2021

α-glucosidase inhibitors from dendrobium delacourii, dendrobium gibsonii and aerides multiflora

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Recommended Citation

Thant, May Thazin, "α-glucosidase inhibitors from dendrobium delacourii, dendrobium gibsonii and aerides multiflora" (2021). *Chulalongkorn University Theses and Dissertations (Chula ETD)*. 4849.
https://digital.car.chula.ac.th/chulaetd/4849

α-GLUCOSIDASE INHIBITORS FROM *DENDROBIUM DELACOURII*, *DENDROBIUM GIBSONII* AND *AERIDES MULTIFLORA*

Miss May Thazin Thant

A Dissertation Submitted in Partial Fulfillment of the Requirements
for the Degree of Doctor of Philosophy in Pharmaceutical Sciences and Technology
Common Course
FACULTY OF PHARMACEUTICAL SCIENCES
Chulalongkorn University
Academic Year 2020

สารยับยั้งเอนไซม์แอลฟากลูโคสิเดสจากเอื้องดอกมะขาม เอื้องคำตาและมาลัยแดง

น.ส.เมย์ ทาซิน ทันต์

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรดุษฎีบัณฑิต
สาขาวิชาเภสัชศาสตร์และเทคโนโลยี ไม่สังกัดภาควิชา/เทียบเท่า
คณะเภสัชศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย
ปีการศึกษา 2563

Thesis Title α-GLUCOSIDASE INHIBITORS FROM *DENDROBIUM DELACOURII*, *DENDROBIUM GIBSONII* AND *AERIDES MULTIFLORA*
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เมย์ ทาซิน ทันต์ : สารยับยั้งเอนไซม์แอลฟากลูโคสิเดสจากเอื้องดอกมะขาม เอื้องคำตาและมาลัยแดง. (α-GLUCOSIDASE INHIBITORS FROM *DENDROBIUM DELACOURII*, *DENDROBIUM GIBSONII* AND *AERIDES MULTIFLORA*) อ.ที่ปรึกษาหลัก : ศ.ภก. ดร.กิตติศักดิ์ ลิขิตวิทยาวุฒิ, อ.ที่ปรึกษาร่วม : รศ. ภก. ดร.บุญชู ศรีตุลารักษ์

การศึกษาองค์ประกอบทางเคมีที่มีฤทธิ์ยับยั้งแอลฟากลูโคซิเดสจากพืชสามชนิดในวงศ์กล้วยไม้คือ เอื้องดอกมะขาม, เอื้องคำตา และ มาลัยแดง สามารถแยกสารและหาโครงสร้างได้ 30 ชนิด จำแนกได้เป็นสาร 11 ชนิดจากเอื้องดอกมะขามได้แก่ hircinol, ephemeranthoquinone, densiflorol B, moscatin, 4,9-dimethoxy-2,5-phenanthrenediol, gigantol, batatasin III, lusianthridin, 4,4',7,7'-tetrahydroxy-2,2'-dimethoxy-9,9',10,10'-tetrahydro-1,1'-biphenanthrene, phoyunnanin E, และ phoyunnanin C สารจากเอื้องคำตาแบ่งเป็นสารใหม่ 2 ชนิดได้แก่ dihydrodengibsinin และ dendrogibsol และสารอีก 7 ชนิดคือ ephemeranthol A, dengibsinin, nobilone, aloifol I, lusianthridin, denchrysan A และ 4-methoxy-*9H*-fluorene-2,5,9-triol สารจากมาลัยแดงแบ่งเป็นสารใหม่ 4 ชนิดได้แก่ aerimultin A, aerimultin B, aerimultin C และ dihydrosinapyl dihydroferulate และสารอีก 6 ชนิดคือ methoxycoelonin, gigantol, imbricatin, agrostonin, dihydroconiferyl dihydro-*p*-coumarate และ 5-methoxy-9,10-dihydrophenanthrene-2,3,7-triol. เมื่อนำสารที่แยกได้มาทดสอบฤทธิ์ยับยั้งแอลฟากลูโคซิเดส เปรียบเทียบกับยา acarbose (ค่า IC_{50} 514.4 ± 9.2 ไมโครโมลาร์) พบว่าสารซึ่งมีโครงสร้างเป็นไดเมอร์ 8 ชนิดมีฤทธิ์แรง (ค่า IC_{50} 5.2 – 77.0 ไมโครโมลาร์) ได้แก่ 4,4',7,7'-tetrahydroxy-2,2'-dimethoxy-9,9',10,10'-tetrahydro-1,1'-biphenanthrene, phoyunnanin E, phoyunnanin C, dendrogibsol, aerimultins A-C และ agrostonin สาร 7 ชนิดซึ่งมีโครงสร้างเป็นโมโนเมอร์ มีฤทธิ์ปานกลาง (ค่า IC_{50} 115.2 - 390.1 ไมโครโมลาร์) ซึ่งได้แก่ moscatin, gigantol, lusianthridin, 6-methoxycoelonin, imbricatin, dihydroconiferyl dihydro-*p*-coumarate และ 5-methoxy-9,10-dihydrophenanthrene-2,3,7-triol สารที่ไม่มีฤทธิ์ (ค่ายับยั้งน้อยกว่าร้อยละ 50 ที่ความเข้มข้น 100 ไมโครกรัม/มิลลิลิตร) ได้แก่ hircinol, ephemeranthoquinone, densiflorol B, 4,9-dimethoxy,2,5-phenanthrenediol, batatasin III, dihydrodengibsinin, ephemeranthol A, dengibsinin, nobilone, aloifol I, dechrysan A, 4-methoxy-*9H*-fluorene 2,5,9-triol และ dihydrosinapyl dihydroferulate เมื่อนำสารที่มีฤทธิ์แรงที่สุดซึ่งได้แก่ phoyunnanin C, phoyunnanin E, dendrogibsol และ aerimultin C มาศึกษากลไกการออกฤทธิ์พบว่าสารดังกล่าวทั้งหมดออกฤทธิ์ยับยั้งแบบไม่แข่งขัน และมีสามารถจับกับเอนไซม์แอลฟากลูโคซิเดสได้ดีกว่ายา acarbose

สาขาวิชา	เภสัชศาสตร์และเทคโนโลยี	ลายมือชื่อนิสิต ....
ปีการศึกษา	2563	ลายมือชื่อ อ.ที่ปรึกษาหลัก ....
		ลายมือชื่อ อ.ที่ปรึกษาร่วม ....

6176459833 : MAJOR PHARMACEUTICAL SCIENCES AND TECHNOLOGY

KEYWORD: α-glucosidase, Dendrobium delacourii, Dendrobium gibsonii, Aerides multiflora

May Thazin Thant : α-GLUCOSIDASE INHIBITORS FROM *DENDROBIUM DELACOURII*, *DENDROBIUM GIBSONII* AND *AERIDES MULTIFLORA*. Advisor: Prof. KITTISAK LIKHITWITAYAWUID, Ph.D. Co-advisor: Assoc. Prof. BOONCHOO SRITULARAK, Ph.D.

In this study, three plants from the Orchidaceae family, i.e., *Dendrobium delacourii, Dendrobium gibsonii*, and *Aerides multiflora*, were investigated for their chemical constituents and α-glucosidase inhibitory activities. A total of thirty compounds were isolated and structurally characterized. Eleven known compounds were identified from *Dendrobium delacourii*, including hircinol, ephemeranthoquinone, densiflorol B, moscatin, 4,9-dimethoxy-2,5-phenanthrenediol, gigantol, batatasin III, lusianthridin, 4,4',7,7'-tetrahydroxy-2,2'-dimethoxy-9,9',10,10'-tetrahydro-1,1'-biphenanthrene, phoyunnanin E, and phoyunnanin C. Two new compounds, i.e., dihydrodengibsinin and dendrogibsol, were isolated from *Dendrobium gibsonii*, along with seven known compounds including ephemeranthol A, dengibsinin, nobilone, aloifol I, lusianthridin, denchrysan A, and 4-methoxy-9*H*-fluorene-2,5,9-triol. Four new compounds, i.e., aerimultins A-C and dihydrosinapyl dihydroferulate, and six known compounds, which include methoxycoelonin, gigantol, imbricatin, agrostonin, dihydroconiferyl dihydro-*p*-coumarate and 5-methoxy-9,10-dihydrophenanthrene-2,3,7-triol, were obtained from *Aerides multiflora*. All the isolated compounds were evaluated for α-glucosidase inhibitory activity. When compared with the drug acarbose (IC_{50} value 514.4 ± 9.2 µM), eight dimeric compounds showed potent activity: 4,4',7,7'-tetrahydroxy-2,2'-dimethoxy-9,9',10,10'-tetrahydro-1,1'-biphenanthrene, phoyunnanin E, phoyunnanin C, dendrogibsol, aerimultins A-C and agrostonin) (IC_{50} values 5.2 – 77.0 µM). Seven monomeric compounds exhibited moderate activity: moscatin, gigantol, lusianthridin, 6-methoxycoelonin, imbricatin, dihydroconiferyl dihydro-*p*-coumarate, and 5-methoxy-9,10-dihydrophenanthrene-2,3,7-triol (IC_{50} values 115.2 - 390.1 µM). The other compounds displayed no activity, including hircinol, ephemeranthoquinone, densiflorol B, 4,9-dimethoxy-2,5-phenanthrenediol, batatasin III, dihydrodengibsinin, ephemeranthol A, dengibsinin, nobilone, aloifol I, dechrysan A, 4-methoxy-9*H*-fluorene 2,5,9-triol, and dihydrosinapyl dihydroferulate (less than 50 % inhibition at 100 µg/ml). The kinetic studies on the most potent compounds, i.e., phoyunnanin C, phoyunnanin E, dendrogibsol, and aerimultin C revealed that all were non-competitive inhibitors with a higher affinity to the α-glucosidase enzyme than the drug acarbose.

Field of Study:	Pharmaceutical Sciences and Technology	Student's Signature ....
Academic Year:	2020	Advisor's Signature ....
		Co-advisor's Signature ....

ACKNOWLEDGEMENTS

First, I wish to express my deep respect and gratitude towards my thesis advisor, Professor Dr. Kittisak Likhitwitayawuid and my co-advisor Associate Professor Dr. Boonchoo Sritularak, for their excellent supervision, invaluable suggestions, encouragement, constructive criticism, and continuous support throughout my research work.

I would like to express my sincere thanks to the members of my thesis committee for their inestimable advice. My special thanks go to the staff members of the Department of Pharmacognosy and Pharmaceutical Botany, Faculty of Pharmaceutical Sciences, Chulalongkorn University, for their kind help and support.

My gratitude is also expressed to my seniors and friends in Thailand for their friendly manners, kindness, and help. I am also thankful to all my teachers, seniors, and friends from the University of Pharmacy, Yangon, for their encouragement.

I am grateful for financial support in the form of a CU-ASEAN Ph.D. scholarship from the Graduate School, Chulalongkorn University.

Finally, my warmest gratitude towards my family for their love, support, and encouragement whenever I feel weary.

May Thazin Thant

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ABBREVIATIONS AND SYMBOLS

Acetone-d_6 = Deuterated acetone

AcO = Acetone

APCI-MS = Atmospheric Pressure Chemical Ionization Mass Spectrometry

br s = Broad singlet (for NMR spectra)

°C = Degree celsius

CC = Column chromatography

$CDCl_3$ = Deuterated chloroform

CH_2Cl_2 = Dichloromethane

cm = Centimeter

^{13}C-NMR = Carbon-13 Nuclear Magnetic Resonance

1-D NMR = One-dimensional Nuclear Magnetic Resonance

2-D NMR = Two-dimensional Nuclear Magnetic Resonance

d = Doublet (for NMR spectra)

dd = Doublet of doublets (for NMR spectra)

δ = Chemical shift

DMSO-d_6 = Deuterated dimethylsulfoxide

ε = Molar absorptivity

ESI-MS = Electrospray Ionization Mass Spectrometry

EtOAc = Ethyl acetate

FCC = Flash Column Chromatography

g = Gram

Gal = Galactose

GF = Gel Filtration

Glc = Glucose
HMBC = ^{1}H-detected Heteronuclear Multiple Bond Correlation
HR-ESI-MS = High Resolution Electrospray Ionization Mass Spectrometry
^{1}H-NMR = Proton Nuclear Magnetic Resonance
HSQC = ^{1}H-detected Heteronuclear Single Quantum Coherence
Hz = Hertz
IC_{50} = Concentration exhibiting 50% inhibition
IR = Infrared
J = Coupling constant
Kg = Kilogram
L = Liter
λ_{max} = Wavelength at maximal absorption
$[M-H]^-$ = Deprotonated molecular ion
$[M+H]^+$ = Protonated molecular ion
$[M+Na]^+$ = Sodium-adduct molecular ion
m = Multiplet (for NMR spectra)
MeOH = Methanol
mg = Milligram
µg = Microgram
min = Minute
ml = Milliliter
µl = Microliter
µM = Micromolar
mm = Millimeter
mM = Millimolar
MS = Mass spectrum

MW = Molecular weight

m/z = Mass to charge ratio

NA = No inhibitory activity

nm = Nanometer

nM = Nanomolar

NMR = Nuclear Magnetic Resonance

NOESY = Nuclear Overhauser Effect Spectroscopy

ν_{max} = Wave number at maximal absorption

OEt = Ethoxy group

OMe = Methoxy group

Rha = Rhamnose

s = Singlet (for NMR spectra)

t = Triplet (for NMR spectra)

TLC = Thin Layer Chromatography

UV-VIS = Ultraviolet and Visible spectrophotometry

VLC = Vacuum Liquid Column Chromatography

Xyl = Xylose

CHAPTER I

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disease associated with hyperglycemia which is due to deficiency in insulin secretion or lack of insulin action (Abo, 2008). The complications of DM can reduce life expectancy and increase health-care costs. In 2017, globally, about 8.8% of adult population suffered from diabetes, and this number is projected to rise to 9.9% by 2045 (Standl *et al.*, 2019). DM has become the world’s main disablers and killers, with significantly high rates of morbidity and mortality. Four types of DM are recognized, including (1) type I DM (insulin dependent diabetes mellitus), (2) type II DM (non-insulin dependent diabetes mellitus), (3) gestational DM (GDM), and (4) diabetes due to other causes such as genetic disorders or medicines. Statistics show that about 90% of all diabetic patients suffer from type II DM (Rosak & Mertes, 2012).

Antidiabetic drugs can be classified into several classes, including insulin secretagogues (e.g. glipizide and repaglinide), insulin sensitizers (e.g. pioglitazone and metformin), α-glucosidase inhibitors (e.g. acarbose and voglibose), dipeptidyl peptidase-4 (DPP-4) inhibitors (e.g. saxagliptin and linagliptin) and sodium glucose cotransporter-2 (SGLT-2) inhibitors (e.g. empagliflozin and canagliflusin) (Khalil & Ebeid, 2016).

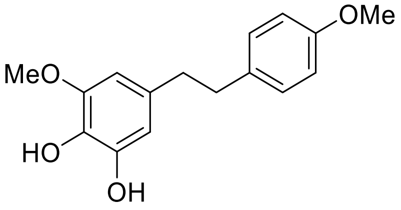
α-Glucosidase inhibitors (AGIs), such as acarbose and miglitol, have been used in combination with other anti-DM drugs for the treatment of type II DM (Baron, 1998). α-Glucosidase is a key enzyme produced from intestinal cells and is responsible for converting oligosaccharides into monosaccharides (glucose) (Peng *et al.*, 2016). Thus, glucose absorption can be reduced by inhibition of this enzyme (Sugihara *et al.*, 2014). However, these AGIs have several undesirable side-effects including bloating, flatulence, diarrhea, and abdominal pain (Feng *et al.*, 2011).

Recently, several AGIs of botanical origin have been reported, and the family Orchidaceae has been found to be a rich source (Kumar *et al.*, 2011). Orchidaceae is one of the largest families of flowering plants (Sut *et al.*, 2017), and several of its members have been traditionally used for treating various diseases, such as diabetes, inflammations, and infections (Bulpitt *et al.*, 2007). Previous studies revealed that orchids produce various classes of secondary metabolites, such as stilbenoids, anthraquinones, flavonoids, terpenoids, steroids, and alkaloids (Nongdam, 2014). So far, the AGIs obtained from Orchidaceae can be chemically classified into 7 major groups: (i) bibenzyl derivatives, for example, 4,5-dihydroxy-3,4′-dimethoxybibenzyl and dendrofalconerol A from *Dendrobium tortile*, gigantol from *Dendrobium devonianum*, batatasin III and dendrosinen B from *Dendrobium infundibulum,* and dendroscabrol B from *Dendrobium scabrilingue* (Limpanit *et al.*, 2016a; Na Ranong *et al.*, 2019; Sarakulwattana *et al.*, 2020; Sun *et al.*, 2014); (ii) phenanthrene-related compounds, for example, 4,5-dihydroxy-2-methoxy-9,10-dihydrophenanthrene from *Dendrobium christyanum*, lusianthridin, and coelonin from *Dendrobium scabrilingue* (San *et al.,* 2020; Sarakulwattana *et al.,* 2020), bobulretin A from *Bulbophyllum retusiusculum* (Sun *et al.,* 2018), gastrobellinol C from *Gastrochilus bellinus* (San *et al.*, 2021), and 5-methoxy-7-hydroxy-9,10-dihydro-1,4-phenanthrenequinone from *Dendrobium formosum* (Inthongkaew *et al.*, 2017); (iii) flavonoids, for example, rutin from *Pholida chinensis*, naringenin from *Dendrobium densiflorum*, and 5-hydroxy-3-methoxy-flavone-7-*O*-[β-D-apiosyl-(1→6)]-β-D-glucoside from *Dendrobium devonianum* (Fan *et al.,* 2001; Ren *et al.*, 2020; Sun *et al.*, 2014); (iv) diterpene glycosides, for example, flifimdioside A from *Flickingeria fimbriata* (Chen *et al.*, 2018); (v) lignans, for example, syringaresinol-4′-*O*-D-glucopyranoside from *Flickingeria fimbriata* (Chen *et al.*, 2018); (vi) phenylpropanoids, for example, coniferyl aldehyde from *Gastrochilus bellinus* (San *et al.*, 2021); and (vii) benzylmalate glycosides, for example, arundinoside D from *Arundina graminifolia* (Auberon *et al.*, 2019). These are illustrated in **Table 1** and **Figure 1**.

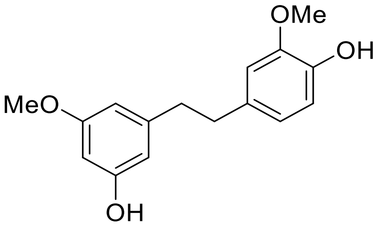
Table 1 Examples of α-glucosidase inhibitors from Orchidaceae family

Category and compound	Plant	Parts used	References
(i) Bibenzyl derivatives			
4,5-Dihydroxy-3,4′-dimethoxybibenzyl [**1**]	*Dendrobium tortile*	Whole plant	(Limpanit *et al.*, 2016a)
Gigantol [**2**]	*D. devonianum*	Whole plant	(Sun *et al.*, 2014)
Batatasin III [**3**]	*D. infundibulum*	Whole plant	(Na Ranong *et al.*, 2019)
Dendrosinen B [**4**]	*D. infundibulum*	Whole plant	(Na Ranong *et al.*, 2019)
Dendroscabrol B [**5**]	*D. scabrilingue*	Whole plant	(Sarakulwattana *et al.*, 2020)
Dendrofalconerol A [**6**]	*D. tortile*	Whole plant	(Limpanit *et al.*, 2016a)
(ii) Phenanthrene-related compounds			
4,5-Dihydroxy-2-methoxy-9,10-dihydrophenanthrene [**7**]	*D. christyanum*	Root	(San *et al.*, 2020)
Lusianthridin [**8**]	*D. scabrilingue*	Whole plant	(Sarakulwattana *et al.*, 2020)
Coelonin [**9**]	*D. scabrilingue*	Whole plant	(Sarakulwattana *et al.*, 2020)
Bobulretin A [**10**]	*Bulbophyllum retusiusculum*	Whole plant	(Sun *et al.*, 2018)

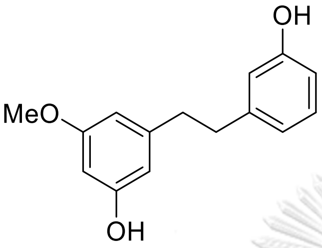
Category and compound	Plant	Parts used	References
Gastrobellinol C [**11**]	*Gastrochilus bellinus*	Whole plant	(San *et al.*, 2021)
5-Methoxy-7-hydroxy-9,10-dihydro-1,4-phenanthrenequinone [**12**]	*D. formosum*	stem	(Inthongkaew *et al.*, 2017)
(iii) Flavonoids			
Rutin [**13**]	*Pholidota chinensis*	Whole plant	(Ren *et al.*, 2020)
Naringenin [**14**]	*D. densiflorum*	Stem	(Fan *et al.*, 2001)
5-hydroxy-3-methoxyflavone-7-*O*-[β-D-apiosyl-(1→6)]-β-D-glucoside [**15**]	*D. devonianum*	Whole plant	(Sun *et al.*, 2014)
(iv) Diterpene glycosides			
Flifimdioside A [**16**]	*Flickingeria fimbriata*	Stem	(Chen *et al.*, 2018)
(v) Lignans			
Syringaresinol-4′-*O*-D-glucopyranoside [**17**]	*F. fimbriata*	Stem	(Chen *et al.*, 2018)
(vi) Phenylpropanoids			
Coniferyl aldehyde [**18**]	*Gastrochilus bellinus*	Whole plant	(San *et al.*, 2021)
(vii) Benzylmalate glycosides			
Arundinoside D [**19**]	*Arundina graminifolia*	Root and rhizomes	(Auberon *et al.*, 2019)



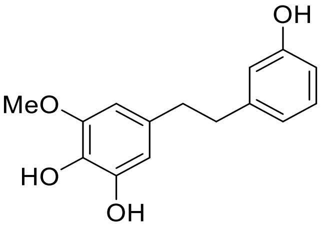
4,5-Dihydroxy-3,4′-dimethoxybibenzyl [**1**]



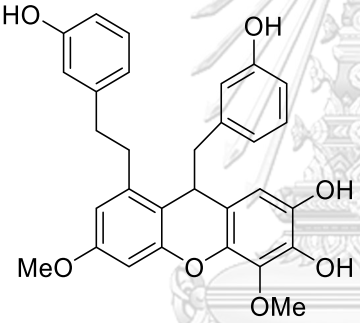
Gigantol [**2**]



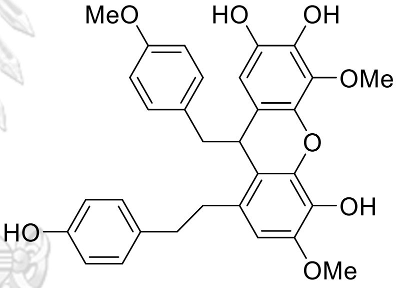
Batatasin III [**3**]



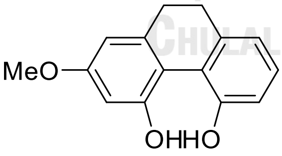
Dendrosinen B [**4**]

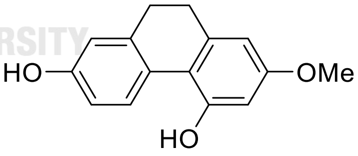


Dendroscabrol B [**5**]



Dendrofalconerol A [**6**]

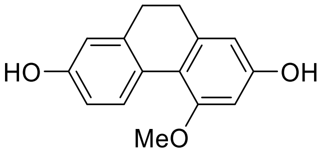




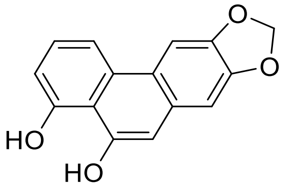
4,5-Dihydroxy-2-methoxy-
9,10-dihydrophenanthrene [**7**]

Lusianthridin [**8**]

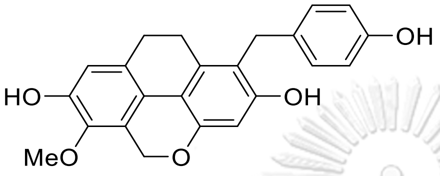
Figure 1 Structures of α-glucosidase inhibitors from Orchidaceae family



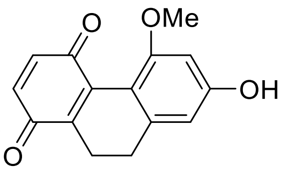
Coelonin [**9**]



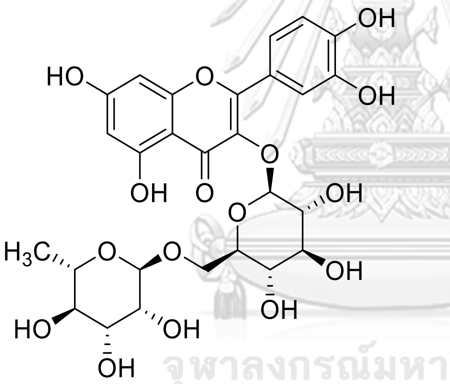
Bobulretin A [**10**]



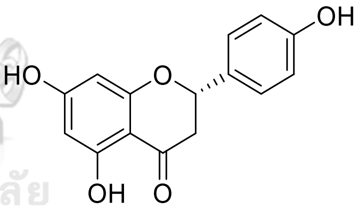
Gastrobellinol C [**11**]



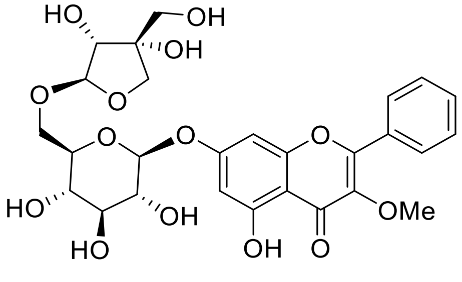
5-Methoxy-7-hydroxy-9,10-dihydro-1,4-phenanthrenequinone [**12**]



Rutin [**13**]

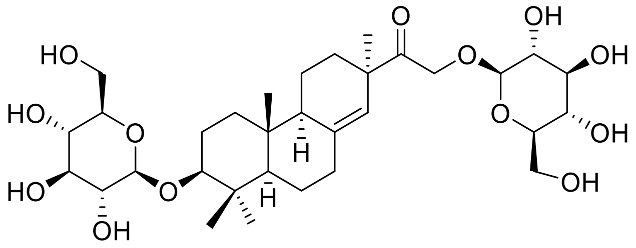


Naringenin [**14**]

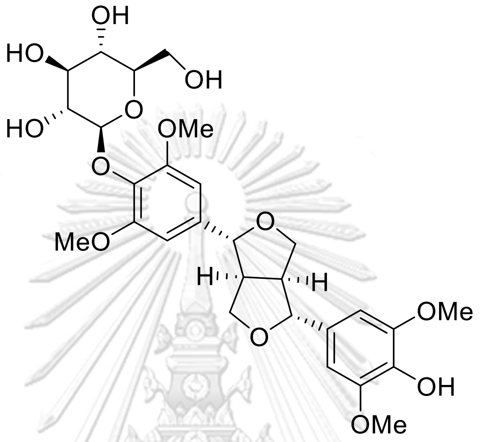


5-Hydroxy-3-methoxyflavone-7-*O*-[β-D-apiosyl-(1→6)]-β-D-glucoside [**15**]

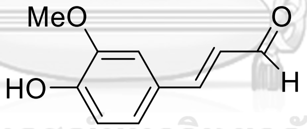
Figure 1 (continued)



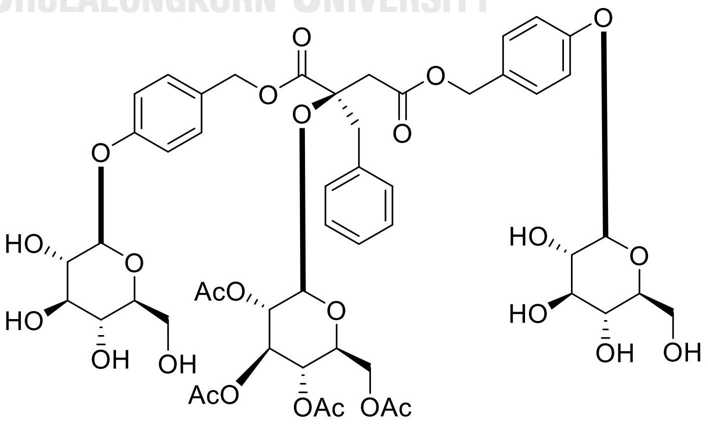
Flifimdioside A [**16**]



Syringaresinol-4′-*O*-D-glucopyranoside [**17**]



Coniferyl aldehyde [**18**]



Arundinoside D [**19**]

Figure 1 (continued)

In primary screening, the MeOH extracts of *Dendrobium delacourii, Dendrobium gibsonii*, and *Aerides multiflora* (each at 100 µg/mL) exhibited inhibitory activity against α-glucosidase enzyme, with 80 %, 79 %, and 82 % inhibition, respectively (see the Experimental), and thus were subjected to further studies to identify the active principles. In this study, the following objectives have been put forwards:

1. To isolate, purify, and determine the structures of the chemical constituents of *Dendrobium delacourii, D. gibsonii* and *Aerides multiflora.*
2. To evaluate α-glucosidase inhibitory activity of the isolated compounds.

CHAPTER II

LITERATURE REVIEW

1 Botanical considerations and traditional uses

Several plants from different genera of the Orchidaceae family have been used in Traditional Chinese Medicine (Dahlgren *et al.*, 2012). Examples are *Aerides odoratum*, *Bulbophyllum odoratissimum, Dendrobium nobile, Flickingeria fugax*, and *Pholidota articulata* (Pant, 2013). However, there have been relatively few reports of their bioactive constituents (Gutiérrez, 2010). This section describes the botanical characteristics and traditional medicinal uses of *Dendrobium delacourii*, *Dendrobium gibsonii*, and *Aerides multiflora*.

1.1 *Dendrobium*

Dendrobium is one of the largest genera in the family Orchidaceae. The genus consists of more than 1400 species, with about 1,217 species distributed in the tropical and subtropical areas (Yuan *et al.*, 2019). Several plants in this genus are collectively known as the crude drug “Shi-Hu” in Traditional Chinese Medicine (TCM). Studies have shown that these plants contain a wide variety of secondary metabolites, such as phenanthrenes, bibenzyls, fluorenones, sesquiterpenes, and alkaloids (Cardile *et al.*, 2020), with various biological activities, including cytotoxicity, anti-inflammatory, antifibrotic, immunomodulatory, and antioxidant activities (Zhang *et al.*, 2019). Although the medicinal potentials of *Dendrobium* have attracted immense research interest, so far only a few species have been fully investigated (Chen *et al.*, 2014).

1.1.1 *Dendrobium delacourii*

Dendrobium delacourii Guillaumin, also known as Delacour's Dendrobium, is called in Thai as Ueang Dok Ma Kham. It is an epiphytic ornamental plant with no records of medicinal uses. Recently, this plant species has been suggested to be treated as a variety of *Dendrobium venustum*, and the name

Dendrobium venustum var. *delacourii* has been proposed (Prommanut, 2017). *Dendrobium delacourii* has short pseudobulbs. The flower is yellow, having untwisted petals and bright yellow flabellate labellum with reddish-brown lines along the veins **(Figure 2)**. *D. delacourii* is distributed throughout Thailand, Myanmar, Laos, and Vietnam. Up to the present, there have been no previous phytochemical and biological studies on this plant.

Figure 2 *Dendrobium delacourii* Guillaumin

1.1.2 *Dendrobium gibsonii*

Dendrobium gibsonii Paxton, known in Thai as Ueang Kham Ta, has slender stems, lanceolate leaves, and orange to yellow-colored flowers **(Figure 3).** The common name is Gibson's Dendrobium. It is widely distributed in India, Nepal, Bhutan, Myanmar, Thailand, China, and Vietnam. The plant is regarded as a fragrant orchid in India, and its volatile oils are prepared from the floral parts by hydro and steam distillation, maceration, or supercritical fluid extraction (Singh *et al.*, 2016). In TCM, *D. gibsonii* is used as an immunostimulant (Cheng *et al.*, 2019; De, 2020; Wang *et al.*, 2018). Previous reports on this plant revealed the presence of two fluorenone derivatives, namely, dengibsin and dengibsinin (Talapatra *et al.*, 1988; Talapatra *et al.*, 1985). However, there have been no studies on the α-glucosidase inhibitory activity of this plant.

Figure 3 *Dendrobium gibsonii* Paxton

1.2 *Aerides*

Aerides is a small epiphytic orchid genus in the Orchidaceae family. This genus consists of approximately 21 species, native to south and south-east Asia (Christenson, 1993; Kocyan *et al.*, 2008). The *Aerides* species with medicinal reputations include *Aerides falcata, Aerides multiflora* and *Aerides odorata.* These plants are known for immunostimulant, antimicrobial, antibacterial and anticancer activities. Previous phytochemical investigations revealed the presence of alkaloids, coumarins, flavonoids, glycosides, phenols, and terpenoids (Katta *et al.*, 2019).

1.2.1 *Aerides multiflora*

Aerides multiflora Roxb is an epiphytic orchid growing on a tree trunk (Bhowmik & Rahman, 2020). It is commonly known as the Multi-flowered Aerides and called Malai Dang in Thai. The plant is native to Bangladesh, India, Nepal, Myanmar, Thailand, Malaysia, Philippines, Laos, Cambodia, and Vietnam. The leaves are bilobed, deeply channeled, and the inflorescences bear purple or pink fragrant flowers **(Figure 4).** The flowering period is May-June. *A. multiflora* has been used to treat cuts and wounds (Gogoi *et al.*, 2012; Pant, 2013) and also used as a tonic (Subedi *et al.*, 2013). The tubers exhibited an antibacterial effect *in vitro* (Ghanaksh &

Kaushik, 1999). No studies on the chemical constituents and α-glucosidase inhibitory activity of this plant have been reported.

Figure 4 *Aerides multiflora* Roxb

2 Chemical constituents

2.1 Chemical constituents of *Dendrobium* species

According to the previous reports, the chemical constituents of *Dendrobium* can be categorized into 9 major classes, including bibenzyls and derivatives, flavonoids, terpenoids, aliphatic acid derivatives, benzoic acid derivatives, coumarins, lignans and neolignans, fluorenones, and miscellaneous compounds. Bibenzyls are the largest group. The distribution of secondary metabolites in this genus is summarized in **Table 2** and **Figure 5.**

Table 2 Distribution of secondary metabolites in the genus *Dendrobium*

Category and compound	Plant	Plant part	References
Bibenzyls and derivatives: (a)Simple bibenzyls			
Aloifol I [**20**]	*D. infundibulum*	whole plant	(Na Ranong *et al.*, 2019)
	D. longicornu	stem	(Hu *et al.*, 2008)
	D. williamsonii	whole plant	(Yang *et al.*, 2018)
	D. scabrilingue	whole plant	(Sarakulwattana *et al.*, 2020)
	D. christiyanum	root	(San *et al.*, 2020)
Amoenylin [**21**]	*D. amoenum*	whole plant	(Majumder, Guha, *et al.*, 1999)
	D. williamsonii	whole plant	(Yang *et al.*, 2018)
Batatasin [**22**]	*D. longicornu*	stem	(Hu *et al.*, 2008)
	D. plicatile	stem	(Yamaki & Honda, 1996)
Batatasin III [**3**]	*D. aphyllum*	stem	(Yang *et al.*, 2015a)
	D. cariniferum	stem	(Chen *et al.*, 2008c)
	D. chrysotoxum	whole plant	(Li *et al.*, 2009a)
	D. draconis	stem	(Sritularak *et al.*, 2011b)
	D. formosum	whole plant	(Inthongkaew *et al.*, 2017)
	D. gratiosissimum	stem	(Zhang *et al.*, 2008a)

Table 2 (continued)

Category and compound	Plant	Plant part	References
Batatasin III [**3**] (continued)	*D. infundibulum*	whole plant	(Na Ranong *et al.*, 2019)
	D. loddigesii	stem	(Ito *et al.*, 2010)
	D. venustum	whole plant	(Sukphan *et al.*, 2014)
	D. scabrilingue	whole plant	(Sarakulwattana *et al.*, 2020)
	D. christiyanum	root	(San *et al.*, 2020)
Brittonin A [**23**]	*D. secundum*	stem	(Sritularak *et al.*, 2011)
Chrysotobibenzyl [**24**]	*D. aurantiacum* var. *denneanum*	stem	(Yang *et al.*, 2006b)
	D. capillipes	stem	(Phechrmeekha *et al.*, 2012)
	D. chrysanthum	stem	(Yang *et al.*, 2006a)
	D. chrysotoxum	stem	(Hu *et al.*, 2012)
	D. nobile	stem	(Zhang *et al.*, 2007)
	D. pulchellum	stem	(Chanvorachote *et al.*, 2013)

Table 2 (continued)

Category and compound	Plant	Plant part	References
Crepidatin [**25**]	*D. aurantiacum*	stem	(Yang *et al.*, 2006b)
	D. capillipes	stem	(Phechrmeekha *et al.*, 2012)
	D. chrysanthum	stem	(Yang *et al.*, 2006a)
	D. crepidatum	whole plant	(Majumder & Chatterjee, 1989)
Cumulatin [**26**]	*D. cumulatum*	whole plant	(Majumder & Pal, 1993)
Chrysotoxine [**27**]	*D. lindleyi*	Whole plant	(Khoonrit *et al.*, 2020)
3,4′-Dihydroxy-3′,4,5-trimethoxybibenzyl [**28**]	*D. lindleyi*	whole plant	(Khoonrit *et al.*, 2020)
Dendrobin A [**29**]	*D. nobile*	stem	(Wang *et al.*, 1985)
Dendromoniliside E [**30**]	*D. nobile*	stem	(Miyazawa *et al.*, 1999)
3,3′-Dihydroxy-4,5-dimethoxybibenzyl [**31**]	*D. williamsonii*	whole plant	(Rungwichaniwat *et al.*, 2014)
3,4′-Dihydroxy-5-methoxybibenzyl [**32**]	*D. amoenum*	whole plant	(Majumder, Guha, *et al.*, 1999)
3,4′-Dihydroxy-5,5′-di-methoxydihydrostilbene [**33**]	*D. nobile*	stem	(Hwang *et al.*, 2010)

Table 2 (continued)

Category and compound	Plant	Plant part	References
3,4′-Dihydroxy-3′,4,5-trimethoxybibenzyl [**34**]	*D. infundibulum*	whole plant	(Na Ranong *et al.*, 2019)
Erianin [**35**]	*D. chrysotoxum*	stem	(Hu *et al.*, 2012)
Gigantol [**2**]	*D. aphyllum*	whole plant	(Chen *et al.*, 2008c)
	D. aurantiacum var. *denneanum*	whole plant	(Ying *et al.*, 2009)
	D. brymerianum	whole plant	(Klongkumnuankarn *et al.*, 2015)
	D. densiflorum	stem	(Fan *et al.*, 2001)
	D. devonianum	whole plant	(Sun *et al.*, 2014)
	D. draconis	stem	(Sritularak *et al.*, 2011b)
	D. longicornu	stem	(Hu *et al.*, 2008)
	D. nobile	stem	(Zhang *et al.*, 2007)
	D. officinale	stem	(Zhao *et al.*, 2018)
	D. palpebrae	whole plant	(Kyokong *et al.*, 2019)
	D. polyanthum	stem	(Hu *et al.*, 2009)
	D. scabrilingue	whole plant	(Sarakulwattana *et al.*, 2020)
	D. trigonopus	stem	(Hu *et al.*, 2008a)
	D. venustum	whole plant	(Sukphan *et al.*, 2014)

Table 2 (continued)

Category and compound	Plant	Plant part	References
Gigantol [**2**] (continued)	*D. wardianum*	stem	(Zhang *et al.*, 2017)
	D. lindleyi	whole plant	(Khoonrit *et al.*, 2020)
	D. christiyanum	root	(San *et al*., 2020)
	D. pachyglossum	whole plant	(Warinhomhoun *et al.*, 2021)
Gigantol-5-*O*-β-D-glucopyranoside [**36**]	*D. fimbriatum*	stem	(Xu *et al.*, 2017)
4-Hydroxy-3,5,3′-trimethoxybibenzyl [**37**]	*D. nobile*	stem	(Zhang *et al.*, 2007)
5-Hydroxy-3,4,3′,4′,5′-pentamethoxybibenzyl [**38**]	*D. secundum*	stem	(Phechrmeekha *et al.*, 2012)
Isoamoenylin [**39**]	*D. amoenum*	whole plant	(Majumder, Guha*, et al.*, 1999)
Moscatilin [**40**]	*D. amoenum*	whole plant	(Majumder, Guha*, et al.*, 1999)
	D. aurantiacum var. *denneanum*	stem	(Yang *et al.*, 2006b)
	D. brymerianum	whole plant	(Klongkumnuankarn *et al.*, 2015)
	D. chrysanthum	stem	(Yang *et al.*, 2006a)
	D. densiflorum	stem	(Fan *et al.*, 2001)

Table 2 (continued)

Category and compound	Plant	Plant part	References
Moscatilin [**40**] (continued)	*D. ellipsophyllum*	whole plant	(Tanagornmeatar *et al.*, 2014)
	D. formosum	whole plant	(Inthongkaew *et al.*, 2017)
	D. gratiosissimum	stem	(Zhang *et al.*, 2008a)
	D. infundibulum	whole plant	(Na Ranong *et al.*, 2019)
	D. loddigesii	whole plant	(Chen *et al.*, 1994)
	D. longicornu	stem	(Hu *et al.*, 2008)
	D. moscatum	whole plant	(Majumder & Sen, 1987)
	D. nobile	stem	(Miyazawa *et al.*, 1999)
	D. palpebrae	whole plant	(Kyokong *et al.*, 2019)
	D. parishii	whole plant	(Kongkatitham *et al.*, 2018)
	D. polyanthum	stem	(Hu *et al.*, 2009)
	D. pulchellum	stem	(Chanvorachote *et al.*, 2013)
	D. secundum	stem	(Sritularak *et al.*, 2011)
	D. wardianum	stem	(Zhang *et al.*, 2017)
	D. williamsonii	whole plant	(Yang *et al.*, 2018)
	D. lindleyi	whole plant	(Khoonrit *et al.*, 2020)
	D. christiyanum	root	(San *et al.*, 2020)
	D. pachyglossum	whole plant	(Warinhomhoun *et al.*, 2021)

Table 2 (continued)

Category and compound	Plant	Plant part	References
Moscatilin diacetate [**41**]	*D. loddigesii*	stem	(Chen *et al.*, 1994)
3,3′,4-Trihydroxy bibenzyl [**42**]	*D. longicornu*	stem	(Hu *et al.*, 2008)
3,3′,5-Trihydroxy bibenzyl [**43**]	*D. cariniferum*	whole plant	(Chen *et al.*, 2008c)
3,5,4′-Trihydroxy bibenzyl [**44**]	*D. gratiosissimum*	stem	(Zhang *et al.*, 2008a)
4,5,4′-Trihydroxy-3,3′-dimethoxy bibenzyl [**45**]	*D. ellipsophyllum*	whole plant	(Tanagornmeatar *et al.*, 2014)
	D. palpebrae	whole plant	(Kyokong *et al.*, 2019)
	D. parishii	whole plant	(Kongkatitham *et al.*, 2018)
	D. secundum	stem	(Sritularak *et al.*, 2011)
4,3′,4′-Trihydroxy-3,5-dimethoxy bibenzyl [**46**]	*D. parishii*	whole plant	(Kongkatitham *et al.*, 2018)
Tristin [**47**]	*D. aphyllum*	stem	(Yang *et al.*, 2015a)
	D. chrysotoxum	stem	(Hu *et al.*, 2012)
	D. densiflorum	stem	(Fan *et al.*, 2001)
	D. gratiosissimum	stem	(Zhang *et al.*, 2008a)
	D. longicornu	stem	(Hu *et al.*, 2008)

Table 2 (continued)

Category and compound	Plant	Plant part	References
Tristin [**47**] (continued)	*D. officinale*	stem	(Zhao *et al.*, 2018)
	D. trigonopus	stem	(Hu *et al.*, 2008a)
Dendrophenol [**48**]	*D. candidum*	stem	(Li *et al.*, 2008)
Dendrocandin E [**49**]	*D. candidum*	stem	(Li *et al.*, 2009c)
	D. parishii	whole plant	(Kongkatitham *et al.*, 2018)
Dendrosinen B [**50**]	*D. sinense*	whole plant	(Chen *et al.*, 2014)
	D. infundibulum	whole plant	(Na Ranong *et al.*, 2019)
	D. christiyanum	root	(San *et al.*, 2020)
3,4-Dihydroxy-5,4′-dimethoxy bibenzyl [**51**]	*D. candidum*	stem	(Li *et al.*, 2008)
	D. signatum	whole plant	(Mittraphab *et al.*, 2016)
	D. tortile	whole plant	(Limpanit *et al.*, 2016a)
	D. wardianum	stem	(Zhang *et al.*, 2017)
	D. williamsonii	whole plant	(Yang *et al.*, 2018)

Table 2 (continued)

Category and compound	**Plant**	**Plant part**	**References**
4,4′-Dihydroxy-3,5-dimethoxy bibenzyl [**52**]	*D. candidum*	stem	(Li *et al.*, 2008)
	D. ellipsophyllum	whole plant	(Tanagornmeatar *et al.*, 2014)
	D. williamsonii	whole plant	(Yang *et al.*, 2018)
3-*O*-Methylgigantol [**53**]	*D. candidum*	stem	(Li *et al.*, 2008)
	D. plicatile	stem	(Yamaki & Honda, 1996)
(b) Bibenzyls with substitution at ethylene bridge			
Dendrocandin A [**54**]	*D. candidum*	stem	(Li *et al.*, 2008)
	D. wardianum	stem	(Zhang *et al.*, 2017)
Dendrocandin C [**55**]	*D. candidum*	stem	(Li *et al.*, 2009c)
Dendrocandin D [**56**]	*D. candidum*	stem	(Li *et al.*, 2009c)
Dendrosinen A [**57**]	*D. sinense*	whole plant	(Chen *et al.*, 2014)
4,5-Dihydroxy-3,α,3′,4′-tetramethoxybibenzyl [**58**]	*D. lindleyi*	whole plant	(Shang *et al.*, 2020)
4,4′,5-Trihydroxy-3,3′,α-trimethoxybibenzyl [**59**]	*D. lindleyi*	whole plant	(Shang *et al.*, 2020)
4-[2-(3-Hydroxyphenol)-1-methoxyethyl]-2,6-dimethoxyphenol [**60**]	*D. longicornu*	stem	(Hu *et al.*, 2008)
Loddigesiinol C [**61**]	*D. loddigesii*	whole plant	(Ito *et al.*, 2010)

Table 2 (continued)

Category and compound	Plant	Plant part	References
Nobilin A [**62**]	*D. nobile*	stem	(Zhang *et al.*, 2006)
Nobilin B [**63**]	*D. nobile*	stem	(Zhang *et al.*, 2006)
Nobilin C [**64**]	*D. nobile*	stem	(Zhang *et al.*, 2006)
Nobilin D [**65**]	*D. nobile*	stem	(Zhang *et al.*, 2007)
(c) Bibenzyls with other substitutions			
Dendrosinen C [**66**]	*D. sinense*	whole plant	(Chen *et al.*, 2014)
Loddigesiinol D [**67**]	*D. loddigesii*	whole plant	(Ito *et al.*, 2010)
Densiflorol A [**68**]	*D. densiflorum*	stem	(Fan *et al.*, 2001)
Crepidatuol A [**69**]	*D. crepidatum*	stem	(Li *et al.*, 2013)
Crepidatuol B [**70**]	*D. crepidatum*	stem	(Li *et al.*, 2013)
Trigonopol B [**71**]	*D. chrysotoxum*	stem	(Hu *et al.*, 2012)
Longicornuol A [**72**]	*D. longicornu*	stem	(Hu *et al.*, 2008)
Trigonopol A [**73**]	*D. trigonopus*	stem	(Hu *et al.*, 2008a)
Dendrocandin B [**74**]	*D. candidum*	stem	(Li *et al.*, 2008)
	D. signatum	whole plant	(Mittraphab *et al.*, 2016)
	D. officinale	stem	(Yang *et al.*, 2015)
Dendrocandin T [**75**]	*D. officinale*	stem	(Yang *et al.*, 2015)

Table 2 (continued)

Category and compound	Plant	Plant part	References
Dendrocandin U [**76**]	*D. officinale* *D. wardianum*	stem stem	(Yang *et al.*, 2015) (Zhang *et al.*, 2017)
Dendrocandin V [**77**]	*D. wardianum*	stem	(Zhang *et al.*, 2017)
(d)Dihydrophenanthrenes			
1,5-Dihydroxy-3,4,7-trimethoxy-9,10-dihydrophenanthrene [**78**]	*D. moniliforme*	whole plant	(Zhao *et al.*, 2016)
Coelonin [**9**]	*D. aphyllum* *D. formosum* *D. nobile* *D. scabrilingue*	whole plant whole plant stem whole plant	(Hu *et al.*, 2008) (Inthongkaew *et al.*, 2017) (Yang *et al.*, 2007) (Sarakulwattana *et al.*, 2020)
Dendroinfundin A [**79**]	*D. infundibulum*	whole plant	(Na Ranong *et al.*, 2019)
Dendroinfundin B [**80**]	*D. infundibulum*	whole plant	(Na Ranong *et al.*, 2019)
4,5-Dihydroxy-2,3-dimethoxy-9,10-dihydrophenanthrene [**81**]	*D. ellipsophyllum* *D. sinense*	whole plant whole plant	(Tanagornmeatar *et al.*, 2014) (Chen *et al.*, 2014)
4,5-Dihydroxy-2,6-dimethoxy-9,10-dihydrophenanthrene [**82**]	*D. chrysotoxum*	stem	(Hu *et al.*, 2012)

Category and compound	Plant	Plant part	References
4,5-Dihydroxy-3,7-dimethoxy-9,10-dihydrophenanthrene [**83**]	*D. nobile*	stem	(Ye *et al.*, 2002)
4,5-Dihydroxy-2-methoxy-9,10-dihydrophenanthrene (Orchinol) [**7**]	*D. nobile*	stem	(Zhang *et al.*, 2007)
9,10-Dihydromoscatin [**84**]	*D. polyanthum*	stem	(Hu *et al.*, 2009)
9,10-Dihydrophenanthrene-2,4,7-triol [**85**]	*D. officinale*	stem	(Zhao *et al.*, 2018)
	D. polyanthum	stem	(Hu *et al.*, 2009)
2,7-Dihydroxy-3,4,6-trimethoxy-9,10-dihydrophenanthrene [**86**]	*D. densiflorum*	stem	(Fan *et al.*, 2001)
2,8-Dihydroxy-3,4,7-trimethoxy-9,10-dihydrophenanthrene [**87**]	*D. nobile*	stem	(Yang *et al.*, 2007)
4,7-Dihydroxy-2,3,6-trimethoxy-9,10-dihydrophenanthrene [**88**]	*D. rotundatum*	whole plant	(Majumder & Pal, 1992)
3,4-Dimethoxy-1-(methoxymethyl)-9,10-dihydrophenanthrene-2,7-diol [**89**]	*D. hainanense*	aerial part	(Zhang *et al.*, 2018)
Ephemeranthol A [**90**]	*D. infundibulum*	whole plant	(Na Ranong *et al.*, 2019)

Table 2 (continued)

Category and compound	Plant	Plant part	Reference
Ephemeranthol A [**90**]	*D. nobile*	stem	(Yang *et al.*, 2007)
(continued)	*D. officinale*	stem	(Zhao *et al.*, 2018)
Ephemeranthol C [**91**]	*D. nobile*	stem	(Yang *et al.*, 2007)
Erianthridin [**92**]	*D. nobile*	stem	(Hwang *et al.*, 2010)
	D. formosum	whole plant	(Inthongkaew *et al.*, 2017)
	D. plicatile	stem	(Yamaki & Honda, 1996)
Flavanthridin [**93**]	*D. nobile*	stem	(Hwang *et al.*, 2010)
Hircinol [**94**]	*D. aphyllum*	stem	(Yang *et al.*, 2015a)
	D. draconis	stem	(Sritularak *et al.*, 2011b)
	D. formosum	whole plant	(Inthongkaew *et al.*, 2017)
3-Hydroxy-2,4,7-trimethoxy-9,10-dihydrophenanthrene [**95**]	*D. nobile*	stem	(Yang *et al.*, 2007)
7-Hydroxy-2,3,4-trimethoxy-9,10-dihydro-phenanthrene [**96**]	*D. hainanense*	aerial part	(Zhang *et al.*, 2018)
	D. brymerianum	whole plant	(Klongkumnuankarn *et al.*, 2015)
	D. formosum	whole plant	(Inthongkaew *et al.*, 2017)

Table 2 (continued)

Category and compound	Plant	Plant part	Reference
7-Hydroxy-2,3,4-trimethoxy-9,10-dihydrophenanthrene [**96**] (continued)	*D. palpebrae*	whole plant	(Kyokong *et al.*, 2019)
Lusianthridin [**97**]	*D. plicatile*	stem	(Yamaki & Honda, 1996)
	D. venustum	whole plant	(Sukphan *et al.*, 2014)
	D. scabrilingue	whole plant	(Sarakulwattana *et al.*, 2020)
2-Hydroxy-4,7-dimethoxy-9,10-dihydrophenanthrene [**98**]	*D. nobile*	stem	(Yang *et al.*, 2007)
7-Methoxy-9,10-dihydrophenanthrene-2,4,5-triol [**99**]	*D. draconis*	stem	(Sritularak *et al.*, 2011b)
2,5,7-Trimethoxy-4-methoxy-9,10-dihydrophenanthrene [**100**]	*D. formosum*	whole plant	(Inthongkaew *et al.*, 2017)
Plicatol C [**101**]	*D. plicatile*	stem	(Honda & Yamaki, 2000)

Table 2 (continued)

Category and compound	**Plant**	**Plant part**	**Reference**
Rotundatin [**102**]	*D. rotundatum*	whole plant	(Majumder & Pal, 1992)
(*S*)-2,4,5,9-Tetrahydroxy-9,10-dihydrophenanthrene [**103**]	*D. fimbriatum*	stem	(Xu *et al.*, 2014)
(e) Phenanthrenes			
2,5-Dihydroxy-3,4-dimethoxyphenanthrene [**104**]	*D. nobile*	stem	(Yang *et al.*, 2007)
2,5-Dihydroxy-4,9-dimethoxyphenanthrene [**105**]	*D. nobile*	stem	(Zhang *et al.*, 2008b)
	D. palpebrae	whole plant	(Kyokong *et al.*, 2019)
2,8-Dihydroxy-3,4,7-trimethoxyphenanthrene [**106**]	*D. nobile*	stem	(Yang *et al.*, 2007)
Epheranthol B [**107**]	*D. chrysotoxum*	stem	(Hu *et al.*, 2012)
	D. plicatile	stem	(Yamaki & Honda, 1996)
Fimbriol B [**108**]	*D. nobile*	stem	(Yang *et al.*, 2007)
Flavanthrinin [**109**]	*D. brymerianum*	whole plant	(Klongkumnuankarn *et al.*, 2015)

Table 2 (continued)

Category and compound	Plant	Plant part	Reference
Flavanthrinin [**109**] (continued)	*D. venustum*	whole plant	(Sukphan *et al.*, 2014)
	D. nobile	stem	(Zhang *et al.*, 2008b)
	D. parishii	whole plant	(Kongkatitham *et al.*, 2018)
Moscatin [**110**]	*D. aphyllum*	whole plant	(Hu *et al.*, 2008)
	D. chrysanthum	stem	(Yang *et al.*, 2006a)
	D. chrysotoxum	whole plant	(Li *et al.*, 2009a)
	D. densiflorum	stem	(Fan *et al.*, 2001)
	D. polyanthum	stem	(Hu *et al.*, 2009)
Loddigesiinol A [**111**]	*D. loddigesii*	whole plant	(Ito *et al.*, 2010)
	D. wardianum	stem	(Zhang *et al.*, 2017)
Dendroscabrol A [**112**]	*D. scabrilingue*	whole plant	(Sarakulwattana *et al.*, 2020)
Nudol [**113**]	*D. formosum*	whole plant	(Inthongkaew *et al.*, 2017)
	D. nobile	stem	(Yang *et al.*, 2007)
	D. rotundatum	whole plant	(Majumder & Pal, 1992)

Table 2 (continued)

Category and compound	Plant	Plant part	Reference
Plicatol A [**114**]	*D. nobile* *D. plicatile*	stem stem	(Yang *et al.*, 2007) (Honda & Yamaki, 2000)
Plicatol B [**115**]	*D. plicatile*	stem	(Honda & Yamaki, 2000)
2,3,5-Trihydroxy-4,9-dimethoxyphenanthrene [**116**]	*D. nobile*	stem	(Yang *et al.*, 2007)
3,4,8-Trimethoxyphenan-threne-2,5-diol [**117**]	*D. nobile*	stem	(Hwang *et al.*, 2010)
Bulbophyllanthrin [**118**]	*D. nobile*	stem	(Yang *et al.*, 2007)
Denthyrsinin [**119**]	*D. thyrsiforum*	stem	(Zhang *et al.*, 2005)
5-Hydroxy-2,4-dimethoxyphenanthrene [**120**]	*D. loddigesii*	whole plant	(Ito *et al.*, 2010)
3-Hydroxy-2,4,7-trimethoxyphenanthrene [**121**]	*D. nobile*	stem	(Yang *et al.*, 2007)
Confusarin [**122**]	*D. chrysotoxum* *D. formosum* *D. nobile* *D. officinale*	stem whole plant stem stem	(Hu *et al.*, 2012) (Inthongkaew *et al.*, 2017) (Zhang *et al.*, 2008b) (Zhao *et al.*, 2018)

Table 2 (continued)

Category and compound	**Plant**	**Plant part**	**Reference**
2,6-Dihydroxy-1,5,7-trimethoxyphenanthrene [**123**]	*D. densiflorum*	stem	(Fan *et al.*, 2001)
	D. palpebrae	whole plant	(Kyokong *et al.*, 2019)
1,5,7-Trimethoxy-phenanthren-2-ol [**124**]	*D. nobile*	stem	(Yang *et al.*, 2007)
(f) Phenanthrene-1,4-dione			
Cypripedin [**125**]	*D. densiflorum*	stem	(Fan *et al.*, 2001)
	D. lindleyi	whole plant	(Khoonrit *et al.*, 2020)
Densiflorol B [**126**]	*D. venustum*	whole plant	(Sukphan *et al.*, 2014)
	D. densiflorum	stem	(Fan *et al.*, 2001)
Denbinobin [**127**]	*D. moniliforme*	stem	(Lin *et al.*, 2001)
	D. nobile	stem	(Yang *et al.*, 2007)
	D. wardianum	stem	(Zhang *et al.*, 2017)
(g) 9,10-dihydrophenanthrene-1,4-dione			
Dendronone [**128**]	*D. chrysanthum*	stem	(Yang *et al.*, 2006a)

Table 2 (continued)

Category and compound	Plant	Plant part	Reference
Dendronone [**128**] (continued)	*D. longicornu*	stem	(Hu *et al.*, 2008)
Ephemeranthoquinone [**129**]	*D. plicatile*	stem	(Yamaki & Honda, 1996)
5-Methoxy-7-hydroxy-9,10-dihydro-1,4-phenanthrenequinone [**12**]	*D. draconis*	stem	(Sritularak *et al.*, 2011b)
	D. formosum	whole plant	(Inthongkaew *et al.*, 2017)
Moniliformin [**130**]	*D. moniliforme*	stem	(Lin *et al.*, 2001)
(h) Phenanthropyran derivatives			
Amoenumin [**131**]	*D. amoenum*	whole plant	(Veerraju *et al.*, 1989)
Fimbriatone [**132**]	*D. nobile*	stem	(Zhang *et al.*, 2008b)
	D. pulchellum	stem	(Chanvorachote *et al.*, 2013)
Crystalltone [**133**]	*D. chrysotoxum*	stem	(Hu *et al.*, 2012)
	D. polyanthum	stem	(Hu *et al.*, 2009)
Chrysotoxol A [**134**]	*D. chrysotoxum*	stem	(Hu *et al.*, 2012)
Chrysotoxol B [**135**]	*D. chrysotoxum*	stem	(Hu *et al.*, 2012)

Table 2 (continued)

Category and compound	Plant	Plant part	References
(i) 9,10-dihydrophenanthrodioxine			
Dendrocandin P2 [**136**]	*D. officinale*	stem	(Zhao *et al.*, 2018)
(j) Phenanthrodioxine			
Dendrocandin P1 [**137**]	*D. officinale*	stem	(Zhao *et al.*, 2018)
(k) Others			
Dendrochrysanene [**138**]	*D. chrysanthum*	stem	(Yang *et al.*, 2006a)
Aphyllone [**139**]	*D. nobile*	stem	(Hwang *et al.*, 2010)
9,10-Dihydro-aphyllone A-5-*O*-β-D-glucopyranoside [**140**]	*D. fimbriatum*	stem	(Xu *et al.*, 2017)
2,4,5,9*S*-Tetrahydroxy-9,10-dihydrophenanthrene-4-*O*-β-D-glucopyranoside [**141**]	*D. primulinum*	whole plant	(Ye *et al.*, 2016)
(l) Dimeric bibenzyls			
Dendrocandin I [**142**]	*D. candidum* *D. signatum*	stem whole plant	(Li *et al.*, 2009c) (Mittraphab *et al.*, 2016)
Dendrocandin F [**143**]	*D. candidum*	stem	(Li *et al.*, 2009c)
Dendrocandin G [**144**]	*D. candidum*	stem	(Li *et al.*, 2009c)
Dendrosinen D [**145**]	*D. sinense*	whole plant	(Chen *et al.*, 2014)

Table 2 (continued)

Category and compound	Plant	Plant part	References
Dendrofalconerol B [**146**]	*D. falconeri*	stem	(Sritularak & Likhitwitayawuid, 2009)
Nobilin E [**147**]	*D. nobile*	stem	(Zhang *et al.*, 2007)
Dendroscabrol B [**5**]	*D. scabrilingue*	whole plant	(Sarakulwattana *et al.*, 2020)
Dendropachol [**148**]	*D. pachyglossum*	whole plant	(Warinhomhoun *et al.*, 2021)
Dengraol A [**149**]	*D. gratiosissimum*	stem	(Zhang *et al.*, 2008a)
Dengraol B [**150**]	*D. gratiosissimum*	stem	(Zhang *et al.*, 2008a)
Dencryol A [**151**]	*D. crystallinum*	stem	(Wang *et al.*, 2009)
Dencryol B [**152**]	*D. crystallinum*	stem	(Wang *et al.*, 2009)
2,2′-Dihydroxy-3,3′,4,4′,7,7′-hexamethoxy-9,9′,10,10′-tetrahydro-1,1′-biphenanthrene [**153**]	*D. nobile*	stem	(Yang *et al.*, 2007)
2,2′-Dimethoxy-4,4′,7,7′-tetrahydroxy-9,9′,10,10′-tetrahydro-1,1′-biphenanthrene [**154**]	*D. plicatile*	stem	(Yamaki & Honda, 1996)
Flavanthrin [**155**]	*D. aphyllum*	whole plant	(Chen, Li, *et al.*, 2008)

Table 2 (continued)

Category and compound	Plant	Plant part	Reference
Phoyunnanin C [**156**]	*D. venustum*	whole plant	(Sukphan *et al.*, 2014)
Phoyunnanin E [**157**]	*D. venustum*	whole plant	(Sukphan *et al.*, 2014)
Dendrosignatol [**158**]	*D. signatum*	whole plant	(Mittraphab *et al.*, 2016)
Dendroparishiol [**159**]	*D. parishii*	whole plant	(Kongkatitham *et al.*, 2018)
Dendrocandin H [**160**]	*D. candidum*	stem	(Li *et al.*, 2009c)
Loddigesiinol G [**161**]	*D. loddigesii*	stem	(Lu *et al.*, 2014)
Loddigesiinol H [**162**]	*D. loddigesii*	stem	(Lu *et al.*, 2014)
Loddigesiinol I [**163**]	*D. loddigesii*	stem	(Lu *et al.*, 2014)
Loddigesiinol J [**164**]	*D. loddigesii*	stem	(Lu *et al.*, 2014)
Dendropalpebrone [**165**]	*D. palpebrae*	whole plant	(Kyokong *et al.*, 2019)
Dendrofalconerol A [**6**]	*D. falconeri*	stem	(Sritularak & Likhitwitayawuid, 2009)
	D. signatum	whole plant	(Mittraphab *et al.*, 2016)
	D. tortile	whole plant	(Limpanit *et al.*, 2016)

Table 2 (continued)

Category and compound	Plant	Plant part	Reference
Flavonoids			
(a) Flavones			
Apigenin [**166**]	*D. crystallinum*	stem	(Wang *et al.*, 2009)
	D. williamsonii	whole plant	(Rungwichaniwat *et al.*, 2014)
Apigenin 6-C-glucosyl-(1→2)-α-L-arabinoside [**167**]	*D. officinale*	leaves	(Zhang *et al.*, 2017a)
6-*C*-(α-Arabinopyrano-syl)-8-*C*-[(2-*O*-α-rhamnopyranosyl)-β-galactopyranosyl] apigenin [**168**]	*D. huoshanense*	aerial part	(Chang *et al.*, 2010)
6-*C*-[(2-*O*-α-Rhamno-pyranosyl)-β-glucopyra-nosyl]-8-*C*-(α-arabinopyranosyl) apigenin [**169**]	*D. huoshanense*	aerial part	(Chang *et al.*, 2010)
6-*C*-(β-Xylopyranosyl)-8-*C*-[(2-*O*-α-rhamnopyra-nosyl)-β-glucopyranosyl] apigenin [**170**]	*D. huoshanense*	aerial part	(Chang *et al.*, 2010)
5,6-Dihydroxy-4′-methoxyflavone [**171**]	*D. chrysotoxum*	stem	(Hu *et al.*, 2012)
6‴-Glucosyl-vitexin [**172**]	*D. crystallinum*	stem	(Wang *et al.*, 2009)

Table 2 (continued)

Category and compound	Plant	Plant part	Reference
5-Hydroxy-3-methoxy-flavone-7-*O*-[β-D-apiosyl-(1→6)]-β-D-glucoside [**15**]	*D. devonianum*	whole plant	(Sun *et al.*, 2014)
Isoschaftoside [**173**]	*D. huoshanense*	aerial part	(Chang *et al.*, 2010)
Isoviolanthin [**174**]	*D. crystallinum*	stem	(Wang *et al.*, 2009)
Kaempferol [**175**]	*D. aurantiacum* var. *denneanum*	stem	(Yang *et al.*, 2006b)
Kaempferol-3-*O*-α-L-rhamnopyranoside [**176**]	*D. secundum*	stem	(Phechrmeekha *et al.*, 2012)
Kaempferol-3,7-*O*-di-α-L-rhamnopyranoside [**177**]	*D. secundum*	stem	(Phechrmeekha *et al.*, 2012)
Kaempferol-3-*O*-α-L-rhamnopyranosyl-(1→2)-β-D-glucopyranoside [**178**]	*D. capillipes*	stem	(Phechrmeekha *et al.*, 2012)
Kaempferol-3-*O*-α-L-rhamnopyranosyl-(1→2)-β-D-xylopyranoside [**179**]	*D. capillipes*	stem	(Phechrmeekha *et al.*, 2012)
Luteolin [**180**]	*D. aurantiacum* var. *denneanum*	whole plant	(Ying *et al.*, 2009)
	D. ellipsophyllum	whole plant	(Tanagornmeatar *et al.*, 2014)
	D. longicornu	stem	(Hu *et al.*, 2008)

Table 2 (continued)

Category and compound	Plant	Plant part	Reference
Vicenin-2 [**181**]	*D. aurantiacum* var. *denneanum*	stem	(Xiong *et al.*, 2013)
Quercetin-3-*O*-L-rhamnopyranoside [**182**]	*D. secundum*	stem	(Phechrmeekha *et al.*, 2012)
Quercetin-3-*O*-α-L-rhamnopyranosyl-(1→2)-β-D-xylopyranoside [**183**]	*D. capillipes*	stem	(Phechrmeekha *et al.*, 2012)
(b) Flavanones			
(2*S*)-Homoeriodictyol [**184**]	*D. densiflorum*	stem	(Fan *et al.*, 2001)
	D. ellipsophyllum	whole plant	(Tanagornmeatar *et al.*, 2014)
Naringenin **[14]**	*D. aurantiacum* var. *denneanum*	stem	(Yang *et al.*, 2006b)
	D. densiflorum	stem	(Fan *et al.*, 2001)
	D. longicornu	stem	(Hu *et al.*, 2008)
(2*S*)-Eriodictyol [**185**]	*D. ellipsophyllum*	whole plant	(Tanagornmeatar *et al.*, 2014)
	D. trigonopus	stem	(Hu *et al.*, 2008a)
	D. tortile	whole plant	(Limpanit *et al.*, 2016a)
Terpenoids			
Amoenin [**187**]	*D. amoenum*	whole plant	(Dahmén & Leander, 1978)
	D. williamsonii	whole plant	(Yang *et al.*, 2018)

Table 2 (continued)

Category and compound	Plant	Plant part	Reference
Asiatic acid [**188**]	*D. parishii*	whole plant	(Kongkatitham *et al.*, 2018)
Corchoionoside C [**189**]	*D. wardianum*	stem	(Fan *et al.*, 2013)
Crystallinin [**190**]	*D. wardianum*	stem	(Fan *et al.*, 2013)
Dendrobane A [**191**]	*D. moniliforme*	stem	(Bi *et al.*, 2004)
Dendromoniliside A-D [**192**]	*D. moniliforme*	stem	(Zhao *et al.*, 2003)
Dendronobiloside A [**193**]	*D. moniliforme*	stem	(Zhao *et al.*, 2003)
	D. nobile	stem	(Zhao *et al.*, 2001)
Dendronobiloside B [**194**]	*D. nobile*	stem	(Zhao *et al.*, 2001)
Dendronobiloside C [**195**]	*D. nobile*	stem	(Zhao *et al.*, 2001)
Dendronobiloside D [**196**]	*D. nobile*	stem	(Zhao *et al.*, 2001)
Dendronobiloside E [**197**]	*D. nobile*	stem	(Zhao *et al.*, 2001)
Dendronobilin A **[198]**	*D. wardianum*	stem	(Zhang *et al.*, 2017)
Dendronobilin B **[199]**	*D. wardianum*	stem	(Zhang *et al.*, 2017)
	D. nobile	stem	(Zhang *et al.*, 2007)
Dendronobilin C [**200**]	*D. crystallium*	stem	(Wang *et al.*, 2009)
Dendronobilin D [**201**]	*D. nobile*	stem	(Zhang *et al.*, 2007)
Dendronobilin E [**202**]	*D. nobile*	stem	(Zhang *et al.*, 2007)
Dendronobilin F [**203**]	*D. nobile*	stem	(Zhang *et al.*, 2007)
Dendronobilin G [**204**]	*D. nobile*	stem	(Zhang *et al.*, 2007)
Dendronobilin H [**205**]	*D. nobile*	stem	(Zhang *et al.*, 2007)
Dendronobilin I [**206**]	*D. nobile*	stem	(Zhang *et al.*, 2007)
Dendronobilin J [**207**]	*D. nobile*	stem	(Zhang *et al.*, 2007)
Dendronobilin K [**208**]	*D. wardianum*	stem	(Fan *et al.*, 2013)

Table 2 (continued)

Category and compound	Plant	Plant part	Reference
Dendronobilin L [**209**]	*D. nobile*	stem	(Zhang *et al.*, 2007)
Dendronobilin M [**210**]	*D. nobile*	stem	(Zhang *et al.*, 2008b)
Dendronobilin N [**211**]	*D. nobile*	stem	(Zhang *et al.*, 2008b)
Dendroside A [**212**]	*D. moniliforme*	stem	(Zhao *et al.*, 2003)
	D. nobile	stem	(Zhao *et al.*, 2001)
Dendroside B [**213**]	*D. nobile*	stem	(Ye & Zhao, 2002)
	D. williamsonii	whole plant	(Yang *et al.*, 2018)
Dendroside C [**214**]	*D. moniliforme*	stem	(Zhao *et al.*, 2003)
	D. nobile	stem	(Ye & Zhao, 2002)
Dendroside D [**215**]	*D. nobile*	stem	(Ye & Zhao, 2002)
Dendroside E [**216**]	*D. nobile*	stem	(Ye *et al.*, 2002)
Dendroside F [**217**]	*D. moniliforme*	stem	(Zhao *et al.*, 2003)
Dendroside G [**218**]	*D. nobile*	stem	(Ye *et al.*, 2002)
Dendrowardol A [**219**]	*D. wardianum*	stem	(Fan *et al.*, 2013)
Dendrowardol B [**220**]	*D. wardianum*	stem	(Fan *et al.*, 2013)
Dendrowardol C [**221**]	*D. wardianum*	stem	(Fan *et al.*, 2013)
Amotin [**222**]	*D. amoenum*	whole plant	(Majumder, Guha, *et al.*, 1999)
Dendrowillin A [**223**]	*D. williamsonii*	whole plant	(Yang *et al.*, 2018)
Dendrowillin B [**224**]	*D. williamsonii*	whole plant	(Yang *et al.*, 2018)
α-Dihydropicrotoxinin [**225**]	*D. amoenum*	whole plant	(Majumder, Guha, *et al.*, 1999)

Table 2 (continued)

Category and compound	Plant	Plant part	Reference
Dendroterpene A [**226**]	*D. nobile*	stem	(Dai *et al.*, 2019)
Dendroterpene B [**227**]	*D. nobile*	stem	(Dai *et al.*, 2019)
Dendroterpene C [**228**]	*D. nobile*	stem	(Dai *et al.*, 2019)
Dendroterpene D [**229**]	*D. nobile*	stem	(Dai *et al.*, 2019)
Picrotin **[230]**	*D. williamsonii*	whole plant	(Yang *et al.*, 2018)
Findlayanin **[231]**	*D. nobile*	stem	(Meng *et al.*, 2017)
	D. polyanthum	stem	(Hu *et al.*, 2009)
3-Hydroxy-2-oxodendrobine [**232**]	*D. findlayanum*	whole plant	(Qin *et al.*, 2011)
Wardianumine A [**233**]	*D. wardianum*	stem	(Zhang *et al.*, 2017)
Aliphatic acid derivatives			
Aliphalic acids [**234**]	*D. clavatum* var. *aurantiacum*	stem	(Chang *et al.*, 2001)
Aliphatic alcohols [**235**]	*D. clavatum* var. *aurantiacum*	stem	(Chang *et al.*, 2001)
Decumbic acid [**236**]	*D. nobile*	stem	(Zhou *et al.*, 2017)
Dimethyl malate [**237**]	*D. huoshanense*	aerial part	(Chang *et al.*, 2010)
Malic acid [**238**]	*D. huoshanense*	aerial part	(Chang *et al.*, 2010)
Isopentyl butyrate [**239**]	*D. huoshanense*	aerial part	(Chang *et al.*, 2010)
(-)-Shikimic acid [**240**]	*D. fuscescens*	whole plant	(Talapatra *et al.*, 1989)
	D. huoshanense	aerial part	(Chang *et al.*, 2010)
	D. longicornu	stem	(Hu *et al.*, 2008)

Table 2 (continued)

Category and compound	**Plant**	**Plant part**	**Reference**
(-)-Shikimic acid [**240**] (continued)	*D. pulchellum*	stem	(Chanvorachote *et al.*, 2013)
Benzoic acid derivatives			
Antiarol **[241]**	*D. chrysotoxum*	stem	(Hu *et al.*, 2012)
Ethylhaematommate [**242**]	*D. longicornu*	whole plant	(Li *et al.*, 2009b)
Methylhaematommate [**243**]	*D. christyanum*	root	(San *et al.*, 2020)
Gallic acid **[244]**	*D. longicornu*	whole plant	(Li *et al.*, 2009b)
p-Hydroxybenzaldehyde [**245**]	*D. tortile*	whole plant	(Limpanit *et al.*, 2016a)
p-Hydroxybenzoic acid [**246**]	*D. williamsonii*	whole plant	(Yang *et al.*, 2018)
3-Hydroxy-2-methoxy-5,6-dimethylbenzoic acid [**247**]	*D. crystallinum*	stem	(Wang *et al.*, 2009)
Methyl 4-hydroxybenzoate [**248**]	*D. williamsonii*	whole plant	(Yang *et al.*, 2018)
Methyl 2,4-dihydroxy-3,6-dimethylbenzoate	*D. christyanum*	root	(San *et al.*, 2020)
Methyl β-orsellinate [**249**]	*D. longicornu*	stem	(Li *et al.*, 2009b)

Table 2 (continued)

Category and compound	Plant	Plant part	Reference
Methyl β-orsellinate [**249**] (continued)	*D. williamsonii*	whole plant	(Rungwichaniwat *et al.*, 2014)
Protocatechuic acid [**250**]	*D. nobile*	stem	(Ye & Zhao, 2002)
Salicylic acid [**251**]	*D. huoshanense*	aerial part	(Chang *et al.*, 2010)
	D. williamsonii	whole plant	(Yang *et al.*, 2018)
Syringic acid [**252**]	*D. crystallinum*	stem	(Wang *et al.*, 2009)
Tachioside [**253**]	*D. denneanum*	stem	(Pan *et al.*, 2012)
Vanillic acid [**254**]	*D. crystallinum*	stem	(Wang *et al.*, 2009)
Vanillin [**255**]	*D. williamsonii*	whole plant	(Yang *et al.*, 2018)
Vanilloside [**256**]	*D. denneanum*	stem	(Pan *et al.*, 2012)
Phenylpropanoids			
Alkyl 4′-hydroxy-*trans*-cinnamates [**257**]	*D. clavatum* var. *aurantiacum*	stem	(Chang *et al.*, 2001)
Alkyl *trans*-ferulates [**258**]	*D. clavatum* var. *aurantiacum*	stem	(Chang *et al.*, 2001)
Defuscin [**259**]	*D. aurantiacum* var. *denneanum*	stem	(Yang *et al.*, 2006b)
	D. moniliforme	stem	(Bi *et al.*, 2004)
n-Octacosyl ferulate [**260**]	*D. aurantiacum var. denneanum*	stem	(Yang *et al.*, 2006b)
	D. moniliforme	stem	(Bi *et al.*, 2004)
n-Triacontyl *p*-hydroxy-*cis*-cinnamate [**261**]	*D. moniliforme*	stem	(Bi *et al.*, 2004)

Table 2 (continued)

Category and compound	**Plant**	**Plant part**	**Reference**
Tetratriacontanyl-*trans*-*p*-coumarate [**262**]	*D. williamsonii*	whole plant	(Rungwichaniwat *et al.*, 2014)
n-Docosyl *trans*-ferulate [**263**]	*D. longicornu*	whole plant	(Li *et al.*, 2009b)
n-Eicosyl *trans*-ferulate [**264**]	*D. christyanum*	root	(San *et al.*, 2020)
n-Docosyl 4-hydroxy-*trans*-cinnamate [**265**]	*D. christyanum*	root	(San *et al.*, 2020)
trans-Tetracosyl ferulate [**266**]	*D. tortile*	whole plant	(Limpanit *et al.*, 2016a)
	D. scabrilingue	whole plant	(Sarakulwattana *et al.*, 2020)
Ferulaldehyde [**267**]	*D. longicornu*	whole plant	(Li *et al.*, 2009b)
Ferulic acid [**268**]	*D. secundum*	stem	(Sritularak *et al.*, 2011)
2-(*p*-Hydroxyphenyl)ethyl *p*-coumarate [**269**]	*D. falconeri*	stem	(Sritularak & Likhitwitayawuid, 2009)
Coniferyl alcohol [**270**]	*D. trigonopus*	stem	(Hu *et al.*, 2008a)
	D. christyanum	root	(San *et al.*, 2020)
Dendroside [**271**]	*D. nobile*	stem	(Zhou *et al.*, 2017)
cis-Hexacosanoyl ferulate [**272**]	*D. tortile*	whole plant	(Limpanit *et al.*, 2016a)

Table 2 (continued)

Category and compound	Plant	Plant part	Reference
cis-Tetracosanoyl ferulate [**273**]	*D. scabrilingue*	whole plant	(Sarakulwattana *et al.*, 2020)
Tetracosyl(*Z*)-*p*-coumarate [**274**]	*D. falconeri*	whole plant	(Sritularak & Likhitwitayawuid, 2009)
Dihydroconiferyl dihydro-*p*-coumarate [**275**]	*D. formosum*	whole plant	(Inthongkaew *et al.*, 2017)
	D. nobile	stem	(Zhang *et al.*, 2006)
	D. williamsonii	whole plant	(Yang *et al.*, 2018)
1-[4-(β-D-Glucopyranosyloxy)-3,5-dimethoxyphenyl]-1-propanone [**276**]	*D. aurantiacum* var. *denneanum*	stem	(Xiong *et al.*, 2013)
p-Hydroxyphenyl propionic methyl ester [**277**]	*D. aphyllum*	whole plant	(Chen, Li, *et al.*, 2008)
Phloretic acid [**278**]	*D. ellipsophyllum*	whole plant	(Tanagornmeatar *et al.*, 2014)
Dihydroconiferyl alcohol [**279**]	*D. longicornu*	stem	(Hu *et al.*, 2008)
Salidrosol [**280**]	*D. chrysotoxum*	stem	(Hu *et al.*, 2012)
Shashenoside I [**281**]	*D.aurantiacum* var. *denneanum*	stem	(Xiong *et al.*, 2013)

Table 2 (continued)

Category and compound	Plant	Plant part	Reference
Syringin [**282**]	*D.aurantiacum* var. *denneanum*	stem	(Xiong *et al.*, 2013)
Coumarins and lactone			
Ayapin [**283**]	*D. densiflorum*	stem	(Fan *et al.*, 2001)
Coumarin [**284**]	*D. aurantiacum* var. *denneanum*	stem	(Yang *et al.*, 2006b)
	D. clavatum var. *aurantiacum*	stem	(Chang *et al.*, 2001)
Dendrocoumarin [**285**]	*D. nobile*	stem	(Zhou *et al.*, 2018)
Denthyrsin [**286**]	*D. thyrsiflorum*	stem	(Zhang *et al.*, 2005)
Scoparone [**287**]	*D. densiflorum*	stem	(Fan *et al.*, 2001)
	D. palpebrae	whole plant	(Kyokong *et al.*, 2019)
	D. thyrsiflorum	stem	(Zhang *et al.*, 2005)
	D. williamsonii	whole plant	(Yang *et al.*, 2018)
Scopoletin [**288**]	*D. densiflorum*	stem	(Fan *et al.*, 2001)
Dendrolactone [**289**]	*D. nobile*	stem	(Zhou *et al.*, 2016a)

Table 2 (continued)

Category and compound	Plant	Plant part	Reference
Lignans and neolignans			
Dehydrodiconiferyl alcohol-4-*O*-β-D-glucoside [**290**]	*D. chrysanthum*	stem	(Ye *et al.*, 2004)
Balanophonin [**291**]	*D. williamsonii*	whole plant	(Yang *et al.*, 2018)
Acanthoside B [**292**]	*D. chrysanthum*	stem	(Ye *et al.*, 2004)
Liriodendrin [**293**]	*D. aurantiacum* var. *denneanum*	stem	(Xiong *et al.*, 2013)
	D. pulchellum	stem	(Chanvorachote *et al.*, 2013)
Syringaresinol [**294**]	*D. secundum*	stem	(Sritularak *et al.*, 2011)
	D. williamsonii	whole plant	(Yang *et al.*, 2018)
Syringaresinol-4-*O*-D-monoglucopyranoside [**17**]	*D. aurantiacum* var. *denneanum*	stem	(Xiong *et al.*, 2013)
Episyringaresinol [**295**]	*D. chrysotoxum*	stem	(Hu *et al.*, 2012)
	D. longicornu	stem	(Hu *et al.*, 2008)
	D. nobile	stem	(Zhang *et al.*, 2008b)
Episyringaresinol $4''$-*O*-β-D-glucopyranoside [**296**]	*D. moniliforme*	stem	(Zhao *et al.*, 2003)

Table 2 (continued)

Category and compound	Plant	Plant part	Reference
(-)-(7*S*,8*R*,7′*E*)-4-Hydroxy-3,3′,5,5′tetramethoxy-8,4′-oxyneolign-7′-ene-7,9,9′-triol-7,9′-bis-*O*-β-D-glucopyranoside [**297**]	*D. aurantiacum* var. *denneanum*	stem	(Xiong *et al.*, 2013)
Lyoniresinol [**298**]	*D. chrysanthum*	stem	(Ye *et al.*, 2004)
(-)-Medioresinol [**299**]	*D. loddigesii*	whole plant	(Ito *et al.*, 2010)
(-)-Pinoresinol [**300**]	*D. loddigesii*	whole plant	(Ito *et al.*, 2010)
Erythro-1-(4-*O*-β-D-glucopyranosyl-3-methoxyphenyl)-2-[4-(3-hydroxypropyl)-2,6-dimethoxyphenoxy]-1,3-propanediol [**301**]	*D. longicornu*	stem	(Hu *et al.*, 2008)
(-)-(8*R*,7′*E*)-4-Hydroxy-3,3′,5,5′-tetra-methoxy-8,4′-oxyneolign-7′-ene-9,9′-diol-4,9-bis-*O*-β-D-glucopyranoside [**302**]	*D. auranticum*	stem	(Li *et al.*, 2014)

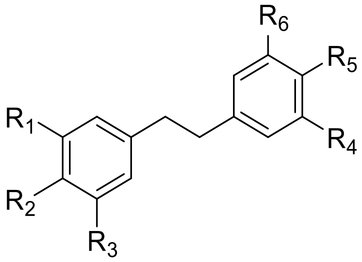
Table 2 (continued)

Category and compound	Plant	Plant part	Reference
(-)-(8*S*,7′*E*)-4-Hydroxy-3,3′,5,5′-tetramethoxy-8,4′-oxyneolign-7′-ene-9,9′-diol,4,9-bis-*O*-β-D-glucopyranoside [**303**]	*D. auranticum*	stem	(Li *et al.*, 2014)
(-)-(8*R*,7′*E*)-4-hydroxy-3,3′,5,5′,9′-pentamethoxy-8,4′-oxyneolign-7′-ene-9-ol-4,9-bis-*O*-β-D-glucopyranoside [**304**]	*D. auranticum*	stem	(Li *et al.*, 2014)
Fluorenones			
Denchrysan A [**305**]	*D. chrysotoxum*	whole plant	(Li *et al.*, 2009a)
Dendroflorin [**306**]	*D. aurantiacum* var. *denneanum*	stem	(Yang *et al.*, 2006b)
	D. brymerianum	whole plant	(Klongkumnuankarn *et al.*, 2015)
	D. palpebrae	whole plant	(Kyokong *et al.*, 2019)
Dengibsin [**307**]	*D. aurantiacum* var. *denneanum*	stem	(Yang *et al.*, 2006b)
	D. chrysanthum	stem	(Yang *et al.*, 2006a)
	D. chrysotoxum	whole plant	(Li *et al.*, 2009a)

Table 2 (continued)

Category and compound	Plant	Plant part	Reference
Nobilone [**308**]	*D. brymerianum*	whole plant	(Klongkumnuankarn *et al.*, 2015)
	D. nobile	stem	(Zhang *et al.*, 2007)
	D. palpebrae	whole plant	(Kyokong *et al.*, 2019)
1,4,5-Trihydroxy-7-methoxy-9*H*-fluoren-9-one [**309**]	*D. chrysotoxum*	whole plant	(Chen *et al.*, 2008b)
2,4,7-Trihydroxy-5-methoxy-9-fluorenone [**310**]	*D. chrysotoxum*	stem	(Yang *et al.*, 2004)
2,4,7-Trihydroxy-1,5-dimethoxy-9-fluorenone [**311**]	*D. chrysotoxum*	stem	(Yang *et al.*, 2004)
Denchrysan B [**312**]	*D. brymerianum*	whole plant	(Klongkumnuankarn *et al.*, 2015)
	D. chrysanthum	whole plant	(Ye *et al.*, 2003)
Alkaloids			
(-)-(1*R*,2*S*,3*R*,4*S*,5*R*,6*S*,9*S*,11*R*)-11-Carboxy-methyldendrobine [**313**]	*D. nobile*	stem	(Meng *et al.*, 2017)
Dendrobine [**314**]	*D. nobile*	stem	(Meng *et al.*, 2017)
Crepidatumine A [**315**]	*D. crepidatum*	stem	(Xu *et al.*, 2020)

Category and compound	Plant	Plant part	Reference
Crepidatumine B [**316**]	*D. crepidatum*	stem	(Xu *et al.*, 2020)
Crepidatumine C [**317**]	*D. crepidatum*	stem	(Xu *et al.*, 2019)
Crepidatumine D [**318**]	*D. crepidatum*	stem	(Xu *et al.*, 2019)
Miscellaneous compounds			
3,6,9-Trihydroxy-3,4-dihydroanthracen-1-(2*H*)-one [**319**]	*D. chrysotoxum*	stem	(Hu *et al.*, 2012)
Palmarumycin JC2 [**320**]	*D. crystallinum*	stem	(Wang *et al.*, 2009)
Dehydrovomifoliol [**321**]	*D. loddigesii*	whole plant	(Ito *et al.*, 2010)
4-(2-Hydroxypropyl)-2(5*H*)-furanone [**322**]	*D. tortile*	whole plant	(Limpanit *et al.*, 2016a)
5,7-Dihydroxychromen-4-one [**323**]	*D. ellipsophyllum*	whole plant	(Tanagornmeatar *et al.*, 2014)
RF-3192C [**324**]	*D. scabrilingue*	whole plant	(Sarakulwattana *et al.*, 2020)



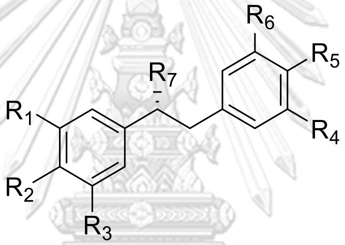
	R_1	R_2	R_3	R_4	R_5	R_6
[**20**] Aloifol I	OMe	OH	OMe	OH	H	H
[**21**] Amoenylin	OMe	OH	OMe	H	OMe	H
[**22**] Batatasin	OMe	H	H	OH	H	OH
[**3**] Batatasin III	OH	H	OMe	H	H	OH
[**23**] Brittonin A	OMe	OMe	OMe	OMe	OMe	OMe
[**24**] Chrysotobibenzyl	OMe	OMe	OMe	OMe	OMe	H
[**25**] Crepidatin	OMe	OMe	OMe	OMe	OH	H
[**26**] Cumulatin	OMe	OMe	OH	OH	OMe	OMe
[**28**] 4,5-Dihydroxy-3,3′,4′-trimethoxybibenzyl	OMe	OH	OH	H	OMe	OMe
[**27**] Chrysotoxine	OMe	OH	OMe	H	OMe	OMe
[**29**] Dendrobin A	OH	OH	OMe	H	H	OMe
[**30**] Dendromoniliside E	OGlc	OGlc	OMe	H	OMe	H
[**31**] 3,3′-Dihydroxy-4,5-dimethoxybibenzyl	OMe	OMe	OH	H	H	OH
[**32**] 3,4′-Dihydroxy-5-methoxybibenzyl	OH	H	OMe	H	OH	H
[**33**] 3,4′-Dihydroxy-5,5′-dimethoxydihydrostilbene	OH	H	OMe	OMe	OH	H

Figure 5 Structures of compounds isolated from *Dendrobium*

	R_1	R_2	R_3	R_4	R_5	R_6
[**34**] 3,4′-Dihydroxy-3′,4,5-trimethoxybibenzyl	OMe	OMe	OH	H	OH	OMe
[**35**] Erianin	OMe	OMe	H	OMe	OH	OMe
[**2**] Gigantol	OMe	H	OH	H	OH	OMe
[**36**] Gigantol-5-*O*-β-D-glucopyranoside	OMe	H	OGlc	H	OH	OMe
[**37**] 4-Hydroxy-3,5,3′-trimethoxybibenzyl	OMe	OH	OMe	H	H	OMe
[**38**] 5-Hydroxy-3,4,3′,4′,5′-pentamethoxybibenzyl	OMe	OMe	OH	OMe	OMe	OMe
[**39**] Isoamoenylin	OMe	OMe	OMe	H	H	OH
[**40**] Moscatilin	OMe	OH	OMe	H	OH	OMe
[**41**] Moscatilin diacetate	OMe	OAc	OMe	H	OAc	OMe
[**42**] 3,3′,4-Trihydroxy bibenzyl	OH	OH	H	H	H	OH
[**43**] 3,3′,5-Trihydroxy bibenzyl	OH	H	OH	H	H	OH
[**44**] 3,5,4′-Trihydroxy bibenzyl	OH	H	OH	H	OH	H
[**45**] 4,5,4′-Trihydroxy-3,3′-dimethoxy bibenzyl	OMe	OH	OH	H	OH	OMe
[**46**] 4,3′,4′-Trihydroxy-3,5-dimethoxy bibenzyl	OMe	OH	OMe	H	OH	OH
[**47**] Tristin	OH	H	OH	H	OH	OMe

