CHEMICAL CONSTITUENTS AND BIOLOGICAL ACTIVITIES FROM *CLAUSENA HARMANDIANA, CLAUSENA LANSIUM,* AND *CLAUSENA WALLICHII*

WISANU MANEERAT

DOCTOR OF PHILOSOPHY
IN
APPLIED CHEMISTRY

SCHOOL OF SCIENCE
MAE FAH LUANG UNIVERSITY
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Wisanu Maneerat

Thesis Title	Chemical Constituents and Biological Activities from *Clausena harmandiana*, *Clausena lansium*, and *Clausena wallichii*
Author	Wisanu Maneerat
Degree	Doctor of Philosophy (Applied Chemistry)
Advisor	Asst. Prof. Dr. Surat Laphookhieo

ABSTRACT

Phytochemical investigation and biological activity studies from *Clausena* plants including *Clausena harmandiana*, *Clausena lansium*, and *Clausena wallichii* led to the isolation and identification of twenty-one new compounds (**WM22**, **WM23**, **WM25-WM27**, **WM29**, **WM32-WM35**, **WM37**, **WM42**, **WM56-WM54**, **WM57**, **WM62**, and **WM66**) along with fifty-three known compounds (**WM1-WM21**, **WM24**, **WM28**, **WM30**, **WM32**, **WM36**, **WM38**, **WM39-WM41**, **WM43-WM47**, and **WM67-WM74**). All structures were characterized by spectroscopic methods, including NMR, UV, IR, and MS spectral data for structural characterization. Some of isolated compounds were exhibited cytotoxicity and antibacterial activities.

Three new carbazole alkaloids, harmandianamines A (**WM50**), B (**WM49**), and C (**WM37**), together with fifteen known compounds (**WM3**, **WM5**, **WM14**, **WM15**, **WM36**, **WM38**, **WM39**, **WM43-WM48**, **WM70**, and **WM71**) were isolated from the twigs of *Clausena harmandiana*. The antibacterial activity against *Escherichia coli* TISTR 780, *Salmonella typhimurium* TISTR 292, *Staphylococcus aureus* TISTR 1466, and methicillin-resistant *Staphylococcus aureus* (MRSA) SK1

ofsome isolated compounds were also evaluated. Compound **WM47** exhibited significant antibacterial activity against MRSA SK1 with an MIC value of 0.25 μg/mL which was higher than that of the standard drug, vancomycin (MIC value = 1 μg/mL) whereas compounds **WM44** and **WM46** showed strong activity with MIC values of 4 and 8 μg/mL, respectively. Only compound **WM44** showed strong antibacterial activity against *Staphylococcus aureus* TISTR 1466 with an MIC value of 4 μg/mL

A new phenylpropanoid derivative, harmandianone (**WM66**), along with five known compounds (**WM67**–**WM70** and **WM74**) were isolated from the acetone extract of *Clausena harmandiana* fruits. Compounds **WM66**, **WM68**-**WM70**, and **WM74** demonstrated weak antibacterial activities against *Escherichia coli* TISTR 780, *Salmonella typhimurium* TISTR 292, *Staphylococcus aureus* TISTR 1466 and methicillin-resistant *Staphylococcus aureus* (MRSA) SK1, with MIC values between 64 and 128 μg/mL.

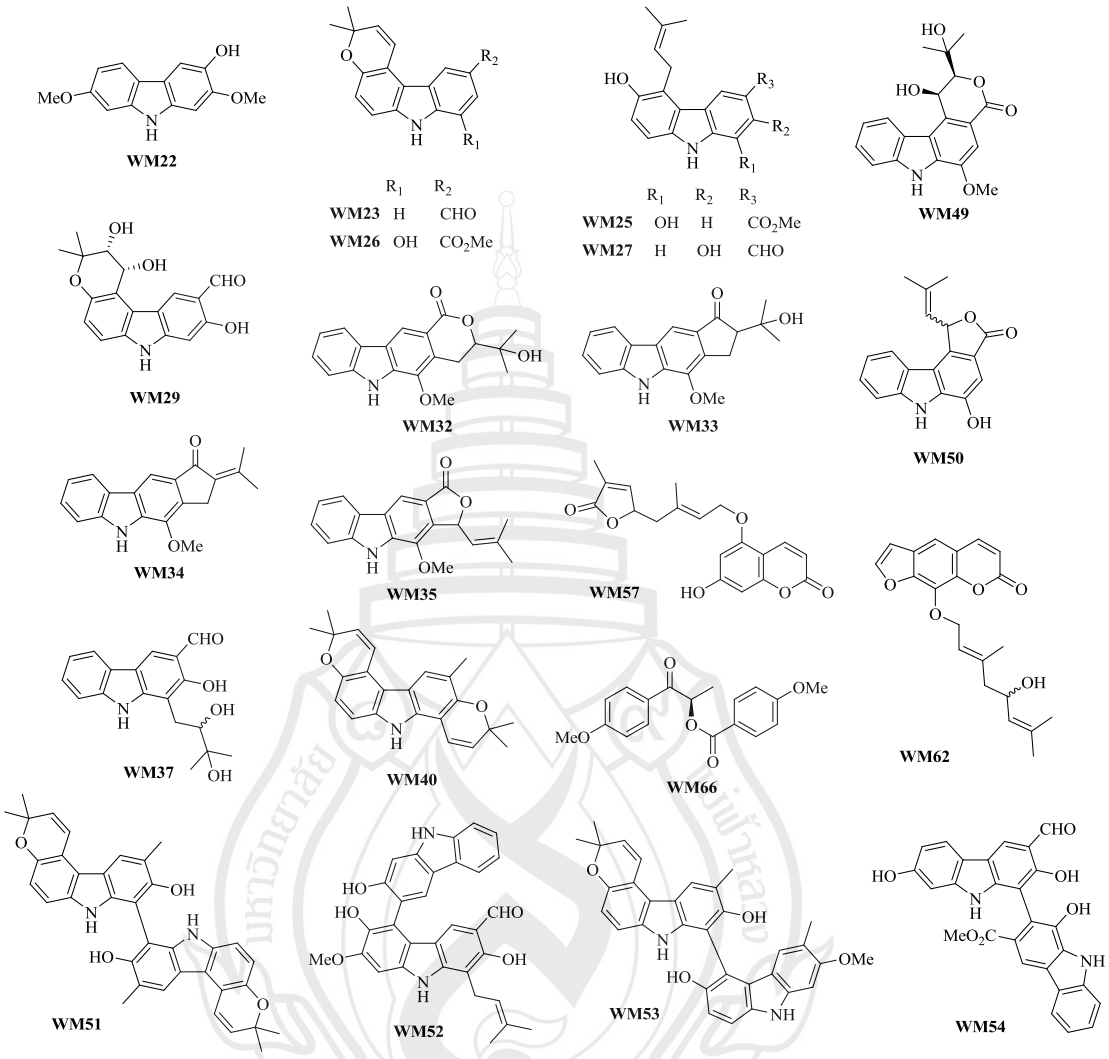
Three new carbazole alkaloids, mafaicheenamines A, (**WM32**), D (**WM34**), and E (**WM35**), together with eleven known compounds (**WM3**, **WM4**, **WM10**, **WM11**, **WM16**, **WM17**, **WM30**, **WM55**, **WM59**, **WM63**, and **WM64**) were isolated from the roots of *Clausena lansium*. Some of the isolates were evaluated for their cytotoxicity against three human cancer cell lines including oral cavity cancer (KB), breast cancer (MCF-7), and small-cell lung cancer (NCI-H187).

Four new compounds including two carbazole alkaloids, mafaicheenamines A (**WM32**) and C (**WM33**) and two new coumarins, clausenalansimins A (**WM57**) and B (**WM62**), along with fourteen known compounds (**WM4**, **WM16**, **WM17**, **WM30**, **WM31**, **WM58** – **WM61**, **WM63**, **WM64**, **WM56**, **WM65**, and **WM73**) were isolated from the twigs of *C. lansium*. Some of the isolated compounds were evaluated for their cytotoxicity against three human cancer cell lines including oral

cavity cancer (KB), breast cancer (MCF7), and small-cell lung cancer (NCI-H187) and antibacterial activity.

Six new carbazole alkaloids, clausenawallines A (**WM51**), B (**WM52**), C (**WM42**), D (**WM22**), E (**WM53**), and F (**WM54**), along with sixteen known compounds (**WM2**, **WM5**, **WM6**, **WM8**, **WM9**, **WM12**, **WM13**, **WM17**-**WM19**, **WM21**, **WM28**, **WM36**, **WM39**, **WM40**, and **WM41**) were isolated from the roots of *Clausena wallichii*. Compounds **WM40**, **WM52**, and **WM53** exhibited significant antibacterial activity against *Staphylococcus aureus* TISTR 1466 and methicillin-resistant *Staphylococcus aureus* (MRSA) SK1 with MIC values in the range of 4-16 μg/mL, whereas compound **WM54** showed the highest cytotoxicity against oral cavity cancer (KB) and small-cell lung cancer (NCI-H187) with IC_{50} values of 10.2 and 4.5 μM, respectively.

Five carbazole alkaloids, clausenawallines G (**WM25**), H (**WM27**), I (**WM23**), J (**WM26**), and K (**WM29**), along with twelve known alkaloids (**WM1**, **WM2**, **WM6**, **WM14**-**WM16**, **WM19**, **WM20**, **WM24**, **WM28**, **WM79**, and **WM80**) were isolated from the twigs of *Clausena wallichii*. Their structures were established using spectroscopic methods. The antibacterial activity of compounds **WM23**, **WM25**-**WM27**, and **WM29** were also evaluated.



Keywords: Rutaceae/*Clausena*/*Clausena harmandiana*/*Clausena lansium*/*Clausena wallichii*/Cytotoxicity/Antibacterial activity

TABLE OF CONTENTS

TABLE OF CONTENTS (continued)

LIST OF TABLES

LIST OF TABLES (continued)

Table **Page**

LIST OF FIGURES

ABBREVIATIONS AND SYMBOLS

s	=	singlet
d	=	doublet
t	=	triplet
q	=	quartet
m	=	multiplet
dd	=	doublet of doublet
ddd	=	doublet of doublet of doublet
t	=	triplet
td	=	triplet of doublet
br s	=	broad singlet
g	=	Gram
nm	=	Nanometer
mp	=	Melting Point
cm^{-1}	=	Reciprocol Centimeter (wave number)
δ	=	Chemical Shift Relative to TMS
J	=	Coupling Constant
$[\alpha]_D$	=	Specific Rotation
λ_{max}	=	Maximum Wavelength
ν	=	Absorption Frequencies
m/z	=	a Value of Mass Divided by Charge
°C	=	Degree Celsius
MHz	=	Megahertz
ppm	=	Part per Million
c	=	Concentration
IR	=	Infrared
UV	=	Ultraviolet-visible

ABBREVIATIONS AND SYMBOLS (continued)

HR-EI-MS	=	High Resolution Electron Impact Mass Spectroscopy
ESI-TOF-MS	=	Electrospray Ionization Time-of-Fight Mass Spectroscopy
NMR	=	Nuclear Magnetic Resonance
2D NMR	=	Two Dimensional Nuclear Magnetic Resonance
COSY	=	Correlation Spectroscopy
DEPT	=	Distortionless Enhancement by Polarization Transfer
HMBC	=	Heteronuclear Multiple Bond Correlation
HMQC	=	Heteronuclear Multiple Quantum Coherence
CC	=	Column Chromatography
QCC	=	Quick Column Chromatography
PLC	=	Preparative Thin Layer Chromatography
TMS	=	Tetramethylsilane
$CDCl_3$	=	Deuterochloroform

CHAPTER 1

INTRODUCTION

1.1 Botanical Description of *Clausena* Genus

Clausena plants belonging to the Rutacea family is shrubs or trees, unarmed, without rust-colored villosulous indumentum on terminal and axillary buds or young inflorescences. Leaves are alternate, odd-pinnate. Inflorescences are terminal or axillary, paniculate or in loose racemes. Flowers are bisexual or very rarely female, globose to pyriform or rarely ovoid in bud which containing 4 or 5 sepals, 4 or 5 petals, and 8 or 10 stamens. Fruits are a berry, with neither pulp nor pulp vesicles; endocarp membranous. Seeds have membranous seed coat. (Swingle & Reece, 1996)

Clausena genus consists of twenty-three species such as *C. abyssinica*, *C. anisata*, *C. anisum-olens*, *C. brevistyla*, *C. cambodiana*, *C. dunniana*, *C. excavata*, *C. guillauminii*, *C. harmandiana*, *C. heptaphylla*, *C. inaequalis*, *C. indica*, *C. lansium*, *C. laxiflora*, *C. lenis*, *C. mollis*, *C. pentaphylla*, *C. suffruitcosa*, *C. todayensis*, *C. vistita*, *C. wallichii*, and *C. willdenovii*. However, only six species were found in Thailand including *C. excavata*, *C. guillauminii*, *C. harmandiana*, *C. lenis*, *C. lansium*, and *C. wallichii* (Smitinand, 2001).

1.1.1 *Clausena harmandiana* (Pierre)

C. harmandiana (Pierre) is small evergreen trees of shrubs. Branches rounded, pubescent. Leaves are imparipinnate, with 6-9 opposite or alternate leaflets, which are subdeltoid, ovate-acuminate, obtuse at both ends, 5-14 cm long, 5-8 cm wide, submembranous, coriaceous, with 7-8 pairs of small lateral veins. Inflorescences

terminal, pubescent, 10-20 cm long, much branched with rather large (5-6 mm diam.), sessile flowers. Sepals 1 mm long, very coriaceous, pubescent on the outside and ciliate. Petals 3.5-4 mm long, very concave, obovate, veinless, red spotted. Stamens 7-10, 2.5 mm long, with the filaments flattened below and subulate above, longer than the anther, which is oval and without an a pical gland. Disk cupuliform. Ovary 2.5 mm long, with 5 locules, each carrying on the outside 2 large glands. Ovules 2 in each locule (Swingle & Reece, 1996). Several parts of this plant have been used as traditional medicines for the treatment of illnesses, stomach pains and headaches (Thongthoom, Songsiang, Phaosiri & Yenjai, 2010). The young leaves of the plant are edible and are used as a vegetable in Thailand (Songsiang, Thongthoom, Booonyarat & Yenjai, 2011).

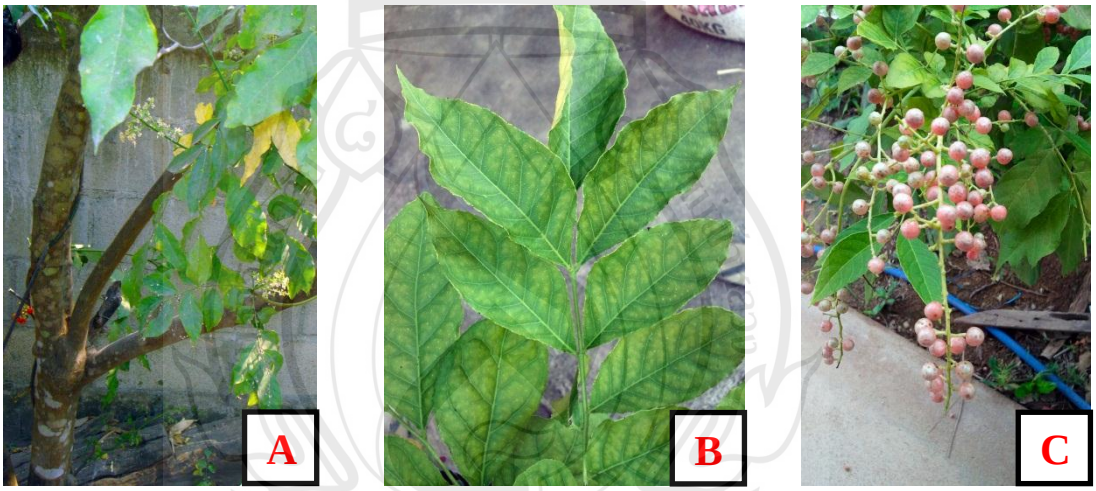


Figure 1.1 Stems (A), Leaves (B), and Fruits (C) of *C. harmandiana*

1.1.2 *Clausena lansium* (Lour.) Skeels

Clausena lansium (Lour.) Skeels or “wampee” have been known in Thai local name as “mafaicheen”. Its tree or shrub, branches at first pubescent or puberulous, leaves 5-7-9-foliolate, 20–25 cm long, leaflets ovate-elliptic, lanceolate or ovate, with petiolules 2–6 mm, more or less oblique at the base, apex obtuse or subemarginate, sometimes almost mucronulate, slightly acuminate, margin undulate-crenate or

slightly serrulate, becoming glabrous or glabrescent, the midrib and veins often sparsely scabrous, glabrescent below, terminal leaflet often 6-10 cm long, flowers subsessile or shortly pedicellate, in many-flowered cymose panicles, lobes triangular or ovate, stamens 10, alternate ones shorter, filaments dilated above the middle, flattened, subulate above, anthers oblong or elliptic, cordate-sagittate at base, with a dorsal gland, ovary shortly stipitate, glandular, very often 5-locular ovules in pairs [in each locule], superposed, the upper one peltate on the side or toward the base, the lower one subpendulous, style very short, distinct, glabrous above, stigma 5-lobed, slightly wider than style, fruit usually with 5 locules, 5-seeded, or be abortion 1-seeded, or sterile, ovoid-globose, pubescent, 1 in. (25 cm) or less diam., cotyledons fleshy, equal (Swingle & Reece, 1996). Several parts of this plant have been used as traditional medicines in China, Taiwan, and Philippines for treatments of coughs, asthma, ulcers, and gastrointestinal diseases (Lin 1989, Adebajo et al., 2009)

Figure 1.2 Leaves (A), Fruits (B), and Seeds (C) of *C. lansium*

1.1.3 *Clausena wallichii*

Clausena wallichii is a small tree, leaves with the rachis narrowly winged; leaflets rhomboid-lanceolate, or oblong, acumainate, glabrous, margins crenulate. Inflorescences paniculate, many-flowered, branches close together, flowers few. Calyx 5-merous, lobes ovate. Petals 5, margins slightly imbricate in the bud, thin. Stamens 10, free, filaments thickened at the middle, at first slightly arched below.

Orary short and narrowly stalked, 5- (or 4-) locular, ovules obliquely superimposed. Style very short, furrowed, equaling the stigma in width (Swingle & Reece, 1996).

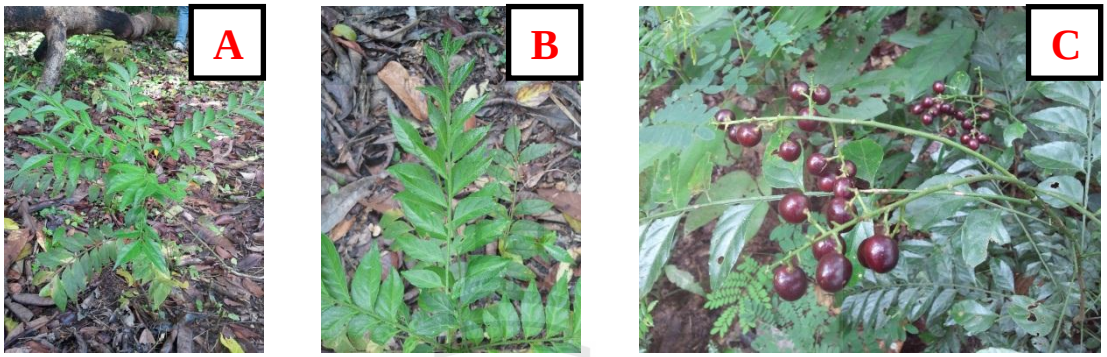


Figure 1.3 Tree (A), Leaves (B), and Fruits (C) of *C. wallichii*

1.2 Constituents Isolated from *Clausena* Plants

Clausena genus is well known to be rich source of amides, carbazole alkaloids, coumarins, and limonoids. The information from SciFider scholar database reveals several types of compounds as presented in the plants of *Clausena* genus as summarized in Table 1.1.

Table 1.1 Compounds isolated from *Clausena* genus

A = Amides **B** = Carbazole alkaloids **C** = Coumarins
D = Glycoside **E** = Limonoids **F** = Peptides
G = Phenylpropanoid **H** = Quinolene **I** = Quinolone
J = Quinones **K** = Terpenes

Plant	Part	Compound	Biliography
C. anisata	Aerial	2′,3′-Epoxyanisolactone (**C24**)	Lakshmi, Prakash,
		Anisolactone (**C23**)	Raj, Kapil, &
		Imperatorin (**C26**)	Popli, 1984
		Indicolactone (**C32**)	
		Xanthotoxol (**C25**)	
	Roots	Anisatin (**B60**)	Okorie, 1975
		Chalepin (**C94**)	
		Clausanitin (**B59**)	
		Coumarrayin (**C7**)	
		Imperatorin (**C26**)	
	Root barks	3-(1,1-Dimethyallyl)-xanthoxyletin (**C102**)	Mester, Szendrei & Reisch, 1997
		Chalepin (**C94**)	
		Coumarrayin (**C7**)	
		Imperatorin (**C26**)	
		Osthol (**C6**)	

Table 1.1 (Continued)

Plant	Part	Compound	Biliography
C. anisata	Stem barks and roots	Xanthoxyletin (**C14**) 3-(1,1)-Dimethyallyl-Xanthoxyletin (**C102**) Anisocoumarin A (**C93**) Anisocoumarin B (**C3**) Anisocoumarin C (**C95**) Anisocoumarin D (**C96**) Gravelliferone methyl ether (**C91**) Heliettin (**C98**) Imperatorin (**C26**) Swietenocoumarin I (**C92**)	Ngadjui Ayafor, Sondengam & Connolly, 1989a
		Xanthoxyletin (**C14**) Clausenarin (**E4**) Clausenolide (**E1**) Clausenolide-1-ethyl ester (**E3**) Zapoterin (**E5**)	Ngadjui, Ayafor & Sondengam, 1989b

Table 1.1 (Continued)

Plant	Part	Compound	Biliography
C. anisata	Stem barks and roots	Heptaphylline (**B48**) Ekeberginine (**B63**) Girinimbine (**B68**) *O*-Demethylmurrayanine (**B4**) 3-Methylcarbazole (**B1**) *N*-Methylswietenidine B (**I2**)	Ngadjui, Ayafor, Sondengam & Connolly, 1989a
		Aurantiamide acetate (**A15**) Ekeberginine (**B63**) Girinimbine (**B68**) Murrayamine A (**B69**) *N*-Benzoylphenylalaninyl-*N*-benzoylphenylalaninate (**A16**)	Songue, Kouam, Dongo, Mpondo & White, 2012
	Stem barks	Clausenine (**B27**) Clausenol (**B23**)	Charkraborty, Chowdhury & Battacharyya, 1995
	Stems	Clausamine B (**B91**) Clausamine C (**B92**) Clausamine D (**B64**) Clausamine E (**B66**)	Ito, et al., 2009

Table 1.1 (Continued)

Plant	Part	Compound	Biliography
C. anisata	Stems	Clausine F (**B62**)	Ito, et al., 2009
		Furanoclausamine A (**B93**)	
		Furanoclausamine B (**B94**)	
		Glycosinine (**B12**)	
		Mukonal (**B10**)	
		Mukonidine (**B11**)	
	Branches	Clausamine A (**B90**)	Ito, Katsuno,
		Clausamine B (**B91**)	Ruangrungsi &
		Clausamine C (**B92**)	Furukawa, 1998
		Clausine F (**B62**)	
		Clausamine A (**B90**)	Ito et al., 2000
		Clausamine B (**B91**)	
		Clausamine C (**B92**)	
		Clausine F (**B62**)	
		Clausamine D (**B64**)	
		Clausamine E (**B66**)	
		Clausamine F (**B65**)	
		Clausamine G (**B67**)	
		Ekeberginine (**B63**)	
		O-Demethylmurrrayanine (**B4**)	

Table 1.1 (Continued)

Plant	Part	Compound	Biliography
C. anisata	Branches	Methyl carbazole-3-carboxylate (**B3**)	Ito et al., 2000
		Clausine E (**B5**)	
		Clausamine A (**B90**)	
	Leaves	Anisocoumarin E (**C10**)	Ngadjui, Ayafor,
		Anisocoumarin F (**C11**)	Sondengem &
		Anisocoumarin G (**C12**)	Connolly, 1989b
		Anisocoumarin H (**C37**)	
		Capnolactone (**C43**)	
		Imperatorin (**C26**)	
		Triphasiol (**C9**)	
		Anisocoumarin I (**C72**)	Ngadjui,
		Anisocoumarin J (**C73**)	Mouncherou,
		Capnolactone (**C43**)	Ayafor,
		Imperatorin (**C26**)	Sondengam &
		Isoponcimarin (**C8**)	Tillequin, 1991
		Triphasiol (**C9**)	
		Umbelliferone (**C1**)	

Table 1.1 (Continued)

Plant	Part	Compound	Biliography
C. anisum-olens	Aerial	Clausenain I (**F1**)	Wang, He, Yang, Shen, Zhou & Hao, 2005
		Clausenain B (**F2**)	Wang, Xu, Wang & Yang, 2009
	Leaves and twigs	Anisucumarin A (**C77**) Anisucumarin B (**C78**) Hekumarone (**C70**)	Wang, He, Yang, Di & Hao, 2008
		Anisocoumarin H (**C37**) Aurapten (**C36**) Capnolactone (**C43**) Umbelliferone (**C1**)	Wang, Huang, Li & Yang, 2010
C. dentata	Root barks	Imperatorin (**C26**) Dentatin (**C17**)	Govindachari, Pai, Subramaniam & Muthukumaraswany 1968
C. dunniana	Aerial	Dunniana acid A (**K1**) Dunniana acid B (**K2**)	He, Shen, Hong, Zhao, Zhou & Hao, 2002

Table 1.1 (Continued)

Plant	Part	Compound	Biliography
C. dunniana	Aerial	2-Oxoclerod-3-en-15-oic acid (**K3**)	He, Shen, Zuo, Yang & Hao, 2003
		14,15-Dinorclerod-3-ene-2,13-dione (**K4**)	
		2α-Methoxyclerod-3-en-15-oic acid (**K5**)	
		2β-(Acetyloxy)clerod-3-en-15-oic acid (**K6**)	
		2β-(Formyloxy)clerod-3-en-15-oic acid (**K7**)	
		4α-Hydroxyclerodan-15-oic acid (**K8**)	
		14α,18-Dihydroxyclerodan-15-oic acid (**K9**)	
		4′-Hydroxyclerodan-15-oic acid (**K10**)	
		Clerodan-3-en-15-oic acid (**K11**)	
		3α,4α-Dihydroxyclerodan-15-oic acid (**K12**)	

Table 1.1 (Continued)

Plant	Part	Compound	Biliography
C. dunniana	Aerial	3β-Hydroxyclerodan-4(18)-en-15-oic acid (**K13**)	He, Shen, Zuo, Yang & Hao, 2003
		Clerodan-4(18)-en-15-oic acid (**K14**)	
		Ethyl clerodan-4(18)-en-15-oate (**K15**)	
		Ethyl clerodan-3-en-15-oate (**K16**)	
		(2*S*)-1-[(6,7-Dimethoxyfuro [2,3b]quinolone-4-yl)oxyl-3-methylbutane-2,3-diol (**H3**)	
	Stems	3-Methylcarbazole (**B1**)	Cui, Yan, Cai & Yao, 2002
		Murrayafoline (**B6**)	
		Girinimbine (**B68**)	
		Mahanimbine (**B81**)	
		Bicyclomahanimbine (**B82**)	
C. excavata	Aerial part	Excavatin D (**C43**)	He, Shen, He, Yang, Zuo & Hao, 2000
		Excavacoumarin B (**C50**)	
		Excavacoumarin C (**C64**)	
		Excavacoumarin D (**C48**)	

Table 1.1 (Continued)

Plant	Part	Compound	Biliography
C. excavata	Aerial part	Excavacoumarin E (**C49**)	He, Zhang, Shen, He, Chen, & Hao, 2002
		Excavacoumarin F (**C57**)	
		Excavacoumarin G (**C46**)	
		Zapoterin (**E5**)	
		21,23-Dihydro-21-hydroxy-23-oxozapoterin (**E6**)	
		21,23-Dihydro-23-hydroxy-21-oxozapoterin (**E7**)	
		21,23-Dihydro-23-hydroxy-21-oxoclausenarin (**E8**)	
		23-Ethoxy-21,23-dihydro-21-oxoclausenarin (**E9**)	
		(11′)-1,2,21,23-Tetrahydro-11,23-dihydroxy-21-oxoobacunoic acid (**E10**)	
		Excavacoumarin H (**C42**)	He, She, Du, Zhao & Hao, 2004
		Excavacoumarin I (**C47**)	
	Branch	Cladimarin A (**C80**)	Takemura et. al., 2004
		Cladimarin B (**C81**)	

Table 1.1 (Continued)

Plant	Part	Compound	Biliography
C. excavata	Fruits	Clausenaexcavin (**C68**)	Laphookhieo,
		Scopoletin (**C2**)	Sripisut, Prawat &
		Seselin (**C21**)	Karalai, 2009
	Leaves	Clausine L (**B13**)	Wu, Huang, Lai, Teng, Ko & Kuon, 1993
		Clauszoline M (**B43**)	Ito, Katsuno, Ohta, Omura, Kaijiura & Furukawa, 1997
		1-*O*-Methylclausenolide (**E2**)	Thuy, Ripperger,
		7-Geranyloxy-5-hydroxycoumarin (**C4**)	Prozel, Sung & Adam, 1999
		Anisocoumarin H (**C37**)	
		Clausenarin (**E4**)	
		Clausenolide (**E1**)	
		Clauszoline M (**B43**)	
		Excavatin A (**C38**)	
		Excavatin B (**C39**)	
		Excavatin C (**C40**)	
		Excavatin D (**C43**)	

Table 1.1 (Continued)

Plant	Part	Compound	Biliography
C. excavata	Leaves	Excavatin E (**C52**)	Thuy, Ripperger,
		Excavatin F (**C44**)	Prozel, Sung &
		Excavatin G (**C54**)	Adam, 1999
		Excavatin H (**C55**)	
		Excavatin I (**C62**)	
		Excavatin J (**C65**)	
		Excavatin K (**C45**)	
		Excavatin L (**C53**)	
		Excavatin M (**C63**)	
		Excavacoumarin A (**C56**)	He, Shen, He,
		Excavatin M (**C63**)	Yang, Zhu & Hao,
			2000
		Clauslactone A (**C82**)	Ito et al., 2000
		Clauslactone B (**C83**)	
		Clauslactone C (**C84**)	
		Clauslactone D (**C85**)	
		Clauslactone E (**C67**)	
		Clauslactone F (**C59**)	
		Clauslactone G (**C60**)	

Table 1.1 (Continued)

Plant	Part	Compound	Biliography
C. excavata	Leaves	Clauslactone H (**C63**)	Ito et al., 2000
		Clauslactone I (**C65**)	
		Clauslactone J (**C66**)	
		Clauszoline M (**B43**)	
		Umbelliferone (**C1**)	
		Excavacoumarin A (**C56**)	He, Shen, Zuo,
		Excavacoumarin B (**C50**)	Zhu, Yang & Hao,
			2000
		3-Formyl-2,7-dimethoxycarbazole (**B40**)	Muhd Sharif et. al., 2011
		Excavarin A (**C58**)	Kumar, Saha & Saha, 2012
	Rhizomes	2-Hydroxy-3-formyl-7-methoxycarbazole (**B39**)	Sunthitikawinsakul et al., 2003
		3-Formylcarbazole (**B2**)	
		Methyl carbazole-3-carboxylate (**B3**)	
		Clausenidin (**C19**)	
		Clauszoline J (**B41**)	
		Dentatin (**C17**)	

Table 1.1 (Continued)

Plant	Part	Compound	Biliography
C. excavata	Rhizomes	Mukonal (**B10**)	Sunthitikawinsakul
		Murrayanine (**B7**)	et al., 2003
		Nordentatin (**C16**)	
		Xanthoxyletin (**C14**)	
	Rhizomes	Clausenolide-1-ethyl ether (**E3**)	Sunthitikawinsakul
	and roots	Dentatin (**C17**)	et al., 2003
		Nordentatin (**C16**)	
		3-Formyl-2,7-dimethoxycarbazole (**B40**)	Kongkathip, Kongkathip,
		Clausenidin (**C19**)	Sunthitikawinsakul,
		Clauszoline J (**B41**)	Napaswat &
		O-Methylmukonal (**B12**)	Soosook, 2005
	Root	Clausenidin (**C19**)	Wu & Furukawa,
	barks	Clausenidinaric acid (**G1**)	1982
		Clauserin (**C97**)	
		Heptaphylline (**B48**)	
		Nordentatin (**C16**)	
		Xanthoxyletin (**C14**)	

Table 1.1 (Continued)

Plant	Part	Compound	Biliography
C. excavata	Root barks	Clausine T (**B78**)	Wu, Huang & Wu, 1997
		Clausine W (**B76**)	
		Furoclausine A (**B80**)	
		Furoclausine B (**B79**)	
		Claucavatin A (**C100**)	Huang, Wu & Wu, 1997
		Claucavatin B (**C101**)	
		Clausarin (**C99**)	
		Clausenidin (**C19**)	
		Kinocoumarin (**C20**)	
		Nordentatin (**C16**)	
		Osthol (**C6**)	
		Xanthoxyletin (**C14**)	
		Clausenatine A (**B102**)	Wu, Huang, Wu & Kuoh, 1999
		Clausine O (**B36**)	
		Clausine P (**B44**)	
		Clausine Q (**B31**)	
		Clausine R (**B30**)	
		Clausine S (**B56**)	
		Clausine U (**B55**)	

Table 1.1 (Continued)

Plant	Part	Compound	Biliography
C. excavata	Root barks	Clausine V (**B45**)	Wu, Huang, Wu & Kuoh, 1999
		Clausine M (**B21**)	
		Clausine N (**B19**)	
	Roots	Clauszoline H (**B98**)	Ito, Katsuno, Ohta, Omura, Kajiura & Furukawa, 1997
		Clauszoline I (**B5**)	
		Clauszoline J (**B41**)	
		Clausarin (**C99**)	Su et al., 2009
		Clausenidin (**C19**)	
		Dentatin (**C17**)	Muhd Sharif et. al., 2011
		Nordentatin (**C16**)	
		Xanthoxyletin (**C14**)	
		Xanthyltin (**C13**)	
	Stem barks	Clausine B (**B48**)	Wu, Huang, Wu & Teng, 1996
		Clausine E (**B5**)	
		Clausine H (**B42**)	
		Clausine I (**B25**)	
		Clausine K (**B40**)	
		Glycozolidal (**B34**)	
		Lansine (**B37**)	

Table 1.1 (Continued)

Plant	Part	Compound	Biliography
C. excavata	Stem barks	Mukonal (**B10**)	Wu, Huang, Wu & Teng, 1996
		Mukonine (**B8**)	
		5-Geranyloxy-7-hydroxycoumarin (**C5**)	Ito, Ohta, Tan & Furukawa, 1996
		Clauszoline A (**B100**)	
		Clauszoline B (**B97**)	
		Clauszoline C (**B42**)	
		Clauszoline D (**B54**)	
		Clauszoline E (**B77**)	
		Clauszoline F (**B101**)	
		Clauszoline G (**B74**)	
		Clausine B (**B48**)	Taufiq Yap et al., 2007
		Clausine H (**B42**)	
		Clausine TY (**B38**)	
		Clausenarin (**E4**)	Muhd Sharif et al., 2011
		Clausenolide-1-methyl ether (**E2**)	
		Clausine K (**B40**)	

Table 1.1 (Continued)

Plant	Part	Compound	Biliography
C. excavata	Stems	Dectamine (**H1**) Mukonine (**B8**) Nordentatin (**C16**) 3-Formylcarbazole (**B2**) Clausine Z (**B24**) Clauszoline I (**B5**) Lansine (**B37**) Methyl 1,6-dihydroxy-9*H*-carbazole-3-carboxylate (**B26**) Methyl carbazole-3-carboxylate (**B3**) Mukonidine (**B11**) Mukonine (**B8**) Murrayanine (**B7**) *O*-Demethylmurrayanine (**B4**) *O*-Methylmukonal (**B12**) Sansoakamine (**B35**)	Laphookhieo, Sripisut, Prawat & Karalai, 2009 Sripisut & Laphookhieo 2010

Table 1.1 (Continued)

Plant	Part	Compound	Biliography
C. excavata	Stems and leaves	Clauslactone R (**C79**) Clauslactone S (**C75**) Clauslactone T (**C86**) Clauslactone K (**C69**) Clauslactone L (**C71**) Clauslactone M (**C54**) Clauslactone N (**C74**) Clauslactone O (**C61**) Clauslactone P (**C76**) Clauslactone Q (**C51**)	Xin, Lu, Ke, Hu, Lin & Ye, 2008 Nakamura, Takemura, Ju-ichi, Ito, & Furukawa, 1998 Takemura, Nakamura, Hirusawa, Ju-ichi, Ito & Furukawa, 2000
C. guillauminii	Root barks	7-Methoxyheptaphylline (**B51**) Heptaphylline (**B49**) Osthol (**C6**) Poncitrin (**C15**) Xanthoxyletin (**C14**)	Nakamura et al., 2009

Table 1.1 (Continued)

Plant	Part	Compound	Biliography
C. harmandiana	Root barks	Clausarin (**C99**) Dentatin (**C17**) Heptaphylline (**B49**) Nordentatin (**C16**) Osthol (**C6**) Xanthoxyletin (**C14**)	Wangboondkul, Pummagura & Chichantipyuth, 1984
		7-Methoxylmukonal (**B38**) 7-Methoxyheptaphylline (**B51**)	Chichantipyuth, Pummangura, Naowsaran & Thanyavuthi, 1998
	Roots	Clausarin (**C99**) Clausine K (**B41**) Dentatine (**C17**) Heptaphylline (**B49**)	Yenjai et al., 2000
		7-Methoxymukonal (**B39**) Clausine C (**B22**) Clausine V (**B45**) Clauszoline K (**B20**) Glycosinine (**B12**)	Thongthoom, Songsiang, Phaosiri & Yenjai, 2010

Table 1.1 (Continued)

Plant	Part	Compound	Biliography
C. harmandiana	Roots	Heptazoline (**B52**)	Thongthoom,
		Methyl carbazole-3-carboxylate (**B3**)	Songsiang, Phaosiri & Yenjai, 2010
		Mukonal (**B10**)	
		Osthol (**C6**)	
		3-Formyl-1-hydroxy-7-methyxycarbazole (**B29**)	Songsiang et al., 2011
		7-Hydroxyheptaphylline (**B50**)	
		7-Methoxyheptaphylline (**B51**)	
		7-Methoxymurrayanine (**B73**)	
		Clauraila A (**B32**)	
		Clauraila B (**B70**)	
		Clauraila C (**B95**)	
		Clauraila D (**B96**)	
		Clausine E (**B5**)	
		Clausine K (**B40**)	
		Clausine O (**B36**)	
		Dentatin (**C17**)	
		Girinimbine (**B68**)	

Table 1.1 (Continued)

Plant	Part	Compound	Biliography
		Heptaphylline (**B49**)	
C. harmandiana	Roots	Lansine (**B37**)	Songsiang et al.,
		Murrayanine (**B7**)	2011
		Nordentatin (**C16**)	
		O-Demethylmurrayanine (**B4**)	
		Xanthoxyletin (**C14**)	
		7-Hydroxyheptaphylline (**B50**)	Songsiang et al.,
		7-Methoxymukonal (**B39**)	2012
		7-Methoxyheptaphylline (**B51**)	
		Clausine C (**B22**)	
		Clausine E (**B5**)	
		Clausine K (**B40**)	
		Dentatin (**C17**)	
		Heptaphylline (**B49**)	
		Lansine (**B37**)	
		Nordentatin (**C16**)	
		Xanthoxyletin (**C14**)	
C. heptaphylla	Leaves	Clausenal (**B46**)	Chakraborty, Sena, Podder, Chowdhury & Bhattacharyya, 1995

Table 1.1 (Continued)

Plant	Part	Compound	Biliography
C. heptaphylla	Leaves	Lunamarin A (**C34**)	Sohrab, Hasan &
		Lunamarin B (**C35**)	Rashid, 1999
		Clausmarin A (**C103**)	Sohrab, Hansan & Rashid, 2000
	Roots	Clausenidin (**C19**)	Joshi, Kamat &
		Clausenin (**C18**)	Saksena, 1976
		3-Methylcarbazole (**B1**)	Roy, Bhattacharyya & Chakaraborty, 1974
		Girinimbine (**B68**)	Roy &
		Murrayacine (**B71**)	Chakraborty, 1976
		2-Methylantraquinone (**J1**)	Chakraborty, Islam & Roy, 1978
		Clausenolide (**E1**)	Chakraborty, Bhattacharyya & Bhattacharyya, 1979
		Heptazolicine (**B75**)	Bhattacharyya, Biswas, Barua, Saha, Roy & Chowdhury, 1984

Table 1.1 (Continued)

Plant	Part	Compound	Biliography
C. heptaphylla	Stem barks	Clausenalene (**B99**)	Bhattacharyya, Biswas, Barua, Saha, Roy & Chowdhury, 1993
		Clausenolide-1-methyl ether (**E2**)	Begum et al., 2011
C. indica	Roots	Indicolactonediol (**C33**)	Rakash, Raj, Kapil & Popli, 1978
C. lansium	Aerial parts	Lansiol (**K17**)	Lakshmi, Raj & Kapil, 1989
		Clausenamide (**A12**)	Cheng, Yeng, He & Zheng, 1989
		neo-Clausenamide (**A11**)	
		seco-Clausenamide (**A9**)	Yang, Chen & Huang, 1991
		seco-Demethylclausenamide (**A8**)	
		homo-Clausenamide (**A13**)	
		zeta-Clausenamide (**A14**)	
	Branches	Lansiumarin A (**C30**)	Ito Katsuni & Furukawa, 1998
		Lansiumarin B (**C31**)	
		Lansiumarin C (**C29**)	

Table 1.1 (Continued)

Plant	Part	Compound	Biliography
C. lansium	Fruit peels	8-Hydroxylpsoralen (**C25**)	Prasad et al., 2010
	Leaves	*N*-Methyl-3-phenyloxirane-2-carboxamide (**A1**)	Li et al., 1996
		Lansiumamide B (**A4**)	
		SB-204900 (**A5**)	Milner, Coates, Gilpin & Spear, 1996
	Root barks	Wampetin (**C32**)	Khan, Naqvi & Ishratullah, 1983
		7-Hydroxyheptaphylline (**B50**)	Kumar, Vallipuram, Adebajo & Reisch, 1995
		Angustifolin (**C89**)	
		Chalepensin (**C97**)	
		Chalepin (**C94**)	
		Gravalliferone (**C90**)	
	Roots	3-Formyl-1,6-dimethoxy carbazole (**B28**)	Li, McChesney & El-Feraly, 1991
		3-Formyl-6-methoxycarbazole (**B16**)	
		3-Formylcarbazole (**B2**)	
		Glycozoline (**B15**)	

Table 1.1 (Continued)

Plant	Part	Compound	Biliography
C. lansium	Roots	Indizoline (**B58**)	Li, McChesney &
		Methyl 6-methoxy carbazole-3-carboxylate (**B17**)	El-Feraly, 1991
		Methyl carbazole-3-carboxylate (**B3**)	
		Murrayanine (**B7**)	
	Seeds	Lansiumamide A (**A3**)	Lin, 1989
		Lansiumamide B (**A4**)	
		Lansiumamide C (**A6**)	
		Lansiumamide I (**A7**)	
		N-*cis*-Styryl-cinnamamide (**A10**)	
	Stems	3-Formyl-6-methoxycarbazole (**B16**)	Lin et al., 2012
		3-Formylcarbazole (**B2**)	
		Claulansine A (**B83**)	
		Claulansine B (**B84**)	
		Claulansine C (**B86**)	
		Claulansine D (**B88**)	
		Claulansine E (**B89**)	
		Claulansine F (**B69**)	

Table 1.1 (Continued)

Plant	Part	Compound	Biliography
C. lansium	Stems	Claulansine H (**B53**)	Lin et al., 2012
		Claulansine I (**B57**)	
		Claulansine J (**B47**)	
		Clausine D (**B61**)	
		Clausine I (**B25**)	
		Glycozolidal (**B34**)	
		Methyl 6-methoxy carbazole-3-carboxylate (**B17**)	
		Murrayanine (**B7**)	
		Claulamine A (**B87**)	Shen et al., 2012
		Claulamin B (**B84**)	
		Clausenoside A (**D1**)	
		Clausenoside B (**D2**)	
		Clausine D (**B61**)	
		Dectamnine (**H1**)	
		Dihydroalatamide (**A2**)	
		Imperatorin (**C26**)	
		Indizoline (**B58**)	
		Isogospherol (**C27**)	
		Isoheraclenin (**C28**)	

Table 1.1 (Continued)

Plant	Part	Compound	Biliography
C. lansium	Stems	Isoimperatorin (**C22**)	Shen et al., 2012
		Isotachioside (**D4**)	
		Lansiumarin A (**C30**)	
		Lansiumarin C (**C29**)	
		Mafaicheenamine A (**B85**)	
		Osthol (**C6**)	
		Wampetin (**C32**)	
		Xanthotoxol (**C25**)	
C. lenis	Aerial parts	Diseselin A (**C87**)	He, Chen, Shen, Chen, Zhao & Hao, 2003
		Diseselin B (**C88**)	He, Shen, Chen, He & Hao, 2006
		Lenisin A (**G2**)	
		Lenisin B (**G3**)	
		Lenisin C (**G4**)	
C. pentaphylla	Areal parts	*O*-Methylclausenol (**K18**)	Mannadhad, Shoeb, Kapil & Popli, 1977
		Clausmarin A (**C103**)	Shoeb, Manandhar,

Table 1.1 (Continued)

Plant	Part	Compound	Biliography
C. pentaphylla	Areal parts	Clausmarin B (**C104**)	Kapil & Popli, 1977
		Clausmarin C (**C105**)	Rai, Sharma & Misra, 2009
	Roots	Clausarin (**C99**)	Anwer, Shoeb,
		Clausenidin (**C19**)	Kapil & Popli,
		Dentatin (**C17**)	1997
		Heptaphylline (**B49**)	
		5,7-Dihydroxy-3′,4′-dimethoxyflavanone 6-C-[α-rhamnopyranosyl-(1→6)]-β-glucopyranoside (**D3**)	Intekhab, Aslam, Bhadauria & Singh, 2012
C. vestita	Whole plants	γ-Fagarine (**H2**)	Shi, Ye, Tang & Zhao, 2010
		2,3-Dimethoxycarbazole (**B14**)	
		2-Hydroxy-3-methylcarbazole (**B9**)	
		7-Hydroxyheptaphylline (**B50**)	
		Lansine (**B37**)	
		4-Methoxy-1-methylquinoline-2-one (**I1**)	

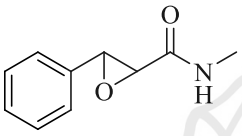
Table 1.1 (Continued)

Plant	Part	Compound	Biliography
C. vestita	Whole plants	7-Hydroxy-3-methylcarbazole (**C18**)	Shi, Ye, Tang & Zhao, 2010
		Clausine O (**B36**)	
		Clausine P (**B44**)	
		Clausine Z (**B24**)	
		Clauslactone U (**C106**)	
		Clauszoline C (**B42**)	
		Clauszoline I (**B5**)	
		Clauszoline J (**B41**)	
		Clauszoline M (**B43**)	
		Clauszoline N (**B33**)	
		Clauszoline K (**B20**)	
		Dectamine (**H1**)	
		Girinimbine (**B68**)	
		Methyl 6-methoxy carbazole-3-carboxylate (**B17**)	
		Methyl carbazole-3-carboxylate (**B3**)	
		Mukonal (**B10**)	
		Mukonidine (**B11**)	

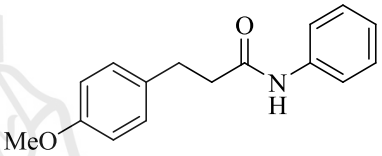
Table 1.1 (Continued)

Plant	Part	Compound	Biliography
C. suffruticoca	Leaves	7-[(2′*E*,6′*E*)-7′-carboxy-5′(ξ)-hydroxy-3′-methylocta-2′,6′-dienyloxy] coumarin (**C41**)	Begum, Rahman, Chowdhury, Rahman, Gibbons & Rashid, 2010

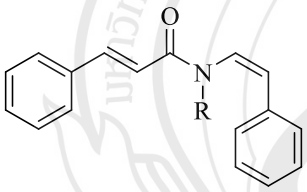
A = Amides



N-Methyl-3-phenyloxirane-2-carboxamide (**A1**)

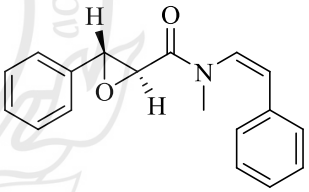


Dihydroalatamide (**A2**)

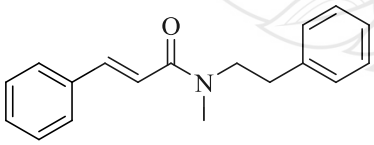


Lansiumamide A (**A3**): R = H

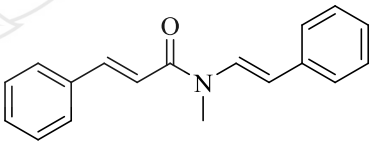
Lansiumamide B (**A4**): R = Me



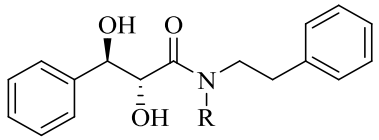
SB-204900 (**A5**)



Lansiumamide C (**A6**)

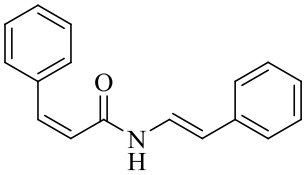


Lansiumamide I (**A7**)

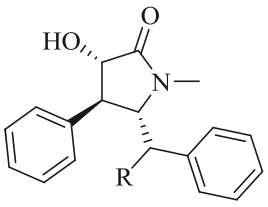


Seco-Demethylclausenamide (**A8**): R = H

Seco-Clausenamide (**A9**): R = Me

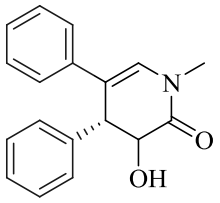


N-cis-Styryl-cinnamamide (**A10**)

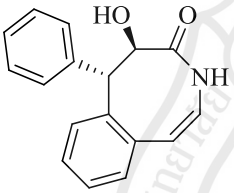


Neo-Clausenamide (**A11**): R = H

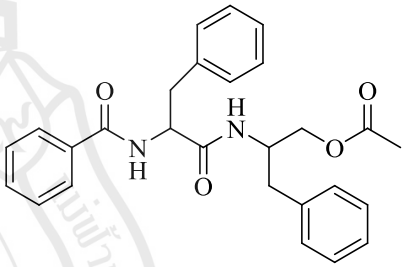
Clausenamide (**A12**): R = OH



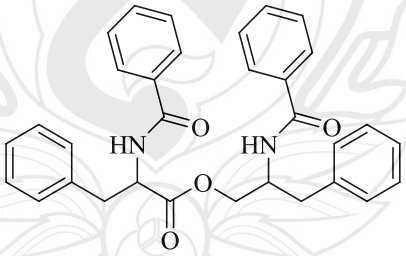
Homo-Clausenamide (**A13**)



Zeta-Clausenamide (**A14**)

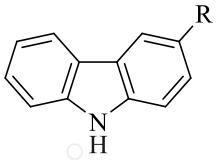


Aurantiamide acetate (**A15**)



N-Benzoylphenylalaninyl-*N*-benzoylphenylalaninate (**A16**)

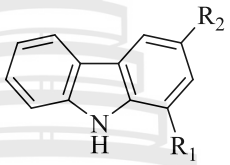
B = Carbazole alkaloids



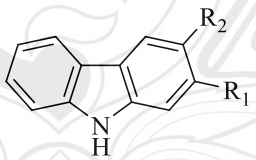
3-Methylcarbazole (**B1**): R = Me

3-Formylcarbazole (**B2**): R = CHO

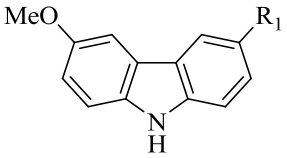
Methyl carbazole-3-carboxylate (**B3**): R = CO_2Me



	R_1	R_2
O-Demethylmurrayanine (**B4**):	OH	CHO
Clauszoline I or Clausine E (**B5**):	OH	CO_2Me
Murrayafoline (**B6**):	OMe	Me
Murrayanine (**B7**):	OMe	CHO
Mukonine (**B8**):	OMe	CO_2Me



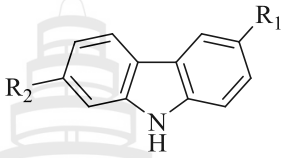
	R_1	R_2
2-Hydroxy-3-methylcarbazole (**B9**):	OH	Me
Mukonal (**B10**):	OH	CHO
Mukonidine (**B11**):	OH	CO_2Me
Glycosinine or *O*-Methylmukonal (**B12**):	OMe	CHO
Clausine L (**B13**):	OMe	CO_2Me
2,3-Dimethoxycabazole (**B14**):	OMe	OMe



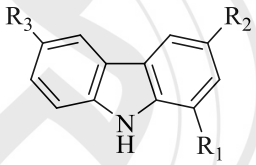
Glycozoline (**B15**): R = Me

3-Formyl-6-methoxycarbazole (**B16**): R = CHO

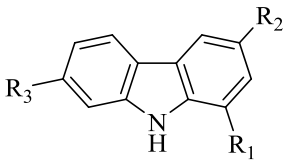
Methyl 6-methoxy carbazole-3-carboxylate (**B17**): R = CO_2Me



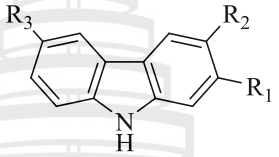
	R_1	R_2
7-Hydroxy-3-methylcarbazole (**B18**):	Me	OH
Clausine N (**B19**):	CHO	OH
Clauszoline K (**B20**):	CHO	OMe
Clausine M (**B21**):	CO_2Me	OH
Clausine C or Clauzoline L (**B22**):	CO_2Me	OMe



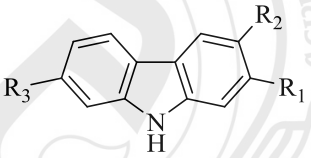
	R_1	R_2	R_3
Clausenol (**B23**):	OH	Me	OMe
Clausine Z (**B24**):	OH	CHO	OH
Clausine I (**B25**):	OH	CHO	OMe
Methyl 1,6-dihydroxy-9*H*-carbazole-3-carboxylate (**B26**):	OH	CO_2Me	OH
Clausenine (**B27**):	OMe	Me	OMe
3-Formyl-1,6-dimethoxycarbazole (**B28**):	OMe	CHO	OMe



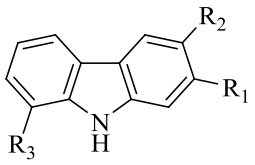
	R_1	R_2	R_3
3-Formyl-1-hydroxy-7-methyxycarbazole (**B29**):	OH	CHO	OMe
Clausine R (**B30**):	OH	CO_2Me	OH
Clausine Q (**B31**):	OMe	CHO	OH
Clauraila A (**B32**):	OMe	CHO	OMe



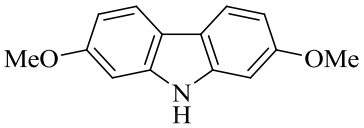
	R_1	R_2	R_3
Clauszoline N (**B33**):	OH	CHO	OH
Glycozolidal (**B34**):	OH	CHO	OMe
Sansoakamine (**B35**):	OH	CO_2Me	OMe



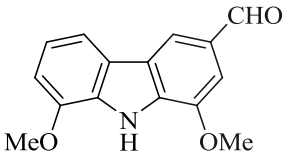
	R_1	R_2	R_3
Clausine O (**B36**):	OH	CHO	OH
Lansine (**B37**):	OH	CHO	OMe
Clausine TY or Clauszoline J (**B38**):	OH	CO_2Me	OMe
2-Hydroxy-3-formyl-7-methoxycarbazole or 7-Methoxymukonal (**B39**):	OH	CHO	OMe
3-Formyl-2,7-dimethoxycarbazole (**B40**):	OMe	CHO	OMe
Clauszoline J or Clausine K (**B41**):	OMe	CO_2H	OMe
Clauszoline C or Clausine H (**B42**):	OMe	CO_2Me	OMe



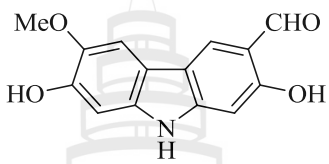
	R_1	R_2	R_3
Clauszoline M (**B43**):	OH	CHO	OH
Clausine P (**B44**):	OMe	Me	OMe



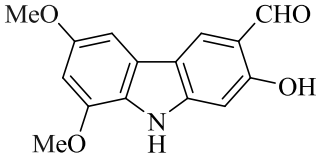
Clausine V (**B45**)



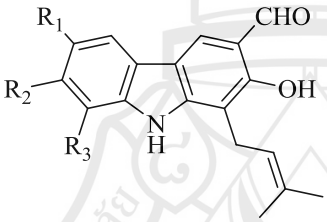
Clausenal (**B46**)



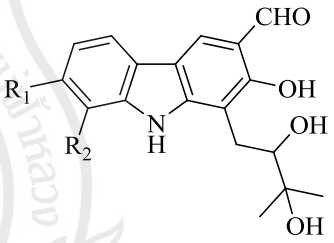
Claulansine J (**B47**)



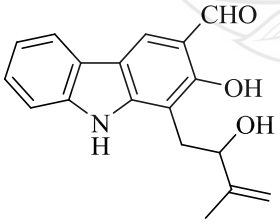
Clausine B (**B48**)



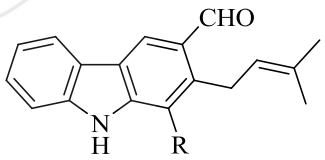
	R_1	R_2	R_3
Heptaphylline (**B49**):	H	H	H
7-Hydroxyheptaphylline (**B50**):	H	OH	H
7-Methoxyheptaphylline (**B51**):	H	OMe	H
Heptazoline (**B52**):	H	H	OH
Claulansine H (**B53**):	OMe	OH	H



	R_1	R_2
Clauszoline D (**B54**):	H	OH
Clausine U (**B55**):	OH	H

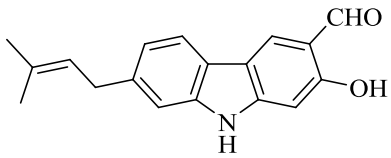


Clausine S (**B56**)

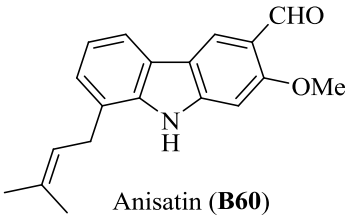


Claulansine I (**B57**): R = OH

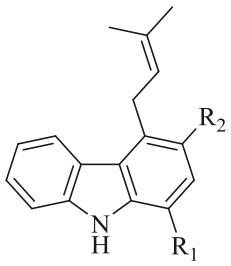
Indizoline (**B58**): R = OMe



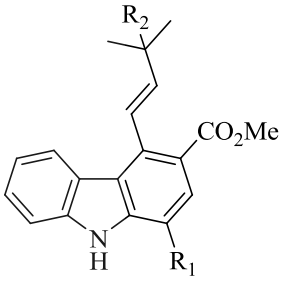
Clausanitin (**B59**)



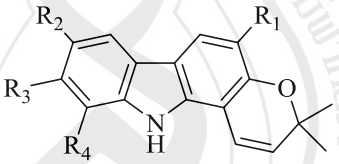
Anisatin (**B60**)



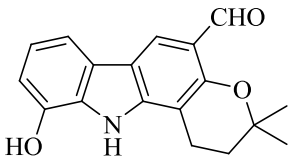
	R_1	R_2
Clausine D (**B61**):	OH	CHO
Clausine F (**B62**):	OH	CO_2Me
Ekeberginine (**B63**):	OMe	CHO
Clausamine D (**B64**):	OMe	CO_2Me



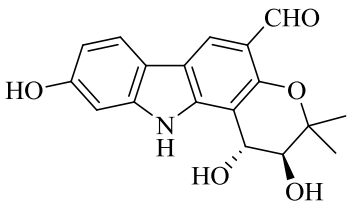
	R_1	R_2
Clausamine F (**B65**):	OH	OH
Clausamine E (**B66**):	OMe	OH
Clausamine G (**B67**):	OMe	OOH



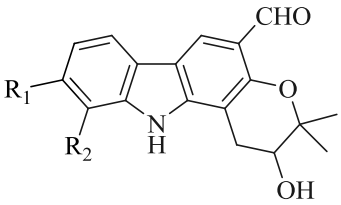
	R_1	R_2	R_3	R_4
Girinimbine (**B68**):	Me	H	H	H
Murrayamine A (**B69**):	Me	H	OH	H
Clauraila B (**B70**):	Me	H	H	OH
Murrayacine (**B71**):	CHO	H	H	H
Claulansine F (**B72**):	CHO	OMe	H	H
7-Methoxymurrayanine (**B73**):	CHO	H	OMe	H
Clauszoline G (**B74**):	CHO	H	H	OH



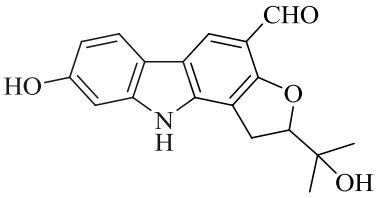
Heptazolicine (**B75**)



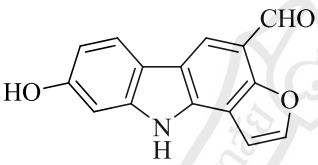
Clausine W (**B76**)



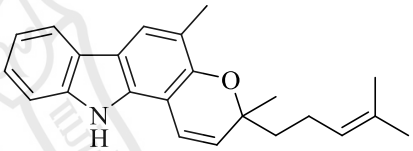
	R_1	R_2
Clauszoline E (**B77**):	H	OH
Clausine T (**B78**):	OH	H



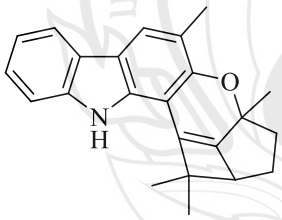
Furoclausine B (**B79**)



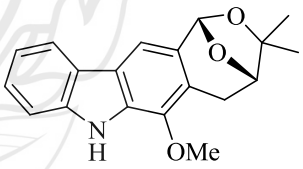
Furoclausine A (**B80**)



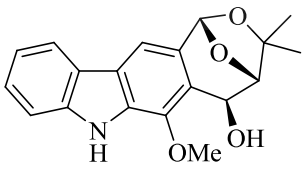
Mahanimbine (**B81**)



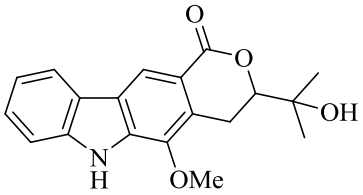
Bicyclomahanimbine (**B82**)



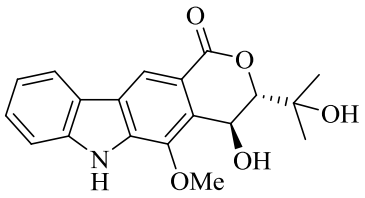
Claulansine A (**B83**)



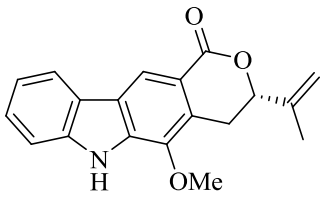
Claulansine B or Claulamin B (**B84**)



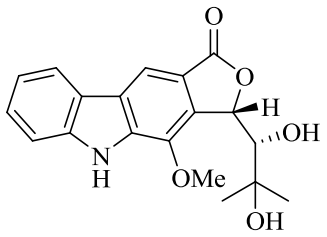
Mafaicheenamine A (**B85**)



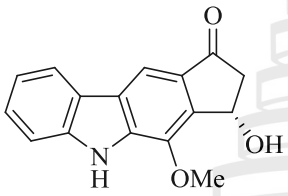
Claulansine C (**B86**)



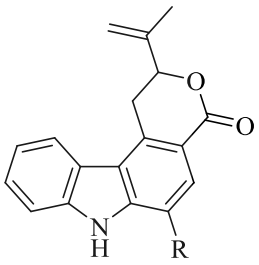
Claulamine A (**B87**)



Claulansine D (**B88**)

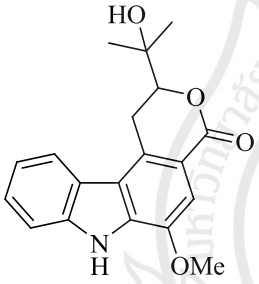


Claulansine E (**B89**)

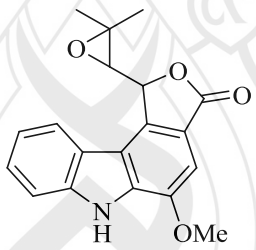


Clausamine A (**B90**): R = OH

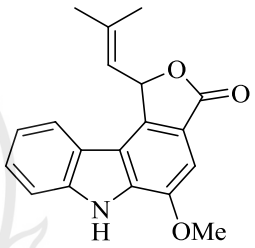
Clausamine B (**B91**): R = OMe



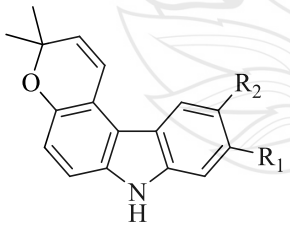
Clausamine C (**B92**)



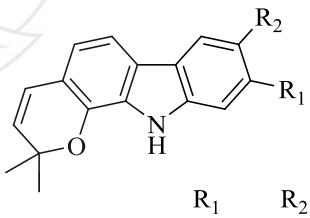
Furanoclausamine A (**B93**)



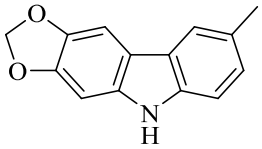
Furanoclausamine B (**B94**)



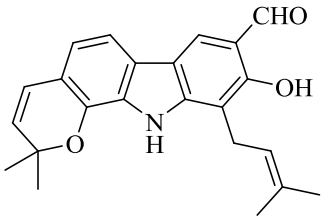
	R_1	R_2
Clauraila C (**B95**):	H	CO_2Me
Clauraila D (**B96**):	OH	CHO



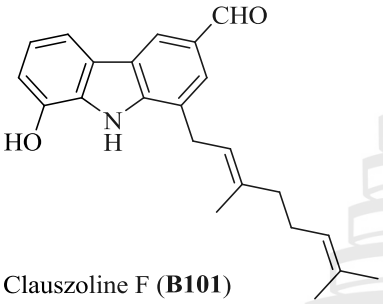
	R_1	R_2
Clauszoline B (**B97**):	OH	CHO
Clauszoline H (**B98**):	OMe	Me



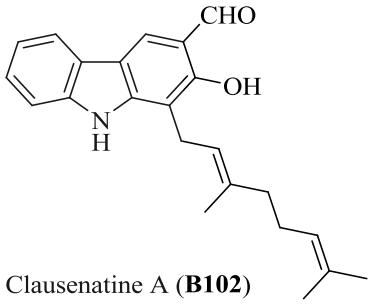
Clausenalene (**B99**)



Clauszoline A (**B100**)

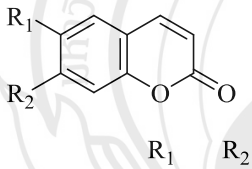


Clauszoline F (**B101**)

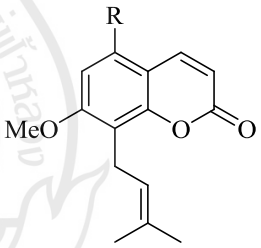


Clausenatine A (**B102**)

C = Coumarins

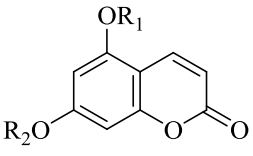


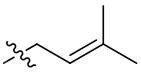
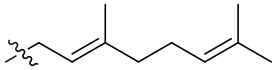
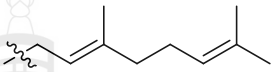
	R_1	R_2
Umbelliferone (**C1**): H		OH
Scopoletin (**C2**):	OH	OMe

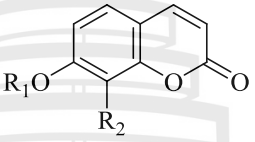


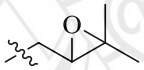
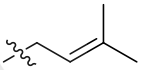
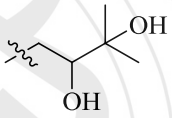
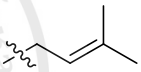
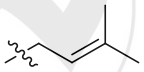
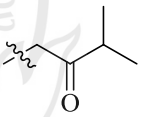
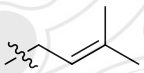
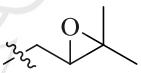
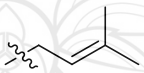
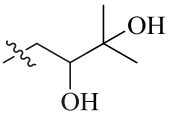
Osthol (**C6**): R = H

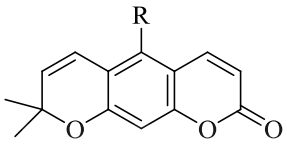
Coumarrayin (**C7**): R = OMe



	R_1	R_2
Anisocoumarin B (**B3**):	H	
7-Geranyloxy-5-hydroxycoumarin (**C4**):	H	
5-Geranyloxy-7-hydroxycoumarin (**C5**):		H

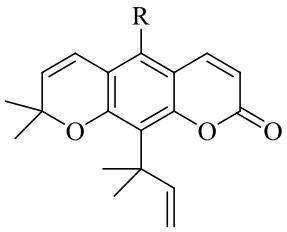


	R_1	R_2
Isoponcimarin (**C8**):		
Triphasiol (**C9**):		
Anisocoumarin E (**C10**):		
Anisocoumarin F (**C11**):		
Anisocoumarin G (**C12**):		



Xanthyltin (**C13**): R = H

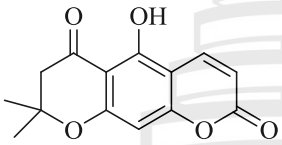
Xanthoxyletin (**C14**): R = OMe



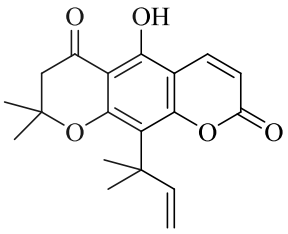
Poncitrin (**C15**): R = H

Nordentatin (**C16**): R = OH

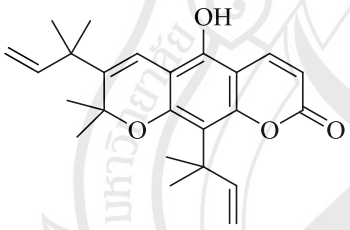
Dentatin (**C17**): R = OMe



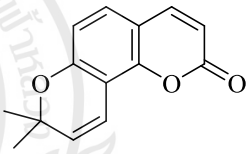
Clausenin (**C18**)



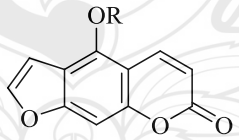
Clausenidin (**C19**)



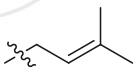
Kinocoumarin (**C20**)



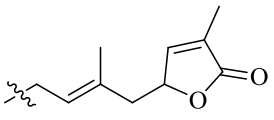
Seselin (**C21**)



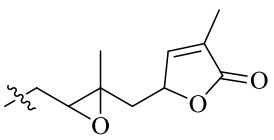
Isoimperatorin (**C22**): R =

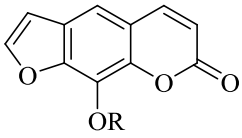


Anisolactone (**C23**): R =

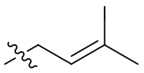


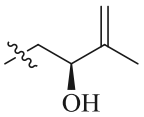
2',3'-Epoxyanisolactone (**C24**): R =

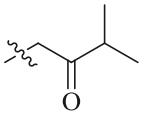


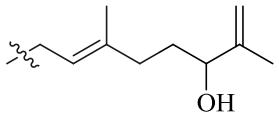


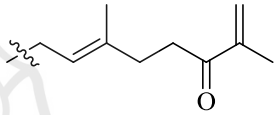
8-Hydroxypsoralen or Xanthotoxol (**C25**): R = H

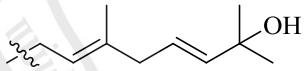
Imperatorin (**C26**): R = 

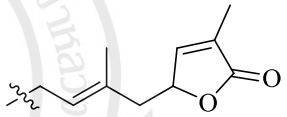
Isogospherol (**C27**): R = 

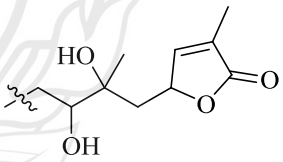
Isoheraclenin (**C28**): R = 

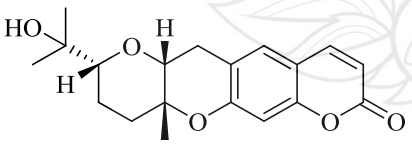
Lansiumarin C (**C29**): R = 

Lansiumarin A (**C30**): R = 

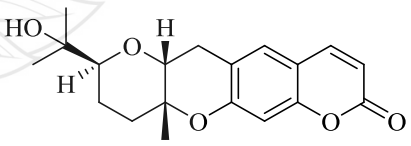
Lansiumarin B (**C31**): R = 

Wampetin or Indicolactone (**C32**): R = 

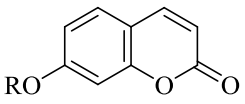
Indicolactonediol (**C33**): R = 



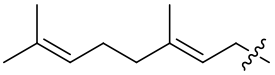
Lunamarin A (**C34**)



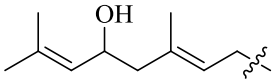
Lunamarin B (**C35**)



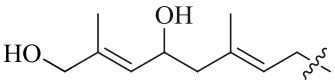
Aurapten (**C36**): R =



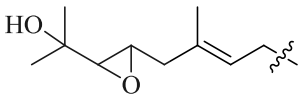
Anisocoumarin H (**C37**): R =



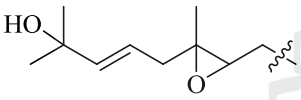
Excavatin A (**C38**): R =



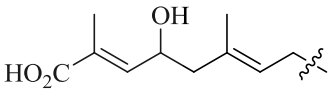
Excavatin B (**C39**): R =



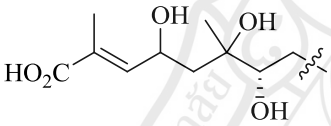
Excavatin C(**C40**): R =



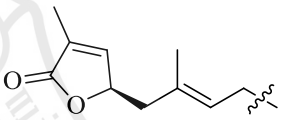
7-[(2'*E*,6'*E*)-7'-carboxy-5'(z)-hydroxy-3'-methylocta-2',6'-dienyloxy] coumarin (**C41**): R =



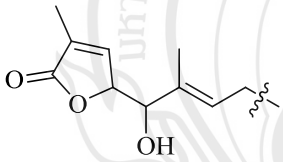
Excavacoumarin H (**C42**): R =



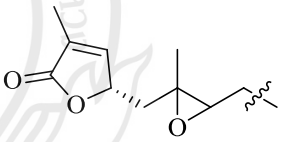
Excavatin D or Capnolactone (**C43**): R =



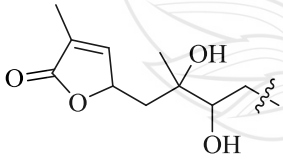
Excavatin F (**C44**): R =



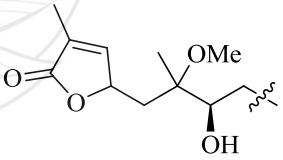
Excavatin K (**C45**): R =

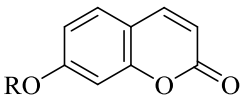


Excavacoumarin G (**C46**): R =

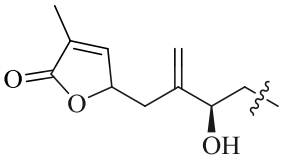


Excavacoumarin I (**C47**): R =

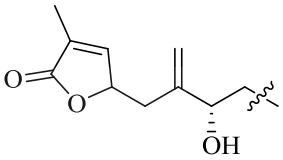




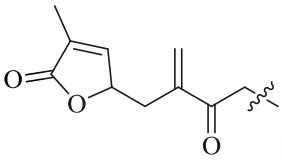
Excavacoumarin D (**C48**): R =



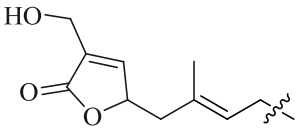
Excavacoumarin E (**C49**): R =



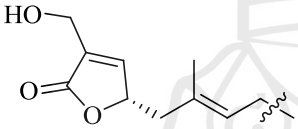
Excavacoumarin B (**C50**): R =



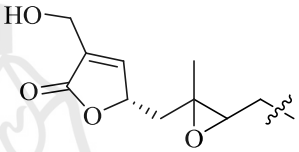
Clauslactone Q (**C51**): R =



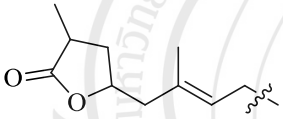
Excavatin E (**C52**): R =



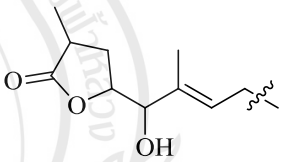
Excavatin L (**C53**): R =



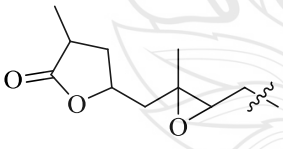
Clauslactone M or
Excavatin G (**C54**): R =



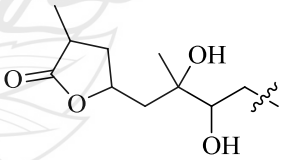
Excavatin H (**C55**): R =



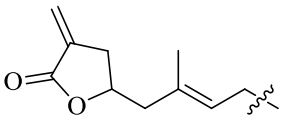
Excavacoumarin A (**C56**): R =



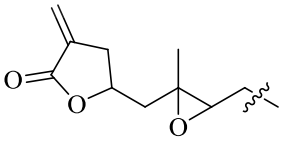
Excavacoumarin F (**C57**): R =

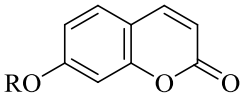


Excavarin A (**C58**): R =

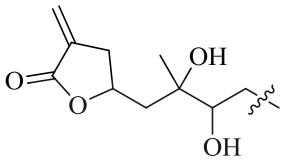


Clauslactone F (**C59**): R =

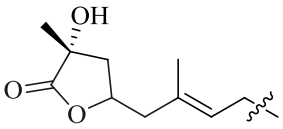




Clauslactone G (**C60**): R =

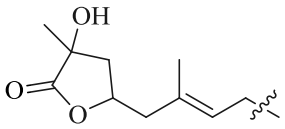


Clauslactone O (**C61**): R =

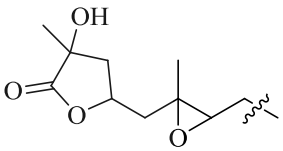


Clauslactone H or

Excavatin I (**C62**): R =

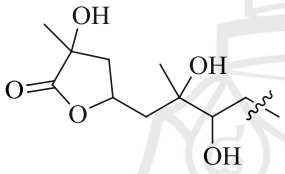


Excavatin M (**C63**): R =

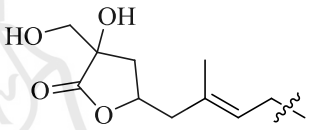


Clauslactone I or

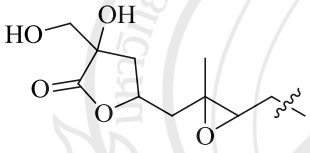
Excavacoumarin C (**C64**): R =

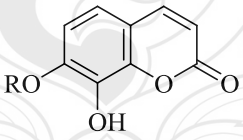


Excavatin J (**C65**): R =

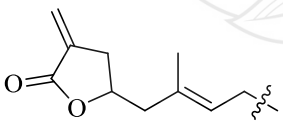


Clauslactone J (**C66**): R =

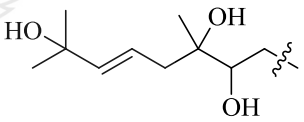


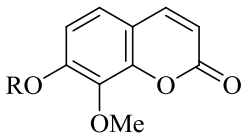


Clauslactone E (**C67**): R =

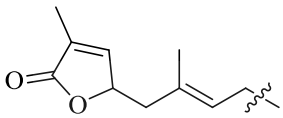


Clausenaexcavin (**C68**): R =

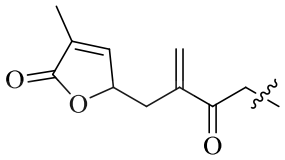




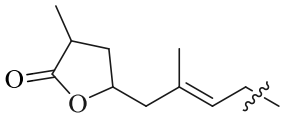
Clauslactone K (**C69**): R =



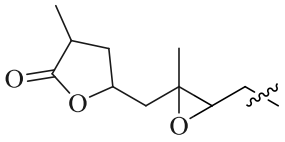
Hekumarone (**C70**): R =



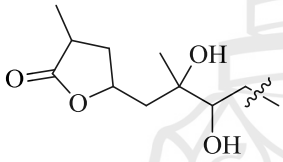
Clauslactone L (**C71**): R =



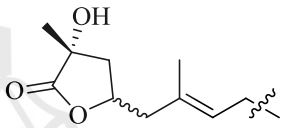
Anisocoumarin I (**C72**): R =



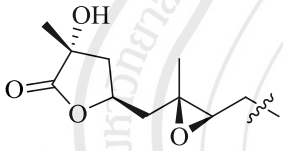
Anisocoumarin J (**C73**): R =



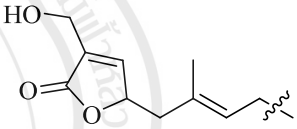
Clauslactone N (**C74**): R =



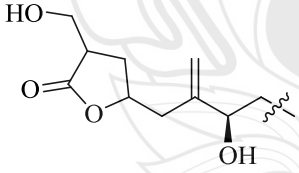
Clauslactone S (**C75**): R =



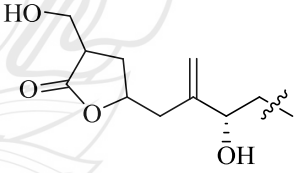
Clauslactone P (**C76**): R =



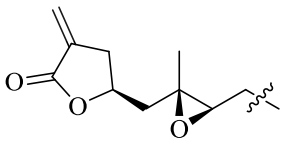
Anisucumarin A (**C77**): R =

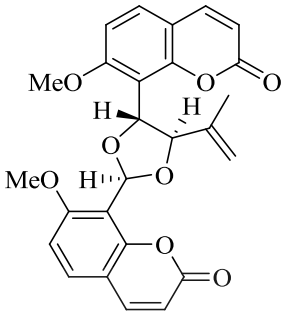


Anisucumarin B (**C78**): R =

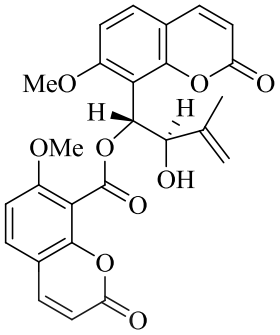


Clauslactone R (**C79**): R =

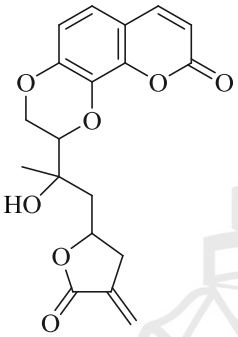




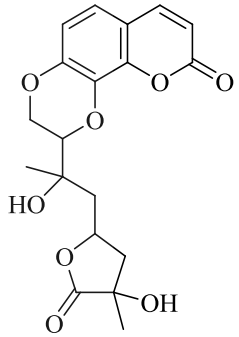
Cladimarin A (**C80**)



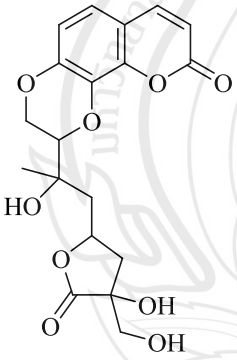
Cladimarin B (**C81**)



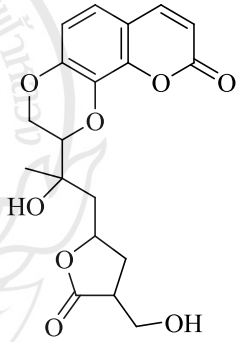
Clauslactone A (**C82**)



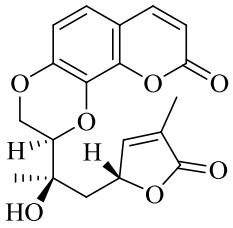
Clauslactone B (**C83**)



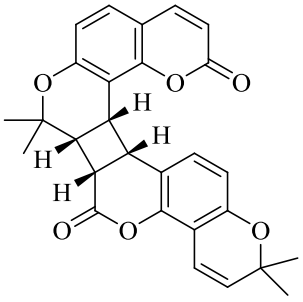
Clauslactone C (**C84**)



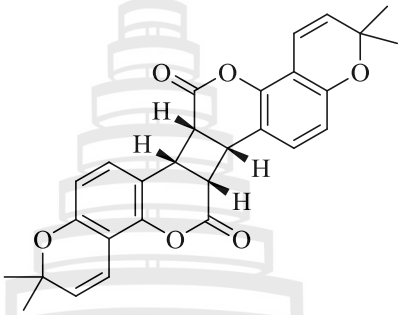
Clauslactone D (**C85**)



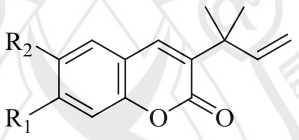
Clauslactone T (**C86**)

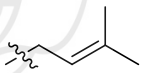
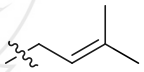
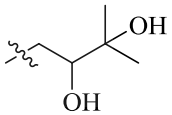


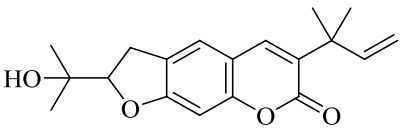
Diseselin A (**C87**)



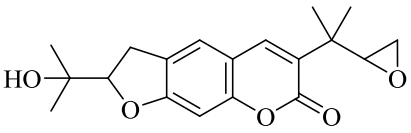
Diseselin B (**C88**)



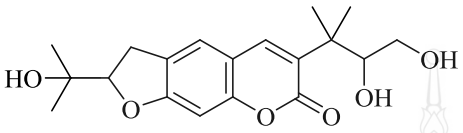
	R_1	R_2
Angustifolin (**C89**):	OH	H
Gravalliferone (**C90**):	OH	
Gravelliferone methyl ether (**C91**):	OMe	
Swietenocoumarin I (**C92**):	OMe	
Anisocoumarin A (**C93**):	OMe	CHO



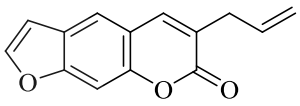
Chalepin (**C94**)



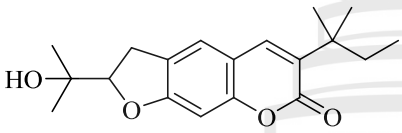
Anisocoumarin C (**C95**)



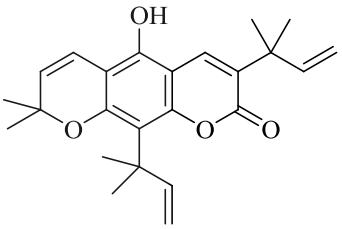
Anisocoumarin D (**C96**)



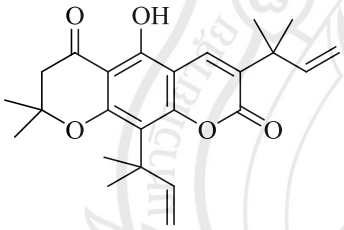
Chalepensin (**C97**)



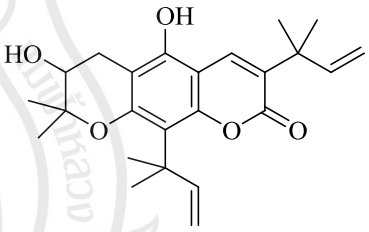
Heliettin (**C98**)



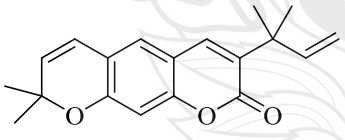
Clausarin (**C99**)



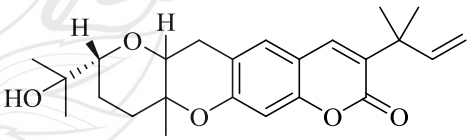
Claucavatin A (**C100**)



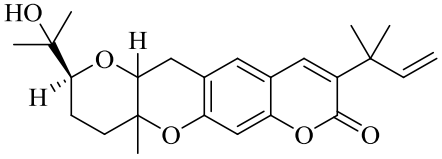
Claucavatin B (**C101**)



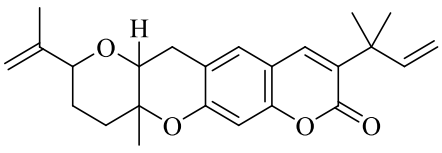
3-(1,1-Dimethylallyl)-xanthoxyletin (**C102**)



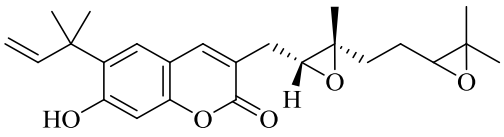
Clausmarin A (**C103**)



Clausmarin B (**C104**)

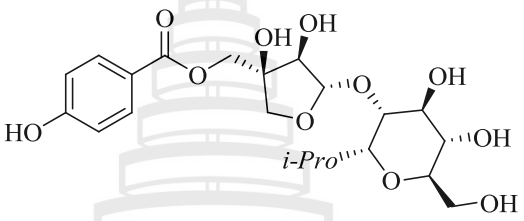


Clausmarin C (**C105**)

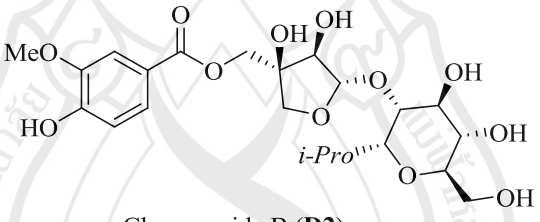


Clauslactone U (**C106**)

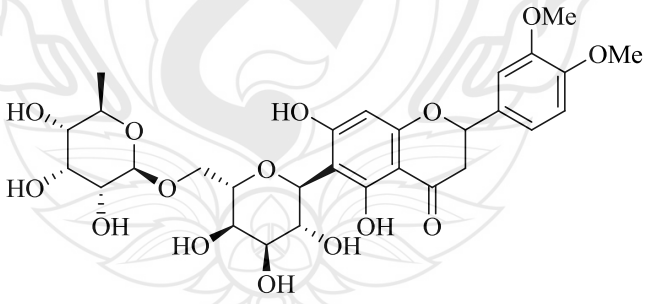
D = Glycosides



Clausenoside A (**D1**)

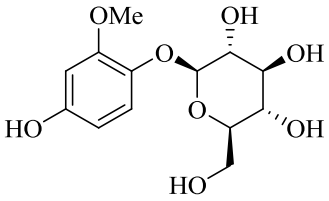


Clausenoside B (**D2**)



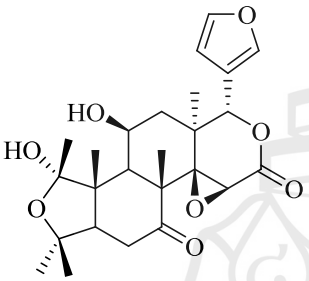
5,7-Dihydroxy-3',4' -dimethoxyflavanone

6-C-[α-rhamnopyranosyl-(1->6)]-β -glucopyranoside (**D3**)

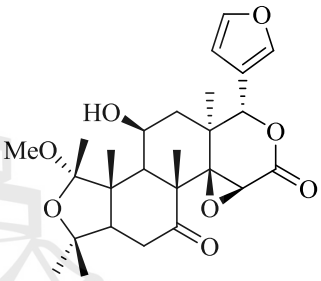


Isotachioside (**D4**)

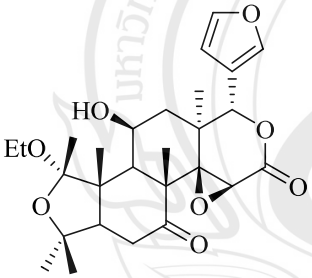
E = Limonoids



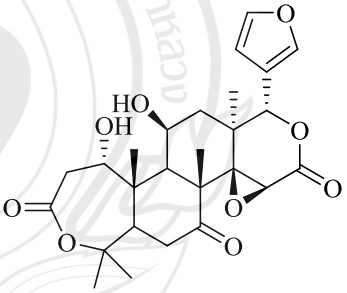
Clausenolide (**E1**)



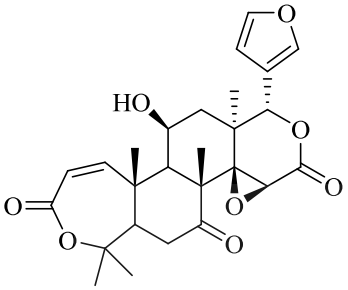
1-*O*-Methylclausenolide or
Clausenolide-1-methyl ether (**E2**)



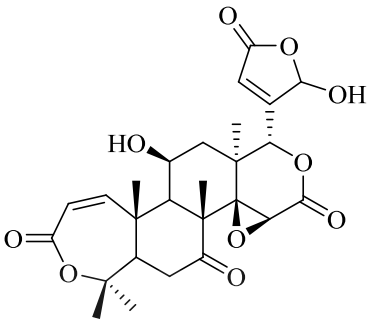
Clausenolide-1-ethyl ester (**E3**)



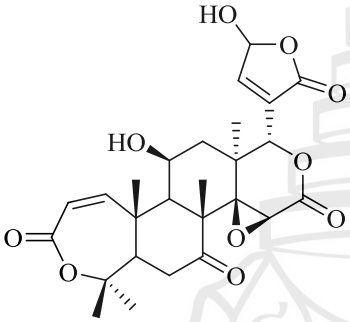
Clausenarin (**E4**)



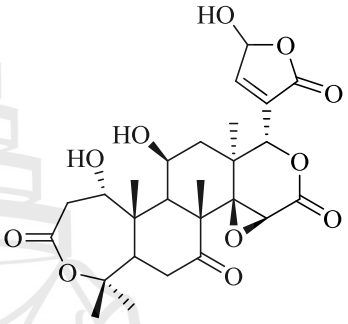
Zapoterin (**E5**)



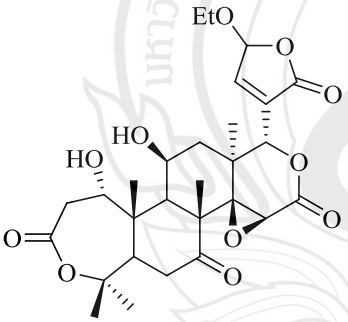
21,23-Dihydro-21-hydroxy-23-oxozapoterin (**E6**)



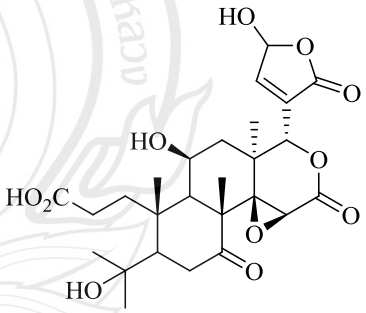
21,23-Dihydro-23-hydroxy-21-oxozapoterin (**E7**)



21,23-Dihydro-23-hydroxy-21-oxoclausenarin (**E8**)

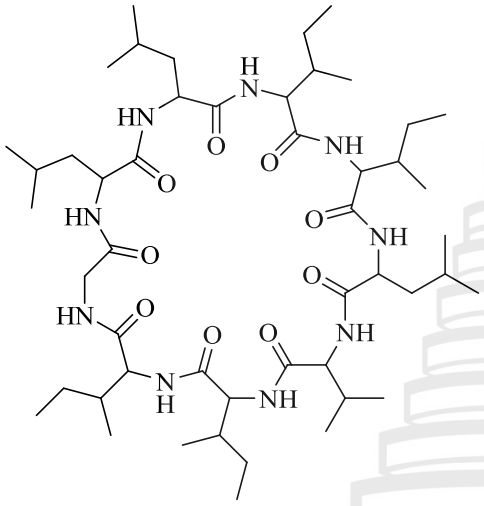


23-Ethoxy-21,23-dihydro-21-oxoclausenarin (**E9**)

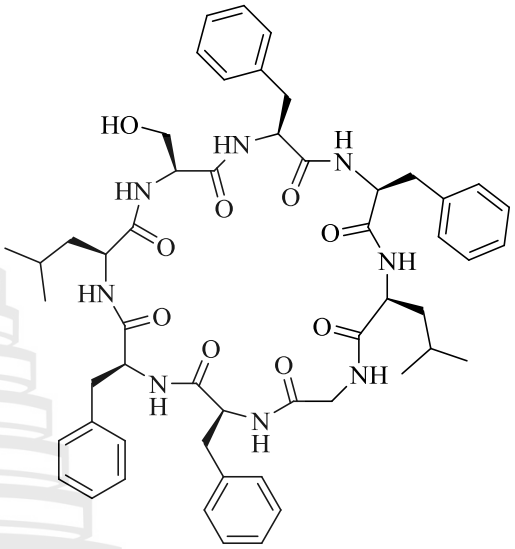


(11')-1,2,21,23-tetrahydro-11,23-dihydroxy-21-oxoobacunoic acid (**E10**)

F = Peptides

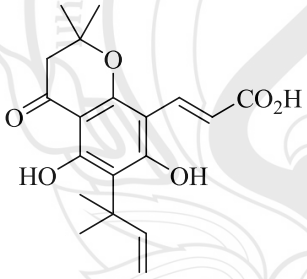


Clausenain I (**F1**)

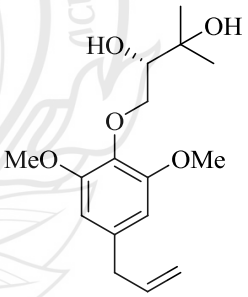


Clausenain B (**F2**)

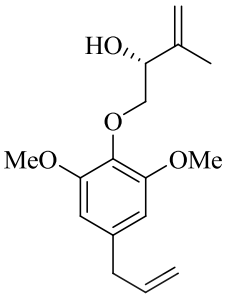
G = Phenylpropanoids



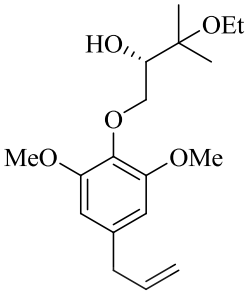
Clausenidinaric acid (**G1**)



Lenisin A (**G2**)

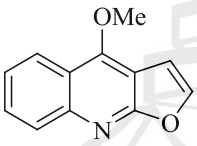


Lenisin B (**G3**)

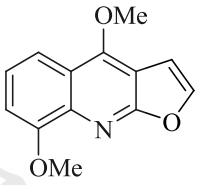


Lenisin C (**G4**)

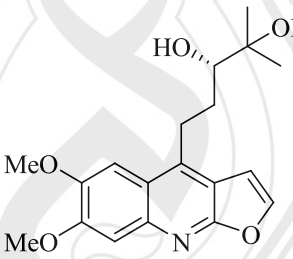
H = Quinolenes



Dectamine (**H1**)

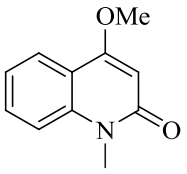


y-Fagarine (**H2**)

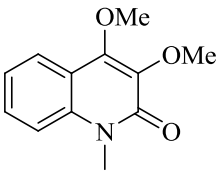


(2*S*)-1-[(6,7-Dimethoxyfuro[2,3-b]
quinolin-4-yl)oxy]-3-methylbutane-2,3-diol (**H3**)

I = Quinolones

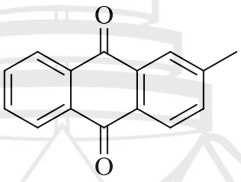


4-Methyl-1-methyl quinoline-2-one (**I1**)



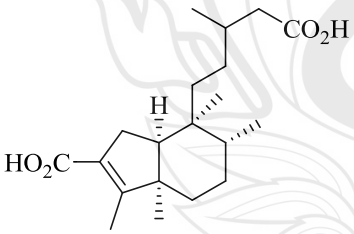
N-Methylswietenidine B (**I2**)

J = Quinones

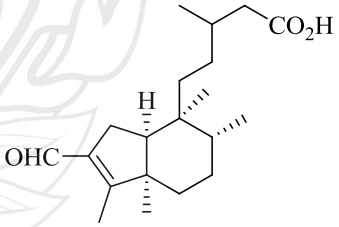


2-Methylantraquinone (**J1**)

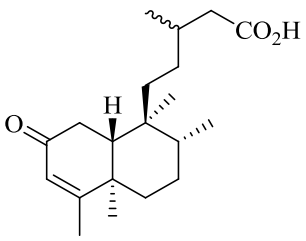
K = Terpenoids



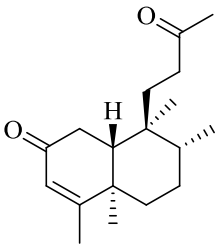
Dunniana acid A (**K1**)



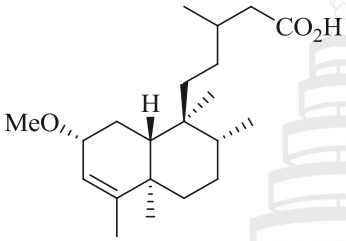
Dunniana acid B (**K2**)



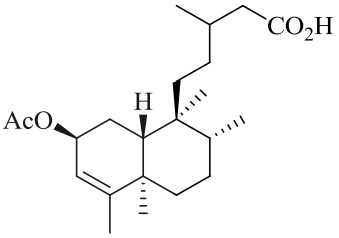
2-Oxoclerod-3-en-15-oic acid (**K3**)



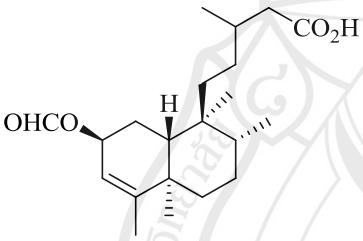
14,15-Dinorclerod-3-ene-2,13-dione (**K4**)



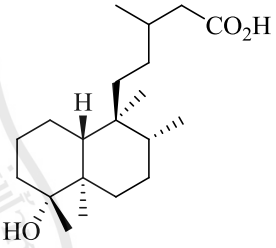
2a-Mehoxyclerod-3-en-15-oic acid (**K5**)



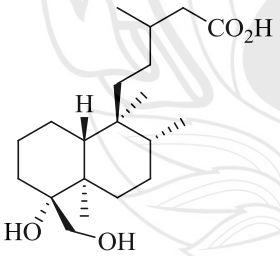
2β-(Acetyloxy)clerod-3-en-15-oic acid (**K6**)



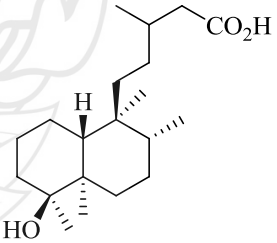
2β-(Formyloxy)clerod-3-en-15-oic acid (**K7**)



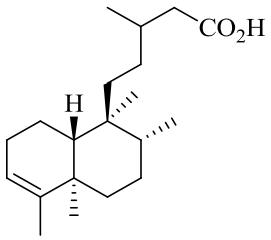
4α-Hydroxyclerodan-15-oic acid (**K8**)



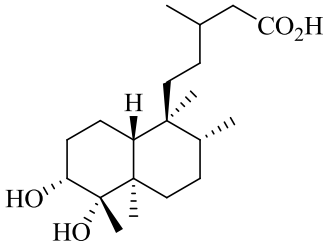
4α,18-Dihydroxyclerodan-15-oic acid (**K9**)



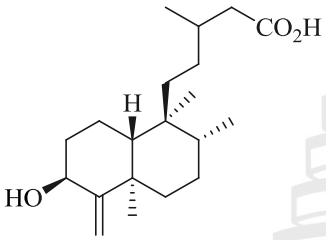
4β-Hydroxyclerodan-15-oic acid (**K10**)



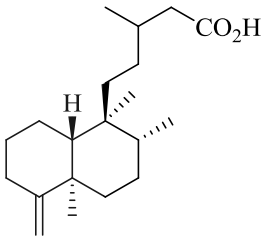
Clerodan-3-en-15-oic acid (**K11**)



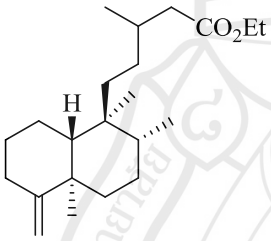
3α,4α-Dihydroxyclerodan-15-oic acid (**K12**)



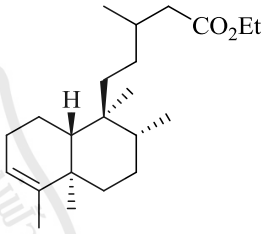
3β-Hydroxyclerodan-4(18)-en-15-oic acid (**K13**)



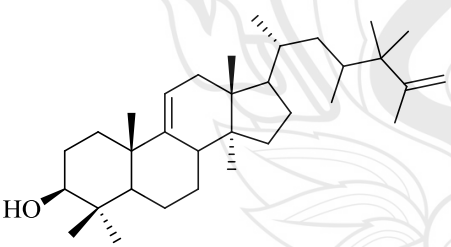
Clerodan-4(18)-en-15-oic acid (**K14**)



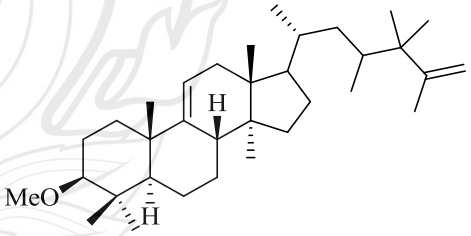
Ethyl clerodan-4(18)-en-15-oate (**K15**)



Ethyl clerodan-3-en-15-oate (**K16**)



Lansiol (**K17**)



O-Methylclausenol (**K18**)

1.3 Bioactivities from *Clausena* Plants

Various parts of *Clausena* plants are used for traditional medicine, such as the treatment of coughs, asthma, influenza, colds, and snake-bites (Kongkathip & Kongkathip, 2009). Many isolated compounds from this genus showed interesting pharmacological activities.

