พฤกษเคมีและฤทธิ์ทางชีวภาพของลำต้นตากวางและม้ากระทืบโรง

นายปฐม โสมวงศ์

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรดุษฎีบัณฑิต
สาขาวิชาเภสัชเวท ภาควิชาเภสัชเวทและเภสัชพฤกษศาสตร์
คณะเภสัชศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย
ปีการศึกษา 2555

PHYTOCHEMISTRY AND BIOACTIVITIES OF *SALACIA VERRUCOSA* AND *FICUS FOVEOLATA* STEMS

Mr. Pathom Somwong

A Dissertation submitted in Partial Fulfillment of the Requirements
for the Degree of Doctor of Philosophy Program in Pharmacognosy
Department of Pharmacognosy and Pharmaceutical Botany
Faculty of Pharmaceutical Sciences
Chulalongkorn University
Academic Year 2012

Thesis Title	PHYTOCHEMISTRY AND BIOACTIVITIES OF *SALACIA VERRUCOSA* AND *FICUS FOVEOLATA* STEMS
By	Mr. Pathom Somwong
Field of Study	Pharmacognosy
Thesis Advisor	Associate Professor Rutt Suttisri, Ph.D.

Accepted by the Faculty of Pharmaceutical Sciences, Chulalongkorn University in Partial Fulfillment of the Requirements for the Doctor's Degree

……………………………………………Dean of the Faculty of Pharmaceutical Sciences
(Associate Professor Pintip Pongpech, Ph.D.)

THESIS COMMITTEE

……………………………………………Chairman
(Professor Kittisak Likhitwitayawuid, Ph.D.)
……………………………………………Thesis Advisor
(Associate Professor Rutt Suttisri, Ph.D.)
……………………………………………Examiner
(Associate Professor Surattana Amnuoypol, Ph.D.)
……………………………………………Examiner
(Witchuda Thanakijcharoenpath, Ph.D.)
……………………………………………External Examiner
(Duangpen Pattamadilok, Ph.D.)

ปฐม โสมวงศ์: พฤกษเคมีและฤทธิ์ทางชีวภาพของลำต้นตากวางและม้ากระทืบโรง (PHYTOCHEMISTRY AND BIOACTIVITIES OF *SALACIA VERRUCOSA* AND *FICUS FOVEOLATA* STEMS) อ. ที่ปรึกษาวิทยานิพนธ์หลัก : รศ.ดร.รุทธ์ สุทธิศรี, 262 หน้า.

การศึกษาองค์ประกอบทางเคมีของลำต้นตากวาง (*Salacia verrucosa* Wight) วงศ์ Celastraceae สามารถแยกสารใหม่ในกลุ่ม 1,3-diketofriedelane triterpeneได้ 1 ชนิดคือ 21α-hydroxyfriedelane-1,3-dione และที่เคยมีรายงานแล้ว 3 ชนิดคือ friedelane-1,3-dione, 26-hydroxyfriedelane-1,3-dione และ 30-hydroxyfriedelane-1,3-dione, สารในกลุ่ม friedelane triterpene 3 ชนิดคือ friedelin, kokoonol และ 21α-hydroxyfriedelan-3-one และ สารในกลุ่ม oleanane triterpene 1 ชนิดคือ 3β,22α-dihydroxyolean-12-en-29-oic acid สำหรับการศึกษาองค์ประกอบทางเคมีของลำต้นม้ากระทืบโรง [*Ficus foveolata* (Wall. ex Miq.) Miq.] วงศ์ Moraceae สามารถแยกสารใหม่ในกลุ่ม eudesmane sesquiterpene ได้ 2 ชนิดคือ foveolide A และ foveoeudesmenone และที่เคยมีรายงานแล้ว 2 ชนิดคือ 4(15)-eudesmene-1β,6α-diol และ 4(15)-eudesmene-1β,5α-diol, สารใหม่ในกลุ่ม sesquiterpenoid dimer 1 ชนิดคือ foveolide B, สารใหม่ในกลุ่ม phenolic 1 ชนิดคือ foveospirolide และที่เคยมีรายงานแล้ว 1 ชนิดคือ ethyl rosmarinate นอกจากนี้ยังพบสารในกลุ่ม triterpene 3 ชนิดคือ friedelin, taraxerol และ betulin พิสูจน์โครงสร้างทางเคมีขององค์ประกอบของพืชเหล่านี้โดยอาศัยการวิเคราะห์เชิงสเปกตรัมด้วย UV, IR, MS และ NMR ร่วมกับการเปรียบเทียบข้อมูลที่เคยมีรายงานมาก่อนแล้ว

สาร friedelane-1,3-dione มีความเป็นพิษระดับสูงต่อเซลล์มะเร็งลำไส้ของมนุษย์ (SW620) ด้วยค่า IC_{50} 2.02 ไมโครโมลาร์ ในขณะที่สาร 26-hydroxyfriedelane-1,3-dione และ 21α-hydroxyfriedelan-3-one มีความเป็นพิษในระดับปานกลางต่อเซลล์มะเร็งลำไส้, เซลล์มะเร็งตับ (HepG2) และ เซลล์มะเร็งกระเพาะอาหาร (KATO-III) นอกจากนี้สาร 26-hydroxyfriedelane-1,3-dione ยังแสดงความเป็นพิษระดับปานกลางต่อเซลล์มะเร็งปอด (CHAGO) และเซลล์มะเร็งเต้านม (BT474) สาร foveolide A แสดงความเป็นพิษระดับปานกลางต่อเซลล์มะเร็งลำไส้, เซลล์มะเร็งตับ, เซลล์มะเร็งเต้านม และเซลล์มะเร็งกระเพาะอาหาร ขณะที่สาร foveolide B แสดงความเป็นพิษระดับปานกลางเฉพาะต่อเซลล์มะเร็งลำไส้ นอกจากนี้สาร foveolide A ยังแสดงฤทธิ์ต้านเชื้อวัณโรค *Mycobacterium tuberculosis* โดยมีค่าความเข้มข้นต่ำสุดที่สามารถยับยั้งเชื้อได้คือ 200 ไมโครโมลาร์

ภาควิชา เภสัชเวทและเภสัชพฤกษศาสตร์ ลายมือชื่อนิสิต..
สาขาวิชา เภสัชเวท ลายมือชื่อ อ.ที่ปรึกษาวิทยานิพนธ์หลัก..........................
ปีการศึกษา 2555

#5276952633: MAJOR PHARMACOGNOSY

KEYWORDS: *SALACIA VERRUCOSA* / CELASTRACEAE / *FICUS FOVEOLATA* / MORACEAE / CYTOTOXICITY

PATHOM SOMWONG: PHYTOCHEMISTRY AND BIOACTIVITIES OF *SALACIA VERRUCOSA* AND *FICUS FOVEOLATA* STEMS. ADVISOR: ASSOC.PROF. RUTT SUTTISRI, Ph.D., 262 PP.

Chemical investigation of the stems of *Salacia verrucosa* Wight (family Celastraceae) led to the isolation of one new (21α-hydroxyfriedelane-1,3-dione) and three known 1,3-diketofriedelane triterpenes (friedelane-1,3-dione, 26-hydroxyfriedelane-1,3-dione and 30-hydroxyfriedelane-1,3-dione), three friedelane-type triterpenes (friedelin, kokoonol and 21α-hydroxyfriedelan-3-one), and one oleanane-type triterpene (3β,22α-dihydroxyolean-12-en-29-oic acid). From the stems of *Ficus foveolata* (Wall. ex Miq.) Miq. (family Moraceae), two new (foveolide A and foveoeudesmenone) and two known eudesmane-type sesquiterpenes [4(15)-eudesmene-1β,6α-diol and 4(15)-eudesmene-1β,5α-diol], a new sesquiterpenoid dimer (foveolide B), one new (foveospirolide) and one known phenolic compound (ethyl rosmarinate), together with three known triterpenes (friedelin, taraxerol and betulin) were isolated. The chemical structures of these plant constituents were determined by spectroscopic analyses, including UV, IR, MS and NMR, and comparison with previously reported data.

Friedelane-1,3-dione was strongly cytotoxic against human colon cancer cell line (SW620) with an IC_{50} value of 2.02 μM, whereas 26-hydroxyfriedelane-1,3-dione and 21α-hydroxyfriedelan-3-one were moderately cytotoxic against colon, liver (HepG2) and gastric (KATO-III) cancer cell lines. 26-Hydroxyfriedelane-1,3-dione also exhibited moderate cytotoxicity against lung (CHAGO) and breast (BT474) cancer cell lines. Foveolide A was moderately cytotoxic against colon, liver, breast and gastric cancer cell lines, while foveolide B was specifically cytotoxic toward colon cancer cell line. In addition, foveolide A exhibited anti-tuberculosis activity against *Mycobacterium tuberculosis* with a minimum inhibitory concentration of 200 μM.

Department: Pharmacognosy and Pharmaceutical Botany Student's signature……………………

Field of Study: Pharmacognosy Advisor's signature……………………

Academic Year: 2012

ACKNOWLEDGEMENTS

I would like to express my deepest gratitude to my thesis advisor, Associate Professor Dr. Rutt Suttisri of the Department of Pharmacognosy and Pharmaceutical Botany, Faculty of Pharmaceutical Sciences, Chulalongkorn University. I greatly appreciate his valuable advice, kindness, patience, and constant encouragement throughout my research study.

My appreciations are extended to Professor Dr. Masataka Moriyasu and Associate Professor Dr. Kazuko Kawanishi of the Department of Natural Medicinal Chemistry, Kobe Pharmaceutical University, for their kindness, hospitality and guidance during my research experience at Kobe Pharmaceutical University, Kobe, Japan.

I would like to thank members of my thesis committee, including Professor Dr. Kittisak Likhitwitayawuid, Associate Professor Dr. Surattana Amnuoypol, Dr. Witchuda Thanakijcharoenpath, and Dr. Duangpen Pattamadilok, for their critical review and constructive suggestions for this thesis.

I am grateful for the financial support from a Royal Golden Jubilee Ph. D. scholarship (grant no. PHD/0268/2550) from Thailand Research Fund (TRF).

I would like to thank Mr. Anumart Buakeaw of the Institute of Biotechnology and Genetic Engineering, Chulalongkorn University, for his assistance in the *in vitro* cytotoxicity assay.

My appreciation is also extended to the Faculty of Pharmacy, Rangsit University, for continuing support during my graduate study.

I am thankful to all staff members and other graduate students of the Department of Pharmacognosy and Pharmaceutical Botany, Faculty of Pharmaceutical Sciences, Chulalongkorn University, for their assistance, friendship and kind support throughout the period of my study.

Finally, I would like to express my special and deepest appreciation to my family for their love, understanding and encouragement.

CONTENTS

CHAPTER **Page**

CHAPTER **Page**

CHAPTER **Page**

LIST OF TABLES

Table **Page**

Table **Page**

LIST OF FIGURES

Figure **Page**

Figure **Page**

Figure **Page**

Figure **Page**

LIST OF SCHEMES

LIST OF ABBREVIATIONS

acetone-d_6 = Deuterated acetone

α = Alpha

β = Beta

br s = Broad singlet (for NMR spectra)

^{o}C = Degree Celsius

Calc = Calculate

CC = Column chromatography

$CDCl_3$ = Deuterated chloroform

CD_3OD = Deuterated methanol

CH_2Cl_2 = Dichloromethane

cm = Centimeter

cm^{-1} = Reciprocal centimeter (unit of wave number)

^{13}C NMR = Carbon-13 Nuclear Magnetic Resonance

DEPT = Distortionless Enhancement by Polarization Transfer

2D NMR = Two dimensional Nuclear Magnetic Resonance

d = Doublet (for NMR spectra)

dd = Doublet of doublets (for NMR spectra)

ddd = Doublet of doublets of doublets (for NMR spectra)

dddd = Doublet of doublets of doublets of doublets (for NMR spectra)

DMSO = Dimethyl sulfoxide

δ = Chemical shift

ε = Molar absorptivity

ESI-MS = Electrospray Ionization Mass Spectrometry

EtOAc = Ethyl acetate

Fu_c = Fluorescent unit from untreated

Fu_t = Fluorescent unit from treated

g = Gram

h = Hour

^{1}H NMR = Proton Nuclear Magnetic Resonance

^{1}H-^{1}H COSY = Homonuclear (Proton-Proton) Correlation Spectroscopy

HMBC = ^{1}H-detected Heteronuclear Multiple Bond Coherence

HR = High Resolution

HSQC = Heteronuclear Single Quantum Correlation

Hz = Hertz

IC_{50} = Median Inhibitory Concentration

IR = Infrared

J = Coupling constant

KBr = Potassium bromide

Kg = Kilogram

L = Liter

λ_{max} = Wavelength at maximal absorption

µg = Microgram

µg/ml = Microgram per milliliter

µl = Microliter

$[M]^+$ = Molecular ion

$[M+H]^+$ = Pseudomolecular ion

$[M+Na]^+$ = Pseudomolecular ion

$[M+H+Na]^+$ = Pseudomolecular ion

m = Multiplet (for NMR spectra)

MeOH = Methanol

mg = Milligram

MHz = Megahertz

MIC = Minimum inhibitory concentration

min = Minute

ml = Milliliter

mm = Millimeter

mp = Melting point

MS = Mass Spectrometry

MW = Molecular weight

m/z = Mass to charge ratio

Na = Sodium

ν_{max} = Wave number at maximal absorption

nm = Nanometer

NMR = Nuclear Magnetic Resonance

NOESY = Nuclear Overhauser Enhancement Spectroscopy

OD = Optical density

PBS = Phosphate buffered saline

ppm = Part-per-million

q = Quartet (for NMR spectra)

rel int = Relative intensity

s = Singlet (for NMR spectra)

t = Triplet

td = Triplet of doublets (for NMR spectra)

TLC = Thin Layer Chromatography

TOF = Time of flight

UV = Ultraviolet

CHAPTER I

INTRODUCTION

Several members of the family Celastraceae have been traditionally used as medicinal plants. Many of them belong to the genus *Salacia* which has been found throughout. For example, the decoction of *S. reticulata* roots is used in the treatment of gonorrhea, rheumatism, skin diseases, itching and swelling, hemorrhoids, asthma, amenorrhoea and dysmenorrhoea (Arunakumara and Subasinghe, 2010). *Salacia* species (e.g. *S. chinensis*, *S. oblonga*, *S. reticulata*), known as ‘Ponkoranti’ in Ayurvedic medicine, are widely distributed in India and Sri Lanka (Li, Huang, and Yamahara, 2008) and these species have been used in the treatment of diabetes (Matsuda *et al*., 2005; Mukherjee *et al*., 2006; Li *et al*., 2008). Further investigation into the anti-diabetic activity of the extract of *S. oblonga* in patients with type 2 diabetes showed that it could lower acute glycemia and insulinemia after high carbohydrate consumption (Williams *et al*., 2007). In addition, *S. oblonga* also displayed anti-inflammatory activity *in vivo* by inhibiting the formation of mediators of inflammation (Ismail *et al*., 1997). The chloroform and alcoholic extract of *S. chinensis* roots possessed significant antihyperlipidemic activity in triton-induced and atherogenic diet-induced hyperlipidemic rats (Sikarwar and Patil, 2012). These *Salacia* species are an important source of medicinal compounds, which are effective as antidiabetic, antiobesity, hypolipidemic, hepatoprotective and antioxidant agents (Paarakh, Patil, and Thanga, 2008).

