. The ^{1}H-NMR and ^{1}H,^{1}H-COSY spectra (see *Table 1*) showed the presence of one $NHCH_2CH_2$ moiety (2.74 (*t*, *J* = 7.1), 3.45–3.51 (*m*), 7.21 (br. *s*, NH)), one *trans* C=C bond (7.43 (*d*, *J* = 15.6), 6.52 (*d*, *J* = 15.6)), one *p*-substituted Ph group (7.05 (*d*, *J* = 8.3, 2 H), 6.75 (*d*, *J* = 8.3, 2 H)), and one 1,3,4-trisubstituted aromatic ring (7.11 (*d*, *J* = 2.1), 7.07 (*dd*, *J* = 8.3, 2.1), 6.90 (*d*, *J* = 8.3)). The above data suggested the presence of a caffeoyltyramine-like unit, which was constructed as *Unit A* by analysis of HSQC and HMBC data (*Fig.*). The remaining

Table 1. *^{1}H- and ^{13}C-NMR Data for Compounds* **1**, **2**, *and* **4** (δ in ppm, J in Hz)[1])

	1			**2**			**4**	
	δ(H)[a])[b])	δ(C)[a])[c])		δ(H)[a])[b])	δ(C)[a])[c])		δ(H)[b])[d])	δ(C)[c])[d])
C(1)		129.3	C(1)		129.9	C(1)		49.9
H–C(2)	7.08 (br. *s*)	111.2	H–C(2)	7.11 (*d*, *J* = 2.1)	116.6	CH_2(2)	1.61–1.68 (*m*), 1.85 (*dd*, *J* = 6.8, 13.6)	45.0
C(3)		145.2	C(3)		144.8	H–C(3)	4.06–4.16 (*m*)	66.5
C(4)		150.2	C(4)		146.2	CH_2(4)	1.72 (*dd*, *J* = 10.0, 13.6), 2.03 (*ddd*, *J* = 1.2, 6.8, 13.6)	46.5
C(5)		128.9	H–C(5)	6.90 (*d*, *J* = 8.3)	118.1	C(5)		88.3
H–C(6)	6.58 (br. *s*)	118.5	H–C(6)	7.07 (*dd*, *J* = 8.3, 2.1)	121.7	C(6)		83.8
H–C(7)	7.42 (*d*, *J* = 15.6)	140.8	H–C(7)	7.43 (*d*, *J* = 15.6)	139.7	H–C(7)	6.55 (*d*, *J* = 16.2)	136.3
H–C(8)	6.48 (*d*, *J* = 15.6)	119.1	H–C(8)	6.52 (*d*, *J* = 15.6)	121.1	H–C(8)	7.99 (*d*, *J* = 16.2)	132.2
C(9)		167.0	C(9)		166.1	C(9)		152.9
C(1′)		132.2	C(1′)		127.9	Me(10)	2.10 (*s*)	21.7
H–C(2′)	6.98 (br. *s*)	110.4	H–C(2′)	6.81 (br. *s*)	106.2	CH_2(11)	3.70, 3.80 (overlapped)	77.8
C(3′)		150.2	C(3′)		148.8	Me(12)	0.92 (*s*)	16.9
H–C(4′)	6.80 (br. *s*)	115.5	C(4′)		137.5	Me(13)	1.12 (*s*)	20.1
C(5′)		147.4	C(5′)		148.8	CH(14)	5.85 (*s*)	118.8
H–C(6′)	6.80 (br. *s*)	119.5	H–C(6′)	6.81 (br. *s*)	106.2	C(15)		167.9
H–C(7′)	6.01 (*d*, *J* = 8.4)	88.6	H–C(7′)	4.98 (*d*, *J* = 8.0)	77.7	H–C(1′)	4.76 (*d*, *J* = 7.2)	103.4
H–C(8′)	4.18 (*d*, *J* = 8.4)	57.3	H–C(8′)	4.10–4.16 (*m*)	79.5	H–C(2′)	3.43 (*d*, *J* = 9.3)	75.3
C(9′)		170.1	CH_2(9′)	3.50–3.56 (*m*), 3.70–3.76 (*m*)	61.8	H–C(3′)	3.45 (*d*, *J* = 9.3)	78.4
3-OMe	3.82 (*s*)	56.1	3′-OMe	3.84 (*s*)	56.7	H–C(4′)	3.39 (*d*, *J* = 9.3)	72.3
3′-OMe	3.78 (*s*)	56.0	5′-OMe	3.84 (*s*)	56.7	H–C(5′)	3.63–3.68 (*m*)	76.0
C(1″)		130.4	C(1″)		131.2	CH_2(6′)	4.28 (*dd*, *J* = 7.2, 12.0), 4.48 (*dd*, *J* = 2.0, 12.0)	64.8
H–C(2″)	7.05 (*d*, *J* = 8.3)	130.2	H–C(2″)	7.05 (*d*, *J* = 8.3)	130.5	C(1″)		156.2
H–C(3″)	6.78 (*d*, *J* = 8.3)	116.2	H–C(3″)	6.75 (*d*, *J* = 8.3)	116.1	H–C(2″)	6.27 (*s*)	99.4
C(4″)		156.5	C(4″)		156.7	C(3″)		152.4
H–C(5″)	6.78 (*d*, *J* = 8.3)	116.2	H–C(5″)	6.75 (*d*, *J* = 8.3)	116.1	C(4″)		133.8
H–C(6″)	7.05 (*d*, *J* = 8.3)	130.2	H–C(6″)	7.05 (*d*, *J* = 8.3)	130.5	C(5″)		155.3
CH_2(7″)	2.75 (*t*, *J* = 7.3)	35.2	CH_2(7″)	2.74 (*t*, *J* = 7.1)	35.7	H–C(6″)	6.27 (*s*)	95.5
CH_2(8″)	3.56 (*t*, *J* = 7.3)	41.7	CH_2(8″)	3.45–3.51 (*m*)	41.9	4″-OMe	3.72 (*s*)	61.7
C(1‴)		130.4	NH	7.21 (br. *s*)		5″-OMe	3.79 (*s*)	56.9
H–C(2‴)	7.03 (*d*, *J* = 8.3)	130.3						
H–C(3‴)	6.74 (*d*, *J* = 8.3)	115.7						
C(4‴)		156.4						
H–C(5‴)	6.74 (*d*, *J* = 8.3)	115.7						
H–C(6‴)	7.03 (*d*, *J* = 8.3)	130.3						
CH_2(7‴)	2.68–2.73 (*m*), 2.77–2.83 (*m*)	34.2						
CH_2(8‴)	3.33–3.39 (*m*), 3.62–3.68 (*m*)	41.2						

