Chemical Constituents from the Stems of *Goniothalamus macrophyllus*

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A Thesis Submitted in Partial Fulfillment of the Requirements
for the Degree of Master of Science in Organic Chemistry
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Thesis Title	Chemical Constituents from the Stems of *Goniothalamus macrophyllus*
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Dean of Graduate School

ชื่อวิทยานิพนธ์ องค์ประกอบทางเคมีจากลำต้นชิงดอกเดียว (*Goniothalamus macrophyllus*)

ผู้เขียน นางสาวอุไรวรรณ เพ็ชรกูล

สาขาวิชา เคมีอินทรีย์

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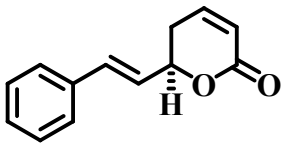
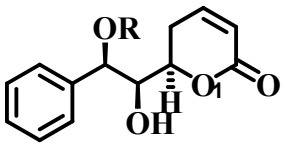
บทคัดย่อ

การศึกษาองค์ประกอบทางเคมีของลำต้นชิงดอกเดียว (*Goniothalamus macrophyllus*) แยกได้สารประกอบที่ยังไม่มีรายงานการวิจัย ประเภท naphthoquinones 3 สาร ได้แก่ 3-amino-5-hydroxy-2-methoxynaphthalene-1,4-dione **(GMS3)**, 3-hydroxymethyl-1-methyl-1*H*-benzo[*f*] indole-4,9-dione **(GMS8)** และ 2-acetyl-3-amino-5-hydroxy-6-methoxynaphthalene-1,4-dione **(GMS12)**, ประเภท aristolactams 2 สาร ได้แก่ 10-amino-3,4-methylenedioxyphenyl-*N*-methoxy-9,10-dihydrophenanthrene-1-carboxylic acid lactam **(GMS7)** และ 10-amino-3,4-dimethoxy-*N*-methoxy-9,10-dihydrophenanthrene-1-carboxylic acid lactam **(GMS9)** นอกจากนี้ยังได้สารที่มีรายงานแล้ว 11 สาร ได้แก่ 6-methylene-2-styryl-3,6-dihydro-2*H*-pyran **(GMS1)**, 2-methyl-naphthalene-1,4-dione **(GMS2)**, 6-(1-hydroxy-2-methoxy-2-phenylethyl)-5,6-dihydro-2*H*-pyran-2-one **(GMS4)**, 6-methylene-2-(3-phynyloxiranyl)-3,6-dihydro-2*H*-pyran **(GMS5)**, 5-hydroxy-3-amino-2-aceto-3,1,4-naphthoquinone (**GMS6**), 10-amino-3,4-methylenedioxyphenylphenanthrene-1-carboxylic acid lactam **(GMS10)**, 3-methoxy-4-methylbenzo[*f*]quinoline-2,5,10-(1*H*)-trione **(GMS11)**, 1-(6-methylene-3,6-dihydro-2*H*-pyran-2-yl)-2-phenyl-ethane-1,2-diol **(GMS13)**, 8-hydroxy-7-phenyl-2,6-dioxabicycle[3.3.1]nonan-3-one **(GMS14)**, Liriodenine **(GMS15)** และ 10-amino-3-hydroxy-4-methoxyphenanthrene-1-carboxylic acid lactam **(GMS16)**. โครงสร้างของสารประกอบเหล่านี้วิเคราะห์โดยใช้ข้อมูลทางสเปกโทรสโกปี UV IR NMR MS และเปรียบเทียบกับสารที่มีรายงานการวิจัยแล้ว

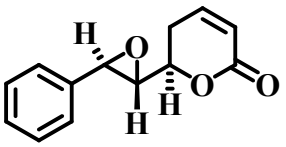


GMS1

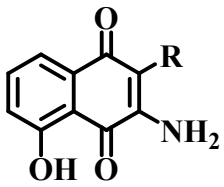


GMS4: R = CH_3

GMS14: R = H

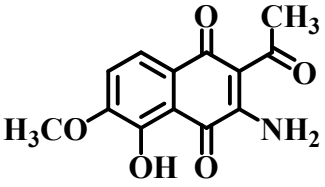


GMS4

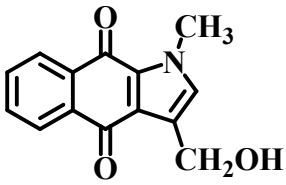


GMS3: R = OCH_3

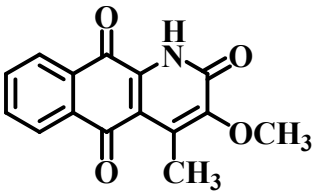
GMS6: R = $COCH_3$



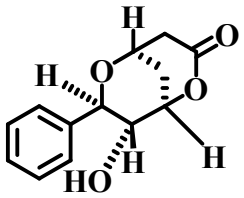
GMS12



GMS8



GMS11



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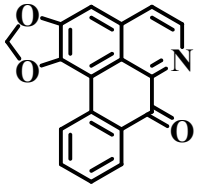
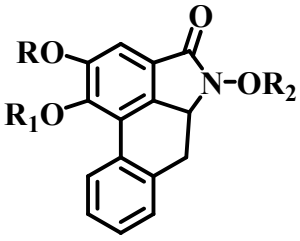
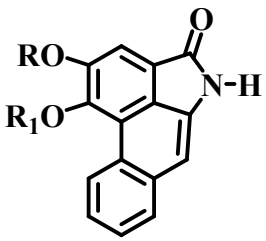


GMS15



GMS7: R = R_1 = R_2 = CH_3

GMS9: R = R_1 = -CH_2- , R = CH_3



GMS10: R = H, R_1 = CH_3

GMS16: R = R_1 = -CH_2-

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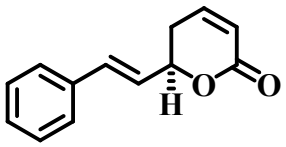
Author Miss Uraiwan Phetkul

Major Program Organic Chemistry

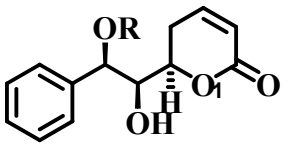
Academic Year 2008

ABSTRACT

Investigation of the constituents from the stems of *G. macrophyllus* yielded three new naphthoquinones: 3-amino-5-hydroxy-2-methoxynaphthalene-1,4-dione **(GMS3)**, 3-hydroxymethyl-1-methyl-1*H*-benzo[*f*]indole-4,9-dione **(GMS8)** and 2-acetyl-3-amino-5-hydroxy-6-methoxynaphthalene-1,4-dione **(GMS12)**; two new aristolactams: 10-amino-3,4-methylenedioxyphenyl-*N*-methoxy-9,10-dihydro phenanthrene-1-carboxylic acid lactam **(GMS7)** and 10-amino-3,4-dimethoxy-*N*-methoxy-9,10-dihydrophenanthrene-1-carboxylic acid lactam **(GMS9)**. Eleven known compounds were also obtained: 6-methylene-2-styryl-3,6-dihydro-2*H*-pyran **(GMS1)**, 2-methylnaphthalene-1,4-dione **(GMS2)**, 6-(1-hydroxy-2-methoxy-2-phenylethyl)-5,6-dihydro-2*H*-pyran-2-one **(GMS4)**, 6-methylene-2-(3-phynyloxiranyl)-3,6-dihydro-2*H*-pyran **(GMS5)**, 5-hydroxyl-3-amino-2-aceto-3,1,4-naphthoquinone (**GMS6**), 10-amino-3,4-methylenedioxyphenylphenanthrene-1-carboxylic acid lactam **(GMS10)**, 3-methoxy-4-methylbenzo[*f*]quinoline-2,5,10-(1*H*)-trione **(GMS11)**, 1-(6-methylene-3,6-dihydro-2*H*-pyran-2-yl)-2-phenyl-ethane-1,2-diol **(GMS13)** and 8-hydroxy-7-phenyl-2,6-dioxabicycle[3.3.1]nonan-3-one **(GMS14)**, Liriodenine **(GMS15)** and 10-amino-3-hydroxy-4-methoxyphenanthrene-1-carboxylic acid lactam **(GMS16)**. Their structures were determined on the basis of UV, IR, NMR, MS and by comparison of their spectroscopic data with those reported.



GMS1



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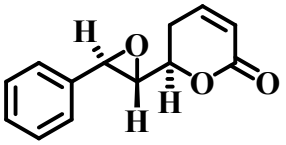

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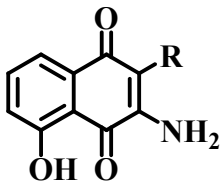

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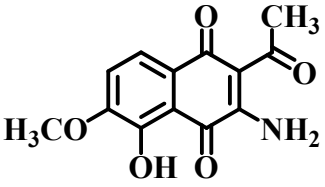

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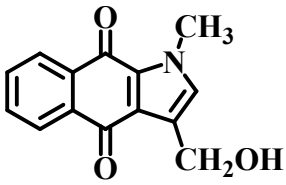
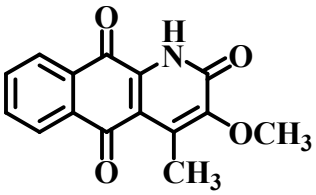
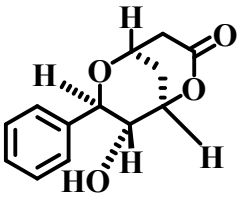


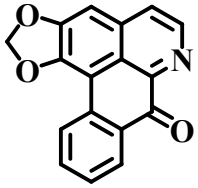
GMS8



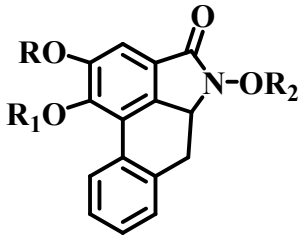
GMS11



GMS14



GMS15



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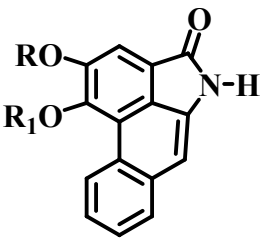

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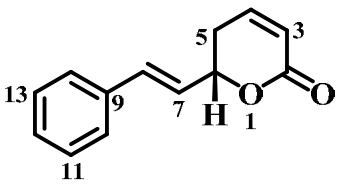

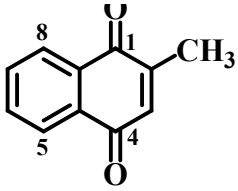

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Uraiwan Phetkul

THE RELEVANCE OF THE RESERCH WORK TO THAILAND

The purpose of this research is to investigate the chemical constituents of *Goniothalamus macrophyllus*. Five styryllactones, five napthoquinones, four aristolactams, one azaanthraquinone and one aporphine were isolated from this plants. The crude methylene chloride and crude acetone showed strong cytotoxic activity. Many known compounds from this plant have been reported to have cytotoxicity, antimicrobial activity, embryotoxic activity and antibacterial activity. This project demonstrated that *G. macrophyllus,* a Thai plant, can be utilized as a potential source of bioactive compounds.

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LIST OF ABBREVIATIONS AND SYMBOLS

s	=	singlet
d	=	doublet
t	=	triplet
m	=	multiplet
dd	=	doublet of doublet
dt	=	doublet of triplet
td	=	triplet of doublet
ddd	=	doublet of doublet of doublet
dddd	=	doublet of doublet of doublet of doublet
br s	=	broad singlet
br m	=	broad multiplet
g	=	gram
kg	=	kilogram
mg	=	milligram
%	=	percent
nm	=	nanometer
m.p.	=	melting point
cm^{-1}	=	reciprocal centimeter (wave number)
δ	=	chemical shift relative to TMS
J	=	coupling constant
λ_{max}	=	maximum wavelength
ν	=	absorption frequencies
ε	=	molar extinction coefficient
$^{\circ}C$	=	degree celcius
MHz	=	Megahertz
ppm	=	part per million
IR	=	Infrared

LIST OF ABBREVIATIONS AND SYMBOLS (Continued)

UV	=	Ultraviolet-Visible
NMR	=	Nuclear Magnetic Resonance
2D NMR	=	Two Dimentional Nuclear Magnetic Resonance
COSY	=	Correlated Spectroscopy
DEPT	=	Distortionless Enhancement by Polarization Transfer
HMBC	=	Heteronuclear Multiple Bond Correlation
HMQC	=	Heteronuclear Multiple Quantum Coherence
CC	=	column chromatography
TMS	=	tetramethylsilane
DMSO-d_6	=	deuterodimethylsulphoxide
$CDCl_3$	=	deuterochloroform
MeOH	=	Methanol
CH_2Cl_2	=	Dichloromethane
TLC	=	Thin-Layer Chromatography
MIC	=	Minimum Inhibition Concentration

CHAPTER 1
INTRODUCTION

1.1 Introduction

Thailand is a tropical country abundance with many kinds of herbal plants that can cure many diseases. Herbal plants are sources of natural remedy which are neglected for a long time since the modern science occupied the livelihood of Thai people. Thai scientists have realized that it is necessary to conduct a research on new substances from the herbal plants which have pharmacological and biological activities. Various parts of the plants, such as bulbs, barks, stems, roots and leaves can be used to treat illness. Medicinal plants especially herbs have played important roles in every day life such as *Andrographis paniculata* Wall. ex Ness (ฟ้าทะลายโจร) relieves the symptom of cold, *Curcuma longa* Linn. (ขมิ้นชัน) prevents and heals ulcer.

The genus *Goniothalamus* (Annonaceae) consists of 115 species, mostly distributed throughout the tropical and subtropical countries. Many of them are used in the folk medicine in several countries. Plants in this genus have been studied for bioactive constituents by medicinal chemists due to their proven use in folk medicine for treatment of various diseases (Blazquez, *et al*., 1999).

G. macrophyllus is locally known as Ching Dok Diao (ชิงดอกเดียว) or Rajchakru (ราชครู). Its leaves are used to allay fever and a decoction of the roots is given as a post-partum remedy and to cause abortion (Burkill, 1953) and a decoction of *G. macrophyllus* was used by the ethnic group, Sakai, to nourish the blood and invigorate the body (Thonghom, 1993). Styryllactones and flavonoids have been isolated and identified from the *G. macrophyllus* (Sam, *et al*., 1987 and Ee, *et al*., 2001). Goniothalamin and goniothalamin oxide isolated from this species display important biological activities such as embryotoxic and teratogenic activities (Sam, *et al*., 1987). Our preliminary screening of the crude methylene chloride extract for cytotoxicity have shown interesting activity against glial tumor (9.0 μg/ml), bone

cancer (36.2 μg/ml), colon cancer (3.7 μg/ml) and prostate cancer (3.7 μg/ml) whereas the crude acetone exhibited cytotoxicity against colon cancer (8.25 μg/ml)
cancer (36.2 μg/ml), colon cancer (3.7 μg/ml) and prostate cancer (3.7 μg/ml) whereas the crude acetone exhibited cytotoxicity against colon cancer (8.25 μg/ml)
and prostate cancer (55.6 μg/ml). However, there are only a few reports on the chemical constituents from the stems of *Goniothalamus macrophyllus*. We were therefore motivated to investigate its constituents in detail.

1.2 Review of Literatures

Goniothalamus is in the family of Annonaceae and is distributed in Asia and Australia (Leboeuf, *et al*., 1982). In Thailand twenty five species of *Goniothalamus* have been found. They are *G. aurantiacus* (ปาหนันเมืองกาญจน์), *G. cheliensis* (ปาหนันยักษ์), *G. elegans* (ปาหนันจิ๋ว), *G. expansus* (ปาหนันเตี้ย), *G giganteus* (ปาหนันช้าง), *G. griffithii* (ปาหนันมรกต), *G. laoticus* (ข้าวหลามดง), *G. latestigma* (ส่าเหล้าต้น), *G. maewongensis* (ปาหนันแม่วงก์) *G. malayanus* (ปาหนันพรุ), *G. repevensis* (แสดสยาม), *G. macrophyllus* (ชิงดอกเดียว), *G. rongklanus* (ปาหนันร่องกล้า), *G. ridleyi* (ปาหนันปุ่มราก), *G. rotundisepalus* (ปาหนันหอม), *G. sawtehii* (ปาหนันหยิก), . *scortechinii* (ปาหนันกลีบแผ่), *G. tamirensis* (ข้าวหลาม), *G. tapis* (บุหงาลำเจียก), *G. tavogensis* (ปาหนันกลีบเรียว), *G.tenuifolius* (ปาหนันหนัง), *G. tortilipetalus* (ปาหนันปุ่มต้น), *G. undulatus* (ปาหนันขี้แมว), *G.uvaroides* (ปาหนันเส้นใบ), *G. calvicarpus* (สะบันงาป่า).

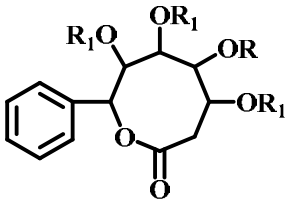
1.2.1 The Chemical Constituents of *Goniothalamus* genus

Various classes of compounds, such as styryllactones, alkaloids, annonaceous acetogenins, flavonoids and chalcones were isolated from *Gonoithalamus* genus. The styryllactones are secondary metabolites mainly isolated from the *Goniothalamus* genus. Goniothalamin and goniothalamin oxide isolated

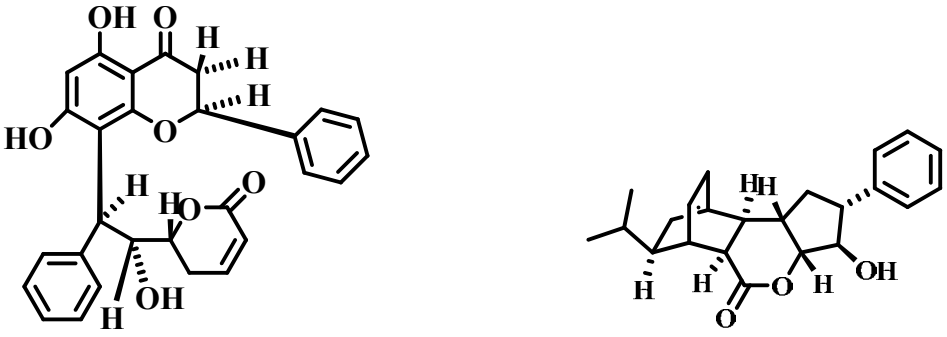
from the stem bark of *G. macrophyllus* (Sam, *et al*., 1987), and (6*R*,7*R*,8*R*)-goniodiol-8-monoacetate and (5*S*,6*R*,7*S*,8*S*)-goniotriol isolated from the leaves of *G. amuyon* (Lan, *et al*., 2003) are some of the styryllactones with six-membered ring lactones. 7-*Epi*–goniofufurone and goniofufurone isolated from the bark of *G. gigantues* (Fang, *et al.,* 1991) are some of styrllactones containing five-membered ring lactones. Furthermore, the eight-membered-ring lactones were also found in this genus such as, gonioheptolides A and gonioheptolides B from the bark of *G. gigantues* (Fang, *et al*., 1993). Recently more complex styryllactones were isolated such as goniolactones A-F from the roots of *G. cheliensis* (Wang, *et al.,* 2002) and cardiopetalolactone from *G. cardiopetalus* (Hisham, *et al.,* 2000).

Some six-membered ring styryllactones

Some five-membered ring styryllactones



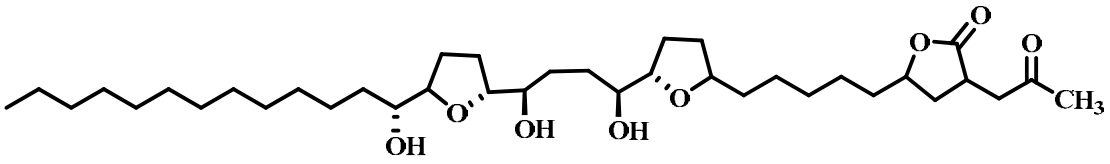
Some eight-membered ring styryllactones



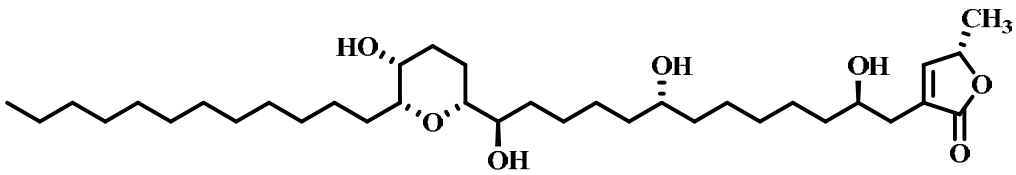
Some more complex styryllactones

Figure 1 Types of styryllactones found in *Goniothalamus* genus

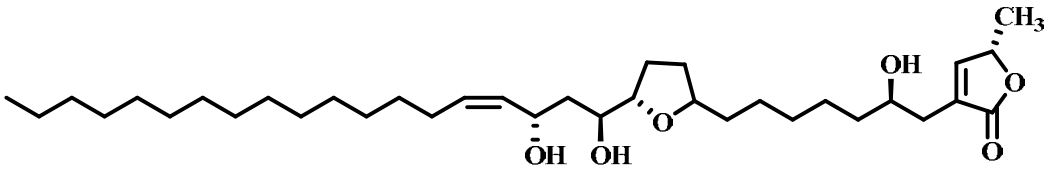
Four types of annonaceous acetogenins, based on different tetrahydrofuran rings, were isolated from the *Goniothalamus* genus. The non adjacent bis-tetrahydrofuran type, such as murisolin, isoannonacin, and a mixture of annonacin and goniothalamicin were isolated from the root of *G. donnaiensis* (Jiang, *et* al., 1997). The mono-tetrahydrofuran type, for example pyranicin, pyragonicin and goniotrionin were isolated from the bark of *G. gigantues*. Pyranicin and pyragonicin are the first mono-tetrahydrofuran annonaceous acetogenins. (Alali, *et al*., 1998). The non-tetrahydrofuran type, for example goniotricin, was isolated from the bark of *G. gigantues* (Alali *et al*., 1999). The tri-tetrahydrofuran type, for example gonionin, was isolated from *G. gigantues* (Gu, *et al*., 1994).



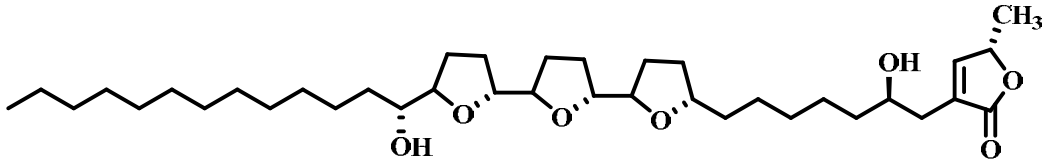
Non adjacent bis-tetrahydrofuran type



Non tetrahydrofuran type



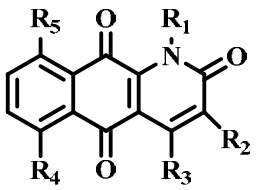
Mono-tetrahydrofuran type



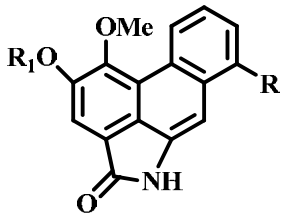
Tri-tetrahydrofuran type

Figure 2 Types of annonaceous acetogenins found in *Goniothalamus* genus

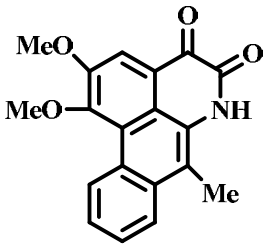
Several classes of compounds such as azaanthraquinones, aristolactams, aporphines and amino-napthoquinones types of alkaloids have been reported in this genus. Cepharanone B, taliscanine, aristolactam AII, velutinam and norcepharadione B, were isolated from the bark of *G. tenuifolius* (Likhitwitayawuid, *et al*., 1997). (3*S*)-2-Oxo-5,12-dimethoxy-3-methylben[*f*]indoline was isolated from the root bark of *G. cheliensis* (Jiang, *et al*., 2008).



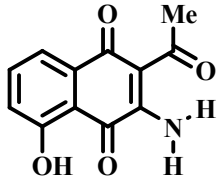
Azaantraquinones



Aristolactams



Aporphine



Amino-napthoquinone

Figure 3 Types of alkaloids found in *Goniothalamus* genus

1.2.2 The Biological Activity of *Goniothalamus* genus

The chemical constituents isolated from the *Goniothalamus* genus were summarized in **Table 1** (Based on SciFinder Scholar database). Some of the plants in *Goniothalamus* genus have been biologically investigated. The roots of *G. giganteus* are used to abort and treat colds and the heated leaves are applied onto swellings (Wiart, 2007). The roots of *G. tapis* are used as abortifacient during early months of pregnancy (Burkill, 1953). In Java, Indonesia, an infusion of the roots is used to treat typhoid fever (Greshoff, 1900). In Taiwan, the seeds of *G. amuyon* are used to treat scabies (Heyne, 1952). In the Philippines, the seeds are used to treat rheumatism and tympanites, and the fruit is for stomachic (Quisumbing, 1951).

The dichloromethane fraction of *G. scortechinii* exhibited antibacterial activity. It showed antibacterial activity against *Staphylococcus aureus* ATCC 25923, *S. aureus* ATCC 29213, *Enterococcus faecalis* ATCC 24922, *Escherichia coli* ATCC 25922, *Bacillus sp*., *Klebsiella pneumoniae*, *Shigella sonnei*, *S. flexneri* and *Proteus sp*. (Wiart, 2007). The ethyl acetate extracts from the flowers and stem bark of *G. grandflorous* showed activity against *Trichophyton mentagrophtye* and *T. verrucosum* (Khan, *et al.,* 1999).

Some of styryllactones from *Goniothalamus* genus showed antibacterial, antimicrobial, teratogenic and embryotoxic activities. Interestingly, some of them are significantly cytotoxic against several human tumor cell lines, such as, goniolactone B isolated from the roots of *G. cheliensis* exhibited cytotoxicity against A2780, HCT-8 and KB cells with IC_{50} values of 7.40, 4.43 and 7.23 μM, respectively (Wang, *et al*., 2002). (6*R*,7*R*,8*R*)-8-Chlorogoniodiol isolated from *G. amuyon* was reported to possess specific cytotoxicity on the HONE-1 cancer cell line and relatively low anti-proliferation effect on NUGC (Lan *et al*., 2003). (*R*)-Goniothalamin isolated from this genus displayed *in vitro* cytotoxicity against lung carcinoma, gastric carcinoma, breast carcinoma, colon carcinoma, leukemia, and ovarian carcinoma (Ali, *et* al., 1997; Inayat-Hussain, *et* al., 1999; Inayat-Hussain, *et* al., 2003 and Pihie, *et* al., 1998).

Some of annonaceous acetogenins from *Goniothalamus* genus have been investigated for biological activity. Gigantransenins A and gigantransenins C isolated from the bark of *G. giganteus* showed selective inhibitory effects on the human breast tumor cell-line (MCF-7) comparable with the potency of adriamycin (Zeng L, *et al*., 1996). Both goniotetracin, and 2,4-*cis*- and *trans*-gonioneninone isolated from *G. giganteus* were selectively and significantly cytotoxic to the human pancreatic tumour cell line (PACA-2), whereas pyranicin exhibited a selective cytotoxicity against the pancreatic cell line (PACA-2) in a panel of six human solid tumor cell lines, with pyranicin showing 10 times of the potency of adriamycin (Alali, *et al*., 1998).

Some of alkaloids in this genus also showed cytotoxicty. For example, marcanines E isolated from the stem bark of *G. marcanii* exhibited cytotoxicity against several human tumor cell lines, A-549, HT-29, MCF7, RPMI, and U251 with ED_{50} in the range of 0.04-3.03 μM, whereas marcanines A, B, and C showed cytotoxicity in all cell lines, with the ED_{50} in the range of 0.18 to 2.12 μM, while dielsiquinone and marcanines C were more active than the other marcanines A in A-549, MCF7, and RPMI cells, with ED_{50} in the range of 0.04 to 0.11 μM. (Soonthornchareonnon, *et al*., 1999).

Furthermore, some of the compounds from *G. macrophyllus* have been reported to show embryotoxic, teratogenic activity in mice (Sam, *et al*., 1987), antiplasmodial (Mohd, *et al*., 2007) and cytotoxic activity (Wattanapiromsakul, *et al*., 2005). The stem extract of this plant was reported to show inhibitory activity against the growth of *Plasmodium falciparum* (Mohd, *et al*., 2007) whereas goniothalamin and goniothalamin oxide displayed embryotoxic and teratogenic activities (Sam, *et al*., 1987). Goniothalamin showed a promising cytotoxicity (SRB assay) against colon cancer cell line (IC_{50} = 0.51 μg/ml), breast cancer cell lines (IC_{50} = 0.95 μg/ml) and lung carcinoma (IC_{50} = 3.51 μg/ml) (Wattanapiromsakul, *et al*., 2005).

1.2.3 *Goniothalamus macrophyllus*

Description

G. macrophyllus is understorey tree up to 7 m tall and 15 cm dbh. Leaves are alternate, simple, penni-veined, rather large. Flowers with ca. 30 mm long petals, white-creamish coloured, fragrant, placed solitary or in small clusters on stem or branches. Fruitlets ca. 20 mm long, green-yellowish coloured, with only one seed, placed in apocarp. Its flowers bloom from March until May, with seeds developing between June and August. This plant can be grown from either seeds or air-layers, although seedlings grow very slowly, reaching only in their first year, and may only bloom beginning in their fifth year. Making air-layers of this plant produces results much more quickly.

Ecology

G. macrophyllus grows in undisturbed forests up to 1240 m altitude. It is often found in disturbed forests, but usually as a pre-disturbance remnant.

Distribution

G. macrophyllus is distributed in Thailand, Peninsular Malaysia, Sumatra, Java and Borneo (Sarawak, West- and East-Kalimantan).

Figure 4 *Goniothalamus macrophyllus*

Table 1 Compounds isolated from the plants of *Goniothalamus* genus

Compounds	Structure	Bibliography
G. amuyon		
stems		
goniothalamin	**53**	Lan, *et al.,* 2003
goniothalamin oxide	**54**	
9-deoxygoniopypyrone	**73**	
8-methoxygoniodiol	**87**	
8-chlorogoniodiol	**88**	
goniodiol-7-monoacetate	**89**	
goniodiol-8-monoacetate	**90**	
(5*R*,6*R*,7*R*,8*R*) goniotriol	**91**	
goniothalesdiol A	**99**	Lan, *et al.,* 2006
goniothalesacetate	**100**	
Leaves		
goniodio-7-monoacetate	**89**	Wu, *et al.,* 1991
(5*R*,6*R*,7*S*,8*S*) goniotriol	**85**	Wu, *et al.,* 1992
goniodiol diacetate	**86**	
goniodiol-7-monoacetate	**89**	
goniodiol-8-monoacetate	**90**	
goniotriol-8-monoacetate	**92**	
G. arvensin		
stem bark		
(-)-ethavensin	**56**	Bermejo, et al., 1997
arvensin	**57**	
goniofufurone	**68**	Bermejo, et al., 1997
(5*R*,6*R*,7*S*,8*S*) goniotriol	**85**	
(5*R*,6*R*,7*R*,8*R*) goniotriol	**91**	

Table1 (continued)

Compounds	Structure	Bibliography
arvensin diacetate	**58**	Bermejo, et al., 1999
(+)-2-*epi*-altholactone	**59**	
3-acetyl-2-*epi*-altholactone	**60**	Bermejo, *et al.,* 1995
(+)-altholactone acetate	**62**	
(+)-goniotharvensin	**63**	
(+)-goniotharvensin monoacetate	**64**	
L-arabino-hept-2-enonic acid	**65**	
G. borneensis		
bark		
goniothalamin	**53**	Cao, *et al.,* 1998
goniothalenol	**61**	
G. cardiopetalus		
stem bark		
goniothalenol	**61**	Hisham, *et al.,* 2000
cardiopetalolactone	**98**	
goniofufurone	**68**	Hisham, *et al.,* 2002
cardiobutanolide	**83**	
G. Cheliensis		
roots		
goniolactone A	**93**	Wang, *et al.,* 2002
goniolactone B	**94**	
goniolactone C	**95**	
goniolactone D	**96**	
goniolactone E	**97**	
root barks		
(3S)-2-oxo-5,12-dimethoxy-methylbenz[*f*]indoline	**34**	Jiang, *et al.,* 2008

Table1 (continued)

Compounds	Structure	Bibliography
G. Donnaiensis		
roots		
donnaienin A	**14**	Jiang, *et al.,* 1997
donnaienin B	**15**	
goniodonin	**16**	Jiang, *et al.,* 1997
cis-goniodonin	**17**	
G. gardneri		
aerial part		
goniothalamusin	**18**	Seidel, *et al.,* 1999
2′-hydroxy-4,4′,6′-trimethoxydihydrochalcone	**35**	Seidel, *et al.,* 2000
2′,4′-dihydroxy-4,6′-dimethoxydihydrochalcone	**36**	
4,2′,4′-trihydroxy-6′-methoxydihydrochalcone	**37**	
flavokawain A	**38**	
2′,4′-dihydroxy-4,6-dimethoxychalcone	**39**	
rel-(1β,2α)-di-(2,4-dihydroxy-6-methoxybenzoyl)-(3β,4α)-di-(4-methoxyphenyl)-cyclobutane	**40**	
naringenin trimethyl ether	**41**	
tsugafolin	**42**	
mearnsitrin	**50**	
annulatin	**51**	
G. giganteus		
bark		
pyranicin	**1**	Alali, *et al.,* 1998
pyragonicin	**2**	
goniotrionin	**3**	
(2,4-*cis* and *trans*)-gigantecinone	**4**	

Table1 (continued)

Compounds	Structure	Bibliography
4-deoxygigantecin	**5**	Alali, *et al.,* 1997
gigantecin	**6**	
gigantetronenin	**7**	Fang, *et al.,* 1992
gigantrionenin	**8**	
gigantrionenin goniocin	**9**	Gu, *et al.,* 1994
goniothalamicin	**10**	
goniotetracin	**11**	Alali, *et al.,* 1997
(2,4-*cis* and *trans*)-gonioninone	**12**	
gonionenin	**13**	Gu, *et al.,* 1994
squamocin	**19**	
goniofufurone	**68**	Fang, *et al.,* 1991
goniobutenolide A	**79**	
goniobutenolide A diacetate	**80**	
goniobutenolide B	**81**	
goniobutenolide B diacetate	**82**	
(5*R*,6*R*,7*R*,8*R*)-goniotriol	**91**	Alkofahi, *et al.,* 1989
D-ido-heptonic acid	**66**	Fang, *et al.,* 1992
gonioheptolide A	**77**	
gonioheptolide B	**78**	
Stem bark		
goniothalamin	**53**	Elzayat, *et al.,* 1985
goniothalenol	**61**	
8-acetylgoniofufurone	**67**	Fang, *et al.,* 1991
goniofufurone	**68**	
7-*epi*-goniofufurone	**69**	
iso-goniopypyrone	**70**	
8-acetyl-9-deoxygoniopypyrone	**71**	

Table1 (continued)

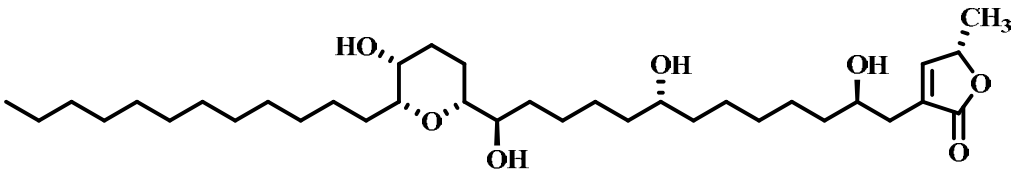
Compounds	Structure	Bibliography
lelocarpin	**72**	
9-deoxygoniopypyrone	**73**	
goniopypyrone	**74**	Jun, *et al.,* 1999
goniodiol	**84**	
G. griffthii		
rhizomes	**55**	
goniofupyrone	**75**	
5-acetylgoniopypyrone	**76**	
7-acetylgoniopypyrone		
Roots		
thliscanine	**26**	Jun, *et al.,* 1999
aristolactam AII	**27**	
cepharanone B	**28**	
velutinam	**29**	
griffithdione	**30**	
griffiazanone A	**32**	
griffiazanone B	**33**	
G. macrophyllus		
stem bark		
goniothalamin	**53**	Sam, *et al.,* 1987
goniothalamin oxide	**54**	
pinocembrin	**52**	Ee, *et al.,* 2001
goniothalamin	**53**	
goniothalamin oxide	**54**	

Table1 (continued)

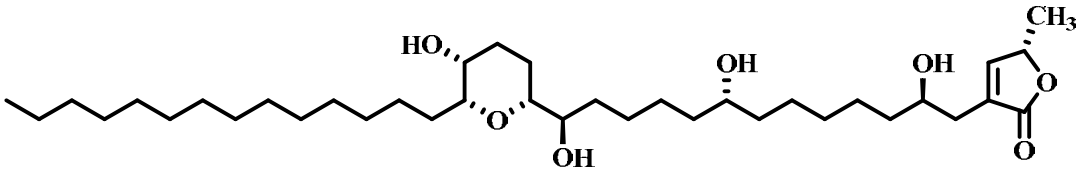
Compounds	Structure	Bibliography
marcanine A	**20**	Soonthornchareonnon,
marcanine B	**21**	*et al.,* 1999
marcanine C	**22**	
marcanine D	**23**	
marcanine E	**24**	
dielsiquinone	**25**	
5-hydroxy-3-amino-2-aceto-3,1,4-naphthoquinone	**31**	
G. tenuifolius		
Leaves		
retusin	**43**	Likhitwitayawuid,
quercetin pentamethyl ether	**44**	*et al*., 2006
quercetin-3-*O*-methyl ether	**45**	
quercetin-3,7-dimethyl ether	**46**	
quercetin-3,7,3′-trimethyl ether	**47**	
3,5,7,3′-tetramethoxy-4′-hydroxyflavone	**48**	
3′-hydroxy-3,5,7,4′-tetramethoxyflavone	**49**	

Structures of Compounds from the *Goniothalamus* genus

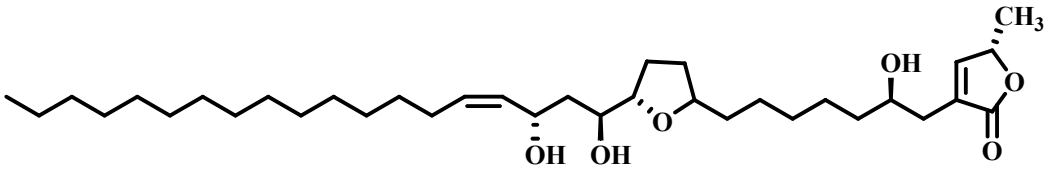
Annonaceous acetogenins



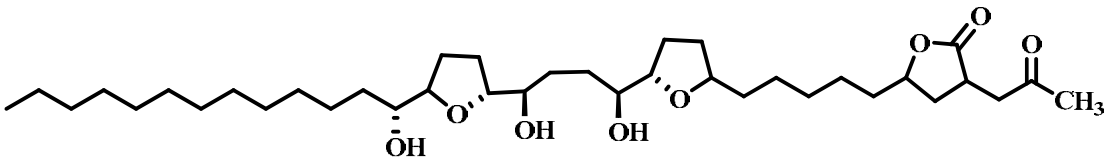
1: pyranicin



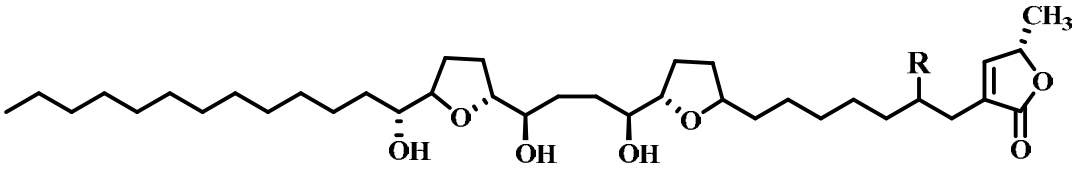
2: pyragonicin



3: goniotrionin

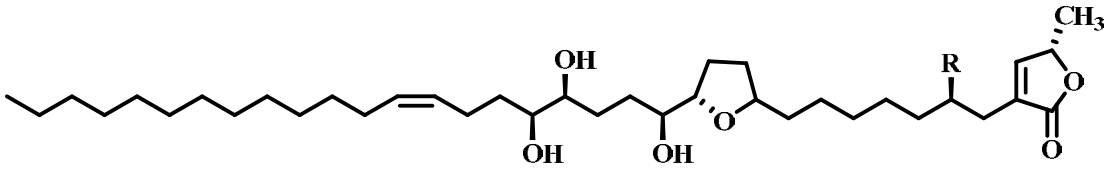


4: (2,4-*cis* and *trans*)-gigantecinone



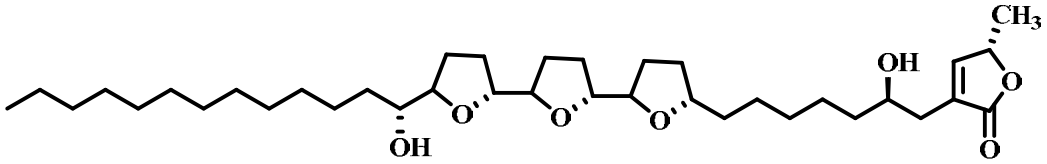
5: 4-deoxygigantecin**:** R = H

6: gigantecin**:** R = OH

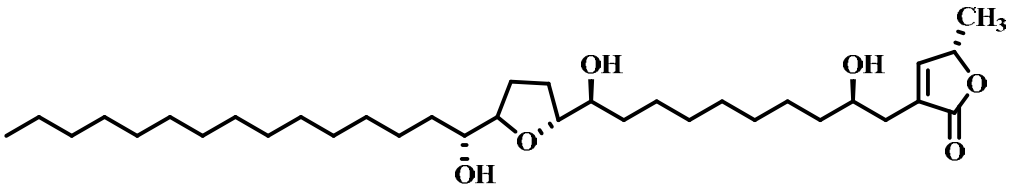


7: gigantetronenin**:** R = OH

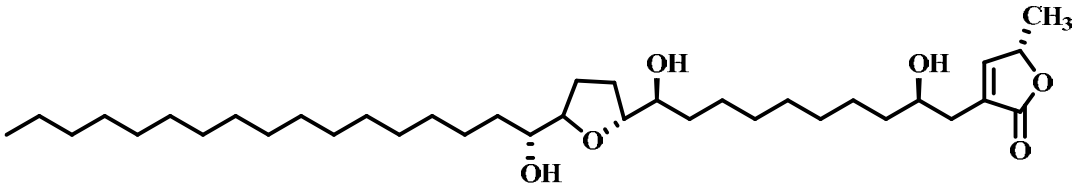
8: gigantrionenin**:** R = H



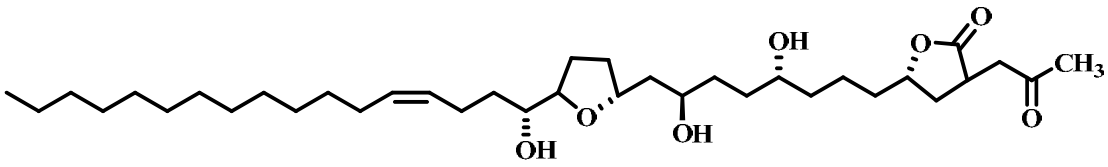
9: goniocin



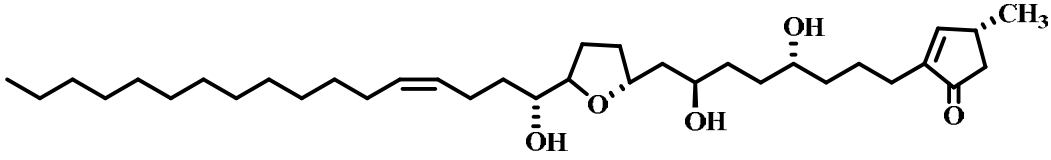
10: goniothalamicin



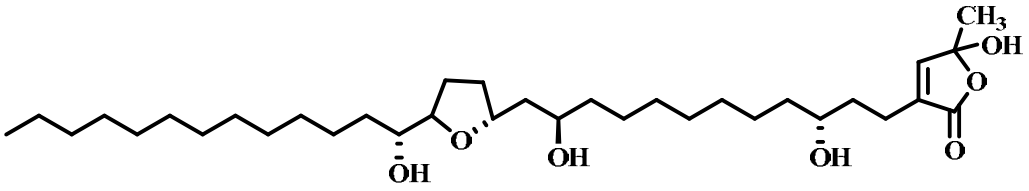
11: goniotetracin



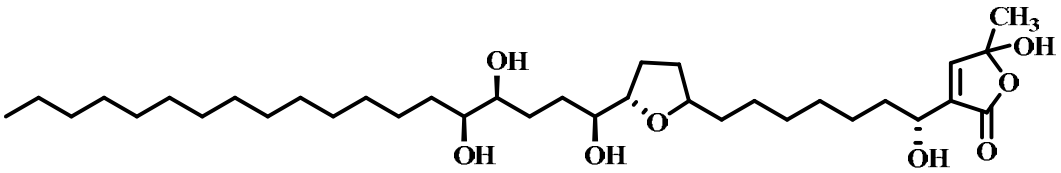
12: (2,4-*cis* and *trans*)-gonioneninone



