องค์ประกอบทางเคมีของกิ่งส้มซ่า

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CHEMICAL CONSTITUENTS OF *GLYCOSMIS PARVA* BRANCHES

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การศึกษาพฤกษเคมีของกิ่งส้มชื่น โดยใช้วิธีทางโครมาโทกราฟี สามารถแยกองค์ประกอบทางเคมีจากสิ่งสกัดได้สาร 5 ชนิด ซึ่งเมื่อวิเคราะห์โครงสร้างด้วยวิธีทางสเปคโตรสโคปี พบของผสมในกลุ่มสตีรอยด์ 2 ชนิด คือ β-Sitosterol และ Stigmasterol และพบสารในกลุ่มอะครีโดน อัลคาลอยด์ 4 ชนิด ได้แก่ *N*-Methylataphilline, 5-Hydroxy-*N*-methylseverifoline, 5-Hydroxy-noracronycine และ อัลคาลอยด์ อะครีโดน อีกหนึ่งชนิดซึ่งจำเป็นต้องมีการยืนยันโครงสร้างด้วย 2D-NMR ต่อไป อนึ่งการพิสูจน์โครงสร้างทางเคมีของสารประกอบที่แยกได้นี้ อาศัยการวิเคราะห์ข้อมูลของ UV, IR, MS และ NMR ร่วมกับการเปรียบเทียบข้อมูลของสารที่ทราบโครงสร้างแล้ว

ภาควิชา……เภสัชเวท…… ลายมือชื่อนิสิต……

สาขาวิชา……..เภสัชเวท…… ลายมือชื่ออาจารย์ที่ปรึกษา……..…

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Phytochemical investigation of *Glycosmis parva* Craib (Rutaceae) branches using several chromatographic led to the chromatographic isolation of 5 compounds. β-sitosterol and stigmasterol were detected as a mixture of steroidal compounds. Three isolated compounds; *N*-methylataphilline, 5-hydroxy-*N*-methylseverifoline and 5-hydroxy-noracronycine were isolated. Inaddition, an unknown acridone analogue was also isolated. This compound still needs more 2D-NMR experiment before its structure can be established. Structure determination of all of the known compounds was accomplished through extensive spectroscopic studies, including comparison of their UV, IR, MS and NMR properties with the previous data of related compounds.

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LIST OF ABBREVIATIONS

AS	=	Anisaldehyde-sulphuric acid spraying reagent
br	=	Broad (for NMR spectra)
^{13}C NMR	=	Carbon-13 nuclear magnetic resonance
c	=	Concentration
°C	=	Degree celsius
$CDCl_3$	=	Deuterated chloroform (Chloroform-*d*)
CD_3OD	=	Deuterated methanol (Methanol-d_4)
$CHCl_3$	=	Chloroform
cm	=	Centimeter
COLOC	=	Correlation spectroscopy via long-range coupling
COSY	=	Correlation spectroscopy
1-D	=	One dimensional
2-D	=	Two dimensional
d	=	Doublet (for NMR spectra)
dd	=	Doublet of doublets (for NMR spectra)
DEPT	=	Distortionless enhancement by polarization transfer
DRG	=	Dragendroff spraying reagent
EI	=	Electron impact
EIMS	=	Electron impact mass spectroscopy
EtOAc	=	Ethyl acetate
EtOH	=	Ethanol
ε	=	Molar absorptivity
FT-IR	=	Fourier transform infared
g	=	Gram
^{1}H NMR	=	Proton nuclear magnetic resonance
Hz	=	Hertz
IC_{50}	=	Median inhibitory concentration
IR	=	Infrared spectrophotometry

J	=	Coupling constant
Kg	=	Kilogram
λ_{max}	=	Wavelength at maximal absorption
L	=	Liter
m	=	Multiplet (for NMR spectra)
M^+	=	Molecular ion
MeOH	=	Methanol
mg	=	Milligram
μg	=	Microgram
MHz	=	Megahertz
min	=	Minute
ml	=	Milliliter
μl	=	Microliter
mm	=	Milimeter
MPLC	=	Medium pressure liquid chromatography
MS	=	Mass spectrometry
m/z	=	Mass to charge ratio
nm	=	Namometer
NMR	=	Nuclear magnetic resonance
NOESY	=	Nuclear overhauser effect correlation spectroscopy
PLC	=	Preparative Thin layer chromatography
ppm	=	Part per million
Pet. ether	=	Petroleum ether
s	=	Singlet (for NMR spectra)
t	=	Triplet (for NMR spectra)
tt	=	Triplet of triplets (for NMR spectra)
TLC	=	Thin layer chromatography
TMS	=	Tetramethylsilane
vis.	=	Visible
UV	=	Ultraviolet
ν_{max}	=	Wave number at maximal absorption

CHAPTER I

INTRODUCTION

The genus *Glycosmis* belongs to the tribe Clauseneae of the sub-family Aurantioideae in the family Rutaceae. This genus consists of about 110 species, distributed in tropical zones, particularly in Ceylon, India, Burma, Indo-China, South-China, Thailand, Malaysia, Indonesia and Papua New Guinea (Jackson, 1895; Ridley, 1922; Merrill, 1968; Jayaweera, 1982).

The plants in the genus *Glycosmis* are evergreen shrubs or undertrees. Leaves alternate, 1-5 foliate. Flowers usually small, axillary panicles. Calyx 4 or 5 partial imbricate. Petals 4 or 5 imbricate. Stamen 8 to 10 free, filaments dilated below. Ovary 2 to 5 celled, the style very short, not jointed, ovule 1 in each cell. Fruits globose, freshy, berry. Seeds 1 to 3 oblong, testa membranous. (Ridley, 1922; Merrill, 1968)

According to Smitinand (1980), five species of genus *Glycosmis* were reported in Thailand. They are as follows.

Glycosmis chlorosperma Tan. (*G. tomentella* Ridl.)

น้ำข้าวเขา Nam khaao khao (Nakhon Si Thammarat).

Glycosmis pentaphylla Corr. (*G. cochinchinensis* Pierre)

กระรอกน้ำ Krarok nam, กระรอกน้ำข้าว Krarok nam khaao (Chon Buri);

กระโรกน้ำข้าว Krarok nam khaao, เขยตาย Khoei taai, ลูกเขยตาย Luuk khoei taai (Central);

Glycosmis pentaphylla Corr. (*G. cochinchinensis* Pierre) (Continued)

เขนทะ Khentha (Northern);

ตาระแป Taa-ra-pae (Malay-Yala);

น้ำข้าว Nam khaao (Central, Peninsular);

ประยงค์ใหญ่ Prayong yai (Bangkok);

พุทธรักษา Phuttharaksaa (Sukhothai);

มันหมู Man muu (Prachuap Khiri Khan);

ส้มชื่น Som chuen (Northern, Northeastern).

Glycosmis subsessilis Craib

ค้างคาวหนู Khaang khaao nuu (Nakhon Ratchasima).

Glycosmis trifolia Spreng.

ขะยงป่า Kha yong paa, ประยงค์ป่า Prayong paa; พะยงป่า Phayong paa (Northern).

However, other species of genus *Glycosmis* have been also found in Thailand according to Jackson (1895) and other databases. They are as follows.

Glycosmis chlorosperma var. *paraphyllophora* B.C. Stone

Glycosmis cyanocarpa var. *larsenii* B.C. Stone

Glycosmis elongata Bakh. f.

(*G. augustifolia* Lindl.)

(*G. arborea* DC.)

(*G. citrifolia* Lindl.)

Glycosmis parva Craib

Glycosmis puberula var. *craibii* (Tanaka) B.C. Stone

(*G. craibii* Tanaka)

Glycosmis winitii Craib

(Jackson, 1895)

Glycosmis crassifolia Ridley

(Greger *et al.*, 1996)

Glycosmis cyanocarpa (Bl.) Spreng.

(Talapatra, Chauduri and Talapatra, 1975; Greger *et al.*, 1992b; Seger *et al.*, 1998a)

Glycosmis cyanocarpa var. *wirawanii* B.C. Stone

Glycosmis macrophylla Miq.

(Cannon *et al.*, 1980)

Glycosmis mauritiana (Lamk.) Tanaka

(Greger *et al.*, 1993b; Hofer *et al.*, 1995a&b)

Glycosmis ovoidea Pierre

(Hofer *et al.*, 1995a)

Glycosmis montana Pierre

Glycosmis pentaphylla (Retz.) DC.

(Willaman and Li, 1970; Greger *et al.*, 1993b; Garba, Mustapha and Choudhury, 1993; Ito *et al.*, 1999a; Quader, Nutan and Rashid, 1999)

Glycosmis pseudoracemosa Swingle

Glycosmis trichanthera Guillaumin

(Vajrodaya *et al.*, 1998)

Glycosmis parva Craib is also known in Thai as "Som-Chuen" (ส้มชื่น). (วงศ์สถิตย์ ฉั่วกุล และคณะ 2539) According to Royal Botanic Garden Kew, 1926, the characteristic features of *Glycosmis parva* Craib are described as follows.

Glycosmis parva Craib [Rutaceae-Aurantieae]; a *G. montana* Piere foliis angustioribus, filamentis inferne ampliatis, a *G. dinhense* Pierre ex Guillaumin petalis haud dorso pilosis, foliis haud longe acuminatis recedit.

Frutex circa 1.5 m. altus (ex *Kerr*); ramuli graciles, primo subferrugineo-tomentosi vel pubescentes, compressi, mox puberuli, cortice cinereo vel'brunneo-cinereo obtecti, lenticellis haud conspicuis. *Folia* alterna, interdum subopposita, lanceolata, apice obtusa, interdum retusa, rarius subacuminata, 3.5-9 cm. longa, 1-2.5 cm. lata, chartaceo-coriacea, supra viridia, ad costam breviter subtomentella vel matura fere glabra, subtus pallide viridia, subglabra, costa supra conspicua subtus prominente, nervis lateralibus utrinque 11-14 rectis intra marginem anastomo-santibus supra obscuris vel subconspicuis subtus subprominentibus, aliis paulo minus validis interpositis, nervulis subtus prominulis, margine integra, petiolo 2-6 mm. longo primo puberulo mox fere glabro supra canaliculato suffulta. *Inflorescentia* axillaris, petiolo subaequilonga vel eo paululo longior, pedunculo communi ferrugineo-pubescente perbrevi vel sub fructu circa 1 mm. longo suffulta; flores albi (ex *Kerr*), pedicello brevi articulato subglabro bracteolato suffulti. *Sepala* 5, subrotundata, vix 1.5 mm. diametro, dorso glabra, glandula unica prominente instructa, ciliata. *Petala* 5, oblongo-lanceolata, apice obtusa, basi angustata, 4 mm. longa, 1.5 mm. lata, glabra, glandulosa. *Discus* brevis, crenulatus, glaber. *Filamenta* complanata, apice acuminata, ad 2.5 mm. longa, glabra, antheris 0.75 mm. longis apice glandula parva conspicua globosa ornatis. *Pistillum* globrum, 1.75 mm. altum, glandulosum stylo valido vix distincto. *Fructus* subellipsoideus, circa 7 mm. longus.

Krabin, Sakeo, 50 m., evergreen forest, *Kerr* 9766.

So far, only one phytochemical study on *Glycosmis parva* Craib has been reported (Hofer, Vajrodaya and Greger, 1998). The components of the leaves of *Glycosmis parva* Craib have been shown to be phenethyl sulphur amides derivatives. A number of interesting phytochemical studies on Acridone derivatives of Rutaceous plants and recent reports on their anticancer activity prompted the author to explore the possibility of finding other new Acridone derivatives from *Glycosmis parva* Craib.

Figure 1 *Glycosmis parva* Craib

CHAPTER II

HISTORICAL

1. Chemical constituents of *Glycosmis* spp.

A number of compounds have been isolated from the genus *Glycosmis*. They can be classified as follows.

1. Alkaloids derived from tryptophan
   - Simple tryptamine derivatives
2. Alkaloids derived from anthranilic acid
   - Carbazole alkaloids
   - Quinoline alkaloids
   - Quinazoline alkaloids
   - Acridone alkaloids
3. Alkaloids derived from phenylalanine and tyrosine (Phenethylamides alkaloids)
   - Methylthiopropenoic acid derivatives
   - Methylsulfonylpropenoic acid derivatives
   - Methylthiocarbonic acid derivatives
   - Isovaleric acid
   - Anthranilylamide
4. Miscellaneous
   - Flavonoids
   - Coumarins
   - Quinones
   - Terpenes

Table 1 Distribution of chemical constituents in *Glycosmis* spp.

Compound	Category	Plant part	Reference
***Glycosmis angustifolia* Lindl.**			
Dambullin [**91**]	Phenethyl amides alk.	Leaf	Greger *et al.*, 1994
Methyldambullin [**92**]	Phenethyl amides alk.	Leaf	Greger *et al.*, 1994
Gerambullin [**96**]	Phenethyl amides alk.	Leaf	Greger *et al.*, 1994
Methylgerambullin [**97**]	Phenethyl amides alk.	Leaf	Greger *et al.*, 1994
Gerambullindiol [**102**]	Phenethyl amides alk.	Leaf	Greger *et al.*, 1994
Methyliso gerambullone [**104**]	Phenethyl amides alk.	Leaf	Greger *et al.*, 1994
Methyl gerambullone [**103**]	Phenethyl amides alk.	Leaf	Greger *et al.*, 1994
***Glycosmis arborea* (Roxb.) DC.**			
Arborine [**42**]	Quinazoline alk.	Leaf	Svoboda and Kattau, 1967
Arborinine [**49**]	Acridone alk.	Leaf	Svoboda and Kattau, 1967
Glycoborinine [**15**]	Carbazole alk.	Root	Chakravarty *et al.*, 1999
Glycoric acid [**153**]	Sesquiterpene	Tuber	Chakravarty *et al.*, 1996a
Glycozolidine [**10**]	Carbazole alk.	Root	Chakravarty *et al.*, 1999
Glycozoline [**8**]	Carbazole alk.	Root	Chakravarty *et al.*, 1999
24(*S*)-Methyl-5-α-lanosta-9(11)-25-dien -3-α-ol [**147**]	Triterpene	Tuber	Chakravarty *et al.*, 1996b

Table 1 Distribution of chemical constituents in *Glycosmis* spp. (continued)

Compound	Category	Plant part	Reference
***Glycosmis arborea* (Roxb.) DC. (Continued)**			
24,24-Dimethyl-5-α-lanosta-9(11)-25-dien -3-α-ol [**148**]	Triterpene	Tuber	Chakravarty *et al.*, 1996b
24(*S*)-Methyl-5-α-lanosta-9(11)-25-dien -3-β-ol [**149**]	Triterpene	Tuber	Chakravarty *et al.*, 1996b
24,24-Dimethyl-5-α-lanosta-9(11)-25-dien -3-β-ol [**150**]	Triterpene	Tuber	Chakravarty *et al.*, 1996b
3-(3,3'-Dimethyl-allyl)-4-8-dimethoxy-*N*-methyl quinolin-2-one [**22**]	Quinoline alk.	Root	Chakravarty *et al.*, 1999
Skimmianine [**31**]	Quinoline alk.	Root Leaf	Chakravarty *et al.*, 1999 Willaman and Li, 1970
***Glycosmis bilocularis* Thw.**			
1,5-Dihydroxy-2,3-dimethoxy-10-methyl acrid-9-one [**50**]	Acridone alk.	Leaf	Bowen, Perera and Lewis, 1978
Arborine [**42**]	Quinazoline alk.	Leaf	Bowen, Perera and Lewis, 1978
Arborinine [**49**]	Acridone alk.	Leaf	Bowen, Perera and Lewis, 1978
5-Hydroxy arborinine [**50**]	Acridone alk.	Stem	Bowen, Perera and Lewis, 1980
Dictamnine [**28**]	Quinoline alk.	Stem	Bowen, Perera and Lewis, 1980

Table 1 Distribution of chemical constituents in *Glycosmis* spp. (continued)

Compound	Category	Plant part	Reference
***Glycosmis bilocularis* Thw. (Continued)**			
Glycorine [34]	Quinazoline alk.	Leaf	Bowen, Perera and Lewis, 1978
Kokusaginine [33]	Quinoline alk.	Stem	Bowen, Perera and Lewis, 1980
		Leaf	Bowen, Perera and Lewis, 1978
Skimmianine [31]	Quinoline alk.	Stem	Bowen, Perera and Lewis, 1980
		Leaf	Bowen, Perera and Lewis, 1978
***Glycosmis chlorosperma* (Bl.) Spreng.**			
Dambullin [91]	Phenethyl amides alk.	Leaf	Hofer *et al.*, 2000
Gerambullin [96]	Phenethyl amides alk.	Leaf	Hofer *et al.*, 2000
Gerambullol [95]	Phenethyl amides alk.	Leaf	Hofer *et al.*, 2000
β-Hydroxy gerambullin [99]	Phenethyl amides alk.	Leaf	Hofer *et al.*, 2000
β-Hydroxy gerambullol [100]	Phenethyl amides alk.	Leaf	Hofer *et al.*, 2000
β-Hydroxy gerambullal [101]	Phenethyl amides alk.	Leaf	Hofer *et al.*, 2000
Sakambullin [93]	Phenethyl amides alk.	Leaf	Hofer *et al.*, 2000
O-Methyl sakambullin [94]	Phenethyl amides alk.	Leaf	Hofer *et al.*, 2000

Table 1 Distribution of chemical constituents in *Glycosmis* spp. (continued)

Compound	Category	Plant part	Reference
***Glycosmis chlorosperma* (Bl.) Spreng. (Continued)**			
Sakerine [**105**]	Phenethyl amides alk.	Leaf	Hofer *et al.*, 2000
Sakerinol-A [**107**]	Phenethyl amides alk.	Leaf	Hofer *et al.*, 2000
Sakerinol-B [**106**]	Phenethyl amides alk.	Leaf	Hofer *et al.*, 2000
O-Methyl sakerinol-A [**108**]	Phenethyl amides alk.	Leaf	Hofer *et al.*, 2000
Penangin [**129**]	Alk.-misc	Leaf	Greger *et al.*, 1992b
Isopenangin [**131**]	Alk.-misc	Leaf	Greger *et al.*, 1992b
Glycosmis chlorosperma cf.			
Cis-Bogorin [**38**]	Quinazoline alk.	Leaf	Seger *et al.*, 1998b
Trans-Bogorin [**37**]	Quinazoline alk.	Leaf	Seger *et al.*, 1998b
Penangin [**129**]	Alk.-misc	Leaf	Greger *et al.*, 1993a
Isopenangin [**131**]	Alk.-misc	Leaf	Greger *et al.*, 1993a
Penimide-B [**90**]	Phenethyl amides alk.	Leaf	Greger *et al.*, 1993a
***Glycosmis citrifolia* (Willd.) Lindl.**			
De-*N*-methyl acronycine [**55**]	Acridone alk.	Rootbark+ Stembark	Leu *et al.*, 1998
		Rootbark+ Stembark	Wu *et al.*, 1983
Noracronycine [**60**]	Acridone alk.	Rootbark+ Stembark	Leu *et al.*, 1998
		Rootbark+ Stembark	Wu *et al.*, 1983

Table 1 Distribution of chemical constituents in *Glycosmis* spp. (continued)

Compound	Category	Plant part	Reference
***Glycosmis citrifolia* (Willd.) Lindl. (Continued)**			
Acrifoline [57]	Acridone alk.	Bark	Ono *et al.*, 1995
5-Hydroxy noracronycine [63]	Acridone alk.	Rootbark+ Stembark	Wu *et al.*, 1983
		Rootbark+ Stembark	Leu *et al.*, 1998
De-*N*-methyl noracronycine [66]	Acridone alk.	Rootbark+ Stembark	Leu *et al.*, 1998
		Rootbark+ Stembark	Wu *et al.*, 1983
Atalaphyllidine [67]	Acridone alk.	Rootbark+ Stembark	Leu *et al.*, 1998
		Rootbark+ Stembark	Wu *et al.*, 1983
Citracridone-I [64]	Acridone alk.	Rootbark+ Stembark	Leu *et al.*, 1998
		Rootbark+ Stembark	Wu *et al.*, 1983
γ-Fagarine [32]	Quinoline alk.	Leaf	Wu, Chang and Wu, 1995
Furofoline-I [58]	Acridone alk.	Root	Wu, Furukawa and Hsu, 1982
		Rootbark+ Stembark	Wu *et al.*, 1983
Furofoline-II [59]	Acridone alk.	Root	Wu, Furukawa and Hsu, 1982
		Rootbark+ Stembark	Wu *et al.*, 1983
Glychalcone-A [135]	Flavonoid	Leaf	Wu, Chang and Wu, 1995
Glychalcone-B [136]	Flavonoid	Leaf	Wu, Chang and Wu, 1995

Table 1 Distribution of chemical constituents in *Glycosmis* spp. (continued)

Compound	Category	Plant part	Reference
***Glycosmis citrifolia* (Willd.) Lindl. (Continued)**			
Glycobismine-A [83]	Acridone alk.	Bark	Furukawa *et al.*, 1984
Glycobismine-D [81]	Acridone alk.	Rootbark+ Stembark	Ito *et al.*, 2000
Glycobismine-E [82]	Acridone alk.	Rootbark+ Stembark	Ito *et al.*, 2000
Glycocitlone-A [25]	Acridone alk.	Rootbark+ Stembark	Ito *et al.*, 2000
Glycocitlone-B [26]	Acridone alk.	Rootbark+ Stembark	Ito *et al.*, 2000
Glycocitlone-C [27]	Acridone alk.	Rootbark+ Stembark	Ito *et al.*, 2000
Glycocitridine [18]	Quinoline alk.	Leaf	Wu, Chang and Wu, 1995
Glycocitrine-I [74]	Acridone alk.	Rootbark+ Stembark	Wu, Furukawa and Kuoh, 1982
		Rootbark+ Stembark	Wu *et al.*, 1983
		Rootbark+ Stembark	Leu *et al.*, 1998
Glycocitrine-II [72]	Acridone alk.	Rootbark+ Stembark	Wu, Furukawa and Kuoh, 1982
		Rootbark+ Stembark	Wu *et al.*, 1983
		Rootbark+ Stembark	Leu *et al.*, 1998
Glycocitrine-IV [79]	Acridone alk.	Rootbark+ Stembark	Ito *et al.*, 2000
Glycocitrine-V [54]	Acridone alk.	Rootbark+ Stembark	Ito *et al.*, 2000

Table 1 Distribution of chemical constituents in *Glycosmis* spp. (continued)

Compound	Category	Plant part	Reference
***Glycosmis citrifolia* (Willd.) Lindl. (Continued)**			
Glycocitrine-VI [76]	Acridone alk.	Rootbark+ Stembark	Ito *et al.*, 2000
Glycocitrine-II *O*-methyl ether [73]	Acridone alk.	Rootbark+ Stembark	Wu, Furukawa and Kuoh, 1982
3-*O*-Methyl glycocitrine-II [72]	Acridone alk.	Rootbark+ Stembark	Leu *et al.*, 1998
		Rootbark+ Stembark	Wu *et al.*, 1983
Glycofoline [53]	Acridone alk.	Stembark	Wu and Furukawa, 1982
		Rootbark	Wu and Furukawa, 1982
		Rootbark+ Stembark	Wu *et al.*, 1983
Glycofolinine [47]	Acridone alk.	Bark	Ono *et al.*, 1995
Glycothiomin-A [130]	Alk.-misc	Leaf	Wu, Chang and Wu, 1995
Glycothiomin-B [132]	Alk.-misc	Leaf	Wu, Chang and Wu, 1995
Glyflavanone-A [137]	Flavonoid	Leaf	Wu, Chang and Wu, 1995
Glyflavanone-B [138]	Flavonoid	Leaf	Wu, Chang and Wu, 1995
Glyfoline [48]	Acridone alk.	Rootbark+ Stembark	Wu, Furukawa and Kuoh, 1982
		Rootbark+ Stembark	Wu *et al.*, 1983
Pyranofoline [52]	Acridone alk.	Rootbark+ Stembark	Leu *et al.*, 1998
		Root	Wu, Furukawa and Hsu, 1982
		Rootbark+ Stembark	Wu *et al.*, 1983

Table 1 Distribution of chemical constituents in *Glycosmis* spp. (continued)

Compound	Category	Plant part	Reference
***Glycosmis citrifolia* (Willd.) Lindl. (Continued)**			
Parahydroquinone [144]	Benzenoid	Rootbark+ Stembark	Wu *et al.*, 1983
Penangin [129]	Alk.-misc	Leaf	Wu, Chang and Wu, 1995
4,8-Dimethoxy-1-methyl-3-(3-methyl-but-2-enyl)quinol-2-one [22]	Quinoline alk.	Rootbark+ Stembark	Leu *et al.*, 1998
4,8-Dimethoxy-1-methyl-3-(3-methylbut-2-enyl)-2-quinolone [22]	Quinoline alk.	Rootbark+ Stembark	Wu *et al.*, 1983
N-Methyl severifoline [70]	Acridone alk.	Rootbark+ Stembark	Leu *et al.*, 1998
		Rootbark+ Stembark	Wu *et al.*, 1983
5-Hydroxy-*N*-methylseverifoline [69]	Acridone alk.	Rootbark+ Stembark	Wu *et al.*, 1983
		Rootbark+ Stembark	Leu *et al.*, 1998
β-Sitosterol [145]	Steroid	Rootbark+ Stembark	Leu *et al.*, 1998
Skimmianine [31]	Quinoline alk.	Leaf	Wu, Chang and Wu, 1995
***Glycosmis cochinchinensis* Pierre.**			
Arborinine [49]	Acridone alk.	Leaf	Ito *et al.*, 1999b
Doisuthine [127]	Phenethyl amides alk.	Leaf	Ito *et al.*, 1999b
Glycoamide-A [125]	Phenethyl amides alk.	Leaf	Ito *et al.*, 1999b

Table 1 Distribution of chemical constituents in *Glycosmis* spp. (continued)

Compound	Category	Plant part	Reference
***Glycosmis cochinchinensis* Pierre. (Continued)**			
Glycoamide-B [126]	Phenethyl amides alk.	Leaf	Ito *et al.*, 1999b
Glycozolone-A [43]	Quinazoline alk.	Leaf	Ito *et al.*, 1999b
Glycozolone-B [44]	Quinazoline alk.	Leaf	Ito *et al.*, 1999b
***Glycosmis craibii* Tanaka**			
Sakerine [105]	Phenethyl amides alk.	Leaf	Hofer *et al.*, 1995a
Dihydroisosakerol [111]	Phenethyl amides alk.	Leaf	Hofer *et al.*, 1995a
***Glycosmis crassifolia* Ridley**			
Dehydro thalebanin-A [124]	Phenethyl amides alk.	Leaf	Greger *et al.*, 1996
Thalebanin-B [122]	Phenethyl Amides alk.	Leaf	Greger *et al.*, 1996
Dehydro thalebanin-B [123]	Phenethyl Amides alk.	Leaf	Greger *et al.*, 1996
***Glycosmis cyanocarpa* (Bl.) Spreng.**			
Angelical [139]	Coumarin	Rootbark	Talapatra, Chauduri and Talapatra, 1975
Evolitrine [29]	Quinoline alk.	Leaf	Sarkar, Kundu and Chakraborty, 1978
Glycarpine [30]	Quinoline alk.	Leaf	Sarkar, Kundu and Chakraborty, 1978
Laipol [151]	Diterpene	Leaf	Seger *et al.*, 1998a

Table 1 Distribution of chemical constituents in *Glycosmis* spp. (continued)

Compound	Category	Plant part	Reference
***Glycosmis cyanocarpa* (Bl.) Spreng. (Continued)**			
Isolaipol [152]	Diterpene	Leaf	Seger *et al.*, 1998a
Limettin [140]	Coumarin	Leaf+ Stem	Talapatra, Chauduri and Talapatra, 1975
		Leaf+ Twigs	Talapatra, Chauduri and Talapatra, 1975
Sinharine [84]	Phenethyl Amides alk.	Leaf	Greger *et al.*, 1992b
Methylsinharine [85]	Phenethyl Amides alk.	Leaf	Greger *et al.*, 1992b
Xanthyletin [141]	Coumarin	Rootbark	Talapatra, Chauduri and Talapatra, 1975
		Rootbark	Talapatra, Chauduri and Talapatra, 1975
		Leaf+ Twigs	Talapatra, Chauduri and Talapatra, 1975
Glycosmis cyanocarpa cf.			
Dehydroniranin-A [117]	Phenethyl Amides alk.	Leaf	Greger *et al.*, 1996
Dehydroniranin-B [119]	Phenethyl Amides alk.	Leaf	Greger *et al.*, 1996
Glycosmis cyanocarpa* var. *simplicifolia cf.			
Glycozolidol [9]	Carbazole alk.	Leaf+ Stem	Greger *et al.*, 1992a
Kokusaginine [33]	Quinoline alk.	Leaf+ Stem	Greger *et al.*, 1992a
Sinharine [84]	Phenethyl amides alk.	Leaf+ Stem	Greger *et al.*, 1992a

Table 1 Distribution of chemical constituents in *Glycosmis* spp. (continued)

Compound	Category	Plant part	Reference
***Glycosmis cyanocarpa* var. *simplicifolia* (Continued)**			
Methylsinharine [**85**]	Phenethyl amides alk.	Leaf+ Stem	Greger *et al.*, 1992a
Skimmianine [**31**]	Quinoline alk.	Leaf+ Stem	Greger *et al.*, 1992a
***Glycosmis ovoidea* Pierre**			
Doisuthine [**127**]	Phenethyl Amides alk.	Leaf	Hofer *et al.*, 1995a
Methoxy doisuthine [**128**]	Phenethyl Amides alk.	Leaf	Hofer *et al.*, 1995a
Methylgerambullal [**98**]	Phenethyl Amides alk.	Leaf	Hofer *et al.*, 1995a
Glycosmis mauritiana cf.			
Niranin [**116**]	Phenethyl Amides alk.	Leaf	Greger *et al.*, 1996
***Glycosmis mauritiana* (Lamk.) Tanaka**			
1-Hydroxy-3-methoxy-2-(3-methyl-but-2-enyl)-*N*-methyl-acridan -9-one [**80**]	Acridone alk.	Root	Rastogi, Kapil and Popli, 1980
De-*N*-methyl-acronycine [**55**]	Acridone alk.	Rootbark	Govindachari, Pai and Subramaniam, 1966
Des-*N*-methyl acronycine [**55**]	Acridone alk.	Stembark	Kumar, Reisch and Wickramasinghe, 1989
De-*N*-methyl noracronycine [**66**]	Acridone alk.	Rootbark	Govindachari, Pai and Subramaniam, 1966

Table 1 Distribution of chemical constituents in *Glycosmis* spp. (continued)

Compound	Category	Plant part	Reference
***Glycosmis mauritiana* (Lamk.) Tanaka (Continued)**			
Noracronycine [60]	Acridone alk.	Rootbark	Govindachari, Pai and Subramaniam, 1966
		Stembark	Kumar, Reisch and Wickramasinghe, 1989
Arborine [42]	Quinazoline alk.	Flowers	Sinhababu and Thakur, 1995
		Leaf	Svoboda and Kattau, 1967
Arborinine [49]	Acridone alk.	Leaf	Desai *et al.*, 1967
		Flowers	Sinhababu and Thakur, 1995
		Leaf	Svoboda and Kattau, 1967
		Root	Rastogi, Kapil and Popli, 1980
		Stem	Govindachari *et al.*, 1969
Carbazole [3]	Carbazole alk.	Rootbark	Chowdhury *et al.*, 1987
		Rootbark	Chowdhury, Hirani and Bhattacharyya, 1986
3-Formylcarbazole [5]	Carbazole alk.	Root	Jash *et al.*, 1992
3-Methylcarbazole [4]	Carbazole alk.	Rootbark	Chowdhury *et al.*, 1987
		Rootbark	Chowdhury, Hirani and Bhattacharyya, 1986
Dictamnine [28]	Quinoline alk.	Root	Rastogi, Kapil and Popli, 1980
Friedelin [146]	Triterpene	Leaf+ Stem	Rastogi, Kapil and Popli, 1980

Table 1 Distribution of chemical constituents in *Glycosmis* spp. (continued)

Compound	Category	Plant part	Reference
***Glycosmis mauritiana* (Lamk.) Tanaka (Continued)**			
Glycolone [21]	Quinoline alk.	Rootbark	Sinha and Kumar, 1988
		Leaf	Bhattacharyya and Chowdhury, 1985b
Glycomide [133]	Alk.-misc	Flowers	Sarkar and Chakraborty, 1977
Glycophylone [17]	Quinoline alk.	Seed	Bhattacharyya and Chowdhury, 1984
Glycophymine [41]	Quinazoline alk.	Flowers	Sarkar and Chakraborty, 1977
Glycophymoline [35]	Quinazoline alk.	Flowers	Sarkar and Chakraborty, 1979
Glycorine [34]	Quinazoline alk.	Flowers	Sinhababu and Thakur, 1995
Glycosinine [6]	Carbazole alk.	Root	Jash *et al.*, 1992
Glycosmicine [40]	Quinazoline alk.	Flowers	Sinhababu and Thakur, 1995
Homoglycosolone [19]	Quinoline alk.	Rootbark	Kumar, Das and Sinha, 1986
Glycosolone [24]	Quinoline alk.	Rootbark	Das and Chowdhury, 1978
		Rootbark	Das, Chowdhury and Chowdhury, 1982
Glycozolicine [13]	Carbazole alk.	Root	Jash *et al.*, 1992
Glycozolidal [11]	Carbazole alk.	Root	Bhattacharyya and Chowdhury, 1985a

Table 1 Distribution of chemical constituents in *Glycosmis* spp. (continued)

Compound	Category	Plant part	Reference
***Glycosmis mauritiana* (Lamk.) Tanaka (Continued)**			
Glycozolidine [10]	Carbazole alk.	Rootbark	Anwer, Kapil and Popli, 1972
		Rootbark	Chowdhury, Hirani and-Bhattacharyya, 1986
		Rootbark	Chowdhury and Das, 1978
		Rootbark	Chakraborty, 1980
		Root	Rastogi, Kapil and Popli, 1980
Glycozolidol [9]	Carbazole alk.	Root	Bhattacharyya, Chakrabartty and Chowdhury, 1985
Glycozoline [8]	Carbazole alk.	Rootbark	Chowdhury, Hirani and-Bhattacharyya, 1986
		Rootbark	Chakraborty, 1969
		Rootbark	Chakraborty, 1980
		Root	Rastogi, Kapil and Popli, 1980
Glycozolinine [7]	Carbazole alk.	Seed	Mukherjee, Mukherjee and Ganguly, 1983
Glycozolinol [7]	Carbazole alk.	Root	Bhattacharyya, Sarkar and Chakraborty, 1984
Hentriacontan-1-ol [155]	Alkane	Leaf+ Stem	Rastogi, Kapil and Popli, 1980
		Leaf+ Stem	Bhakuni *et al.*, 1971

Table 1 Distribution of chemical constituents in *Glycosmis* spp. (continued)

Compound	Category	Plant part	Reference
***Glycosmis mauritiana* (Lamk.) Tanaka (Continued)**			
N-Hentriacontane [154]	Alkane	Leaf+ Stem	Rastogi, Kapil and Popli, 1980
		Leaf+ Stem	Bhakuni *et al.*, 1971
Methyl illukumbin-A [88]	Phenethyl Amides alk.	Leaf	Greger *et al.*, 1993b
Illukumbin-B [86]	Phenethyl Amides alk.	Leaf	Greger *et al.*, 1993b
Methyl illukumbin-B [87]	Phenethyl Amides alk.	Leaf	Greger *et al.*, 1993b
Mupamine [14]	Carbazole alk.	Leaf	Kumaruzzman, Roy and Chakraborty, 1989
4,8-Dimethoxy-3-(3-methyl-but-2-enyl)-*N*-methylquinol-2-one [22]	Quinoline alk.	Root	Rastogi, Kapil and Popli, 1980
Ritigalin [118]	Phenethyl Amides alk.	Leaf	Hofer *et al.*, 1995b
Sakerol [110]	Phenethyl Amides alk.	Leaf	Hofer *et al.*, 1995a
Sakerone [109]	Phenethyl Amides alk.	Leaf	Hofer *et al.*, 1995a
Skimmianine [31]	Quinoline alk.	Flowers	Sinhababu and Thakur, 1995
		Rootbark	Govindachari, Pai and Subramaniam, 1966
		Root	Rastogi, Kapil and Popli, 1980

Table 1 Distribution of chemical constituents in *Glycosmis* spp. (continued)

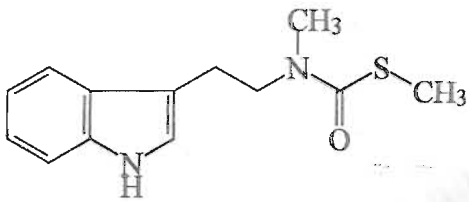
Compound	Category	Plant part	Reference
***Glycosmis mauritiana* (Lamk.) Tanaka (Continued)**			
β-Sitosterol [145]	Steroid	Root	Rastogi, Kapil and Popli, 1980
Vitexin [134]	Flavonoid	Leaf+ Stem	Rastogi, Kapil and Popli, 1980
		Leaf+ Stem	Bhakuni *et al.*, 1971
***Glycosmis parva* Craib**			
Glyparvin-A [112]	Phenethyl Amides alk.	Leaf	Hofer, Vajrodaya and Greger, 1998
Dihydroglyparvin [113]	Phenethyl Amides alk.	Leaf	Hofer, Vajrodaya and Greger, 1998
Khaochamide [120]	Phenethyl Amides alk.	Leaf	Hofer, Vajrodaya and Greger, 1998
Puhinamide [121]	Phenethyl Amides alk.	Leaf	Hofer, Vajrodaya and Greger, 1998
***Glycosmis parviflora* (Sims) Little**			
Ritigalin [118]	Phenethyl Amides alk.	Leaf	Hofer *et al.*, 1995b
***Glycosmis petelotii* Guillaumin**			
Glypetelotine [1]	Indole alk.	Leaf	Cuong, Taylor and Van-Sung, 1999
***Glycosmis pentaphylla* (Retz.) DC.**			
De-*N*-methyl acronycine [55]	Acridone alk.	Stem	Ito *et al.*, 1999a

Table 1 Distribution of chemical constituents in *Glycosmis* spp. (continued)

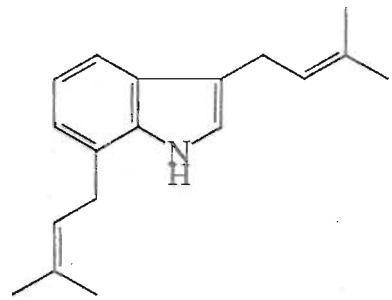
Compound	Category	Plant part	Reference
***Glycosmis pentaphylla* (Retz.) DC.**			
Noracronycine [60]	Acridone alk.	Stem	Ito *et al.*, 1999a
De-*N*-methyl noracronycine [66]	Acridone alk.	Stem	Ito *et al.*, 1999a
Acrifoline [57]	Acridone alk.	Stem	Ito *et al.*, 1999a
Arborinine [49]	Acridone alk.	Entire plant	Quader, Nutan and Rashid, 1999
		Stem	Ito *et al.*, 1999a
		Leaf	Greger *et al.*, 1993b
5-Hydroxy arborinine [50]	Acridone alk.	Stem	Ito *et al.*, 1999a
Carbazole [3]	Carbazole alk.	Rootbark	Garba, Mustapha and Choudhury, 1993
3-Methylcarbazole [4]	Carbazole alk.	Rootbark	Garba, Mustapha and Choudhury, 1993
Citracridone-I [64]	Acridone alk.	Stem	Ito *et al.*, 1999a
Dictamnine [28]	Quinoline alk.	Rootbark	Willaman and Li, 1970
Glycocitrine-III [77]	Acridone alk.	Stem	Ito *et al.*, 1999a
Glycozolidine [10]	Carbazole alk.	Rootbark	Garba, Mustapha and Choudhury, 1993
Glycozoline [8]	Carbazole alk.	Rootbark	Garba, Mustapha and Choudhury, 1993
Glycoquinone [143]	Quinoid	Stem	Ito *et al.*, 1999a
Kokusaginine [33]	Quinoline alk.	Stem	Ito *et al.*, 1999a
Skimmianine [31]	Quinoline alk.	Leaf	Greger *et al.*, 1993b
		Stem	Ito *et al.*, 1999a
		Rootbark	Willaman and Li, 1970

Table 1 Distribution of chemical constituents in *Glycosmis* spp. (continued)

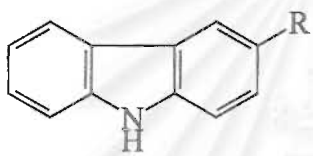
Compound	Category	Plant part	Reference
***Glycosmis rupestris* Ridley**			
De-*N*-methyl acronycine [55]	Acridone alk.	Bark	Rahmani *et al.*, 1998
7-Methoxy glycomaurin [16]	Carbazole alk.	Bark	Rahmani *et al.*, 1998
***Glycosmis trichanthera* Guillaumin**			
γ-Fagarine [32]	Quinoline alk.	Rootbark	Vajrodaya *et al.*, 1998
Methylgerambullin [97]	Phenethyl amides alk.	Leaf	Vajrodaya *et al.*, 1998
Glyparvin-A [112]	Phenethyl amides alk.	Leaf	Vajrodaya *et al.*, 1998
3,7-Diprenyl Carbazole [2]	Indole alk.	Rootbark	Vajrodaya *et al.*, 1998
Skimmianine [31]	Quinoline alk.	Rootbark	Vajrodaya *et al.*, 1998
Trichanthin-A [114]	Phenethyl amides alk.	Leaf	Vajrodaya *et al.*, 1998
Trichanthin-B [115]	Phenethyl amides alk.	Leaf	Vajrodaya *et al.*, 1998
Yukocitrin [51]	Acridone alk.	Stembark	Vajrodaya *et al.*, 1998



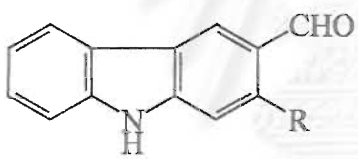
[1] Glypetelotine



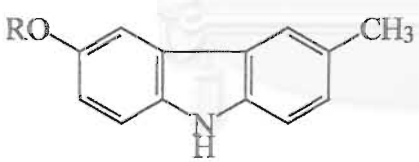
[2] 3,7-Diprenylated indole



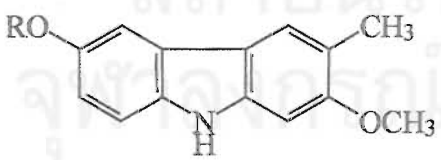
[3] Carbazole R=H
[4] 3-Methylcarbazole R=Me



[5] 3-Formylcarbazole R=H
[6] Glycosinine R=Me

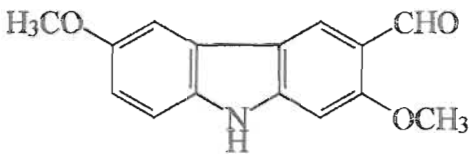


[7] Glycozolinine R=H
(Glycozolinol)
[8] Glycozoline R=Me

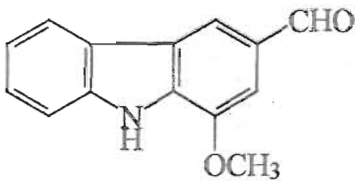


[9] Glycozolidol R=H
[10] Glycozolidine R=Me

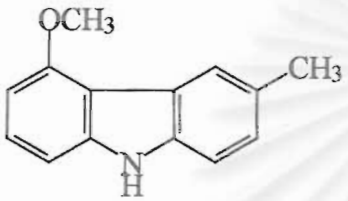
Figure 2 Structures of compounds previously isolated from *Glycosmis* spp.



