

ห้องสมุดงานวิจัย สำนักงานคณะกรรมการวิจัยแห่งชาติ



E41041



BIOACTIVE CONSTITUENTS OF THE ROOTS OF *MAYTENUS*
MEKONGENSIS AND PALLADIUM CATALYZED
CASCADE REACTIONS OF ARYL IODIDES,
ALLENES, AND AMINES

THITIMA LNHATRAKOOL

A DISSERTATION PRESENTED TO RAMKHAMHAENG UNIVERSITY
IN FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY
(APPLIED CHEMISTRY)

2011

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สารออกฤทธิ์จากรากต้นหนามก้านจางและการใช้เพลเลเดียมเป็นตัวเร่งในปฏิกิริยา
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ชิตีมา หลินหะตระกูล

คุษฎีนิพนธ์เสนอต่อมหาวิทยาลัยรามคำแหง
เป็นสาระสมบูรณ์ของการศึกษาตามหลักสูตรปริญญา
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Dissertation Title Bioactive Constituents of the Roots of *Maytenus mekongensis* and Palladium Catalyzed Cascade Reactions of Aryl Iodides, Allenes, and Amines

Student's Name Miss Thitima Lhinhatrakool

Field of Study Applied Chemistry

Advisory Committee

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Ramkhamhaeng University approved this dissertation as a fulfillment of the requirements for the degree of Doctor of Philosophy (Applied Chemistry).

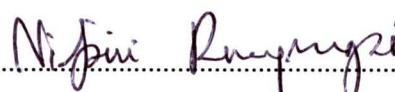
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ABSTRACT

Dissertation Title	Bioactive Constituents of the Roots of <i>Maytenus mekongensis</i> and Palladium Catalyzed Cascade Reactions of Aryl Iodides, Allenes, and Amines
Student's Name	Miss Thitima Lhinhatrakool
Degree Sought	Doctor of Philosophy
Field of Study	Applied Chemistry
Academic Year	2011
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This work consists of two research topics. The first topic is the chemical investigation of the dichloromethane extract of the root of *Maytenus mekongensis* which had led to the isolation of eight new alkaloids, 7-*epi*-euojaponine A (**XIII**), 2-*O*-benzoyl-2-deacetylmayteine (**XIV**), 7-*epi*-5-*O*-benzoyl-5-deacetylperitassine A (**XV**), mekongensine (**XVI**), 7-*epi*-mekongensine (**XVII**), 1-*O*-benzoyl-1-deacetyl mekongensine (**XVIII**), 9'-deacetoxymekongensine (**XIX**), 1-*O*-benzoyl-1-deacetyl-9'-deacetoxymekongensine (**XX**), together with four known alkaloids euonymine (**IX**), 7-*epi*-euonymine (**X**), mayteine (**XI**), and 7-*epi*-mayteine (**XII**). Eight known triterpenes, abruslactone A (**I**), 3 β -29-dihydroxyolean-12-en (**II**), 3 β -hydroxyolean-12-en-29-oic acid (**III**), polpunonic acid (**IV**), salaspermic acid (**V**), cangoronine

(VI), 3-hydroxy-2-oxofriedelan-3-ene-20 α -carboxylic acid (VII), and tingenone (VIII) were also isolated. Compounds XVI-XX were active against *Plasmodium falciparum* with IC₅₀ values of 2.86, 3.60, 3.46, 2.74 and 2.33 $\mu\text{g/mL}$, respectively.

The second research topic is a study of the palladium catalyzed cascade reaction which was carried out using a mono substituted allene, an aryl iodide and secondary amines under Heck reaction condition using Pd(OAc)₂ as catalyst, Cs₂CO₃ as base in MeCN at 80°C. The reaction took place via π -allyl palladium (II) complexes with high regio- and stereoselectivity, to afford nitrogen containing compounds with a trisubstituted double bond in good to moderate yields. The more stable *Z*-isomer was found to be predominant product.

