สารที่มีฤทธิ์ต้านอนุมูลอิสระจากเอื้องมัจฉา

นายณภัทร เกี่ยวข้อง

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาเภสัชศาสตรมหาบัณฑิต
สาขาวิชาเภสัชเวท ภาควิชาเภสัชเวทและเภสัชพฤกษศาสตร์
คณะเภสัชศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย
ปีการศึกษา 2560

FREE RADICAL SCAVENGERS FROM *DENDROBIUM PALPEBRAE*

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A Thesis Submitted in Partial Fulfillment of the Requirements
for the Degree of Master of Science in Pharmacy Program in Pharmacognosy
Department of Pharmacognosy and Pharmaceutical Botany
Faculty of Pharmaceutical Sciences
Chulalongkorn University
Academic Year 2017

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ณภัทร เกี่ยวข้อง : สารที่มีฤทธิ์ต้านอนุมูลอิสระจากเอื้องมัจฉา (FREE RADICAL SCAVENGERS FROM *DENDROBIUM PALPEBRAE*) อ.ที่ปรึกษาวิทยานิพนธ์หลัก: รศ. ภก. ดร.บุญชู ศรีตุลารักษ์, อ.ที่ปรึกษาวิทยานิพนธ์ร่วม: ศ. ภก. ดร.กิตติศักดิ์ ลิขิตวิทยาวุฒิ, หน้า.

การศึกษาทางพฤกษเคมีของเอื้องมัจฉาในวงศ์ Orchidaceae สามารถแยกสารบริสุทธิ์ได้ทั้งหมด 10 ชนิด พบว่าเป็นสารชนิดใหม่ในกลุ่ม phenanthrene-phenanthraquinone 1 ชนิด คือ dendropalpebrone ประกอบกับสารที่เคยมีการรายงานแล้ว 9 ชนิด ได้แก่ gigantol, lusianthridin, nobilone, 3,7-dihydroxy-2,4,8-trimethoxyphenanthrene, 2,5-dihydroxy-4,9-dimethoxyphenanthrene, moscatilin, scoparone, 4,5,4'-trihydroxy-3,3'-dimethoxy-bibenzyl และ dendroflorin จากการทดสอบฤทธิ์ต้านอนุมูลอิสระเบื้องต้นของสารบริสุทธิ์แต่ละชนิดด้วยวิธี oxygen radical absorbance capacity assay, DPPH radical scavenging assay, deoxyribose degradation assay และทดสอบฤทธิ์ยับยั้งอนุมูลอิสระในเซลล์เพาะเลี้ยงมาโครฟาจ (RAW 267.4) ที่ถูกเหนี่ยวนำโดยไฮโดรเจนเปอร์ออกไซด์ พบว่า dendroflorin มีฤทธิ์ต้านอนุมูลอิสระที่สูงที่สุด โดยความเข้มข้นของ dendroflorin ที่สามารถต้านอนุมูลอิสระได้ร้อยละ 50 (IC_{50}) คือ 193 ไมโครโมลาร์ ซึ่ง Trolox® ที่ใช้เป็นชุดควบคุมผลบวกมีค่า IC_{50} อยู่ที่ 160 ไมโครโมลาร์ นอกจากนั้นพบว่า dendroflorin ยับยั้งอนุมูลอิสระในเซลล์ได้สูงกว่ากลุ่มควบคุมอย่างมีนัยสำคัญทางสถิติในลักษณะที่แปรผันตามความเข้มข้น อีกทั้งยังสามารถส่งผลเพิ่มฤทธิ์ต้านอนุมูลอิสระของเอนไซม์ภายในเซลล์ อันได้แก่ superoxide dismutase (SOD), glutathione peroxidase (GPx) และ catalase (CAT) ได้

ภาควิชา	เภสัชเวทและเภสัชพฤกษศาสตร์	ลายมือชื่อนิสิต .....
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ปีการศึกษา	2560	ลายมือชื่อ อ.ที่ปรึกษาร่วม .....

6076103233 : MAJOR PHARMACOGNOSY
KEYWORDS: DENDROBIUM PALPEBRAE / FREE RADICALS / ORCHIDACEAE / BIBENZYLS / PHENANTHRENES / DIHYDROPHENANTHRENES / FLUORENONES

NAPAT KYOKONG: FREE RADICAL SCAVENGERS FROM *DENDROBIUM PALPEBRAE*. ADVISOR: ASSOC. PROF. BOONCHOO SRITULARAK, Ph.D., CO-ADVISOR: PROF. KITTISAK LIKHITWITAYAWUID, Ph.D., pp.

Phytochemical study of Dendrobium palpebrae Lindl. (Orchidaceae) afforded ten pure compounds. One of them was characterized as a new phenanthrene-phenanthraquinone derivative named dendropalpebrone, and nine known compounds were identified as gigantol, lusianthridin, nobilone, 3,7-dihydroxy-2,4,8-trimethoxyphenanthrene, 2,5-dihydroxy-4,9-dimethoxyphenanthrene, moscatilin, scoparone, 4,5,4'-trihydroxy-3,3'-dimethoxybibenzyl and dendroflorin. All of the isolated compounds were initially screened for their free radical scavenging activity via oxygen radical absorbance capacity assay, DPPH radical scavenging assay, deoxyribose degradation assay, and assay for intracellular antioxidant activity in H_2O_2-induced RAW 264.7 murine macrophage cells. Dendroflorin showed the most potent activity in all assays, especially in the deoxyribose degradation assay. It manifested an IC_{50} value of 193 μM approximating to the IC_{50} of Trolox®, a positive control (IC_{50} 160 μM). In a further evaluation, dendroflorin significantly reduced reactive oxygen species in hydrogen peroxide induced RAW 264.7 macrophage cells in a dose-dependent manner, and it also improved the activity of cellular antioxidant enzymes including superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase (CAT).

Department:	Pharmacognosy and Pharmaceutical Botany	Student's Signature .....
		Advisor's Signature .....
Field of Study:	Pharmacognosy	Co-Advisor's Signature .....
Academic Year:	2017	

ACKNOWLEDGEMENTS

I am delighted to express my sincere gratitude to my thesis advisor, Associate Professor Dr. Boonchoo Sritularak and my co-advisor, Professor Dr. Kittisak Likhitwitayawuid, for their invaluable help and constant encouragement throughout the thesis. This thesis would not have been accomplished without all the support, advice and kindness that I have always received from them.

Besides my advisors, I am grateful for all assistance, insightful comments and beneficial advice from the members of my thesis committee, and I would like to thank all staff members of the Department of Pharmacognosy and Pharmaceutical Botany, Faculty of Pharmaceutical Sciences, Chulalongkorn University, especially Mr. Virunh Kongkatitham, for their help and support.

I would like to thank Associate Professor Dr. Pornchai Rojsitthisak, Mr. Chawanphat Muangnoi and Mr. Wuttinont Thaweesest from the Department of Food and Pharmaceutical Chemistry, for guidance, suggestions and all their help.

Additionally, I wish to express my specially thanks to the graduate school of Chulalongkorn university for granting the graduate scholarship to commemorate the 72nd anniversary of his Majesty King Bhumibol Adulyadej, for supporting my research.

Finally, I most gratefully acknowledge my family for all their love, understanding, encouragement and supporting throughout the period of this thesis research.

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ABBREVIATIONS and SYMBOLS

AAPH	=	2,2′-Azobis(2-amidinopropane) dihydrochloride
Acetone-d_6	=	Deuterated acetone
Ara	=	Arabinose
AU	=	Absorbance unit
AUC	=	Area under the curve
br s	=	Broad singlet (for NMR spectra)
°C	=	Degree celsius
CAT	=	Catalase
CC	=	Column chromatography
$CDCl_3$	=	Deuterated chloroform
CH_2Cl_2	=	Dichloromethane
cm	=	Centimeter
^{13}C-NMR	=	Carbon-13 Nuclear Magnetic Resonance
COPD	=	Chronic obstructive pulmonary disease
1-D NMR	=	One-dimensional Nuclear Magnetic Resonance
2-D NMR	=	Two-dimensional Nuclear Magnetic Resonance
d	=	Doublet (for NMR spectra)
DCFH-DA	=	2′,7′-Dichlorofluorescein diacetate
dd	=	Doublet of doublets (for NMR spectra)
δ	=	Chemical shift
DEPT	=	Distortionless Enhancement by Polarization Transfer
DMEM	=	Dulbecco's modified eagle's medium

DPPH	=	2,2-Diphenyl-1-picrylhydrazyl
ε	=	Molar absorptivity
EDTA	=	Ethylene diamine tetraacetic acid
ESI-MS	=	Electrospray Ionization Mass Spectrometry
EtOAc	=	Ethyl acetate
FBS	=	Fetal bovine serum
FCC	=	Flash Column Chromatography
FL	=	Fluorescein
g	=	Gram
Gal	=	Galactose
GF	=	Gel Filtration
Glc	=	Glucose
GPx	=	Glutathione Peroxidase
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
$[M+Na]^+$	=	Sodium-adduct molecular ion
m	=	Multiplet (for NMR spectra)
MeOH	=	Methanol
mg	=	Milligram
µg	=	Microgram
min	=	Minute
mL	=	Milliliter
µL	=	Microliter
µM	=	Micromolar
µmol TE/g	=	Micromole Trolox® equivalent per gram of sample
mm	=	Millimeter
mM	=	Millimolar
MS	=	Mass spectrum
MW	=	Molecular weight
m/z	=	Mass to charge ratio
N/A	=	Thai name not available
nm	=	Nanometer
NMR	=	Nuclear Magnetic Resonance
NOESY	=	Nuclear Overhauser Effect Spectroscopy
ν_{max}	=	Wave number at maximal absorption
OEt	=	Ethoxy group
OMe	=	Methoxy group
ORAC	=	Oxygen Radical Absorbance Capacity

ppm	=	Part per million
Rha	=	Rhamnose
ROS	=	Reactive Oxygen Species
s	=	Singlet (for NMR spectra)
SD	=	Standard deviation
SOD	=	Superoxide Dismutase
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

Oxidative stress is defined as a loss in the balance between free radical generation and free radical detoxification by antioxidants in cells, leading to excessive accumulation that the antioxidants are not enough to neutralize the surplus of free radicals (Conti *et al.*, 2016). This imbalance can be deleterious to cellular structures, resulting in induction of aging process and causing a range of modern chronic diseases, for example, cancer, diabetes, cardiovascular diseases, Parkinson's disease, Alzheimer's disease, chronic obstructive pulmonary disease (COPD), rheumatoid arthritis (RA), chronic renal failure, and cataracts (Pham-Huy *et al.*, 2008; Fiedor and Burda, 2014).

A free radical is an atom or molecule containing unpaired electrons in the valence shell which is unintentionally generated by cell metabolism. The unpaired electrons cause the free radicals to be unstable and easy to react or withdraw electrons from other molecules to obtain their stability. Therefore, the molecules which lose their electron by attacking from free radicals will subsequently become free radicals. This chain reaction leads to the accumulation of free radicals that can be harmful to the living cell (Phaniendra *et al.*, 2015).

The most common free radicals which have been frequently studied are reactive oxygen species (ROS), including hydroxyl radical ($^{\bullet}OH$), superoxide anion ($^{\bullet}O_2^-$), and hydrogen peroxide (H_2O_2) (Koekkoek and Zanten, 2016). ROS can be generated from either endogenous and exogenous sources. For the endogenous sources, ROS mainly occur by metabolic reaction of some organelles within the cells including mitochondria, peroxisomes and endoplasmic reticulum. Other endogenous sources can be auto-oxidation of adrenaline, prostaglandin synthesis, cytochrome P450, inflammation, immune cell activation, mental stress, infection, aging, and excessive exercise. On the other hand, ROS are also generated by numerous exogenous sources such as ultraviolet (UV) light, tobacco smoke, drugs, heavy metals, industrial solvents, pesticides, and high temperature (Phaniendra *et al.*, 2015).

Antioxidant is a substance that is able to hinder or slow oxidation reaction of the free radicals. Human body has numerous mechanisms to quench oxidative stress. In normal state, endogenous antioxidants, which are naturally produced in the cell, stabilize the balance of free radicals and antioxidants. However, if this balance is destabilized by the excess of free radicals, externally supplied antioxidants known as exogenous antioxidants are essential for equilibrating this imbalance (Fusco *et al.*, 2007; Fiedor and Burda, 2014).

The endogenous antioxidants can be classified as enzymatic and non-enzymatic antioxidants. Most of antioxidant enzymes are directly related to the neutralization of cellular free radicals, namely, superoxide dismutase, catalase, glutathione peroxidase and glutathione reductase. In case of the non-enzymatic antioxidants, they are divided into two types i.e. metabolic antioxidants, and nutrient antioxidants which belong to the exogenous antioxidants. The metabolic antioxidants are produced by metabolism in the body, such as L-arginine, glutathione, coenzyme Q10, melatonin, uric acid, transferrin, and bilirubin. On the contrary, the nutrient antioxidants cannot be synthesized within the body, but must to be received through foods or supplements, for example, vitamin C, vitamin E, carotenoids, metals (e.g. zinc and selenium), flavonoids, and omega-3 fatty acids (Pham-Huy *et al.*, 2008).

Under stress conditions, the production of free radical increases in plants, resulting in induction of oxidative stress. To respond to this increasing of oxidative stress, plants have their innate ability to generate non-enzymatic antioxidants. They enhance the production of many low molecular weight antioxidants, namely, vitamin E and vitamin C. They also produce high molecular weight antioxidant secondary metabolites including, tannins, flavonoids, bibenzyls, which act as free radical scavengers, metal chelators, or reducing agents (Kasote *et al.*, 2015). For this reason, plant is one of the most important sources of exogenous antioxidants. It has been the basis of traditional medicines in the world for a long time. Moreover, chemical constituents of plants have many activities, including antioxidant activity which continue to be the source of new drugs (Krishnaiah *et al.*, 2011).

Dendrobium is one of the largest genera in the family Orchidaceae. It contains more than 1100 identified species and is widely distributed throughout Asia, Australia, and Europe (Luo *et al.*, 2016). Numerous plants in this genus have been used in traditional Chinese medicine for a long time as a yin tonic to nourish the stomach, promote the body fluid production, and reduce fever (Lo *et al.*, 2004). On the other hand, several chemical studies on *Dendrobium* species reported many secondary metabolites including alkaloids, aromatic compounds, terpenoids and polysaccharides. These compounds have been studied for various bioactivities, for instance, immunomodulatory, anti-cataract, neuroprotective, anti-angiogenesis, anti-tumor, and hepatoprotective activity (Xu *et al.*, 2013). Furthermore, previous pharmacological studies revealed that some *Dendrobium* plants were potential sources of antioxidant constituents. Several antioxidant compounds have been found from *Dendrobium*, for example, moscatilin and apigenin from *D. williamsonii* (Rungwichaniwat *et al.*, 2014), hircinol and gigantol from *D. draconis* (Sritularak *et al.*, 2011a), and dendrocandins H and I from *D. candidum* (Li *et al.*, 2009b).

At present, more than 150 species of genus *Dendrobium* have been identified in Thailand, as described below (Vaddhanaphuti, 2005; Plant varieties protection office, 2013; Forest herbarium, 2014):

Dendrobium acerosum Lindl.	**กล้วยไม้มือนาง** Kluai mai mue nang
D. aciculare Lindl.	**เอื้องใบเข็ม** Ueang bai khem
D. acinaciforme Roxb.	**เอื้องยอดสร้อย** Ueang yot soi
D. aduncum Lindl.	N/A
D. albosanguineum Lindl.	**เอื้องตางัว** Ueang ta ngua
D. aloifolium (Blume) Rchb.f.	**เอื้องมณี** Ueang mani
D. amethylstoglossum Rchb.f.	N/A
D. anceps Sw.	N/A
D. angulatum Lindl.	N/A

D. anosmum Lindl.	**เอื้องสาย** Ueang sai
D. antennatum Lindl.	**กระต่ายหูบิด** Kratai hu bid
D. aphyllum (Roxb.) C.E.C.Fisch.	**เอื้องงวงช้าง** Ueang nguang chang
D. arcuatum J.J.Sm.	**เอื้องนกกระเรียนขาว** Ueang nok krarien khao
D. bellatulum Rolfe	**เอื้องแซะภู** Ueng sae phu
D. bensoniae Rchb.f.	**เอื้องสายดอกขาว** Ueang sai dok khao
D. bicameratum Lindl.	**เอื้องเข็ม** Ueang khem
D. bifarium Lindl.	N/A
D. bilobulatum Seidenf.	**กล้วยไม้ก้างปลา** Kluai mai kang pla
D. blumei Lindl.	**หวายนายบลูม** Wai nai blum
D. brevimentum Seidenf.	**เอื้องสายสี่ดอกใต้** Ueang sai si dok tai
D. brymerianum Rchb.f.	**เอื้องคำฝอย** Ueang kham foi
D. calicopis Ridl.	**เอื้องสายทะเลบันม่วง** Ueang sai talay bun muang
D. capillipes Rchb.f.	**เอื้องคำกิ่ว** Ueang kham kio
D. cariniferum Rchb.f.	**เอื้องกาจก** Ueang kachok
D. chittimae Seidenf.	**เอื้องจิตติมา** Ueang chittima
D. christyanum Rchb.f.	**เอื้องแซะภูกระดึง** Ueang sae phu kradueng
D. chrysanthum Lindl.	**เอื้องสายมรกต** Ueang sai morakot
D. chryseum Rolfe	N/A
D. chrysocrepis Par. & Rchb.f.	N/A
D. chrysotoxum Lindl.	**เอื้องคำ** Ueang kham
D. ciliatilabellum Seidenf.	**หวายเขาเขียว** Wai khao khiao
D. clavator Ridl.	N/A

D. compactum Rolfe ex Hackett	**เอื้องข้าวตอก** Ueang khao tok
D. compressum Lindl.	**หวายแบนตะนาวศรี** Wai baen tanao si
D. concinnum Miq.	**หางเปีย** Hang pia
D. confinale Kerr	N/A
D. cowenii P.O'Byrne & J.J.Vern.	N/A
D. crepidatum Lindl. & Paxton	**เอื้องสายน้ำเขียว** Ueang sai nam khiao
D. cretaceum Lindl.	**เอื้องสายน้ำนม** Ueang sai nam nom
D. crocatum Hook.f.	**เอื้องนางนวล** Ueang nang nuan
D. cruentum Rchb.f.	**เอื้องนกแก้ว** Ueang nok kaeo
D. crumenatum Sw.	**หวายตะมอย** Wai tamoi
D. crystallinum Rchb.f.	**เอื้องนางฟ่อน** Ueang nang fon
D. cumulatum Lindl.	**เอื้องสายสี่ดอก** Ueang sai si dok
D. curviflorum Rolfe	N/A
D. cuspidatum Lindl.	**เอื้องข้าวตอกปากแหลม** Ueang khao tok pak laem
D. dantaniense Guillaumin	**เอื้องเข็ม** Ueang khem
D. delacourii Guillaumin	**เอื้องดอกมะขาม** Ueang dok ma kham
D. deltatum Seidenf.	N/A
D. denneanum Kerr	N/A
D. densiflorum Lindl.	**เอื้องมอนไข่** Ueang mon khai
D. denudans D.Don	**เอื้องสายจำปา** Ueang sai champa
D. devonianum Paxton	**เอื้องเมี่ยง** Ueang miang
D. dickasonii L.O.Williams	**เอื้องเคี้ยะ** Ueang khia
D. dixanthum Rchb.f.	**เอื้องเทียน** Ueang thian

D. dixonianum Rolfe ex Downie	**เอื้องข้าวตอกเหลือง** Ueang khao tok lueang
D. draconis Rchb.f.	**เอื้องเงิน** Ueang ngoen
D. elliottianum P.O'Byrne	**หวายเจดีย์** Wai chedi
D. ellipsophyllum Tang & F.T.Wang	**เอื้องทอง** Ueang thong
D. eriiflorum Griff.	**เอื้องข้าวตอก** Ueang khao tok
D. erostelle Seidenf.	N/A
D. erosum (Blume) Lindl.	N/A
D. eserre Seidenf.	N/A
D. exile Schltr.	**เอื้องเสี้ยน** Ueang sian
D. falconeri Hook.	**เอื้องสายวิสูตร** Ueang sai wisut
D. farmeri Paxton	**เอื้องมัจฉาณุ** Ueang matchanu
D. fimbriatum Hook.	**เอื้องคำน้อย** Ueang kham noi
*D. findlayanu*m Parish & Rchb.f.	**พวงหยก** Phuang yok
D. flexile Ridl.	N/A
D. formosum Roxb. ex Lindl.	**เอื้องเงินหลวง** Ueang ngoen luang
D. friedericksianum Rchb.f.	**เอื้องเหลืองจันทบูร** Ueang lueang chantabun
D. fuerstenbergianum Schltr.	**เอื้องแซะภูกระดึง** Ueang sae phukradueng
D. fychianum Bateman ex Rchb.f.	**หวายพม่า** Wai phama
D. garrettii Seidenf.	**หวายการ์เร็ต** Wai karet
D. gibsonii Paxton	**เอื้องคำสาย** Ueang kham sai
D. grande Hook.f.	**เอื้องแผงใบใหญ่** Ueang pheang bai yai
D. gratiotissimum Rchb.f.	**เอื้องกิ่งดำ** Ueang king dam
D. gregulus Seidenf.	**เอื้องมะต่อม** Ueang ma tom
D. griffithianum Lindl.	**เอื้องมัจฉาณุ** Ueang matchanu

D. harveyanum Rchb.f.	**เอื้องคำฝอย** Ueang kham foi
D. hendersonii Hawkes & Heller	**หวายตะมอยน้อย** Wai tamoi noi
D. henryi Schltr.	**เอื้องสุริยัน** Ueang suriyan
D. hercoglossum Rchb.f.	**เอื้องดอกมะเขือ** Ueang dok ma kuea
D. heterocarpum Lindl.	**เอื้องสีตาล** Ueang si tan
D. hymenanthum Rchb.f.	**เอื้องน้อยกลีบบาง** Ueang noi klip bang
D. hymenopterum Hook.f.	N/A
D. incurvum Lindl.	N/A
D. indivisum (Blume) Miq. var. *indivisum*	**ตานเสี้ยนไม้** Tan sian mai
D. indivisum (Blume) Miq. var. *lampangense* Rolfe	N/A
D. indivisum (Blume) Miq. var. *pallidum* Seidenf.	**ก้างปลา** Kang pla
D. indragiriense Schltr.	**เอื้องอินทิรา** Ueang inthira
D. infundibulum Lindl.	**เอื้องตาเหิน** Ueang ta hoen
D. intricatum Gagnep.	**เอื้องชมพู** Ueang chomphu
D. jenkinsii Wall. ex Lindl.	**เอื้องผึ้งน้อย** Ueang phueng noi
D. kanburiense Seidenf.	**หวายเมืองกาญจน์** Wai muang kan
D. keithii Ridl.	**หางเปีย** Hang pia
D. kentrophyllum Hook.f.	**ก้างปลาใหญ่** Kang pla yai
D. kontumense Gagnep.	**เอื้องเงินวิลาศ** Ueang ngoen wilat
D. kratense Kerr	**เอื้องข้าวตอกปากจัก** Ueang khao tok pak jak
D. lagarum Seidenf.	N/A
D. lampongense J.J.Sm.	**หวายลำปอง** Wai lum pong

D. lamellatum (Bl.) Lindl.	N/A
D. lamyaiae Seidenf.	**เอื้องครั่งแสดน้อย** Ueang krang saet noi
D. leonis (Lindl.) Rchb.f.	**เอื้องตะขาบใหญ่** Ueang ta khap yai
D. lindleyi Steud.	**เอื้องผึ้ง** Ueang phueng
D. linguella Rchb.f.	**เอื้องดอกมะเขือใต้** Ueang dok ma kuea tai
D. lituiflorum Lindl.	**เอื้องสายม่วง** Ueang sai muang
D. lueckelianum Fessel & Wolff	N/A
D. mannii Ridl.	**เอื้องหางปลา** Ueang hang pla
D. metachilinum Rchb.f.	**เอื้องทองใต้** Ueang thong tai
D. monticola Hunt & Summerh.	**เอื้องข้าวตอกมรกต** Ueang khao tok morakot
D. moschatum (Buch.-Ham.) Sw.	**เอื้องจำปา** Ueang champa
D. mucronatum Seidenf.	N/A
D. nanocompactum Seidenf.	N/A
D. nathanielis Rchb.f.	**เกล็ดนิ่ม** Klet nim
D. nobile Lindl.	**เอื้องเก้ากิ่ว** Ueang kao kio
D. ochreatum Lindl.	**เอื้องตะขาบ** Ueang ta khap
D. oligophyllum Gagnep.	**ข้าวตอกปราจีน** Khao tok prachin
D. pachyglossum Parish & Rchb.f	**เอื้องขนหมู** Ueang khon mu
D. pachyphyllum (Kuntze) Bakh.f.	**เอื้องน้อย** Ueang noi
D. palpebrae Lindl.	**เอื้องมัจฉา** Ueang matcha
D. pandaneti Ridl.	**เอื้องปักษาปากส้ม** Ueang paksa pak som
D. panduriferum Hook.f.	**หวายดินสอ** Wai dinso
D. parciflorum Rchb.f. ex Lindl.	**เอื้องดอกขาวใบแบน** Ueang dok khao bai baen

D. parcum Rchb.f.	**เอื้องก้านกิ่ว** Ueang kan kio
D. parishii Rchb.f.	**เอื้องครั่ง** Ueang khrang
D. parvum Seidenf.	N/A
D. peguanum Lindl.	**หวายเปกู** Wai peku
D. pendulum Roxb.	**เอื้องไม้เท้าฤาษี** Ueang mai thao ruesi
D. perpaulum Seidenf.	**เอื้องข้าวตอกอินทนนท์** Ueang khao tok inthanon
D. planibulbe Lindl.	N/A
D. podagraria Hk. F.	N/A
D. polyanthum Wall. ex Lindl.	**เอื้องสายประสาท** Ueang sai prasat
D. porphyrochilum Lindl.	**เอื้องเฉวียน** Ueang chawian
D. praecinctum Rchb.f.	**หวายภูหลวง** Wai phu luang
D. primulinum Lindl.	**เอื้องสายน้ำผึ้ง** Ueang sai num phueng
D. proteranthum Seidenf.	**หวายน้อยภูหลวง** Wai noi phu luang
D. pulchellum Roxb. ex Lindl.	**เอื้องคำตาควาย** Ueang kham ta khwai
D. pychnostachyum Lindl.	**เศวตสอดสี** Sawet sot si
D. rhodopterygium Rchb.f.	N/A
D. rhodostele Ridl.	**เอื้องแมงเงาแดง** Ueang mang ngao dang
D. salaccense (Blume) Lindl.	**เอื้องใบไผ่** Ueang bai phai
D. sanguinolentum Lindl.	**เอื้องสายทะเลบัน** Ueang sai taley bun
D. scabrilingue Lindl.	**เอื้องแซะ** Ueang sae
D. schilhaueri Ormerod & Pedersen	N/A
D. secundum (Blume) Lindl.	**เอื้องแปรงสีฟัน** Ueang preang si fan
D. senile Parish & Rchb.f.	**เอื้องชะนี** Ueang chani

D. setifolium Ridl.	**เอื้องตุ้มหู** Ueang tum hu
D. signatum Rchb.f.	**เอื้องเค้ากิ่ว** Ueang khao kio
D. singaporense Hawkes & Heller	N/A
D. sinuatum (Lindl.) Lindl. ex Rchb.f.	N/A
D. sociale J.J.Sm.	**เอื้องมะลิปากชมพู** Ueang mali pak chompu
D. strongylanthum Rchb.f.	**เอื้องเย้าลม** Ueang yao lom
D. stuartii Bailey	N/A
D. stuposum Lindl.	**เอื้องสาย** Ueang sai
D. subulatum (Blume) Lindl.	N/A
D. sukhakulii hort.	**หวายสุขะกุล** Wai sukhakun
D. sulcatum Lindl.	**เอื้องจำปาน่าน** Ueang champa nan
D. superbiens Rchb.f.	**หวายคิง** Wai khing
D. sutepense Rolfe ex Downie	**เอื้องมะลิ** Ueang mali
D. terminale Parish & Rchb.f	**เอื้องแผงโสภา** Ueang phaeng sopha
D. tetrodon Rchb.f. ex Lindl.	**เอื้องสายดอกเขียว** Ueang said ok khiao
D. thyrsiflorum Rchb.f	**เอื้องมอนไข่ใบมน** Ueang mon khai bai mon
D. tortile Lindl.	**เอื้องไม้ตึง** Ueang mai tueng
D. trigonopus Rchb.f.	**เอื้องคำเหลี่ยม** Ueang kham liam
D. trinervium Ridl.	**เทียนลิง** Thian ling
D. truncatum Lindl.	N/A
D. umbonatum Seidenf.	**หวายอัมโบ** Wai umbo
D. unicum Seidenf.	**เอื้องครั่งแสด** Ueang krang saet
D. uniflorum Griff.	**เอื้องทอง** Ueang thong
D. venustum Teijsm. & Binn	**ข้าวเหนียวลิง** Khao niao ling

D. villosulum Lindl.	**กล้วยหญ้านา** Kluai ya na
D. viridulum Ridl.	N/A
D. wardianum R.Warner	**เอื้องมณีไตรรงค์** Ueang mani trairong
D. wattii (Hook.f.) Rchb.f.	**เอื้องแซะ** Ueang sae
D. williamsonii Day & Rchb.f.	**เอื้องเงินแสด** Ueang ngoen saet
D. wilmsianum Schltr.	N/A
D. xanthophlebium Lindl.	**เอื้องแซะภูลังกา** Ueang sae phu langka
D. ypsilon Seidenf.	**เอื้องแบนปากตัด** Ueang baen pak tat

D. palpebrae Lindl., locally known as "Ueang matcha" (เอื้องมัจฉา), is distributed in dry evergreen forests in the northern, northeastern and southern region of Thailand. Moreover, this plant has been found in India, China, Myanmar and Laos. *D. palpebrae* is an epiphytic orchid with subclavate and sulcate stems. Its leaves are oblong-elliptic, 3 to 5 leaves sprout at apex of the stem. *D. palpebrae* produces raceme of white colored flowers, 3 cm in diameter of which their sepals and petals are completely white, except their labellum being white with golden yellow base. The flowering period is in January to March. (Vaddhanaphuti, 2005; Plant varieties protection office, 2013; Forest herbarium, 2014)

Although *D. palpebrae* Lindl. has been found growing in several countries, no phytochemical researches have been conducted on this orchid. In this study, we evaluated the DPPH free radical scavenging activity of crude ethyl acetate extract of *D. palpebrae*. This result showed that the extract, at 100 µg/mL, exhibited more than 80% reduction of DPPH free radical scavenging activity. This study thus aimed to investigate the chemical constituents of *D. palpebrae* and to identify the compounds responsible for the free radical scavenging activity. The result might be useful for the antioxidant studies or any related studies in the future.

The major objectives of this study were as follows.

1. To isolate and purify the chemical constituents from *Dendrobium palpebrae*.
2. To characterize the chemical structures of the isolated compounds.
3. To investigate the free radical scavenging activities of the isolated compounds.

Figure 1 *Dendrobium palpebrae* Lindl.

CHAPTER II
HISTORICAL

1. Chemical constituents of *Dendrobium*

A wide variety of secondary metabolites including bibenzyls and derivatives, flavonoids, terpenoids and miscellaneous compounds (**Figures 2-5**) have been identified from several species of the genus *Dendrobium*.

The lists of bibenzyls and flavonoids are shown in **Table 1** and **Table 2**, respectively. Bibenzyls and derivatives are members of the stilbenes which share similar biosynthetic pathway with flavonoids. Stilbenes and flavonoids are plant-specific metabolites with different metabolic functions in plants, for example, increasing immunity against various herbivors and microbial pathogens, coloration and UV protection. In the shikimic acid pathway, stilbenes and flavonoids are synthesized from the combination of a coenzyme A (CoA) activated phenylpropanoid unit and three malonyl-CoA units. Afterward, the diverging point of stilbenes and flavonoids depends on the polyketide synthase activity. In case of stilbene synthase, the product of subsequent folding and cyclization of the generated tetraketide intermediate will be a stilbene structure which can be stilbenes, bibenzyls or dihydrostilbenes, bis-bibenzyls, phenanthrenes and 9,10-dihydrophenanthrenes. On the contrary, if polyketide synthase is chalcone synthase, the product of this biosynthesis will be a chalcone structure which is subsequently modified to be flavonoids (Watts *et al.*, 2006; Dubrovina and Kiselev, 2017).

The terpenoids in *Dendrobium* are shown in **Table 3**. Generally, terpenoids are one of the largest families of natural plant products. In plants, terpenoids are used as signal molecules to attract the insects to support plant's pollination or as defense against biotic and abiotic stresses similar to bibenzyls and flavonoids (Singh and Sharma, 2015). The first step of terpenoid biosynthesis is the generation of a C_5 unit called isopentenyl diphosphate (IPP) via two IPP generating pathways: are the acetate-mevalonate pathway and the non-mevalonate pathway. We can classify the

terpenoids by the homologous series of the number of five-carbon isoprene units in their structures including hemiterpenes (1 isoprene unit; C_5), monoterpenes (2 isoprene units; C_{10}), sesquiterpenes (3 isoprene units; C_{15}), diterpenes (4 isoprene units; C_{20}), sesterterpenes (5 isoprene units; C_{25}), triterpenes (6 isoprene units; C_{30}), tetraterpenes (8 isoprene units; C_{40}), and polyterpenes $(C_5)_n$ where "n" can be 9 to 30,000 isoprene units (Dubey *et al.*, 2003; Singh and Sharma, 2015).

Dendrobium orchids do not produce only bibenzyls, flavonoids, and terpenoids, but they also biosynthesize other small groups of compounds which are displayed together in **Table 4** as miscellaneous compounds, including aliphatic compounds, benzoic acid derivatives, phenylpropanoids, fluorenones, coumarins, lignans and neolignans (Xu *et al.*, 2013).

Table 1 Distribution of bibenzyls and derivatives in the genus *Dendrobium*

Compounds	Plant	Plant part	Reference
Dendrocandin A [**1**]	*D. candidum*	Stem	Li *et al.*, 2008
	D. wardianum	Stem	Zhang *et al.*, 2017
Dendrocandin C [**2**]	*D. candidum*	Stem	Li *et al.*, 2009a
Dendrocandin D [**3**]	*D. candidum*	Stem	Li *et al.*, 2009a
Dendrocandin E [**4**]	*D. candidum*	Stem	Li *et al.*, 2009a)
Dendrocandin B [**5**]	*D. candidum*	Stem	Li *et al.*, 2008
	D. signatum	Whole plant	Mittraphab *et al.*, 2016
	D. officinale	Stem	Yang *et al.*, 2015a
Dendrocandin T [**6**]	*D. officinale*	Stem	Yang *et al.*, 2015a
Dendrocandin U [**7**]	*D. officinale*	Stem	Yang *et al.*, 2015a
	D. wardianum	Stem	Zhang *et al.*, 2017
Dendrocandin V [**8**]	*D. wardianum*	Stem	Zhang *et al.*, 2017
Dendrocandin F [**9**]	*D. candidum*	Stem	Li *et al.*, 2009b
Dendrocandin G [**10**]	*D. candidum*	Stem	Li *et al.*, 2009b
Dendrocandin H [**11**]	*D. candidum*	Stem	Li *et al.*, 2009b
Dendrosinen A [**12**]	*D. sinense*	Whole plant	Chen *et al.*, 2014
Dendrosinen B [**13**]	*D. sinense*	Whole plant	Chen *et al.*, 2014
Dendrosinen C [**14**]	*D. sinense*	Whole plant	Chen *et al.*, 2014
Dendrosinen D [**15**]	*D. sinense*	Whole plant	Chen *et al.*, 2014

Table 1 (continued)

Compounds	Plant	Plant part	Reference
Aloifol I [**16**]	*D. longicornu*	Stem	Hu *et al.*, 2008a
	D. williamsonii	Whole plant	Yang *et al.*, 2017a
Amoenylin [**17**]	*D. amoenum*	Whole plant	Majumder *et al.*, 1999
	D. williamsonii	Whole plant	Yang *et al.*, 2017a
Batatasin [**18**]	*D. longicornu*	Stem	Hu *et al.*, 2008a
	D. plicatile	Stem	Yamaki and Honda, 1996
Batatasin III [**19**]	*D. aphyllum*	Stem	Yang *et al.*, 2015b
	D. cariniferum	Stem	Chen *et al.*, 2008a
	D. chrysotoxum	Whole plant	Li *et al.*, 2009c
	D. draconis	Stem	Sritularak *et al.*, 2011a
	D. formosum	Whole plant	Inthongkaew *et al.*, 2017
	D. gratiosissimum	Stem	Zhang *et al.*, 2008a
	D. loddigesii	Stem	Ito *et al.*, 2010
	D. venustum	Whole plant	Sukphan *et al.*, 2014
Brittonin A [**20**]	*D. secundum*	Stem	Sritularak *et al.*, 2011b
Chrysotobibenzyl [**21**]	*D. aurantiacum* var. *denneanum*	Stem	Yang *et al.*, 2006a
	D. capillipes	Stem	Phechrmeekha *et al.*, 2012
	D. chrysanthum	Stem	Yang *et al.*, 2006b
	D. chrysotoxum	Stem	Hu *et al.*, 2012
	D. nobile	Stem	Zhang *et al.*, 2007a
	D. pulchellum	Stem	Chanvorachote *et al.*, 2013

Table 1 (continued)

Compounds	Plant	Plant part	Reference
Chrysotoxine [**22**]	*D. aurantiacum* var. *denneanum*	Stem	Yang *et al.*, 2006a
	D. chrysanthum	Stem	Yang *et al.*, 2006b
	D. nobile	Stem	Zhang *et al.*, 2007a
	D. pulchellum	Stem	Chanvorachote *et al.*, 2013
Crepidatin [**23**]	*D. aurantiacum* var. *denneanum*	Whole plant	Liu *et al.*, 2009a
	D. capillipes	Stem	Phechrmeekha *et al.*, 2012
	D. chrysanthum	Stem	Yang *et al.*, 2006b
	D. crepidatum	Whole plant	Majumder and Chatterjee, 1989
	D. nobile	Stem	Zhang *et al.*, 2007a
	D. pulchellum	Stem	Chanvorachote *et al.*, 2013
Cumulatin [**24**]	*D. cumulatum*	Whole plant	Majumder and Pal, 1993
Dendrobin A [**25**]	*D. nobile*	Stem	Wang *et al.*, 1985; Ye and Zhao, 2002a
3,3′-Dihydroxy-4,5- dimethoxy-bibenzyl [**26**]	*D. williamsonii*	Whole plant	Rungwichaniwat *et al.*, 2014
3,4′-Dihydroxy-5-methoxybibenzyl [**27**]	*D. amoenum*	Whole plant	Majumder *et al.*, 1999

Table 1 (continued)

Compounds	Plant	Plant part	Reference
3,4′-Dihydroxy-5,5′-dimethoxydihydro stilbene [**28**]	*D. nobile*	Stem	Hwang *et al.*, 2010
Erianin [**29**]	*D. chrysotoxum*	Stem	Hu *et al.*, 2012
Gigantol [**30**]	*D. aphyllum*	Whole plant	Chen *et al.*, 2008c
	D. aurantiacum var. *denneanum*	Whole plant	Liu *et al.*, 2009a
	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.*, 2011a
	D. gratiosissimum	Stem	Zhang *et al.*, 2008a
	D. formosum	Whole plant	Inthongkaew *et al.*, 2017
	D. loddigesii	Whole plant	Ito *et al.*, 2010
	D. longicornu	Stem	Hu *et al.*, 2008a
	D. nobile	Stem	Zhang *et al.*, 2007a
	D. officinale	Stem	Zhao *et al.*, 2018
	D. polyanthum	Stem	Hu *et al.*, 2009

Table 1 (continued)

Compounds	Plant	Plant part	Reference
Gigantol [**30**] (continued)	*D. trigonopus*	Stem	Hu *et al.*, 2008b
	D. venustum	Whole plant	Sukphan *et al.*, 2014
	D. wardianum	Stem	Zhang *et al.*, 2017
Gigantol-5-*O*-β-D-glucopyranoside [**31**]	*D. fimbriatum*	Stem	Xu *et al.*, 2017
4-Hydroxy-3,5,3′-trimethoxybibenzyl [**32**]	*D. nobile*	Stem	Ye and Zhao, 2002a
5-Hydroxy-3,4,3′,4′,5′-pentamethoxy-bibenzyl [**33**]	*D. secundum*	Stem	Phechrmeekha *et al.*, 2012
Isoamoenylin [**34**]	*D. amoenum*	Whole plant	Majumder *et al.*, 1999
Moscatilin [**35**]	*D. amoenum*	Whole plant	Majumder *et al.*, 1999
	D. aurantiacum var. *denneanum*	Stem	Yang *et al.*, 2006a
	D. brymerianum	Whole plant	Klongkumnuankarn *et al.*, 2015
	D. chrysanthum	Stem	Yang *et al.*, 2006b
	D. densiflorum	Stem	Fan *et al.*, 2001
	D. ellipsophyllum	Whole plant	Tanagornmeatar *et al.*, 2014

Table 1 (continued)

Compounds	Plant	Plant part	Reference
Moscatilin [**35**] (continued)	*D. formosum*	Whole plant	Inthongkaew *et al.*, 2017
	D. gratiosissimum	Stem	Zhang *et al.*, 2008a
	D. loddigesii	Whole plant	Chen *et al.*, 1994; Ito *et al.*, 2010
	D. longicornu	Stem	Hu *et al.*, 2008a
	D. moscatum	Whole plant	Majumder and Sen, 1987
	D. nobile	Stem	Miyazawa *et al.*, 1999; Yang *et al.*, 2007b
	D. polyanthum	Stem	Hu *et al.*, 2009
	D. pulchellum	Stem	Chanvorachote *et al.*, 2013
	D. secundum	Stem	Sritularak *et al.*, 2011b
	D. wardianum	Stem	Zhang *et al.*, 2017
	D. williamsonii	Whole plant	Yang *et al.*, 2017a
Moscatilin diacetate [**36**]	*D. loddigesii*	Stem	Chen *et al.*, 1994
3,3′,4-Trihydroxy bibenzyl [**37**]	*D. longicornu*	Stem	Hu *et al.*, 2008a
3,3′,5-Trihydroxy bibenzyl [**38**]	*D. cariniferum*	Whole plant	Liu *et al.*, 2009b
3,5,4′-Trihydroxy bibenzyl [**39**]	*D. gratiosissimum*	Stem	Zhang *et al.*, 2008a

Table 1 (continued)

Compounds	Plant	Plant part	Reference
4,5,4′-Trihydroxy-3,3′-dimethoxy bibenzyl [**40**]	*D. secundum*	Stem	Sritularak *et al.*, 2011b
	D. ellipsophyllum	Whole plant	Tanagornmeatar *et al.*, 2014
Tristin [**41**]	*D. aphyllum*	Stem	Yang *et al.*, 2015b
	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.*, 2008a
	D. officinale	Stem	Zhao *et al.*, 2018
	D. trigonopus	Stem	Hu *et al.*, 2008b
Dendromoniliside E [**42**]	*D. nobile*	Stem	Miyazawa *et al.*, 1999
Dendrophenol [**43**]	*D. candidum*	Stem	Li *et al.*, 2008
3,4-Dihydroxy-5,4′-dimethoxybibenzyl [**44**]	*D. candidum*	Stem	Li *et al.*, 2008
	D. signatum	Whole plant	Mittraphab *et al.*, 2016
	D. tortile	Whole plant	Limpanit *et al.*, 2016
	D. wardianum	Stem	Zhang *et al.*, 2017
	D. williamsonii	Whole plant	Yang *et al.*, 2017a
4,4′-Dihydroxy-3,5-dimethoxybibenzyl [**45**]	*D. candidum*	Stem	Li *et al.*, 2008
	D. ellipsophyllum	Whole plant	Tanagornmeatar *et al.*, 2014
	D. williamsonii	Whole plant	Yang *et al.*, 2017a

Table 1 (continued)

Compounds	Plant	Plant part	Reference
Loddigesiinol C [**46**]	*D. loddigesii*	Whole plant	Ito *et al.*, 2010
3-*O*-Methylgigantol [**47**]	*D. candidum*	Stem	Li *et al.*, 2008
	D. plicatile	Stem	Yamaki and Honda, 1996
Dendrocandin I [**48**]	*D. candidum*	Stem	Li *et al.*, 2009b
	D. signatum	Whole plant	Mittraphab *et al.*, 2016
Densiflorol A [**49**]	*D. densiflorum*	Stem	Fan *et al.*, 2001
Longicornuol A [**50**]	*D. longicornu*	Stem	Hu *et al.*, 2008a
Trigonopol A [**51**]	*D. trigonopus*	Stem	Hu *et al.*, 2008b
Trigonopol B [**52**]	*D. chrysotoxum*	Stem	Hu *et al.*, 2012
	D. trigonopus	Stem	Hu *et al.*, 2008b
Crepidatuol A [**53**]	*D. crepidatum*	Stem	Li *et al.*, 2013
Crepidatuol B [**54**]	*D. crepidatum*	Stem	Li *et al.*, 2013
Loddigesiinol D [**55**]	*D. loddigesii*	Whole plant	Ito et al., 2010
Dencryol A [**56**]	*D. crystallinum*	Stem	Wang *et al.*, 2009
Dencryol B [**57**]	*D. crystallinum*	Stem	Wang *et al.*, 2009
Dengraol A [**58**]	*D. gratiosissimum*	Stem	Zhang *et al.*, 2008a
Dengraol B [**59**]	*D. gratiosissimum*	Stem	Zhang *et al.*, 2008a
4-[2-(3-Hydroxyphenol)-1-methoxyethyl]-2,6-dimethoxy phenol [**60**]	*D. longicornu*	Stem	Hu *et al.*, 2008a

Table 1 (continued)

Compounds	Plant	Plant part	Reference
Nobilin A [**61**]	*D. nobile*	Stem	Zhang *et al.*, 2006
Nobilin B [**62**]	*D. nobile*	Stem	Zhang *et al.*, 2006
Nobilin C [**63**]	*D. nobile*	Stem	Zhang *et al.*, 2006
Nobilin D [**64**]	*D. nobile*	Stem	Zhang *et al.*, 2007a
Nobilin E [**65**]	*D. nobile*	Stem	Zhang *et al.*, 2007a
Dendrofalconerol A [**66**]	*D. falconeri*	Stem	Sritularak and Likhitwitayawuid, 2009
	D. signatum	Whole plant	Mittraphab *et al.*, 2016
	D. tortile	Whole plant	Limpanit *et al.*, 2016
Dendrofalconerol B [**67**]	*D. falconeri*	Stem	Sritularak and Likhitwitayawuid, 2009
Dendrowillol A [**68**]	*D. williamsonii*	Whole plant	Yang *et al.*, 2017a
Dendrosignatol [**69**]	*D. signatum*	Whole plant	Mittraphab *et al.*, 2016
2,2′-Dihydroxy-3,3′,4,4′, 7,7-hexamethoxy-9,9′, 10,10′-tetrahydro-1,1′-biphenanthrene [**70**]	*D. nobile*	Stem	Yang *et al.*, 2007b
2,2′-Dimethoxy-4,4′,7,7′-tetrahydroxy-9,9′,10,10′-tetrahydro-1,1′-biphenanthrene [**71**]	*D. plicatile*	Stem	Yamaki and Honda, 1996

Table 1 (continued)

Compounds	Plant	Plant part	Reference
Flavanthrin [**72**]	*D. aphyllum*	Whole plant	Chen *et al.*, 2008c
Phoyunnanin C [**73**]	*D. venustum*	Whole plant	Sukphan *et al.*, 2014
Phoyunnanin E [**74**]	*D. venustum*	Whole plant	Sukphan *et al.*, 2014
Amoenumin [**75**]	*D. amoenum*	Whole plant	Veerraju *et al.*, 1989
Crystalltone [**76**]	*D. chrysotoxum*	Stem	Hu *et al.*, 2012
	D. crystallinum	Stem	Wang *et al.*, 2009
Chrysotoxol A [**77**]	*D. chrysotoxum*	Stem	Hu *et al.*, 2012
Chrysotoxol B [**78**]	*D. chrysotoxum*	Stem	Hu *et al.*, 2012
Confusarin [**79**]	*D. chrysotoxum*	Stem	Hu *et al.*, 2012
	D. formosum	Whole plant	Inthongkaew *et al.*, 2017
	D. nobile	Stem	Zhang *et al.*, 2008b
	D. officinale	Stem	Zhao *et al.*, 2018
2,6-Dihydroxy-1,5,7-trimethoxyphenanthrene [**80**]	*D. densiflorum*	Stem	Fan *et al.*, 2001
Dendrochrysanene [**81**]	*D. chrysanthum*	Stem	Yang *et al.*, 2006b
Bulbophyllanthrin [**82**]	*D. nobile*	Stem	Yang *et al.*, 2007b
Denthyrsinin [**83**]	*D. thyrsiforum*	Stem	Zhang *et al.*, 2005

