JOURNAL OF NATURAL PRODUCTS

ARTICLE

pubs.acs.org/jnp

Antiplasmodial Sesquiterpene Alkaloids from the Roots of *Maytenus mekongensis*

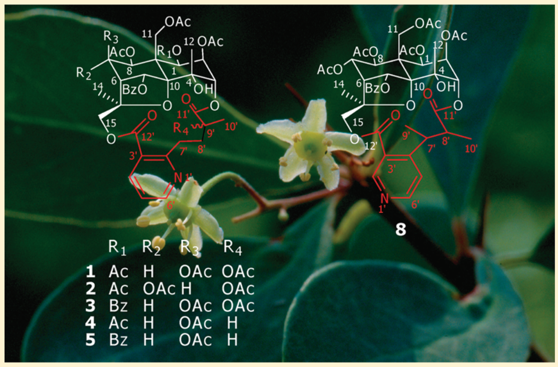
Thitima Lhinhatrakool,[†] Samran Prabpai,[‡] Palangpon Kongsaeree,[‡] and Somyote Sutthivaiyakit*[,†]

[†]Department of Chemistry and Center for Innovation in Chemistry, Faculty of Science, Ramkhamhaeng University, Hua Mark, Bangkapi, Bangkok 10240, Thailand

[‡]Department of Chemistry and Center for Excellence in Protein Structure and Function, Faculty of Science, Mahidol University, Bangkok 10400, Thailand

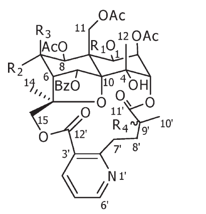
S *Supporting Information*

ABSTRACT: Eight new sesquiterpene alkaloids (**1**−**8**) and four known sesquiterpene alkaloids (**9**−**12**) have been isolated from the roots of *Maytenus mekongensis*. Structures were determined using extensive spectroscopic methods. The relative configuration of 7-*epi*-mekongensine (**2**) was established by single-crystal X-ray crystallographic analysis. The alkaloids were evaluated for antiplasmodial activity against *Plasmodium falciparum*, K1 strain, and for cytotoxicity using a panel of cell lines.

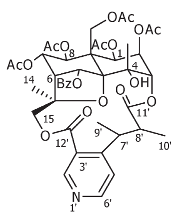


In our search for biologically active compounds from Thai medicinal plants we investigated *Maytenus mekongensis* Ding Hou (Celastraceae), known in Thailand as "Naam Kaan Chaang".[1] Although *Maytenus* species have been reported to possess compounds having cytotoxic,[2] antibiotic,[3] antifeedant,[4] and antileukemic activities,[5] there have been no reports of biological activity or phytochemical investigations of this plant. Preliminary screening of an extract of *M. mekongensis* using breast cancer MCF7 and small cell lung NCI-H187 cancer cell lines indicated inhibitory activity. Column chromatography (CC) of the CH_2Cl_2 solubles of the roots yielded 12 sesquiterpene alkaloids (**1**−**12**), of which eight were new. The known sesquiterpene alkaloids were identified as mayteine (**10**),[6] euonymine (**12**),[7] 7-*epi*-euonymine (**9**),[6] and 7-*epi*-mayteine (**11**).[8]

Compound **1** was obtained as an amorphous solid with the molecular formula $C_{45}H_{51}NO_{20}$ based on HRESIMS. The FTIR spectrum showed absorption bands for OH and ester carbonyl groups. The ^1H NMR spectrum of **1** had signals of six acetyl groups at δ_H 2.27, 2.23, 2.12, 2.10, 1.98, and 1.89. The low-field oxymethine proton signals between δ_H 5.60 and 5.02 and aromatic protons between δ_H 8.18 and 7.45, in conjunction with the $^1H-^1H$ COSY spectrum, which showed sequential correlations from H-1 to H-3 and from H-5 to H-8 with two oxymethylene group signals at δ_H 5.41 and 3.93 (both d, J = 12.2 Hz, H_2-15) and at δ_H 5.20 and 4.55 (both d, J = 13.4 Hz, H_2-11), implied the presence of a dihydro-β-agarofuran moiety commonly found in sesquiterpene pyridine alkaloids from *Maytenus* species.[6] HMBC

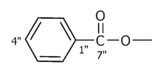


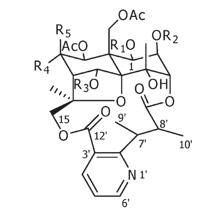
	R1	R2	R3	R4
1	Ac	H	OAc	OAc
2	Ac	OAc	H	OAc
3	Bz	H	OAc	OAc
4	Ac	H	OAc	H
5	Bz	H	OAc	H



8

5-O-Bz





	R1	R2	R3	R4	R5
6	Bz	Ac	H	OAc	H
7	Bz	Bz	Ac	H	OAc
9	Ac	Ac	Ac	OAc	H
10	Bz	Ac	Ac	H	OAc
11	Bz	Ac	Ac	OAc	H
12	Ac	Ac	Ac	H	OAc

cross-peaks between a singlet at δ_H 7.01 (H-5) and the aromatic protons (H-2″, H-6″) at δ_H 8.18 with the carbonyl signal at δ_C 165.6 indicated bonding between an *O*-Bz group and C-5. The singlet at δ_H 1.74 (H_3-10′) and two sets of mutually coupled multiplets of the nonequivalent methylene protons (H_2-7′) at δ_H 3.71 and 3.01 and of H_2-8′ at δ_H 2.65 and 2.17, in addition to the HMBC correlations of H_3-10′/C-8′ (δ_C 37.7), C-9′ (δ_C 80.4), and C-11′ (δ_C 171.5), indicated the presence of an oxygenated wilfordic acid moiety in **1**.[9] Connectivities between C(15)-O/C-12′ and C(3)-O/C-11′ were based on the HMBC cross-peaks of H-15 and H-4′ (δ_H 8.13)/C-12′ (δ_C 167.4) and of H-3 (δ_H 5.02)

Received: January 6, 2011
Published: June 02, 2011

Table 1. ^{13}C NMR (δ) Data of **1**−**9** (100 MHz, $CDCl_3$)[o]