1.3.1 Anti-human Immunodeficiency Virus Activity (anti-HIV)

In 2003, Ayisi and Nyadedzor studied the effects of *C. anisata* leaves in vitro HIV-1 and HIV-2 infections which showed moderate activity at ED_{50} values of 0.70 and 0.12 mg/mL, respectively (Ayisi & Nyadedzor, 2003).

In 2005, Kongkathip and co-worker found that compounds isolated from *C. excavata* rhizomes and roots, *O*-methylmukonal (**B12**), 3-formyl-2,7-dimethoxycarbazole (**B40**), clauszoline J (**B41**), and clausenidin (**C19**), displayed anti HIV-1 activity in syncytial assay with EC_{50} values of 12.0, 29.1, 34.2, and 5.3 µM, respectively, and thus exhibited potential therapeutic index (PTI) values of 56.7, 8.0 , 1.6, and 7.0, respectively (Kongkathip, Kongkathip, Sunthitikawinsakul, Napaswat & Yoosook, 2005).

1.3.2 Anti-hepatitis B Virus Activity (anti-HBV)

In 2009, Su and co-worker reported the study of anti-HBV of natural pyranocoumarins derivatives from *C. excavata*, which found clausenidin (**C19**) with EC_{50} 1.88 µM (Su et al., 2009).

1.3.3 Anti-tumor Promoting Activity

In 2000, Ito and coworker described the inhibitory effects on Epstein–Barr virus early antigen (EBV-EA) activation induced by 12-*O*-tetradecanoylphorbol-13-acetate (TPA) in Raji cells of carbazole alkaloids from the acetone extract of *C. anisata* branches. The results showed that ekeberginine (**B63**) exhibited more effective on EBV-EA inhibition (89.5%, 77.6%, 36.5%, and 9.7% inhibition of

activation at 1×10^3, 5×10^2, 1×10^2, 10 mol ratio/TPA, respectively) (Ito et al., 2000). In addition, Takemura and co-worker also reported the inhibitory effects of bicoumarins on EBV-EA activation induced by TPA in Raji cells. They found cladimarin A (**C80**) showed almost equal inhibitory activity to that of *β*-carotene (Takemura et al., 2004).

1.3.4 Cytotoxicity

Many carbazole alkaloids displaied cytotoxicity against a variety of tumor cell lines. In 2007, Taufiq-Yap and co-worker reported the cytotoxicity against T-lymphoblastic leukeamia cell line (CEM-SS) of carbazole alkaloid derivatives from *C. excavata* stems. 3-Carbomathoxy-2-hydroxy-7-methoxycarbazole (**B35**) showed significant cytotoxicity with an IC_{50} value of 8.2 µg/mL (Taufiq-Yep et al., 2007).

In 2009, Ito and co-worker reported the cytotoxic activity against human leukemia cell line (HL-60) at a concentration of 30 µM and clausamine E (**B91**) exhibited 47.3% cell viability. (Ito et al., 2009).

In 2010, Thongthoom and co-worker reported that some compounds from *C. harmandiana* root, carbazole alkaloid **B52**, showed strong cytotoxicity against human lung cancer cell line (NCI-H187) with an IC_{50} value of 1.63 µg/mL. Compound **B39** also exhibited strong cytotoxicity against human breast cancer (MCF-7) and human epidermoid carcinoma (KB) cell lines with IC_{50} values of 2.21 and 1.74 µg/mL, respectively (Thongthoom, Songsiang, Phaosiri & Yenjai, 2010). In the same year Prasad and co-worker also reported that 8-hydropsorelen (**C25**) exhibited anti-cancer activity against human hepatocellular liver carcinoma (HepG2), human lung adenocarcinoma epithelial (A549), and human cervical carcinoma cell lines (HELA) with IC_{50} values of 0.34, 0.013, and 28.2 µg/mL, respectively (Prasad, et al., 2010).

In 2011, Muhd Sharif and co-worker showed that some limonoid, carbazole alkaloids, and coumarins isolated from the leaves, stem bark, and roots of *C. excavata* exhibited cytotoxicity against HL-60 (human promyelocytic leukemia cancer), MCF-7 (human breast cancer), HeLa (human cervical cancer), and HT-29 (human colon

cancer) and dentatin (**C17**) exhibited the most cytotoxicity against all cancer cell lines with an IC_{50} values ranging from 5 to 10 µg/mL (Muhd Sharif, et al, 2011).

1.3.5 Anti-nociceptive Activity

In 2002, Rahman and co-worker found that the ethanol extract of *C. excavata* leaves showed significant anti-nociceptive activity on acetic acid induced writhing in mice by oral at doses of 125.25 and 500 mg/Kg body weight (Rahman, Alimuzzaman, Shilpi & Hossain, 2002).

1.3.6 Anti-platelet Activity

Clausine D (**B61**), isolated from the leaves of *C. excavata* showed the exhibition of anti-platelet activity in vitro. The inhibitory effect varied depending on the types of aggregation inducers. Their compound inhibited most strongly when induced by arachidonic acid (AA) and collagen-induced platelet aggregation with IC_{50} values of 9.0 ± 1.1 and 58.9 ± 0.9 µM, respectively. On the other hand, inhibition was less when induced by collagen whereas there was no effect when induced by U46619, PAF, and thrombin. Compound **B61** also inhibited increasing intracellular concentration of calcium in platelet aggregation caused by AA and collagen (Wu, Huang, Lai, Teng, Ko & Kuoh, 1993).

1.3.7 Immunimodulatory Activity

In 2003, Manosroi and co-worker proved the immunomodulatory activity of aqueous, acetone, and 35% aqueous-ethanol extract of the woods of *C. excavata* by test in vitro mouse macrophage phagocytosis and splenocyte proliferation assay. The results found that all extracts showed phagocytic modulation, but no dose response relationships (Manosroi, Saraphanchotiwitthaya, & Manosroi, 2003). In addition, the same group reported in 2004 that the hot aqueous extract and the acetone extract were more splenocyte-proliferation active than the folklore extract (Manosroi, Saraphanchotiwitthaya, & Manosroi, 2004). The following year, this group showed the effect *in vivo* of the crude extracts of *C. excavata* on the production of

haemagglutinating antibodies (HA) in mice by intraperitoneal administration and oral route. The results found the 35% aqueous-ethanol extract from the wood of *C. excavata* showed potent in vitro and in vivo immunomodulating activity in mice (Manosroi, Saraphanchotiwitthaya, & Manosroi, 2005).

1.3.8 Anti-malarial Activity

In 2010, Sripisut and Laphookhieo found that *O*-methylmukonal (**B12**), isolated from the stems of *C. excavata*, showed anti-malarial activity against *Plasmodium falciparum* K1 strain with a MIC value of 6.74 µg/mL (Sripisut & Laphookhieo, 2010).

1.3.9 Anti-microbial Activities

1.3.9.1 Anti-mycobacterial activity

Some coumarins and carbazole alkaloids showed anti-mycobacterial activity. In 2003, Sunthitikawinsakul and co-worker reported anti-mycobacterial activity against *Mycobacteriam tuberculosis* H37Ra from the chloroform extract of *C. excavata* rhizomes with a MIC of 25 µg/mL. The isolated compounds **B2**, **B3**, **B10**, **B39**, **B41**, **C16**, **C17**, and **C19** also exhibited anti-mycobacterial activity against *M. tuberculosis* H37Ra with MIC values ranging from 50-200 µg/mL, respectively (Sunthitikawinsakul et al., 2003).

1.3.9.2 Anti-fungal activity

Sunthitikawinsakul and co-worker reported the anti-fungal activity from the rhizome and roots of *C. excavata*. The results showed that carbazole alkaloids **B2**, **B3**, **B10**, and **B39** displayed antifungal activity against *Candida albicans* with IC_{50} values of 13.6, 9.5, 29.3, and 2.8, respectively.

1.3.10 Stimulate Glucose Uptake in L6 Myotubes

In 2010, Noipha and coworker were reported the exhibited glucose uptake activity in L6 myotube of carbazole alkaloids and coumarins from *C. harmandiana*. The result showed that heptaphylline (**B48**) and 7-methoxyheptaphylline **(B51**) with

50 µM, while nordentatin (**C16**) showed the most significant increases in glucose uptake at 25 µM. In addition, compounds **B51** and **C16** were inhibited by P38 mitogen activated protein kinases and phosphatidylimositol 3-kinases, respectively (Noipha, Thongthoom, Songsiang, Boonyarat, & Yenjai, 2010).

1.3.11 Neuroprotective Activity

In 2012, Liu and co-worker reported the neuroprotective effect on neuron-like PC12 cells induced by serum withdrawal, A$\beta_{25\text{-}35}$, and sodium nitroprusside (SNP) in vitro of carbazole alkaloids from *C. lansium*. At 10 µM, compounds **B8**, **B48**, **B53**, **B57**, and **B83** increased the cell survival rate of the A$\beta_{25\text{-}35}$-treated group (Liu et al., 2012).

1.3.12 Anti-inflammatory Activity

Shen and co-worker reported anti-inflammatory activity of compounds isolated from the stems of *C. lansium*. Among the isolated compounds, osthol (**C6**), imperatorin (**C26**), and isoheraclenin (**C28**) exhibited selective and potent inhibition of formyl-L-methionyl-L-leucyl-L-phenylalanine/cytochalasin B (fMLP/CB)-induced superoxide anion generation. Lansiumarin C (**C29**) decreased nitric oxide (NO) and tumor necrosis factor-α (TNF-α) production in lipopolysaccharide (LPS)-induced macrophages (Shen et al., 2012).

1.4 Research Objectives

The purpose of this research involved extraction, isolation, purification and structure elucidation of chemical constituents from *Clausena* plants in the northern part of Thaland, including *C. harmandiana*, *C. lansium*, and *C. wallichii*. Some of the isolated compounds will be further evaluated for their cytotoxicity and antibacterial activities.

CHAPTER 2

RESEARCH METHODOLOGY

2.1 Instruments and Chemicals

Melting points were recorded in °C was determined using a Buchi melting point B-540 apparatus. The optical rotation $[\alpha]_D$ value were determined with a Bellingham & Stanley APD440 polarimeter. The UV-vis spectra were recorded with a Perkin-Elmer UV-Vis spectrophotometer. The IR spectra were recorded using a Perkin-Elmer FTS FT-IR spectrophotometer. Nuclear magnetic resonance spectra (NMR) were recorded using 400 MHz Bruker and 500 MHz Varian UNITY INOVA spectrometers. The spectra were recorded in deuterochloroform ($CDCl_3$) and deuteroacetone (acetone-d_6) and were reported as δ value in ppm downfield from tetramethylsilane (TMS) as an internal reference. The high resolution mass spectrometry was obtained from a MicroToF, Bruker Daltonics (ESI-TOF-MS) or MAT 95 XL mass spectrometers (HR-EI-MS). Quick column chromatography (QCC) and column chromatography (CC) were carried out on silica gel 60 (Merck, 230-400 Mesh ASTM) and silica gel 100 (Merck, 70-230 Mesh ASTM), respectively. Sephadex™ LH-20 was used for isolation proceduce. Preparative TLC silica gel 60 F_{254} was used for analytical purposes.

2.2 Plant Materials

All plants were collected from the northern part of Thailand. The twigs and fruits of *C. harmandiana* were collected from Chiang Rai Province in March 2010 and July 2011, respectively. The roots and twigs of *C. lansium* were collected from Nan Province in April 2008. In addition, the roots and twigs of *C. wallichii* were collected from Phrae Province in June 2010. All plants were identified by Dr. Monthon Norsaengsri and Mr. James Maxwell and voucher specimen numbers QBG 45335 (*C. harmandiana*), QBG 25077 (*C. lansium*), and QBG 4533 (*C. wallichii*) were deposited at the Herbarium of Queen Sirikit Botanic Garden, Mae Rim, Chiang Mai, Thailand.

2.3 Extraction

2.3.1 Extraction of *C. harmandiana* Twigs

Air-dried twigs of *C. harmandiana* (4.91 Kg) were cut into small pieces and extracted with hexanes and acetone over period of 3 days (2 times per each) at room temperature, respectively. The hexanes and acetone extracts were filtered and concentrated under reduced pressure to give hexanes (14.39 g) and acetone (29.22 g) extracts. Both extracts were combined (CHT, 43.61 g) because of the similarity of the TLC chromatogram (Figure 2.1).

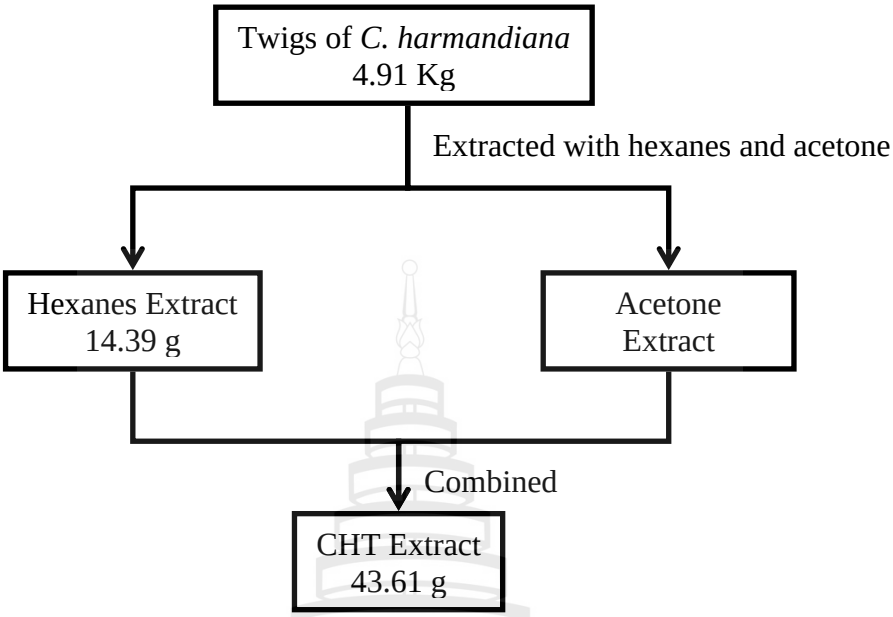


Figure 2.1 Extraction of *C. harmandiana* Twigs

2.3.2 Extraction of *C. harmandiana* Fruits

The fresh fruits of *C. harmandiana* (4.09 Kg) were milled and extracted with acetone over a period of 3 days (2 times) at room temperature. The filtered solution was evaporated to dryness under reduced pressure to afford CHF extract (181.5 g) (Figure 2.2).

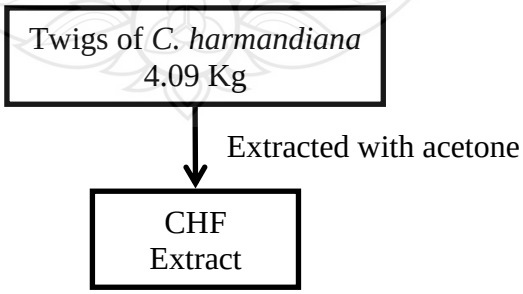


Figure 2.2 Extraction of *C. harmandiana* Fruits

2.3.3 Extraction of *C. lansium* Roots

The air-dried roots of *C. lansium* (2.93 Kg) were cut into small pieces and extracted successively with hexanes and acetone over a period of 3 days (2 times per each) at room temperature. The hexanes and acetone extracts were filtered and concentrated under reduced pressure to give hexanes (15.48 g) and acetone (47.07 g) extracts, respectively. The hexanes and acetone extracts were combined (CLR, 62.55 g) due to the similarity of the TLC chromatogram (Figure 2.3).

2.3.4 Extraction of *C. lansium* Twigs

Air-dried twigs of *C. lansium* (6.73 Kg) were cut into small pieces and extracted successively with CH_2Cl_2 and acetone over a period of 3 days (2 times per each) at room temperature. The filtered of CH_2Cl_2 and acetone extracts were concentrated under reduced pressure yielded CH_2Cl_2 (14.20 g) and acetone (19.82 g) extracts, respectively. The CH_2Cl_2 and acetone crude extracts were combined (CLT, 34.02 g) because of the similarity of the TLC chromatogram (Figure 2.4).

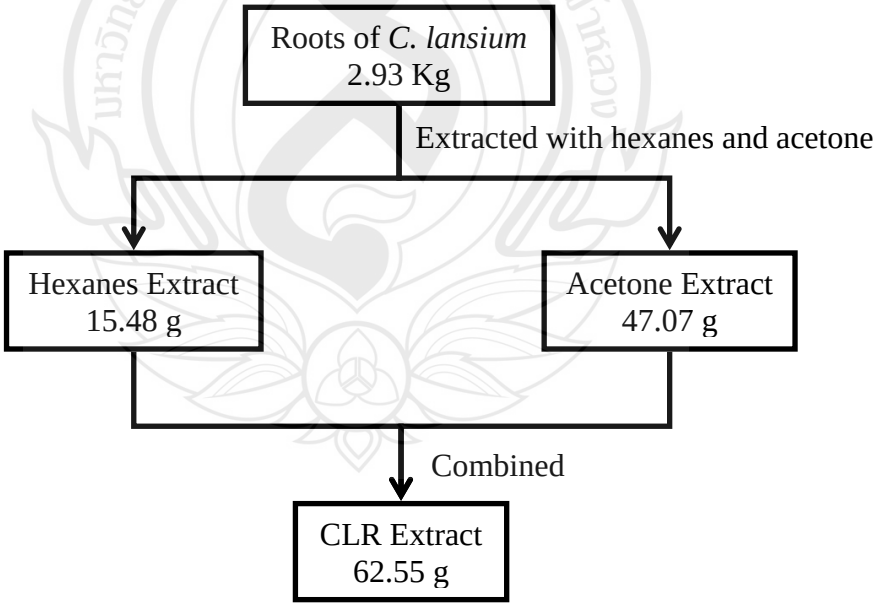


Figure 2.3 Extraction of *C. lansium* Roots

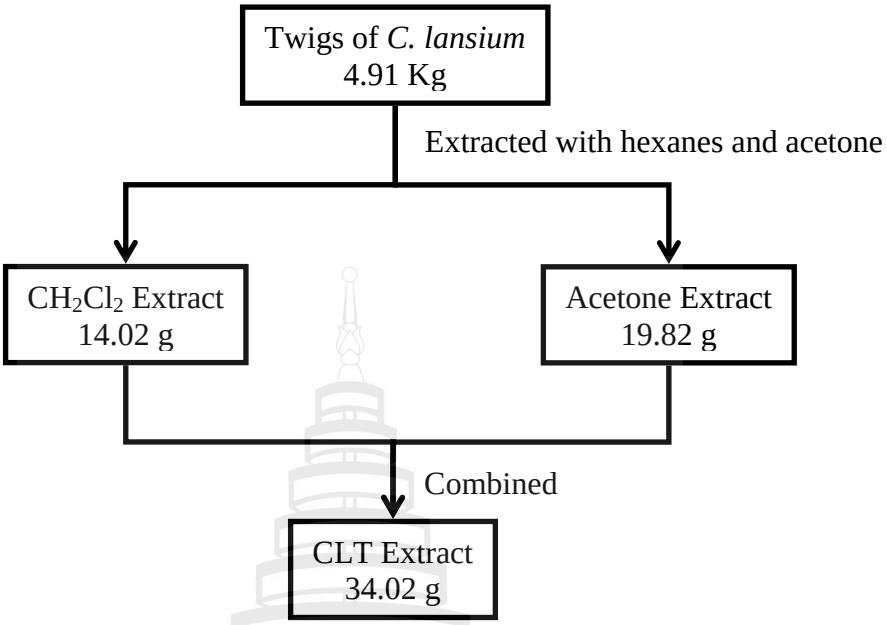


Figure 2.4 Extraction of *C. lansium* Twigs

2.3.5 Extraction of *C. wallichii* Roots

The air-dried roots of *C. wallichii* (1.02 Kg) were cut into small pieces and extracted with acetone over a period of 3 days (2 times per each) at room temperature. The acetone extract was filtered and concentrated under reduced pressure to provide acetone extract (CWR, 18.68 g) (Figure 2.5).

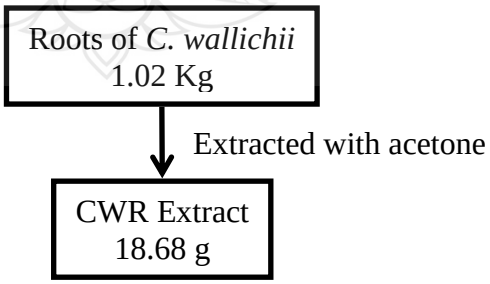


Figure 2.5 Extraction of *C. wallichii* Roots

2.3.6 Extraction of *C. wallichii* Twigs

Air-dried twigs of *C. wallichii* (8.44 Kg) were cut into small pieces and extracted with acetone over a period of 3 days (2 times per each) at room temperature. The filtered of the acetone extract were concentrated under reduced pressure to give acetone extract (CWT, 113.20 g) (Figure 2.6).

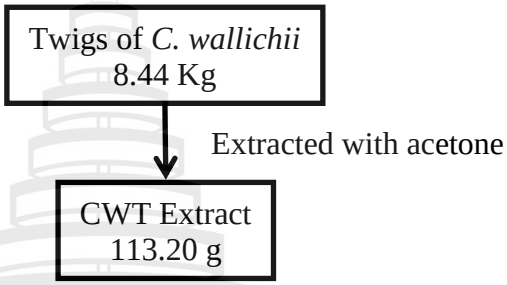


Figure 2.6 Extraction of *C. wallichii* Twigs

2.4 Isolations

2.4.1 Isolation of *C. harmandiana* Twigs

The CHT extract (43.61 g) was subjected to QCC over silica gel using a gradient system of hexanes-EtOAc (100% hexanes to 100% EtOAc) to provide twelve fractions (A-L).

Fraction C (1.10 g) was separated by CC with 50% CH_2Cl_2-hexanes to yield compounds **WM36** (19.9 mg) and **WM39** (2.1 mg).

Compound **WM36** (Heptaphylline): Yellow solid; mp 172-173 °C; UV (MeOH) λ_{max} 236, 250, 277, 298, 342 nm; IR (neat) ν_{max} 3313, 1613, 1474, 1329, 1230 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 11.65 (1H, s, 2-OH), 9.89 (1H, s, 3-CHO), 8.03 (1H, s, H-4), 7.96 (1H, d, *J* = 8.0 Hz, H-5), 7.40 (1H, m, H-8), 7.38 (1H, m, H-7), 7.27 (1H, m, H-6), 5.31 (1H, t, *J* = 3.2 Hz, H-2′), 3.63 (2H, d, *J* = 3.2 Hz, H-1′), 1.89 (3H, s, H-4′), 1.67 (3H, s, H-5′); ^{13}C NMR (100 MHz, $CDCl_3$) 195.4 (3-CHO), 157.8 (C-2), 145.0 (C-9a), 140.1 (C-8a), 134.2 (C-3′), 125.8 (C-7), 125.3 (C-4), 123.6 (C-4b), 121.2 (C-2′), 120.8 (C-5), 119.8 (C-6), 117.3 (C-3), 115.4 (C-4a), 110.8 (C-8), 109.0 (C-1), 25.7 (C-4′), 22.8 (C-1′), 18.1 (C-5′).

Compound **WM39** (Girinimbine): Yellow solid; mp 175-176 °C; UV (MeOH) λ_{max} 241, 247, 255, 268, 310, 322, 335 nm; IR (neat) ν_{max} 3373, 1682, 1605, 1582, 1234 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 7.91 (1H, d, *J* = 8.0 Hz, H-5), 7.83 (1H, br s, 9-NH), 7.67 (1H, s, H-4), 7.38 (1H, d, *J* = 8.0 Hz, H-8), 7.30 (1H, t, *J* = 8.0 Hz, H-7), 7.17 (1H, t, *J* = 8.0 Hz, H-6), 6.64 (1H, d, *J* = 10.0 Hz, H-1′), 5.70 (1H, d, *J* = 10.0 Hz, H-2′), 2.32 (3H, s, 3-Me), 1.47 (6H, s, H-4′ and H-5′); ^{13}C NMR (100 MHz, $CDCl_3$) 149.8 (C-2), 139.5 (C-8a), 134.8 (C-9a), 129.4 (C-7), 124.2 (C-2′), 123.9 (C-4b), 121.1 (C-5), 119.5 (C-1′), 119.3 (C-6), 118.5 (C-3), 117.2 (C-4), 116.7 (C-4a), 110.4 (C-8), 104.4 (C-1), 75.8 (C-3′), 27.6 (C-4′ and C-5′), 16.1 (3-Me).

Fraction D (1.05 g) was performed by CC using silica gel with 50% CH_2Cl_2-hexanes to yielded compound **WM45** (46.0 mg).

Compound **WM45** (Clausemine D): Yellow powder; UV (MeOH) λ_{max} 240, 251, 256, 268, 309, 322, 326 nm; IR (neat) ν_{max} 3386, 1685, 1240 cm^{-1}; ^1H NMR (400

MHz, $CDCl_3$) 8.52 (1H, br s, 9-NH), 8.12 (1H, br d, *J* = 7.6 Hz, H-5), 7.49 (1H, br d, *J* = 7.6 Hz, H-8), 7.45 (1H, s, H-2), 7.43 (1H, td, *J* = 7.6 and 1.2 Hz, H-7), 7.26 (1H, td, *J* = 7.6 and 1.2 Hz, H-6), 5.28 (1H, m, H-2′), 4.30 (2H, d, *J* = 5.6 Hz, H-1′), 4.01 (3H, s, 1-OMe), 3.93 (3H, s, 3-CO_2Me), 1.90 (3H, d, *J* = 1.2 Hz, H-4′), 1.70 (3H, d, *J* = 1.2 Hz, H-5′).

Fraction E (1.16 g) was isolated by CC with 60% CH_2Cl_2-hexanes and followed by Sephadex-LH20 eluting with 100% MeOH to give compound **WM38** (4.6 mg).

Compound **WM38** (Clausine S): Yellow viscous oil; UV (MeOH) λ_{max} 207, 235, 249, 278, 329, 343 nm; IR (neat) ν_{max} 3356, 1612, 1231 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 11.70 (1H, s, 2-OH), 9.90 (1H, s, 3-CHO), 9.46 (1H, br s, 9-NH), 8.07 (1H, s, H-4), 7.97 (1H, d, *J* = 8.0 Hz, H-5), 7.43 (1H, d, *J* = 8.0 Hz, H-8), 7.39 (1H, m, H-7), 7.25 (1H, m, H-6), 5.00 (1H, br s, H-4a′), 4.86 (1H, br s, H4b′), 4.78 (1H, br d, *J* = 8.0 Hz, H-2′), 3.36 (1H, dd, *J* = 14.7 and 2.0, H-1a′), 3.03 (1H, dd, *J* = 14.7 and 8.0 Hz, H-1b′), 2.17 (1H, br s, 2′-OH), 1.91 (3H, s, H-5′); ^{13}C NMR (100 MHz, $CDCl_3$) 195.3 (3-CHO), 158.4 (C-2), 147.6 (C-3′), 146.6 (C-9a), 140.6 (C-8a), 125.8 (C-4 and C-7), 123.8 (C-4b), 120.6 (C-6), 119.7 (C-5), 117.4 (C-4a), 115.1 (C-3), 111.1 (C-8), 110.1 (C-4′), 107.4 (C-1), 76.7 (C-2′), 30.8 (C-1′), 18.6 (C-5′) .

The isolation of fraction G (1.75 g) by repeated Sephadex-LH20 with 100% MeOH and followed by CC using 30% EtOAc-hexanes yielded compounds **WM44** (13.8 mg), **WM47** (18.3 mg), and **WM71** (40.0 mg).

Compound **WM44** (Clausine F): Yellow solid; mp 198-200 °C; UV (MeOH) λ_{max} 208, 224, 241, 269, 312, 324, 338 nm; IR (neat) ν_{max} 3381, 2924, 1689, 1586, 1455, 1340, 1237 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6) 10.66 (1H, br s, 9-NH), 8.90 (1H, br s, 1-OH), 8.14 (1H, br d, *J* = 8.0 Hz, H-5), 7.63 (1H, br d, *J* = 8.0 Hz, H-8), 7.47 (1H, s, H-2), 7.42 (1H, td, *J* = 8.0 and 0.8 Hz, H-7), 7.82 (1H, td, *J* = 8.0 and, 1.2 Hz, H-6), 5.25 (1H, m, H-2′), 4.33 (2H, d, *J* = 5.6 Hz, H-1′), 1.99 (3H, s, H-4′), 1.67 (3H, d, *J* = 1.2 Hz, H-5′); ^{13}C NMR (100 MHz, acetone-d_6) 169.1 (3-$\underline{C}O_2$Me), 141.3 (C-8a), 141.2 (C-1), 132.7 (C-9a), 132.0 (C-3′), 126.3 (C-4), 126.2 (C-7), 124.6 (C-4b) 124.2 (C-4a and C-2′), 123.7 (C-5), 120.3 (C-6), 112.3 (C-2), 51.8 (3-$CO_2\underline{Me}$), 29.1 (C-1′), 25.8 (C-5′), 18.4 (C-4′).

Compound **WM47** (Clausamine B): Yellow viscous oli; UV (MeOH) λ_{max} 208, 238, 249, 269, 279, 322, 335 nm; IR (neat) ν_{max} 3291, 2924, 1690, 1586, 1355, 1309 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6) 11.01 (1H, s, 9-NH), 8.22 (1H, d, *J* = 7.6 Hz, H-5), 7.68 (1H, d, *J* = 8.4 Hz, H-8), 7.56 (1H, s, H-2), 7.48 (1H, td, *J* = 8.4 and 1.2 Hz, H-7), 7.28 (1H, td, *J* = 7.6 and 1.2 Hz, H-6), 5.28 (1H, br s, H-4a′), 5.15 (1H, dd, *J* = 11.0 and 3.6 Hz, H-2′), 5.09 (1H, br s, H-4b′), 4.08 (3H, s, 1-OMe), 3.75 (1H, dd, *J* = 16.4 and 3.6 Hz, H-1a′), 3.56 (1H, m, H-1b′), 1.28 (3H, s, H-5′).

Compound **WM71** (Dectamine): White solid; mp 131-132 °C; UV (MeOH) λ_{max} 236, 308, 314, 329 nm; IR (neat) ν_{max} 1625, 1582, 1087 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6) 8.28 (1H, d, *J* = 8.0 Hz, H-5), 7.91 (1H, d, *J* = 8.0 Hz, H-8), 7. 88 (1H, d, *J* = 2.8 Hz, H-3′), 7.70 (1H, t, *J* = 8.0 Hz, H-7), 7.47 (1H, t, *J* = 8.0 Hz, H-6), 7.41 (1H, d, *J* = 2.8 Hz, H-2′), 4.54 (3H, s, 4-OMe); ^{13}C NMR (100 MHz, $CDCl_3$), 163.8 (C-2), 156.5 (C-4), 145.6 (C-8a), 143.5 (C-3′), 129.6 (C-7), 127.7 (C-8), 123.7 (C-6), 122.3 (C-5), 118.6 (C-4a), 104.2 (C-2′), 103.4 (C-3), 59.0 (4-OMe).

Fraction H (2.98 g) was isolated by CC with 30% EtOAc-hexanes to provide four subfractions (H1-H4). Subfraction H2 (234.1 mg) was repeated by Sephadex-LH20 using 100% MeOH to afford compound **WM43** (5.8 mg) and four subfraction (H2a-H2d). Subfraction H2b (52.7 mg) was purified by CC with 5% acetone-CH_2Cl_2 to give compounds **WM3** (30.3 mg), **WM5** (1.4 mg), and **WM15** (1.9 mg). Fraction H4 (160.3 mg) was subjected to Sephadex-LH20 using 100% MeOH to give compound **WM46** (22.3 mg).

Compound **WM3** (*O*-Demethylmurrayanine): Yellow solid; mp 234-236 °C; UV (MeOH) λ_{max} 221, 239, 248, 273, 288, 332, 342 nm; IR (neat) ν_{max} 3353, 1671 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6) 10.81 (1H, br s, 9-NH), 10.01, (1H, s, 3-CHO), 9.31 (1H, s, 1-OH), 8.27 (1H, s, H-4), 8.20 (1H, d, *J* = 8.0 Hz, H-5), 7.47 (1H, td, *J* = 8.0 and 0.8 Hz, H-7), 7.43 (1H, d, *J* = 1.2 Hz, H-2), 7.27 (1H, td, *J* = 8.0 and 0.8 Hz, H-6); ^{13}C NMR (100 MHz, acetone-d_6) 191.9 (3-CHO), 144.5 (C-1), 141.4 (C-8a), 134.9 (C-9a), 127.2 (C-7), 125.1 (C-4a), 124.5 (C-4b), 121.3 (C-5), 120.8 (C-6), 119.2 (C-4), 112.7 (C-3 and C-8), 108.4 (C-2).

Compound **WM5** (Clauszoline I): Yellow viscous oil; UV (MeOH) λ_{max} 219, 237, 248, 272, 287, 330, 340 nm; IR (neat) ν_{max} 3283, 1701 cm^{-1}; ^{1}H NMR (400 MHz,

$CDCl_3$) 8.52 (1H, br s, 9-NH), 8.45 (1H, s, H-4), 8.10 (1H, d, *J* = 8.0 Hz, H-5), 7.61 (1H, s, H-2), 7.50 (1H, d, *J* = 8.0 Hz, H-8), 7.46 (1H, t, *J* = 8.0 Hz, H-7), 7.28 (1H, t, *J* = 8.0 Hz, H-6), 5.98 (1H, br s, 1-OH), 3.97 (3H, s, 3-CO_2Me).

Compound **WM15** (Clauszoline N): Yellow powder; mp 224-225 °C; UV (MeOH) λ_{max} 203, 231, 281, 309, 341, 361 nm; IR (neat) ν_{max} 3318, 1646, 1629 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6) 11.45 (1H, s, 2-OH), 10.52 (1H, br s, 9-NH), 9.95 (1H, s, 3-CHO), 8.36 (1H, s, H-4), 8.23 (1H, br s, 7-OH), 7.51 (1H, d, *J* = 2.0 Hz, H-5), 7.31 (1H, d, *J* = 8.8 Hz, H-8), 6.94 (1H, dd, *J* = 8.8 and 2.0 Hz, H-7), 6.82 (1H, s, H-1); ^{13}C NMR (100 MHz, acetone-d_6) 196.4 (3-CHO), 161.7 (C-2), 153.0 (C-6), 147.6 (C-9a), 135.8 (C-8a), 128.7 (C-4), 125.1 (C-4b), 115.8 (C-4a), 115.4 (C-7), 112.4 (C-3 and C-8), 106.1 (C-5), 97.0 (C-1).

Compound **WM43** (Clausine D): Brown powder; mp 297-298 °C; UV (MeOH) λ_{max} 224, 241, 253, 275, 289, 344 nm; IR (neat) ν_{max} 3379, 2924, 1655, 1582, 1450, 1334 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6) 10.87 (1H, br s, 9-NH), 10.39 (1H, s, 3-CHO), 8.16 (1H, d, *J* = 8.0 Hz, H-5), 7.67 (1H, d, *J* = 8.0 Hz, H-8), 7.45 (1H, t, *J* = 8.0 Hz, H-7), 7.43 (1H, s, H-2), 7.26 (1H, t, *J* = 8.0 Hz, H-6), 5.31 (1H, m, H-2′), 4.39 (2H, d, *J* = 6.0 Hz, H-1′), 1.93 (3H, s, H-4′), 1.63 (3H, s, H-5′); ^{13}C NMR (100 MHz, acetone-d_6) 189.9 (3-CHO), 141.6 (C-8a), 140.6 (C-1), 134.4 (C-9a), 131.9 (C-3′), 126.3 (C-4b), 123.6 (C-4a), 123.0 (C-2′), 125.6 (C-7), 122.8 (C-4), 122.6 (C-5), 121.0 (C-3), 119.8 (C-6), 111.8 (C-8), 109.2 (C-2), 26.4 (C-1′), 24.8 (C-5′), 17.5 (C-4′).

Compound **WM46** (Clausamine A): Yellow solid; mp 243-245 °C; UV (MeOH) λ_{max} 223, 241, 250, 270, 325, 341 nm; IR (neat) ν_{max} 3502, 2921, 1697, 1365, 1229 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6) 10.87 (1H, br s, 9-NH), 9.33 (1H, br s, 1-OH), 8.20 (1H, d, *J* = 8.0 Hz, H-5), 7.67 (1H, d, *J* = 8.0 Hz, H-8), 7.56 (1H, s, H-2), 7.46 (1H, t, *J* = 8.0 Hz, H-7), 7.25 (1H, t, *J* = 8.0 Hz, H-6), 5.26 (1H, br s, H-4a′), 5.13 (1H, dd, *J* = 11.0 and 3.6 Hz, H-2′), 5.07 (1H, br s, H-4b′), 3.72 (1H, dd, *J* = 16.4 and 3.6 Hz, H-1a′) 3.52 (1H, m, H-1b′), 1.98 (3H, s, H-5′); ^{13}C NMR (100 MHz, acetone-d_6) 166.0 (C-10), 144.2 (C-3′), 142.9 (C-1), 141.4 (C-8a), 134.4 (C-9a), 128.5 (C-4), 126.6 (C-7), 124.0 (C-4b), 122.9 (C-5), 121.5 (C-4a), 120.7 (C-6), 117.0 (C-3), 113.6 (C-8), 112.6 (C-4′), 110.8 (C-2), 81.2 (C-2′), 30.1 (C-1′), 18.6 (C-5′).

Purification of fraction J (2.84 g) by QCC with 5% EtOAc-CH_2Cl_2 and followed by Sephadex-LH20 using 100% MeOH yielded compound **WM72** (2.4 mg).

Compound **WM72** (γ-Fagarine): Colorless solid; mp 155-156 °C; UV (MeOH) λ_{max} 243, 310 nm; IR (neat) ν_{max} 1621, 1518, 1095 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 7.84 (1H, dd, *J* = 8.4, 1.2 Hz, H-5), 7.64 (1H, d, *J* = 2.8 Hz, H-2′), 7.35 (1H, t, *J* = 8.4 Hz, H-6), 7.06 (1H, br d, *J* = 8.4 Hz, H-7), 7.07 (1H, d, *J* = 2.8 Hz, H-3′), 4.44 (3H, s, 4-OMe), 4.08 (3H, s, 8-OMe).

Fraction K (4.42 g) was separated by QCC with a gradient of 20% EtOAc-hexanes to 100% EtOAc to afford seven subfractions (K1-K7). Subfraction K2 (394.6 mg) was purified by Sephadex-LH20 using 100% MeOH followed by CC with 10% acetone-hexanes to give compounds **WM50** (1.1 mg) and **WM37** (1.6 mg). The purification of subfraction K4 (534.5 mg) by Sephadex-LH20 using 100% MeOH to give compound **WM14** (11.5 mg). Compounds **WM49** (1.8 mg) and **WM48** (7.1 mg) were derived from subfraction K6 (442.2 mg) by Sephadex-LH20 with 100% MeOH and followed by CC using 30% EtOAc-CH_2Cl_2.

Compound **WM14** (Clausine Z): Brown powder; mp 231-232 °C; UV (MeOH) λ_{max} 223, 242, 256, 278, 297, 340, 356 nm; IR (neat) ν_{max} 3262, 1652, 1631, 1614, 1583 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ_H 10.55 (1H, br s, 9-NH), 9.97 (1H, s, 3-CHO), 8.16 (1H, br s, H-4), 7.61 (1H, d, *J* = 2.4 Hz, H-5), 7.47 (1H, d, *J* = 8.8 Hz, H-8) 7.38 (1H, d, *J* = 1.2 Hz, H-2), 7.05 (1H, dd, *J* = 8,8 and 2.4 Hz, H-7).

Compound **WM37** (Harmandianamine C): Yellow solid; mp 228-229 °C; $[\alpha]_D^{29}$ = +18.6 (*c* = 0.011, MeOH); UV (MeOH) λ_{max} 204, 236, 247, 277, 298, 327, 342 nm; IR (neat) ν_{max} 3363, 2923, 2853, 1632, 1613, 1232 cm^{-1}; ^1H NMR (500 MHz, acetone-d_6), see Table 3.11; ^{13}C NMR (125 MHz, acetone-d_6), see Table 3.11; EI-MS (*m*/*z*): 312 (51), 253 (38), 223 (100), 166 (20); HR-EI-MS $[M]^+$ (*m*/*z*) 313.1305 (calcd for $C_{18}H_{19}NO_4$, 313.1309).

Compound **WM48** (Clausewatine D): Yellow powder; mp 241-243 °C; UV (MeOH) λ_{max} 222, 240, 250, 270, 325, 339 nm; IR (neat) ν_{max} 3422, 2926, 1686, 1361, 1228 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) 10.08 (1H, br s, 9-NH), 9.31 (1H, br s, 1-OH), 8.20 (1H, d, *J* = 8.0 Hz, H-5), 7.67 (1H, d, *J* = 8.0 Hz, H-8), 7.54 (1H, s, H-2), 7.44 (1H, t, *J* = 8.0 Hz, H-7), 7.26 (1H, t, *J* = 8.0 Hz, H-6), 4.23 (1H, dd, *J* =

12.8 and 3.2 Hz, H-2′) 3.77 (1H, dd, *J* = 16.4 and 3.2 Hz, H-1a′), 3.41 (1H, dd, *J* = 16.5 and 12.8 Hz, H-1b′), 1.42 (6H, s, H-4′ and H-5′).

Compound **WM49** (Harmandianamine B): Yellow solid; mp 216-217 °C; $[\alpha]_D^{29}$ = +36.2 (*c* = 0.012, MeOH); UV (MeOH) λ_{max} 204, 212, 237, 249, 269, 323, 335 nm; IR (neat) ν_{max} 3340, 2921, 2830, 1695, 1584, 1361 cm^{-1}; ^1H NMR (500 MHz, acetone-d_6), see Table 14; ^{13}C NMR (125 MHz, acetone-d_6), see Table 14; EI-MS (*m*/*z*): 340 (88), 263 (100), 236 (46), 224 (22), 209 (20), 153 (14); HR-EI-MS $[M]^+$ (*m*/*z*) 341.1266 (calcd for $C_{19}H_{19}NO_5$, 341.1258).

Compound **WM50** (Harmandianamine A): Yellow solid; mp 203-204 °C; $[\alpha]_D^{28}$ = +6.46 (*c* = 0.008, MeOH); UV (MeOH) λ_{max} 204, 207, 240, 250, 267, 310, 323, 337 nm; IR (neat) ν_{max} 3250, 2923, 2852, 1735, 1798 cm^{-1}; ^1H NMR (500 MHz, acetone-d_6), see Table 15; ^{13}C NMR (125 MHz, acetone-d_6), see Table 15; EI-MS (*m*/*z*): 292 (94), 277 (56), 250 (18), 233 (12), 209 (100), 181 (15); HR-EI-MS $[M]^+$ (*m*/*z*) 293.1054 (calcd for $C_{18}H_{15}NO_3$, 293.1046).

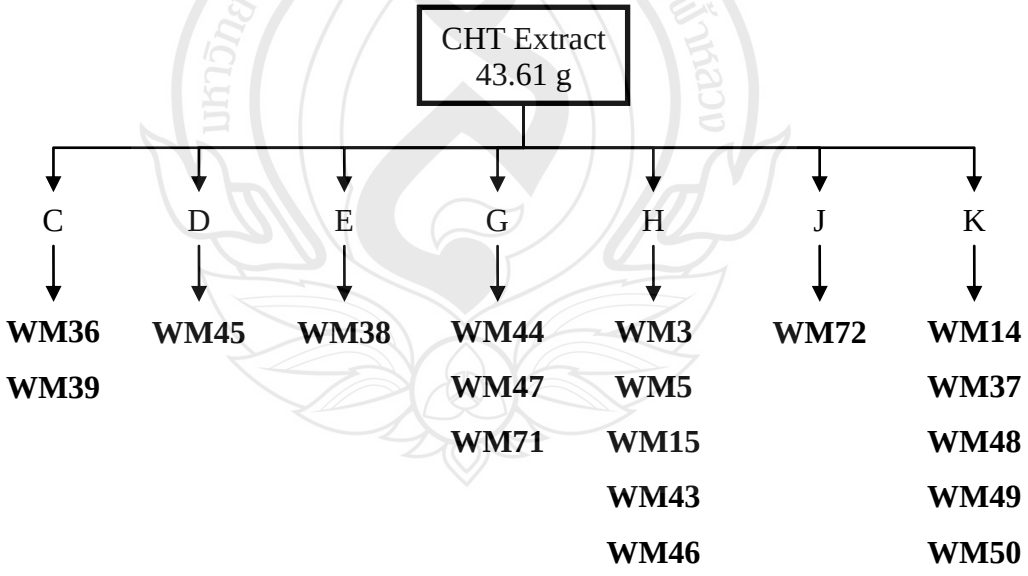


Figure 2.7 Isolation of CHT Extract from the Twigs of *C. harmandiana*

2.4.2 Isolation of *C. harmandiana* Fruits

The CHF crude (181.5 g) was subjected to QCC over silica gel using a gradient of hexanes-EtOAc (100% hexanes to 100% EtOAc) to provide six fractions (A-F). Fraction B (537.9 mg) was separated by CC with 30% CH_2Cl_2-hexanes to afford compound **WM68** (4.2 mg).

Compound **WM68 (**(*E*)-5-Methoxy-2-(prop-1-enyl)phenol): Yellow solid; mp 82-83 °C; UV (MeOH) λ_{max} 205, 257, 265, 310 nm; IR (neat) ν_{max} 3355, 2924, 1775, 1266 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 6.95 (1H, s, H-6), 6.78 (1H, d, *J* = 8.4 Hz, H-4), 6.77 (1H, d, *J* = 8.4 Hz, H-3), 6.29 (1H, d, *J* = 15.6 Hz, H-1′), 6.08 (1H, m, H-2′), 5.55 (1H, br s, 1-OH), 3.87 (3H, s, 5-OMe), 1.85 (3H, d, *J* = 6.8 Hz, H-3′); ^{13}C NMR (100 MHz, $CDCl_3$) 145.6 (C-1 and C-5), 131.8 (C-2), 130.4 (C-1′), 124.0 (C-2′), 118.0 (C-3), 111.4 (C-6), 110.6 (C-4), 56.0 (5-OMe), 18.3 (C-3′).

Compound **WM66** (2.2 mg) was obtained from fraction D (1.45 g) by Sephadex-LH20 eluting with 100% MeOH and followed by repeated CC with 25% EtOAc-hexanes and 2% acetone-hexanes, respectively.

Compound **WM66** (Harmandianone): White solid; mp 114-117 °C; $[\alpha]_D^{27}$ = +60.3 (*c* = 0.014, $CHCl_3$); UV (MeOH) λ_{max} 201, 213, 267, 272 nm; IR (neat) ν_{max} 3350, 2925, 2853, 1712, 1689, 1603, 1259 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$), see Table 3.21; ^{13}C NMR (100 MHz, $CDCl_3$), see Table 3.21; ESI-TOF-MS $[M+Na]^+$ (*m*/*z*) 337.1046 (calcd for $C_{18}H_{18}NaO_5$, 337.1052).

Fraction E (7.05 g) was isolated by QCC with 10% EtOAc-hexanes and followed by Sephadex-LH20 eluting with 100% MeOH to give four subfractions (E1-E4). Subfraction E2 (76.5 mg) was isolated by CC using 30% EtOAc-hexanes to afford four fractions (E2a-E2d). Compounds **WM69** (2.0 mg) and **WM70** (30.9 mg) were derived from fractions E2b (128.6 mg) and E2c (9.7 mg) by CC using 2% acetone-hexanes and Sephadex-LH20 with 100% MeOH, respectively. Fraction E3 (1.37 g) was purified by QCC with 20% EtOAc-hexanes to 100% EtOAc and followed by Sephadex-LH20 using 100% MeOH to afford compound **WM67** (1.1 mg). Up on standing of subfraction E3 (1.26 g) at room temperature provided colorless solid and washed with hexanes to give compound **WM74** (238.2 mg)

Compound **WM67** (Verimol B): Yellow oil; UV (MeOH) λ_{max} 201, 226, 257 nm; IR (neat) ν_{max} 3406, 2925, 1715, 1606, 1252 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$), 8.03 (2H, d, *J* = 8.8 Hz, H-3′ and H-5′), 7.34 (2H, d, *J* = 8.4 Hz, H-3 and H-5), 6.92 (2H, d, *J* = 8.8 Hz, H-2′ and H-6′), 6.88 (2H, d, *J* = 8.4 Hz, H-2 and H-6), 5.71 (1H, d, *J* = 7.2 Hz, H-7), 4.19 (1H, m, H-8), 3.86 (3H, s, 1′-OMe), 3.79 (3H, s, 1-OMe), 1.13 (3H, d, *J* = 6.4 Hz, H-9).

Compound **WM69** ((*E*)-Methyl *p*-coumarate): Yellow solid; mp 96-97 °C; UV (MeOH) λ_{max} 210, 227, 299, 311 nm; IR (neat) ν_{max} 3382, 2952, 1688, 1601, 1434, 1198 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$), 7.64 (1H, d, *J* = 16.0 Hz, H-7), 7.43 (2H, d, *J* = 8.8 Hz, H-3 และ H-5), 6.85 (2H, d, *J* = 8.8 Hz, H-2 และ H-6), 6.30 (1H, d, *J* = 16.0 Hz, H-8), 3.79 (3H, s, 9-OMe).

Compound **WM70** ((*E*)-3-(2-Hydroxy-4-methoxy-phenyl)propanoate): Yellow solid; mp 104-105 °C; UV (MeOH) λ_{max} 204, 216, 234, 290, 324 nm; IR (neat) ν_{max} 3382, 2924, 1715, 1269, 1159 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 7.62 (1H, d, *J* = 16.0 Hz, H-7), 7.07 (1H, dd, *J* = 8.4 and 1.6 Hz, H-3), 7.03 (1H, d, *J* = 1.6 Hz, H-6), 6.91 (1H, d, *J* = 8.4 Hz, H-2), 6.30 (1H, d, *J* = 16.0 Hz, H-8), 5.93 (1H, br s, 4-OH), 3.93 (3H, s, 1-OMe), 3.75 (3H, s, 9-OMe); ^{13}C NMR (100 MHz, $CDCl_3$) 167.7 (C-9), 147.9 (C-5), 146.7 (C-1), 145.9 (C-7), 126.9 (C-4), 123.0 (C-3), 115.2 (C-8), 114.7 (C-2), 109.3 (C-6), 55.9 (1-OMe), 51.6 (9-OMe).

Compound **WM74** (*O*-Methylclausennolide): Colorless solid; mp 192-193 °C; UV (MeOH) λ_{max} 205, 271 nm; IR (neat) ν_{max} 3417, 2938, 1739, 1715, 1027 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6) 7.61 (1H, br s, H-21), 7.58 (1H, br s, H-23), 6.48 (1H, br s, H-22), 5.54 (1H, s, H-17), 4.53 (1H, m, H-11), 3.90 (1H, s, H-15), 3.24 (3H, s, 1-OMe), 3.02 (1H, dd, *J* = 16.0 and 14.0 Hz, H-6β), 2.74 (1H, br s, H-9), 2.68 (1H, dd, *J* = 16.0 and 3.6 Hz, H-5), 2.29 (1H, dd, *J* = 14.0 and 3.6 Hz, H-6α), 1.76 (2H, br d, *J* = 5.6 Hz, H-12), 1.60 (3H, s, H-19), 1.49 (3H, s, H-30), 1.46 (3H, s, H-1), 1.22 (3H, s, H-28), 1.14 (3H, s, H-29), 1.09 (3H, s, H-18) ; ^{13}C NMR (100 MHz, acetone-d_6) 209.7 (C-7), 168.0 (C-16), 144.0 (C-23), 142,4 (C-21), 121.8 (C-20), 111.0 (C-22), 109.5 (C-1), 79.6 (C-4), 78.9 (C-17), 66.7 (C-11), 66.5 (C14), 55.6 (C-13), 56.6 (C-5), 55.1 (C-15), 52.0 (C-10), 51.5 (C-8), 45.5 (C-9), 43.8 (C-12), 37.7 (C-6), 31.1 (C-28), 23.6 (C-29), 20.5 (C-30), 19.8 (C-18), 18.1 (C-2), 17.5 (C-19).

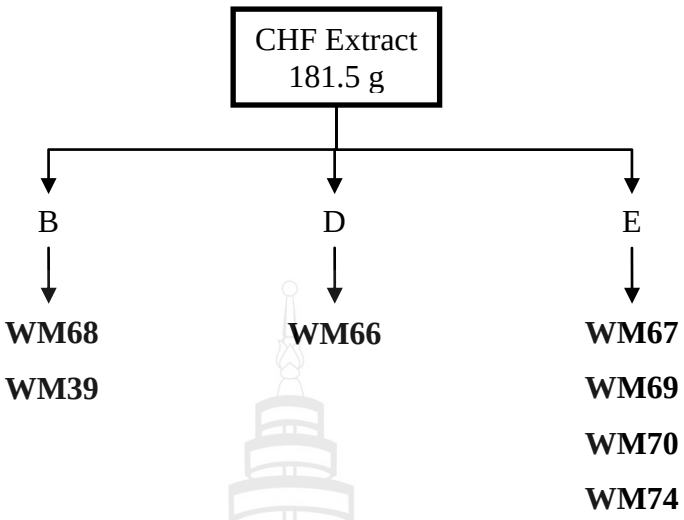


Figure 2.8 Isolation of CHF Extract from *C. harmandiana* Fruits

2.4.3 Isolation of *C. lansium* Roots

Upon standing at room temperature, CLR extract (62.55 g) yielded a yellow crystal which was further washed with hexanes to give compound **WM30** (1.09 g).

Compound **WM30** (Indizoline): Yellow solid; mp 170-171 °C; UV (MeOH) λ_{max} 236, 245, 273, 291, 326 nm; IR (neat) ν_{max} 3312, 2931, 1670, 1601, 1333, 1241 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 10.28 (1H, s, 3-CHO), 8.58 (1H, br s, H-9) 8.44 (1H, s, H-4), 8.07 (1H, d, *J* = 8.0 Hz, H-5), 7.48 (1H, m, H-8), 7.46 (1H, m, H-7), 7.29 (1H, m, H-6), 5.23 (1H, m, H-2′), 3.96 (3H, s, 1-OMe), 3.92 (2H, m, H-1′), 1.84 (3H, s, H-4′), 1.69 (3H, s, H-5′); ^{13}C NMR (100 MHz, $CDCl_3$) 191.8 (3-CHO), 142.8 (C-1), 139.8 (C-8a), 136.9 (C-9a), 133.9 (C-3), 132.0 (C-3′), 127.8 (C-2), 126.7 (C-7), 124.0 (C-4b), 123.8 (C-2′), 123.3 (C-4a), 121.1 (C-4), 120.7 (C-5 and C-6), 111.2 (C-8), 61.4 (1-OMe), 25.6 (C-5′), 24.0 (C-1′), 18.1 (C-4′).

The remaining crude extract (61.46 g) was subjected to QCC over silica gel using a gradient of hexanes-EtOAc (100% hexanes to 100% EtOAc) to provide eight fractions (A-H). Fraction D (1.03 g) was further separated by QCC with a gradient of EtOAc-hexanes (5% EtOAc-hexanes to 100% EtOAc) to afford seven subfractions (D1-D7). Subfraction D2 (86.1 mg) was performed by CC using 40% CH_2Cl_2-

hexanes to yield compounds **WM4** (20.3 mg) and **WM59** (28.4 mg). Separation of subfraction D3 (307.6 mg) was separated by CC with 75% CH_2Cl_2-hexanes and followed by Sephadex-LH20 eluting with 100% MeOH gave compounds **WM31** (4.5 mg) and **WM16** (16.7 mg). Compounds **WM11** (33.9 mg) and **WM17** (30.5 mg) were obtained from repeated CC eluting with 80% CH_2Cl_2-hexanes and Sephadex-LH20 using 100% MeOH from subfractions D5 (169.7 mg) and D6 (135.4 mg), respectively.

Compound **WM4** (Murrayanine): Yellow solid; mp 165-166 °C; UV (MeOH) λ_{max} 221, 238, 249, 273, 4.75, 3.12, 323, 337 nm; IR (neat) ν_{max} 3334, 1665 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 10.05 (1H, s, 3-CHO), 8.64 (1H, br s, 9-NH), 8.19 (1H, d, *J* = 0.8 Hz, H-4), 8.11 (1H, br d, *J* = 8.0 Hz, H-5), 7.52 (1H, br d, *J* = 8.0 Hz, H-8), 7.49 (1H, td, *J* = 8.0 and 1.2 Hz), 7.46 (1H, d, *J* = 0.8 Hz, H-2), 7.32 (1H, td, *J* = 8.0 and 1.2 Hz, H-6), 4.07 (3H, s, 1-OMe); ^{13}C NMR (100 MHz, $CDCl_3$) 191.9 (3-CHO), 146.1 (C-1), 139.4 (C-8a), 134.0 (C-9a), 130.1 (C-3), 126.6 (C-7), 123.6 (C-4a and C-4b), 120.7 (C-5 and C-6), 120.4 (C-4), 111.5 (C-8), 103.5 (C-2), 55.8 (1-OMe).

Compound **WM11** (3-Formyl-6-methoxycarbazole): Brown solid; mp 135-136 °C; UV (MeOH) λ_{max} 229, 246, 280, 297, 334, 354 nm; IR (neat) ν_{max} 3316, 2938, 1674, 1599, 1495, 1213 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) 10.72 (1H, br s, 9-NH), 10.07 (1H, s, 3-CHO), 8.68 (1H, br s, H-4), 7.93 (1H, dd, *J* = 8.4 and 1.6 Hz, H-2), 7.80 (1H, d, *J* = 2.4 Hz, H-5), 7.61 (1H, d, *J* = 8.4 Hz, H-1), 7.50 (1H, d, *J* = 8.8 Hz, H-8), 7.11 (1H, dd, *J* = 8.8 and 2.4 Hz, H-7), 3.92 (3H, s, 6-OMe).

Compound **WM16** (Lansine): Yellow solid; mp 192-193 °C; UV (MeOH) λ_{max} 237, 249, 269, 281, 323, 334 nm; IR (neat) ν_{max} 3354, 2925, 1715, 1371, 1216 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) 11.44 (1H, s, 2-OH), 10.55 (1H, br s, 9-NH), 9.95 (1H, s, 3-CHO), 8.41 (1H, s, H-4), 7.44 (1H, d, *J* = 2.8 Hz, H-5), 7.39 (1H, d, *J* = 8.8 Hz, H-8), 7.01 (1H, dd, *J* = 8.8 and 2.4 Hz, H-7), 6.84 (1H, s, H-1), 3.88 (3H, s, 6-OMe); ^{13}C NMR (100 MHz, acetone-d_6) 196.4 (3-CHO), 161.7 (C-2), 155.7 (C-6), 147.5 (C-9a), 136.3 (C-8a), 128.7 (C-4), 124.8 (C-4b), 118.6 (C-4a), 116.9 (C-3), 115.2 (C-7), 112.6 (C-8), 104.0 (C-5), 97.1 (C-8).

Compound **WM17** (Glycozolidal): Yellow solid; mp 196-197 °C; UV (MeOH) λ_{max} 206, 230, 278, 307, 336, 359 nm; IR (neat) ν_{max} 3333, 2925, 1735, 1606

cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6) 10.44 (1H, s, 3-CHO), 8.49 (1H, s, H-4), 7.75 (1H, d, *J* = 2.4 Hz, H-5), 7.39 (1H, d, *J* = 8.8 Hz, H-8), 7.11 (1H, s, H-1), 6.99 (1H, dd, *J* = 8.8 and 2.4 Hz, H-7), 4.01 (3H, s, 2-OMe), 3.90 (3H, s, 6-OMe).

Compound **WM31** (Claulansine A): Brown viscous oil; $[\alpha]_D^{24}$ +32.47 ° (*c* = 0.02, MeOH); UV (MeOH) λ_{max} 239, 249, 258, 295, 320, 331 nm; IR (neat) ν_{max} 3372, 2921, 2851, 1563 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 8.15 (1H, br s, 9-NH), 7.99 (1H, d, *J* = 8.0 Hz, H-5), 7.55 (1H, s, H-4), 7.39 (1H, ddd, *J* = 8.0, 7.4, and 1.2 Hz, H-7), 7.21 (1H, ddd, *J* = 8.0, 7.4, and 1.2 Hz, H-6), 6.15 (1H, s, H-10), 4.51 (1H, d, *J* = 5.1 Hz, H-2′), 3.96 (3H, s, 1-OMe), 3.37 (1H, dd, *J* = 17.6 and 5.2 Hz, H-1a′), 3.11 (1H, d, *J* = 17.6 Hz, H-1b′), 1.40 (3H, s, H-4′), 1.26 (3H, s, H-5′); ^{13}C NMR (100 MHz, $CDCl_3$) 142.7 (C-1) 130.8 (C-2), 125.8 (C-7), 123.9 (C-4b), 123.4 (C-4a), 120.4 (C-3), 120.3 (C-5), 119.8 (C-6), 112.3 (C-4), 110.8 (C-8), 101.6 (C-10), 80.1 (C-3′), 60.0 (1-OMe), 29.6 (C-4′), 25.9 (C-1′), 23.9 (C-5′); ESI-TOF-MS $[M+H]^+$ (*m*/*z*) 310.1436 (calcd for $C_{19}H_{20}NO_3$, 310.1443).

Compound **WM59** (Imperatorin): Yellow solid; mp 95-96 °C; UV (MeOH) λ_{max} (log ε) 218, 248, 264, 300; IR (neat) ν_{max} 2930, 1715, 1586, 1151, 1094 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 7.74 (1H, d, *J* = 9.6 Hz, H-4), 7.67 (1H, d, *J* = 2.2 Hz, H-2′), 7.34 (1H, s, H-5), 6.80 (1H, d, *J* = 2.2 Hz, H-3′), 5.59 (1H, t, *J* = 7.3 Hz, H-2″), 4.99 (2H, d, *J* = 7.3 Hz, H-1″), 1.72 (3H, s, H-4″), 1.70 (3H, s, H-5″); ^{13}C NMR (100 MHz, $CDCl_3$) 160.5 (C-2), 148.7 (C-7), 146.5 (C-2′), 144.9 (C-8a), 144.3 (C-4), 139.7 (C-3″), 132.7 (C-8), 125.8 (C-6), 119.7 (C-2″), 116.4 (C-4a), 114.6 (C-3), 113.1 (C-5), 106.6 (C-3′), 70.1 (C-1″), 25.7 (C-4″), 18.0 (C-5″).

Fraction E (5.70 g) was isolated by QCC using a gradient of 10% EtOAc-hexanes to 100% EtOAc to provide five subfractions (E1-E5). Subfraction E2 (94.7 mg) was purified by CC with 30% CH_2Cl_2-hexanes to afford compound **WM10** (5.0 mg). Fraction E4 (1.35 g) was subjected to CC using 50% CH_2Cl_2-hexanes to give seven subfractions (E4a-E4g). Purification of subfraction E4b (14.6 mg) by CC with 10% EtOAc-hexanes yielded compounds **WM34** (2.3 mg) and **WM35** (6.9 mg). Compounds **WM3** (65.0 mg) and **WM55** (11.7 mg) were purified by Sephadex-LH20 using 100% MeOH from subfractions E4d (111.6 mg) and E4f (163.2 mg), respectively.

Compound **WM10** (Glycozoline): Yellow solid; mp 175-176 °C; UV (MeOH) λ_{max} 227, 252, 264, 295, 303, 342, 359 nm; IR (neat) ν_{max} 3400, 1471, 1210 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 7.80 (1H, br s, 9-NH), 7.82 (1H, br s, H-4), 7.52 (1H, d, *J* = 2.4 Hz, H-5), 7.29 (1H, d, *J* = 8.4 Hz, H-1), 7.23 (1H, d, *J* = 8.8 Hz, H-8), 7.21 (1H, dd, *J* = 8.4 and 1.2 Hz, H-2), 7.03 (1H, dd, *J* = 8.8 and 2.4 Hz, H-7), 3.92 (3H, s, 6-OMe), 2.52 (3H, s, 3-Me).

Compound **WM34** (Mafaicheenamine D): Yellow solid; mp 202-203 °C; UV (MeOH) λ_{max} 246, 266, 278, 296, 303, 321, 334, 357 nm; IR (neat) ν_{max} 3286, 1675, 1610 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$), see Table 3.9; ^{13}C NMR (125 MHz, $CDCl_3$), see Table 3.9; ESI-TOF-MS $[M+H]^+$ (*m*/*z*) 292.1332 (calcd for $C_{19}H_{18}NO_2$, 292.1338).

Compound **WM35** (Mafaicheenamine E): Yellow solid; mp 209 – 212 °C; $[\alpha]^{27}_D$ –14.3 (*c* 0.012, MeOH); UV (MeOH) λ_{max} 246, 264, 278, 295, 310, 325, 339 nm; IR (neat) ν_{max} 3300, 1730, 1612 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6), see Table 3.10; ^{13}C NMR (100 MHz, acetone-d_6), see Table 3.10; ESI-TOF-MS $[M+H]^+$ (*m*/*z*) 308.1281 (calcd for $C_{19}H_{18}NO_3$, 308.1287).

Compound **WM55** (Umbelliferone): Yellow solid; mp 227 – 228 °C; UV (MeOH) λ_{max} 202, 216, 296, 324; IR (neat) ν_{max} 3166, 2925, 1712, 1684, 1609, 1236 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) 9.66 (1H, s, 7-OH), 7.86 (1H, d, *J* = 9.6 Hz, H-4), 7.51 (1H, d, *J* = 8.4 Hz, H-5), 6.84 (1H, dd, *J* = 8.4 and 2.0 Hz, H-6), 6.74 (1H, d, *J* = 2.0 Hz, H-8), 6.16 (1H, d, *J* = 9.6 Hz, H-3); ^{13}C NMR (100 MHz, acetone-d_6) 161.6 (C-7), 160.6 (C-2), 156.4 (C-8a), 144.2 (C-4), 129.9 (C-5), 113.3 (C-6), 112.3 (C-4a), 111.3 (C-3), 102.8 (C-8).

Fraction G (7.94 g) was separated by QCC with a gradient of 20% EtOAc-hexanes to 100% EtOAc to afford four subfractions (G1-G4). Subfraction G3 (967.0 mg) was purified by CC with 10% EtOAc-CH_2Cl_2 to give compounds **WM63** (184.4 mg) and **WM64** (109.6 mg).

Compound **WM63** (Wampetin): Yellow solid; mp 75 – 76 °C; UV (MeOH) λ_{max} 213, 248, 265, 299; IR (neat) ν_{max} 2925, 1751, 1731, 1586, 1401, 1147 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 7.77 (1H, d, *J* = 9.6 Hz, H-4), 7.70 (1H, d, *J* = 2.0 Hz, H-2′), 7.39 (1H, s, H-4), 6.92 (1H, t, *J* = 1.6 Hz, H-6′), 6.82 (1H, d, *J* = 2.0 Hz, H-3′),

6.37 (1H, d, *J* = 9.6 Hz, H-3), 5.72 (1H, td, *J* = 7.2 and 1.2 Hz, H-2′′), 5.04 (2H, m, H-1′′), 4.92 (1H, m, H-5′′), 2.41 (1H, dd, *J* = 14.0 and 7.6 Hz, H-4b′′), 2.30 (1H, dd, *J* = 14.0 and 6.8 Hz, H-4a′′), 1.84 (3H, t, *J* = 1.6 Hz, H-10′′), 1.79 (3H, s, H-9′′); ^{13}C NMR (100 MHz, $CDCl_3$) 173.9 (C-8′′), 160.4 (C-2), 148.5 (C-7), 148.3 (C-6′′), 146.7 (C-2′), 144.3 (C-2), 143.8 (C-8a), 137.0 (C-3′′), 131.3 (C-8), 130.1 (C-7′′), 125.9 (C-6), 123.8 (C-2′′), 116.5 (C-4a), 114.7 (C-3), 113.2 (C-5), 106.8 (C-3′), 79.5 (C-5′′), 69.6 (C-1′′), 40.3 (C-4′′), 17.2 (C-9′′), 10.6 (C-10′′).

Compound **WM64** (Indicolactonediol): Yellow solid; 113 – 114 °C; UV (MeOH) λ_{max} 204, 212, 247, 296; IR (neat) ν_{max} 3382, 2936, 1745, 1729, 1587, 1149, 1097 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 7.78 (1H, d, *J* = 9.6 Hz, H-4), 7.71 (1H, d, *J* = 2.0 Hz, H-2′), 7.42 (1H, s, H-5), 7.13 (1H, t, *J* = 1.6 Hz, H-6′′), 6.84 (1H, d, *J* = 2.0 Hz, H-3′), 6.37 (1H, d, *J* = 9.6 Hz, H-3), 4.92 (2H, m, H-5′′), 4.66 (1H, dd, *J* = 11.2 and 5.6 Hz, H-1b′′), 4.56 (1H, dd, *J* = 11.2 and 5.6 Hz, H-1a′′), 3.52 (1H, t, *J* = 5.6 Hz, H-2′′), 2.11 (1H, dd, *J* = 14.8 and 8.4 Hz, H-4b′′), 1.84 (1H, dd, *J* = 14.8 and 5.2 Hz, H-4a′′), 1.92 (3H, t, *J* = 1.6 Hz, H-10′′), 1.39 (3H, s, H-9′′); ^{13}C NMR (100 MHz, $CDCl_3$) 174.2 (C-8′′), 160.4 (C-2), 148.5 (C-6′′), 148.3 (C-7), 146.8 (C-2′), 144.3 (C-4), 143.5 (C-8a), 131.4 (C-8), 130.2 (C-7′′), 126.0 (C-6), 116.5 (C-4a), 114.8 (C-3), 114.0 (C-5), 106.8 (C-3′), 73.9 (C-3′′), 72.0 (C-1′′ and C-5′′), 59.6 (C-2′′), 41.5 (C-4′′), 18.1 (C-9′′), 10.6 (C-10′′).

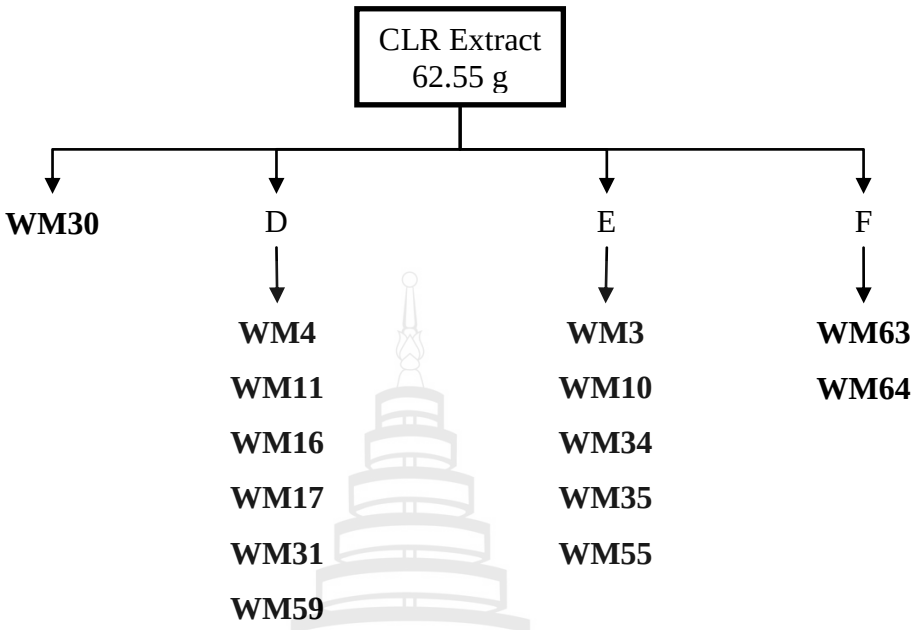


Figure 2.9 Isolation of CLR Extract from Roots of *C. lansium*

2.4.4 Isolation of *C. lansium* Twigs

The CLT extract (34.02 g) was subjected to QCC over silica gel eluted with a gradient of hexanes-acetone (100% hexanes to 100% acetone) to provide seventeen fractions (A-Q).

Fraction F (207.1 mg) was separated by CC with 20% EtOAc-hexanes yielding compound **WM30** (13.5 mg).

Upon standing at room temperature, fraction G (562.9 mg) gave compound **WM59** (247.1 mg).

The isolation of fraction J (1.83 g) was performed by CC with 20% EtOAc-hexanes to afford thirteen subfractions (J1-J13). Subfraction J3 (33.9 mg) was subjected to repeated CC with 65% CH_2Cl_2-hexanes to afford compound **WM16** (4.2 mg). Subfraction J4 (173.3 mg) was separated by CC eluting a gradient of 70% CH_2Cl_2-hexanes to 2% MeOH-CH_2Cl_2 yielding compounds **WM1** (1.3 mg), **WM4** (2.6 mg), **WM65** (10.5 mg), and fifteen fractions (J4a-J4o). Compound **WM31** (2.2 mg) was derived from fraction J2n (25.1 mg) by repeated CC with a gradient of 90%

CH_2Cl_2-hexanes to 10% EtOAc-CH_2Cl_2. Subfraction J7 (546.4 mg) was further purified by CC with 30% hexanes-CH_2Cl_2 yielding compound **WM60** (207.8 mg).

Compound **WM1** (3-Formyl carbazole): Brown powder; mp 156-157 °C; UV (MeOH) λ_{max} 232, 248, 273, 288, 324 nm; IR (neat) ν_{max} 3311, 1679 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) 10.94 (1H, br s, 9-NH), 10.09 (1H, s, 3-CHO), 8.71 (1H, s, H-4), 8.26 (1H, d, *J* = 8.0 Hz, H-5), 7.97 (1H, dd, *J* = 8.4 and 1.6 Hz, H-2), 7.66 (1H, d, *J* = 8.4 Hz, H-1), 7.60 (1H, d, *J* = 8.0 Hz, H-8), 7.48 (1H, t, *J* = 8.0 Hz, H-7), 7.29 (1H, t, *J* = 8.0 Hz, H-6).

Compound **WM60** (Heraclenin): Yellow solid; mp 125-126 °C; UV (MeOH) λ_{max} 232, 248, 273, 288, 324 nm; IR (neat) ν_{max} 2967, 1728, 1587, 1401, 1149, 1097 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 7.71 (1H, d, *J* = 9.6 Hz, H-4), 7.63 (1H, d, *J* = 2.0 Hz, H-2′), 7.33 (1H, s, H-5), 6.76 (1H, d, *J* = 2.0 Hz, H-3′), 6.27 (1H, d, *J* = 9.6 Hz, H-3), 4.50 (2H, d, *J* = 5.6 Hz, H-1′′), 3.23 (1H, t, *J* = 5.6 Hz, H-2′′), 1.26 (3H, s, H-4′′), 1.19 (3H, s, H-5′′); ^{13}C NMR (100 MHz, $CDCl_3$) 160.1 (C-2), 148.0 (C-7), 146.6 (C-2′), 144.2 (C-4), 143.3 (C-8a), 131.0 (C-8), 125.8 (C-6), 116.2 (C-4a), 114.4 (C-3), 113.8 (C-5), 106.6 (C-3′), 72.2 (C-1′′), 61.1 (C-2′′), 57.9 (C-3′′), 24.3 (C-4′′), 18.6 (C-5′′).

Compound **WM65** (Phenetyl cinnamide): Yellow solid; mp 128-129 °C; UV (MeOH) λ_{max} 205, 209, 216, 222, 273 nm; IR (neat) ν_{max} 3791, 2926, 1776, 1657, 1619, 1343, 1226 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 7.62 (1H, d, *J* = 15 Hz, H-7), 7.48 (2H, m, H-2 and H-6), 7.34 (5H, m, H-3, H-4, H-5, H-15, and H-17), 7.22 (3H, m, H-14, H-16 and H-18), 6.32 (1H, d, *J* = 15 Hz, H-8), 5.67 (1H, br s, H-10), 3.66 (2H, dd, *J* = 12.8 and 7.2 Hz, H-11), 2.89 (2H, t, *J* = 7.2 Hz, H-12); ^{13}C NMR (100 MHz, $CDCl_3$), 165.8 (C-9), 141.0 (C-7), 138.8 (C-13), 134.7 (C-1), 129.6 (C-4), 128.7 (C-2, C-6, C-15, and C-17), 128.6 (C-3 and C-5), 127.7 (C-13 C-16 and C-18), 120.5 (C-8), 40.7 (C-11), 35.6 (C-12).

Fraction K (4.64 g) was performed by CC using a gradient of EtOAc-CH_2Cl_2 (5% EtOAc-CH_2Cl_2 to 100% EtOAc) to yield compounds **WM17** (1.8 mg), **WM58** (5.6 mg), and nine subfractions (K1-K9). Subfraction K6 (124.2 mg) was subjected to repeated CC with 2% acetone-CH_2Cl_2 to afford compounds **WM33** (9.7 mg) and

WM62 (8.7 mg), while subfraction K8 was purefied by CC with 10% EtOAc-hexanes to give compound **WM73** (16.2 mg).

Compound **WM33** (Mafaicheenamine C): Brown solid; mp 165 – 166 °C; $[\alpha]^{26}_{D}$ +64.2 (*c* = 0.02, MeOH); UV (MeOH) λ_{max} 232, 245, 269, 291, 332, 347 nm; IR (neat) ν_{max} 3607, 2935, 1731, 1563 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$), see Table 3.8; ^{13}C NMR (100 MHz, $CDCl_3$), see Table 3.8. HR-EI-MS $[M]^+$ (*m*/*z*) 309.1364 (calcd for $C_{19}H_{19}NO_3$, 309.1365).

Compound **WM58** (Xanthotoxol): Brown solid; mp 162 -163 °C; UV (MeOH) λ_{max} 218, 241, 249, 261, 267, 306 nm; IR (neat) ν_{max} 3320, 2924, 2708, 1595, 1450, 1155 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 7.80 (1H, d, *J* = 9.6 Hz, H-4), 7.71 (1H, d, *J* = 2.4 Hz, H-2′), 7.27 (1H, s, H-4), 6.82 (1H, d, *J* = 2.4 Hz, H-3′), 6.37 (1H, d, *J* = 9.6 Hz, H-3); ^{13}C NMR (100 MHz, $CDCl_3$) 160.2 (C-2), 158.3 (C-8), 147.0 (C-2′), 144.8 (C-4), 144.5 (C-7), 139.3 (C-8a), 126.0 (C-6), 117.9 (C-4a), 114.2 (C-3), 110.5 (C-5), 106.7 (C-3′).

Compound **WM62** (Clausenalansimin A): Yellow viscous oil; $[\alpha]^{27}_{D}$ +48.1 (*c* = 0.02, $CHCl_3$); UV (MeOH) λ_{max} (log ε) 204, 216, 247, 299 nm; IR (neat) ν_{max} 3442, 2924, 2855, 1722, 1626, 1587 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$), see Table 3.20; ^{13}C NMR (100 MHz, $CDCl_3$), see Table 3.20; ESI-TOF-MS $[M+Cl]^-$ (*m*/*z*) 389.1161 (calcd for $C_{21}H_{22}O_5Cl$, 389.1156).

Compound **WM73** (4-Methoxyl-1- methyl-2-quinolone): Brown solid; mp 102-103 °C; UV (MeOH) λ_{max} 228, 258, 278, 316, 329 nm; IR (neat) ν_{max} 2938, 1638, 1588, 1390, 1234 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 7.96 (1H, d, *J* = 8.0 Hz, H-4), 7.57 (1H, t, *J* = 8.0 Hz, H-7), 7.33 (1H, d, *J* = 8.0 Hz, H-8), 7.22 (1H, t *J* = 8.0 Hz, H-6), 6.03 (1H, s, H-3), 3.94 (3H, s, 4-OMe), 3.67 (3H, s, 1-Me); ^{13}C NMR (100 MHz, $CDCl_3$) 163.9 (C-2), 162.7 (C-4), 139.7 (C-8a), 131.2 (C-7), 123.3 (C-5), 121.6 (C-6), 116.5 (C-4a), 114.0 (C-8), 96.4 (C-3), 55.8 (4-OMe), 29.0 (1-Me).

Purification of fraction M (806.5 mg) was performed by sephadex-LH20 with 60% CH_2Cl_2-MeOH, yielding five subfractions (M1-M5). Subfraction M2 (199.9 mg) was further subjected to repeated CC with a gradient of $CHCl_3$-hexanes (70% $CHCl_3$-hexane to 100% $CHCl_3$) to afford eleven subfractions (M2a-M2k). Subfraction M2b (49.9 mg) was further subjected to repeated CC with 80% $CHCl_3$-hexanes to yield

four fractions (M2b1-M2b4). Compound **WM63** (4.8 mg) was derived from fraction M2b2 (18.5 mg) by repeated CC using 60% $CHCl_3$-hexanes whereas compound **WM64** (1.7 mg) was obtained from fraction M2b3 (21.5 mg) by repeated CC with 5% EtOAc-$CHCl_3$. Subfraction M2d (8.6 mg) was further purified by prep. TLC with 5% EtOAc-$CHCl_3$ to afford **WM56** (7.3 mg). Compound **WM32** (9.8 mg) was derived from subfraction M2f (18.7 mg) by prep. TLC with 50% EtOAc-hexanes.

Compound **WM32** (Mafaicheenamine A): Brown solid; mp 148-149 °C; $[\alpha]^{26}_{D}$ +81.37° (*c* = 0.02, MeOH); UV (MeOH) λ_{max} 234, 244, 267, 282, 319, 322 nm; IR (neat) ν_{max} 3525, 2973, 1694, 1608 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6), see Table 3.7; ^{13}C NMR (100 MHz, acetone-d_6), see Table 3.7; HR-EI-MS $[M]^+$ (*m*/*z*) 325.1315 (calc. for $C_{19}H_{19}NO_4$, 325.1314).

Compound **WM56** (Isoscopoletin): Yellow solid; mp 205-206 °C; UV (MeOH) λ_{max} 204, 228, 253, 261, 295, 344 nm; IR (neat) ν_{max} 3254, 2926, 1715, 1293, 1142 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 7.82 (1H, d, *J* = 9.6 Hz, H-4), 7.15 (1H, s, H-5), 6.77 (1H, s, H-8), 6.13 (1H, d, *J* = 9.6 Hz, H-3), 3.88 (3H, s, 7-OMe); ^{13}C NMR (100 MHz, $CDCl_3$) 160.9 (C-2), 152.3 (C-6), 150.4 (C-8a), 146.0 (C-7), 143.8 (C-4), 111.8 (C-3), 110.6 (C-4a), 108.9 (C-5), 102.8 (C-8), 55.7 (7-OMe).

Fraction N (621.1 mg) was performed by CC with 40% EtOAc-hexanes, yielding eleven subfractions (N1-N11). Subfraction N8 (65.5 mg) was separated by CC using a gradient of EtOAc-CH_2Cl_2 (10% EtOAc-CH_2Cl_2 to 25% EtOAc-CH_2Cl_2) to yield compound **WM57** (4.0 mg), while subfraction N10 (39.4 mg) was purified by prep. TLC with 7% EtOAc-CH_2Cl_2 to give compound **WM61** (9.8 mg).

Compound **WM57** (Clausenalansimin B): Yellow viscous oil; $[\alpha]^{27}_{D}$ +17.2 (*c* 0.02, $CHCl_3$); UV (MeOH) λ_{max} 207, 329 nm; IR (neat) ν_{max} 2921, 1726, 1609, 1454 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$), see Table 3.19; ^{13}C NMR (100 MHz, $CDCl_3$), see Table 3.19; HR-EI-MS $[M]^+$ (*m*/*z*) 342.1158 (calcd for $C_{19}H_{18}O_6$, 342.1103).

Compound **WM61** (Heraclenol): Yellow viscous oil; UV (MeOH) λ_{max} 217, 248, 264, 299 nm; IR (neat) ν_{max} 3382, 2925, 1721, 1587, 1402, 1152, 1105 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 7.77 (1H, d, *J* = 9.6 Hz, H-4), 7.70 (1H, d, *J* = 2.0 Hz, H-2′), 7.39 (1H, s, H-5), 6.83 (1H, d, *J* = 2.0 Hz, H-3′), 6.37 (1H, d, *J* = 9.6 Hz, H-3),

4.75 (1H, dd, *J* = 10.4 and 2.4 Hz, H-1a′′), 4.41 (1H, dd, *J* = 10.4 and 8.0 Hz, H-1b′′), 3.87 (1H, d, *J* = 8.0 and 2.4 Hz, H-2′′), 1.33 (3H, s, H-4′′), 1.29 (3H, s, H-5′′).

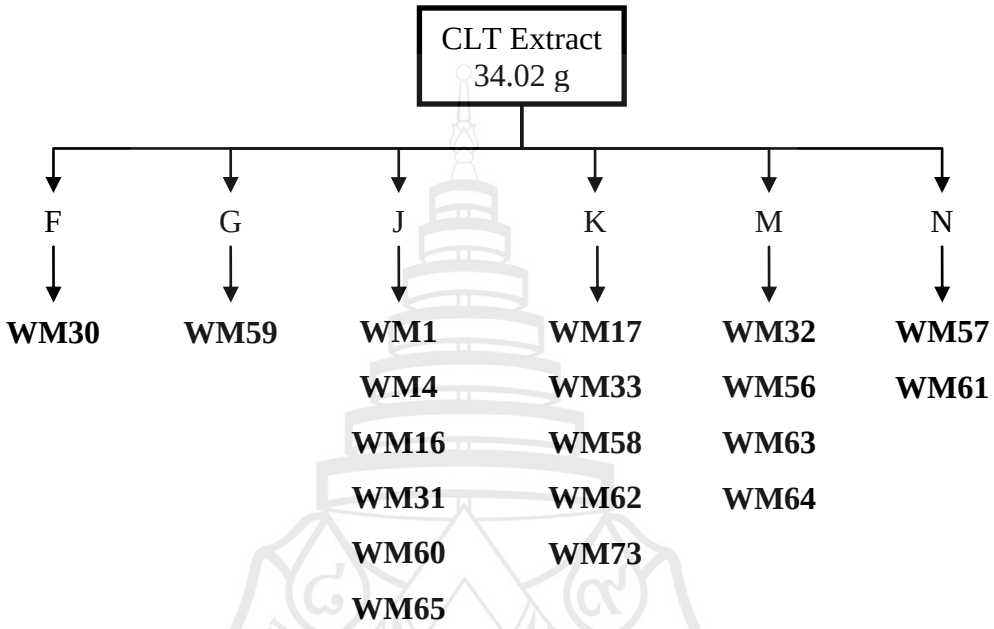


Figure 2.10 Isolation of CLT Extract from the Twigs of *C. lansium*

2.4.5 Isolation of *C. wallichii* Roots

The CWR crude (18.68 g) was isolated by QCC over silica gel eluting hexanes and increasing the polarity of the elution solvents system with EtOAc (100% hexanes to 100 % EtOAc) to afford five fractions (A-E). Fraction B (1.83 g) was further isolated by QCC with 5% EtOAc-hexanes to give four subfractions (B1-B4). Subfraction B2 (281.4 g) was separated by repeated CC using 30% CH_2Cl_2-hexanes to yield compound **WM39** (17.1 mg). Compounds **WM2** (2.1 mg), **WM7** (2.1 mg), **WM28** (17.0 mg), and **WM36** (3.8 mg) were derived from subfraction B4 (176.8 mg) by repeated CC with 50% CH_2Cl_2-hexanes.

Compound **WM2** (Methyl carbazole-3-carboxylate): Brown viscous oil; UV (MeOH) λ_{max} 231, 241, 276, 304, 328, 353 nm; IR (neat) ν_{max} 3288, 2952, 1686, 1246 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 10.07 (1H, br s, 9-NH), 8.81 (1H, s, H-4), 8.24

(1H, d, *J* = 8.0 Hz, H-5), 8.08 (1H, dd, *J* = 8.4 and 1.6 Hz, H-2), 7.58 (1H, d, *J* = 8.0 Hz, H-1), 7.57 (1H, d, *J* = 8.0 Hz, H-8), 7.46 (1H, t, *J* = 8.0 Hz, H-7), 7.26 (1H, d, *J* = 8.0 Hz, H-6), 3.91 (3H, s, 3-CO_2Me).

Compound **WM7** (Mukonal): Brown solid; mp 238-239 °C; UV (MeOH) λ_{max} 232, 277, 296, 332, 343 nm; IR (neat) ν_{max} 3613, 3331, 2924, 1714, 1638, 1470, 1328, 1244 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6) 11.48 (1H, s, 2-OH), 10.02 (1H, s, 3-CHO), 8.49 (1H, s, H-4), 8.11 (1H, d, *J* = 7.6 Hz, H-5), 7.51 (1H, d, *J* = 7.6 Hz, H-8), 7.40 (1H, t, *J* = 7.6 Hz, H-6), 7.25 (1H, t, *J* = 7.6 Hz, H-7), 6.92 (1H, s, H-1).

Compound **WM28** (Clauraila D): Yellow solid; mp 219-220 °C; UV (MeOH) λ_{max} 204, 239, 305, 326 nm; IR (neat) ν_{max} 3346, 2925, 1740, 1636, 1463, 1286 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 11.43 (1H, s, 2-OH), 9.91 (1H, s, 3-CHO), 8.17 (1H, s, H-4), 8.14 (1H, br s, 9-NH), 7.15 (1H, d, *J* = 10.0 Hz, H-1′), 7.12 (1H, d, *J* = 8.4 Hz, H-8), 6.90 (1H, d, *J* = 8.4 Hz, H-7), 6.81 (1H, s, H-1), 5.88 (1H, d, *J* = 10.0 Hz, H-2′), 1.50 (6H, s, H-4′ and H-5′); ^{13}C NMR (100 MHz, $CDCl_3$) 195.0 (3-CHO), 160.9 (C-2), 147.8 (C-6), 146.5 (C-9a), 135.2 (C-8a), 132.3 (C-2′), 129.6 (C-4), 119.4 (C-1′), 118.6 (C-4b), 117.9 (C-4a), 115.6 (C-4 and C-5), 115.3 (C-7), 110.4 (C-8), 96.7 (C-1), 75.5 (C-3′), 27.2 (C-4′ and C-5′).

Fraction C (2.01 g) was further separated by QCC with 10% EtOAc-hexanes to 20% EtOAc-hexanes to afford five subfractions (C1-C5). Subfraction C2 (285.4 mg) was subjected to CC with 20% EtOAc-hexanes to give seven fractions (C2a-C2g). Fractions C2b (30.2 mg), C2d (34.3 mg), C2f (11.5 mg) were repeatedly purified by CC using 20% CH_2Cl_2-hexanes to yield compounds **WM42** (5.8 mg), **WM41** (16.6 mg), and **WM51** (4.5 mg), respectively, while compound **WM6** (2.8 mg) was isolated from fraction C2f (27.6 mg) by CC with 45% CH_2Cl_2-hexanes. Fraction C4 (181.9 mg) was subjected to repeated CC using 20% EtOAc-hexanes to give five subfractions (C4a-C4d). Subfractions C4b (55.4 mg) and C4d (24.6 mg) were further purified by CC with 80% CH_2Cl_2-hexanes to give compounds **WM8** (3.7 mg) and **WM13** (6.5 mg), respectively.

Compound **WM6** (Mukonine): Yellow solid; mp 193-194 °C; UV (MeOH) λ_{max} 236, 247, 267, 276, 307, 320 nm; IR (neat) ν_{max} 3323, 2948, 1693, 1350, 1257 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6) 10.78 (1H, br s, 9-NH), 8.47 (1H, s, H-4), 8.20

(1H, d, *J* = 8.0 Hz, H-5), 7.63 (1H, d, *J* = 8.0 Hz, H-8), 7.59 (1H, s, H-2), 7.45 (1H, t, *J* = 8.0 Hz, H-7), 7.26 (1H, t, *J* = 8.0 Hz, H-6), 4.07 (3H, s, 1-OMe), 3.91 (3H, s, 3-CO_2Me).

Compound **WM8** (2-Methoxy-3-formyl carbazole or *O*-Methylmukonal): Brow solid; mp 186-187 °C; UV (MeOH) λ_{max} 220, 237, 248, 272, 258, 330, 340 nm; IR (neat) ν_{max} 3316, 2836, 1668, 1578, 1345, 1135 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 10.05 (1H, s, 3-CHO), 8.64 (1H, br s, 9-NH), 8.19 (1H, s, H-4), 8.11 (1H, d, *J* = 8.0 Hz, H-5), 7.52 (1H, m, H-8), 7.46 (1H, s, H-1), 7.48 (1H, m, H-6), 7.32 (1H, td, *J* = 8.0 and 1.6 Hz, H-7), 4.07 (3H, s, 2-OMe).

Compound **WM13** (Clausine C): Yellow solid; mp 197-198 °C; UV (MeOH) λ_{max} 224, 237, 248, 281, 320 nm; IR (neat) ν_{max} 3282, 2924, 1698, 1607, 1440, 1251, 1097 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 8.07 (1H, s, H-4), 8.23 (1H, br s, 9-NH), 8.06 (1H, d, *J* = 8.4 Hz, H-5), 7.98 (1H, d, *J* = 8.8 Hz, H-2), 7.38 (1H, d, *J* = 8.4 Hz, H-6), 6.93 (1H, s, H-8), 6.91 (1H, d, *J* = 8.8 Hz, H-1), 3.96 (3H, s, 3-CO_2Me), 3.90 (3H, s, 7-OMe); ^{13}C NMR (100 MHz, $CDCl_3$) 168.1 (3-$\underline{C}O_2$Me), 159.7 (C-7), 142.7 (C-8a), 141.5 (C-9a), 126.4 (C-5), 123.4 (C-4a), 122.0 (C-4), 121.5 (C-2), 120.3 (C-3), 117.2 (C-4b), 109.9 (C-6), 109.1 (C-1), 95.2 (C-8), 55.8 (7-OMe), 52.0 (3-CO_2Me).

Compound **WM41** (7-Methoxy heptaphylline): Yellow solid; mp 166-167 °C; UV (MeOH) λ_{max} 221, 236, 254, 301, 340 nm; IR (neat) ν_{max} 3502, 2924, 1731, 1617, 1233 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 11.64 (1H, s, 2-OH), 9.89 (1H, s, 3-CHO), 8.13 (1H, br s, 9-NH), 7.92 (1H, s, H-4), 7.43 (1H, d, *J* = 8.4 Hz, H-5), 6.90 (1H, d, *J* = 2.4 Hz, H-8), 6.87 (1H, dd, *J* = 8.4 and 2.4 Hz, H-6), 5.31 (1H, t, *J* = 6.8, H-2′), 3.89 (3H, s, 7-OMe), 3.62 (2H, d, *J* = 6.8 Hz, H-1′), 1.89 (3H, s, H-4′), 1.77 (3H, s, H-5′); ^{13}C NMR (100 MHz, $CDCl_3$) 195.5 (3-CHO), 159.1 (C-7), 157.4 (C-2), 145.3 (C-9a), 141.6 (C-8a), 134.2 (C-4′), 124.2 (C-4), 121.4 (C-2′), 120.6 (C-5), 117.6 (C-4b), 117.4 (C-4a), 115.5 (C-3), 109.0 (C-6), 95.8 (C-8), 25.8 (C-5′), 23.0 (C-1′), 18.2 (C-4′).

Compound **WM42** (Clausenawalline C): Yellow solid; mp 239-240 °C; UV (MeOH) λ_{max} 206, 235, 295, 310 ,337, 349, 390, 399 nm; IR (neat) ν_{max} 3299, 2970, 1639, 1659 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$), see Table 3.12; ^{13}C NMR (100 MHz,

$CDCl_3$), see Table 3.12; ESI-TOF-MS $[M+H]^+$ (*m*/*z*) 346.1790 (calcd for $C_{23}H_{24}NO_2$, 346.1807).

Compound **WM51** (Clausenawalline A): Brown solid; mp 203-204 °C; UV (MeOH) λ_{max} 230, 273, 334, 379, 391 nm; IR (neat) ν_{max} 3523, 3302, 2916, 1212, 1438, 1205, 1076 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6), see Table 3.15; ^{13}C NMR (100 MHz, acetone-d_6), see Table 3.15; ESI-TOF-MS $[M+H]^+$ (*m*/*z*) 557.2421 (calcd for $C_{36}H_{32}N_2O_4$, 557.2440).

Fraction D (3.21 g) was subjected to QCC and eluted with increasing the polarity of the elution solvents system of hexanes and EtOAc (20% EtOAc-hexanes to 100% EtOAc) to provide seven subfractions (D1-D7). Subfraction D2 (118.9 mg) was further isolated by CC with 30% EtOAc-hexanes to yield compound **WM18** (12.8 mg). Fractions D3 (1.18 g) and D5 (862.0 mg) were subjected to Sephadex-LH20 using 100% MeOH to afford four (D3a-D3d) and five (D5a-D5e) subfractions, respectively. Subfraction D3b (751.0 mg) was separated by CC with 2% EtOAc-CH_2Cl_2 to yield compounds **WM40** (3.0 mg), **WM52** (1.8 mg), and six subfractions (D3b1-D3b6). Subfractions D3b2 (25.1 mg) and D3b4 (30.5 mg) were further separated by CC with 25% EtOAc-hexanes to give compounds **WM9** (9.5 mg) and **WM12** (2.1 mg), respectively, while compound and **WM5** (3.0 mg) was derived from subfraction D3d (114.2 mg) by repeated CC with 20 % EtOAc-hexanes. Fraction D5b (259.1 mg) was further isolated by CC with 5% EtOAc-CH_2Cl_2 to afford compounds **WM22** (2.1 mg), **WM19** (19.0 mg), and **WM21** (8.5 mg). Finally, compounds **WM53** (1.7 mg) and **WM54** (6.2 mg) were isolated from fraction D5d (51.6 mg) by CC using 5% EtOAc-CH_2Cl_2.

Compound **WM9** (3-Hydroxy-2-methoxy-9*H*-carbazole): Yellow solid; mp 203-204 °C; UV (MeOH) λ_{max} 209, 234, 265, 305, 347, 350 nm; IR (neat) ν_{max} 3394, 2925, 1312, 1181 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) 9.98 (1H, br s, 9-NH), 7.93 (1H, d, *J* = 8.0 Hz, H-5), 7.51 (1H, s, H-4), 7.40 (1H, d, *J* = 8.0 Hz, H-8), 7.24 (1H, td, *J* = 8.0 and 1.2 Hz, H-7), 7.15 (1H, s, 3-OH), 7.08 (1H, s, H-1), 7.07 (1H, td, *J* = 8.0 and 1.2 Hz, H-6), 3.92 (3H, s, 2-OMe); ^{13}C NMR (100 MHz, acetone-d_6) 148.5 (C-2), 141.9 (C-3), 140.9 (C-8a), 135.2 (C-9a), 124.3 (C-4b), 123.6 (C-7), 119.0 (C-5), 118.3 (C-4a), 118.0 (C-6), 110.3 (C-8), 105.7 (C-4), 93.8 (C-1), 56.4 (2-OMe).

Compound **WM12** (Clauszoline K): Yellow solid; mp 254-255 °C; UV (MeOH) λ_{max} 204, 234, 243, 292, 325 nm; IR (neat) ν_{max} 3321, 2923, 1674, 1604, 1323, 1159 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6) 10.73 (1H, br s, 9-NH), 10.06 (1H, s, 3-CHO), 8.58 (1H, s, H-4), 8.12 (1H, d, *J* = 8.4 Hz, H-5), 7.87 (1H, dd, *J* = 8.0 and 1.4 Hz, H-2), 7.59 (1H, d, *J* = 8.0 Hz, H-1), 7.11 (1H, d, *J* = 2.0 Hz, H-8), 6.91 (1H, dd, *J* = 8.4 and 2.0 Hz, H-6), 3.89 (3H, s, 7-OMe).

Compound **WM18** (2-Hydroxy-3-formyl-7-methoxycarbazole): Yellow solid; mp 223-224 °C; UV (MeOH) λ_{max} 223, 238, 253, 299, 319, 340 nm; IR (neat) ν_{max} 3373, 2925, 1619, 1155 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6) 11.44 (1H, s, 2-OH), 10.60 (1H, br s, 9-NH), 9.97 (1H, s, 3-CHO), 8.31 (1H, s, H-4), 7.96 (1H, d, *J* = 8.4 Hz, H-5), 7.04 (1H, d, *J* = 2.4 Hz, H-8), 6.85 (1H, s, H-1), 6.85 (1H, dd, *J* = 8.4 and 2.4 Hz, H-6), 3.87 (3H, s, 7-OMe); ^{13}C NMR (100 MHz, acetone-d_6) 193.7 (3-CHO), 160.3 (C-2), 159.3 (C-7), 146.3 (C-9a), 142.4 (C-8a), 126.2 (C-4), 120.4 (C-5), 117.8 (C-4a), 116.7 (C-4b), 115.2 (C-3), 108.7 (C-6), 96.3 (C-1), 95.5 (C-8), 54.9 (7-OMe).