Table 1 (continued)

Compounds	Plant	Plant part	Reference
5-Hydroxy-2,4-dimethoxyphenanthrene [**84**]	*D. loddigesii*	Whole plant	Ito *et al.*, 2010
3-Hydroxy-2,4,7-trimethoxyphenanthrene [**85**]	*D. nobile*	Stem	Yang *et al.*, 2007b
Cypripedin [**86**]	*D. densiflorum*	Stem	Fan *et al.*, 2001
Densiflorol B [**87**]	*D. densiflorum*	Stem	Fan *et al.*, 2001
	D. venustum	Whole plant	Sukphan *et al.*, 2014
Denbinobin [**88**]	*D. moniliforme*	Stem	Lin *et al.*, 2001
	D. nobile	Stem	Yang *et al.*, 2007b
	D. wardianum	Stem	Zhang *et al.*, 2017
Fimbriatone [**89**]	*D. nobile*	Stem	Zhang *et al.*, 2008b
	D. pulchellum	Stem	Chanvorachote *et al.*, 2013
Loddigesiinol B [**90**]	*D. loddigesii*	Whole plant	Ito *et al.*, 2010
Dendronone [**91**]	*D. chrysanthum*	Stem	Yang *et al.*, 2006b
	D. longicornu	Stem	Hu *et al.*, 2008a
Ephemeranthoquinone [**92**]	*D. plicatile*	Stem	Yamaki and Honda, 1996

Table 1 (continued)

Compounds	Plant	Plant part	Reference
5-Methoxy-7-hydroxy-9,10-dihydro-1,4-phenanthrenequinone [**93**]	*D. draconis*	Stem	Sritularak *et al.*, 2011a
	D. formosum	Whole plant	Inthongkaew *et al.*, 2017
Moniliformin [**94**]	*D. moniliforme*	Stem	Lin *et al.*, 2001
Moscatin [**95**]	*D. aphyllum*	Whole plant	Chen *et al.*, 2008
	D. chrysanthum	Stem	Yang *et al.*, 2006b
	D. chrysotoxum	Whole plant	Li *et al.*, 2009c
	D. densiflorum	Stem	Fan *et al.*, 2001
	D. polyanthum	Stem	Hu *et al.*, 2009
Coelonin [**96**]	*D. aphyllum*	Whole plant	Chen *et al.*, 2008
	D. formosum	Whole plant	Inthongkaew *et al.*, 2017
	D. nobile	Stem	Yang *et al.*, 2007b
9,10-Dihydromoscatin [**97**]	*D. polyanthum*	Stem	Hu *et al.*, 2009
9,10-Dihydrophenanthrene-2,4,7-triol [**98**]	*D. officinale*	Stem	Zhao *et al.*, 2018
	D. polyanthum	Stem	Hu *et al.*, 2009

Table 1 (continued)

Compounds	Plant	Plant part	Reference
4,5-Dihydroxy-2,3-dimethoxy-9,10-dihydrophenanthrene [**99**]	*D. ellipsophyllum*	Whole plant	Tanagornmeatar *et al.*, 2014
	D. sinense	Whole plant	Chen *et al.*, 2013
4,5-Dihydroxy-2,6-dimethoxy-9,10-dihydrophenanthrene [**100**]	*D. chrysotoxum*	Stem	Hu *et al.*, 2012
4,5-Dihydroxy-3,7-dimethoxy-9,10-dihydrophenanthrene [**101**]	*D. nobile*	Stem	Ye and Zhao, 2002a
4,5-Dihydroxy-2-methoxy-9,10-dihydrophenanthrene (Orchinol) [**102**]	*D. nobile*	Stem	Zhang *et al.*, 2007b
	D. officinale	Stem	Zhao *et al.*, 2018
Lusianthridin [**103**]	*D. brymerianum*	Whole plant	Klongkumnuankarn *et al.*, 2015
	D. formosum	Whole plant	Inthongkaew *et al.*, 2017
	D. plicatile	Stem	Yamaki and Honda, 1996
	D. venustum	Whole plant	Sukphan *et al.*, 2014

Table 1 (continued)

Compounds	Plant	Plant part	Reference
2,7-Dihydroxy-3,4,6-trimethoxy-9,10-dihydrophenanthrene [**104**]	*D. densiflorum*	Stem	Fan *et al.*, 2001
2,8-Dihydroxy-3,4,7-trimethoxy-9,10-dihydrophenanthrene [**105**]	*D. nobile*	Stem	Yang *et al.*, 2007b
4,7-Dihydroxy-2,3,6-trimethoxy-9,10-dihydrophenanthrene [**106**]	*D. rotundatum*	Whole plant	Majumder and Pal, 1992
Ephemeranthol A [**107**]	*D. nobile*	Stem	Yang *et al.*, 2007b; Hwang *et al.*, 2010
	D. officinale	Stem	Zhao *et al.*, 2018
Ephemeranthol C [**108**]	*D. nobile*	Stem	Yang *et al.*, 2007b; Hwang *et al.*, 2010
Erianthridin [**109**]	*D. nobile*	Stem	Hwang *et al.*, 2010
	D. formosum	Whole plant	Inthongkaew *et al.*, 2017
	D. plicatile	Stem	Yamaki and Honda, 1996
Flavanthridin [**110**]	*D. nobile*	Stem	Hwang *et al.*, 2010

Table 1 (continued)

Compounds	Plant	Plant part	Reference
Hircinol [**111**]	*D. aphyllum*	Stem	Yang *et al.*, 2015b
	D. draconis	Stem	Sritularak *et al.*, 2011a
	D. formosum	Whole plant	Inthongkaew *et al.*, 2017
3-Hydroxy-2,4,7-trimethoxy-9,10-dihydrophenanthrene [**112**]	*D. nobile*	Stem	Yang *et al.*, 2007b
2-Hydroxy-4,7-dimethoxy-9,10-dihydrophenanthrene [**113**]	*D. nobile*	Stem	Yang *et al.*, 2007b
7-Methoxy-9,10-dihydrophenanthrene-2,4,5-triol [**114**]	*D. draconis*	Stem	Sritularak *et al.*, 2011a
2,5,7-Trimethoxy-4-methoxy-9,10-dihydrophenanthrene [**115**]	*D. formosum*	Whole plant	Inthongkaew *et al.*, 2017
	D. longicornu	Stem	Hu *et al.*, 2008a
Plicatol C [**116**]	*D. plicatile*	Stem	Honda and Yamaki, 2000
Rotundatin [**117**]	*D. rotundatum*	Whole plant	Majumder and Pal, 1992

Table 1 (continued)

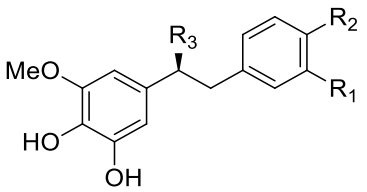
Compounds	Plant	Plant part	Reference
2,5-Dihydroxy-3,4 dimethoxyphenanthrene [**118**]	*D. nobile*	Stem	Yang *et al.*, 2007b
2,5-Dihydroxy-4,9-dimethoxyphenanthrene [**119**]	*D. nobile*	Stem	Zhang *et al.*, 2008b
2,8-Dihydroxy-3,4,7-trimethoxyphenanthrene [**120**]	*D. nobile*	Stem	Yang *et al.*, 2007b
Epheranthol B [**121**]	*D. chrysotoxum*	Stem	Hu *et al.*, 2012
	D. plicatile	Stem	Yamaki and Honda, 1996
Fimbriol B [**122**]	*D. nobile*	Stem	Yang *et al.*, 2007b; Hwang *et al.*, 2010
Flavanthrinin [**123**]	*D. brymerianum*	Whole plant	Klongkumnuankarn *et al.*, 2015
	D. nobile	Stem	Zhang *et al.*, 2008b
	D. venustum	Whole plant	Sukphan *et al.*, 2014
Loddigesiinol A [**124**]	*D. loddigesii*	Whole plant	Ito *et al.*, 2010
	D. wardianum	Stem	Zhang *et al.*, 2017

Table 1 (continued)

Compounds	Plant	Plant part	Reference
Nudol [**125**]	*D. formosum*	Whole plant	Inthongkaew *et al.*, 2017
	D. nobile	Stem	Yang *et al.*, 2007b
	D. rotundatum	Whole plant	Majumder and Pal, 1992
Plicatol A [**126**]	*D. nobile*	Stem	Yang *et al.*, 2007b
	D. plicatile	Stem	Honda and Yamaki, 2000
Plicatol B [**127**]	*D. plicatile*	Stem	Honda and Yamaki, 2000
2,3,5-Trihydroxy-4,9-dimethoxyphenanthrene [**128**]	*D. nobile*	Stem	Yang *et al.*, 2007b
3,4,8-Trimethoxyphenanthrene-2,5-diol [**129**]	*D. nobile*	Stem	Hwang *et al.*, 2010
Aphyllone [**130**]	*D. nobile*	Stem	Hwang *et al.*, 2010
9,10-Dihydro-aphyllone A-5-*O*-β-D-glucopyranoside [**131**]	*D. fimbriatum*	Stem	Xu *et al.*, 2017
(*S*)-2,4,5,9-Tetrahydroxy-9,10-dihydro-phenanthrene [**132**]	*D. fimbriatum*	Stem	Xu *et al.*, 2014

Table 1 (continued)

Compounds	Plant	Plant part	Reference
1,5,7-Trimethoxy-phenanthrene-2-ol [**133**]	*D. nobile*	Stem	Kim *et al.*, 2015
1,5-Dihydroxy-3,4,7-trimethoxy-9,10-dihydro-phenanthrene [**134**]	*D. moniliforme*	Whole plant	Zhao *et al.*, 2016
2,4,5,9*S*-Tetrahydroxy-9,10-dihydrophenanthrene-4-*O*-β-D-glucopyranoside [**135**]	*D. primulinum*	Whole plant	Ye *et al.*, 2016
Loddigesiinol G [**136**]	*D. loddigesii*	Stem	Lu *et al.*, 2014
Loddigesiinol H [**137**]	*D. loddigesii*	Stem	Lu *et al.*, 2014
Loddigesiinol I [**138**]	*D. loddigesii*	Stem	Lu *et al.*, 2014
Loddigesiinol J [**139**]	*D. loddigesii*	Stem	Lu *et al.*, 2014
Dendrocandin P1 [**140**]	*D. officinale*	Stem	Zhao *et al.*, 2018
Dendrocandin P2 [**141**]	*D. officinale*	Stem	Zhao *et al.*, 2018

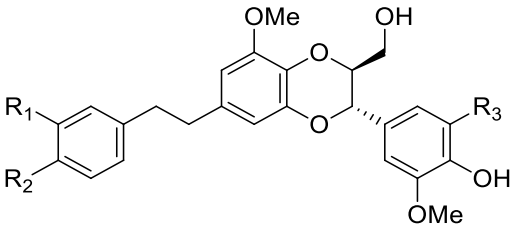


[**1**] Dendrocandin A: R_1 = H, R_2 = R_3 = OMe

[**2**] Dendrocandin C: R_1 = H, R_2 = OH, R_3 = OMe

[**3**] Dendrocandin D: R_1 = H, R_2 = OH, R_3 = OEt

[**4**] Dendrocandin E: R_1 = R_2 = OH, R_3 = H

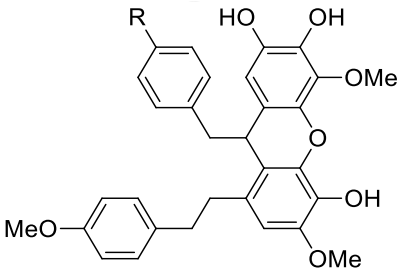


[**5**] Dendrocandin B: R_1 = H, R_2 = R_3 = OMe

[**6**] Dendrocandin T: R_1 = R_3 = OMe, R_2 = OH

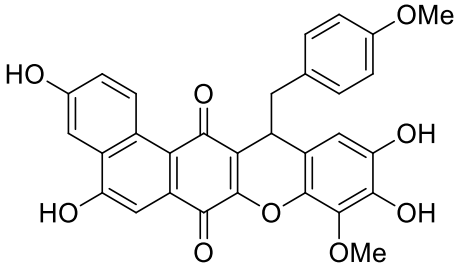
[**7**] Dendrocandin U: R_1 = H, R_2 = OH, R_3 = OMe

[**8**] Dendrocandin V: R_1 = R_3 = H, R_2 = OMe



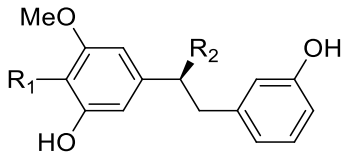
[**9**] Dendrocandin F: R = OMe

[**10**] Dendrocandin G: R= OH



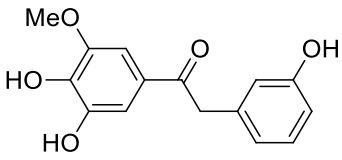
[**11**] Dendrocandin H

Figure 2 Structures of bibenzyls and derivatives previously isolated from *Dendrobium* species

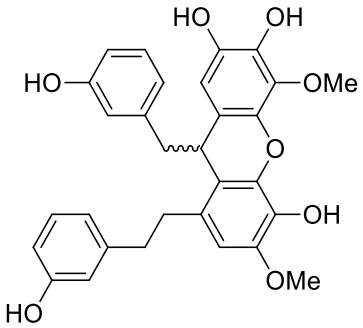


[**12**] Dendrosinen A: R_1 = OMe, R_2 = OH

[**13**] Dendrosinen B: R_1 = OH, R_2 = H

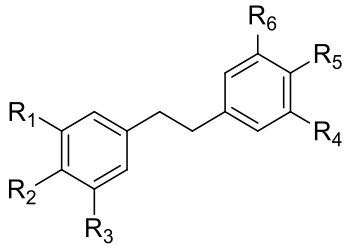


[**14**] Dendrosinen C



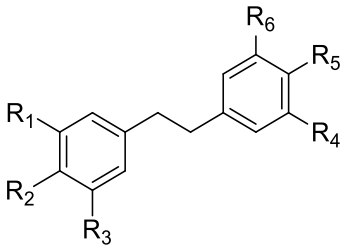
[**15**] Dendrosinen D

Figure 2 Structures of bibenzyls and derivatives previously isolated from *Dendrobium* species (continued)



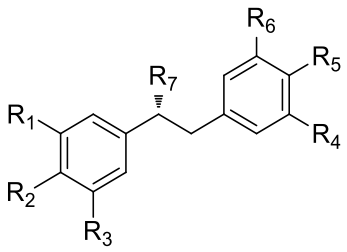
	R_1	R_2	R_3	R_4	R_5	R_6
[**16**] Aloifol I	OMe	OH	OMe	OH	H	H
[**17**] Amoenylin	OMe	OH	OMe	H	OMe	H
[**18**] Batatasin	OMe	H	H	OH	H	OH
[**19**] Batatasin III	OH	H	OMe	H	H	OH
[**20**] Brittonin A	OMe	OMe	OMe	OMe	OMe	OMe
[**21**] Chrysotobibenzyl	OMe	OMe	OMe	OMe	OMe	H
[**22**] Chrysotoxine	OMe	OH	OMe	OMe	OMe	H
[**23**] Crepidatin	OMe	OMe	OMe	OMe	OH	H
[**24**] Cumulatin	OMe	OMe	OH	OH	OMe	OMe
[**25**] Dendrobin A	OH	OH	OMe	H	H	OMe
[**26**] 3,3′-Dihydroxy-4,5-dimethoxybibenzyl	OMe	OMe	OH	H	H	OH
[**27**] 3,4′-Dihydroxy-5-methoxybibenzyl	OH	H	OMe	H	OH	H
[**28**] 3,4′-Dihydroxy-5,5′-Dimethoxydihydrostilbene	OH	H	OMe	OMe	OH	H

Figure 2 Structures of bibenzyls and derivatives previously isolated from *Dendrobium* species (continued)

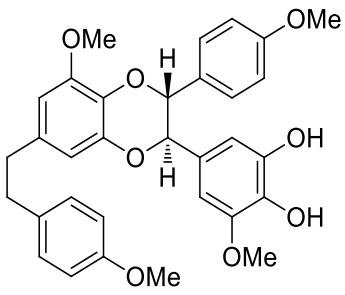


	R_1	R_2	R_3	R_4	R_5	R_6
[**29**] Erianin	OMe	OMe	OMe	H	OMe	OH
[**30**] Gigantol	OMe	H	H	H	OH	OMe
[**31**] Gigantol-5-*O*-β-D-glucopyranoside	OMe	H	OGlc	H	OH	OMe
[**32**] 4-Hydroxy-3,5,3′ trimethoxybibenzyl	OMe	OH	OMe	H	H	OMe
[**33**] 5-Hydroxy-3,4,3′,4′,5′ pentamethoxybibenzyl	OMe	OMe	OH	OMe	OMe	OMe
[**34**] Isoamoenylin	OMe	OMe	OMe	H	H	OH
[**35**] Moscatilin	OMe	OH	OMe	H	OH	OMe
[**36**] Moscatilin diacetate	OMe	OAc	OMe	H	OAc	OMe
[**37**] 3,3′,4-Trihydroxybibenzyl	OH	OH	H	H	H	OH
[**38**] 3,3′,5-Trihydroxybibenzyl	OH	H	OH	H	H	OH
[**39**] 3,5,4′-Trihydroxybibenzyl	OH	H	OH	H	OH	H
[**40**] 4,5,4′-Trihydroxy-3-3′-dimethoxybibenzyl	OMe	OH	OH	H	OH	OMe
[**41**] Tristin	OH	H	OH	H	OH	OMe
[**42**] Dendromoniliside E	OGlc	OGlc	OMe	H	OMe	H

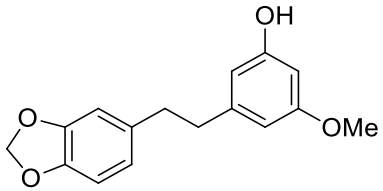
Figure 2 Structures of bibenzyls and derivatives previously isolated from *Dendrobium* species (continued)



	R_1	R_2	R_3	R_4	R_5	R_6	R_7
[**43**] Dendrophenol	OMe	OH	OMe	OH	OH	H	H
[**44**] 3,4-Dihydroxy-5,4′-dimethoxybibenzyl	OH	OH	OMe	H	OMe	H	H
[**45**] 4,4′-Dihydroxy-3,5-dimethoxybibenzyl	OMe	OH	OMe	H	OH	H	H
[**46**] Loddigesiinol C	OMe	OH	OMe	H	OH	OMe	OMe
[**47**] 3-*O*-Methylgigantol	OMe	H	OH	OMe	OMe	H	H

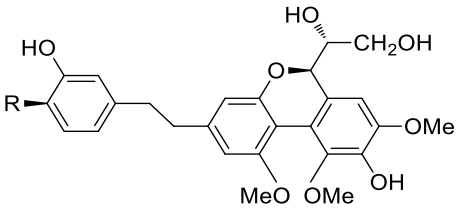


[**48**] Dendrocandin I



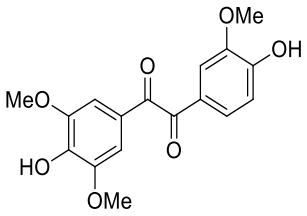
[**49**] Densiflorol A

Figure 2 Structures of bibenzyls and derivatives previously isolated from *Dendrobium* species (continued)

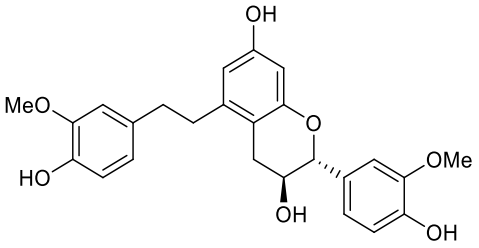


[**50**] Longicornuol A: R = H

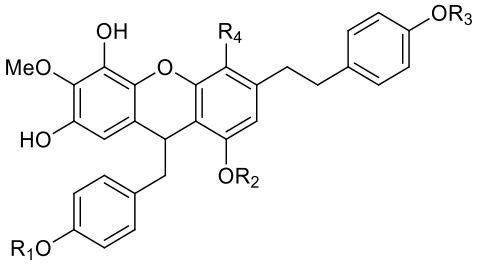
[**51**] Trigonopol A: R = OMe



[**55**] Loddigesiinol D

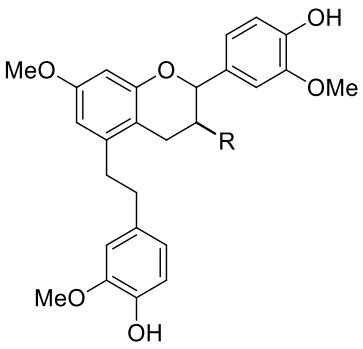


[**52**] Trigonopol B



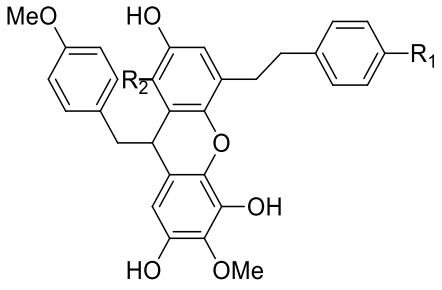
[**56**] Dencryol A: R_1 = OMe, R_2 = R_3 = OH, R_4 = H

[**57**] Dencryol B: R_1 = OH, R_2 = R_3 = OMe, R_4 = OH



[**53**] Crepidatuol A: R = H

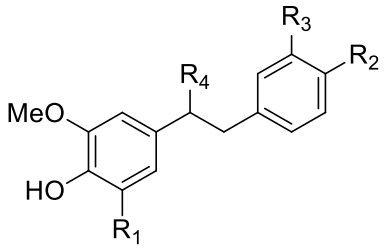
[**54**] Crepidatuol B: R = OH



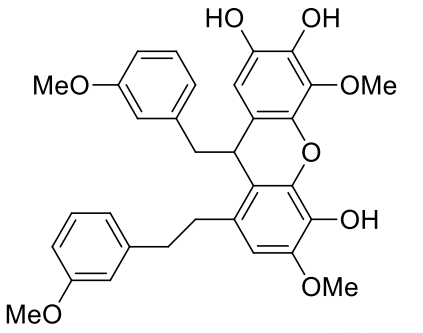
[**58**] Dengraol A: R_1 = OH, R_2 = H

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

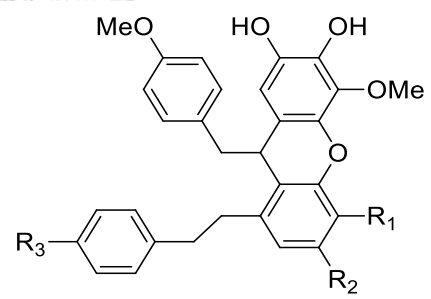
Figure 2 Structures of bibenzyls and derivatives previously isolated from *Dendrobium* species (continued)



	R_1	R_2	R_3	R_4
[**60**] 4-[2-(3-Hydroxyphenol)-1-methoxyethyl]-2,6-dimethoxyphenol	OMe	H	OH	OMe
[**61**] Nobilin A	OH	H	OMe	OMe
[**62**] Nobilin B	OMe	OH	OMe	OMe
[**63**] Nobilin C	OMe	OMe	OMe	OMe
[**64**] Nobilin D	OMe	OH	OMe	OH

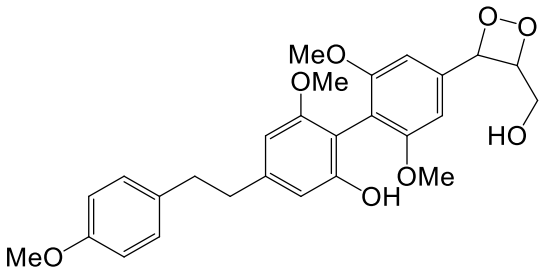


[**65**] Nobilin E

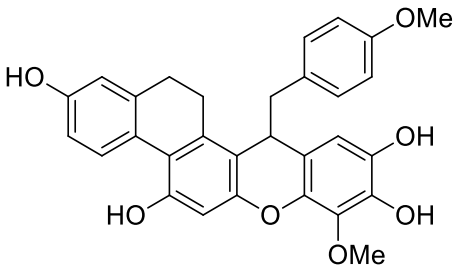


[**66**] Dendrofalconerol A: R_1 = OH, R_2 = R_3 = OMe

[**67**] Dendrofalconerol B: R_1 = H, R_2 = R_3 = OH

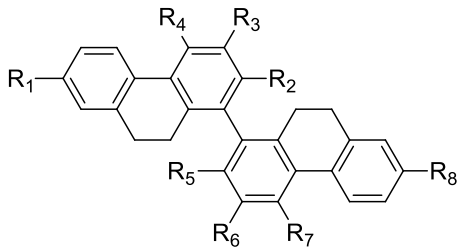


[**68**] Dendrowillol A

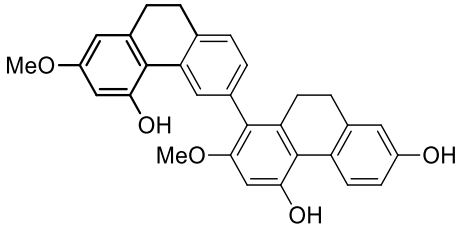


[**69**] Dendrosignatol

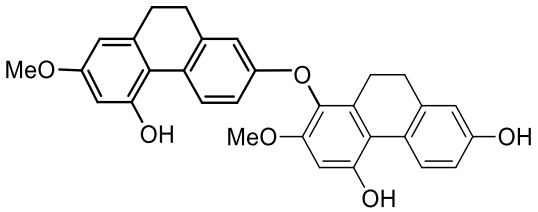
Figure 2 Structures of bibenzyls and derivatives previously isolated from *Dendrobium* species (continued)



	R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8
[**70**] 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
[**71**] 2,2′-Dimethoxy-4,4′,7,7′-tetrahydroxy-9,9′,10, 10′-tetrahydro-1,1′-biphenanthrene	OH	OMe	H	OH	OMe	H	OH	OH
[**72**] Flavanthrin	OH	OH	H	OMe	OH	H	OMe	OH

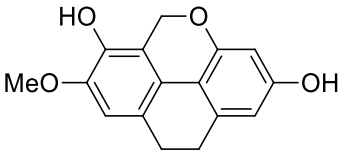


[**73**] Phoyunnanin C

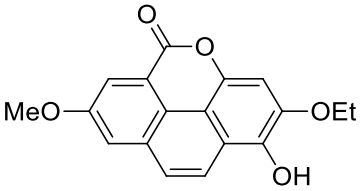


[**74**] Phoyunnanin E

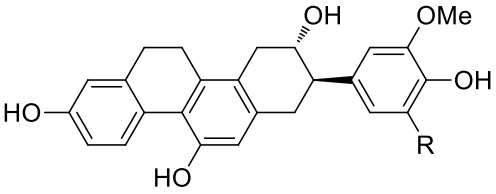
Figure 2 Structures of bibenzyls and derivatives previously isolated from *Dendrobium* species (continued)



[**75**] Amoenumin

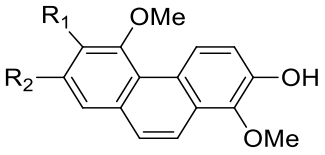


[**76**] Crystalltone



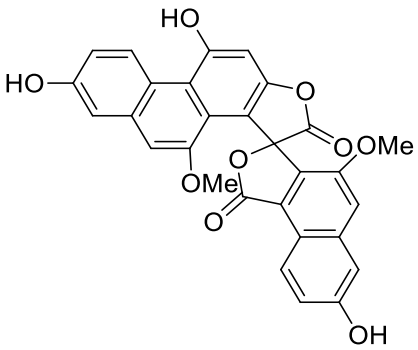
[**77**] Chrysotoxol A: R = H

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



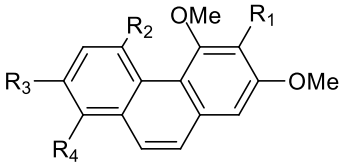
[**79**] Confusarin: R_1 = OMe, R_2 = OH

[**80**] 2,6-Dihydroxy-1,5,7-trimethoxy phenanthrene: R_1 = OH, R_2 = OMe

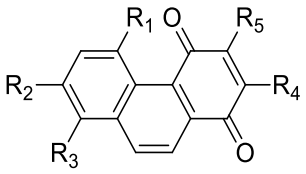


[**81**] Dendrochrysanene

Figure 2 Structures of bibenzyls and derivatives previously isolated from *Dendrobium* species (continued)

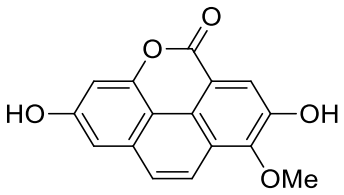


	R_1	R_2	R_3	R_4
[**82**] Bulbophyllanthrin	OH	OH	H	H
[**83**] Denthyrsinin	OH	H	OH	OMe
[**84**] 5-Hydroxy-2,4-dimethoxy phenanthrene	H	OH	H	H
[**85**] 3-Hydroxy-2,4,7-trimethoxy phenanthrene	OH	H	OMe	H

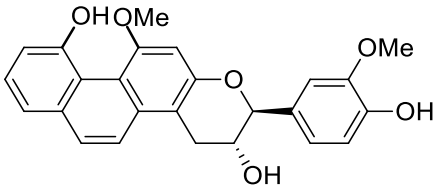


	R_1	R_2	R_3	R_4	R_5
[**86**] Cypripedin	H	OH	OMe	OMe	H
[**87**] Densiflorol B	H	OH	H	OMe	H
[**88**] Denbinobin	OH	OMe	H	H	OMe

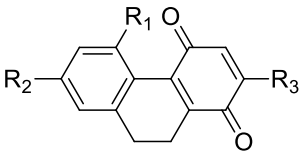
Figure 2 Structures of bibenzyls and derivatives previously isolated from *Dendrobium* species (continued)



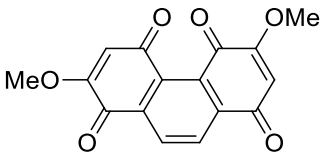
[**89**] Fimbriatone



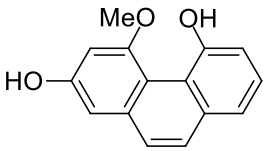
[**90**] Loddigesiinol B



	R_1	R_2	R_3
[**91**] Dendronone	OH	OMe	H
[**92**] Ephemeranthoquinone	H	OH	OMe
[**93**] 5-Methoxy-7-hydroxy-9,10-dihydro-1,4 phenanthrenequinone	OMe	OH	H

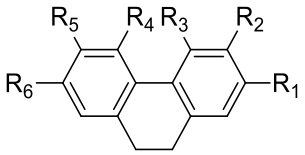


[**94**] Moniliformin



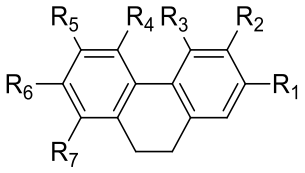
[**95**] Moscatin

Figure 2 Structures of bibenzyls and derivatives previously isolated from *Dendrobium* species (continued)



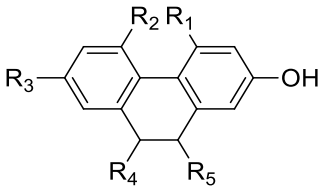
	R_1	R_2	R_3	R_4	R_5	R_6
[**96**] Coelonin	OH	H	OMe	H	H	OH
[**97**] 9,10-Dihydromoscatin	H	H	OH	OMe	H	OH
[**98**] 9,10-Dihydrophenanthrene-2,4,7-triol	OH	H	OH	H	H	OH
[**99**] 4,5-Dihydroxy-2,3-dimethoxy-9,10-dihydrophenanthrene	OMe	OMe	OH	OH	H	H
[**100**] 4,5-Dihydroxy-2,6-dimethoxy-9,10-dihydrophenanthrene	OMe	H	OH	OH	OMe	H
[**101**] 4,5-Dihydroxy-3,7-dimethoxy-9,10-dihydrophenanthrene	H	OMe	OH	OH	H	OMe
[**102**] 4,5-Dihydroxy-2-methoxy-9,10-dihydrophenanthrene (Orchinol)	OMe	H	OH	OH	H	H
[**103**] Lusianthridin	OMe	H	OH	H	H	OH

Figure 2 Structures of bibenzyls and derivatives previously isolated from *Dendrobium* species (continued)



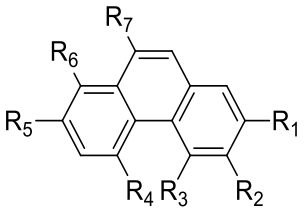
	R_1	R_2	R_3	R_4	R_5	R_6	R_7
[**104**] 2,7-Dihydroxy-3,4,6-trimethoxy-9,10-dihydro phenanthrene	OH	OMe	OMe	H	OMe	OH	H
[**105**] 2,8-Dihydroxy-3,4,7-trimethoxy-9,10-dihydro phenanthrene	OH	OMe	OMe	H	H	OMe	OH
[**106**] 4,7-Dihydroxy-2,3,6-trimethoxy-9,10-dihydro phenanthrene	OMe	OMe	OH	H	OMe	OH	H
[**107**] Ephemeranthol A	OH	H	H	OH	OMe	OMe	H
[**108**] Ephemeranthol C	OH	OH	OMe	OH	H	H	H
[**109**] Erianthridin	OH	OMe	OMe	H	H	OH	H
[**110**] Flavanthridin	OH	H	H	OMe	OH	OMe	H
[**111**] Hircinol	OH	H	OMe	OH	H	H	H
[**112**] 3-Hydroxy-2,4,7-trimethoxy-9,10-dihydro phenanthrene	OMe	OH	OMe	H	H	OMe	H

Figure 2 Structures of bibenzyls and derivatives previously isolated from *Dendrobium* species (continued)



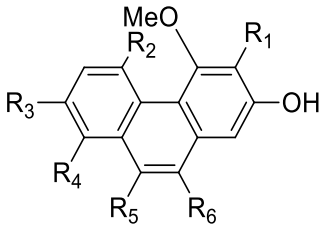
	R_1	R_2	R_3	R_4	R_5
[**113**] 2-Hydroxy-4,7-dimethoxy-9,10-dihydro phenanthrene	OMe	H	OMe	H	H
[**114**] 7-Methoxy-9,10-dihydrophenanthrene-2,4,5-triol	OH	OH	OMe	H	H
[**115**] 2,5,7-Trihydroxy-4-methoxy-9,10-dihydrophenanthrene	OMe	OH	OH	H	H
[116] Plicatol C	OMe	OH	H	OMe	OMe
[**117**] Rotundatin	OMe	OH	H	OH	OH

Figure 2 Structures of bibenzyls and derivatives previously isolated from *Dendrobium* species (continued)



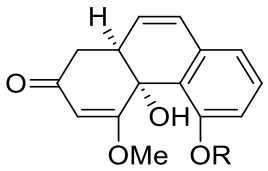
	R_1	R_2	R_3	R_4	R_5	R_6	R_7
[**118**] 2,5-Dihydroxy-3,4-dimethoxyphenanthrene	OH	OMe	OMe	OH	H	H	H
[**119**] 2,5-Dihydroxy-4,9-dimethoxyphenanthrene	OH	H	OMe	OH	H	H	OMe
[**120**] 2,8-Dihydroxy-3,4,7-trimethoxyphenanthrene	OH	OMe	OMe	H	OMe	OH	H
[**121**] Epheranthol B	H	H	OMe	OH	OMe	H	H
[**122**] Fimbriol B	OH	OMe	OH	H	H	H	H
[**123**] Flavanthrinin	H	H	OMe	H	OH	H	H

Figure 2 Structures of bibenzyls and derivatives previously isolated from *Dendrobium* species (continued)



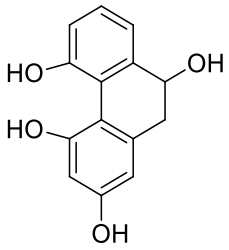
	R_1	R_2	R_3	R_4	R_5	R_6
[**124**] Loddigesiinol A	H	OMe	H	H	OH	H
[**125**] Nudol	OMe	H	OH	H	H	H
[**126**] Plicatol A	H	OH	H	H	OMe	OMe
[**127**] Plicatol B	H	OH	H	H	H	H
[**128**] 2,3,5-Trihydroxy-4,9-dimethoxyphenanthrene	OH	OH	H	H	OMe	H
[**129**] 3,4,8-Trimethoxy phenanthrene-2,5-diol	OMe	OH	H	OMe	H	H

Figure 2 Structures of bibenzyls and derivatives previously isolated from *Dendrobium* species (continued)

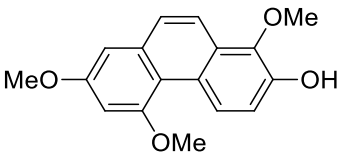


[**130**] Aphyllone: R = H

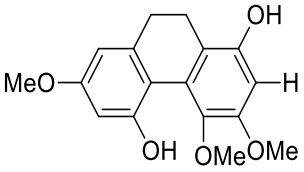
[**131**] 9,10-Dihydro-aphyllone A-5-*O*-β-D-glucopyranoside: R = Glc



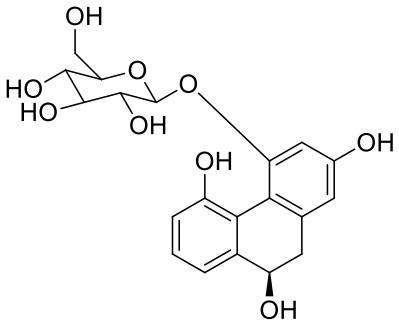
[**132**] (*S*)-2,4,5,9-Tetrahydroxy-9,10-dihydrophenanthrene



[**133**] 1,5,7-Trimethoxyphenanthren-2-ol

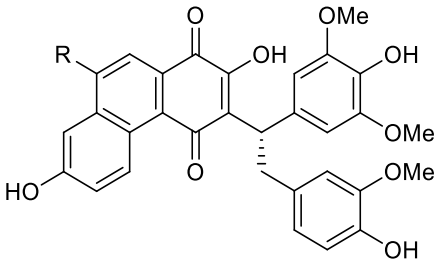


[**134**] 1,5-dihydroxy-3,4,7-trimethoxy-9,10-dihydrophenanthrene



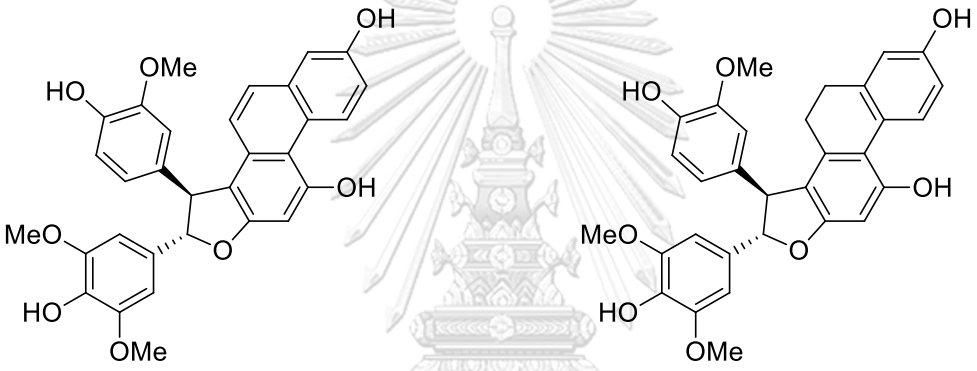
[**135**] 2,4,5,9*S*-Tetrahydroxy-9,10-dihydrophenanthrene 4-*O*-β-D-glucopyranoside

Figure 2 Structures of bibenzyls and derivatives previously isolated from *Dendrobium* species (continued)



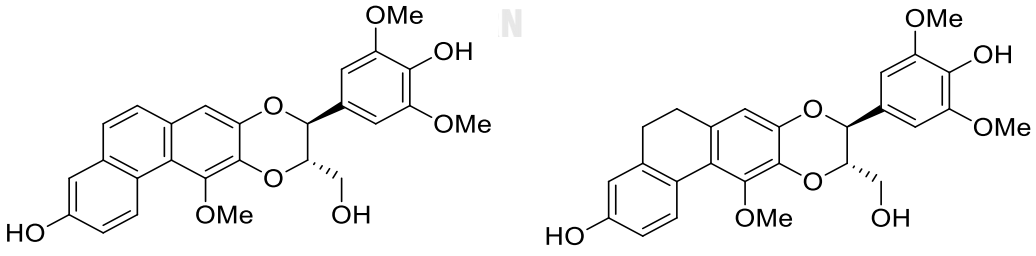
[**136**] Loddigesiinol G: R = H

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



[**138**] Loddigesiinol I

[**139**] Loddigesiinol J



[**140**] Dendrocandin P1

[**141**] Dendrocandin P2

Figure 2 Structures of bibenzyls and derivatives previously isolated from *Dendrobium* species (continued)

Table 2 Distribution of flavonoids in the genus *Dendrobium*

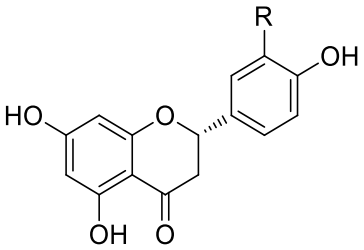
Compounds	Plant	Plant part	Reference
(2*S*)-Homoeriodictyol [**142**]	*D. densiflorum*	Stem	Fan *et al.*, 2001
	D. ellipsophyllum	Whole plant	Tanagornmeatar *et al.*, 2014
Naringenin [**143**]	*D. aurantiacum* var. *denneanum*	Stem	Yang *et al.*, 2006a
	D. densiflorum	Stem	Fan *et al.*, 2001
	D. longicornu	Stem	Hu *et al.*, 2008a
(2*S*)-Eriodictyol [**144**]	*D. trigonopus*	Stem	Hu *et al.*, 2008b
	D. ellipsophyllum	Whole plant	Tanagornmeatar *et al.*, 2014
	D. tortile	Whole plant	Limpanit *et al.*, 2016
Vicenin-2 [**145**]	*D. aurantiacum* var. *denneanum*	Stem	Xiong *et al.*, 2013
Apigenin [**146**]	*D. crystallinum*	Stem	Wang *et al.*, 2009
	D. williamsonii	Whole plant	Rungwichaniwat *et al.*, 2014
5,6-Dihydroxy-4′-methoxyflavone [**147**]	*D. chrysotoxum*	Stem	Hu *et al.*, 2012
Luteolin [**148**]	*D. aurantiacum* var. *denneanum*	Whole plant	Liu *et al.*, 2009a
	D. ellipsophyllum	Whole plant	Tanagornmeatar *et al.*, 2014

Table 2 (continued)

Compounds	Plant	Plant part	Reference
Chrysoeriol [**149**]	*D. ellipsophyllum*	Whole plant	Tanagornmeatar *et al.*, 2014
6-*C*-(α-Arabinopyranosyl)-8-*C*-[(2-*O*-α-rhamnopyranosyl)-β-galactopyranosyl] apigenin [**150**]	*D. huoshanense*	Aerial part	Chang *et al.*, 2010
6-*C*-(α-Arabinopyranosyl)-8-*C*-[(2-*O*-α-rhamnopyranosyl)-β-glucopyranosyl] apigenin [**151**]	*D. huoshanense*	Aerial part	Chang *et al.*, 2010
6‴-Glucosyl-vitexin [**152**]	*D. crystallinum*	Stem	Wang *et al.*, 2009
Isoschaftoside [**153**]	*D. huoshanense*	Aerial part	Chang *et al.*, 2010
Isoviolanthin [**154**]	*D. crystallinum*	Stem	Wang *et al.*, 2009
6-*C*-[(2-*O*-α-Rhamnopyranosyl)-β-glucopyranosyl]-8-*C*-(α-arabinopyranosyl) apigenin [**155**]	*D. huoshanense*	Aerial part	Chang *et al.*, 2010
6-*C*-(β-Xylopyranosyl)-8-*C*-[(2-*O*-α-rhamnopyranosyl)-β-glucopyranosyl] apigenin [**156**]	*D. huoshanense*	Aerial part	Chang *et al.*, 2010

Table 2 (continued)

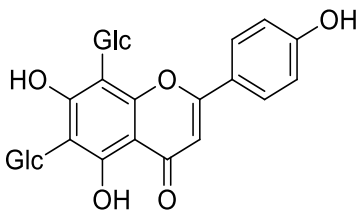
Compounds	Plant	Plant part	Reference
Kaempferol [**157**]	*D. aurantiacum var. denneanum*	Stem	Yang *et al.*, 2006a)
Kaempferol-3-*O*-α-L-rhamnopyranoside [**158**]	*D. secundum*	Stem	Phechrmeekha *et al.*, 2012
Kaempferol-3,7-*O*-di-α-L-rhamnopyranoside [**159**]	*D. secundum*	Stem	Phechrmeekha *et al.*, 2012
Kaempferol-3-*O*-α-L-rhamnopyranosyl-(1⟶2)-β-D-gluco pyranoside [**160**]	*D. capillipes*	Stem	Phechrmeekha *et al.*, 2012
Kaempferol-3-*O*-α-L-rhamnopyranosyl-(1⟶2)-β-D-xylopyranoside [**161**]	*D. capillipes*	Stem	Phechrmeekha *et al.*, 2012
Quercetin-3-*O*-L-rhamnopyranoside [**162**]	*D. secundum*	Stem	Phechrmeekha *et al.*, 2012
Quercetin-3-*O*-α-L-rhamnopyranosyl-(1′,2)-β-D-xylopyranoside [**163**]	*D. capillipes*	Stem	Phechrmeekha *et al.*, 2012
5-Hydroxy-3-methoxy-flavone-7-*O*-[β-D-apiosyl-(1⟶6)]-β-D-glucoside [**164**]	*D. devonianum*	Stem	Sun *et al.*, 2014



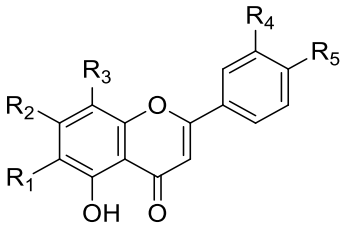
[**142**] (2*S*)-Homoeriodictyol: R = OMe

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

[**144**] (2*S*)-Eriodictyol: R = OH

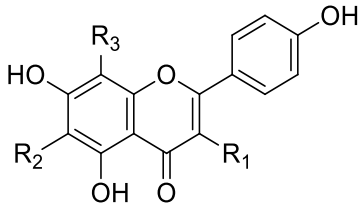


[**145**] Vicenin-2



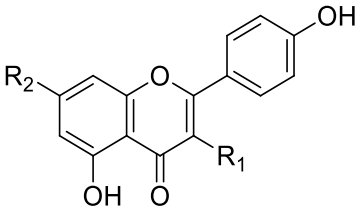
	R_1	R_2	R_3	R_4	R_5
[**146**] Apigenin	H	OH	H	H	OH
[**147**] 5,6-Dihydroxy-4′-methoxy-flavone	OH	H	H	H	OMe
[**148**] Luteolin	H	OH	H	OH	OH
[**149**] Chrysoeriol	H	OH	H	OMe	OH
[**150**] 6-*C*-(α-Arabinopyranosyl)-8-*C*-[(2-*O*-α-rhamnopyranosyl) -β-galactopyranosyl] apigenin	-Ara	OH	-Gal-Rha	H	OH
[**151**] 6-*C*-(α-Arabinopyranosyl)-8-*C*-[(2-*O*-α-rhamnopyranosyl) -β-glucopyranosyl] apigenin	-Ara	OH	-Glc-Rha	H	OH

Figure 3 Structures of flavonoids previously isolated from *Dendrobium* species

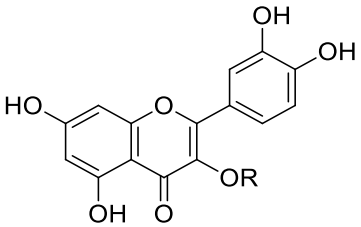


	R_1	R_2	R_3
[**152**] 6‴-Glucosyl-vitexin	H	H	-Glc
[**153**] Isoschaftoside	H	-Ara	-Glc
[**154**] Isoviolanthin	H	-Rha	-Glc
[**155**] 6-*C*-[(2-*O*-α-Rhamnopyranosyl)-β-glucopyranosyl]-8-*C*-(α-arabinopyranosyl) apigenin	H	-Glc-Rha	-Ara
[**156**] 6-*C*-(β-Xylopyranosyl)-8-*C*-[(2-*O*-α-rhamnopyranosyl)-β-glucopyranosyl] apigenin	H	-Xyl	-Glc-Rha
[**157**] Kaempferol	OH	H	H

Figure 3 Structures of flavonoids previously isolated from *Dendrobium* species (continued)