Moraceae is another important plant family of which several members of its genera have been utilized as medicinal plants; some with similar indications as plants belonging to the family Celastraceae. Members of this family that have been used traditionally include plants in the genus *Ficus* (fig). A number of *Ficus* species are generally used as food and for their medicinal properties in Ayurvedic and traditional Chinese medicine (Lansky *et al*., 2008). In India, decoction of *F. religiosa* bark has been used as a treatment for various disorders such as fever, gonorrhea and skin diseases; its leaf juice has also been used to treat asthma and cough (Makhija, Sharma, and Khamar, 2010). The plant is also a good source of traditional medicine for the treatment of diabetes, diarrhea, epilepsy, gastric problems, inflammatory and infectious disorders

(Singh, Singh, and Goel, 2011). Powdered *F. racemosa* leaves, mixed with honey, are given in bilious infections and its fruits are useful in regulating diarrhea and constipation (Joseph and Raj, 2010). In Nepal, powdered *F. foveolata* bark is taken as a cure for boils and to promote milk secretion during child birth (Kunwar and Bussmann, 2006).

In Thailand, several plants belonging to both families have been employed as medicinal plants, especially in the northeastern part. Celastraceous plants that have been utilized in traditional medicine include *Euonymus cochinchinensis* Craib (Thai name: Nang yai, Maha kanang), *Siphonodon celastrineus* Griff. (Thai name: Duk khao, Ma duk), *Salacia chinensis* L. (Thai name: Ta kai, Kamphaeng chet chan) and *Salacia verrucosa* Wight (Thai name: Ta kwang, Kamphaeng kao chan), whereas members of the family Moraceae popular in herbal medicine are *Ficus hispida* L.f. (Thai name: Ma duea plong), *Ficus racemosa* L. (Thai name: Ma duea uthumphon), *Ficus foveolata* (Wall. ex Miq.) Miq. (Thai name: Ma kra thuep rong) and *Maclura cochinchinensis* Corner (Thai name: Khe, Wua thaloeng). Different parts of these medicinal plants (e.g. stems, leaves and roots) are used as crude drugs and ingredients in medicinal preparations (Chuakul, Saralamp, and Boonpleng, 2002). In northeastern Thailand, crude drugs derived from the stems of these plants are frequently used. For example, the decoctions of *S. chinensis* and *S. verrucosa* stems are prescribed as laxative, whereas the alcoholic maceration of *F. foveolata* stems, prepared solely or mixed with other herbal ingredients, is taken as a tonic (Suksri *et al*., 2005).

Based on traditional uses of *Salacia* species, many researches were conducted in order to investigate their active compounds and biological activities. Potent α-glucosidase inhibitors, which are thiosugars sulfonium sulfate such as kotalanol (Matsuda *et al*., 1999; Yoshikawa *et al*., 2008a), ponkoranol (Yoshikawa *et al*., 2008a), salacinol (Matsuda *et al*., 1999; Yoshikawa *et al*., 1997, 2008a) and salaprinol (Yoshikawa *et al*., 2008a), were isolated from *S. oblonga*, *S. prinoides* and *S. reticulata*. Several investigated *Salacia* species yielded various triterpenoid compounds, which possessed significant biological activities including antimalarial (Figueiredo, Raz, and Sequin, 1998), antileishmanial (Thiem *et al*., 2005), antileukemic (Sneden, 1981), cytotoxic (Setzer *et al*., 2001; Minh *et al*., 2010), aldose reductase (Matsuda *et al*., 1999; Morikawa *et al*., 2003), and α-glucosidase inhibitory (Gao *et al*., 2010; Huang *et al*., 2012) and radical scavenging activities (Kishi *et al*., 2003). Furthermore, phytochemical studies of *S.*

chinensis have revealed various types of triterpenoid constituents such as the salasones (friedelane-type) (Kishi *et al*., 2003; Morikawa *et al*., 2003), foliasalacin A (dammarane-type), foliasalacin B (lupane-type), foliasalacin C (oleanane-type) (Yoshikawa *et al*., 2008b) and foliasalacin D (baccharane-type) (Zhang *et al*., 2008b). In addition, eudesmane-type sesquiterpenes, i.e. the salasols (Kishi *et al*., 2003; Morikawa *et al*., 2003), megastigmane glycosides, i.e. the foliasalaciosides (Nakamura *et al*., 2008a, 2011; Zhang *et al*., 2008a) and phenolic glycosides, i.e. the foliachinenosides (Nakamura *et al*., 2008b), were also isolated from this plant.

A series of works on *Ficus* species demonstrated various bioactive chemical constituents including antimalarial macrocyclic trichothecene sesquiterpenoids from the leaves and stem bark of *F. fistulosa* (Zhang *et al*., 2002), anti-inflammatory phenolic glucosides from the bark of *F. racemosa* (Li *et al*., 2004), antimicrobial triterpenes and isoflavones from the stem bark of *F. ovata* (Kuete *et al*., 2009), insecticidal and antifungal flavonoids and coumarins from the leaves and stems of *F. sarmentosa* var. *henryi* (Wang *et al*., 2010, 2011b). Several of these studies on *Ficus* species focused on anticancer and anti-inflammatory activities (Lansky *et al*., 2008). Different types of compounds such as triterpenes from *F. microcarpa* (Chiang *et al*., 2005), flavonoids and chromenes from *F. formosana* f. *formosana* (Sheu *et al*., 2005), phenanthroindolizidine alkaloids from *F. septica* (Wu *et al*., 2002; Damu *et al*., 2005, 2009) and a ceramide from *F. elastica* (Mbosso *et al*., 2012) demonstrated significant cytotoxicity against cancer cell lines *in vitro*. Recently, stilbenoid compounds isolated from the methanolic extract of *F. foveolata* stems were able to potently inhibit butyrylcholinesterase, an enzyme involved in the etiology of Alzheimer's disease (Sermboonpaisarn and Sawasdee, 2012).

From these literature data, it can be observed that members of *Salacia* and *Ficus* genera are important Asian medicinal plants and their utilization in traditional medicine is also widespread throughout Thailand. However, although chemical and biological studies of these plants have been widely performed, phytochemical study of two well-known Thai medicinal plants such as *S. verrucosa* and *F. foveolata* has rarely been conducted. A previous study of *S. verrucosa* stems reported the presence of three friedelane-type triterpenes and one sugar (Jangruang *et al*., 2009), whereas the similar investigation of *F. foveolata* stems demonstrated four stilbenes, four flavonoids, one alkyl ferulate and a mixture of two alkyl diferulates

(Sermboonpaisarn and Sawasdee, 2012). Therefore, these two plants were selected for further investigation of their chemical constituents and biological activities. The phytochemical data obtained in this study would contribute to the knowledge on chemotaxonomy of these plant families and would be valuable information in the studies of Thai medicinal plants.

The purposes of this research were as follows:

1. Isolation and purification of compounds from the stems of *S. verrucosa* and *F. foveolata*.
2. Determination of chemical structures and physical properties of each isolated compound.
3. Evaluation of biological activities of the isolated compounds

CHAPTER II

HISTORICAL

1. Family Celastraceae

Celastraceae is the dicotyledonous plants belonging to the order Celastrales (including Hippocrateaceae). Members of plants in this family can be found in both hemispheres except the arctic regions, predominantly distributed in the tropics and subtropics. Plants in the family of Celastraceae, including trees and erect or scandent shrubs, were classified into 90 genera and over 1,000 species (Mabberley, 1990). Fruit of the family is often colourful. Leaves are frequently leathery and flowers are small, with four to five sepals and petals; alternating between the petals, stamens rise from a usually conspicuous nectar disk (Celastraceae, 2013). In Thailand, there are 16 genera consisting of 58 species with several subspecies and varieties (Hou, Savinov, and Van Welzen, 2010). Examples of plant genera belonging to this family that can be found are *Euonymus, Siphonodon*, *Celastrus*, *Kokoona* and *Salacia*. Several plants of this family have been used in traditional medicine of different countries and one of them, i.e. the genus *Salacia*, has been reported as Thai medicinal plants (Chuakul *et al*., 2002; Suksri *et al.*, 2005).

2. Genus *Salacia*

The genus *Salacia*, native to tropical Asia and India, comprises about 200 species. Eleven of these species can be found in evergreen and deciduous forests throughout Thailand. *Salacia* plant is usually climbing shrub or, rarely, small tree. Their leaves are opposite decussate, glabrous and entire. The flowers are in axillary fascicles or on very short bracteate tubercles, in cymes, panicles or thyrses and are bisexual. The calyx is deeply 5-lobed. The numbers of petals are 4-7, imbricate or erect. The stamens are 3 or 2, with slender filaments tapering to the anthers, which mostly open transversely. The ovary, partly or completely immersed in the disc, has 3 or 2 locules with 2-8 ovules in each locule. The subglobose or drupaceous fruits have 1-3 locules with coriaceous pericarp when dried. The seeds usually are 1 to several, embedded in mucilaginous pulp (Hou *et al*., 2010).

Salacia species found growing in Thailand have been recorded as follows (Royal Forest Department, 2001; Hou *et al*., 2010).

1. *S. chinensis* L. (Thai name: Kamphaeng chet chan)
2. *S. dongnaiensis* Pierre
3. *S. grandiflora* Kurz (Thai name: Ta som)
4. *S. korthalsiana* Miq. (Thai name: Kamphaeng talang)
5. *S. laotica* Pit.
6. *S. macrophylla* Blume (Thai name: Sadao yen)
7. *S. noronhioides* Pierre (Thai name: Krado yen)
8. *S. oblongifolia* Blume (Thai name: Sadao hot)
9. *S. rostrata* Pierre
10. *S. verrucosa* Wight (Thai name: Ta kwang)
11. *S. viminea* Wall. ex M.A. Lawson (Thai name: Sadao tan)

3. *Salacia verrucosa* Wight

The plant is a straggling shrub (up to 4 m tall) or, rarely, small tree (up to 9 m tall). Its branches are usually densely covered with lenticels. The leaves are opposite or opposite decussate. The leaf texture is usually subcoriaceous. Their shape is elliptic or obovate, 8-20 by 4-7.5 cm. The leaf base is cuneate or obtuse, while the apex is short-acuminate. The leaf margin is slightly crenulate with 6-10 veins per side. The petiole is 3-10 mm long. The flowers are several to many on short, bracteate tubercles. The pedicels are 9-14.5 mm long. The calyx lobes are slightly erose or shortly fimbriate, about 1 mm long. The petals are broad-elliptic or obovate, 2-3 by 1.5-2 mm. The receptacle disk is round, flat and slightly concave at the center, with the margin slightly extended outward into a narrow membranous rim, about 1.5 mm in diameter. The stamens are 3, about 0.5 mm long. The ovary has 3 locules with 2 ovules in each locule. The subglobose fruits are 2.5-3.5 cm in diameter with orange or red colors. The ellipsoid seeds are about 1.5-1.8 by 1-1.5 cm (Hou *et al*., 2010).

The habitat of *S. verrucosa* is in the evergreen and deciduous forests of India, Myanmar, Laos, Cambodia, Vietnam, Malaysia, Indonesia and Philippines. In Thailand, this plant is distributed in the northern and the northeastern parts, for example, Lampang, Phrae, Nakhon Phanom and Nong Khai (Royal Forest Department, 2001).

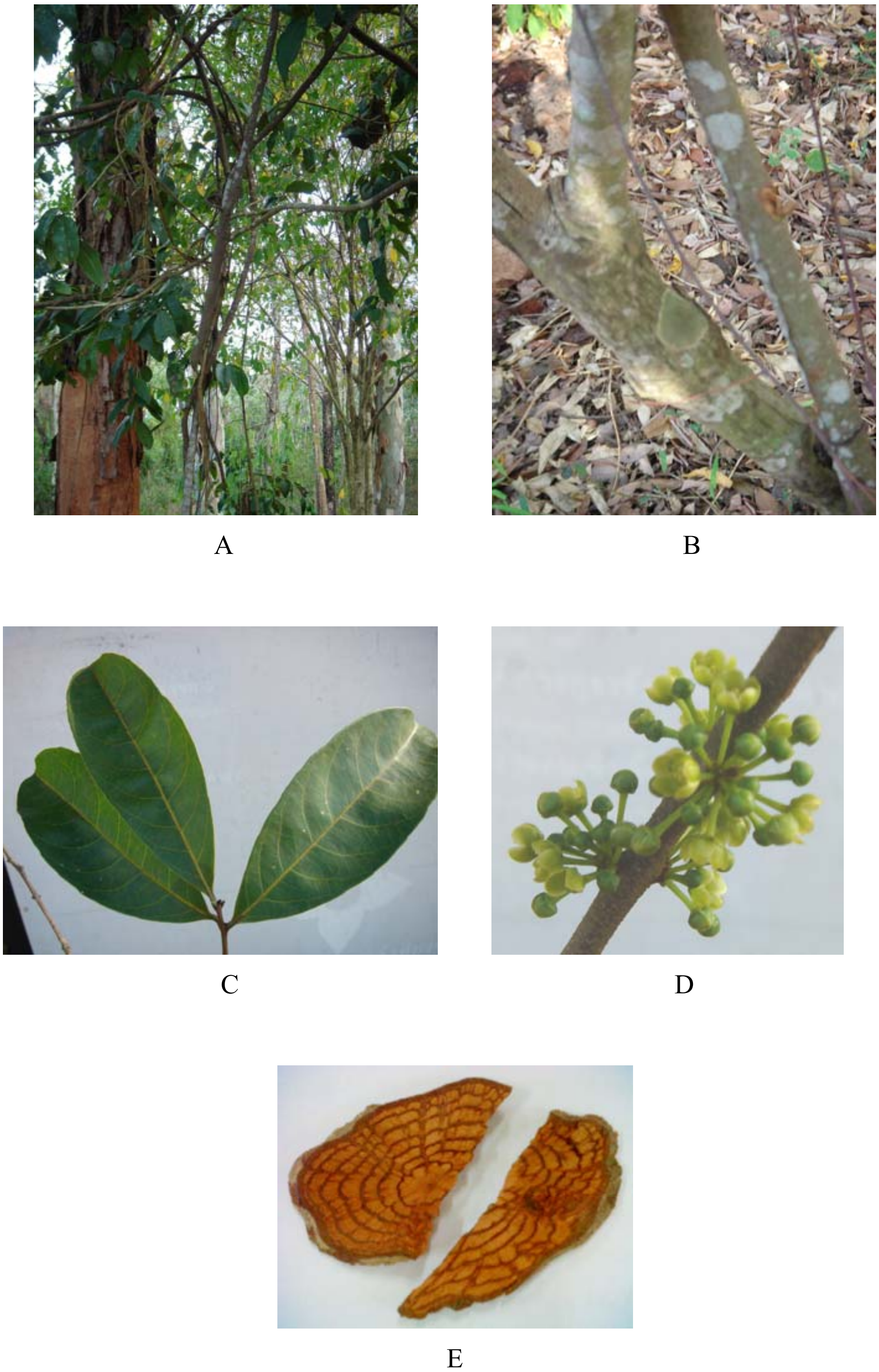


Figure 1. *Salacia verrucosa* Wight

A) Habit, B) Stem, C) Leaves, D) Flowers, E) Cross sections of stem

4. Family Moraceae

Moraceae, the mulberry family of the rose order (Rosales), consists of about 40 genera and over 1,000 species. Most are widely distributed in tropical and subtropical regions, less common in temperate areas (Mabberley, 1990). Plants of the family include trees, shrubs, vines, or rarely herbs often with milky or watery latex and sometimes spines and have small alternate or opposite leaves, along with petalless male or female flowers. The fruits of many species are multiple because fruits from different flowers become joined together (Moraceae, 2013). Examples of the plant genera in this family are *Antiaris*, *Artocarpus*, *Broussonetia*, *Ficus*, *Maclura* and *Morus*. Parts of these plants have been utilized as food and also important in various industries. In India, fruits of these plants are eaten raw and cooked or pickled, while woods are used as fuel woods and furniture. Young leaves of *Morus spp.* are used for rearing silkworms (Chhetri, 2010). In China, the most economically important species are those of *Morus* and *Maclura* associated with the production of silk. Some species in *Broussonetia*, *Maclura* and *Morus* are used for paper making, whereas some species in *Artocarpus*, *Ficus* and *Morus* are edible fruits (Zhekun and Gilbert, 2003).