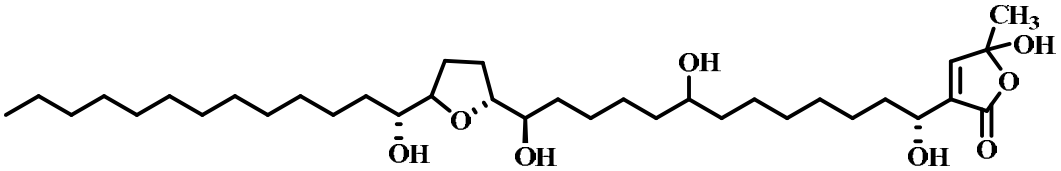
13: gonionenin



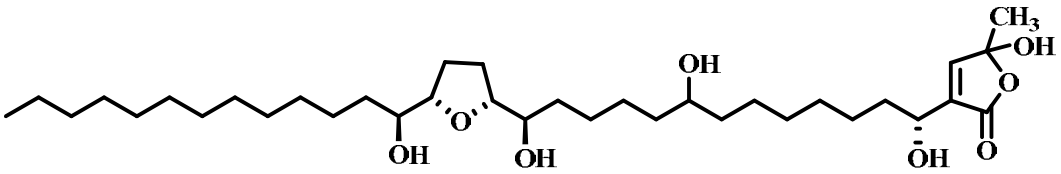
14: donnaienin A



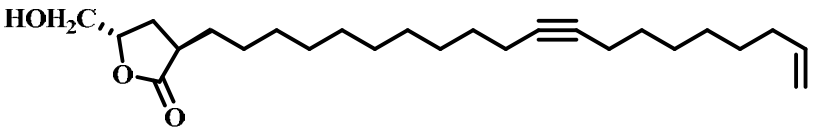
15: donnaienin B



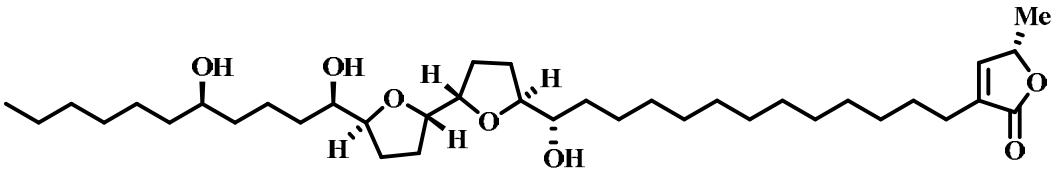
16: goniodonin



17: *cis*-goniodonin

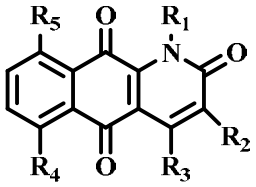


18: goniothalamusin

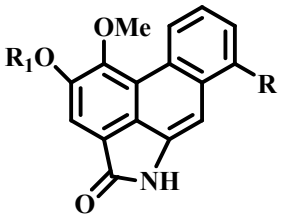


19: squamocin

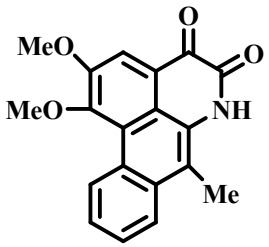
Alkaloids



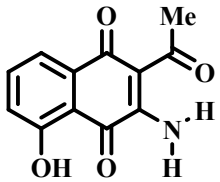
	R_1	R_2	R_3	R_4	R_5
20: marcanine A**:**	H	H	CH_3	H	H
21: marcanine B**:**	H	OCH_3	CH_3	H	H
22: marcanine C**:**	CH_3	OCH_3	CH_3	H	H
23: marcanine D**:**	CH_3	OCH_3	CH_2OH	H	H
24: marcanine E**:**	H	OCH_3	CH_3	OH	H
25: dielsiquinone**:**	CH_3	OCH_3	CH_3	H	OH



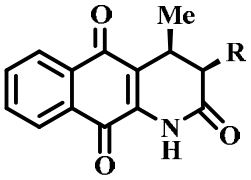
	R	R_1
26: taliscanine **:**	OCH_3	CH_3
27: aristolactam AII**:**	H	H
28: cepharanone B**:**	H	CH_3
29: velutinam**:**	OH	OCH_3



30: griffithdione

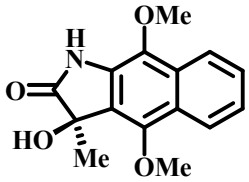


31: 5-hydroxy-3-amino-2-aceto-3,1,4-naphthoquinone



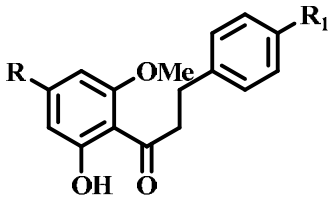
32: griffiazanone A**:** R = OH

33: griffiazanone B**:** R = H

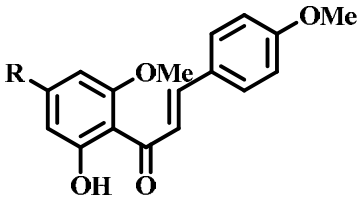


34: (3*S*)-2-oxo-5,12-dimethoxymethylbenz[*f*]indoline

Chalcones



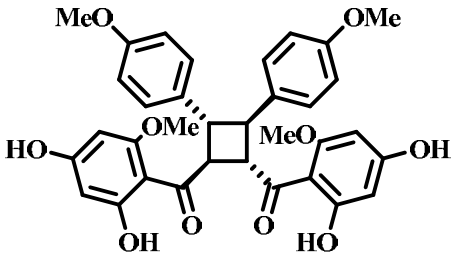
	R	R_1
35: 2′-hydroxy-4,4′,6′-trimethoxydihydrochalcone**:**	OCH_3	OCH_3
36: 2′,4′-dihydroxy-4,6′-dimethoxydihydrochalcone**:**	OH	OCH_3
37: 4,2′,4′-trihydroxy-6′-methoxydihydrochalcone**:**	OH	OH



38: flavokawain A**:** R= OCH_3

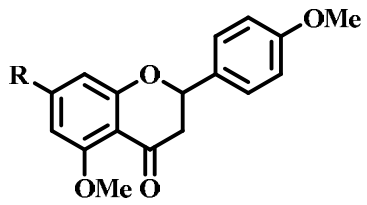
39: 2′,4′-dihydroxy-4,6-dimethoxychalcone**:** R = OH

Dihydrochalcones



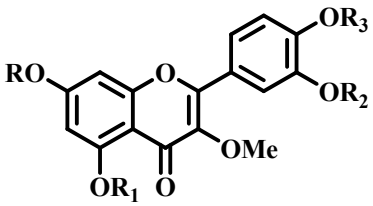
40: rel-(1β,2α)-di-(2,4-dihydroxy-6-methoxybenzoyl)-(3β,4α)-di-(4-methoxyphenyl)-cyclobutane

Flavonoids

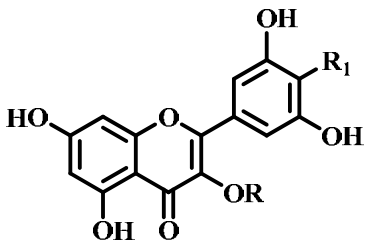


41: naringenin trimethyl ether**:** R = OCH_3

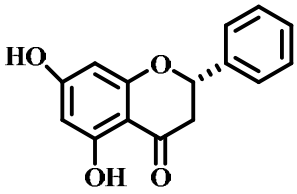
42: tsugafolin**:** R = OH



	R	R_1	R_2	R_3
43: retusin**:**	CH_3	H	CH_3	CH_3
44: quercetin pentamethyl ether**:**	CH_3	CH_3	CH_3	CH_3
45: quercetin-3-*O*-methyl ether**:**	H	H	H	H
46: quercetin-3,7-dimethyl ether**:**	CH_3	H	H	H
47: quercetin-3,7,3′-trimethyl ether**:**	CH_3	H	CH_3	H
48: 3,5,7,3′-tetramethoxy-4′-hydroxyflavone**:**	CH_3	CH_3	CH_3	H
49: 3′-hydroxy-3,5,7,4′-tetramethoxyflavone**:**	CH_3	CH_3	CH_3	H

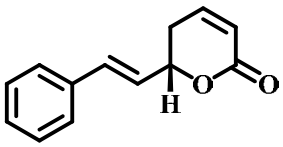


	R	R_1
50: mearnsitrin**:**	rhamnose	OCH_3
51: annulatin**:**	CH_3	OH

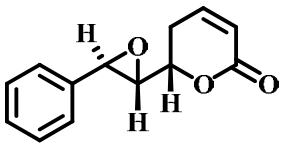


52: pinocembrin

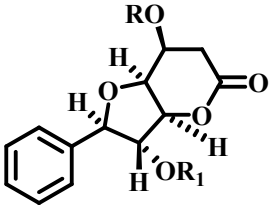
Styryllactones

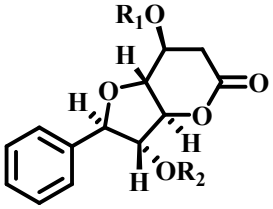


53: goniothalamin

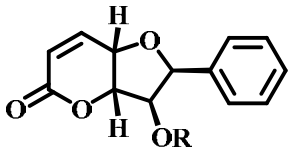


54: goniothalamin oxide



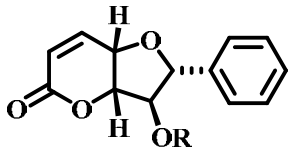


	R	R_1		R	R_1
55: goniofupyrone**:**	H	H	**57:** arvensin**:**	H	H
56: (-)-ethavensin**:**	Et	H	**58:** arvensin diacetate **:**	Ac	Ac



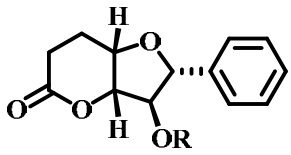
59: (+)-2-*epi*-altholactone**:** R = H

60: 3-acetyl-2-*epi*-altholactone**:** R = Ac



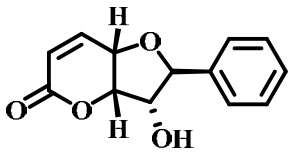
61: goniothalenol**:** R = H

62: (+)- altholactone acetate **:** R = Ac

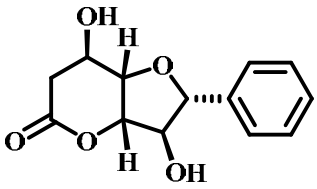


63: (+)-goniotharvensin**:** R = H

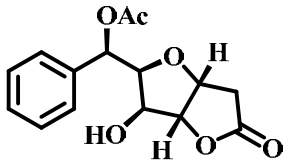
64: goniotharvensin monoacetate**:** R = Ac



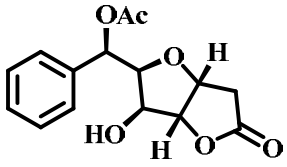
65: L-arabino-hept-2-enonic acid

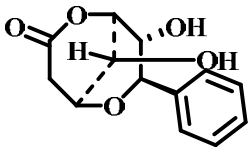


66: D-ido-heptonic acid



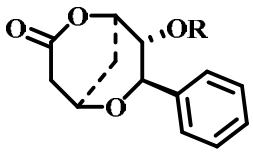
67: 8-acetylgoniofufurone

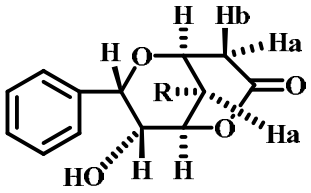




	R	R_1
68: goniofufurone**:**	H	OH
69: 7-*epi*-goniofufurone**:**	OH	H

70: *iso*-goniopypyrone



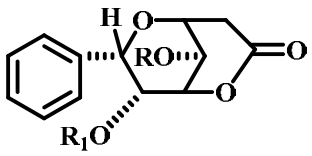


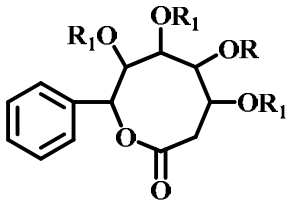
71: 8-acetyl-9-deoxygoniopypyrone**:** R = Ac

72: lelocarpin**:** R = H

73: 9-deoxygoniopypyrone**:** R = H

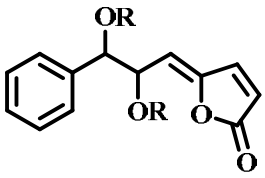
74: goniopypyrone**:** R = OH

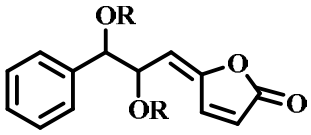




	R	R_1
75: 5-acetylgoniopypyrone**:**	H	Ac
76: 7-acetylgoniopypyrone**:**	Ac	H

	R	R_1
77: gonioheptolide A**:**	CH_3	H
78: gonioheptolide B**:**	Et	H



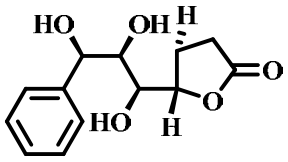


79: goniobutenolide A**:** R = H

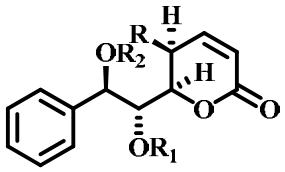
80: goniobutenolide A diacetate**:** R = Ac

81: goniobutenolide B**:** R = H

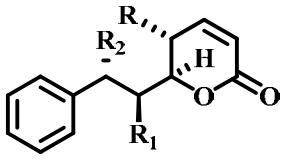
82: goniobutenolide B diacetate**:** R = Ac



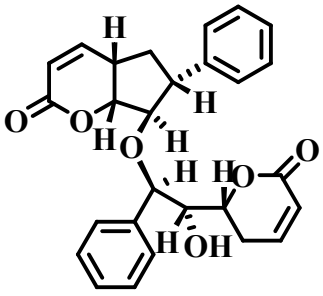
83: cardiobutanolide



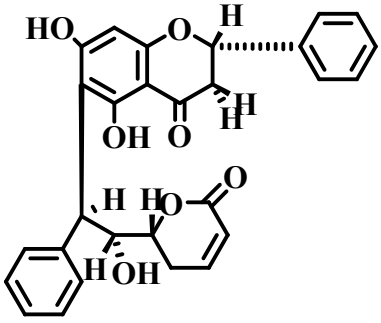
	R	R_1	R_2
84: goniodiol**:**	H	H	H
85: (5*S*,6*R*,7*S*,8*S*)goniotriol**:**	OH	OH	OH
86: goniodiol diacetate**:**	H	Ac	Ac



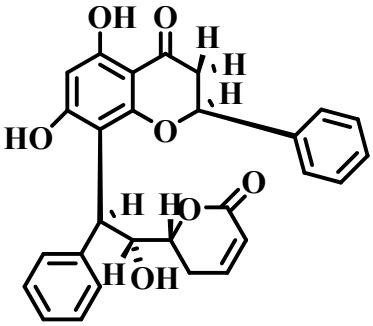
	R	R_1	R_2
87: 8-methoxygoniodiol**:**	H	OH	OCH_3
88: 8-chlorogoniodiol**:**	H	H	Cl
89: goniodiol-7-monoacetate**:**	H	OAc	OH
90: goniodiol-8-monoacetate**:**	H	OH	OAc
91: (5*S*,6*R*,7*R*,8*R*) goniotriol**:**	OH	OH	OH
92: goniotriol-8-monoacetate**:**	OH	H	OAc



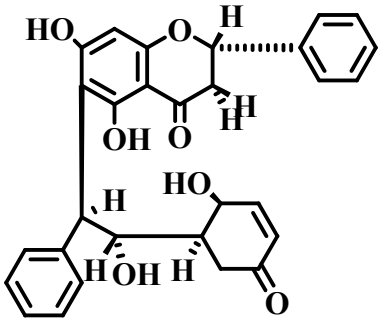
93: goniolactone A



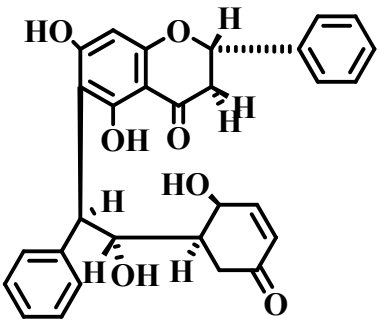
94: goniolactone B



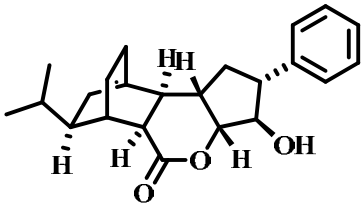
95: goniolactone C



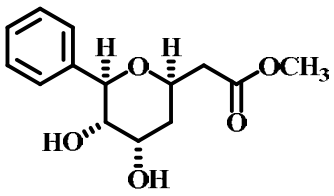
96: goniolactone D



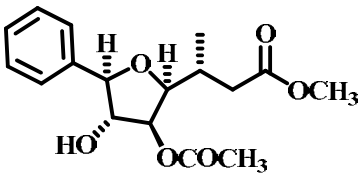
97: goniolactone E



98: cardiopetalolactone



99: goniothalesdiol A



100: goniothalesacetate

1.3 The Objective

The objective of this work is to investigate the chemical constituents from the stems of *G. macrophyllus*.

CHAPTER 2
EXPERIMENTAL

2.1 General Method

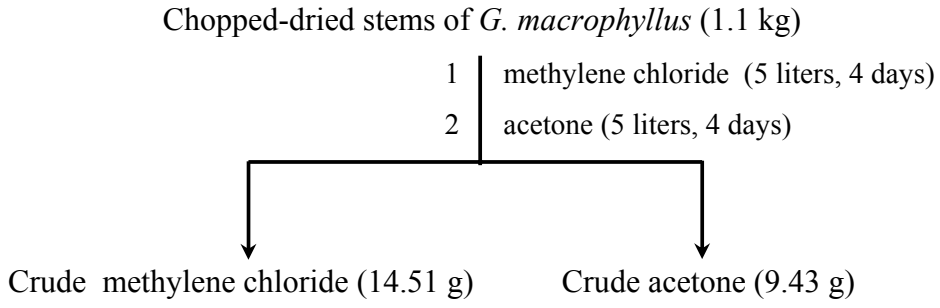
Melting point was recorded in ^{o}C on a digital Electrothermal 9100 Melting Point Apparatus. Ultraviolet spectra were measured with UV-160A spectrophotometer (SHIMADZU). Principle bands (λ_{max}) were recorded as wavelengths (nm) and log ε in methanol solutions. Infrared spectra were obtained on a FTS165 FT-IR spectrophotometer and were recorded in wave number (cm^{-1}). ^{1}H and ^{13}C–Nuclear magnetic resonance spectra were recorded on a FT-NMR Bruker Ultra Shield^{TM} 300 and 500 MHz spectrometer at Department of Chemistry, Faculty of Science, Prince of Songkla University. Spectra were recorded in deuterochloroform, hexadeutero-dimethylsulphoxide and were recored as δ value in ppm down field from TMS (internal standard δ 0.00). Solvents for extraction and chromatography were distilled at their boiling ranges prior to use. For thin-layer chromatography (TLC), aluminum sheets of silica gel 60 F254 (20×20 cm, layer thickness 0.2 mm, Merck) were used for analytical purposes and the compounds were visualized under ultraviolet light. Column chromatography was performed by using siliga gel 100 (70-230 Mesh ASTM, Merck).

2.2 Plant material

G. macrophyllus were collected from Songkhla province in the Southern part of Thailand, in September, 2007. Identification was made by Mr. Ponlawat Pattarakulpisutti, Department of Biology, Facutly of Science, Prince of Songkla University. The specimen (Uraiwan 01) has been deposited in the Herbarium of Department of Biology, Facutly of Science, Prince of Songkla University, Thailand.

2.3 Extraction and Isolation

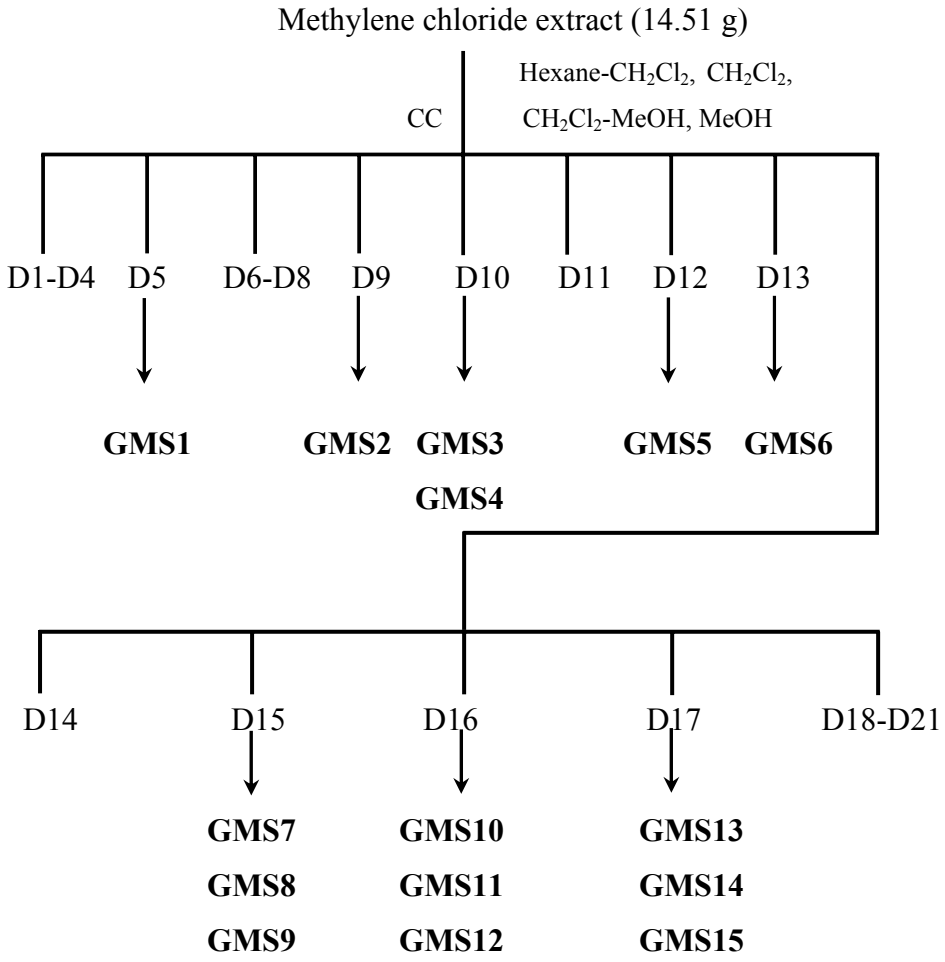
Chopped-dried stems of *G. macrophyllus* (1.1 kg) were immersed in methylene chloride and acetone at room temperature for 4 days successively. After evaporation, a dark brown gum of methylene chloride extract (14.51 g) and a brown gum of acetone extract (9.43 g) were obtained. The process of extraction was shown in **Scheme 1**.



Scheme 1 Extraction of crude extracts from the stems of *G. macrophyllus*

2.3.1 Purification of methylene chloride extract

Methylene chloride extract (14.51 g) was subjected to column chromatography using silica gel as the stationary phase and gradienthy eluted with hexane-methylene chloride, methylene chloride, methylene chloride-methanol and methanol. On the basis of their TLC characteristics, the fractions containing the same major components were combined to give fractions D1-D21. Further purification of subfractions gave fifteen pure compounds (**Scheme 2**).



Scheme 2 Isolation of compounds **GMS1-GMS15** from methylene chloride extract

Table 2 Physical characteristics and weights of the fractions from methylene chloride extract

Fraction	Weight (g)	Physical characteristic
D1	0.0955	white viscous liquid
D2	0.1477	yellow viscous liquid
D3	0.3122	orange viscous liquid
D4	0.4755	yellow viscous liquid mixed with white solid
D5	4.6610	white solid
D6	0.1557	yellow viscous liquid
D7	0.2958	yellow solid
D8	0.6511	yellow viscous mixed with yellow solid
D9	0.0243	red solid
D10	0.1101	red solid
D11	0.0415	yellow solid
D12	0.0519	yellow solid
D13	0.0470	yellow solid
D14	0.0899	yellow solid
D15	0.8482	brown solid
D16	0.9100	brown solid
D17	0.6146	brown solid
D18	0.9371	brown solid
D19	0.4106	brown solid
D20	0.6734	brown solid
D21	0.5911	brown solid

Isolation of GMS1

Fraction D5 (4.6610 g), containing one major component, was dissolved in hexane to form a white solid of **GMS1** (4.6 g).

GMS1:

6-Methylene-2-styryl-3,6-dihydro-2*H*-pyran

$[\alpha]^{29}_{D}$ +176.7° (*c* = 2.0, $CHCl_3$)

IR (Neat) ν (cm^{-1}): 1718 (C=O stretching), 1238 (C-O stretching)

^{1}H NMR ($CDCl_3$) (*δ* ppm): 7.23-7.30 (5H, *m*, H-10, H-11, H-12, H-13, H-14), 6.91 (1H, *dt*, *J* = 9.9, 4.0 Hz, H-4), 6.72 (1H, *d*, *J* = 16.0 Hz, H-8), 6.25 (1H, *dd*, *J* = 16.0, 6.0 Hz, H-7), 6.06 (1H, *dt*, *J* = 9.9, 0.9 Hz, H-3), 5.08 (1H, *ddd*, *J* = 15.3, 6.0, 0.9 Hz, H-6), 2.52 (2H, *m*, H-5)

^{13}C NMR ($CDCl_3$) (*δ* ppm): 163.9 (C-2), 144.8 (C-4), 135.8 (C-9), 133.1 (C-8), 128.7 (C-11, C-13), 128.4 (C-12), 126.7 (C-10, C-14), 125.7 (C-7), 121.6 (C-3), 78.0 (C-6), 29.9 (C-5)

Isolation of GMS2

Fraction D9 (24.3 mg) was further purified by column chromatography over silica gel and eluted with a step gradient of hexane-methylene chloride (7:3) to hexane-methylene chloride (2:8) to afford **GMS2** (3.5 mg) as a yellow solid.

GMS2:

2-Methylnaphthalene-1,4-dione

UV (CH_3OH) λ_{max} nm (log ε) : 255 (3.17), 263 (3.03), 331 (1.7), 409 (3.0)

IR (Neat) ν (cm^{-1}) : 1661, 1640 (C=O stretching)

^{1}H NMR ($CDCl_3$) (*δ* ppm): 8.20 (1H, *dd*, *J* = 7.2, 2.4 Hz, H-5), 8.14 (1H, *dd*, *J* = 7.2, 2.4 Hz, H-8), 7.72 (1H, *ddd*, *J* = 7.2, 7.2, 2.4 Hz, H-6), 7.66 (1H, *ddd*, *J* = 7.2, 7.2, 2.4 Hz, H-7), 6.92 (1H, *d*, *J* = 2.7 Hz, H-3), 2.45 (3H, *d*, *J* = 2.7 Hz, 2-CH_3)

^{13}C NMR ($CDCl_3$) (*δ* ppm): 181.9 (C-1), 175.6 (C-4), 134.7 (C-4a, C-8a), 133.4 (C-6), 132.8 (C-7), 126.8 (C-5), 126.1 (C-8), 124.4 (C-3), 123.1 (C-2), 11.2 (2-CH_3)

Isolation of GMS3 and GMS4

Fraction D10 (110.1 mg) was purified by crystallization in acetone to afford **GMS3** (3.5 mg) as a red solid. The filtrate of fraction D10 (106.6 mg) was further subjected to column chromatography and eluted with hexane-methylene chloride-acetone (6:2:2) to give a brown gum of **GMS4** (3.1 mg).

GMS3:

3-Amino-5-hydroxy-2-methoxynaphthalene-1,4-dione

UV (CH_3OH) λ_{max} nm (log ε) : 232 (3.88), 271 (4.15), 408 (1.08)

IR (Neat) ν (cm^{-1}) : 3421 (O-H stretching), 1638 (C=O stretching)

^{1}H NMR ($CDCl_3$) (δ ppm): 11.56 (1H, *s*, 5-OH), 7.56 (1H, *dd*, *J* = 7.5, 2.1 Hz, H-8), 7.52 (1H, *t*, *J* = 7.5 Hz, H-7), 7.11 (1H, *dd*, *J* = 7.5, 2.1 Hz, H-6), 4.98 (2H, *brs*, NH_2), 4.02 (3H, *s*, OCH_3)

^{13}C NMR ($CDCl_3$) (δ ppm): 186.4 (C-4), 177.8 (C-1), 160.9 (C-5), 138.4 (C-2), 138.0 (C-3), 136.6 (C-8), 132.0 (C-8a), 123.0 (C-6), 118.9 (C-7), 113.2 (C-4a), 60.4 (OCH_3)

EIMS *m/z* (% rel inte) : 219 (9), 218 (100), 188 (7), 176 (19), 149 (18), 120 (9), 65 (10)

HR-EIMS *m/z* : 219.0537 for $C_{11}H_9NO_4$ (calcd. 219.0532)

GMS4:

6-(1-Hydroxy-2-methoxy-2-phenylethyl)-5,6-dihydro-2*H*-pyran-2-one

$[\alpha]^{29}_{D} = +15.6^{o}$ (*c* = 0.67, $CDCl_3$)

IR (Neat) ν (cm^{-1}) : 3431 (O-H stretching), 1723 (C=O stretching), 1253 (C-O stretching)

^{1}H NMR ($CDCl_3$) (δ ppm): 7.34-7.40 (5H, *m*, H-10, H-11, H-12, H-13, H-14), 6.92 (1H, *ddd*, *J* = 10.8, 6.0, 2.4 Hz, H-4), 6.01 (1H, *ddd*, *J* = 10.8, 2.7, 0.9 Hz, H-3), 4.38 (1H, *d*, *J* = 5.7 Hz, H-8), 4.33 (1H, *ddd*, *J* = 11.7, 5.7, 4.2 Hz, H-6), 4.17 (1H, *t*, *J* = 5.7 Hz, H-7), 3.25 (3H, *s*, OCH_3), 2.72 (1H, *tdd*, *J* = 18.6, 11.7, 2.7 Hz, H-5), 2.48 (1H, *J* = *dddd*, 18.6, 11.7, 4.2, 0.9 Hz, H-5)

^{13}C NMR ($CDCl_3$) (δ ppm): 163.7 (C-2), 145.5 (C-4), 136.9 (C-9), 128.5 (C-11, C-13), 128.4 (C-10, C-14), 127.9 (C-12), 120.9 (C-3), 82.6 (C-8), 77.4 (C-6), 74.4 (C-7), 56.8 (8-OCH_3), 24.5 (C-5)

Isolation of GMS5

Fraction D12 (51.9 mg) was crystallized in hexane:acetone (1:1) to give a yellow solid of **GMS5** (20.0 mg).

GMS5:

6-Methylene-2-(3-phynyl-oxiranyl)-3,6-dihydro-2*H*-pyran

$[\alpha]^{29}_{D} = +99.6^{o}$ (*c* = 0.7, $CHCl_3$)

IR (Neat) ν (cm^{-1}): 1723 (C=O stretching), 1250 (C-O stretching)

^{1}H NMR ($CDCl_3$) (δ ppm): 7.26-7.39 (5H, *m*, H-10, H-11, H-12, H-13, H-14), 6.95 (1H, *ddd*, *J* = 9.5, 5.1, 3.6 Hz, H-4), 6.07 (1H, *td*, *J* = 9.5, 1.8 Hz, H-3), 4.46 (1H, *td*, *J* = 11.4, 5.7 Hz, H-6), 3.90 (1H, *d*, *J* = 1.8 Hz, H-8), 3.28 (1H, *dd*, *J* = 5.7, 1.8 Hz, H-7), 2.60 (2H, *m*, H-5)

^{13}C NMR ($CDCl_3$) (δ ppm): 162.8 (C-2), 144.3 (C-4), 135.7 (C-9), 128.7 (C-11, C-13), 128.6 (C-10, C-14), 125.7 (C-12), 121.6 (C-3), 77.1 (C-6), 61.5 (C-7), 57.3 (C-8), 25.9 (C-5)

Isolation of GMS6

Fraction D13 (47.0 mg) was further purified by column chromatography over silica gel and eluted with hexane-acetone (7:3) and acetone to give fractions D13.1-D13.13. Fraction D13.3 (8.0 mg) was rechromatographed on column chromatography and eluted with a mixed solvent of hexane-methylene chloride-acetone (3:1:1) to give a yellow solid of **GMS6** (2.5 mg).

GMS6:

5-hydroxy-3-amino-2-aceto-3,1,4-naphthoquinone

UV (CH_3OH) λ_{max} nm (log ε) : 234 (3.84), 266 (2.09), 277 (2.00), 391 (2.10)

IR (Neat) ν (cm^{-1}) : 3359 (N-H, O-H stretching), 1586 (C=O stretching)

^{1}H NMR ($CDCl_3$) (δ ppm): 11.38 (1H, *s*, 5-OH), 10.71, 7.19 (2H, *brs*, NH_2), 7.76 (1H, *dd*, J = 7.2, 2.7 Hz, H-8), 7.70 (1H, *t*, J = 7.2 Hz, H-7), 7.22 (1H, *dd*, J = 7.2, 2.7 Hz, H-6), 2.73 (3H, *s*, CH_3)

^{13}C NMR ($CDCl_3$) (δ ppm): 202.2 (CO), 184.7 (C-4), 180.4 (C-1), 161.8 (C-5), 152.5 (C-3), 139.1 (C-8), 133.7 (C-8a), 124.7 (C-2), 122.2 (C-6), 119.7 (C-7), 114.0 (C-4a), 33.1 (CH_3)

Isolation of GMS7, GMS8 and GMS9

Fraction D15 (0.8482 g) was further purified by column chromatography over silica gel and eluted with a step gradient of hexane-methylene chloride (7:3), methylene chloride, methylene chloride-methanol and methanol to give fractions D15.1-D15.6. Fraction D15.5 (0.2177 g) was rechromatographed on column chromatography and gradienthy eluted with hexane-methylene chloride (4:1), methylene chloride, methylene chloride-acetone and acetone to give fractions D15.5.1-D15.5.6. Fraction D15.5.3 was rechromatographed on column chromatography and eluted with a mixed solvent of hexane-acetone (7:3) to give a white solid of **GMS7** (4.1 mg). Fraction D15.5.5 was purified by crystallization in acetone to afford a yellow solid of **GMS8** (3.5 mg). The filtrate of fractions D15.5.5

was further subjected to column chromatography, eluted with hexane-acetone (4:1) and acetone to give fractions D15.5.5.1-D15.5.5.10. Fraction D15.5.5.1 was rechromatographed on column chromatography and eluted with a mixed solvent of hexane-acetone (7:3) to afford **GMS9** (6.0 mg) as a white solid.

GMS7:

10-Amino-3,4-methylenedioxyphenyl-*N*-methoxy-9,10-dihydrophenanthrene -1-carboxylic acid lactam

UV (CH_3OH) λ_{max} nm (log ε) : 271 (3.99), 293 (1.38), 403 (2.21)

IR (Neat) ν (cm^{-1}) : 1718 (C=O stretching)

^{1}H NMR ($CDCl_3$) (δ ppm): 7.97 (1H, *d*, *J* =7.5 Hz, H-5), 7.39 (1H, *dd*, *J* =7.5, 1.2 Hz, H-6), 7.35 (1H, *dd*, *J* = 7.5, 1.2 Hz, H-8), 7.32 (1H, *dd*, *J* = 7.5, 1.2 Hz, H-7), 7.15 (1H, *s*, H-2), 6.23 (1H, *d*, *J* = 1.2 Hz, -OCH_2O-), 6.14 (1H, *d*, *J* = 1.2 Hz, -OCH_2O-), 4.64 (1H, *dd*, *J* = 14.5, 6.0 Hz, H-10), 4.03 (3H, *s*, *N*-OMe), 3.47 (1H, *dd*, *J* = 14.5, 6.0 Hz, H-9), 2.87 (1H, *d*, *J* = 14.5 Hz, H-9)

^{13}C NMR ($CDCl_3$) (δ ppm): 169.6 (C-12), 150.2 (C-3), 147.4 (C-4), 136.0 (C-11), 133.7 (C-5a), 129.9 (C-6), 129.6 (C-8a), 128.8 (C-7), 128.0 (C-8), 127.1 (C-5), 120.9 (C-1), 113.8 (C-4a), 102.6 (C-2), 102.3 (-OCH_2O-), 64.9 (*N*-OMe), 58.0 (C-10), 34.7 (C-9)

EIMS *m/z* (% relalive intesity) : 295 (15), 294 (100), 263 (92), 234 (37), 176 (35), 150 (29), 71 (14)

HR-EIMS m/z : 295. 0841 for $C_{17}H_{13}NO_4$ (calcd. 295.0845)

GMS8:

3-Hydroxymethyl-1-methyl-1*H*-benzo[*f*]indole-4,9-dione

UV (CH_3OH) λ_{max} nm (log ε) : 217 (3.95), 225 (4.03), 289 (2.26), 350 (3.15), 431 (3.59)

IR (Neat) ν (cm^{-1}) : 3400 (O-H stretching), 1640, 1594 (C=O stretching)

^{1}H NMR ($CDCl_3$) (*δ* ppm): 8.17 (1H, *dd*, *J* = 6.0, 2.4 Hz, H-7), 8.14 (1H, *dd*, *J* = 6.0, 2.4 Hz, H-4), 7.71 (1H, *dd*, *J* = 6.0, 2.4 Hz, H-6), 7.69 (1H, *dd*, *J* = 6.0, 2.4 Hz, H-5), 6.85 (1H, *s*, H-2), 4.71 (2H, *d*, *J* = 6.9 Hz, 3-CH_2), 4.40 (1H, *t*, *J* = 6.9 Hz, OH), 4.06 (3H, *s*, *N*-Me)

^{13}C NMR ($CDCl_3$) (*δ* ppm): 182.7 (C-8), 176.3 (C-9), 133.8 (C-9a), 133.7 (C-7a), 133.4 (C-5), 133.3 (C-6), 131.7 (C-8a), 129.1 (C-2), 126.7 (C-4), 126.5 (C-7), 126.2 (C-3), 126.0 (C-3a), 57.0 (3-CH_2), 36.7 (*N*-Me)

EIMS *m/z* (% relative intensity) : 241 (15), 241 (100), 239 (30), 211 (45), 154 (20)

HR-MS m/z : 241.0740 for $C_{14}H_{11}NO_3$ (calcd. 241.0739)

GMS9:

10-Amino-3,4-dimethoxy-*N*-methoxy-9,10-dihydrophenanthrene-1-carboxylic acid lactam

UV (CH_3OH) λ_{max} nm (log ε) : 223 (3.70), 250 (3.86), 273 (2.24), 315 (1.78)

IR (Neat) ν (cm^{-1}) : 1705 (C=O stretching)

^{1}H NMR ($CDCl_3$) (*δ* ppm): 8.30 (1H, *d*, *J* = 7.5 Hz, H-5), 7.34 (1H, *ddd*, *J* = 7.5, 7.5, 1.2 Hz, H-6), 7.28 (1H, *ddd*, *J* = 7.5, 7.5, 1.2 Hz, H-7), 7.25 (1H, *dd*, *J* = 7.5, 1.2 Hz, H-8), 7.23 (1H, *s*, H-2), 4.53 (1H, *dd*, *J* = 13.8, 6.0 Hz, H-10), 3.96 (3H, *s*, *N*-OCH_3), 3.88 (3H, *s*, 3-OCH_3), 3.81 (3H, *s*, 4-OCH_3), 3.34 (1H, *dd*, *J* = 13.8, 6.0 Hz, H-9), 2.74 (1H, *d*, *J* = 13.8 Hz, H-9)

^{13}C NMR ($CDCl_3$) (*δ* ppm): 168.9 (C-12), 155.4 (C-3), 150.5 (C-4), 134.4 (C-4a), 134.2 (C-8a), 131.4 (C-5a), 129.8 (C-8), 128.6 (C-7), 128.1 (C-6), 127.9 (C-5), 124.0 (C-11), 122.8 (C-1), 105.9 (C-2), 64.8 (*N*-OCH_3), 60.4 (4-OCH_3), 57.8 (3-OCH_3), 56.4 (C-10), 35.3 (C-9)

EIMS *m/z* (% relative intesity) : 311 (20), 310 (100), 280 (70), 250 (87), 235 (35), 71 (22)

HR-EIMS *m/z* : 311.1158 for $C_{18}H_{17}NO_4$ (calcd. 311.1158)

Isolation of GMS10, GMS11 and GMS12

Fraction D16 (0.9100 g) was further rechromatographed on column chromatography and gradienthy eluted with hexane-methylene chloride (4:1), methylene chloride and acetone to give fractions D16.1-D16.7. Fraction D16.1 (0.2147 g) was rechromatographed on column chromatography and gradienthy eluted with of hexane-methylene chloride (4:1), methylene chloride, methylene chloride-acetone and acetone to give fractions D16.1.1-D16.1.5. Fraction D16.1.1 was rechromatographed on column chromatography and eluted with of hexane-acetone (3:2) to give a yellow solid of **GMS10** (0.9 mg). Fraction D16.2 (0.0347 g) was rechromatographed on column chromatography and gradienthy eluted with of hexane-acetone (4:1) to hexane-acetone (3:2) to give a yellow solid of **GMS11** (2.5 mg). Fraction D16.3 (4.1 mg) was further purified by crystallization from hexane:acetone (1:1) to afford **GMS12** (3.7 mg) as a red solid.

GMS10:

10-Amino-3,4-methylenedioxyphenylphenanthrene-1-carboxylic acid lactam

UV (CH_3OH) λ_{max} nm (log ε) : 230 (4.33), 264 (4.05), 275 (3.84), 327 (2.75), 341 (3.75)

IR (Neat) ν (cm^{-1}) : 3395 (O-H stretching), 1687 (C=O stretching)

^{1}H NMR ($CDCl_3$) (δ ppm): 8.66 (1H, *dd*, *J* = 7.5, 0.9 Hz, H-5), 7.82 (1H, *dd*, *J* = 7.5, 0.9, H-8), 7.60 (1H, *s*, H-2), 7.58 (1H, *ddd*, *J* = 7.5, 7.5, 0.9 Hz, H-7), 7.56 (1H, *ddd*, *J* = 7.5, 7.5, 0.9 Hz, H-6), 7.07 (1H, *s*, H-9), 6.40 (2H, *s*, -OCH_2O-)

^{13}C NMR ($CDCl_3$) (δ ppm): 168.6 (C-12), 148.8 (C-3), 153.3 (C-4), 134.1 (C-8a), 134.1 (C-10), 128.7 (C-8), 127.7 (C-7), 127.2 (C-5), 125.8 (C-6), 125.5 (C-5a), 123.9 (C-11), 105.9 (C-2), 105.2 (C-9), 103.0 (-OCH_2O-)

GMS11:

3-Methoxy-4-methylbenzo[*f*]quinoline-2,5,10(1*H*)-trione

UV (CH_3OH) λ_{max} nm (log ε) : 244 (3.83), 266 (2.43), 296 (2.97), 315 (1.48), 424 (1.7)

IR (Neat) ν (cm^{-1}) : 3390 (N-H stretching), 1653, 1638 (C=O stretching)

^{1}H NMR ($CDCl_3$) (*δ* ppm): 8.22 (1H, *dd*, *J* = 7.5, 1.2 Hz, H-8), 8.17 (1H, *dd*, *J* = 7.5, 1.2 Hz, H-5), 7.84 (1H, *ddd*, *J* = 7.5, 1.2 Hz, H-7), 7.76 (1H, *ddd*, *J* = 7.5, 7.5, 1.2 Hz, H-6), 4.06 (3H, *s*, 3-OCH_3), 2.66 (3H, *s*, 4-CH_3)

^{13}C NMR ($CDCl_3$) (*δ* ppm): 180.0 (C-9), 177.3 (C-10), 156.8 (C-2) 152.8 (C-3), 138.1 (C-4), 137.6 (C-9a), 135.6 (C-7), 134.7 (C-10a), 133.6 (C-6), 130.0 (C-8a), 127.5 (C-8), 126.7 (C-5), 117.8 (C-4a), 59.9 (3-OCH_3), 13.8 (4-CH_3)

GMS12:

2-Acetyl-3-amino-5-hydroxy-6-methoxynaphthalene-1,4-dione

UV (CH_3OH) λ_{max} nm (log ε) : 223 (3.98), 254 (2.89), 264 (3.86), 271 (2.77), 401 (3.46)

IR (Neat) ν (cm^{-1}) : 3416-3338 (N-H, O-H stretching), 1628, 1568 (C=O stretching)

^{1}H NMR ($CDCl_3$) (*δ* ppm): 11.70 (1H, *s*, 5-OH), 10.63 and 7.19 (2H, *brs*, NH_2), 7.76 (1H, *d*, *J* = 8.4 Hz, H-8), 7.21 (1H, *d*, *J* = 8.4 Hz, H-7), 4.00 (3H, *s*, 3-OCH_3), 2.73 (3H, *s*, 4-CH_3)

^{13}C NMR ($CDCl_3$) (*δ* ppm): 202.2 (CO), 185.7 (C-4), 180.3 (C-1), 152.6 (C-5), 152.4 (C-3), 152.0 (C-6), 125.0 (C-8a), 120.8 (C-8), 117.9 (C-7), 114.0 (C-4a), 109.0 (C-2), 56.4 (3-OCH_3), 33.3 (2-$COCH_3$)

Isolation of GMS13, GMS14 and GMS15

Fraction D17 (0.6146 g) was rechromatographed on column chromatography and eluted with mixed solvent of hexane-methylene chloride (4:1), methylene chloride, methylene chloride-acetone and acetone to give fractions D17.1-D17.7. Fraction D17.3 was rechromatographed on column chromatography and eluted with mixed solvent of hexane-acetone (7:3) to give fractions D17.3.1-D17.3.5. Fraction D17.3.1 was rechromatographed on column chromatography and eluted with mixed solvent hexane-acetone (7:3) to (3:6) to give a brown gum of **GMS13** (21.3 mg) and a brown gum of **GMS14** (25.0 mg). Fraction D17.5 was rechromatographed on column chromatography and eluted with mixed solvent of hexane-acetone (6:4) to give a yellow solid of **GMS15** (4.0 mg).