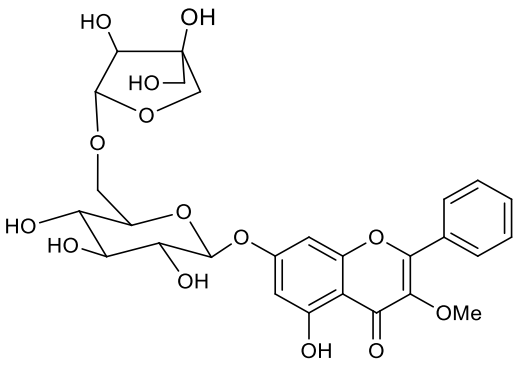


	R_1	R_2
[**158**] Kaempferol-3-*O*-α-L-rhamnopyranoside	O-Rha	OH
[**159**] Kaempferol-3,7-*O*-di-α-L-rhamnopyranoside	O-Rha	O-Rha
[**160**] Kaempferol-3-*O*-α-L-rhamnopyranosyl (1⟶2)-α-D-glucopyranoside	O-Glc-Rha	OH
[**161**] Kaempferol-3-O-α-L-rhamnopyranosyl (1⟶2)-β-D-xylopyranoside	O-Xyl-Rha	OH



	R
[**162**] Quercetin-3-*O*-α-L-rhamnopyranoside	O-Rha
[**163**] Quercetin-3-*O*-α-L-rhamnopyranosyl-(1⟶2)-β-D-xylopyranoside	O-Xyl-Rha

Figure 3 Structures of flavonoids previously isolated from *Dendrobium* species (continued)



[**164**] 5-Hydroxy-3-methoxyflavone-7-*O*-[β-D-apiosyl-(1⟶6)]-β-D-glucoside

Figure 3 Structures of flavonoids previously isolated from *Dendrobium* species (continued)

Table 3 Distribution of terpenoids in the genus *Dendrobium*

Compounds	Plant	Plant part	Reference
Aduncin [**165**]	*D. longicornu*	Stem	Hu *et al.*, 2008a
Amoenin [**166**]	*D. amoenum*	Whole plant	Dahmen and Leander, 1978
	D. williamsonii	Whole plant	Yang *et al.*, 2017b
Amotin [**167**]	*D. amoenum*	Whole plant	Majumder *et al.*, 1999
Dendrowillin A [**168**]	*D. williamsonii*	Whole plant	Yang *et al.*, 2017b
Dendrowillin B [**169**]	*D. williamsonii*	Whole plant	Yang *et al.*, 2017b
α-Dihydropicrotoxinin [**170**]	*D. amoenum*	Whole plant	Majumder *et al.*, 1999
	D. williamsonii	Whole plant	Yang *et al.*, 2017b
Picrotin [**171**]	*D. williamsonii*	Whole plant	Yang *et al.*, 2017b
Dendrobane A [**172**]	*D. moniliforme*	Stem	Bi *et al.*, 2004
Dendronobilin A [**173**]	*D. nobile*	Stem	Zhang *et al.*, 2007a
Dendronobilin B [**174**]	*D. wardianum*	Stem	Zhang *et al.*, 2007b
	D. nobile	Stem	Wang *et al.*, 2009; Meng *et al.*, 2017
Dendronobilin C [**175**]	*D. crystallium*	Stem	Wang *et al.*, 2009
Dendronobilin D [**176**]	*D. nobile*	Stem	Zhang *et al.*, 2007b
Dendronobilin E [**177**]	*D. nobile*	Stem	Zhang *et al.*, 2007b
Dendronobilin F [**178**]	*D. nobile*	Stem	Zhang *et al.*, 2007b
Dendronobilin G [**179**]	*D. nobile*	Stem	Zhang *et al.*, 2007b
Dendronobilin H [**180**]	*D. nobile*	Stem	Zhang *et al.*, 2007b

Table 3 (continued)

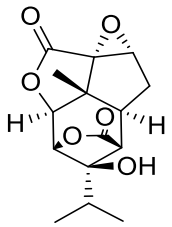
Compounds	Plant	Plant part	Reference
Dendronobilin I [**181**]	*D. nobile*	Stem	Zhang *et al.*, 2007b
Dendronobilin J [**182**]	*D. nobile*	Stem	Zhang *et al.*, 2007b
Dendronobilin K [**183**]	*D. wardianum*	Stem	Fan *et al.*, 2013
Dendronobilin L [**184**]	*D. nobile*	Stem	Zhang *et al.*, 2007b
Dendronobilin M [**185**]	*D. nobile*	Stem	Zhang *et al.*, 2008c; Meng *et al.*, 2017
Dendronobilin N [**186**]	*D. nobile*	Stem	Zhang *et al.*, 2008c
Dendrowardol A [**187**]	*D. nobile*	Stem	Zhang *et al.*, 2008c
Dendrowardol B [**188**]	*D. nobile*	Stem	Zhang *et al.*, 2008c
Dendrowardol C [**189**]	*D. wardianum*	Stem	Fan *et al.*, 2013
Corchoionoside C [**190**]	*D. wardianum*	Stem	Fan *et al.*, 2013
Crystallinin [**191**]	*D. wardianum*	Stem	Fan *et al.*, 2013
Findlayanin [**192**]	*D. nobile*	Stem	Meng et al., 2017
	D. polyánthum	Stem	Hu *et al.*, 2009
3-Hydroxy-2-oxodendrobine [**193**]	*D. findlayanum*	Whole plant	Qin *et al.*, 2011
Dendrobine [**194**]	*D. nobile*	Stem	Wang *et al.*, 1985 Meng *et al.*, 2017
(-)-(1*R*,2*S*,3*R*,4*S*,5*R*,6*S*,9*S*, 11*R*)-11-Carboxymethyl dendrobine [**195**]	*D. nobile*	Stem	Meng *et al.*, 2017
Dendromoniliside A [**196**]	*D. nobile*	Stem	Zhang *et al.*, 2007b

Table 3 (continued)

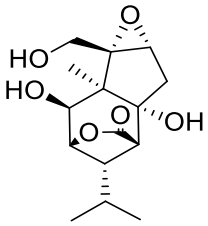
Compounds	Plant	Plant part	Reference
Dendromoniliside B [**197**]	*D. moniliforme*	Stem	Zhao *et al.*, 2003
Dendromoniliside C [**198**]	*D. moniliforme*	Stem	Zhao *et al.*, 2003
Dendromoniliside D [**199**]	*D. moniliforme*	Stem	Zhao *et al.*, 2003
Dendronobiloside A [**200**]	*D. moniliforme*	Stem	Zhao *et al.*, 2003
	D. nobile	Stem	Zhao *et al.*, 2001; Ye and Zhao, 2002a
Dendronobiloside B [**201**]	*D. nobile*	Stem	Zhao *et al.*, 2001; Ye and Zhao, 2002a
Dendronobiloside C [**202**]	*D. nobile*	Stem	Zhao *et al.*, 2001; Ye and Zhao, 2002a
Dendronobiloside D [**203**]	*D. nobile*	Stem	Zhao *et al.*, 2001; Ye and Zhao, 2002a
Dendronobiloside E [**204**]	*D. nobile*	Stem	Zhao *et al.*, 2001; Ye and Zhao, 2002a
Dendroside A [**205**]	*D. moniliforme*	Stem	Zhao *et al.*, 2003
	D. nobile	Stem	Zhao *et al.*, 2001; Ye and Zhao, 2002a
Dendroside B [**206**]	*D. nobile*	Stem	Ye and Zhao, 2002a; Zhao *et al.*, 2003
Dendroside C [**207**]	*D. moniliforme*	Stem	Zhao *et al.*, 2003
	D. nobile	Stem	Ye and Zhao, 2002a

Table 3 (continued)

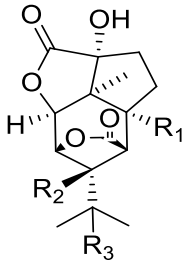
Compounds	Plant	Plant part	Reference
Dendroside D [**208**]	*D. nobile*	Stem	Ye and Zhao, 2002a
Dendroside E [**209**]	*D. nobile*	Stem	Ye *et al.*, 2002b
Dendroside F [**210**]	*D. moniliforme*	Stem	Zhao *et al.*, 2003
Dendroside G [**211**]	*D. nobile*	Stem	Ye *et al.*, 2002b
Wardianumine A [**211**]	*D. wardianum*	Stem	Zhang *et al.*, 2017



[**165**] Aduncin



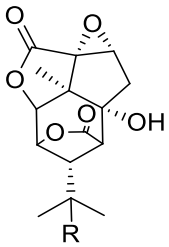
[**166**] Amoenin



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

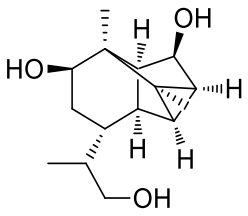
[**168**] Dendrowillin A: R_1 = R_3 = OH, R_2 = H

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

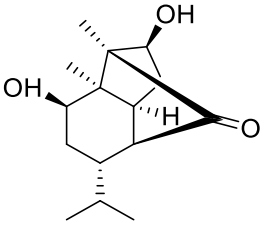


[**170**] α-Dihydropicrotoxinin: R = H

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

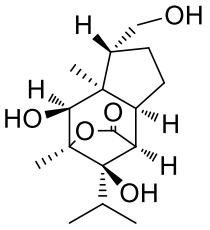


[**172**] Dendrobane A

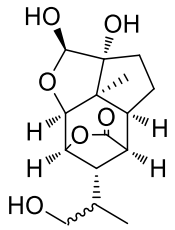


[**173**] Dendronobilin A

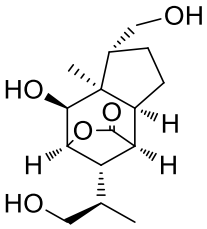
Figure 4 Structures of terpenoids previously isolated from *Dendrobium* species



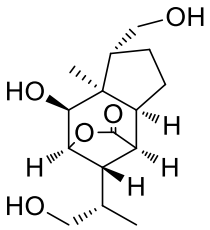
[**174**] Dendronobilin B



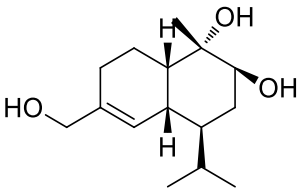
[**175**] Dendronobilin C



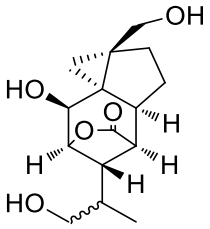
[**176**] Dendronobilin D



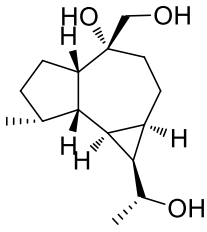
[**177**] Dendronobilin E



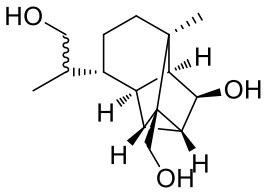
[**178**] Dendronobilin F



[**179**] Dendronobilin G

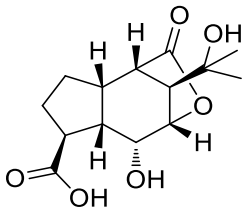


[**180**] Dendronobilin H

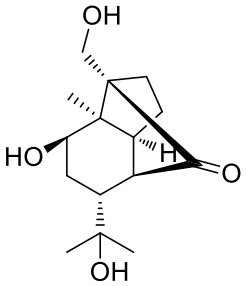


[**181**] Dendronobilin I

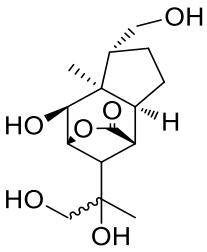
Figure 4 Structures of terpenoids previously isolated from *Dendrobium* species (continued)



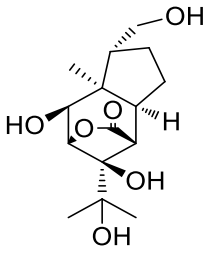
[**182**] Dendronobilin J



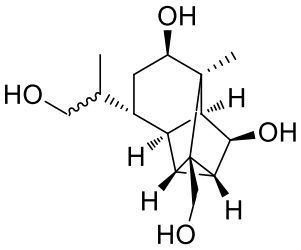
[**183**] Dendronobilin K



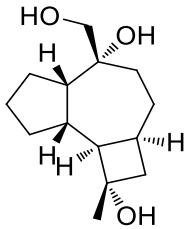
[**184**] Dendronobilin L



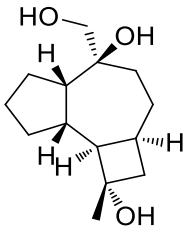
[**185**] Dendronobilin M



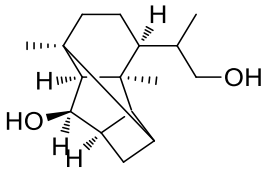
[**186**] Dendronobilin N



[**187**] Dendrowardol A

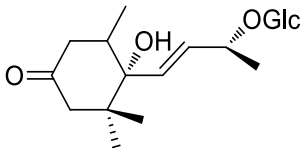


[**188**] Dendrowardol B

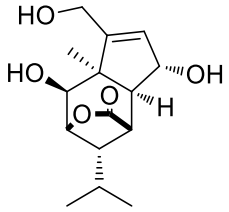


[**189**] Dendrowardol C

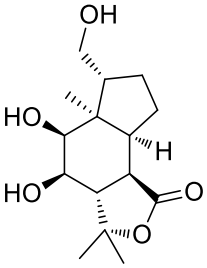
Figure 4 Structures of terpenoids previously isolated from *Dendrobium* species (continued)



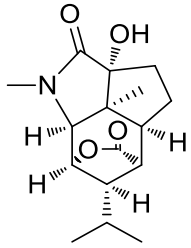
[**190**] Corchoionoside C



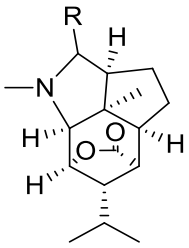
[**191**] Crystallinin



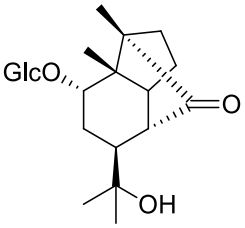
[**192**] Findlayanin



[**193**] 3-Hydroxy-2-oxodendrobine

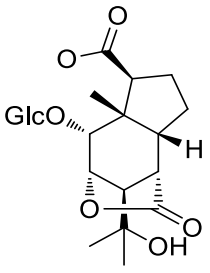


[**194**] Dendrobine: R = H

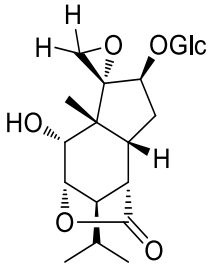


[**196**] Dendromoniliside A

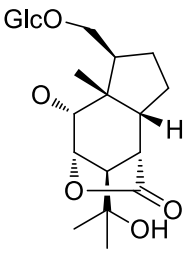
[**195**] (-)-(1*R*,2*S*,3*R*,4*S*,5*R*,6*S*,9*S*,11*R*)-11-Carboxymethyldendrobine: R = CH_2COOH



[**197**] Dendromoniliside B

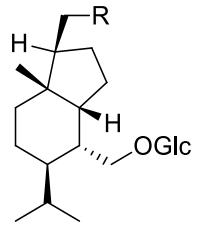


[**198**] Dendromoniliside C



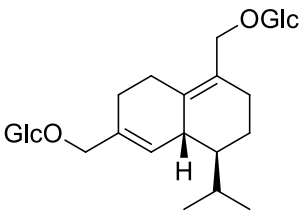
[**199**] Dendromoniliside D

Figure 4 Structures of terpenoids previously isolated from *Dendrobium* species (continued)

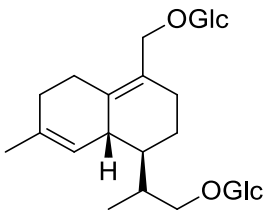


[**200**] Dendronobiloside A: R = OGlc

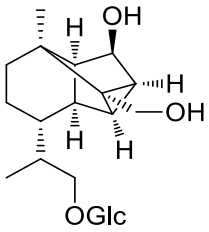
[**201**] Dendronobiloside B: R = OH



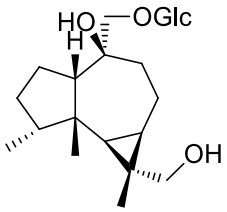
[**202**] Dendronobiloside C



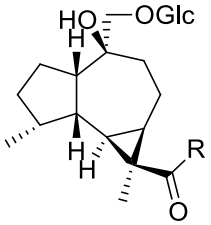
[**203**] Dendronobiloside D



[**204**] Dendronobiloside E



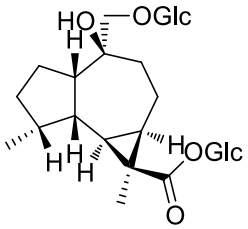
[**205**] Dendroside A



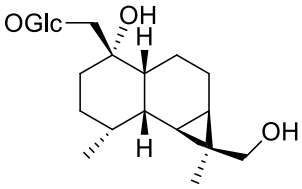
[**206**] Dendroside B: R = OGlc

[**207**] Dendroside C: R = OH

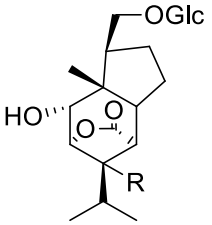
Figure 4 Structures of terpenoids previously isolated from *Dendrobium* species (continued)



[**208**] Dendroside D

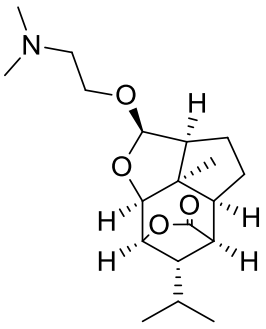


[**209**] Dendroside E



[**210**] Dendroside F: R = H

[**211**] Dendroside G: R = OH



[**212**] Wardianumine A

Figure 4 Structures of terpenoids previously isolated from *Dendrobium* species (continued)

Table 4 Distribution of miscellaneous compounds in the genus *Dendrobium*

Category and Compound	**Plant**	**Plant part**	**References**
Aliphatic acid derivatives			
Aliphalic acids [**213**]	*D. clavatum* var. *aurantiacum*	Stem	Chang *et al.*, 2001
Aliphatic alcohols [**214**]	*D. clavatum* var. *aurantiacum*	Stem	Chang *et al.*, 2001
Malic acid [**215**]	*D. huoshanense*	Aerial part	Chang *et al.*, 2001
Dimethyl malate [**216**]	*D. huoshanense*	Aerial part	Chang *et al.*, 2010
(-)-Shikimic acid [**217**]	*D. fuscescens*	Whole plant	Talapatra *et al.*, 1989
	D. huoshanense	Aerial part	Chang *et al.*, 2010
	D. longicornu	Stem	Hu *et al.*, 2008a
	D. pulchellum	Stem	Chanvorachote *et al.*, 2013
Isopentyl butyrate [**218**]	*D. huoshanense*	Aerial part	Chang *et al.*, 2010
Decumbic acid [**219**]	*D. nobile*	Stem	Zhou *et al.*, 2016
Benzoic acid derivatives and phenolic compounds			
3-Hydroxy-2-methoxy-5,6-dimethylbenzoic acid [**220**]	*D. crystallinum*	Stem	Wang *et al.*, 2009
Salicylic acid [**221**]	*D. huoshanense*	Aerial part	Chang *et al.*, 2010
	D. williamsonii	Whole plant	Yang *et al.*, 2017a

Table 4 (continued)

Category and Compound	**Plant**	**Plant part**	**Reference**
Vanilloside [**222**]	*D. denneanum*	Stem	Pan *et al.*, 2012
p-Hydroxybenzoic acid [**223**]	*D. williamsonii*	Whole plant	Yang *et al.*, 2017a
Gallic acid [**224**]	*D. longicornu*	Whole plant	Li *et al.*, 2009d
Syringic acid [**225**]	*D. crystallinum*	Stem	Wang *et al.*, 2009
Vanillic acid [**226**]	*D. crystallinum*	Stem	Hu *et al.*, 2012
	D. williamsonii	Whole plant	Li *et al.*, 2009d
Protocatechuic acid [**227**]	*D. nobile*	Stem	Ye and Zhao, 2002a
Antiarol [**228**]	*D. chrysotoxum*	Stem	Sun *et al.*, 2014
Ethylhaematommate [**229**]	*D. longicornu*	Whole plant	Sritularak and Likhitwitayawuid, 2009
p-Hydroxybenz-aldehyde [**230**]	*D. devonianum*	Whole plant	Limpanit *et al.*, 2016
	D. falconeri	Stem	Yang *et al.*, 2017a
	D. tortile	Whole plant	Yang *et al.*, 2017a
Vanillin [**231**]	*D. williamsonii*	Whole plant	Hu *et al.*, 2008a
Methyl 4-hydroxy-benzoate [**232**]	*D. williamsonii*	Whole plant	Hu *et al.*, 2012

Table 4 (continued)

Category and Compound	**Plant**	**Plant part**	**Reference**
Methyl β-orsellinate [**233**]	*D. longicornu*	Stem	Li *et al.*, 2009d
Tachioside [**234**]	*D. denneanum*	Stem	Pan *et al.*, 2012
Dendroside [**235**]	*D. nobile*	Stem	Zhou *et al.*, 2017
Phenylpropanoids			
Alkyl 4′-hydroxy-*trans*-cinnamates [**236**]	*D. clavatum* var. *aurantiacum*	Stem	Chang *et al.*, 2001
Alkyl *trans*-ferulates [**237**]	*D. clavatum* var. *aurantiacum*	Stem	Chang *et al.*, 2001
Defuscin [**238**]	*D. aurantiacum* var. *denneanum*	Stem	Yang *et al.*, 2006a
	D. moniliforme	Stem	Bi *et al.*, 2004
n-Octacosyl ferulate [**239**]	*D. aurantiacum var. denneanum*	Stem	Yang *et al.*, 2006a
	D. moniliforme	Stem	Bi *et al.*, 2004
n-Triacontyl *p*-hydroxy-*cis*-cinnamate [**240**]	*D. moniliforme*	Stem	Bi *et al.*, 2004

Table 4 (continued)

Category and Compound	**Plant**	**Plant part**	**Reference**
Tetratriacontanyl-*trans*-*p*-coumarate [**241**]	*D. williamsonii*	Whole plant	Rungwichaniwat *et al.*, 2014)
n-Docosyl *trans*-ferulate [**242**]	*D. longicornu*	Whole plant	Li *et al.*, 2009d
	D. williamsonii	Whole plant	Rungwichaniwat *et al.*, 2014
trans-Tetracosyl ferulate [**243**]	*D. tortile*	Whole plant	Limpanit *et al.*, 2016
cis-Hexacosanoyl ferulate [**244**]	*D. tortile*	Whole plant	Limpanit *et al.*, 2016
Ferulaldehyde [**245**]	*D. longicornu*	Whole plant	Li *et al.*, 2009d
Ferulic acid [**246**]	*D. secundum*	Stem	Sritularak *et al.*, 2011b
2-(*p*-Hydroxyphenyl) ethyl *p*-coumarate [**247**]	*D. falconeri*	Stem	Sritularak and Likhitwitayawuid, 2009
Dihydroconiferyl dihydro-*p*-coumarate [**248**]	*D. formosum*	Whole plant	Inthongkaew *et al.*, 2017
	D. nobile	Stem	Zhang *et al.*, 2006
	D. williamsonii	Whole plant	Yang *et al.*, 2017a

Table 4 (continued)

Category and Compound	**Plant**	**Plant part**	**Reference**
1-[4-(β-D-Glucopyranosyloxy)-3,5-dimethoxyphenyl]-1- propanone [**249**]	*D. aurantiacum* var. *denneanum*	Stem	Xiong *et al.*, 2013
Coniferyl alcohol [**250**]	*D. trigonopus*	Stem	Hu *et al.*, 2008b
p-Hydroxyphenyl propionic methyl ester [**251**]	*D. aphyllum*	Whole plant	Chen *et al.*, 2008c
Phloretic acid [**252**]	*D. ellipsophyllum*	Whole plant	Tanagornmeatar *et al.*, 2014
Dihydroconiferyl alcohol [**253**]	*D. longicornu*	Stem	Hu *et al.*, 2008a
Salidrosol [**254**]	*D. chrysotoxum*	Stem	Hu *et al.*, 2012
Shashenoside I [**255**]	*D. aurantiacum* var. *denneanum*	Stem	Xiong *et al.*, 2013
Syringin [**256**]	*D. aurantiacum* var. *denneanum*	Stem	Xiong *et al.*, 2013
Tetracosyl(*Z*)-*p*-coumarate [**257**]	*D. falconeri*	Whole plant	Sritularak and Likhitwitayawuid, 2009
Coumarins			
Ayapin [**258**]	*D. densiflorum*	Stem	Fan *et al.*, 2001

Table 4 (continued)

Category and Compound	**Plant**	**Plant part**	**Reference**
Coumarin [**259**]	*D. aurantiacum* var. *denneanum*	Stem	Yang *et al.*, 2006a
	D. clavatum var. *aurantiacum*	Stem	Chang *et al.*, 2001
Denthyrsin [**260**]	*D. thyrsiflorum*	Stem	Zhang *et al.*, 2005
Scoparone [**261**]	*D. densiflorum*	Stem	Fan *et al.*, 2001
	D. thyrsiflorum	Stem	Zhang *et al.*, 2005
	D. williamsonii	Whole plant	Yang *et al.*, 2017a
Scopoletin [**262**]	*D. densiflorum*	Stem	Fan *et al.*, 2001
Lignans and neolignans			
Dehydrodiconiferyl alcohol-4-*O*-β-D-glucoside [**263**]	*D. chrysanthum*	Stem	Ye *et al.*, 2004
Balanophonin [**264**]	*D. williamsonii*	Whole plant	Yang *et al.*, 2017a
Episyringaresinol [**265**]	*D. chrysotoxum*	Stem	Hu *et al.*, 2012
	D. longicornu	Stem	Hu *et al.*, 2008a
	D. nobile	Stem	Zhang *et al.*, 2008b
Episyringaresinol 4″-*O*-β-D-glucopyranoside [**266**]	*D. moniliforme*	Stem	Zhao *et al.*, 2003

Table 4 (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 [**267**]	*D. aurantiacum var. denneanum*	Stem	Xiong *et al.*, 2013
Lyoniresinol [**268**]	*D. chrysanthum*	Stem	Ye *et al.*, 2004
(-)-Syringaresinol-4,4′-bis-*O*-β-D-glucopyranoside [**269**]	*D. aurantiacum* var. *denneanum*	Stem	Xiong *et al.*, 2013
Syringaresinol-4-*O*-D-monoglucopyranoside [**270**]	*D. aurantiacum* var. *denneanum*	Stem	Xiong *et al.*, 2013
(-)-Medioresinol [**271**]	*D. loddigesii*	Whole plant	Ito *et al.*, 2010
(-)-Pinoresinol [**272**]	*D. loddigesii*	Whole plant	Ito *et al.*, 2010
Dendrolactone [**273**]	*D. nobile*	Stem	Zhou *et al.*, 2016
Erythro-1-(4-*O*-β-D-glucopyranosyl-3-methoxyphenyl)-2-[4-(3-hydroxypropyl)-2,6-dimethoxyphenoxy]-1,3-propanediol [**274**]	*D. longicornu*	Stem	Hu *et al.*, 2008a

Table 4 (continued)

Category and Compound	**Plant**	**Plant part**	**Reference**
Syringaresinol [**275**]	*D. secundum*	Stem	Sritularak *et al.*, 2011b
	D. williamsonii	Whole plant	M. Yang *et al.*, 2017a
Acanthoside B [**276**]	*D. chrysanthum*	Stem	Ye *et al.*, 2004
Liriodendrin [**277**]	*D. pulchellum*	Stem	Chanvorachote *et al.*, 2013
(-)-(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 [**278**]	*D. auranticum*	Stem	Li *et al.*, 2014
(-)-(8*S*,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 [**279**]	*D. auranticum*	Stem	Li *et al.*, 2014

Table 4 (continued)

Category and Compound	**Plant**	**Plant part**	**Reference**
(-)-(8*R*,7′*E*)-4-hydroxy-3,3′,5,5′,9′-penta-methoxy-8,4′-oxyneolign-7′-ene-9-ol-4,9-bis-*O*-β-D-gluco-pyranoside [**280**]	*D. auranticum*	Stem	Li *et al.*, 2014
Fluorenones			
Denchrysan A [**281**]	*D. chrysotoxum*	Whole plant	Li *et al.*, 2009c
Denchrysan B [**282**]	*D. brymerianum*	Whole plant	Klongkumnuankarn *et al.*, 2015
	D. chrysanthum	Whole plant	Ye *et al.*, 2003
Dendroflorin [**283**]	*D. aurantiacum* var. *denneanum*	Stem	Yang *et al.*, 2006a
	D. brymerianum	Whole plant	Klongkumnuankarn *et al.*, 2015
Dengibsin [**284**]	*D. aurantiacum var. denneanum*	Stem	Yang *et al.*, 2006a
	D. chrysanthum	Stem	Yang *et al.*, 2006b
	D. chrysotoxum	Whole plant	Li *et al.*, 2009c

Table 4 (continued)

Category and Compound	**Plant**	**Plant part**	**Reference**
Nobilone [**285**]	*D. brymerianum*	Whole plant	Klongkumnuankarn *et al.*, 2015
	D. nobile	Stem	Zhang *et al.*, 2007a
1,4,5-Trihydroxy-7-methoxy-9H-fluoren-9-one [**286**]	*D. chrysotoxum*	Whole plant	Chen *et al.*, 2008b
2,4,7-Trihydroxy-5-methoxy-9-fluorenone [**287**]	*D. chrysotoxum*	Stem	Yang *et al.*, 2004
2,4,7-Trihydroxy-1,5-dimethoxy-9-fluorenone [**288**]	*D. chrysotoxum*	Stem	Yang *et al.*, 2004
Others			
3,6,9-Trihydroxy-3,4-dihydroanthracen-1-(2*H*)-one [**289**]	*D. chrysotoxum*	Stem	Hu *et al.*, 2012
Palmarumycin JC2 [**290**]	*D. crystallinum*	Stem	Wang *et al.*, 2009
Dehydrovomifoliol [**291**]	*D. loddigesii*	Whole plant	Ito *et al.*, 2010

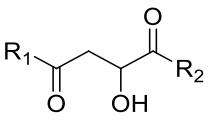
Table 4 (continued)

Category and Compound	**Plant**	**Plant part**	**Reference**
4-(2-Hydroxypropyl)-2(5H)-furanone [**292**]	*D. tortile*	Whole plant	Limpanit *et al.*, 2016
5,7-Dihydroxy-chromen-4-one [**293**]	*D. ellipsophyllum*	Whole plant	Tanagornmeatar *et al.*, 2014

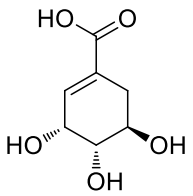
$CH_3\text{-}(CH_2)_n\text{-}CH_2\text{-}R$

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

[**214**] Aliphatic alcohol: R = OH, n = 22-32

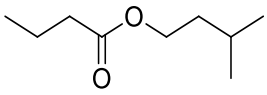


[**215**] Malic acid: R_1 = R_2 = OH

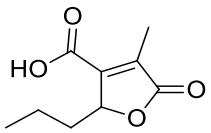


[**216**] Dimethyl malate: R_1 = R_2 = OMe

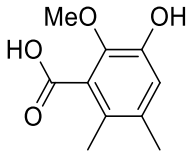
[**217**] (-)-Shikimic acid



[**218**] Isopentyl butyrate

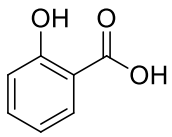


[**219**] Decumbic acid

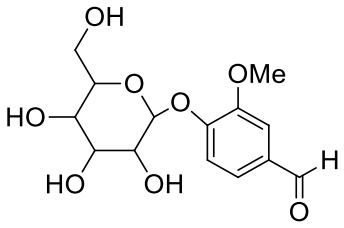


[**220**] 3-Hydroxy-2-methoxy-5,6-dimethylbenzoic acid

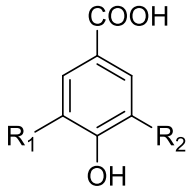
Figure 5 Structures of miscellaneous compounds previously isolated from *Dendrobium* species



[**221**] Salicylic acid



[**222**] Vanilloside



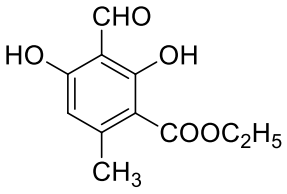
[**223**] *p*-Hydroxybenzoic acid: $R_1 = R_2 = H$

[**224**] Gallic acid: $R_1 = OH$, $R_2 = OH$

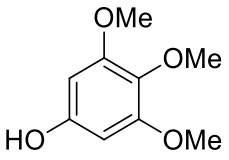
[**225**] Syringic acid: $R_1 = R_2 = OMe$

[**226**] Vanillic acid: $R_1 = H$, $R_2 = OMe$

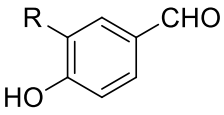
[**227**] Protocatechuic acid: $R_1 = H$, $R_2 = OH$



[**228**] Antiarol

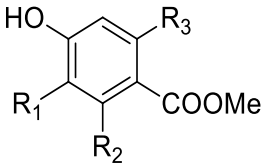


[**229**] Ethylhaematommate



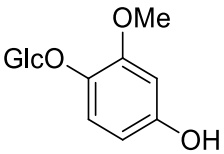
[**230**] *p*-Hydroxybenzaldehyde: R = H

[**231**] Vanillin: R = OMe



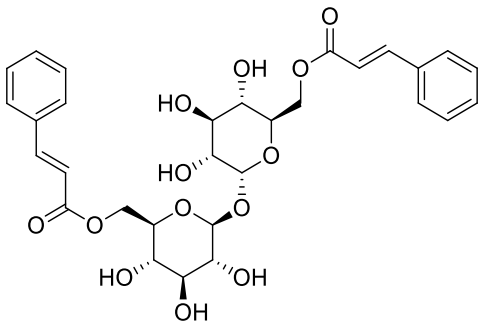
[**232**] Methyl 4-hydroxybenzoate $R_1 = R_2 = R_3 = H$

[**233**] Methyl β-orsellinate: $R_1 = R_3 = CH_3$, $R_2 = OH$

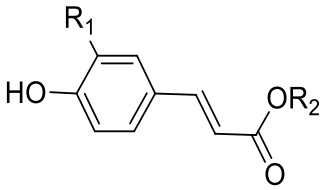


[**234**] Tachioside

Figure 5 Structures of miscellaneous compounds previously isolated from *Dendrobium* species (continued)



[**235**] Dendroside



[**236**] Alkyl 4′-hydroxy-*trans*-cinnamates: R_1 = H, R_2 = C_nH_{2n+1}, n =22-32

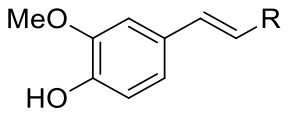
[**237**] Alkyl *trans*-ferulates: R_1 = OMe, R_2 = C_nH_{2n+1}, n = 18-28, 30

[**238**] Defuscin: R_1 = OMe, R_2 = $(CH_2)_{27}CH_3$

[**239**] *n*-Octacosyl ferulate: R_1 = OMe, R_2 = $(CH_2)_{28}CH_3$

[**240**] *n*-Triacontyl *p*-hydroxy-*cis*-cinnamate: R_1 = H, R_2 = $C_{30}H_{61}$

[**241**] Tetratriacontanyl-*trans*-*p*-coumarate: R_1 = H, R_2 = $(CH_2)_{33}CH_3$



[**242**] *n*-Docosyl *trans*-ferulate: R = $COOCH_2(CH_2)_{20}CH_3$

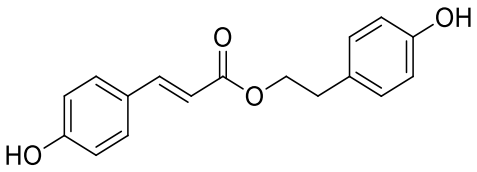
[**243**] *trans*-Tetracosylferulate: R = $COOCH_2(CH_2)_{22}CH_3$

[**244**] *cis*-Hexacosanoyl ferulate: R = $COOCH_2(CH_2)_{24}CH_3$

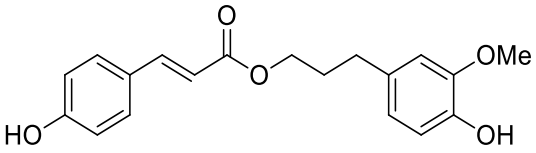
[**245**] Ferulaldehyde: R = CHO

[**246**] Ferulic acid: R = COOH

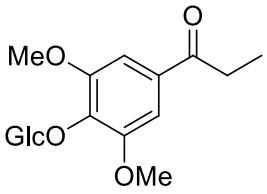
Figure 5 Structures of miscellaneous compounds previously isolated from *Dendrobium* species (continued)



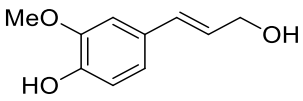
[**247**] 2-(*p*-Hydroxyphenyl) ethyl *p*-coumarate



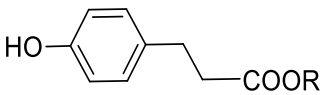
[**248**] Dihydroconiferyl dihydro-*p*-coumarate



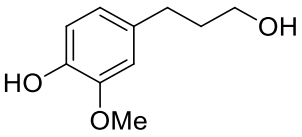
[**249**] 1-[4-(β-D-glucopyranosyloxy)-3,5-dimethoxyphenyl]-1-propanone



[**250**] Coniferyl alcohol

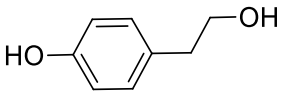


[**251**] *p*-Hydroxyphenyl propionic methyl ester: R = CH_3

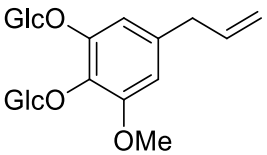


[**253**] Dihydroconiferyl alcohol

[**252**] Phloretic acid: R = OH

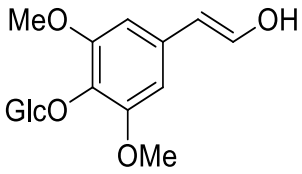


[**254**] Salidrosol

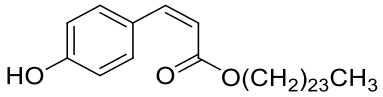


[**255**] Shashenoside I

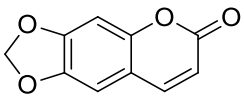
Figure 5 Structures of miscellaneous compounds previously isolated from *Dendrobium* species (continued)



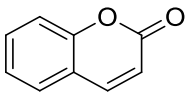
[**256**] Syringin



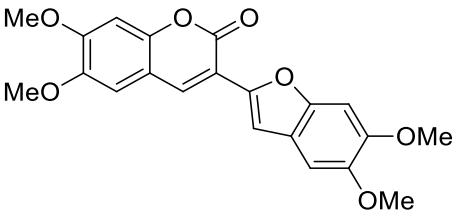
[**257**] Tetracosyl (*Z*)-*p*-coumarate



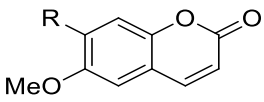
[**258**] Ayapin



[**259**] Coumarin



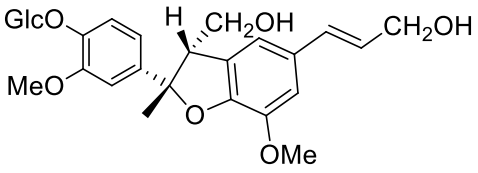
[**260**] Denthyrsin



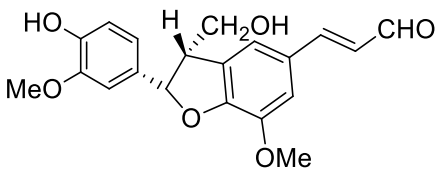
[**261**] Scoparone: R = OMe

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

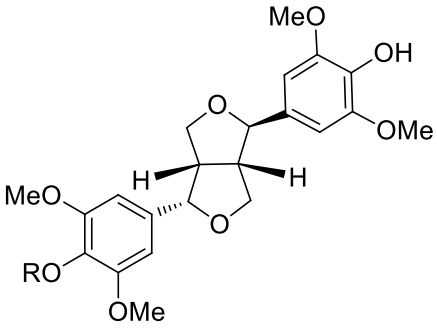
Figure 5 Structures of miscellaneous compounds previously isolated from *Dendrobium* species (continued)



[**263**] Dehydrodiconiferyl alcohol-4-*O*-β-D-glucoside

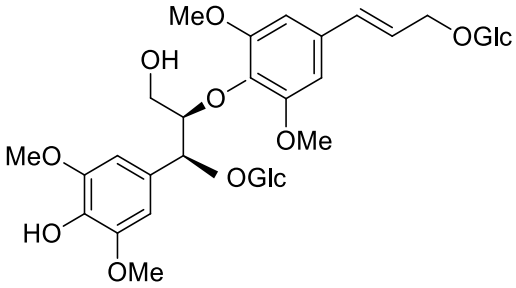


[**264**] Balanophonin

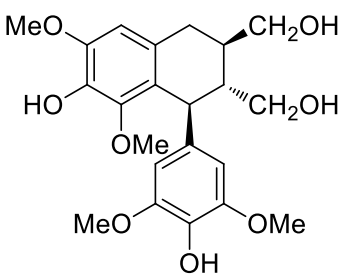


[**265**] Episyringaresinol: R = H

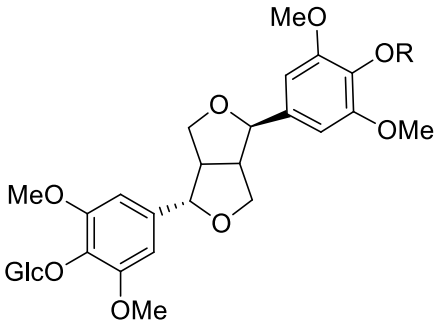
[**266**] Episyringaresinol 4″-*O*-β-D-glucopyranoside: R = Glc



[**267**] (-)-(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



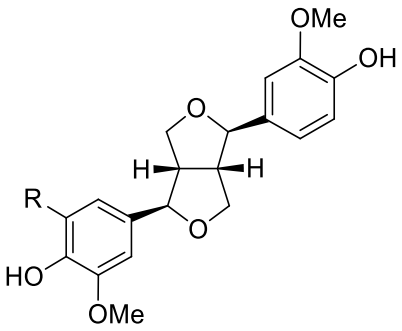
[**268**] Lyoniresinol



[**269**] (-)-Syringaresinol-4,4′-bis-*O*-β-D-glucopyranoside: R = Glc

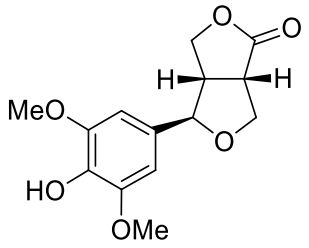
[**270**] Syringaresinol-4-*O*-D-monoglucopyranoside: R = H

Figure 5 Structures of miscellaneous compounds previously isolated from *Dendrobium* species (continued)

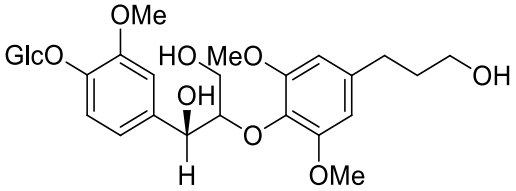


[**271**] (-)-Medioresinol: R = OMe

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

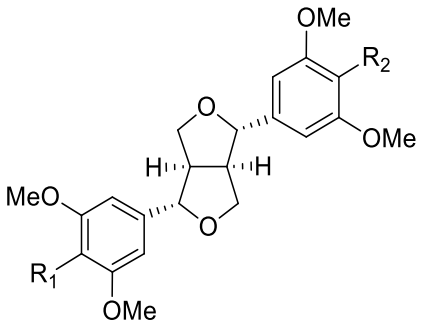


[**273**] Dendrolactone

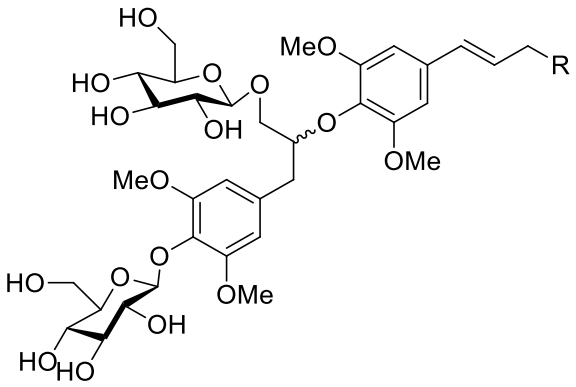


[**274**] Erythro-1-(4-*O*-β-D-glucopyranosyl-3-methoxyphenyl)-2-[4-(3-hydroxypropyl)-2,6-dimethoxyphenoxy]-1,3-propanediol

Figure 5 Structures of miscellaneous compounds previously isolated from *Dendrobium* species (continued)



	R_1	R_2
[**275**] Syringaresinol	OH	OH
[**276**] Acanthoside B	OGlc	OH
[**277**] Liriodendrin	OGlc	OGlc

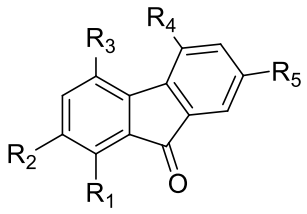


[**278**] (-)-(8*R*,7′*E*)-4-Hydroxy-3,3′,5,5′-tetramethoxy-8,4′-oxyneolign-7′-ene-9,9′-diol 4,9-bis-*O*-β-D-glucopyranoside: R = OH; 8*R*

[**279**] (-)-(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*

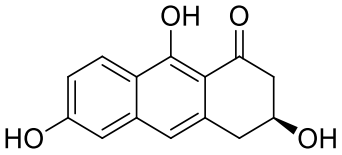
[**280**] (-)-(8*R*,7′*E*)-4-Hydroxy-3,3′,5,5′,9′-pentamethoxy-8,4′-oxyneolign-7′-ene-9-ol 4,9-bis-*O*-β-D-glucopyranoside: R = OMe; 8*R*

Figure 5 Structures of miscellaneous compounds previously isolated from *Dendrobium* species (continued)

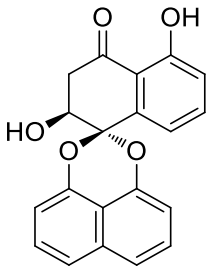


	R_1	R_2	R_3	R_4	R_5
[**281**] Denchrysan A	H	OH	OH	OMe	OH
[**282**] Denchrysan B	H	OH	OMe	OH	H
[**283**] Dendroflorin	OH	H	OH	OMe	OH
[**284**] Dengibsin	H	OH	OMe	OH	H
[**285**] Nobilone	H	OH	H	OMe	OH
[**286**] 1,4,5-Trihydroxy-7-methoxy-9*H*-fluoren-9-one	OH	H	OH	OH	OMe
[**287**] 2,4,7-Trihydroxy-5-methoxy-9-fluorenone	OMe	OH	OH	H	OH
[**288**] 2,4,7-Trihydroxy-1,5-dimethoxy-9-fluorenone	OMe	OH	OH	OMe	OH

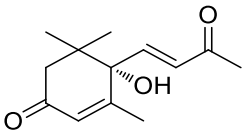
Figure 5 Structures of miscellaneous compounds previously isolated from *Dendrobium* species (continued)



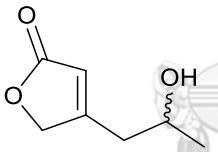
[**289**] 3,6,9-Trihydroxy-3,4-dihydroanthracen-1-(2*H*)-one



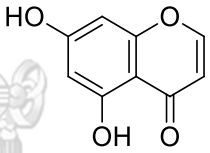
[**290**] Palmarumycin JC2



[**291**] Dehydrovomifoliol



[**292**] 4-(2-Hydroxypropyl)-2(5*H*)-furanone



[**293**] 5,7-Dihydroxy-chromen-4-one

Figure 5 Structures of miscellaneous compounds previously isolated from *Dendrobium* species (continued)

2. Traditional uses and biological activities of *Dendrobium* species

Several *Dendrobium* species have been used as folk medicine for a thousand years in many countries, for example, China, India, and Japan. In China, more than seventy species of *Dendrobium* were mentioned in many Chinese pharmacopoeias under the same Chinese name "Shi hu". Their ethnopharmacological properties were recorded that they are a source of astringent, tonic, analgesic, antipyretic, and anti-inflammatory substances. Thus, they have been used to treat plenty of disorders, such as, enhancing the production of body fluids, supplementing the stomach, clearing heat and nourishing Yin (Xu *et al.*, 2013; Cakova *et al.*, 2017). In addition, they are also used as medicinal herbs for reducing fever, eye, kidney and lung disorders, stomach diseases, red tongue, swelling, dry mouth, hyperglycemia, diabetes, and immunomodulatory as well as anti-aging effects (Yang *et al.*, 2007a; Rungwichaniwat *et al.*, 2014).

Dendrobium orchids are known to produce a variety of secondary metabolites, for instance, bibenzyls, phenanthrenes, sesquiterpenes, fluorenones, and alkaloids, which have been studied for a number of pharmacological activities (Lo *et al.*, 2004). At present, accumulating researches provide evidence that different *Dendrobium* species demonstrate numerous medicinal activities, including anti-inflammatory, antiplatelet aggregation, hemagglutinating, anti-fibrotic, anti-viral, anti-fungal, antimicrobial, antimalarial, anti-diabetic, inhibition of cataractogenesis, anticancer, anti-angiogenesis, hepatoprotective, neuroprotective, immunomodulatory, free radical scavenging and antioxidant activities (Ng *et al.*, 2012; Cakova *et al.*, 2017).