[a]) Measured in (D_6)DMSO. [b]) Measured at 600 MHz. [c]) Measured at 150 MHz. [d]) Measured in CD_3OD.

^{1}H-NMR signals, corresponding to two aromatic H-atoms (6.81 (*s*)), two MeO groups (3.84 (*s*)), and one CH(O)–CH(O)–CH_2(O) moiety (4.98 (*d*, *J* = 8.0), 4.10–4.16 (*m*), 3.70–3.76 (*m*), 3.50–3.56 (*m*)), were assigned by ^{1}H,^{1}H-COSY and HMQC. These signals, together with HMBC correlations of H–C(2′,6′)/C(4′)[1]) and MeO/C(3′,5′), completed a symmetrical 1,3,4,5-tetrasubstituted aromatic ring with MeO groups attached to C(3) and C(5). HMBC Correlations of H–C(7′)/C(1), H–C(8′)/C(1′), and H–C(7′)/C(2′,6′) indicated that the CH(O)–CH(O)–CH_2(O) moiety was connected to C(1′) of the tetrasubstituted aromatic ring. Thus, a phenylpropanoid unit, *Unit B*, was established (*Fig.*). Since *Units A* and *B* accounted for 14 degrees of unsaturation of the molecule, the remaining degree of unsaturation suggested a dioxane ring between these two units. This dioxane moiety was verified by close similarities of its NMR data with those of americanol A, a typical benzodioxane type lignan [14]. This connection was further confirmed by the long range selective proton decoupling method (LSPD). The selective irradiation at H–C(8′) and H–C(7′) led to the sharpness of the C-atom signals of C(4) and C(3), respectively. The *trans* orientation for H–C(7′) and H–C(8′) on the 1,4-dioxane ring was evident from the *J*(7′,8′) value (8.0 Hz). Moreover, in view of the optical inactivity, the presence of racemic **2** was assumed.