position	1	2	3	4	5	6	7	8	9
1	72.5	71.7	72.4	73.5	73.5	72.3	73.3	72.3	72.3
2	69.3	69.0	68.8	69.2[a−i]a	69.8	68.4	69.8	68.4	68.5
3	77.9	77.3	77.6	76.1	76.1	74.3[a−i]b	75.6	75.4	75.1
4	70.1	70.3	70.1	70.1	70.8	70.5	70.5	70.8	70.5
5	75.0	75.7	75.1	74.9	74.9	76.7[n]	73.8	75.8	74.7
6	50.9	50.1	50.8	51.0	50.9	51.4[j−m]j	51.4	49.7	49.4
7	68.8	73.1	68.8	69.3[a−i]a	69.1	73.2	68.9	73.2	73.6
8	71.9	74.8	72.7	71.1	71.8	74.2[a−i]b	71.3	74.1	73.9
9	52.4	51.8	52.8	52.2	52.6	51.4[j−m]j	52.5	51.7	51.4
10	93.0	93.1	93.0	93.4	93.6	94.3	94.1	94.1	94.3
11	60.3	60.5	60.6	60.3	60.4	60.4	60.6	60.6	60.6
12	23.1	23.8	23.1	22.8	22.8	24.0	23.2	23.7	23.8
13	84.0	85.5	84.1	84.4	84.6	86.1	84.4	83.9	85.6
14	18.0	19.0	18.0	17.9	17.8	19.6	18.5	19.4	19.4
15	69.9	70.0	70.0	70.5	70.5	70.8	70.0	70.2	69.9
2′	160.6	160.5	161.0	163.6	163.2	165.9	165.4	150.9	168.4
3′	125.7	126.0	125.7	125.0	125.4	125.4	125.0	125.3	125.0
4′	139.3	139.9	139.4	139.4	139.0	138.2	137.8	156.3	137.7
5′	121.5	121.8	121.4	121.5	121.8	121.2	121.1	121.6	121.1
6′	151.8	151.8	151.9	152.2	152.9	151.7	151.5	152.8	151.5
7′	31.0	30.8	30.1	32.5	33.4[j−m]k	36.1	36.5	33.2	36.4
8′	37.7	44.8	37.5	33.3	33.4[j−m]k	45.3	44.9	45.6	44.8
9′	80.4	80.4	80.4	38.5	38.5	11.5	11.9	11.5	12.0
10′	22.3	21.8	22.7	18.5	18.6	9.7	9.8	10.0	11.5
11′	171.5	171.3	171.4	175.0	175.0	173.7	173.9	173.5	174.0
12′	167.4	167.0	167.5	166.6	165.8	168.8	168.5	168.0	168.4
1″	129.2	128.9[j−m]l	129.3	129.3	129.4	129.5	129.5	129.3	
2″, 6″	130.3	130.3	130.3	130.3	130.3	129.3	130.0	130.3	
3″, 5″	128.9	128.9[j−m]l	128.5	128.9	128.9	128.4	128.8	128.8	
4″	133.7	133.9	133.5	133.6	133.7	133.2	133.4	133.7	
7″	165.6	165.6	165.6	165.8	164.9	164.4	164.7	165.7	
1-OAc	20.6	20.6		20.5				20.5	20.5
	168.7	168.5		169.4				169.1	169.0
2-OAc	21.0[a−i]c	20.9	20.9	21.0[a−i]d	20.9	20.8		21.0	21.0[a−i]e
	168.3	168.3	168.0	168.7[a−i]f	168.4	168.0		168.6	168.6
5-OAc							21.6		21.5
							169.9		169.6
7-OAc	20.1	20.8	21.1	21.1[a−i]d	21.0	20.8	21.0	20.9	20.8[a−i]e
	170.2	170.0	170.0	170.1[a−i]f	170.1[a−i]f	169.8	169.9	169.7[j−m]m	169.8
8-OAc	20.5	20.7[a−i]h	19.8[a−i]i	20.5	20.0	20.1	19.8	20.7	20.7
	168.9	169.7	168.9	169.0	169.0	169.5	168.9	169.7[j−m]m	169.6
11-OAc	21.4[a−i]c	21.3[a−i]h	21.5[a−i]i	21.4	21.5	21.3	21.3	21.3	21.2
	170.1	169.7	170.2	170.2	170.2[a−i]g	170.0	170.5	170.0	170.0
9′-OAc	20.1	21.2	21.0						
	170.9	171.0	170.9						

[a−i] Interchangeable signals. [j−m] Overlapping signals. [n] Obscured by solvent signal. [o] **3**: [1-OBz: δ 164.6 (C, C-7‴), 133.8 (CH, C-4‴), 129.7 (CH, C-2‴,6‴), 129.1 (C, C-1‴), 128.9 (CH, C-3‴,5‴)]; **5**: [1-OBz: δ 164.9 (C, C-7‴), 133.5 (CH, C-4‴), 129.5 (CH, C-2‴,6‴), 129.3 (C, C-1‴), 128.5 (CH, C-3‴,5‴)]; **7**: [2-OBz: δ 164.7 (C, C-7‴), 133.4 (CH, C-4‴), 129.6 (CH, C-2‴,6‴), 129.5 (C, C-1‴), 128.4 (CH, C-3‴,5‴)].

and H_2-8′/C-11′ (δ_C 171.5), respectively. The long-range HMBC correlation between OCOCH_3-9′/C-9′ required the presence of an OAc group at C-9′. The signal at δ_H 5.60, assigned to H-7, was observed as a doublet of doublets with $J_{7,8}$ = 6.6 and $J_{6,7}$ = 3.8 Hz, respectively. The NOE difference experiment, which revealed NOE interactions between H-5/H-6 and H_3-12 and no NOE effect between H-5/H-7, implied the α-orientation of H-7. On the basis of the spectroscopic data (Experimental Section and Table 1), compound **1** was identified as 2,9′-di-*O*-acetyl-5-*O*-benzoyl-5-deacetylwilforidine[9] and was given the name mekongensine.

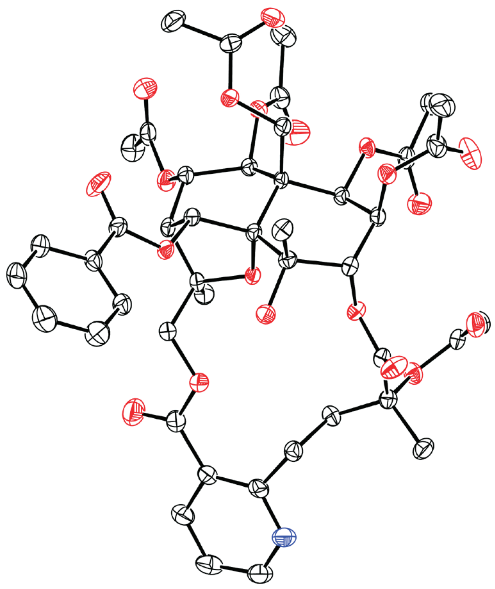


Figure 1. ORTEP drawing of **2**. Hydrogen atoms are omitted for clarity.

Compound **2** was isolated as a colorless solid with same molecular formula as **1**. The FTIR spectrum showed absorption bands for OH and ester groups. The ^{1}H and ^{13}C NMR spectra closely resembled those of **1**. However, the signal at δ_H 5.77 (H-7, a doublet of doublets with $J_{7,8}$ = 9.5 and $J_{6,7}$ = 3.6 Hz) indicated that **2** differed from **1** in configuration at C-7. The NOE difference spectrum showed interactions between H-5/H-6, H-7, and H_3-12, which provided support for the β-orientation of H-7. Compound **2** was accordingly the 7-epimer of **1** and was given the name 7-*epi*-mekongensine.[9] The structure of **2** was confirmed by X-ray crystallographic analysis (Figure 1).

Compound **3** has the molecular formula $C_{50}H_{53}NO_{20}$, and it showed ^{1}H and ^{13}C NMR signals similar to those of **1** and **2**. However, the ^{1}H NMR spectrum of **3** showed only five acetyl groups, and the aromatic proton signals at δ_H 8.20−7.45 indicated the presence of two benzoyl groups. Long-range HMBC correlations of H-1 (δ_H 5.99)/C-7‴ (δ_C 164.6) and of H-5 (δ_H 6.95)/C-7″ (δ_C 165.6) indicated bonding of one *O*-Bz group at C-1 and the second one at C-5. Compound **3** was thus identified as 1-*O*-benzoyl-1-deacetylmekongensine.