บทคัดย่อ

ชื่อเรื่องคุณฉันทิพนธ์ สารออกฤทธิ์จากรากต้นหนามก้านจางและการใช้เพลลเดียมเป็นตัวเร่งในปฏิกิริยาเชื่อมต่อระหว่างเอริลไอโอโอดี อัลลีนและเอมีน

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งานวิจัยนี้ประกอบด้วยสองส่วน ส่วนแรกคือ การศึกษาองค์ประกอบทางเคมีจากส่วนสกัดชั้นไดคลอโรมีเทน ของส่วนรากของต้นหนามก้านจาง (*Maytenus mekongensis*) สามารถแยกสารอัลคาลอยด์ชนิดใหม่ได้ 8 ชนิด คือ 7-*epi*-cuojaponine A (XIII), 2-*O*-benzoyl-2-deacetylmayteine (XIV), 7-*epi*-5-*O*-benzoyl-5-deacetylperitassine A (XV), mekongensine (XVI), 7-*epi*-mekongensine (XVII), 1-*O*-benzoyl-1-deacetyl mekongensine (XVIII), 9'-deacetoxymekongensine (XIX), 1-*O*-benzoyl-1-deacetyl-9'-deacetoxymekongensine (XX) และสามารถแยกสารอัลคาลอยด์ที่เคยมีรายงานการค้นพบจากแหล่งอื่นอีก 4 ชนิด ได้แก่ euonymine (IX), 7-*epi*-euonymine (X), mayteine (XI), 7-*epi*-mayteine (XII) และสารกลุ่มไตรเทอร์ปีนที่เคยมีรายงานการค้นพบแล้ว จากแหล่งอื่น 8 ชนิด ได้แก่ abruslactone A (I), 3 β ,29-dihydroxyolean-12-en (II), 3 β -hydroxyolean-12-en-29-oic acid (III), polpunonic acid (IV), salaspermic acid (V), cangoronine (VI), 3-hydroxy-2-oxofriedelan-3-ene-20 α -carboxylic acid

(VII) และ tingenone (VIII) สารบริสุทธิ์ XVI-XX แสดงฤทธิ์ต้านเชื้อ *Plasmodium falciparum* โดยแสดงค่า IC₅₀ 2.86, 3.60, 3.46, 2.74 และ 2.33 $\mu\text{g}/\text{mL}$ ตามลำดับ

ส่วนที่สองคือ การศึกษาปฏิกิริยาใหม่ ที่ใช้แพลเลเดียมเป็นตัวเร่งในการเชื่อมต่อระหว่างสารอัลลีน เอริลไอโอโคด์ และเอมีนทุติยภูมิ ภายใต้สภาวะของ Heck โดยใช้ Pd(OAc)₂ เป็นตัวเร่ง Cs₂CO₃ เป็นเบส ในตัวทำละลาย MeCN ที่อุณหภูมิ 80 องศาเซลเซียส ปฏิกิริยาเกิดโดยผ่านสารประกอบเชิงซ้อนไพอัลไลของแพลเลเดียม ปฏิกิริยามีความจำเพาะแบบสเตอริโอซีเลคทีฟ และทำให้เกิดสารผลิตภัณฑ์ที่มีใน โตรเจนเป็นองค์ประกอบและมีพันธะคู่แบบ trisubstituted ในปริมาณสูงถึงปานกลาง โดยซี-ไอโซเมอร์เกิดได้ดีกว่าอี-ไอโซเมอร์

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LIST OF ABBREVIATIONS

<i>s</i>	singlet
<i>d</i>	doublet
<i>t</i>	triplet
<i>q</i>	quartet
<i>qint</i>	quintet
<i>brs</i>	broad singlet
<i>brd</i>	broad doublet
<i>brt</i>	broad triplet
<i>m</i>	multiplet
<i>dd</i>	doublet of doublets
<i>dt</i>	doublet of triplets
<i>td</i>	triplet of doublets
<i>tt</i>	triplet of triplets
<i>ddd</i>	doublet of doublet of doublets
δ	chemical shift
<i>J</i>	coupling constant
<i>m/z</i>	mass-to-charge ratio
mp	melting point
calcd	calculated
equiv	molar equivalents
UV	ultraviolet

LIST OF ABBREVIATIONS (cont.)