Compound **WM19** (3-Formyl-2,7-dimethoxycarbazole): Yellow solid; mp 217-218 °C; UV (MeOH) λ_{max} 223, 247, 278, 306, 317 nm; IR (neat) ν_{max} 3384, 2925, 1715, 1615 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6) 10.60 (1H, br s, 9-NH), 10.44 (1H, s, 3-CHO), 8.37 (1H, s, H-4), 8.09 (1H, d, *J* = 8.8 Hz, H-5), 7.11 (1H, s, H-1), 7.03 (1H, d, *J* = 2.4 Hz, H-8), 6.84 (1H, dd, *J* = 8.8 and 2.4 Hz, H-6), 3.99 (3H, s, 2-OMe), 3.85 (3H, s, 7-OMe); ^{13}C NMR (100 MHz, acetone-d_6)): 188.5 (3-CHO), 161.7 (C-2), 160.0 (C-7), 146.6 (C-9a), 143.0 (C-8a), 121.5 (C-5), 120.1 (C-4), 119.4 (C-3), 118.2 (C-4a), 117.8 (C-4b), 109.6 (C-6), 96.2 (C-8), 93.8 (C-1), 56.3 (2-OMe), 55.8 (7-OMe).

Compound **WM21** (Clauszoline C): Yellow solid; mp 241-242 °C; UV (MeOH) λ_{max} 240, 298, 348 nm; IR (neat) ν_{max} 3394, 3252, 1607, 1153 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6) 10.38 (1H, br s, 9-NH), 8.41 (1H, s, H-4), 7.94 (1H, d, *J* = 8.4 Hz, H-5), 7.10 (1H, s, H-1), 7.02 (1H, s, H-8), 6.82 (1H, dd, *J* = 8.4, H-6), 3.89 (3H, s, 2-OMe), 3.85 (3H, s, 7-OMe), 3.83, (3H, s, 3-CO_2<u>Me</u>)

Compound **WM22** (Clausenawalline D): Brown solid; mp 247-247 °C; UV (MeOH) λ_{max} 234, 265, 312, 326 nm; IR (neat) ν_{max} 3508, 3395, 1618, 1580 cm^{-1}; ^{1}H

NMR (400 MHz, acetone-d_6), see Table 3.1; ^{13}C NMR (100 MHz, acetone-d_6), see Table 3.1; ESI-TOF-MS $[M+H]^+$ (*m*/*z*) 278.1175 (calcd for $C_{18}H_{15}NO_2$, 278.1181).

Compound **WM40** (2,7-dihydroxy-3-formyl-1-(3′-methyl-2′-butenyl) carbazole): Brown solid; mp 193-194 °C; UV (MeOH) λ_{max} 220, 237, 243, 252, 302, 341 nm; IR (neat) ν_{max} 3330, 2923, 1614, 1471, 1325, 1152 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6) 11.74 (1H, s, 2-OH), 10.39 (1H, br s, 9-NH), 9.94 (1H, s, 3-CHO), 8.53 (1H, s, H-4), 8.16 (1H, br s, 7-OH), 7.87 (1H, d, *J* = 8.0 Hz, H-5), 6.94 (1H, d, *J* = 2.4 Hz, H-8), 6.77 (1H, dd, *J* = 8.0 and 2.4 Hz, H-6), 5.34 (1H, t, *J* = 7.2 Hz, H-2′), 3.61 (2H, d, *J* = 7.2 Hz, H-1′), 1.82 (3H, s, H-4′), 1.66 (1H, s, H-5′).

Compound **WM52** (Clausenawalline B): Brown solid; mp 214-215 °C; UV (MeOH) λ_{max} 214, 236, 256, 306, 349, 538 nm; IR (neat) ν_{max} 3372, 1725, 1615 cm^{-1}; ^{1}H NMR (500 MHz, acetone-d_6), see Table 3.16; ^{13}C NMR (125 MHz, acetone-d_6), see Table 3.16; ESI-TOF-MS $[M+H]^+$ (*m*/*z*) 507.1901 (calcd for $C_{31}H_{27}N_2O_5$, 507.1920).

Compound **WM53** (Clausenawalline E): Brown solid; mp 196-197 °C; UV (MeOH) λ_{max} 230, 266, 303, 311, 336 nm; IR (neat) ν_{max} 3849, 3396, 2923, 1620 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$), see Table 3.17; ^{13}C NMR (125 MHz, $CDCl_3$), see Table 3.17; ESI-TOF-MS $[M+H]^+$ (*m*/*z*) 505.2121 (calcd for $C_{32}H_{29}N_2O_4$, 505.2127).

Compound **WM54** (Clausenawalline F): Brown solid; mp 236-237 °C; UV (MeOH) λ_{max} 222, 233, 277, 300, 340 nm; IR (neat) ν_{max} 3346, 1704, 1614, 1564 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6), see Table 3.18; ^{13}C NMR (100 MHz, acetone-d_6), see Table 3.18; ESI-TOF-MS $[M+H]^+$ (*m*/*z*) 481.1394 (calcd for $C_{28}H_{21}N_2O_6$, 481.1400).

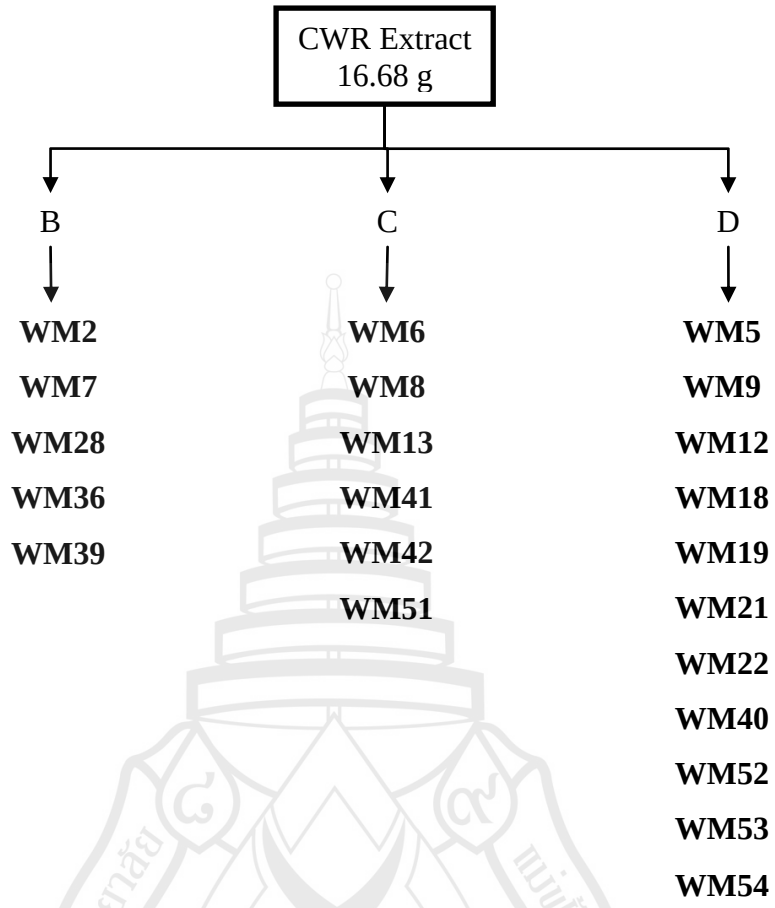


Figure 2.11 Isolation of CWR Extract from the Roots of *C. wallichii*

2.4.6 Isolation of *C. wallichii* Twigs

The isolation of CWT extract (113.20 g) with QCC using a gradient system from 100% hexanes to 100 % acetone gave eight fractions (A-H). Fraction B (2.07 g) was further isolated by Sephadex- LH20 using 20% CH_2Cl_2-MeOH and followed by repeated CC with 25% EtOAc-hexanes and 60% CH_2Cl_2-hexanes to yield compound **WM71** (4.5 mg).

Fraction C (4.13 g) was subjected to QCC with 20% CH_2Cl_2-hexanes to give four subfractions (C1-C4). Subfraction C3 (2.18 g) was further separated by Sephadex LH-20 with 100% MeOH to give compound **WM28** (31.6 mg) and six fractions (C3a-

C3f). Compounds **WM6** (1.4 mg) and **WM24** (8.5 mg) were derived from fractions C3d (11.0 mg) and C3e (14.6 mg), respectively, by CC with 85% CH_2Cl_2-hexanes.

Compound **WM24** (Clauraila C): Yellow solid; mp 249-250 °C; UV (MeOH) λ_{max} 226, 240, 290, 302, 373, 392 nm; IR (neat) ν_{max} 3280, 2924, 1695, 1289 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) 10.63 (1H, br s, 9-NH), 8.83 (1H, s, H-4), 8.04 (1H, dd, *J* = 8.4 and 1.2 Hz, H-2), 7.54 (1H, d, *J* = 8.4 Hz, H-1), 7.34 (1H, d, *J* = 8.4 Hz, H-8), 7.33 (1H, d, *J* = 10.0 Hz, H-1′), 6.93 (1H, d, *J* = 8.4 Hz, H-7), 6.00 (1H, d, *J* = 10.0 Hz, H-2′), 3.91 (3H, s, 3-CO_2Me), 1.47 (6H, s, H-4′ and H-5′).

Fraction D (5.50 g) was isolated by QCC with 10% EtOAc-hexanes to afford five subfractions (D1-D5). Compound **WM2** (8.2 mg) was obtained from subfraction D2 (284.5 mg) by CC using 90% CH_2Cl_2-hexanes. Subfraction D4 (492.2 mg) was separated by Sephadex-LH20 with 100% MeOH to provide four fractions (D4a-D4d). Fraction D4b (12.5 mg) was further purified by CC with 30% acetone-hexanes to yield compounds **WM1** (2.3 mg) and **WM13** (2.2 mg). Compounds **WM23** (2.9 mg) and **WM16** (2.7 mg) were derived from fraction D4c (19.6 mg) by CC using 20% acetone-hexanes.

Compound **WM23** (Clausenawalline I): Yellow solid; mp 253-254 °C; UV (MeOH) 204, 231, 297, 312 nm; IR (neat) ν_{max} 3302, 2923, 2852, 1671, 1609, 1583 cm^{-1}; ^1H NMR (500 MHz, acetone-d_6), see Table 3.2; ^{13}C NMR (125 MHz, acetone-d_6), see Table 3.2; ESI-TOF-MS $[M+H]^+$ (*m*/*z*) 278.1175 (calcd for $C_{18}H_{16}NO_2$, 278.1175).

Fraction E (8.78 g) was subjected to QCC with a gradient of hexanes-EtOAc (10% EtOAc-hexanes to 100% EtOAc) to afford six subfractions (E1-E6). Subfraction E2 (1.28 g) was further separated by Sephadex LH-20 using 100% MeOH and followed by CC with 2% acetone-CH_2Cl_2 to give compounds **WM29** (2.2 mg) and **WM15** (12.1 mg). Subfraction E3 (991.3 mg) was isolated by Sephadex LH-20 with 100% MeOH and further purified by CC with 5% acetone-CH_2Cl_2 to yield compounds **WM19** (1.9 mg) and **WM72** (1.6 mg). Compounds **WM27** (12.1 mg) and **WM26** (8.6 mg) were derived from subfraction E5 (107.3 mg) by CC with 5% acetone-CH_2Cl_2.

Compound **WM26** (Clausenawalline J): Yellow solid; mp 217-218 °C; UV (MeOH) λ_{max} 225, 237, 265, 278, 295, 377, 369, 390 nm; IR (neat) ν_{max} 3337, 2973, 1697, 1629, 1585 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6), see Table 3.4; ^{13}C NMR (100 MHz, acetone-d_6), see Table 3.4; ESI-TOF-MS $[M+H]^+$ (*m*/*z*) 324.1236 (calcd for $C_{19}H_{18}NO_4$, 324.1236)

Compound **WM27** (Clausenawalline H): Yellow solid; mp 232-233 °C; UV (MeOH) λ_{max} 233, 280, 310, 345, 362 nm; IR (neat) ν_{max} 3331, 2924, 1683, 1620, 1455 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6), see Table 3.5; ^{13}C NMR (100 MHz, acetone-d_6), see Table 3.5; ESI-TOF-MS $[M+H]^+$ (*m*/*z*) 296.1288 (calcd for $C_{18}H_{18}NO_3$, 296.1281)

Compound **WM29** (Clausenawalline K): Yellow solid; mp 240-241 °C; $[\alpha]_D^{27}$ –20.4 (*c* = 0.011, MeOH); UV (MeOH) λ_{max} 203, 233, 251, 284, 310, 341, 361 nm; IR (neat) ν_{max} 3322, 2922, 2852, 1734, 1637 cm^{-1}; ^{1}H NMR (500 MHz, acetone-d_6), see Table 3.6; ^{13}C NMR (125 MHz, acetone-d_6), see Table 3.6; ESI-TOF-MS $[M+H]^+$ (*m*/*z*) 328.1172 (calcd for $C_{18}H_{18}NO_5$, 328.1179)

Fraction F (3.63 g) was subjected to QCC with 20% EtOAc-hexanes and increasing polarity to 100% EtOAc to give seven subfractions (F1-F7). Subfraction F3 (205 mg) was further purified by CC with 5% acetone-CH_2Cl_2 to yield compound **WM25** (2.1 mg).

Compound **WM25** (Clausenawalline G): Yellow solid; mp 213-214 °C; UV (MeOH) λ_{max} 255, 243, 254, 269, 284, 3.18, 334, 353 nm; IR (neat) ν_{max} 3301, 2922, 2852, 1687, 1435 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6), see Table 3.3; ^{13}C NMR (100 MHz, acetone-d_6), see Table 3.3; ESI-TOF-MS $[M+H]^+$ (*m*/*z*) 326.1380 (calcd for $C_{19}H_{20}NO_4$, 326.1387)

Compound **WM20** (2.8 mg) was derived from fraction G (7.05 g) by QCC using a gradient of hexanes-EtOAc (30% EtOAc-hexanes to 100% EtOAc) and followed by Sephadex LH-20 with 100% MeOH.

Compound **WM20** (Clauszoline J): Brown solid; mp 255-257 °C; UV (MeOH) λ_{max} 223, 249, 278, 306, 317 nm; IR (neat) ν_{max} 3384, 2925, 1715, 1615, 1158 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6) 10.51 (1H, br s, 9-NH), 8.64 (1H, s, H-4), 8.02 (1H, d, *J* = 8.4 Hz, H-5), 7.23 (1H, s, H-1), 7.00 (1H, d, *J* = 2.0 Hz, H-8), 6.86

(1H, dd, J = 8.4 and 2.0 Hz, H-6), 4.12 (3H, s, 2-OMe), 3.86 (3H, s, 7-OMe); ^{13}C NMR (100 MHz, acetone-d_6) 166.6 (3-CO_2H), 160.0 (C-7), 158.1 (C-2), 145.1 (C-9a), 143.1 (C-8a), 125.1 (C-4), 121.5 (C-5), 118.6 (C-4a), 117.7 (C-4b), 111.4 (C-3), 109.5 (C-6), 96.1 (C-8), 94.7 (C-1), 57.2 (2-OMe), 55.8 (7-OMe).

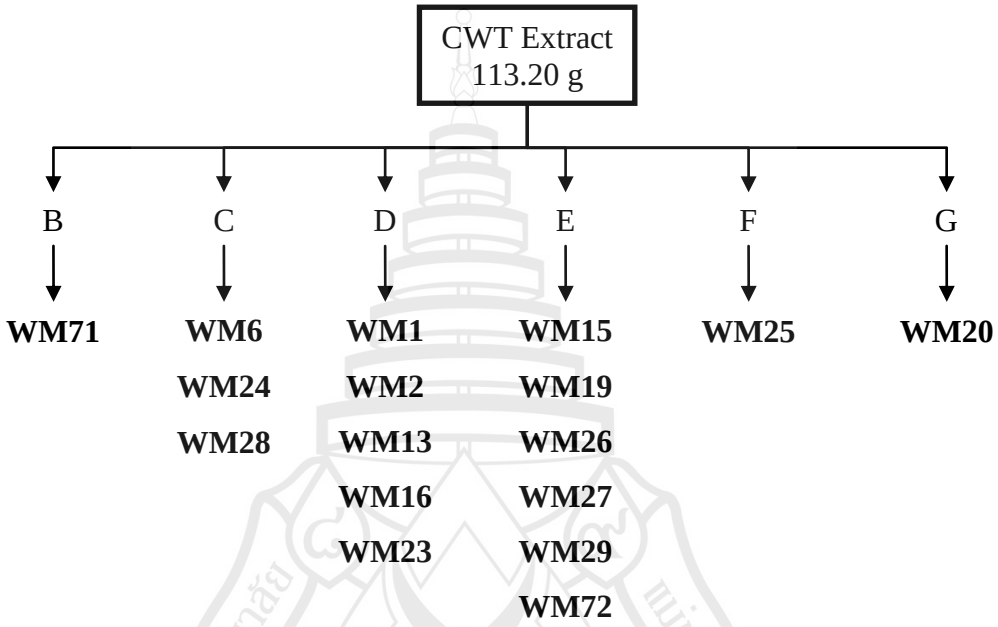


Figure 2.12 Isolation of CWT Extract from the Twigs of *C. wallichii*

2.5 Biological Assays

2.5.1 Antibacterial Assay

Escherichia coli TISTR 780, *Salmonella typhimurium* TISTR 292, *Staphylococcus aureus* TISTR 1466 were obtained from the Microbiological Resources Center of the Thailand Institute of Scientific and Technological Research, whereas MRSA SK1 was obtained from the Department of Microbiology, Faculty of Science, Prince of Songkla University, Thailand. The minimum inhibitory concentrations (MICs) were determined by a 2-fold serial dilution method using Mueller-Hinton broth, according to the Clinical and Laboratory Standards Institute

recommendations (CLSI, 2002). The test substances were dissolved in DMSO. Vancomycin and gentamycin were used as standard drugs. All compounds, except compound **WM67**, were evaluated for their antibacterial activity as summarized in Table 3.22

2.5.2 Cytotoxic Assay

The cytotoxic assay against the three cancer cell lines, including oral cavity cancer (KB), breast cancer (MCF-7), and small-cell lung cancer (NCI-H187) were performed using the resazurin microplate assay, which was modified for mammalian cell cytotoxicity (Brien, Wilsonn, Orton & Pognan, 2000). Compounds **WM1-WM14**, **WM16-WM18**, **WM21**, **WM22**, **WM28**, **WM30-WM32**, **WM35**, **WM36**, **WM39**, **WM40-WM42**, **WM51**, **WM54**, **WM56-WM65**, **WM71**, and **WM73** were evaluated for their cytotoxicity. Its values are summarized in Table 3.23.

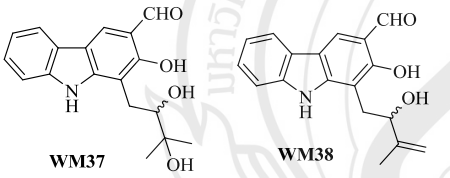
CHAPTER 3

RESULTS AND DISCUSSION

3.1 Isolated Compounds

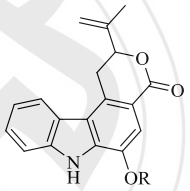
3.1.1 Isolated Compounds from the Twigs of *C. harmandiana*

The combination of hexanes and acetone extracts of *C. harmandiana* twigs (CHT extract) was subjected to silica gel column chromatography to yield three new carbazole alkaloids, harmandianamines A (**WM50**), B (**WM49**), and C (**WM37**), along with fifteen known alkaloids: *O*-demethylmurayanine (**WM3**) (Ngadjui, Ayafor, Sondengam, & Connolly, 1989), clauszoline I (**WM5**) (Ito, Katsuno, Ohta,

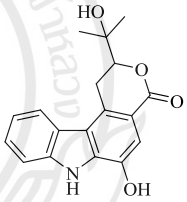


WM37

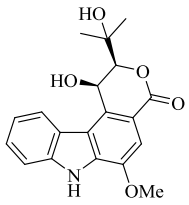
WM38



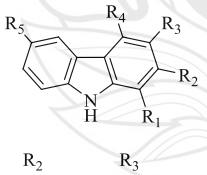
WM46: R = H
WM47: R = Me



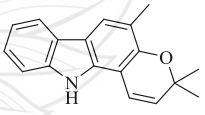
WM48



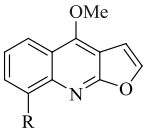
WM49



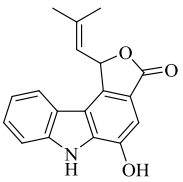
	R_1	R_2	R_3	R_4	R_5
WM3:	OH	H	CHO	H	H
WM5:	OH	H	CO_2Me	H	H
WM14:	OH	H	CHO	H	OH
WM15:	H	OH	CHO	H	OH
WM36:	Isoprene	OH	CHO	H	H
WM43:	OH	H	CHO	Isoprene	H
WM44:	OH	H	CO_2Me	Isoprene	H
WM45:	OMe	H	CO_2Me	Isoprene	H



WM39



WM71: R = H
WM72: R = OMe

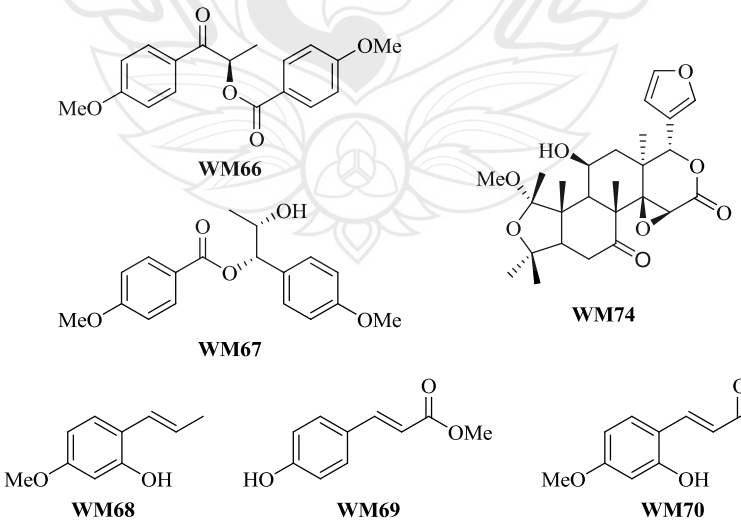


WM50

Omura, Kajiura, & Frukawa, 1997), clausine Z (**WM14**) (Potterat et al., 2005, clauszoline N (**WM15**) (Shi, Ye, Tang, & Zhao, 2010), heptaphylline (**WM36**) (Wu & Furukawa, 1982), clausine S (**WM38**) (Wu, Huang, Wu & Kuoh, 1999), girinimbine (**WM39**) (Furukawa, Wu, Ohta, & Kuoh, 1985), clausine D (**WM43**) (Wu, Huang & Lai, 1992), clausine F (**WM44**) (Wu, Huang & Lai, 1992), clausemine D (**WM45**) (Ito et al., 2000), clausamine A (**WM46**) (Ito, Katsuno & Furukawa, 1998), clausamine B (**WM47**) (Ito, Katsuno & Furukawa, 1998), clausevatine D (**WM48**) (Wu, Huang & Wu, 1998), dectamine (**WM71**) (Wu & Furokawa, 1982), and γ-fagarine (**WM72**) (Terezan et al., 2010).

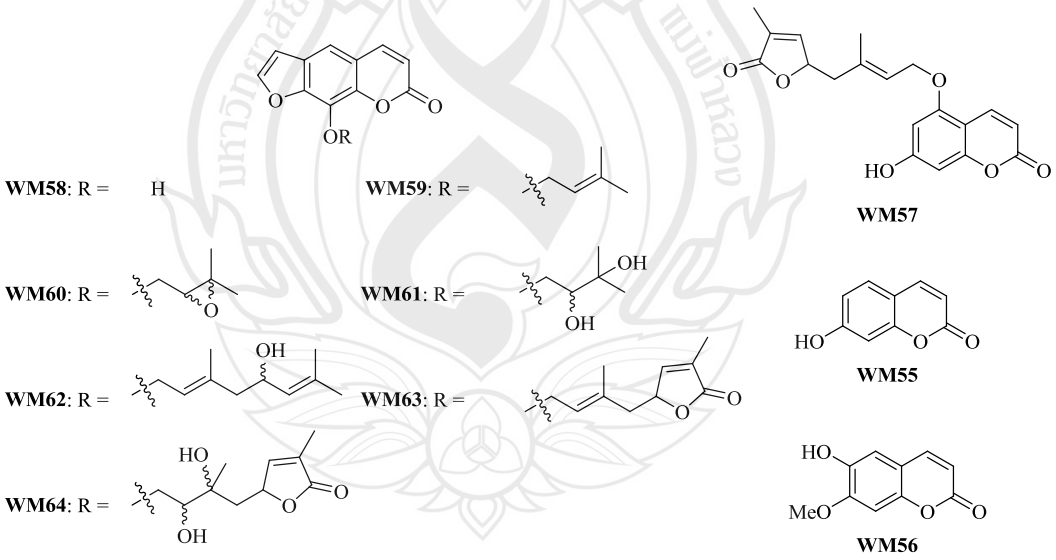
3.1.2 Isolated Compounds from the Fruits of *C. harmandiana*

Phytochemical investigation of acetone extract of *C. harmandiana* fruits using chromatographic techniques led to the isolation and structural identification of a new phenylpropanoid (**WM66**), along with five known compounds: verimol B (**WM67**) (Sy & Brown, 1998), (*E*)-5-methoxy-2-(prop-1-enyl)phenol (**WM68**) (Bottini et al., 1986), (*E*)-methyl *p*-coumarate (**WM69**) (Muhammed, Nasim, Naheed, Shaiq & Abdul, 2011), (*E*)-3-(2-hydroxy-4-methoxy-phenyl)propanoate (**WM70**) (Cordoba, Tormo. Medared & Plumet, 2007), and *O*-methylclausenolide (**WM74**) (Wu, Huang & Lai, 1992).



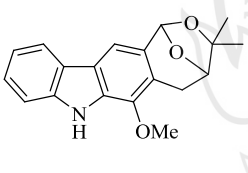
3.1.3 Isolated Compounds from the Roots of *C. lansium*

The combination of hexanes and acetone extracts from air-dried roots of *C. lansium* were purified by chromatographic techniques which led to the isolation of two new carbazole alkaloids (**WM34** and **WM35**), together with twelve known compounds including *O*-demethylmurrayanine (**WM3**) (Ngadjui, Ayafor, Sondengam, & Connolly, 1989), murrayanine (**WM4**) (Li, McChesney & El-Feraly, 1991), glycozoline (**WM10**) (Chakravarty, Sarkar, Masuda & Shiojima, 1999), 3-formyl-6-methoxycarbazole (**WM11**) (Li, McChesney & El-Feraly, 1991), lansine (**WM16**) (Prakash, Kanwal, Kapil & Popli, 1980; Ma et al., 2005), glycozolidal (**WM17**) (Li, McChesney & El-Feraly, 1991), indizoline (**WM30**) (Li, McChesney & El-Feraly, 1991), claulansine A (**WM31**) (Liu et al., 2012), umbelliferone (**WM55**) (Ngadjui, Mouncherou, Ayafor, Sondengam & Tillequin, 1991), imperatorin (**WM59**) (Masuda, Takasugi & Anetai, 1998), wampetin (**WM63**) (Khan, Naqvi & Ishratullah, 1983), and indicolactonediol (**WM64**) (Rakash, Raj, Kapil & Popli, 1978)

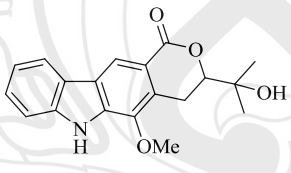


3.1.4 Isolated Compounds from the Twigs of *C. lansium*

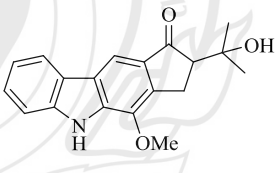
The combination of CH_2Cl_2 and acetone extracts of *C. lansium* twigs was subjected to silica gel chromatography to yield four new compounds, including two new carbazole alkalids: mafiacheenamines A (**WM32**) and C (**WM33**) and two novel coumarins: clausenalansimins A (**WM62**) and B (**WM57**). The remaining fifteen known compounds including 3-formyl carbazole (**WM1**) (Li, McChesney & El-Feraly, 1991), murrayanine (**WM4**) (Li, McChesney & El-Feraly, 1991), lansine (**WM16**) (Prakash, Kanwal, Kapil & Popli, 1980; Ma et al., 2005), glycozolidal (**WM17**) (Li, McChesney & El-Feraly, 1991), indizoline (**WM30**) (Li, McChesney & El-Feraly, 1991), claulansine A (**WM31**) (Liu et al., 2012), isoscopoletin (**WM56**) (Al-Barwani & Eltayeb, 2005), xanthotoxol (**WM58**) (Ito, Katsuno, Ruangrungsi & Furukawa, 1998), imperatorin (**WM59**) (Masuda, Takasugi & Anetai, 1998), heraclenin (**WM60**) (Appendino et al., 2004), heraclenol (**WM61**) (Razdan, Kachroo, Harkar& Koul, 1982), wampetin (**WM63**) (Khan, Naqvi & Ishratullah, 1983), indicolactonediol (**WM64**) (Rakash, Raj, Kapil & Popli, 1978), phenethyl cinnamide (**WM65**) (Riemer, Hofer & Greger, 1997), and 4-methoxyl-1-methyl-2-quinolone (**WM73**) (Nayer, Sutar & Bhan, 1971) (Figure 6 and 7) were isolated.



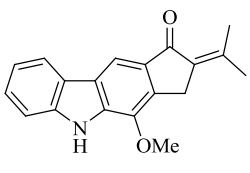
WM31



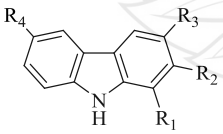
WM32



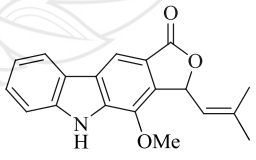
WM33



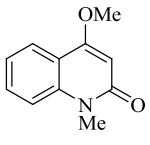
WM34



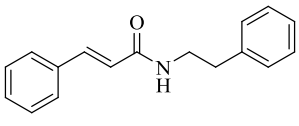
	R_1	R_2	R_3	R_4
WM1:	H	H	CHO	H
WM3:	OH	H	CHO	H
WM4:	OMe	H	CO_2Me	H
WM10:	H	H	Me	OMe
WM11:	H	H	CHO	OMe
WM16:	H	OH	CHO	OMe
WM17:	H	OMe	CHO	OMe
WM30:	OMe	Isoprene	CHO	H



WM35



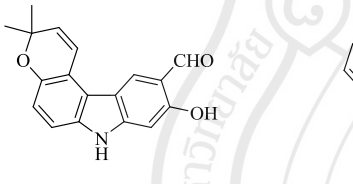
WM73



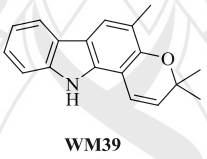
WM65

3.1.5 Isolated Compounds from the Roots of *C. wallichii*

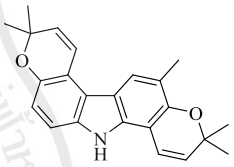
The acetone extract of the roots of *C. wallichii* was subjected to column chromatography over silica gel to give six new carbazole alkaloids (**WM22**, **WM42**, and **WM51-WM54**) together with sixteen known compounds were characterized as methyl carbazole-3-carboxylate (**WM2**) (Li, McChesney & El-Feraly, 1991), clauszoline I (**WM5**) (Ito, Katsuno, Ohta, Omura, Kajiura & Furukawa, 1997), mukonine (**WM6**) (Wu, Huang & Wu, 1996), mukonal (**WM7**) (Bhattacharyya & Chakraborty, 1984), 2-methoxy-3-formylcarbazole (**WM8**) (Jash, Biswas, Bhattacharyya, Bhattacharyya, Chakraborty & Chowdhury, 1992), 3-hydroxy-2-methoxy-9*H*-carbazole (**WM9**) (Knölker, Bauermeister, Pannek & Wolpert, 1995), clauszoline K (**WM12**) (Ito, Tan & Furukawa, 1996), clausine C (**WM13**) (Wu, Huang & Wu, 1996), 2-hydroxy-3-formyl-7-methoxycarbazole (**WM18**) (Chaichantipyuth, Pummangura, Naowsaran & Thanyavuthi, 1998), 3-formyl-2,7-



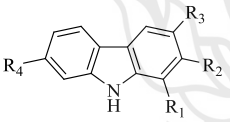
WM28

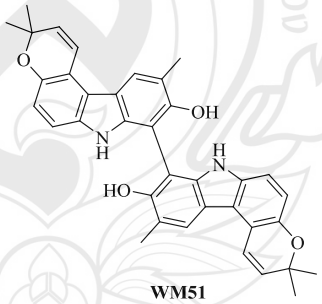


WM39

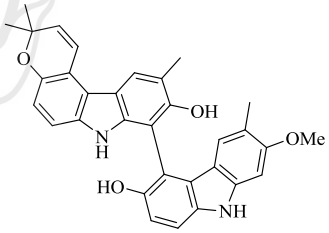


WM42



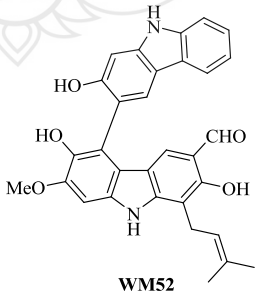


WM51

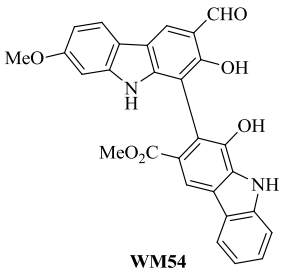


WM53

	R_1	R_2	R_3	R_4
WM2:	H	H	CO_2Me	H
WM5:	OH	H	CO_2Me	H
WM6:	OMe	H	CO_2Me	H
WM7:	H	OH	CHO	H
WM8:	H	OMe	CHO	H
WM9:	H	OMe	OH	H
WM12:	H	H	CHO	OMe
WM13:	H	H	CO_2Me	OMe
WM18:	H	OH	CHO	OMe
WM19:	H	OMe	CHO	OMe
WM21:	H	OMe	CO_2Me	OMe
WM22:	H	OMe	OH	OMe
WM36:	Isoprene	OH	CHO	H
WM40:	Isoprene	OH	CHO	OH
WM41:	Isoprene	OH	CHO	OMe



WM52

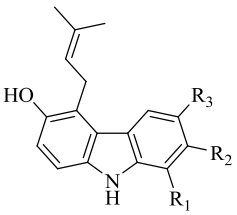


WM54

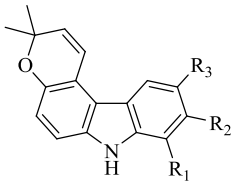
dimethoxycarbazole (**WM19**) (Ruangrungsi & Ariyaprayoon, 1990), clauszoline C (**WM21**) (Ito, Tan & Furukawa, 1996), clauraila D (**WM28**) (Songsiang, Thongthoom, Boonyarat & Yenjai, 2011), heptaphylline (**WM36**) (Wu & Furukawa, 1982), girinimbine (**WM39**) (Furukawa, Wu, Ohta & Kuoh, 1985), 2,7-dihydorxy-3-formyl-1-(3′-methyl-2′-butenyl)carbazole (**WM40**) (Kumar, Vallipuram, Adebajo & Reisch, 1995), and 7-methoxyheptaphylline (**WM41**) (Chaichantipyuth, Pummangura, Naowsaran & Thanyavuthi, 1998).

3.1.6 Isolated Compounds from the Twigs of *C. wallichii*

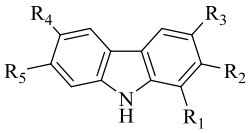
The acetone extract of *C. wallichii* twigs was purified by column chromatography to yield five new carbazole alkaloids, clausenawallines G-K (**WM23**, **WM25**-**WM27**, and **WM29**), along with twelve known alkaloids which were identified as clauraila C (**WM24**) (Songsiang, Thongthoom, Boonyarat & Yenjai, 2011), clauraila D (**WM28**) (Songsiang, Thongthoom, Boonyarat & Yenjai, 2011), 3-formyl carbazole (**WM1**) (Li, McChesney & El-Feraly, 1991), methyl carbazole-3-carboxylate (**WM2**) (Li, McChesney & El-Feraly, 1991), mukonine (**WM6**) (Wu, Huang & Wu, 1996), clausine C (**WM13**) (Wu, Huang & Wu, 1996), clauszoline N (**WM15**) (Shi, Ye, Tang & Zhao, 2010), lansine (**WM16**) (Prakash, Kanwal, Kapil & Popli, 1980; Ma et al., 2005), 3-formyl-2,7-dimethoxycarbazole (**WM19**) (Prakash, Kanwal, Kapil & Popli, 1980; Ma et al., 2005), clauszoline J (**WM20**) (Ito, Katsuno, Ohta, Omura, Kajiura & Furukawa, 1997), dectamine (**WM71**) (Wu & Furokawa, 1982), and γ-fagarine (**WM72**) (Terezan et al., 2010).



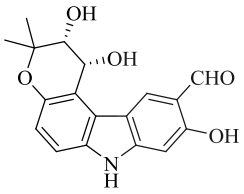
	R_1	R_2	R_3
WM25:	OH	H	CO_2Me
WM27:	H	OH	CHO



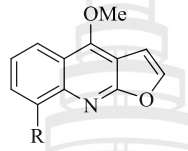
	R_1	R_2	R_3
WM23:	H	H	CHO
WM24:	H	H	CO_2Me
WM26:	OH	H	CO_2Me
WM28:	H	OH	CHO



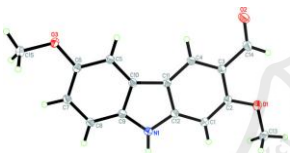
	R_1	R_2	R_3	R_4	R_5
WM1:	H	H	CHO	H	H
WM2:	H	H	CO_2Me	H	H
WM6:	OMe	H	CO_2Me	H	H
WM13:	H	H	CO_2Me	H	OMe
WM15:	H	OH	CHO	OH	H
WM16:	H	OH	CHO	OMe	H
WM19:	H	OMe	CHO	H	OMe
WM20:	H	OMe	CO_2H	H	OMe



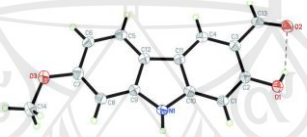
WM29



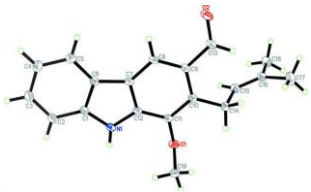
WM71: R = H
WM72: R = OMe



WM17



WM18

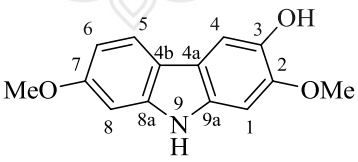


WM30

3.2 Structural Elucidation of Selected Compounds

3.2.1 Carbazole Alkaloids

3.2.1.1 Compound **WM22**



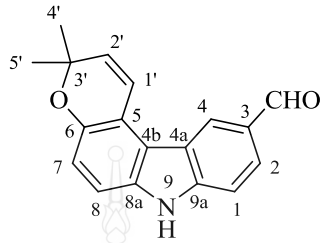
Compound **WM22**, mp 247-249 °C, was isolated as a brown solid. Its molecular formula was determined as $C_{14}H_{14}NO_3$ ($[M+H]^+$ *m/z* 244.0968, calcd for

244.0974) by ESI-TOF-MS. UV spectrum showed absorption maxima bands at λ_{max} 234, 265, 312, and 326. IR spectrum indicated the presence of OH and NH stretching bands at 3508 and 3395 cm^{-1}, respectively. Analysis of its NMR spectra, including COSY, HMQC, and HMBC data, allowed unambiguous assignment of all proton and carbon signals. The ^1H NMR data (Table 3.1) showed a broad NH singlet at δ_H 9.85, an ABX aromatic system [δ_H 7.78 (1H, d, *J* = 8.4 Hz, H-5), 6.94 (1H, d, *J* = 2.0 Hz, H-8), and 6.71 (1H, dd, *J* = 8.4 and 2.0 Hz, H-6)], and two para-romatic protons [δ_H 7.43 (1H, s, H-4) and 7.03 (1H, s, H-1)]. On the basis of HMBC correlations (Table 3.1), two methoxy groups were observed at δ_H 3.90 and 3.82 (br s, 3H) and located at C-2 and C-7, respectively. The C-3 resonance at δ_C 142.0 was assigned to a nonprotonated aromatic carbon carrying a hydroxy group. Detailed assignments of the protons and carbons as well as HMBC correlations are shown in Table 3.1, facilitating assignment of structure **WM22** to clausenawalline D.

Table 3.1 ^1H NMR (400 MHz), ^{13}C NMR (100 MHz), COSY, and HMBC Spectral Data of **WM22** in Acetone-d_6

Positions	**δ_H (mult., *J* in Hz)**	**δ_C**	**COSY ($^1H \rightarrow ^1H$)**	**HMBC ($^1H \rightarrow ^{13}C$)**
1	7.03 (s)	144.5	–	C-2, C-3, C-4a
2	–	108.4	–	–
3	–	112.7	–	–
4	7.43 (s)	119.2	–	C-2, C-3, C-4b, C-9a
4a	–	125.1	–	–
4b	–	124.5	–	–
5	7.78 (d, 8.4)	121.3	H-6	C-4a, C-7, C-8a
6	6.71 (dd, 8.4, 2.0)	120.8	H-5	C-4b, C-7, C-8
7	–	127.2	–	–
8	6.94 (d, 2.0)	112.7	–	C-4b, C-6, C-7
8a	–	141.4	–	–
9a	–	134.9	–	–
2-OMe	3.90 (s)	56.5	–	C-2
3-OH	7.05 (br s)	–	–	C-3
7-OMe	3.82 (s)	55.6	–	C-7
9-NH	9.85 (br s)	–	–	–

3.2.1.2 Compound **WM23**

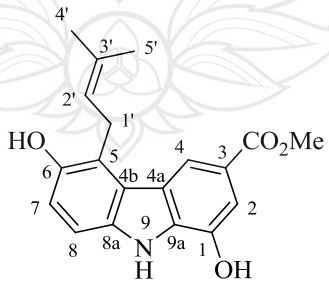


Compound **WM23** was obtained as a yellow solid with mp 253-254 °C. The ESI-TOF-MS gave a pseudomolecular ion peak at *m*/*z* 278.1175 $[M+H]^+$ (calcd for 278.1181) consistent with the molecular formula $C_{18}H_{15}NO_2$. The ^1H NMR spectrum of **WM23** showed a singlet formyl proton at δ_H 10.10 (1H, 3-CHO), two sets of aromatic protons including an ABX system [δ_H 8.77 (1H, d, *J* = 1.2, H-4), 7.93 (1H, dd, *J* = 8.4, 1.2 Hz, H-2), and 7.62 (1H, d, *J* = 8.4 Hz, H-1)] and an ortho-coupled aromatic proton [δ_H 7.36 (1H, d, *J* = 8.4 Hz, H-8) and 6.96 (1H, d, *J* = 8.4 Hz, H-7)], together with a pyran moiety [δ_H 7.44 (1H, d, *J* = 10.0 Hz, H-1′), 6.07 (1H, d, *J* = 10.0 Hz, H-2′), and 1.47 (6H, s, H-4′ and H-5′)]. The pyran moiety was placed at C-5/C-6 due to the HMBC correlations of H-1′ (δ_H 7.44) to C-4b (δ_C 119.2), C-5 (δ_C 116.3), and C-6 (δ_C 148.1), whereas the formyl group was located on C-3 due to the ^3J HMBC correlations of H-2 (δ_H 7.93) and H-4 (δ_H 8.77) with 3-CHO (δ_C 191.9) (Table 3.2). Therefore, structure **WM23** was identified as clausenawalline I. Detailed assignments of the ^1H, ^{13}C, COSY, and HMBC NMR spectral data are shown in Table 3.2.

Table 3.2 ^{1}H NMR (500 MHz), ^{13}C NMR (125 MHz), COSY, and HMBC Spectral Data of **WM23** in Acetone-d_6

Positions	δ_H (mult., *J* in Hz)	δ_C	COSY (^{1}H→^{1}H)	HMBC (^{1}H→^{13}C)
1	7.62 (d, 8.4)	112.5	H-2	C-3, C-4a
2	7.93 (dd, 8.4, 1.2)	126.3	H-1	C-4, C-9a, 3-CHO
3	–	129.8	–	–
4	8.77 (d, 1.2)	126.7	–	C-2, C-4b, C-9a, 3-CHO
4a	–	123.5	–	–
4b	–	119.2	–	–
5	–	116.3	–	–
6	–	148.1	–	–
7	6.96 (d, 8.4)	117.1	H-8	C-5, C-8a
8	7.36 (d, 8.4)	112.5	H-7	C-4b, C-6
8a	–	136.6	–	–
9a	–	145.4	–	–
1′	7.44 (d, 10.0)	120.4	H-2′	C-4b, C-6, C-3′
2′	6.07 (d, 10.0)	132.9	H-1′	C-5, C-4′, C-5′
3′	–	75.9	–	–
4′	1.47 (s)	27.4	–	C-2′, C-3′, C-5′
5′	1.47 (s)	27.4	–	C-2′, C-3′, C-4′
3-CHO	10.10 (s)	191.9	–	–
9-NH	10.84 (br s)	–	–	–

3.2.1.3 Compound **WM25**



Compound **WM25** was obtained as a yellow solid, mp 213-214 °C. The molecular formula, $C_{19}H_{19}NO_4$, was assigned by the ESI-TOF-MS ion peak at *m*/*z* 326.1380 $[M+H]^+$ (calcd for 326.1387). The ^{1}H NMR signals at δ_H 10.54 (1H, br s, 9-

NH), 8.44 (1H, d, *J* = 1.2 Hz, H-4), 7.52 (1H, d, *J* = 1.2 Hz, H-2), 7.31 (1H, d, *J* = 8.4 Hz, H-8), and 7.10 (1H, d, *J* = 8.4 Hz, H-7) corresponded to the 1,3,5,6-tetrasubstituted of carbazole alkaloid. The correlation between methoxy protons (δ_H 3.87) and the carbonyl carbon (δ_C 167.2) in the HMBC experiment (Table 3.3) indicated the presence of a methyl ester group. This group was placed on C-3 due to the ^3J HMBC correlations between H-2 (δ_H 7.52), H-4 (δ_H 8.44), and 3-CO_2Me (δ_H 3.87) with a carbonyl ester at δ_C 167.2 (3-$\underline{C}O_2$Me). In addition, resonances of isoprenyl protons were also observed in the ^{1}H NMR spectrum at δ_H 5.29 (1H, t, *J* = 6.0 Hz, H-2′), 3.98 (2H, d, *J* = 6.0 Hz, H-1′), 1.98 (3H, s, H-5′), and 1.68 (3H, s, H-4′) which was placed on C-5 due to the HMBC correlations of H-1′ (δ_H 3.98) with C-4b (δ_C 124.0) and C-6 (δ_C 150.2). Therefore, structure **WM25** was identified as clausenawalline G. Detailed assignments of the ^{1}H, ^{13}C, and HMBC NMR spectral data are shown in Table 3.3.

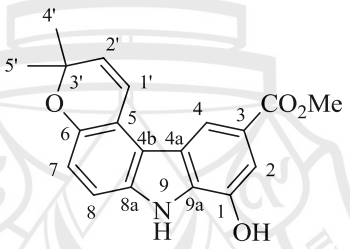
Table 3.3 ^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz), and HMBC Spectral Data of **WM25** in Acetone-d_6

Positions	**δ_H (mult., *J* in Hz)**	**δ_C**	**HMBC (^{1}H→^{13}C)**
1	–	143.2	–
2	7.52 (d, 1.2)	110.6	C-1, C-4, C-9a, 3-$\underline{C}O_2$Me
3	–	124.1	–
4	8.44 (d, 1.2)	118.3	C-2, C-4b, 3-$\underline{C}O_2$Me
4a	–	120.3	–
4b	–	124.0	–
5	–	117.3	–
6	–	150.2	–
7	7.10 (d, 8.4)	116.2	C-5, C-6, C-8a
8	7.31 (d, 8.4)	110.2	C-4b, C-6
8a	–	136.0	–
9a	–	135.0	–
1′	3.98 (d, 6.0)	26.2	C-4b, C-6, C-2′, C-3′
2′	5.29 (t, 6.0)	123.7	C-5, C-4′, C-5′
3′	–	132.4	–

Table 3.3 (continued)

Positions	δ_H (mult., *J* in Hz)	δ_C	HMBC ($^1H \rightarrow ^{13}C$)
4′	1.68 (s)	25.8	C-2′, C-3′, C-5′
5′	1.98 (s)	18.3	C-2′, C-3′, C-4′
3-$\underline{C}O_2Me$	–	167.2	–
3-$CO_2\underline{Me}$	3.87 (s)	51.8	3-$\underline{C}O_2Me$
9-NH	10.54 (br s)	–	–

3.2.1.4 Compound **WM26**

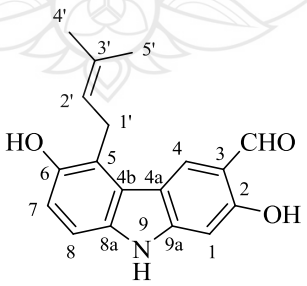


Compound **WM26**, obtained as a yellow solid, which showed a pseudomolecular ion peak $[M+H]^+$ at *m/z* 324.1236 (calcd for 324.1236) in the ESI-TOF-MS corresponding to a molecular formula of $C_{19}H_{17}NO_4$. The ^1H and ^{13}C NMR spectra of **WM26** were similar to those of **WM23** (Table 3.2), except compound **WM26** displayed the presence of a methyl ester group [δ_H 3.88 (3H, s, 3-$CO_2\underline{Me}$)/δ_C 51.9 and δ_C 168.0, 3-$\underline{C}O_2Me$] instead of the formyl group at C-3 in **WM23**. In addition, a set of meta-coupled aromatic protons [δ_H 8.41 (1H, d, *J* = 1.2 Hz, H-4) and 7.65 (1H, d, *J* = 1.2 Hz, H-2)] also replaced the ABX system of **WM23**. The ^3J HMBC correlations (Table 3.4) of the methyl ester (δ_H 3.88), H-4 (δ_H 8.41), and H-2 (δ_H 7.65) to δ_C 168.0 (3-$\underline{C}O_2Me$), and H-2 (δ_H 7.65) to δ_C 117.3 (C-4) and 134.8 (C-9a) supported the location of the methyl ester and hydroxy group at C-3 and C-1, respectively. Thus, compound **WM26** was assigned as clausenawalline J. Detailed assignments of the ^1H, ^{13}C, and HMBC NMR spectroscopic data are shown in Table 3.4.

Table 3.4 ^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz), and HMBC Spectral Data of **WM26** in Acetone-d_6

Positions	**δ_H (mult., *J* in Hz)**	**δ_C**	**HMBC (^{1}H→^{13}C)**
1	–	143.5	–
2	7.65 (d, 1.2)	110.8	C-1, C-4, C-9a, 3-$\underline{C}O_2$Me
3	–	124.3	–
4	8.41 (d, 1.2)	117.3	C-2, C-4b, C-9a, 3-CO_2Me
4a	–	120.4	–
4b	–	119.7	–
5	–	116.0	–
6	–	147.8	–
7	6.90 (d, 8.4)	116.7	C-5, C-6, C-8a
8	7.39 (d, 8.4)	112.5	C-4b, C-6
8a	–	136.5	–
9a	–	134.8	–
1′	7.30 (d, 10.0)	120.4	C-4b, C-6, C-3′
2′	5.97 (d, 10.0)	132.6	C-5, C-4′, C-5′
3′	–	75.8	–
4′	1.46 (s)	27.4	C-2′, C-3′, C-5′
5′	1.46 (s)	27.4	C-2′, C-3′, C-4′
3-$\underline{C}O_2$Me	–	168.0	–
3-$CO_2\underline{Me}$	3.88 (s)	51.9	3-$\underline{C}O_2$Me
9-NH	10.54 (br s)	–	–

3.2.1.5 Compound **WM27**



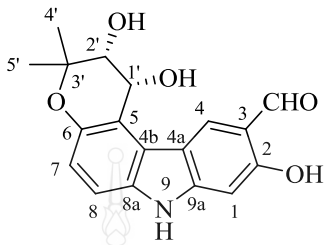
Compound **WM27** was obtained as a yellow solid. Its molecular formula, $C_{18}H_{17}NO_3$ was determined on the basis of its ESI-TOF-MS ($[M+H]^+$ *m*/*z* 296.1288,

calcd for 296.1281). The ^{1}H NMR spectroscopic data of **WM27** was similar to those of **WM25**; however, the main differences were that the ^{1}H NMR spectrum of **WM27** showed a chelated formyl proton at δ_H 9.44 (1H, s, 3-CHO) with the hydroxy proton at δ_H 11.47 (1H, br s, 2-OH). Moreover, an aromatic proton H-1 at δ_H 6.82 (1H, s) was also observed in the ^{1}H NMR spectrum. The HMBC correlations between the formyl proton (δ_H 9.44) with C-3 (δ_C 115.8), H-4 (δ_H 8.30) with 3-CHO (δ_C 195.5), and H-1 (δ_H 6.82) with C-3 (δ_C 115.8) also supported this observation (Table 3.5). Thus, structure **WM27** was assigned as clausenawalline H. Detailed assignments of the ^{1}H, ^{13}C, and HMBC NMR spectroscopic data are shown in Table 3.5.

Table 3.5 ^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz), and HMBC Spectral Data of **WM27** in Acetone-d_6

Positions	**δ_H (mult., *J* in Hz)**	**δ_C**	**HMBC (^{1}H→^{13}C)**
1	6.82 (s)	96.8	C-2, C-3, C-4a, C-9a
2	–	161.3	–
3	–	115.8	–
4	8.30 (s)	131.1	C-2, C-4b, C-9a, 3-CHO
4a	–	118.8	–
4b	–	123.4	–
5	–	122.5	–
6	–	149.8	–
7	6.99 (d, 8.4)	109.6	C-5, C-8a
8	7.16 (d, 8.4)	115.3	C-4b, C-6
8a	–	136.1	–
9a	–	147.8	–
1′	3.94 (d, 6.0)	15.2	C-4b, C-6, C-3′
2′	5.30 (t, 6.0)	123.2	C-5, C-4′, C-5′
3′	–	132.7	–
4′	1.68 (s)	24.9	C-2′, C-3′, C-5′
5′	1.94 (s)	17.5	C-2′, C-3′, C-4′
2-OH	11.47 (br s)	–	–
3-CHO	9.44 (s)	195.5	–
9-NH	10.56 (br s)	–	–

3.2.1.6 Compound **WM29**

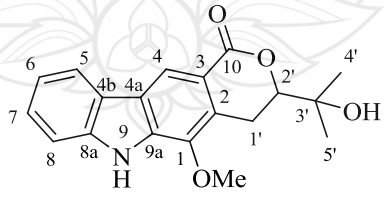


Compound **WM29** was obtained as a yellow solid and showed molecular formula, $C_{18}H_{17}NO_5$, determined by ESI-TOF-MS (*m*/*z* 328.1172, calcd for 328.1179). Compound **WM29** also displayed ^{1}H NMR signals similar to that of **WM27** at δ_H 11.44 (1H, br s, 2-OH), 10.68 (1H, br, s, 9-NH), 9.98 (1H, s, 3-CHO), 8.87 (1H, s, H-4), 7.76 (1H, d, *J* = 8.4 Hz, H-7), 7.36 (1H, d, *J* = 8.4 Hz, H-8), and 6.86 (1H, s, H-1). This remaining resonances were characteristic of a 2,2-dimethyl-3,4-chroman diol [δ_H 5.35 (1H, d, *J* = 4.8 Hz, H-1′), 3.95 (1H, d, *J* = 4.8 Hz, H-2′), 1.42 (3H, s, H-4′), and 1.45 (3H, s, H-5′)] (Grougnet et al., 2005; Wu et al., 1997) which was placed on C-5/C-6 due to the ^2J and ^3J HMBC correlations of H-1′ (δ_H 5.35) to δ_C 136.4 (C-6), 123.7 (C-4b), and 116.2 (C-5) (Table 3.6). The diol should have pseudo-diequatorial or *cis*-configuration due to the small coupling constant value of H-1′ and H-2′ (each 4.8 Hz) (Grougnet et al., 2005; Wu et al., 1997). Thus, the structure of **WM29** was identified as clausenawalline K. Detailed assignments of the ^{1}H, ^{13}C, and HMBC NMR spectroscopic data are shown in Table 3.6.

Table 3.6 ^{1}H NMR (500 MHz), ^{13}C NMR (125 MHz), and HMBC Spectral Data of **WM29** in Acetone-d_6

Positions	δ_H (mult., *J* in Hz)	δ_C	HMBC ($^{1}H \rightarrow ^{13}C$)
1	6.86 (s)	96.6	C-3, C-4a
2	–	161.2	–
3	–	118.1	–
4	8.87 (s)	133.5	C-2, C-4b, C-9a, 3-CHO
4a	–	117.4	–
4b	–	123.7	–
5	–	116.2	–
6	–	136.4	–
7	7.76 (d, 8.4)	116.7	C-6, C-8a
8	7.36 (d, 8.4)	112.8	C-4b, C-6
8a	–	148.1	–
9a	–	147.5	–
1′	5.35 (d, 4.8)	64.7	C-4b, C-6, C-3′
2′	3.95 (d, 4.8)	73.4	C-5, C-4′, C-5′
3′	–	77.5	–
4′	1.42 (s)	26.1	C-2′, C-3′, C-5′
5′	1.45 (s)	21.5	C-2′, C-3′, C-4′
2-OH	11.44 (br s)	–	
3-CHO	9.98 (s)	196.7	–
9-NH	10.68 (br s)	–	–

3.2.1.7 Compound **WM32**



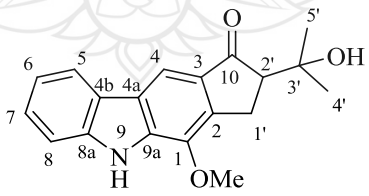
Compound **WM32**, $[\alpha]_D^{26}$ + 81.37 (*c* 0.02, MeOH), was obtained as brown solid. The molecular formula of $C_{19}H_{19}NO_4$ was determined by a molecular ion peak at $[M]^+$ *m*/*z* 325.1315 (calcd for $C_{19}H_{19}NO_4$, 325.1314) in HR-EI-MS. By comparison the ^{1}H and ^{13}C NMR spectral data (Table 3.7) of **WM32** with that of clausevatine D

(**WM48**) (Wu et al., 1998), which was isolated from the roots of *C. excavata*, both of them showed similar ^{1}H and ^{13}C NMR signals, indicating that compound **WM32** was a lactonic carbazole alkaloid skeleton which appeared ^{1}H NMR signals of a four mutually coupling aromatic protons of ring A at δ_H 8.23 (1H, d, *J* = 8.0 Hz, H-5), 7.56 (1H, d, *J* = 8.0 Hz, H-8), 7.46 (1H, ddd, *J* = 8.0, 7.2, 1.2 Hz, H-7) and 7.26 (1H, ddd, *J* = 8.0, 7.2, 1.2 Hz, H-6) and a lactonic moiety at δ_H 3.47 (1H, dd, *J* = 16.4, 2.4 Hz, H-1a′), 3.02 (1H, dd, *J* = 16.4, 12.4 Hz, 1b′), 4.29 (1H, dd, *J* = 12.4, 2.4 Hz, H-2′), 1.37 (6H, s, H-4′ and H-5′). However, two main differences were observed in ^{1}H NMR spectrum. Firstly, an additional methoxyl group was observed at δ_H 3.99 which was placed on C-1 due to the HMBC correlations between proton H-1′ (δ_H 3.47 and 3.02) and methoxyl protons (δ_H 3.99) with C-1 (δ_C 142.1). Secondly, the singlet aromatic proton on ring C was shifted from δ_H 7.55 (for clausevatine D, acetone-d_6) to δ_H 8.59 (for carbazole **WM32**, acetone-d_6). These results implied that the lactonic ring of **WM32** should be placed on C-2 and C-3 instead C-3 and C-4 as appeared in **WM48**. Therefore, the proton signal at δ_H 8.59 was identified to H-4 in which showed ^{2}J and ^{3}J correlations with C-4a (δ_C 124.4), C-4b (δ_C 124.9), and C-10 (δ_C 166.4) in HMBC spectrum. Thus, the structure of **WM32** was indentified to be mafaicheenamine A.

Table 3.7 ^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz), COSY, and HMBC Spectral Data of **WM32** in Acetone-d_6

Positions	δ_H (mult., *J* in Hz)	δ_C	COSY (^{1}H→^{1}H)	HMBC (^{1}H→^{13}C)
1	–	142.1	–	–
2	–	129.6	–	–
3	–	118.0	–	–
4	8.59 (s)	119.8	–	C-2, C-4b, C-9a, C-10
4a	–	124.4	–	–
4b	–	124.9	–	–
5	8.23 (d, 8.0)	121.5	H-6	C-7, C-8a
6	7.26 (ddd, 8.0, 7.2, 1.2)	121.0	H-5, H-7	C-4b, C-8
7	7.46 (ddd, 8.0, 7.2, 1.2)	127.5	H-6, H-8	C-6, C-8a
8	7.56 (d, 8.0)	112.5	H-7	C-4b, C-6
8a	–	141.6	–	–
9a	–	137.4	–	–
10	–	166.4	–	–
1a′	3.47 (dd, 16.4, 2.4)	23.2	H-2′	C-1, C-2, C-3
1b′	3.02 (dd, 16.4, 12.4)		H-2′	C-1, C-2, C-3
2′	4.29 (dd, 12.4, 2.4)	85.1	H-1′a, H-1′b	C-2, C-3′
3′	–	71.2	–	–
4′	1.37 (s)	26.8	–	C-2′, C-3′, C-5′
5′	1.37 (s)	25.3	–	C-2′, C-3′, C-4′
1-OMe	3.99 (s)	61.3	–	C-1
9-NH	10.96 (br s)	–	–	–

3.2.1.8 Compound **WM33**



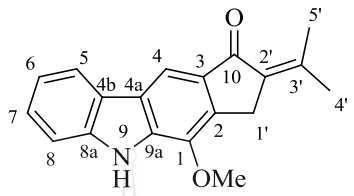
Compound **WM33** was obtained as a brown solid, $[\alpha]_D^{26}$ +64.25 (*c* 0.02, MeOH). It showed molecular ion peak at $[M]^+$ *m/z* 309.1364 (calcd for $C_{19}H_{19}NO_3$, 309.1365) in HR-EI-MS. The ^{1}H NMR signals of **WM33** were similar to those of

WM32 (Table 3.7) but differed in the higher field shift of non-oxygenated proton H-2′ which appeared at δ_H 2.95 instead of an oxymethine proton at δ_H 4.29. In addition, the ^{13}C NMR signal of C-10 of **WM33** (δ_C 208.5) also resonated lower field than those of **WM32** (δ_C 166.4). This result implied that the lactonic ring of **WM32** was replaced by the five membered ring of ketone. Finally, the structure of **WM33** was confirmed by HMBC correlation as shown in Table 3.8. Therefore, the structure of **WM33** was identified to be mafaicheenamine C. Detailed assignments of the protons and carbons as well as COSY and HMBC correlations are shown in Table 3.8.

Table 3.8 ^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz), COSY, and HMBC Spectral Data of **WM33** in $CDCl_3$

Positions	**δ_H (mult., *J* in Hz)**	**δ_C**	**COSY ($^1H \rightarrow {}^1H$)**	**HMBC ($^1H \rightarrow {}^{13}C$)**
1	–	140.8	–	–
2	–	138.9	–	–
3	–	114.1	–	–
4	8.27 (s)	112.3	–	C-2, C-4b, C-9a, C-10
4a	–	123.8	–	–
4b	–	124.0	–	–
5	8.07 (d, 7.6)	121.0	H-6	C-4a, C-7, C-8a
6	7.28 (ddd, 8.0, 7.6, 2.4)	120.7	H-5, H-7	C-4b, C-8
7	7.47 (ddd, 8.0, 7.6, 2.4)	127.1	H-6, H-8	C-6, C-8a
8	7.48 (d, 7.6)	111.2	H-7	C-4b, C-6
8a	–	140.2	–	–
9a	–	137.9	–	–
10	–	208.5	–	–
1a′	3.52 (dd, 16.8, 8.0)	27.6	H-2′	C-1, C-3, C-10, C-2′
1b′	2.99 (dd, 16.8, 4.8)		H-2′	C-1, C-3, C-10, C-2′
2′	2.95 (dd, 8.0, 4.8)	57.0	H-1′a, H-1′b	C-3′
3′	–	72.9	–	–
4′	1.37 (s)	28.6	–	C-2′, C-3′, C-5′
5′	1.16 (s)	24.4	–	C-2′, C-3′, C-4′
1-OMe	4.13 (br s)	60.2	–	C-1
9-NH	8.65 (br s)	–	–	–

3.2.1.9 Compound **WM34**

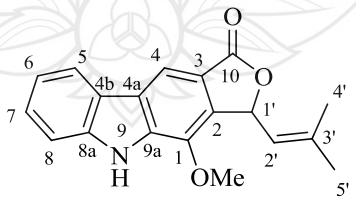


Compound **WM34** was isolated as a yellow solid (mp 202-203 °C) and its molecular formula was determined as $C_{19}H_{18}NO_2$ ($[M+H]^+$ *m*/*z* 292.1332, calcd for 292.1338) by ESI-TOF-MS. Its UV and IR spectra showed typical of carbazole alkaloid and similar to that of **WM33**. Analysis of its NMR spectral data including COSY, HMQC, and HMBC spectra, allowed unambiguous assignment of all proton and carbon signals. The ^{1}H and ^{13}C NMR displayed signals similar to those of **WM33** (Table 3.8), except **WM34** contained an exocylic α,β-unsaturated ketone which was placed on C-2/C-3 due to the ^3J HMBC correlations of H-4 (δ_H 8.33) and H-1′ (δ_H 3.89) with carbonyl carbon (C-10, δ_C 193.3). The ^4J HMBC correlation of H-4′ (δ_H 2.51) with C-10 was also observed. Finally, the methoxyl group was located on C-1 by process of elimination and also supported with the HMBC correlations of methoxyl group (δ_H 4.16) and a methylene group (δ_H 3.89, H-1′) with C-1 (δ_C 140.5). Therefore, mafaicheenamine D was indentified to the structure **WM34**. Detailed assignments of the protons and carbons as well as HMBC correlations are shown in Table 3.9.

Table 3.9 ^{1}H NMR (500 MHz), ^{13}C NMR (125 MHz), and HMBC Spectral Data of **WM34** in $CDCl_3$

Positions	δ_H (mult., *J* in Hz)	δ_C	HMBC ($^{1}H \rightarrow ^{13}C$)
1	–	140.5	–
2	–	133.3	–
3	–	120.7	–
4	8.33 (s)	112.1	C-2, C-4a, C-9a, C-10
4a	–	124.0	–
4b	–	125.5	–
5	8.12 (d, 7.6)	121.0	C-6, C-7, C-8a
6	7.29 (m)	120.3	C-4b, C-7, C-8
7	7.47 (m)	126.6	C-5, C-6, C-8a
8	7.48 (m)	111.0	C-4b, C-6, C-7
8a	–	139.9	–
9a	–	136.7	–
10	–	193.3	–
1′	3.89 (s)	29.9	C-1, C-2, C-10, C-2′
2′	–	130.7	–
3′	–	148.1	–
4′	2.51 (s)	24.4	C-10, C-2′, C-3′, C-5′
5′	2.07 (s)	20.3	C-2′, C-3′, C-4′
1-OMe	4.16 (s)	60.0	C-1
9-NH	8.39 (br s)	–	–

3.2.1.10 Compound **WM35**



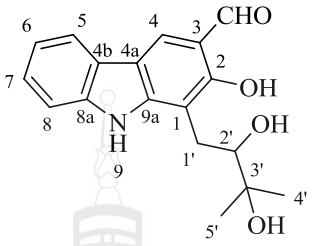
Compound **WM35** was obtained as a yellow solid (mp 209-212 °C), $[\alpha]_D^{27}$ – 14.3. The ESI-TOF-MS gave a pseudomolecular ion peak at $[M+H]^+$ *m/z* 308.1281 (calcd for 308.1287) consistent with the molecular formula $C_{19}H_{17}NO_3$. The

^{1}H and ^{13}C NMR spectral data of **WM35** were similar to those of **WM34** except compound **WM35** showed ^{1}H and ^{13}C NMR signals of γ-lactone moiety [oxymethine proton at δ_H 6.41 (1H, d, *J* = 9.2 Hz, H-1′)/δ_C 75.9 (C-1′), an olefinic proton at δ_H 5.19 (1H, d, *J* = 9.2 Hz, H-2′)/δ_C 121.4 (C-2′), two allyl methyl groups at δ_H 2.04 (3H, d, *J* = 1.2 Hz, H-4′)/δ_C 25.0 (C-4′) and 1.85 (3H, d, *J* = 1.2 Hz, H-5′)/δ_C 17.7 (C-5′), and δ_C 169.9 (lactone carbonyl)] instead of an exocylic α,β-unsaturated ketone moiety. Therefore, mafaicheenamine E was assigned to be **WM35**. Detailed assignments of the protons and carbons as well as COSY and HMBC correlations are shown in Table 3.10)

Table 3.10 ^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz), COSY, and HMBC Spectral Data of **WM35** in Acetone-d_6

Positions	**δ_H (mult., *J* in Hz)**	**δ_C**	**COSY (^{1}H→^{1}H)**	**HMBC (^{1}H→^{13}C)**
1	–	139.4	–	–
2	–	118.5	–	–
3	–	135.7	–	–
4	8.35 (s)	112.9	–	C-2, C-9a, C-10
4a	–	118.5	–	–
4b	–	123.1	–	–
5	8.29 (d, 8.4)	120.8	H-6	C-8a, C-7
6	7.29 (dd, 8.4 and 8.0)	120.0	H-5, H-7	C-4a, C-8
7	7.50 (dd, 8.4 and 8.0)	126.8	H-6, H-8	C-5, C-8a
8	7.61 (d, 8.4)	111.6	H-7	C-4b, C-6
8a	–	141.1	–	–
9a	–	136.8	–	–
10	–	169.9	–	–
1′	6.41 (d, 9.2)	75.9	H-2′	C-1, C-3, C-10, C-2′
2′	5.19 (d, 9.2)	121.4	H-1′	C-4′, C-5′
3′	–	139.4	–	–
4′	2.04 (d, 1.2)	25.0	–	C-2′, C-3′, C-5′
5′	1.85 (d, 1.2)	17.7	–	C-2′, C-3′, C-4′
1-OMe	4.04 (s)	60.0	–	C-1
9-NH	10.94 (br s)	–	–	–

3.2.1.11 Compound **WM37**

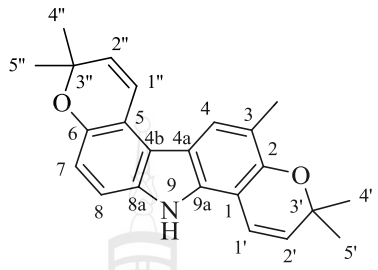


Compound **WM37** was isolated as a yellow solid (mp 228-229 °C). The molecular formula of $C_{18}H_{19}NO_4$ was inferred by HR-EI-MS ($[M]^+$ *m*/*z* 313.1305, calcd for 313.1309). The ^{1}H NMR spectral data of **WM37** displayed signals of NH at δ_H 10.61 (1H, br s), a chelated hydrogen at δ_H 11.78 (1H, br s, 2-OH), a formyl proton at δ_H 9.97 (1H, s, 3-CHO), a set of 1,2-disubstituted benzene ring at δ_H 8.07 (1H, d, *J* = 8.0 Hz, H-5), 7.50 (1H, d, *J* = 8.0 Hz, H-8), 7.35 (1H, td, *J* = 8.0 and 1.0 Hz, H-7), and 7.20 (1H, td, *J* = 8.0 and 1.0 Hz, H-6), and a singlet aromatic proton at δ_H 8.34 (1H, s, H-4). The presence of $-CH_2CH(OH)C(CH_3)_2OH$ unit was also observed in the ^{1}H NMR at δ_H 3.73 (1H, dd, *J* = 9.5 and 2.0 Hz, H-2′), 3.36 (1H, dd, *J* = 14.5 and 2.0 Hz, H-1a′), 2.81 (1H, m, H-1b′), 1.31 (3 H, s, H-4′), and 1.30 (3 H, s, H-5′) (Wu et al., 1999), which was placed at C-1 due to the correlations of H-1′ (δ_H 3.36 and 2.81) and H-4 (δ_H 8.34) with C-2 (δ_C 158.9) and C-9a (δ_C 147.2) in the HMBC experiment. The structure of **WM37** was, therefore, assigned to harmandianamine C. Detailed assignments of the protons and carbons as well as HMBC correlations are shown in Table 3.11.

Table 3.11 ^{1}H NMR (500 MHz), ^{13}C NMR (125 MHz), and HMBC Spectral Data of **WM37** in Acetone-d_6

Positions	**δ_H (mult., *J* in Hz)**	**δ_C**	**HMBC (^{1}H→^{13}C)**
1	–	109.6	–
2	–	158.9	–
3	–	116.0	–
4	8.34 (s)	126.4	C-2, C-4b, C-9a, 3-CHO
4a	–	118.1	–
4b	–	124.5	–
5	8.07 (d, 8.0)	121.0	C-4a, C-7, C-8a
6	7.20 (td, 8.0 and 1.0)	120.4	C-4b, C-8
7	7.35 (td, 8.0 and 1.0)	126.4	C-5, C-8a
8	7.50 (d, 8.0)	112.7	C-4b, C-6
8a	–	142.0	–
9a	–	147.2	–
1a′	3.36 (dd, 14.5 and 2.0)	27.4	C-1, C-2, C-9a, C-2′
1b′	2.81 (m)	–	–
2′	3.73 (dd, 9.5 and 2.0)	79.2	C-3′
3′	–	73.1	–
4′	1.31 (s)	25.2	C-2′, C-3′, C-5′
5′	1.30 (s)	26.0	C-2′, C-3′, C-4′
2-OH	11.78 (br s)	–	–
3-CHO	9.97 (s)	196.8	C-2, C-3
9-NH	10.61 (br s)	–	–

3.2.1.12 Compound **WM42**

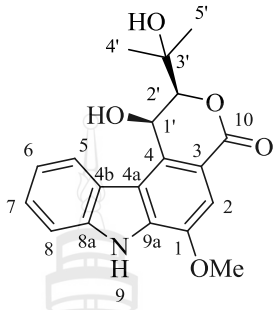


Compound **WM42** was obtained as a yellow solid with mp 239-240 °C. The molecular formula, $C_{23}H_{23}NO_2$, was assigned from the ESI-TOF-MS ion peak at *m*/*z* 346.1790 $[M+H]^+$ (calcd for 346.1807). The UV spectrum showed absorption maxima bands at λ_{max} 206, 235, 295, 310, 337, 349, 390, and 399 nm. The IR spectrum indicated the presence of an NH stretching band at 3299 cm^{-1}, which was further supported by NH resonance at δ_H 7.71 (br s) in the ^{1}H NMR spectrum (Table 3.12). A methyl singlet at δ_H 2.32 was assigned to the aryl methyl group located at C-3 of the carbazole skeleton based on its ^2J and ^3J HMBC correlations to C-2 (δ_C 149.5), C-3 (δ_C 119.3), and C-4 (δ_C 123.2). The ^{1}H NMR spectrum also displayed a set of ortho-coupled aromatic signals at δ_H 7.12 (1H, d, *J* = 8.8 Hz, H-8) and 6.82 (1H, d, *J* = 8.8 Hz, H-7), together with an aromatic singlet at δ_H 7.71 (1H, s, H-4). Two 2H-pyran moieties were also evident. First unit [δ_H 6.59 (1H, d, *J* = 9.6 Hz, H-1′), 5.68 (1H, d, *J* = 9.6 Hz, H-2′), and 1.47 (6H, s, H-4′ and H- 5′)] was located at C-1/C-2 on the basis of the ^2J and ^3J correlations between H-1′ (δ_H 6.59) and C-2 (δ_C 149.5), C-9a (δ_C 136.0), C-1 (δ_C 104.3), and C-3′ (δ_C 75.8) in the HMBC spectrum. The another unit [δ_H 7.20 (1H, d, *J* = 9.6 Hz, H-1″), 5.79 (1H, d, *J* = 9.6 Hz, H-2″), and 1.47 (6H, s, H-4″and H-5″)] was located at C-5/C-6 on the basis of the HMBC correlations between H-1″ (δ_H 7.20) and C-6 (δ_C 146.6), C-4b (δ_C 119.3), C-5 (δ_C 114.9), and C-3″ (δ_C 75.0). Detailed assignments of the protons and carbons as well as COSY and HMBC correlations are shown in Table 3.12, facilitating assignment of structure **WM42** to clausenawalline C.

Table 3.12 ^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz), COSY, and HMBC Spectral Data of **WM42** in $CDCl_3$

Positions	**δ_H (mult., *J* in Hz)**	**δ_C**	**COSY ($^{1}H \rightarrow {}^{1}H$)**	**HMBC ($^{1}H \rightarrow {}^{13}C$)**
1	–	104.3	–	–
2	–	149.5	–	–
3	–	119.3	–	–
4	7.71 (s)	123.2	–	C-2, C-4b, C-9a, 3-Me
4a	–	110.1	–	–
4b	–	119.3	–	–
5	–	114.9	–	–
6	–	146.6	–	–
7	6.82 (d, 8.8)	113.7	H-8	C-5, C-6, C-8a
8	7.12 (d, 8.8)	110.1	H-7	C-4b, C-6
8a	–	134.7	–	–
9a	–	136.0	–	–
1′	6.59 (d, 9.6)	117.1	H-2′	C-1, C-2, C-9a, C-3′
2′	5.68 (d, 9.6)	120.2	H-1′	C-1, C-3′, C-4′, C-5′
3′	–	75.8	–	–
4′	1.47 (s)	27.5	–	C-2′, C-3′, C-5′
5′	1.47 (s)	27.5	–	C-2′, C-3′, C-4′
1″	7.20 (d, 9.6)	120.2	H-2″	C-4b, C-5, C-6, C-3″
2″	5.79 (d, 9.6)	123.2	H-1″	C-5, C-3″, C-4″, C-5″
3″	–	75.0	–	–
4″	1.47 (s)	27.2	–	C-2″, C-3″, C-5″
5″	1.47 (s)	27.2	–	C-2″, C-3″, C-4″
3-Me	2.32 (s)	16.1	–	C-2, C-3, C-4
3-OH	–	–	–	–
7-OMe	–	–	–	–
9-NH	7.71 (br s)	–	–	–

3.2.1.13 Compound **WM49**

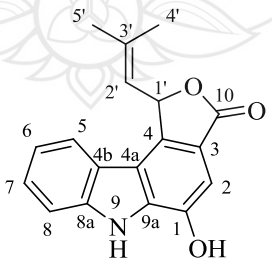


Compound **WM49** was obtained as a yellow solid (mp 216-217 °C). The HR-EI-MS showed themolecular ion peak at $[M]^+$ *m/z* 341.1266 (calcd for 341.1258) corresponding to the molecular formula of $C_{19}H_{19}NO_5$. The ^1H NMR spectrum displayed similar signals of 1,3,4-trisubstituted carbazole alkaloids pattern at δ_H 11.01 (1H, br s, 9-NH), 8.30 (1H, d, *J* = 8.0 Hz, H-5), 7.67 (1H, d, *J* = 8.0 Hz, H-8), 7.54 (1H, s, H-2), 7.48 (1H, td, *J* = 8.0 and 1.5 Hz, H-7), and 7.29 (1H, td, *J* = 8.0 and 1.5 Hz, H-6). In addition, the methoxyl group was also observed at δ_H 4.08 in ^1H NMR spectrum which was placed at C-1 because of the HMBC correlation between methoxyl protons with C-1 (δ_C 147.9). By comparison of NMR spectral data of **WM49** with that of clausevatine E (Wu et al., 1998) isolated from *C. excavata*, all remaining signals [δ_H 5.83 (1H, dd, *J* = 4.0 and 2.0, H-1′), 5.39 (1H, d, *J* = 4.0 Hz, 1′-OH), 4.71 (1H, br s, 3′-OH), 4.39 (1H, d, *J* = 2.0, H-2′), 1.60 (3 H, s, H-4′), and 1.52 (3 H, s, H-5′)] were similar. The small coupling constant, 2.0 Hz, of H-1′ (δ_H 5.83) and H-2′ (δ_H 4.39) should be recognized as *syn* orientation of both protons. However, the stereochemistry at C-1′ and C-2′ of lactone ring was different with those of clausevatine E because of the opposite optical rotation (+36.2 (MeOH) for **WM49**; -92.4 (MeOH) for clausevatine E) (Wu et al., 1998). The structure of **WM49** was, therefore, identified as harmandianamine B. Detailed assignments of the protons and carbons as well as HMBC correlations are shown in Table 3.13.

Table 3.13 ^{1}H NMR (500 MHz), ^{13}C NMR (125 MHz), and HMBC Spectral Data of **WM49** in Acetone-d_6

Positions	δ_H (mult., *J* in Hz)	δ_C	HMBC (^{1}H→^{13}C)
1	–	147.9	–
2	7.54 (s)	106.1	C-1, C-3, C-4, C-10
3	–	116.9	–
4	–	130.4	–
4a	–	116.8	–
4b	–	120.5	–
5	8.30 (d, 8.0)	123.4	C-4a, C-7, C-8a
6	7.29 (td, 8.0 and 1.5)	121.0	C-4b, C-8
7	7.48 (td, 8.0 and 1.5)	127.0	C-5, C-8a
8	7.67 (d, 8.0)	112.7	C-4b, C-6
8a	–	141.3	–
9a	–	135.2	–
10	–	166.3	–
1′	5.83 (dd, 4.0 and 2.0)	63.6	C-4, C-4a
2′	4.39 (d, 2.0)	84.2	–
3′	–	73.1	–
4′	1.60 (s)	27.0	C-2′
5′	1.52 (s)	26.8	C-2′
1-OMe	4.08 (s)	56.2	C-1
9-NH	11.01 (br s)	–	–
1′-OH	5.39 (d, 4.0)	–	–
3′-OH	4.71 (br s)	–	–

3.2.1.14 Compound **WM50**



Compound **WM50** was obtained as a yellow solid (mp 203-204 °C) which showed the molecular ion peak at $[M]^{+}$ *m*/*z* 293.1054 (calcd for 293.1046) in HR-EI-

MS corresponding to the molecular formula of $C_{18}H_{15}NO_3$. The ^{1}H NMR spectral data of **WM50** displayed signals of NH at δ_H 11.01 (br s), a set of 1,2-disubstituted benzene ring at δ_H 7.82 (1H, d, *J* = 8.0 Hz, H-5), 7.67 (1H, d, *J* = 8.0 Hz, H-8), 7.46 (1H, td, *J* = 8.0 and 1.5 Hz, H-7), and 7.24 (1H, td, *J* = 8.0 and 1.5 Hz, H-6), and an aromatic proton at δ_H 7.20 (1H, s, H-2). The ^{1}H and ^{13}C NMR spectrum also showed signals of γ-lactone group at δ_H/δ_C 6.59 (1H, d, *J* = 10.5 Hz, H-1′)/77.5 (C-1′), 5.23 (1H, m, H-2′)/121.7 (C-2′), 2.20 (3H, d, *J* = 1.5 Hz, H-4′)/30.2 (C-4′), and 1.86 (3 H, d, *J* = 1.5 Hz, H-5′)/30.2 (C-5), which was placed on C-3/C-4 due to the ^3J HMBC correlations of H-2 (δ_H 7.20) and H-1′ (δ_H 6.59) with carbonyl carbon C-10 (δ_C 170.9). In addition, the hydroxy proton signal at δ_H 9.64 (1H, br s) was located at C-1 due to the HMBC correlations of this proton with C-1 (δ_C 144.2) and C-9a (δ_C 132.8). Therefore, the structure **WM50** was assigned as harmandianamine A. Detailed assignments of the protons and carbons as well as HMBC correlations are shown in Table 3.14.

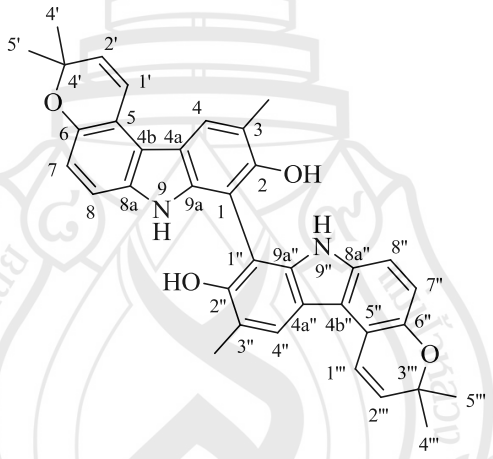
Table 3.14 ^{1}H NMR (500 MHz), ^{13}C NMR (125 MHz), and HMBC Spectral Data of **WM50** in Acetone-d_6

Positions	**δ_H (mult., *J* in Hz)**	**δ_C**	**HMBC (^{1}H→^{13}C)**
1	–	144.2	–
2	7.20 (s)	104.5	C-1, C-3, C-9a, C-10
3	–	138.7	–
4	–	115.9	–
4a	–	118.7	–
4b	–	121.0	–
5	7.82 (d, 8.0)	123.1	C-4a, C-7
6	7.24 (td, 8.0 and 1.5)	120.9	C-4b, C-8
7	7.46 (td, 8.0 and 1.5)	126.9	C-5, C-8a
8	7.67 (d, 8.0)	112.7	C-4b, C-6
8a	–	142.3	–
9a	–	132.8	–
10	–	170.9	–
1′	6.59 (d, 10.5)	77.5	C-3, C-10, C-2′, C-3′
2′	5.23 (m)	121.7	–
3′	–	141.9	–

Table 3.14 (continued)

Positions	**δ_H (mult., *J* in Hz)**	**δ_C**	**HMBC ($^1H \rightarrow ^{13}C$)**
4′	2.20 (d, 1.5)	30.2	C-3′, C-5′
5′	1.86 (d, 1.5)	30.2	C-2′, C-4′
1-OH	9.64 (br s)	–	C-1, C-9a
9-NH	11.01 (br s)	–	–

3.2.1.15 Compound **WM51**



Compound **WM51** was obtained as a brown solid, mp 203-204 °C. The molecular formula, $C_{36}H_{32}N_2O_4$, was deduced from the ESI-TOF-MS spectrum which showed the pseudomolecular ion peak at *m*/*z* 557.2421 $[M+H]^+$ (calcd for 557.2440). The IR spectrum showed OH and NH stretching bands at 3523 and 3302 cm^{-1}, respectively, and the UV spectrum showed typical absorbances at λ_{max} 230, 273, 334, 379, and 391 nm which were characteristic of the carbazole alkaloid skeleton in **WM51**. The fragment ion $[M^+–C_{18}H_{16}NO_2+H^\bullet]^+$ at *m*/*z* 279, representative of half the molecule, in the MS spectrum as well as ^1H and ^{13}C NMR spectral data suggested that the structure of **WM51** was a highly symmetrical carbazole alkaloid dimer. The ^1H NMR spectral data of **WM51** (Table 3.15) demonstrated the presence of NH and aromatic methyl groups at δ_H 9.49 and 2.49, respectively. The methyl group was

placed on C-3 because of the ^{2}J and ^{3}J HMBC correlations (Table 3.15) of this signal with C-2 (δ_H 152.8), C-4 (δ_C 123.6), and C-3 (δ_C 117.7). The chemical shift of C-2 at δ_C 152.8 suggested that this carbon was attached to a hydroxyl group. A singlet aromatic proton at δ_H 8.03 was assigned to H-4 and correlated with C-2 (δ_C 152.8), C-4b (δ_C 119.5), and 3-Me (δ_C 16.5) in the HMBC spectrum. A set of ortho-coupled aromatic protons at δ_C 7.08 (1H, d, J = 8.8 Hz) and 6.73 (1H, d, J = 8.8 Hz) were assigned as H-7 and H-8, respectively, and was supported by the ^{2}J and ^{3}J HMBC correlation of H-8 with C-4b (δ_C 119.5) and C-6 (δ_C 146.6). A pyran moiety showed resonances at δ_H 7.42 (1H, d, J = 10.0 Hz, H-1′), 5.95 (1H, d, J = 10.0 Hz, H-2′), and 1.50 (6H, s, H-4′ and H-5′) which was placed at C-5 and C-6 due to the ^{2}J and ^{3}J correlations of H-1′ (δ_H 7.42) with C-4b (δ_C 119.5), C-5 (δ_C 114.7), C-6 (δ_C 146.6), of H-7 (δ_H 6.73) with C-5 (δ_C 114.7), C-6 (δ_C 146.6), C-8a (δ_C 135.9), and of H-8 (δ_H 7.08) with C-6 (δ_C 146.6) and C-4b (δ_C 119.5) in the HMBC spectrum. These findings, along with the presence of a low-field singlet due to proton H-4 (and H-4′′, δ_H 8.03) and the lack of protons at C-1 (and C-1′′) in the ^{1}H NMR spectral data revealed the C-1/C-1′′ carbon–carbon linkage between the two carbazole moieties as in glycoborinine (Chakravarty et al., 1999). The ^{3}J HMBC correlation of the NH proton (δ_H 9.49) with C-1 (δ_C 110.9) also supported the assigned structure. A detailed assignment of the protons, carbons, COSY, and HMBC of **WM51** is shown in Table 3.15.

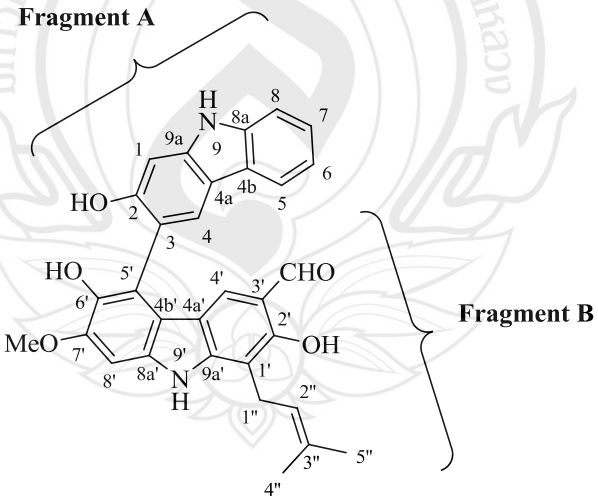
Table 3.15 ^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz), COSY, and HMBC Spectral Data of **WM51** in Acetone-d_6

Positions	**δ_H (mult., J in Hz)**	**δ_C**	**COSY (^{1}H→^{1}H)**	**HMBC (^{1}H→^{13}C)**
1	–	110.9	–	–
2	–	152.8	–	–
3	–	117.7	–	–
4	8.03 (s)	123.6	–	C-2, C-5a, 3-Me
4a	–	116.4	–	–
4b	–	119.5	–	–

Table 3.15 (continued)

Positions	δ_H (mult., *J* in Hz)	δ_C	COSY ($^1H \rightarrow {}^1H$)	HMBC ($^1H \rightarrow {}^{13}C$)
5	–	114.7	–	–
6	–	146.6	–	–
7	6.73 (d, 8.8)	113.6	H-8	C-5, C-6, C-8a
8	7.08 (d, 8.8)	111.9	H-7	C-4a, C-6
8a	–	135.9	–	–
9a	–	141.0	–	–
1′	7.42 (d, 10.0)	120.7	H-2′	C-4b, C-5, C-6, C-3′
2′	5.95 (d, 10.0)	131.4	H-1′	C-5, C-3′, C-4′, C-5′
3′	–	74.9	–	–
4′	1.50 (s)	26.9	–	C-2′, C-3′, C-5′
5′	1.50 (s)	27.0	–	C-2′, C-3′, C-4′
3-Me	2.49 (s)	16.5	–	C-4a, C-4b, C-8a, C-9a
9-NH	9.49 (br s)	–	–	–

3.2.1.16 Compound **WM52**



Compound **WM52** was obtained as a brown solid, mp 214-215 °C. It showed a pseudomolecular ion peak at $[M+H]^+$ *m/z* 507.1901 (calcd for $C_{31}H_{27}N_2O_5$, 507.1920) in the ESI-TOF-MS. The IR and UV spectra were similar to those of **WM51** suggesting the presence of a carbazole alkaloid skeleton in **WM52** as well.

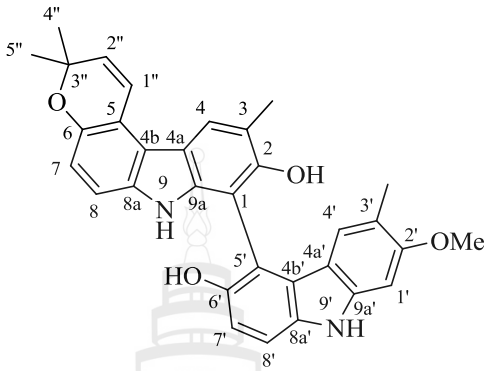
The ^{1}H, ^{13}C, NMR, and HMBC spectral data (Table 3.16) established the unsymmetrical carbazole-dimer of clausenawalline B. The ^{1}H NMR data showed two fragments (A and B) for the carbazole moieties. Fragment B was a 7-methoxyheptaphylline derivative (**WM41**), which displayed a broad singlet for the NH at δ_H 10.48 (9′-NH), a chelated hydrogen at δ_H 11.70 (2′-OH), a singlet due to a formyl proton at δ_H 9.87 (3′-CHO) and a singlet aromatic proton due to H-4′ at δ_H 8.27. The location of the formyl group was determined from HMBC correlations of 3′-CHO (δ_H 9.87) with C-2′ (δ_C 158.1), C-4′ (δ_C 124.9), and C-3′ (δ_C 116.0). The prenyl moiety was evident from ^{1}H NMR signals at δ_H 5.41 (1H, td, J = 6.8 and 1.3 Hz, H-2″), 3.67 (2H, d, J = 6.8 Hz, H-1″), 1.85 (3H, s, H-4″), and 1.70 (3H, s, H-5″). This moiety was placed at C-1′ because of the correlations of H-1″ (δ_H 3.67) with C-2′ (δ_H 158.1), C-9a′ (δ_C 146.2), and C-1′ (δ_C 110.2). The ^{1}H NMR spectrum also showed a singlet aromatic proton at δ_H 7.16 and the presence of a methoxyl group at δ_H 4.00 which were identified as H-8′ and 7′-OMe, respectively, on the basis of the ^{2}J and ^{3}J correlations of C-7′ (δ_C 148.5) with H-8′ (δ_H 7.16) and 7′-OMe (δ_H 4.00) in the HMBC spectrum.

In fragment A, the ^{1}H NMR spectral data displayed a set of four spin proton signals at δ_H 7.38 (1H, d, J = 7.8 Hz, H-5), 7.12 (1H, ddd, J = 8.2, 7.8, and 1.3 Hz, H-6), 6.97 (1H, d, J = 8.2 Hz, H-8), and 6.69 (1H, ddd, J = 8.2, 7.8, and 1.3 Hz, H-7) which were attributed to H-5, H-6, H-8, and H-7, respectively, and two singlets for the aromatic protons at δ_H 7.17 and 7.96 were assigned to H-1 and H-4, respectively. The connectivity of both fragments was confirmed by HMBC correlations. The ^{2}J and ^{3}J HMBC correlations of H-4 (δ_H 7.96) with C-3 (δ_C 117.8) and C-5′ (δ_C 118.7) confirmed the carbon–carbon linkage of carbazole fragments A and B at C-3 and C-5′, respectively, as well as the lack of proton signals for H-3 and H-5′ in the ^{1}H NMR spectrum. Detailed assignments of the protons, carbons, and HMBC of **WM52** are shown in Table 3.16.

Table 3.16 ^{1}H NMR (500 MHz), ^{13}C NMR (125 MHz), and HMBC Spectral Data of **WM52** in Acetone-d_6

Positions	**δ_H (mult., *J* in Hz)**	**δ_C**	**HMBC (^{1}H→^{13}C)**
1	7.17 (s)	98.9	C-2, C-3, C-4a, C-9a
2	–	155.3	–
3	–	117.8	–
4	7.96 (s)	123.4	C-2, C-9a, C-5′
4a	–	118.9	–
4b	–	124.7	–
5	7.38 (d, 7.8)	111.0	C-7, C-8a
6	7.12 (ddd, 8.2, 7.8, 1.2)	124.3	C-5a, C-8
7	6.69 (ddd, 8.2, 7.8, 1.2)	118.7	C-5, C-6, C-8a
8	6.97 (d, 8.2)	121.6	C-5a, C-6, C-8a
8a	–	141.1	–
9a	–	143.4	–
1′	–	110.2	–
2′	–	158.1	–
3′	–	116.0	–
4′	8.27 (s)	124.9	C-2′, C-4a′, C-9a′, 3′-CHO
4a′	–	118.6	–
4b′	–	117.7	–
5′	–	118.7	–
6′	–	139.7	–
7′	–	148.5	–
8′	7.16 (s)	94.3	C-5a′, C-7′, C-8a′
8a′	–	135.0	–
9a′	–	146.2	–
1″	3.67 (d, 6.8)	23.5	C-1′, C-2′, C-9a′, C-3″
2″	5.41 (td, 6.8, 1.3)	122.4	C-1′, C-1″, C-4″, C-5″
3″	–	133.1	–
4″	1.85 (s)	25.8	C-2″, C-3″, C-5″
5″	1.70 (s)	18.1	C-2″, C-3″, C-4″
2-OH	7.55 (br s)	–	–
2′-OH	11.70 (s)	–	C-1′, C-2′, C-3′
3′-CHO	9.87 (s)	196.7	C-2′, C-3′, C-4′
6′-OH	6.95 (br s)	–	–
7′-OMe	4.00 (s)	56.6	C-7′
9-NH	10.06 (br s)	–	C-4a, C-5a, C-8a, C-9a
9′-NH	10.48 (br s)	–	C-4a′, C-5a′, C-8a′, C-9a′

3.2.1.17 Compound **WM53**

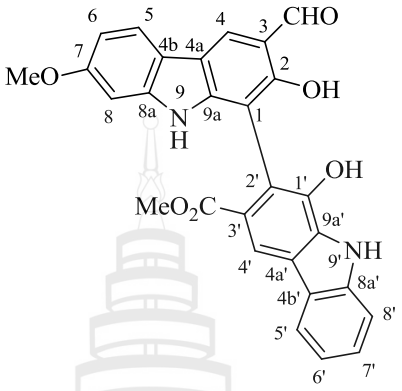


Compound **WM53** was obtained as a yellow solid, mp 196-197 °C. The ESI-TOF-MS gave a pseudomolecular ion peak at *m*/*z* 505.2121 $[M+H]^+$ (calcd for 505.2127), consistent with the molecular formula $C_{32}H_{28}N_2O_4$. The IR and UV spectra were similar to those of **WM51**. The NMR data (Table 3.17) indicated an unsymmetrical carbazole-type heterodimeric structure for compound **WM53**. One carbazole unit was similar to that of glycoborinine (Chakrawarty et al., 1999) except that in **WM53** the H-1 signal was absent in the ^{1}H NMR spectrum, indicating substitution at this position. The second unit was identified as 6-hydroxy-2-methoxy-3-methylcarbazole, which showed ^{1}H NMR signals for two ortho-coupled aromatic protons at δ_H 7.41 (1H, d, *J* = 8.5 Hz, H-8′) and 7.15 (1H, d, *J* = 8.5 Hz, H-7′), two aromatic singlets at δ_H 6.77 (1H, s, H-1′) and 6.57 (1H, s, H-4′), a NH at δ_H 7.94 (1H, br s, 9′-NH), a methoxyl group at δ_H 3.82 (3H, s, 2′-OMe), and an aryl methyl group at δ_H 1.93 (3H, s, 3′-Me). The HMBC correlations (Table 3.17) as well as an MS fragment ion at *m*/*z* 227.0933 $[M-C_{18}H_{16}NO_2+H]^+$ gave further support for this structural unit. The carbazole units were connected by a carbon−carbon linkage between C-1 and C-5′ because of the lack of signals for H-1 in the glycoborinine unit and for H-5′ of the 6-hydroxy-2-methoxy-3-methylcarbazole moiety. The detailed assignments of the protons, carbons, and HMBC correlations are summarized in Table 3.17. Thus, the structure of **WM53** was identified as clausenawalline E.

Table 3.17 ^{1}H NMR (500 MHz), ^{13}C NMR (125 MHz), and HMBC Spectral Data of **WM53** in $CDCl_3$

Positions	δ_H (mult., *J* in Hz)	δ_C	HMBC ($^{1}H \rightarrow ^{13}C$)
1	–	101.0	–
2	–	150.9	–
3	–	119.2	–
4	8.05 (s)	128.8	C-2, C-3, C-4b, C-9a
4a	–	116.8	–
4b	–	119.5	–
5	–	114.8	–
6	–	146.6	–
7	6.76 (d, 8.5)	114.0	C-5, C-6, C-8a
8	6.91 (d, 8.5)	110.4	C-4b, C-6, C-8a
8a	–	134.7	–
9a	–	138.8	–
1′	6.77 (s)	91.9	C-2′, C-3′, C-4a′, C-9a′
2′	–	157.8	–
3′	–	117.4	–
4′	6.57 (s)	122.5	C-2′, C-3′, C-4b′, C-9a′, 3′-CH_3
4a′	–	115.1	–
4b′	–	122.3	–
5′	–	108.2	–
6′	–	148.0	–
7′	7.15 (d, 8.5)	113.2	C-5′, C-6′, C-8a′
8′	7.41 (d, 8.5)	112.3	C-4b′, C-6′
8a′	–	134.4	–
9a′	–	140.3	–
1″	7.30 (d, 9.5)	120.2	C-4b, C-6, C-3″
2″	5.84 (d, 9.5)	131.2	C-5, C-3″, C-4″, C-5″
3″	–	75.1	–
4″	1.49 (s)	27.3	C-3″, C-5″
5″	1.49 (s)	27.2	C-3″, C-4″
2-OH	4.95 (br s)	–	C-3
3-Me	2.50 (s)	16.5	C-2, C-3, C-4
9-NH	7.45 (br s)	–	C-4a, C-4b, C-8a, C-9a
2′-OMe	3.82 (s)	55.4	C-2′
3′-Me	1.93 (s)	16.6	C-2′, C-3′, C-4′
6′-OH	5.25 (br s)	–	–
9′-NH	7.94 (br s)	–	C-4a′, C-4b′, C-8a′, C-9a′

3.2.1.18 Compound **WM54**



Compound **WM54** was obtained as a brown solid, mp 236-237 °C, which showed a pseudomolecular ion $[M + H]^+$ at *m*/*z* 481.1394 (calcd for 481.1400) from the ESI-TOF-MS, corresponding to a molecular formula of $C_{28}H_{20}N_2O_6$. The NMR data (Table 3.18) showed the combination of two unsymmetrical carbazole units including a 2-hydroxy-7-methoxy-9*H*-carbazole-3-carbaldehyde and a methyl 1-hydroxy-9*H*-carbazole-3-carboxylate moieties (Table 3.18). The ^{1}H NMR data of the 2-hydroxy-7-methoxy-9*H*-carbazole-3-carbaldehyde moiety displayed signals for an NH at δ_H 10.23 (1H, br s, 9-NH), a formyl proton at δ_H 10.01 (1H, s, 3-CHO), a methoxyl group at δ_H 3.80 (3H, s, 7-OMe), H-4 at δ_H 8.33 (1H, s, H-4), and an ABX aromatic proton system at δ_H 7.99 (1H, d, *J* = 8.8 Hz, H-5), 6.90 (1H, d, *J* = 2.4 Hz, H-8), and 6.85 (1H, dd, *J* = 8.8 and 2.4 Hz, H-6). The ^{1}H NMR spectrum of the methyl 1-hydroxy-9*H*-carbazole-3-carboxylate subunit showed the protons of a 1,2-disubstituted aromatic ring at δ_H 8.25 (1H, d, *J* = 8.0 Hz, H-5′), 7.65 (1H, d, *J* = 8.0 Hz, H-8′), 7.48 (1H, dd, *J* = 8.0 and 7.6 Hz, H-7′), and 7.29 (1H, dd, *J* = 8.0 and 7.6 Hz, H-6′), a singlet aromatic proton at δ_H 8.50 (1H, H-4′), and a methyl ester signal at δ 3.51 (3H, s, 3′-CO_2Me). These carbazole moieties were linked between C-1 and C-2′ due to the lack of proton signals of H-1 and H-2′ as well as the HMBC correlation of H-4′ (δ_H 8.50) with δ_C 115.6 (C-2′). The detailed assignments of the protons, carbons, COSY and HMBC correlations are summarized in Table 3.18. Thus, the structure of **WM54** was identified as clausenawalline F.