In Thailand, the members of plants in genus *Artocarpus* and *Ficus* are predominantly used as food and also described as medicinal plants (Suksri *et al*., 2005).

5. Genus *Ficus*

Ficus, commonly known as ‘Fig’, is a plant genus easily characterized by its very distinctive inflorescence. It is one of the largest plant genera consisting of about 1,000 species that can be found mainly in tropical and subtropical regions throughout the world. The genus can be divided into six subgenera including *Urostigma*, *Pharmacosycea*, *Sycomorus*, *Ficus*, *Sycidium* and *Synoecia* (Chaudhary *et al*., 2012). The genus *Ficus* includes plants like trees, shrubs, climbers, stragglers and woody epiphytes with latex. The leaves are usually alternate. The leaf margin is entire to lobed, rarely palmate. The leaf blade is glabrous or hairy and contained pinnate veins. The inflorescences are axillary or on specialized cauliflorous branches. *Ficus* plant is either monoecious with male, gall (sterile female) and female flowers in each fig, or dioecious with either male and gall flowers or only female flowers in each fig. The male flowers have 2-6 calyx lobes with 1-3 stamens, while the female flowers have 0-6 calyx lobes with a free ovary.

The gall flowers are similar to female flowers but do not produce seeds. The fruits are a seed-like achene, usually enclosed within a syconium formed from the enlarged hollow fleshy receptacle (hypanthodium). The seeds are pendulous with small amount of endosperm (Zhekun and Gilbert, 2003).

In Thailand, about 77 *Ficus* species have been recorded as follows (Royal Forest Department, 2001; Berg, 2007).

1. *F. acuminata* Roxb. (Thai name: Duea)
2. *F. albipila* (Miq.) King (Thai name: Liang phueng)
3. *F. altissima* Blume (Thai name: Krang)
4. *F. annulata* Blume (Thai name: Sai)
5. *F. anserina* (Corner) C.C. Berg
6. *F. arnottiana* (Miq.) Miq.
7. *F. aurantiaca* Griff. (Thai name: Duea thao)
8. *F. auriculata* Lour. (Thai name: Duea wa)
9. *F. benghalensis* L. (Thai name: Ni khrot)
10. *F. benjamina* L. (Thai name: Sai yoi)
11. *F. bistipulata* Griff.
12. *F. botryocarpa* Miq. (Thai name: Duea ching)
13. *F. calcicola* Corner (Thai name: Hai)
14. *F. callosa* Willd. (Thai name: Ma duea kwang)
15. *F. capillipes* Gagnep. (Thai name: Kariang)
16. *F. carica* L. (Thai name: Ma duea farang)
17. *F. chartacea* Wall. ex King
    var. *chartacea* (Thai name: Ma duea khi nok)
    var. *torulosa* Wall. (Thai name: Sai nok)
18. *F. consociata* Blume var. *murtonii* King (Thai name: Sai yai)
19. *F. curtipes* Corner (Thai name: Sai hin)
20. *F. drupacea* Thunb.
    var. *drupacea* (Thai name: Lung khon)
    var. *pubescens* Corner (Thai name: Sai)

21. *F. elastica* Roxb. ex Hornem. (Thai name: Yang india)
22. *F. fistulosa* Reinw. ex Blume (Thai name: Ching khao)
23. *F. foveolata* (Wall. ex Miq.) Miq. (Thai name: Ma kra thuep rong)
24. *F. geniculata* Kurz (Thai name: Hai)
25. *F. glabella* Blume var. *concinna* Miq. (Thai name: Krai)
26. *F. glaberrima* Blume
    var. *glaberrima* (Thai name: Duea sai)
    var. *siamensis* Corner (Thai name: Pho hin)
27. *F. globosa* Blume (Thai name: Sai luk klom)
28. *F. griffithii* (Miq.) Miq.
29. *F. heterophylla* L.f. (Thai name: Salot nam)
30. *F. heteropleura* Blume (Thai name: Sai)
31. *F. heterostyla* Merr.
32. *F. hirta* Vahl (Thai name: Ma duea hom)
33. *F. hispida* L.f. (Thai name: Ma duea plong)
34. *F. indica* L. (Thai name: Sai tok)
35. *F. infectoria* Roxb. (Thai name: Liap)
36. *F. laevis* Blume (Thai name: Ma duea thao)
37. *F. lepicarpa* Blume (Thai name: Cha luk pho)
38. *F. lyrata* Warb. ex De Wild. & Durand (Thai name: Yang bai so)
39. *F. malayana* C.C.Berg & Chantaras.
40. *F. montana* Burm.f. (Thai name: Ma duea hin)
41. *F. nervosa* Heyne (Thai name: Pho kha nun)
42. *F. obpyramidata* King (Thai name: Pho)
43. *F. obscura* Blume
    var. *borneensis* (Miq.) Corner (Thai name: Sai chueak)
    var. *obscura* (Thai name: Sai tok)
44. *F. oligodon* Miq. (Thai name: Duea wa)
45. *F. parietalis* Blume (Thai name: Ma duea khon)
46. *F. pellucidopunctata* Griff. (Thai name: Sai tok)

47. *F. praetermissa* Corner (Thai name: Duea nam)
48. *F. prostrata* Wall. (Thai name: Ma not)
49. *F. pubilimba* Merr. (Thai name: Sai)
50. *F. pumila* L. (Thai name: Ma duea thao)
51. *F. punctata* Thunb. (Thai name: Duea thao bai yai)
52. *F. pyriformis* Hook. & Arn. (Thai name: Luk khlai)
53. *F. racemosa* L. (Thai name: Ma duea uthumphon)
54. *F. religiosa* L. (Thai name: Pho si maha pho)
55. *F. retusa* L. var. retusa (Thai name: Sai yoi bai thu)
56. *F. ribes* Reinw. ex Blume (Thai name: Ma not)
57. *F. ridleyana* C.C.Berg & Chantaras.
58. *F. rostrata* Lam. (Thai name: Salot hin)
59. *F. rumphii* Blume (Thai name: Pho khi nok)
60. *F. saemocarpa* Miq. (Thai name: Duea pha)
61. *F. saxophila* Blume subsp. *cardiophylla* (Merr.) C.C. Berg
62. *F. schwarzii* Koord. (Thai name: Duea pho)
63. *F. scortechinii* King (Thai name: Duea din)
64. *F. semicordata* Buch.-Ham. ex Sm. (Thai name: Duea plong hin)
65. *F. subcordata* Blume (Thai name: Sai)
66. *F. subgelderi* Corner var. *rigida* (Miq.) Corner (Thai name: Sai krang)
67. *F. subincisa* Sm. (Thai name: Ma duea noi)
68. *F. subpisocarpa* Gagnep.
69. *F. superba* (Miq.) Miq. var. *superba* (Thai name: Krai)
70. *F. talbotii* King (Thai name: Khan laen)
71. *F. tinctoria* G.Forst.

    subsp. *gibbosa* (Blume) Corner (Thai name: Krang)

    subsp. *parasitica* Willd. (Thai name: Sai krang)
72. *F. triloba* Buch.-Ham. ex Voigt
73. *F. tuphapensis* Drake var. *annamensis* Corner (Thai name: Ma duea khon)
74. *F. variegata* Blume (Thai name: Phuk)

75. *F. vasculosa* Wall. ex Miq. (Thai name: Ma duea thong)
76. *F. virens* Aiton
    - var. *glabella* (Blume) Corner (Thai name: Krang)
    - var. *virens* (Thai name: Phak lueat)
77. *F. viridicarpa* Corner (Thai name: Duea phlong)

6. *Ficus foveolata* (Wall. ex Miq.) Miq.

A synonym of this plant is *F. sarmentosa* Buch.-Ham. ex Sm. The plant is a climber or woody vine belonging to the subgenus *Synoecia*. Its branchlets are grayish white when dried, wrinkled, glabrous or densely white-hairy. The thinly membranous stipules are lanceolate-ovate, about 8 mm long. The leaves are arranged alternately in 2 vertical rows on opposite sides of the stem; the petiole is about 1 cm long. The leaf blade is ovate, ovate-elliptic, elliptic-lanceolate, lanceolate or oblong, 8-12 by 3-4 cm; both surfaces are glabrous or sparsely brown pubescent on the lower surface. The leaf base is rounded to broadly cuneate, while the apex is acute to acuminate. The secondary veins are 4-12 on each side of the midvein. The globose fruits are axillary on leafy or on leafless branchlets, solitary or occasionally paired, blackish purple when matured. They are 0.5-2 cm in diameter and are densely covered with brown hairs. The peduncle is 0.5-1.5 cm or shorter along with triangular involucral bracts. The male flowers are pedicellate with 3-4 oblanceolate calyx lobes, 2 stamens with short filaments and mucronate anthers. The gall flowers are pedicellate with 4 obovate-spatulate calyx lobes, elliptic ovary and shallowly funnelform stigma. The female flowers are pedicellate with spatulate calyx lobes, obovate ovary and thin and long stigma. The achenes are ovoid-ellipsoid with sticky liquid (Zhekun and Gilbert, 2003).

F. foveolata has been found growing in the forests of East, South and South-East Asia, including the northern and northeastern parts of Thailand, at 600-2,500 m above sea level (Royal Forest Department, 2001; Zhekun and Gilbert, 2003).

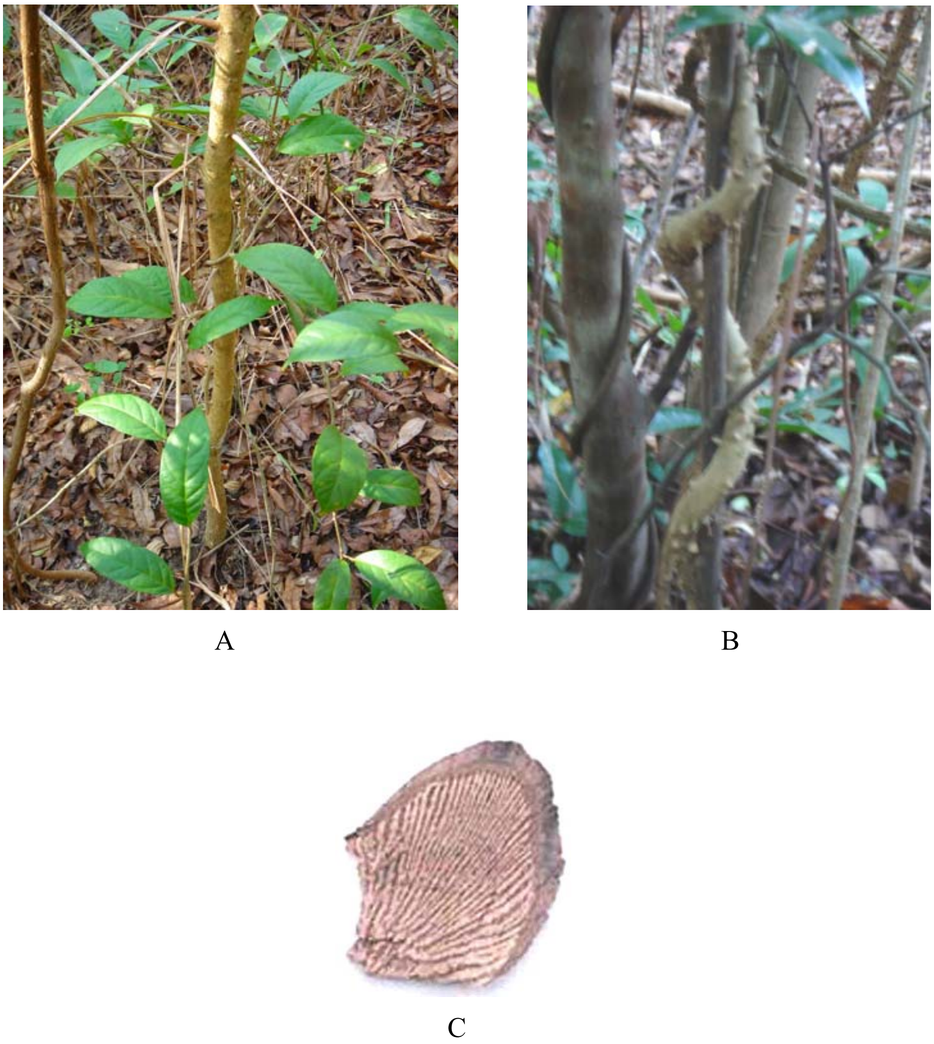
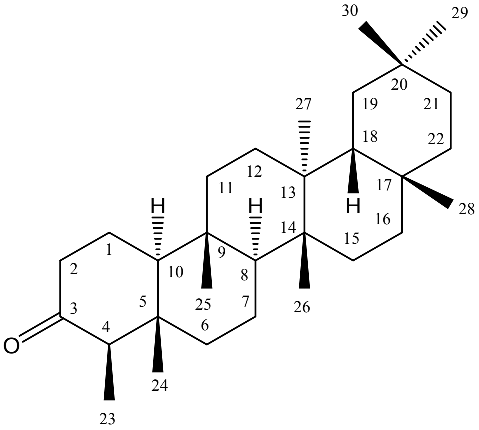


Figure 2. *Ficus foveolata* (Wall. ex Miq.) Miq.

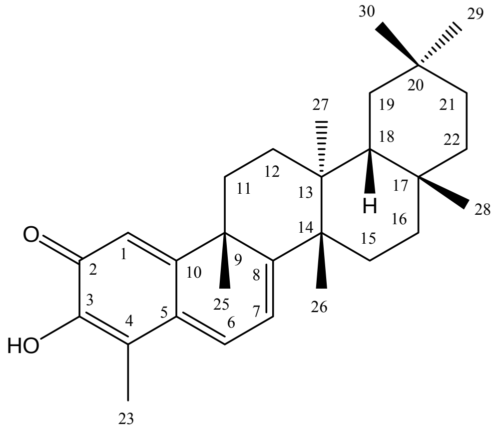
A) Habit, showing young stem and leaves, B) Stem, C) Cross section of stem

7. Friedelane and Quinone-methide Triterpenes in the Family Celastraceae

Quinone-methide triterpenes (celastroloids) are secondary metabolites related to friedelane-type triterpenes and are restricted to the higher plant families including Celastraceae and Hippocrateaceae. The biosynthesis of quinone-methides requires an oxidosqualene as a central intermediate, which would be converted by a cyclase into the first cyclic intermediate, 3β-friedelanol and then, by an oxidoreductase, into friedelin. Transformation of friedelin to quinone-methide required many biosynthetic steps involving various enzymes. Due to the enzyme activities and their localizations, friedelin and its derivatives usually accumulate in the leaves and stems, whereas the quinone-methides are mostly found in the root bark. These compounds have been predominantly isolated from the plant genera *Maytenus* and *Salacia* (Corsino *et al.*, 2000).