V_{\max}	maximum absorption frequencies
α	optical rotation
R_f	in TLC ratio of movement of the band to the front of the solvent
$\mu\text{g/mL}$	microgram per milliliter
μM	micromolar
μg	microgram
mg	milligram
g	gram
kg	kilogram
mL	milliliter
L	liter
mmol	millimol
ppm	part per million
cm^{-1}	reciprocal centimeter (wave number)
t_R	retention time
min.	minute
h	hour
CC	column chromatography
TLC	thin layer chromatography
RP-18	reversed phase C-18

LIST OF ABBREVIATIONS (cont.)

FTIR	fourier transform infrared spectroscopy
HREIMS	high resolution electronic impact mass spectrometry
^1H NMR	proton nuclear magnetic resonance spectroscopy
^{13}C NMR	carbon-13 nuclear magnetic resonance spectroscopy
MHz	mega hertz
HPLC	high performance liquid chromatography
COSY	correlated spectroscopy
HMQC	heteronuclear multiple quantum correlation
HMBC	heteronuclear multiple bond correlation
NOE	nuclear overhauser enhancement
CDCl_3	deuteriochloroform
$\text{MeOH-}d_4$	deuteromethanol
pyridine- d_5	deuteropyridine
TMS	tetramethylsilane
TFP	tri(2-furyl)phosphine
ORTEP	oak ridge thermal ellipsoid plot
Nic	nicotinoyl
OBz	<i>O</i> -benzoyl

Antiplasmodial Sesquiterpene Alkaloids from the Roots of *Maytenus mekongensis*

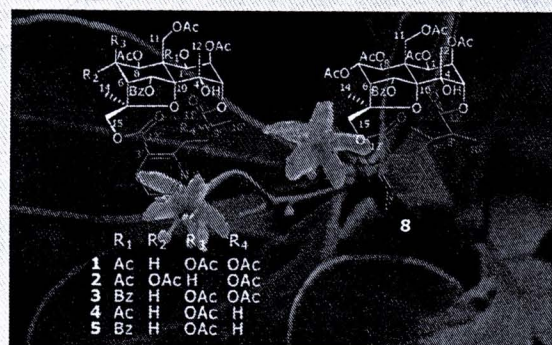
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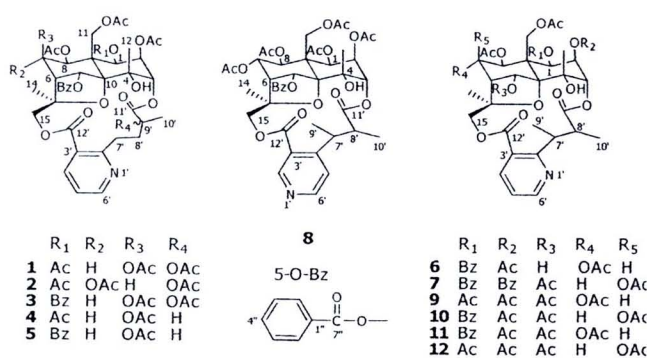
S Supporting Information

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 CH₂Cl₂ 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 C₄₅H₅₁NO₂₀ 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, H₂-15) and at δ_H 5.20 and 4.55 (both d, J = 13.4 Hz, H₂-11), implied the presence of a dihydro-β-agarofuran moiety commonly found in sesquiterpene pyridine alkaloids from *Maytenus* species.⁶ HMBC



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 (H₃-10') and two sets of mutually coupled multiplets of the nonequivalent methylene protons (H₂-7') at δ_H 3.71 and 3.01 and of H₂-8' at δ_H 2.65 and 2.17, in addition to the HMBC correlations of H₃-10'/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)