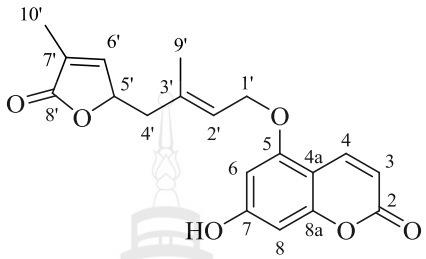
Table 3.18 ^{1}H NMR (500 MHz), ^{13}C NMR (125 MHz), COSY, and HMBC Spectral Data of **WM54** in Acetone-d_6

Positions	**δ_H (mult., *J* in Hz)**	**δ_C**	**COSY (^{1}H→^{1}H)**	**HMBC (^{1}H→^{13}C)**
1	–	96.1	–	–
2	–	159.3	–	–
3	–	106.5	–	–
4	8.33 (s)	126.7	–	C-2, C-3, C-4b, C-9a, 3-CHO
4a	–	116.4	–	–
4b	–	118.3	–	–
5	7.99 (d, 8.8)	121.3	H-6	C-4b, C-7, C-8a
6	6.85 (dd, 8.8, 2.4)	109.4	H-5	C-4b, C-8
7	–	160.0	–	–
8	6.90 (d, 2.4)	96.5	–	C-4b, C-6, C-8a
8a	–	143.5	–	–
9a	–	147.2	–	–
1′	–	160.0	–	–
2′	–	115.6	–	–
3′	–	121.1	–	–
4′	8.50 (s)	117.0	–	C-2′, C-4b′, C-9a′, 3′-$\underline{C}O_2Me$
4a′	–	123.8	–	–
4b′	–	124.1	–	–
5′	8.25 (d, 8.0)	121.3	H-6′	C-7′, C-8a′
6′	7.29 (dd, 8.0, 7.6)	120.6	H-5′, H-7′	C-4b′, C-8′
7′	7.48 (dd, 8.0, 7.6)	127.6	H-6′, H-8′	C-5′, C-8a′
8′	7.65 (d, 8.0)	112.4	H-7′	C-4b′, C-6′
8a′	–	141.5	–	–
9a′	–	142.3	–	–
3-CHO	10.01 (s)	196.7	–	C-2, C-3, C-4
7-OMe	3.80 (s)	55.8	–	C-7
9-NH	10.23 (br s)*	–	–	–
3′-$\underline{C}O_2Me$	–	172.4	–	–
3′-$CO_2\underline{Me}$	3.51 (s)	51.6	–	3′-$\underline{C}O_2Me$
9′-NH	10.74 (br s)*	–	–	–

Note. *The chemical shift maybe interchangeable

3.2.2 Coumarins

3.2.2.1 Compound **WM57**

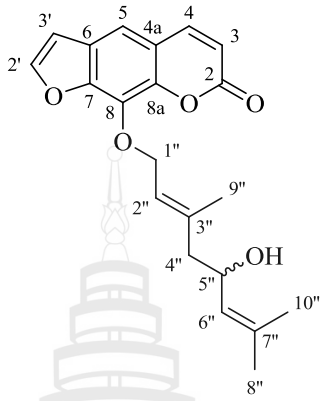


Compound **WM57** was isolated as a yellow viscous oil with a molecular formula of $C_{19}H_{18}O_6$ on the basis of HR-EI-MS. The ^{1}H NMR spectral data of **WM57** revealed an α,β-unsaturated lactone at δ_H 6.12 (1H, d, *J* = 9.6 Hz, H-3) and 7.96 (1H, d, *J* = 9.6 Hz, H-4) and two meta-coupling aromatic protons at δ_H 6.48 (1H, d, *J* = 1.6 Hz, H-6) and 6.26 (1H, d, *J* = 1.6 Hz, H-8). These results implied that this molecule is a 5,7-oxygenated coumarin nucleus. Moreover, the ^{1}H NMR spectrum also showed signals of –OCH_2CH=C– unit at δ_H 4.66 (2H, m, H-1′) and 5.53 (1H, t, *J* = 5.6 Hz, H-2′) and an α,β-unsaturated γ-lactone moiety at δ_H 2.35 (1H, dd, *J* = 17.0 and 7.2 Hz, H-4a′), 2.61 (1H, dd, *J* = 17.0, 5.2 Hz, H-4b′), 5.11 (1H, m, H-5′), 7.09 (1H, br t, H-6′), 1.92 (3H, br s, H-10′). The side chain unit was also supported by COSY and HMBC experiments (Table 3.19) and located at C-5 due to the ^2J and ^3J HMBC correlations of the H-4 (δ_H 7.96), H-6 (δ_H 6.48) and H-1′ (δ_H 4.66) with C-5 (δ_H 156.1). The structure of clausenalansimin B, therefore, was assigned to **WM57**. The detailed assignments of the protons, carbons, COSY, and HMBC correlations are summarized in Table 3.19.

Table 3.19 ^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz), COSY, and HMBC Spectral Data of **WM54** in $CDCl_3$

Positions	δ_H (mult., *J* in Hz)	δ_C	COSY ($^1H \rightarrow {}^1H$)	HMBC ($^1H \rightarrow {}^{13}C$)
2	–	162.1	–	–
3	6.12 (d, 9.6)	110.3	H-4	C-4a
4	7.96 (d, 9.6)	139.2	H-3	C-2, C-5, C-8a
4a	–	103.8	–	–
5	–	156.1	–	–
6	6.48 (d, 1.6)	96.4	H-8	C-4a, C-5
7	–	161.0	–	–
8	6.26 (d, 1.6)	96.9	H-6	C-4a
8a	–	156.6	–	–
1′	4.66 (m)	66.0	H-2′	C-5, C-3′
2′	5.53 (t, 5.6)	125.1	H-1′, H-9′	C-4′, C-9′
3′	–	133.4	–	–
4′	2.35 (dd, 17.0, 7.2) 2.61 (dd, 17.0, 5.2)	42.6	H-5′	C-2′, C-6′, C-9′
5′	5.11 (m)	79.6	H-4′	–
6′	7.09 (br t)	148.9	H-10′	C-4′, C-7′, C-8′, C-10′
7′	–	130.4	–	–
8′	–	177.0	–	–
9′	1.74 (s)	17.6	H-2′	C-2′, C-4′
10′	1.92 (br s)	10.6	H-6′	C-6′, C-8′

3.2.2.1 Compound **WM62**



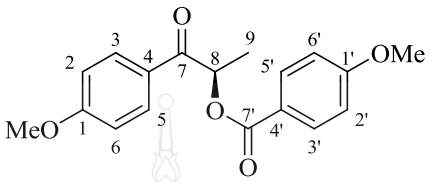
Compound **WM62** was isolated as a yellow viscous oil. Its molecular formula was established as $C_{21}H_{22}O_5$ by ESI-TOF-MS. The UV-Vis spectrum showed an absorption band of a conjugated furanocoumarin at 204-300 nm (Ito et al., 1998), whereas IR spectroscopic data displayed absorption bands of hydroxy and carbonyl functionalities at 3442 and 1722 cm^{-1}, respectively. The ^1H NMR spectrum (Table 3.20) of **WM62** showed the common signals of furanocoumarin skeleton at δ_H 6.36 (1H, d, *J* = 9.6 Hz, H-3), 7.36 (1H, d, *J* = 2.0 Hz, H-2′), 6.81 (1H, s, H-5), 7.68 (1H, d, *J* = 2.0 Hz, H-3′) and 7.76 (1H, d, *J* = 9.6 Hz, H-4). In addition, ^1H NMR signals were observed δ_H 5.68 (1H, dt, *J* = 7.2 and 1.2 Hz, H-2″), 5.11 (1H, m, H-6″), 5.04 (2H, d, *J* = 7.2 Hz, H-1″), 4.41 (1H, m, H-5″), 2.17 (2H, m, H-4″), 1.76 (3H, s, H-9″), 1.68 (3H, s, H-8″) 1.65 (3H, s, H-10″) and could be identified as the 5-hydroxy-3,7-dimethylocta-2,7-dienyloxy moiety. This moiety was also confirmed by COSY and HMBC correlations (Table 21) and located at C-8 because the H-1″ (δ_H 5.04) showed ^3J HMBC correlation with the carbon at C-8 (δ_C 131.5). Therefore, clausenalansimin A was deduced to be **WM62**. The detailed assignments of the protons, carbons, COSY, and HMBC correlations are summarized in Table 3.20.

Table 3.20 ^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz), COSY, and HMBC Spectral Data of **WM62** in $CDCl_3$

Positions	δ_H (mult., *J* in Hz)	δ_C	COSY ($^1H \rightarrow {}^1H$)	HMBC ($^1H \rightarrow {}^{13}C$)
2	–	160.4	–	–
3	6.36 (d, 9.6)	114.7	H-4	–
4	7.76 (d, 9.6)	144.3	H-3	C-5
4a	–	116.5	–	–
5	7.36 (s)	113.4	–	C-4a, C-7, C-8a, C-3′
6	–	125.8	–	–
7	–	148.6	–	–
8	–	131.5	–	–
8a	–	143.8	–	–
2′	7.68 (d, 2.0)	146.7	H-3′	C-7
3′	6.81 (d, 2.0)	106.8	H-2′	C-6
1″	5.04 (d, 7.2)	69.8	H-2″	C-8
2″	5.68 (td, 7.2, 1.2)	122.9	H-1′, H-9′	C-3″, C-4″, C-9″
3″	–	139.6	–	–
4″	2.17 (m)	47.8	H-5″	C-2′, C-6′, C-9′
5″	4.41 (m)	66.2	H-4″, H-6″	C–8″
6″	5.11 (m)	127.2	–	–
7″	–	135.1	–	–
8″	1.68 (s)	16.9	–	C–6″, C-7″, C-10″
9″	1.76 (s)	25.7	H-2′	C-2′, C-4′
10″	1.65 (s)	18.1	–	C–6″, C-7″, C-8″

3.2.3 Phenylpropanoid Derivative

3.2.3.1 Compound **WM66**



Compound **WM66** was obtained as a white solid (mp 114 - 117 °C). It displayed a pseudomolecular ion peak at $[M+Na]^+$ *m/z* 337.1046 (calcd for 337.1052) in ESI-TOF-MS, corresponding to the molecular formula $C_{18}H_{18}O_5$. The UV spectrum displayed maximal absorption bands at λ_{max} 201, 213, 267, and 272 nm, while the IR spectrum revealed the absorption bands of aryl ester (1689 cm^{-1}) and aryl ketone (1712 cm^{-1}) functional groups. The ^1H and ^{13}C NMR spectra of **WM66** displayed the signals of a *p*-methoxybenzoyl unit at δ_H 7.98 (2H, d, *J* = 8.4 Hz, H-3′ and H-5′)/δ_C 131.9, δ_H 6.95 (2H, d, *J* = 8.4 Hz, H-2′ and H-6′)/δ_C 113.6, δ_H 3.87 (3H, s, 1′-OMe)/δ_C 55.5, δ_C 122.0 (C-4′) and δ_C 163.6 (C-1′) (Sy & Brown, 1998). The correlations between H-3′/H-5′ (δ_H 7.98) with C-1′ (δ_C 163.6) and C-7′ (δ_C 165.9), and 1′-OMe (δ_H 3.87) with C-1′ (δ_C 163.6) in the HMBC spectrum were also supported the *p*-methoxybenzoyl unit. Using a combination of COSY, HMQC and HMBC analyses, the signal of a *p*-methoxyphenyl-1-oxopropanone unit (phenylpropanoids derivative) was also observed in the ^1H and ^{13}C NMR spectra at δ_H 7.80 (2H, d, *J* = 8.4 Hz, H-3 and H-5)/δ_C 130.9, δ_H 6.93 (2H, d, *J* = 8.4 Hz, H-2 and H-6)/δ_C 114.0, δ_H 6.15 (1H, q, *J* = 6.2 Hz, H-8)/δ_C 71.3, δ_H 3.86 (3H, s, 1-OMe)/δ_C 55.4, δ_H 1.63 (3H, d, *J* = 6.2 Hz, H-9)/δ_C 17.3, δ_C 195.3 (C-7), δ_C 163.8 (C-1) and δ_C 127.4 (C-4). The important ^2J and ^3J HMBC correlations of the *p*-methoxyphenyl-1-propanone unit are summarized as: H-3/H-5 (δ_H 7.80) and H-9 (δ_H 1.63) with aryl ketone C-7 (δ_C 195.3), H-2/H-6 (δ_H 6.93) with C-4 (δ_C 127.4), and 1-OMe (δ_H 3.86) with C-1 (δ_C 163.8). Finally, the *p*-methoxyphenyl-1-propanone and *p*-methoxybenzoyl units were linked to each other via ester-linkage at C-8 and C-7′, due

to H-8 (δ_H 6.15) and H-3′/H-5′ (δ_H 7.98) displaying cross peak ^3J HMBC correlations with aryl ester C-7′ (δ_C 165.9). The absolute configuration of **WM66** ($[\alpha]_D^{27}$ = +60.3, *c* = 0.014, $CHCl_3$) at C-8 was determined as an R configuration by comparison with specific rotation of (2*S*)-hydroxy-1-phenyl-propanone ($[\alpha]_D^{20}$ = –86, *c* = 2, $CHCl_3$) (Kihumbu et al., 2002) and (2*R*)-hydroxy-1-phenyl-propanone ($[\alpha]_D^{20}$ = +70, *c* = 1.7, $CHCl_3$) (Demir et al., 2001). Thus, the structure of **WM66** was identified as harmandianone. Detailed assignments of the protons, carbons, COSY and HMBC correlations of **WM66** are summarized in Table 3.21.

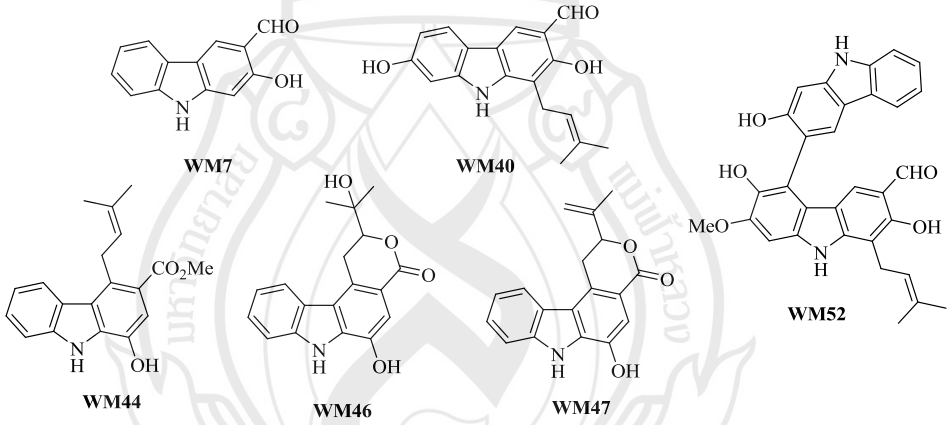
Table 3.21 ^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz), COSY, and HMBC Spectral Data of **WM66** in $CDCl_3$

Positions	**δ_H (mult., *J* in Hz)**	**δ_C**	**COSY (^{1}H→^{1}H)**	**HMBC (^{1}H→^{13}C)**
1	–	163.8	–	–
2/6	6.93 (d, 8.4)	114.0	H-3/ H-5	C-1, C-2 or C-6, C-4
3/5	7.80 (d, 8.4)	130.9	H-2/ H-6	C-1, C-3 or C-5, C-7
4	–	127.4	–	–
7	–	195.3	–	–
8	6.15 (q, 6.2)	71.3	H-9	C-9, C-7′
9	1.63 (d, 6.2)	17.3	H-8	C-7, C-8
1′	–	163.6	–	–
2′/6′	6.95 (d, 8.4)	113.6	H-3′/ H-5′	C-1′, C-4′
3′/5′	7.98 (d, 8.4)	131.9	H-2′/ H-6′	C-1′, C-7′
4′	–	122.0	–	–
7′	–	165.9	–	–
1-OMe	3.86 (s)	55.4	–	C-1
1′-OMe	3.87 (s)	55.5	–	C-1′

3.3 Biological Activities

Some isolated compounds were selected for the evaluation of antibacterial activity against Gram-positive bacteria (*Staphylococcus aureus* TISTR 1466 and methicillin-resistant *S. aureus* SK1) and Gram-negative bacteria (*Escherichia coli* TISTR 780 and *Salmonella typhimurium* TISTR 292), as well as the cytotoxicity against three human cancer cell lines, oral cancer (KB), breast cancer (MCF-7), and small-cell lung cancer (NCI-H187).

3.3.1 Antibacterial Activity



All compounds, except compound **WM67**, were evaluated for their antibacterial activities against Gram-positive bacteria (*S. aureus* TISTR1466 and MRSA SK1) and Gram-negative bacteria (*E. coli* TISTR 780 and *S. typhimurium* TISTR 292) as summarized in Table 3.22. All tested compounds showed weak (64-128 µg/mL) or no activity against Gram-negative bacteria (*E. coli* TISTR 780 and *S. typhimuriun* TISTR 292), except compound **WM7** showed moderate activity against *S. typhimurium* TISTR 292 with an MIC value of 32 µg/mL. However, compound **WM47** was found to be potent antibacterial activity against MRSA SK1 with MIC value of 0.25 µg/mL which was higher than a standard drug, vancomycin (MIC value = 1 µg/mL) while compounds **WM40**, **WM44**, **WM46**, and **WM52** showed good

antibacterial activity against MRSA SK1 with MIC values of 4 and 8 µg/mL. Also, compound **WM44** displayed strong antibacterial activity against *Staph. aureus* TISTR 1466 with an MIC value of 4 µg/mL (Table 3.22).

Table 3.22 Antibacterial Activity of Compounds **WM1-WM66** and **WM68-WM74**

Compounds	Minimum Inhibitory Concentration (µg/mL)			
	Gram-positive		Gram-negative	
	Staph. aureus	**MRSA SK1**	***E. coli***	***S. typhimurium***
WM1	Inactive	64	128	128
WM2	Inactive	Inactive	128	128
WM3	64	64	128	128
WM4	Inactive	128	128	128
WM5	64	64	128	128
WM6	Inactive	Inactive	128	128
WM7	Inactive	64	128	32
WM8	Inactive	128	Inactive	128
WM9	Inactive	Inactive	128	128
WM10	Inactive	Inactive	128	128
WM11	Inactive	16	128	64
WM12	Inactive	128	Inactive	128
WM13	Inactive	Inactive	Inactive	128
WM14	Inactive	32	Inactive	128
WM15	Inactive	16	63	128
WM16	Inactive	32	128	128
WM17	Inactive	128	128	128
WM18	Inactive	128	Inactive	129
WM19	Inactive	Inactive	Inactive	128
WM20	Inactive	128	Inactive	Inactive
WM21	Inactive	Inactive	Inactive	128
WM22	Inactive	Inactive	128	128
WM23	Inactive	Inactive	128	128
WM24	Inactive	Inactive	128	128
WM25	128	128	64	64
WM26	128	128	128	128
WM27	Inactive	128	128	128
WM28	Inactive	Inactive	128	Inactive
WM29	128	128	128	128
WM30	Inactive	Inactive	128	128
WM31	Inactive	Inactive	Inactive	128
WM32	128	128	128	128
WM33	Inactive	128	Inactive	128

Table 3.22 (Continued)

Compounds	Minimum Inhibitory Concentration (µg/mL)			
	Gram-positive		Gram-negative	
	Staph. aureus	**MRSA SK1**	***E. coli***	***S. typhimurium***
WM34	128	32	128	128
WM35	Inactive	Inactive	128	128
WM36	Inactive	Inactive	128	128
WM37	128	128	Inactive	128
WM38	32	32	64	128
WM39	Inactive	128	Inactive	128
WM40	8	4	64	64
WM41	Inactive	Inactive	128	128
WM42	Inactive	Inactive	128	128
WM43	Inactive	64	128	128
WM44	4	4	128	64
WM45	Inactive	Inactive	128	128
WM46	32	8	128	128
WM47	Inactive	0.25	Inactive	128
WM48	Inactive	32	Inactive	128
WM49	Inactive	64	Inactive	128
WM50	128	32	128	128
WM51	62	128	Inactive	128
WM52	8	8	128	128
WM53	64	64	128	Inactive
WM54	16	32	128	128
WM55	Inactive	Inactive	128	128
WM56	Inactive	Inactive	128	128
WM57	Inactive	Inactive	128	128
WM58	Inactive	Inactive	128	128
WM59	Inactive	128	128	128
WM60	Inactive	128	128	128
WM61	Inactive	Inactive	128	128
WM62	128	128	128	128
WM63	128	Inactive	128	128
WM64	Inactive	Inactive	128	128
WM65	Inactive	Inactive	128	128
WM66	Inactive	Inactive	128	128
WM68	Inactive	Inactive	128	128
WM69	Inactive	Inactive	128	128
WM70	128	128	128	128
WM71	Inactive	Inactive	Inactive	128
WM72	Inactive	Inactive	129	128
WM73	Inactive	Inactive	128	128

Table 3.22 (Continued)

Compounds	Minimum Inhibitory Concentration (µg/mL)			
	Gram-positive		Gram-negative	
	Staph. aureus	**MRSA SK1**	***E. coli***	***S. typhimurium***
WM73	Inactive	Inactive	128	128
WM74	Inactive	Inactive	128	128
Vancomycin	0.25	1	Not Test	Not Test
Gentamycin	Not Test	Not Test	0.25	0.25

Note. *Inactive > 128 µg/mL

3.3.2 Cytotoxic Activity

Compounds **WM1-WM14**, **WM16-WM18**, **WM21**, **WM22**, **WM28**, **WM30-WM32**, **WM35**, **WM36**, **WM39**, **WM40-WM42**, **WM51**, **WM54**, **WM56-WM65**, **WM71**, and **WM73** were evaluated for their cytotoxicity against oral cancer (KB), breast cancer (MCF-7), and small cell lung cancer (NCI-H187) cell lines (Table 3.23). Compounds **WM6**, **WM7**, **WM12**, **WM13**, **WM21**, **WM42** and **WM56** had no cytotoxicity against all three cancer cell lines. Compounds **WM14**, **WM16**, **WM17**, **WM32**, and **WM35** exhibited selective cytotoxicity against MCF-7 cell line with IC_{50} values of 7.09, 3.24, 2.47, 9.11, 10.13 µM, respectively, which were higher than positive controls (doxorubicin and tamoxifen). With respect to cytotoxicity against the MCF-7 cell line, compounds **WM2-WM5**, **WM8-WM11**, **WM18**, **WM22**, **WM28**, **WM30**, **WM31**, **WM36**, **WM39**, **WM41**, **WM51**, **WM54**, **WM57-WM59**, **WM61**, **WM62**, **WM64**, **WM65**, and **WM71** exhibited weakly activity (IC_{50} 16.21-171.08 µM). Compounds **WM1-WM5**, **WM8**, **WM9**, **WM14-WM18**, **WM22**, **WM28**, **WM30-WM32**, **WM35**, **WM36**, **WM39-WM41**, **WM51**, **WM54**, **WM57-WM63**, **WM65**, **WM71**, and **WM73** showed cytotoxicity against the NCI-H187 cell line with IC_{50} values ranging from 3.90 to 200.05 µM. Compounds **WM1-WM5**, **WM8**, **WM9**, **WM11**, **WM14**, **WM16**, **WM17**, **WM18**, **WM22**, **WM28**, **WM30-WM32**, **WM35**, **WM36**, **WM39**, **WM40**, **WM51**, **WM54**, **WM57-WM60**, **WM62**, **WM63**, **WM65**, **WM71**, and **WM73** were also weakly active cytotoxicity against KB cell line (IC_{50} 8.69 - 183.92 µM).

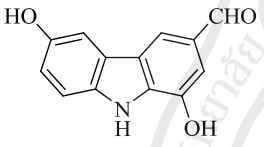
Table 3.23 Cytotoxicity of Compounds **WM1-WM14**, **WM16-WM18**, **WM21**, **WM22**, **WM28**, **WM30-WM32**, **WM35**, **WM36**, **WM39**, **WM40-WM42**, **WM51**, **WM54**, **WM56-WM65**, **WM71**, and **WM73**

Compounds	Cytotoxicity (IC_{50}, µM)		
	KB[a]	MCF-7[b]	NCI-H187[c]
WM1	24.00	Inactive	66.82
WM2	59.73	170.13	95.87
WM3	59.43	73.13	44.45
WM4	85.96	16.71	47.64
WM5	73.69	64.02	38.92
WM6	Inactive	Inactive	Inactive
WM7	Inactive	Inactive	Inactive
WM8	103.16	111.11	18.27
WM9	91.88	21.46	27.42
WM10	Inactive	51.14	Inactive
WM11	127.64	59.42	Inactive
WM12	Inactive	Inactive	Inactive
WM13	Inactive	Inactive	Inactive
WM14	55.07	7.09	4.17
WM16	28.38	3.24	32.12
WM17	44.53	2.47	18.53
WM18	181.49	69.17	45.93
WM21	Inactive	Inactive	Inactive
WM22	37.53	16.21	11.93
WM28	49.56	66.18	60.89
WM30	90.44	39.11	42.66
WM31	48.35	75.76	63.59
WM32	23.63	9.11	40.83
WM35	125.64	10.13	96.71
WM36	94.30	171.08	20.25
WM39	8.75	28.82	58.97
WM40	107.22	Inactive	20.24
WM41	Inactive	53.95	42.36
WM42	Inactive	Inactive	Inactive
WM51	12.19	45.74	19.73
WM54	10.28	62.35	2.53
WM56	Inactive	Inactive	Inactive
WM57	79.82	72.22	89.65
WM58	133.51	59.01	200.05
WM59	35.56	139.33	143.89
WM60	66.54	Inactive	60.84
WM61	Inactive	146.78	155.95
WM62	62.40	87.63	81.44

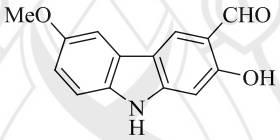
Table 3.23 (Continue)

Compounds	Cytotoxicity (IC_{50}, µM)		
	KB[a]	**MCF-7**[b]	**NCI-H187**[c]
WM63	48.99	Inactive	71.67
WM64	Inactive	90.45	Inactive
WM65	161.71	45.38	100.88
WM71	183.92	28.54	108.84
WM73	150.32	Inactive	186.67
Doxorubicin	1.70	16.88	0.12
Tamoxifen	Not Test	13.30	Not Test
Ellipticine	5.21	Not Test	3.14

Note. [a]KB = Oral cavity cancer; [b]MCF-7 = Breast cancer; [c]NCI-H187 = Small cell lung cancer



WM14



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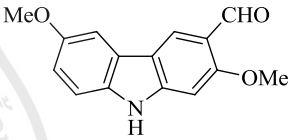

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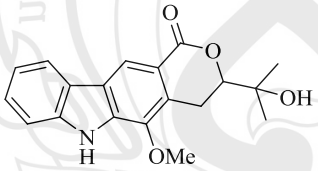

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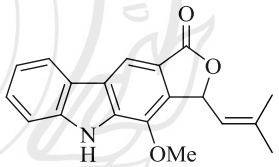
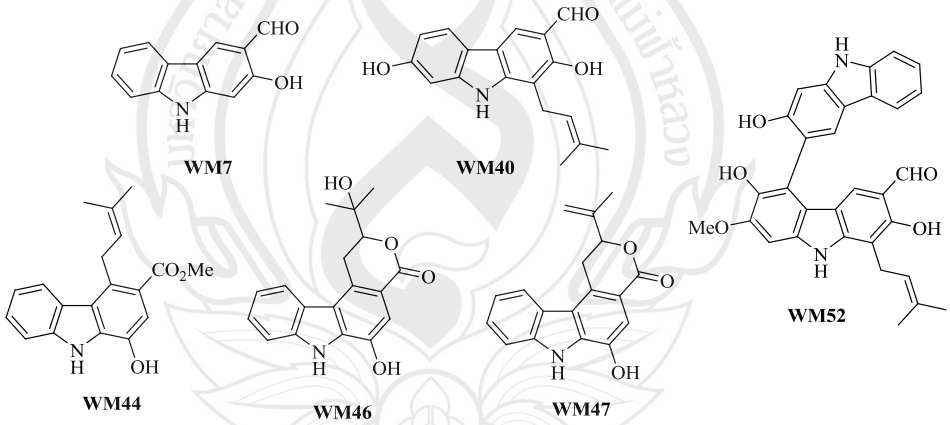


WM35

CHAPTER 4

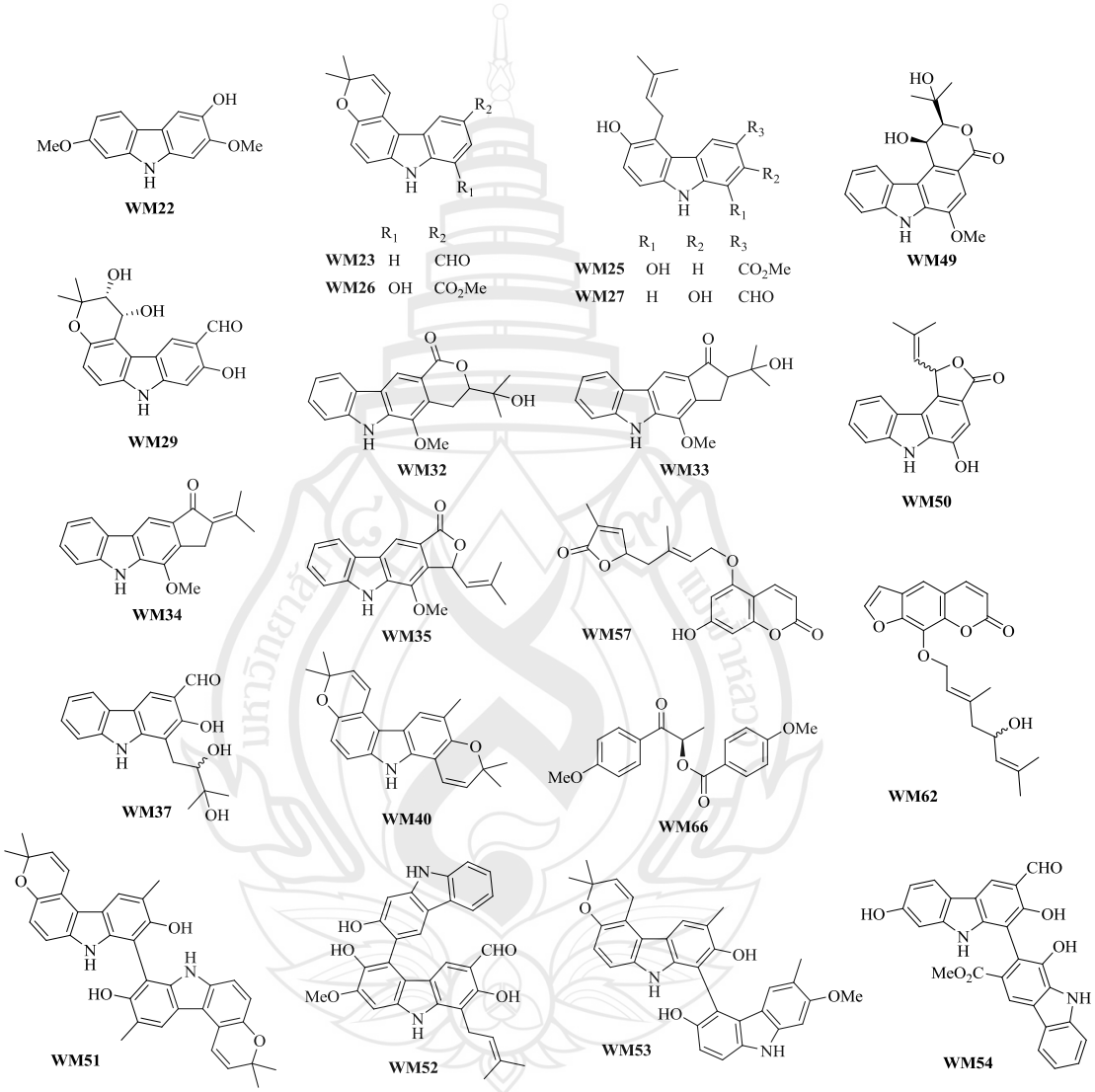
CONCLUSION

In conclusion, the chemical investigation of *Clausena* plants from the Northern part of Thailand; *C. harmandiana*, *C. lansium*, and *C. wallichii* led to the isolation and identification of twenty one new compounds (**WM22**, **WM23**, **WM25-WM27**, **WM29**, **WM32-WM35**, **WM37**, **WM42**, **WM56-WM54**, **WM57**, **WM62**, and **WM66**) and fifty-three known compounds (**WM1-WM21**, **WM24**, **WM28**, **WM30**, **WM32**, **WM36**, **WM38**, **WM39-WM41**, **WM43-WM47**, and **WM67-WM74**).

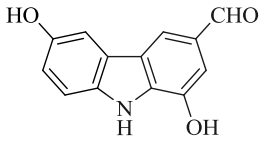


Their structures were elucidated by intensive spectroscopic analyses. All compounds, except compound **WM67**, were evaluated for their antibacterial activity. All tested compounds showed weak (MIC 64 - 128 µg/mL) or no activity against Gram-negative bacteria (*E. coli* TISTR 780 and *S. typhimuriun* TISTR 292), except compound **WM7** showed moderate activity against *S. typhimurium* TISTR 292 with an MIC value of 32 µg/mL. In addition, compound **WM47** showed significant potent antibacterial activity against MRSA SK1 with MIC value of 0.25 µg/mL, along with

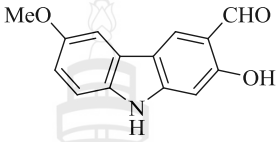
good antibacterial activity against MRSA SK1 (MIC, 4 and 8 µg/mL) from compounds **WM40**, **WM44**, **WM46**, and **WM52**. However, only compound **WM44** was displayed strong antibacterial activity against *Staph. aureus* TISTR 1466 with MIC value of 4 µg/mL.



Some of isolated compounds were further evaluated for their cytotoxicity against KB, MCF-7, and NCI-H187 cell lines. Compounds **WM14**, **WM16**, **WM17**, **WM32**, and **WM35** exhibited selective cytotoxicity against MCF-7 cell line with IC_{50} values of 7.09, 3.24, 2.47, 9.11, 10.13 µM, respectively.



WM14



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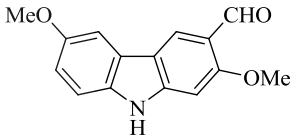

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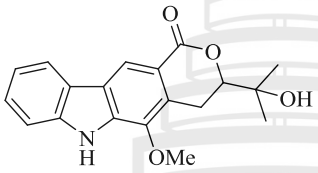
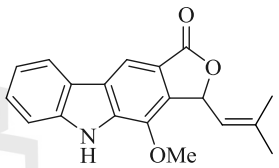


WM32



WM35

The carbazole alkaloids, which contained a methyl, formyl or methylester group at position C-3 of the carbazole skeleton are found as majority in the genera of *Clausena*. It is implied that the rich source of carbazole alkaloids and this might be a useful chemotaxonomic marker of this genus.

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APPENDIX

APPENDIX

NMR Spectra of Isolated Compounds from *C. harmandiana*, *C. lansium*, and *C. wallichii*

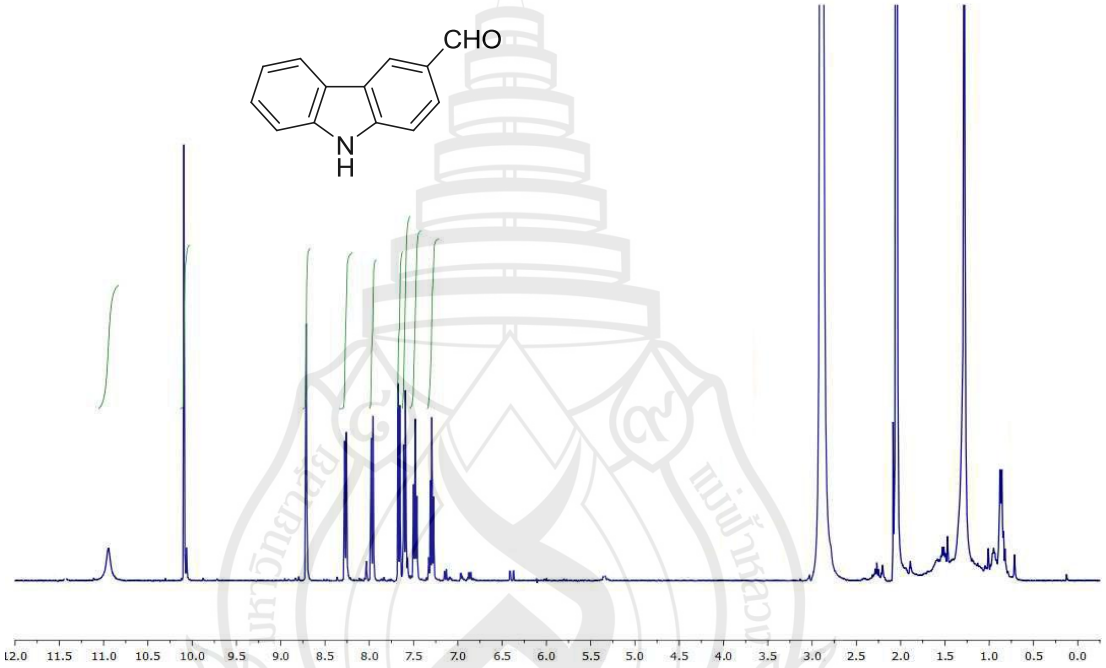

Figure A1 ^{1}H NMR Spectrum of **WM1** in Acetone-d_6 (400 MHz)

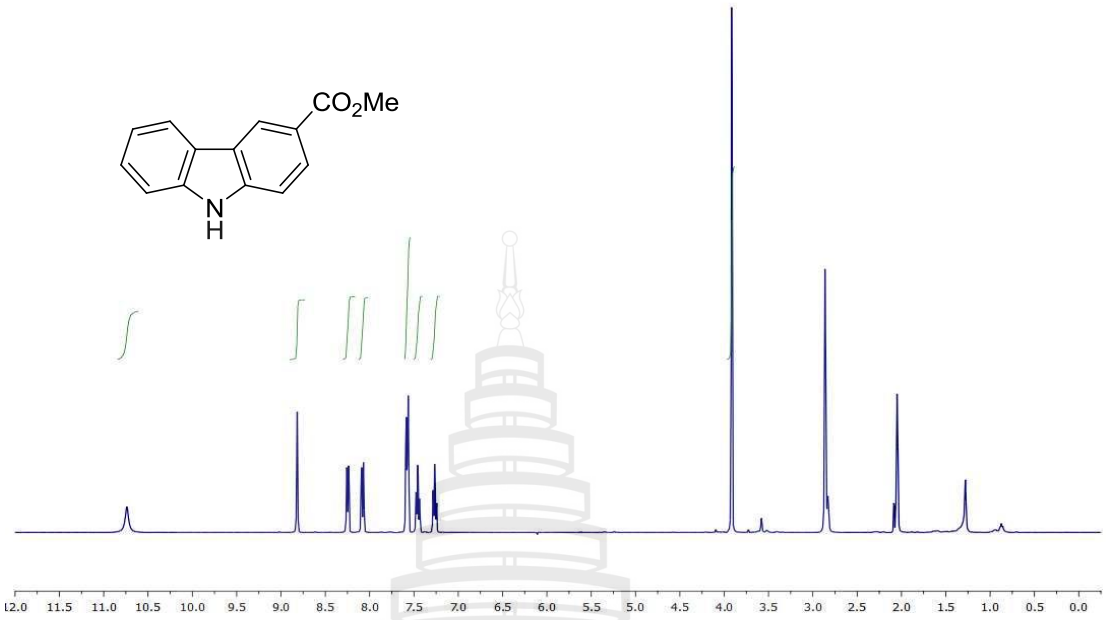

Figure A2 ^{1}H NMR Spectrum of **WM2** in Acetone-d_6 (400 MHz)

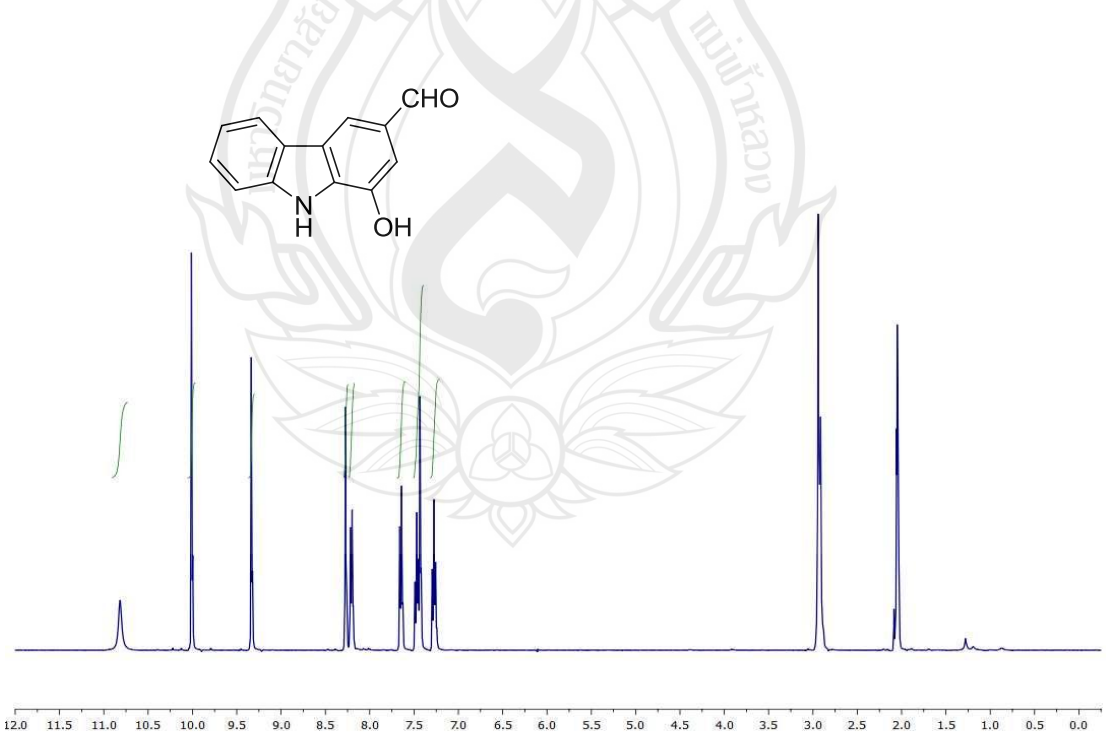

Figure A3 ^{1}H NMR Spectrum of **WM3** in Acetone-d_6 (400 MHz)

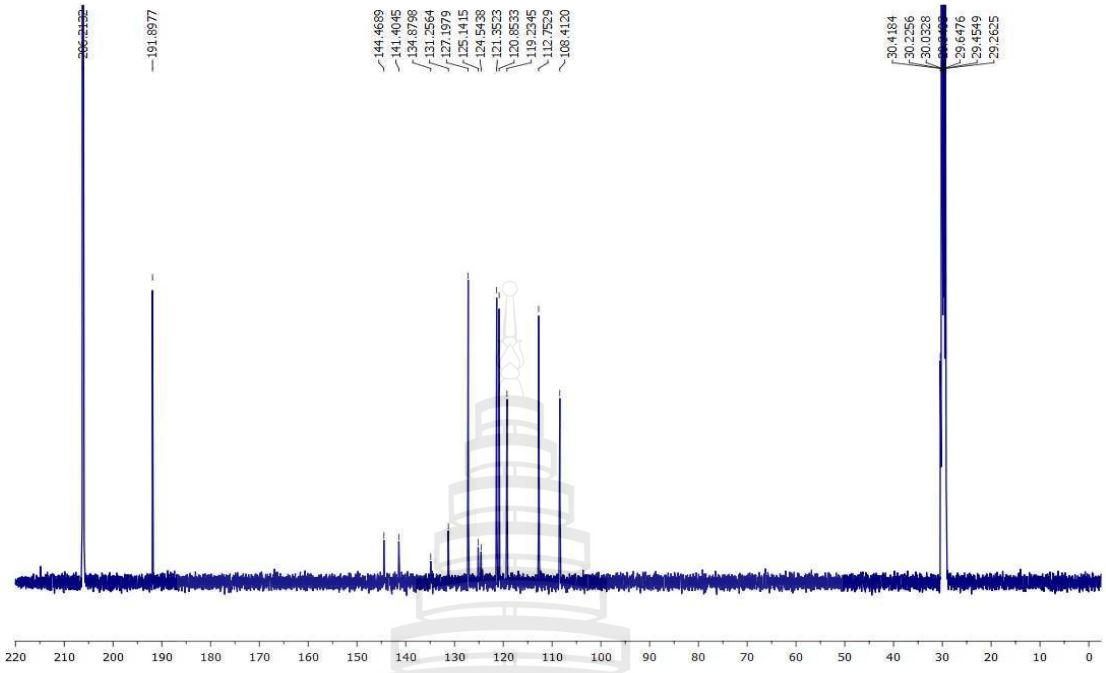

Figure A4 ^{13}C NMR Spectrum of **WM3** in Acetone-d_6 (100 MHz)

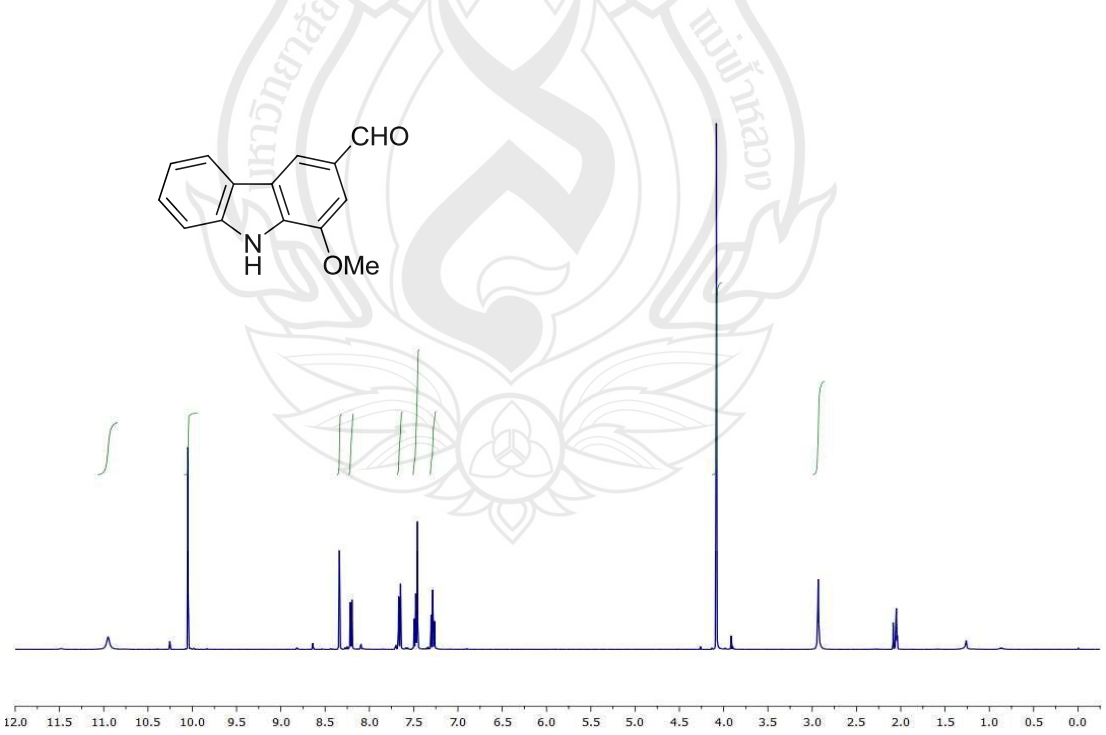

Figure A5 ^{1}H NMR Spectrum of **WM4** in Acetone-d_6 (400 MHz)

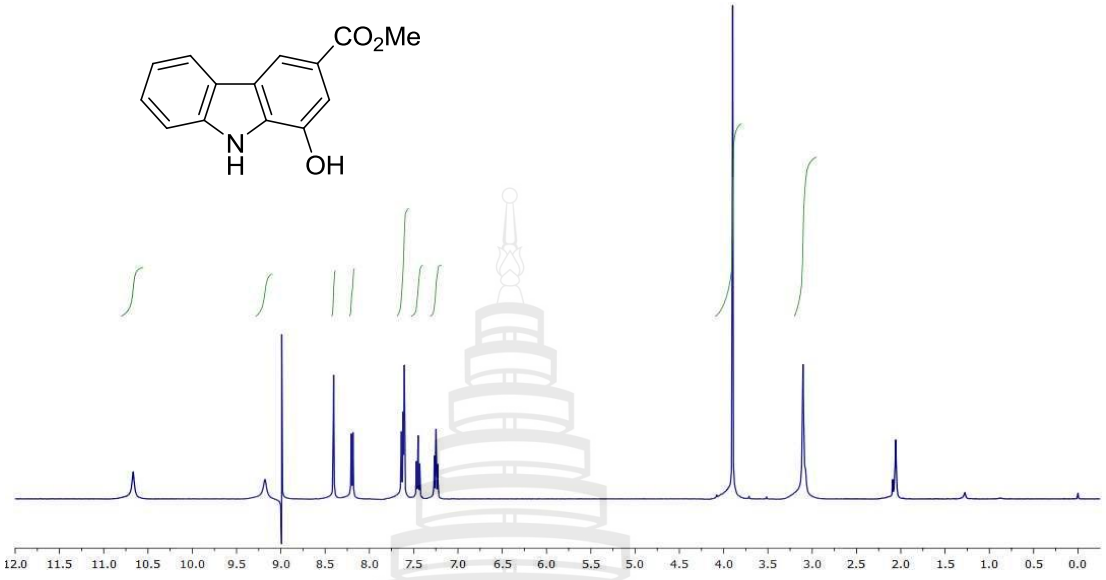

Figure A6 ^{1}H NMR Spectrum of **WM5** in Acetone-d_6 (400 MHz)

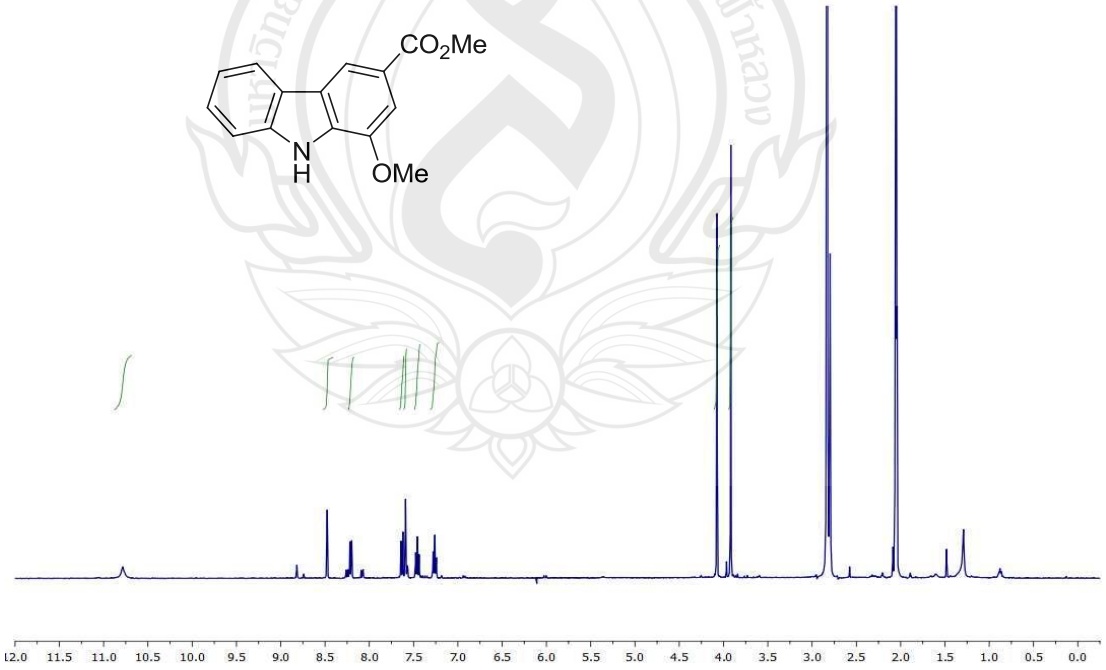

Figure A7 ^{1}H NMR Spectrum of **WM6** in Acetone-d_6 (400 MHz)

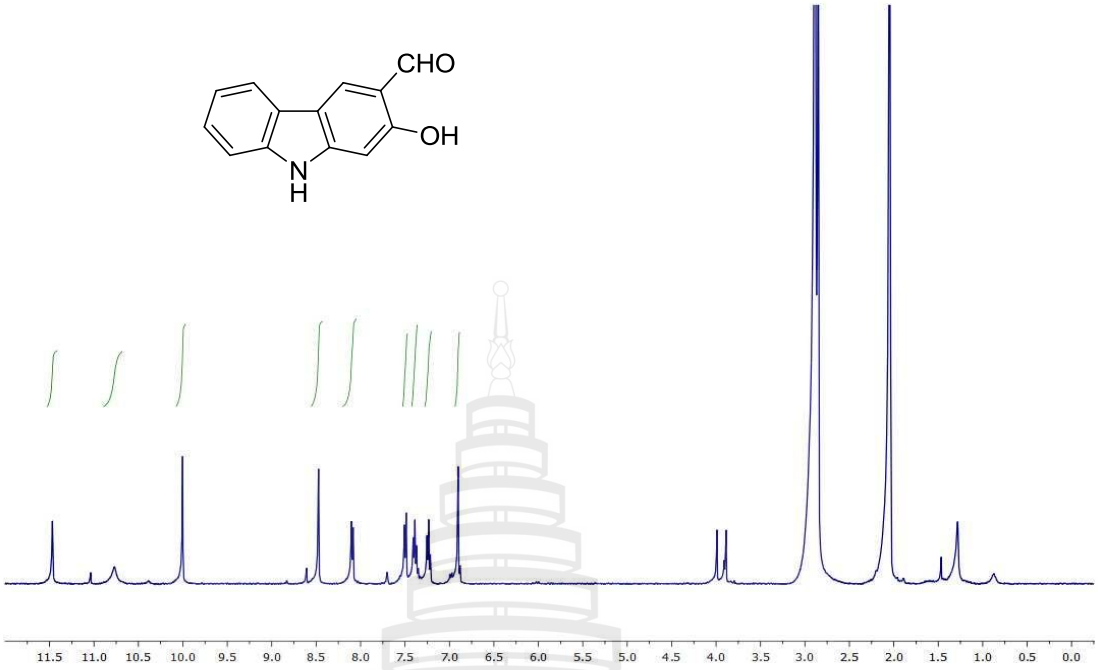

Figure A8 ^{1}H NMR Spectrum of **WM7** in Acetone-d_6 (400 MHz)

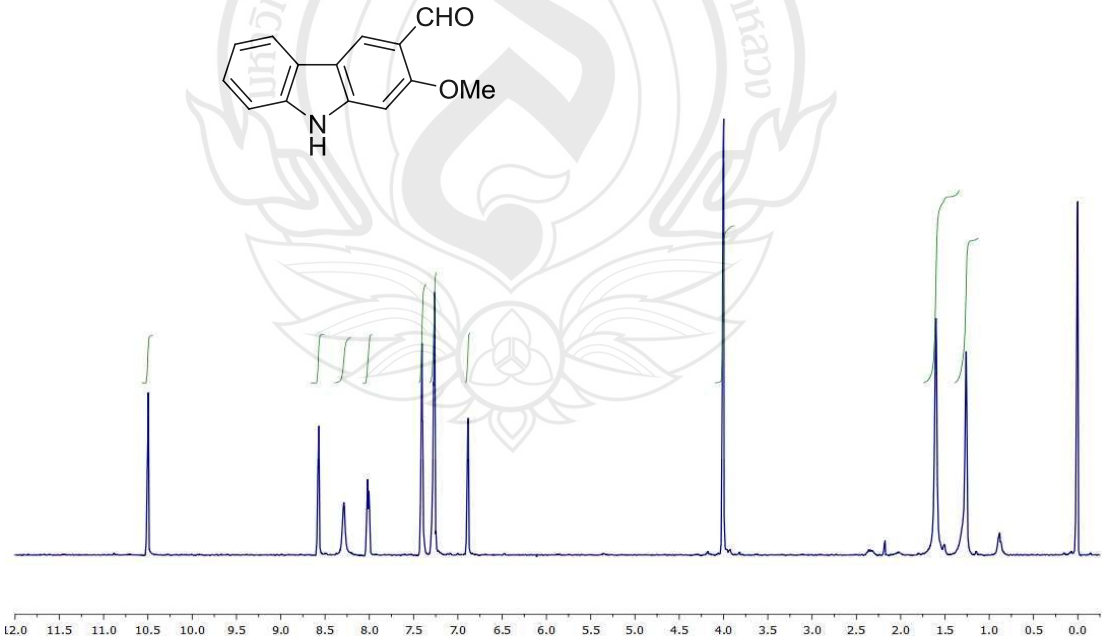

Figure A9 ^{1}H NMR Spectrum of **WM8** in $CDCl_3$ (400 MHz)

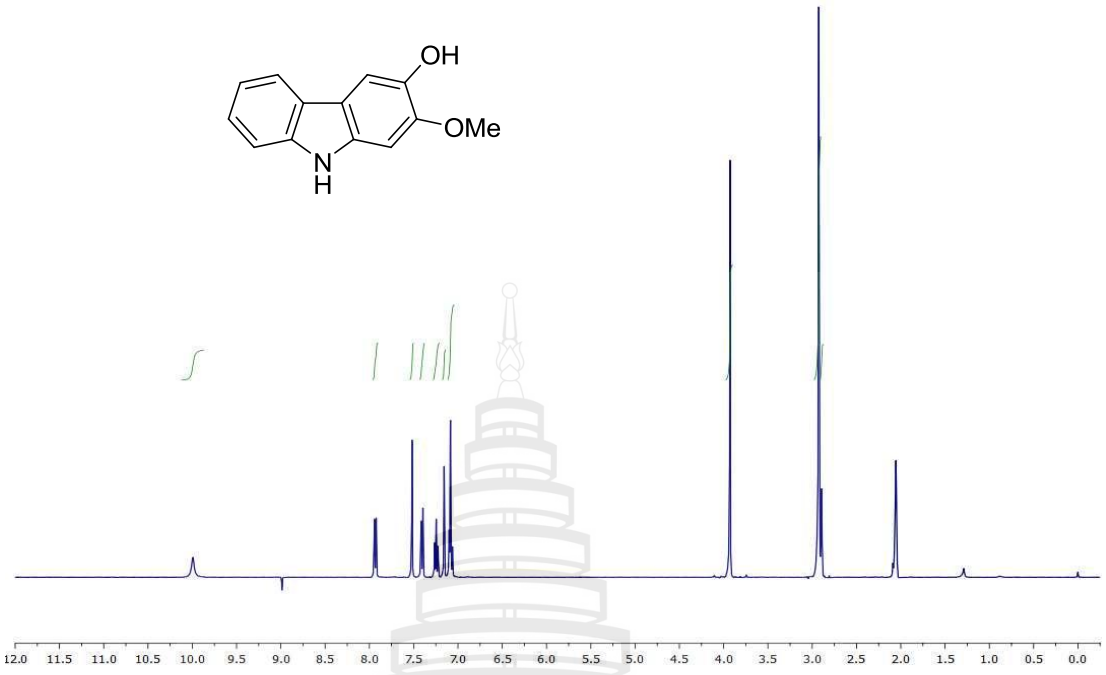

Figure A10 ^{1}H NMR Spectrum of **WM9** in Acetone-d_6 (400 MHz)

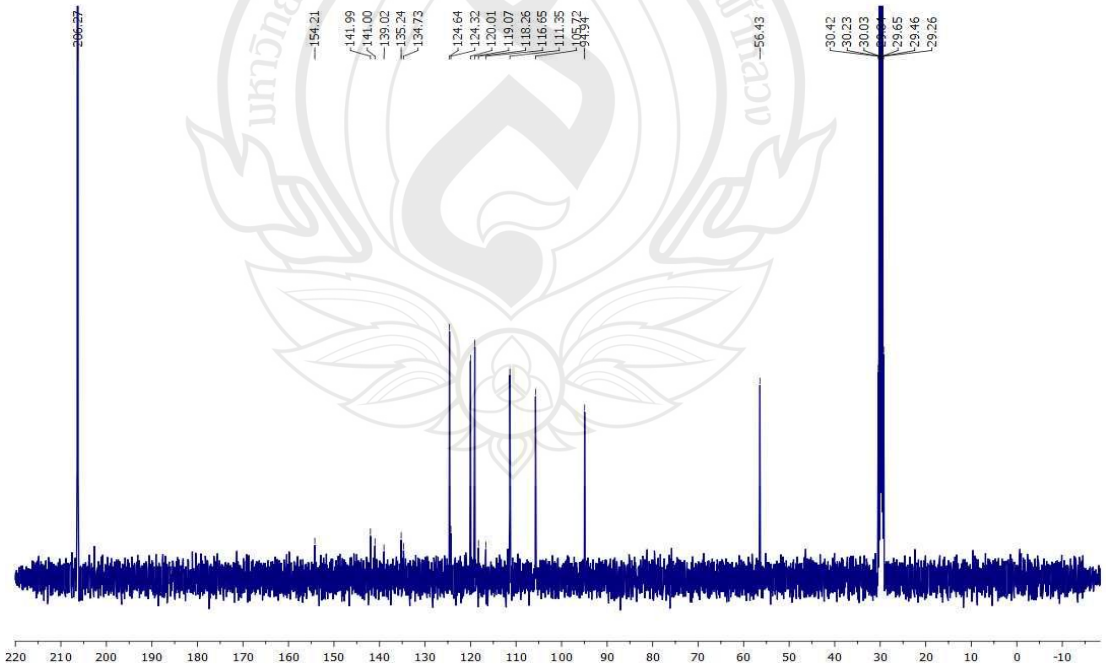

Figure A11 ^{13}C NMR Spectrum of **WM9** in Acetone-d_6 (100 MHz)

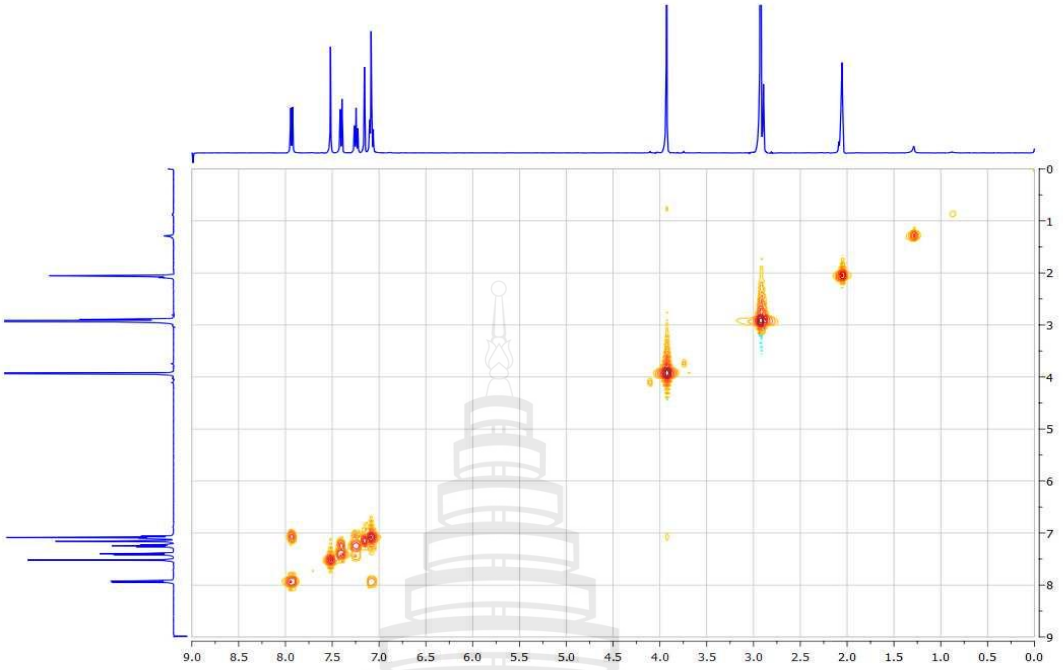

Figure A12 COSY Spectrum of **WM9** in Acetone-d_6

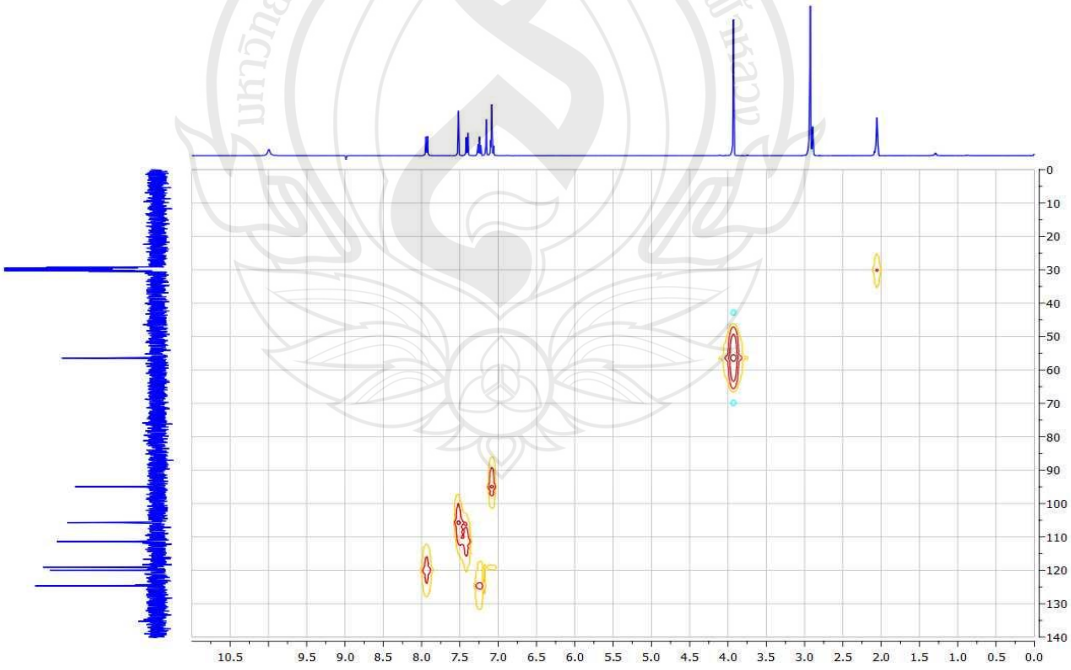

Figure A13 HMQC Spectrum of **WM9** in Acetone-d_6

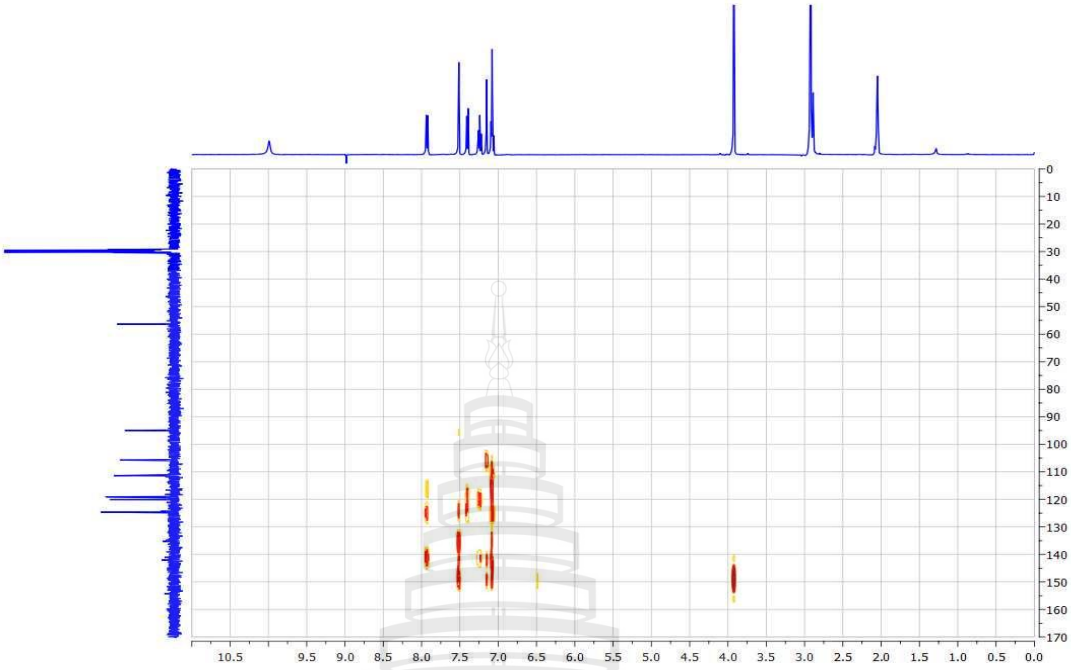

Figure A14 HMBC Spectrum of **WM9** in Acetone-d_6

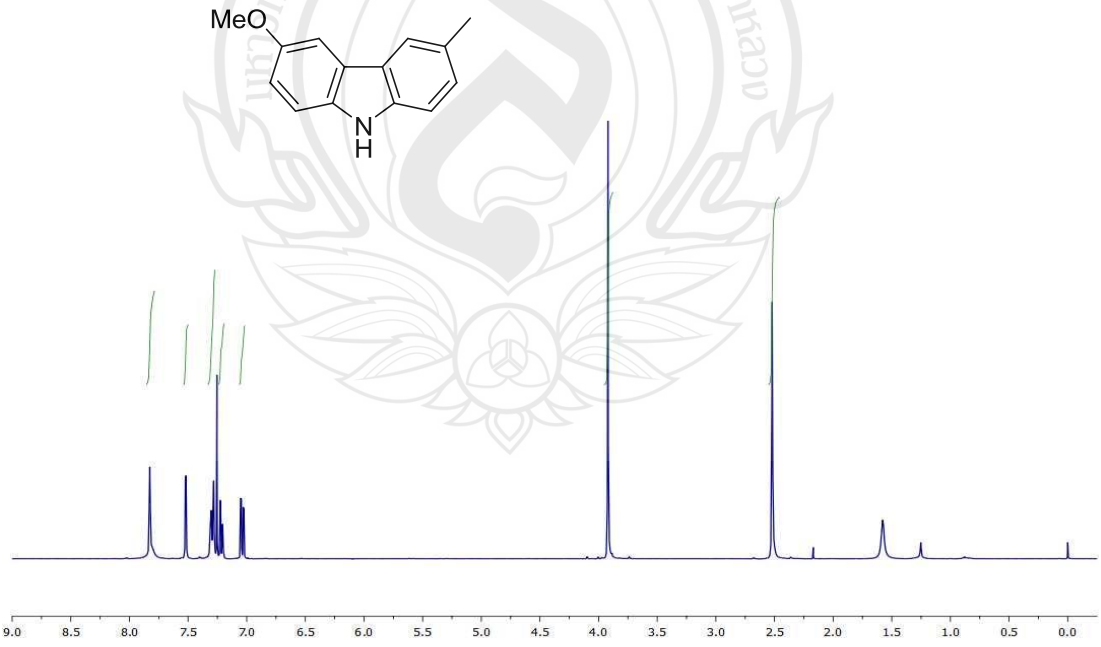

Figure A15 ^{1}H NMR Spectrum of **WM10** in $CDCl_3$ (400 MHz)

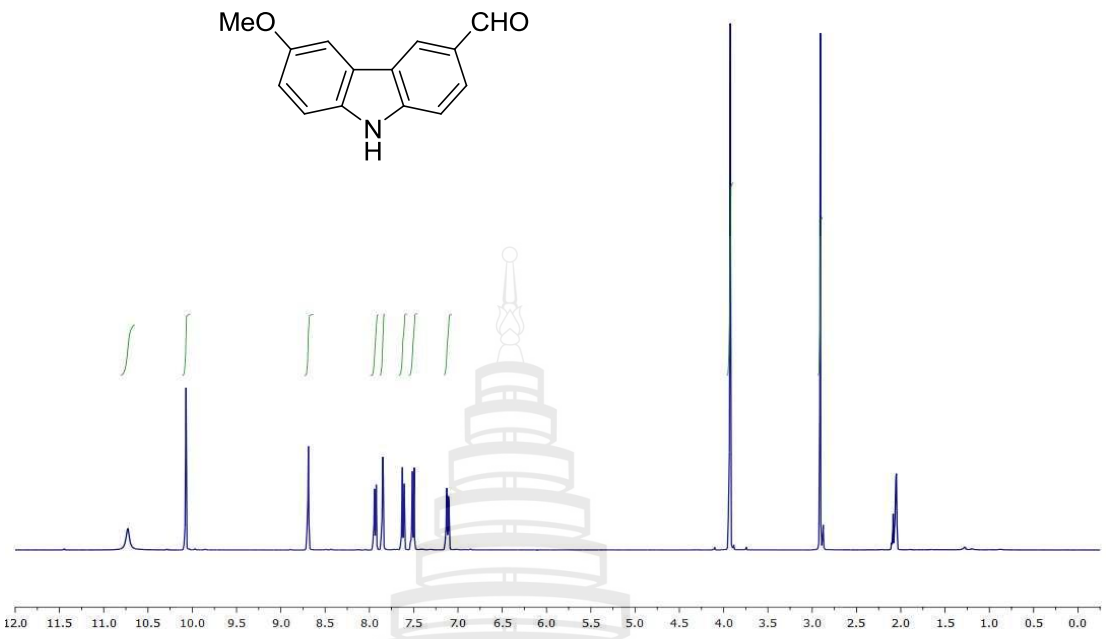

Figure A16 ^{1}H NMR Spectrum of **WM11** in Acetone-d_6 (400 MHz)

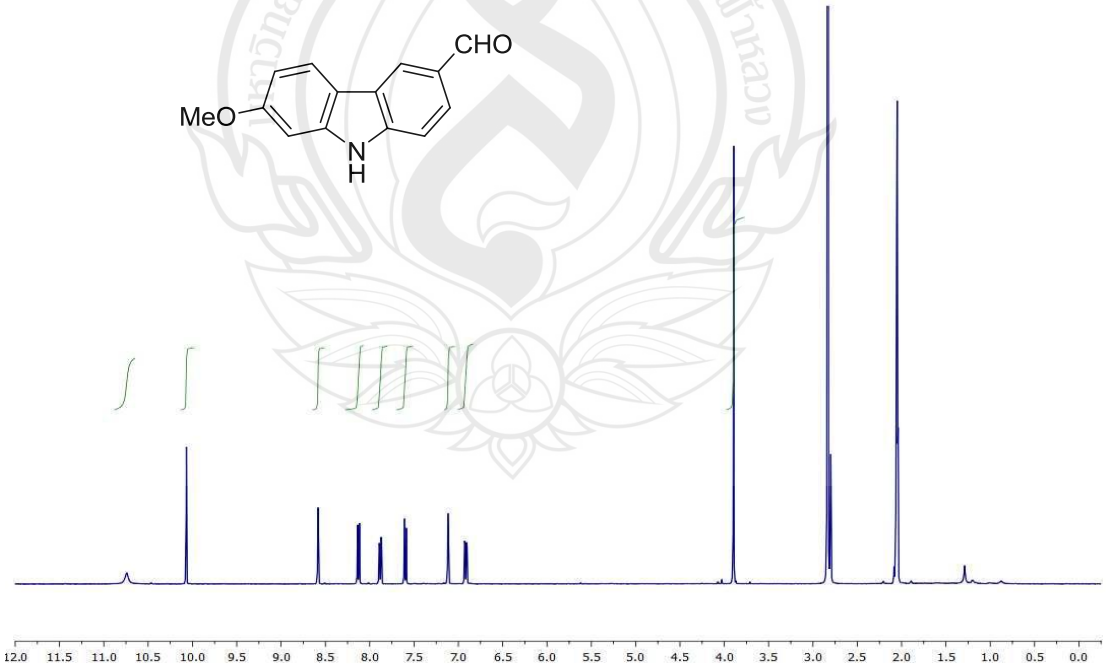

Figure A17 ^{1}H NMR Spectrum of **WM12** in Acetone-d_6 (400 MHz)

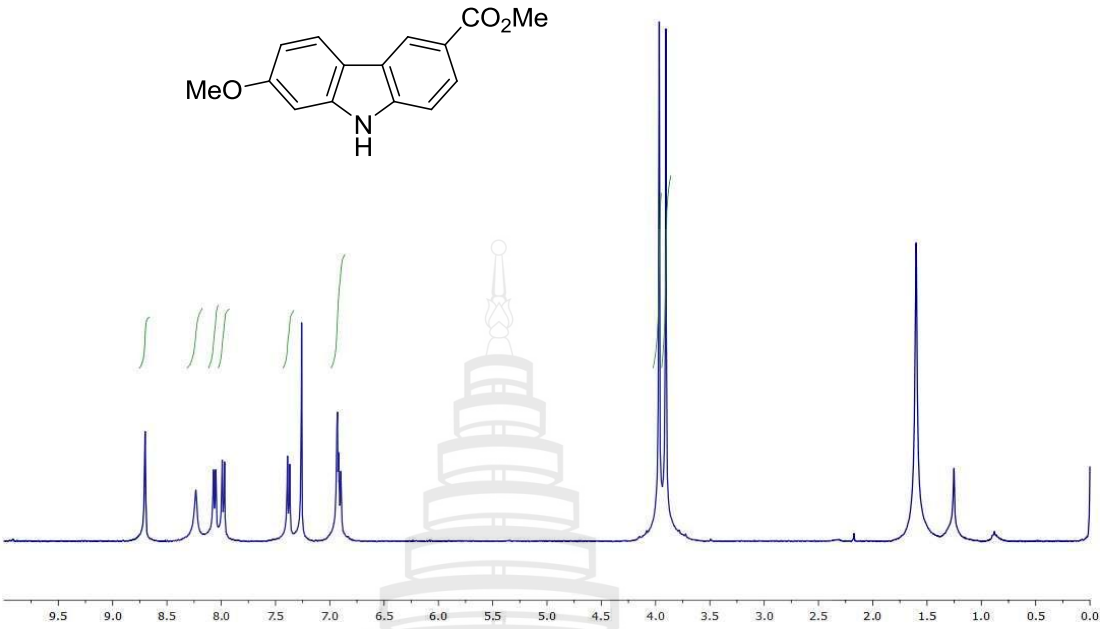

Figure A18 ^{1}H NMR Spectrum of **WM13** in $CDCl_3$ (400 MHz)

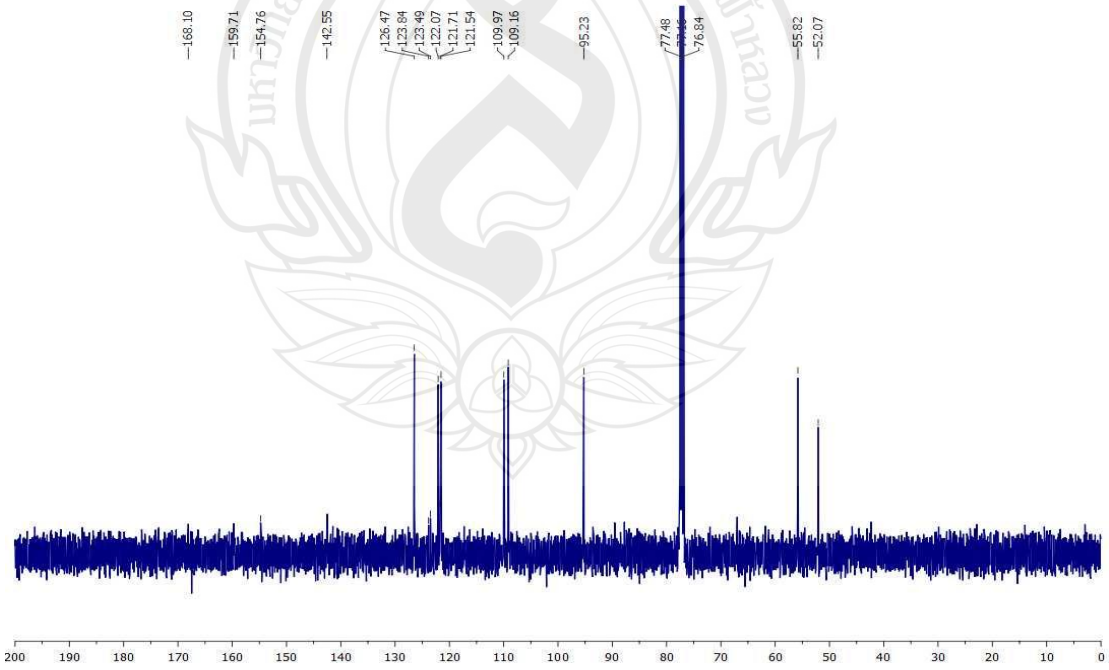

Figure A19 ^{13}C NMR Spectrum of **WM13** in $CDCl_3$ (100 MHz)

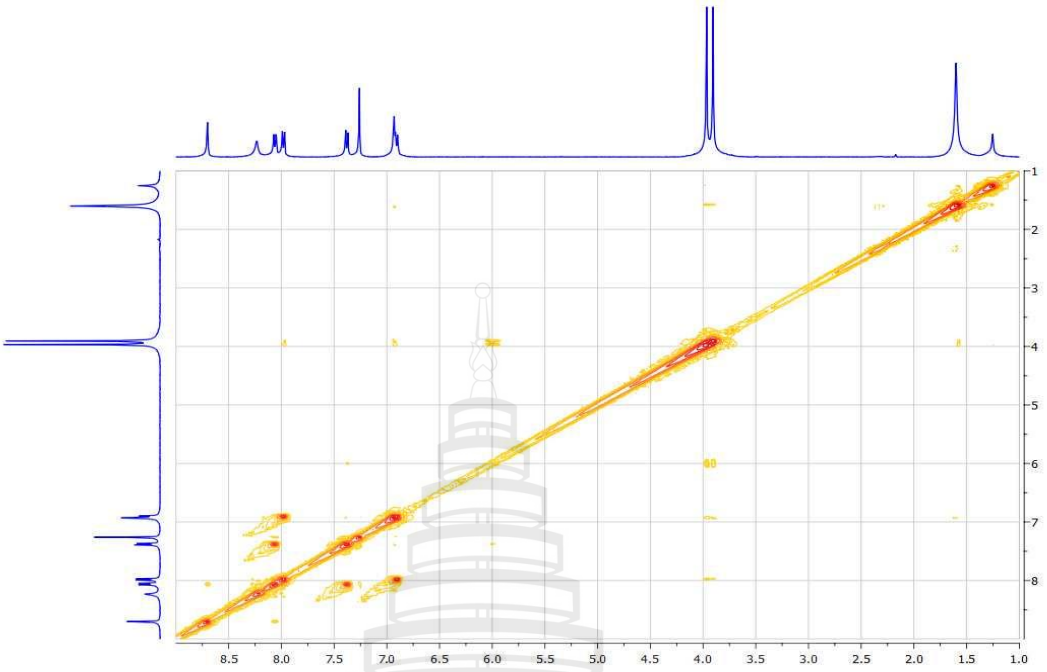

Figure A20 COSY Spectrum of **WM13** in $CDCl_3$

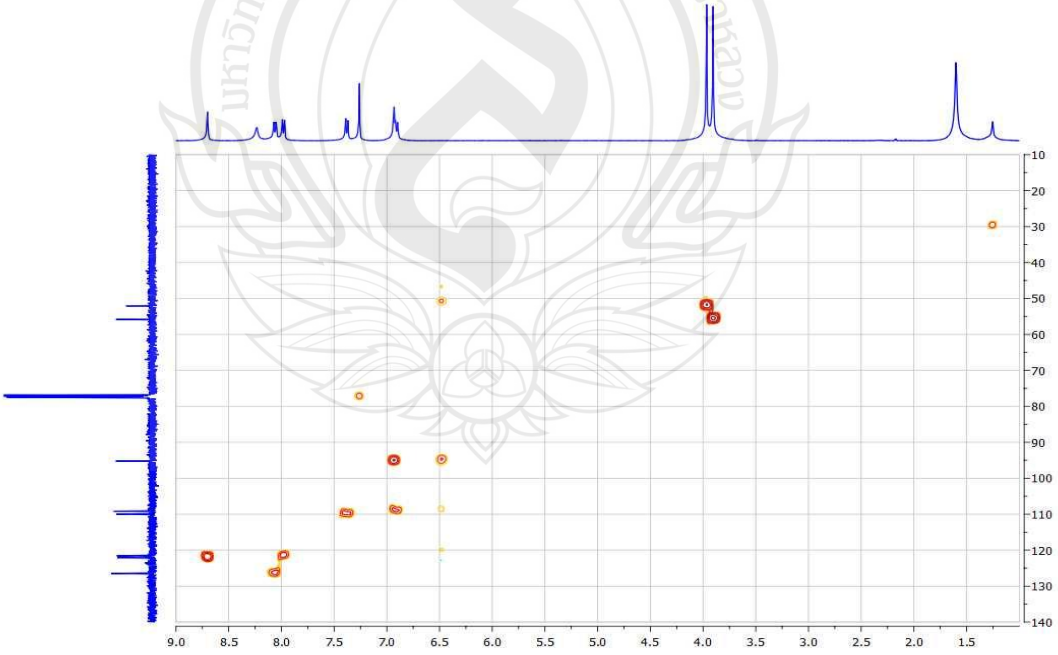

Figure A21 HMQC Spectrum of **WM13** in $CDCl_3$

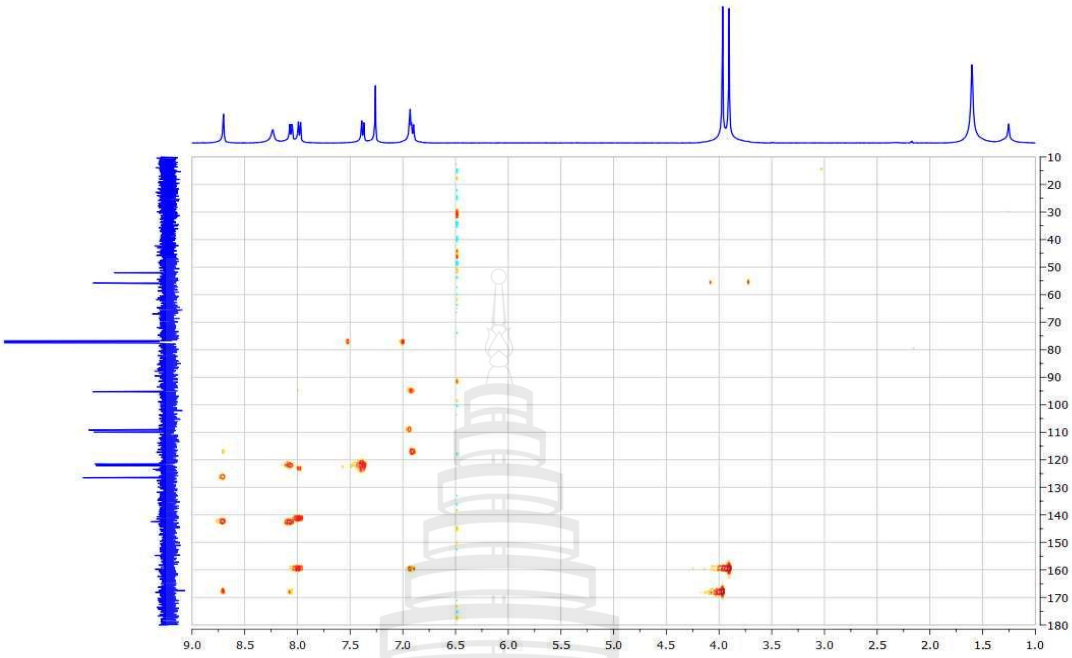

Figure A22 HMBC Spectrum of **WM13** in $CDCl_3$

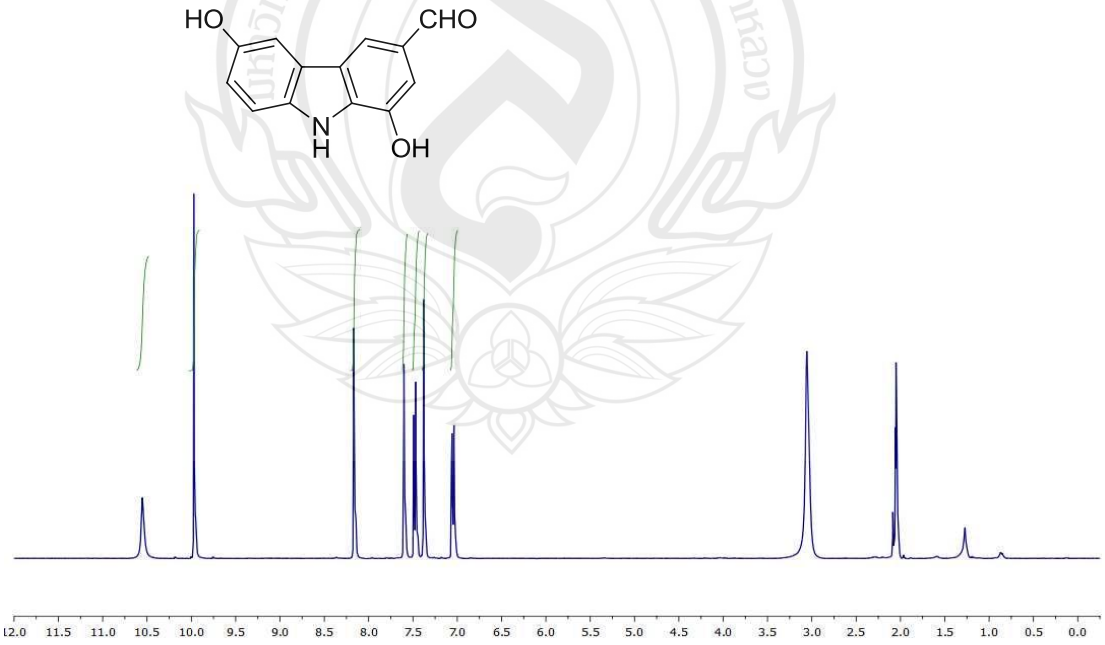

Figure A23 ^{1}H NMR Spectrum of **WM14** in Acetone-d_6 (400 MHz)

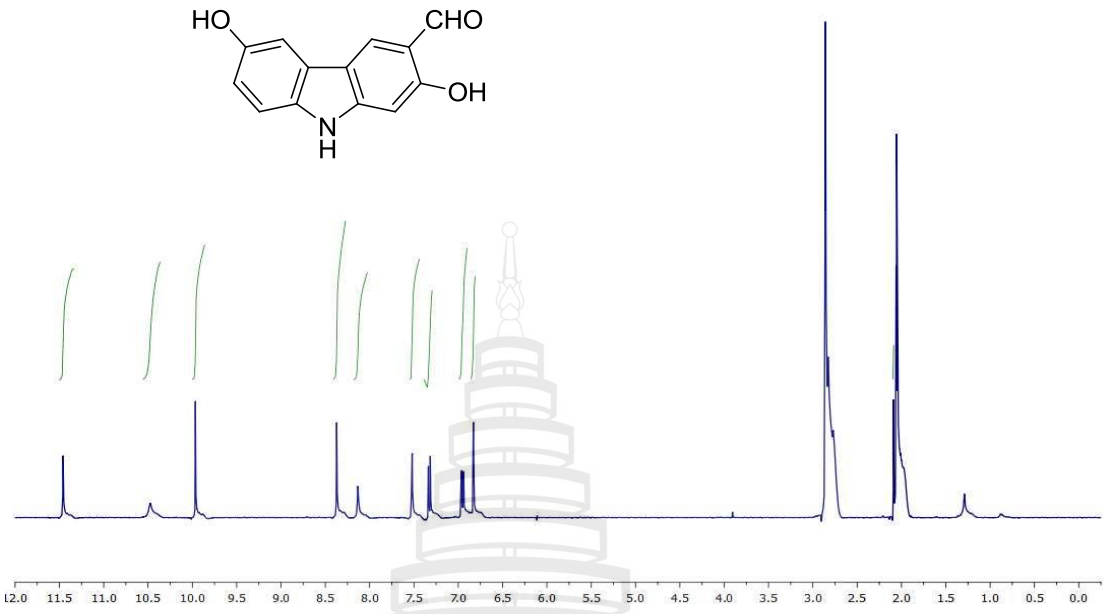

Figure A24 ^{1}H NMR Spectrum of **WM15** in Acetone-d_6 (400 MHz)

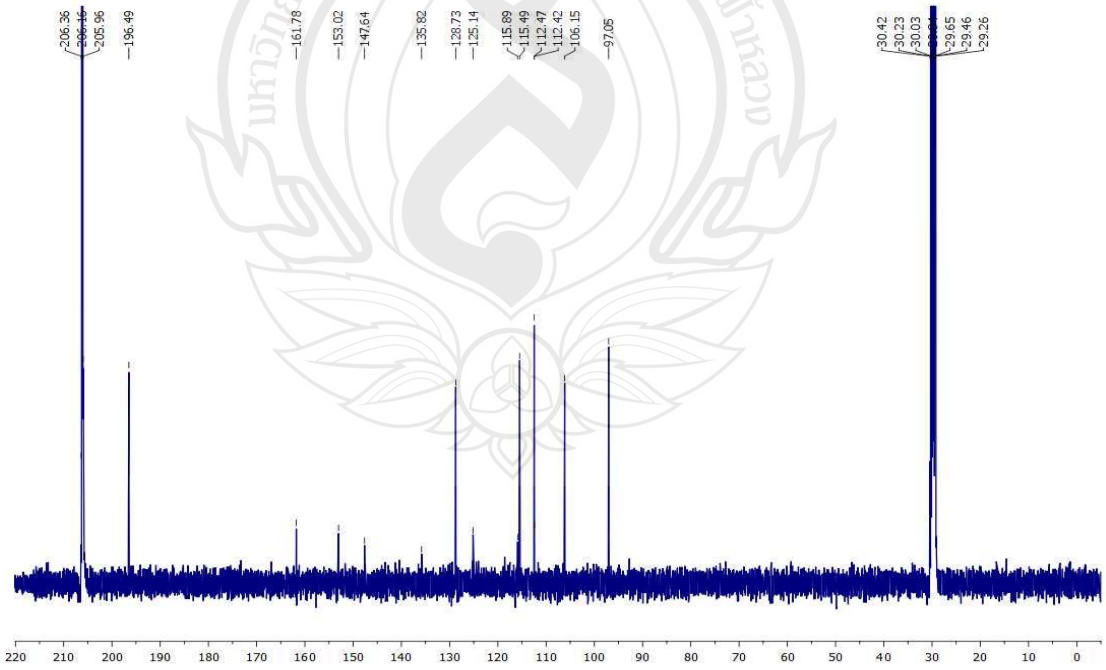

Figure A25 ^{13}C NMR Spectrum of **WM15** in Acetone-d_6 (100 MHz)

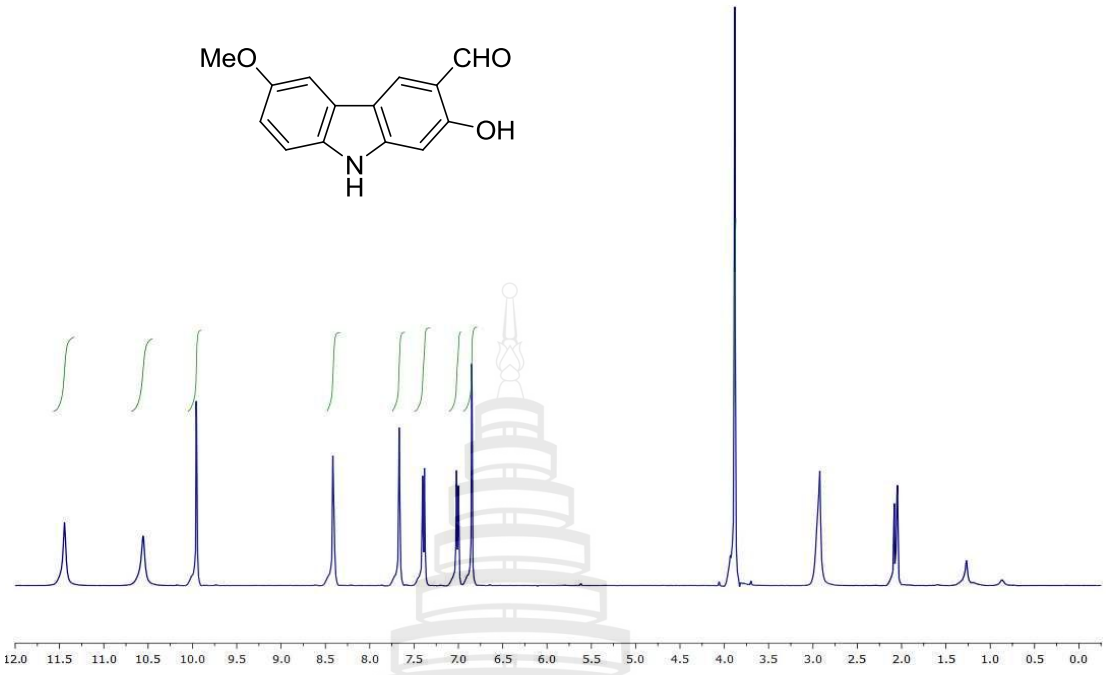

Figure A26 ^{1}H NMR Spectrum of **WM16** in Acetone-d_6 (400 MHz)

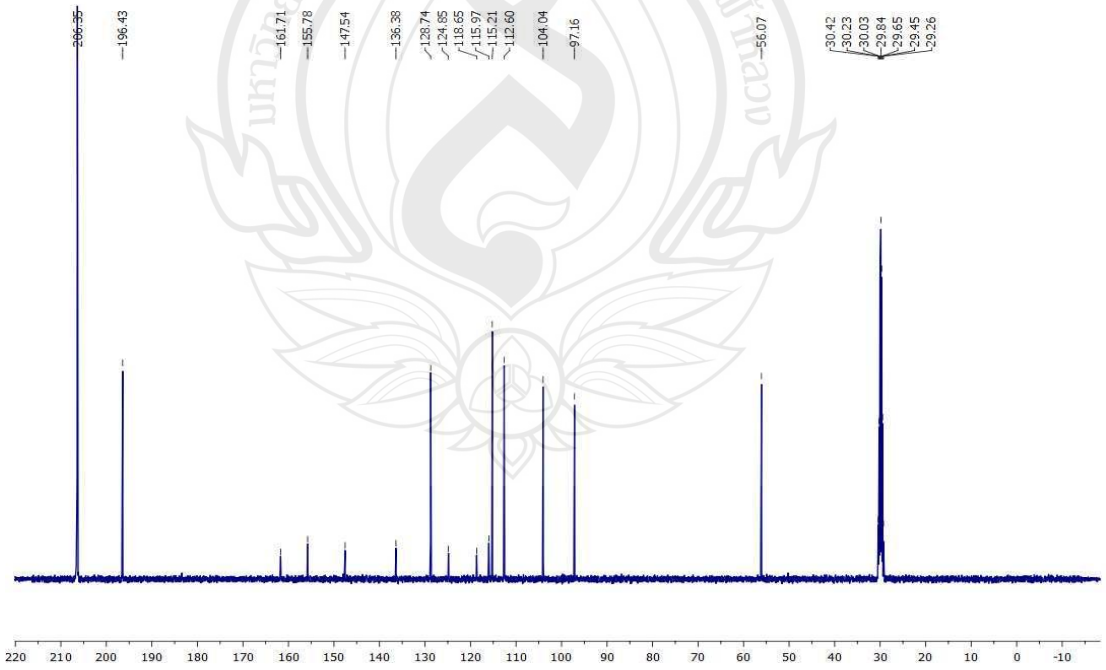

Figure A27 ^{13}C NMR Spectrum of **WM16** in Acetone-d_6 (100 MHz)