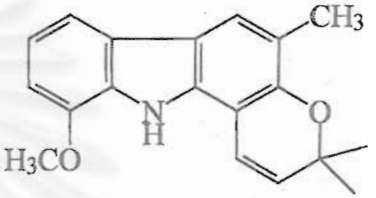
[11] Glycozolidal



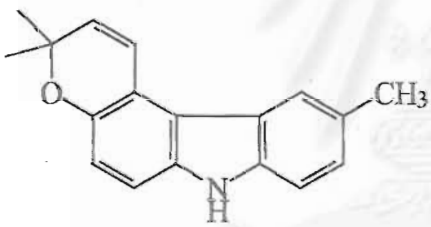
[12] Murrayanine



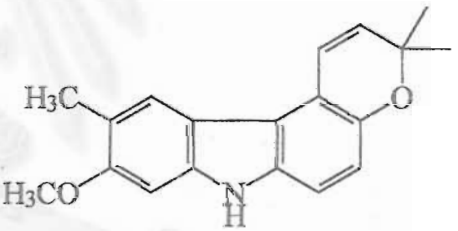
[13] Glycozolicine



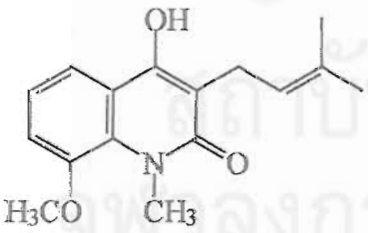
[14] Mupamine



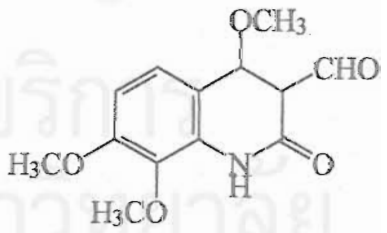
[15] Glycoborinine



[16] 7-Methoxyglycomaurin

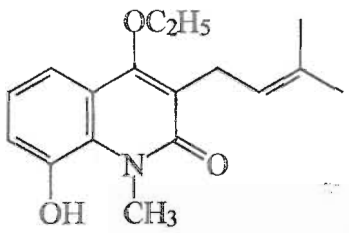


[17] Glycophylone

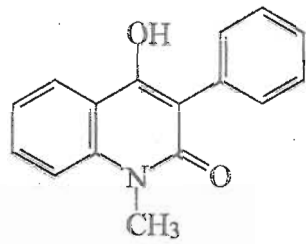


[18] Glycocitridine

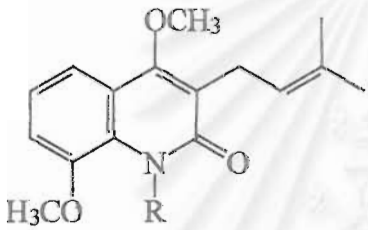
Figure 2 Structures of compounds previously isolated from *Glycosmis* spp. (Continued)



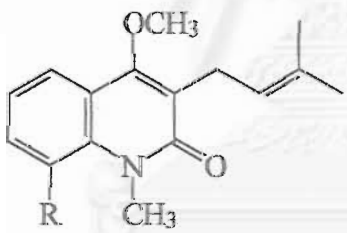
[19] Homoglycosolone



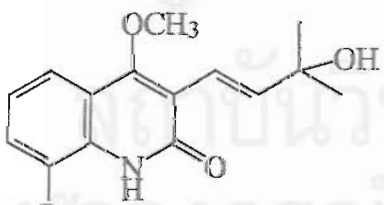
[20] Arboricine



[21] Glycolone R=H
[22] *O*-Methylglycosolone R=Me

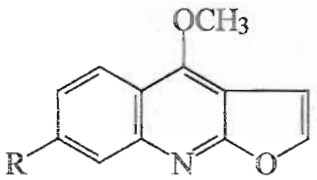


[23] *N*-Methylatanine R=H
[24] Glycosolone R=Me

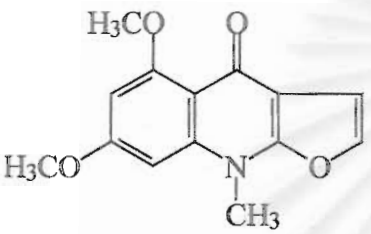


[25] Glycocitlone-A R=H
[26] Glycocitlone-B R=OH
[27] Glycocitlone-C R=OMe

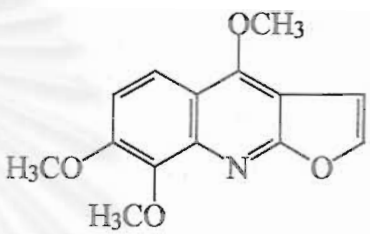
Figure 2 Structures of compounds previously isolated from *Glycosmis* spp. (Continued)



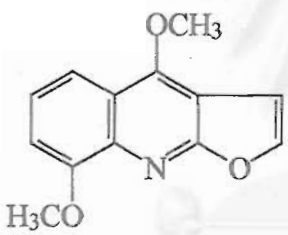
[28] Dictamnine R=H
[29] Evolitrine R=OMe



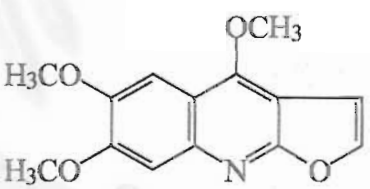
[30] Glycarpine



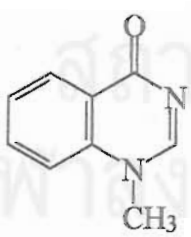
[31] Skimmianine



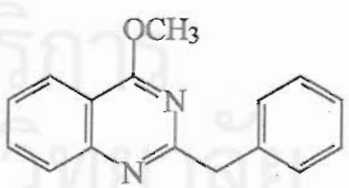
[32] γ-Fagarine



[33] Kokusaginine

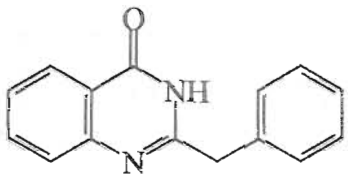


[34] Glycorine

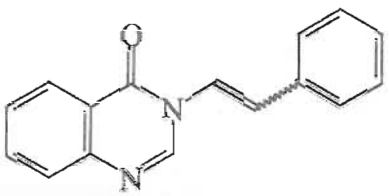


[35] Glycophymoline
(Glycophymine)

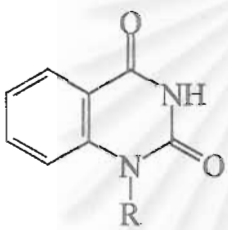
Figure 2 Structures of compounds previously isolated from *Glycosmis* spp. (Continued)



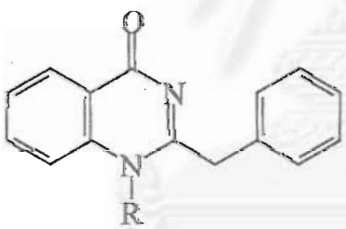
[36] Glycosminine



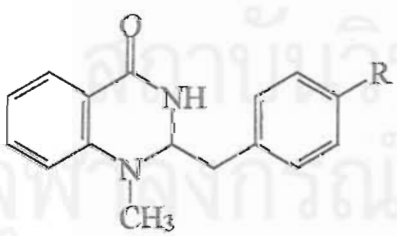
[37] (E)-Bogorine
[38] (Z)-Bogorine



[39] 2,4-Quinazolinedione R=H
[40] Glycosmicine R=Me

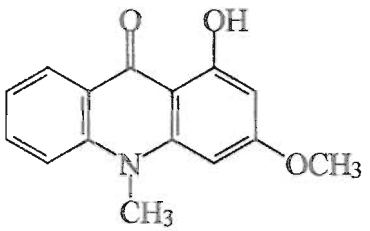


[41] Glycophymine R=H
[42] Arborine R=Me
(Glycosine)

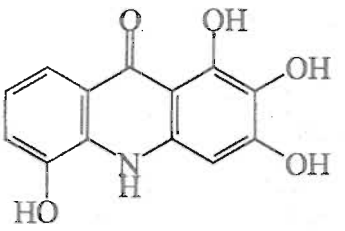


[43] Glycozolone-A R=H
[44] Glycozolone-B R=OMe

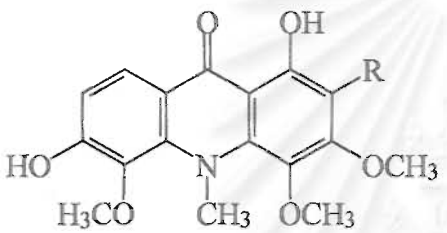
Figure 2 Structures of compounds previously isolated from *Glycosmis* spp. (Continued)



[45] 1-Hydroxy-3-methoxy
-10-methylacridone

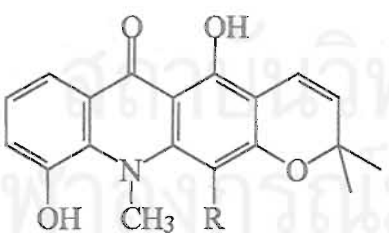


[46] 2, 3, 5-Hydroxyarborine



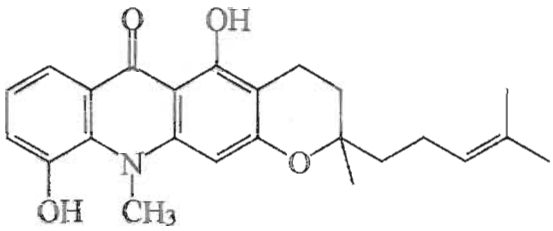
[47] Glycofolinine R=H
[48] Glyfoline R=OMe

[49] Arborinine R=H
[50] 5-Hydroxyarborinine R=OMe

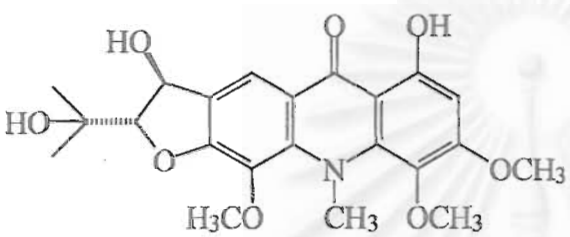


[51] Yukocitrin R=H
[52] Pyranofoline R=OMe

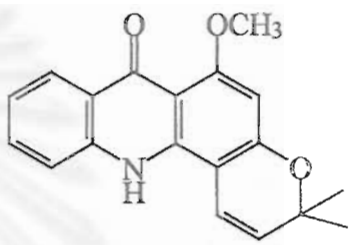
Figure 2 Structures of compounds previously isolated from *Glycosmis* spp.
(Continued)



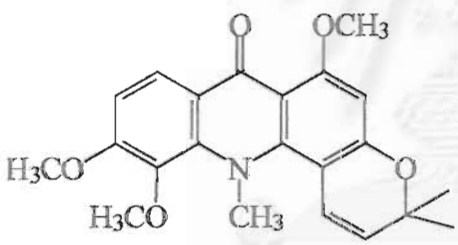
[53] Glycofoline



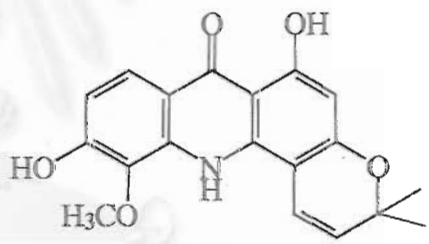
[54] Glycocitrine-V



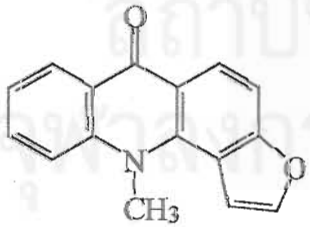
[55] Des-*N*-Methylacronycine
(De-*N*-Methylacronycine)



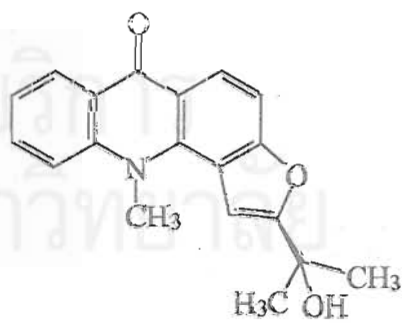
[56] Dimethoxyacronycine



[57] Acrifoline

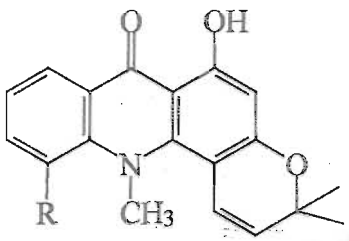


[58] Furofoline-I

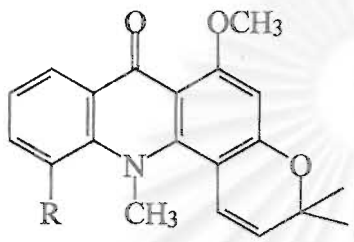


[59] Furofoline-II

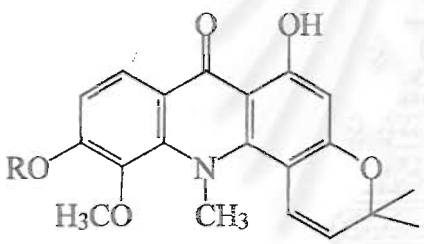
Figure 2 Structures of compounds previously isolated from *Glycosmis* spp.
(Continued)



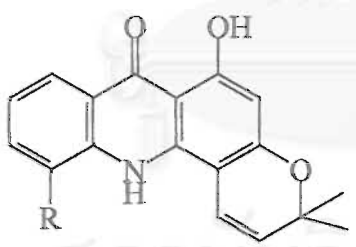
[60] Noracronycine R=H
[61] 5-Hydroxynoracronycine R=OH



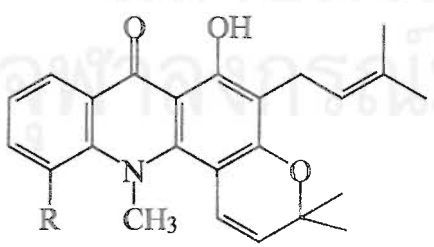
[62] Acronycine R=H
[63] 5-Methoxyacronycine R=OMe



[64] Citracridone-I R=H
[65] Citracridone-II R=Me

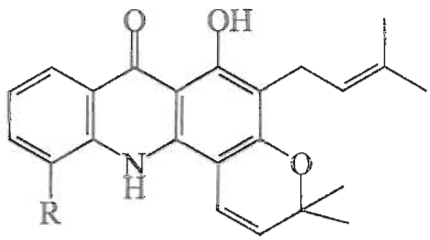


[66] Des-*N*-Methyl-noracronycine (De-*N*-Methyl-noracronycine) R=H
[67] Atalaphillidine R=OH

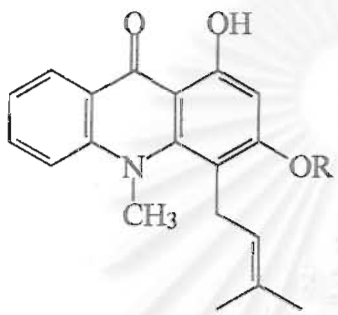


[68] *N*-Methylseverifoline R=H
[69] 5-Hydroxy-*N*-methyl-severifoline (*N*-Methylatalaphillinine) R=OH

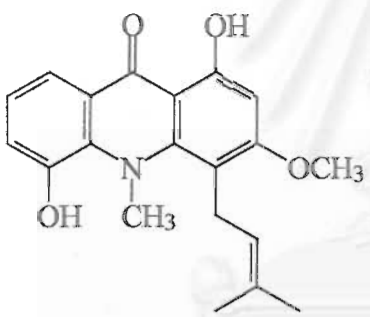
Figure 2 Structures of compounds previously isolated from *Glycosmis* spp. (Continued)



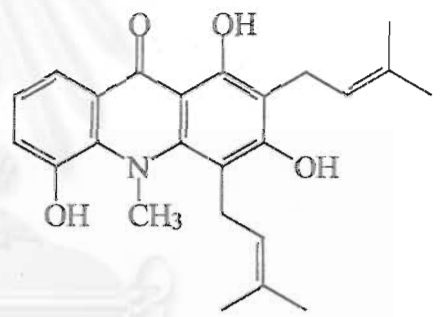
[70] Severifoline R=H
[71] Atalaphillinine R=OH



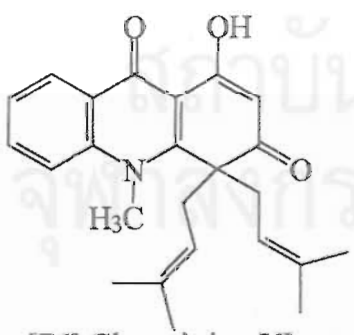
[72] Glycocitrine-II R=H
[73] 3-*O*-Methyl- R=Me
glycocitrine-II



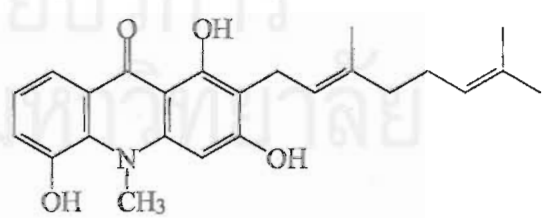
[74] Glycocitrine-I



[75] *N*-Methylatalaphilline

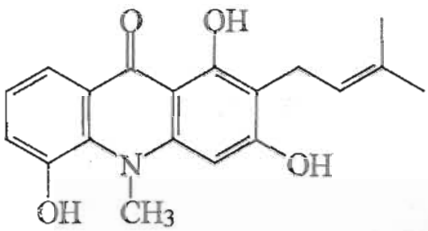


[76] Glycocitrine-VI

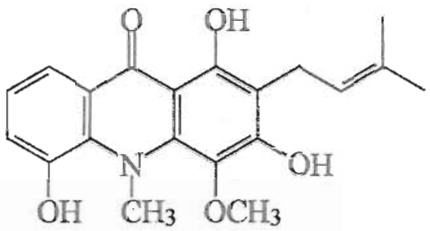


[77] Glycocitrine-III

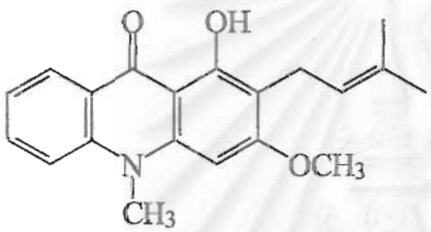
Figure 2 Structures of compounds previously isolated from *Glycosmis* spp. (Continued)



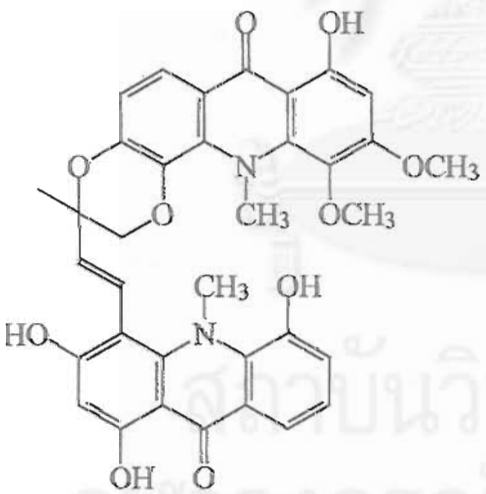
[78] Junosin



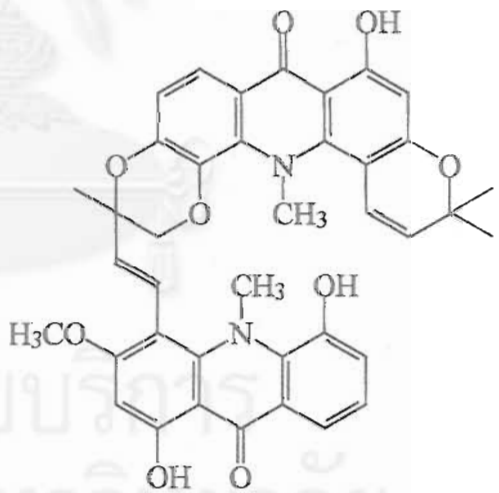
[79] Glycocitrine-IV



[80] 1-Hydroxy-3-methoxy-2-(3-methylbut-2-enyl)-*N*-methylacridan-9-one

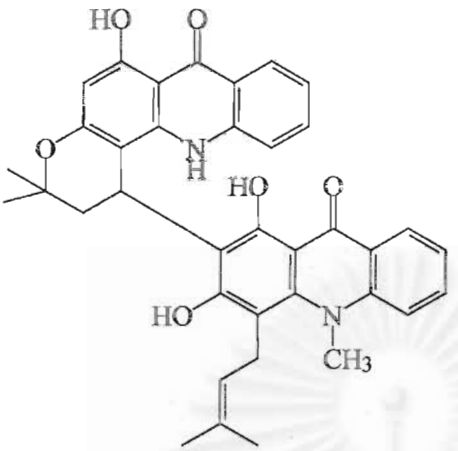


[81] Glycobismine-D

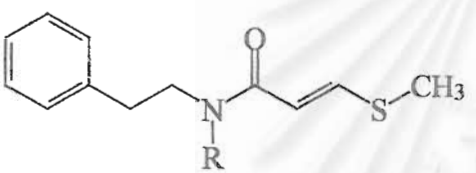


[82] Glycobismine-E

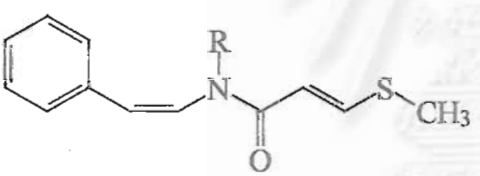
Figure 2 Structures of compounds previously isolated from *Glycosmis* spp. (Continued)



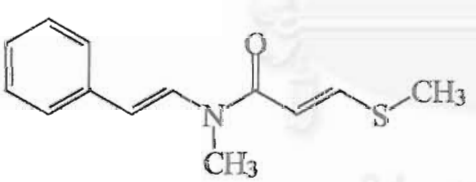
[83] Glycobismin-A



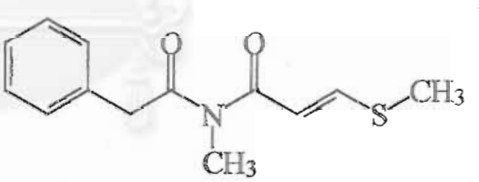
[84] Sinharine R=H
[85] Methylsinharine R=Me



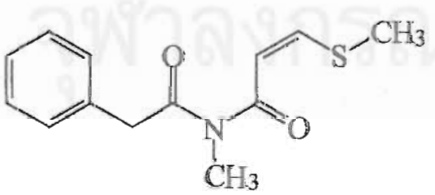
[86] Illukumbin-B R=H
[87] Methylillukumbin-B R=Me



[88] Methylillukumbin-A

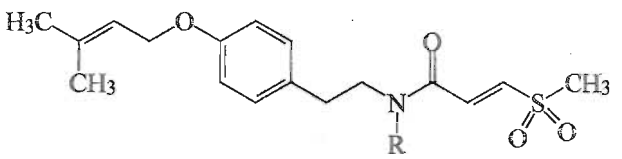


[89] Penimide-A

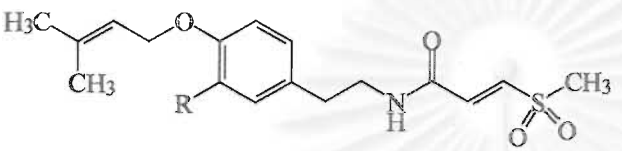


[90] Penimide-B

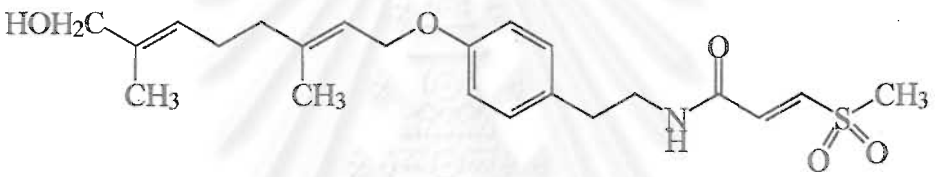
Figure 2 Structures of compounds previously isolated from *Glycosmis* spp. (Continued)



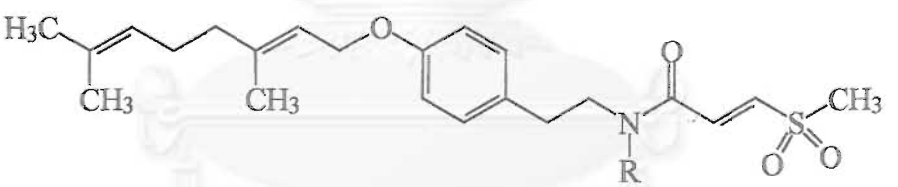
[91] Dambullin R=H
[92] Methyldambullin R=Me



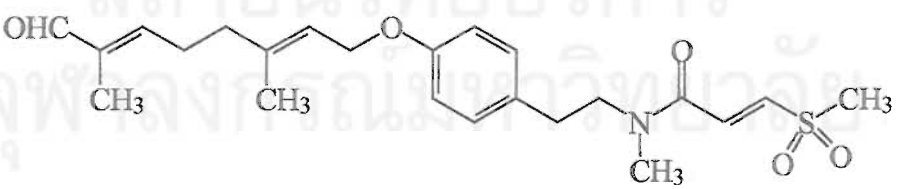
[93] Sakambullin R=OH
[94] *O*-Methyl sakambullin R=OMe



[95] Gerambullol

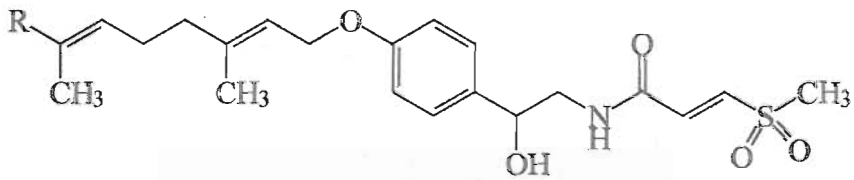


[96] Gerambullin R=H
[97] Methylgerambullin R=Me

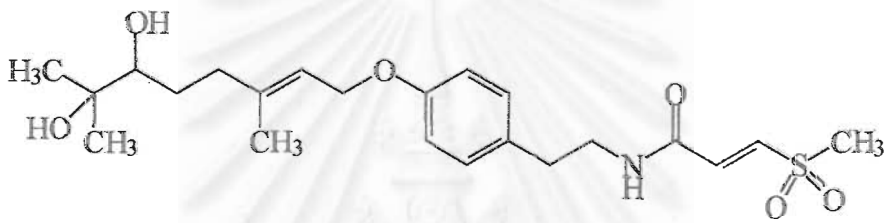


[98] Methylgerambullal

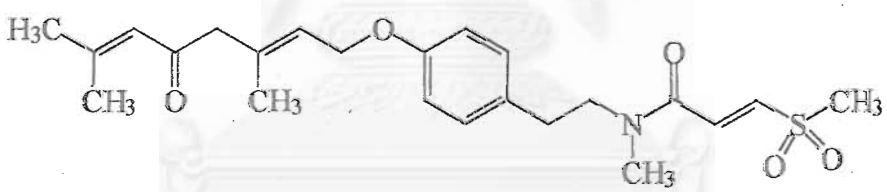
Figure 2 Structures of compounds previously isolated from *Glycosmis* spp. (Continued)



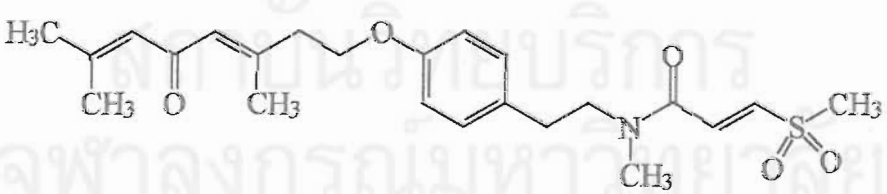
[99] β-Hydroxygerambullin R=Me
[100] β-Hydroxygerambullol R=CH_2OH
[101] β-Hydroxygerambullal R=CHO



[102] Gerambullindiol

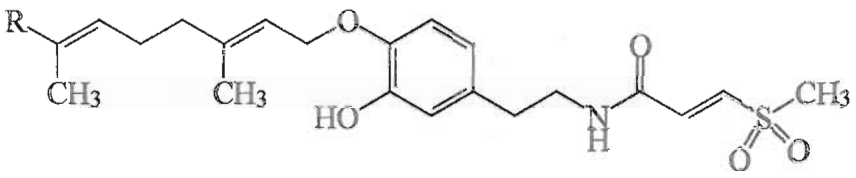


[103] Methylgerambullone

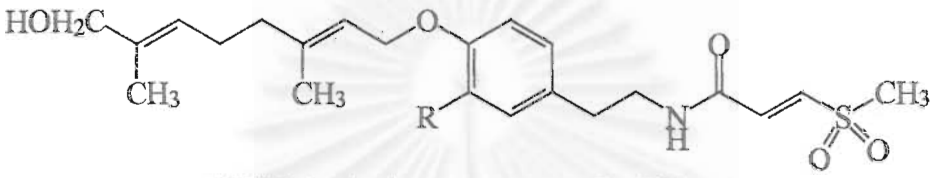


[104] Methylisogerambullone

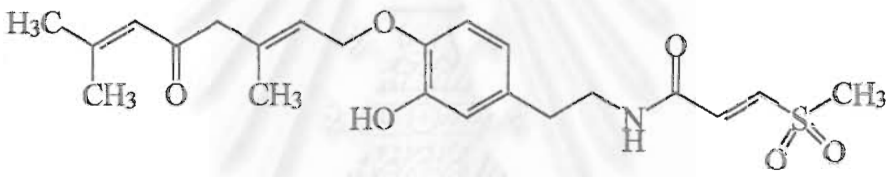
Figure 2 Structures of compounds previously isolated from *Glycosmis* spp. (Continued)



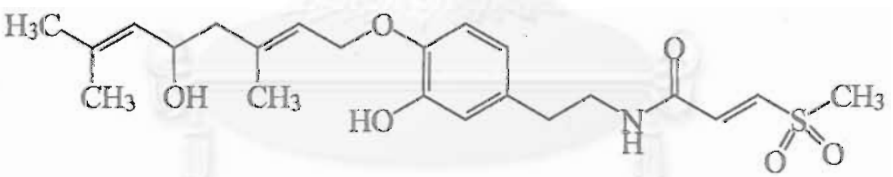
[105] Sakerine R=Me
[106] Sakerinol-B R=CH_2OH



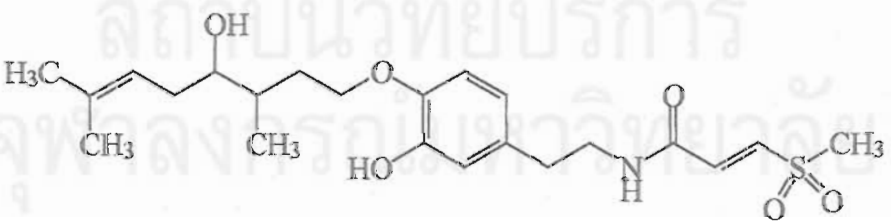
[107] Sakerinol-A R=OH
[108] *O*-Methylsakerinol-A R=OMe



[109] Sakerone

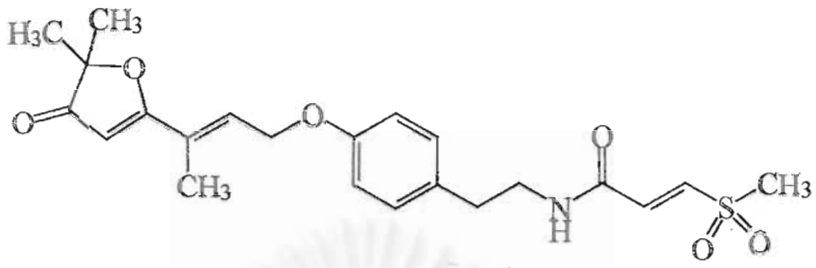


[110] Sakerol

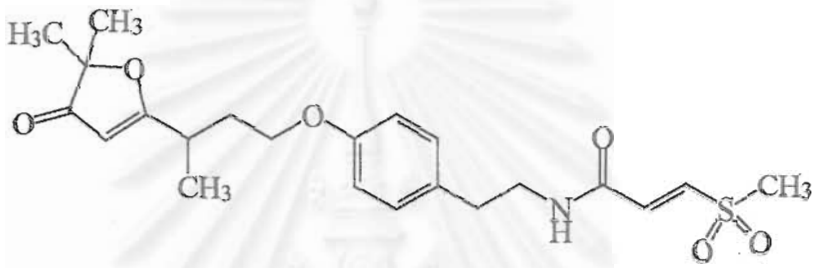


[111] Dihydroisosakerol

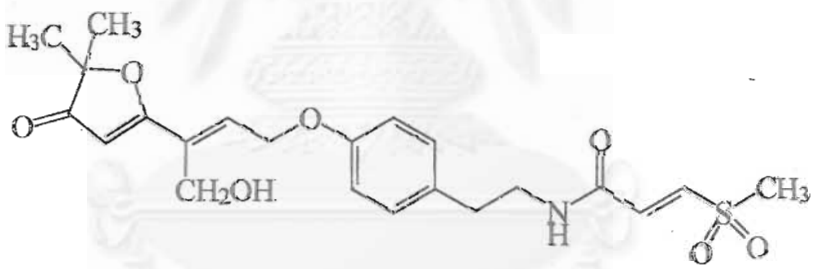
Figure 2 Structures of compounds previously isolated from *Glycosmis* spp. (Continued)



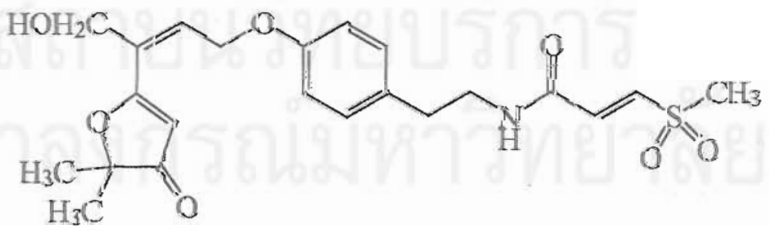
[112] Glypavin-A



[113] Dihydroglypavin

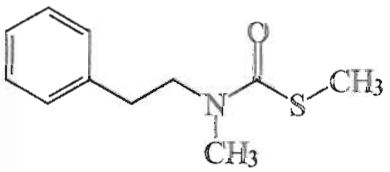


[114] Trichanthin-A

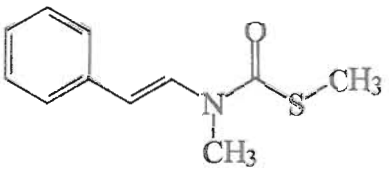


[115] Trichanthin-B

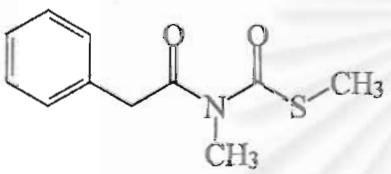
Figure 2 Structures of compounds previously isolated from *Glycosmis* spp. (Continued)



