ไฟโตอเล็กซินจากเปลือกต้นขนุน

นางสาว ธิดาวรรณ โพธิดารา

สถาบันวิทยบริการ
จุฬาลงกรณ์มหาวิทยาลัย

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PHYTOALEXINS FROM *ARTOCARPUS HETEROPHYLLUS* STEM BARK.

Miss. Thidawan Phothidara

สถาบันวิทยบริการ
จุฬาลงกรณ์มหาวิทยาลัย

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การศึกษาทางพฤกษเคมีของไฟโตอเล็กซินจากเปลือกต้นขนุน (*Artocarpus heterophyllus*) ได้ทำการแยกสารประกอบจากสิ่งสกัดโทลูอีนได้สารประกอบสองชนิดคือ Artonin A และ Cycloheterophyllin ซึ่งเป็นสารประกอบฟลาโวนซึ่งมีหมู่พรีนีลในสูตรโครงสร้าง และสารประกอบจากสิ่งสกัด เมททานอล ได้สารประกอบหนึ่งชนิดคือ Artonin D ซึ่งเป็นสารประกอบ chalcone ชนิด Diel-Alder type adduct

การพิสูจน์เอกลักษณ์ และสูตรโครงสร้างทางเคมีของสารประกอบที่แยกได้นี้ อาศัยการวิเคราะห์ข้อมูล จากสเปกตรัมของ UV, IR, MS และ NMR ร่วมกับการเปรียบเทียบข้อมูลของสารที่พบสูตรโครงสร้างแล้ว

สถาบันวิทยบริการ
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ภาควิชา เภสัชพฤกษศาสตร์	ลายมือชื่อนิสิต……
สาขาวิชา เภสัชพฤกษศาสตร์	ลายมือชื่ออาจารย์ที่ปรึกษา……..……
ปีการศึกษา 2546	ลายมือชื่ออาจารย์ที่ปรึกษาร่วม……..

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KEY WORD : *ARTOCARPUS HETEROPHYLLUS.* / PHYTOALEXINS

THIDAWAN PHOTHIDARA : PHYTOALEXINS FROM *ARTOCARPUS HETEROPHYLLUS* STEM BARK.THESIS ADVISOR : ASSOCIATE PROFESSOR RAPEPOL BAVOVADA , Ph.D., THESIS CO-ADVISOR: ASSISTANT PROFESSOR SUNTAREE VITAYANATPAISAN, 157 pp.

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Phytochemical study of the phytoalexins from *Artocarpus heterophyllus* stem bark led to the isolated two prenylated flavones, artonin A and cycloheterophyllin from toluene extract and one Diels-Alder type adduct of chalcone derivative, artonin D from methanol extract.

The structures of all of these isolated compound were determined by extensive spectroscopic studies, including comparison of their UV, IR, MS and NMR properties with previously reported data.

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Department Pharmaceutical Botany Student's signature……..

Field of study Pharmaceutical Botany Advisor's signature…….…….

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LIST OF ABBREVIATIONS AND SYMBOLS

Acetone-d_6	=	Deuterated acetone
br	=	Broad (for NMR spectra)
^{o}C	=	Degree Celsius
CA	=	Chemical Abstract
$CDCl_3$	=	Deuterated chloroform
$CH\ Cl_3$	=	Chloroform
cm	=	Centimeter
^{13}C NMR	=	Carbon-13 Nuclear Magnetic Resonance
^{1}H-^{1}H COSY	=	Homonuclear (Proton- Proton) Correlation Spectroscopy
1-D	=	One Dimensional
2-D	=	Two Dimensional
d	=	Doublet (for NMR spectra)
dd	=	Doublet of doublet (for NMR spectra)
DEPT	=	Distortionless Enhancement by Polarization Transfer
DMSO- d_6	=	Deuterated dimethysulfoxide
δ	=	Chemical shift
EIMS	=	Electric Impact Mass Spectrometry
EtOAc	=	Ethyl acetate
ES TOF MS	=	Electro spray time of flight Mass Spectrometry
g	=	Gram
hr	=	Hour
^{1}H NMR	=	Proton Nuclear Magnetic Resonance
HMBC	=	^{1}H-detected Heteronuclear Multiple Bond Coherence
HMQC	=	^{1}H-detected Heteronuclear Multiple Quantum Coherence
Hz	=	Hertz
IR	=	Infrared spectrum
KBr	=	Potassium bromide
J	=	Coupling constant
λ_{max}	=	Wavelength at maximal absorption
ε	=	Molar absorptivity

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LIST OF ABBREVIATIONS AND SYMBOLS (continued)

M^+	=	Molecular ion
m	=	Multiplet (for NMR spectra)
MeOH	=	Methanol
mg	=	Miligram
$[M+H]^+$	=	Protonated molecular ion
min	=	Minute
ml	=	Mililiter
MW	=	Molecular weight
m/z	=	Mass to charge ratio
MS	=	Mass Spectrometry
nm	=	Nanometer
NMR	=	Nuclear Magnetic Resonance
NOESY	=	Nuclear Overhauser Effect Spectroscopy
spp.	=	Species
V_{max}	=	Wave number at maximal absorption
s	=	Singlet (for NMR spectra)
t	=	Triplet (for NMR spectra)
TLC	=	Thin layer Chromatography
UV	=	Ultraviolet
VLC	=	Vacuum Liquid Column Chromatography

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CHAPTER I

INTRODUCTION

The genus *Artocarpus* belongs to the family Moraceae of the order Urticarles.This genus consisted of about 47 species distributed in Ceylon, India, Pakistan, Burma, Siam , Indo-china, South-China, Malesia and Solomon Islands. Three species (*A.communis, A.heterohhyllus and A.interger*) are cultivated throughout the tropic; 20 spp. in Malaya including the cultivated species (Kochummen, 1978).

Plants in the genus *Artocarpus* are evergreen trees with milky juice. Leaves alternate, coriaceous , often very large, entire, lobe or pinnatifid, penninerved. Flower monoecious, densely crowded on globose or oblong, 1-sexual solitary usually axillary receptacles, often mixed with scales which are often thickened or peltate at the apex. Male flower: Perianth 2-4 lobed or partite; lobes obtus, valvate or slightly imblicate. Stamens 1, erect. Pistillode 0.Female flower; Perianths tubular, confluent below with the receptacle; mouth minute. Ovary straight; ovule pendulous; style central or lateral; stigma entire (rarely 2-3 fid) . Fruit much enlarged fleshy oblong cylindric or subglobose entire or lobed receptacle clothed with the greatly accrescent fleshy perianths and carpels (anthocarps) which have hardened spinescent or truncate or pyramidal or flat apices. Seed pendulous; testa membranous ; albumen 0; embryo straight or incurved; cotyledons freshy equal or unequal; radical short, superior (Kirtikar and Basu,1980)

According to Smitinand (2001) ,the species of genus *Artocarpus* found in Thailand are as follows.

Artocarpus altilis (Parkinson)Fosberg (*A.communis* J.R & G. Forst., *A.incisa* Linn. F.)	ขนุนสำปะลอ Khanun sampalo (Central); สาเก Sake (Central); Bread fruit tree; Bread nut tree.
A.altissimus J.J Smith	ไสน Sanai (Surat Thani)
A.chaplasha Roxb.	หาดส้าน Haat san (Chiang Rai)
A.dadah Miq.	ทังคัน Thang khan; ม่วงกวาง Muang kwang, (Yala); หาดรุม Hat rum, หาดลูกใหญ่, Hat luk yai (Trang); หาดขน Hat khon (Narathiwat)

A.elasticus Reinw.ex Blume	กะออก Ka ok, กะเอาะ Ka-o (Peninsular); ตือกะ Tue-ka (Malay-Yala); เอาะ O (Trang,Ranong).
A.gomezianus Wall.ex Trecul	ตะปัง Ta pang, ตำปัง Tam-pang (Malay-Peninsular); หาดหนุน Hat nun (Northern) ; อีโป้ I po(Trang)
A.heterophyllus Lamk. (*A.integrifolious* Linn.f.)	ขนุนKhanun (General); ขะนูน Kha-nu (Chong-Chanthaburi) ;ขะเนอ Kha-noe (Khmer); ซีคึย Si-Khue, ปะหน่อย Pa-noi (Karen-Mae Hong Son); นะยวนซะ Na-yaui-sa (Karen-Kanchanaburi); นากอ Na-ko (Malay-Pattani); เนน Nen (Chaobon-Nakhon Ratchasima) ; มะหนุน Manun (Northern,Peninsular); ล้าง , ลาง Lang (Shan- Northern) หมักหมี้ Makmi (Northeastern); หมากกลาง Mak glang (Shan-Mee Hong Son); Jack fruit tree
A.kemando Miq.	ขนุนป่า Khanun pa (Narathiwat); ยาตู Yatu (Malay-Narathiwat)
A.integer (Thunb.) Merr.	จำปาดะ Champada(General) ; จำปาเดาะ Champado (Peninsular); Champadak.
A.lacucha Roxb. (*A.lakoocha* Roxb.)	กาแย kaa-yae, ตาแป Ta-pae, ตาแปง Ta-paeng (Maley-Narathiwat); มะหาด Mahat (Peninsular) ; มะหาดใบใหญ่ Mahat bai yai (Trang) : หาด Hat (General)
A.lanceifolius Roxb.	ขนุนป่า Khanun pa (Peninsular); หนังกาปิโต Nang-ka pi-to; หนังกาปีปิ๊ต Nang-ka-pi-pit (Malay-Peninsular); นั่งกาปีแป๊ะ Nang-ka-pi-pae (Malay-Narathiwat)
A.nitidus Trec subsp.lingnanesis Jarrett. (*A.parva* Gagnep.)	มะหาดข่อย Mahat khoi (Surat Thani)
A.rigidus Blume subsp. rigidus	ขนุนป่า Khanun pa (Peninsular)
A.rigidus bl. subsp.asoerulus Jarrett. (*A.calophyllus* Kurz)	ขนุนปาน Khannun pan (Surat Thani)

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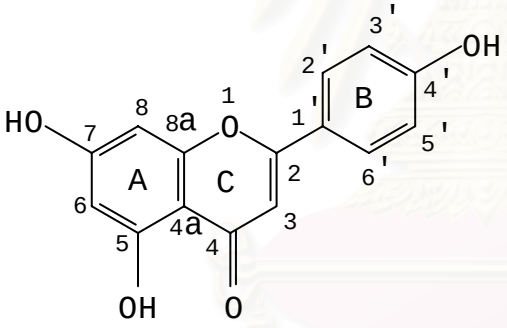
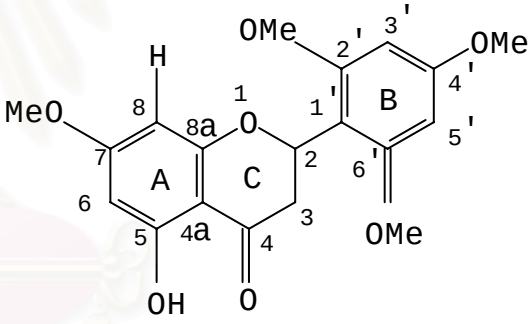
A. heterophyllus Lamk. is plant known in Thai as Khanun. Young twings, petioles and midrib of young leaves covered with minute, erecto -patent, acute bristles, older ones glabrous; leaves elliptic-oblong- ovate with cuneate, subdecurrent base, firmly coriaceous, 10-20 cm by 5-10 cm; petiole 2-4 cm; stipules 1 1/2-5 cm. Inflorescences borne on short, thick, few-flowered lateral shoots (arising from stem and thick branches), light green, 4-6 cm long; female 1-2 together in axils of lowest leave; male higher, more numerous; female inflorescence on thicker stalk than male, with fleshy ring at base; stigma clavate; syncarp ellipsoid, light yellow, 30-90 cm by 25-50 cm. Cultivated as a fruit-tree, often spontaneously springing up. (Backer C. A , D. Sc and R. C. Bakhuizen, 1965)

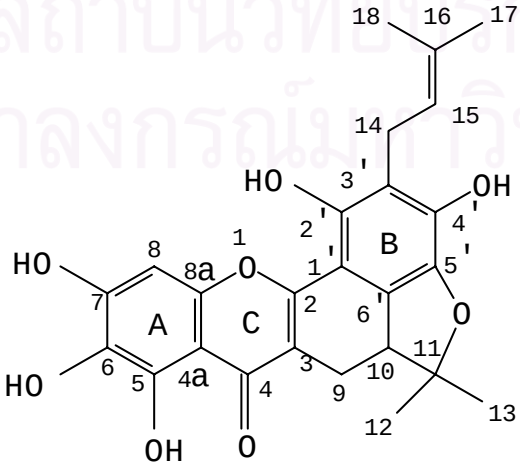
Most of chemical constituents of genus *Artocarpus* have been reported were flavonoids and in the very less triterpenoids extent and sterols. Flavonoids having structure variation among flavone , flavonol, prenylated flavone and chalcone of which some structure were shown below



Epigenin (Flavones)



Heteroflavanones (Flavanones)



Artonin J (Prenylated flavones)

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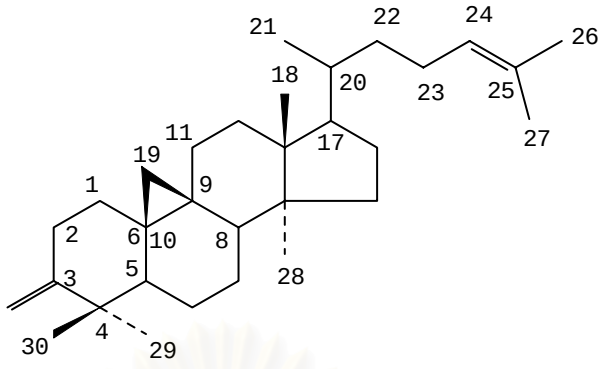

Cycloartenone (Triterpenoids)

Of the various flavonoid derivatives conjugates known to accumulate in plants, the occurrence of isoprenoids as natural plant constituent came to be recognized fairly recently. This form of conjugation was thought to be associated with the prenylated flavones and isoflavones. Most of the latter compounds (in the Leguminosae) are inducible metabolites (phytoalexin) that are synthesized in response to fungal attack. Phytoalexins were products of higher plant metabolism , absent from healthy tissues or present only in negligible traces , which accumulate in significant amount in response to fungal or bacterial challenge . (Stoessl , 1980).

In this study, the plant material (red colour patch) was collected from damage areas of bark of which distinctly different from the normal bark (brown colour).These isolated constituents of the plant material could be correctly called phytoalexin. These prompted the author to investigate the chemical compounds of this plant for more information in the field of chemotaxonomy and phytochemistry.

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Figure 1 *A.Heterophyllus* Lamk.

Figure 2 *A.Heterophyllus* Lamk. stem bark

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CHAPTER II

HISTORICAL

1.Chemical Constituents of Genus *Artocarpus*

Chemical constituents of genus *Artocarpus* have been investigated for more than 50 years. These compounds were reported as steroids, triterpenoids, flavonoids, and several miscellaneous substances. However, the two main group are flavonoids and triterpenoids. The distribution of flavonoids in the genus *Artocarpus* are shown in table 1.

Table 1. Distribution of flavonoids in the *Artocarpus.*

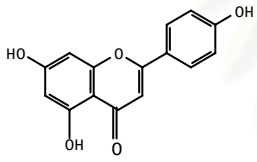
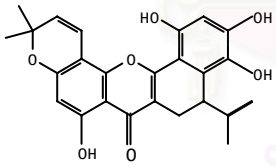
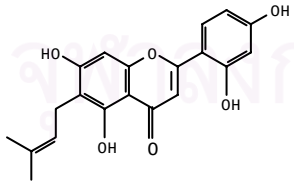
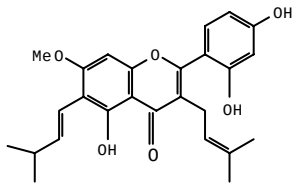
Chemical compound	Source	Reference
Artocarpus altilis		
Apigenin**[1]** 	Heartwood	Shimizu *et al*., 1998
Artobiloxanthone **[2]** 	Stem bark	Aida *et al* ., 1997
Artocarpesin **[3]** 	Heartwood	Shimizu *et al*., 1998
Artocarpin **[4]** 	Heartwood	Venkataraman, 1972

Table 1 (Continued)

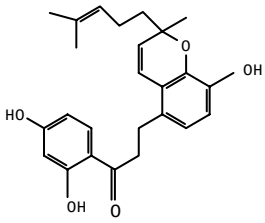
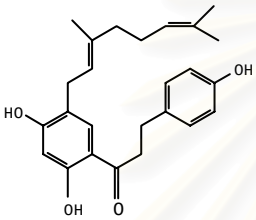
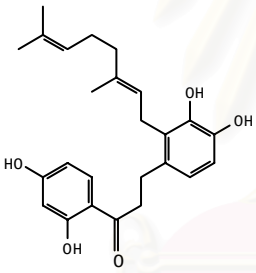
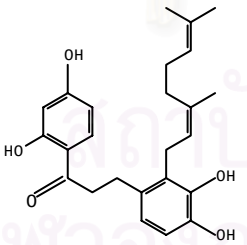
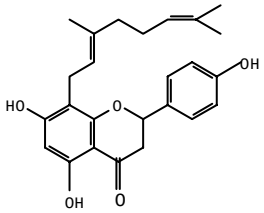
Chemical compound	Source	Reference
Artocarpus chalcone AC-3-1**[5]** 	Flower	Fujimoto *et al* ., 1987
Artocarpus chalcone AC-3-2**[6]** 	Flower	Fujimoto *et al* ., 1987
Artocarpus chalcone AC-5-1**[7]** 	Flower	Fujimoto *et al* ., 1987
Artocarpus chalconel **[8]** 	Flower	Fujimoto , Augustein, and Made, 1987
Artocarpus flavone AC-3-3**[9]** 	Flower	Fujimoto *et al* ., 1987

Table 1 (Continued)

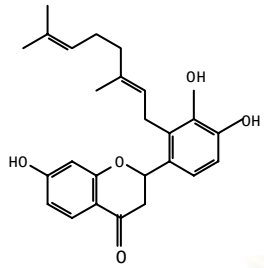
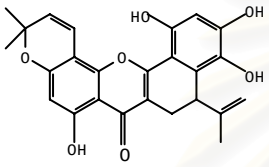
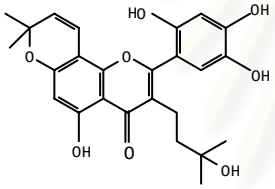
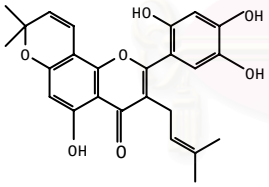
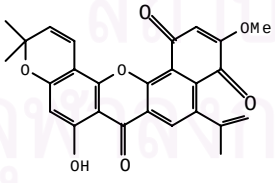
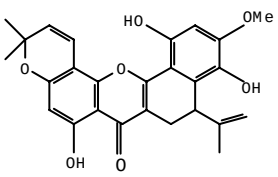
Chemical compound	Source	Reference
Artocarpus flavone AC-5-2 **[10]** 	Flower	Fujimoto *et al* ., 1987
Artocarpus flavone KB-1 **[11]** 	Stem bark	Fujimoto *et al* ., 1990
Artocarpus flavone KB-2 **[12]** 	Stem bark	Fujimoto *et al* ., 1990
Artocarpus flavone KB-3(artonin E)**[13]** 	Stem bark	Fujimoto *et al* ., 1990
Artomunoxanthentrione**[14]** 	Root bark	Shieh and Lin, 1992
Artomunoxanthone**[15]** 	Root bark	Shieh and Lin, 1992

Table 1 (Continued)

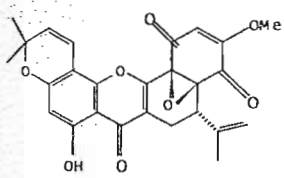
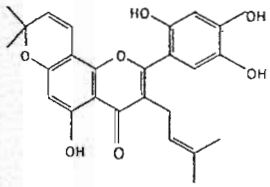
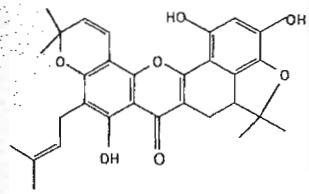
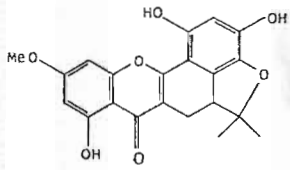
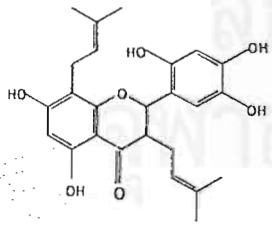
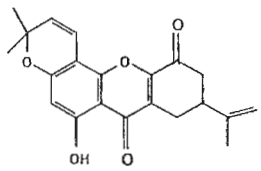
Chemical compound	Source	Reference
Artomunoxanthotrione epoxide**[16]** 	Root bark	Lin , Shieh and Jong , 1992
Artonin E**[13]** 	Stem bark	Hano *et al* ., 1990
Artonin F**[17]** 	Stem bark	Hano *et al* ., 1990
Artonin K**[18]** 	Stem bark	Aida *et al.*, 1997
Artonin V**[19]** 	Root bark	Hano , Inami,and Nomura, 1994
Artonol A **[20]** 	Stem bark	Aida *et al.*, 1997

Table 1 (Continued)

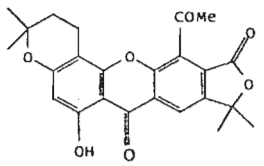
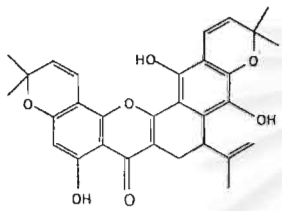
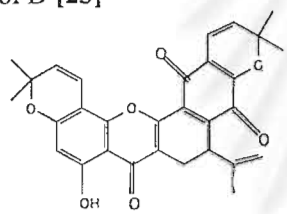
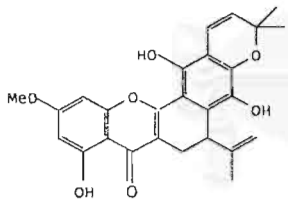
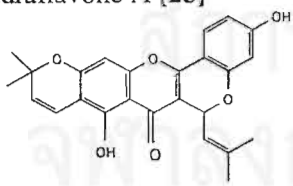
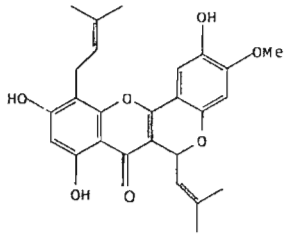
Chemical compound	Source	Reference
Artonol B [21] 	Stem bark	Aida *et al.*, 1997
Artonol C [22] 21 	Stem bark	Aida *et al.*, 1997
Artonol D [23] 	Stem bark	Aida *et al.*, 1997
Artonol E [24] 	Stem bark	Aida *et al.*, 1997
Cudraflavone A [25] 	Root bark	Shieh and Lin, 1992
Cycloaltilisin [26] 	Stem	Chen *et al.*, 1993

Table 1 (Continued)

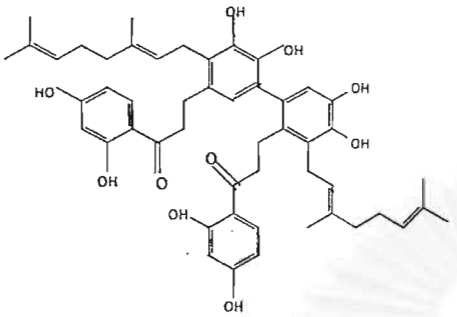
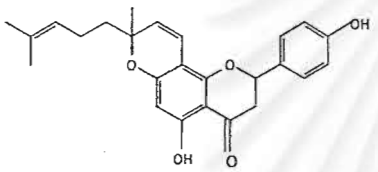
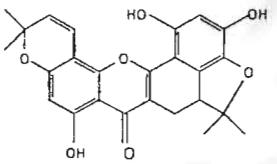
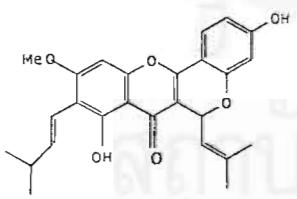
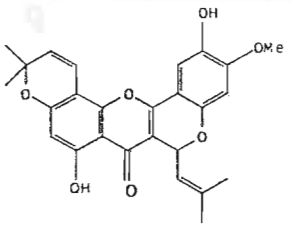
Chemical compound	Source	Reference
Cycloatilisin 6 **[27]** 	Bud cover	Patil *et al.*, 2002
Cycloatilisin 7 **[28]** 	Bud cover	Patil *et al.*, 2002
Cycloartobiloxanthone **[29]** 	Stem bark	Hano *et al* ., 1990
Cycloartocarpin **[30]** 	Heartwood	Venkataraman, 1972
Cycloartomunin **[31]** 	Root bark	Lin and Shieh, 1991

Table 1 (Continued)

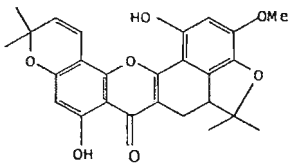
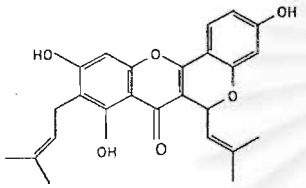
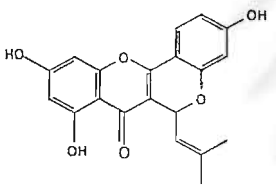
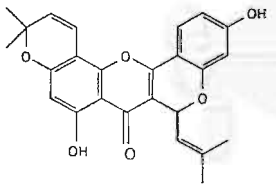
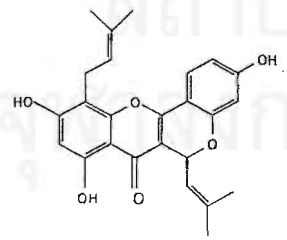
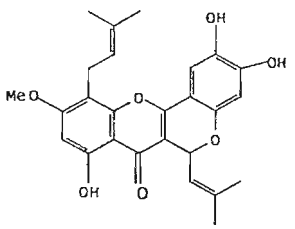
Chemical compound	Source	Reference
Cycloartomunoxanthone **[32]** 	Root bark	Lin and Shieh, 1991
Cyclocommunin **[33]** 	Root bark	Lin and Shieh, 1991
Cyclocommunol **[34]** 	Root bark	Lin and Shieh, 1991
Cyclomorusin **[35]** 	Root bark Stem	Lin and Shieh, 1991 Chen *et al.*,1993
Cyclomulberrin **[36]** 	Root bark Stem	Lin and Shieh, 1991 Chen *et al.*, 1993
Dihydrocycloartomunin **[37]** 	Root bark	Lin and Shieh, 1991

Table 1 (Continued)

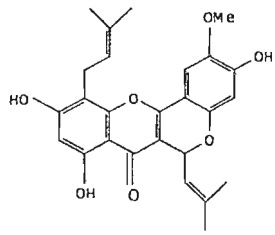
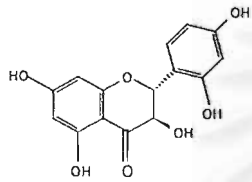
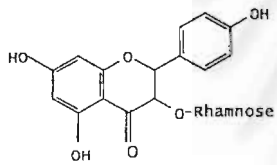
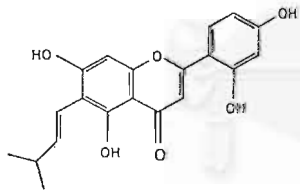
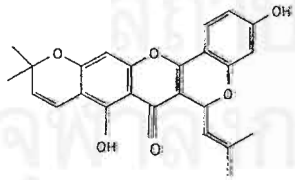
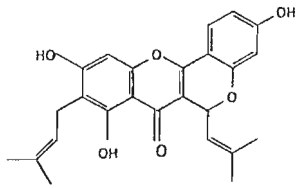
Chemical compound	Source	Reference
Dihydroisocycloartomunin **[38]** 	Root bark	Lin and Shieh, 1992
Dihydromorin **[39]** 	Heartwood	Shimizu *et al.*, 1998
Engeletin **[40]** 	Stem	Chen *et al.*, 1993
Isoartocarpesin **[41]** 	Heartwood	Shimizu *et al.*, 1998
Isocyclomorusin (Cudraflavone A) **[25]** 	Stem	Chen *et al.*, 1993
Isocyclomuberrin (Cyclocommunin) **[33]** 	Stem	Chen *et al.*, 1993

Table 1 (Continued)

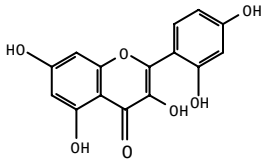
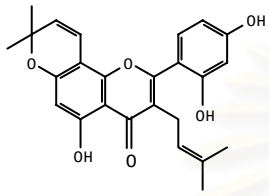
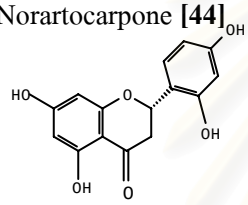
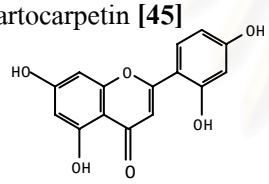
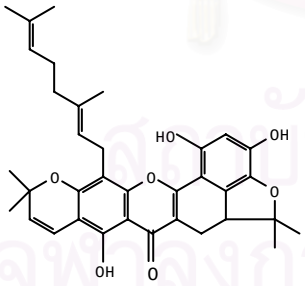
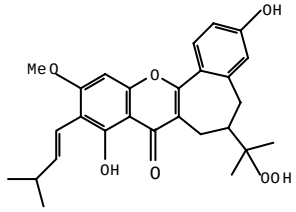
Chemical compound	Source	Reference
Morin **[42]** 	Heartwood	Venkataraman, 1972
Morusin **[43]** 	Stem bark	Fujimoto *et at*., 1990
(+)-Norartocarpone **[44]** 	Heartwood	Shimizu *et al*., 1998
Norartocarpetin **[45]** 	Heartwood	Venkataraman, 1972
A.champeden		
Artoindonesianin A **[46]** 	Root	Hakim *et al*., 1999
Artoindonesianin B **[47]** 	Root	Hakim *et al*., 1999

Table 1 (continued)

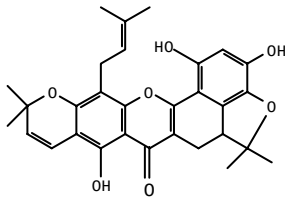
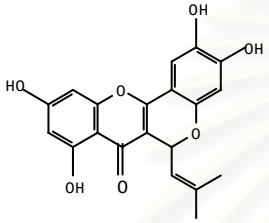
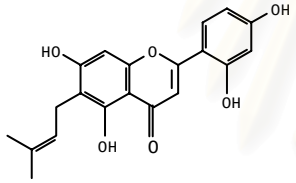
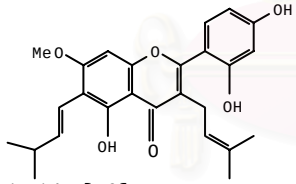
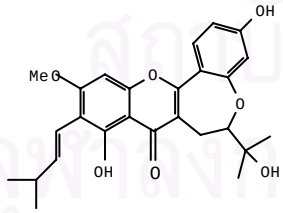
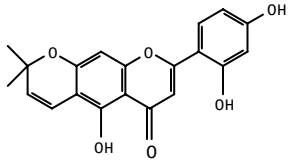
Chemical compound	Source	Reference
Artonin A **[48]** 	Root	Hakim *et al*., 1999
Cyclochampedol **[49]** 	Stem bark	Achmad *et al*., 1996; Paolo *et al*, 1998
A.chaplacha		
Artocarpicin **[3]** 	Heartwood	Rao, Rathi, and Venkataraman 1972
Artocarpin **[4]** 	Heartwood	Rao *et al*., 1972
Chaplashin **[50]** 	Heartwood	Rao *et al*., 1972
Cycloartocarpesin **[51]** 	Heartwood	Rao *et al*., 1972

Table 1 (continued)

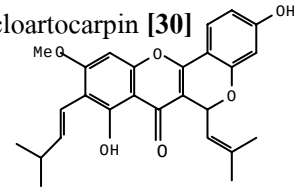
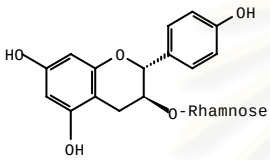
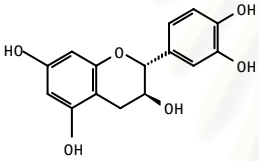
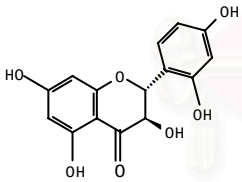
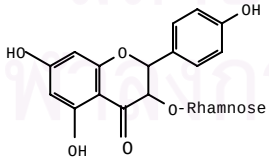
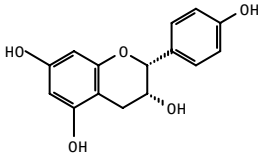
Chemical compound	Source	Reference
Cycloartocarpin **[30]** 	Heart wood	Rao *et al*., 1972
A.dadah		
Afzelechin-3-*O*-α-L-rhamnopyra-Noside **[52]** 	Stem bark Twing	Su *et al*., 2002
(+)-Catechin **[53]** 	Stem bark Twing	Su *et al*., 2002
Dihydromorin **[39]** 	Stem bark	Su *et al*., 2002
Engeletin **[40]** 	Twing	Su *et al*., 2002
(-)-Epiafzelechin **[54]** 	Stem bark	Su *et al*., 2002

Table 1 (continued)

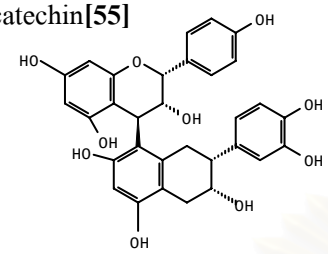
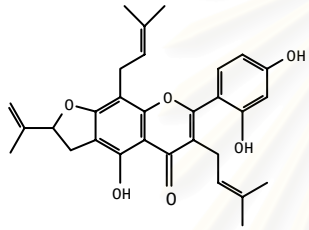
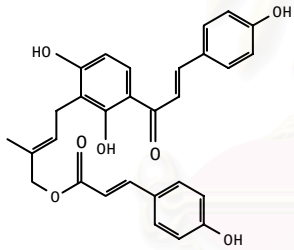
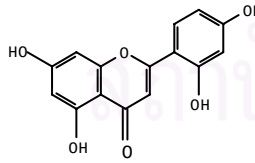
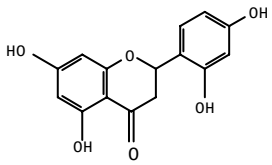
Chemical compound	Source	Reference
(-)-Epiafzelechin-(4β→8)-epicatechin**[55]** 	Stem bark	Su *et al*. ,2002
Gemichalcole B **[56]** 	Twig	Su *et al*., 2002
Isogemichalcole B **[57]** 	Twig	Su *et al*., 2002
Norartocarpetin **[45]** 	Twig	Su *et al*., 2002
Steppogenin **[58]** 	Twig	Su *et al*., 2002

Table 1 (continued)

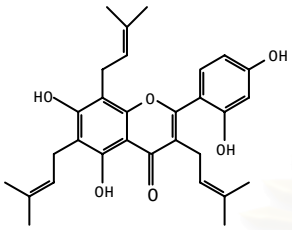
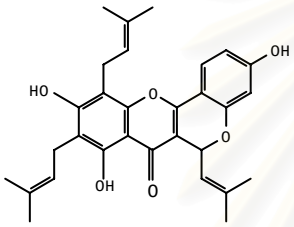
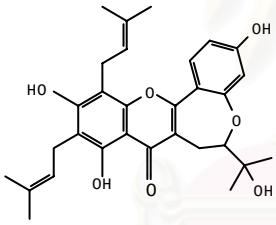
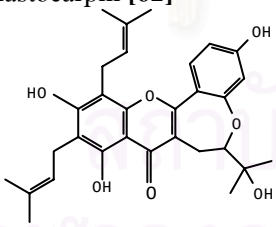
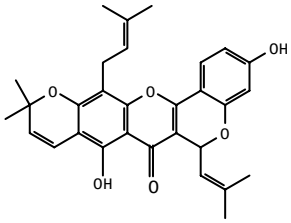
Chemical compound	Source	Reference
A.elasticus		
Artelasticin **[59]** 	Heartwood	Kijjoa *et al*., 1996
Artelastin **[60]** 	Heartwood	Kijjoa *et al*., 1996
Artelastinin **[61]** 	Heartwood	Kijjoa *et al*., 1976
Artelastocarpin **[62]** 	Heartwood	Kijjoa *et al*., 1996
Artelastochromene **[63]** 	Heratwood	Kijjoa *et al*., 1996

Table 1 (continued)

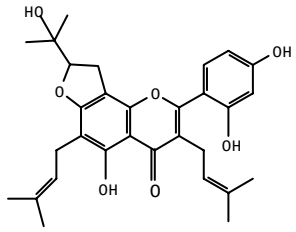
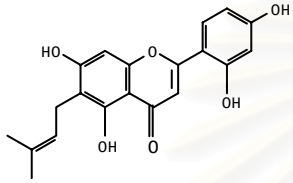
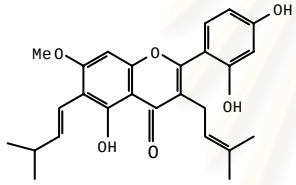
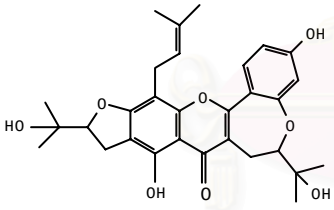
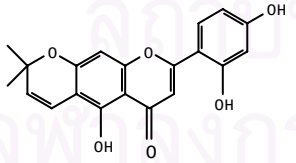
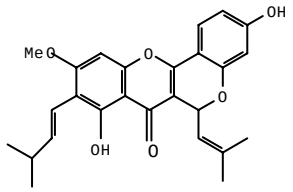
Plant and chemical compound	Plant part	Reference
Artelastofuran **[64]** 	Heratwood	Kijjoa *et al* ., 1998
Artocarpicin **[3]** 	Heartwood	Kijjoa *et al*., 1996
Artocarpin **[4]** 	Heratwood	Kijjoa *et al*., 1976
Carpelastofuran **[65]** 	Heratwood	Cidade *et al*., 2001
Cycloartocarpesin **[51]** 	Heratwood	Pendse *et al*., 1976
Cycloartocarpin **[30]** 	Heratwood	Pendse *et al*., 1976

Table 1 (continued)

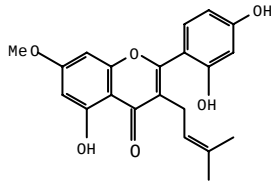
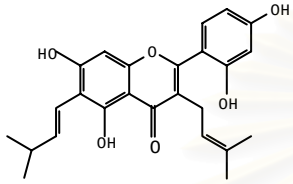
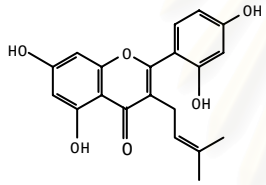
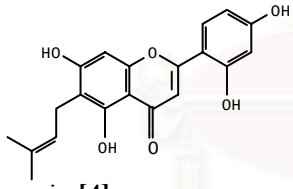
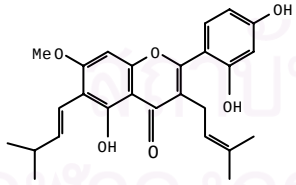
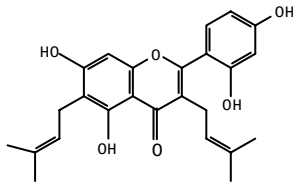
Plant and chemical compound	Plant part	Reference
Integrin **[66]** 	Heartwood	Pendse *et al*., 1976
Norartocarpin **[67]** 	Heartwood	Pendse *et al*., 1976
A.gomezianus		
Albanin A **[68]** 	Root	Sritularak, 1998; Likhitwitayawuid, Sritularak, and De-Ek-NamKul, 2000
Artocarpesin **[3]** 	Heartwood	Venkataraman, 1972
Artocarpin **[4]** 	Heartwood	Venkataraman, 1972
Cudraflavone C **[69]** 	Root	Sritularak, 1998; Likhitwitayawuid, Sritularak, and De-Ek-NamKul, 2000

Table 1 (continued)

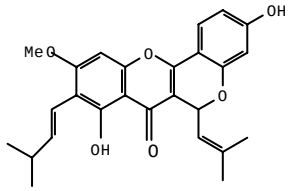
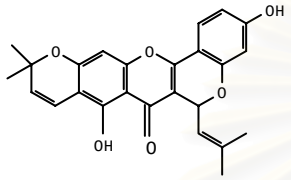
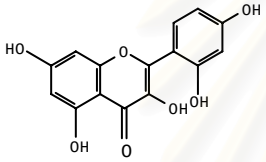
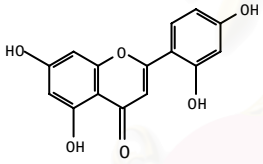
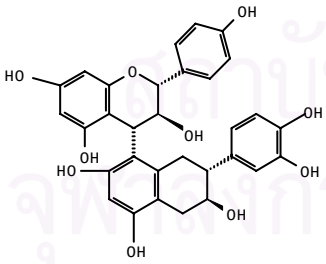
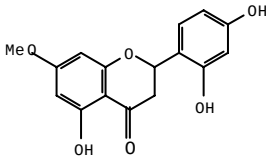
Plant and chemical compound	Plant part	Reference
Cycloartocarpin **[30]** 	Heartwood	Venkataraman, 1972
Isocyclomorusin **[25]** 	Root	Sritularak,1998; Likhitwitayawuid, Sritularak, and De-Ek-NamKul, 2000
Morin **[42]** 	Heartwood	Venkataraman, 1972
Norartocarpetin **[45]** 	Heartwood	Venkataraman, 1972
A.heterophyllus		
Afzelechin-(4α→8)-catechin **[70]** 	Leaf	An *et al*., 1992
Artocarpanone **[71]** 	Heartwood	Radhakrishnan, Roa, and Venkarataraman, 1965

Table 1 (continued)

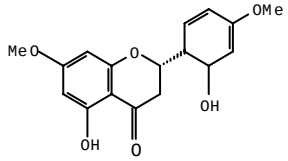
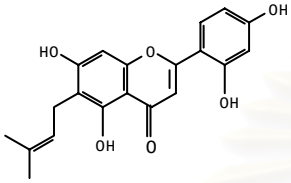
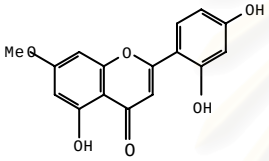
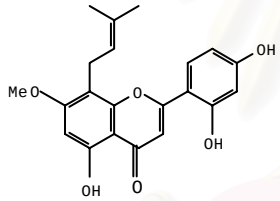
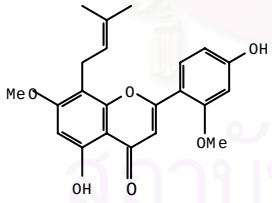
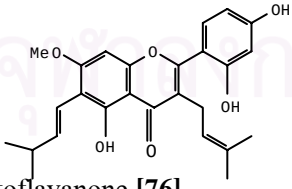
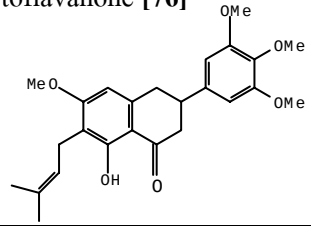
Plant and chemical compound	Plant part	Reference
Artocarpanone A **[72]** 	Root bark	Lin *et al*., 1995
Artocarpesin **[3]** 	Heartwood	Radhakrishnan *et al*., 1965
Artocarpetin **[73]** 	Heartwood	Venkataraman, 1972
Artocarpetin A **[74]** 	Root bark	Lin *et al*., 1995
Artocarpetin B **[75]** 	Root	Chung *et al*., 1995
Artocarpin **[4]** 	Heartwood	Radhakrishnan *et al*., 1965
Artoflavanone **[76]** 	Root	Dayal and Seshadri, 1974

Table 1 (continued)

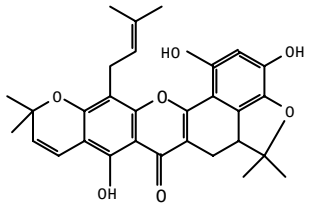
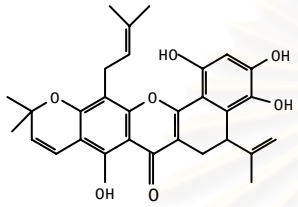
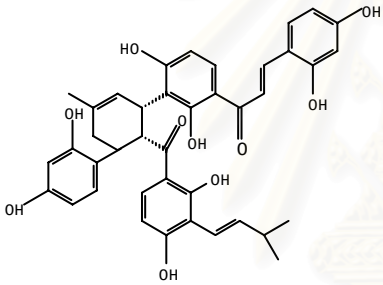
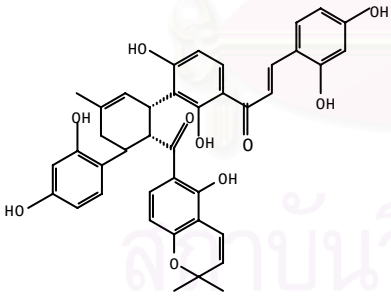
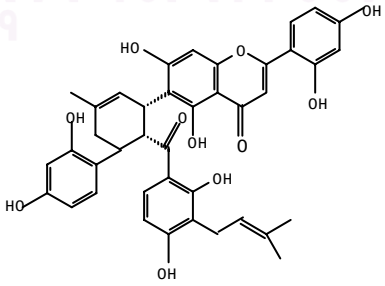
Plant and chemical compound	Plant part	Reference
Artonin A **[77]** 	Root bark	Hano *et al*., 1989
Artonin B **[78]** 	Root bark	Hano *et al*., 1989
Artonin C **[79]** 	Root bark	Hano, Aida, and Nomura, 1990
Artonin D **[80]** 	Root bark	Hano, Aida, and Nomura, 1990
Artonin I **[81]** 	Root bark	Hano *et al*., 1989

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Table 1 (continued)

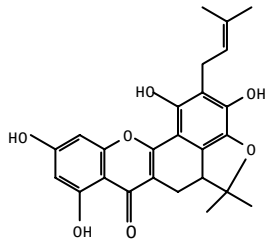
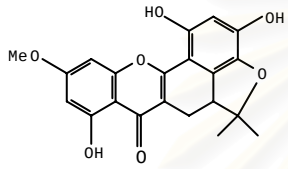
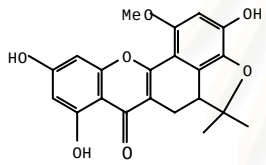
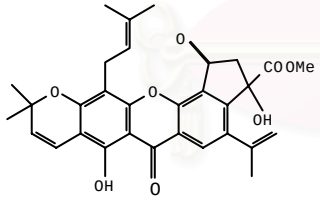
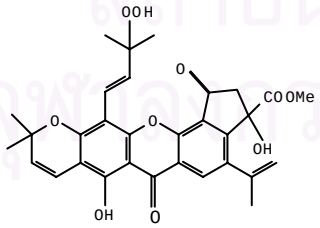
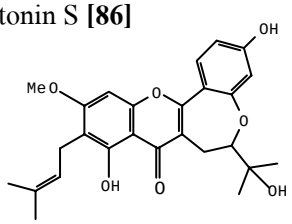
Plant and chemical compound	Plant part	Reference
Artonin J **[82]** 	Root bark	Aida *et al*., 1993
Artonin K **[18]** 	Root bark	Aida *et al*., 1993
Artonin L **[83]** 	Root bark	Aida *et al*., 1993
Artonin Q **[84]** 	Stem bark	Aida *et al*., 1994
Artonin R **[85]** 	Stem bark	Aida *et al*., 1994
Artonin S **[86]** 	Stem bark	Aida *et al*., 1994

Table 1 (continued)