Friedelin



A quinone-methide

Maytenus species constitute a rich source of friedelane-type triterpenes. Compounds isolated from these plants have shown a variety of biological activities such as antitumour (Nozaki *et al.*, 1986), antiulcerogenic (Andrade *et al.*, 2008), cytotoxicity (Oramas-Royo *et al.*, 2010) and antidiabetic activities (Ardiles *et al.*, 2012). For example, maytenfoliol (**54**), an antileukemic agent, was isolated along with canophyllal (**3**), canophyllol (**4**), friedelin (**27**), 29-hydroxyfriedelan-3-one (**34**), 30-hydroxyfriedelan-3-one (**35**), maytensifolins A-C (**56-58**) and pachysonol (**67**) from *M. diversifolia* (Nozaki *et al.*, 1986, 1991). 3,15-Dioxo-21α-hydroxyfriedelane (**18**), isolated from *M. robusta*, exhibited antiulcerogenic activity in mice afflicted with gastric ulcers comparable with omeprazole as the positive control (54.6 and 57.9% inhibition, respectively) (Andrade *et al.*, 2008). The aromatic and quinone-methide triterpenes isolated from *M. retusa*, such as 23-*nor*-blepharodol (**1**), 6,23-dioxo-7,8-dihydropristimerol-23-oic acid (**17**), 3-methoxy-6-oxotingenol-23-oic acid (**60**), 7-oxo-7,8-dihydroscutione (**62**) and 21-oxopristimerine (**65**), showed cytotoxic activity against the human tumor cell lines HL-60 and MCF-7 (Oramas-Royo *et al.*, 2010). 7β,29-Dihydroxy-D:A-friedooleanan-3-one (**13**) and 7β-hydroxy-3-oxo-D:A-friedooleanan-28-oic acid (**40**) from the root bark of *M. jelskii* appeared to increase insulin-mediated signaling, suggesting their potential in the treatment of type 2 diabetes mellitus (Ardiles *et al.*, 2012).

The friedelane-type triterpenes were also isolated from plants in the genera *Celastrus*, *Euonymus* and *Kokoona*. Cassinolide (**5**), a triterpenoid lactone, was isolated along with 7β,29-dihydroxy-D:A-friedooleanan-3-one (**13**), friedelin (**27**), 29-hydroxyfriedelan-3-one (**34**) and 7β-hydroxy-3-oxo-D:A-friedooleanan-28-oic acid (**40**) from *C. vulcanicola* (Nunez *et al.*, 2012; Torres-Romero *et al.*, 2010). 30-Hydroxyfriedelan-3-one (**35**), isolated from *E. alatus*, exhibited cytotoxic activity against MDA-MB-435 cell line with an inhibition percentage of 57.38% at the concentration of 10 μg/ml (Tu *et al.*, 2011). Demethylzeylasterone (**7**), a 6-oxophenolic triterpenoid from *K. zeylanica*, was found to be an inhibitor of the enzyme topoisomerase IIα (IC_{50} = 17.6 μM). The compound was also selectively cytotoxic against MCF-7 cancer cell line (IC_{50} = 12.5 μM) (Furbacher and Gunatilaka, 2001). The same plant also contains other friedelane-type triterpenoids including D:A-friedo-olean-3,21-dione (**28**), 21α-hydroxyfriedelan-3-one (**33**), zeylandiol (**82**), zeylanol (**83**) and zeylanonol (**84**) (Gunatilaka, Nanayakkara, and Sultanbawa, 1979; Gunatilaka *et al.*, 1982).

The presence of friedelane-type triterpenes and quinone-methides in *Salacia* species has been reported and some of them have been shown to be bioactive. For example, 17-methoxycarbonyl-28-*nor*-isoiguesterin (**59**) from the roots of *S. kraussii* displayed antimalarial activity against the multidrug-resistant strain K1 and the drug-sensitive strain NF_{54} of *Plasmodium falciparum*, with IC_{50} values of 27.6 and 37.1 ng/ml, respectively (Figueiredo *et al.*, 1998). Regeol A (**69**) and tingenone (**81**), from *S. chinensis* stems, showed an inhibitory effect on rat lens aldose reductase, with IC_{50} values of 30 and 13 μM, respectively (Morikawa *et al.*, 2003). Two triterpenoids isolated from the roots of *S. madagascariensis*, isoiguesterin (**46**) and 20-*epi*-isoiguesterinol (**49**), were potently active against the protozoa *Leishmania* (Thiem *et al.*, 2005).

Friedelane triterpenoids isolated from *Salacia* species also include celastrol (**6**), 30-hydroxypristimerin (**42**), 22β-hydroxytingenone (**44**), isoiguesterin (**46**), isoiguesterinol (**48**), netzahualcoyene (**61**), pristimerin (**68**), salacenonal (**70**), salaciquinone (**71**) and tingenone (**81**) found in the root bark of *S. reticulata* (Dhanabalasingham *et al.*, 1996), friedelane-1,3-dione (**24**) from the stems of *S. verrucosa* (Jangruang *et al.*, 2009), 15α-hydroxyfriedelan-1,3-dione (**30**) from the stem bark of *S. beddomei* (Hisham *et al.*, 1996b), 26-hydroxyfriedelan-1,3-dione (**31**) from the roots of *S. oblonga* (Matsuda *et al*., 1999) and the stems of *S. verrucosa* (Jangruang *et al*., 2009), and kokoonol (**52**), salaquinone A (**72**) and salasones A-C (**74-76**) from the stems of *S. chinensis* (Morikawa *et al*., 2003).

Phytochemical investigation of plants in the family Celastraceae has resulted in the isolation of various friedelane and quinone-methide triterpenes. Distribution of these compounds in this plant family is summarized in **Table 1**, and their chemical structures are shown in **Figure 3**.

Table 1. Distribution of friedelane and quinone-methide triterpenes in the family Celastraceae

Compound	**Source**	**Plant part**	**References**
23-*nor*-Blepharodol (**1**)	*Maytenus retusa*	Root bark	Oramas-Royo *et al*., 2010
Cangoronine (**2**)	*M. ilicifolia*		Itokawa *et al*., 1991
Canophyllal (**3**)	*M. diversifolia*	Stems	Nozaki *et al*., 1986
Canophyllol (**4**)	*Celastrus vulcanicola* *Lepidobotrys staudtii* *M. diversifolia* *M. macrocarpa* *Salacia elliptica*	Stems Leaves, Stem bark Stems Stem bark Branches	Torres-Romero *et al*., 2010 Tane *et al*., 1996 Nozaki *et al*., 1986 Chavez *et al*., 1998 Duarte *et al*., 2009
Cassinolide (**5**)	*Cassine xylocarpa* *Celastrus vulcanicola*	Root bark Stems	Nunez *et al*., 2012 Torres-Romero *et al*., 2010
Celastrol (**6**)	*S. kraussii* *S. reticulata*	Roots Root bark	Figueiredo *et al*., 1998 Dhanabalasingham *et al*., 1996

Table 1. (continued)

Compound	**Source**	**Plant part**	**References**
Demethylzeylasterone (**7**)	*Kokoona zeylanica*	Inner bark	Furbacher and Gunatilaka, 2001
1β,15α-Dihydroxy-friedelan-3-one (**8**)	*Salacia beddomei*	Stem bark	Hisham *et al*., 1996b
2α,29-Dihydroxy-3-friedelanone (**9**)	*Lepidobotrys staudtii*	Leaves, stem bark	Tane *et al*., 1996
2β,21α-Dihydroxy-3-friedelanone (**10**)			
6β,21α-Dihydroxy-3-friedelanone (**11**)			
16α,28-Dihydroxyfriedelin (**12**)	*S. elliptica*	Branches	Duarte *et al*., 2009
7β,29-Dihydroxy-D:A-friedooleanan-3-one (**13**)	*Maytenus jelskii*	Root bark	Ardiles *et al*., 2012
21α,26-Dihydroxy-D:A-friedooleanan-3-one (**14**)	*S. reticulata* var. *diandra*	Stem bark	Kumar, Wazeer, and Wijeratne, 1985
21α,30-Dihydroxy-D:A-friedooleanan-3-one (**15**)			Kumar, Wijeratne, and Abeygunawardena, 1990
28,29-Dihydroxyfriedelan-3-one (**16**)	*Elaeodendron balae*	Stems	Weeratunga *et al*., 1982
6,29-Dioxo-7,8-dihydropristimerol-23-oic acid (**17**)	*M. retusa*	Root bark	Oramas-Royo *et al*., 2010
3,15-Dioxo-21α-hydroxyfriedelane (**18**)	*M. robusta*	Aerial parts	Andrade *et al*., 2008

Table 1. (continued)

Compound	**Source**	**Plant part**	**References**
Elaeodendradiol (**19**)	*Elaeodendron glaucum*	Bark	Anjaneyulu and Rao, 1980
Elaeodendrol (**20**)			
2,4(23)-Friedeladien-22β-hydroxy-21-one (**21**)	*Acanthothamnus aphyllus*	Roots	Estrada *et al*., 1994
2,4(23)-Friedeladien-29-oic acid (**22**)			
Friedelan-3β-ol (**23**)	*Celastrus vulcanicola* *Pleurostylia opposita* *Salacia elliptica*	Stems Leaves Branches	Torres-Romero *et al*., 2010 Dantanarayana *et al*., 1983 Duarte *et al*., 2009
Friedelane-1,3-dione (**24**)	*Peritassa compta* *S. verrucosa*	Stems	Klass and Tinto, 1992 Jangruang *et al*., 2009
Friedelane-3,15-dione (**25**)	*P. compta*	Stems	Klass and Tinto, 1992
3,4-*seco*-Friedelan-3-oic acid (**26**)	*Maytenus obtusifolia*	Roots	Silva *et al*., 2008
Friedelin (**27**)	*Celastrus vulcanicola* *Euonymus alatus* *Kokoona zeylanica* *M. diversifolia* *M. macrocarpa*	Stems Root bark Inner bark Stems Stem bark	Torres-Romero *et al*., 2010 Tu *et al*., 2011 Gunatilaka *et al*., 1982 Nozaki *et al*., 1986 Chavez *et al*., 1998

Table 1. (continued)

Compound	**Source**	**Plant part**	**References**
Friedelin **(27)**	*Maytenus obtusifolia* *M. salicifolia* *Peritassa compta* *P. opposita* *Salacia beddomei* *S. elliptica* *S. verrucosa*	Roots Fruits Stems Leaves Stem bark Branches Stems	Silva *et al*., 2008 Valladao *et al*., 2010 Klass and Tinto, 1992 Dantanarayana *et al*., 1983 Hisham *et al*., 1996b Duarte *et al*., 2009 Jangruang *et al*., 2009
D:A-Friedo-olean-3,21-dione (**28**)	*Kokoona zeylanica*	Inner bark	Gunatilaka *et al*., 1982
15α-Hydroxyfriedelan-3-one (**29**)	*P. compta* *S. amplifolia* *S. beddomei*	Stems Roots Stem bark	Klass and Tinto, 1992 Wang *et al*., 2011a Hisham *et al*., 1996b
15α-Hydroxyfriedelan-1,3-dione (**30**)	*P. compta* *S. beddomei*	Stems Stem bark	Klass and Tinto, 1992 Hisham *et al*., 1996b
26-Hydroxyfriedelan-1,3-dione (**31**)	*S. oblonga* *S. reticulata* *S. verrucosa*	Roots Roots Stems	Matsuda *et al*., 1999 Yoshikawa *et al*., 2002 Jangruang *et al*., 2009
28-Hydroxyfriedelan-1,3-dione (**32**)	*M. macrocarpa*	Stem bark	Chavez *et al*., 1998

Table 1. (continued)

Compound	**Source**	**Plant part**	**References**
21α-Hydroxyfriedelan-3-one (**33**)	*Kokoona zeylanica*	Inner bark	Gunatilaka *et al.*, 1982
	Lepidobotrys staudtii	Leaves, stem bark	Tane *et al.*, 1996
29-Hydroxyfriedelan-3-one (**34**)	*Catha cassinoides*	Stems	Betancor *et al.*, 1980
	Celastrus vulcanicola	Stems	Torres-Romero *et al.*, 2010
	Euonymus alatus	Root bark	Tu *et al.*, 2011
	L. staudtii	Leaves, stem bark	Tane *et al.*, 1996
	Maytenus diversifolia	Stems	Nozaki *et al.*, 1986
	M. ilicifolia	Root bark	Itokawa *et al.*, 1991
	M. macrocarpa	Stem bark	Chavez *et al.*, 1998
	M. nemerosa	Stems	Fang *et al.*, 1984
	M. obtusifolia	Roots	Silva *et al.*, 2008
	Salacia chinensis	Stems	Morikawa *et al.*, 2003
	S. reticulata	Root bark	Dhanabalasingham *et al.*, 1996
30-Hydroxyfriedelan-3-one (**35**)	*C. cassinoides*	Stems	Betancor *et al.*, 1980
	E. alatus	Root bark	Tu *et al.*, 2011
	L. staudtii	Leaves, stem bark	Tane *et al.*, 1996
	M. diversifolia	Stems	Nozaki *et al.*, 1986
	M. nemerosa	Stems	Fang *et al.*, 1984
	S. elliptica	Branches	Duarte *et al.*, 2009
16α-Hydroxyfriedelin (**36**)	*S. elliptica*	Branches	Duarte *et al.*, 2009

Table 1. (continued)

Compound	**Source**	**Plant part**	**References**
28-Hydroxyisoiguesterin (**37**)	*Salacia kraussii*	Roots	Figueiredo *et al.*, 1998
3-Hydroxy-2-oxofriedelan-3-en-20α-carboxylic acid (**38**)	*Austroplenckia populnea*	Root bark	Sousa *et al.*, 1990
3β-Hydroxy-2-oxofriedelan-20α-carboxylic acid (**39**)			
7β-Hydroxy-3-oxo-D:A-friedooleanan-28-oic acid (**40**)	*Maytenus jelskii*		Ardiles *et al.*, 2012
2α-Hydroxypopulnonic acid (**41**)	*Acanthothamnus aphyllus*	Roots	Estrada *et al.*, 1994
30-Hydroxypristimerin (**42**)	*S. reticulata*	Root bark	Dhanabalasingham *et al.*, 1996
20α- Hydroxytingenone (**43**)	*A. populnea*		Sousa *et al.*, 1990
22β-Hydroxytingenone (**44**)	*A. aphyllus* *S. reticulata*	Roots Root bark	Estrada *et al.*, 1994 Dhanabalasingham *et al.*, 1996
Ilicifoline (**45**)	*M. ilicifolia*	Root bark	Itokawa *et al.*, 1991
Isoiguesterin (**46**)	*S. amplifolia* *S. madagascariensis* *S. reticulata*	Roots Roots Root bark	Wang *et al.*, 2011a Thiem *et al.*, 2005 Dhanabalasingham *et al.*, 1996
28-*nor*-Isoiguesterin-17-carbaldehyde (**47**)	*S. kraussii*	Roots	Figueiredo *et al.*, 1998
Isoiguesterinol (**48**)	*S. madagascariensis* *S. reticulata*	Roots Root bark	Thiem *et al.*, 2005 Dhanabalasingham *et al.*, 1996

Table 1. (continued)

Compound	Source	Plant part	References
20-*epi*-Isoiguesterinol (**49**)	*Salacia madagascariensis*	Roots	Thiem *et al*., 2005
Isopristimerin III (**50**)	*Maytenus ilicifolia*	Root bark	Itokawa *et al*., 1991
Isotingenone III (**51**)			
Kokoonol (**52**)	*Kokoona zeylanica* *S. chinensis*	Stems Stems	Gunatilaka *et al*., 1983a Morikawa *et al*., 2003
Kotalagenin 16-acetate (**53**)	*S. oblonga*	Roots	Matsuda *et al*., 1999
Maytenfoliol (**54**)	*M. diversifolia*	Stems	Nozaki *et al*., 1986
Maytenoic acid (**55**)	*Austroplenckia populnea* *Catha cassinoides* *Celastrus vulcanicola* *Gymnosporia emarginata* *M. ilicifolia*	Root bark Stems Stems Bark Root bark	Sousa *et al*., 1990 Betancor *et al*., 1980 Torres-Romero *et al*., 2010 Ramaiah *et al*., 1984 Itokawa *et al*., 1991
Maytensifolin-A (**56**)	*M. diversifolia*	Stems	Nozaki *et al*., 1986
Maytensifolin-B (**57**)			
Maytensifolin-C (**58**)			Nozaki *et al*., 1991
17-Methoxycarbonyl-28-*nor*-isoiguesterin (**59**)	*S. kraussii*	Roots	Figueiredo *et al*., 1998
3-Methoxy-6-oxotingenol-23-oic acid (**60**)	*M. retusa*	Root bark	Oramas-Royo *et al*., 2010