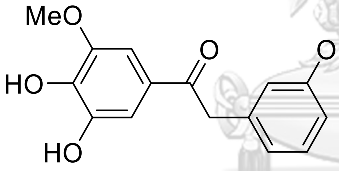
Figure 5 (continued)

	R_1	R_2	R_3	R_4	R_5	R_6
[**48**] Dendrophenol	OMe	OH	OMe	OH	H	OH
[**49**] Dendrocandin E	OMe	OH	OH	OH	OH	H
[**50**] Dendrosinen B	OMe	OMe	OH	H	OH	H
[**51**] 3,4-Dihydroxy-5,4′-dimethoxy bibenzyl	OH	OH	OMe	H	OMe	H
[**52**] 4,4′-Dihydroxy-3,5-dimethoxy bibenzyl	OMe	OH	OMe	H	OH	H
[**53**] 3-*O*-Methylgigantol	OMe	H	OH	OMe	OMe	H

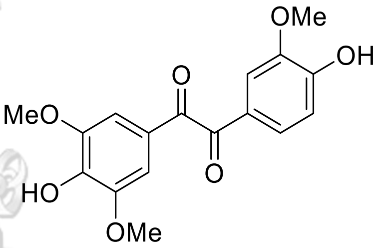


	R_1	R_2	R_3	R_4	R_5	R_6	R_7
[**54**] Dendrocandin A	OMe	OH	OH	H	OMe	H	OMe
[**55**] Dendrocandin C	OMe	OH	OH	H	OH	H	OMe
[**56**] Dendrocandin D	OMe	OH	OH	H	OH	H	OEt
[**57**] Dendrosinen A	OMe	OMe	OH	H	OH	H	OH
[**58**] 4,5-Dihydroxy-3,α,3′,4′-tetramethoxybibenzyl	OMe	OH	OH	OMe	OMe	H	OMe

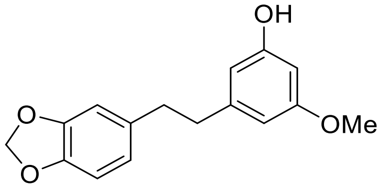
	R_1	R_2	R_3	R_4	R_5	R_6	R_7
[**59**] 4,4′,5-trihydroxy-3,3′,α-trimethoxybibenzyl	OMe	OH	OH	OMe	OH	H	OMe
[**60**] 4-[2-(3-Hydroxyphenol)-1-methoxyethyl]-2,6-dimethoxyphenol	OMe	OH	OMe	H	H	OH	OMe
[**61**] Loddigesiinol C	OMe	OH	OMe	H	OH	OMe	OMe
[**62**] Nobilin A	OMe	OH	OH	H	H	OMe	OMe
[**63**] Nobilin B	OMe	OH	OMe	H	OH	OMe	OMe
[**64**] Nobilin C	OMe	OH	OMe	H	OMe	OMe	OMe
[**65**] Nobilin D	OMe	OH	H	OMe	OH	OMe	OH



[**66**] Dendrosinen C

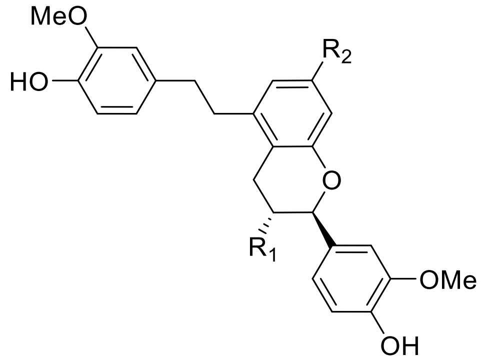


[**67**] Loddigesiinol D

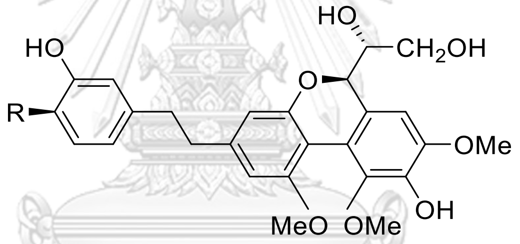


[**68**] Densiflorol A

Figure 5 (continued)



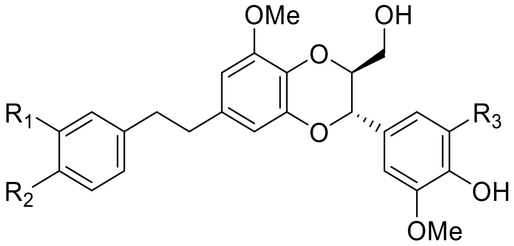
	R_1	R_2
[**69**] Crepidatuol A	H	OMe
[**70**] Crepidatuol B	OH	OMe
[**71**] Trigonopol B	OH	OH



[**72**] Longicornuol A: R = H

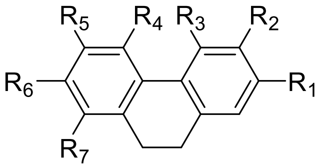
[**73**] Trigonopol A: R = OMe

Figure 5 (continued)



	R_1	R_2	R_3
[**74**] Dendrocandin B	H	OMe	OMe
[**75**] Dendrocandin T	OMe	OH	OMe
[**76**] Dendrocandin U	H	OH	OMe
[**77**] Dendrocandin V	H	OMe	H

Figure 5 (continued)



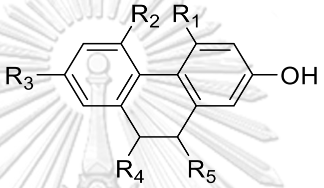
	R_1	R_2	R_3	R_4	R_5	R_6	R_7
[**78**] 1,5-Dihydroxy-3,4,7-trimethoxy-9,10-dihydrophenanthrene	H	OMe	OMe	OH	H	OMe	H
[**9**] Coelonin	OH	H	OMe	H	H	OH	H
[**79**] Dendroinfundin A	OMe	OMe	OH	H	H	OMe	H
[**80**] Dendroinfundin B	OMe	OMe	OH	OH	H	H	OMe
[**81**] 4,5-Dihydroxy-2,3-dimethoxy-9,10-dihydrophenanthrene	OMe	OMe	OH	OH	H	H	H
[**82**] 4,5-Dihydroxy-2,6-dimethoxy-9,10-dihydrophenanthrene	OMe	H	OH	OH	OMe	H	H
[**83**] 4,5-Dihydroxy-3,7-dimethoxy-9,10-dihydro phenanthrene	H	OMe	OH	OH	H	OMe	H
[**7**] 4,5-Dihydroxy-2-methoxy-9,10-dihydrophenanthrene (Orchinol)	OMe	H	OH	OH	H	H	H

Figure 5 (continued)

	R_1	R_2	R_3	R_4	R_5	R_6	R_7
[**84**] 9,10-Dihydromoscatin	H	H	OH	OMe	H	OH	H
[**85**] 9,10-Dihydrophenanthrene-2,4,7-triol	OH	H	OH	H	H	OH	H
[**86**] 2,7-Dihydroxy-3,4,6-trimethoxy-9,10-dihydrophenanthrene	OH	OMe	OMe	H	OMe	OH	H
[**87**] 2,8-Dihydroxy-3,4,7-trimethoxy-9,10-dihydrophenanthrene	OH	OMe	OMe	H	H	OMe	OH
[**88**] 4,7-Dihydroxy-2,3,6-trimethoxy-9,10-dihydrophenanthrene	OMe	OMe	OH	H	OMe	OH	H
[**89**] 3,4-Dimethoxy-1-(methoxymethyl)-9,10-dihydrophenanthrene-2,7-diol	OH	H	H	OMe	OMe	OH	CH_2-OMe
[**90**] Ephemeranthol A	OH	H	H	OH	OMe	OMe	H
[**91**] Ephemeranthol C	OH	OH	OMe	OH	H	H	H
[**92**] Erianthridin	OH	OMe	OMe	H	H	OH	H
[**93**] Flavanthridin	OH	H	H	OMe	OH	OMe	H
[**94**] Hircinol	OH	H	OMe	OH	H	H	H

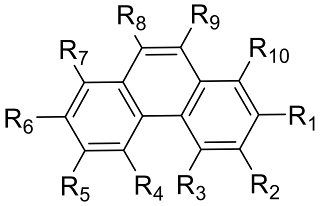
Figure 5 (continued)

	R_1	R_2	R_3	R_4	R_5	R_6	R_7
[**95**] 3-Hydroxy-2,4,7-trimethoxy-9,10-dihydrophenanthrene	OMe	OH	OMe	H	H	OMe	H
[**96**] 7-Hydroxy-2,3,4-trimethoxy-9,10-dihydrophenanthrene	OMe	OMe	OMe	H	H	OH	H
[**97**] Lusianthridin	OMe	H	OH	H	H	OH	H



	R_1	R_2	R_3	R_4	R_5
[**98**] 2-Hydroxy-4,7-dimethoxy-9,10-dihydrophenanthrene	OMe	H	OMe	H	H
[**99**] 7-Methoxy-9,10-dihydrophenanthrene-2,4,5-triol	OH	OH	OMe	H	H
[**100**] 2,5,7-Trihydroxy-4-methoxy-9,10-dihydrophenanthrene	OMe	OH	OH	H	H
[**101**] Plicatol C	OMe	OH	H	OMe	OMe
[**102**] Rotundatin	OMe	OH	H	OH	OH
[**103**] (*S*)-2,4,5,9-Tetrahydroxy-9,10-dihydrophenanthrene	OH	OH	H	OH	H

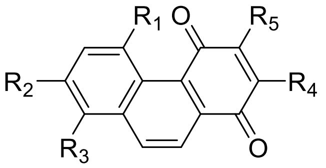
Figure 5 (continued)



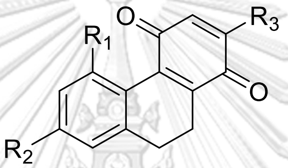
	R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8	R_9	R_{10}
[**104**] 2,5-Dihydroxy-3,4-dimethoxyphenanthrene	OH	OMe	OMe	OH	H	H	H	H	H	H
[**105**] 2,5-Dihydroxy-4,9-dimethoxy-phenanthrene	OH	H	OMe	OH	H	H	H	OMe	H	H
[**106**] 2,8-Dihydroxy-3,4,7-trimethoxy-phenanthrene	OH	OMe	OMe	H	H	OMe	OH	H	H	H
[**107**] Epheranthol B	H	H	OMe	OH	H	OMe	H	H	H	H
[**108**] Fimbriol B	OH	OMe	OH	H	H	H	H	H	H	H
[**109**] Flavanthrinin	H	H	OMe	H	H	OH	H	H	H	H
[**110**] Moscatin	H	H	OH	OMe	H	OH	H	H	H	H
[**111**] Loddigesiinol A	OH	H	OMe	OMe	H	H	H	OH	H	H
[**112**] Dendroscabrol A	OH	OMe	OMe	H	H	OMe	H	H	H	H
[**113**] Nudol	OH	OMe	OMe	H	H	OH	H	H	H	H
[**114**] Plicatol A	OH	H	OMe	OH	H	H	H	OMe	OMe	OH
[**115**] Plicatol B	OH	H	OMe	OH	H	H	H	H	H	H

	R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8	R_9	R_{10}
[**116**] 2,3,5-Trihydroxy-4,9-dimethoxyphenanthrene	OH	OH	OMe	OH	H	H	H	OMe	H	H
[**117**] 3,4,8-Trimethoxyphenanthrene-2,5-diol	OH	OMe	OMe	OH	H	H	OMe	H	H	H
[**118**] Bulbophyllanthrin	OMe	OH	OMe	OH	H	H	H	H	H	H
[**119**] Denthyrsinin	OMe	OH	OMe	H	H	OH	OMe	H	H	H
[**120**] 5-Hydroxy-2,4-dimethoxy phenanthrene	OMe	H	OMe	OH	H	H	H	H	H	H
[**121**] 3-Hydroxy-2,4,7-trimethoxyphenanthrene	OMe	OH	OMe	H	OMe	H	H	H	H	H
[**122**] Confusarin	OH	H	H	OMe	OMe	OH	H	H	H	OMe
[**123**] 2,6-Dihydroxy-1,5,7trimethoxyphenanthrene	OH	H	H	OMe	OH	OMe	H	H	H	OMe
[**124**] 1,5,7-Trimethoxyphenanthre-2ol	OH	H	H	OMe	H	OMe	H	H	H	OMe

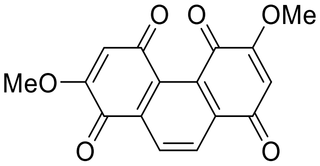
Figure 5 (continued)



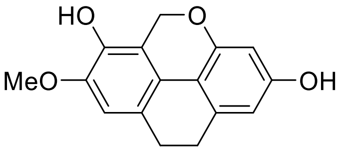
	R_1	R_2	R_3	R_4	R_5
[**125**] Cypripedin	H	OH	OMe	OMe	H
[**126**] Densiflorol B	H	OH	H	OMe	H
[**127**] Denbinobin	OH	OMe	H	H	OMe



	R_1	R_2	R_3
[**128**] Dendronone	OH	OMe	H
[**129**] Ephemeranthoquinone	H	OH	OMe
[**12**] 5-Methoxy-7-hydroxy-9,10-dihydro-1,4-phenanthrenequinone	OMe	OH	H

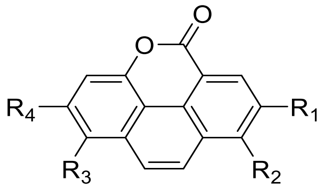


[**130**] Moniliformin

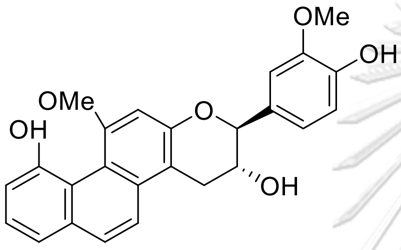


[**131**] Amoenumin

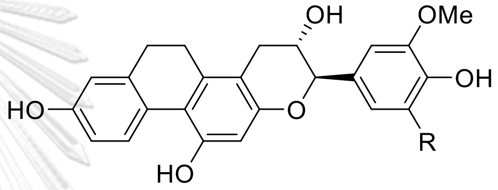
Figure 5 (continued)



	R_1	R_2	R_3	R_4
[**132**] Fimbriatone	OH	OMe	H	OH
[**133**] Crystalltone	OMe	H	OH	EtO

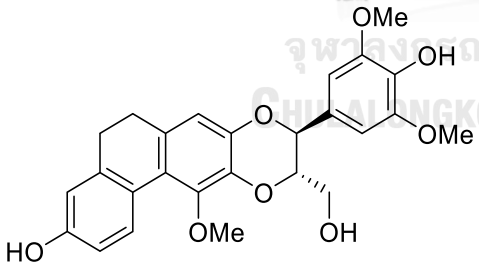


[**133**] Loddigesiinol B

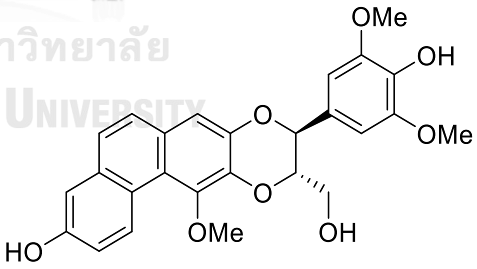


[**134**] Chrysotoxol A: R = H

[**135**] Chrysotoxol B: R = OMe

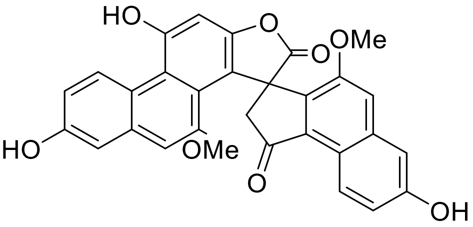


[**136**] Dendrocandin P2

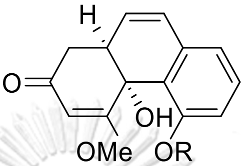


[**137**] Dendrocandin P1

Figure 5 (continued)

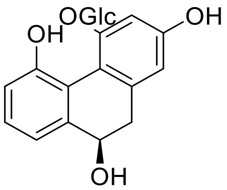


[**138**] Dendrochrysanene

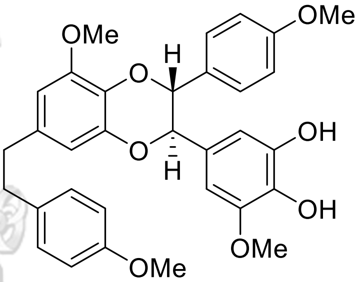


[**139**] Aphyllone: R = H

[**140**] 9,10-Dihydro-aphyllone A-5-*O*-β-D-glucopyranoside: R = Glc

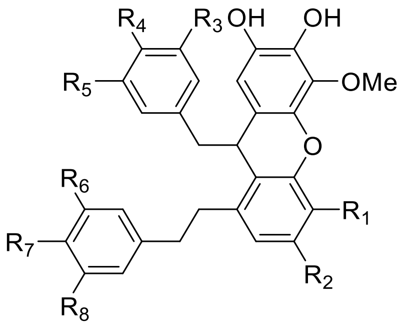


[**141**] 2,4,5,9*S*-Tetrahydroxy-9,10-dihydro-phenanthrene-4-*O*-β-D-glucopyranoside

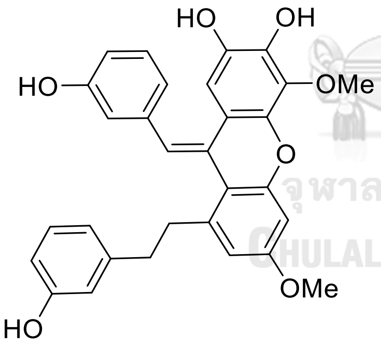


[**142**] Dendrocandin I

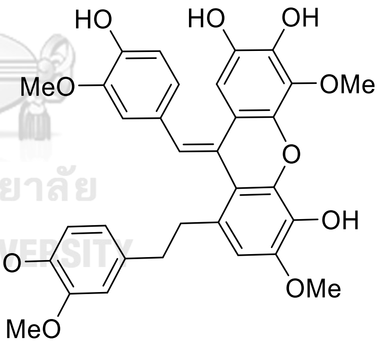
Figure 5 (continued)



	R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8
[**143**] Dendrocandin F	H	OMe	H	OMe	H	H	OMe	H
[**144**] Dendrocandin G	OH	OMe	H	OH	H	H	OMe	H
[**145**] Dendrosinen D	OH	OMe	OH	H	H	OH	H	H
[**146**] Dendrofalconerol B	H	OH	H	OMe	H	H	OH	H
[**147**] Nobilin E	OH	OMe	H	H	OMe	H	H	OMe

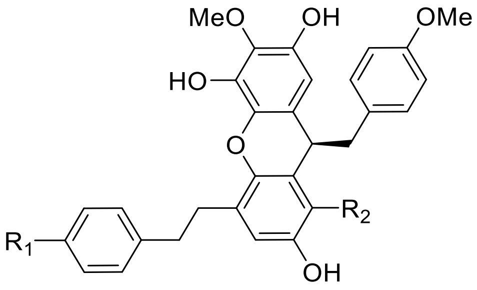


[**5**] Dendroscabrol B



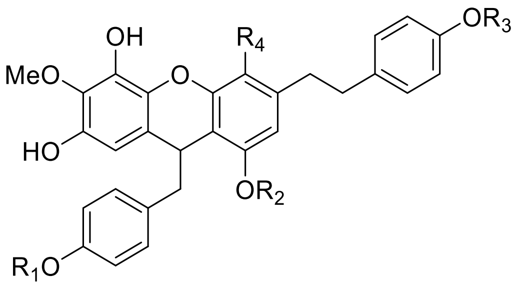
[**148**] Dendropachol

Figure 5 (continued)

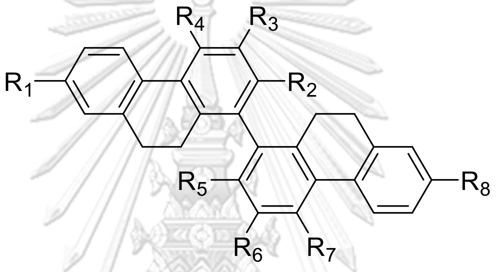


[**149**] Dengraol A: R_1 = OH, R_2 = H

[**150**] Dengraol B: R_1 = R_2 = OMe

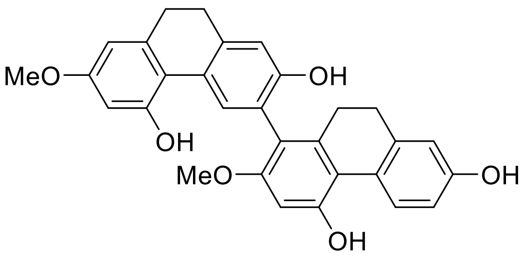


	R_1	R_2	R_2	R_4
[**151**] Dencryol A	OMe	OH	OH	H
[**152**] Dencryol B	OH	OMe	OMe	OH

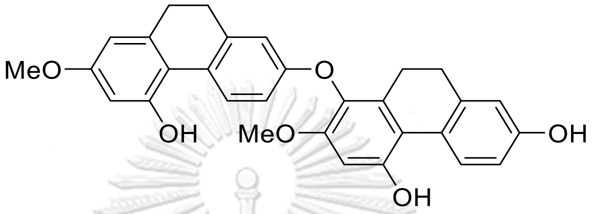


	R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8
[**153**] 2,2′-Dihydroxy-3,3′,4,4′,7,7′-hexamethoxy-9,9′,10,10′-tetrahydro-1,1′-biphenanthrene	OMe	OH	OMe	OMe	OH	OMe	OMe	OMe
[**154**] 2,2′-Dimethoxy-4,4′,7,7′-tetrahydroxy-9,9′,10,10′-tetrahydro-1,1′-biphenanthrene	OH	OMe	H	OH	OMe	H	OH	OH
[**155**] Flavanthrin	OH	OH	H	OMe	OH	H	OMe	OH

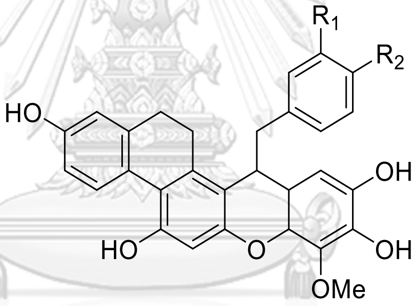
Figure 5 (continued)



[**156**] Phoyunnanin C



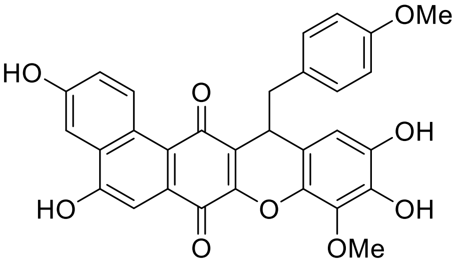
[**157**] Phoyunnanin E



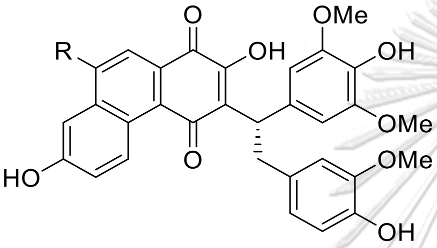
[**158**] Dendrosignatol: R_1 = H, R_2 = OMe

[**159**] Dendroparishiol: R_1 = OMe, R_2 = OH

Figure 5 (continued)

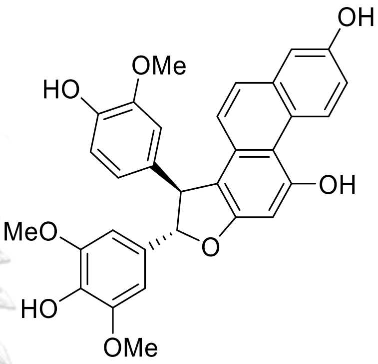


[**160**] Dendrocandin H

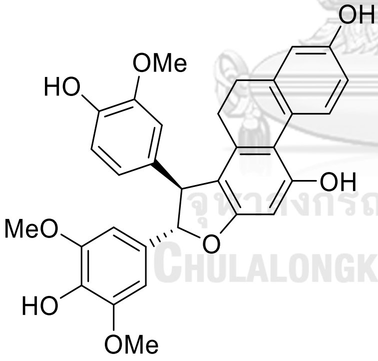


[**161**] Loddigesiinol G: R = H

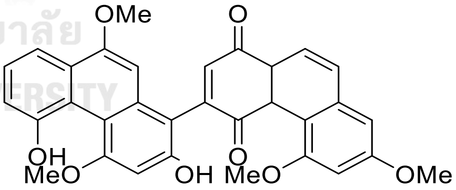
[**162**] Loddigesiinol H: R = OH



[**163**] Loddigesiinol I

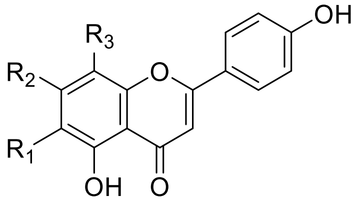


[**164**] Loddigesiinol J



[**165**] Dendropalpebrone

Figure 5 (continued)



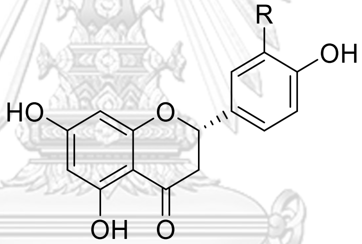
	R$_1$	R$_2$	R$_3$
[**166**] Apigenin	H	OH	H
[**167**] Apigenin-6-*C*-glucosyl-(1→2)-α-L-arabinoside	[Ara-]$_2$	OH	H
[**168**] 6-*C*-(α-Arabinopyranosyl)-8-*C*-[(2-*O*-α-rhamnopyranosyl)-β-galactopyranosyl]apigenin	-Ara	OH	-Gal-Rha
[**169**] 6-*C*-[(2-*O*-α-Rhamnopyranosyl)-β-glucopyranosyl]-8-*C*-(α-arabinopyranosyl)apigenin	-Glc-Rha	OH	-Ara

Figure 5 (continued)

	R_1	R_2	R_3	R_4	R_5	R_6
[**170**] 6-*C*-(β-Xylopyranosyl)-8-*C*-[(2-*O*-α-rhamnopyranosyl)-β-glucopyranosyl]apigenin	-Xyl	OH	-Glc-Rha	H	OH	H
[**171**] 5,6-Dihydroxy-4′-methoxyflavone	OH	H	H	H	OMe	H
[**172**] 6‴-Glucosyl-vitexin	H	OH	-(Glc)$_2$	H	OH	H
[**15**] 5-Hydroxy-3-methoxyflavone-7-*O*-[β-D-apiosyl-(1→6)]-β-D-glucoside	H	-Glc- Api	H	H	H	OMe
[**173**] Isoschaftoside	-Ara	OH	-Glc	H	OH	H
[**174**] Isoviolanthin	-Rha	OH	-Glc	H	OH	H
[**175**] Kaempferol	H	OH	H	H	OH	OH
[**176**] Kaempferol-3-*O*-α-L-rhamnopyranoside	H	OH	H	H	OH	O-Rha
[**177**] Kaempferol-3,7-*O*-di-α-L-rhamnopyranoside	H	O-Rha	H	H	OH	O-Rha
[**178**] Kaempferol-3-*O*-α-L-rhamnopyranosyl-(1→2)-β-D-glucopyranoside	H	OH	H	H	OH	O-Glc-Rha

Figure 5 (continued)

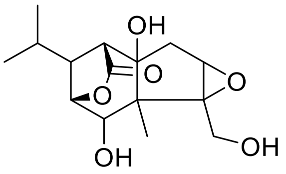
	R_1	R_2	R_3	R_4	R_5	R_6
[**179**] Kaempferol-3-*O*-α-L-rhamnopyranosyl(1→2)-β-D-xylopyranoside	H	OH	H	H	OH	O-Xyl- Rha
[**180**] Luteolin	H	OH	H	OH	OH	H
[**181**] Vicenin-2	-Glc	OH	-Glc	H	OH	H
[**182**] Quercetin-3-*O*-α-L-rhamnopyranoside	H	OH	H	OH	OH	-O-Rha
[**183**] Quercetin-3-*O*-α-L-rhamnopyranosyl-(1→2)-β-D-xylopyranoside	H	OH	H	OH	OH	-O-Xyl-Rha



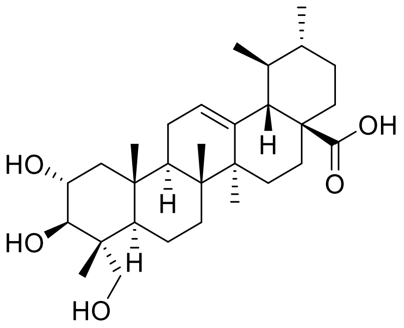
[**184**] (2*S*)-Homoeriodictyol: R = OMe

[**14**] Naringenin: R = H

[**185**] (2*S*)-Eriodictyol: R = OH

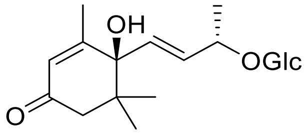


[**187**] Amoenin

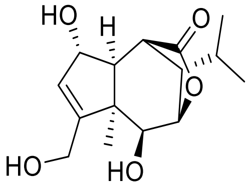


[**188**] Asiatic acid

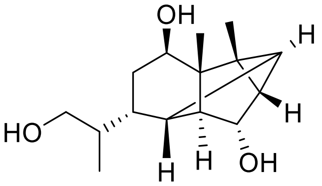
Figure 5 (continued)



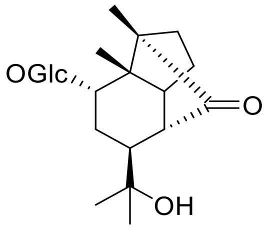
[**189**] Corchoionoside C



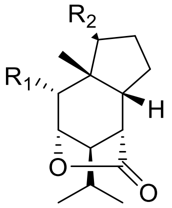
[**190**] Crystallinin

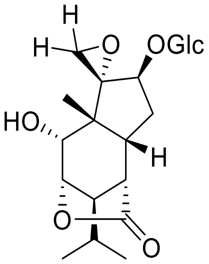


[**191**] Dendrobane A



[**192**] Dendromoniliside A

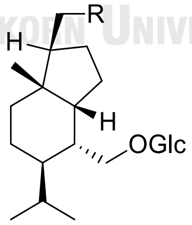




[**192**] Dendromoniliside B, R_1 = OGlc, R_2 = COOH

[**192**] Dendromoniliside C

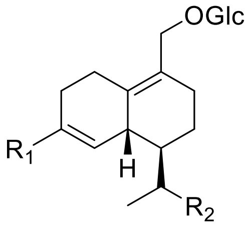
[**192**] Dendromoniliside D, R_1 = OH, R_2 = OGlc



[**193**] Dendronobiloside A: R = OGlc

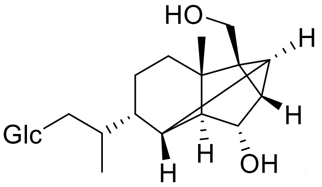
[**194**] Dendronobiloside B: R = OH

Figure 5 (continued)

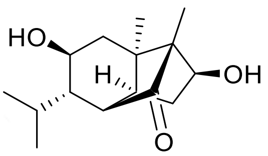


[**195**] Dendronobiloside C, R_1= $-CH_2OGlc$, R_2=H

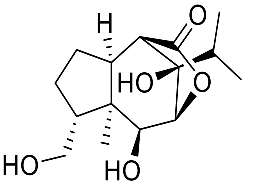
[**196**] Dendronobiloside D, R_1=H, R_2= OGlc



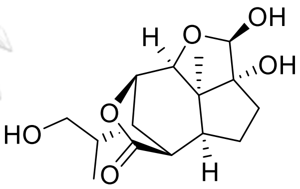
[**197**] Dendronobiloside E



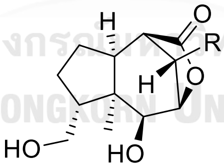
[**198**] Dendronobilin A

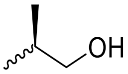


[**199**] Dendronobilin B



[**200**] Dendronobilin C



[201] Dendronobilin D; R = 

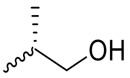
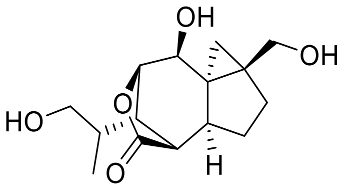
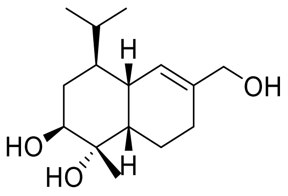
[202] Dendronobilin E; R = 

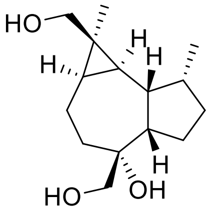
Figure 5 (continued)



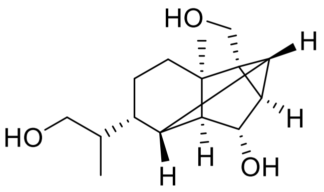
[**203**] Dendronobilin F



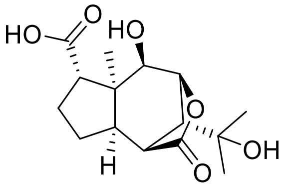
[**204**] Dendronobilin G



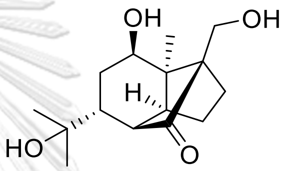
[**205**] Dendronobilin H



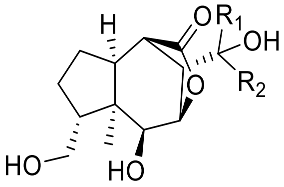
[**206**] Dendronobilin I

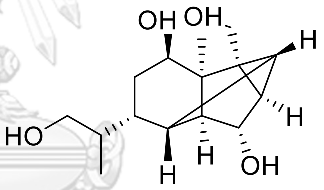


[**207**] Dendronobilin J



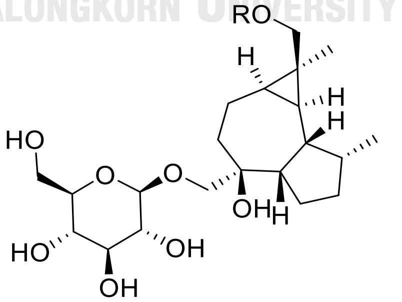
[**208**] Dendronobilin K





[**209**] Dendronobilin L, R_1=Me, R_2=CH_2 [**211**] Dendronobilin N

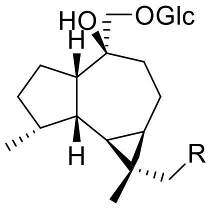
[**210**] Dendronobilin M, R_1=CH_2OH, R_2=OH

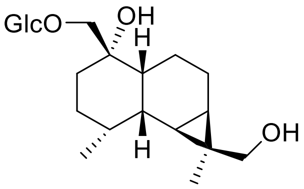


[**212**] Dendroside A: R = H

[**213**] Dendroside B: R = Glc

Figure 5 (continued)

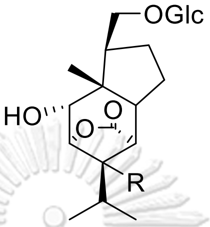




[**214**] Dendroside C; R = OH

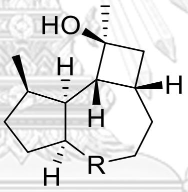
[**215**] Dendroside D; R= OGlc

[**216**] Dendroside E



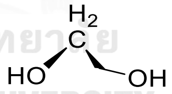
[**217**] Dendroside F; R = H

[**218**] Dendroside G; R = OH

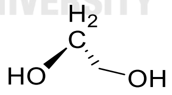


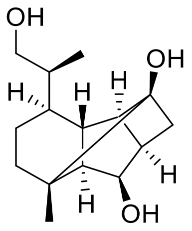
R

[**219**] Dendrowardol A



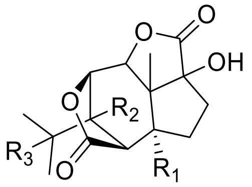
[**220**] Dendrowardol B





[**221**] Dendrowardol C

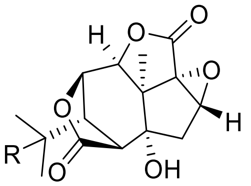
Figure 5 (continued)



[**222**] Amotin: $R_1 = R_3 = H$, $R_2 = OH$

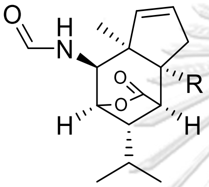
[**223**] Dendrowillin A: $R_1 = R_3 = OH$, $R_2 = H$

[**224**] Dendrowillin B: $R_1 = R_2 = H$, $R_3 = OH$



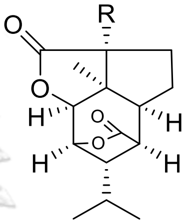
[**225**] α-Dihydropicrotoxinin: R = H

[**230**] Picrotin: R = OH



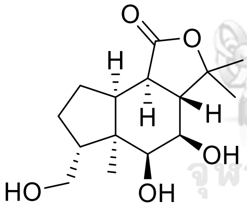
[226] Dendroterpene A; R =H

[227] Dendroterpene B; R =OH

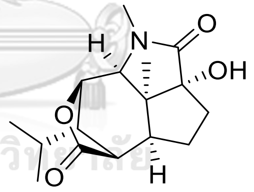


[228] Dendroterpene C; R =H

[229] Dendroterpene D; R =OH

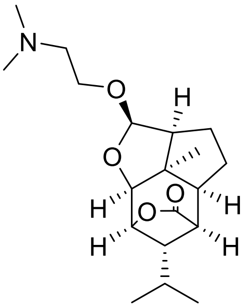


[**231**] Findlayanin



[**232**] 3-Hydroxy-2-oxodendrobine

Figure 5 (continued)

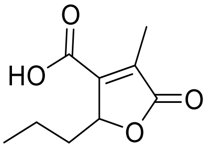


[**233**] Wardianumine A

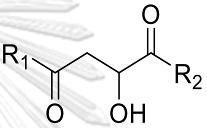
CH_3-(CH_2)n-CH_2-R

[**234**] Aliphatic acids: R = COOH, n = 19-31

[**235**] Aliphatic alcohols: R = OH, n = 22-32

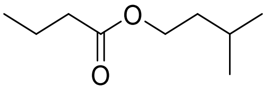


[**236**] Decumbic acid

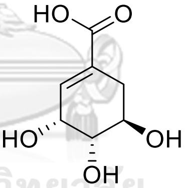


[**237**] Dimethyl malate: R_1=R_2= OMe

[**238**] Malic acid: R_1 = R_2 = OH

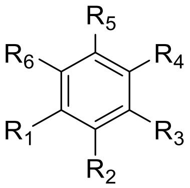


[**239**] Isopentyl butyrate



[**240**] (-)-Shikimic acid

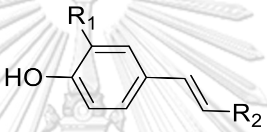
Figure 5 (continued)



	R_1	R_2	R_3	R_4	R_5	R_6
[**241**] Antiarol	OMe	OMe	H	OH	H	OMe
[**242**] Ethylhaematommate	H	Me	COO-C_2H_5	OH	CHO	OH
[**243**] Methylhaematommate	H	Me	COOMe	OH	CHO	OH
[**244**] Gallic acid	OH	OH	OH	H	COOH	H
[**245**] *p*-Hydroxybenzaldehyde	OH	H	H	CHO	H	H
[**246**] *p*-Hydroxybenzoic acid	H	OH	H	H	H	COOH
[**247**] 3-Hydroxy-2-methoxy-5,6-dimethylbenzoic acid	COOH	Me	Me	H	OH	OMe
[**248**] Methyl-4-hydroxybenzoate	H	H	COOMe	H	H	OH
[**248**] Methyl 2,4-dihydroxy-3,6-dimethylbenzoate	OH	H	Me	COOMe	OH	Me
[**249**] Methyl β-orsellinate	H	OH	COOMe	Me	H	OH

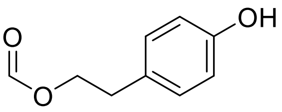
Figure 5 (continued)

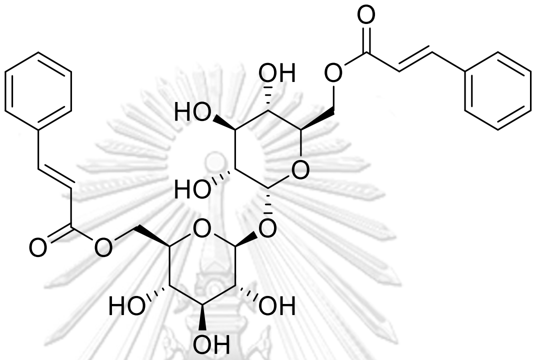
	R_1	R_2	R_3	R_4	R_5	R_6
[**250**] Protocatechuic acid	H	OH	OH	H	COOH	H
[**251**] Salicylic acid	H	H	H	COOH	OH	H
[**252**] Syringic acid	OMe	OH	OMe	H	COOH	H
[**253**] Tachioside	H	H	OH	OMe	H	-OGlc
[**254**] Vanillic acid	H	OH	OMe	H	COOH	H
[**255**] Vanillin	OH	H	H	CHO	H	OMe
[**256**] Vanilloside	-OGlc	H	H	CHO	H	OMe



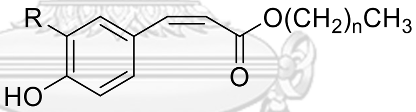
	R_1	R_2	
[**257**] Alkyl 4′-hydroxy-*trans*-cinnamates	H	COO-C_nH_{2n+1}	n =22-32
[**258**] Alkyl *trans*-ferulates	OMe	COO-C_nH_{2n+1}	n=18-28,30
[**259**] Defuscin	H	COO-$(CH_2)_{29}CH_3$	
[**260**] *n*-Octacosyl ferulate	OMe	COO- $(CH_2)_{27}CH_3$	
[**261**] *n*-Triacontyl *p*-hydroxy-*cis*-cinnamate	H	COO-$C_{30}H_{61}$	
[**262**] Tetratriacontanyl-*trans*-*p*-coumarate	H	COO-$(CH_2)_{33}CH_3$	
[**263**] *n*-Docosyl *trans*-ferulate	OMe	COO-$(CH_2)_{21}CH_3$	
[**264**] *n*-Eicosyl *trans*-ferulate	OMe	COO-$(CH_2)_{19}CH_3$	
[**265**] *n*-Docosyl 4-hydroxy-*trans*-cinnamate	H	COO-$(CH_2)_{21}CH_3$	
[**266**] *trans*-Tetracosyl ferulate	OMe	COO-$(CH_2)_{23}CH_3$	
[**267**] Ferulaldehyde	OMe	CHO	
[**268**] Ferulic acid	OMe	COOH	

Figure 5 (continued)

	R_1	R_2
[**269**] 2-(*p*-Hydroxyphenyl)-ethyl-*p*-coumarate	OMe	
[**270**] Coniferyl alcohol	OMe	OH



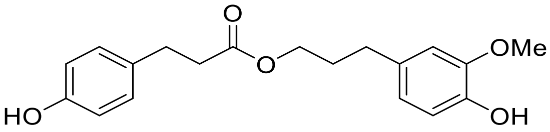
[**271**] Dendroside



[**272**] *cis*-Hexacosanoyl ferulate: R= OMe, n=25

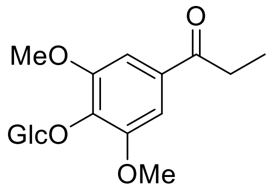
[**273**] *cis*-Tetracosanoyl ferulate: R= OMe, n=22

[**274**] Tetracosyl (*Z*)-*p*-coumarate: R= H, n=23

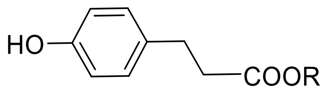


[**275**] Dihydroconiferyl dihydro-*p*-coumarate

Figure 5 (continued)



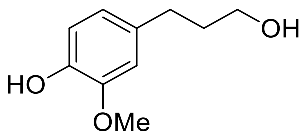
[**276**] 1-[4-(β-D-glucopyranosyloxy)-3,5-dimethoxyphenyl]-1-propanone



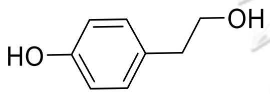
[**277**] *p*-Hydroxyphenyl propionic

methyl ester: R = Me

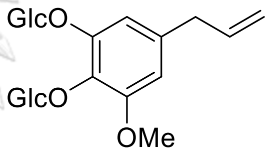
[**278**] Phloretic acid: R =H



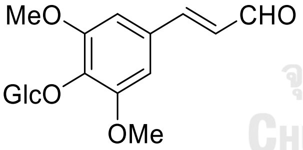
[**279**] Dihydroconiferyl alcohol



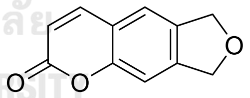
[**280**] Salidrosol



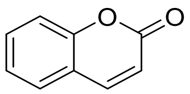
[**281**] Shashenoside I



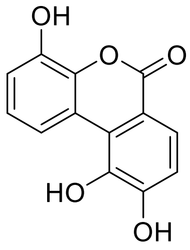
[**282**] Syringin



[**283**] Ayapin

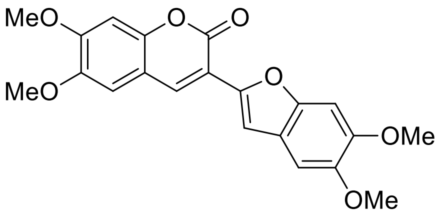


[**284**] Coumarin

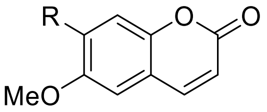


[**285**] Dendrocoumarin

Figure 5 (continued)

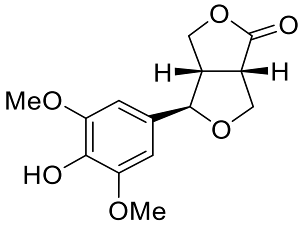


[**286**] Denthyrsin

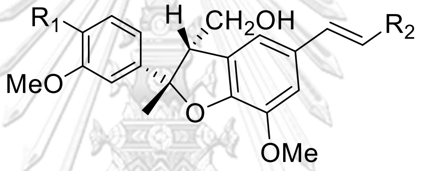


[**287**] Scoparone: R = OMe

[**288**] Scopoletin: R = OH

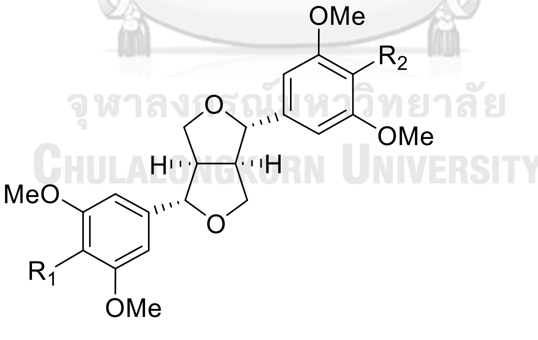


[**289**] Dendrolactone



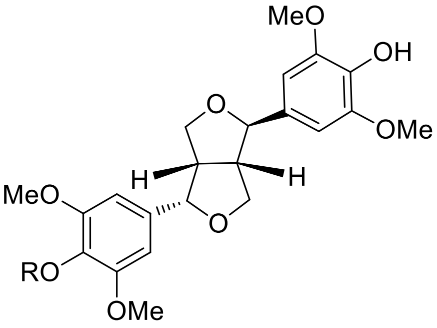
[**290**] Dehydrodiconiferyl alcohol-4-*O*-β-D-glucoside: R_1=OGlc, R_2=CH_2OH

[**291**] Balanophonin,: R_1=OH, R_2=CHO



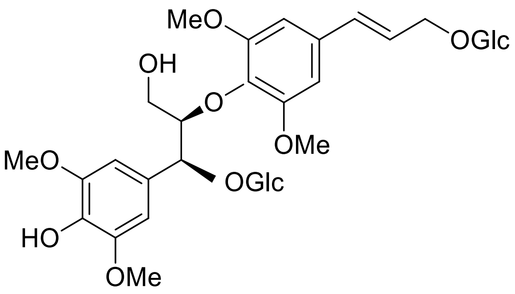
	R_1	R_2
[**292**] Acanthoside B	OGlc	OH
[**293**] Liriodendrin	OGlc	OGlc
[**294**] Syringaresinol	OH	OH
[**17**] Syringaresinol-4-*O*-D-monoglucopyranoside	OGlc	H

Figure 5 (continued)

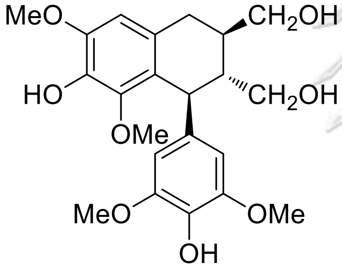


[**295**] Episyringaresinol: R = H

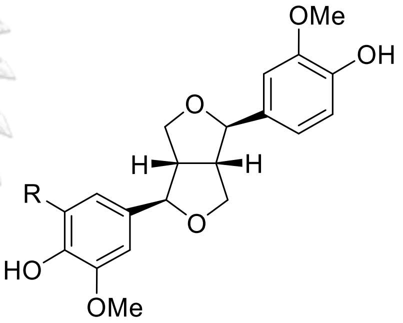
[**296**] Episyringaresinol 4″-*O*-β-D-glucopyranoside: R = Glc



[**297**] (-)-(7*S*,8*R*,7′*E*)-4-Hydroxy-3,3′,5,5-tetramethoxy-8,4′-oxyneolign-7′-ene-7,9,9′-triol-7,9′-bis-*O*-β-D-glucopyranoside

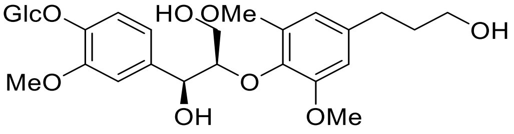


[**298**] Lyoniresinol



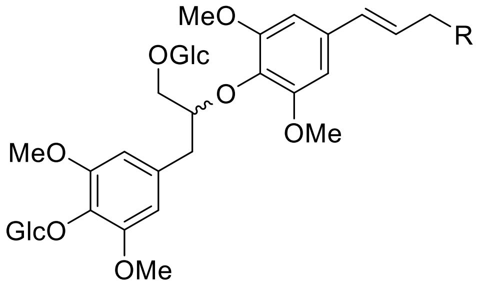
[**299**] (-)-Medioresinol: R = OMe

[**300**] (-)-Pinoresinol: R = H



[**301**] *Erythro*-1-(4-*O*-β-D-glucopyranosyl-3-methoxyphenyl)-2-[4-(3-hydroxypropyl)-2,6-dimethoxyphenoxy]-1,3-propanediol

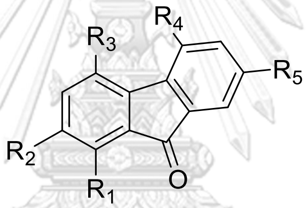
Figure 5 (continued)



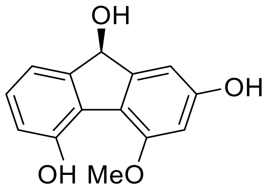
[**302**] (-)-(8*R*,7′*E*)-4-Hydroxy-3,3′,5,5′-tetramethoxy-8,4′-oxyneolign-7′-ene-9,9′-diol,4,9-bis-*O*-β-D-glucopyranoside: R = OH; 8*R*

[**303**] (-)-(8*S*,7′*E*)-4-Hydroxy-3,3′,5,5′-tetramethoxy-8,4′-oxyneolign-7′-ene-9,9′-diol,4,9-bis-*O*-β-D-glucopyranoside: R = OH; 8*S*

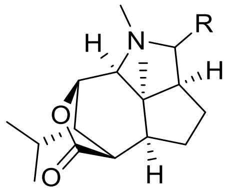
[**304**] (-)-(8*R*,7′*E*)-4-Hydroxy-3,3′,5,5′,9′-pentamethoxy-8,4′-oxyneolign-7′-ene-9-ol,4,9-bis-*O*-β-D-glucopyranoside: R = OMe; 8*R*



	R_1	R_2	R_3	R_4	R_5
[**305**] Denchrysan A	H	OH	OH	OMe	OH
[**306**] Dendroflorin	OH	H	OH	OMe	OH
[**307**] Dengibsin	H	OH	OMe	OH	H
[**308**] Nobilone	H	OH	H	OMe	OH
[**309**] 1,4,5-Trihydroxy-7-methoxy-9*H*-fluoren-9-one	OH	H	OH	OH	OMe
[**310**] 2,4,7-Trihydroxy-5-methoxy-9-fluorenone	OMe	OH	OH	H	OH
[**311**] 2,4,7-Trihydroxy-1,5-dimethoxy-9-fluorenone	OMe	OH	OH	OMe	OH

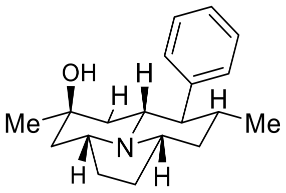


[**312**] Denchrysan B

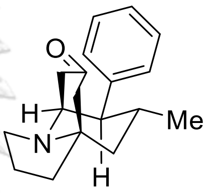


[**313**] (-)-(1*R*,2*S*,3*R*,4*S*,5*R*,6*S*,9*S*,11*R*)-11-carboxymethyldendrobine: R = CH_2COOH

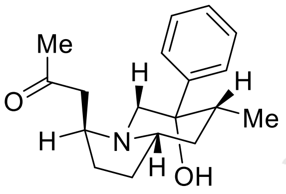
[**314**] Dendrobine: R = H



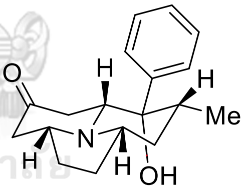
[**315**] Crepidatumine A



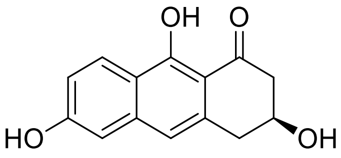
[**316**] Crepidatumine B



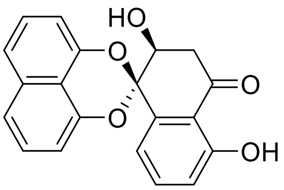
[**317**] Crepidatumine C



[**318**] Crepidatumine D

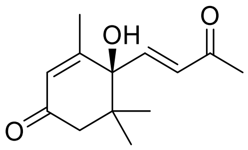


[**319**] 3,6,9-Trihydroxy-3,4-dihydroanthracen-1-(2*H*)-one

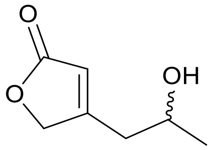


[**320**] Palmarumycin JC2

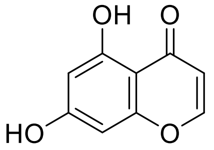
Figure 5 (continued)



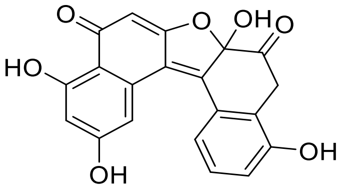
[**321**] Dehydrovomifoliol



[**322**] 4-(2-Hydroxypropyl)-2(5*H*)-furanone



[**323**] 5,7-Dihydroxy-chromen-4-one

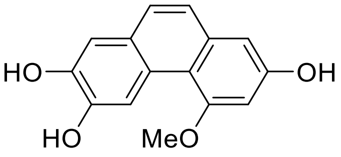


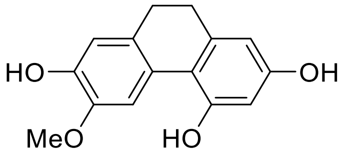
[**324**] RF-3192C

Figure 5 (continued)

2.2 Chemical constituents of *Aerides* species

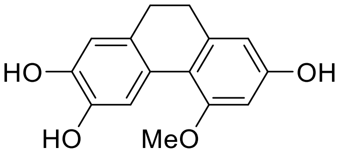
There are only a few reports on the chemical constituents of the genus *Aerides* (**Figure 6**). The methanolic extract obtained from *Aerides odoratum* was found to contain alkaloids, glycosides, flavonoids, saponins, tannins, terpenoids, steroids, and anthroquinones (Akter *et al.*, 2018). Nine secondary metabolites, including aerosanthrene (5-methoxyphenanthrene-2,3,7-triol) [**325**] aerosin (3-methoxy-9,10-dihydro-2,5,7-phenanthrenetriol) [**326**], 5-methoxy-9,10-dihydro-2,3,7-phenanthrenetriol [**327**], 3,5-dimethoxy phenanthrene-2,7-diol [**328**], 3-methoxy-2,7-dihydroxy-5*H*-phenanthro[4,5-bcd]pyran [**329**], imbricatin [**330**], coelonin [**331**], methoxycoelonin [**332**], and gigantol [**2**] were reported from the ethyl acetate extract of *Aerides rosea* (Cakova *et al.*, 2015). A phenanthropyran derivative named aeridin [**333**] was reported from *Aerides crispum* (Anuradha & Rao, 1998).

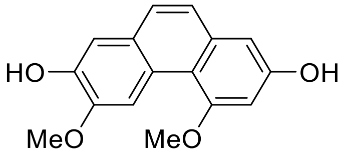




[**325**] Aerosanthrene

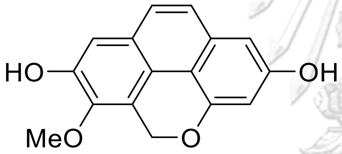
[**326**] Aerosin

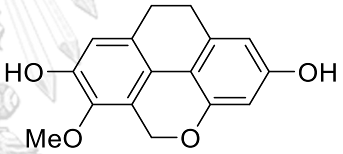




[**327**] 5-Methoxy-9,10-dihydro-2,3,7-phenanthrenetriol

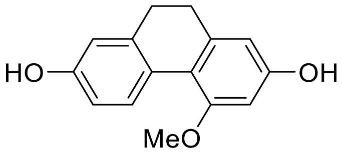
[**328**] 3,5-Dimethoxyphenanthrene-2,7-diol

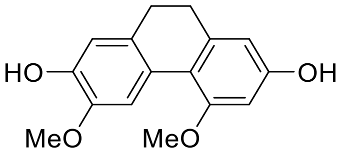




[**329**] 3-Methoxy-2,7-dihydroxy-5*H*-phenanthro[4,5-bcd]pyran

[**330**] Imbricatin

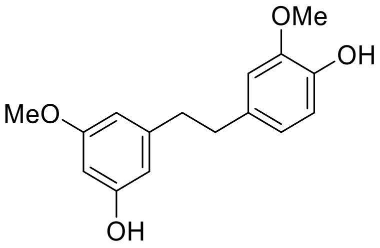




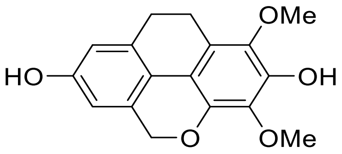
[**331**] Coelonin

[**332**] 6-Methoxycoelonin

Figure 6 Structures of compounds isolated from *Aerides*



[**2**] Gigantol



[**333**] Aeridin

Figure 6 (continued)

3 Biological studies

3.1 Biological activities of *Dendrobium* species

Various biological activities, such as cytotoxic, antioxidant, anti-inflammatory, immunomodulatory, neuroprotective, antimalarial, antiplatelet aggregation, and α-glucosidase inhibition activities, have been reported for several plants of *Dendrobium* (Da Silva & Ng, 2017; Gutiérrez, 2010; Inthongkaew *et al.*, 2017).

Several compounds isolated from *Dendrobium* have been studied for cytotoxic activity using different types of cancer cells. Denthyrsininin [**119**] from *D. thyrsiflorum* showed cytotoxic activity against Hela, K-562, and MCF-7 cancer cell lines (Zhang *et al.*, 2005). Batatasin III [**3**] from *D. draconis* has been reported for cytotoxicity against H460 lung cancer cells (Pinkhien *et al.*, 2017). Bibenzyl derivatives including dendrofalconerol A [**6**] and dendrocandin B [**74**] from *D. signatum*, were reported for cytotoxic activity against human breast cancer cells, liver hepatocellular carcinoma, and colorectal tumor cells (Mittraphab *et al.*, 2016).

Many studies revealed that *Dendrobium* species produce different types of compounds with antioxidant properties. Moscatilin [**40**], syringaresinol [**294**], 4,5,4′-trihydroxy-3,3′-dimethoxybibenzyl [**45**], and ferulic acid [**268**] from *D. secundum* were reported as DPPH radical scavengers with IC_{50} values of 5.14, 11.38, 15.87, and 37.52 μM respectively (Sritularak *et al.*, 2011). Dendrocandin C [**55**], dendrocandin D [**56**], and dendrocandin E [**49**] from *D. candidum* showed potential antioxidant activity with IC_{50} values of 34.2, 34.5, and 15.6 mM, respectively (Li *et al.*, 2009). The bibenzyl derivatives moscatilin [**40**] and nobilin D [**65**] from *D. nobile* exhibited antioxidant activity with IC_{50} values of 19.9 and 21.0 μM, respectively, in the DPPH assay (Zhang *et al.*, 2007). Dendropachol [**148**] from *Dendrobium pachyglossum* showed antioxidant activities and protected keratinocytes against hydrogen peroxide-induced oxidative stress (Warinhomhoun *et al.*, 2021).

Nobilin D [**65**], nobilin E [**66**], and dendroflorin [**306**] from *D. nobile* were reported as potent anti-inflammatory agents having IC_{50} values of 15.3, 19.2 and 13.4 μM, respectively (Zhang *et al.*, 2007).

Several sesquiterpene glycosides, i.e., dendrosides A, B, D, E, F, and G [**212, 213, 215-218**], from *D. nobile* were studied for immunomodulatory activity. Dendroside A, dendroside B, dendroside D, and dendroside G showed enhancement of *in vitro* cell proliferation of murine T and B lymphocytes. Dendroside E and dendroside F responsed to both T cell and B cell proliferation after induction with concanavalin A or lipopolysaccharide (Ye *et al.*, 2002). 4,5-Dihydroxy-3,3′,4′-trimethoxybibenzyl from *Dendrobium lindleyi* showed dose-dependent immune modulatory activity in lipopolysaccharide (LPS)-treated $CD14^{lo}$ and $CD14^{hi}$ monocytes (Khoonrit *et al*., 2020).

The lignan and neolignan glucosides (-)-syringaresinol-4,4′-bis-*O*-β–D-glucopyranoside [**17**] and (-)-(7*S*,8*R*,7′*E*)-4-Hydroxy-3,3′,5,5′-tetramethoxy-8,4′-oxyneolign-7′-ene-7,9,9′-triol,7,9′-bis-*O*-β-D-glucopyranoside [**297**] from *D. aurantiacum* var. *denneanum* showed neuroprotective activity against glutamate-induced neurotoxicity in PC12 cells (Xiong *et al.*, 2013).

Densiflorol B [**126**], phoyunnanin E [**157**], batatasin III [**3**], gigantol [**2**], and phoyunnanin C [**156**] from *D. venustum* were studied for antimalarial activity.

Densiflorol B and phoyunnanin E showed potent activity with IC_{50} values of 1.3 and 1.1 μM, respectively, as compared with positive controls (dihydroartemisinin IC_{50} = 0.002 nM; mefloquine IC_{50} = 0.031 nM) (Sukphan *et al.*, 2014).

Moscatilin [**40**] and moscatin [**110**] from *D. longicornu* showed anti-platelet aggregation activity (Chen *et al.*, 1994). Trigonopol A [**73**] from *D. trigonopus* and gigantol [**2**], homoeriodictyol [**184**], scopoletin [**288**], and scoparone [**287**] from *D. densiflorum* also exhibited anti-platelet aggregation activity (Fan *et al.*, 2001).

Regarding α-glucosidase inhibitory activity, a few compounds from *Dendrobium* were investigated. Dendrofalconerol A [**6**] and (2*S*)-eriodictyol [**185**] from *D. tortile* showed activity with IC_{50} values of 18.0 and 276.2 μM, respectively (Limpanit *et al.*, 2016a). Confusarin [**122**] (IC_{50} = 189.78 μM) and 5-methoxy-7-hydroxy-9,10-dihydro-1,4-phenanthrenequinone [**120**] (IC_{50} = 126.88 μM) from *D. formosum* exhibited stronger α-glucosidase inhibitory activity than the positive control acarbose (IC_{50} = 745.9 μM) (Inthongkaew *et al.*, 2017). Dendroscabrol B [**5**] from *D. scabrilingue* and *n*-docosyl-4-hydroxy-*trans*-cinnamate [**265**] from *D. christyanum* showed potent α-glucosidase inhibitory activity with IC_{50} values of 9.4 μM and 4.61 μM respectively (San *et al.*, 2020; Sarakulwattana *et al.*, 2020).

3.2 Biological activities of *Aerides* species

Some *Aerides* species have been used in traditional medicine, for example, *Aerides falcata* for boosting immune system; *Aerides multiflora* and *Aerides odorata* for antibaterial properties (Pant, 2013). However, up to the present, there has been only one report on the biological activities of *Aerides*, describing the cytotoxicity of the methanolic and ethyl acetate extracts of *Aerides odorata* against MCF-7 cancer cells with 60.69 and 61.128 % growth inhibition at 100 μg/mL, respectively (Katta *et al.*, 2019).

CHAPTER III

EXPERIMENTAL

1 Materials

1.1 Plant materials

Dendrobium delacourii

The whole plants of *Dendrobium delacourii* were purchased from Chatuchak market in May 2018. Plant identification was performed by Dr. B. Sritularak. A voucher specimen (BS-Ddela-052561) has been deposited at the Department of Pharmacognosy and Pharmaceutical Botany, Faculty of Pharmaceutical Sciences, Chulalongkorn University.

Dendrobium gibsonii

The whole plants of *Dendrobium gibsonii* were purchased from Chatuchak market, Bangkok, in February 2018. Plant identification was performed by Dr. B. Sritularak. A voucher specimen (BS-DG-022561) has been deposited at the Department of Pharmacognosy and Pharmaceutical Botany, Faculty of Pharmaceutical Sciences, Chulalongkorn University.

Aerides multiflora

The whole plants of *Aerides multiflora* were purchased from Chatuchak market in May 2019. Plant identification was performed by Mr. Yanyong Punpreuk, Department of Agriculture, Bangkok, Thailand. A voucher specimen BS-AM-052562 has been deposited at the Department of Pharmacognosy and Pharmaceutical Botany, Faculty of Pharmaceutical Sciences, Chulalongkorn University.

1.2 Chemicals

Organic solvents (methanol, acetone, ethyl acetate, dichloromethane, and hexane) used in this study were of commercial grade and redistilled before use. Yeast α-glucosidase enzyme and *p*-nitrophenol-α-D-glucopyranoside were purchased from Sigma Chemical, Inc. (St. Louis, MO, USA), and acarbose was obtained from Fluka Chemical (Buchs, Switzerland).

2. General techniques

2.1 Analytical thin-layer chromatography (TLC)

2.1.1 Normal-phase thin-layer chromatography

Technique : One-dimension ascending

Absorbent : Silica gel 60 F_{254} precoated plate (E. Merck)

Temperature : Laboratory temperature (30-35 °C)

Detection :

1. Ultraviolet light at wavelengths of 254 and 365 nm.
2. Spraying with anisaldehyde reagent (*p*-anisaldehyde 15 g in ethanol 250 mL and concentrated sulfuric acid 2.5 mL), followed by heating at 105 °C for 10 minutes.

2.1.2 Reverse-phase thin-layer chromatography

Technique : One-dimension ascending

Absorbent : RP C-18 precoated on aluminum sheet (Anal Tech)

Temperature : Laboratory temperature (30-35 °C)

Detection : Ultraviolet light at wavelengths of 254 and 365 nm.

2.2 Column chromatography (CC)

2.2.1 Vacuum liquid chromatography (VLC)

Adsorbent : Silica gel 60 (No. 1.07734.2500), size 0.063-0.200 mm (E. Merck)

Packing method : Dry packing

Sample loading : The sample was dissolved in a small volume of organic solvent, adsorbed by a small quantity of the adsorbent, dried and then gradually placed on top of the column.

Detection : Each fraction was examined by TLC as described in section 2.1.1.

2.2.2 Flash column chromatography (FCC), normal phase

Adsorbent : Silica gel 60 (No. 1.09385.2500), size 0.040-0.063 mm (E. Merck)

Packing method : Wet packing

Sample loading : The sample was dissolved in a small volume of organic solvent, adsorbed by a small quantity of the adsorbent, dried and then gradually placed on top of the column.

Detection : Fractions were examined as described in section 2.1.1

2.2.3 Flash column chromatography (FCC), reverse phase

Adsorbent : C-18 (No. 1.10167.1000), size 40-63 µm (E. Merck)

Packing method : Wet packing

Sample loading : The sample was dissolved in a small volume of organic solvent and then gradually loaded on top of the column.

Detection : Fractions were examined as described in section 2.1.1

2.2.4 Gel filtration chromatography

Gel filter : Sephadex LH-20 particle size 25-100 µm (GE Healthcare)

Packing method : An appropriate organic solvent was used as the eluent. Gel filter was suspended in the eluent, left standing about 24 hours and then poured into the column and left to set tightly.

Sample loading : The sample was dissolved in a small volume of the eluent and then gradually distributed on top of the column.

Detection : Fractions were examined in a similar manner as described in section 2.1.1

2.2.5 Semi-preparative high-pressure liquid chromatography (HPLC)

Column : COSMOSIL 5C$_{18}$-AR-II (10ID x 250 mm)

Flow rate : 3 ml/min

Mobile phase : Isocratic 50% methanol in water

Sample preparation: The sample was dissolved in a small volume of the eluent and filtered through Millipore filter paper before injection.

Injection volume : 1 ml

Pump : LC-8A (Shimadzu)

Detector : SPD-10A UV-Vis Detector (Shimadzu)

Recorder : C-R6A Chromatopac (Shimadzu)

Temperature : Room temperature

2.2.6 Diaion HP-20 column chromatography

Adsorbent : Non-polar copolymer styrene-divinylbenzene adsorbent resin with particle size 0.5 mm in diameter (E. Merck)

Mobile phase : (Water : Methanol) in gradient elution

Packing method : Diaion resin was suspended in 25% methanol in water, poured into the column and packed.

Sample loading : The sample was dissolved in 25% methanol in water, and then gradually loaded on top of the column.

Detection : Fractions were examined as described in section 2.1.1

2.3 Spectroscopy

2.3.1 Mass spectra

Mass spectra were recorded on a Bruker micro TOF mass spectrometer (ESI-MS) (Department of Chemistry, Faculty of Sciences, Mahidol University or Department of Chemistry, Faculty of Science, Chulalongkorn University).

2.3.2 Ultraviolet (UV) spectra

UV spectra were measured with a Milton Roy Spectronic 3000 Array spectrophotometer (Pharmaceutical Research Instrument Center, Faculty of Pharmaceutical Sciences, Chulalongkorn University).

2.3.3 Infrared (IR) spectra

IR spectra were recorded on a Perkin-Elmer FT-IR 1760X spectrophotometer (Scientific and Technology Research Equipment Center, Chulalongkorn University).

2.3.4 Proton and carbon-13 nuclear magnetic resonance (^{1}H and ^{13}C-NMR) spectra

^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on a Bruker Avance DPX-300 FT-NMR spectrometer (Faculty of Pharmaceutical Sciences, Chulalongkorn University).

^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectra were recorded on a Bruker Avance III HD 500 NMR spectrometer (Scientific and Technology Research Equipment Center, Chulalongkorn University).

Solvents for NMR spectra were deuterated acetone (acetone-d_6), deuterated dimethyl sulfoxide (DMSO-d_6) and deuterated chloroform ($CDCl_3$). Chemical shifts were reported in ppm scale using the chemical shift of the solvent as the reference signal.

2.3.5 Optical rotations

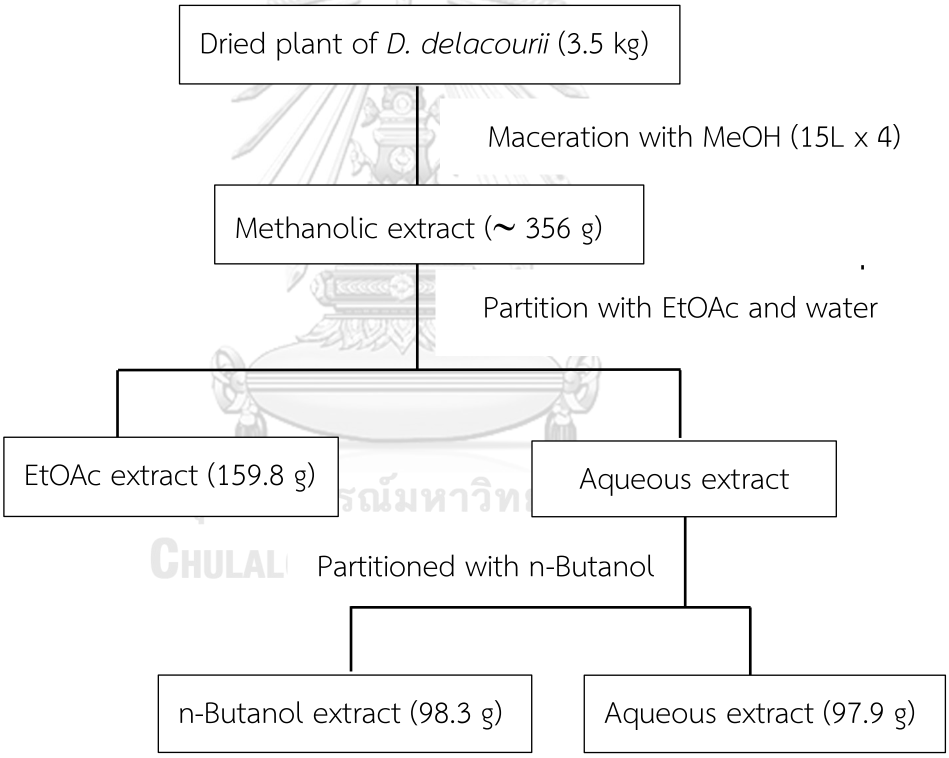
Optical rotations were measured on a Perkin-Elmer 341 polarimeter (Pharmaceutical Research Instrument Center, Faculty of Pharmaceutical Sciences, Chulalongkorn University).

3 Extraction and isolation

3.1 Extraction, separation, and isolation of compounds from *D. delacourii*

3.1.1 Extraction

The dried powder of whole plant *D. delacourii* (3.5 kg) was macerated with MeOH (4 x 15 L), and a MeOH extract (300.7 g) was obtained. The MeOH extract, at a concentration of 100 μg/mL, showed 80 ± 9.7 % inhibition of α-glucosidase. This extract was suspended in water and then partitioned with EtOAc and butanol to give an EtOAc extract (159.79 g), a butanol extract (98.29 g) and an aqueous extract (97.93 g), respectively, after evaporation of the solvent.



Scheme 1 Extraction steps of *Dendrobium delacourii*

3.1.2 Separation and isolation

The EtOAc extract was then separated by vacuum liquid chromatography (silica gel, acetone-hexane, gradient) to give five fractions (A-E). Fraction D (54.2 g) was further separated on a silica gel column (acetone-hexane, gradient) to give 4 fractions (DA-DD).

3.1.2.1 Isolation of compounds DD1 and DD2 (hircinol and ephemeranthoquinone)

Fraction DB (5.4 g) was separated on Sephadex LH20 (methanol) to yield 6 fractions (DBA-DBF). Fraction DBB (612 mg) was subjected to CC (silica gel, acetone-hexane, gradient) to yield pure compounds **DD1** (11.4 mg) and **DD2** (6.4 mg) which were identified as hircinol and ephemeranthoquinone, respectively.

3.1.2.2 Isolation of compound DD3 (densiflorol B)

DD3 (7.9 mg) was obtained from fraction DBD after purification on a silica gel column (acetone-hexane, gradient) and then identified as densiflorol B.

3.1.2.3 Isolation of compound DD4 (moscatin)

DD4 (17.1 mg) was obtained from DBE fraction by purification by CC (silica gel, acetone-hexane, gradient).

3.1.2.4 Isolation of compound DD5 (4,9-dimethoxy,2,5-pheneanthrenediol)

DD5 (3.6 mg) was obtained from DBF fraction by purifying on a silica gel column (acetone-hexane, gradient) and then identified as 4,9- dimethoxy, 2,5-pheneanthrenediol.

3.1.2.5 Isolation of compound DD6 (gigantol)

Fraction DC (6.1 g) was separated on a Sephadex LH-20 column (methanol) to yield 4 fractions (DCA-DCD). Separation of fraction DCA (1.2 g) by CC (silica gel, acetone-hexane, gradient) gave **DD6** (166.5 mg) which was identified as gigantol.

3.1.2.6 Isolation of compound DD7 (batatasin III)

Fraction DCB (170.9 mg) was further separated on a silica gel column (ethyl acetate-dichloromethane, gradient); **DD7** (33.7 mg) was obtained and identified as batatasin III.

3.1.2.7 Isolation of compound DD8 (lusianthridin)

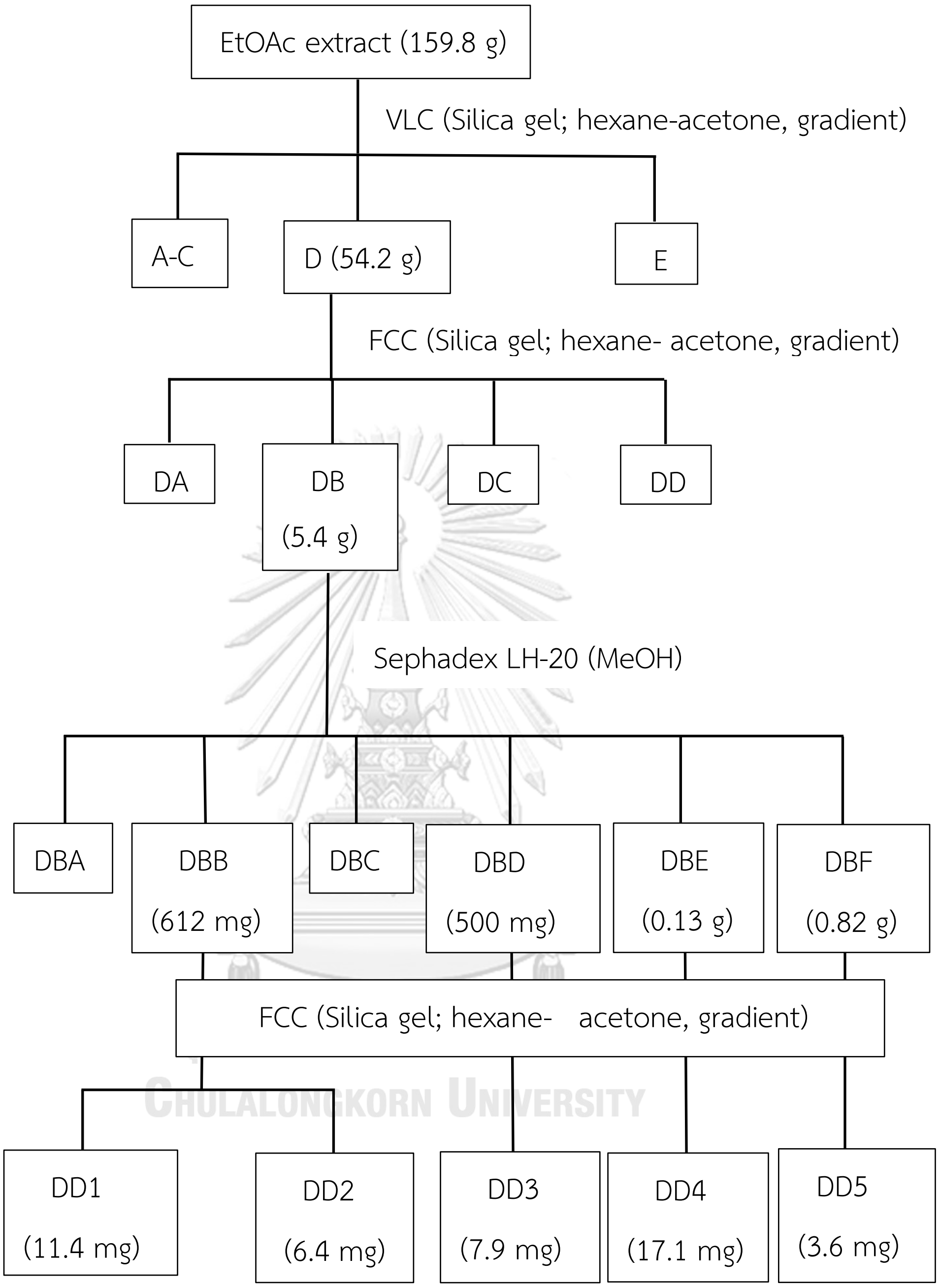
Fraction DCD (428 mg) was separated on a silica gel column (acetone-hexane, gradient) to give **DD8** (183.3 mg) which was identified as lusianthridin.

3.1.2.8 Isolation of compounds DD9 and DD10 (4,4′,7,7′-tetrahydroxy-2,2′-dimethoxy-9,9′,10,10′-tetrahydro-1,1′-biphenanthrene and phoyunnanin E)

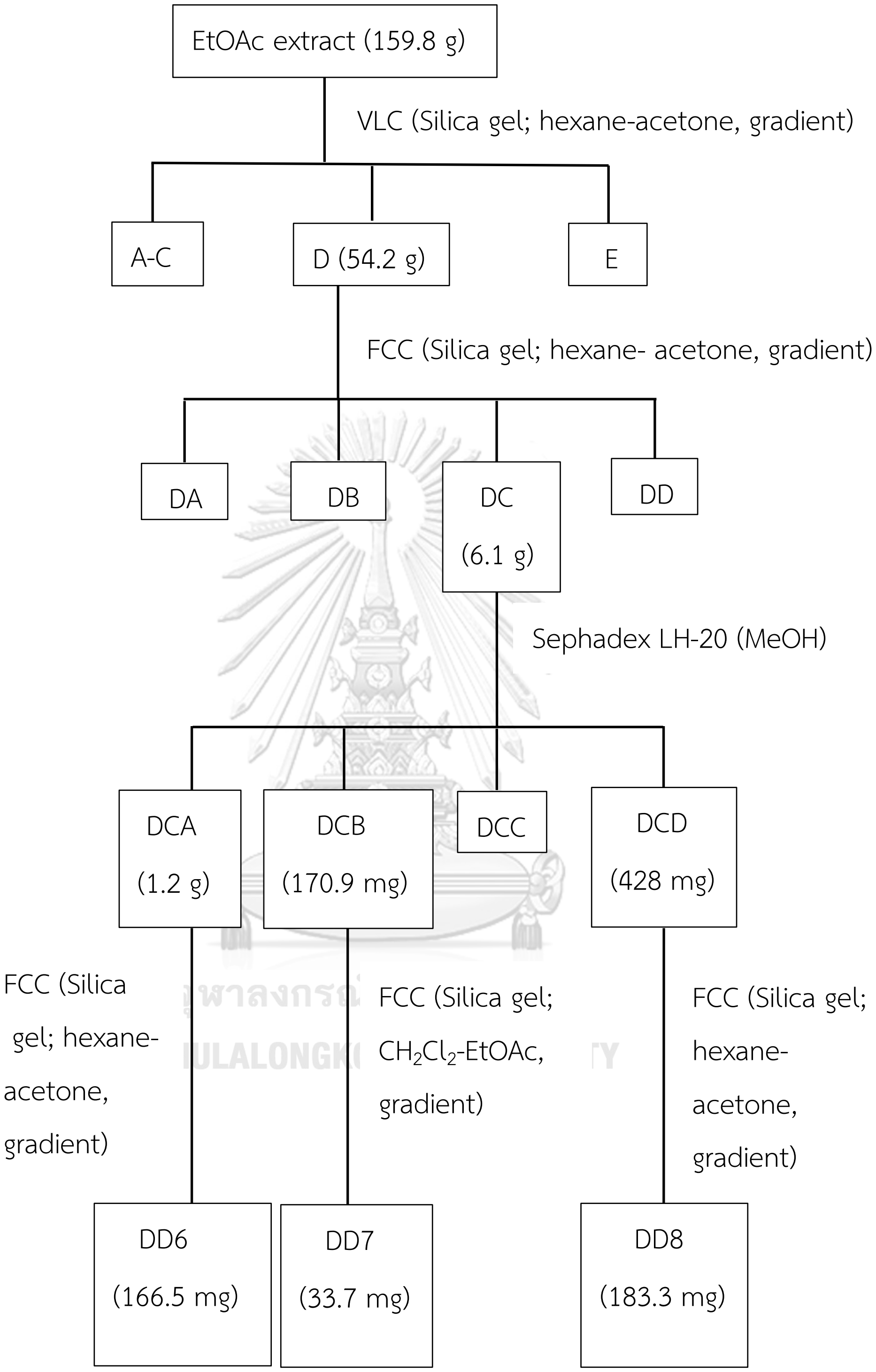
Fraction DD (6.7 g) was separated with Sephadex LH-20 (methanol) to yield 3 fractions (DDA-DDC). **DD9** (4.7 mg) and **DD10** (7mg) were obtained from fraction DDB (290 mg) through separation by CC (silica gel; methanol-dichloromethane, gradient) and then identified as 4,4′,7,7′-tetrahydroxy-2,2′-dimethoxy-9,9′,10,10′-tetrahydro-1,1′-biphenanthrene and phoyunnanin E, respectively.

3.1.2.9 Isolation of compound DD11 (phoyunnanin C)

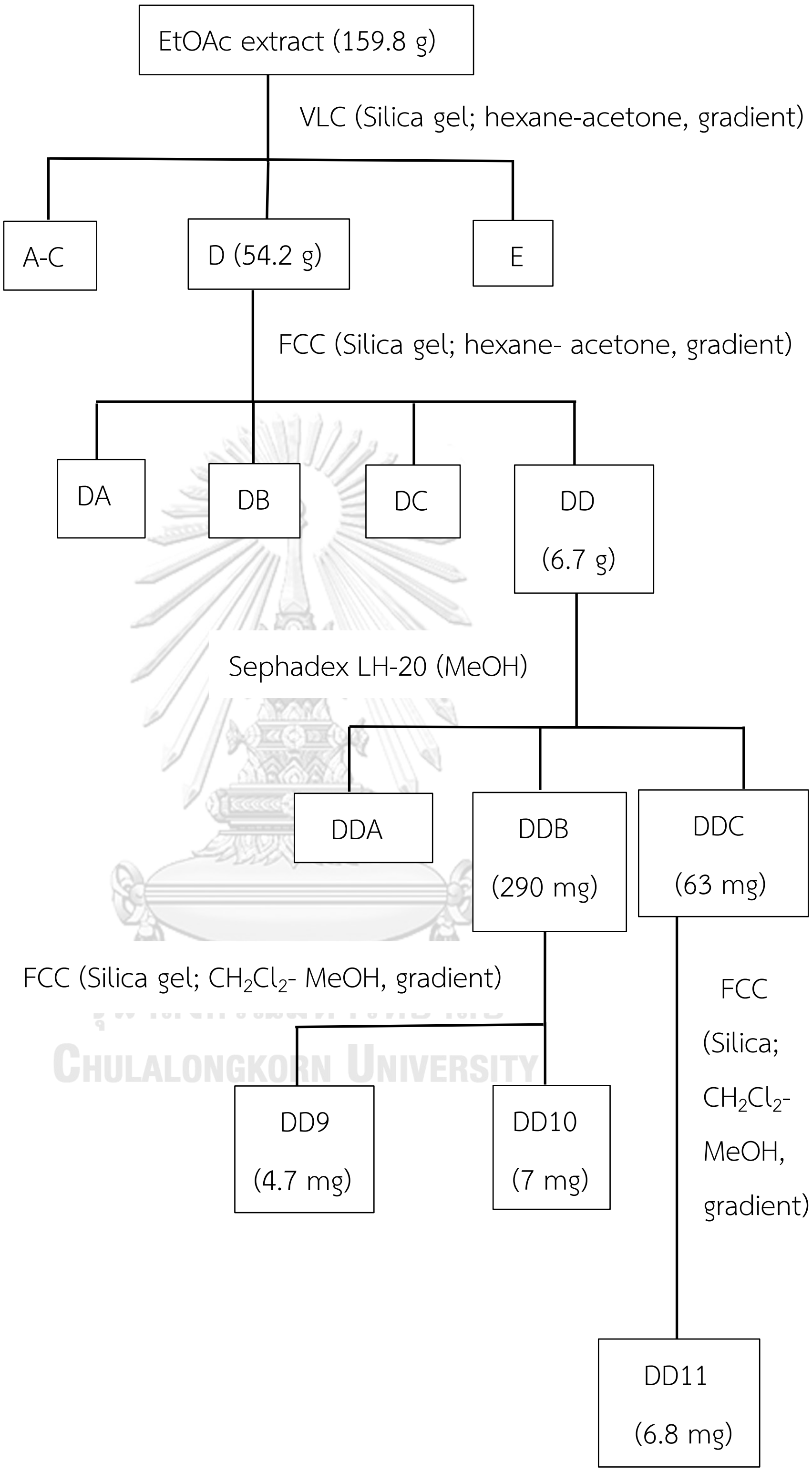
DD11 (6.8 mg) was obtained from fraction DDC through separation on a silica gel column (methanol- dichloromethane, gradient) and identified as phoyunnanin C.



Scheme 2 Separation and isolation of compounds from *Dendrobium delacourii*



Scheme 2 (Continued)

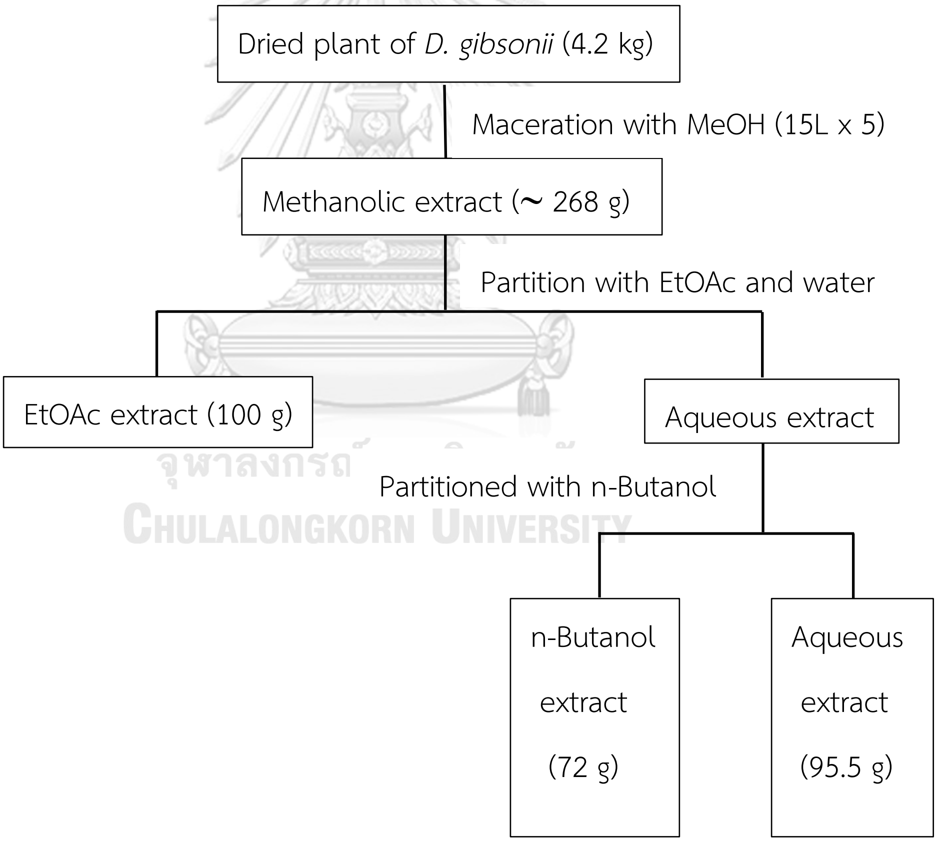


Scheme 2 (Continued)

3.2 Extraction, separation, and isolation of compounds from *Dendrobium gibsonii*

3.2.1 Extraction

The dried powder of whole-plant *D. gibsonii* (4.2 kg) was macerated with methanol (MeOH) (5 x 15 L), and a MeOH extract (371 g) was obtained after drying. The MeOH extract, at a concentration of 100 µg/mL, showed 78.7 ± 3.2 % inhibition of α-glucosidase. This extract was suspended in water and then partitioned with EtOAc and BuOH to give an EtOAc extract (100 g), a BuOH extract (72 g) and an aqueous extract (95.5 g) after evaporation of the solvent.



Scheme 3 Extraction steps of *Dendrobium gibsonii*

3.2.2 Separation and Isolation

The EtOAc extract was then further separated by vacuum liquid chromatography (silica gel, EtOAc–dichloromethane, gradient) to give five fractions (A–E).

3.2.2.1 Isolation of compounds DG3 and DG4 (ephemeranthol A and dengibsinin)

Fraction B (8.3 g) was fractionated on a silica gel column (acetone–hexane, gradient) to give three fractions (BA–BC). Fraction BB (170 mg) was separated by Sephadex LH-20 (acetone) chromatography to yield BBA and BBB fractions. Fraction BBB (190 mg) was subjected to column chromatography (CC) (silica gel, EtOAc–hexane, gradient) to give **DG3** (18 mg) and **DG4** (15.7 mg) which were then identified as ephemeranthol A and dengibsinin, respectively.