Thoreliamide C (**3**) was obtained as a colorless amorphous powder. Its IR absorptions (3380, 1654, 1612 and 1515 cm^{-1}) indicated that it contained similar *N-trans*-feruloyltyramine units in the molecule. The molecular ion $[M+Na]^+$ at *m*/*z* 958.3582 in HR-ESI-MS suggested a molecular formula $C_{54}H_{53}N_3O_{12}$, consistent with that of an *N-trans*-feruloyltyramine trimer. Comparison of the NMR data of **3** and cannabisin D [15] revealed a cannabasin D-like unit in this molecule. Partial NMR data of **3** (*Table 2*) resembled strongly those of cannabisin D, such as H-atom signals of two HN–CH_2CH_2 groups (δ(H) 2.68 (*t*, *J* = 7.3), 3.38 (*t*, *J* = 7.3), 7.58 (br. *s*, NH), 2.52 (*t*, *J* = 7.1), 3.16–3.21 (*m*), 3.25–3.30 (*m*), 7.66 (br. *s*, NH), two *p*-substituted Ph groups (6.66 (*d*, *J* = 8.5, 2 H), 6.88 (*d*, *J* = 8.5, 2 H), 6.71 (*d*, *J* = 8.5, 2 H), 6.98 (*d*, *J* = 8.5, 2 H)), two MeO groups (3.57 and 3.88), and other H-atom signals (6.97 (*s*), 6.58 (*s*), 7.26 (*s*), 6.10 (*dd*, *J* = 8.1, 2.0), 6.45 (*d*, *J* = 8.1), 6.58 (*d*, *J* = 2.0), 4.33 (br. *s*), 3.73 (*d*, *J* = 1.8)) as well as the corresponding C-atom signals. The remaining signals, ascribed to a tyramine moiety (one HN–CH_2CH_2 group: δ(H) 2.52–2.55 (*m*), 2.61–2.66 (*m*), 3.31–3.36 (*m*), 3.45–3.50 (*m*), 7.12 (br. *s*, NH); two *p*-substituted Ph groups (6.61 (*d*, *J* = 8.3, 2 H), 6.80 (*d*, *J* = 8.3, 2 H)), one MeO group (3.58 (*s*)), an *ABX* system (6.69 (*d*, *J* = 8.5), 7.00 (*dd*, *J* = 8.5, 1.9), 7.18 (*d*, *J* = 1.9)), and a single H-atom (7.16), suggested an 8-*O*-substituted[1]) *N-trans*-feruloyltyramine moiety as in cannabisin F [10]. These two moieties were deduced to be connected by C(8″) and C(4′) *via* an O-atom. This elucidation was supported by the ROESY correlations of H–N(γ) (δ(H) 7.12 (br. *s*))/MeO–C(3′) (3.88 (*s*)), MeO–C(3′)/H–C(2′) and H–C(2′)/H–C(7′), as well as the down-field chemical shift of C(8″) (δ(C) 141.8). This 8-*O*-4 linkage is common in dimers of this type as demonstrated in literature [16]. According to *Lajide et al.* [12], the relative configuration of H–C(8) and H–C(7) was determined to be *trans*, since the *J*(7,8) value (1.8 Hz) was close to zero, which was consistent with that of rabdosiin (1.5 Hz) and thomasic acid dimethyl ester (1.0 Hz) [17]. Therefore, the structure of **3** was fully established.

Thorelinin (**4**) was obtained as a colorless amorphous powder. Its molecular ion $[M+Na]^+$ in HR-ESI-MS was consistent with the molecular formula $C_{29}H_{40}O_{13}$. IR

Table 2. *^{1}H- and ^{13}C-NMR Data for Compound* **3** *in (D_6)Acetone at 600 and 150 MHz, resp.* (δ in ppm, J in Hz)[1])