The HRESIMS of compound **4** indicated a molecular formula of $C_{43}H_{49}NO_{18}$, and the ^{1}H NMR spectrum of **4** showed five acetyl groups and aromatic protons of one benzoyl group. The singlet at ca. δ_H 1.74 was absent and had been replaced by a doublet at δ_H 1.20. The ^{1}H−^{1}H COSY spectrum indicated correlations of signals at δ_H 1.20 (d, H-10′)/δ_H 2.40 (H-9′); H-9′/H-8′ (δ_H 2.00), and H-8′/H-7′ (δ_H 3.96, 3.03). The ^{1}H−^{1}H COSY correlations implied the presence of a wilfordic acid moiety in **4**. Connectivities from C(15)-*O* to C-12″ and C(3)-*O* to C-11″ were detected from the HMBC cross-peaks of H_2-15/C-12″ and of H-3/C-11″, respectively. Thus, compound **4** was determined to be 9′-deacetoxymekongensine.

Compound **5**, isolated as a colorless, amorphous solid with the molecular formula $C_{48}H_{51}NO_{18}$, showed sets of ^{1}H and ^{13}C NMR signals similar to those of **4**. The ^{1}H NMR spectrum of **5** showed only four acetyl signals, but had aromatic proton signals characteristic of two benzoyl groups. Long-range HMBC correlations of H-1 (δ_H 6.50)/C-7‴ (δ_C 164.9) and of H-5 (δ_H 7.03)/C-7″ (δ_C 164.9) indicated connections of one *O*-Bz group to C-1 and the second group to C-5. Complete assignments of ^{1}H and ^{13}C NMR chemical shifts are shown in the Experimental Section and Table 1. Compound **5** was thus 1-*O*-benzoyl-1-deacetyl-9′-deacetoxymekongensine.

Compound **6** was isolated as a colorless, amorphous solid with the molecular formula $C_{41}H_{47}NO_{17}$ (HRESIMS). The FTIR spectrum showed absorption bands of OH (ν_{max} 3400 cm^{-1}) and ester carbonyl (ν_{max} 1748 cm^{-1}) functions. The ^{1}H NMR spectrum of compound **6** revealed four acetyl groups (δ_H 2.24, 2.13, 1.92, and 1.36). The ^{1}H−^{1}H COSY spectrum showed sequential correlations from H-1 to H-3 and from H-5 to H-8 of a dihydroagarofuran nucleus, as also observed in **1**−**5**, but the signal assignable to H-5 resonated at δ_H 5.21 (d, J = 2.6 Hz), which was more shielded than those in **1**−**5**, thus indicating a free OH group at C-5. The presence of an evoninic acid moiety[6] was implied from the ^{1}H−^{1}H COSY correlations of signals at δ_H 1.40 (d, H-9′)/4.79 (q, H-7′) and at 1.18 (d, H-10′)/2.58 (q, H-8′) and correlations of pyridyl ring protons H-5′/H-4′, H-6′, in addition to the ^3J ^{1}H−^{13}C correlations between H-7′/C-3′, C-10′, and C-11′ and between H-4′/ C-2′, C-6′, and C-12′. Connectivities from the oxygen at C-1 to C-7″ (of a benzoyl group), from the oxygen atom at C-3 to C-11′, and from the oxygen atom at C-15 to C-12′ were detected from the HMBC correlations between H-1 (δ_H 5.84)/C-7″ (δ_C 164.4) and C-11 (δ_C 60.4), as well as H-3 (δ_H 4.77)/C-11′ (δ_C 173.7), and between H_2-15 (6.07 and 3.66)/C-12′ (δ_C 168.8), respectively. Connectivities of each OAc group to a particular oxymethine carbon were also observed from HMBC correlations. Assignments of ^{1}H and ^{13}C NMR signals are shown in the Experimental Section and Table 1, and most of the ^{1}H and ^{13}C NMR shifts are similar to those reported for euojaponine A previously isolated from *Euonymus japonica*.[6b] However, the doublet of doublets assignable to H-7 at δ_H 5.47 showed $J_{7,8}$ values of 9.8 Hz and $J_{6,7}$ of 3.0 Hz, indicating the β-orientation of H-7. The NOE experiment indicated interactions between H-5/H-6, H-7, and H_3-12 and provided further support to the assignment. Compound **6** was thus concluded to be 7-*epi*-euojaponine A.[6b]

Compound **7**, $C_{48}H_{51}NO_{18}$, had NMR signals similar to those of **6**, but with four acetyl groups (δ_H 2.29, 2.21, 2.11, and 1.31), and signals revealing the presence of two benzoyl groups. HMBC correlations between H-1 (δ_H 6.02)/the higher field carbonyl signal at δ_C 164.7 (C-7″) and between H-2 (δ_H 5.60)/C-7‴ (δ_C 164.7) indicated that one *O*-Bz group connected to C-1 and the second group to C-2. The broad singlet at δ_H 7.04 (H-5) showed a long-range HMBC correlation with a carbonyl carbon at δ_C 169.9 and implied a C(5)−OAc linkage. Most of the ^{1}H and ^{13}C NMR resonances were similar to those reported for mayteine (**10**).[6] Compound **7** was thus identified as 2-*O*-benzoyl-2-deacetylmayteine.

Compound **8** showed an $[M + H]^+$ ion at m/z 868.3049 corresponding to the molecular formula $C_{43}H_{49}NO_{18}$. The ^{1}H NMR spectrum indicated five acetyl groups and one benzoyl group. The ^{1}H−^{1}H COSY spectrum indicated the connectivity between protons of the dihydroagrarofuran moiety and also connectivity between H-8′/H-10′ and H-7′ and between H-7′/H-9′. Signals of the pyridyl nucleus appeared, however, as a singlet at δ_H 8.95 and two doublets at δ_H 8.69 and 7.37, both with J = 5.2 Hz, which are different from those found in the evoninic acid nucleus as observed in **6** and **7**,[6] thus indicating compound **8** to possess an isomeric evoninic acid moiety. The HMBC spectrum showed ^3J correlations between H_2-15 and H-2′/C-12′ and between H-5′/C-7′, thus requiring the pyridyl ring to be 3,4-disubstituted.[10] HMBC correlations between

H-5, H-2″, and H-6″/a higher field carbonyl carbon (δ_C 165.7, C-7″) indicated connection of C-5 to an *O*-benzoyl group. Complete ^1H and ^{13}C NMR assignments are provided in the Experimental Section and Table 1. Compound **8** was thus assigned to be 7-*epi*-5-*O*-benzoyl-5-deacetylperitassine A.[10,11]

7-*epi*-Euonymine (**9**) has the molecular formula $C_{38}H_{47}NO_{18}$ and ^1H and ^{13}C NMR spectra very similar to euonymine (**12**)[6] previously reported and also obtained in this study. The doublet of doublets at δ_H 5.49 of H-7 showing $J_{7,8}$ = 9.7 Hz indicated a β-oriented H-7. This compound was reported previously as a transformation product of evonine;[7] however no detailed NMR data were given; we therefore included these data in the Experimental Section and Table 1.