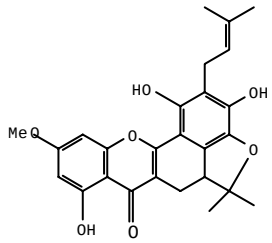
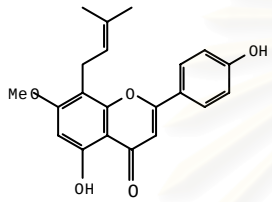
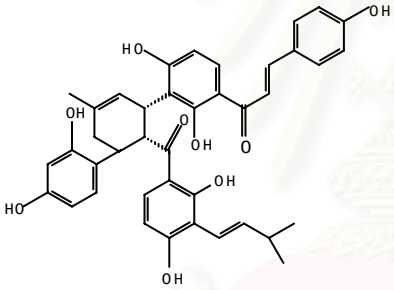
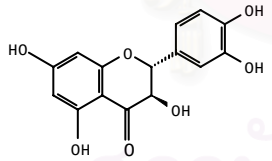
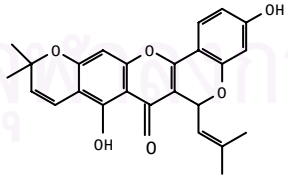
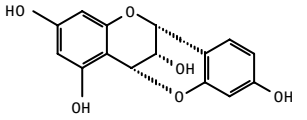
Plant and chemical compound	Plant part	Reference
Artonin T **[87]** 	Stem bark	Aida *et al*., 1994
Artonin U **[88]** 	Stem bark	Aida *et al*., 1994
Artonin X **[89]** 	Stem bark	Shinomiya *et al*., 1995
Catechin **[90]** 	Leaf	Yamazaki *et al*., 1987
Cudraflavone A **[25]** 	Root bark	Lin *et al*., 1995
Cyanomaclurin **[91]** 	Heartwood	Radhakrishnan *et al*., 1965

Table 1 (continued)

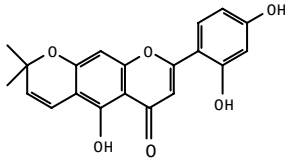
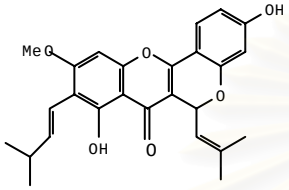
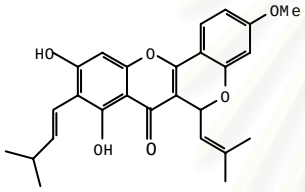
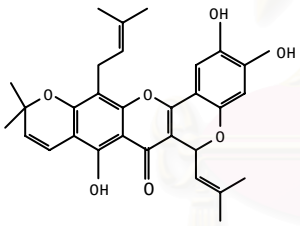
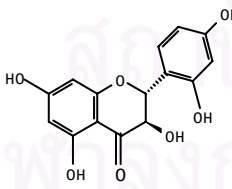
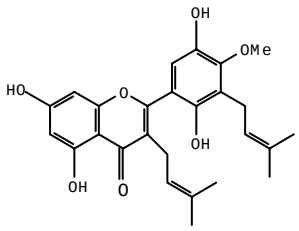
Plant and chemical compound	Plant part	Reference
Cycloartocarpesin **[51]** 	Heartwood	Parthasarathy *et al*., 1969
Cycloartocarpin **[30]** 	Heartwood	Venkataraman, 1972
Cycloartocarpin A **[92]** 	Root bark	Lu and Lin, 1994
Cycloheterophyllin **[93]** 	Stem bark Root bark	Rao, Varadan, and Venkataraman, 1971; Hano *et al*., 1989
Dihydromorin **[39]** 	Heartwood	Venkataraman, 1972
Heteroartonin A **[94]** 	Root	Chung *et al*., 1995

Table 1 (continued)

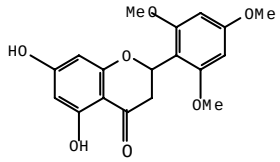
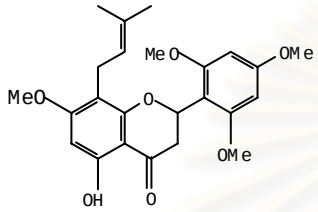
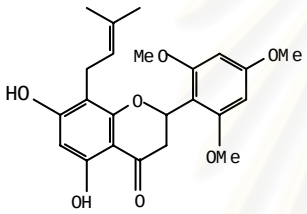
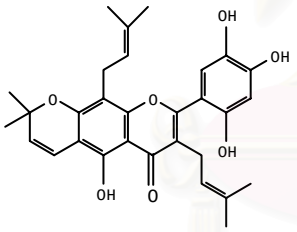
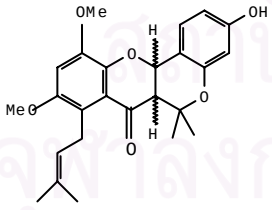
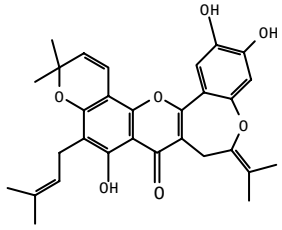
Plant and chemical compound	Plant part	Reference
Heteroflavanone A **[95]** 	Root bark	Lu and Lin, 1993
Heteroflavanone B **[96]** 	Root bark	Lu and Lin, 1993
Heteroflavanone C **[97]** 	Root bark	Lu and Lin, 1994
Heterophyllin **[98]** 	Root bark	Hano *et al*., 1989
Heterophylol **[99]** 	Root bark	Lin and Lu, 1993
Isocycloheterophyllin **[100]** 	Stem bark	Rao, Varadan ,and Venkatarman, 1973

Table 1 (continued)

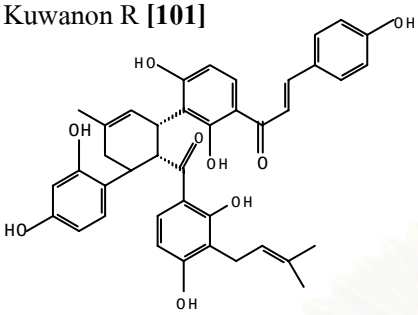
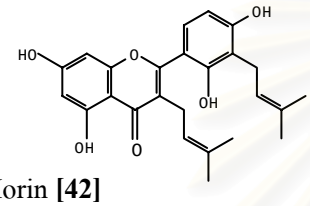
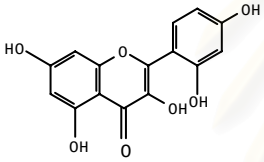
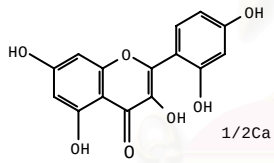
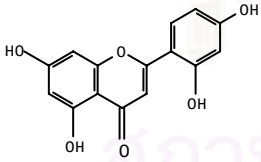
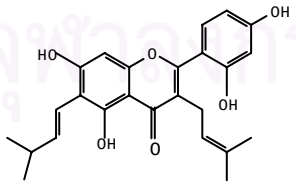
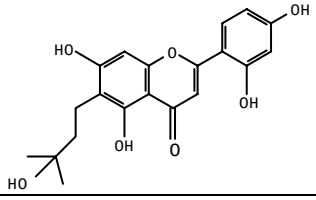
Plant and chemical compound	Plant part	Reference
Kuwanon R **[101]** 	Root bark	Shinomiya *et al*., 1995
Kuwanon T **[102]** 	Root bark	Shinomiya *et al*., 1995
Morin **[42]** 	Heartwood	Radhakrishnan *et al*., 1965 Parthasarathy *et al*., 1969
Morin-calcium-chelate **[103]** 	Heartwood	Mu and Li, 1982
Norartocarpetin **[45]** 	Heartwood	Radhakrishnan *et al*., 1965
Norartocarpin **[67]** 	Heartwood	Venkataraman, 1972
Oxydihydroartocarpesin **[104]** 	Heartwood	Pathasarathy *et al*., 1969

Table 1 (continued)

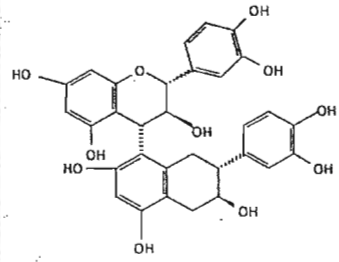
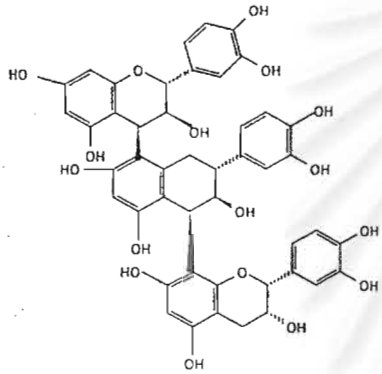
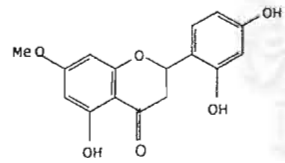
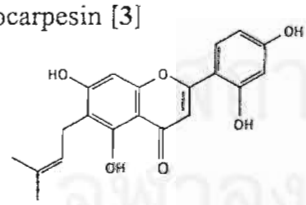
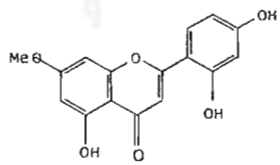
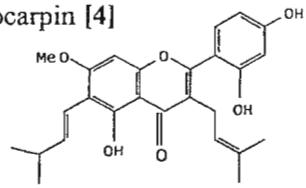
Plant and chemical compound	Plant part	Reference
Procyanidin B-3 **[105]** 	Leaf	An *et al.*,1 992
Procyanidin C-1 **[106]** 	Leaf	An *et al.*, 1992
A.hirsuta		
Artocarpanone **[71]** 	Heartwood	Venkataraman, 1972
Artocarpesin [3] 	Heartwood	Venkataraman, 1972
Artocarpetin **[73]** 	Heartwood	Venkataraman, 1972
Artocarpin **[4]** 	Heartwood	Venkataraman, 1972

Table 1 (continued)

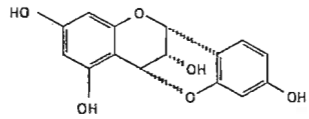
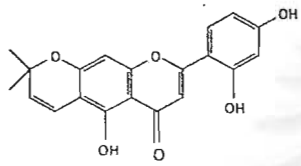
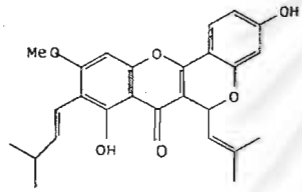
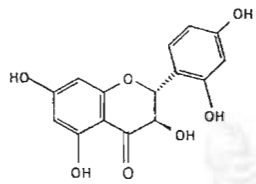
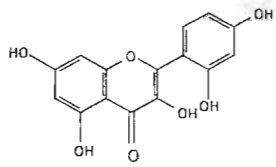
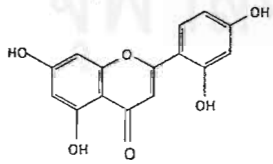
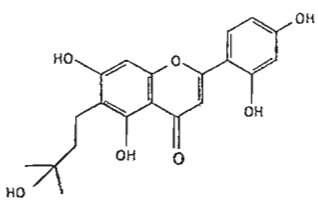
Plant and chemical compound	Plant part	Reference
Cyanomaclurin **[91]** 	Heartwood	Venkataraman, 1972
Cycloartocarpesin **[51]** 	Heartwood	Venkataraman, 1972
Cycloartocarpin **[30]** 	Heartwood	Venkataraman, 1972
Dihydromorin **[39]** 	Heartwood	Venkataraman, 1972
Morin **[42]** 	Heartwood	Venkataraman, 1972
Norartocarpetin **[45]** 	Heartwood	Venkataraman, 1972
Oxydihydroartocarpesin **[104]** 	Heartwood	Venkataraman, 1972

Table 1 (continued)

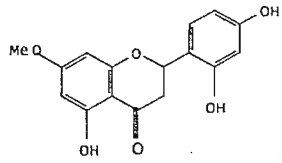
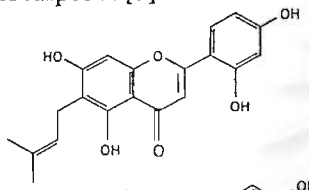
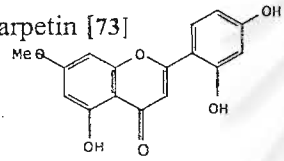
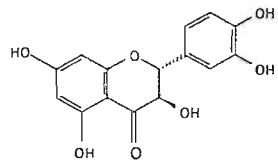
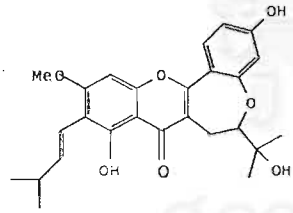
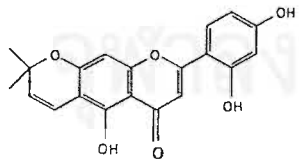
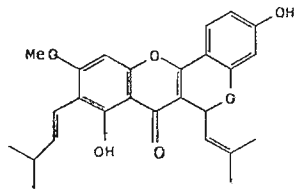
Plant and chemical compound	Plant part	Reference
A.integer		
Artocarpanone [71] 	Heartwood	Pendse *et al.*, 1976
Artocarpesin [3] 	Heartwood	Pendse *et al.*, 1976
Artocarpetin [73] 	Heartwood	Pendse *et al.*, 1976
Catechin [90] 	Leaf	Yamazaki *et al.*, 1987
Chaplashin [50] 	Heartwood	Pendse *et al.*, 1976
Cycloartocarpesin [51] 	Heartwood	Pendse *et al.*, 1976
Cytoartocarpin [30] 	Heartwood	Pendse *et al.*, 1976

Table 1 (continued)

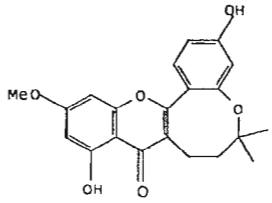
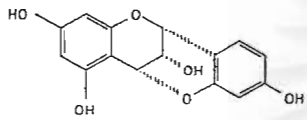
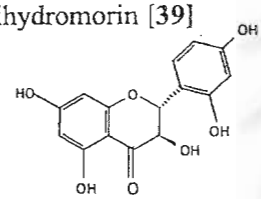
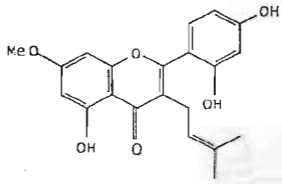
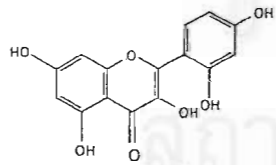
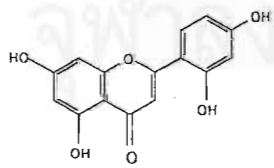
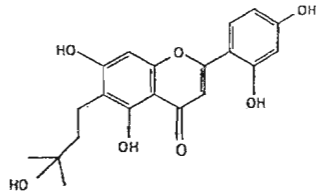
Plant and chemical compound	Plant part	Reference
Cyclointegrin **[107]** 	Heartwood	Pendse *et al.*, 1976
Cyanomaclurin **[91]** 	Heartwood	Pendse *et al.*, 1976
Dihydromorin **[39]** 	Heartwood	Pendse *et al.*, 1976
Integrin **[66]** 	Heartwood	Pendse *et al.*, 1976
Morin **[42]** 	Heartwood	Pendse *et al.*, 1976
Norartocarpetin **[45]** 	Heartwood	Pendse *et al.*, 1976
Oxydihydroartocarpesin **[104]** 	Heartwood	Pendse *et al.*, 1976

Table 1 (continued)

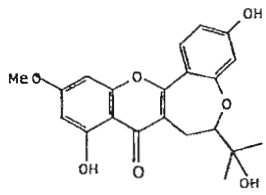
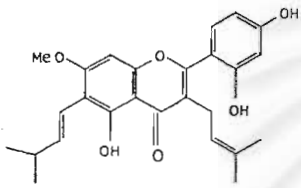
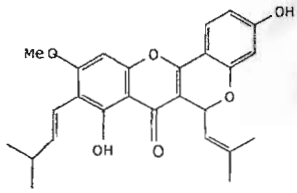
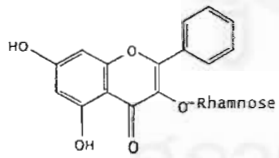
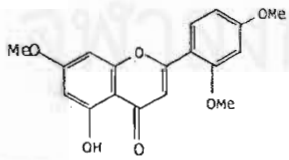
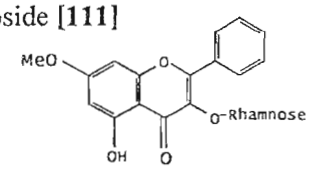
Plant and chemical compound	Plant part	Reference
Oxyisocyclointegrin **[108]** 	Heartwood	Pendse *et al.*, 1976
A.lakoocha		
Artocarpin **[4]** 	Heartwood	Ventakaraman, 1972
Cycloartocarpin **[30]** 	Heartwood	Ventakaraman, 1972
5,7-Dihydroxyflavone-3-*O*-α-L-rhamnoside **[109]** 	Root bark	Chauhan and Kumari, 1979
5-Hydroxy-7,2',4'-trimethoxyflavone**[110]** 	Stem wood	Pavaro and Reutrakul, 1976
Galangin-3- *O*-α-L-(-)-rhamnoside-Pyranoside **[111]** 	Root bark	Chauhan and Kumari, 1979

Table 1 (continued)

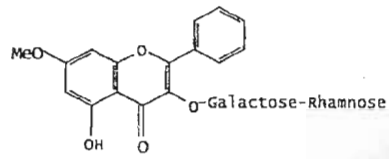
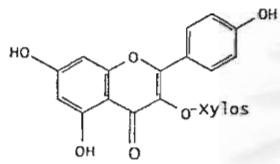
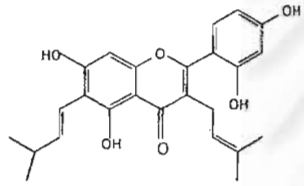
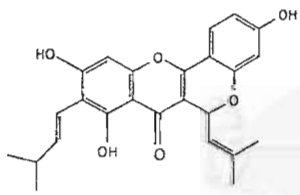
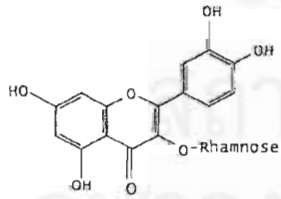
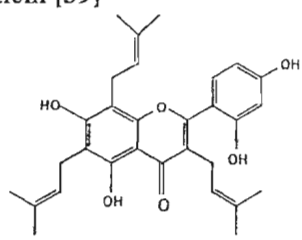
Plant and chemical compound	Plant part	Reference
Galangin-3- *O*-β-D-galactopyranosyl-(1→4)-α-L-rhamnosidepyranoside **[112]** 	Root bark	Chauhan,Kumari and Saraswat, 1979
Kaempferol-3-*O*-β-D-xylanopyranoside **[113]** 	Root bark	Chauhan *et al.*, 1982
Norartocarpin **[67]** 	Heartwood	Venkataraman, 1972
Norcycloartocarpin **[114]** 	Heartwood	Venkataraman, 1972
Quercetin-3-*O*-α-L-rhamnopyranoside **[115]** 	Rootbark	Chauhan *et al.*, 1982
A.lanceifolius		
Artelasticin **[59]** 	Heartwood	Syah *et al.*, 2001

Table 1 (continued)

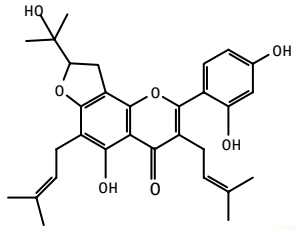
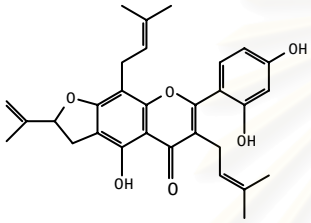
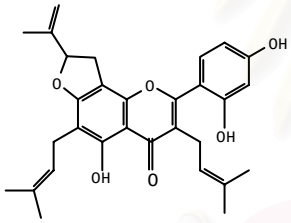
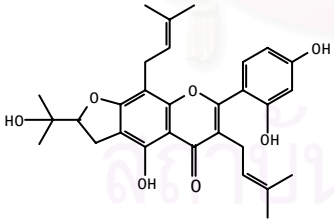
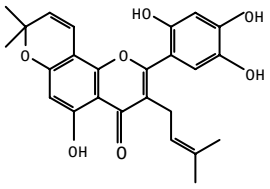
Plant and chemical compound	Plant part	Reference
Artelastofuran **[64]** 	Heartwood	Syah *et al*., 2001
Artoindonesianin G **[116]** 	Heartwood	Syah *et al*., 2001
Artoindonesianin H **[117]** 	Heartwood	Syah *et al*., 2001
Artoindonesianin I **[118]** 	Heartwood	Syah *et al*., 2001
A.nobilis Artobilochromen **[13]** (Artonin E) 	Stem bark	Pavanasasivam,Sultanbawa And Mageswaran, 1974; Kumar *et al*., 1977; Sultanbawa and Surendrakumar, 1989

Table 1 (continued)

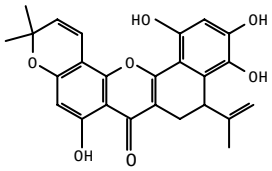
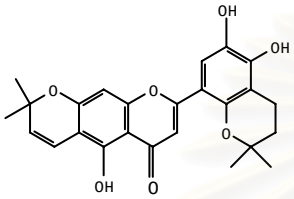
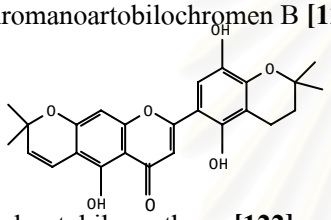
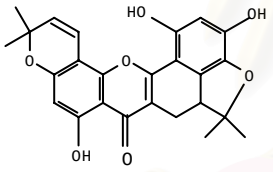
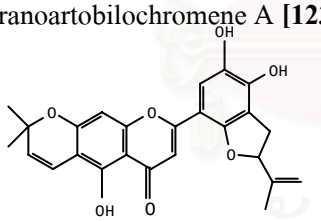
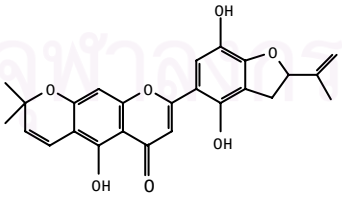
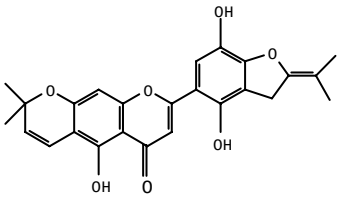
Plant and chemical compound	Plant part	Reference
Artobiloxanthone **[119]** 	Stem bark	Sultanbawa and Surendrakumar, 1989
Chromanoartobilochromen A **[120]** 	Stem bark	Kumar *et al*., 1977
Chromanoartobilochromen B **[121]** 	Stem bark	Pavanasivum *et al*., 1974; Kumar *et al*., 1977
Cycloartobiloxanthone **[122]** 	Stem bark	Sultanbawa and Surendrakumar, 1989
Furanoartobilochromene A **[123]** 	Stem bark	Pavanasivum *et al*., 1974; Kumar *et al*., 1977
Furanoartobilochromene B-1 **[124]** 	Stem bark	Pavanasivum *et al*., 1974; Kumar *et al*., 1977
Furanoartobilochromene B-2 **[125]** 	Stem bark	Pavanasivum *et al*., 1974 Kumar *et al*., 1977

Table 1 (continued)

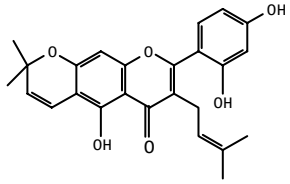
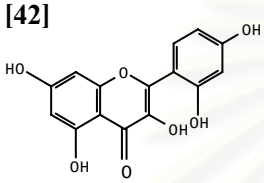
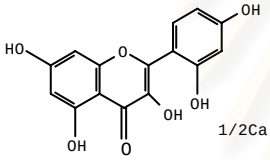
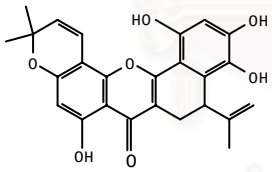
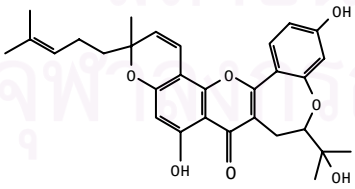
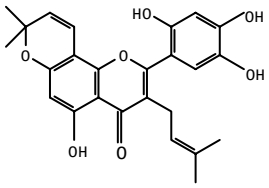
Plant and chemical compound	Plant part	Reference
Oxydihydromorusin **[126]** 	Stem bark	Kumar *et al*., 1977; Fukai and Nomura, 1993
A.pithecogalla		
Morin **[42]** 	Heartwood	Mu and Li, 1982
Morin-calcium-chelate **[103]** 	Heartwood	Mu and Li, 1982
A.rigida		
Artobiloxanthone **[119]** 	Stem bark	Hano, Inami, and Nomura, 1990
Artocarpol B **[127]** 	Root bark	Ko, Lin, and Yang, 2000
Artonin E **[13]** 	Stem bark	Hano, Inami, and Nomura, 1990

Table 1 (continued)

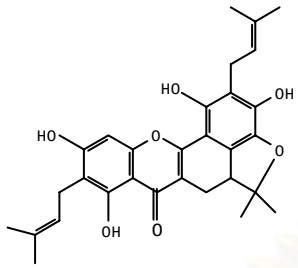
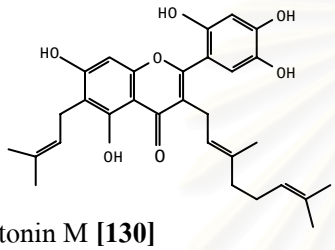
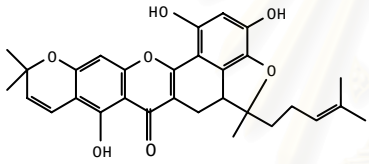
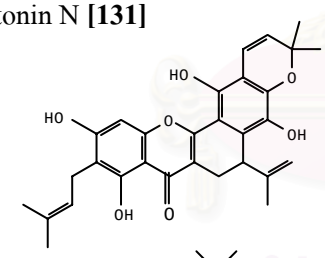
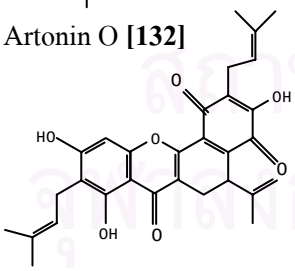
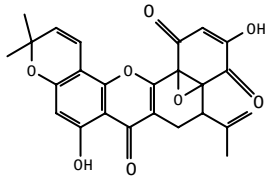
Plant and chemical compound	Plant part	Reference
Artonin G **[128]** 	Stem bark	Hano, Inami, and Nomura, 1990
Artonin H **[129]** 	Stem bark	Hano, Inami, and Nomura, 1990
Artonin M **[130]** 	Root bark	Hano, Inami, and Nomura, 1993
Artonin N **[131]** 	Stem bark	Hano, Inami, and Nomura, 1993
Artonin O **[132]** 	Stem bark	Hano, Inami, and Nomura, 1993
Artonin P **[133]** 	Stem bark	Hano, Inami, and Nomura, 1993

Table 1 (continued)

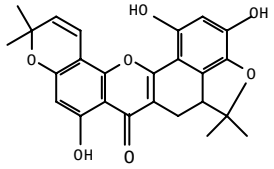
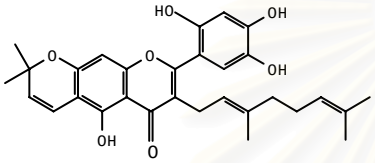
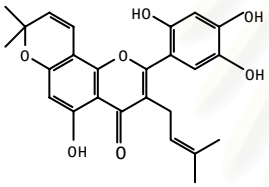
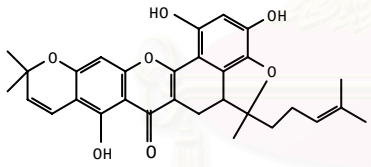
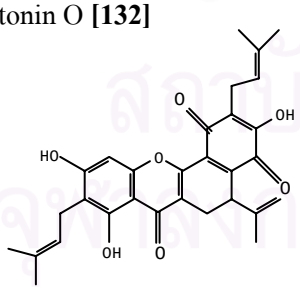
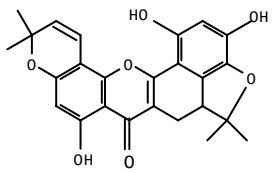
Plant and chemical compound	Plant part	Reference
Cycloartobiloxanthone **[122]** 	Stem bark	Hano, Inami, and Nomura, 1990
A.rotunda		
Artoindonesianin L **[134]** 	Root bark	Suhartati *et at*., 2001
Artonin E **[13]** 	Root bark	Suhartati *et al*., 2001
Artonin M **[130]** 	Root bark	Suhartati *et al*., 2001
Artonin O **[132]** 	Root bark	Suhartati *et al*., 2001
Cycloartobiloxanthone **[122]** 	Root bark	Suhartati *et al*., 2001

Table 1 (continued)

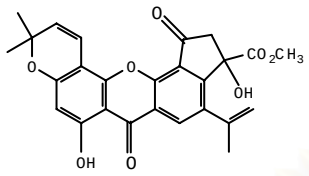
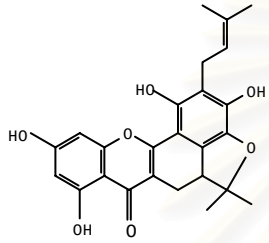
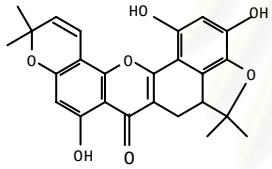
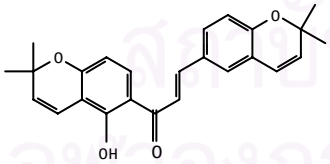
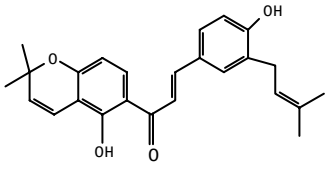
Plant and chemical compound	Plant part	Reference
A.teysmanii		
Artoindonesianin C **[135]** 	Root bark	Makmur *et al*., 2000
Artonin J **[82]** 	Root bark	Makmur *et al*., 2000
Cycloartobiloxanthone **[122]** 	Root bark	Makmur *et al*., 2000
A.tonkiensis		
Artotonkin **[136]**	Stem bark	Lein *et al*., 1998
A.venenosa		
Paratocarpin A **[137]** 	Stem bark	Hano *et al*.,1995a; Nomura, Hano, and Aida, 1998
Paratocarpin B **[138]** 	Stem bark	Hano *et al*.,1995a; Nomura, Hano, and Aida, 1998

Table 1 (continued)

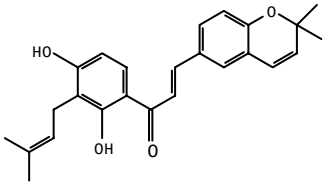
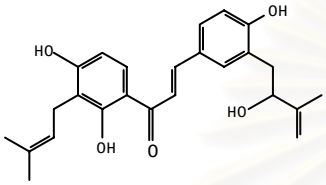
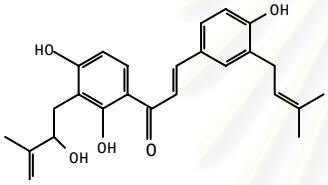
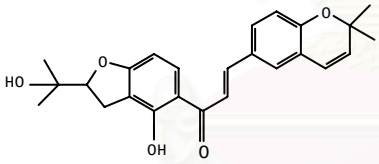
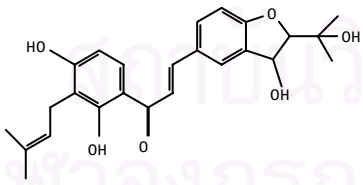
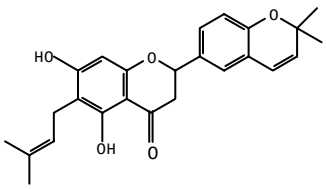
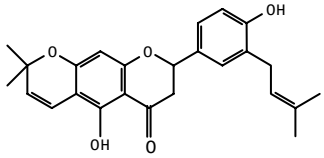
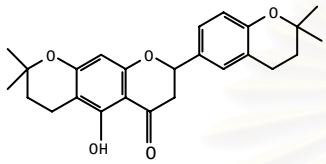
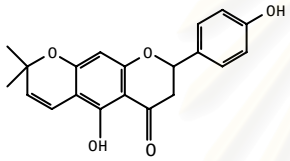
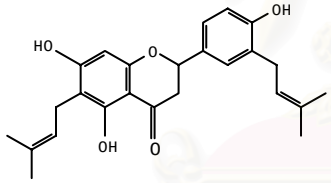
Plant and chemical compound	Plant part	Reference
Paratocarpin C **[139]** 	Stem bark	Hano *et al*., 1995a; Nomura, Hano, and Aida, 1998
Paratocarpin D **[140]** 	Stem bark	Hano *et al*., 1995a; Nomura, Hano, and Aida, 1998
Paratocarpin E **[141]** 	Stem bark	Hano *et al*.,1 995a; Nomura, Hano, and Aida, 1998
Paratocarpin F **[142]** 	Stem bark	Hano *et al*., 1995b; Nomura, Hano, and Aida, 1998
Paratocarpin G **[143]** 	Stem bark	Hano *et al*., 1995b; Nomura, Hano, and Aida, 1998
Paratocarpin H **[144]** 	Stem bark	Hano *et al*., 1995b; Nomura, Hano, and Aida, 1998

Table 1 (continued)

Plant and chemical compound	Plant part	Reference
Paratocarpin I **[145]** 	Stem bark	Hano *et al*., 1995b; Nomura, Hano, and Aida, 1998
Paratocarpin J **[146]** 	Stem bark	Hano *et al*., 1995b; Nomura, Hano, and Aida, 1998
Paratocarpin K **[147]** 	Stem bark	Hano *et al*., 1995b; Nomura, Hano, and Aida, 1998
Paratocarpin L **[148]** 	Stem bark	Hano *et al*., 1995b; Nomura, Hano, and Aida, 1998

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The distribution of triterpenoids in the genus *Artocarpus* are shown in table 2.

Table 2. Distribution of triterpenoids in the *Artocarpus*.

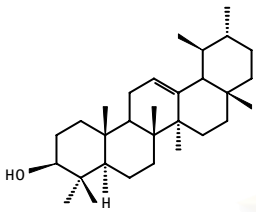
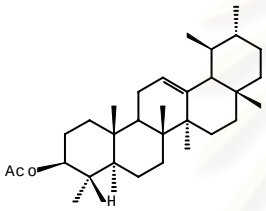
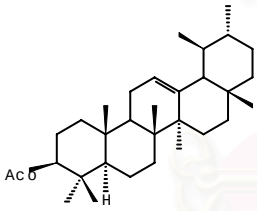
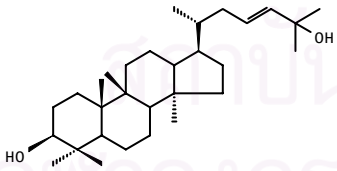
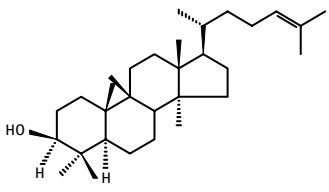
Plant and chemical compound	Plant part	Reference
A.altilis		
α-Amyrin **[149]** 	Latex	Ultee, 1949
α-Amyrin acetate**[150]** 	Fruit	Altman and Zito, 1976
β-Amyrin acetate**[151]** 	Latex	Ultee, 1949
Cycloart-23-ene-3β-25-diol **[152]** 	Fruit	Altman and Zito, 1976
Cycloart-24-ene-3β-25-ol **[153]** 	Fruit	Altman and Zito, 1976

Table 2 (Continued)

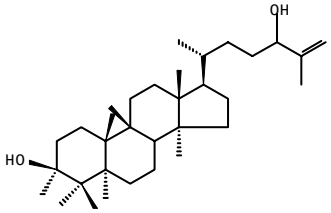
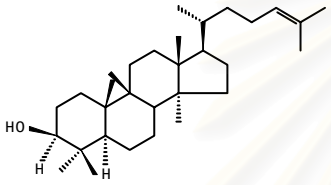
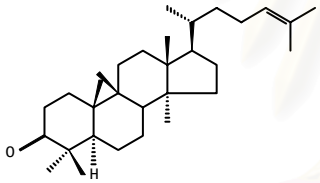
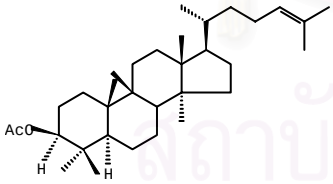
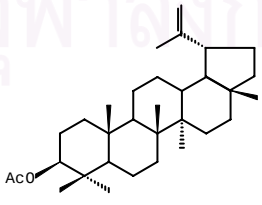
Plant and chemical compound	Plant part	Reference
Cycloart-25-ene-3β-24-diol **[154]** 	Fruit	Altman and Zito, 1976
Cycloartenol **[153]** (Cycloart-24-ene-3β-ol) 	Stem bark	Pavanasasivam and Sultanbawa, 1973
Cycloartonone **[155]** 	Stem bark	Pavanasasivam and Sultanbawa, 1973
Cycloartenyl acetate **[156]** 	Stem bark	Pavanasasivam and Sultanbawa, 1973
Lupeol acetate **[157]** 	Root bark	Shieh and Lin, 1992

Table 2 (Continued)

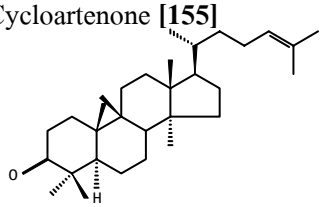
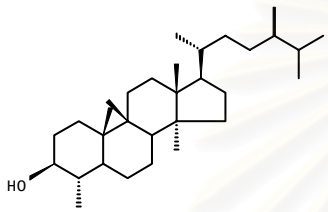
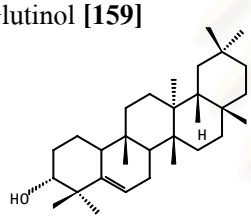
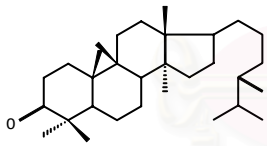
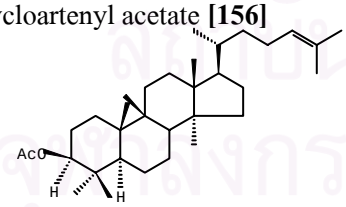
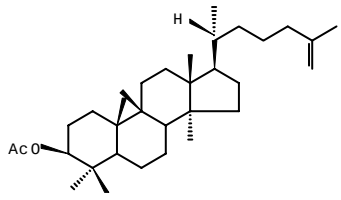
Plant and chemical compound	Plant part	Reference
A.Champeden		
Cycloartenone **[155]** 	Stem bark	Achmad *et al*., 1996
Cycloeucalenol **[158]** 	Stem bark	Achmad *et al*., 1996
Glutinol **[159]** 	Stem bark	Achmad *et al*., 1996
24-Methylenecycloartanone **[160]** 	Stem bark	Achmad *et al*., 1996
A.chaplasha		
Cycloartenyl acetate **[156]** 	Stem bark	Mahato, Banerjee, and Chakravarti, 1971
Isocycloartenol acetate **[161]** 	Stem bark	Mahato *et al*., 1971

Table 2 (Continued)

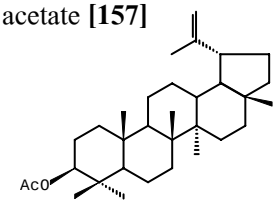
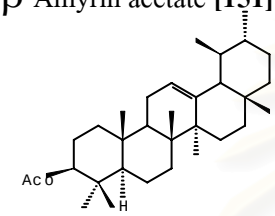
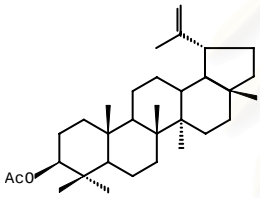
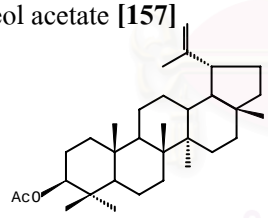
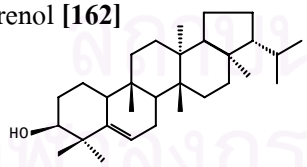
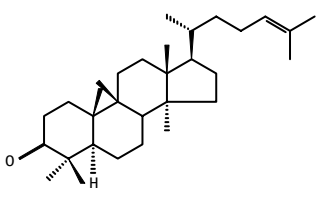
Plant and chemical compound	Plant part	Reference
Lupeol acetate **[157]** 	Stem bark	Mahato *et al*., 1971
A.elasticus		
β-Amyrin acetate **[151]** 	Latax	Ultee, 1949
Lupeol acetate **[157]** 	Latex	Ultee, 1949
A.gomezianus		
Lupeol acetate **[157]** 	Leaf	Kingroungpet, 1994
Simiarenol **[162]** 	Leaf	Kingroungpet, 1994
A.heterophyllus		
Artostenone (Cycloartonone) **[155]** 	Fruit	Nath and Mukherjee, 1939

Table 2 (Continued)

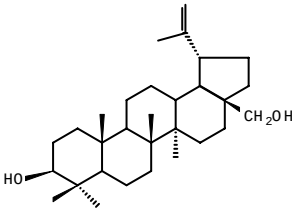
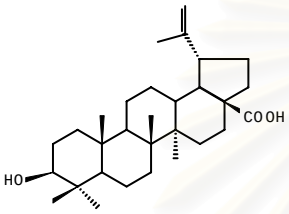
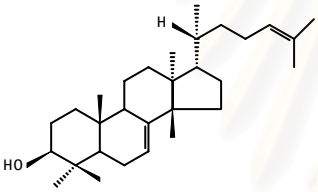
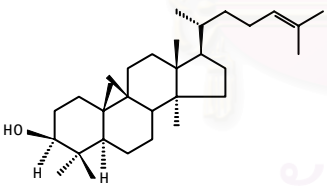
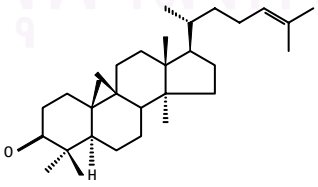
Plant and chemical compound	Plant part	Reference
Betulin **[163]** 	Root bark	Lu and Lin, 1994
Betulinic acid **[164]** 	Root Root bark	Dayal and Seshadri, 1974 Lu and Lin, 1994
Butyrospermol **[165]** 	Fruit	Barton, 1951
Cycloartenol **[153]** 	Fruit Wood Stem bark Latex	Barton, 1951 Nogueira and Correia, 1958; Pavanasasivam and Sultanbawa, 1973 Barik *et al*., 1994
Cycloartenone**[155]** 	Fruit Stem bark Root Latex	Barton, 1951; Pavanasasivam and Sultanbawa, 1973 Dayal and Seshadri, 1974; Pant and Chaturvedi, 1989; Barik *et al*., 1994

Table 2 (Continued)

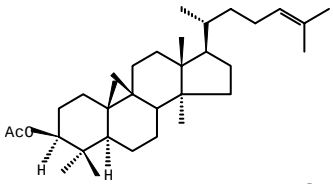
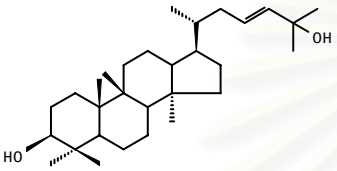
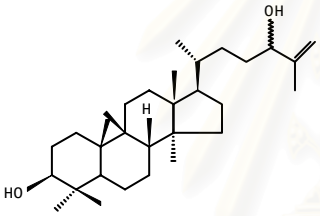
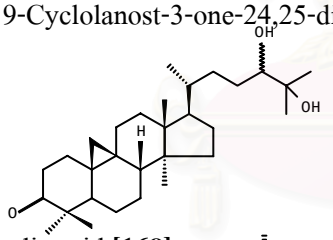
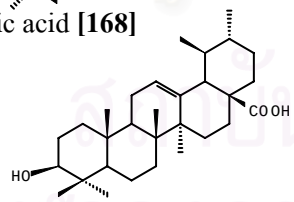
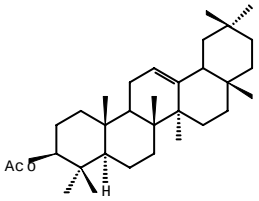
Plant and chemical compound	Plant part	Reference
Cycloartenyl acetate **[156]** 	Stem bark	Pavanasasivam and Sultanbawa, 1973
9,19-Cyclolanost-23-ene-3β,25-diol(Cycloart-23-ene-3,25-diol) **[152]** 	Fruit	Kielland and Malterud, 1994
9,19-Cyclolanost-25-ene-3β,24-diol **[166]** 	Fruit	Kielland and Malterrud, 1994 Barik *et al*., 1997
9,19-Cyclolanost-3-one-24,25-diol **[167]** 	Latex	Barik *et al*., 1994
Ursolic acid **[168]** 	Root Root bark	Dayal and Seshadri, 1974; Lu and Lin, 1994
A.lakoocha β-Amyrin acetate **[151]** 	Stem bark	Kapil and Joshi, 1960

Table 2 (Continued)

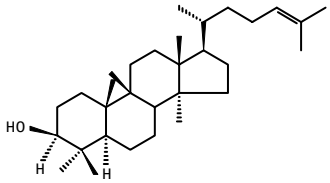
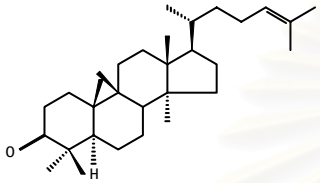
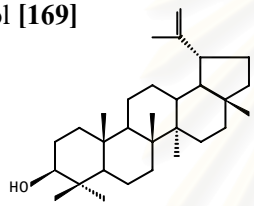
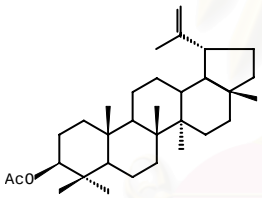
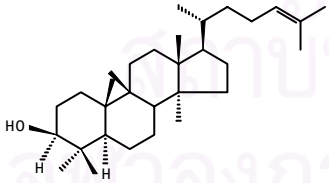
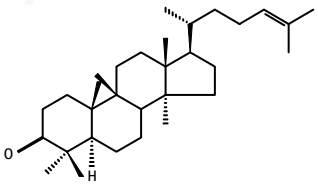
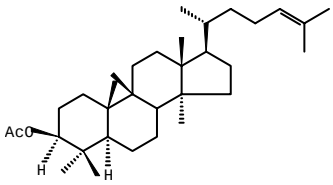
Plant and Chemical compound	Plant part	Reference
Cycloartenol **[153]** 	Stem bark	Pavanasasivam and Sultanbawa, 1973
Cycloartenone **[155]** 	Stem bark	Pavanasasivam and Sultanbawa, 1973
Lupeol **[169]** 	Root bark	Chauhan and Kumari, 1979
Lupeol acetate **[157]** 	Stem bark	Kapil and Joshi, 1960
A.nobilis		
Cycloartenol **[153]** 	Stem bark Heartwood	Pavanasasivam and Sultanbawa, 1973
Cycloartenone **[155]** 	Stem bark Heartwood	Pavanasasivam and Sultanbawa, 1973

Table 2 (Continued)

Plant and Chemical compound	Plant part	Reference
Cycloartenyl acetate **[156]** 	Stem bark Heartwood	Pavanasasivam and Sultanbawa, 1973

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The distribution of miscellaneous compound in the genus *Artocarpus* are shown in table 3.