	δ(H)	δ(C)		δ(H)	δ(C))		δ(H)	δ(C)
C(1)		135.6	C(1′)		127.3	C(1″)		124.9
H–C(2)	6.58 (*d*, *J* = 2.0)	111.4	C(2′)	6.97 (*s*)	112.9	H–C(2″)	7.18 (*d*, *J* = 1.7)	113.2
C(3)		147.6	C(3′)		148.5	C(3″)		147.8
C(4)		145.4	C(4′)		146.3	C(4″)		148.5
H–C(5)	6.45 (*d*, *J* = 8.1)	115.0	H–C(5′)	6.58 (*s*)	115.8	C(5″)	6.69 (*d*, *J* = 8.5)	115.5
H–C(6)	6.10 (*dd*, *J* = 8.1, 2.0)	120.0	C(6′)		131.8	H–C(6″)	7.00 (*dd*, *J* = 8.5, 1.9)	125.1
H–C(7)	4.33 (br. *s*)	45.3	H–C(7′)	7.26 (*s*)	131.8	H–C(7″)	7.16 (*s*)	123.5
H–C(8)	3.73 (*d*, *J* = 1.8)	48.8	C(8′)		129.2	H–C(8″)		141.8
C(9)		171.7	C(9′)		168.6	C(9″)		163.3
3-OMe	3.57 (*s*)	55.5	3′-OMe	3.88 (*s*)	56.0	3″-OMe	3.58 (*s*)	55.7
C(1‴)		130.4	C(1⁗)		130.6	C(1⁗′)		129.9
H–C(2‴)	6.88 (*d*, *J* = 8.5)	130.2	H–C(2⁗)	6.98 (*d*, *J* = 8.5)	130.1	H–C(2⁗′)	6.80 (*d*, *J* = 8.3)	130.2
H–C(3‴)	6.66 (*d*, *J* = 8.5)	115.6	H–C(3⁗)	6.71 (*d*, *J* = 8.5)	115.6	H–C(3⁗′)	6.61 (*d*, *J* = 8.3)	115.7
C(4‴)		156.3	C(4⁗)		156.3	C(4⁗′)		156.3
H–C(5‴)	6.66 (*d*, *J* = 8.5)	115.6	H–C(5⁗)	6.71 (*d*, *J* = 8.5)	115.6	H–C(5⁗′)	6.61 (*d*, *J* = 8.3)	115.7
H–C(6‴)	6.88 (*d*, *J* = 8.5)	130.2	H–C(6⁗)	6.98 (*d*, *J* = 8.5)	130.1	H–C(6⁗′)	6.80 (*d*, *J* = 8.3)	130.2
CH_2(7‴)	2.52 (*t*, *J* = 7.1)	34.9	CH_2(7⁗)	2.68 (*t*, *J* = 7.3)	35.1	CH_2(7⁗′)	2.52–2.55 (*m*), 2.61–2.66 (*m*)	34.7
CH_2(8‴)	3.16–3.21 (*m*), 3.25–3.30 (*m*)	41.3	CH_2(8⁗)	3.38 (*t*, *J* = 7.3)	41.9	CH_2(8⁗′)	3.31–3.36 (*m*), 3.45–3.50 (*m*)	41.2
NH(α)	7.66 (br. *s*)		NH(β)	7.58 (br. *s*)		NH(γ)	7.12 (br. *s*)	

absorptions at 3415, 1700, 1600 and 1506 cm^{-1} showed the existence of OH, CO, and Ph groups. The ^{1}H-NMR spectrum displayed signals of a β-glucose unit (4.76 (*d*, *J* = 7.2), 3.43 (*d*, *J* = 9.3), 3.45 (*d*, *J* = 9.3), 3.39 (*d*, *J* = 9.3), 3.63–3.68 (*m*), 4.28 (*dd*, *J* = 7.2, 12.0), 4.48 (*dd*, *J* = 2.0, 12.0)), three Me groups (0.92 (*s*), 1.12 (*s*), 2.10 (*s*)), two MeO groups (3.72 (*s*), 3.79 (*s*)), one (*E*)-C=C bond (6.55 (*d*, *J* = 16.2 Hz), 7.99 (*d*, *J* = 16.2)), three aromatic *singlet*s (5.85, 6.27 × 2), and high-field H-atoms at 4.06–4.16 (*m*), 3.70, 3.80 (overlaped by MeO groups), 2.03 (*ddd*, *J* = 1.2, 6.8, 13.6), 1.85 (*dd*, *J* = 6.8, 13.6), 1.72 (*dd*, *J* = 10.0, 13.6), and 1.61–1.68 (*m*). The above data were in good agreement with those of dihydrophaseic acid [18], except for a β-glucose unit, as well as two MeO groups and two aromatic H-atoms at δ(H) 6.27. These MeO and aromatic resonances, together with the corresponding C-atom signals[1]) at 156.2 (C(1″)), 99.4 (C(2″)), 152.4 (C(3″)), 133.8 (C(4″)), 155.3 (C(5″)), and 95.5 (C(6″)), revealed the presence of a 1,3,4,5-tetrasubstituted benzene ring. HMBC Correlations from the anomeric H-atom to C(1″) indicated a 1′-*O*-1″ linkage between the sugar moiety and the benzene ring. The correlation of H–C(6′)/C(15) suggested that the carboxy group of the dihydrophaseic acid moiety was connected to C(6′) of the sugar unit by an ester bond. The two MeO groups (δ(H) 3.72 and 3.79) were connected to C(4″) and C(5″), respectively, as shown by HMBC and ROESY experiments. As dihydrophaseic acid is regarded as a metabolite of abscisic acid, a plant growth hormone, the absolute configurations of C(1), C(5), and C(6) were deduced to be (*R*), (*R*), and (*S*), respectively, by biogenetic consideration [19]. Furthermore, a ROESY correlation of CH_2(11)/H–C(3) indicated an (*S*)-configuration for C(3). Thus, the structure of **4** was fully established.