The isolated alkaloids were evaluated for their cytotoxic, antiplasmodial, and antituberculous activity. Compounds (**1**−**5**) having wilfordic acid moieties, either with or without a 9′-OAc group, exhibited comparable antiplasmodial activities, with IC_{50} values of 3.1×10^{-3}, 3.9×10^{-3}, 3.5×10^{-3}, 3.1×10^{-3}, and 2.5×10^{-3} mM, respectively, while compounds (**10**−**12**) with evoninic acid moieties showed no inhibitory activity. Only compounds **1** and **4** showed very weak cytotoxic activity against the human oral epidermal carcinoma (KB) cell line, with IC_{50} values of 28.2 and 46.7 μg/mL, respectively, and no inhibitory activity was observed with human breast adenocarcinoma (MCF7) and human small cell lung (NCI-H187) cell lines. Compound **1** showed no antimycobacterial activity against *Mycobacterium tuberculosis* H37Ra at 200 μg/mL.

EXPERIMENTAL SECTION

General Experimental Procedures. Melting points were measured using an Electrothermal melting point apparatus and are uncorrected. Optical rotations were recorded on a JASCO DIP 1020 polarimeter. IR spectra were obtained on a Perkin-Elmer 1760x FT-IR spectrophotometer. ^1H and ^{13}C NMR spectra were recorded with a Bruker Avance 400 MHz spectrometer. Chemical shifts are referenced to the residual solvent signals ($CDCl_3$: δ_H 7.24 and δ_C 77.0 ppm). HRESIMS was recorded on a Bruker Daltonics microTOF mass spectrometer. HPLC separation was performed using a Merck LiChrospher 100 RP-18 (5 μm, 250 × 4.0 mm) column, with a TSP SpectraSYSTEM P2000 pump and a TSP SpectraSYSTEM UV2000 detector.

Plant Material. The roots of *Maytenus mekongensis*, known in Thailand as "Naam Kaan Chaang", were collected from Don Muu, Kampeae Subdistrict, Trakarnpoepon District, Ubonratchatani Province, Thailand, in June 2004. The plant was identified by Assoc. Prof. Dr. Wongsatit Chuakul of the Department of Pharmaceutical Botany, Faculty of Pharmacy, Mahidol University, Bangkok, Thailand. A voucher specimen (SSMMe/2004) is maintained at the Department of Chemistry, Ramkhamhaeng University.

Extraction and Isolation. The dried roots (7.5 kg) were extracted successively with hexanes, CH_2Cl_2, and MeOH using Soxhlet extraction to obtain hexanes (51 g), CH_2Cl_2 (54 g), and MeOH (606 g) extracts, respectively. The CH_2Cl_2 extract (54 g) was subjected to column chromatography using a gradient of hexanes−CH_2Cl_2 to CH_2Cl_2−MeOH to obtain seven major fractions. Fraction 2 (7.4 g) was separated by CC [silica gel (Merck), hexanes−CH_2Cl_2 (5:95) to CH_2Cl_2−MeOH (50:50)] to give nine fractions (2.1−2.9). CC (silica gel, CH_2Cl_2−MeOH, 99.5:0.5 to 50:50) of fraction 2.4 (3.6 g) gave fractions 2.4.1−2.4.4. Fraction 2.4.1 (418 mg) was chromatographed [Sephadex LH 20, hexanes−CH_2Cl_2, 50:50] to give three fractions, 2.4.1.1−2.4.1.3. Fraction 2.4.1.2 (258 mg) was separated by CC [silica gel, CH_2Cl_2−MeOH (100:0 to 80:20) then C_{18}, MeOH−H_2O (70:30 to 100:0)] and gave **6** (4.0 g) and **7** (10.4 mg). Fraction 2.4.2 (475 mg) was further purified [Sephadex LH 20 (Sigma), CH_2Cl_2−MeOH, 50:50] to give fractions 2.4.2.1−2.4.2.3. Fraction 2.4.2.2 (208 mg) was chromatographed on Sephadex LH 20 (MeOH), then subjected to HPLC (C_{18}, CH_3CN−H_2O, 63:27) to yield **5** (2.4 mg) and **3** (19.9 mg). Fraction 2.4.3 (821.8 mg) was purified on Sephadex LH 20 (CH_2Cl_2−MeOH, 10:90) and gave three subfractions (2.4.3.1−2.4.3.3). Subfraction 2.4.3.2 (635 mg) was fractionated (Sephadex LH 20, CH_2Cl_2−MeOH, 10:90) and yielded two subfractions (2.4.3.2.1, 2.4.3.2.2). Subfraction 2.4.3.2.1 was subjected to HPLC (C_{18}, CH_3CN−H_2O, 66:34), giving **5** (12.7 mg) and **7** (1.2 mg). Subfraction 2.4.3.2.2 provided **10** (221 mg). Subfraction 2.4.4 (2.0 g) was purified by CC (silica gel, hexanes−EtOAc, 75:25 to 40:60) to give subfractions 2.4.4.1−2.4.4.5. Subfraction 2.4.4.3 (454 mg) yielded **11** (20.2 mg) and **9** (5.3 mg). Purification of fraction 2.4.4.3.2 (112.3 mg) using CC (C_{18}, MeOH−H_2O, 70:30 to 90:10) gave additional **11** (5.4 mg). Fraction 2.4.4.4 (103 mg), using CC (C_{18}, MeOH−H_2O, 65:35 to 100:0), gave **9** (4.4 mg). Subfraction 2.4.4.5 (516.9 mg) was further purified (Sephadex LH 20, MeOH) and gave subfractions 2.4.4.5.1−2.4.4.5.2. Subfraction 2.4.4.5.1 (C_{18}, MeOH−H_2O, 50:50 to 100:0) gave **12** (4.8 mg) and **10** (188 mg). Subfraction 2.4.4.5.2 (109 mg), by HPLC (C_{18}, CH_3CN−H_2O, 56:44), gave **2** (6.8 mg) and **8** (3.9 mg). Subfraction 2.5 (686 mg) [CC on Sephadex LH 20, CH_2Cl_2−MeOH (50:50) followed by RP-CC on C_{18}, MeOH−H_2O (55:45 to 100:0)] gave subfractions 2.5.2.1−2.5.2.5. Fraction 2.5.2.2 contained **12** (18.0 mg), and fraction 2.5.2.4 (142.2 mg) gave **4** (21.3 mg), **1** (44.6 mg), and **2** (17.4 mg) after purification by HPLC (CH_3CN−H_2O, 50:50).