3.2.2.2 Isolation of compound DG5 (nobilone)

Fraction C (10.8 g) was re-separated on a silica gel column (acetone–hexane, gradient) to give four fractions (CA–CD). Fraction CB (1.3 g) was separated by Sephadex LH-20 (acetone) gel filtration to yield CBA and CBB fractions. Fraction CBA (740 mg) was subjected to CC (silica gel, EtOAc–CH_2Cl_2, gradient) to yield **DG5** (98 mg) which was identified as nobilone.

3.2.2.3 Isolation of compound DG6 (aloifol I)

Fraction CC (1 g) was separated with Sephadex LH-20 (acetone) to give three fractions (CCA, CCB and CCC). Fraction CCB (60 mg) was subjected to CC (silica gel, EtOAc–hexane, gradient) to furnish **DG6** (11.2 mg) which was identified as aloifol I.

3.2.2.4 Isolation of compounds DG7 and DG1 (lusianthridin and dihydrodengibsinin)

Fraction CCC (100 mg) was subjected to CC (silica gel, EtOAc–hexane, gradient) to give **DG7** (6.2 mg) and **DG1** (25.3 mg). **DG7** was identified as lusianthridin, and **DG1** was characterized as a new naturally occurring compound and named dihydrodengibsinin.

3.2.2.5 Isolation of compound DG2 (dendrogibsol)

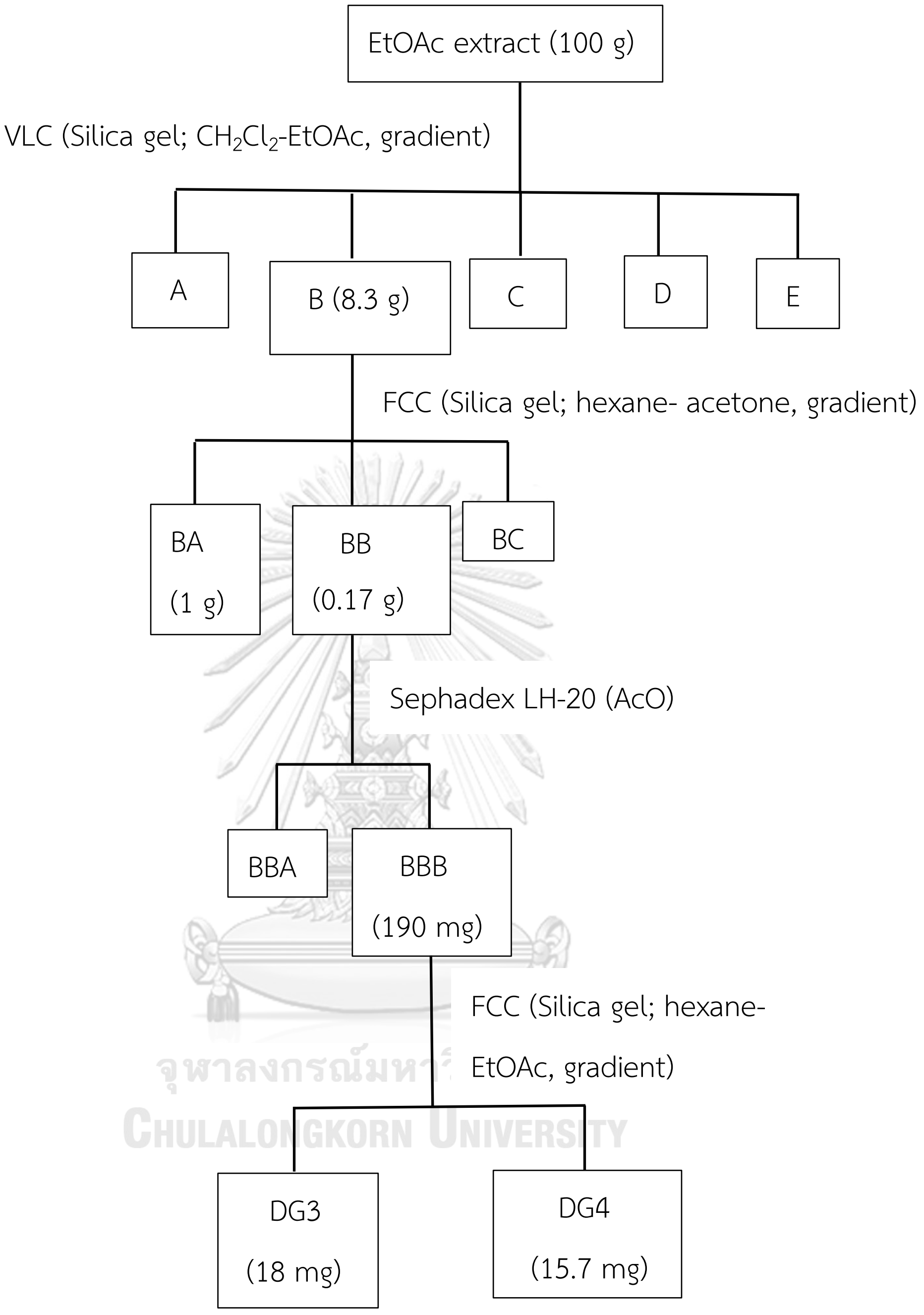
Fraction CD (805 mg) was separated on a Sephadex LH-20 (acetone) column to give fractions CDA and CDB. Fraction CDA (50 mg) was purified by CC (silica gel, EtOAc–dichloromethane, gradient) to yield **DG2** (5 mg). **DG2** was characterized as a new compound and named dendrogibsol.

3.2.2.6 Isolation of compound DG8 (denchrysan A)

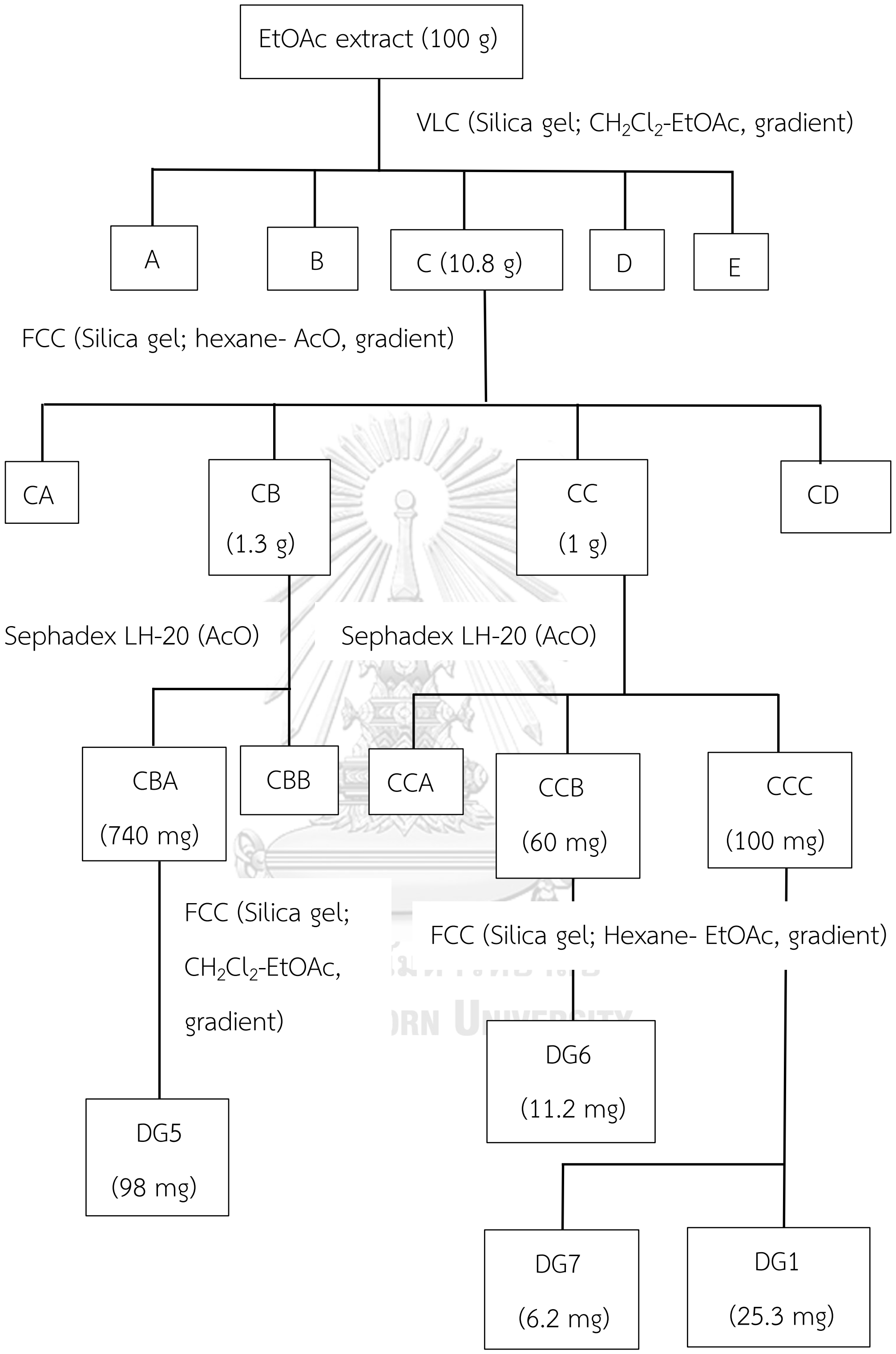
Fraction D (5.5 g) was further fractionated on a silica gel column (acetone–dichloromethane, gradient) to give three fractions (DA–DC). Fraction DB (1 g) was separated with Sephadex LH-20 (acetone) to yield DBA and DBB fractions. Fraction DBA (30 mg) was subjected to CC (silica gel, MeOH–toluene, gradient) to furnish **DG8** (14 mg) which was later identified as denchrysan A.

3.2.2.7 Isolation of compound DG9 (4-methoxy-9*H*-fluorene-2,5,9-triol)

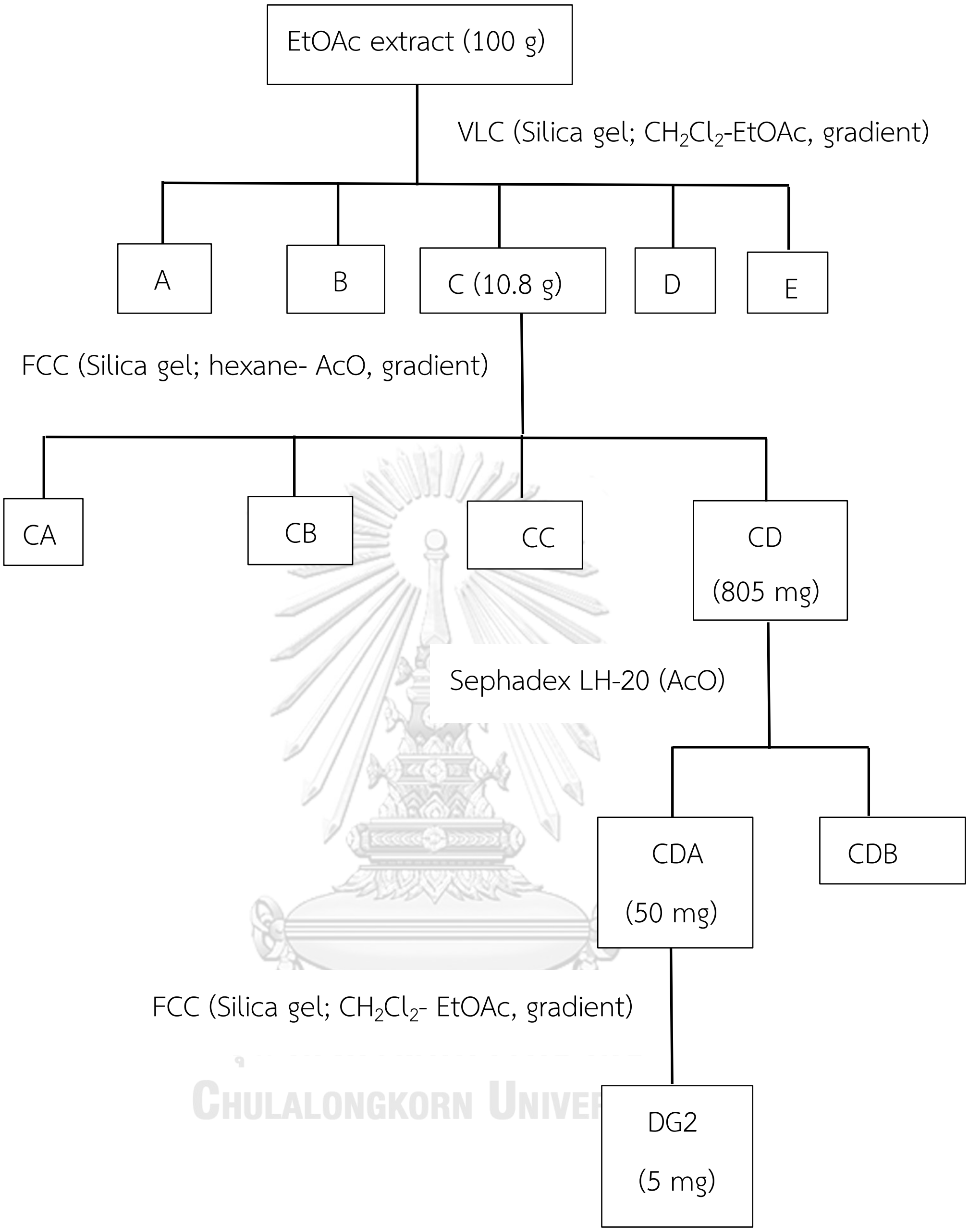
Fraction E (8.2 g) was fractionated on a silica gel column (acetone–dichloromethane, gradient) to give fractions EA and EB. **DG9** (10.3 mg) was obtained after purification of fraction EA (1g) with Sephadex LH-20 (methanol) and identified as 4-methoxy-9*H*-fluorene-2,5,9-triol.



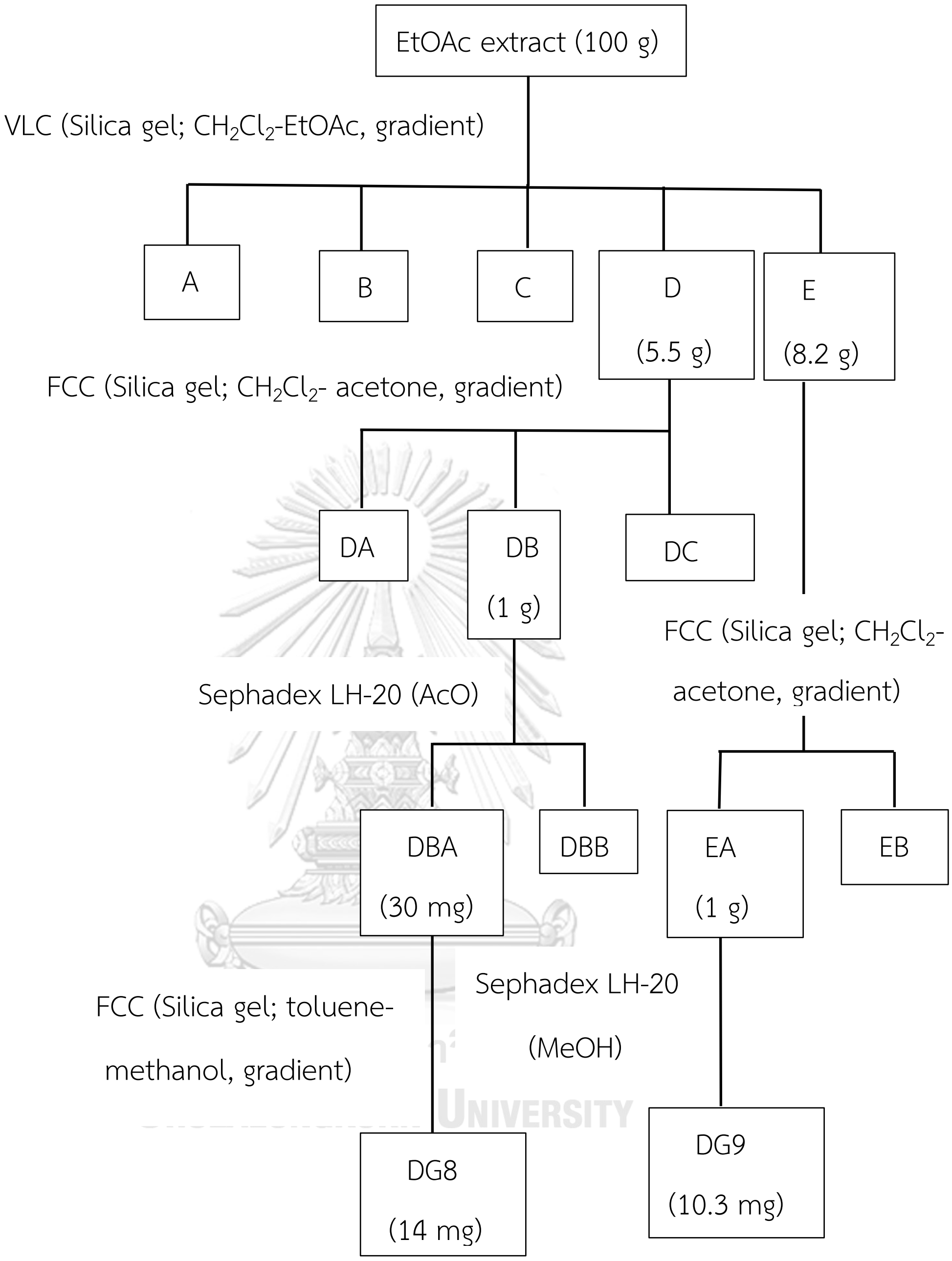
Scheme 4 Separation and isolation of compounds from *Dendrobium gibsonii*



Scheme 4 (Continued)



Scheme 4 (Continued)

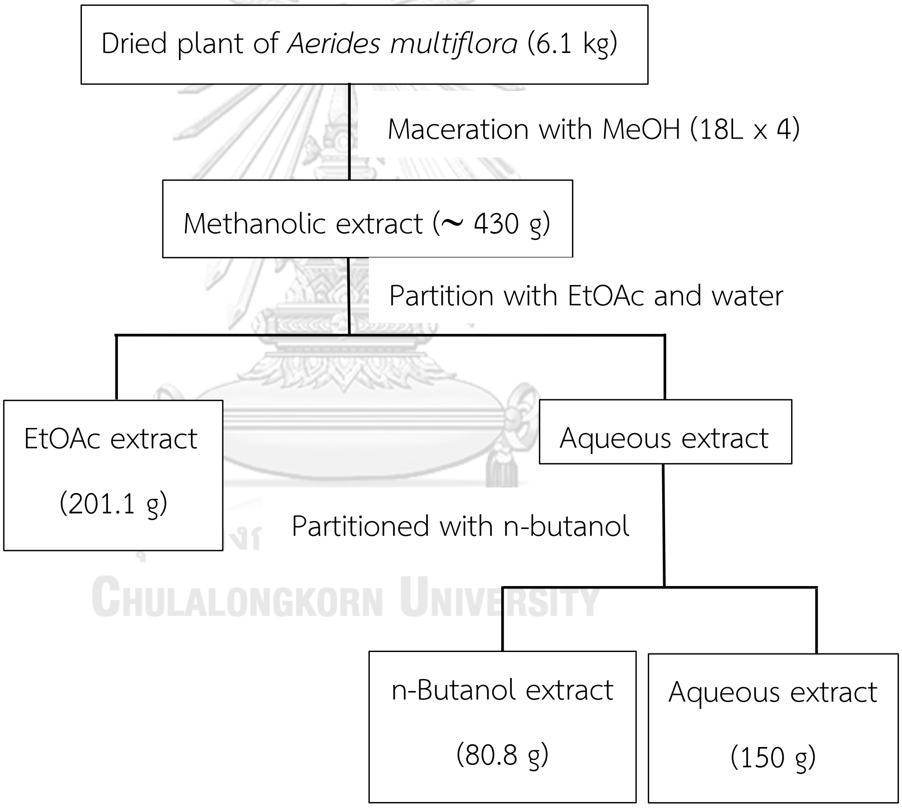


Scheme 4 (Continued)

3.3 Extraction, separation, and isolation of compounds from *Aerides multiflora*

3.3.1 Extraction

The dried powder of whole plant *Aerides multiflora* (6.1 kg) was macerated with MeOH (4 x 18 L). The MeOH extract, at a concentration of 100 µg/mL, showed 82.4 ± 9.5 % inhibition of α-glucosidase. This MeOH extract (550 g) was then suspended in water and partitioned with EtOAc and butanol to give an EtOAc extract (201.1 g), a butanol extract (80.8 g) and an aqueous extract (150 g), respectively.



Scheme 5 Extraction steps of *Aerides multiflora*

3.3.2 Separation and Isolation

The EtOAc extract was separated by vacuum liquid chromatography (silica gel, EtOAc-CH_2Cl_2, gradient) to give five fractions (A-E).

3.3.2.1 Isolation of compound AMF5 (6-methoxycoelonin)

Fraction B (11.4 g) was fractionated on a silica gel column (EtOAc-hexane, gradient) to give 3 fractions (BA-BC). Fraction BA (1 g) was separated on a Sephadex LH-20 (methanol) column to yield fractions BAA, BAB, and BAC. Fraction BAA (200 mg) was subjected to column chromatography (CC, silica gel, EtOAc-CH_2Cl_2, gradient) to give **AMF5** (65.4 mg) which was identified as 6-methoxycoelonin.

3.3.2.2 Isolation of compound AMF1 (aerimultin A)

Fraction BAB (300 mg) was subjected to CC (silica gel, EtOAc-CH_2Cl_2, gradient) to give fractions BAB1 and BAB2. Fraction BAB1 (160.2 mg) was separated by CC (silica gel, acetone-hexane, 3:7) to yield **AMF1** (2.3 mg), which was later characterized as new compound and named aerimultin A.

3.3.2.3 Isolation of compound AMF6 (gigantol)

AMF6 (14.5 mg) was obtained from fraction BAB2 (100 mg) after purification on Sephadex LH-20 (acetone) and identified as gigantol.

3.3.2.4 Isolation of compounds AMF7 and AMF8 (imbricatin and agrostonin)

Fraction BB (1 g) was separated with Sephadex LH-20 (acetone) to yield fractions BBA and BBB. Fraction BBA (195.8 mg) was subjected to CC (silica gel, EtOAc-CH_2Cl_2, gradient) to yield fractions BBA1 and BBA2. Fraction BBA1 (132.2 mg) was subjected to CC (silica gel, acetone-hexane, 3:7) to furnish **AMF7** (39 mg) and **AMF8** (7 mg), which were identified as imbricatin and agrostonin, respectively.

3.3.2.5 Isolation of compounds AMF9 and AMF10 (dihydroconiferyl dihydro-*p*-coumarate and 5-methoxy-9,10-dihydrophenanthrene-2,3,7-triol)

Fraction C (10.5 g) was fractionated on a silica gel column (EtOAc-CH_2Cl_2, gradient) to give 3 fractions (CA-CC). Fraction CB (500 mg) was separated on Sephadex LH-20 (acetone) to yield fractions CBA and CBB. Fraction CBA (236.9 mg) was further isolated by CC (silica gel, EtOAc-hexane, gradient) to give **AMF9** (74.1 mg) and **AMF10** (9.2 mg), which were identified as dihydroconiferyl dihydro-*p*-coumarate and 5-methoxy-9,10-dihydrophenanthrene-2,3,7-triol, respectively.

3.3.2.6 Isolation of compound AMF2 (aerimultin B)

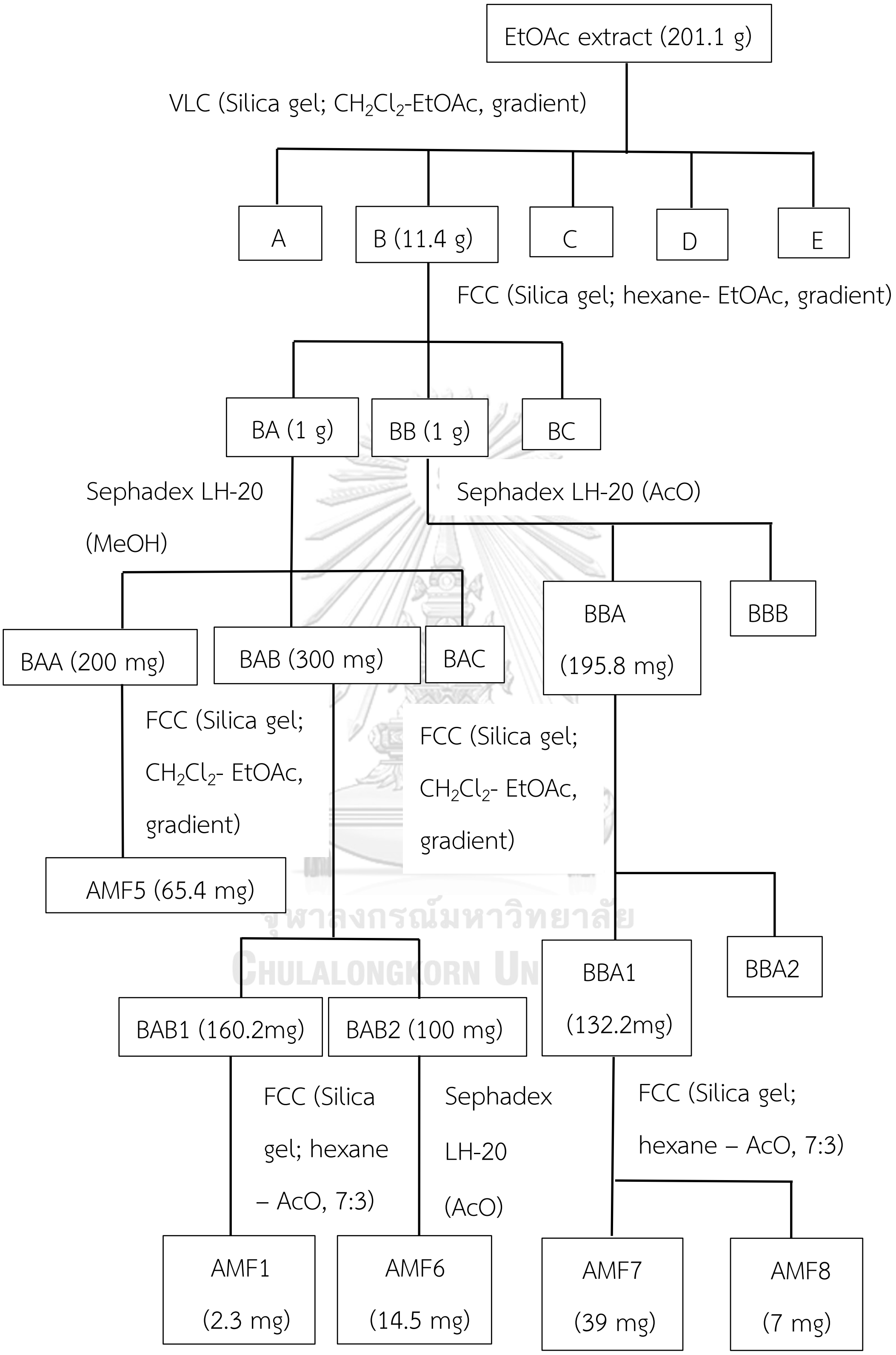
Fraction CC (100 mg) was separated with Sephadex LH-20 (acetone) to yield fractions CCA, CCB, and CCC. Fraction CCB (10 mg) was subjected to CC (silica gel, EtOAc-CH_2Cl_2, 0.2: 9.8) to yield **AMF2** (3.9 mg), which was determined as a new compound and named aerimultin B.

3.3.2.7 Isolation of compound AMF4 (dihydrosinapyl dihydroferulate)

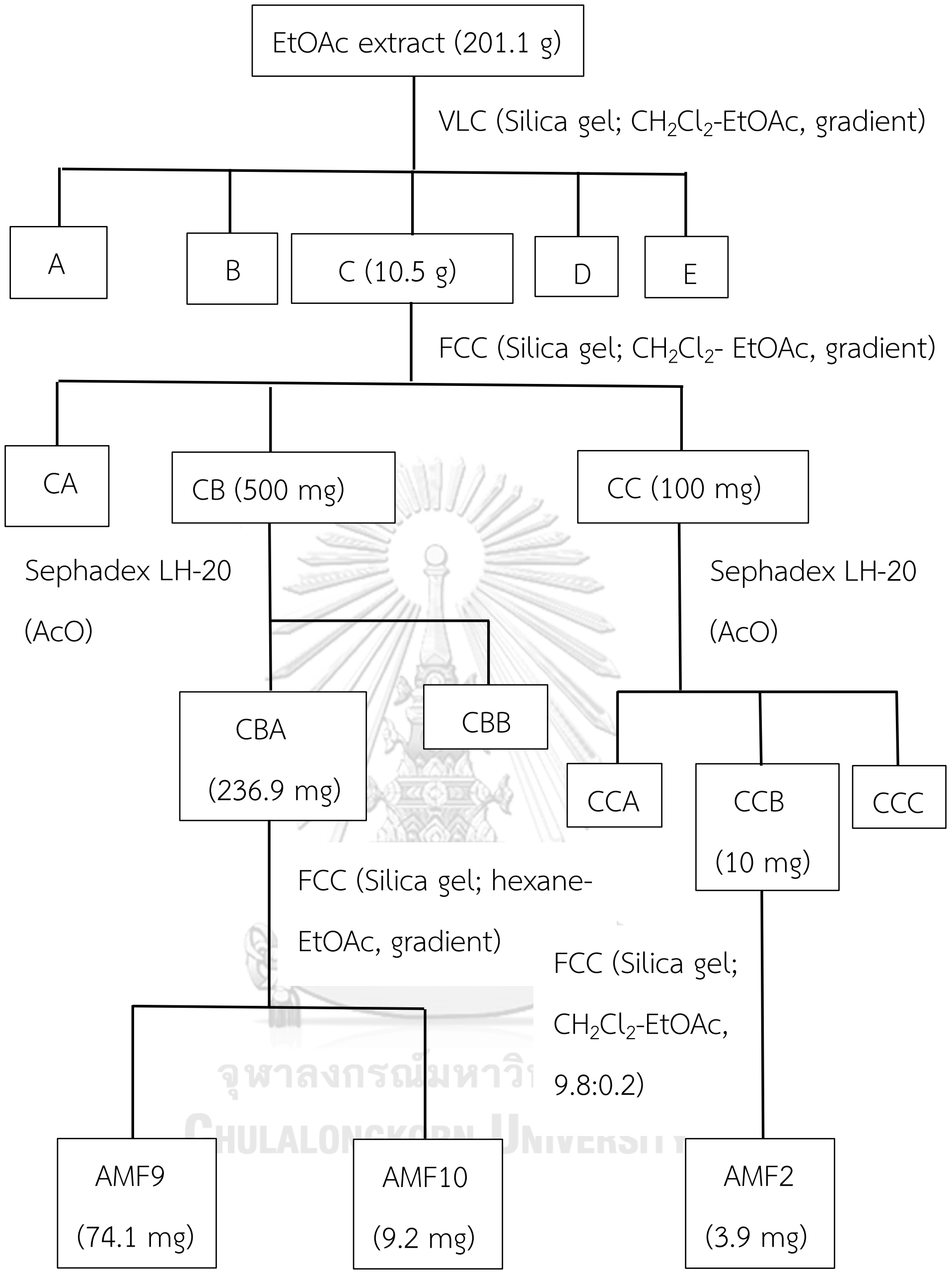
Fraction D (72 g) was fractionated on a silica gel column (EtOAc-CH_2Cl_2, gradient) to give 3 fractions (DA-DC). Fraction DA (1 g) was separated with Sephadex LH-20 (methanol) to yield fractions DAA and DAB. Fraction DAA (300 mg) was re-separated on a Sephadex LH20 (acetone) column to yield fractions DAA1 and DAA2. Fraction DAA1 (100 mg) was further purified by CC (silica gel, EtOAc-hexane, 3:7) to give **AMF4** (4.2 mg). It was identified as a new natural compound named dihydrosinapyl dihydroferulate.

3.3.2.8 Isolation of compound AMF3 (aerimultin C)

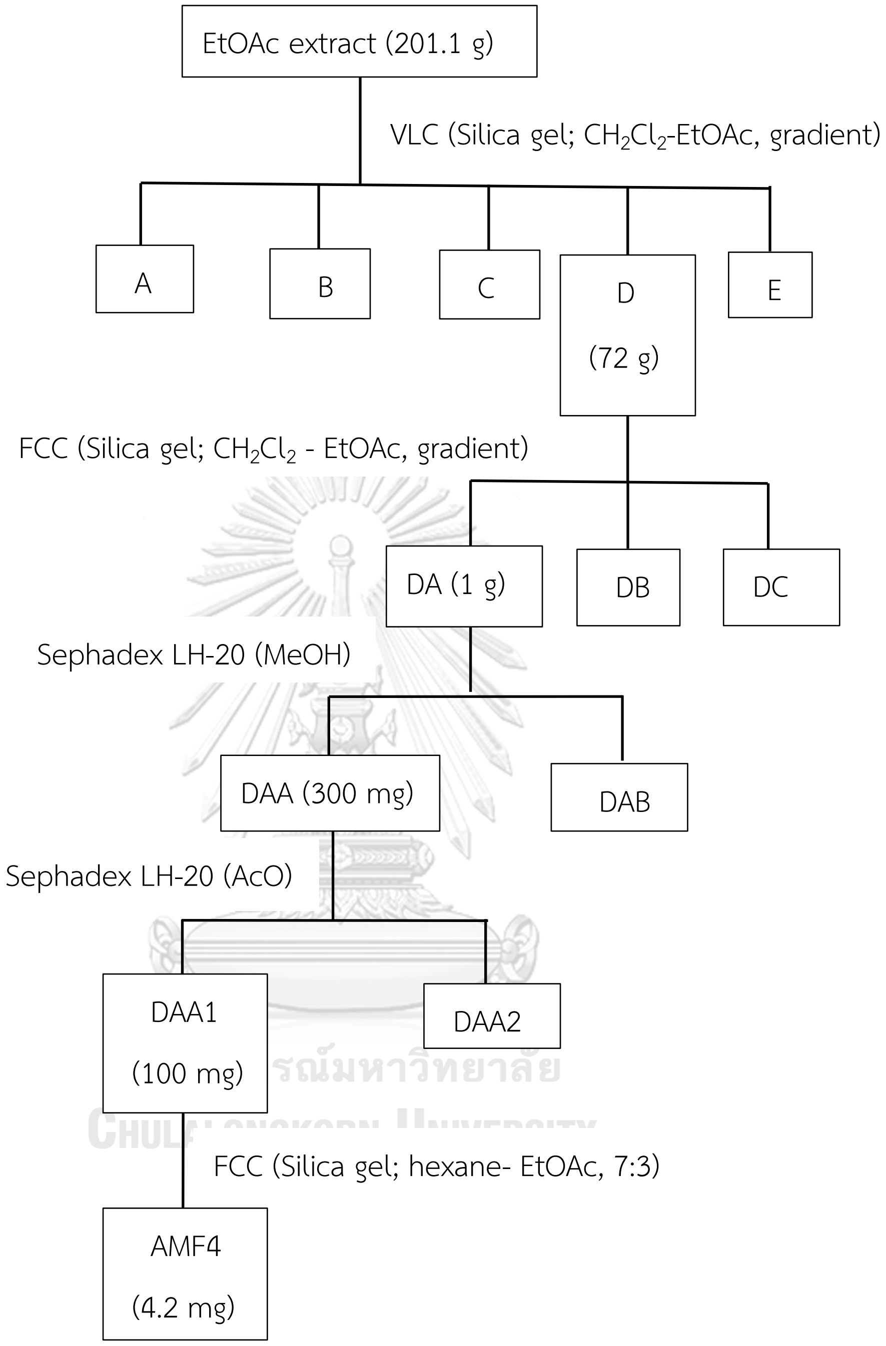
Fraction E (84.8 g) was separated on a Diaion HP-20 column (water-methanol, gradient) to yield five fractions (EA-EE). Fraction EC (1.7 g) was separated with Sephadex LH-20 (methanol) to yield fractions ECA, ECB and ECC. Fraction ECC (40 mg) was subjected to CC (silica gel, methanol- CH_2Cl_2, 0.5:9.5) to furnish **AMF3** (8.8 mg). **AMF3** was elucidated as a new compound and named aerimultin C.



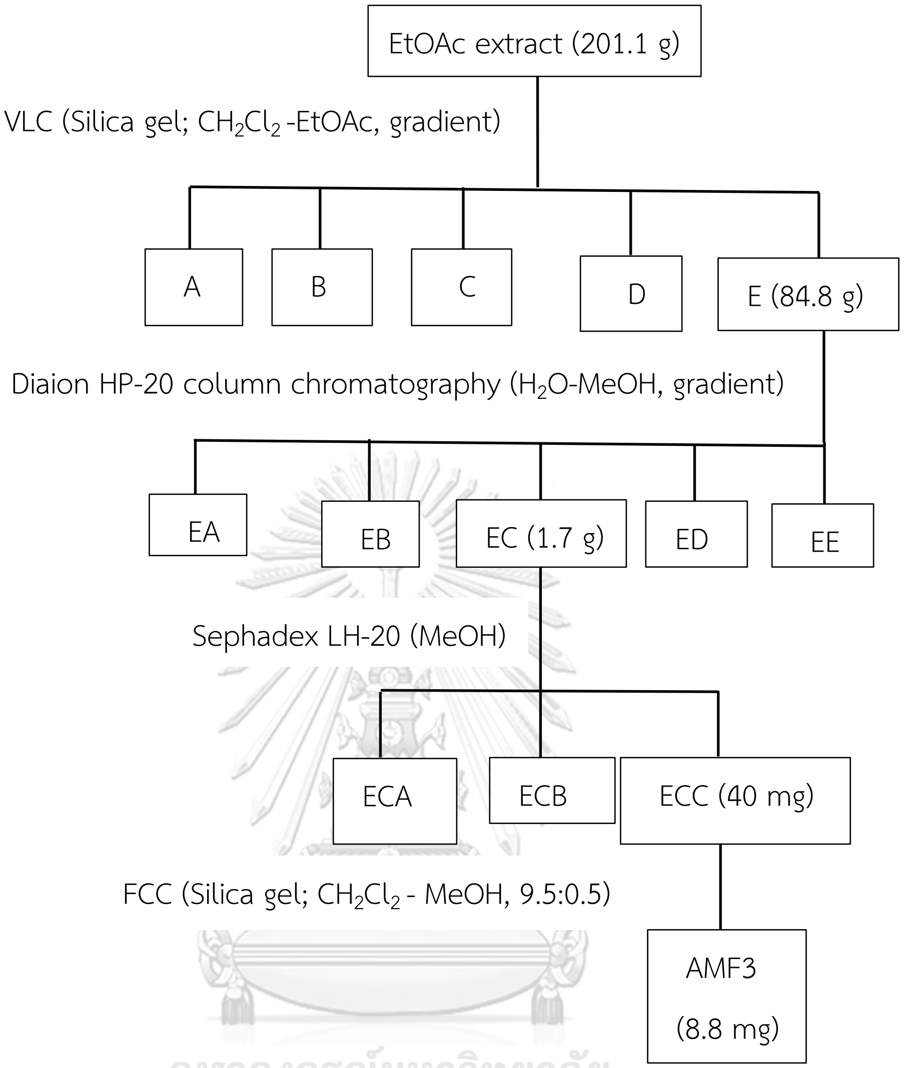
Scheme 6 Separation and isolation of compounds from *Aerides multiflora*



Scheme 6 (Continued)



Scheme 6 (Continued)



Scheme 6 (Continued)

4. Physical and spectral data of isolated compounds

4.1 Compound DD1 (hircinol) [94]

Compound **DD1** was obtained as a yellow amorphous solid (11.4 mg, 0.00033% of the dry weight of the plant). It was soluble in acetone.

HR-ESIMS: $[M+H]^+$ ion at *m/z* 243.1059 ($C_{15}H_{15}O_3$)

^1H NMR: δ ppm, 500 MHz, in acetone-d_6; **Table 6**

^{13}C NMR: δ ppm, 125 MHz, in acetone-d_6; **Table 6**

4.2 Compound DD2 (ephemeranthoquinone) [129]

Compound **DD2** was obtained as a reddish powder (6.4 mg, 0.0018% of the dry weight of the plant). It was soluble in acetone.

HR-ESIMS: $[M+Na]^+$ ion at *m/z* 279.06185 ($C_{15}H_{12}O_4Na$)

^1H NMR: δ ppm, 300 MHz, in acetone-d_6; **Table 7**

^{13}C NMR: δ ppm, 75 MHz, in acetone-d_6; **Table 7**

4.3 Compound DD3 (densiflorol B) [126]

Compound **DD3** was obtained as an orange powder (7.9 mg, 0.00023% of the dry weight of the plant). It was soluble in acetone.

HR-ESIMS: $[M+Na]^+$ ion at *m/z* 277.0473 ($C_{15}H_{10}O_4Na$)

^1H NMR: δ ppm, 300 MHz, in acetone-d_6; **Table 8**

^{13}C NMR: δ ppm, 75 MHz, in acetone-d_6; **Table 8**

4.4 Compound DD4 (moscatin) [110]

Compound **DD4** was obtained as a brown amorphous solid (17.1 mg, 0.00049% of the dry weight of the plant). It was soluble in acetone.

HR-ESIMS: $[M+H]^+$ ion at *m/z* 241.0888 ($C_{15}H_{13}O_3$)

^1H NMR: δ ppm, 500 MHz, in acetone-d_6; **Table 9**

^{13}C NMR: δ ppm, 125 MHz, in acetone-d_6; **Table 9**

4.5 Compound DD5 (4,9-dimethoxy-2,5-phenanthrenediol) [105]

Compound **DD5** was obtained as a brown amorphous solid (3.6 mg, 0.0001% of the dry weight of the plant). It was soluble in acetone.

HR-ESIMS: $[M+H]^+$ ion at *m/z* 271.1009 ($C_{16}H_{15}O_4$)

^1H NMR: δ ppm, 500 MHz, in acetone-d_6; **Table 10**

^{13}C NMR: δ ppm, 125 MHz, in acetone-d_6; **Table 10**

4.6 Compound DD6 (gigantol) [2]

Compound **DD6** was obtained as a brown amorphous solid (166.5 mg, 0.0048% of the dry weight of the plant). It was soluble in acetone.

HR-ESIMS: $[M+Na]^+$ ion at *m/z* 297.1102 ($C_{16}H_{18}O_4Na$)

^1H NMR: δ ppm, 300 MHz, in acetone-d_6; **Table 11**

^{13}C NMR: δ ppm, 75 MHz, in acetone-d_6; **Table 11**

4.7 Compound DD7 (batatasin III) [3]

Compound **DD7** was obtained as a brown amorphous solid (33.7 mg, 0.0009% of the dry weight of the plant). It was soluble in acetone.

HR-ESIMS: $[M+Na]^+$ ion at *m/z* 267.10556 ($C_{15}H_{16}O_3Na$)

^1H NMR: δ ppm, 300 MHz, in acetone-d_6; **Table 12**

^{13}C NMR: δ ppm, 75 MHz, in acetone-d_6; **Table 12**

4.8 Compound DD8 (lusianthridin) [97]

Compound **DD8** was obtained as a brown amorphous solid (183.3 mg, 0.0053% of the dry weight of the plant). It was soluble in acetone.

HR-ESIMS: $[M+Na]^+$ ion at *m/z* 265.08251 ($C_{15}H_{14}O_3Na$)

^1H NMR: δ ppm, 300 MHz, in acetone-d_6; **Table 13**

^{13}C NMR: δ ppm, 75 MHz, in acetone-d_6; **Table 13**

4.9 Compound DD9 (4,4′,7,7′-tetrahydroxy-2,2′-dimethoxy-9,9′,10,10′-tetrahydro-1,1′-biphenanthrene) [154]

Compound **DD9** was obtained as a yellow amorphous powder (4.7 mg, 0.0001% of the dry weight of the plant). It was soluble in acetone.

HR-ESIMS: $[M+Na]^+$ ion at *m/z* 505.1630 ($C_{30}H_{26}O_6Na$)

^1H NMR: δ ppm, 300 MHz, in acetone-d_6; **Table 14**

^{13}C NMR: δ ppm, 75 MHz, in acetone-d_6; **Table 14**

4.10 Compound DD10 (phoyunnanin E) [157]

Compound **DD10** was obtained as a brown amorphous powder (7 mg, 0.0002% of the dry weight of the plant). It was soluble in acetone.

HR-ESIMS: $[M+Na]^+$ ion at *m/z* 505.1628 ($C_{30}H_{26}O_6Na$)

^1H NMR: δ ppm, 300 MHz, in acetone-d_6; **Table 15**

^{13}C NMR: δ ppm, 75 MHz, in acetone-d_6; **Table 15**

4.11 Compound DD11 (phoyunnanin C) [156]

Compound **DD11** was obtained as a brown amorphous powder (6.8 mg, 0.00019% of the dry weight of the plant). It was soluble in acetone.

HR-ESIMS: $[M+Na]^+$ ion at *m/z* 505.1635 ($C_{30}H_{26}O_6Na$)

^1H NMR: δ ppm, 300 MHz, in acetone-d_6; **Table 16**

^{13}C NMR: δ ppm, 75 MHz, in acetone-d_6; **Table 16**

4.12 Compound DG1 (dihydrodengibsinin) [335]

Compound **DG1** was obtained as a brownish-white amorphous solid (25.3 mg, 0.0006% of the dry weight of the plant). It was soluble in acetone.

HR-ESIMS: $[M - H]^-$ ion at *m/z* 273.0764 ($C_{15}H_{13}O_5$)

UV: λ_{max} nm (log ε), in methanol: 220 (3.82), 255 (4.02), 300 (4.24)

FT-IR: ν cm^{-1} (film): 3420, 3240, 2925, 1618, 1484, 1459, 1373, 1314, 1144, 1084, 720

Optical rotation: $[\alpha]_{D}^{20}$: - 100.0 (c 0.01, MeOH)

^{1}H NMR: δ ppm, 300 MHz, in acetone-d_6; **Table 17**

^{13}C NMR: δ ppm, 75 MHz, in acetone-d_6; **Table 17**

4.13 Compound DG2 (dendrogibsol) [336]

Compound **DG2** was obtained as a brownish amorphous solid (5 mg, 0.0001% of the dry weight of the plant). It was soluble in acetone.

HR-ESIMS: [M + H]$^{+}$ ion at *m/z* 557.1849 ($C_{32}H_{29}O_9$)

UV: λ_{max} nm (log ε), in methanol: 260 (5.10), 310 (4.76), 325 (4.61)

FT-IR: ν cm^{-1} (film): 3434, 2930, 2848, 1723, 1607, 1485, 1461, 1365, 1303, 1282, 1236, 1198, 1092

Optical rotation: $[\alpha]_{D}^{20}$: + 156.0 (c 0.002, MeOH)

^{1}H NMR: δ ppm, 500 MHz, in acetone-d_6; **Table 18**

^{13}C NMR: δ ppm, 125 MHz, in acetone-d_6; **Table 18**

4.14 Compound DG3 (ephemeranthol A) [90]

Compound **DG3** was obtained as a white amorphous solid (18 mg, 0.0004% of the dry weight of the plant). It was soluble in acetone.

HR-ESIMS: [M + Na]$^{+}$ ion at *m/z* 295.0965 ($C_{16}H_{16}O_4Na$)

^{1}H NMR: δ ppm, 300 MHz, in acetone-d_6; **Table 19**

^{13}C NMR: δ ppm, 75 MHz, in acetone-d_6; **Table 19**

4.15 Compound DG4 (dengibsinin) [309]

Compound **DG4** was obtained as an orange-colored powder (15.7 mg, 0.0004% of the dry weight of the plant). It was soluble in acetone.

HR-ESIMS: [M + Na]$^{+}$ ion at *m/z* 295.05740 ($C_{15}H_{12}O_5Na$)

^{1}H NMR: δ ppm, 300 MHz, in acetone-d_6; **Table 20**

^{13}C NMR: δ ppm, 75 MHz, in acetone-d_6; **Table 20**

4.16 Compound DG5 (nobilone) [308]

Compound **DG5** was obtained as a reddish powder (98 mg, 0.0023% of the dry weight of the plant). It was soluble in acetone.

HR-ESIMS: $[M + Na]^+$ ion at *m/z* 265.04825 ($C_{14}H_{10}O_4Na$)

^{1}H NMR: δ ppm, 300 MHz, in acetone-d_6; **Table 21**

^{13}C NMR: δ ppm, 75 MHz, in acetone-d_6; **Table 21**

4.17 Compound DG6 (aloifol I) [20]

Compound **DG6** was obtained as a brown amorphous solid (11.2 mg, 0.0003% of the dry weight of the plant). It was soluble in acetone.

HR-ESIMS: $[M + Na]^+$ ion at *m/z* 297.11083 ($C_{16}H_{18}O_4Na$)

^{1}H NMR: δ ppm, 300 MHz, in acetone-d_6; **Table 22**

^{13}C NMR: δ ppm, 75 MHz, in acetone-d_6; **Table 22**

4.18 Compound DG7 (lusianthridin) [97]

Compound **DG7** was obtained as a brown amorphous solid (6.2 mg, 0.0001% of the dry weight of the plant). It was soluble in acetone.

HR-ESIMS: $[M + Na]^+$ ion at *m/z* 265.0840 ($C_{15}H_{14}O_3Na$)

^{1}H NMR: δ ppm, 300 MHz, in acetone-d_6; **Table 23**

^{13}C NMR: δ ppm, 75 MHz, in acetone-d_6; **Table 23**

4.19 Compound DG8 (denchrysan A) [305]

Compound **DG8** was obtained as a reddish powder (14 mg, 0.0003% of the dry weight of the plant). It was soluble in acetone.

HR-ESIMS: $[M + Na]^+$ ion at *m/z* 281.03781 ($C_{14}H_{10}O_5Na$)

^{1}H NMR: δ ppm, 300 MHz, in acetone-d_6; **Table 24**

^{13}C NMR: δ ppm, 75 MHz, in acetone-d_6; **Table 24**

4.20 Compound DG9 (4 methoxy-9*H*-fluorene-2,5,9-triol) [312]

Compound **DG9** was obtained as a white powder (10.3 mg, 0.0002% of the dry weight of the plant). It was soluble in acetone.

HR-ESIMS: [M + Na]$^+$ ion at *m/z* 267.06364 ($C_{14}H_{12}O_4Na$)

^{1}H NMR: δ ppm, 300 MHz, in acetone-d_6; **Table 25**

^{13}C NMR: δ ppm, 75 MHz, in acetone-d_6; **Table 25**

4.21 Compound AMF1 (aerimultin A) [337]

Compound **AMF1** was obtained as a whitish-brown amorphous solid (2.3 mg, 0.00004% of the dry weight of the plant). It was soluble in acetone.

HR-ESIMS: [M + Na]$^+$ ion at *m/z* 565.1841 ($C_{32}H_{30}O_8Na$)

UV: λ_{max} nm (log ε), in methanol: 265 (4.31), 305 (4.2), 315 (4.19)

FT-IR: ν cm^{-1} (film): 3350, 2923, 2850, 1696, 1605, 1462, 1442, 1221, 1201

^{1}H NMR: δ ppm, 500 MHz, in acetone-d_6; **Table 26**

^{13}C NMR: δ ppm, 125 MHz, in acetone-d_6; **Table 26**

4.22 Compound AMF2 (aerimultin B) [338]

Compound **AMF2** was obtained as a brown amorphous solid (3.9 mg, 0.00006% of the dry weight of the plant). It was soluble in acetone.

HR-ESIMS: [M + Na]$^+$ ion at *m/z* 559.1376 ($C_{32}H_{24}O_8Na$)

UV: λ_{max} nm (log ε), in methanol: 265 (4.67), 315 (4.09), 370 (3.99)

FT-IR: ν cm^{-1} (film): 3368, 2919, 2850, 1736, 1587, 1463,1259

Optical rotation: $[\alpha]^{20}_{D}$: - 108 (c 0.005, MeOH)

^{1}H NMR: δ ppm, 500 MHz, in acetone-d_6; **Table 27**

^{13}C NMR: δ ppm, 125 MHz, in acetone-d_6; **Table 27**

4.23 Compound AMF3 (aerimultin C) [339]

Compound **AMF3** was obtained as a brown amorphous solid (8.8 mg, 0.00001% of the dry weight of the plant). It was soluble in acetone.

HR-ESIMS: $[M + Na]^+$ ion at *m/z* 533.1218 ($C_{30}H_{22}O_8Na$)

UV: λ_{max} nm (log ε), in methanol: 265 (4.1), 315 (3.42), 355 (3.47), 370 (3.48)

FT-IR: ν cm^{-1} (film): 3360, 2921, 2851, 1712, 1588, 1461, 1371

Optical rotation: $[\alpha]^{20}_{D}$: +67.5 (c 0.008, MeOH)

^1H NMR: δ ppm, 300 MHz, in acetone-d_6; **Table 28**

^{13}C NMR: δ ppm, 75 MHz, in acetone-d_6; **Table 28**

4.24 Compound AMF4 (dihydrosinapyl dihydroferulate) [340]

Compound **AMF4** was obtained as a yellow amorphous solid (4.2 mg, 0.00006% of the dry weight of the plant). It was soluble in acetone.

HR-ESIMS: $[M + Na]^+$ ion at *m/z* 413.1585 ($C_{21}H_{26}O_7Na$)

UV: λ_{max} nm (log ε), in methanol: 280 (3.76), 315 (3.12)

FT-IR: ν cm^{-1} (film): 3432, 2937, 2841, 1723, 1608, 1514, 1455, 1427, 1208, 1111

^1H NMR: δ ppm, 300 MHz, in acetone-d_6; **Table 29**

^{13}C NMR: δ ppm, 75 MHz, in acetone-d_6; **Table 29**

4.25 Compound AMF5 (6-methoxycoelonin) [332]

Compound **AMF5** was obtained as a brown amorphous solid (65.4 mg, 0.001% of the dry weight of the plant). It was soluble in acetone.

HR-ESIMS: $[M + Na]^+$ ion at *m/z* 295.09358 ($C_{16}H_{16}O_4Na$)

^1H NMR: δ ppm, 300 MHz, in acetone-d_6; **Table 30**

^{13}C NMR: δ ppm, 75 MHz, in acetone-d_6; **Table 30**

4.26 Compound AMF6 (gigantol) [2]

Compound **AMF6** was obtained as a brown amorphous solid (14.5 mg, 0.0002% of the dry weight of the plant). It was soluble in acetone.

HR-ESIMS: [M + Na]$^+$ ion at *m/z* 297.10851 ($C_{16}H_{18}O_4Na$)

^{1}H NMR: δ ppm, 300 MHz, in acetone-d_6; **Table 31**

^{13}C NMR: δ ppm, 75 MHz, in acetone-d_6; **Table 31**

4.27 Compound AMF7 (imbricatin) [330]

Compound **AMF7** was obtained as a brown amorphous solid (39 mg, 0.0006% of the dry weight of the plant). It was soluble in acetone.

HR-ESIMS: [M + Na]$^+$ ion at *m/z* 293.07781 ($C_{16}H_{14}O_4Na$)

^{1}H NMR: δ ppm, 300 MHz, in acetone-d_6; **Table 32**

^{13}C NMR: δ ppm, 75 MHz, in acetone-d_6; **Table 32**

4.28 Compound AMF8 (agrostonin) [341]

Compound **AMF8** was obtained as a brown amorphous solid (7 mg, 0.0001% of the dry weight of the plant). It was soluble in acetone.

HR-ESIMS: [M + Na]$^+$ ion at *m/z* 561.1527 ($C_{32}H_{26}O_8Na$)

^{1}H NMR: δ ppm, 300 MHz, in acetone-d_6; **Table 33**

^{13}C NMR: δ ppm, 75 MHz, in acetone-d_6; **Table 33**

4.29 Compound AMF9 (dihydroconiferyl dihydro-*p*-coumarate) [275]

Compound **AMF9** was obtained as a yellow amorphous solid (74.1 mg 0.0012% of the dry weight of the plant). It was soluble in acetone.

HR-ESIMS: [M + Na]$^+$ ion at *m/z* 353.1369 ($C_{19}H_{22}O_5Na$)

^{1}H NMR: δ ppm, 300 MHz, in acetone-d_6; **Table 34**

^{13}C NMR: δ ppm, 75 MHz, in acetone-d_6; **Table 34**

4.30 Compound AMF10 (5-methoxy-9,10-dihydrophenanthrene-2,3,7-triol) [342]

Compound **AMF10** was obtained as a brown amorphous solid (9.2 mg, 0.0002% of the dry weight of the plant). It was soluble in acetone.

HR-ESIMS:	[M + Na]$^+$ ion at *m/z* 281.0791 ($C_{15}H_{14}O_4Na$)
^{1}H NMR:	δ ppm, 300 MHz, in acetone-d_6; **Table 35**
^{13}C NMR:	δ ppm, 75 MHz, in acetone-d_6; **Table 35**

5 Assay for α- glucosidase inhibitory activity

5.1 Evaluation of α-glucosidase inhibitory activity

In this assay, inhibition of the enzyme α-glucosidase was determined from the release of *p*-nitrophenol from the substrate *p*-nitrophenol-α-D-glucopyranoside (*p*NPG) in the presence of the test compound. The samples were initially prepared in 50 % DMSO solution. The sample solution (10 µL) and 0.1 U/ml α-glucosidase (40 µL) in phosphate buffer (pH 6.8) were added to a 96-well plate. The mixture was pre-incubated at 37°C for 10 minutes before the addition of 2 mM *p*NPG (50 µL). The final concentration of DMSO in each well was 5 %. Then, the mixture was further incubated at 37°C for 20 minutes. Finally, 1 M Na_2CO_3 solution (100 µL) was added to stop the reaction. The absorbance of the mixture was determined at 405 nm using a micro-plate reader. In this assay, acarbose was used as the positive control (Inthongkaew *et al*., 2017).

The percentage of α-glucosidase enzyme inhibition was calculated as follows:

$\% \text{ inhibition} = [(A_c-A_s)/A_c] \times 100$

A_c = Absorbance of 5 % DMSO in H_2O (negative control)

A_s = Absorbance of test sample or acarbose

All the extracts and compounds isolated from the three plants were initially tested at a concentration of 100 μg/ml as described above. An extract was considered as active if it showed more than 70% inhibition of the enzyme. An IC_{50} (the concentration that shows 50% inhibition) was determined for compounds that showed more than 70% inhibition. Two-fold serial dilution was done for each sample for the IC_{50} determination.

5.2 Kinetic study

The most potent compounds from the three plants (DD10, DD11, DG2 and AMF3) were selected for enzyme kinetic studies. The *p*NPG substrate concentrations were varied from 0.25 to 2 mM in the absence or presence of the test compound or acarbose at different concentrations. The reaction was monitored at 405 nm using a microplate reader every 5 min for a total time of 25 min. The mode of inhibition was determined by analysis of the double-reciprocal Lineweaver–Burk plots (1/V vs. 1/[S]). A secondary plot was constructed from the slopes of the double-reciprocal lines, and the K_i value was calculated from the line equation of this plot (Chatsumpun *et al.*, 2017). The graphpad prism software was used to analyze the data.

CHAPTER IV

RESULTS AND DISCUSSION

In this research, the dried powders of *Dendrobium delacourii, Dendrobium gibsonii and Aerides multiflora* were each extracted with methanol (MeOH) to yield methanolic extracts (300.7 g, 371 g and 550 g, respectively). During the preliminary investigation, all the MeOH extracts showed more than 70 % inhibition of α-glucosidase at 100 µg/ml, and therefore were subjected to further investigation to identify the active principles.

1 Preliminary evaluation of α-glucosidase inhibitory activity

1.1 Evaluation of *Dendrobium delacourii* extracts

The MeOH extract prepared from *Dendrobium delacourii*, at 100 µg/ml, exhibited 80 % inhibition of α-glucosidase enzyme. This extract was suspended in water and then partitioned with EtOAc and butanol to give an EtOAc extract (159.79 g), a butanol extract (98.29 g), and an aqueous extract (97.93 g), respectively. Only the EtOAc extract was active (85.5 ± 5.2 % inhibition at 100 µg/mL) **(Table 3)** and therefore was selected for further investigation to identify the active principles.

Table 3 α-Glucosidase inhibitory activity of extracts from *D. delacourii*

Extracts (100 µg/mL)	% Inhibition of α-glucosidase
Methanol	80 ± 9.7
Ethyl acetate	85.5 ± 5.2
n-Butanol	9.1 ± 0.1
Acarbose (Positive control)	41.5 ± 0.5

1.2 Evaluation of *Dendrobium gibsonii* extracts

The MeOH extract prepared from *Dendrobium gibsonii*, at 100 µg/ml, exhibited 78.7 ± 3.2 % inhibition of α-glucosidase enzyme. This extract was suspended in water and then partitioned with EtOAc and butanol to give an EtOAc extract (100 g), a butanol extract (72 g) and an aqueous extract (95.5 g), respectively. Only EtOAc extract was active, exhibiting 77.7 ± 1.8 % inhibition at 100 μg/mL (more than 70 % inhibition) **(Table 4)** and therefore was chosen for further investigation.

Table 4 α-Glucosidase inhibitory activity of extracts from *D. gibsonii*

Extracts (100 μg/mL)	% Inhibition of α-glucosidase
Methanol	78.7 ± 3.2
Ethyl acetate	77.7 ± 1.8
n-Butanol	8.4 ± 3.0
Acarbose (Positive control)	41.5 ± 0.5

1.3 Evaluation of *Aerides multiflora* extracts

The MeOH extract prepared from *Aerides multiflora*, at 100 μg/ml, exhibited 82.4 ± 9.5 % inhibition of α-glucosidase enzyme. This MeOH extract (550 g) was then suspended in water and partitioned with EtOAc and butanol to give an EtOAc extract (201.1 g), a butanol extract (80.8 g), and an aqueous extract (150 g), respectively. Only the EtOAc extract was active, exhibiting 92.9 ± 3.2 % inhibition at 100 μg/mL (more than 70 % inhibition) **(Table 5)** and therefore was selected for further investigation.

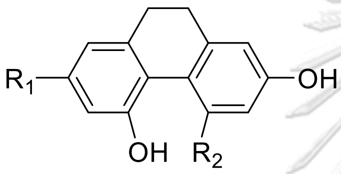
Table 5 α-Glucosidase inhibitory activity of extracts from *A. multiflora*

Extracts (100 μg/mL)	% Inhibition of α-glucosidase
Methanol	82.4 ± 9.5
Ethyl acetate	92.9 ± 3.2
n-Butanol	5.9 ± 1.8
Acarbose (Positive control)	41.5 ± 0.5

2 Chemical investigation

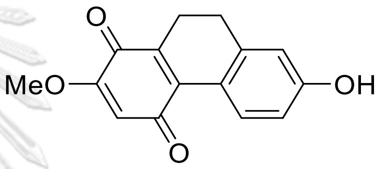
2.1 Chemical investigation of EtOAc extract of *Dendrobium delacourii*

The phytochemical investigation of the EtOAc extract resulted in the isolation of 11 compounds, including hircinol [**94**], ephemeranthoquinone [**129**], densiflorol B [**126**], moscatin [**110**], 4,9-dimethoxy-2,5-phenanthrenediol [**105**], gigantol [**2**], batatasin III [**3**], lusianthridin [**97**], 4,4′,7,7′-tetrahydroxy-2,2′-dimethoxy-9,9′,10,10′-tetrahydro-1,1′-biphenanthrene [**154**], phoyunnanin E [**157**], and phoyunnanin C [**156**] (**Figure 7**).

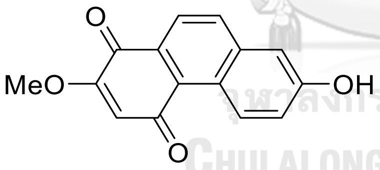


hircinol [**94**]; R_1=H; R_2 = OMe

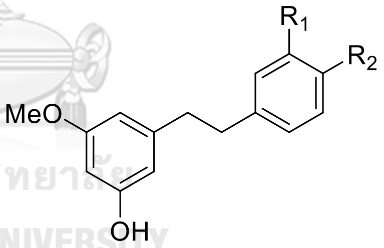
lusianthridin [**97**]; R_1= OMe; R_2 = H



ephemeranthoquinone [**129**]



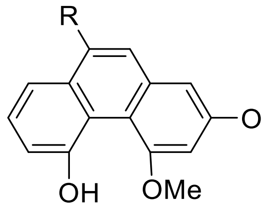
densiflorol B [**126**]



gigantol [**2**]; R_1 = OMe, R_2 = OH

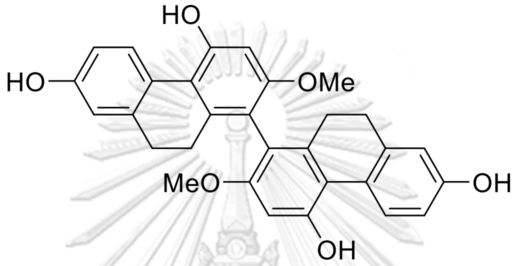
batatasin III [**3**]; R_1 = OH, R_2 = H

Figure 7 Structures of compounds isolated from *Dendrobium delacourii*

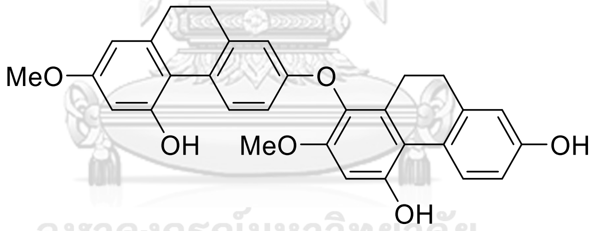


moscatin [**110**]; R = H

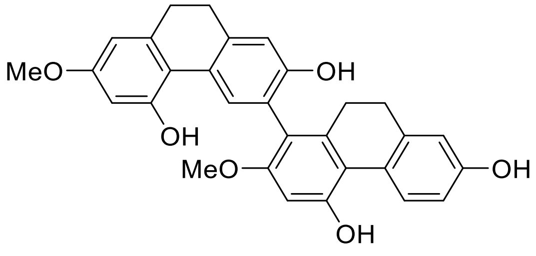
4,9-dimethoxy, 2,5- phenanthrenediol [**105**]; R = OMe



4,4′,7,7′-tetrahydroxy-2,2′-dimethoxy-9,9′,10,10′-tetrahydro-1,1′-biphenanthrene [**154**]



phoyunnanin E [**157**]



phoyunnanin C [**156**]

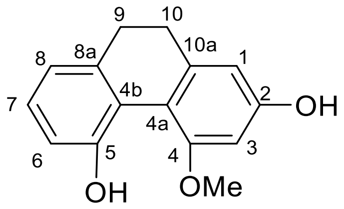
Figure 7 (Continued)

2.1.1 Identification of compound DD1 (hircinol)

Compound DD1 was obtained as a yellow amorphous solid. The APCI mass spectrum (**Figure 8**) showed a protonated molecular ion $[M+H]^+$ at *m/z* 243.1059 (calculated for $C_{15}H_{15}O_3$, 243.1021), suggesting the molecular formula $C_{15}H_{14}O_3$. The ^{1}H-NMR spectrum of compound DD1 in acetone-d_6 (**Figure 9 and Table 6**) displayed two pairs of methylene protons at δ_H 2.59 (4H, m, H_2-9 and H_2-10), five aromatic protons at δ_H 6.60 (1H, d, *J*=2.5 Hz, H-1), 6.49 (1H, d, *J*=2.5 Hz, H-3), 6.80 (1H, d, *J*=8.0 Hz, H-6), 7.06 (1H, t, *J*=8.0 Hz, H-7), and 6.79 (1H, d, *J*=8.0 Hz, H-8), a hydroxy group at δ_H 7.80 (1H, s, 5-OH) and one methoxy group at δ_H 3.97 (3H, s, 4-OMe). These NMR data suggested a dihydrophenanthrene skeleton (Fisch *et al.,* 1973).

The ^{13}C-NMR spectrum (**Figure 10 and Table 6**) showed a methoxy carbon at δ_C 57.2, two methylene carbons at δ_C 31.8 (C-9) and 31.6 (C-10), five methine carbons at δ_C 99.8 (C-3), 109.8 (C-1), 118.2 (C-6), 120.1 (C-8), and 128.1 (C-7), and seven quaternary carbons at δ_C 114.6 (C-4b), 130.4 (C-4a), 141.3 (C-8a), 144.2 (C-10a), 154.7 (C-4), 156.3 (C-5), and 158.5 (C-2). The methoxy group was placed at C-4, as evidenced by its NOESY cross peaks with H-3 and 5-OH protons (**Figure 11**).

The above spectroscopic data of compound DD1 were in accordance with the values reported for hircinol [**94**] (Fisch *et al.*, 1973). Thus, compound DD1 was identified as hircinol. This compound was previously isolated from several *Dendrobium* species, for example *D. aphyllum* (Yang *et al.,* 2015a), *D. draconis* (Sritularak *et al.,* 2011b) and *D. formosum* (Inthongkaew *et al.,* 2017).

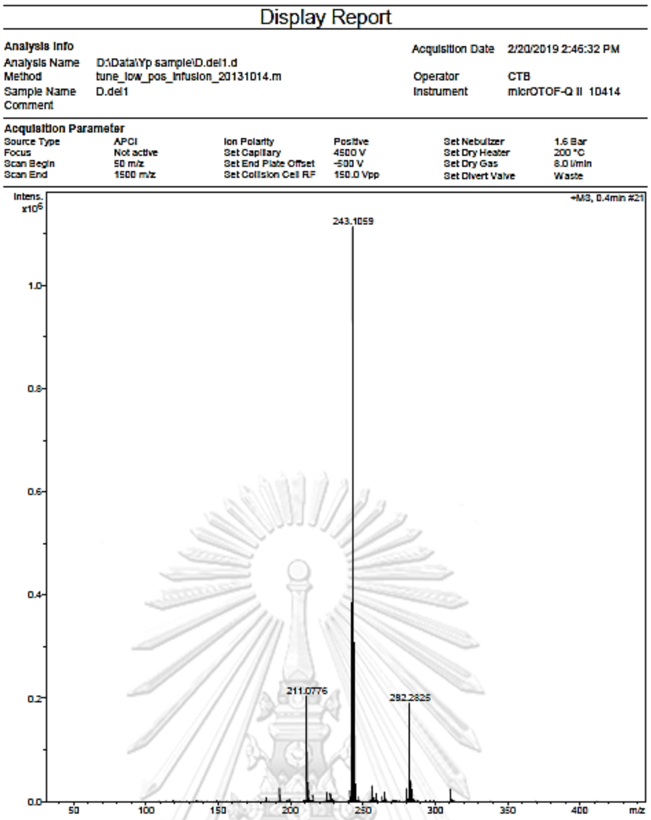


hircinol [**94**]

Table 6 NMR spectral data of compound DD1 and hircinol

Position	DD1 (acetone-d_6)		Hircinol ($CDCl_3$)	
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
1	6.60 (1H, d, 2.5)	109.8	6.51 (1H, s)	109.9
2	-	158.5	-	158.4
3	6.56 (1H, d, 2.5)	99.8	6.51 (1H, s)	100.0
4	-	154.7	-	154.6
4a	-	130.4	-	128.7
4b	-	114.6	-	114.7
5	-	156.3	-	156.3
6	6.80 (1H, d, 8.0)	118.2	6.77-7.32 (m)	118.2
7	7.06 (1H, t, 8.0)	128.1		128.1
8	6.80 (1H, d, 8.0)	120.1		120.0
8a	-	141.3	-	141.3
9	2.59 (2H, m)	31.8	2.64 (2H, br s)	31.6
10	2.59 (2H, m)	31.6	2.64 (2H, br s)	31.8
10a	-	144.2	-	144.1
4-OMe	3.97 (3H, s)	57.2	3.89 (3H, s)	57.3
5-OH	7.80 (1H, s)	-	7.95 (1H, s)	-

(Fisch *et al.*, 1973)



Display Report

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Acquisition Parameter

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Figure 8 Mass spectrum of compound DD1

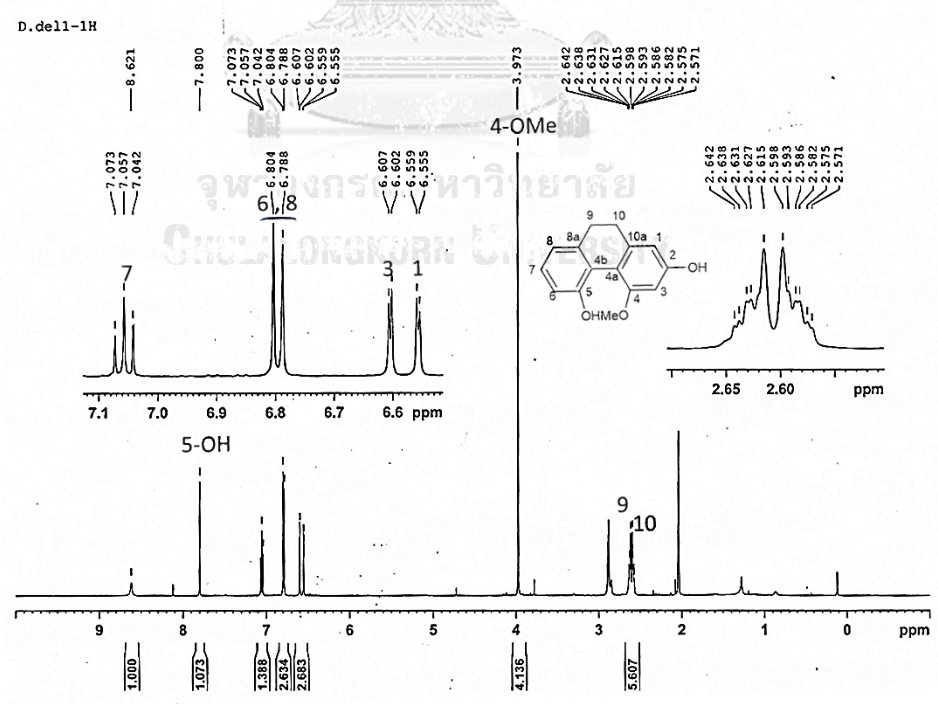


Figure 9 ^{1}H-NMR (500 MHz) spectrum of compound DD1

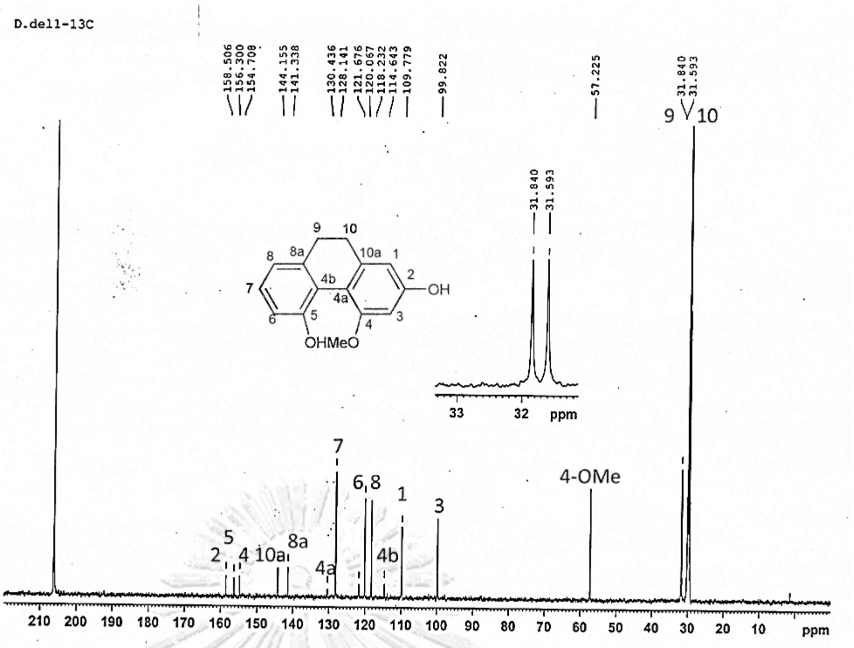


Figure 10 ^{13}C-NMR (125 MHz) spectrum of compound DD1

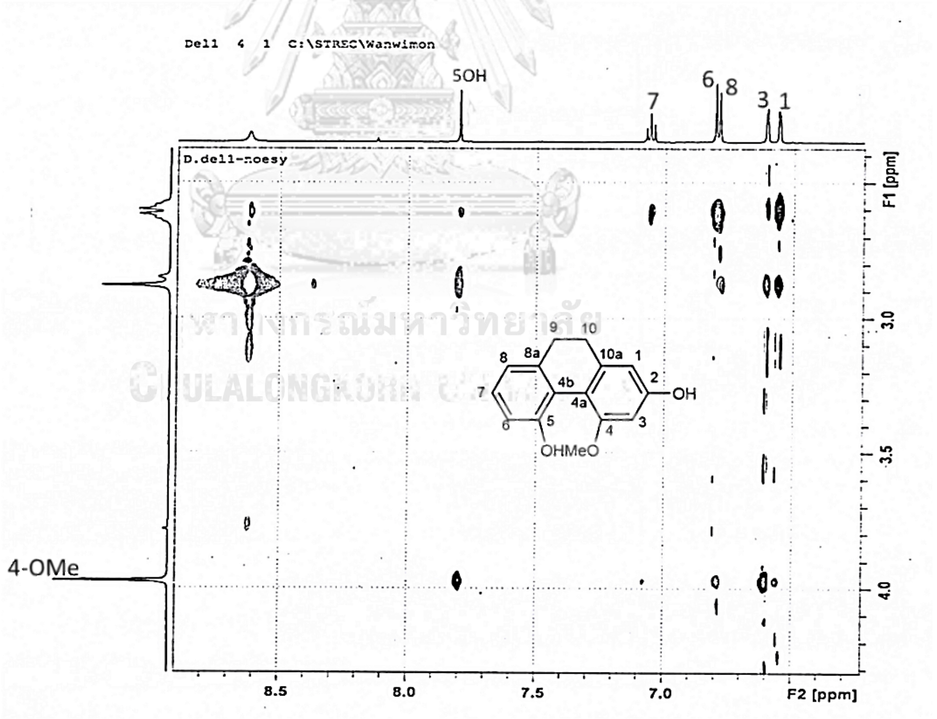


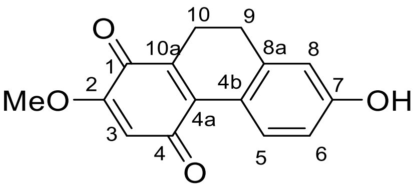
Figure 11 NOESY spectrum of compound DD1

2.1.2 Identification of compound DD2 (ephemeranthoquinone)

Compound DD2 was obtained as a reddish powder. The HR-ESI mass spectrum (**Figure 12**) showed a sodium adduct molecular ion $[M+Na]^+$ at *m/z* 279.06185 (calculated for $C_{15}H_{12}O_4Na$, 279.06333), suggesting the molecular formula $C_{15}H_{12}O_4$. The ^{1}H-NMR spectrum of compound DD2 in acetone-d_6 (**Figure 13 and Table 7**) displayed signals for four aromatic protons at δ_H 5.98 (1H, s, H-3), 7.97 (1H, d, *J*= 9.3 Hz, H-5), 6.76 (1H, m, H-6) and 6.76 (1H, d, *J*= 2.4 Hz, H-8); two pairs of methylene protons at δ_H 2.69 (2H, m, H_2-9) and 2.62 (2H, m, H_2-10); one hydroxy group at δ_H 8.89 (1H, s, 7-OH) and one methoxy signal at δ_H 3.85 (3H, s, 2-OMe).

The ^{13}C-NMR spectrum (**Figure 14 and Table 7**) showed the presence of two carbonyl carbons at δ_C 180.8 (C-1) and 187.2 (C-4); two methylene carbons at δ_C 20.0 (C-10) and 27.2 (C-9); six quaternary carbons at δ_C 121.2 (C-4b), 136.1 (C-4a), 136.2 (C-10a), 141.5 (C-8a), 158.6 (C-2), and 159.1 (C-7); four methine carbons at δ_C 107.4 (C-3), 113.4 (C-5), 114.8 (C-8) and 132.0 (C-6); and a methoxy carbon at δ_C 55.7 (2-OMe). The position of 2-OMe was indicated from its NOESY cross peak with H-3 (**Figure 15**).

The above NMR data were in agreement with the values previously reported for ephemeranthoquinone (Majumder & Sen, 1987; Tezuka *et al.*, 1991), and therefore compound DD2 was identified as ephemeranthoquinone [**129**]. It was also earlier isolated from *D. hongdie* (Chen *et al.*, 2015).



ephemeranthoquinone [**129**]

Table 7 NMR spectral data of compound DD2 and ephemeranthoquinone

Position	DD2 (acetone-d_6)		Ephemeranthoquinone (acetone-d_6)	
	δ_H (mult., J in Hz)	δ_C	δ_H (mult., J in Hz)	δ_C
1	-	180.8	-	182.0
2	-	158.6	-	159.5
3	5.98 (1H, s)	107.4	5.92 (1H, s)	108.7
4	-	187.2	-	188.5
4a	-	136.1	-	136.9
4b	-	121.2	-	123.2
5	7.97 (1H, d, 9.3)	113.4	8.01 (1H, d, 9)	115.3
6	6.76 (1H, m)	132.0	6.76 (1H, d, 8.6)	133.6
7	-	159.1	-	161.7
8	6.76 (1H, d, 2.4)	114.8	6.72 (1H, s)	116.7
8a	-	141.5	-	142.7
9	2.69 (2H, m)	27.2	2.73 (2H, m)	28.5
10	2.62 (2H, m)	20.0	2.73 (2H, m)	21.3
10a	-	136.2	-	137.5
2-OMe	3.85 (3H, s)	55.7	3.85 (3H, s)	56.8
7-OH	8.89 (1H, s)	-	-	-

(Majumder & Sen, 1987; Tezuka *et al.*, 1991)

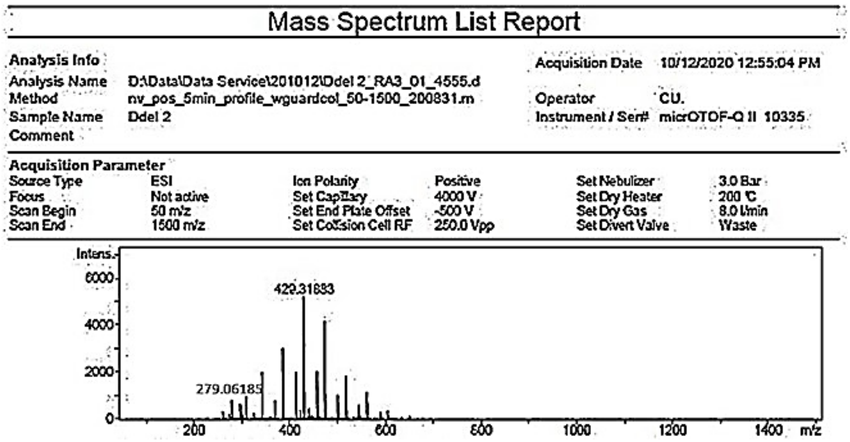


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Figure 12 Mass spectrum of compound DD2

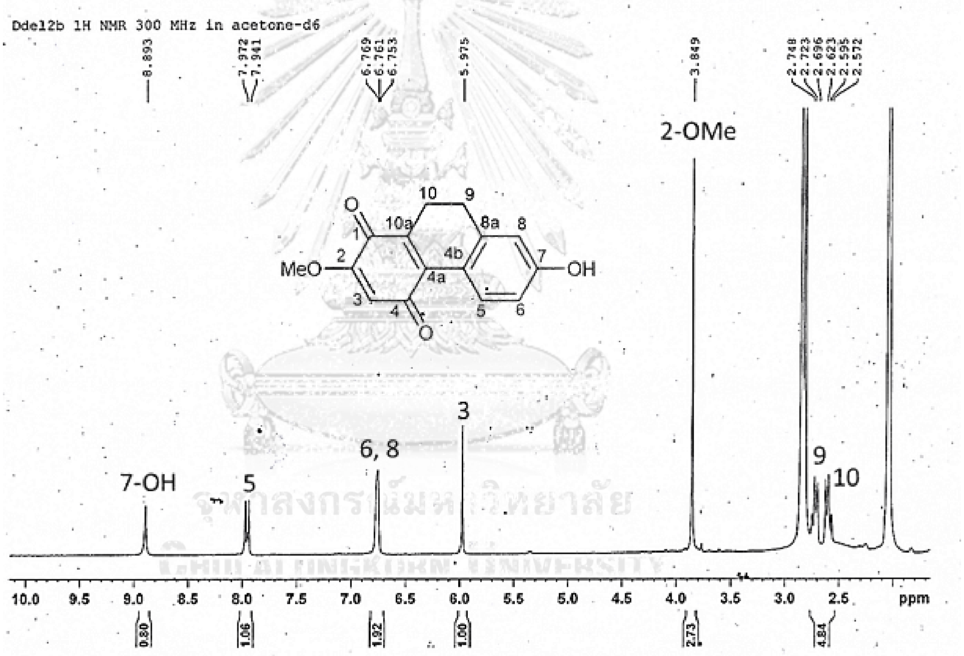


Figure 13 ^{1}H-NMR (300 MHz) spectrum of compound DD2

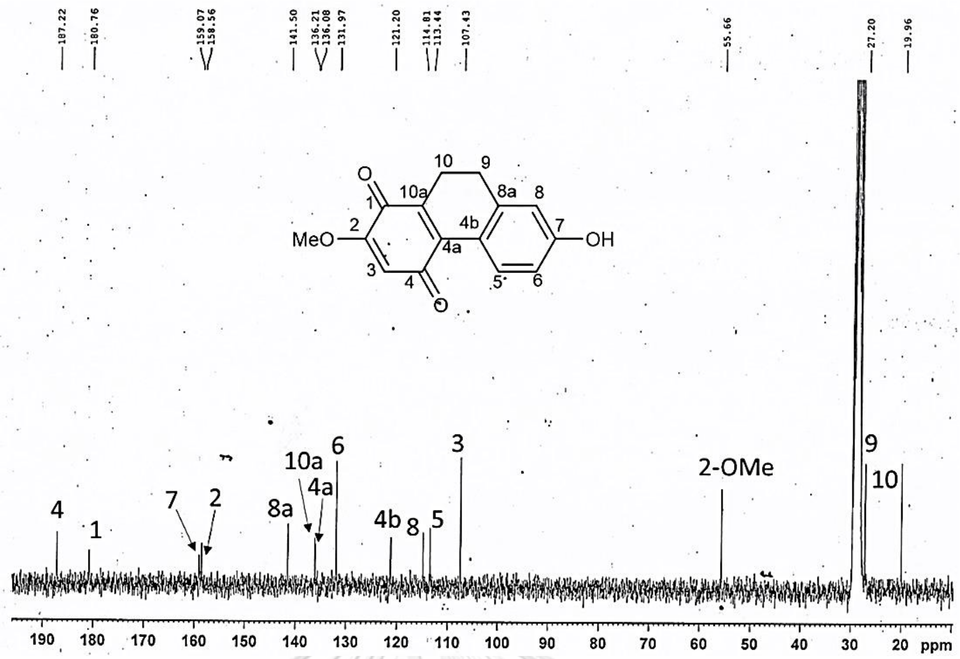


Figure 14 ^{13}C-NMR (75 MHz) spectrum of compound DD2

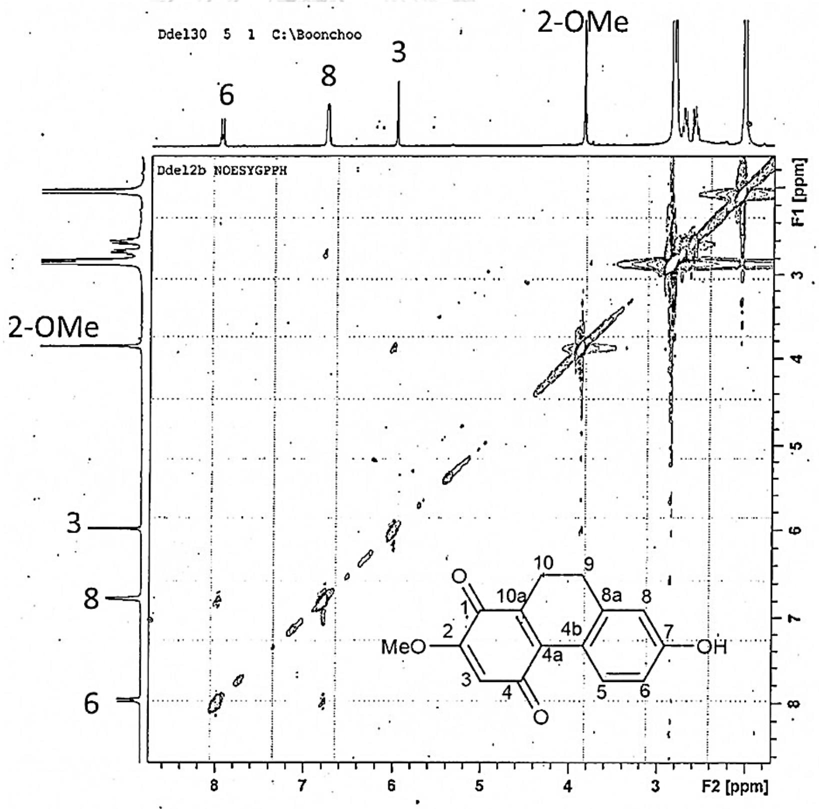


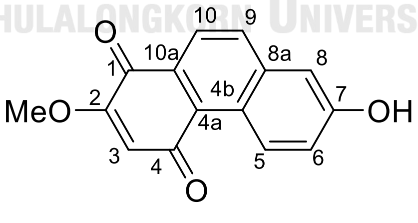
Figure 15 NOESY spectrum of compound DD2

2.1.3 Identification of compound DD3 (densiflorol B)

Compound DD3 was obtained as an orange powder. The HR-ESI mass spectrum (**Figure 16**) showed a sodium adduct molecular ion $[M+Na]^+$ at *m/z* 277.0473 (calculated for $C_{15}H_{10}O_4Na$, 277.0477), suggesting the molecular formula $C_{15}H_{10}O_4$. The ^{1}H-NMR spectrum of DD3 in acetone-d_6 (**Figure 17 and Table 8**) revealed signals for six aromatic protons at δ_H 6.20 (1H, s, H-3), 9.49 (1H, d, *J*= 9.3 Hz, H-5), 7.35 (1H, dd, *J*= 2.4, 9.3 Hz, H-6), 7.31 (1H, d, *J*= 2.4 Hz, H-8), and 8.04 (2H, br s, H-9 and H-10); and one methoxy group at δ_H 3.92 (3H, s, 2-OMe).

The ^{13}C NMR spectrum (**Figure 18 and Table 8**) also showed the presence of two carbonyl carbons at δ_C 180.5 (C-1) and 188.4 (C-4); six quaternary carbons at δ_C 160.2 (C-2), 157.8 (C-7), 139.4 (C-8a), 130.1 (C-10a), 127.5 (C-4a), and 124.2 (C-4b); six methine carbons at δ_C 134.2 (C-9), 132.3 (C-10), 122.0 (C-5), 122.0 (C-6), 110.9 (C-3), and 109.9 (C-8); and a methoxy group at δ_C 55.8 (2-OMe). The position of 2-OMe group was supported by its NOESY correlation with H-3 (**Figure 19**).

The ^{1}H-NMR and ^{13}C-NMR data of DD3 showed close similarities with those of densiflorol B [**126**], which was earlier reported from *Dendrobium densiflorum* (Fan *et al.*, 2001). Thus, compound DD3 was identified as densiflorol B.