Scientific literature reports a large number of studies on the free radical scavenging activity or antioxidative activity of the extracts from *Dendrobium* orchids. For instance, the methanolic extracts of *D. tosaense* and *D. moniliforme* at a concentration of 0.4 mg/mL were able to scavenge DPPH radical at 95.9 and 83.4%, respectively (Lo *et al.*, 2004). In another study, several compounds isolated from the aerial part of *D. secundum* (moscatilin [**35**], 4,5,4′-trihydroxy-3,3′-dimethoxybibenzyl [**40**], ferulic acid [**246**], and syringaresinol [**275**]) were measured for their DPPH radical scavenging activity and found to appreciable activity (IC_{50} = 5.14, 15.87, 37.52, and 0.24 μM, respectively) compared with quercetin and Trolox® as the positive controls (IC_{50} =

2.47 and 11.68 μM, respectively) (Sritularak *et al.*, 2011b). Batatasin III [**19**], gigantol [**31**], 5-methoxy-7-hydroxy-9,10-dihydro-1,4-phenanthrenequinone [**93**], and hircinol [**111**] also showed DPPH free radical scavenging activity similar to quercetin and Trolox® (Sritularak *et al.*, 2011a). Moscatilin [**35**] demonstrated the strongest DPPH radical scavenging activity with IC_{50} 8.5 μM, whereas 3,3′-dihydroxy-4,5-dimethoxybibenzyl [**26**] and apigenin [**146**] exhibited appreciable activity (IC_{50} 19.5 and 19.3 μM, respectively) compared with the positive controls quercetin and vitamin C (IC_{50} 8.3 and 42.4 μM, respectively) (Rungwichaniwat *et al.*, 2014). In the ORAC assay, chrysotoxine [**22**], crepidatin [**23**], gigantol [**30**], moscatilin [**35**], nobilin D [**64**], dendroflorin [**283**], and nobilone [**285**] showed higher antioxidant activity than vitamin C (Zhang *et al.*, 2007a). In another study, polysaccharides isolated from *D. denneanum*, *D. fimbriatum*, *D. huoshanense*, *D. nobile*, and *D. officinale* manifested potential antioxidant and free radical scavenging activities toward DPPH, hydroxyl, and ABTS free radicals (Luo *et al.*, 2009; Luo *et al.*, 2011; Luo and Fan, 2011; Tian *et al.*, 2013; Luo *et al.*, 2016).

With regard to the antidiabetic activity of contituents of *Dendrobium*, research has been focused on hypoglycemic and α-glucosidase inhibitory activity. The polyphenolic loddigesiinols G-J [**136**-**139**] and a bibenzyl derivative named crepidatuol B [**54**] from *D. loddigesii* were examined for the α-glucosidase inhibitory activity by spectrophotometry. All compounds were significantly stronger α-glucosidase inhibitors than the positive control *trans*-resveratrol (Lu *et al.*, 2014). In another study in *D. formosum*, confusarin [**79**] and 5-methoxy-7-hydroxy-9,10-dihydro-1,4-phenanthrenequinone [**93**] at a concentration of 50 μg/ml, were evaluated. They inhibited α-glucosidase more than 50% and their IC_{50} (189.78 and 126.88 μM, respectively) are lower than that of acarbose (745.9 μM). Moscatilin [**36**] at 100 μg/ml and lusianthridin [**103**] at 1 and 10 μg/ml, isolated from *D. formosum* in the same study, demonstrated glucose uptake stimulatory effect without toxicity in L6 skeletal muscle cells (Inthongkaew *et al.*, 2017). In addition, a flavonol glycoside named 5-hydroxy-3-methoxy-flavone-7-*O*-[β-D-apiosyl-(1-6)]-β-D-glucoside [**164**] and a bibenzyl named gigantol [**30**] from *D. devonianum* were also analyzed for their α-glucosidase

inhibitory activity. Their enzyme inhibition at the concentration of 437.5 mmol/L were 43.4 and 36.7%, respectively, and these results were higher than that of acarbose (Sun *et al.*, 2014).

An investigation on the antiplatelet aggregation activity of the stem of *D. loddigesii* revealed that the phenanthrene moscatin [**95**], and the bibenzyls moscatilin [**35**] and moscatilin diacetate [**36**] could significantly inhibit rabbit platelet aggregation induced by arachidonic acid, collagen, and platelet-activating factor or PAF (Chen *et al.*, 1994). In another *in vitro* study with coherent results, gigantol [**30**], moscatilin [**35**], homoeriodictyol [**142**], scoparone [**261**], and scopoletin [**262**] isolated from *D. densiflorum* also demonstrated potent antiplatelet aggregation activity on rat platelet aggregation in preliminary tests *in vitro* (Fan *et al.*, 2001). Moreover, trigonopol A [**51**], a compound from *D. trigonopus*, at 0.0014 M exhibited antiplatelet aggregation activity with a moderate inhibitory ratio (67.55%) in a preliminary pharmacological test *in vitro* (Hu *et al.*, 2008b).

In the search for new anticancer substances, the bibenzyls and related compounds from *D. brymerianum* including gigantol [**30**], moscatilin [**35**], lusianthridin [**103**], and dendroflorin [**283**] displayed appreciable cytotoxic properties against human lung cancer cell lines with IC_{50} values of 196.7, 23.4, 65.0, and 125.8 μg/mL, respectively. Moreover, lusianthridin [**103**] and dendroflorin [**283**] also exhibited antimigratory activity at nontoxic concentrations (Klongkumnuankarn *et al.*, 2015). Moscatilin [**35**] from *D. pulchellum* could suppress the motility and invasion of human non-small cell lung cancer H23 cells at nontoxic concentrations, which indicated the antimetastatic potential of this agent (Kowitdamrong *et al.*, 2013). Gigantol [**30**] from *D. draconis* could hinder the non-small cell lung cancer H460 cell migration (Charoenrungruang *et al.*, 2014). 4,5,4′-Trihydroxy-3,3′-dimethoxybibenzyl [**40**], 4,4′-dihydroxy-3,5-dimethoxybibenzyl [**45**], chrysoeriol [**148**] and luteolin [**149**] from *D. ellipsophyllum*, at non-toxic concentrations, manifested anoikis-sensitizing effect and apoptosis induction (Tanagornmeatar *et al.*, 2014). Dendrocandin B [**5**], 3,4-dihydroxy-5,4′-dimethoxybibenzyl [**44**], dendrocandin I [**48**], dendrofalconerol A [**66**], and dendrosignatol [**69**] from *D. signatum* showed potential cytotoxic property against

many human cancer cell lines, including HepG2, HT-29, and MDA-231 cells (Mittraphab *et al.*, 2016).

In addition, 2-(*p*-hydroxyphenyl) ethyl *p*-coumarate [**247**], a phenylpropanoid from *D. falconeri* was evaluated for anti-herpes simplex virus type 1 (HSV-1) activity using the plaque reduction method with acyclovir as the positive control. It exhibited moderate anti-HSV-1 activity with an EC_{50} value of 352.1 μM, whereas the EC_{50} of acyclovir was 0.25 μM (Sritularak and Likhitwitayawuid, 2009). Another study on, densiflorol B [**87**] and phoyunnanin E [**73**] from *D. venustum* demonstrated moderate antimalarial activity (IC_{50} = 1.3 and 1.1 μM, respectively) compared with dihydroartemisinin and mefloquine as positive controls (IC_{50} = 0.002 and 0.031 nM) (Sukphan *et al.*, 2014).

CHAPTER III

EXPERIMENTAL

1. Source of plant materials

The whole plant of *Dendrobium palpebrae* Lindl. was purchased from Jatujak market, Bangkok, Thailand, in November 2012. Authentication was performed by Associate Professor Thatree Phadungcharoen (Faculty of Pharmacy, Rangsit University) and comparison with the database of the Botanical Garden Organization. A voucher specimen (BS-DPal-112555) has been deposited at the herbarium of the Department of Pharmacognosy and Pharmaceutical Botany, Faculty of Pharmaceutical Sciences, Chulalongkorn University.

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 F254 precoated plate (E. Merck)

Temperature : Laboratory temperature (30-35 ºC)

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) and heating at 105 ºC 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 ºC)

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, mixed with a small quantity of the adsorbent, triturated, dried and then gradually placed on top of the column.

Detection : Each fraction was examined by TLC under UV light at the wavelengths of 254 and 365 nm.

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 : Dry packing

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

Detection : Fractions were examined as described in section 2.2.1

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 2.2.1

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 prior to use 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 2.2.1

2.3 Spectroscopy

2.3.1 Ultraviolet (UV) spectra

UV spectra were recorded on a Milton Roy Spectronic 3000 Array spectrophotometer (Faculty of Pharmaceutical Sciences, Chulalongkorn University).

2.3.2 Infrared (IR) spectra

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

2.3.3 Mass spectra

Mass spectra were recorded on a Bruker micro TOF mass spectrometer (ESI-MS) (Department of Chemistry, Faculty of Sciences, Mahidol 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 methanol (CD_3OD) and deuterated chloroform ($CDCl_3$). Chemical shifts were reported in ppm scale using the chemical shift of the solvent as the reference signal.

2.4 Solvents

All organic solvents employed throughout this work were of commercial grade and were redistilled prior to use.

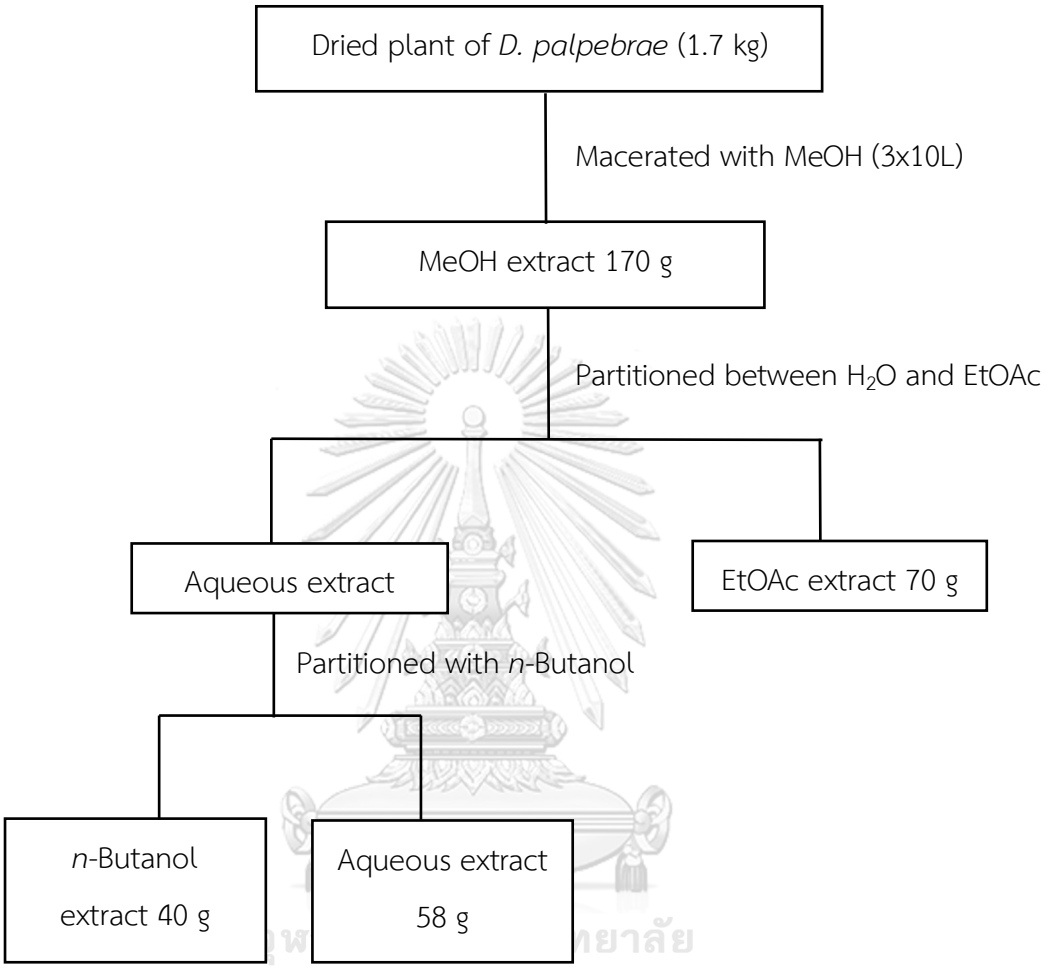
3. Extraction and isolation

3.1 Extraction

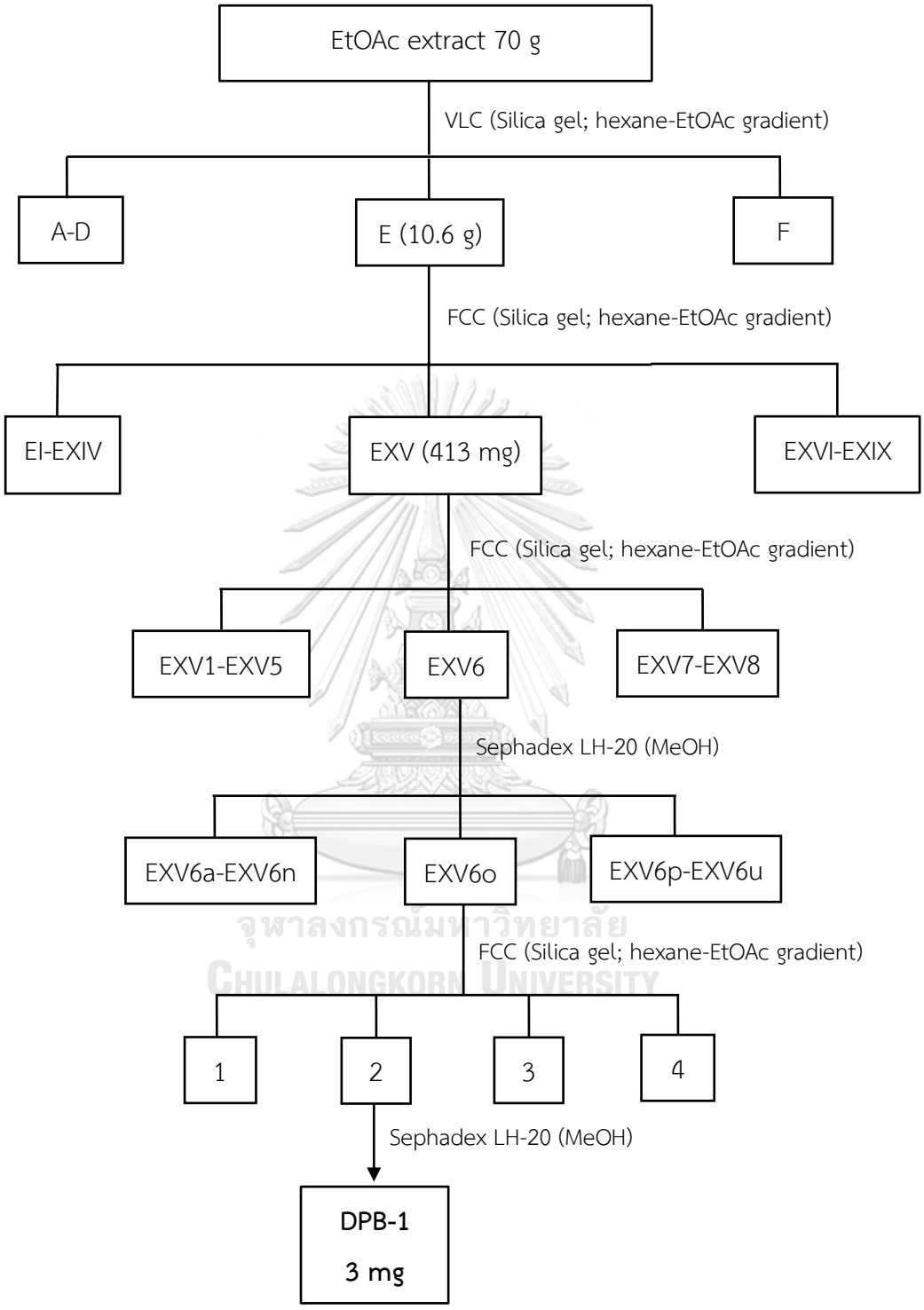
The dried and ground whole plants of *D. palpebrae* (1.7 kg) were macerated with 10 liters of methanol for 72 hours three times. The organic solvent was evaporated under reduced pressure to give 170 g of methanol crude extract. This extract was suspended in water and partitioned with EtOAc and then *n*-butanol to give an EtOAc extract (70 g), an *n*-butanol extract (40 g), and an aqueous extract (58 g). All three extracts were screened for free radical scavenging activity by DPPH radical scavenging assay. The EtOAc extract showed the highest activity with >80% reduction at 100 µg/mL. Thus, the EtOAc extract was selected for further investigation (**Scheme 1**).

3.2 Isolation

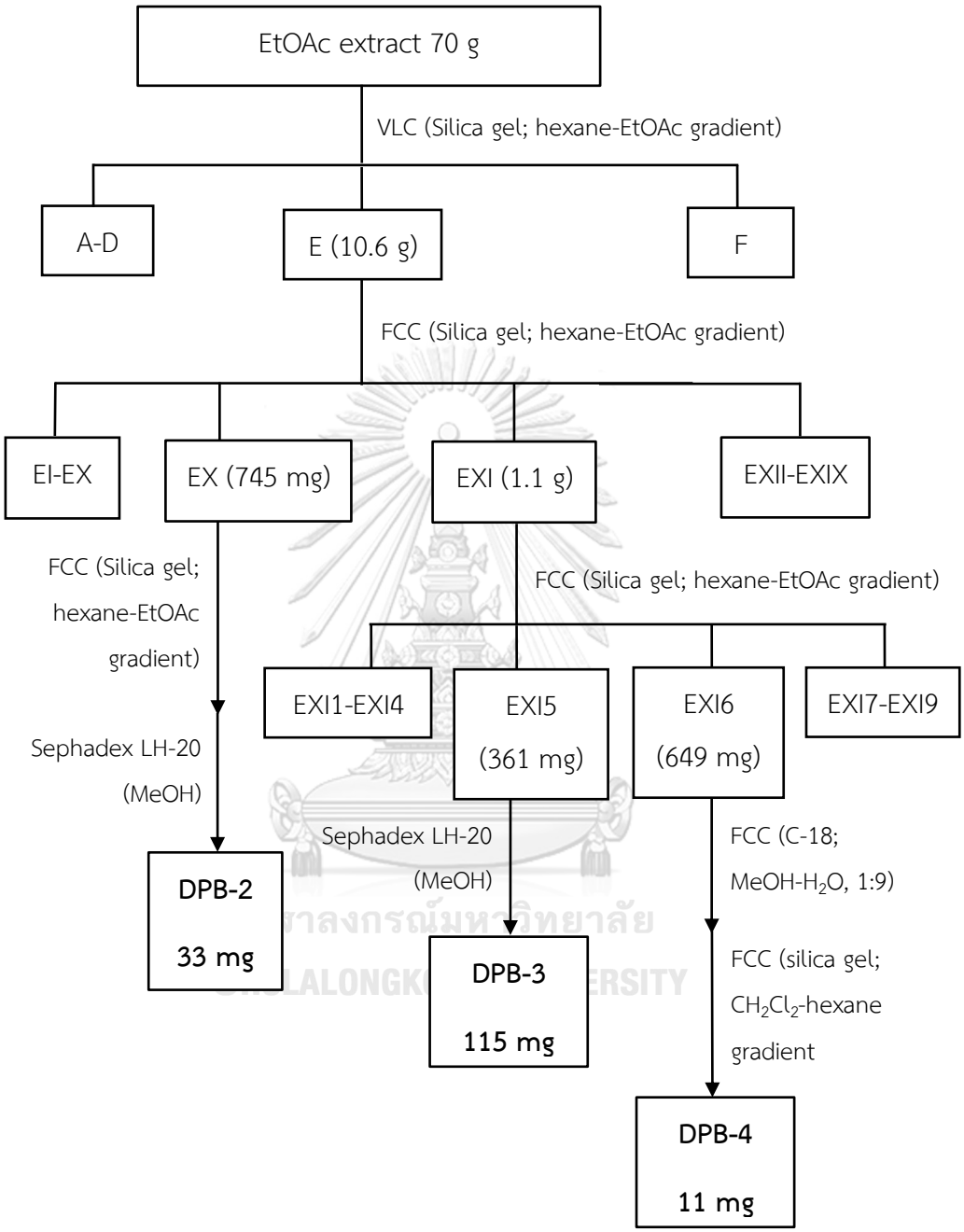
The EtOAc extract (70 g) was initially fractionated by vacuum liquid chromatography (VLC) as described in section 2.2.1. (**Scheme 2**) Silica gel (No.7734) was used as the stationary phase and a step gradient of hexane-EtOAc (1:0 to 0:1) as the mobile phase. The eluates were collected about 500 mL per fraction, examined by TLC (silica gel, hexane-EtOAc) and combined to give six fractions (A-F).



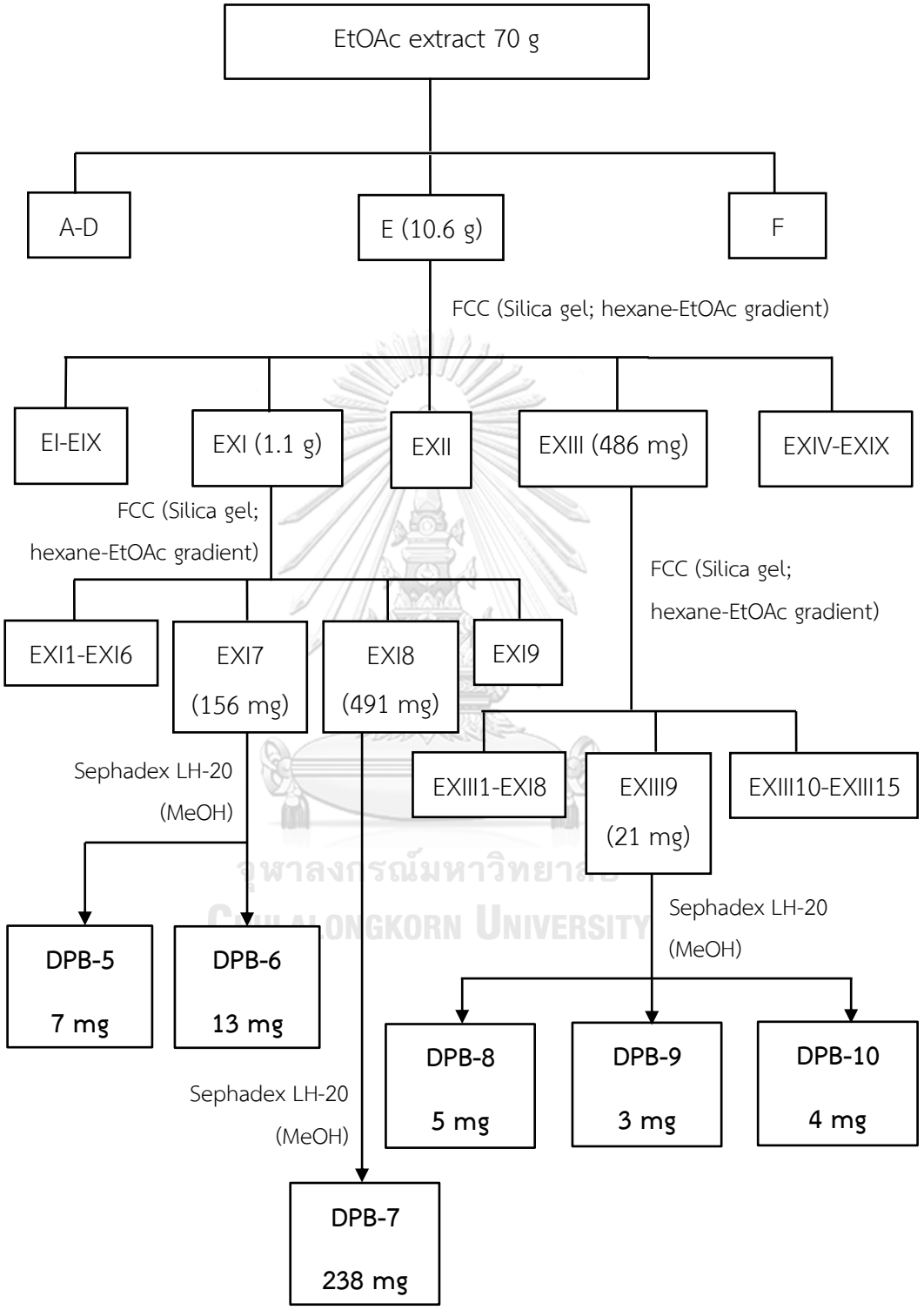
Scheme 1 Separation of the MeOH extract of *Dendrobium palpebrae*



Scheme 2 Separation of the EtOAc extract of *Dendrobium palpebrae*



Scheme 2 Separation of the EtOAc extract of *Dendrobium palpebrae* (continued)



Scheme 2 Separation of the EtOAc extract of *Dendrobium palpebrae* (continued)

3.2.1 Isolation of compound DPB-1 (Dendropalpebrone)

Fraction E (10.6 g) was separated by FCC over silica gel (No. 9385) as the stationary phase with a gradient mixture of hexane-EtOAc (1:0 to 0:1) to give nineteen fractions (EI-EXIX).

Fraction EXV (413 mg) was further separated by FCC using silica gel as the stationary phase with a gradient of hexane-EtOAc (1:0 to 0:1) to afford eight fractions (EXV1-EXV8).

Fraction EXV6 was purified on a Sephadex LH-20 column, eluted with methanol, to give twenty-one fractions (EXV6a-EXV6u). Fraction EXV6o was subjected to repeated separation by FCC over silica gel with a gradient mixture of hexane-EtOAc (1:0 to 0:1) to give four sub-fractions (1-4)

Finally, sub-fraction 2 was purified on a Sephadex LH-20 column (methanol) to yield compound DPB-1 as an orange amorphous solid (3 mg). DPB-1 was characterized as a new dimeric structure consisting of a phenanthrene and a phenanthraquinone unit and named as dendropalpebrone.

3.2.2 Isolation of compound DPB-2 (Gigantol)

Fraction EX (745 mg) was fractionated on a silica gel column using as a gradient mixture of hexane-EtOAc (1:0 to 0:1) as the mobile phase. Then, it was further purified on Sephadex LH-20 (methanol) to give compound DPB-2 (33 mg). It was identified as gigantol.

3.2.3 Isolation of compound DPB-3 (Lusianthridin)

Fraction EXI (1.1 g) was fractionated by FCC using silica gel (No. 9385) as the stationary phase with a step gradient mixture of hexane-EtOAc (1:0 to 0:1). Nine sub-fractions (EXI1-EXI9) were obtained.

Fraction EXI5 (361 mg) was further purified on Sephadex LH-20 (methanol) to give compound DPB-3 (115 mg) as a brown amorphous solid. It was later identified as lusianthridin.

3.2.4 Isolation of compound DPB-4 (Nobilone)

Fraction EXI6 (649 mg) was separated by CC using C-18 as the stationary phase with a mixture of methanol-H_2O (1:9) as the mobile phase. Compound DPB-4 was obtained after purification on CC over silica gel (CH_2Cl_2-hexane gradient (1:0 to 0:1)) as a red amorphous solid (11 mg) and was later identified as nobilone.

3.2.5 Isolation of compound DPB-5 (3,7-Dihydroxy-2,4,8-trimetho-xyphenanthrene) and DPB-6 (2,5-Dihydroxy-4,9-dimethoxyphenanthrene)

Fraction EXI7 (156 mg) was purified by CC over Sephadex LH-20, eluted with methanol to give compound DPB-5 as a yellowish white crystal (7 mg). It was identified as 3,7-dihydroxy-2,4,8-trimethoxyphenanthrene and compound DPB-6 as a light-yellow powder (13 mg). It was identified as 2,5-dihydroxy-4,9-dimethoxyphenanthrene.

3.2.6 Isolation of compound DPB-7 (Moscatilin)

Fraction EXI8 (491 mg) was further fractionated on a Sephadex LH-20 column and methanol as mobile phase to afford DPB-7 as a brown amorphous solid (238 mg). It was later identified as moscatilin.

3.2.7 Isolation of compound DPB-8 (Scoparone), DPB-9 (4,5,4′-Trihydroxy-3,3′-dimetho-xybibenzyl), and DPB-10 (Dendroflorin)

Fraction EXIII (486 mg) was separated by FCC using silica gel (No. 9385) as the stationary phase with a step gradient mixture of hexane-EtOAc (1:0 to 0:1). Fifteen fractions (EXIII1-EXIII15) were obtained.

Then, fraction EXIII9 (21 mg) was further purified on Sephadex LH20 (methanol) to yield compound DPB-8 as a pale brown powder (5 mg), DPB-9 as a brown amorphous solid (3 mg), and DPB-10 as a red amorphous solid (4 mg). These compounds were later identified as scoparone, 4,5,4′-trihydroxy-3,3′-dimethoxybibenzyl, and dendroflorin, respectively.

4. Physical and spectral data of isolated compounds

4.1 Compound DPB-1 (Dendropalpebrone)

Compound DPB-1 was obtained as an orange amorphous solid (3.0 mg, 0.00018% based on dried weight of whole plant). It was soluble in methanol.

UV : λ_{max} nm (log ε), in methanol: 221 (4.28), 258 (4.23), 283 (4.14); see **Figure 6**

FT-IR : ν cm^{-1} (film): 3433, 2918, 2850, 1731, 1627, 1469, 1180; see **Figure 7**

HR-ESI-MS : $[M+H]^+$ ion at *m/z* 559.1368 ($C_{32}H_{24}O_8$); see **Figure 8**

^{1}H NMR : δ ppm, 500 MHz, in CD_3OD; see **Table 5, Figure 9**

^{13}C NMR : δ ppm, 125 MHz, in CD_3OD; see **Table 5, Figure 10**

4.2 Compound DPB-2 (Gigantol)

Compound DPB-2 was obtained as a brown amorphous solid (33.0 mg, 0.00194% based on dried weight of whole plant). It was soluble in acetone.

HR-ESI-MS : $[M+H]^+$ ion at *m/z* 297.1111 ($C_{16}H_{18}O_4$); see **Figure 14**

^{1}H NMR : δ ppm, 300 MHz, in acetone-d_6; see **Table 6, Figure 15**

^{13}C NMR : δ ppm, 75 MHz, in acetone-d_6; see **Table 6, Figure 16**

4.3 Compound DPB-3 (Lusianthridin)

Compound DPB-3 was obtained as a brown amorphous solid (115.0 mg, 0.00676% based on dried weight of whole plant). It was soluble in acetone.

HR-ESI-MS : $[M+H]^+$ ion at *m/z* 265.0845 ($C_{15}H_{14}O_3$); see **Figure 18**

^{1}H NMR : δ ppm, 300 MHz, in acetone-d_6; see **Table 7, Figure 19**

^{13}C NMR : δ ppm, 75 MHz, in acetone-d_6; see **Table 7, Figure 20**

4.4 Compound DPB-4 (Nobilone)

Compound DPB-4 was obtained as a red amorphous solid (11.0 mg, 0.00065% based on dried weight of whole plant). It was soluble in acetone.

HR-ESI-MS : $[M+H]^+$ ion at *m/z* 265.0479 ($C_{14}H_{10}O_4$); see **Figure 24**

^{1}H NMR : δ ppm, 300 MHz, in acetone-d_6; see **Table 8, Figure 25**

^{13}C NMR : δ ppm, 75 MHz, in acetone-d_6; see **Table 8, Figure 26**

4.5 Compound DPB-5 (3,7-Dihydroxy-2,4,8-trimethoxyphenanthrene)

Compound DPB-5 was obtained as pale-yellow crystals (7.0 mg, 0.00041% based on dried weight of whole plant). It was soluble in acetone.

HR-ESI-MS : $[M+H]^+$ ion at *m/z* 323.0896 ($C_{17}H_{16}O_5$); see **Figure 30**

^{1}H NMR : δ ppm, 300 MHz, in acetone-d_6; see **Table 9, Figure 31**

^{13}C NMR : δ ppm, 75 MHz, in acetone-d_6; see **Table 9, Figure 32**

4.6 Compound DPB-6 (2,5-Dihydroxy-4,9-dimethoxyphenanthrene)

Compound DPB-6 was obtained as a light-yellow powder (13.0 mg, 0.00076% based on dried weight of whole plant). It was soluble in acetone.

HR-ESI-MS : $[M+H]^+$ ion at *m/z* 293.0791 ($C_{16}H_{14}O_4$); see **Figure 36**

^{1}H NMR : δ ppm, 300 MHz, in acetone-d_6; see **Table 10, Figure 37**

^{13}C NMR : δ ppm, 75 MHz, in acetone-d_6; see **Table 10, Figure 38**

4.7 Compound DPB-7 (Moscatilin)

Compound DPB-7 was obtained as a brown amorphous solid (238.0 mg, 0.014% based on dried weight of whole plant). It was soluble in acetone.

HR-ESI-MS : $[M+H]^+$ ion at *m/z* 327.1219 ($C_{17}H_{20}O_5$); see **Figure 42**

^{1}H NMR : δ ppm, 300 MHz, in acetone-d_6; see **Table 11, Figure 43**

^{13}C NMR : δ ppm, 75 MHz, in acetone-d_6; see **Table 11, Figure 44**

4.8 Compound DPB-8 (Scoparone)

Compound DPB-8 was obtained as a pale brown powder (5.0 mg, 0.00029% based on dried weight of whole plant). It was soluble in chloroform.

HR-ESI-MS : $[M+H]^+$ ion at *m/z* 229.0470 ($C_{11}H_{10}O_4$); see **Figure 48**

^{1}H NMR : δ ppm, 300 MHz, in $CDCl_3$; see **Table 12, Figure 49**

^{13}C NMR : δ ppm, 75 MHz, in $CDCl_3$; see **Table 12, Figure 50**

4.9 Compound DPB-9 (4,5,4′-Trihydroxy-3,3′-dimethoxybibenzyl)

Compound DPB-9 was obtained as a brown amorphous solid (3.0 mg, 0.00018% based on dried weight of whole plant). It was soluble in acetone.

HR-ESI-MS : $[M+H]^+$ ion at *m/z* 313.1060 ($C_{16}H_{18}O_5$); see **Figure 53**

^{1}H NMR : δ ppm, 300 MHz, in acetone-d_6; see **Table 13, Figure 54**

^{13}C NMR : δ ppm, 75 MHz, in acetone-d_6; see **Table 13, Figure 55**

4.10 Compound DPB-10 (Dendroflorin)

Compound DPB-10 was obtained as a red amorphous solid (4.0 mg, 0.00024% based on dried weight of whole plant). It was soluble in acetone.

HR-ESI-MS : $[M+H]^+$ ion at *m/z* 281.0417 ($C_{14}H_{10}O_5$); see **Figure 59**

^{1}H NMR : δ ppm, 300 MHz, in acetone-d_6; see **Table 14, Figure 60**

^{13}C NMR : δ ppm, 75 MHz, in acetone-d_6; see **Table 14, Figure 61**

5. Free radical scavenging activity assays

5.1 Sample preparation

Approximately 3 mg of the sample was dissolved in 300 µL of dimethyl sulfoxide (DMSO) to give a "stock solution". The stock solution was further diluted with DMSO for the oxygen radical absorbance capacity assay and 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity assay. For the deoxyribose degradation assay, results can be interfered by high concentration of DMSO. Therefore, the stock solution in this case was diluted with distilled water before use.

5.2 Oxygen radical absorbance capacity assay (ORAC assay)

At present, there are many methods for evaluation of antioxidant proper *in vitro*. The oxygen radical absorbance capacity (ORAC) assay has been widely used to determine the antioxidant property in the pharmaceutical, nutraceutical, and food

industries (Huang *et al*, 2002). The ORAC assay is based on a competitive reaction between an agent with antioxidation activity and a fluorescent probe, which is fluorescein (FL), for a radical (usually peroxyl radical) initiated by the thermal decomposition of azo-compounds, namely, 2,2′-azobis(2-amidinopropane)-dihydrochloride (AAPH). The removal of peroxyl radicals by the sample or the positive control which has antioxidant property, decreases the degradation of fluorescein. Results of the attack of radicals and defense by the antioxidant are displayed as area under the curve (AUC) of the fluorescence declination. A standard calibration line is plotted by evaluating the radical clearing activity of a standard antioxidant, for example, Trolox® (Lucas-Abellán *et al.*, 2008; Roy *et al.*, 2010).

5.2.1 Materials and instruments

- 2,2′-Azobis(2-amidinopropane) dihydrochloride (AAPH) (Sigma-Aldrich)
- Trolox® (Sigma-Aldrich)
- Fluorescein (FL) (Sigma-Aldrich)
- Black 96-well microplate (Corning)
- Microplate reader (CLARIOstar, BMG LABTECH)
- Ultrasonic bath (Transsonic 570/H, Elma)
- Vortex mixer (Vortex-Genie2, Scientific Industries)

5.2.2 Determination of oxygen radical absorbance capacity assay

The ORAC assay in this study used black 96-well plates with a microplate reader. The assay was conducted at 37 °C under pH 7.4 with a blank sample in parallel. FL was used as the substrate, and Trolox®, which is a water-soluble analogue of vitamin E, was applied as a positive control at concentrations 0 – 100 µM. 2,2'-Azobis(2-amidinopropane) dihydrochloride (AAPH) was used to generate peroxyl radical. The reaction mixture contained the sample, at 50 µg/mL, or in positive control, Trolox® (25 µL), fluorescein in buffer pH 7.4 (150 µL) and AAPH (25 µL), while the blank was a reaction mixture without sample or Trolox®. The fluorescence of FL was recorded every minute

after addition of AAPH by microplate reader at an excitation wavelength of 485 nm and an emission wavelength of 530 nm. The fluorescent results were expressed relative to the initial reading. Moreover, the results were calculated using net areas under the FL decay curves (AUC) obtained by subtracting the AUC of the blank from the AUC of the sample. Trolox® concentrations against the average net AUC of the two measurements (Trolox® and sample) for each concentration were plotted as the standard curve. The final values were expressed as micromole Trolox® equivalent (TE) per gram of sample (μmol TE/g) (Huang *et al.*, 2002).

5.3 2,2-Diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity assay

2,2-Diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity assay was popularly used as the first method to screen the antioxidant property of a crude extract, a compound, or other biological sources. This is due to the speed and simplicity of the method. DPPH radicals are stable. They can delocalize the spare electron over another DPPH molecules. Thus, unlike most other free radicals, they do not bind each other to become dimeric molecule. Moreover, because of the delocalization, their color is deep violet with absorbance at around 517 nm. If DPPH radicals are mixed with a substance which is able to donate a hydrogen atom, they will change to the reduced form and gradually become yellow (Kedare and Singh, 2011).

5.3.1 Materials and instruments

- 2,2-Diphenyl-1-picrylhydrazyl (DPPH) (Sigma-Aldrich)
- 96-well microplate (Corning)
- Microplate reader (CLARIOstar, BMG LABTECH, Germany)
- Ultrasonic bath (Transsonic 570/H, Elma)
- Vortex mixer (Vortex-Genie2, Scientific Industries)

5.3.2 Determination of DPPH radical scavenging activity assay

The DPPH assay was carried out according to Lu *et al*. (Lu *et al.*, 2014). The radical scavenging activity (RSA) was evaluated by the change of color from violet to yellow. A diluted sample at 50 µg/mL or 22 µL of stock solution was added to wells in a 96-well microplate, and 200 µL of 150 µM DPPH in methanol was added to the well subsequently. The microplate was covered and kept in the dark at room temperature for 30 minutes. The absorbance was monitored at wavelength of 517 nm by microplate reader. The result was expressed as percentage of radical scavenging activity (%RSA) calculated by the following formula:

$$\%\text{RSA} = [\frac{(\text{Absorbance of blank} - \text{Absorbance of sample})}{\text{Absorbance of blank}}] \text{ x } 100$$

5.4 Deoxyribose degradation assay

The reaction of the complex of iron and ethylene diamine tetraacetic acid (Fe^{2+}-EDTA) with hydrogen peroxide (H_2O_2) in the presence of ascorbic acid generates the hydroxy radical ($^{\bullet}OH$). Then, this radical attacks deoxyribose to produce malondialdehyde (MDA). The reaction of MDA with thiobarbituric acid (TBA) at low pH and high temperature condition produces a pink chromogen of MDA-TBA adduct. Its absorbance can be measured at 532 nm. If a compound with antioxidant activity interrupts the degradation of deoxyribose by hydroxy radical attack, the absorbance at 532 nm of the pink chromogen will decrease (Halliwell *et al.*, 1987; Cheeseman *et al.*, 1988).

5.4.1 Materials and instruments

- KH_2PO_4 (Merck)
- KOH (Merck)
- Deoxyribose (Sigma-Aldrich)
- Ferric chloride ($FeCl_3$) (Sigma-Aldrich)
- Ethylene diamine tetraacetic acid (EDTA) (Merck)

- Ascorbic acid (Sigma-Aldrich)

- Hydrogen peroxide (H_2O_2) (Merck)

- Thiobarbituric acid (TBA) (Sigma-Aldrich)

- Trichloroacetic Acid (TCA) (Merck)

- 96-well microplate (Corning)

- Microplate reader (CLARIOstar, BMG LABTECH, Germany)

- Ultrasonic bath (Transsonic 570/H, Elma)

- Vortex mixer (Vortex-Genie2, Scientific Industries)

5.4.2 Determination of deoxyribose degradation assay

The reaction mixture contained, in a final volume of 1 mL, the following reagents:

- 200 µL of 100 mM KH_2PO_4/KOH buffer

- 200 µL of 15 mM deoxyribose

- 200 µL of 500 µM $FeCl_3$

- 100 µL of 1 mM EDTA

- 100 µL of 1 mM ascorbic acid

- 100 µL of 10 mM H_2O_2

- 100 µL of diluted sample at concentration 50 µg/mL or diluted Trolox® used as positive control

The mixture was incubated at 37 °C for 1 hour. One mL of 1 %w/v TBA was added to each mixture followed by the addition of 1 mL of 2.8 %w/v TCA. The mixture solution was heated at 90 °C for 20 minutes by water bath to develop the pink color of malondialdehyde–thiobarbituric acid, and the absorbance was measured at 532 nm. The percent of hydroxyl radical scavenging activity of the sample was calculated using the following formula:

$$\%\ \text{Hydroxyl radical scavenging activity} = \left[\frac{(\text{AB} - \text{AS})}{\text{AB}}\right] \text{x } 100$$

where, AB is absorbance of blank, and AS is absorbance of sample

5.5 Intracellular antioxidant activity in cell culture

Cells were simultaneously treated with the test sample and H_2O_2. The antioxidant ability of each test compound was assessed by measuring the reduction of cellular ROS synthesis.

Nonfluorescent DCFH-DA (2′,7′-dichlorofluorescein diacetate) diffuses into cells containing esterase that has the ability to cleave diacetate to form DCFH (2′,7′-dichlorodihydrofluorescein). ROS can oxidize the nonfluorescent DCFH to yield fluorescent DCF (2′,7′-dichlorofluorescein). Therefore, the ROS level in the cell was evaluated by observing fluorescent signal generated from oxidized DCFH-DA (Soh, 2006).

5.5.1 Materials and instruments

- RAW 264.7 murine macrophage cell lines (ATCC TIB71)
- Dulbecco's modified eagle's medium (DMEM) (Invitrogen)
- Heat-inactivated fetal bovine serum (FBS) (Invitrogen)
- Streptomycin (Invitrogen)
- Penicillin (Invitrogen)
- 2′,7′-Dichlorofluorescein diacetate (DCFH-DA) (Sigma-Aldrich)
- Hydrogen peroxide (H_2O_2) (Merck)
- Quercetin (Sigma-Aldrich)
- Black 96-well culture plate (Corning)
- Fluorescence microplate reader (CLARIOstar, BMG LABTECH)
- Incubator (Forma Series II, Thermo Scientific)
- Ultrasonic bath (Transsonic 570/H, Elma)
- Vortex mixer (Vortex-Genie2, Scientific Industries)

5.5.2 Determination of intracellular antioxidant activity in cell culture

For cell culturing, RAW 264.7 cells, which are murine macrophage cells, were cultured in DMEM supplemented with 10% heat-inactivated FBS, 100 µg/mL streptomycin, and penicillin. This study was done at the controlled temperature of 37 °C and humidified atmosphere of 5% CO_2/95% air.

RAW 264.7 cells were plated at 2×10^4 cells/mL in black 96-well culture plates and incubated for 24 hours. Cells were washed with serum-free medium and treated with 50 µg/mL of each compound for 24 hours. Therefrom, the cells were washed and treated with 5 µM of DCFH-DA in serum-free medium for 30 minutes before the addition of 1 mM of H_2O_2 for 30 minutes to induce ROS production. The fluorescence intensity was monitored by using a fluorescence microplate reader with excitation at 485 nm and emission at 530 nm. The ROS production in the cells related to the monitored fluorescence intensity and the %ROS inhibition was calculated using the following formula:

$$\%\text{ROS inhibition} = \left[\frac{\left(\text{Fluorescence}_{Control} - \text{Fluorescence}_{Sample}\right)}{\text{Fluorescence}_{Control}}\right] \text{x } 100$$

In addition, dendroflorin was selected for further evaluation for intracellular antioxidant activity in cell culture, at concentrations which were not toxic to cell (12.5, 25.0, and 50.0 µg/mL), by the above-mentioned procedure.

5.6 Activity of antioxidant enzymes in cell culture

A cellular imbalance between the ROS system and antioxidant levels is known as oxidative stress. Mechanisms of action of several anti-oxidative compounds are related to antioxidant enzymes, namely, superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase (CAT). SOD can convert the superoxide radical into H_2O_2 and O_2 which are less toxic, while CAT can convert H_2O_2 into O_2 and H_2O. In case of GPx, H_2O_2 were converted into H_2O only. In summary, the net result is that the two

potentially harmful species, superoxide radical and H_2O_2, are changed to H_2O by these enzymes (Weydert and Cullen, 2010).

5.6.1 Materials and instruments

- RAW 264.7 murine macrophage cell lines (ATCC TIB71)
- Dulbecco's modified eagle's medium (DMEM) (Invitrogen)
- Heat-inactivated fetal bovine serum (FBS) (Invitrogen)
- Streptomycin (Invitrogen)
- Penicillin (Invitrogen)
- Hydrogen peroxide (H_2O_2) (Merck)
- Lysis buffer (Sigma-Aldrich)
- Quercetin (Sigma-Aldrich)
- SOD, GPx, and CAT cellular activity assay kit (Cayman Chemical)
- Six-well culture plates (Corning)
- Fluorescence microplate reader (CLARIOstar, BMG LABTECH)
- Incubator (Forma Series II, Thermo Scientific)
- Ultrasonic bath (Transsonic 570/H, Elma)
- Vortex mixer (Vortex-Genie2, Scientific Industries)

5.6.2 Determination of effect of dendroflorin on antioxidant enzymes activity in cell culture

Murine macrophage cells (RAW 264.7) were cultured according to the protocol, reagents and conditions previously described in 5.5.2.

RAW 264.7 cells were plated at 1×10^6 cells/mL in six-well culture plates. Cells were incubated at 37 °C in a humidified atmosphere of 5% CO_2/95% air for 24 hours. Cells were washed with serum-free medium (free phenol red) and treated with 12.5, 25.0 and 50.0 µg/mL of dendroflorin for 24 hours. Cellular oxidative stress was induced by adding 1 mM of H_2O_2 for 30 minutes. Treated

and induced cells were resuspended in an ice-cold lysis buffer at 4°C for 30 minutes and centrifuged at 13,500×g at 4°C for 5 minutes to attain cell lysate for evaluation of antioxidant enzyme activities. The SOD, GPx, and CAT activity was monitored by using SOD, GPx, and CAT cellular activity assay kits.

CHAPTER IV
RESULTS AND DISCUSSION

In this research, the methanol extract of the dried and ground whole plants of *Dendrobium palpebrae* (1.7 kg) were suspended in water and partitioned with ethyl acetate (EtOAc) and *n*-butanol, respectively. The EtOAc extract demonstrated the strongest DPPH radical scavenging activity with more than 80% inhibition at a concentration of 100 µg/mL. The EtOAc extract was further separated using several chromatographic techniques to afford ten compounds. The structures of these compounds were characterized using several spectroscopic techniques, including MS and NMR, as follows.

1. Structure determination of isolated compounds

1.1 Structure determination of compound DPB-1

Compound DPB-1 was obtained as an orange amorphous solid. The UV spectrum (**Figure 6**) of DPB-1 displayed absorptions at 221, 258, and 283 nm, and the IR spectrum (**Figure 7**) presented absorption bands for hydroxyl (3433 cm^{-1}), ketone (1731 cm^{-1}), and aromatic (2918 and 1627 cm^{-1}) functionalities. The HR-ESI mass spectrum (**Figure 8**) showed a sodium-adduct molecular ion $[M+Na]^+$ at *m/z* 559.1368 (calculated for $C_{32}H_{24}O_8Na$; 559.1369), suggesting the molecular formula $C_{32}H_{24}O_8$.