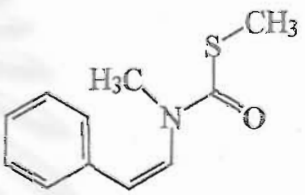
[116] Niranin



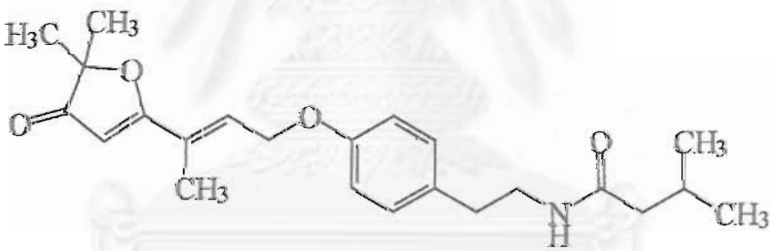
[117] Dehydroniranin-A



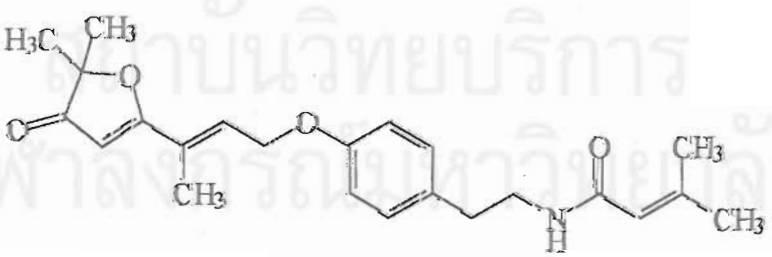
[118] Ritigalin



[119] Dehydroniranin-B

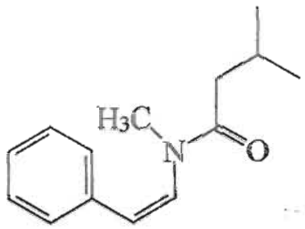


[120] Khaocharnide

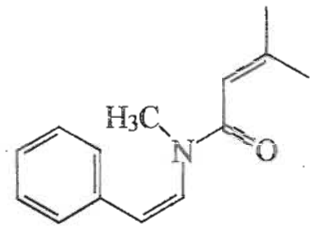


[121] Puhinamide

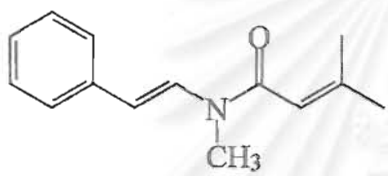
Figure 2 Structures of compounds previously isolated from *Glycosmis* spp. (Continued)



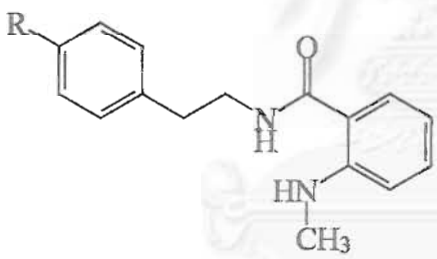
[122] Thalebanin-B



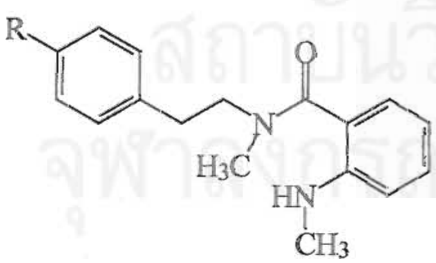
[123] Dehydrothalebanin-B



[124] Dehydrothalebanin-A

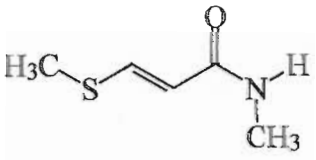


[125] Glycoamide-A R=H
[126] Glycoamide-B R=OMe

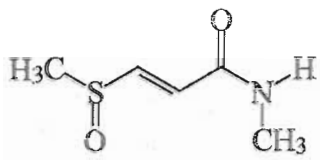


[127] Doisuthine R=H
[128] Methoxydoisuthine R=OMe

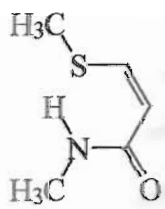
Figure 2 Structures of compounds previously isolated from *Glycosmis* spp. (Continued)



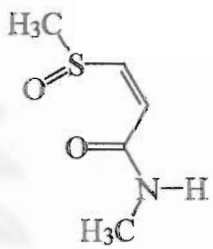
[129] Penangin



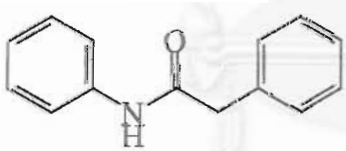
[130] Glycothiomin-A



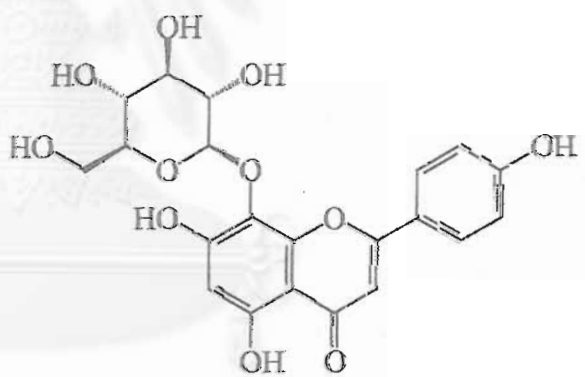
[131] Isopenangin



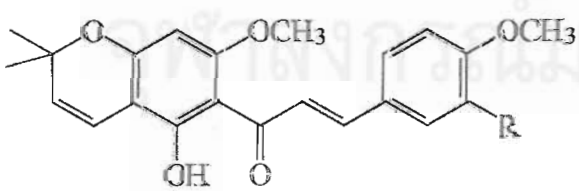
[132] Glycothiomin-B



[133] Glycomide

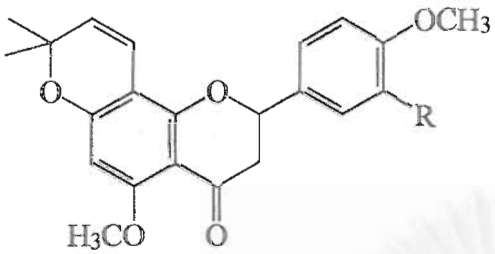


[134] Vitexin

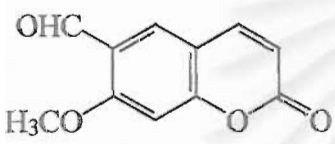


[135] Glychalcone-A R=H
[136] Glychalcone-B R=OMe

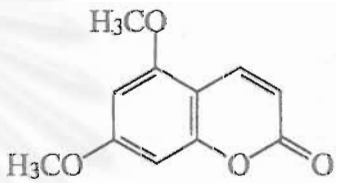
Figure 2 Structures of compounds previously isolated from *Glycosmis* spp. (Continued)



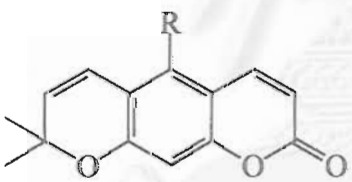
[137] Glyflavanone-A R=H
[138] Glyflavanone-B R=OMe



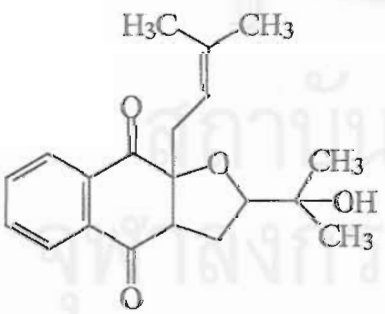
[139] Angelical



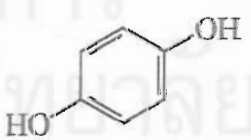
[140] Limettin



[141] Xanthyletin R=H
[142] Xanthoxyletin R=OMe

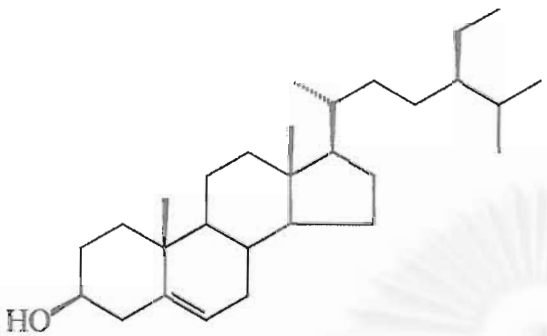


[143] Glycoquinone

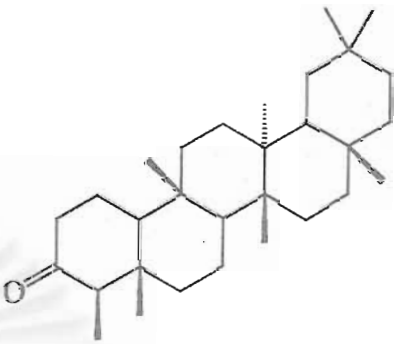


[144] Parahydroquinone

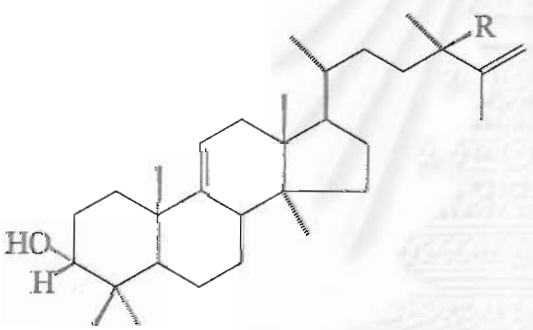
Figure 2 Structures of compounds previously isolated from *Glycosmis* spp. (Continued)



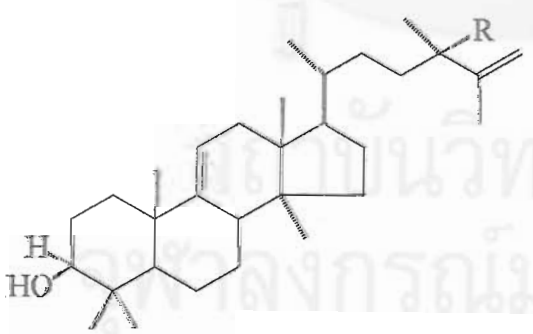
[145] β-Sitosterol



[146] Friedelin

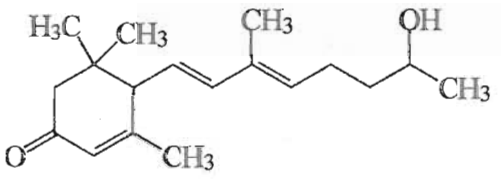


[147] (24*S*)-Methyl-5α-lanosta
-9(11),25-dien-3α-ol R=H
[148] 24,24-Dimethyl-5α-lanosta
-9(11),25-dien-3α-ol R=Me

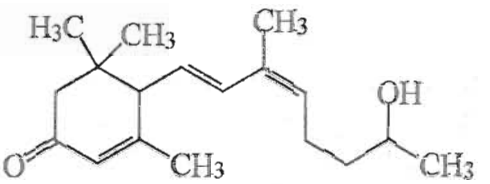


[149] (24*S*)-Methyl-5α-lanosta
-9(11),25-dien-3β-ol R=H
[150] 24,24-Dimethyl-5α-lanosta
-9(11),25-dien-3β-ol R=Me

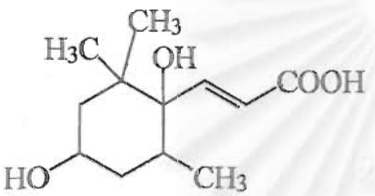
Figure 2 Structures of compounds previously isolated from *Glycosmis* spp. (Continued)



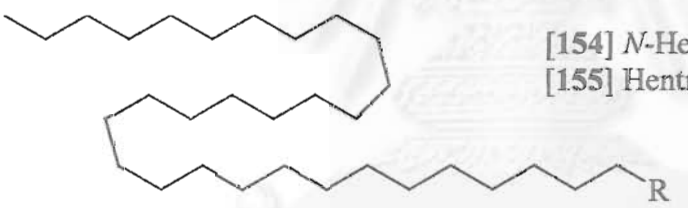
[151] Laipol



[152] Isolaipol



[153] Glycoric acid



[154] *N*-Hentriacontane R=H
[155] Hentriacontan-1-ol R=OH

Figure 2 Structures of compounds previously isolated from *Glycosmis* spp. (Continued)

2. Biological activities of compounds isolated from *Glycosmis* spp.

Several biological activities of the compounds isolated from *Glycosmis* spp. have been studied. Many acridone alkaloids such as atalaphyllidine (**67**), 5-hydroxy-*N*-methylseverifoline (**69**), atalaphyllinine (**71**) and des-*N*-methylnoracronycine (**66**) showed potent antiproliferative activity against tumor cell lines [human lung carcinoma (A-549), melanin pigment producing mouse melanoma (B-16 melanoma 4A5), T-cell leukemia (CCRF-HSB-2), human gastric cancer cell and lymph-node metastasized (TGBC 11TKB)], whereas they have weak cytotoxicity on normal human cell lines.(Kawaii *et al.*, 1999a)

According to a review by Kawaii and Co-workers in 1999b, atalaphyllidine (**67**), atalaphyllinine (**71**) and des-*N*-methylnoracronycine (**66**) showed induction of human promyelocytic leukemia cell (HL-60) differentiation, supposed to be clinically effective against myeloproliferative disorders and human colon, mammary and lung xenografts and melanoma.

The antimalarial activity of *Glycosmis* acridone alkaloids have been studied. Several compounds such as glycocitrine-I (**74**), *N*-methylataphilline (**75**), des-*N*-methylnoracronycine (**66**), atalaphillidine (**67**), atalaphillinine (**71**), 5-hydroxy-*N*-methylseverifoline (**69**) and glycobismine-A (**83**) showed antimalarial activity against rodent malaria both *in vitro* and *in vivo*. (Fujioka *et al.*, 1989)

Two sulfur-containing amides [methylillukumbin-A (**88**), methylillukumbin-B (**87**)] from leaf extracts of *Glycosmis mauritiana* and *G. pentaphylla* showed antifungal activity. (Greger *et al.*, 1993b)

Insecticidal activities of the plants in the genus *Glycosmis* have been relatively little studied. Roots of *Glycosmis pentaphylla* may represent a source of root resistant to larval *Diaprepes abbreviatus* in live root or diet-incorporation assays. (Shapiro *et al.*, 1997)

The EtOAc fraction of *Glycosmis pentaphylla* leaf extract inhibited the juvenile hormone III (JH-III) biosynthesis *in vitro* of corpora allata of the field cricket *Gryllus bimaculatus*. It also showed a larvicidal activity against the mosquito *Culex quinquefasciatus*. (Muthukrishnan *et al*., 1999)

CHAPTER III

EXPERIMENTAL

1. Plant Materials

The branches of *Glycosmis parva* Craib were collected from The World Biosphere Reserve, Sakaerat Environmental Research Station, Nakorn-ratchasima Province, Thailand in January 2000. The plant was identified by Associate Professor Dr. Nijsiri Ruangrungsi, Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok, Thailand. A voucher specimen has been deposited in the herbarium of the 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. Merck) pre-coated plate
Layer Thickness	: 0.2 mm
Distance	: 5 cm
Temperature	: Laboratory temperature (30-35°C)

2.1 Analytical Thin-Layer Chromatography (TLC) (Continued)

Detection : 1. Ultraviolet light at wavelengths of 254 and 365 nm
2. Dragendorff spraying reagent
3. Anisaldehyde sulfuric acid reagent and heated at 100-105 °C for 5-10 min
4. 10% Sulfuric acid in ethanol and heated at 100-105°C for 5-10 min
5. Iodine vapor

2.2 High Performance Thin-Layer Chromatography (HPTLC)

Technique : One dimension, ascending

Adsorbent : Silica gel RP-18 $WF_{254}s$ (E. Merck) pre-coated plate for reverse phase chromatography

Layer Thickness : 0.2 mm

Distance : 3.5 cm

Temperature : Laboratory temperature (18-25°C)

Detection : Ultraviolet light at wavelengths of 254 and 365 nm

2.3 Preparative Thin-Layer Chromatography (PLC)

Technique : One dimension, ascending

Adsorbent : Silica gel 60 F_{254} (E. Merck) pre-coated plate for preparative layer chromatography

Layer Thickness : 2 mm

Distance : 10 cm

Temperature : Laboratory temperature (30-35°C)

Detection : Ultraviolet light at wavelengths of 254 and 365 nm

2.4 Column Chromatography (CC)

2.4.1 Quick Column Chromatography

Adsorbent : Silica gel 60 (No. 7734) particle size 0.063-0.200 mm (70-230 mesh ASTM, E. Merck)

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, dried and placed gently on top of the column.

Detection : Fractions were examined by TLC in the same manner as described in section 2.1

2.4.2 Flash Column Chromatography

Adsorbent : Silica gel 60 (No. 7734) particle size 0.063-0.200 mm (70-230 mesh ASTM, E. Merck) & Silica gel 60 (No. 9385) particle size 0.040-0.063 mm (230-400 mesh ASTM, E. Merck)

Packing method : Dry & Wet packing

Sample loading : The sample was dissolved in a small amount of eluant and then applied gently on top of the column.

Detection : Fractions were examined by TLC in the same manner as described in section 2.1

2.4.3 Medium Pressure Liquid Chromatography (MPLC)

Adsorbent : LICHROPREP Si-60 (40-63 μm, E. Merck) pre-packed column & LICHROPREP RP-18 (40-63 μm, E. Merck) pre-packed column for reverse phase chromatography

Chromatographic pump : YAMAZEN PUMP 540, pressure 1-2 kg/ cm^2

Flow rate : 6 ml/ min

Saturation time : Column was saturated with eluant prior to add the sample for 45 min

Sample loading : The sample was dissolved in a small volumn of eluant, filtered through filter and loaded on the bottom of the column

Detection : Fractions were examined by UV-Detector YAMAZEN PREP-UV 254 and automatically fractionated in 5 ml each by fraction collector.

2.4.4 Gel Filtration Chromatography

Adsorbent : Sephadex LH 20 (Phamacia)

Packing method : Gel filter was suspended in the eluant and left standing to swell for 24 hours prior to use. It was then poured into the column and allowed to set tightly.

Sample loading : The sample was dissolved in a small amount of eluant and then applied gently on top of the column.

Detection : Fractions were examined by TLC in the same manner as described in section 2.1

2.5 Spectroscopy

2.5.1 Ultraviolet (UV) Absorption Spectra

Ultraviolet spectra (in chloroform) were measured on a HITACHI U-3200 Spectrophotometer (Faculty of Pharmaceutical Sciences, Chiba University, Chiba, Japan).

2.5.2 Infrared (IR) Absorption Spectra

Infrared spectra (KBr disc.) were measured on a JASCO FT/IR-300E spectrometer (Faculty of Pharmaceutical Sciences, Chiba University, Chiba, Japan) or a PERKIN-ELMER Spectrum 2000 FT-IR spectrometer (Pharmaceutical Research Instrument Center, Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok, Thailand).

2.5.3 Mass Spectra (MS)

Electron impact mass spectra (EIMS) were measured on a HITACHI RMU-7M mass spectrometer (Faculty of Pharmaceutical Sciences, Chiba University, Chiba, Japan) or a FISON MICROMASS VG PLATFORM II mass spectrometer (Pharmaceutical Research Instrument Center, Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok, Thailand).

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

^{1}H-NMR (500 MHz) and ^{13}C-NMR (125 MHz) spectra were obtained with a JEOL JMN-A 500 NMR spectrometer (Faculty of Pharmaceutical Sciences, Chiba University, Chiba, Japan).

Solvents for NMR spectra were deuterated chloroform (Chloroform-*d*) and deuterated methanol (Methanol-d_4). Chemical shifts were reported in ppm scale using the chemical shift of the TMS as the internal standard.

2.6 Physical Properties

2.6.1 Melting Points

Melting points were obtained on a Gallenkamp melting point apparatus (Faculty of Pharmaceutical Sciences, Chiba University, Chiba, Japan).

2.7 Solvents

Throughout this work, all organic solvents were of commercial grade and were distilled prior to use. Except solvents for NMR experiment were deuterated solvents as described in section 2.5.4.

2.8 Spraying Reagents

2.8.1 Dragendroff Spraying Reagent (DRG; MUNiER and MACHEBOEUF)

Solution (a) : Dissolve 0.85 g basic bismuth nitrate in 10 ml glacial acetic acid and 40 ml water under heating. If necessary, filter.

Solution (b) : Dissolve 8 g potassium idodide in 30 ml water

Stock solution : (a) and (b) are mixed 1:1

Spraying reagent : One ml stock solution is mixed with two ml glacial acetic acid and 10 ml water.

The alkaloids appear as brown or orange-brown (vis.) zones immediately on spraying. The color is fairly stable.

2.8.2 Anisaldehyde-Sulphuric Acid Spraying Reagent (AS)

Anisaldehyde (0.5 ml) is mixed with 10 ml glacial acetic acid, followed by 85 ml methanol and 5 ml concentrated sulphuric acid, in that order. The reagent has only limited stability and is no longer useable when the color has turned to red-violet.

3. Extraction and Isolation

3.1 Extraction

The dried, coarsely powdered branches of *Glycosmis parva* Craib (3.5 Kg) were macerated with ethanol (40 L) four times and filtered. The filtrates were pooled and evaporated under reduced pressure at temperature not exceeding than 40°C to yield an ethanol extract (syrupy mass 410 g, 11.71% based on dried weight of the branches). The ethanol extract was partitioned with hexane 20 L (40x500 ml) and the obtained extract was evaporated as the above manner to yield a hexane extract (39.0 g, 1.11% based on dried weight of the branches). The residue from hexane extraction was partitioned with chloroform (25 L) and the obtained extract was evaporated *in vacuo* to yield a chloroform extract (64.0 g, 1.83% based on dried weight of the branches).

3.2 Isolation

3.2.1 Isolation of Compounds from Hexane Extract

The hexane extract (39.0 g) was dissolved in a small amount of organic solvent (hexane and chloroform), triturated with silica gel 60 (No. 7734), dried under reduced pressure and then fractionated by quick column chromatography using sintered glass filter column of silica gel 60 (No. 7734). Elution was performed in a polarity gradient manner with hexane and chloroform. The ratios and volumes of solvents used in this quick column chromatography are summarized in Table 2.

Table 2 The ratios and volumes of solvents for quick column chromatography of hexane extract of *Glycosmis parva* Craib

Fraction	Ratio of hexane : chloroform	Volume of solvent (L)
1-17	100% Hexane	5.1 (17x300 ml)
18-51	1 : 1	10.2 (34x300 ml)
52-56	2 : 3	1.5 (5x300 ml)
57-60	3 : 7	1.2 (4x300 ml)
61-66	1 : 4	1.8 (6x300 ml)
67-88	100% Chloroform	6.6 (22x300 ml)

The eluates were examined by TLC which using chloroform as the developing system. Fractions with similar chromatographic pattern were combined to yield 11 fractions, as shown in Table 3.

Table 3 Combination of fractions from quick column chromatography of hexane extract from *Glycosmis parva* Craib

Combined fraction	Fraction	Volume of solvent (L)
GH1	1-2	0.6 (2x300 ml)
GH2	3-8	1.8 (6x300 ml)
GH3	9-18	3.0 (10x300 ml)
GH4	19	0.3 (1x300 ml)
GH5	20-24	1.5 (5x300 ml)
GH6	25-39	4.5 (15x300 ml)
GH7	40-61	6.6 (22x300 ml)
GH8	62-71	3.0 (10x300 ml)
GH9	72-76	1.5 (5x300 ml)
GH10	77-83	2.1 (7x300 ml)
GH11	84-88	1.5 (5x300 ml)

3.2.1.1 Isolation of Isolate j1-2

Fraction GH6 (2.4 g) was fractionated on a column using silica gel 60 (No. 9385) as the adsorbent with chloroform as the eluant. Twenty-nine fractions approximately of 15 ml were collected. The eluates were examined by TLC using methanol : chloroform (1 : 200) as the developing solvent. Fractions showing similar chromatographic pattern were combined to yield four fractions as shown below.

fractions 1-3 = combined fraction GH6.1
fractions 4-6 = combined fraction GH6.2
fractions 7-13 = combined fraction GH6.3
fractions 14-29 = combined fraction GH6.4

Isolate j1-1A (3 mg) was obtained as colorless needles from fraction GH6.2 through recrystallization from hexane. The yield was $8.6x10^{-5}$ % based on dried weight of the branches, Rf 0.35 [Silica gel 60 F_{254} (No.9385), methanol : chloroform (1:200)].

Fraction GH6.3 was separated on a column using silica gel 60 (No.9385) as the adsorbent with chloroform as the eluant. Forty fractions, approximately of 10 ml, were collected. Fractions with the same chromatographic pattern examined by TLC using methanol : chloroform (1:150) as the developing solvent were combined to yield three fractions. The TLC chromatogram of fractions 2-23 showed only one spot under UV light at 365 nm and 10% sulfuric acid in ethanol, Rf 0.35 [Silica gel 60 F_{254} (No.9385), methanol : chloroform (1:200)]. Evaporation of this fraction under reduced pressure gave 6 mg of compound j1-1B as colorless needles. The yield was $1.7x10^{-4}$ % based on dried weight of the branches. It was later combined with isolated j1-1A as j1-2 and identified as a mixture of β-sitosterol [145] and stigmasterol [156].

3.2.1.2 Isolation of Compounds j2-1 & j2-2

Fraction GH8A (736 mg) was obtained as orange powder from fraction GH8 through recrystallization from hexane. The yield was $2.1x10^{-2}$ % based on dried weight of the branches, Rf 0.25 [Silica gel 60 F_{254} (No.9385), methanol : chloroform (1:100)]. The TLC chromatogram of GH8A showed only one spot under UV light at 254, 365 nm, dragendroff spraying reagent, anisaldehyde-sulfuric acid reagent and 10% sulfuric acid in ethanol.

As the same as fraction GH8A, fraction GH9A (520 mg) was obtained as orange powder from fraction GH9 through recrystallization from hexane. The yield was $1.5x10^{-2}$ % based on dried weight of the branches, Rf 0.25 [Silica gel 60 F_{254} (No.9385), methanol : chloroform (1:100)]. The TLC chromatograms of GH9A showed only one spot as the same character as GH8A.

Fractions GH8A (736 mg) and GH9A (520 mg) were combined and further separated by Medium Pressure Liquid Chromatography (MPLC), and then by the LICHROPREP RP-18 pre-packed column for reverse phase chromatography with water : methanol (1:5) as the eluant. Fifty fractions, approximately of 5 ml, were collected. The eluates were examined by TLC using water : methanol (2:5) as the developing solvent. Fractions showing similar chromatographic pattern were combined to yield four fractions.

The TLC chromatogram of fractions 1-16 and 22-36 showed only one spot under UV light at 254 and 365 nm [Silica gel RP-18 $WF_{254}S$ for reverse phase TLC, water : methanol (2:5)]. Evaporation of fractions 1-16 under reduced pressure gave 32 mg of compound j2-1 as an orange powder, Rf 0.2 [Silica gel RP-18 $WF_{254}S$ for reverse phase TLC, water : methanol (2:5)]. It was later identified as *N*-methylataphilline [**75**].

Fractions 22-36 were evaporated under reduced pressure gave 31 mg of compound j2-2 as an orange powder, Rf 0.4 [Silica gel RP-18 $WF_{254}S$ for reverse phase TLC, water : methanol (2:5)]. It was later identified as 5-hydroxy-*N*-methylseverifoline (*N*-methylatalaphillinine) [**69**].

3.2.2 Isolation of Compounds from Chloroform Extract

The chloroform extract (64.0 g) was dissolved in a small amount of organic solvent (chloroform and methanol), triturated with silica gel 60 (No. 7734), dried under reduced pressure and then fractionated by quick column chromatography using sintered glass filter column of silica gel 60 (No. 7734). Elution was performed in a polarity gradient manner with dichloromethane and methanol. The ratios and volumes of solvents used in this quick column chromatography are summarized in Table 4.

Table 4 The ratios and volumes of solvents for quick column chromatography of chloroform extract of *Glycosmis parva* Craib

Fraction	Ratio of Dichloromethane : methanol	Volume of solvent (L)
1-89	100% dichloromethane	26.7 (89x300 ml)
90-99	19 : 1	3.0 (10x300 ml)
100-110	9 : 1	3.3 (11x300 ml)
111-120	4 : 1	3.0 (10x300 ml)

The eluates were examined by TLC which using methanol : dichloromethane (1:100) as the developing system. Fractions with similar chromatographic pattern were combined to yield 15 fractions, as shown in Table 5.

Table 5 Combination of fractions from quick column chromatography of chloroform extract from *Glycosmis parva* Craib

Combined fraction	Fraction	Volume of solvent (L)
GC1	1-4	1.2 (4x300 ml)
GC2	5-10	1.8 (6x300 ml)
GC3	11-32	6.6 (22x300 ml)
GC4	33-41	2.7 (9x300 ml)
GC5	42-54	3.9 (13x300 ml)
GC6	55-63	2.7 (9x300 ml)
GC7	64	0.3 (1x300 ml)
GC8	65-69	1.5 (5x300 ml)
GC9	70	0.3 (1x300 ml)
GC10	71-73	0.9 (3x300 ml)

Table 5 Combination of fractions from quick column chromatography of chloroform extract from *Glycosmis parva* Craib (Continued)

Combined fraction	Fraction	Volume of solvent (L)
GC11	74-76	0.9 (3x300 ml)
GC12	77-84	2.4 (8x300 ml)
GC13	85-88	1.2 (4x300 ml)
GC14	89-90	0.6 (2x300 ml)
GC15	91-120	9.0 (30x300 ml)

3.2.2.1 Isolation of Compound j6-1

Fraction GC6 (1.2 g) was fractionated on a column using silica gel 60 (No. 9385) as the adsorbent with chloroform as the eluant. Forty fractions approximately of 15 ml were collected. The eluates were examined by TLC using methanol : chloroform (1:100) as the developing solvent. Fractions showing the same chromatographic pattern were combined to yield 7 fractions as shown below.

fractions 1-6 = combined fraction GC6.1
fractions 7-11 = combined fraction GC6.2
fractions 12-16 = combined fraction GC6.3
fractions 17-19 = combined fraction GC6.4
fractions 20-29 = combined fraction GC6.5
fractions 30-31 = combined fraction GC6.6
fractions 32-40 = combined fraction GC6.7

Fraction GC6.5 (371 mg) was separated on a column using silica gel 60 (No.9385) as the adsorbent with chloroform as the eluant. Thirty fractions, approximately of 10 ml, were collected. The eluates were examined by TLC using methanol : chloroform (1:100) as the developing solvent. Fractions with the same chromatographic pattern were combined to yield 7 fractions as shown below.

fractions 1 = combined fraction GC6.5.1
fractions 2-8 = combined fraction GC6.5.2
fractions 9-11 = combined fraction GC6.5.3
fractions 12-18 = combined fraction GC6.5.4
fractions 19-22 = combined fraction GC6.5.5
fractions 23-25 = combined fraction GC6.5.6
fractions 26-30 = combined fraction GC6.5.7

Fraction GC6.5.2 (106 mg) was isolated on a column using silica gel 60 (No.9385) as the adsorbent with chloroform as the eluant. Eighty fractions, approximately of 10 ml, were collected. The eluates were examined by TLC using methanol : chloroform (1:200) as the developing solvent. Fractions with the similar chromatographic pattern were combined to yield 13 fractions as shown below.

fractions 1-6 = combined fraction GC6.5.2.1
fractions 7-16 = combined fraction GC6.5.2.2
fractions 17-23 = combined fraction GC6.5.2.3
fractions 24 = combined fraction GC6.5.2.4
fractions 25-28 = combined fraction GC6.5.2.5
fractions 29-33 = combined fraction GC6.5.2.6
fractions 34-36 = combined fraction GC6.5.2.7
fractions 37-39 = combined fraction GC6.5.2.8
fractions 40-58 = combined fraction GC6.5.2.9

fractions 59-63 = combined fraction GC6.5.2.10
fractions 64-68 = combined fraction GC6.5.2.11
fractions 69-71 = combined fraction GC6.5.2.12
fractions 72-80 = combined fraction GC6.5.2.13

Fraction GC6.5.2.9 (35 mg) was separated by Medium Pressure Liquid Chromatography (MPLC) using LICHROPREP Si-60 pre-packed column as the adsorbent with methanol : chloroform (1:125) as the eluant. Seventy-five fractions, approximately of 5 ml, were collected. Eluates with similar chromatograhpic TLC pattern were combined to yield four fractions.

The TLC chromatogram of fractions 4-18 showed only one spot under UV light at 254 and 365, Rf 0.4 [Silica gel 60 F_{254} (No.9385), methanol : chloroform (1:100)]. Evaporation of this fraction under reduced pressure gave 5 mg of compound j6-1 as yellow powder. The yield was 1.4×10^{-4} % based on dried weight of the branches.

3.2.2.2 Isolation of Compound j7-1

Fraction GC5 (1.0 g) was fractionated by gel filtration, using a column of Sephadex LH 20 as the adsorbent with methanol as the eluant. Seventy-five fractions approximately of 30 ml were collected and examined by TLC using methanol : chloroform (1:100) as the developing solvent. Fractions showing the similar chromatographic pattern were combined to yield 20 fractions as shown below.

fractions 1-2 = combined fraction GC5.1
fractions 3-7 = combined fraction GC5.2
fractions 8-11 = combined fraction GC5.3
fractions 12-15 = combined fraction GC5.4
fractions 16-17 = combined fraction GC5.5

fractions 18-20 = combined fraction GC5.6
fractions 21-24 = combined fraction GC5.7
fractions 25 = combined fraction GC5.8
fractions 26-28 = combined fraction GC5.9
fractions 29-31 = combined fraction GC5.10
fractions 32-36 = combined fraction GC5.11
fractions 37-40 = combined fraction GC5.12
fractions 41-45 = combined fraction GC5.13
fractions 46-49 = combined fraction GC5.14
fractions 50-55 = combined fraction GC5.15
fractions 56-59 = combined fraction GC5.16
fractions 60-62 = combined fraction GC5.17
fractions 63-64 = combined fraction GC5.18
fractions 65-67 = combined fraction GC5.19
fractions 68-75 = combined fraction GC5.20

Fraction GC5.12 (57 mg) was isolated on a column using silica gel 60 (No.9385) as the adsorbent with chloroform as the eluant. Thirty fractions, approximately of 10 ml, were collected. The eluates were examined by TLC using methanol : chloroform (1:200) as the developing solvent. The same chromatographic TLC pattern of fractions was combined to yield 6 fractions as shown below.

fractions 1-4 = combined fraction GC5.12.1
fractions 5-7 = combined fraction GC5.12.2
fractions 8-11 = combined fraction GC5.12.3
fractions 12-16 = combined fraction GC5.12.4
fractions 17-20 = combined fraction GC5.12.5
fractions 21-30 = combined fraction GC5.12.6

Fraction GC5.12.3 (6 mg) was isolated using preparative TLC [pre-coated silica gel 60 F_{254} (2 mm, 10x10 cm) plates] with triple development in chloroform. It gave 4 mg of compound j7-1 as orange powder. The yield was $1.1x10^{-4}$ % based on dried weight of the branches. It was later identified as 5-hydroxynoracronycine [**61**].

4. Physical and Spectra data of Isolated Compounds

4.1 Compound j1-2

Compound j1-2 was obtained as colorless needles (6 mg). It was soluble in chloroform.

Melting Point : 118-136°C

EIMS : ***m/z* (%relative intensity); Figure 3**

414 (M^+, 16), 412 (M^+, 14), 396 (8), 351 (8), 329 (5), 300 (16), 273 (11), 255 (25), 231 (9), 213 (16), 159 (24), 145 (26), 133 (24), 119 (22), 105 (30), 95 (33), 81 (54), 69 (51), 55 (100)

IR : **ν_{max} cm^{-1}, KBr disc; Figure 4**

3449 (br), 2932, 1655, 1562, 1543, 1508, 1457

^{13}C NMR : **δ ppm, 125 MHz, in CDCl3; Figure 6**

11.85 (C-18), 11.97 (C-29″), 12.03 (C-18″), 12.25 (C-29), 18.77 (C-21), 18.97 (C-27″), 19.01 (C-27), 19.39 (C-19 and C-19″), 19.81 (C-26), 21.07 (C-11, C-11″ and C-21″), 21.20 (C-26″), 23.04 (C-28), 24.29 (C-15), 24.35 (C-15″), 25.40 (C-28″), 26.04 (C-23), 28.24 (C-16), 28.91 (C-16″), 29.12 (C-25), 31.65 (C-2 and C-2″), 31.88 (C-7, C-7″, C-8, C-8″ and C-25″), 33.92 (C-22), 36.14 (C-20), 36.49 (C-10 and C-10″), 37.24 (C-1 and C-1″), 39.66 (C-12″), 39.76 (C-12), 40.49 (C-20″), 42.20 (C-4″), 42.29 (C-13, C-13″ and C-4), 45.81 (C-24), 50.11 (C-9 and C-9″), 51.22 (C-24″), 55.93 (C-17), 56.03 (C-17″), 56.75 (C-14), 56.85 (C-14″), 71.80 (C-3 and C-3″), 121.71 (C-6 and C-6″), 129.25 (C-23″), 138.31 (C-22″) and 140.74 (C-5 and C-5″).

4.2 Compound j2-1

Compound j2-1 was obtained as orange powder (32 mg). It was soluble in chloroform.

Melting Point : 191-193°C

EIMS : ***m/z* (%relative intensity); Figure 7**

393 (M^+, 100), 378 (18), 350 (38), 338 (50), 322(69), 294 (37), 282 (46)

UV : **λ_{max} nm, in chloroform; Figure 8**

273, 324, 336, 408

IR : **ν_{max} cm^{-1}, KBr disc; Figure 9**

3463 (br), 2928, 1654, 1560, 1542, 1509, 1459

^{1}H NMR : **δ ppm, 500 MHz, in $CDCl_3$; Figures 10-11**

1.75 (3H, s, H-5″), 1.80 (3H, s, H-5′), 1.84 (3H, s, H-4″), 1.86 (3H, s, H-4′), 3.48 (2H, d, *J*=7 Hz, H-1″), 3.55 (5H, s, H_2-1′ and H_3-N-Me), 5.30 (2H, tt, *J*=6, 1.5 Hz, H-2″), 5.35 (2H, tt, *J*=6, 1.5 Hz, H-2′), 5.56 (1H, br s, 5-OH), 6.41 (1H, s, 3-OH), 7.12 (1H, dd, *J*=8, 1.5 Hz, H-6), 7.16 (1H, t, *J*=8 Hz, H-7), 7.90 (1H, dd, *J*=8, 1.5 Hz, H-8) and 14.23 (1H, s, 1-OH).

^{13}C NMR : **δ ppm, 125 MHz, in $CDCl_3$; Figure 12**

17.72 (C-5″), 17.96 (C-5′), 21.48 (C-1″), 25.63 (C-4′ and C-4″), 26.70 (C-1′), 48.16 (N-Me), 106.34 (C-2), 107.33 (C-4), 108.61 (C-9a), 116.43 (C-8), 119.17 (C-7), 121.88 (C-2″), 122.58 (C-2′), 122.72 (C-6), 124.90 (C-8a), 133.85 (C-3″), 135.10 (C-3′), 137.97 (C-10a), 148.07 (C-4a), 149.08 (C-5OH), 159.16 (C-1OH), 161.39 (C-3OH) and 182.80 (C-9)

4.3 Compound j2-2

Compound j2-2 was obtained as orange powder (31 mg). It was soluble in chloroform.