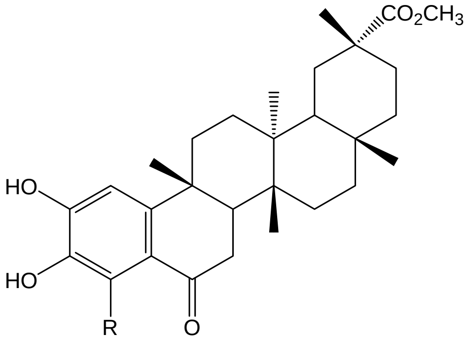
Table 1. (continued)

Compound	**Source**	**Plant part**	**References**
Netzahualcoyene (**61**)	*Salacia amplifolia* *S. reticulata*	Roots Root bark	Wang *et al*., 2011a Dhanabalasingham *et al*., 1996
7-Oxo-7,8-dihydroscutione (**62**)	*Maytenus retusa*	Root bark	Oramas-Royo *et al*., 2010
7-Oxofriedelin (**63**)	*M. obtusifolia*	Roots	Silva *et al*., 2008
6-Oxoisoiguesterin (**64**)	*S. madagascariensis*		Thiem *et al*., 2005
21-Oxopristimerine (**65**)	*M. retusa*	Root bark	Oramas-Royo *et al*., 2010
Pachysandiol-B (**66**)	*M. acanthophylla*	Leaves	Oliveira *et al*., 2009
Pachysonol (**67**)	*M. diversifolia*	Stems	Nozaki *et al*., 1986
Pristimerin (**68**)	*Acanthothamnus aphyllus* *Austroplenckia populnea* *M. ilicifolia* *S. amplifolia* *S. beddomei* *S. kraussii* *S. reticulata*	Roots Root bark Root bark Roots Stem bark Roots Root bark	Estrada *et al*., 1994 Sousa *et al*., 1990 Itokawa *et al*., 1991 Wang *et al*., 2011a Hisham, 1995 Figueiredo *et al*., 1998 Dhanabalasingham *et al*., 1996
Regeol A (**69**)	*S. amplifolia* *S. chinensis*	Roots Stems	Wang *et al*., 2011a Morikawa *et al*., 2003
Salacenonal (**70**)	*S. reticulata*	Root bark	Dhanabalasingham *et al*., 1996

Table 1. (continued)

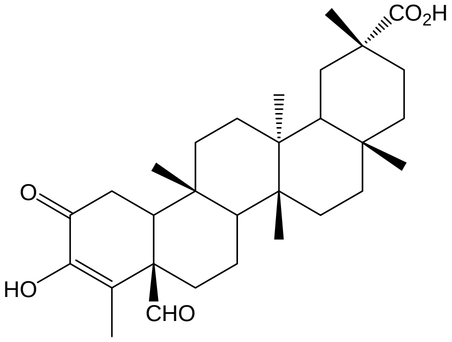
Compound	**Source**	**Plant part**	**References**
Salaciquinone (**71**)	*Salacia reticulata*	Root bark	Dhanabalasingham *et al*., 1996
Salaquinone A (**72**)	*S. chinensis*	Stems	Morikawa *et al*., 2003
Salaquinone B (**73**)			Kishi *et al*., 2003
Salasone A (**74**)			Morikawa *et al*., 2003
Salasone B (**75**)			
Salasone C (**76**)			
Salasone D (**77**)			Kishi *et al*., 2003
Salasone E (**78**)			
Salaspermic acid (**79**)	*Maytenus ilicifolia*	Root bark	Itokawa *et al*., 1991
7-Tetraene-24-*nor*-friedelane-29-oic acid methylester (**80**)	*S. amplifolia*	Roots	Wang *et al*., 2011a
Tingenone (**81**)	*Acanthothamnus aphyllus* *M. nemerosa* *S. chinensis* *S. reticulata*	Roots Stems Stems Root bark	Estrada *et al*., 1994 Fang *et al*., 1984 Morikawa *et al*., 2003 Dhanabalasingham *et al*., 1996
Zeylandiol (**82**)	*Kokoona zeylanica*	n.i.	Gunatilaka *et al*., 1979
Zeylanol (**83**)			
Zeylanonol (**84**)			

n.i. = not indicated

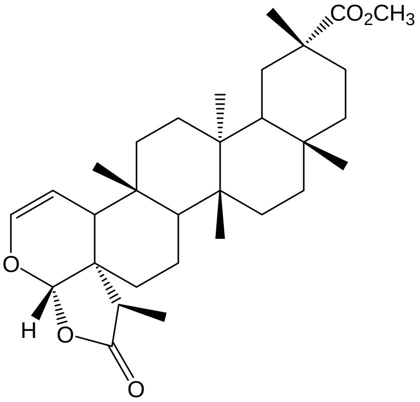


23-*nor*-Blepharodol (**1**) R = H

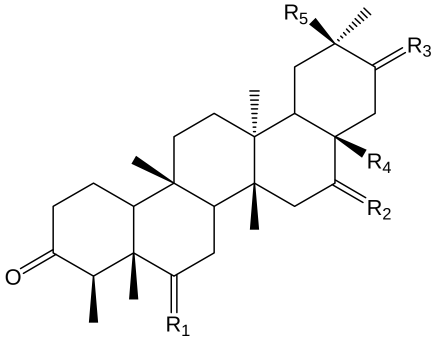
6,29-Dioxo-7,8-dihydropristimerol-23-oic acid (**17**) R = CO_2H



Cangoronine (**2**)

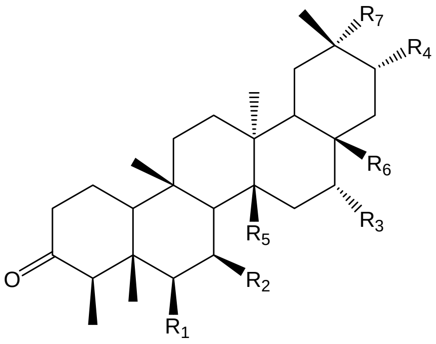


Cassinolide (**5**)



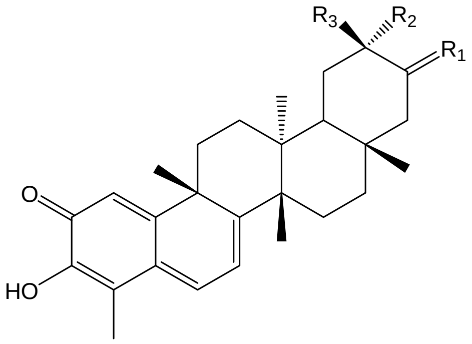
	R_1	R_2	R_3	R_4	R_5
Canophyllal (**3**)	H_2	H_2	H_2	CHO	CH_3
Maytenfoliol (**54**)	H_2	H_2	H_2	CH_2OH	CH_2OH
Maytensifolin-B (**57**)	H_2	O	H_2	CH_3	CH_3
Maytensifolin-C (**58**)	β-OH, α-H	O	O	CH_3	CH_3
Pachysonol (**67**)	H_2	β-OH, α-H	H_2	CH_3	CH_3

Figure 3. Friedelane and quinone-methide triterpenes isolated from plants in the family Celastraceae

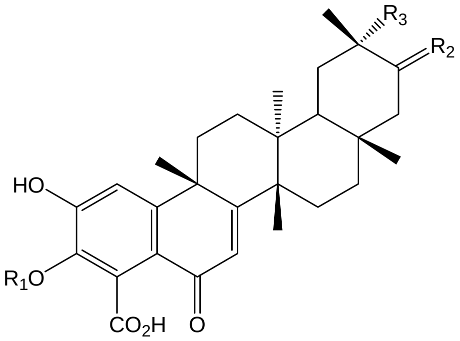


	R_1	R_2	R_3	R_4	R_5	R_6	R_7
Canophyllol (**4**)	H	H	H	H	CH_3	CH_2OH	CH_3
6β,21α-Dihydroxy-3-friedelanone (**11**)	OH	H	H	OH	CH_3	CH_3	CH_3
16α,28-Dihydroxy friedelin (**12**)	H	H	OH	H	CH_3	CH_2OH	CH_3
7β,29-Dihydroxy-D:A-friedooleanan-3-one (**13**)	H	OH	H	H	CH_3	CH_3	CH_2OH
21α,26-Dihydroxy-D:A-friedooleanan-3-one (**14**)	H	H	H	OH	CH_2OH	CH_3	CH_3
28,29-Dihydroxy friedelan-3-one (**16**)	H	H	H	H	CH_3	CH_2OH	CH_2OH
16α-Hydroxy friedelin (**36**)	H	H	OH	H	CH_3	CH_3	CH_3
7β-Hydroxy-3-oxo-D:A-friedooleanan-28-oic acid (**40**)	H	OH	H	H	CH_3	CO_2H	CH_3
Kokoonol (**52**)	H	H	H	H	CH_2OH	CH_3	CH_3

Figure 3. (continued)

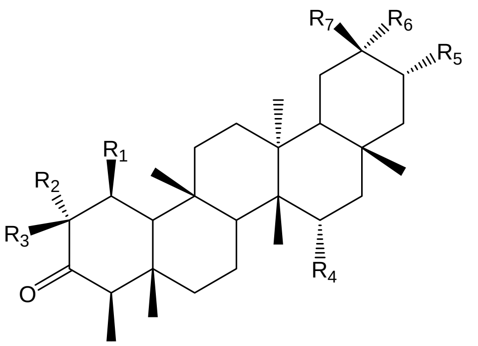


	R_1	R_2	R_3
Celastrol (**6**)	H_2	CO_2H	CH_3
30-Hydroxypristimerin (**42**)	H_2	CO_2CH_3	CH_2OH
Isoiguesterinol (**48**)	H_2	CH_2OH	H
20-*epi*-Isoiguesterinol (**49**)	H_2	H	CH_2OH
21-Oxopristimerine (**65**)	O	CO_2CH_3	CH_3
Pristimerin (**68**)	H_2	CO_2CH_3	CH_3



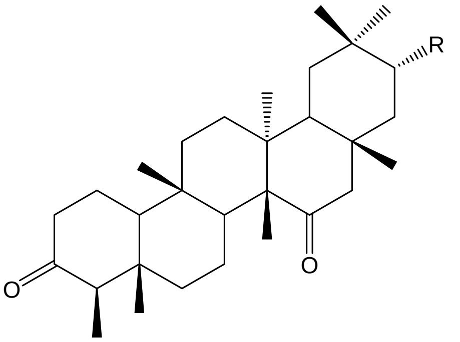
	R_1	R_2	R_3
Demethylzeylasterone (**7**)	H	H_2	CO_2H
3-Methoxy-6-oxotingenol-23-oic acid (**60**)	CH_3	O	H

Figure 3. (continued)



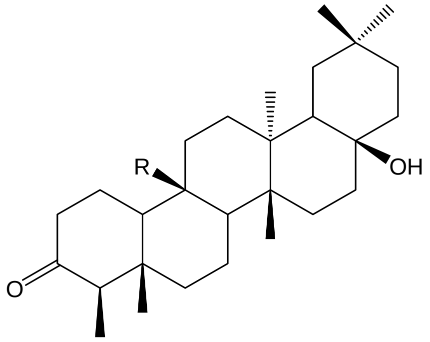
	R_1	R_2	R_3	R_4	R_5	R_6	R_7
1β,15α-Dihydroxy-friedelan-3-one (**8**)	OH	H	H	OH	H	CH_3	CH_3
2α,29-Dihydroxy-3-friedelanone (**9**)	H	OH	H	H	H	CH_2OH	CH_3
2β,21α-Dihydroxy-3-friedelanone (**10**)	H	H	OH	H	OH	CH_3	CH_3
21α,30-Dihydroxy-D:A-friedooleanan-3-one (**15**)	H	H	H	H	OH	CH_3	CH_2OH
Friedelin (**27**)	H	H	H	H	H	CH_3	CH_3
15α-Hydroxyfriedelan-3-one (**29**)	H	H	H	OH	H	CH_3	CH_3
21α-Hydroxyfriedelan-3-one (**33**)	H	H	H	H	OH	CH_3	CH_3
29-Hydroxyfriedelan-3-one (**34**)	H	H	H	H	H	CH_2OH	CH_3
30-Hydroxyfriedelan-3-one (**35**)	H	H	H	H	H	CH_3	CH_2OH
2α-Hydroxypopulnonic acid (**41**)	H	OH	H	H	H	CO_2H	CH_3
Maytenoic acid (**55**)	H	H	H	H	H	CO_2H	CH_3

Figure 3. (continued)



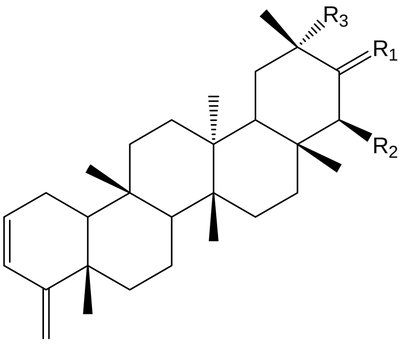
3,15-Dioxo-21α-hydroxyfriedelane (**18**) R = OH

Friedelane-3,15-dione (**25**) R = H

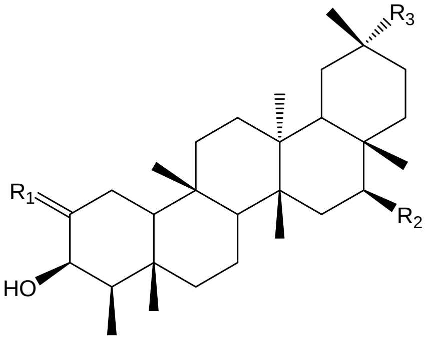


Elaeodendradiol (**19**) R = CH_2OH

Elaeodendrol (**20**) R = CH_3

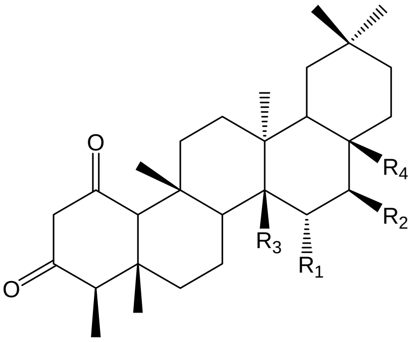


	R_1	R_2	R_3
2,4(23)-Friedeladien-22β-hydroxy-21-one (**21**)	O	OH	CH_3
2,4(23)-Friedeladien-29-oic acid (**22**)	H_2	H	CO_2H

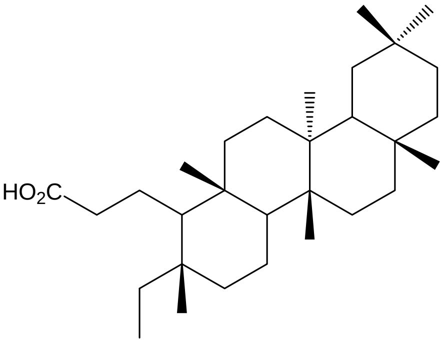


	R_1	R_2	R_3
Friedelan-3β-ol (**23**)	H_2	H	CH_3
3β-Hydroxy-2-oxofriedelan -20α-carboxylic acid (**39**)	O	H	CO_2H
Pachysandiol-B (**66**)	H_2	OH	CH_3