Table 3. Distribution of miscellaneous compounds in the *Artocarpus.*

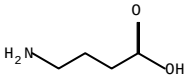
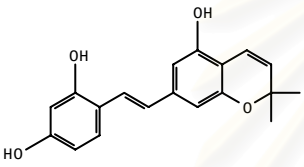
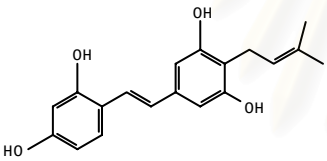
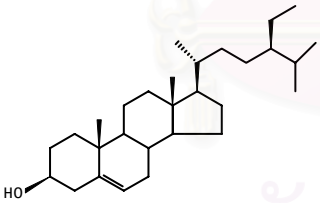
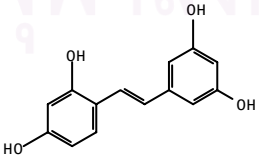
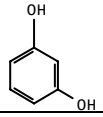
Plant and Chemical compound	Category	Plant part	Reference
A.altilis			
γ-Aminobutyric acid **[170]** 	Amino acid	Leaf	Durand *et al*., 1962
Artocarbene **[171]** 	Stilbebe	Heartwood	Shimizu *et al*., 1997
4-Prenyloxyresveratrol **[172]** 	Stilbene	Heartwood	Shimizu *et al*., 1997
β-Sitosterol **[173]** 	Steroid	Root bark	Shieh and Lin, 1992
A.chaplasha			
Oxyresveratrol **[174]** 	Stilbene	Heartwood	Rao *et al*., 1972
Resorcinol **[175]** 	Benzenoid	Heartwood	Rao *et al*., 1972

Table 3 (Continues)

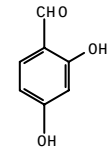
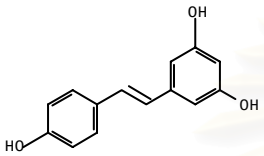
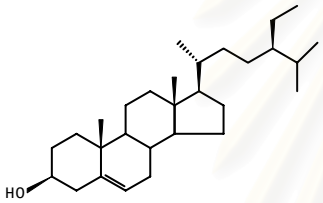
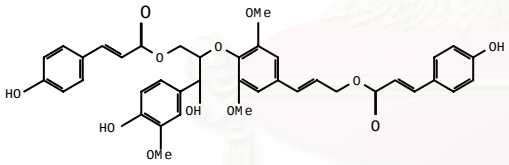
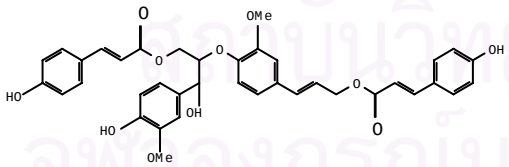
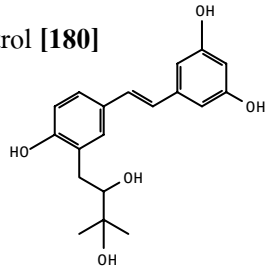
Plant and Chemical compound	Category	Plant part	Reference
β-Resorcyaldehyde **[176]** 	Benzenoid	Heartwood	Rao *et al*., 1972
Resveratrol **[177]** 	Stilbene	Heartwood	Rao *et al*., 1972
β-Sitosterol **[173]** 	Steroid	Stem bark	Mahato *et al*., 1971
A.dadah Dadahol A **[178]** 	Neolignan	Twing	Su *et al*., 2002
Dadahol B **[179]** 	Neolignan	Twing	Su *et al*., 2002
3-(2,3-dihydroxy-3-methylbutyl)-resveratrol **[180]** 	Stilbene	Stem bark	Su *et al*., 2002

Table 3 (Continues)

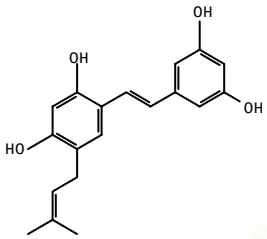
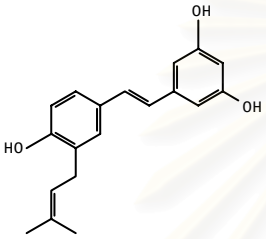
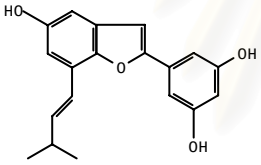
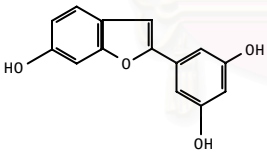
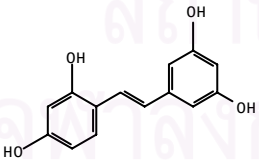
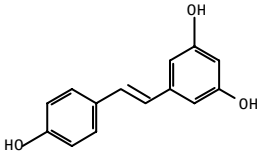
Plant and chemical compound	Category	Plant part	Reference
3-(γ,γ-dimethylally)oxyresveratrol **[181]** 	Stibene	Stem bark	Su *et al*.,2002
3-(γ,γ-dimethylally) resveratrol **[182]** 	Stilbene	Stem bark	Su *et al*.,2002
3-(γ,γ-dimethypropenyl)moracinM**[183]** 	Stilbene	Stem bark	Su *et al*.,2002
Moracin M **[184]** 	Stilbene	Twing	Su *et al*.,2002
Oxyresveratrol **[174]** 	Stilbene	Stem bark Twig	Su *et al*.,2002
Resveratrol **[177]** 	Stilbene	Twig	Su *et al*.,2002

Table 3 (Continues)

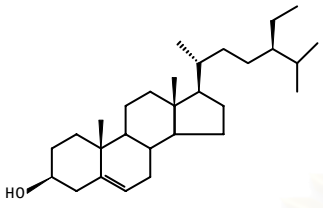
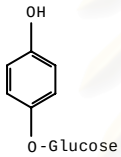
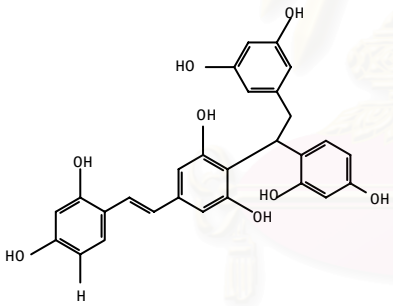
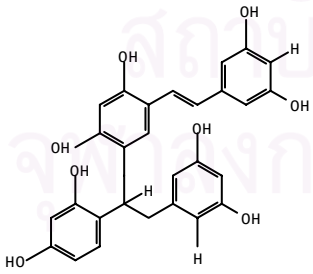
Plant and chemical compound	Category	Plant part	Reference
A.elasticus			
β-Sitosterol **[173]** 	Steroid	Heartwood	Pendese *et al*., 1976
A.gomezianus			
Arbutin **[185]** 	Phenolic Glycoside	Leaf	Kingroungpet, 1994
Andaracin A **[186]** 	Stilbene	Root	Likhitwitayawuid , and Sritularak, 2001
Artogomezianol**[187]** 	Stilbene	Root	Likhitwitayawuid , and Sritularak, 2001
1-Dotriacontanol **[188]** $HOCH_2CH_2(CH_2)_{29}CH_3$	Alcohol	Leaf	Kingroungpet, 1994

Table 3 (Continues)

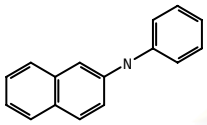
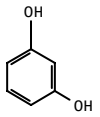
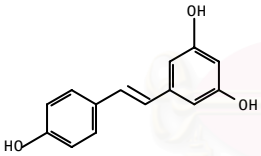
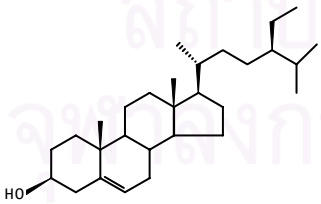
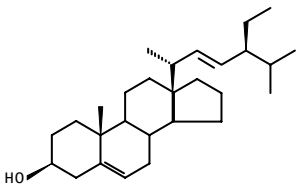
Plant and chemical compound	Category	Plant part	Reference
Mesoerythritol **[189]**	Phenolic Compound	Heart wood	Venkataraman, 1972
Phenyl-β-naphthylamine **[190]** 	Naphalene	Root	Sritularak, 1998; Likhiwitayawuid, Sritularak and De-Ek-Namkul, 2000
Resorcinol **[175]** 	Benzenoid	Root	Sritularak, 1998
Resveratrol **[177]** 	Stibene	Root	Sritularak, 1998; Likhiwitayawuid, Sritularak and De-Ek-Namkul, 2000
β-Sitosterol **[173]** 	Steroid	Leaf	Kingroungpet, 1994
Stigmasterol**[189]** 	Steroid	Root	Sritularak, 1998

Table 3 (Continues)

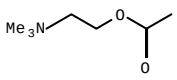
Plant and chemical compound	Category	Plant part	Reference
A.heterophylllus			
Acetycholine**[191]** 	Amine	Seed	Pereria,Medina and Bustor, 1962
Artocarpus integra α-D-Galactose specific lactin **[192]**	Lectin	Seed	Suresh,Appukuttan,and Basu,1982
Artocarpus integrifolia lectin **[193]**	Lectin	Seed	Chatterjee,Sarkar,and Rao,1982; Namjuntra and Culavanatol,1984
Artocarpus lectin CE-A-I **[194]**	Lectin	Seed	Ferreira *et al*.,1992
Aurantiamine acetate **[195]**	Protein	Seed	Chakraborty and Mandal, 1981
9-Hydroxytridecyl docosanoate **[196]** $CH_3(CH_2)_{20}COO(CH_2)_8CH(OH)(CH_2)_3CH_3$	Lipid	Root bark	Lu and Lin,1994
4-Hydroxyundecyl docosanoate**[197]** $CH_3(CH_2)_{20}COO(CH_2)_3CH(OH)(CH_2)_6CH_3$	Lipid	Latex	Pant and Chaturvedi,1989
Jacatin **[198]**	Lectin	Seed	Hagiwara *et al*.,1988 Ferreira *et al*.,1992
Lymphoagglutinin **[199]**	Lectin	Seed	Arora *et al*.,1987

Table 3 (continued)

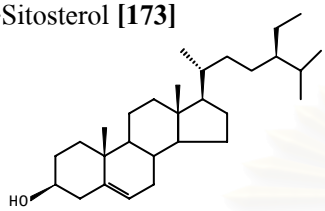
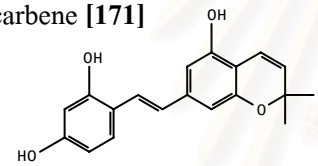
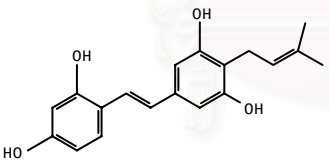
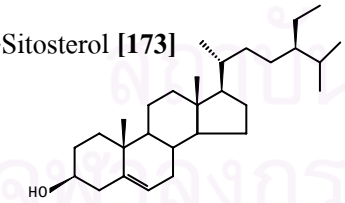
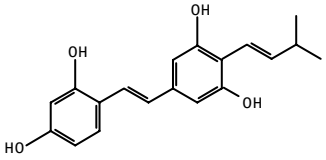
Plant and chemical compound	Category	Plant part	Reference
Recinoleic acid **[200]** $CH_3(CH_2)_5CH(OH)CH_2CH=CH(CH_2)_7COOH$	Lipid	Seed	Daulabad and Mirajkar, 1989
β-Sitosterol **[173]** 	Steroid	Heartwood Root Root bark	Pathasarsthy *et al*.,1969; Dayal and Seshadri,1974 Lu and Lin ,1994
A.hirsuta Lymphoagglutinin **[201]**	Lectin	Seed	Arora *et al*.,1987
A.integer Artocarbene **[171]** 	Stilbene	Aerial part	Boonlaksiri *et al*.,2000
Artocarpus lectin **[202]**	Lectin	Seed	Hashim,Gendel and Jaafar,1992
4-Prenyloxyresveratrol **[172]** 	Stilbene	Aerial part	Boonlaksiri *et al*.,2000
β-Sitosterol **[173]** 	Steroid	Heartwood	Pendse *et al*.,1976
Tran-4-(3-methy-E-but-1-enyl)-3,5,2',4'-tetrahydroxystilbene **[203]** 	Stilbene	Aerial part	Boonlaksiri *et al*.,2000

Table 3 (continued)

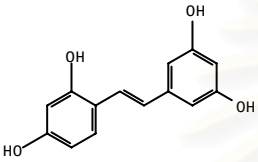
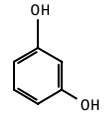
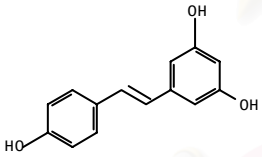
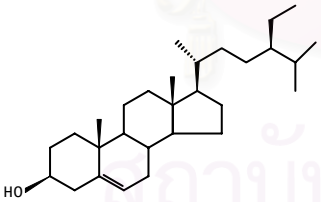
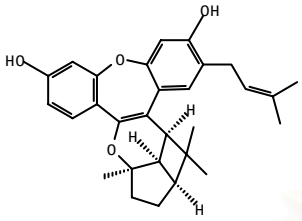
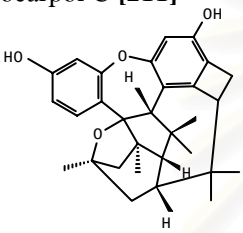
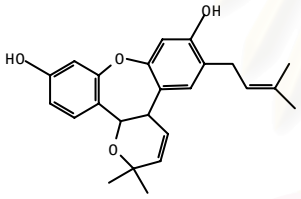
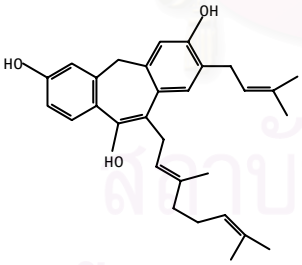
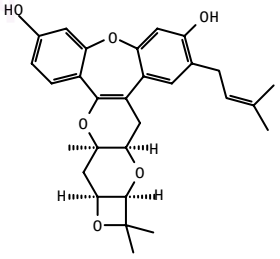
Plant and chemical compound	Category	Plant part	Reference
A.lakoocha			
ALA-I **[204]**	Isolectin	Seed	Wongkham *et al*.,1995
ALA-II **[205]**	Isolectin	Seed	Wongkham *et al*.,1995
Artocarpus lakoocha lectin **[206]**	Lectin	Seed	Chatterjee *et al*.,1982
Lymphoagglutinin **[201]**	Lectin	Seed	Arora *et al*.,1987
Oxyresveratrol **[174]** 	Stilbene	Heartwood	Venkataraman,1972; Mongolsuk,Robertson and Towers,1957
Resorcinol **[175]** 	Benzenoid	Heartwood	Venkataraman,1972
Resveratrol **[177]** 	Stilbene	Heartwood	Venkataraman,1972
β-Sitosterol **[173]** 	Steroid	Root bark	Chauhan and Kumari 1979
A.lignansis			
Artocarpus lectin **[207]**		Seed	Zhang *et al*.,1999
A.masticatus			
Artocarpus lectin AM **[208]**		Seed	Blasco *et al*.,1996
A.melinoxylus			
Artocarpus lectin AME **[209]**		Seed	Blasco *et al*.,1996

Table 3(continued)

Plant and chemical compound	Category	Plant part	Reference
A.rigida			
Artocarpus A **[210]** 	Phenolic	Root bark	Chung *et al*.,2000
Artocarpol C **[211]** 	Phenolic	Root bark	Ko,Lin,and Yang,2000
Artocarpol D **[212]** 	Phenolic	Root bark	Ko,Lin,and Yang,2000
Artocarpol E **[213]** 	Phenolic	Root bark	Ko,Lin,and Yang,2000
Artocarpol F **[214]** 	Phenolic	Root bark	Ko,, Yang and Lin,2000

Biosynthesis of flavonoids

1. General aspects

All classes of flavonoids are biosynthetically closely related, with a chalcone being the first common intermediate (Scheme 1 and 2). Earlier feeding experiments with radioactivety labelled precursor have established that the chalcone skeleton is derived from acetate and phenylalanine: A ring is form by head to tail condensation of three acetate unit and B ring as well as carbon 2, 3 and 4 of the heterocyclic C ring arise from phenylalanine (Wollenweber, 1982)

The common substituents of flavonoid compounds are hydroxyl groups, which may be methylated or glycosylated. The location of some hydroxyl groups is a consequence of the general biosynthetic pathway. Thus, in most flavonoid compounds ring A has hydroxyl groups either at C-7 or at both C-5 and C-7. These are rarely methylated. Ring B is virtually always hydroxylated at C-4′ and commonly also at C-3′ and C-5′ ; hydroxyl groups at this latter two positions are often methylated (Britton, 1983)

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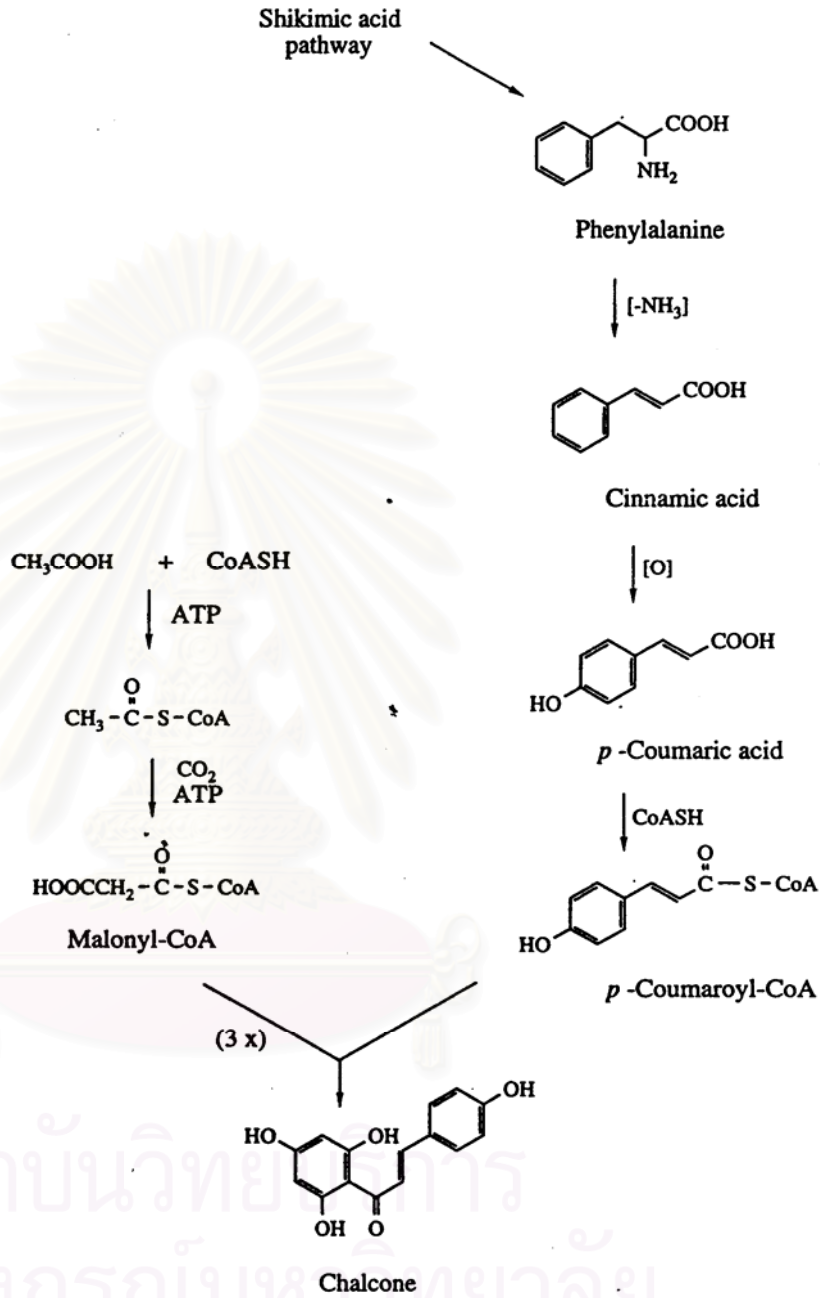

Scheme 1 Biosynthetic pathway of flavonoids

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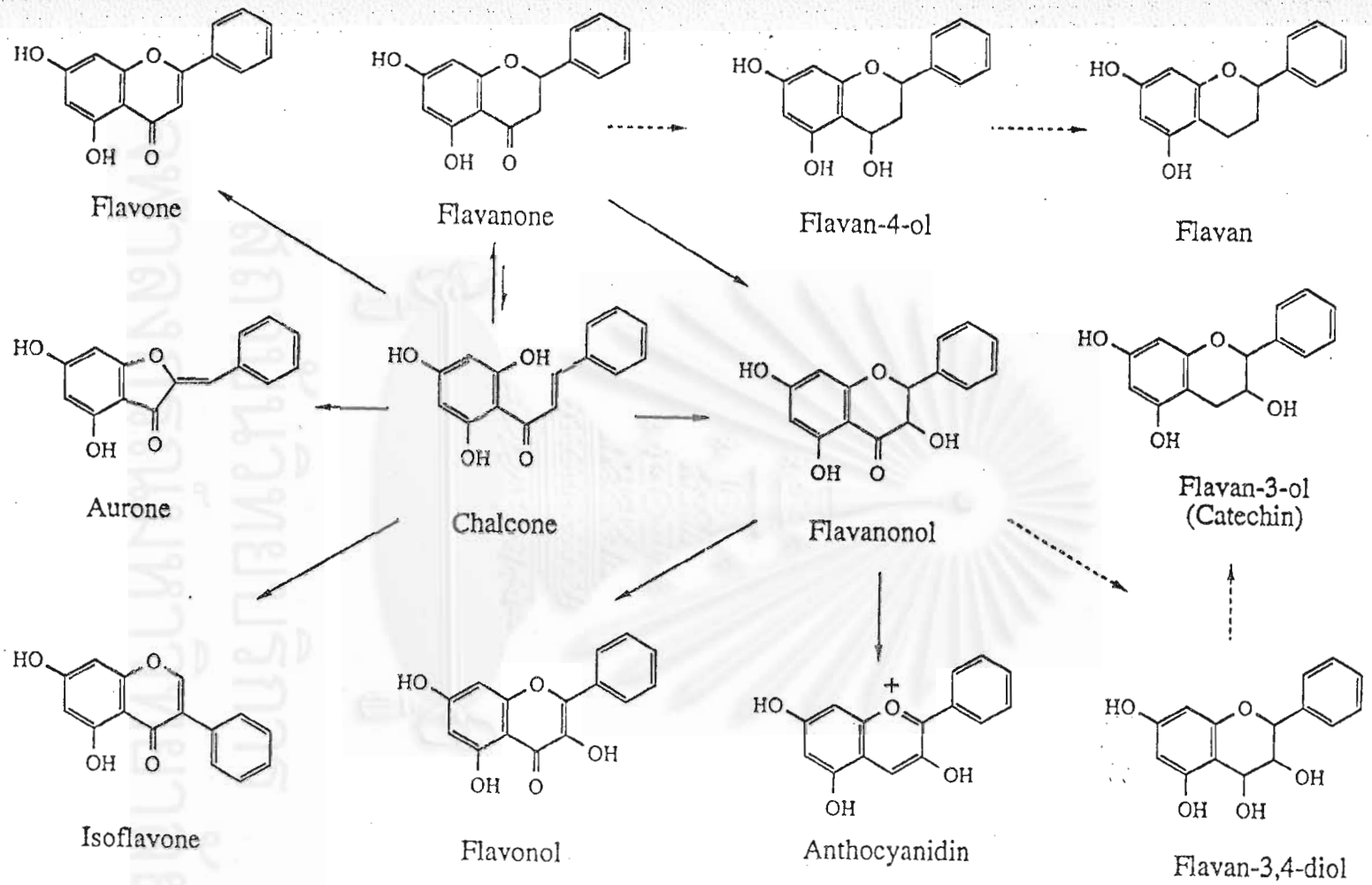
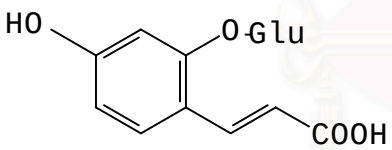


Scheme 2 Overall scheme of flavonoid biosynthesis illustrating demonstrated (⟶) and postulated (------>) biogenetic relationships among the various flavonoid classes.

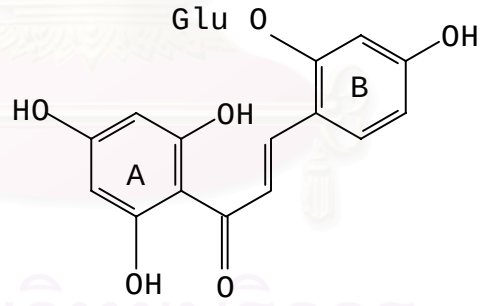
2. Biogenetic aspect of Moraceous Flavonoids

The biogenesis of *Artocarpus* pigments is of special interest because of their unique structural features; the β- resorcylic acid orientation of hydroxyl group in the B-ring in all the compounds (with an additional hydroxyl in cycloheterophyllin) and the C-5 substituent in the 3-position in artocarpin , cycloartocarpin and cycloheterphyllin . All the flavonoids isolated so far from *Artocarpus heterophyllus* fit into a biosynthetic scheme
(Scheme 3) in which the hydroxylation pattern of both the A and B ring is fixed at the chalcone stage; an exception is cycloheterophyllin.

The only other flavone having 2′,4′-hydroxylation is morin, the colouring matter of 'old fustic', *Morus tinctoria*, which also occurs in *M. alba*, *M. bambycis* and *Maclura pomifera* , and the flavones, mulberrin, cyclomulberrin, mulberrochromene, and cyclomulb errochromene , isolated from *Morus alba* bark, which are similar to some of the *Artocarpus* pigments in having a C-5 unit attached to the 3-and 6- positions of the chromene ring.Both species appear to be unique among plants in possessing an enzyme system which directed [215] to a pathway in which it condenses with a phloroglucinol precursor in the acetate route to form the chalcone [216] (Rao *et al.* , 1971)

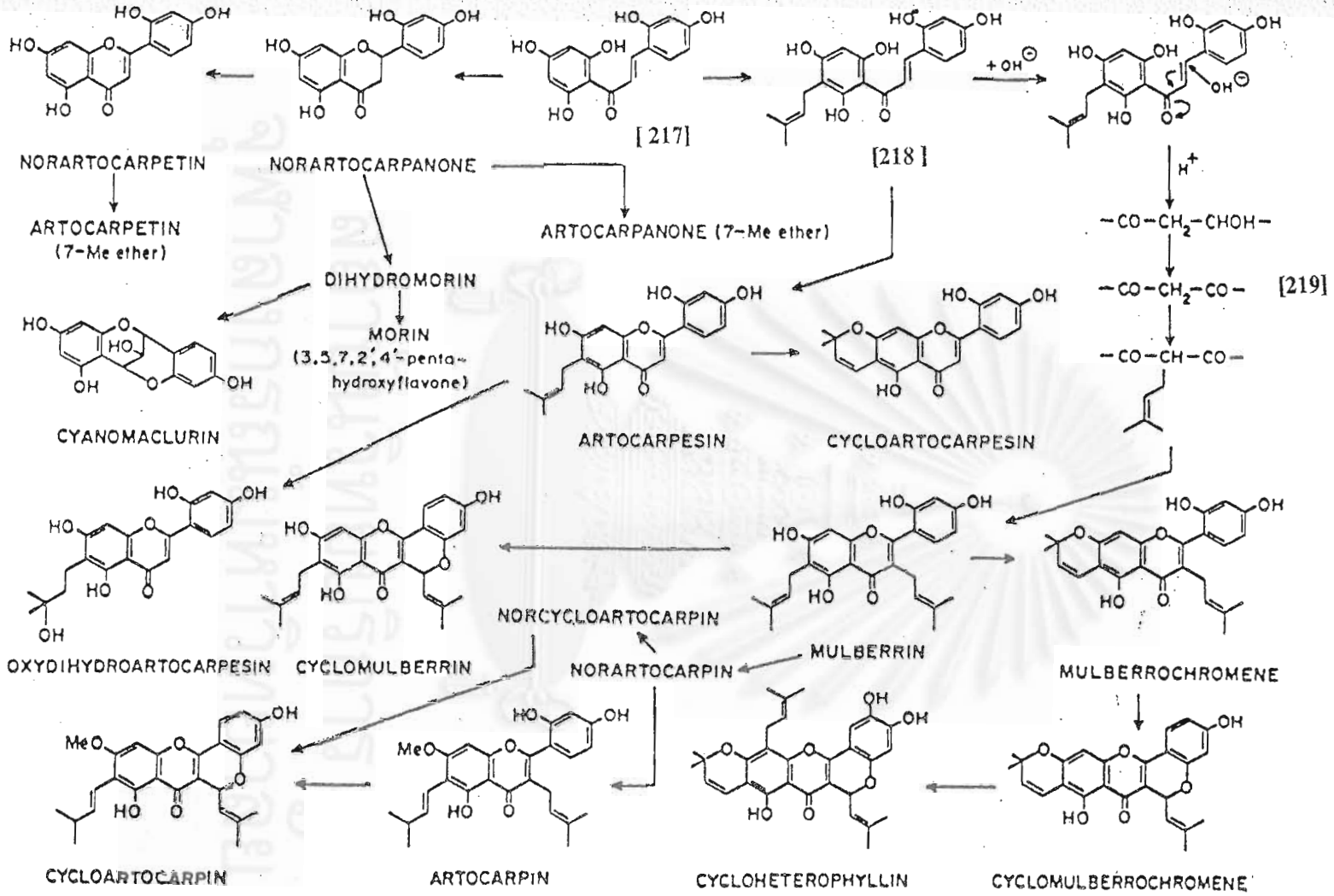


[215]



[216]

Attachment of the phloroglucinol nucleus of the chalcone [217] by one unit of γ,γ-dimethylallyl pyrophosphate leads the prenylated chalcone [218] and artocarpin.The dibezoylmethan [219] may be formed as indicated, and attack by a second unit of dimethylallyl pyrophosphate, followed by cyclization and shift of an olefinic bond to conjugate with the benzene ring, will lead to artocarpin. Further cyclization of artocarpin to cycloartocarpin involves the oxidation of the boubly allylic CH_2 to CHOH (Radhakrishnan, Rao and Venkataraman, 1965)



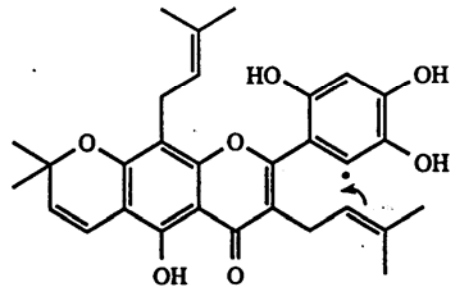
Scheme 3 Biogenesis of the flavonoids isolated from *A.heterophyllus*

In the biosynthetic of cycloheterophyllin [93] the attack of the third γ,γ-dimethylallyl group may occur at any stage; but the additional hydroxylation in the B ring probably represents the final step (Rao *et al*., 1971). Although a number of isoflavones having 2′, 4′, 5′ pattern of oxygenation are know, few such flavones with this unusual oxygenation pattern are report (e.g. cycloheterophyllin [93], and isocycloheterophyllin [100] from the bark of *Artocarpus heterophyllus* and artobilochromen [13], chromanoartobilo -chromen B[121]).The other flavones isolated thus far from *Artocarpus* have the 2′-4′-oxygenetion pattern; it is likely that the additional hydroxylation on B ring occurs during the final step of biosynthesis (Kumar *et al*., 1977).

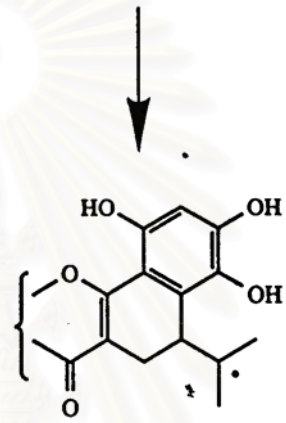
Both artonin A [77] and B [78] have unique structure in which the C-C linkage takes place between the C-6′ position of the B ring and C-10 position of isoprenoid moiety located at the C-3 position. Taking no optical activities into account, artonin A and B are biogenetically assumed to be derived from heterophyllin [98] through the oxidation coupling reaction as shown in Scheme 4 (Hano *et al*., 1989)

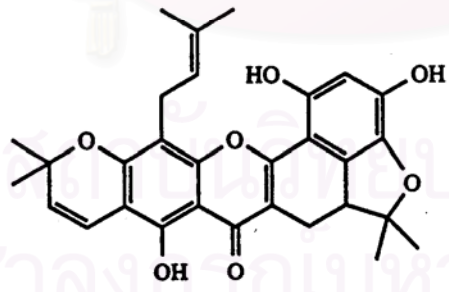
As artobiloxanthone [2] and artobilochromen [13] have the same oxygenation pattern as the simple flavone [218], a biogenetic relationship between dihydrozoxanthones and flavones seems likely. A feasible biosynthetic route for the formation of artobiloxanthone [2] and cycloartobiloxanthone [122] from simple flavone is suggested in Scheme 5. The epoxidation-dehydration mechanism is similar to that proposed for the biosynthesis of the rotenoid, amorphigenin. (Sultanbawa and Surendrakumar, 1989)

Biogenesis of integrin [66] and the two related flavones, cyclointegrin[107], and oxyisocyclointegrin [108], is of interest because they are the first natural flavones in which the A-ring is derived from phloroglucinol and C-prenylation occurs in the 3-position,and not on one of the strongly nucleophillic carbon atoms of the phloroglucinol moiety. If the dibenzoylmethane derivative [219] is the intermediate in the biosynthesis of the *Artocarpus* pigments, the presence of a specific enzyme in *A.integer* and *A.elasticus*, which preferentially prenylates the $-COCH_2CO-$ group and not the phloroglucinol nucleus, must be assumed. Other possibilities are the attack of the prenyl cation on the 3-position of a flavone in which the electron density at this position is increased by 2′-and 4′-hydroxyl group or the α-carbon of the chalcone intermediate (Pendse *et al*., 1976)

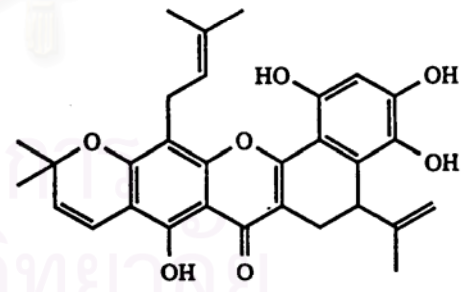


Heterophyllin



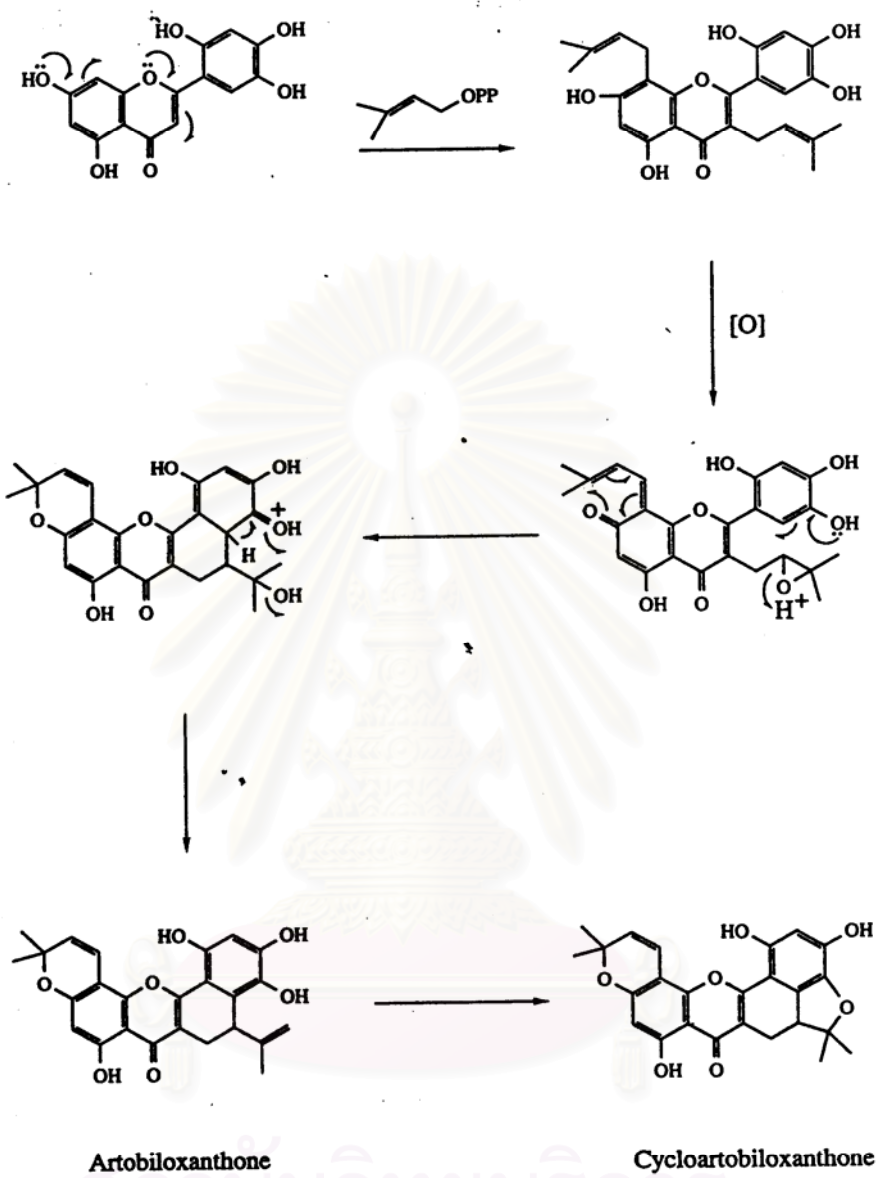


Artonin A

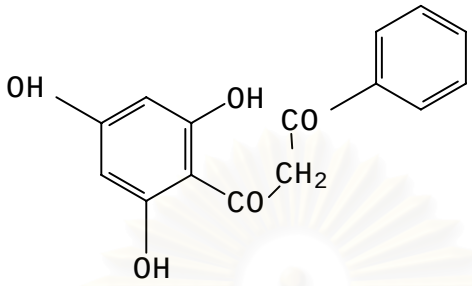


Artonin B

Scheme 4 Biogenesis of artonins A and B from heterophyllin



Scheme 5 A feasible biosynthetic route for the formation of artobilozanthone and cycloartobiloxanthone



[220]

The isoprenoid- substitued flavonoid compounds from the mulberry tree (*Morus alba*), optically active Diels – Alder - type adducts, such as Kuwanons G [221] and H [222], are attractive compounds from biosynthetic point of view because of their structural features and large optical rotation. In the biosynthetic study of mulberry Diels-Alder-type adducts, it has been established that adducts are biosynthesized through an intermolecular Diels-Alder-Type reaction between an isoprenyl portion of an isoprenyl phenol as the diene and an α, β- double bond of a chalcone derivative as the dienophile (Scheme 6)

Artonin C [79], D[80] ,and I [81] from *Artocarpus heterophyllus* can also be regarded as typical intermolecular Diels-Alder-type adducts (Nomora and Hano, 1994).

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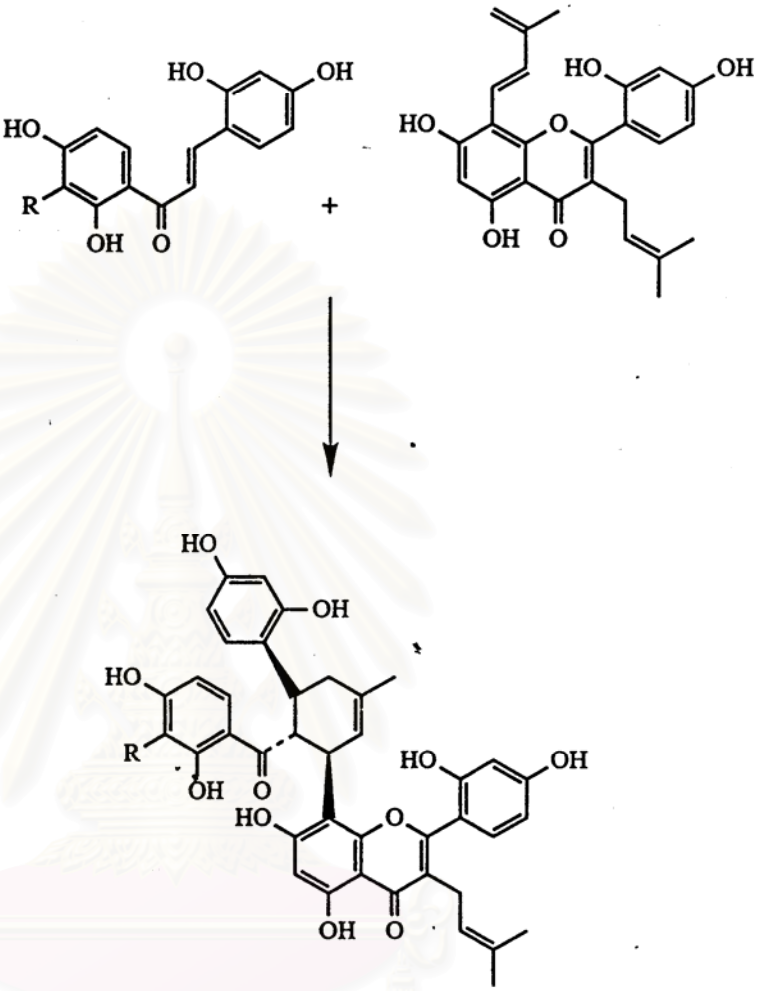

Kuwanon G R = H

Kuwanon H R =

Scheme 6 Biosynthesis of mulberry Diels-Alder-type adducts Kuwanons G and H

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CHAPTER III

EXPERIMENTAL

1.Source of Plant Materials

Dried orange red stem bark of *Artocarpus heterophyllus* was distincted from the normal brown part were collected from Nakornprathom ,Thailand in october 2002. The plant was identified by Dr.Rapepol Bavovada Department of the Pharmaceutical Botany , Faculty of Pharmaceutical Sciences, Chulalongkorn University.

2.General Techniques

2.1 Analytical Thin-layer Chromatography (TLC)

Technique : One dimension, ascending

Adsorbent : Silica gel 60 F_{254} (E.Merch) precoated plate

Layer thickness : 0.25 mm

Distance : 5 cm

Temperature :Laboratory temperature (30-35 °C)

Detection :1.Ultraviolet light at the wavelength of 254 and 365 nm

: 2. 10% Sulfuric acid in ethanol and heated at 105 °C for 10 min.

2.2 Column Chromatography

2.2.1 Flash Column Chromatography

Adsorbent : Silica gel 60 (No.9385) particle size 0.040-0.063 mm (230-400 mesh ASTM) (E.Merch)

Packing method : Dry packing

Sample loading : The sample was dissolved in a small amount of organic solvent, mixed with a small quantity of adsorbent, triturated, then dried and added gently to the top of the column

Examination of eluates : Fractions were examined by TLC observing under ultraviolet light at wavelength of 254 and 365 nm and followed by spraying with 10 % sulfuric acid in ethanol before being heated at 105°C for 10 min. Those fractions of similar pattern were combined.

2.2.2 Gel Filtration Chromatography

Gel filter : Sephadex LH-20 (Pharmacia)

Packing method : Gel filter was suspentded in the eluent and left standing to swell for 24 hours prior to use. Then poured into column and was allowed to set tightly.

Sample loading :The sample was dissolved in small volumn of eluent and loaded on the top of the column

Examination of eluates: Fractions were examined in the same manner as descrided in section 2.2.1

2.3 Spectroscopy

2.3.1 Ultraviolet (UV) Absorption Spectra

The spectra were obtained on a UV (in methanol) spectra were obtained on a shimazu UV-160A UV / VIS spectrophotometer (Pharmaceutical Research Instrument Center, Faculty of Pharmaceutical Sciences, Chulalongkorn University)

2.3.2 Infrared (IR) Absorption Spectra

The IR spectra were obtained from a Perkin Elmer FT-IR spectrometer 1760 x (Scientific and Technological Research Equipment Center, Chulalongkorn University) in potassium bromide (KBr) disc and as a solution in acetone.

2.3.3 Mass Spectra

The Electron Impact Mass Spectra (EIMS) were performed on a Finnigan MAT Incos 50 mass spectrometer (Department of Chemistry , Faculty of Sciences, Mahidol University).

The Electro spray time of flight Mass Spectrometry (ESTOFMS) were obtained using a Micromass LCT mass spectrometer, and the rock mass calibration was applied for the determination of accurate mass. (The Nation Center for Genetic Engineering and Biotechnology, Nation Science and Technology Development, Agency, Thailand Science Park)

2.3.4 Proton and Carbon-13 Nuclear Magnetic Resonance (^{1}H and ^{13}C NMR) Spectra

The 300 MHz ^{1}H NMR and 75 MHz ^{13}C NMR spectra obtained with a Bruker avance DPX-300 FT-NMR spectrometer (Faculty of Pharmaceutical Sciences, Chulalongkorn University)

The 500 MHz ^{1}H NMR and 125 MHz ^{13}C NMR spectra were obtained with JEOL JMN-A 500 spectrometer (Scientific and Technological Research Equipment Center, Chulalongkorn University)

The solvent for NMR spectra was deuterated acetone (CD_3COCD_3) deuterated chloroform ($CDCl_3$) and Deuterated dimethysulfoxide (DMSO- d_6)

The chemical shifts were report in ppm scale using the chemical shift of tetramethylsilane (TMS) at 0 ppm as reference signal.

2.4 Physical Properties

2.4.1 Melting points

Melting points were obtained on a Fisher/ Johns melting point apparatus (Department of Pharmaceutical Botany, Faculty of Pharmaceutical Sciences , Chulalongkorn University)

2.5 Solvents

Throughout this work, all organic solvents were of commercial grade and were be redistilled prior to use.

3. Extraction Procedure

The characteristic orange red , stem bark of *Artocarpus heterophyllus* (600 g) was dried chopped, ground and then extracted with toluene (5x20 L), chloroform (6x20 L) and methanol (2x20 L) to give after removal of the organic solvent, a toluene extract (31.38 g, 5.23% based on dried weight of stem bark), a chloroform extract (7.2 g , 8.4 % based on dried weight of stem bark) and methanol extract (28.59g, 4.765 % based on weight of stem bark) (Scheme 7)

4. Isolation Procedure

4.1 The Isolation of compound AHT1 (Scheme 8)

The toluene extract (7.46 g) was fractionated by column chromatography using silica gel 60 (400g) as adsorbent. Mixtures of chloroform, ethylacetate and methanol (1: 0.2: 0.0128) were used as mobile phase. Three hundred and thirty one fractions (50 ml each) were collect and examined by TLC (Silica gel, chloroform: ethylacetate : methanol 1:0.2:0.0128). Fractions with similar chromatographic pattern were combined and grouped into 5 major fractions as follow ; Fraction A-1 (1.2 g), A-2 (780 mg), A-3 (102 mg), A-4 (391 mg), and A-5 (2.1 g)

Fraction A–2 (780 mg) was separated by column chromatography using silica gel 60 (35 g) as adsorbent. Mixtures of acetone and hexane (1:2) were used as mobile phase. Fifty four fractions (30 ml each) were collected. The eluates were examined by TLC (silica gel, acetone: hexane , 1:2). Combination of fractions which showing similar chromatographic pattern gave fractions B-1 (130 mg) ,B-2 (100 mg), B-3 (150 mg), B-4 (160 mg) and B-5 (180 mg).

Fraction B-2 (100 mg) was purified by column chromatography using silica gel 60 (35 g) as adsorbent. Mixture of acetone and hexane (1: 2) was used as mobile phase. Twenty seven fractions (30 ml each) were collected. The elutes were examined by TLC (silica gel , acetone: hexane, 1:2). Combination of fractions showing similar chromatographic pattern gave fractions C-1 (10 mg) , C-2 (30 mg) ,C-3(25 mg) and C-4 (25 mg) .

Fraction C-2 (30 mg) was purified by column chromatography using silica gel 60 (No.9385, 30 g) as adsorbent. Mixtures of acetone and hexane (3:10) were used as mobile phase.Twenty fractions (30 ml each) were collected. The elutes were examined by TLC (silica gel, acetone: hexane, 1:2). Combination of fractions D-2 (14- 16) of which showing similar chromatographic pattern gave compound AHT1 (2 mg).