Melting Point : 189-191°C

EIMS : ***m/z* (%relative intensity); Figure 14**

391 (M^+, 100), 377 (32), 376 (81), 348 (56), 322 (27), 318 (17)

UV : **λ_{max} nm, in chloroform; Figure 15**

308, 416

IR : **ν_{max} cm^{-1}, KBr disc; Figure 16**

3448 (br), 1654, 1561, 1540, 1508. 1458

^{1}H NMR : **δ ppm, 500 MHz, in $CDCl_3$; Figure 17**

1.52 (6H, br s, H_3-4′ and H_3-5′), 1.73 (3H, s, H-5″), 1.80 (3H, s, H-4″), 3.48 (2H, d, *J*=6, H-1″), 3.57 (3H, s, N-Me), 5.29 (2H, tt, *J*=6, 1.5 Hz, H-2″), 5.58 (1H, d, *J*=10, H-2′), 5.72 (1H, br s, 5-OH), 6.77 (1H, d, *J*=10, H-1′), 7.11 (1H, dd, *J*=8, 1.5 Hz, H-6), 7.16 (1H, t, *J*=8 Hz, H-7), 7.87 (1H, dd, *J*=8, 1.5 Hz, H-8) and 14.27 (1H, s, 1-OH).

^{13}C NMR : **δ ppm, 125 MHz, in $CDCl_3$; Figures 18-19**

18.14 (C-5″), 25.73 (C-4″), 25.83 (C-1″), 28.38 (C-4′), 30.97 (C-5′), 47.74 (N-Me), 77.89 (C-3′), 104.11 (C-2), 107.52 (C-4), 109.18 (C-9a), 116.05 (C-8), 118.00 (C-7), 119.89 (C-2″), 123.18 (C-1′), 123.79 (C-6), 125.53 (C-8a), 126.94 (C-2′), 131.37 (C-3″), 138.15 (C-10a), 146.89 (C-4a), 150.22 (C-5OH), 157.14 (C-1OH), 159.08 (C-3) and 182.90 (C-9).

4.4 Compound j7-1

Compound j7-1 was obtained as orange powder (4 mg). It was soluble in chloroform.

Melting Point : 250-252°C

EIMS : ***m/z* (%relative intensity); Figure 21**

323 (M^+, 43), 308 (100), 294 (12), 293 (60), 280 (7), 268 (3)

UV : **λ_{max} nm, in chloroform; Figure 22**

297, 308, 413

IR : **ν_{max} cm^{-1}, KBr disc; Figure 23**

3447 (br), 2919, 1654, 1638, 1558, 1541, 1505, 1460

^{1}H NMR : **δ ppm, 500 MHz, in $CDCl_3$; Figure 24**

1.52 (6H, br s, H_3-4′ and H_3-5′), 1.73 (3H, s, H-5″), 1.80 (3H, s, H-4″), 3.48 (2H, d, *J*=6, H-1″), 3.57 (3H, s, N-Me), 5.29 (2H, tt, *J*=6, 1.5 Hz, H-2″), 5.58 (1H, d, *J*=10, H-2′), 5.72 (1H, br s, 5-OH), 6.77 (1H, d, *J*=10, H-1′), 7.11 (1H, dd, *J*=8, 1.5 Hz, H-6), 7.16 (1H, t, *J*=8 Hz, H-7), 7.87 (1H, dd, *J*=8, 1.5 Hz, H-8) and 14.27 (1H, s, 1-OH).

^{13}C NMR : **δ ppm, 125 MHz, in $CDCl_3$; Figures 25-26**

18.14 (C-5″), 25.73 (C-4″), 25.83 (C-1″), 28.38 (C-4′), 30.97 (C-5′), 47.74 (N-Me), 77.89 (C-3′), 104.11 (C-2), 107.52 (C-4), 109.18 (C-9a), 116.05 (C-8), 118.00 (C-7), 119.89 (C-2″), 123.18 (C-1′), 123.79 (C-6), 125.53 (C-8a), 126.94 (C-2′), 131.37 (C-3″), 138.15 (C-10a), 146.89 (C-4a), 150.22 (C-5OH), 157.14 (C-1OH), 159.08 (C-3) and 182.90 (C-9).

4.5 Compound j6-1

Compound j6-1 was obtained as yellow powder (5 mg). It was soluble in chloroform.

^{1}H NMR : **δ ppm, 500 MHz, in $CDCl_3$; Figure 27**

1.75 (3H, s), 1.78 (3H, s), 3.42 (2H, d, *J*=8 Hz), 3.78 (6H, d, *J*=5 Hz), 3.88 (3H, s), 3.96 (3H, s), 5.38 (1H, s), 6.38 (1H, s), 7.91 (1H, s), 14.22 (1H, s)

^{13}C NMR : **δ ppm, 125 MHz, in $CDCl_3$; Figures 28-29**

17.85, 25.87, 28.18, 45.46, 56.18, 60.34, 60.88, 94.11, 105.84, 117.13, 121.23, 122.11, 124.52, 130.04, 133.66, 135.01, 139.75, 141.60, 153.02, 159.36, 160.54, 181.67

CHAPTER IV

RESULTS AND DISCUSSION

The dried branches of *Glycosmis parva* Craib (3.5 Kg) were extracted with 95% ethanol. The ethanol extract was partitioned with hexane and chloroform, respectively. The hexane extract was then separated using several chromatographic techniques to afford two pure compounds (j2-1 & j2-2) and a mixture of two steroids (j1-2). The chloroform extract, after repetitive chromatography yielded two compounds (j7-1 & j6-1).

The structure determinations of all the isolates were accomplished by interpretation of their MS, UV, IR and NMR data and then confirmed by comparison with literature values of previously related compounds.

1. Structure Determination of Isolated Compounds

1.1 Structure Determination of Isolate j1-2

Isolate j1-2 was obtained as colorless needles. A Libermann-Burchard test gave a positive green color, indicative of a steroidal skeleton. Two molecular ions at *m/z* 412 and 414 were observed in EIMS (Figure 3). The IR spectrum (Figure 4) exhibited absorption bands for a hydroxyl group at 3449 cm^{-1} and aromatic rings at 1457-1655 cm^{-1}. In the present investigation, isolate j1-2 was identified as a mixture of β-sitosterol [**145**] and stigmasterol [**156**] by comparison of its ^{1}H and ^{13}C-NMR data with reported values (Khalil and Idler, 1980; Iribarren and Pomilio, 1985; Heupel *et al.*, 1986 and Wright *et al.*, 1978).

In the ^{1}H-NMR spectrum (Figure 5), the signals at δ 4.99 (1H, dd, *J*=15.1, 8.7 Hz) and 5.13 (1H, dd, *J*=15.3, 8.9 Hz) were assigned to H-23 and H-22 of stigmasterol. The signals at δ 3.50 (2.2H, m) and 5.33 (2.2H, d, *J*=3.7 Hz) were assigned to H-3 and H-6 of both β-sitosterol and stigmasterol respectively. The integration steps of H-3, H-6, H-22, H-23 were approximately in the ratios of 2.2 : 1. Therefore, it could be deduced that the ratio of β-sitosterol and stigmasterol in j1-2 was approximately in 1.2 : 1.

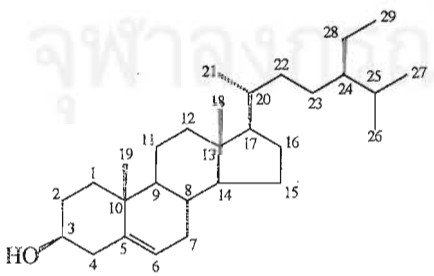
The ^{13}C-NMR spectrum (Figure 6) of compound j1-2 displayed forty-six signals. Comparison of these data with reported ^{13}C-NMR values of β-sitosterol and stigmasterol (Wright *et al.*, 1978) is shown in Table 6.

Table 6 ^{13}C-NMR spectral data of β-sitosterol, stigmasterol and isolate j1-2 (in $CDCl_3$)

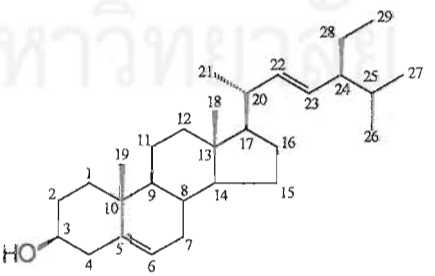
Carbon	Chemical shift (ppm)		
	β-sitosterol	Stigmasterol	Isolate j1-2
1	37.31	37.31	37.24
2	31.57	31.67	31.65
3	71.69	71.81	71.80
4	42.45	42.35	42.29, 42.20
5	140.76	140.80	140.74
6	121.59	121.69	121.71
7	31.92	31.94	31.88
8	31.92	31.94	31.88
9	50.17	50.20	50.11
10	36.51	36.56	36.49
11	21.11	21.11	21.07
12	39.81	39.74	39.76, 39.66
13	42.33	42.35	42.29

Table 6 ^{13}C-NMR spectral data of β-sitosterol, stigmasterol and isolate j1-2 (in $CDCl_3$) (Continued)

Carbon	Chemical shift (ppm)		
	β-sitosterol	Stigmasterol	Isolate j1-2
14	56.79	56.91	56.75, 56.85
15	24.32	24.39	24.29, 24.35
16	28.26	28.96	28.24, 28.91
17	56.11	56.06	55.93, 56.03
18	11.87	12.07	11.85, 12.03
19	19.40	19.42	19.39
20	36.17	40.54	36.14, 40.49
21	18.82	21.11	18.77, 21.07
22	33.95	138.37	33.92, 138.31
23	26.13	129.32	26.04, 129.25
24	45.85	51.29	45.81, 51.22
25	29.18	31.94	29.12, 31.88
26	19.84	21.26	19.81, 21.20
27	19.04	19.02	19.01, 18.97
28	23.09	25.44	23.04, 25.40
29	12.32	12.27	12.25, 11.97



β-Sitosterol [145]



Stigmasterol [156]

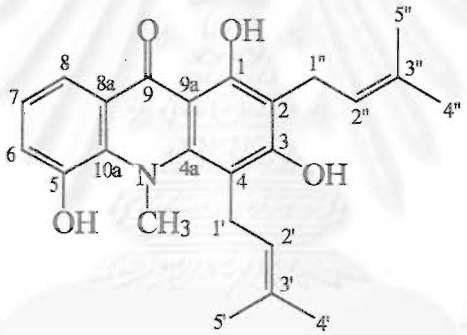
1.2 Structure Determination of Compound j2-1

Compound j2-1 was obtained as an orange powder. It showed UV absorption maxima at 273, 324, 336 and 408 nm (Figure 8). The IR specturm (Figure 9) exhibited a hydroxyl group at 3463, an aromatic ring at 1459-1654 cm^{-1}. The EIMS of compound j2-1 (Figure 7) revealed a molecular ion peak at *m/z* 393, corresponding to the molecular formula $C_{24}H_{27}NO_4$.

Compound j2-1 was identified as *N*-methylataphilline [**75**] by analyses of ^1H and ^{13}C-NMR data with previously published ^1H-NMR in $CDCl_3$ (Wu, Kuoh and Furukawa, 1982) and ^{13}C-NMR in DMSO-d_6 (Banerji *et al.*, 1981) values. Comparison of these data with reported ^1H and ^{13}C-NMR values of *N*-methylataphilline [**75**] is shown in Table 7.

The ^1H-NMR spectrum in $CDCl_3$ (Figure 10) showed three singlets at δ 14.23, 6.41 and 5.56 (broad). These signals disappeared on CD_3OD (Figure 11), indicating the presence of three phenolic hydroxyl groups in compound j2-1. Probably one of them (at δ 14.23) was characteristically H-bonded with 9-carbonyl moiety. In the aromatic proton region, three protons signals (ABX-pattern) at δ 7.90 (dd, *J*=8, 1.5 Hz), 7.16 (t, *J*=8 Hz) and 7.12 (dd, *J*=8, 1.5 Hz) could be assigned to H-8, H-7 and H-6 respectively, according to their coupling constants. The presence of two similar prenyl moieties in positions 2 and 4 was indicated as shown in table 7 (H-1′ to H-5′ and H-1″ to H-5″). The signal at δ 3.55 (3H, singlet) was assigned to an *N*-methyl group.

In the ^{13}C-NMR ($CDCl_3$+CD_3OD) spectrum (Figure 12), j2-1 exhibited twenty-four signals representing one carbonyl group, five methyl groups, two methylene carbons, five methine carbons and eleven quaternary carbons. A characteristic carbonyl carbon of 9-acridone compound appeared at δ 182.80 (C-9). *N*-methyl carbon signal was observed at δ 48.16. This downfield chemical shift is an characteristic of *N*-methyl carbon having substituents at both peri-positions (C-4 & C-5) in 9-acridone nucleus. According to the steric effects (or γ-effect), the downfield signal at δ 25.63 could be assigned to C-4′ and C-4″ (*trans* positions). The signals at δ 17.96 and 17.72 could be assigned to C-5″ and C-5′ position, respectively.



N-methylataphilline [75]

Table 7 ^{1}H-NMR spectral data of compound J2-1 (in $CDCl_3$+CD_3OD) and *N*-Methylataphilline [75]

Position	*N*-Methylataphilline		Compound J2-1	
	δ_H (ppm) (multiplicity, *J* in Hz)	δ_C (ppm)	δ_H (ppm) (multiplicity, *J* in Hz)	δ_C (ppm)
1	-	159.1	-	159.16
2	-	106.6	-	106.34
3	-	161.4	-	161.39
4	-	108.3	-	107.33
4a	-	148.4	-	148.07
5	-	148.9	-	149.08
6	7.16 (m)	123.9	7.12 (1H, dd, 8, 1.5)	122.72
7	7.07 (t, 8)	119.7	7.16 (1H, t, 8)	119.17
8	7.78 (br, d)	115.5	7.90 (1H, dd, 8, 1.5)	116.43
8a	-	124.4	-	124.90
9	-	182.1	-	182.80
9a	-	109.7	-	108.61
10a	-	138.0	-	137.97
N-CH_3	3.61 (3H, s)	47.8	3.55 (3H, s)	48.16
1′	3.48 (m)	26.3	3.55 (2H, s)	26.70
2′	5.36 (m)	123.0	5.35 (2H, tt, 6, 1.5)	122.58
3′	-	131.2	-	135.10
4′	1.82 (6H)	25.6	1.86[a] (3H, s)	25.63[d]
5′		18.0	1.80[a] (3H, s)	17.96
1″	3.48 (2H, m)	21.5	3.48 (2H, d, 7)	21.48
2″	5.28 (m)	122.9	5.30 (2H, tt, 6, 1.5)	121.88
3″	-	130.7	-	133.85
4″	1.72[b] (3H)	25.6	1.84[c] (3H, s)	25.63[d]
5″	1.77[b] (3H)	18.0	1.75[c] (3H, s)	17.72
1-OH	14.43 (1H, s)	-	14.23 (1H, s)	-
3-OH	#	-	6.41 (1H, s)	-
5-OH	#	-	5.56 (1H, br s)	-

a, b, c, d : Interchangable within the same column

\# : No reported data

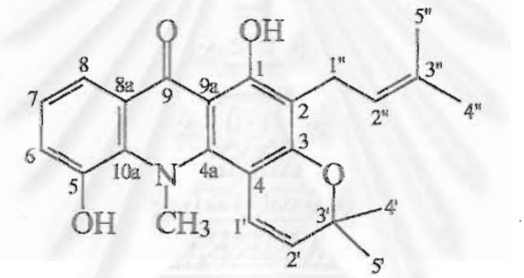
1.3 Structure Determination of Compound j2-2

Compound j2-2, an orange powder, showed UV absorptions at 308 and 416 nm (Figure 15). The IR spectrum (Figure 16) exhibited absorption bands for a hydroxyl group at 3448 and aromatic ring at 1458-1654 cm^{-1}. Its EIMS (Figure 14) revealed a molecular ion at *m/z* 391, consistent with the molecular formula $C_{24}H_{25}NO_4$.

Comparison of its ^1H and ^{13}C-NMR spectral data (Table 8) with previously published ^1H-NMR in $CDCl_3$+10%$(CD_3)_2SO$ (Kuoh and Furukawa, 1982) and ^{13}C-NMR in acetone-d_6 (Banerji *et al.*, 1981) suggested that compound j2-2 was identical with 5-hydroxy-*N*-methylseverifoline [**69**].

The ^1H-NMR data (Figure 16) for compound j2-2 showed two methylene protons (AB type) at δ 6.77 (d, *J*=10 Hz) and 5.58 (d, *J*=10 Hz), and a six-proton singlet at δ 1.52 reflect the presence of a dimethylchromen system. Similar to compound j2-1, j2-2 displayed aromatic proton signals (ABX-type) for H-8, H-7 and H-6 at δ 7.87 (dd, *J*=8, 1.5 Hz), 7.16 (t, *J*=8 Hz) and 7.11 (dd, *J*=8, 1.5 Hz) respectively. The presence of two one-proton singlets at δ 14.27 and 5.72 (broad) due to two hydroxyl protons of positions 1 & 5. The *N*-methyl proton signal appeared at δ 3.57. Other signals at δ 5.29 (tt, *J*=6, 1.5 Hz), 3.48 (2H, d, *J*=6 Hz), 1.80 (3H, s) and 1.73 (3H, s) could be assigned to prenyl moiety at position 2.

The ^{13}C-NMR (in $CDCl_3$) spectrum (Figure 17) and DEPT-135 spectra (Figure 18) suggested the presence of twenty-four signals representing one carbonyl group, five methyl groups, a methylene carbon, six methine carbons and eleven quarternary carbons. Similar to j2-1, compound j2-2 exhibited the characteristic carbonyl carbon of 9-acridone compound at δ 182.90 (C-9). Its *N*-methyl carbon signal was observed at δ 47.74.



5-Hydroxy-*N*-methylseverifoline [**69**]

Table 8 ^{1}H-NMR spectral data of compound J2-2 (in $CDCl_3$) and 5-Hydroxy-*N*-methylseverifoline [69]

Position	5-Hydroxy-*N*-methylseverifoline		Compound J2-2	
	δ_H (ppm) (multiplicity, *J* in Hz)	δ_C (ppm)	δ_H (ppm) (multiplicity, *J* in Hz)	δ_C (ppm)
1	-	159.7	-	157.14
2	-	102.2	-	104.11
3	-	163.2	-	159.08
4	-	106.7	-	107.52
4a	-	149.2	-	146.89
5	-	149.2	-	150.22
6	7.24 (dd, 8, 2)	123.2	7.11 (1H, dd, 8, 1.5)	123.79
7	7.12 (t, 8)	120.7	7.16 (1H, t, 8)	118.00
8	7.83 (dd, 8, 2)	117.2	7.87 (1H, dd, 8, 1.5)	116.05
8a	-	126.2	-	125.53
9	-	182.1	-	182.90
9a	-	110.2	-	109.18
10a	-	138.2	-	138.15
N-CH_3	3.80 (3H, s)	48.4	3.57 (3H, s)	47.74
1′	6.59 (d, 10)	123.2	6.77 (1, d, 10)	123.18
2′	5.59 (d, 10)	124.2	5.58 (1H, d, 10)	126.94
3′	-	77.0	-	77.89
4′	1.48 (6H)	27.2	1.52 (6H, s)	28.38[d]
5′		27.2		30.97[d]
1″	3.32 (2H, d, 7)	21.7	3.48 (2H, d, 6)	25.83
2″	5.24 (t, 7)	121.7	5.29 (2H, tt, 6, 1.5)	119.89
3″	-	130.7	-	131.37
4″	1.67[b] (3H)	25.4	1.73[c] (3H, s)	25.73
5″	1.81[b] (3H)	17.7	1.80[c] (3H, s)	18.14
1-OH	14.63 (1H, s)	-	14.27 (1H, s)	-
5-OH	#	-	5.72 (1H, br s)	-

a, b, c, d : Interchangable within the same column

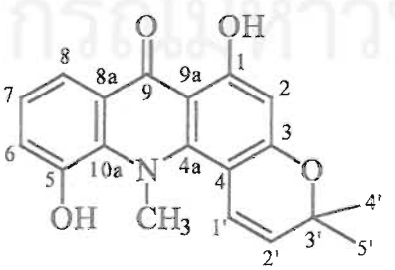
\# : No reported data

1.4 Structure Determination of Compound j7-1

Compound j7-1 was obtained as an orange powder. The UV spectrum showed maximal absorptions at 297, 308 and 413 nm. (Figure 22). It also exhibited IR bands (Figure 23) at 3447 (hydroxyl group) and 1460-1654 cm-1 (aromatic ring). The EIMS (Figure 21) revealed a molecular ion peak at *m/z* 323, corresponding to the molecular formula $C_{19}H_{17}NO_4$.

The ^{1}H-NMR (in $CDCl_3$) spectrum (Figure 24) of compound j7-1 exhibited nine proton signals in the olefinic and aromatic proton regions. Two methylene protons (AB type) at δ 6.79 (d, *J*=10 Hz) and 5.58 (d, *J*=10 Hz) with a six-proton singlet at δ 1.49 reflected the presence of a dimethylchromen system. Three proton signals (ABX-type) at δ 8.04 (dd, *J*=8, 1.5 Hz), 7.12 (t, *J*=8 Hz) and 7.07 (dd, *J*=8, 1.5 Hz) for H-8, H-7 and H-6 also showed the same splitting pattern as compound j2-2. Furthermore the presence of a proton signal at δ 14.87 showed the characteristic phenolic hydroxyl group of position 1.

By comparing the above spectral information with reported ^{1}H-NMR data (Fraser *et al*, 1973), compound j7-1 was identified as 5-hydroxynoracronycine [**61**] (Table 9). Its ^{13}C-NMR data, it was tentatively assigned and presented here. Since no previous work has been reported, it needs more 2D-NMR experiments to confirm the exact ^{13}C-NMR assignment.



5-Hydroxynoracronycine [**61**]

Table 9 NMR spectral data of compound J7-1 (in $CDCl_3$) and [61]

Position	5-Hydroxy-noracronycine	Compound J7-1	
	δ_H (ppm) (multiplicity, *J* in Hz)	δ_H (ppm) (multiplicity, *J* in Hz)	δ_C (ppm)
1	-	-	159.26
2	6.11 (s)	6.29 (1H, s)	92.03
3	-	-	160.15
4	-	-	102.55
4a	-	-	144.91
5	-	-	146.89
6	7.22-7.32 (m)	7.07 (1H, dd, 8, 1.5)	122.00
7		7.12 (1H, t, 8)	118.89
8	7.78 (dd)	8.04 (1H, dd, 8, 1.5)	115.92
8a	-	-	124.17
9	-	-	180.57
9a	-	-	105.38
10a	-	-	133.55
N-CH_3	3.83 (s)	4.01 (3H, s)	41.03
1′	6.72 (d)	6.79 (1, d, 10)	120.17
2′	5.68 (d)	5.58 (1H, d, 10)	126.75
3′	-	-	77.95
4′	1.49 (s)	1.49 (6H, s)	28.43
5′			30.95
1-OH	14.20 (s)	14.87 (1H, s)	-

a, b, c, d : Interchangable within the same column

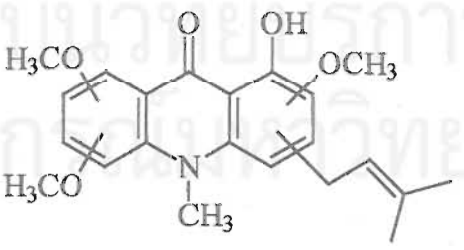
\# : No reported data

1.5 Structure Determination of Compound j6-1

Compound j6-1 was obtained as a yellow powder. The ^{1}H-NMR spectrum (Figure 27) recorded in $CDCl_3$ indicated the presence of a phenolic hydroxyl group at δ 14.22 (1H, s) which was chelated with carbonyl moiety. In the aromatic proton region, it showed two proton singlets at δ 7.91 (1H, s) and 6.38 (1H, s). Three signals at δ 3.78 (6H, d), 3.88 (3H, s) and 3.96 (3H, s) probably assigned to three methoxy groups with a *N*-methyl group. Other signals appeared at δ 5.38 (s), 3.42 (2H, d, *J*=8 Hz), 1.75 (3H, s) and 1.78 (3H, s) which could be assigned to a prenyl moiety, similar to compounds j2-1 and j2-2.

The ^{13}C-NMR in $CDCl_3$ spectrum (Figure 28) and DEPT-135 spectrum (Figure 29) suggested the presence of twenty-two signals representing one carbonyl group (at δ 181.67), six methyl groups, a methylene carbon, four methine carbons and ten quarternary carbon.

From the information above, several possible structures can be proposed for compound j6-1. It might be a new compound in this acridone alkaloid group; however, more data from 2D-NMR experiments are needed to establish its structure.



CHAPTER V

CONCLUSION

The investigation of the hexane extract of *Glycosmis parva* Craib led to the isolation of two acridone alkaloids, namely *N*-methylataphilline [**75**] and 5-hydroxy-*N*-methylseverifoline [**69**]. Additionally, the presence of two steroids *viz* β–sitosterol [**145**] and stigmasterol [**156**] were revealed. While, the separation of the chloroform extract of *Glycosmis parva* Craib yielded two pure compounds, j7-1 and j6-1. Compound j7-1 was deduced to 5-hydroxynoracronycine [**61**]. It needs more 2D-NMR information to reveal the explicit ^{13}C-NMR assignment. Moreover, compound j6-1 might be a new acridone, but more information from the 2D-NMR experiment is needed before any conclusion can be drawn.

With regard to the biological activities experiment data, no previous work of *N*-methylataphilline [**75**] has been reported. Whereas, 5-hydroxy-*N*-methylseverifoline [**69**] showed potent antiproliferative activity against tumor cell lines (Kawaii *et al.*, 1999a & 1999b). It also exhibited potent antimalarial activity with more than 90% suppression of the growth of *Plasmodium yoelii*, which causes malaria in rodents (Fujioka *et al.*, 1989). Meanwhile, 5-hydroxynoracronycine [**61**] also showed antimalarial acitivity by suppressing more than 80% of *Plasmodium yoelii* growth (Fujioka *et al.*, 1989).

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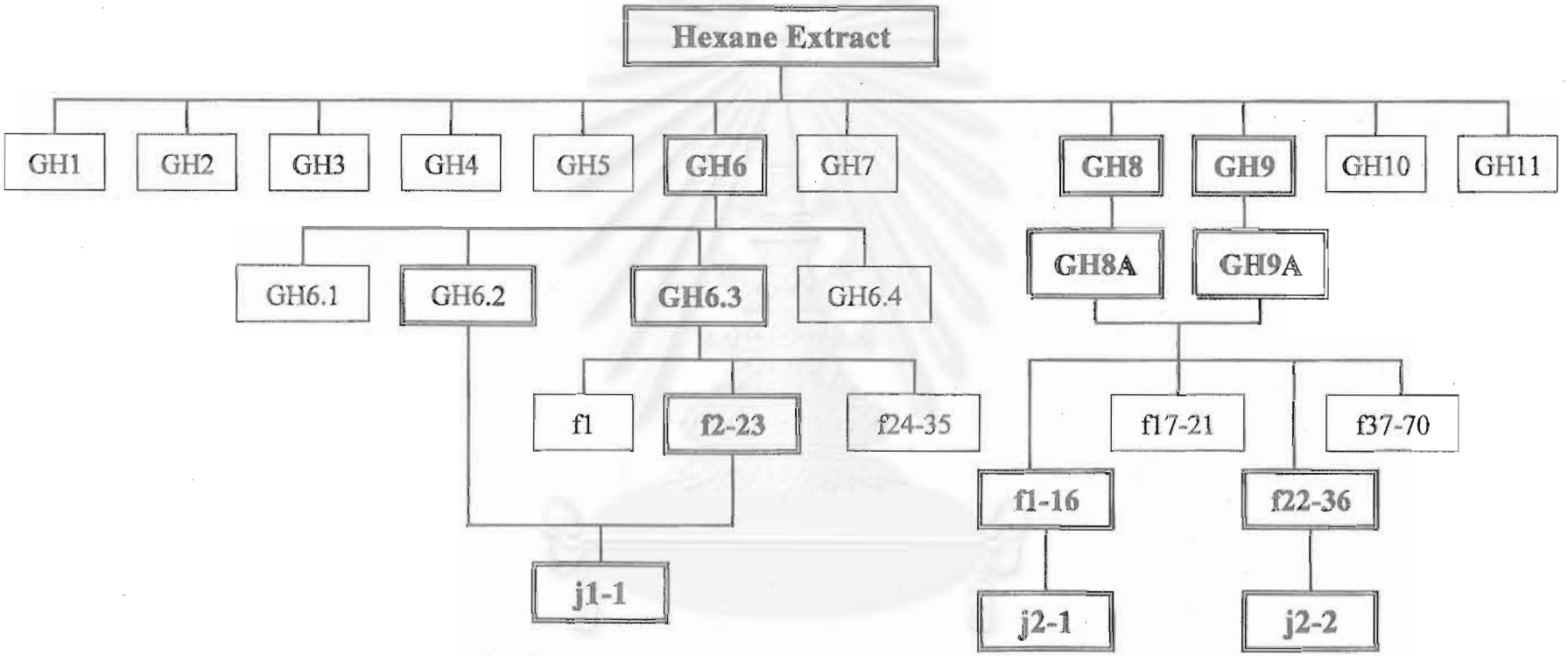
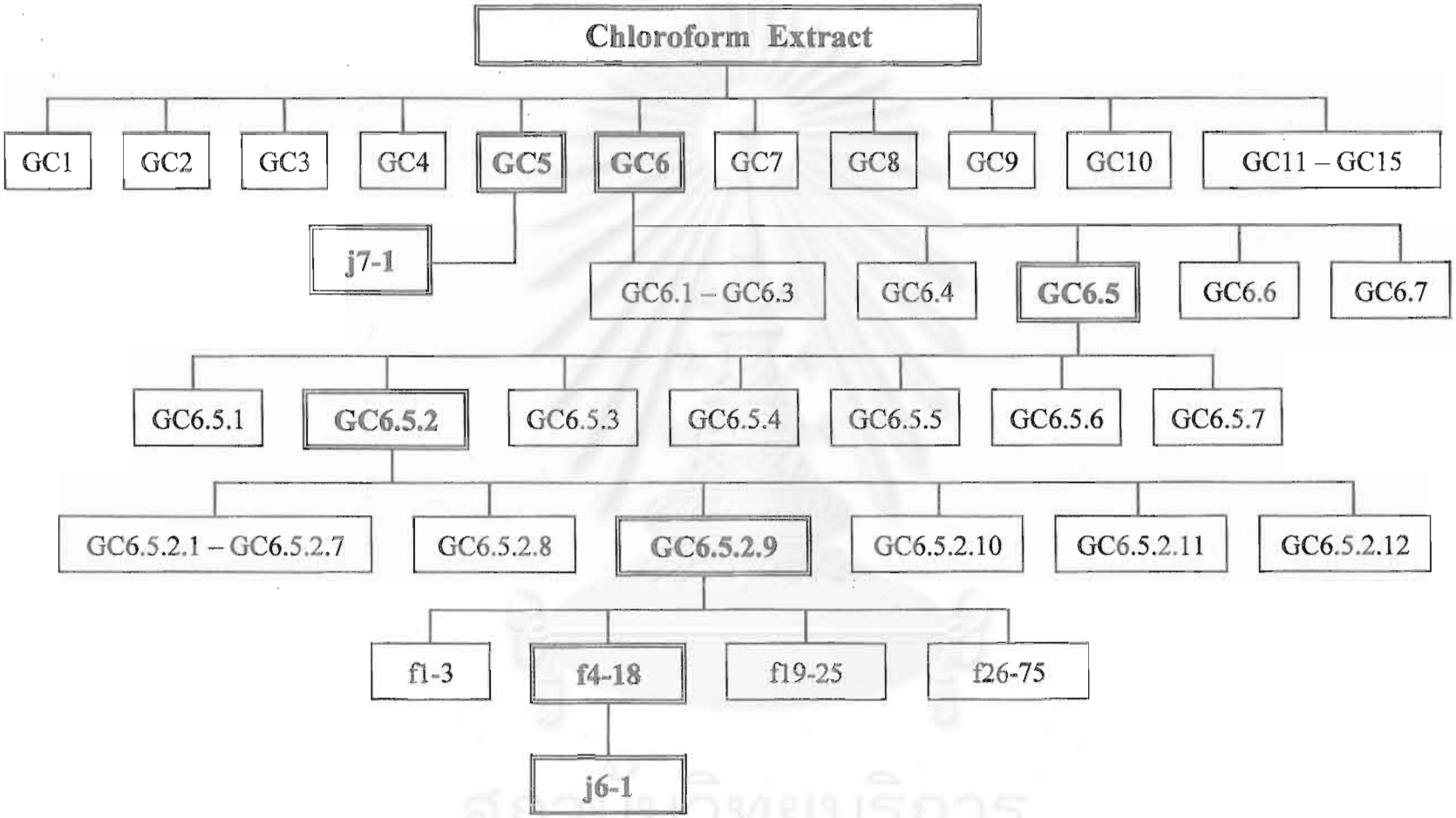
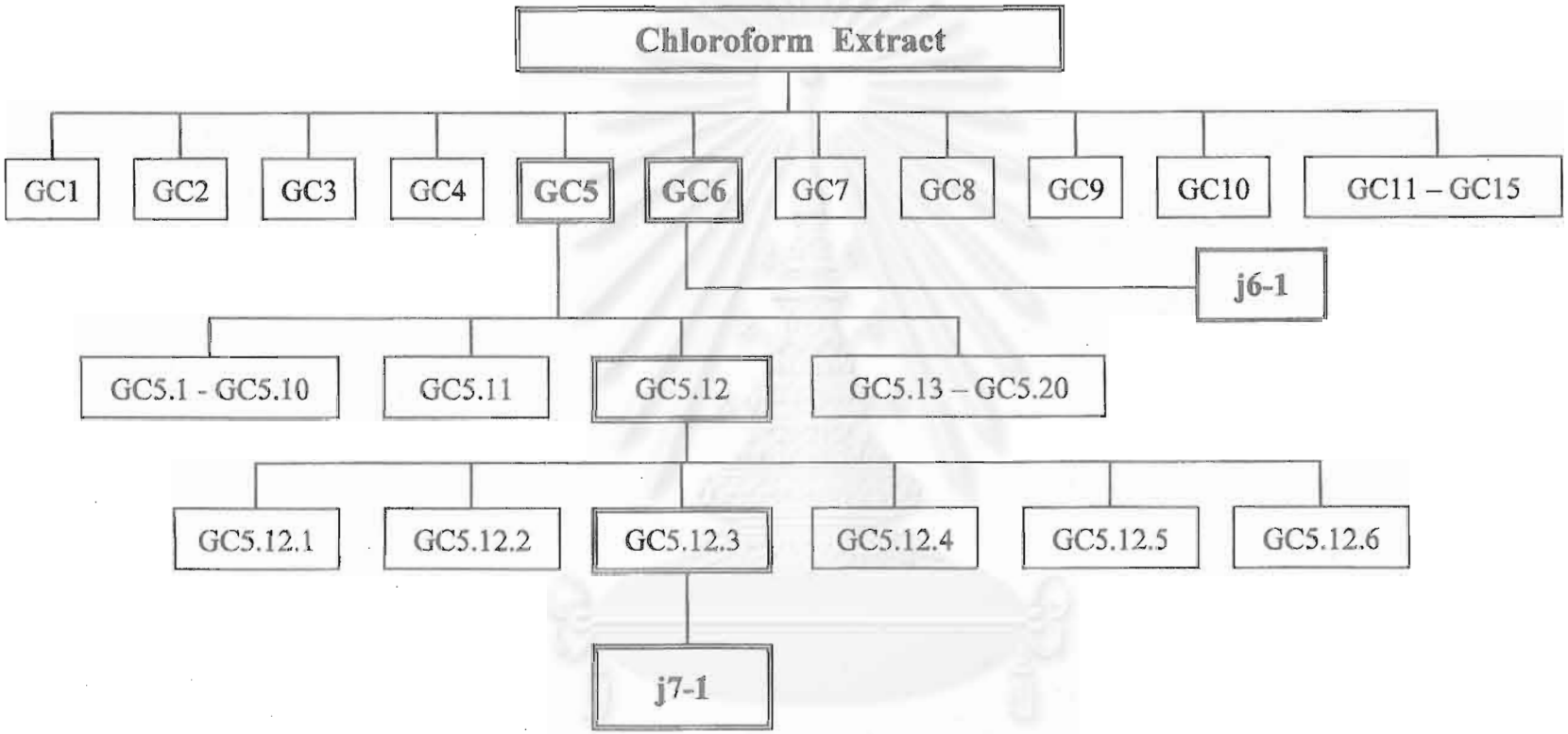
APPENDIX



Scheme 1 Isolation of isolates j1-2, j2-1 and j2-2 from hexane extract of *Glycosmis parva* Craib



Scheme 2 Isolation of compound j6-1 from chloroform extract of *Glycosmis parva* Craib



Scheme 3 Isolation of compound j7-1 from chloroform extract of *Glycosmis parva* Craib