Mekongensine (***1***): colorless, amorphous solid; mp 171−173 °C; $[\alpha]_D^{26}$ +11.8 (*c* 0.65, $CHCl_3$); FT-IR (KBr) ν_{max} 3542, 2945, 1748, 1585, 1568, 1451, 1434, 1372, 1254, 1237, 1183, 1133, 1098, 1050, 1025, 1007, 932, 899, 763, 714, 623, 590 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ_H 8.67 (1H, dd, *J* = 4.8, 1.8, H-6′), 8.18 (2H, dd, *J* = 7.6, 1.3 Hz, H-2″,6″), 8.13 (1H, dd, *J* = 7.8, 1.8, H-4′), 7.56 (1H, tt, *J* = 7.6, 1.3 Hz, H-4″), 7.45 (2H, t, *J* = 7.6 Hz, H-3″,5″), 7.26 (1H, dd, *J* = 7.8, 4.8, H-5′), 7.01 (1H, brs, H-5), 5.60 (1H, dd, *J* = 6.6, 3.8, H-7), 5.59 (1H, d, *J* = 3.8 Hz, H-1), 5.41 (1H, d, *J* = 12.2 Hz, H-15a), 5.39 (1H, d, *J* = 6.6 Hz, H-8), 5.20 (1H, d, *J* = 13.4 Hz, H-11a), 5.19 (1H, dd, *J* = 3.8, 2.7 Hz, H-2), 5.02 (1H, d, *J* = 2.7 Hz, H-3), 4.55 (1H, d, *J* = 13.4 Hz, H-11b), 4.15 (1H, d, *J* = 1.0 Hz, 4-OH), 3.93 (1H, d, *J* = 12.2 Hz, H-15b), 3.71 (1H, ddd, *J* = 14.3, 12.5, 4.2 Hz, H-7′a), 3.01 (1H, ddd, *J* = 14.3, 12.5, 4.2 Hz, H-7′b), 2.65 (1H, ddd, *J* = 13.9, 12.5, 4.3 Hz, H-8′a), 2.53 (1H, d, *J* = 3.8 Hz, H-6), 2.27 (3H, s, 11-OAc), 2.23 (3H, s, 7-OAc), 2.17 (1H, m, H-8′b), 2.12 (3H, s, 8-OAc), 2.10, (3H, s, 9′-OAc), 1.98 (3H, s, 1-OAc), 1.89 (3H, s, 2-OAc), 1.74 (3H, s, H-10′), 1.63 (3H, s, H-14), 1.57 (3H, d, *J* = 0.6 Hz, H-12); ^{13}C NMR ($CDCl_3$, 100 MHz), see Table 1; HRESIMS *m/z* 948.2902 $[M + Na]^+$ (calcd for $C_{45}H_{51}NO_{20}Na$, 948.2902).

7-epi-Mekongensine (***2***): colorless, rhombic crystals from MeOH−H_2O; mp 280−282 °C; $[\alpha]_D^{26}$ +7.2 (*c* 0.4850, $CHCl_3$); IR (KBr) ν_{max} 3540, 2946, 1755, 1732, 1601, 1586, 1569, 1451, 1434, 1371, 1250, 1224, 1180, 1135, 1094, 1053, 955, 905, 827, 761, 714, 625, 592, 463 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ_H 8.71 (1H, dd, *J* = 4.8, 1.7 Hz, H-6′), 8.20 (2H, dd, *J* = 7.7, 1.4 Hz, H-2″,6″), 8.13 (1H, dd, *J* = 7.8, 1.7 Hz, H-4′), 7.57 (1H, t, *J* = 7.7 Hz, H-4″), 7.45 (2H, t, *J* = 7.7 Hz, H-3″,5″), 7.28 (1H, dd, *J* = 7.8, 4.8 Hz, H-5′), 6.69 (1H, brs, H-5), 5.77 (1H, dd, *J* = 9.5, 3.6 Hz, H-7), 5.68 (1H, d, *J* = 9.5 Hz, H-8), 5.62 (1H, d, *J* = 3.5 Hz, H-1), 5.46 (1H, d, *J* = 12.0 Hz, H-15a), 5.17 (1H, dd, *J* = 3.5, 2.6 Hz, H-2), 5.00 (1H, d, *J* = 2.6 Hz, H-3), 4.82 (1H, d, *J* = 13.3 Hz, H-11a), 4.60 (1H, d, *J* = 13.3 Hz, H-11b), 4.24 (1H, d, *J* = 1.0 Hz, 4-OH), 3.89 (1H, d, *J* = 12.0 Hz, H-15b), 3.61 (1H, dt, *J* = 13.3, 4.4 Hz, H-7′a), 3.02 (1H, dt, *J* = 13.3, 4.4 Hz, H-7′b), 2.61 (1H, d, *J* = 3.6 Hz, H-6), 2.61 (1H, dt, *J* = 13.7, 4.4 Hz, H-8′a), 2.36 (3H, s, 11-OAc), 2.19 (1H, m, H-8′b), 2.15 (3H, s, 9′-OAc), 2.11 (3H, s, 2-OAc), 1.99 (3H, s, 7-OAc), 1.97 (3H, s, 8-OAc), 1.86 (3H, s, 1-OAc), 1.75 (3H, s, H-10′), 1.67 (3H, s, H-14), 1.60 (3H, s, H-12); ^{13}C NMR ($CDCl_3$, 100 MHz), see Table 1 ;

HRESIMS m/z 948.2885 $[M + Na]^+$ (calcd for $C_{45}H_{51}NO_{20}Na$, 948.2902).

1-O-Benzoyl-1-deacetylmekongensine (**3**): colorless, amorphous solid; mp 166−168 °C; $[\alpha]_D^{30}$ +22.3 (c 0.49, $CHCl_3$); IR (KBr) ν_{max} 3543, 2926, 2854, 1747, 1732, 1602, 1585, 1451, 1434, 1372, 1315, 1247, 1179, 1132, 1107, 1057, 1025, 933, 897, 761, 712, 626, 594 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ_H 8.71 (1H, dd, J = 4.8, 1.7 Hz, H-6′), 8.20 (2H, dd, J = 7.7, 1.5 Hz, H-2″,6″), 8.15 (1H, dd, J = 7.9, 1.8 Hz, H-4′), 7.87 (2H, dd, J = 7.8, 1.4 Hz, H-2‴,6‴), 7.56 (1H, m, H-4‴), 7.56 (1H, m, H-4″), 7.45 (2H, t, J = 7.7 Hz, H-3″,5″), 7.40 (2H, t, J = 7.8 Hz, H-3‴,5‴), 7.27 (1H, dd, J = 7.9, 4.8 Hz, H-5′), 6.95 (1H, s, H-5), 5.99 (1H, d, J = 3.7 Hz, H-1), 5.64 (1H, dd, J = 5.8, 3.8 Hz, H-7), 5.48 (1H, d, J = 5.8 Hz, H-8), 5.43 (1H, d, J = 13.2 Hz, H-11a), 5.40 (1H, d, J = 11.9 Hz, H-15a), 5.31 (1H, dd, J = 3.7, 2.6 Hz, H-2), 5.11 (1H, d, J = 2.6 Hz, H-3), 4.70 (1H, d, J = 13.2 Hz, H-11b), 4.16 (1H, d, J = 0.9 Hz, 4-OH), 3.97 (1H, d, J = 11.9 Hz, H-15b), 3.74 (1H, dt, J = 14.7, 4.1 Hz, H-7′a), 3.04 (1H, dt, J = 14.7, 4.1 Hz, H-7′b), 2.72 (1H, dt, J = 14.0, 4.1 Hz, H-8′a), 2.58 (1H, d, J = 3.8 Hz, H-6), 2.25 (3H, s, 11-OAc), 2.20 (1H, m, H-8′b), 2.19 (3H, s, 7-OAc), 2.16 (3H, s, 2-OAc), 2.12 (3H, s, 9′-OAc), 1.76 (3H, s, H-10′), 1.70 (3H, s, H-14), 1.62 (3H, s, H-12), 1.34 (3H, s, 8-OAc); ^{13}C NMR ($CDCl_3$, 100 MHz), see Table 1; HRESIMS m/z 1010.3015 $[M + Na]^+$ (calcd for $C_{50}H_{53}NO_{20}Na$, 1010.3059).