In addition , fraction B-3 (150 mg) containing a yellow amorphous precipitated and little impurities was further purified by washing with methanol to give purified precipitate (4.4 mg) showing similar chromatographic patterns (three solvent systems) with those of compound AHT1 . (Table 4)

Table 4 Chromatographic equivalence between fraction C-2 and fraction B-3

Solven system	R_f AHT1 from Fraction C-2	R_f AHT1 from Fraction B-3
$CHCl_3$: MeOH (97.4 : 2.6)	0.55	0.55
Hexane : Acetone (2 : 1)	0.595	0.595
$CHCl_3$: Acetone (1: 0.1)	0.44	0.44

4.2 The Isolation of compound AHT2 (Scheme 9)

Remains material often AHT1 was removed from fraction B-7 (145.6 mg) was purified by column chromatography using silica gel 60 (No.9385, 35 g) as adsorbent. Mixture of chloroform and acetone (1: 0.1) was used as mobile phase. Twenty fractions (30 ml each) were collected. The elutes were examined by TLC (silica gel, chloroform :acetone, 1:0.1). Combination of fractions showing similar chromatographic pattern gave collective fractions E-1 (5 mg) , E-2 (90 mg) ,E-3 (15 mg) ,E-4 (10 mg) , E-5 (10 mg) , and E-6 (15mg)

Fraction E-2 (90 mg) was separated by gel filtration on a sephadex LH20 ($CHCl_3$ and MeOH, 1:1) column. Twenty fractions (15 ml each) were collected and subsequently combined according to their TLC behavior (silica gel, acetone: hexane, 1:2) to yield 3 main fractions : F-1(15 mg) , F-2 (61 mg) , and F-3(10 mg) .

Fraction F-2 (61 mg) was purified by column chromatography using silica gel 60 (30 g) as adsorbent. Mixture of chloroform and methanol (97.4 : 2.6) was used as mobile phase. Nineteen fractions (20 ml each) were collected. The elutes were examined by TLC (silica gel, chloroform : methanol, 97.4 : 2.6).Combination of fractions showing similar chromatographic pattern gave 3 main fractions G-1(18 mg) ,G-2 (25.3 mg) and G-3 (10.52 mg)

Fraction G-2 (25.3 mg) was purified by column chromatography using silica gel 60 (30 g) as adsorbent. Mixture of chloroform and methanol (97.4 : 2.6) was used as mobile phase. Eleven fractions (15 ml each) were collected. The elutes were examined by TLC (silica gel, chloroform : methanol, 97.4 : 2.6). Combination of fractions showing similar chromatographic patterns resulted in the isolation of compound AHT2 (2 mg) from the fraction 8-11.

Fraction G-3 (10.52 mg) re-purified on sephadex LH20 with ($CHCl_3$: MeOH 1:1) as eluent to afford 1.2 mg of compound AHT2.

4.3 The Isolation of compound AHM3 (Scheme 10)

The methanol extract (16.14 g) was separated by flash chromatography of silica gel 60 (300 g). The elutes 300 ml per fractions were collected . Elution was performed in a polarity gradient manner with mixtures of chloroform and methanol (100:0 - 0:100). Ninety fractions were collected. Fractions with similar TLC pattern (silica gel, hexane : acetone, 1:0.8) were combined to yield 9 fractions :fraction H-1(150 mg), H-2 (200 mg), H-3 (90. Mg), H-4 (894.1 mg) , H-5 (300 mg), H-6 (2.7 g), H-7 (2.7 g), H-8 (2.8 g) , and H-9 (3.6 g)

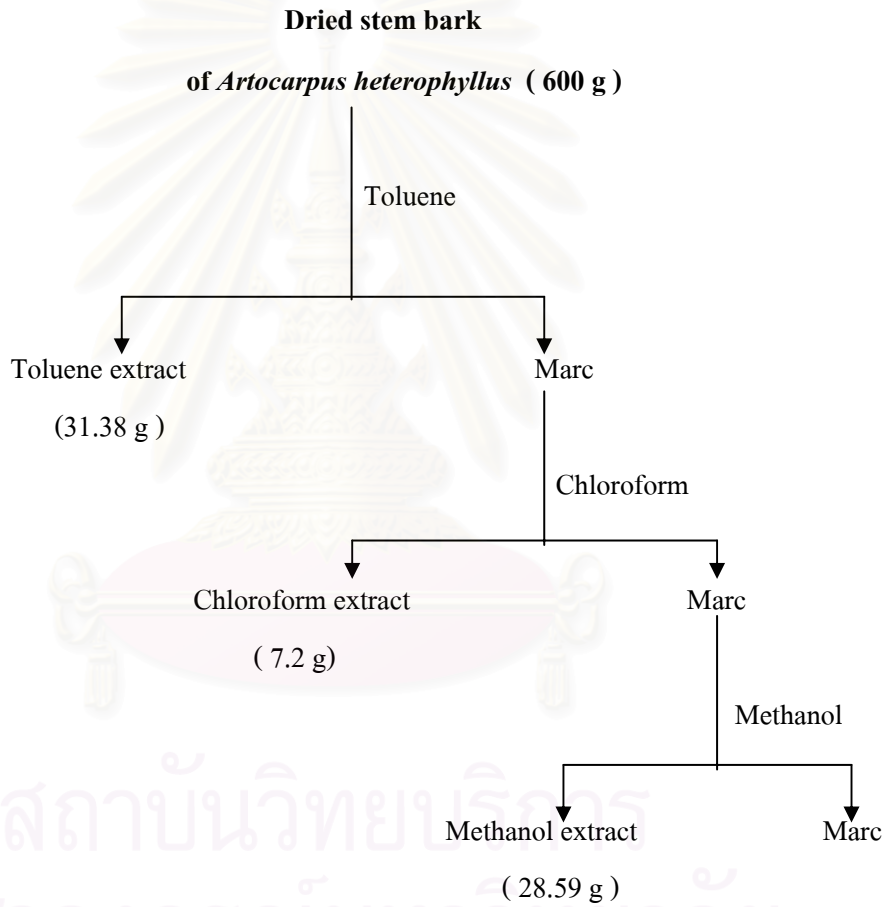
Fraction H-6 (2.7 g) was purified by column chromatography using silica gel 60 (30 g) as adsorbent. Mixture of hexane and acetone (1:0.8) was used as mobile phase. Thirty five fractions (30 ml each) were collected. Combination of fractions showing similar chromatographic pattern gave collective portions I-1(100 mg) , I-2 (840 mg) , and I-3 (770.9 mg)

Fraction I-2 (840 mg) was purified by column chromatography using silica gel 60 (No.9385, 30 g) as adsorbent. Mixtures of chloroform and methanol (1:0.1) were used as mobile phase. Twenty five fractions (20 ml each) were collected and combined according to their similarity of TLC pattern (silica gel, chloroform : methanol , 1:0.1) into 3 fractions of J-1 (130 mg) J-2 (180.5 mg) and J-3 (360.8 mg) respectively.

Fraction J-2 (180.5 mg) was fractionated by gel filtration chromatography using a column of sephadex LH 20 (1.3x50 cm, $CHCl_3$ and MeOH 1:1).The eluates were collected (10 ml per fractions) and combined according to their similarity of TLC pattern (silica gel, chloroform : methanol , 1:0.1) to give 3 fractions of K-1 (50.3 mg) K-2 (60.5 mg) and K-3 (30 mg).

Fraction K-2 (60.5 mg) was fractionated by gel filtration chromatography using a column of sephadex LH 20 (1.3x50 cm, chloroform : methanol, 1:1).The eluates were collected (10 ml per fractions) and combined according to their similarity of TLC pattern (silica gel, chloroform : methanol, 1:0.1) Twelve fractions, (10 ml each) were collected to obtains 3 fractions of L-1(5.6 mg), L-2 (7.6 mg) and L-3 (45.3 mg)

Fractions L-3 (45.3 mg) was further purified by column chromatography using silica gel 60 (10 g) as adsorbent. Mixture of chloroform and methanol (1:0.1) were used as mobile phase. Twenty two fractions, (15 ml each) were collected and combined according to similarity of TLC pattern (silica gel, chloroform : methanol, 1:0.1) the combined fraction 11-22 offer 27.5 mg of compound AHM3 (amorphous yellow powder R_f0.46, silica gel, chloroform: methanol (1:0.1).



Scheme 7 Extraction Procedure of *Artocarpus heterophyllus* stem bark

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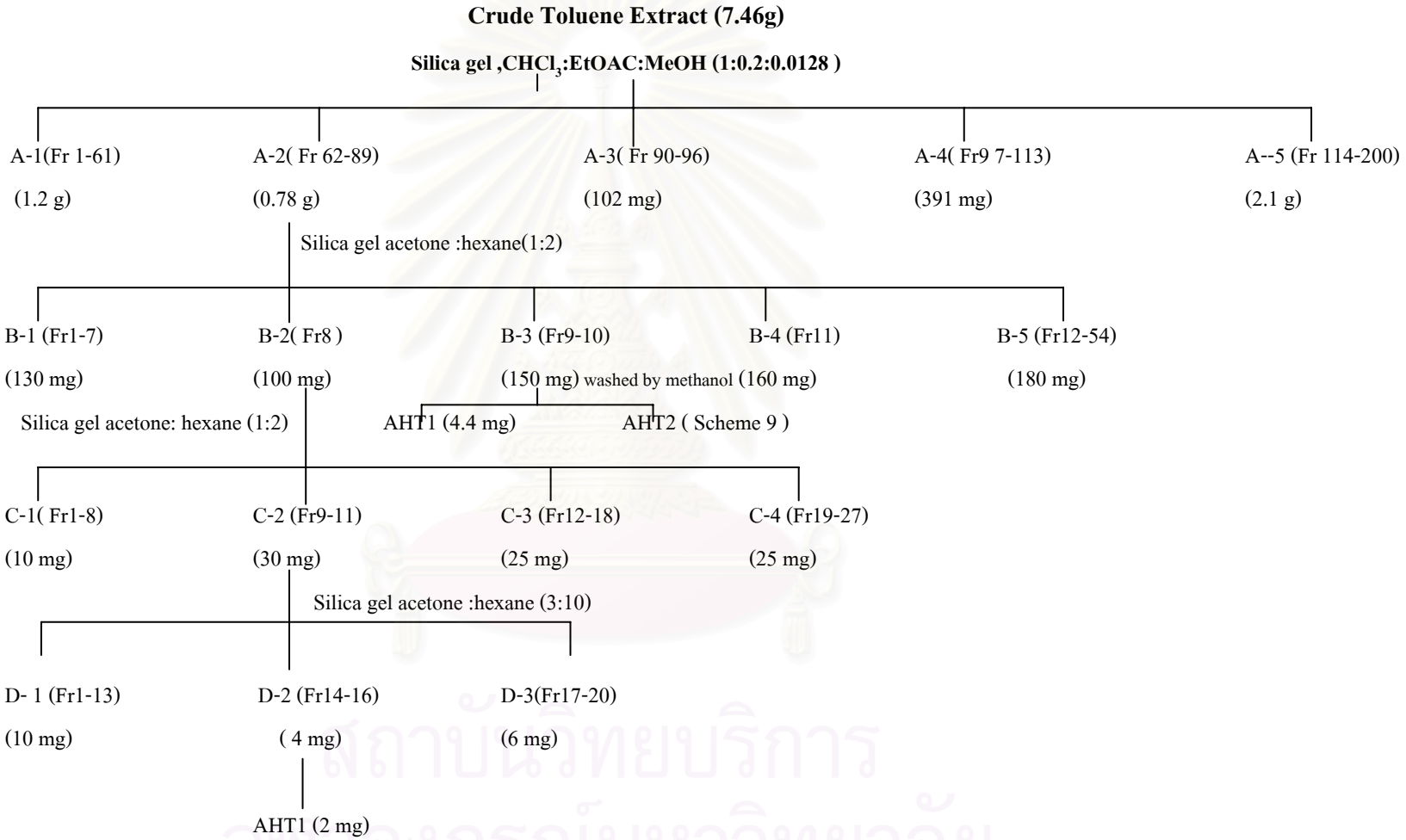
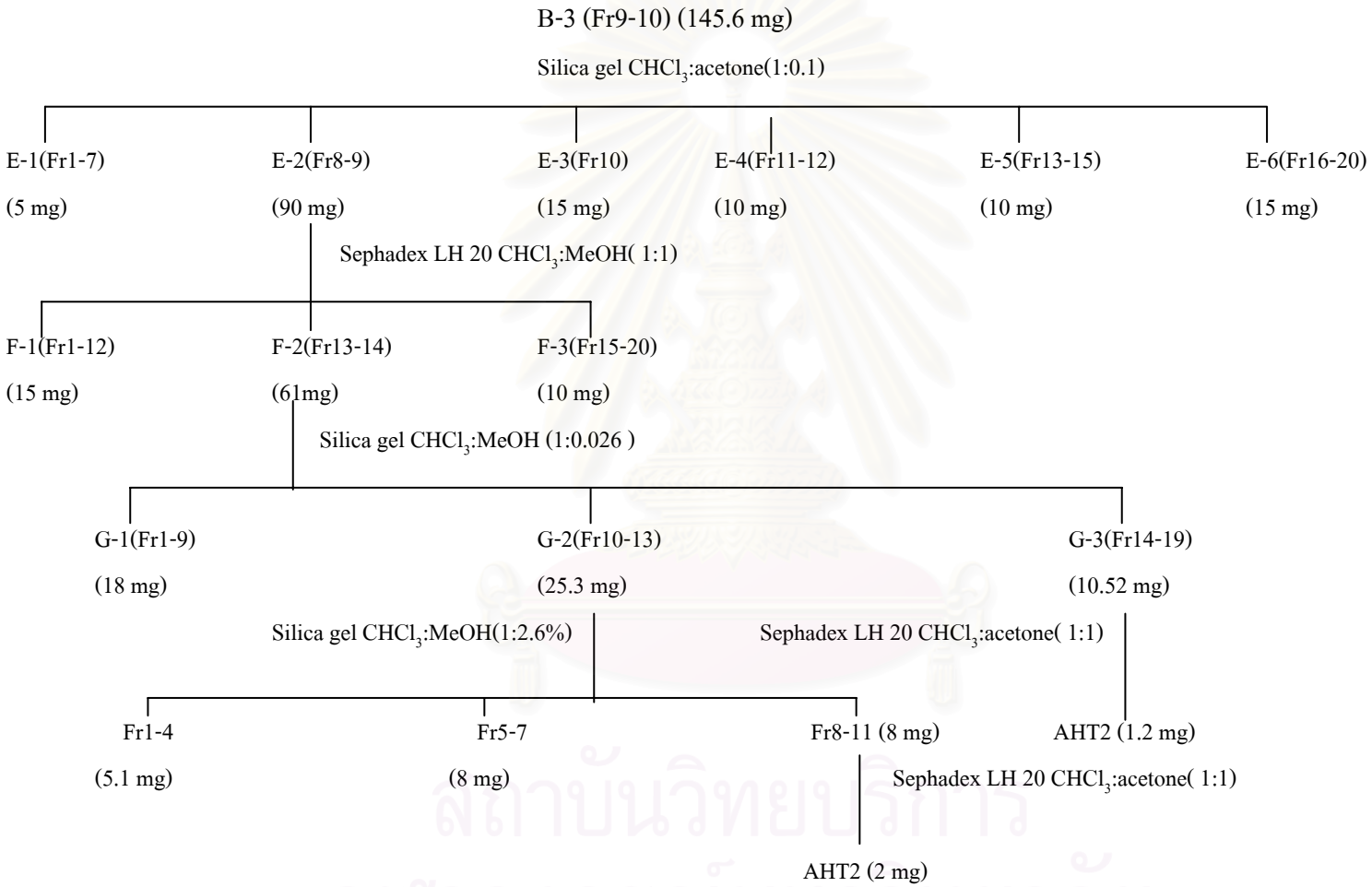
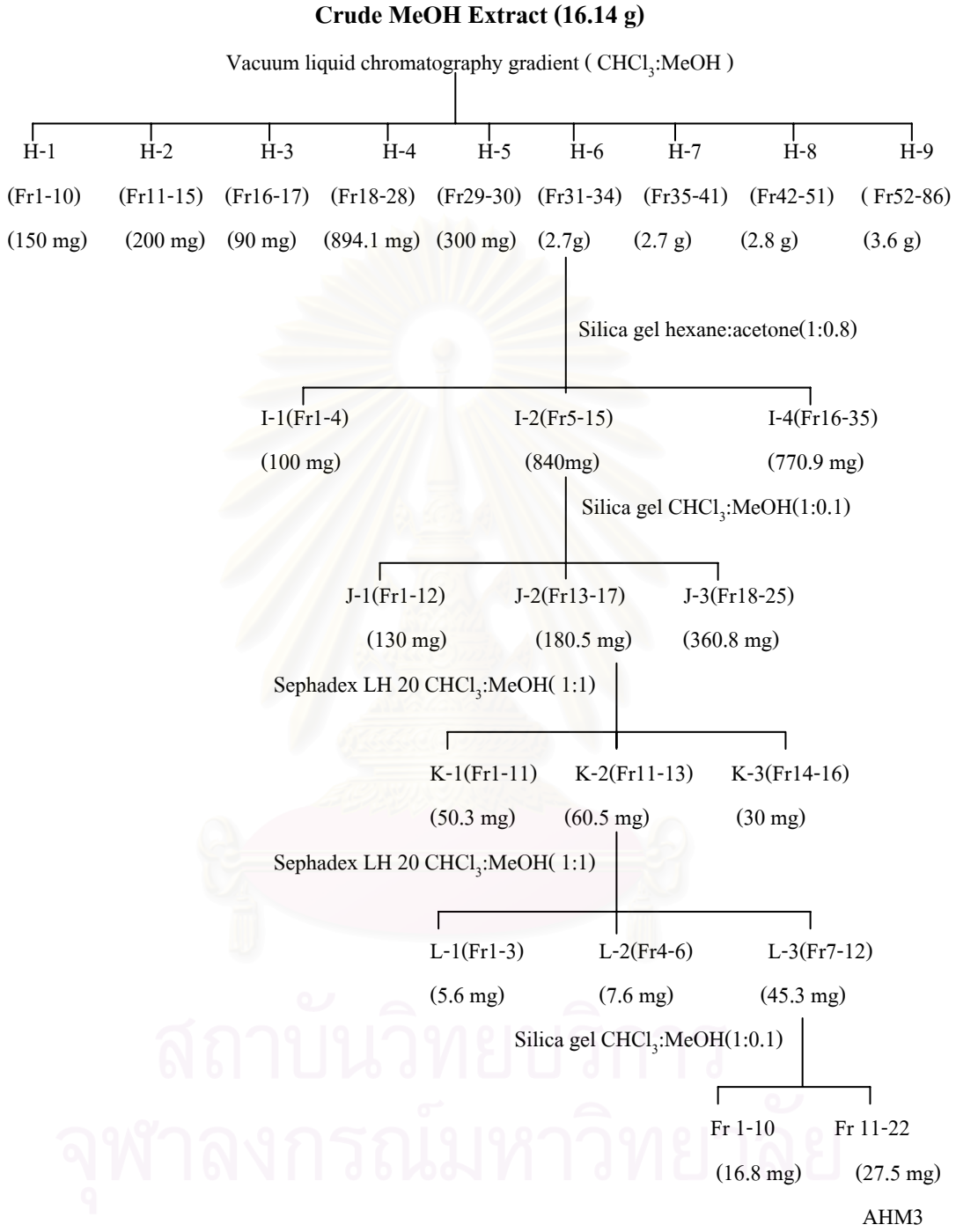


Scheme 8 Fractionation of the toluene extract of the stem bark of *Artocarpus heterophyllus*.



Scheme 9 Fractionation of the toluene extract of the stem bark of *Artocarpus heterophyllus*.



Scheme 10 Fractionation of the methanol extract of the stem bark of *Artocarpus heterophyllus*.

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5. Characterization of Isolated compounds

5.1 Characterization of AHT1

Compound AHT1(8 mg, $1.33x10^{-5}$ % based on dried weight of stem bark) was obtained as yellow needle . It was soluble in acetone

EIMS: m/z (% relative intensity); Figure 9

502 (26.32), 487 (42.86), 447 (68.97), 446 (100), 444 (12.35), 403(32.69), 389 (18.24), 388 (21.5), 385 (10.46), 361 (7.38), 357 (9.89), 215 (11.76), 171 (7)

IR: νcm^{-1}, KBr disc; Figure 10

3546, 3194 (br), 2974, 2929, 1651, 1605, 1551, 1476, 1429, 1342, 1298, 1169, 1148, 988, 824, 775

UV: λ_{max} nm , in methanol; Figure 11

295 nm , 385 nm

^{1}H-NMR: δ ppm, 500 MHz, in acetone-d_6 ; Figure 12

1.32(s), 1.45(s), 1.46(s), 1.62(br, s), 1.65(s), 1.79(s), 2.35(t, *J*=15.2), 3.2(q, *J*=7), 3.4(tt, *J*=7), 3.45(tt, *J*=7.2), 3.63(q, *J*=7.9), 5.38(t, *J*=7), 5.72(d, *J*=10), 6.39(s), 6.68(d, *J*=10) 13.69(s)

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

18.1, 20.4, 22.0, 22.8, 25.9, 28.3, 28.3, 47.5, 78.3, 93.6 , 105.0, 105.2, 105.2, 108.2, 112.5, 116.4, 123.6, 128.8, 131.6, 133.7, 137.9, 147.0, 151.4, 154.4, 155.2, 156.9, 161.5, 181.7

Melting points 238-240 °C

5.2 Characterization of AHT2

Compound AHT2 (3.2 mg, 5.33 x 10^{-6} % based on dried weight of stem bark)was obtained as amorphous yellow brown solid. It was soluble in chloroform

EIMS: m/z (% relative intensity); Figure 24

504 (14.84), 502 (23.74), 487 (34.17), 447 (100) , 205 (31.67), 153 (22.23), 105 (16.74), 77 (14.82)

IR: νcm^{-1}, KBr disc; Figure 25

3363, 2968, 2926, 2857, 1704, 1654, 1629, 1596, 1594, 1465, 1377, 1301, 1189, 1124, 974, 871

UV: λ_{max} nm , in methanol; Figure 26

268 nm , 299 nm, 394 nm

^{1}H-NMR: δ ppm, 500 MHz, in chloroform-d_6 ; Figure 27

1.23 (s), 1.43 (d, *J*=4.6), 1.61 (s, br), 1.67 (s), 1.83 (s), 1.93 (s), 3.45(m), 5.22 (m), 5.43 (d, *J*=9.16), 5.58 (d, *J*=10.07), 6.18 (d,*J*=9.46), 6.48 (s, br), 6.69 (d, *J*=9.76), 12.95(s)

^{13}C-NMR: δ ppm, 125 MHz, in chloroform-d_6 ; Figure 29, 30

18.1, 18.6, 21.5, 25.6, 25.7, 28.1, 28.2, 69.4, 77.6, 104.8, 104.8, 105.4, 105.4, 107.5, 108.3, 110.0, 115.9, 120.9, 122.0, 127.8, 131.7, 139.1, 151.7, 153.6, 154.5, 155.0, 156.4, 178.8

^{13}C-NMR: δ ppm, 125 MHz, in deuterated dimethysulfoxide- d_6 ; Figure 31

17.9, 18.4, 21.1, 25.4, 25.5, 27.6, 27.7, 68.4, 77.8, 104.5, 104.5, 104.7, 105.6, 107.2, 108.3, 109.0, 114.9, 121.1, 121.8, 128.8, 131.3, 137.8, 141.0, 152.3, 153.6, 155.8, 155.7, 177.8

Melting points 196-200 °C

5.3 Characterization of AHM3

Compound AHM3 (27.5 mg, $4.58x10^{-5}$ % based on dried weight of stem bark) was obtained as amorphous yellow powder . It was soluble in acetone.

ES-TOFMS: m/z (% relative intensity); Figure 41

675 (6.06), 674 (100), 183 (24.24)

IR: νcm^{-1}, KBr disc; Figure 42

3340, 2974, 2975, 1702, 1612, 1369, 1272, 1206, 1115, 978

UV: λ_{max} nm , in methanol; Figure 43

263 nm , 315 nm , 389 nm

^{1}H-NMR: δ ppm, 500 MHz, in acetone-d_6 ; Figure 44

1.38 (s),1.41(s), 1.91(s, br), 2.24 (d, br , *J*=18), 2.50 (d, br, *J*=17), 3.8 (m), 4.18 (br), 4.64 (dd, *J*=5.19), 5.63 (d, *J*=10), 5.65 (s, br), 6.25 (d, *J*=9), 6.27 (d, *J*=2.44) , 6.29 (d, *J*=2.44), 6.33 (dd, *J*=2, 8) , 6.35 (dd, *J*=2, 8), 6.40 (d, *J*=2.44), 6.42 (d, *J*=2.44) ,6.47(d , *J*=2.44), 6.49(d, *J*=2.44), 6.94(d, *J*=8.55), 7.63 (d, *J*=8.85) ,7.71 (d, *J*=18.57), 7.84 (d, *J*=9.15), 8.14 (d, *J*=15.26), 8.2 (s, br), 8.36 (d, *J*=9.16), 8.6 (s, br), 8.85 (s, br), 9.05 (s, br), 9.35 (s,br), 12.88 (s), 14.36 (s)

^{13}C-NMR: δ ppm, 125 MHz, in acetone-d_6; Figure 45, 46, 47

23.8, 28.4, 28.5, 32.8, 32.9, 36.1, 47.6, 78.5, 103.5, 103.6, 107.5, 108.8, 109.1, 109.5, 109.8, 114.0, 114.1, 115.1, 116.0, 116.0, 117.2, 121.8, 123.2, 128.8, 129.1, 130.7, 131.7, 133.8, 135.0, 141.0, 156.5, 158, 160.0, 160.7, 160.9, 162.3, 163.5, 165.7, 193.3, 209.7

Melting points 139- 140 °C

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CHAPTER IV

RESULT AND DISCUSSION

Three characteristic orange red compounds were isolated from the toluene and methanol extracts of the stem bark of *Artocarpus heterophyllus* (600 g) . The toluene extract (31.38 g) was further purified using several chromatographic techniques to offer two pure compounds (AHT1, AHT2). The methanol extract gave one pure compound (AHM3). Structure elucidation of these compounds will be discussed in this chapter.

1. Structure elucidation of Compound AHT1

AHT1 was obtained as yellow needle, it gives a green colour with alcoholic ferric chloride suggestion the presence of phenolic hydroxy group. The EIMS of AHT1 (Figure 9) revealed the molecular ion peak at *m/z* 502 (9.54 %) showed the following significant fragment ions m / z 487 (M^+- CH_3), 459 (M^+-C_3H_7), 446 (M^+-C_4H_8) (scheme 11) of which analysed for the molecular formula of $C_{30}H_{30}O_7$ The IR spectrum of AHT1 (Figure10) showed the maximum absorption bands due to hydroxyl (3194 cm^{-1}), and ketone carbonyl (1651 cm^{-1}), ether linkage(1148 cm^{-1}), and conjugated carbon moieties (1476 cm^{-1}).

Compound AHT1 was assigned as a known prenylflavone, artonin A (Figure 3) by analyses of ^{1}H and ^{13}C-NMR spectra and comparison with the literature values.

The ^{1}H-NMR spectra of AHT1(Figure 12 and table 5) displayed 3 hydroxyl protons at δ 8.6, 9.85, 13.66 ppm 4 aromatic proton between δ 5.2-6.7 ppm , 6 methyl protons at δ 1.3 ppm, 1.57 ppm, 1.45 ppm, 1.46 ppm, 1.69 ppm and δ 1.52 ppm. Two broad signals at δ 8.6 ppm and 8.93 ppm were assigned for OH at C-2′ and C-4′ .The five methine carbon, two methylene carbon, 15 quaternary carbon one carbonyl and 6 methyl carbon were seen in ^{13}C-NMR (Figure 13) and the DEPT spectrum (Figure14).

The chelated hydroxyl group of C-5 position showed up at δ13.66 ppm in the ^{1}H-NMR spectrum (Figure 12). The characteristic signal of two vinyl protons were observed at δ 6.68 ppm (d, *J* 10.1 Hz, H-14) and δ 5.72 ppm (d, *J* 10 Hz, H-15) .

An aromatic proton signal, at δ 6.39 ppm was observed and assigned to the protons located at C-3′.

The ^{13}C-NMR spectrum of AHT1 displayed thirty carbon atoms The most downfiend at δ181.66 ppm was assigned to carbonyl carbon of C-4.

Compound AHT1 was identified as artonin A based on the analyes of its spectral data comparisons with previous published results (Hano , 1989).

However ,an intensive examination of its HMBC spectra revealed some wrong assignments in the previous record especially the ^{13}C-NMR chemical shifts at C-8a and C-5.The correct assignment of C-8a should be δ154.5 ppm where as C-5 should beδ 155.2 ppm instead of C-8a (δ155.2) and C-5 (δ154.4) as previously reported.

The HMBC spectra concerning those two carbons (Figure 22 and Figure 23) clearly demonstrated that, the obvious chelated C-5 OH proton (δ13.65 ppm) correlated to the carbon at δ155.2 ppm and a carbon at δ105.0 ppm (C-4a) , 105.8 (C-6) thus , the chemical shifts at 155.2 should belong to C-5 not the unseen correlation at δ154.5 as in the previous report.

The methylene proton at C-19 (δ 3.45 ppm andδ 3.63 ppm) (Figure 20 Figure 21) correlated with carbon having chemical shifts at 108.2 (C-8) ,123.6 (C-20), 131.6 (C-21), 154.4 and 157.0 ppm (C-7) respectively. Nearly all of those ^{13}C chemical shifts were in agreements with previous report (Table 5, Hano , 1989) except one at 154.5 ppm (155.3 previous report). Thus chemical shifts of C-5 , and C-8a could be alternately revised to 155.2 and 154.5 ppm respective.

The unambiguous proton and carbon assignment with long-range correlation between carbons and proton observed from HMBC spectrum (Figure 4) and comparison with the data previously report were summarized in Table 5

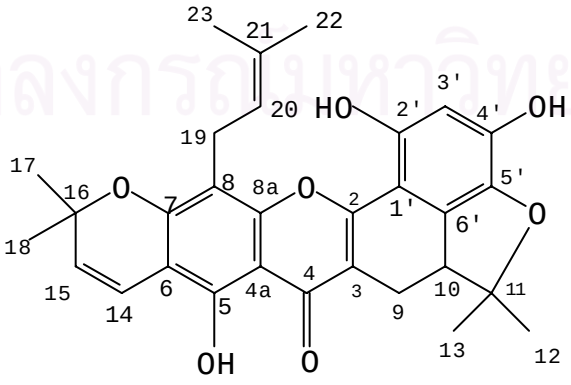


Figure 3 The structure of AHT1

Table 5 NMR spectral data of compound AHT1(acetone- d_6) as compared with artonin A (acetone- d_6)

Position	Compound AHT1		Artonin A		HMBC (correlation with ^{1}H)
	^{1}H(mult.,*J* in Hz)	^{13} C ppm.	^{1}H(mult.,*J* in Hz)	^{13} C ppm.	
2		161.5		161.6	H-9
3		112.5		112.6	H-9,H-10
4		181.7		181.7	
4a		105.0		105.0	
5		155.2		154.5	5-OH
6		105.8		105.9	H-15, 5- OH
7		157.0		157.0	H-19, H-15
8		108.2		108.3	H-19
8a		154.4		155.3	H-19
1′		105.2		105.3	H-3′,H-10
2′		151.4		151.5	H-3′
3′	6.39 (s)	105.2	6.68 (s)	105.4	
4′		147.0		147.0	H-3′
5′		137.9		138.0	H-3′
6′		133.7		133.7	H-9 , H-10
9	2.35 (t,15.2) 3.4(tt, 7)	20.4	2.44, 3.42	20.5	H-10
10	3.4 (tt, 7)	47.5		47.6	H-9, H-12, H-13
11		93.6		93.7	H-9,H-10 , H-12, H-13
12	1.65 (s)	28.3		28.4	H-10, , H-13
13	1.32 (s)	22.8	1.78 (s)	22.9	H-10, H-12
14	6.68 (d, 10)	116.4	6.68 (d, 10)	116.4	H-15
15	5.72(d, 10)	128.8	5.72(d, 10)	128.9	H-17, H-18
16		78.3		78.4	H-14, H-15, H-17, H-18

Table 5 (continued)

Position	Compound AHT1		Artonin A		HMBC (correlation with ^{1}H)
	^{1}H(mult.,*J* in Hz)	^{13} C ppm.	^{1}H(mult.,*J* in Hz)	^{13} C ppm.	
17	1.45 (s)	28.3	1.45 (s)	28.4	H-15, H-18
18	1.46 (s)	28.3	1.45(s)	28.4	H-15, H-17
19	3.45 (m), 3.63(q,8)	22.0	3.41,3.64	22.0	H-20
20	5.38 (t,7)	123.6	5.3 (m)	123.7	H-19, H-22, H-23,
21		131.6		131.7	H-22, H-23
22	1.62 (s, br)	25.9	1.69	25.9	H-20, H-23
23	1.79 (s)	18.1	1.52	18.2	H-20, H-22
5-OH	13.69 (s)			13.66(s)	
2′-OH	8.95 (s ,br)				
4′-OH	8.6 (s, br)				

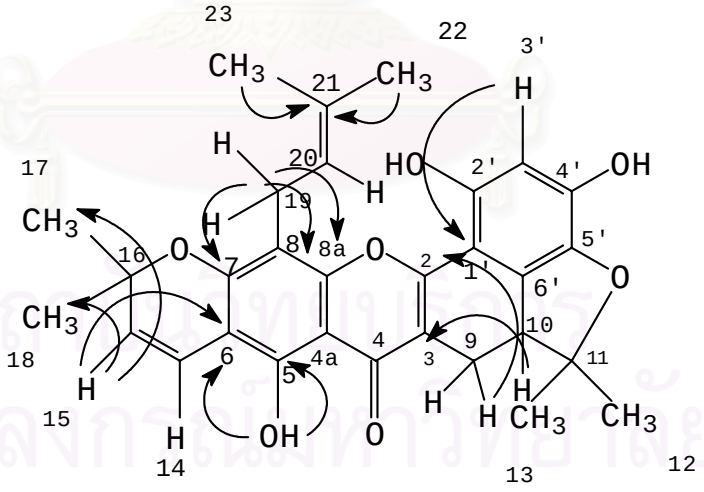
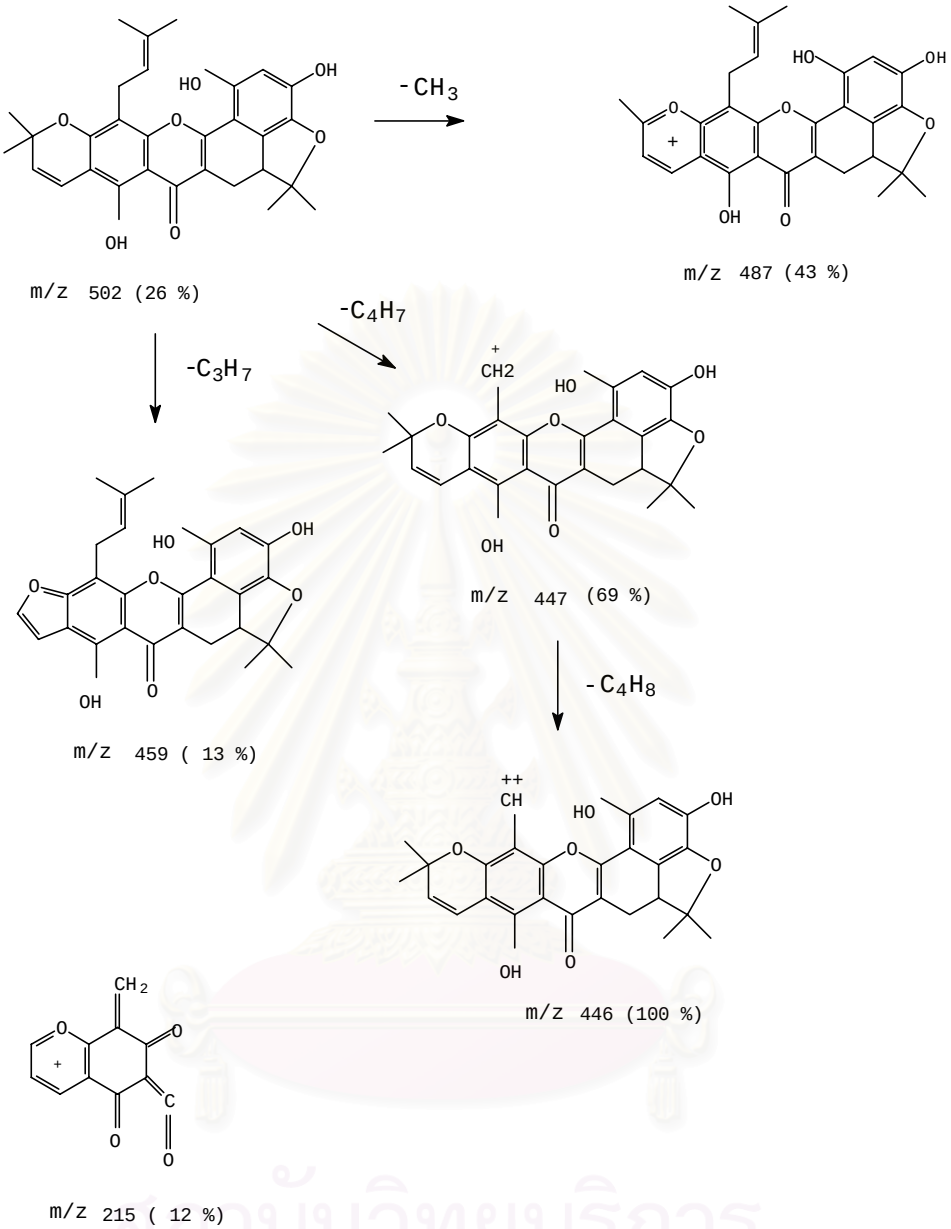


Figure 4 Selected HMBC correlations of compound AHT1



Scheme 11 Propose mass fragmentation of AHT1

2. Structure elucidation of compound AHT2

AHT2 was obtained as yellow brown amorphous solid it gives a green colour with alcoholic ferric chloride suggestion the presence of phenolic hydroxy group. The EIMS of AHT2 (Figure 24) revealed the molecular ion peak at *m/z* 502 (23.74 %) showed the following significant fragment ions m / z 487 (M^+- CH_3), 448 (M^+-C_4H_6), 447 (M^+-C_4H_7)

(scheme 12) of which analysed for the molecular formula of $C_{30}H_{30}O_7$.The IR spectrum of AHT2 (Figure 25) showed the maximum absorption bands due to hydroxyl (3293 cm^{-1}), and carbonyl unsaturated ketone (1655cm^{-1}) and conjugated carbon moieties(1465.47 cm^{-1})

The ^{1}H-NMR spectra of AHT2 (Figure 27 , 28and table 6) displayed a chelated hydroxyl proton at 13.8 ppm, 6 methyl proton at δ 1.44 ppm, 1.66 ppm, 1.83 ppm, 1.93 ppm , one methylene proton at 3.5 ppm and seven methine between 5.2-7.25 ppm.

The ^{13}C-NMR spectrum of AHT2 (Figure 29, 30,31) displayed 30 carbon peaks but have 6 addition peaks of impurities at δ 29.67 , 99.62 , 135.1,149.3 ,162.2 and 165.2 ppm not corelated with majority of peak in the spectrum. (Figure 29, 30 ,31) The most downfield signal at δ 178.8 ppm was assigned to carbonyl carbon of C-4.

Compound AHT2 was assigned as a known prenylflavone, cycloheterophyllin (Figure 5) by analyses of ^{1}H and ^{13}C-NMR spectra and comparison with the literature values.(Hano , 1989)(Rao, 1971).

The unambiguous proton and carbon assignment with long-range correlation between carbons and proton observed from HMBC spectrum (Figure 6)and comparison with the data previously report were summarized in Table 6

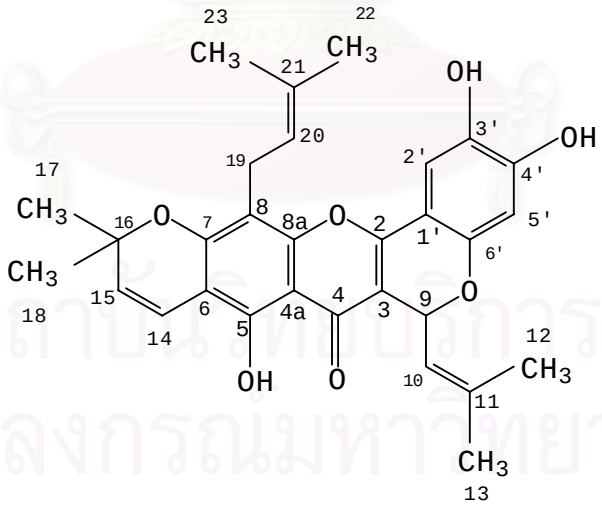


Figure 5 The structure of AHT2

Table 6 NMR spectral data of compound AHT2 (in $CDCl_3$) and (in DMSO) as compared with cycloheterophyllin (in $CDCl_3$)

position	Compound AHT2			Cycloheterophyllin		HMBC (correlation with ^1H)
	^1H(mult.,*J* in Hz)	^{13} C ppm. DMSO	^{13} C (mult.)in $CDCl_3$	^1H(mult.,*J* in Hz)	^{13} C ppm. in DMSO	
2		155.8	155.0		155.7	
3		108.3	108.3		108.3	
4		177.8	178.8		177.8	
4a		104.5	104.8		104.5	
5			154.5		152.8	
6		104.7	105.4		104.7	
7		155.7	156.4		155.5	
8		107.2	107.5		107.1	
8a		153.6	153.6		153.7	
1′		105.6	105.4		105.6	
2′		152.3	151.7		152.3	
3′		104.5	104.8		104.5	
4′					150.4	
5′		141			141.0	
6′		109	110		109.0	
9	6.15 (d, 9.5)	68.4	69.4	6.07	68.5	
10	5.42 (d,9)	121.1	120.9	5.42	121.1	H-12 , H-13
11		137.8	139.1		137.6	H- 12 ,H- 13
12	1.66 (s)	25.4	25.7	1.63	25.4	H- 10 ,H- 11
13	1.97 (s)	18.4	18.6	1.97	18.3	H- 10 ,H- 11
14	6.7 (d,9.7)	114.9	115.9	6.58	114.9	H-5
15	5.58(d,10)	128.8	127.8	5.73	128.5	H-6 ,H-16
16		77.8	77.6		77.6	H-14, H-15, H-17 , H-18

Table 6 (continued)

Position	Compound AHT2			Cycloheterophyllin		HMBC (correlation with ^{1}H)
	^{1}H(mult.,*J* in Hz)	^{13}C (ppm.)in DMSO	^{13}C (ppm.) in $CDCl_3$	^{1}H(mult.,*J* in Hz)	^{13}C (ppm.) in DMSO	
17	1.44 (s)	27.7	28.2	1.48	27.6	H-18, H-15 ,H-16
18	1.44 (s)	27.6	28.1	1.48	27.5	H-17, H-15, H-16
19	3.45 (m)	21.1	21.5	3.48	21.0	H-20, H-21
20	5.2(t , 7)	121.8	122	5.23	121.9	H-22, H-23
21		131.3	131.7		131.1	
22	1.66 (s)	25.5	25.6	1.63	25.4	H- 20
23	1.85 (s)	17.9	18.1	1.88	17.8	H- 20 ,H- 21

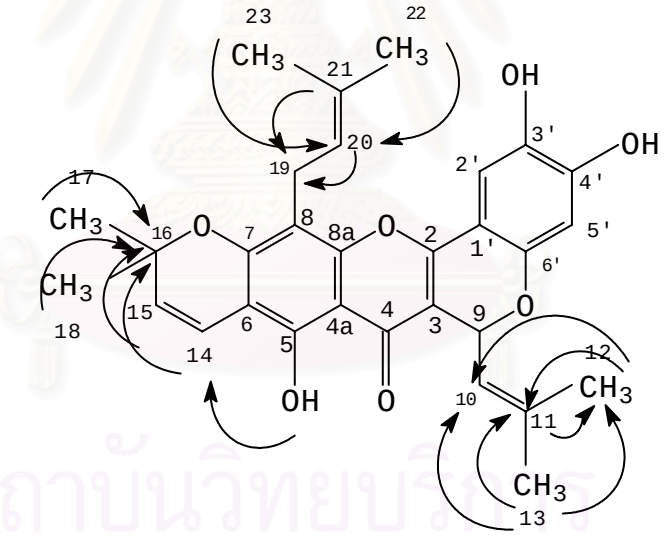
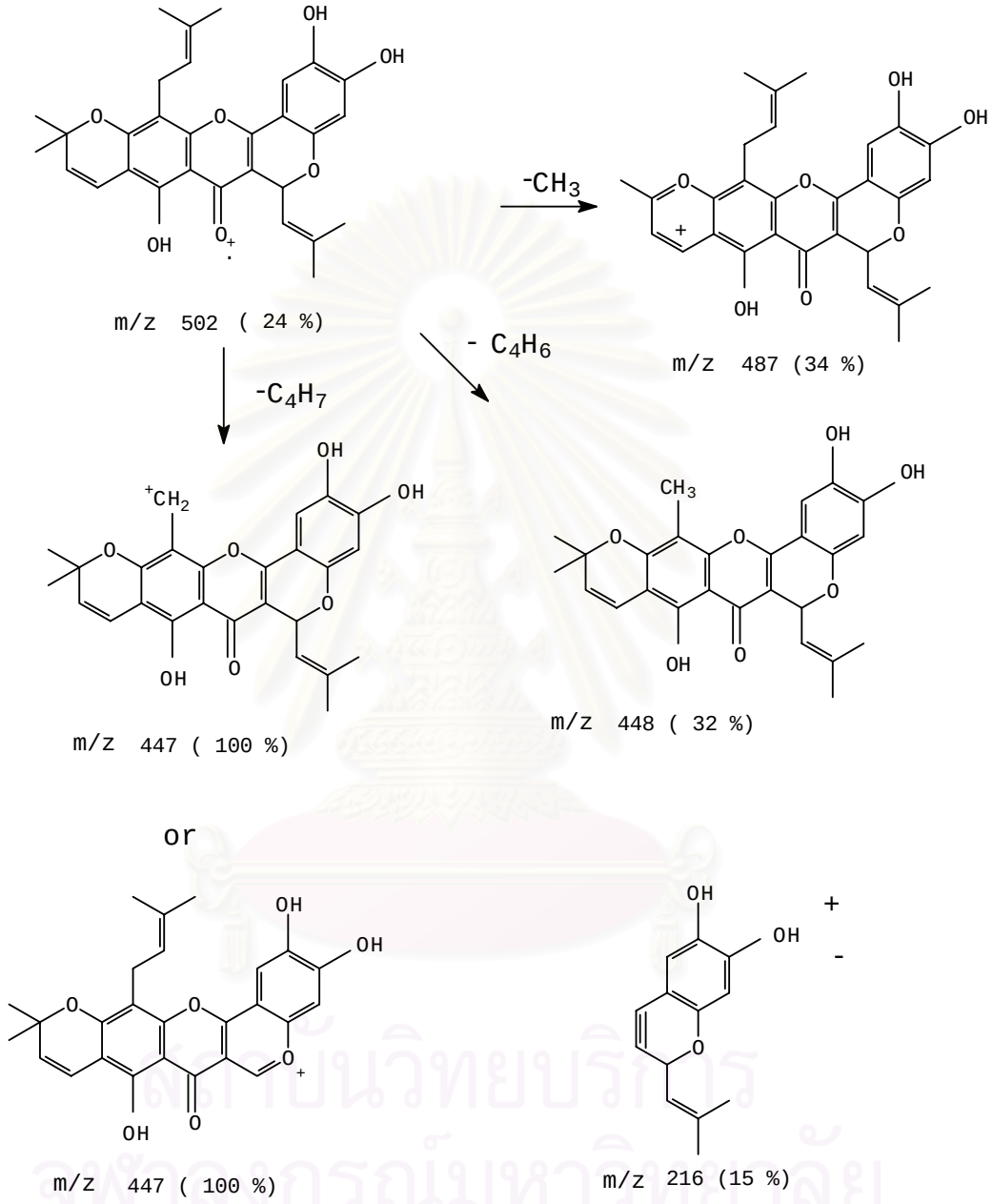


Figure 6 Selected HMBC correlations of compound AHT2



Scheme 12 Propose mass fragmentation of AHT2

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3. Structure elucidation of compound AHM3

AHM3 was obtained as amorphous yellow powder .The ES-TOFMS of AHM3 (Figure 41) revealed the molecular ion peak at *m/z* 676 which analysed for the molecular formula of $C_{40}H_{36}O_{10}$ .The IR spectrum of AHM3 (Figure42) showed hydroxyl vibration at 3340 , carbonyl (1702) conjugate carbon (1612), and aromatic stretching carbon (1570). The UV absorption maxima were seen at 263 nm, 315 nm and 389 nm indicate a chalcone chromophore. (Markham, 1982)

Compound AHM3 was assigned as an Diels-Alder type adducts, artonin D (Figure 7) by analyeses of ^{1}H and ^{13}C-NMR spectra and comparison with the literature values.(Hano, 1990) .The ^{1}H-NMR spectra of AHM3 (Figure 44 and table7) displayed thirtysix protons classified as these methyl protons at δ 1.38 ppm (s), 1.41 ppm (s), 1.93 ppm (br, s), fifteen olifinic aromatic protons between 5.6-8.4, five of which were vinyl protons at δ 7.71 ppm (d, *J*=15, C-2), 8.14 ppm (d, *J*=15, C-β), 5.65 ppm (br, s, C-2$''$), 6.56 ppm (d, *J*=9, C-21$''$), 5.63 ppm (d, *J*=10, C-22$''$),two chelated hydroxyl protons atδ 12.88 ppm (s, C-10$'$), 14.53 ppm (s, C-2$'$) and five hydroxy groups show broad single peak at δ 8.2, 8.6, 8.85, 9.05 and 9.35.