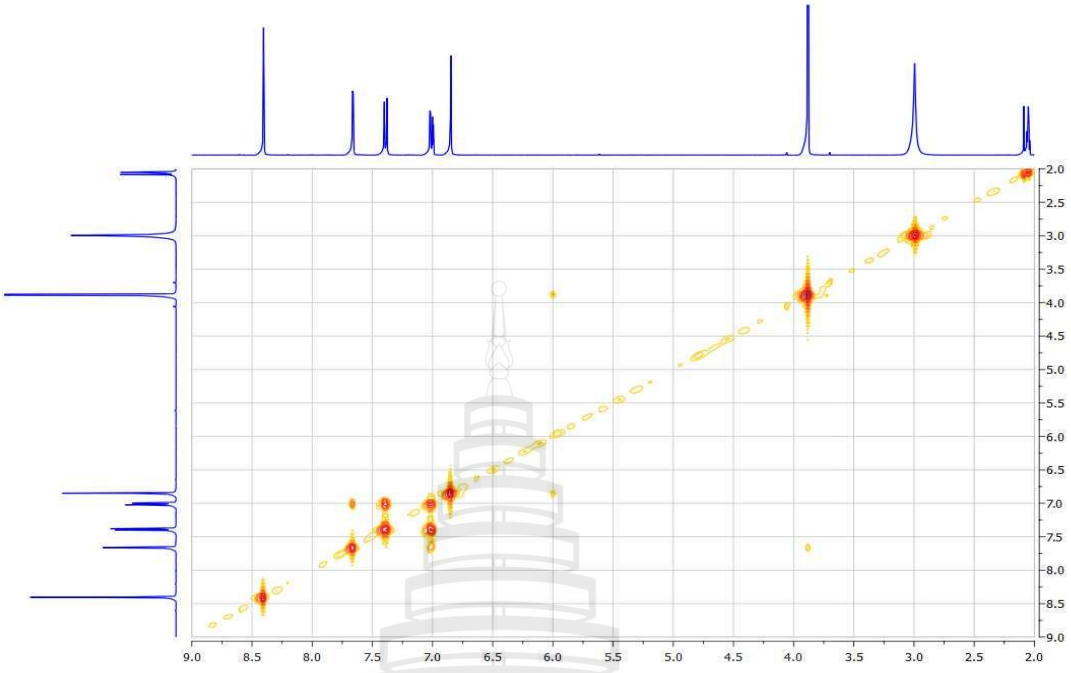

Figure A28 COSY Spectrum of **WM16** in Acetone-d_6

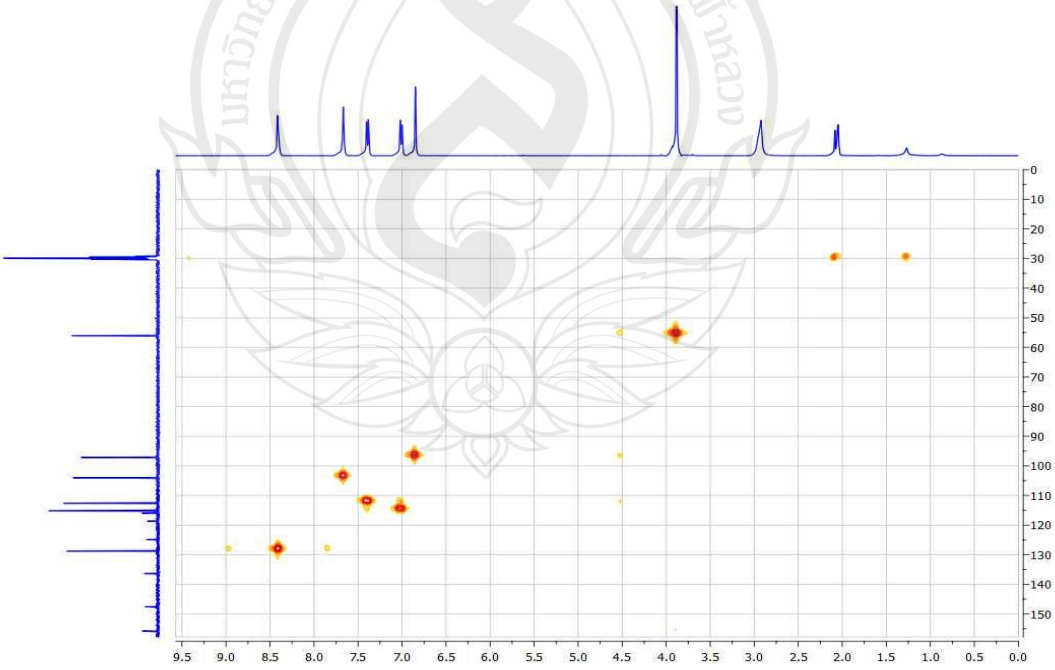

Figure A29 HMQC Spectrum of **WM16** in Acetone-d_6

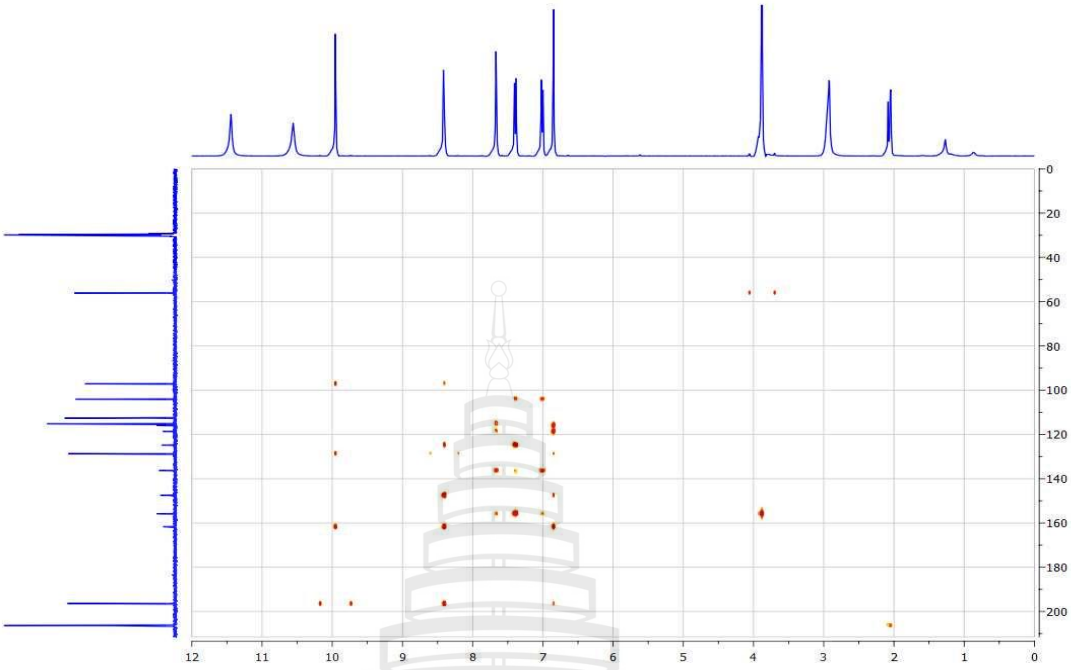

Figure A30 HMBC Spectrum of **WM16** in Acetone-d_6

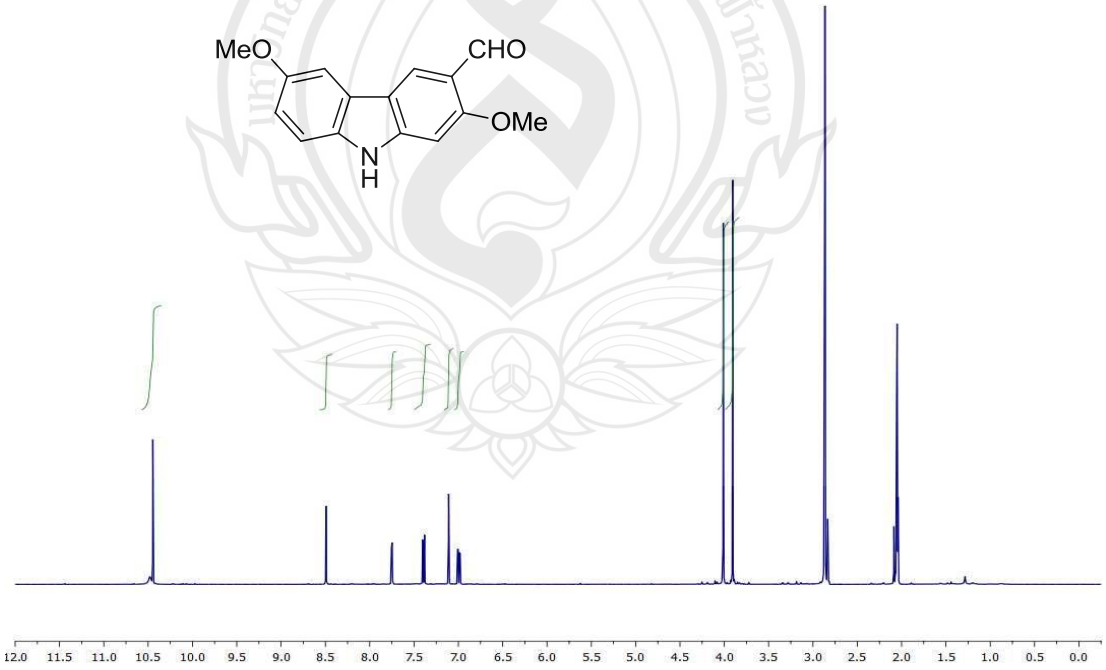

Figure A31 ^{1}H NMR Spectrum of **WM17** in Acetone-d_6 (400 MHz)

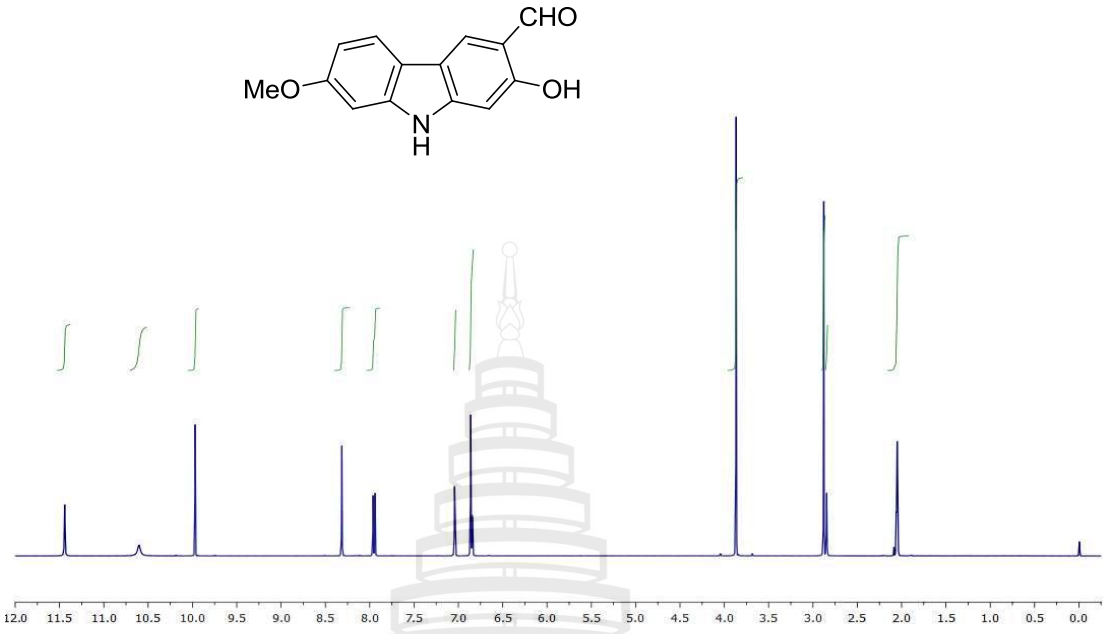

Figure A32 ^{1}H NMR Spectrum of **WM18** in Acetone-d_6 (400 MHz)

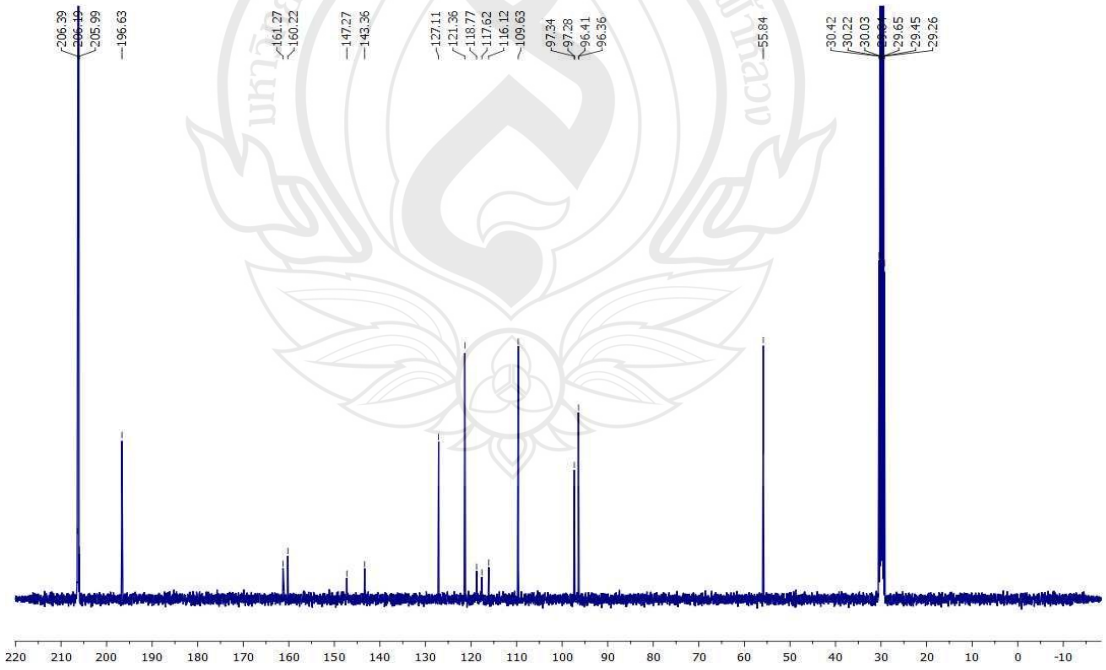

Figure A33 ^{13}C NMR Spectrum of **WM18** in Acetone-d_6 (100 MHz)

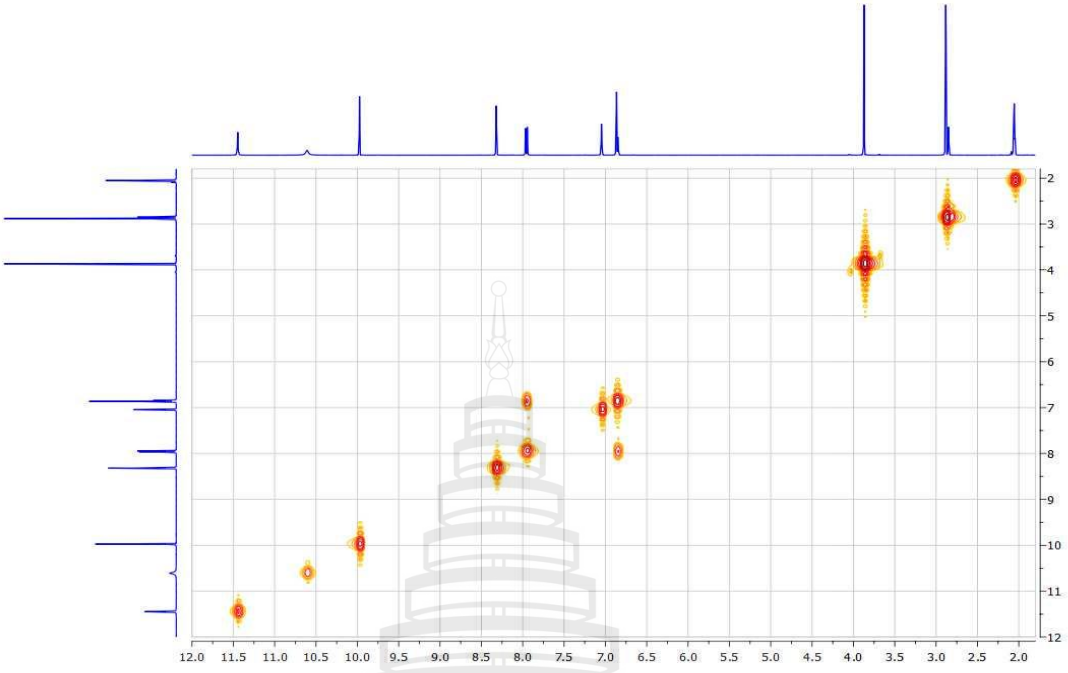

Figure A34 COSY Spectrum of **WM18** in Acetone-d_6

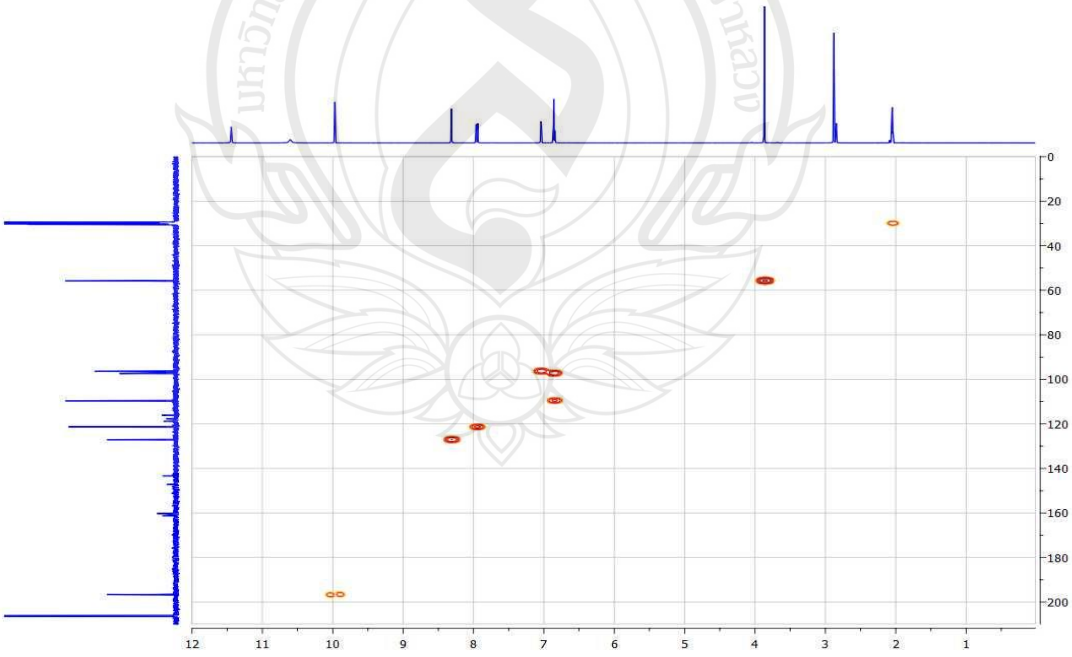

Figure A35 HMQC Spectrum of **WM18** in Acetone-d_6

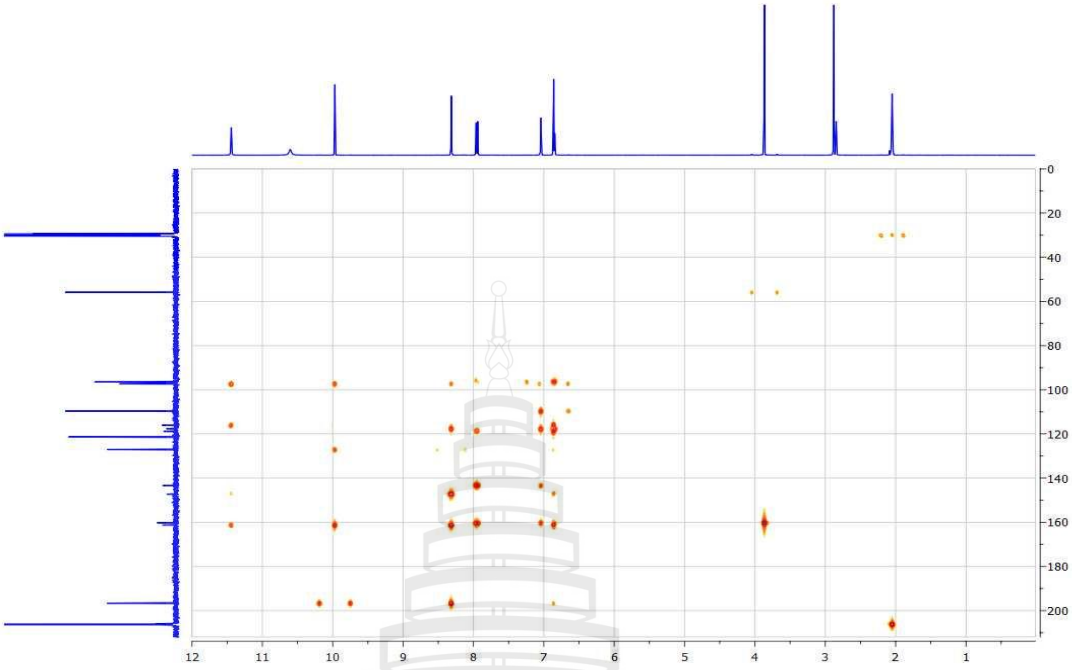

Figure A36 HMBC Spectrum of **WM18** in Acetone-d_6

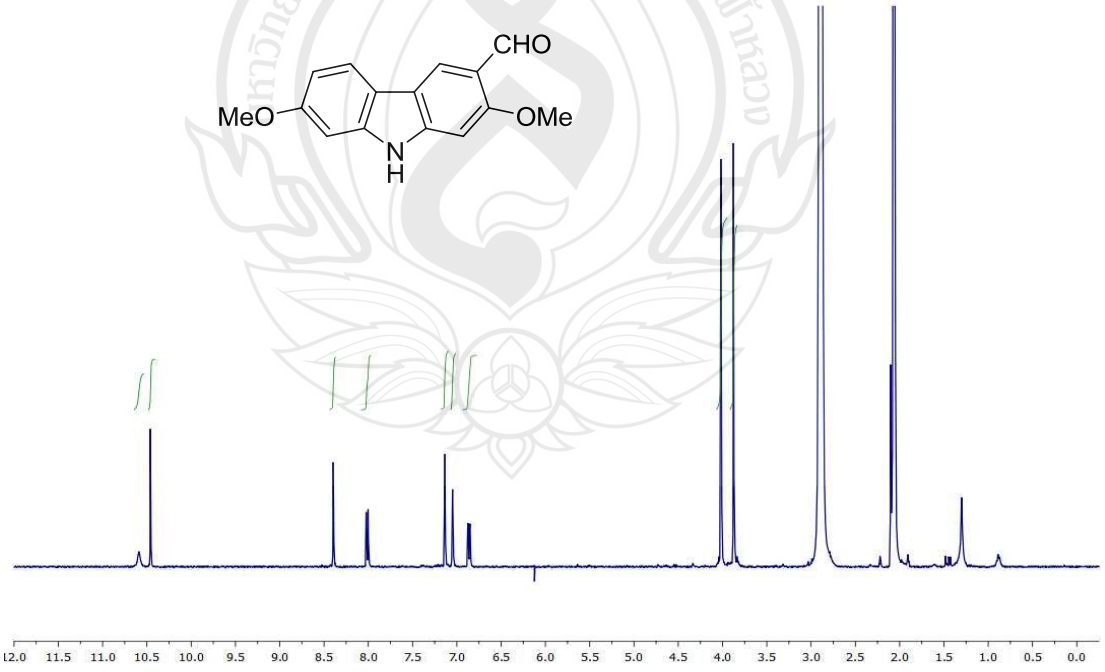

Figure A37 ^{1}H NMR Spectrum of **WM19** in Acetone-d_6 (400 MHz)

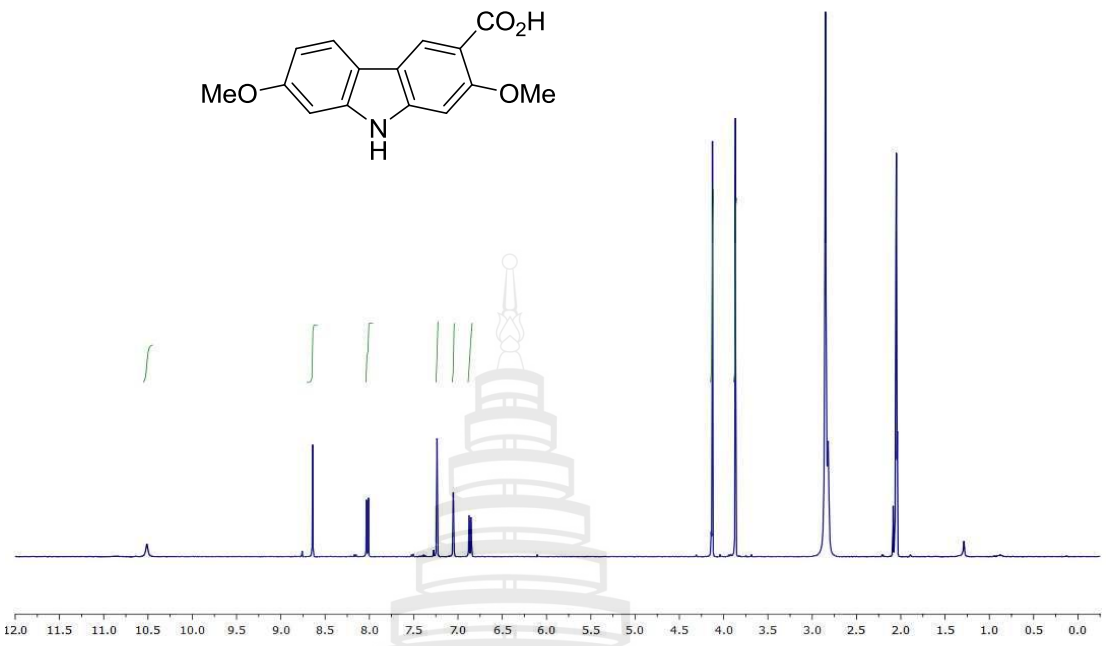

Figure A38 ^{1}H NMR Spectrum of **WM20** in Acetone-d_6 (400 MHz)

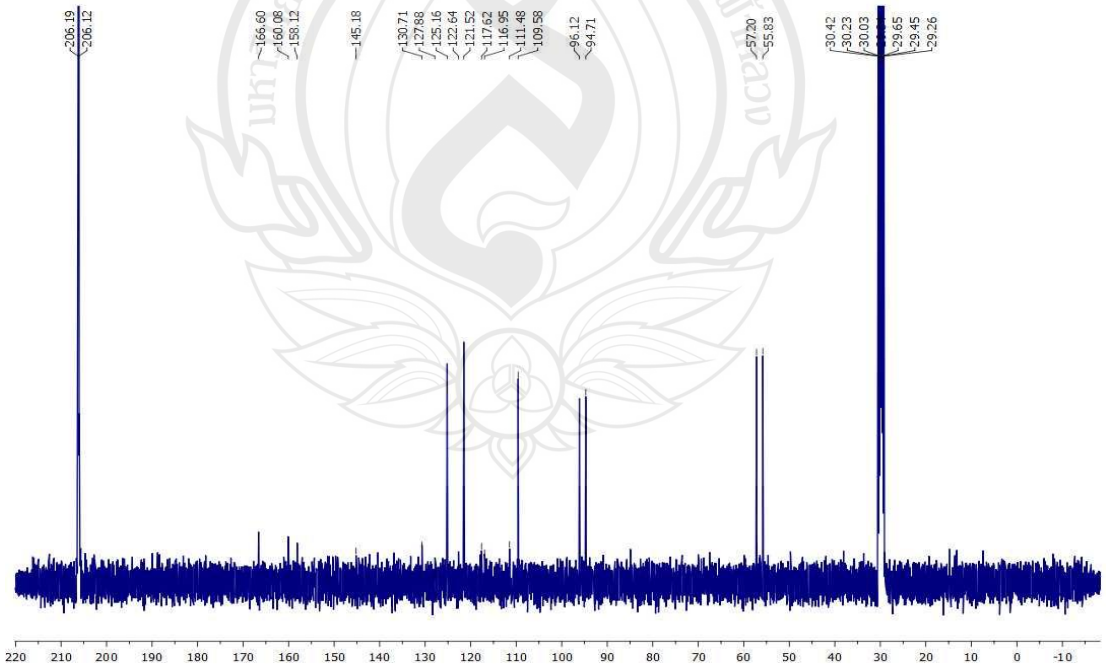

Figure A39 ^{13}H NMR Spectrum of **WM20** in Acetone-d_6 (100 MHz)

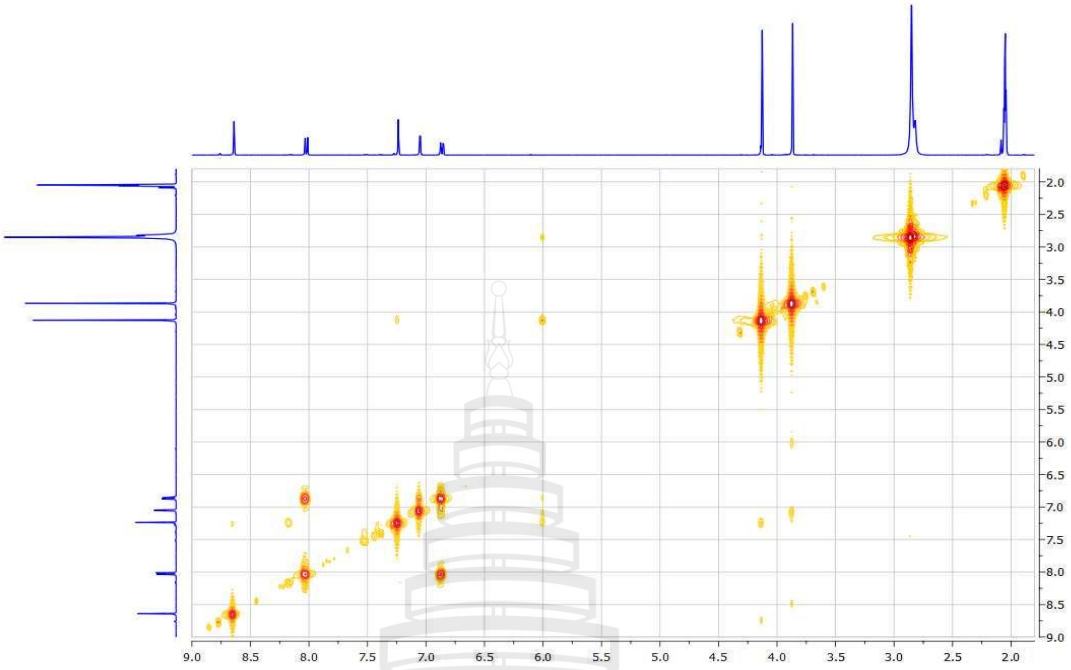

Figure A40 COSY Spectrum of **WM20** in Acetone-d_6

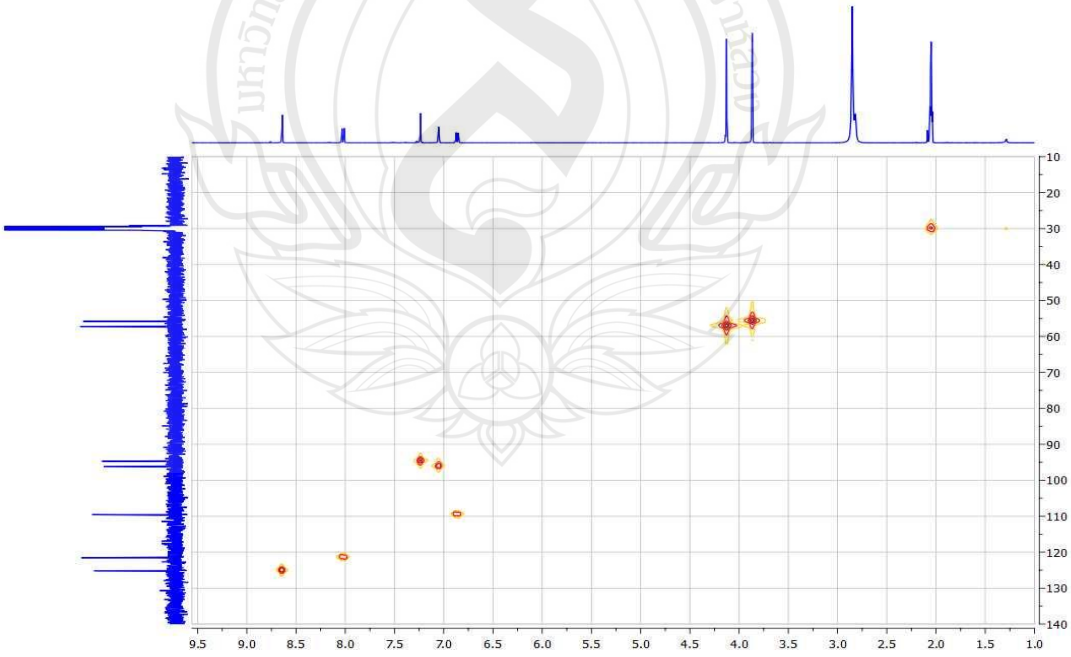

Figure A41 HMQC Spectrum of **WM20** in Acetone-d_6

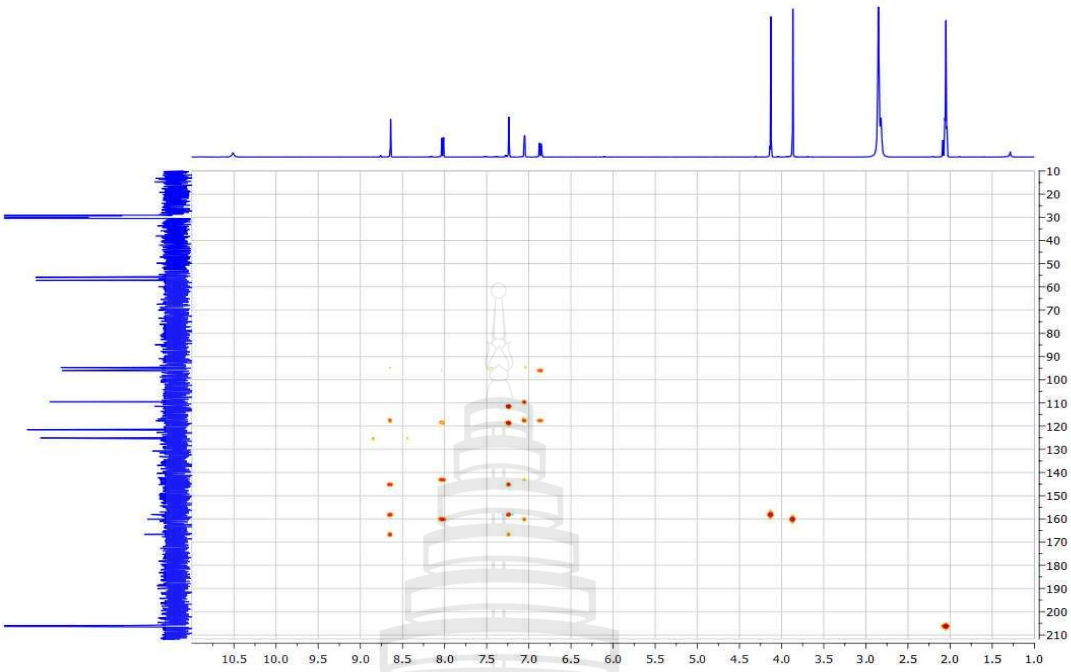

Figure A42 HMBC Spectrum of **WM20** in Acetone-d_6

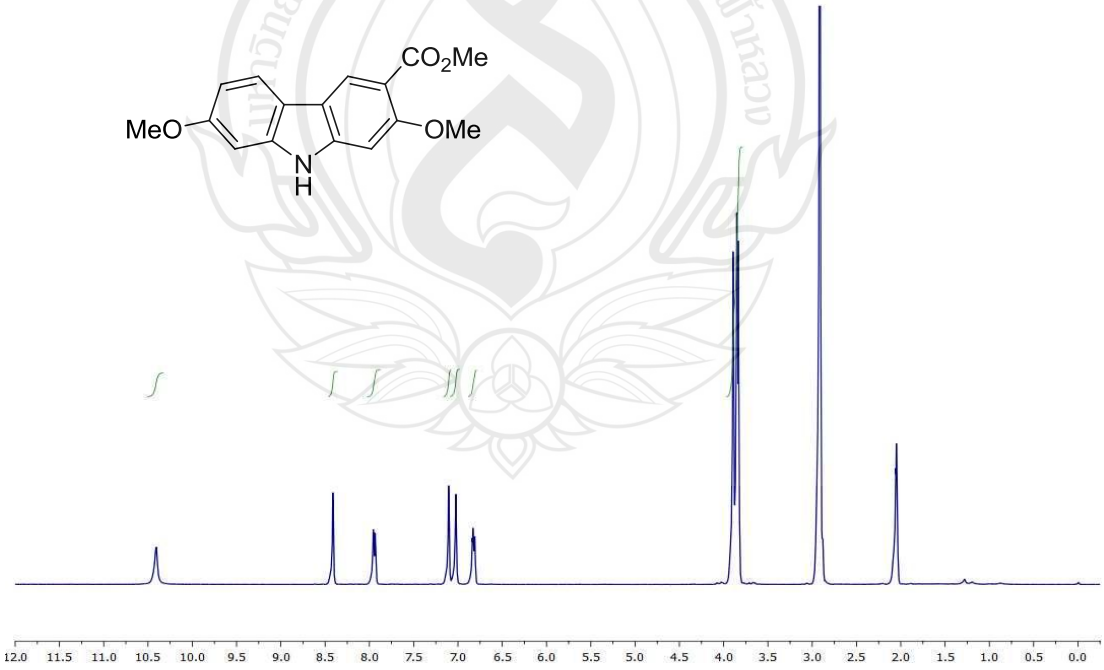

Figure A43 ^{1}H NMR Spectrum of **WM21** in Acetone-d_6 (400 MHz)

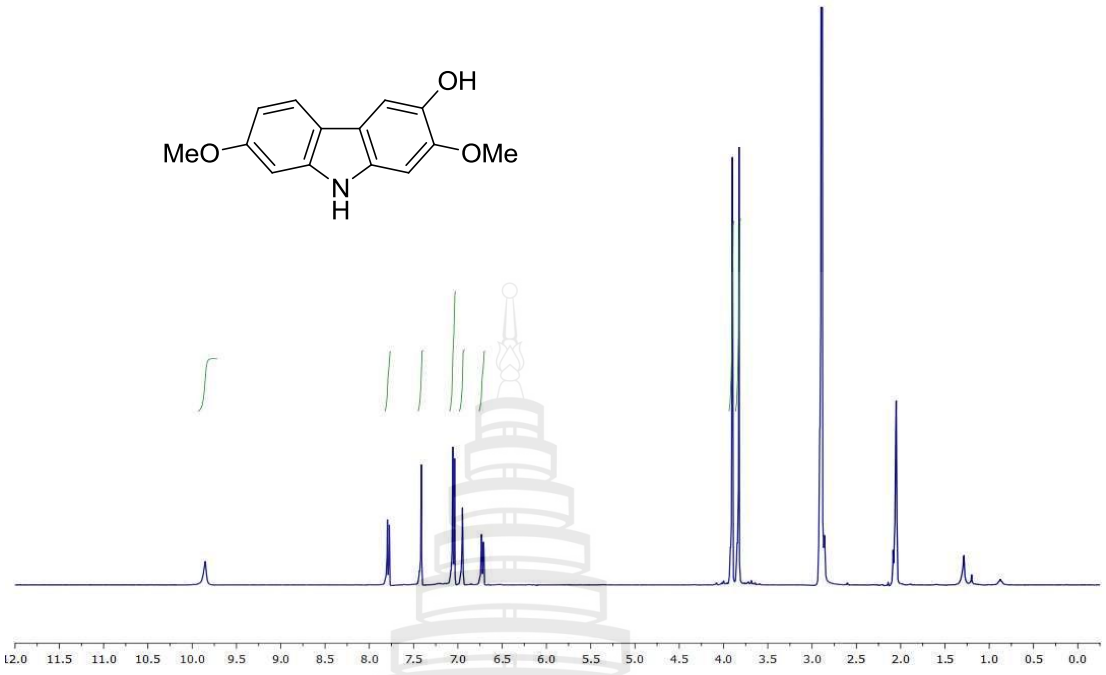

Figure A44 ^{1}H NMR Spectrum of **WM22** in Acetone-d_6 (400 MHz)

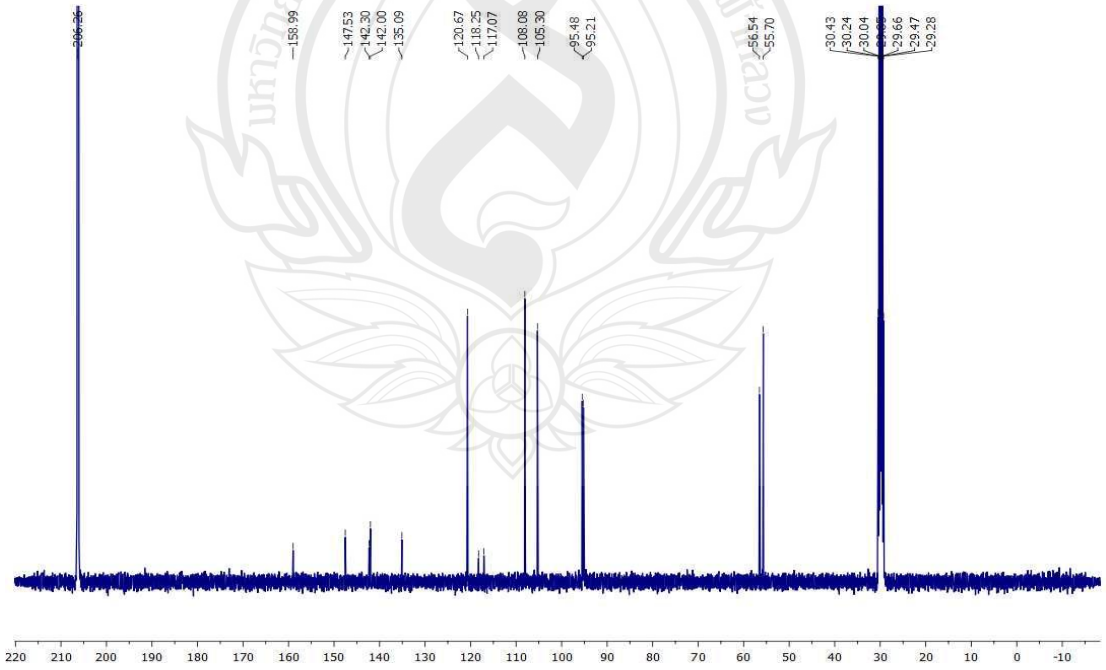

Figure A45 ^{13}C NMR Spectrum of **WM22** in Acetone-d_6 (100 MHz)

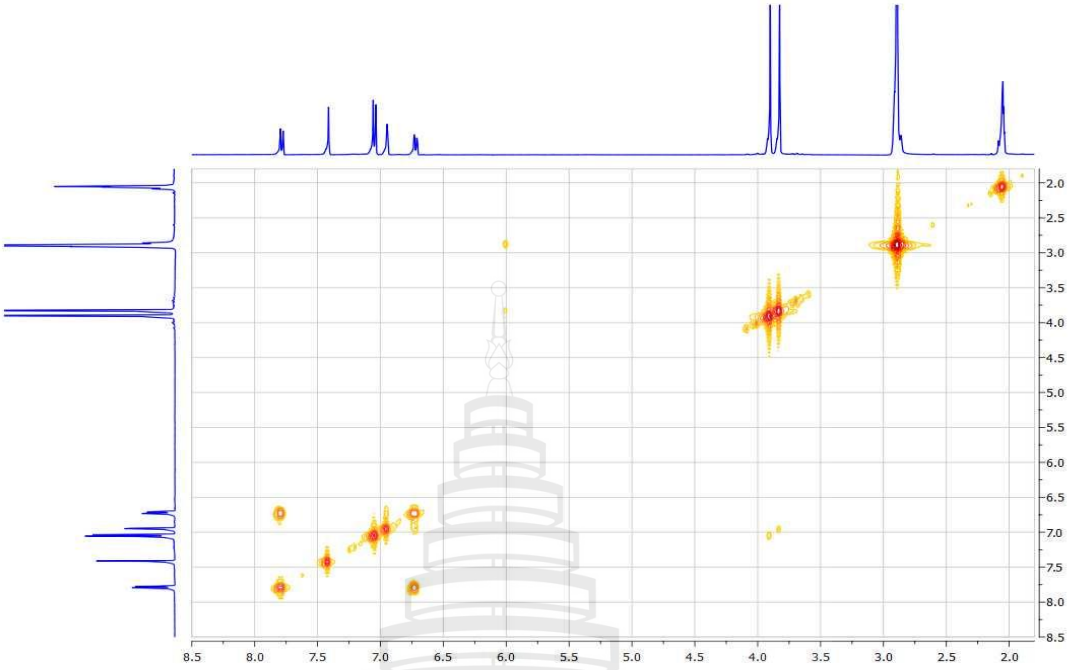

Figure A46 COSY Spectrum of **WM22** in Acetone-d_6

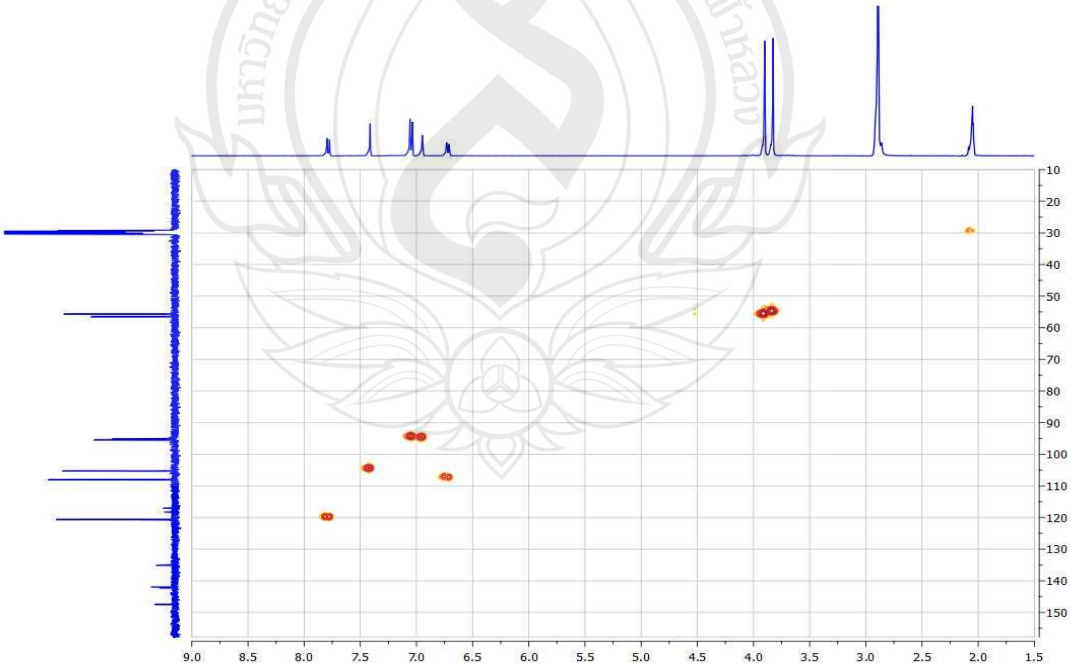

Figure A47 HMQC Spectrum of **WM22** in Acetone-d_6

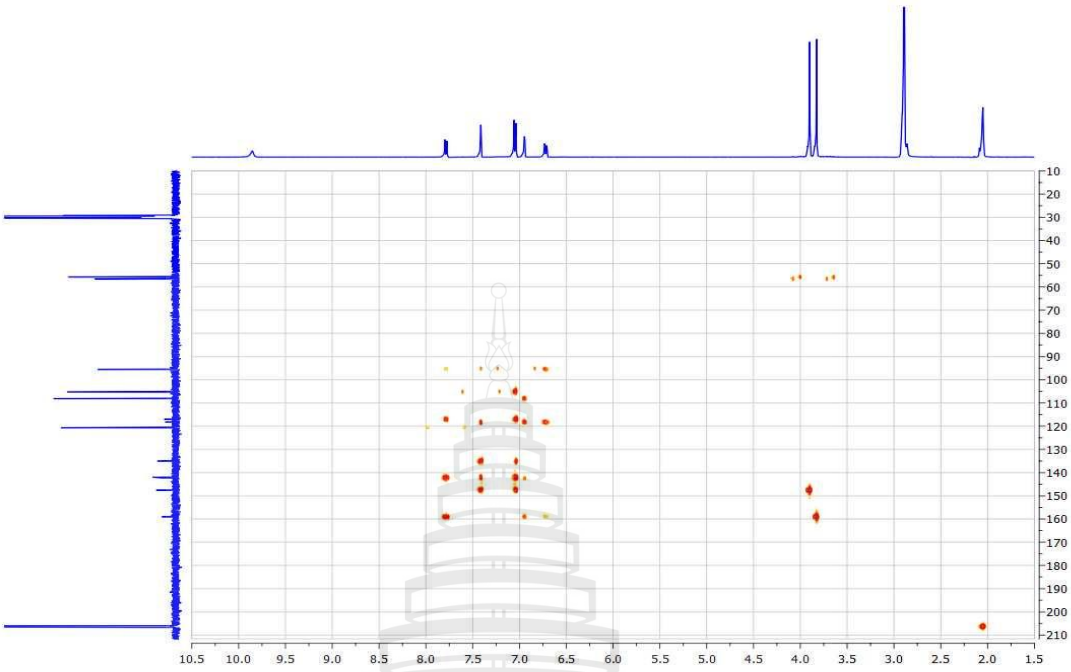

Figure A48 HMBC Spectrum of **WM22** in Acetone-d_6

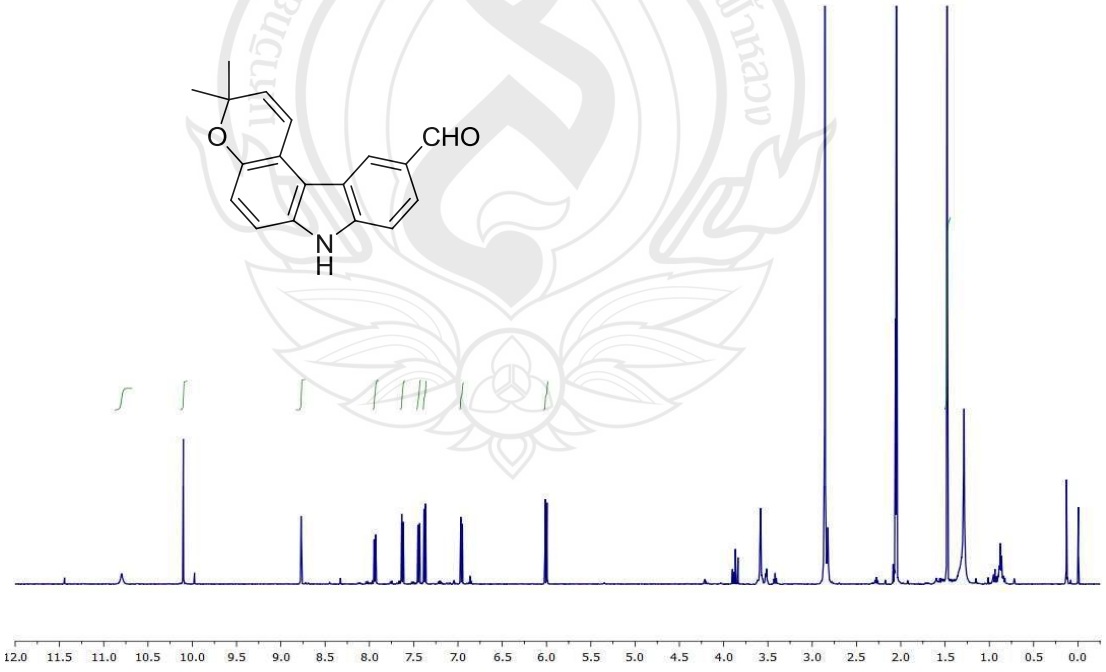

Figure A49 ^{1}H NMR Spectrum of **WM23** in Acetone-d_6 (400 MHz)

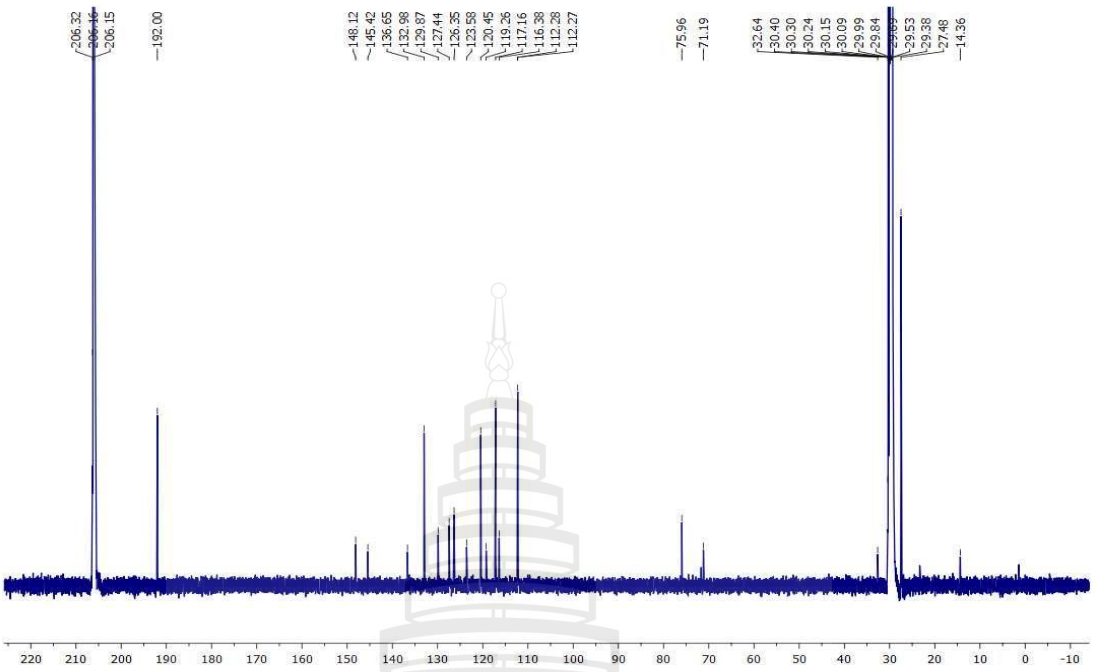

Figure A50 ^{13}C NMR Spectrum of **WM23** in Acetone-d_6 (100 MHz)

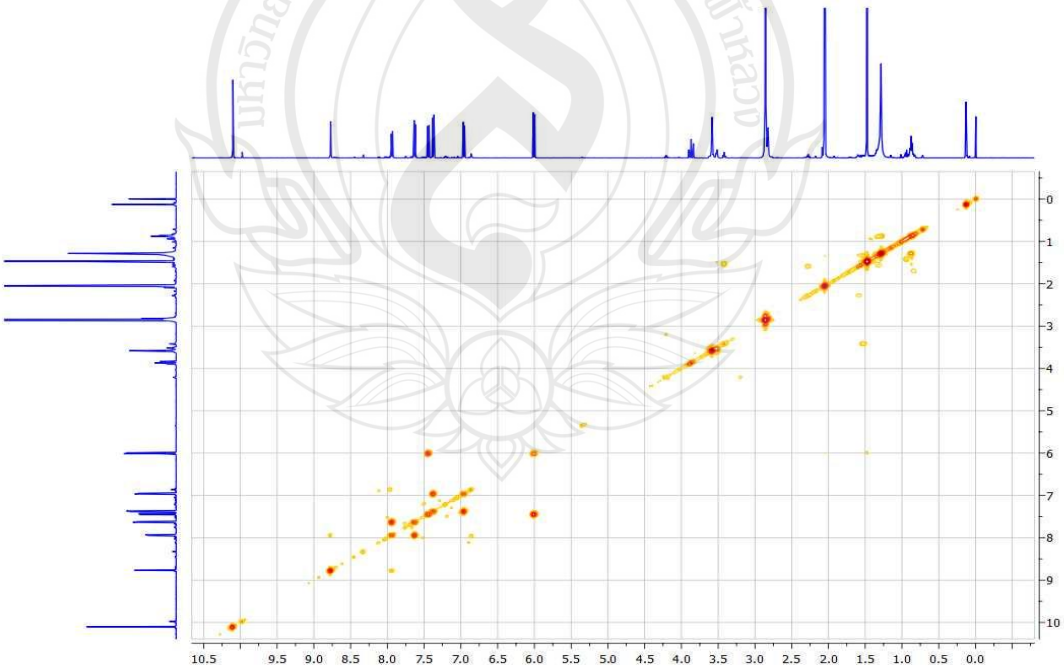

Figure A51 COSY Spectrum of **WM23** in Acetone-d_6

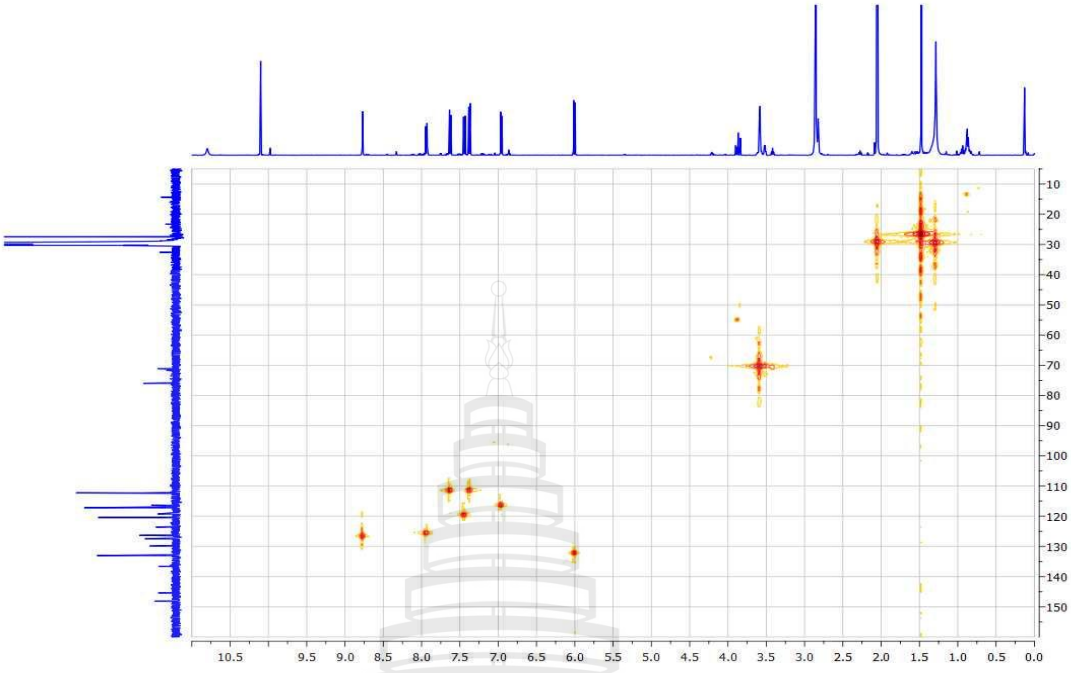

Figure A52 HMQC Spectrum of **WM23** in Acetone-d_6

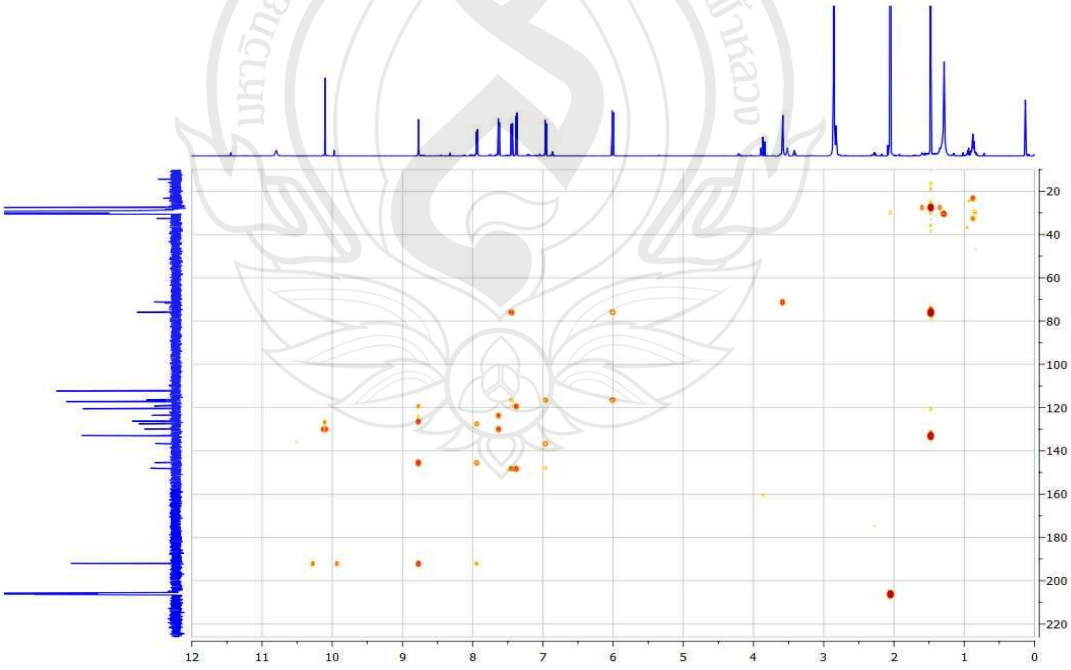

Figure A53 HMBC Spectrum of **WM23** in Acetone-d_6

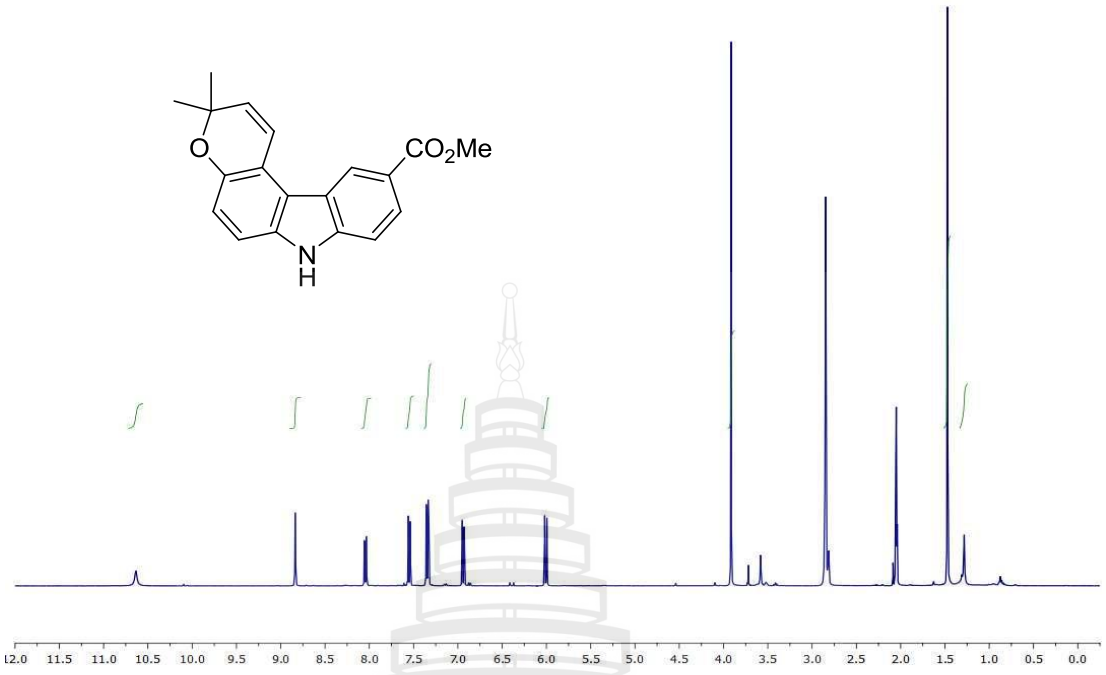

Figure A54 ^{1}H NMR Spectrum of **WM24** in Acetone-d_6 (400 MHz)

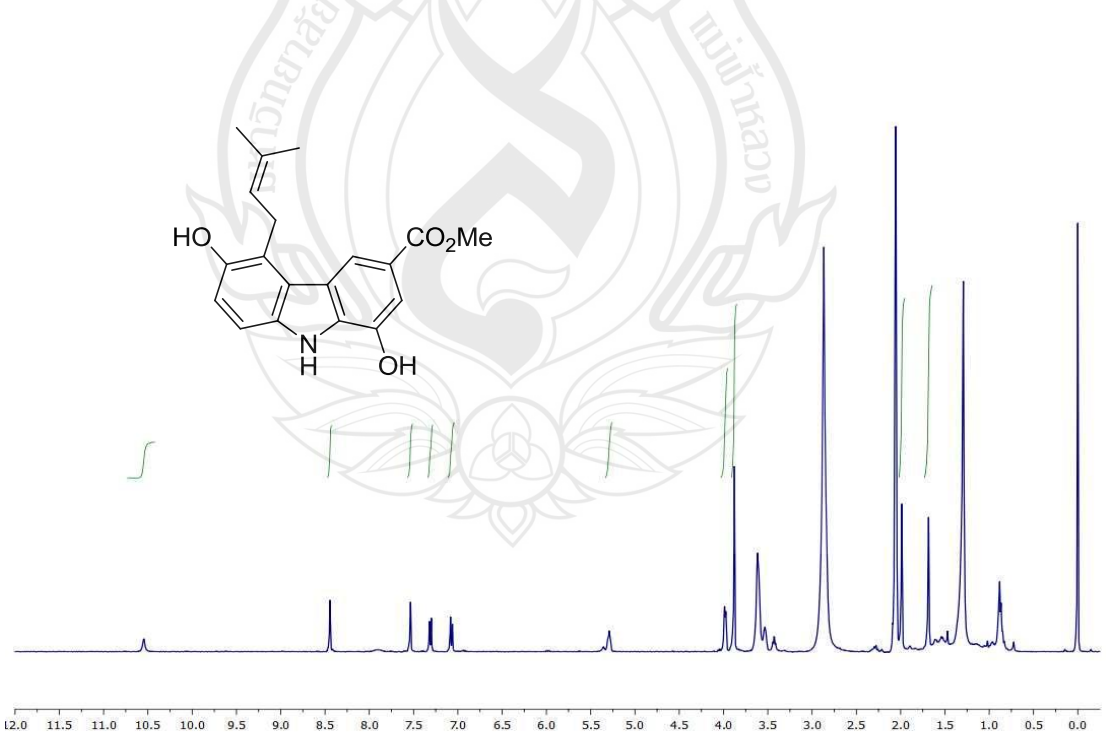

Figure A55 ^{1}H NMR Spectrum of **WM25** in Acetone-d_6 (400 MHz)

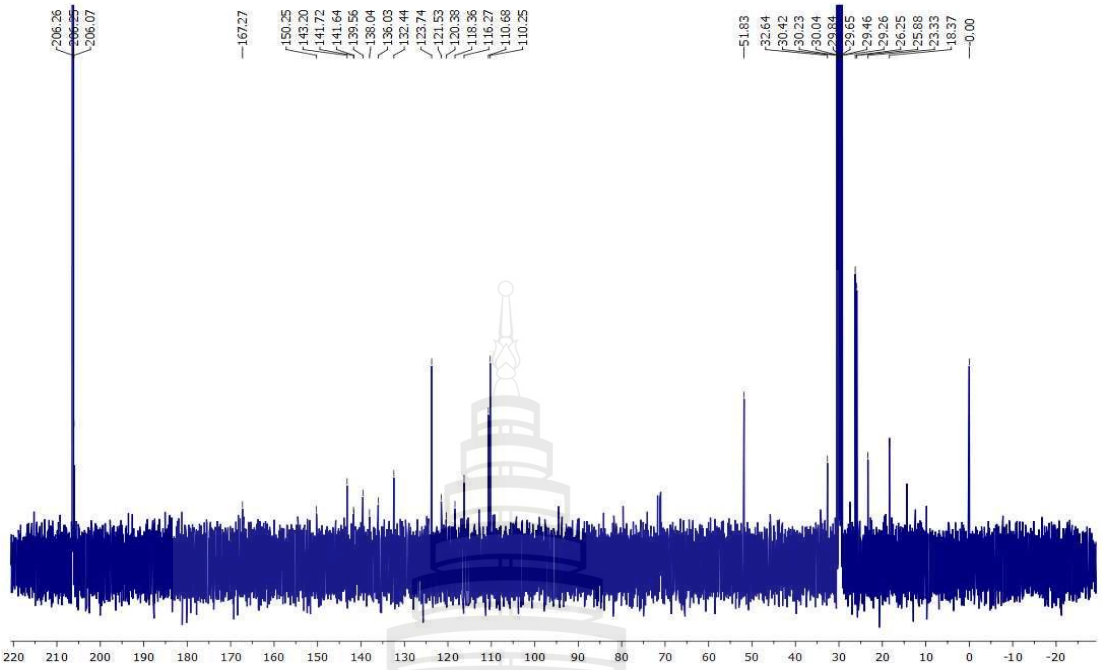

Figure A56 ^{13}C NMR Spectrum of **WM25** in Acetone-d_6 (100 MHz)

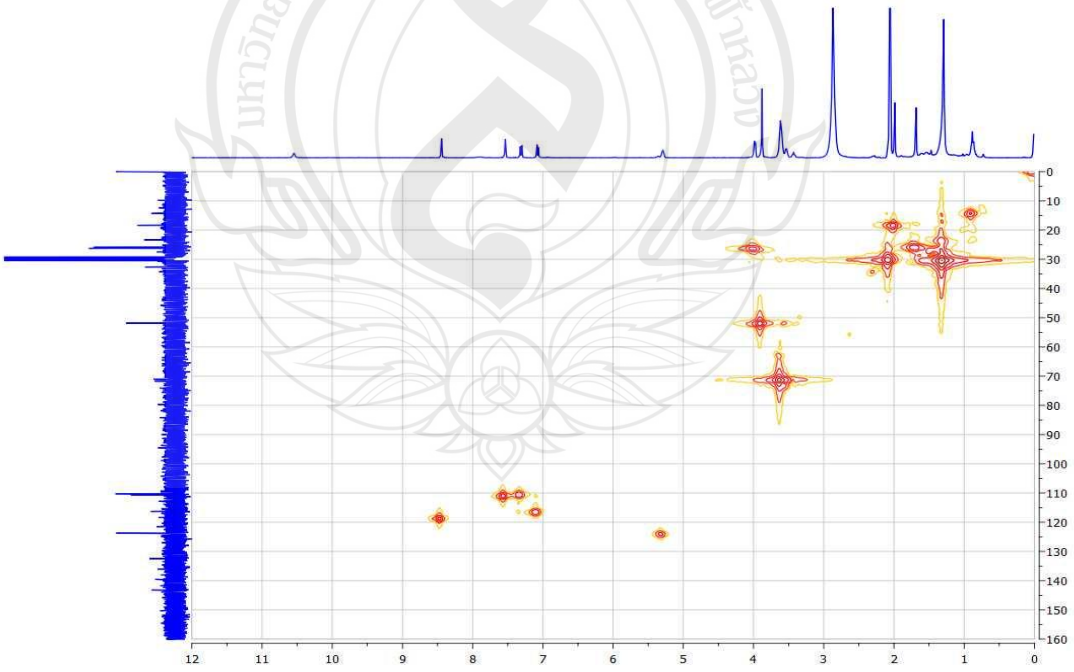

Figure A57 HMQC Spectrum of **WM25** in Acetone-d_6

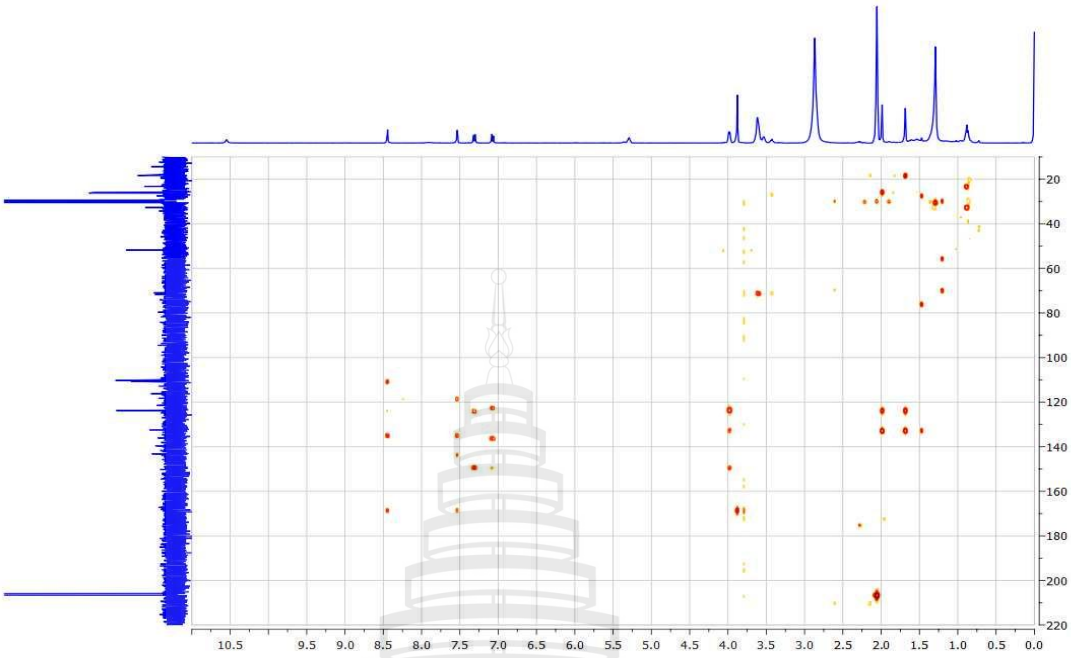

Figure A58 HMBC Spectrum of **WM25** in Acetone-d_6

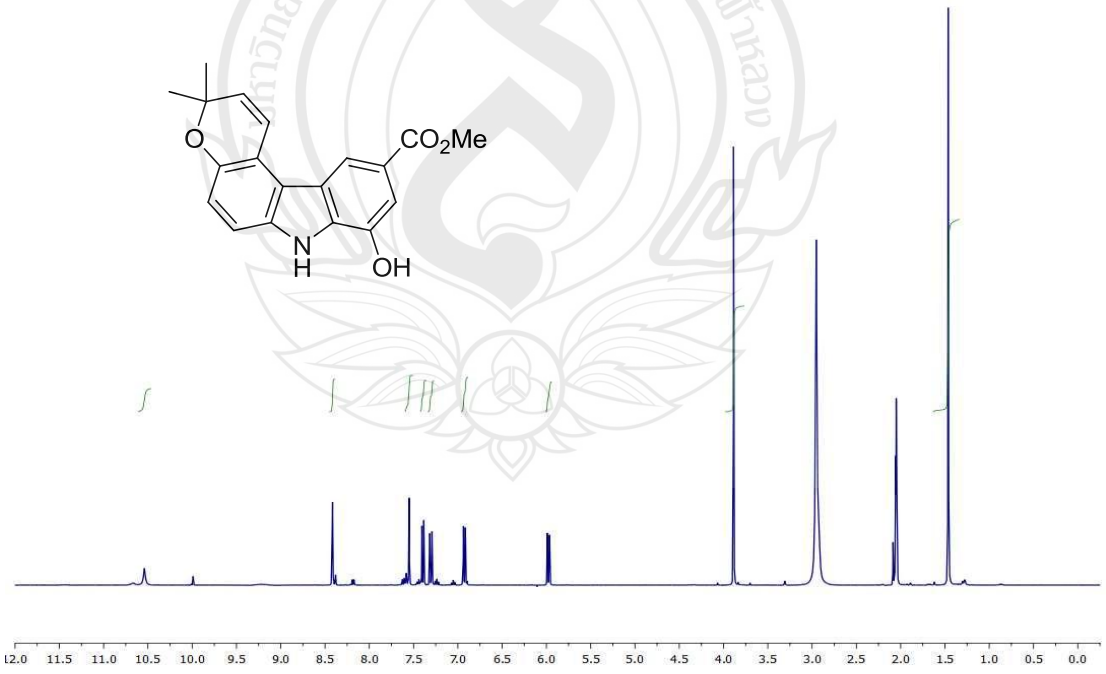

Figure A59 ^{1}H NMR Spectrum of **WM26** in Acetone-d_6 (400 MHz)

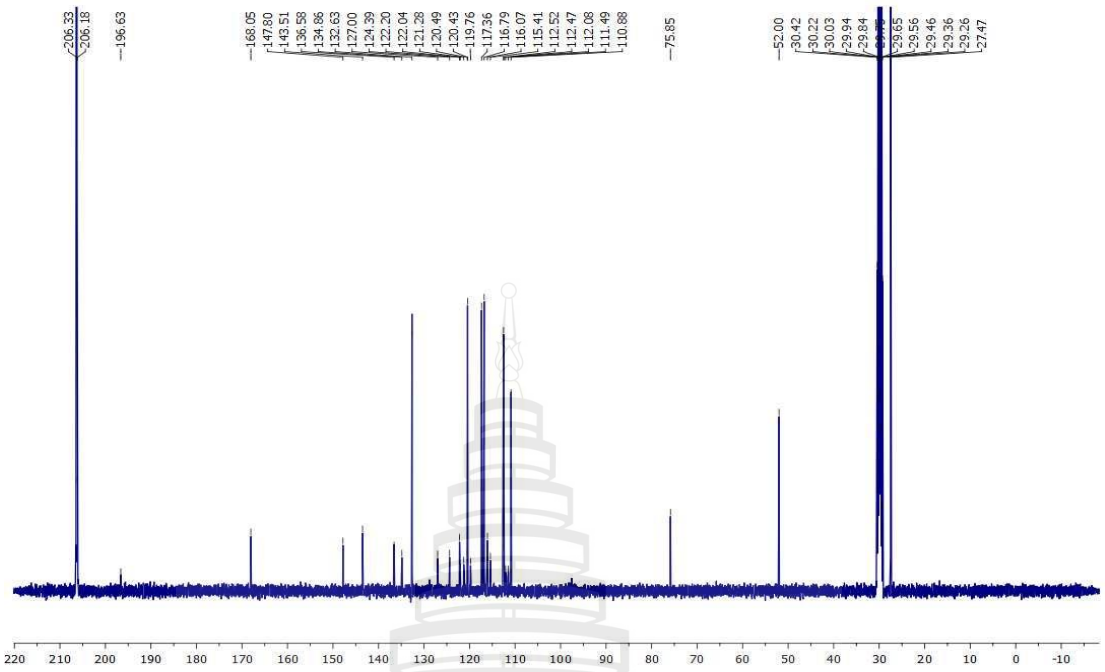

Figure A60 ^{1}H NMR Spectrum of **WM26** in Acetone-d_6 (400 MHz)

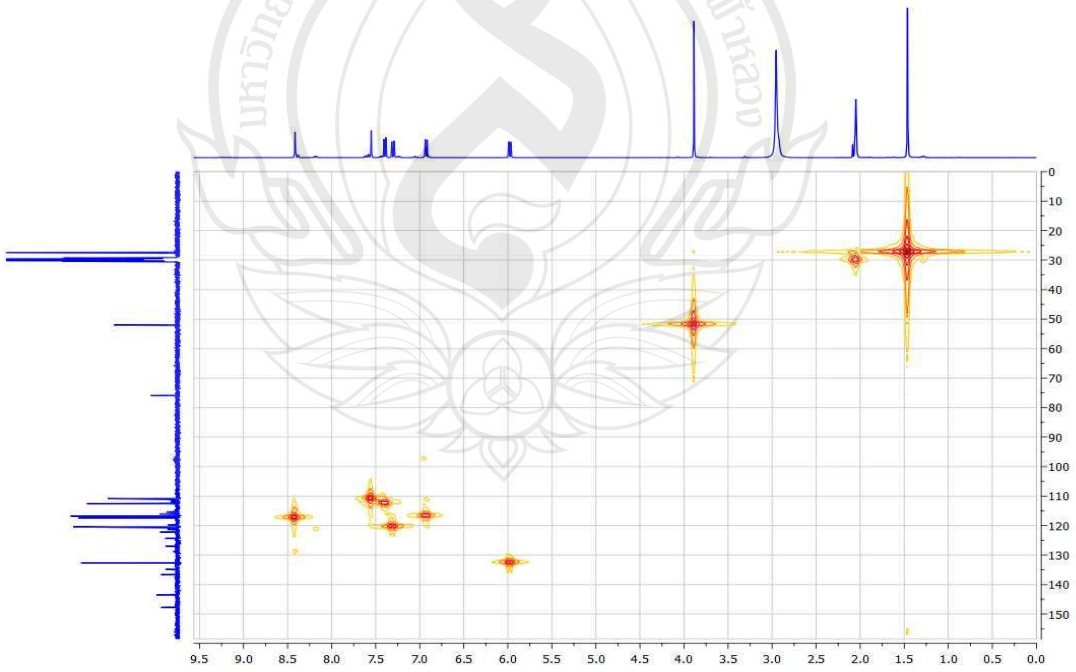

Figure A61 HMQC Spectrum of **WM26** in Acetone-d_6

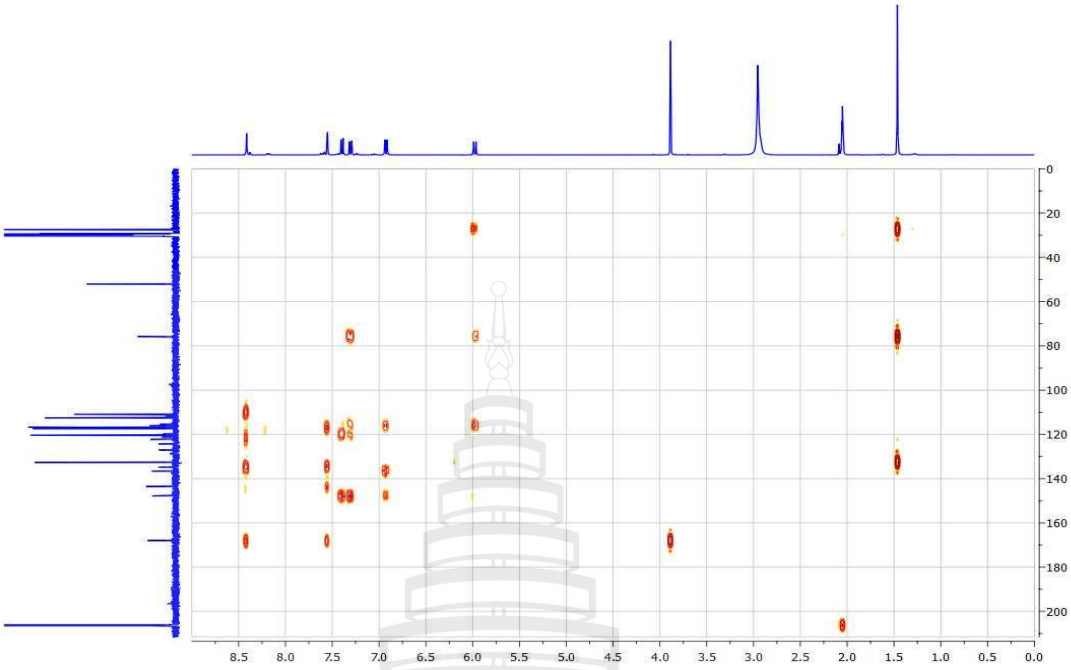

Figure A62 HMBC Spectrum of **WM26** in Acetone-d_6

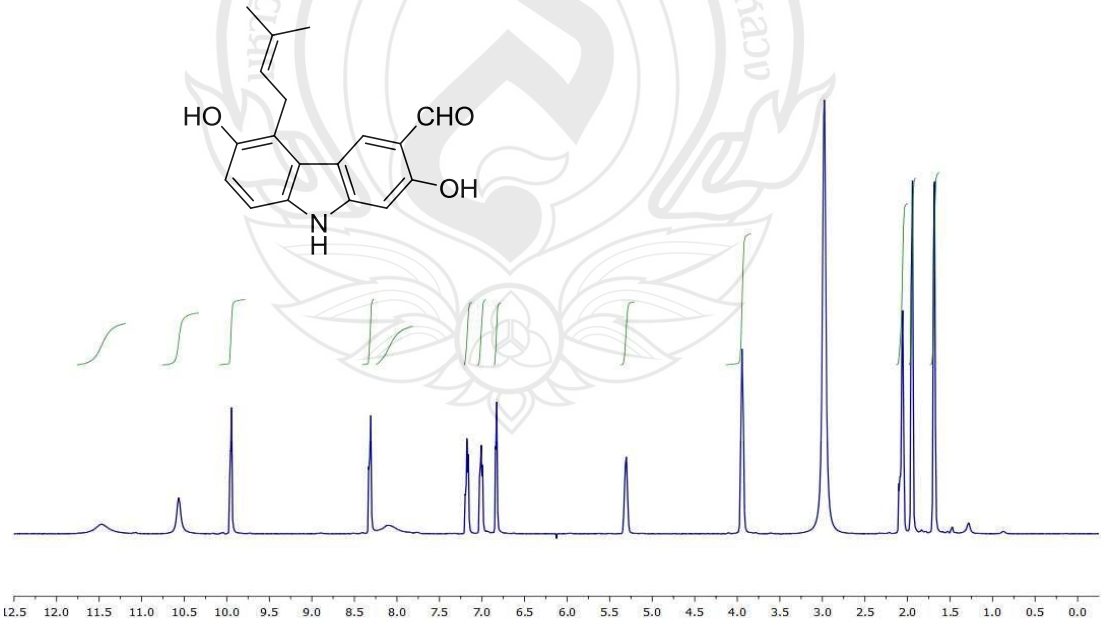

Figure A63 ^{1}H NMR Spectrum of **WM27** in Acetone-d_6 (400 MHz)

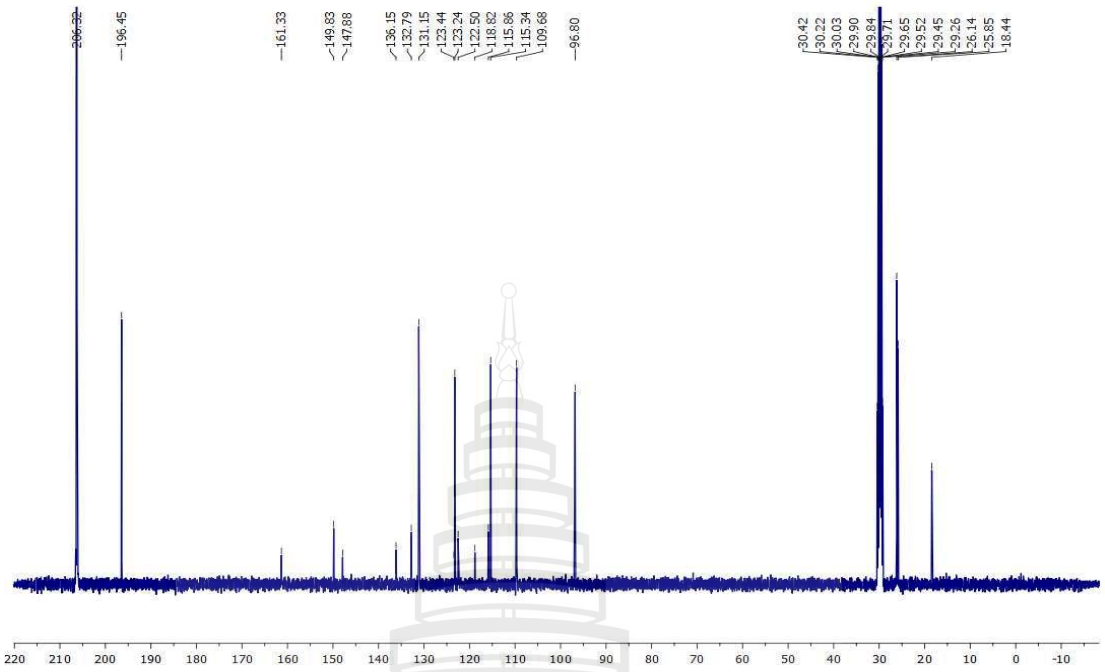

Figure A64 ^{13}C NMR Spectrum of **WM27** in Acetone-d_6 (100 MHz)

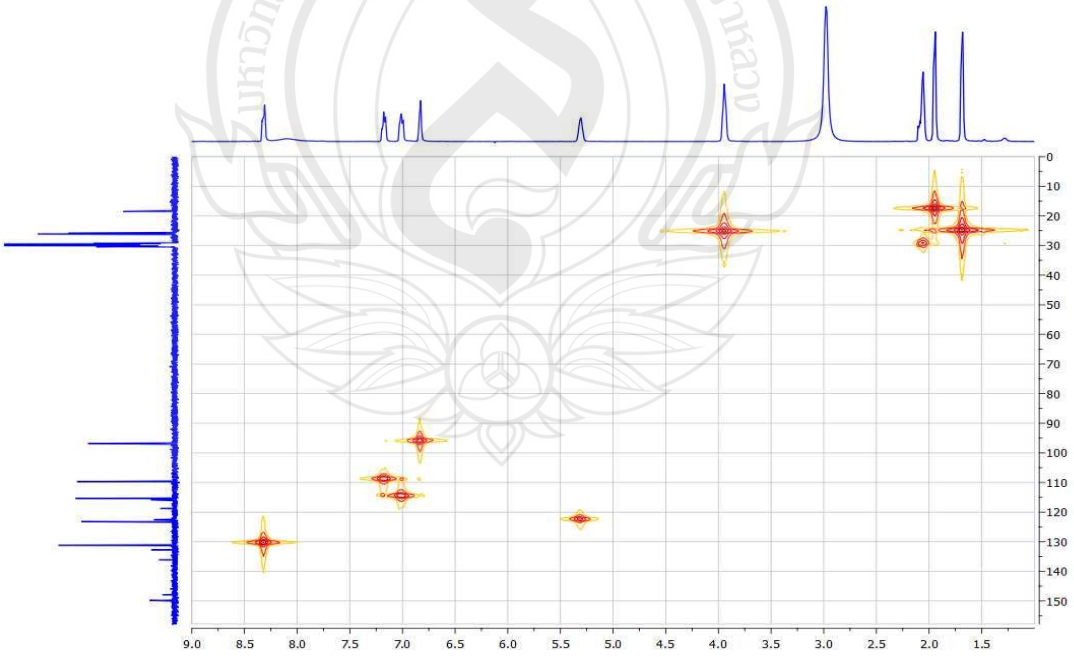

Figure A65 HMQC Spectrum of **WM27** in Acetone-d_6

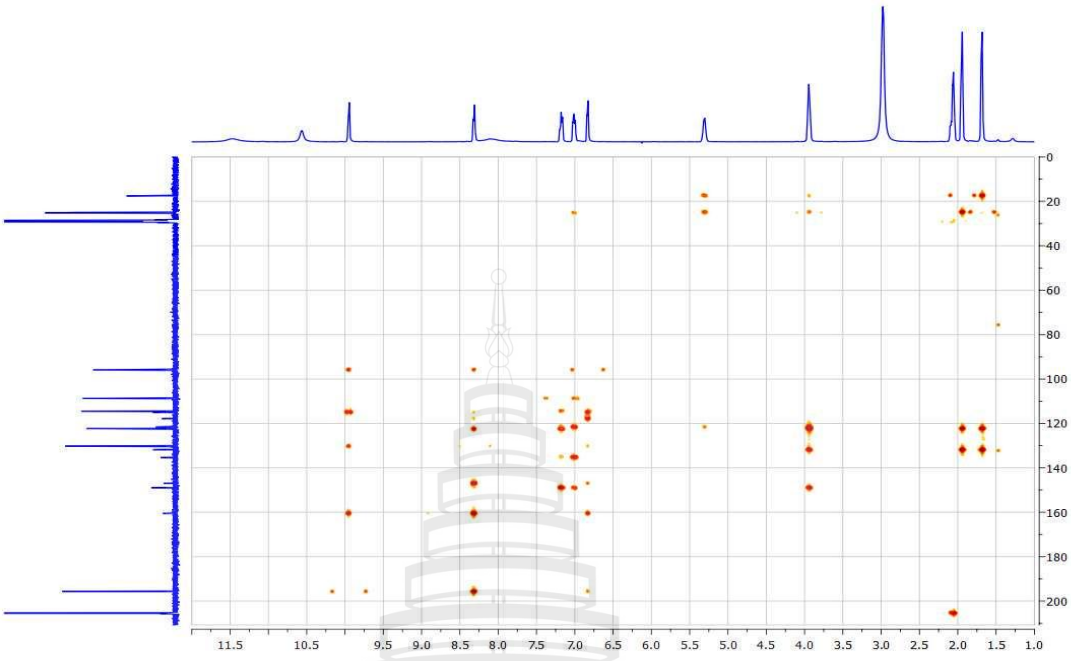

Figure A66 HMBC Spectrum of **WM27** in Acetone-d_6

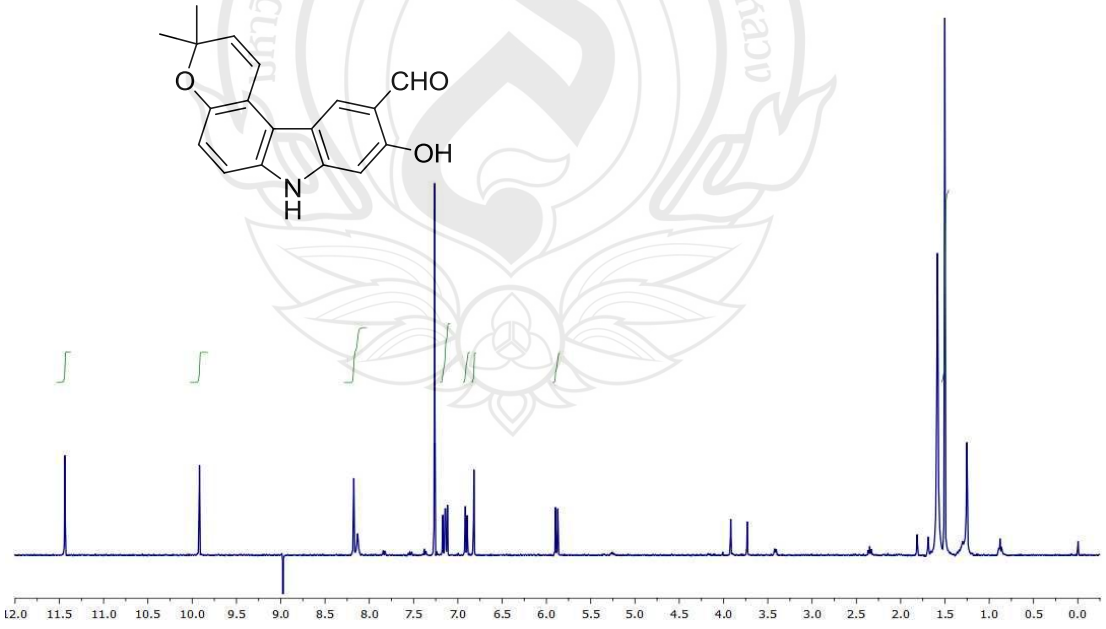

Figure A67 ^{1}H NMR Spectrum of **WM28** in $CDCl_3$ (400 MHz)

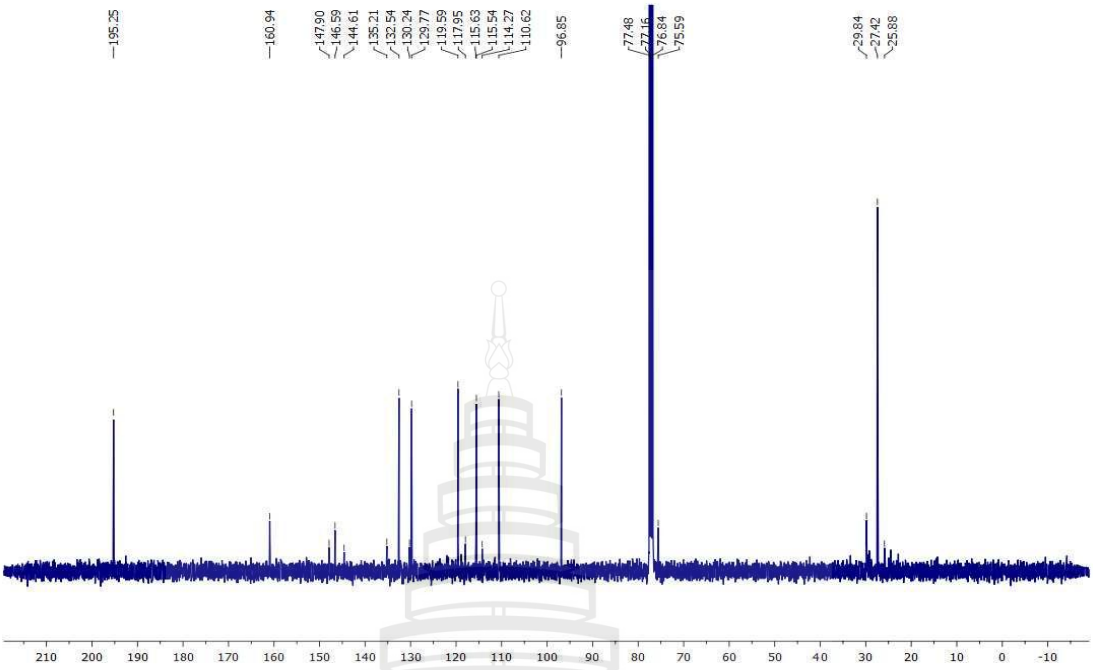

Figure A68 ^{13}C NMR Spectrum of **WM28** in $CDCl_3$ (100 MHz)

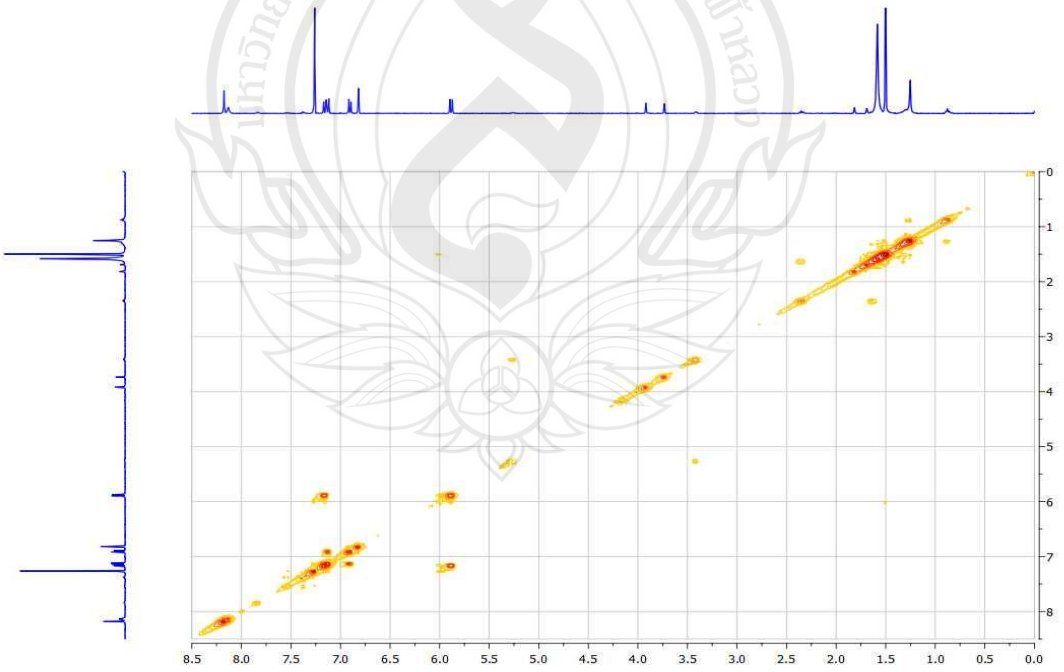

Figure A69 COSY Spectrum of **WM28** in $CDCl_3$

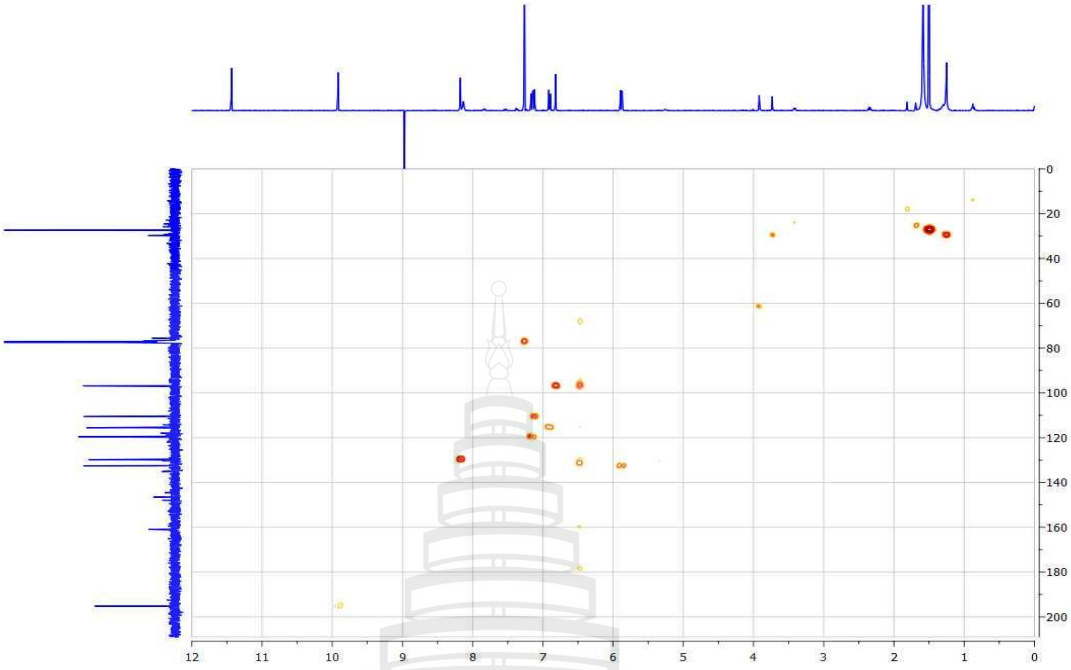

Figure A70 HMQC Spectrum of **WM28** in $CDCl_3$

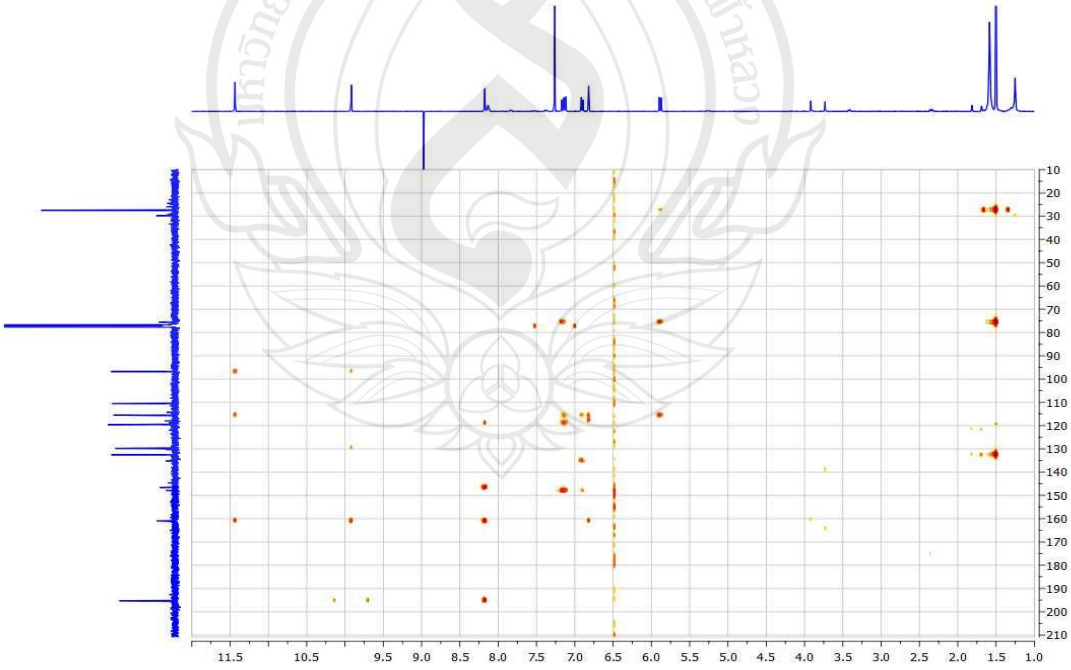

Figure A71 HMBC Spectrum of **WM28** in $CDCl_3$

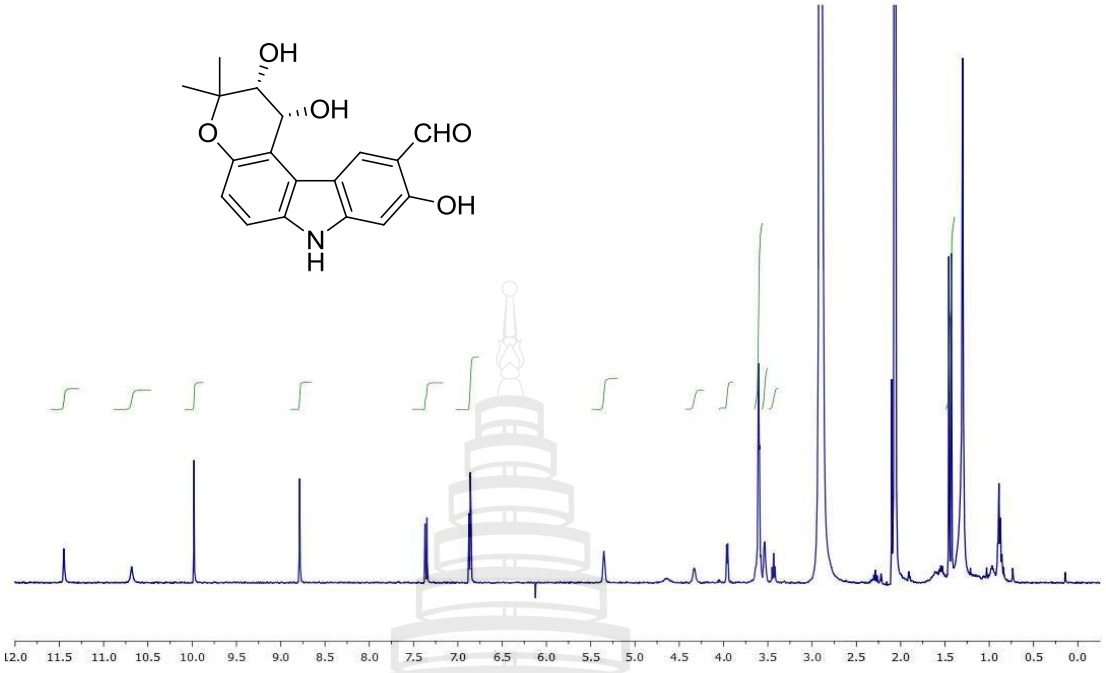

Figure A72 ^{1}H NMR Spectrum of **WM29** in Acetone-d_6 (500 MHz)