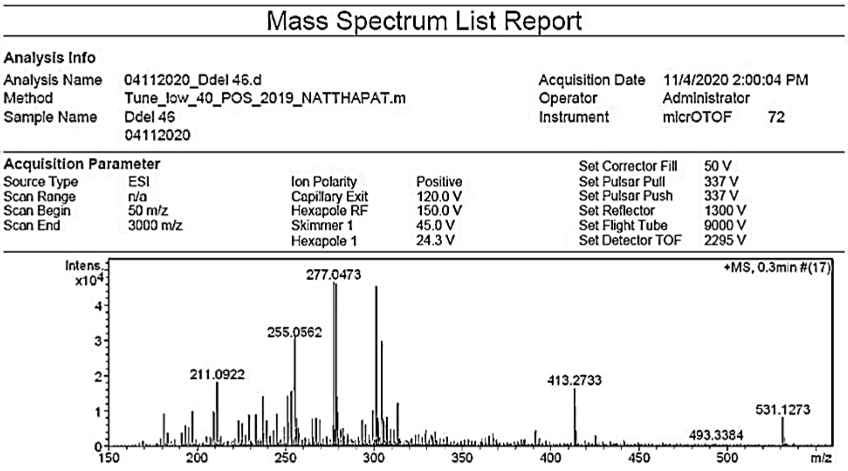


densiflorol B [**126**]

Table 8 NMR spectral data of compound DD3 and densiflorol B

Position	DD3 (acetone-d_6)		Densiflorol B (DMSO-d_6)	
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
1	-	180.5	-	180.2
2	-	160.2	-	158.3
3	6.20 (1H, s)	110.9	6.30 (1H, s)	111.1
4	-	188.4	-	188.4
4a	-	127.5	-	126.8
4b	-	124.2	-	123.3
5	9.49 (1H, d, 9.3)	122.0	9.35 (1H, d, 9.5)	121.8
6	7.35 (1H, dd, 2.4, 9.3)	122.0	7.35 (1H, dd, 2.2, 9.5)	122.4
7	-	157.8	-	157.5
8	7.31 (1H, d, 2.4)	109.9	7.25 (1H, d, 2.2)	109.7
8a	-	139.4	-	138.9
9	8.04 (1H, br s)	134.2	8.1 (1H, d, 8.6)	132.3
10	8.04 (1H, br s)	132.3	7.95 (1H, d, 8.6)	129.7
10a	-	130.2	-	128.3
2-OMe	3.92 (3H, s)	55.8	3.9 (3H, s)	56.4

(Fan *et al.*, 2001)



Mass Spectrum List Report

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Scan End	3000 m/z	Skimmer 1	45.0 V	Set Reflector	1300 V
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Figure 16 Mass spectrum of compound DD3

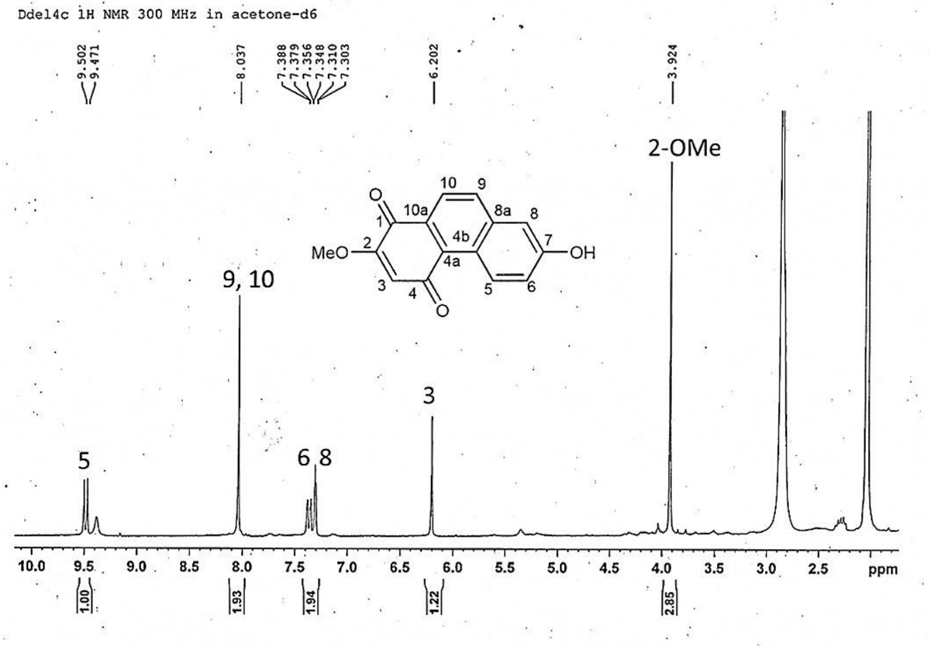


Figure 17 ^{1}H-NMR (300 MHz) spectrum of compound DD3

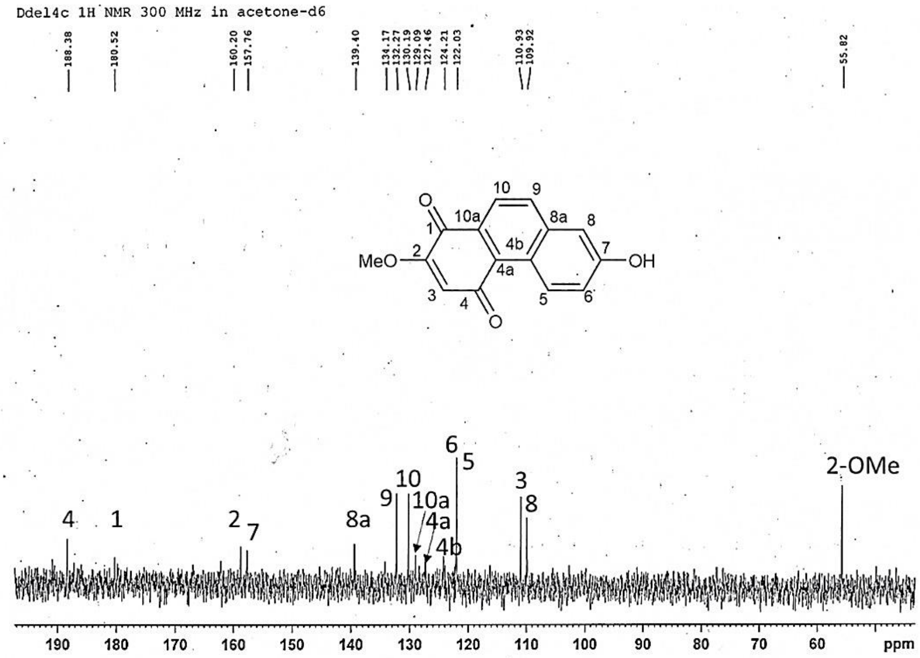


Figure 18 ^{13}C-NMR (75 MHz) spectrum of compound DD3

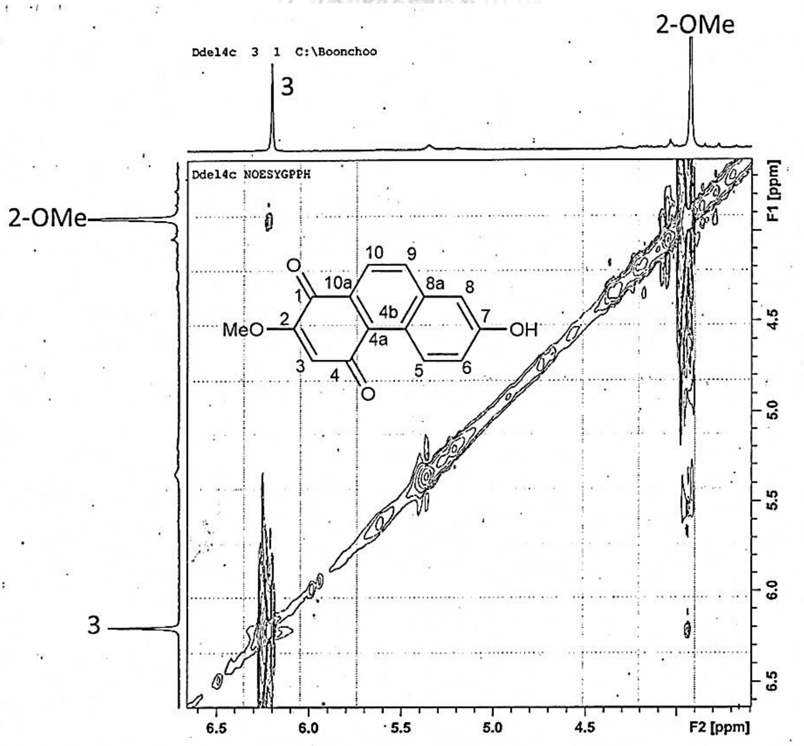


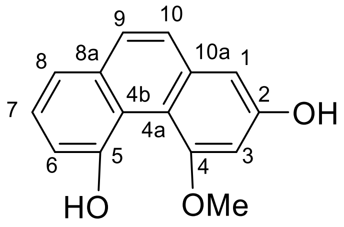
Figure 19 NOESY spectrum of compound DD3

2.1.4 Identification of compound DD4 (moscatin)

Compound DD4 was obtained as a brown amorphous solid. The APCI mass spectrum (**Figure 20**) showed a protonated molecular ion $[M+H]^+$ at *m/z* 241.0888 (calculated for $C_{15}H_{13}O_3$ 241.0865), suggesting the molecular formula $C_{15}H_{12}O_3$. The ^{1}H-NMR spectrum of DD4 in acetone-d_6 (**Figure 21 and Table 9**) suggested the presence of a phenanthrene skeleton. It showed signals for a pair of *ortho*-coupled aromatic protons at δ_H 7.63 (1H, d, *J*= 9.0 Hz, H-9) and 7.49 (1H, d, *J*= 8.5 Hz, H-10); an ABC coupling system at δ_H 7.10 (1H, dd, *J*= 7.5, 2.0 Hz, H-6), 7.43 (1H, t, *J*= 7.5 Hz, H-7), 7.41 (1H, dd, *J*= 1.5, 7.5 Hz, H-8), a pair of *meta*-coupled aromatic protons at δ_H 7.07 (1H, d, *J*= 2.5 Hz, H-1) and 6.99 (1H, d, *J*= 2.5 Hz, H-3); two hydroxy groups at δ_H 8.94 (1H, s, 2-OH) and 9.51 (1H, s, 5-OH); and a methoxy group at 4.15 (3H, s, 4-OMe).

The ^{13}C-NMR (**Figure 22 and Table 9**) spectrum displayed fifteen carbon signals, representing a methoxy group at δ_C 58.6; seven methine carbons at δ_C 107.8 (C-1), 102.5 (C-3), 116.9 (C-6), 127.4 (C-7), 121.0 (C-8), 129.7 (C-9), and 126.9 (C-10), and seven quaternary carbons at δ_C 156.4 (C-2), 157.3 (C-4), 155.2 (C-5), 113.9 (C-4a), 119.8 (C-4b), 135.0 (C-8a), and 137.1 (C-10a). The NOESY spectrum (**Figure 23**), showed correlations from the 4-OMe protons to H-3 and 5-OH protons, indicating the position of the methoxyl group at C-4. The assignment of 2-OH proton was based on its NOESY correlations with H-1 and H-3.

Based on the above data and comparison with previously reported data (Ono *et al.*, 1995), DD4 was identified as moscatin [**110**]. This compound was previously reported from several *Dendrobium* species, such as *D. aphyllum* (Chen *et al.,* 2008), *D. chrysanthum* (Yang *et al.,* 2006a), *D. chrysotoxum* (Li *et al.,* 2009a), *D. densiflorum* (Fan *et al.,* 2001), and *D. polyanthum* (Hu *et al.,* 2009).



Moscatin [**110**]

Table 9 NMR spectral data of compound DD4 and moscatin

Position	DD4 (acetone-d_6)		Moscatin ($CDCl_3$)	
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
1	7.07 (1H, d, 2.5)	107.8	6.96 (1H, d, 2.5)	107.4
2	-	156.4	-	154.4
3	6.99 (1H, d, 2.5)	102.5	6.82 (1H, d, 2.5)	101.7
4	-	157.3	-	155.4
4a	-	113.9	-	114.2
4b	-	119.8	-	118.8
5	-	155.2	-	153.8
6	7.10 (1H, dd, 7.5, 2.0)	116.9	7.23 (1H, dd, 8.0, 1.2)	116.6
7	7.43 (1H, t, 7.5)	127.4	7.48 (1H, dd, 8.0, 1.2)	129.4
8	7.41 (1H, dd, 1.5, 7.5)	121.0	7.41 (1H, dd, 1.2, 8.0)	120.8
8a	-	135.0	-	134.1
9	7.63 (1H, d, 9)	129.7	7.61 (1H, d, 9.2)	127.0
10	7.49 (1H, d, 8.5)	126.9	7.41 (1H, d, 9.2)	125.9
10a	-	137.1	-	136.1
4-OMe	4.15 (3H, s)	58.6	4.04 (3H, s)	58.4
2-OH	8.94 (1H, s)	-	-	-
5-OH	9.51 (1H, s)	-	-	-

(Ono *et al.*, 1995)

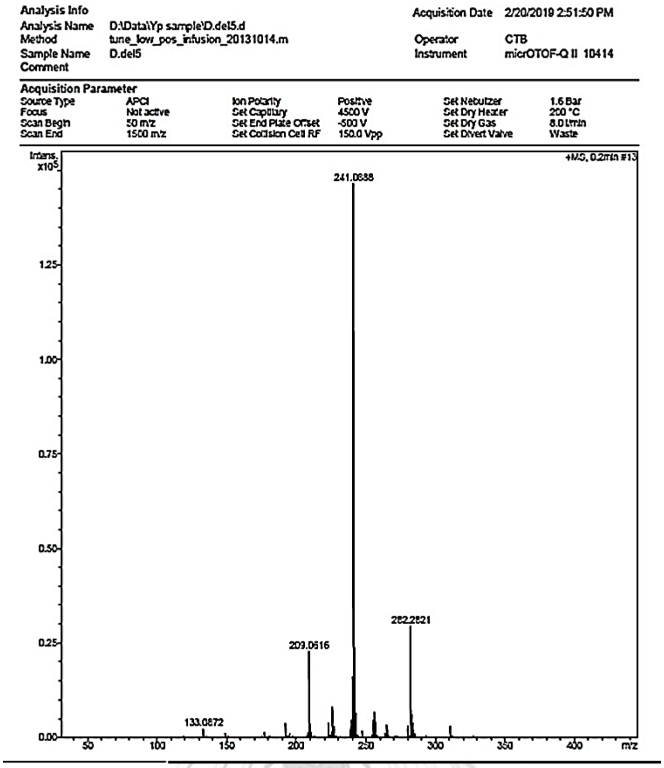


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Figure 20 Mass spectrum of compound DD4

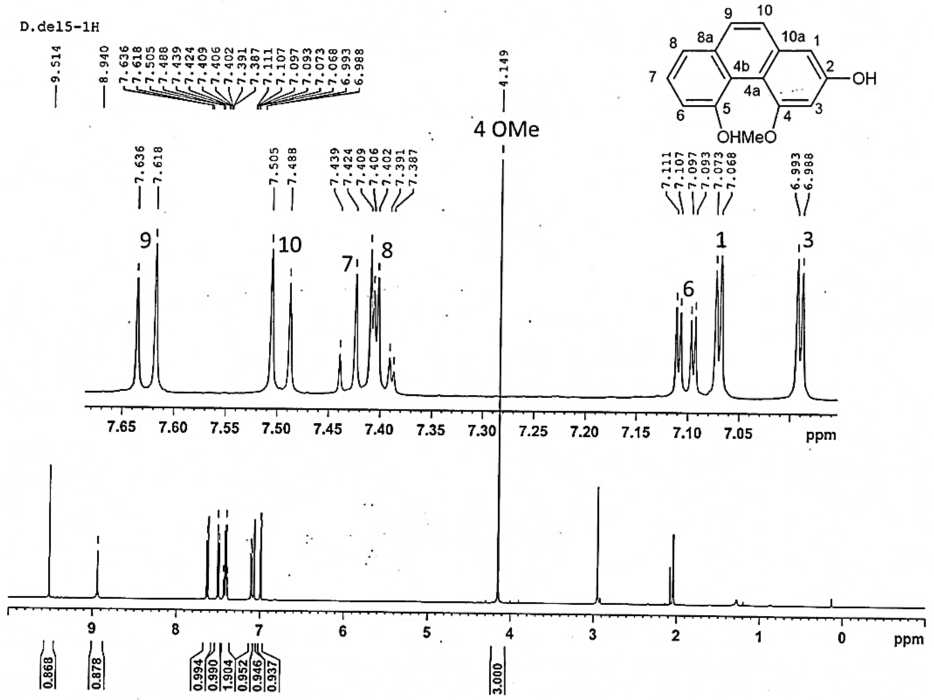


Figure 21 ^{1}H-NMR (500 MHz) spectrum of compound DD4

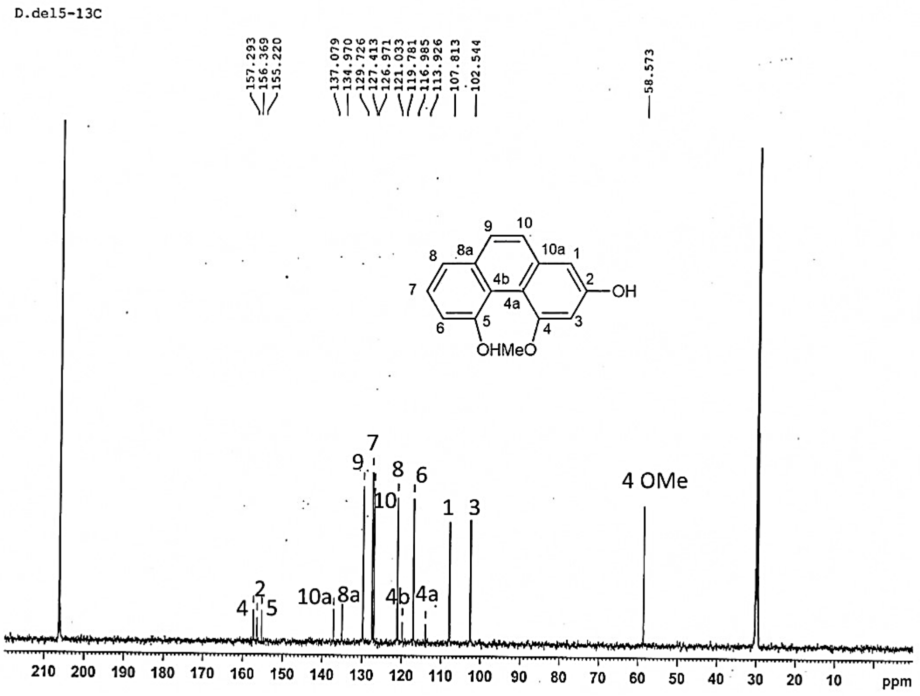


Figure 22 ^{13}C-NMR (125 MHz) spectrum of compound DD4

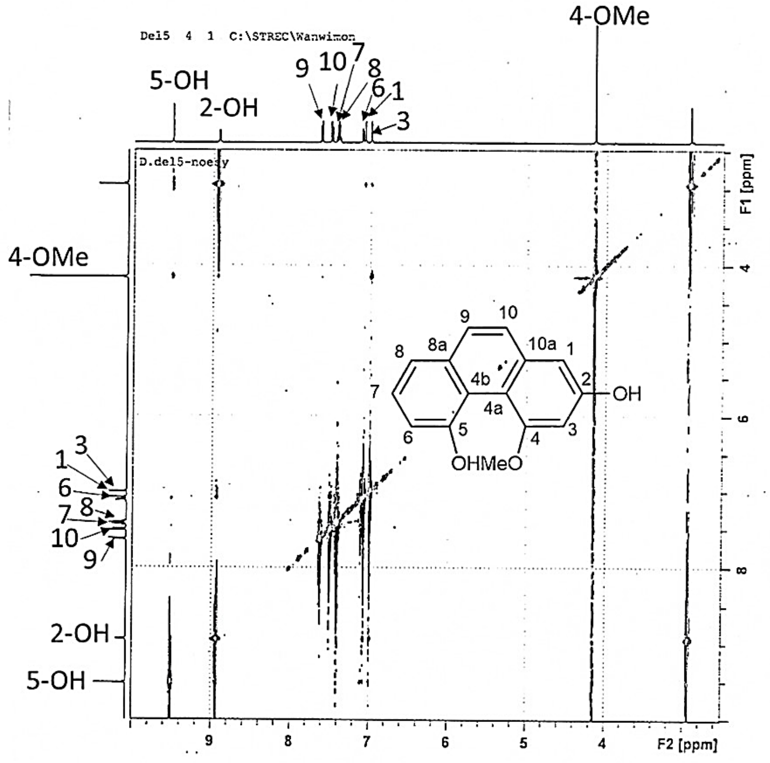


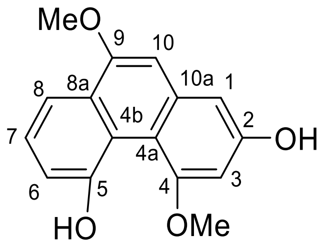
Figure 23 NOESY spectrum of compound DD4

2.1.5 Identification of compound DD5 (4,9-dimethoxy-2,5-phenanthrenediol)

Compound DD5 was obtained as a brown amorphous solid. The APCI mass spectrum (**Figure 24**) showed a protonated molecular ion $[M+H]^+$ at *m/z* 271.1009, (calculated for $C_{16}H_{15}O_4$; 271.0970), suggesting the molecular formula $C_{16}H_{14}O_4$. The ^{1}H-NMR spectrum of compound DD5 (**Figure 25 and Table 10**) showed signals for six aromatic protons, appearing as a singlet at δ_H 6.92 (1H, s, H-10), two *meta*-coupled doublets at δ_H 6.99 (1H, d, *J* = 2.5 Hz, H-1) and 6.81 (1H, d, *J* = 2.5 Hz, H-3), a triplet at δ_H 7.43 (1H, t, *J* = 7.5 Hz, H-7) and two double doublets at 7.12 (1H, dd, *J* = 1.5, 7.5 Hz, H-6) and 7.85 (1H, dd, *J* = 1.5, 8.0 Hz, H-8). In addition, two singlet signals representing two methoxy groups showed at δ_H 4.11 (3H, s, 4-OMe) and 4.03 (3H, s, 9-OMe); two singlet signals for two hydroxy groups at δ_H 9.43 (1H, s, 5-OH) and 8.82 (1H, s, 2-OH).

The ^{13}C-NMR spectrum (**Figure 26 and Table 10**) displayed 16 carbon signals, including two methoxy carbons at δ_C 58.5 (4-OMe) and 55.9 (9-OMe), eight quaternary carbons at 157.5 (C-2), 156.3 (C-4), 110.0 (C-4a), 120.9 (C-4b), 155.2 (C-5), 129.2 (C-8a), 154.9 (C-9), and 137.9 (C-10a), and six methine carbons at 106.9 (C-1), 100.3 (C-3), 117.6 (C-6), 127.9 (C-7), 114.3 (C-8), and 102.8 (C-10). The NOESY correlations from H-3 and 5-OH to the protons at δ_H 4.11 (4-OMe) and from H-10 to the protons at δ_H 4.03 (9-OMe) supported the positions of methoxy groups at C-4 and C-9, respectively (**Figure 27**). The 2-OH proton showed NOESY correlations with H-1 and H-3.

The results from comparison of the above NMR data with reported values (Leong *et al.*, 1997) indicated that compound DD5 was 4,9-dimethoxy-2,5-phenanthrenediol [**105**]. It was also previously isolated from *D. nobile* (Zhang *et al*., 2008b) and *D. palpebrae* (Kyokong *et al*., 2019).



4,9-dimethoxy-2,5-phenanthrenediol [**105**]

Table 10 NMR spectral data of compound DD5 and 4,9-dimethoxy-2,5-phenanthrenediol

Position	**DD5 (acetone-d_6)**		**4,9-dimethoxy-2,5-phenanthrenediol ($CDCl_3$)**	
	δ_H (mult., J in Hz)	**δ_C**	**δ_H (mult., J in Hz)**	**δ_C**
1	6.99 (1H, d, 2.5)	106.9	6.88 (1H, d, 2.6)	106.3
2	-	157.5	-	154.3
3	6.81 (1H, d, 2.5)	100.3	6.69 (1H, d,2.6)	99.4
4	-	156.3	-	155.4
4a	-	110.0	-	110.5
4b	-	120.9	-	119.9
5	-	155.2	-	153.8
6	7.12 (1H, dd, 1.5, 7.5)	117.6	7.25 (1H, dd, 1.5, 7.9)	117.3
7	7.43 (1H, t, 7.5)	127.9	7.5 (1H, t, 7.9)	126.9
8	7.85 (1H, dd, 1.5, 8.0)	114.3	7.94 (1H, dd, 1.5, 7.9)	114.1
8a	-	129.2	-	128.5
9	-	154.9	-	154.6
10	6.92 (1H, s)	102.8	6.73 (1H, s)	101.5
10a	-	137.9	-	136.8
4-OMe	4.11 (3H, s)	58.5	4.06 (3H, s)	58.3
9-OMe	4.03 (3H, s)	55.9	4.04 (3H, s)	55.5
2-OH	8.82 (1H, s)	-	-	-
5-OH	9.43 (1H, s)	-	-	-

(Leong *et al.*, 1997)

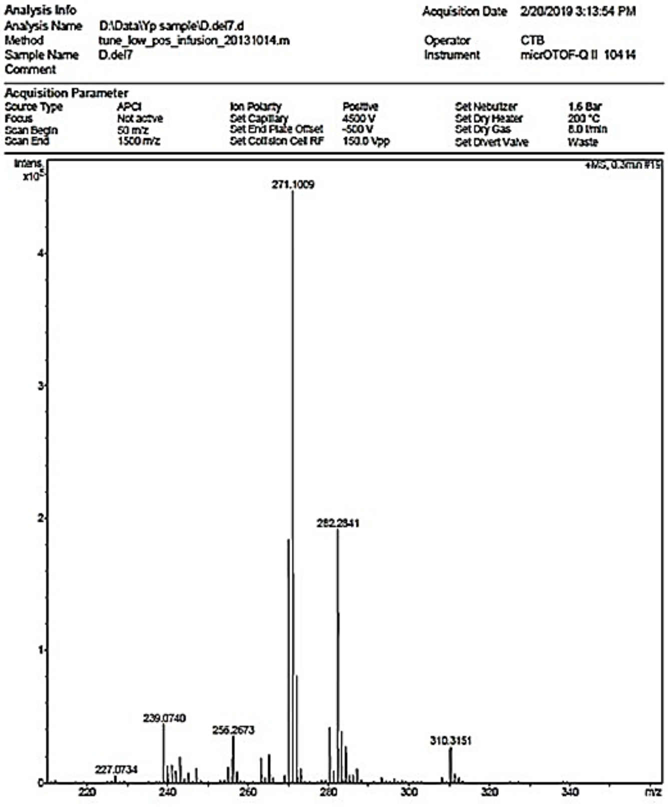


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Figure 24 Mass spectrum of compound DD5

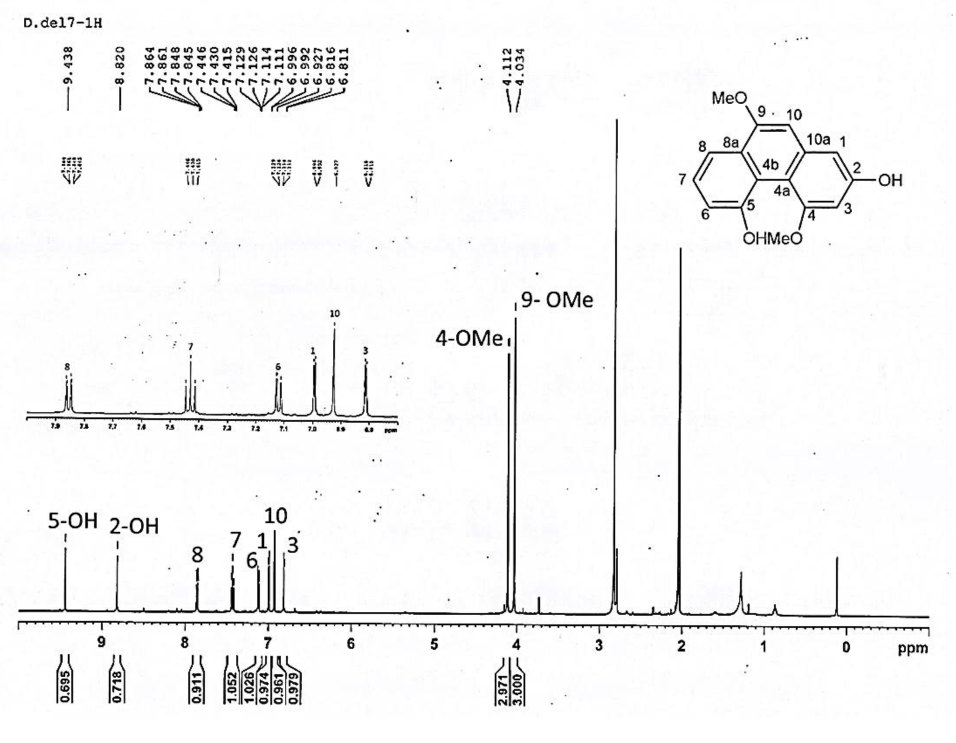


Figure 25 ^{1}H-NMR (500 MHz) spectrum of compound DD5

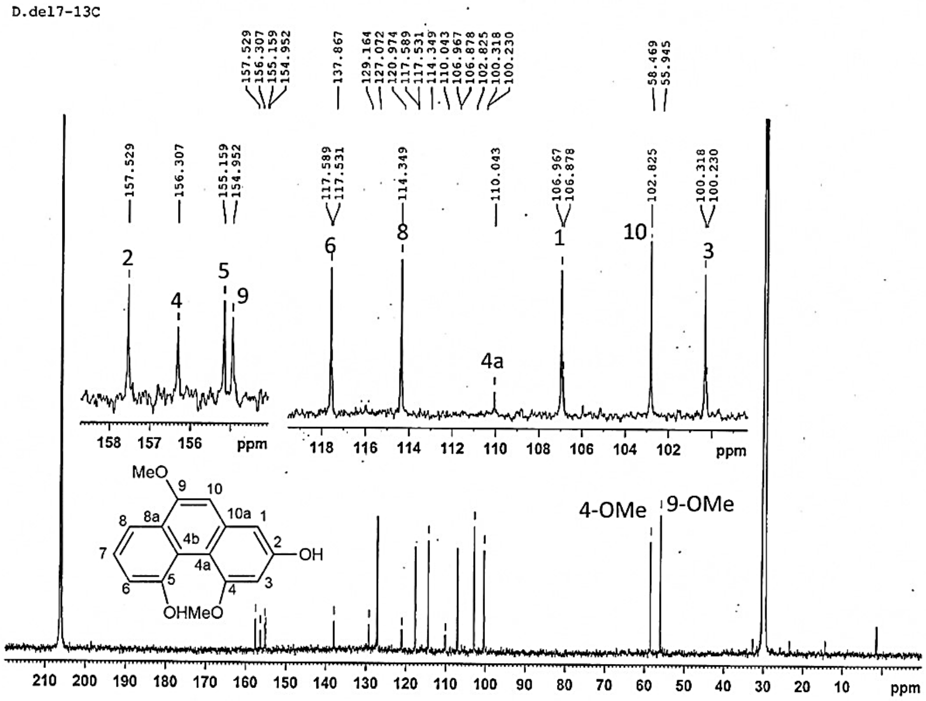


Figure 26 ^{13}C-NMR (125 MHz) spectrum of compound DD5

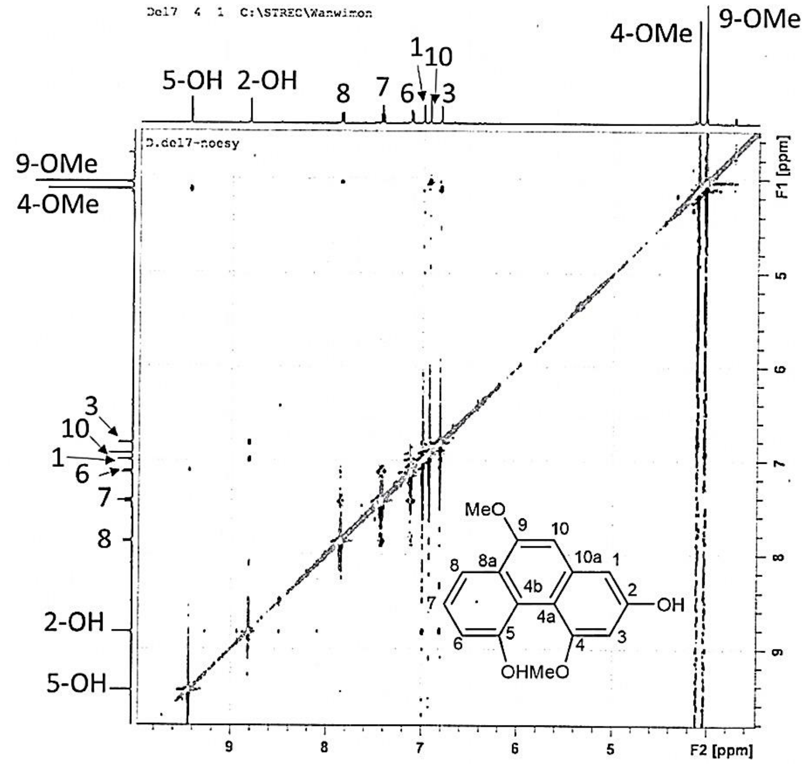


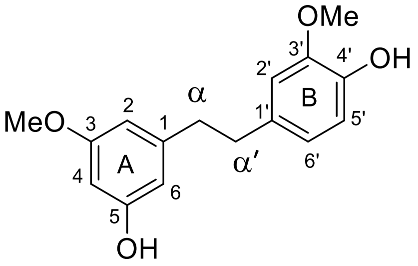
Figure 27 NOESY spectrum of compound DD5

2.1.6 Identification of compound DD6 (gigantol)

Compound DD6 was obtained as a brown amorphous solid. The HR-ESI mass spectrum (**Figure 28**) showed a sodium adduct molecular ion $[M+Na]^+$ at *m/z* 297.1102, (calculated for $C_{16}H_{18}O_4Na$; 297.1102), suggesting the molecular formula $C_{16}H_{18}O_4$. The ^{1}H-NMR spectrum (**Figure 29 and Table 11**) exhibited signals for two methoxy groups at δ_H 3.69 (3H, s, 3-OMe) and 3.77 (3H, s, 3′-OMe), two pairs of methylene protons at δ_H 2.79 (4H, m, H_2-α, H_2-α'), and two sets of aromatic protons. The first set appeared at δ_H 6.79 (1H, br t, *J* = 1.5 Hz, H-2), 6.25 (1H, t, *J* = 1.5 Hz, H-4), and 6.29 (1H, br dd, *J* = 1.5, 1.5 Hz, H-6), representing the protons on the A ring (1,3,5-trisubstitution). The second set consisted of signals at δ_H 6.79 (1H, d, *J* = 2.0 Hz, H-2′), 6.73 (1H, d, *J* = 8.0 Hz, H-5′), and 6.65 (1H, dd, *J* = 8.0, 2.0 Hz, H-6′), due to the B ring protons (1′,3′,4′-trisubstitution).

The ^{13}C-NMR spectrum (**Figure 30 and Table 11**) showed two methylene carbons at δ_C 38.9 (C- α) and 37.9 (C- α'); two methoxy carbons at δ_C 56.1 (3-OMe) and 55.2 (3′-OMe); six quaternary carbons at δ_C 145.4 (C-1), 159.2 (C-3), 161.8 (C-5), 134.1 (C-1′), 147.9 (C-3′), and 145.1 (C-4′); and six methine carbons at δ_C 108.9 (C-2), 99.7 (C-4), 106.3 (C-6), 115.5 (C-2′), 112.8 (C-5′), and 121.5 (C-6′).

The above NMR spectra of DD6 were in accordance with those reported for gigantol (Chen, Xu*, et al.*, 2008). Thus, compound DD6 was identified as gigantol [**2**]. It was frequently found in *Dendrobium* species, for example, *D. aphyllum* (Chen *et al*., 2008c), *D. brymerianum* (Klongkumnuankarn *et al.*, 2015), *D. officinale* (Zhao *et al*., 2018), and *D. palpebrae* (Kyokong *et al*., 2019).



gigantol [**2**]

Table 11 NMR spectral data of compound DD6 and gigantol

Position	DD6 (acetone-d_6)		Gigantol (acetone-d_6)	
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
1	-	145.4	-	144.5
2	6.79 (1H, br t, 1.5)	108.9	6.33 (1H, dd, 2.0, 2.0)	107.9
3	-	159.2	-	158.2
4	6.25 (1H, t, 1.5)	99.7	6.26 (1H, dd, 2.0, 2.0)	98.7
5	-	161.8	-	160.8
6	6.29 (1H, br dd, 1.5, 1.5)	106.3	6.30 (1H, dd, 2.0, 2.0)	105.3
α	2.79 (2H, m)	38.9	2.79 (2H, s)	37.9
α′	2.79 (2H, m)	37.9	2.78 (2H, s)	36.9
1′	-	134.1	-	133.1
2′	6.79 (1H, d, 2.0)	115.5	6.80 (1H, d, 2.0)	114.6
3′	-	147.9	-	147.0
4′	-	145.1	-	144.2
5′	6.73 (1H, d, 8.0)	112.8	6.74 (1H, d, 8.0)	111.9
6′	6.65 (1H, dd, 8.0, 2.0)	121.5	6.66 (1H, dd, 8.0, 2.0)	120.6
3′OMe	3.78 (3H, s)	55.2	3.78 (3H, s)	54.3
3-OMe	3.69 (3H, s)	56.1	3.69 (3H, s)	55.2

(Chen, Xu*, et al.*, 2008)

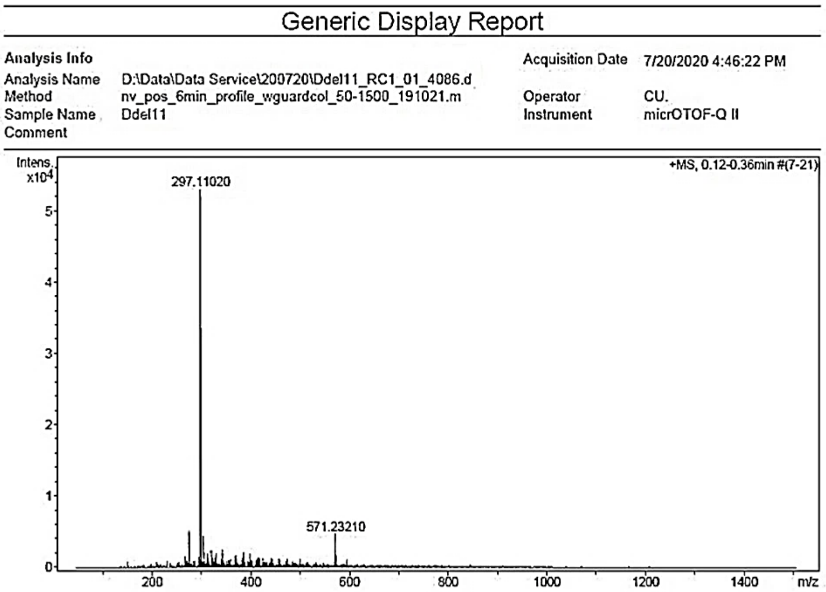


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Figure 28 Mass spectrum of compound DD6

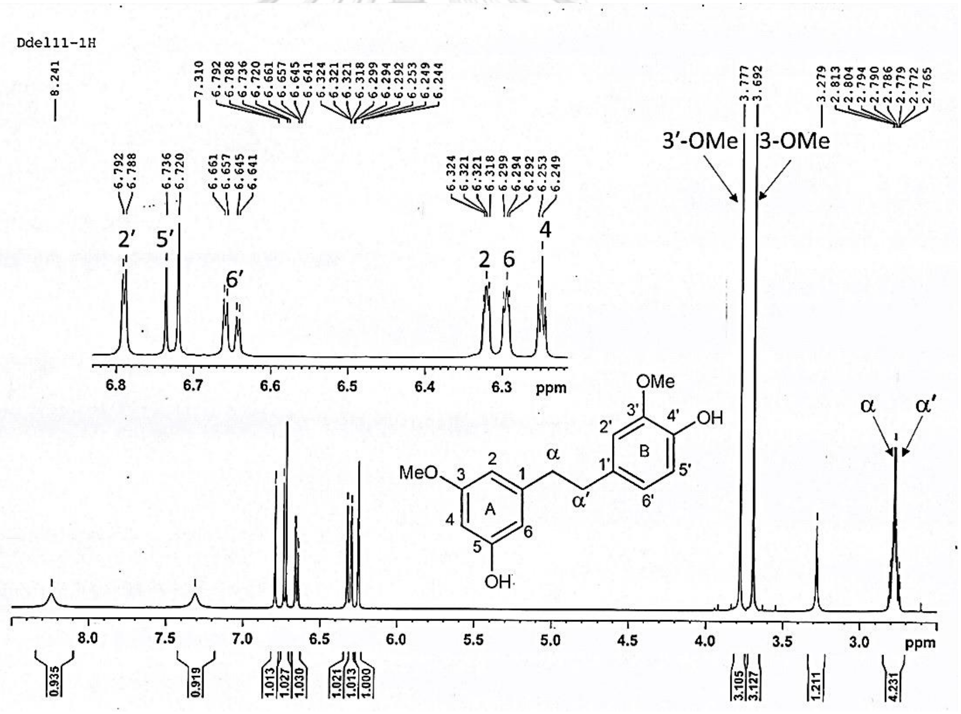


Figure 29 ^{1}H-NMR (500 MHz) spectrum of compound DD6

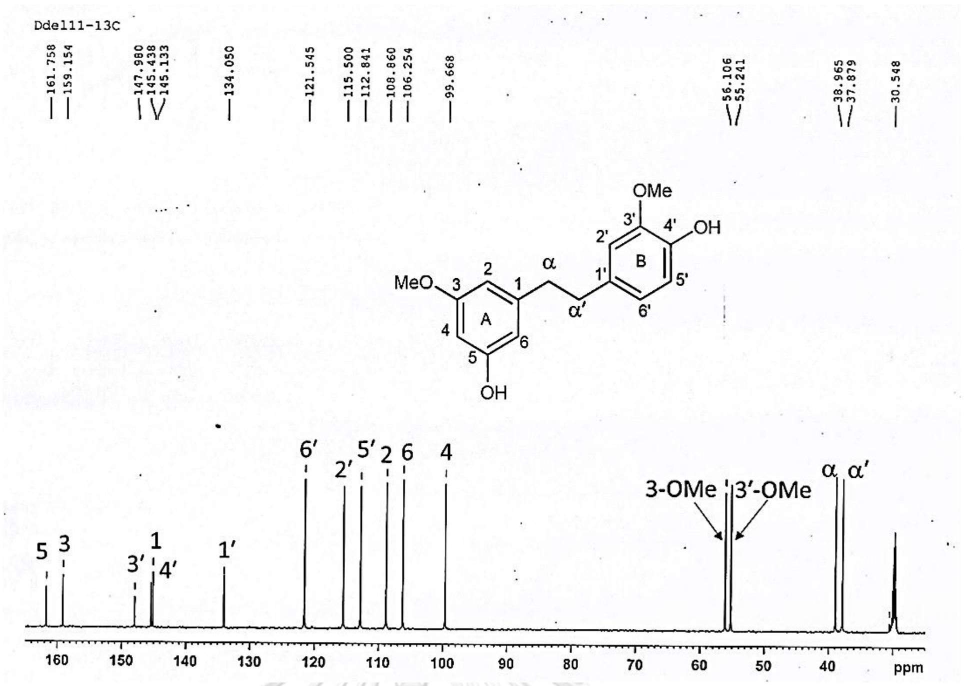
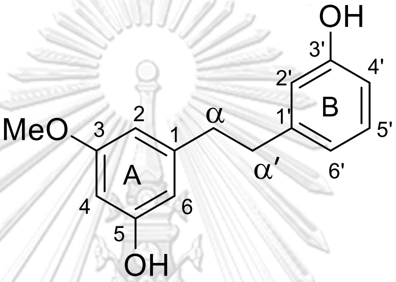


Figure 30 ^{13}C-NMR (125 MHz) spectrum of compound DD6

2.1.7 Identification of compound DD7 (batatasin III)

Compound DD7 was obtained as a brown amorphous solid. The HR-ESI mass spectrum (**Figure 31**) showed a sodium adduct molecular ion $[M+Na]^+$ at *m/z* 267.10556, (calculated for $C_{15}H_{16}O_3Na$; 267.099715), suggesting the molecular formula $C_{15}H_{16}O_3$. The ^{1}H-NMR spectrum (**Figure 32 and Table 12**) showed resonances for four methylene protons at δ_H 2.79 (4H, m, H_2-α and H_2-α'). In addition, seven aromatic proton resonances appeared as two separate coupling systems: (a) δ_H 6.30 (1H, br t, *J* = 2.0 Hz, H-2), 6.23 (1H, t, *J* = 2.0 Hz, H-4), and 6.32 (1H, br t, *J* = 2.0 Hz, H-6) for 1,3,5-trisubstituted ring A; (b) δ_H 6.71 (1H, br d, *J* = 2.4 Hz, H-2′), 6.63 (1H, m, H-4′), 7.07 (1H, t, *J* = 8.0 Hz, H-5′), and 6.69 (1H, br d, *J* = 9.0 Hz, H-6′) for 1′,3′-disubstituted ring B.

The ^{13}C-NMR spectrum (**Figure 33 and Table 12**) showed two methylene carbons [δ_C 38.5 (C-α) and 38.2 (C-α')], a methoxy carbon [δ_C 55.2 (3-OMe)], five quaternary carbons [δ_C 145.0 (C-1), 159.2 (C-3), 161.8 (C-5), 144.3 (C-1′), and 158.2 (C-3′)], and seven aromatic methine carbons [δ_C 106.2 (C-2), 99.8 (C-4), 108.8 (C-6), 116.2 (C-2′), 113.6 (C-4′), 130.0 (C-5′), and 120.4 (C-6′)]. By comparison of these spectral data with the literature values of batatasin III (Yang *et al.*, 2018), compound DD6 was identified as batatasin III [**3**]. It was also earlier reported from some other species of *Dendrobium*, such as *D. infundibulum* (Na Ranong*, et al.,* 2019), *D. scabrilingue* (Sarakulwattana*, et al.,* 2020) and *D. christyanum* (San*, et al.,* 2020).



batatasin III [**3**]

Table 12 NMR spectral data of compound DD7 and batatasin III

Position	DD7 (acetone-d_6)		Batatasin III (CD_3OD)	
	δ_H (mult., J in Hz)	δ_C	δ_H (mult., J in Hz)	δ_C
1	-	145.0	-	144.1
2	6.3 (1H, br t, 2.0)	106.2	6.24 (1H, dd, 2.0, 2.2)	107.6
3	-	159.2	-	158.0
4	6.23 (1H, t, 2.0)	99.8	6.20 (1H, dd, 2.0, 2.2)	98.5
5	-	161.8	-	160.8
6	6.32 (1H, br t, 2.0)	108.8	6.24 (1H, dd, 2.0, 2.2)	105.6
α	2.79 (2H, m)	38.5	2.79 (2H, m)	37.5
α'	2.79 (2H, m)	38.2	2.79 (2H, m)	37.8
1′	-	144.3	-	143.3
2′	6.71 (1H, br d, 2.4)	116.2	6.63 (1H, m)	115.0
3′	-	158.2	-	156.9
4′	6.63 (1H, m)	113.6	6.63 (1H, m)	112.4
5′	7.07 (1H, t, 8.0)	130.0	7.08 (1H, dd, 7.5, 8.0)	128.9
6′	6.69 (1H, br d, 9)	120.4	6.63 (1H, m)	119.5
3- OMe	3.70 (3H, s)	55.2	3.70 (3H, s)	54.1

(Yang *et al.*, 2018)

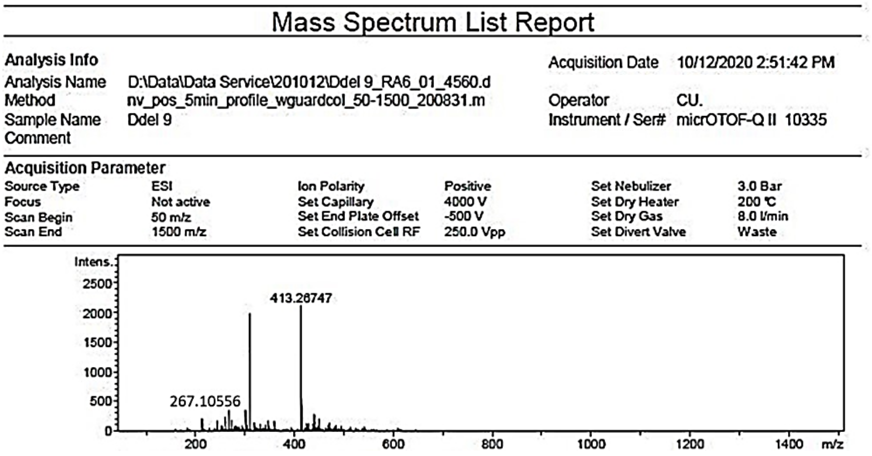


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Figure 31 Mass spectrum of compound DD7

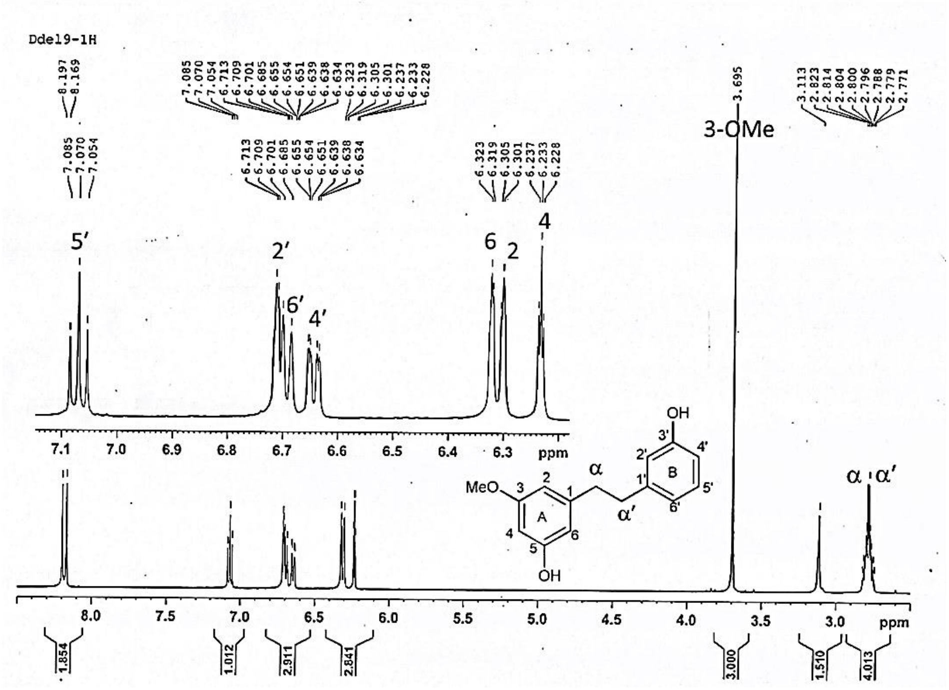


Figure 32 ^{1}H-NMR (500 MHz) spectrum of compound DD7

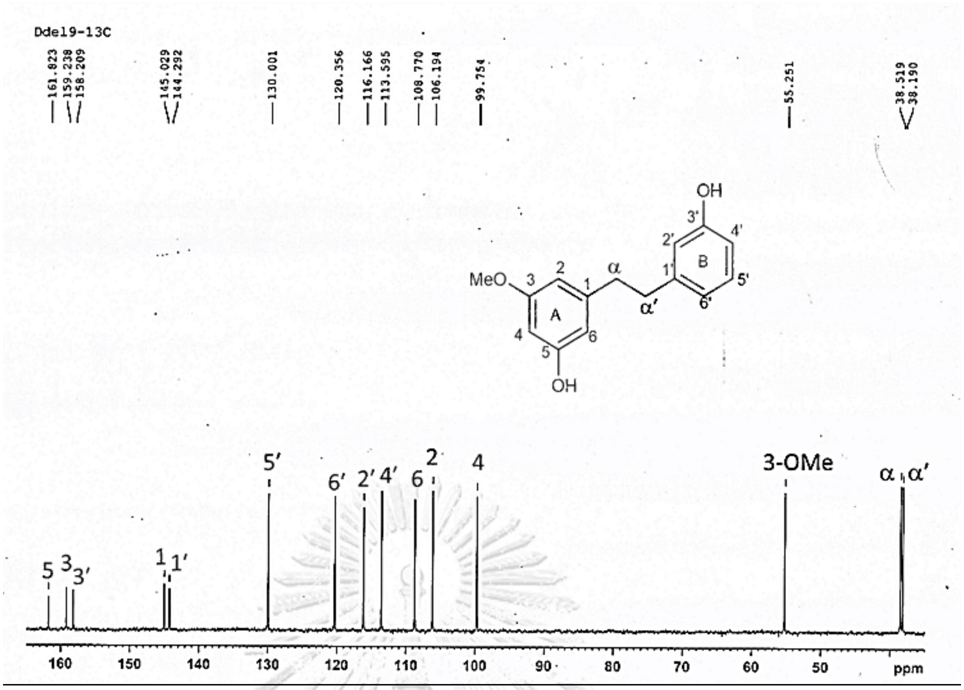
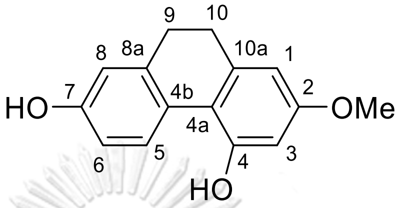


Figure 33 ^{13}C-NMR (125 MHz) spectrum of compound DD7

2.1.8 Identification of compound DD8 (lusianthridin)

Compound DD8 was obtained as a brown amorphous solid. The HR-ESI mass spectrum (**Figure 34**) showed a sodium adduct molecular ion $[M+Na]^+$ at *m/z* 265.08251, (calculated for $C_{15}H_{14}O_3Na$; 265.084065), suggesting the molecular formula $C_{15}H_{14}O_3$. The ^{1}H-NMR spectrum of DD8 (**Figure 35 and Table 13**) exhibited signals for five aromatic protons [δ_H 6.37 (1H, d, J = 2.5 Hz, H-1), 6.45 (1H, d, J = 2.5 Hz, H-3), 8.24 (1H, br s, H-5), 6.73 (1H, br d, J = 2.7 Hz, H-6), and 6.73 (1H, d, J = 2.7 Hz, H-8)] and four methylene protons [δ_H 2.67 (4H, m, H_2-9, and -10)], indicating a dihydrophenanthrene skeleton. The ^{1}H-NMR spectrum also showed a resonance for a methoxy group at δ_H 3.72 (3H, s, 2-OMe).

The ^{13}C-NMR spectrum of DD8 (**Figure 36 and Table 13**) revealed fifteen carbon signals, including a methoxy carbon [δ_C 55.2 (2-OMe)], five aromatic methine carbons [δ_C 105.8 (C-1), 101.5 (C-3), 129.8 (C-5), 113.4 (C-6), and 115.0 (C-8)], and seven quaternary carbon signals [δ_C 159.1 (C-2), 155.7 (C-4), 115.7 (C-4a), 125.8 (C-4b), 155.8 (C-7), 139.7 (C-8a), and 141.3 (C-10a)]. By comparing the above ^{1}H- and ^{13}C-NMR data with previously reported values for lusianthridin from *Pholidota yunnanensis* (Guo *et al.*, 2007), compound DD8 was identified as lusianthridin [**97**]. This compound was also reported from several other *Dendrobium* species, such as *D. plicatile* (Yamaki & Honda, 1996) and *D. scabrilingue* (Sarakulwattana, 2020).



lusianthridin [**97**]

Table 13 NMR spectral data of compound DD8 and lusianthridin

Position	DD8 (acetone-d_6)		Lusianthridin (acetone-d_6)	
	δ_H (mult., J in Hz)	δ_C	δ_H (mult., J in Hz)	δ_C
1	6.37 (1H, d, 2.5)	105.8	6.37 (1H, d, 2.6)	106.0
2	-	159.1	-	159.3
3	6.45 (1H, d, 2.5)	101.5	6.44 (1H, d, 2.6)	101.6
4	-	155.7	-	155.9
4a	-	115.7	-	115.9
4b	-	125.8	-	125.9
5	8.25 (1H, d, 7)	129.8	8.22 (1H, d, 7.5)	129.9
6	6.73 (1H, dd, 2.5, 7.5)	113.4	6.68 (1H, dd, 2.7, 7.5)	113.5
7	-	155.8	-	156.1
8	6.72 (1H, br s)	115.0	6.69 (1H, m)	115.0
8a	-	139.7	-	139.8
9	2.67 (2H, m)	30.6	2.67 (2H, m)	30.8
10	2.67 (2H, m)	31.3	2.67 (2H, m)	31.5
10a	-	141.3	-	141.4
2-OMe	3.72 (3H, s)	55.2	3.74 (3H, s)	55.3

(Guo *et al.*, 2007)

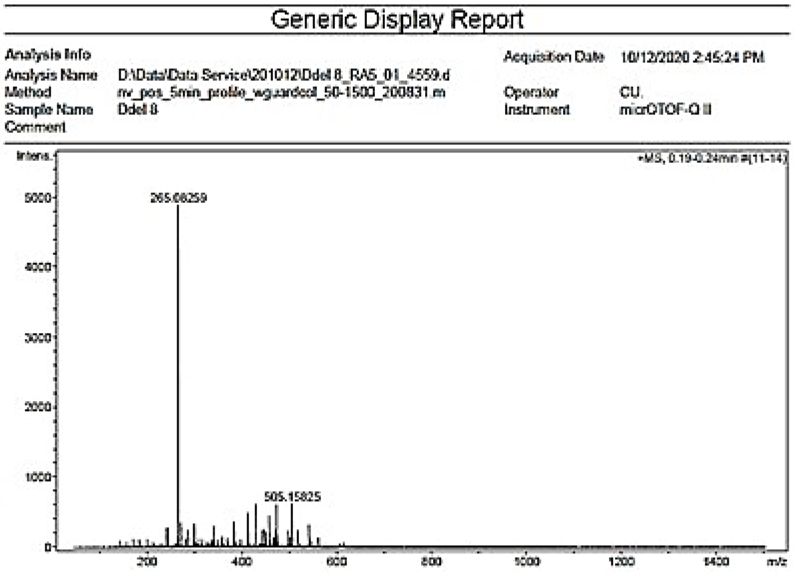


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Figure 34 Mass spectrum of compound DD8

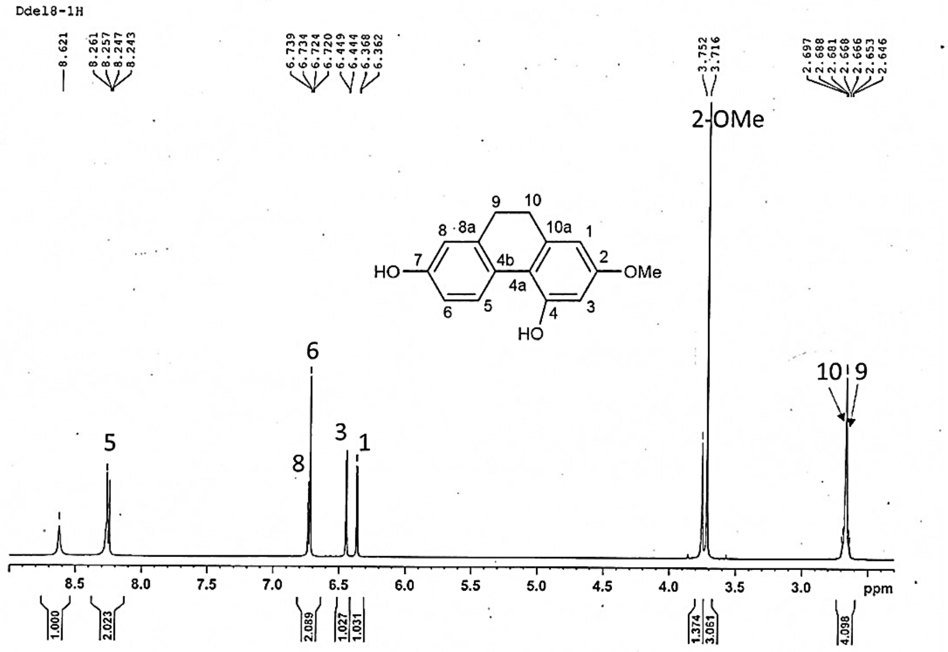


Figure 35 ^{1}H-NMR (500 MHz) spectrum of compound DD8

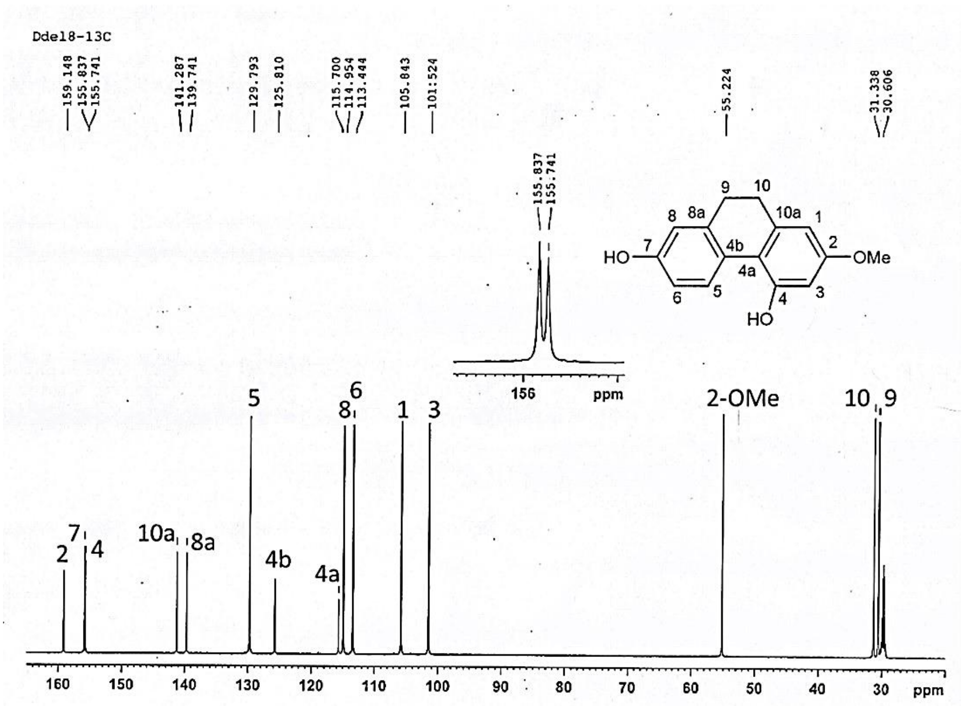


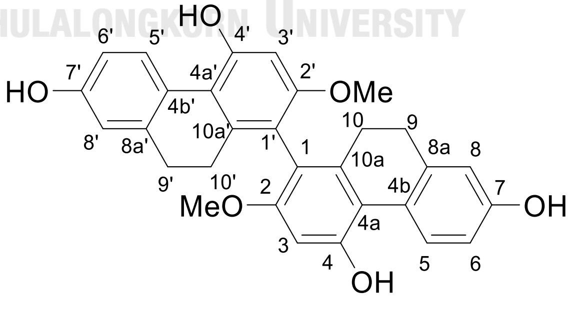
Figure 36 ^{13}C-NMR (125 MHz) spectrum of compound DD8

2.1.9 Identification of compound DD9 (4,4′,7,7′-tetrahydroxy-2,2′-dimethoxy-9,9′,10,10′-tetrahydro-1,1′-biphenanthrene)

Compound DD9 was obtained as a yellow amorphous powder. The HR-ESI mass spectrum (**Figure 37**) showed a sodium adduct molecular ion $[M+Na]^+$ at *m/z* 505.1630, (calculated for $C_{30}H_{26}O_6Na$; 505.1627), suggesting the molecular formula $C_{30}H_{26}O_6$. The ^{1}H and ^{13}C NMR spectra (**Table 14**) suggested that DD9 was a dimeric compound consisting of two identical units of a 9,10-dihydrophenanthrene. The ^{1}H-NMR spectrum (**Figure 38**) indicated the presence of four pairs of methylene protons [δ_H 2.51 (4H, m, H_2-9, H_2-9′) and 2.31 (4H, m, H_2-10, H_2-10′)], six protons for two methoxy groups [δ_H 3.60 (6H, s, 2-OMe and 2′-OMe)], two uncoupled aromatic protons [δ_H 6.57 (2H, s, H-3 and H-3′)], four hydroxy protons [δ_H 8.41 (2H, s, 4-OH and 4′-OH) and 8.08 (2H, s, 7-OH and 7′-OH)] and two sets of three aromatic protons with an ABM coupling pattern [δ_H 6.69 (2H, dd, *J*= 8.4, 2.4 Hz, H-6 and H-6′), 8.25 (2H, d, *J*= 8.4 Hz, H-5 and H-5′), and δ_H 6.65 (2H, d, *J*= 2.4 Hz, H-8 and H-8′)]. The methoxy groups were placed at C-2- and C-2′ based on the NOESY correlations from the methoxy protons with H-3 and H-3′(**Figure 39**). The NOESY spectrum also showed the correlations of 4-OH/4′-OH protons to H-3/H-3′ and 7-OH/7′-OH protons to H-6/H-6′.

The ^{13}C-NMR and HSQC spectra of DD9 (**Figures 40 and 41**) showed thirty signals representing four methylene carbons, two methoxy carbons and twenty-four aromatic carbons. The NMR assignments of protons and carbons were obtained through analysis of the HSQC, and HMBC and NOESY spectra (**Figures 41, 42, and 39**).

The ^{1}H and ^{13}C NMR spectra of DD9 were similar to those of DD8 (lusianthridin), suggesting its structure as a dimeric lusianthridin. The two units should be linked through a C-C bond between C-1 and C-1′, as supported by the HMBC correlations from C-1/C-1′ to H-3/H-3′ and H-10/H-10′ (Liu *et al.*, 2016). From the above data and through comparison of the NMR spectral data of DD9 with literature values (Guo *et al.*, 2007), compound DD9 was identified as 4,4′,7,7′-tetrahydroxy-2,2′-dimethoxy-9,9′,10,10′-tetrahydro-1,1′-biphenanthrene [**154**]. It was previously reported from *Pholidota yunnanensis* (Guo *et al.*, 2007) and *Dendrobium plicatile* (Yamaki & Honda, 1996).

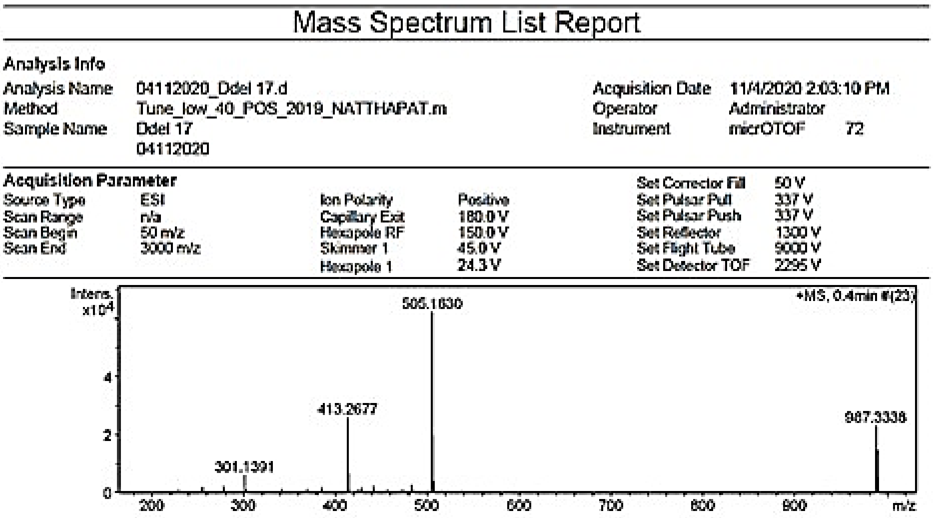


4,4′,7,7′-Tetrahydroxy-2,2′-dimethoxy-9,9′,10,10′-tetrahydro-1,1′-biphenanthrene [**154**]

Table 14 NMR spectral data of compound DD9 and 4,4′,7,7′-tetrahydroxy-2,2′-dimethoxy-9,9′,10,10′-tetrahydro-1,1′-biphenanthrene

Position	**DD9 (acetone-d_6)**		**4,4′,7,7′-Tetrahydroxy-2,2′-dimethoxy-9,9′,10,10′-tetrahydro-1,1′-biphenanthrene (acetone-d_6)**	
	δ_H (mult., *J* in Hz)	**δ_C**	**δ_H (mult., *J* in Hz)**	**δ_C**
1,1′	-	116.5	-	117.4
2,2′	-	156.4	-	157.4
3,3′	6.57 (2H, s)	98.3	6.58 (2H, s)	99.2
4,4′	-	154.0	-	154.9
4a,4a′	-	114.6	-	115.5
4b,4b′	-	125.5	-	126.5
5,5′	8.25 (2H, d, 8.4)	129.3	8.27 (2H, d, 8.6)	130.2
6,6′	6.69 (2H, dd, 8.4, 2.4)	112.5	6.7 (2H, d, 2.7)	113.4
7,7′	-	155.1	-	156.0
8,8′	6.65 (2H, d, 2.4)	113.8	6.66 (2H, d, 2.7)	114.7
8a,8a′	-	139.3	-	140.2
9,9′	2.51 (4H, m)	29.7	2.53 (4H, m)	30.6
10,10′	2.31 (4H, m)	27.0	2.33 (4H, m)	27.9
10a,10a′	-	139.7	-	140.6
2-OMe, 2′-OMe	3.60 (6H, s)	54.7	3.61 (6H, s)	55.6
4-OH, 4′-OH	8.41 (2H, s)	-	-	-
7-OH, 7′-OH	8.08 (2H, s)	-	-	-

(Guo *et al.*, 2007)



Mass Spectrum List Report

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Acquisition Parameter

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Hexapole 1 24.3 V
Set Corrector Fill 50 V
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Figure 37 Mass spectrum of compound DD9

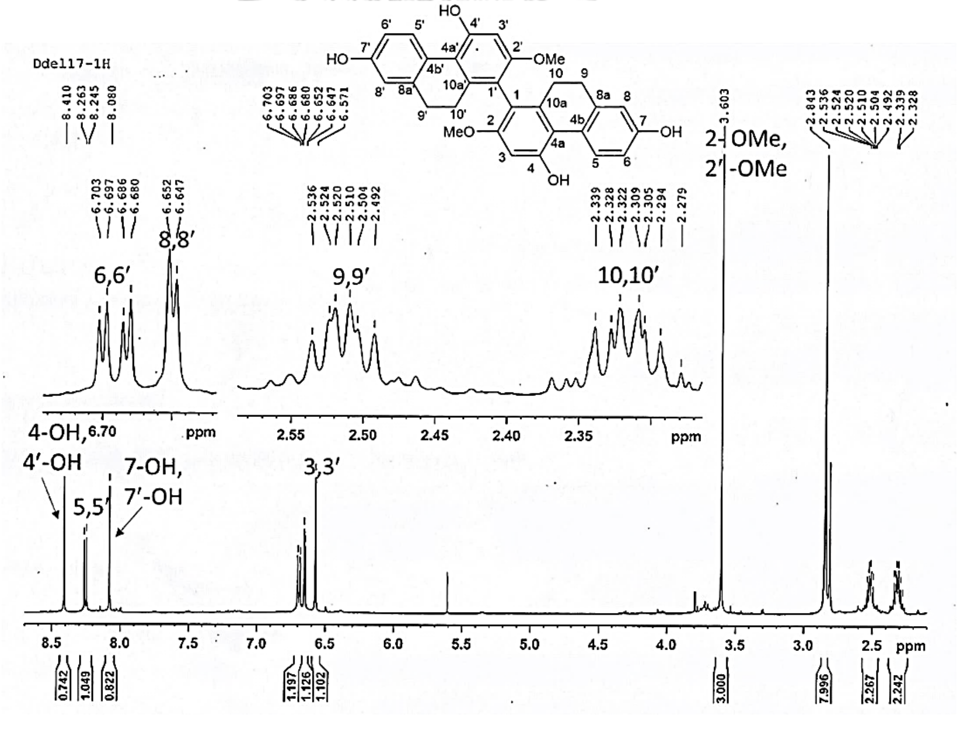


Figure 38 ^{1}H-NMR (300 MHz) spectrum of compound DD9

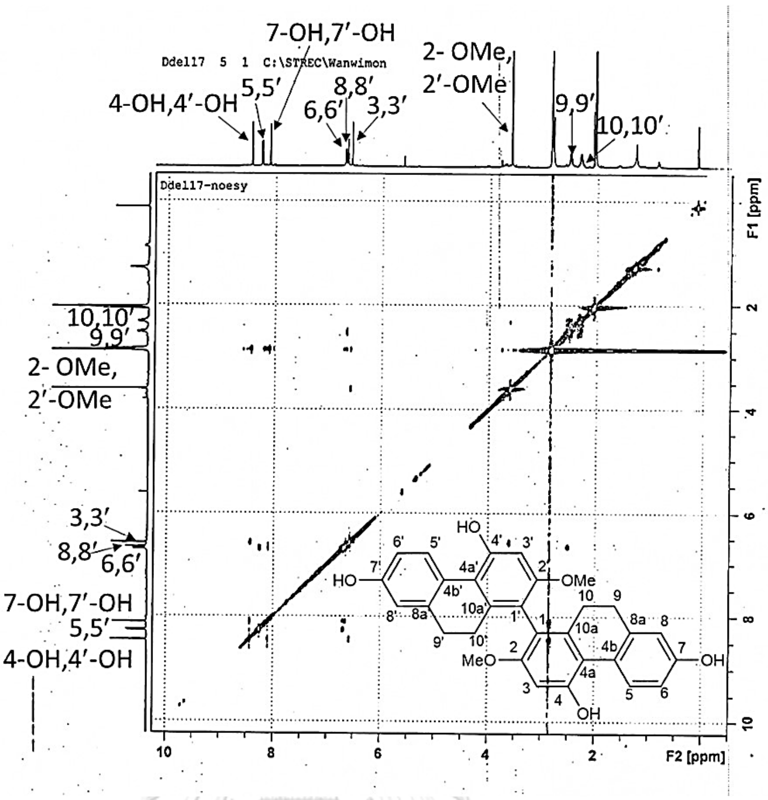


Figure 39 NOESY spectrum of compound DD9

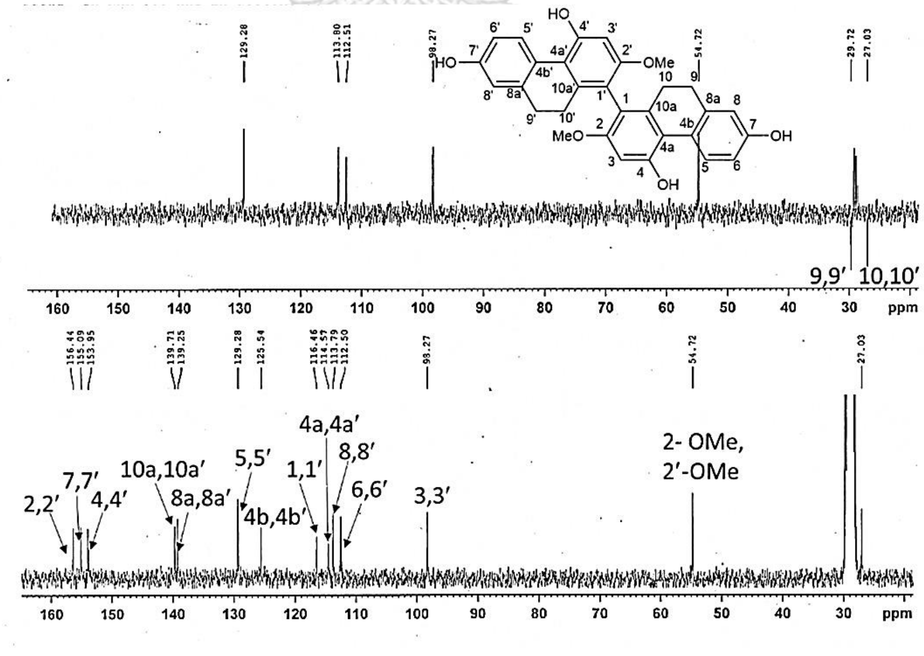


Figure 40 ^{13}C-NMR (75 MHz) spectrum of compound DD9

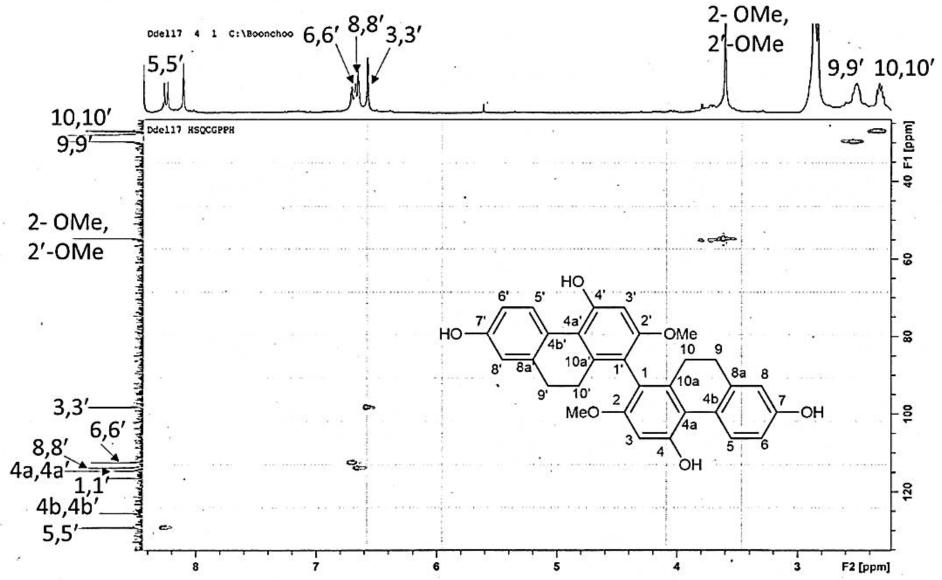


Figure 41 HSQC spectrum of compound DD9

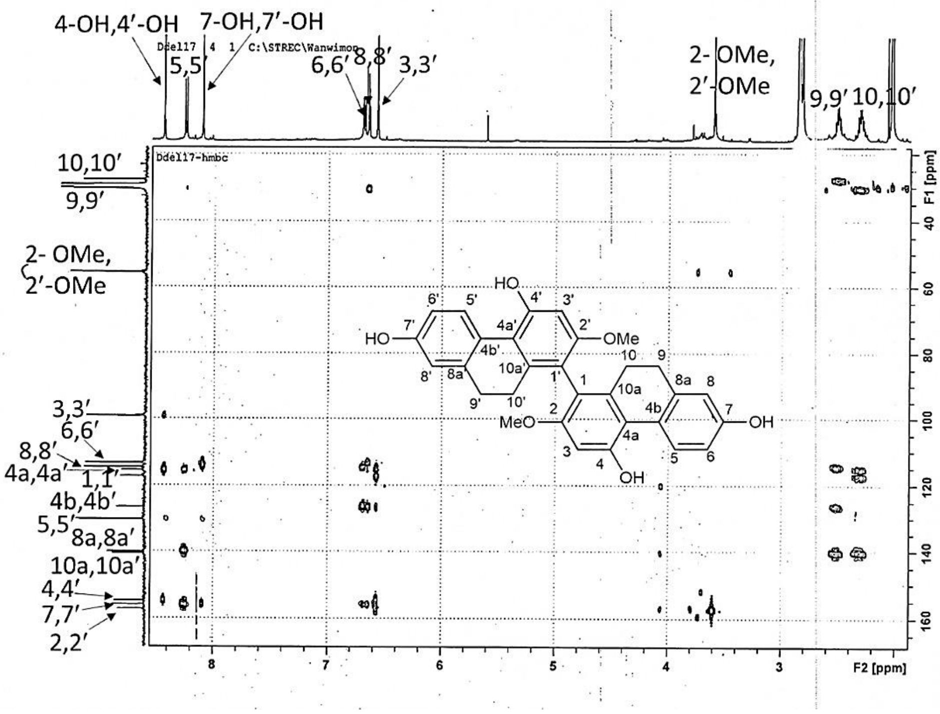


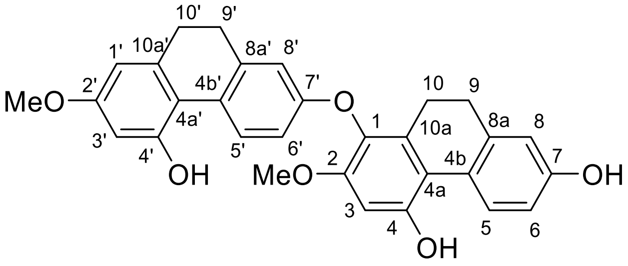
Figure 42 HMBC spectrum of compound DD9

2.1.10 Identification of compound DD10 (phoyunnanin E)

Compound DD10 was obtained as a brown amorphous powder. The HR-ESI mass spectrum (**Figure 43**) showed a sodium adduct molecular ion $[M+Na]^+$ at *m/z* 505.1628, (calculated for $C_{30}H_{26}O_6Na$; 505.1627), suggesting a molecular of $C_{30}H_{26}O_6$. The ^{1}H-NMR spectrum of DD10 (**Figures 44 and Table 15**) exhibited signals for four pairs of methylene protons [δ_H 2.6 (4H, m, H_2-9 and -10) and 2.67 (4H, m, H_2 -9′ and -10′], suggesting a dimeric dihydrophenanthrene structure. In addition to a ^{1}H NMR signal for an uncoupled aromatic proton [δ_H 6.66 (1H, s, H-3)], resonances for two sets of three aromatic protons with an ABM coupling patten were observed: (a) δ_H 8.27 (1H, d, *J*= 9.0 Hz, H-5), 6.71 (1H, dd, *J*= 9.0, 2.5 Hz, H-6), and 6.69 (1H, d, *J*= 2.5 Hz, H-8); (b) δ_H 8.25 (1H, d, *J*= 8.5 Hz, H-5′), 6.62 (1H, dd, *J*= 8.5, 2.5 Hz, H-6′), and 6.67 (1H, d, *J*= 2.5 Hz, H-8′). Besides, two methoxy groups [δ_H 3.71 (3H, s, 2-OMe) and 3.73 (3H, s, 2′-OMe)] were present and placed at C-2 and C-2′ because of the NOESY correlations from 2-OMe protons to H-3, and from 2′-OMe protons to H-1′ and H-3′(**Figure 45**).

The ^{13}C-NMR and HSQC spectra (**Figures 46 and 47 and Table 15**) of DD10 revealed signals for four methylene carbons, two methoxy carbons and twenty-four aromatic carbons. The signal of C-1 appeared as an aromatic quaternary carbon at a downfield position at δ_C 133.9. The HMBC correlations of DD10 (**Figure 48**) suggested that the two dihydrophenanthrene units were connected through an ether linkage at C-1 and C-7′.

By comparing these spectroscopic properties with previously reported values (Guo *et al.*, 2006), compound DD10 was identified as phoyunnanin E [**157**]. This dihydrophenanthrene dimer was previously reported from *Dendrobium venustum* (Sukphan *et al*., 2014).



phoyunnanin E [**157**]

Table 15 NMR spectral data of compound DD10 and phoyunnanin E

Position	DD10 (acetone-d_6)		Phoyunnanin E (acetone-d_6)	
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
1	-	133.9	-	133.9
2	-	152.0	-	152.0
3	6.66 (1H, s)	100.8	6.68 (1H, s)	100.8
4	-	152.5	-	152.6
4a	-	115.7	-	115.8
4b	-	125.6	-	125.6
5	8.27 (1H, d, 9.0)	130.2	8.29 (1H, d, 8.2)	130.2
6	6.71 (1H, dd, 9.0, 2.5)	113.6	6.72 (1H, dd, 8.2, 2.7)	113.6
7	-	156.4	-	156.4
8	6.69 (1H, d, 2.5)	115.0	6.7 (1H, d, 2.7)	115.0
8a	-	139.8	-	139.8
9	2.6 (2H, m)	30.7	2.62 (2H, m)	30.0
10	2.6 (2H, m)	23.8	2.62 (2H, m)	23.8
10a	-	134.0	-	134.0
1′	6.37 (1H, d, 2.5)	106.0	6.38 (1H, d, 2.5)	106.0
2′	-	159.6	-	159.6
3′	6.42 (1H, d, 2.5)	101.6	6.43 (1H, d, 2.5)	101.6
4′	-	156.1	-	156.1
4a′	-	115.5	-	115.5

Position	DD10 (acetone-d_6)		Phoyunnanin E (acetone-d_6)	
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
4b′	-	127.6	-	127.6
5′	8.25 (1H, d, 8.5)	129.8	8.26 (1H, d, 8.7)	129.8
6′	6.62 (1H, dd, 8.5, 2.5)	112.6	6.64 (1H, dd, 8.7, 2.8)	112.6
7′	-	157.7	-	157.7
8′	6.67 (1H, d, 2.5)	114.2	6.69 (1H, d, 2.8)	114.2
8a′	-	139.7	-	139.7
9′	2.67 (2H, m)	30.7	2.68 (2H, m)	30.7
10′	2.67 (2H, m)	31.3	2.68 (2H, m)	31.4
10a′	-	141.6	-	141.6
2-OMe	3.71 (3H, s)	56.0	3.72 (3H, s)	56.0
2′-OMe	3.73 (3H, s)	55.3	3.74 (3H, s)	55.3

(Guo *et al.*, 2006)

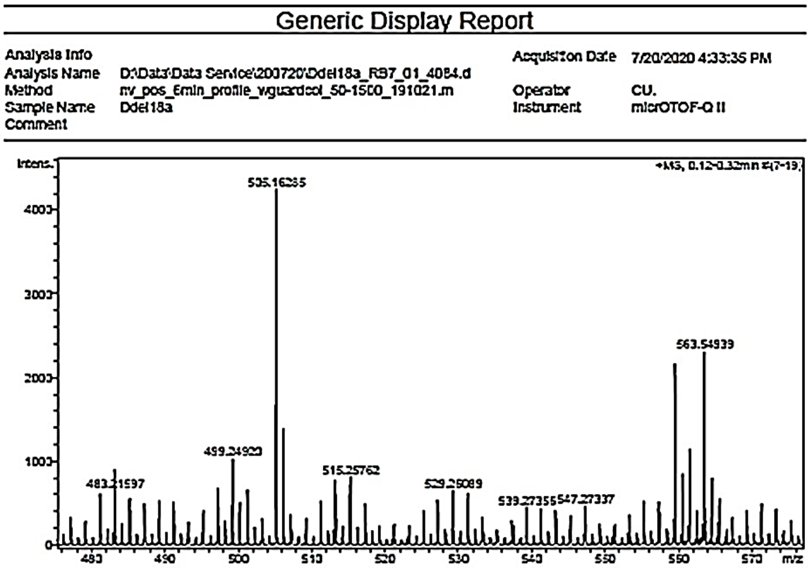


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Figure 43 Mass spectrum of compound DD10

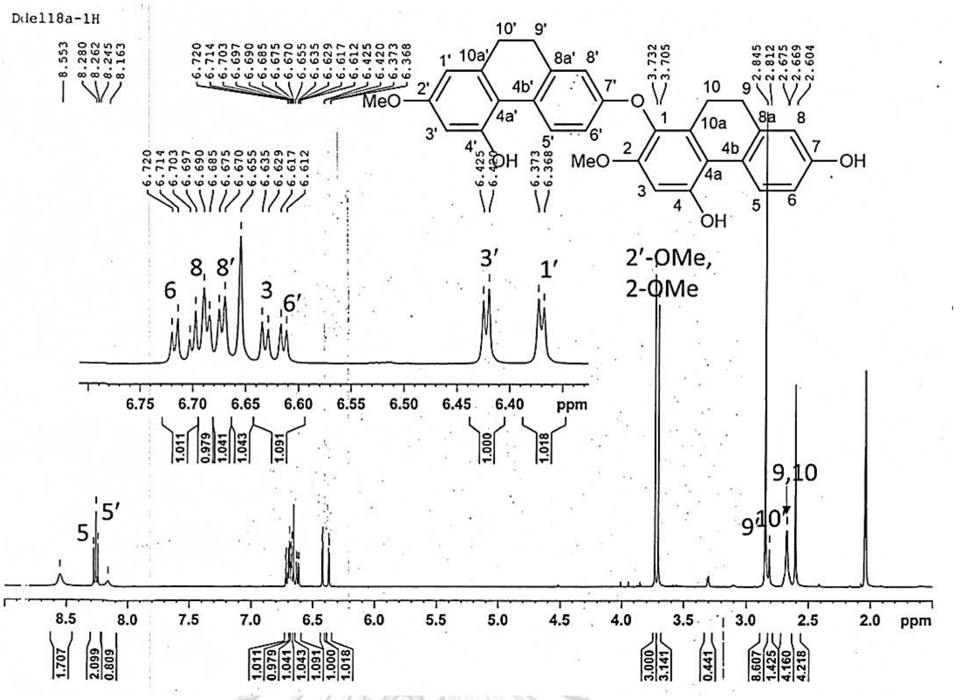


Figure 44 ^{1}H-NMR (500 MHz) spectrum of compound DD10

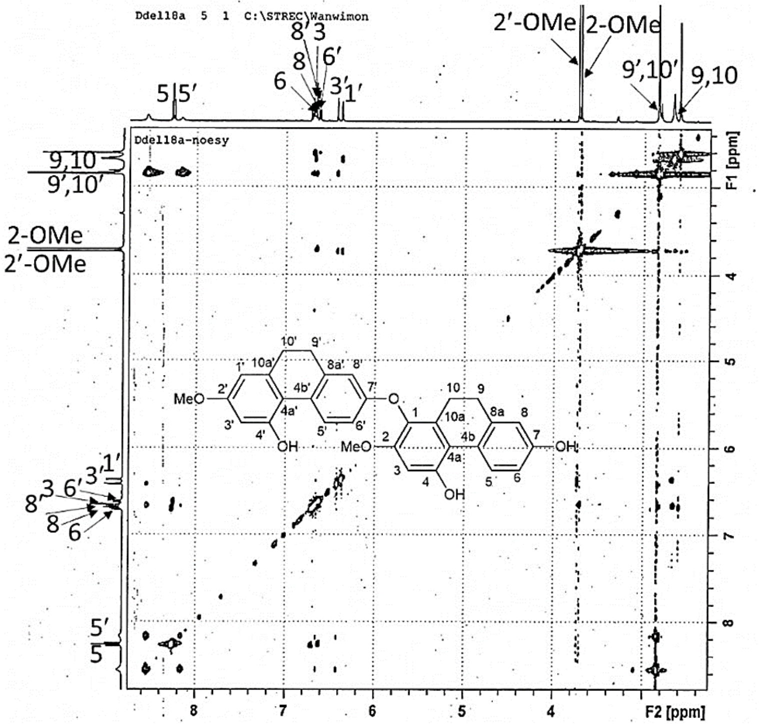


Figure 45 NOESY spectrum of compound DD10

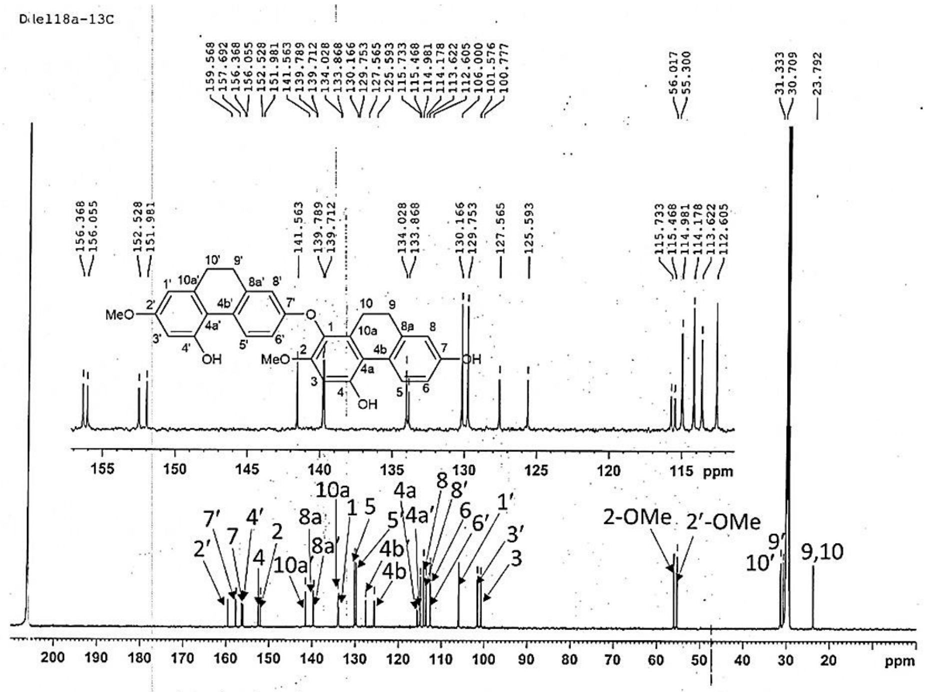


Figure 46 ^{13}C-NMR (125 MHz) spectrum of compound DD10

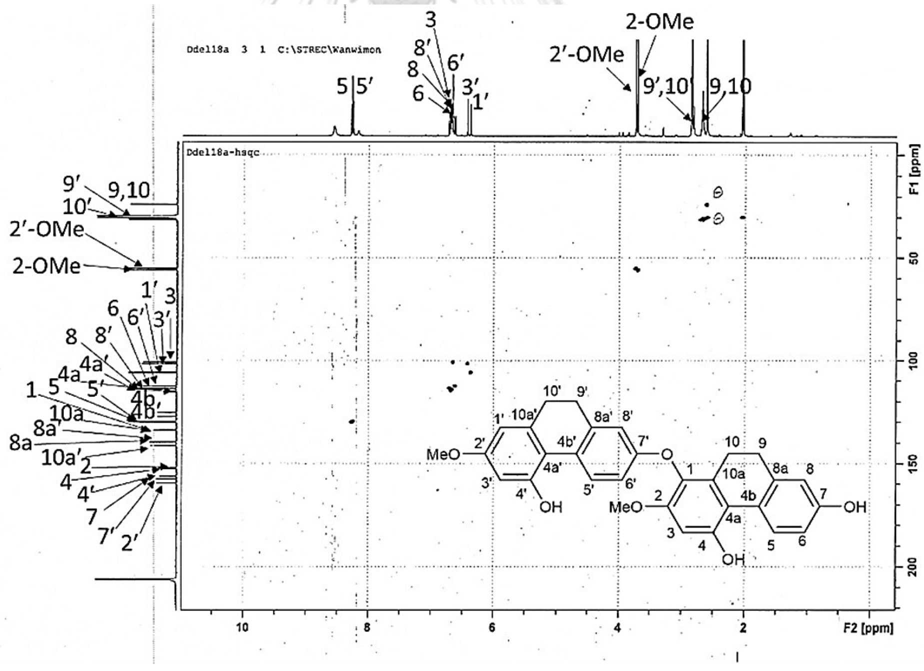


Figure 47 HSQC spectrum of compound DD10

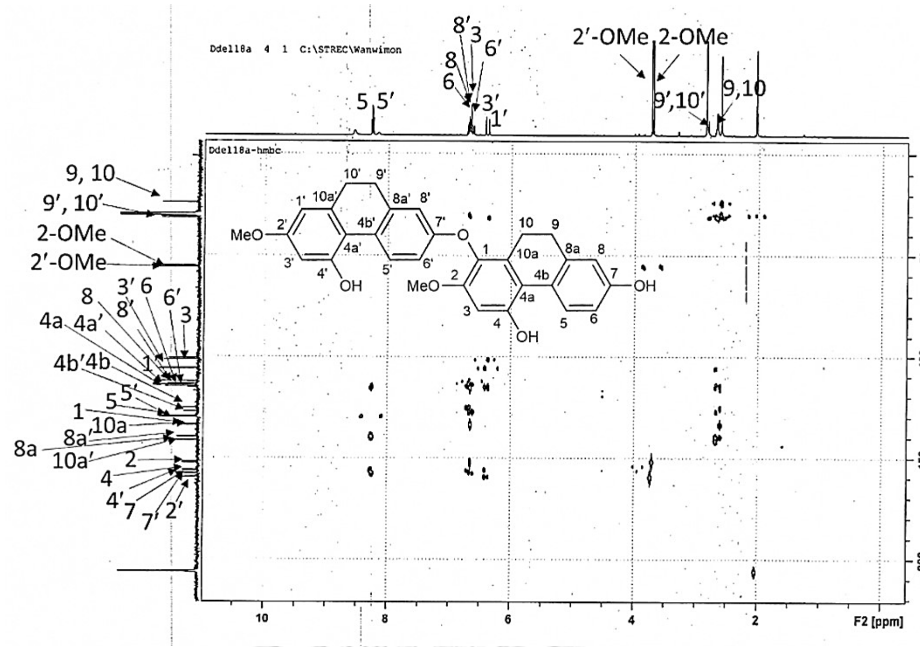


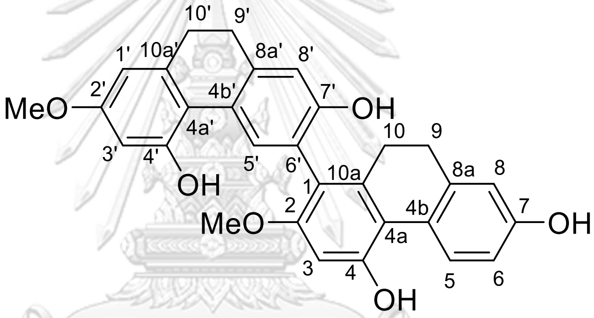
Figure 48 HMBC spectrum of compound DD10

2.1.11 Identification of compound DD11 (phoyunnanin C)

Compound DD11 was obtained as a brown amorphous powder. The HR-ESI mass spectrum (**Figure 49**) showed a sodium adduct molecular ion $[M+Na]^+$ at *m/z* 505.1635, (calculated for $C_{30}H_{26}O_6Na$; 505.1627), suggesting a molecular formula of $C_{30}H_{26}O_6$. The ^{1}H-NMR spectrum of DD11 (**Figure 50 and Table 16**) showed signals for two pairs of methylene protons [δ_H 2.53 (2H, m, H_2-9), 2.51 (2H, m, H_2-10) and 2.73 (2H, m, H_2-9′, H_2-10′)], two methoxy groups [δ_H 3.64 (3H, s, 2-OMe) and 3.72 (3H, s, 2′-OMe)], and eight aromatic protons [δ_H 6.57 (1H, s, H-3), 8.23 (1H, d, *J* = 8.4 Hz, H-5), 6.69 (1H, dd, *J* = 8.4, 2.7 Hz, H-6), 6.66 (1H, d, *J* = 2.7 Hz, H-8), 6.38 (2H, br s, H-1′, H-3′), 8.08 (1H, s, H-5′) and 6.76 (1H, s, H-8′)].