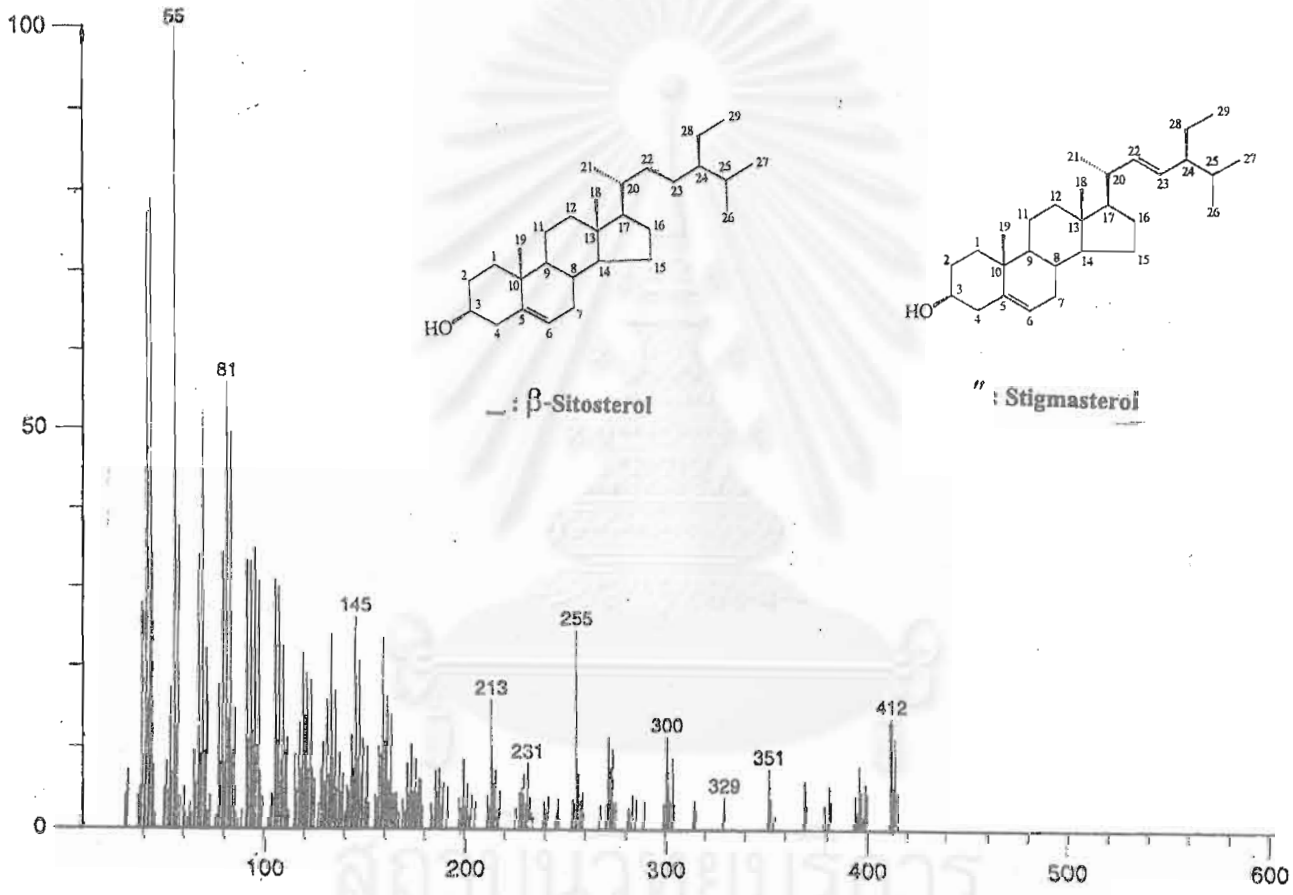
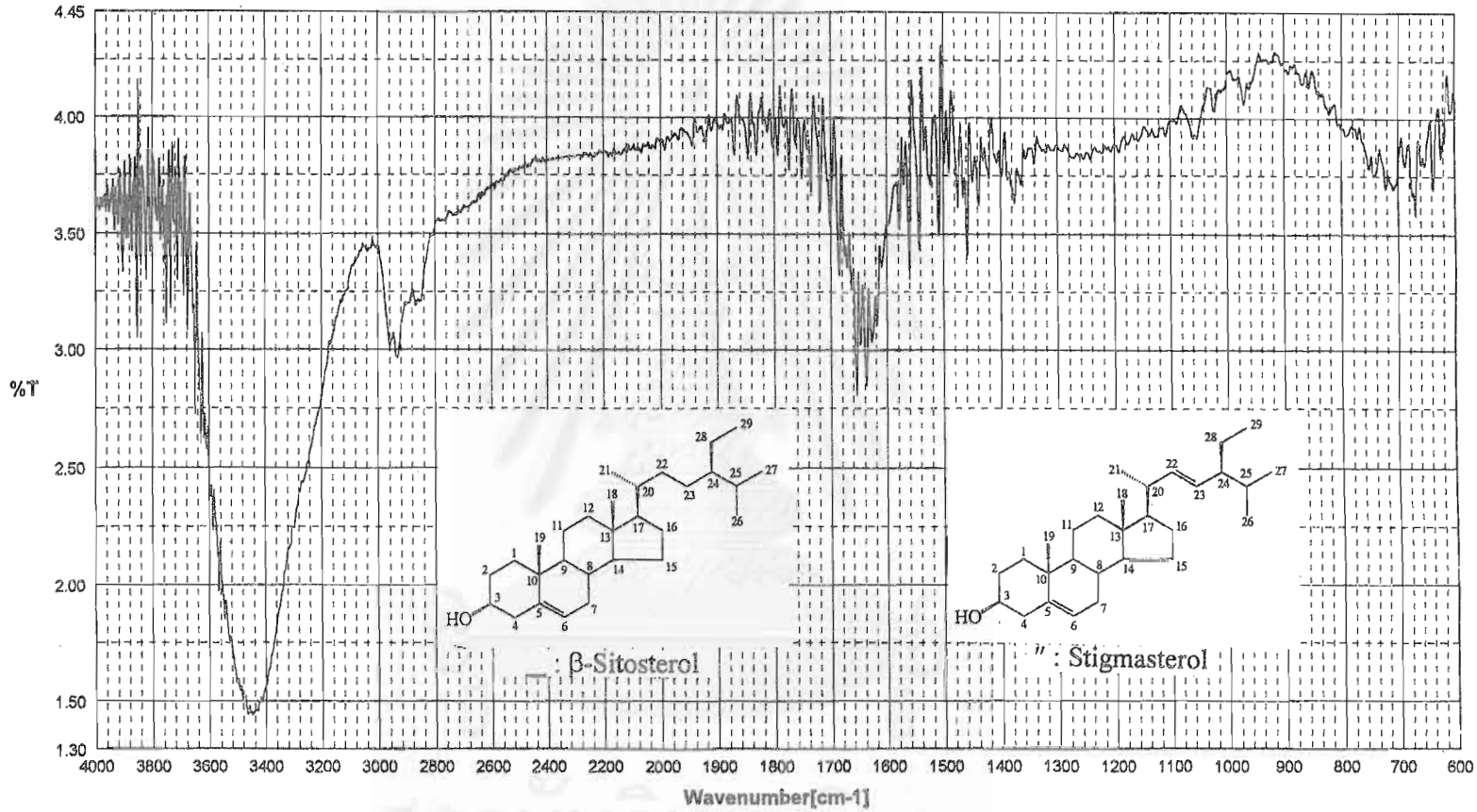


Figure 3 EI mass spectrum of isolated j1-2



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日付: 100/10/20 14:01

Figure 4 Infrared spectrum of isolated j1-2 (in KBr disc)

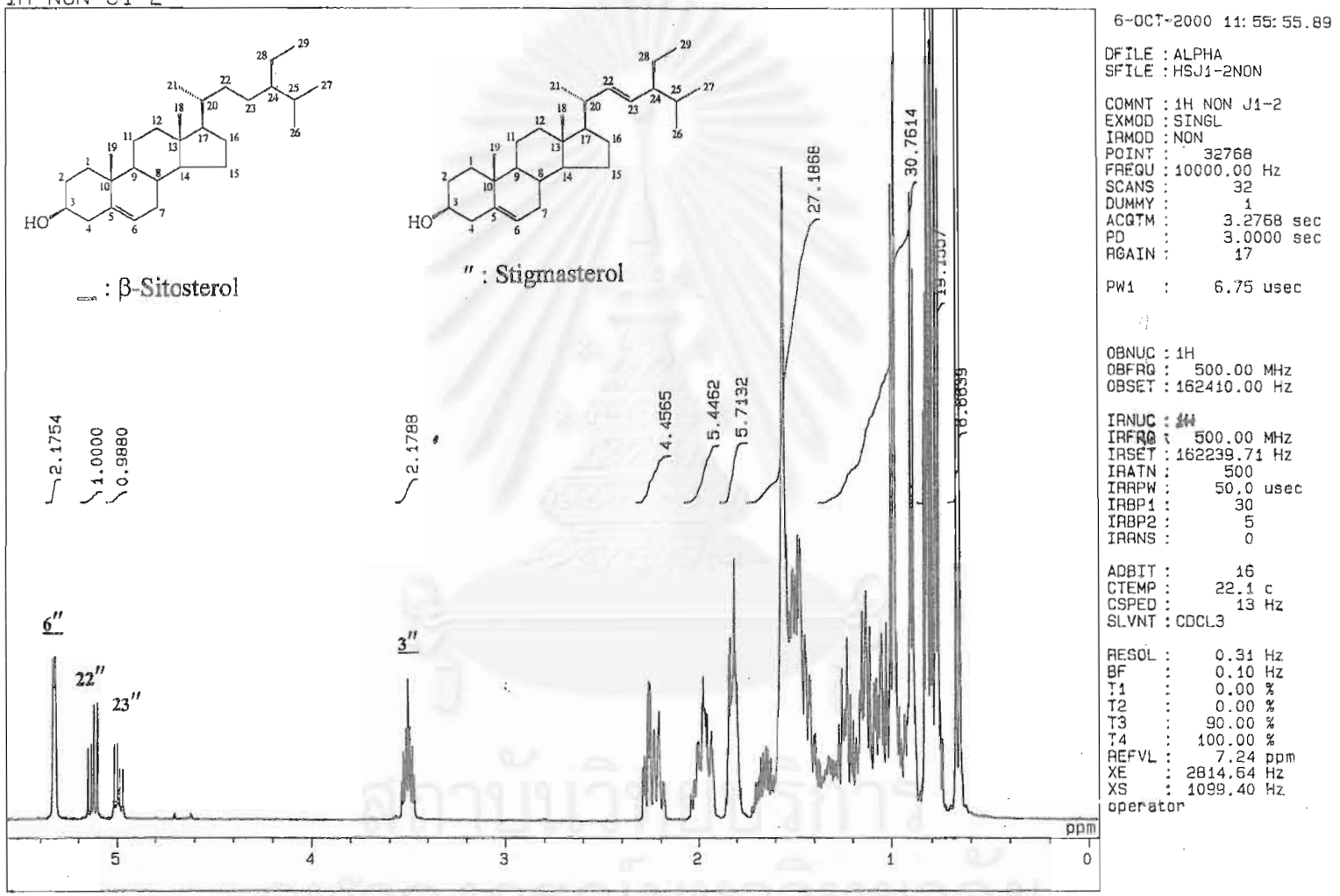


Figure 5a 500 MHz ^{1}H-NMR spectrum of isolated j1-2 (in $CDCl_3$)

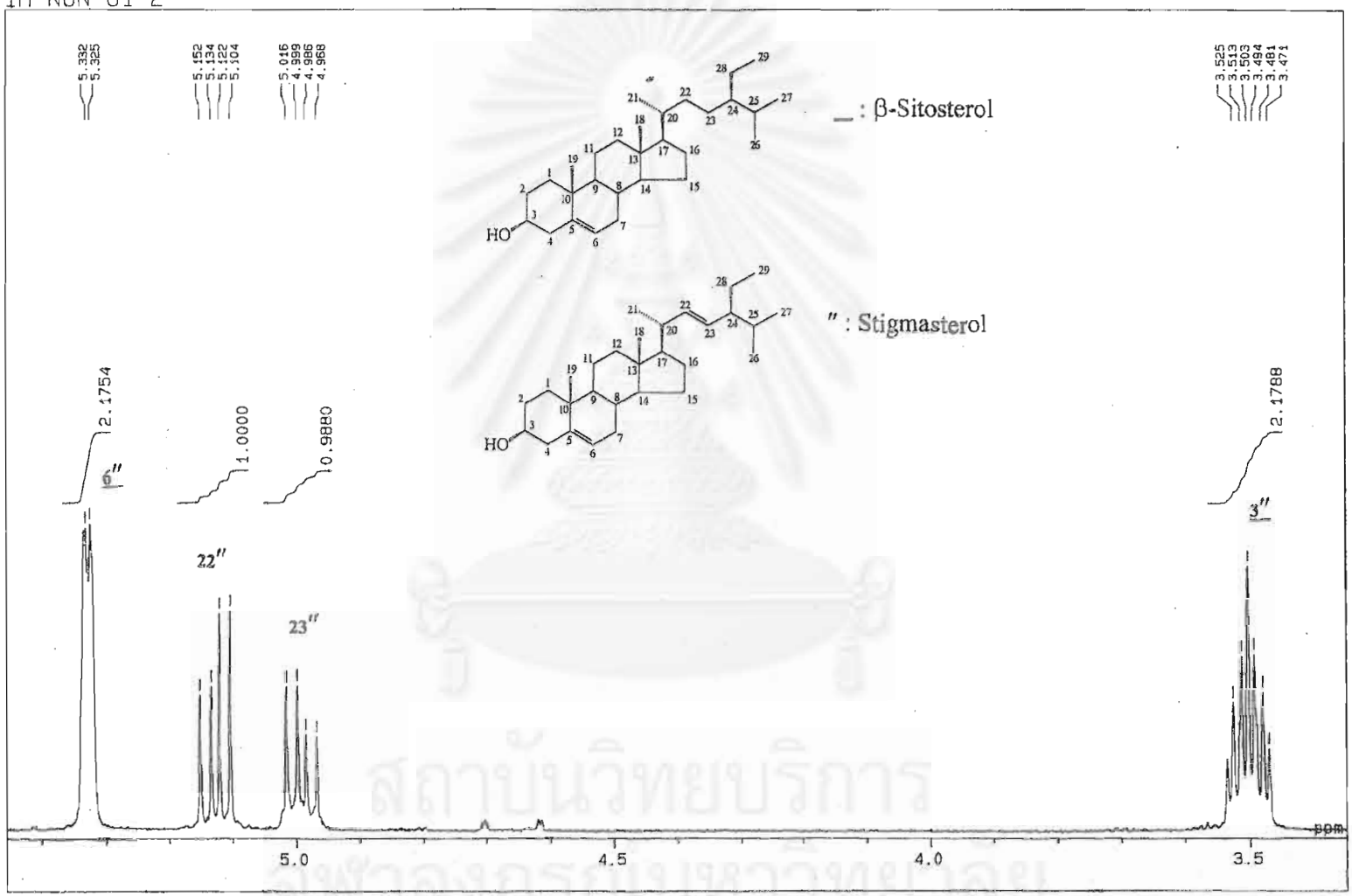


Figure 5b 500 MHz ^{1}H-NMR spectrum of isolated j1-2 (in $CDCl_3$) (expanded from 3.4 to 5.4 ppm)

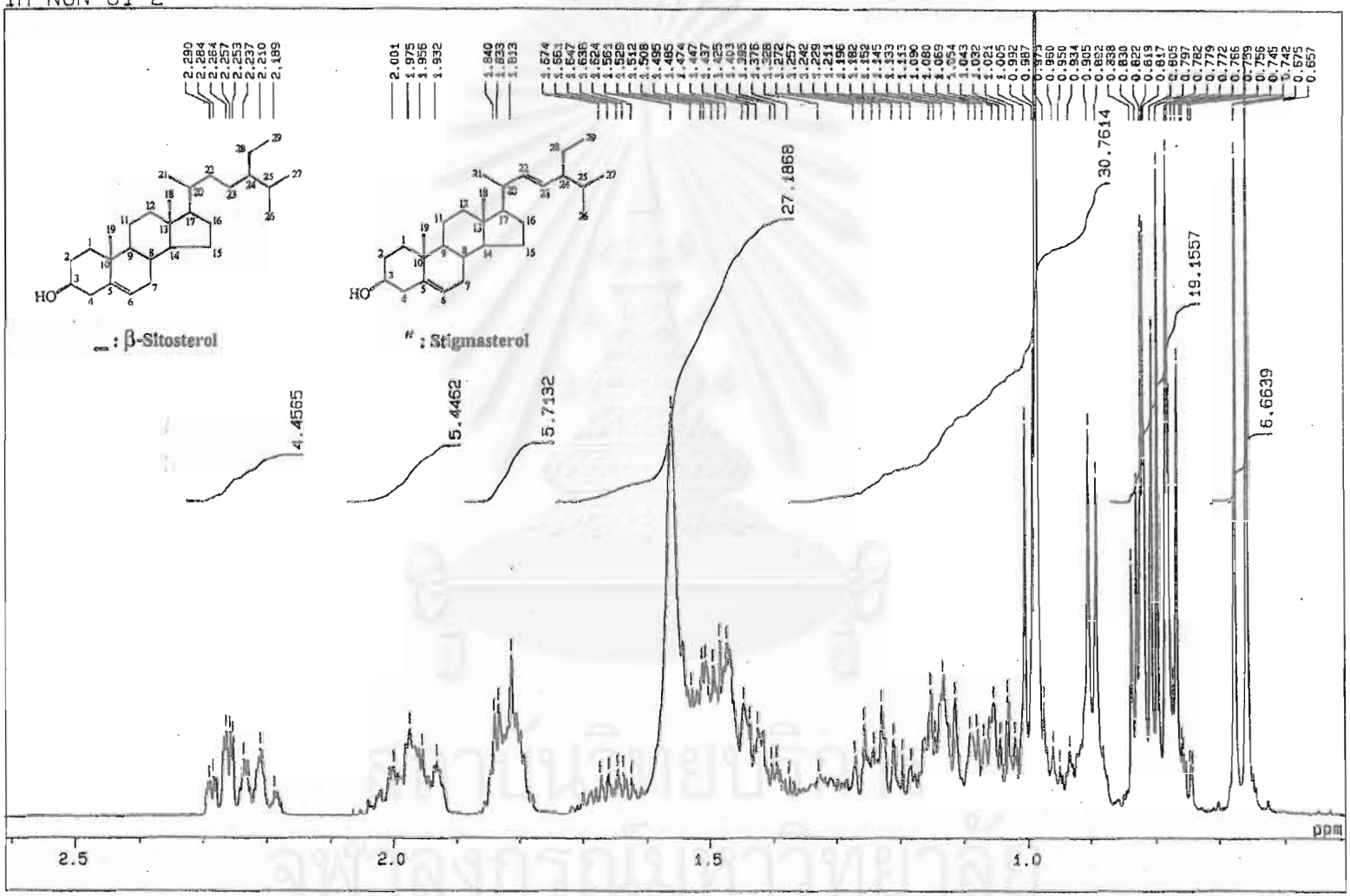
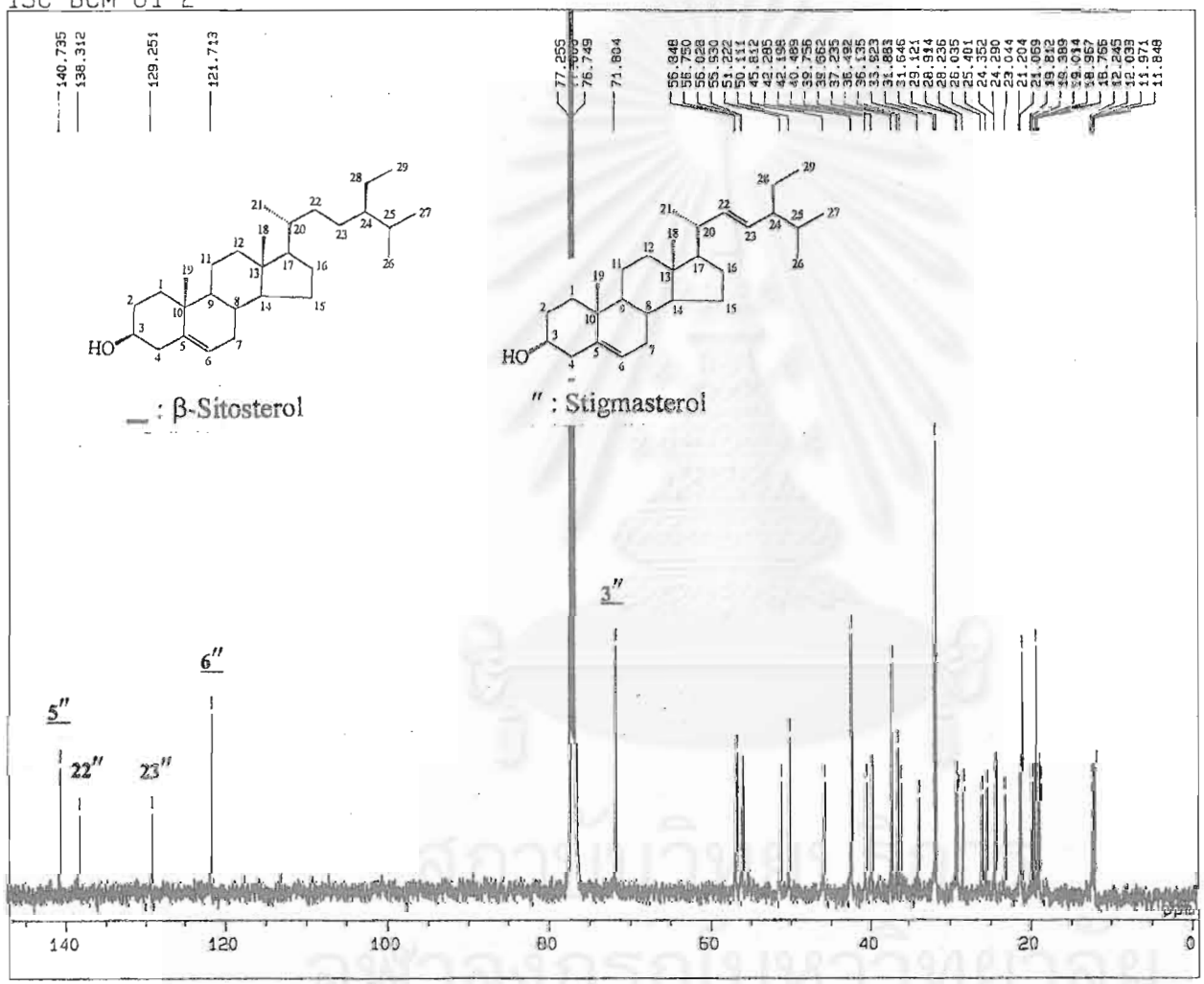


Figure 5c 500 MHz ^{1}H-NMR spectrum of isolated j1-2 (in $CDCl_3$) (expanded from 0.5 to 2.6 ppm)

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IRMOD : BCM
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FREQU : 30030.03 Hz
SCANS :     1200
DUMMY :        4
ACQTM :   2.1823 sec
PD    :   1.5000 sec
RGAIN :       23

PW1   :    4.50 usec


OBNUC : 13C
OBFRQ :  125.65 MHz
OBSET : 127782.65 Hz

IRNUC : 1H
IRFRQ :  500.00 MHz
IRSET : 162410.00 Hz
IRATN :      511
IRRPW :   50.0 usec
IRBP1 :       30
IRBP2 :        5
IRRNS :        0

ADBIT :       16
CTEMP :     21.1 c
CSPED :       13 Hz
SLVNT : CDCL3

RESOL :     0.46 Hz
BF    :     3.00 Hz
T1    :     0.00 %
T2    :     0.00 %
T3    :    90.00 %
T4    :   100.00 %
REFVL :    77.00 ppm
XE    : 18591.90 Hz
XS    :  3271.70 Hz
operator
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Figure 6a 125 MHz ^{13}C-NMR spectrum of isolated j1-2 (in $CDCl_3$)

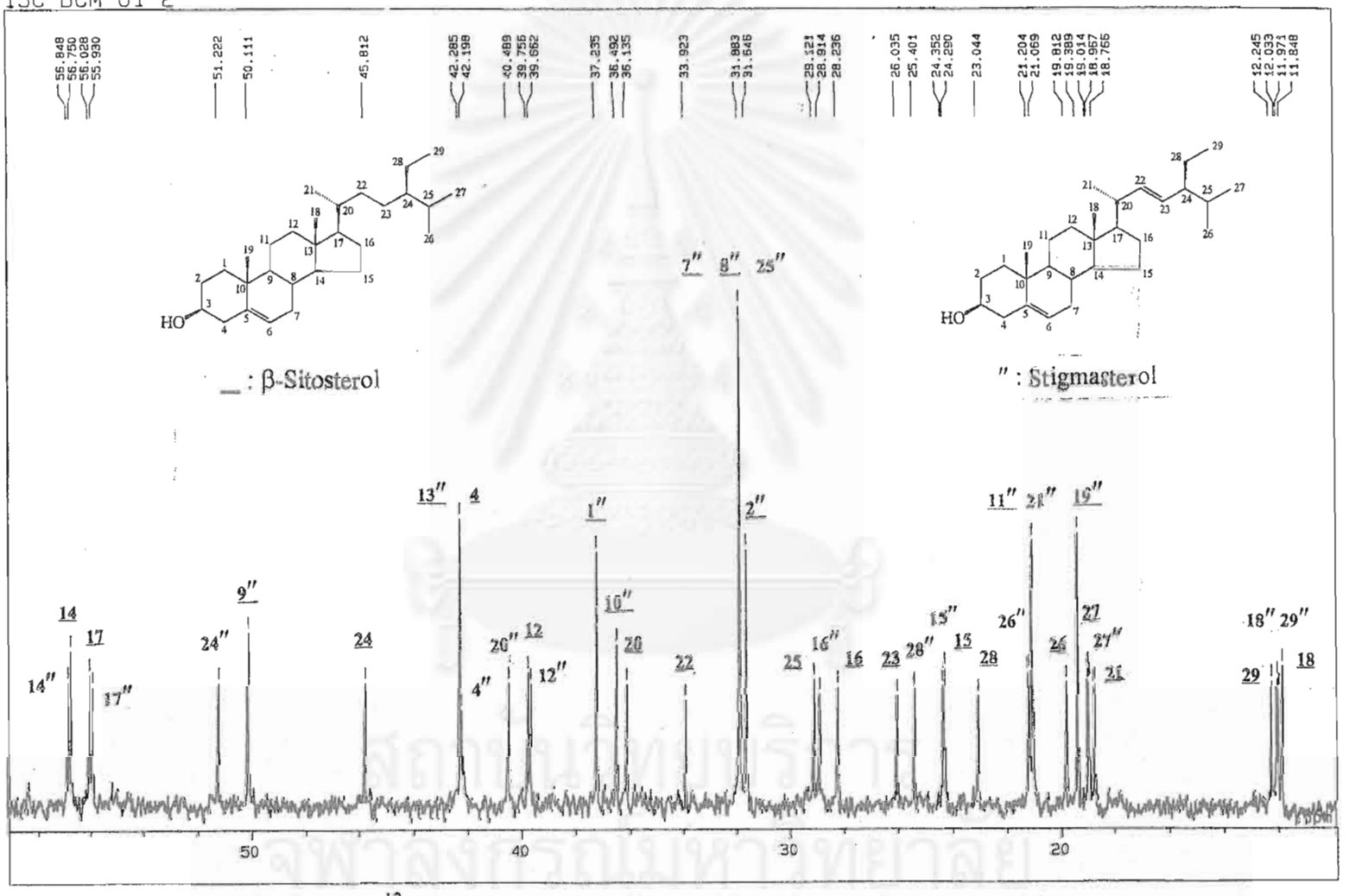

Figure 6b 125 MHz ^{13}C-NMR spectrum of isolated j1-2 (in $CDCl_3$) (expanded from 10 to 58 ppm)

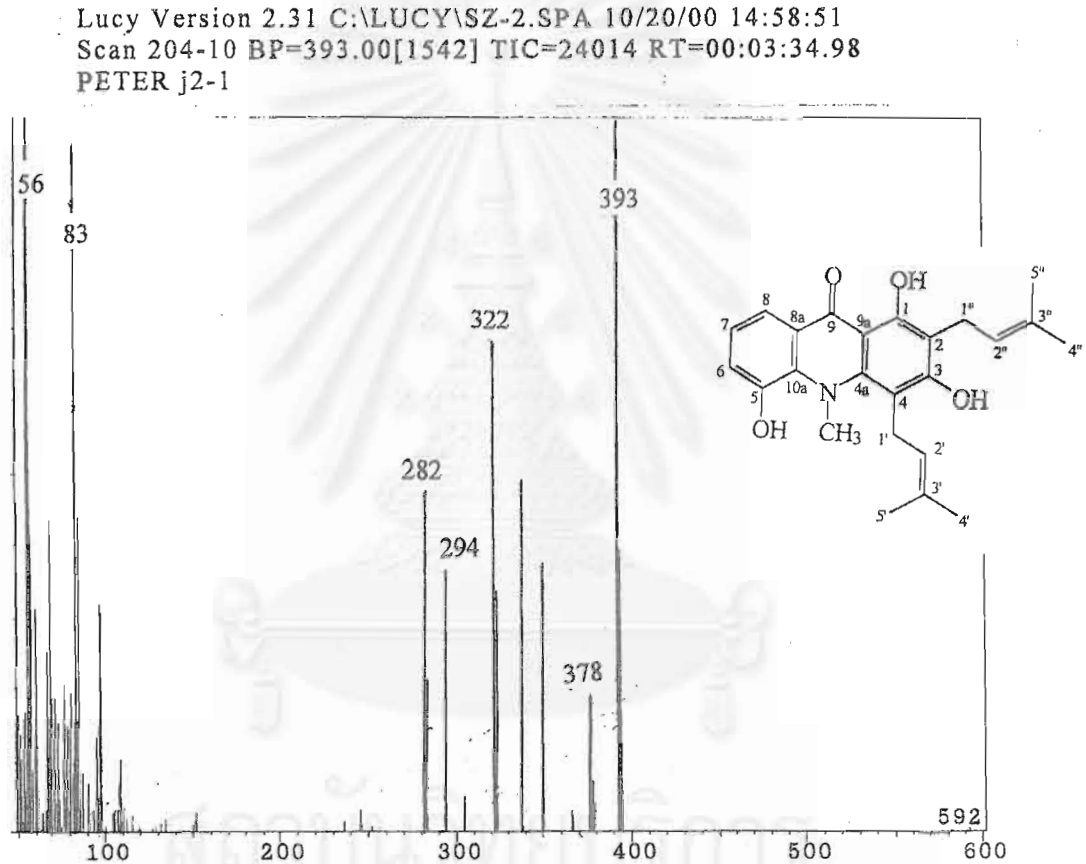

Figure 7 EI mass spectrum of compound j2-1

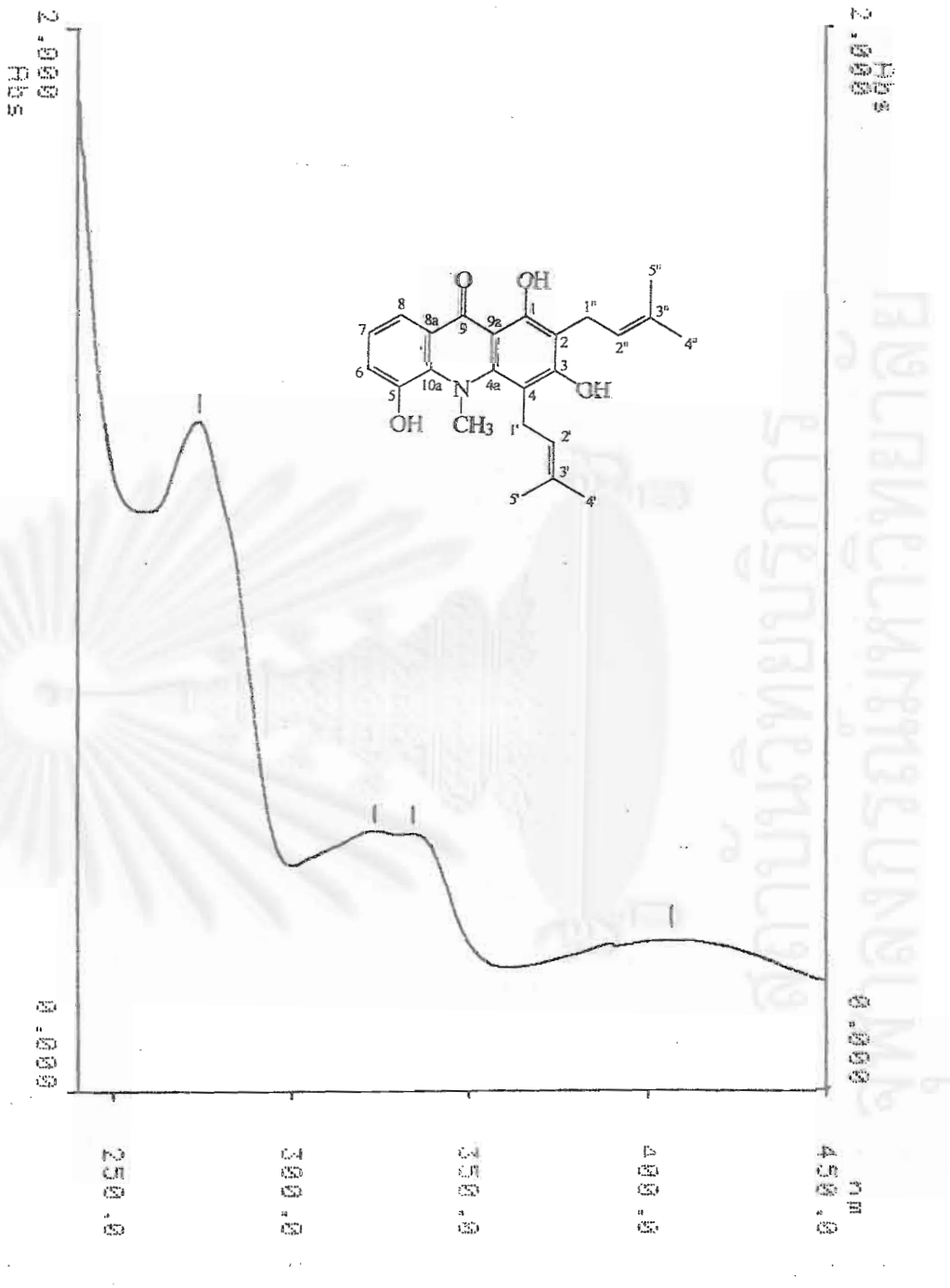

Figure 8 Ultraviolet spectrum of compound j2-1 (in $CHCl_3$)

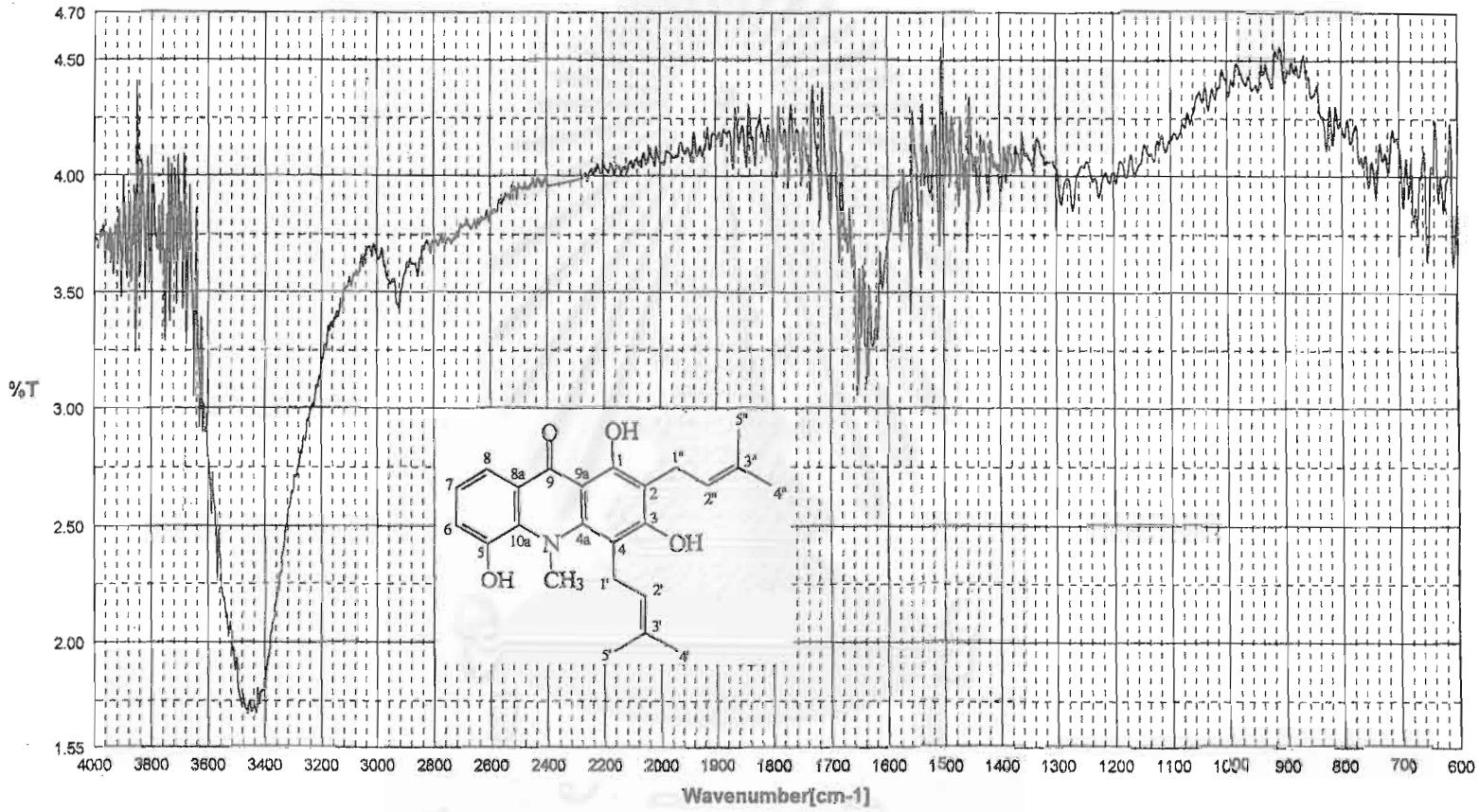

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Figure 9 Infrared spectrum of compound j2-1 (in KBr disc)

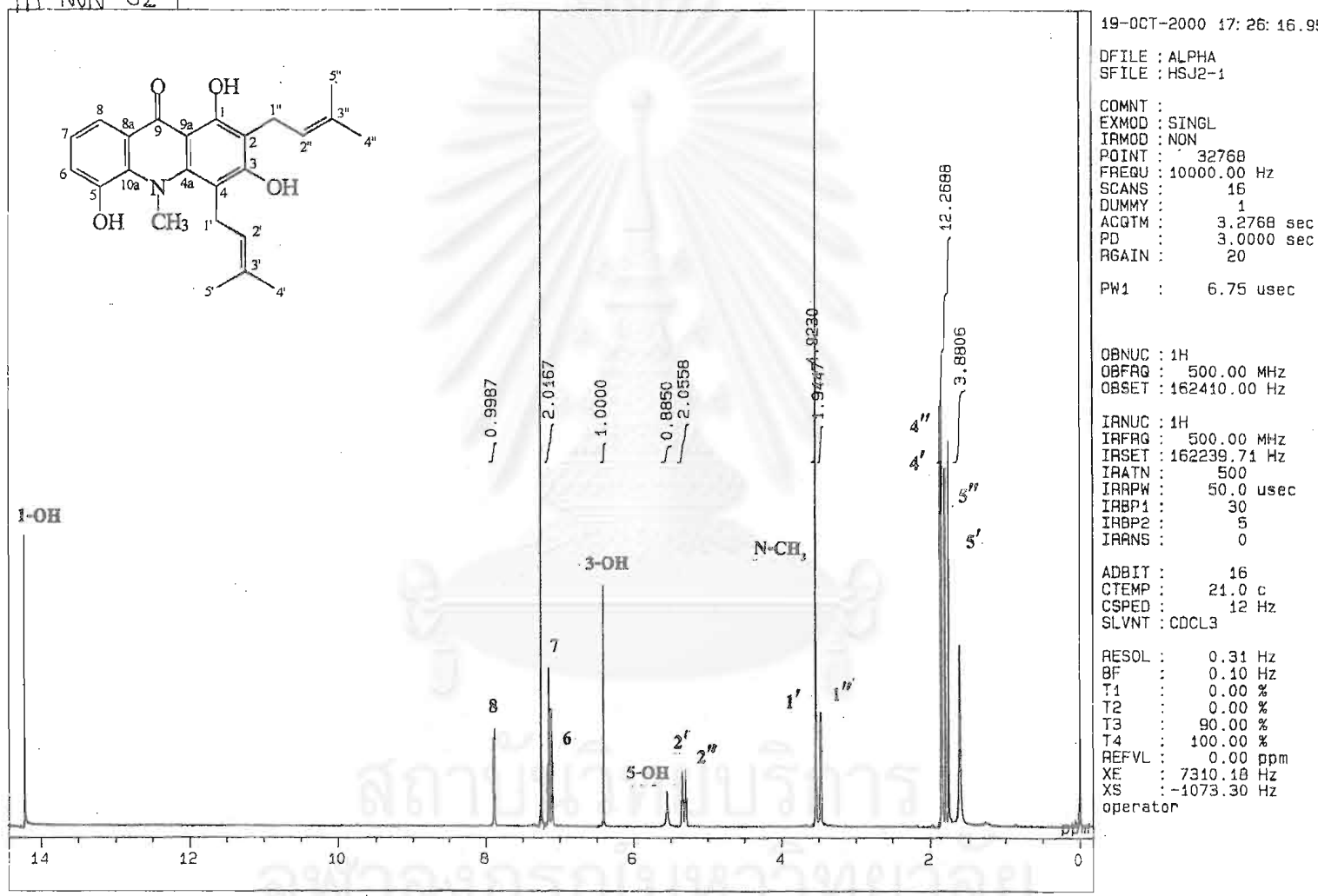

Figure 10a 500 MHz ^{1}H-NMR spectrum of compound j2-1 (in $CDCl_3$)