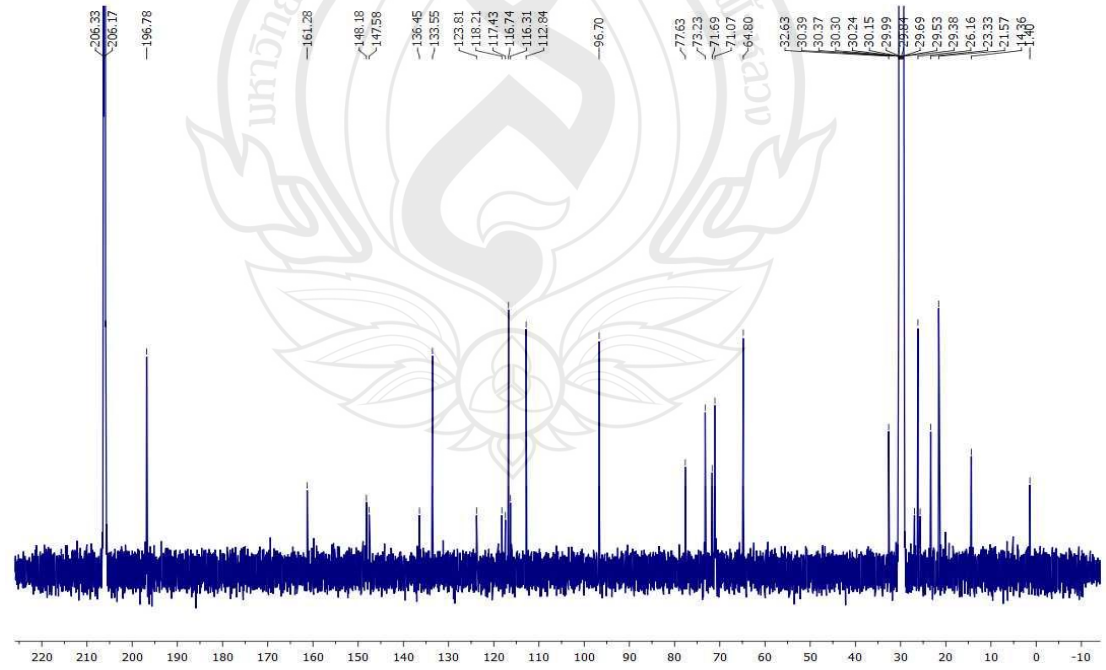

Figure A73 ^{13}C NMR Spectrum of **WM29** in Acetone-d_6 (125 MHz)

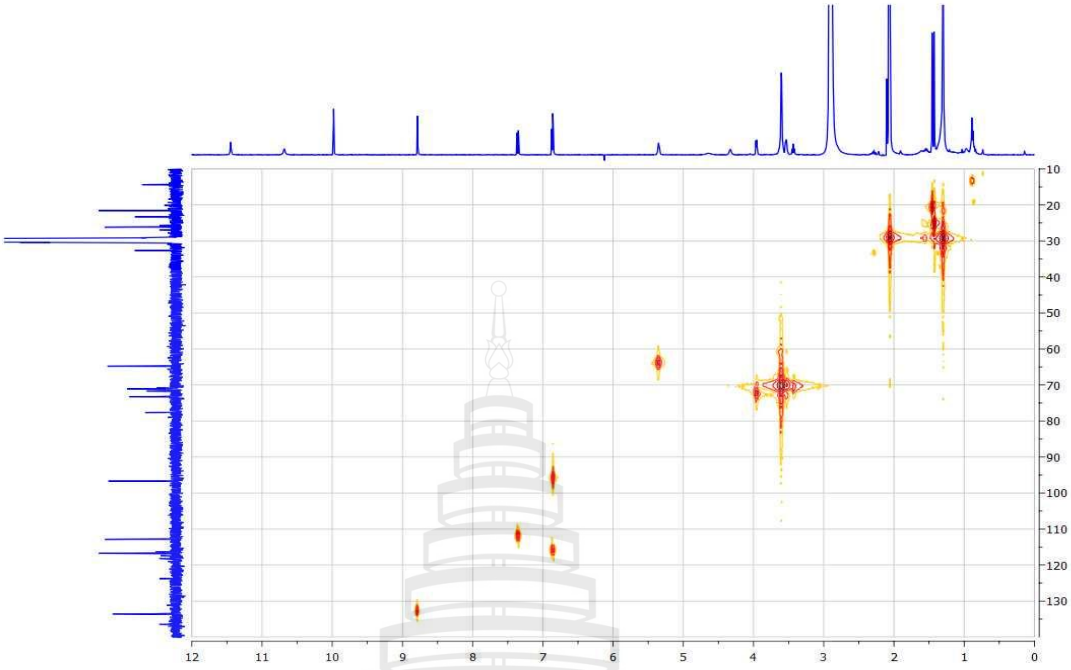

Figure A74 HMQC Spectrum of **WM29** in Acetone-d_6

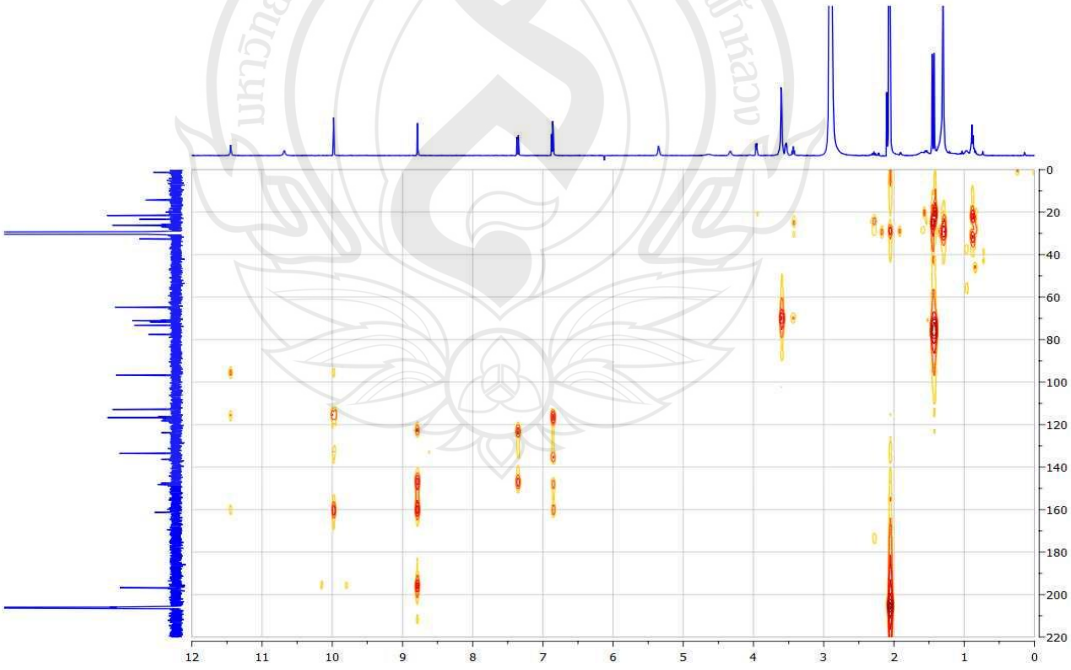

Figure A75 HMBC Spectrum of **WM29** in Acetone-d_6

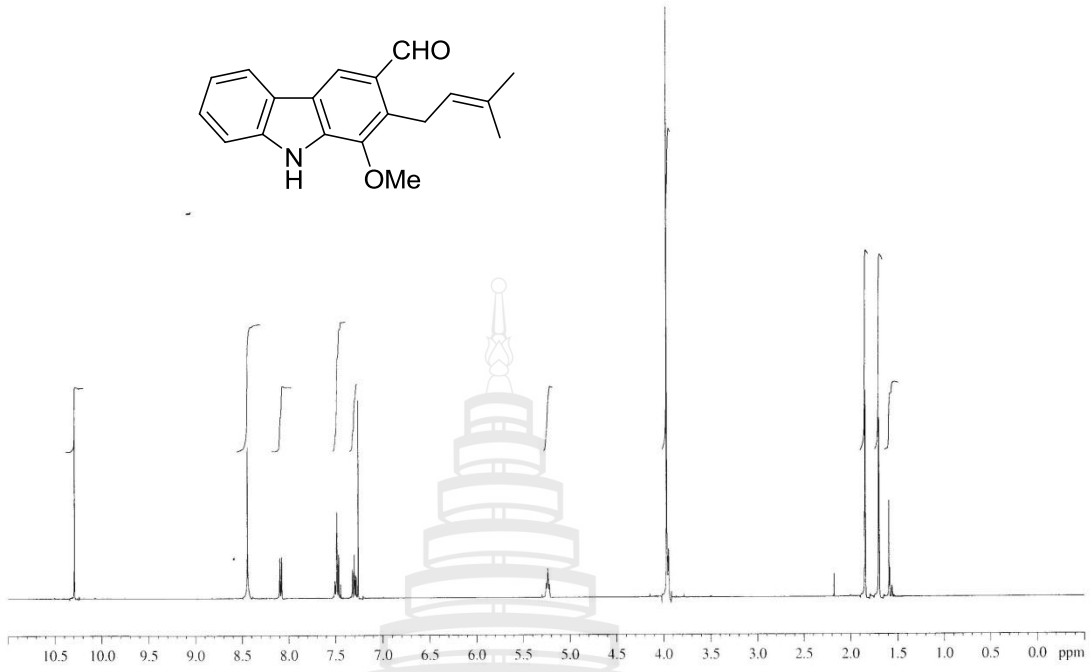

Figure A76 ^{1}H NMR Spectrum of **WM30** in $CDCl_3$ (400 MHz)

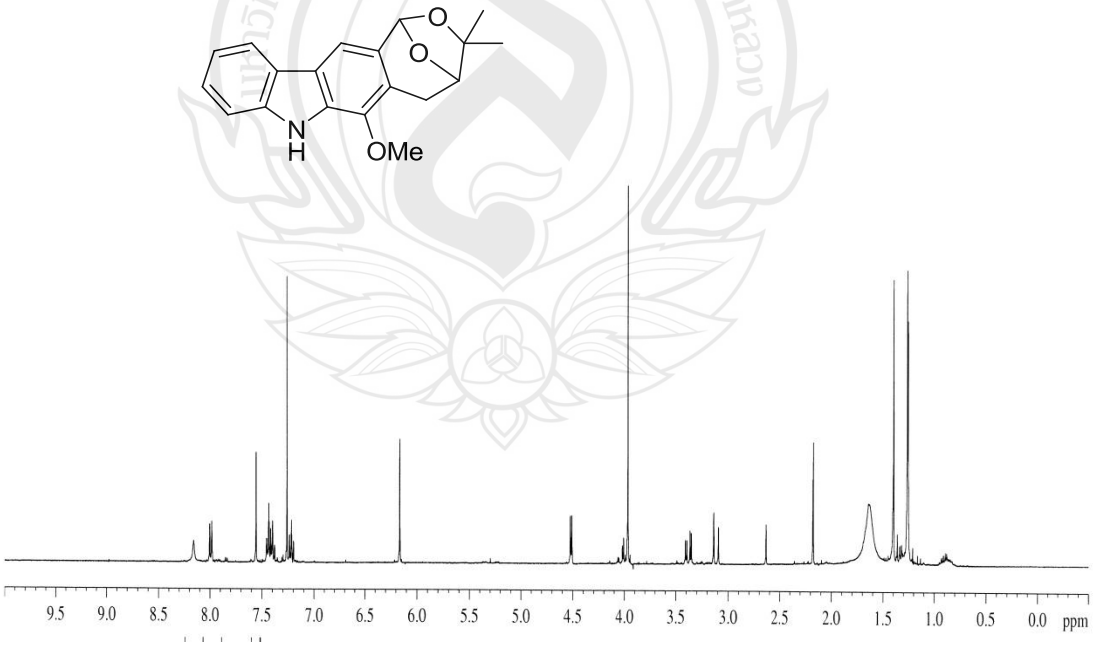

Figure A77 ^{1}H NMR Spectrum of **WM31** in $CDCl_3$ (400 MHz)

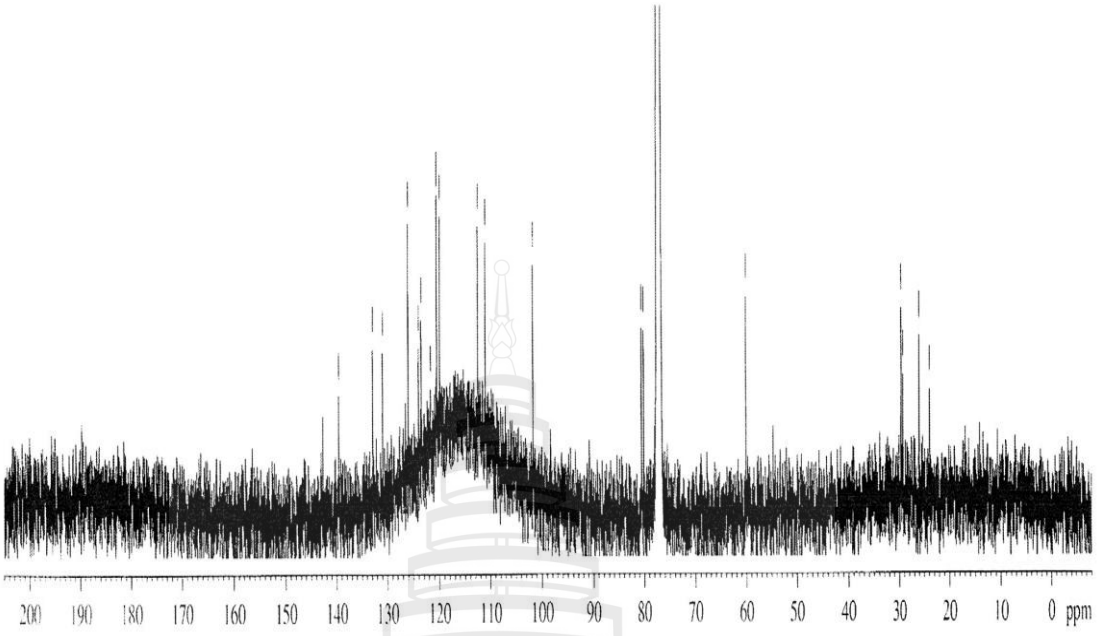

Figure A78 ^{13}C NMR Spectrum of **WM31** in $CDCl_3$ (100 MHz)

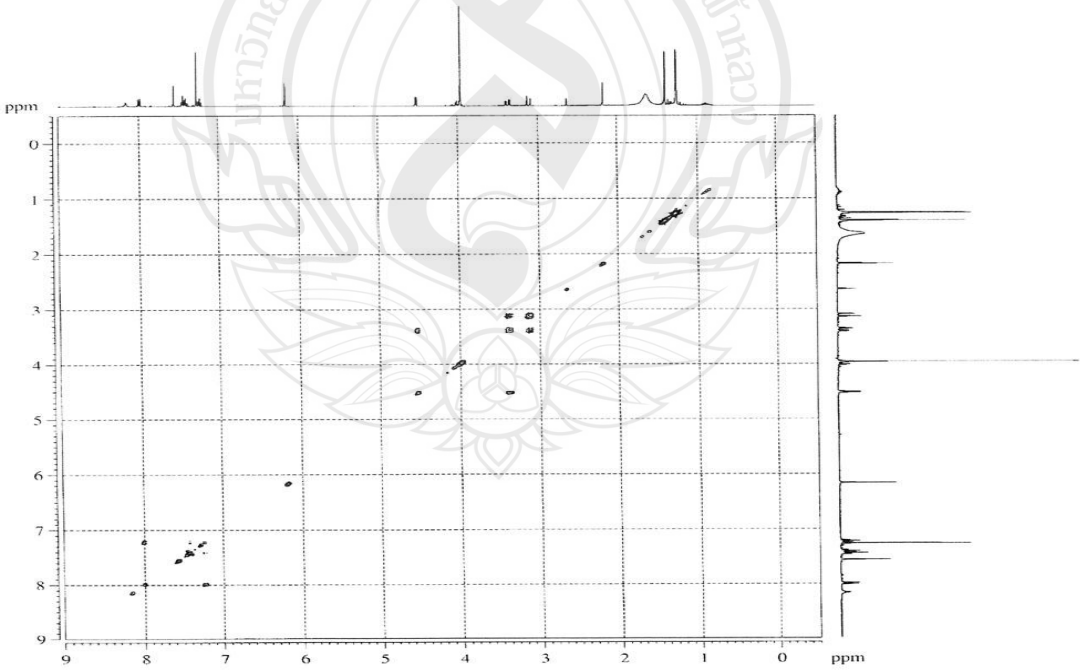

Figure A79 COSY Spectrum of **WM31** in $CDCl_3$

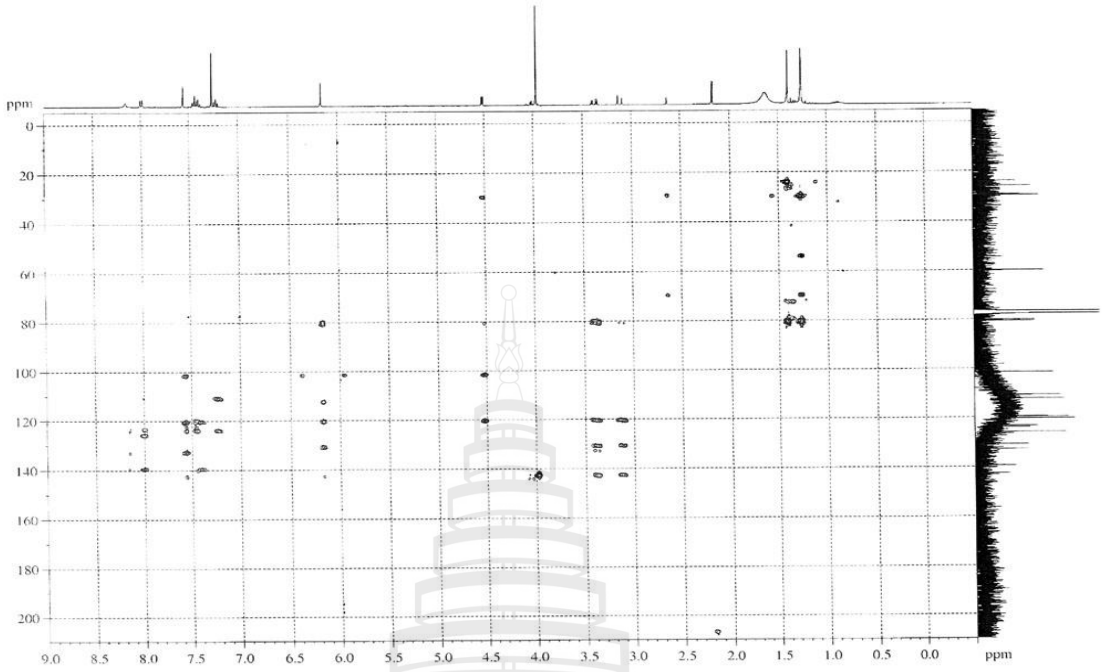

Figure A80 HMQC Spectrum of **WM31** in $CDCl_3$

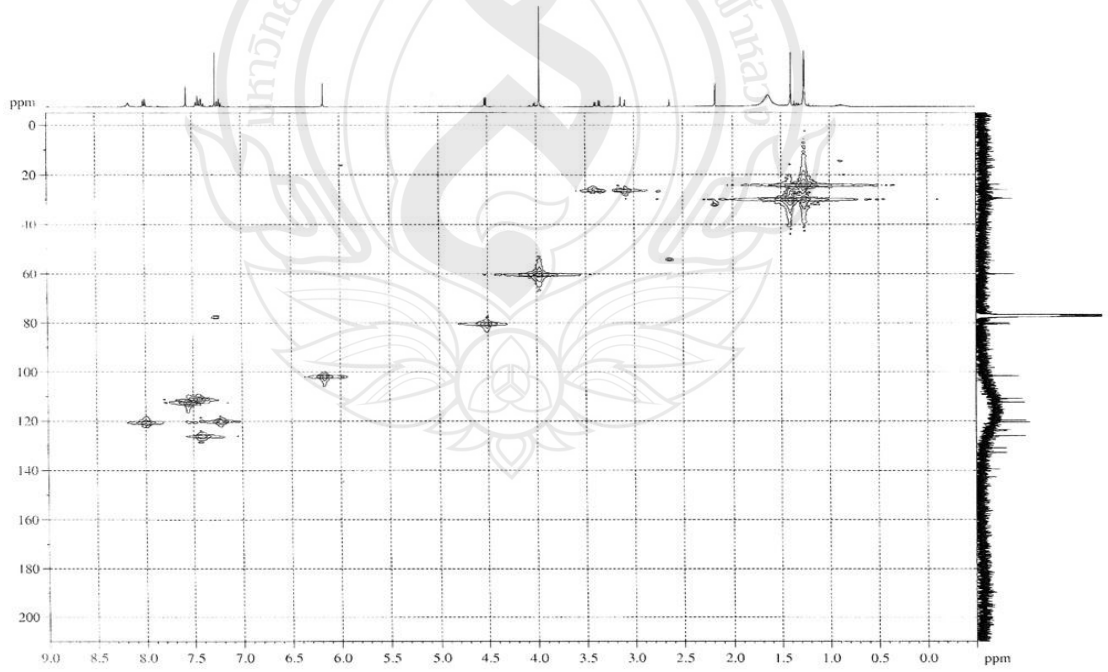

Figure A81 HMBC Spectrum of **WM31** in $CDCl_3$

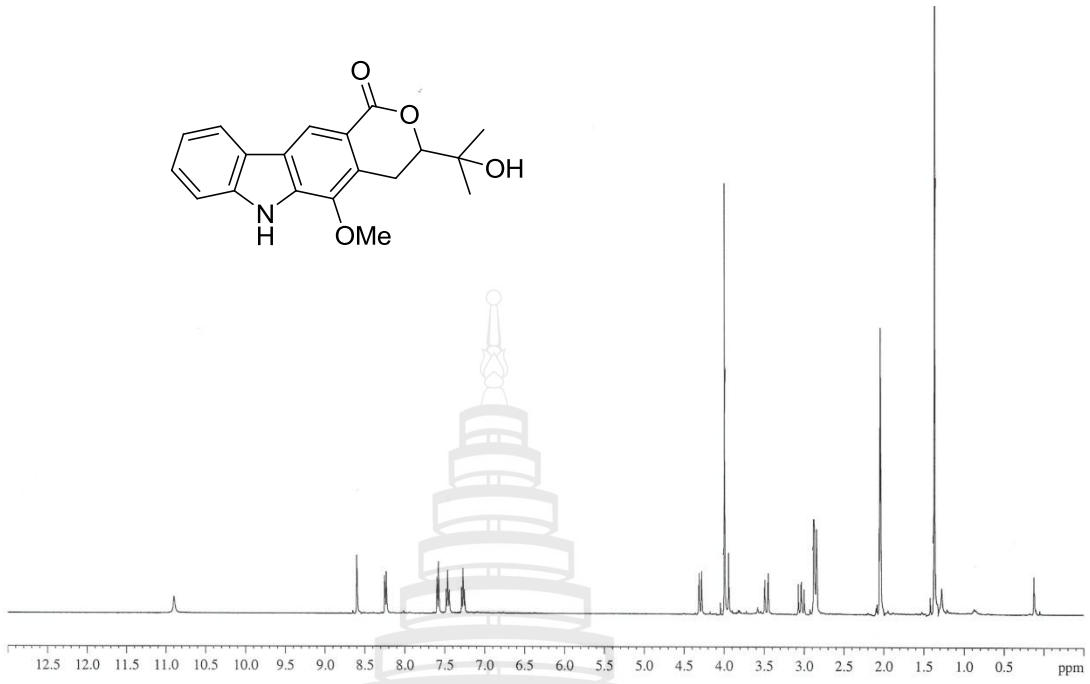

Figure A82 ^{1}H NMR Spectrum of **WM32** in Acetone-d_6 (400 MHz)

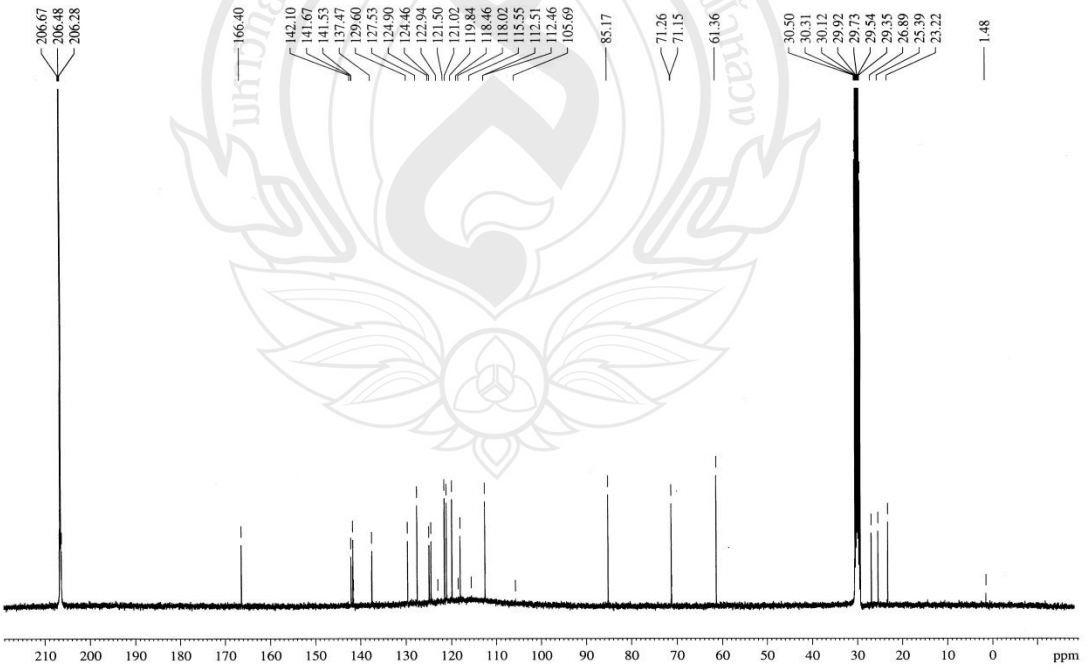

Figure A83 ^{13}C NMR Spectrum of **WM32** in Acetone-d_6 (100 MHz)

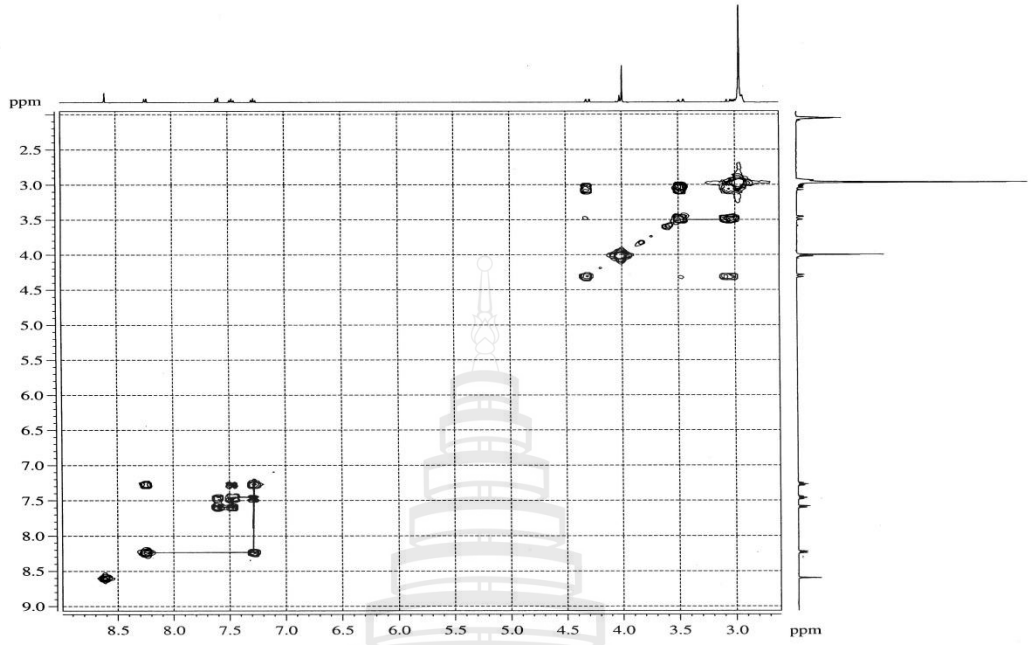

Figure A84 COSY Spectrum of **WM32** in Acetone-d_6

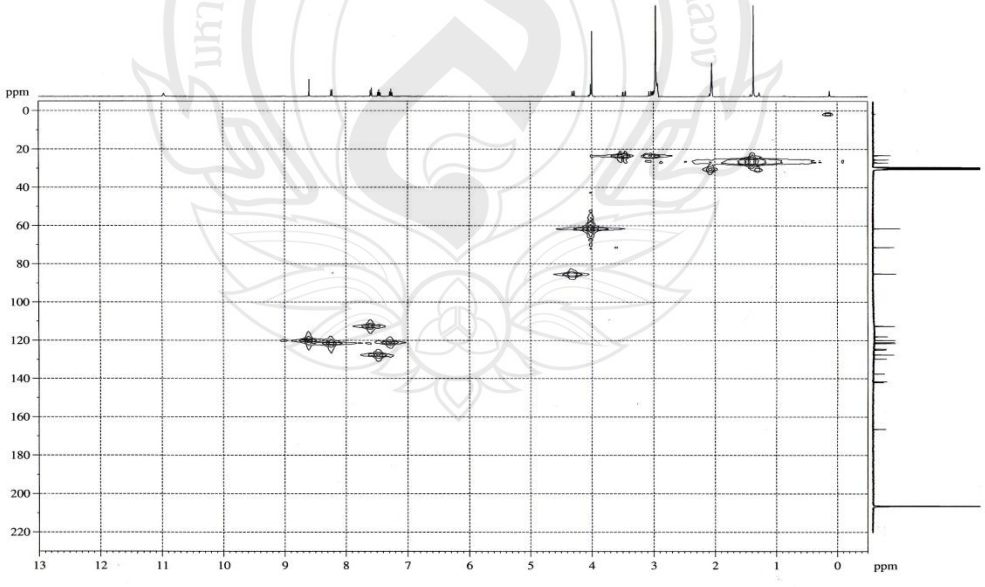

Figure A85 HMQC Spectrum of **WM32** in Acetone-d_6

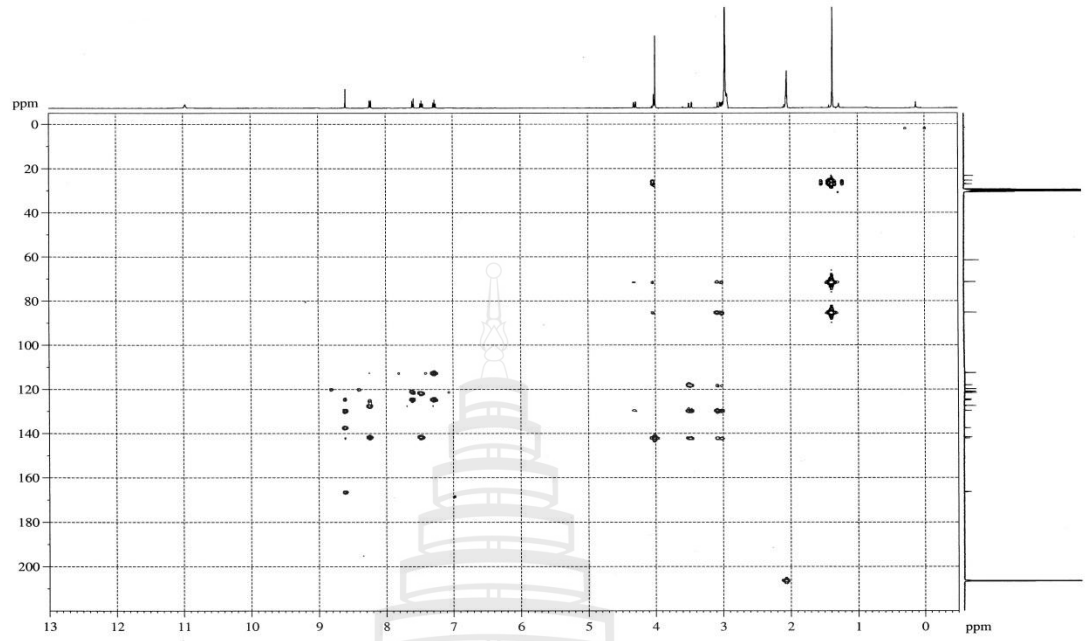

Figure A86 HMBC Spectrum of **WM32** in Acetone-d_6

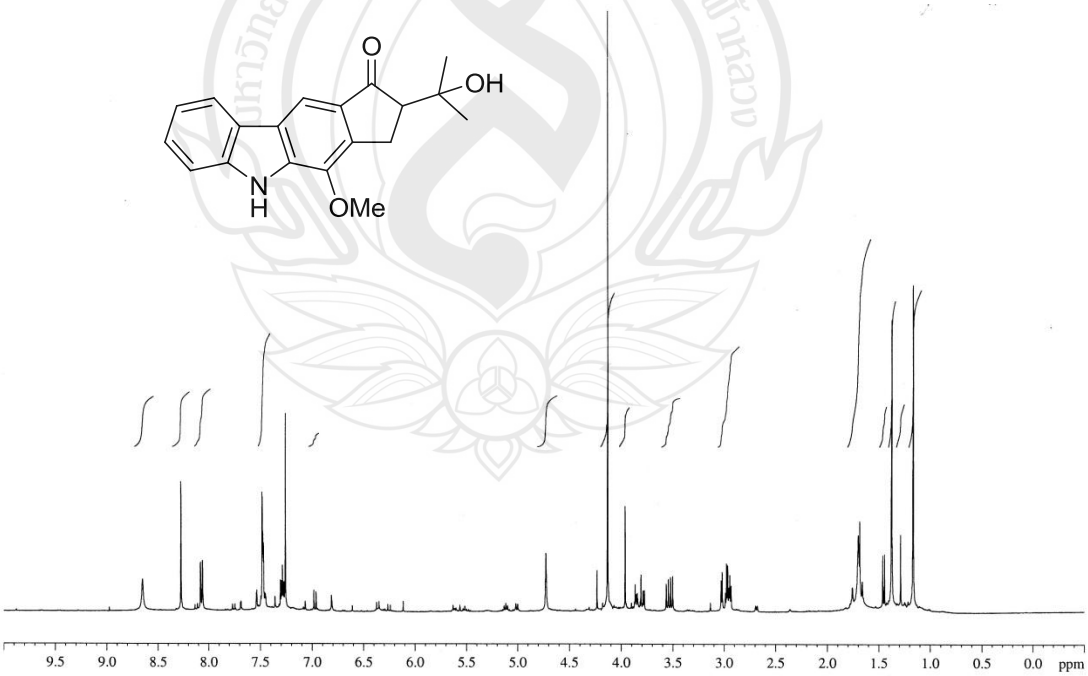

Figure A87 ^{1}H NMR Spectrum of **WM33** in $CDCl_3$ (400 MHz)

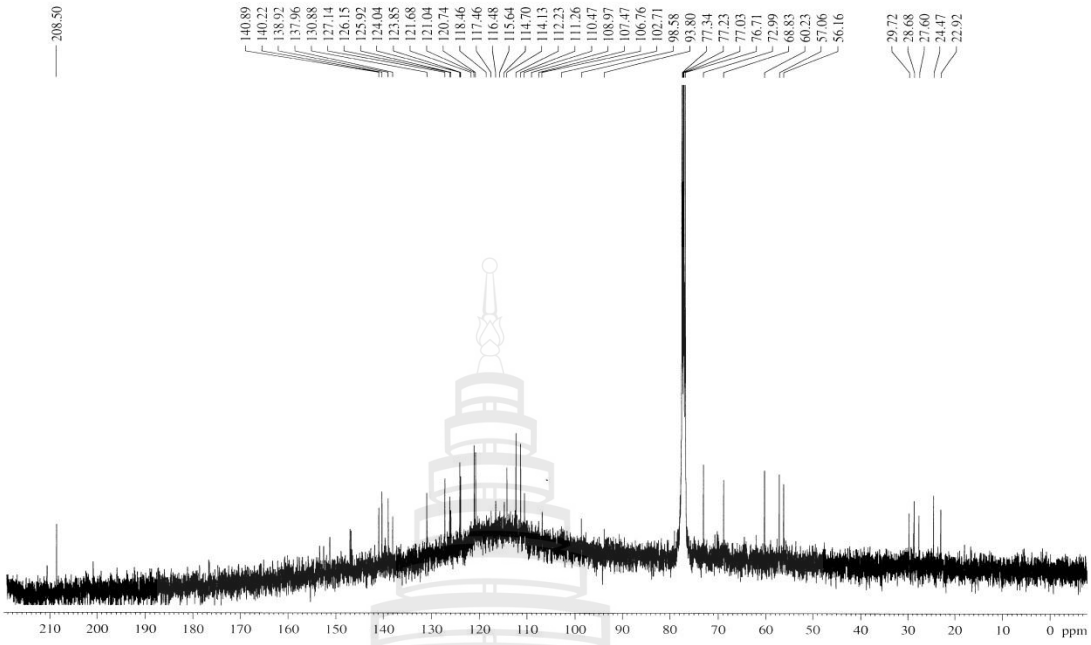

Figure A88 ^{13}C NMR Spectrum of **WM33** in $CDCl_3$ (100 MHz)

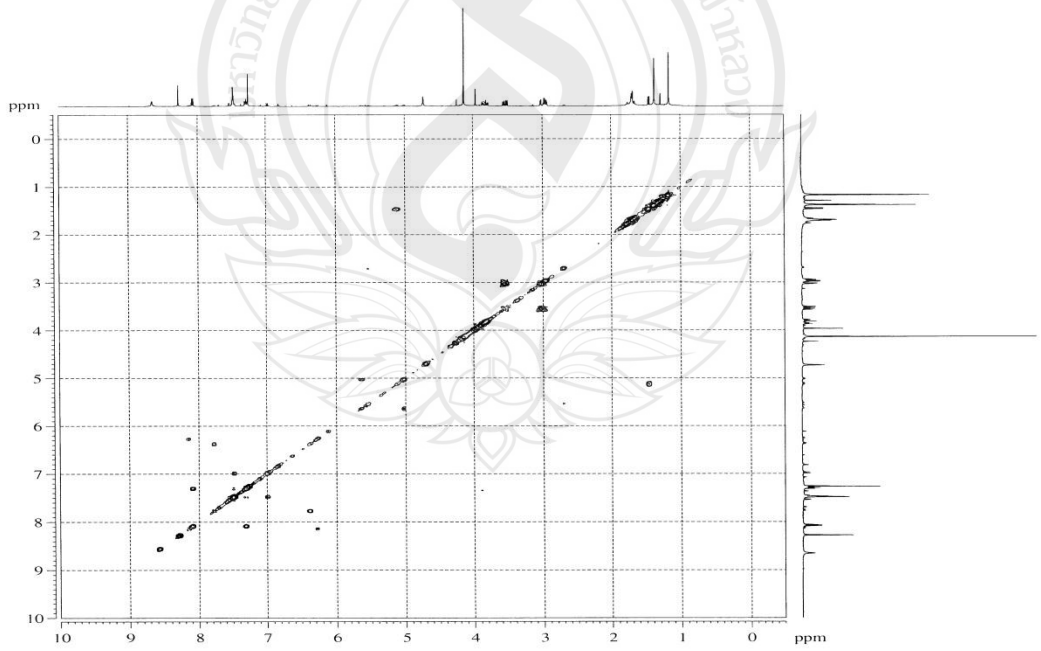

Figure A89 COSY Spectrum of **WM33** in $CDCl_3$

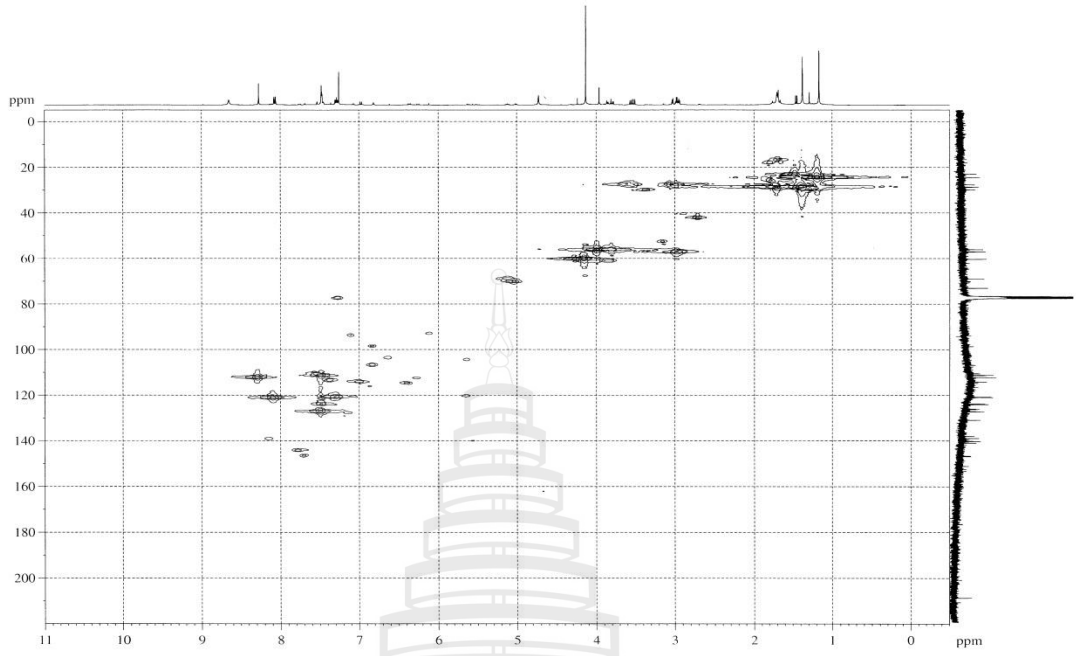

Figure A90 HMQC Spectrum of **WM33** in $CDCl_3$

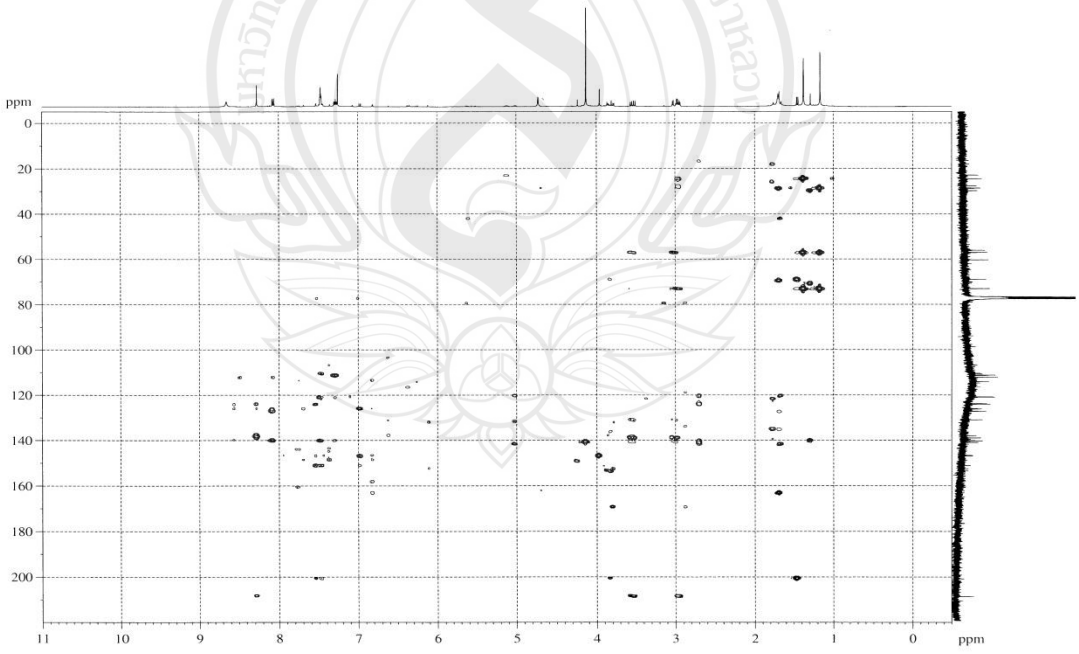

Figure A91 HMBC Spectrum of **WM33** in $CDCl_3$

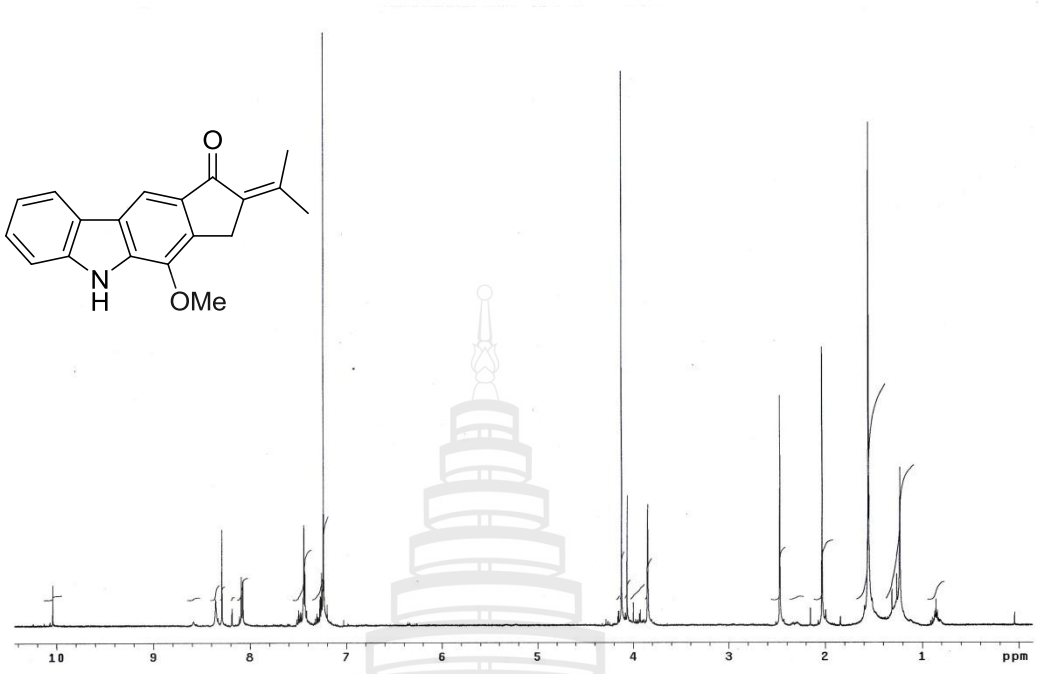

Figure A92 ^{1}H NMR Spectrum of **WM34** in $CDCl_3$ (500 MHz)

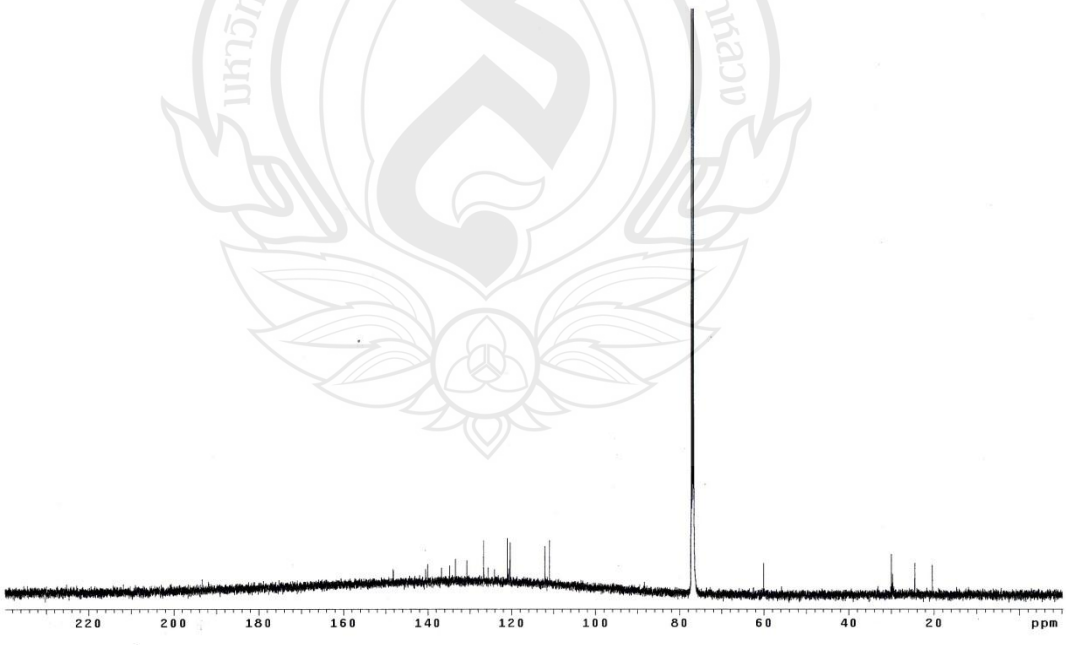

Figure A93 ^{13}C NMR Spectrum of **WM34** in $CDCl_3$ (125 MHz)

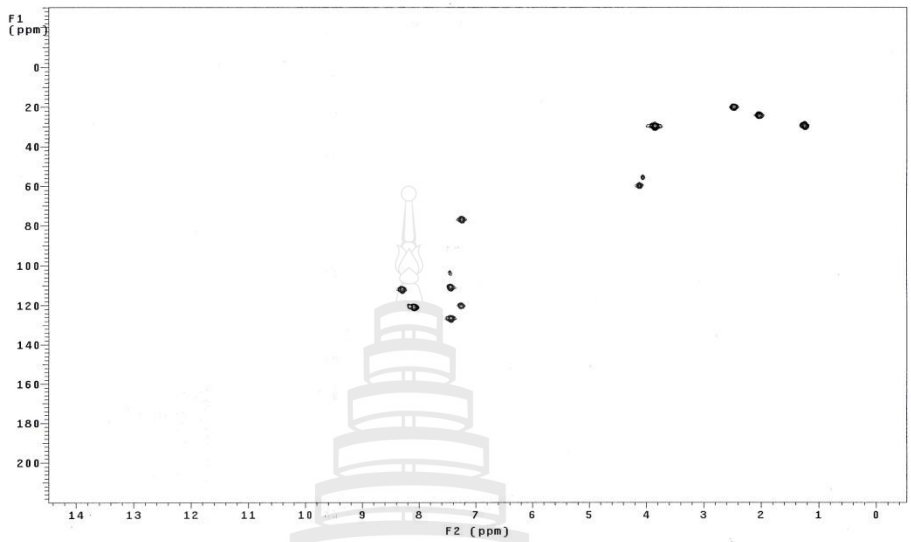

Figure A94 HMQC Spectrum of **WM34** in $CDCl_3$

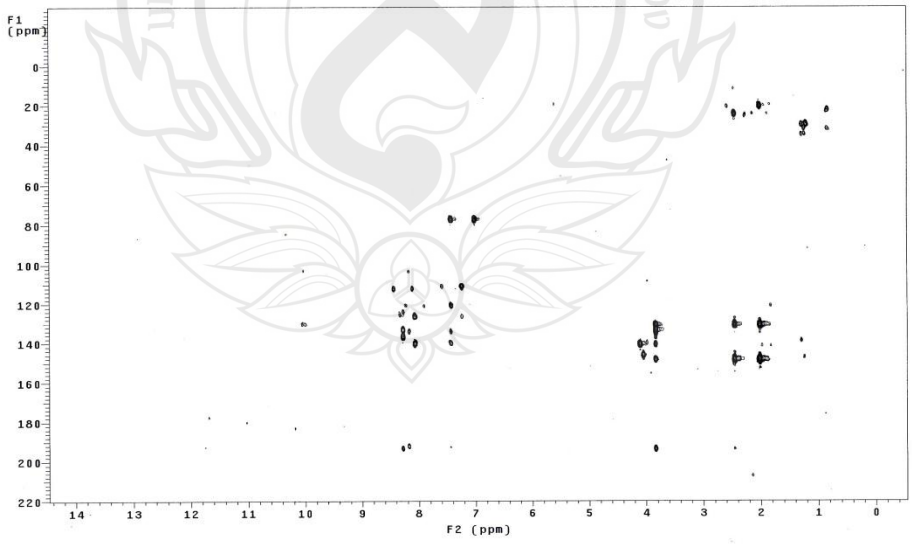

Figure A95 HMBC Spectrum of **WM34** in $CDCl_3$

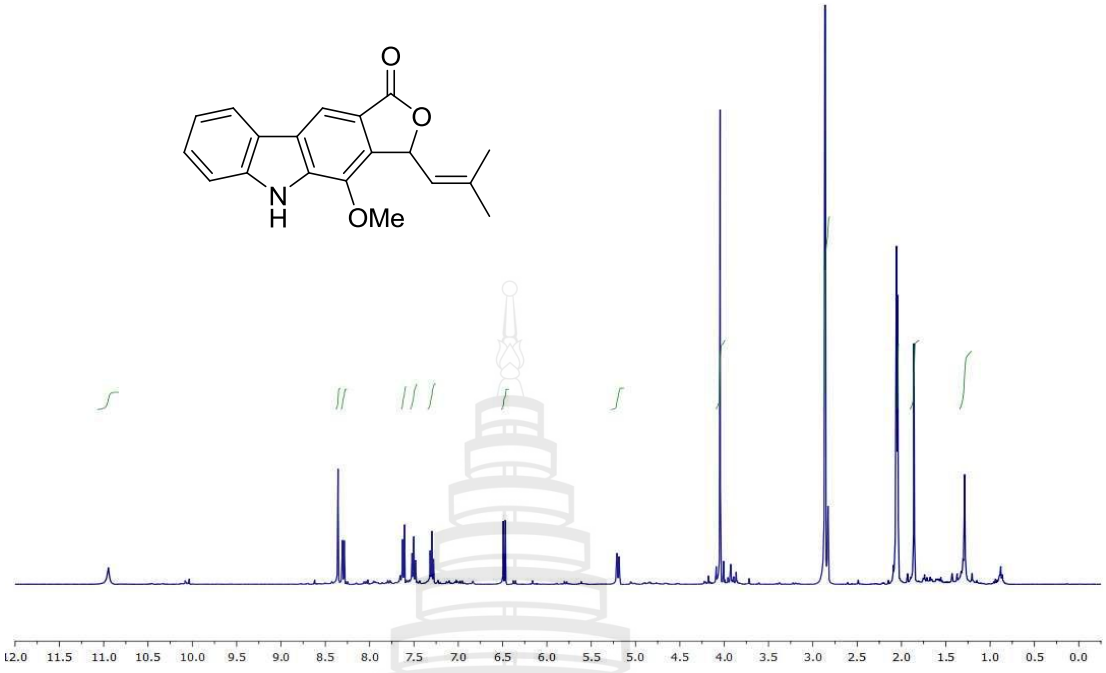

Figure A96 ^{1}H NMR Spectrum of **WM35** in Acetone-d_6 (400 MHz)

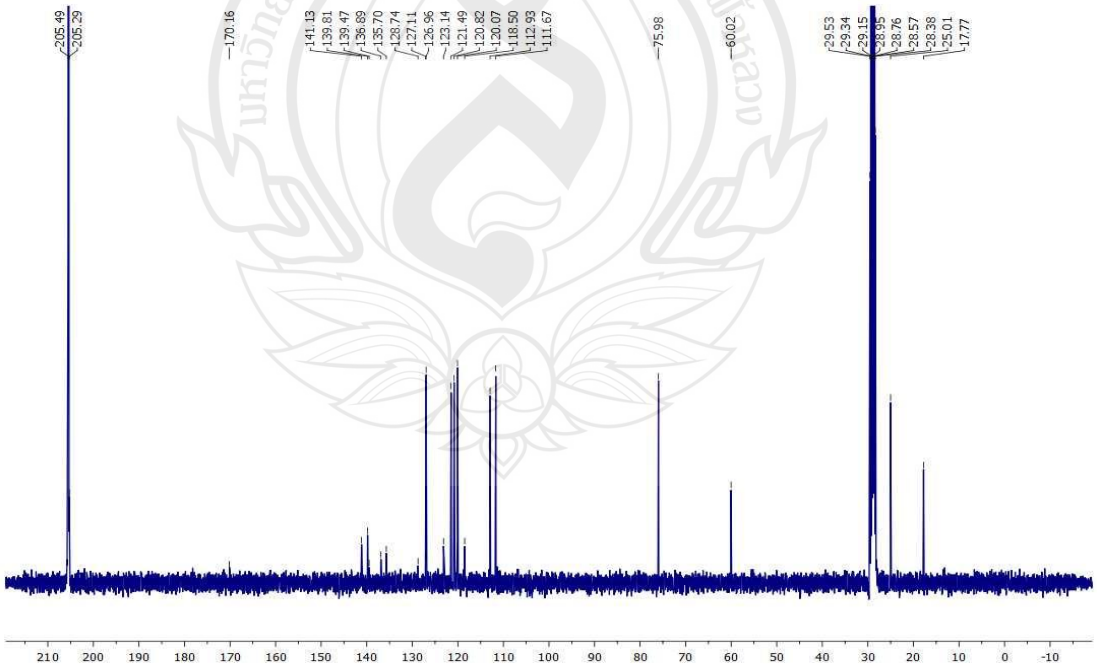

Figure A97 ^{13}C NMR Spectrum of **WM35** in Acetone-d_6 (100 MHz)

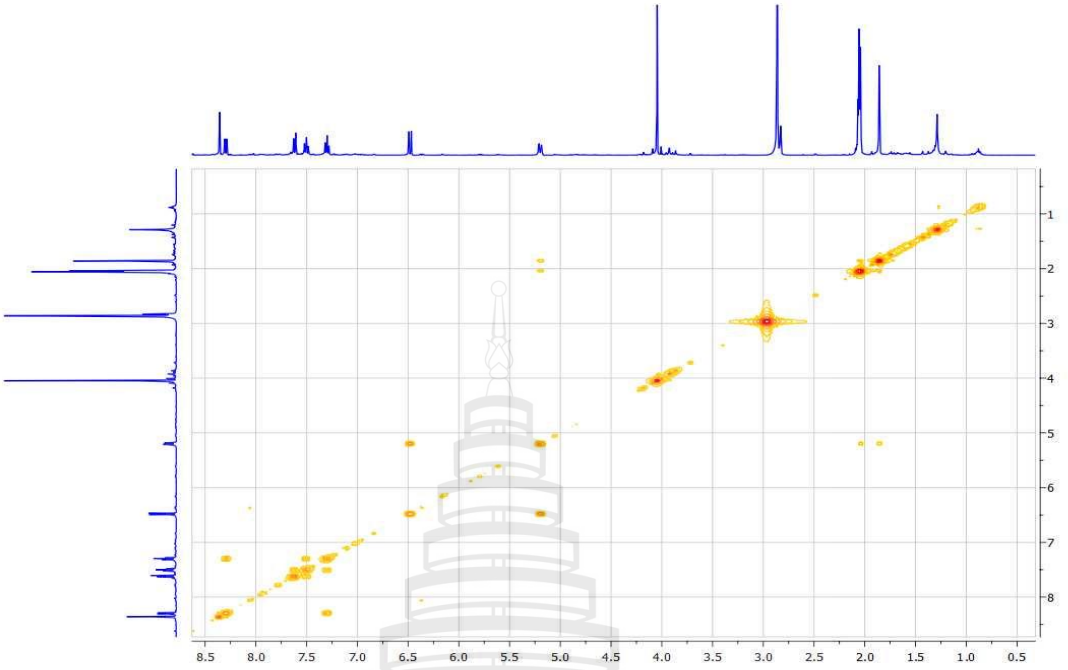

Figure A98 COSY Spectrum of **WM35** in Acetone-d_6

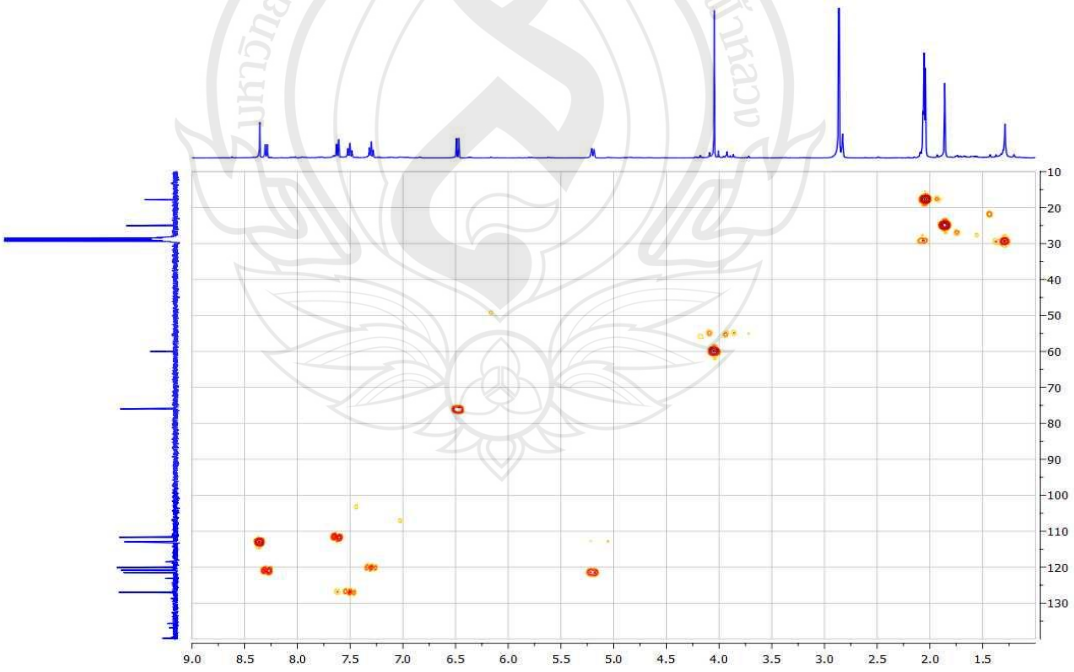

Figure A99 HMQC Spectrum of **WM35** in Acetone-d_6

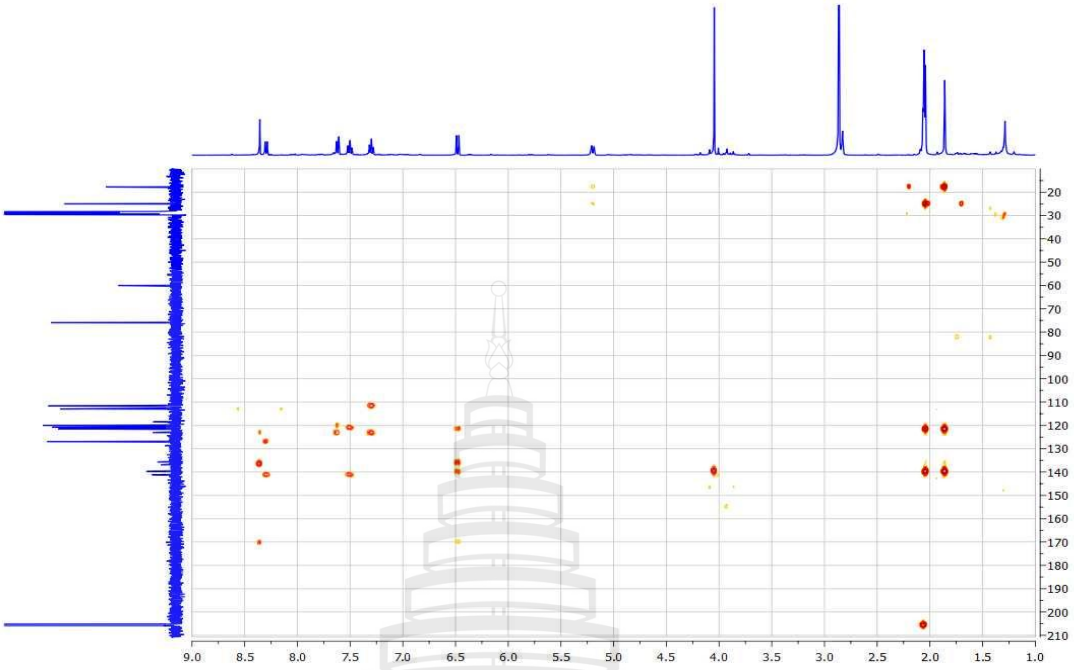

Figure A100 HMBC Spectrum of **WM35** in Acetone-d_6

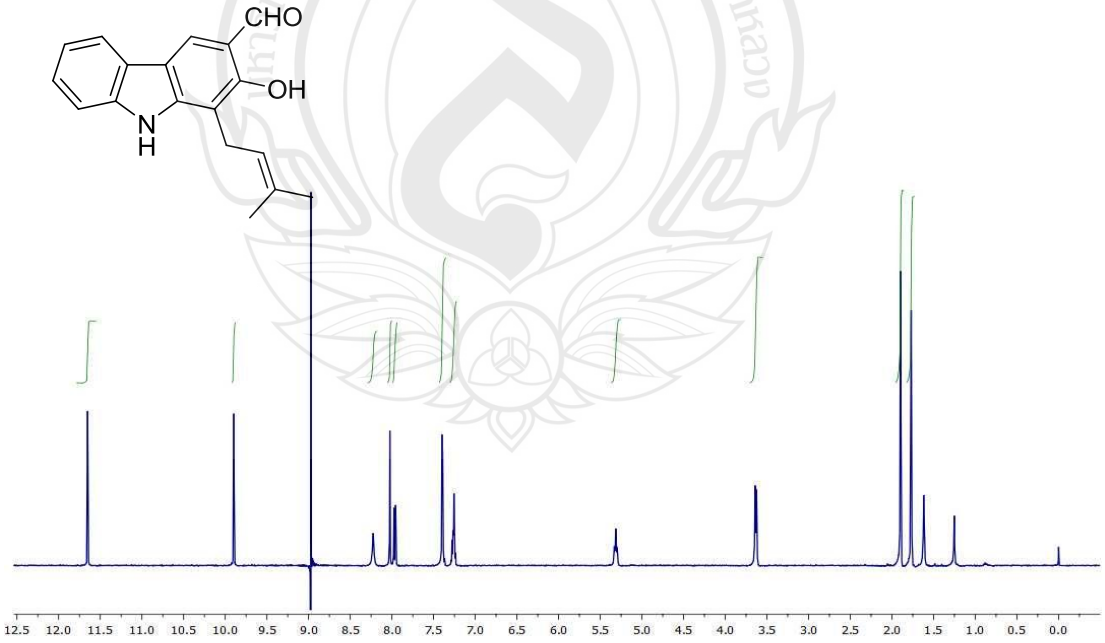

Figure A101 ^{1}H NMR Spectrum of **WM36** in $CDCl_3$ (400 MHz)

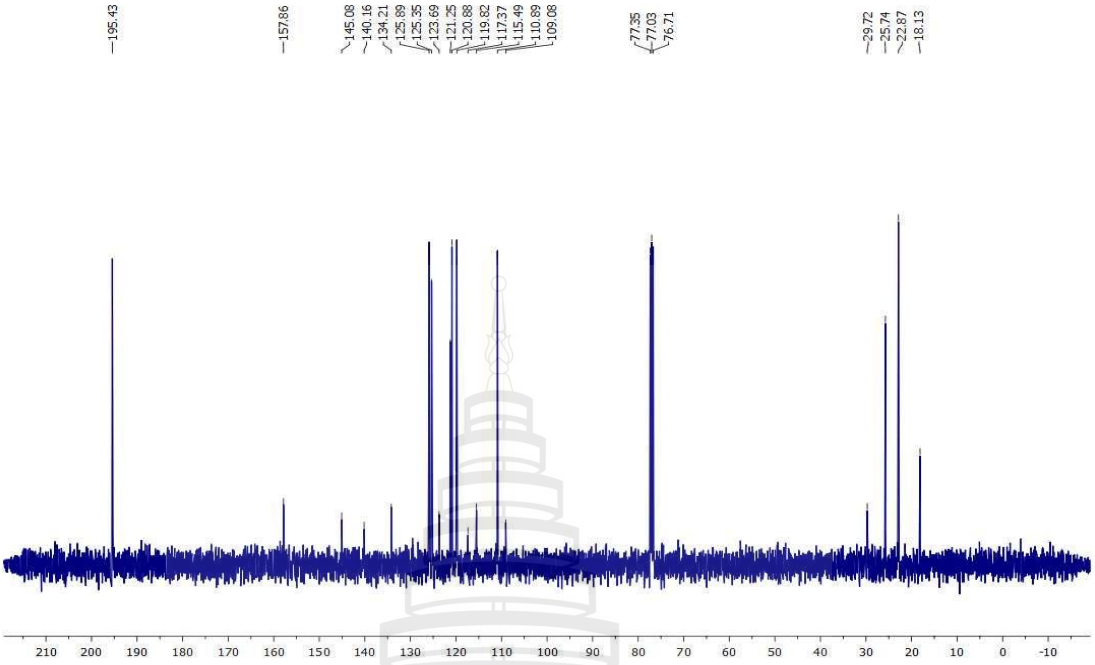

Figure A102 ^{13}C NMR Spectrum of **WM36** in $CDCl_3$ (100 MHz)

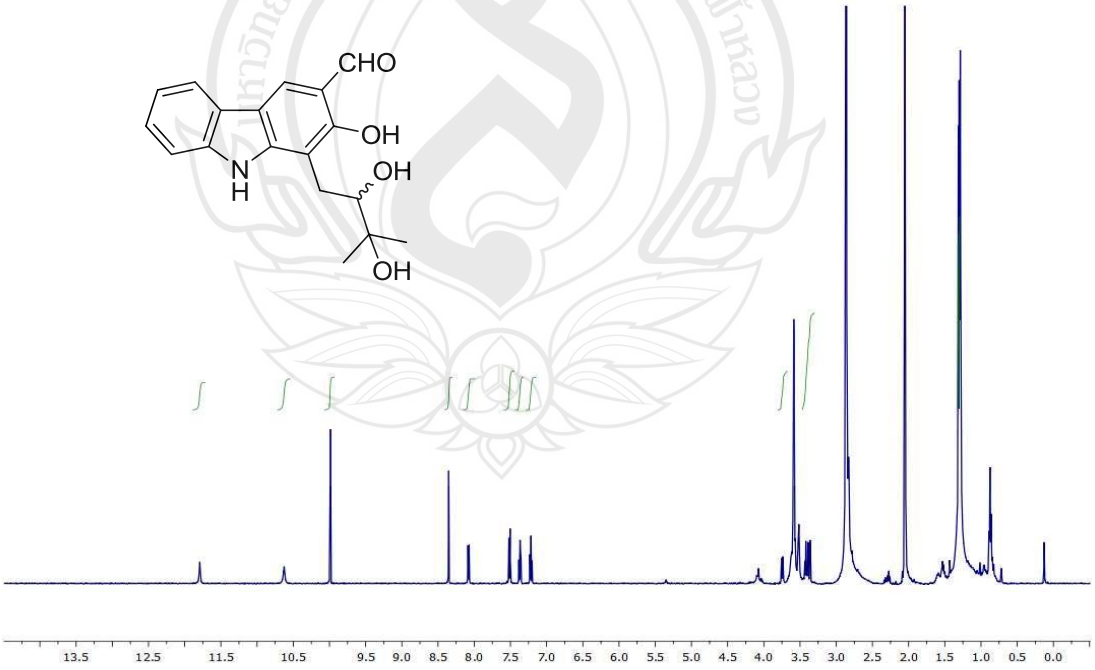

Figure A103 ^{1}H NMR Spectrum of **WM37** in Acetone-d_6 (500 MHz)

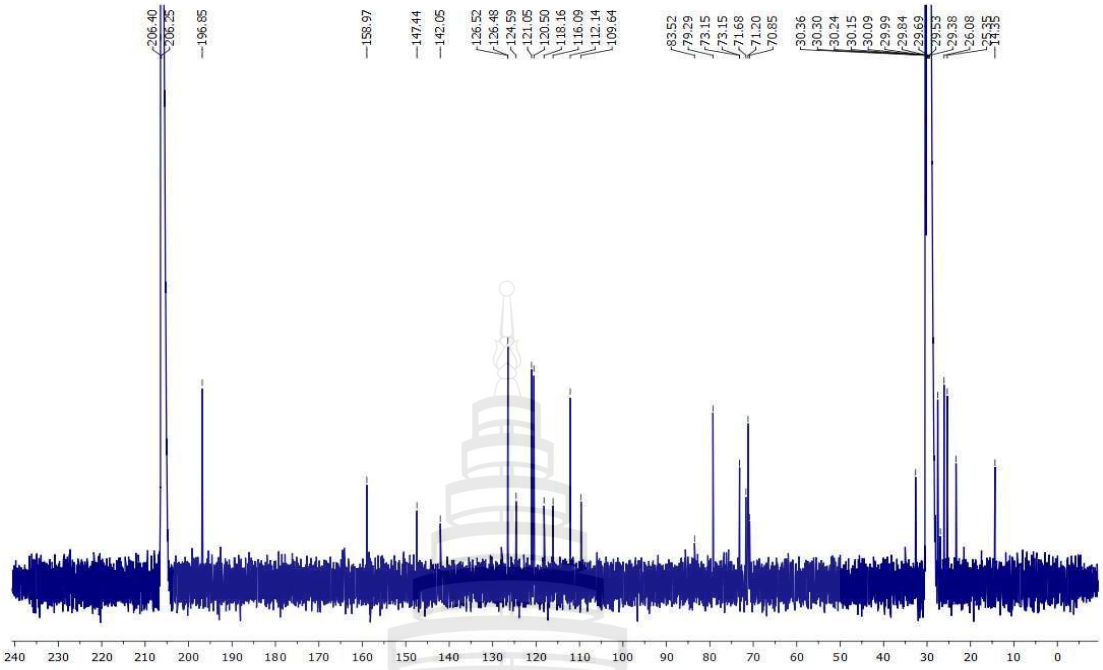

Figure A104 ^{13}C NMR Spectrum of **WM37** in Acetone-d_6 (125 MHz)

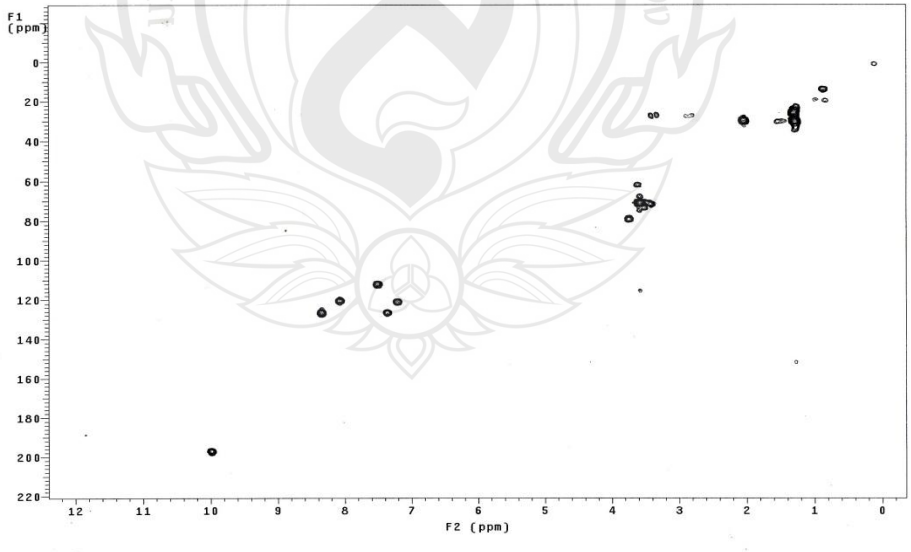

Figure A105 HMQC Spectrum of **WM37** in Acetone-d_6

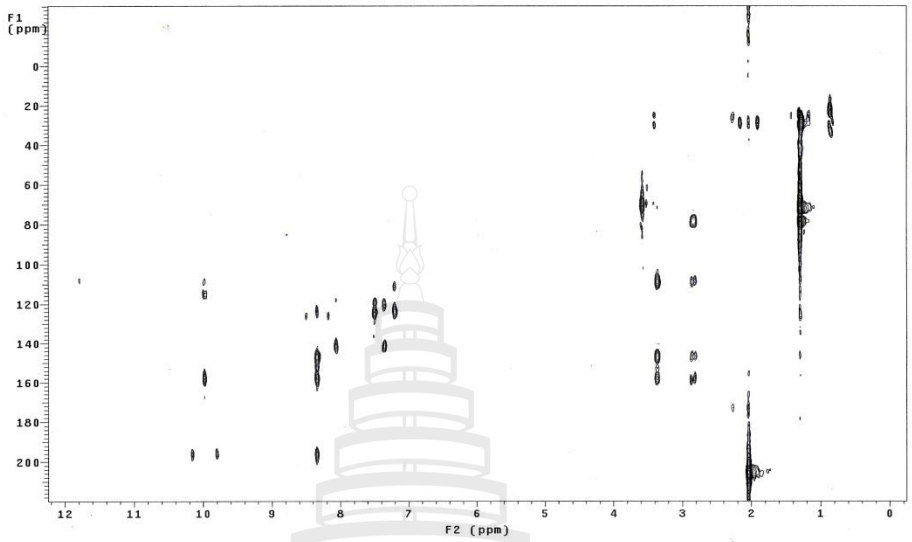

Figure A106 HMBC Spectrum of **WM37** in Acetone-d_6

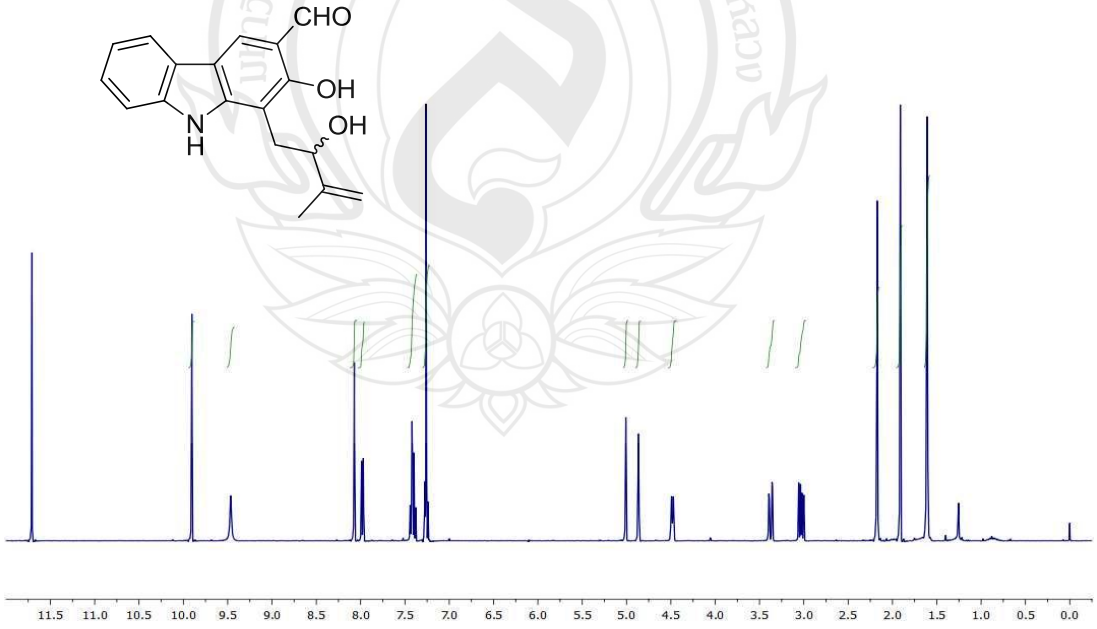

Figure A107 ^{1}H NMR Spectrum of **WM38** in $CDCl_3$ (400 MHz)

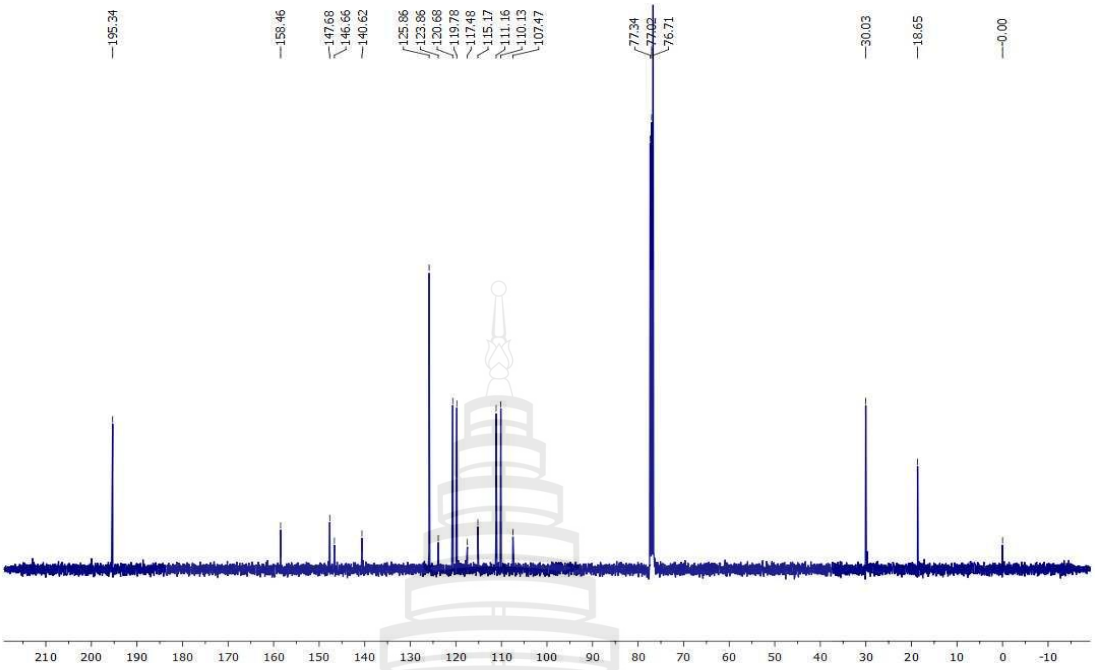

Figure A108 ^{13}C NMR Spectrum of **WM38** in $CDCl_3$ (100 MHz)

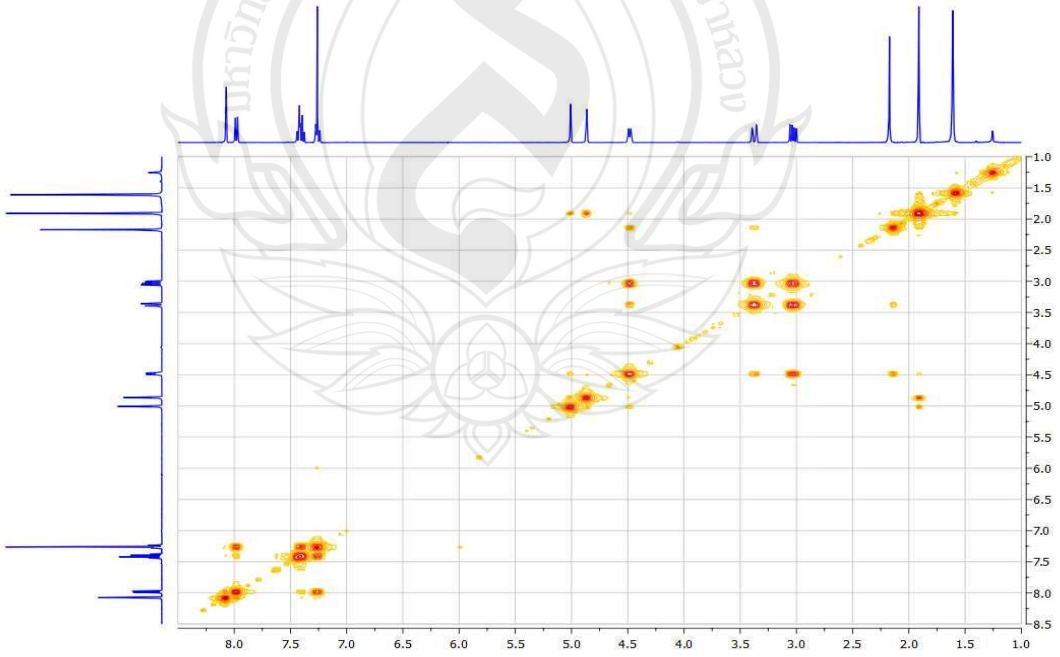

Figure A109 COSY Spectrum of **WM38** in $CDCl_3$

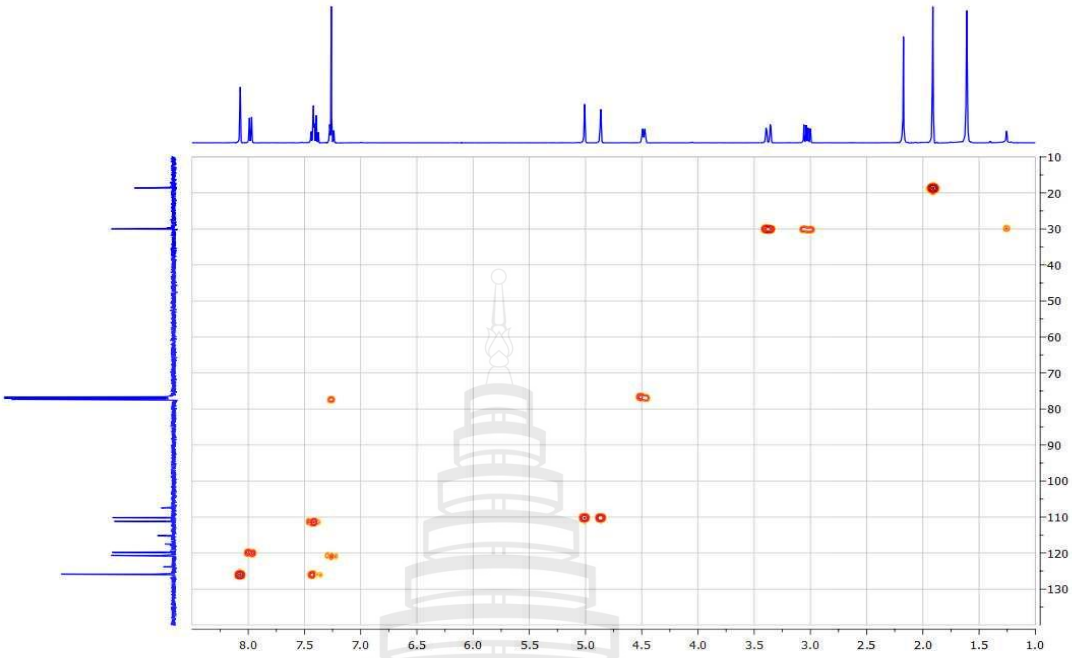

Figure A120 HMQC Spectrum of **WM38** in $CDCl_3$

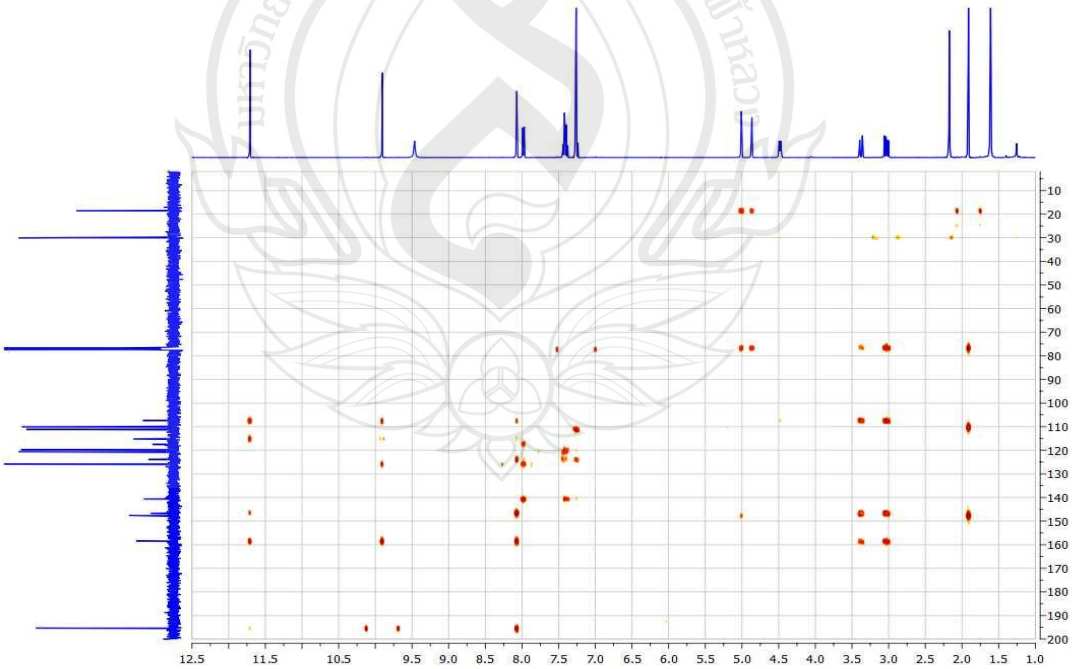

Figure A121 HMBC Spectrum of **WM38** in $CDCl_3$

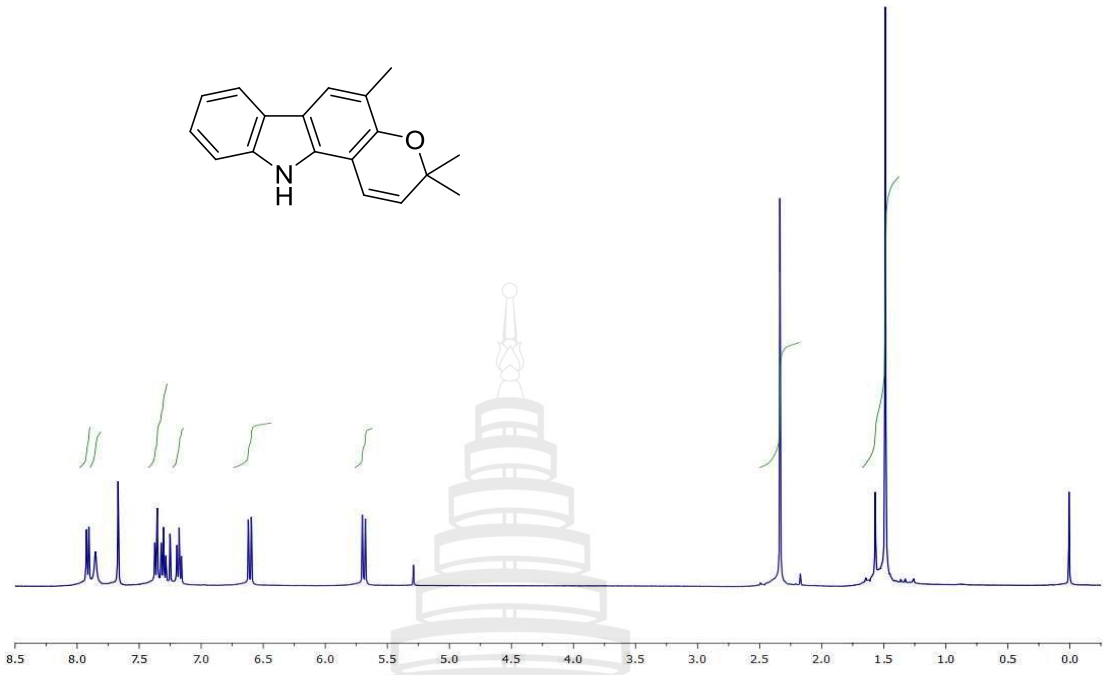

Figure A122 ^{1}H NMR Spectrum of **WM39** in $CDCl_3$ (400 MHz)

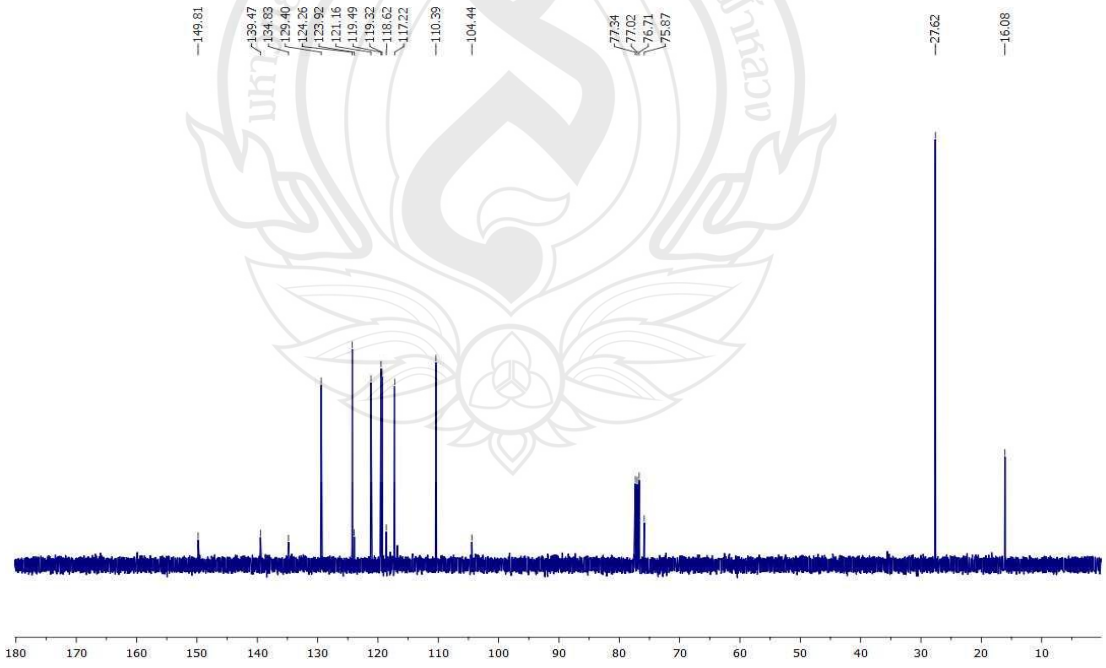

Figure A123 ^{13}C NMR Spectrum of **WM39** in $CDCl_3$ (100 MHz)

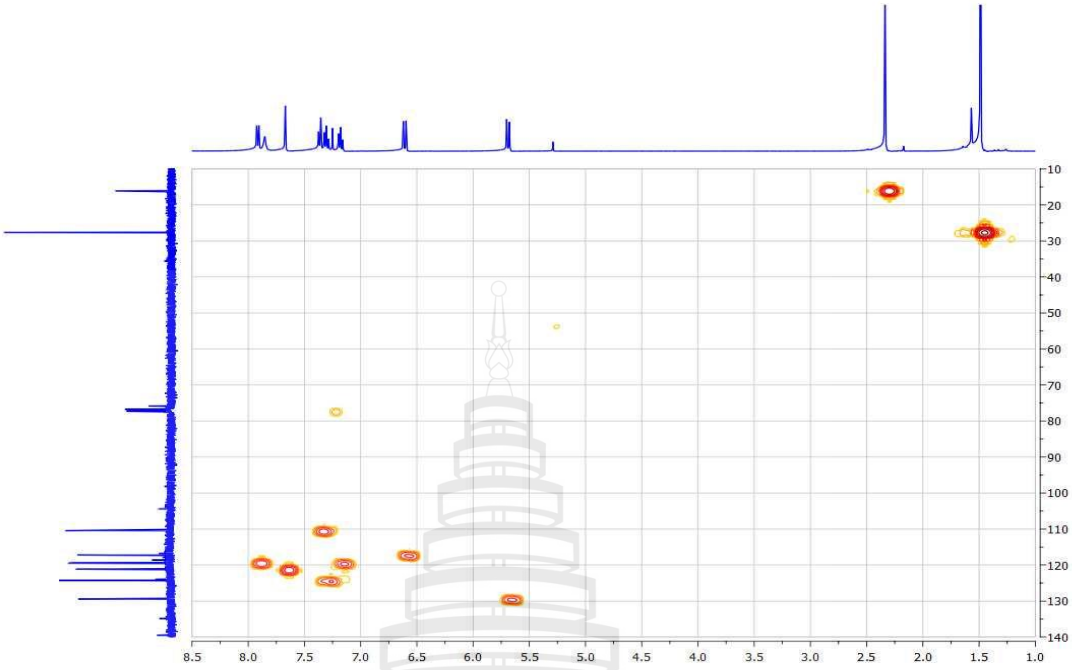

Figure A124 HMQC Spectrum of **WM39** in $CDCl_3$

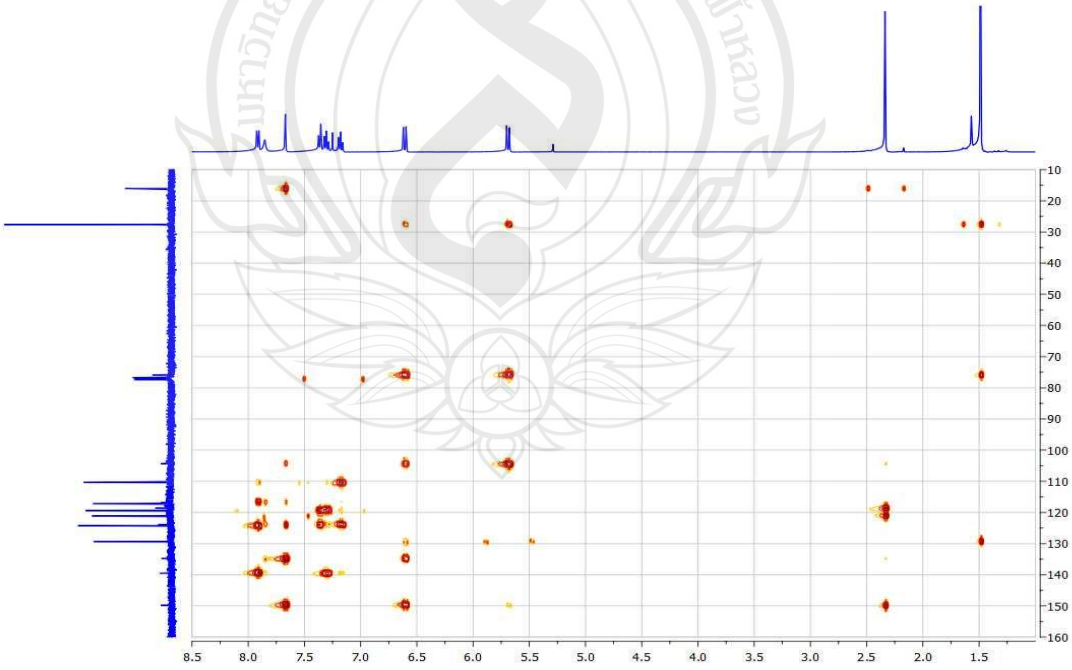

Figure A125 HMBC Spectrum of **WM39** in $CDCl_3$

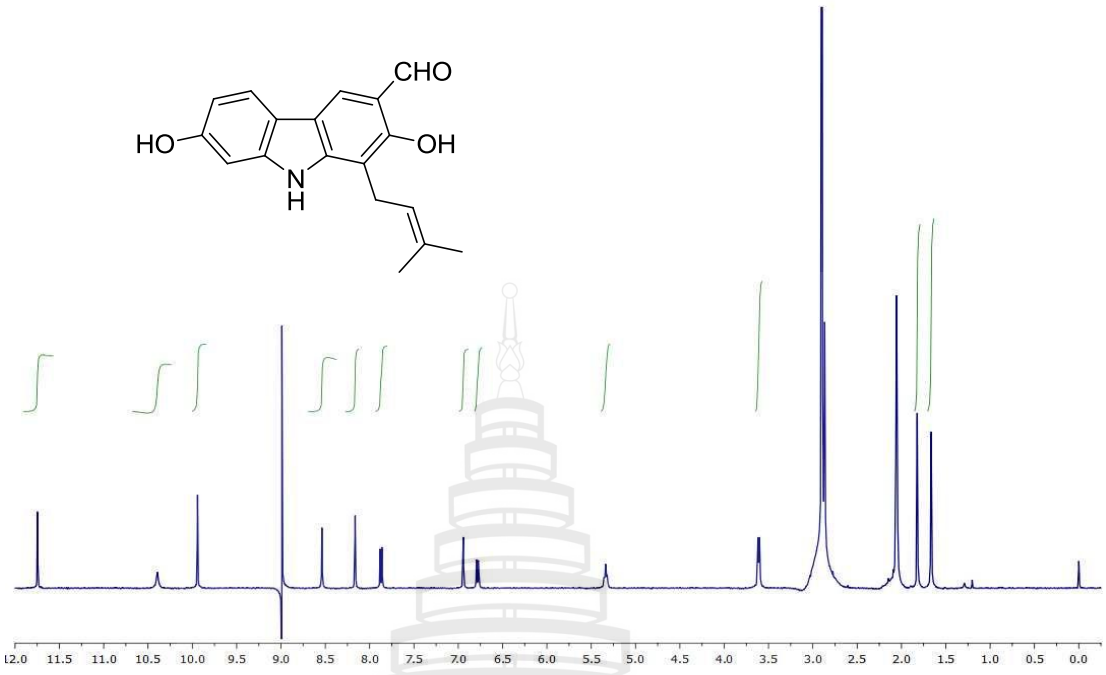

Figure A126 ^{1}H NMR Spectrum of **WM40** in Acetone-d_6 (400 MHz)