GMS13:

1-(6-Methylene-3,6-dihydro-2*H*-pyran-2-yl)-2-phenyl-ethane-1,2-diol

$[\alpha]^{29}_{D} = +89.2^{o}$ (*c* = 0.3, $CHCl_3$)

^{1}H NMR ($CDCl_3$) (δ ppm): 7.30-7.37 (5H, *m*, H-10, H-11, H-12, H-13, H-14), 6.90 (1H, *ddd*, *J* = 9.9, 6.0, 2.7 Hz, H-4), 5.96 (1H, *dd*, *J* = 9.9, 1.8 Hz, H-3), 4.87 (1H, *d*, *J* = 4.8 Hz, H-8), 4.39 (1H, *td*, *J* = 11.7, 4.8 Hz, H-6), 3.92 (1H, *t*, *J* = 4.8 Hz, H-7), 2.60 (1H, *tdd*, *J* = 18.6, 11.7, 2.7 Hz, H-5), 2.46 (1H, *td*, *J* = 18.6, 4.8 Hz, H-5), 3.13 (1H, *br s*, OH), 3.10 (1H, *br s*, OH)

^{13}C NMR ($CDCl_3$) (δ ppm): 164.0 (C-2), 145.9 (C-4), 140.3 (C-9), 128.7 (C-11, C-13), 128.2 (C-10, C-14), 126.4 (C-12), 120.8 (C-3), 77.4 (C-6), 76.1 (C-7), 72.0 (C-8), 24.9 (C-5)

GMS14:

8-Hydroxy-7-phenyl-2,6-dioxabicyclo[3.3.1]nonan-3-one

$[\alpha]^{29}_{D}$ = -93.3° (*c* = 0.1, EtOH), $[\alpha]^{29}_{D}$ = -39.5° (*c* = 0.5, $CHCl_3$)

IR (Neat) ν (cm^{-1}) : 3431 (O-H stretching), 1705 (C=O stretching)

^{1}H NMR ($CDCl_3$) (*δ* ppm): 7.30-7.41 (5H, *m*, H-11, H-12, H-13, H-14, H-15), 4.84 (1H, *br s*, H-1), 4.38 (1H, *br s*, H-5), 4.43 (1H, *d*, *J* = 9.6 Hz, H-7), 3.46 (1H, *dd*, *J* = 9.6, 2.7 Hz, H-8), 2.83 (1H, *dd*, *J* = 19.2, 2.1 Hz, H-4), 2.91 (*dd*, *J* = 19.2, 1.5 Hz, H-4), 2.15 (1H, *br m*, H-9)

^{13}C NMR ($CDCl_3$) (*δ* ppm): 169.6 (C-3), 138.3 (C-10), 128.5 (C-12, C-14), 128.4 (C-11, C-15), 127.5 (C-13), 77.1 (C-1), 74.1 (C-7), 72.4 (C-8), 65.7 (C-5), 36.5 (C-4), 29.7 (C-9)

GMS15

Liriodenine

UV (CH_3OH) λ_{max} nm (log ε) : 225 (4.33), 244 (4.05), 266 (2.84), 271 (2.75), 401 (0.75)

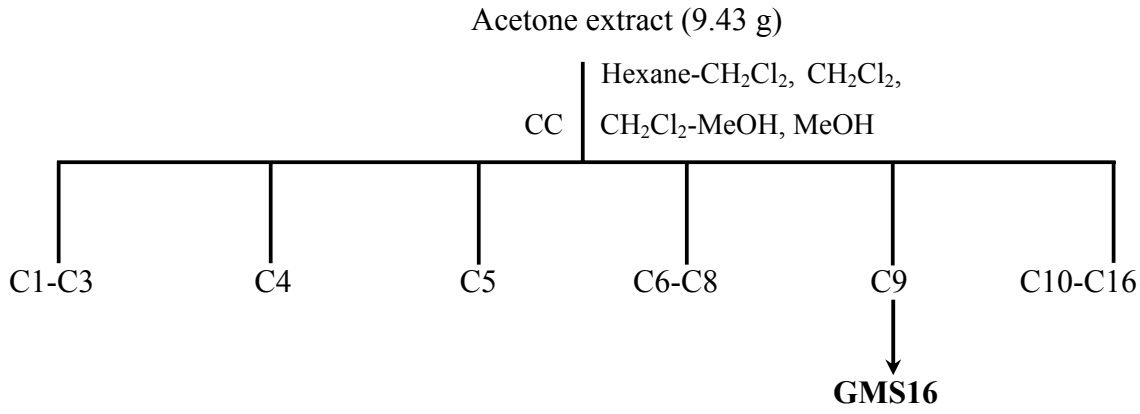
IR (Neat) ν (cm^{-1}) : 1653 (C=O stretching)

^{1}H NMR ($CDCl_3$) (*δ* ppm): 8.82 (1H, *d, J* = 5.1 Hz, H-5), 8.57 (1H, *d, J* = 8.1 Hz, H-11), 8.51 (1H, *dd, J* = 8.1, 1.2 Hz, H-8), 7.70 (1H, *d, J* = 5.1 Hz, H-4), 7.67 (1H, *dd, J* = 8.1, 1.2 Hz, H-10), 7.51 (1H, *dt, J* = 8.1, 1.2 Hz, H-9), 7.12 (1H, *s*, H-3), 6.30 (2H, *s*, -OCH_2O-)

^{13}C NMR ($CDCl_3$) (*δ* ppm): 182.2 (C-7), 152.0 (C-1), 145.0 (C-2), 144.5 (C-5), 136.0 (C-3a), 134.0 (C-10), 132.8 (C-11a), 131.2 (C-8a), 128.9 (C-9), 128.7 (C-8), 127.4 (C-11), 124.3 (C-4), 123.2 (C-1b), 108.1 (C-1a), 103.3 (C-3), 102.6 (-OCH_2O-)

2.3.2 Purification of acetone extract

Acetone extract (9.43 g) was subjected to a column chromatography using silica gel as the stationary phase and gradienthy eluted with hexane-methylene chloride, methylene chloride, methylene chloride-methanol and methanol. On the basis of their TLC characteristics, the fractions containing the same major components were combined to give fractions C1-C16. Further purification of subfractions gave one pure compound. (**Scheme 3)**



Scheme 3 Isolation of compounds **GMS16** from acetone extract

Table 3 Physical characteristics and weights of the fractions from acetone extract

Fraction	Weight (g)	Physical characteristic
C1	0.0435	white viscous liquid
C2	0.0955	yellow viscous liquid
C3	0.0677	orange liquid
C4	0.2103	yellow viscous liquid mixed with white solid
C5	2.9210	white solid
C6	0.3217	orange solid
C7	0.7213	red solid
C8	0.8514	res solid
C9	0.7143	brown solid
C10	0.4126	brown solid
C11	0.3415	brown solid
C12	0.2366	brown solid
C13	0.3511	brown solid
C14	0.2650	brown solid
C15	0.2481	black solid
C16	0.3107	black solid

Isolaton of GMS16

Fraction C9 (0.7143 mg) was crystallized in MeOH to give a yellow solid of **GMS16** (3.2 mg).

GMS16:

10-Amino-3-hydroxy-4-methoxyphenantrene-1-carboxyylic acid lactam

UV (CH_3OH) λ_{max} nm (log ε) : 194 (3.25), 203 (2.10), 226 (3.55), 247 (3.88), 274 (2.41), 280 (1.65), 316 (1.33), 378 (1.11)

IR (Neat) ν (cm^{-1}) : 3426 (O-H stretching), 1640 (C=O stretching)

^{1}H NMR ($CDCl_3$) (δ ppm): 9.77 (1H, *s*, *N*-H), 9.27 (1H, *s*, 3-OH), 8.99 (1H, *dd*, *J* = 6.0, 1.8 Hz, H-5), 7.61 (1H, *dd*, *J* = 6.0, 1.8 Hz, H-8), 7.59 (1H, *s*, H-2), 7.36 (*dd*, *J* = 6.0, 1.8 Hz, H-6), 7.34 (*dd*, *J* = 6.0, 1.8 Hz, H-7), 6.86 (1H, *s*, H-9), 3.90 (3H, *s*, 4-OCH_3)

^{13}C NMR ($CDCl_3$) (δ ppm): 169.5 (C-12), 149.1 (C-3), 152.0 (C-4), 135.1 (C-8a), 134.9 (C-10), 128.7 (C-8), 127.1 (C-6), 127.0 (C-5), 126.5 (C-5a), 125.2 (C-7), 123.0 (C-11), 122.0 (C-1), 121.0 (C-4a), 113.9 (C-2), 104.5 (C-9), 59.9 (4-OCH_3)

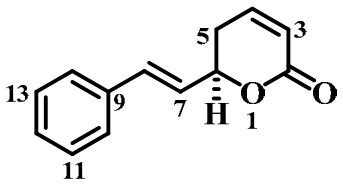
CHAPTER 3
RESULT AND DISCUSSION

3.1 Structural Determination

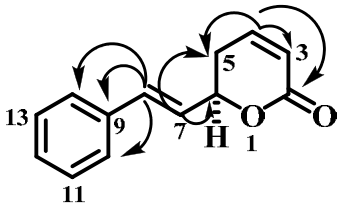
The stems of *Goniothalamus macrophyllus* was extracted with methylene chloride and acetone, successively. Separation of methylene chloride extract by column chromatography produced fifteen compound whereas purification of acetone extract gave one compound. They were identified as 6-methylene-2-styryl-3,6-dihydro-2*H*-pyran **(GMS1)**, 2-methylnaphthalene-1,4-dione **(GMS2)**, 3-amino-5-hydroxy-2-methoxynaphthalene-1,4-dione **(GMS3)**, 6-(1-hydroxy-2-methoxy-2-phenylethyl)-5,6-dihydro-2H-pyran-2-one **(GMS4)**, 6-methylene-2-(3-phynyl-oxiranyl)-3,6-dihydro-2*H*-pyran **(GMS5)**, 5-hydroxy-3-amino-2-aceto-3,1,4-naphthoquinone **(GMS6)**, 10-amino-3,4-methylenedioxyphenyl-*N*-methoxy-9,10-dihydrophenanthrene-1-carboxylic acid lactam **(GMS7)**, 3-hydroxymethyl-1-methyl-1*H*-benzo[*f*]-indole-4,9-dione **(GMS8)**, 10-amino-3,4-dimethoxy-*N*-methoxy-9,10-di-hydrophenanthrene-1-carboxylic acid lactam **(GMS9)**, 10-amino-3,4-methylenediphenylphenanthrene-1-carboxylic acid lactam **(GMS10)**, 3-methoxy-4-methylbenzo[*f*]quinoline-2,5,10-(1*H*)-trione **(GMS11)**, 2-acetyl-3-amino-5-hydroxy-6-methoxynaphthalene-1,4-dione **(GMS12)**, 1-(6-methylene-3,6-dihydro-2*H*-pyran-2-yl)-2-phenylethane-1,2-diol **(GMS13)**, 8-hydroxy-7-phenyl-2,6-dioxabicyclo[3.3.1]nonan-3-one, **(GMS14)**, liriodenine **(GMS15)** and 10-amino-3-hydroxy-4-methoxyphenanthrene-1-carboxlic acid lactam **(GMS16)**. Their structures were elucidated by 1D and 2D spectroscopic data.

GMS1:

6-Methylene-2-styryl-3,6-dihydro-2*H*-pyran



GMS1 was obtained as a white solid, $[\alpha]^{29}_{D} = +176.7^{o}$ (*c* = 2.0, $CHCl_3$). The IR spectrum showed the absorption bands of C=O stretching at 1718 cm^{-1} and C-O stretching at 1238 cm^{-1}. The ^{1}H NMR spectrum showed a multiplet at δ 7.23-7.30 referring to five aromatic protons (H-10 to H-14) from a *mono*-substituted phenyl ring. The resonances of two olefinic protons with a *trans* configuration were observed at δ 6.25 (*dd, J* = 16.0, 6.0 Hz) and 6.72 (*d, J* = 16.0 Hz) ascribable to H-7 and H-8, respectively. The resonances at δ 6.06 (*dt*, *J* = 9.9, 0.9 Hz) and δ 6.91 (*dt, J* = 9.9, 4.0 Hz) were assigned for olefinic protons H-3 and H-4 of an α,β-unsaturated lactone moiety. A multiplet of methylene protons (H-5) was observed at δ 2.52 and a methine proton (H-6) on a carbon bearing the oxygen was detected at δ 5.08 as a doublet of doublet of doublet (*J* = 15.3, 6.0, 0.9 Hz). The ^{13}C-NMR spectrum exhibited the resonances of one carbonyl carbon (δ 163.9), a quaternary aromatic carbon (δ 135.8), five aromatic methine carbons (δ 128.7×2, 128.4 and 126.7×2), four olefinic carbons (δ 144.8, 133.1, 125.7, and 121.6), a methylene carbon (δ 29.9) and a deshielded oxymethine carbon (δ 78.0). The HMBC correlations of H-7 to C-5, C-6, C-9 and of H-8 to C-7, C-9 and C-10 confirmed that H-7 was next to the lactone ring whereas H-8 was linked to the aromatic moiety. **GMS1** was assigned as 6-methylene-2-styryl-3,6-dihydro-2*H*-pyran. The assigned structure and its optical rotation of $+176.7^{o}$ as well as spectroscopic data were in agreement with those of a known compound, (+)-goniothalamin ($[\alpha]^{29}_{D} = +178.5^{o}$, *c* = 2.0, $CHCl_3$) (Sam, *et al*., 1987). Thus **GMS1** was identified as (+)-goniothalamin.



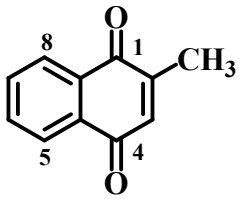
Major HMBC of **GMS1**

Table 4 NMR spectral data of **GMS1**

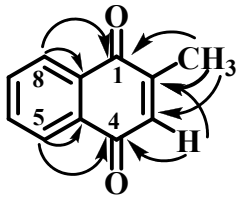
Position	**δ_H (multiplicity)**	**δ_C (C-type)**	**HMBC**
1			
2		163.9 (C=O)	
3	6.06 (*dt*, *J* = 9.9, 0.9 Hz)	121.6 (CH)	C-2, C-5
4	6.91 (*dt, J* = 9.9, 4.0 Hz)	144.8 (CH)	C-2, C-5, C-6
5	2.52 (*m*)	29.9 (CH_2)	C-2, C-4, C-6
6	5.08 (*ddd, J* = 15.3, 6.0, 0.9 Hz)	78.0 (CH)	C-4, C-7
7	6.25 (*dd, J* = 16.0, 6.0 Hz)	125.7 (CH)	C-5, C-6, C-8
8	6.72 (*d, J* = 16.0 Hz)	133.1 (CH)	C-6, C-7, C-9, C-10
9		135.8 (C)	
10-14	7.23-7.30 (*m*)	126.7 (CH)	
		128.7 (CH)	
		128.4 (CH)	
		128.7 (CH)	
		126.7 (CH)	

GMS2:

2-Methylnaphthalene-1,4-dione



GMS2 was obtained as a yellow solid. The IR spectrum showed the absorption bands of C=O stretching at 1640 and 1661 cm^{-1}. The UV spectrum exhibited absorption maxima at 255, 263, 331 and 409 nm, indicating a quinone as the basic structure. The ^{1}H NMR spectral data showed signals of four coupled aromatic protons at δ 8.20 (*dd*, *J* = 7.2, 2.4 Hz), δ 7.72 (*ddd*, *J* = 7.2, 7.2, 2.4 Hz), δ 7.66 (*ddd*, *J* = 7.2, 7.2, 2.4 Hz) and δ 8.14 (*dd*, *J* = 7.2, 2.4 Hz) which were assigned for H-5, H-6, H-7 and H-8, respectively. The spectrum further showed a doublet signal of a methyl group (δ 2.45) and a doublet signal of H-3 at δ 6.92. In the COSY experiment the correlation of these two protons were shown indicating the occurance of a long range coupling. The HMBC correlations of CH_3 to C-1 (δ 181.9), C-2 (δ 123.1) and C-3 (δ 124.4) suggested that CH_3 group was next to a lower field carbonyl group C-1 (δ 181.9) rather than C-4 (δ 175.6). The ^{13}C NMR spectrum showed two carbonyl carbons (δ 181.9 and 175.6), three quaternary carbons (δ 134.7×2 and 123.1), five methine carbons (δ 133.4, 132.8, 126.8, 126.1 and 124.4) and one methyl carbon (δ 11.2). **GMS2** was then assigned to be 2-methylnaphthalene-1,4-dione which was known as aecol (Shapovalov, *et al*., 1989).



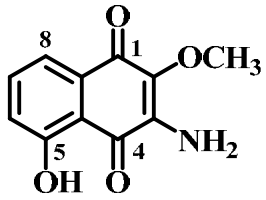
Major HMBC of **GMS2**

Table 5 NMR spectral data of **GMS2**

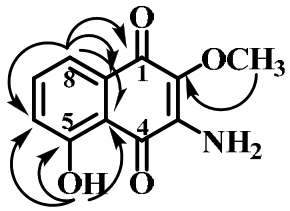
Position	**δ_H (multiplicity)**	**δ_C (C-type)**	**HMBC**
1		181.9 (C=O)	
2		123.1 (C)	
3	6.92 (*d*, *J* = 2.7 Hz)	124.4 (CH)	C-2, C-4
4		175.6 (C=O)	
4a		134.7 (C)	
5	8.20 (*dd*, *J* = 7.2, 2.4 Hz)	126.8 (CH)	C-1, C-4a, C-6, C-7
6	7.72 (*ddd*, *J* = 7.2, 7.2, 2.4 Hz)	133.4 (CH)	C-5, C-7, C-8
7	7.66 (*ddd*, *J* = 7.2, 7.2, 2.4 Hz)	132.8 (CH)	C-5, C-6, C-8
8	8.14 (*dd*, *J* = 7.2, 2.4 Hz)	126.1 (CH)	C-4, C-8a
8a		134.7 (C)	
2-CH_3	2.45 (*d*, *J* = 2.7 Hz)	11.2 (CH_3)	C-1, C-2, C-3

GMS3:

3-Amino-5-hydroxy-2-methoxynaphthalene-1,4-dione



GMS3 was obtained as a red solid. The IR spectrum of **GMS3** indicated the presence of amino and hydroxyl group at 3421 cm^{-1} and C=O stretching at 1638 cm^{-1}. The UV spectrum exhibited absorption maxima at 232, 271 and 408 nm, indicating a quinone as the basic structure. The presence of carbonyl groups was also observed from the carbon resonances at δ 177.8 (C-1) and 186.4 (C-4). The ^{1}H NMR spectrum showed a sharp singlet signal of a chelated hydroxy proton at δ 11.56 (5-OH), a broad singlet signal of an amino group at δ 4.98 and a sharp singlet signal of a methoxyl group at δ 4.02. The spectrum further showed an ABM pattern of aromatic protons H-6, H-7 and H-8 at δ 7.11 (*dd*, J = 7.5, 2.1 Hz), δ 7.52 (*t*, J = 7.5 Hz) and δ 7.56 (*dd*, J = 7.5, 2.1 Hz), respectively. The HMBC correlations of H-8 to C-1, C-4a, C-6 and C-8a confirmed the position of H-8. The correlations of OH to C-5, C-4a, and C-6 confirmed that the -OH group was at C-5 position. The evidence from HMBC correlation was insufficient to indicate the location of the amino group (NH_2) and the methoxyl group (OCH_3). However, the amino group was placed at C-3 rather than at C-2 according to the higher field shift of C-1 (δ 177.8) which resulted from transferring of electron density by cross conjugation between NH_2 and C-1 (Soonthornchareonnon, *et al*., 1999). Consequently the methoxyl group was determined at C-2 position. **GMS3** was therefore proposed as 3-amino-5-hydroxy-2-methoxynaphthalene-1,4-dione.



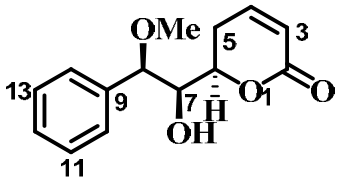
Major HMBC of **GMS3**

Table 6 NMR spectral data of **GMS3**

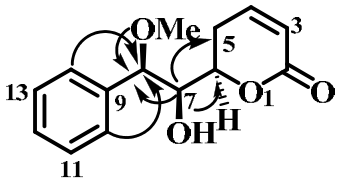
Position	**δ_H (multiplicity)**	**δ_C (C-type)**	**HMBC**
1		177.8 (C=O)	
2		138.4 (C)	
3		138.0 (C)	
4		186.4 (C=O)	
4a		113.2 (C)	
5		160.9 (C)	
6	7.11 (*dd*, *J* = 7.5, 2.1 Hz)	123.0 (CH)	C-4a, C-5, C-7
7	7.52 (*t*, *J* = 7.5 Hz)	118.9 (CH)	C-5, C-6, C-8a
8	7.56 (*dd*, *J* = 7.5, 2.1 Hz)	136.6 (CH)	C-1, C-4a, C-6, C-8a
8a		132.0 (C)	
-OCH_3	4.02 (*s*)	60.4 (CH_3)	C-2
-NH_2	4.98 (*brs*)		
5-OH	11.56 (*s*)		C-4a, C-5, C-6

GMS4:

6-(1-Hydroxy-2-methoxy-2-phenylethyl)-5,6-dihydro-2*H*-pyran-2-one



GMS4 was obtained as a brown gum, $[\alpha]^{29}_{D}$ = +15.6° (*c* = 0.67, $CHCl_3$). The IR spectrum showed the absorption bands of O-H stretching at 3431 cm^{-1}, C=O stretching at 1723 cm^{-1} and C-O stretching at 1253 cm^{-1}. The ^1H NMR spectrum showed signals of five coupled aromatic protons at *δ* 7.40-7.34 (H-10 to H-14), two olefinic protons of an α,β-unsaturated lactone at *δ* 6.01 (H-3) and *δ* 6.92 (H-4), two oxymethine protons at *δ* 4.17 (H-7) and *δ* 4.38 (H-8) and non-equivalent methylene protons at *δ* 2.48 (H-5) and 2.72 (H-5), and methoxy protons at *δ* 3.25 (*s*) The data corresponded to a methoxy derivative of 1-(6-methylene-3,6-dihydro-2*H*-pyran-2-yl)-2-phenyl-ethane-1,2-diol (Fang, *et al*., 1991), with an additional signal of a methoxyl group shown at *δ* 3.25 (*s*). The HMBC correlations of H-7 to C-5, C-6, C-9 and H-8 to C-7, C-9, C-10 confirmed that H-7 was next to a lactone ring whereas H-8 was linked to the aromatic moiety. The correlations of the methoxyl group to C-8 and aromatic protons (H-10, H-11) to C-8 indicated that the methoxyl group was nearby the aromatic moiety rather than a lactone ring. **GMS4** was then assigned to be 6-(1-hydroxy-2-methoxy-2-phenylethyl)-5,6-dihydro-2*H*-pyran-2-one. Its optical rotation of +15.6° was in agreement with those of a known compound (6*R*,7*R*,8*R*)-8-methoxygoniodiol ($[\alpha]_D$ = +24.2°, *c* = 0.68, $CHCl_3$) (Lan, *et al*., 2003). **GMS4** then was assigned as (6*R*,7*R*,8*R*)-8-methoxygoniodiol.



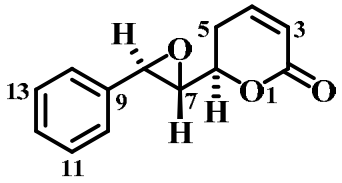
Major HMBC of **GMS4**

Table 7 NMR spectral data of **GMS4**

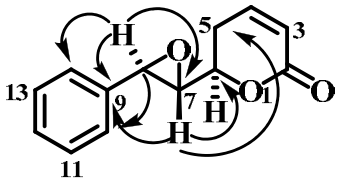
Position	**δ_H (multiplicity)**	**δ_C (C-type)**	**HMBC**
1			
2		163.7 (C=O)	
3	6.01 (*ddd*, *J* = 10.8, 2.7, 0.9 Hz)	120.9 (CH)	C-2, C-5
4	6.92 (*ddd*, *J* = 10.8, 6.0, 2.4 Hz)	145.5 (CH)	C-2, C-5, C-6
5	2.72 (*tdd*, *J* = 18.6, 11.7, 2.7 Hz)	24.5 (CH_2)	C-2,C-4, C-6
	2.48 (*dddd*, *J* = 18.6, 11.7, 4.2, 0.9 Hz)		
6	4.33 (*ddd*, *J* = 11.7, 5.7, 4.2 Hz)	77.4 (CH)	C-4, C-7
7	4.17 (*t*, *J* = 5.7 Hz)	74.4 (CH)	C-5, C-6, C-8
8	4.38 (*d*, *J* = 5.7 Hz)	82.6 (CH)	C-6, C-7, C-9, C-10
9		136.9 (C)	
10-14	7.34-7.40 (*m*)	128.4 (CH)	C-8
		128.5 (CH)	
		127.9 (CH)	
		128.5 (CH)	
		128.4 (CH)	
8-OMe	3.25 (*s*)	56.8 (CH_3)	C-8

GMS5:

6-Methylene-2-(3-phynyl-oxiranyl)-3,6-dihydro-2*H*-pyran



GMS5 was obtained as a yellow solid, $[\alpha]^{29}_{D} = +99.6^{o}$ (*c* = 0.7, $CHCl_3$). The IR spectrum showed the absorption bands of C=O stretching at 1723 cm^{-1} and of C-O stretching 1250 cm^{-1}. The ^{1}H NMR spectral data showed resonances at δ 7.26-7.39 (5H) indicating the presence of a *mono*-substituted phenyl moiety. The resonances at δ 6.95 (*ddd, J* = 9.5, 5.1, 3.6 Hz) and 6.07 (*td*, *J* = 9.5, 1.8 Hz) were assigned to H-4 and H-3 of an α,β-unsaturated lactone moiety. The resonances of two oxymethine protons with a *trans* configuration were observed at δ 3.28 (*dd, J* = 5.7, 1.8 Hz) and 3.90 (*d, J* = 1.8 Hz) ascribable to H-7 and H-8, respectively. The high field shift of the oxycarbons C-7 (δ 61.5) and C-8 (δ 57.3) in the ^{13}C NMR spectrum were assigned for those of an oxirane ring rather than of two free hydroxyl groups which in general the signals were shown at δ 70-80 ppm. The HMBC correlations of H-7 to the C-5, C-6, C-9 and of H-8 to C-7, C-9, C-10, C-14 confirmed the position of protons at C-7 and C-8, respectively. A multiplet of methylene protons (H-5) was observed at δ 2.60. **GMS5** was then assigned to be 6-methylene-2-(3-phynyl-oxiranyl)-3,6-dihydro-2*H*-pyran. Its optical rotation of $+99.6^{o}$ and spectral data were in agreement with those of a known compound (+)-goniothalamin oxide ($[\alpha]_D = +100.7^{o}$, *c* = 0.7, $CHCl_3$) (Sam, *et al*., 1987). **GMS5** then was assigned as (+)-goniothalamin oxide.



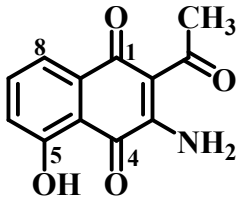
Major HMBC of **GMS5**

Table 8 NMR spectral data of **GMS5**

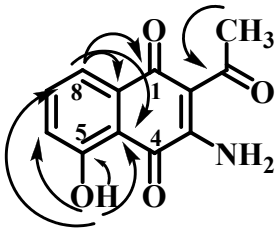
Position	**δ_H (multiplicity)**	**δ_C (C-type)**	**HMBC**
1			
2		162.8 (C=O)	
3	6.07 (*td*, *J* = 9.5, 1.8 Hz)	121.6 (CH)	C-2, C-5
4	6.95 (*ddd*,, *J* = 9.5, 5.1, 3.6 Hz)	144.3 (CH)	C-2, C-5, C-6
5	2.60 (*m*)	25.9 (CH_2)	C-2, C-4, C-6
6	4.46 (*td*, *J* = 11.4, 5.7 Hz)	77.1 (CH)	C-4, C-7
7	3.28 (*dd*, *J* = 5.7, 1.8 Hz)	61.5 (CH)	C-5, C-6, C-8
8	3.90 (*d*, *J* = 1.8 Hz)	57.3 (CH)	C-6, C-7, C-9, C-10
9		135.7 (C)	
10-14	7.26-7.39 (*m*)	128.6 (CH)	
		128.7 (CH)	
		125.7 (CH)	
		128.7 (CH)	
		128.6 (CH)	

GMS6:

5-hydroxy-3-amino-2-aceto-3,1,4-naphthoquinone



GMS6 was obtained as a yellow solid. The IR spectrum showed absorption bands of amino and hydroxyl at 3359 cm^{-1} and C=O stretching at 1586 cm^{-1}. The UV spectrum exhibited absorption maxima at 234, 266, 277 and 391 nm, indicating a quinone as the basic structure. The ^{1}H NMR spectrum showed a sharp singlet signal of a chelated hydroxy proton at δ 11.38, broad singlet signals of an amino group at δ 7.19 and δ 10.71, and a sharp singlet signal of a methyl group at δ 2.73. The spectrum further showed an ABM pattern of aromatic protons H-6, H-7 and H-8 at δ 7.22 (*dd*, J = 7.2, 2.7 Hz), δ 7.70 (*t*, J = 7.2 Hz) and δ 7.76 (*dd*, J = 7.2, 2.7 Hz), respectively. The presence of an acyl group was indicated from the proton resonance of methyl protons at δ 2.73 (*s*) and a carbon resonance of C=O at δ 202.2. The HMBC correlations of a chelated hydroxy proton (δ 11.38) to C-5, C-4a, C-6 and C-7 and of H-8 to C-1, C-4a and C-8a confirmed the position of -OH at C-5 and H-8 at C-8. The evidence from HMBC correlation was not able to indicate the location of amino group (NH_2) and acyl group ($COCH_3$). However, the amino group was placed at C3 rather than at C2 according to the higher field shift of C-1 (δ 180.4) which resulted from transferring of electron density by cross conjugation between NH_2 and C-1 (Soonthornchareonnon, *et al*., 1999). Its ^{1}H and ^{13}C NMR spectral data were compatible with those of known compound name 5-hydroxy-3-amino-2-aceto-3,1,4-naphthoquinone (Soonthornchareonnon, *et al*., 1999).



Major HMBC of **GMS6**

Table 9 NMR spectral data of **GMS6**

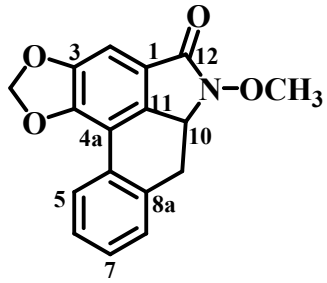
Position	**δ_H (multiplicity)**	**δ_C (C-type)**	**HMBC**
1		180.4 (C=O)	
2		124.7 (C)	
3		152.5 (C)	
4		184.7 (C=O)	
4a		114.0 (C)	
5		161.8 (C)	
6	7.22 (*dd*, *J* = 7.2, 2.7 Hz)	122.2 (CH)	C-4a, C-5, C-8
7	7.70 (*t*, *J* = 7.2 Hz)	119.7 (CH)	C-5, C-6, C-8a
8	7.76 (*dd*, *J* = 7.2, 2.7 Hz)	139.1 (CH)	C-1, C-4a, C-8
8a		133.7 (C)	
CH_3	2.73 (*s*)	33.1 (CH_3)	C=O
C=O		202.2 (C=O)	
-NH_2	7.19, 10.71 (*brs*)		
5-OH	11.38 (*s*)		C-4a, C-5, C-6, C-7

Table 10 Comparison of the ^{1}H NMR spectral data of **GMS6** and **5-hydroxy-3-amino-2-aceto-1,4-napthoquinone**

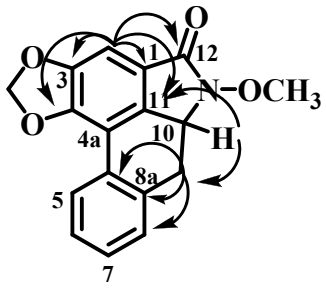
Position	GMS6		5-hydroxy-3-amino-2-aceto-1,4-napthoquinone	
	δ_H (multiplicity)	**δ_C (C-type)**	**δ_H (multiplicity)**	**δ_C (C-type)**
1		180.4 (C=O)		180.4 (C=O)
2		124.7 (C)		124.7 (C)
3		152.5 (C)		152.5 (C)
4		184.7 (C=O)		184.8 (C=O)
4a		114.0 (C)		114.0 (C)
5		161.8 (C)		161.9 (C)
6	7.22 (*dd*, *J* = 7.2, 2.7 Hz)	122.2 (CH)	7.21 (*dd*, *J* = 7.9, 1.8 Hz)	122.2 (CH)
7	7.70 (*t*, *J* = 7.2 Hz)	119.7 (CH)	7.73	119.7 (CH)
8	7.76 (*dd*, *J* = 7.2, 2.7 Hz)	139.1 (CH)	7.76	139.1 (CH)
8a		133.7 (C)		133.7 (C)
CH_3	2.73 (*s*)	33.1 (CH_3)	2.73 (*s*)	33.1 (CH_3)
C=O		202.2 (C=O)		202.2 (C=O)
-NH_2	7.19, 10.71 (*brs*)		7.12, 10.69 (*brs*)	
5-OH	11.38 (*s*)		11.38 (*s*)	

GMS7:

10-Amino-3,4-methylenedioxyphenyl-*N*-methoxy-9,10-dihydrophenanthrene-1-carboxylic acid lactam



GMS7 was obtained as a white solid. The IR spectrum showed the absorption band of C=O stretching at 1718 cm^{-1}. The UV spectrum exhibited absorption maxima at 271, 293 and 403 nm, indicating an aristolactam as the basic structure. The existence of a lactam carbonyl group was confirmed by the carbon signal at δ 169.6 in the ^{13}C NMR spectrum. The ^{1}H NMR spectrum showed the resonances of an isolated aromatic proton at δ 7.15 (*s*, H-2) and four adjacent aromatic protons H-5, H-6, H-7 and H-8 at δ 7.97 (*d*, *J* = 7.5 Hz), δ 7.39 (*dd*, *J* = 7.5, 1.2 Hz), δ 7.32 (*dd*, *J* = 7.5, 1.2 Hz) and δ 7.35 (*dd*, *J* = 7.5, 1.2 Hz), respectively. An aromatic proton H-2 was confirmed being at *peri* position to C=O from the ^{3}J correlation of H-2 to C=O (δ 169.6). The signal of *N*-OCH_3 was detected at δ 4.03 (*s*) whereas the signal of a methylenedioxyphenyl was shown at δ 6.14 (*d*, *J* = 1.2 Hz) and δ 6.23 (*d*, *J* = 1.2 Hz). The spectrum further showed a doublet of doublet signal of a methine proton H-10 at δ 4.64 (*J* = 14.5, 6.0 Hz). This proton was coupled with methylene protons H-9 resonating at δ 3.47 (*dd*, *J* = 14.5, 6.0 Hz) and δ 2.87 (*d*, *J* = 14.5 Hz). The HMBC correlations of an aromatic proton H-2 to C-1, C-3, C-4, C-11, C-12 and of H-10 to C-1, C-4a, C-9, C-11 as well as of methylene protons H-9 to C-5a, C-8, C-8a confirmed the assigned structure. Compound **GMS7** therefore was identified as 10-amino-3,4-methylenedioxyphenyl-*N*-methoxy-9,10-dihydrophenan threne-1 carboxylic acid lactam. It was a new aristolactam.



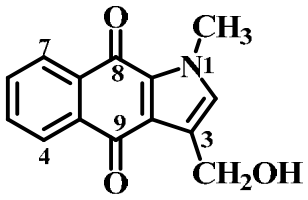
Major HMBC of **GMS7**

Table 11 NMR spectral data of **GMS7**

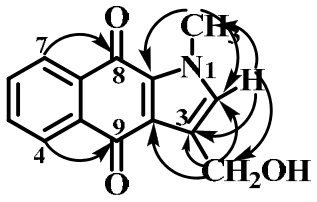
Position	δ_H (multiplicity)	δ_C (C-type)	HMBC
1		120.9 (C)	
2	7.15 (*s*)	102.6 (CH)	C-1, C-3, C-4, C-4a C-11, C-12
3		150.2 (C)	
4		147.4 (C)	
4a		113.8 (C)	
5	7.97 (*d*, *J* = 7.5 Hz)	127.1 (CH)	C-4a, C-5a, C-7
5a		133.7 (C)	
6	7.39 (*dd*, *J* = 7.5, 1.2 Hz)	129.9 (CH)	C-5, C-5a, C-8
7	7.32 (*dd*, *J* = 7.5, 1.2 Hz)	128.8 (CH)	C-5a, C-6, C-8
8	7.35 (*dd*, *J* = 7.5, 1.2 Hz)	128.0 (CH)	C-7, C-8a
8a		129.6 (C)	
9	3.47 (*dd*, *J* = 14.5, 6.0 Hz) 2.87 (*d*, *J* = 14.5 Hz)	34.7 (CH_2)	C-5a, C-8, C-8a
10	4.64 (*dd*, *J* = 14.5, 6.0 Hz)	58.0 (CH)	C-1, C-4a, C-9, C-11
11		136.0 (C)	
12		169.6 (C=O)	
N-OCH_3	4.03 (*s*)	64.9 (CH_3)	
-OCH_2O-	6.14 (*d*, *J* = 1.2 Hz) 6.23 (*d*, *J* = 1.2 Hz)	102.3 (CH_2)	C-3, C-4

GMS8:

3-Hydroxymethyl-1-methyl-1*H*-benzo[*f*]indole-8,9-dione



GMS8 was obtained as a yellow solid. The IR spectrum showed the absorption bands of O-H stretching at 3400 cm^{-1} and of C=O stretching at 1640 and 1594 cm^{-1}. The UV spectrum exhibited absorption maxima at 217, 225, 289, 350 and 431 nm, indicating a quinone as the basic structure. The presence of C=O was also observed from the carbon resonance at δ 182.7 (C-8) and 176.3 (C-9). The ^{1}H NMR spectral data (Table 13) showed signals of four coupled aromatic protons at δ 8.14 (*dd*, *J* = 6.0, 2.4 Hz), δ 7.69 (*dd*, *J* = 6.0, 2.4 Hz), δ 7.71 (*dd*, *J* = 6.0, 2.4 Hz) and δ 8.17 (*dd*, *J* = 6.0, 2.4 Hz). These signals were assigned for H-4, H-5, H-6 and H-7, respectively. The presence of hydroxymethylene protons (3-CH_2OH) was observed from the resonances of methylene protons at δ 4.71 (*d*, *J* = 6.9 Hz) and a hydroxyl proton at δ 4.40 (*t*, *J* = 6.9 Hz). It was assigned to be at C-3 according to the correlations of CH_2 to C-2, C-3 and C-3a. The appearance of a singlet resonance at δ 4.06 was assigned for a *N*-CH_3 and a singlet signal at δ 6.85 was deduced for an olefinic proton H-2. The HMBC correlations of H-2 (δ 6.85) to *N*-$\underline{CH_3}$, 3-$\underline{CH_2}$OH, C-3 and of *N*-CH_3 to C-2, C-8a confirmed the structure of a pyrone ring. Compound **GMS8** therefore was identified as 3-hydroxymethyl-1-methyl-1*H*-benzo[*f*]indole-8,9-dione. It was a new alkaloid.



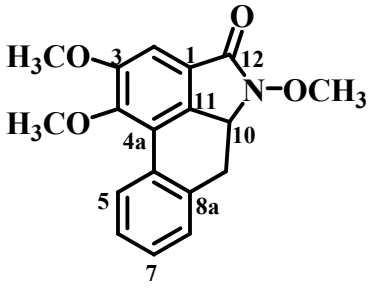
Major HMBC of **GMS8**

Table 12 NMR spectral data of **GMS8**

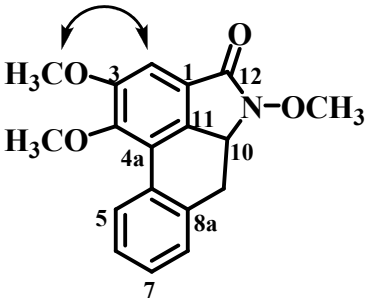
Position	δ_H (multiplicity)	δ_C (C-type)	HMBC
1			
2	6.85 (s)	129.1 (CH)	*N*-CH_3, C-3, 3-CH_2OH
3		126.2 (C)	
3a		126.0 (C)	
4	8.14 (*dd*, *J* = 6.0, 2.4 Hz)	126.7 (CH)	C-5, C-6, C-9
5	7.69 (*dd*, *J* = 6.0, 2.4 Hz)	133.4 (CH)	C-6, C-7
6	7.71 (*dd*, *J* = 6.0, 2.4 Hz)	133.3 (CH)	C-4, C-5
7	8.17 (*dd*, *J* = 6.0, 2.4 Hz)	126.5 (CH)	C-5, C-6, C-8
7a		133.7 (C)	
8		182.7 (C=O)	
8a		131.7 (C)	
9		176.3 (C=O)	
9a		133.8 (C)	
N-CH_3	4.06 (s)	36.7 (CH_3)	C-2, C-8a
3-$\underline{CH_2}$OH	4.71 (*d*, *J* = 6.9 Hz)	57.0 (CH_2)	C-2. C-3, C-3a
3-$CH_2\underline{OH}$	4.40 (*t*, *J* = 6.9 Hz)		

GMS9:

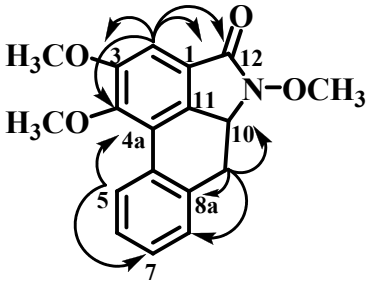
10-Amino-3,4-dimethoxy-*N*-methoxy-9,10-dihydrophenanthrene-1-carboxylic acid lactam



GMS9 was obtained as a white solid. The IR spectrum showed the absorption bands of C=O stretching at 1705 cm^{-1}. The UV spectrum exhibited absorption maxima at 223, 250, 273 and 315 nm, indicating an aristolactam as the basic structure. The ^{1}H NMR spectrum showed resonances of an isolated aromatic proton H-2 (δ 7.23), four adjacent aromatic protons H-5 (δ 8.30), H-6 (δ 7.34), H-7 (δ 7.28) and H-8 (δ 7.25), *N*-methoxyl protons (*N*-OCH_3) (δ 3.96), two methoxyl group (δ 3.81 and 3.88), a methine proton H-10 (δ 4.53) and methylene protons H-9 (δ 3.34 and 2.74). These signals were in agreement with the parent structure of aristolactam **GMS7**, with the addition of two methoxyl groups at C-3 and C-4 instead of a methylenedioxyphenyl. The aromatic proton H-2 was confirmed being at *peri* position to C=O from the ^{3}J correlation of H-2 to C=O (δ 168.9). The HMBC correlations of 3-OCH_3 (δ 3.88) to C-3 and 4-OCH_3 (δ 3.81) to C-4 as well as H-2 to C-3 and C-4 confirmed the positions of OCH_3 at C-3 and C-4, respectively. In the NOEDIFF experiment, irradiation of the aromatic signal at δ 7.23 resulted in enhancement of the methoxyl signal at δ 3.88, indicating methoxy protons (δ 3.88) at *ortho* position to H-2. Compound **GMS9** therefore was identified as 10-amino-3,4-dimethoxy-*N*-methoxy-9,10-dihydrophenanthrene-1-carboxylic acid lactam. It was a new aristolactam.



NOE of **GMS9**



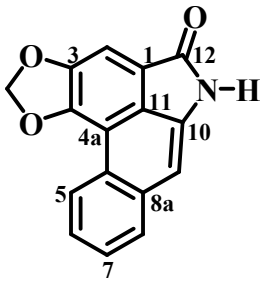
Major HMBC of **GMS9**

Table 13 NMR spectral data of **GMS9**

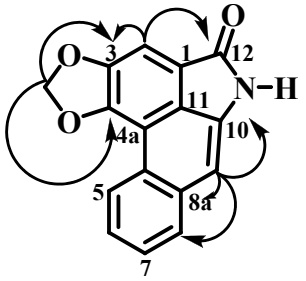
Position	δ_H (multiplicity)	δ_C (C-type)	HMBC
1		122.8 (C)	
2	7.23 (*s*)	105.9 (CH)	C-1, C-3, C-4, C-11, C-12
3		155.4 (C)	
4		150.5 (C)	
4[a]		134.4 (C)	
5	8.30 (*d*, *J* = 7.5 Hz)	127.9 (CH)	C-4a, C-7, C-11
5a		131.4 (C)	
6	7.34 (*ddd*, *J* = 7.5, 7.5, 1.2 Hz)	128.1 (CH)	C-5a, C-8
7	7.28 (*ddd*, *J* = 7.5, 7.5, 1.2 Hz)	128.6 (CH)	C-5, C-5a, C-8a
8	7.25 (*dd*, *J* =7.5, 1.2 Hz)	129.8 (CH)	C-5, C-5a, C-8a
8a		134.2 (C)	
9	3.34 (*dd*, *J* = 13.8, 6.0 Hz) 2.74 (*d*, *J* = 13.8 Hz)	35.3 (CH_2)	C-5a, C-8, C-8a, C-10
10	4.53 (*dd*, *J* = 13.8, 6.0 Hz)	56.4 (CH)	C-1, C-8a, C-9
11		124.0 (C)	
12		168.9 (C)	
N-OCH_3	3.96 (*s*)	64.8 (CH_3)	
3-OCH_3	3.88 (*s*)	57.8 (CH_3)	C-3
4-OCH_3	3.81 (*s*)	60.4 (CH_3)	C-4

GMS10:

10-Amino-3,4-methylenediphenylphenanthrene-1-carboxylic acid lactam



GMS10 was obtained as a yellow solid. The IR spectrum showed the absorption bands of O-H stretching at 3395 cm^{-1} and C=O stretching at 1687 cm^{-1}. The UV spectrum exhibited absorption maxima at 230, 264, 275, 327, 341 nm, indicating an aristolactam as the basic structure. The ^{1}H NMR spectrum showed resonances of a methylenedioxyphenyl group by the signal at δ 6.40 (2H, *s*). The remaining resonances indicated the presence of six aromatic protons, the singlet resonances at δ 7.60 and 7.07 were revealed to H-2 and H-9 whereas resonances at δ 8.66 (*dd*), 7.56 (*ddd*), 7.58 (*ddd*) and 7.82 (*dd*) suggested four adjacent aromatic protons H-5, H-6, H-7 and H-8, respectively. The HMBC correlations of H-9 to C-8, C-8a, C-10 and C-11 confirmed that the aromatic proton H-9 was conjugated to H-8. The correlations of H-2 to C-1, C-3, C-4, C-11, C-12 and H-9 to C-8, C-8a, C-10 and C-11 confirmed the assignement of H-2 and H-9, respectively. Furthermore the aromatic proton H-2 was supported being at *peri* position to C=O from the ^{3}J correlation of H-2 to C=O (δ 168.6). In ^{13}C NMR spectrum the carbon signals of carbonyl carbon and methylenedioxy carbon were shown at δ 168.6 and 103.0, respectively. Compound **GMS10** therefore was identified as 10-amino-3,4-methylene diphenylphenanthrene-1-carboxylic acid lactam (Michirori, *et al*., 1974).