In conclusion, the major new isolated compounds in this study are cinnamic acid amide derivatives, except for the new triterpenoid **4** and two aporphine alkaloids, liriodenine and oxoputerine. The aporphine alkaloids were previously reported from *Mitrephora* genus [7], the existence of cinnamic acid amide derivatives in this genus is reported here for the first time. It is known from the literature that the dimerization of cinnamic acid amides is a common phenomenon in higher plants [8][10][12][13][15]. For example, grossamide and cannabisin G and F are all dimerized from two cinnamic acid amides possessing coupling sites at 8–8, 8–5, and 8-*O*-4, respectively. The dimers from *M. thorelii* exhibited the same dimerization patterns with the reported ones. Furthermore, thoreliamide C (**3**) was the first cinnamic acid amide trimer found in the plant kingdom, whereas the coupling patterns among its three structural units were consistent with those in dimers. The occurrence of **3** suggested the possibility of further polymerization of cinnamic acid amides in plants.

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Experimental Part

General. TLC: Precoated silica gel GF_{254} plates (*Yan Tai Chemical Industry*). Column chromatography (CC): commercial SiO_2 (200–300 and 300–400 mesh, *Qing Dao Hai Yang Chemical Group Co.*). Prep. HPLC: *PrepStar SD-1* solvent delivery modules, a *ProStar UV-VIS 320* detector and a *ProStar 701* Fraction Collector (all from *Varian*, Walnut Creek, CA, USA); *LinChrospher 100 RP-18* (*Merck*, Darmstadt, Germany) column (25 × 220 mm; 12 μm). Optical rotation: *Perkin-Elmer 341* polarimeter. UV Spectra: *Hewlett-Packard 8452A* diode-array spectrophotometer; λ_{max} in nm (log ε). IR Spectra: *Nicolet Magna-FT-IR-750* spectrometer; ν_{max} in cm^{-1}. ^1H- and ^{13}C-NMR Spectra: *Bruker AM-400* and *INVOR-600* NMR spectrometers; chemical shifts, δ in ppm, with residual MeOH (δ(H) 3.30, δ(C) 49.0) or DMSO (δ(H) 2.05, δ(C) 29.92) as internal standard, coupling constant *J* in Hz, assignments supported by ^1H,^1H-COSY, HSQC, HMBC, and ROESY experiments. EI: *Finnigan MAT-95* mass spectrophotometer; in *m*/*z*. ESI- and HR-ESI-MS: *Micromass LC-MS-MS* apparatus; in *m*/*z*.

Plant Material. The fresh stems of *M. thorelii* were collected in Nanning, Guangxi Province, China, in October 2005, and identified by Prof. *Jin-gui Shen* of the Shanghai Institute of Materia Medica, Chinese Academy of Sciences. A voucher specimen (2005007) is deposited in the Herbarium of the Institute.

Extraction and Isolation. The air-dried and powdered stems of *M. thorelii* (8.5 kg) were percolated with 95% EtOH (3 × 35 l) at r.t. for 10 d. The EtOH extract was filtered and concentrated under reduced pressure. Then, the concentrated extract (360 g) was suspended in MeOH/H_2O (1:5, *v*/*v*, 1.5 l) and partitioned successively with petroleum ether (PE) (60–90°), $CHCl_3$, AcOEt, and BuOH (each 3 × 1 l). The AcOEt fraction (45 g) was fractionated by CC (SiO_2, PE/AcOEt/MeOH 10:1:0 to 0:1:0 to 0:0:1) to give four fractions (*Fr. A*–*Fr. D*). *Fr. B* (7.0 g) was separated by CC (SiO_2, $CHCl_3$/MeOH 100:1 to 0:1) to give six fractions (*Fr. B1*–*Fr. B6*). *Fr. B2* (724 mg) was submitted to CC (*Sephadex LH-20*, $CHCl_3$/MeOH 1:1) to afford **1** (380 mg). *Fr. B4* (463 mg) was separated by CC (SiO_2, $CHCl_3$/MeOH 50 to 0:1) to give four fractions (*Fr. B4a*–*Fr. B4d*). *Fr. B4a* (126 mg) was purified by prep. HPLC (MeCN/H_2O 30–70%) and then CC (*Sephadex LH-20*) to afford **2** (9 mg). *Fr. B5* (724 mg) was separated by CC (*Sephadex LH-20*, $CHCl_3$/MeOH 1:1) to give three fractions (*Fr. B5a*–*Fr. B5c*). *Fr. B5a* (126 mg) was purified by prep. HPLC (MeCN/H_2O gradient 70:30 to 30:70) and then CC (*Sephadex LH-20*) to afford **3** (3 mg). *Fr. C* (126 mg) was separated by prep. HPLC (MeCN/H_2O 80:20 to 50:50) to give two fractions. *Fr. C1* (50 mg) was subjected repeatedly to CC (*Sephadex LH-20*, MeOH) to afford **4** (18 mg).