The ^{13}C-NMR spectrum of AHM3 (Figure 45) displayed fourty carbon atoms the signals at δ193.3 ppm, 209.7 ppm were assigned to carbonyl carbons. The DEPT (Figure 48) spectrum showed nineteen methine, one methylene , three methyl and fifteen quarternary carbons.

The unambiguous proton and carbon assignment with long-range correlation between carbons and proton observed from HMBC spectrum (Figure 8) and comparison with the data previously report were summarization Table 7

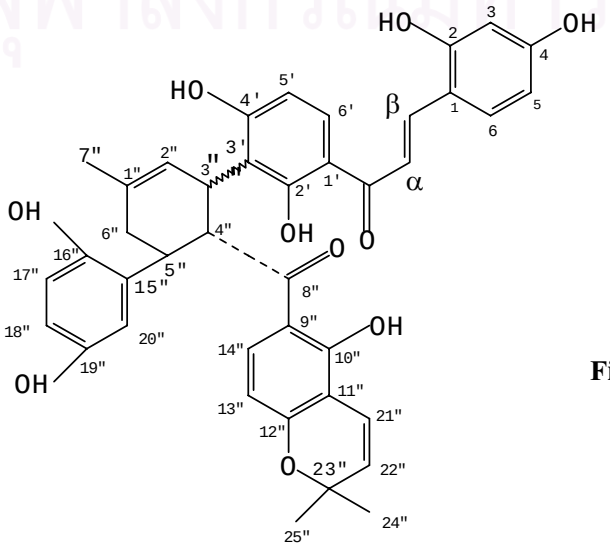


Figure 7 The structure of AHM3

Table 7 NMR spectral data of compound AHM3 (acetone- d_6) as compared with artonin D (acetone- d_6)

position	Compound AHM3		Artonin D		HMBC (correlation with ^{1}H)
	^{1}H(mult., *J* in Hz	^{13} C ppm.	^{1}H(mult., *J* in Hz	^{13} C ppm.	
1		115.2		115.3	H-6, H-α
2		160		159.9	H-6, H-β
3	6.47(d, 2)	103.6	6.49(d, 2)	103.7	
4		162.3		162.3	H-6
5	6.42(dd, 2, 6)	109.1	6.43(dd, 2, 8)	109.2	
6	7.63(d, 8)	131.7	7.65(d, 8)	131.8	H-β
α	7.71(d, 15)	117.2	7.72(d, 15)	117.5	
β	8.14(d, 15)	141.0	8.15(d, 15)	141.0	H-6
C=O		193.3		193.4	
1′		114.2		114.3	H-5′
2′		163.5		163.3	H-6′
3′		116.0		116.0	H-5′
4′		165.7		165.8	H-6′
5′	6.35(d, 8)	109.8	6.35(d, 9)	110.0	
6′	7.84(d, 9)	130.7	7.85(d, 9)	130.8	H-2′ , H-4′
1″		135		135.1	H-3″, H-6″
2″	5.65(br, s)	123.2	5.67(br, s)	123.3	H-3″, H-6″
3″	4.18(br, m)	32.8	4.20(br, m)	32.9	H-4″, H-7″ , H-2″
4″	4.65(dd, 5)	47.6	4.67(d, 4,5)	47.7	H-3″, H-6″, H-5″
5″	3.8(m), 2.24(br,d, 18)	36.1	3.82(m), 2.27 (br,d, 17)	36.2	H-20″, H-4″
6″	2.5(br,d, 17)	32.9	2.52(br,d, 17)	33.0	H-4″, H-7″, H-2″
7″		23.8		23.8	H-3″, H-6″
8″		209.7		209.7	
9″		114.0		114.1	H-13″

Table 7 (continued)

position	Compound AHM3		Artonin D		HMBC (correlation with ^{1}H)
	^{1}H(mult.,*J* in Hz	^{13} C ppm.	^{1}H(mult.,*J* in Hz	^{13} C ppm.	
10″		160.7		160.8	H-14″
11″		109.6		109.7	10′- OH
12″		160.8		160.8	H-14″
13″	6.25 (d,*J*=9)	108.8	6.26(d,*J*=9)	108.9	H-23″
14″	8.36(d,*J*=9)	133.8	8.37(d,*J*=9)	133.8	
15″		121.8		121.9	
16″		156.5		156.5	
17″	6.49(d,*J*=2)	103.6	6.51(d,*J*=2)	103.7	
18″		158.0		158.0	H-20 ″
19″	6.29(dd,*J*=2,6)	107.5	6.30(d,*J*=2,8)	107.6	H-17″
20″	6.95(d,*J*=8)	128.8	6.96(d,*J*=8)	128.9	H-5″, H-16″, H-18″
21″	6.56(d,*J*=9)	116.1	6.58(d,*J*=10)	116.1	
22″	5.63(d,*J*=10)	129.1	5.65(d,*J*=10)	129.1	
23″		78.5		78.6	H-24″, H-25″, H-13″
24″		28.5		28.6	
25″		28.4		28.5	
7″-Me	1.91(3H,br,s)		1.93(3H,br,s)		
23"-Me	1.37,1.39(3H,s)		1.38,1.41(3H, s)		
2′-OH	14.53(s)		14.53(s)		
10′-OH	12.88(s)		12.89(s)		

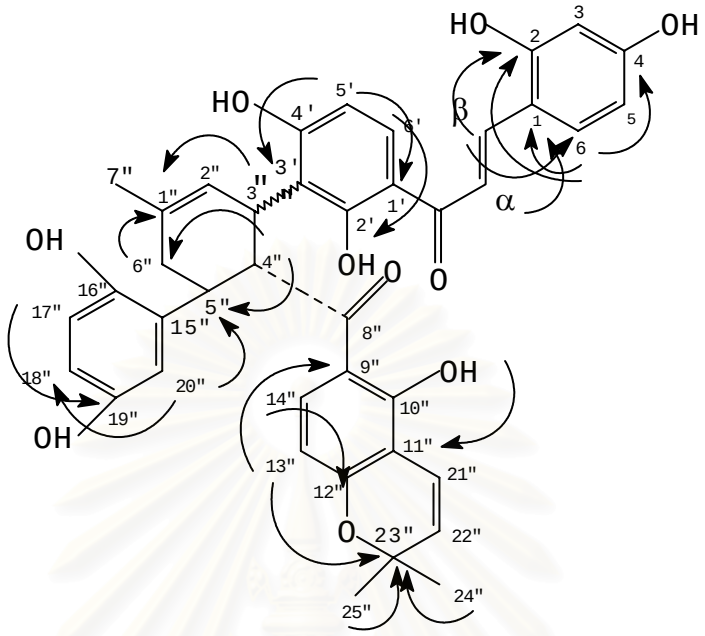
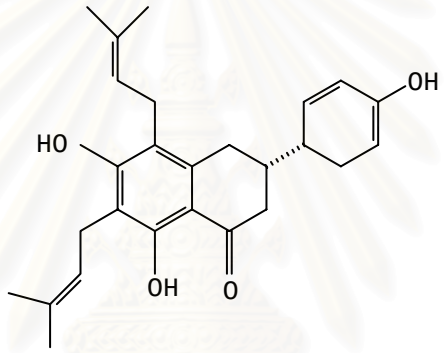


Figure 8 Selected HMBC correlations of compound AHM3

Artonin A , artonin D and cycloheterophyllin were isolated from stem bark of *Artocarpus heterophyllus* .These compounds were known Jack fruit tree isoprenylated flavonoids. Artonin A and artonin D were founded in root bark by Hano in 1989 Hano , Aida and Nomura in 1990 , cycloheterophyllin was founded in stem bark by Rao Varada and Venkataraman in 1971 and root bark by Hano in 1989.

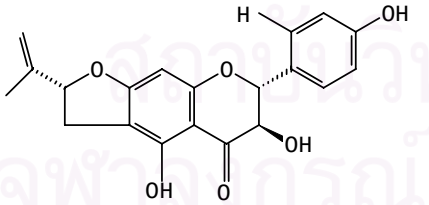
Artonin A , artonin D were found in stem bark for the first time in this investigation and there pure compounds (artonin A , artonin D ,cycloheterophyllin) could be considered as phytoalexin because those compounds could only be isolated from part of the damage stem bark giving characteristic orange red patch of which markedly different from normal stem bark (Figure 2). According to Barron .D and Ibrahim.R K in 1996 revision , isoprenylated flavonoid compounds are considered as constitutive antimicrobial substances especially those belonging to isoflavonoid and stilbenoids . The definition of the different type of antimicrobial metabolites , whether they are constitutive or induced by biotic / abiotic elieitors (phytoalexins) ,has recently been discussed by Grayer and Harborn .The antifungal / antimicrobial effect of flavonoids is mainly attributed to the presence of

phenolic hydroxyl group which have high affinity for proteins and therefore act as inhibitor of microbial enzymes. In addition of the flavonoid ring system with prenyl groups is through to increase their lipophilicity and , consequently, enhances their antimicrobial activity through interaction with cellular membranes. Although no particular pattern for a structure- activity relationship could be established, it is generally agreed that at least one phenolic hydroxyl group and a certain degree of lipophilicity are required for the biocidal of flavonoid compounds. However , on the nature of the flavonoid in question. In fact every prenylflavonoid has antimicrobial activity some of the compound were shown below Lonchocarpol A [220] isolateted from yellow lupin root showed strong growth inhibited of *Cladosporium herbarum*. (Tahara,1994)

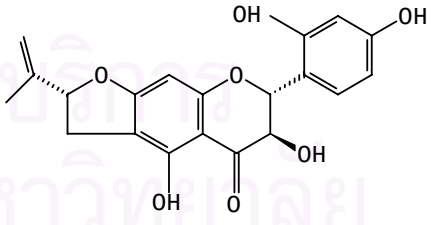


Lonchocarpol A [220]

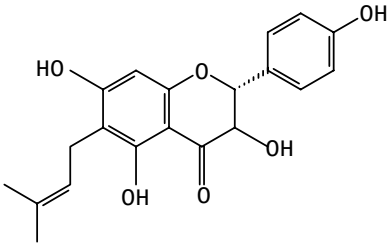
Shuterol [221],shuterone A [222] ,shuterone[223], and shuteron B [224] isolated from *Shuteria vestita* showed inhibited the growth of *Cladosporium herbarum*. (Ingham ,1986)



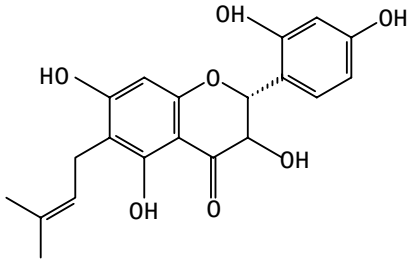
Shuterol [221]



Shuterone A [222]

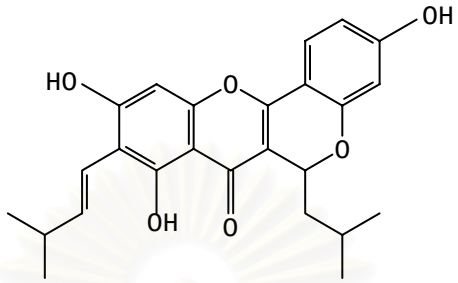


Shuterone [223]



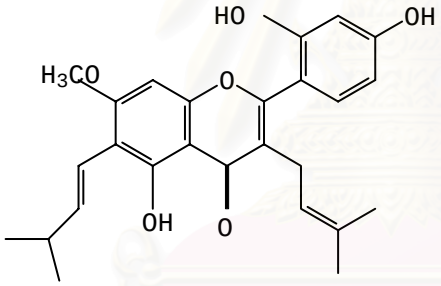
Shuteron B [224]

Brosimone I [225] isolated from root of *Brosimopsis oblongifolia* showed antifungal and antibacterial activity . (Ferrari, 1988)

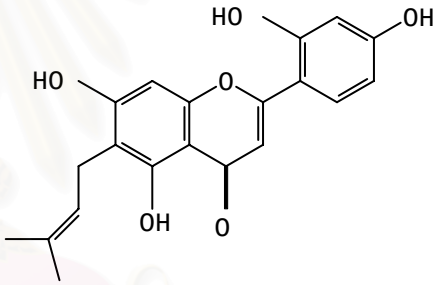


Brosimone I [225]

Artocarpin [4] and artocarpesin [3] from the heartwood of *Artocarpus heterophyllus*. Inhibited growth of *Streptococci mutans* . (Sato, 1996)



Artocarpin [4]



Artocarpesin [3]

Conclusively, other isoprenylated flavonoids from *Artocarpus* species should be studied for their of antimicrobial activities . In addition to this study , comparison of TLC properties between normal bark and damage bark extract would conclusively confirm the present of phytoalexin in the later extract.

CHAPTER V

CONCLUSION

In this present investigation of *Atocarpus heterophyllus* stem bark , two prenylated flavones and one Diels- Alder-type adduct were isolated. The flavones were identified as artonin A and cycloheterophyllin. The Diels –Ader type adduct identified as artonin D. The identification of these compounds were based on the data from various spectroscopic techniques.

This work offers some knowledge in supporting chemotaxonomic information and phytochemical notification. Revision of ^{13}C chemical shift , at C-5 , and C-8a of artonin A were achieved through careful examination of its HMBC spectra.

The complete carbon and proton assignments of all isolated compounds were made through extensive studies of one and two dimentional NMR spectra.

The occurrence of prenylated flavones in the damaged stem bark was considered as phytoalexin was also discussed.

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APPENDIX

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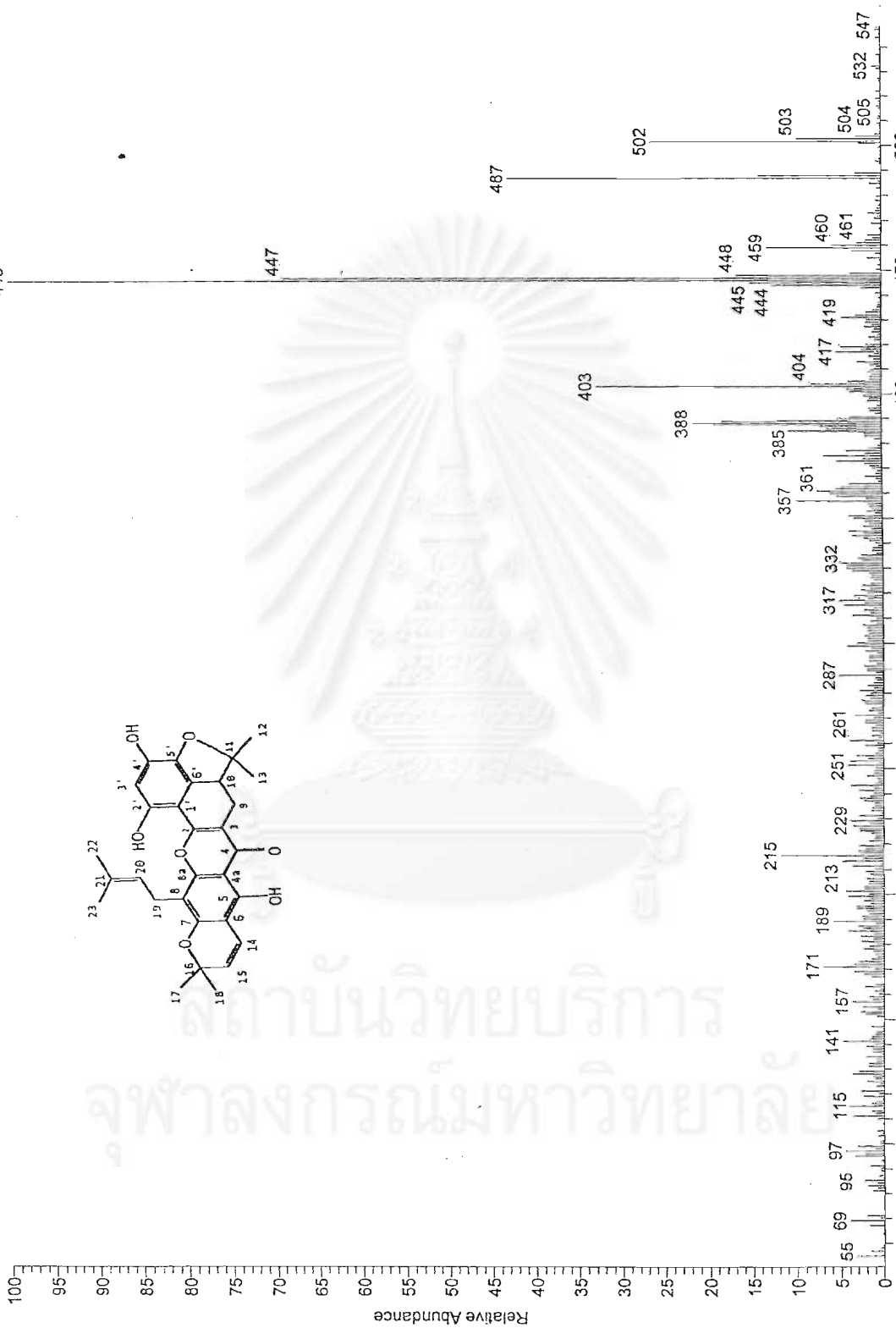

Figure 9 EIMS spectrum of AHT1

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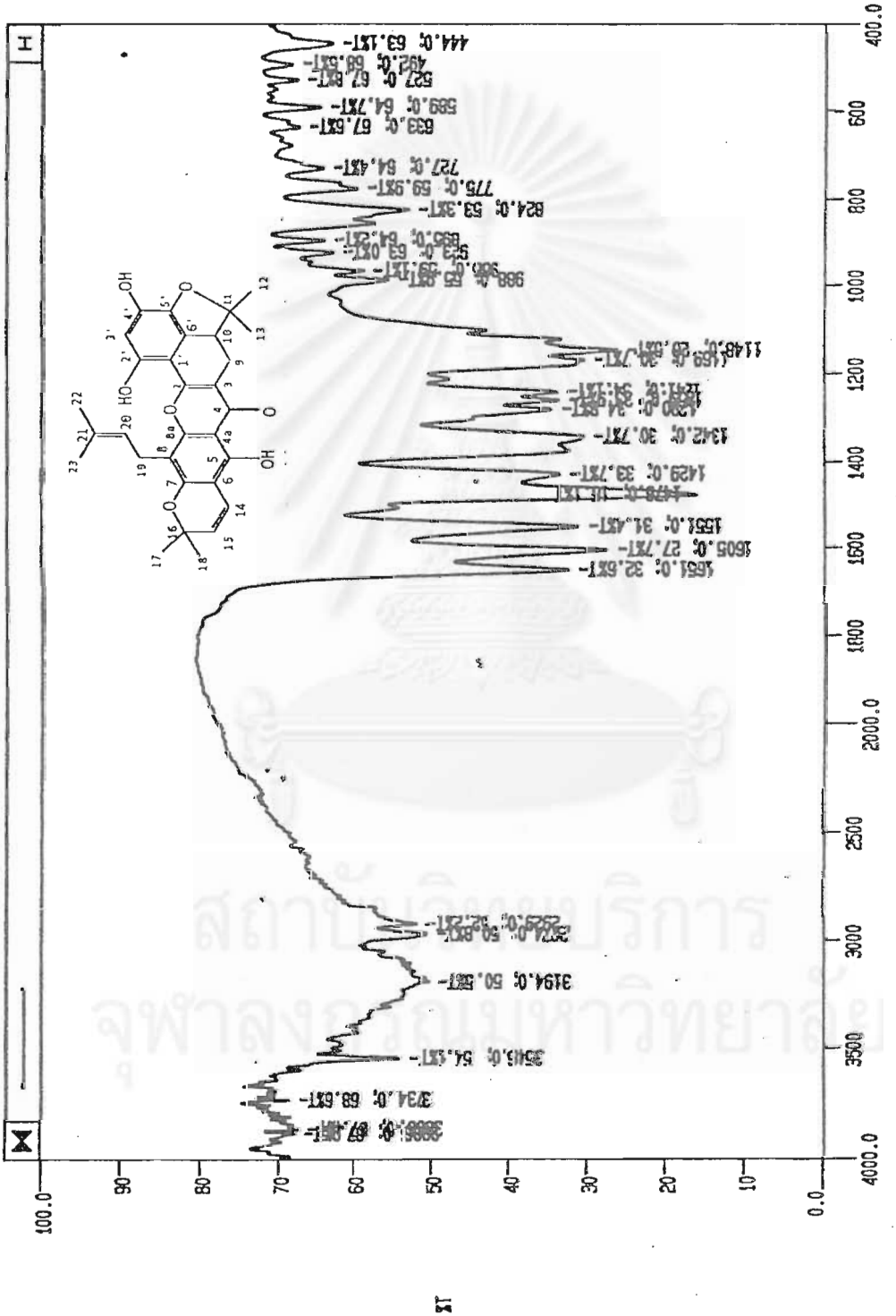

CM-1

Figure 10 IR spectrum of AHT1 (in acetone)

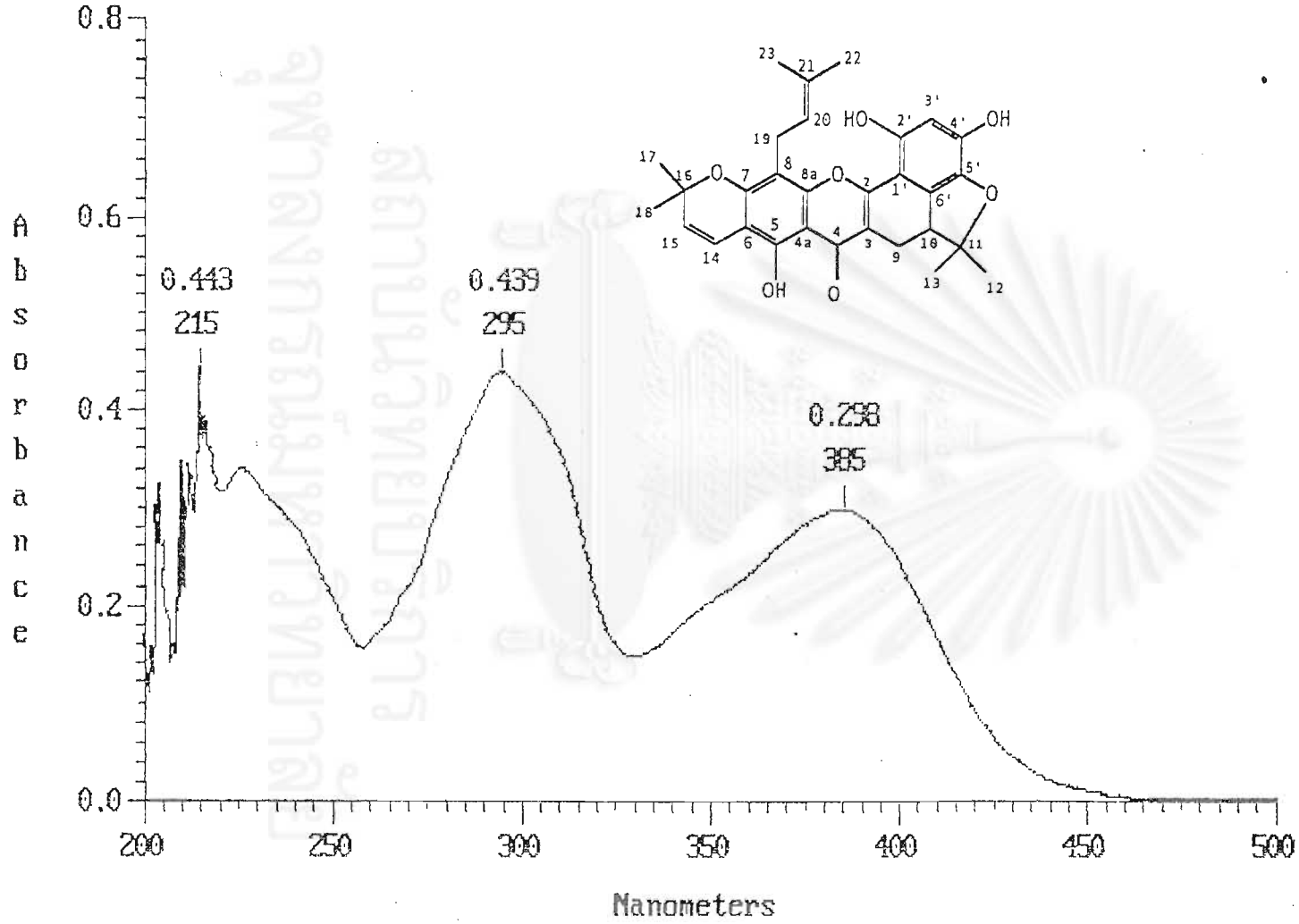

Figure 11 UV spectrum of AHT1 (in methanol)

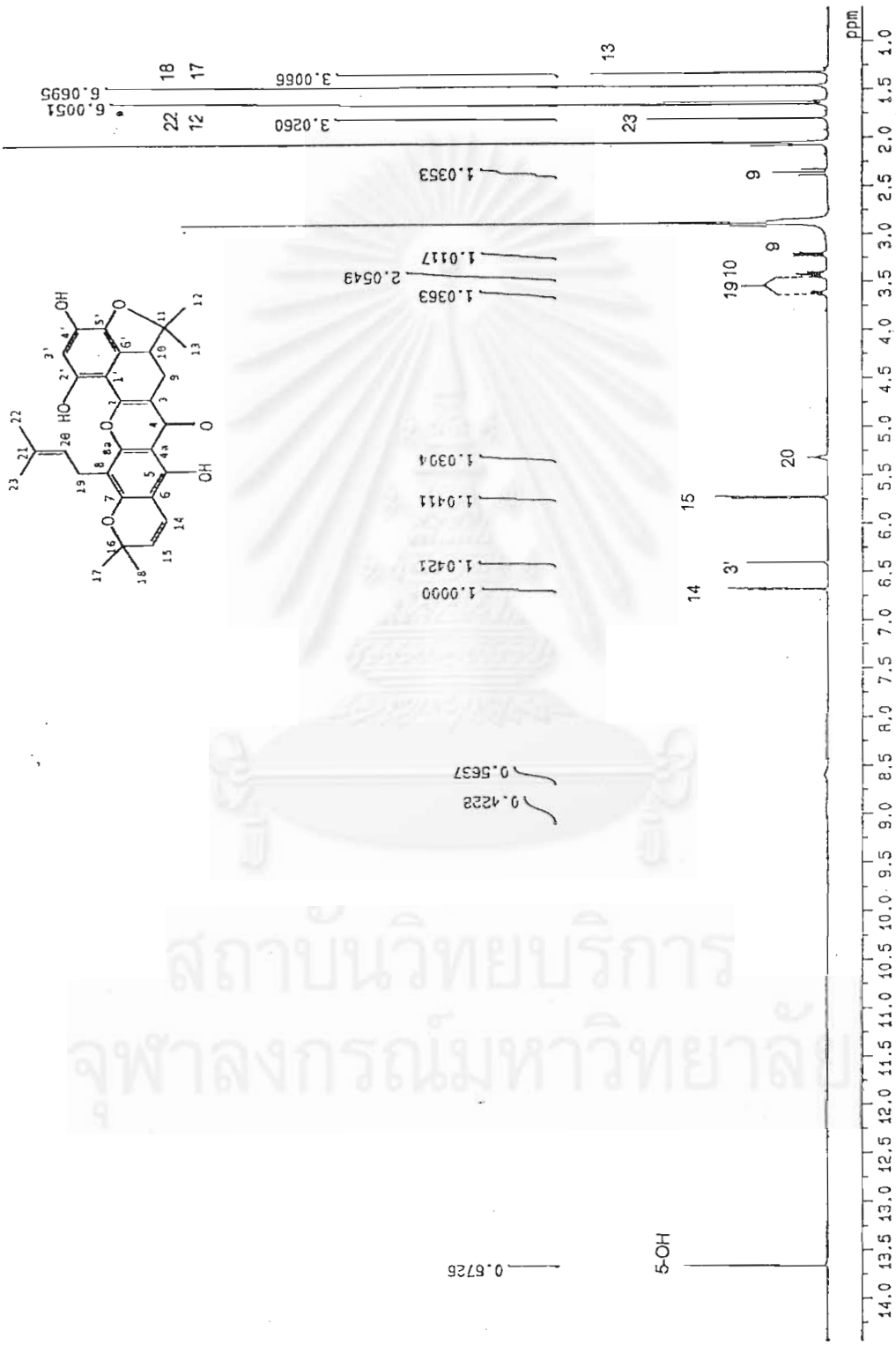

Figure 12 The 500 MHz ^{1}H-NMR spectrum of AHT1 (in acetone-d_6)

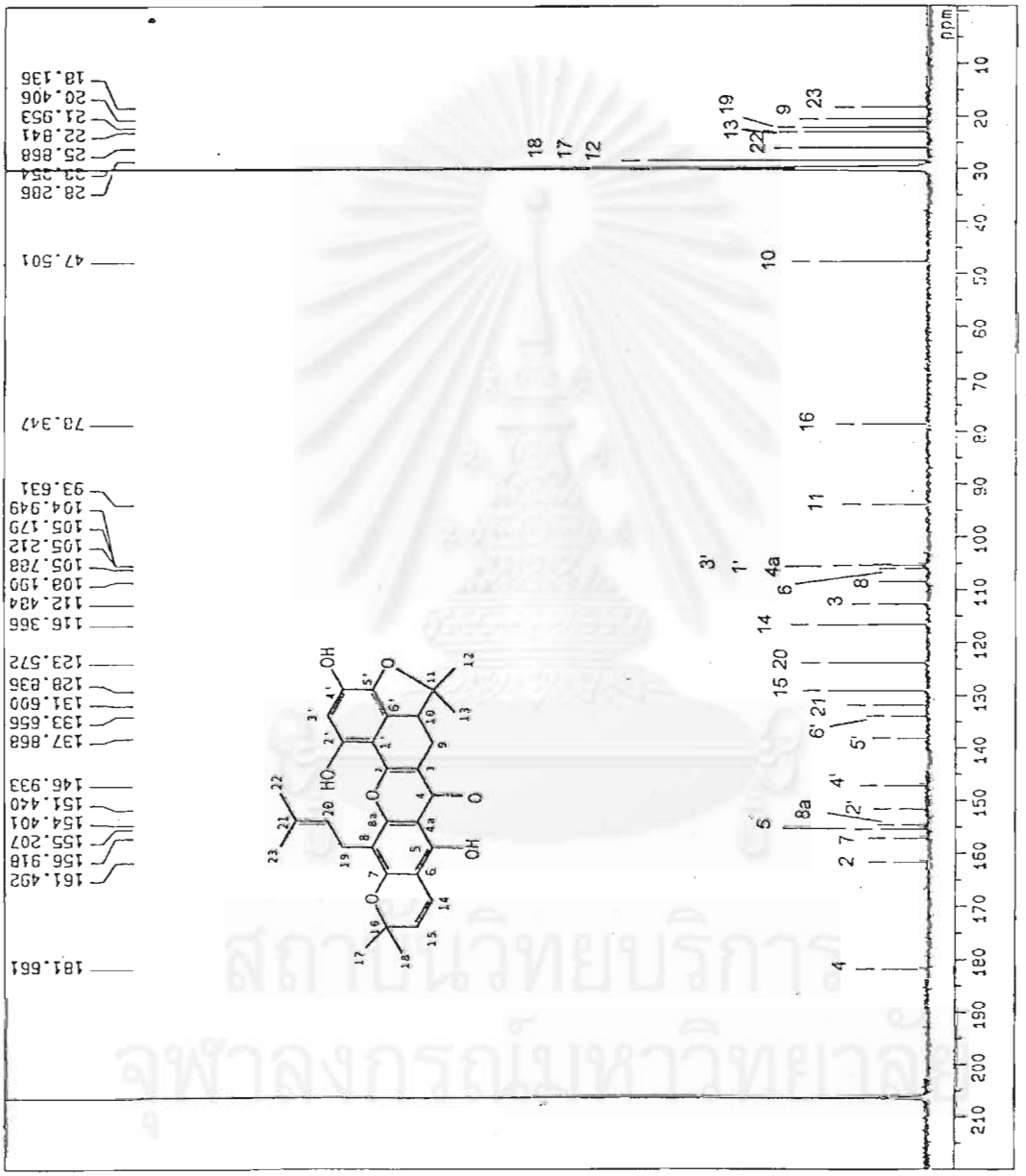

Figure 13 The 125 MHz ^{13}C-NMR spectrum of AHT1 (in acetone-d_6)

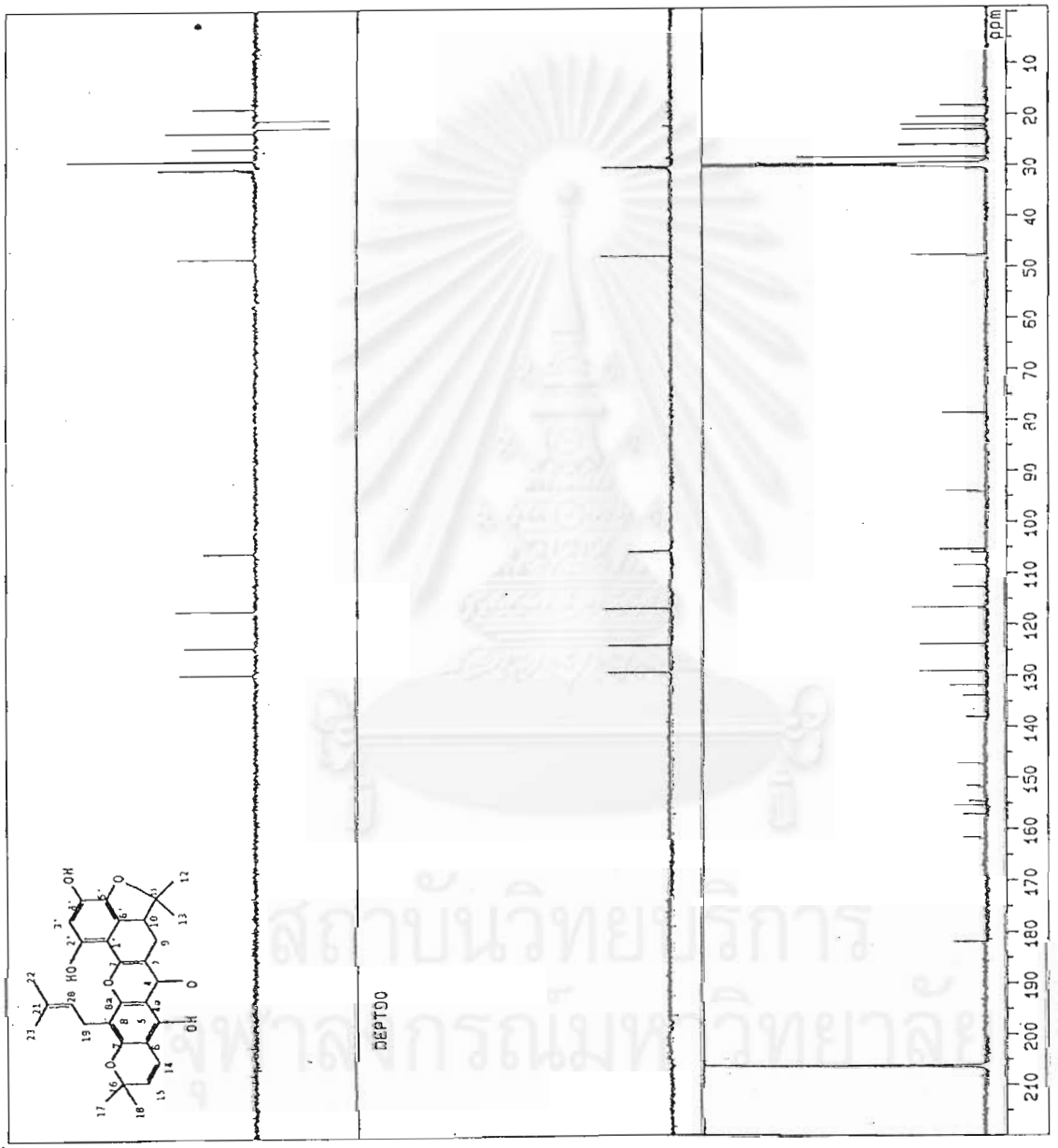

Figure14 The 125 MHz DEPT spectra of AHT1 (in acetone $-d_6$)

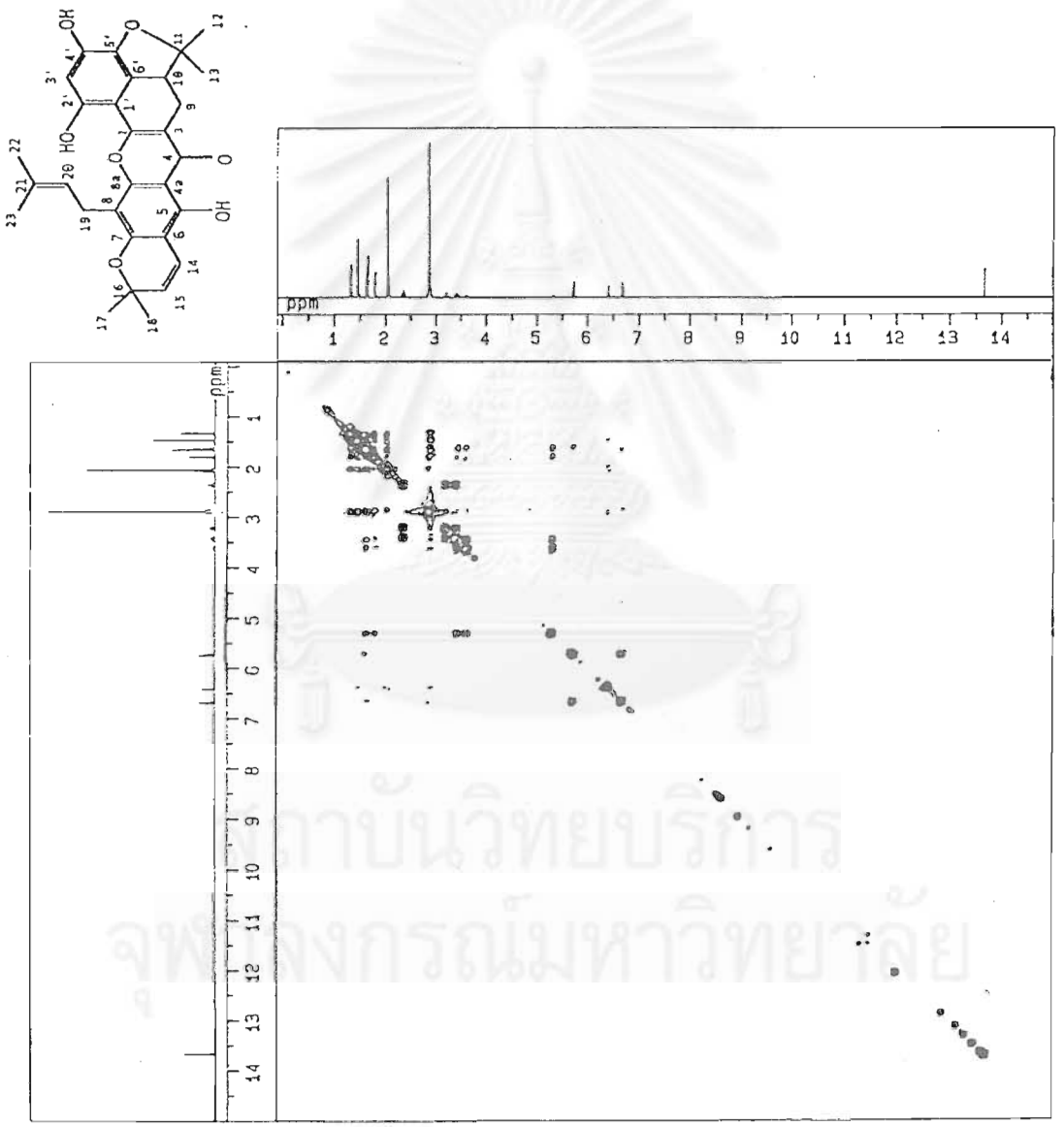

Figure 15 The500 MHz ^{1}H-^{1}H COSY spectrum of AHT1 (in acetone-d_6)

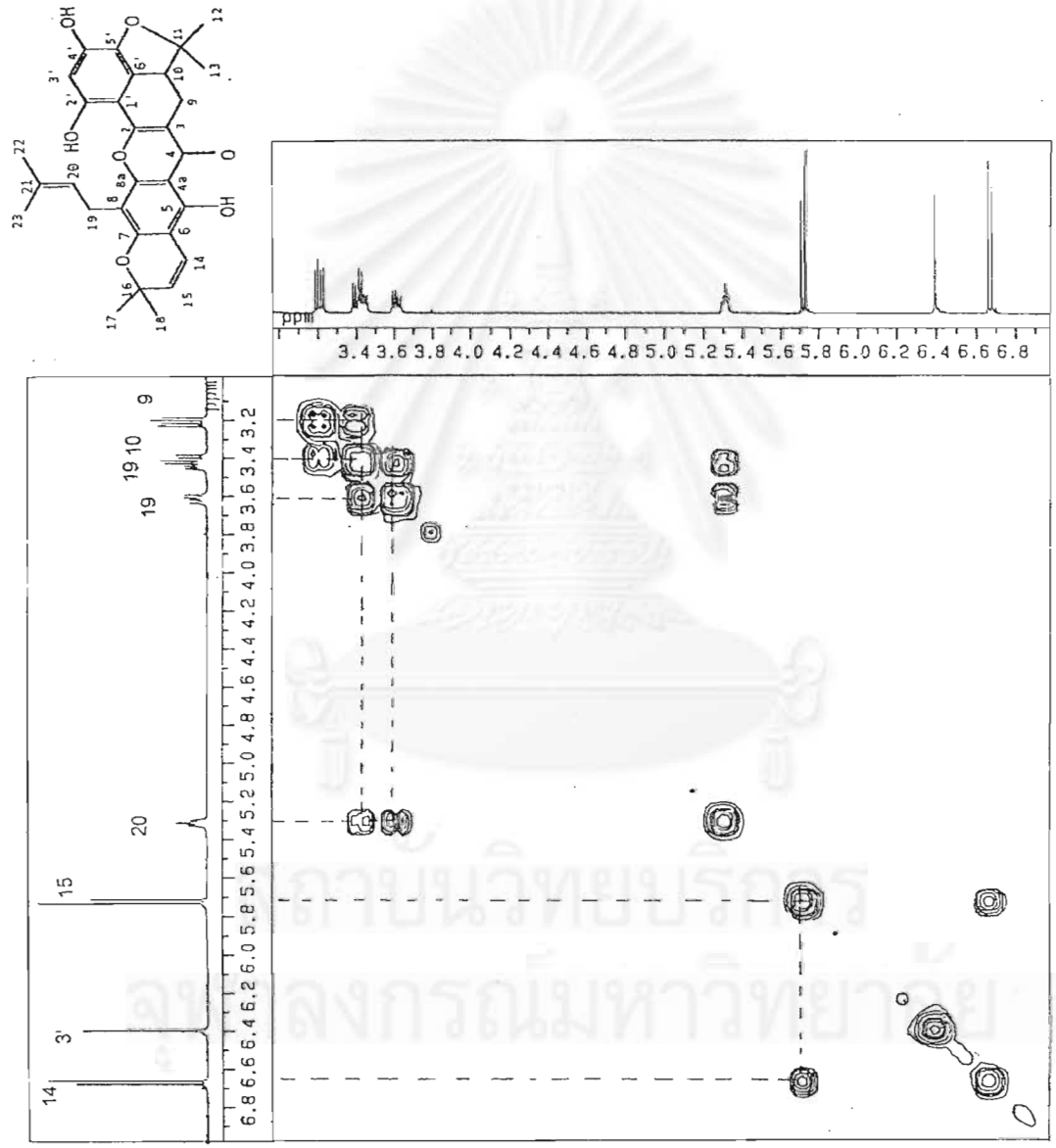

Figure 16 Expansion of the 500 MHz ^{1}H-^{1}H COSY spectrum of AHT1 (in acetone-d_6)

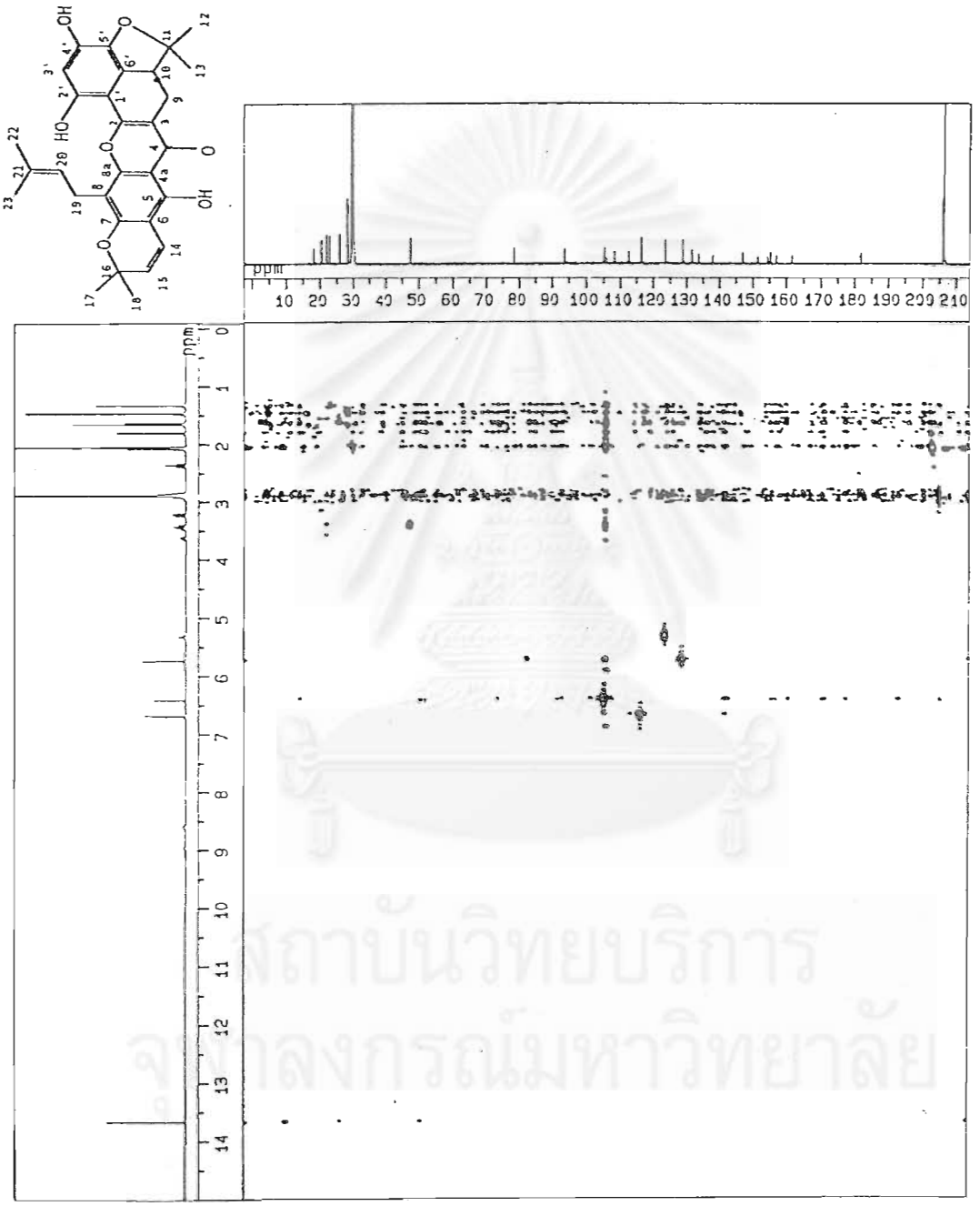

Figure 17 HMQC spectrum of AHT1 (in acetone-d_6)