9′-Deacetoxymekongensine (**4**): colorless, amorphous solid; mp 134−136 °C; $[\alpha]_D^{31}$ −7.1 (c 0.30, $CHCl_3$); IR (KBr) ν_{max} 3568, 230, 1748, 1723, 1585, 1568, 1451, 1371, 1254, 1231, 1160, 1096, 1071, 1047, 1007, 1007, 903, 767, 715, 620, 596, 462 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ_H 8.30 (1H, d, J = 7.8 Hz, H-4′), 8.25 (1H, dd, J = 4.8, 1.7 Hz, H-6′), 8.25 (2H, dd, J = 7.4, 1.4 Hz, H-2″,6″), 7.57 (1H, tt, J = 7.4, 1.4 Hz, H-4″), 7.46 (2H, t, J = 7.4 Hz, H-3″,5″), 7.30 (1H, dd, J = 7.8, 4.8 Hz, H-5′), 6.98 (1H, s, H-5), 5.76 (1H, d, J = 11.9 Hz, H-15a), 5.65 (1H, d, J = 3.6 Hz, H-1), 5.55 (1H, dd, J = 5.8, 3.8 Hz, H-7), 5.39 (1H, d, J = 5.8 Hz, H-8), 5.26 (1H, d, J = 13.2 Hz, H-11a), 5.17 (1H, dd, J = 3.6, 2.6 Hz, H-2), 5.14 (1H, d, J = 1.0 Hz, 4-OH), 4.98 (1H, d, J = 2.6 Hz, H-3), 4.52 (1H, d, J = 13.2 Hz, H-11b), 3.96 (1H, ddd, J = 12.8, 9.7, 6.2 Hz, H-7′a), 3.67 (1H, d, J = 11.9 Hz, H-15b), 3.03 (1H, m, H-7′b), 2.52 (1H, d, J = 3.8 Hz, H-6), 2.40 (1H, m, H-9′), 2.27 (3H, s, 11-OAc), 2.24 (3H, s, 7-OAc), 2.12 (3H, s, 2-OAc), 2.00 (2H, m, H-8′), 1.99 (3H, s, 8-OAc), 1.86 (3H, s, H-14), 1.86 (3H, s, 1-OAc), 1.56 (3H, d, J = 1.1 Hz, H-12), 1.20 (3H, d, J = 6.9 Hz, H-10′); ^{13}C NMR ($CDCl_3$, 100 MHz), see Table 1; HRESIMS m/z 890.2856 $[M + Na]^+$ (calcd for $C_{43}H_{49}NO_{18}Na$, 890.2847).

1-O-Benzoyl-1-deacetyl-9′-deacetoxymekongensine (**5**): colorless, amorphous solid; mp 152−154 °C; $[\alpha]_D^{31}$ +3.4 (c 0.30, $CHCl_3$); IR (KBr) ν_{max} 3467, 3068, 2935, 1747, 1723,1602, 1585, 1567, 1451, 1371, 1314, 1255, 1224, 1158, 1097, 1048, 1025, 1009, 932, 893, 768, 713, 688, 604, 566, 491 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ_H 8.30 (1H, d, J = 7.8 Hz, H-4′), 8.25 (1H, dd, J = 4.8, 1.7 Hz, H-6′), 8.25 (2H, dd, J = 7.4, 1.4 Hz, H-2″,6″), 7.57 (1H, tt, J = 7.4, 1.4 Hz, H-4″), 7.46 (2H, t, J = 7.4 Hz, H-3″,5″), 7.30 (1H, dd, J = 7.8, 4.8 Hz, H-5′), 6.98 (1H, s, H-5), 5.76 (1H, d, J = 11.9 Hz, H-15a), 5.65 (1H, d, J = 3.6 Hz, H-1), 5.55 (1H, dd, J = 5.8, 3.8 Hz, H-7), 5.39 (1H, d, J = 5.8 Hz, H-8), 5.26 (1H, d, J = 13.2 Hz, H-11a), 5.17 (1H, dd, J = 3.6, 2.6 Hz, H-2), 5.14 (1H, d, J = 1.0 Hz, 4-OH), 4.98 (1H, d, J = 2.6 Hz, H-3), 4.52 (1H, d, J = 13.2 Hz, H-11b), 3.96 (1H, ddd, J = 12.8, 9.7, 6.2 Hz, H-7′a), 3.67 (1H, d, J = 11.9 Hz, H-15b), 3.03 (1H, m, H-7′b), 2.52 (1H, d, J = 3.8 Hz, H-6), 2.40 (1H, m, H-9′), 2.27 (3H, s, 11-OAc), 2.24 (3H, s, 7-OAc), 2.12 (3H, s, 2-OAc), 2.00 (2H, m, H-8′), 1.99 (3H, s, 8-OAc), 1.86 (3H, s, H-14), 1.86 (3H, s, 1-OAc), 1.56 (3H, d, J = 1.1 Hz, H-12), 1.20 (3H, d, J = 6.9 Hz, H-10′); ^{13}C NMR ($CDCl_3$, 100 MHz), see Table 1; HRESIMS m/z found 952.3005 $[M + Na]^+$ (calcd for $C_{48}H_{51}NO_{18}Na$, 952.3004).

7-epi-Euojaponine A (**6**): colorless, amorphous solid; mp 147−148 °C; $[\alpha]_D^{32}$ +25.7 (c 0.20, $CHCl_3$); IR (KBr) ν_{max} 3400, 2929, 1748, 1715, 1602, 1584, 1566, 1452, 1433, 1369, 1314, 1269, 1218, 1168, 1107, 1063, 1036, 962, 917, 857, 755, 712, 603, 594, 564 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ_H 8.69 (1H, dd, J = 4.8, 1.7 Hz, H-6′), 8.13 (1H, dd, J = 7.7, 1.7 Hz, H-4′), 7.76 (2H, d, J = 7.6 Hz, H-2″,6″), 7.50 (1H, brt, J = 7.7 Hz, H-4″), 7.37 (2H, brt, J = 7.7 Hz, H-3″,5″), 7.27 (1H, dd, J = 7.8, 4.8 Hz, H-5′), 6.12 (1H, d, J = 2.9 Hz, 5-OH), 6.07 (1H, d, J = 12.0 Hz, H-15a), 5.84, (1H, d, J = 3.5 Hz, H-1), 5.76 (1H, d, J = 9.8 Hz, H-8), 5.71 (1H, brs, 4-OH), 5.47 (1H, dd, J = 9.8, 3.0 Hz, H-7), 5.37 (1H, t, J = 3.1 Hz, H-2), 5.21 (1H, d, J = 2.6 Hz, H-5), 5.02 (1H, d, J = 13.3 Hz, H-11a), 4.79 (1H, q, J = 6.7 Hz, H-7′), 4.77 (1H, d J = 2.6 Hz, H-3), 4.70 (1H, d, J = 13.2 Hz, H-11b), 3.66 (1H, d, J = 12.0 Hz, H-15b), 2.58 (1H, q, J = 7.2 Hz, H-8′), 2.54 (1H, brd, J = 2.9 Hz, H-6), 2.24 (3H, s, 11-OAc), 2.13 (3H, s, 2-OAc), 1.92 (3H, s, 7-OAc), 1.88 (3H, s, H-12), 1.74 (3H, s, H-14), 1.40 (3H, d, J = 7.0 Hz, H-9′), 1.36 (3H, s, 8-OAc), 1.18 (3H, d, J = 7.1 Hz, H-10′); ^{13}C NMR ($CDCl_3$, 100 MHz), see Table 1; HRESIMS m/z 848.2736 $[M + Na]^+$ (calcd for $C_{41}H_{47}NO_{17}Na$, 848.2742).