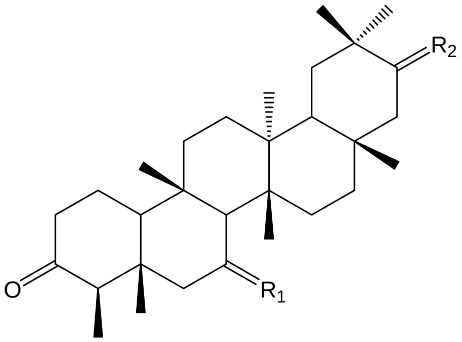
Figure 3. (continued)



	R_1	R_2	R_3	R_4
Friedelane-1,3-dione (**24**)	H	H	CH_3	CH_3
15α-Hydroxyfriedelan-1,3-dione (**30**)	OH	H	CH_3	CH_3
26-Hydroxyfriedelan-1,3-dione (**31**)	H	H	CH_2OH	CH_3
28-Hydroxyfriedelan-1,3-dione (**32**)	H	H	CH_3	CH_2OH
Kotalagenin 16-acetate (**53**)	H	OAc	CH_2OH	CH_3

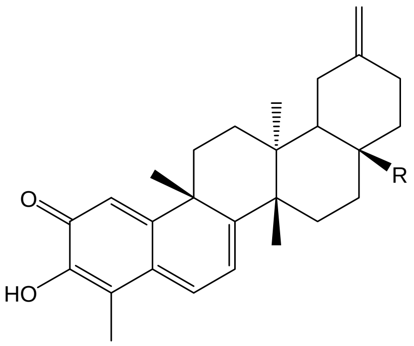


3,4-*seco*-Friedelan-3-oic acid (**26**)



	R_1	R_2
D:A-Friedo-olean-3,21-dione	H_2	O
7-Oxofriedelin (**63**)	O	H_2

Figure 3. (continued)

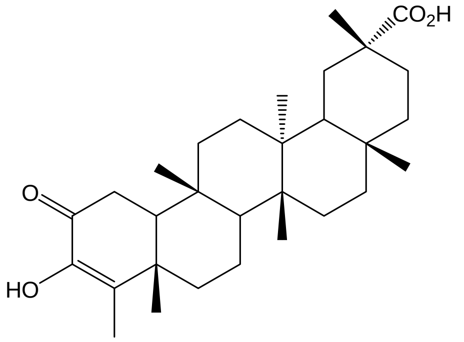


28-Hydroxyisoiguesterin (**37**) R = CH_2OH

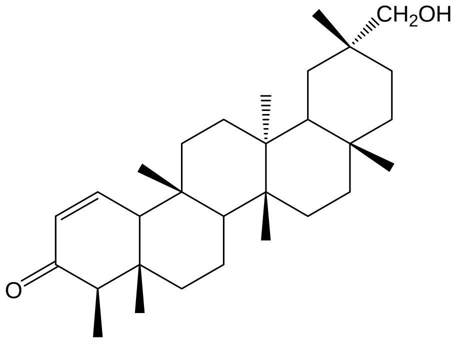
Isoiguesterin (**46**) R = CH_3

28-*nor*-Isoiguesterin-17-carbaldehyde (**47**) R = CHO

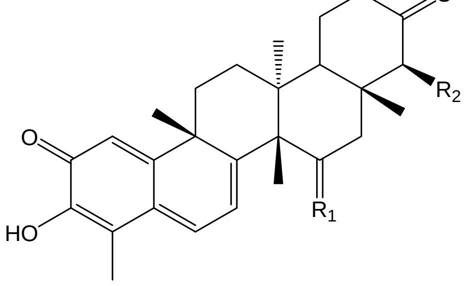
17-Methoxycarbonyl-28-*nor*-isoiguesterin (**59**) R = CO_2CH_3



3-Hydroxy-2-oxofriedelan-3-en-20α-carboxylic acid (**38**)

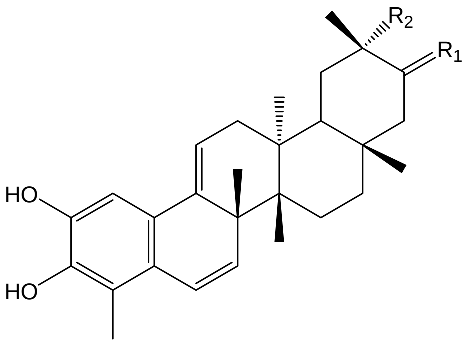


Ilicifoline (**45**)

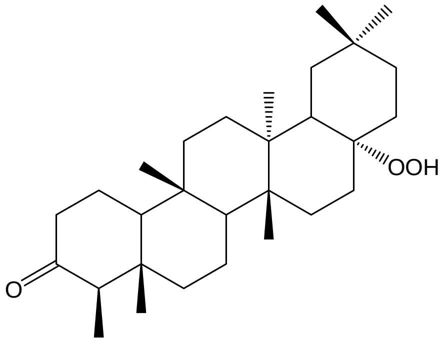


	R_1	R_2	R_3
20α- Hydroxytingenone (**43**)	H_2	H	OH
22β-Hydroxytingenone (**44**)	H_2	OH	H
Salaquinone A (**72**)	O	OH	H
Tingenone (**81**)	H_2	H	H

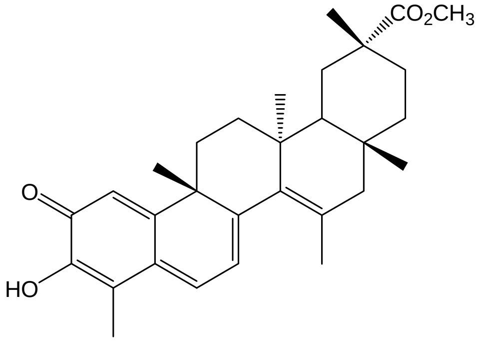
Figure 3. (continued)



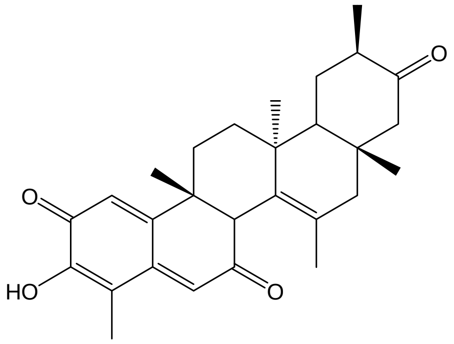
	R_1	R_2
Isopristimerin III (**50**)	H_2	CO_2CH_3
Isotingenone III (**51**)	O	H



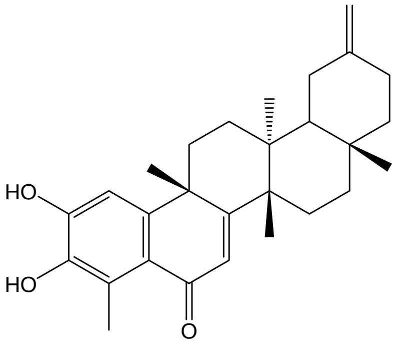
Maytensifolin-A (**56**)



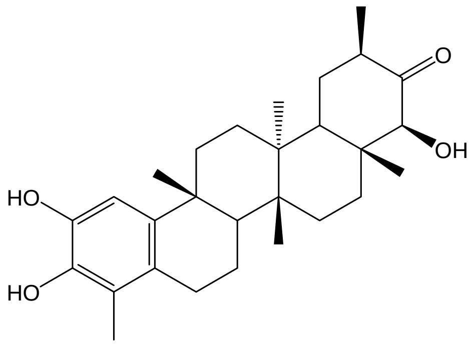
Netzahualcoyene (**61**)



7-Oxo-7,8-dihydroscutione (**62**)

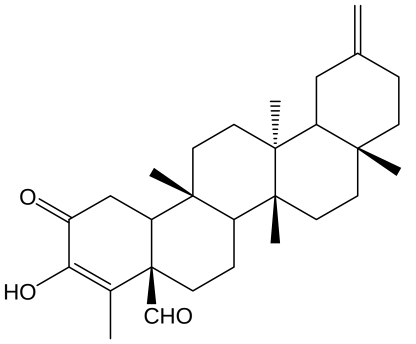


6-Oxoisoiguesterin (**64**)

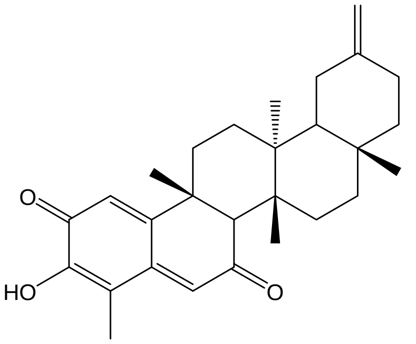


Regeol A (**69**)

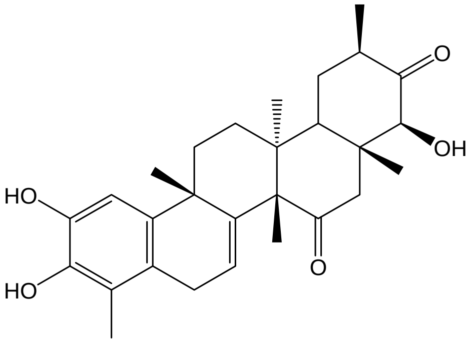
Figure 3. (continued)



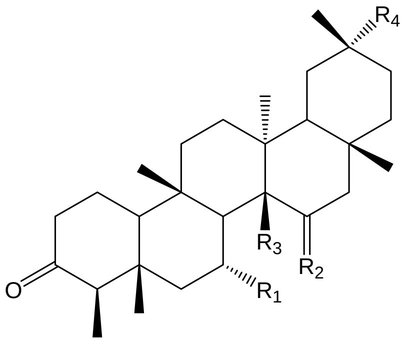
Salacenonal (**70**)



Salaciquinone (**71**)

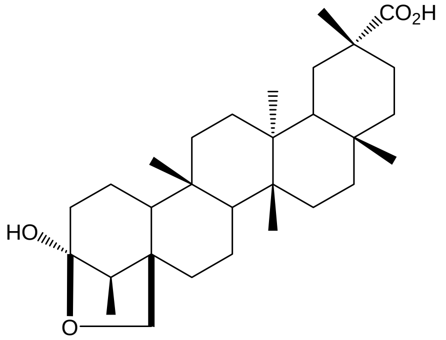


Salaquinone B (**73**)

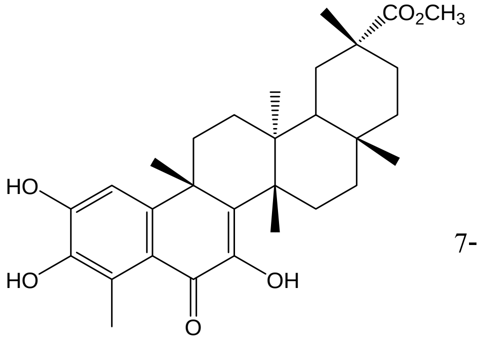


	R_1	R_2	R_3	R_4
Salasone A (**74**)	H	O	CH_2OH	CH_3
Salasone B (**75**)	OH	O	CH_3	CH_3
Salasone C (**76**)	H	α-OH, β-H	CH_3	CH_2OH
Salasone D (**77**)	H	α-OH, β-H	CH_2OH	CH_3
Salasone E (**78**)	OH	H_2	CH_2OH	CH_3

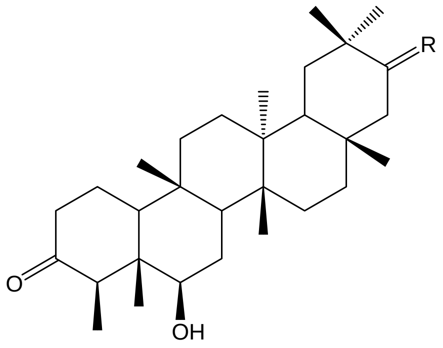
Figure 3. (continued)



Salaspermic acid (**79**)



7-Tetraene-24-*nor*-friedelane-29-oic acid methylester (**80**)



Zeylandiol (**82**) R = β-OH, α-H

Zeylanol (**83**) R = H_2

Zeylanonol (**84**) R = O

Figure 3. (continued)

8. Chemical Constituents of Plants in the Genus *Salacia*

Plants in the genus *Salacia* such as *S. reticulata* and *S. oblonga* have been widely used in the treatment for the initial stages of diabetes in the Ayurvedic system of Indian traditional medicine. The mode of administration usually consists of an aqueous decoction prepared from the roots of these plants (Matsuda, Morikawa, and Yoshikawa, 2002). Investigations of the bioactive chemical constituents of these plants led to the identification of a xanthone glucoside, mangiferin (**153**), from the root bark of *S. reticulata* (Karunanayake and Sirimanne, 1985) and the stems of *S. chinensis* (Kishi *et al*., 2003), as the hypoglycemic and radical scavenging principle.

Various studies on *Salacia* species have reported the isolation of α-glucosidase inhibitors involved in the treatment of diabetes mellitus. Thiosugar sulfonium salts, including kotalanol (**145**), ponkoranol (**162**), salaprinol (**167**) and salacinol (**166**) (Yoshikawa *et al*., 1997, 2008a; Matsuda *et al*., 1999), isolated from the roots of *S. oblonga*, *S. prinoides* and *S. reticulata*, exhibited potent inhibitory activity on the enzyme α-glucosidase (Matsuda *et al*., 1999). Neoponkoranol (**157**) and Neosalaprinol (**158**), the de-*o*-sulfonate derivatives of **162** and **167** respectively, obtained from the stems of *S. chinensis*, also showed inhibitory activity toward this enzyme(Xie *et al*., 2011). A polyhydroxylated cyclic 13-membered sulfoxide (**161**) found in the stems of *S. reticulata* showed even higher α-glucosidase inhibitory activity than the thiosugar sulfonium salts kotalanol (**145**) and salacinol (**166**) (Ozaki, Oe, and Kitamura, 2008). Furthermore, four lupane-type triterpenes i.e. 2β,3β-dihydroxylup-20(29)-ene (**91**), 3α,28-dihydroxylup-20(29)-en-2-one (**92**), 3α-hydroxylup-20(29)-en-2-one (**141**) and 2,3-*seco*-lup-20(29)-en-2,3-dioic acid (**152**), along with three dammarane-type triterpenes, 24*S*,25-dihydroxytirucall-7-en-3-one (**95**), olibanumol (**159**) and 24,25,26-trihydroxytirucall-7-en-3-one (**175**), from the roots of *S. hainanensis*, showed stronger inhibiting activity on α-glucosidase than the anti-diabetic drug acarbose (Gao *et al*., 2010; Huang *et al*., 2012).

Phytochemical studies of *Salacia* species have yielded various types of chemical constituents. For example, lupane-type triterpenes such as betulin (**87**), 15,28-dihydroxylup-20(29)-en-3-one (**93**), 28-hydroxylup-20(29)-en-3-one (**142**), and 30-hydroxylup-20(29)-en-3-one (**143**), were isolated from the stem bark of *S. cordata* (Tinto, Blair, and Alli, 1992), while 2α,3β-dihydroxylup-20(29)-ene (**90**), 20,29-epoxysalacianone (**97**), 6β-hydroxysalacianone

(**144**), salacianol (**164**) and salacianone (**165**) were isolated from the stem bark of *S. beddomei* (Hisham *et al*., 1995, 1996a).