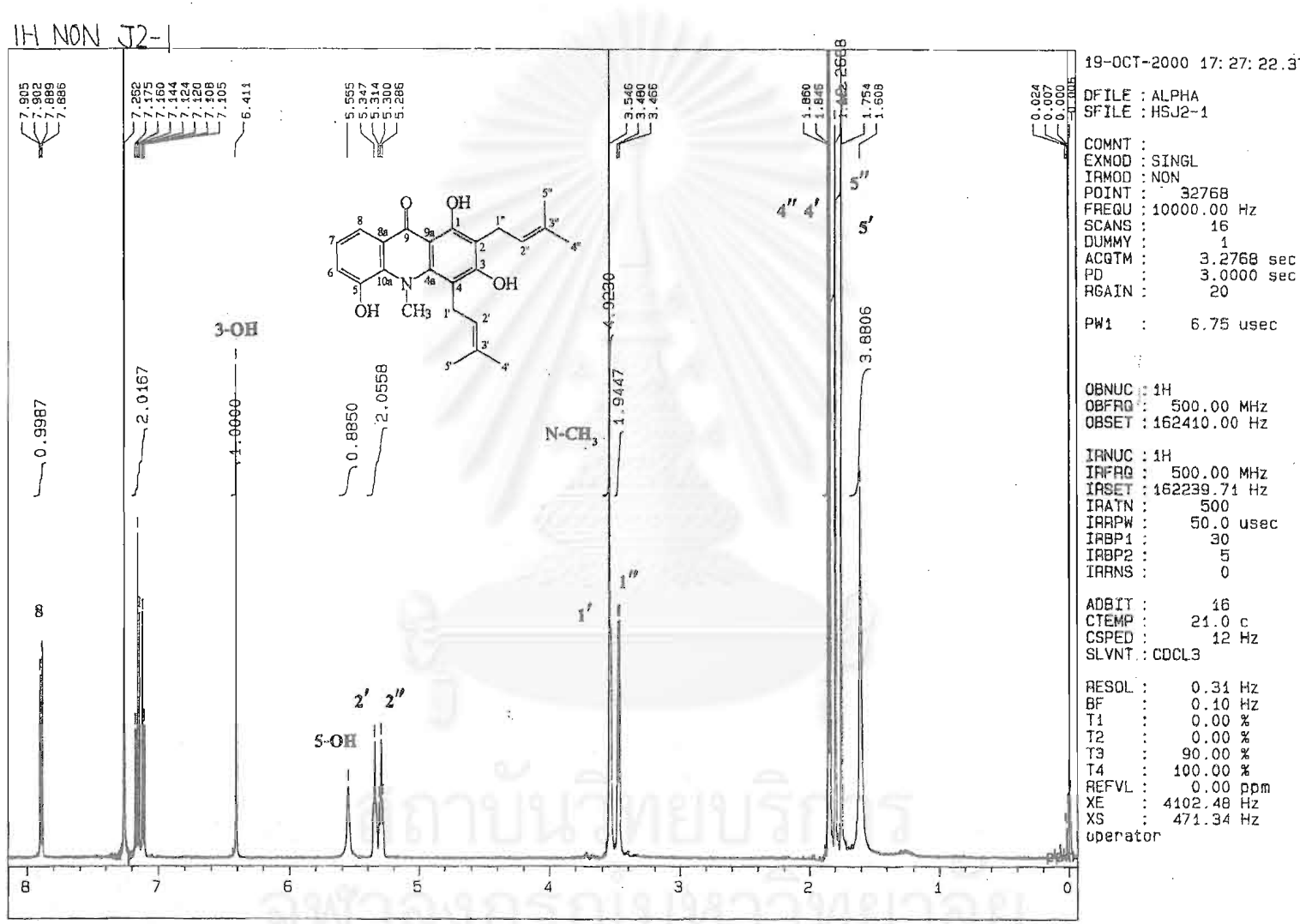

Figure 10b 500 MHz ^{1}H-NMR spectrum of compound j2-1 (in $CDCl_3$) (expanded from 0 to 8.0 ppm)

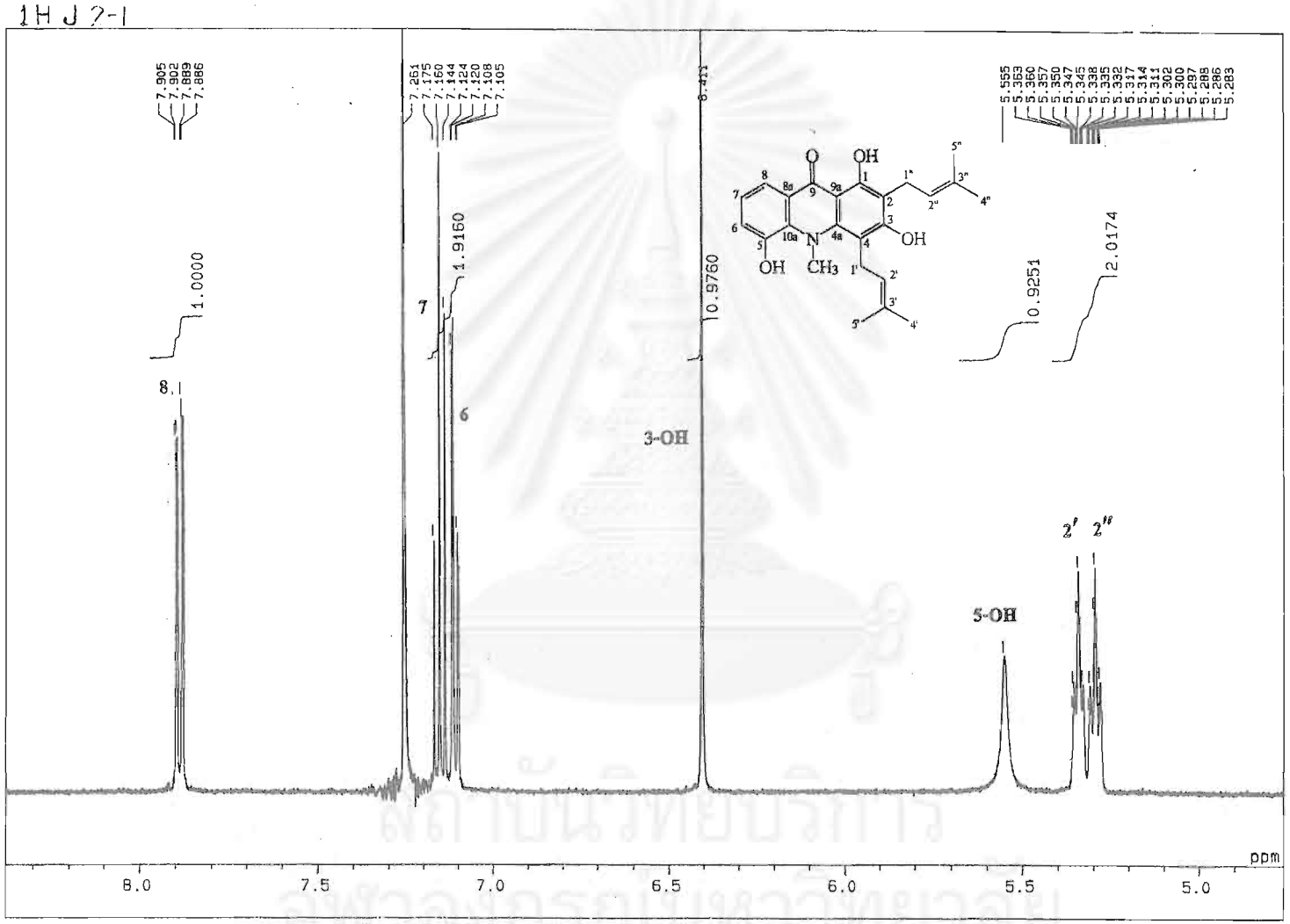

Figure 10c 500 MHz ^{1}H-NMR spectrum of compound j2-1 (in $CDCl_3$)
(expanded from 4.8 to 8.3 ppm)

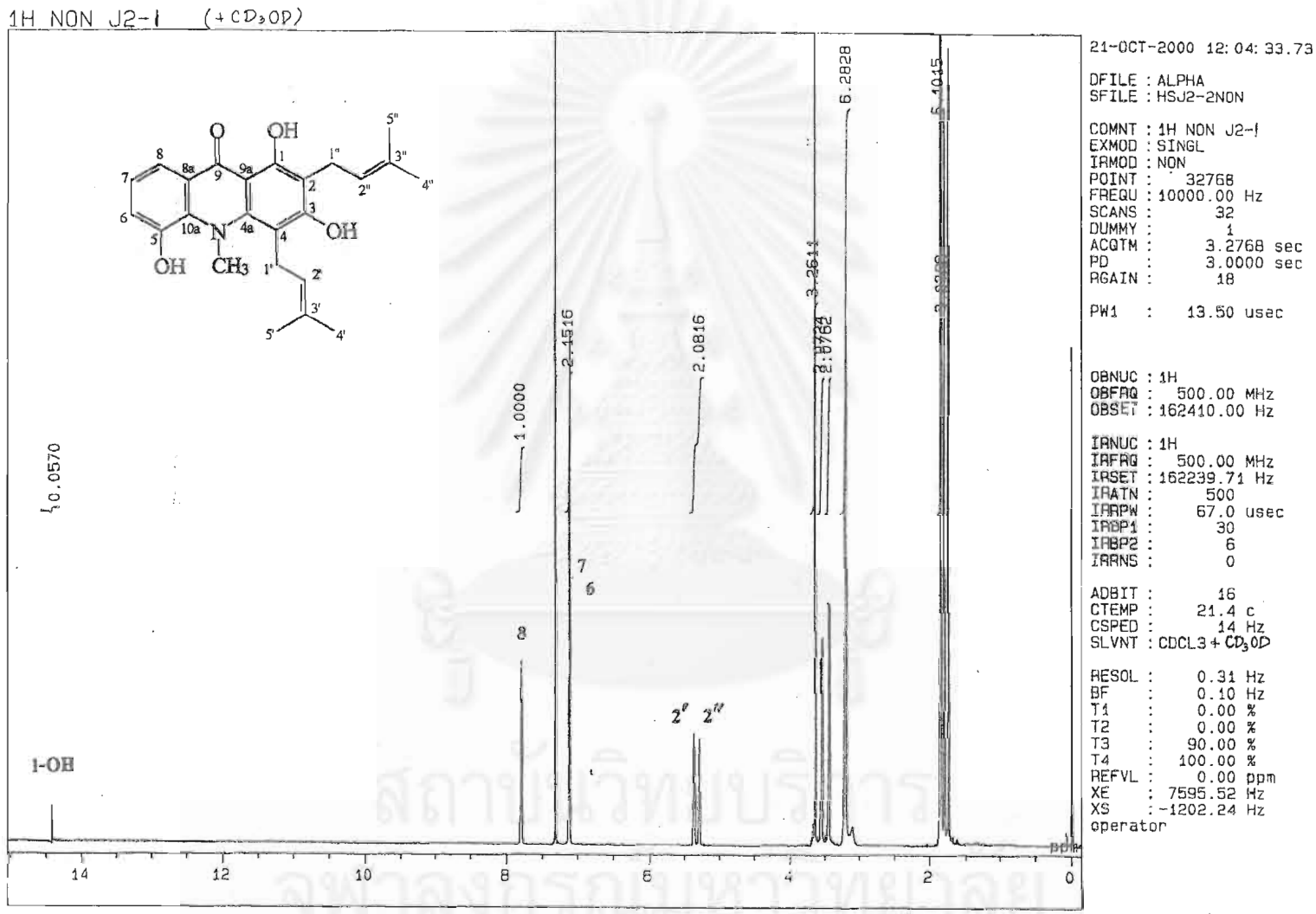

Figure 11a 500 MHz ^{1}H-NMR spectrum of compound j2-1 (in $CDCl_3$+CD_3OD)

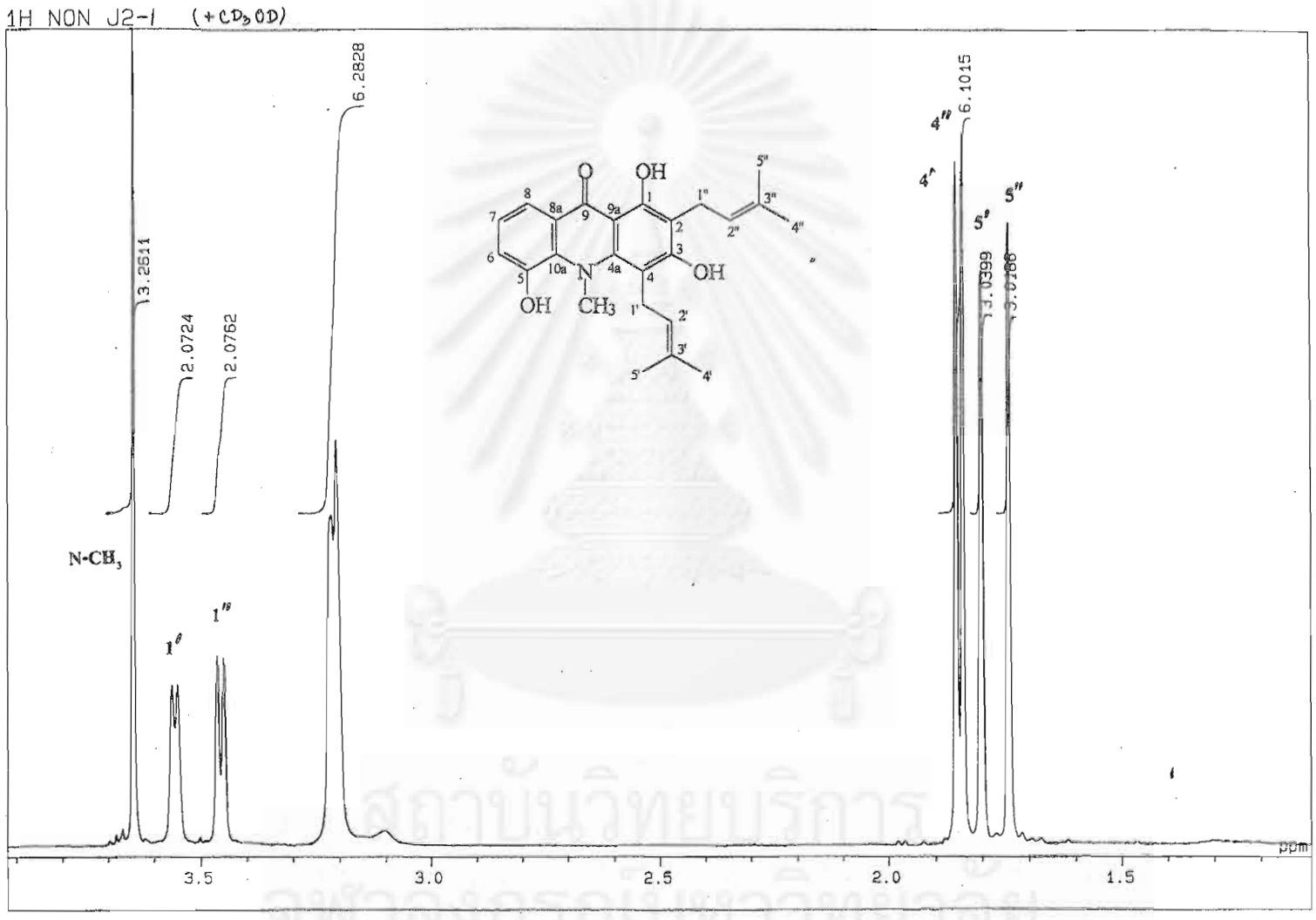

Figure 11b 500 MHz 1H-NMR spectrum of compound j2-1 (in CDCl3+CD3OD) (expanded from 1.2 to 3.9 ppm)

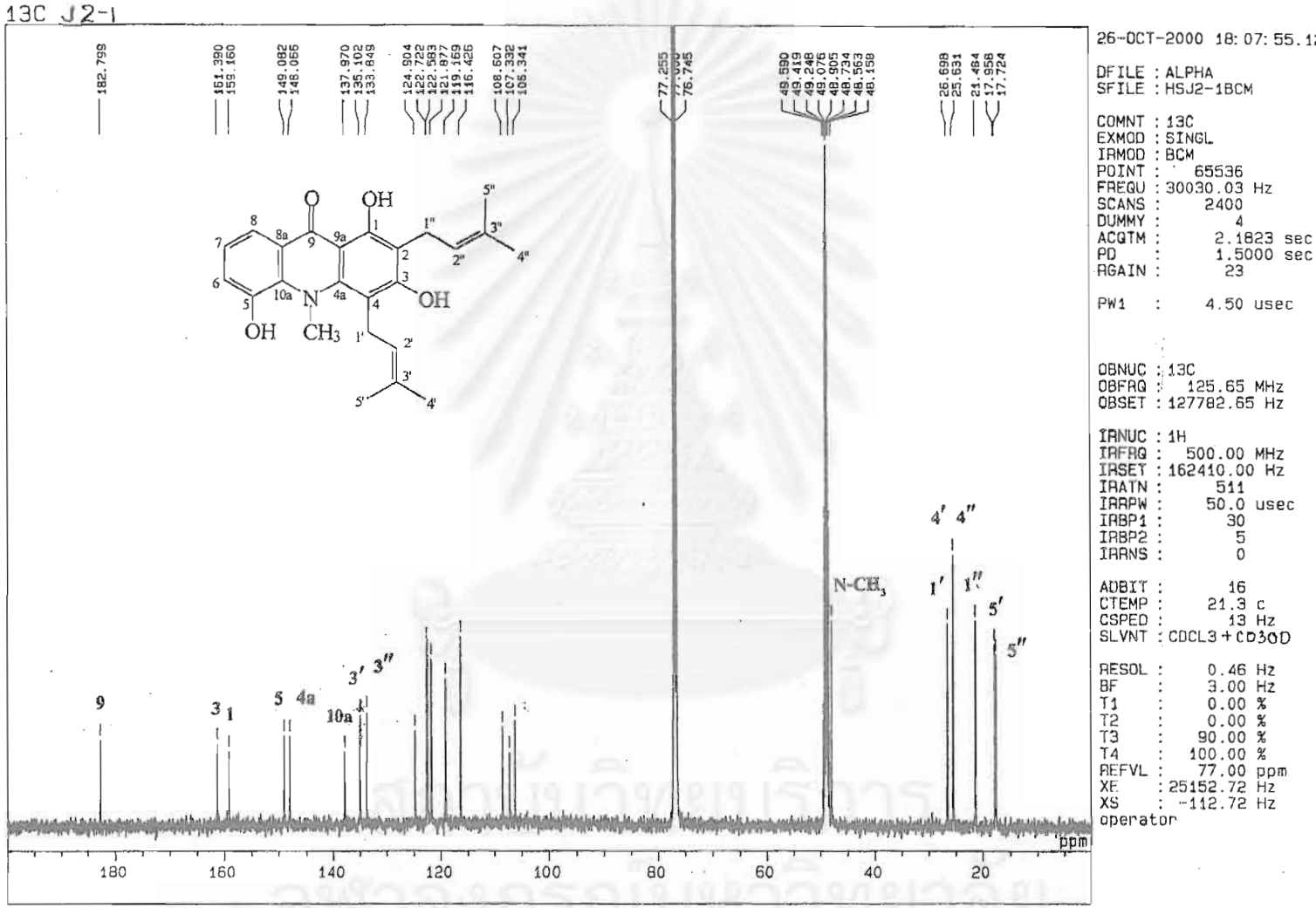

Figure 12a 125 MHz ^{13}C-NMR spectrum of compound j2-1 (in $CDCl_3$+CD_3OD)

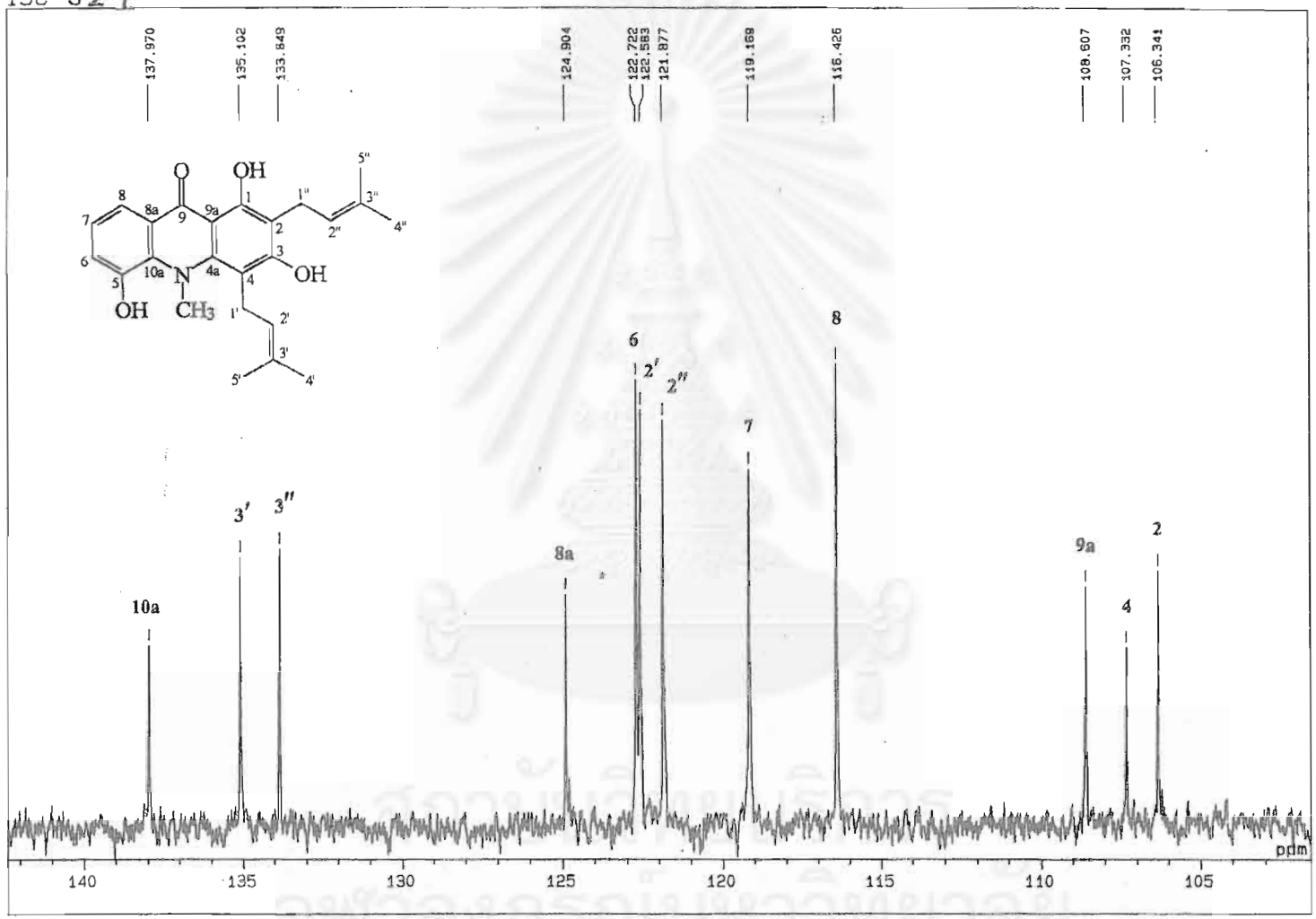

Figure 12b 125 MHz 13C-NMR spectrum of compound j2-1 (in CDCl3+CD3OD) (expanded from 103 to 142 ppm)

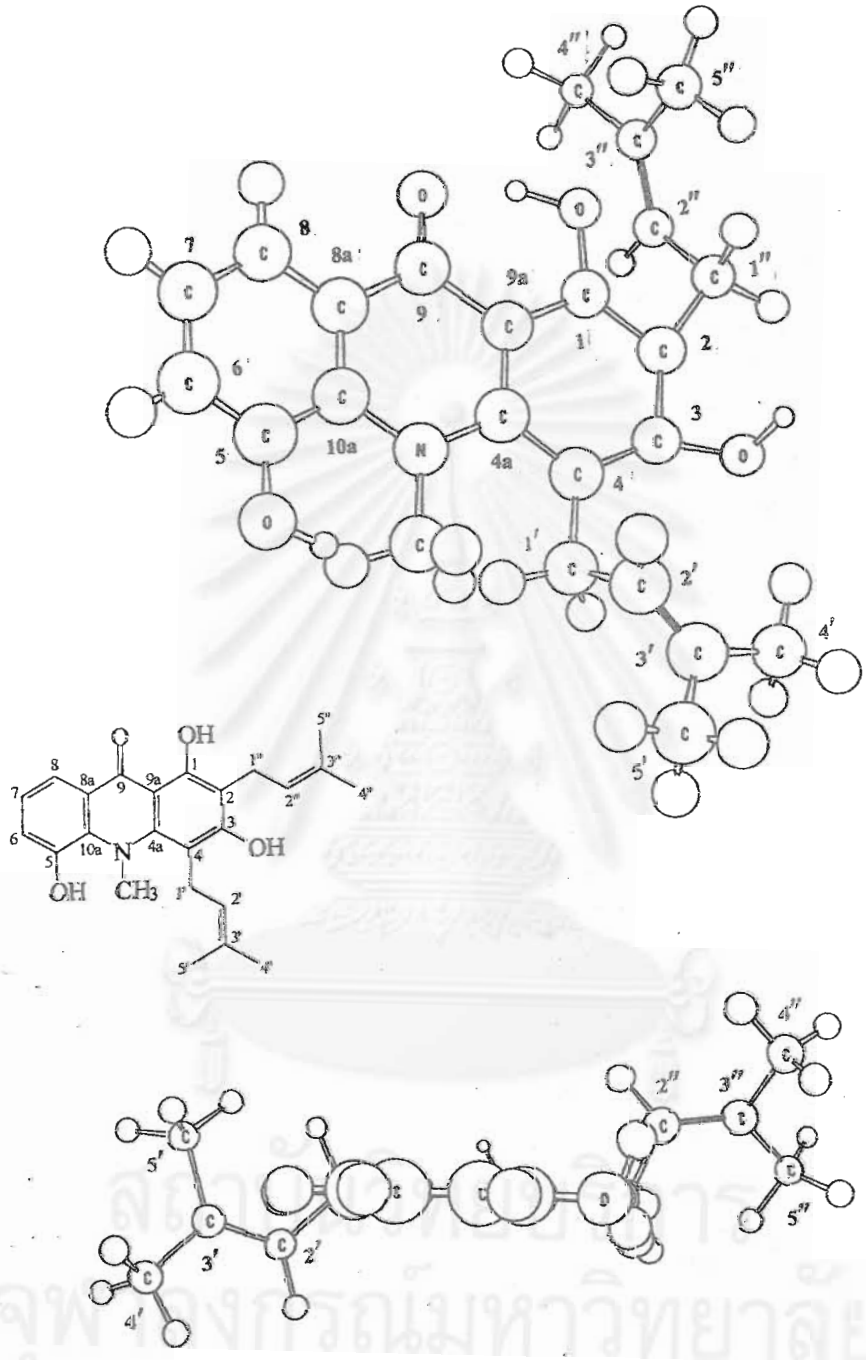

Figure 13 Computer modeling of compound j2-1 structure

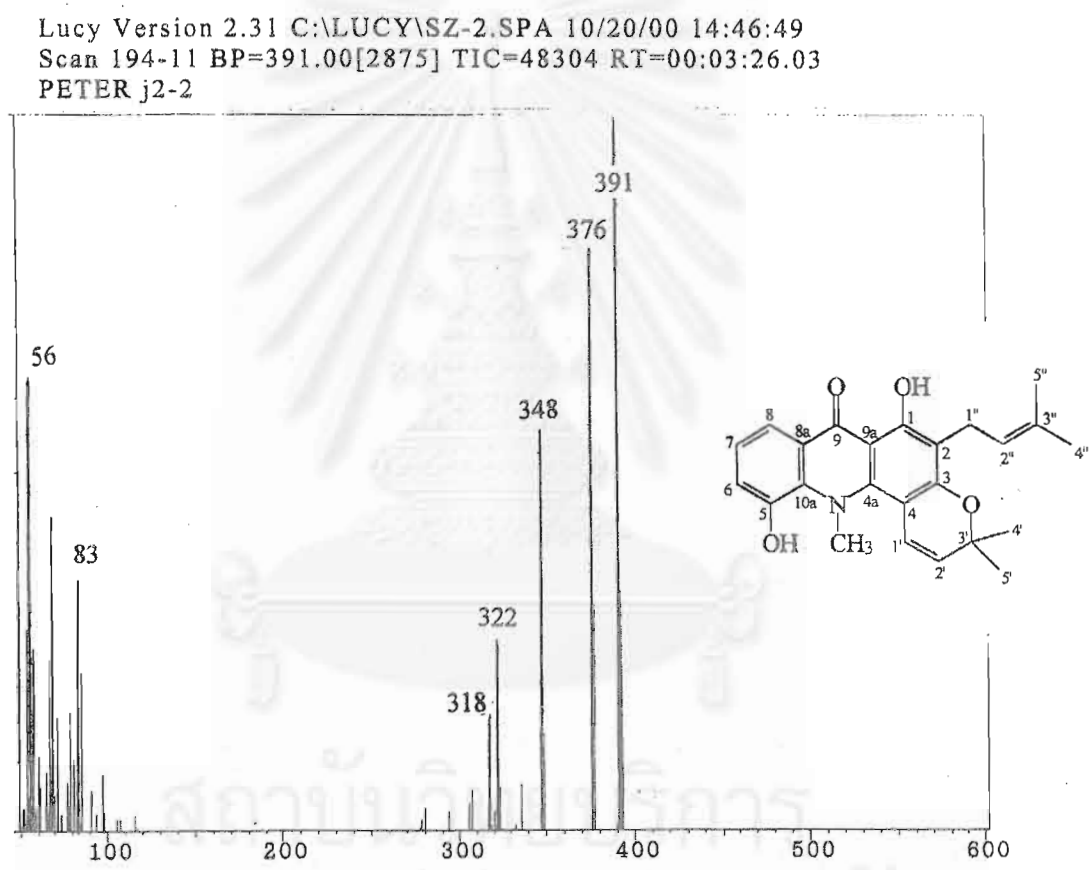

Figure 14 EI mass spectrum of compound j2-2

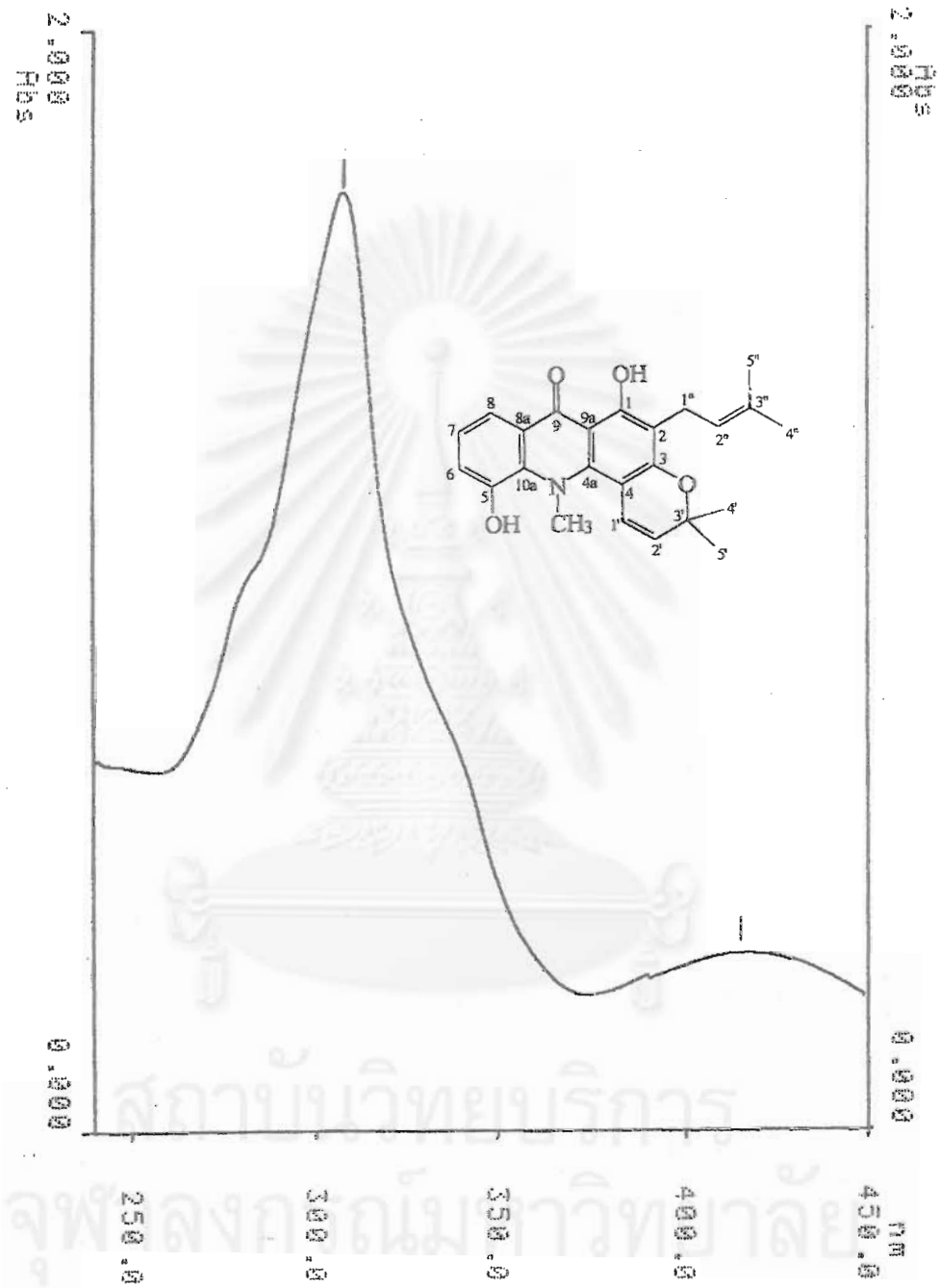

Figure 15 Ultraviolet spectrum of compound j2-2 (in $CHCl_3$)

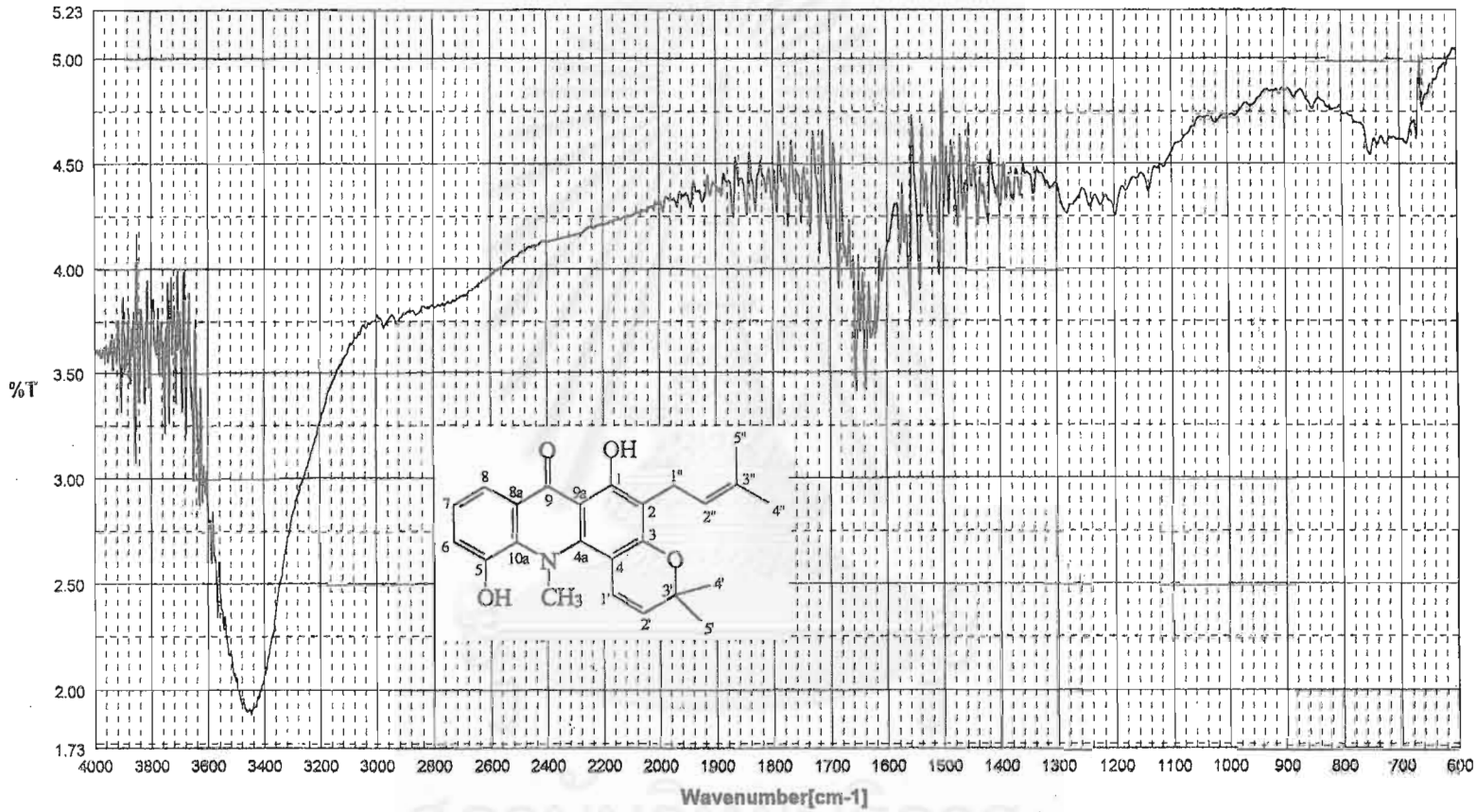

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Figure 16 Infrared spectrum of compound j2-2 (in KBr disc)