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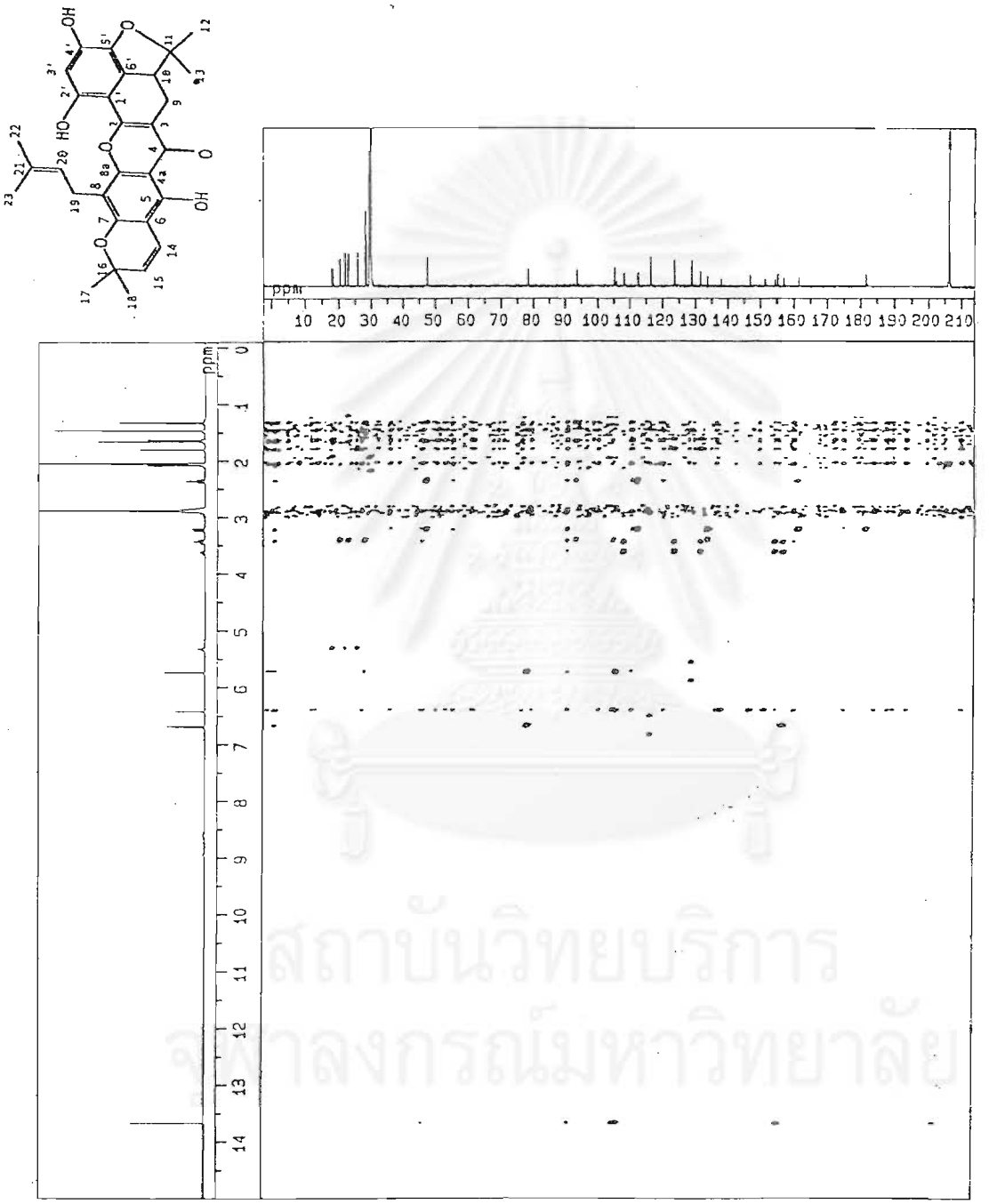


Figure 18 The125 MHz HMBC spectrum of AHT1 (in acetone-d_6)

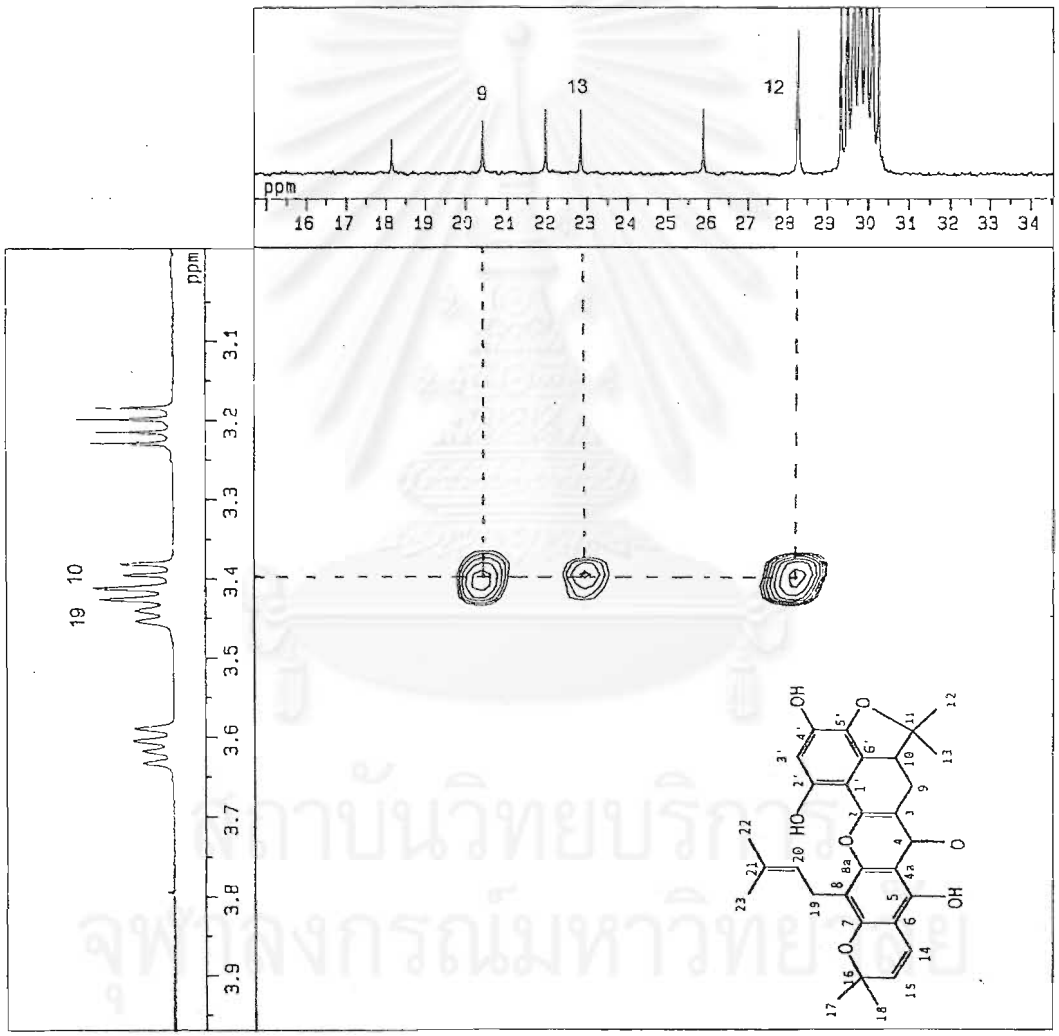


Figure 19 Expansion of an area of 125 MHz HMBC spectrum of AHT1 (in acetone-d_6)

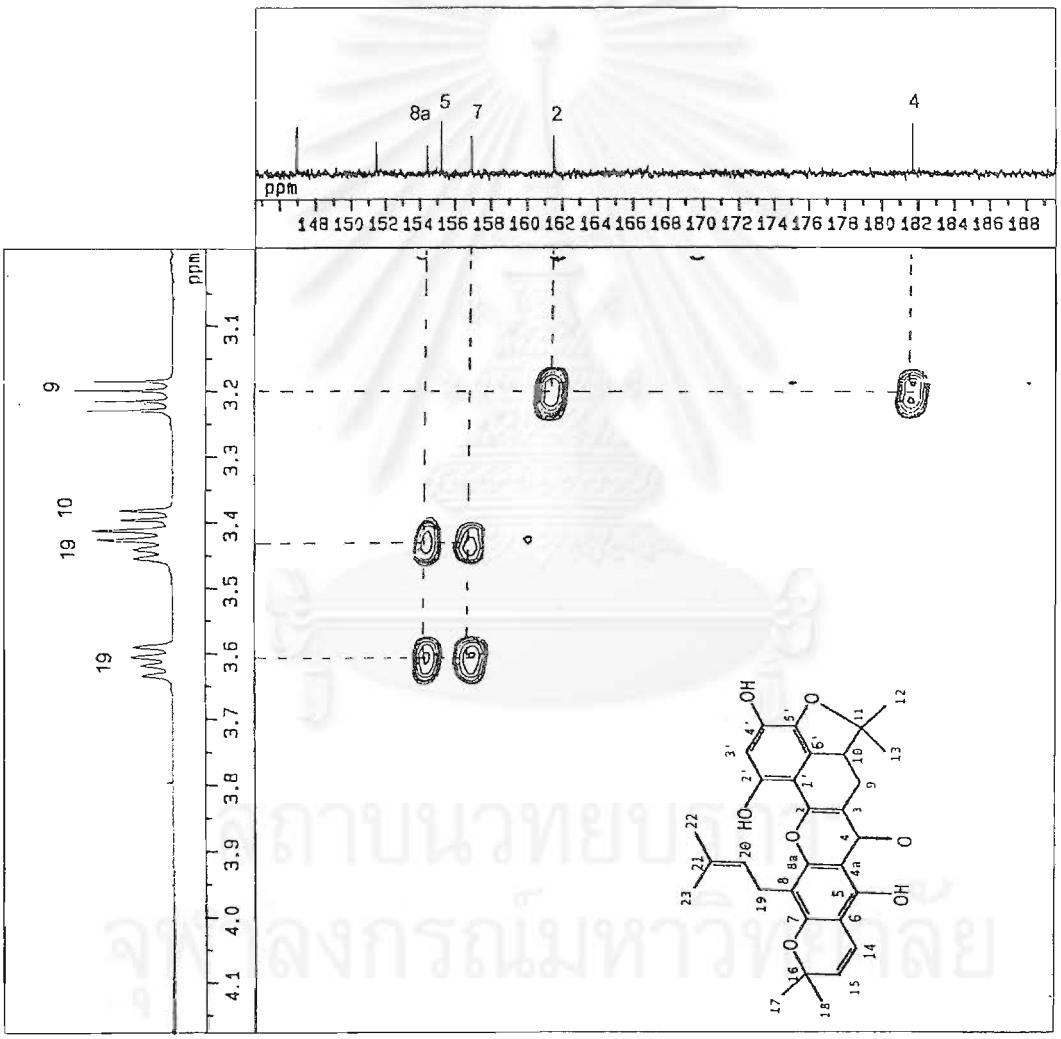


Figure 20 Expansion of an area of 125 MHz HMBC spectrum of AHT1 (in acetone-d_6)

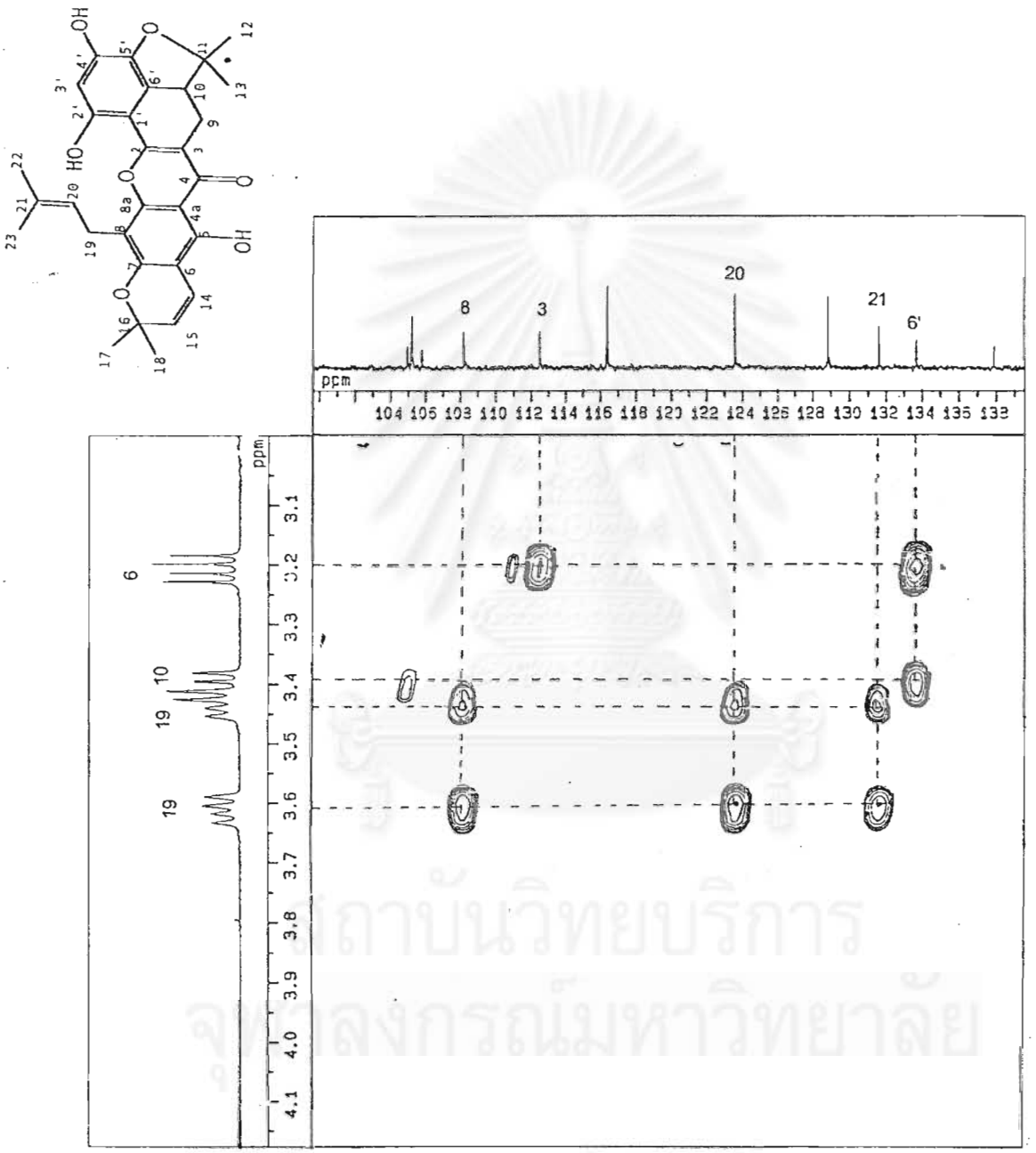


Figure 21 Expansion of an area of 125 MHz HMBC spectrum of AHT1 (in acetone-d_6)

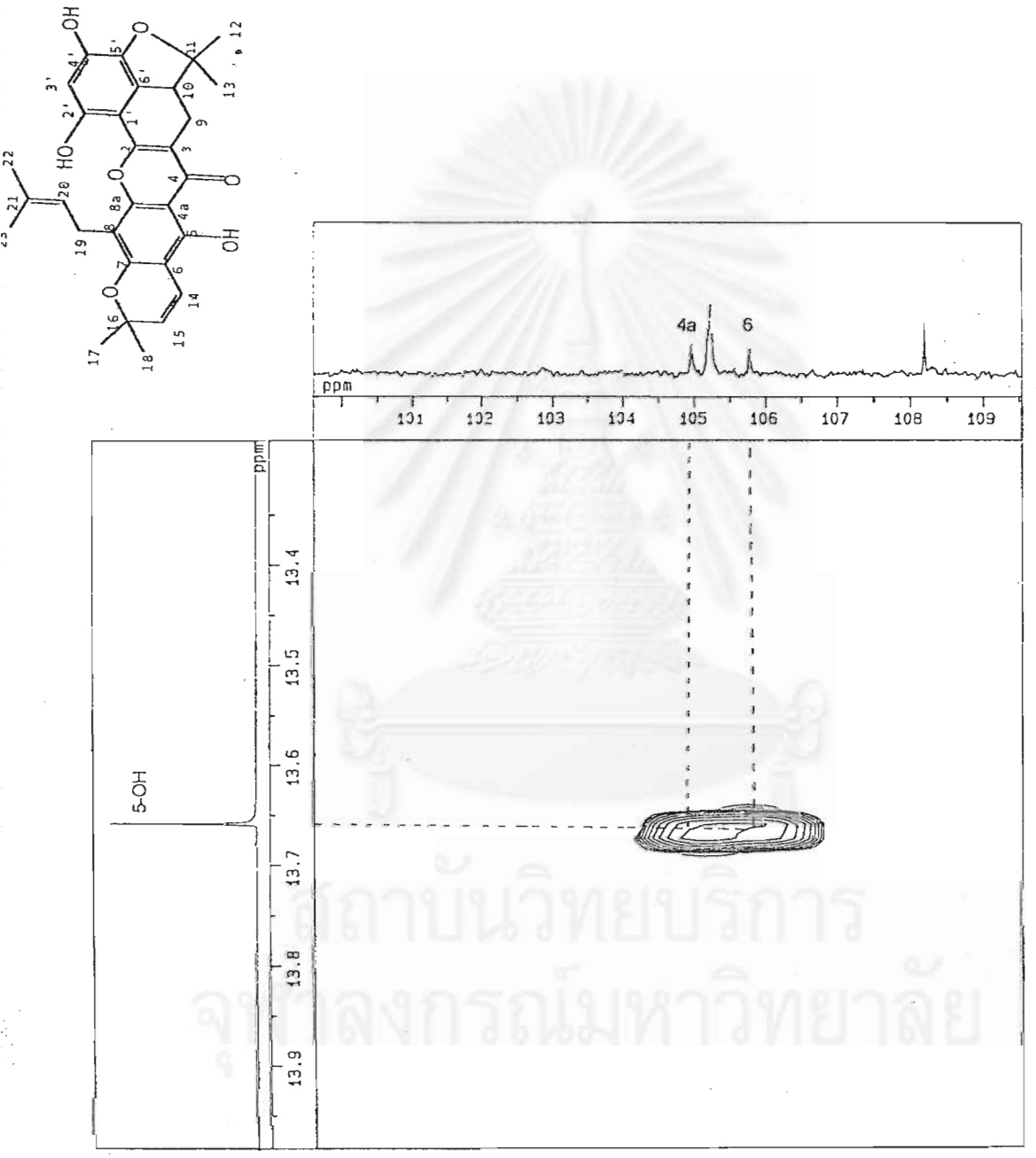


Figure 22 Expansion of an area of 125 MHz HMBC spectrum of AHT1 (in acetone-d_6)

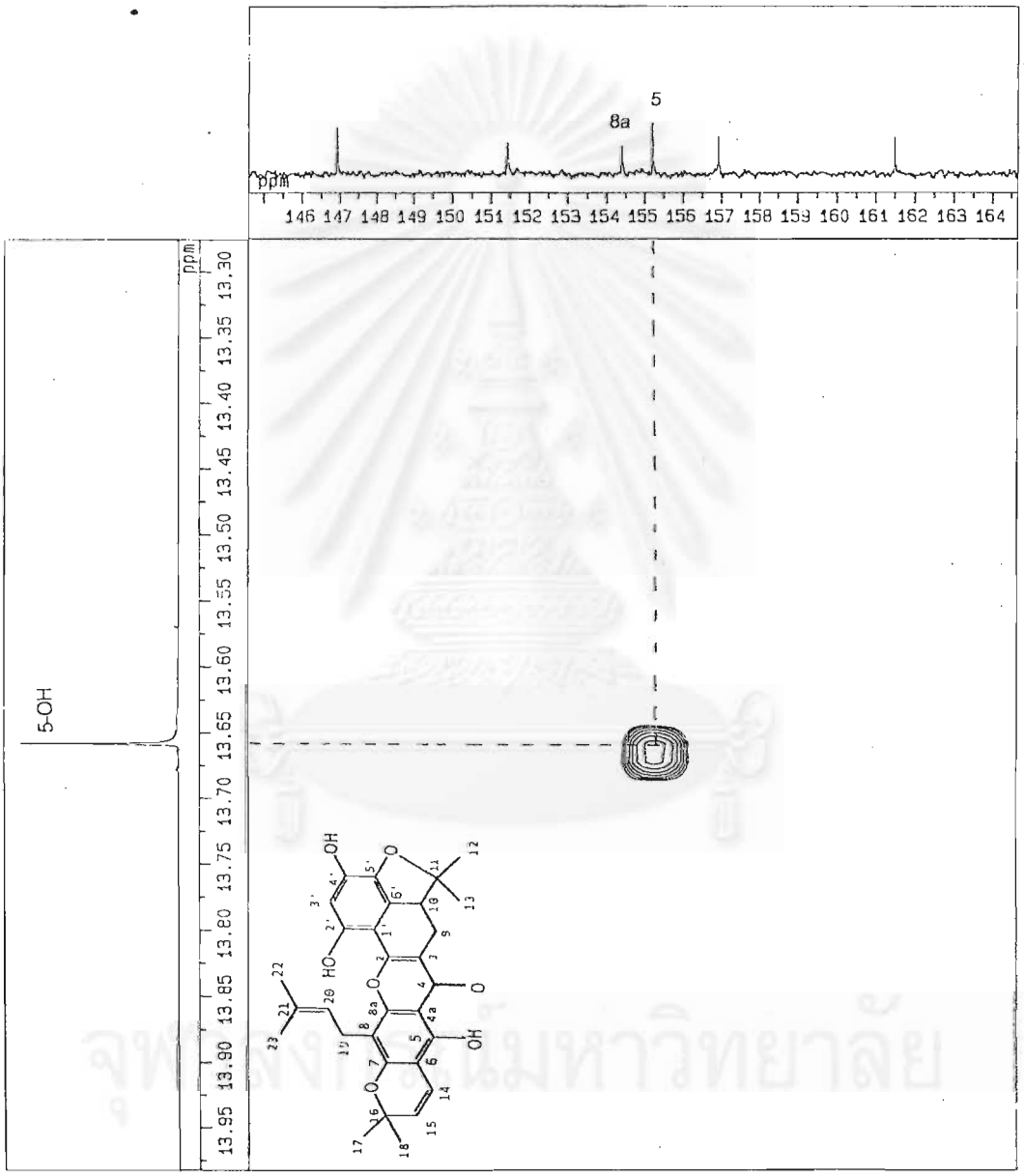


Figure 23 Expansion of an area of 125 MHz HMBC spectrum of AHT1 (in acetone-d_6)

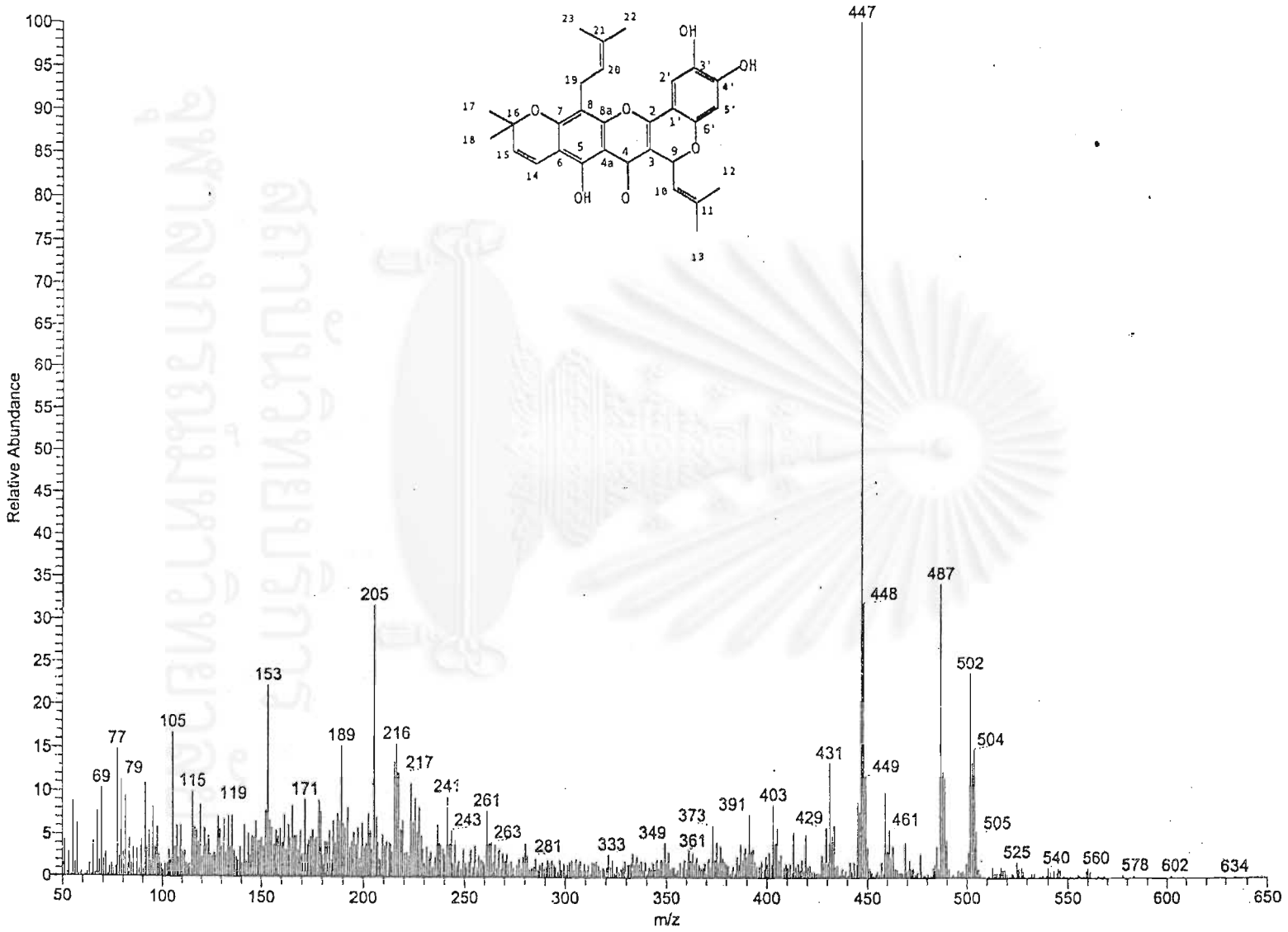


Figure 24 EIMS spectrum of AHT2

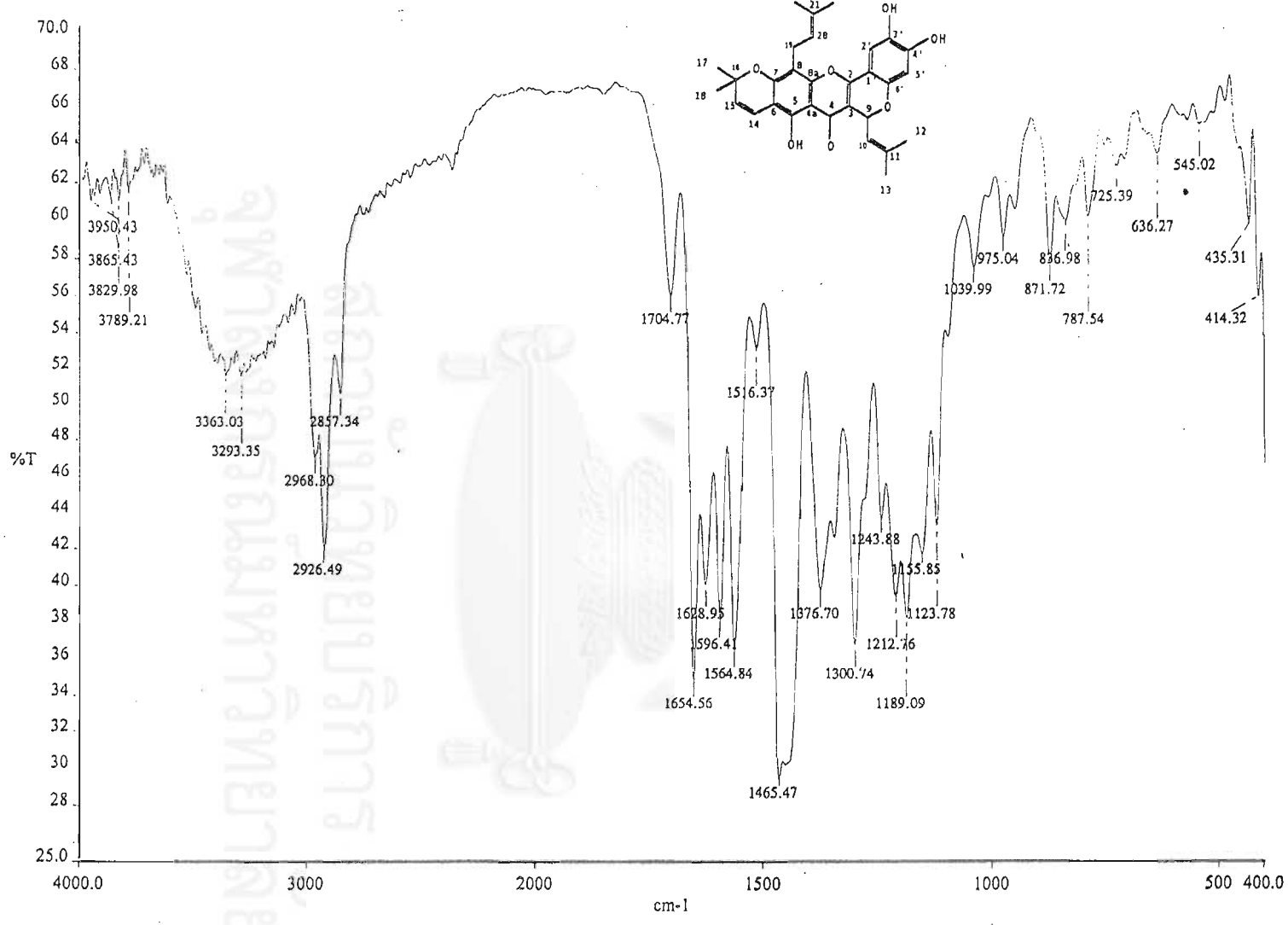


Figure 25 IR spectrum of AHT2 (in acetone)

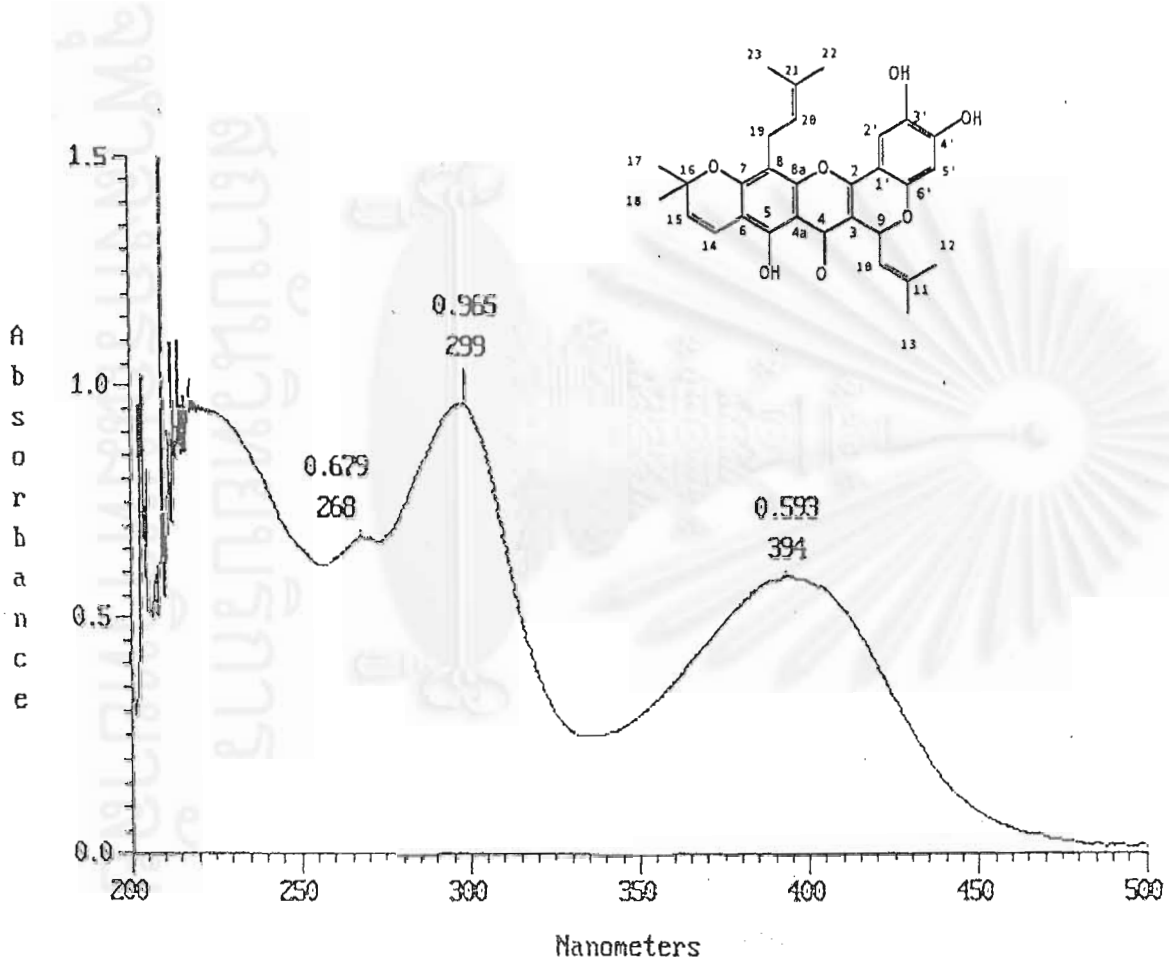


Figure 26 UV spectrum of AHT2 (in methanol)

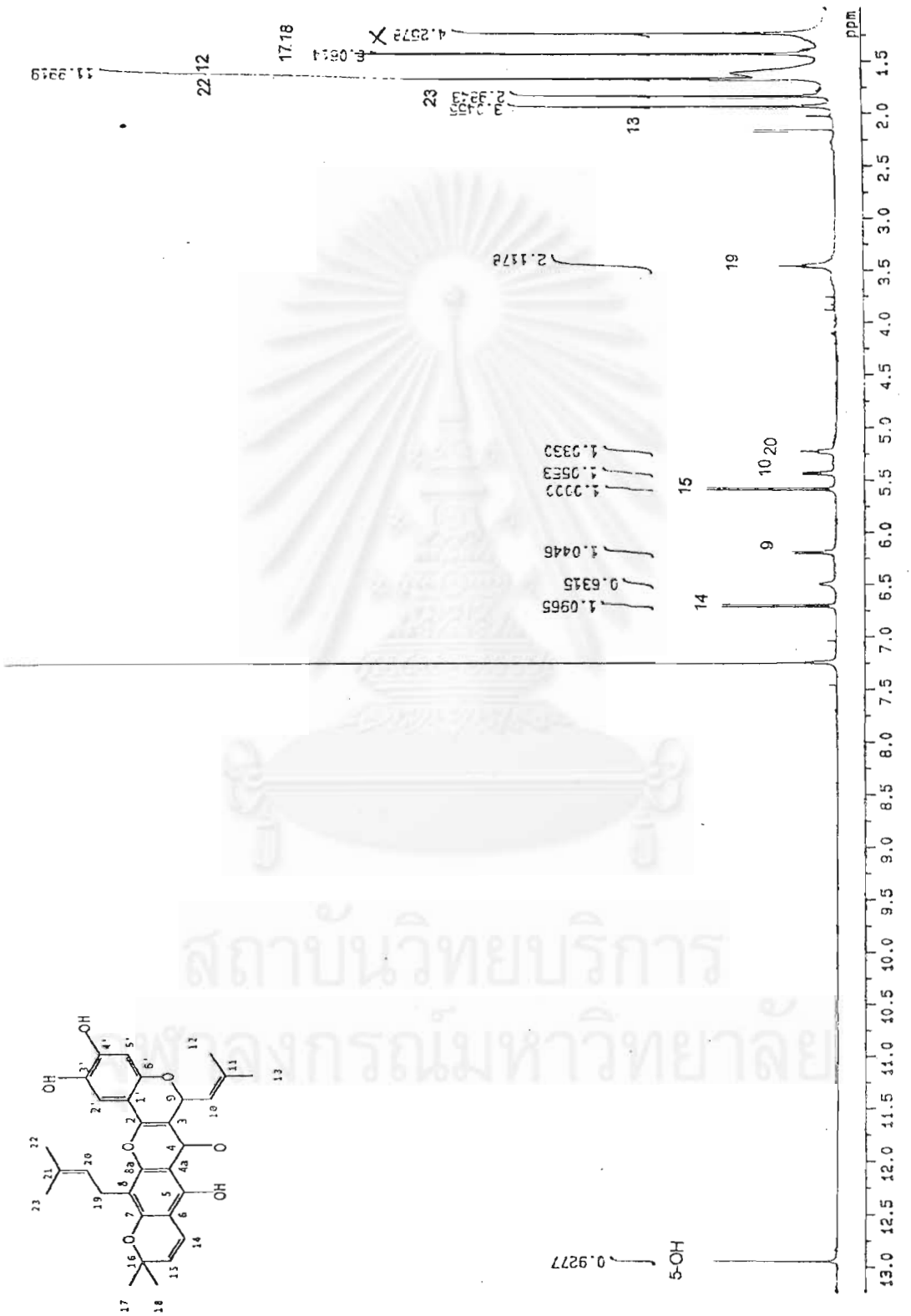


Figure 27 The 500 MHz ^{1}H-NMR spectrum of AHT2 (in $CDCl_3$)

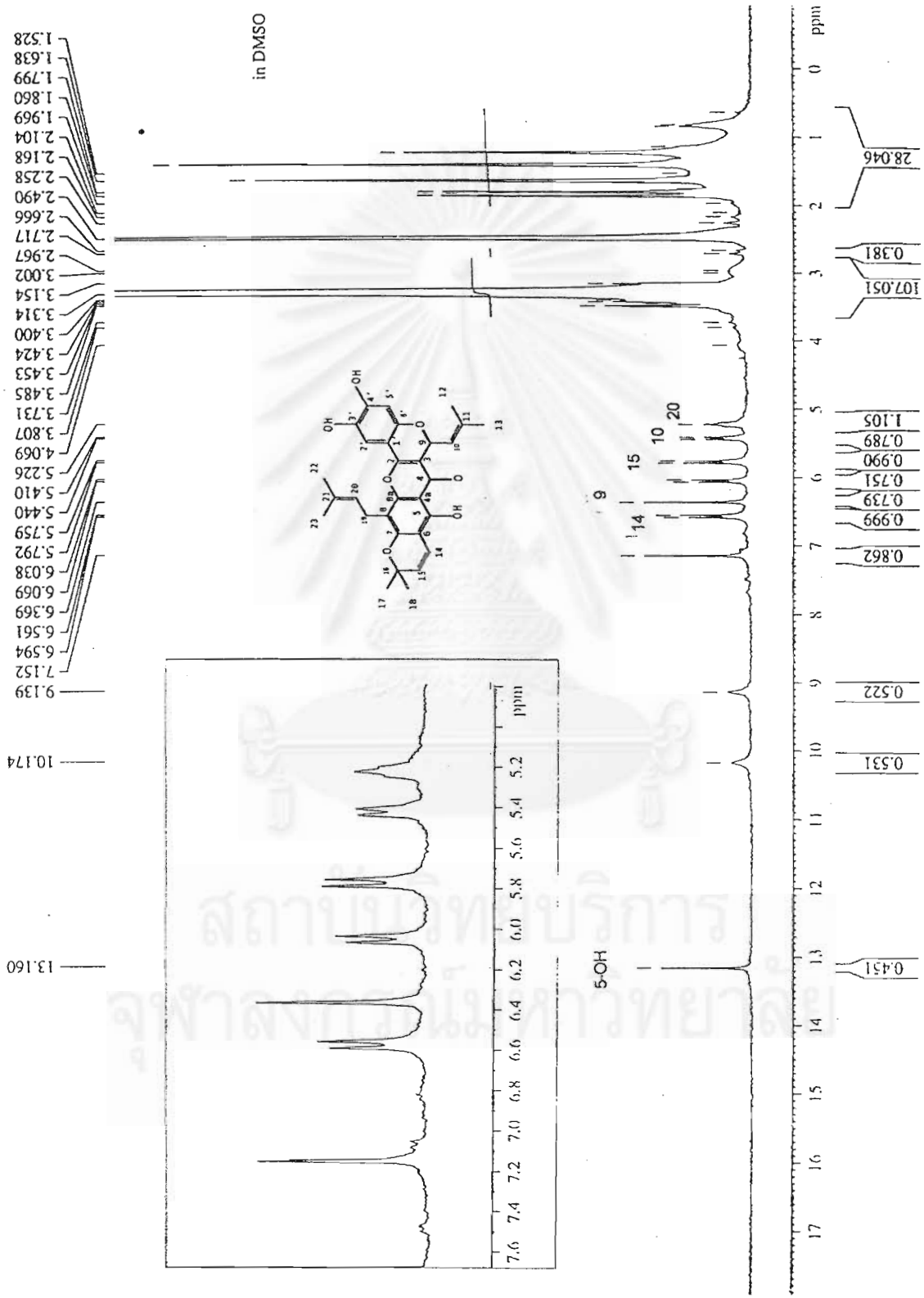
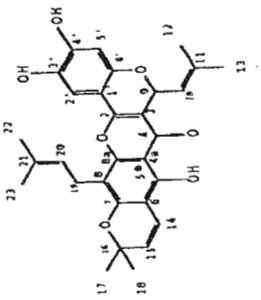


Figure 28 The 500 MHz ^{1}H-NMR spectrum of AHT2 (in DMSO)



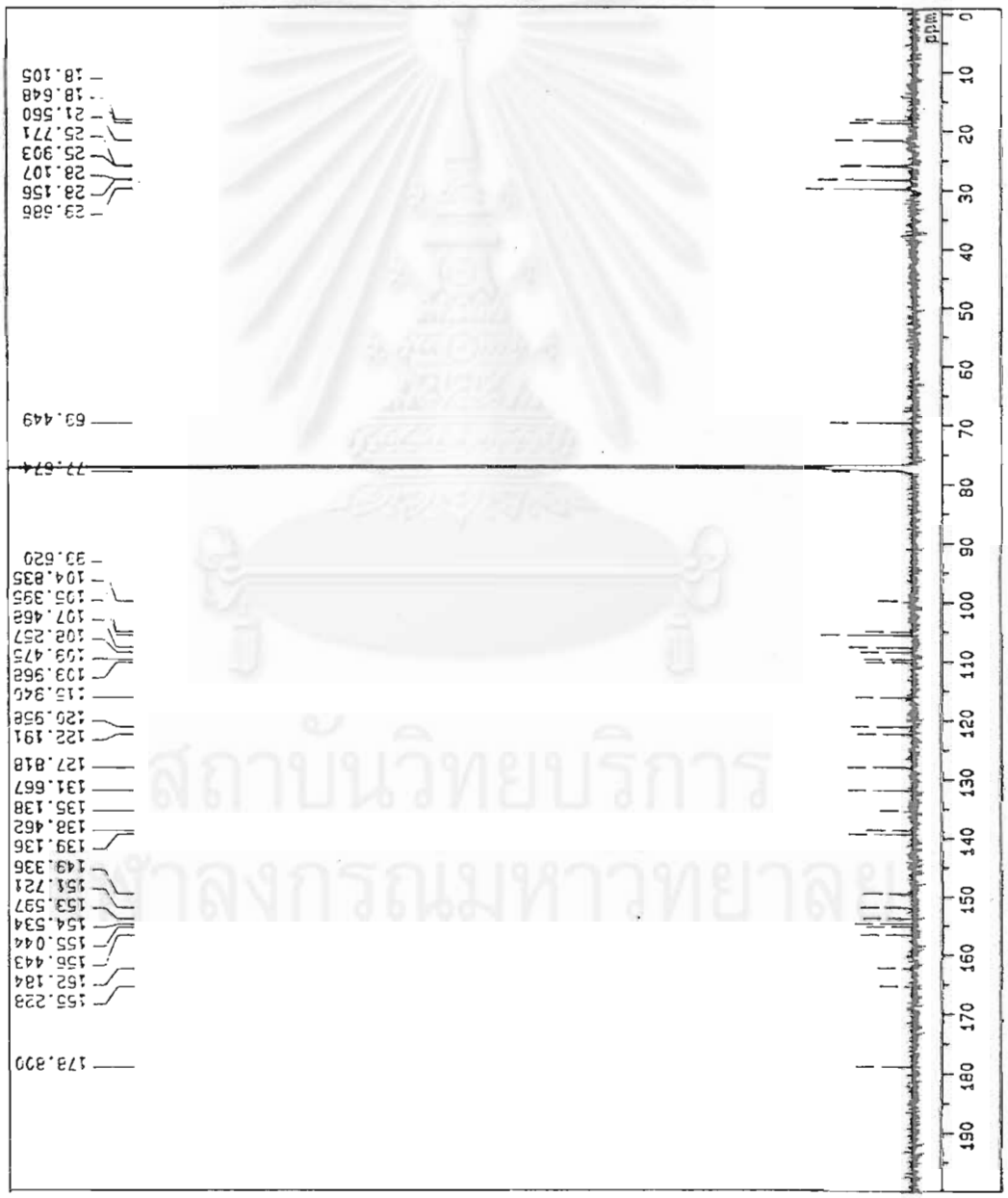


Figure 29 The 125 MHz ^{13}C-NMR spectrum of AHT2 (in $CDCl_3$)