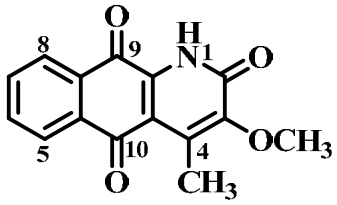
Major HMBC of **GMS10**

Table 14 NMR spectral data of **GMS10**

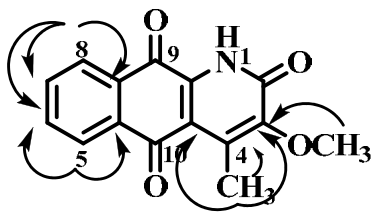
Position	δ_H (multiplicity)	δ_C (C-type)	HMBC
1		*	
2	7.60 (*s*)	105.9 (CH)	C-3, C-4, C-12
3		148.8 (C)	
4		153.3 (C)	
4a		*	
5	8.66 (*dd*, *J* = 7.5, 0.9 Hz)	127.2 (CH)	C-6, C-8a
5a		125.5 (C)	
6	7.56 (*ddd*, *J* =7.5, 7.5, 0.9 Hz)	125.8 (CH)	C-5a, C-8
7	7.58 (*ddd*, *J* =7.5, 7.5, 0.9 Hz)	127.7 (CH)	C-6, C-8a
8	7.82 (*dd*, *J* =7.5, 0.9 Hz)	128.7 (CH)	C-7, C-9
8a		134.1 (C)	
9	7.07 (*s*)	105.2 (CH)	C-8, C-8a, C-10, C-11
10		134.1 (C)	
11		123.9 (C)	
12		168.6 (C)	
-OCH_2O-	6.40 (*s*)	103.0 (CH_2)	C-3, C-4

*** Not observed**

GMS11: 3-methoxy-4-methylbenzo[*f*]quinoline-2,9,10(1*H*)-trione



GMS11 was obtained as a yellow solid. The IR spectrum indicated the presence of C=O stretching at 1653 and 1638 cm^{-1}. The UV spectrum exhibited absorption maxima at 244, 266, 296, 315 and 424 nm, indicating a quinone as the basic structure. The presence of C=O of quinone moiety was also observed from the carbon resonances at δ 180.0 (C-9) and 177.3 (C-10). The high field shift of C-10 might result from transferring of electron density by cross conjugation between N-1 and C-10 (Soonthornchareonnon, *et al*., 1999). The ^{1}H NMR spectrum showed signals of four coupled aromatic protons [δ 8.22 (*dd*, *J* = 7.5, 1.2 Hz), 8.17 (*dd*, *J* = 7.5, 1.2 Hz), 7.76 (*ddd*, *J* = 7.5, 7.5, 1.2 Hz) and 7.84 (*ddd*, *J* = 7.5, 7.5, 1.2 Hz)], indicating an *ortho*-disubstituted benzene moiety. The lower field resonances (δ 8.22 and δ 8.17) were assigned for H-8 and H-5 as affected by a *peri* carbonyl group whereas the higher field (δ 7.76 and δ 7.84) ones were proposed for H-6 and H-7. The spectrum further showed a singlet signal of a methyl group at δ 2.66 and a singlet signal of a methoxyl group at 4.06. The long-range HMBC correlations of -CH_3 to C-3 (δ 152.8), C-4 (δ 138.1) and C-4a (δ 117.8) confirmed the substitution of the methyl group at C-4 positon. The HMBC spectrum also revealed correlations of H-8 and H-5 to C-10a and C-8a, respectively. **GMS11** was then assigned to be 3-methoxy-4-methylbenzo[*f*]quinoline-2,9,10(1*H*)-trione. Its ^{1}H NMR and ^{13}C NMR and assignd structure were compatible to those of a known compound named dielsiquinone (Soonthornchareonnon, *et al*., 1999).



Major HMBC of **GMS11**

Table 15 NMR spectral data of **GMS11**

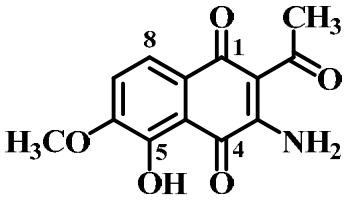
Position	**δ_H (multiplicity)**	**δ_C (C-type)**	**HMBC**
1			
2		156.8 (C)	
3		152.8 (C)	
4		138.1 (C)	
4a		117.8 (C)	
5	8.17 (*dd*, *J* = 7.5, 1.2 Hz)	126.7 (CH)	C-6, C-10a
6	7.76 (*ddd*, *J* = 7.5, 7.5, 1.2 Hz)	133.6 (CH)	C-5, C-8, C-10a
7	7.84 (*ddd*, *J* = 7.5, 7.5, 1.2 Hz)	135.6 (CH)	C-6, C-8
8	8.22 (*dd*, *J* = 7.5, 1.2 Hz)	127.5 (CH)	C-6, C-7, C-8a
8a		130.0 (C)	
9		180.0 (C)	
9a		137.6 (C)	
10		177.3 (C)	
10a		134.7 (C)	
3-OCH_3	4.06 (*s*)	59.9 (OCH_3)	C-3, C-4, C-4a
4-CH_3	2.66 (*s*)	13.8 (CH_3)	C-3

Table 16 Comparison of the ^{1}H NMR spectral data of **GMS11** and **dielsiquinone**

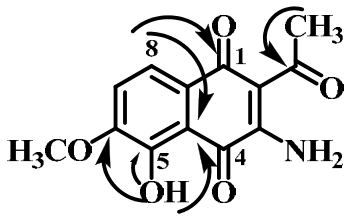
Position	**GMS11** δ_H **(multiplicity)**	**dielsiquinone** δ_H **(multiplicity)**
5	8.17 (*dd*, *J* = 7.5, 1.2 Hz)	8.16 (*dd*, *J* = 7.6, 0.9 Hz)
6	7.76 (*ddd*, *J* = 7.5, 7.5, 1.2 Hz)	7.76 (*ddd*, *J* = 7.7, 7.7, 0.9 Hz)
7	7.84 (*ddd*, *J* = 7.5, 7.5, 1.2 Hz)	7.83 (*ddd*, *J* = 7.7, 7.7, 0.9 Hz)
8	8.22 (*dd*, *J* = 7.5, 1.2 Hz)	8.22 (*dd*, *J* = 7.6, 0.9 Hz)
3-OCH_3	4.06 (*s*)	4.06 (*s*)
4-CH_3	2.66 (*s*)	2.66 (*s*)

GMS12:

2-Acetyl-3-amino-5-hydroxy-6-methoxynaphthalene-1,4-dione



GMS12 was obtained as a red solid. The IR spectrum of **GMS12** indicated the presence of amino and hydroxyl (3416-3338 cm^{-1}), C=O stretching at 1628 and 1568 cm^{-1}. The UV spectrum exhibited absorption maxima at 223, 254, 264, 271 and 401 nm, indicating a quinone as the basic structure. The carbonyl carbons of the quinone moiety were shown at δ 180.3 (C-1) and δ 185.7 (C-4) in ^{13}C NMR spectrum. The ^{1}H NMR spectrum showed singlet signals of a hydrogen bonded hydroxyl group at δ 11.70, a methoxyl group at δ 4.00, a singlet of an acyl group at δ 2.73 and a broad singlet signal of an amino group at δ 7.19 and δ 10.63. The spectrum further showed two doublet signals with an ortho coupling constant of 8.4 Hz at δ 7.76 (H-8) and δ 7.21 (H-7). Amino acetyl naphthoquinone derivative then was assigned for **GMS12**. The HMBC experiment, a ^{3}J correlation of an aromatic proton H-8 to carbonyl carbon C-1 (δ 180.3) verified the *peri* positon of H-8 and carbonyl carbon C-1. In the same manner as **GMS6** the amino group was placed at C-3 position due to the high field shift of C-1 (δ 180.3). Consequently the acyl group was placed at C-2 position. The structure of **GMS12** was therefore proposed as 2-acetyl-3-amino-5-hydroxy-6-methoxynaphthalene-1,4-dione.



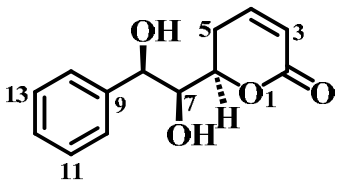
Major HMBC of **GMS12**

Table 17 NMR spectral data of **GMS12**

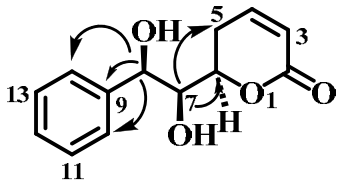
Position	**δ_H (multiplicity)**	**δ_C (C-type)**	**HMBC**
1		180.3 (C=O)	
2		109.0 (C)	
3		152.4 (C)	
4		185.7 (C=O)	
4a		114.0 (C)	
5		152.6 (C)	
6		152.0 (C)	
7	7.21 (*d*, *J* = 8.4 Hz)	117.9 (CH)	C-5, C-6, C-8a
8	7.76 (*d*, *J* = 8.4 Hz)	120.8 (CH)	C-1, C-4a, C-8
8a		125.0 (C)	
CH_3	2.73 (*s*)	33.3 (CH_3)	C=O
C=O		202.2 (C=O)	
NH_2	7.19, 10.63 (*brs*)		
5-OH	11.70 (*s*)		C-5, C-4a, C-6, C-7
OCH_3	4.00 (*s*)	56.4 (CH_3)	C-6

GMS13:

1-(6-Methylene-3, 6-dihydro-2*H*-pyran-2-yl)-2-phenyl-ethane-1,2-diol



GMS13 was obtained as a brown gum, $[\alpha]^{29}_{D}$ = +89.2° (*c* = 0.3, $CHCl_3$). The ^{1}H NMR spectrum showed signals at *δ* 7.30-7.37 (5H) representation of a *mono*-substituted phenyl moiety. The presence of the resonances of two methine protons (H-3, *δ* 5.96, *dd*; H-4, *δ* 6.90, *ddd*), non-equivalent methylene protons (H-5, *δ* 2.46, *td*; *δ* 2.60, *tdd*) and an oxymethine proton (H-6, *δ* 4.39, *td*) suggested the presence protons of an *α,β*-unsaturated lactone moiety. The resonances of two hydroxyl protons (*δ* 3.13 and 3.15), two oxymethine protons H-7 (3.92, *t*, *J* = 4.8 Hz) and H-8 (4.87, *d*, *J* = 4.8 Hz), as well as resonances of two low-field oxymethine carbons (*δ* 76.0, C-7 and *δ* 72.0, C-8) were verified for a diol structure. The spectrum further showed a triplet of doublet of an oxymethine proton (H-6) at *δ* 4.39. This proton was coupled with methylene protons H-5 resonating at 2.46 (*td*, *J* = 18.6, 4.8 Hz) and 2.60 (*tdd*, *J* = 18.6, 11.7, 2.7 Hz). The assignments of protons and carbons were confirmed by COSY and HMBC experiment **(Table 19)**. **GMS13** was then assigned to be 1-(6-Methylene-3,6-dihydro-2*H*-pyran-2-yl)-2-phenyl-ethane-1,2-diol. Its optical rotation of +89.2° was in agreement with those of a known compound goniodiol ($[\alpha]_D$ = +96.4°, *c* = 0.3, $CHCl_3$) (Mu, *et al*., 1999). **GMS13** then was assigned as goniodiol.



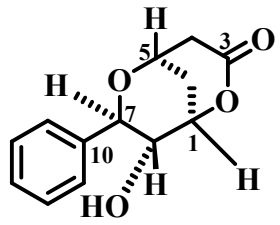
Major HMBC of **GMS13**

Table 18 NMR spectral data of **GMS13**

Position	**δ_H (multiplicity)**	**δ_C (C-type)**	**HMBC**
1			
2		164.0 (C=O)	
3	5.96 (*dd*, *J* = 9.9, 1.8 Hz)	120.8 (CH)	C-2, C-5
4	6.90 (*ddd*, *J* = 9.9, 6.0, 2.7 Hz)	145.9 (CH)	C-2, C-5, C-6
5	2.46 (*td*, *J* = 18.6, 4.8 Hz)	24.9 (CH_2)	C-2,C-4, C-6
	2.60 (*tdd*, *J* = 18.6, 11.7, 2.7 Hz)		
6	4.39 (*td*, *J* = 11.7, 4.8 Hz)	77.4 (CH)	C-4, C-7
7	3.92 (*t*, *J* = 4.8 Hz)	76.1 (CH)	C-5, C-6, C-8
8	4.87 (*d*, *J* = 4.8 Hz)	72.0 (CH)	C-6, C-7, C-9, C-10
9		140.3 (C)	
10-14	7.30-7.37 (*m*)	128.2 (CH)	
		128.7 (CH)	
		126.4 (CH)	
		128.7(CH)	
		128.2 (CH)	

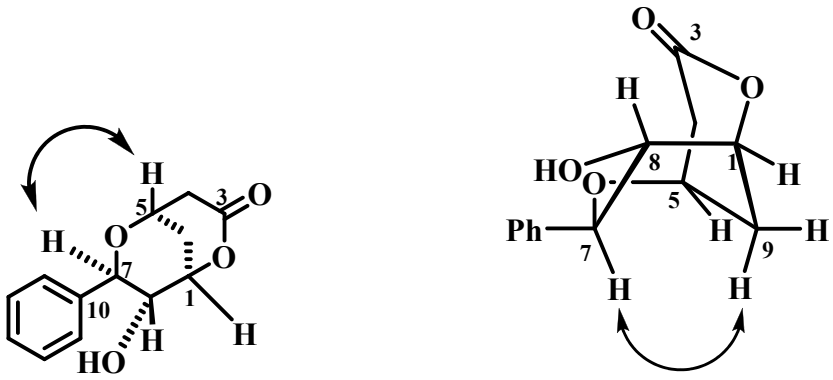
GMS14:

8-Hydroxy-7-phenyl-2,6-dioxabicyclo[3.3.1]nonan-3-one

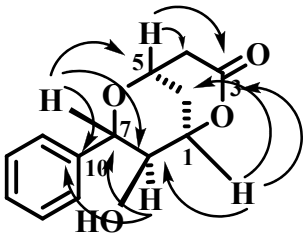


GMS14 was obtained as a brown gum, $[\alpha]^{29}_{D} = -39.7^{o}$ (*c* = 0.5, $CHCl_3$). The IR spectrum showed the absorption bands of O-H stretching at 3431 cm^{-1} and C=O stretching at 1705 cm^{-1}. The ^{1}H NMR data showed the signals represented a *mono*-substituted phenyl moiety at δ 7.31-7.37. Oxymethine protons H-1, H-5, H-7 and H-8 were suggested from the proton resonances at δ 4.84 (*br s*), δ 4.38 (*br s*), δ 4.43 (*d*, *J* = 9.6 Hz) and δ 3.46 (*dd*, *J* = 9.6, 2.7 Hz) as well as the carbon resonances at δ 77.1 (C-1), δ 65.7 (C-5), δ 74.1 (C-7) and δ 72.4 (C-8), respectively. The resonances of methylene proton H-9 were observed at δ 2.15 (*m*) whereas those of non-equivalent methylene protons H-4 were shown at δ 2.83 (*dd*, *J* = 19.2, 2.1 Hz) and 2.91 (*dd*, *J* = 19.2, 1.5 Hz). The results from COSY experiments also confirmed the assignments of protons. The HMBC correlations of H-7 to C-5, C-8, C-10 confirmed that the aromatic moiety was linked to C-7. The correlations of H-1 to C-3, C-8, C-9 and H-4a, H-4b to C-4, C-5, as well as of H-5 to C-3, C-7, C-9 supported the assignment of a lactone ring. The ^{13}C NMR spectrum exhibited the resonances of a carbonyl ester carbon (δ 169.6), a quarternary aromatic carbon (δ 138.3), five aromatic methine carbons (δ 127.5., 128.4x2 and 128.5x2), four oxymethine carbons (δ 65.7, 72.4, 74.1 and 77.1) and two methylene carbons (δ 29.7 and 36.5). The coupling constant of 9.6 Hz indicated that H-7 and H-8 were in *trans* position. In NOESY experiment, the correlations of H-1 to H-5 and H-7 to H-9 (CH_2) were observed suggesting that the bicyclic were arranged in a boat-chair conformation rather than chart-chair conformation. Compound **GMS14** therefore was identified as 8-hydroxy-7-phenyl-2,6-dioxabicyclo[3.3.1]nonan-3-one. Its optical rotation of -39.7^{o} was in agreement with those of a known compound 8-*epi*-9-deoxygoniopypyrone

($[\alpha]^{20}_{D}$ = -90.0°, *c* = 0.7, $CHCl_3$) (Surivet, *et al*., 1999). **GMS13** then was assigned as 8-*epi*-9-deoxygoniopypyrone.



NOESY of **GMS14**



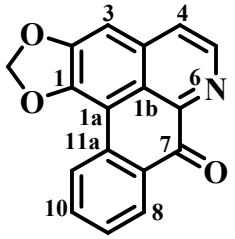
Major HMBC of **GMS14**

Table 19 NMR spectral data of **GMS14**

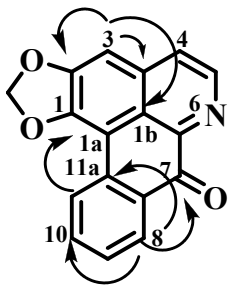
Position	δ_H (multiplicity)	δ_C (C-type)	HMBC
1	4.84 (*br m*)	77.1 (CH)	C-3, C-8, C-9
2			
3		169.6 (C=O)	
4	2.83 (*dd*, *J* = 19.2, 2.1 Hz)	36.5 (CH_2)	C-3, C-5
	2.91 (*dd*, *J* = 19.2, 1.5 Hz)		
5	4.38 (*br s*)	65.7 (CH)	C-1, C-3, C-4, C-9
6			
7	4.43 (*d*, *J* = 9.6 Hz)	74.1 (CH)	C-1, C-5, C-9, C-10
8	3.46 (*dd*, *J* = 9.6, 2.7 Hz)	72.4 (CH)	C-8, C-9, C-10
9	2.15 (*br s*)	29.7 (CH_2)	C-1, C-5, C-8
10		138.3 (C)	
11-15	7.31-7.37 (*m*)	128.4 (CH)	
		128.5 (CH)	
		127.5 (CH)	
		128.5 (CH)	
		128.4 (CH)	

GMS15:

Liriodenine



GMS15 was obtained as a yellow solid. The IR spectrum showed the absorption band of C=O stretching at 1653 cm^{-1}. The ^{1}H NMR spectrum showed signals corresponding to seven aromatic protons. The resonances at δ 8.51 (*dd*, *J* = 8.1, 1.2 Hz), 7.51 (*dt*, *J* = 8.1, 1.2 Hz), 7.67 (*dd*, *J* = 8.1, 1.2 Hz) and 8.57 (*d*, *J* = 8.1 Hz) belonged to four adjacent aromatic protons H-8, H-9, H-10 and H-11, respectively, whereas the singlet resonance at δ 7.12 was revealed to H-3 and the doublet resonances at δ 7.70 (*J* = 5.1 Hz) and 8.82 (*J* = 5.1 Hz) were assigned for H-4 and H-5, respectively. The HMBC correlations of H-4 to C-3, C-5 and of H-5 to C-3a, C-4 confirmed their positions at C-4 and C-5, respectively. The correlations of H-3 to C-1, C-2, C-1b, C-4 supported the location of H-3. The correlations of H-8 to C-7, C-10, C-11a and H-11 to C-9, C-1a, C-8a confirmed that H-8 was at *peri* position to C=O and H-11 was at C-11. Compound **GMS15** therefore was identified identical with Liriodenine (Wijeratine, *et al*., 1996).



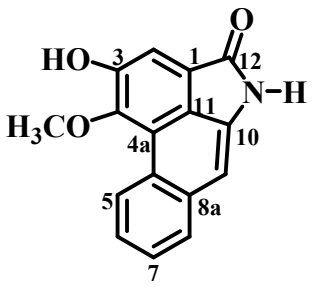
Major HMBC of **GMS15**

Table 20 NMR spectral data of **GMS15**

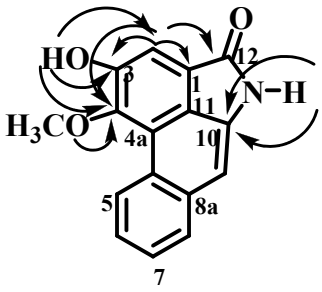
Position	δ_H (multiplicity)	δ_C (C-type)	HMBC
1		152.0 (C)	
1a		108.1 (C)	
1b		123.2 (C)	
2		145.0 (C)	
3	7.12 (*s*)	103.3 (CH)	C-1, C-1b, C-2, C-4
3a		136.0 (C)	
4	7.70 (*d*, *J* = 5.1 Hz)	124.3 (CH)	C-3, C-5
5	8.82 (*d*, *J* = 5.1 Hz)	144.5 (CH)	C-3a, C-4
6			
6a		*	
7		182.2 (C=O)	
8	8.51 (*dd*, *J* = 8.1, 1.2 Hz)	128.7 (CH)	C-7, C-10, C-11a
8a		131.2 (C)	
9	7.51 (*dt*, *J* = 8.1, 1.2 Hz)	128.9 (CH)	C-8a, C-11
10	7.67 (*dd*, *J* = 8.1, 1.2 Hz)	134.0 (CH)	C-11, C-11a
11	8.57 (*d*, *J* = 8.1 Hz)	127.4 (CH)	C-1a, C-8a, C-9
11a		132.8 (C)	
-OCH_2O-	6.30 (*s*)	102.6 (CH_2)	

GMS16:

10-Amino-3-hydroxy-4-methoxyphenanthrene-1-carboxylic acid lactam



GMS16 was obtained as a white solid. The IR spectrum showed the absorption bands of O-H stretching at 3426 cm^{-1} and of C=O stretching at 1640 cm^{-1}. The ^{1}H NMR spectrum showed the resonances of two isolated aromatic protons, H-2 (δ 7.59, *s*) and H-9 (δ 6.86, *s*), and four adjacent aromatic protons, H-5 (δ 8.99, *dd*), H-6 (δ 7.36, *dd*), H-7 (δ 7.34, *dd*) and H-8 (δ 7.61, *dd*). The spectrum further showed signals of a methoxyl group (δ 3.90, *s*) and two hydroxyl protons (δ 9.27, 3-OH; δ 9.77, *N*-H). The HMBC correlations of H-9 to C-1, C-8, C-8a, C-10 confirmed that H-9 was in between H-8 and H-10. The proton H-2 was confirmed at *peri* position to C=O from the ^{3}J correlation of H-2 to C=O (δ 169.5). The hydroxyl group was placed at C-3 rather than C-4 according to the HMBC correlation of -OH to C-3, C-2 and C-4. In addition, long range correlations of *N*-H (δ 9.77) to C-1 (δ 122), C-10 (δ 134.9) and C-11 (δ 123.0) confirmed the lactam structure. Compound **GMS16** therefore was identified as 10-amino-3-hydroxy-4-methoxyphenantrene-1-carboxylic acid lactam which was known as aristolactam A-II (Talapatra, *et al*., 1988).



Major HMBC of **GMS16**

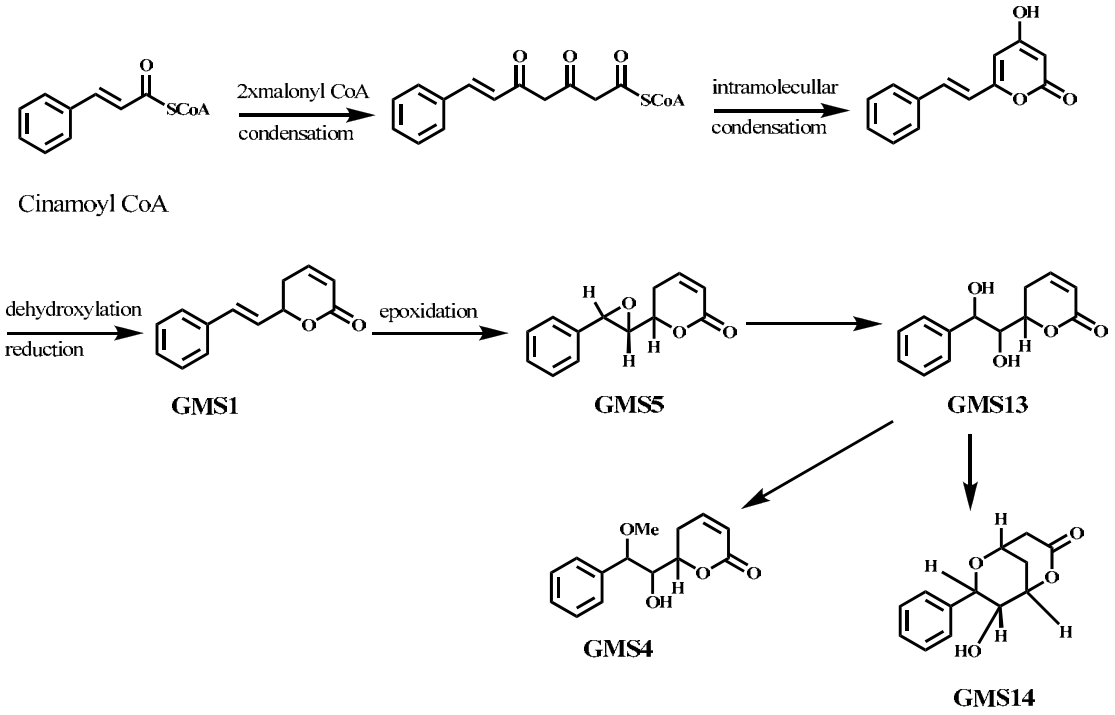
Table 21 NMR spectral data of **GMS16**

Position	δ_H (multiplicity)	δ_C (C-type)	HMBC
1		122.0 (C)	
2	7.59 (*s*)	113.9 (CH)	C-1, C-3, C-4, C-11, C-12
3		149.1 (C)	
4		152.0 (C)	
4a		121.0 (C)	
5	8.99 (*dd*, *J* = 6.0, 1.8 Hz)	127.0 (CH)	C-4a, C-5a, C-6
5a		126.5 (C)	
6	7.36 (*dd*, *J* = 6.0, 1.8 Hz)	127.1 (CH)	C-5a, C-8
7	7.34 (*dd*, *J* = 6.0, 1.8 Hz)	125.2 (CH)	C-5, C-5a, C-8
8	7.61 (*dd*, *J* = 6.0, 1.8 Hz)	128.7 (CH)	C-7, C-8[a]
8a		135.1 (C)	
9	6.86 (*s*)	104.5 (CH)	C-1, C-8, C-8a, C-10
10		134.9 (C)	
11		123.0 (C)	
12		169.5 (C)	
4-OCH_3	3.90 (*s*)	59.9 (CH_3)	C-4
3-OH	9.27		C-2, C-3, C-4
N-H	9.77		C-1, C-10, C-11

3.2 Proposed biosynthetic routes

3.2.1 Proposed biosynthetic routes of GMS1, GMS4, GMS5, GMS13 and GMS14

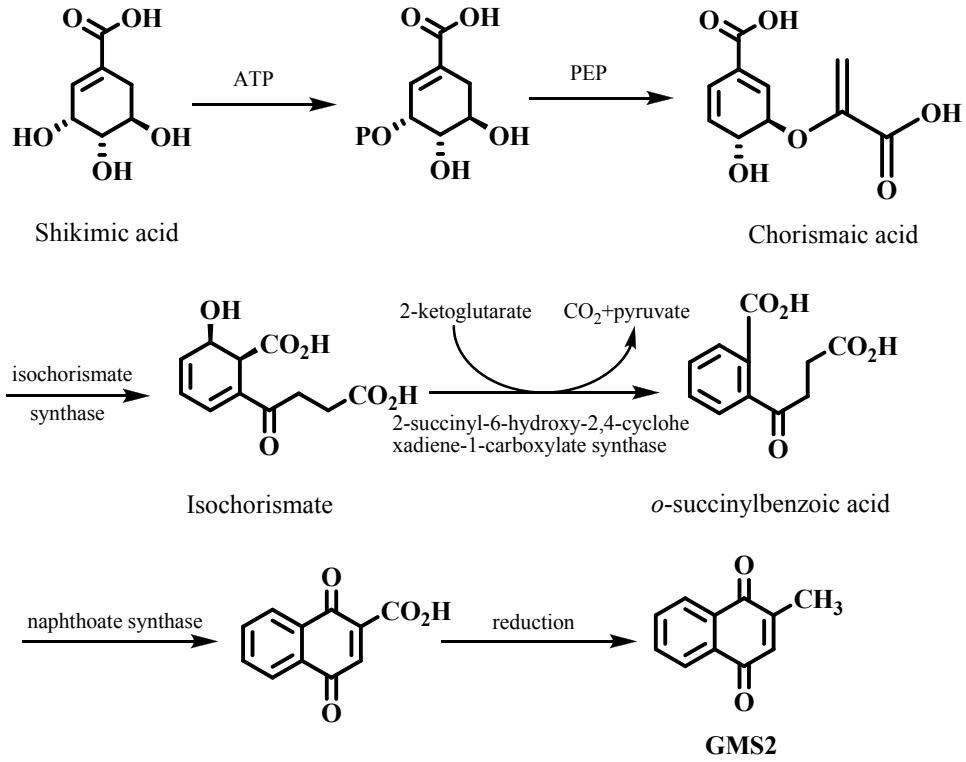
Biosynthetic routes for the formation of **GMS1**, **GMS4**, **GMS5**, **GMS13** and **GMS14** from simple styryllactones is proposed in **Scheme 4** (Pizzolatti, *et al*., 2004).



Scheme 4 Proposed biosynthetic routes of **GMS1**, **GMS4**, **GMS5**, **GMS13** and **GMS14**

3.2.2 Proposed biosynthetic route of GMS2

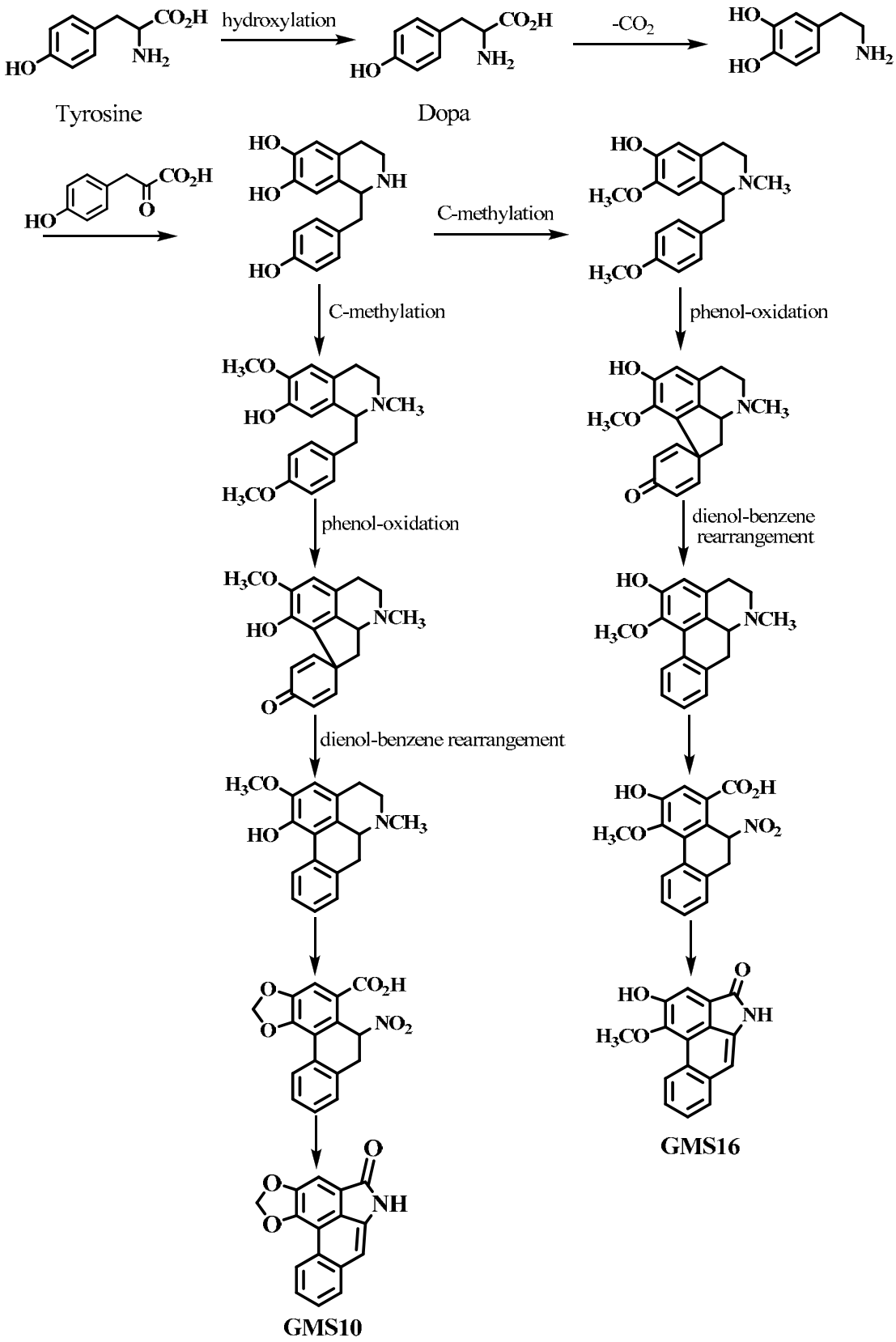
Biosynthetic route for the formation of **GMS2** from simple naphthoquinone is proposed in **Scheme 4** (Palaniappan, *et al*., 1992; Seto, *et al*., 2008; Simantiras, *et al*., 1989).

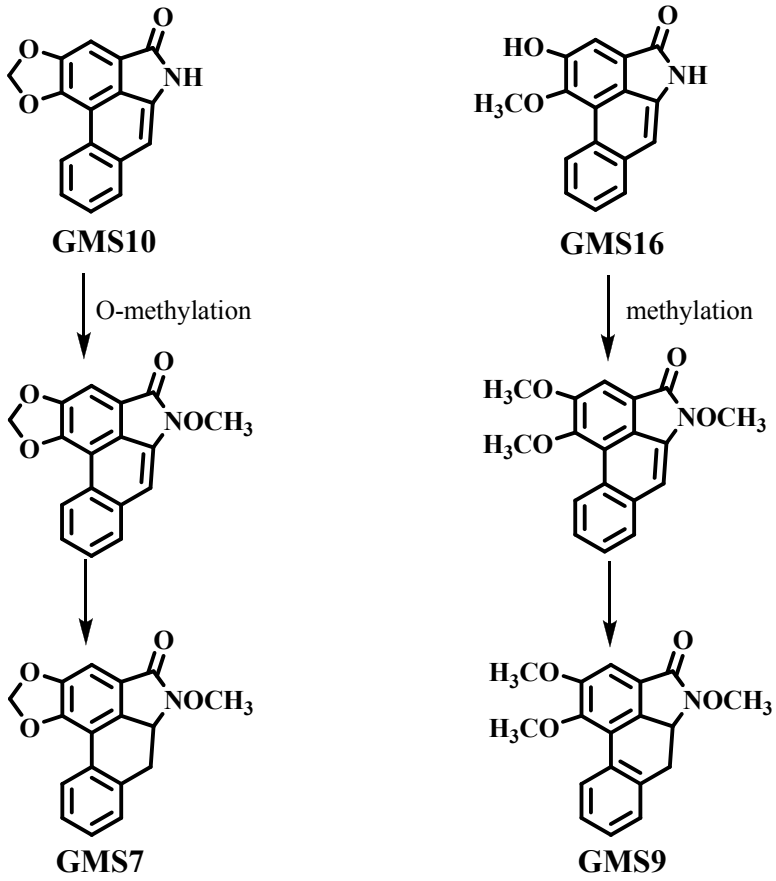


Scheme 5 Proposed biosynthetic route of **GMS2**

3.2.3 Proposed biosynthetic routes of GMS7, GMS9, GMS10 and GMS16

Biosynthetic routes for the formation of **GMS7**, **GMS9**, **GMS10** and **GMA16** from simple aristolactams is proposed in **Scheme 6** (Comer, *et al*., 1968).


hydroxylation
-CO2
Tyrosine
Dopa
C-methylation
C-methylation
phenol-oxidation
phenol-oxidation
dienol-benzene rearrangement
dienol-benzene rearrangement
GMS16
GMS10



Scheme 6 Proposed biosynthetic routes of **GMS7**, **GMS9**, **GMS10** and **GMS16**

3.3 Evaluation of biological activities of crude extracts

The methylene chloride extract (SD) and acetone extract (SC) of *G. macrophyllus* were tested for antibacterial, antifungal and cytotoxic activitiy.

3.3.1 Antibacterial activity

The antibacterial activity of the extracts of *G. macrophyllus* were tested on *Staphylococcus aureus* ATCC25923, methicillin-resistant strain MRSA SK1, *Pseudomonas aeruginosa* ATCC27853 and *Escherichia coli* ATCC25922. The standard drugs, vancomycin and gentamicin were used as the references. It was found that the extracts of *G. macrophyllus* showed no activity at MIC 200 μg/ml (**Table 22**).

Table 22 Antibacterial activity of crude extracts from the stems of *G. macrophyllus*

Fractions	Antibacterial activity (MIC, μg/ml)			
	SA	MRSA SK1	PA	EC
SD	>200	>200	>200	>200
SC	>200	>200	>200	>200
vancomycin	1	1		
gentamicin			1	1

* SA = *S. aureus* ATCC25923, MRSA SK1 = methicillin-resistant strain MRSA SK1, PA = *P. aeruginosa* ATCC27853, EC = *E. coli* ATCC25922, SD = methylene chloride extract, SC = acetone extract

3.3.2 Antifugal activity

The antifungal activity of the extracts of *G. macrophyllus* were tested on *Cryptococcus neoformans* ATCC90112, *Cryptococcus neoformans* ATCC90113 and *Microsporum gypseum.* The standard drugs, amphotericin B and miconazole were used as the references. The result indicated that the methylene chloride extract (SD) was able to inhibit the growth of *C. neoformans* ATCC90112, *C. neoformans* ATCC90113 and *M. gypseum* with MIC 128, 64 and 200 μg/ml, respectively, whereas the acetone extract (SC) showed less activity (**Table 23**).

Table 23 Antifugal activity of crude extracts from the stems of *G. macrophyllus*

Fractions	Antifugal activity (MIC, μg/ml)		
	CN90112	CN90113	*Mg*
SD	128	64	64
SC	200	128	200
amphotericin B	0.25	0.5	
miconazole			1

* CN90112 = *C. neoformans* ATCC90112, CN90113 = *C. neoformans* ATCC90113, Mg = *M. gypseum,* SD = methylene chloride extract, SC = acetone extract

3.3.3 Cytotoxic activity

The extracts were evaluated for cytotoxicity against glial tumor, bone cancer, colon cancer and prostate cancer cell lines. The results indicated that methylene chloride extract inhibited the growth of glial tumor, bone cancer, colon cancer and prostate cancer cell lines with IC_{50} 9.0, 36.2, 3.7 and 3.7 μg/ml, respectively. The acetone extract was found to be cytotoxic against colon cancer and prostate cancer cell lines with IC_{50} 8.25 and 55.6 μg/ml and inactive for glial tumor and bone cancer.

Table 24 Cytotoxic activity of crude extracts from the stems of *G. macrophyllus*

Part of the plant	Fractions	Antibacterial activity (IC_{50}, μg/ml)			
		Glial tumor	Bone cancer	Colon cancer	Prostate cancer
Stems	SD	9.0	36.2	3.7	3.7
	SC	NA	NA	8.25	55.6

* NA = no activity

SD = methylene chloride extract, SC = acetone extract

3.4 Review of biological activities of the known compounds obtained from this study

Biological activities some compounds obtained from this study have been previously investigated. Base on the search from SciFinder Scholar, the biological activities of goniothalamin (**GMS1**), goniothalamin oxide (**GMS5**), 3-methoxy-4-methylbenzo[*f*]quino-line-2,5,10-(1*H*)-trione (**GMS11**) and **Liriodenine (GMS15)** are summarized.

Goniothalamin (**GMS1**) is the major component of *G. macrophyllus*. It have been tested on antimicrobial activity against *Plasmodium berghei* and *P. yoelii* with percentage of parasitemia reduction 26.8 and 63.5, respectively. (Mohd Ridzuan, 2006). The embryotoxic, teratogenic activity were studied (LD_{50}, mice, i.p., = 76 mg/kg and 32.5 % abnormality) (Sam, *et al*., 1987). It showed cytotoxicity to cell lines such as breast cancer (MCF-7, ED_{50} = 0.7-1.0 μg/ml), mouse leukemia (P-388, ED_{50} = 0.75 μg/ml) (Mereyala, *et al*., 2001), human hepatocellular carcinoma (HepG2, IC_{50} = 8.83 μg/ml) (Tian, *et al*., 2006), promyclocytic leukemia (HL-60, IC_{50} = 2.9 μg/ml), hepato carcinoma (Bel-7402, IC_{50} = 20.6 μg/ml), human lung carcinoma (A549, IC_{50} = 1.7 μg/ml), human stomach cancer (SGC-7901, IC_{50} = 5.3 μg/ml), human melanoma (UACC62, IC_{50} = 17.4 μg/ml), human breast cancer (MCF-7, IC_{50} = 17.4 μg/ml), human kidney cancer (786-0, IC_{50} = 6.4 μg/ml), (human ovarian cancer, IC_{50} = 39.0 μg/ml), colon canceer (HT-29, IC_{50} = 11.2 μg/ml) while it was inactive against human prostate cancer (PCO.3, IC_{50} = >100μg/ml) (Fatima, *et al*., 2006).

Goniothalamin oxide **(GMS5)** have been reported to showed embryotoxic and teratogenic activity (LD_{50}, mice, i.p., = 36 mg/kg and 16.2% abnormality) (Sam, *et al*., 1987). It was also exhibited cytotoxicity against human hepatocellular carcinoma (HepG2, IC_{50} = 0.9 μg/ml; Hep3B, IC_{50} = 15.2 μg/ml), and breast cancer cells (MDA-MB-231, IC_{50} = 5.7 μg/ml, MCF-7, IC_{50} = 8.8 μg/ml) while it was inactive against human gastric (NUGC, IC_{50} = >100 μg/ml) and hunman nasopharyngeal cancer cells (HONE-1, IC_{50} = > 100 μg/ml) (Lan, *et* al., 2003).

3-Methoxy-4-methylbenzo[*f*]quino-line-2,5,10-(1*H*)-trione **(GMS11)** have been tested on cytotoxic activity against human nonsmall cell lung carcinoma (A-549, ED_{50} = 0.04 μg/ml), human colon adreno carcinoma (HT-29, ED_{50} = 0.35 μg/ml), human melanoma (RPMI, ED_{50} = 0.08 μg/ml), human breast carcinoma (MAF-7, ED_{50} = 0.08 μg/ml) and human brain carcinoma (U251, ED_{50} = 0.08 μg/ml) (Soonthornchareonnon, *et al*., 1999).

Liriodenine **(GMS15)** have been tested on antibacterial activity against gram-positive bacteria (Clark, *et al.,* 1987). It was reported to induce vasodilation in rat thoracic aorta (Chulia, *et al*., 1995). It inhibited the proliferation of human hepatoma cell lines, including Hep-G2 and SK Hep-1 (Heieh, *et al*., 2005).

Conclusion

Investigation of the constituents from the stems of *G. macrophyllus* led to the isolation of sixteen compounds including five styryllactones: 6-methylene-2-styryl-3,6-dihydro-2*H*-pyran **(GMS1)**, 6-(1-hydroxy-2-methoxy-2-phenylethyl)-5,6-dihydro-2*H*-pyran-2-one **(GMS4)**, 6-methylene-2-(3-phynyloxiranyl)-3,6-dihydro-2*H*-pyran **(GMS5)**, 1-(6-methylene-3,6-dihydro-2*H*-pyran-2-yl)-2-phenyl-ethane-1,2-diol **(GMS13)** and 8-hydroxy-7-phenyl-2,6-dioxabicycle[3.3.1]nonan-3-one **(GMS14)**, five napthoquinones: 2-methylnaphthalene-1,4-dione **(GMS2)**, 3-amino-5-hydroxy-2-methoxynaphthalene-1,4-dione**(GMS3)**, 5-hydroxy-3-amino-2-aceto-3,1,4-naphthoquinone (**GMS6**), 3-hydroxymethyl-1-methyl-1*H*-benzo[*f*]indole-4,9-dione **(GMS8)** and 2-acetyl-3-amino-5-hydroxy-6-methoxynaphthalene-1,4-dione **(GMS12)**, four aristolactams: 10-amino-3,4-methylenedoxyiphenyl-*N*-methoxy-9,10-dihydrophenanthrene-1-carboxylic acid lactam **(GMS7)**, 10-amino-3,4-dimethoxy-*N*-methoxy-9,10-dihydrophenanthrene-1-carboxylic acid lactam **(GMS9)**, 10-amino-3,4-methylene-dioxyphenylphenanthrene-1-carboxylic acid lactam **(GMS10)** and 10-amino-3-hydroxy-4-methoxyphenanthrene-1-carboxylic acid lactam **(GMS16)**, one azaanthraquinone: 3-methoxy-4-methylbenzo[*f*]quinoline-2,5,10-(1*H*)-trione **(GMS11)** and one aporphine: liriodenine **(GMS15)**. **GMS3**, **GMS7**, **GMS8**, **GMS9** and **GMS12** are new compounds. **GMS2**, **GMS4**, **GMS6**, **GMS10**, **GMS11**, **GMS13**, **GMS14**, **GMS15** and **GMS16** were obtained for the first time from this plants. **GMS1** and **GMS5** were previously isolated from this plant. The crude methylene chloride and crude acetone showed strong cytotoxic activity but weak antibacterial and antifungal activity. Further study on the biological activity of the isolated compound should be performed.