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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}	69.8	68.4	69.8	68.4	68.5
3	77.9	77.3	77.6	76.1	76.1	74.3 ^{a-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 ^{-m}	51.4	49.7	49.4
7	68.8	73.1	68.8	69.3 ^{a-i}	69.1	73.2	68.9	73.2	73.6
8	71.9	74.8	72.7	71.1	71.8	74.2 ^{a-b}	71.3	74.1	73.9
9	52.4	51.8	52.8	52.2	52.6	51.4 ^{-m}	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}	36.1	36.5	33.2	36.4
8'	37.7	44.8	37.5	33.3	33.4 ^{j-m}	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 ^{-m}	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 ^{-m}	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-c}	20.9	20.9	21.0 ^{a-d}	20.9	20.8		21.0	21.0 ^{a-e}
	168.3	168.3	168.0	168.7 ^{a-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-d}	21.0	20.8	21.0	20.9	20.8 ^{a-e}
	170.2	170.0	170.0	170.1 ^{a-f}	170.1 ^{a-f}	169.8	169.9	169.7 ^{-m}	169.8
8-OAc	20.5	20.7 ^{a-h}	19.8 ^{a-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 ^{-m}	169.6
11-OAc	21.4 ^{a-c}	21.3 ^{a-h}	21.5 ^{a-i}	21.4	21.5	21.3	21.3	21.3	21.2
	170.1	169.7	170.2	170.2	170.2 ^{a-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 H₂-8'/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 H₃-12 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-deacetylwilfordine⁹ and was given the name mekongensine.

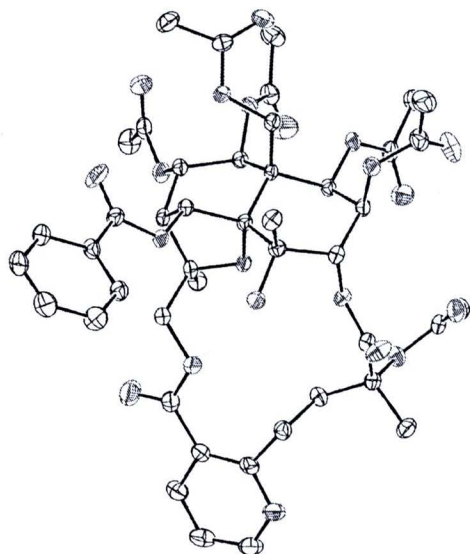


Figure 1. ORTEP drawing of **2**. Hydrogen atoms are omitted for clarity.

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 ^1H 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 H₃-12, 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 $\text{C}_{50}\text{H}_{53}\text{NO}_{20}$, and it showed ^1H and ^{13}C NMR signals similar to those of **1** and **2**. However, the ^1H 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 $\text{C}_{43}\text{H}_{49}\text{NO}_{18}$, and the ^1H 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 ^1H – ^1H 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 ^1H – ^1H 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 H₂-15/C-12'' and of H-3/C-11'', respectively. Thus, compound **4** was determined to be 9'-deacetoymekongensine.

Compound **5**, isolated as a colorless, amorphous solid with the molecular formula $\text{C}_{48}\text{H}_{51}\text{NO}_{18}$, showed sets of ^1H and ^{13}C NMR signals similar to those of **4**. The ^1H 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 ^1H 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'-deacetoymekongensine.

Compound **6** was isolated as a colorless, amorphous solid with the molecular formula $\text{C}_{41}\text{H}_{47}\text{NO}_{17}$ (HRESIMS). The FTIR spectrum showed absorption bands of OH (ν_{max} 3400 cm^{-1}) and ester carbonyl (ν_{max} 1748 cm^{-1}) functions. The ^1H NMR spectrum of compound **6** revealed four acetyl groups (δ_{H} 2.24, 2.13, 1.92, and 1.36). The ^1H – ^1H 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 moiety⁶ was implied from the ^1H – ^1H 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 ^1H – ^{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 H₂-15 (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 ^1H and ^{13}C NMR signals are shown in the Experimental Section and Table 1, and most of the ^1H 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 H₃-12 and provided further support to the assignment. Compound **6** was thus concluded to be 7-epi-euojaponine A.^{6b}

Compound **7**, $\text{C}_{48}\text{H}_{51}\text{NO}_{18}$, 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(S)–OAc linkage. Most of the ^1H 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 $[\text{M} + \text{H}]^+$ ion at m/z 868.3049 corresponding to the molecular formula $\text{C}_{43}\text{H}_{49}\text{NO}_{18}$. The ^1H NMR spectrum indicated five acetyl groups and one benzoyl group. The ^1H – ^1H COSY spectrum indicated the connectivity between protons of the dihydroagarofuran 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 H₂-15 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 $\text{C}_{38}\text{H}_{47}\text{NO}_{18}$ 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 $\mu\text{g}/\text{mL}$, 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 $\mu\text{g}/\text{mL}$.