The ^1H NMR spectrum of DPB-1 (**Figure 9** and **Table 5**) displayed ten aromatic proton signals between 6.75 and 8.09 ppm and signals of four methoxy groups at δ_H 3.56 (5-OMe), 3.81 (9′-OMe), 3.95 (7-OMe), and 4.13 (4′-OMe).

The ^{13}C-NMR spectrum of this compound (**Figure 10** and **Table 5**) and the HSQC (**Figure 11**) spectral data displayed thirty-two carbon signals, including signals for four methoxy groups at δ_C 55.5 (9′-OMe), 55.7 (5-OMe), 56.2 (7-OMe) and 58.5 (4′-OMe). The other twenty-eight carbon signals could be differentiated into ten methine carbon signals at 99.6 (C-3′), 100.6 (C-8), 101.6 (C-10′), 102.8 (C-6), 115.1 (C-8′), 118.1 (C-6′), 123.3 (C-10), 128.6 (C-7′), 133.0 (C-9) and 136.6 (C-2) and eighteen quaternary carbon

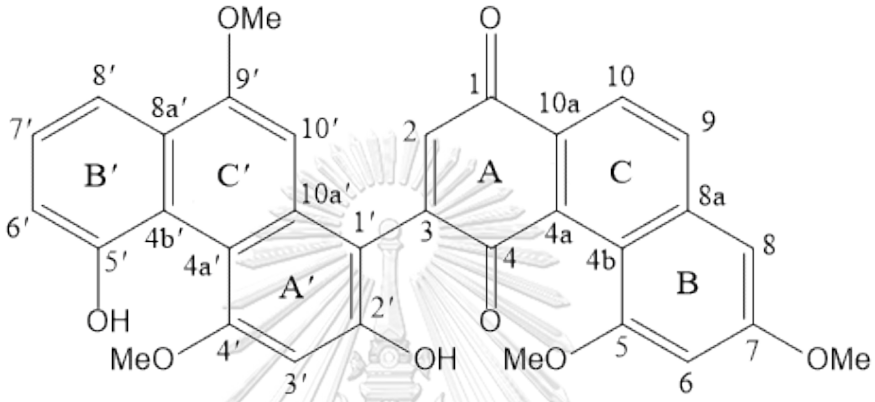
signals at 110.7 (C-4a′), 112.2 (C-1′), 118.1 (C-4b), 121.4 (C-4b′), 129.0 (C-8a′), 131.8 (C-10a), 136.7 (C-4a), 136.8 (C-10a′), 140.9 (C-8a), 151.1 (C-3), 155.1 (C-5′), 155.6 (C-9′), 156.2 (C-2′), 157.6 (C-4′), 159.5 (C-5), 162.9 (C-7), 186.0 (C-1) and 190.1 (C-4). Moreover, two quaternary carbons at δ_C 186.0 (C-1) and 190.1 (C-4) were carbonyl carbon, which is characteristic of a ketone group (δ_C 190-215 ppm) (Hishinuma, *et al.*, 2015). The above spectral data were suggestive of a phenanthrene-phenanthraquinone dimeric structure.

For the phenanthraquinone unit, the following ^{1}H NMR signals appeared: a singlet proton signal at δ_H 6.99 (1H, s, H-2), two pairs of doublet proton signals at δ_H 6.75 (1H, *d*, *J* = 1.7 Hz, H-6), 7.01 (1H, *d*, *J* = 1.7 Hz, H-8), 8.04 (1H, *d*, *J* = 8.6 Hz, H-9), and 8.09 (1H, *d*, *J* = 8.6 Hz, H-10), and two methoxy groups at δ_H 3.56 (3H, *s*, 5-OMe) and 3.95 (3H, *s*, 7-OMe). The phenanthrene unit showed ^{1}H NMR resonances for four aromatic protons and two methoxyls at δ_H 6.75 (1H, *s*, H-10′), 6.88 (1H, *s*, H-3′) 7.18 (1H, *dd*, *J* = 7.8, 1.4 Hz, H-6′), 7.45 (1H, *t*, *J* = 7.8 Hz, H-7′), 7.88 (1H, *dd*, *J* = 7.8, 1.4 Hz, H-8′), 3.81 (3H, *s*, 9′-OMe), and 4.13 (3H, *s*, 4′-OMe). The NMR data of the phenanthrene unit were similar to those of 2,5-dihydroxy-4,9-dimethoxyphenanthrene [**119**] which was previously reported (Leong *et al.*, 1997). However, the ^{1}H NMR spectrum of DPB-1 demonstrated the absence of the doublet proton of H-1′ and the presence of a singlet proton of H-3′ at δ_H 6.88 (1H, *s*), as compared with 2,5-dihydroxy-4,9-dimethoxyphenanthrene [**119**].

The NOESY (**Figure 12**) and HMBC (**Figure 13**) experiments were performed to confirm the proposed structure. The NOESY spectrum displayed interactions of 5-OMe with H-6, 7-OMe with H-6 and H-8, 4′-OMe with H-3′, and 9′-OMe with H-8′ and H-10′. These interactions confirmed the locations of the methoxy groups at C-5, C-7, C-4′, and C-9′, respectively. The locations of H-6, H-8, and H-9 were supported by the NOESY cross-peaks of H-8 and H-9 and their HMBC correlations with C-4b (δ_C 118.1). The assignment of H-2 was confirmed from its HMBC correlations with C-4 (δ_C 190.1) and C-10a (δ_C 131.8). The linkage between C-1′ of the phenanthrene unit and C-3 of the phenanthraquinone unit was deduced from the HMBC correlation between the signals

of H-2 and C-1′. This was corroborated by the absence of H-3 in phenanthraquinone unit and H-1′ in phenanthrene unit of DPB-1.

Based on there spectral data, the structure of DPB-1 was established as shown, and this compound was named dendropalpebrone [**294**].



Dendropalpebrone [**294**]

Table 5 NMR spectral data of compound DPB-1 (in CD_3OD)

Position	δ_H (mult., *J* in Hz)	δ_C	HMBC (correlation with ^1H)
1	-	186.0	10
2	6.99 (*s*)	136.6	-
3	-	151.1	2*
4	-	190.1	2
4a	-	136.7	10
4b	-	118.1	6, 8, 9
5	-	159.5	5-OMe, 6*
6	6.75 (*d*, 1.7)	102.8	8
7	-	162.9	6*, 7-OMe, 8*
8	7.01 (*d*, 1.7)	100.6	6, 9
8a	-	140.9	9*, 10

* Two-bonding coupling

Table 5 NMR spectral data of compound DPB-1 (in CD_3OD) (continued)

Position	δ_H (mult., *J* in Hz)	δ_C	HMBC (correlation with ^1H)
9	8.04 (*d*, 8.6)	133.0	8
10	8.09 (*d*, 8.6)	123.3	-
10a	-	131.8	2, 9
1′	-	112.2	2, 3′, 10′
2′	-	156.2	3′*
3′	6.88 (*s*)	99.6	-
4′	-	157.6	3′*,4′-OMe
4a′	-	110.7	3′, 10′
4b′	-	121.4	6′, 8′
5′	-	155.1	6′*, 7′
6′	7.18 (*dd*, 7.8, 1.4)	118.1	8′
7′	7.45 (*t*, 7.8)	128.6	-
8′	7.88 (*dd*, 7.8, 1.4)	115.1	6′
8a′	-	129.0	7′, 10′
9′	-	155.6	8′, 9′-OMe, 10′*
10′	6.75 (*s*)	101.6	-
10a′	-	136.8	-
5-OMe	3.56 (*s*)	55.7	-
7-OMe	3.95 (*s*)	56.2	-
4′-OMe	4.13 (*s*)	58.5	-
9′-OMe	3.81 (*s*)	55.6	-

* Two-bonding coupling

1.2 Structure determination of compound DPB-2

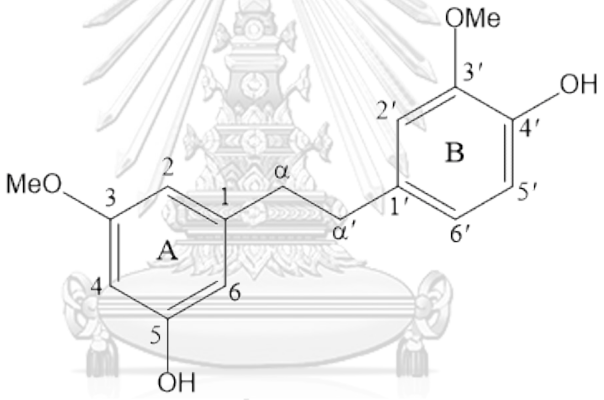
Compound DPB-2 was obtained as a brown amorphous solid. The HR-ESI mass spectrum (**Figure 14**) showed a sodium-adduct molecular ion $[M+Na]^+$ at *m/z* 297.1111 (calculated for $C_{16}H_{18}O_4Na$; 297.1103), suggesting the molecular formula $C_{16}H_{18}O_4$.

The ^1H NMR spectrum of compound DPB-2 (**Figure 15** and **Table 6**) indicated the presence of four methylene proton signals at δ_H 2.80 (4H, *m*, H_2-α, H_2-α'). The ^1H NMR data also displayed six aromatic proton signals at δ_H 6.28 (1H, *t*, *J* = 2.1 Hz, H-2), 6.31 (1H, *t*, *J* = 2.1 Hz, H-4), 6.35 (1H, *t*, *J* = 2.1 Hz, H-6), 6.67 (1H, *dd*, *J* = 8.1, 1.5 Hz, H-6′), 6.76 (1H, *d*, *J* = 8.1 Hz, H-5′), and 6.81 (1H, *d*, *J* = 1.5 Hz, H-2′), together with two methoxy signals at δ_H 3.71 (3H, *s*, 3-OMe) and 3.79 (3H, *s*, 3′-OMe).

The ^{13}C NMR data (**Figure 16** and **Table 6**) demonstrated sixteen carbon signals, including two methoxyl carbons at δ_C 54.5 (C-3-OMe) and 55.3 (C-3′-OMe), two methylene carbons at δ_C 37.1 (C-α') and 38.2 (C-α), six methine carbons at δ_C 98.9 (C-4), 105.5 (C-6), 108.1 (C-2), 112.1 (C-5′), 114.7 (C-2′) and 120.8 (C-6′), and six quaternary carbons at δ_C 133.3 (C-1′), 144.4 (C-4′), 144.6 (C-1), 147.2 (C-3′), 158.4 (C-3) and 161.0 (C-5). These NMR data suggested that DPB-2 was a bibenzyl compound. The locations of methoxy groups were assigned at C-3′ and C-3 according to the NOESY interactions (**Figure 17**) of 3′-OMe with H-2′, and 3-OMe with H-2 and H-4, respectively.

Through comparison of ^1H and ^{13}C NMR data of this compound with previously reported values (Klongkumnuankarn *et al.*, 2015), compound DPB-2 was identified as gigantol [**30**]. Gigantol [**30**] is a bibenzyl which is a major constituent frequently discovered in several species in the genus *Dendrobium*, for instance, *D. aphyllum* (Chen *et al.*, 2008c), *D. aurantiacum* var. *denneanum* (Liu *et al.*, 2009a), *D. brymerianum* (Klongkumnuankarn *et al.*, 2015), *D. densiflorum* (Fan *et al.*, 2001), *D. devonianum* (Sun *et al.*, 2014), *D. draconis* (Sritularak *et al.*, 2011a), *D. gratiosissimum* (Zhang *et al.*, 2008a), *D. formosum* (Inthongkaew *et al.*, 2017), *D. loddigesii* (Ito *et al.*, 2010), *D. longicornu* (Hu *et al.*, 2008a), *D. nobile* (Zhang *et al.*, 2007a), *D. officinale* (Zhao *et al.*, 2018), *D. polyanthum* (Hu *et al.*, 2009), *D. trigonopus* (Hu *et al.*, 2008b), *D. venustum* (Sukphan *et al.*, 2014), and *D. wardianum* (Zhang *et al.*, 2017).

Furthermore, gigantol [**30**] was previously reported that it had many pharmacological activities including appreciable DPPH radical scavenging activity (Sritularak *et al.*, 2011a), antiplatelet aggregation activity (Fan *et al.*, 2001), potent α-glucosidase inhibitory activity (Sun *et al.*, 2014), antimigratory of lung cancer cells activity in a time-dependent manner (Klongkumnuankarn *et al.*, 2015), moderate antimalarial activity and weak anti-herpetic activity (Sukphan *et al.*, 2014). It also exhibited appreciable cytotoxic activity against human lung cancer H460 cells (Klongkumnuankarn *et al.*, 2015), human leukemic promyelocytic HL-60 cells (Zhang *et al.*, 2008a), human acute monocytic leukemia THP-1 cells (Zhao *et al.*, 2018).



Gigantol [**30**]

Table 6 NMR spectral data of compound DPB-2 and gigantol (in acetone-d_6)

Position	Compound DPB-2		Gigantol[a]	
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
1	-	144.6	-	145.4
2	6.28 (*t*, 2.1)	108.1	6.22 (*t*, 2.0)	108.8
3	-	158.4	-	159.1
4	6.31 (*t*, 2.1)	98.9	6.28 (*t*, 2.0)	99.6
5	-	161.0	-	161.7
6	6.35 (*t*, 2.1)	105.5	6.30 (*t*, 2.0)	106.2
1′	-	133.3	-	134.0
2′	6.81 (*d*, 1.5)	114.7	6.79 (*d*, 1.5)	115.4
3′	-	147.2	-	147.9
4′	-	144.4	-	145.1
5′	6.76 (*d*, 8.1)	112.1	6.69 (*d*, 8.0)	112.8
6′	6.67 (*dd*, 8.1, 1.5)	120.8	6.64 (*dd*, 8.0, 1.5)	121.5
α	2.80 (*m*)	38.2	2.78 (*m*)	39.0
α′	2.80 (*m*)	37.1	2.78 (*m*)	37.9
3-OMe	3.71 (*s*)	55.3	3.78 (*s*)	55.2
3′-OMe	3.79 (*s*)	54.5	3.69 (*s*)	56.0

[a] Klongkumnuankarn *et al.*, 2015

1.3 Structure determination of compound DPB-3

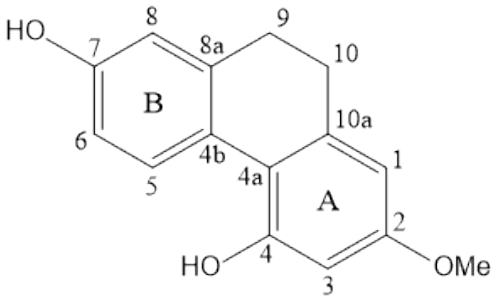
Compound DPB-3 was obtained as a brown amorphous solid. The HR-ESI mass spectrum (**Figure 18**) showed a sodium-adduct molecular ion $[M+Na]^+$ at *m/z* 265.0845 (calculated for $C_{15}H_{14}O_3Na$; 265.0841), suggesting the molecular formula $C_{15}H_{14}O_3$.

The ^{1}H-NMR spectrum of compound DPB-3 (**Figure 19** and **Table 7**) exhibited five aromatic proton signals at δ_H 6.37 (1H, *d*, *J* = 2.1 Hz, H-1), 6.44 (1H, *d*, *J* = 2.1 Hz, H-3), 6.69 (1H, *dd*, *J* = 9.3, 2.7 Hz, H-6), 6.71 (1H, *d*, *J* = 2.7 Hz, H-8), and 8.22 (1H, *d*, *J* = 9.3 Hz, H-5), together with a methoxy signal at δ_H 3.74 (3H, *s*, 2-OMe). Additional NMR signals were observed for two methylene groups at δ_H 2.68 (4H, *s*, H_2-9, H_2-10).

The ^{13}C-NMR and DEPT 135° (**Figure 20** and **Table 7**) spectra presented fifteen carbon signals, corresponding to one methoxy carbon, five aromatic methine carbons, two methylene carbons, and seven quaternary carbons. The appearance of the methylene proton signals at δ_H 2.68 (4H, *s*, H_2-9, H_2-10), which showed HSQC correlations (**Figure 21**) to two carbon signals at δ_C 29.9 (C-9), 30.6 (C-10), indicated a dihydrophenanthrene skeleton. Therefore, the structure of DPB-3 should be a dihydrophenanthrene with a methoxyl and two hydroxyl substitutions.

On ring B, the proton signal at δ_H 8.22 (1H, *d*, *J* = 9.3 Hz, H-5) showed a NOESY interaction (**Figure 22**) with the proton at δ_H 6.69 (1H, *dd*, *J* = 9.3, 2.7 Hz, H-6). The H-1 assignment was obtained from its NOESY interaction with protons at C-10 and C-2-OMe. Moreover, the position of H-8 was assigned from its NOESY interaction with protons at C-9. The position of 2-OMe was confirmed by its NOESY interaction with H-1 and H-3. Moreover, the HMBC correlation (**Figure 23**) from 2-OMe to C-2 supported the location of a methoxy group at C-2.

On the basis of these ^{1}H and ^{13}C NMR data, compound DPB-3 was identified as lusianthridin [**103**] which was previously reported from *Pholidota yunnanensis*, a plant in the family Orchidaceae (Guo *et al.*, 2007). Furthermore, lusianthridin has also been found in *Dendrobium* species such as *D. brymerianum* (Klongkumnuankarn *et al.*, 2015), *D. venustum* (Sukphan *et al.*, 2014), and *D. formosum* (Inthongkaew *et al.*, 2017).



Lusianthridin [**103**]

Table 7 NMR spectral data of compound DPB-3 and lusianthridin (in acetone-d_6)

Position	Compound DPB-3		Lusianthridin[a]	
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
1	6.37 (*d*, 2.1)	105.0	6.37 (*d*, 2.6)	106.0
2	-	158.4	-	159.3
3	6.44 (*d*, 2.1)	100.7	6.44 (*d*, 2.6)	101.6
4	-	155.1	-	155.9
4a	-	114.9	-	115.9
4b	-	125.0	-	125.9
5	8.22 (*d*, 9.3)	129.0	8.22 (*d*, 7.5)	129.9
6	6.69 (*dd*, 2.7, 9.3)	112.6	6.68 (*dd*, 2.7, 7.5)	113.5
7	-	155.2	-	156.1
8	6.71 (*d*, 2.7)	114.1	6.69 (*m*)	115.0
8a	-	138.9	-	139.8
9	2.68 (*s*)	29.9	2.67 (*m*)	30.8
10	2.68 (*s*)	30.6	2.67 (*m*)	31.5
10a	-	140.5	-	141.4
2-OMe	3.74 (*s*)	54.4	3.74 (*s*)	55.3

[a] Guo *et al.*, 2007

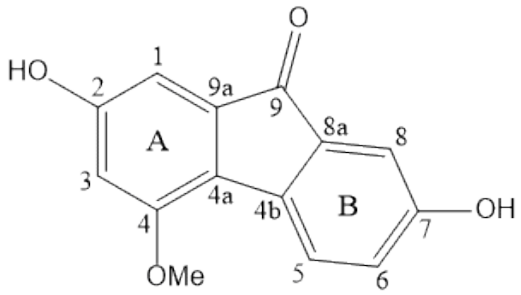
1.4 Structure determination of compound DPB-4

Compound DPB-4 was obtained as a red amorphous solid. The HR-ESI mass spectrum (**Figure 24**) demonstrated a sodium-adduct molecular ion $[M+Na]^+$ at *m/z* 265.0479 (calculated for $C_{14}H_{10}O_4Na$; 265.0477), and its molecular formula was determined as $C_{14}H_{10}O_4$.

The ^{1}H-NMR spectrum of compound DPB-4 (**Figure 25** and **Table 8**) exhibited signals for a methoxy proton at δ_H 4.15 (3H, *s*, 4-OMe), and five aromatic protons at δ_H 6.80 (1H, *d*, *J* = 2.1 Hz, H-3), 6.82 (1H, *d*, *J* = 2.1 Hz, H-1), 6.96 (1H, *dd*, *J* = 7.2, 1.8 Hz, H-6), 7.12 (1H, *d*, *J* = 1.8 Hz, H-8), and 7.16 (1H, *d*, *J* = 7.2 Hz, H-5). In the ^{13}C-NMR spectrum (**Figure 26** and **Table 8**), fourteen carbon signals were observed, including those of a methoxyl, five aromatic methines, seven aromatic quaternary carbons and a carbonyl carbon at δ_C 192.4 (C-9), which is characteristic of a ketone group (δ_C 190-215 ppm) (Hishinuma, *et al.*, 2015). The HSQC data (**Figure 27**) confirmed the presence of protons at C-1, C-3, C-5, C-6, and C-8.

The assignment of substitutions on ring A started with the proton at C-1, which was confirmed by HMBC correlation (**Figure 28**) between the signal of C-9 (ketone group) and H-1. Secondly, *meta*-coupling constant of H-1 doublet led to the assignment of the coupled proton at H-3. Thirdly, the NOESY experiment (**Figure 29**) illustrated correlations of 4-OMe with H-3, therefore a methoxy group could be located at C-4. For the assignment of protons on ring B, the proton at C-8 could be deduced by the HMBC cross-peak between C-4b and this proton signal. Then, *meta*-coupling constant of H-6/H-8 supported the assignment of H-6, which, in turn, *ortho*-coupled to H-5.

From the above data, and through comparison of its ^{1}H-NMR and ^{13}C-NMR spectra with previously reported data (Klongkumnuankarn *et al.*, 2015), compound DPB-4 was identified as the fluorenone nobilone [**285**]. Nobilone has been found in several of *Dendrobium* species, for example, *D. brymerianum* (Klongkumnuankarn *et al.*, 2015), and *D. nobile* (Zhang *et al.*, 2007a).



Nobilone [**285**]

Table 8 NMR spectral data of compound DPB-4 and nobilone (in acetone-d_6)

Position	Compound DPB-4		Nobilone[a]	
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
1	6.82 (*d*, 2.1)	105.1	6.80 (*d*, 2.0)	105.9
2	-	160.1	-	160.9
3	6.80 (*d*, 2.1)	105.4	6.78 (*d*, 2.0)	106.2
4	-	152.7	-	153.5
4a	-	121.7	-	122.6
4b	-	127.1	-	128.0
5	7.16 (*d*, 7.2)	129.3	7.13 (*d*, 7.5)	130.2
6	6.96 (*dd*, 1.8, 7.2)	124.2	6.93 (*dd*, 1.5, 7.5)	125.0
7	-	150.8	-	151.6
8	7.12 (*d*, 1.8)	115.9	7.10 (*d*, 1.5)	116.7
8a	-	135.0	-	135.8
9	-	192.4	-	193.2
9a	-	136.4	-	137.2
4-OMe	4.15 (*s*)	56.7	4.13 (*s*)	57.5

[a] Klongkumnuankarn *et al.*, 2015

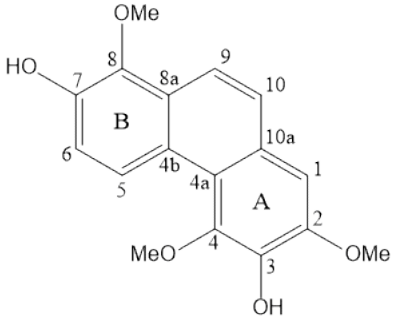
1.5 Structure determination of compound DPB-5

Compound DPB-5 was obtained as pale-yellow crystals. The HR-ESI mass spectrum (**Figure 30**) showed a sodium-adduct molecular ion $[M+Na]^+$ at *m/z* 323.0896 (calculated for $C_{17}H_{16}O_5Na$; 323.0895), suggesting the molecular formula $C_{17}H_{16}O_5$.

The ^{1}H-NMR spectrum of DPB-5 (**Figure 31** and **Table 9**) showed the presence of a singlet aromatic proton at δ_H 7.26 (1H, *s*, H-1), along with two pairs of *ortho*-coupled aromatic protons at δ_H 7.25 (1H, *d*, *J* = 9.3 Hz, H-6) with 9.17 (1H, *d*, *J* = 9.3 Hz, H-5) and δ_H 7.68 (1H, *d*, *J* = 9.0 Hz, H-10) with 7.86 (1H, *d*, *J* = 9.0 Hz, H-9). Besides, the ^{13}C-NMR (**Figure 32** and **Table 9**) and HSQC (**Figure 33**) spectral exhibited three signals representing three methoxy groups at δ_C 55.4, 58.7 and 60.4 ppm.

The assignment of the singlet proton at C-1 on ring A was based on the NOESY cross peak (**Figure 34**) between δ_H 7.26 (H-1) and δ_H 7.68 (H-10), together with the HMBC correlation (**Figure 35**) from δ_C 127.2 (C-10) to this proton signal. The locations of the methoxy groups were also confirmed from NOESY interactions. The NOESY cross peaks were observed for the following pairs of protons: H-1 (δ_H 7.26) and 2-OMe (δ_H 3.92), H-5 (δ_H 9.17) and 4-OMe (δ_H 3.94), and H-9 (δ_H 7.86) and 8-OMe (δ_H 4.00).

On the basis of there spectral evidence and through comparison of its NMR and MS data with previously reported data (Tuchinda *et al.*, 1988; Majumder and Sen, 1991), DPB-5 was identified as 3,7-dihydroxy-2,4,8-trimethoxyphenanthrene [**80**] (another reported name: 1,5,7-trimethoxyphenanthrene-2,6-diol). This compound has been earlier reported from *Dendrobium densiflorum* (Fan *et al.*, 2001). It has also been identified from other plants in the family Orchidaceae, for example, *Eulophia nuda* (Tuchinda *et al.*, 1988) and *Cymbidium pendulum* (Majumder and Sen, 1991).



3,7-dihydroxy-2,4,8-trimethoxyphenanthrene [**80**]

Table 9 NMR spectral data of compound DPB-5 (in acetone-d_6) and 3,7-dihydroxy-2,4,8-trimethoxyphenanthrene (in $CDCl_3$)

Position	Compound DPB-5		3,7-Dihydroxy-2,4,8-trimethoxyphenanthrene	
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)[a]	δ_C[b]
1	7.26 (*s*)	105.0	7.25 (*s*)	104.8
2	-	147.7	-	146.8
3	-	140.3	-	139.3
4	-	144.5	-	144.0
4a	-	119.2	-	119.2
4b	-	123.8	-	124.2
5	9.17 (*d*, 9.3)	123.3	9.16 (*dd*, 0.8, 9.3)	123.9
6	7.25 (*d*, 9.3)	117.0	7.24 (*d*, 9.3)	116.0
7	-	146.4	-	145.5
8	-	141.2	-	140.8
8a	-	127.5	-	126.5
9	7.86 (*d*, 9.0)	117.7	7.85 (*dd*, 0.8, 9.2)	117.8
10	7.68 (*d*, 9.0)	127.2	7.67 (*d*, 9.2)	127.3
10a	-	125.4	-	125.6
2-OMe	3.92 (*s*)	55.4	3.92 (*s*)	56.0
4-OMe	3.94 (*s*)	58.7	3.93 (*s*)	59.6
8-OMe	4.00 (*s*)	60.4	4.00 (*s*)	61.7

[a] Tuchinda *et al.*, 1988

[b] Majumder and Sen, 1991

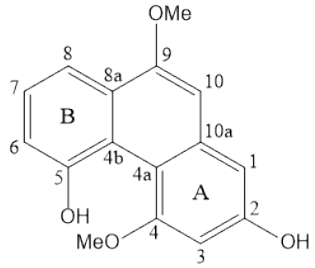
1.6 Structure determination of compound DPB-6

Compound DPB-6 was obtained as a light-yellow powder. The HR-ESI mass spectrum (**Figure 36**) showed a sodium-adduct molecular ion $[M+Na]^+$ at *m/z* 293.0791 (calculated for $C_{16}H_{14}O_4Na$; 293.0790), suggesting the molecular formula $C_{16}H_{14}O_4$.

The ^{1}H-NMR and ^{13}C-NMR spectra of compound DPB-6 (**Figure 37** and **38** and **Table 10**) revealed signals which were suggestive of a phenanthrene skeleton, and were similar to those of DPB-5. The ^{1}H-NMR spectrum of DPB-6 showed a singlet at δ_H 6.93 (1H, *s*, H-10), two *meta*-coupled doublets at δ_H 6.81 (1H, *d*, *J* = 2.4 Hz, H-3) and 6.99 (1H, *d*, *J* = 2.4 Hz, H-1), a triplet at δ_H 7.43 (1H, *t*, *J* = 8.1 Hz, H-7), and two double doublets at δ_H 7.11 (1H, *dd*, *J* = 8.1, 1.2 Hz, H-6) and 7.85 (1H, *dd*, *J* = 8.1, 1.2 Hz, H-8). The HSQC data (**Figure 39**) supported the presence of protons at C-1, C-3, C-6, C-7, C-8, and C-10.

The positions of the aromatic protons and methoxyl groups were deduced from NOESY correlations (**Figure 40**), together with HMBC correlations (**Figure 41**). At the beginning on ring A, the position of H-1 was confirmed by the HBMC correlation of δ_H 6.99 (H-1) and δ_C 101.9 (H-10). The *meta*-coupling peak of H-1 led to placing of proton at C-3. The NOSEY correlations from δ_H 6.81 (H-3) to δ_H 4.11 (4-OMe), and from δ_H 6.93 (H-10) to δ_H 4.03 (9-OMe) supported the locations of the methoxyl groups at C-4 and C-9, respectively. Then, the HMBC correlations from δ_C 154.1 (C-9) to δ_H 4.03 (9-OMe), 6.93 (H-10), and 7.85 (H-8) were used to assign the proton at C-8. Then, the location of protons at C-6 and C-7 were deduced by their coupling patterns displayed at δ_H 7.11 (H-6), 7.43 (H-7), and 7.85 (H-8).

From the above data and through comparison with previously reported data (Leong *et al.*, 1997), DPB-6 was identified as 2,5-dihydroxy-4,9-dimethoxyphenanthrene [**119**]. It was earlier isolated from the stems of *Dendrobium nobile* (Zhang *et al.*, 2008b). Previously, it was found in another orchid, *Bulbophyllum vaginatum* (Leong *et al.*, 1997).



2,5-dihydroxy-4,9-dimethoxyphenanthrene [**119**]

Table 10 NMR spectral data of compound DPB-6 (in acetone-d_6) and 2,5-dihydroxy-4,9-dimethoxyphenanthrene (in $CDCl_3$)

Position	Compound DPB-6		2,5-Dihydroxy-4,9-dimethoxyphenanthrene[a]	
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
1	6.99 (*d*, 2.4)	106.1	6.88 (*d*, 2.6)	106.3
2	-	156.7	-	154.3
3	6.81 (*d*, 2.4)	99.4	6.69 (*d*, 2.6)	99.4
4	-	155.4	-	155.4
4a	-	109.1	-	110.5
4b	-	120.1	-	119.9
5	-	154.3	-	153.8
6	7.11 (*dd*, 1.2, 8.1)	116.7	7.25 (*dd*, 1.5, 7.9)	117.3
7	7.43 (*t*, 8.1)	126.2	7.50 (*t*, 7.9)	126.9
8	7.85 (*dd*, 1.2, 8.1)	113.5	7.94 (*dd*, 1.5, 7.9)	114.1
8a	-	128.3	-	128.5
9	-	154.1	-	154.6
10	6.93 (*s*)	101.9	6.73 (*s*)	101.5
10a	-	136.9	-	136.8
4-OMe	4.11 (*s*)	57.6	4.06 (*s*)	58.3
9-OMe	4.03 (*s*)	55.1	4.04 (*s*)	55.5

[a] Leong *et al.*, 1997

1.7 Structure determination of compound DPB-7

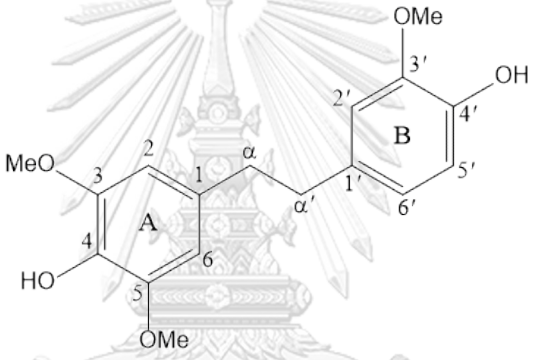
Compound DPB-7 was obtained as a brown amorphous solid. The HR-ESI mass spectrum (**Figure 42**) showed a sodium-adduct molecular ion $[M+Na]^+$ at *m/z* 327.1219 (calculated for $C_{17}H_{20}O_5Na$; 327.1208), suggesting the molecular formula $C_{17}H_{20}O_5$.

The ^{1}H-NMR spectrum of DPB-7 (**Figure 43** and **Table 11**) showed characteristics of a bibenzyl skeleton, it similar to the spectrum of compound DPB-2. The differences were on ring A, showing the presence of another methoxy group at C-5, and a hydroxyl group at C-4, making ring A of DPB-7 symmetrically substituted. This was confirmed by the ^{1}H-NMR signals of this ring which displayed a two-protons singlet at δ_H 6.38 (H-2/H-6), instead of three *meta*-coupled triplets (of H-2, H-4 and H-6) as observed in DPB-2.

The ^{13}C NMR (**Figure 44** and **Table 11**) and HSQC (**Figure 45**) spectra displayed seventeen carbon signals, including five methine carbons at δ_C 105.2 (C-2), 105.2 (C-6), 111.3 (C-2′), 114.2 (C-5′) and 121.1 (C-6′), seven quaternary carbons at δ_C 132.9 (C-1), 132.9 (C-4), 133.7 (C-1′), 143.8 (C-4′), 146.3 (C-3′), 146.9 (C-3) and 146.9 (C-5)), two methylene carbons δ_C 37.9 (C-α) and 38.5 (C-α'), and three methoxy carbons δ_C 56.3 (C-3-OMe,C-5-OMe) and 55.9 (C-3′-OMe). The positions of these methoxyl groups were deduced from the NOESY (**Figure 46**) and HMBC (**Figure 47**) correlations.

Through comparison of the ^{1}H, ^{13}C-NMR and MS data of this compound with reported values (Majumder and Sen, 1987), DPB-7 was identified as moscatilin [**35**]. Moscatilin [**35**] is a major compound isolated from several *Dendrobium* species, for example, *D. amoenum* (Majumder *et al.*, 1999), *D. aurantiacum* var. *denneanum* (Yang *et al.*, 2006a), *D. brymerianum* (Klongkumnuankarn *et al.*, 2015), *D. chrysanthum* (Yang *et al.*, 2006b), *D. densiflorum* (Fan *et al.*, 2001), *D. ellipsophyllum* (Tanagornmeatar *et al.*, 2014), *D. formosum* (Inthongkaew *et al.*, 2017), *D. gratiosissimum* (Zhang *et al.*, 2008a), *D. loddigesii* (Chen *et al.*, 1994), *D. longicornu* (Hu *et al.*, 2008a), *D. moscatum* (Majumder and Sen, 1987), *D. nobile* (Miyazawa *et al.*, 1999), *D. polyanthum* (Hu *et al.*, 2009), *D. pulchellum* (Chanvorachote *et al.*, 2013), *D. secundum* (Sritularak *et al.*, 2011b), *D. wardianum* (Zhang *et al.*, 2017), and *D. williamsonii* (Yang *et al.*, 2017a).

In addition, moscatilin [**35**] was previously evaluated for several pharmacological activities, for example, antiplatelet DPPH radical scarvenging activity (Sritularak *et al.*, 2011b), aggregation activity (Chen *et al.*, 1994; Fan *et al.*, 2001), antimutagenic activity (Miyazawa *et al.*, 1999). It also showed various activities against many types of cancer cell lines including cytotoxic and antimigratory activities in human lung cancer H460 cells (Klongkumnuankarn *et al.*, 2015), cytotoxic and anoikis sensitizing activities in human lung cancer H23 cells (Chanvorachote *et al.*, 2013), and cytotoxic activity in human leukemia HL-60 cells (Zhang *et al.*, 2008a; Yang *et al.*, 2017a).



Moscatilin [**35**]

Table 11 NMR spectral data of compound DPB-7 (in acetone-d_6) and moscatilin (in $CDCl_3$)

Position	Compound DPB-7		Moscatilin[a]	
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
1	-	132.9	-	132.8
2	6.38 (*s*)	105.2	6.30 (*s*)	105.2
3	-	146.9	-	146.8
4	-	132.9	-	133.53
5	-	146.9	-	146.8
6	6.38 (*s*)	105.2	6.30 (*s*)	105.2
1′	-	133.7	-	132.8
2′	6.64 (*d*, 2.0)	111.3	6.60 (*d*, 2.0)	111.2
3′	-	146.3	-	146.1
4′	-	143.8	-	143.7
5′	6.86 (*d*, 8.0)	114.2	6.77 (*d*, 8.0)	114.1
6′	6.70 (*dd*, 2.0, 8.0)	121.1	6.74 (*dd*, 2.0, 8.0)	121.0
α	2.84 (*s*)	38.5	2.79 (*s*)	38.3
α′	2.84 (*s*)	37.9	2.79 (*s*)	37.8
3-OMe	3.86 (*s*)	56.3	3.81 (*s*)	56.2
5-OMe	3.86 (*s*)	56.3	3.81 (*s*)	56.2
3′-OMe	3.85 (*s*)	55.9	3.81 (*s*)	55.8

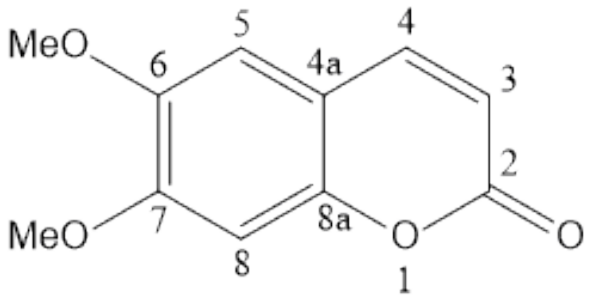
[a] Majumder and Sen, 1987

1.8 Structure determination of compound DPB-8

Compound DPB-8 was obtained as colorless needles. The HR-ESI mass spectrum (**Figure 48**) showed a sodium-adduct molecular ion $[M+Na]^+$ at *m/z* 229.0470 (calculated for $C_{11}H_{10}O_4Na$; 229.0477), suggesting the molecular formula $C_{11}H_{10}O_4$.

The ^1H NMR spectrum of compound DPB-8 (**Figure 49** and **Table 12**) showed signals largely different from those of the other compounds isolated from *D. palpebrae*. This suggested that compound DPB-8 should not have a bibenzyl, phenanthrene, dihydrophenanthrene or fluorenone structure. The ^1H NMR spectrum illustrated signals for six methoxy protons at δ_H 3.92 (3H, *s*, 6-OMe) and 3.94 (3H, *s*, 7-OMe), and four aromatic protons at δ_H 6.27 (1H, *d*, *J* = 9.6 Hz, H-3), 6.82 (1H, *s*, H-8), 6.86 (1H, *s*, H-5) and 7.64 (1H, *d*, *J* = 9.6 Hz, H-4). Furthermore, in the ^{13}C-NMR and HSQC spectra (**Figures 50-51** and **Table 12**), eleven carbon signals were detected, comprising two methoxyl carbons, four aromatic methines, four quaternary carbons, and an ester carbonyl carbon which resonated at δ_C 161.4 (C-2). The HMBC correlations (**Figure 52**) supported the placement of the methoxyl groups at C-6 and C-7.

Based on the above ^1H NMR, ^{13}C NMR, HMBC and MS data, DPB-8 should be a coumarin substituted with two methoxy groups. It was identified as scoparone [**261**] (Fan *et al.*, 2001). This compound has been isolated from many *Dendrobium* species such as *D. densiflorum* (Fan *et al.*, 2001), *D. thyrsiflorum* (Zhang *et al.*, 2005), and *D. williamsonii* (Yang *et al.*, 2017a).



Scoparone [**261**]

Table 12 NMR spectral data of compound DPB-8 and scoparone (in $CDCl_3$)

Position	Compound DPB-8		Scoparone[a]	
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
2	-	161.4	-	161.4
3	6.27 (*d*, 9.6)	113.5	6.28 (*d*, 9.5)	113.5
4	7.64 (*d*, 9.6)	143.3	7.63 (*d*, 9.5)	143.3
4a	-	111.4	-	111.4
5	6.86 (*s*)	108.0	6.87 (*s*)	108.0
6	-	146.3	-	146.3
7	-	152.8	-	152.8
8	6.82 (*s*)	100.0	6.84 (*s*)	99.9
8a	-	150.0	-	150.0
6-OMe	3.92 (*s*)	56.4	3.92 (*s*)	56.3
7-OMe	3.94 (*s*)	56.4	3.95 (*s*)	56.4

[a] Jerezano *et al.*, 2011

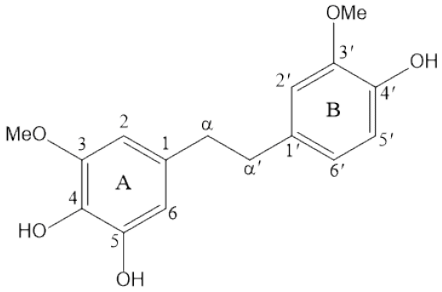
1.9 Structure determination of compound DPB-9

Compound DPB-9 was obtained as a brown amorphous solid. The HR-ESI mass spectrum (**Figure 53**) showed a sodium-adduct molecular ion $[M+Na]^+$ at *m/z* 313.1060 (calculated for $C_{16}H_{18}O_5Na$; 313.1052), suggesting the molecular formula $C_{16}H_{18}O_5$.

The ^{1}H-NMR spectrum of compound DPB-9 (**Figure 54** and **Table 13**) revealed signals for four methylene protons at δ_H 2.73 (2H, *m*, H_2-α) and 2.76 (2H, *m*, H_2-α'), and two methoxyl singlet peaks at δ_H 3.75 (3H, *s*, 3-OMe) and 3.79 (3H, *s*, 3′-OMe). In the aromatic region, the ^{1}H NMR spectrum displayed two *meta*-coupled doublets of ring A at δ_H 6.34 (1H, *d*, *J* = 1.8 Hz, H-2) and 6.36 (1H, *d*, *J* = 1.8 Hz, H-6). In the part of ring B, three signals of a 1,3,4- trisubstituted aromatic ring at δ_H 6.65 (1H, *dd*, *J* = 1.8, 8.1 Hz, H-6′), 6.71 (1H, *dd*, *J* = 8.1 Hz, H-5′), and 6.79 (1H, *dd*, *J* = 1.8 Hz, H-2′) could be observed.

The ^{13}C-NMR and HSQC spectra (**Figures 55** and **56** and **Table 13**) showed sixteen carbon signals, corresponding to two methoxyls at δ_C 55.3 (C-3′) and 55.5 (C-3), two aliphatic methylenes at 37.6 (C-α') and 38.0 (C-α). Other aromatic carbon signals could be separated into those of five methine carbons at δ_C 103.7 (C-2), 108.9 (C-6), 112.1 (C-2′), 114.6 (C-5′), 120.8 (C-6′), and seven quaternary carbons at δ_C 131.8 (C-1), 132.9 (C-4), 133.4 (C-1′), 144.7 (C-4′), 145.2 (C-5), 147.2 (C-3′), and 147.9 (C-3). The locations of the methoxy groups were assigned by the NOESY (**Figure 57**) and HMBC spectra (**Figure 58**). The first methoxy group at δ_H 3.75 could be located at C-3 according to its NOESY correlation with H-2 and HMBC correlation from 3-OMe to C-3. The other methoxy group at δ_H 3.79 was placed at C-3′ based on its NOESY interaction with H-2′, together with the HMBC correlation from 3′-OMe to C-3′.

Through analysis of there spectroscopic data and comparison with previously reported values (Sritularak *et al.*, 2011b), DPB-9 was identified as 4,5,4′-trihydroxy-3,3′-dimethoxybibenzyl [**40**]. The presence of this bibenzyl in *Dendrobium* species has been previously reported from *D. secundum* (Sritularak *et al.*, 2011b; Phechrmeekha *et al.*, 2012), and *D. ellipsophyllum* (Tanagornmeatar *et al.*, 2014).



4,5,4′-trihydroxy-3,3′-dimethoxybibenzyl [**40**]

Table 13 NMR spectral data of compound DPB-9 (in acetone-d_6) and 4,5,4′-trihydroxy-3,3′-dimethoxybibenzyl (in $CDCl_3$)

Position	Compound DPB-9		4,5,4′-Trihydroxy-3,3′-dimethoxybibenzyl[a]	
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
1	-	131.8	-	130.4
2	6.34 (*d*, 1.8)	103.7	6.21 (*d*, 2.0)	103.5
3	-	147.9	-	146.6
4	-	132.9	-	133.7
5	-	145.2	-	143.7
6	6.36 (*d*, 1.8)	108.9	6.42 (*d*, 2.0)	108.6
1′	-	133.4	-	133.8
2′	6.79 (*d*, 1.8)	112.1	6.60 (*d*, 2.0)	111.2
3′	-	147.2	-	146.2
4′	-	144.7	-	143.7
5′	6.71 (*d*, 8.1)	114.6	6.80 (*d*, 8.0)	114.1
6′	6.65 (*dd*, 1.8, 8.1)	120.8	6.65 (*dd*, 2.0, 8.0)	121.0
α	2.73 (*m*)	38.0	2.75 (*m*)	38.7
α′	2.76 (*m*)	37.6	2.78 (*m*)	37.7
3-OMe	3.75 (*s*)	55.5	3.80 (*s*)	56.1
3′-OMe	3.79 (*s*)	55.3	3.83 (*s*)	55.9

[a] Sritularak *et al.*, 2011b

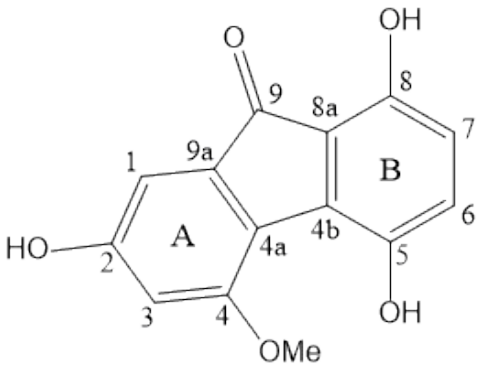
1.10 Structure determination of compound DPB-10

Compound DPB-10 was obtained as a red amorphous solid. The HR-ESI mass spectrum (**Figure 59**) showed a sodium-adduct molecular ion $[M+Na]^+$ at *m/z* 281.0417 (calculated for $C_{14}H_{10}O_5Na$; 281.0426), suggesting the molecular formula $C_{14}H_{10}O_5$.

The ^1H NMR spectrum (**Figure 60** and **Table 14**) revealed signals for four aromatic protons at δ_H 6.59 (1H, *d*, *J* = 9.0 Hz, H-7), 6.77 (1H, *d*, *J* = 1.5 Hz, H-3), 6.79 (1H, *d*, *J* = 1.5 Hz, H-1), and 6.86 (1H, *d*, *J* = 9.0 Hz, H-6). The ^1H-NMR spectrum also showed methoxyl protons at δ_H 4.10 (3H, *s*, 4-OMe). In addition, the ^{13}C NMR and HSQC spectra (**Figures 61-62** and **Table 14**) exhibited fourteen carbon signals, consisting of one methoxyl, four aromatic methines, and eight aromatic quaternary carbons. A keto carbon signal appeared at δ_C 194.4 (C-9).

These ^1H and ^{13}C NMR data resembled those of DPB-4 or nobilone [**286**]. The ^1H NMR spectrum showed one less proton signal from ring B and the presence of an additional hydroxy group which exhibit proton signal at δ_H 8.44 (1H, *s*, 5-OH). DPB-10 exhibited only two *ortho*-coupled protons in ring B. On ring A, the location of the methoxy group was confirmed by the NOESY (**Figure 63**) and HMBC (**Figure 64**) correlations, which were similar to those of DPB-4.

On the basis of the above ^1H NMR and ^{13}C NMR evidence, compound DPB-10 was determined to be dendroflorin [**283**]. This compound has been earlier isolated from several *Dendrobium* species, namely, *D. densiflorum* (Fan *et al.*, 2001), *D. brymerianum* (Klongkumnuankarn *et al.*, 2015), and *D. nobile* (Zhang *et al.*, 2007a).