The ^{13}C-NMR and HSQC spectra (**Figures 51 and 52**) of DD11 showed signals for twenty-four aromatic carbons, four methylene carbons and two methoxy carbons. These NMR data suggested that the structure of DD11 consisted of two dihydrophenanthrene units, and this was further confirmed by the HMBC correlations (**Figure 53**). The position of the methoxy groups were deduced from the NOESY correlations between 2-OMe protons and H-3, and between 2′-OMe protons and H-1′ and H-3′(**Figure 54**).

Through comparison of NMR data of DD11 with DD8 (lusianthridin), compound DD11 was also characterized as a dimer of lusianthridin. However, DD11 was different from DD9 in the points of connection between the two dihydrophenanthrene units. In DD11, the two components were connected directly through C-1 and C-6′, and this was further confirmed by the HMBC correlation between H-5′ and C-1. By comparing the above NMR data with previously reported values (Guo *et al.*, 2007), compound DD11 was identified as phoyunnanin C [**156**]. It was also reported from *Dendrobium venustum* (Sukphan *et al.*, 2014).



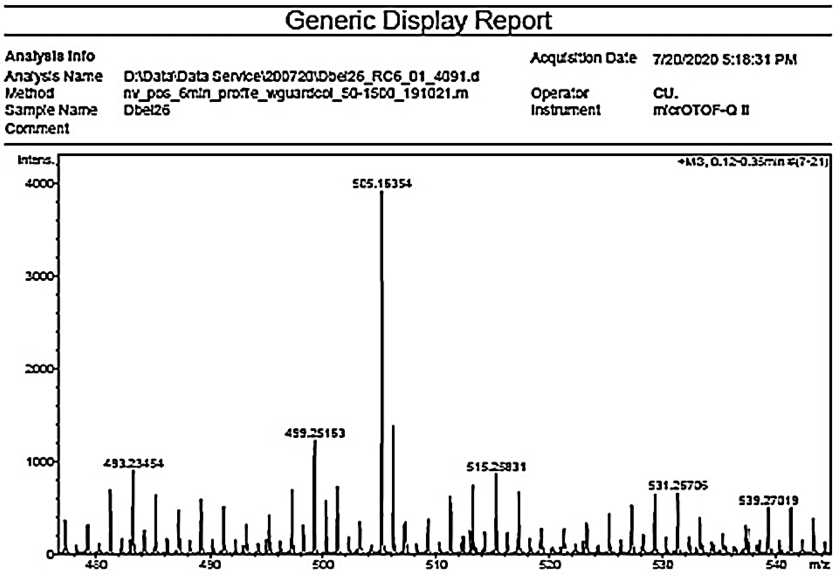
phoyunnanin C [**156**]

Table 16 NMR spectral data of compound DD11 and phoyunnanin C

Position	DD11 (acetone-d_6)		Phoyunnanin C (acetone-d_6)	
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
1	-	117.4	-	118.4
2	-	156.6	-	157.6
3	6.57 (1H, s)	98.5	6.58 (1H, s)	99.4
4	-	154.3	-	155.1
4a	-	114.9	-	115.8
4b	-	125.3	-	126.3
5	8.23 (1H, d, 8.4)	129.3	8.24 (1H, d, 8.5)	130.2

Position	DD11 (acetone-d_6)		Phoyunnanin C (acetone-d_6)	
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
6	6.69 (1H, dd, 8.4, 2.7)	112.5	6.70 (1H, dd, 8.5, 2.7)	113.4
7	-	155.2	-	156.1
8	6.66 (1H, d, 2.7)	113.8	6.67 (1H, d, 2.7)	114.7
8a	-	139.2	-	140.2
9	2.53 (2H, m)	30.7	2.56 (2H, m)	30.6
10	2.51 (2H, m)	27.5	2.52 (2H, m)	28.4
10a	-	140.1	-	141.1
1′	6.38 (1H, br s)	105.1	6.40 (1H, br s)	106.1
2′	-	158.3	-	159.3
3′	6.38(1H, br s)	100.7	6.40 (1H, br s)	101.6
4′	-	155.1	-	155.9
4a′	-	115.1	-	116.0
4b′	-	124.8	-	125.7
5′	8.08 (1H, s)	131.7	8.10 (1H, s)	132.6
6′	-	121.7	-	122.6
7′	-	152.8	-	153.7
8′	6.76 (1H, s)	114.3	6.78 (1H, s)	115.2
8a′	-	137.7	-	138.6
9′	2.73 (2H, m)	30.7	2.75 (2H, m)	30.5
10′	2.73 (2H, m)	30.7	2.75 (2H, m)	31.6
10a′	-	140.5	-	141.4
2-OMe	3.64 (3H, s)	54.4	3.66 (3H, s)	55.7
2′-OMe	3.72 (3H, s)	54.8	3.73 (3H, s)	55.2

(Guo *et al.*, 2007)



Generic Display Report

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Operator CU.
Instrument micrOTOF-Q II

Figure 49 Mass spectrum of compound DD11

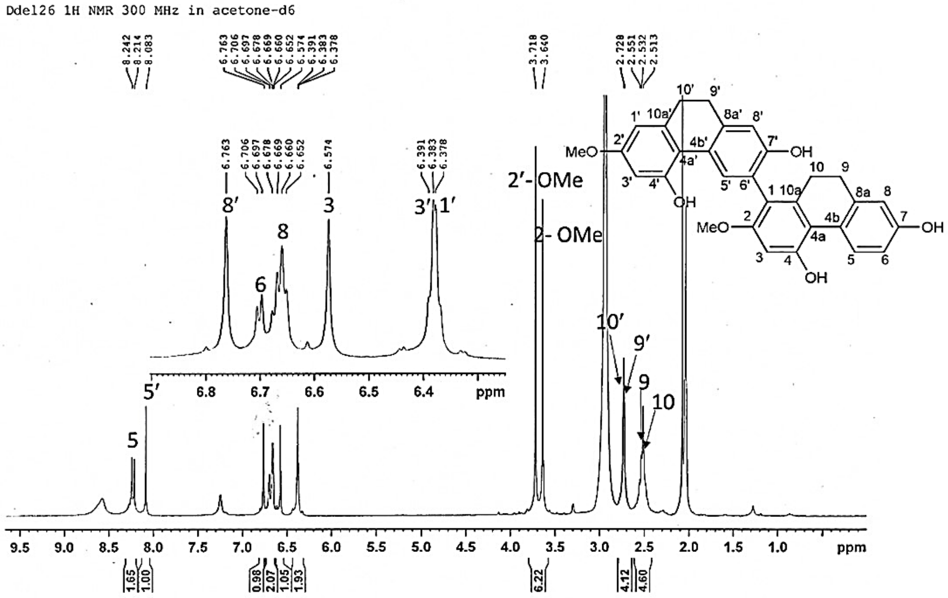


Figure 50 ^{1}H-NMR (300 MHz) spectrum of compound DD11

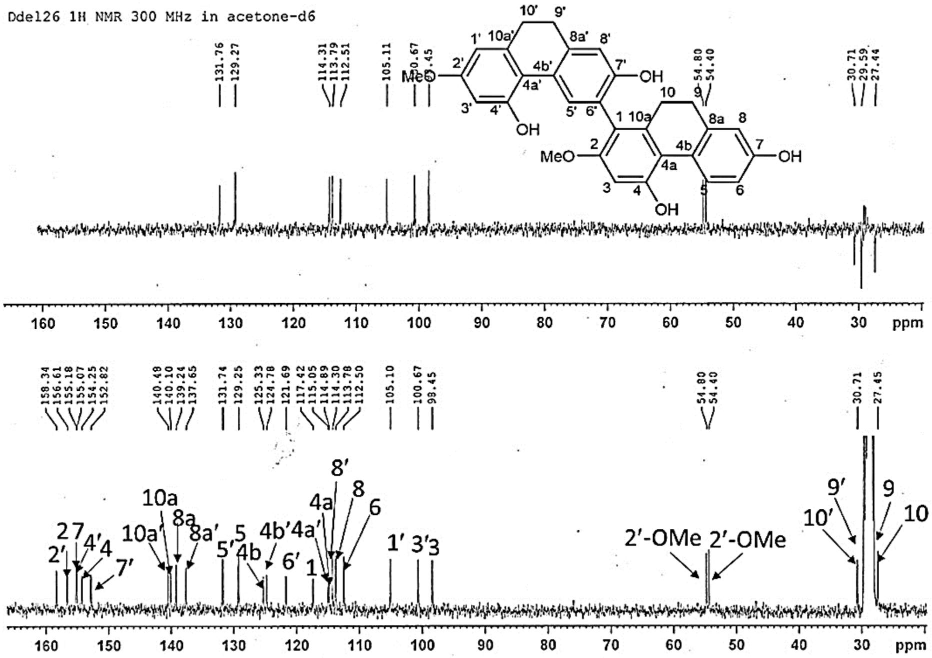


Figure 51 ^{13}C-NMR (75 MHz) spectrum of compound DD11

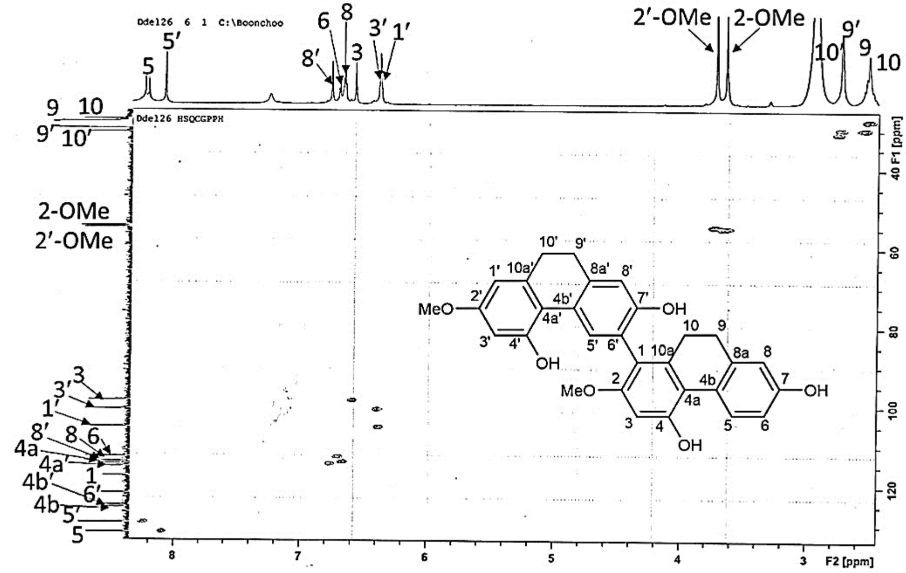


Figure 52 HSQC spectrum of compound DD11

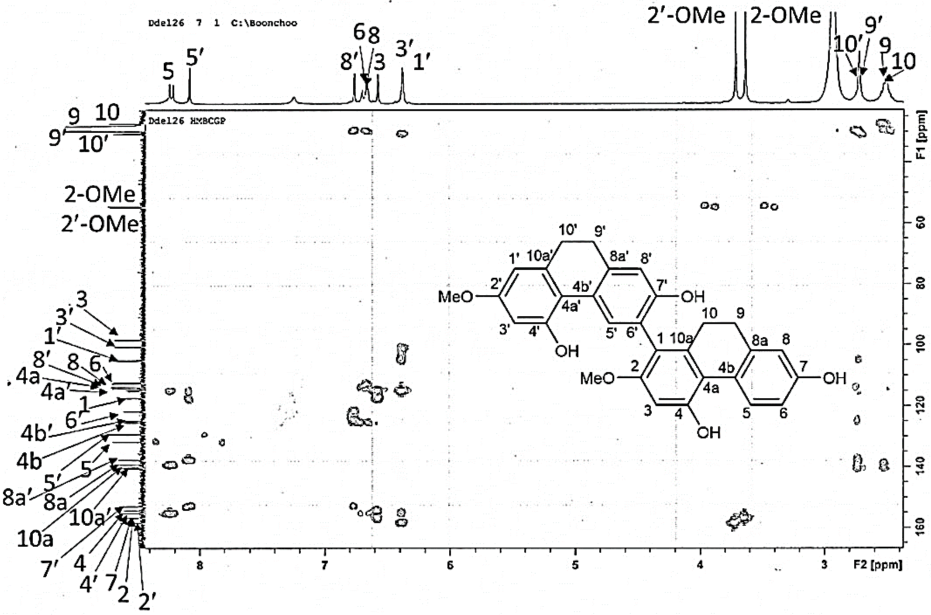


Figure 53 HMBC spectrum of compound DD11

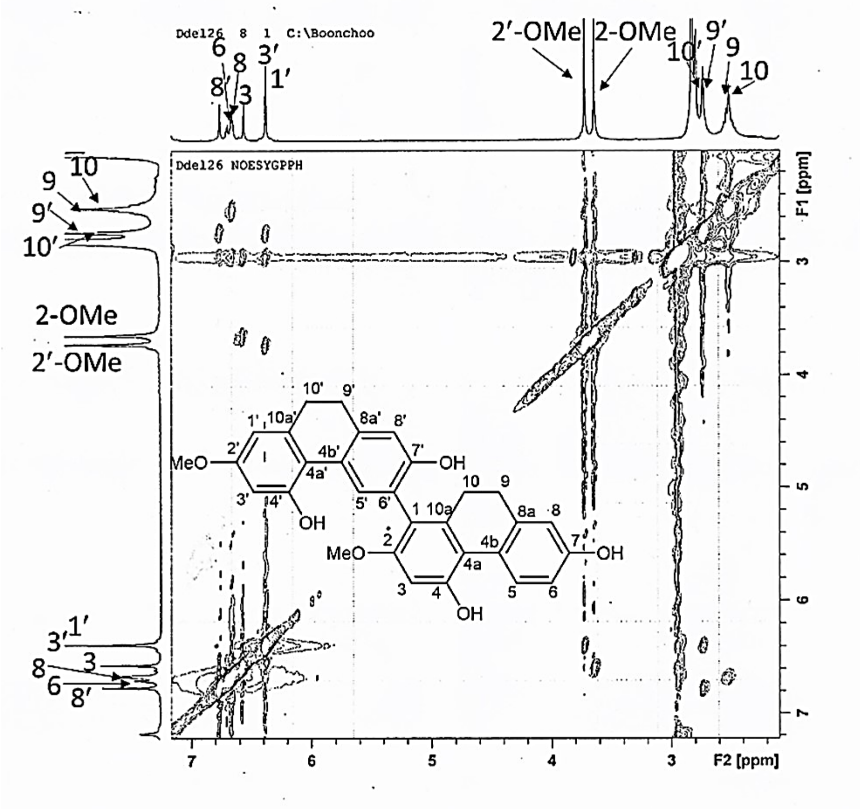
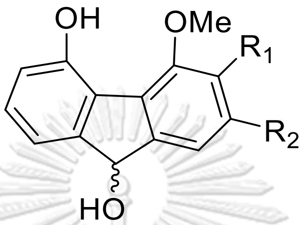


Figure 54 NOESY spectrum of compound DD11

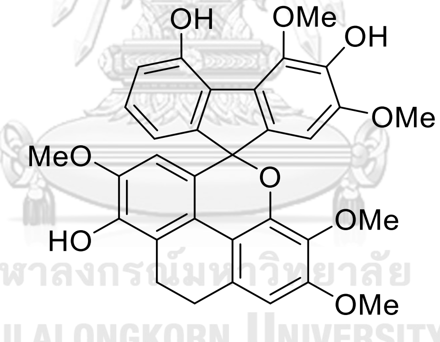
2.2 Chemical investigation of EtOAc extract of *Dendrobium gibsonii*

From the EtOAc extract of *D. gibsonii*, two new compounds named dihydrodengibsinin [**335**] and dendrogibsol [**336**] were isolated, together with seven known compounds, namely ephemeranthol A [**90**], dengibsinin [**309**], nobilone [**310**], aloifol I [**20**], lusianthridin [**97**], denchrysan A [**307**], and 4-methoxy-9*H*-fluorene-2,5,9-triol [**312**] **(Figure 55).**

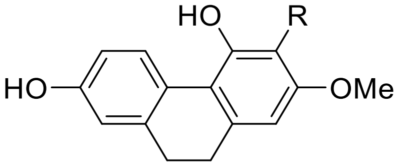


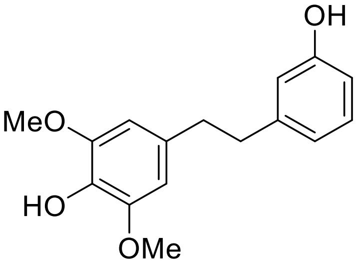
dihydrodengibsinin [**335**]; R_1 = OH, R_2 = OMe

4-methoxy-9*H*-fluorene-2,5,9-triol [**312**]; R_1 = H, R_2 = OH



dendrogibsol [**336**]



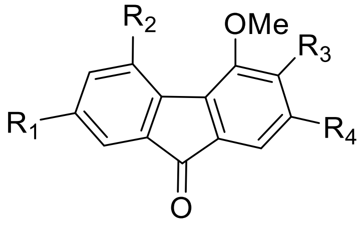


ephemeranthol A [**90**]; R = OMe

aloifol I [**20**]

lusianthridin [**97**]; R = H

Figure 55 Structures of compounds isolated from *Dendrobium gibsonii*



dengibsinin [**309**]; R_1 = H, R_2 = OH, R_3= OH, R_4 = OMe

nobilone [**308**]; R_1 = OH, R_2 = H, R_3= H, R_4 = OH

denchrysan A [**305**]; R_1 = OH, R_2 = OH, R_3= H, R_4 = OH

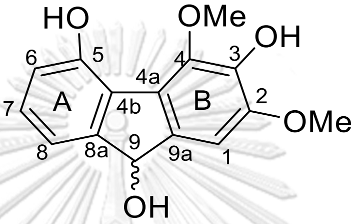
Figure 55 (Continued)

2.2.1 Structural characterization of compound DG1 (dihydrodengibsinin)

Compound DG1 was obtained as a brownish-white amorphous solid. The molecular formula $C_{15}H_{14}O_5$ was analyzed from the deprotonated molecular ion $[M-H]^-$ at *m/z* 273.0764 (calculated for $C_{15}H_{13}O_5$ 273.0763) (**Figure 56**). The UV spectrum (**Figure 57**) exhibited absorption peaks at 220, 255 and 300 nm, indicating a fluorene structure (Ye *et al.*, 2003). The IR spectrum (**Figure 58**) showed absorption bands for hydroxyl (3420 cm^{-1}) and aromatic (2925, 1618 cm^{-1}) functionalities.

The ^{1}H-NMR spectrum of DG1 (**Figure 59**) showed signals for four aromatic protons at δ_H 6.77–7.13 and two methoxy groups at δ_H 3.93 (3H, s, MeO-2) and δ_H 4.12 (3H, s, MeO-4). In addition to a singlet aromatic proton signal at δ_H 7.10 (1H, s, H-1), three aromatic proton resonances with an ABM coupling pattern were observed at δ_H 6.77 (1H, d, *J* = 7.5 Hz, H-6), 7.05 (1H, d, *J* = 7.5 Hz, H-8) and 7.13 (1H, t, *J* = 7.5 Hz, H-7). The ^{13}C-NMR spectrum showed the presence of twelve aromatic carbons and an oxygenated methine carbon of C-9 (δ_C 74.5), which was correlated to the proton at δ_H 5.38 (1H, d, *J* = 7.8 Hz, H-9) in the HSQC spectrum (**Figure 61**). The HO-9 proton at δ_H 4.57 (d, *J* = 7.8 Hz) displayed a two-bond HMBC correlation with C-9, which showed 3-bonds coupling with H-8 of ring A (**Figure 62**). The HO-5 proton at δ_H 9.44 (s) showed correlations with C-5 (δ_C 151.1) and C-6 (δ_C 116.1) in the HMBC spectrum. On ring B, the singlet proton signal δ_H 7.10 was assigned to H-1 from its HMBC correlation with C-9. One of the methoxy groups (δ_H 3.93) should be located at C-2 as supported by its NOESY correlation with H-1 (**Figure 63**) and 4-OMe group at δ_H 4.12 was placed by its HMBC correlation with C-4 (δ_C 139.5) (**Figure 62**).

Based on the above spectral data, compound DG1 was characterized as 2,4-dimethoxy-9*H*-fluorene-3,5,9-triol and given the trivial name dihydrodengibsinin [**335**]. Prior to this study, its natural occurrence was not known. This compound, however, was earlier synthesized by reduction of the corresponding fluorenone dengibsinin (Talapatra *et al.*, 1988; Talapatra *et al.*, 1985).

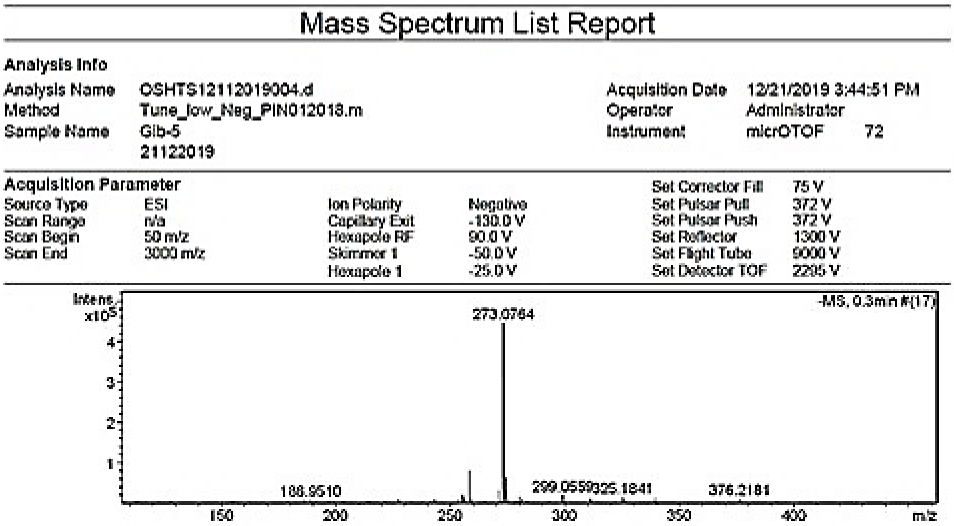


Dihydrodengibsinin [**335**]

Table 17 ^{1}H-NMR (300 MHz) and ^{13}C-NMR (75 MHz) spectral data of compound DG1

Position	DG1 (acetone-d_6)		
	δ_H (mult., *J* in Hz)	δ_C	HMBC (correlation with ^{1}H)
1	7.10 (1H, s)	105.2	9
2	-	148.4	1*, HO-3, MeO-2
3	-	139.0	1, HO-3
4	-	139.5	MeO-4, HO-3
4a	-	123.5	1, 9
4b	-	123.6	6, 8, HO-5
5	-	151.1	7, HO-5
6	6.77 (1H, d, 7.5)	116.1	8, HO-5
7	7.13 (1H, t, 7.5)	128.2	-
8	7.05 (1H, d, 7.5)	116.0	6, 9
8a	-	148.6	7, 9*, HO-9
9	5.38 (1H, d, 7.8)	74.5	1, 8, HO-9
9a	-	137.4	9*, HO-9
MeO-2	3.93 (3H, s)	56.0	-
MeO-4	4.12 (3H, s)	61.4	-
HO-3	7.91 (s)	-	-
HO-5	9.44 (s)	-	-
HO-9	4.57 (d, 7.8)	-	-

* Two-bond coupling



Mass Spectrum List Report

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Acquisition Parameter

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Scan Begin	50 m/z	Hexapole RF	90.0 V	Set Reflector	1300 V
Scan End	3000 m/z	Skimmer 1	-50.0 V	Set Flight Tube	9000 V
		Hexapole 1	-25.0 V	Set Detector TOF	2205 V

Figure 56 Mass spectrum of compound DG1

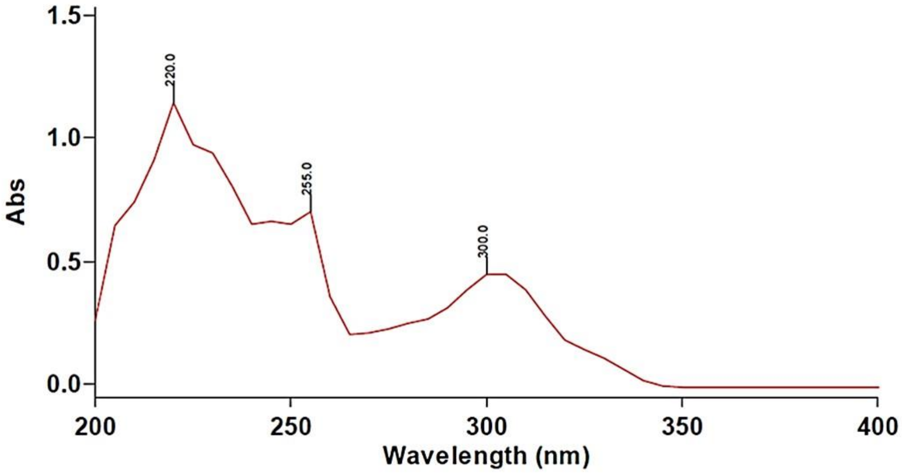


Figure 57 UV spectrum of compound DG1

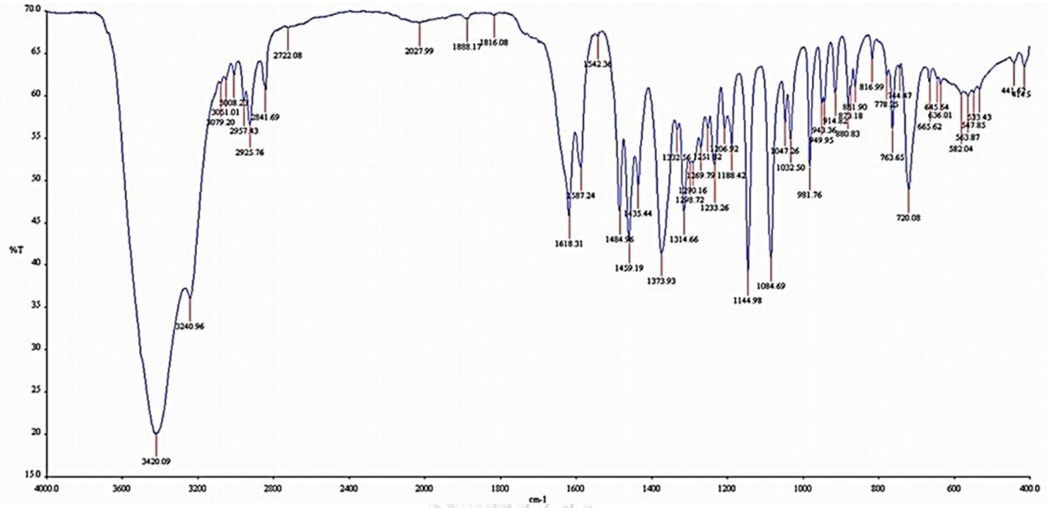


Figure 58 IR spectrum of compound DG1

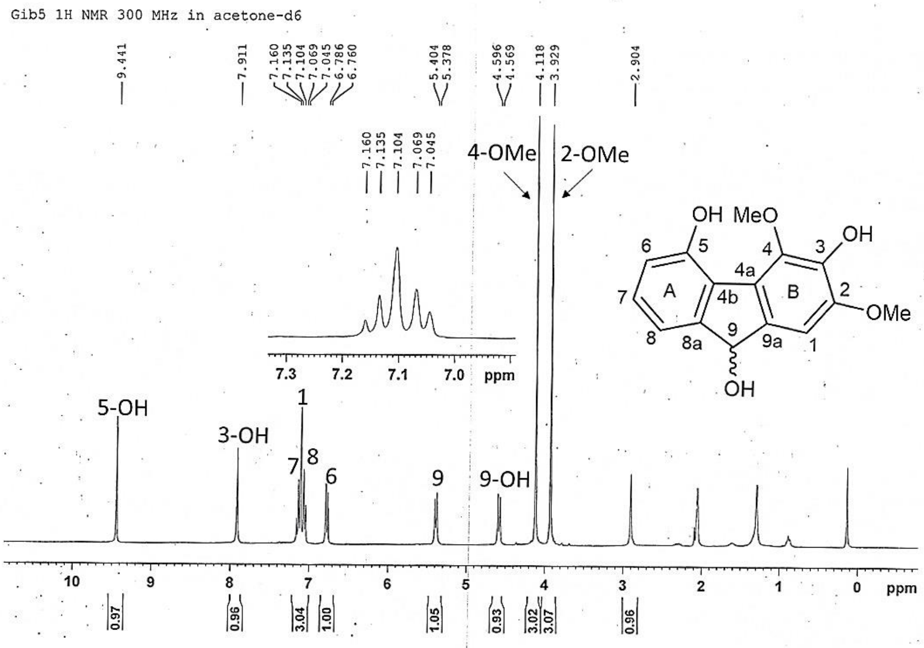


Figure 59 ^{1}H-NMR (300 MHz) spectrum of compound DG1

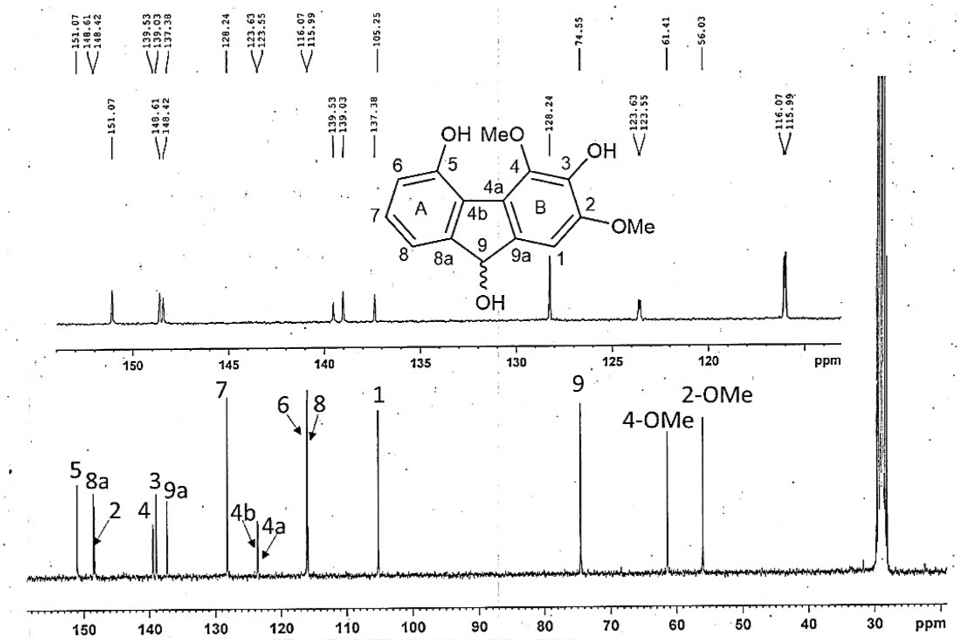


Figure 60 ^{13}C-NMR (75 MHz) of compound DG1

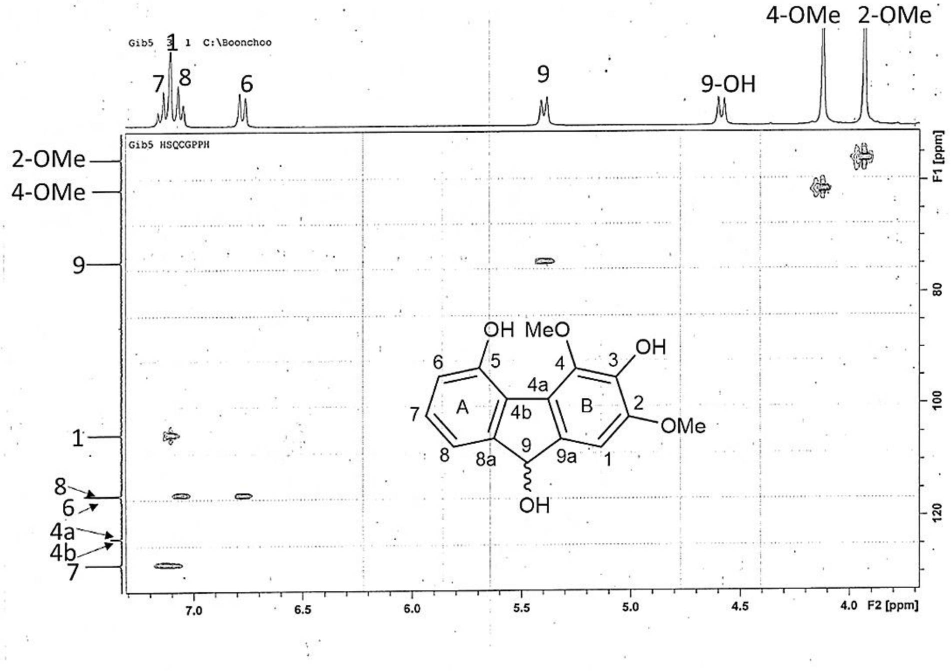


Figure 61 HSQC spectrum of compound DG1

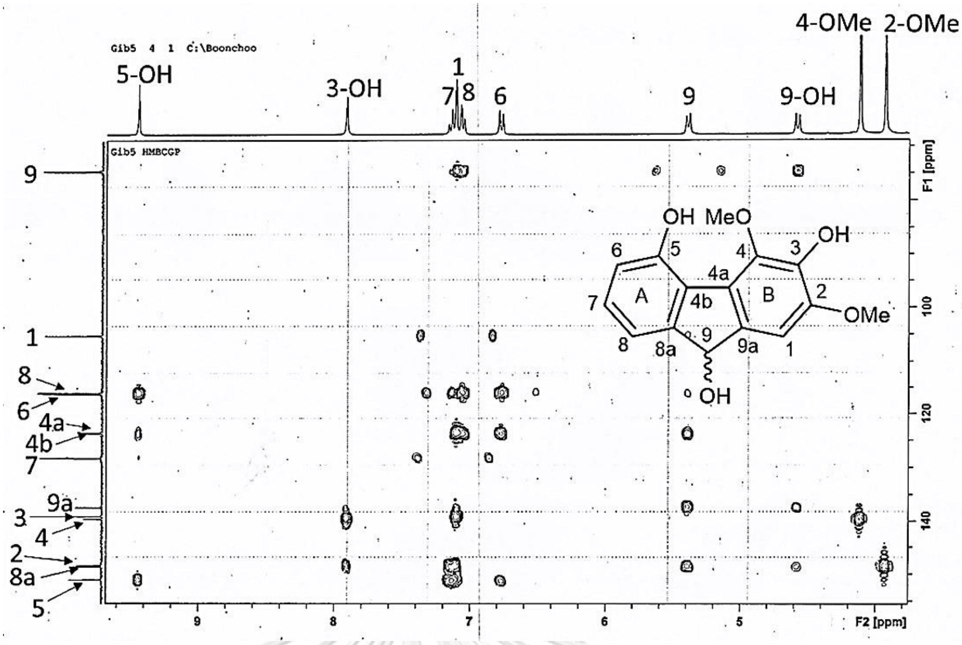


Figure 62 HMBC spectrum of compound DG1

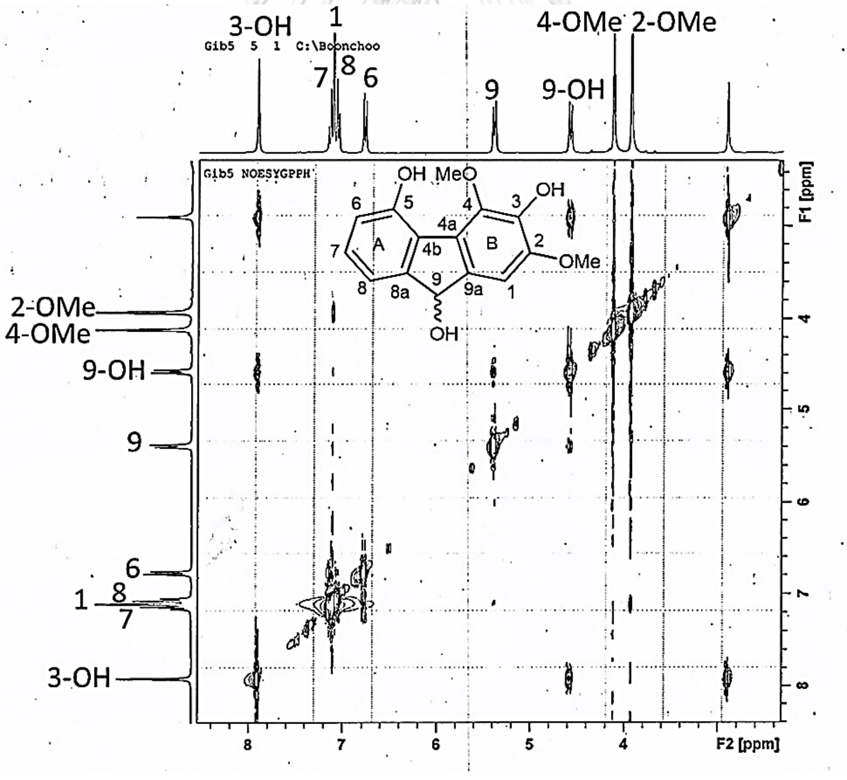


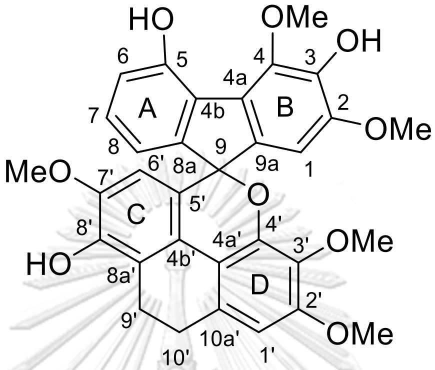
Figure 63 NOESY spectrum of compound DG1

2.2.2 Structural characterization of compound DG2 (dendrogibsol)

Compound DG2 was obtained as a brownish amorphous solid. The molecular formula $C_{32}H_{28}O_9$ was deduced from its protonated molecular ion $[M+H]^+$ at *m/z* 557.1849 (calculated for $C_{32}H_{29}O_9$ 557.1811) (**Figure 64**). The UV spectrum (**Figure 65**) exhibited absorption peaks at 260, 310 and 325 nm. The IR spectrum (**Figure 66**) showed absorption bands at 3334 (hydroxyl), 2930, 1607 (benzene ring), 1485 (methylene) and 1236 (ether) cm^{-1}. Comparison of ^1H and ^{13}C-NMR data of DG2 with DG1 suggested that DG2 was an adduct of a fluorene and a dihydrophenanthrene. DG2 showed several ^1H-NMR resonances similar to those of the DG1, representing four aromatic protons at δ_H 6.65 (1H, dd, *J* = 8.0, 1.0 Hz, H-8), 6.76 (1H, dd, *J* = 8.0, 1.0 Hz, H-6), 6.85 (1H, s, H-1), and 6.93 (1H, t, *J* = 8.0 Hz, H-7), and two methoxy groups at C-2 (δ_H 3.77, 3H, s) and C-4 (δ_H 4.18, 3H, s). The presence of a dihydrophenanthrene unit in DG2 was deduced from the characteristic signals for two methylene carbons at δ_C 20.9 (C-9′) and 26.9 (C-10′), in addition to twelve aromatic carbon resonances.

In the ^1H-NMR spectrum (**Figure 67 and Table 18**), the dihydrophenanthrene unit displayed signals for two aromatic protons at δ_H 6.04 (1H, s, H-6′) and 6.61 (1H, s, H-1′), and three methoxy groups at δ_H 3.37 (3H, s, MeO-3′), 3.54 (3H, s, MeO-7′) and 3.82 (3H, s, MeO-2′). The assignment of H-6′ of ring C was supported by its HBMC correlations with C-4b′ (δ_C 120.6) and C-8′ (δ_C 143.4) (**Figure 70**). On ring C, the first methoxy group should be placed at C-7′ according to its NOESY correlation (**Figure 71**) with H-6′. On ring D, the assignment of H-1 was deduced from its HMBC correlations with C-10′. The NOESY cross-peak between H-1′ and H_2-10′ was also observed. The second methoxy group was located at C-2′, as supported by its NOESY correlation with H-1′. The HMBC correlations of C-3′ (δ_C 137.3) with H-1′ and MeO-3′ indicated the location of the third methoxy group at C-3′.

DG2 had the fluorene moiety connected to the dihydrophenanthrene unit through a C–C linkage between C-5′ (δ_C 123.4) and C-9 (87.4) and an ether bond between C-9 and the oxygen atom at C-4′ (δ_C 145.3), forming a spiro structure. This was supported by the HMBC correlations of C-9 with H-1, H-8, and H-6′. Thus, it was concluded that DG2 was a fluorene–dihydrophenanthrene adduct and was given the trivial name dendrogibsol [**336**]. It is the first representative of this class of dimeric compounds.



Dendrogibsol [**336**]

Table 18 ^{1}H-NMR (500 MHz) and ^{13}C-NMR (125 MHz) spectral data of compound DG2

Position	DG2 (acetone-d_6)		
	δ_H (mult., *J* in Hz)	δ_C	HMBC (correlation with ^{1}H)
1	6.85 (1H, s)	105.6	-
2	-	148.6	HO-3, MeO-2
3	-	140.1	1, HO-3*
4	-	139.6	MeO-4, HO-3
4a	-	124.2	1
4b	-	122.5	6, 8, HO-5
5	-	151.2	6*,7, HO-5*
6	6.76 (1H, dd, 8.0, 1.0)	117.3	7*,8, HO-5
7	6.93 (1H, t, 8.0)	128.6	6*
8	6.65 (1H, dd, 8.0, 1.0)	115.6	6
8a	-	148.8	7
9	-	87.4	6′, 1, 8
9a	-	137.2	1*

Position	DG2 (acetone-d_6)		
	δ_H (mult., *J* in Hz)	δ_C	HMBC (correlation with ^{1}H)
MeO-2	3.77 (3H, s)	56.0	-
MeO-4	4.18 (3H, s)	61.6	-
HO-3	8.11 (s)	-	-
HO-5	9.56 (s)	-	-
1′	6.61 (1H, s)	105.3	10′
2′	-	152.9	1′*, MeO-2′
3′	-	137.3	1′, MeO-3′
4′	-	145.3	-
4a′	-	114.0	1′, 10′
4b′	-	120.6	6′, 9′
5′	-	123.4	6′*
6′	6.04 (1H, s)	105.4	-
7′	-	146.5	6′*, MeO-7′, HO-8′
8′	-	143.4	6′, 9′, HO-8′*
8a′	-	119.2	10′, HO-8′
9′	3.09 (1H, m), 2.78 (1H, m)	20.9	10′*
10′	2.93 (2H, m)	26.9	1′, 9′*
10a′	-	128.6	1′*, 9′
MeO-2′	3.82 (3H, s)	55.5	-
MeO-3′	3.37 (3H, s)	59.6	-
MeO-7′	3.54 (3H, s)	55.4	-
HO-8′	7.61 (s)	-	-

* Two-bond coupling

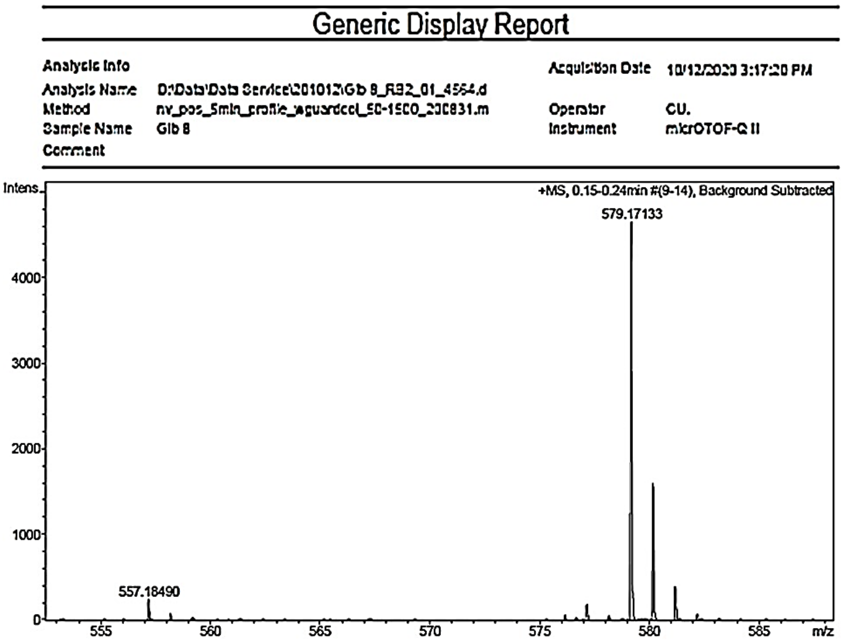


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Figure 64 Mass spectrum of compound DG2

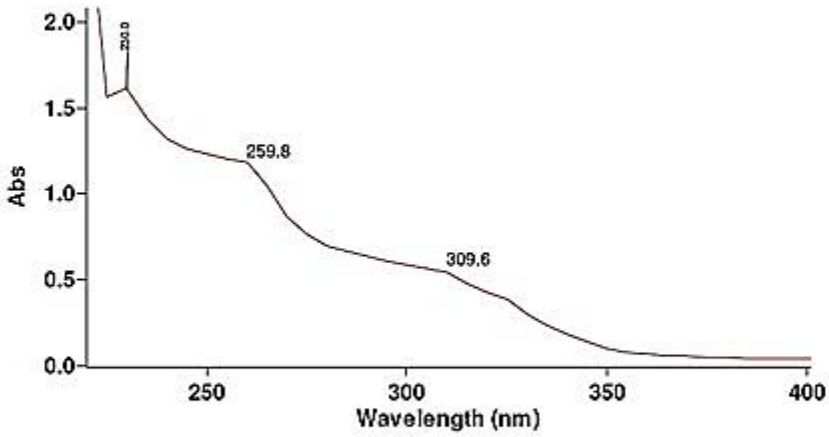


Figure 65 UV spectrum of compound DG2

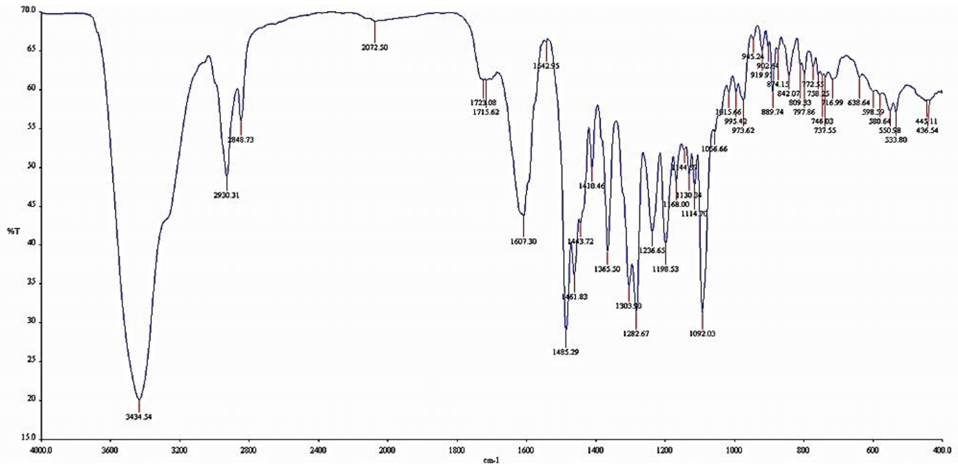


Figure 66 IR spectrum of compound DG2

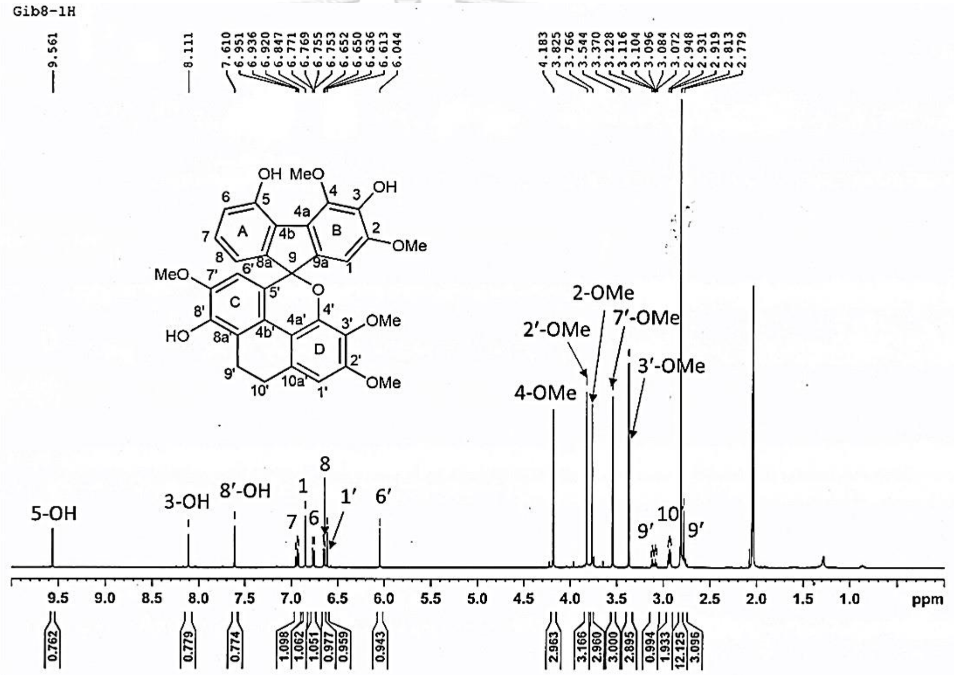


Figure 67 ^{1}H-NMR (500 MHz) spectrum of compound DG2

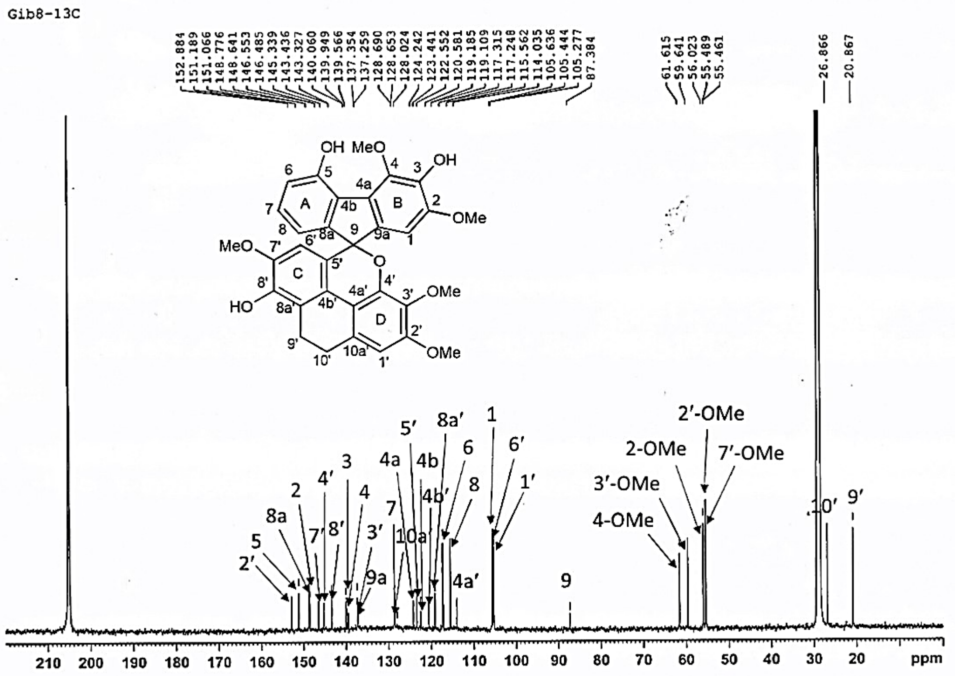


Figure 68 ^{13}C-NMR (125 MHz) of compound DG2

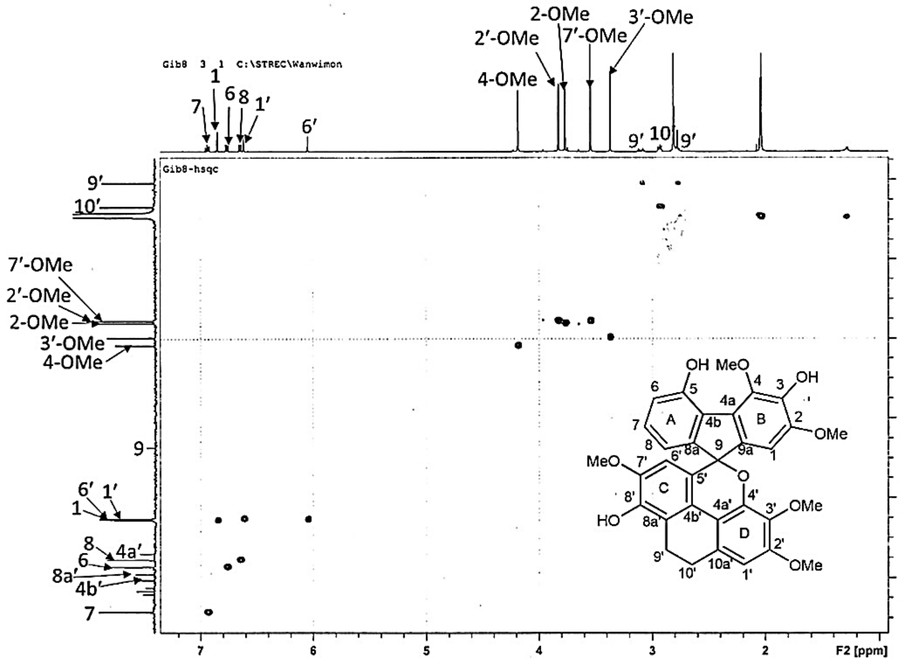


Figure 69 HSQC spectrum of compound DG2

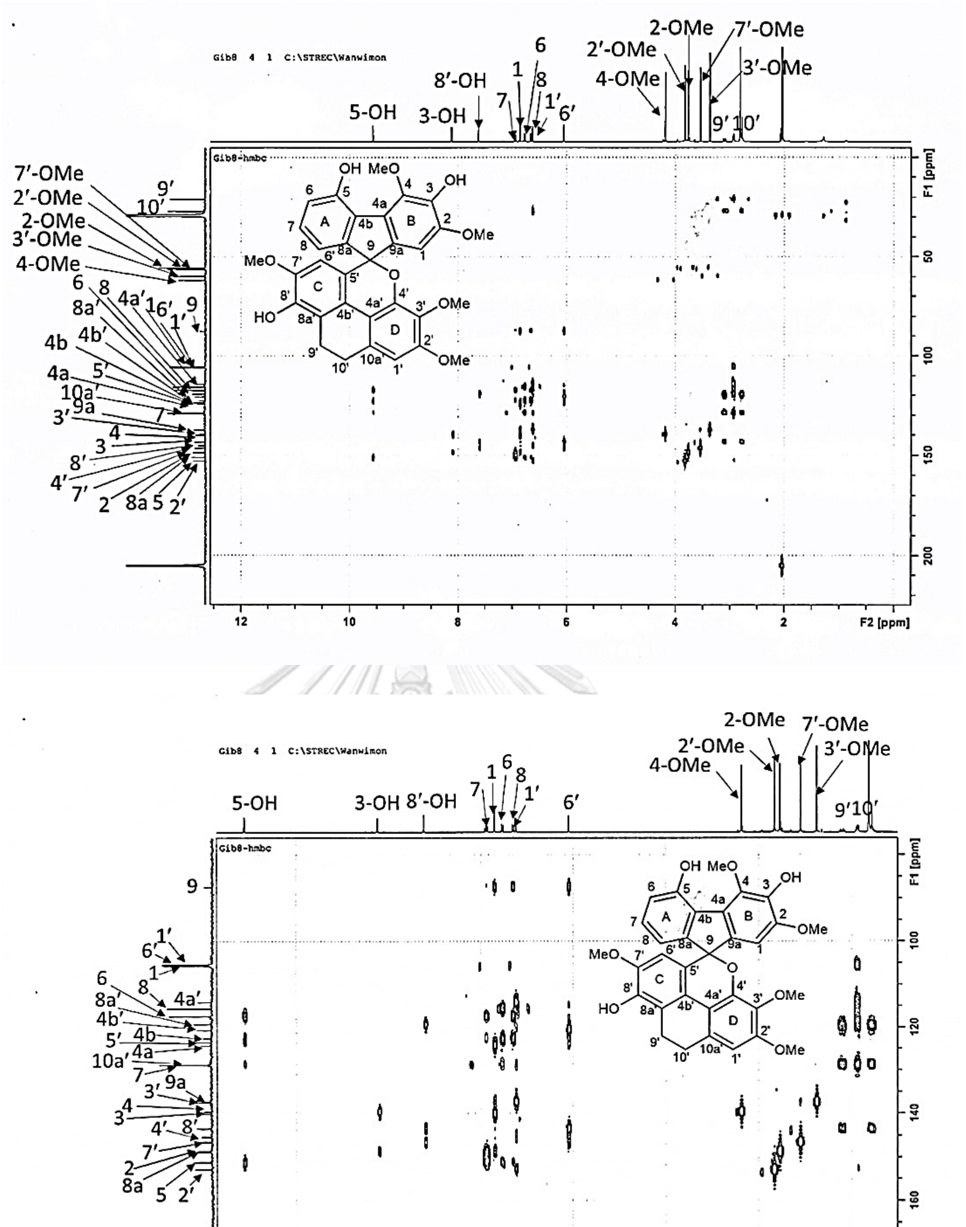


Figure 70 HMBC spectrum of compound DG2 (full and expanded spectrum)

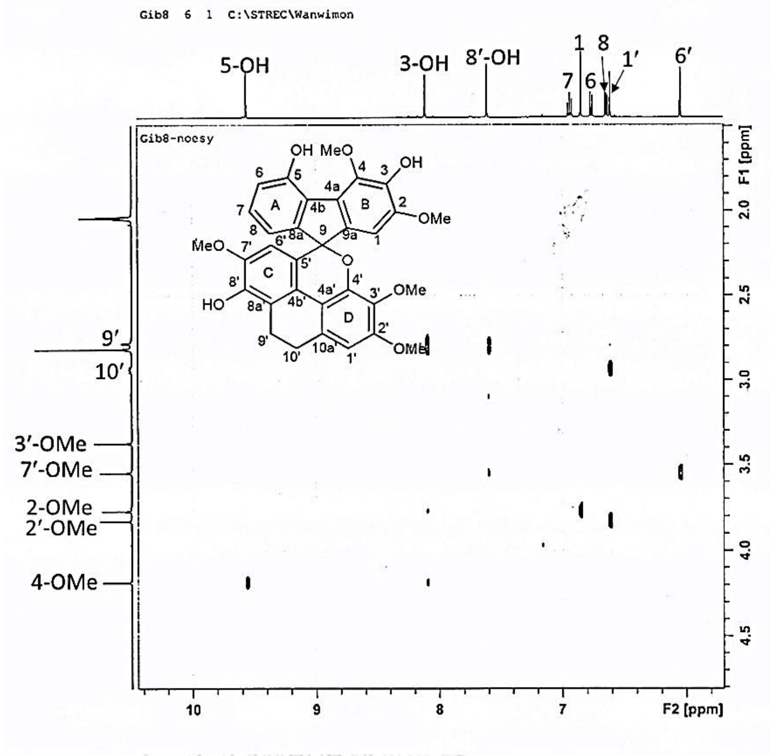


Figure 71 NOESY spectrum of compound DG2

2.2.2.1 Biogenesis of dendrogibsol

The biogenesis of the unprecedented fluorene–dihydrophenanthrene adduct, DG2, is proposed to occur as shown in **Figure 72**. The coupling reaction is initiated by the nucleophilic attack from C-5′ of the dihydrophenanthrene unit (II) onto the keto carbon (C-9) of the fluorenone (I) to give a quinone-like structure (III). This structure subsequently isomerizes to form intermediate IV. Finally, a nucleophilic attack by the oxygen of the OH-4′ group of the dihydrophenanthrene unit occurs at the carbinol carbon (C-9) of the fluorene part, with concomitant loss of H_2O, to generate DG2.

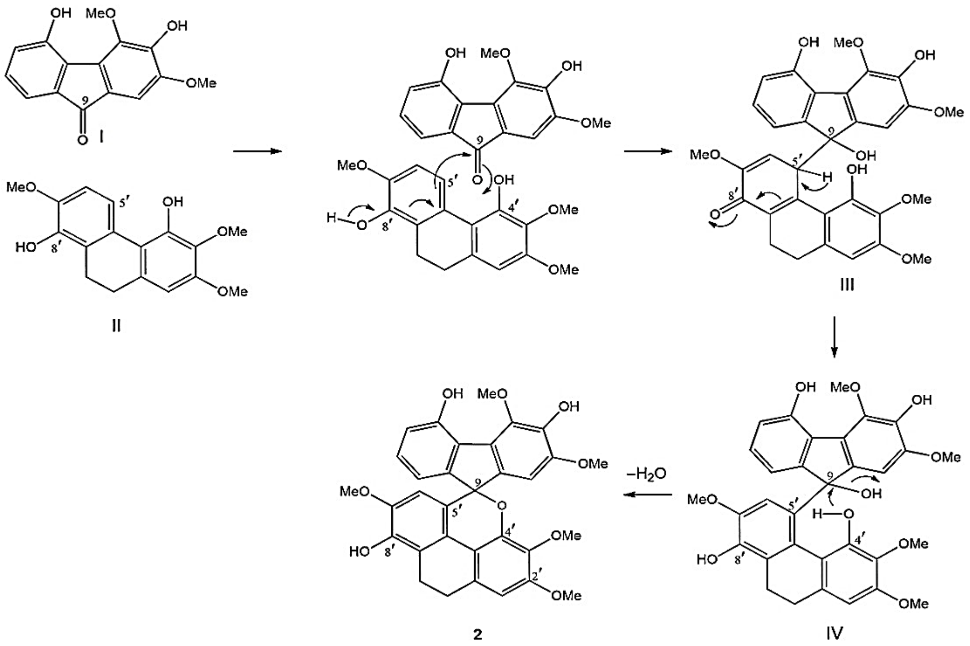


Figure 72 Possible biogenesis of dendrogibsol

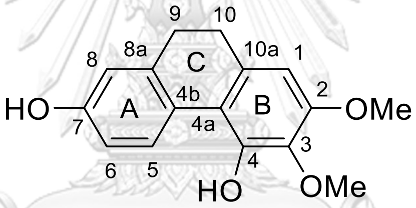
2.2.3 Identification of compound DG3 (ephemeranthol A)

Compound DG3 was obtained as a white amorphous solid. The HR-ESI mass spectrum (**Figure 73**) showed a sodium adduct molecular ion $[M+Na]^+$ at *m/z* 295.0965, (calculated for $C_{16}H_{16}O_4Na$; 295.0964), suggesting the molecular formula $C_{16}H_{16}O_4$. The ^{1}H-NMR spectrum of DG3 (**Figure 74 and Table 19**) exhibited signals for four aromatic protons [δ_H 6.48 (1H, s, H-1), 8.25 (1H, d, *J* = 9.3 Hz, H-5), 6.71 (2H, br d, *J* = 2.4 Hz, H-6, H-8)], two methylene protons [δ_H 2.68 (4H, br s, H_2-9, H_2-10)], two hydroxy protons [δ_H 8.17 (1H, s, 7-OH) and 7.92 (1H, s, 4-OH)] and two methoxy groups [δ_H 3.86 (3H, s, 2-OMe) and 3.81 (3H, s, 3-OMe)]. The ^{13}C-NMR and HSQC spectra (**Figure 75 and 76**) revealed the presence of eight quaternary carbons, four methine carbons, two methylene carbons, and two methoxy carbons. The above NMR data indicated a dihydrophenanthrene skeleton.

The assignment of H-5 on ring A was deduced from its HMBC correlations (**Figure 77**) to C-7 (δ_C 155.4) and C-8a (δ_C 138.8). H-6 showed HMBC correlation to C-8 (δ_C 114.2), and H-8 showed correlation peaks with C-6 (δ_C 112.7) and C-9 (δ_C 30.2).

On ring B, H-1 displayed HMBC correlations to C-2 (δ_C 150.5), C-3 (δ_C 134.9), C-4a (δ_C 114.9) and C-10 (δ_C 29.9). On ring C, two methylene carbons at C-9 and C-10 showed HMBC correlations with H-8 and H-1, respectively. The proton at δ_H 7.92 (s) exhibited HMBC correlations to C-3, C-4 (δ_C 147.4), and C-4a indicating the position of 4-OH. The position of 2-OMe was confirmed by the NOESY interaction (**Figure 78**) of H-1 to the protons of 2-OMe. The position of 3-OMe was confirmed by the NOESY cross peak between 4-OH proton and 3-OMe protons. The NOESY spectrum also showed correlations of 7-OH proton to H-6 and H-8.

From comparison of the above NMR data with the values in a previous report on *Ephemerantha lonchophylla* (Tezuka *et al.*, 1991), DG3 was identified as ephemeranthol A [**90**]. It was also reported from *Dendrobium nobile* (Yang *et al.*, 2007) and *Dendrobium officinale* (Zhao *et al.*, 2018).

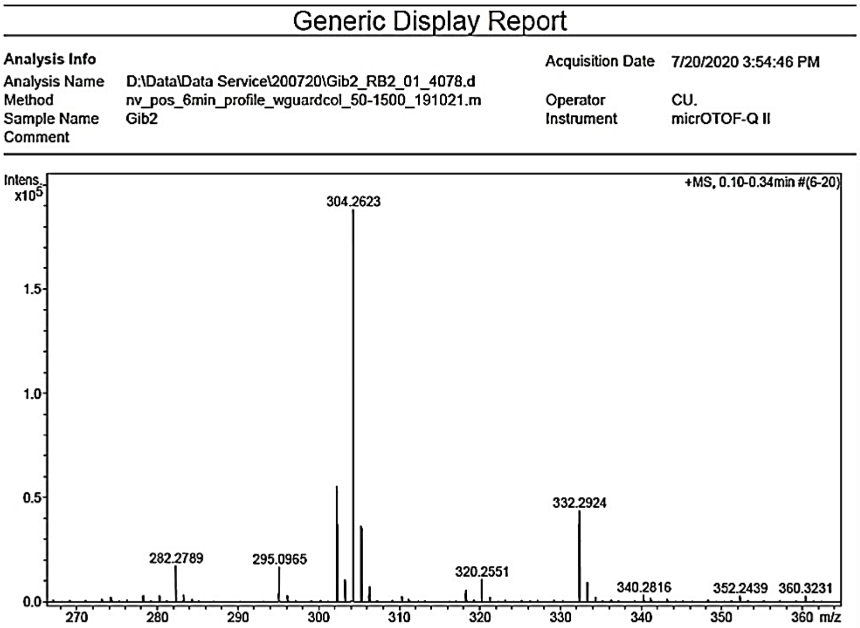


ephemeranthol A [**90**]

Table 19 NMR spectral data of compound DG3 and ephemeranthol A

Position	DG3 (acetone-d_6)		Ephemeranthol A ($CDCl_3$)
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)
1	6.48 (1H, s)	103.3	6.39 (1H, s)
2	-	150.5	-
3	-	134.9	-
4	-	147.4	-
4a	-	114.9	-
4b	-	124.9	-
5	8.25 (1H, d, 9.3)	128.8	8.22 (1H, d, 8.5)
6	6.71 (1H, br d, 9.3)	112.7	6.74 (1H, dd, 8.5, 3.0)
7	-	155.4	-
8	6.71 (1H, d, 2.4)	114.2	6.71 (1H, d, 3.0)
8a	-	138.8	-
9	2.68 (2H, br s)	30.2	2.74 (2H, m)
10	2.68 (2H, br s)	29.9	2.74 (2H, m)
10a	-	133.5	-
2-MeO	3.86 (3H, s)	55.2	3.89 (3H, s)
3-MeO	3.81 (3H, s)	59.9	3.93 (3H, s)
4-OH	7.92 (1H, s)	-	-
7-OH	8.17 (1H, s)	-	-

(Tezuka *et al.*, 1991)



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Sample Name	Gib2	Instrument	micrOTOF-Q II
Comment			

Figure 73 Mass spectrum of compound DG3

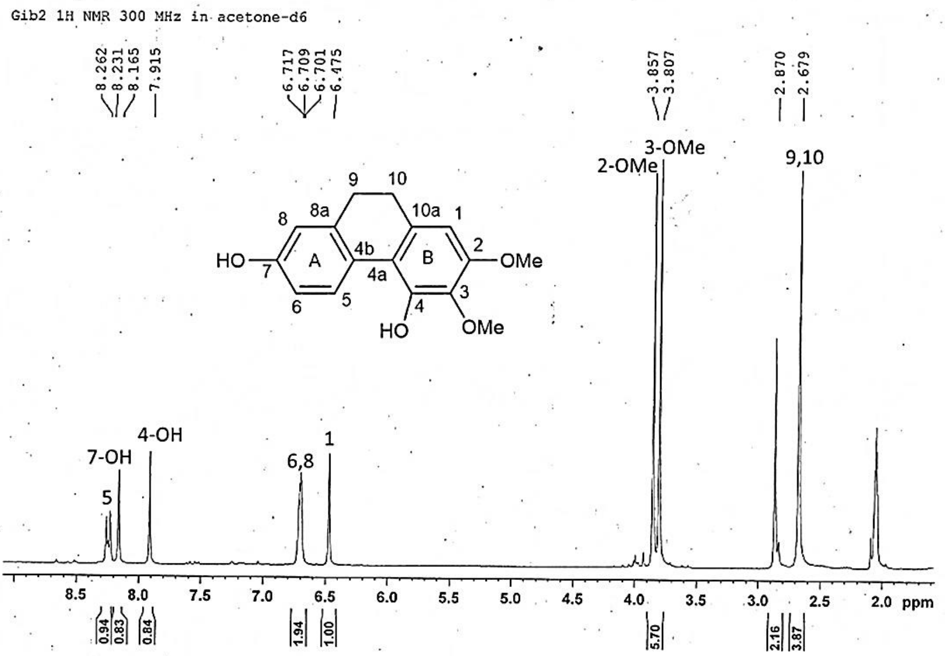


Figure 74 ^{1}H-NMR (300 MHz) spectrum of compound DG3

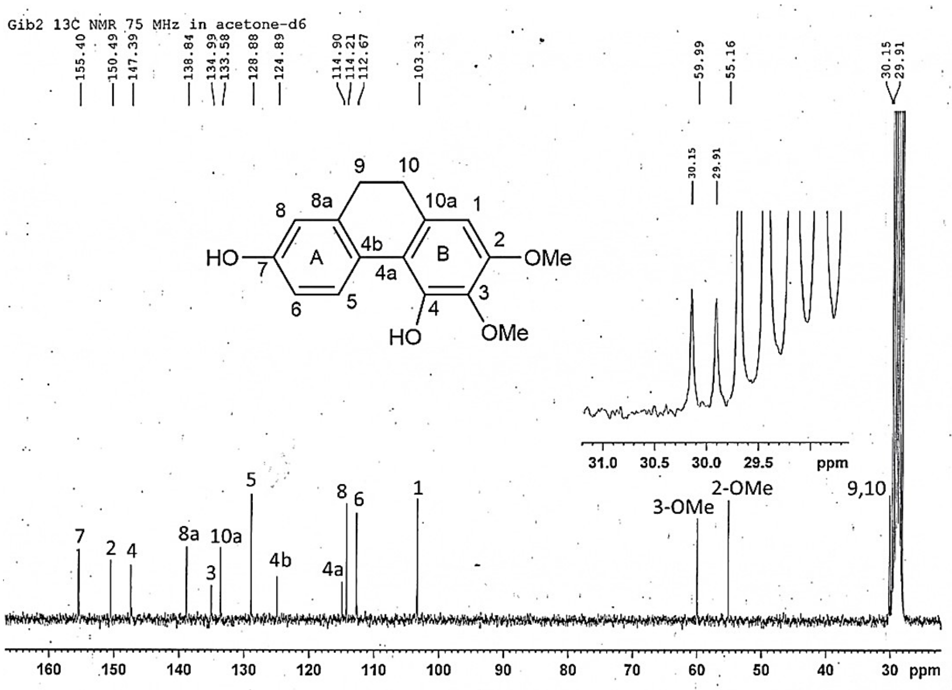


Figure 75 ^{13}C-NMR (75 MHz) spectrum of compound DG3

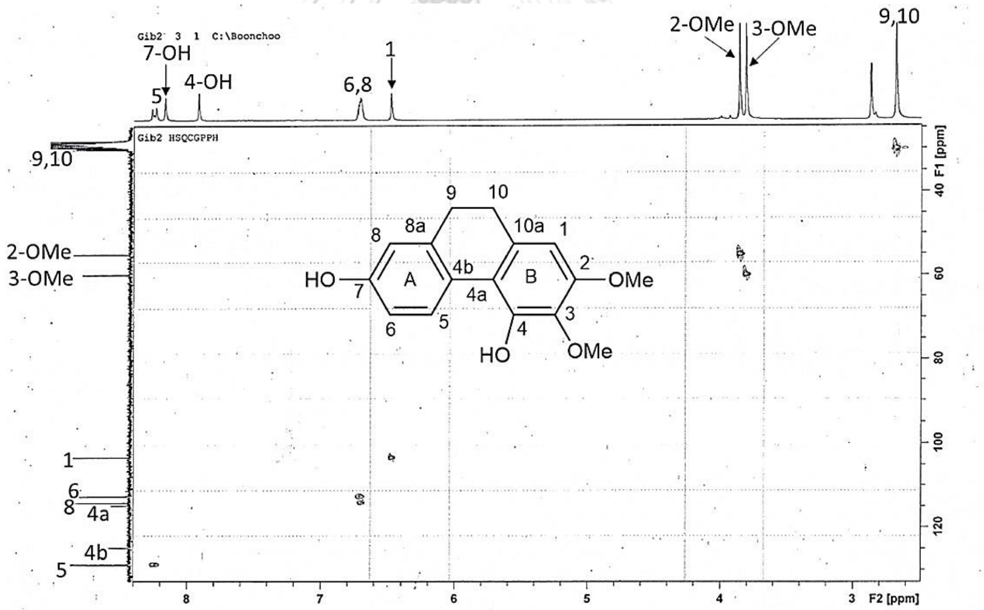


Figure 76 HSQC spectrum of compound DG3

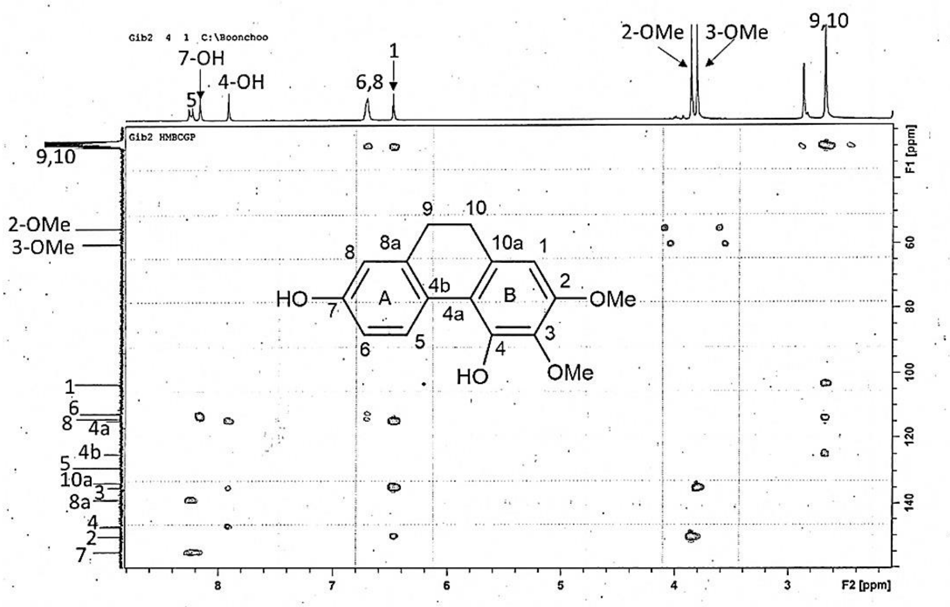


Figure 77 HMBC spectrum of compound DG3

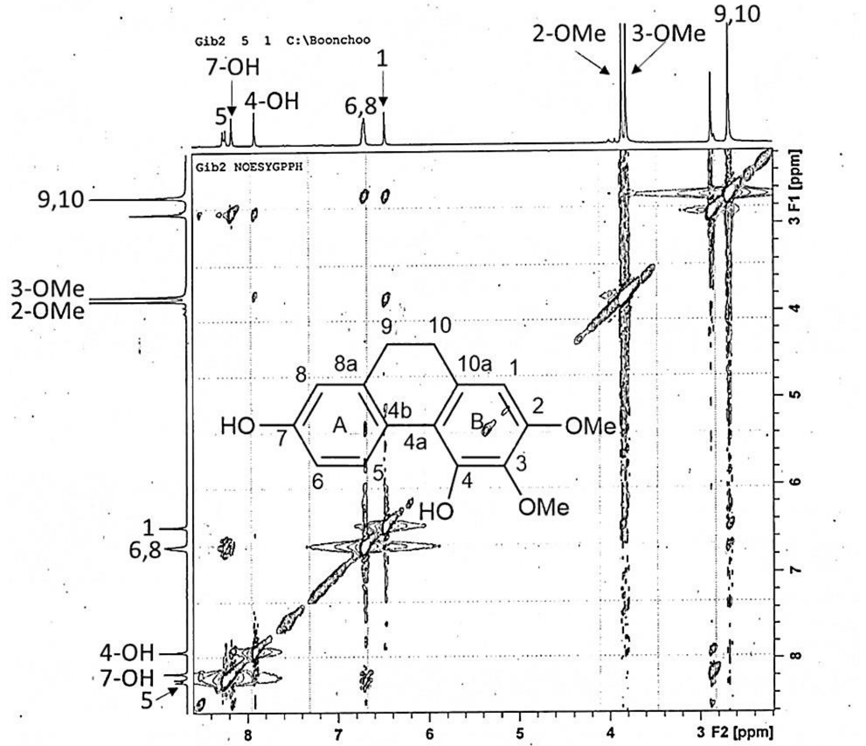


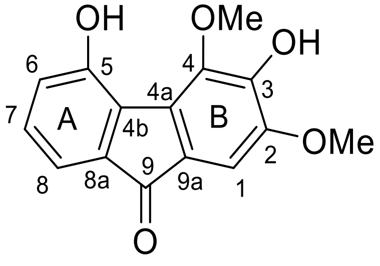
Figure 78 NOESY spectrum of compound DG3

2.2.4 Identification of compound DG4 (dengibsinin)

Compound DG4 was obtained as an orange-colored powder. The HR-ESI mass spectrum (**Figure 79**) showed a sodium adduct molecular ion $[M+Na]^+$ at *m/z* 295.0574, (calculated for $C_{15}H_{12}O_5Na$; 295.0582), suggesting the molecular formula $C_{15}H_{12}O_5$. The ^{1}H-NMR spectrum of DG4 (**Figure 80 and Table 20**) showed four aromatic protons at δ_H 7.11 (1H, s, H-1), 6.97 (1H, dd, *J* = 7.5, 0.6 Hz, H-6), 7.19 (1H, dd, *J* = 7.8, 7.5 Hz, H-7), and 7.08 (1H, br d, *J* = 7.8, 0.6 Hz, H-8), free phenolic groups [δ_H 9.24 (1H, s, 5-OH) and 8.91 (1H, s, 3-OH)], and two methoxy groups at δ_H 3.97 (3H, s, 2-OMe) and 4.18 (3H, s, 4-OMe). The presence of a fluorenone skeleton was indicated from the ^{13}C-NMR and HSQC spectral data (**Figures 81 and 82 and Table 20**) which showed the presence of twelve aromatic carbons and a carbonyl carbon (C-9) at δ_C 191.2. The ^{1}H and ^{13}C NMR spectra were similar to those of compound DG1, except that there was no HO-9 proton in DG4.

The assignment of H-8 on ring A, was obtained from its HMBC correlation (**Figure 83**) with C-6 (δ_C 123.7). The HO-5 proton at δ_H 9.24 (s) showed correlations with C-5 (δ_C 151.2) and C-6 in the HMBC spectrum. On ring B, H-1 was assigned from its HMBC correlation with C-9 (δ_C 191.2). The position of 2-OMe was supported by its NOESY correlations (**Figure 84**) with H-1 and 3-OH; and 4-OMe showed correlation with 5-OH.

By comparing the above spectral data with previously report values (Talapatra *et al.*, 1988; Talapatra *et al.*, 1985), compound DG4 was characterized as dengibsinin [**309**]. Dengibsinin was earlier reported from *Dendrobium aduncum* (Zhiminga *et al.*, 2006).

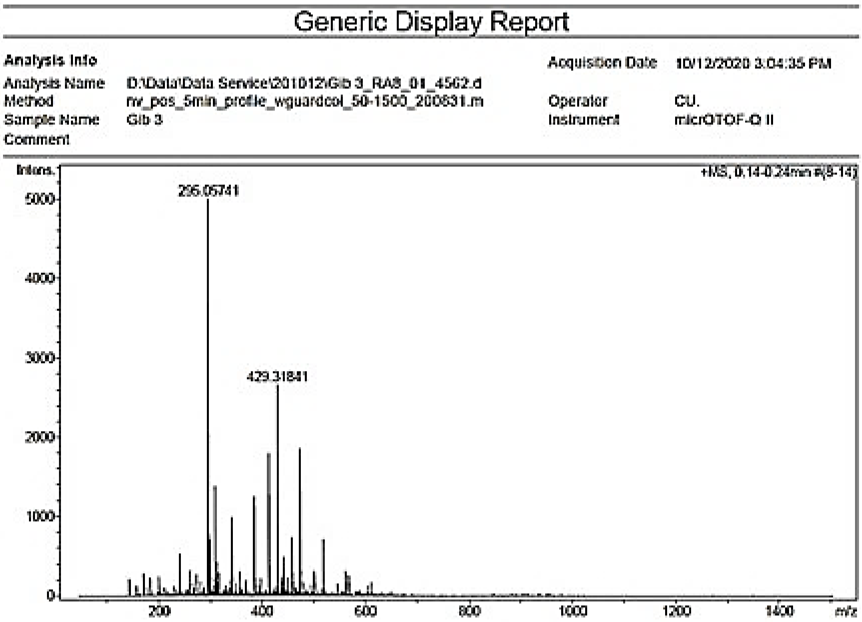


dengibsinin [**309**]

Table 20 NMR spectral data of compound DG4 and dengibsinin

Position	DG4 (acetone-d_6)		Dengibsinin ($CDCl_3$)
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)
1	7.11 (1H, s)	104.5	7.10 (1H, s)
2	-	148.9	-
3	-	136.0	-
4	-	140.1	-
4a	-	124.7	-
4b	-	125.5	-
5	-	151.2	-
6	6.97 (1H, br d, 7.5)	123.7	6.98 (1H, dd, 7.3, 2)
7	7.19 (1H, dd, 7.8, 7.5)	130.2	7.13 (1H, dd, 7.3, 6.8)
8	7.08 (1H, br d, 7.8)	115.3	7.19 (1H, dd, 6.8, 2)
8a	-	145.3	-
9	-	191.2	-
9a	-	129.2	-
2-OMe	3.97 (3H, s)	56.2	3.96 (3H, s)
4-OMe	4.18 (3H, s)	61.8	4.11 (3H, s)
3-OH	8.91 (1H, s)	-	-
5-OH	9.24 (1H, s)	-	-

(Talapatra *et al.*, 1988; Talapatra *et al.*, 1985)



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Instrument microTOF-Q II

Figure 79 Mass spectrum of compound DG4

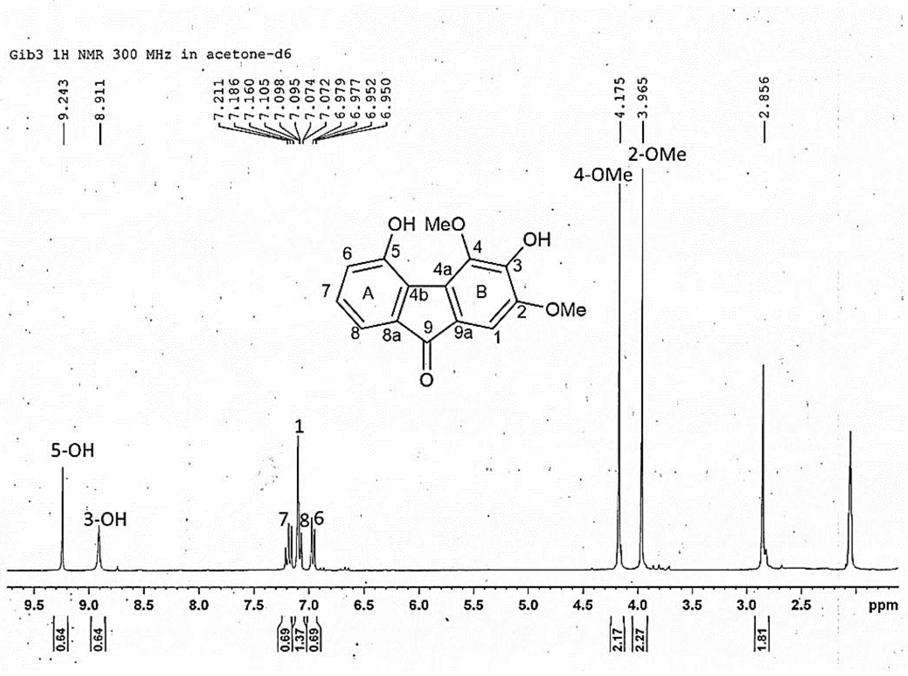


Figure 80 ^{1}H-NMR (300 MHz) spectrum of compound DG4

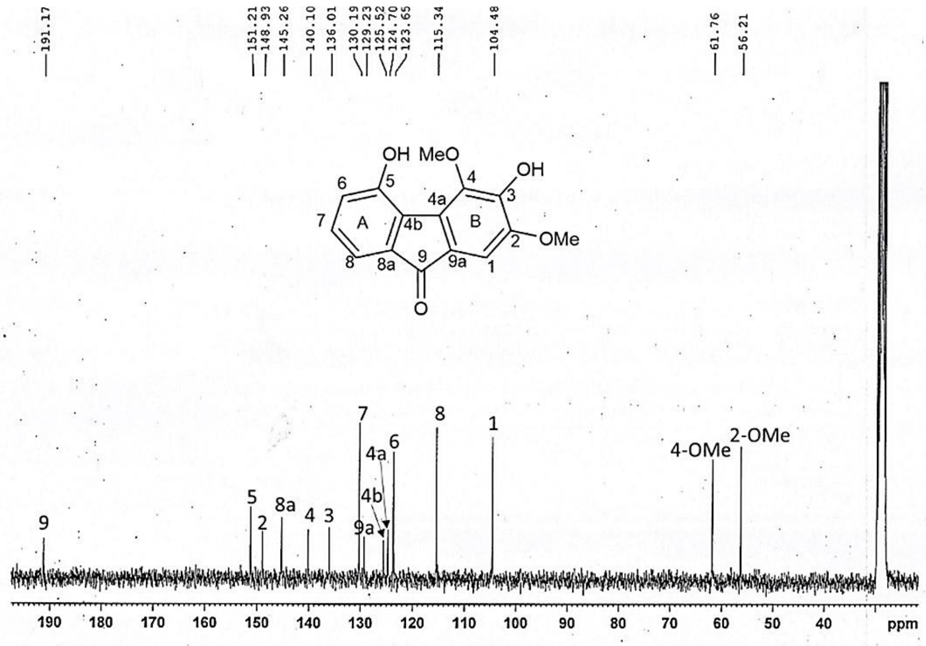


Figure 81 ^{13}C-NMR (75 MHz) spectrum of compound DG4

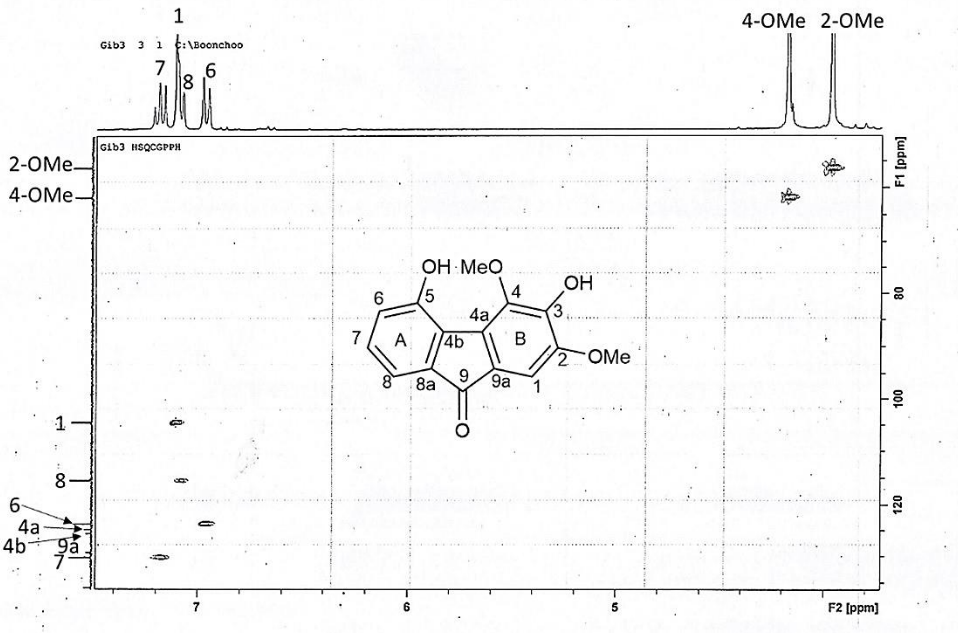


Figure 82 HSQC spectrum of compound DG4

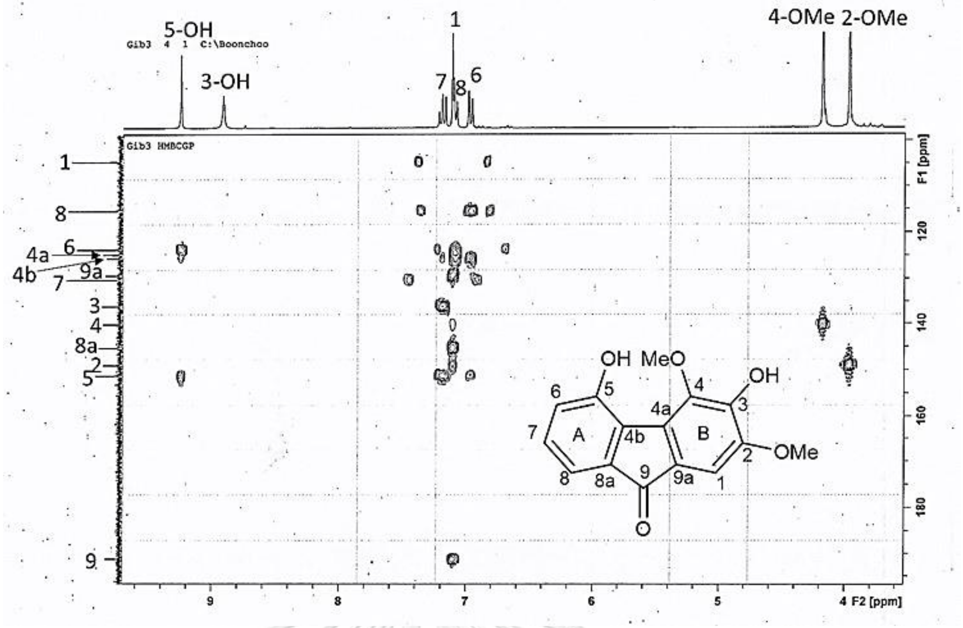


Figure 83 HMBC spectrum of compound DG4

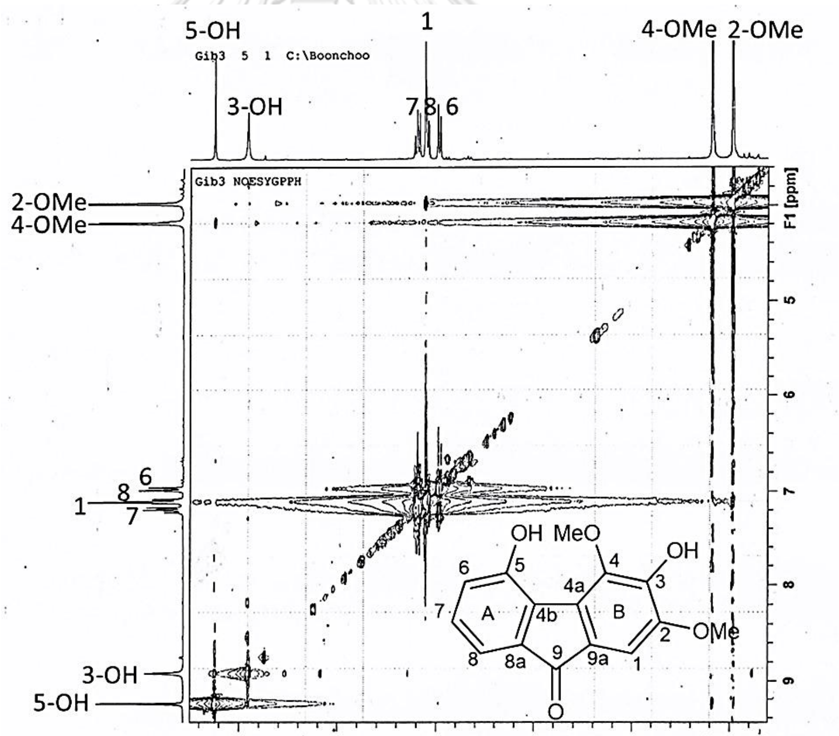


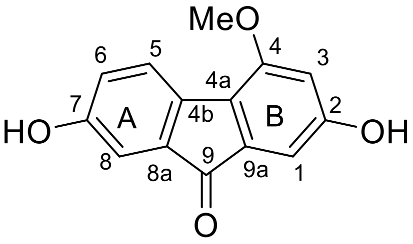
Figure 84 NOESY spectrum of compound DG4

2.2.5 Identification of compound DG5 (nobilone)

Compound DG5 was obtained as a reddish powder. The HR-ESI mass spectrum (**Figure 85**) showed a sodium adduct molecular ion $[M+Na]^+$ at *m/z* 265.04825, (calculated for $C_{14}H_{10}O_4Na$; 265.0476), suggesting the molecular formula $C_{14}H_{10}O_4$. The ^1H-NMR spectrum of DG5 (**Figure 86 and Table 21**) revealed signals for five aromatic protons at δ_H 6.81 (1H, d, J = 2.1 Hz, H-1), 6.78 (1H, d, J = 1.8 Hz, H-3), 7.15 (1H, d, J = 7.2 Hz, H-5), 6.94 (1H, dd, J = 2.1, 7.2 Hz, H-6) and 7.11 (1H, br s, H-8); two hydroxy protons at δ_H 9.14 (1H, s, 2-OH) and 8.93 (1H, s, 7-OH); one methoxy group at δ_H 4.13 (3H, s, 4-OMe). The ^{13}C-NMR and HSQC spectra of DG5 (**Figure 87, 88 and Table 21**) showed fourteen carbon signals, including a methoxy carbon, five methine carbons, seven aromatic quaternary carbons, and a carbonyl carbon (C-9) at δ_C 192.4. These NMR data indicated a fluorenone skeleton.