2-O-Benzoyl-2-deacetylmayteine (**7**): colorless, amorphous solid; mp 180−182 °C; $[\alpha]_D^{28}$ +14.2 (c 0.52, $CHCl_3$); IR (KBr) ν_{max} 3494, 2975, 1746, 1723,1602, 1584, 1566, 1451, 1433, 1370, 1314, 1274, 1246, 1175, 1107, 1059, 1024, 937, 883, 802, 784, 711, 603 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ_H 8.69 (1H, dd, J = 4.9, 1.8 Hz, H-6′), 8.09 (2H, m, H-2″,6″), 8.07 (1H, m, H-4′), 7.71 (2H, dd, J = 7.3, 1.0 Hz, H-2‴,6‴), 7.50 (2H, brt, J = 7.8 Hz, H-3″,5″), 7.61 (1H, brt, J = 7.4 Hz, H-4″), 7.46 (1H, brt, J = 7.3 Hz, H-4‴), 7.28 (2H, m, H-3‴,5‴), 7.27 (1H, t, J = 4.9 Hz, H-5′), 7.04 (1H, brs, H-5), 6.02 (1H, d, J = 4.2 Hz, H-1), 5.98 (1H, d, J = 11.6 Hz, H-15a), 5.63 (1H, d, J = 13.4 Hz, H-11a), 5.60 (1H, dd, J = 4.2, 2.4 Hz, H-2), 5.53 (1H, dd, J = 5.9, 4.1 Hz, H-7), 5.45 (1H, d, J = 5.9 Hz, H-8), 4.93 (1H, d, J = 2.4 Hz, H-3), 4.67 (1H, q, J = 7.0 Hz, H-7′), 4.56 (1H, d, J = 13.4 Hz, H-11b), 4.56 (1H, d, J = 1.0 Hz, 4-OH), 3.71 (1H, d, J = 11.6 Hz, H-15b), 2.64 (1H, q, J = 7.1 Hz, H-8′), 2.37 (1H, d, J = 4.1 Hz, H-6), 2.29 (3H, s, 11-OAc), 2.21 (3H, s, 5-OAc), 2.11 (3H, s, 7-OAc), 1.73 (3H, s, H-14), 1.66 (3H, s, H-12), 1.39 (3H, d, J = 7.0 Hz, H-9′), 1.31 (3H, s, 8-OAc), 1.22 (3H, d, J = 7.1 Hz, H-10′); ^{13}C NMR ($CDCl_3$, 100 MHz), see Table 1; HRESIMS m/z 930.3193 $[M + H]^+$ (calcd for $C_{48}H_{52}NO_{18}$, 930.3184).

7-epi-5-O-Benzoyl-5-deacetylperitassine A (**8**) (refs 10, 11): colorless, amorphous solid; mp 146−148 °C; $[\alpha]_D^{32}$ −17.5 (c 0.20, $CHCl_3$); IR (KBr) ν_{max} 3493, 2926, 2854, 1748, 1723, 1587, 1553, 1452, 1370, 1250, 1225, 1182, 1119, 1056, 971, 910, 828, 789, 715, 600 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ_H 8.95 (1H, s, H-2′), 8.69 (1H, d, J = 5.2 Hz, H-6′), 8.29 (2H, dd, J = 7.1, 1.4 Hz, H-2″,6″), 7.57 (1H, tt, J = 7.3, 1.3 Hz, H-4″), 7.47 (2H, brt, J = 7.6 Hz, H-3″,5″), 7.37 (1H, d, J = 5.2 Hz, H-5′), 6.75 (1H, brs, H-5), 6.05 (1H, d, J = 11.6 Hz, H-15a), 5.72 (1H, d, J = 9.8 Hz, H-8), 5.69 (1H, dd, J = 9.8, 2.9 Hz, H-7), 5.59 (1H, d, J = 3.5 Hz, H-1), 5.27 (1H, t, J = 3.1 Hz, H-2), 5.02 (1H, d, J = 1.3 Hz, 4-OH), 4.76 (1H, d, J = 13.3 Hz, H-11a), 4.73 (1H, d, J = 2.9 Hz, H-3), 4.73 (1H, m, H-7′), 4.71 (1H, d, J = 13.3 Hz, H-11b), 3.58 (1H, d, J = 11.6 Hz, H-15b), 2.61 (1H, d, J = 2.6 Hz, H-6), 2.49 (1H, q, J = 7.2 Hz, H-8′), 2.36 (3H, s, 11-OAc), 2.13 (3H, s, 2-OAc), 2.01 (3H, s, 7-OAc), 1.98 (3H, s, 8-OAc), 1.83 (3H, s, 1-OAc), 1.75 (3H, s, H-14), 1.57 (3H, d, J = 1.1 Hz, H-12), 1.39 (3H, d, J = 7.2 Hz, H-9′), 1.10 (3H, d, J = 7.2 Hz, H-10′); ^{13}C NMR ($CDCl_3$, 100 MHz), see Table 1; HRESIMS m/z 868.3049 $[M + H]^+$ (calcd for $C_{43}H_{50}NO_{18}$, 868.3028).

7-epi-Euonymine (**9**): colorless, amorphous solid; mp 158−160 °C; $[\alpha]_D^{31}$ −18.6 (c 0.27, $CHCl_3$); IR (KBr) ν_{max} 3487, 2930, 1755, 1584, 1566, 1433, 1370, 1316, 1251, 1228, 1169, 1119, 1092. 1060, 1039, 967, 943, 903, 827, 784, 753, 718, 633, 602 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ_H 8.67 (1H, dd, J = 4.8, 1.8 Hz, H-6′), 8.04 (1H, dd, J = 7.8, 1.8 Hz, H-4′), 7.25 (1H, dd, J = 7.8, 4.8 Hz, H-5′), 6.62 (1H, s, H-5), 5.94 (1H, d, J = 11.5 Hz, H-15a), 5.65 (1H, d, J = 9.7 Hz, H-8), 5.54 (1H, d, J = 3.7 Hz, H-1), 5.49 (1H, dd, J = 9.7, 3.4 Hz, H-7), 5.23 (1H, t, J = 3.1 Hz, H-2), 4.75 (1H, d, J = 13.4 Hz, H-11a), 4.70 (1H, d, J = 2.7 Hz, H-3), 4.63 (1H, q, J = 6.8 Hz, H-7′), 4.61 (1H, d, J = 13.4 Hz, H-11b), 4.49 (1H, d, J = 1.3 Hz, 4-OH), 3.64 (1H, d, J = 11.5 Hz, H-15b), 2.57 (1H, q, J = 6.6 Hz, H-8′), 2.45 (1H, d, J = 3.1 Hz, H-6), 2.29 (3H, s, 11-OAc), 2.19 (3H, s, 5-OAc), 2.12 (3H, s, 2-OAc), 2.00 (3H, s, 7-OAc), 1.96 (3H, s, 8-OAc), 1.81 (3H, s, 1-OAc), 1.70 (3H, s, H-14), 1.55 (3H, d, J = 1.0 Hz, H-12), 1.38 (3H, d, J = 7.0 Hz, H-9′), 1.19 (3H, d, J = 7.1 Hz, H-10′); ^{13}C NMR ($CDCl_3$, 100 MHz), see Table 1; HRESIMS m/z 828.2685 $[M + Na]^+$ (calcd for $C_{38}H_{47}NO_{18}Na$, 828.2691).