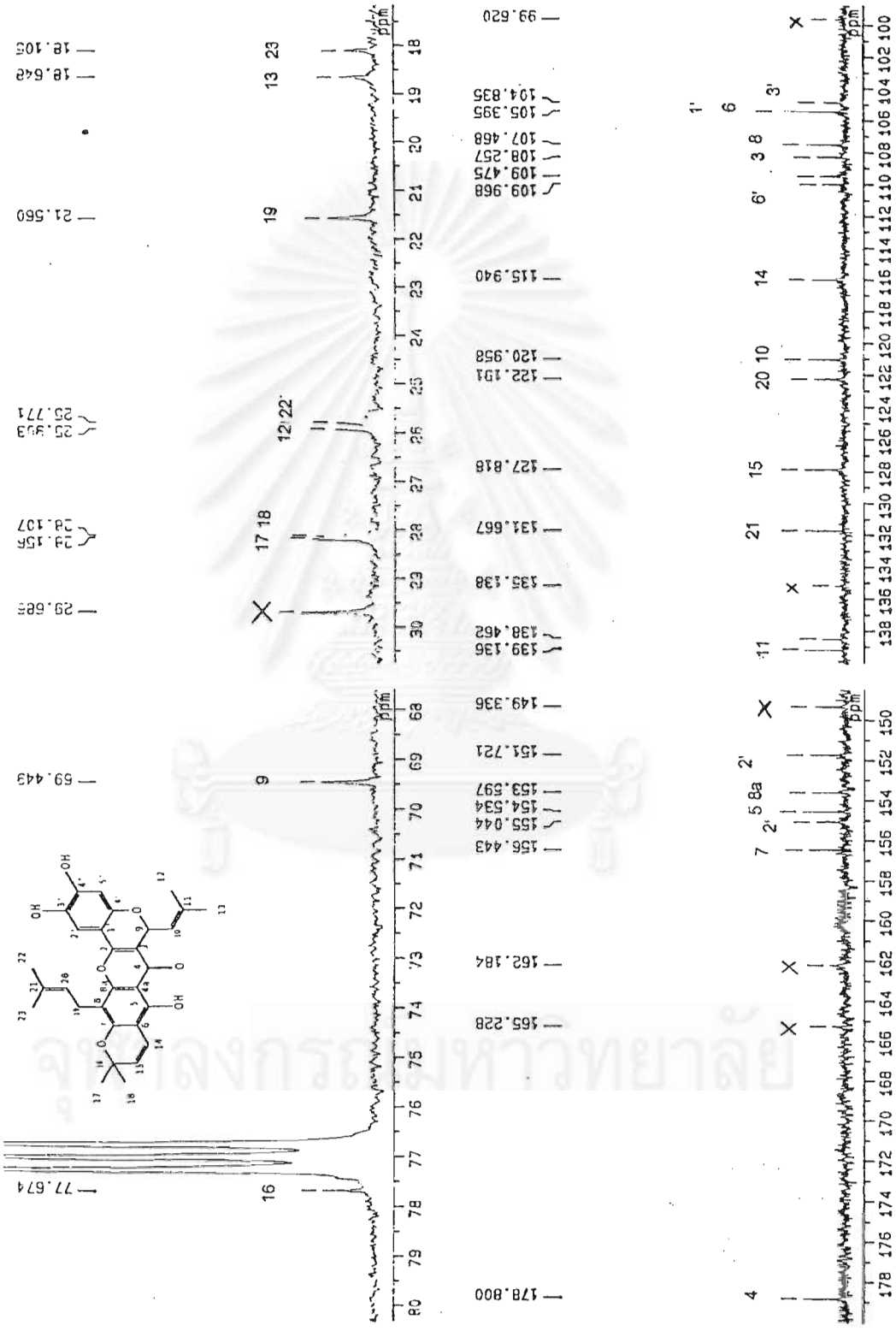


Figure 30 Expansion the 125 MHz ^{13}C-NMR spectrum of AHT2 (in $CDCl_3$)

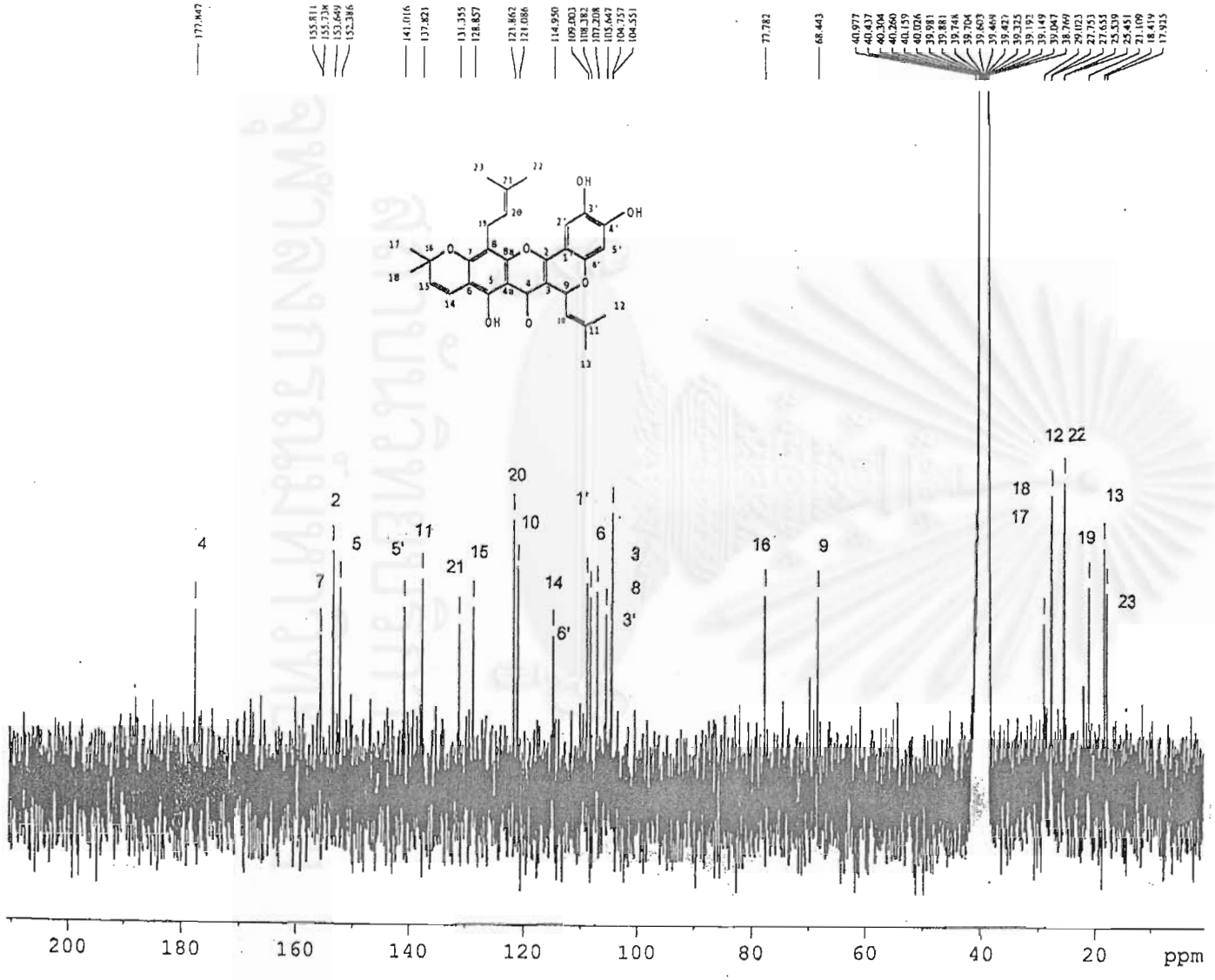
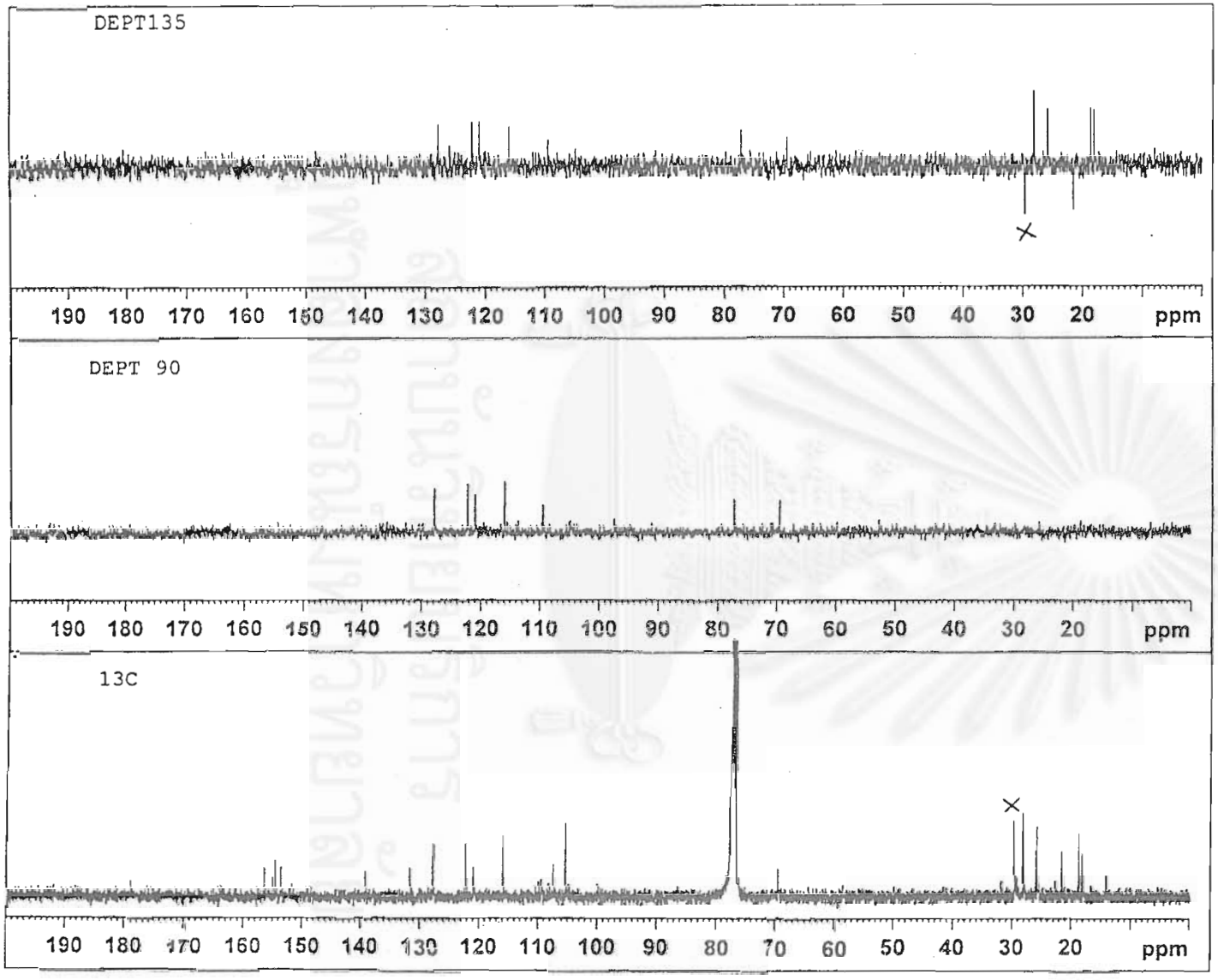


Figure 31 The 125 MHz ^{13}C-NMR spectrum of AHT2 (in DMSO)



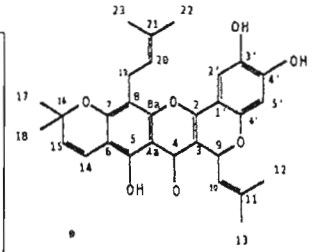


Figure 32 The 125 MHz DEPT spectra of AHT2 (in $CDCl_3$)

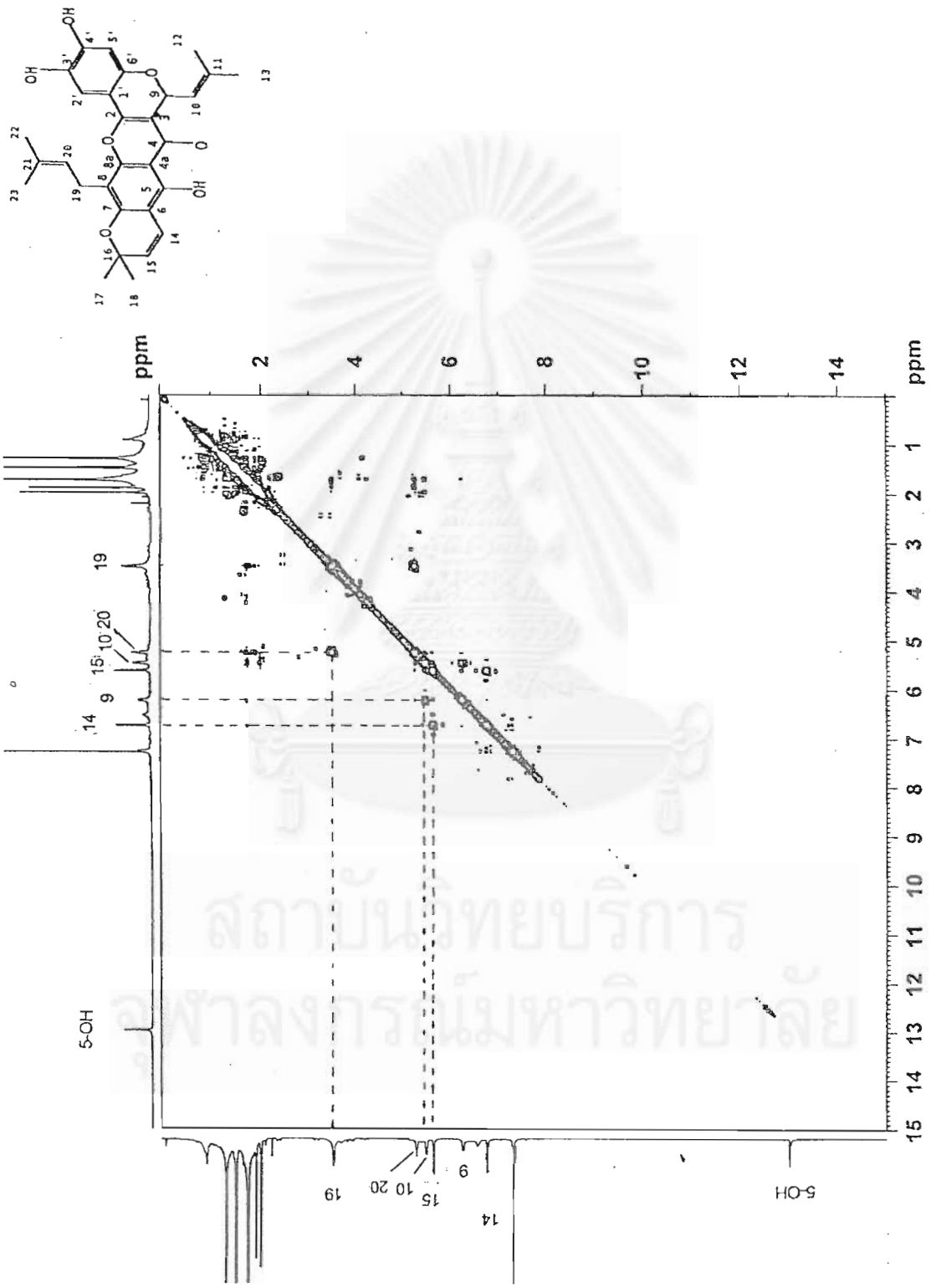


Figure 33 The500 MHz ^{1}H-^{1}H COSY spectrum of AHT2 (in $CDCl_3$)

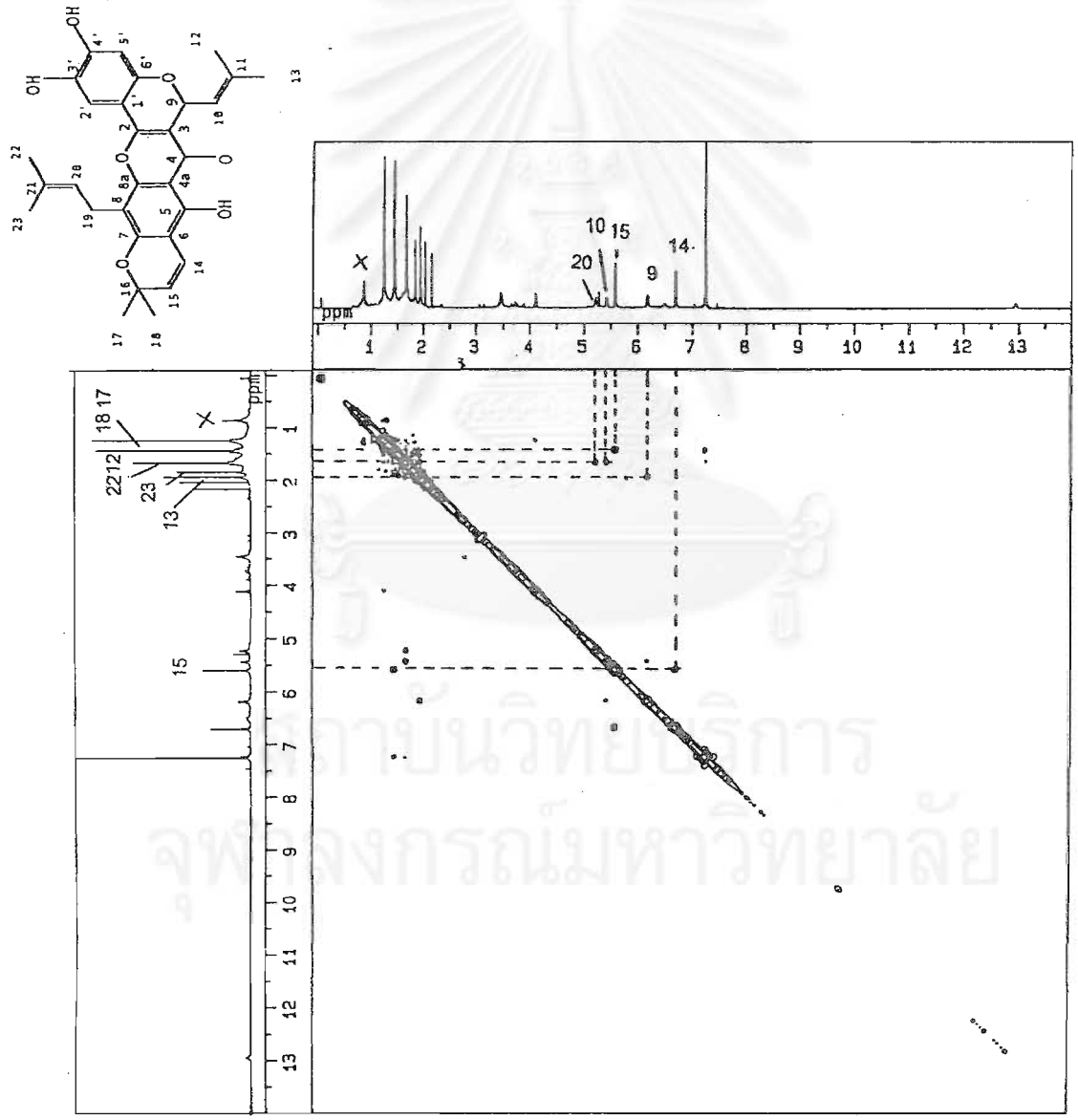


Figure 34 The500 MHz ^{1}H-^{1}H NOESY spectrum of AHT2 (in $CDCl_3$)

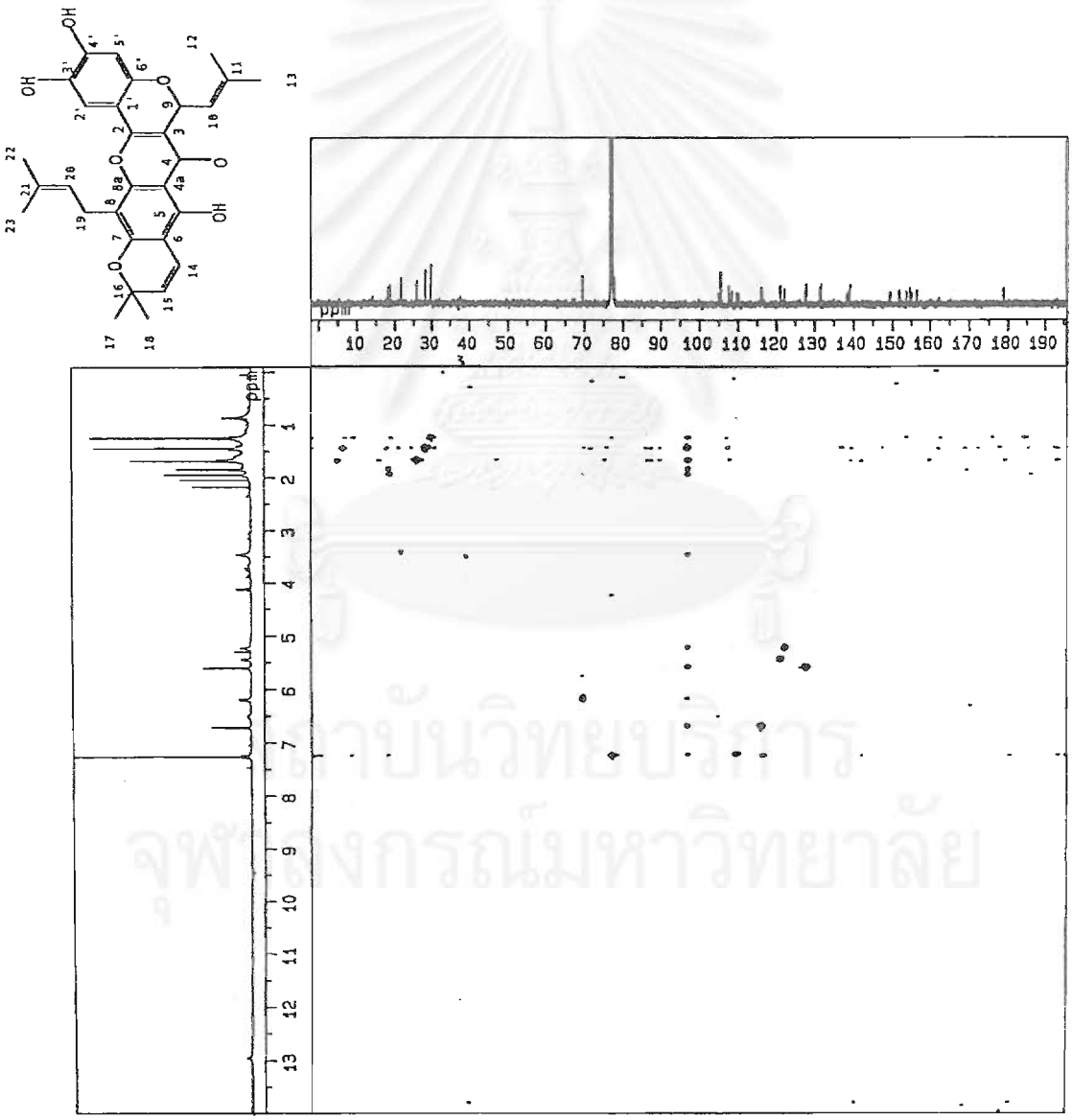


Figure 35 HMQC spectrum of AHT2 (in $CDCl_3$)

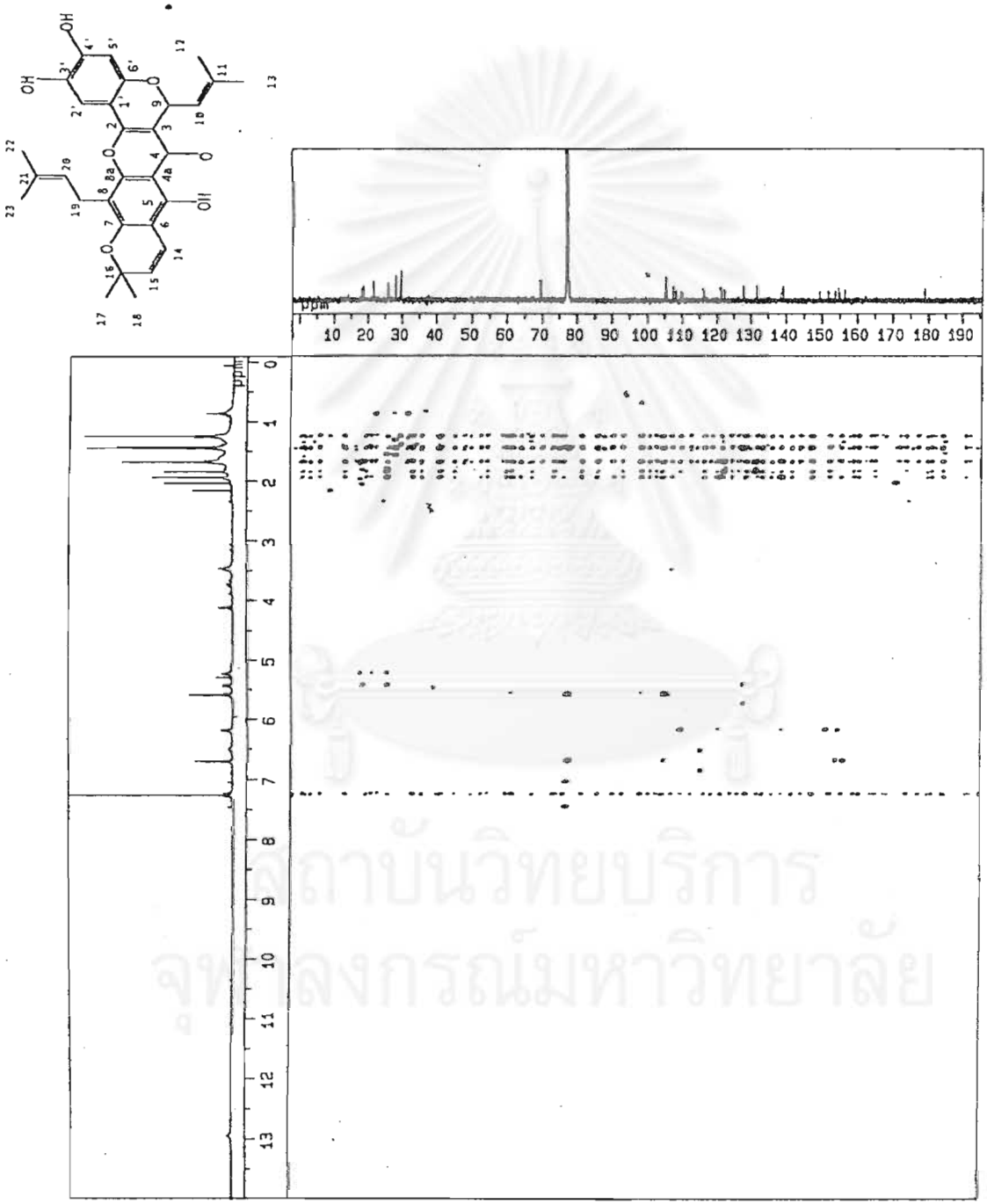


Figure 36 The125 MHz HMBC spectrum of AHT2 (in $CDCl_3$)

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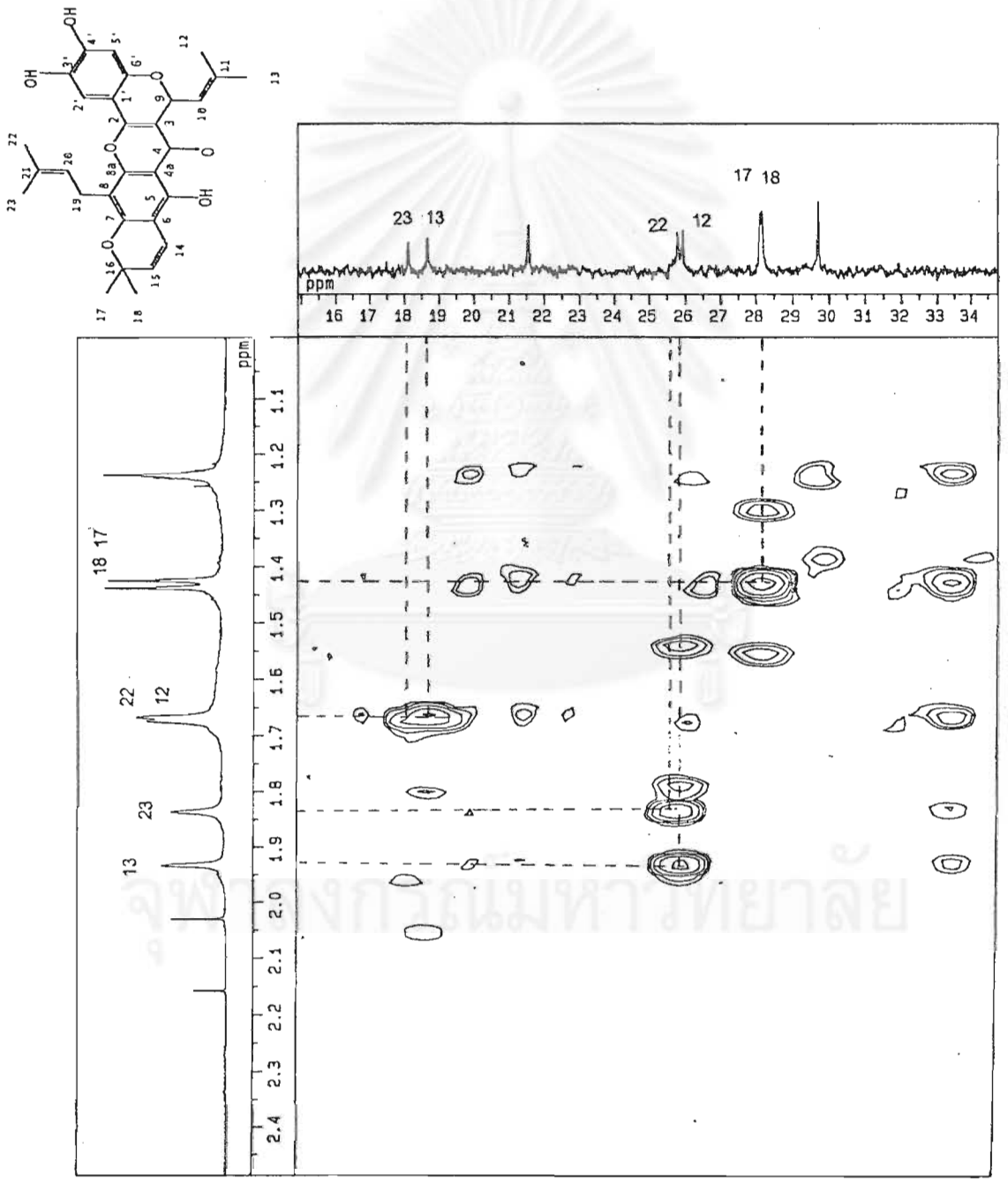

Figure 37 Expansion of an area of 125 MHz HMBC spectrum of AHT2 (in $CDCl_3$)

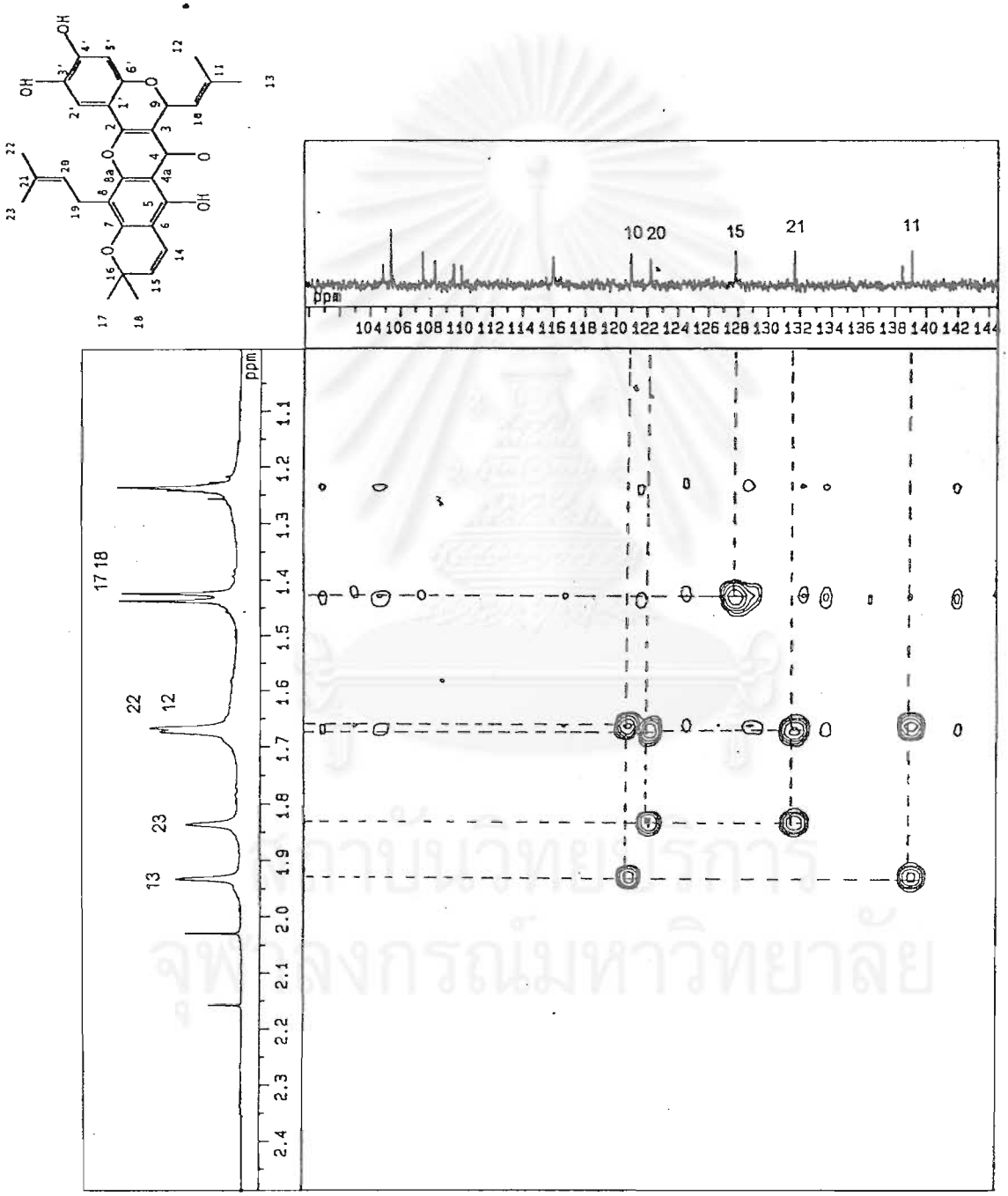

Figure 38 Expansion of an area of 125 MHz HMBC spectrum of AHT2 (in $CDCl_3$)

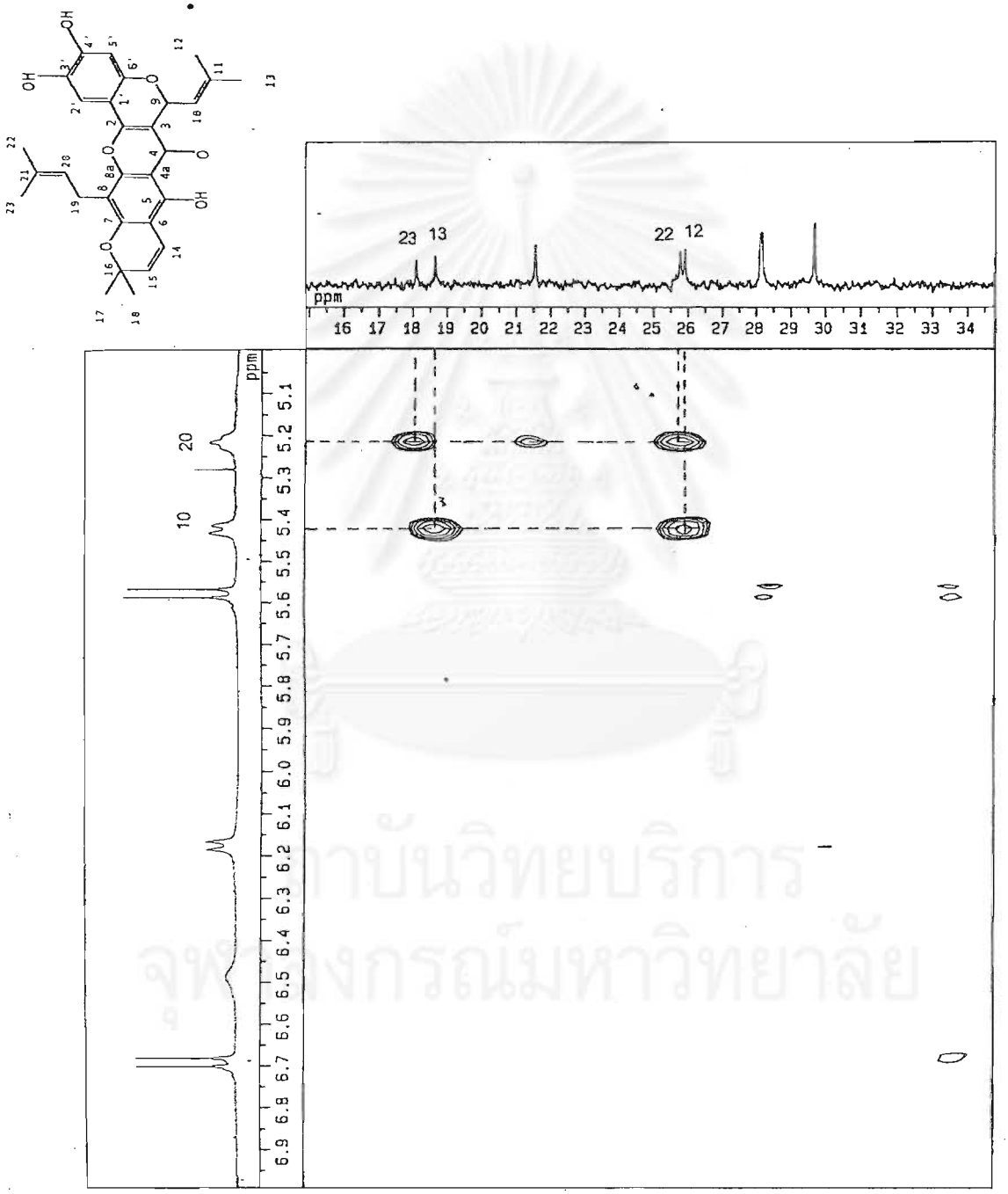

Figure 39 Expansion of an area of 125 MHz HMBC spectrum of AHT2 (in $CDCl_3$)

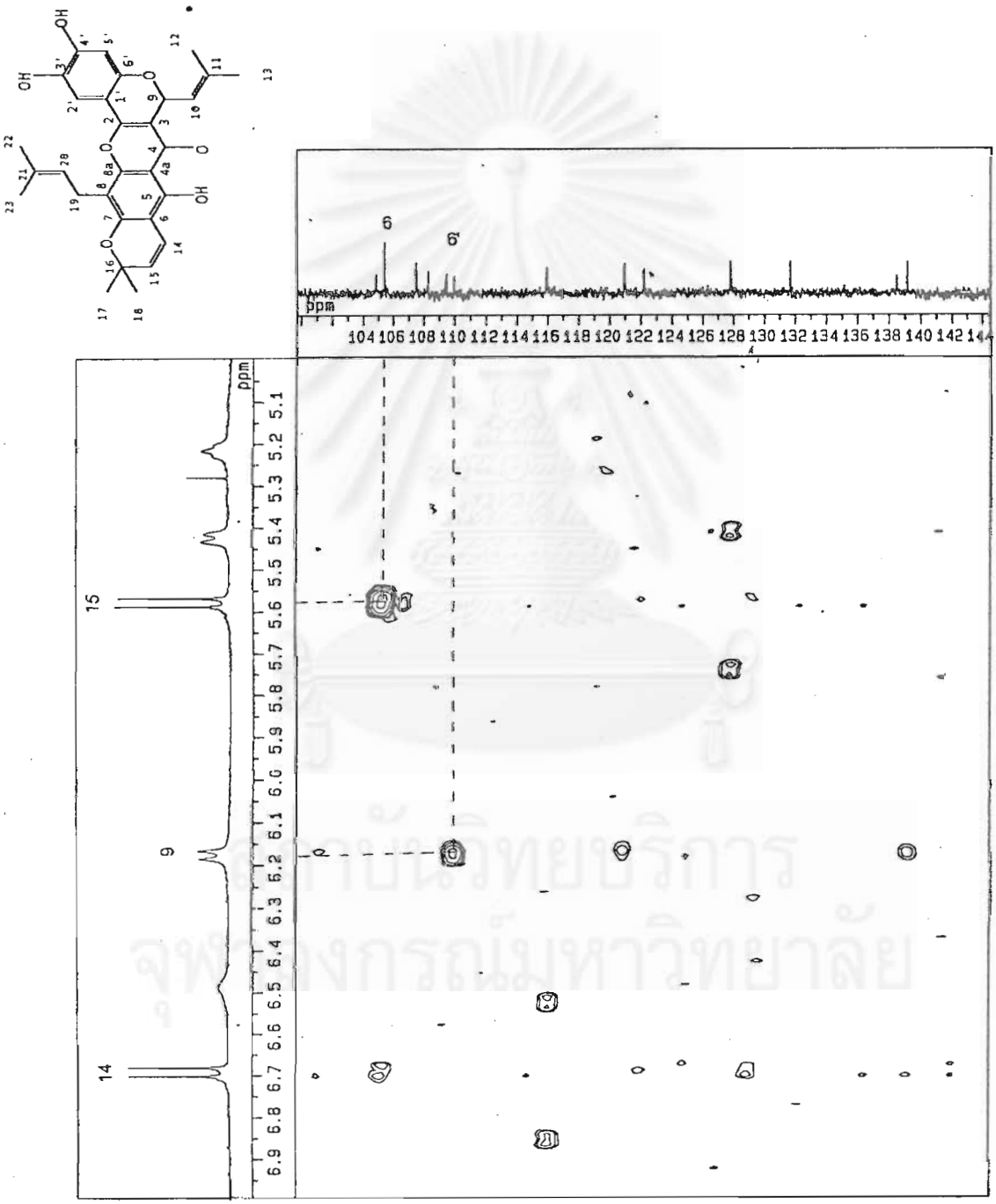

Figure 40 Expansion of an area of 125 MHz HMBC spectrum of AHT2 (in $CDCl_3$)

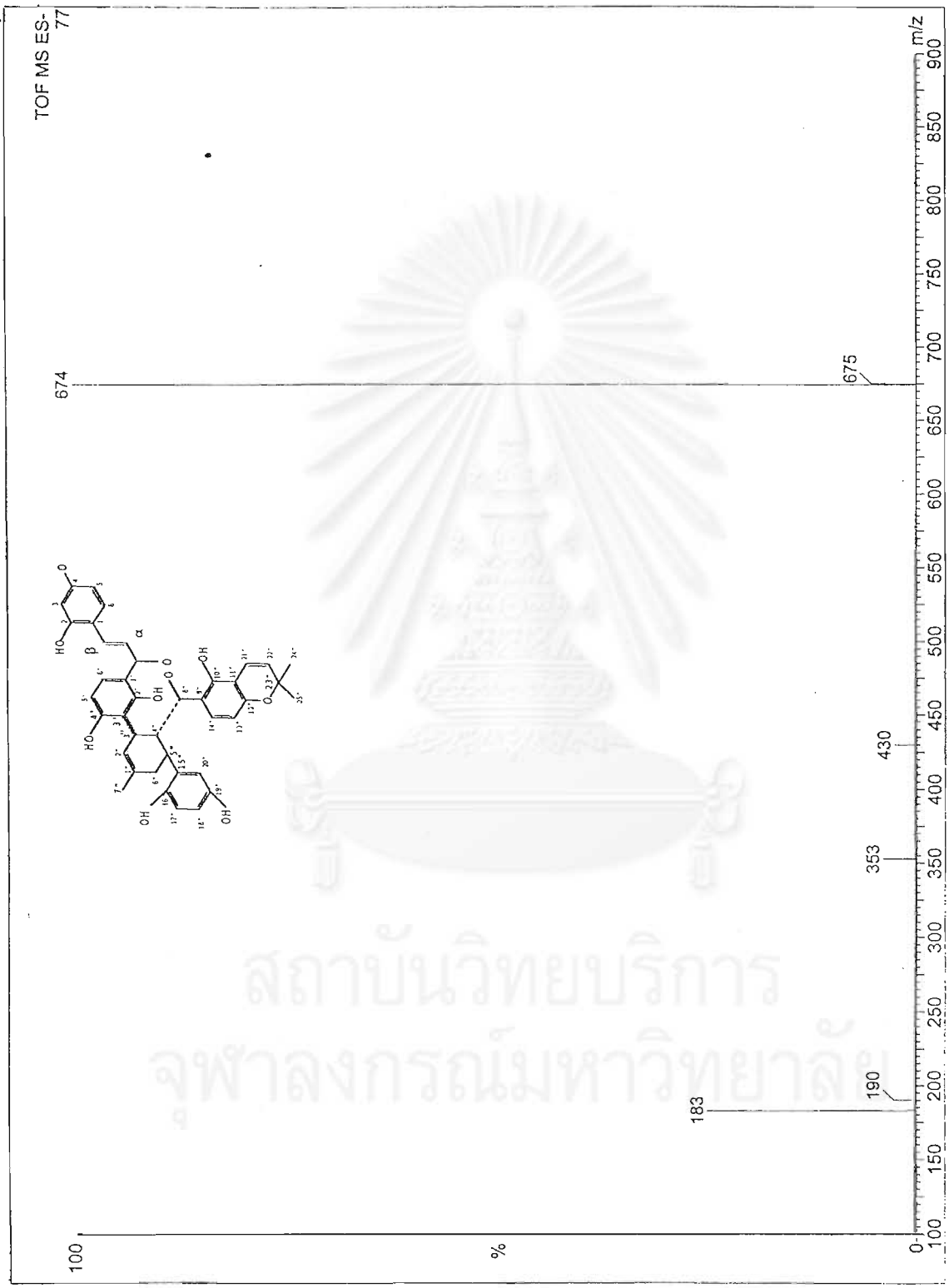

Figure 41 ES- TOF MS spectrum of AHM3

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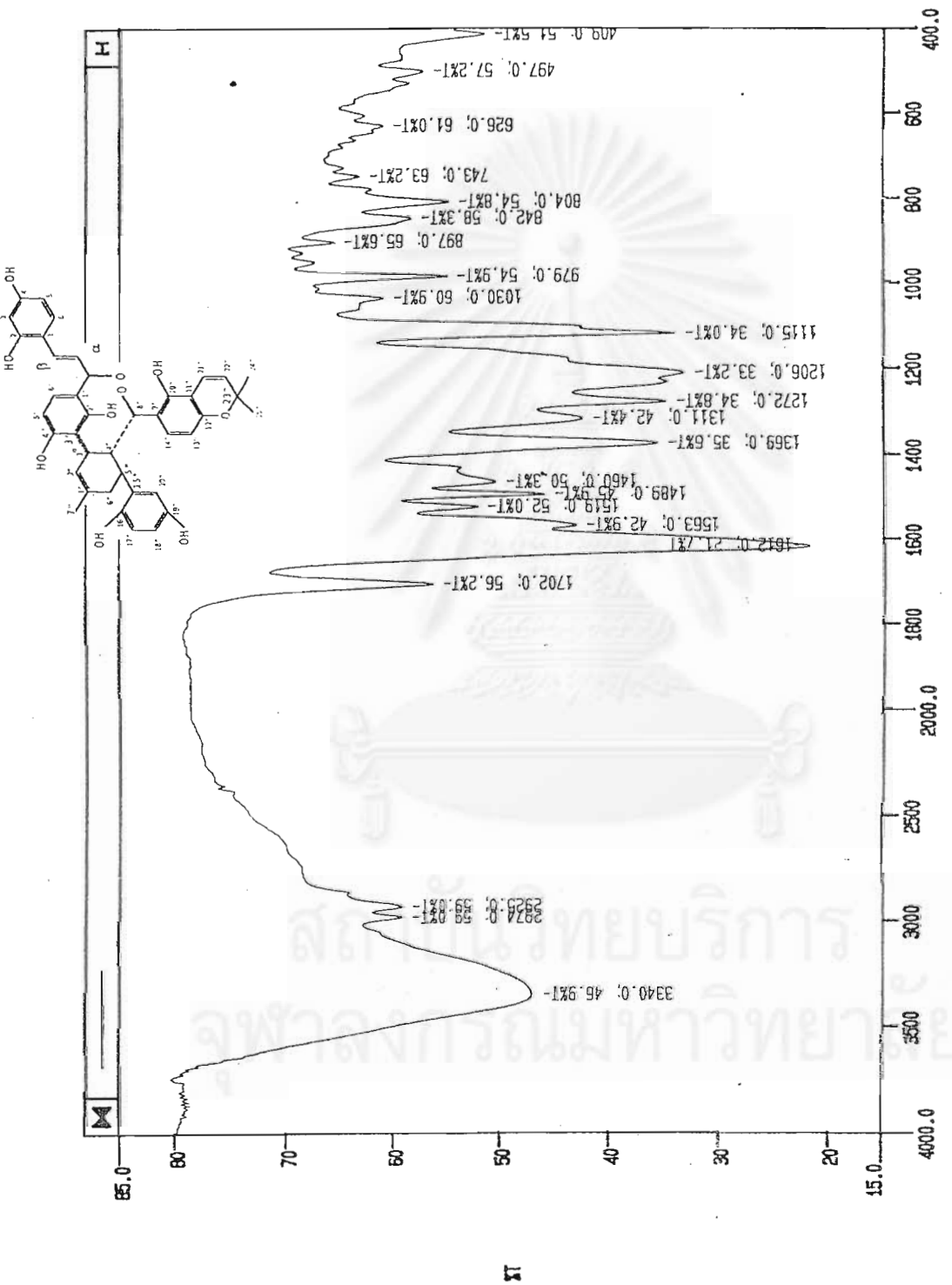