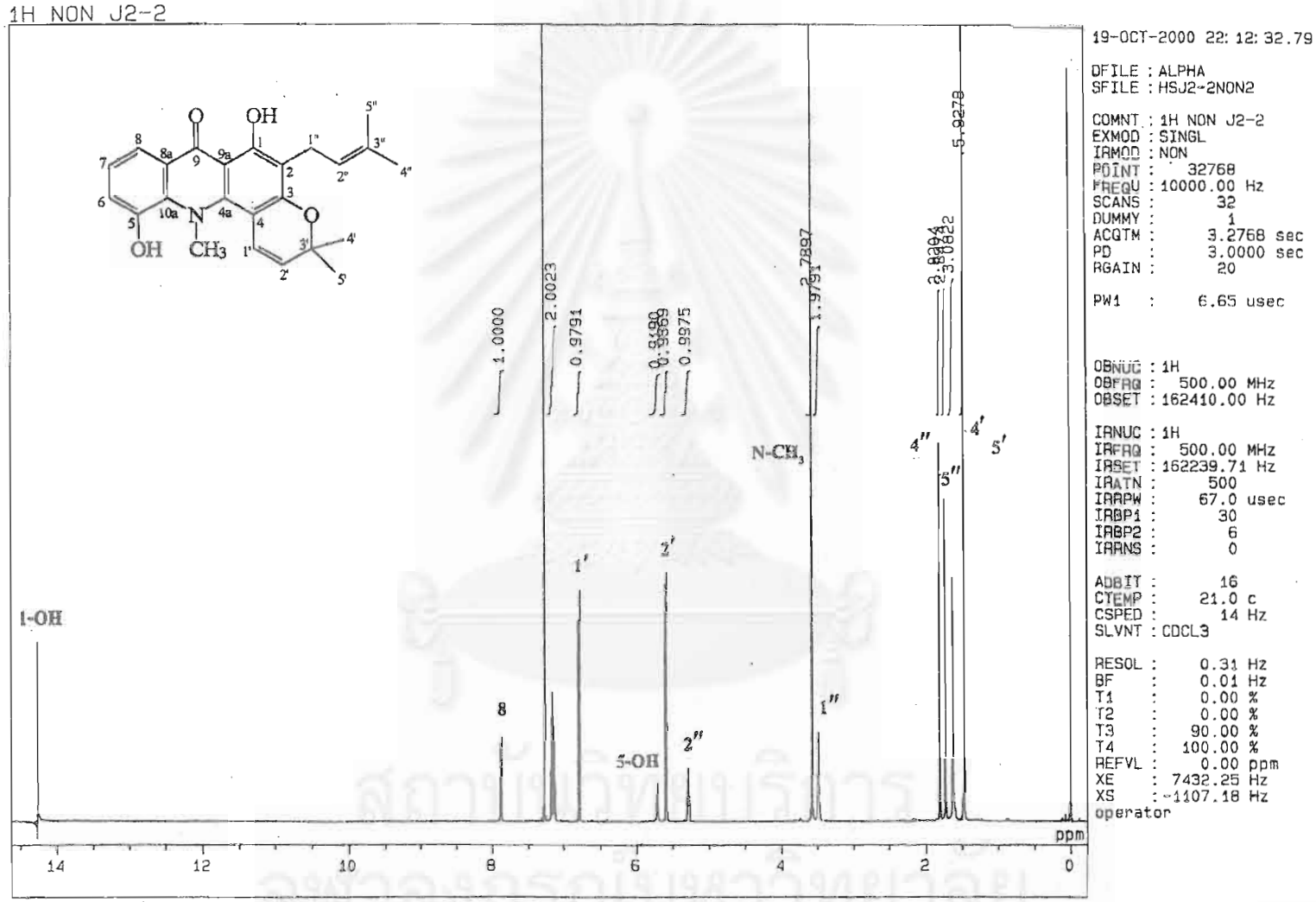

Figure 17a 500 MHz ^{1}H-NMR spectrum of compound j2-2 (in $CDCl_3$)

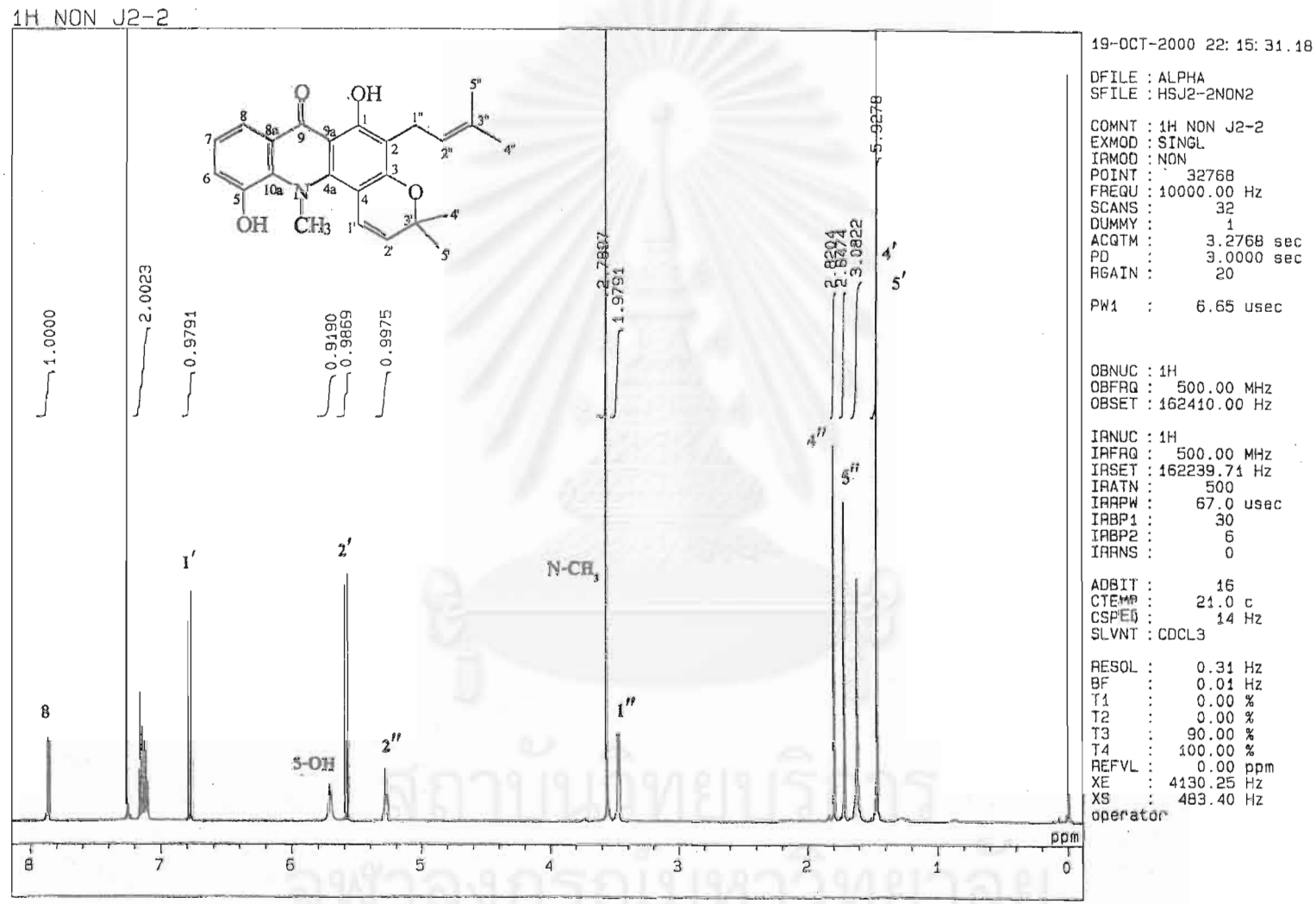

Figure 17b 500 MHz ^{1}H-NMR spectrum of compound j2-2 (in $CDCl_3$) (expanded from 0 to 8.0 ppm)

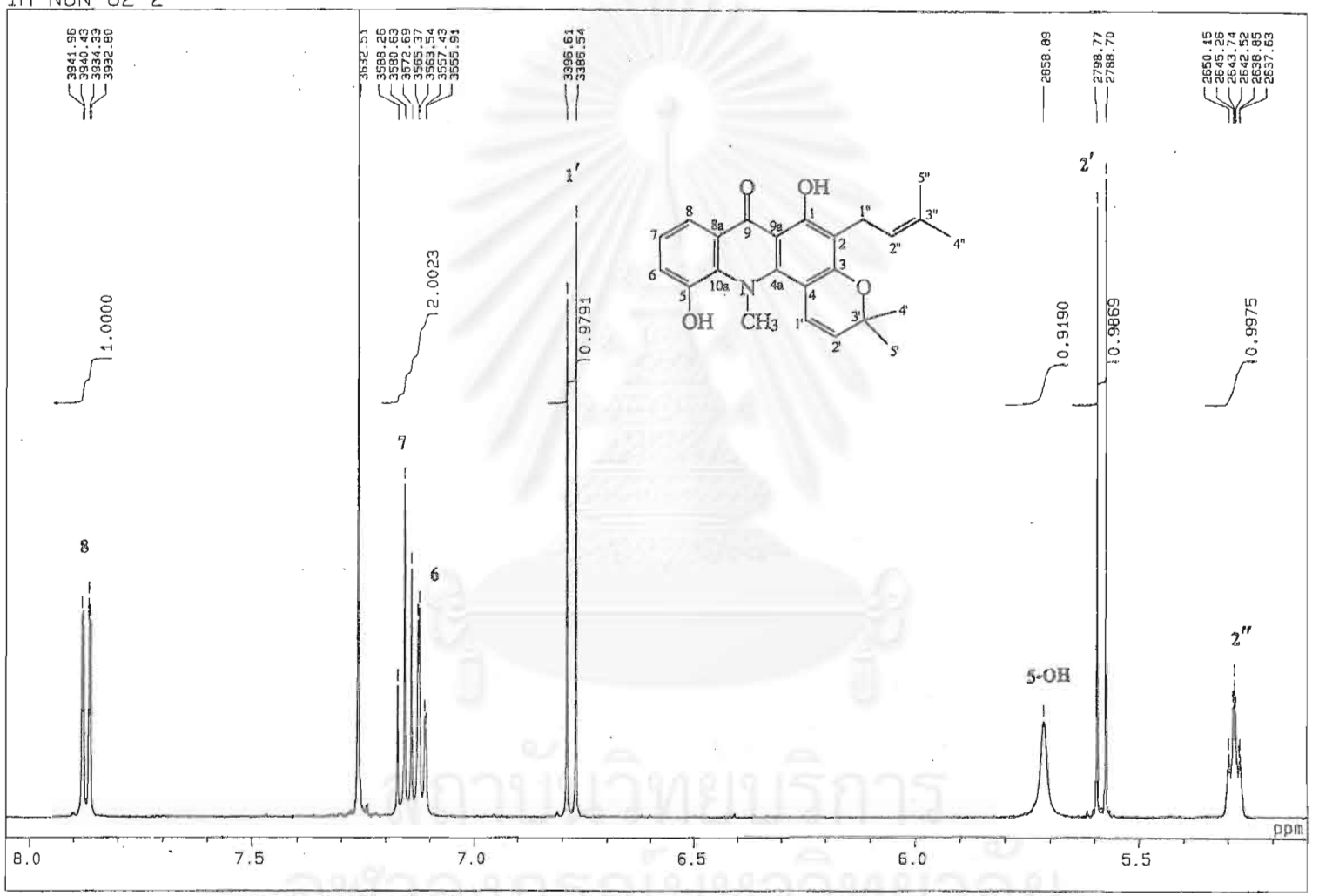

Figure 17c 500 MHz ^{1}H-NMR spectrum of compound j2-2 (in $CDCl_3$)
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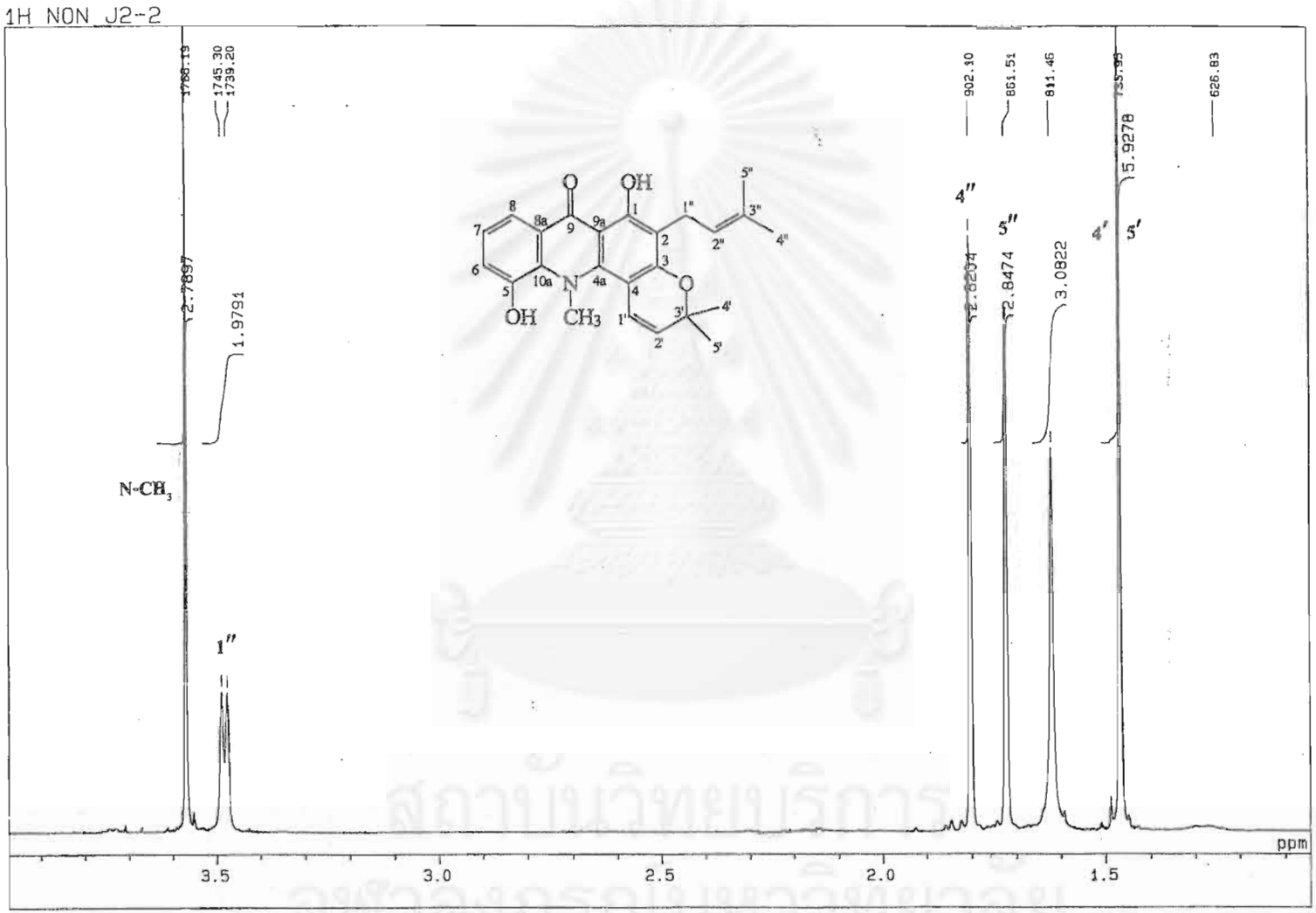

Figure 17d 500 MHz ^{1}H-NMR spectrum of compound j2-2 (in $CDCl_3$)
(expanded from 1.1 to 3.9 ppm)

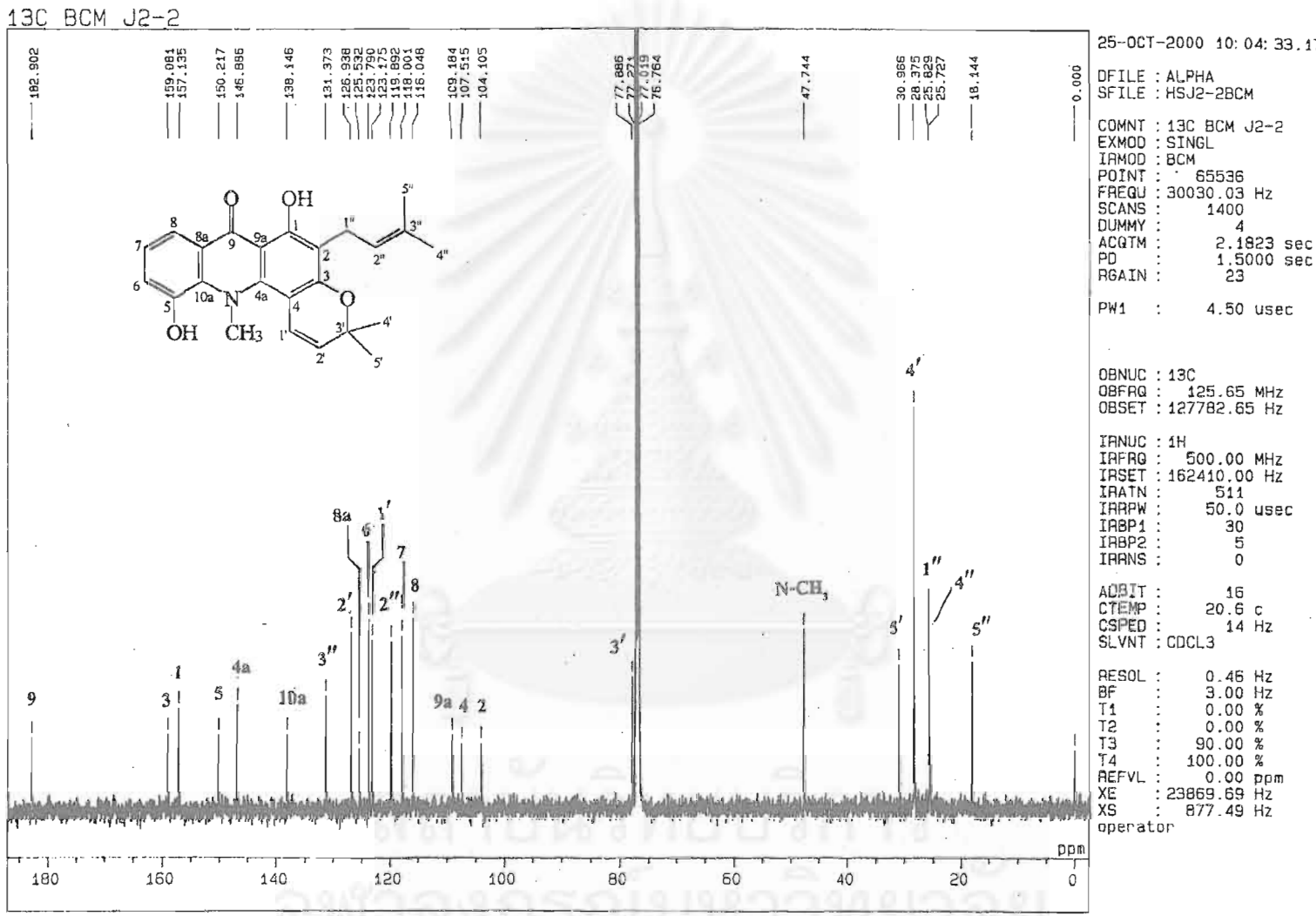

Figure 18 125 MHz ^{13}C-NMR spectrum of compound j2-2 (in $CDCl_3$)

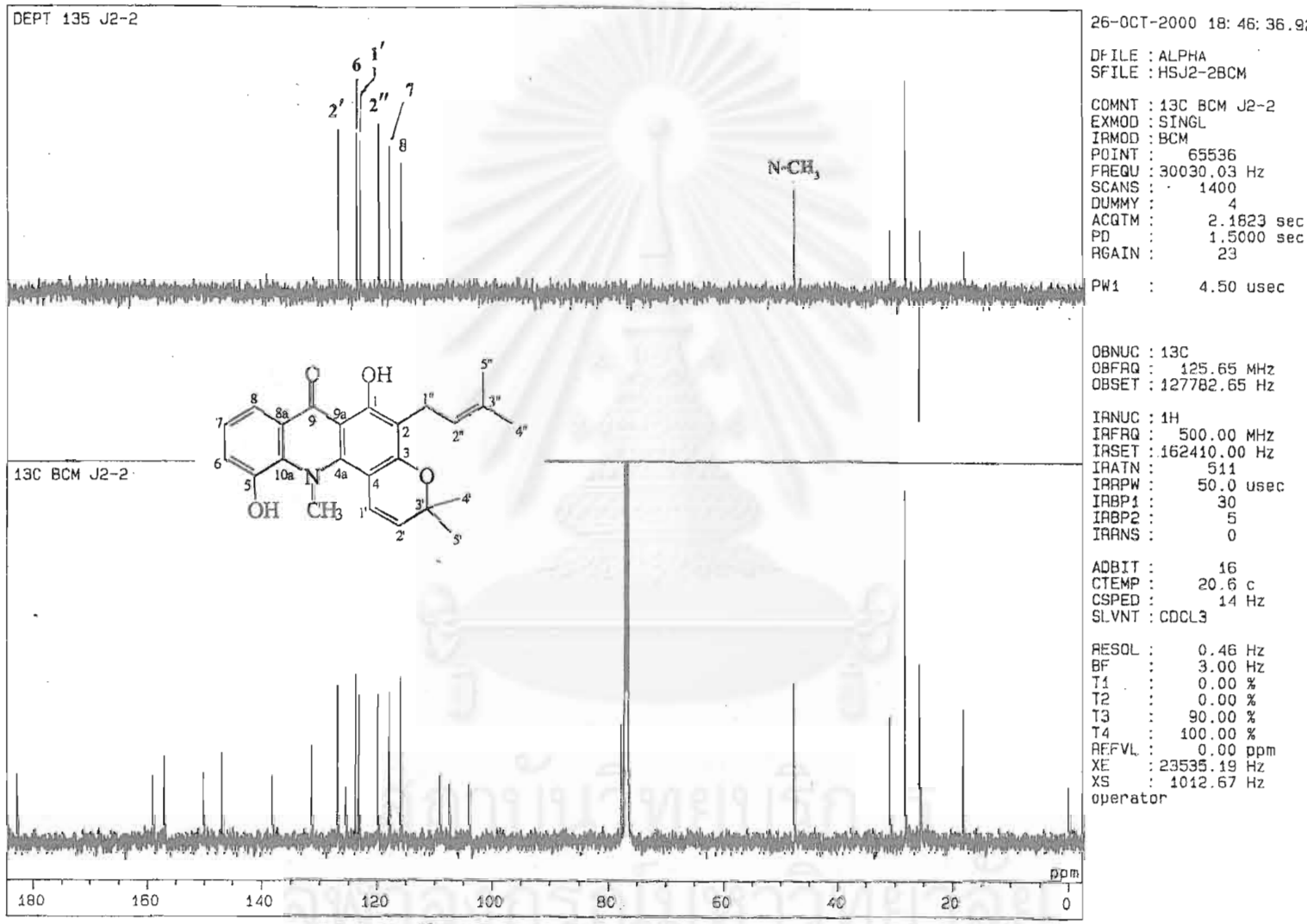

Figure 19a 125 MHz ^{13}C-NMR, DEPT-135 spectra of compound j2-2 (in $CDCl_3$)

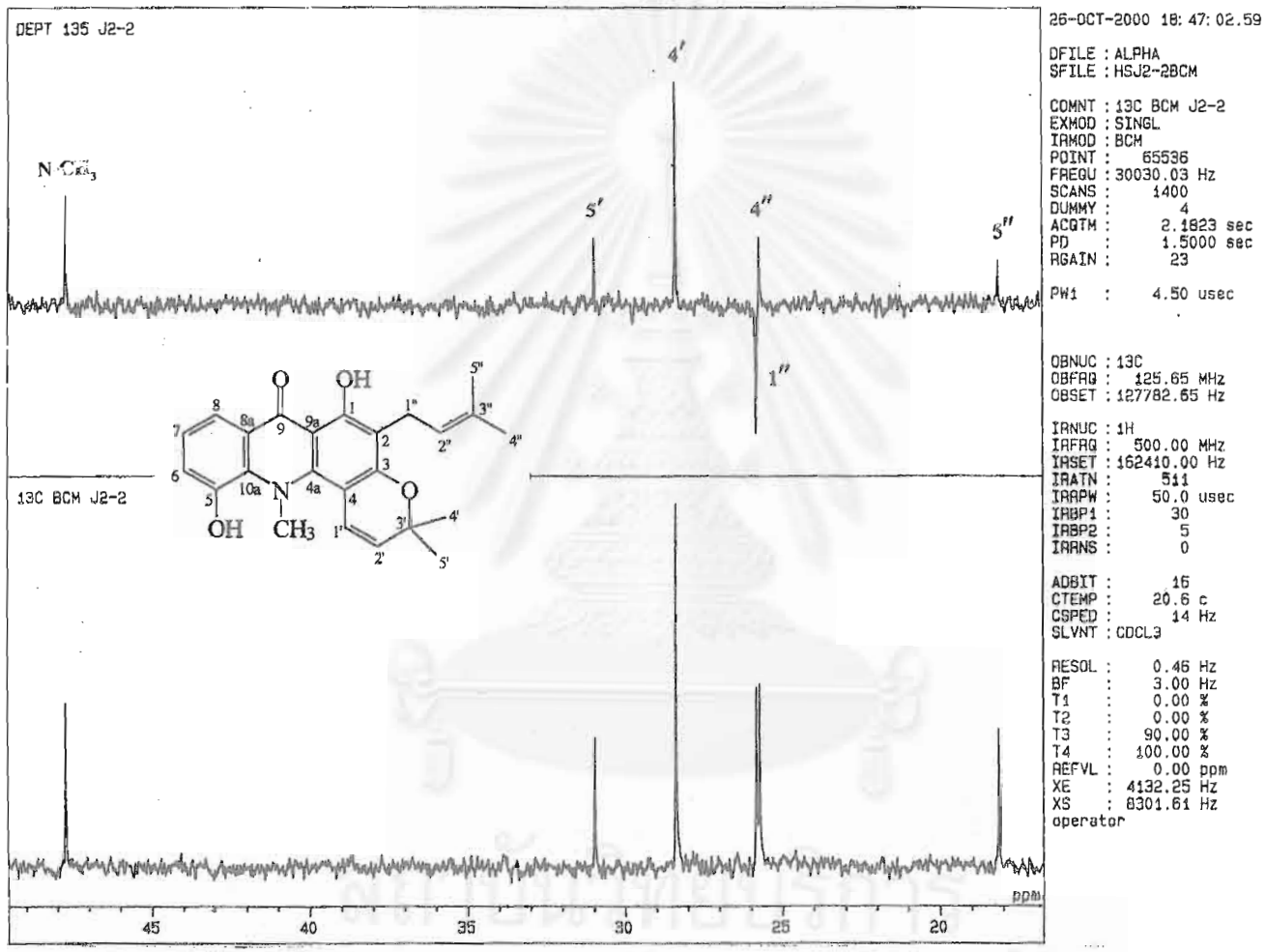

Figure 19b 125 MHz 13C-NMR, DEPT-135 spectra of compound j2-2 (in CDCl3) (expanded from 18 to 49 ppm)

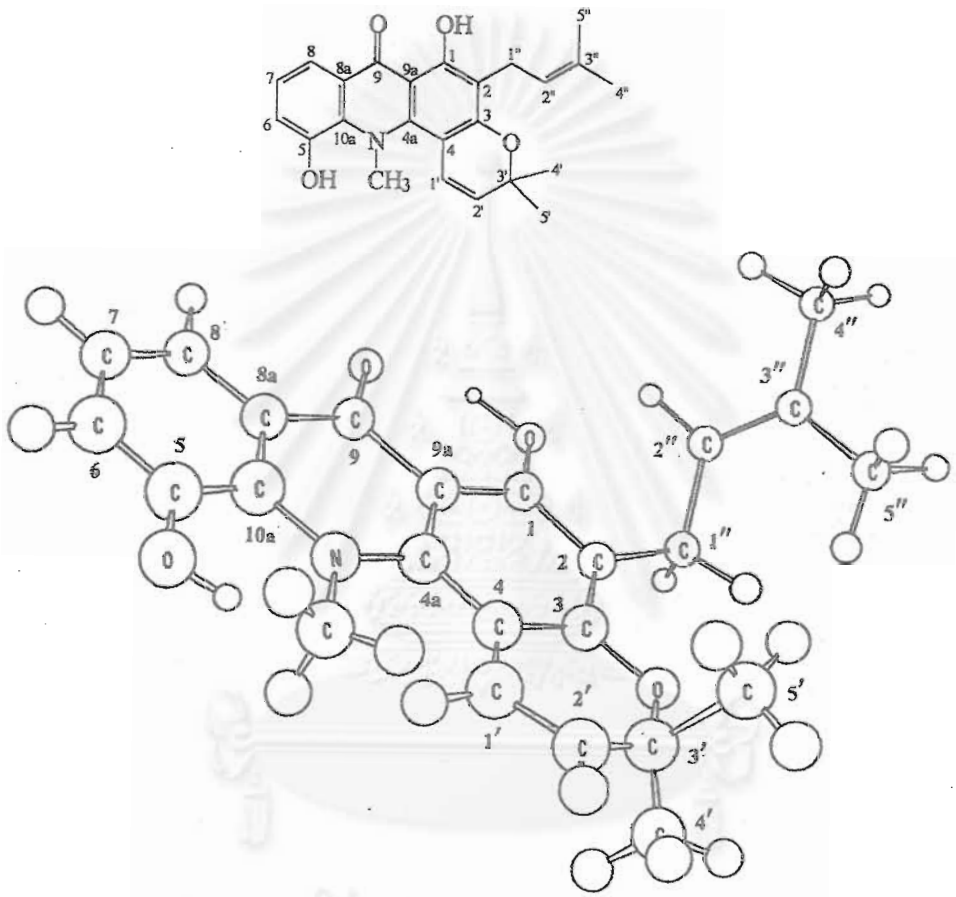

Figure 20 Computer modeling of compound j2-2 structure

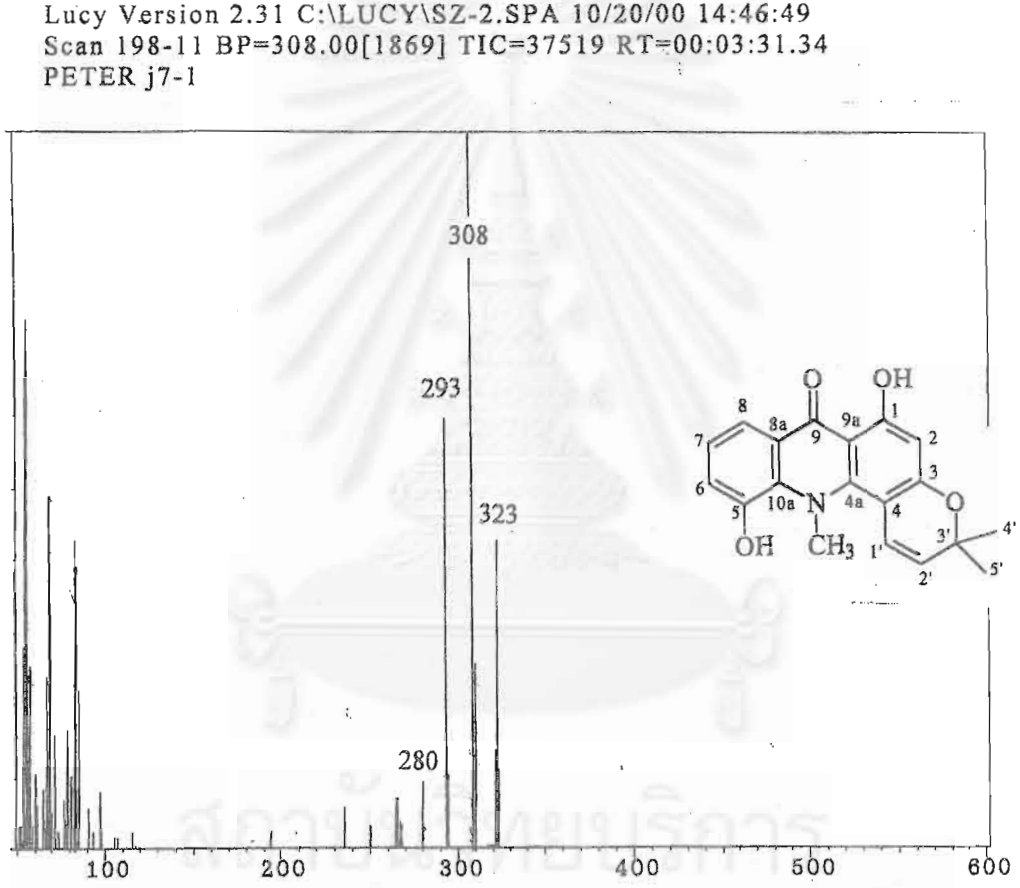

Figure 21 EI mass spectrum of compound j7-1

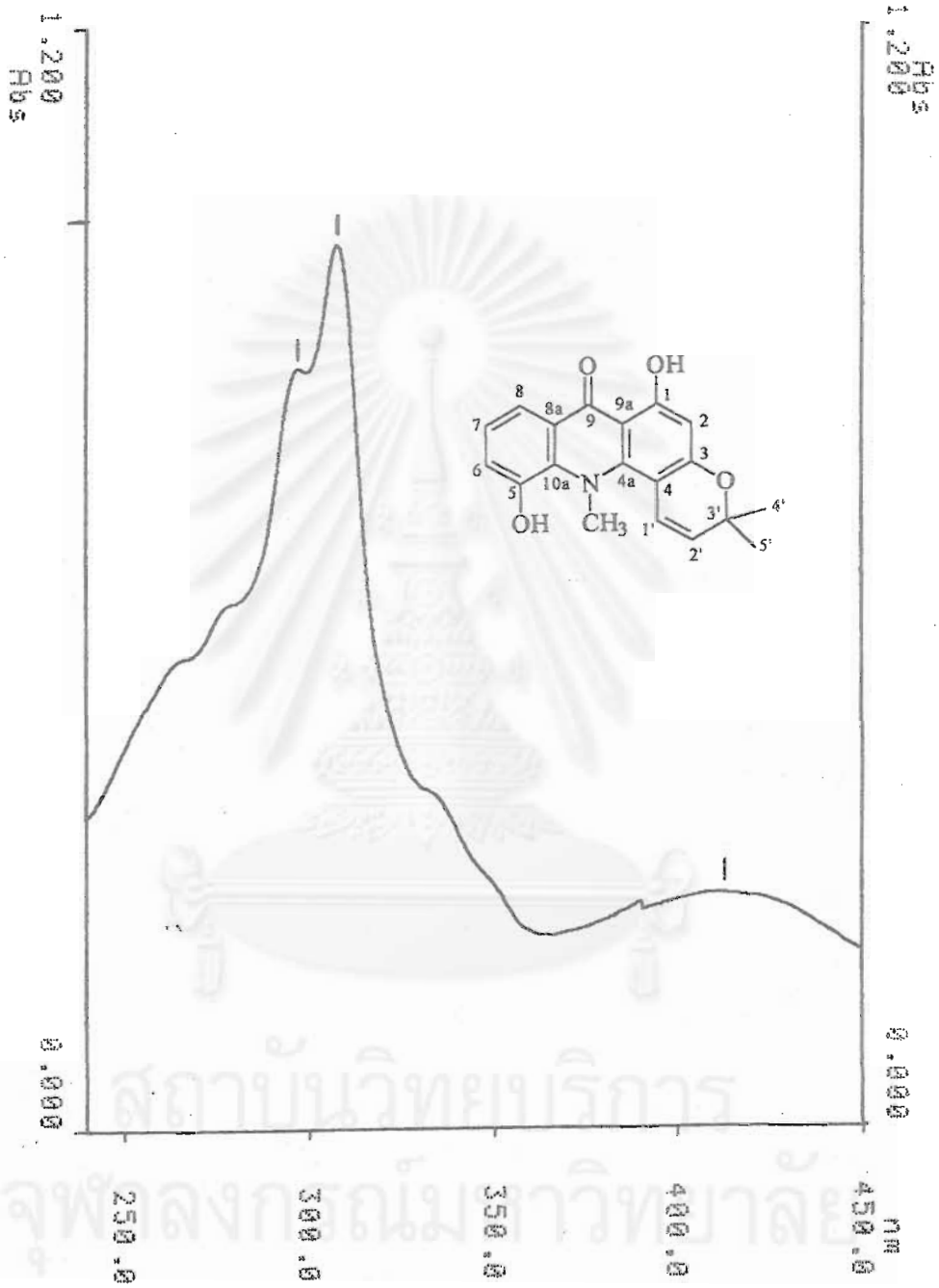

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Figure 22 Ultraviolet spectrum of compound j7-1 (in $CHCl_3$)

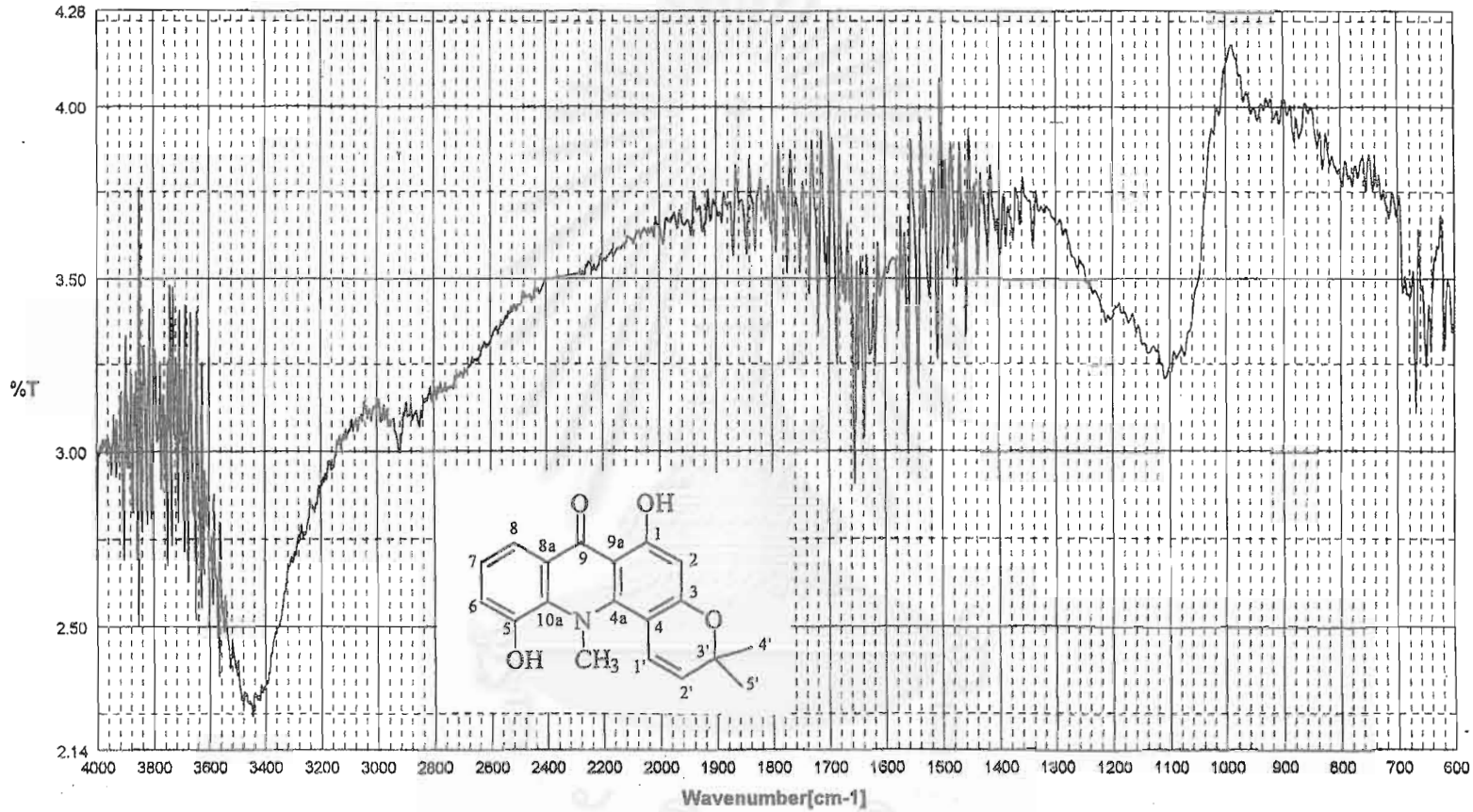

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Figure 23 Infrared spectrum of compound j7-1 (in KBr disc)