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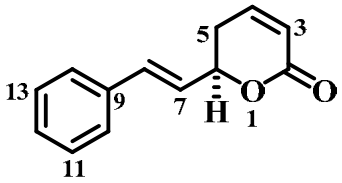
APPENDIX



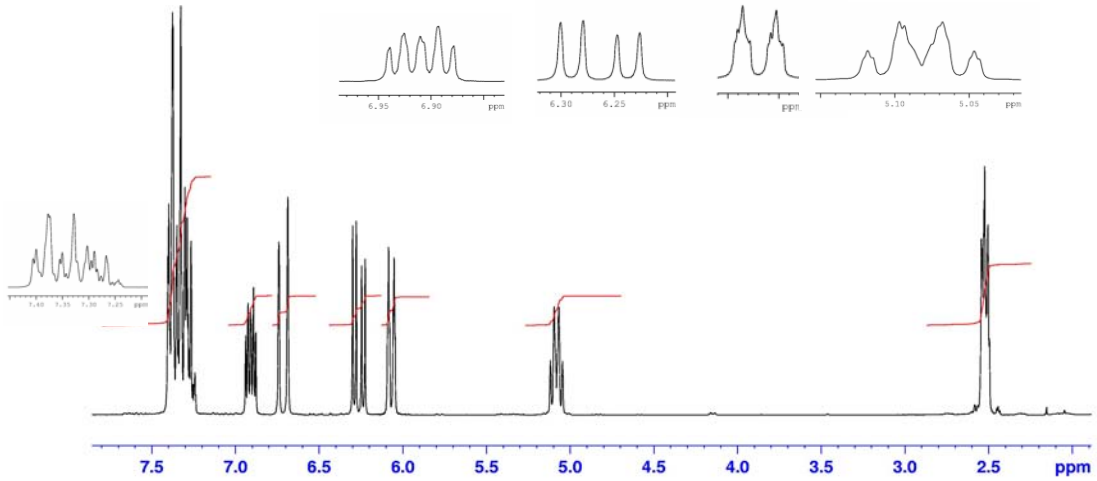


Figure 5 ^{1}H NMR (300 MHz) ($CDCl_3$) spectrum of **GMS1**

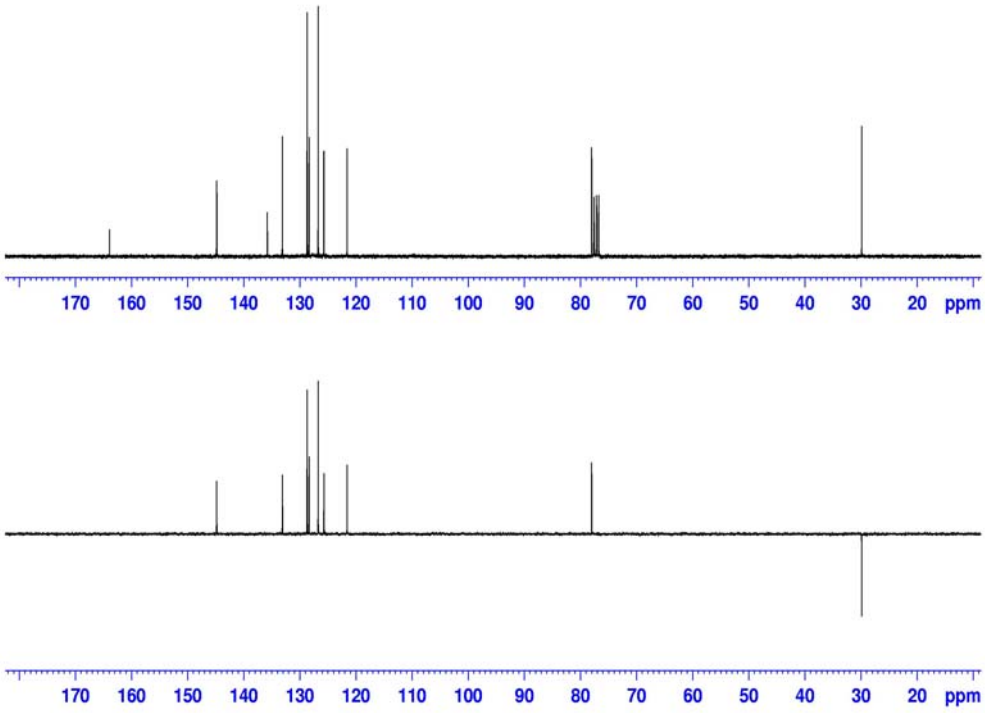


Figure 6 ^{13}C NMR (75 MHz) and DEPT 135 ($CDCl_3$) spectrum of **GMS1**

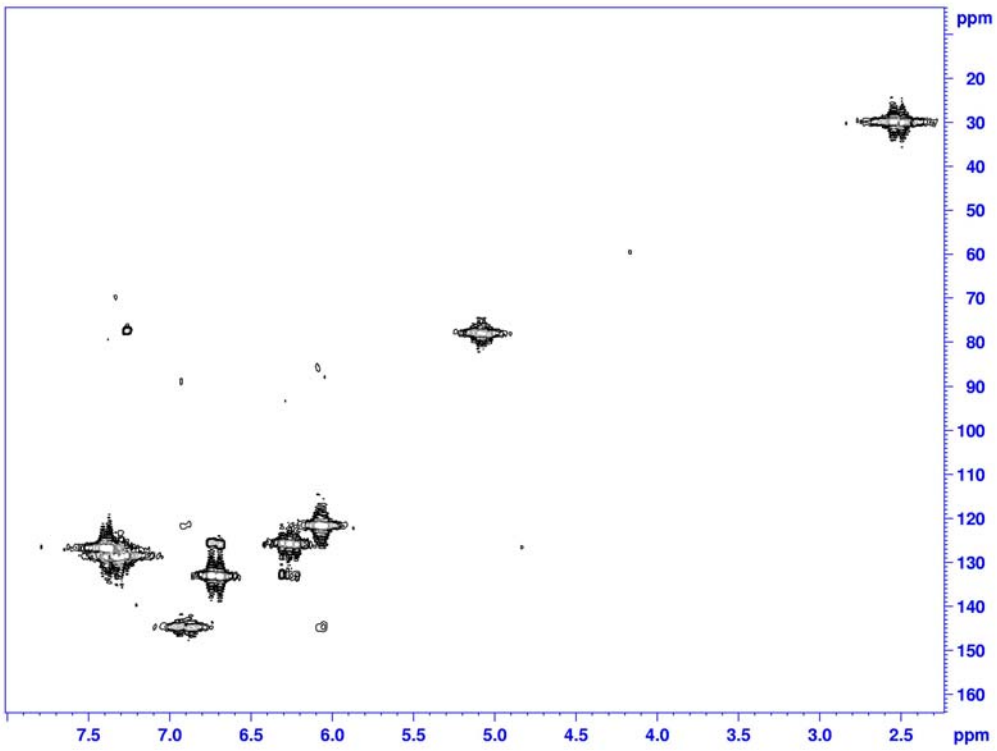


Figure 7 2D HMQC spectrum of **GMS1**

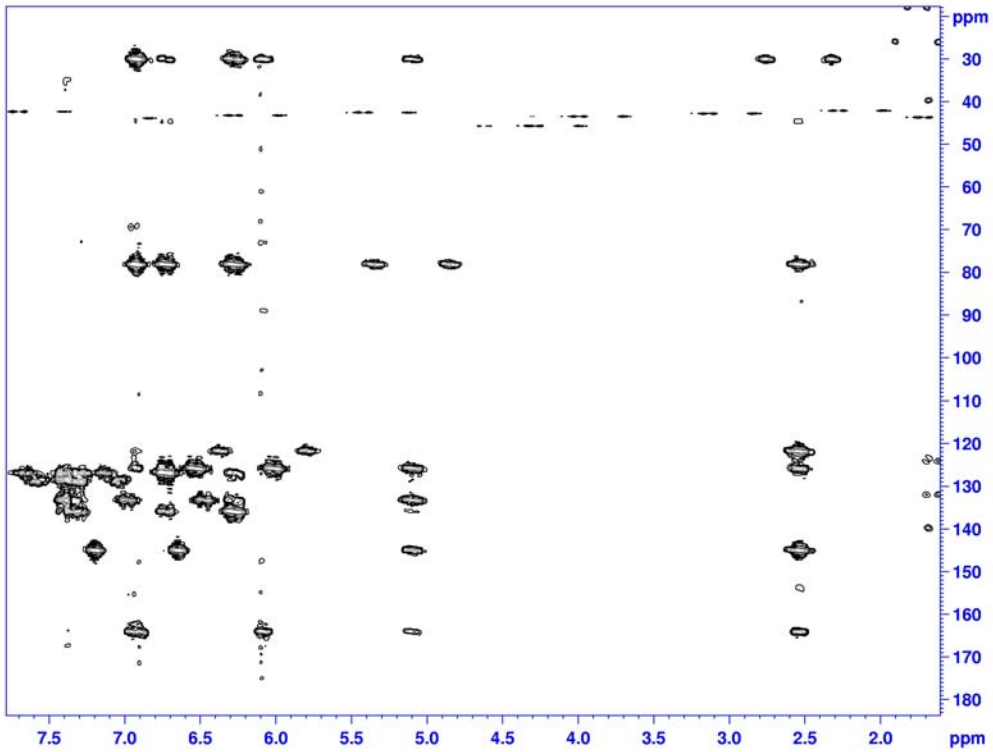


Figure 8 2D HMBC spectrum of **GMS1**

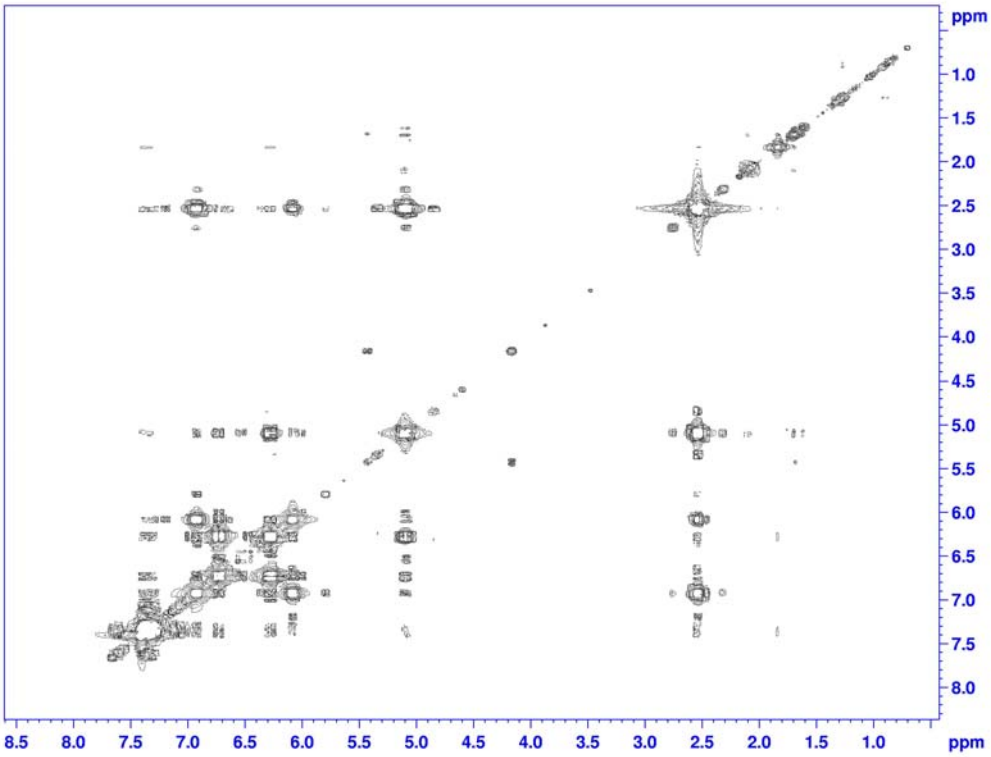


Figure 9 ^{1}H-^{1}H COSY spectrum of **GMS1**

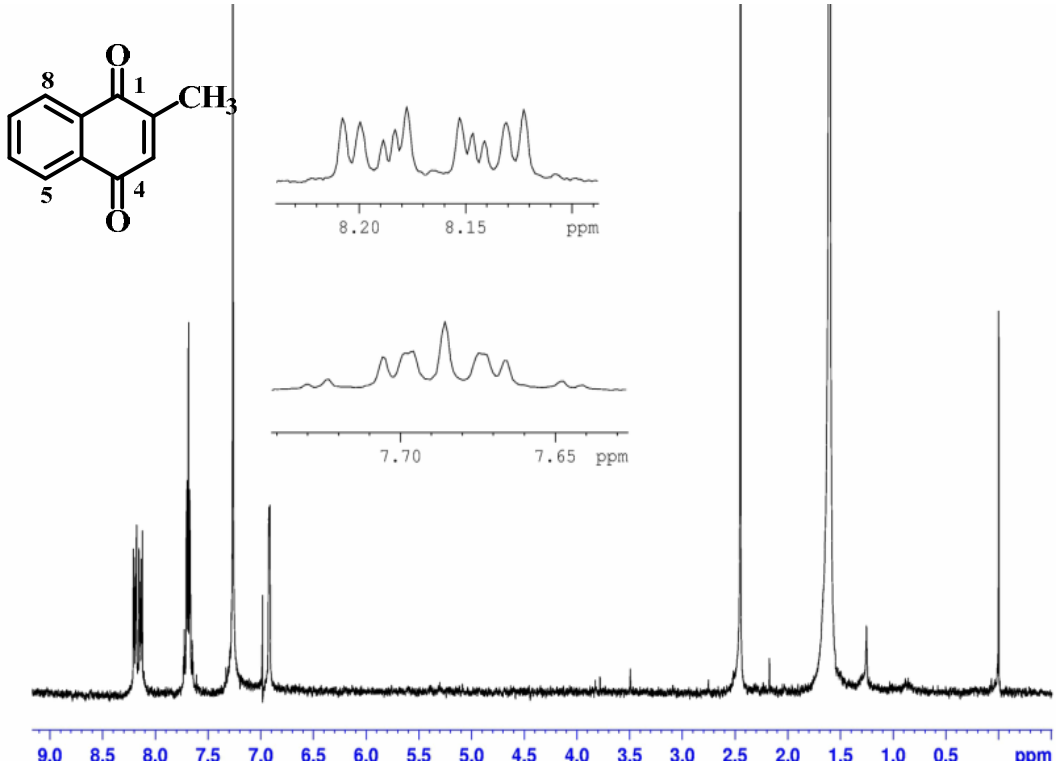


Figure 10 ^{1}H NMR (300 MHz) ($CDCl_3$) spectrum of **GMS2**

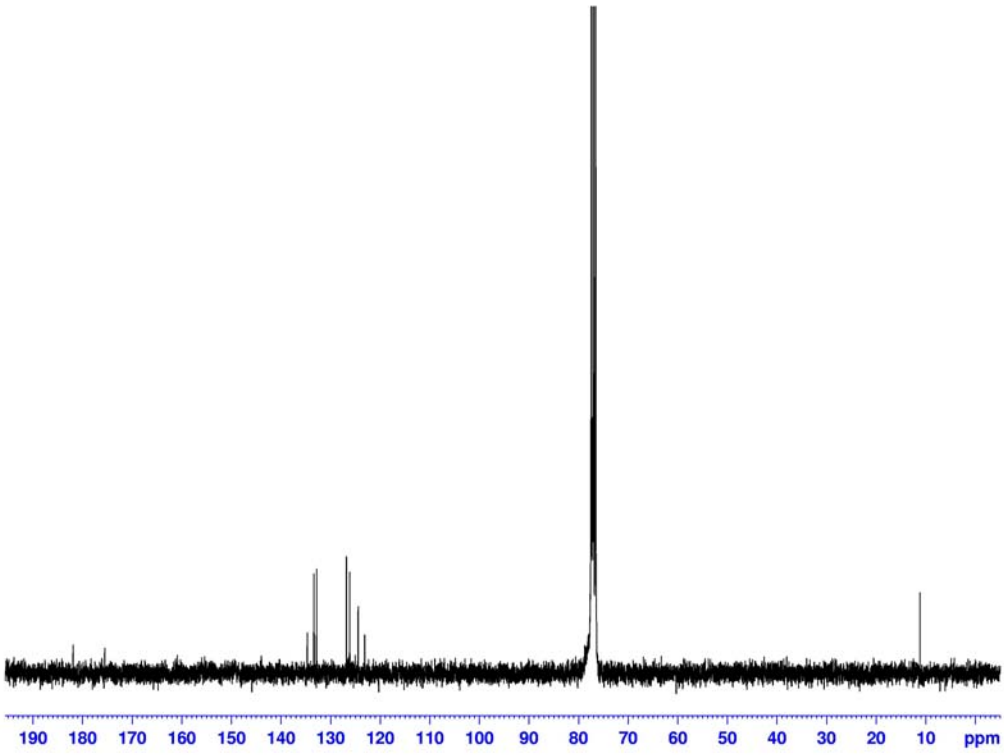


Figure 11 ^{13}C NMR (75 MHz) spectrum of **GMS2**

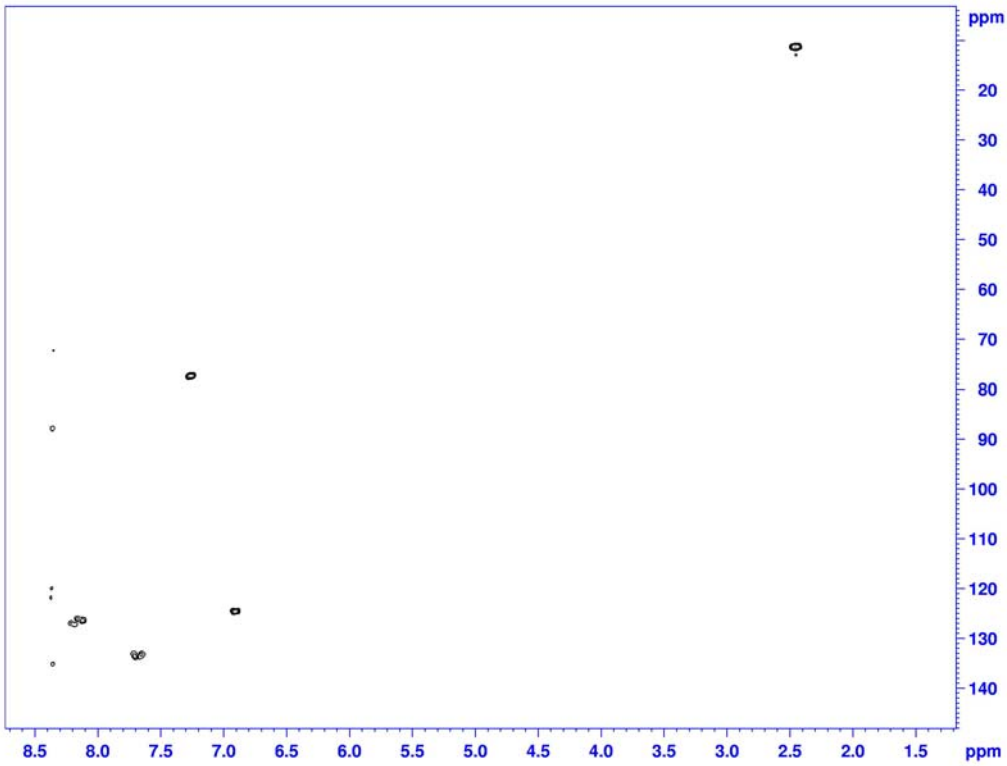


Figure 12 2D HMQC spectrum of **GMS2**

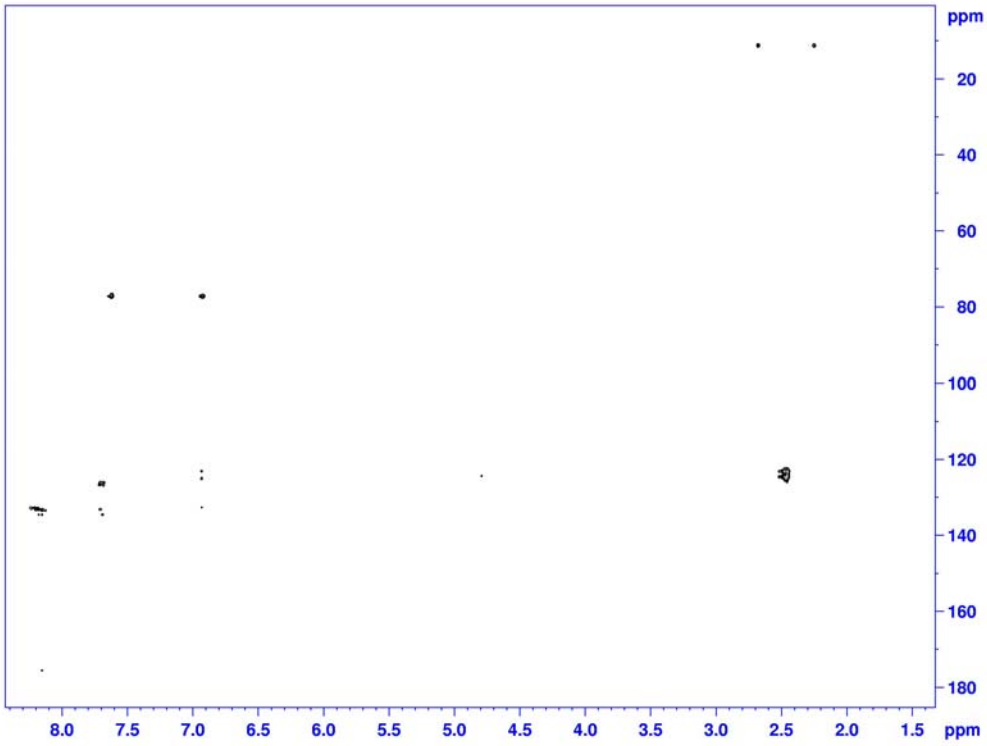


Figure 13 2D HMBC spectrum of **GMS2**

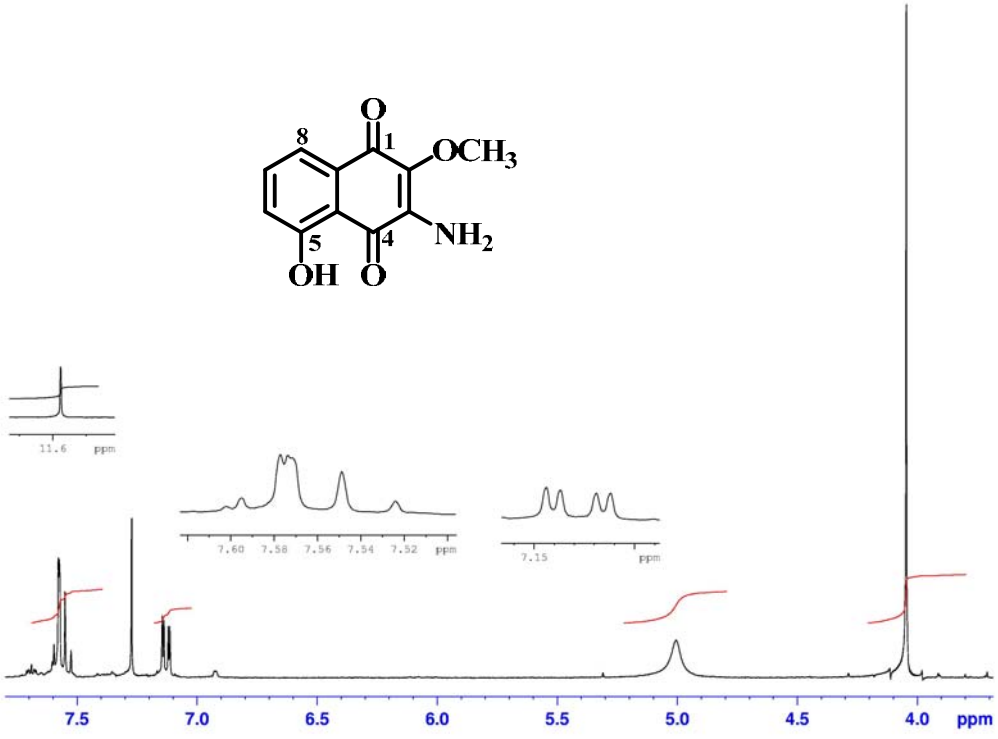


Figure 14 ^{1}H NMR (300 MHz) ($CDCl_3$) spectrum of **GMS3**

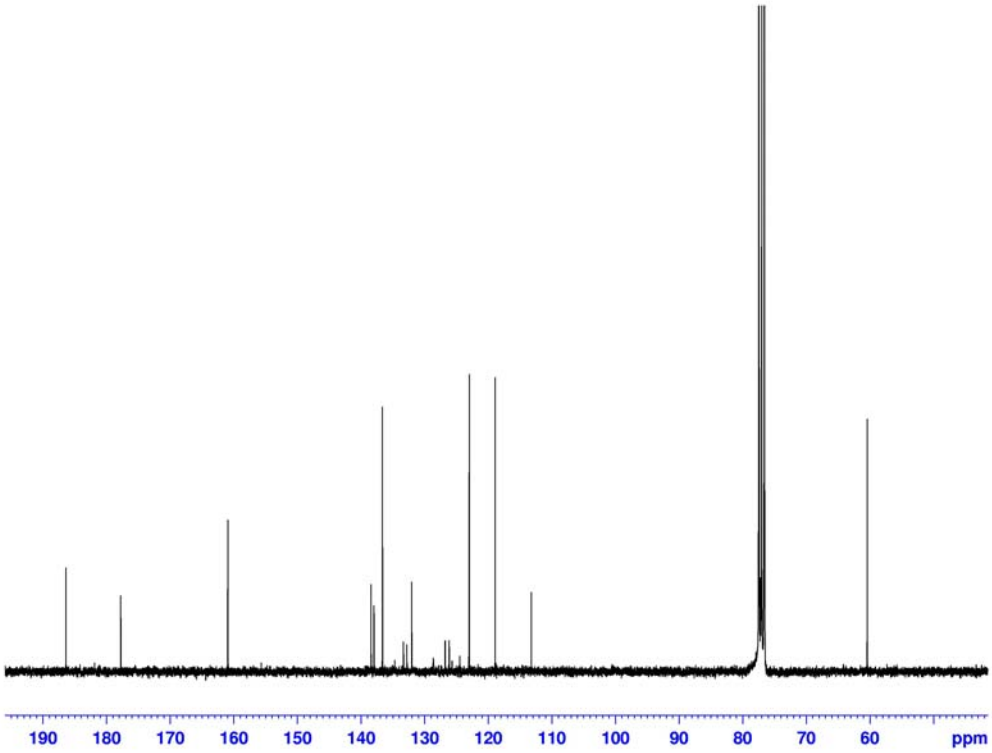


Figure 15 ^{13}C NMR (75 MHz) ($CDCl_3$) spectrum of **GMS3**

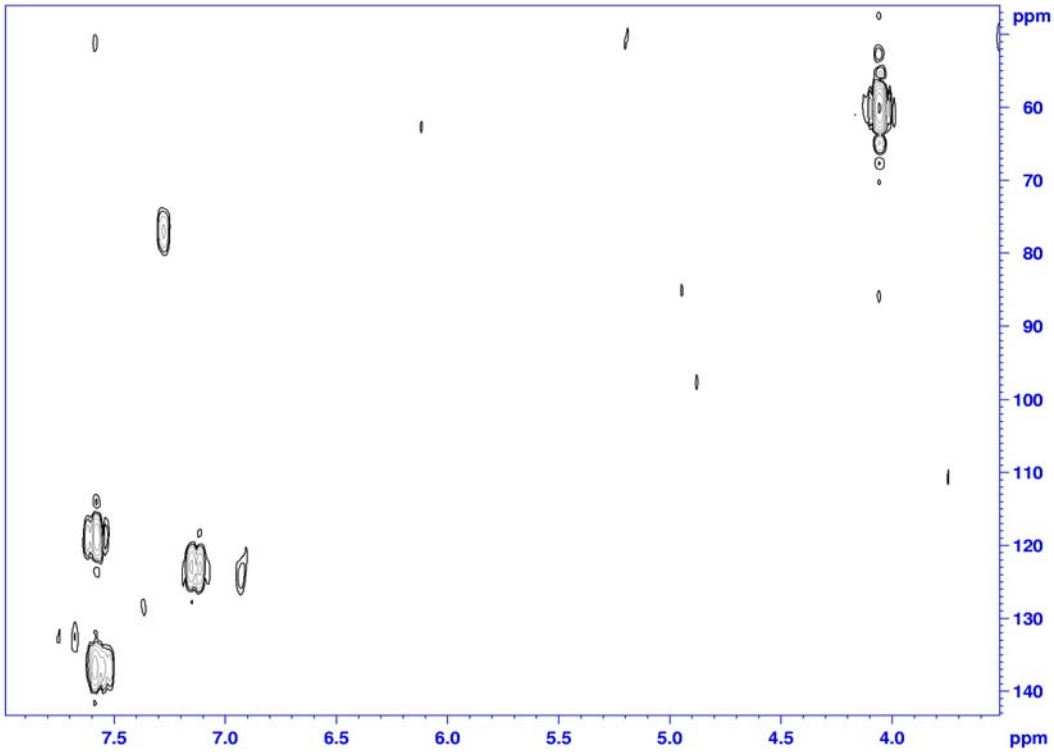


Figure 16 2D HMQC spectrum of **GMS3**

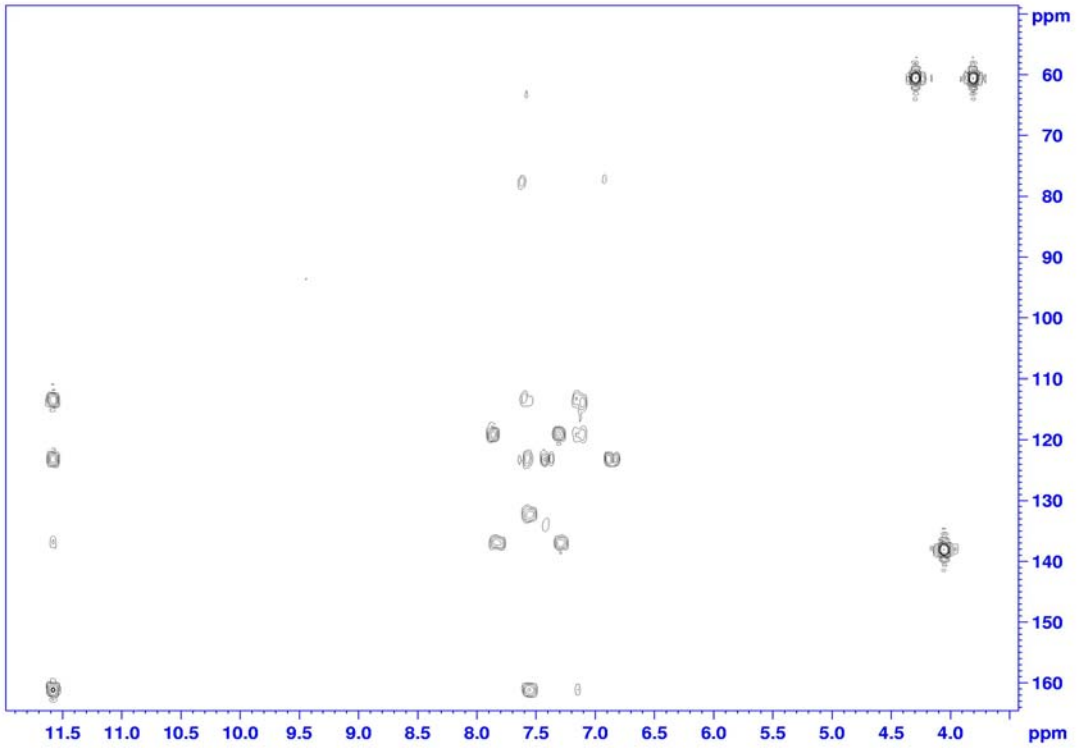


Figure 17 2D HMBC spectrum of **GMS3**

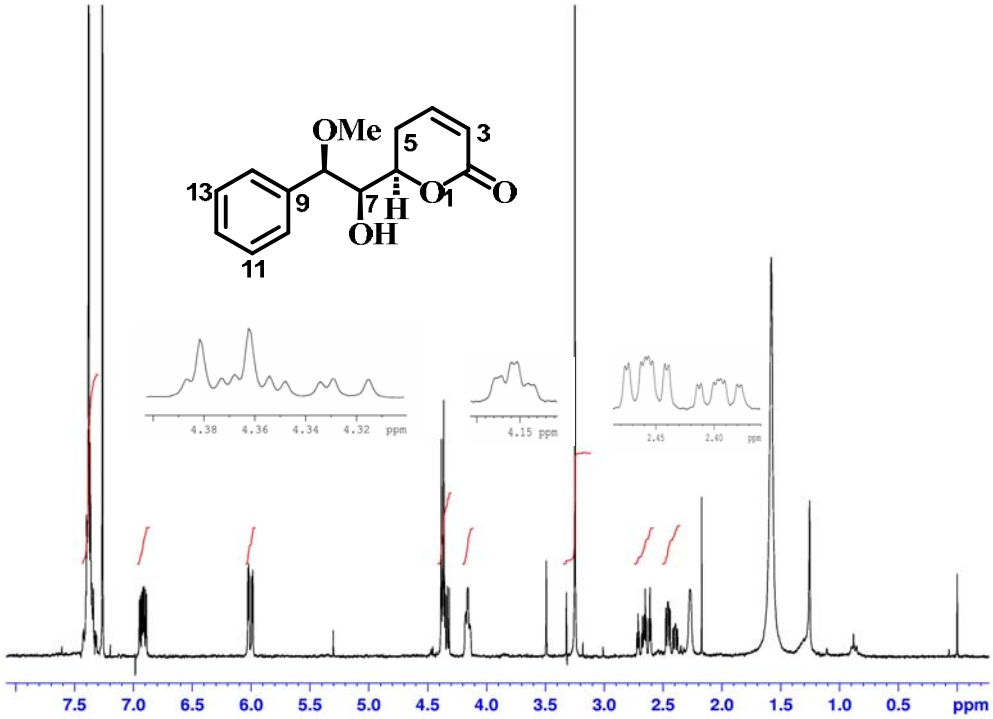


Figure 18 ^{1}H NMR (300 MHz) ($CDCl_3$) spectrum of **GMS4**

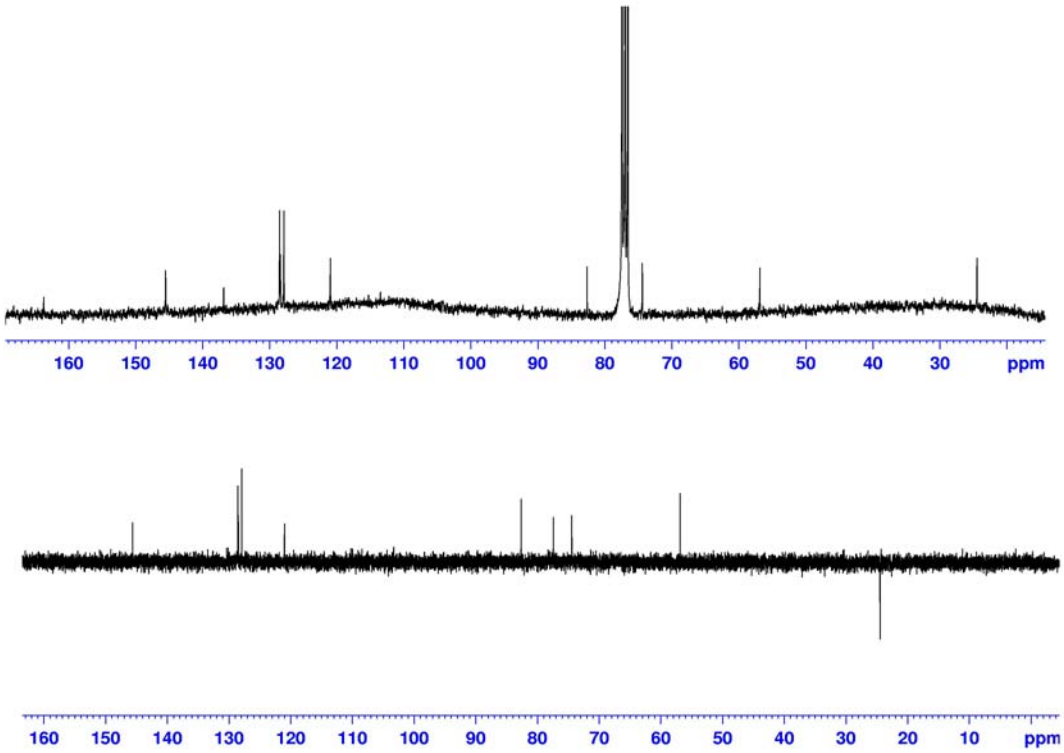


Figure 19 ^{13}C NMR and DEPT 135 (75 MHz) ($CDCl_3$) spectrum of **GMS4**

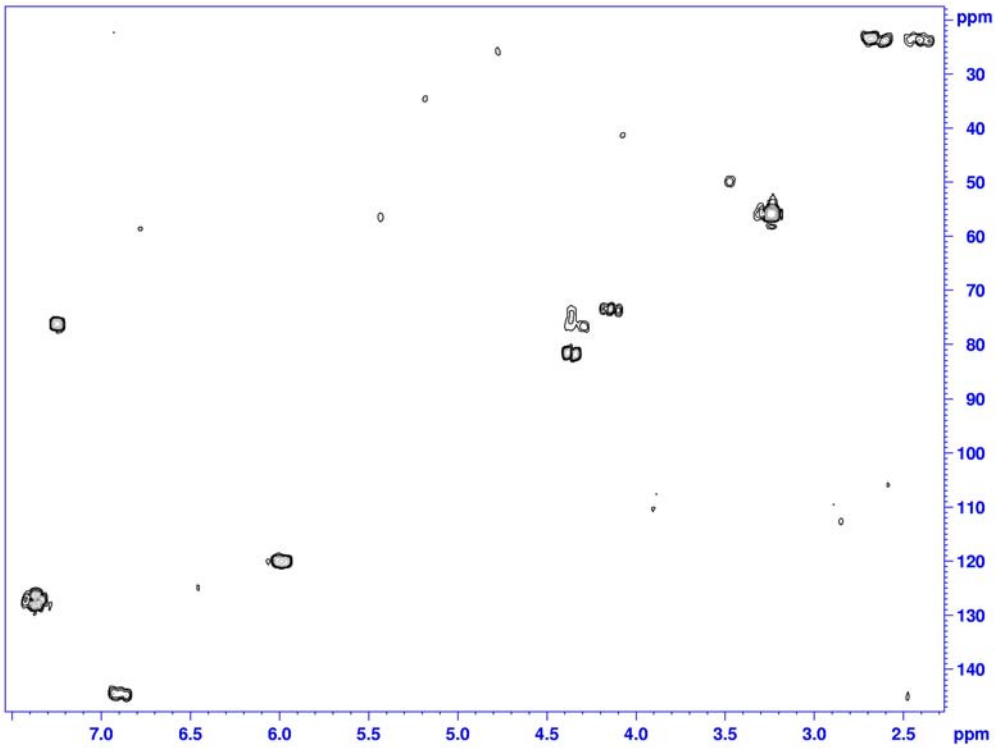


Figure 20 2D HMQC spectrum of **GMS4**

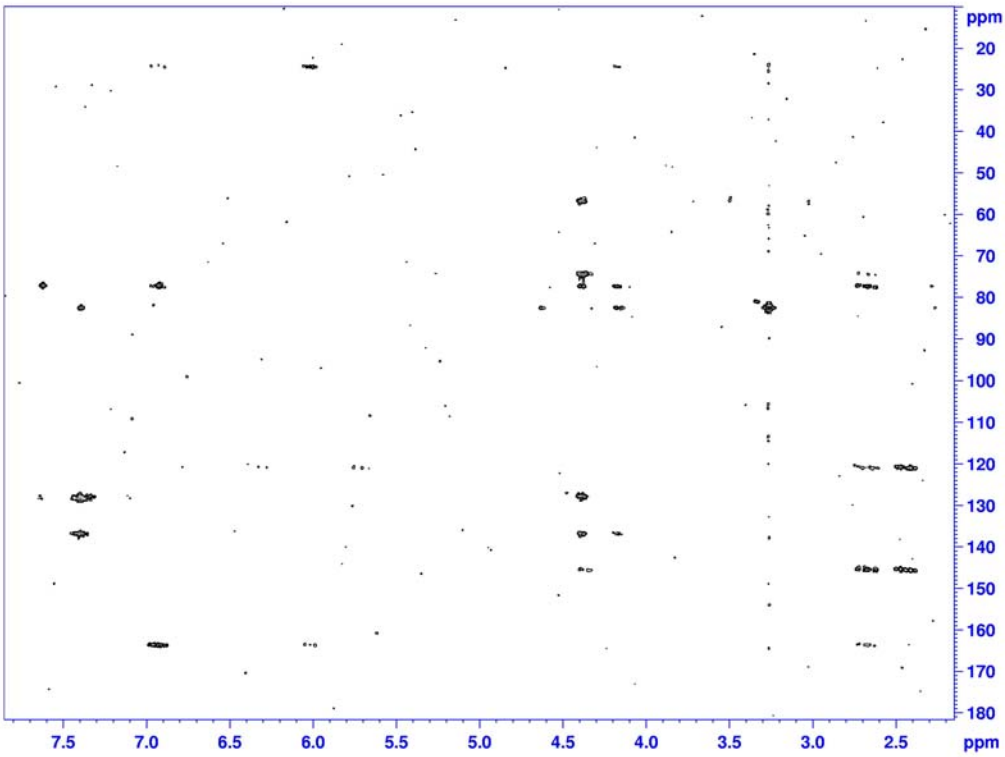


Figure 21 2D HMBC spectrum of **GMS4**

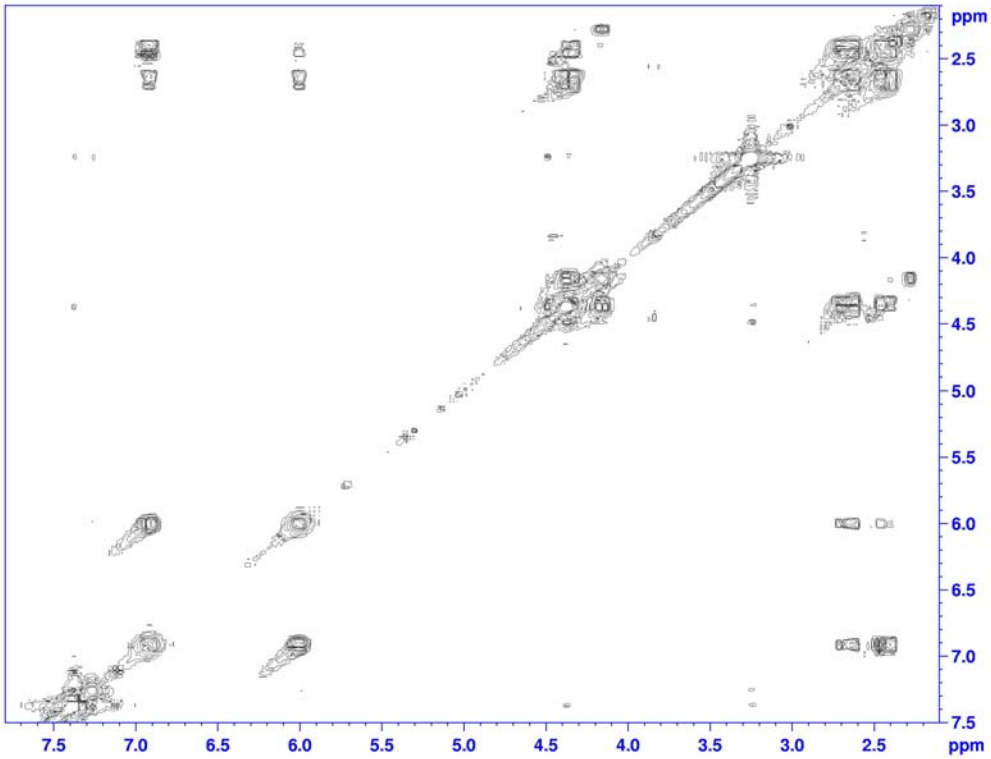


Figure 22 ^{1}H-^{1}H COSY spectrum of **GMS4**

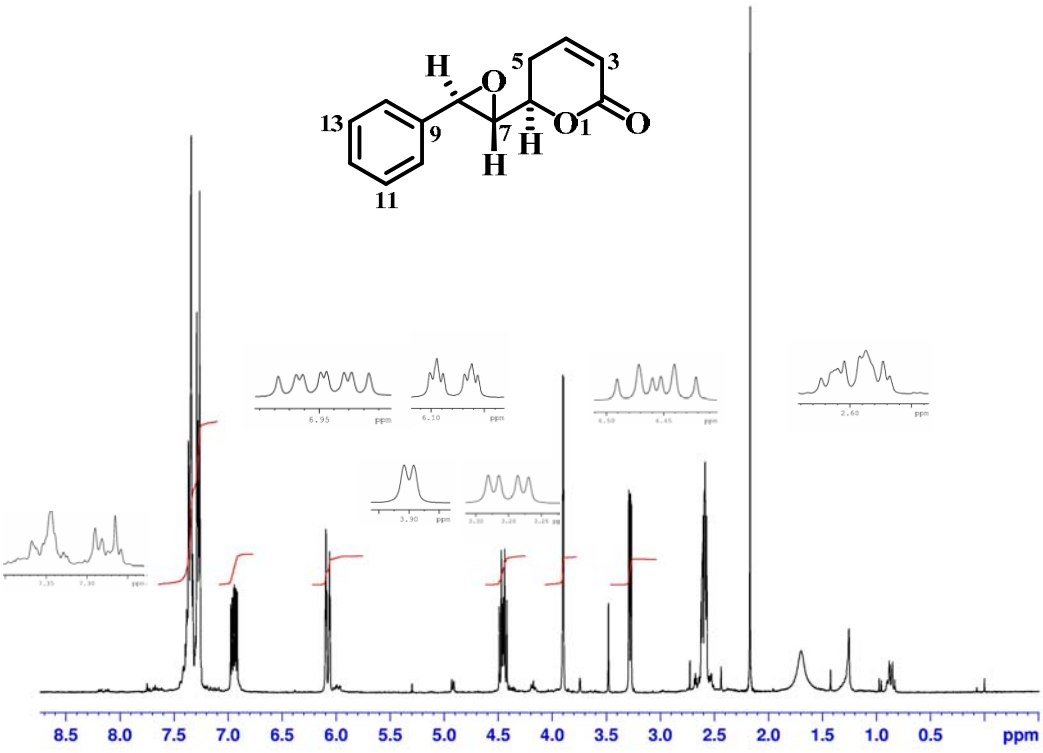


Figure 23 ^{1}H NMR (300 MHz) ($CDCl_3$) spectrum of **GMS5**

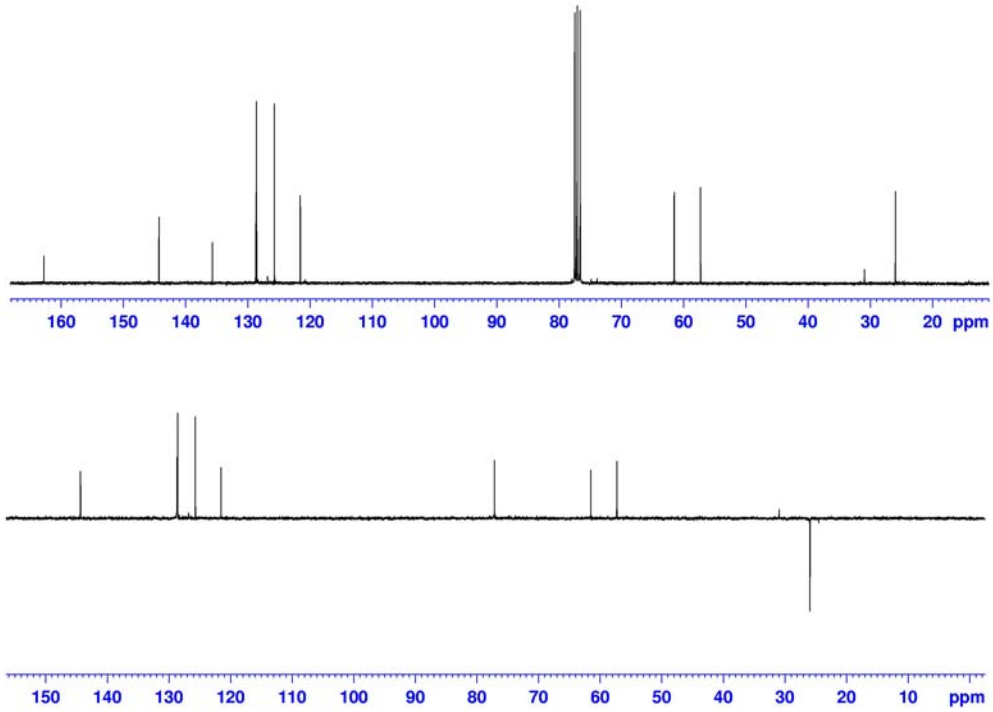


Figure 24 ^{13}C NMR and DEPT 135 (75MHz) ($CDCl_3$) spectrum of **GMS5**