On ring A, the assignment of H-5 was obtained from its HMBC correlations (**Figure 89**) to C-7 (δ_C 150.8) and C-8a (δ_C 134.9). H-6 showed HMBC correlations to C-4b (δ_C 127.1) and C-8 (δ_C 115.9). The position of H-8 was assigned from its HMBC correlations to C-4b and C-6 (δ_C 124.2). In addition, 7-OH proton showed HMBC correlations with C-7 and C-6. On ring B, H-1 showed HMBC correlations to C-3 (δ_C 105.3) and C-4a (δ_C 121.8). The methoxy group was placed at C-4 from the NOESY correlation of 4-OMe protons to H-3 (**Figure 90**).

Through comparison the above NMR data with previously reported values (Klongkumnuankarn *et al*., 2015), DG5 was identified as nobilone [**308**]. Nobilone was also previously reported from other *Dendrobium* species, such as *D. brymerianum* (Klongkumnuankarn *et al*., 2015) *D. nobile* (Zhang *et al*., 2007), and *D. palpebrae* (Kyokong *et al*., 2018).

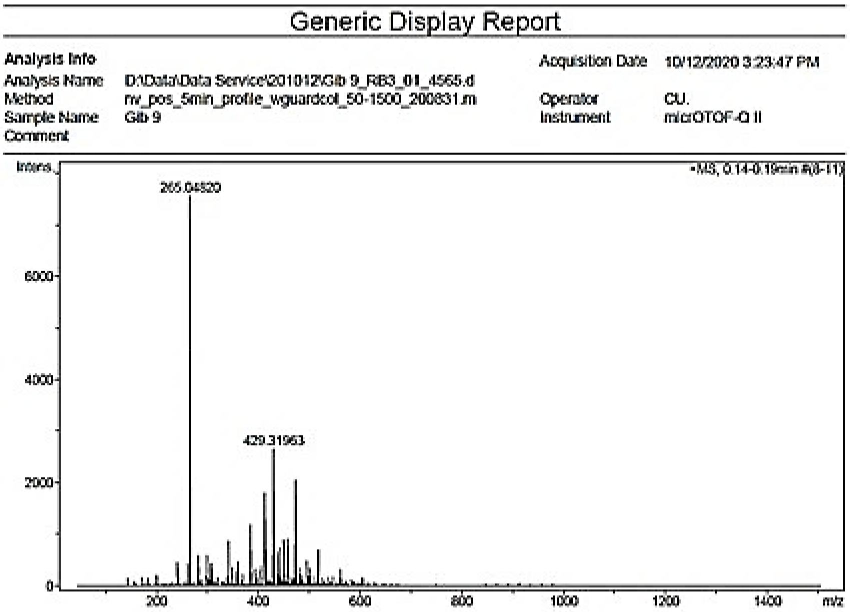


Nobilone [**308**]

Table 21 NMR spectral data of compound DG5 and nobilone

Position	DG5 (acetone-d_6)		Nobilone (acetone-d_6)	
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
1	6.81 (1H, d, 2.1)	105.1	6.80 (1H, d, 2.0)	105.9
2	-	160.0	-	160.9
3	6.78 (1H, d, 2.1)	105.3	6.78 (1H, d, 2.0)	106.2
4	-	152.7	-	153.5
4a	-	121.8	-	122.6
4b	-	127.1	-	128.0
5	7.15 (1H, d, 7.2)	129.3	7.13 (1H, d, 7.5)	130.2
6	6.94 (1H, dd, 2.1, 7.2)	124.2	6.93 (1H, dd, 1.5, 7.5)	125.0
7	-	150.8	-	151.6
8	7.11 (1H, br s)	115.9	7.10 (1H, d, 1.5)	116.7
8a	-	134.9	-	135.8
9	-	192.4	-	193.2
9a	-	136.4	-	137.2
4-OMe	4.13 (3H, s)	56.7	4.13 (3H, s)	57.5
2-OH	9.14 (1H, s)	-	-	-
7-OH	8.93 (1H, s)	-	-	-

(Klongkumnuankarn *et al*., 2015)



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Instrument micrOTOF-Q II

Figure 85 Mass spectrum of compound DG5

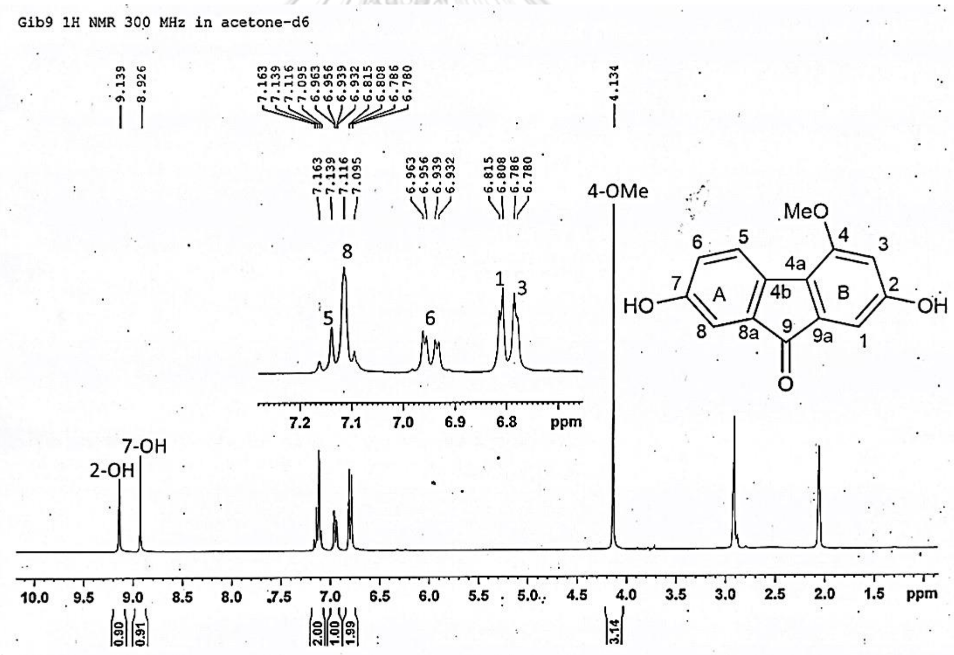


Figure 86 ^{1}H-NMR (300 MHz) spectrum of compound DG5

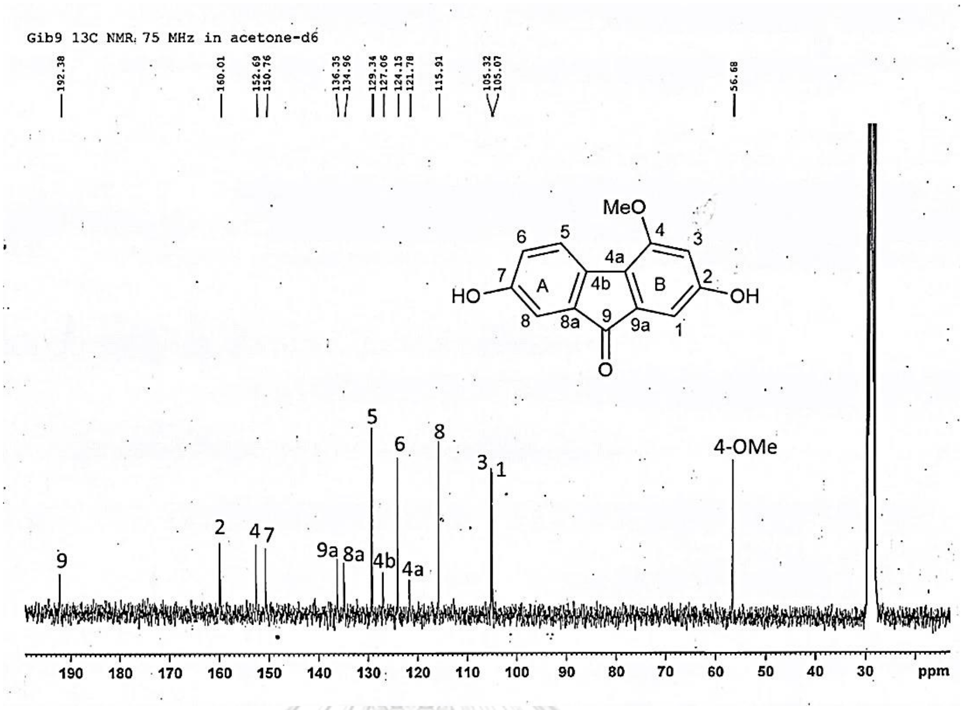


Figure 87 ^{13}C-NMR (75 MHz) spectrum of compound DG5

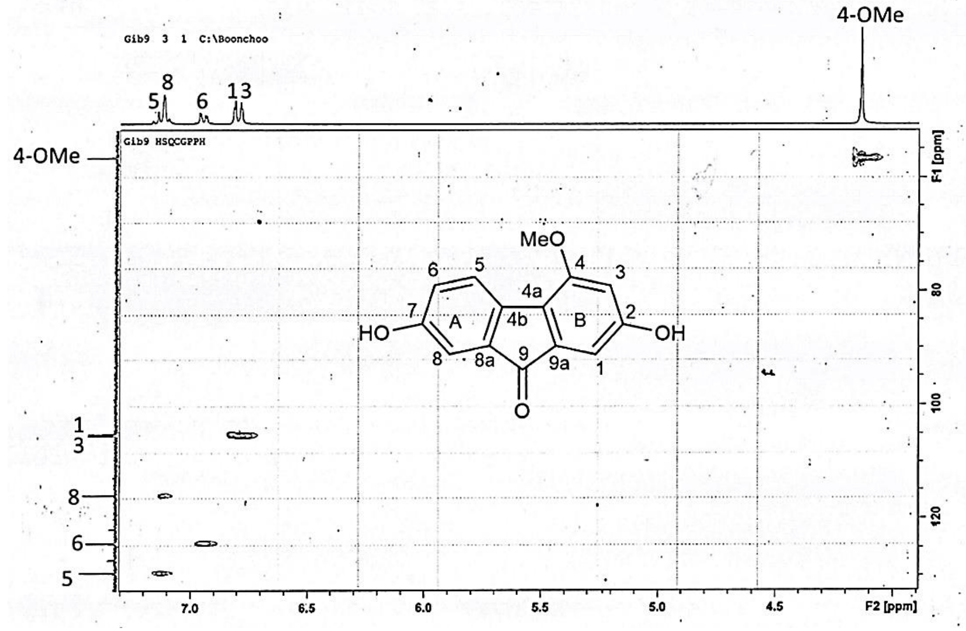


Figure 88 HSQC spectrum of compound DG5

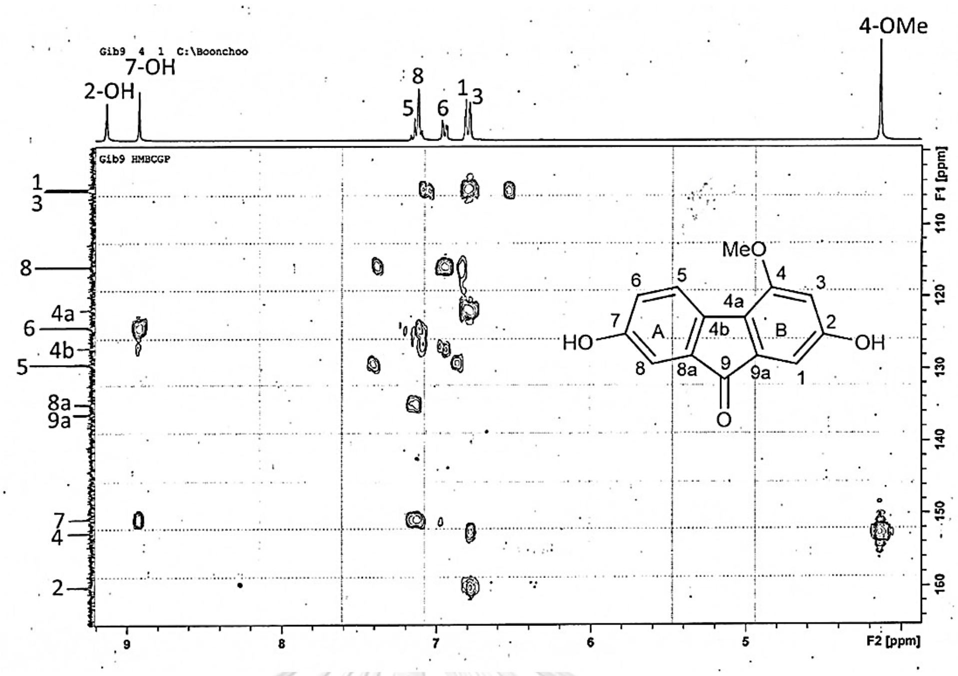


Figure 89 HMBC spectrum of compound DG5

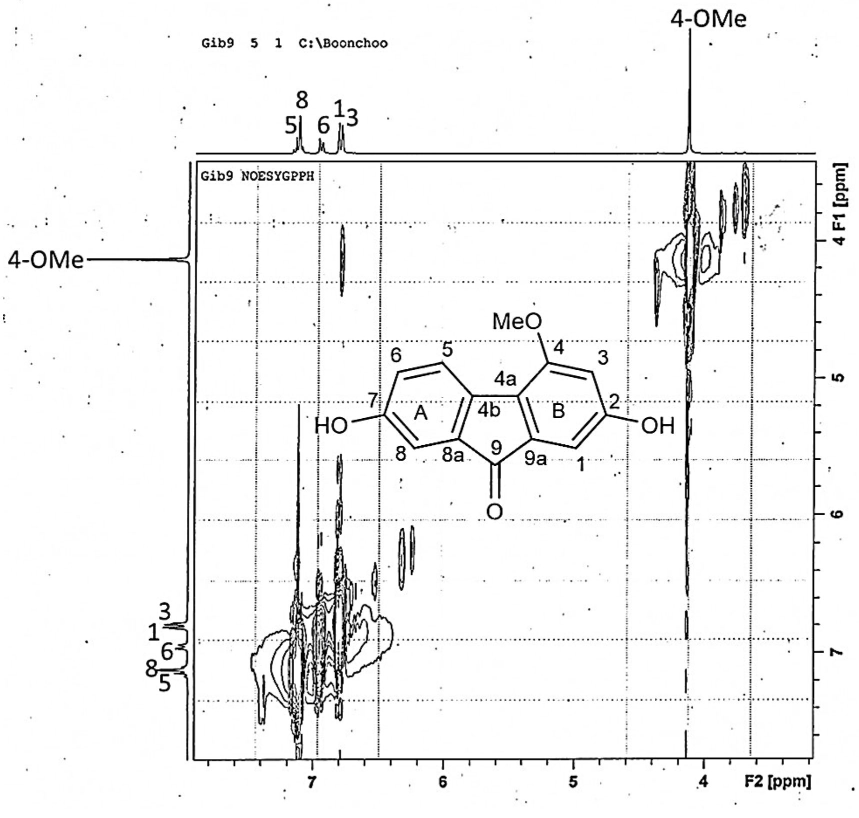


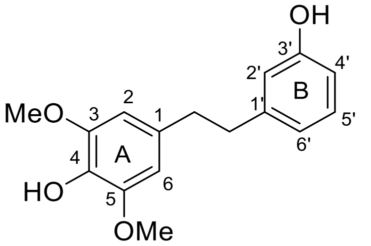
Figure 90 NOESY spectrum of compound DG5

2.2.6 Identification of compound DG6 (aloifol I)

Compound DG6 was obtained as a brown amorphous solid. The HR-ESI mass spectrum (**Figure 91**) showed a sodium adduct molecular ion $[M+Na]^+$ at *m/z* 297.1108, (calculated for $C_{16}H_{18}O_4Na$; 297.1102), suggesting the molecular formula $C_{16}H_{18}O_4$. The ^{1}H-NMR and ^{13}C-NMR spectra (**Figures 92 and 93 and Table 22**) showed signals of four methylene protons at δ_H 2.81 (4H, br s, H$_2$-α, H$_2$-α') and two methylene carbons at δ_C 37.9 (C-α), 37.7 (C-α'), characteristics of a bibenzyl derivative. The ^{13}C-NMR and HSQC spectra (**Figures 93 and 94**) of DG6 also showed sixteen carbon signals including two methylene carbons, two methoxy carbons at δ_C 55.7 (3-OMe and 5-OMe), six quaternary carbons and six methine carbons.

The signals for aromatic protons of ring A at δ_H 6.49 (2H, s, H-2/H-6) and methoxy groups at δ_H 3.78 (6H, s, 3-OMe/5-OMe) suggested symmetrical substitution. This was supported by the HMBC correlations (**Figure 95**) from H-2/H-6 to C-4 at δ_C 132.2; and from 3-OMe/5-OMe protons to C-3/C-5 at δ_C 147.6. The 4-OH proton at δ_H 6.92 showed HMBC correlations with C-3 and C-5. On ring B, four aromatic proton signals at δ_H 6.65 (1H, br d, *J* =7.8 Hz, H-2′), 6.65 (1H, br d, *J* =7.8 Hz, H-4′), 7.08 (1H, t, *J* =8.1 Hz, H-5′) and 6.65 (1H, br d, *J* = 7.8 Hz, H-6′) suggested 1′,3′-disubstitution, which was supported by the HMBC correlations from H-2′ and H-6′ to C-4′ (δ_C 112.7), from H-4′ to C-2′ (δ_C 115.4), and from H-5′ to C-1′ (δ_C 143.6) and C-3′ (δ_C 157.4). In addition, 3′-OH proton at δ_H 8.15 showed its HMBC correlations with C-2′ and C-4′.

The above spectroscopic studies suggested that compound DG6 was aloifol I [**20**], a bibenzyl earlier obtained from *Cymbidium aloifolium* (Juneja *et al.*, 1987). Aloifol I was previously reported from several *Dendrobium* species, such as *D. infundibulum* (Na Ranong, *et al.,* 2019), *D. longicornu* (Hu *et al.*, 2008), and *D. scabrilingue* (Sarakulwattana, *et al.,* 2020).

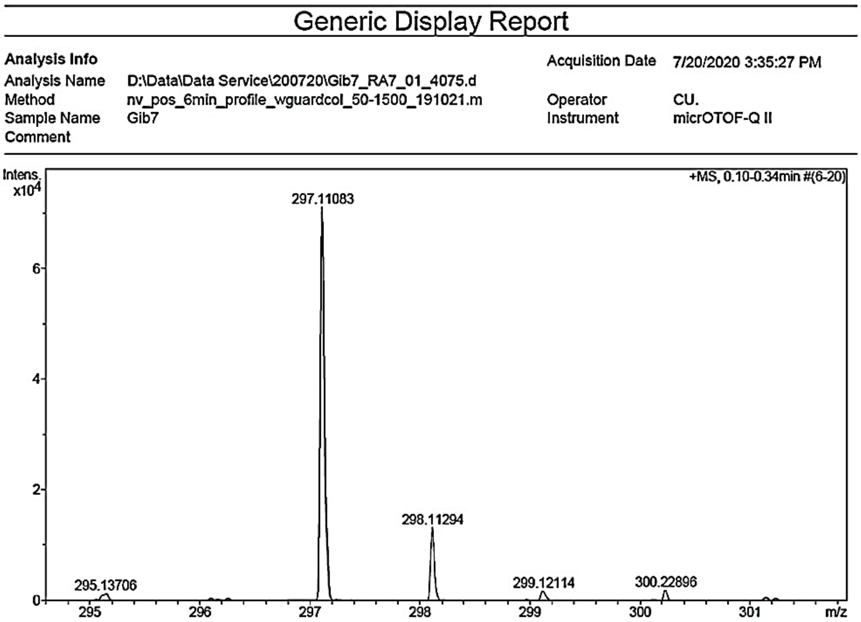


aloifol I [**20**]

Table 22 NMR spectral data of compound DG6 and aloifol I

Position	DG6 (acetone-d_6)		Aloifol I ($CDCl_3$)	
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
1	-	132.2	-	132.8
2	6.49 (1H, s)	105.9	6.27 (1H, s)	105.4
3	-	147.6	-	146.8
4	-	132.2	-	132.9
5	-	147.6	-	146.8
6	6.49 (1H, s)	105.9	6.27 (1H, s)	105.4
α	2.81 (2H, br s)	37.9	2.75 (2H, m)	36.7
α′	2.81 (2H, br s)	37.7	2.75 (2H, m)	37.7
1′	-	143.6	-	143.3
2′	6.65 (1H, br d, 7.8)	115.4	6.62 (1H, dd, 9.0, 2.5)	115.2
3′	-	157.4	-	155.9
4′	6.65 (1H, br d, 7.8)	112.7	6.62 (1H, dd, 9.0, 2.5)	112.9
5′	7.08 (1H, t, 7.8)	129.1	7.03 (1H, t, 9.0)	129.2
6′	6.65 (1H, br d, 7.8)	119.6	6.62 (1H, dd, 9.0, 2.5)	120.5
3-OMe	3.78 (3H, s)	55.7	3.72 (3H, s)	56.2
5-OMe	3.78 (3H, s)	55.7	3.76 (3H, s)	56.2
4-OH	6.92 (1H, s)	-	-	-
3′-OH	8.15 (1H, s)	-	-	-

(Juneja *et al.*, 1987)



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Comment			

Figure 91 Mass spectrum of compound DG6

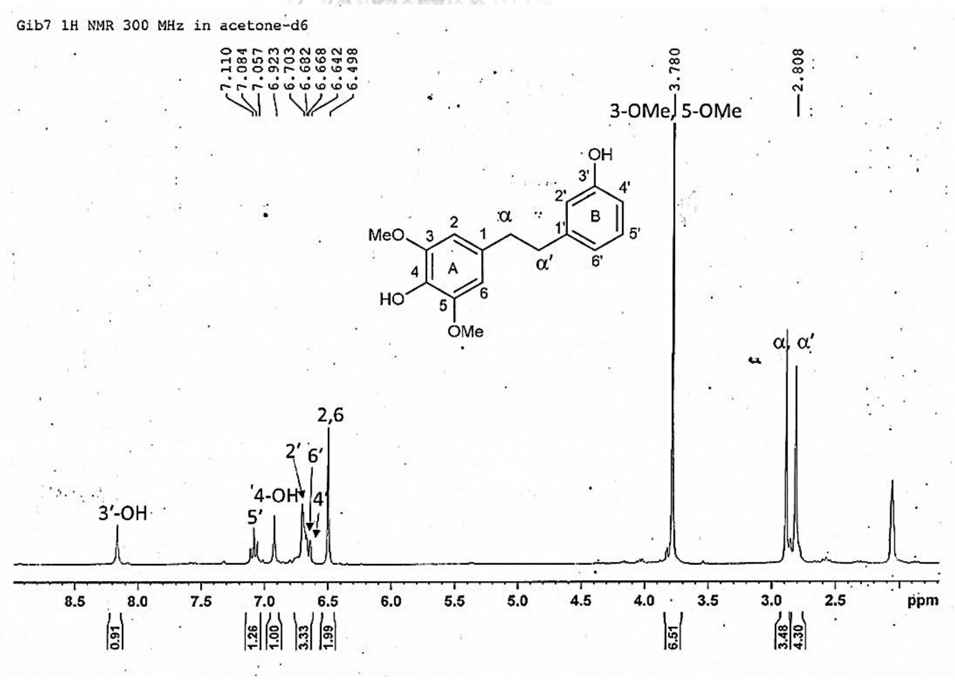


Figure 92 ^{1}H-NMR (300 MHz) spectrum of compound DG6

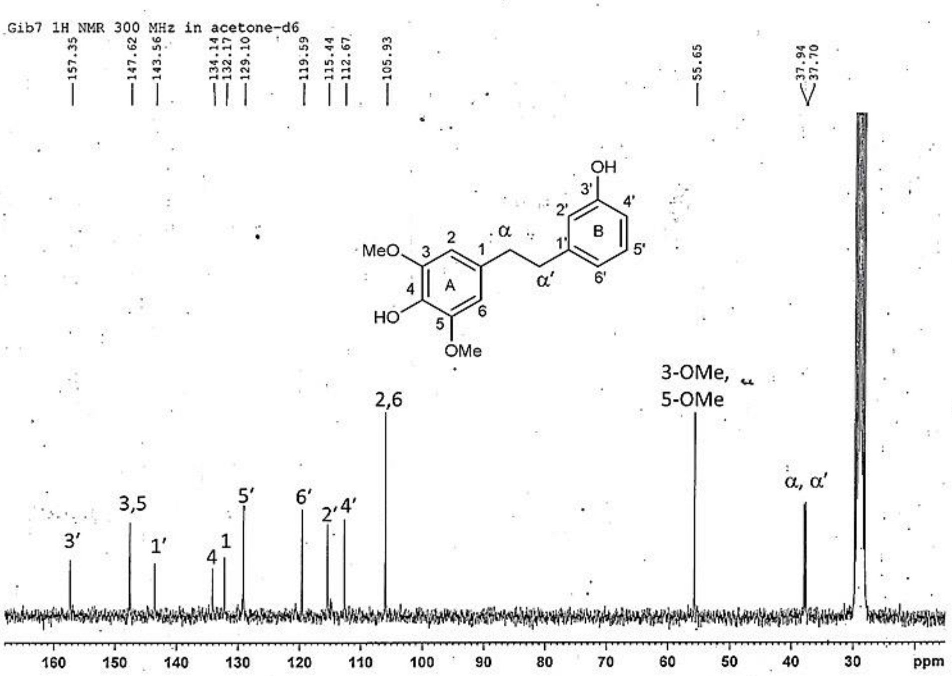


Figure 93 ^{13}C-NMR (75 MHz) spectrum of compound DG6

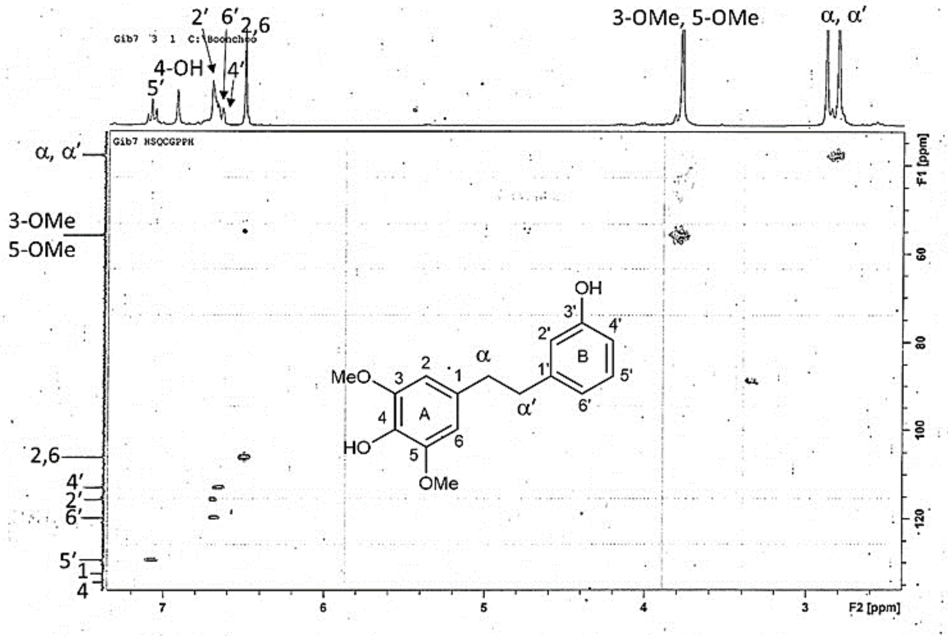


Figure 94 HSQC spectrum of compound DG6

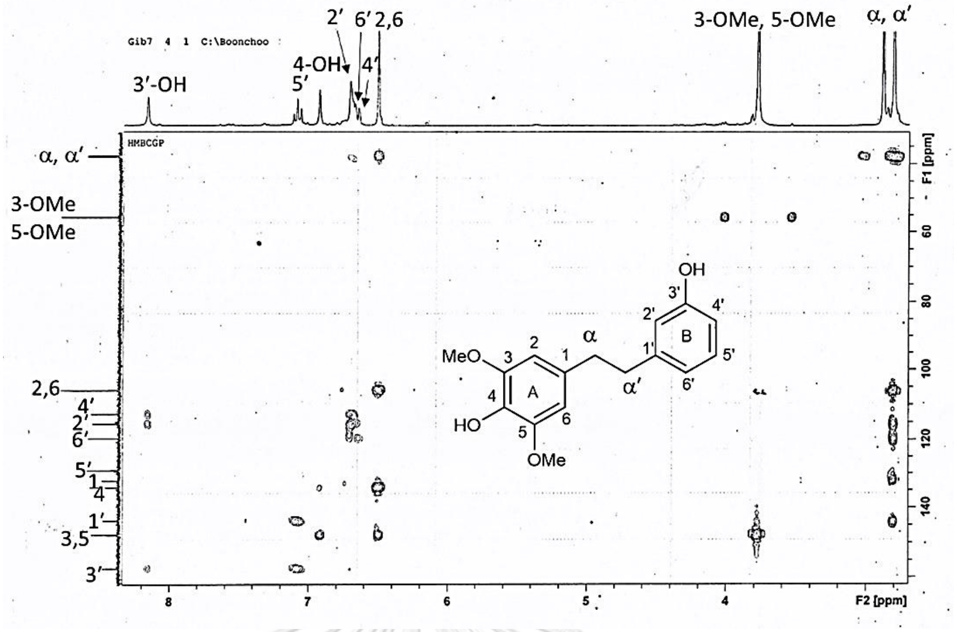


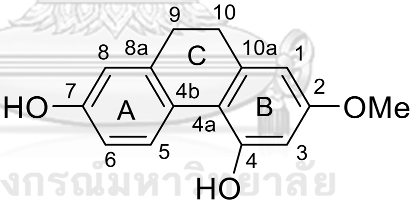
Figure 95 HMBC spectrum of compound DG6

2.2.7 Identification of compound DG7 (lusianthridin)

Compound DG7 was obtained as a brown amorphous solid. The HR-ESI mass spectrum (**Figure 96**) showed a sodium adduct molecular ion $[M+Na]^+$ at *m/z* 265.0840, (calculated for $C_{15}H_{14}O_3Na$; 265.08406), suggesting the molecular formula $C_{15}H_{14}O_3$. The ^{1}H-NMR spectrum of DG7 (**Figure 97 and Table 23**) exhibited five aromatic proton signals at δ_H 6.38 (1H, d, *J* = 2.1 Hz, H-1), 6.43 (1H, d, *J* = 2.4 Hz, H-3), 8.31 (1H, d, *J* = 9.3 Hz, H-5), 6.68 (1H, br d, *J* = 9.3 Hz, H-6), and 6.68 (1H, br s, H-8), four methylene protons at δ_H 2.68 (4H, m, H_2-9, H_2-10), two hydroxy protons at δ_H 8.56 (1H, s, 4-OH) and 8.16 (1H, s, 7-OH), and a methoxy signal at δ_H 3.74 (3H, s, 2-OMe). The ^{13}C-NMR and HSQC spectra (**Figures 98 and 99**) displayed fifteen carbon signals, representing two methylene carbons at C-9 (δ_C 29.8) and C-10 (δ_C 30.6), a methoxy carbon at δ_C 54.4, five aromatic methine carbons, and seven quaternary carbons. The above NMR data indicated a dihydrophenanthrene skeleton, which was further confirmed by the HMBC correlations (**Figure 100**) from the methylene carbons C-9 to H-8 and C-10 to H-1.

The H-5 proton of ring A showed *ortho*-coupling with H-6 and HMBC correlation with C-7 (δ_C 155.2). H-6 exhibited HMBC correlation with C-8 (δ_C 114.1), and H-8 displayed correlation with C-6 (δ_C 112.6). The 7-OH proton showed its HMBC correlation with C-6. On ring B, H-1 showed *meta*-coupling with H-3 and HMBC correlations with C-3 (δ_C 100.7) and C-10 (δ_C 30.6). H-3 showed HMBC correlation with C-1 (δ_C 105.1). The HMBC spectrum also revealed correlations of 4-OH proton to C-3, C-4 (δ_C 155.0) and C-4a (δ_C 114.9). The position of the methoxy group at C-2 was supported by the HMBC correlation from its protons to C-2 and further confirmed by the NOESY correlation between 2-OMe protons and H-3 (**Figure 101**).

The above NMR data suggested that compound DG7 was lusianthridin [**97**], and this was confirmed by comparing with the previously reported NMR values of lusianthridin from *Pholidota yunnanensis* (Guo *et al.*, 2007). Lusianthridin was also reported from several *Dendrobium* species (Yamaki & Honda, 1996; Sarakulwattana *et al.*, 2020).

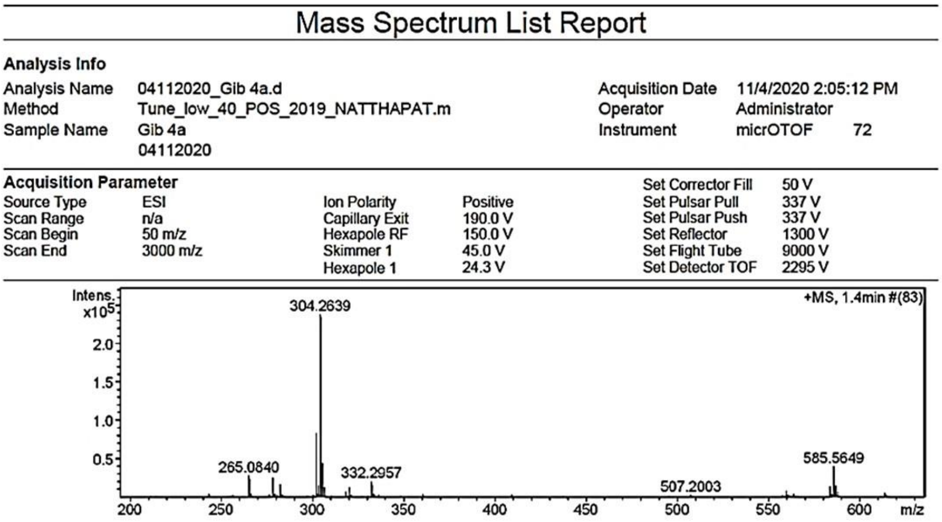


lusianthridin [**97**]

Table 23 NMR spectral data of compound DG7 and lusianthridin

Position	DG7 (acetone-d_6)		Lusianthridin (acetone-d_6)	
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
1	6.38 (1H, d, 2.4)	105.1	6.37 (1H, d, 2.6)	106.0
2	-	158.4	-	159.3
3	6.43 (1H, d, 2.4)	100.7	6.44 (1H, d, 2.6)	101.6
4	-	155.0	-	155.9
4a	-	114.9	-	115.9
4b	-	124.9	-	125.9
5	8.31 (1H, d, 9.3)	129.0	8.22 (1H, d, 7.5)	129.9
6	6.68 (1H, br d, 9.3)	112.6	6.68 (1H, dd, 2.7, 7.5)	113.5
7	-	155.2	-	156.1
8	6.68 (1H, br s)	114.1	6.69 (1H, m)	115.0
8a	-	138.9	-	139.8
9	2.68 (2H, m)	29.8	2.67 (2H, m)	30.8
10	2.68 (2H, m)	30.6	2.67 (2H, m)	31.5
10a	-	140.5	-	141.4
2-OMe	3.74 (3H, s)	54.4	3.72 (3H, s)	55.3
4-OH	8.56 (1H, s)	-	-	-
7-OH	8.16 (1H, s)	-	-	-

(Guo *et al.*, 2007)



Mass Spectrum List Report

Analysis Info

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Sample Name	Gib 4a 04112020	Instrument	micrOTOF 72

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Corrector Fill	50 V
Scan Range	n/a	Capillary Exit	190.0 V	Set Pulsar Pull	337 V
Scan Begin	50 m/z	Hexapole RF	150.0 V	Set Pulsar Push	337 V
Scan End	3000 m/z	Skimmer 1	45.0 V	Set Reflector	1300 V
		Hexapole 1	24.3 V	Set Flight Tube	9000 V
				Set Detector TOF	2295 V

Figure 96 Mass spectrum of compound DG7

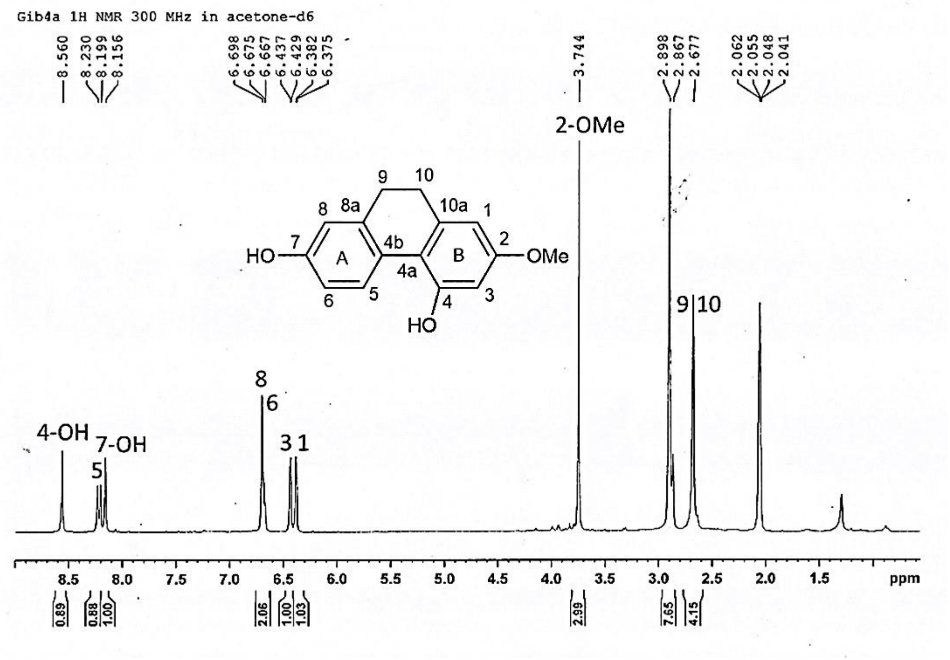


Figure 97 ^{1}H-NMR (300 MHz) spectrum of compound DG7

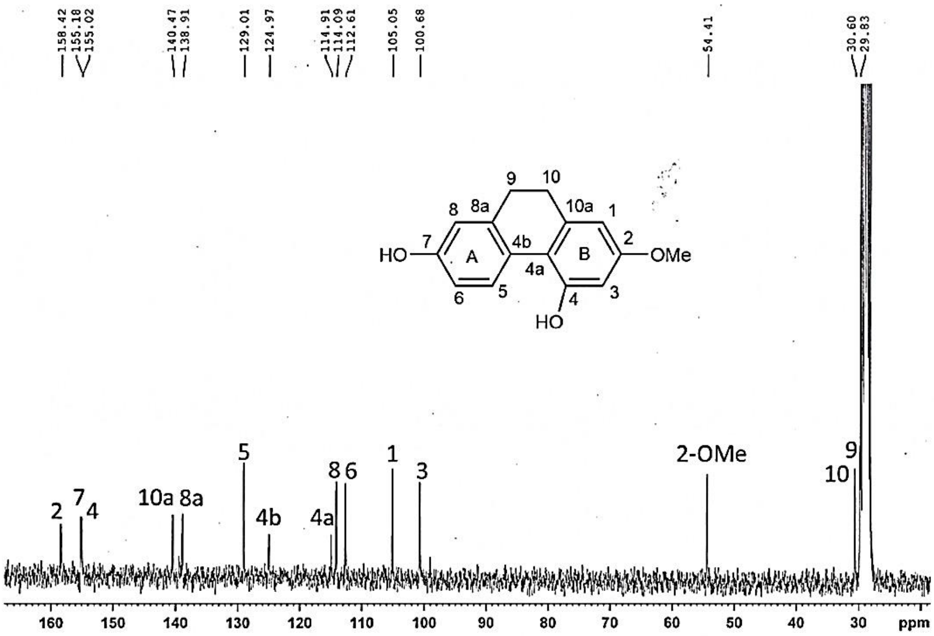


Figure 98 ^{13}C-NMR (75 MHz) spectrum of compound DG7

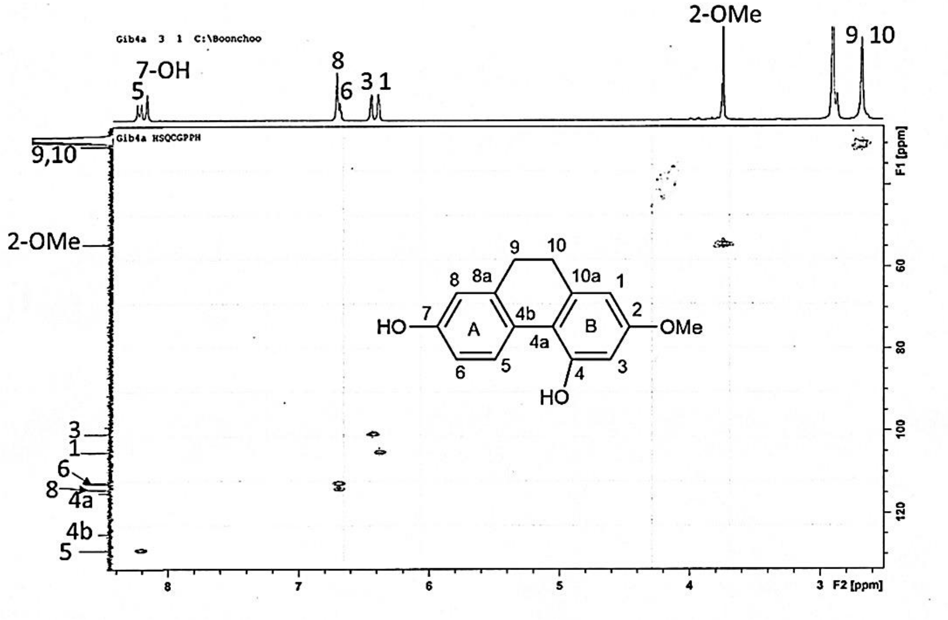


Figure 99 HSQC spectrum of compound DG7

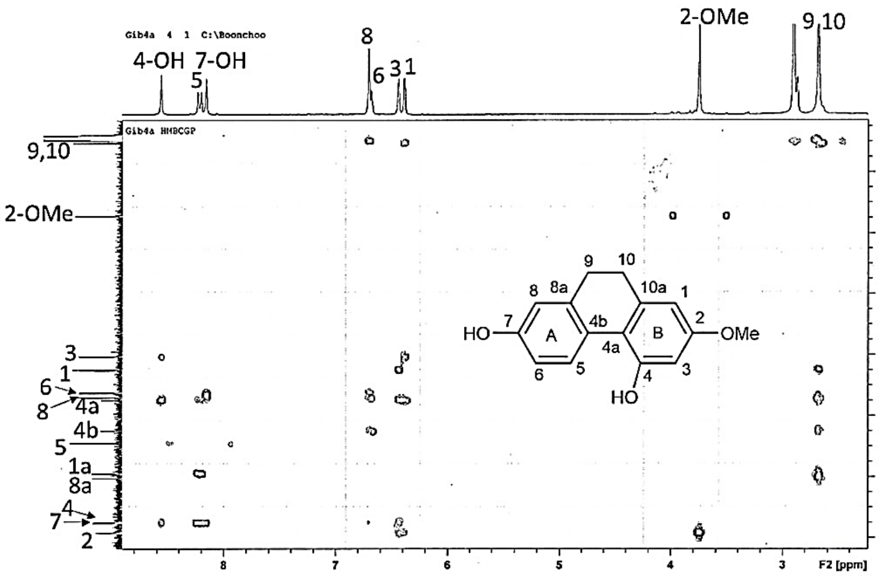


Figure 100 HMBC spectrum of compound DG7

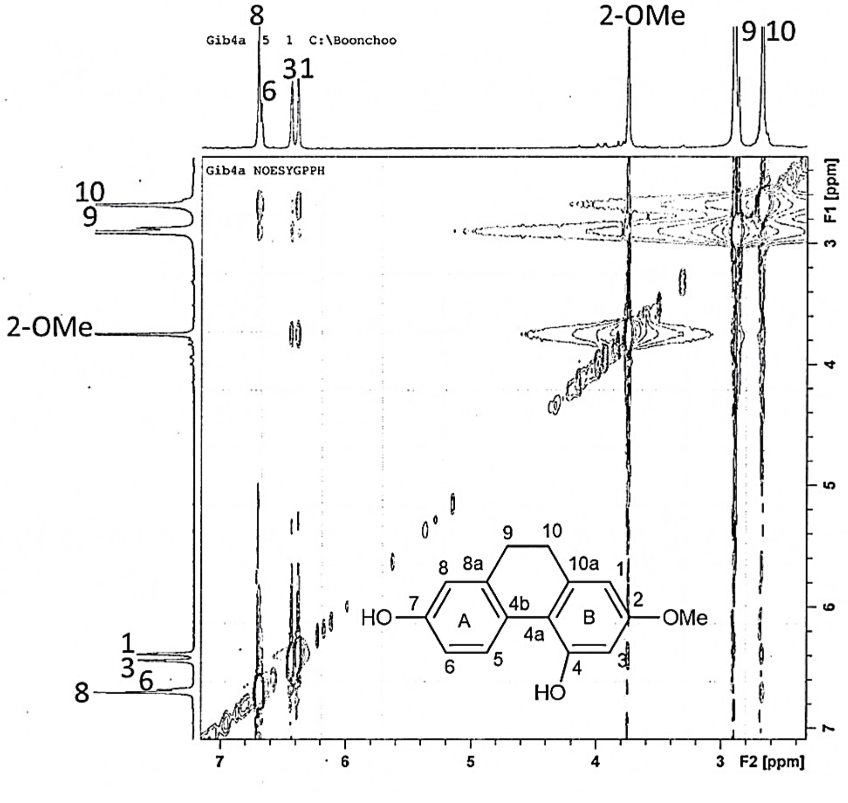


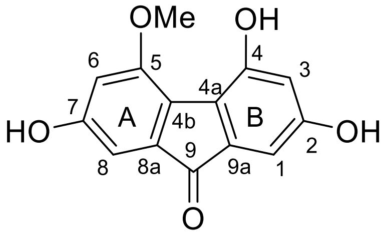
Figure 101 NOESY spectrum of compound DG7

2.2.8 Identification of compound DG8 (denchrysan A)

Compound DG8 was obtained as a reddish powder. The HR-ESI mass spectrum (**Figure 102**) showed a sodium adduct molecular ion $[M+Na]^+$ at *m/z* 281.0378, (calculated for $C_{14}H_{10}O_5Na$; 281.0425), suggesting the molecular formula $C_{14}H_{10}O_5$. The ^{1}H-NMR spectrum of DG8 (**Figure 103 and Table 24**) showed signals for four aromatic protons at δ_H 6.65 (1H, d, *J* = 2.1 Hz, H-1), 6.39 (1H, d, *J* = 2.1 Hz, H-3), 6.74 (1H, br s, H-6), and 6.76 (1H, br s, H-8), a free phenolic OH at δ_H 8.84 (1H, s, 4-OH) and a methoxy group at δ_H 4.10 (3H, s, 5-OMe). The ^{13}C-NMR and HSQC spectra (**Figures 104 and 105**) showed 14 carbon signals representing a methoxy carbon at δ_C 56.6 (5-OMe), four methine and nine quaternary carbons including a carbonyl carbon (C-9 at δ_C 192.5). These NMR signals indicated a fluorenone skeleton.

The H-6 proton of ring A showed HMBC correlations (**Figure 106**) with C-4b (δ_C 122.7) and C-8 (δ_C 105.1), and H-8 showed correlations with C-4b, C-6 (δ_C 105.4) and C-9 (δ_C 192.5). On ring B, H-1 and H-3, a pair of *meta*-coupled aromatic protons, showed HMBC correlations with C-4a (δ_C 119.1). The methoxy group at C-5 was confirmed by the NOESY correlation of 5-OMe protons with H-6 and 4-OH (**Figure 107**).

Based on the above NMR spectral data, compound DG8 was identified as denchrysan A [**305**]. This was confirmed by comparing the NMR data with the previously reported values for denchrysan A, which was earlier isolated from *Dendrobium chrysotoxum* (Chen *et al.*, 2008b).

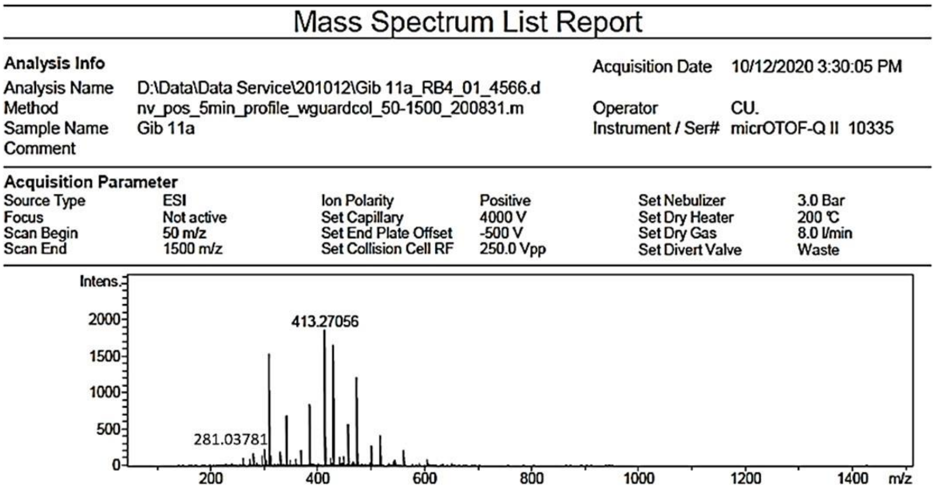


denchrysan A [**305**]

Table 24 NMR spectral data of compound DG8 and denchrysan A

Position	DG8 (acetone-d_6)		Denchrysan A (acetone-d_6)	
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
1	6.65 (1H, d, 2.1)	104.5	6.77 (1H, d, 1.6)	105.8
2	-	158.8	-	160.2
3	6.39 (1H, d, 2.1)	109.1	6.75 (1H, d, 1.6)	110.4
4	-	151.7	-	153.0
4a	-	119.1	-	120.4
4b	-	122.7	-	124.1
5	-	151.7	-	153.0
6	6.74 (1H, br s)	105.4	6.4 (1H, d, 2.2)	104.8
7	-	159.2	-	160.5
8	6.76 (1H, br s)	105.1	6.65 (1H, d, 2.2)	106.5
8a	-	136.2	-	137.5
9	-	192.5	-	193.8
9a	-	136.2	-	137.5
5- OMe	4.10 (3H, s)	56.6	4.10 (3H, s)	57.9
4-OH	8.84 (1H, s)	-	-	-

(Chen *et al.*, 2008b)



Mass Spectrum List Report

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Sample Name	Gib 11a	Instrument / Ser#	micrOTOF-Q II 10335
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	3.0 Bar
Focus	Not active	Set Capillary	4000 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	8.0 l/min
Scan End	1500 m/z	Set Collision Cell RF	250.0 Vpp	Set Divert Valve	Waste

Figure 102 Mass spectrum of compound DG8

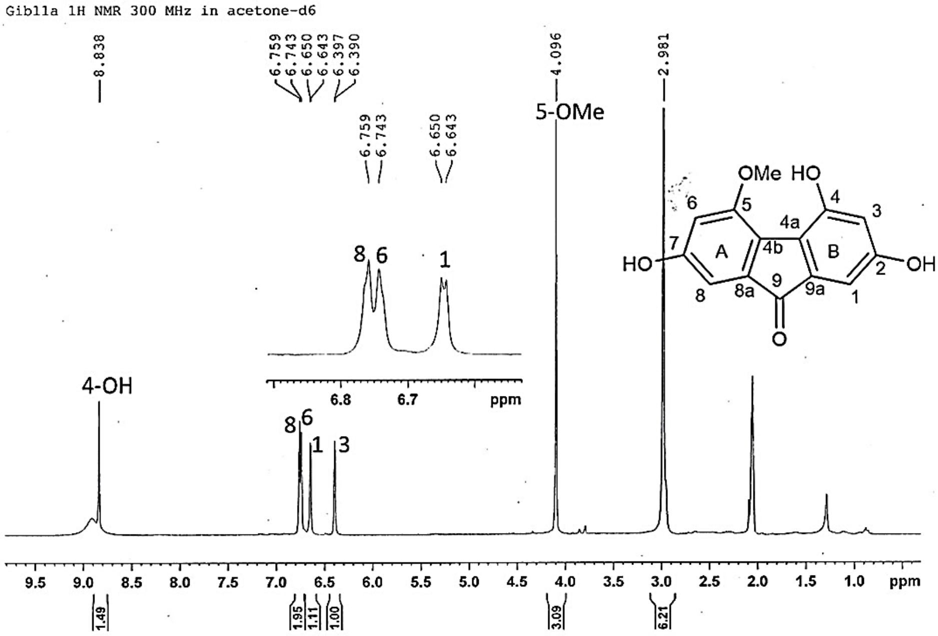


Figure 103 ^{1}H-NMR (300 MHz) spectrum of compound DG8

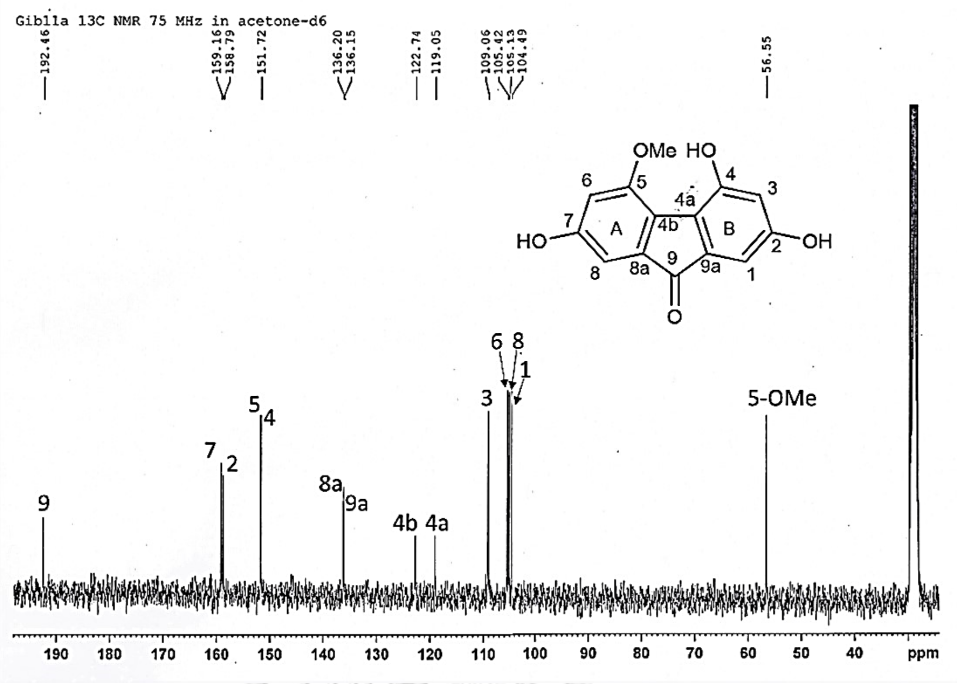


Figure 104 ^{13}C-NMR (75 MHz) spectrum of compound DG8

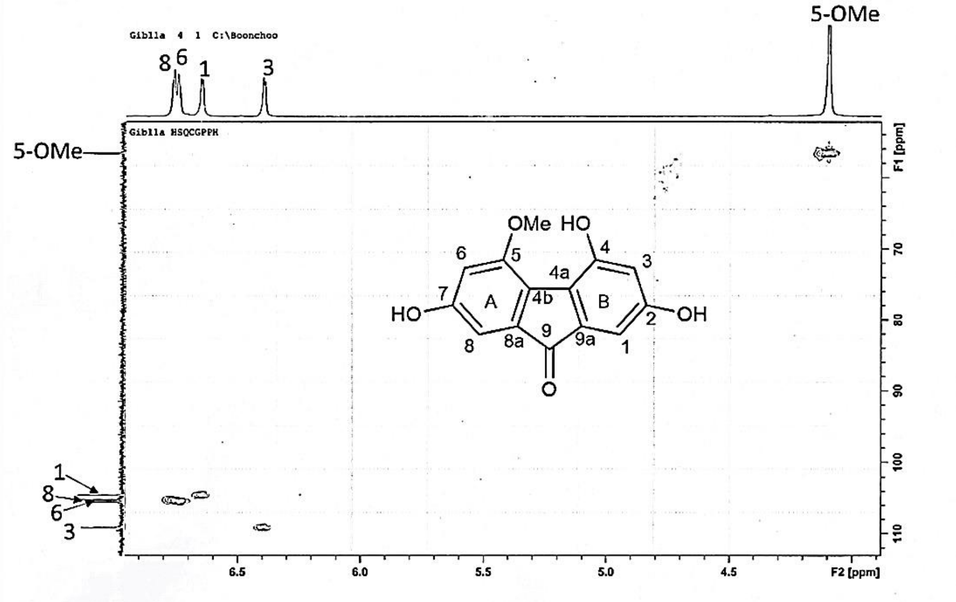


Figure 105 HSQC spectrum of compound DG8

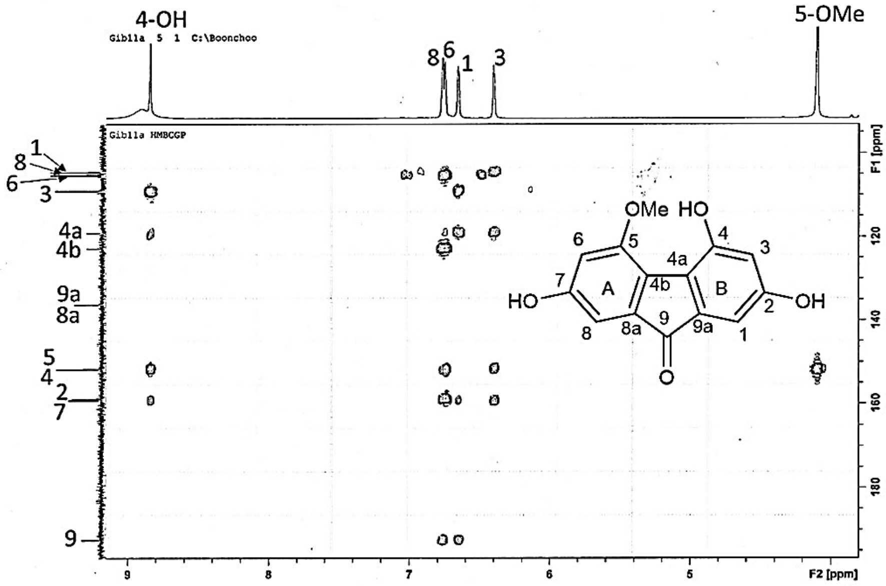


Figure 106 HMBC spectrum of compound DG8

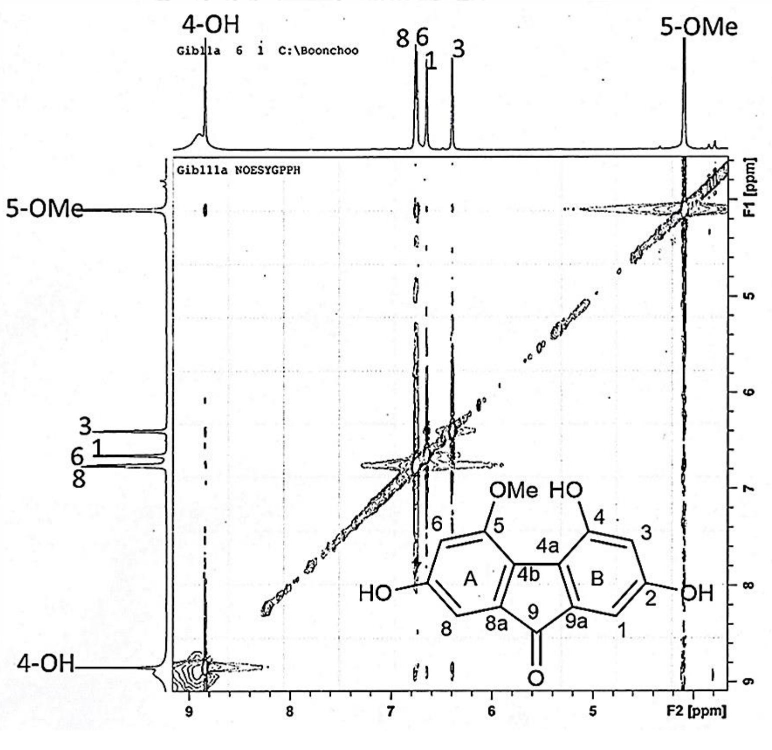


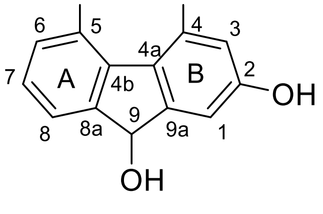
Figure 107 NOESY spectrum of compound DG8

2.2.9 Identification of compound DG9 (4-methoxy-9H-fluorene-2,5,9-triol)

Compound DG9 was obtained as a white powder. The HR-ESI mass spectrum (**Figure 108**) showed a sodium adduct molecular ion $[M+Na]^+$ at *m/z* 267.0636, (calculated for $C_{14}H_{12}O_4Na$; 267.0633), suggesting a molecular formula of $C_{14}H_{12}O_4$. The ^{1}H-NMR spectrum of DG9 (**Figure 109 and Table 25**) displayed signals for five aromatic protons at δ_H 6.73 (1H, d, *J* = 7.5 Hz, H-6), 7.09 (1H, t, *J* = 7.8 Hz, H-7), 7.04 (1H, d, *J* = 6.6 Hz, H-8), 6.84 (1H, br s, H-1), and 6.61 (1H, br s, H-3); hydroxy proton at δ_H 9.09 (1H, s, 5-OH) and a signal for a methoxy group at δ_H 4.08 (3H, s, 4-OMe). The ^{1}H-NMR spectrum also showed resonances at δ_H 5.39 (2H, d, *J* = 7.2 Hz, H-9) and 4.63 (d, *J* = 7.8 Hz, 9-OH), suggesting a fluorene structure. This was supported by the ^{13}C-NMR and HSQC spectra (**Figures 110 and 111**) which showed 14 carbon signals representing a methoxy carbon at δ_C 56.2 (4-OMe), five methine, and seven quaternary carbons, and an oxygenated methine carbon at δ_C 74.6 (C-9).

Three aromatic protons with *ortho*-couplings on ring A were assigned to H-6, H-7, and H-8 from their HMBC correlations (**Figure 112**). H-7 showed HMBC correlations with C-5 (δ_C 150.6) and C-8a (δ_C 147.7). On ring B, H-1 showed HMBC correlations with C-3 (δ_C 99.5) and C-4a (δ_C 99.5), and in return, H-3 showed correlations with C-1 (δ_C 106.3) and C-4a. The position of 4-OMe was confirmed by the NOESY correlation of 4-OMe protons with H-3 and 5-OH (**Figure 113**).

Through comparison of ^{1}H-NMR and ^{13}C-NMR data with literature values (Yang *et al.*, 2004), DG9 was identified as 4-methoxy-9*H*-fluorene-2,5,9-triol and its trivial name was denchrysan B [**312**]. It was previously reported from *Dendrobium chrysotoxum* (Yang *et al*., 2004).

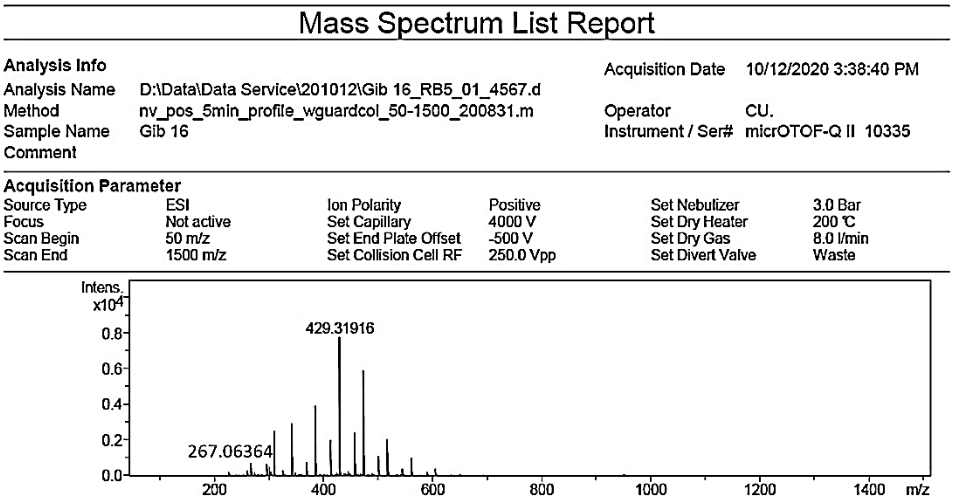


4-methoxy-9*H*-fluorene-2,5,9-triol [**312**]

Table 25 NMR spectral data of compound DG9 and 4-methoxy-9*H*-fluorene-2,5,9-triol

Position	DG9 (acetone-d_6)		4-methoxy-9*H*-fluorene-2,5,9-triol (DMSO-d_6)	
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
1	6.84 (1H, br s)	106.3	6.71 (1H, d, 1.7)	106.2
2	-	158.7	-	158.6
3	6.61 (1H, br s)	99.5	6.52 (1H, d, 1.7)	99.3
4	-	152.1	-	151.6
4a	-	118.1	-	116.9
4b	-	123.8	-	123.5
5	-	150.6	-	149.5
6	6.73 (1H, d, 7.5)	116.1	6.73 (1H, d, 7.2)	115.8
7	7.09 (1H, t, 7.8)	127.6	7.14 (1H, t, 7.2)	127.3
8	7.04 (1H, d, 6.6)	116.1	7.10 (1H, d, 7.2)	116.1
8a	-	147.7	-	147.6
9	5.39 (2H, d, 7.2)	74.6	5.28 (2H, d, 7.7)	73.6
9a	-	149.9	-	149.7
4-MeO	4.08 (3H, s)	56.2	4.03 (3H, s)	56.6
5-OH	9.09 (1H, s)	-	9.11 (1H, s)	-
9-OH	4.63 (1H, d, 7.8)	-	5.74 (1H, d, 7.7)	-

(Yang *et al.*, 2004)



Mass Spectrum List Report

Analysis Info

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Sample Name	Gib 16	Instrument / Ser#	micrOTOF-Q II 10335
Comment			

Acquisition Parameter

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Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	8.0 l/min
Scan End	1500 m/z	Set Collision Cell RF	250.0 Vpp	Set Divert Valve	Waste

Figure 108 Mass spectrum of compound DG9

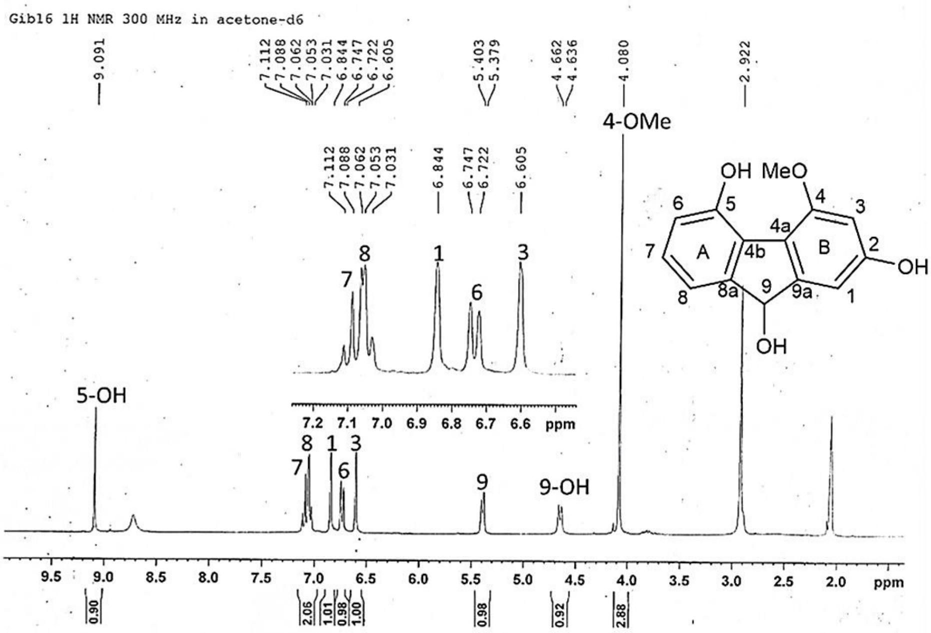


Figure 109 ^{1}H-NMR (300 MHz) spectrum of compound DG9

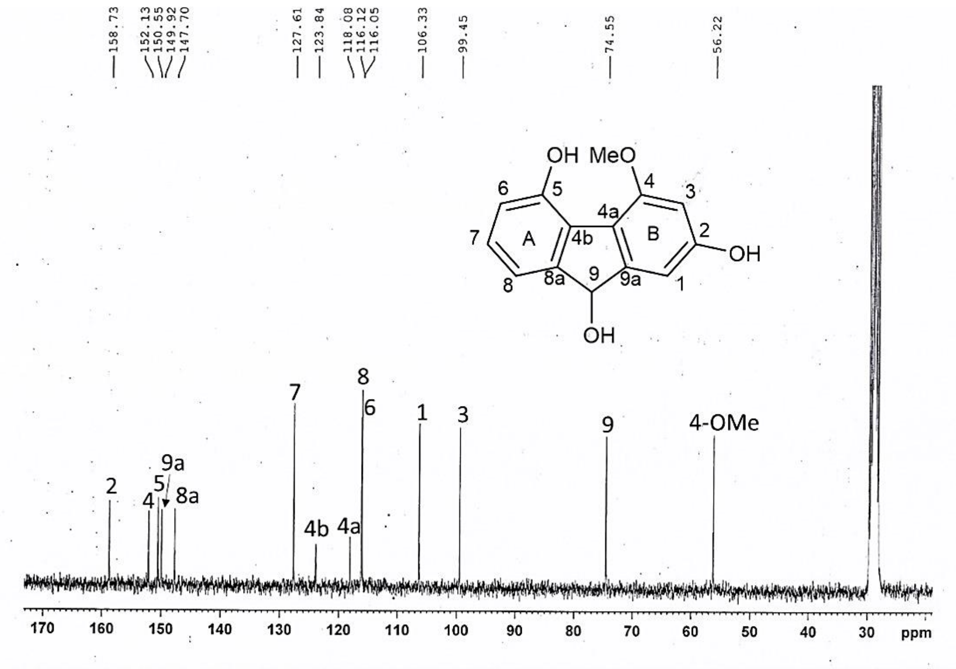


Figure 110 ^{13}C-NMR (75 MHz) spectrum of compound DG9

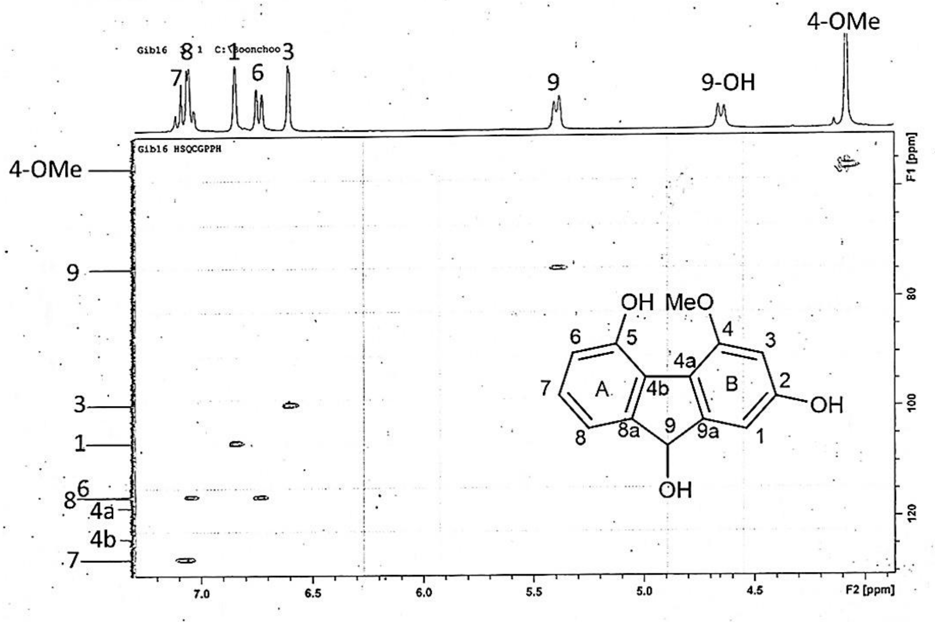


Figure 111 HSQC spectrum of compound DG9

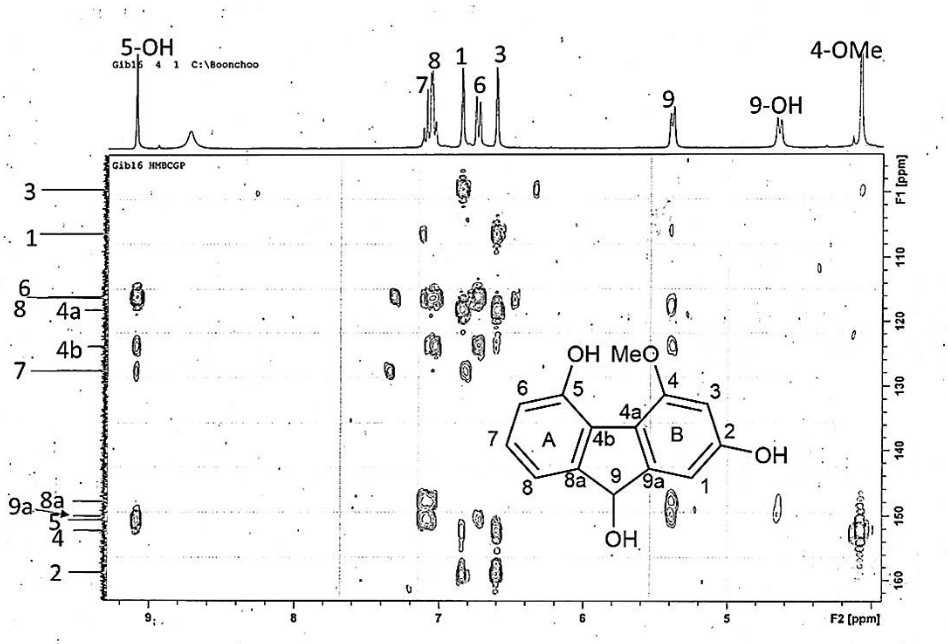


Figure 112 HMBC spectrum of compound DG9

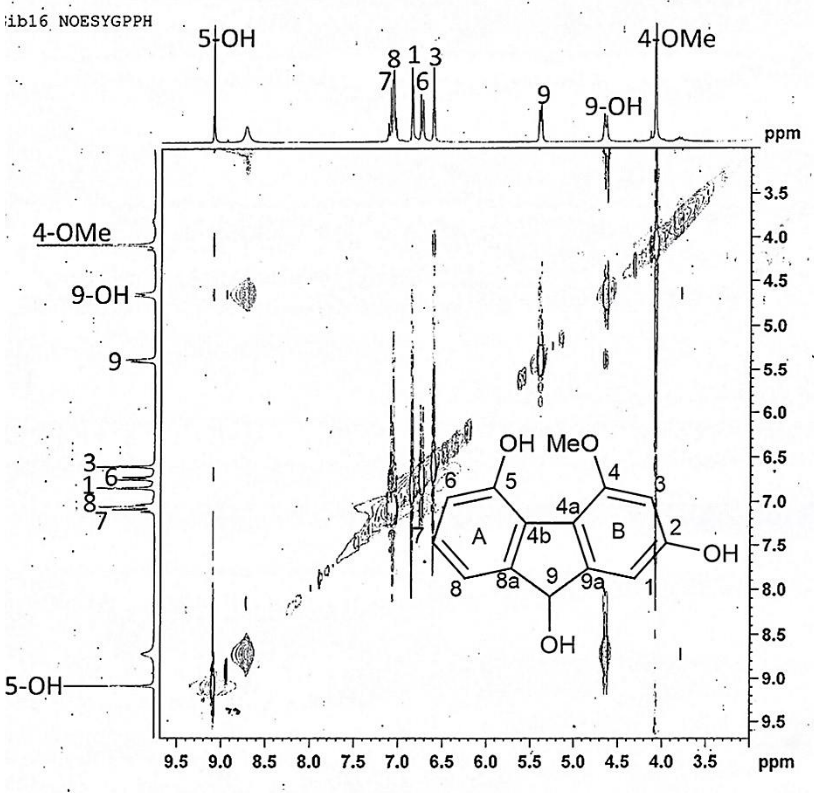
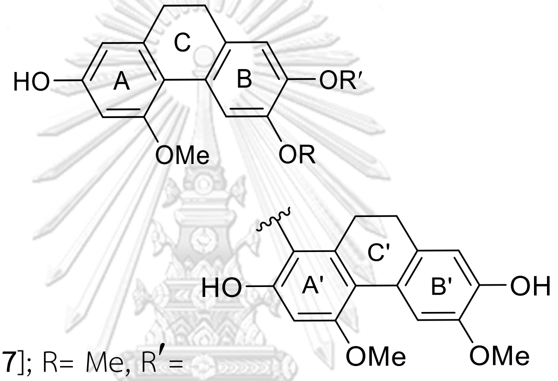


Figure 113 NOESY spectrum of compound DG9

2.3 Chemical investigation of EtOAc extract of *Aerides multiflora*

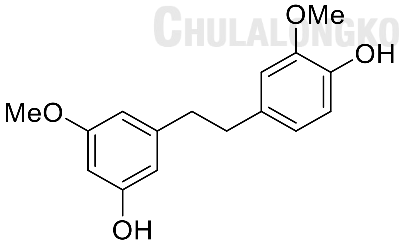
Three new compounds namely aerimultins A-C [**337**–**339**] and a new natural product, dihydrosinapyl dihydroferulate [**340**] were isolated from the EtOAc extract of *Aerides multiflora*. In addition, six known compounds were obtained, including 6-methoxycoelonin [**332**], gigantol [**2**], imbricatin [**330**], agrostonin [**341**], dihydroconiferyl dihydro-*p*-coumarate [**277**], and 5-methoxy-9,10-dihydrophenanthrene-2,3,7-triol [**342**] (**Figure 14**).



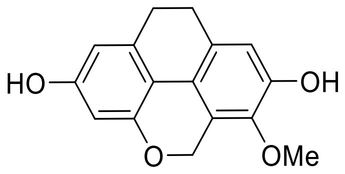
aerimultin A [**337**]; R= Me, R′ =

6-methoxycoelonin [**332**]; R= Me, R′ = H

5-methoxy-9,10-dihydrophenanthrene-2,3,7-triol [**342**]; R= H, R′ = H

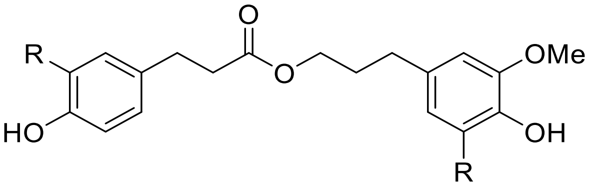


gigantol [**2**]



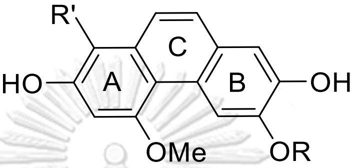
imbricatin [**330**]

Figure 114 Structures of compounds isolated from *Aerides multiflora*

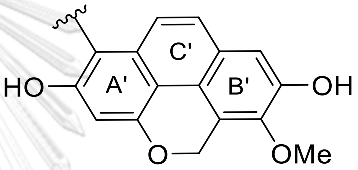


dihydrosinapyl dihydroferulate [**340**]; R = OMe

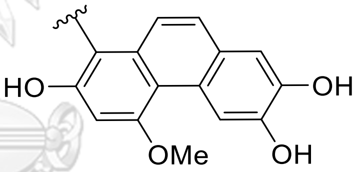
dihydroconiferyl dihydro-*p*-coumarate [**275**]; R = H



aerimultin B [**338**]; R = Me, R′=



aerimultin C [**339**]; R = H, R′=



agrostonin [**341**]; R = H, R′=

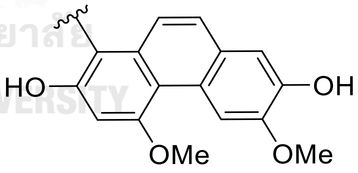


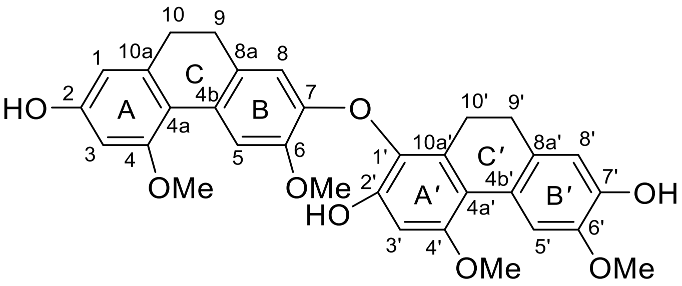
Figure 114 (Continued)

2.3.1 Structural characterization of compound AMF1 (aerimultin A)

Compound AMF1 was isolated as a whitish-brown amorphous solid. It showed a $[M+Na]^+$ at *m/z* 565.1841 (calculated for $C_{32}H_{30}O_8Na$, 565.1838) in the HR-ESI-MS (**Figure 115**). The UV absorptions at 265, 305, and 315 nm (**Figure 116**) were indicative of a dihydrophenanthrene skeleton (Estrada *et al.*, 1999). The IR spectrum (**Figure 117**) showed absorption bands for hydroxyl (3350 cm^{-1}), aromatic ring (2923, 1605 cm^{-1}), methylene (1462 cm^{-1}), and ether (1221 cm^{-1}) groups.

The ^{13}C NMR and HSQC spectra (**Figures 119 and 120)** revealed signals for twenty-four aromatic carbons, plus eight aliphatic carbons representing four methoxy and four methylene groups. The four CH_2 carbons at δ_C 29.0 (C-9), 31.4 (C-10), 29.9 (C-9′), and 24.1 (C-10′) displayed HSQC correlations to the protons at δ_H 2.45 (2H, m, H_2-9), 2.56 (2H, m, H_2-10) and 2.52 (4H, br s, H_2-9′ and H_2-10′), respectively. These NMR signals suggested that AMF1 should be a dimeric compound consisting of two units of 9,10-dihydrophenanthrene (**Table 26**). The first unit of AMF1 (rings A, B, and C) should be derived from 6-methoxycoelonin (AMF5, see 2.3.5), a dihydrophenanthrene also obtained in this study because its ^1H and ^{13}C-NMR properties bore a close resemblance to those of AMF5. For example, in ring A of the first unit of AMF1, the proton at C-1 (δ_H 6.35, 1H, d, J = 2.5 Hz) exhibited HMBC correlation (**Figures 121 and 122**) with C-10 (δ_C 31.4) and NOESY interaction with H_2-10. H-3 (δ_H 6.46, 1H, d, J = 2.5 Hz) of AMF1 showed a NOESY cross peak with MeO-4 protons (δ_H 3.89, 3H, s). The hydroxyl proton at C-2 was observed at δ_H 8.35 (1H, s). For ring B of AMF1, the following ^1H NMR signals were found: two one-proton singlets at δ_H 6.33 (1H, s, H-8) and 7.98 (1H, s, H-5) and a three-proton singlet at δ_H 3.92 (3H, s, MeO-6) which showed a NOESY cross-peak (**Figure 123**) with H-5. The second unit of AMF1 (rings A′, B′, and C′) also exhibited ^1H and ^{13}C NMR data similar to those of AMF5 (see 2.3.5). For instance, the ^1H NMR spectrum of AMF1 exhibited two one-proton singlets at δ_H 6.66 (1H, s, H-8′) and 7.93 (1H, s, H-5′), two methoxy groups at δ_H 3.84 (3H, s, MeO-6′) and 3.91 (3H, s, MeO-4′), and two hydroxyl groups at δ_H 7.44 (s, HO-7′) and 8.25 (s, HO-2′). The HMBC spectrum of AMF1 showed correlation from H-3′ to C-1′ (δ_C 133.7) and C-4a′ (δ_C 117.1), and from H-5′ to C-4a′ (δ_C 117.1), C-8a′ (δ_C 131.4) and C-7′ (δ_C 145.6). H-8′ (δ_C 6.66, 1H, s) displayed HMBC correlation with C-9′ (δ_C 29.9) and NOESY interaction with H_2-9′. The methoxy protons at C-4′ (δ_C 155.3) and C-6′ (δ_C 146.1) showed NOESY correlations with H-3′ and H-5′, respectively. However, in the second dihydrophenanthrene unit of AMF1, the H-1′ signal was absent and the signal for H-3′ appeared as a singlet at δ_H 6.65.

In the ^{13}C NMR spectrum of compound AMF1, the signal for C-1′ of this unit was downfield shifted and observed as a quaternary carbon at δ_C 133.7, with HMBC correlations with H-3′ (δ_H 6.65, s), H_2-10′ (δ_H 2.52, br s), and HO-2′ (δ_H 8.25, s). These NMR properties indicated that the structure of AMF1 consisted of two methoxycoelonin (AMF5) units, connected to each other through an ether linkage at C-7 and C-1′. This was also supported by the absence of a hydroxyl proton at C-7 (δ_C 146.6). Based on the above spectral data, compound AMF1 was characterized as a new dimeric 9,10-dihydrophenanthrene derivative and given the trivial name aerimultin A [**337**].