Several types of glycosides named foliachinenosides A_1-A_3, B_1- B_2, C-I (**99-110**) (Nakamura *et al*., 2008b, 2011), along with the megastigmane glycosides foliasalaciosides A_1-A_2, B_1-B_2, C-D, E_1-E_3, F-L (**122-137**) (Nakamura *et al*., 2008a, 2011; Zhang *et al*., 2008a), the dammarane-type triterpenes foliasalacins A_1-A_4 (**111-114**), the lupane-type triterpenes foliasalacins B_1- B_3 (**115-117**), the oleanane-type triterpene foliasalacin C (**118**) (Yoshikawa *et al*., 2008b), the baccharane triterpenes foliasalacins D_1-D_3(**119-121**) (Zhang *et al*., 2008b) and the acylated eudesmane-type sesquiterpenes salasols A-B (**168-169**) (Kishi *et al*., 2003; Morikawa *et al*., 2003), were isolated from the leaves of *S. chinensis* collected in Thailand.

A number of stilbene derivatives, named lehmbachols A-D (**147-150**), have been isolated from the bark of *S. lehmbachii*, collected in Papua New Guinea (Kawazoe *et al*., 1997).

Other chemical constituents reported as constituents of members of the genus *Salacia* are shown in **Table 2**, and their chemical structures are presented in **Figure 4**.

Table 2. Chemical constituents of plants in the genus *Salacia*

Compound	**Source**	**Plant part**	**References**
α-Amyrin (**85**)	*Salacia amplifolia*	Roots	Wang *et al*., 2011a
β-Amyrin (**86**)	*S. amplifolia* *S. hainanensis*		Wang *et al*., 2011a Gao *et al*., 2010
Betulin (**87**)	*S. beddomei* *S. cordata*	Stem bark	Hisham *et al*., 1996a Tinto *et al*., 1992
Coniferaldehyde (**88**)	*S. amplifolia*	Roots	Wang *et al*., 2011a
Dibutyl phthalate (**89**)			
2α,3β-Dihydroxylup-20(29)-ene (**90**)	*S. beddomei*	Stem bark	Hisham *et al*., 1996a
2β,3β-Dihydroxylup-20(29)-ene (**91**)	*S. hainanensis*	Roots	Huang *et al*., 2012
3α,28-Dihydroxylup-20(29)-en-2-one (**92**)			Gao *et al*., 2010
15,28-Dihydroxylup-20(29)-en-3-one (**93**)	*S. cordata*	Stem bark	Tinto *et al*., 1992
3β,22β -Dihydroxyolean-12-en-29-oic acid (**94**)	*S. oblonga*	Roots	Matsuda *et al*., 1999
24*S*,25-Dihydroxytirucall-7-en-3-one (**95**)	*S. hainanensis*		Gao *et al*., 2010
Dulcitol (**96**)	*S. amplifolia* *S. elliptica* *S. oblonga* *S. verrucosa*	Roots Leaves Roots Stems	Wang *et al*., 2011a Duarte *et al*., 2010 Matsuda *et al*., 1999 Jangruang *et al*., 2009
20,29-Epoxysalacianone (**97**)	*S. beddomei*	Stem bark	Hisham *et al*., 1996a
Ethyl glucopyranoside (**98**)	*S. elliptica*	Leaves	Duarte *et al*., 2010

Table 2. (continued)

Compound	**Source**	**Plant part**	**References**
Foliachinenoside A_1 (**99**)	*Salacia chinensis*	Leaves	Nakamura *et al*., 2008b
Foliachinenoside A_2 (**100**)			
Foliachinenoside A_3 (**101**)			
Foliachinenoside B_1 (**102**)			
Foliachinenoside B_2 (**103**)			
Foliachinenoside C (**104**)			
Foliachinenoside D (**105**)			
Foliachinenoside E (**106**)			Nakamura *et al*., 2011
Foliachinenoside F (**107**)			
Foliachinenoside G (**108**)			
Foliachinenoside H (**109**)			
Foliachinenoside I (**110**)			
Foliasalacin A_1 (**111**)			Yoshikawa *et al*., 2008b
Foliasalacin A_2 (**112**)			
Foliasalacin A_3 (**113**)			
Foliasalacin A_4 (**114**)			
Foliasalacin B_1 (**115**)			
Foliasalacin B_2 (**116**)			
Foliasalacin B_3 (**117**)			
Foliasalacin C (**118**)			
Foliasalacin D_1 (**119**)			Zhang *et al*., 2008b
Foliasalacin D_2 (**120**)			
Foliasalacin D_3 (**121**)			
Foliasalacioside A_1 (**122**)			Nakamura *et al*., 2008a
Foliasalacioside A_2 (**123**)			
Foliasalacioside B_1 (**124**)			

Table 2. (continued)

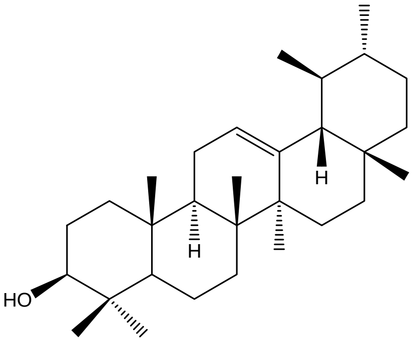
Compound	Source	Plant part	References
Foliasalacioside B_2 (**125**)	*Salacia chinensis*	Leaves	Nakamura *et al*., 2008a
Foliasalacioside C (**126**)			
Foliasalacioside D (**127**)			
Foliasalacioside E_1 (**128**)			Zhang *et al*., 2008a
Foliasalacioside E_2 (**129**)			
Foliasalacioside E_3 (**130**)			
Foliasalacioside F (**131**)			
Foliasalacioside G (**132**)			
Foliasalacioside H (**133**)			
Foliasalacioside I (**134**)			
Foliasalacioside J (**135**)			Nakamura *et al*., 2011
Foliasalacioside K (**136**)			
Foliasalacioside L (**137**)			
Gult-5-en-3β-ol (**138**)	*S. amplifolia*	Roots	Wang *et al*., 2011a
(-)-Gynuraone (**139**)			
19-Hydroxyferruginol (**140**)	*S. oblonga*		Matsuda *et al*., 1999
3α-Hydroxylup-20(29)-en-2-one (**141**)	*S. hainanensis*		Gao *et al*., 2010
28-Hydroxylup-20(29)-en-3-one (**142**)	*S. cordata*	Stem bark	Tinto *et al*., 1992
30-Hydroxylup-20(29)-en-3-one (**143**)			
6β-Hydroxysalacianone (**144**)	*S. beddomei*		Hisham *et al*., 1996a
Kotalanol (**145**)	*S. oblonga* *S. prinoides*	Roots Roots, Stems	Matsuda *et al*., 1999 Yoshikawa *et al*., 2008a

Table 2. (continued)

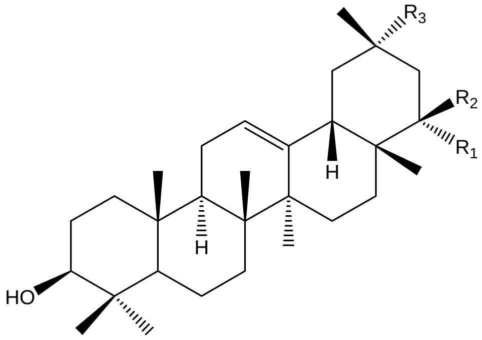
Compound	**Source**	**Plant part**	**References**
Lambertic acid (**146**)	*Salacia oblonga*	Roots	Matsuda *et al*., 1999
Lehmbachol A (**147**)	*S. lehmbachii*	Bark	Kawazoe *et al*., 1997
Lehmbachol B (**148**)			
Lehmbachol C (**149**)			
Lehmbachol D (**150**)			
Lup-20(29)-en-3-one (**151**)	*S. beddomei*	Stem bark	Hisham *et al*., 1995
2,3-*seco*-Lup-20(29)-en-2,3-dioic acid (**152**)	*S. hainanensis*	Roots	Gao *et al*., 2010
Mangiferin (**153**)	*S. chinensis* *S. reticulata*	Stems Root bark	Kishi *et al*., 2003 Karunanayake and Sirimanne, 1985
Maytenfolic acid (**154**)	*S. oblonga*	Roots	Matsuda *et al*., 1999
Methyl-2,4-dihydroxy -3,6-dimethylbenzoate (**155**)	*S. elliptica*	Branches	Duarte *et al*., 2010
(-)-4′-*O*-Methylepigallocatechin (**156**)	*S. oblonga*	Roots	Matsuda *et al*., 1999
Neoponkoranol (**157**)	*S. chinensis*	Stems	Xie *et al*., 2011
Neosalaprinol (**158**)			
Olibanumol J (**159**)	*S. hainanensis*	Roots	Huang *et al*., 2012
Palmitic acid (**160**)	*S. elliptica*	Leaves	Duarte *et al*., 2010
Polyhydroxylated cyclic -13-membered sulfoxide (**161**)	*S. reticulata*	Stems	Ozaki *et al*., 2008
Ponkoranol (**162**)	*S. prinoides*	Roots, Stems	Yoshikawa *et al*., 2008a
Pyracrenic acid (**163**)	*S. cordata*	Stem bark	Tinto *et al*., 1992
Salacianol (**164**)	*S. beddomei*		Hisham *et al*., 1995

Table 2. (continued)

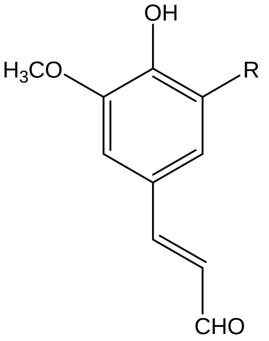
Compound	**Source**	**Plant part**	**References**
Salacianone (**165**)	*Salacia beddomei* *S. hainanensis*	Stem bark Roots	Hisham *et al*., 1995 Gao *et al*., 2010
Salacinol (**166**)	*S. oblonga* *S. prinoides* *S. reticulata*	Roots Roots, Stems Roots	Matsuda *et al*., 1999 Yoshikawa *et al*., 2008a Yoshikawa *et al*., 1997
Salaprinol (**167**)	*S. prinoides*	Roots, Stems	Yoshikawa *et al*., 2008a
Salasol A (**168**)	*S. chinensis*	Stems	Morikawa *et al*., 2003
Salasol B (**169**)			Kishi *et al*., 2003
Sinapic aldehyde (**170**)	*S. amplifolia*	Roots	Wang *et al*., 2011a
β-Sitosterol (**171**)	*S. elliptica*	Leaves	Duarte *et al*., 2010
β-Sitosterol glucoside (**172**)			
3β-Stearyloxyolean-12-en (**173**)			
3β-Stearyloxyurs-12-en (**174**)			
24,25,26-Trihydroxytirucall-7-en-3-one (**175**)	*S. hainanensis*	Roots	Huang *et al*., 2012
Wilforlide A (**176**)	*S. amplifolia*		Wang *et al*., 2011a
Wilforlide B (**177**)			



α-Amyrin (**85**)

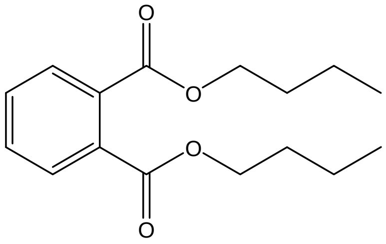


	R_1	R_2	R_3
β-Amyrin (**86**)	H	H	CH_3
3β,22β-Dihydroxyolean-12-en-29-oic acid (**94**)	H	OH	CO_2H
Maytenfolic acid (**154**)	OH	H	CO_2H



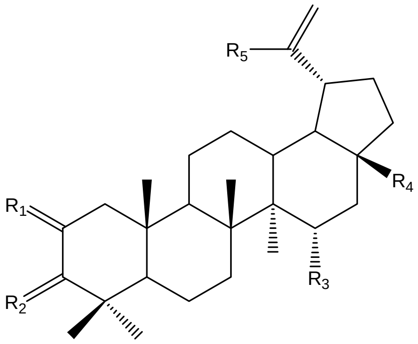
Coniferaldehyde (**88**) R = H

Sinapic aldehyde (**170**) R = OCH_3



Dibutyl phthalate (**89**)

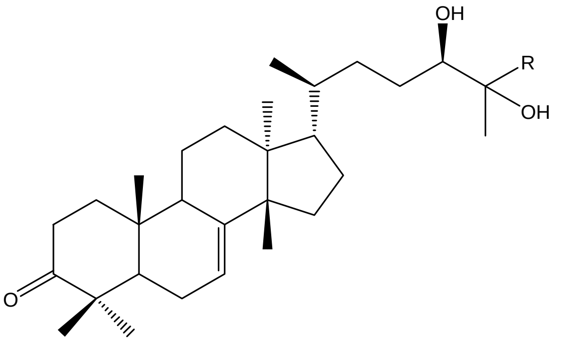
Figure 4. Chemical constituents of plants in the genus *Salacia*



	R_1	R_2	R_3	R_4	R_5
Betulin (**87**)	H_2	β-OH, α-H	H	CH_2OH	CH_3
2α,3β-Dihydroxylup-20(29)-ene (**90**)	α-OH, β-H	β-OH, α-H	H	CH_3	CH_3
2β,3β-Dihydroxylup-20(29)-ene (**91**)	β-OH, α-H	β-OH, α-H	H	CH_3	CH_3
3α,28-Dihydroxylup-20(29)-en-2-one (**92**)	O	α-OH, β-H	H	CH_2OH	CH_3
15,28-Dihydroxylup-20(29)-en-3-one (**93**)	H_2	O	OH	CH_2OH	CH_3
3α-Hydroxylup-20(29)-en-2-one (**141**)	O	α-OH, β-H	H	CH_3	CH_3
28-Hydroxylup-20(29)-en-3-one (**142**)	H_2	O	H	CH_2OH	CH_3
30-Hydroxylup-20(29)-en-3-one (**143**)	H_2	O	H	CH_3	CH_2OH
Lup-20(29)-en-3-one (**151**)	H_2	O	H	CH_3	CH_3
Pyracrenic acid (**163**)	H_2	β-OCaf*, α-H	H	CO_2H	CH_3

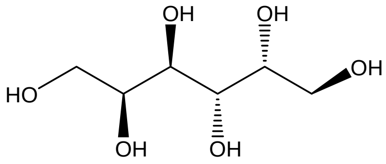
*Caf = 3,4-dihydroxycinnamoyl

Figure 4. (continued)

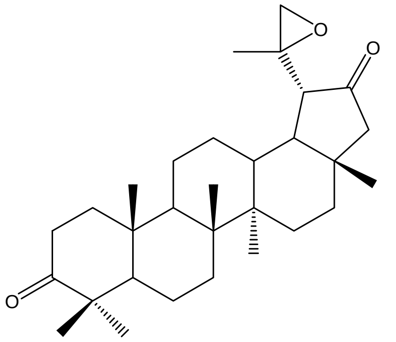


24*S*,25-Dihydroxytirucall-7-en-3-one (**95**) R = CH_3

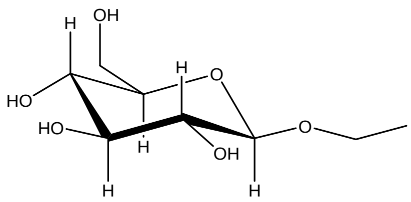
24,25,26-Trihydroxytirucall-7-en-3-one (**175**) R = CH_2OH



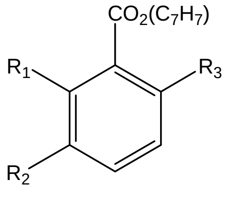
Dulcitol (**96**)



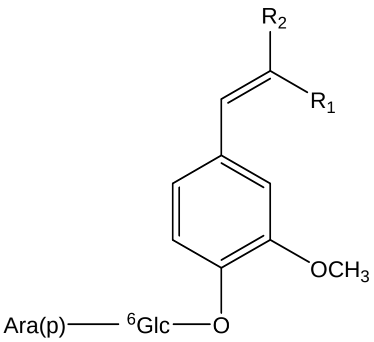
20,29-Epoxysalacianone (**97**)