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 \times 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 $^\circ\text{C}$; $[\alpha]_{\text{D}}^{25} +11.8$ (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, $J = 4.8, 1.8, \text{H-6}'$), 8.18 (2H, dd, $J = 7.6, 1.3$ Hz, H-2'',6''), 8.13 (1H, dd, $J = 7.8, 1.8, \text{H-4}'$), 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, $J = 7.8, 4.8, \text{H-5}'$), 7.01 (1H, brs, H-5), 5.60 (1H, dd, $J = 6.6, 3.8, \text{H-7}$), 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 [$\text{M} + \text{Na}$]⁺ (calcd for $\text{C}_{45}\text{H}_{51}\text{NO}_{20}\text{Na}$, 948.2902).

7-*epi*-Mekongensine (**2**): colorless, rhombic crystals from MeOH– H_2O ; mp 280–282 $^\circ\text{C}$; $[\alpha]_{\text{D}}^{25} +7.2$ (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; $[\alpha]_D^{20} +22.3$ (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-S'), 6.95 (1H, s, H-S), 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'-Deacetoymekongensine (4): colorless, amorphous solid; mp 134–136 °C; $[\alpha]_D^{25} -7.1$ (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-S'), 6.98 (1H, s, H-S), 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'-deacetoymekongensine (5): colorless, amorphous solid; mp 152–154 °C; $[\alpha]_D^{25} +3.4$ (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-S'), 6.98 (1H, s, H-S), 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; $[\alpha]_D^{25} +25.7$ (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-S'), 6.12 (1H, d, $J = 2.9$ Hz, S-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; $[\alpha]_D^{25} +14.2$ (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''), 7.46 (1H, brt, $J = 7.8$ Hz, H-3'',5''), 7.61 (1H, brt, $J = 7.4$ Hz, H-4''), 7.46 (1H, d, $J = 7.3$ Hz, H-4''), 7.28 (2H, m, H-3'',5''), 7.27 (1H, t, $J = 4.9$ Hz, H-S'), 7.04 (1H, brs, H-S), 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; $[\alpha]_D^{25} -17.5$ (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-S'), 6.75 (1H, brs, H-S), 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; $[\alpha]_D^{25} -18.6$ (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-S'), 6.62 (1H, s, H-S), 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 $[\text{M} + \text{Na}]^+$ (calcd for $\text{C}_{38}\text{H}_{47}\text{NO}_{18}\text{Na}$, 828.2691).

X-ray crystal data of 2: $\text{C}_{45}\text{H}_{51}\text{NO}_{20}$, MW = 925.89, monoclinic, $P2_1$, $a = 10.3372(3)$ Å, $b = 16.3424(3)$ Å, $c = 13.1251(4)$ Å, $\beta = 93.298(1)^\circ$, $V = 2213.6(1)$ Å³, $D_x = 1.389$ g/cm³, $Z = 2$, $F(000) = 976$. 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 $0.20 \times 0.10 \times 0.10$ mm³ colorless crystal using graphite-monochromated Mo $K\alpha$ radiation ($\lambda = 0.71073$ 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-97¹³ 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* (KI multi-drug-resistant strain) according to a standard protocol.¹⁵

■ ASSOCIATED CONTENT

Supporting Information. ^1H 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>.

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THE RELEVANCE OF THIS RESEARCH WORK

This thesis consists of two parts. The first part is the chemical investigation of the dichloromethane extract of the roots of *Maytenus mekongensis* which led to the isolation of several pure compounds which might be potentially useful lead compounds for further anti-cancer and anti-plasmodium drug development. The work will contribute significantly to scientific basis of traditional medicine.

The second part is palladium catalyzed cascade reaction which although is the basic research but was aimed on the development of synthetic method to synthesize biologically active compounds for pharmaceutical purposes. The work will further be the goal of developing new synthetic methodology.