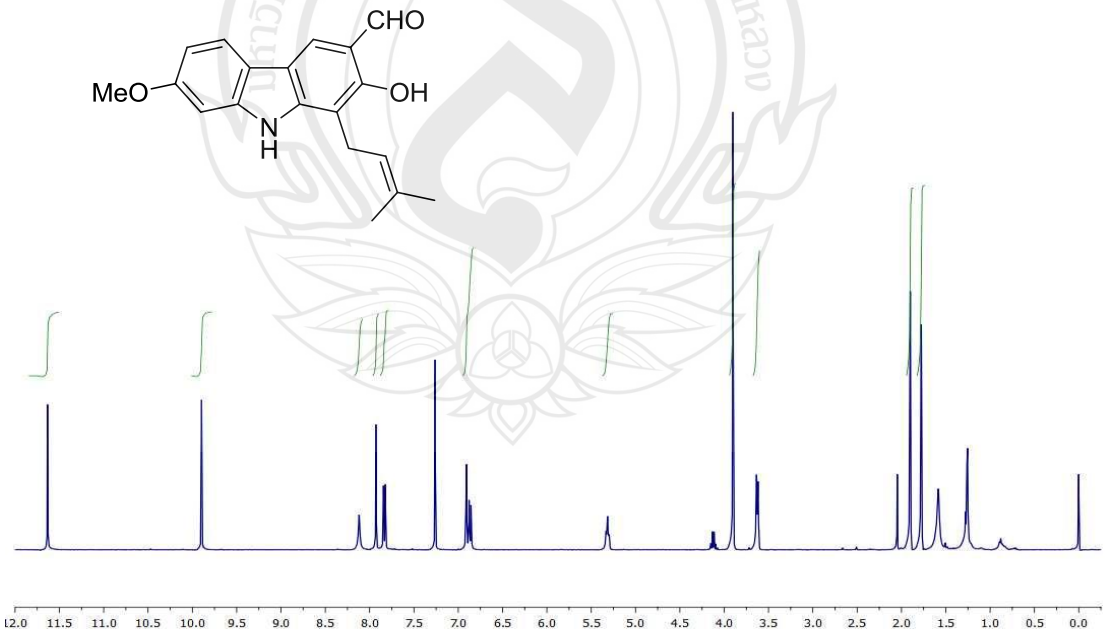

Figure A127 ^{1}H NMR Spectrum of **WM41** in $CDCl_3$ (400 MHz)

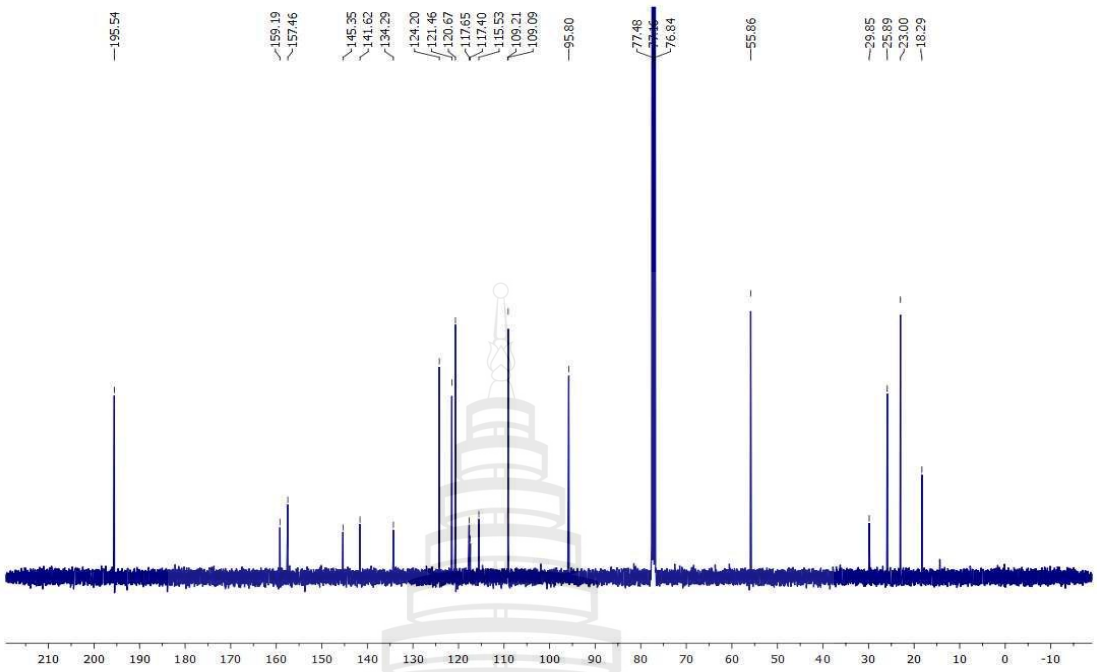

Figure A128 ^{13}C NMR Spectrum of **WM41** in $CDCl_3$ (100 MHz)

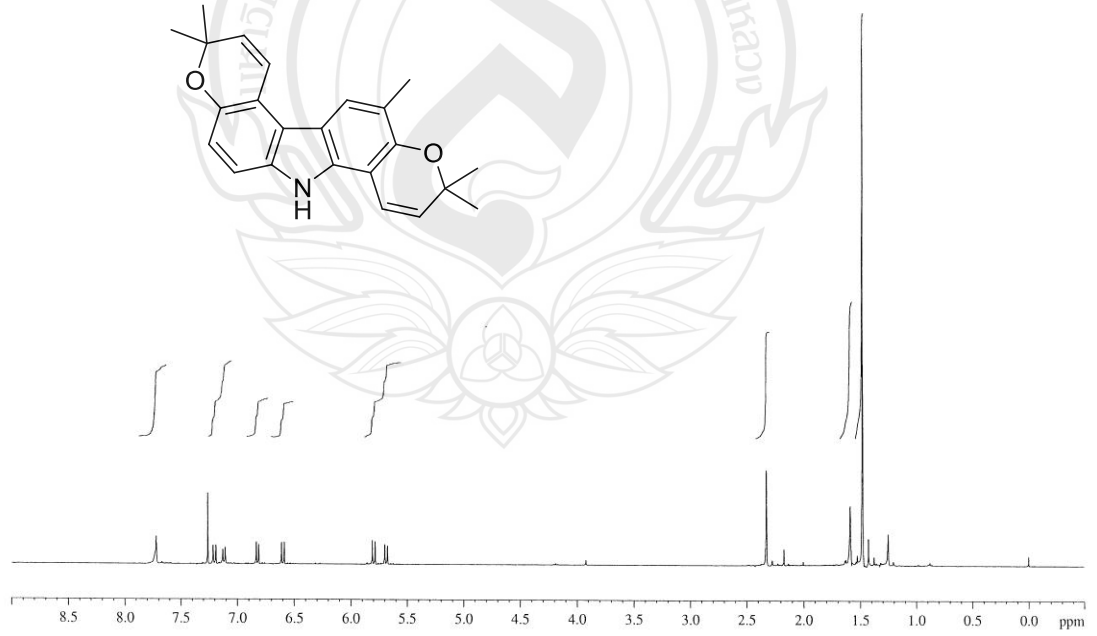

Figure A129 ^{1}H NMR Spectrum of **WM42** in $CDCl_3$ (400 MHz)

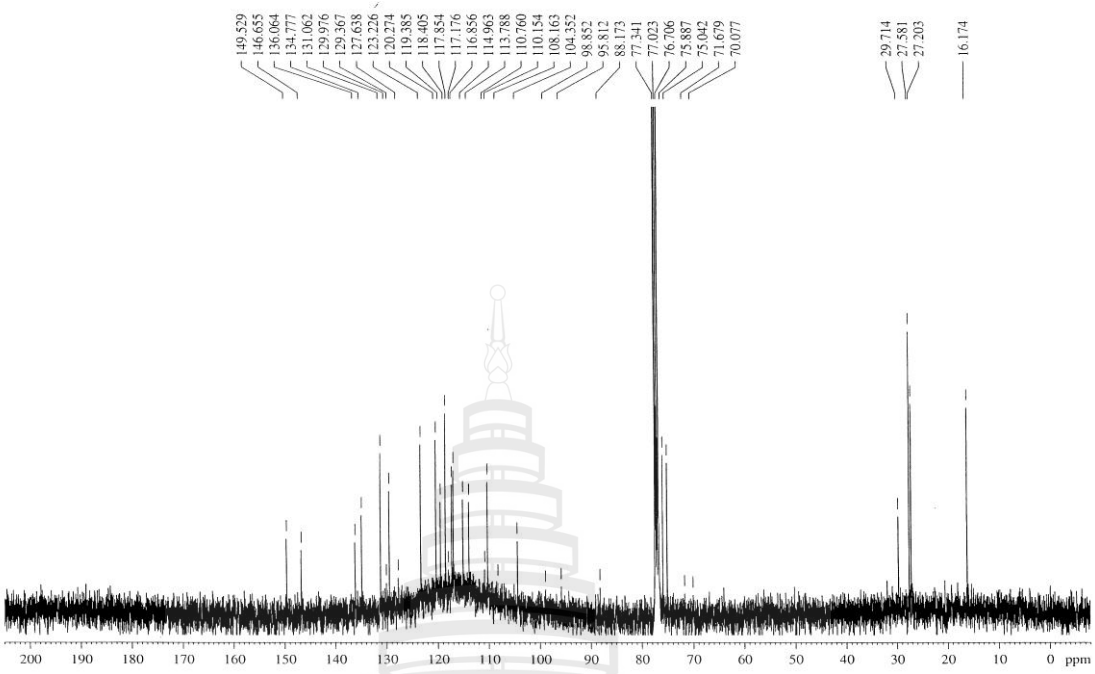

Figure A130 ^{13}C NMR Spectrum of **WM42** in $CDCl_3$ (100 MHz)

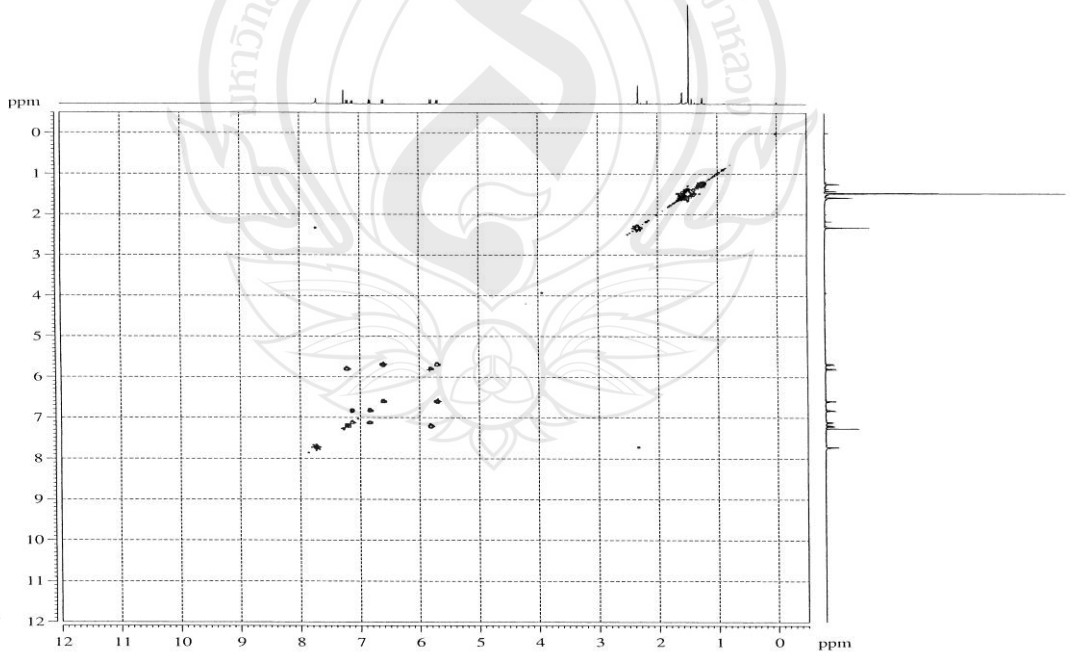

Figure A131 COSY Spectrum of **WM42** in $CDCl_3$

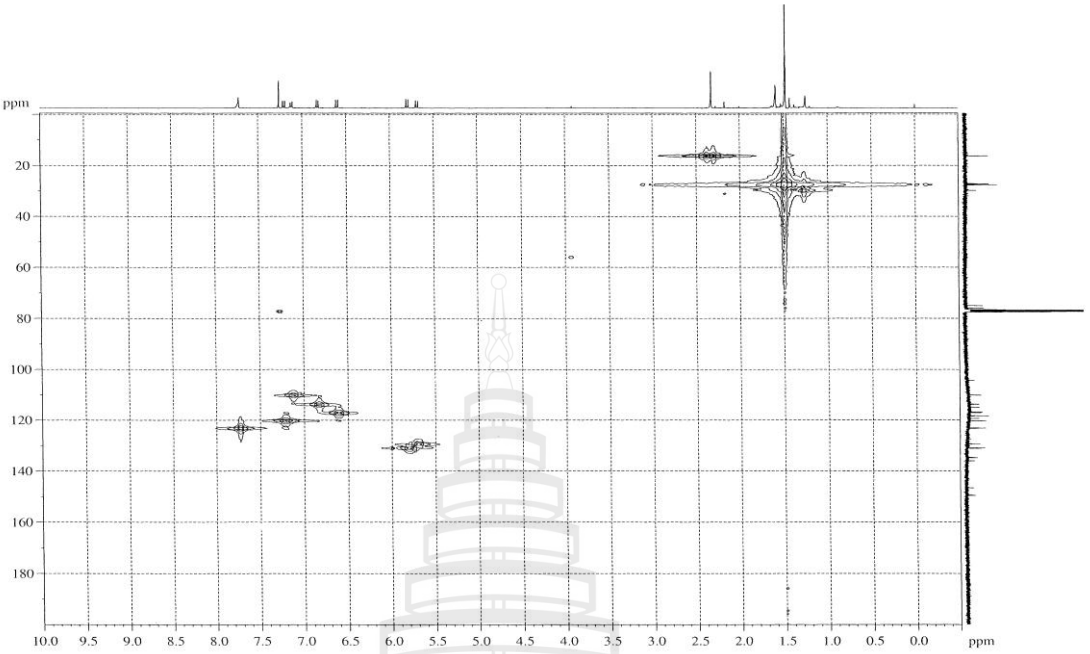

Figure A132 HMQC Spectrum of **WM42** in $CDCl_3$

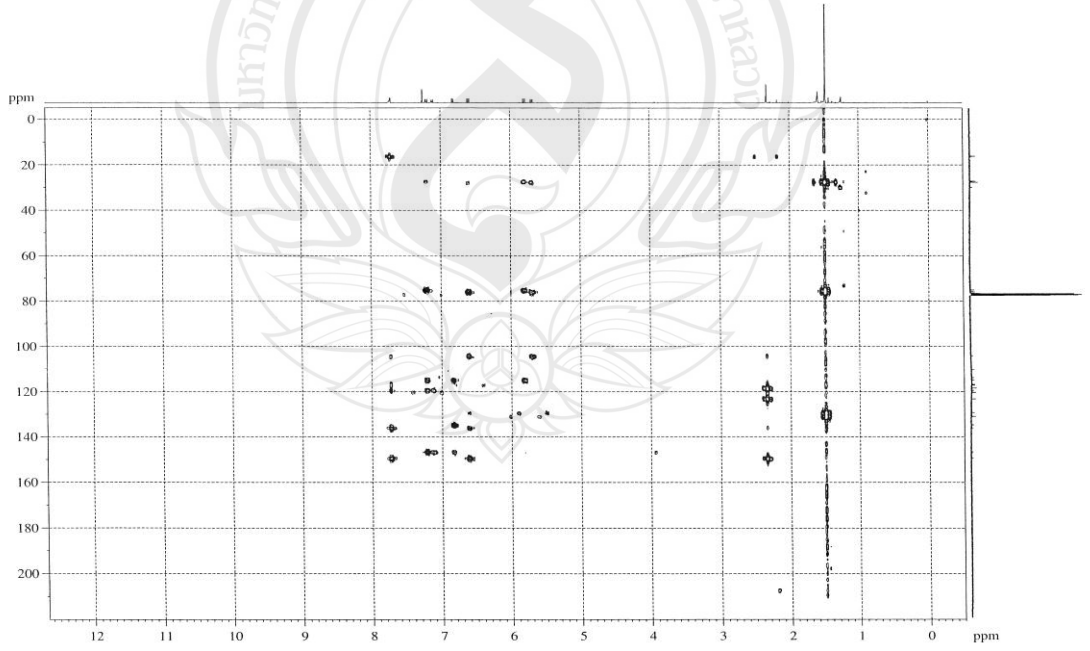

Figure A133 HMBC Spectrum of **WM42** in $CDCl_3$

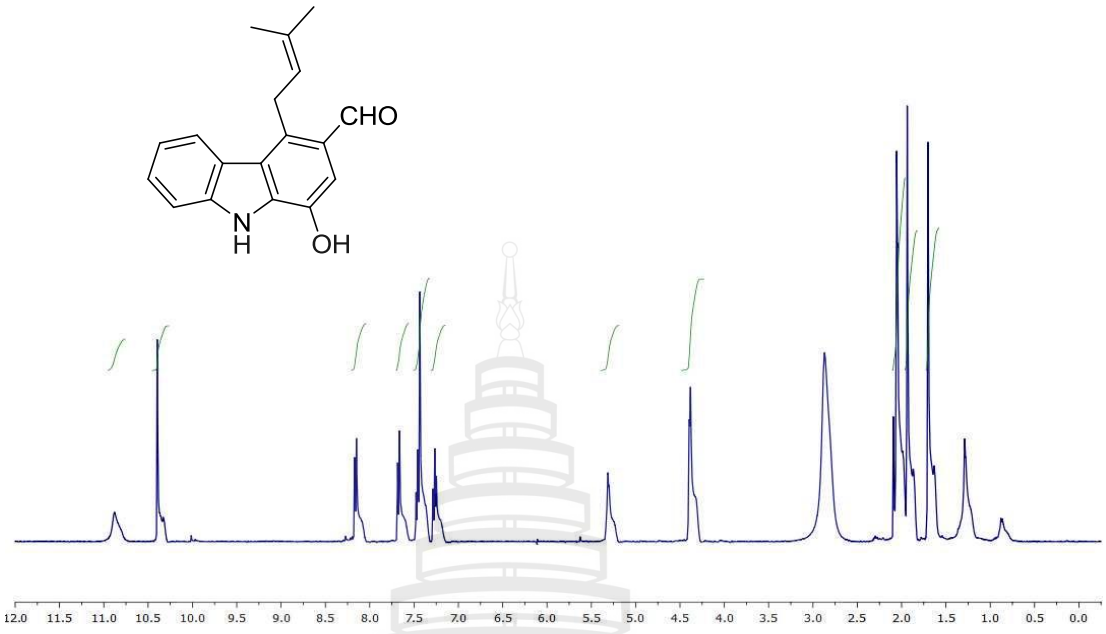

Figure A134 ^{1}H NMR Spectrum of **WM43** in Acetone-d_6 (400 MHz)

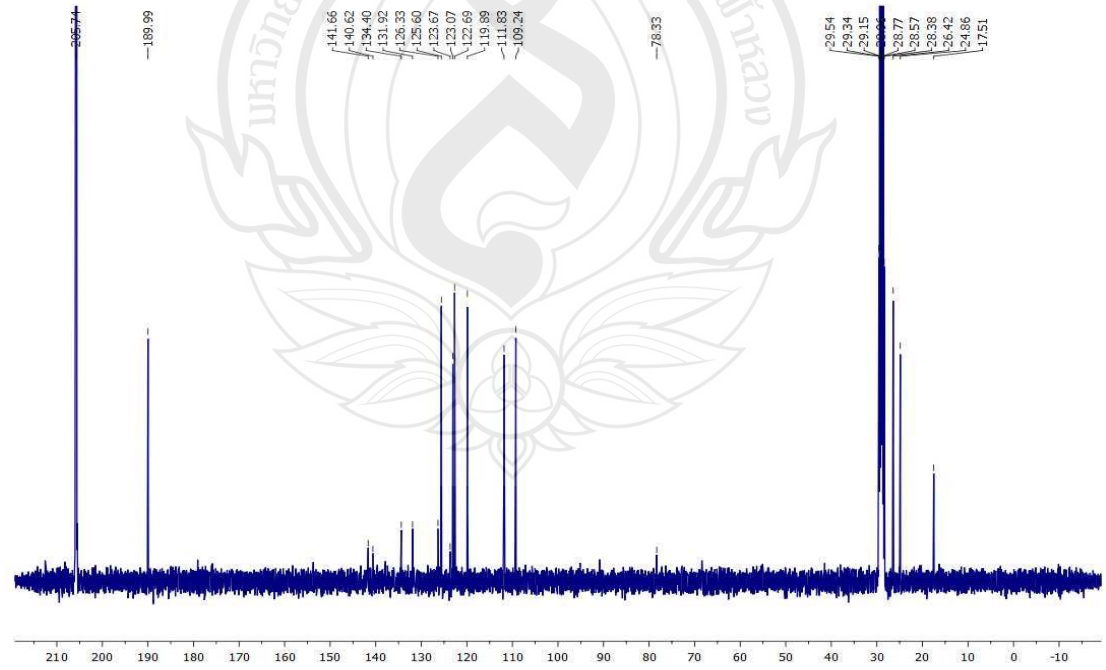

Figure A135 ^{13}C NMR Spectrum of **WM43** in Acetone-d_6 (100 MHz)

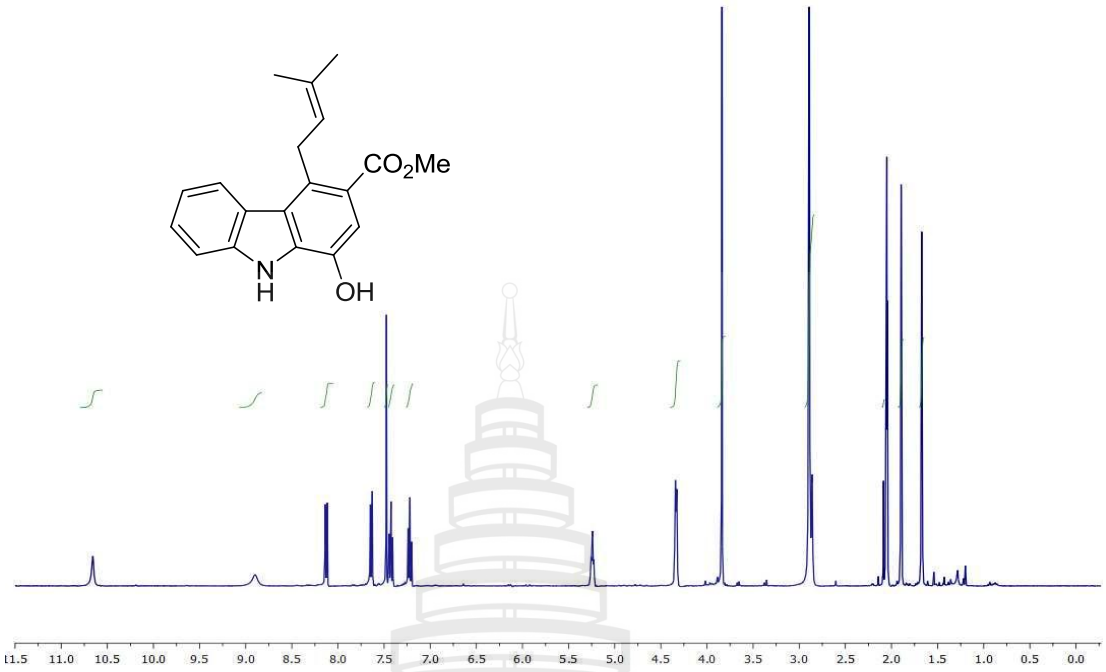

Figure A136 ^{1}H NMR Spectrum of **WM44** in Acetone-d_6 (400 MHz)

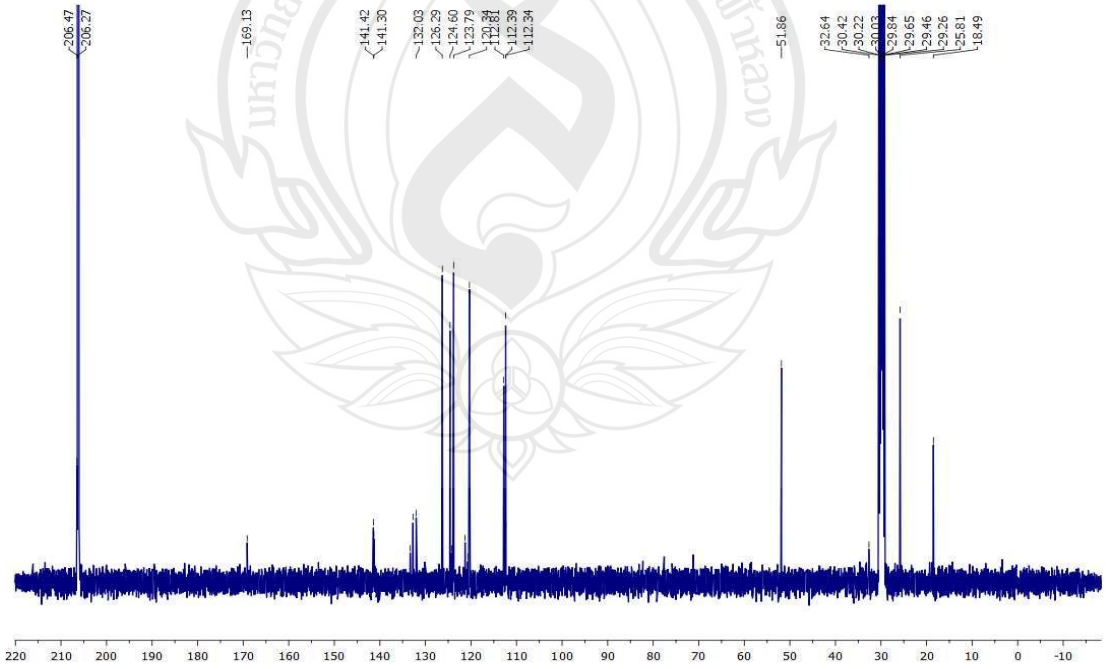

Figure A137 ^{13}C NMR Spectrum of **WM44** in Acetone-d_6 (100 MHz)

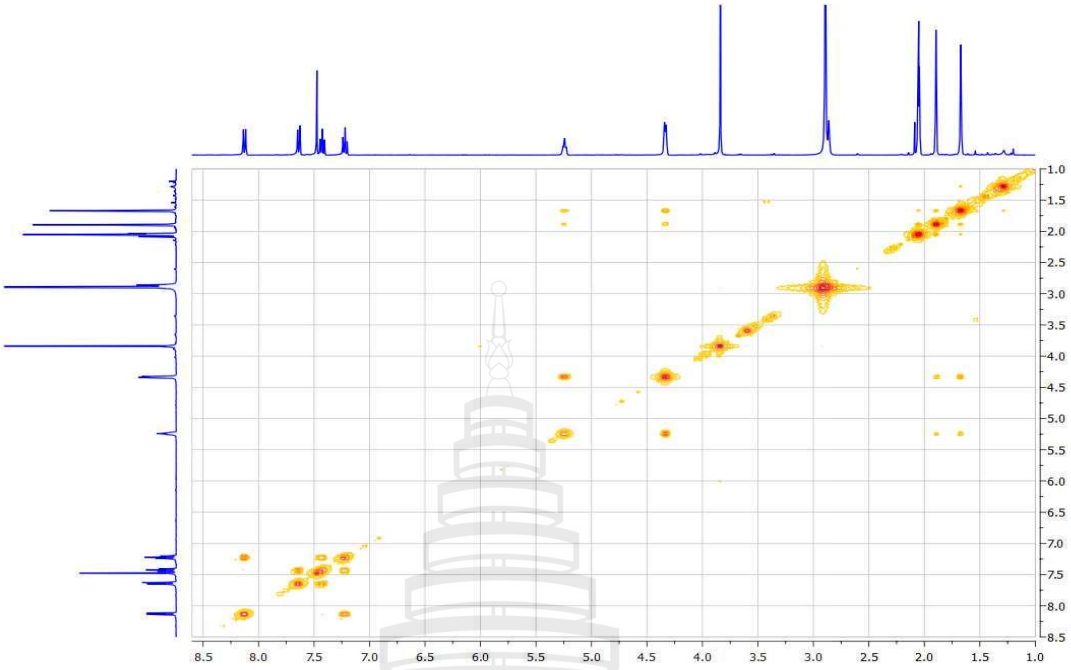

Figure A138 COSY Spectrum of **WM44** in Acetone-d_6

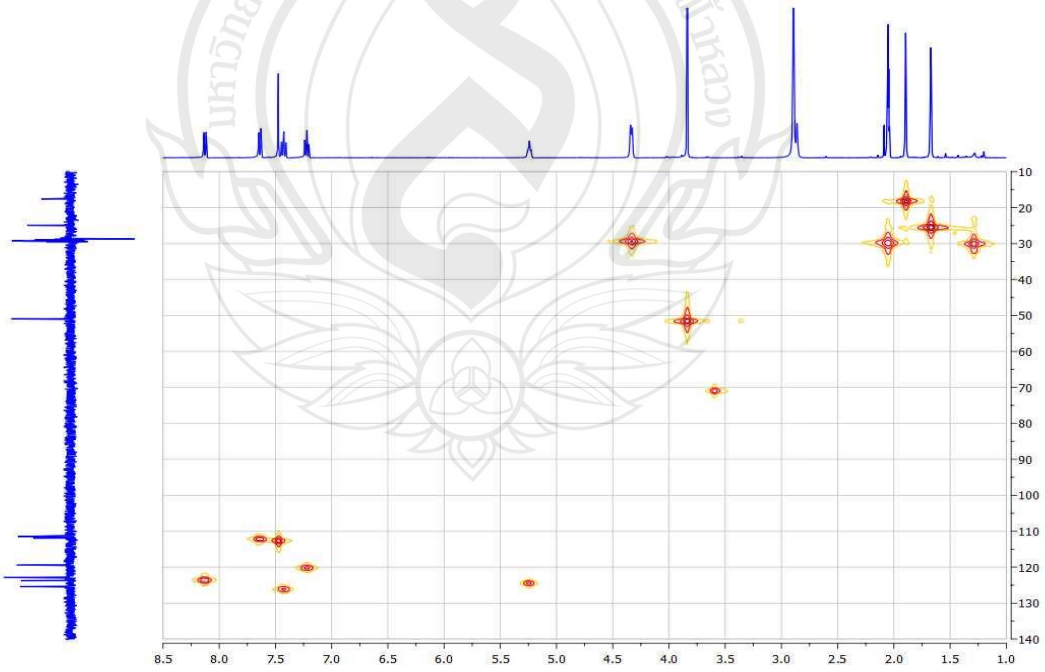

Figure A139 HMQC Spectrum of **WM44** in Acetone-d_6

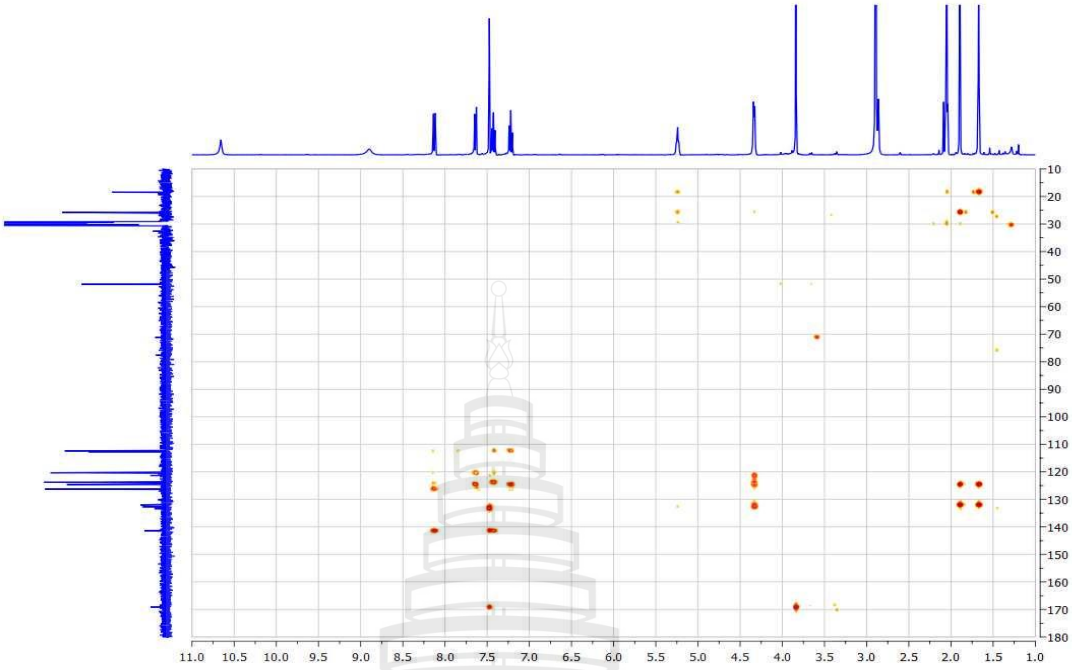

Figure A140 HMBC Spectrum of **WM44** in Acetone-d_6

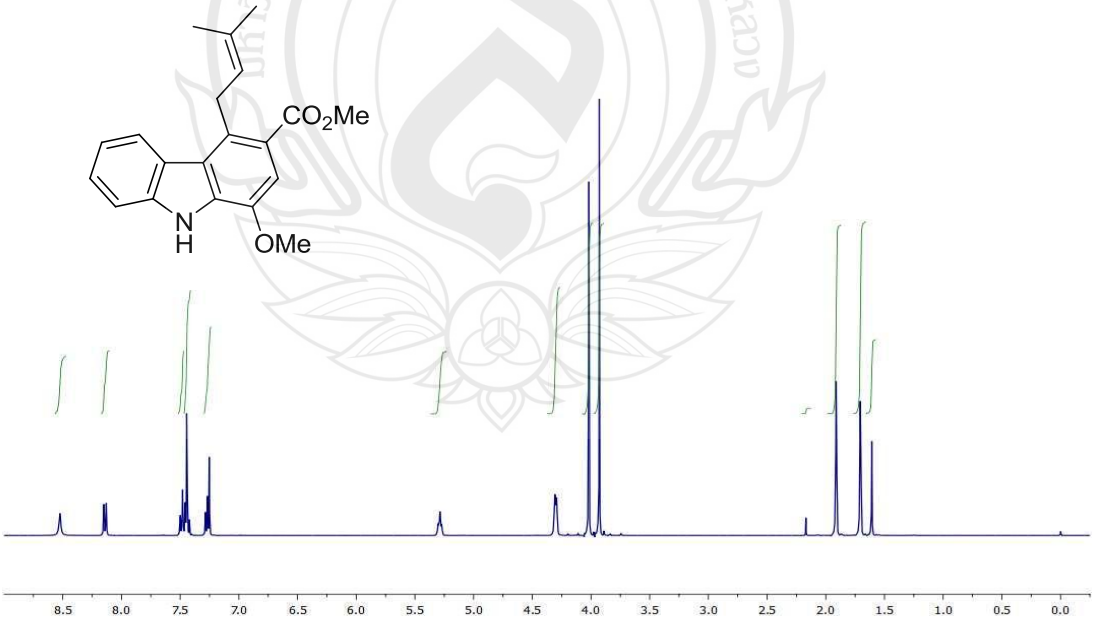

Figure A141 ^{1}H NMR Spectrum of **WM45** in $CDCl_3$ (400 MHz)

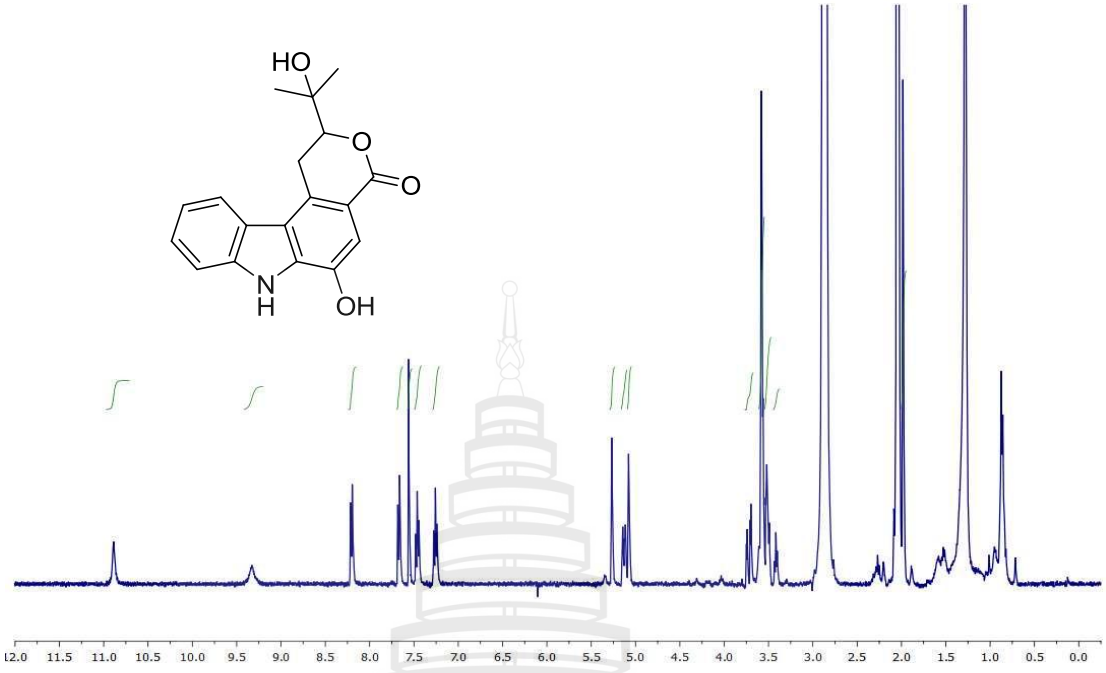

Figure A142 ^{1}H NMR Spectrum of **WM46** in Acetone-d_6 (400 MHz)

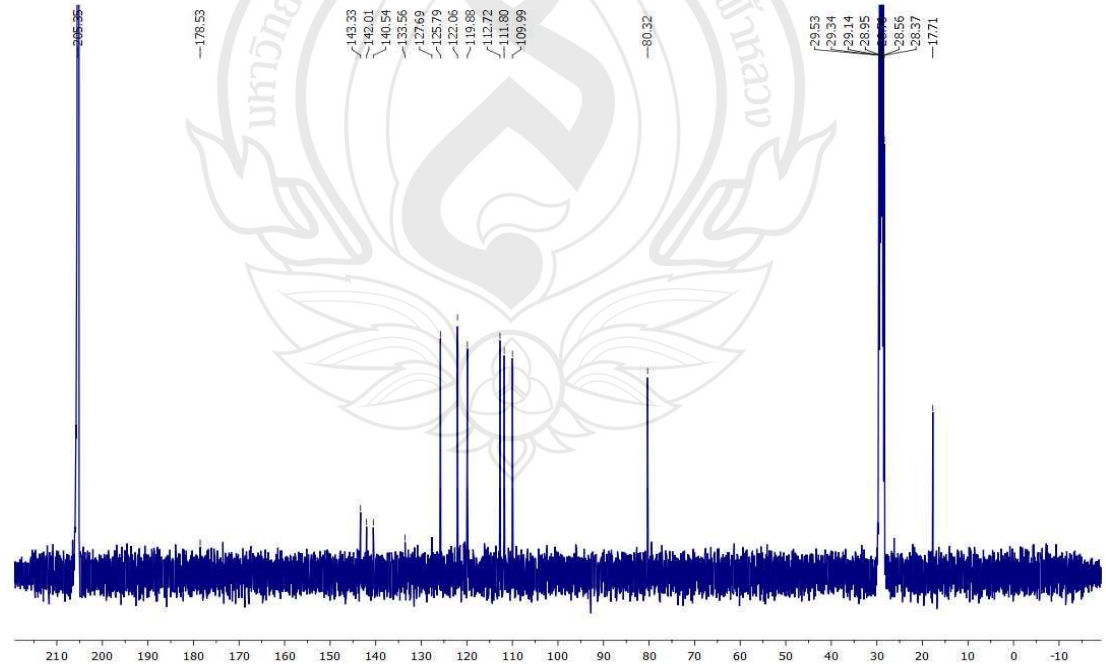

Figure A143 ^{13}C NMR Spectrum of **WM46** in Acetone-d_6 (100 MHz)

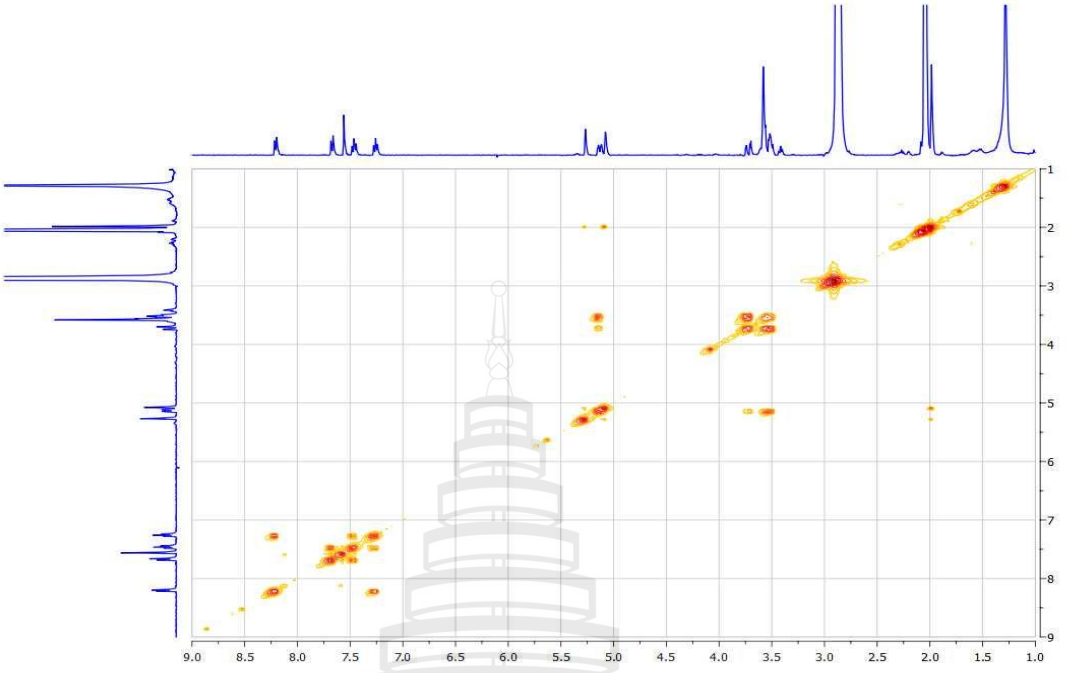

Figure A144 COSY Spectrum of **WM46** in Acetone-d_6

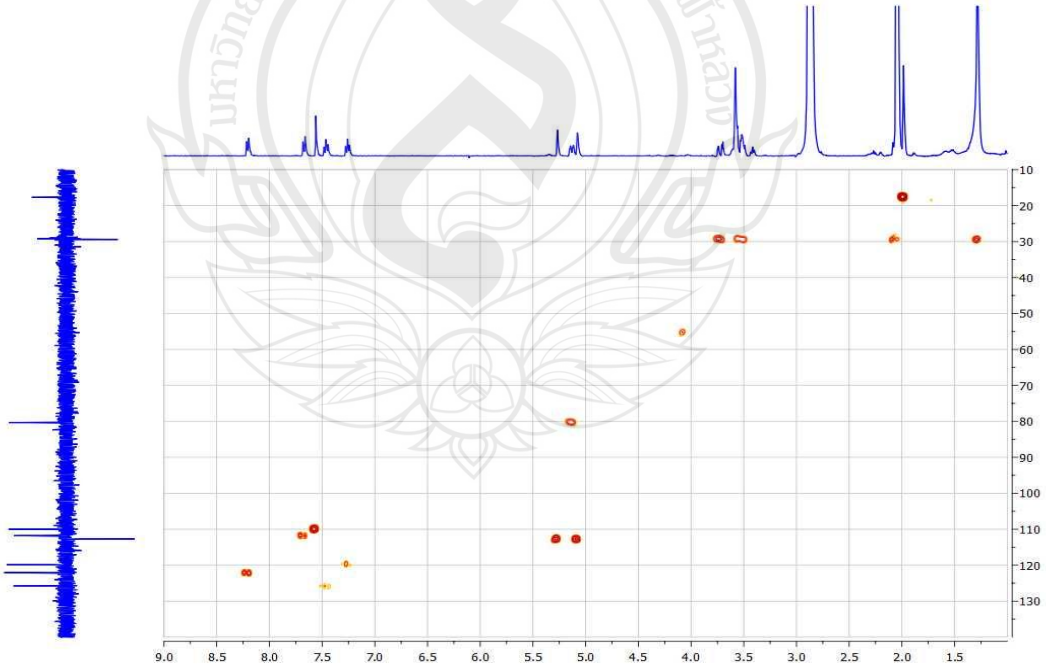

Figure A145 HMQC Spectrum of **WM46** in Acetone-d_6

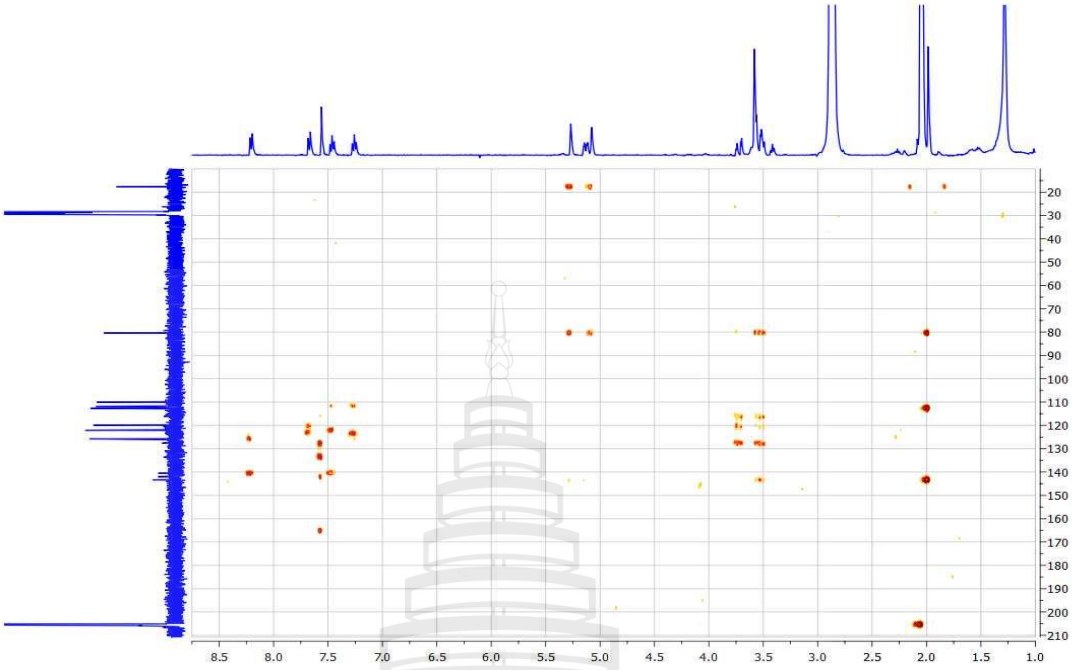

Figure A146 HMBC Spectrum of **WM46** in Acetone-d_6

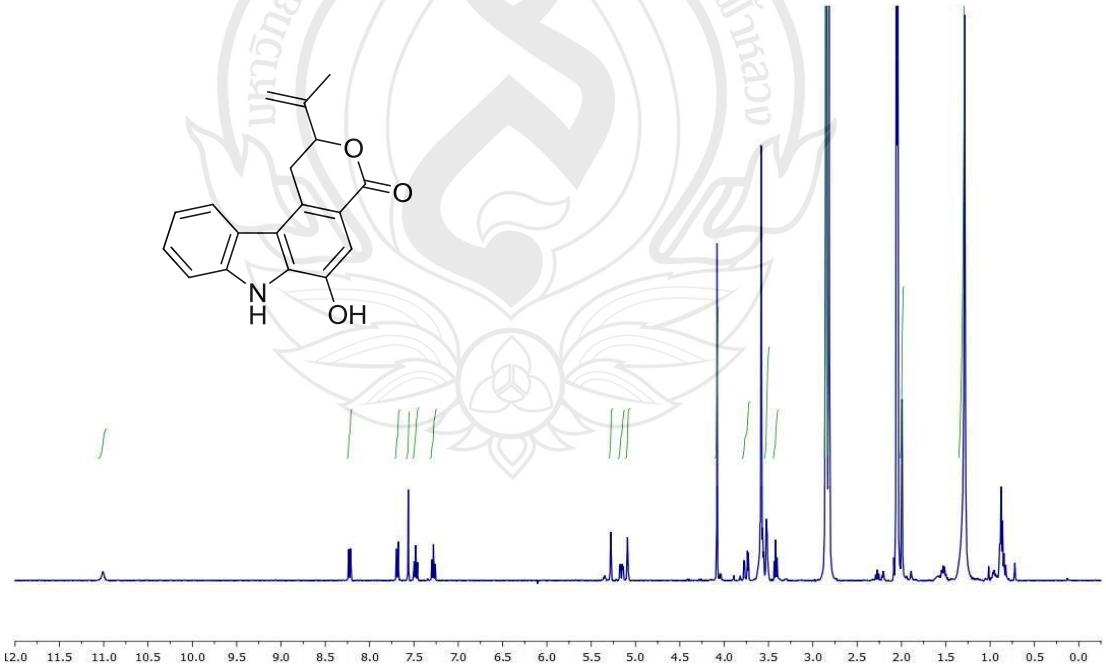

Figure A147 ^{1}H NMR Spectrum of **WM47** in Acetone-d_6 (400 MHz)

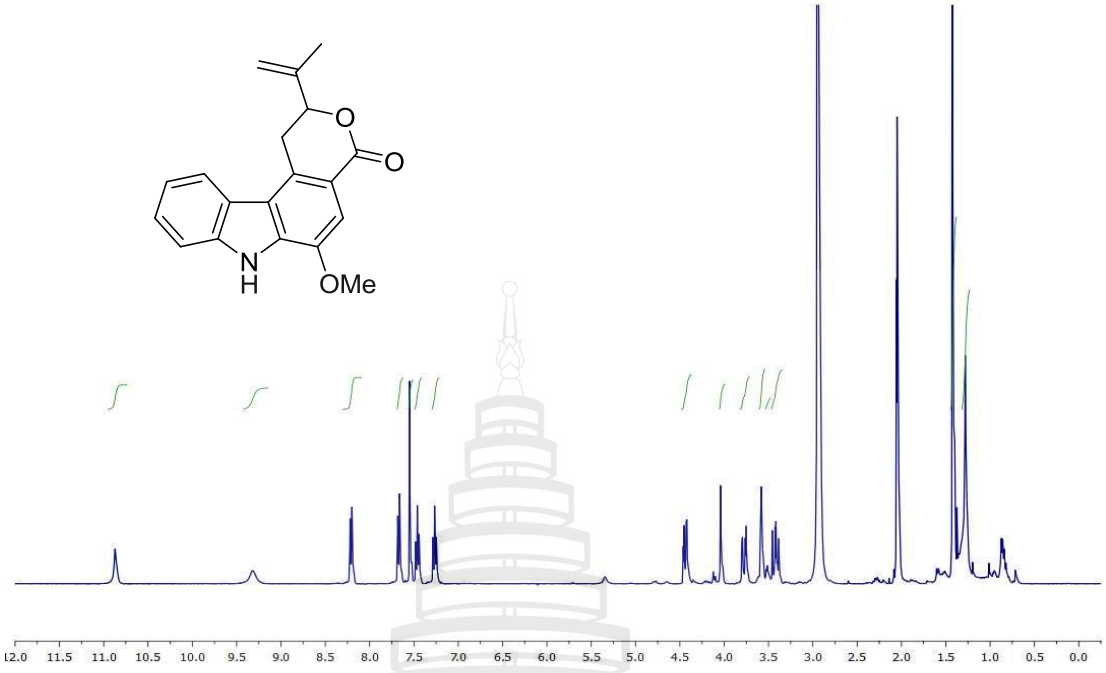

Figure A148 ^{1}H NMR Spectrum of **WM48** in Acetone-d_6 (400 MHz)

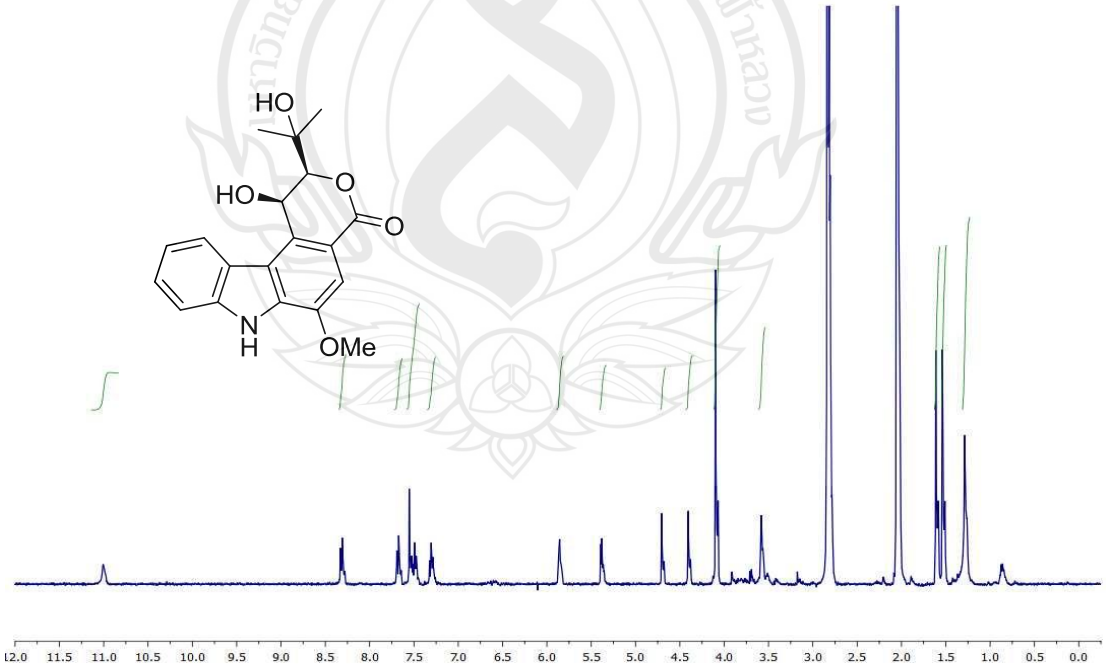

Figure A149 ^{1}H NMR Spectrum of **WM49** in Acetone-d_6 (500 MHz)

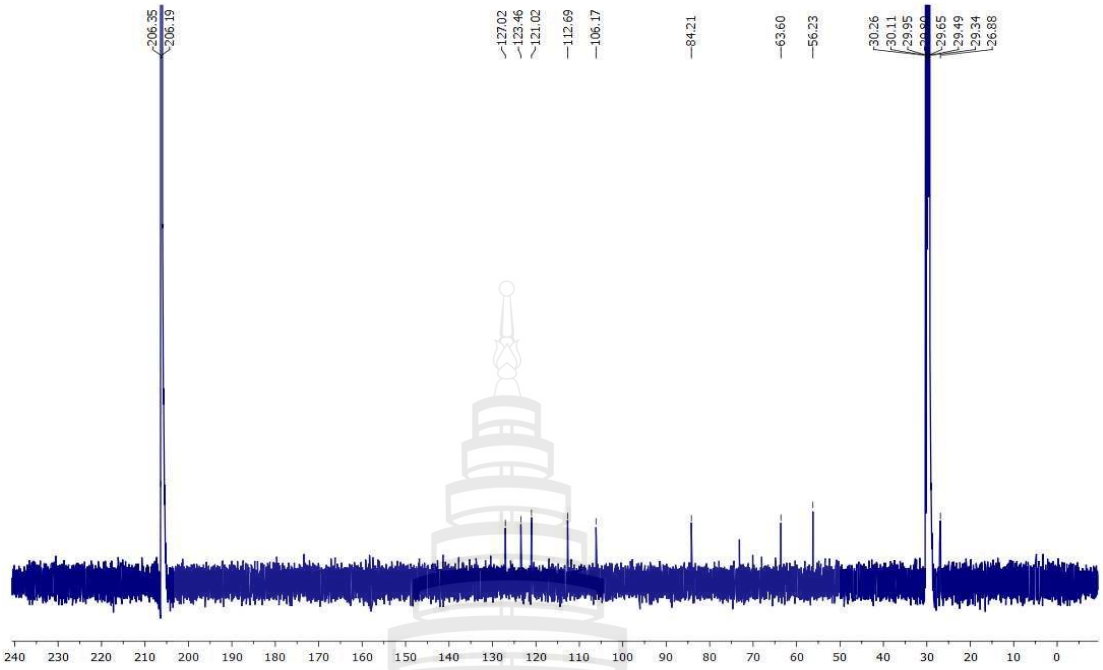

Figure A150 ^{13}C NMR Spectrum of **WM49** in Acetone-d_6 (125 MHz)

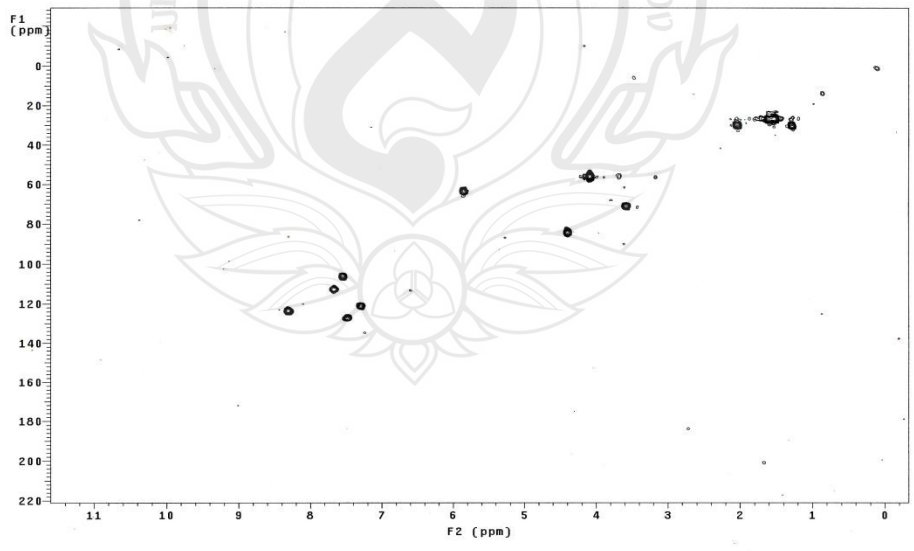

Figure A151 HMQC Spectrum of **WM49** in Acetone-d_6

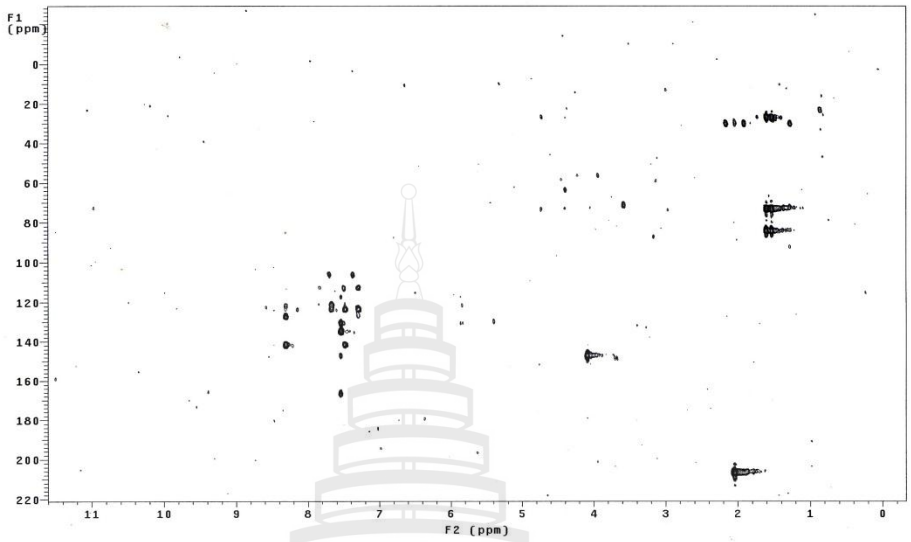

Figure A152 HMBC Spectrum of **WM49** in Acetone-d_6

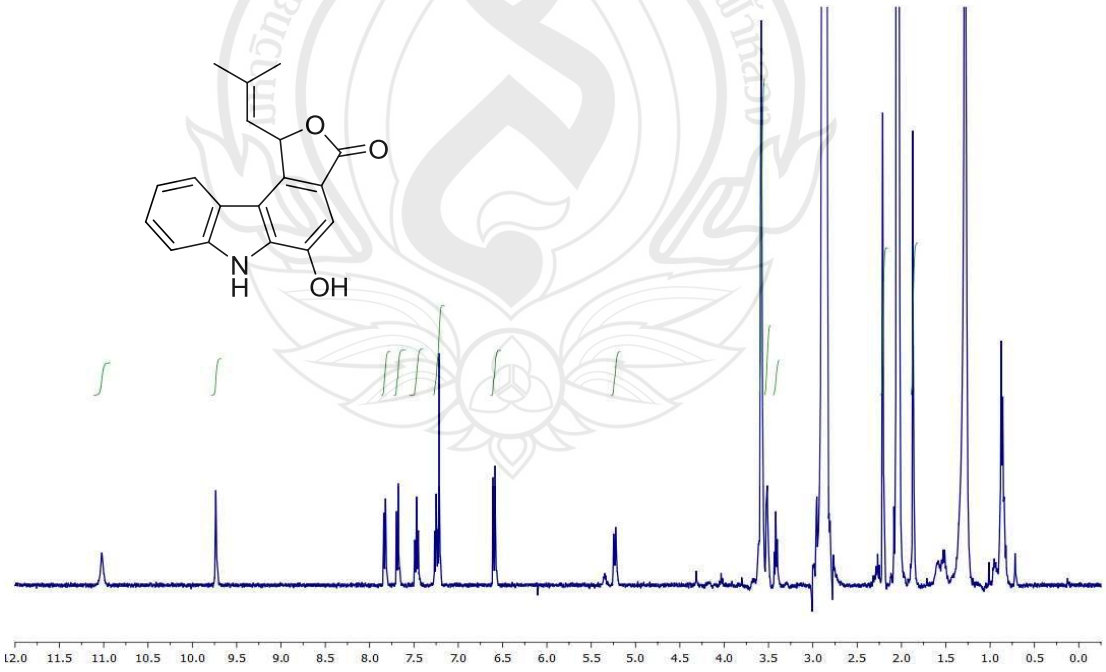

Figure A153 ^{1}H NMR Spectrum of **WM50** in Acetone-d_6 (500 MHz)

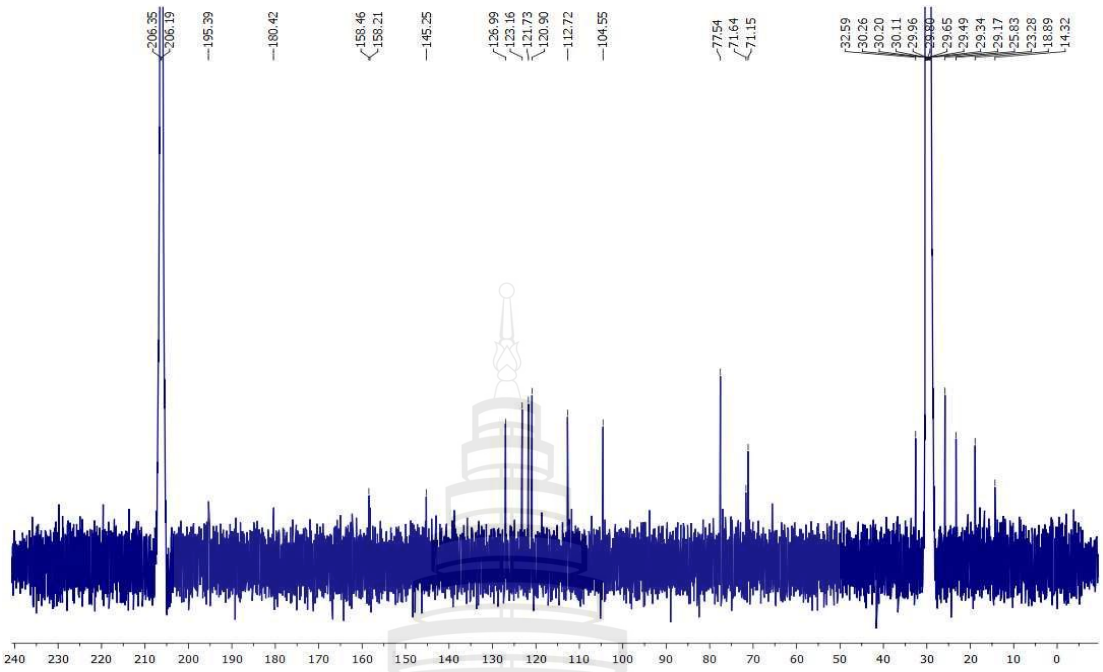

Figure A154 ^{13}C NMR Spectrum of **WM50** in Acetone-d_6 (125 MHz)

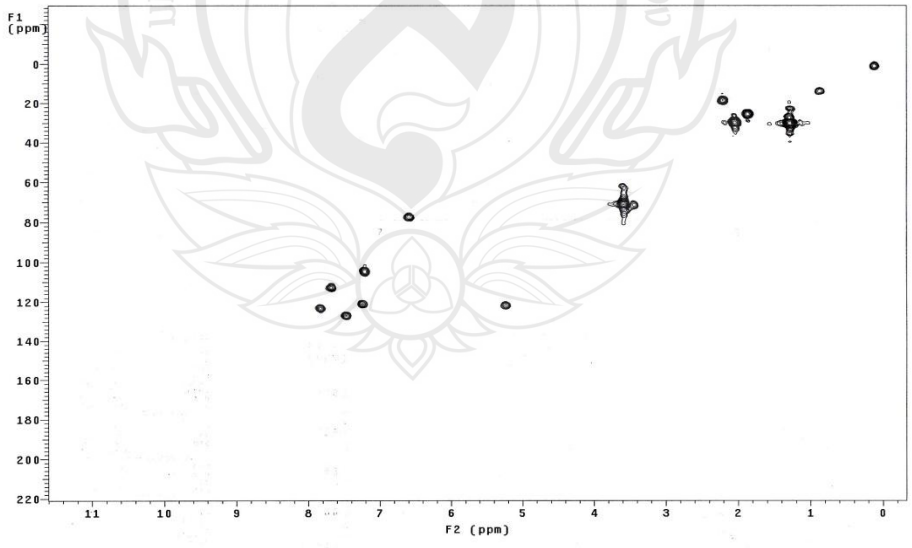

Figure A155 HMQC Spectrum of **WM50** in Acetone-d_6

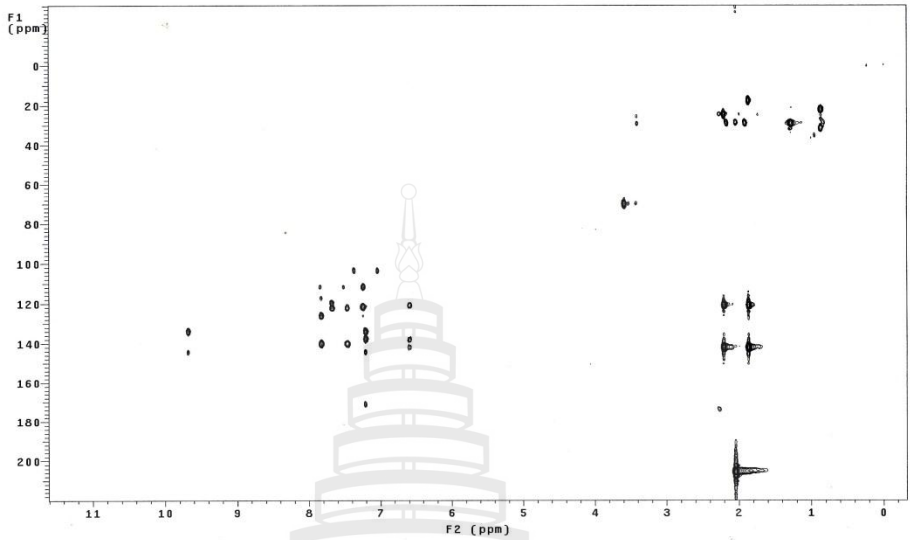

Figure A156 HMBC Spectrum of **WM50** in Acetone-d_6

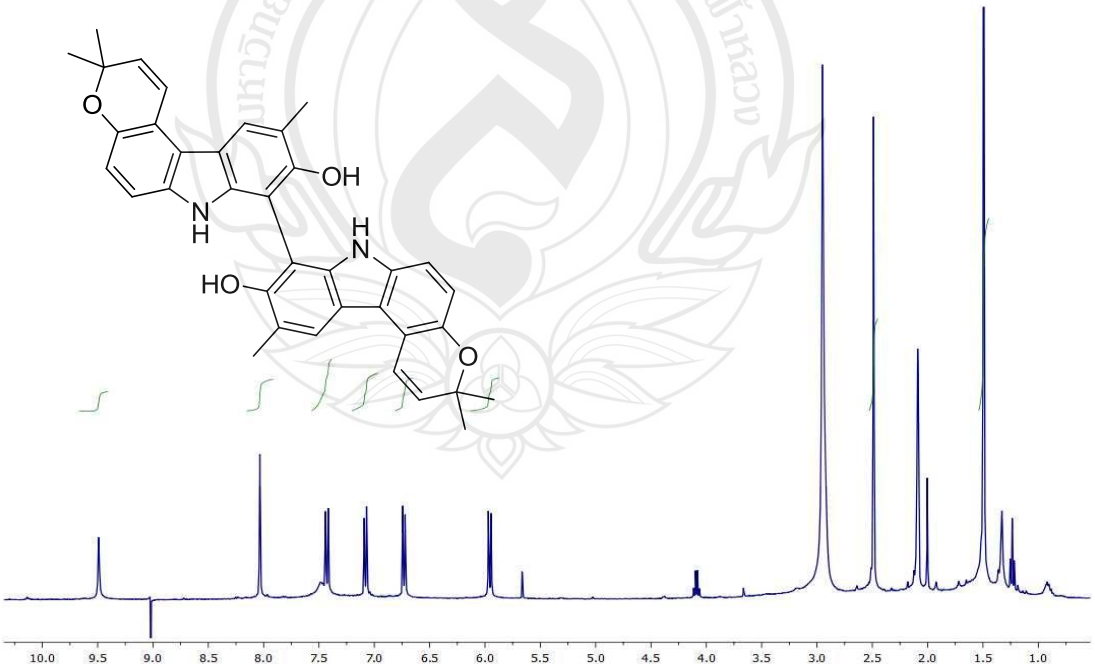

Figure A157 ^{1}H NMR Spectrum of **WM51** in Acetone-d_6 (400 MHz)

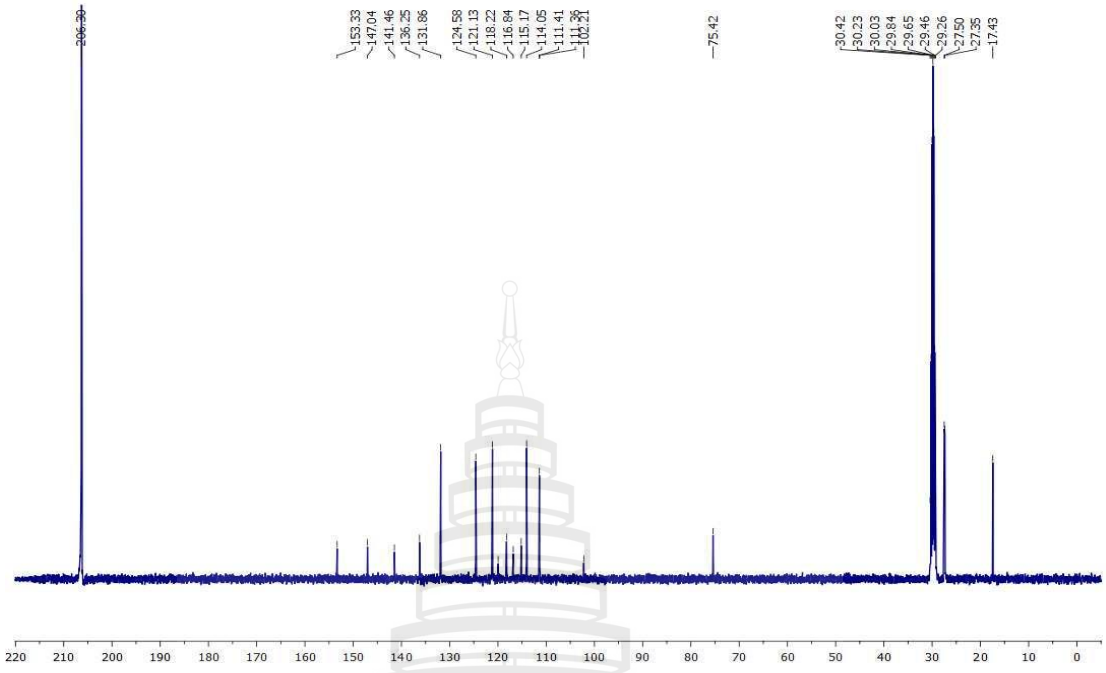

Figure A158 ^{13}C NMR Spectrum of **WM51** in Acetone-d_6 (100 MHz)

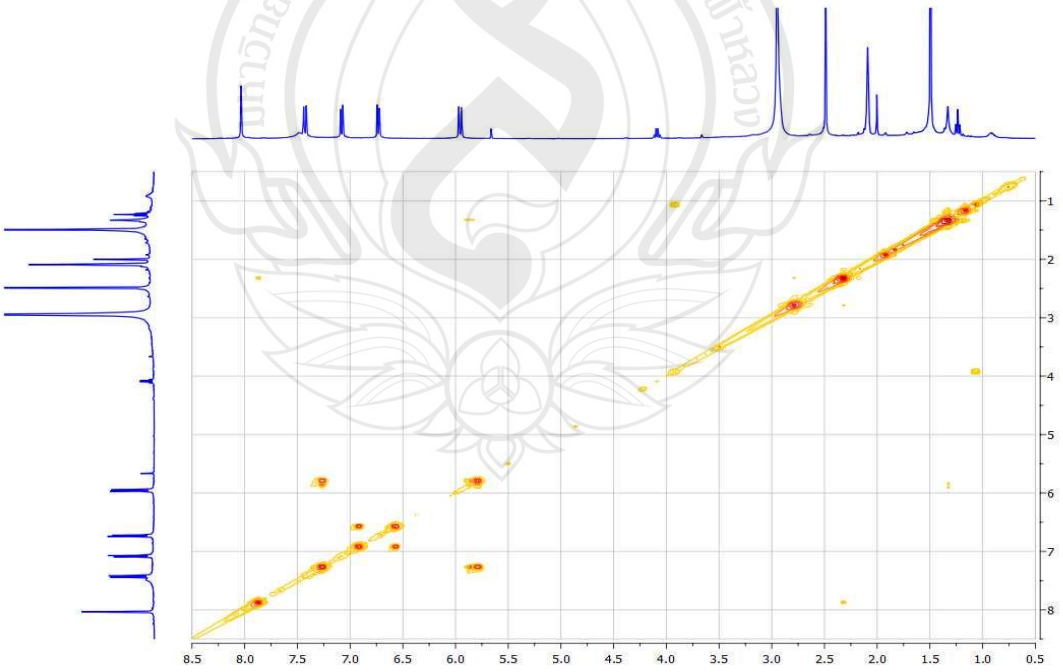

Figure A159 COSY Spectrum of **WM51** in Acetone-d_6

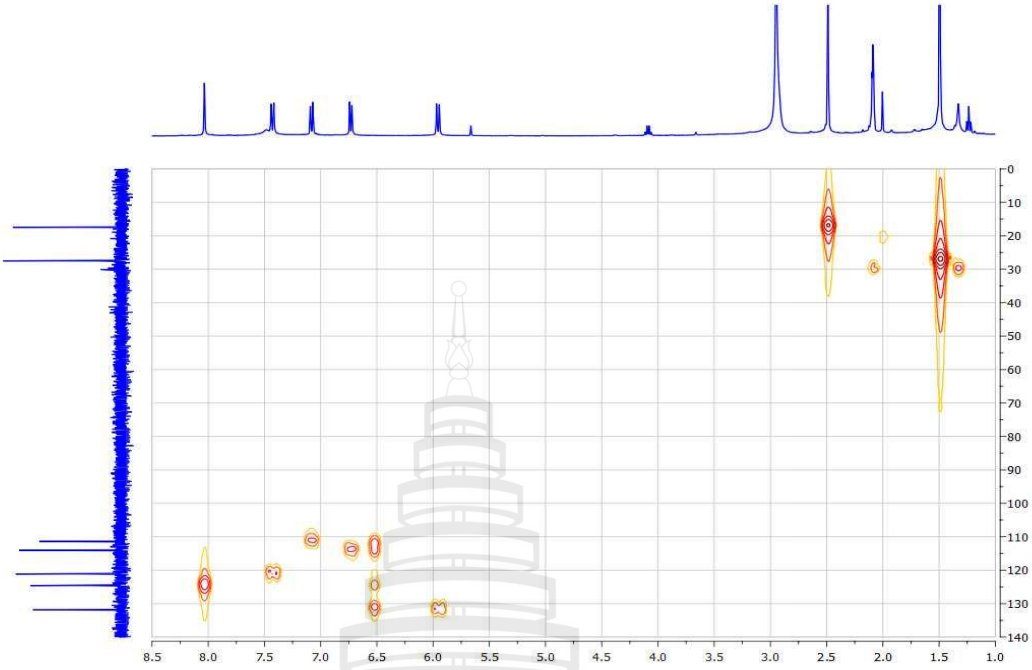

Figure A160 HMQC Spectrum of **WM51** in Acetone-d_6

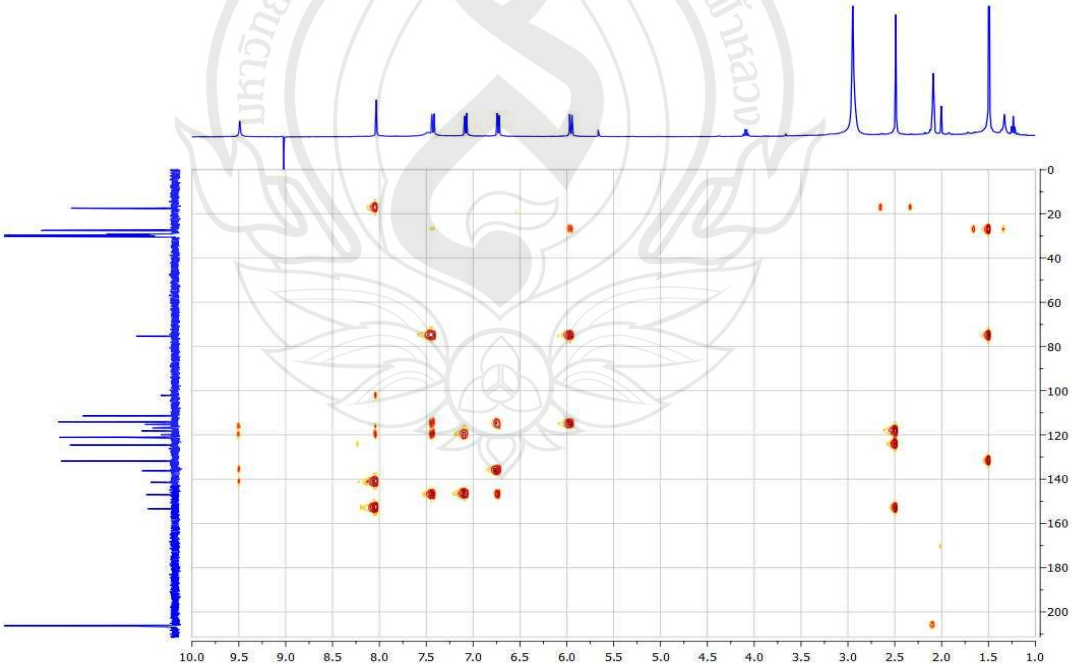

Figure A161 HMBC Spectrum of **WM51** in Acetone-d_6

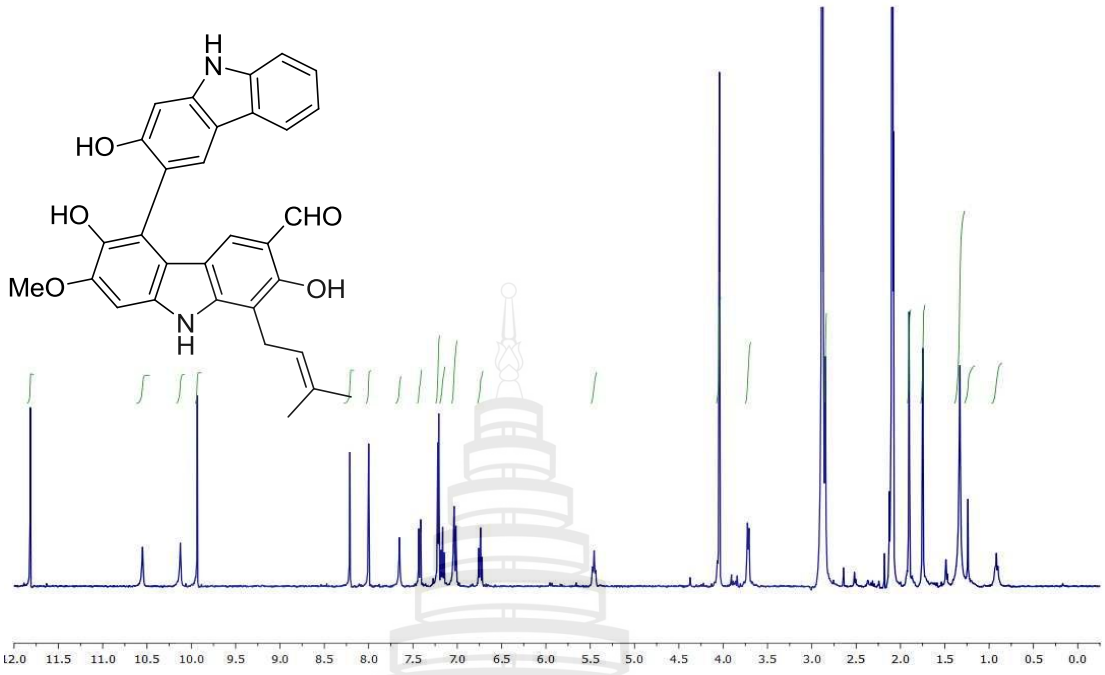

Figure A162 ^{1}H NMR Spectrum of **WM52** in Acetone-d_6 (500 MHz)

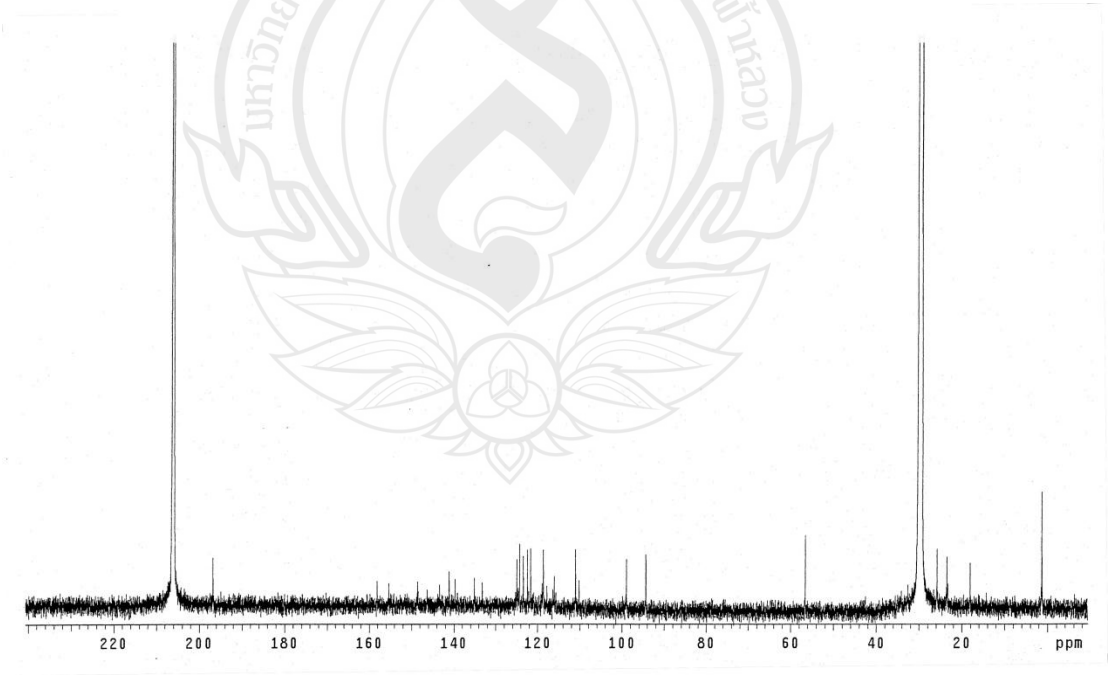

Figure A163 ^{13}C NMR Spectrum of **WM52** in Acetone-d_6 (125 MHz)

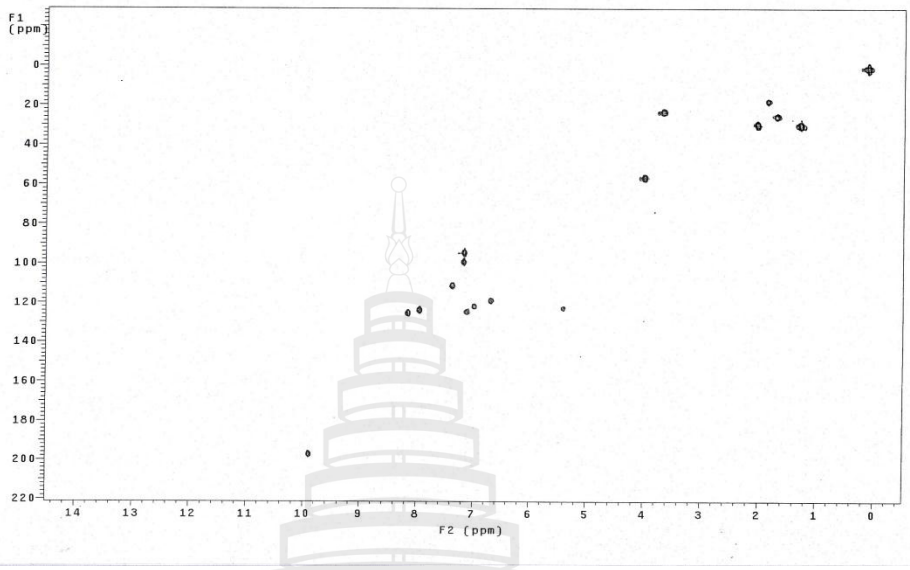

Figure A164 HMQC Spectrum of **WM52** in Acetone-d_6

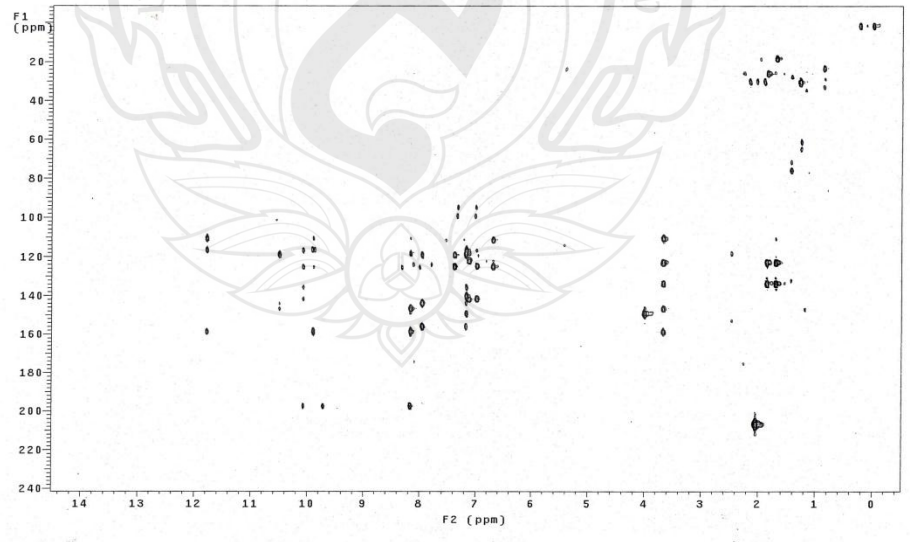

Figure A165 HMBC Spectrum of **WM52** in Acetone-d_6

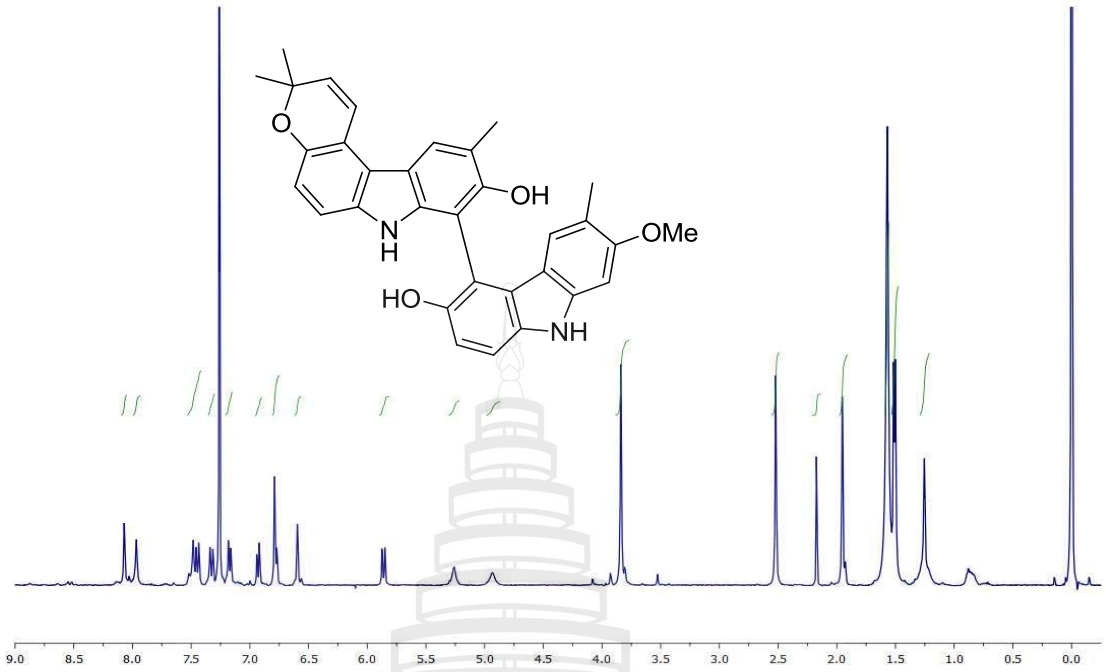

Figure A166 ^{1}H NMR Spectrum of **WM53** in $CDCl_3$ (500 MHz)

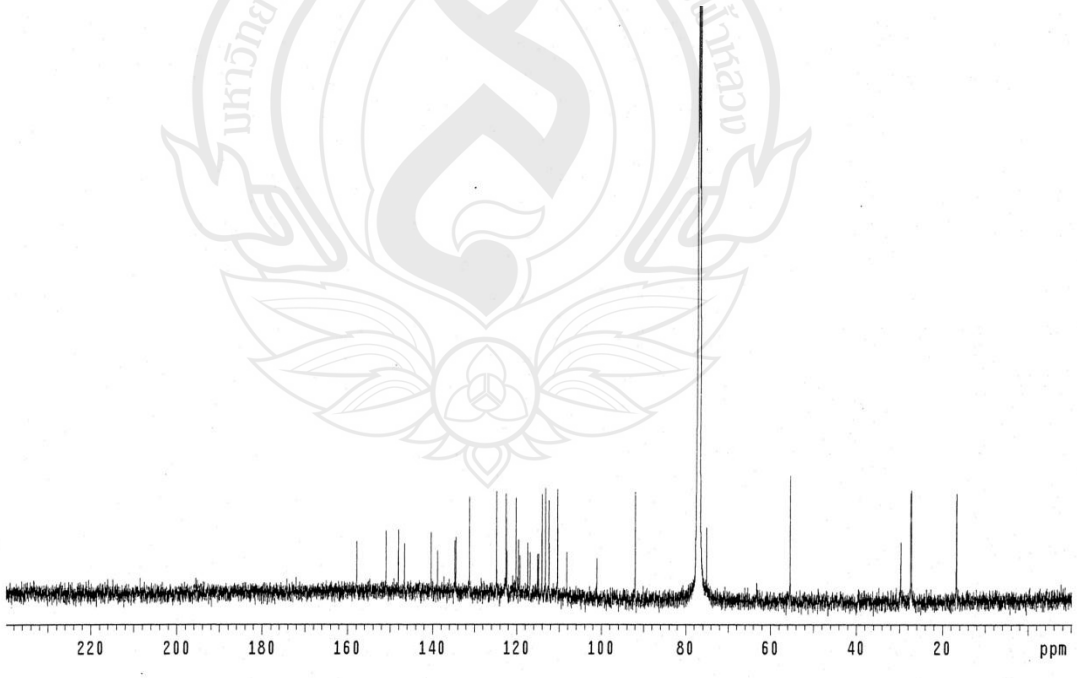

Figure A167 ^{13}C NMR Spectrum of **WM53** in $CDCl_3$ (125 MHz)

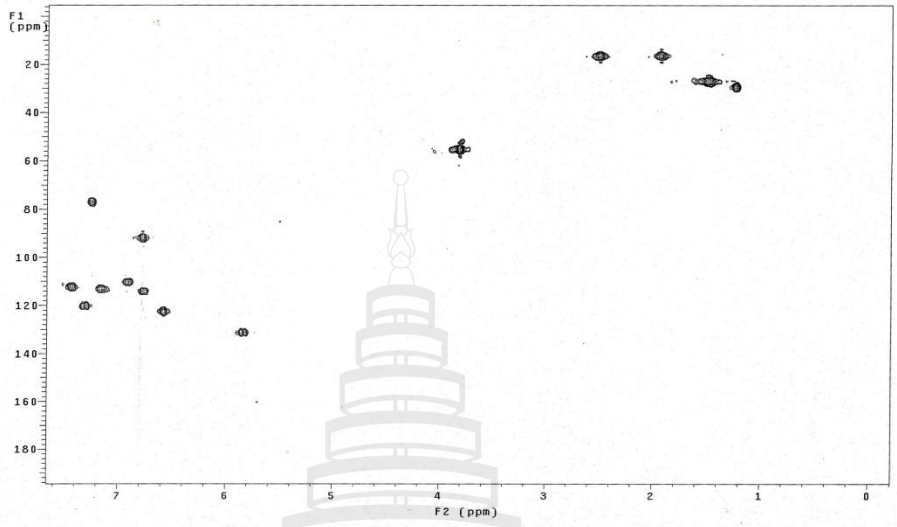

Figure A168 HMQC Spectrum of **WM53** in $CDCl_3$

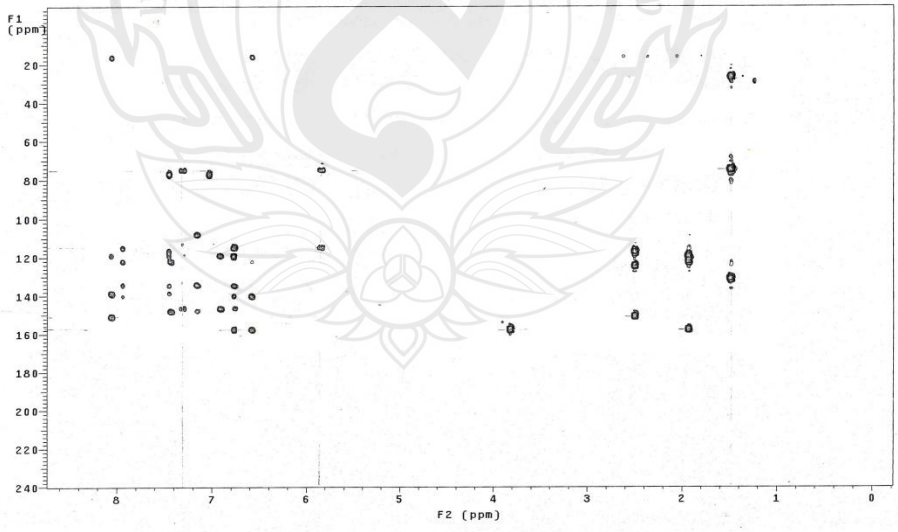

Figure A169 HMBC Spectrum of **WM53** in $CDCl_3$

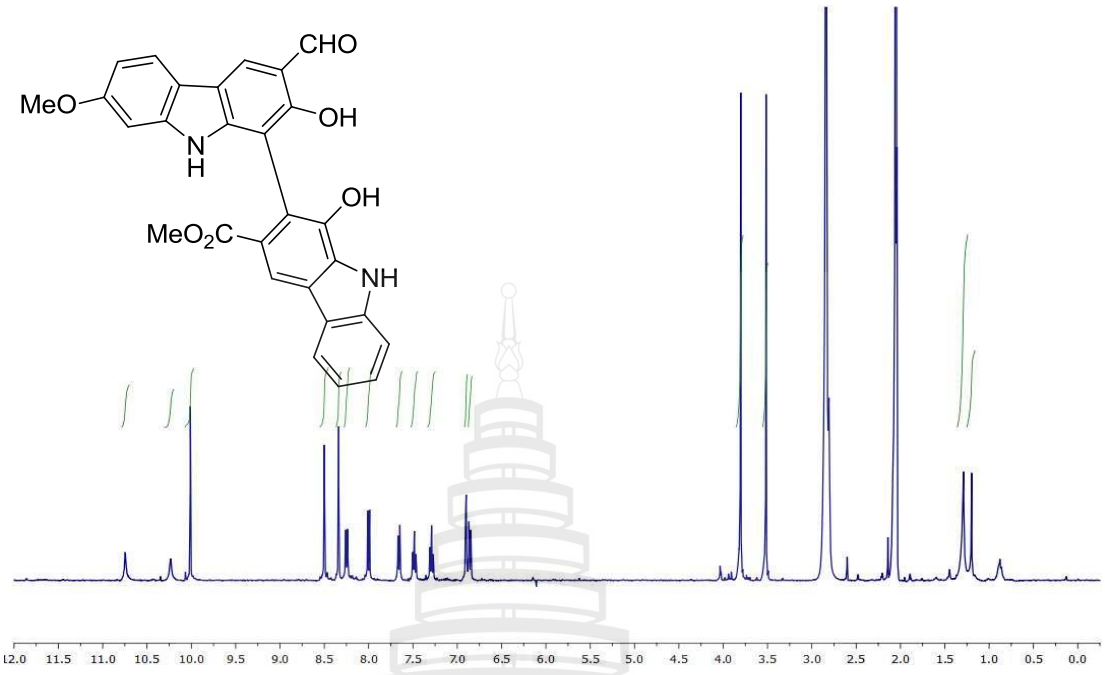

Figure A170 ^{1}H NMR Spectrum of **WM54** in Acetone-d_6 (400 MHz)

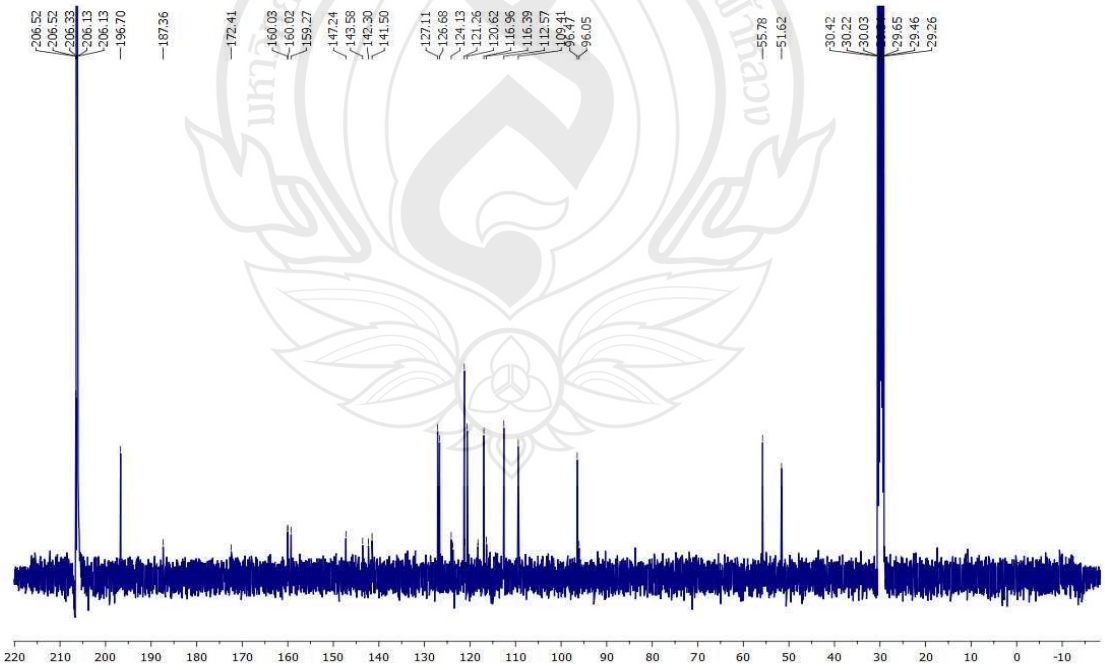

Figure A171 ^{13}C NMR Spectrum of **WM54** in Acetone-d_6 (100 MHz)