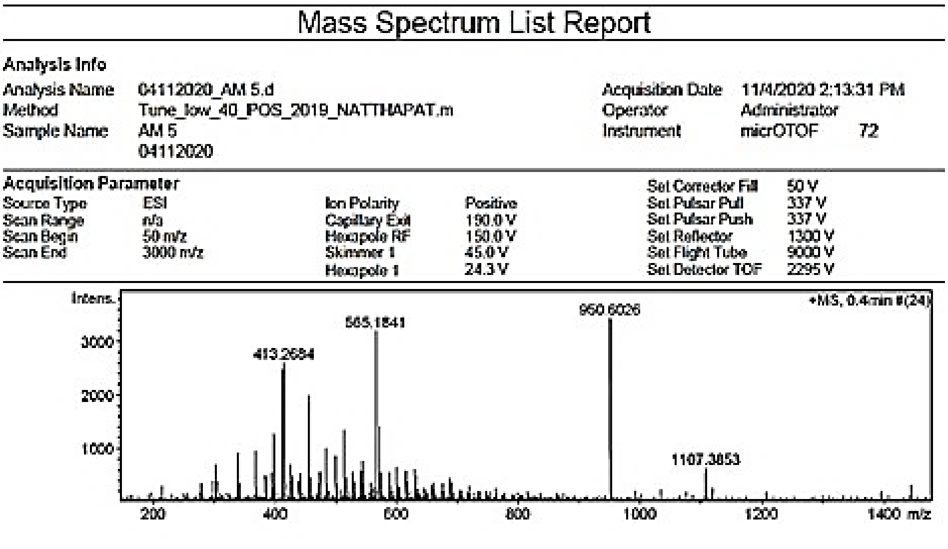
aerimultin A [**337**]

Table 26 ^{1}H (500 MHz) and ^{13}C NMR (125 MHz) spectral data of compound AMF1

Position	AMF1 (acetone-d_6)		
	δ_H (mult., J in Hz)	δ_C	HMBC (Correlation with ^{1}H)
1	6.35 (d, J = 2.5 Hz)	108.3	3, 10, HO-2
2	-	157.8	1*, 3*, HO-2*
3	6.46 (d, J = 2.5 Hz)	99.1	1, HO-2
4	-	158.8	3*, MeO-4
4a	-	115.9	1, 3, 5, 10
4b	-	127.8	5*, 8, 9
5	7.98 (s)	114.3	-
6	-	147.4	8, MeO-6
7	-	146.6	5
8	6.33 (s)	113.6	9
8a	-	131.1	5, 10
9	2.45 (m)	29.0	8
10	2.56 (m)	31.4	1
10a	-	141.6	9, 10*
1′	-	133.7	3′, 10′, HO-2′
2′	-	149.8	3′*, HO-2′*
3′	6.65 (s)	100.2	HO-2′
4′	-	155.3	3′*, MeO-4′
4a′	-	117.1	3′, 5′, 10′
4b′	-	125.2	5′*, 8′, 9′
5′	7.93 (s)	113.4	-
6′	-	146.1	8′, MeO-6′, HO-7′
7′	-	145.6	5′, HO-7′*
8′	6.66 (s)	114.9	9′, HO-7′
8a′	-	131.4	5′, 10′

Position	AMF1 (acetone-d_6)		
	δ_H (mult., J in Hz)	δ_C	HMBC (Correlation with ^1H)
9′	2.52 (br s)	29.9	8′
10′	2.52 (br s)	24.1	-
10a′	-	133.8	9′
MeO-4	3.89 (s)	56.1	-
MeO-6	3.92 (s)	56.5	-
MeO-4′	3.91 (s)	56.4	-
MeO-6′	3.84 (s)	55.8	-
HO-2	8.35 (s)	-	-
HO-2′	8.25 (s)	-	-
HO-7′	7.44 (s)	-	-

* Two-bond coupling



Mass Spectrum List Report

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Acquisition Parameter

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Scan End	3000 m/z	Skimmer 1	45.0 V	Set Reflector	1300 V
		Hexapole 1	24.3 V	Set Flight Tube	9000 V
				Set Detector TOF	2295 V

Figure 115 Mass spectrum of compound AMF1

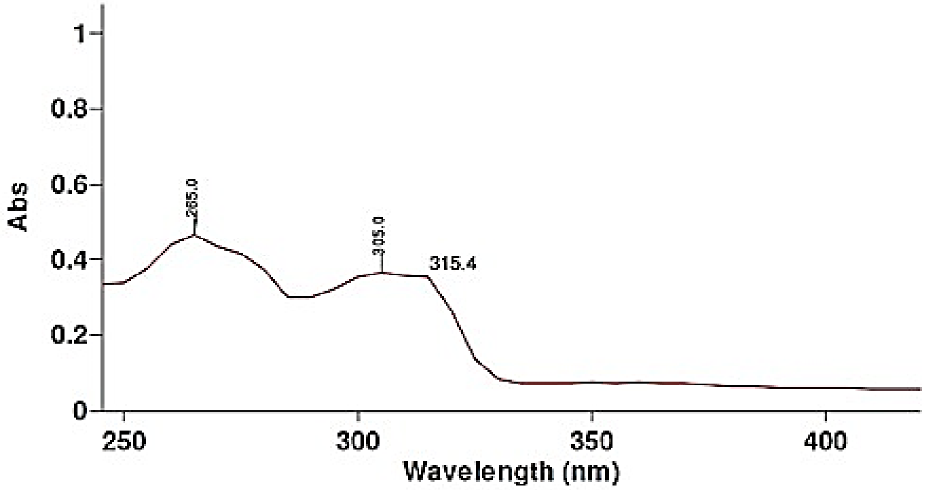


Figure 116 UV spectrum of compound AMF1

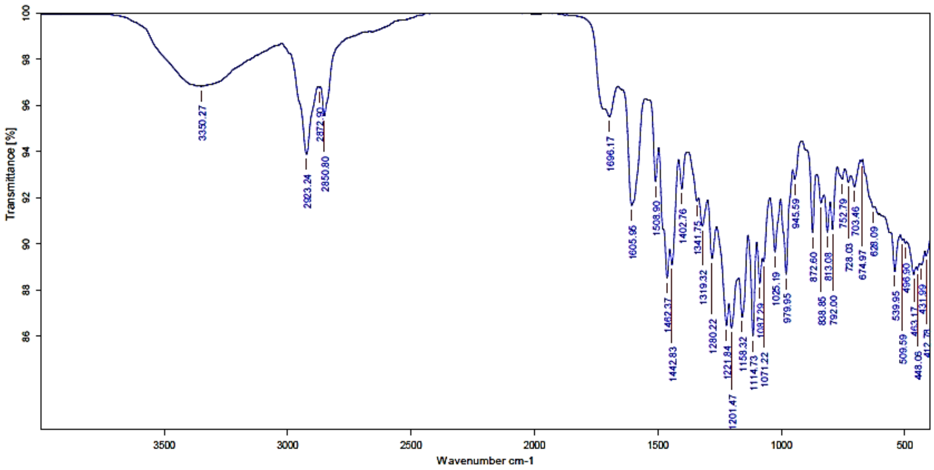


Figure 117 FT-IR spectrum of compound AMF1

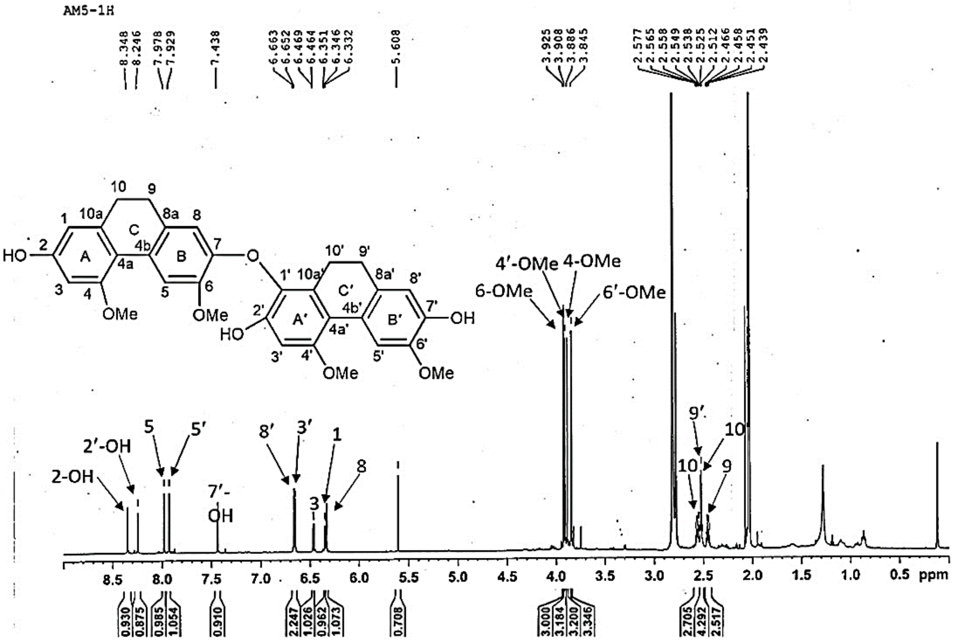


Figure 118 ^{1}H-NMR (500 MHz) spectrum of compound AMF1

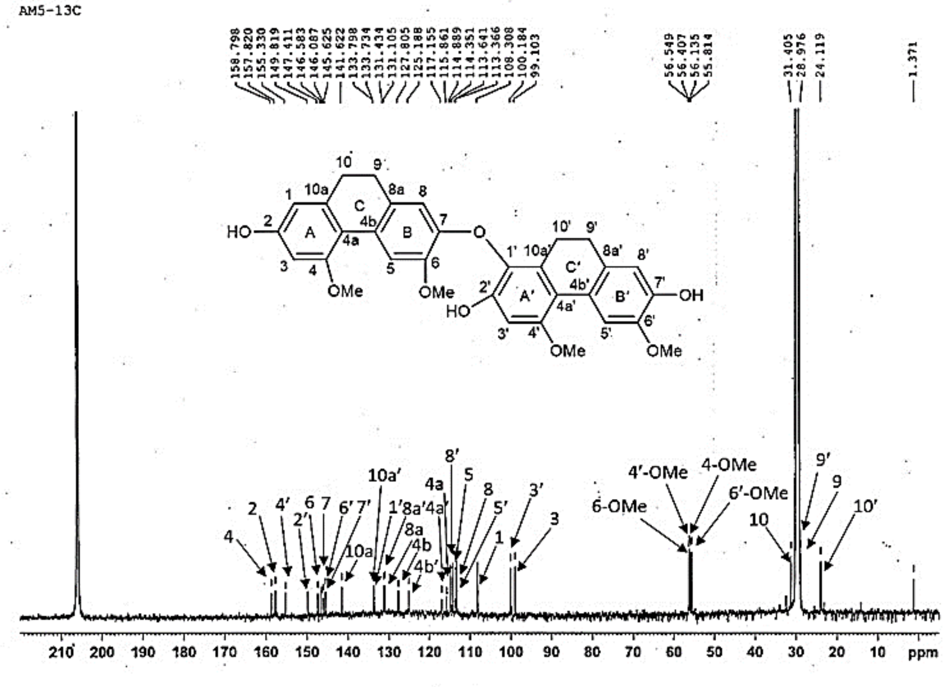


Figure 119 ^{13}C-NMR (125 MHz) spectrum of compound AMF1

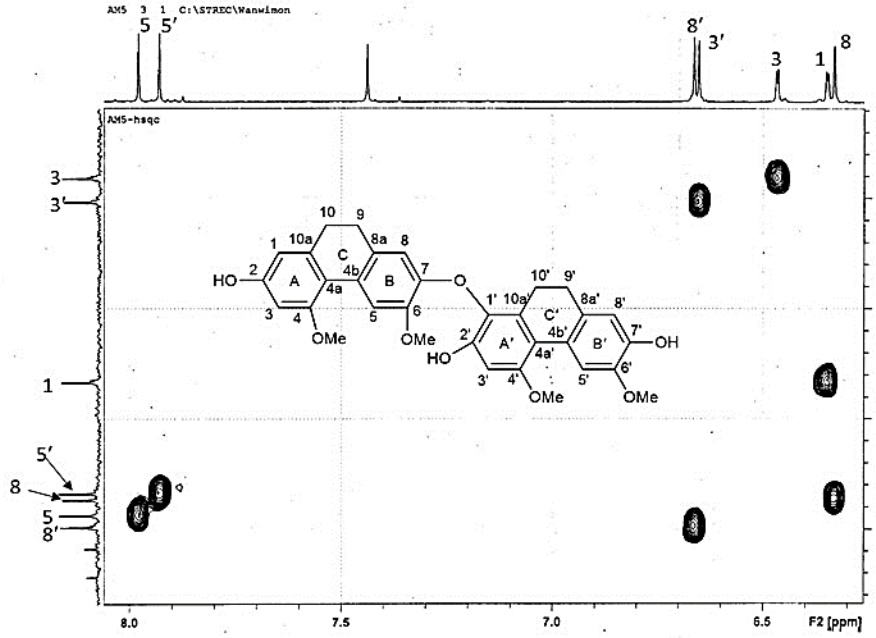


Figure 120 HSQC spectrum of compound AMF1

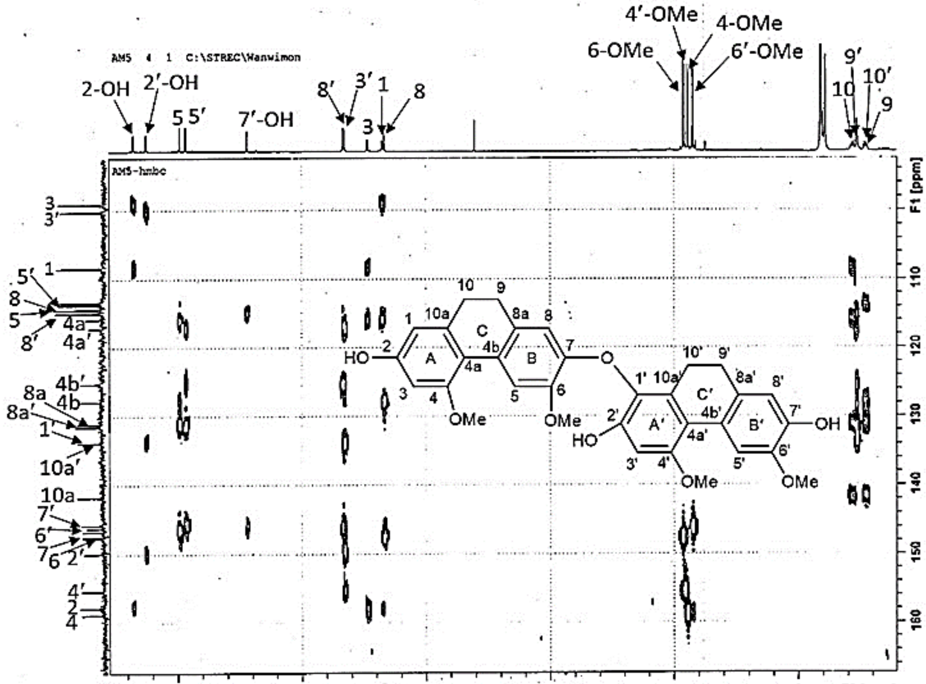


Figure 121 HMBC (full) spectrum of compound AMF1

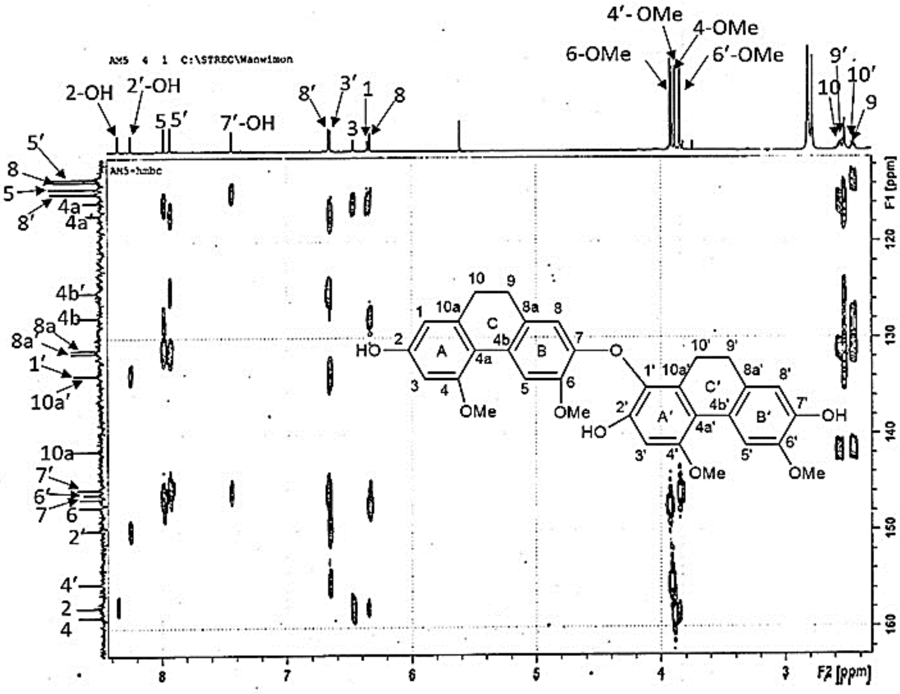


Figure 122 HMBC (expanded) spectrum of compound AMF1

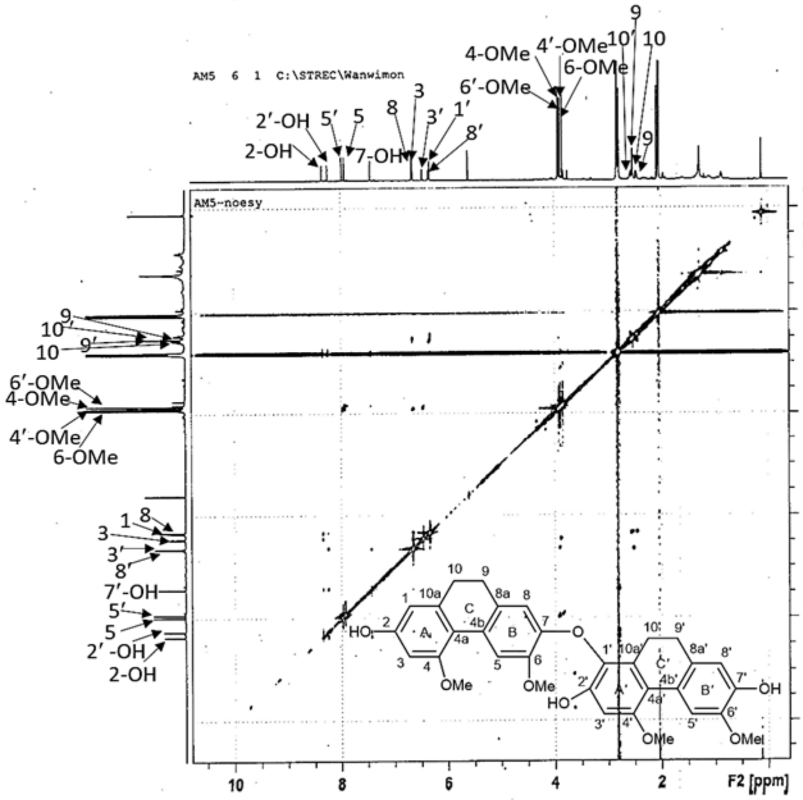
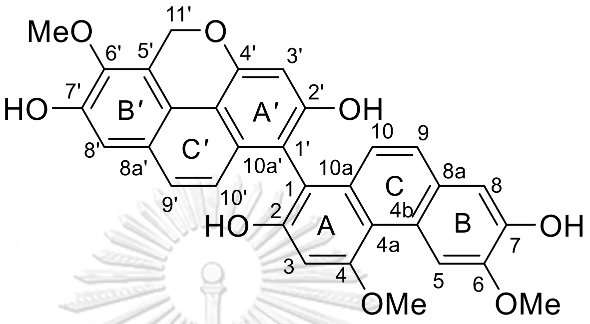


Figure 123 NOESY spectrum of compound AMF1

2.3.2 Structural characterization of compound AMF2 (aerimultin B)

Compound AMF2, a brown amorphous solid, exhibited $[M+Na]^+$ at *m/z* 559.1376 (calculated for $C_{32}H_{24}O_8Na$, 559.1368) in the HR-ESI-MS (**Figure 124**), corresponding to the molecular formula $C_{32}H_{24}O_8$. The UV absorptions (**Figure 125**) at 265, 315.5 and 370 nm were suggestive of a phenanthrene skeleton (Leong *et al.*, 1997). The IR spectrum (**Figure 126**) showed absorption bands due to the presence of hydroxyl (3368 cm^{-1}), aromatic ring (2919, 1587 cm^{-1}), and ether (1259 cm^{-1}) functionalities. AMF2 should be a dimeric phenanthrene, as suggested from the ^1H NMR signals for two pairs of *ortho*-coupled doublets, representing H-9 (δ_H 7.36, 1H, d, *J* = 9.5 Hz), H-10 (δ_H 6.98, 1H, d, *J* = 9.5 Hz), H-9′ (δ_H 7.37, 1H, d, *J* = 9.0 Hz), and H-10′ (δ_H 6.92, 1H, d, *J* = 9.0 Hz) (**Figure 127 and Table 27**). The first phenanthrene unit of AMF2 (rings A, B, and C) exhibited ^1H and ^{13}C NMR resonances similar to those of agrostonin (AMF8), a biphenantherene also isolated from this plant (see 2.3.8). These included three one-proton singlets at δ_H 6.99 (1H, s, H-3), 7.19 (1H, s, H-8) and 9.24 (1H, s, H-5) and two methoxy groups at δ_H 4.06 (3H, s, MeO-6), and 4.22 (3H, s, MeO-4). The proton at C-8 showed HMBC correlation with C-9 (δ_C 126.5). The protons H-3 and H-5 exhibited three-bond couplings with C-4a (δ_C 116.2) in the HMBC spectrum (**Figure 130**). The NOESY correlations (**Figure 131**) of the MeO-4 and MeO-6 protons with H-3 and H-5, respectively, supported the attachment of these methoxy groups at C-4 and C-6. The quaternary carbon at δ_C 109.3 was assigned to C-1 according to its HMBC cross-peaks with H-3 and H-10. For the second phenanthrene unit (rings A′, B′, and C′), the presence of oxymethylene protons at δ_H 5.79 (2H, d, *J* = 1.5 Hz, H_2-11′) indicated a phenanthropyran structure (Majumder & Sabzabadi, 1988). The ^1H NMR spectrum also displayed two sharp one-proton singlets at δ_H 6.81 (1H, s, H-3′) and 7.21 (1H, s, H-8′) and a methoxy group at δ_H 3.95 (3H, s, MeO-6′). The assignments of H-8′ and H-3′ were supported by their HMBC correlations with C-9′ (δ_C 127.9) and C-1′ (δ_C 110.2), respectively. The HMBC correlations of C-6′ (δ_C 144.2) with MeO-6′ protons and H_2-11′ indicated the location of the methoxy group at C-6′. The C-1′ of this second unit showed HMBC correlations with H-3′ and H-10′.

The chemical shifts of C-1 (δ_C 109.3) and C-1′ (δ_C 110.2) suggested that these two carbons were not oxygenated, but, instead, they formed a C─C bridge linking the two monomers (Liu *et al.*, 2016). Therefore, it was concluded that AMF2 had the structure as shown, and the compound was given the trivial name aerimultin B [**338**].



aerimultin B [**338**]

Table 27 ^{1}H (500 MHz) and ^{13}C NMR (125 MHz) spectral data of compound AMF2

Position	AMF2 (acetone-d_6)		
	δ_H (mult., J in Hz)	δ_C	HMBC (correlation with ^{1}H)
1	-	109.3	3, 10
2	-	155.0	3*
3	6.99 (s)	100.0	-
4	-	160.2	3*, MeO-4
4a	-	116.2	3, 5, 10
4b	-	125.8	8, 9
5	9.24 (s)	109.8	-
6	-	148.5	5*, 8, MeO-6
7	-	146.0	5, 8*
8	7.19 (s)	112.2	9
8a	-	128.0	5, 10
9	7.36 (d, J = 9.5 Hz)	126.5	8
10	6.98 (d, J = 9.5 Hz)	123.3	-
10a	-	135.4	9

Position	AMF2 (acetone-d_6)		
	δ_H (mult., J in Hz)	δ_C	HMBC (correlation with ^{1}H)
1′	-	110.2	3′, 10′
2′	-	156.3	3′*
3′	6.81 (s)	103.1	-
4′	-	153.7	3′*, 11′
4a′	-	113.0	3′, 10′
4b′	-	119.1	8′, 9′, 11′
5′	-	120.6	11′*
6′	-	144.2	8′, 11′, MeO-6′
7′	-	150.3	8′*
8′	7.21 (s)	111.6	9′
8a′	-	126.2	10′
9′	7.37 (d, J = 9.0 Hz)	127.9	8′
10′	6.92 (d, J = 9.0 Hz)	124.6	-
10a′	-	132.2	9′
11′	5.79 (d, J = 1.5 Hz)	64.8	-
MeO-4	4.22 (s)	56.1	-
MeO-6	4.06 (s)	56.0	-
MeO-6′	3.95 (s)	61.3	-

* Two-bond coupling

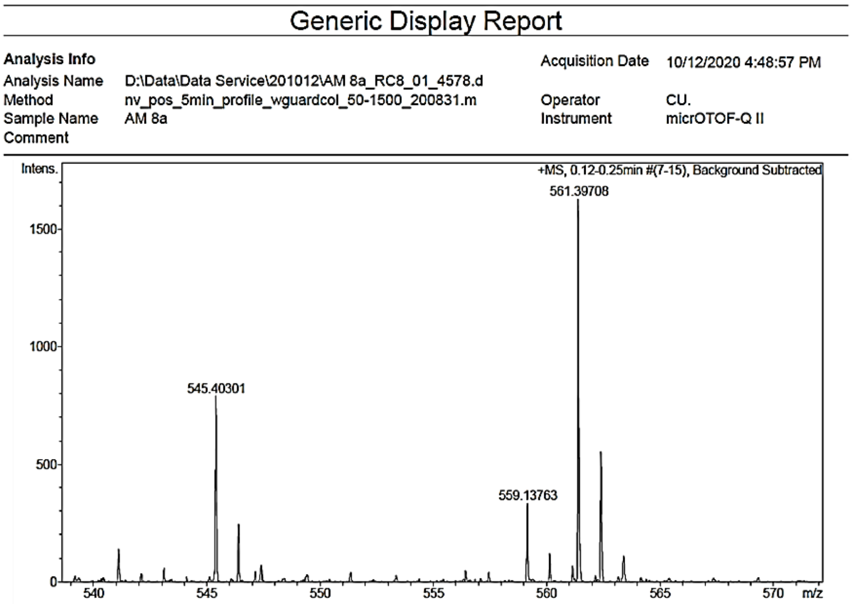


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Figure 124 Mass spectrum of compound AMF2

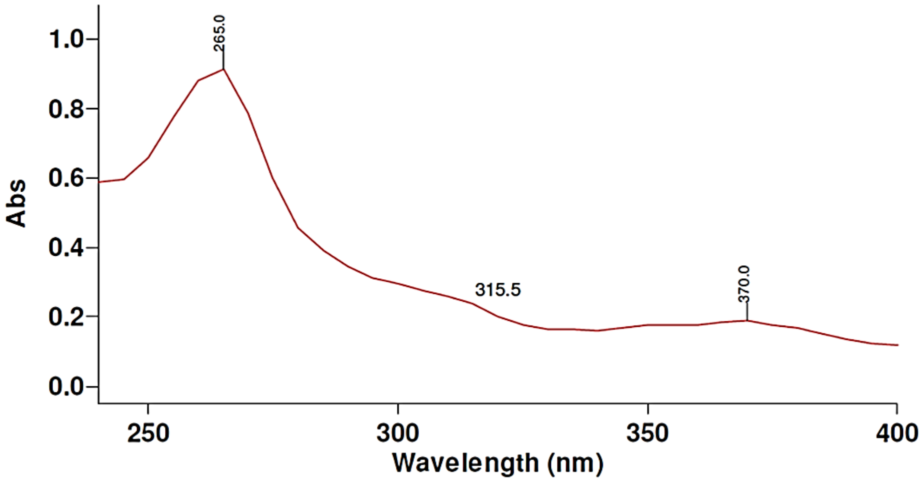


Figure 125 UV spectrum of compound AMF2

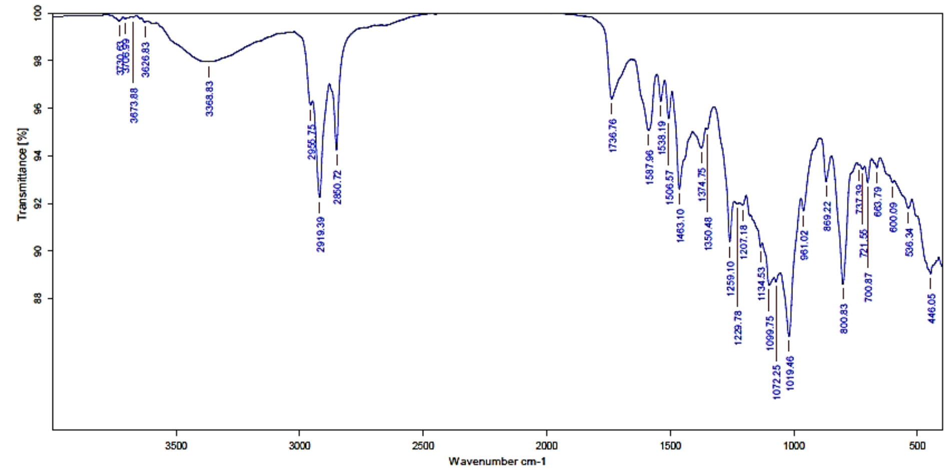


Figure 126 FT-IR spectrum of compound AMF2

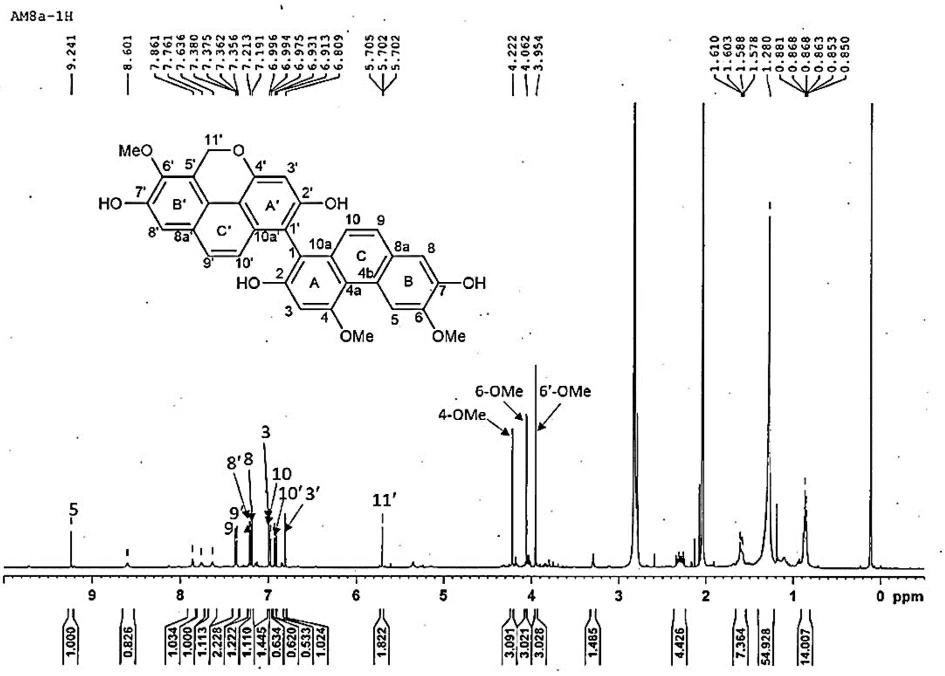


Figure 127 ^{1}H-NMR (500 MHz) spectrum of compound AMF2

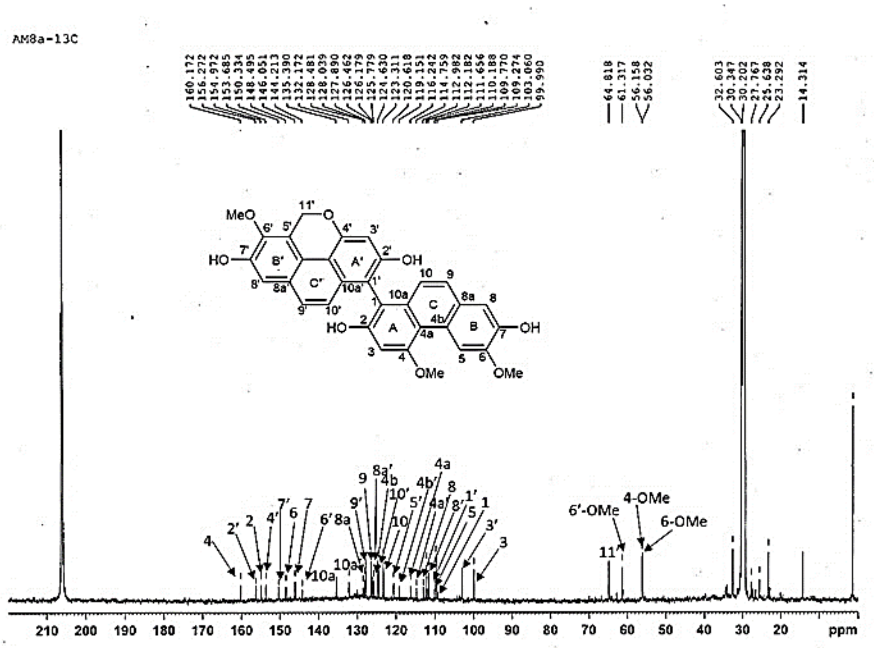


Figure 128 ^{13}C-NMR (125 MHz) spectrum of compound AMF2

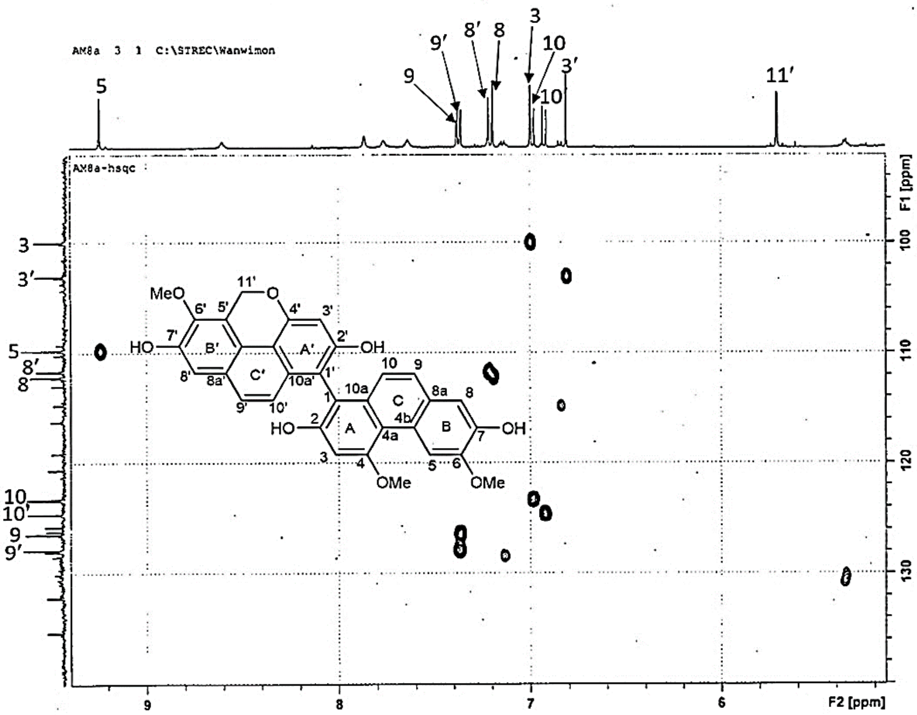


Figure 129 HSQC spectrum of compound AMF2

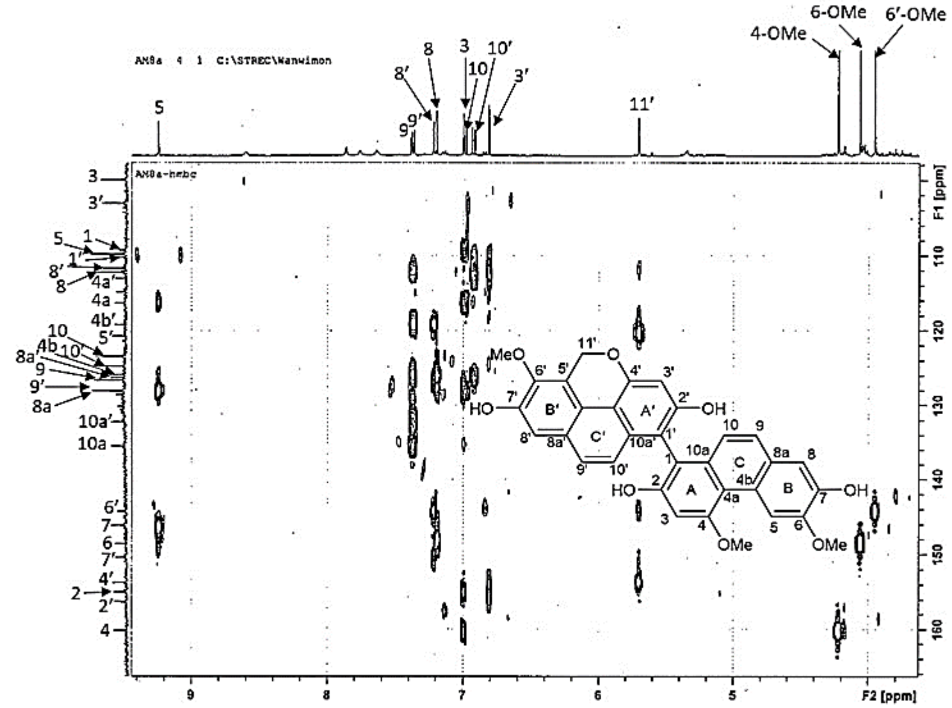


Figure 130 HMBC spectrum of compound AMF2

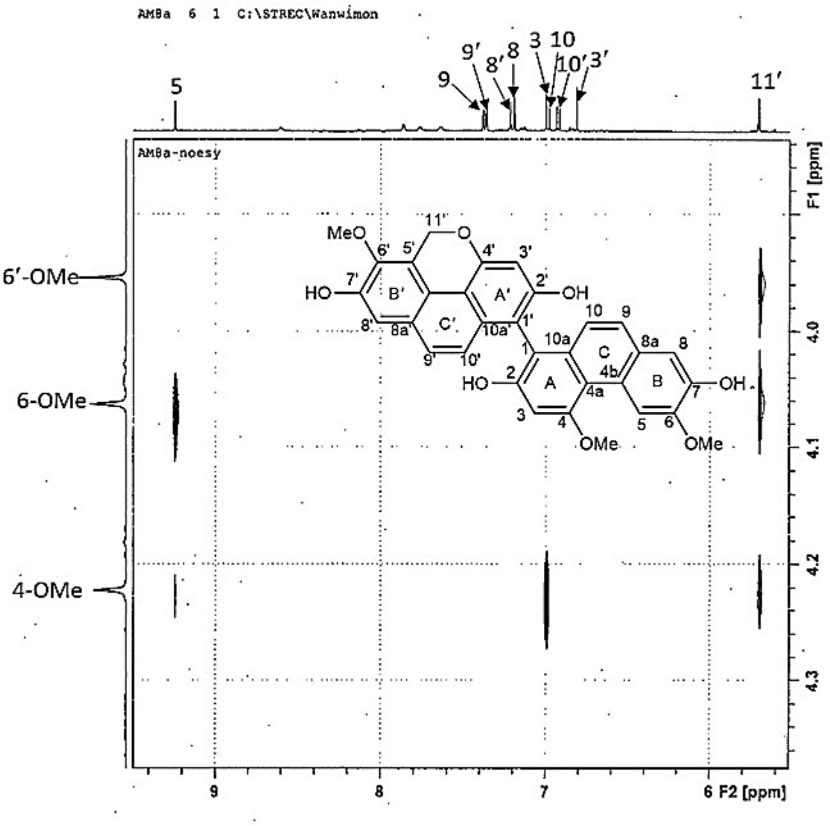
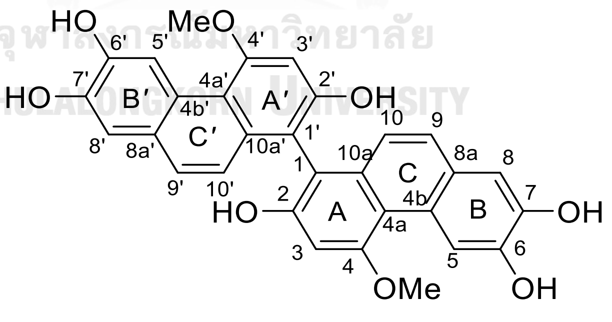


Figure 131 NOESY spectrum of compound AMF2

2.3.3 Structural characterization of compound AMF3 (aerimultin C)

Compound AMF3 was obtained as a brown amorphous solid. The HR-ESI-MS (**Figure 132)** exhibited $[M+Na]^+$ at *m/z* 533.1218 (calculated for $C_{30}H_{22}O_8Na$, 533.1212), suggesting the molecular formula $C_{30}H_{22}O_8$. Its UV absorptions and IR absorption bands were similar to those of AMF2, indicating a phenanthrene derivative (**Figures 133 and 134**). However, the ^{13}C NMR spectrum (**Figure 136 and Table 28**) showed only fifteen carbon signals, suggesting that AMF3 should be a dimeric phenanthrene with two identical units. Comparison of the ^1H and ^{13}C NMR (**Table 28**) of AMF3 with those of agrostonin (AMF8, see 2.3.8) revealed their structural similarity, except for the presence of a hydroxyl group at C-6/C-6′ in AMF3, instead of a methoxy group. Moreover, the two phenanthrene units were symmetrically linked to each other through a C-C bond between C-1 and C-1′ as supported by the HMBC correlations **(Figure 138 and Table 28)** from C-1/C-1′ to H-3/H-3′, H-10/H-10′ and HO-2/HO-2′ (Liu *et al*., 2016). Based on the above spectral evidence, the structure of compound AMF3 was established as shown, and the trivial name aerimultin C was given to the compound.



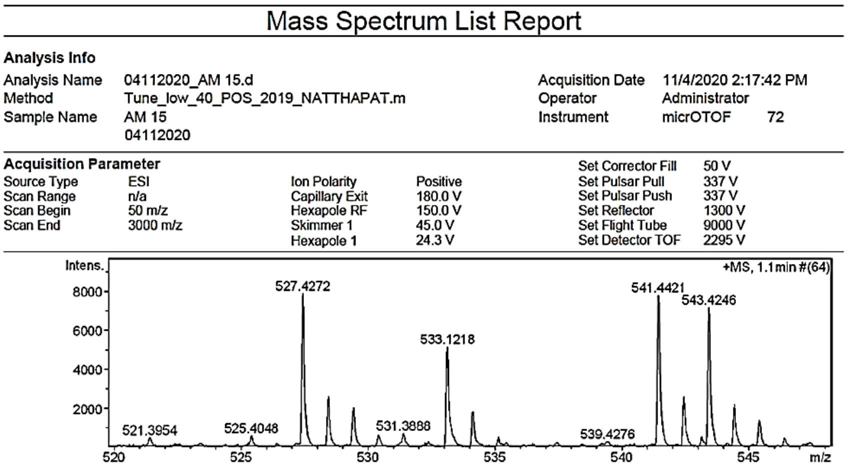
aerimultin C [**339**]

Table 28 ^{1}H (300 MHz) and ^{13}C NMR (75 MHz) spectral data of compound AMF3

Position	AMF3 (acetone-d_6)		
	δ_H (mult., *J* in Hz)	δ_C	HMBC (correlation with ^{1}H)
1	-	108.8	3, 10, HO-2
2	-	154.1	3*, HO-2*
3	6.95 (1H, s)	98.8	HO-2
4	-	159.4	3*, MeO-4
4a	-	115.1	3, 5, 10
4b	-	125.3	8, 9
5	9.19 (1H, s)	112.7	-
6	-	145.3	8
7	-	144.1	5
8	7.19 (1H, s)	111.5	9
8a	-	126.7	5, 10
9	7.31 (1H, d, 9.0)	127.2	8
10	6.87 (1H, d, 9.0)	121.8	-
10a	-	134.6	9
1′	-	108.8	3′, 10′, HO-2′
2′	-	154.1	3′*, HO-2′*
3′	6.95 (1H, s)	98.8	HO-2′
4′	-	159.4	3′*, MeO-4′
4a′	-	115.1	3′, 5′, 10′
4b′	-	125.3	8′, 9′
5′	9.19 (1H, s)	112.7	-
6′	-	145.3	8′
7′	-	144.1	5′
8′	7.19 (1H, s)	111.5	9′
8a′	-	126.7	5′, 10′

Position	AMF3 (acetone-d_6)		
	δ_H (mult., J in Hz)	δ_C	HMBC (correlation with ^{1}H)
9′	7.31 (1H, d, 9.0)	127.2	8′
10′	6.87 (1H, d, 9.0)	121.8	-
10a′	-	134.6	9′
MeO-4	4.18 (3H, s)	55.0	-
MeO-4′	4.18 (3H, s)	55.0	-
HO-2	7.54 (1H, s)	-	-
HO-2′	7.54 (1H, s)	-	-
HO-6	8.32 (br s)	-	-
HO-6′	8.23 (br s)	-	-

* Two-bond coupling



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Analysis Info

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Method	Tune_low_40_POS_2019_NATTHAPAT.m	Operator	Administrator
Sample Name	AM 15 04112020	Instrument	micrOTOF 72

Acquisition Parameter

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Scan End	3000 m/z	Skimmer 1	45.0 V	Set Flight Tube	9000 V
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Figure 132 Mass spectrum of compound AMF3

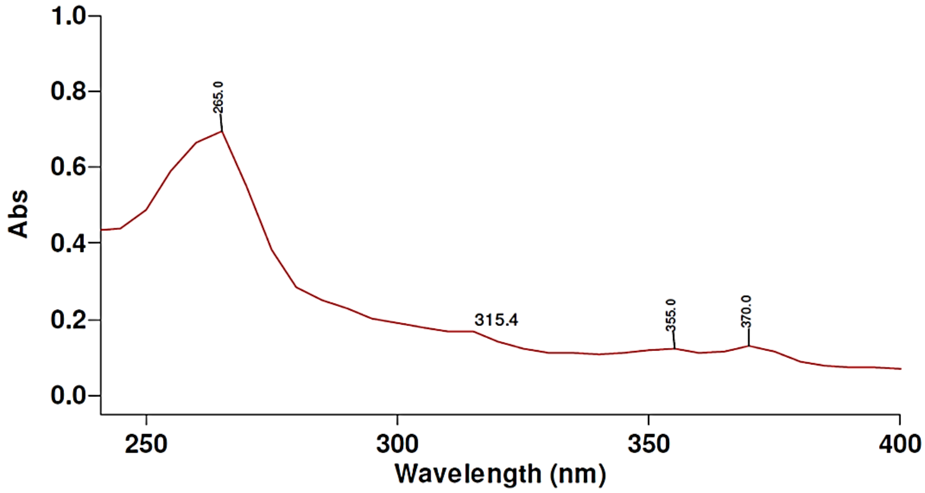


Figure 133 UV spectrum of compound AMF3

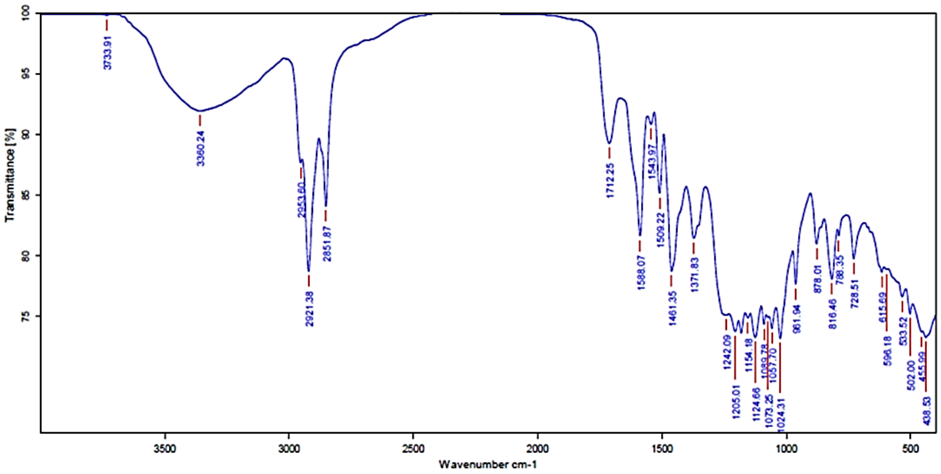


Figure 134 FT-IR spectrum of compound AMF3

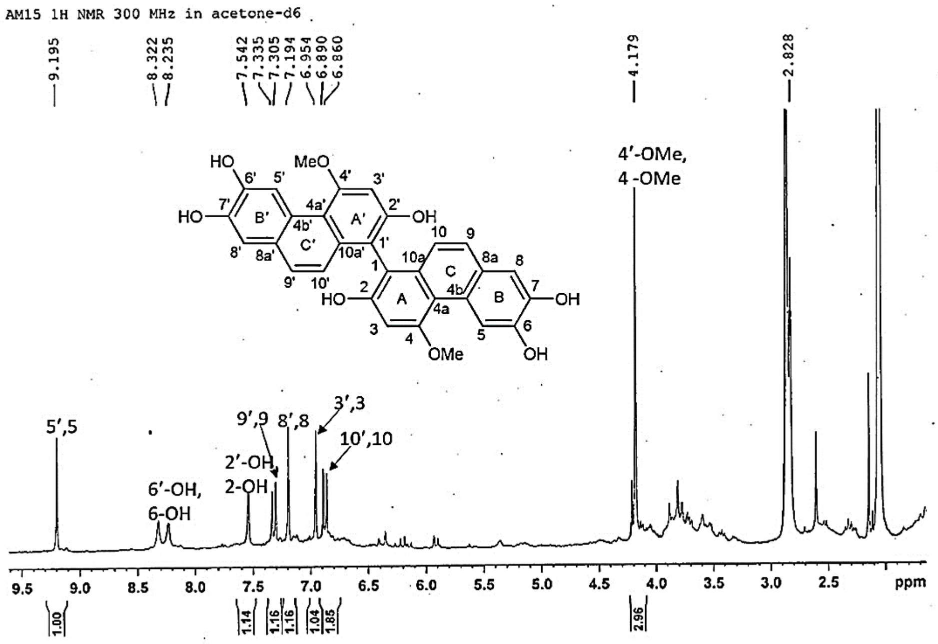


Figure 135 ^{1}H-NMR (300 MHz) spectrum of compound AMF3

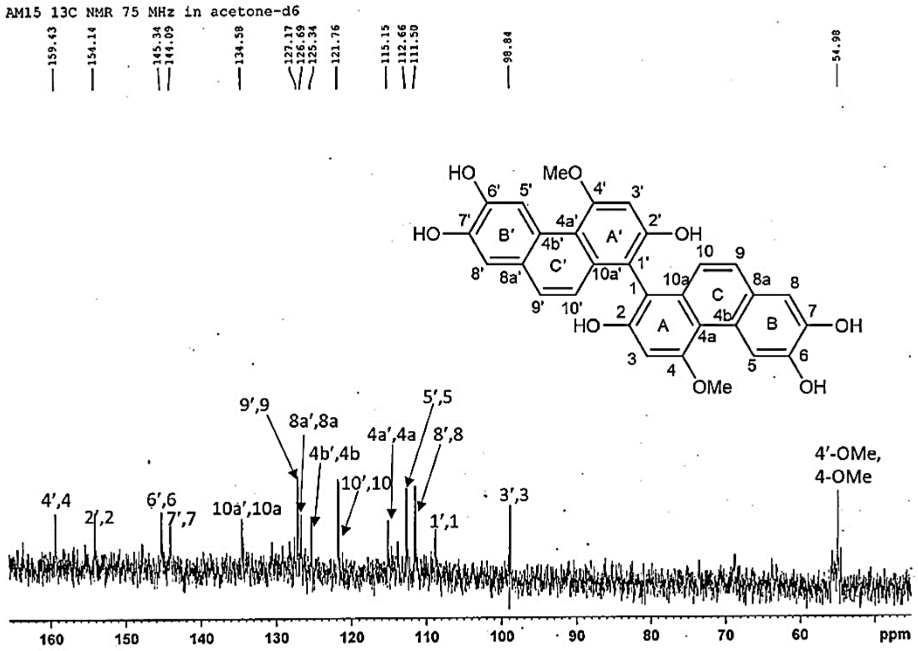


Figure 136 ^{13}C-NMR (75 MHz) spectrum of compound AMF3

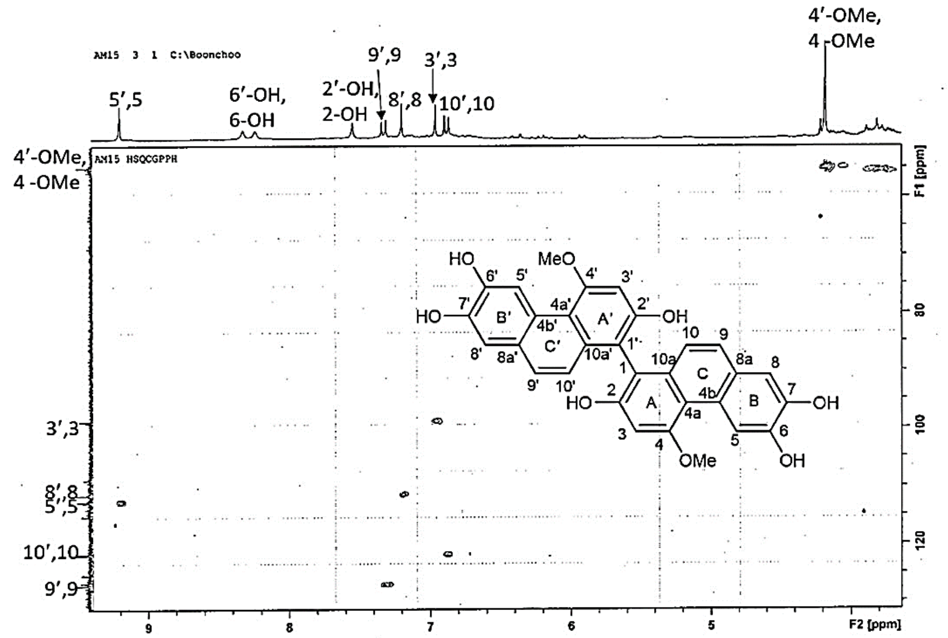


Figure 137 HSQC spectrum of compound AMF3

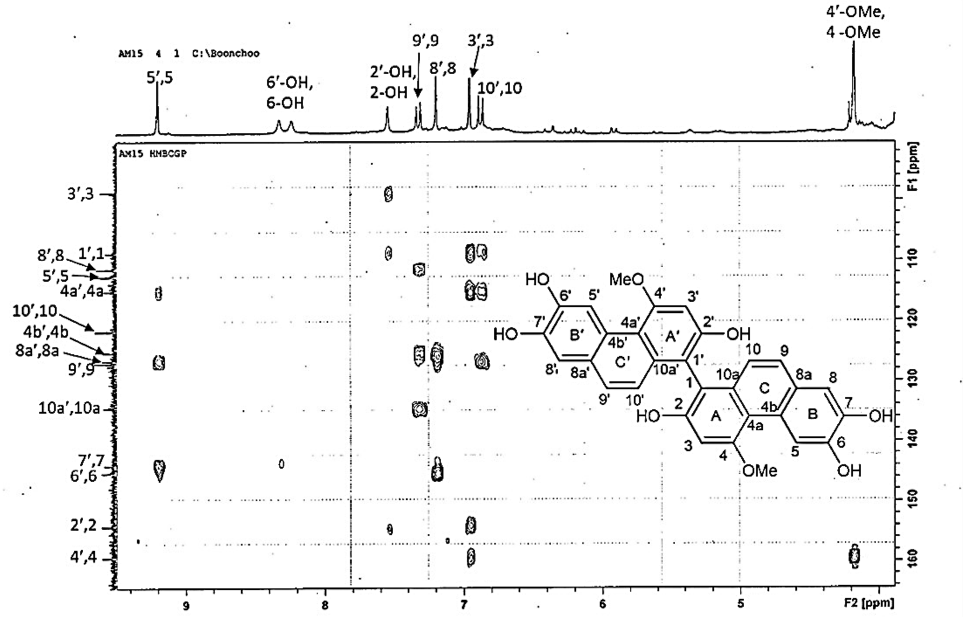


Figure 138 HMBC spectrum of compound AMF3

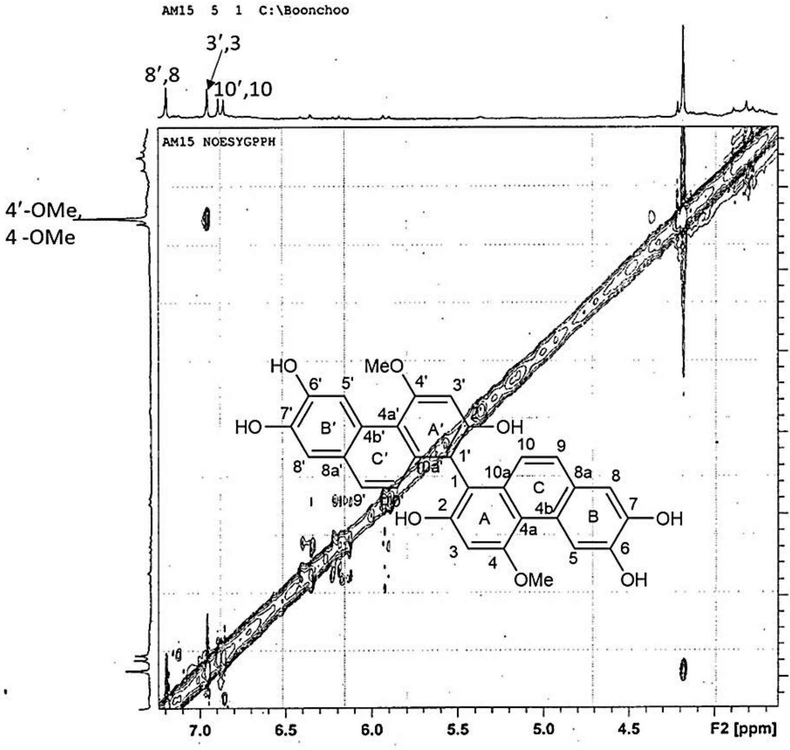


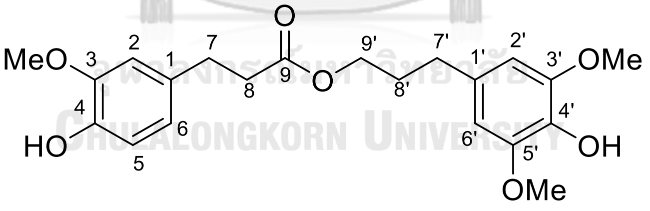
Figure 139 NOESY spectrum of compound AMF3

2.3.4 Identification of compound AMF4 (dihydrosinapyl dihydroferulate)

Compound AMF4 was obtained as a yellow amorphous solid. The molecular formula was determined as $C_{21}H_{26}O_7$ from $[M+Na]^+$ at *m/z* 413.1584 (calculated for $C_{21}H_{26}O_7Na$, 413.1576) in the HR-ESI mass spectrum (**Figure 140**). The UV spectrum (**Figure 141**) exhibited maximum absorptions at 280 and 315 nm. The IR spectrum (**Figure 142**) showed absorption bands for hydroxyl (3432 cm^{-1}), aromatic ring (2937, 1608 cm^{-1}), carbonyl ester (1723, 1208, 1111 cm^{-1}), and methylene (1455 cm^{-1}) groups. The ^{1}H NMR spectrum (**Figure 143 and Table 29**) exhibited signals for a dihydroferulate structure [δ_H 2.59 (2H, t, *J* = 7.5 Hz, H_2-8), 2.81 (2H, m, H_2-7), 3.82 (3H, s, MeO-3), 6.68 (1H, dd, *J* = 8.1, 1.5 Hz, H-6), 6.73 (1H, d, *J* = 8.1 Hz, H-5), and 6.85 (1H, d, *J* = 1.5 Hz, H-2)] (Beck *et al.*, 2007). This was confirmed by the HMBC correlations of C-2 (δ_C 111.8), C-6 (δ_C 120.6) and C-9 (δ_C 172.2) with H_2-7 (**Figure 146 and Table**

29). The location of the MeO-3 group was supported by its NOESY correlation with H-2 (**Figure 147)**. The ^{1}H NMR spectrum also showed signals for a dihydrosinapyl structure [δ_H 1.89 (2H, m, H_2-8′), 2.57 (2H, t, *J* = 7.5 Hz, H_2-7′), 3.80 (6H, s, MeO-3′, MeO-5′), 4.05 (2H, t, *J* = 7.5 Hz, H_2-9′), and 6.49 (2H, s, H-2′, H-6′)] (Zhuo *et al.*, 2016). The HMBC correlations of C-2′/C-6′ (δ_C 105.8) and C-9′ (δ_C 63.2) with H_2-7′ supported the presence of this unit. The NOESY cross-peak between MeO-3′/MeO-5′ protons and H-2′/H-6′ confirmed the locations of the methoxy groups at C-3′/C-5′ (δ_C 147.7).

The two phenylpropanoid units were connected by an ester bond at C-9 and C-9′, as determined from the HMBC correlation of C-9 (δ_C 172.2) with H_2-9′. Based on the above spectroscopic evidence, AMF4 was identified as dihydrosinapyl dihydroferulate. Prior to this study, the natural occurrence of AMF4 was unknown. However, the compound was earlier synthesized by acylation of the lignins obtained from *Arabidopsis thaliana* (Sibout *et al.*, 2016).

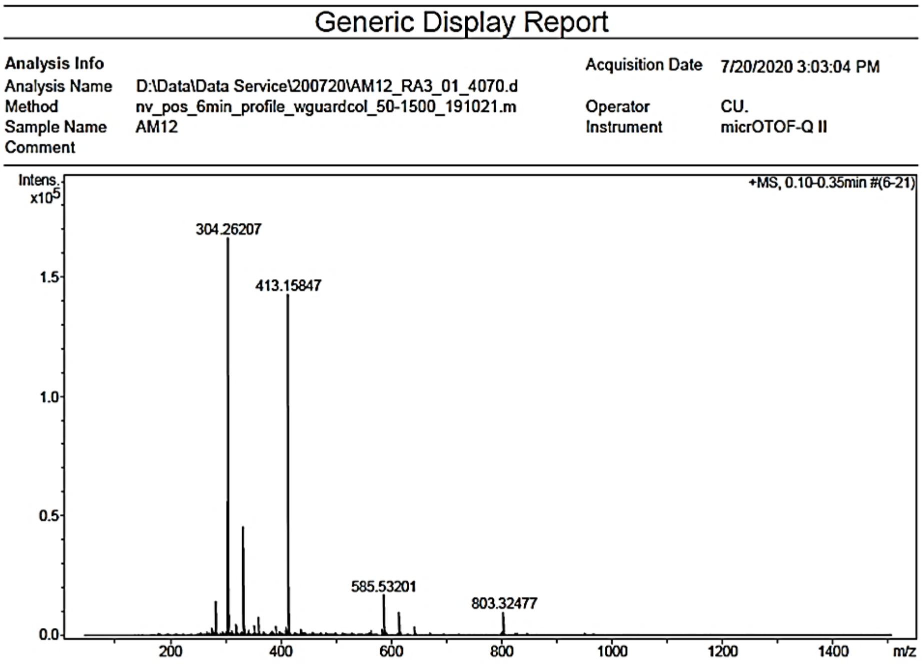


dihydrosinapyl dihydroferulate [**340**]

Table 29 ^{1}H (300 MHz) and ^{13}C NMR (75 MHz) spectral data of AMF4

Position	AMF4 (acetone-d_6)		
	δ_H (mult., J in Hz)	δ_C	HMBC (correlation with ^{1}H)
1	-	132.1	5, 7*, 8
2	6.85 (1H, d, 1.5)	111.8	6, 7
3	-	147.3	5, MeO-3, HO-4
4	-	144.9	2, 6, HO-4*
5	6.73 (1H, d, 8.1)	114.8	HO-4
6	6.68 (1H, dd, 8.1, 1.5)	120.6	2, 7
7	2.81 (2H, m)	30.4	2, 6, 8*
8	2.59 (2H, t, 7.5)	35.8	7*
9	-	172.2	7, 8*, 9′
1′	-	131.7	8′
2′	6.49 (1H, s)	105.8	6′, 7′
3′	-	147.7	2′*, HO-4′, MeO-3′
4′	-	134.2	2′, 6′, HO-4′*
5′	-	147.7	6′*, HO-4′, MeO-5′
6′	6.49 (1H, s)	105.8	2′, 7′
7′	2.57 (2H, t, 7.5)	31.8	2′, 6′, 8′*, 9′
8′	1.89 (2H, m)	30.4	7′*, 9′*
9′	4.05 (2H, t, 7.5)	63.2	7′, 8′*
MeO-3	3.82 (3H, s)	55.3	-
MeO-3′	3.80 (3H, s)	55.7	-
MeO-5′	3.80 (3H, s)	55.7	-
HO-4	7.35 (1H, s)	-	-
HO-4′	6.94 (1H, s)	-	-

* Two-bond coupling



Generic Display Report

Analysis Info

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Sample Name	AM12	Instrument	micrOTOF-Q II
Comment			

Figure 140 Mass spectrum of compound AMF4

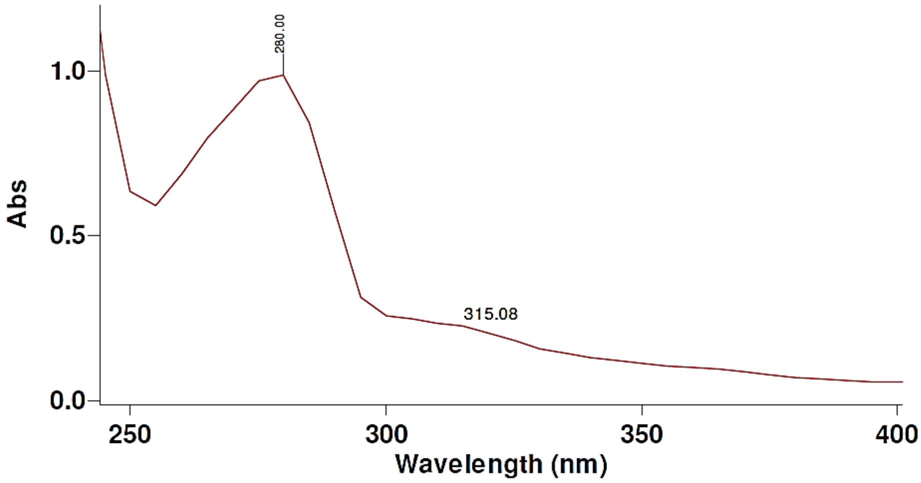


Figure 141 UV spectrum of compound AMF4

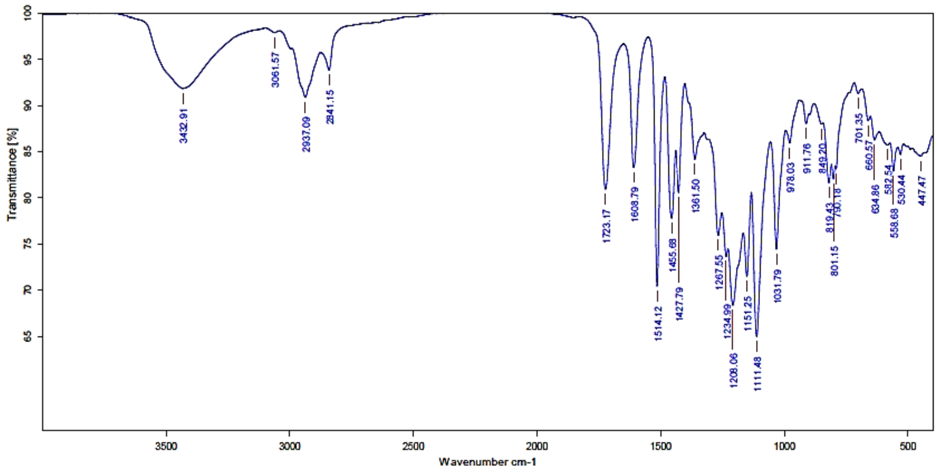


Figure 142 FT-IR spectrum of compound AMF4

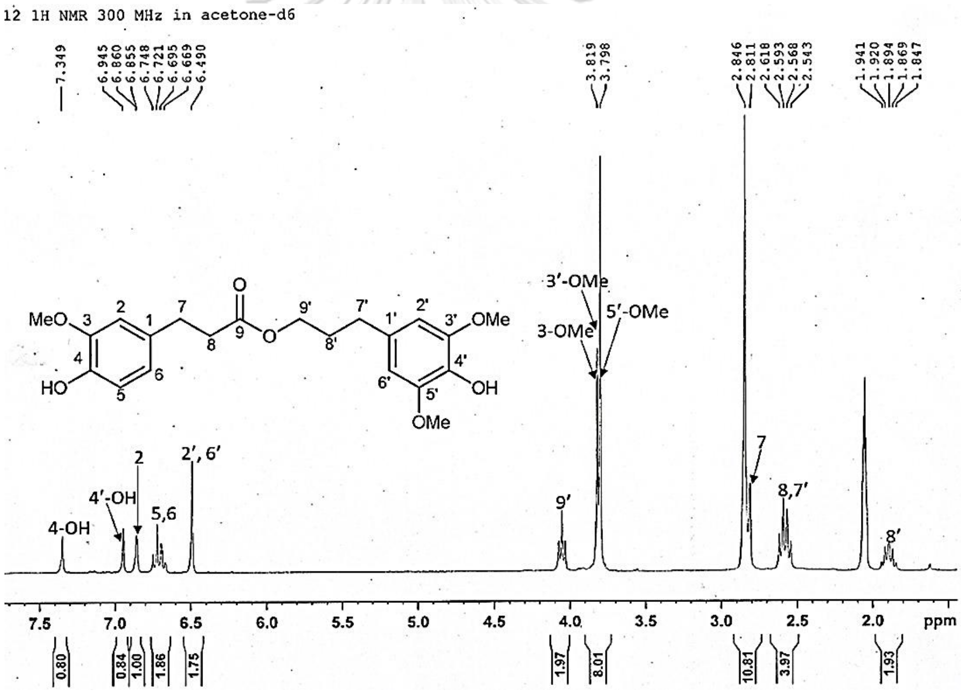


Figure 143 ^{1}H-NMR (300 MHz) spectrum of compound AMF4

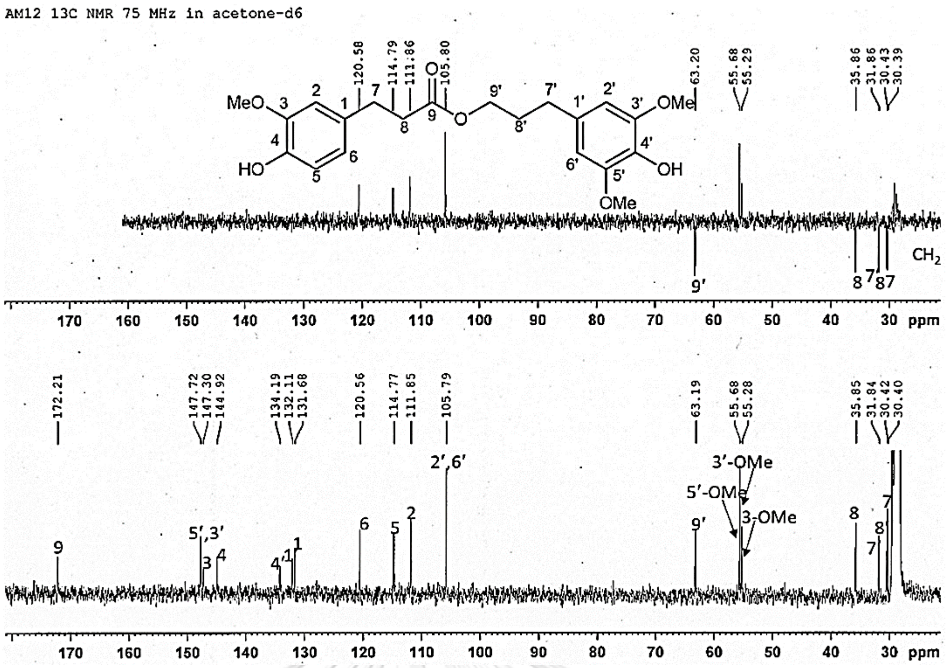


Figure 144 ^{13}C-NMR (75 MHz) spectrum of compound AMF4

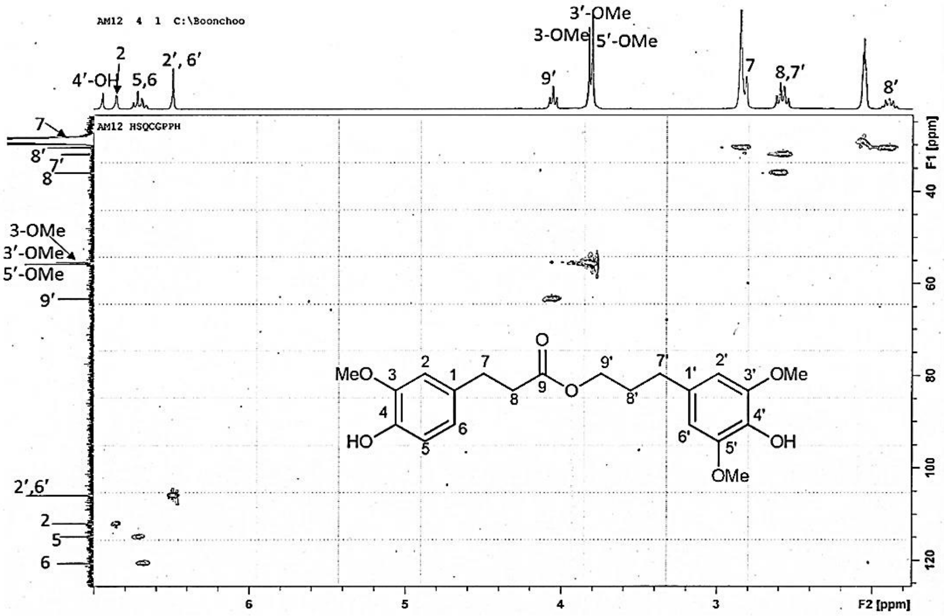


Figure 145 HSQC spectrum of compound AMF4

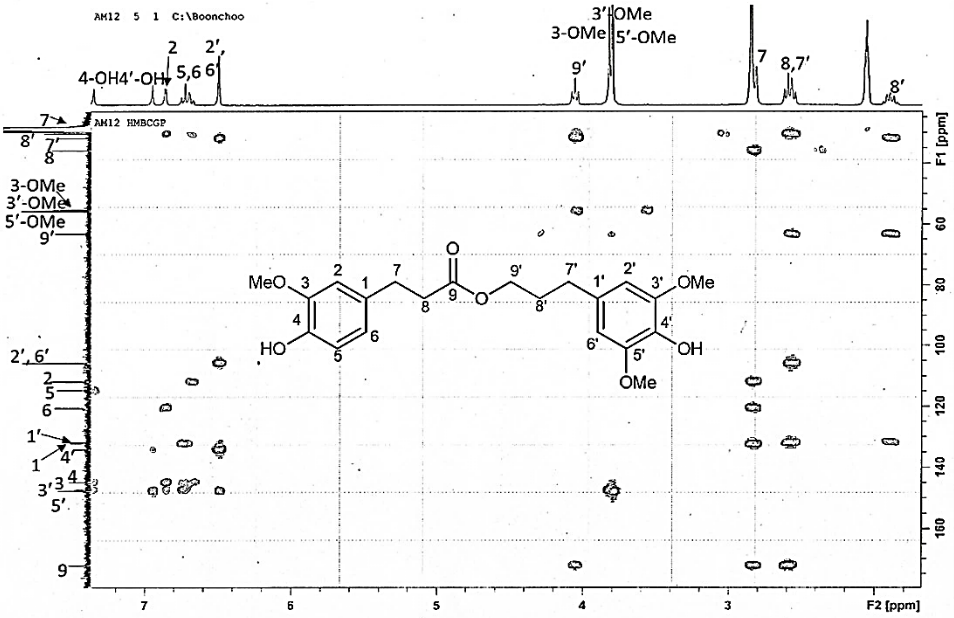


Figure 146 HMBC spectrum of compound AMF4

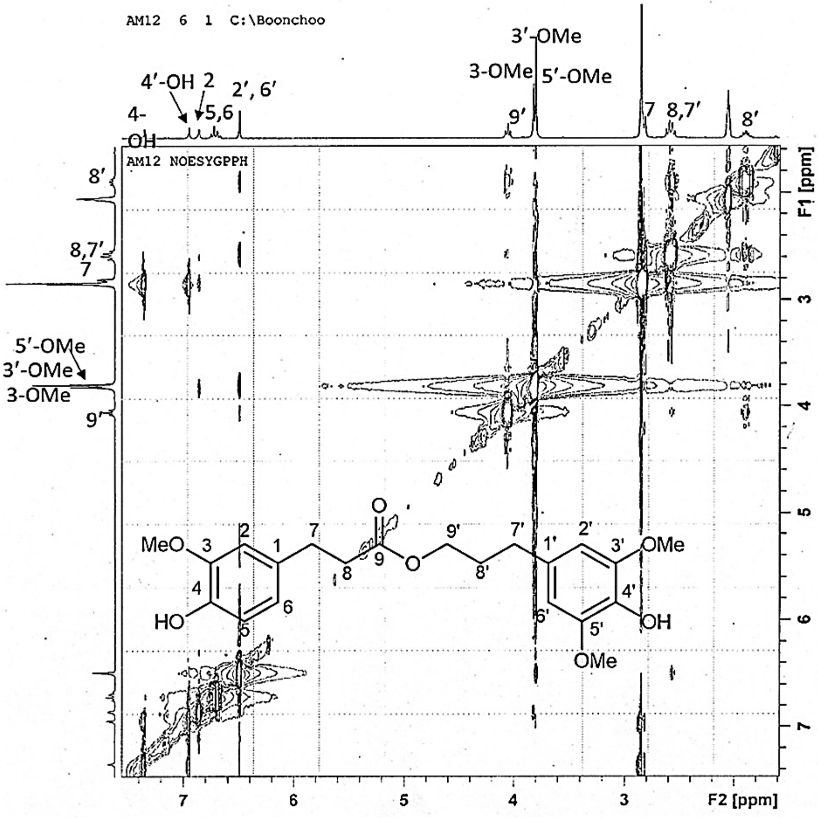


Figure 147 NOESY spectrum of compound AMF4

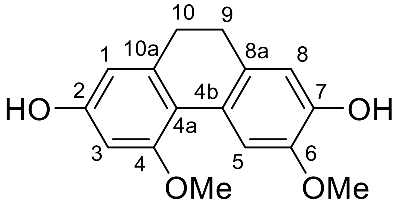
2.3.5 Identification of compound AMF5 (6-methoxycoelonin)

Compound AMF5 was obtained as a brown amorphous solid. The molecular formula was determined as $C_{16}H_{16}O_4$ from $[M+Na]^+$ at *m/z* 295.09368 (calculated for $C_{16}H_{16}O_4Na$, 295.09463) in the HR-ESI-MS (**Figure 148**).

The ^{1}H and ^{13}C-NMR spectra of AMF5 (**Figures 149, 150 and Table 30**) showed signals of four aliphatic protons at δ_H 2.61 (*s,* H_2-9, H_2-10) and two methylene carbons at δ_C 28.9 (C-9) and 30.7 (C-10), suggesting the presence of a dihydrophenanthrene structure. The ^{1}H-NMR spectrum also showed signals for four aromatic protons at δ_H 6.39 (1H, br s, H-1), 6.65 (1H, br s, H-3), 7.89 (1H, s, H-5), and 6.69 (1H, s, H-8), and two methoxy groups at δ_H 3.86 (3H, s, 4-OMe) and 3.83 (3H, s, 6-OMe).

Furthermore, the dihydrophenanthrene structure was confirmed from the HMBC correlation peaks from H-1 to C-3 (δ_C 98.3), C-4a (δ_C 115.5), and C-10 (δ_C 30.7); from H-3 to C-1 (δ_C 107.4) and C-4a; H-5 to C-4a, C-7 (δ_C 144.3) and C-8a (δ_C 130.7); and from H-8 to C-4b (δ_C 124.7), C-6 (δ_C 145.1) and C-9 (δ_C 28.9) (**Figure 152**). In the NOESY spectrum (**Figure 153**), the cross peaks from 4-OMe to H-3 and from 6-OMe to H-5 confirmed the locations of these methoxy groups.

Through comparison of the above NMR spectral data with previously report values (Leong *et al.,* 1997), compound AMF5 was determined as 6-methoxycoelonin [**332**], a dihydrophenanthrene earlier isolated from *Bulbophyllum vaginatum.* This compound was also reported from *Agrostophyllum callosum* (Majumder *et al.*, 1996).

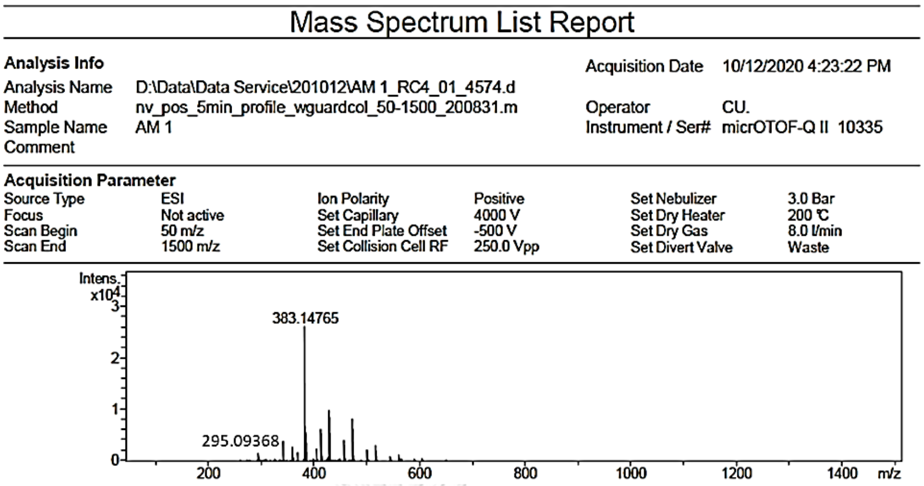


6-methoxycoelonin [**332**]

Table 30 NMR spectral data of compound AMF5 and 6-methoxycoelonin

Position	AMF5 (acetone-d_6)		6-Methoxycoelonin ($CDCl_3$)	
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
1	6.39 (1H, br s)	107.4	6.35 (1H, d, 2.4)	107.6
2	-	156.5	-	154.7
3	6.65 (1H, br s)	98.3	6.42 (1H, d, 2.4)	98.4
4	-	157.7	-	157.6
4a	-	115.5	-	116.6
4b	-	124.7	-	124.8
5	7.89 (1H, s)	112.2	7.86 (1H, s)	113.6
6	-	145.1	-	144.4
7	-	144.3	-	143.5
8	6.69 (1H, s)	114.0	6.78 (1H, s)	111.4
8a	-	130.7	-	131.4
9	2.61 (2H, m)	28.9	2.68 (2H, m)	30.8
10	2.61 (2H, m)	30.7	2.68 (2H, m)	29.0
10a	-	140.5	-	141.2
MeO-4	3.86 (3H, s)	55.5	3.87 (3H, s)	56.2
MeO-6	3.83 (3H, s)	54.9	3.91 (3H, s)	55.7

(Leong *et al.,* 1997)



Mass Spectrum List Report

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Sample Name	AM 1	Instrument / Ser#	micrOTOF-Q II 10335
Comment			

Acquisition Parameter

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Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	8.0 l/min
Scan End	1500 m/z	Set Collision Cell RF	250.0 Vpp	Set Divert Valve	Waste

Figure 148 Mass spectrum of compound AMF5

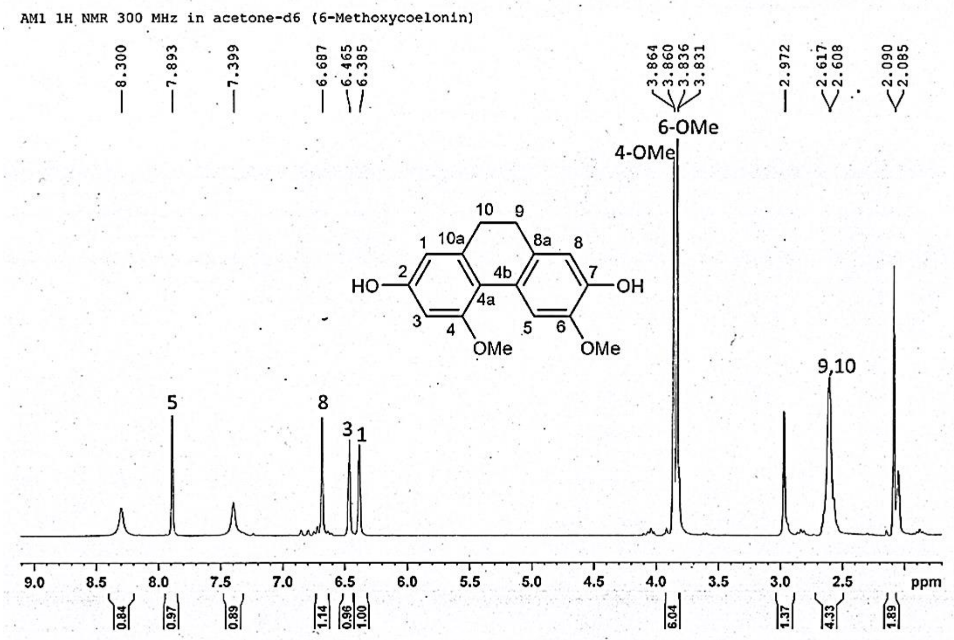


Figure 149 ^{1}H-NMR (300 MHz) spectrum of compound AMF5

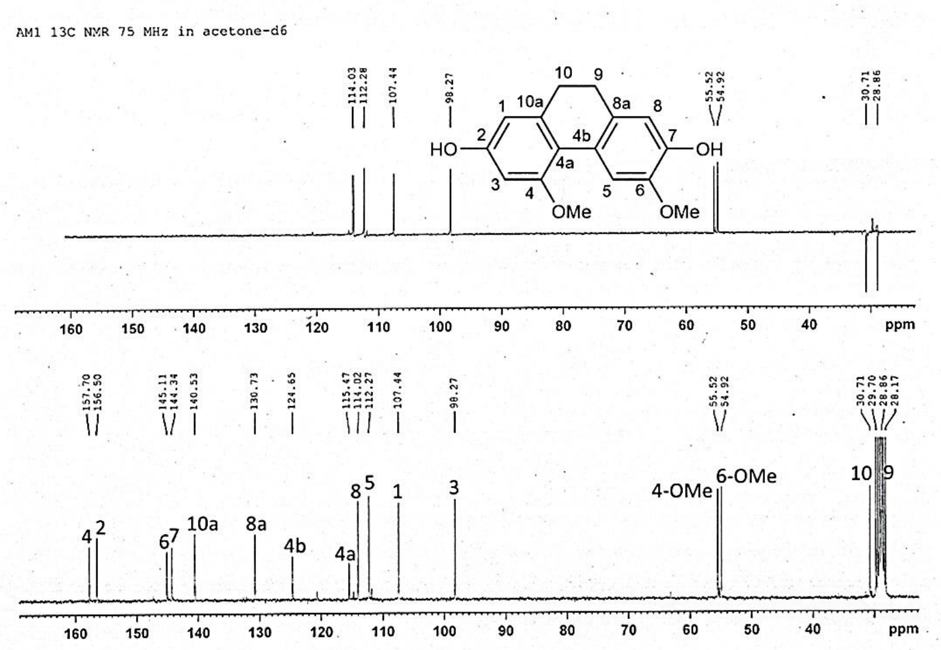


Figure 150 ^{13}C-NMR (75 MHz) spectrum of compound AMF5

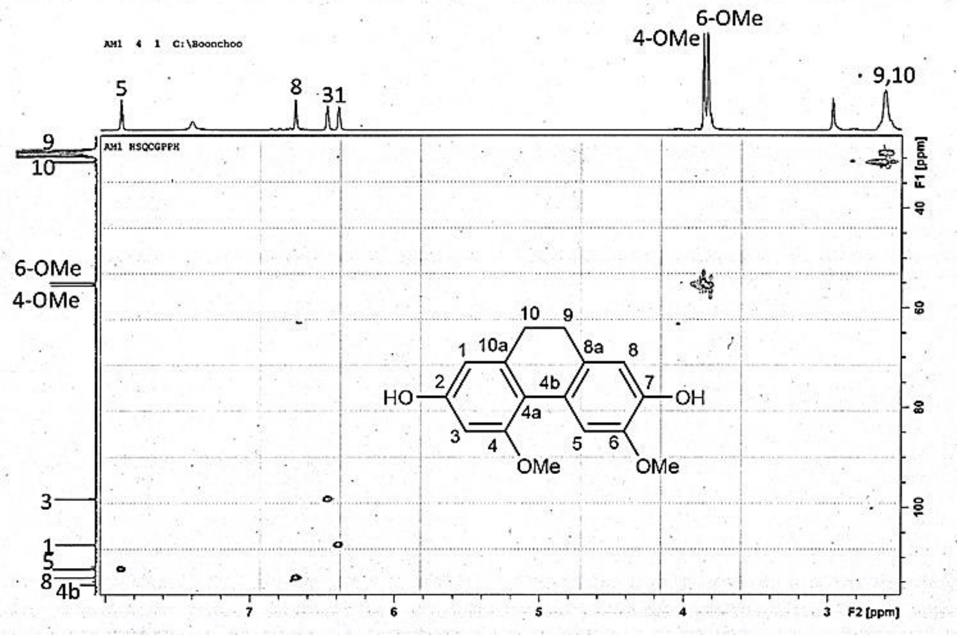


Figure 151 HSQC spectrum of compound AMF5

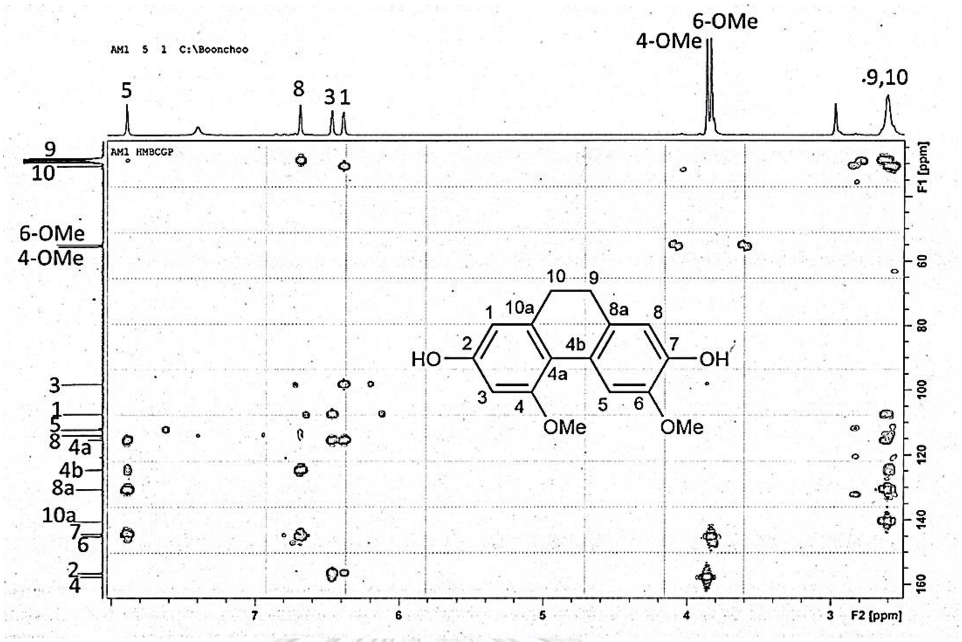


Figure 152 HMBC spectrum of compound AMF5

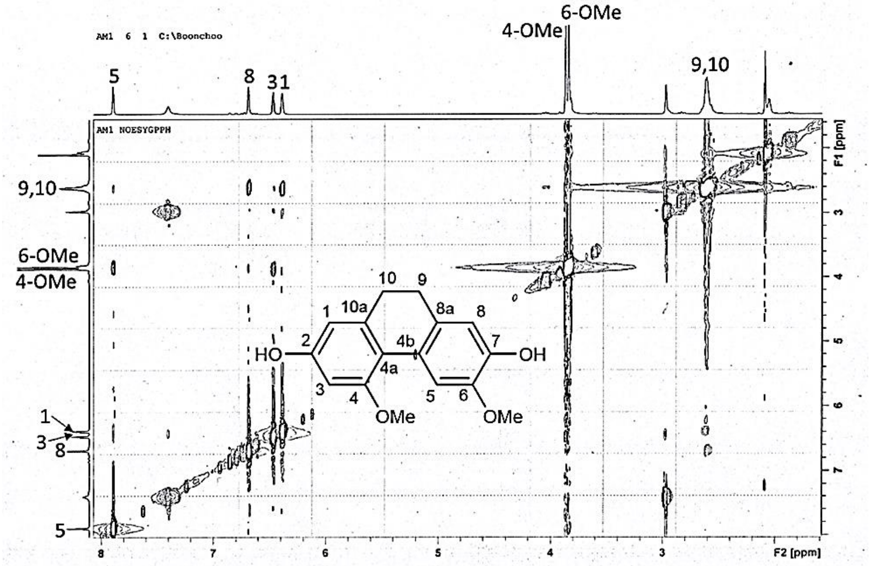


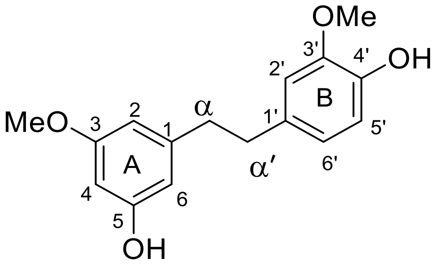
Figure 153 NOESY spectrum of compound AMF5

2.3.6 Identification of compound AMF6 (gigantol)

AMF6 was obtained as a brown amorphous solid. The HR-ESI mass spectrum (**Figure 154**) showed a sodium adduct molecular ion $[M+Na]^+$ at m/z 297.1085, (calculated for $C_{16}H_{18}O_4Na$; 297.1102), suggesting the molecular formula $C_{16}H_{18}O_4$. The ^{1}H-NMR and ^{13}C-NMR spectra (**Figures 155, 156 and Table 31**) showed characteristic signals of a bibenzyl derivative. The ^{1}H-NMR spectrum (**Figure 155)** showed four methylene protons at δ_H 2.89 (4H, br s, H_2-α, H_2-α') and two coupling systems of aromatic protons for 1,3,5-trisubstituted ring A [δ_H 6.31 (1H, br s, H-2), 6.24 (1H, br d, *J* = 2.1 Hz, H-4) and 6.31 (1H, br s, H-6] and 1′,3′,4′-trisubstituted ring B [δ_H 6.81 (1H, br s, H-2′), 6.73 (1H, d, *J* = 7.8 Hz, H-5′) and 6.66 (1H, dd, *J* = 7.8, 1.5 Hz, H-6′)]. The ^{13}C-NMR spectrum (**Figure 156)** showed two methylene carbons at δ_C 38.9 (C-α) and 37.9 (C-α'), two methoxy carbons at δ_C 3.69 (3-OMe) and 3.78 (3′-OMe), in addition to six quaternary carbons and six methine carbons.