Dendroflorin [**283**]

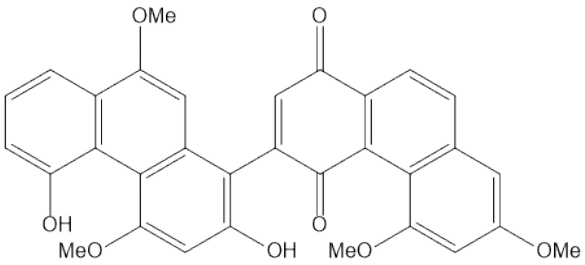
Table 14 NMR spectral data of compound DPB-10 and dendroflorin (in acetone-d_6)

Position	Compound DPB-10		Dendroflorin[a]	
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
1	6.79 (*d*, 1.5)	104.7	6.79 (*d*, 1.6)	105.6
2	-	160.1	-	160.9
3	6.77 (*d*, 1.5)	105.1	6.76 (*d*, 1.6)	106.1
4	-	153.2	-	154.1
4a	-	121.4	-	122.4
4b	-	123.5	-	124.3
5	-	144.2	-	145.1
6	6.86 (*d*, 9.0)	128.1	6.87 (*d*, 9.0)	128.9
7	6.59 (*d*, 9.0)	118.9	6.58 (*d*, 9.0)	119.7
8	-	151.9	-	152.8
8a	-	116.6	-	117.4
9	-	194.4	-	195.3
9a	-	136.5	-	137.4
4-OMe	4.10 (*s*)	56.5	4.10 (*s*)	57.4

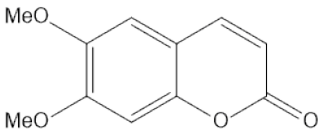
[a] Klongkumnuankarn *et al.*, 2015

2. Free radical scavenging activities

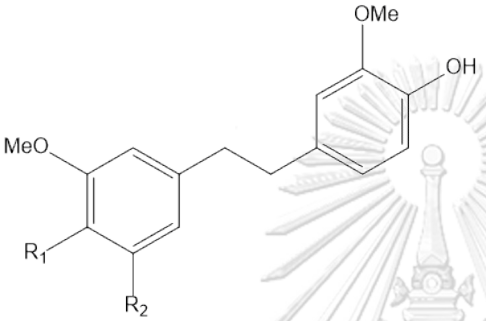
The ethyl acetate (EtOAc) extract of *Dendrobium palpebrae* was preliminarily tested for its free radical scavenging property by DPPH radical scavenging assay, and demonstrated more than 80% inhibition at a concentration of 100 µg/ml. Thus, the EtOAc extract was subjected to further chemical investigation. Ten pure compounds were isolated (DPB 1-10) and identified as dendropalpebrone [**294**], gigantol [**30**], lusianthridin [**103**], nobilone [**285**], 3,7-dihydroxy-2,4,8-trimethoxyphenanthrene [**80**], 2,5-dihydroxy-4,9-dimethoxyphenanthrene [**119**], moscatilin [**35**], scoparone [**261**], 4,5,4′-trihydroxy-3,3′-dimethoxybibenzyl [**40**], and dendroflorin [**283**], respectively. All compounds were further examined for their free radical scavenging activity at a concentration of 50 µg/mL, using ORAC, DPPH radical scavenging, and deoxyribose degradation assays (**Table 15**). Additionally, their inhibitory effects on reactive oxygen species (ROS) production in murine macrophage cells (RAW 264.7) induced by hydrogen peroxide (H_2O_2) were examined, and the results are displayed in **Table 16**.



Dendropalpebrone [**294**]



Scoparone [**261**]



Gigantol [**30**]: R_1 = H, R_2 = OH

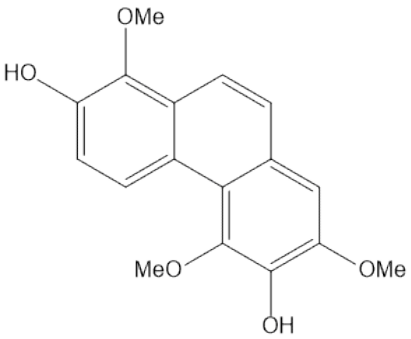
Moscatilin [**35**]: R_1 = OH, R_2 = OMe

4,5,4′-Trihydroxy-3,3′-dimethoxy-bibenzyl [**40**]: R_1 = R_2 = OH

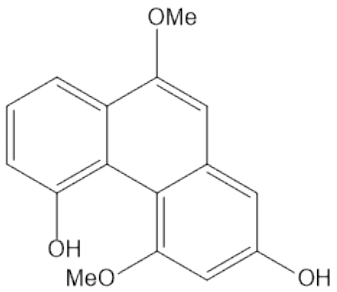
Lusianthridin [**103**]

Nobilone [**285**]: R_1 = R_3 = H, R_2 = OH

Dendroflorin [**283**]: R_1 = R_3 = OH, R_2 = H



3,7-Dihydroxy-2,4,8-trimethoxyphenanthrene [**80**]



2,5-Dihydroxy-4,9-dimethoxyphenanthrene [**119**]

As shown in **Table 15**, scoparone (DPB-8, [**261**]), which does not have any phenolic group showed the least potent free radical scavenging activities in all assays. On the other hand, dendroflorin (DPB-10, [**283**]), which have three phenolic groups exhibited the most potent free radical scavenging properties in all assays. In deoxyribose degradation assay, it manifested an outstanding effect with IC_{50} value of 193 μM approximating to the IC_{50} of the positive control Trolox® (IC_{50} value of 160 μM). However, other isolated compounds (DPB 1-9) were devoid of hydroxy radical inhibitory activity, producing less than 50% inhibition at a concentration of 50 μg/ml.

Table 15 Free radical scavenging activity of isolated compounds from *D. palpebrae*

Compounds	ORAC value (μmol TE/g)	% Radical scavenging activity (%RSA)	% Hydroxy radical inhibition
Dendropalpebrone (DPB-1) [**294**]	292.13 ± 17.44	18.07 ± 1.91	32.40 ± 0.71
Gigantol (DPB-2) [**30**]	386.64 ± 13.50	15.15 ± 1.00	42.06 ± 4.05
lusianthridin (DPB-3) [**103**]	297.24 ± 34.18	26.73 ± 1.02	24.89 ± 0.97
Nobilone (DPB-4) [**285**]	383.15 ± 38.76	17.94 ± 0.71	32.40 ± 0.94
3,7-Dihydroxy-2,4,8-trimethoxy-phenanthrene (DPB-5) [**80**]	308.10 ± 26.51	7.74 ± 0.88	27.04 ± 0.95
2,5-Dihydroxy-4,9-dimethoxy-phenanthrene (DPB-6) [**119**]	270.89 ± 9.70	18.86 ± 0.47	45.28 ± 0.70
Moscatilin (DPB-7) [**35**]	272.33 ± 17.44	15.36 ± 1.32	22.75 ± 3.88
Scoparone (DPB-8) [**261**]	241.50 ± 36.91	3.04 ± 0.33	20.60 ± 0.48
4,5,4′-Trihydroxy-3,3′-dimethoxy-bibenzyl (DPB-9) [**40**]	306.91 ± 41.34	7.16 ± 1.13	25.97 ± 0.61
Dendroflorin (DPB-10) [**283**]	414.17 ± 22.54	31.14 ± 0.31	51.72 ± 0.76

This agreed with a previous study (Bendary *et al.*, 2013) which suggested that the phenols in natural compounds played an important role in free radical scavenging ability and may contribute directly to their antioxidative effects.

For the inhibitory effects on intracellular ROS production in activated murine macrophage cells (**Table 16**), dendroflorin also showed the highest % ROS inhibition, which correlated with the results from ORAC, DPPH and deoxyribose degradation assays. Therefore, dendroflorin was further investigated for antioxidant activity in stimulated murine macrophage-like cell line RAW 264.7 at non-toxic concentrations (12.5 – 50.0 µg/mL). It could significantly reduce the H_2O_2-activated generation of ROS in RAW 264.7 cells in a dose-dependent manner, as shown in **Table 17**. Moreover, dendroflorin at a concentration of 50 µg/ml could reduce ROS more than 50% when compared with control group which was treated with 1 mM of H_2O_2 only.

Table 16 Inhibitory effects on ROS production in RAW 264.7 murine macrophage cells induced by H_2O_2 of isolated compounds from *D. palpebrae*

Compounds	% ROS inhibition
Dendropalpebrone (DPB-1) [**294**]	27.19 ± 1.84
Gigantol (DPB-2) [**30**]	50.67 ± 2.51
lusianthridin (DPB-3) [**103**]	23.22 ± 2.95
Nobilone (DPB-4) [**285**]	48.70 ± 4.84
3,7-Dihydroxy-2,4,8-trimethoxyphenanthrene (DPB-5) [**80**]	17.37 ± 1.40
2,5-Dihydroxy-4,9-dimethoxyphenanthrene (DPB-6) [**119**]	20.45 ± 3.67
Moscatilin (DPB-7) [**35**]	22.23 ± 0.93
Scoparone (DPB-8) [**261**]	13.71 ± 1.51
4,5,4′-Trihydroxy-3,3′-dimethoxybibenzyl (DPB-9) [**40**]	21.85 ± 1.85
Dendroflorin (DPB-10) [**283**]	58.43 ± 6.13

Regarding the effects of dendroflorin [**283**] on the antioxidant enzymes in H_2O_2-induced RAW 264.7 cells, the results indicated that in cellular SOD, GPx and CAT activities RAW 264.7 cells that were pre-incubated with dendroflorin at concentration 12.5 - 50 µg/mL before inducing with H_2O_2 were significantly enhanced ($p < 0.05$), in a dose-dependent manner (**Table 18**). Therefore, dendroflorin might manifest antioxidant activities by preventing cellular oxidative stress in RAW 264.7 murine macrophage cells.

Table 17 Inhibitory effects of dendroflorin on ROS production in RAW 264.7 murine macrophage cells induced by H_2O_2 at non-toxic concentration

Groups	ROS production (AU)	%ROS inhibition
Blank	293.67 ± 9.61^{a}	-
Control: H_2O_2 (1 mM)	1023.00 ± 7.55^{b}	-
Dendroflorin (12.5 µg/mL) + H_2O_2	937.33 ± 14.74^{c}	8.37 ± 1.77
Dendroflorin (25.0 µg/mL) + H_2O_2	774.33 ± 10.69^{d}	24.30 ± 1.44
Dendroflorin (50.0 µg/mL) + H_2O_2	453.33 ± 8.50^{e}	55.68 ± 1.16
Dendroflorin (50.0 µg/mL)	311.33 ± 11.59^{a}	-

Note: Data present in mean ± SD ($n = 3$) in the same column followed by different superscript letters are significantly different ($p < 0.05$).

Table 18 Effects of dendroflorin on antioxidant enzymes in induced RAW 264.7 macrophage cells

Groups	Antioxidant enzymes		
	SOD (Unit/mg protein)	GPx (nmol min^{-1} mg^{-1} protein)	CAT (nmol min^{-1} mg^{-1} protein)
Blank	31.85 ± 0.57[a]	77.53 ± 2.70[a]	32.48 ± 2.30[a]
Control: H_2O_2 (1 mM)	13.03 ± 0.67[b]	47.98 ± 1.35[b]	14.98 ± 2.13[b]
Dendroflorin (12.5 µg/mL) + H_2O_2	14.17 ± 0.98[b]	54.35 ± 1.32[c]	16.78 ± 2.64[b]
Dendroflorin (25.0 µg/mL) + H_2O_2	19.54 ± 1.14[c]	60.51 ± 1.96[d]	18.69 ± 2.48[c]
Dendroflorin (50.0 µg/mL) + H_2O_2	23.66 ± 0.20[d]	75.27 ± 2.03[e]	23.18 ± 2.97[d]
Dendroflorin (50.0 µg/mL)	30.94 ± 0.41[a]	79.23 ± 3.46[a]	37.80 ± 1.90[a]

Note: Data present in mean ± SD (n = 3) in the same column followed by different superscript letters are significantly different ($p < 0.05$).

CHAPTER V
CONCLUSION

Ten pure compounds were isolated from the methanol extract of whole plant of *Dendrobium palpebrae*. One of them was characterized as a new phenanthrene-phenanthraquinone derivative named dendropalpebrone. The other compounds were identified as gigantol [**30**], lusianthridin [**103**], nobilone [**285**], 3,7-dihydroxy-2,4,8-trimethoxyphenanthrene [**80**], 2,5-dihydroxy-4,9-dimethoxyphenanthrene [**119**], moscatilin [**35**], scoparone [**261**], 4,5,4′-trihydroxy-3,3′-dimethoxybibenzyl [**40**] and dendroflorin [**283**]. All compounds were evaluated for their free radical scavenging activity by ORAC, DPPH, deoxyribose degradation assays, and were examined for intracellular antioxidant activity in H_2O_2-treated RAW 264.7 murine macrophage cells. Dendroflorin [**283**] exhibited the strongest antioxidant activities in all assays. It also significantly inhibited ROS production in H_2O_2-induced RAW 264.7 cells at non-toxic concentration in a dose-dependent manner. Further investigation of its anti-oxidative mechanism revealed that dendroflorin [**283**] could protect the RAW 264.7 cells against the oxidative stress by its ability to significant increase the activities of cellular antioxidant enzymes (SOD, GPx and CAT) in a dose-dependent manner.

This study is the first report of natural constituents and biological activities of *D. palpebrae.* All the chemical data obtained in this research should be useful for further phytochemical study of other plants in the genus *Dendrobium*. The information on antioxidant activities of the compounds isolated from *D. palpebrae* should provide a basis for research and development of new antioxidative agents in the future.

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APPENDIX

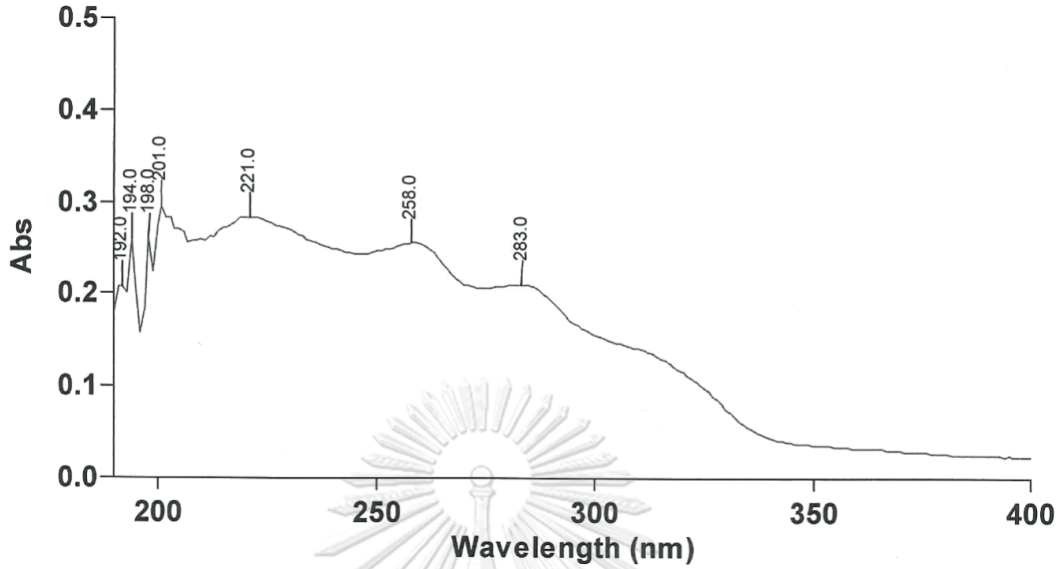

Figure 6 UV spectrum of compound DPB-1

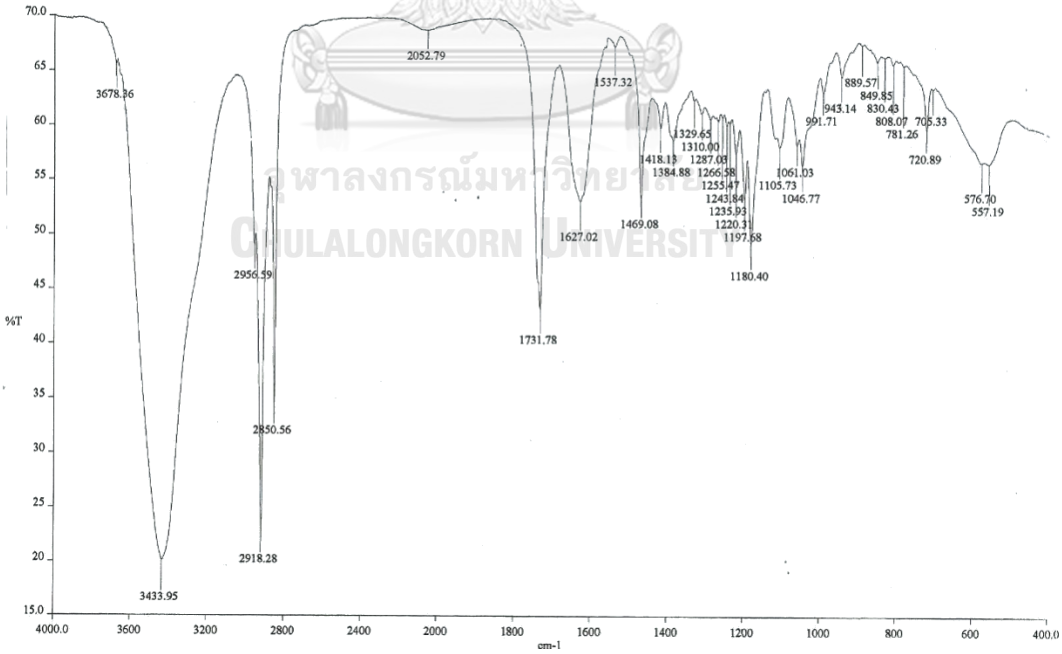

Figure 7 IR spectrum of compound DPB-1

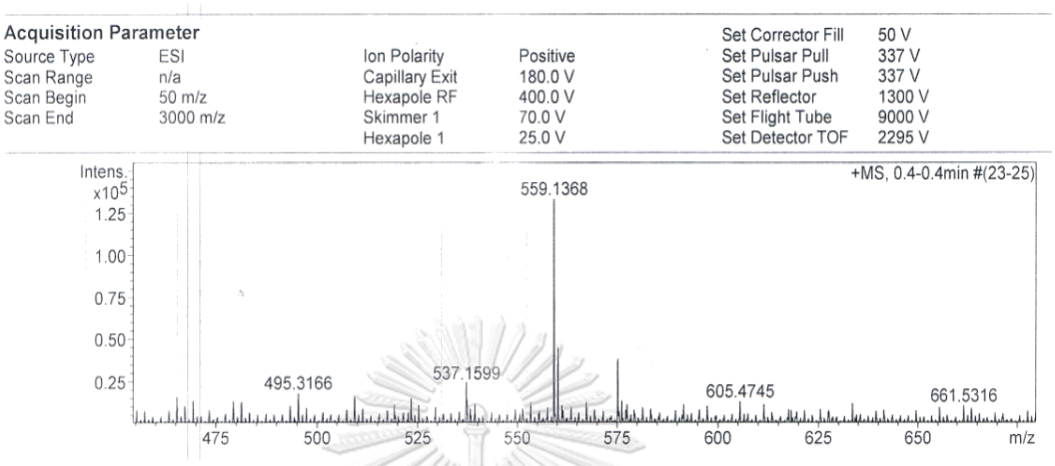

Figure 8 Mass spectrum of compound DPB-1

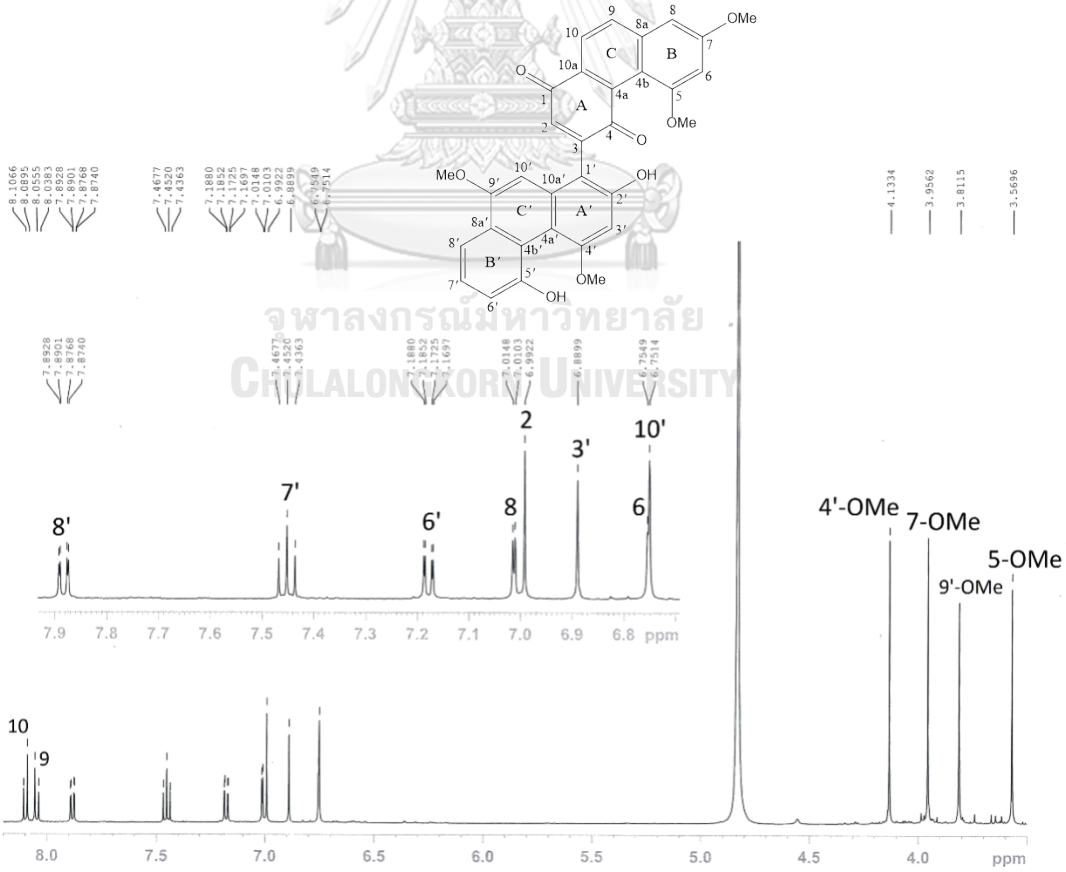

Figure 9 ^{1}H-NMR (500 MHz) spectrum of compound DPB-1 (in CD_3OD)

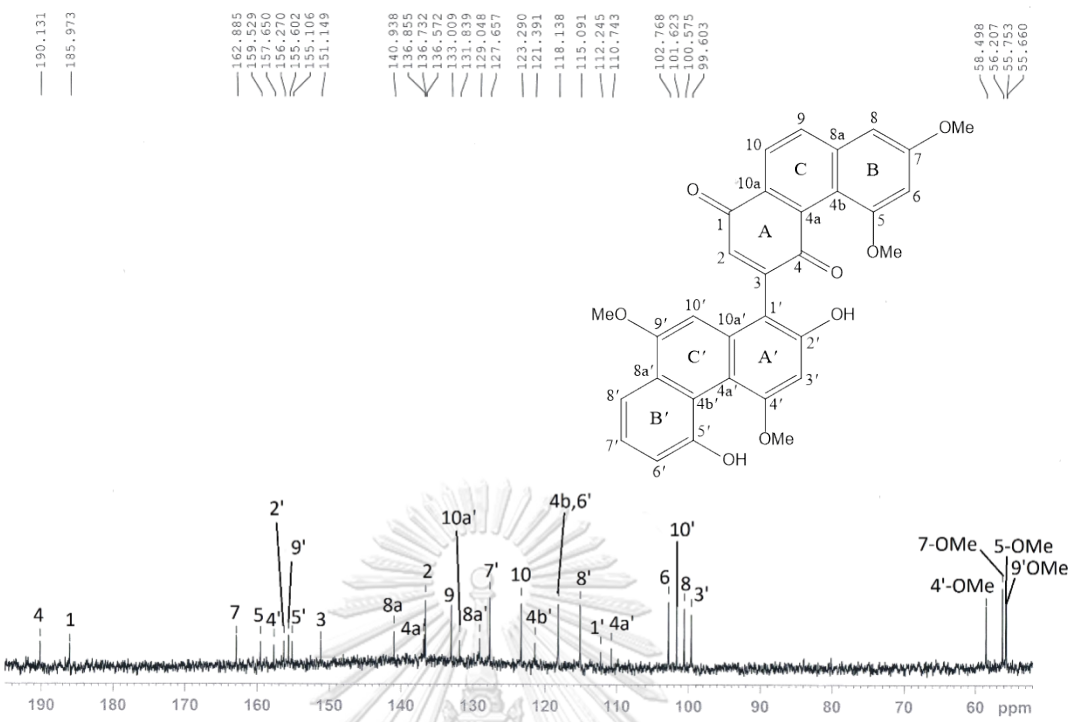

Figure 10 ^{13}C-NMR (125 MHz) spectrum of compound DPB-1 (in CD_3OD)

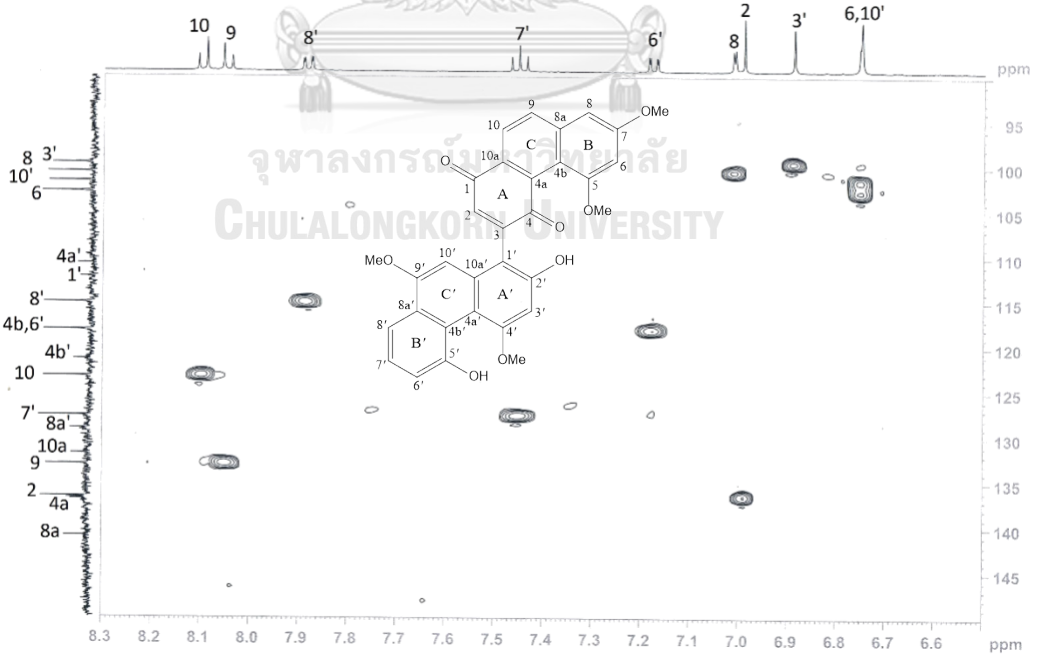

Figure 11 HSQC spectrum of compound DPB-1 (in CD_3OD)

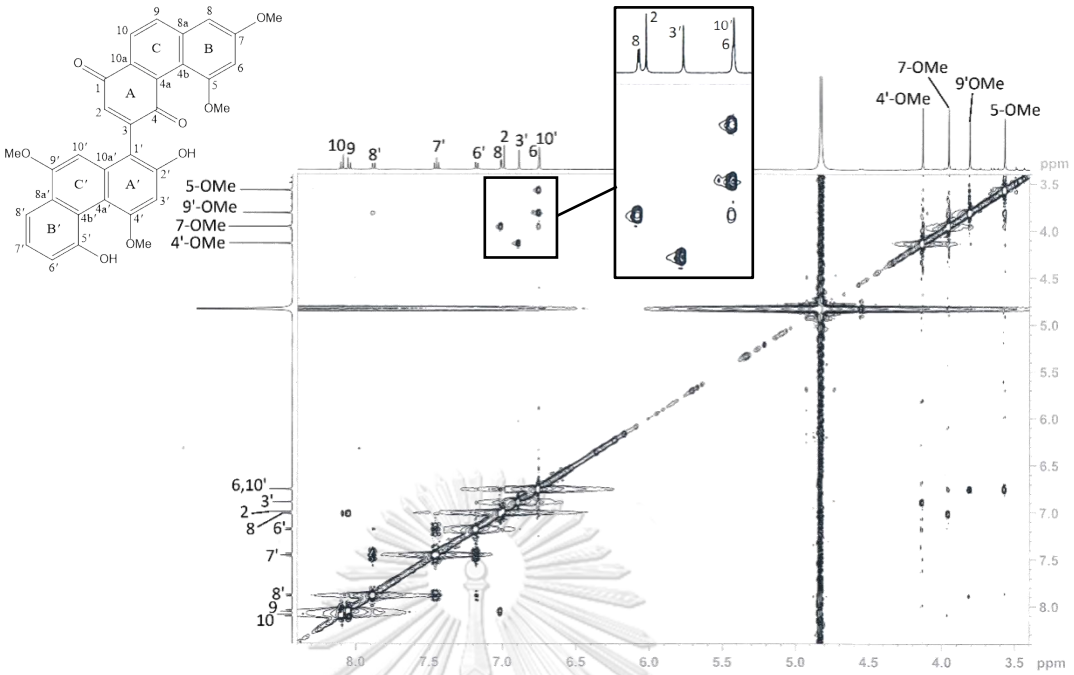

Figure 12 NOSEY spectrum of compound DPB-1 (in CD_3OD)

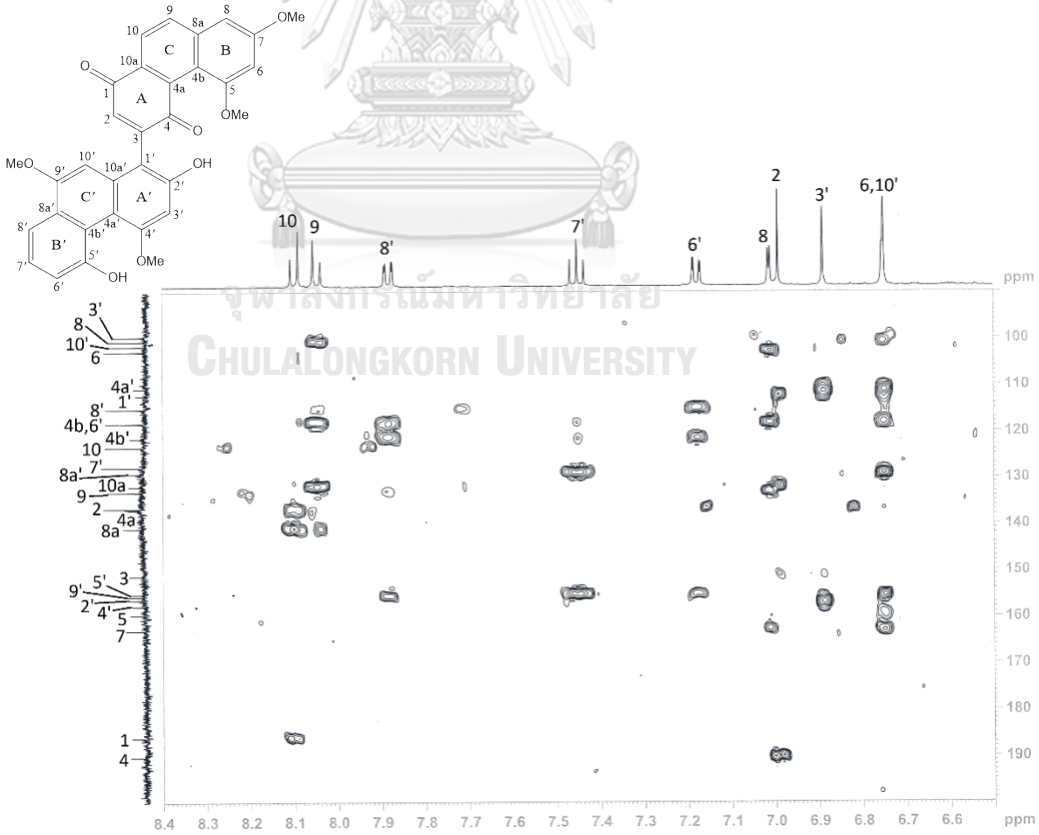

Figure 13 HMBC spectrum of compound DPB-1 (in CD_3OD)

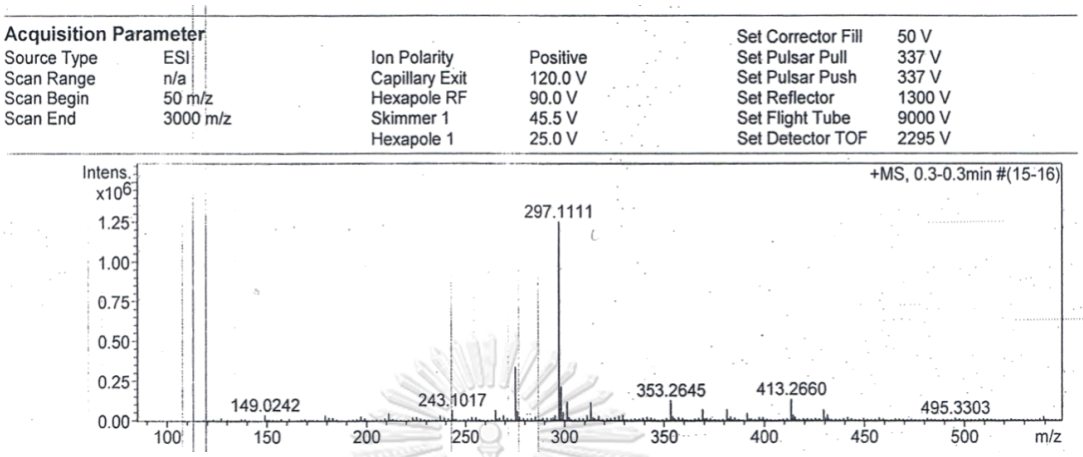

Figure 14 Mass spectrum of compound DPB-2

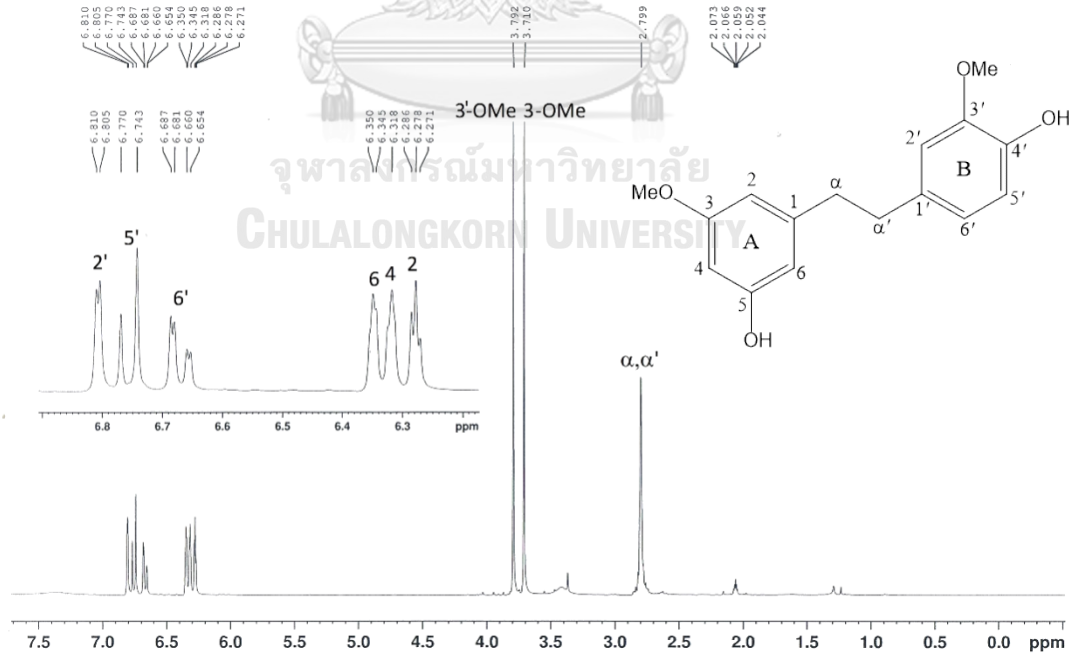

Figure 15 ^{1}H-NMR (300 MHz) spectrum of compound DPB-2 (in acetone-d_6)

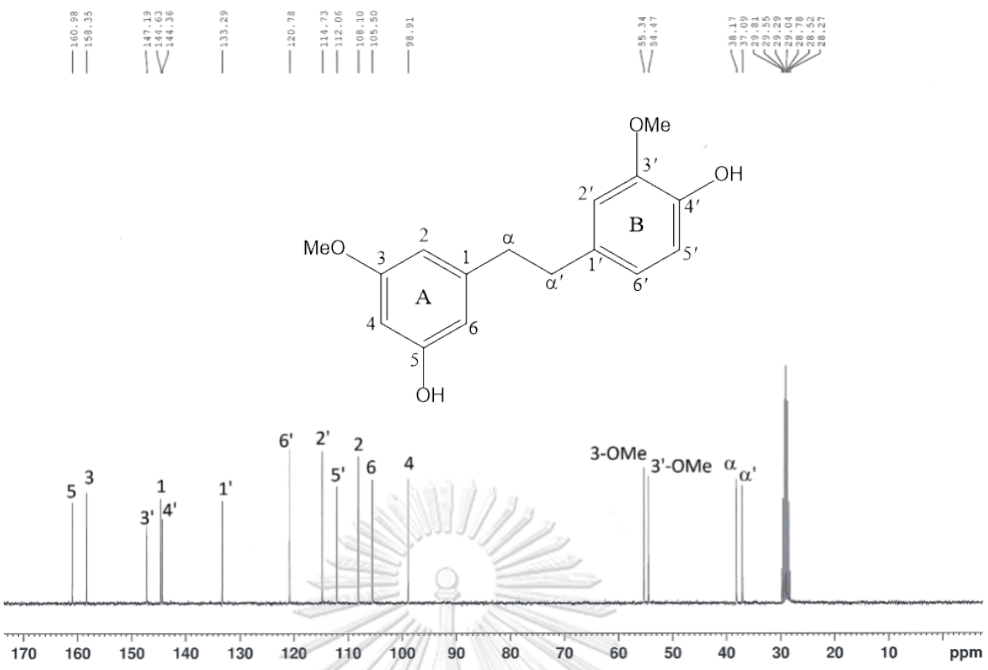

Figure 16 ^{13}C-NMR (75 MHz) spectrum of compound DPB-2 (in acetone-d_6)

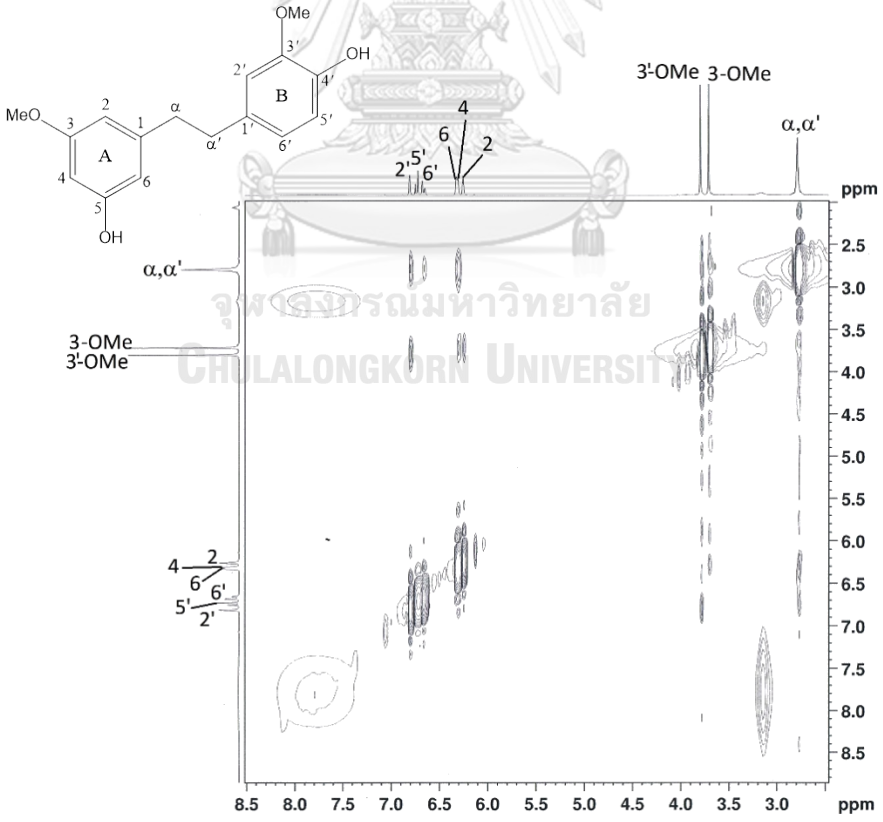

Figure 17 NOESY spectrum of compound DPB-2 (in acetone-d_6)

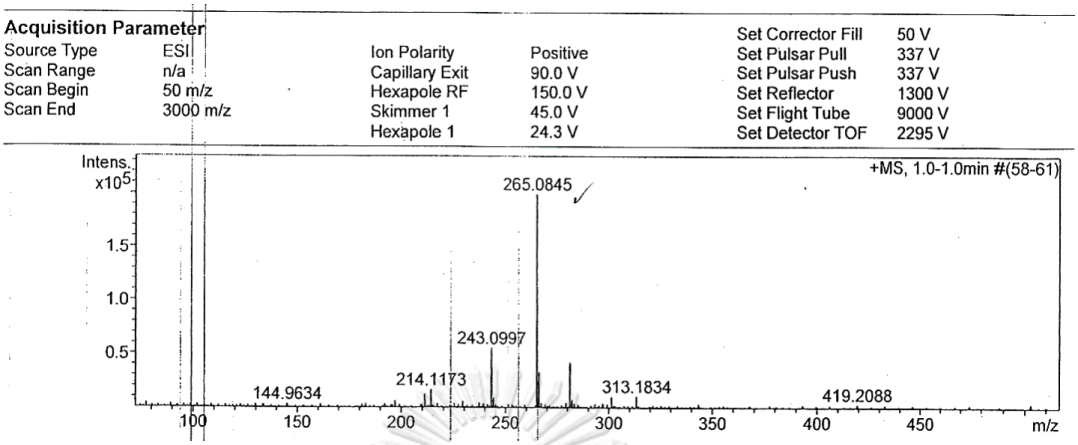

Figure 18 Mass spectrum of compound DPB-3

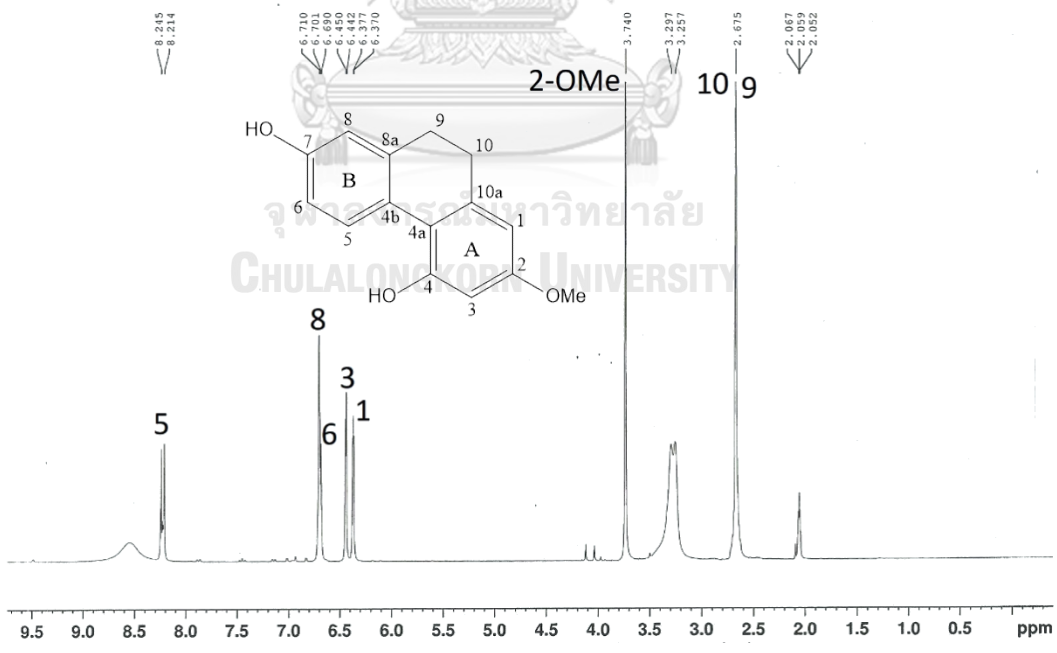

Figure 19 ^{1}H-NMR (300 MHz) spectrum of compound DPB-3 (in acetone-d_6)

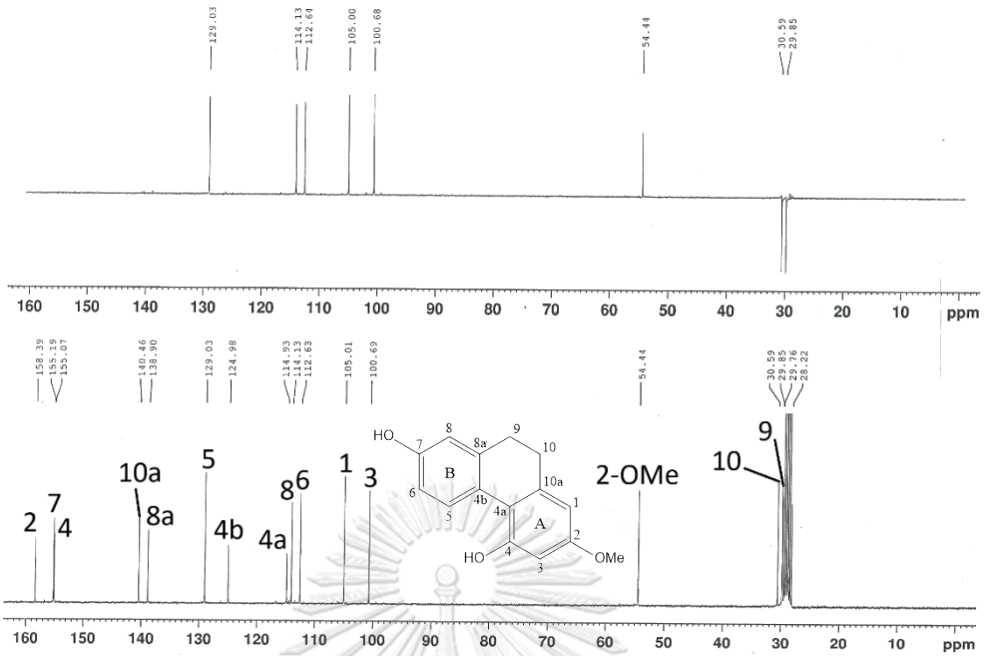

Figure 20 ^{13}C-NMR (75 MHz) and DEPT 135 spectrum of compound DPB-3 (in acetone-d_6)

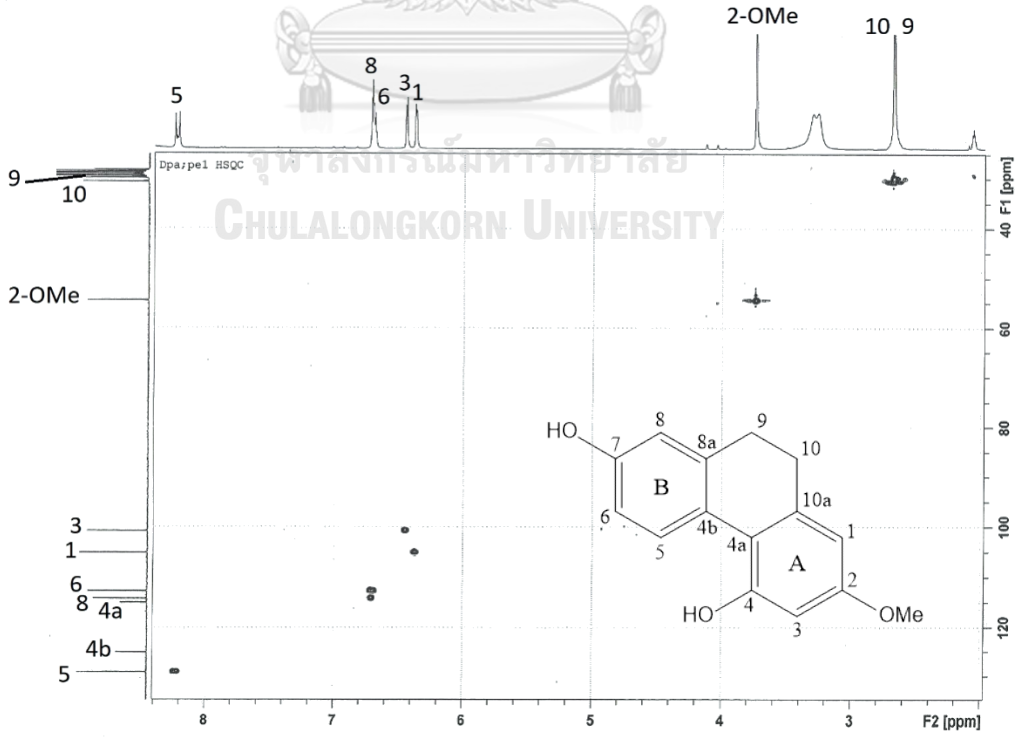

Figure 21 HSQC spectrum of compound DPB-3 (in acetone-d_6)