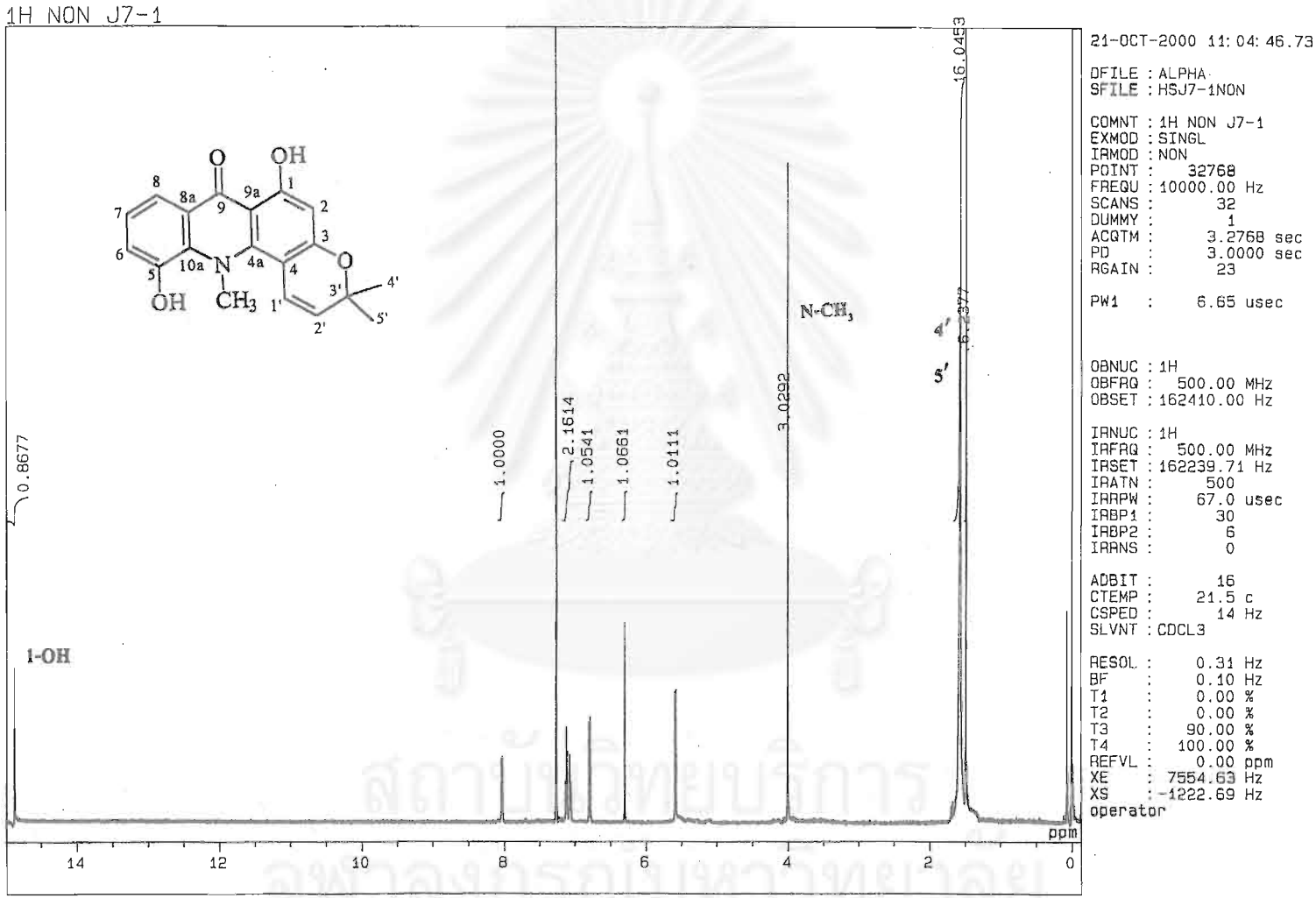


Figure 24a 500 MHz ^{1}H-NMR spectrum of compound j7-1 (in $CDCl_3$)

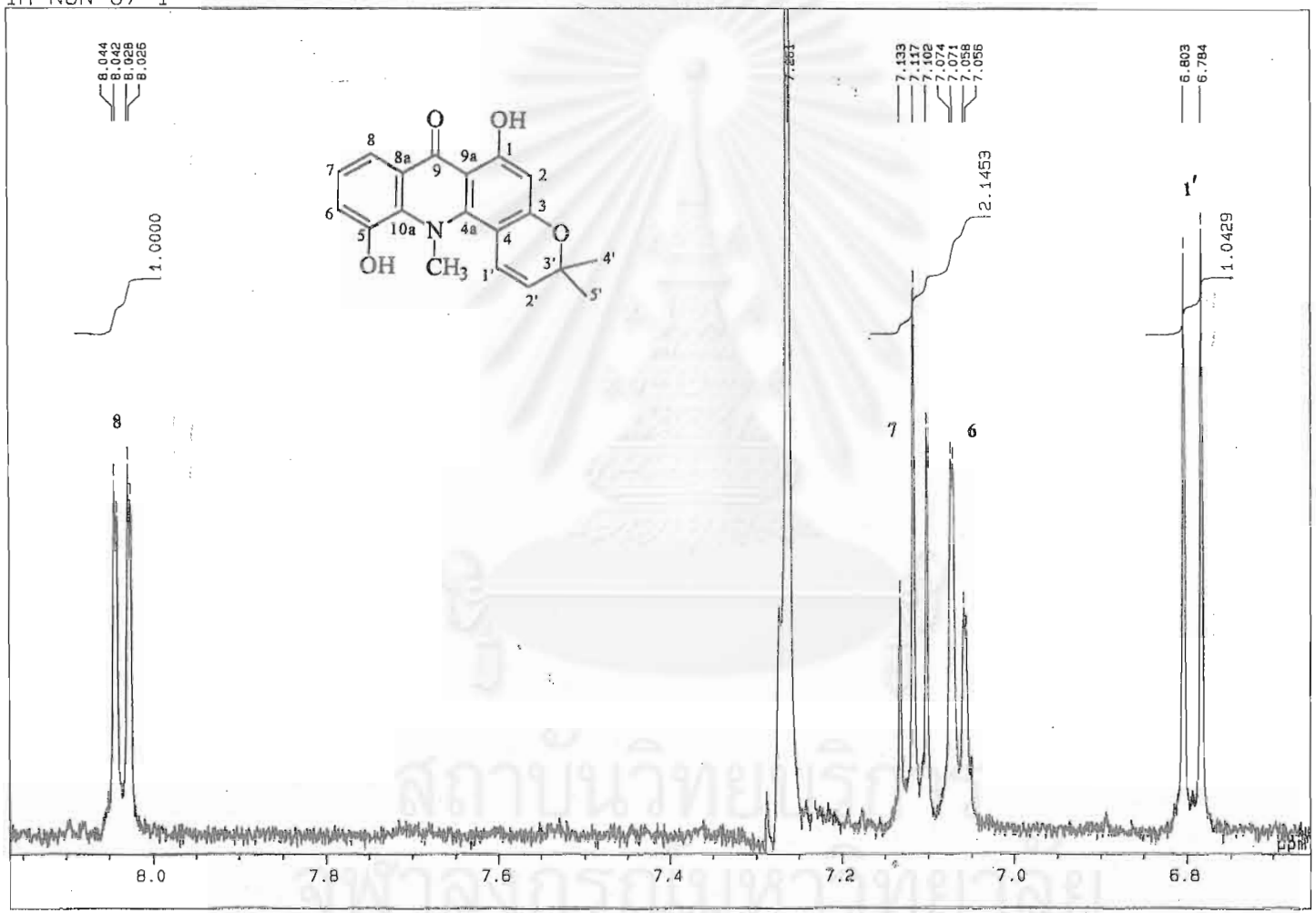


Figure 24b 500 MHz ^{1}H-NMR spectrum of compound j7-1 (in $CDCl_3$)

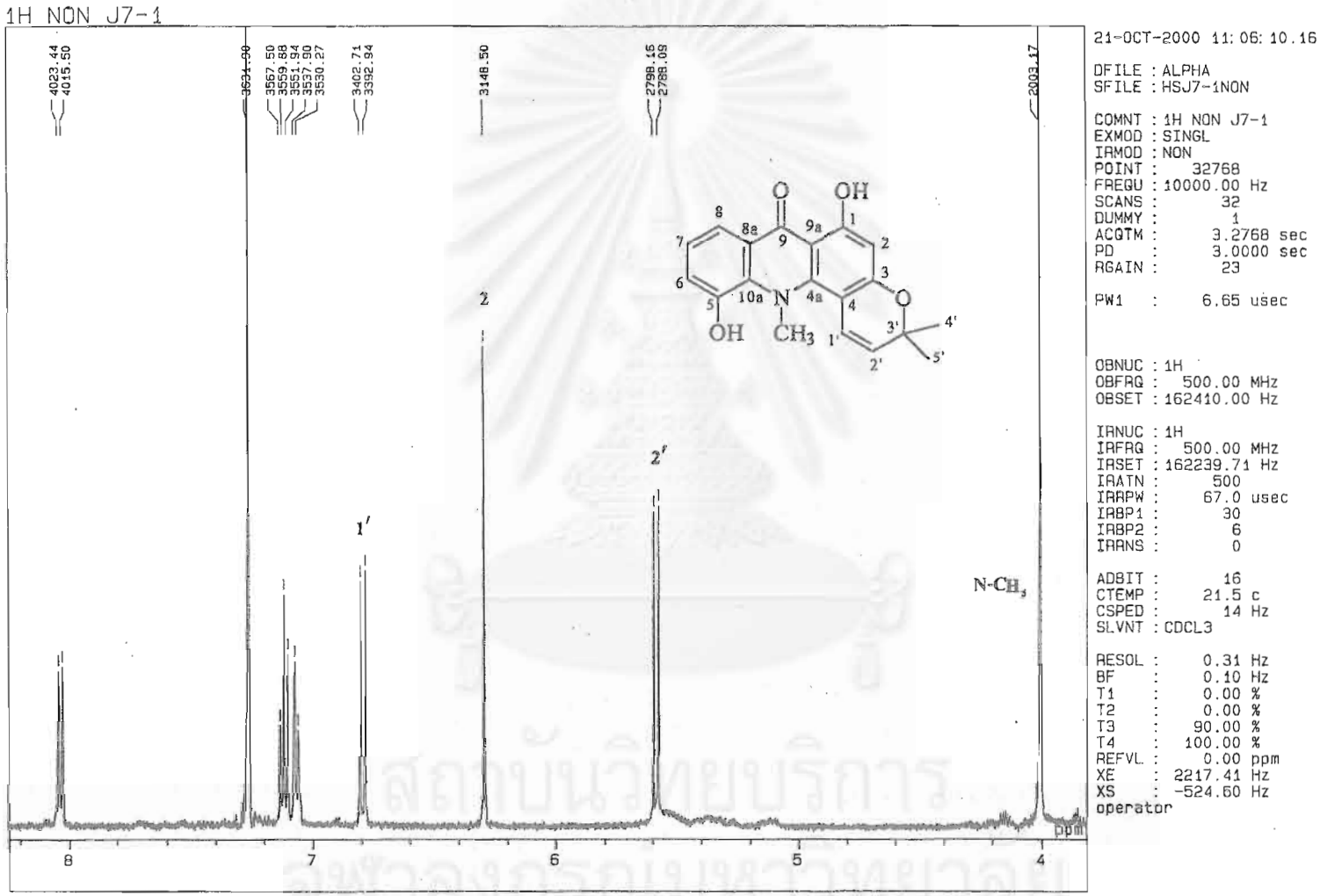
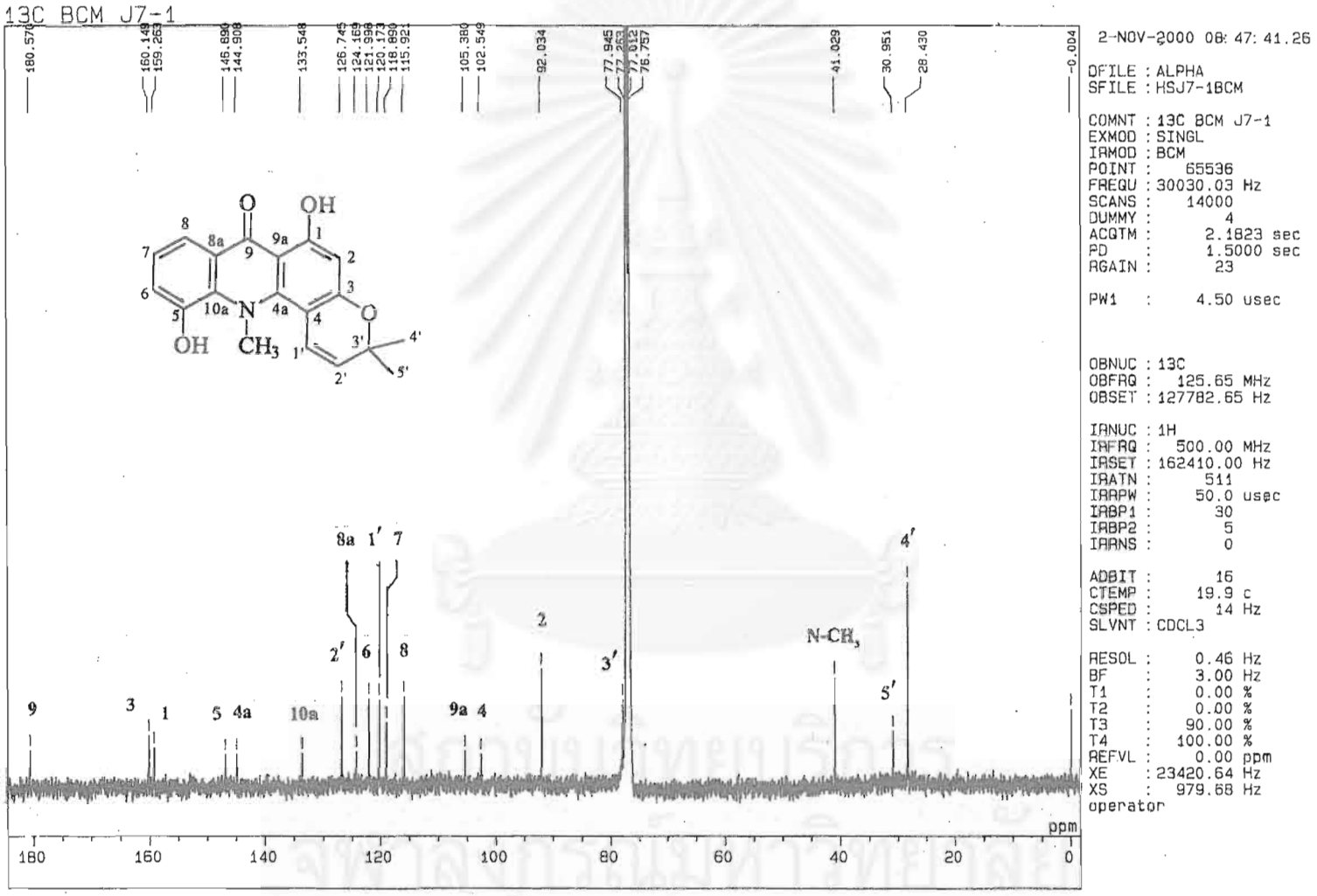


Figure 24c 500 MHz 1H-NMR spectrum of compound j7-1 (in CDCl3)



2-NOV-2000 08:47:41.26

```
DFILE : ALPHA
SFILE : HSJ7-1BCM

COMNT : 13C BCM J7-1
EXMOD : SINGL
IRMOD : BCM
POINT :    65536
FREQU : 30030.03 Hz
SCANS :    14000
DUMMY :        4
ACQTM :   2.1823 sec
PD    :   1.5000 sec
RGAIN :       23

PW1   :    4.50 usec


OBNUC : 13C
OBFRQ :  125.65 MHz
OBSET : 127782.65 Hz

IRNUC : 1H
IRFRQ :  500.00 MHz
IRSET : 162410.00 Hz
IRATN :      511
IRAPW :    50.0 usec
IRBP1 :       30
IRBP2 :        5
IRRNS :        0

ADBIT :       16
CTEMP :     19.9 c
CSPED :       14 Hz
SLVNT : CDCL3

RESOL :     0.46 Hz
BF    :     3.00 Hz
T1    :     0.00 %
T2    :     0.00 %
T3    :    90.00 %
T4    :   100.00 %
REFVL :     0.00 ppm
XE    : 23420.64 Hz
XS    :   979.68 Hz
operator
```

Figure 25 125 MHz ^{13}C-NMR spectrum of compound j7-1 (in $CDCl_3$)

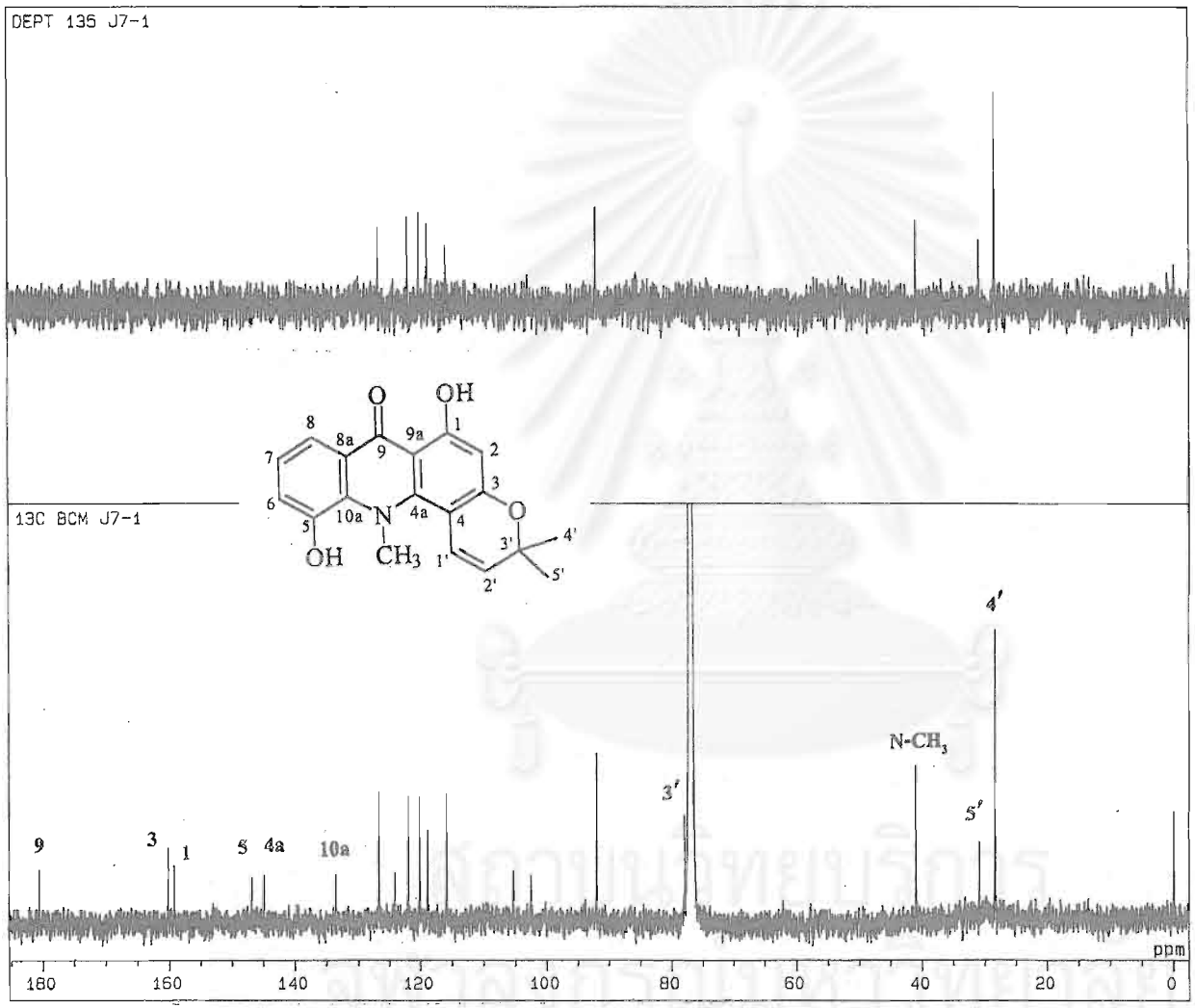


Figure 26a 125 MHz ^{13}C-NMR, DEPT-135 spectra of compound j7-1 (in $CDCl_3$)

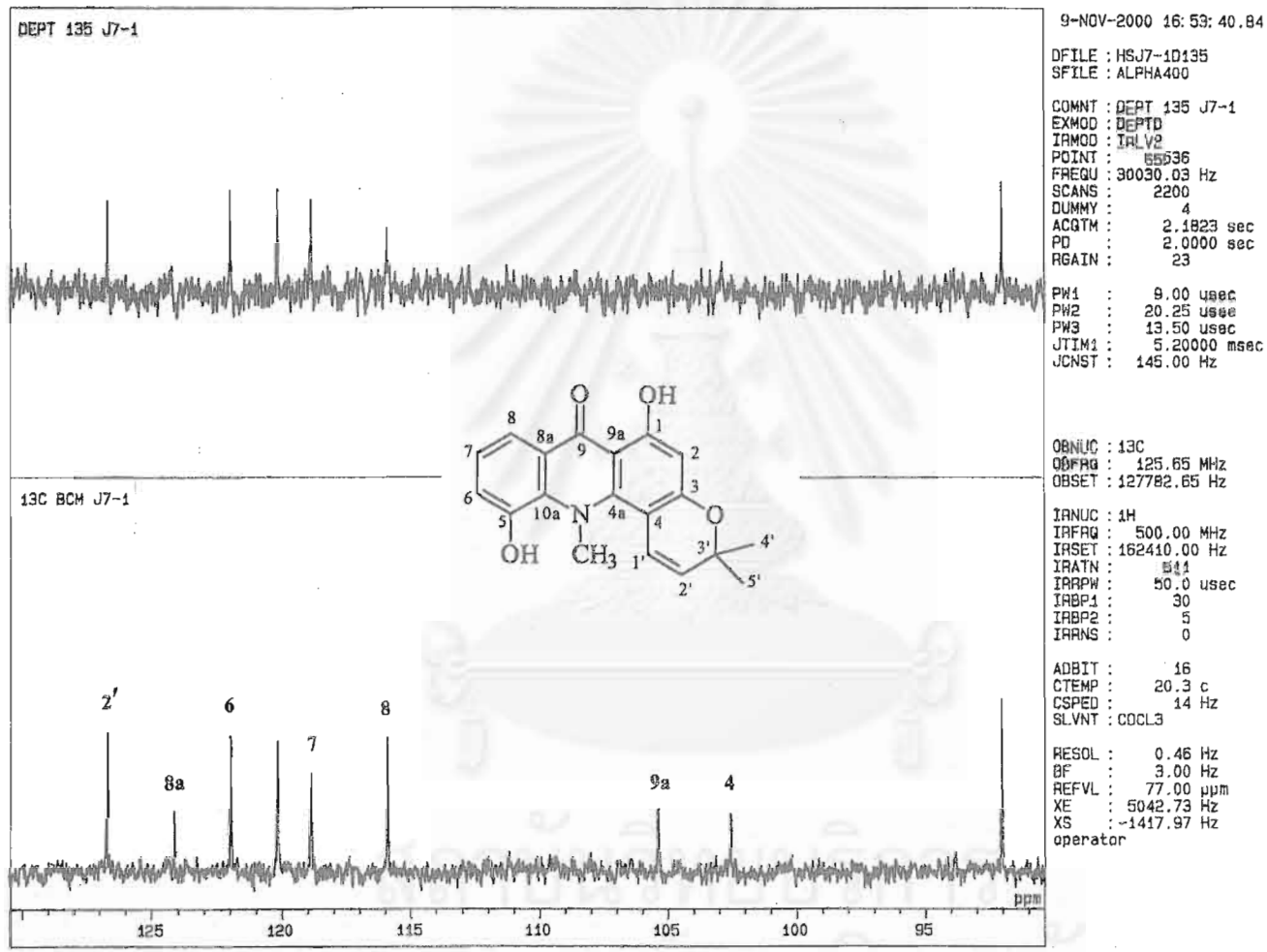


Figure 26b 125 MHz ^{13}C-NMR, DEPT-135 spectra of compound j7-1 (in $CDCl_3$)

(expanded from 91 to 130 ppm)

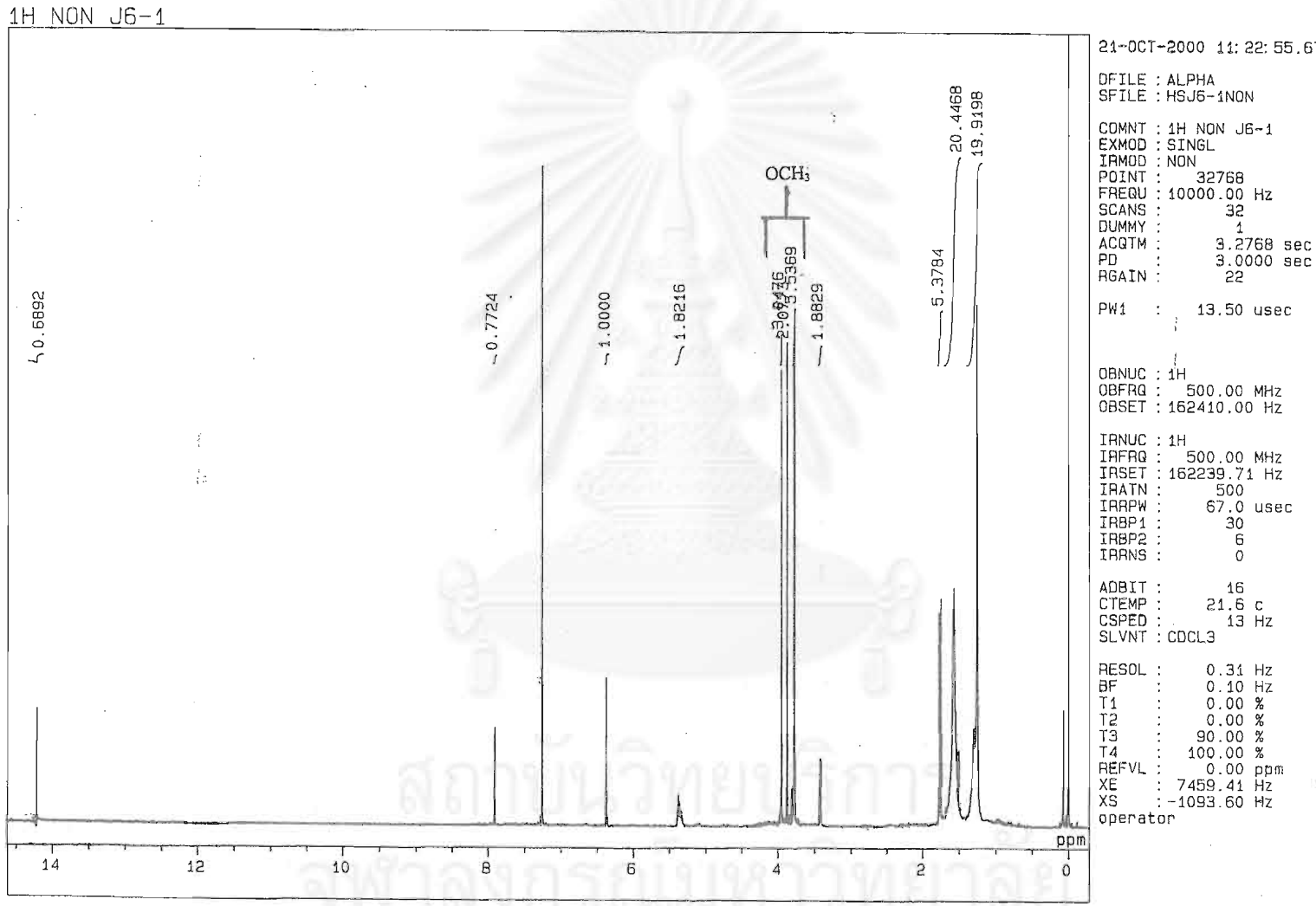


Figure 27a 500 MHz ^{1}H-NMR spectrum of compound j6-1 (in $CDCl_3$)

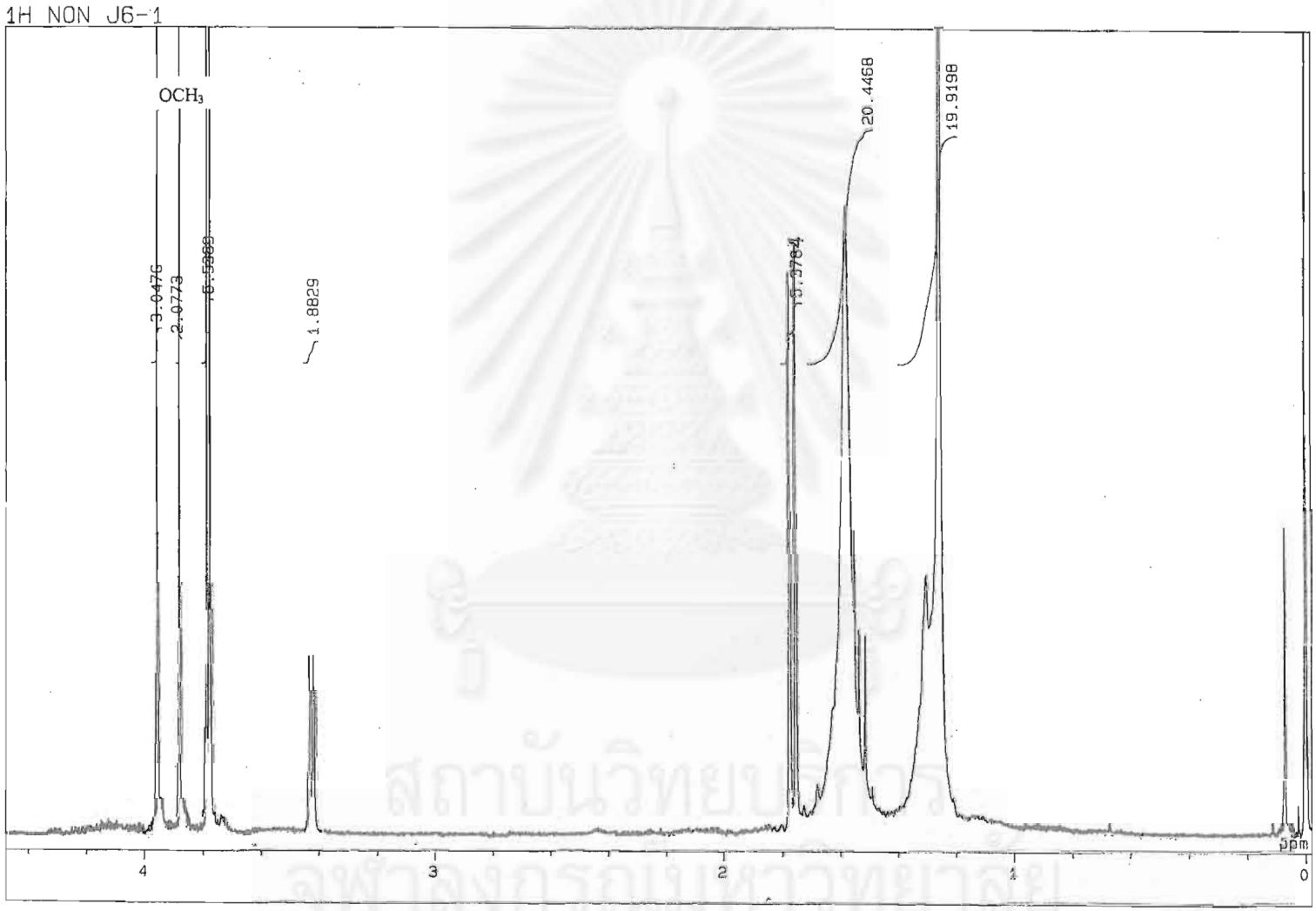


Figure 27b 500 MHz ^{1}H-NMR spectrum of compound j6-1 (in $CDCl_3$)

(expanded from 0 to 4.4 ppm)

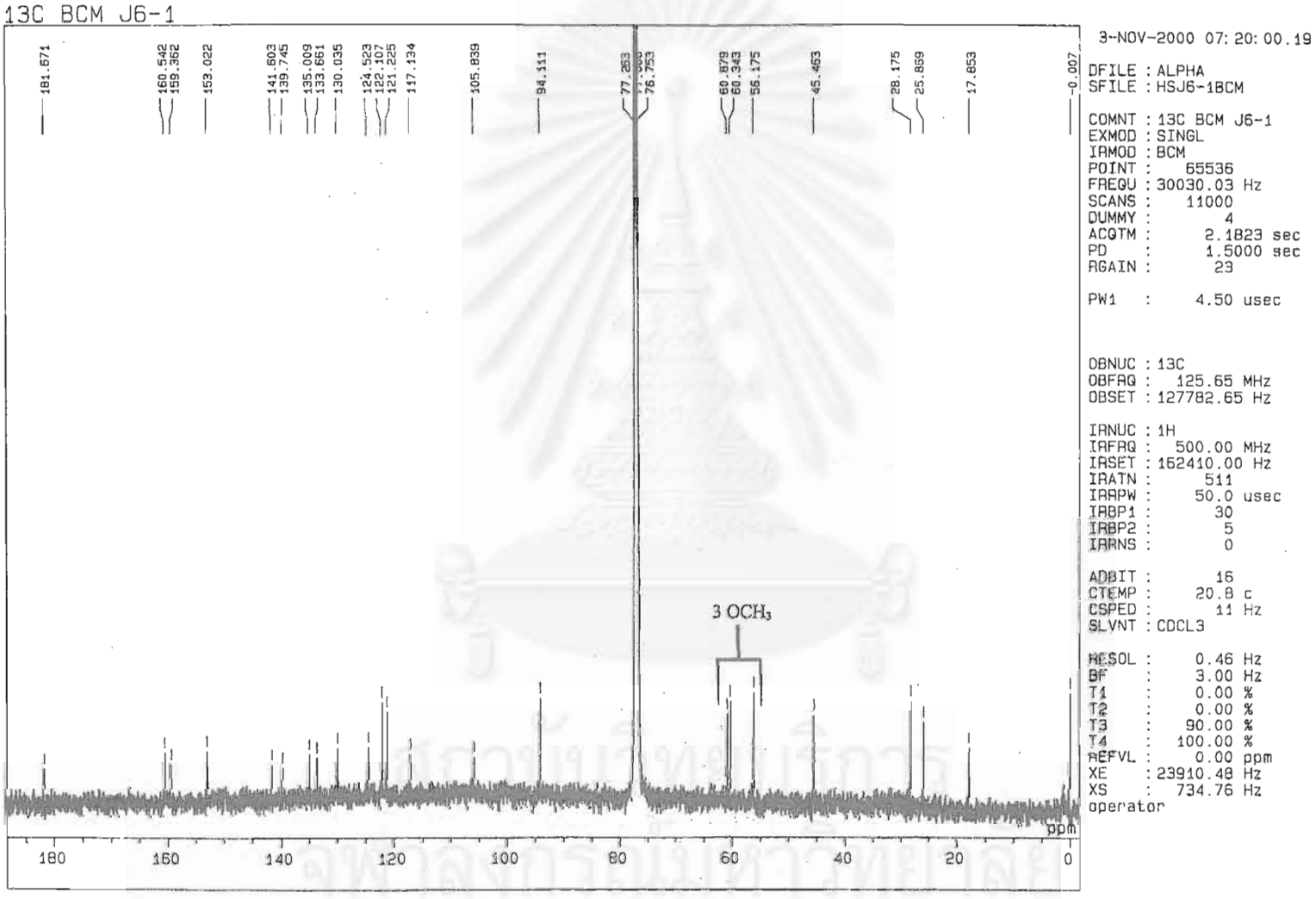


Figure 28 125 MHz ^{13}C-NMR spectrum of compound j6-1 (in $CDCl_3$)

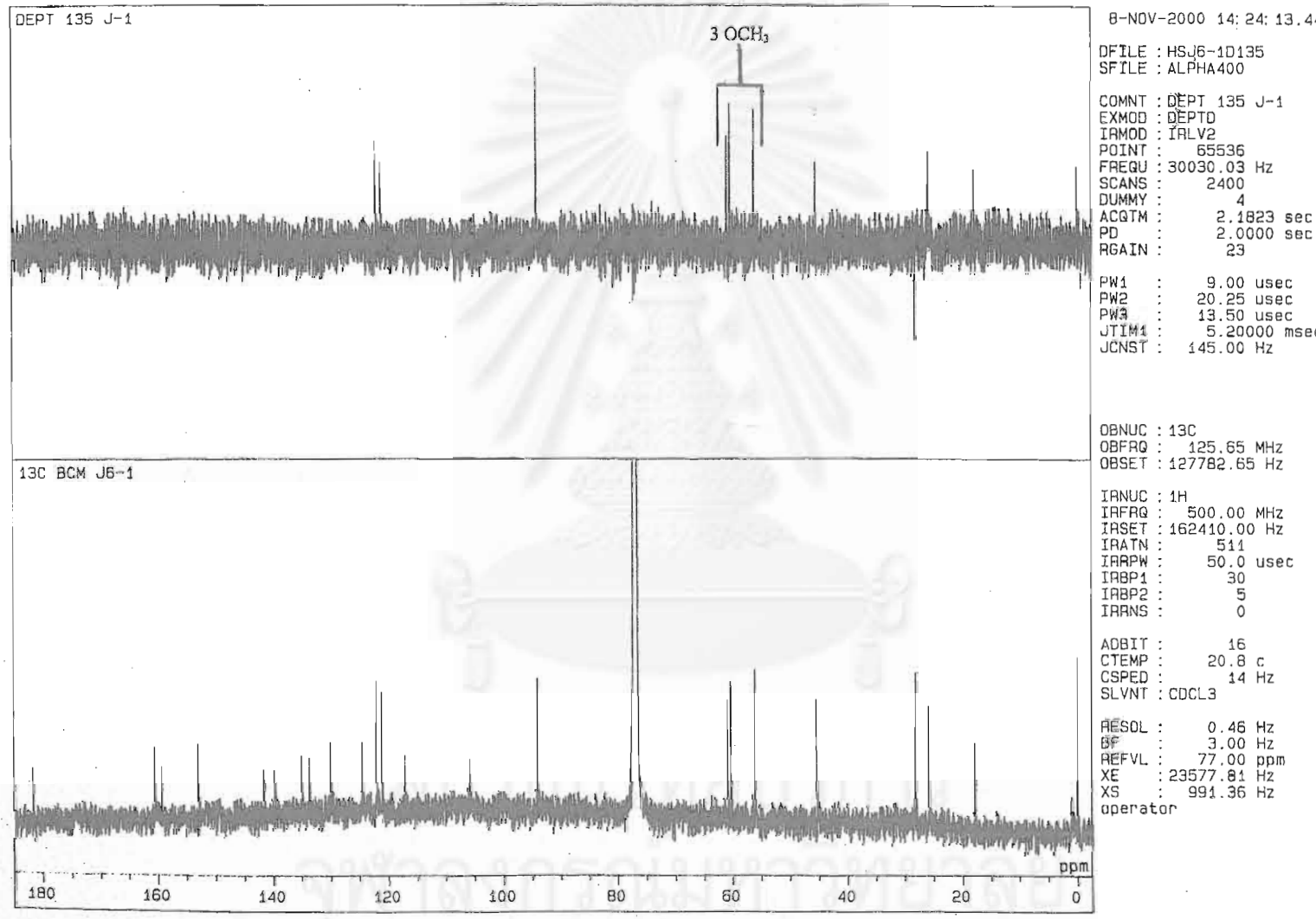


Figure 29 125 MHz ^{13}C-NMR, DEPT-135 spectra of compound j6-1 (in $CDCl_3$)

VITA

Mr. Jakawut Kongsubsopa was born on April 6th, 1975 in Bangkok, Thailand. He received his Bachelor's degree of Science in Pharmacy in 1997 from the Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok, Thailand. After graduation, he had worked as the Medical Representative of the Pharmaceutical sector, Novartis (Thailand) Limited for 2 years. During his master degree study in the Department of Pharmacognosy, Faculty of Pharmaceutical Sciences, Chulalongkorn University, he received the Chiba-Chulalongkorn University Student Exchange Program Scholarship for the study program in Chiba University, Japan.