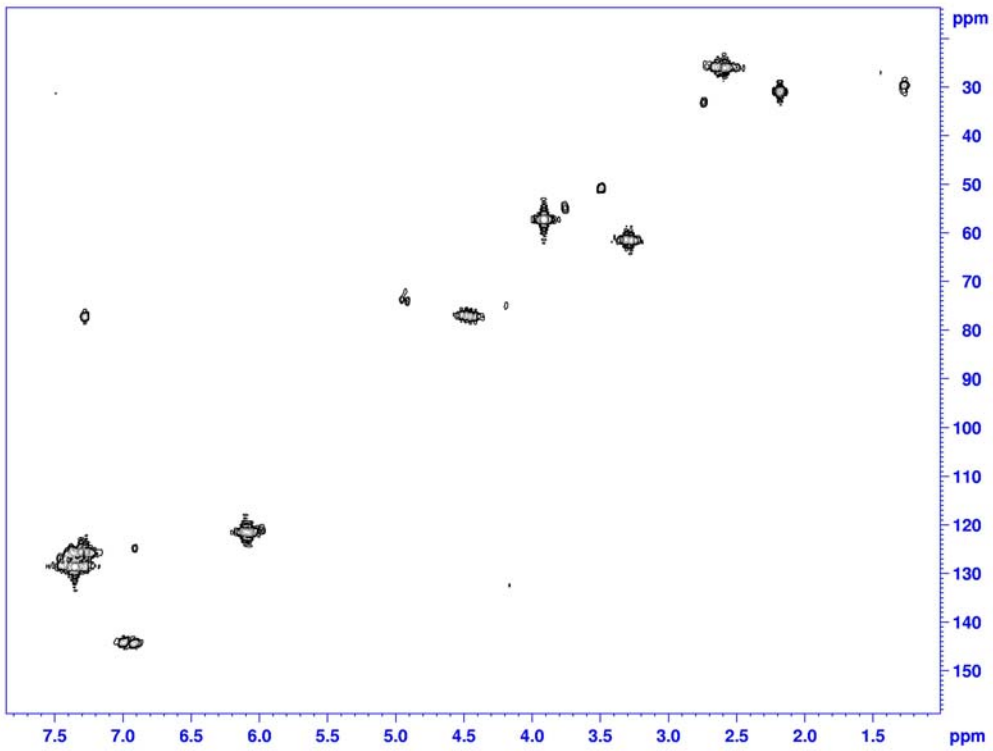


Figure 25 2D HMQC spectrum of **GMS5**

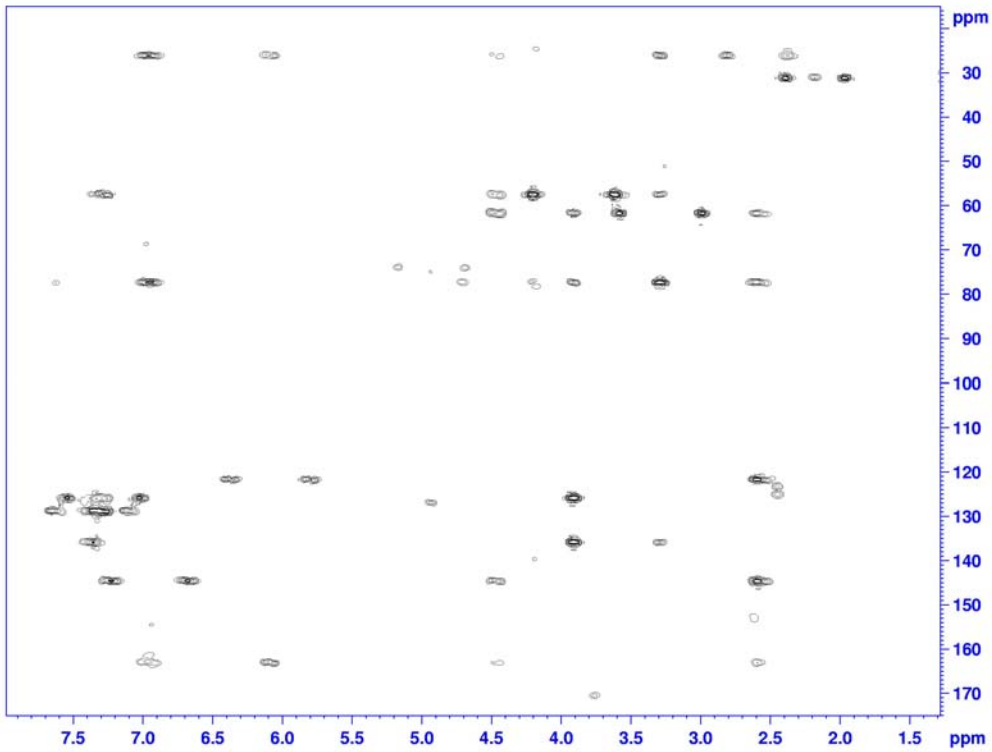


Figure 26 2D HMBC spectrum of **GMS5**

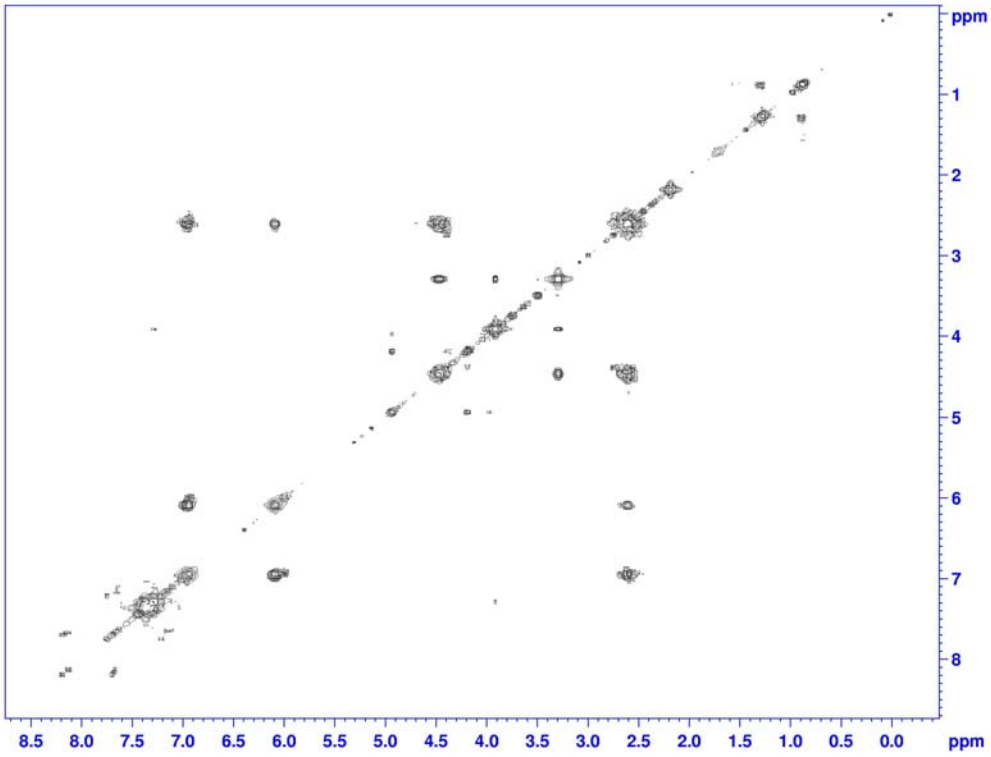


Figure 27 ^{1}H-^{1}H COSY spectrum of **GMS5**

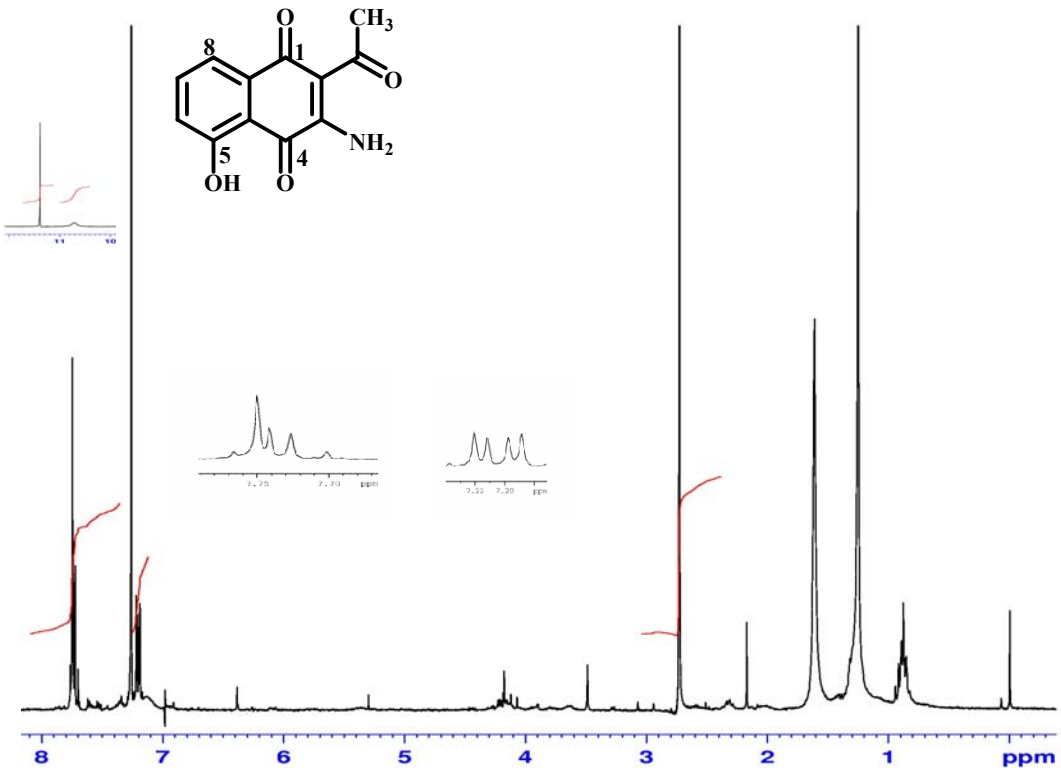


Figure 28 ^{1}H NMR (300 MHz) ($CDCl_3$) spectrum of **GMS6**

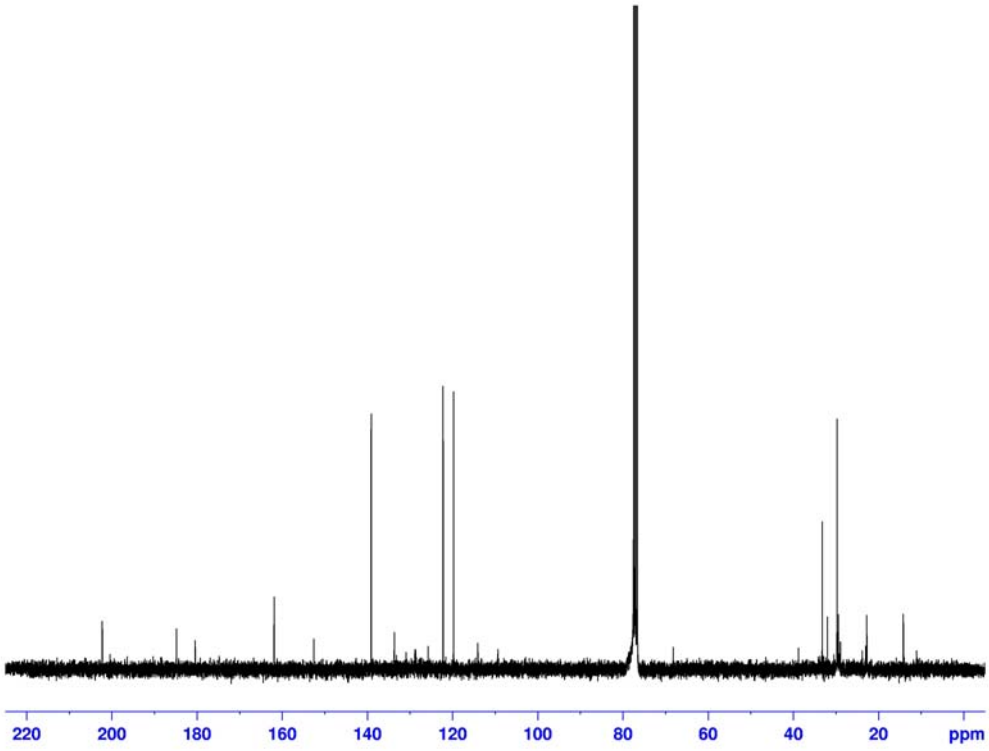


Figure 29 ^{13}C NMR (75 MHz) spectrum of **GMS6**

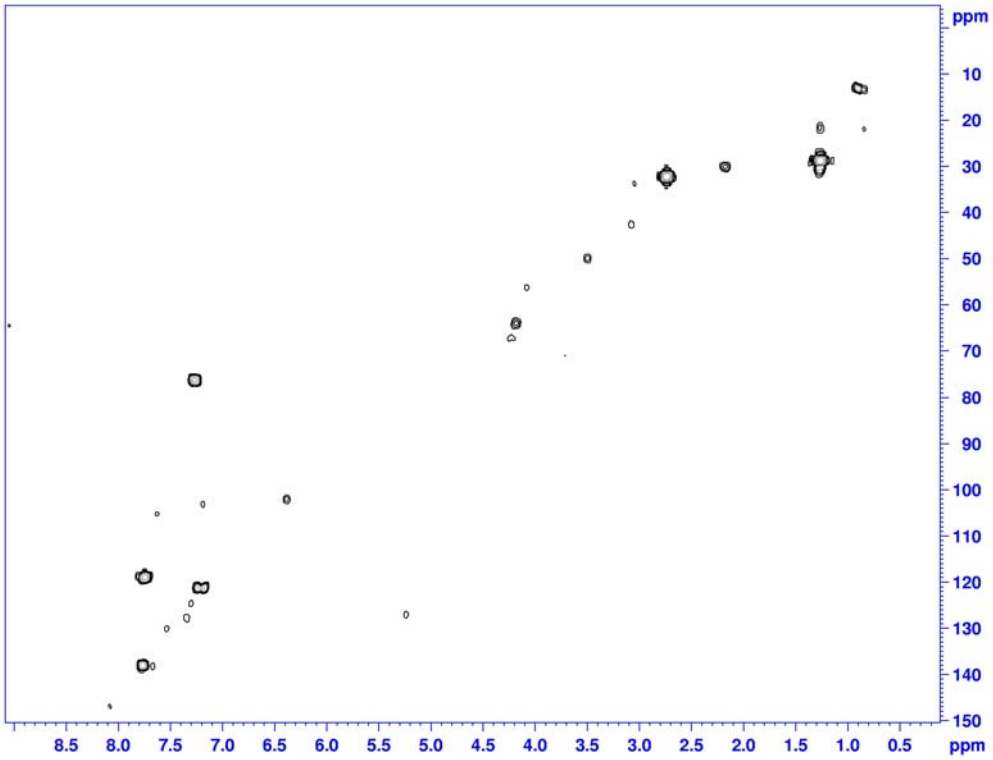


Figure 30 2D HMQC spectrum of **GMS6**

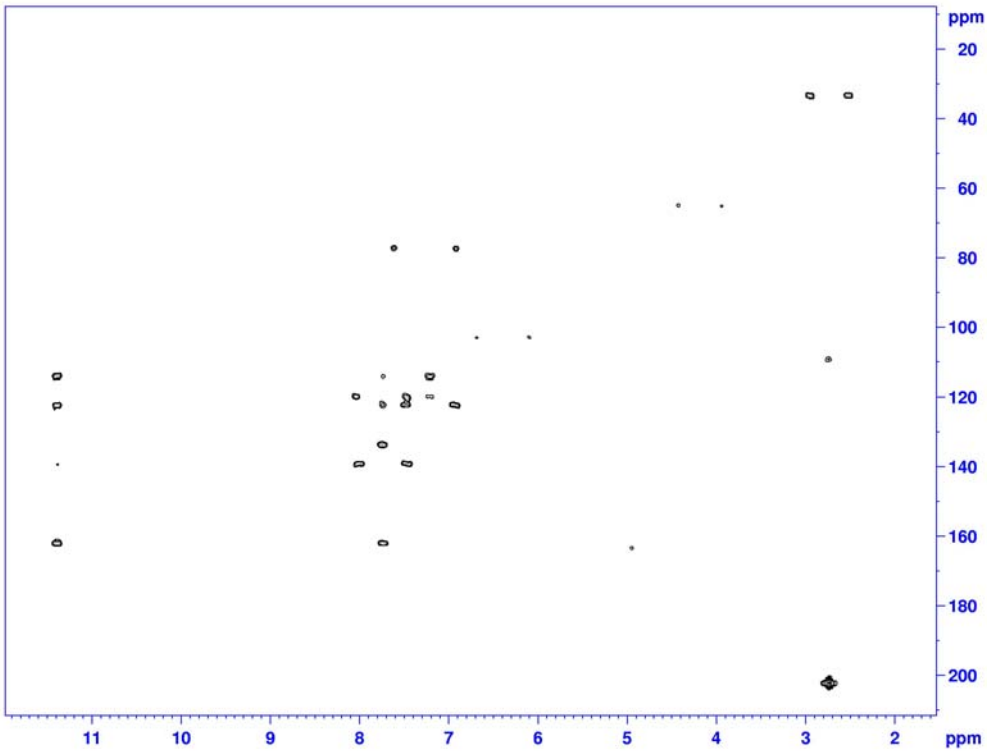


Figure 31 2D HMBC spectrum of **GMS6**

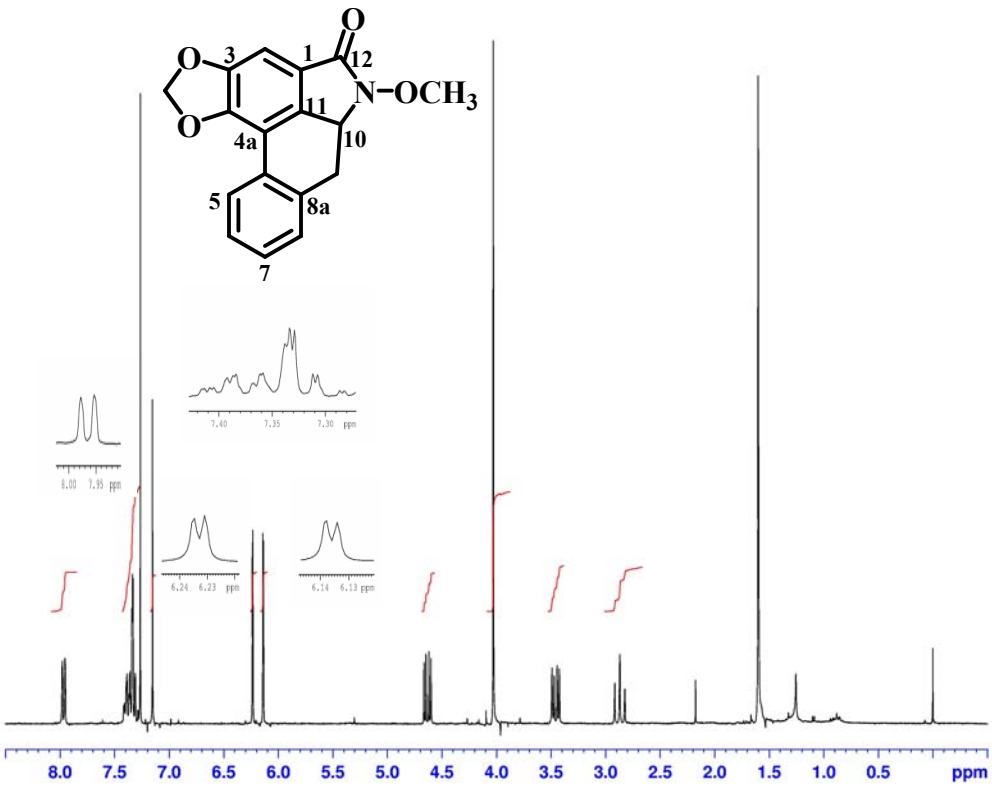


Figure 32 ^{1}H NMR (300 MHz) ($CDCl_3$) spectrum of **GMS7**

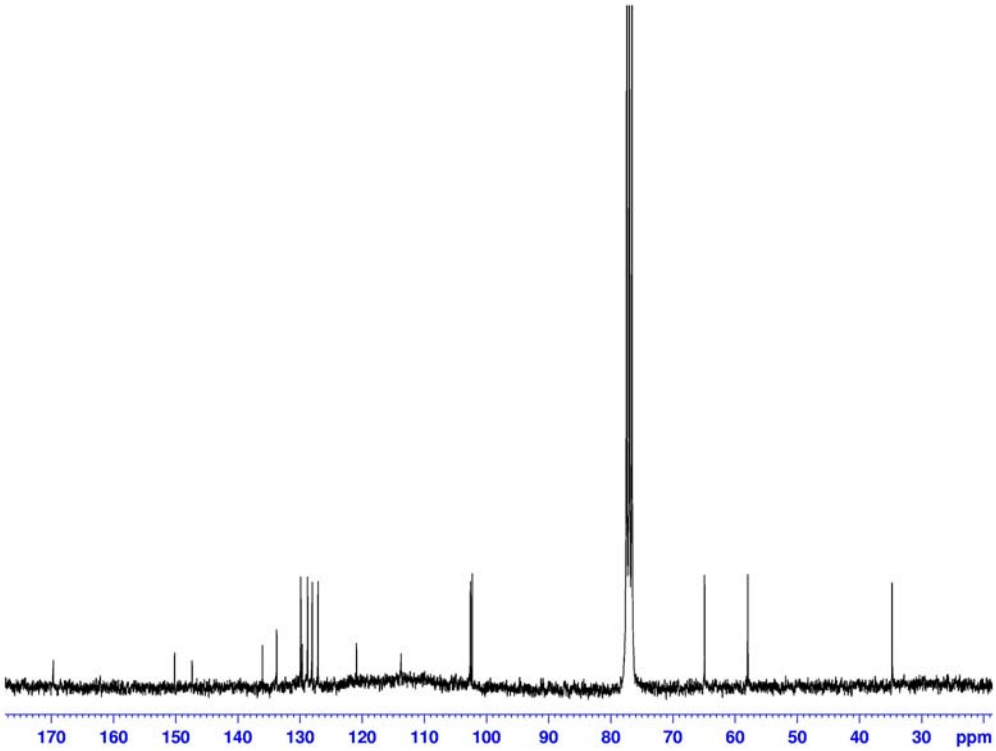


Figure 33 ^{13}C NMR (75 MHz) ($CDCl_3$) spectrum of **GMS7**

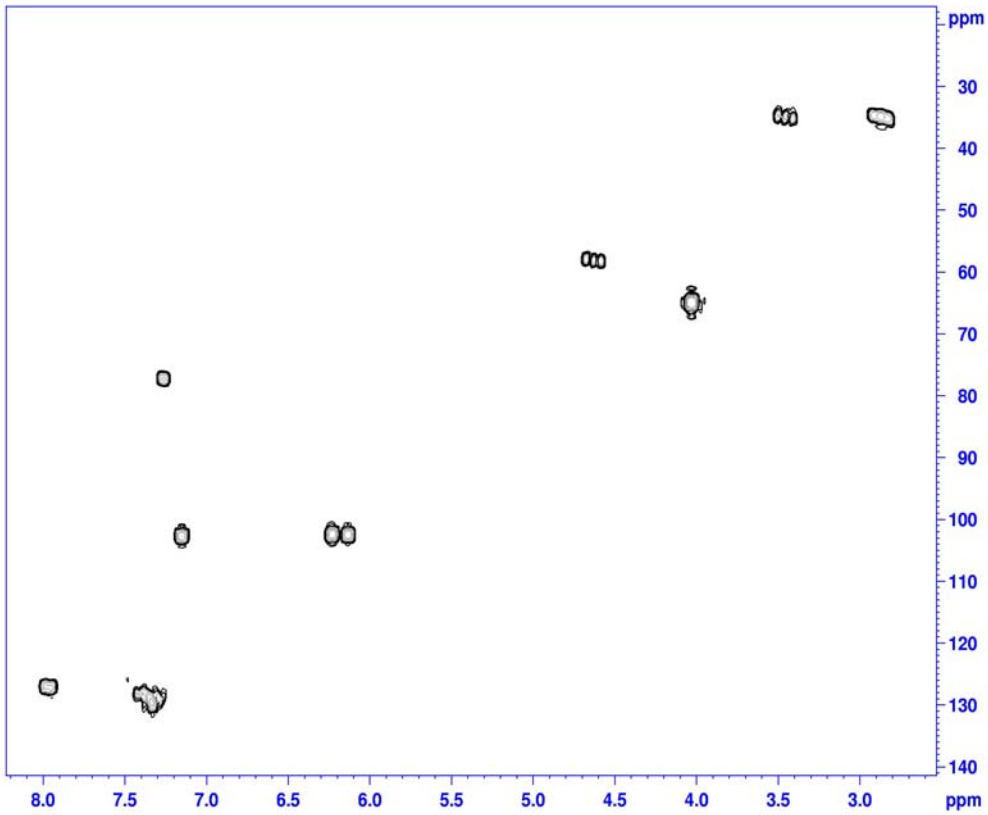


Figure 34 2D HMQC spectrum of **GMS7**

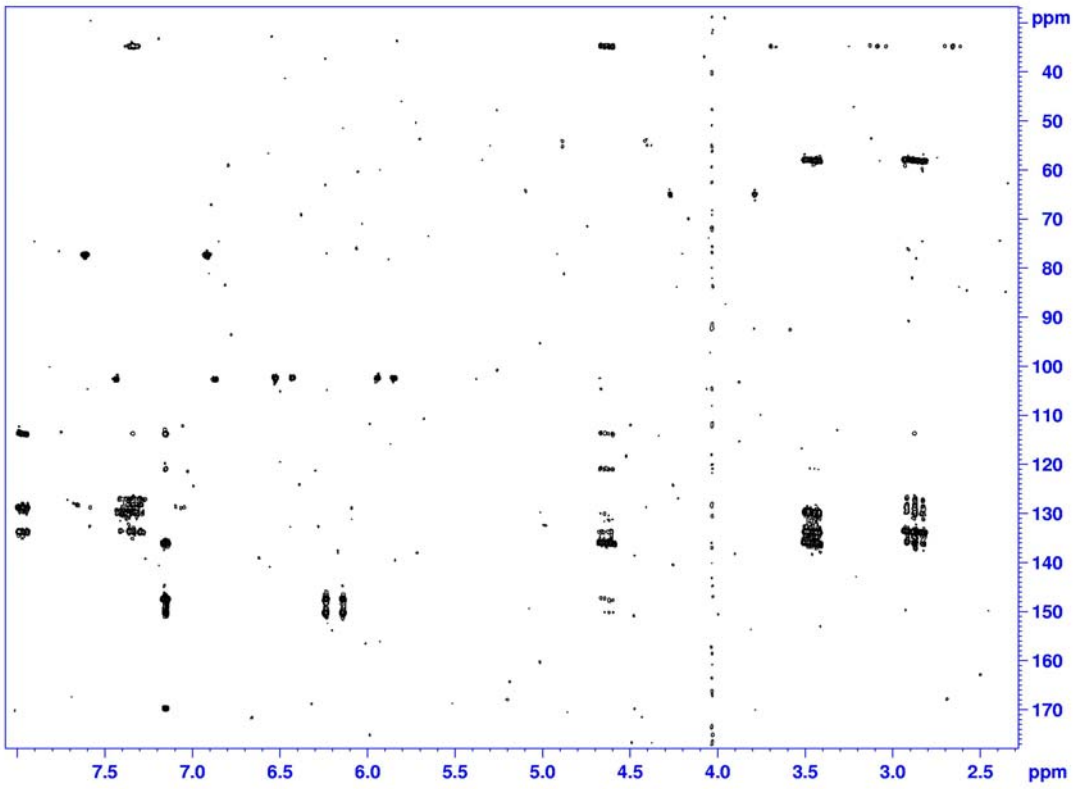


Figure 35 2D HMBC spectrum of **GMS7**

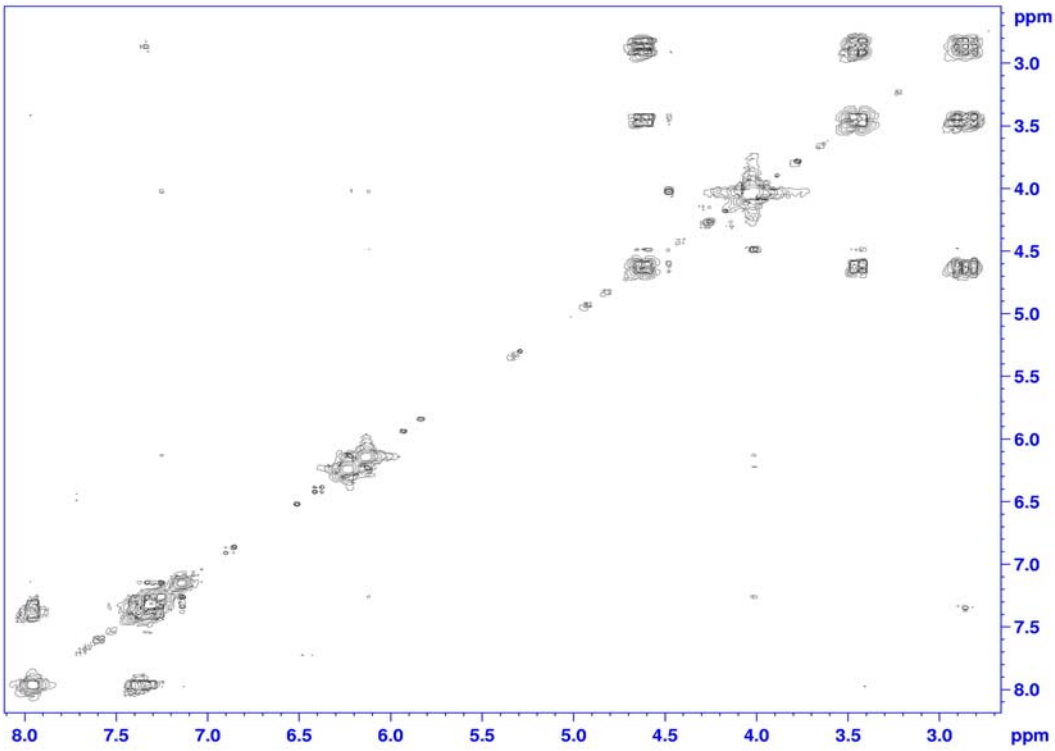


Figure 36 ^{1}H-^{1}H COSY spectrum of **GMS7**

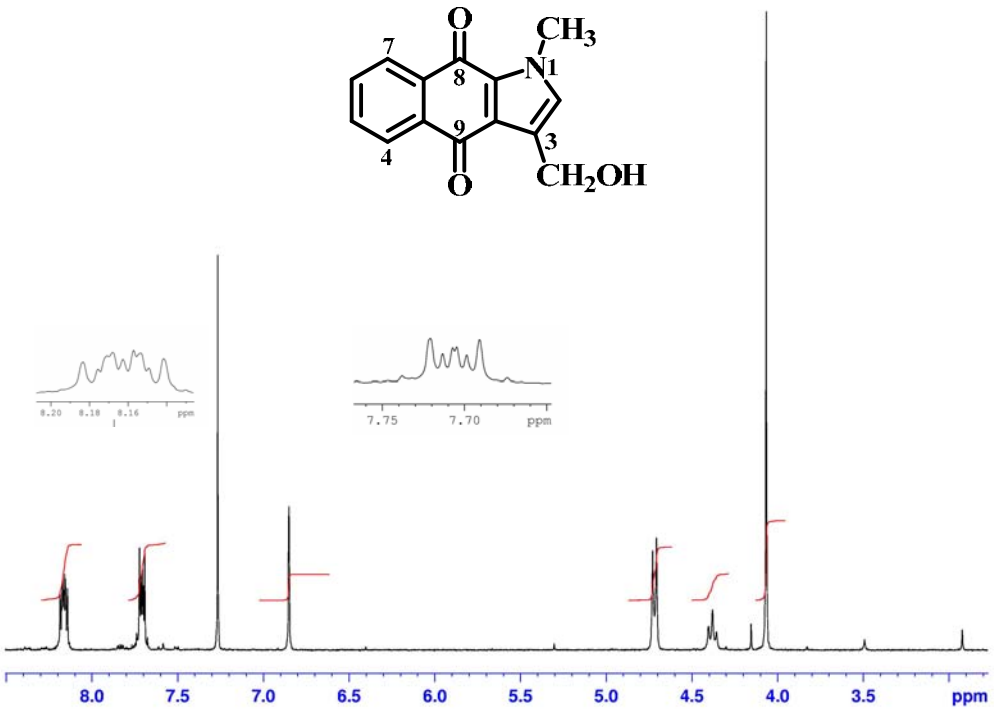


Figure 37 ^{1}H NMR (300 MHz) ($CDCl_3$) spectrum of **GMS8**

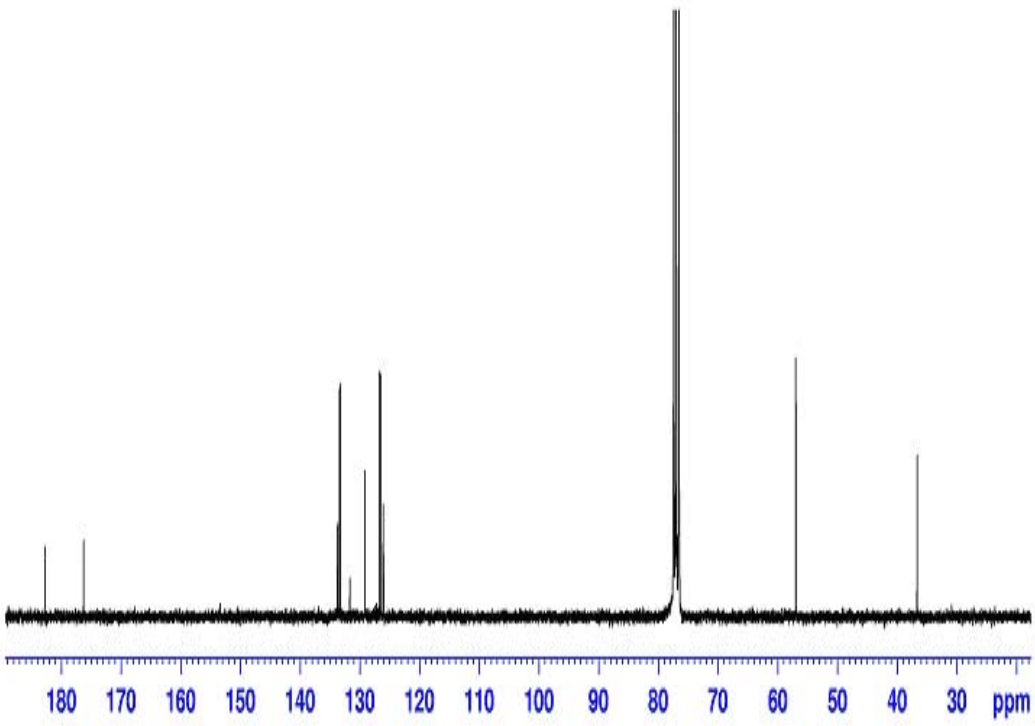


Figure 38 ^{13}C NMR (75 MHz) ($CDCl_3$) spectrum of **GMS8**

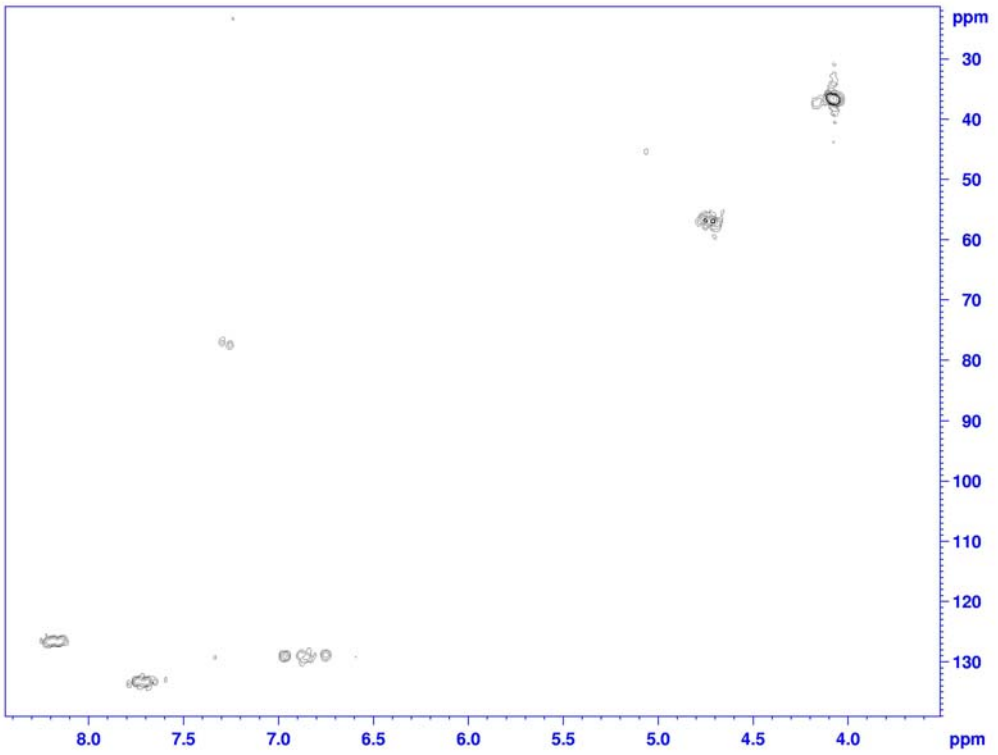


Figure 39 2D HMQC spectrum of **GMS8**

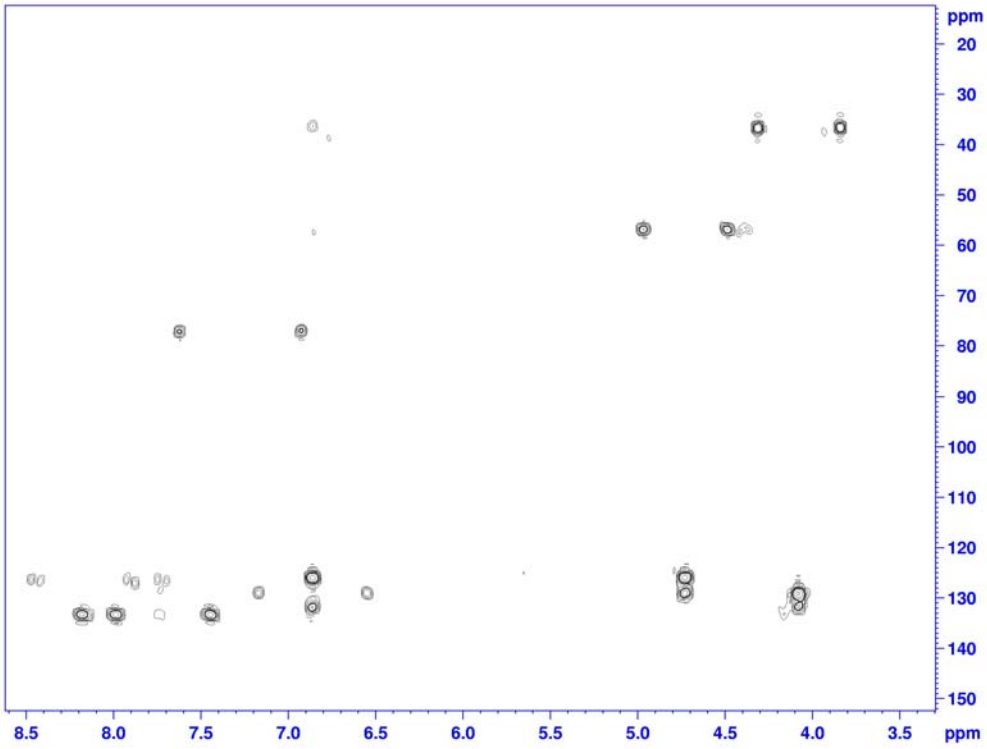


Figure 40 2D HMBC spectrum of **GMS8**

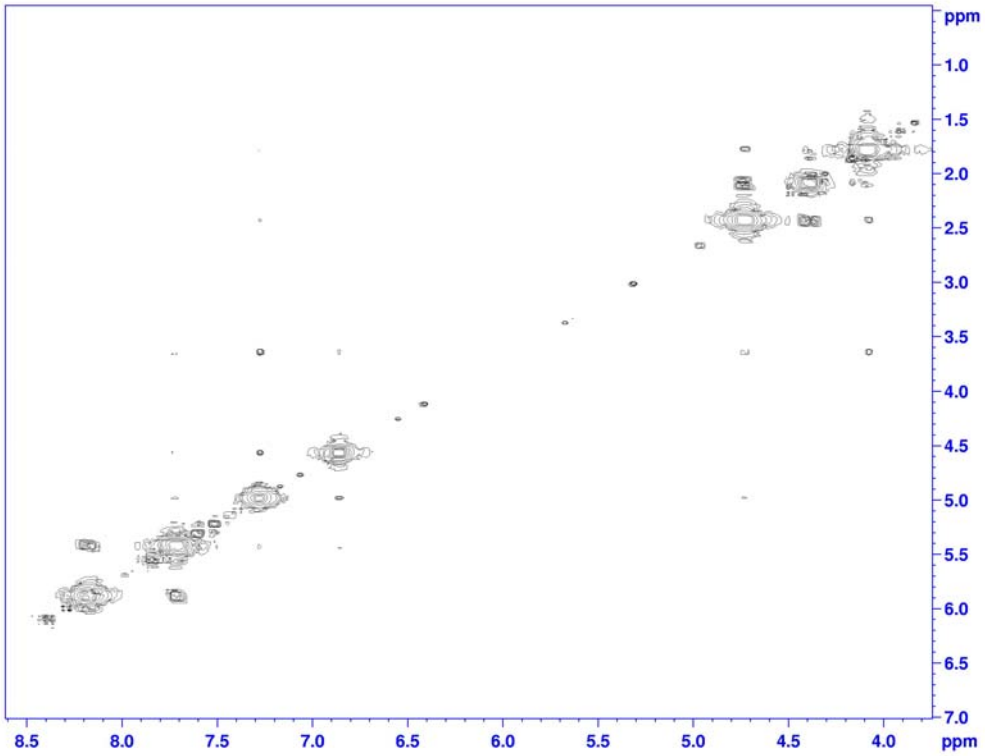


Figure 41 ^{1}H-^{1}H COSY spectrum of **GMS8**

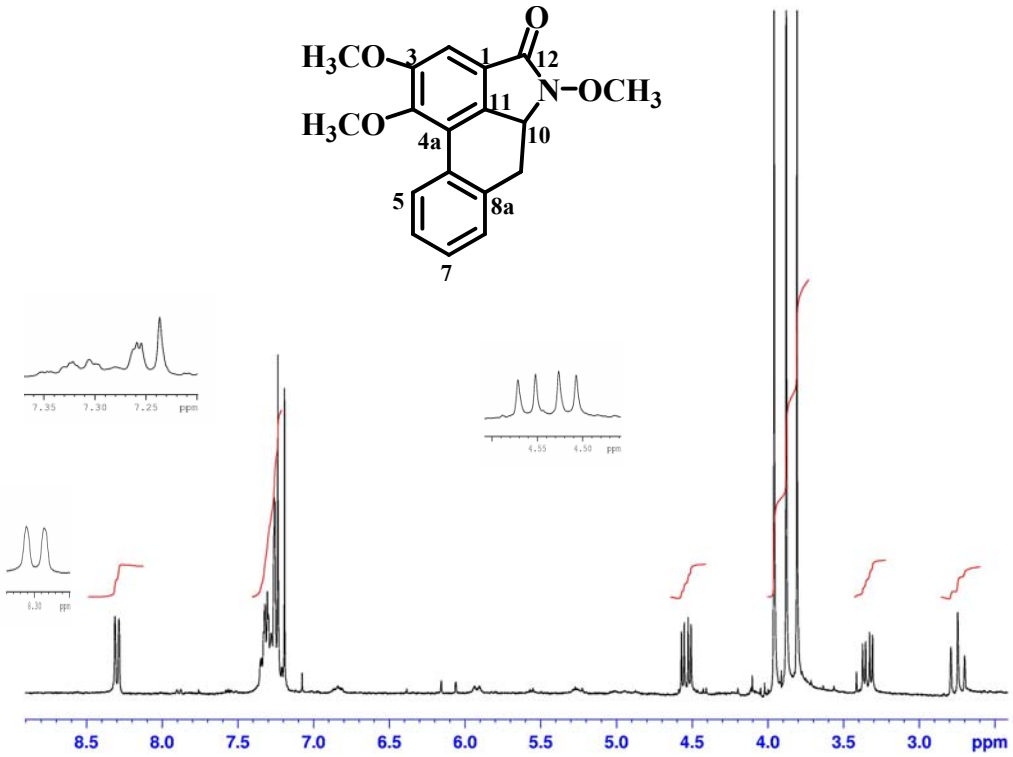


Figure 42 ^{1}H NMR (300 MHz) ($CDCl_3$) spectrum of **GMS9**

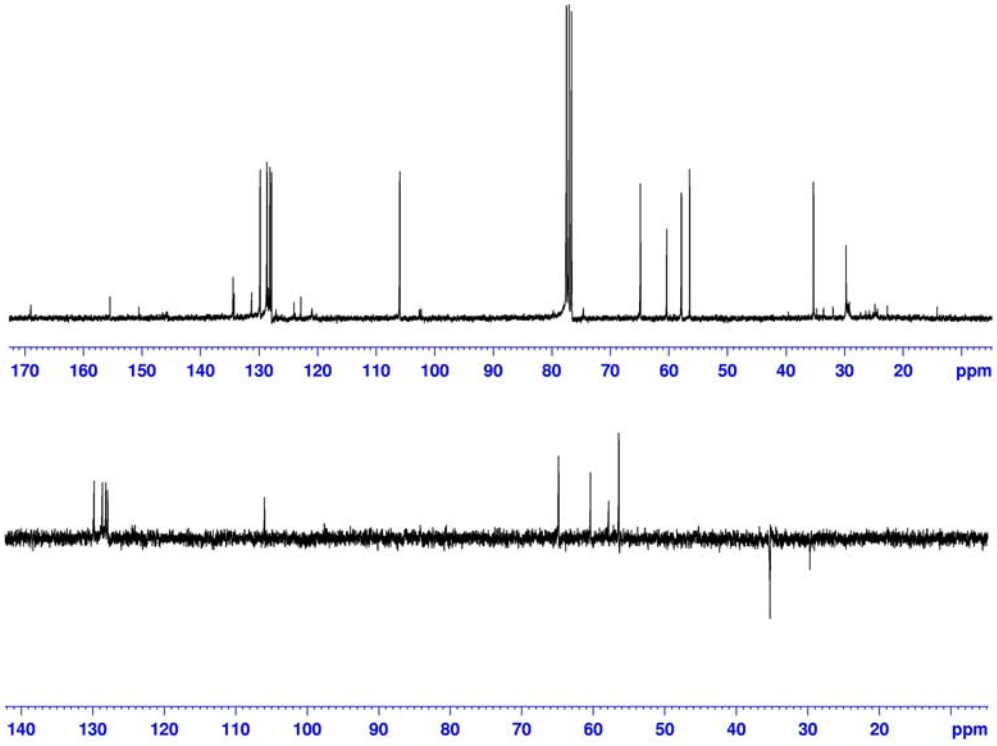


Figure 43 ^{13}C NMR and DEPT 135 (75 MHz) ($CDCl_3$) spectrum of **GMS9**

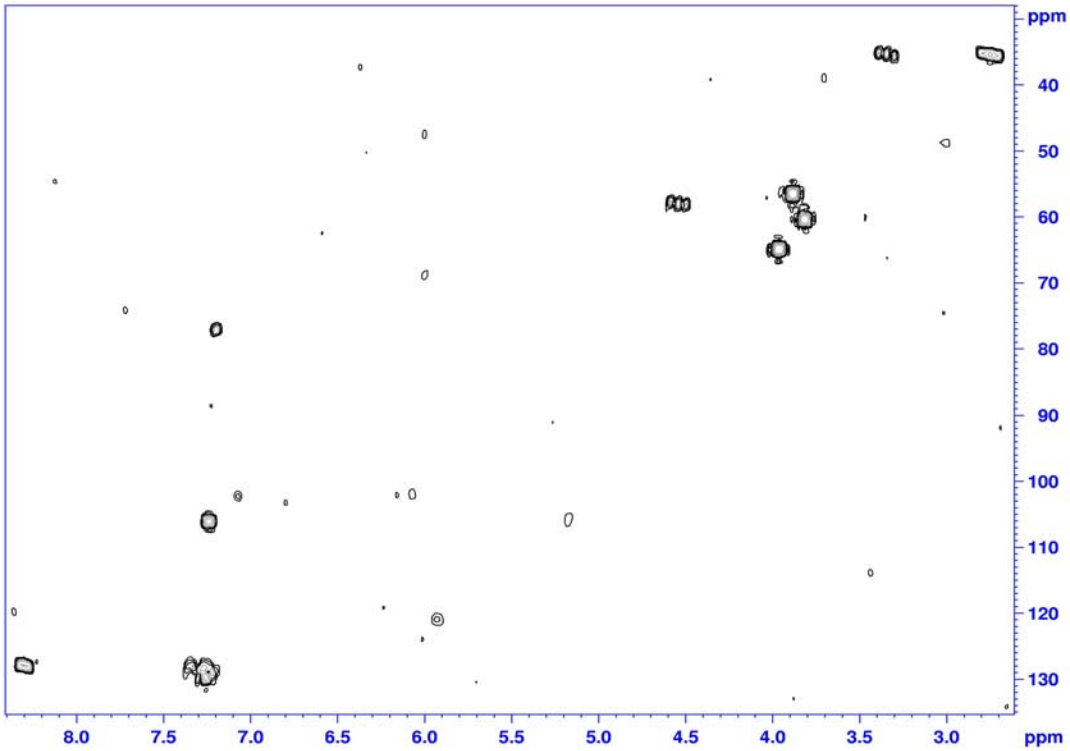


Figure 44 2D HMQC spectrum of **GMS9**

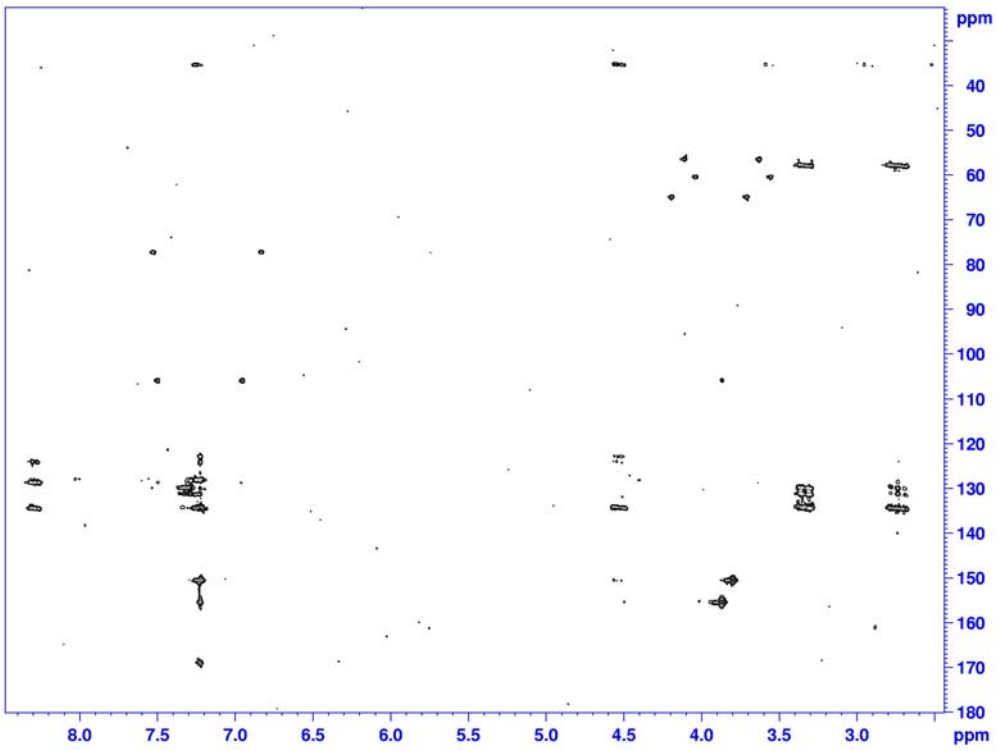


Figure 45 2D HMBC spectrum of **GMS9**

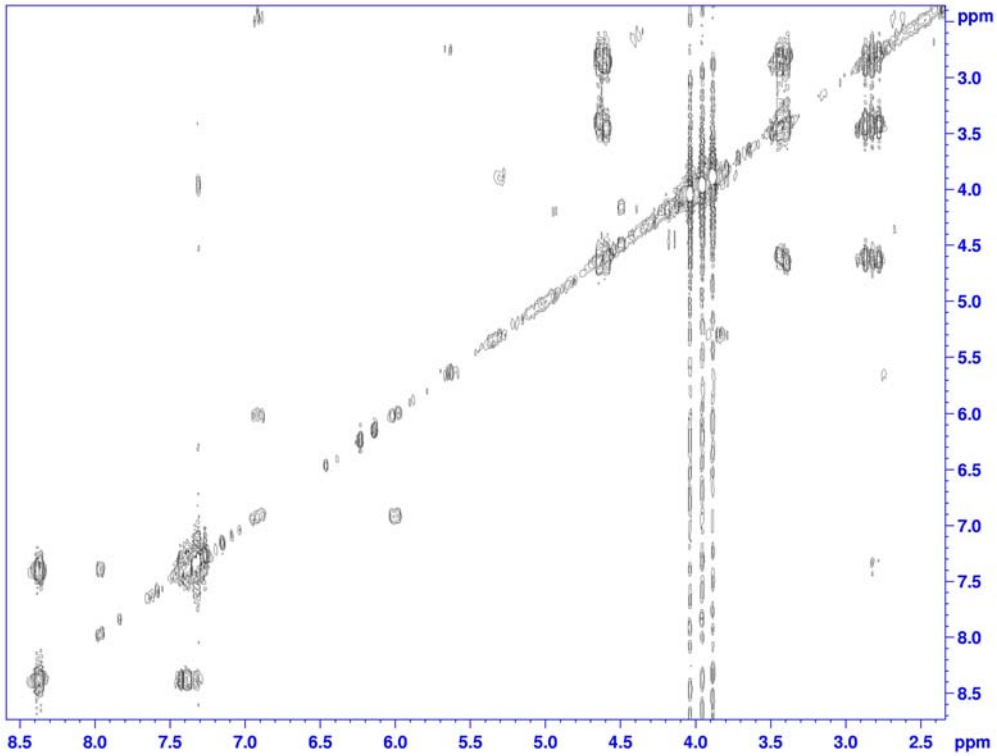


Figure 46 ^{1}H-^{1}H COSY spectrum of **GMS9**