Figure 42 IR spectrum of AHM3 (in acetone)

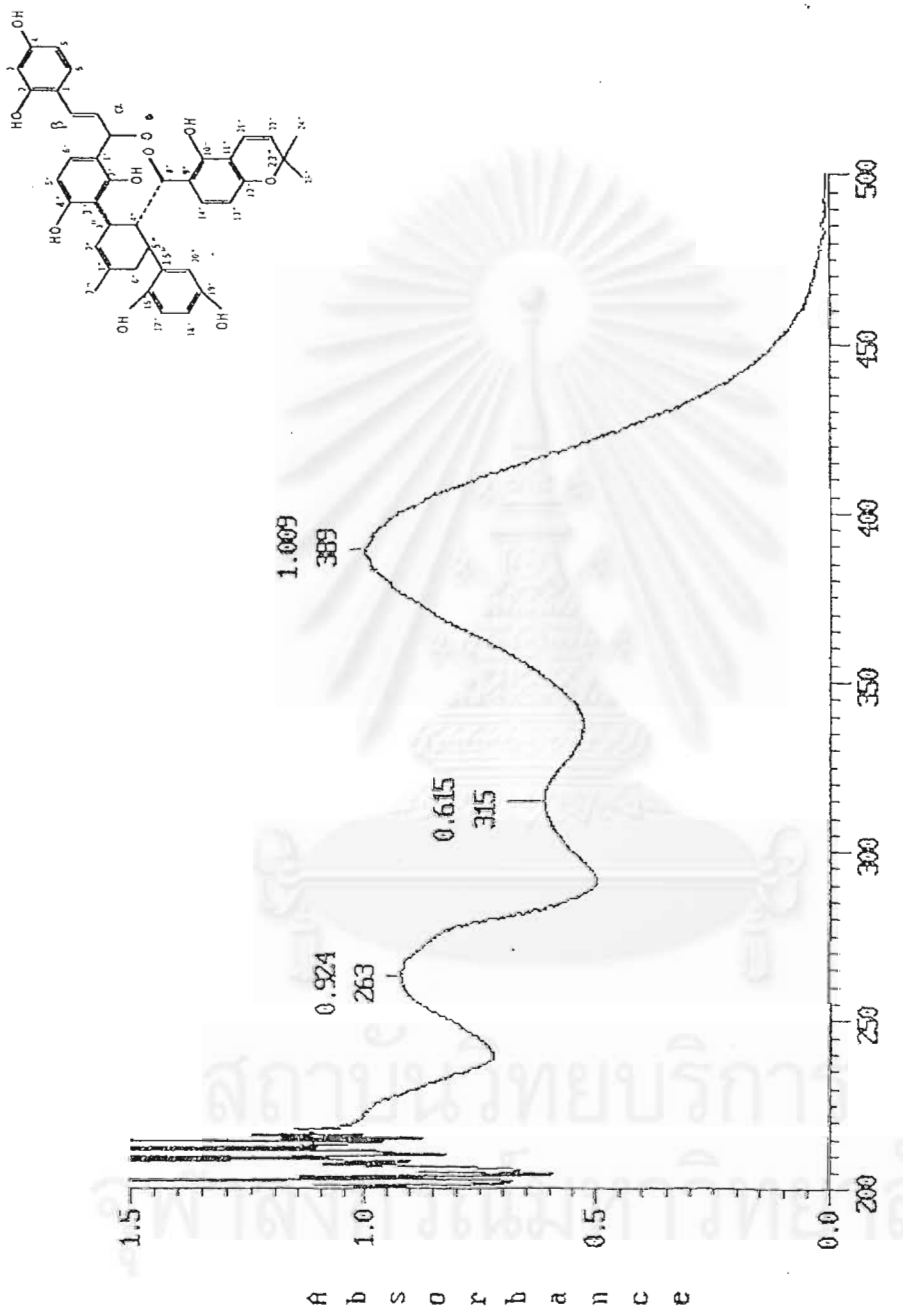

Figure 43 UV spectrum of AHM3 (in methanol)

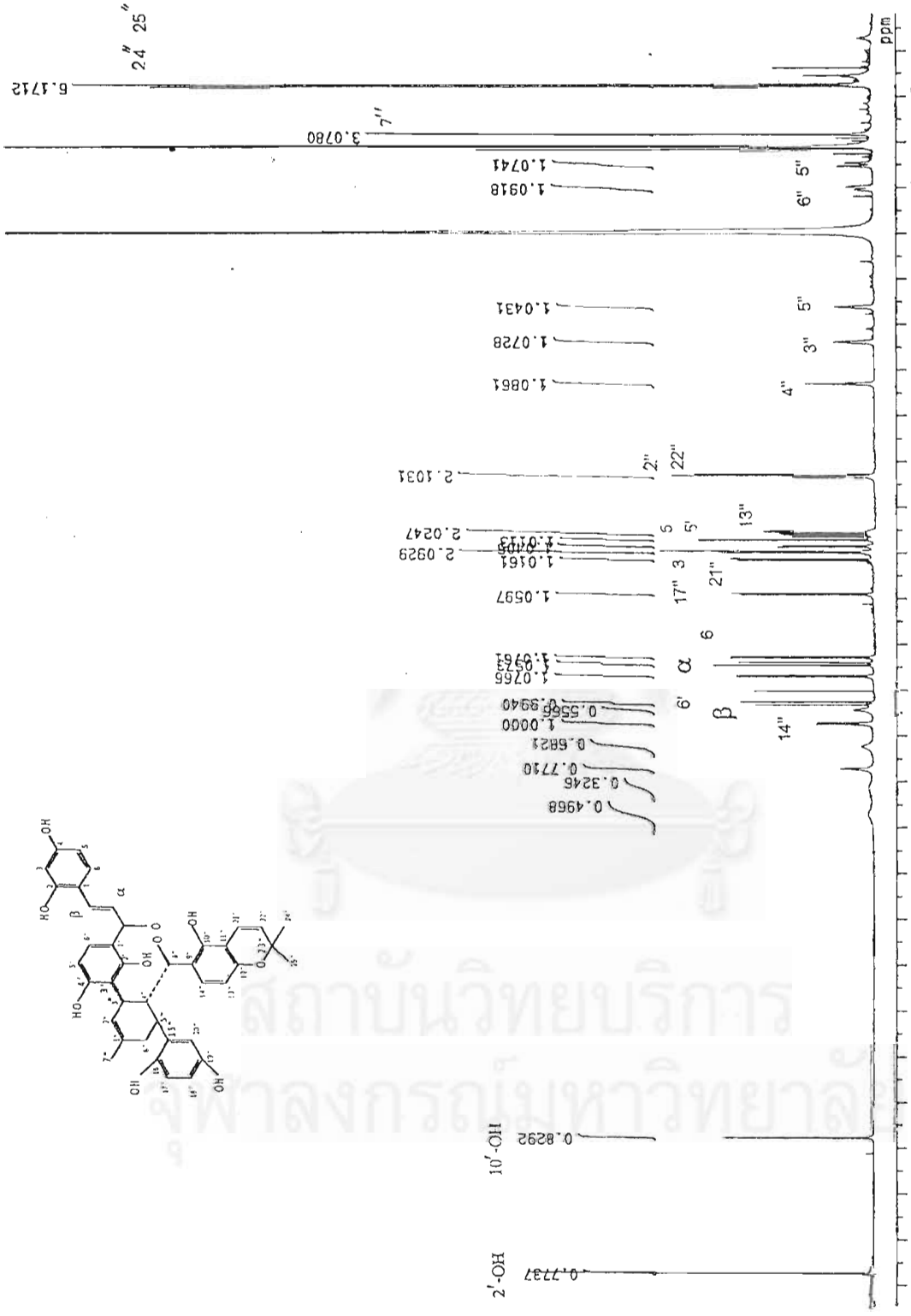

Figure 44 The 500 MHz ^{1}H-NMR spectrum of AHM3 (in acetone-d_6)

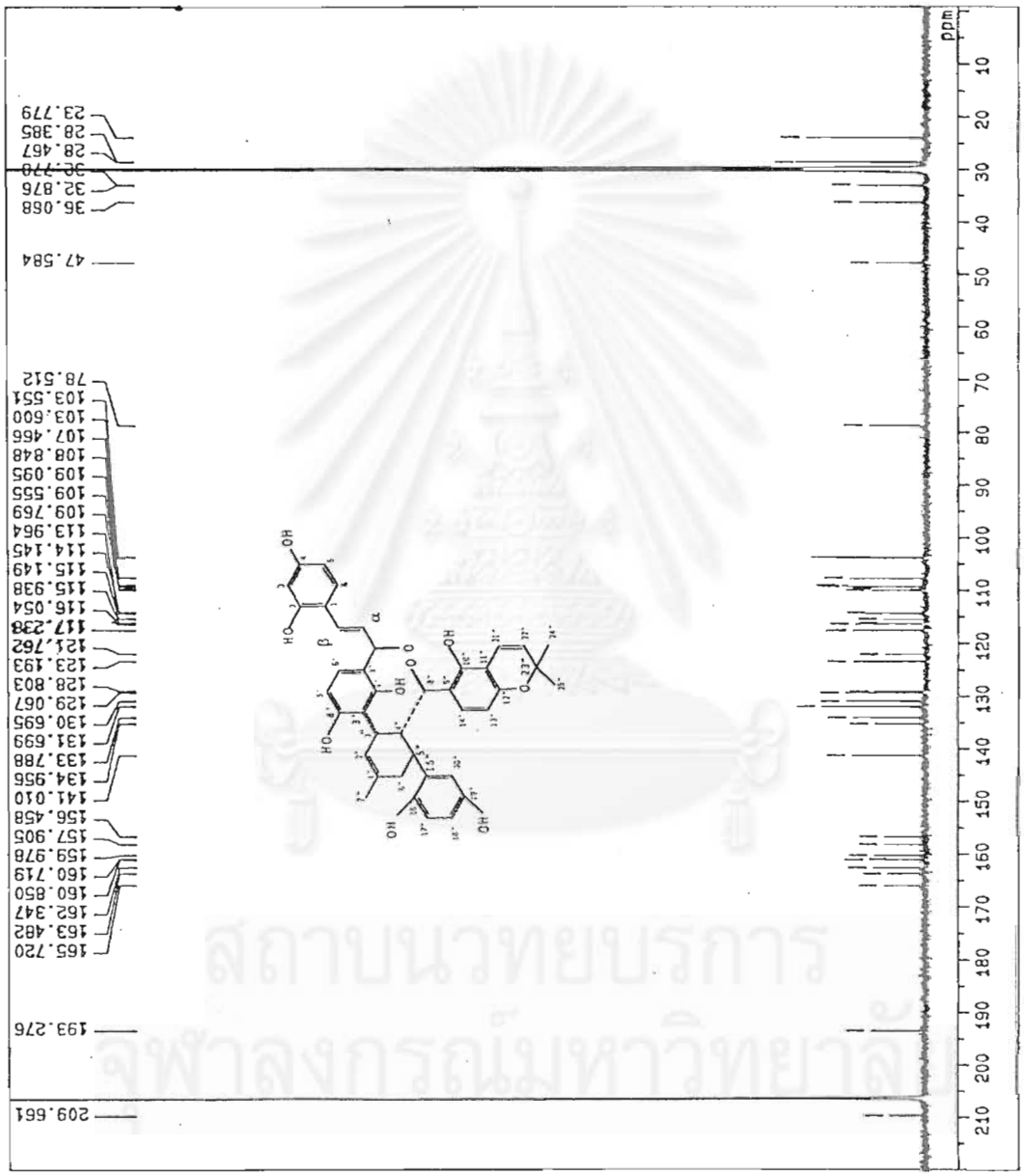

Figure 45 The 125 MHz ^{13}C-NMR spectrum of AHM3 (in acetone $-d_6$)

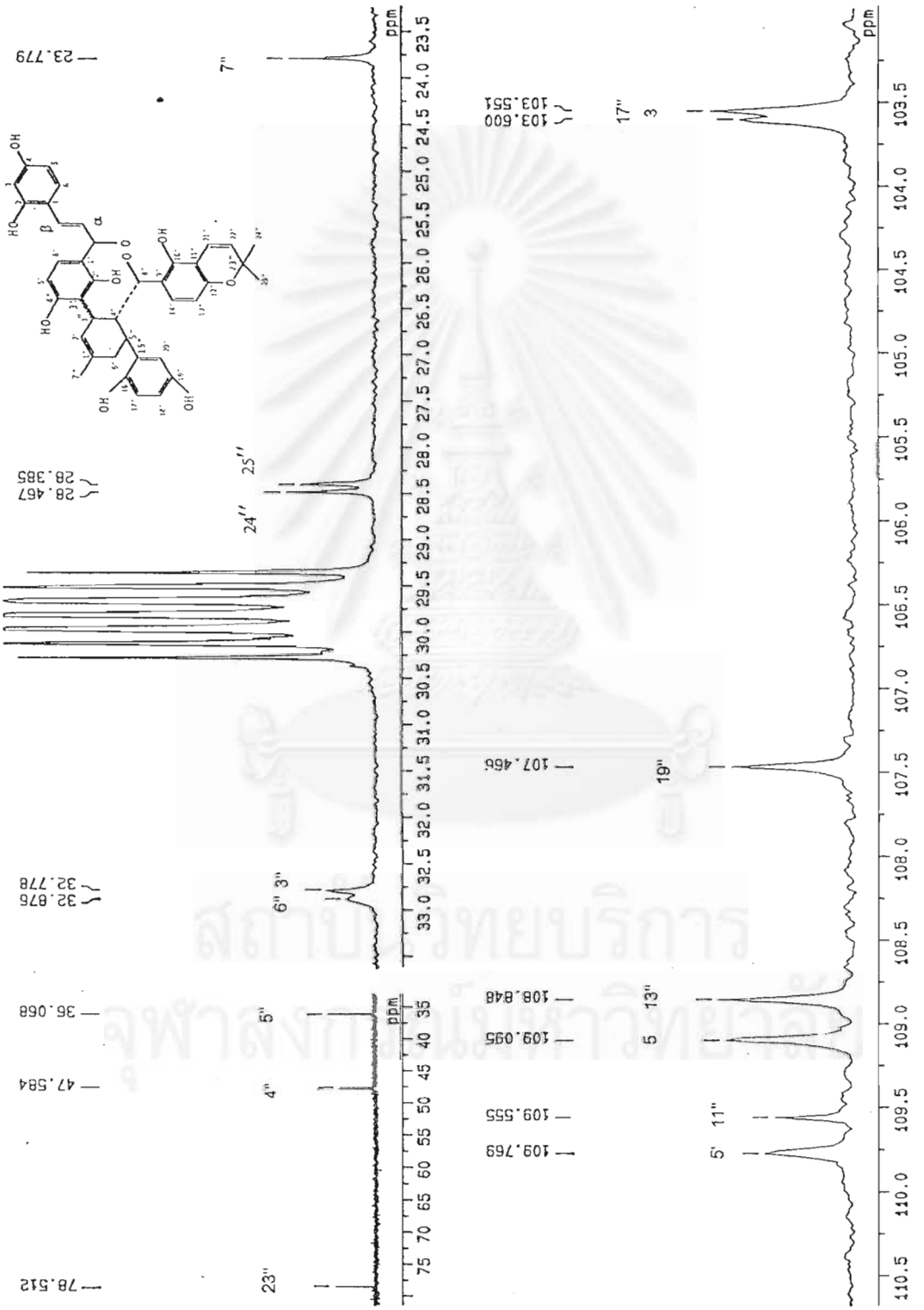

Figure 46 Expansion the 125 MHz ^{13}C-NMR spectrum of AHM3 (in acetone-d_6)

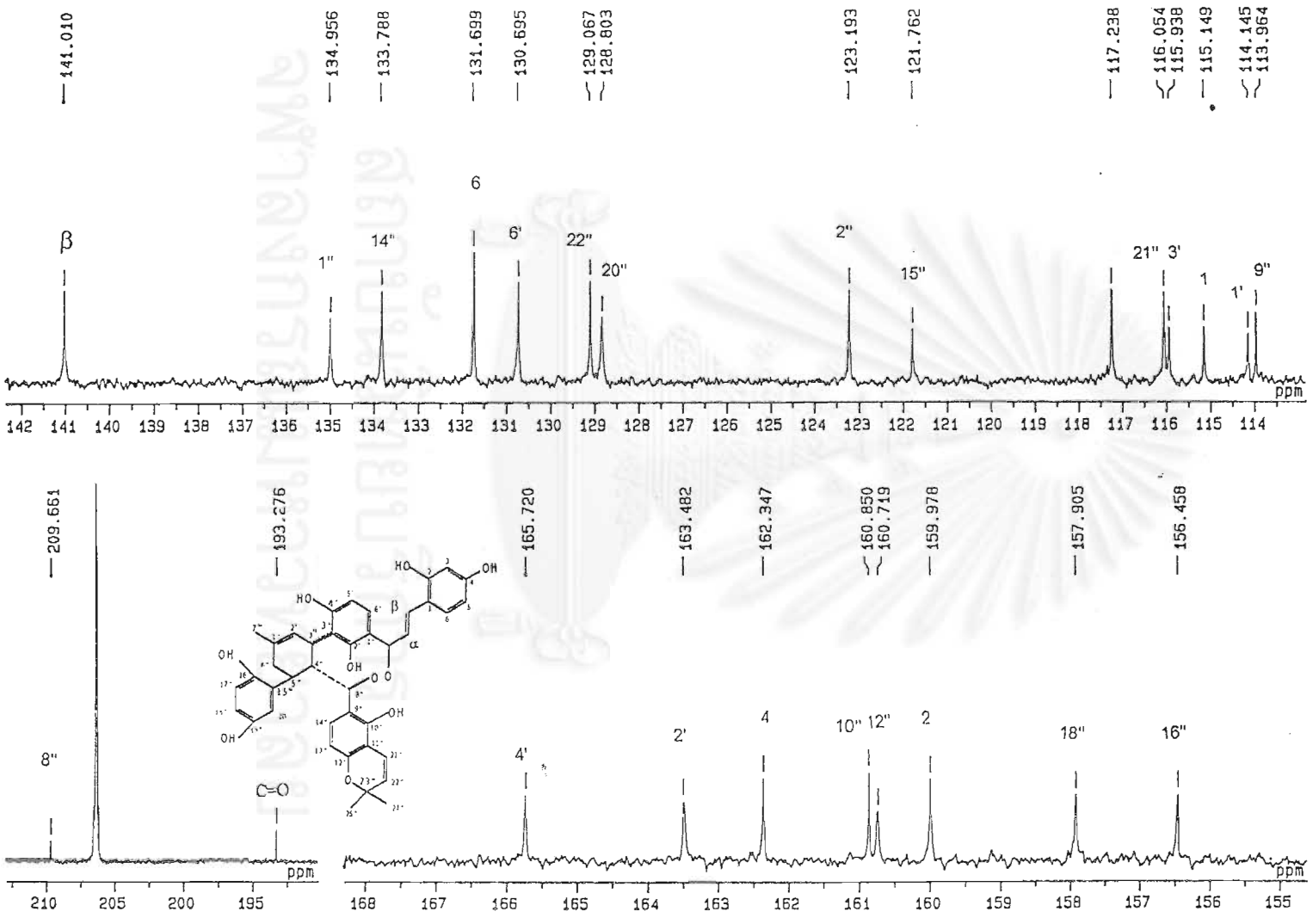

Figure 47 Expansion the 125 MHz ^{13}C-NMR spectrum of AHM3 (in acetone $-d_6$)

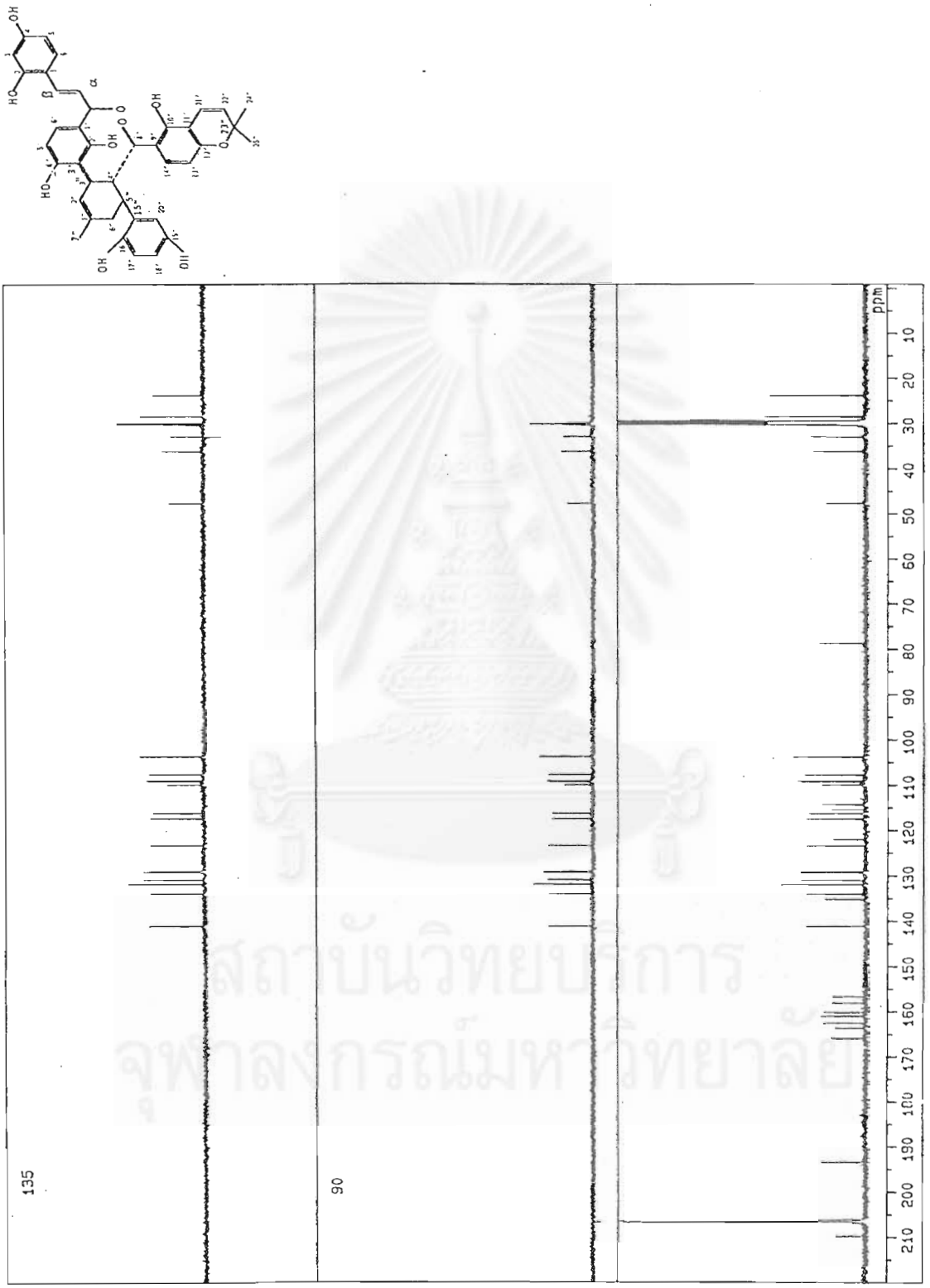

Figure 48 The 125 MHz DEPT spectra of AHM3(in acetone $-d_6$)

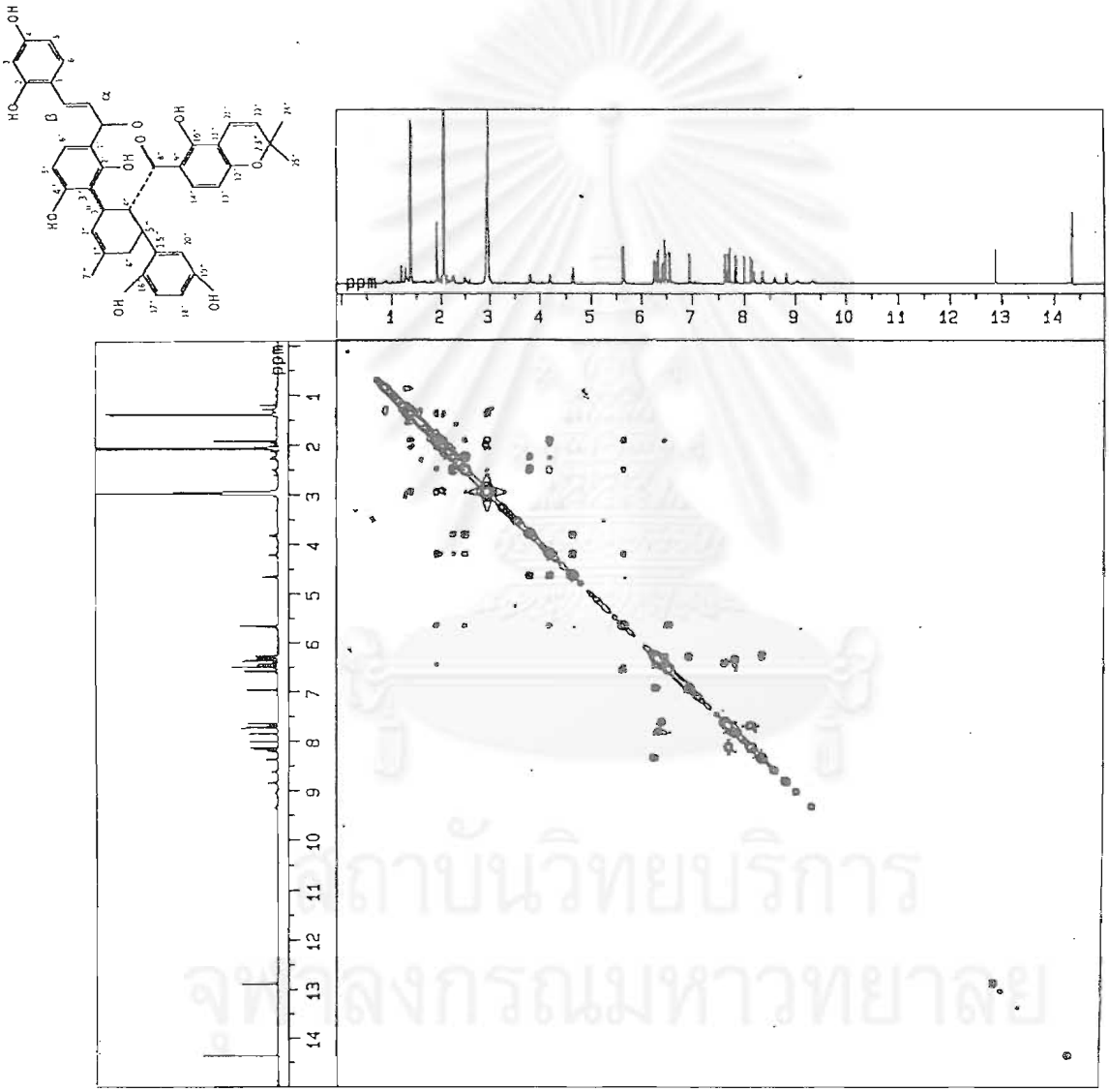

Figure 49 The500 MHz ^{1}H-^{1}H COSY spectrum of AHM3 (in acetone-d_6)

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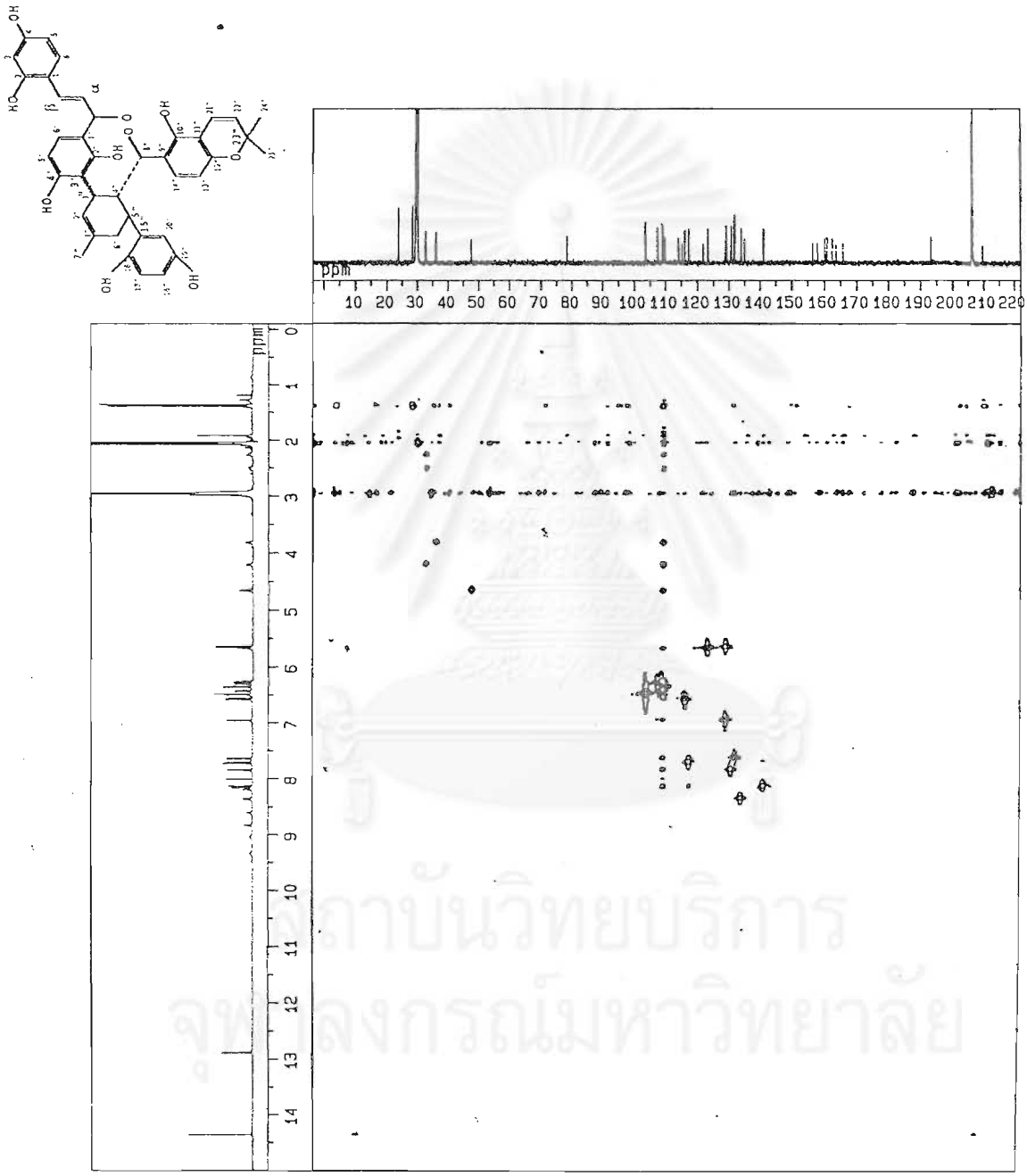

Figure 50 HMQC spectrum of AHM3 (in acetone-d_6)

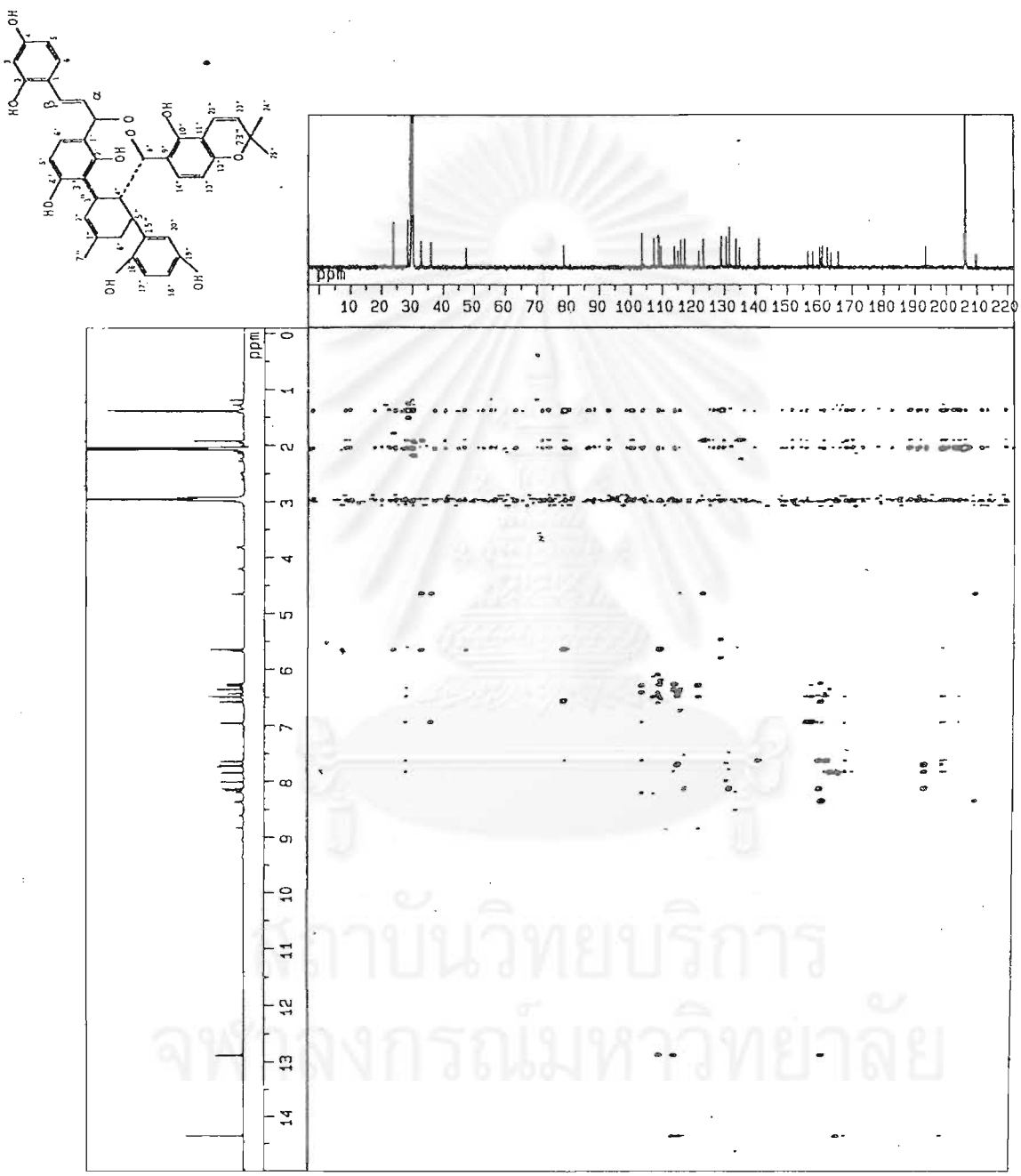

Figure 51 The125 MHz HMBC spectrum of AHM3 (in acetone-d_6)

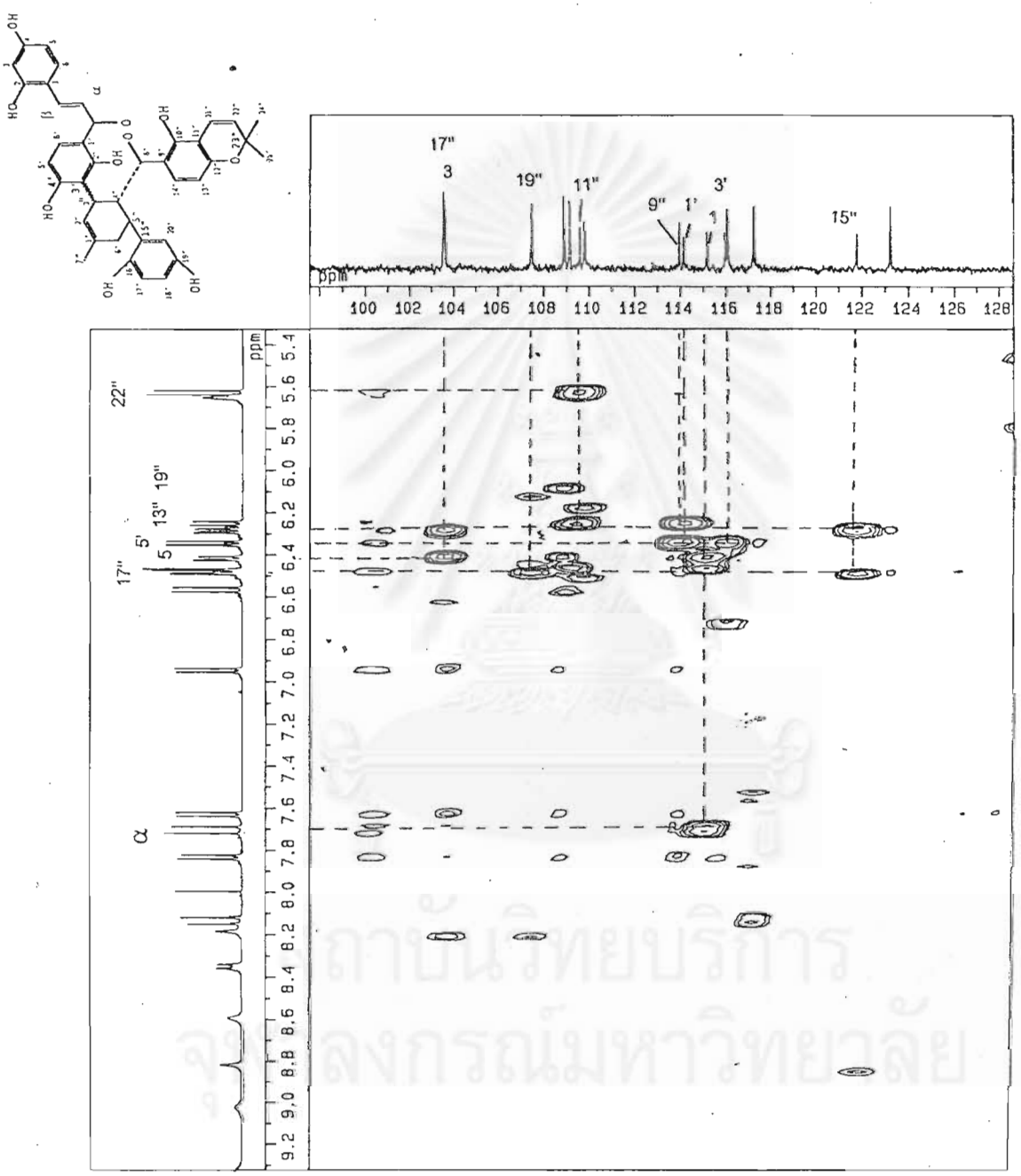

Figure 52 Expansion of an area of 125 MHz HMBC spectrum of AHM3 (in acetone-d_6)

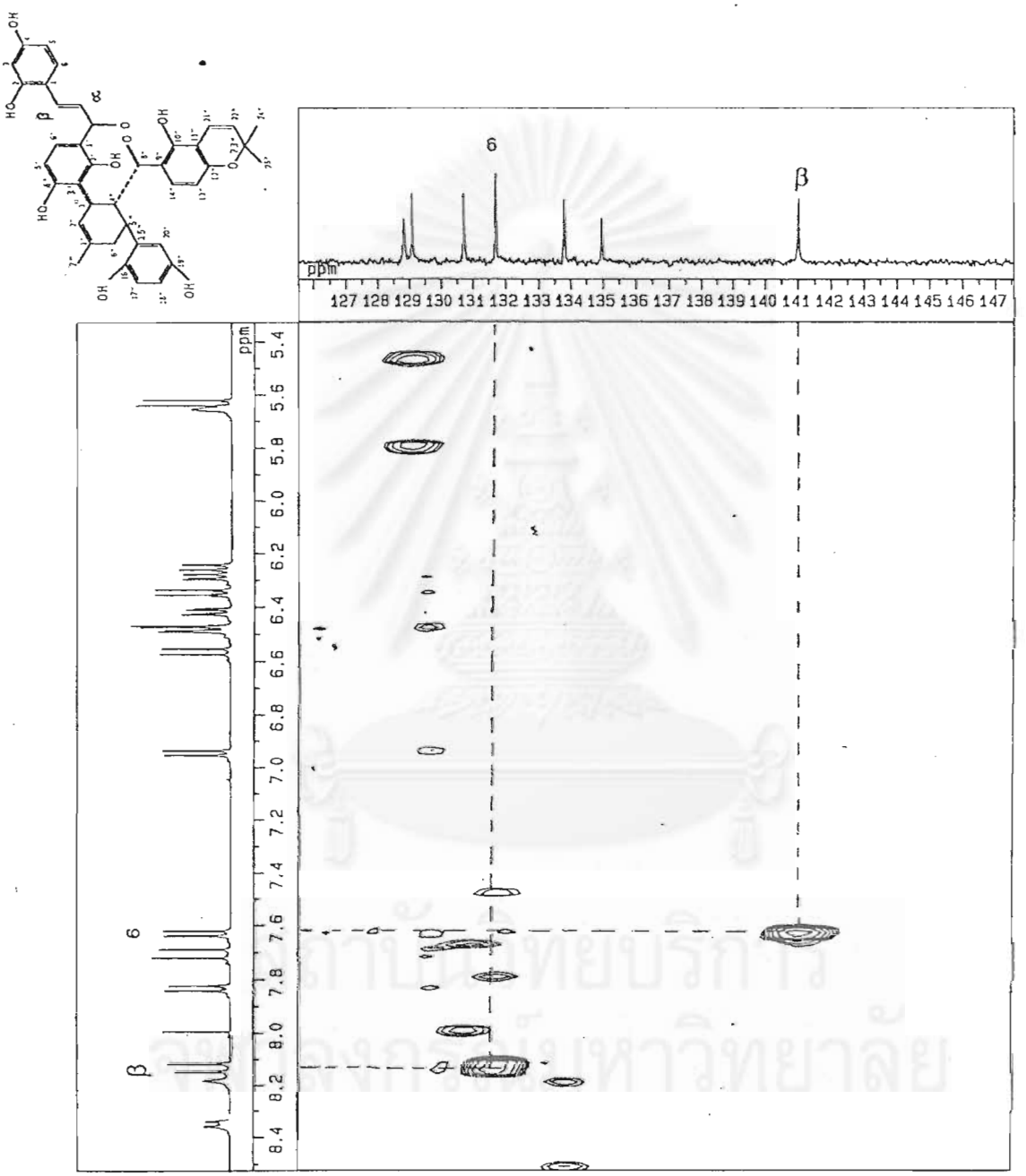

Figure 53 Expansion of an area of 125 MHz HMBC spectrum of AHM3 (in acetone-d_6)

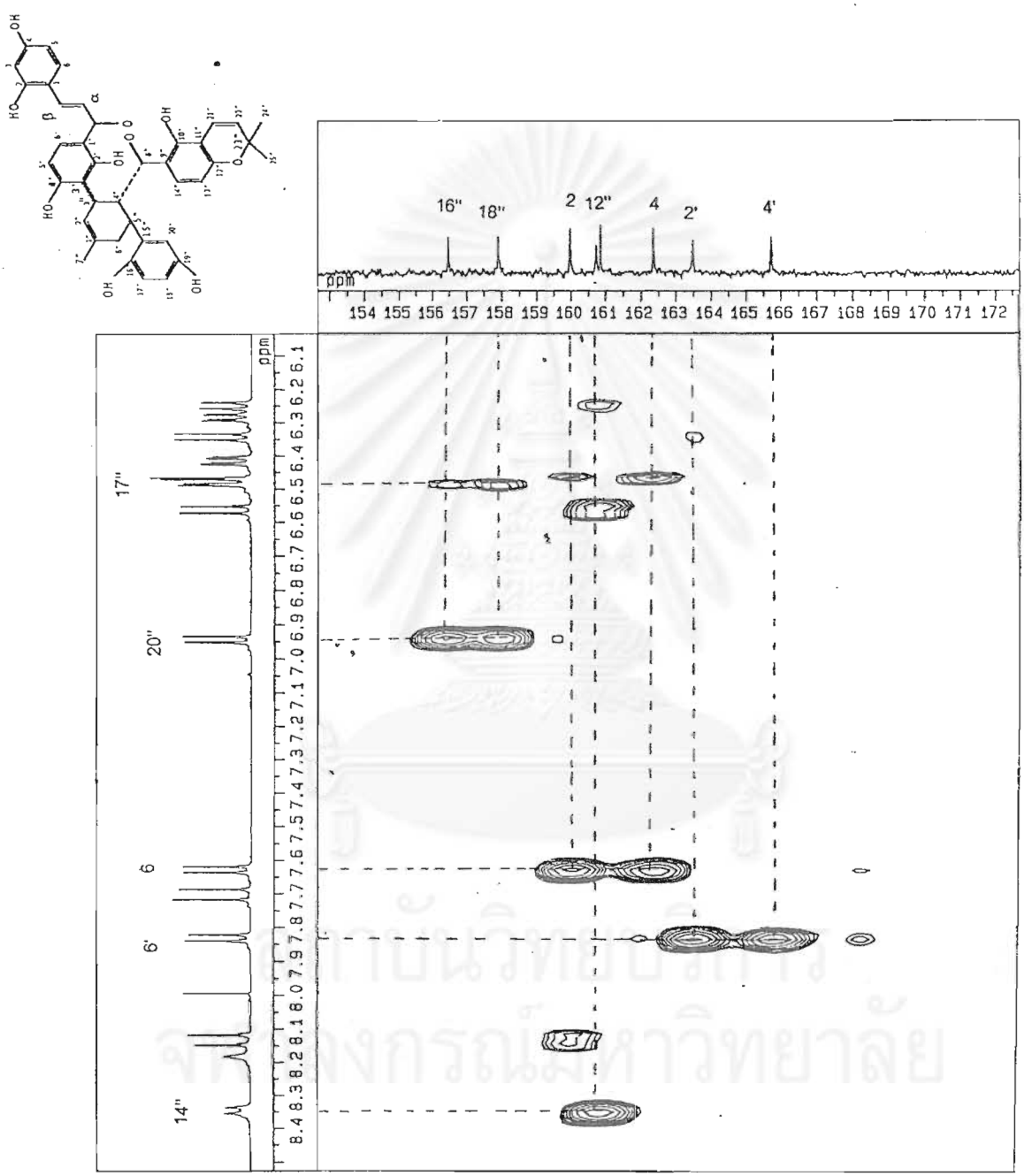

Figure 54 Expansion of an area of 125 MHz HMBC spectrum of AHM3 (in acetone-d_6)

VITA

Miss. Thidawan Phothidara was born on April 22 ,1973 in Bureerum,Thailand. She received her Bachelor's degree of Sciences in Pharmacy in 1997 from the Faculty of Pharmaceutical Sciences , Silpakorn University, Thailand. At present, she is working for the Department of Medical Sciences, Ministry of Public Health, Thailand.

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