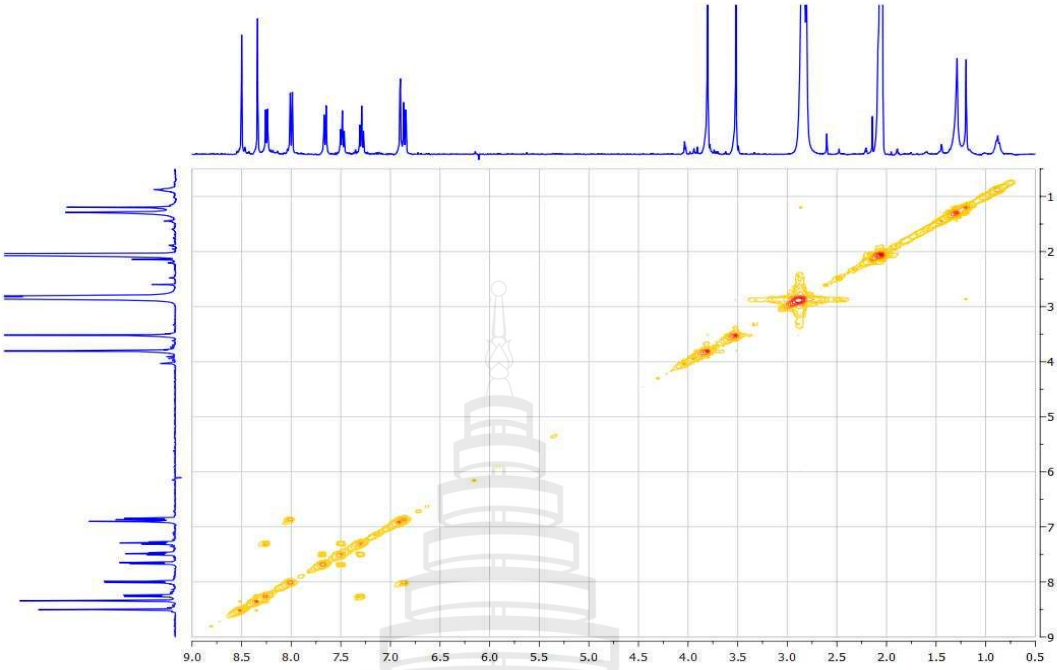

Figure A172 COSY Spectrum of **WM54** in Acetone-d_6

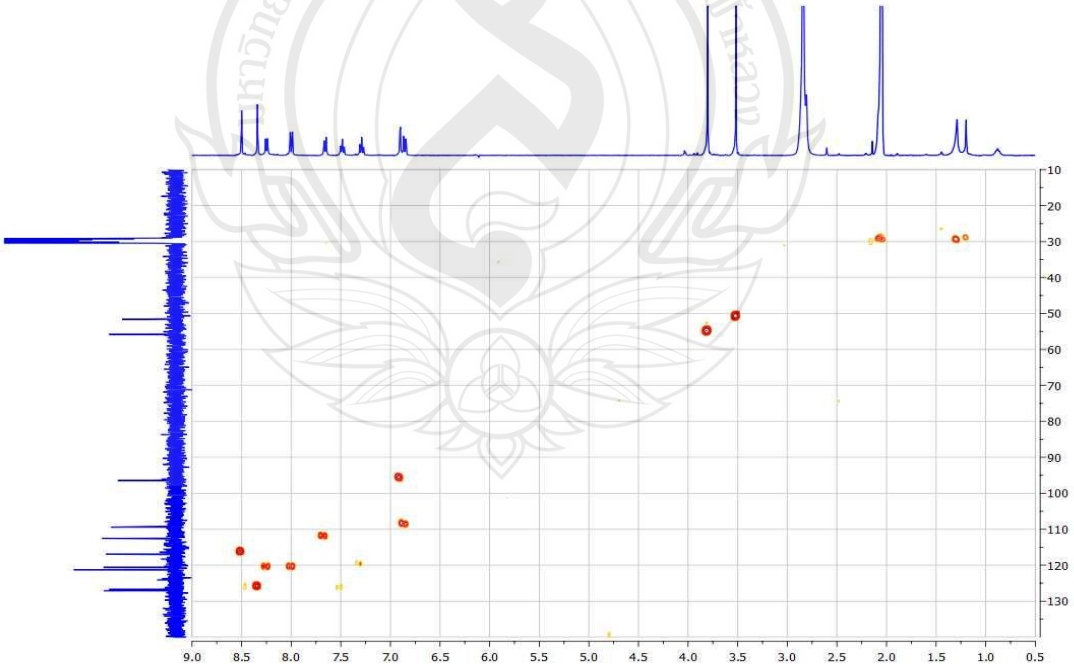

Figure A173 HMQC Spectrum of **WM54** in Acetone-d_6

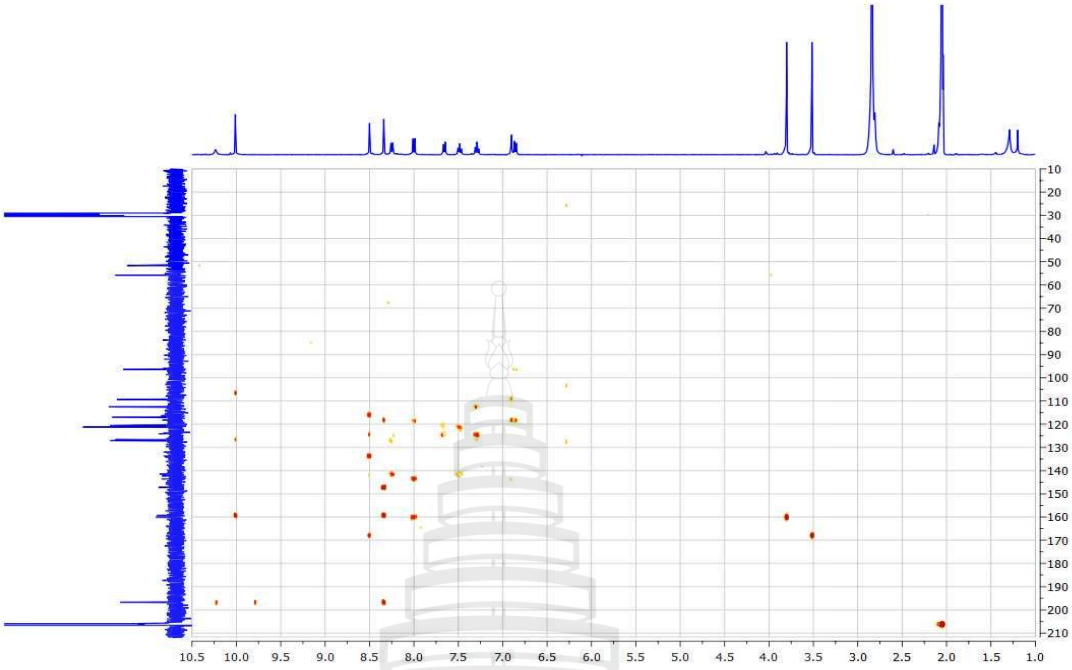

Figure A174 HMBC Spectrum of **WM54** in Acetone-d_6

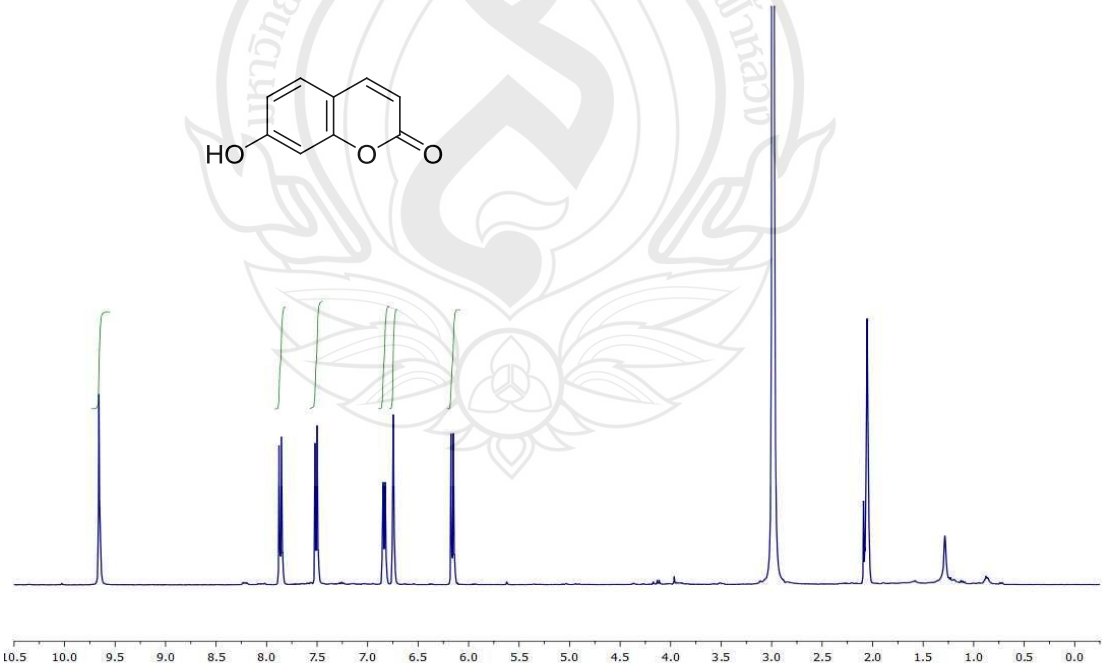

Figure A175 ^{1}H NMR Spectrum of **WM55** in Acetone-d_6 (400 MHz)

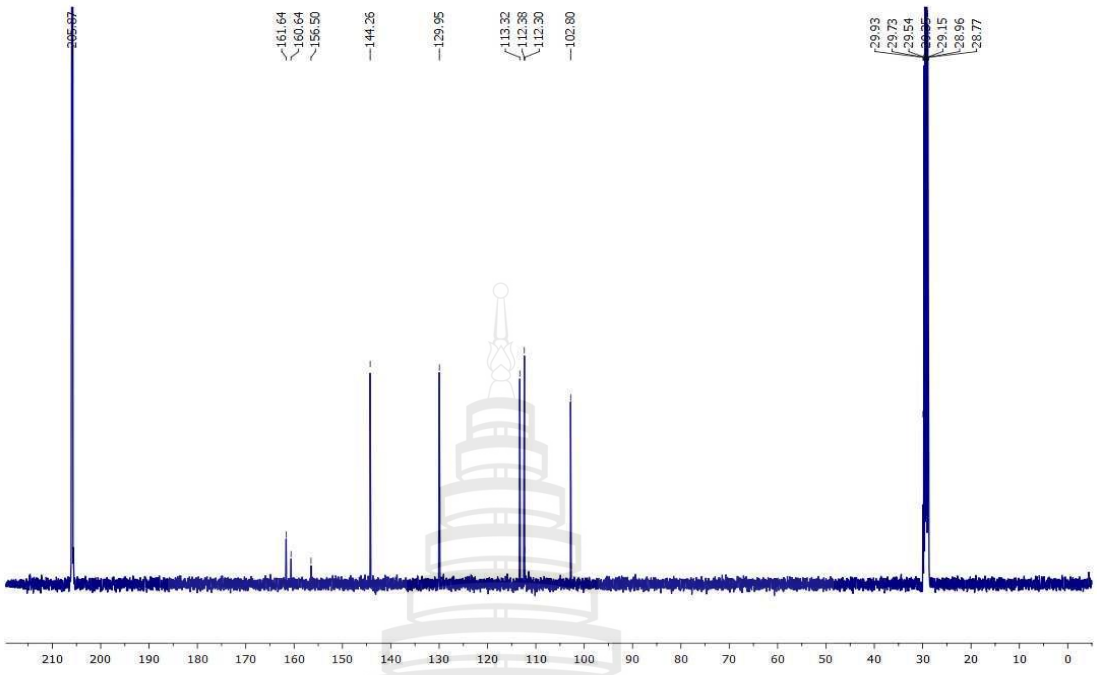

Figure A176 ^{13}C NMR Spectrum of **WM55** in Acetone-d_6 (100 MHz)

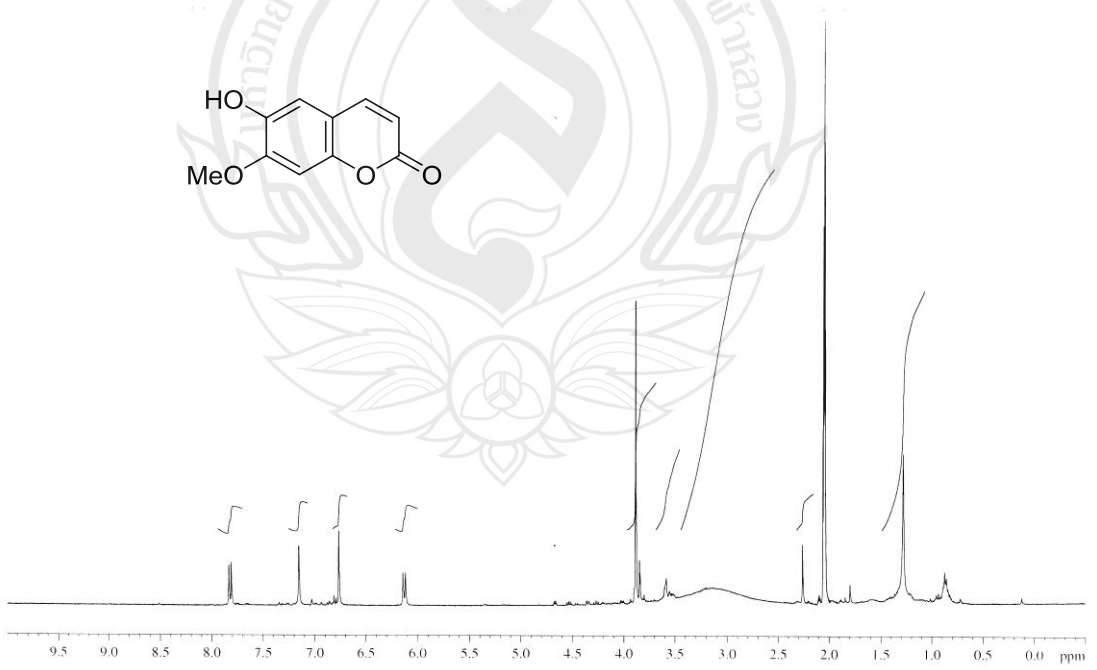

Figure A177 ^{1}H NMR Spectrum of **WM56** in Acetone-d_6 (400 MHz)

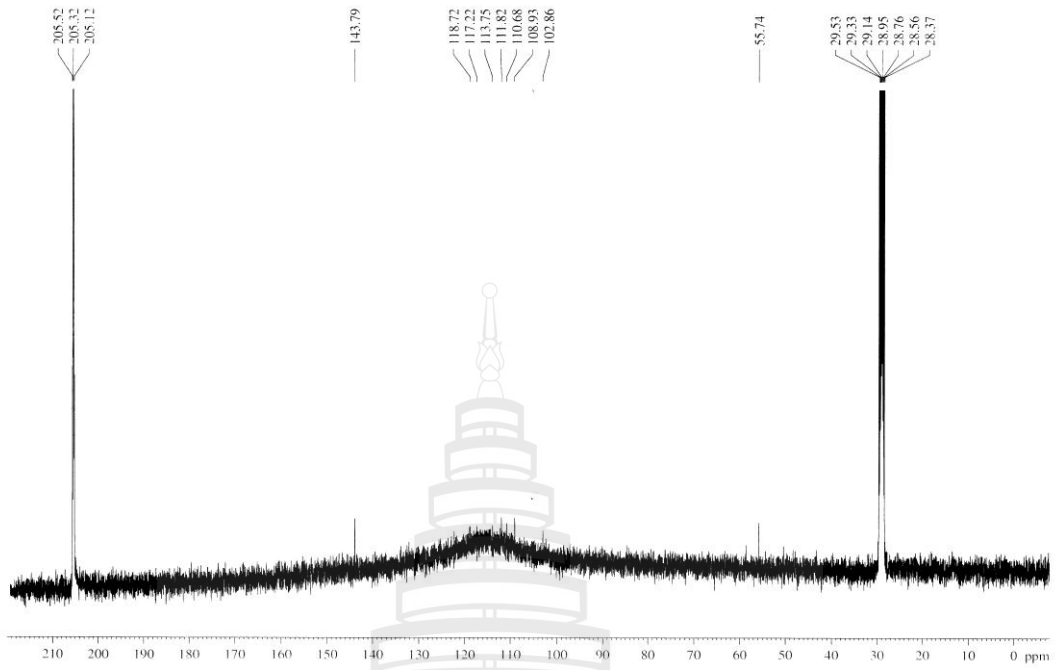

Figure A178 ^{13}C NMR Spectrum of **WM56** in Acetone-d_6 (100 MHz)

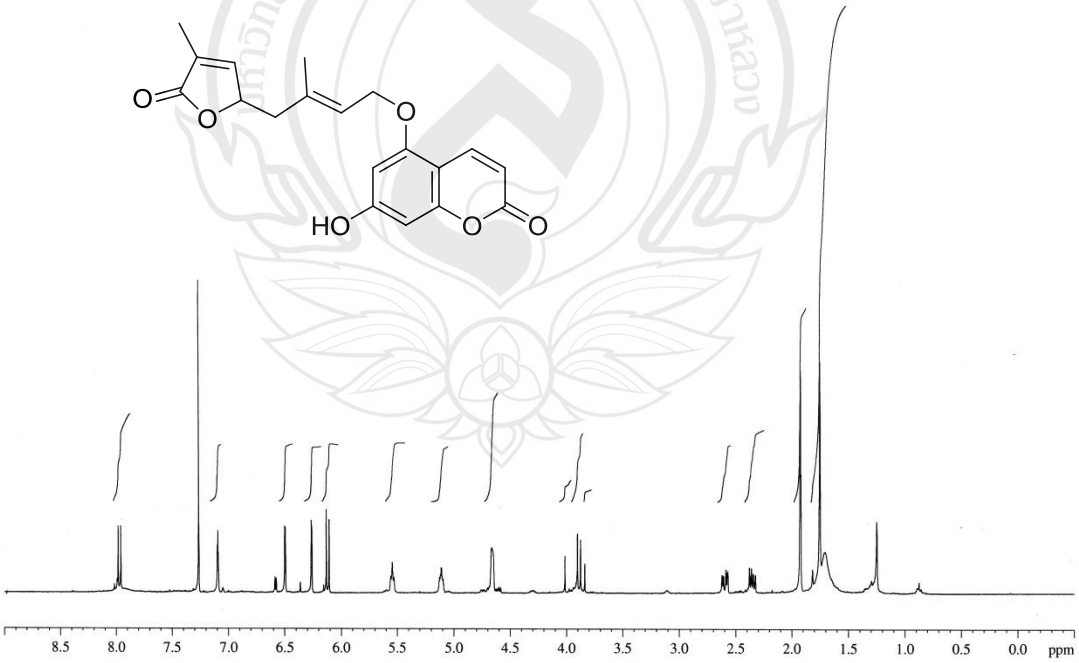

Figure A179 ^{1}H NMR Spectrum of **WM57** in $CDCl_3$ (400 MHz)

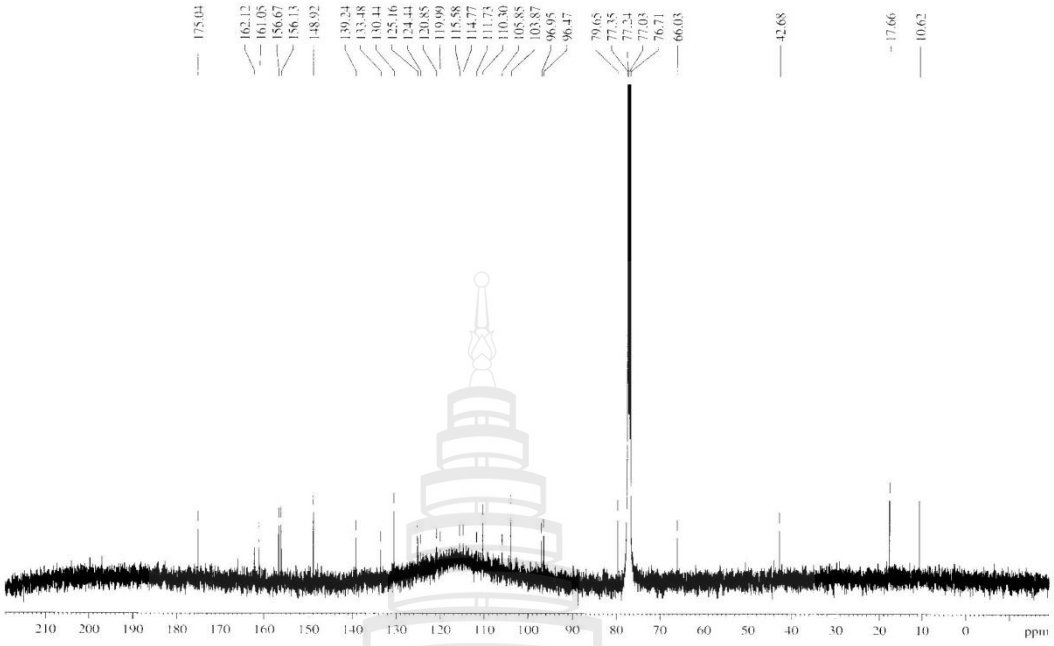

Figure A180 ^{13}C NMR Spectrum of **WM57** in $CDCl_3$ (100 MHz)

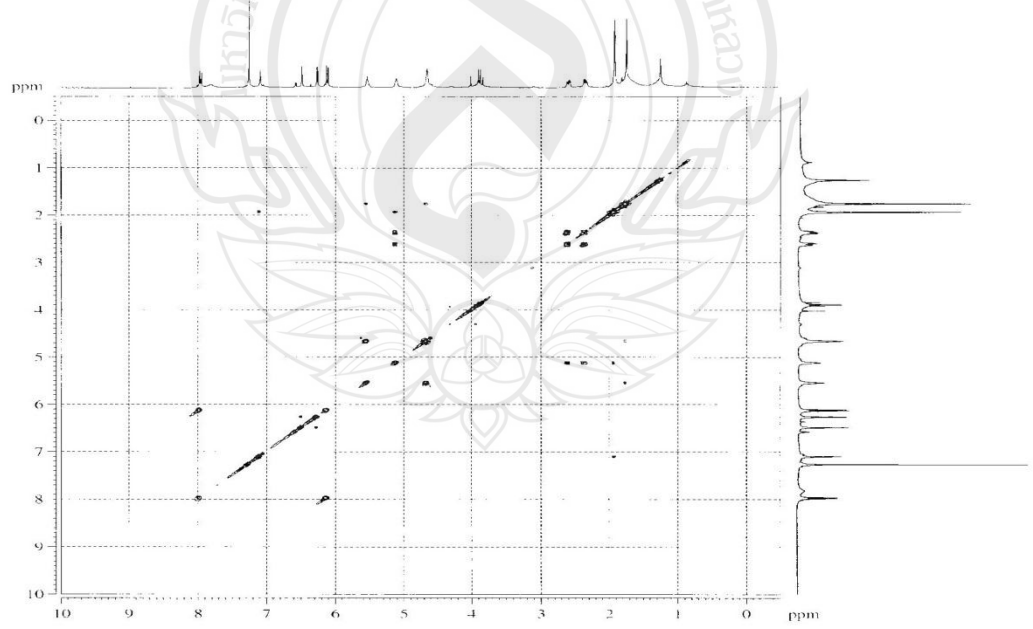

Figure A181 COSY Spectrum of **WM57** in $CDCl_3$

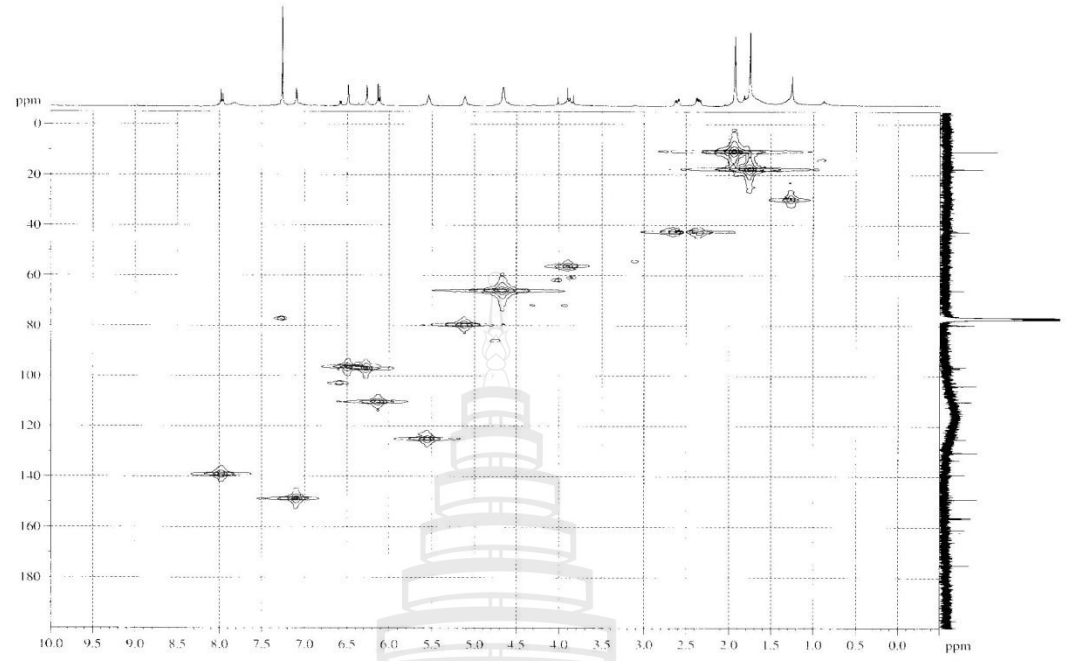

Figure A182 HMQC Spectrum of **WM57** in $CDCl_3$

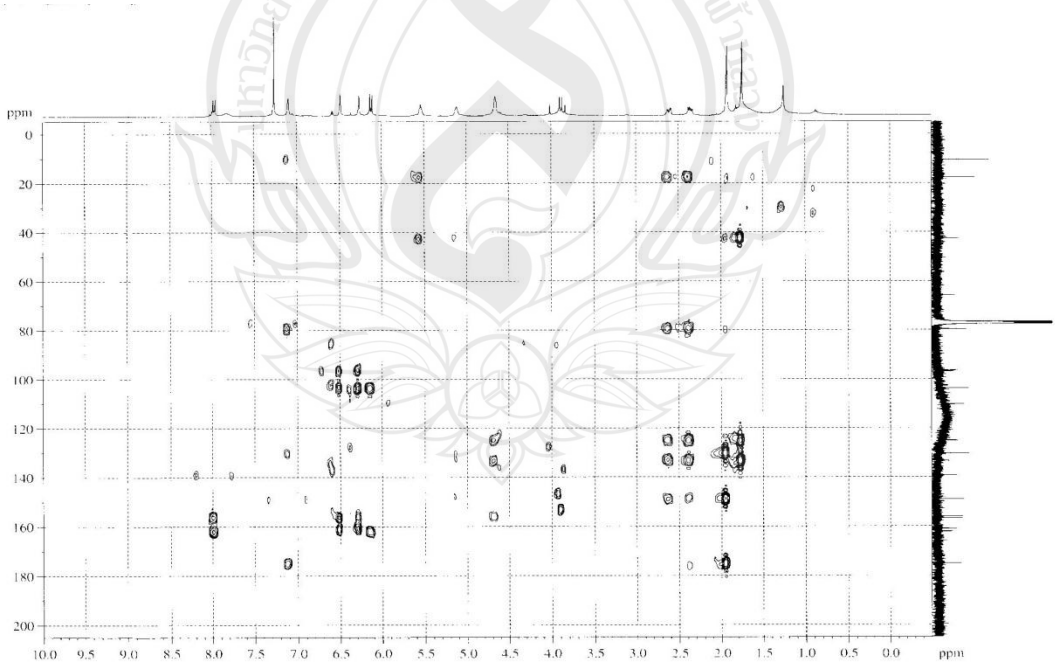

Figure A183 HMBC Spectrum of **WM57** in $CDCl_3$

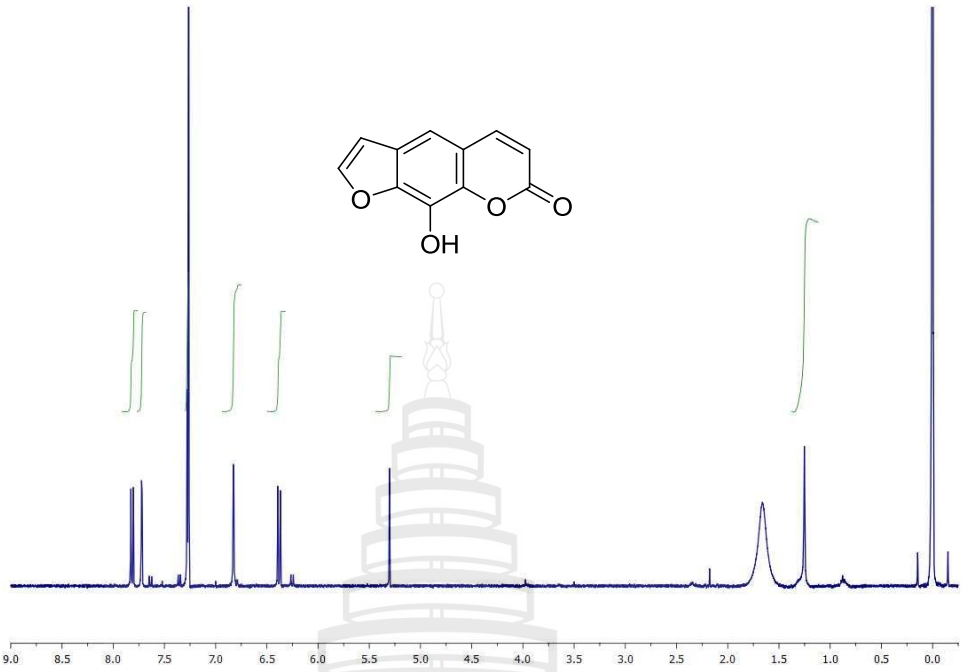

Figure A184 ^{1}H NMR Spectrum of **WM58** in $CDCl_3$ (400 MHz)

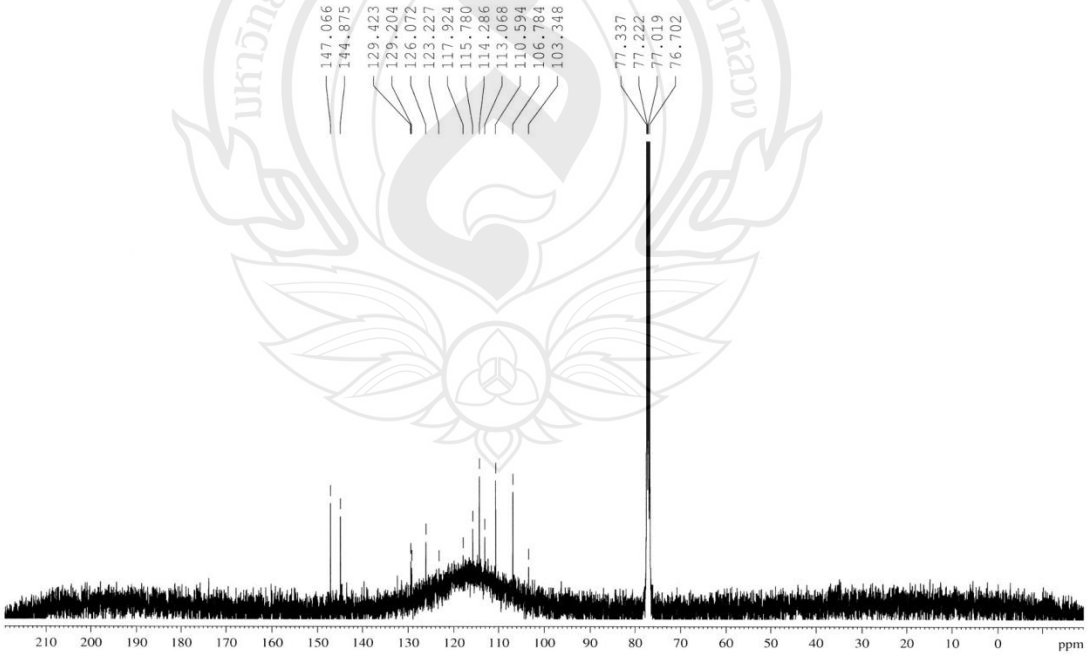

Figure A185 ^{13}C NMR Spectrum of **WM58** in $CDCl_3$ (100 MHz)

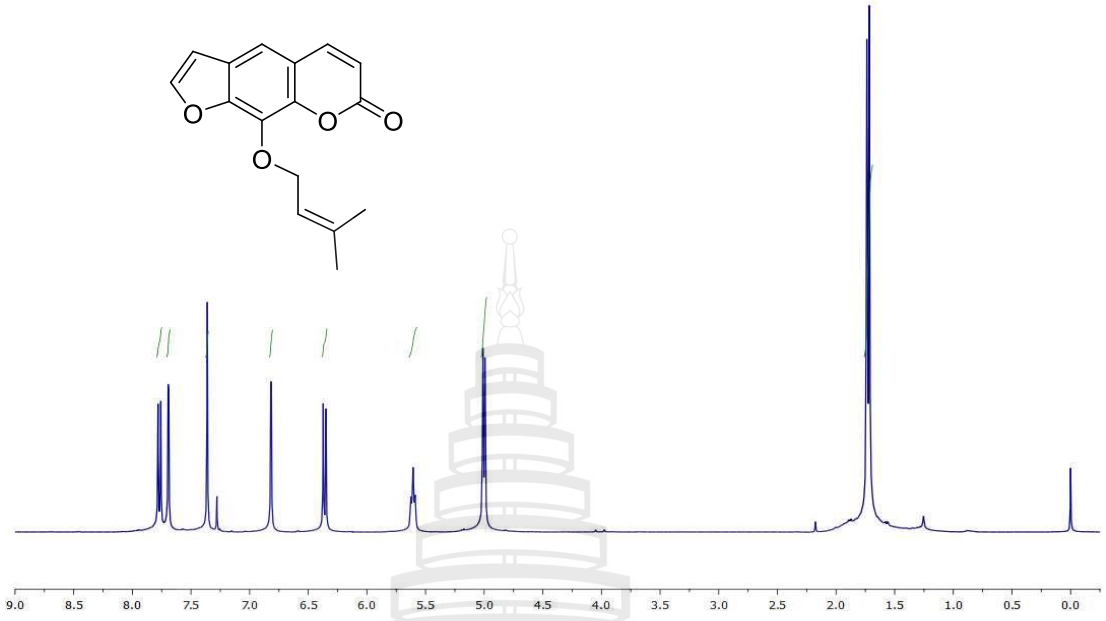

Figure A186 ^{1}H NMR Spectrum of **WM59** in $CDCl_3$ (400 MHz)

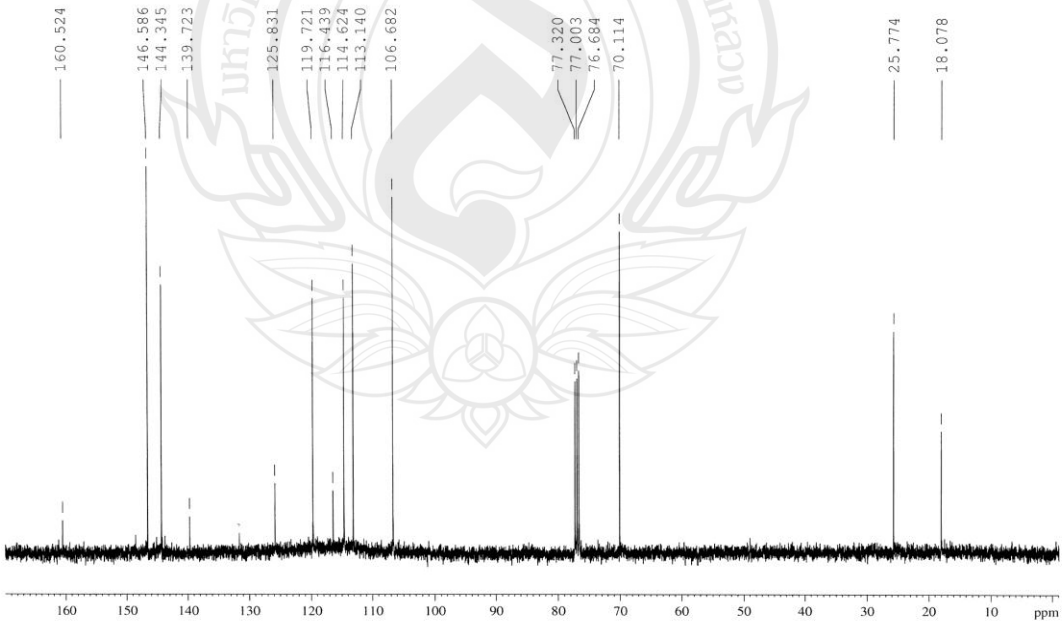

Figure A187 ^{13}C NMR Spectrum of **WM59** in $CDCl_3$ (100 MHz)

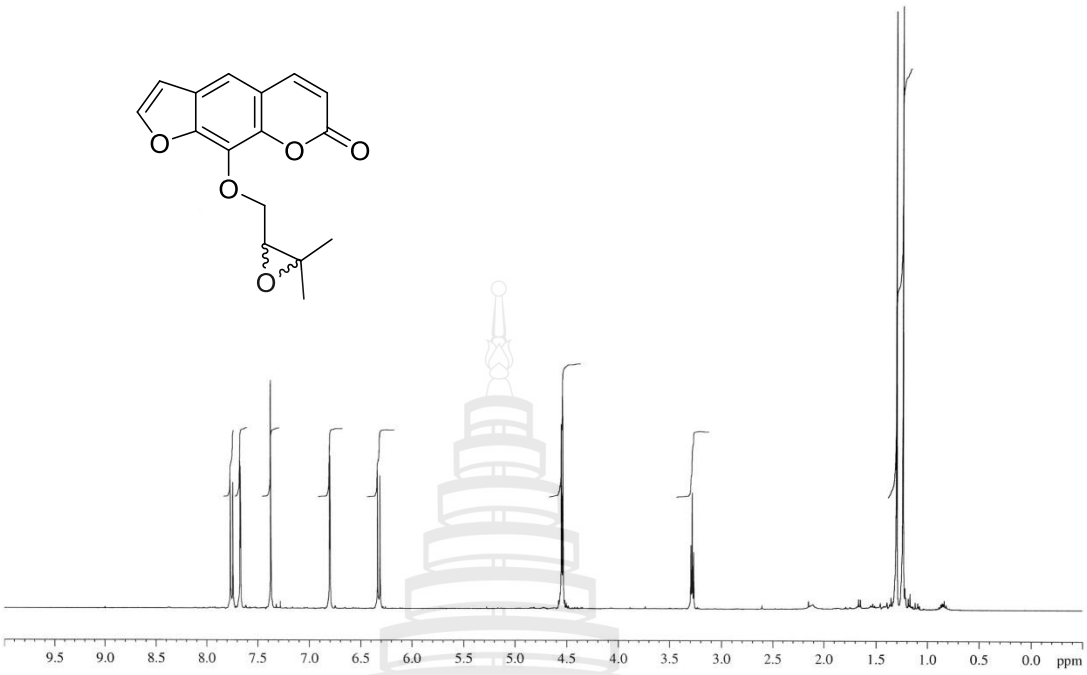

Figure A188 ^{1}H NMR Spectrum of **WM60** in $CDCl_3$ (400 MHz)

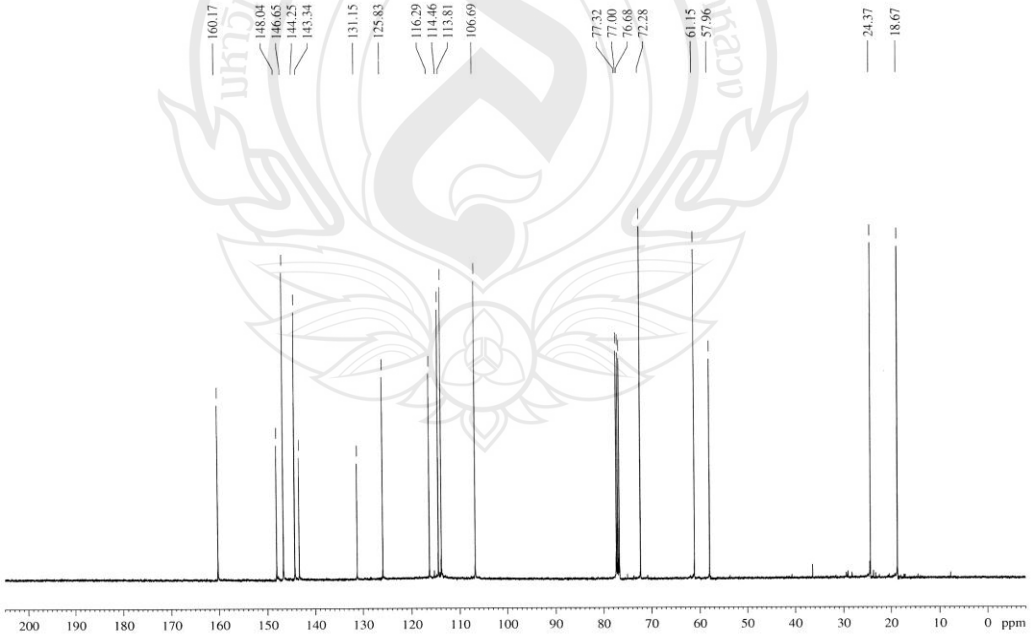

Figure A189 ^{13}C NMR Spectrum of **WM60** in $CDCl_3$ (100 MHz)

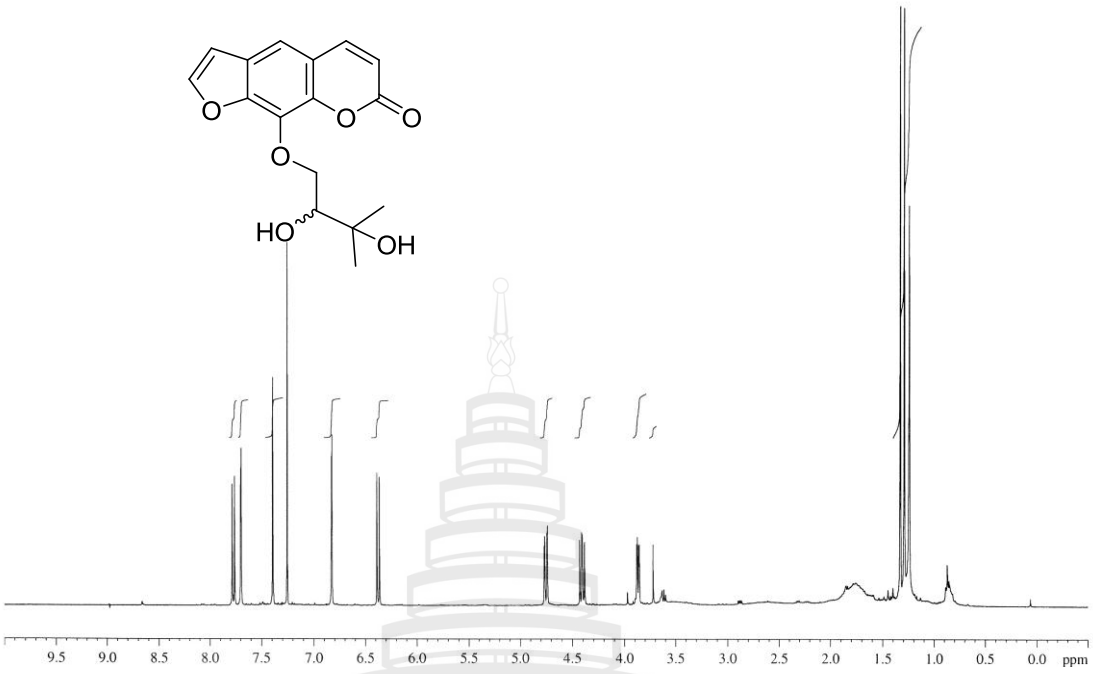

Figure A190 ^{1}H NMR Spectrum of **WM61** in $CDCl_3$ (400 MHz)

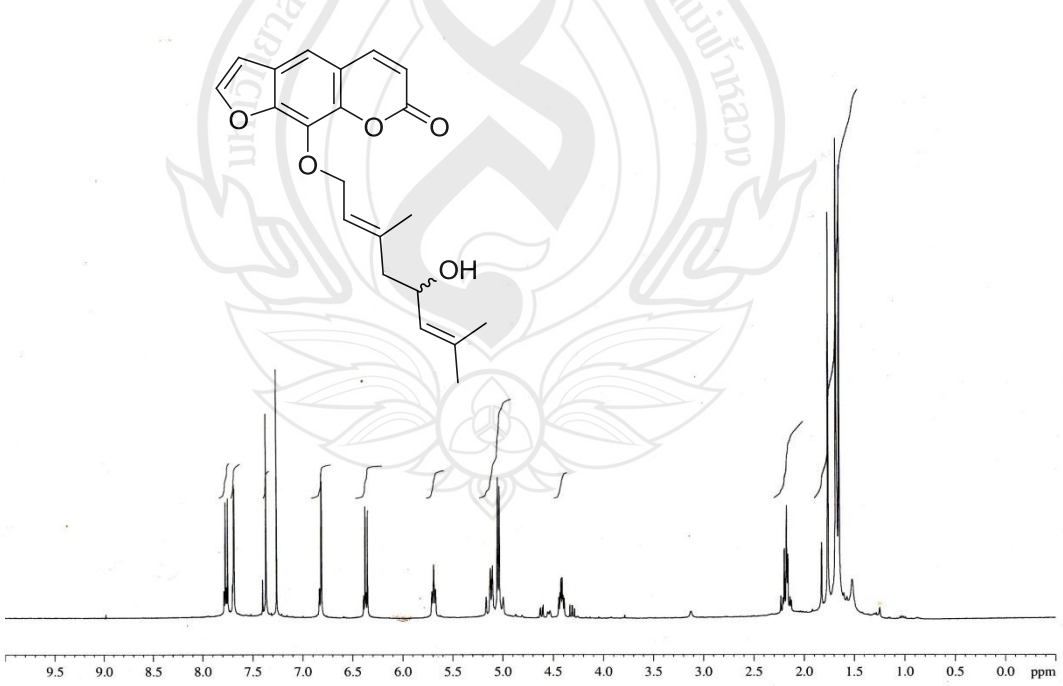

Figure A191 ^{1}H NMR Spectrum of **WM62** in $CDCl_3$ (400 MHz)

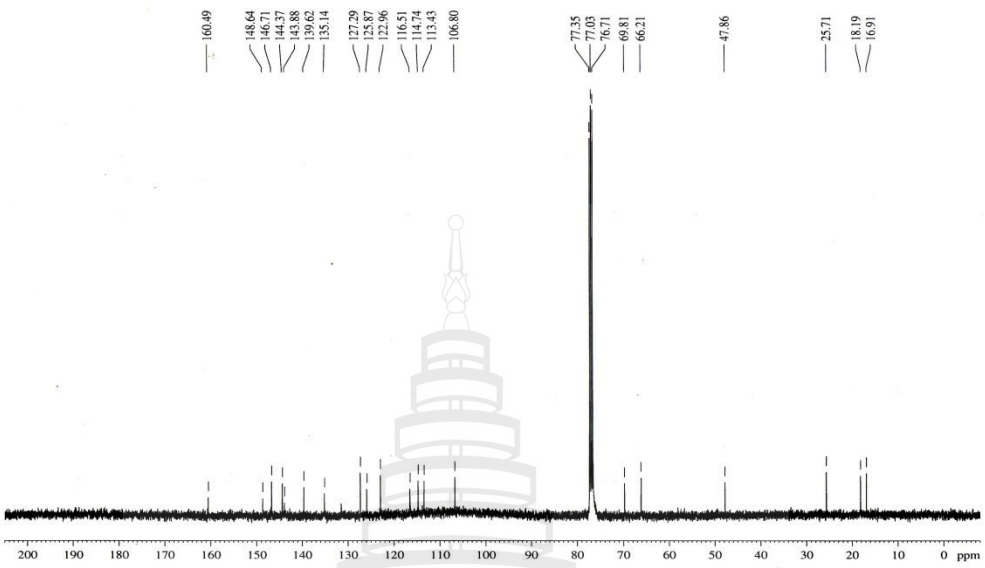

Figure A192 ^{13}C NMR Spectrum of **WM62** in $CDCl_3$ (100 MHz)

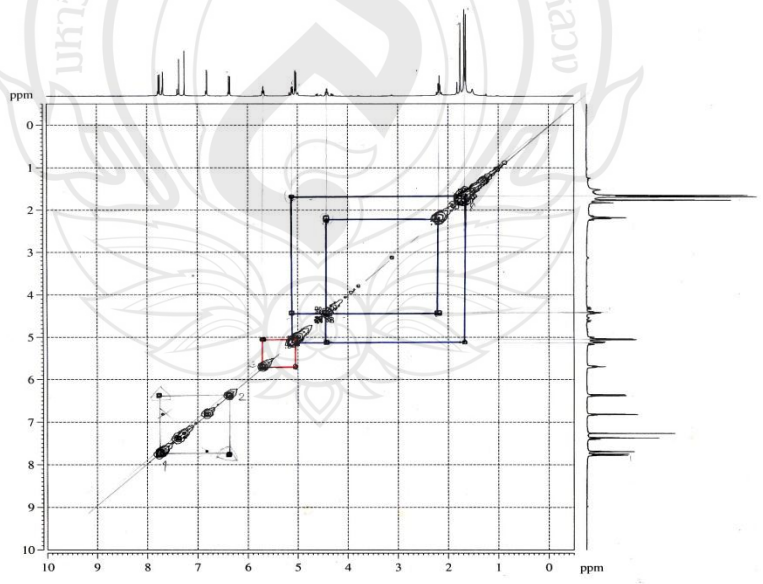

Figure A193 COSY Spectrum of **WM62** in $CDCl_3$

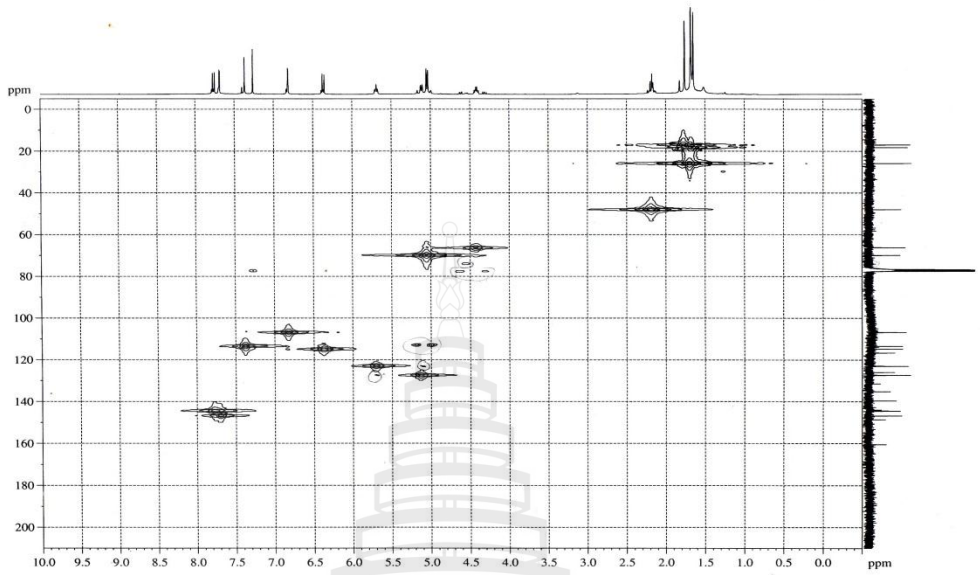

Figure A194 HMQC Spectrum of **WM52** in $CDCl_3$

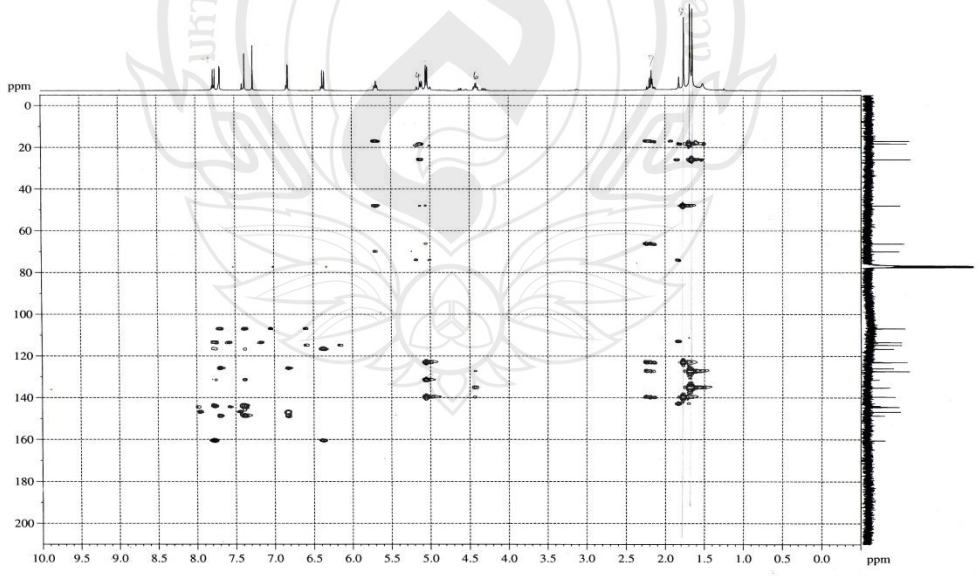

Figure A195 HMBC Spectrum of **WM62** in $CDCl_3$

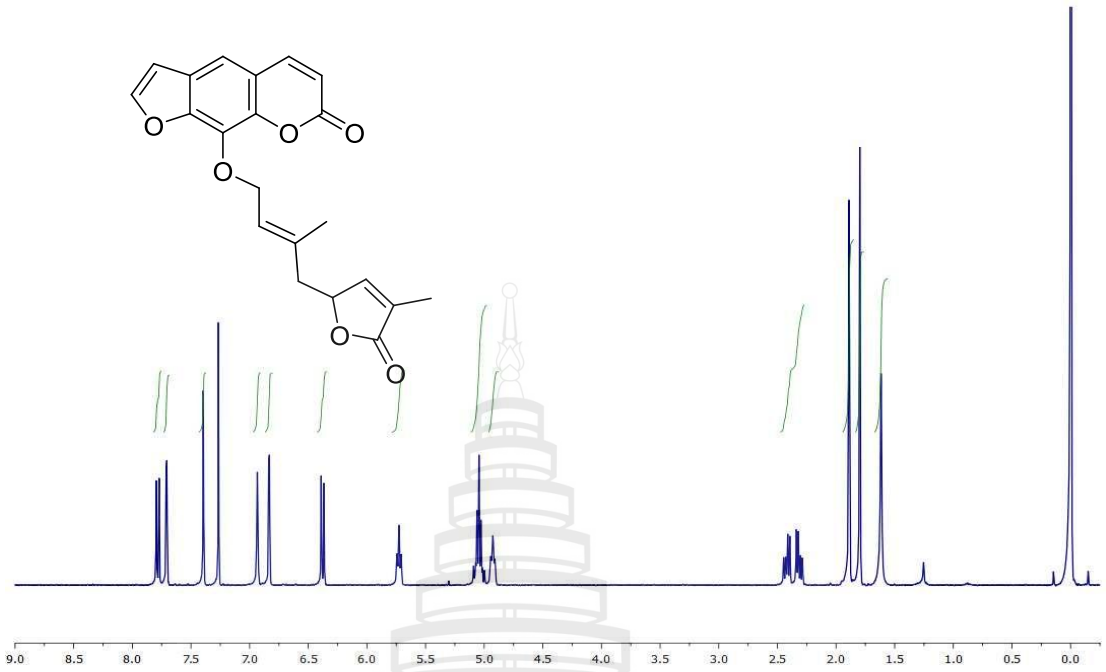

Figure A196 ^{1}H NMR Spectrum of **WM63** in $CDCl_3$ (400 MHz)

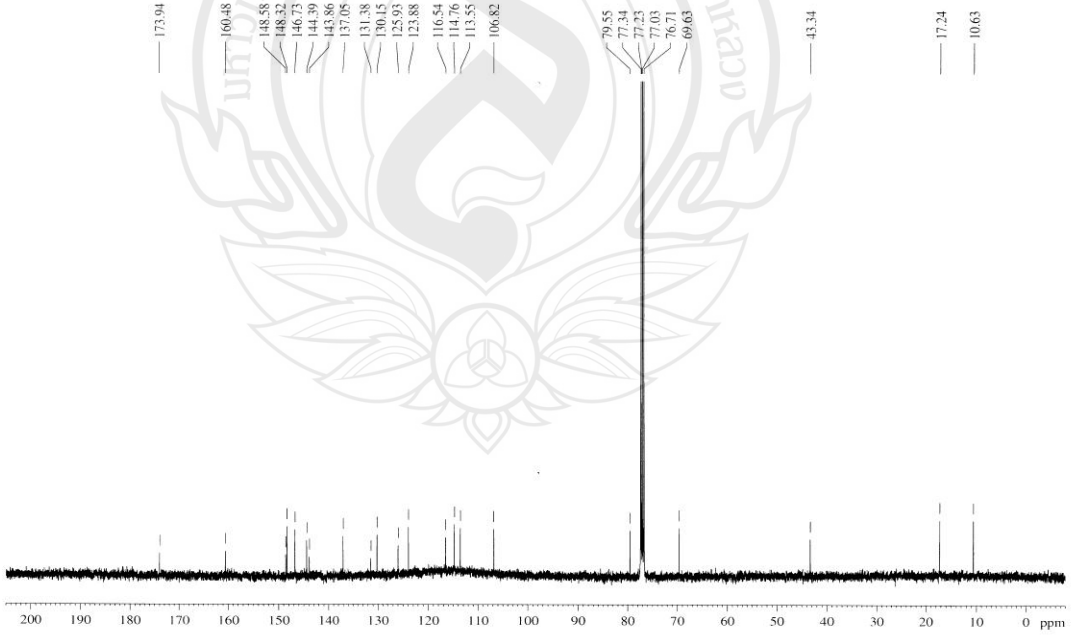

Figure A197 ^{13}C NMR Spectrum of **WM63** in $CDCl_3$ (100 MHz)

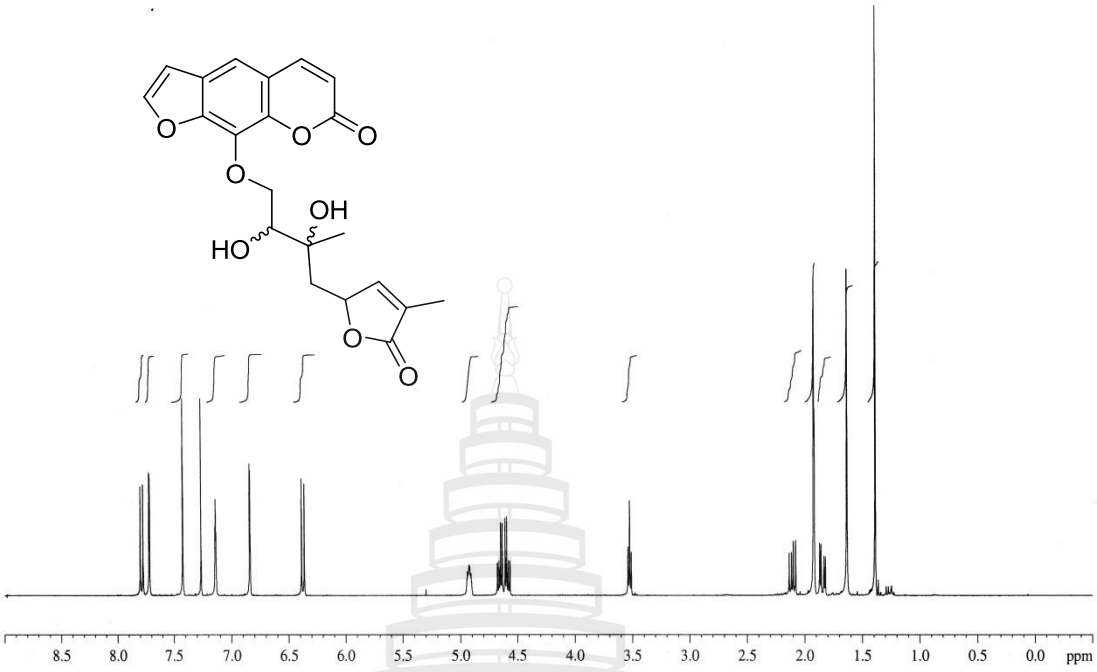

Figure A198 ^{1}H NMR Spectrum of **WM64** in $CDCl_3$ (400 MHz)

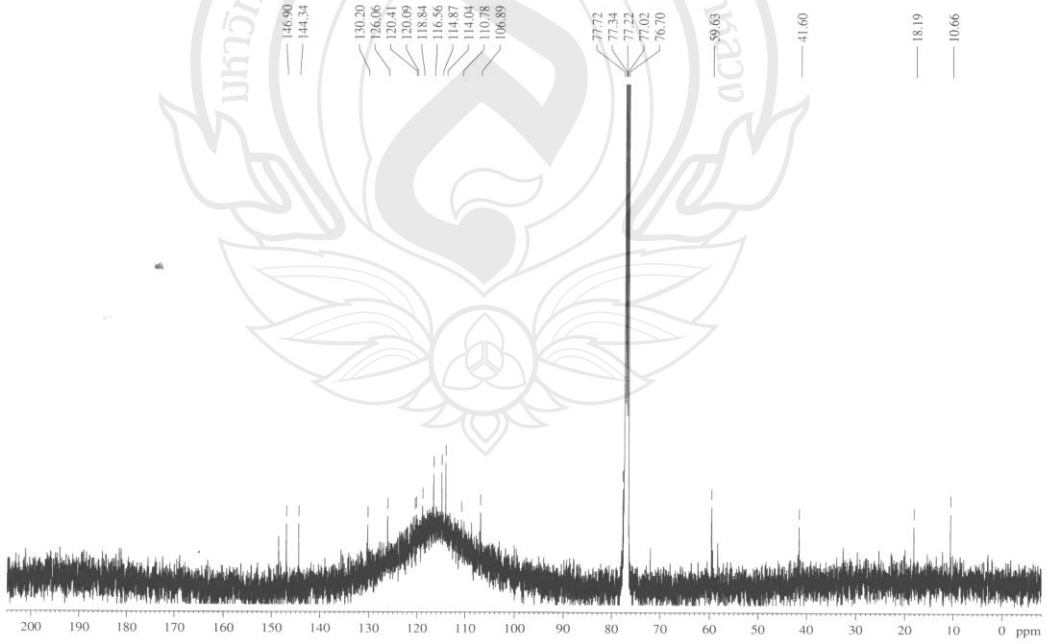

Figure A199 ^{13}C NMR Spectrum of **WM64** in $CDCl_3$ (100 MHz)

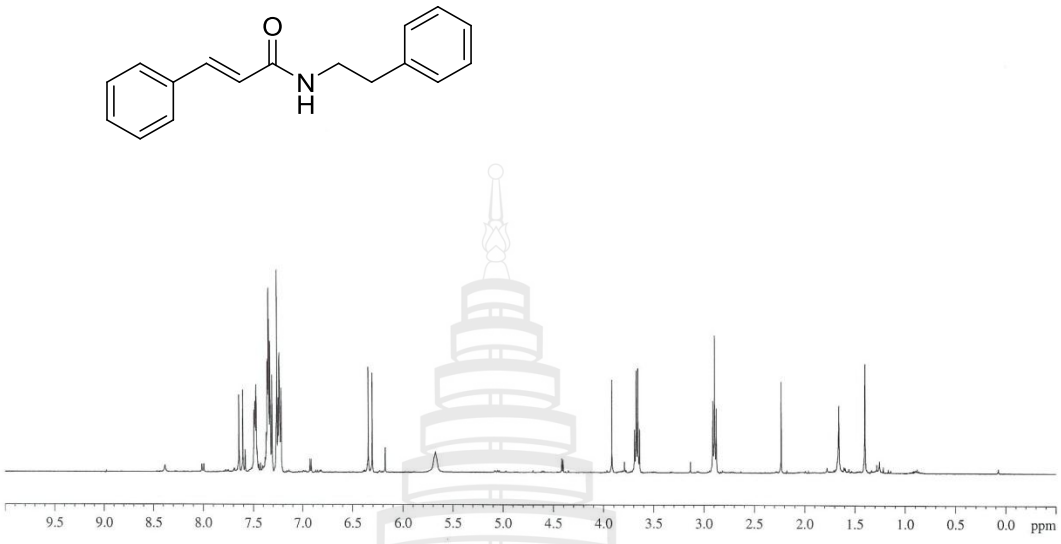

Figure A200 ^{1}H NMR Spectrum of **WM65** in $CDCl_3$ (400 MHz)

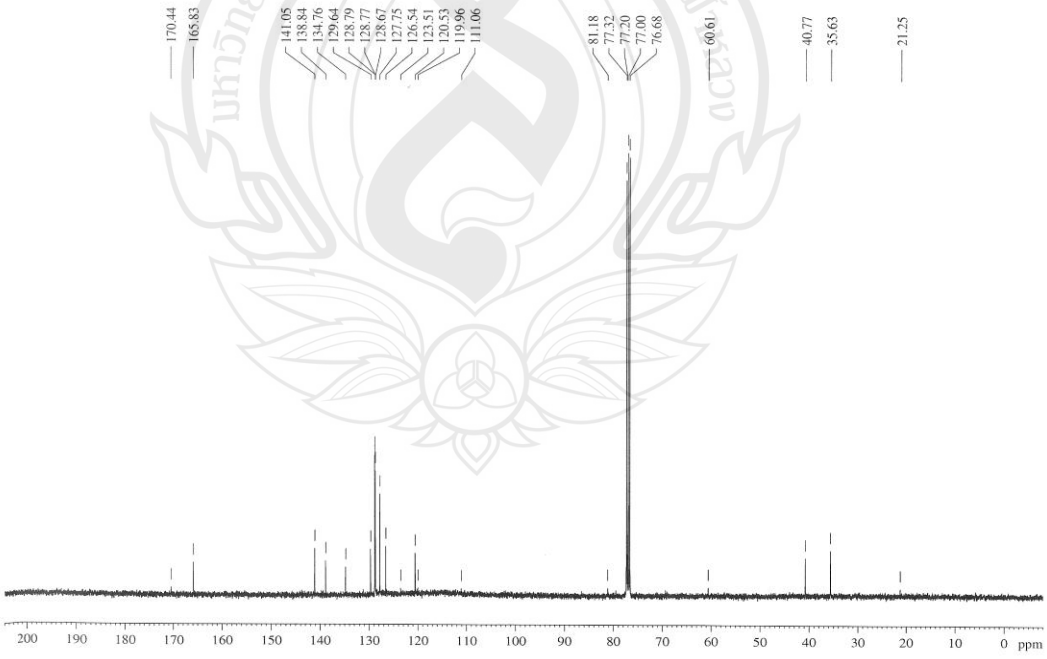

Figure A201 ^{13}C NMR Spectrum of **WM65** in $CDCl_3$ (100 MHz)

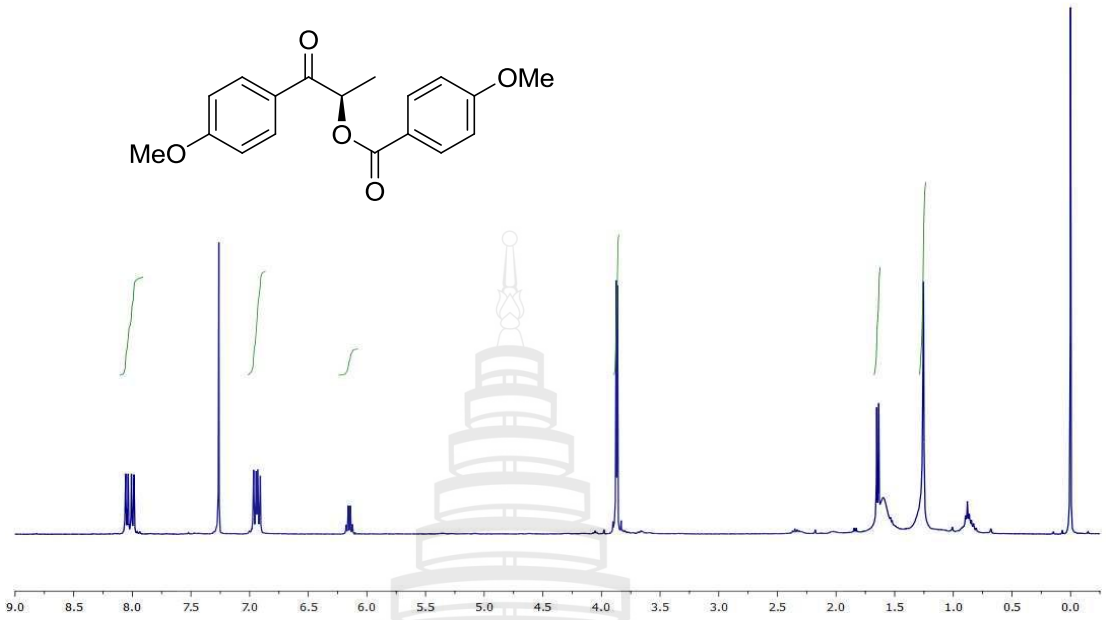

Figure A202 ^{1}H NMR Spectrum of **WM66** in $CDCl_3$ (400 MHz)

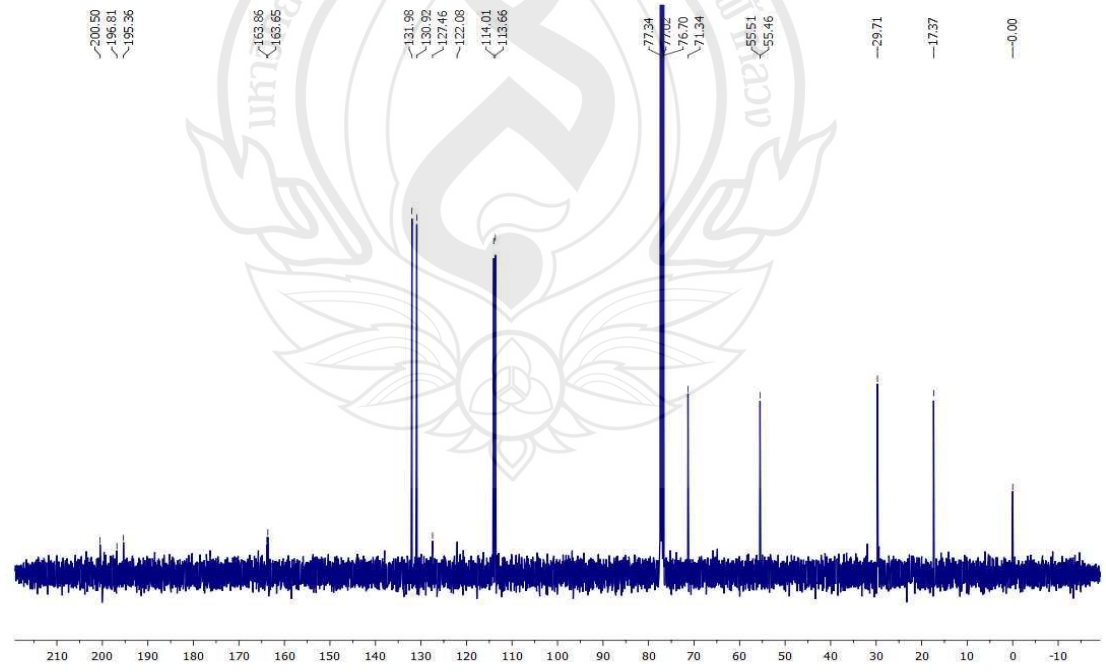

Figure A203 ^{13}C NMR Spectrum of **WM66** in $CDCl_3$ (100 MHz)

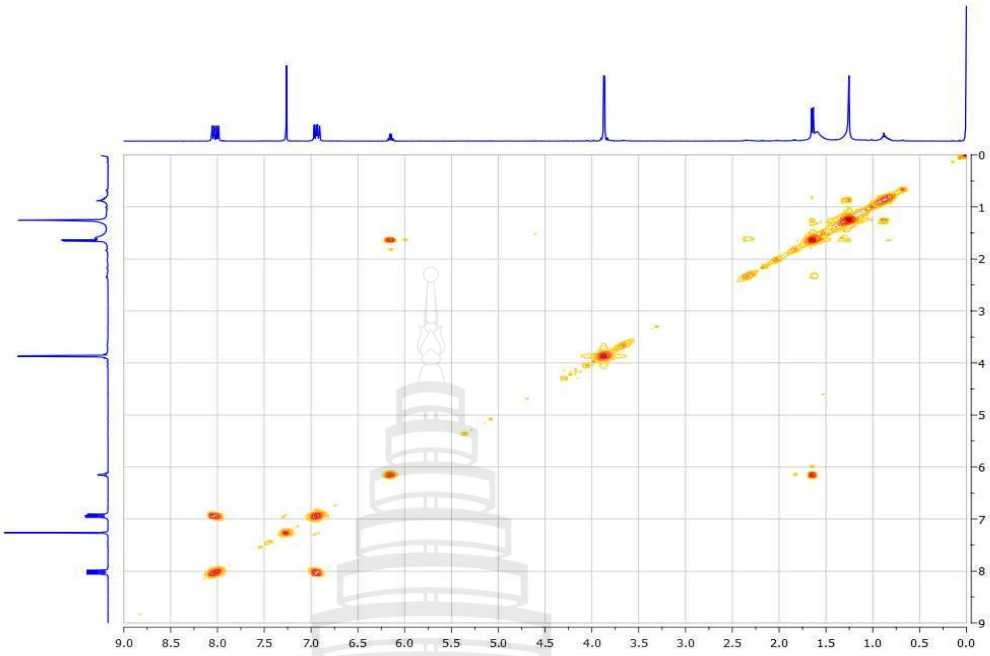

Figure A204 COSY Spectrum of **WM66** in $CDCl_3$

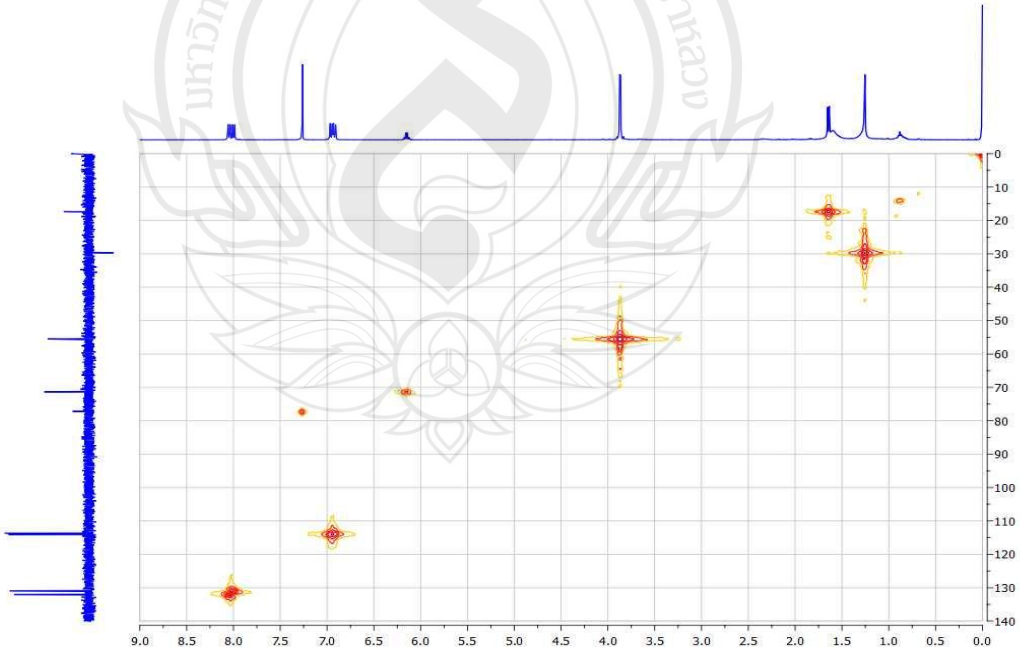

Figure A205 HMQC Spectrum of **WM66** in $CDCl_3$

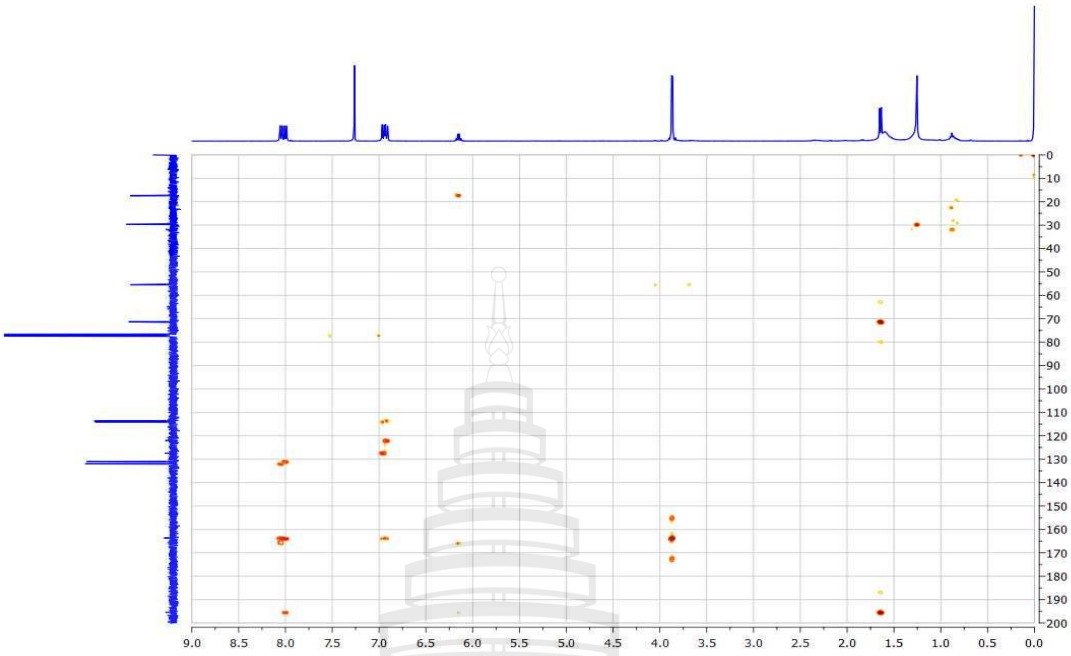

Figure A206 HMBC Spectrum of **WM66** in $CDCl_3$

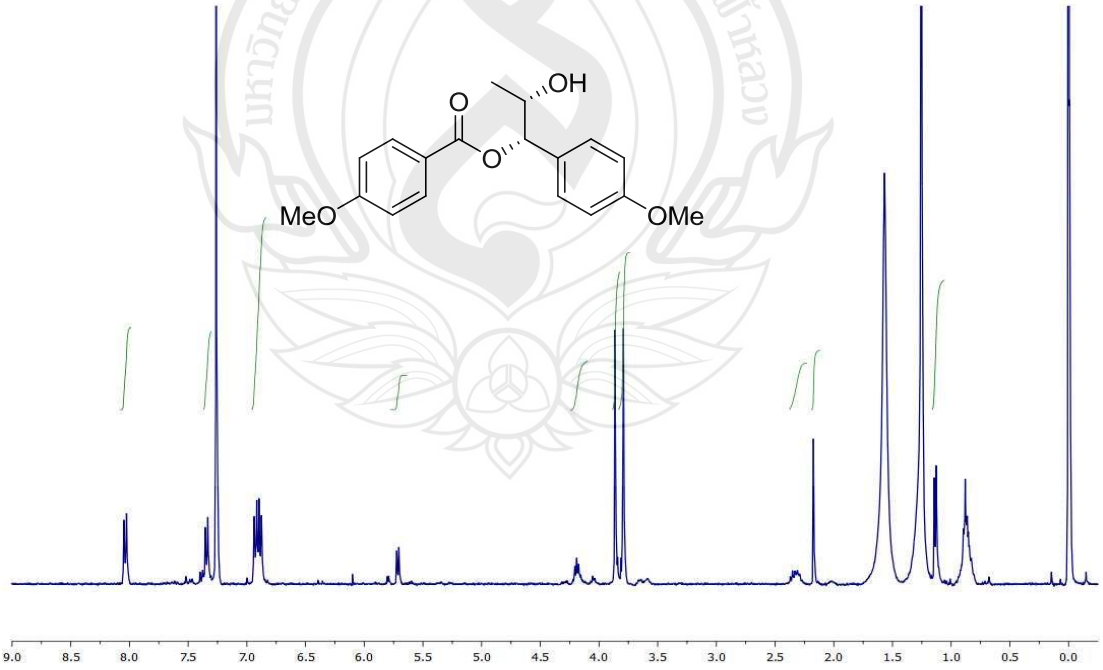

Figure A207 ^{1}H NMR Spectrum of **WM67** in $CDCl_3$ (400 MHz)

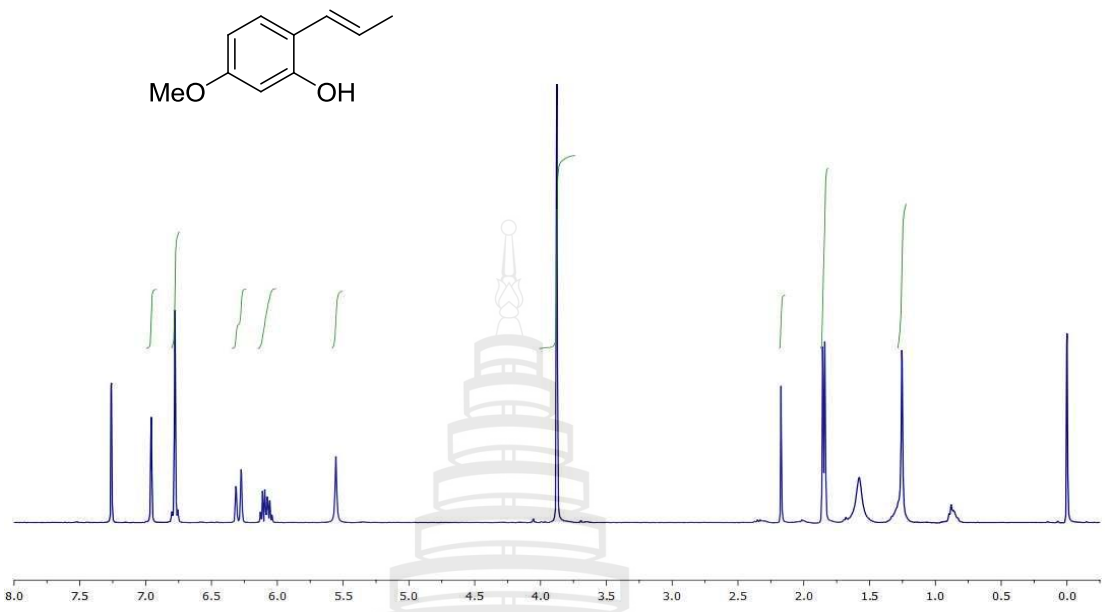

Figure A208 ^{1}H NMR Spectrum of **WM68** in $CDCl_3$ (400 MHz)

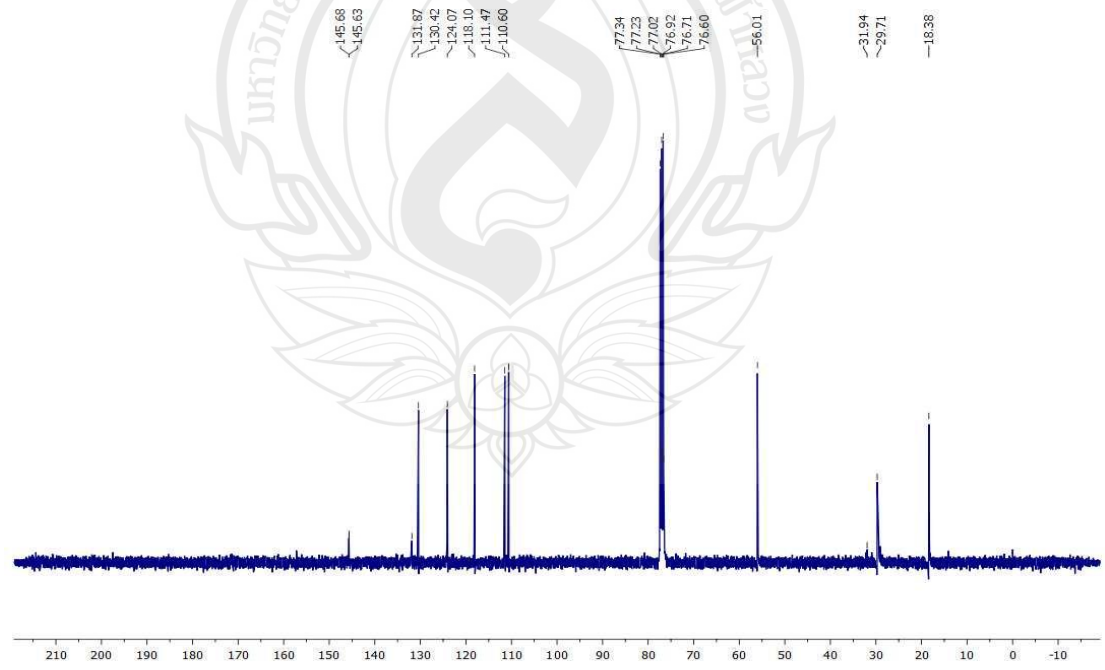

Figure A209 ^{13}C NMR Spectrum of **WM68** in $CDCl_3$ (100 MHz)

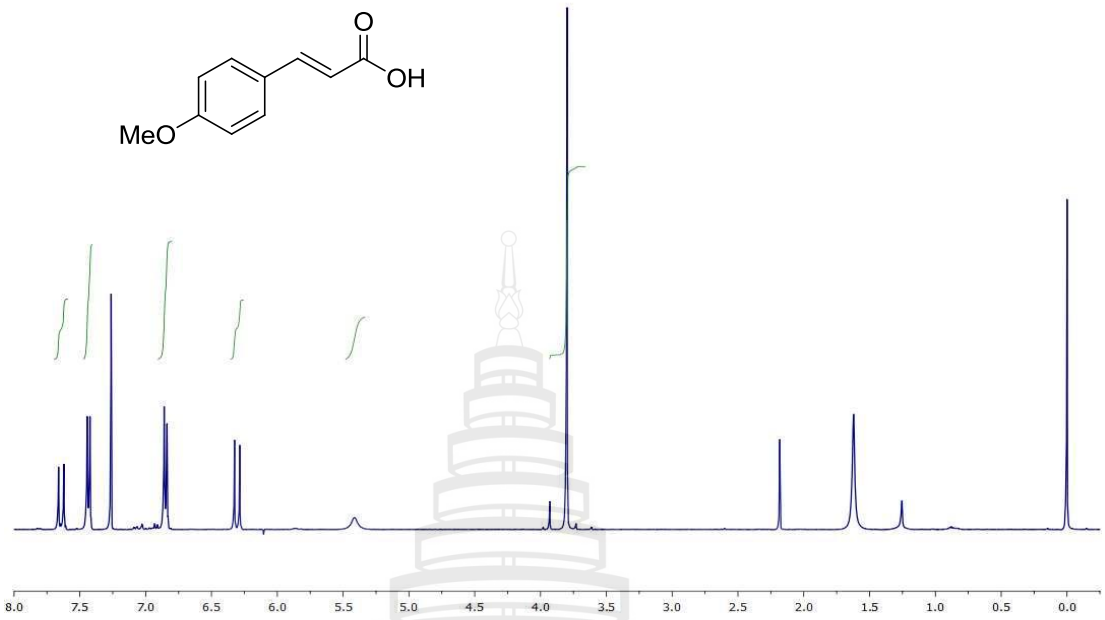

Figure A210 ^{1}H NMR Spectrum of **WM69** in $CDCl_3$ (400 MHz)

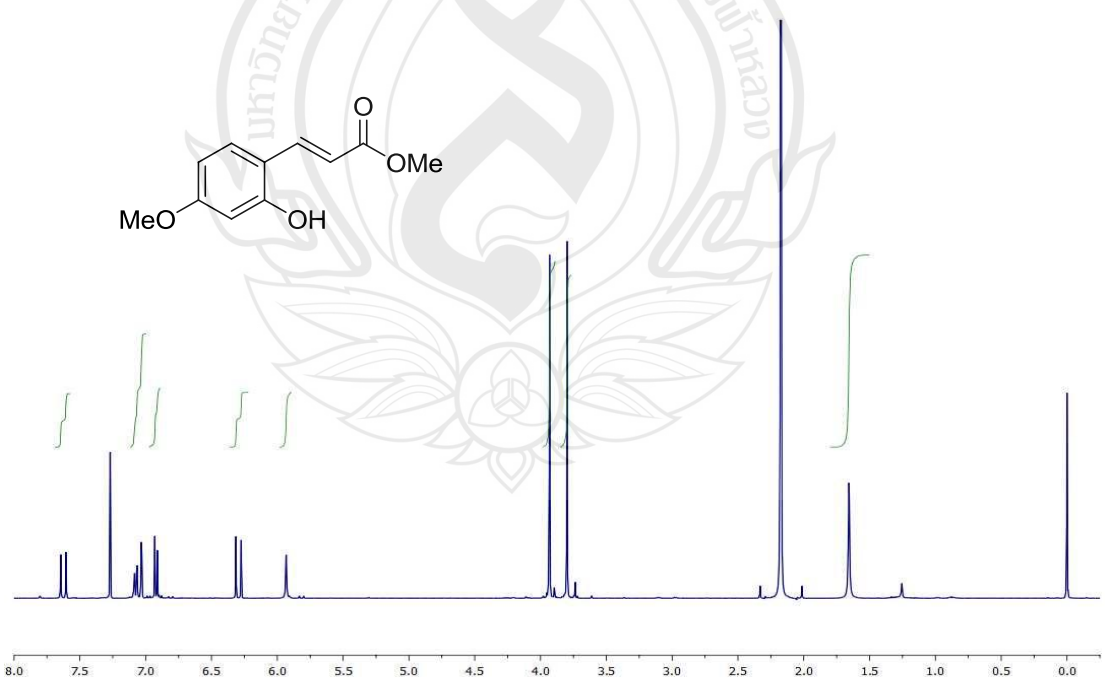

Figure A211 ^{1}H NMR Spectrum of **WM70** in $CDCl_3$ (400 MHz)

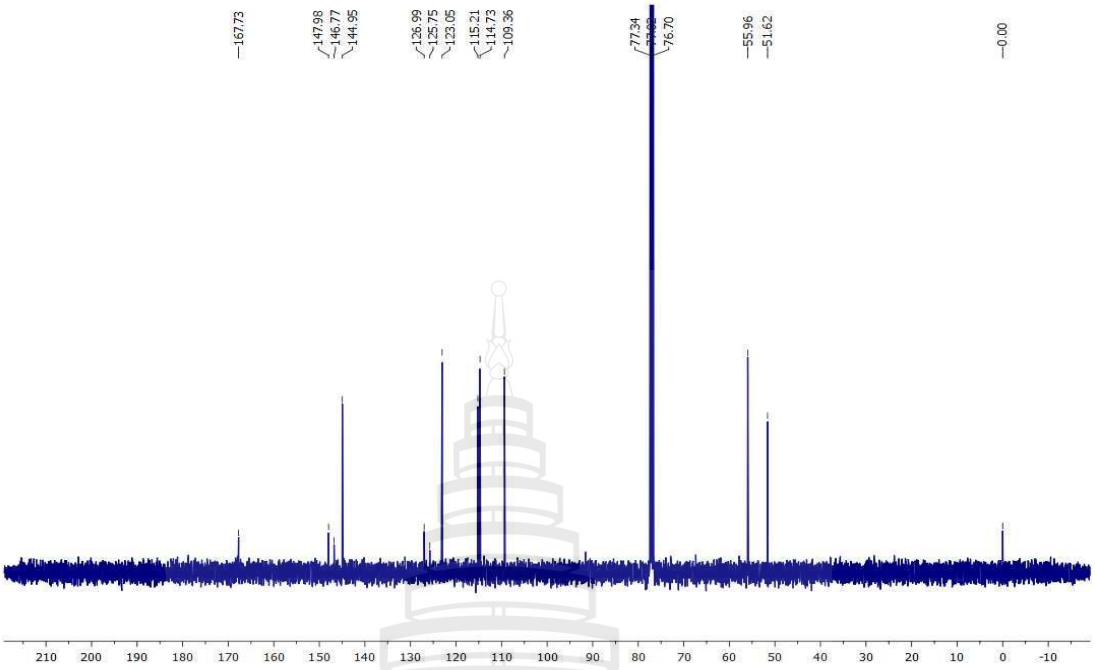

Figure A212 ^{13}C NMR Spectrum of **WM70** in $CDCl_3$ (100 MHz)

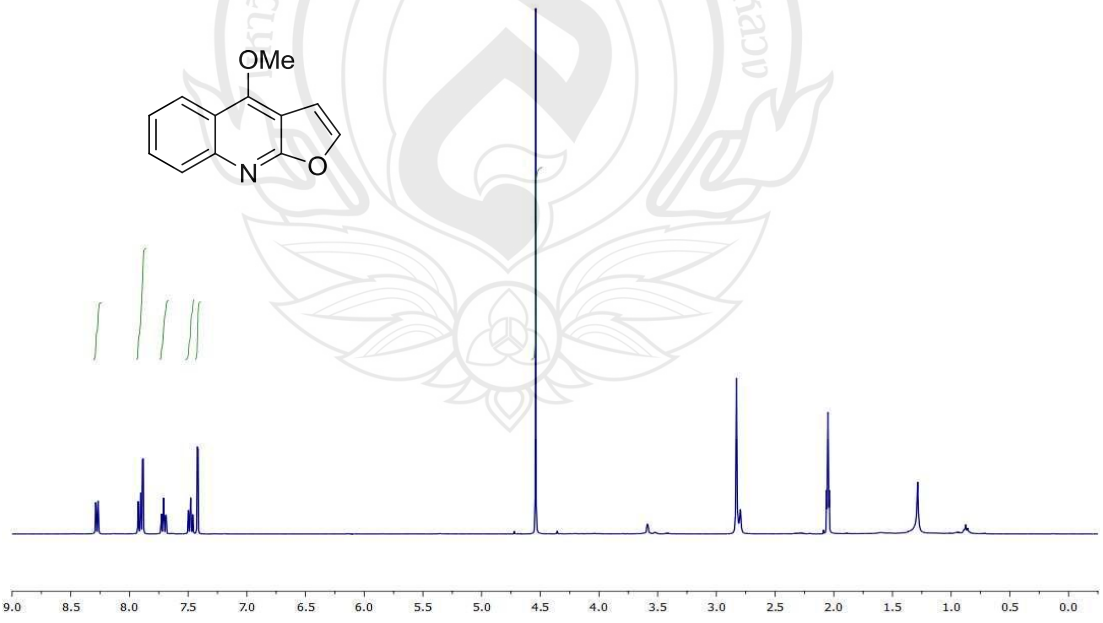

Figure A213 ^{1}H NMR Spectrum of **WM71** in $CDCl_3$ (400 MHz)

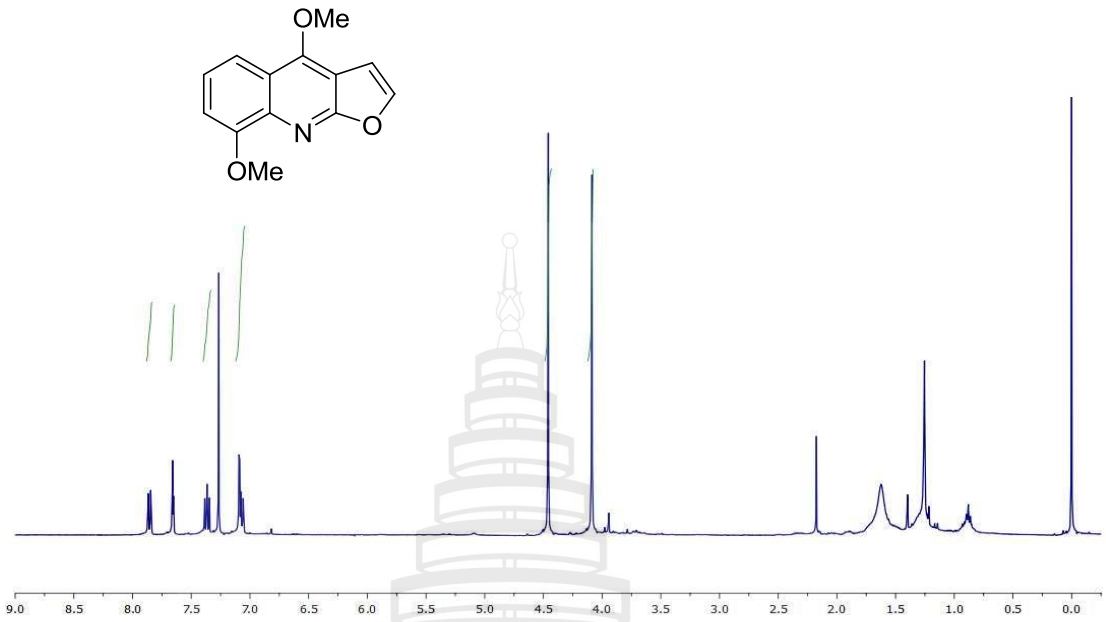

Figure A214 ^{1}H NMR Spectrum of **WM72** in $CDCl_3$ (400 MHz)

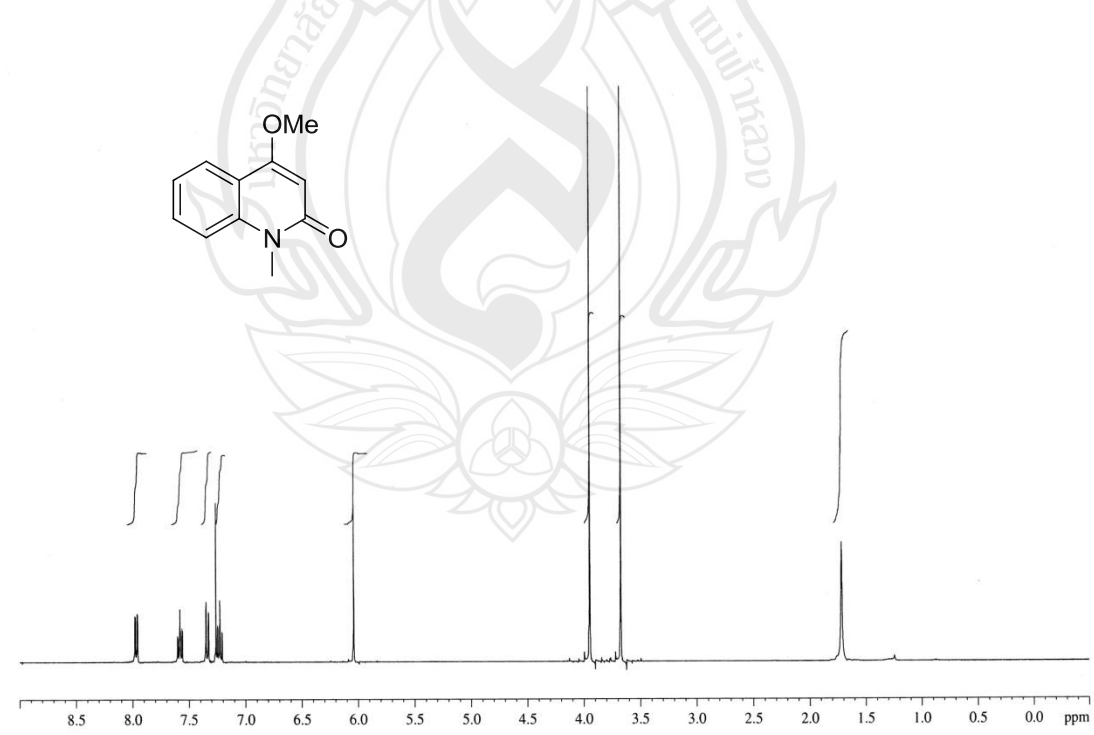

Figure A215 ^{1}H NMR Spectrum of **WM73** in $CDCl_3$ (400 MHz)

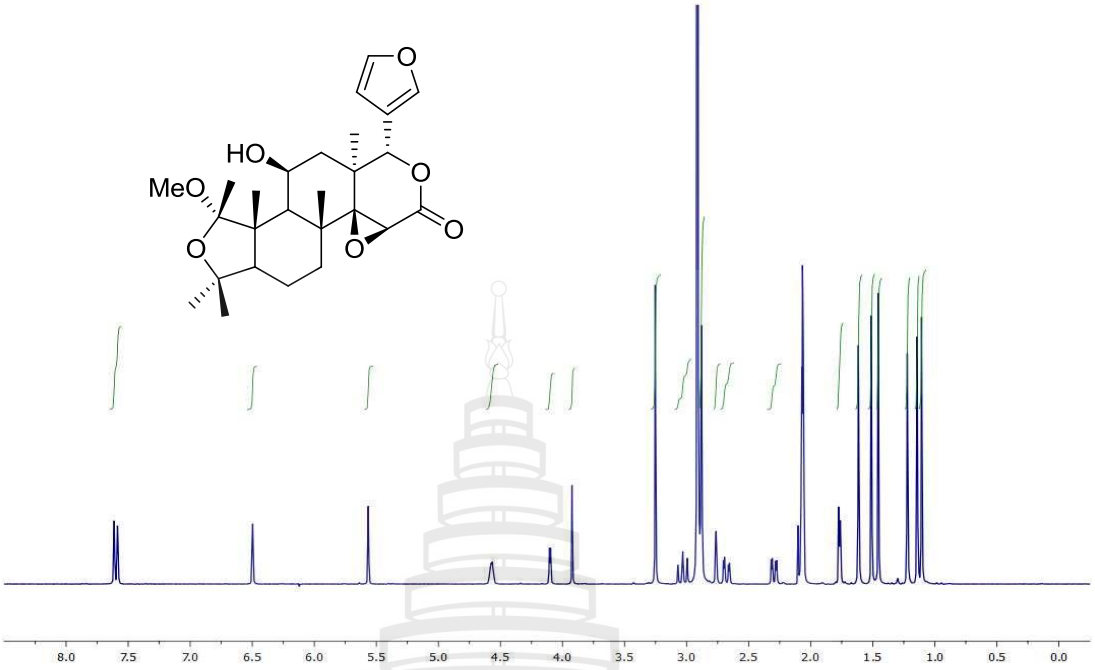

Figure A216 ^{1}H NMR Spectrum of **WM74** in $CDCl_3$ (400 MHz)

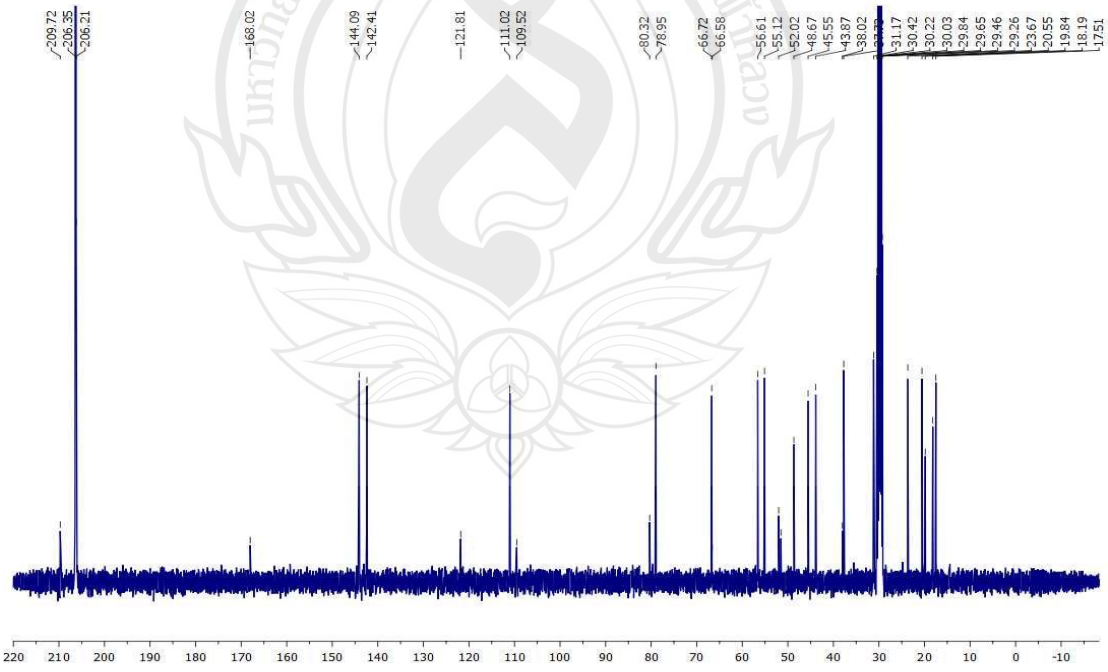

Figure A217 ^{13}C NMR Spectrum of **WM74** in $CDCl_3$ (100 MHz)

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