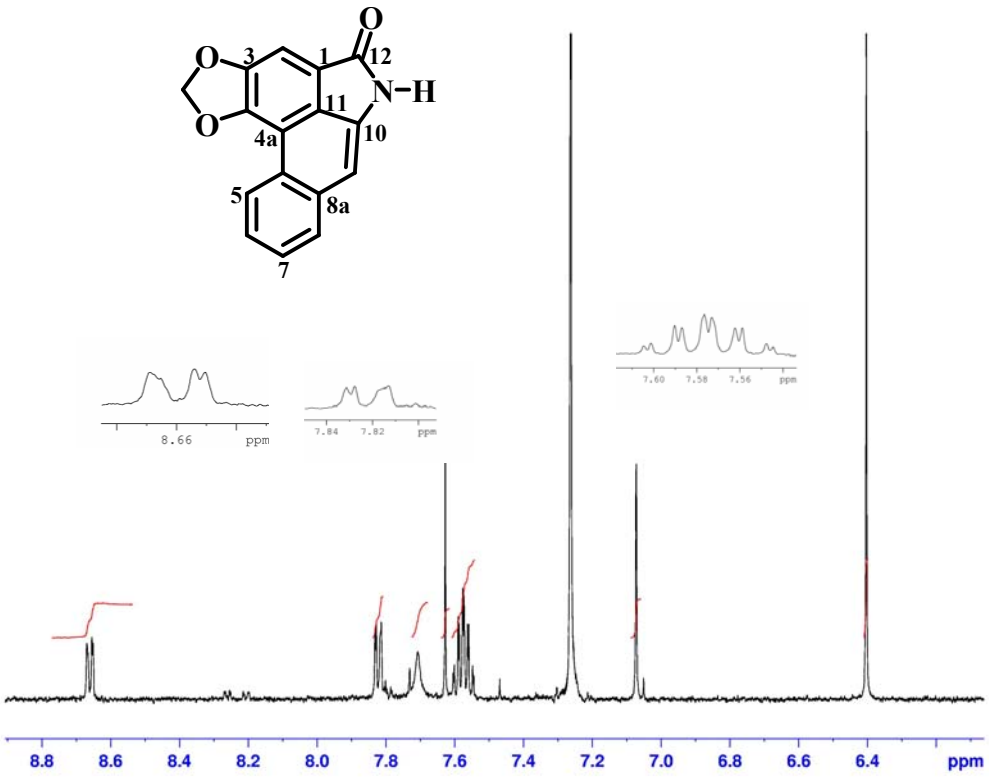


Figure 47 ^{1}H NMR (500 MHz) ($CDCl_3$) spectrum of **GMS10**

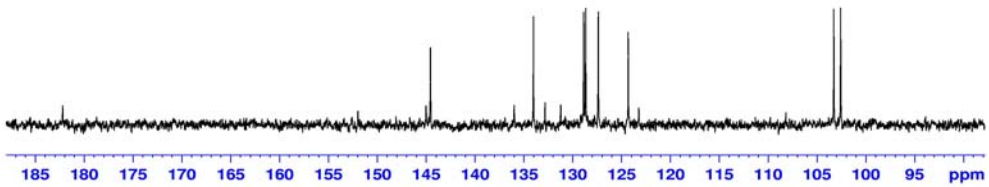


Figure 48 ^{13}C NMR (125 MHz) ($CDCl_3$) spectrum of **GMS10**

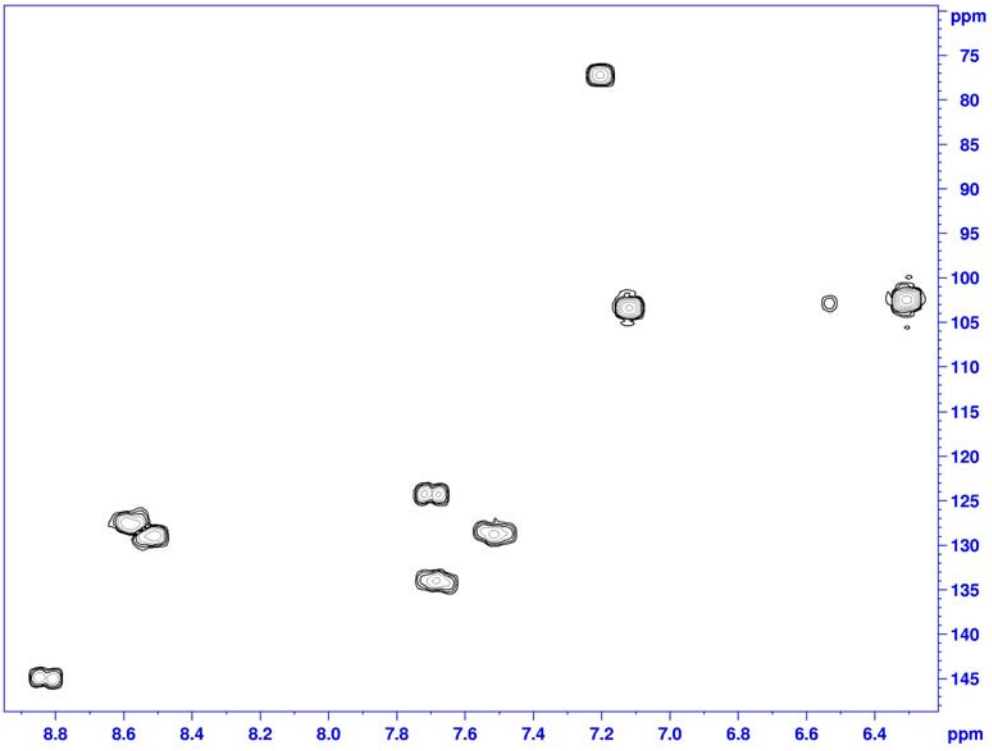


Figure 49 2D HMQC spectrum of **GMS10**

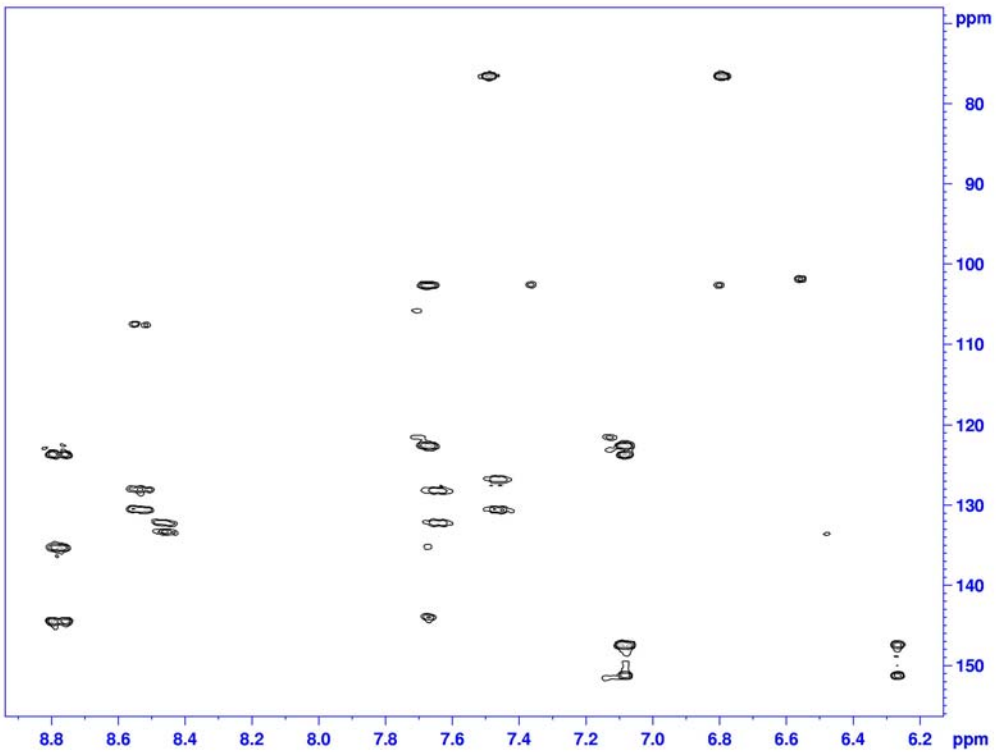


Figure 50 2D HMBC spectrum of **GMS10**

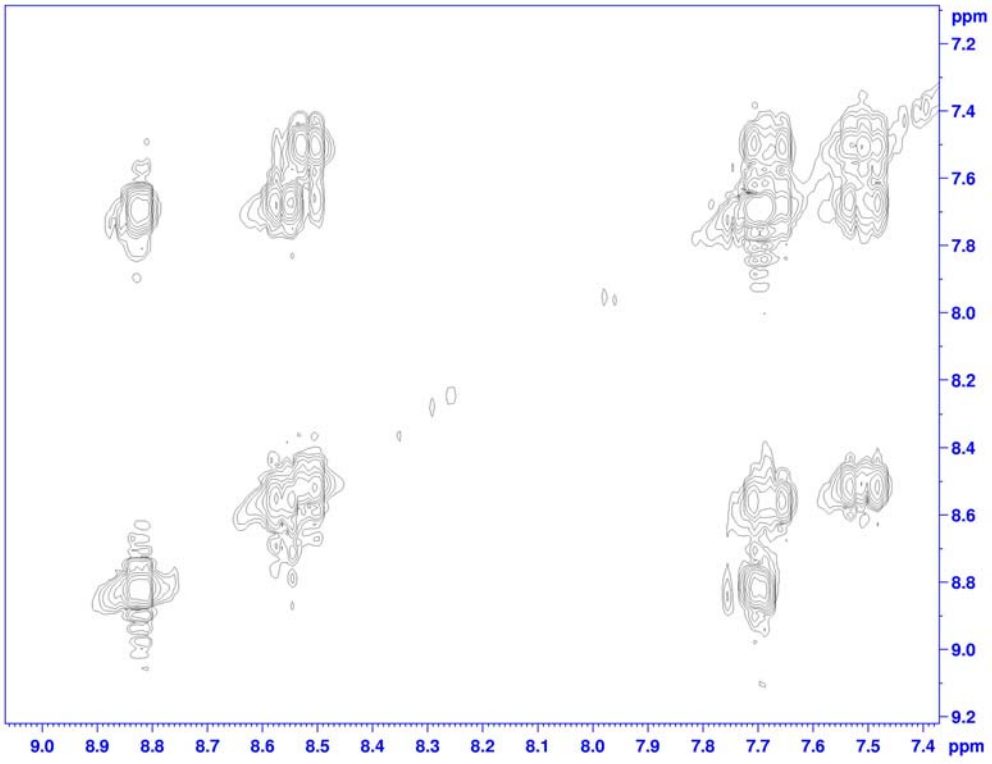


Figure 51 ^{1}H-^{1}H COSY spectrum of **GM10**

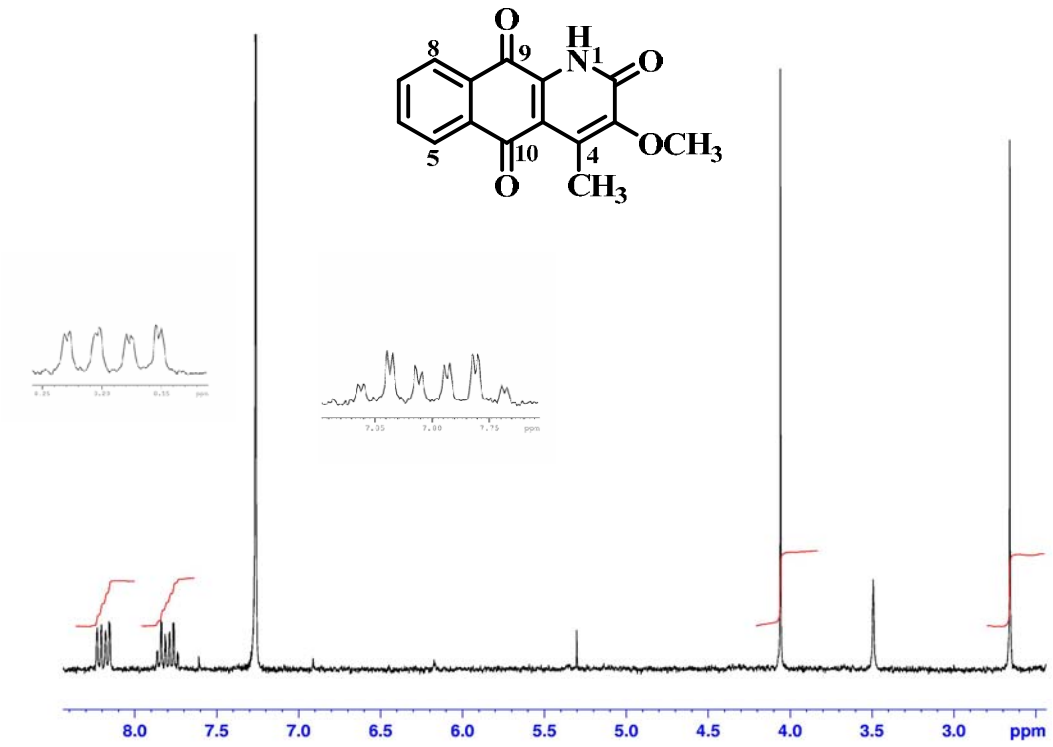


Figure 52 ^{1}H NMR (300 MHz) ($CDCl_3$) spectrum of **GMS11**

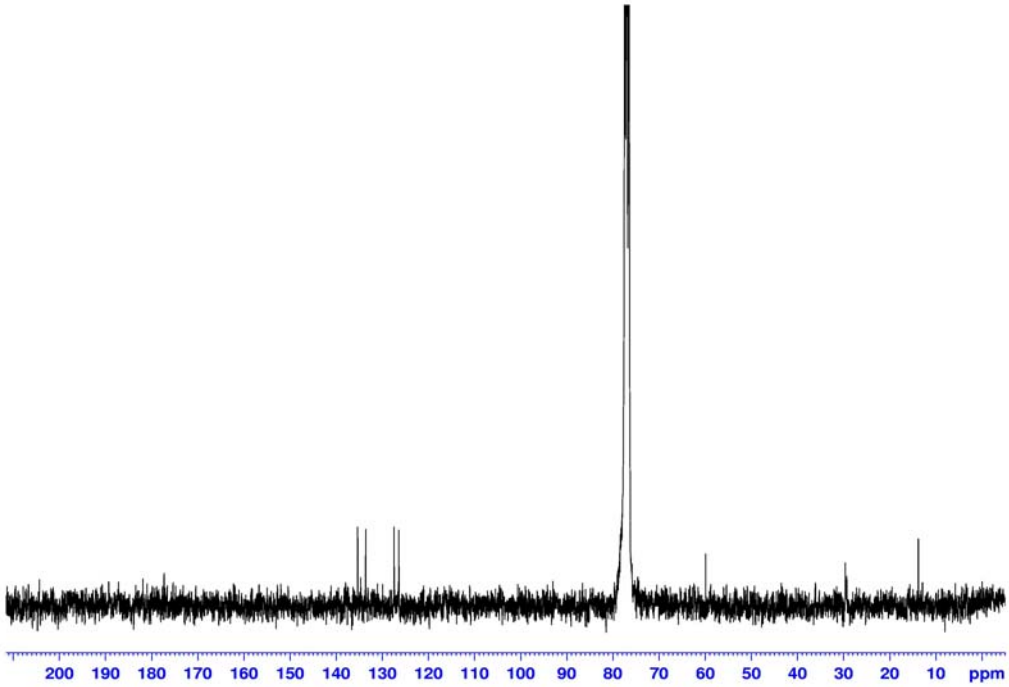


Figure 53 ^{13}C NMR (75 MHz) ($CDCl_3$) spectrum of **GMS11**

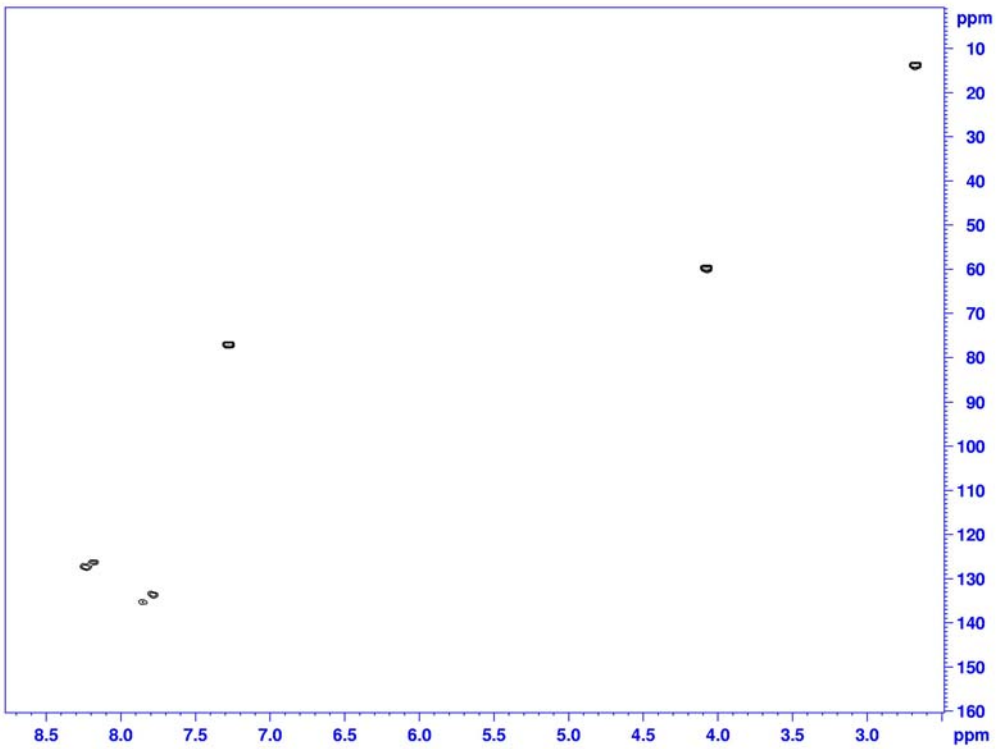


Figure 54 2D HMQC spectrum of **GMS11**

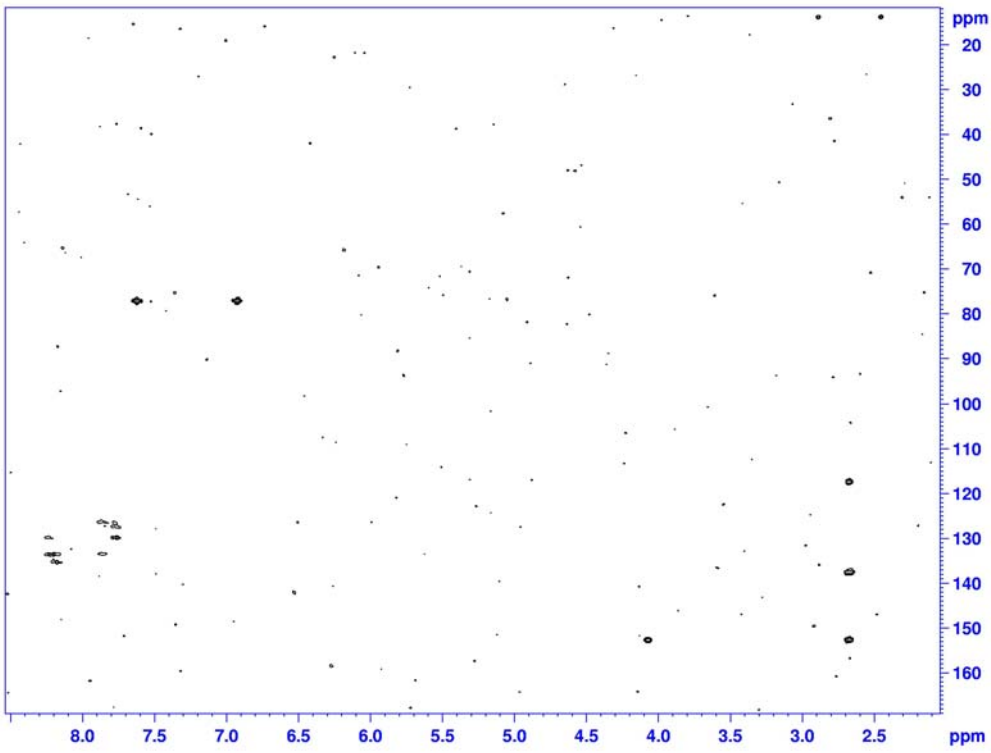


Figure 55 2D HMBC spectrum of **GMS11**

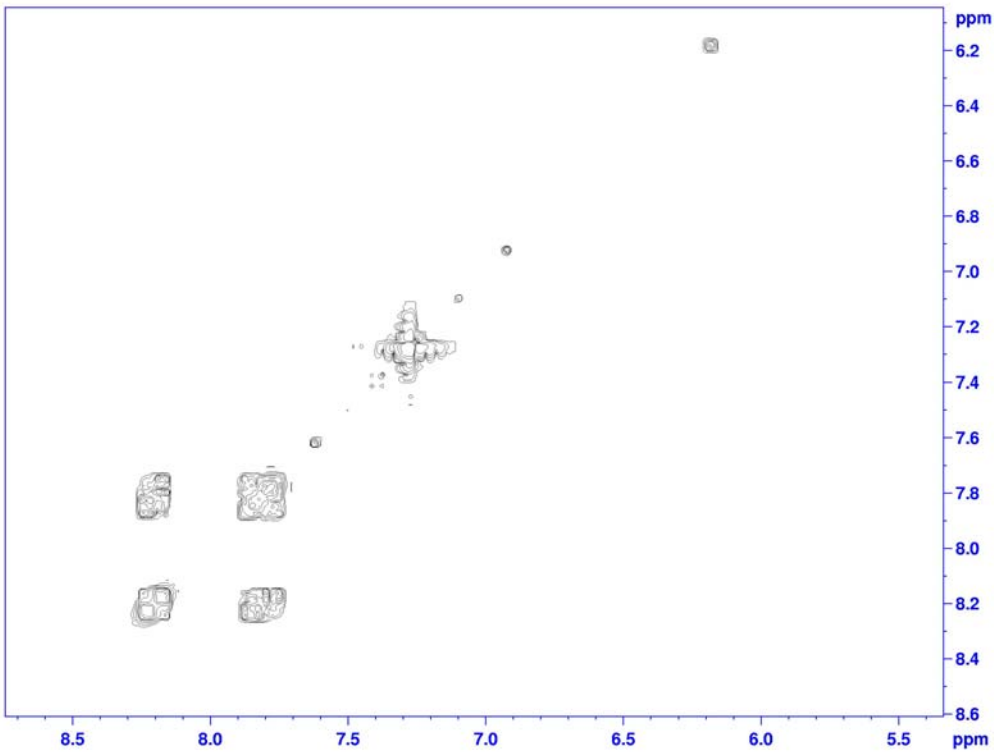


Figure 56 ^{1}H-^{1}H COSY spectrum of **GMS11**

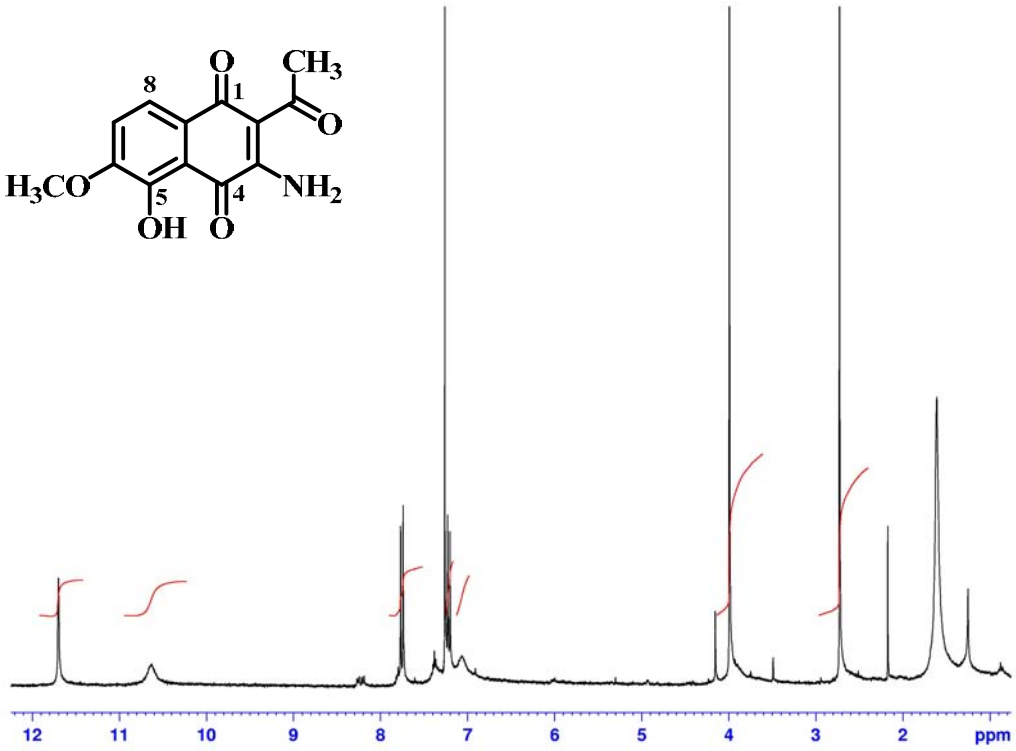


Figure 57 ^{1}H NMR (500 MHz) ($CDCl_3$) spectrum of **GMS12**

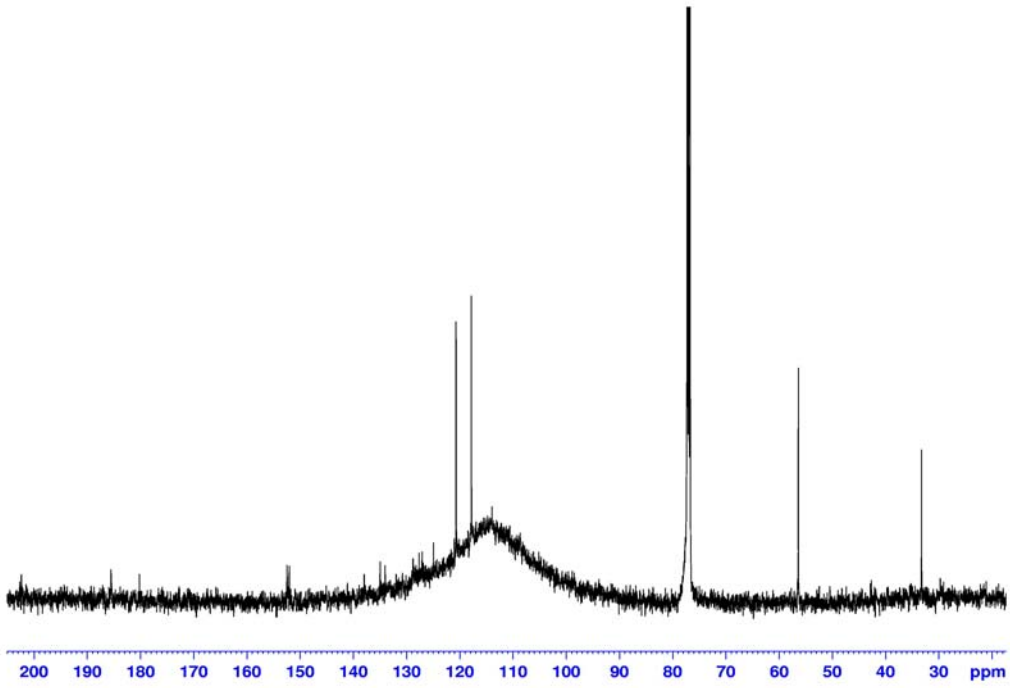


Figure 58 ^{13}C NMR (125 MHz) ($CDCl_3$) spectrum of **GMS12**

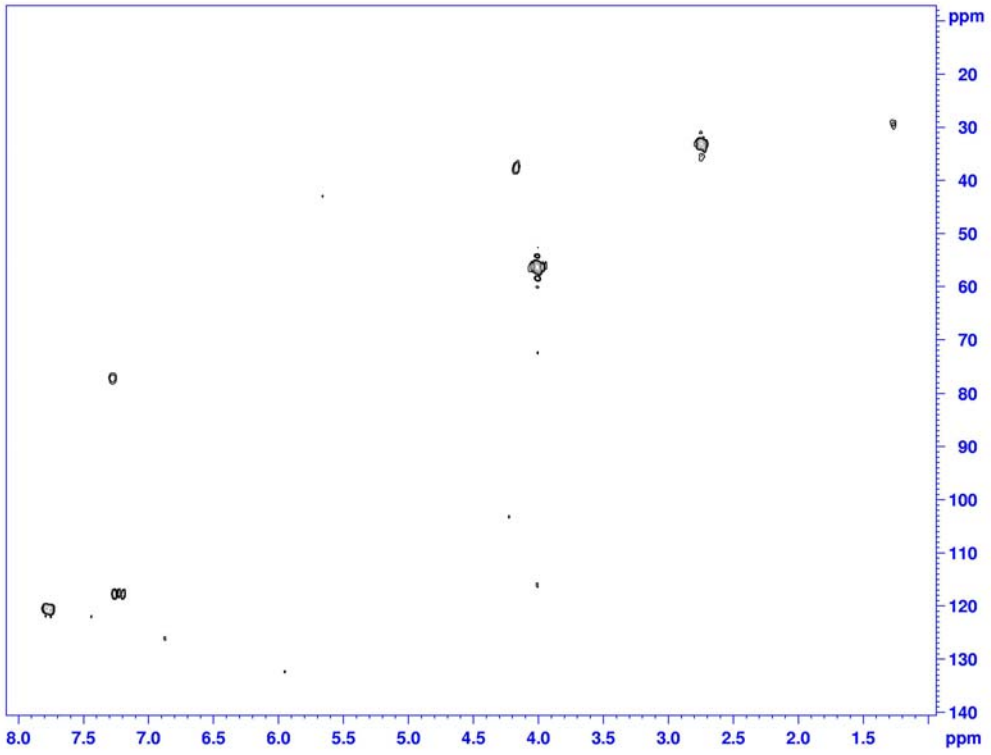


Figure 59 2D HMQC spectrum of **GMS12**

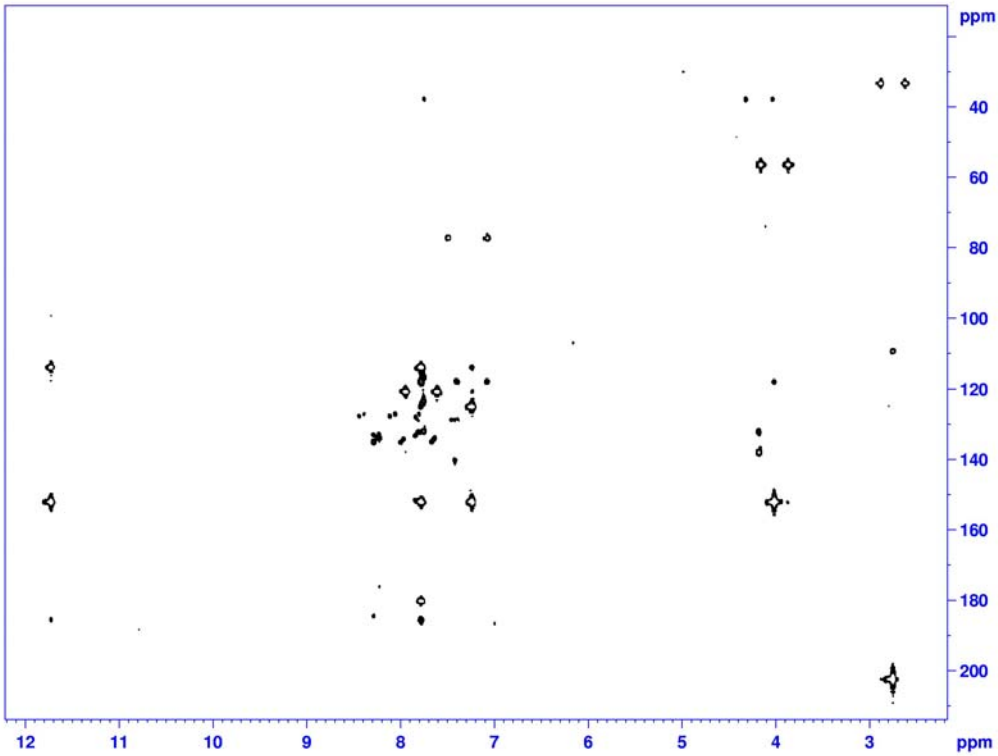


Figure 60 2D HMBC spectrum of **GMS12**

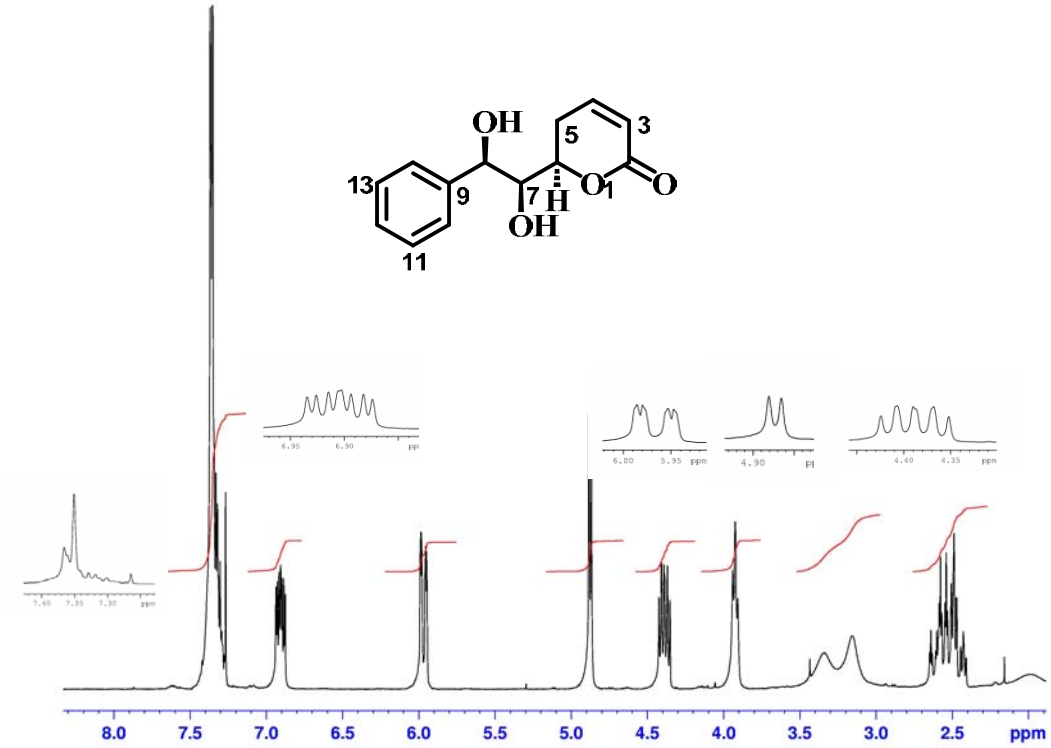


Figure 61 H NMR (300 MHz) ($CDCl_3$) spectrum of **GMS13**

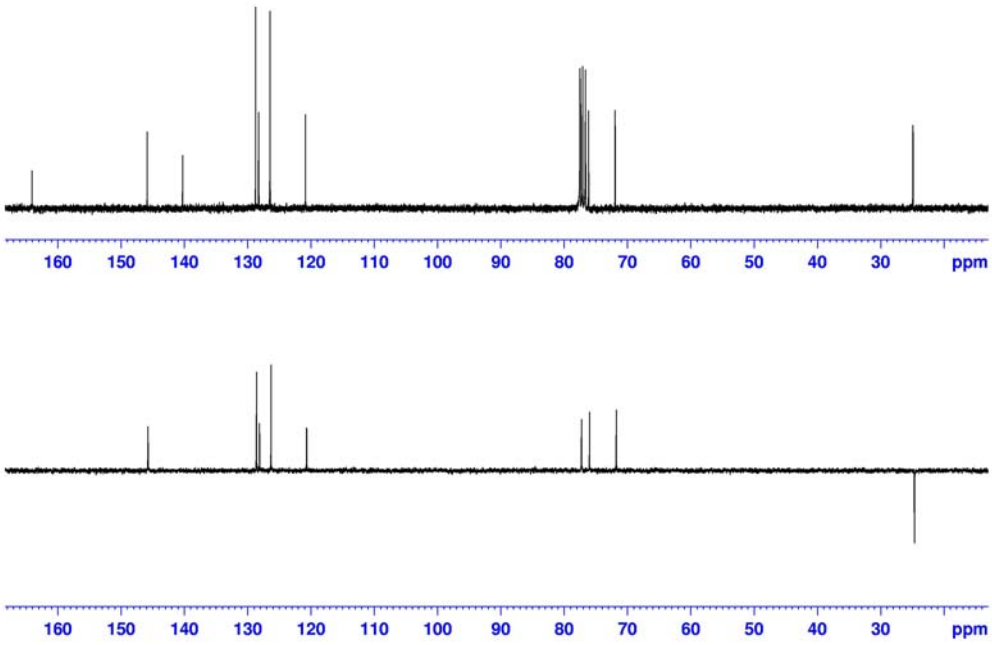


Figure 62 ^{13}C NMR and DEPT 135 (75 MHz) ($CDCl_3$) spectrum of **GMS13**

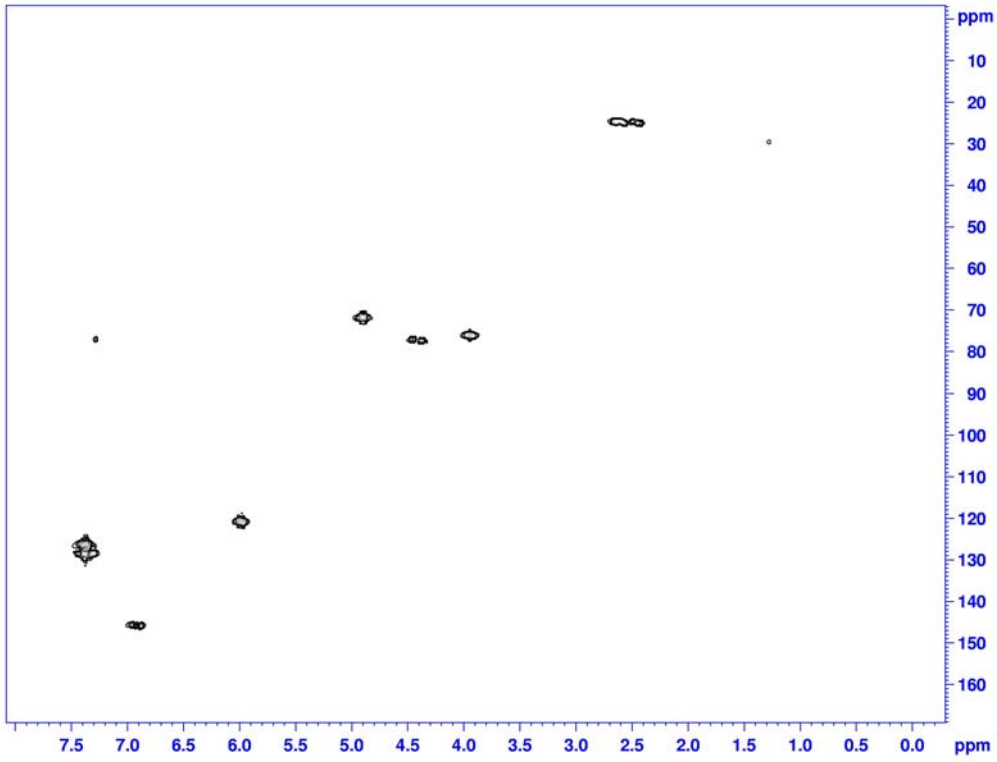


Figure 63 2D HMQC spectrum of **GMS13**

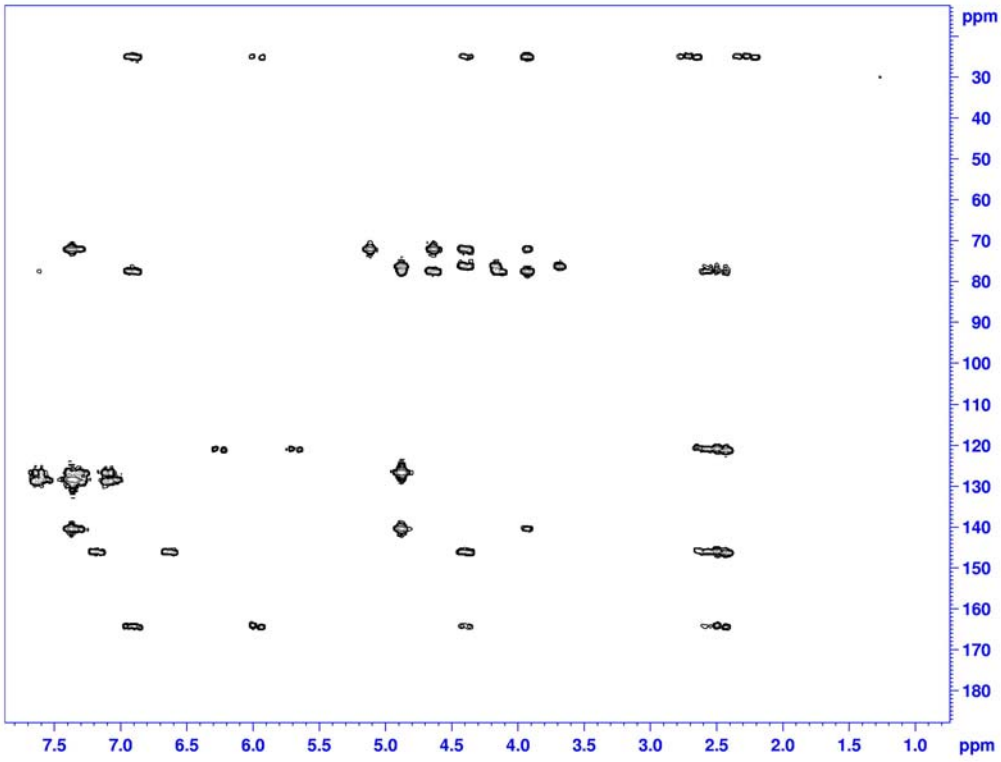


Figure 64 2D HMBC spectrum of **GMS13**

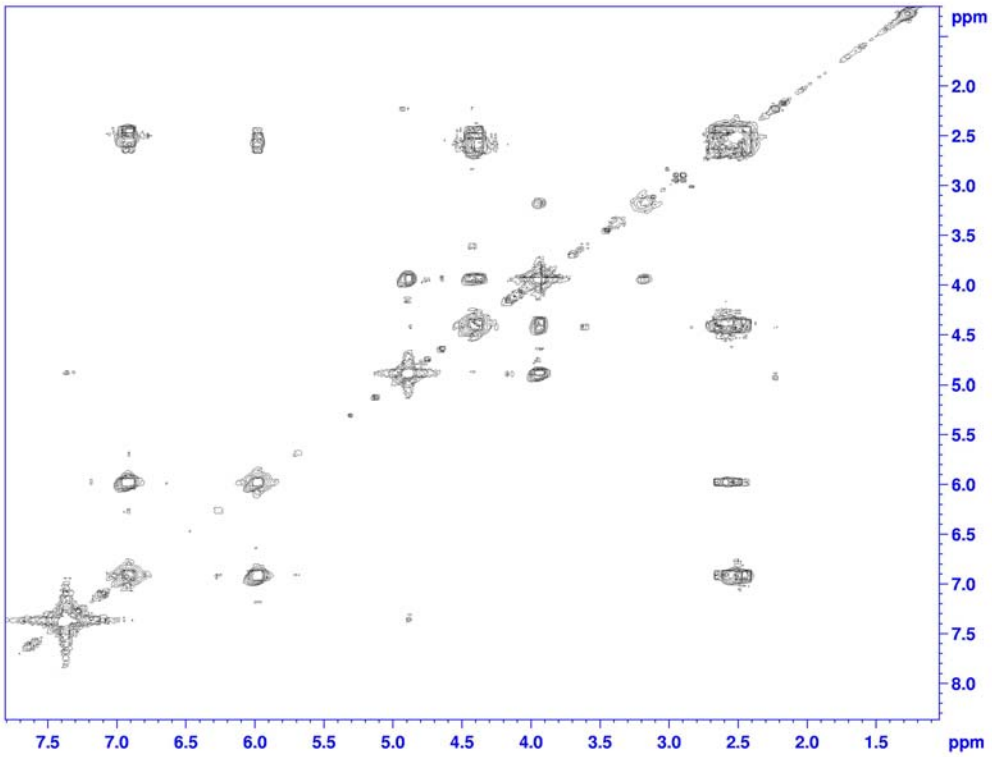


Figure 65 2D ^{1}H-^{1}H COSY spectrum of **GMS13**

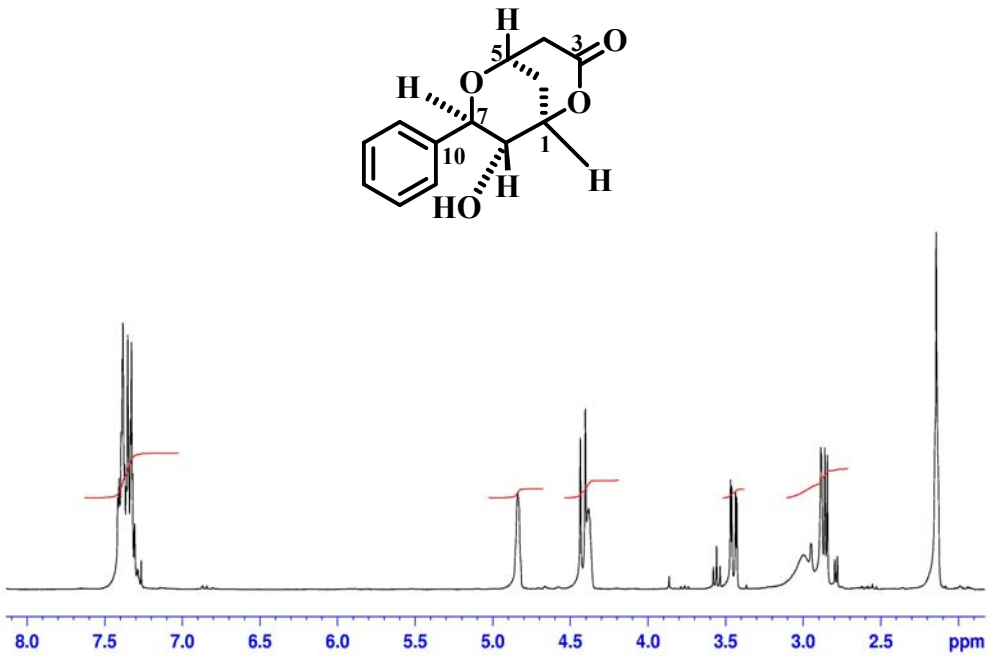


Figure 66 ^{1}H NMR (300 MHz) ($CDCl_3$) spectrum of **GMS14**

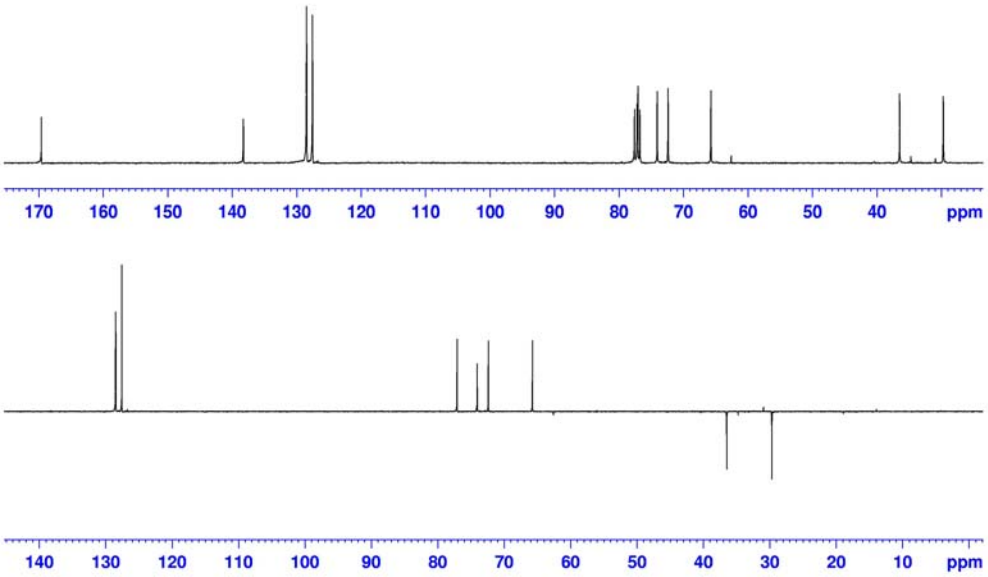


Figure 67 ^{13}C NMR and DEPT 135 (75 MHz) ($CDCl_3$) spectrum of **GMS14**