Thoreliamide A (= rac-*(2*R,*3*S*)-2,3-Dihydro-2-(3-hydroxy-5-methoxyphenyl)*-N-*[2-(4-hydroxyphenyl)ethyl]-5-((1*E*)-3-{[2-(4-hydroxyphenyl)ethyl]amino}-3-oxoprop-1-en-1-yl)-7-methoxybenzofuran-3-carboxamide*; **1**). Colorless amorphous powder. UV (MeOH): 225.0 (4.67), 286.5 (4.39), 321.5 (4.41). IR

(KBr): 3345, 2935, 1654, 1612, 1515, 1270, 1147, 1031, 823. ^{1}H- and ^{13}C-NMR: *Table 1*. EI-MS: 624 (M^+), 487 (50), 367 (75), 351 (96), 350 (100), 137 (32), 120 (48). HR-ESI-MS: 647.2397 ($[M+Na]^+$, $C_{36}H_{36}N_2NaO_8^+$; calc. 647.2369).

Thoreliamide B (=*(2*E*)-3-[2,3-Dihydro-2-(4-hydroxy-3,5-dimethoxyphenyl)-3-(hydroxymethyl)-1,4-benzodioxin-6-yl]*-N-*[2-(4-hydroxyphenyl)ethyl]prop-2-enamide*; **2**). Colorless amorphous powder. UV (MeOH): 293.5 (4.23), 318.0 (4.22). IR (KBr): 3386, 2935, 1656, 1612, 1515, 1463, 1270, 1116, 1047, 827. ^{1}H- and ^{13}C-NMR: *Table 1*. HR-ESI-MS: 508.1989 ($[M+H]^+$, $C_{28}H_{30}NO_8^+$; calc. 508.1971).

Thoreliamide C (=*1,2-Dihydro-1-(4-hydroxy-3-methoxyphenyl)-7-{[(*Z*)-2-(4-hydroxy-3-methoxyphenyl)-1-({[2-(4-hydroxyphenyl)ethyl]amino}carbonyl)ethenyl]oxy}*-N^2,N^3*-bis[2-(4-hydroxyphenyl)ethyl]-6-methoxynaphthalene-2,3-dicarboxamide*; **3**). Colorless amorphous powder. $[\alpha]_D^{25} = 24$ ($c = 0.1$, acetone). UV (MeOH): 223.0 (4.69), 287.0 (4.35), 321.5 (4.37). IR (KBr): 3380, 2923, 1654, 1612, 1515, 1450, 1249, 1130, 1031, 823. ^{1}H- and ^{13}C-NMR: *Table 2*. HR-ESI-MS: 958.3582 ($[M+Na]^+$, $C_{54}H_{53}N_3NaO_{12}^+$; calc. 958.3527).

Thorelinin (=*3-Hydroxy-4,5-dimethoxyphenyl 6-*O-*{(2*E*,4*E*)-5-[(1*R*,3*S*,5*R*,8*S*)-3,8-dihydroxy-1,5-dimethyl-6-oxabicyclo[3.2.1]oct-8-yl]-3-methyl-1-oxopenta-2,4-dien-1-yl}-α-*L*-glucopyranoside*; **4**). Colorless amorphous powder. $[\alpha]_D^{25} = -37.8$ ($c = 0.1$, MeOH). UV (MeOH): 269.5 (4.24). IR (KBr): 3415, 2933, 1700, 1600, 1506, 1456, 1228, 1164, 1105, 1074, 1047, 1012. ^{1}H- and ^{13}C-NMR: *Table 1*. HR-ESI-MS: 619.2339 ($[M+Na]^+$, $C_{29}H_{40}NaO_{13}^+$; calc. 619.2367).

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