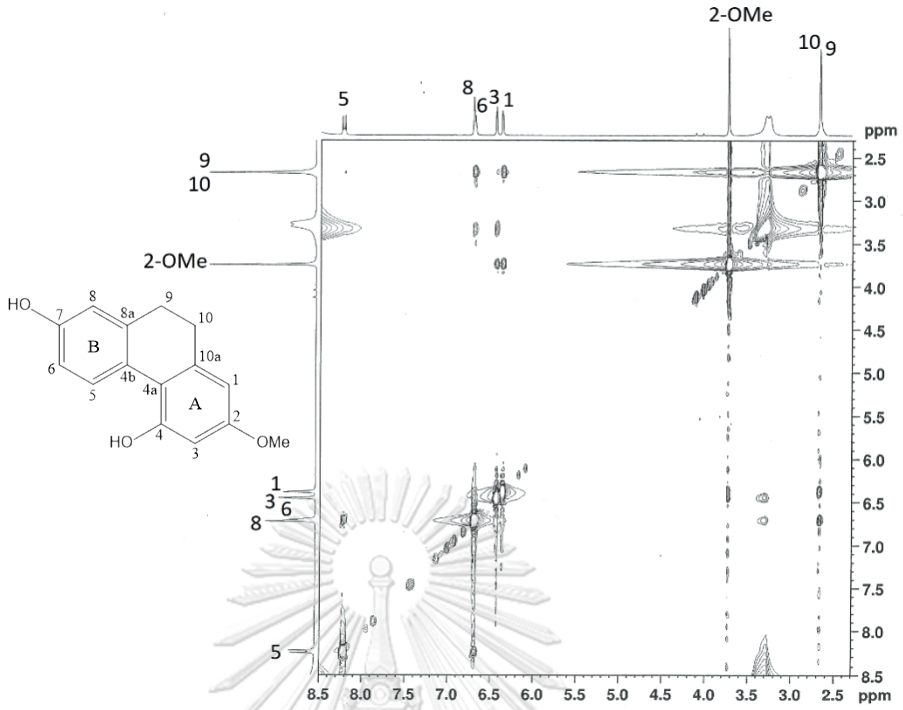

Figure 22 NOESY spectrum of compound DPB-3 (in acetone-d_6)

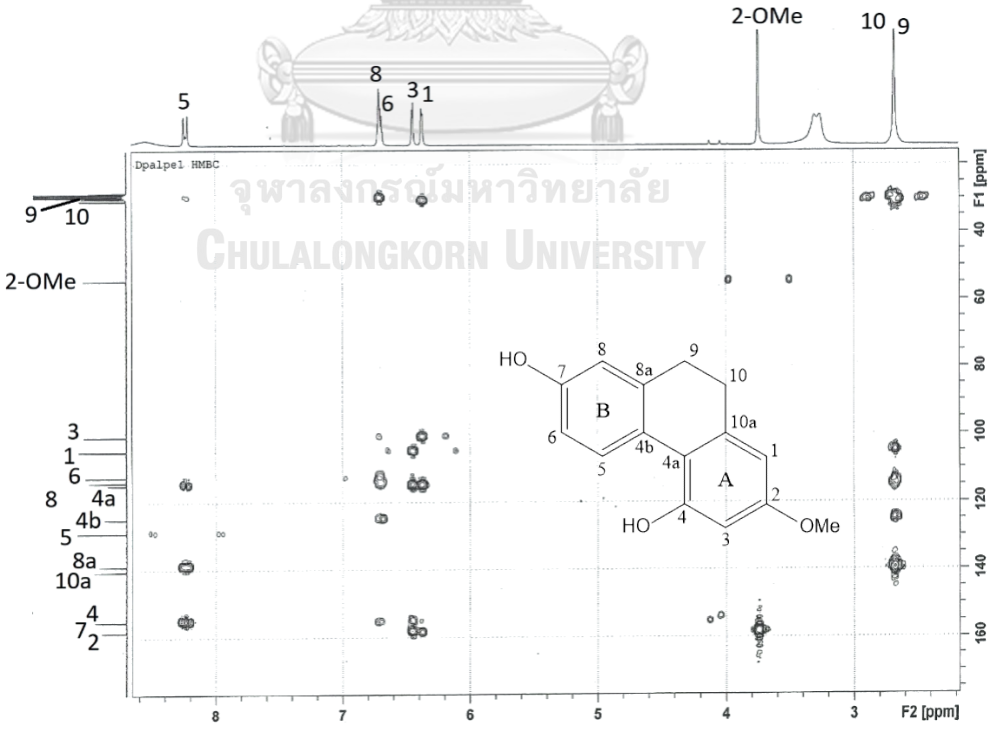

Figure 23 HMBC spectrum of compound DPB-3 (in acetone-d_6)

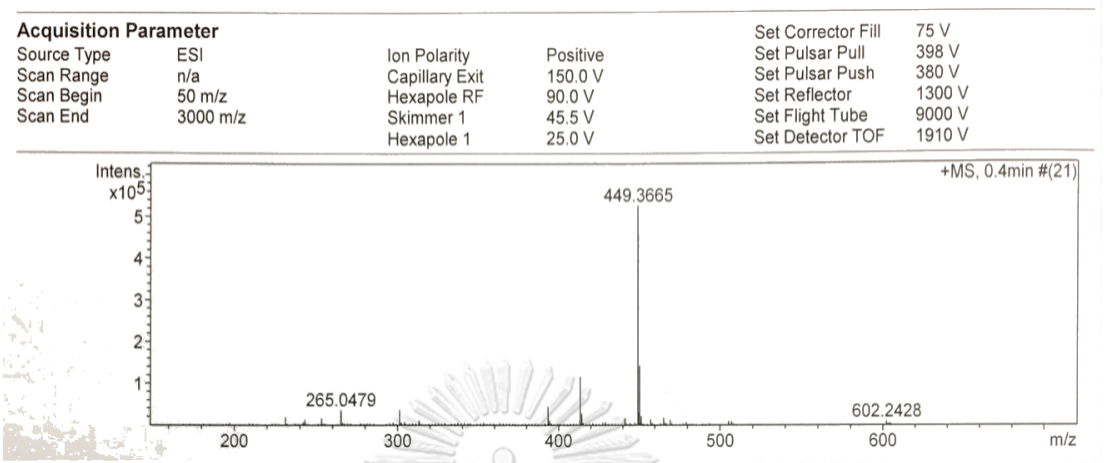

Figure 24 Mass spectrum of compound DPB-4

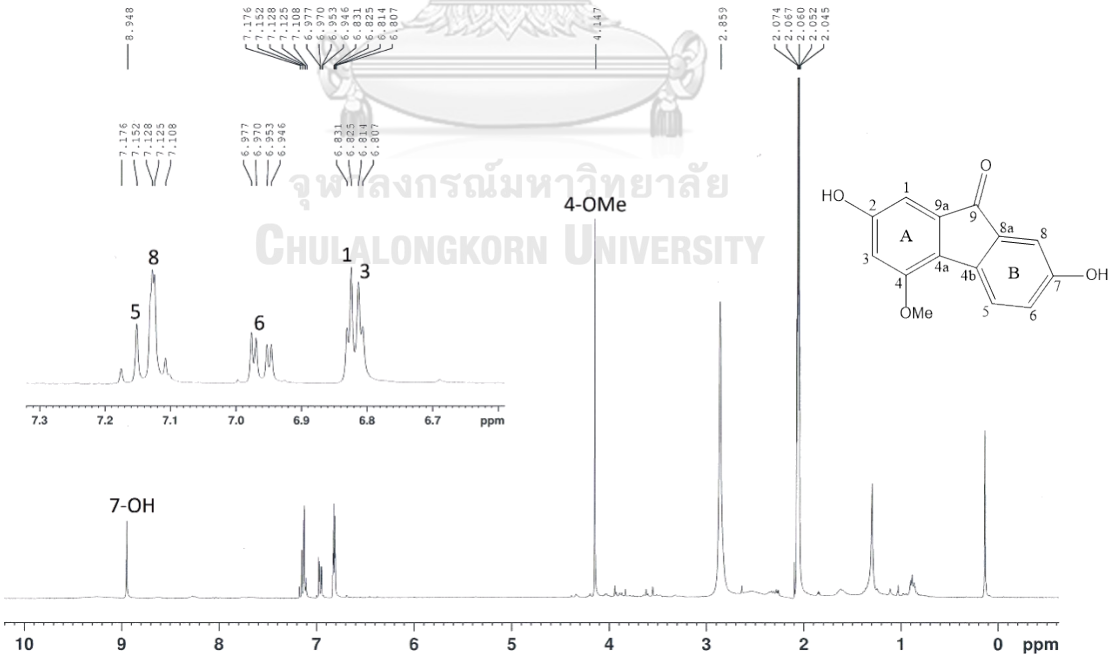

Figure 25 ^{1}H-NMR (300 MHz) spectrum of compound DPB-4 (in acetone-d_6)

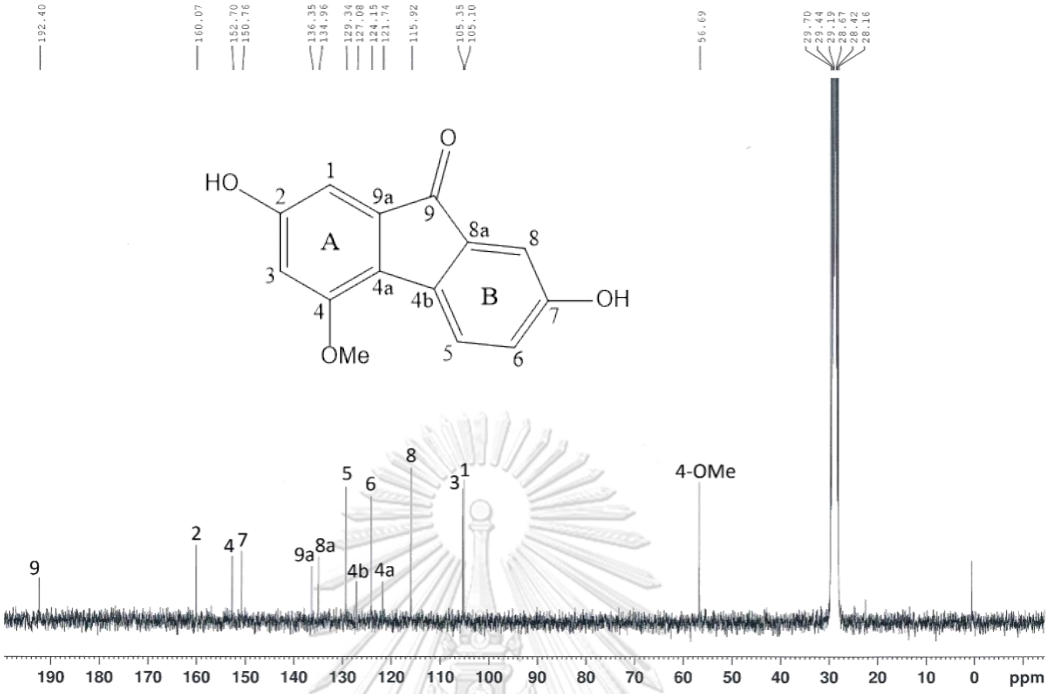

Figure 26 ^{13}C-NMR (75 MHz) spectrum of compound DPB-4 (in acetone-d_6)

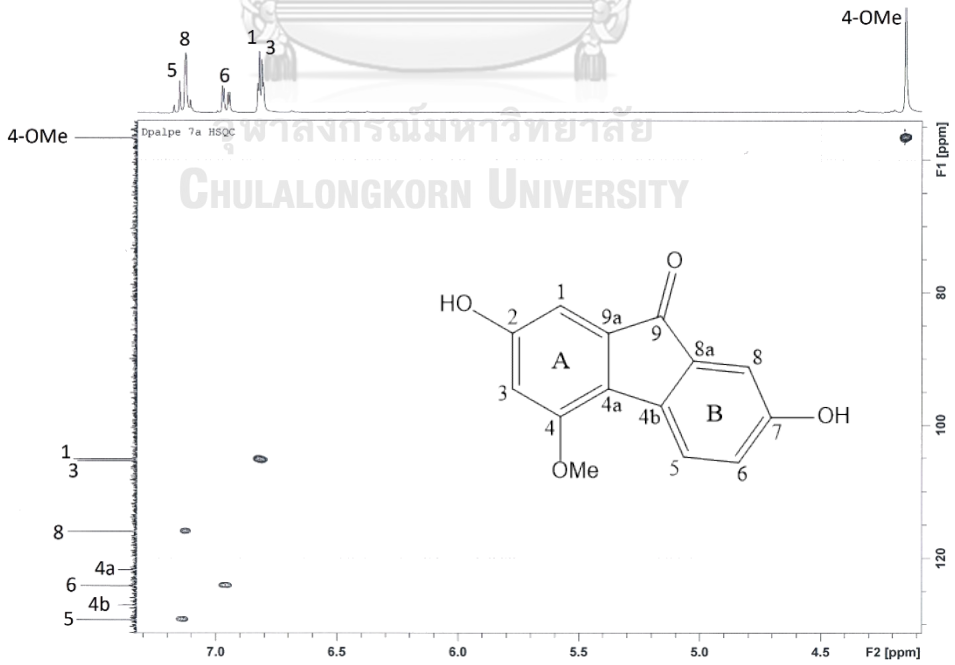

Figure 27 HSQC spectrum of compound DPB-4 (in acetone-d_6)

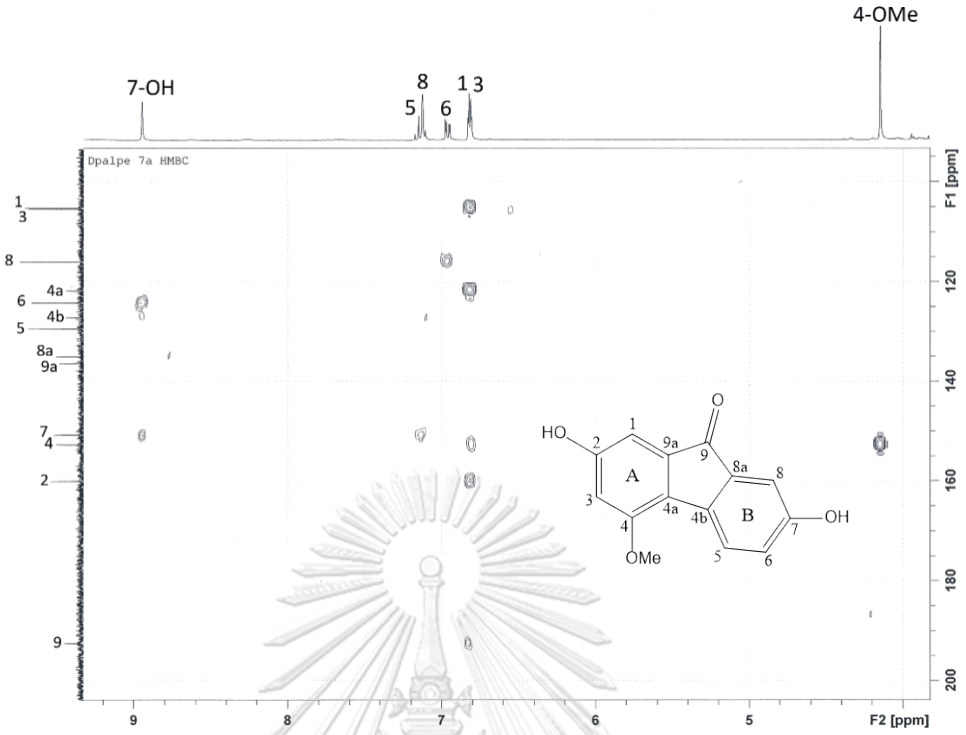

Figure 28 HMBC spectrum of compound DPB-4 (in acetone-d_6)

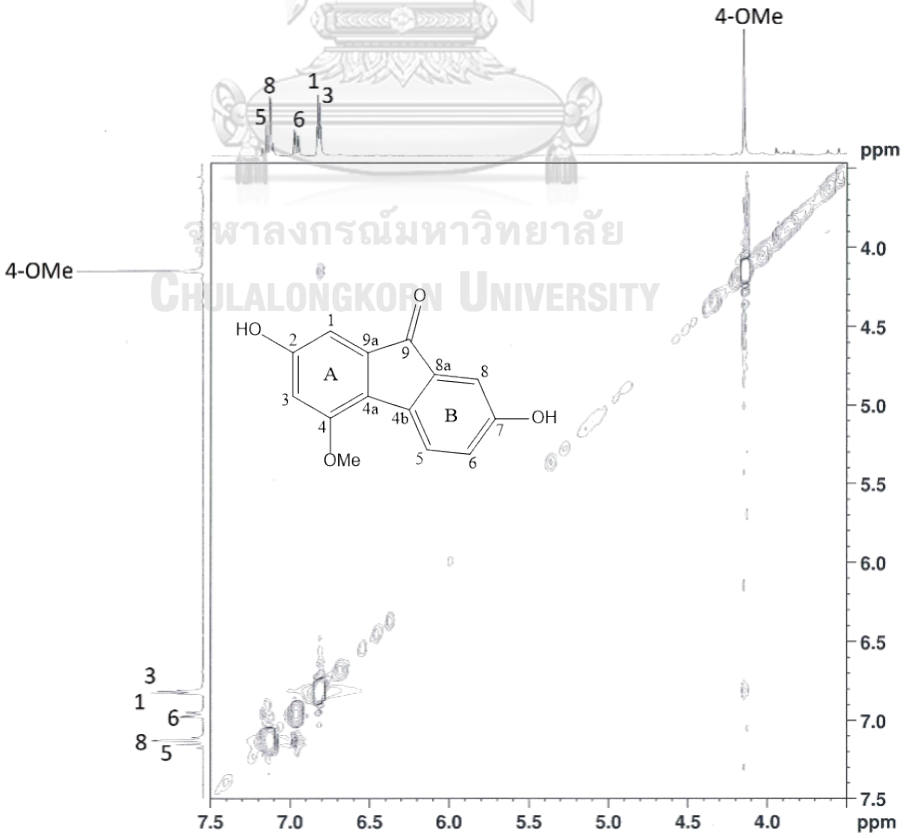

Figure 29 NOESY spectrum of compound DPB-4 (in acetone-d_6)

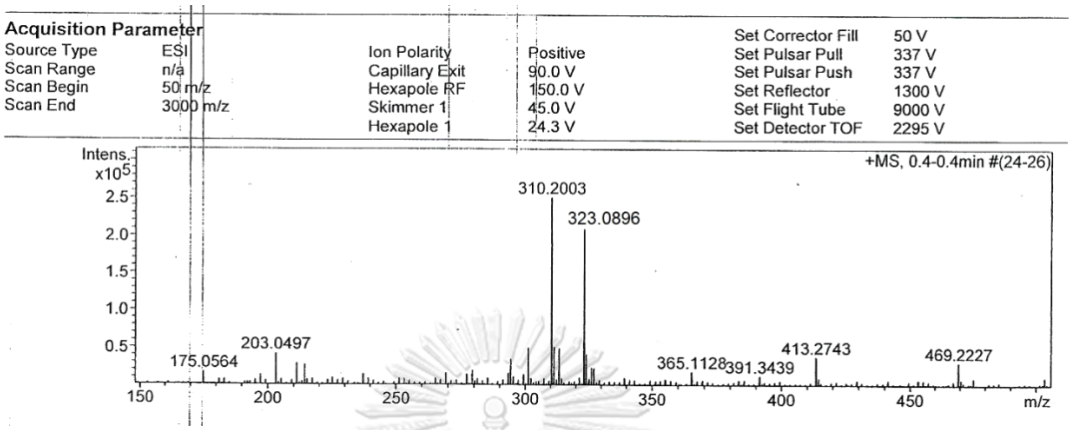

Figure 30 Mass spectrum of compound DPB-5

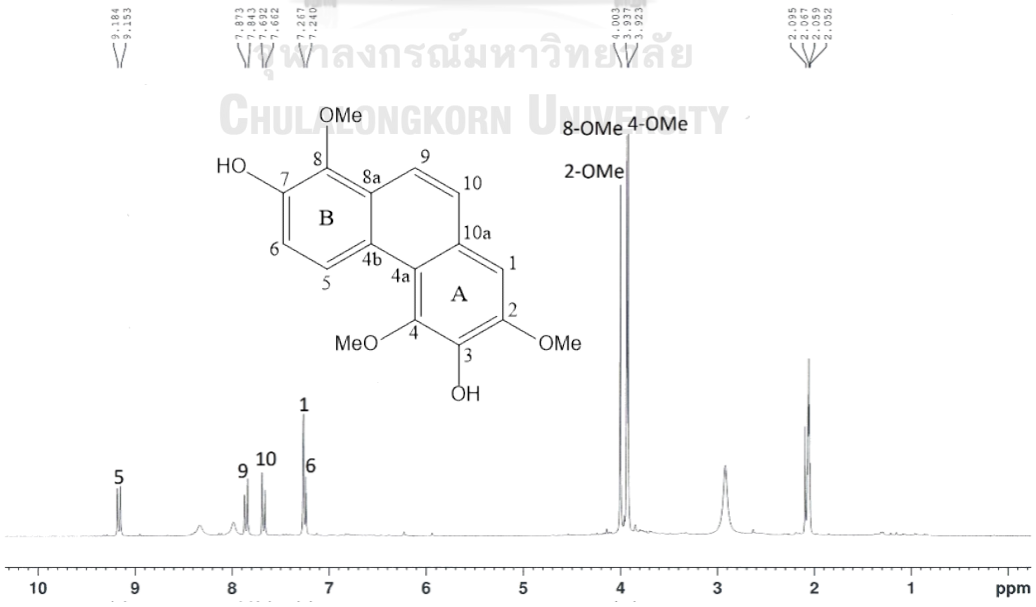

Figure 31 ^{1}H-NMR (300 MHz) spectrum of compound DPB-5 (in acetone-d_6)

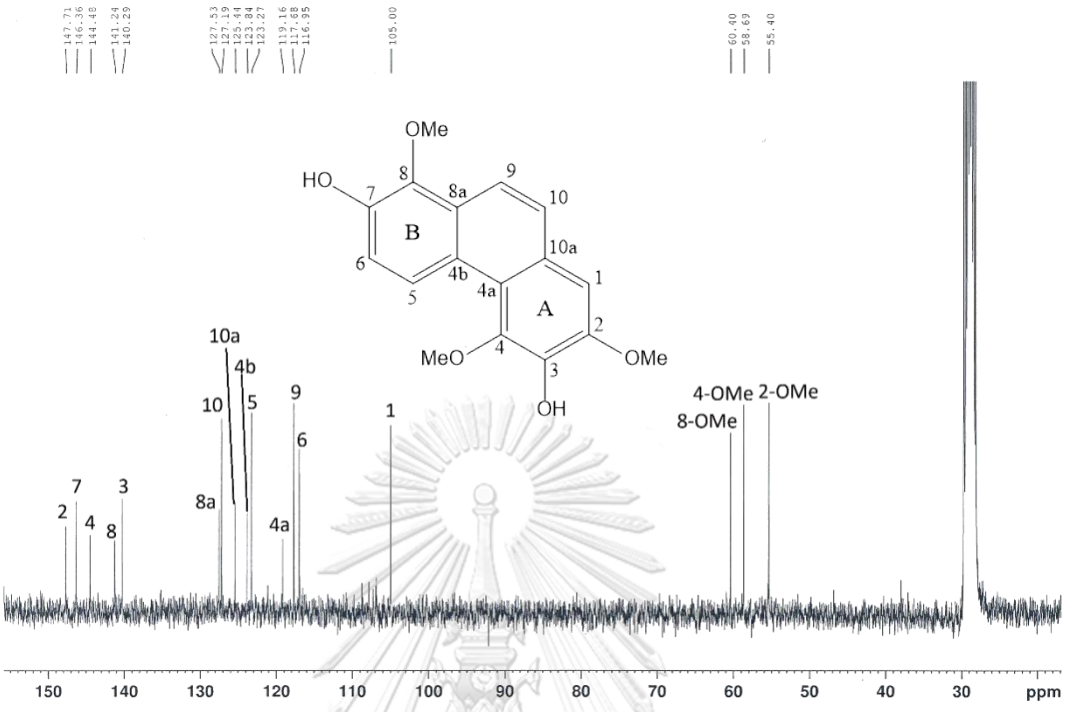

Figure 32 ^{13}C-NMR (75 MHz) spectrum of compound DPB-5 (in acetone-d_6)

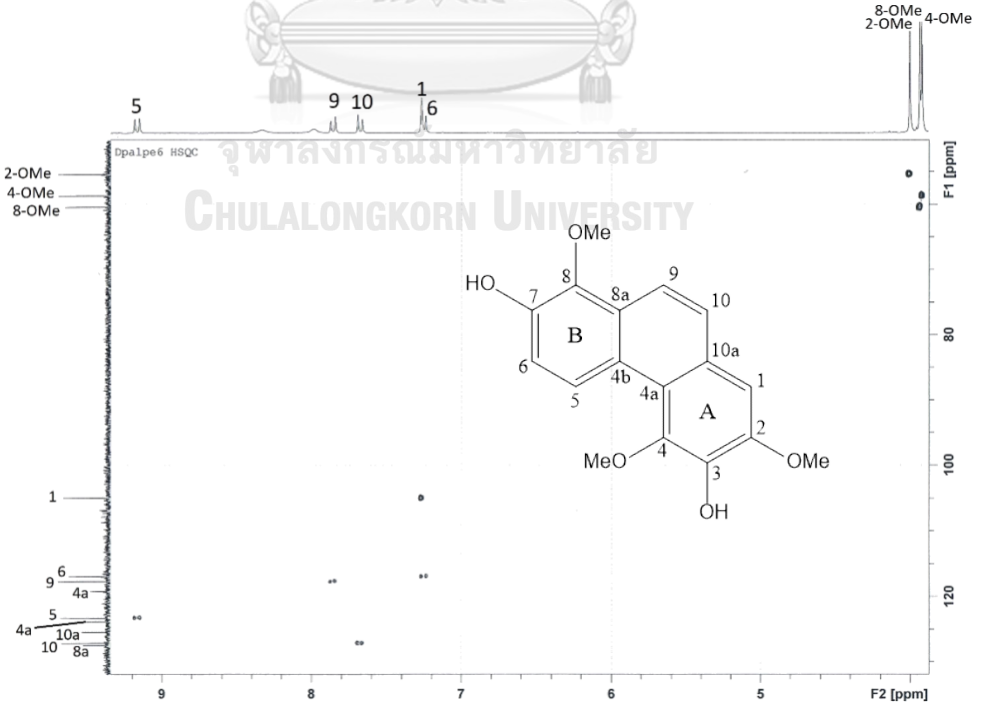

Figure 33 HSQC spectrum of compound DPB-5 (in acetone-d_6)

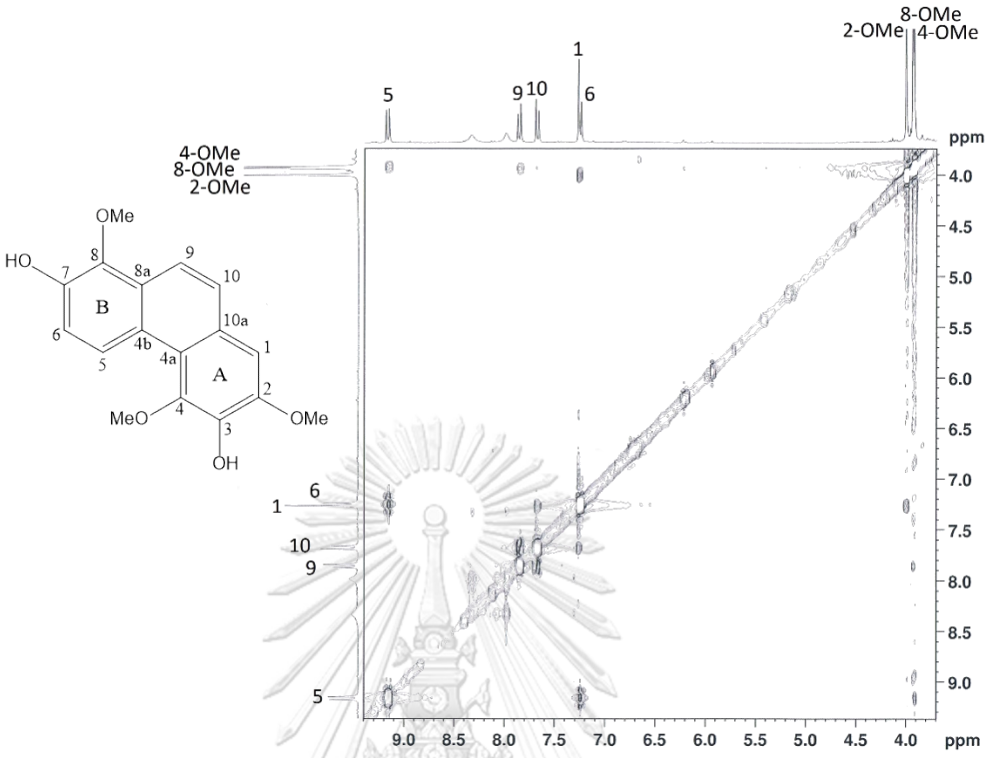

Figure 34 NOESY spectrum of compound DPB-5 (in acetone-d_6)

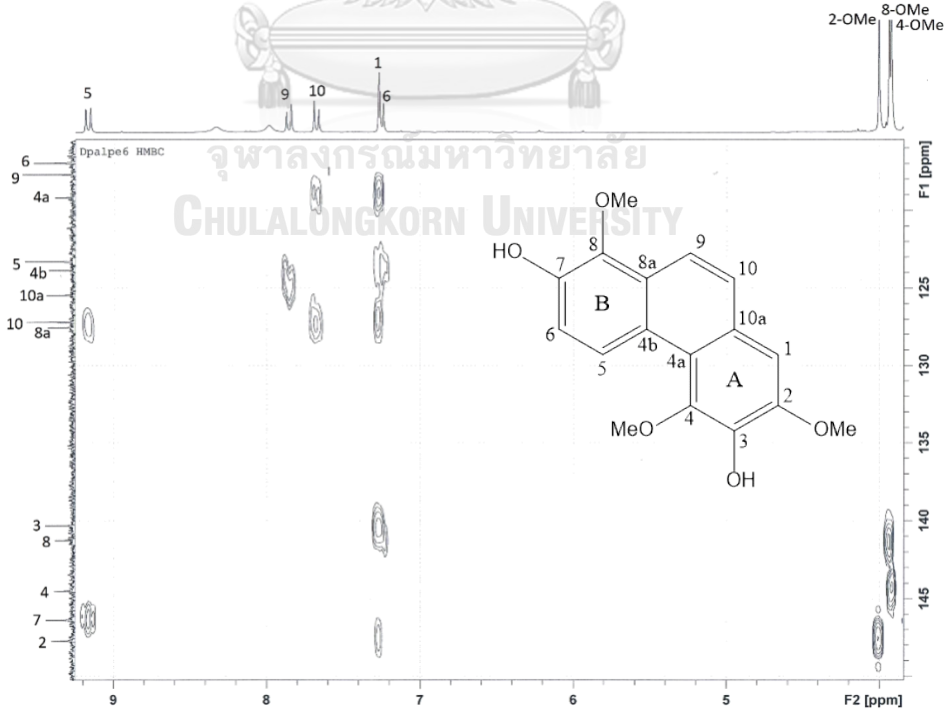

Figure 35 HMBC spectrum of compound DPB-5 (in acetone-d_6)

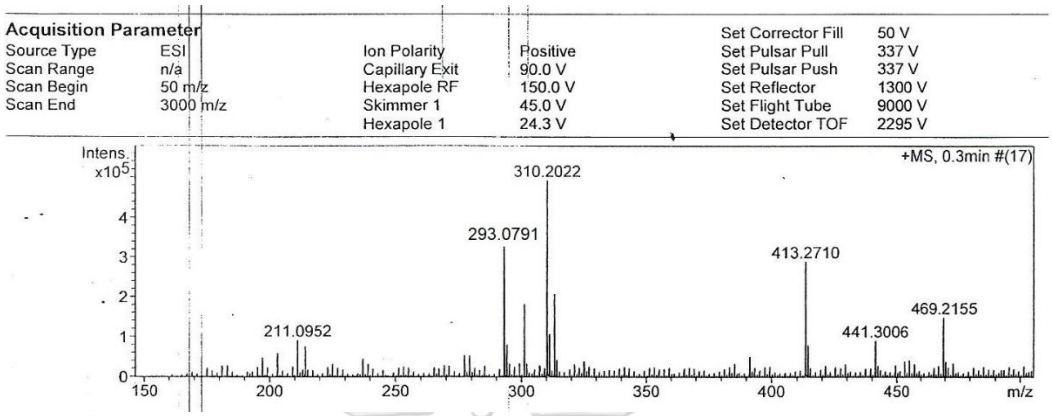

Figure 36 Mass spectrum of compound DPB-6

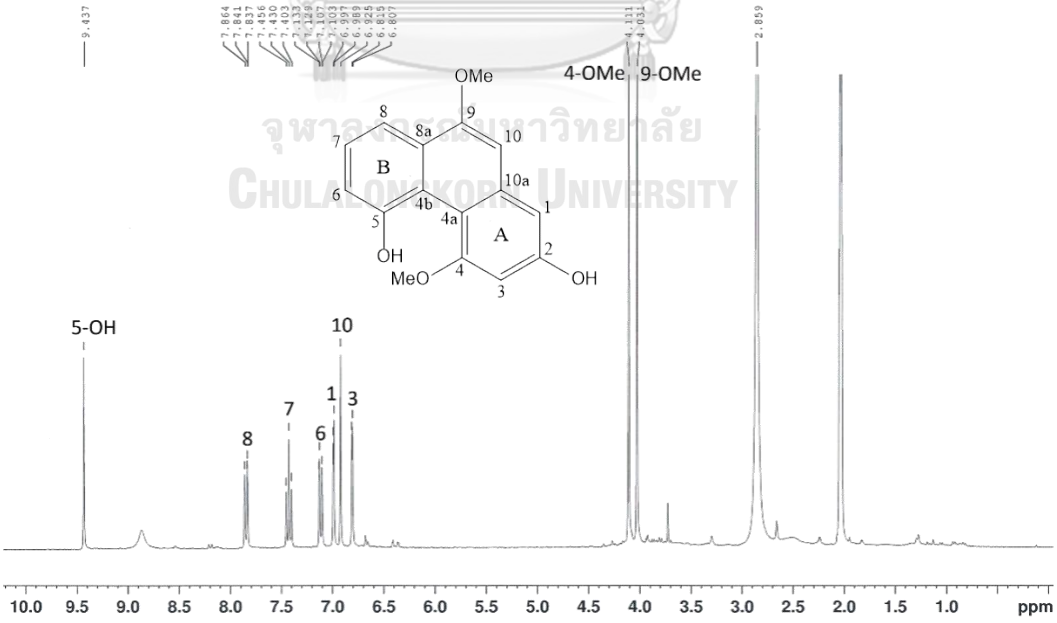

Figure 37 ^{1}H-NMR (300 MHz) spectrum of compound DPB-6 (in acetone-d_6)

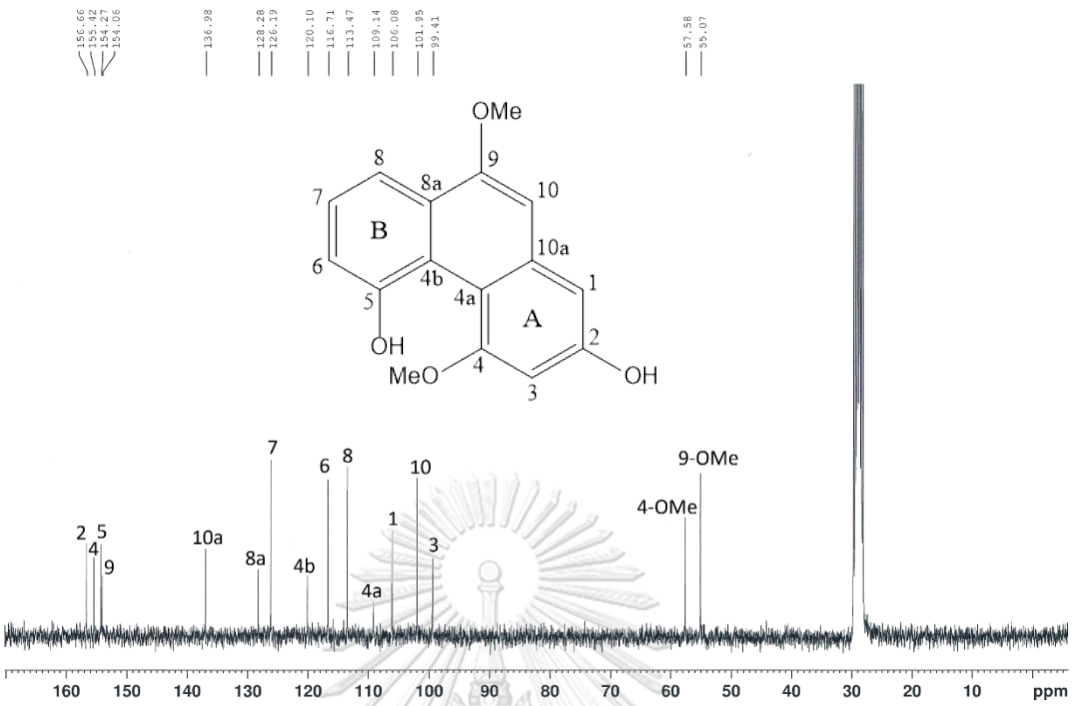

Figure 38 ^{13}C-NMR (75 MHz) spectrum of compound DPB-6 (in acetone-d_6)

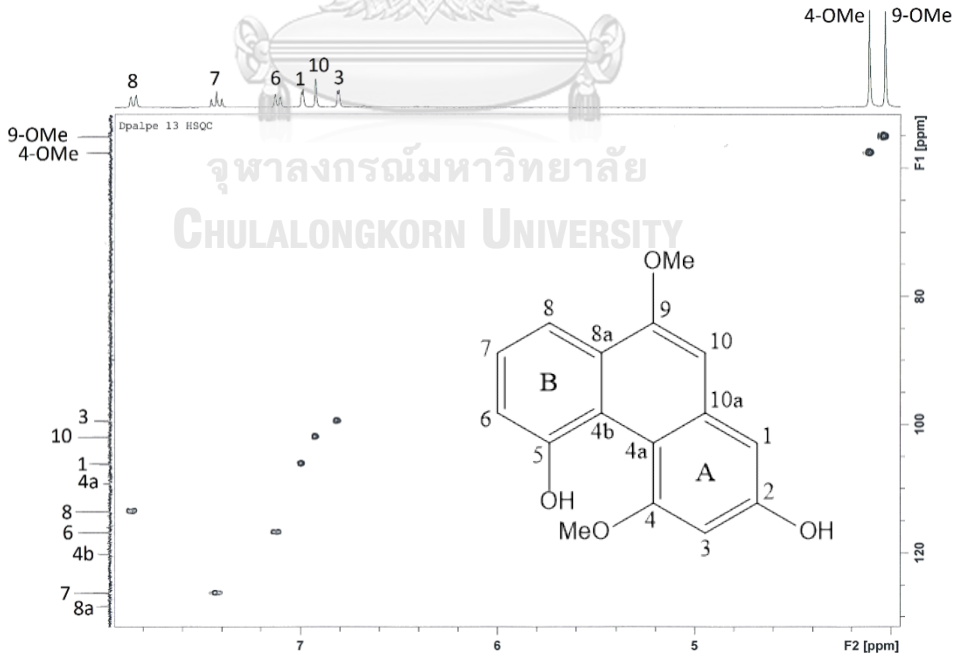

Figure 39 HSQC spectrum of compound DPB-6 (in acetone-d_6)

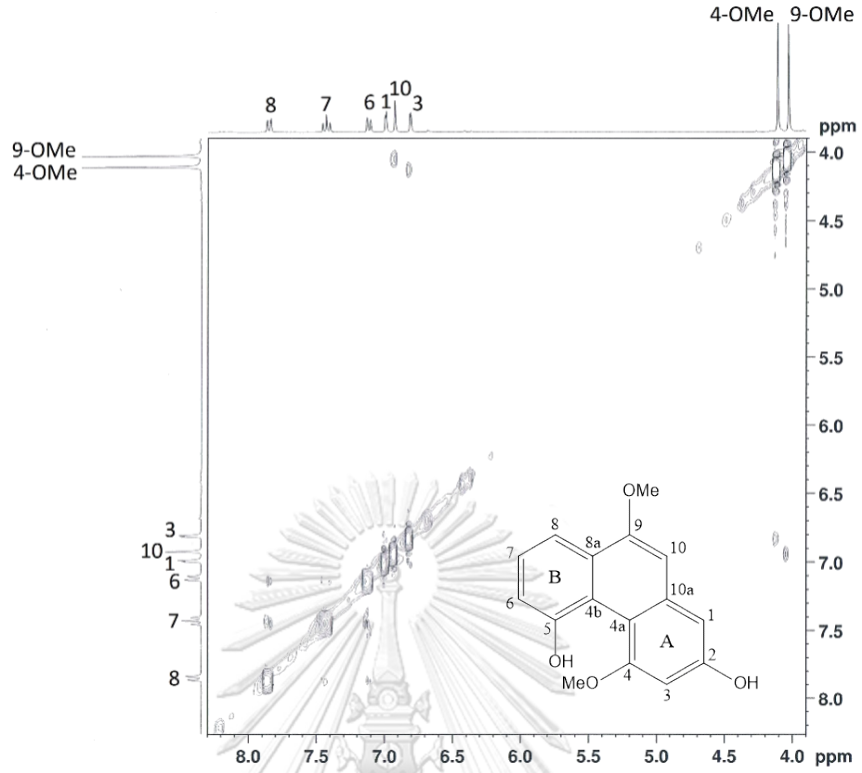

Figure 40 NOESY spectrum of compound DPB-6 (in acetone-d_6)

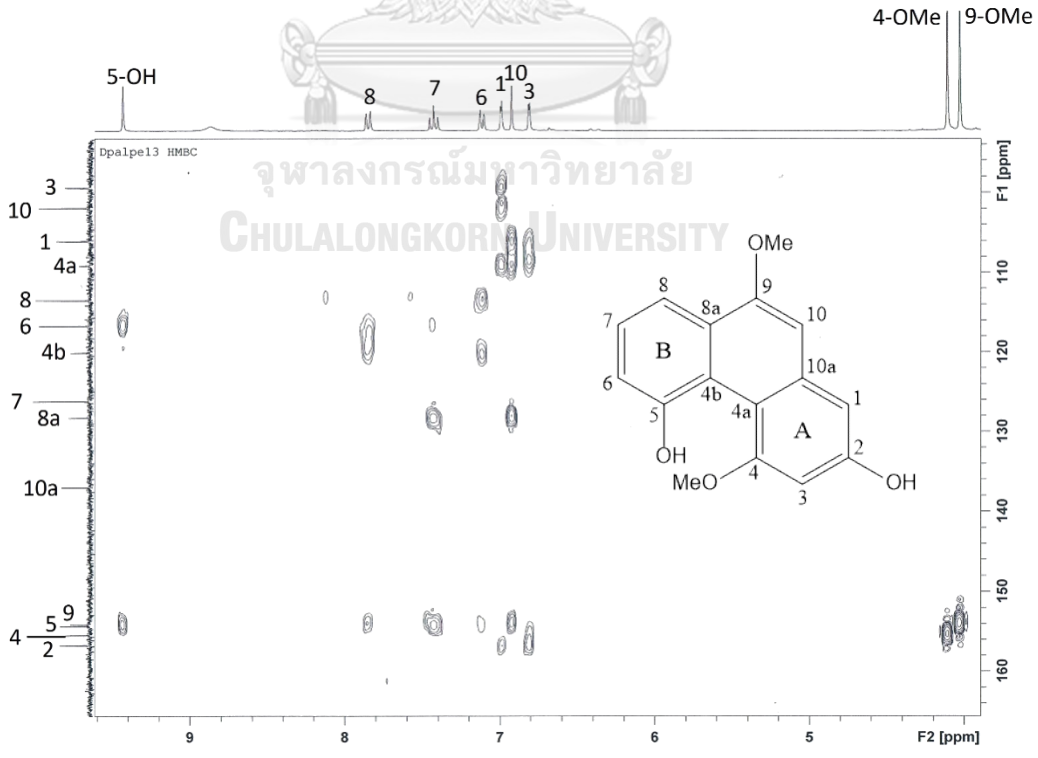

Figure 41 HMBC spectrum of compound DPB-6 (in acetone-d_6)

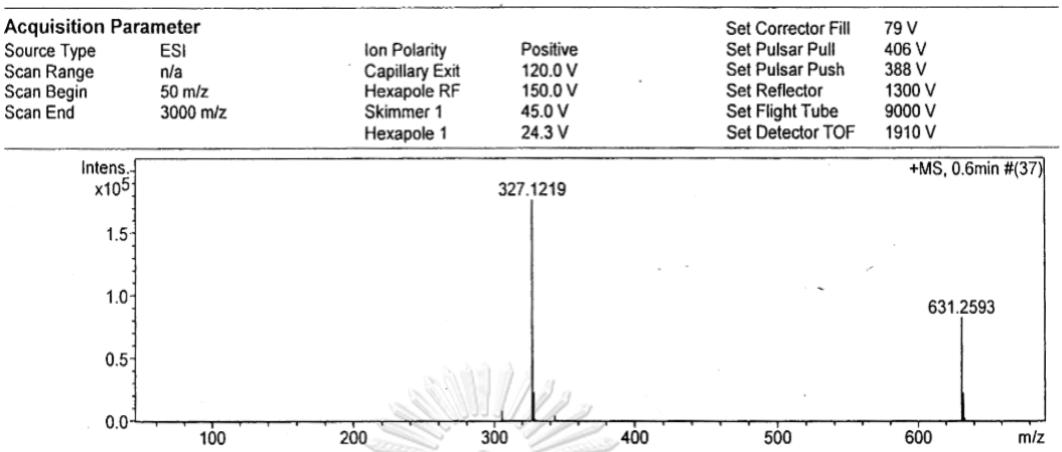

Figure 42 Mass spectrum of compound DPB-7

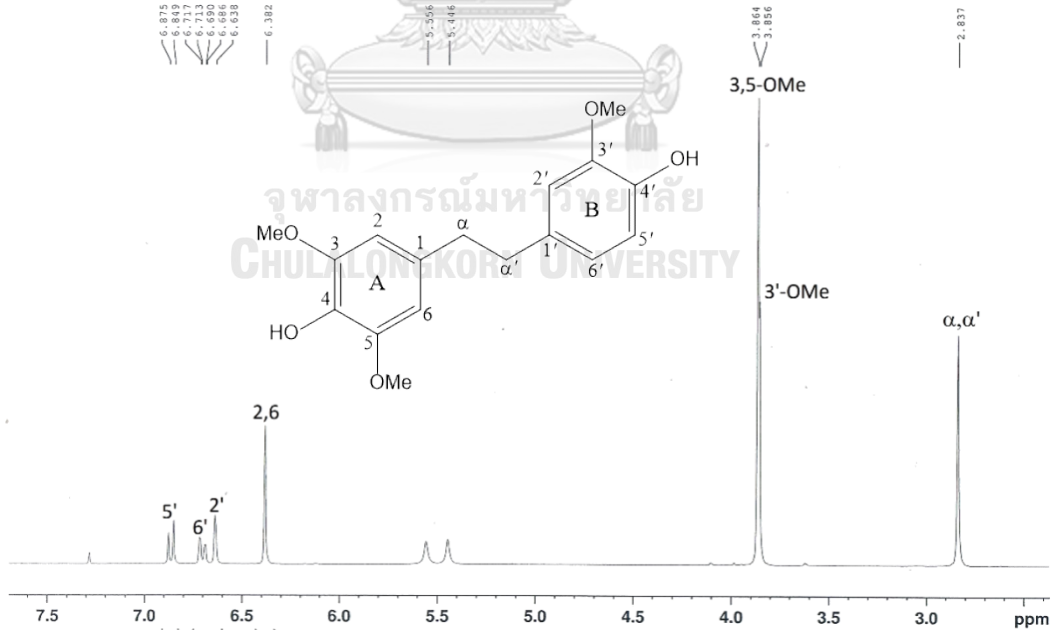

Figure 43 ^{1}H-NMR (300 MHz) spectrum of compound DPB-7 (in acetone-d_6)