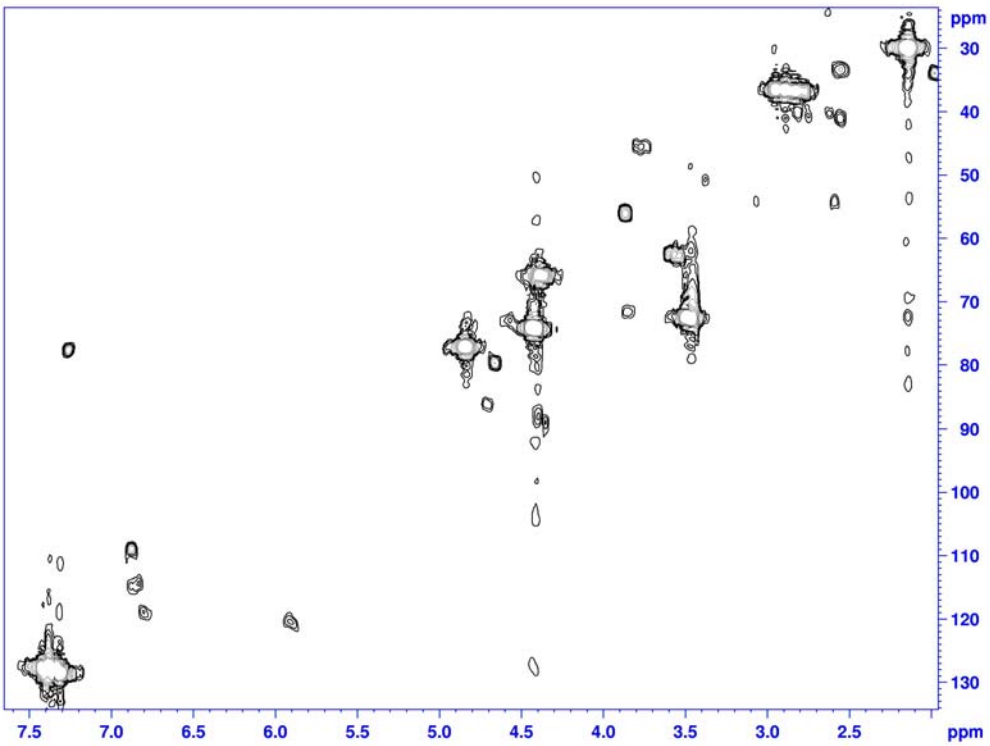


Figure 68 2D HMQC spectrum of **GMS14**

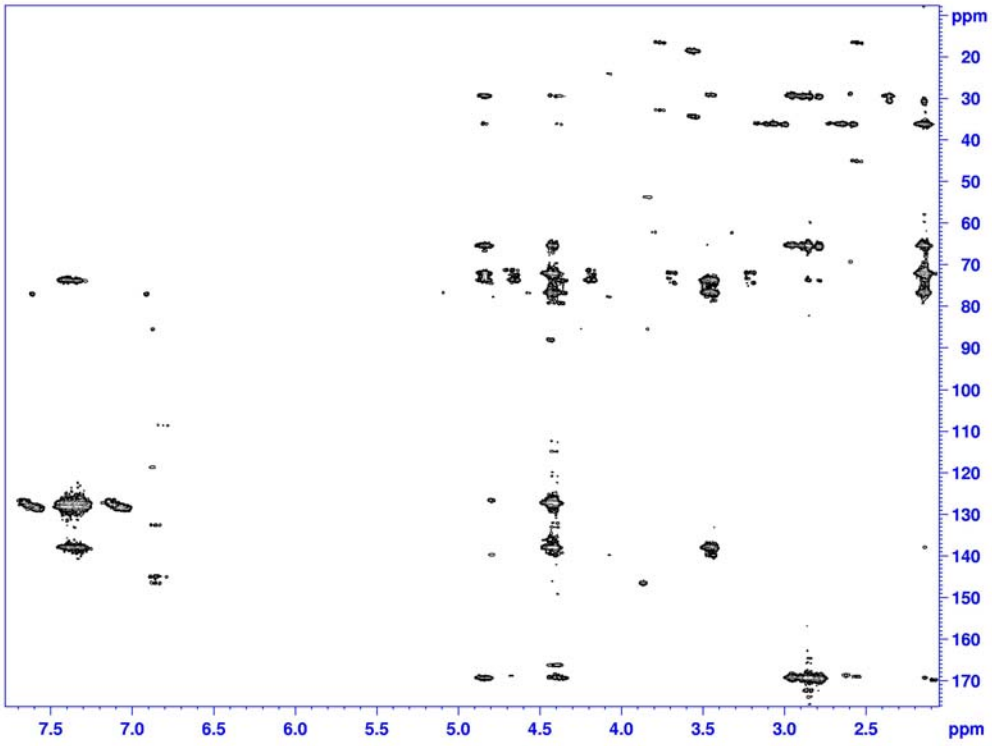


Figure 69 2D HMBC spectrum of **GMS14**

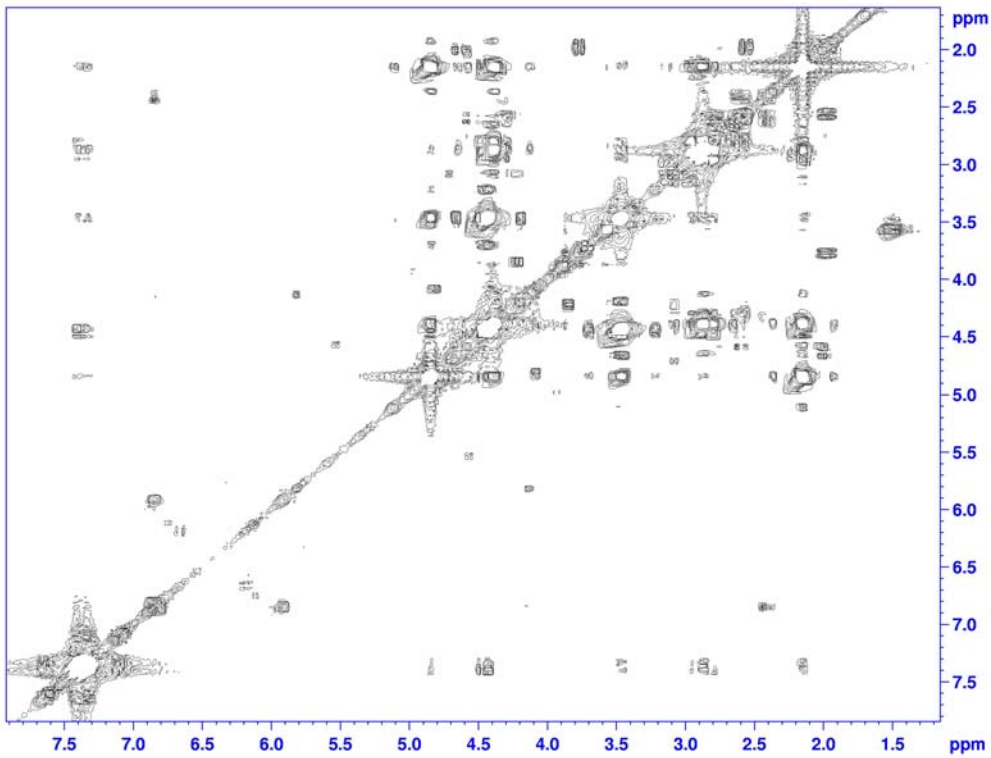


Figure 70 ^{1}H-^{1}H COSY spectrum of **GMS14**

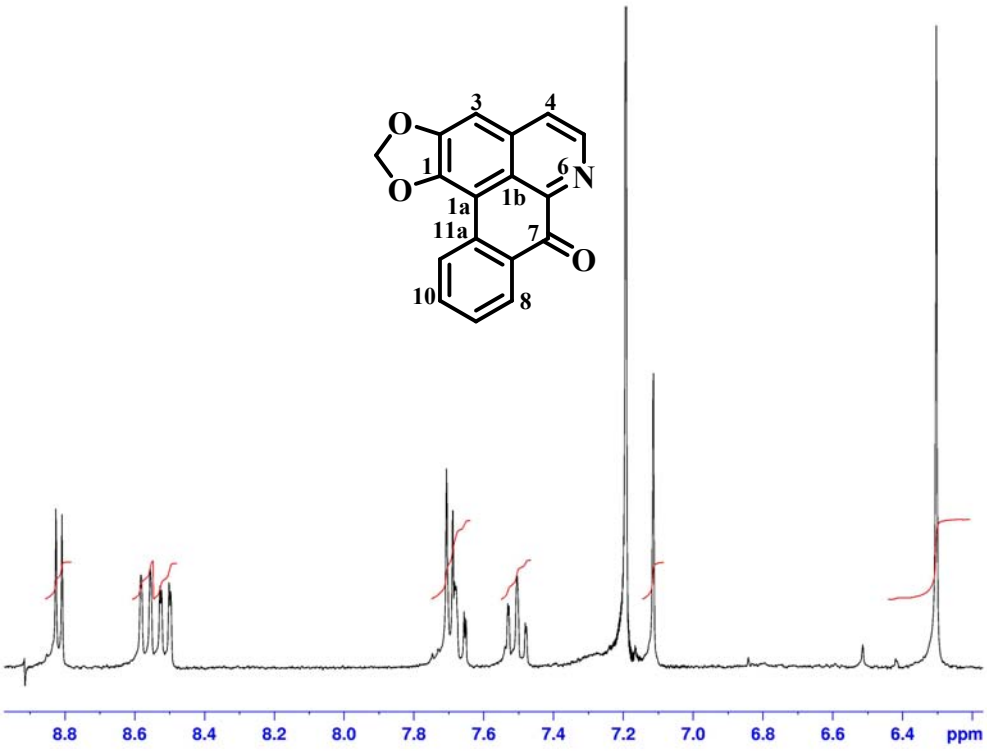


Figure 71 ^{1}H NMR (300 MHz) ($CDCl_3$) spectrum of **GMS15**

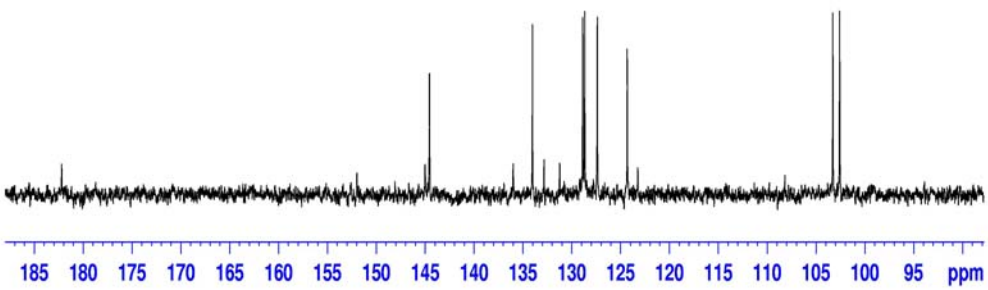


Figure 72 ^{13}C NMR (75 MHz) ($CDCl_3$) spectrum of **GMS15**

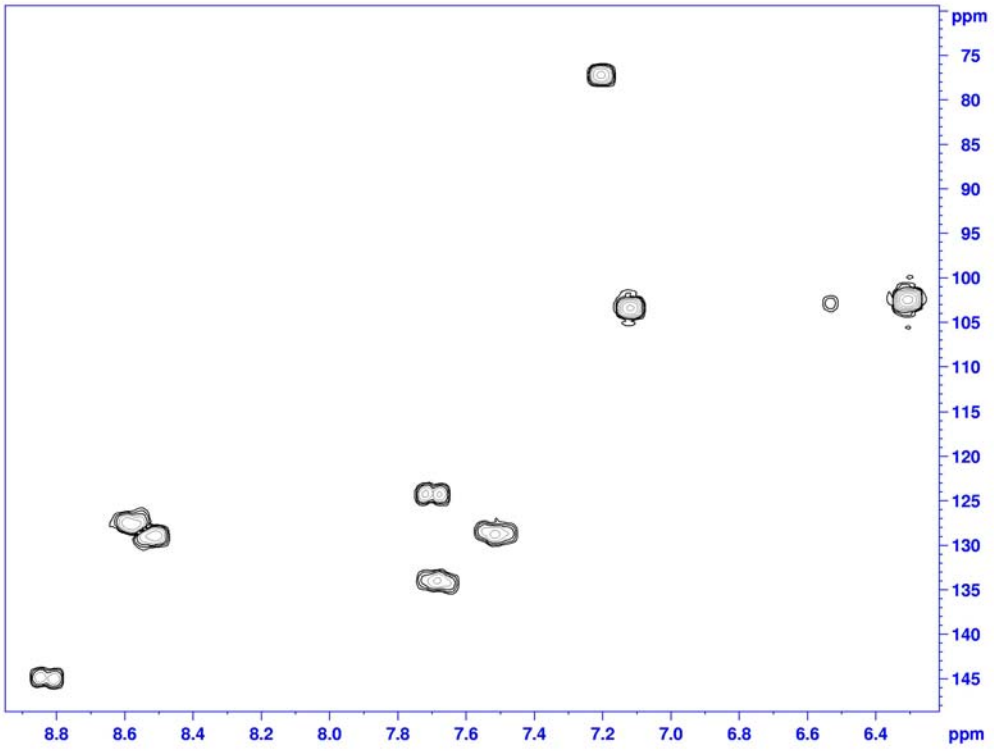


Figure 73 **2**D HMQC spectrum of **GMS15**

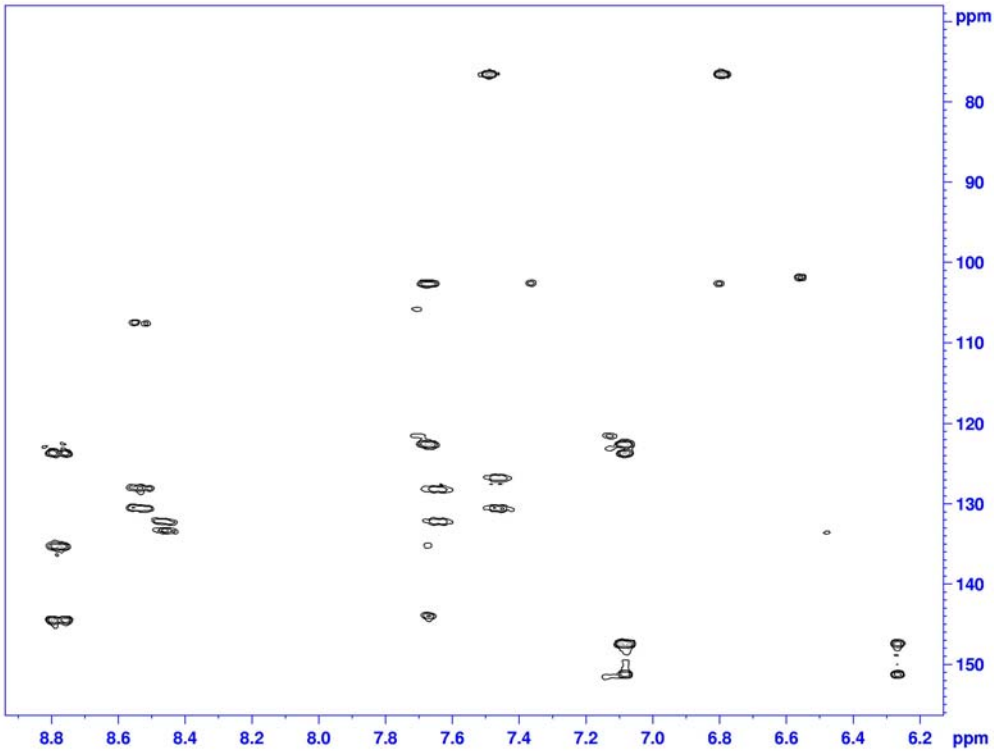


Figure 74 2D HMBC spectrum of **GMS15**

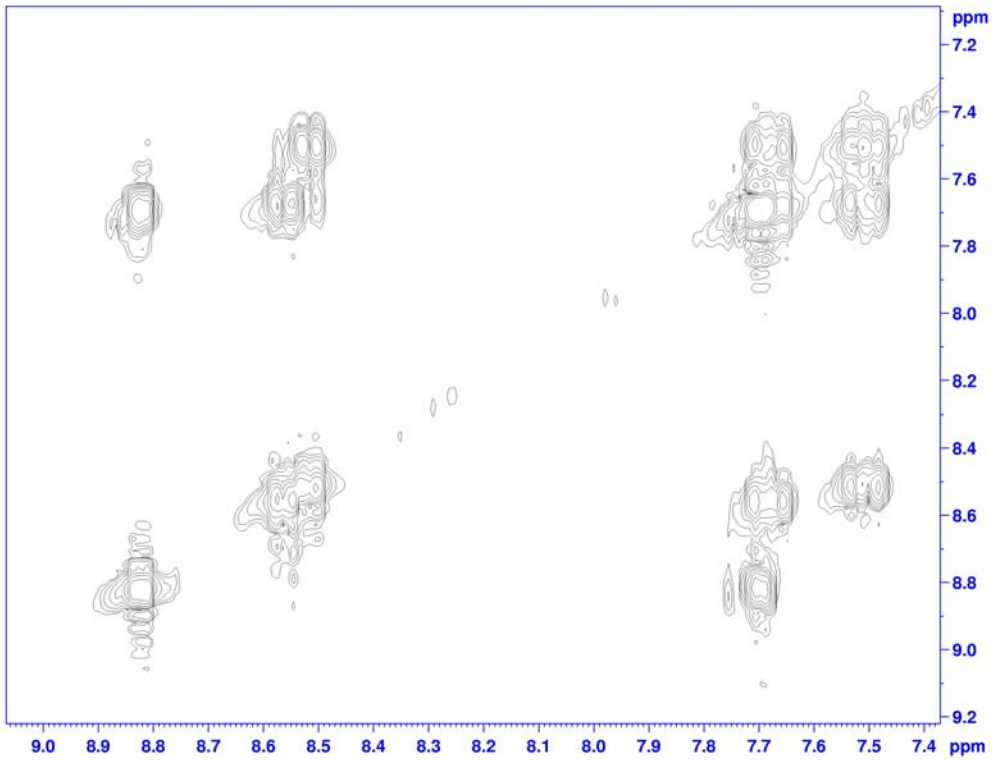


Figure 75 ^{1}H-^{1}H COSY spectrum of **GMS15**

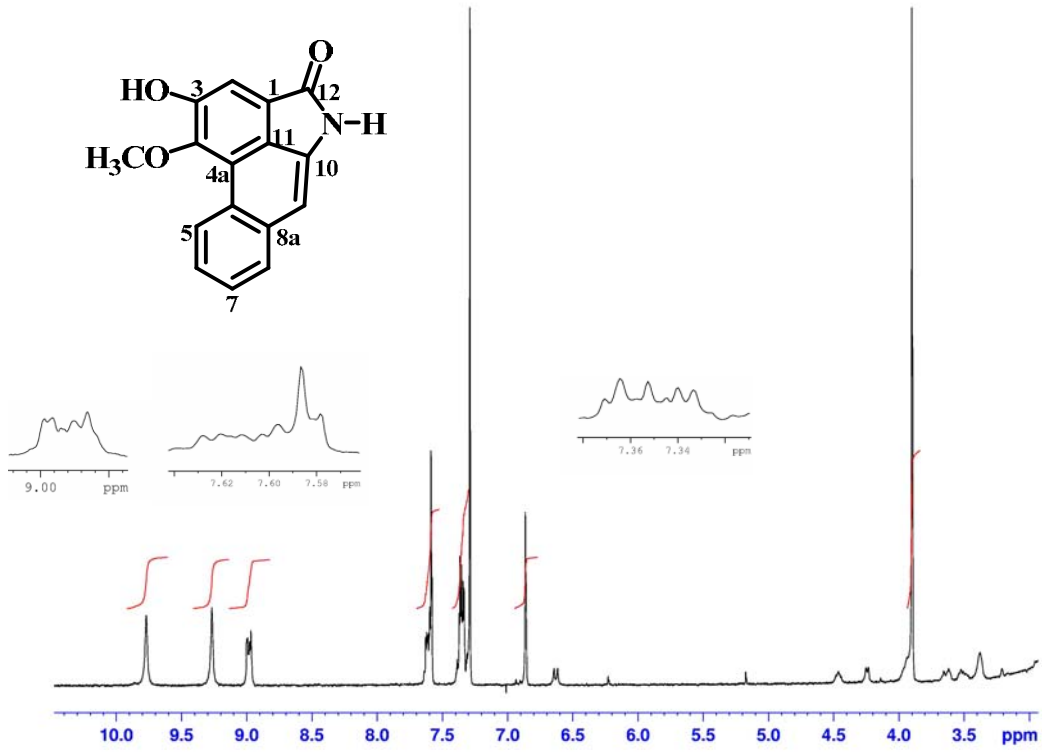


Figure 76 ^{1}H NMR (300 MHz) ($CDCl_3$+DMSO) spectrum of **GMS16**

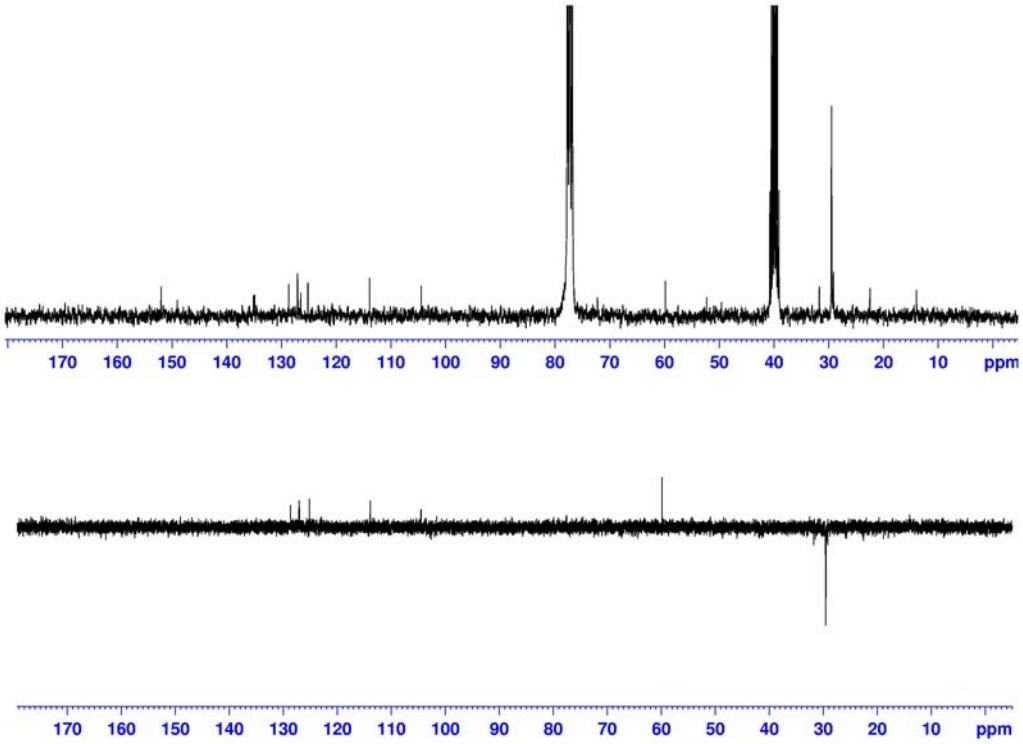


Figure 77 ^{13}C NMR and DEPT 135 (75 MHz) ($CDCl_3$+DMSO) spectrum of **GMS16**

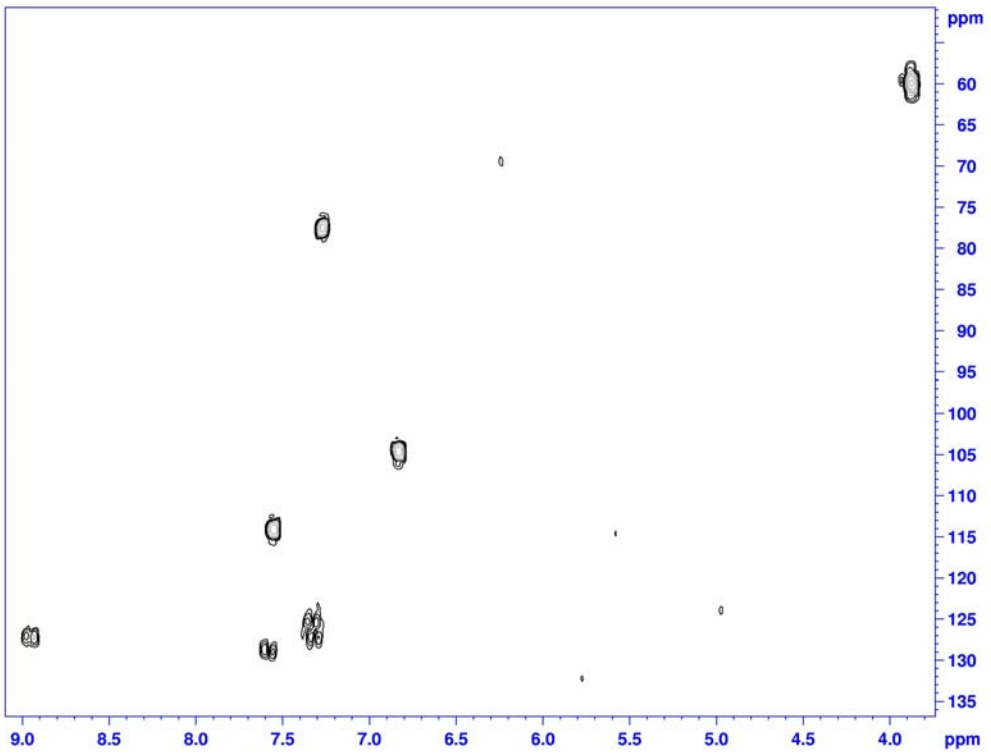


Figure 78 2D HMQC spectrum of **GMS16**

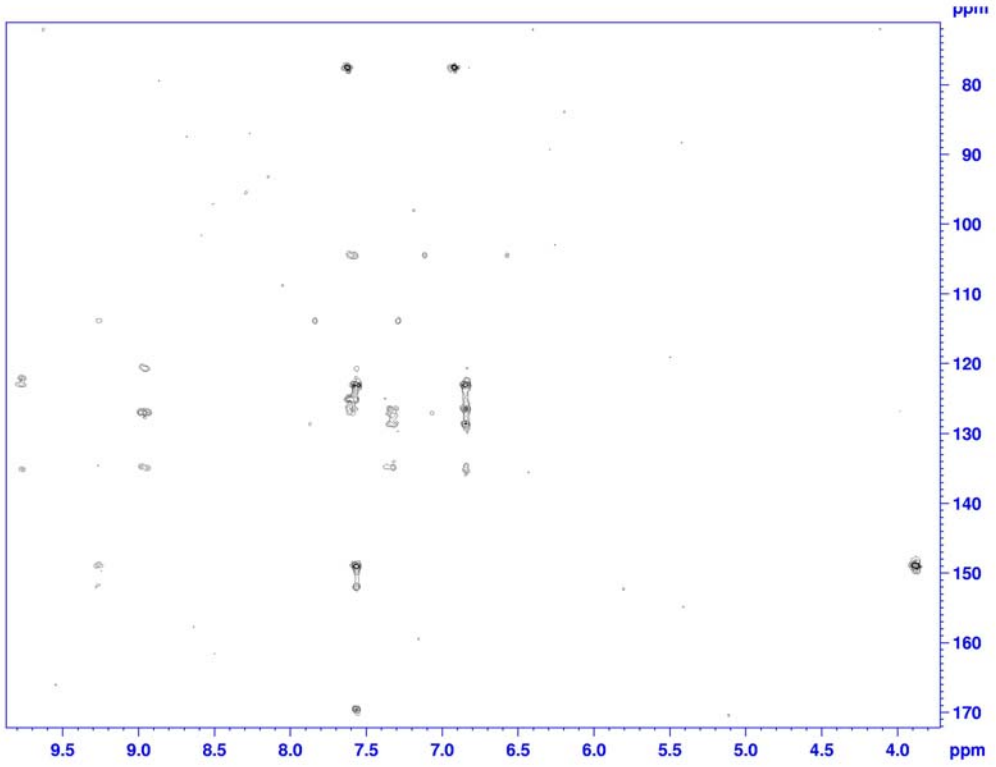


Figure 79 2D HMQC spectrum of **GMS16**

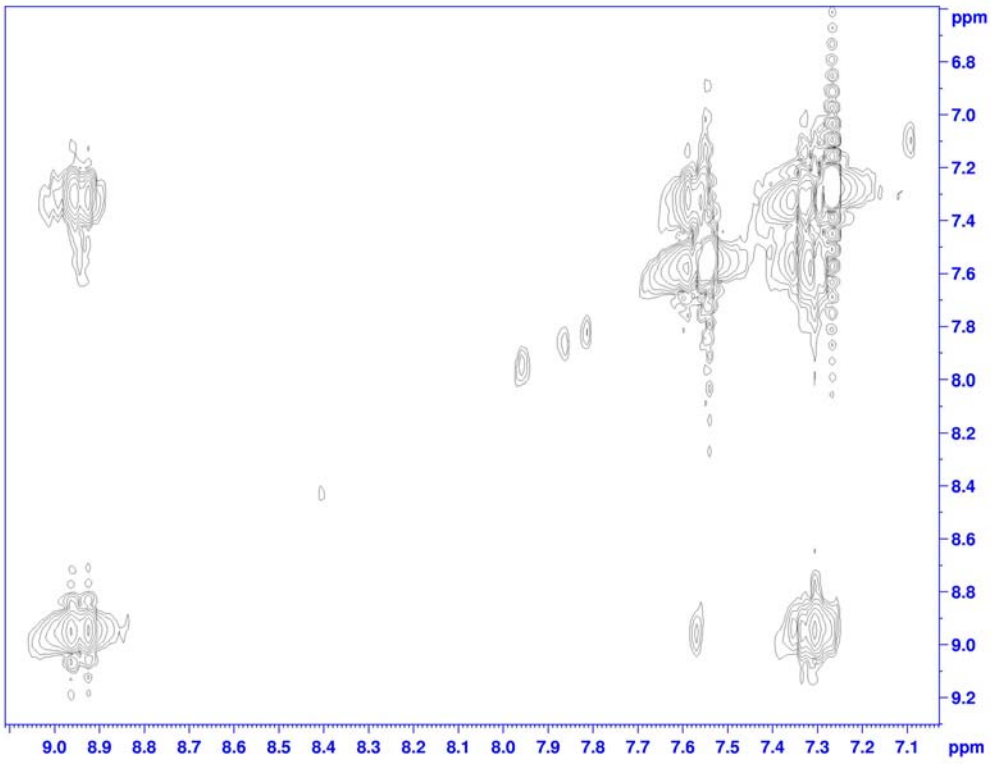


Figure 80 ^{1}H-^{1}H COSY spectrum of **GMS16**

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Bachelor of Science (Education)	Prince of Songkla University	2006

Scholarship Awards during Enrolment

Center of Excellence for Innovation in Chemistry (PERCH-CIC), Commission on Higher Education, Ministry of Education

List of Publications and Proceedings

1. Uraiwan Phetkul and Wilawan Mahabusarakam. "Chemical constituents from the stems of *Goniothalamus macrophyllus*". The 6th IMT-GT UNINET CONFERENCE 2008, The Gurney Resort Hotel & Residences Penang, Penang, Malaysia, 28-30 August 2008. (Poster presentation)
2. Uraiwan Phetkul and Wilawan Mahabusarakam. "Styryllactones and napthoquinone from the stems of *Goniothalamus macrophyllus*". 4th National Grade Research Conference, Burapha University, Chonburi, Thailand, 13 March 2009. (Oral presentation)