The NOESY spectrum (**Figure 157**) displayed cross peaks from 3-OMe protons to H-2 and H-4 of ring A, confirming this methoxy group at C-3. For ring B, the position of the methoxy group at C-3′ was supported by the NOESY correlation peak from 3′-OMe protons to H-2′.

Based on the above NMR spectra data, AMF6 was identified as gigantol [**2**] (Chen, Xu*, et al.*, 2008). Gigantol was also found in other orchid species (Klonglumnuankarn *et al*., 2015; Zhao *et al*., 2018; Kyokong *et al*., 2019).



gigantol [**2**]

Table 31 NMR spectral data of compound AMF6 and gigantol

Position	AMF6 (acetone-d_6)		Gigantol (acetone-d_6)	
	δ_H (mult., J in Hz)	δ_C	δ_H (mult., J in Hz)	δ_C
1	-	144.7	-	144.5
2	6.31 (1H, br s)	108.0	6.33 (1H, dd, 2.0, 2.0)	107.9
3	-	158.4	-	158.2
4	6.24 (1H, br d, 2.1)	98.8	6.26 (1H, dd, 2.0, 2.0)	98.7
5	-	160.9	-	160.8
6	6.31 (1H, br s)	105.4	6.30 (1H, dd, 2.0,2.0)	105.3
α	2.89 (2H, br s)	38.2	2.79 (2H, s)	37.9
α'	2.89 (2H, br s)	37.1	2.78 (2H, s)	36.9
$1'$	-	133.2	-	133.1
$2'$	6.81 (1H, br s)	114.7	6.80 (1H, d, 2.0)	114.6
$3'$	-	147.2	-	147.0
$4'$	-	144.3	-	144.2
$5'$	6.73 (1H, d, 7.8)	112.0	6.74 (1H, d, 8.0)	111.9
$6'$	6.66 (1H, dd, 7.8, 1.5)	120.7	6.66 (1H, dd, 8.0, 2.0)	120.6
$3'$OMe	3.80 (3H, s)	54.4	3.78 (3H, s)	54.3
3-OMe	3.71 (3H, s)	55.3	3.69 (3H, s)	55.2

(Chen, Xu*, et al.*, 2008)

Mass Spectrum List Report

Analysis Info

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Comment			

Acquisition Parameter

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Scan End	1500 m/z	Set Collision Cell RF	250.0 Vpp	Set Divert Valve	Waste

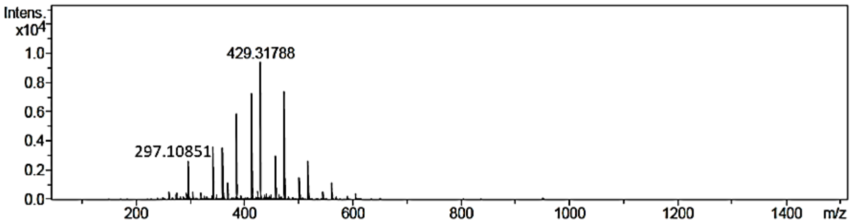


Figure 154 Mass spectrum of compound AMF6

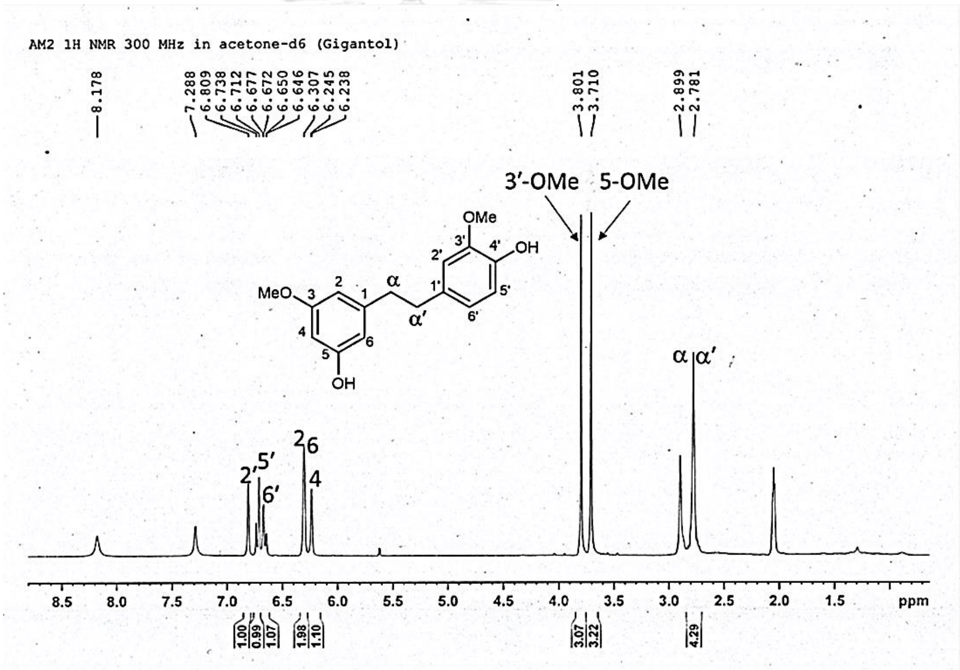


Figure 155 ^{1}H-NMR (300 MHz) spectrum of compound AMF6

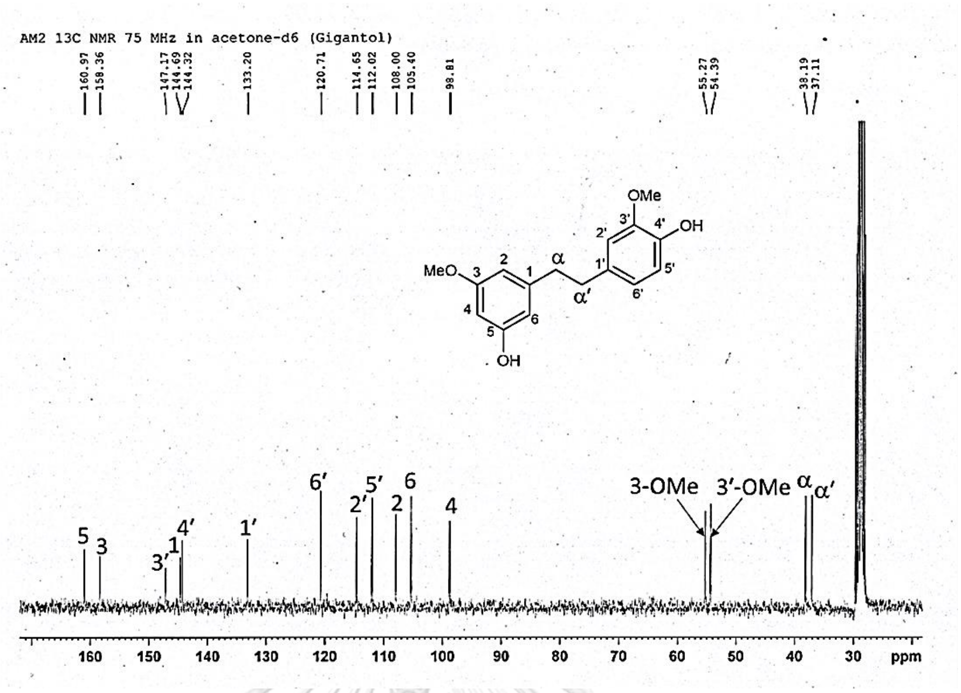


Figure 156 ^{13}C-NMR (75 MHz) spectrum of compound AMF6

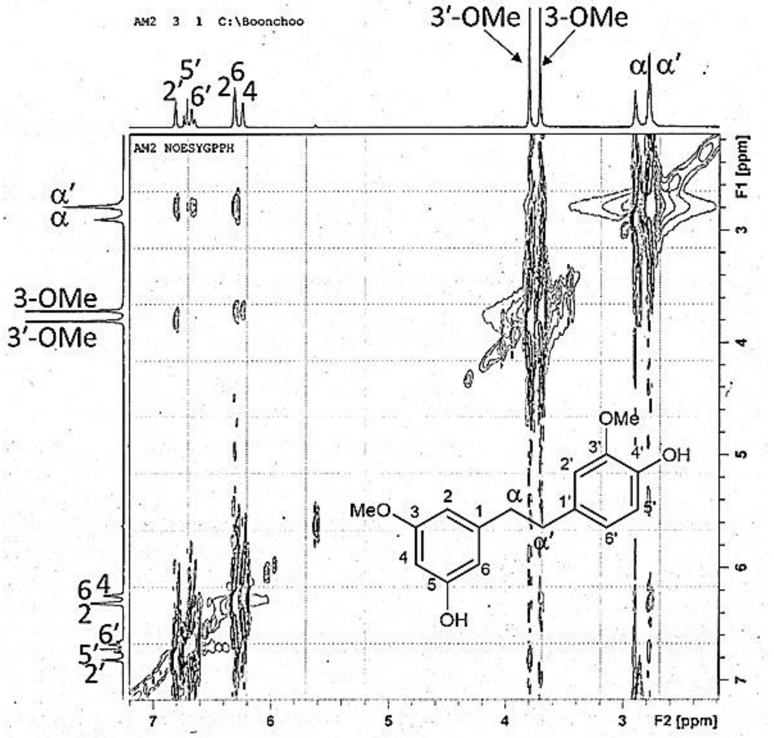


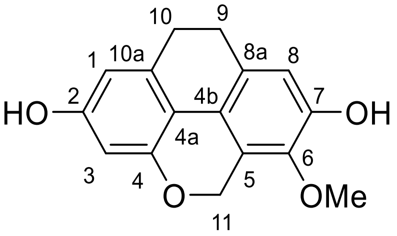
Figure 157 NOESY spectrum of compound AMF6

2.3.7 Identification of compound AMF7 (imbricatin)

Compound AMF7 was obtained as a brown amorphous solid. The HR-ESI mass spectrum (**Figure 158**) showed a sodium adduct molecular ion $[M+Na]^+$ at *m/z* 293.07781, (calculated for $C_{16}H_{14}O_4Na$; 293.07898), suggesting the molecular formula $C_{16}H_{14}O_4$. The ^1H NMR spectrum (**Figure 159 and Table 32**) of AMF7 showed signals for two pairs of methylene protons at δ_H 2.75 (4H, m, H_2-9, H_2-10), a pair of downfield methylene protons at δ_H 5.15 (2H, s, H_2-11), a pair of *meta*-coupled aromatic protons at δ_H 6.35 (1H, d, *J* = 1.8 Hz, H-1) and 6.26 (1H, d, *J* = 1.8 Hz, H-3), an uncoupled aromatic proton at δ_H 6.70 (1H, s, H-8), and a methoxy group at δ_H 3.77 (3H, s, 6-OMe). The positions of the methylene protons (H_2-9 and H_2-10) were further confirmed by their NOESY correlations with H-8 and H-1, respectively. The ^{13}C NMR and HSQC spectra (**Figures 160 and 161**) revealed sixteen carbon signals including an oxygenated methylene carbon C-11 (δ_C 63.3) and a methoxy carbon (δ_C 60.4). The above NMR data of AMF7 suggested a dihydrophenanthropyran skeleton (Majumder, Sen*, et al.*, 1999).

From the HMBC spectrum (**Figure 162**), the assignment of H-1 was deduced from its correlations to C-3 (δ_C 101.1) and C-4a (δ_C 111.6). The assignment of H-3 was based on its HMBC correlations with C-1 (δ_C 108.4), C-2 (δ_C 157.5), C-4 (δ_C 153.1), and C-4a. The position of H-8 was assigned from its HMBC correlations with C-4b (δ_C 119.1), C-6 (δ_C 141.6), and C-7 (δ_C 148.5). The position of 6-OMe was deduced from the NOESY interaction between the methoxy protons at C-6 and the methylene protons at C-11 (**Figure 163**).

Comparison of the NMR data of AMF7 with those of imbricatin obtained from *Vanda coerulea* (Simmler *et al.*, 2010) indicated that AMF7 was imbricatin [**330**]. This compound was previously reported from *Aerides rosea* (Cakova *et al.,* 2015).

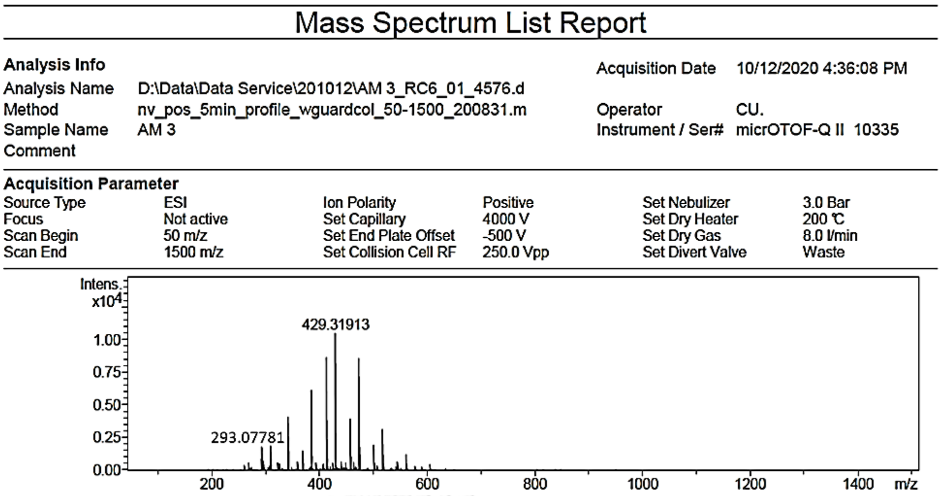


imbricatin [**330**]

Table 32 NMR spectral data of compound AMF7 and imbricatin

Position	AMF7 (acetone-d_6)		Imbricatin (CDCl$_3$)	
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
1	6.35 (1H, d, 1.8)	108.4	6.29 (1H, d, 2.5)	108.7
2	-	157.5	-	155.0
3	6.26 (1H, d, 1.8)	101.1	6.31 (1H, d, 2.5)	101.8
4	-	153.1	-	153.0
5	-	121.2	-	121.0
6	-	141.6	-	141.0
7	-	148.5	-	147.6
8	6.70 (s, 1H)	114.9	6.73 (s, 1H)	114.4
9	2.75 (2H, m)	27.7	2.79-2.78 (4H, d, 3.9)	27.5
10	2.75 (2H, m)	27.0		28.0
4a	-	111.6	-	113.1
4b	-	119.1	-	120.1
8a	-	128.4	-	129.8
10a	-	135.4	-	136.0
11	5.15 (2H, s)	63.3	5.19 (2H, s)	63.8
MeO-6	3.78 (3H, s)	60.4	3.77 (3H, s)	62.2

(Simmler *et al.*, 2010)



Mass Spectrum List Report

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Sample Name	AM 3	Instrument / Ser#	micrOTOF-Q II 10335
Comment			

Acquisition Parameter

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Figure 158 Mass spectrum of compound AMF7

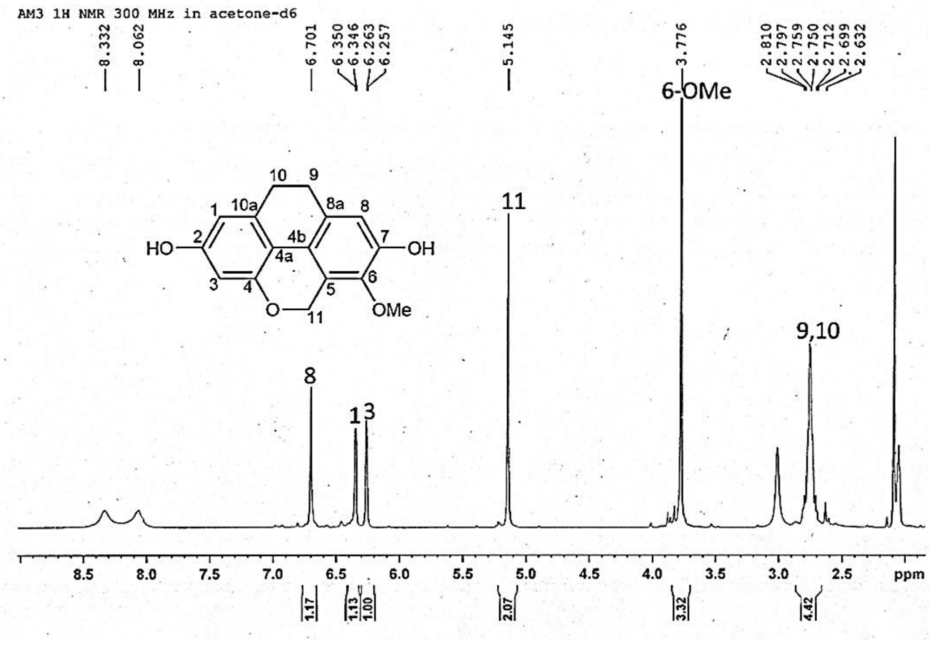


Figure 159 ^{1}H-NMR (300 MHz) spectrum of compound AMF7

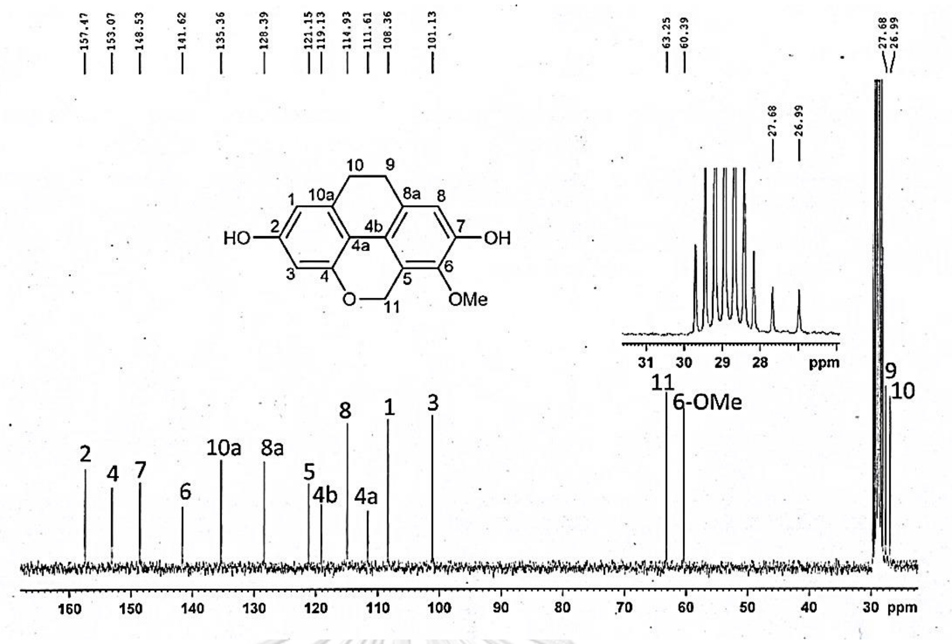


Figure 160 ^{13}C-NMR (75 MHz) spectrum of compound AMF7

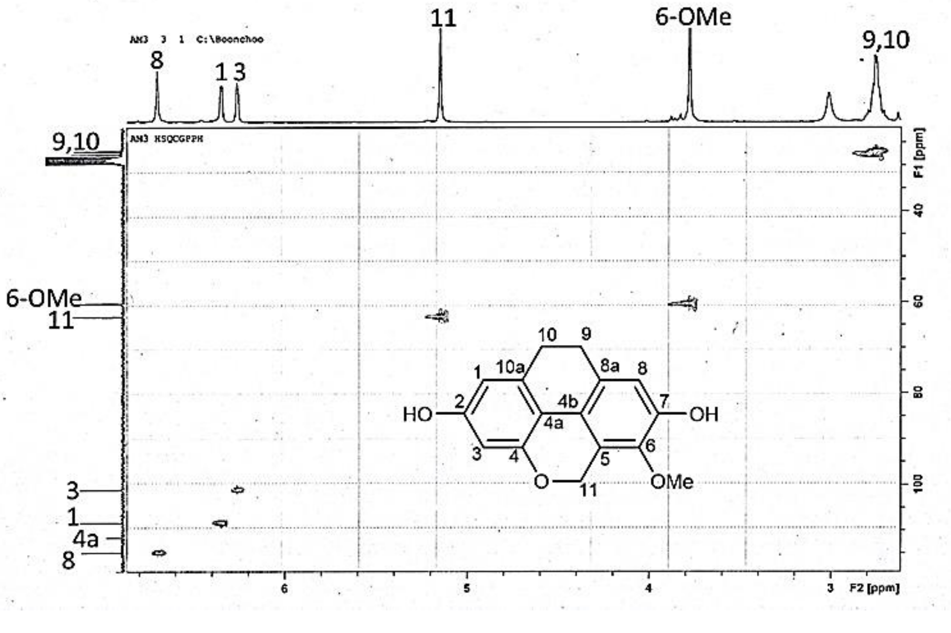


Figure 161 HSQC spectrum of compound AMF7

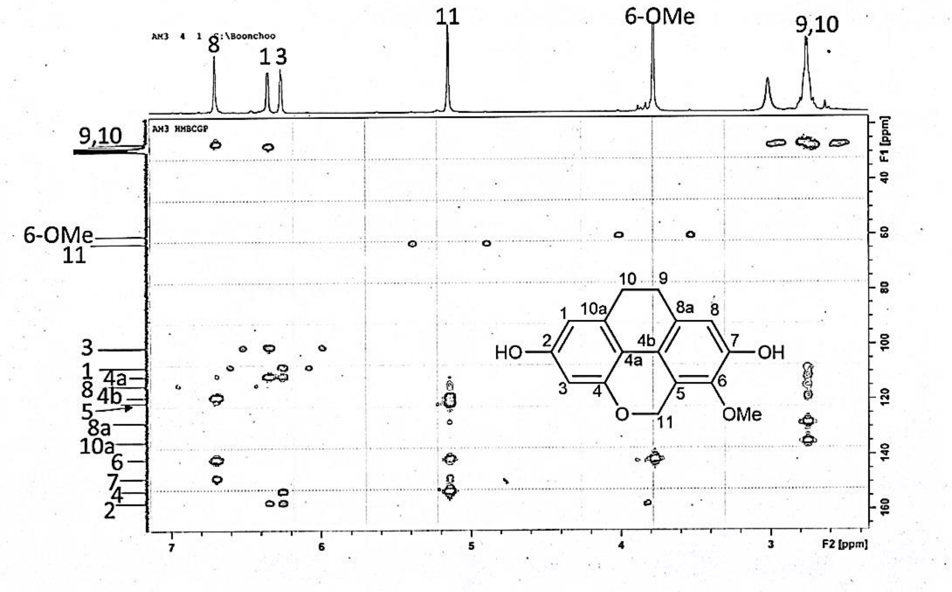


Figure 162 HMBC spectrum of compound AMF7

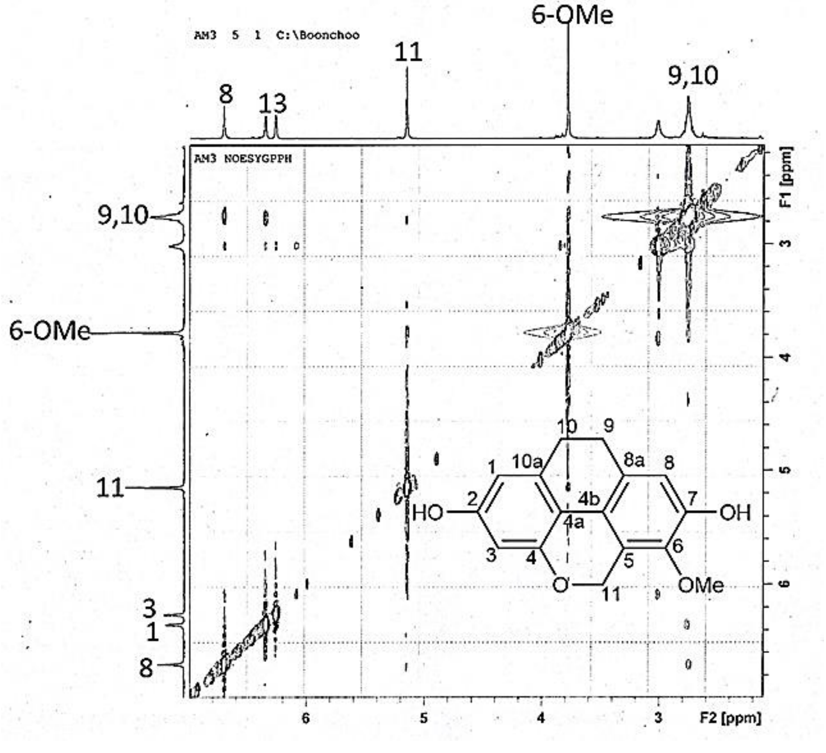


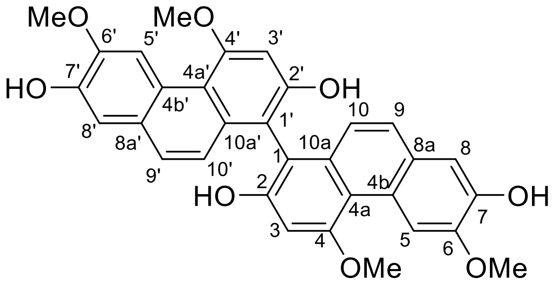
Figure 163 NOESY spectrum of compound AMF7

2.3.8 Identification of compound AMF8 (agrostonin)

AMF8 was obtained as a brown amorphous solid. The HR-ESI mass spectrum (**Figure 164**) showed a sodium adduct molecular ion $[M+Na]^+$ at *m/z* 561.1527, (calculated for $C_{32}H_{26}O_8Na$; 561.1525), suggesting the molecular formula $C_{32}H_{26}O_8$. The ^{13}C-NMR and HSQC spectra (**Figures 165 and 166**) showed only 15 carbon signals, suggesting that AMF8 was a dimeric phenanthrene with two identical subunits. The ^{1}H-NMR spectrum (**Figures 167 and Table 33**) of AMF8 revealed the presence of a pair of two-proton doublets with *ortho*-coupling [δ_H 7.37 (2H, d, *J* = 9.0 Hz, H-9/H-9′) and 6.95 (2H, d, *J* = 9.0 Hz, H-10/H-10′)], three sharp singlets accounting for two protons each [δ_H 7.00 (2H, H-3/H-3′), 9.26 (2H, H-5/H-5′) and 7.20 (2H, H-8/H-8′)], and two singlets representing two methoxy groups each [δ_H 4.24 (6H, s, MeO-4/MeO-4′) and 4.08 (6H, s, MeO-6/MeO-6′)]. Comparison of the ^{1}H and ^{13}C-NMR data of AMF8 with those of AMF3 revealed similarities, except for the presence of the methoxy groups at C-6/C-6′ in AMF8, instead of hydroxyl groups.

The assignments of H-8/H-8′were obtained from their HMBC correlations (**Figure 168**) with C-9/C-9′ (δ_C 127.1). The HMBC correlations of C-4a/C-4a′ (δ_C 115.5) with H-3/H-3′, H-5/H-5′ and H-10/H-10′ were also observed. Four hydroxy groups, 2-OH/2′-OH at δ_H 7.61 and 7-OH/7′-OH at δ_H 7.88, were assigned by their HMBC correlations with C-3/C-3′(δ_C 99.2) and C-8/C-8′ (δ_C 111.3), respectively. The methoxy groups were located at C-4/C-4′ (δ_C 159.3) and C-6/C-6′ (δ_C 147.6) based on their NOESY correlations with H-3/H-3′ and H-5/ H-5′, respectively (**Figure 169**).

These two symmetrical phenanthrene units were connected directly through a C-1 to C-1′ linkage, similar to that of AMF3. The above spectral data were in agreement with agrostonin [**341**], a dimeric phenanthrene earlier reported from *Bletilla formosana* (Lin *et al.*, 2016). Thus, AMF8 was identified as agrostonin. The compound was also found in *Agrostrophyllum khasivanum* and *Agrostrophyllum callosum* (Majumder *et al.*, 1998).



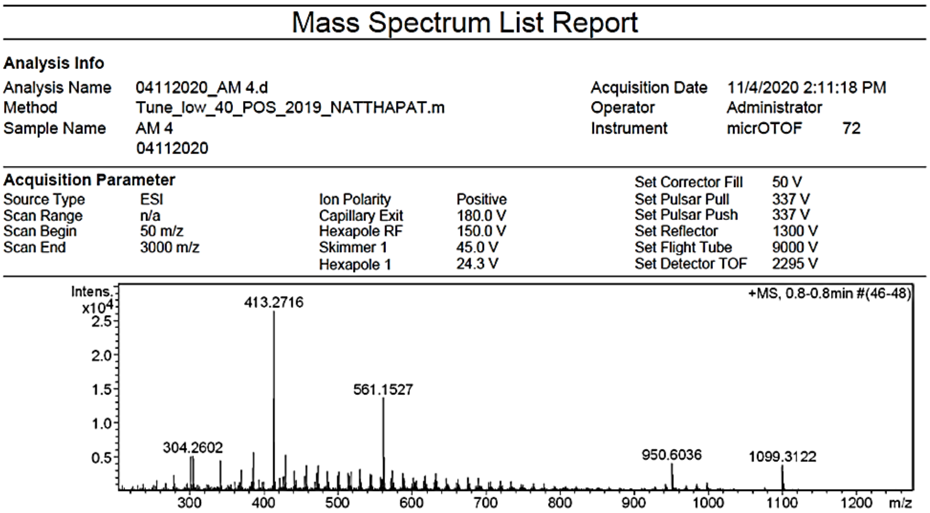
agrostonin [**341**]

Table 33 NMR spectral data of compound AMF8 and agrostonin

Position	AMF8 (acetone-d_6)		Agrostonin (acetone-d_6)	
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
1,1′	-	108.9	-	109.8
2,2′	-	154.2	-	155.1
3,3′	7.00 (2H, s)	99.2	7.00 (2H, s)	100.0
4,4′	-	159.3	-	160.2
4a,4a′	-	115.5	-	116.3
4b, 4b′	-	124.9	-	125.8
5,5′	9.26 (2H, s)	108.9	9.25 (2H, s)	109.7
6,6′	-	147.6	-	148.5
7,7′	-	145.2	-	146.0
8,8′	7.20 (2H, s)	111.3	7.19 (2H, s)	112.2
8a,8a′	-	127.2	-	128.1
9,9′	7.37 (2H, d, 9.0)	127.1	7.36 (2H, d, 9.2)	127.9
10,10′	6.95 (2H, d, 9.0)	122.5	6.93 (2H, d, 9.2)	123.3
10a,10a′	-	134.6	-	135.4
4-OMe, 4′-OMe	4.24 (6H, s)	55.3	4.23 (6H, s)	56.1
6-OMe, 6′-OMe	4.08 (6H, s)	55.2	4.07 (6H, s)	56.0

Position	AMF8 (acetone-d_6)		Agrostonin (acetone-d_6)	
	δ_H (mult., J in Hz)	δ_C	δ_H (mult., J in Hz)	δ_C
2-OH, 2′-OH	7.61 (2H, s)	-	-	-
7-OH, 7′-OH	7.88 (2H, s)	-	-	-

(Lin *et al.*, 2016)



Mass Spectrum List Report

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Acquisition Parameter

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Scan End	3000 m/z	Skimmer 1	45.0 V	Set Reflector	1300 V
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				Set Detector TOF	2295 V

Figure 164 Mass spectrum of compound AMF8

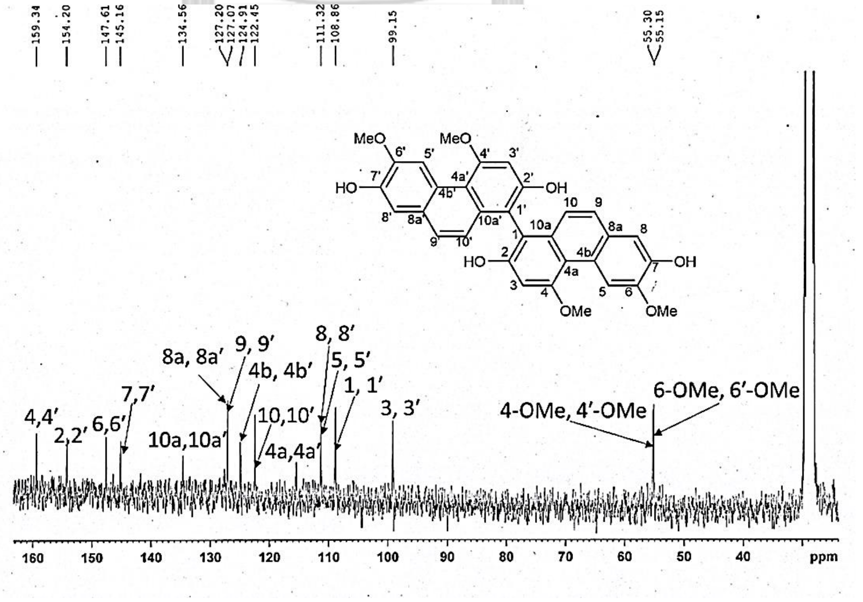


Figure 165 ^{13}C-NMR (75 MHz) spectrum of compound AMF8

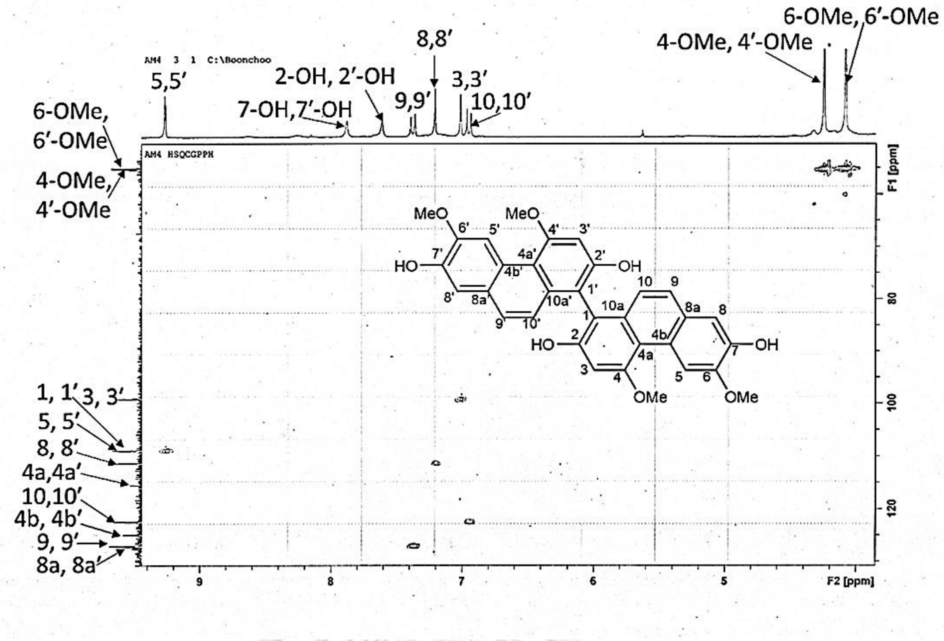


Figure 166 HSQC spectrum of compound AMF8

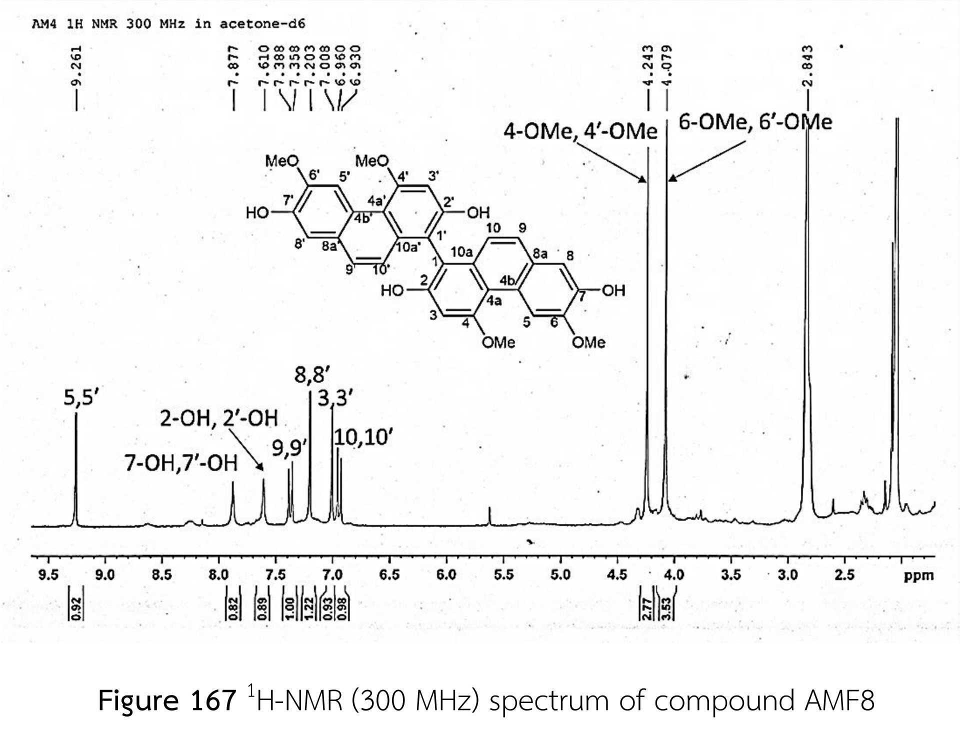


Figure 167 ^{1}H-NMR (300 MHz) spectrum of compound AMF8

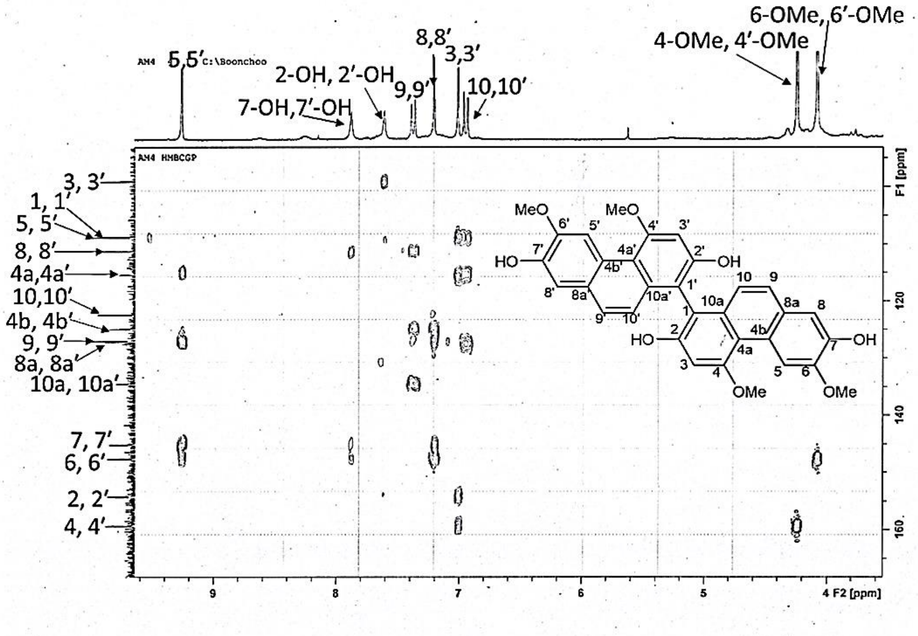


Figure 168 HMBC spectrum of compound AMF8

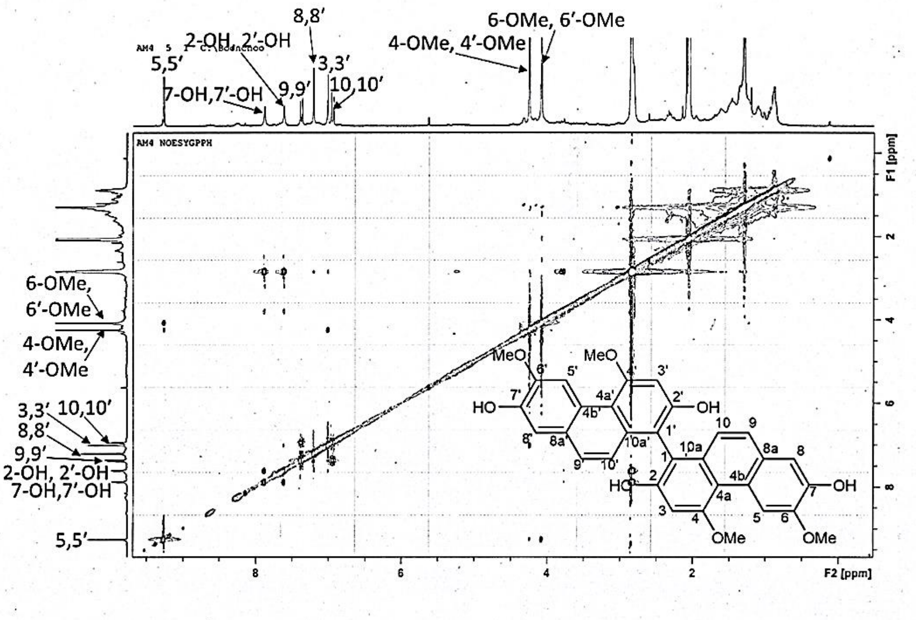
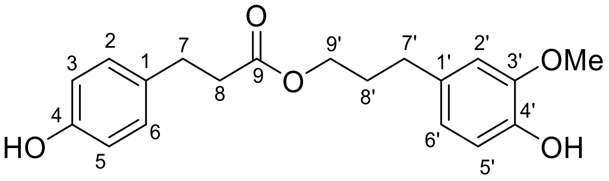


Figure 169 NOESY spectrum of compound AMF8

2.3.9 Identification of compound AMF9 (dihydrocorniferyl dihydro-p-coumarate)

AMF9 was obtained as a yellow amorphous solid. The HR-ESI mass spectrum (**Figure 170**) showed a sodium adduct molecular ion $[M+Na]^+$ at *m/z* 353.1369, (calculated for $C_{19}H_{22}O_5Na$; 353.1365), suggesting the molecular formula $C_{19}H_{22}O_5$. The ^{1}H NMR spectrum (**Figure 171 and Table 34**) of AMF9 indicated five pairs of methylene protons at δ_H 2.83 (2H, t, *J* = 7.8 Hz, H_2-7), 2.57 (2H, m, H_2-7′), 2.57 (2H, m, H_2-8), 1.92 (2H, m, H_2-8′) and 4.04 (2H, t, *J* = 6.6 Hz, H_2-9′), seven aromatic protons at δ_H 7.07 (2H, d, *J* = 8.4 Hz, H-2, H-6), 6.75 (2H, d, *J* = 8.4 Hz, H-3, H-5), 6.80 (1H, d, *J* = 1.8 Hz, H-2′), 6.73 (1H, d, *J* = 8.1 Hz, H-5′), 6.63 (1H, dd, *J* = 8.1, 1.8 Hz, H-6′) and a methoxy group at δ_H 3.81 (s, 3′-OMe). The ^{13}C-NMR and HSQC spectra (**Figures 172 and 173**) of AMF9 displayed nineteen carbon signals, including, five aliphatic methylene carbons, seven aromatic methine carbons, five aromatic quaternary carbons, a methoxy carbon and a carboxyl carbon.

The HMBC spectrum of AMF9 (**Figure 174**) showed correlations from H_2-7 to C-2 (δ_C 129.2), C-6 (δ_C 129.2) and C-9 (δ_C 172.3) for the first phenylpropanoid unit and correlations from H_2-7′ to C-2′ (δ_C 111.9), C-6′ (δ_C 120.7) and C-9′ (δ_C 63.2) for the second unit. The two phenylpropanoid units of AMF9 should be connected through an ester bond between C-9 and C-9′, as indicated by the HMBC correlation between C-9 and H_2-9′. The location of a MeO-3′ group was determined from its NOESY correlation with H-2′ (**Figure 175**). The above NMR spectral data of AMF9 was similar to those of AMF4 except for the absence of the methoxy groups at C-3 and C-5′ in AMF9. Based upon the above spectral evidence, AMF9 was identified as dihydrocorniferyl dihydro-*p*-coumarate [**275**]. This compound was earlier reported from *Dendrobium nobile* (Zhang *et al*., 2006).

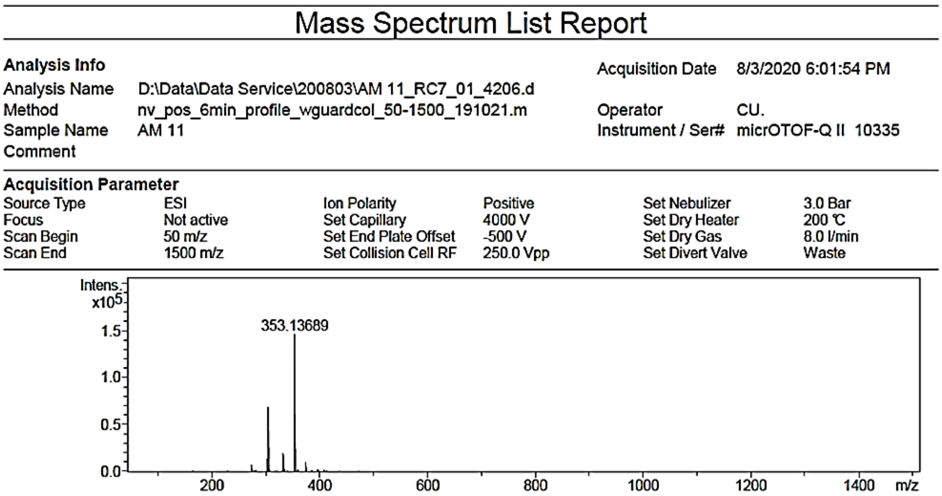


dihydrocorniferyldihydro-*p*-coumarate [**275**]

Table 34 NMR spectral data of AMF9 and dihydrocorniferyl dihydro-*p*-coumarate

Position	AMF 9 (acetone-d_6)		Dihydroconiferyldihydro-*p*-coumarate ($CDCl_3$)	
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
1	-	131.5	-	132.7
2	7.07 (1H, d, 8.4)	129.2	7.06 (1H, d, 8.4)	129.4
3	6.75 (1H, d, 8.4)	115.1	6.74 (1H, d, 8.4)	115.3
4	-	155.7	-	154.0
5	6.75 (1H, d, 8.4)	114.8	6.74 (1H, d, 8.4)	115.3
6	7.07 (1H, d, 8.4)	129.2	7.06 (1H, d, 8.4)	129.4
7	2.83 (2H, t, 7.8)	29.9	2.88 (2H, t, 7.6)	30.2
8	2.57 (2H, m)	35.9	2.59 (2H, t, 7.6)	36.2
9	-	172.3	-	173.1
1′	-	132.7	-	133.1
2′	6.80 (1H, d, 1.8)	111.9	6.65 (1H, br s)	111.0
3′	-	147.3	-	146.4
4′	-	144.7	-	143.8
5′	6.73 (1H, d, 8.1)	114.8	6.82 (1H, d, 8.6)	114.3
6′	6.63 (1H, dd, 8.1, 1.8)	120.7	6.64 (1H, dd, 8.8, 1.8)	121.0
7′	2.57 (2H, m)	31.4	2.56 (2H, t, 7.4)	31.8
8′	1.92 (2H, m)	30.5	1.89 (2H, m)	30.5
9′	4.04 (2H, t, 6.6)	63.2	4.08 (2H, t, 6.5)	63.8
MeO-3′	3.81 (3H, s)	55.3	3.87 (3H, s)	55.9

(Zhang *et al*., 2006)



Mass Spectrum List Report

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Comment

Acquisition Date 8/3/2020 6:01:54 PM
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Instrument / Ser# micrOTOF-Q II 10335

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Figure 170 Mass spectrum of compound AMF9

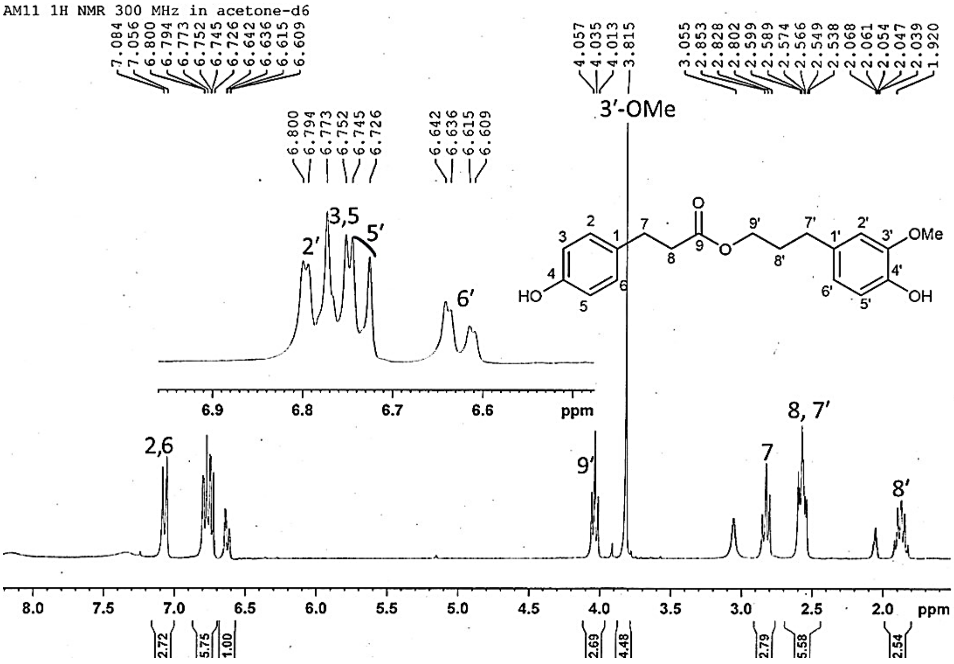


Figure 171 ^{1}H-NMR (300 MHz) spectrum of compound AMF9

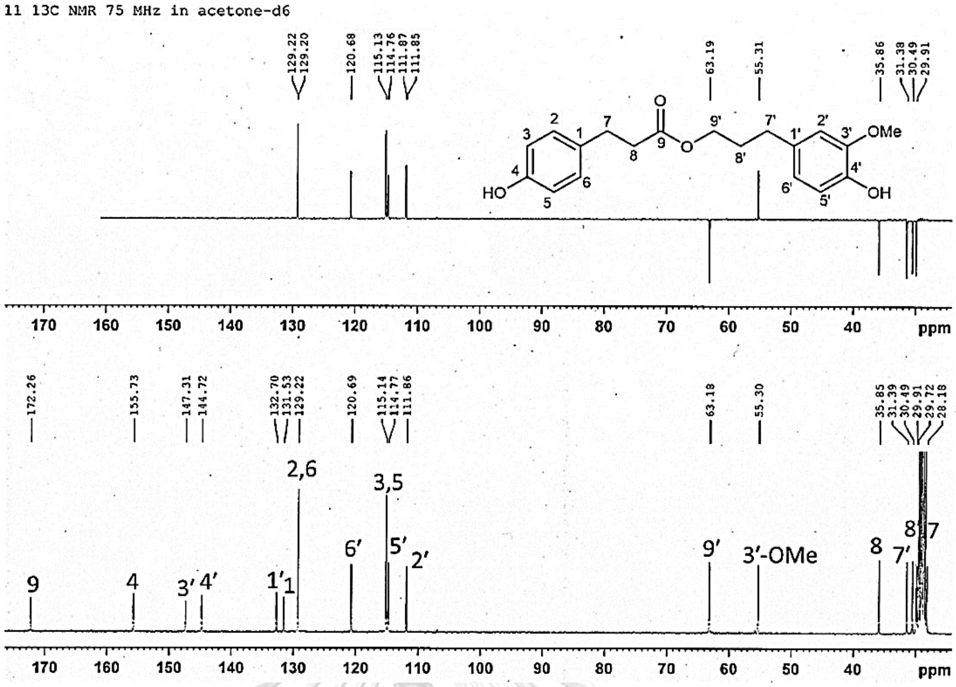


Figure 172 ^{13}C-NMR (75 MHz) spectrum of compound AMF9

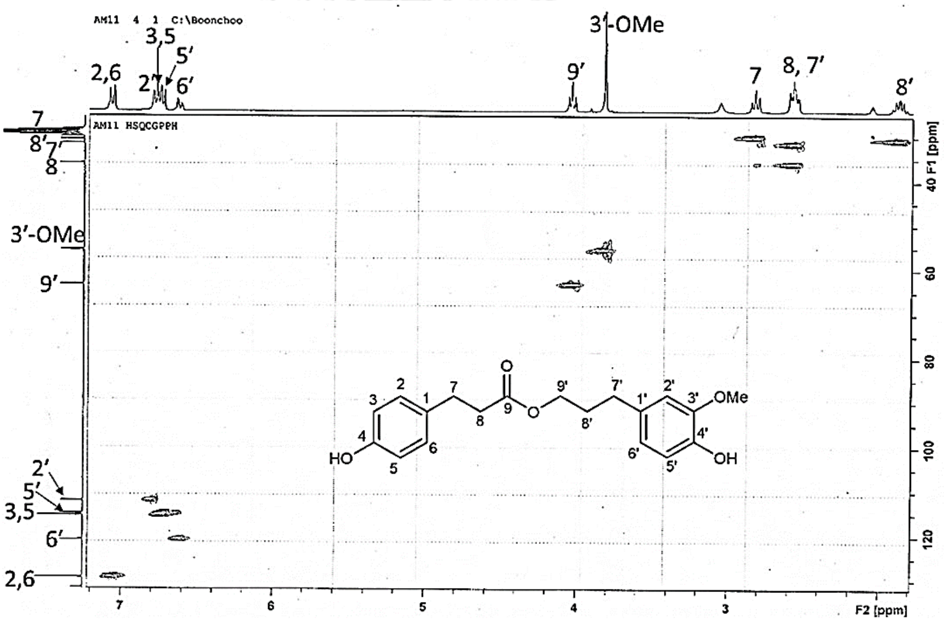


Figure 173 HSQC spectrum of compound AMF9

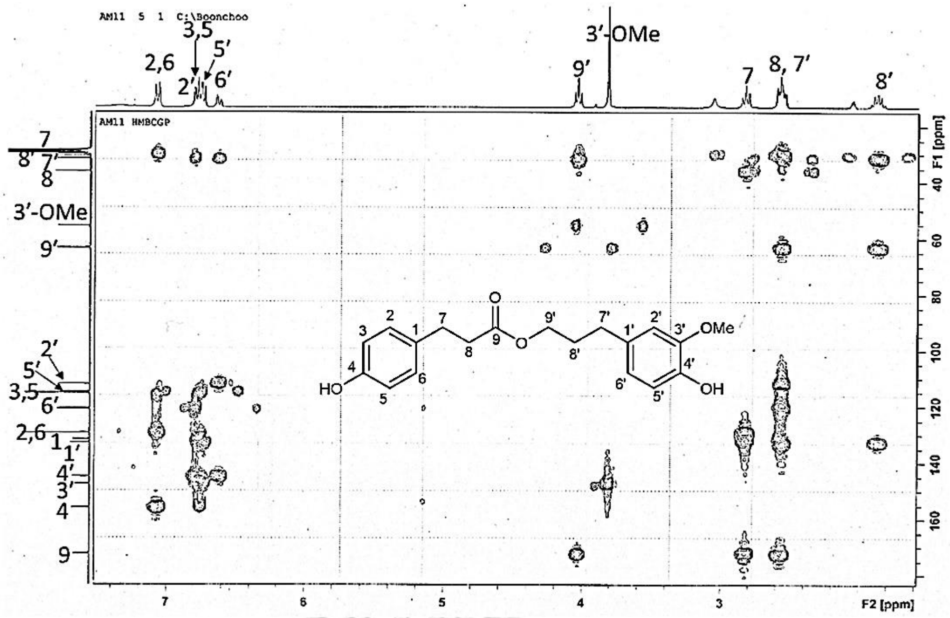


Figure 174 HMBC spectrum of compound AMF9

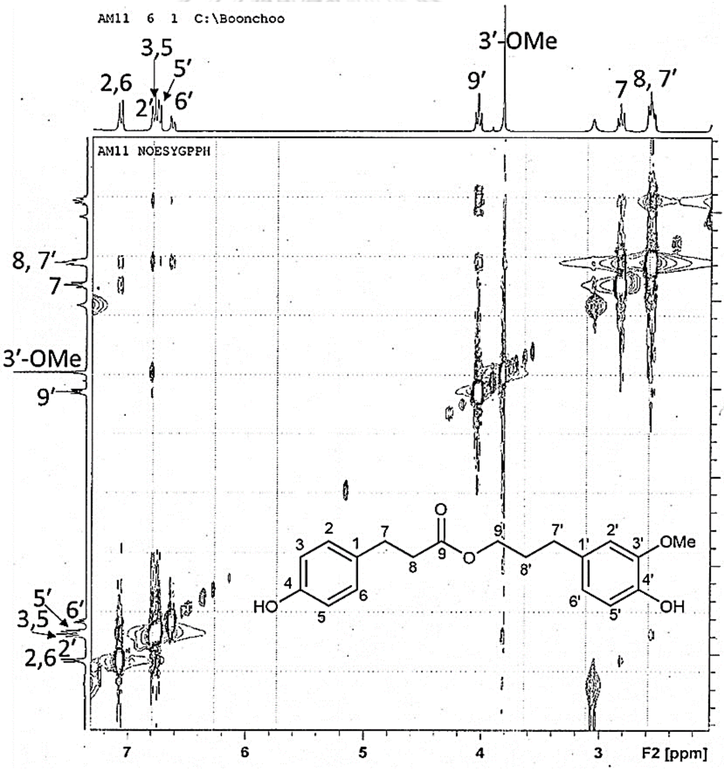


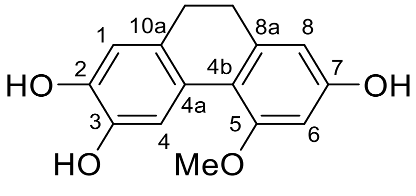
Figure 175 NOESY spectrum of compound AMF9

2.3.10 Identification of compound AMF10 (5-methoxy-9,10-dihydrophenanthrene 2,3,7-triol)

Compound AMF10 was obtained as a brown amorphous solid. The HR-ESI mass spectrum (**Figure 176**) showed a sodium adduct molecular ion $[M+Na]^+$ at *m/z* 281.0791, (calculated for $C_{15}H_{14}O_4Na$; 281.0789), suggesting the molecular formula $C_{15}H_{14}O_4$. The ^{1}H and ^{13}C-NMR spectra of AMF10 (**Figures 177 and 178, and Table 35**) showed signals for four methylene protons at δ_H 2.60 (4H, m, H_2-9, H_2-10) and two methylene carbons at δ_C 30.9 (C-9) and 28.9 (C-10), suggesting a dihydrophenanthrene nucleus. The ^{1}H NMR spectrum also showed four aromatic protons at δ_H 6.67 (1H, s, H-1), 7.81 (1H, s, H-4), 6.45 (1H, d, *J* = 1.8 Hz, H-6), and 6.36 (1H, br s, H-8), and a methoxy group at δ_H 3.82 (3H, s, 5-OMe).

The HMBC spectrum (**Figure 180**) showed correlations from H-1 to C-3 (δ_C 142.5), C-4a (δ_C 124.9) and C-10; from H-4 to C-2 (δ_C 142.7), C-4b (δ_C 115.5) and C-10a (δ_C 129.4); H-6 to C-4b and C-8 (δ_C 107.4); and from H-8 to C-4b, C-6 (δ_C 98.2) and C-9. The NOESY spectrum (**Figure 181**) showed a cross peak from 5-OMe protons to H-6; H_2-9 to H-8; and H_2-10 to H-1.

The above NMR spectral data agreed with those reported for 5-methoxy-9,10-dihydrophenanthrene-2,3,7-triol [**342**], a dihydrophenanthrene earlier obtained from *Bulbophyllum vaginatum* (Leong *et al*., 1997). Thus, compound AMF10 was identified as 5-methoxy-9,10-dihydrophenanthrene 2,3,7-triol [**342**].

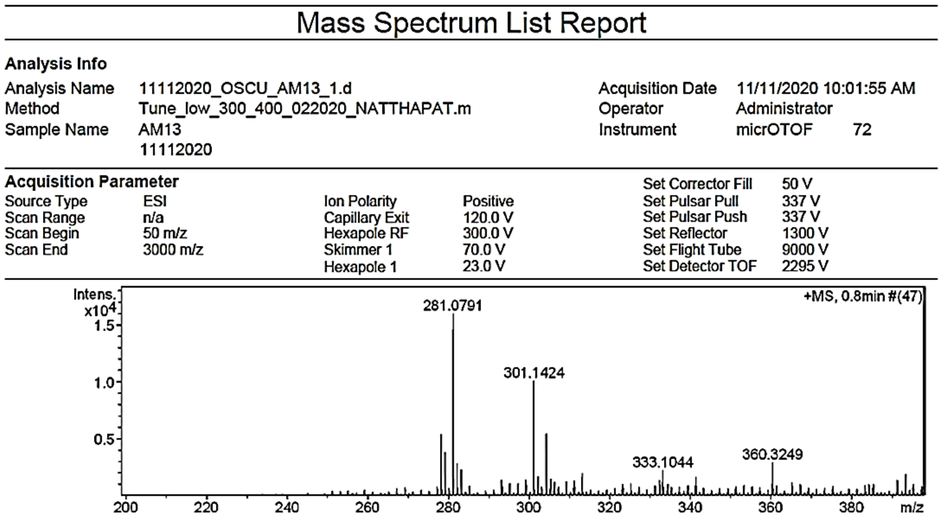


5-methoxy-9,10-dihydrophenanthrene-2,3,7-triol [**342**]

Table 35 NMR spectral data of AMF10 and 5-methoxy-9,10-dihydrophenanthrene-2,3,7-triol

Position	AMF10 (acetone-d_6)		5-Methoxy-9,10-dihydrophenanthrene-2,3,7-triol (acetone-d_6)	
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
1	6.67 (1H, s)	114.1	6.66 (1H, s)	116.4
2	-	142.7	-	143.6
3	-	142.5	-	143.3
4	7.81 (1H, s)	115.5	7.81 (1H, s)	115.0
4a	-	124.9	-	125.8
4b	-	115.5	-	116.4
5	-	157.7	-	158.6
6	6.45 (1H, d, 1.8)	98.2	6.43 (1H, d, 2.4)	99.1
7	-	156.4	-	157.3
8	6.36 (1H, br s)	107.4	6.36 (1H, d, 2.4)	108.3
9	2.60 (4H, m)	30.9	2.58 (4H, m)	31.8
10		28.9		29.8
8a	-	140.6	-	141.4
10a	-	129.4	-	130.3
MeO-5	3.82 (3H, s)	54.8	3.82 (3H, s)	55.7

(Leong *et al.,* 1997)



Mass Spectrum List Report

Analysis Info

Analysis Name	11112020_OSCU_AM13_1.d	Acquisition Date	11/11/2020 10:01:55 AM
Method	Tune_low_300_400_022020_NATTHAPAT.m	Operator	Administrator
Sample Name	AM13 11112020	Instrument	micrOTOF 72

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Corrector Fill	50 V
Scan Range	n/a	Capillary Exit	120.0 V	Set Pulsar Pull	337 V
Scan Begin	50 m/z	Hexapole RF	300.0 V	Set Pulsar Push	337 V
Scan End	3000 m/z	Skimmer 1	70.0 V	Set Reflector	1300 V
		Hexapole 1	23.0 V	Set Flight Tube	9000 V
				Set Detector TOF	2295 V

Figure 176 Mass spectrum of compound AMF10

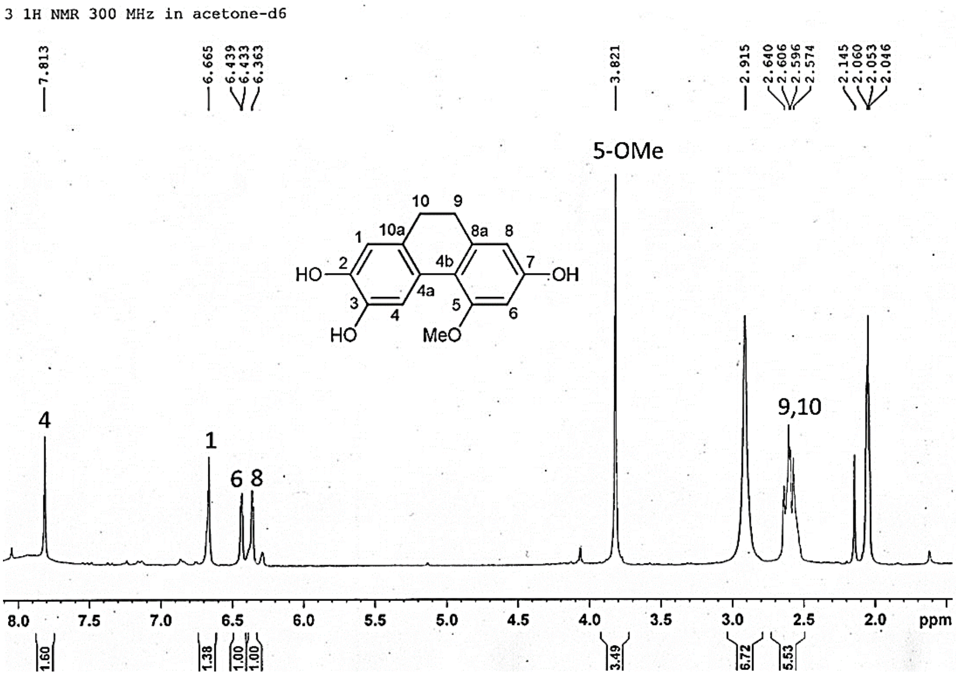


Figure 177 ^{1}H-NMR (300 MHz) spectrum of compound AMF10

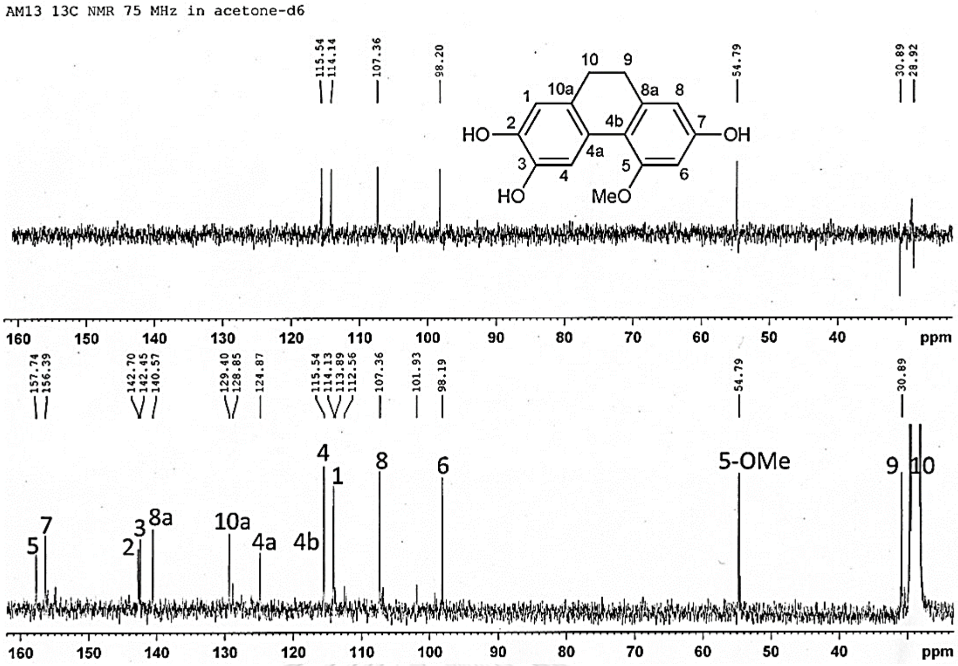


Figure 178 ^{13}C-NMR (75 MHz) spectrum of compound AMF10

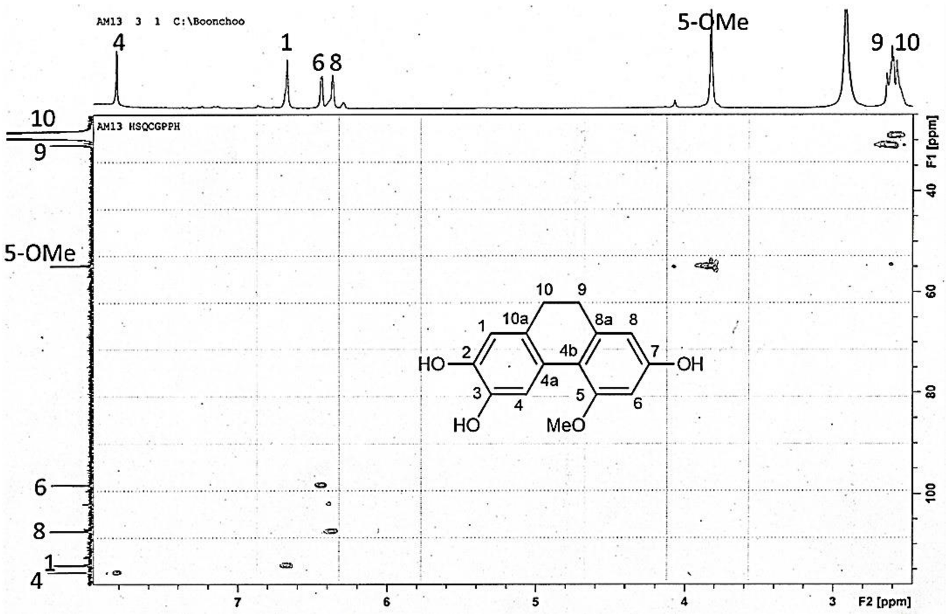


Figure 179 HSQC spectrum of compound AMF10

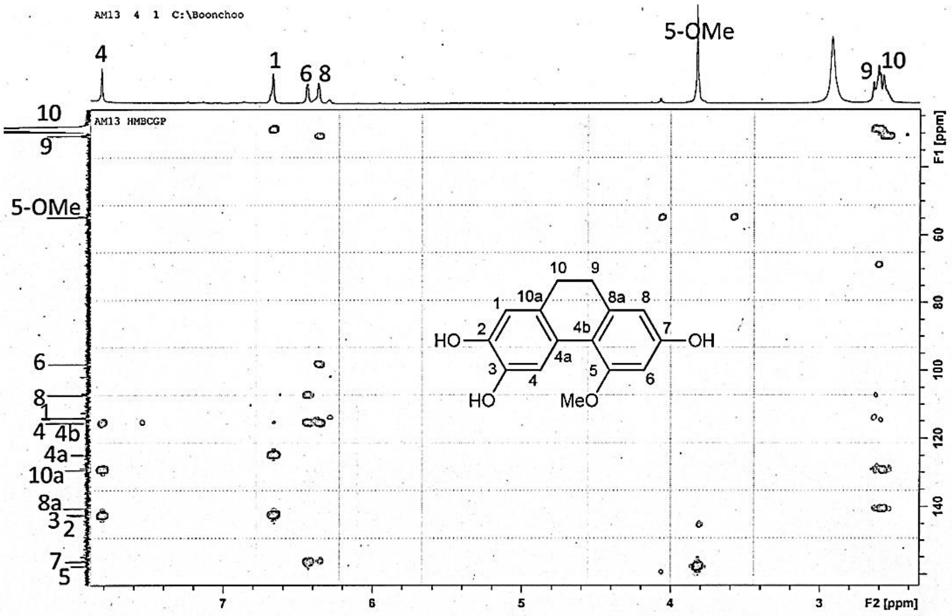


Figure 180 HMBC spectrum of compound AMF10

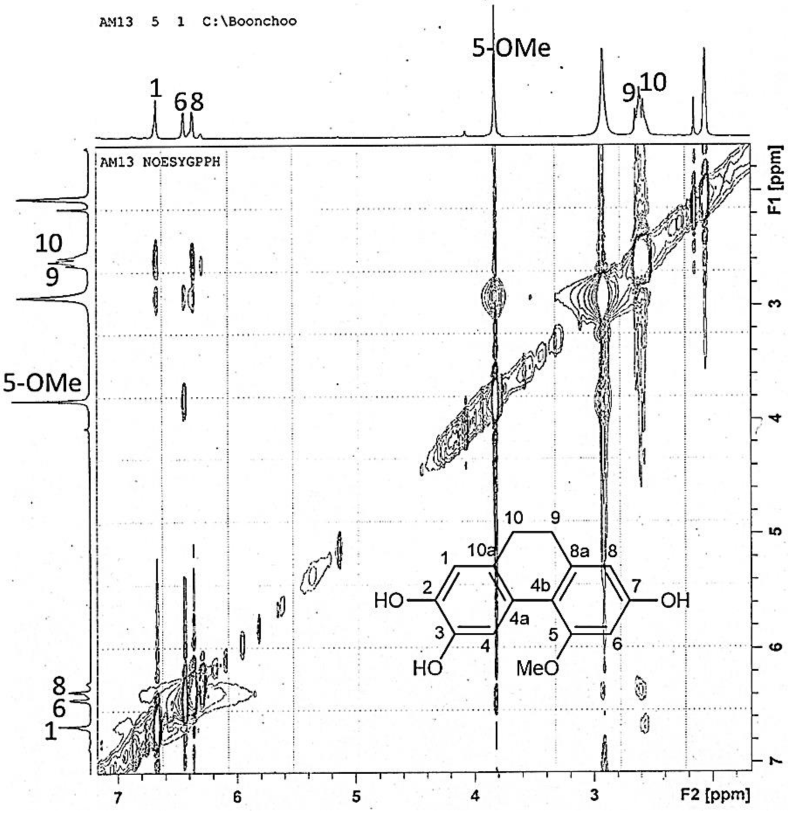


Figure 181 NOESY spectrum of compound AMF10

3 Evaluation of α-glucosidase inhibitory activity

3.1 α-Glucosidase inhibitory activity of compounds from *Dendrobium delacourii*

All the isolated compounds **(Figure 7)** were evaluated for α-glucosidase inhibitory activity. Moscatin [**110**], gigantol [**2**], and lusianthridin [**97**] showed moderate activity, with IC_{50} values of 390.1 ± 9.8 µM, 191.3 ± 6.8 µM, and 195.4 ± 9.6 µM, respectively, as compared with the positive control acarbose (IC_{50} 514.4 ± 9.2 µM). In addition, 4,4′,7,7′-tetrahydroxy-2,2′-dimethoxy-9,9′,10,10′-tetrahydro-1,1′-biphenanthrene [**154**], phoyunnanin E [**157**], and phoyunnanin C [**156**] showed potent α-glucosidase inhibitory activities with IC_{50} values of 18.4 ± 3.4 µM, 8.9 ± 0.8 µM, and 12.6 ± 0.9 µM, respectively. These dimeric compounds showed 10-20 folds stronger inhibitory activity than monomeric compound lusianthridin [**97**]. **(Table 36)**

Table 36 α-Glucosidase inhibitory activity of compounds from *D. delacourii*

Compounds	IC_{50} (µM)
Hircinol (DD1) [**94**]	NA
Ephemeranthoquinone (DD2) [**129**]	NA
Densiflorol B (DD3) [**126**]	NA
Moscatin (DD4) [**110**]	390.1 ± 9.8
4,9-Dimethoxy,2,5-phenanthrenediol (DD5) [**105**]	NA
Gigantol (DD6) [**2**]	191.3 ± 6.8
Batatasin III (DD7) [**3**]	NA
Lusianthridin (DD8) [**97**]	195.4 ± 9.6
4,4′,7,7′-Tetrahydroxy-2,2′-dimethoxy-9,9′,10,10′-tetrahydro-1,1′-biphenanthrene (DD9) [**154**]	18.4 ± 3.4
Phoyunnanin E (DD10) [**157**]	8.9 ± 0.8
Phoyunnanin C (DD11) [**156**]	12.6 ± 0.9
Acarbose	514.4 ± 9.2

NA = no inhibitory activity

The most potent compounds, DD10 [**157**] and DD11 [**156**], were further studied to determine the mode of enzyme inhibition. The experiment was performed by constructing Lineweaver-Burk plots of the reciprocal of velocity (1/V) against the reciprocal of substrate concentration (1/[S]). The substrate *p*-nitrophenol-α-D-glucopyranoside concentration was varied from 0.25 to 2.0 mM in the absence or presence of the test compound (12 µM and 22 µM for DD10; 12 µM and 24 µM for DD11). As summarized in **Table 37**, an increase in the concentration of DD10 or DD11 reduced the V_{max} but did not affect the K_m value, indicating a non-competitive type of enzyme inhibition **(Figures 182 and 183)**. The drug acarbose showed the intersection of the lines on Y-axis, indicating a competitive type of inhibition **(Figure 184)**. The secondary plots were constructed by plotting the slopes of the double-reciprocal lines and inhibitor concentrations. The K_i value is the interception point on the “X” axis and can be calculated from the line equation of the secondary plot.

Line equation of the secondary plot;

$$y = mx + b \text{ (m = slope; b = y-intercept)}$$

When y = 0;

$$0 = mx + b$$

$$x = -b / m$$

$$-K_i = -b / m \quad (x = -K_i)$$

$$K_i = b / m$$

Based on the above calculation, the K_i value (5.89 µM) of DD10 [**157**] was obtained from the line equation of the secondary plot “y = 1.401x + 8.259”, and that of DD11 (5.97 µM) [**156**] was obtained from the line equation “y = 1.387x + 8.289”. The K_i value (190.57 µM) of acarbose was also obtained from the line equation of the secondary plot “y = 0.053x + 10.101”.

$$E + I \rightleftharpoons EI$$

According to the equation, K_i = [E][I] / [EI], K_i is inversely proportional to the [EI] (Bisswanger, 2017). Thus, the smaller the K_i value, the greater binding affinity of the inhibitor [I] with the enzyme [E]. Both compounds DD10 [**157**] (K_i 5.89 μM) and DD11 [**156**] (K_i 5.97 μM) showed much greater affinity to the enzyme than acarbose (K_i 190.57 μM).

Table 37 Kinetic parameters of α-glucosidase inhibition for DD10 and DD11

Inhibitors	Dose (μM)	V_{max} ΔOD/min	K_m (mM)	K_i (μM)
None	-	0.10	1.22	
DD10 [**157**]	22	0.024	1.22	5.89
	12	0.049	1.21	
DD11 [**156**]	24	0.023	1.21	5.97
	12	0.049	1.21	
Acarbose	930	0.11	6.47	190.57
	465	0.10	4.17	

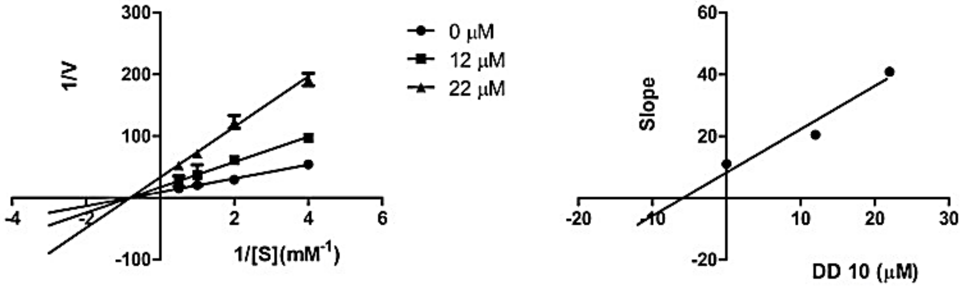


Figure 182 Lineweaver–Burk plot and secondary plot of compound DD10 [**157**]

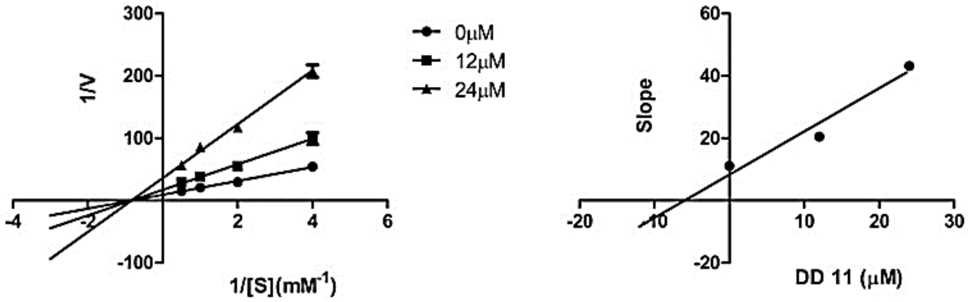


Figure 183 Lineweaver–Burk plot and secondary plot of compound DD11 [**156**]

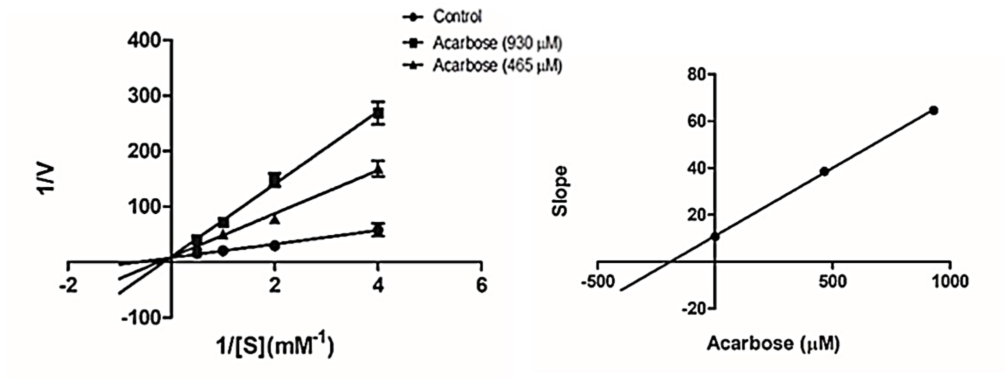


Figure 184 Lineweaver–Burk plot and secondary plot of acarbose

3.2 α-glucosidase inhibitory activity of compounds from *Dendrobium gibsonii*

All the isolated compounds (**Figure 55**) were evaluated for α-glucosidase inhibitory activity. Dendrogibsol [**336**] and lusianthridin [**97**] showed potent α-glucosidase inhibitory activities with IC_{50} values of 19.8 ± 0.9 μM and 185.4 ± 6.9 μM, respectively, when compared with acarbose (IC_{50} 514.4 ± 9.2 μM). The other compounds were devoid of activity as shown in **Table 38**.

Table 38 α-Glucosidase inhibitory activity of compounds from *D. gibsonii*

Compounds	IC_{50} (μM)
Dihydrodengibsinin (DG1) [**335**]	NA
Dendrogibsol (DG2) [**336**]	19.8 ± 0.9
Ephemeranthol A (DG3) [**90**]	NA
Dengibsinin (DG4) [**309**]	NA
Nobilone (DG5) [**308**]	NA
Aloifol I (DG6) [**20**]	NA
lusianthridin (DG7) [**97**]	185.4 ± 6.9
Dechrysan A (DG8) [**305**]	NA
4-methoxy-9*H*-fluorene-2,5,9-triol (DG9) [**312**]	NA
Acarbose	514.4 ± 9.2

NA= no inhibitory activity

The most potent compound DG2 [**336**] was further investigated for kinetic properties regarding the mode of enzyme inhibition, in a similar manner as earlier described in section 3.1, using substrate concentrations in the range of 0.25 - 2.0 mM. DG2 [**336**] showed a non-competitive type of inhibition, as indicated from the decreased values of V_{max} (ΔOD/min) from 0.10 to 0.052 and unchanged a K_m value when the concentrations of DG2 [**336**] were increased (from 11 μM to 22 μM) as shown in **(Table 39 and Figure 185).** A secondary plot was constructed **(Figure 185)** to determine the K_i value. The K_i value of DG2 [**336**] was obtained as 20.38 μM from the line equation of the secondary plot "y = 0.48x + 9.782", and it was much lower than that of acarbose (190.57 μM), as shown in **Table 39**.

Table 39 Kinetic parameters of α-glucosidase inhibition for DG2

Inhibitors	Dose (μM)	V_{max} ΔOD/min	K_m (mM)	K_i (μM)
None	-	0.10	1.22	
DG2 [**336**]	22	0.052	1.19	20.38
	11	0.086	1.23	
Acarbose	930	0.11	6.47	190.57
	465	0.10	4.17	

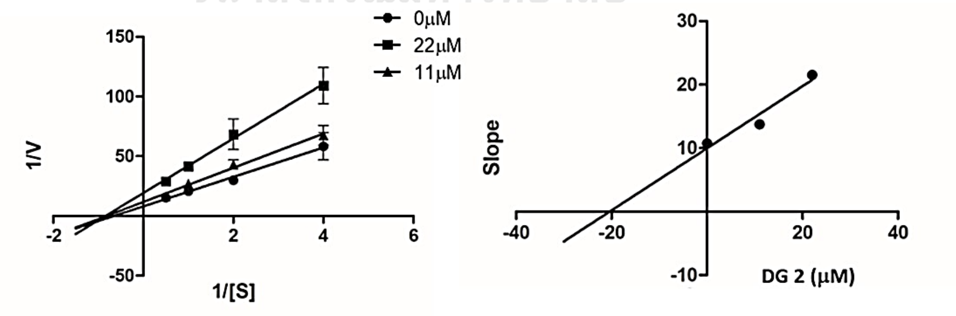


Figure 185 Lineweaver–Burk plot and secondary plot of compound DG2 [336]

3.3 α-glucosidase inhibitory activity of compounds from *Aerides multiflora*

All the isolated compounds **(Figure 114)** were evaluated for α-glucosidase inhibitory activity. All compounds, except for dihydrosinapyl dihydroferulate [**340**], exhibited strong activity (IC_{50} 5.2 - 266.7 μM) when compared with the positive control acarbose (IC_{50} value of 514.4 ± 9.2 μM). Aerimultin C [**339**] was the most potent inhibitor with an IC_{50} value of 5.2 ± 0.7 μM. The IC_{50} values of the dimeric phenanthrene derivatives: [aerimultin A [**337**] (30.9 ± 1.9 μM), aerimultin B [**338**] (77.0 ± 2.5 μM), aerimultin C [**339**] (5.2 ± 0.7 μM), and agrostonin [**341**] (37.2 ± 4.5 μM)] were lower than those of the monomers: [6-methoxycoelonin [**332**] (224.8 ± 7.8 μM), imbricatin [**330**] (165.9 ± 7.7 μM), and 5-methoxy-9,10-dihydrophenanthrene-2,3,7-triol [**342**] (115.2 ± 9.1 μM)] **(Table 40).**

Table 40 α-Glucosidase inhibitory activity of compounds from *Aerides multiflora*

Compounds	IC_{50} (μM)
Aerimultin A (AMF1) [**337**]	30.9 ± 1.9
Aerimultin B (AMF2) [**338**]	77.0 ± 2.5
Aerimultin C (AMF3) [**339**]	5.2 ± 0.7
Dihydrosinapyl dihydroferulate (AMF4) [**340**]	NA
6-Methoxycoelonin (AMF5) [**332**]	224.8 ± 7.8
Gigantol (AMF6) [**2**]	191.3 ± 6.8
Imbricatin (AMF7) [**330**]	165.9 ± 7.7
Agrostonin (AMF8) [**341**]	37.2 ± 4.5
Dihydro-coniferyl dihydro-*p*-coumarate (AMF9) [**277**]	266.7 ± 8.6
5-Methoxy-9,10-dihydrophenanthrene-2,3,7-triol (AMF10) [**342**]	115.2 ± 9.1
Acarbose	514.4 ± 9.2

NA= no inhibitory activity

A kinetic study was performed on the most potent compound AMF3 [**339**] to analyze the mode of enzyme inhibition by varying the substrate concentration (0.25–2.0 mM). From the Lineweaver–Burk plot (**Figure 186)**, an increase in the concentration of compound AMF3 (from 4 to 8 μM) reduced V_{max} from 0.10 to 0.035 but did not affect the K_m value. The results suggested a non-competitive inhibition for AMF3 [**339**]. The K_i value of compound AMF3 (4.18 μM) was calculated from the line equation of the secondary plot “y = 2.296x + 9.613” as previously described in section 3.1 and it was much lower than that of acarbose (190.57 μM), as shown in **Table 41**.

Table 41 Kinetic parameters of α-glucosidase inhibition in the presence of AMF3

Inhibitors	Dose (μM)	V_{max} ΔOD/min	K_m (mM)	K_i (μM)
None	-	0.10	1.22	
AMF3 [**339**]	8	0.035	1.20	4.18
	4	0.055	1.22	
Acarbose	930	0.11	6.47	190.57
	465	0.10	4.17	

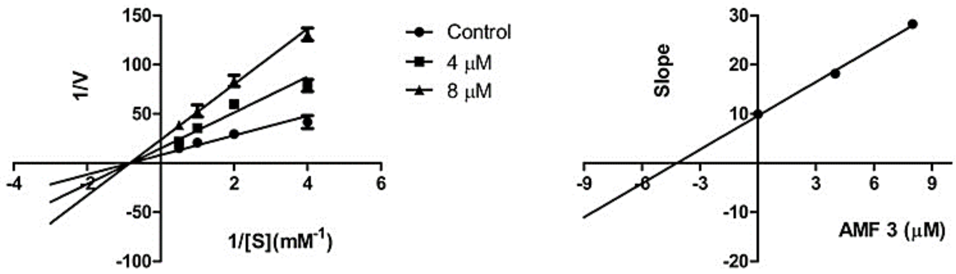


Figure 186 Lineweaver–Burk plot and secondary plot of compound AMF3 [**339**]

CHAPTER V

CONCLUSION

In this study, a total of thirty compounds were isolated from *Dendrobium delacourii* (eleven compounds), *D. gibsonii* (nine compounds), and *Aerides multiflora* (ten compounds). Two compounds (dihydrodengibsinin [**335**] and dendrogibsol [**336**]) from *D. gibsonii* and four compounds (aerimultins A-C [**337-339**] and dihydrosinapyl dihydroferulate [**340**]) from *A. multiflora* were characterized as new compounds **(Figures 55 and 114)**. Dihydrodengibsinin [**335**] was found to be a new natural fluorene. Dendrogibsol [**336**] is the first representative of the fluorene–dihydrophenanthrene adduct. Aerimultins A-C [**337-339**] were characterized as new biphenanthrenes. Dihydrosinapyl dihydroferulate [**340**] was isolated as a new natural compound in this study. All the isolated compounds were evaluated for α-glucosidase inhibitory activity in comparison with acarbose. The dimeric phenanthrenes including phoyunnanin C [**156**], phoyunnanin E [**157**] and 4,4′,7,7′-tetrahydroxy-2,2′-dimethoxy-9,9′,10,10′-tetrahydro-1,1′-biphenanthrene [**154**]) from *D. delacourii*; dendrogibsol [**336**] from *D. gibsonii;* aerimultins A-C [**337-339**] and agrostonin [**341**] from *A. multiflora* showed potent inhibitory activities. Kinetic studies were performed on four selected compounds, phoyunnanin C [**156**], phoyunnanin E [**157**], dendrogibsol [**336**], and aerimultin C [**339**]. The results indicated all the compounds showed a non-competitive type of enzyme inhibition. The K_i values were 5.97 µM for phoyunnanin C [**156**], 5.89 µM for phoyunnanin E [**157**], 20.38 µM for dendrogibsol [**336**] and 4.18 µM for aerimultin C [**339**]; all of them showed much greater affinity to the enzyme than acarbose (190.57 µM). It should be noted that non-competitive inhibitors have some advantages over competitive inhibitors in that they bind to the allosteric site of the enzyme, and thus do not depend upon the substrate concentration. Moreover, they require lower concentrations than competitive inhibitors to produce the same effect.

In summary, this investigation has provided chemical and biological information on the secondary metabolites of three Orchidaceous plants. The data on the effects of the isolated compounds on α-glucosidase enzyme should be useful for the future development of new anti-diabetic drugs from natural sources.

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