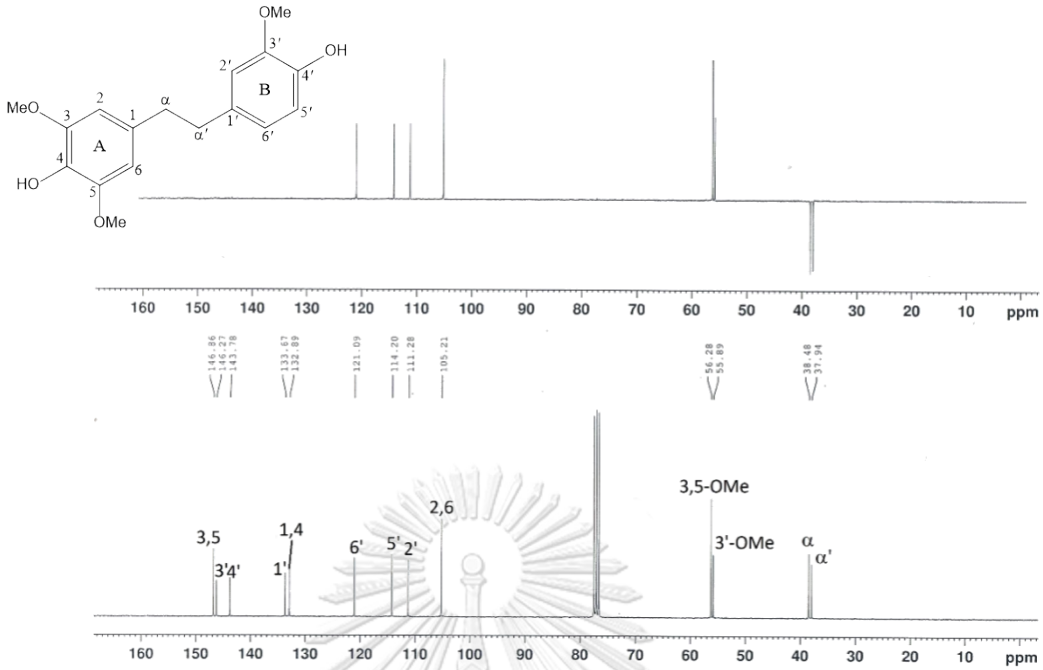

Figure 44 ^{13}C-NMR (75 MHz) and DEPT 135 spectrum of compound DPB-7 (in acetone-d_6)

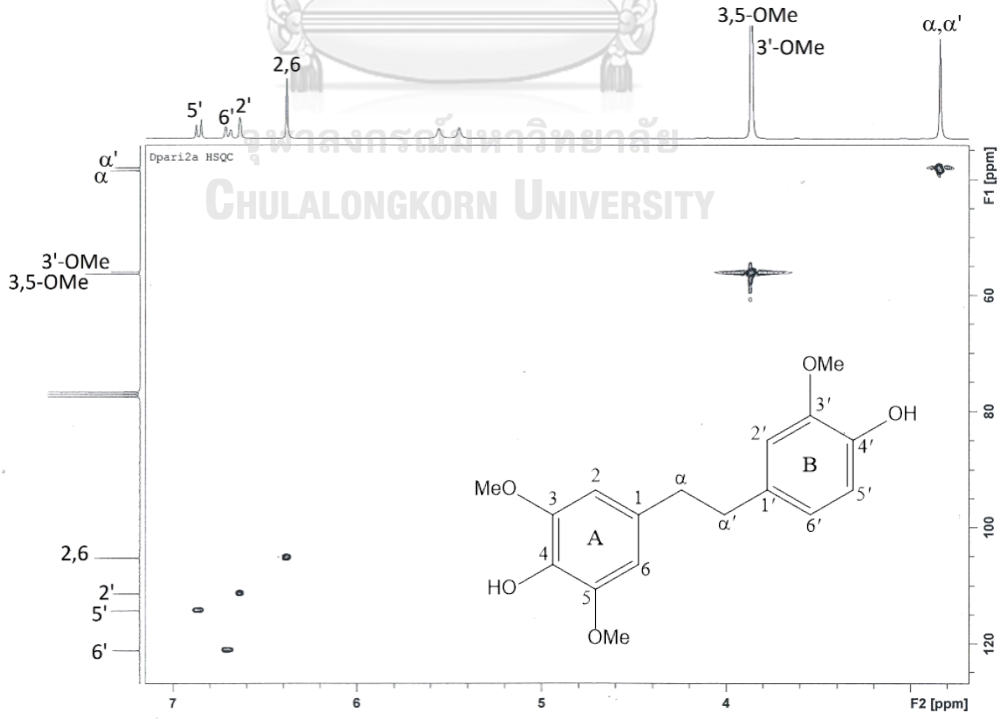

Figure 45 HSQC spectrum of compound DPB-7 (in acetone-d_6)

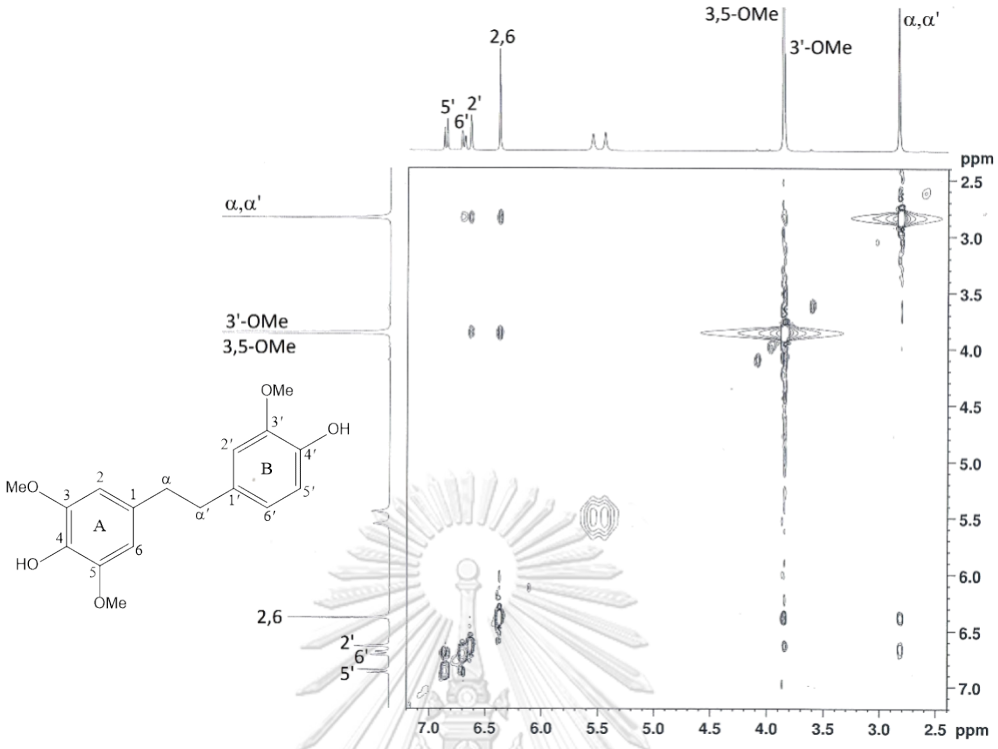

Figure 46 NOESY spectrum of compound DPB-7 (in acetone-d_6)

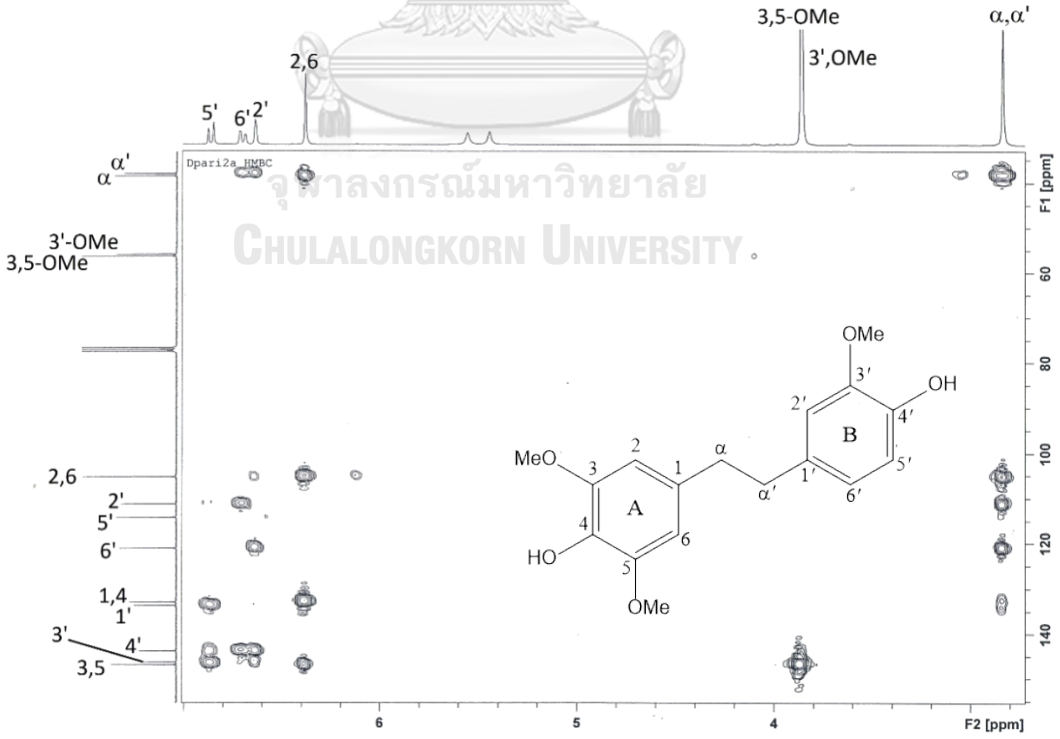

Figure 47 HMBC spectrum of compound DPB-7 (in acetone-d_6)

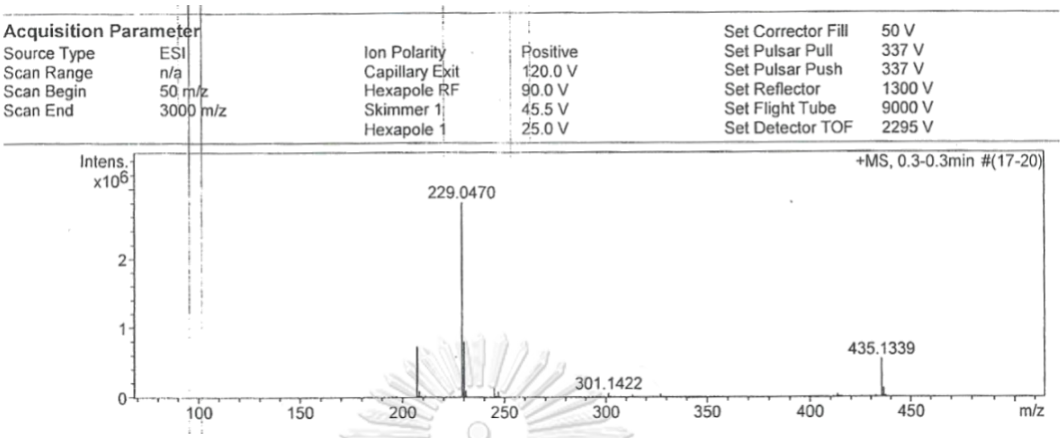

Figure 48 Mass spectrum of compound DPB-8

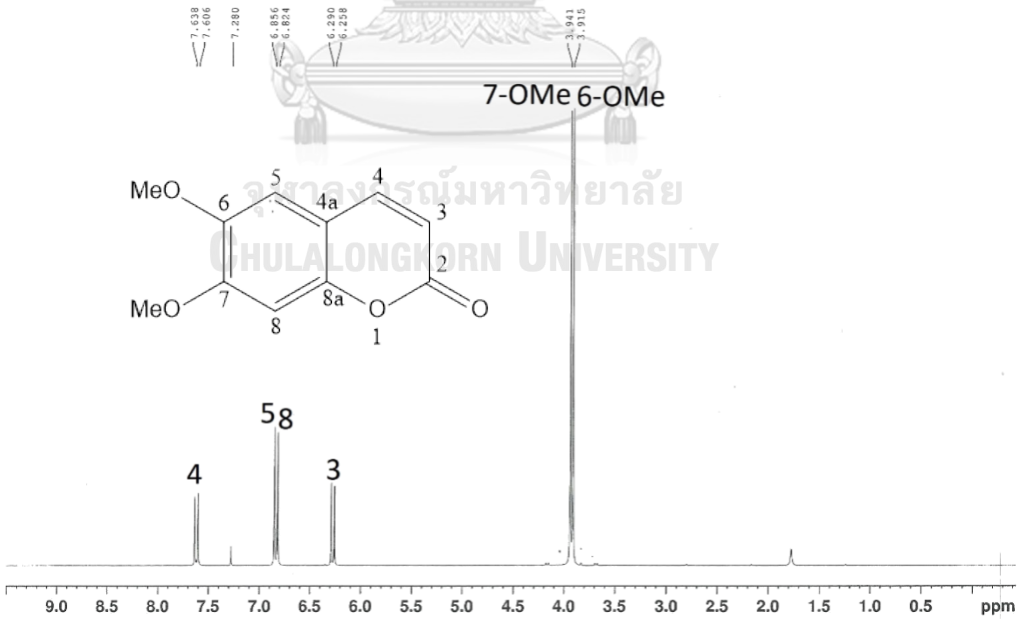

Figure 49 ^{1}H-NMR (300 MHz) spectrum of compound DPB-8 (in $CDCl_3$)

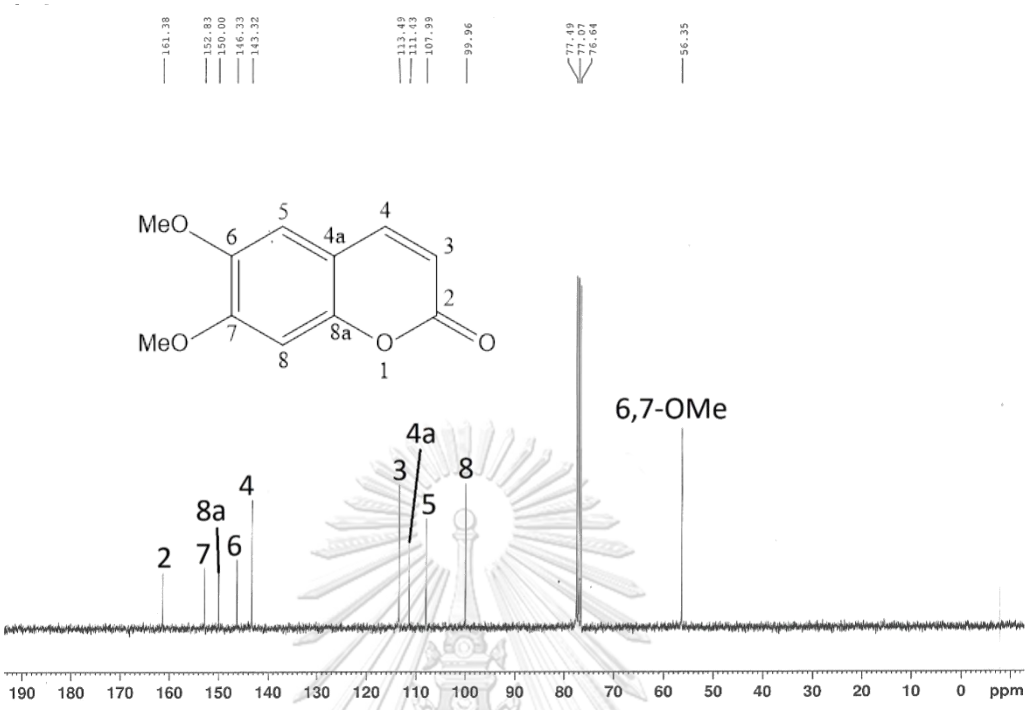

Figure 50 ^{13}C-NMR (75 MHz) spectrum of compound DPB-8 (in $CDCl_3$)

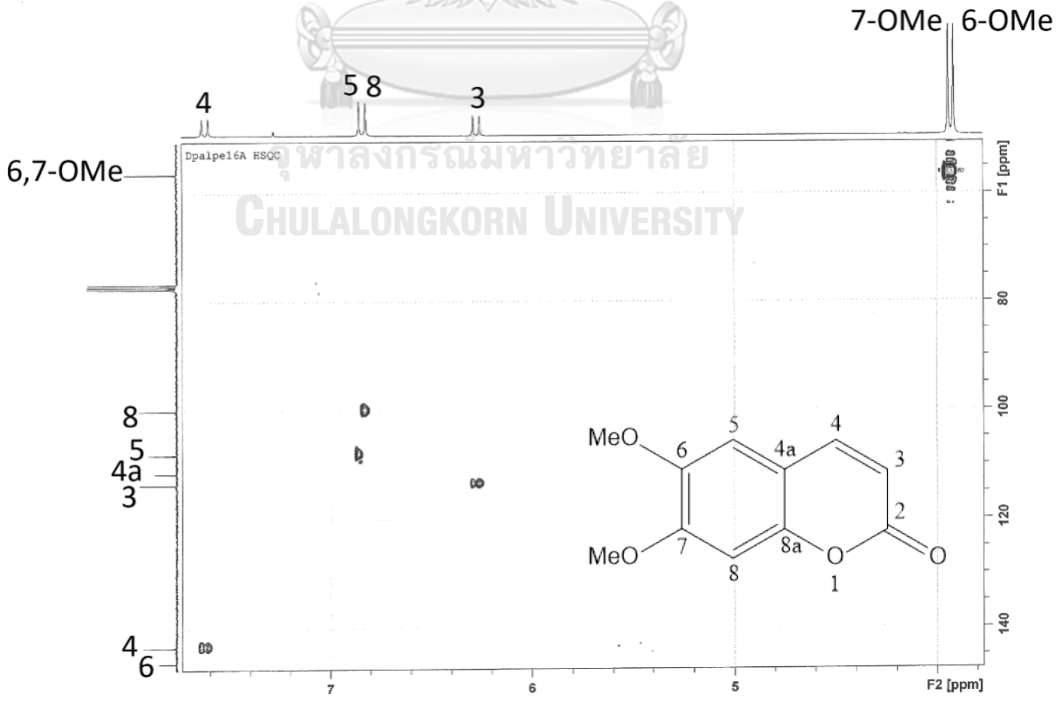

Figure 51 HSQC spectrum of compound DPB-8 (in $CDCl_3$)

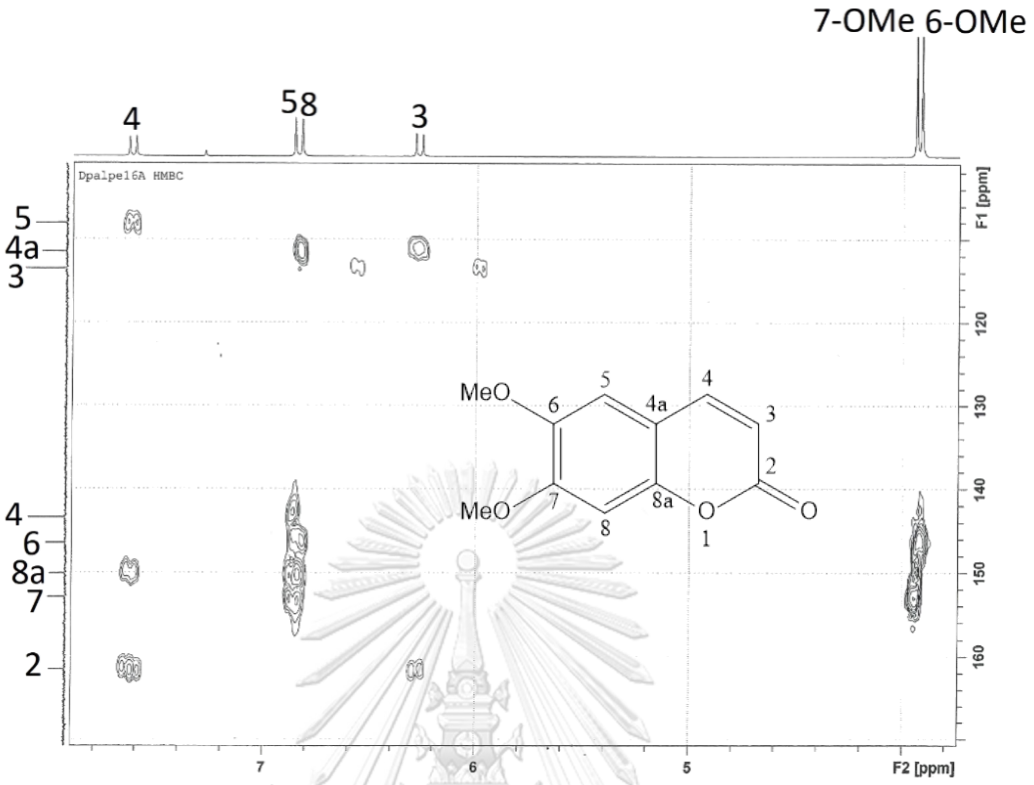

Figure 52 HMBC spectrum of compound DPB-8 (in $CDCl_3$)

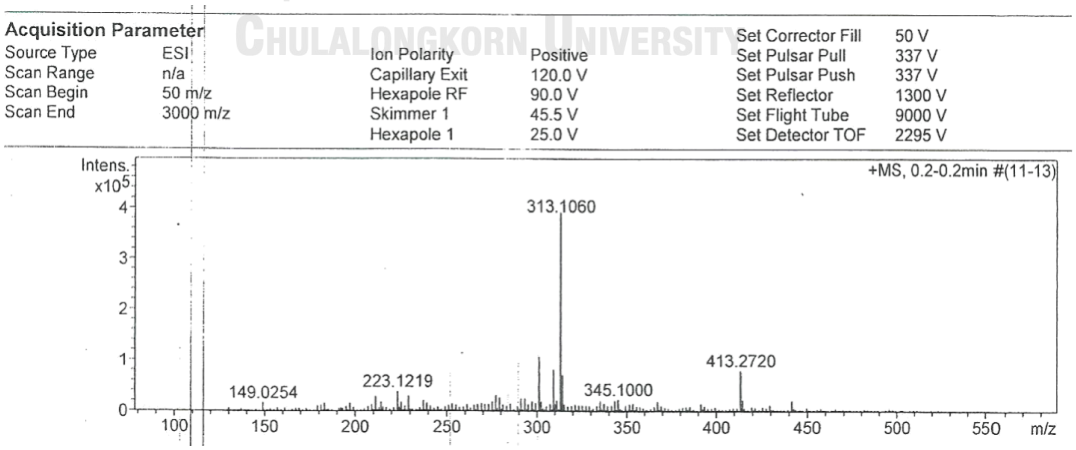

Figure 53 Mass spectrum of compound DPB-9

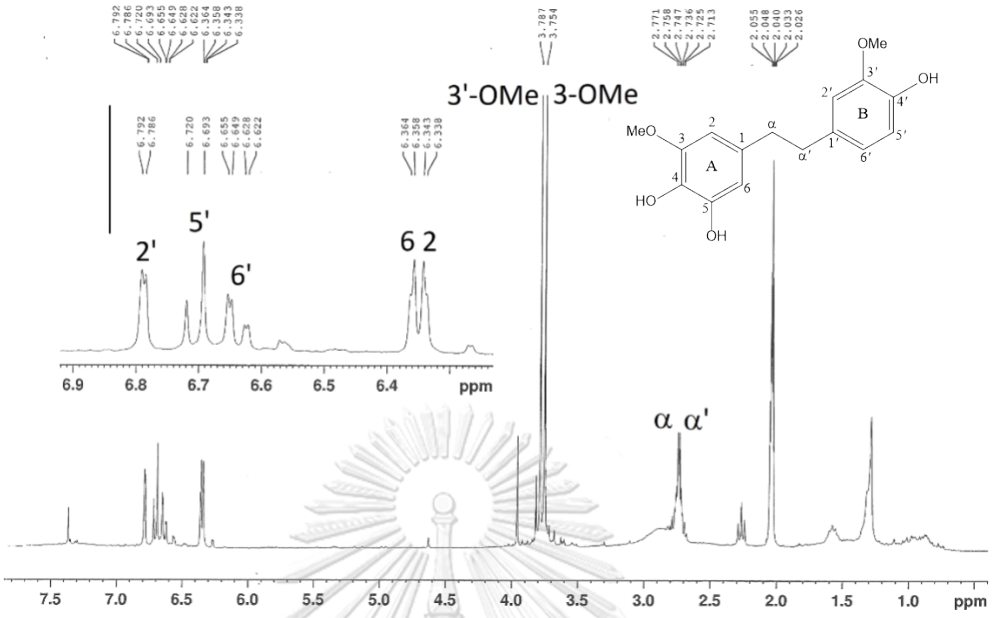

Figure 54 ^{1}H-NMR (300 MHz) spectrum of compound DPB-9 (in acetone-d_6)

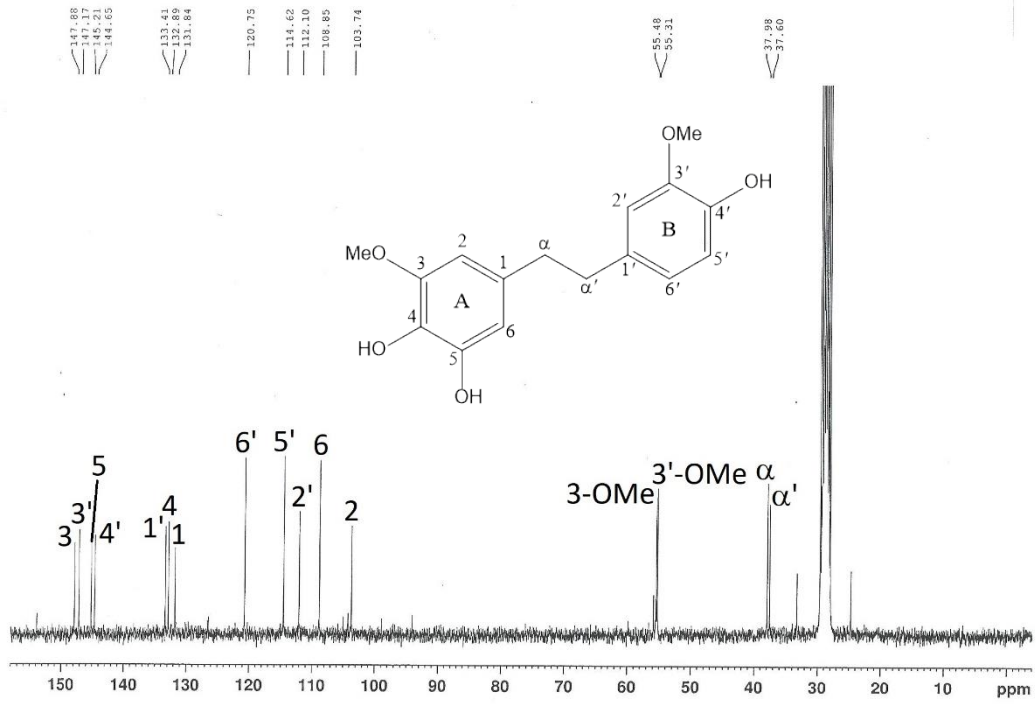

Figure 55 ^{13}C-NMR (75 MHz) spectrum of compound DPB-9 (in acetone-d_6)

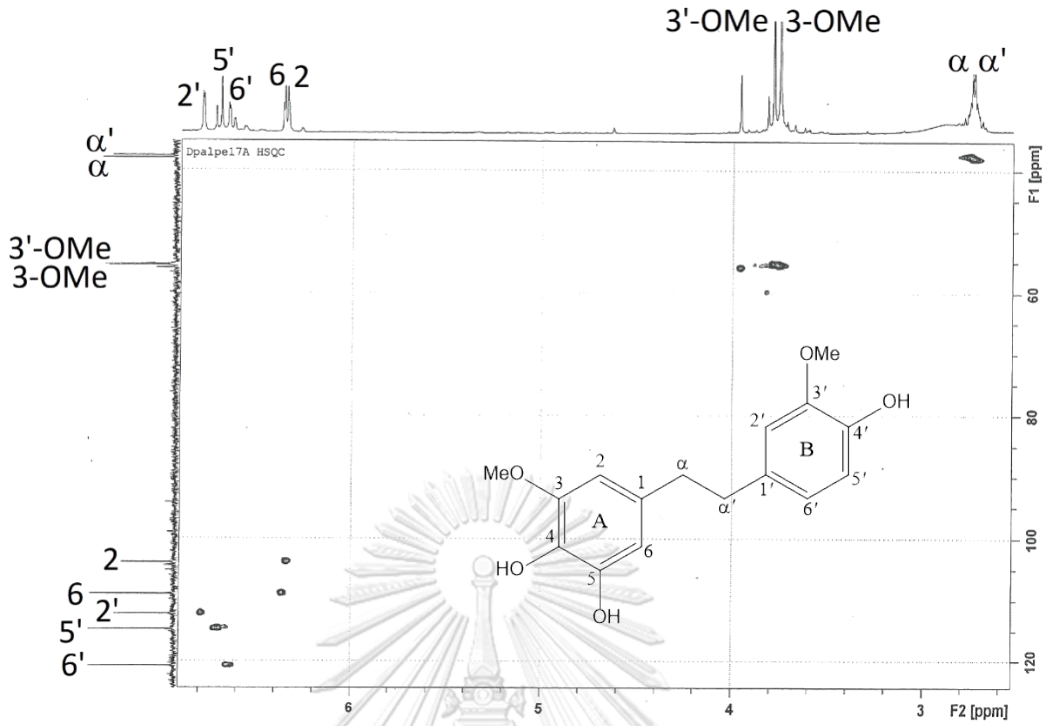

Figure 56 HSQC spectrum of compound DPB-9 (in acetone-d_6)

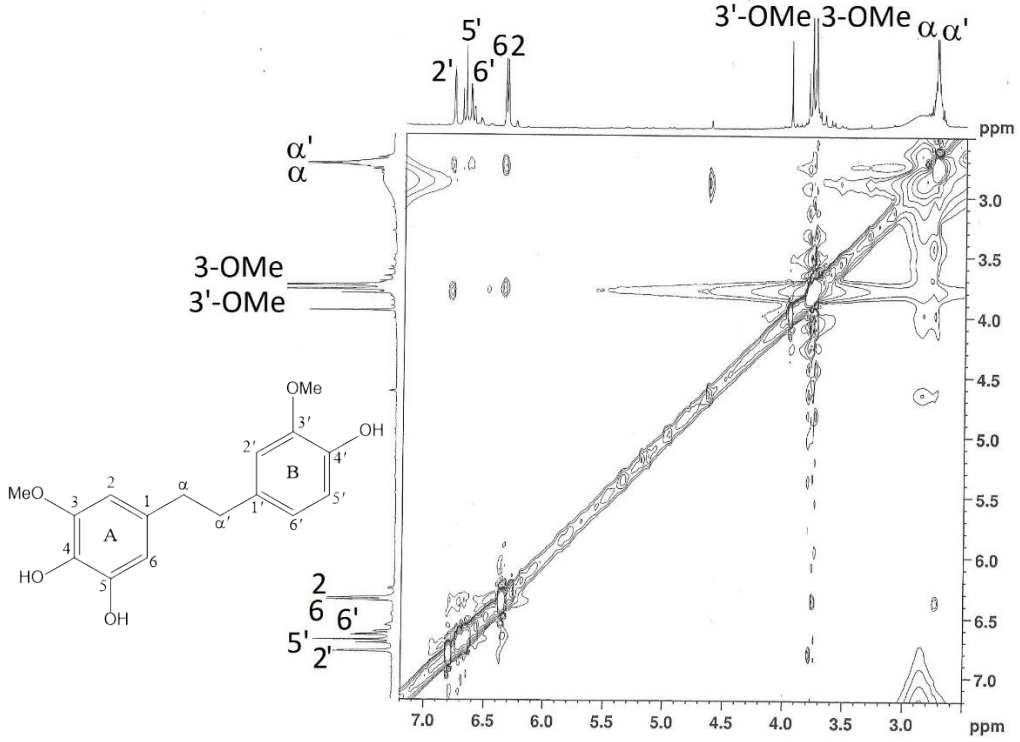

Figure 57 NOESY spectrum of compound DPB-9 (in acetone-d_6)

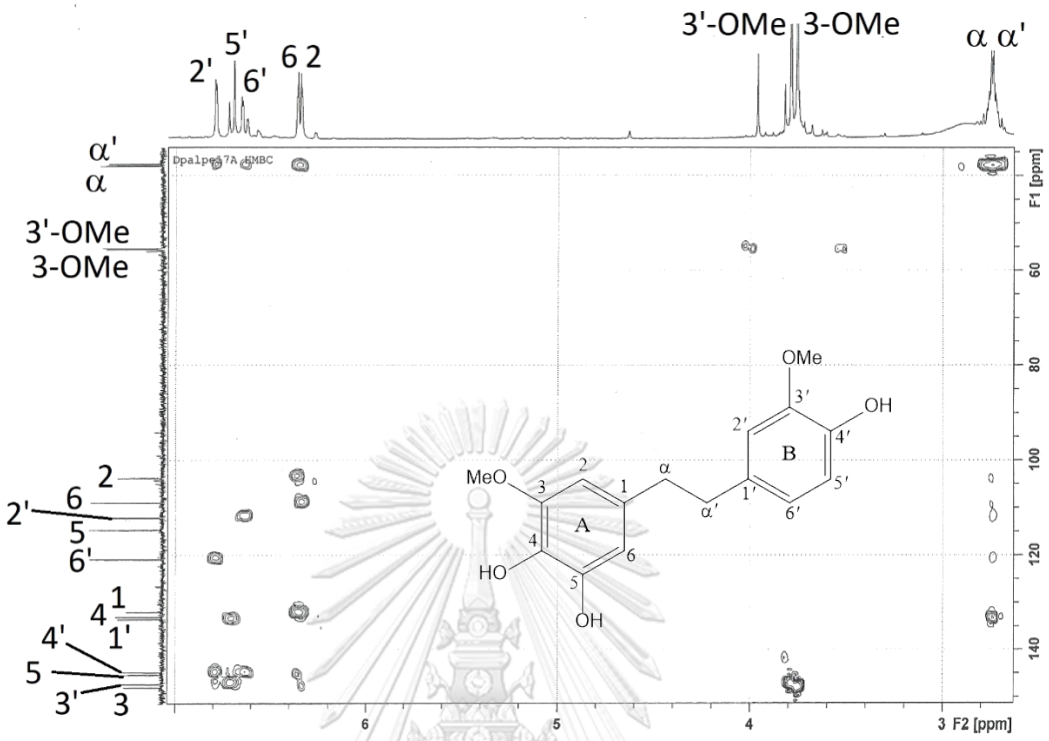

Figure 58 HMBC spectrum of compound DPB-9 (in acetone-d_6)

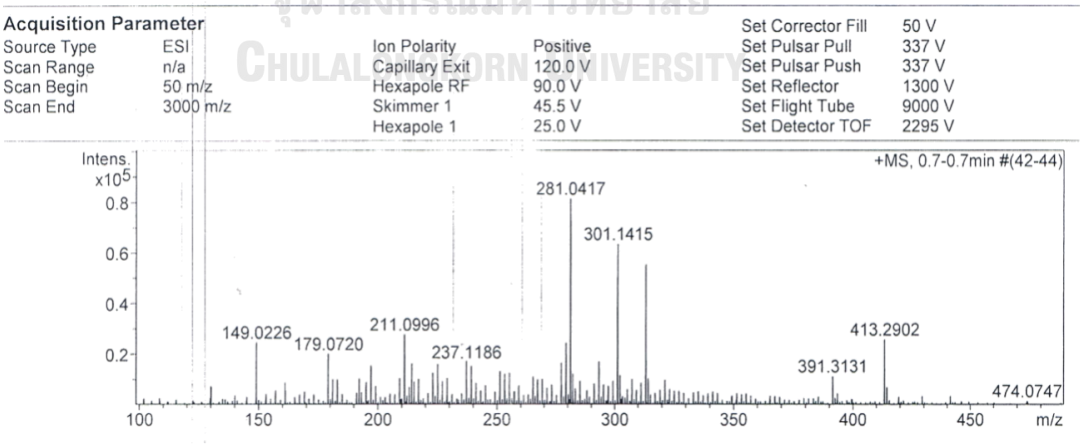

Figure 59 Mass spectrum of compound DPB-10

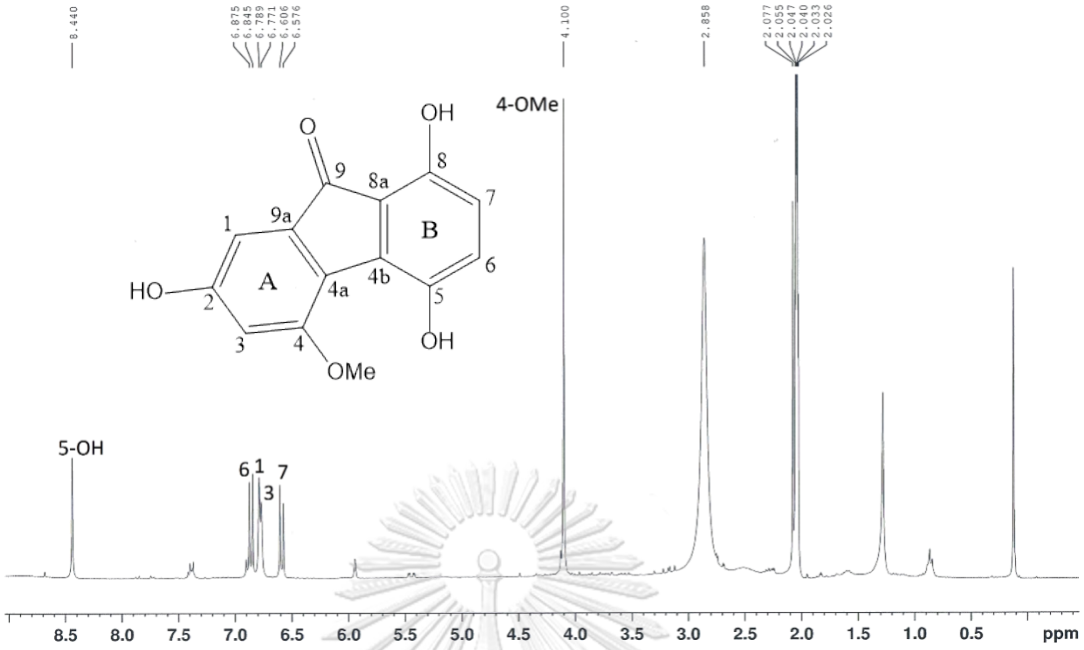

Figure 60 ^{1}H-NMR (300 MHz) spectrum of compound DPB-10 (in acetone-d_6)

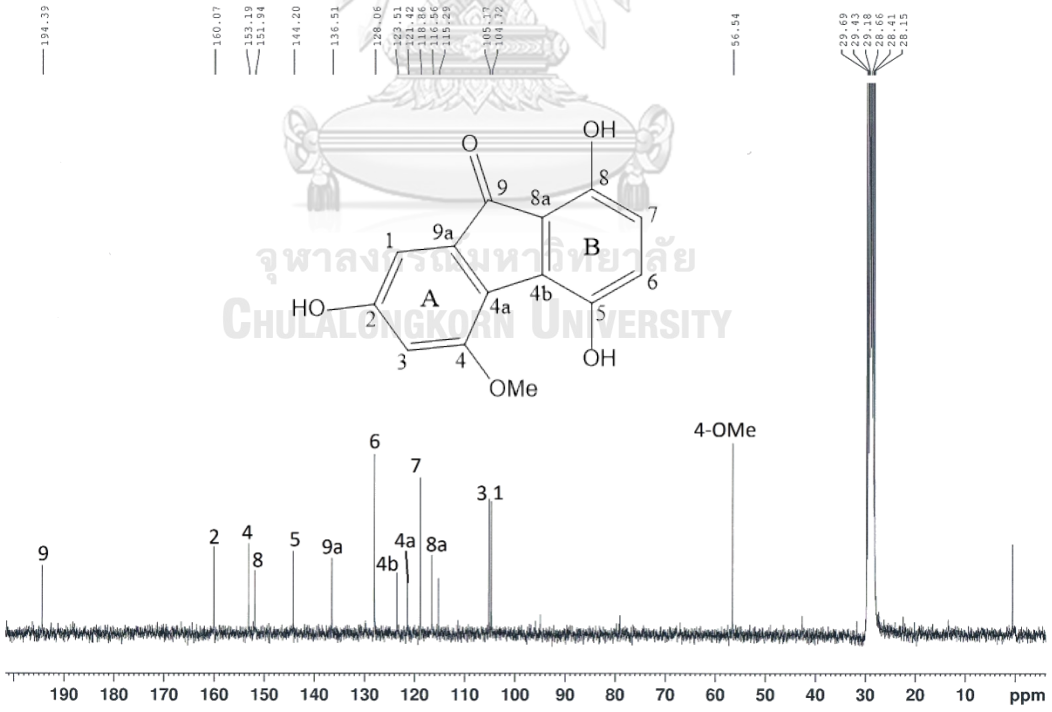

Figure 61 ^{13}C-NMR (75 MHz) spectrum of compound DPB-10 (in acetone-d_6)

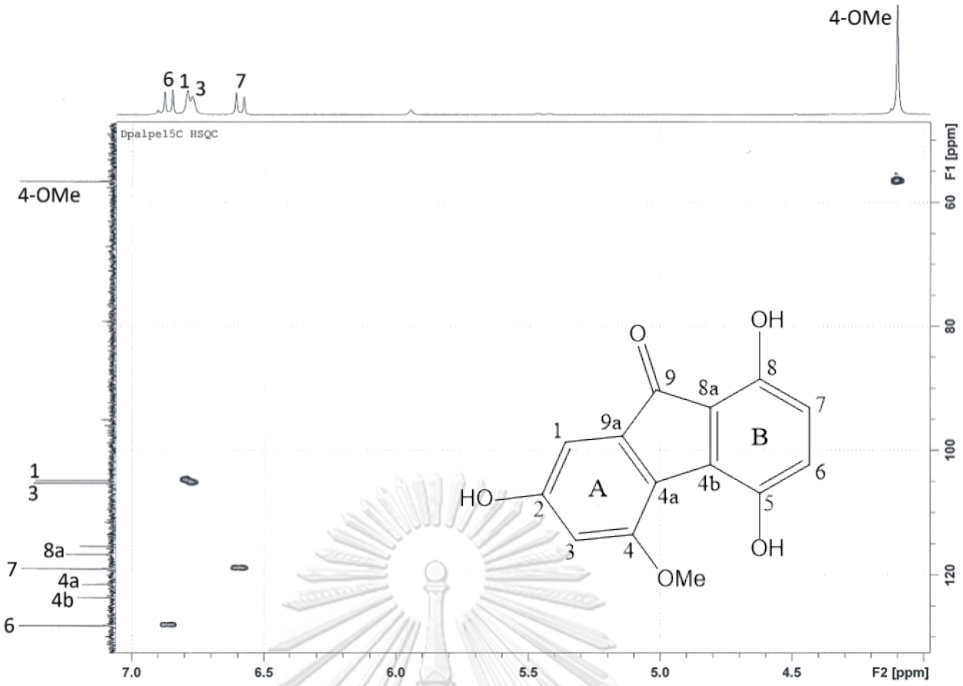

Figure 62 HSQC spectrum of compound DPB-10 (in acetone-d_6)

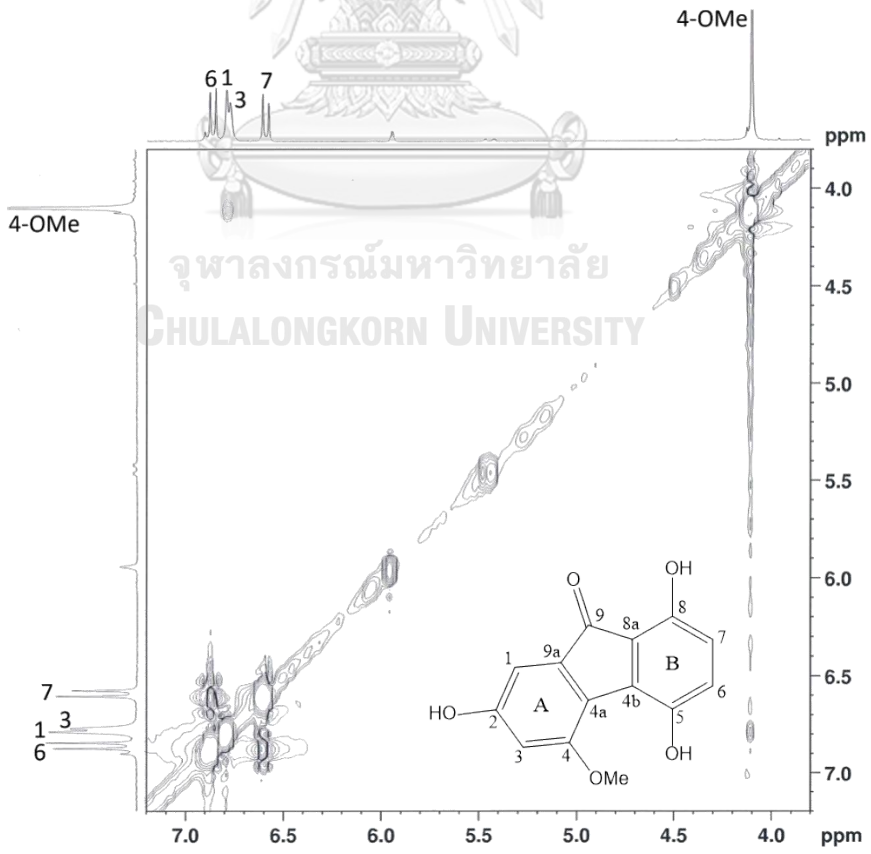

Figure 63 NOESY spectrum of compound DPB-10 (in acetone-d_6)

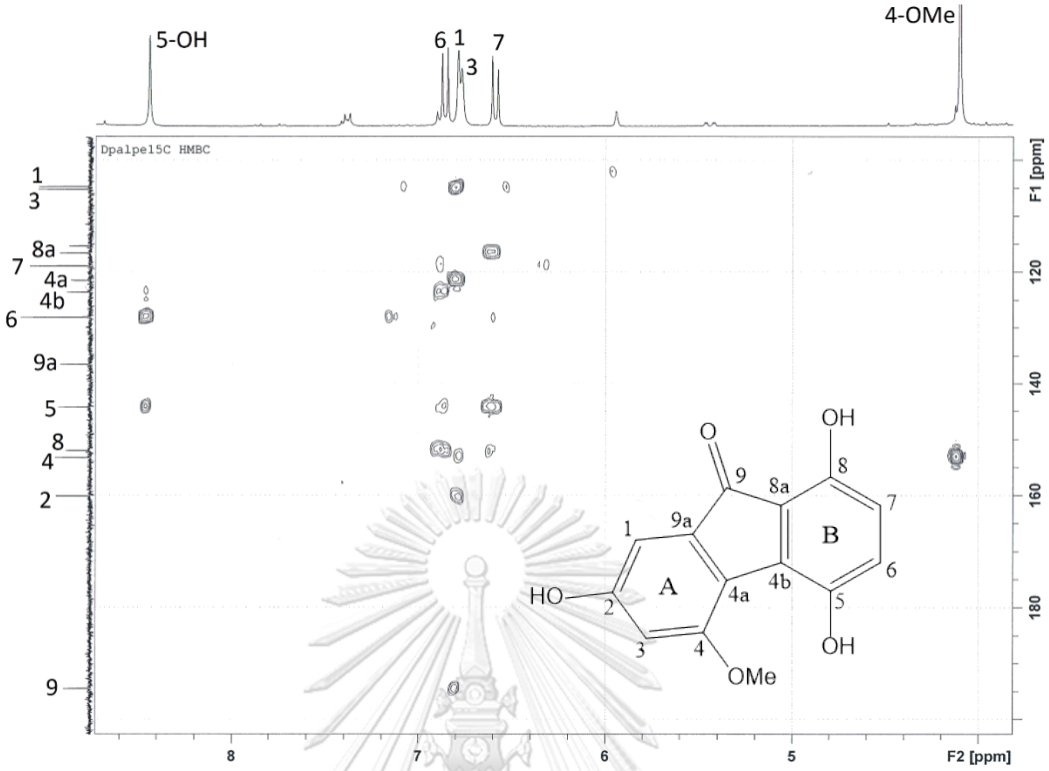

Figure 64 HMBC spectrum of compound DPB-10 (in acetone-d_6)

VITA

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Publications:

Kyokong, N., Muangnoi, C., Thaweesest, W., Kongkatitham, V., Likhitwitayawuid, K., Rojsitthisak, P., Sritularak, B. (2018). A new phenanthrene dimer from Dendrobium palpebrae. Journal of Asian Natural Products Research. Advanced online publication, DOI: 10.1080/10286020.2018.1429416.

Kongkatitham, V., Muangnoi, C., Kyokong, N., Thaweesest, W., Likhitwitayawuid, K., Rojsitthisak, P., Sritularak, B. (2018). Anti-oxidant and anti-inflammatory effects of new bibenzyl derivatives from Dendrobium parishii in hydrogen peroxide and lipopolysaccharide treated RAW264.7 cells. Phytochemistry Letters, 24, 31-38.