X-ray crystal data of 2: $C_{45}H_{51}NO_{20}$, MW = 925.89, monoclinic, $P2_1$, a = 10.3372(3) Å, b = 16.3424(3) Å, c = 13.1251(4) Å, β = 93.298(1)°, V = 2213.6(1) Å^3, D_x = 1.389 g/cm^3, Z = 2, F(000) = 976. A total of 22 699 reflections, 15 631 of which unique reflections (11 705 observed, $|F_o| > 4\sigma|F_o|$), were measured at 150 K from a 0.20 × 0.10 × 0.10 mm^3 colorless crystal using graphite-monochromated Mo Kα radiation (λ = 0.71073 Å) on a Bruker-Nonius kappa CCD diffractometer. The crystal structure was solved by the direct method using SIR-97,[12] and then all atoms except hydrogen atoms were refined anisotropically by a full-matrix least-squares methods on F^2 using SHELXL-97[13] to give a final R-factor of 0.0604 (R_w = 0.1584 for all data). Crystallographic data of compound **2** have been deposited at the Cambridge Crystallographic Data Centre under the reference number CCDC 816693. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (e-mail: deposit@ccdc.cam.ac.uk).

Bioassays. The cytotoxic activity assay was performed using the colorimetric method of Skehan and co-workers.[14] The human oral epidermal carcinoma (KB), human breast adenocarcinoma (MCF7), and human small cell lung (NCI-H187) cell lines were used. Antiplasmodial activity was evaluated against *Plasmodium falciparum* (K1 multi-drug-resistant strain) according to a standard protocol.[15]

■ ASSOCIATED CONTENT

Ⓢ Supporting Information. ^{1}H and ^{13}C NMR spectra of compounds **1**−**8** (Figures S1−S16), COSY and HMBC correlations of compounds **1** and **6**, and cif files of the X-ray data. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*Tel: (662) 319-0931. Fax: (662) 319-1900. E-mail: s_somyote@ru.ac.th.

■ ACKNOWLEDGMENT

We are grateful to the Thailand Research Fund and Ramkhamhaeng University for financial support. T.L. acknowledges the Royal Golden Jubilee Ph.D. Program, Thailand Research Fund, and the Center of Excellence for Innovation in Chemistry (PERCH-CIC), the Commission on Higher Education, the Ministry of Education, for a scholarship. P.K. gratefully acknowledges the support from the Office of the Higher Education Commission and Mahidol University under the National Research Universities Initiative. We acknowledge the Chemistry Departments of Mahidol and Chiangmai Universities, and Chulabhorn Research Institute for HRMS measurements.

■ REFERENCES

(1) Smitinand, T. *Thai Plant Names (Botanical names-Vernacular names)*; Funny Publishing: Bangkok, 1980; p 255.

(2) Chávez, H.; Valdivia, E.; Estévez-Braun, A.; Ravelo, A. G. *Tetrahedron* **1998**, *54*, 13579–13590.

(3) Alvarenga, N. L.; Velazquez, C. A.; Gomez, R.; Canela, N. J.; Bazzocchi, I. L.; Ferro, E. A. *J. Nat. Prod.* **1999**, *62*, 750–751.

(4) (a) Nunez, M. J.; Guadano, A.; Jimenez, I. A.; Ravelo, A. G.; Gonzalez-Coloma, A.; Bazzocchi, I. L. *J. Nat. Prod.* **2004**, *67*, 14–18. (b) González, A. G.; Jiménez, I. A.; Ravelo, A. G.; Sazatornil, J. G.; Bazzocchi, I. L. *Tetrahedron* **1993**, *49*, 697–702.

(5) Kupchan, S. M.; Komoda, Y.; Branfman, A. R.; Sneden, A. T.; Court, W. A.; Thomas, G. J.; Hintz, H. P. J.; Smith, R. M.; Karim, A.; Howie, G. A.; Verma, A. K.; Nagao, Y.; Dailey, R. G.; Zimmerly, V. A.; Sumner, W. C., Jr. *J. Org. Chem.* **1977**, *42*, 2349–2357.

(6) (a) Itokawa, H.; Shirota, O.; Morita, H.; Takeya, K.; Iitaka, Y. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1247–1254. (b) Han, B. H.; Park, M. K.; Ryu, J. H.; Park, J. H.; Naoki, H. *Phytochemistry* **1990**, *29*, 2303–2307.

(7) Yamada, K.; Sugiura, K.; Shizuri, Y.; Wada, H.; Hirata, Y. *Tetrahedron* **1977**, *33*, 1725–1728.

(8) de Almeida, M. T. R.; Ríos-Luci, C.; Padrón, J. M.; Palermo, J. A. *Phytochemistry* **2010**, *71*, 1741–1748.

(9) Sekar, K. V. S.; Campagne, J.-M.; Sneden, A. T. *Planta Med.* **1996**, *62*, 368–370.

(10) Klass, J.; Tinto, W. F.; Reynolds, W. F.; McLean, S. *J. Nat. Prod.* **1993**, *56*, 946–948.

(11) If the numbering is according to ref 10, compound **8** should be named 8-*epi*-6-*O*-benzoyl-6-deacetylperitassine A.

(12) Altomare, A.; Burla, M. C.; Camalli, M.; Cascarano, G. L.; Giacovazzo, C.; Guagliardi, A.; Moliterni, A. G. G.; Polidori, G.; Spagna, R. *J. Appl. Crystallogr.* **1999**, *32*, 115–119.

(13) Sheldrick, G. M. *Acta Crystallogr.* **2008**, *A64*, 112–122.

(14) Skehan, P.; Storeng, R.; Scudiero, D.; Monks, A.; McMahon, J.; Vistica, D.; Warren, J. T.; Bockesch, H.; Kenney, S.; Boyd, M. R. *J. Natl. Cancer Inst.* **1990**, *82*, 1107–1112.

(15) (a) Trager, W.; Jensen, J. B. *Science* **1976**, *193*, 673–675. (b) Desjardins, R. E.; Canfield, C. J.; Haynes, J. D.; Chulay, J. D. *Antimicrob. Agents Chemother.* **1979**, *16*, 710–718.