Ethyl glucopyranoside (**98**)

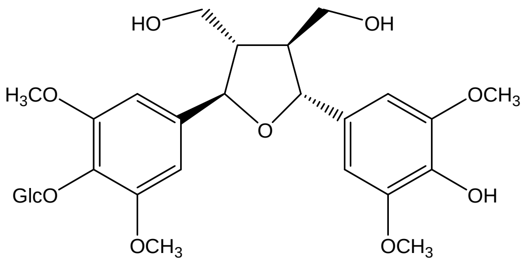


	R_1	R_2	R_3
Foliachinenoside A$_1$ (**99**)	OGlc	H	OGlc
Foliachinenoside A$_2$ (**100**)	OGlc^6-Glc	H	H
Foliachinenoside A$_3$ (**101**)	OGlc	OGlc	H

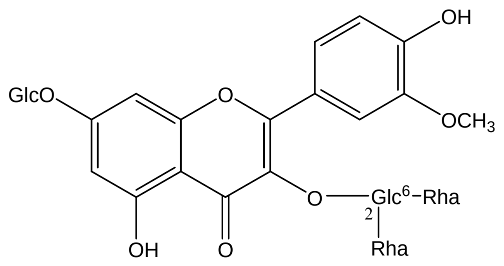


	R_1	R_2
Foliachinenoside B$_1$ (**102**)	CH_3	H
Foliachinenoside B$_2$ (**103**)	H	CH_3

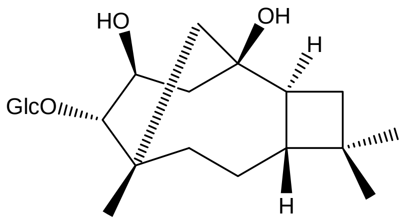
Figure 4. (continued)



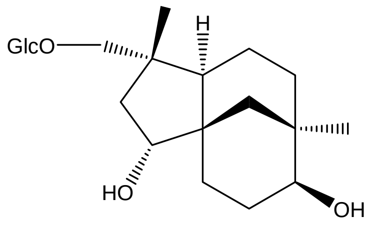
Foliachinenoside C (**104**)



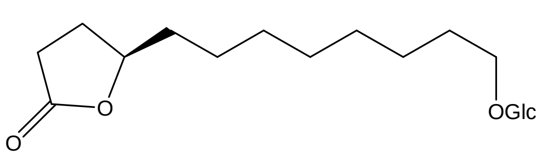
Foliachinenoside D (**105**)



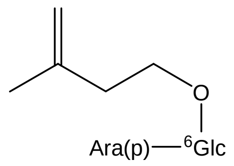
Foliachinenoside E (**106**)



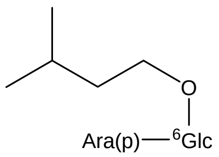
Foliachinenoside F (**107**)



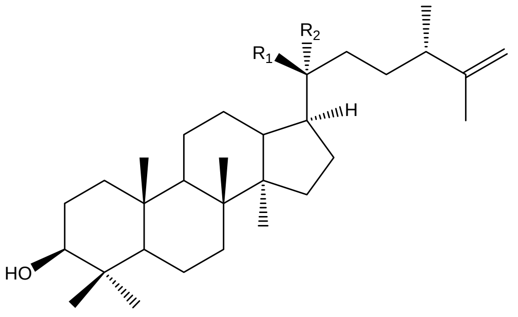
Foliachinenoside G (**108**)



Foliachinenoside H (**109**)

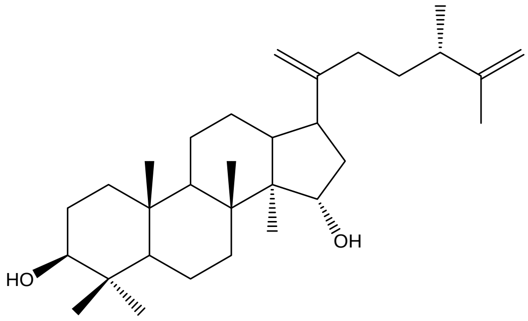


Foliachinenoside I (**110**)

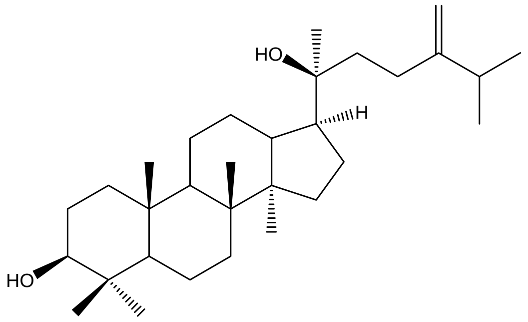


	R_1	R_2
Foliasalacin A_1 (**111**)	OH	CH_3
Foliasalacin A_2 (**112**)	CH_3	OH

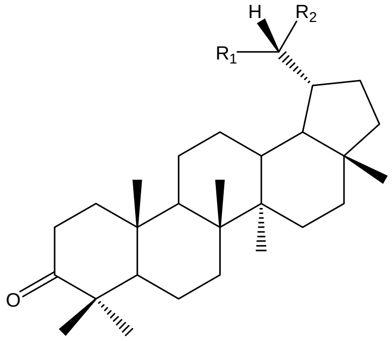
Figure 4. (continued)



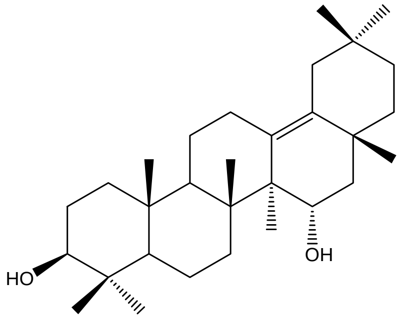
Foliasalacin A$_3$ (**113**)



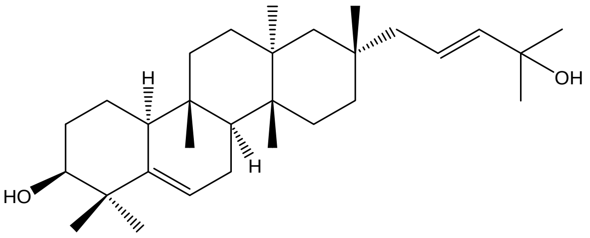
Foliasalacin A$_4$ (**114**)



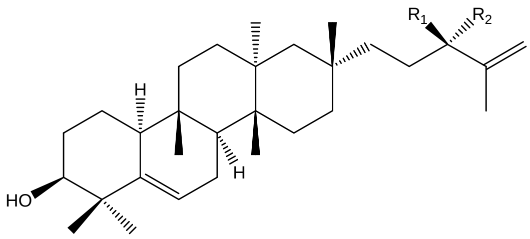
	R$_1$	R$_2$
Foliasalacin B$_1$ (**115**)	CH_2OH	CH_3
Foliasalacin B$_2$ (**116**)	CH_3	CH_2OH
Foliasalacin B$_3$ (**117**)	CO_2H	CH_3



Foliasalacin C (**118**)

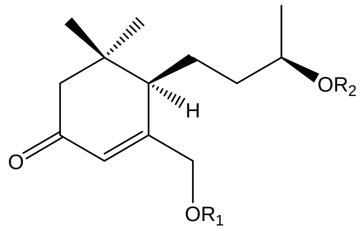


Foliasalacin D$_1$ (**119**)



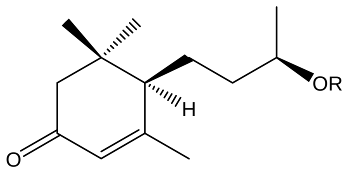
	R$_1$	R$_2$
Foliasalacin D$_2$ (**120**)	OH	H
Foliasalacin D$_3$ (**121**)	H	OH

Figure 4. (continued)



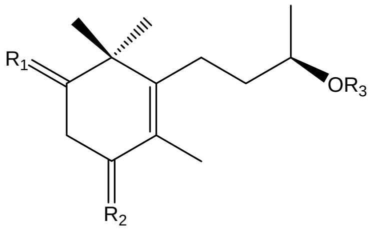
Foliasalacioside A$_1$ (**122**) R$_1$ = Glc, R$_2$ = H

Foliasalacioside A$_2$ (**123**) R$_1$ = H, R$_2$ = Glc

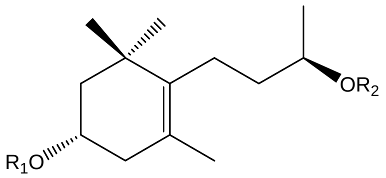


Foliasalacioside B$_1$ (**124**) R = Glc^6-Ara(p)

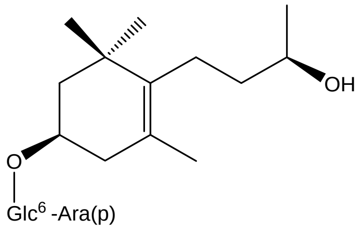
Foliasalacioside B$_2$ (**125**) R = Glc^6-Ara(f)



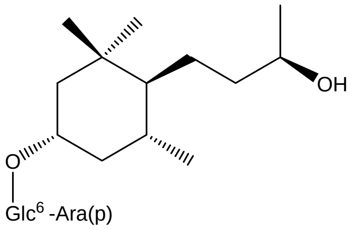
	R$_1$	R$_2$	R$_3$
Foliasalacioside C (**126**)	O	H$_2$	Glc^6-Ara(p)
Foliasalacioside D (**127**)	H$_2$	O	Glc^6-Ara(f)



	R$_1$	R$_2$
Foliasalacioside E$_1$ (**128**)	Glc^6-Ara(p)	H
Foliasalacioside E$_2$ (**129**)	H	Glc^6-Ara(p)
Foliasalacioside E$_3$ (**130**)	H	Glc^6-Ara(f)

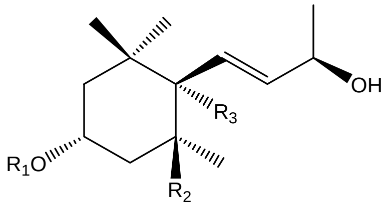


Foliasalacioside F (**131**)

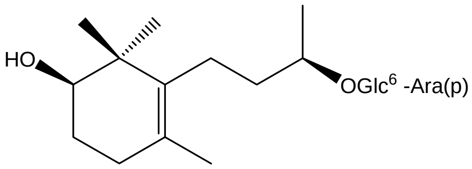


Foliasalacioside H (**133**)

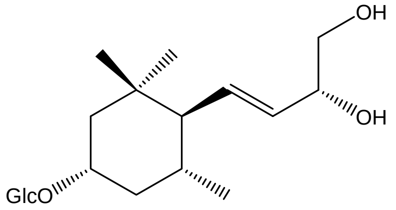
Figure 4. (continued)



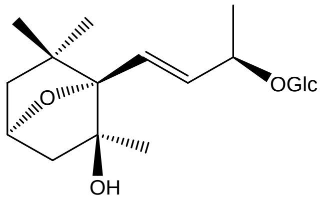
	R_1	R_2	R_3
Foliasalacioside G (**132**)	Glc^6-Ara(p)	H	H
Foliasalacioside K (**136**)	Glc	OH	OH



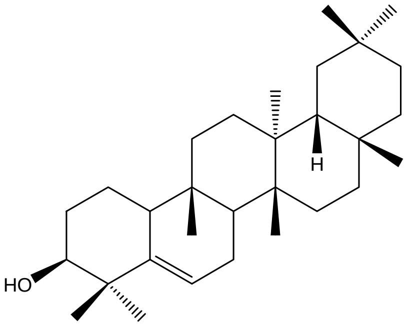
Foliasalacioside I (**134**)



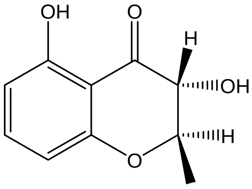
Foliasalacioside J (**135**)



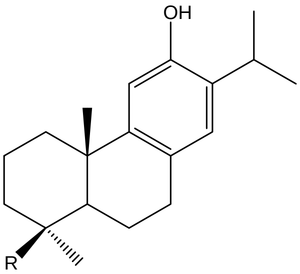
Foliasalacioside L (**137**)



Gult-5-en-3β-ol (**138**)



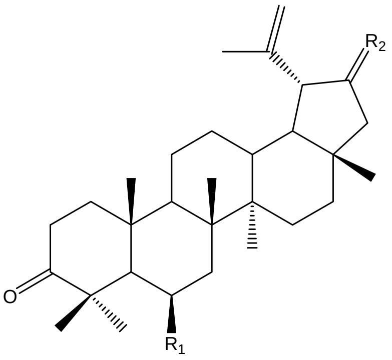
(-)-Gynuraone (**139**)



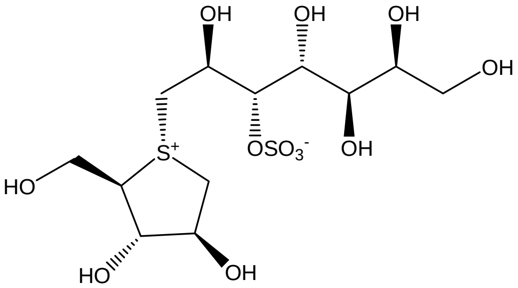
19-Hydroxyferruginol (**140**) R = CH_2OH

Lambertic acid (**146**) R = CO_2H

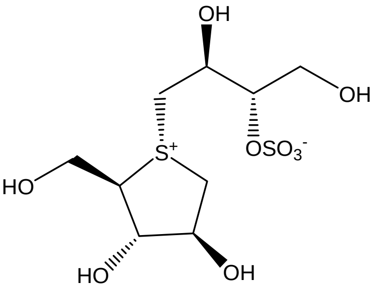
Figure 4. (continued)



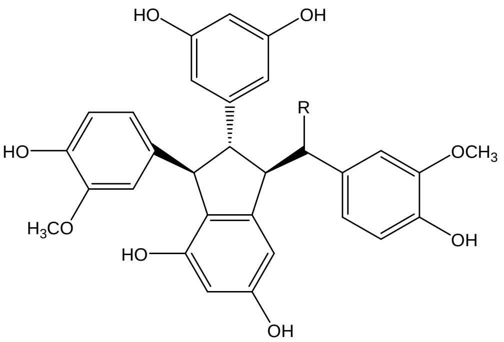
	R_1	R_2
6β-Hydroxysalacianone (**144**)	OH	O
Salacianol (**164**)	H	β-OH, α-H
Salacianone (**165**)	H	O

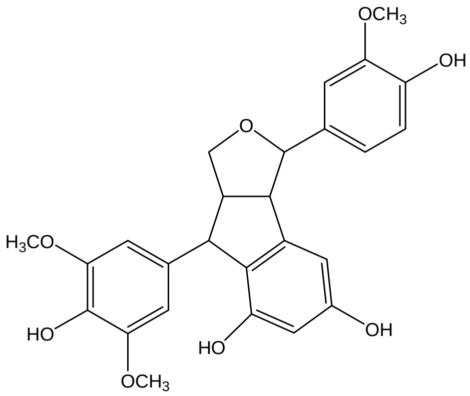


Kotalanol (**145**)



Salacinol (**166**)



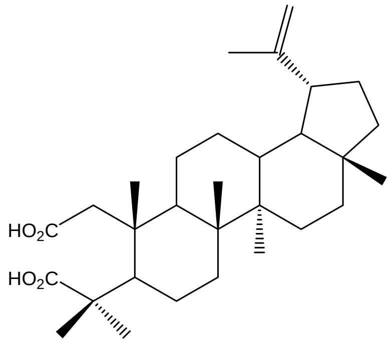


Lehmbachols A, B (**147**, **148**) R = OCH_3 (diastereomers)

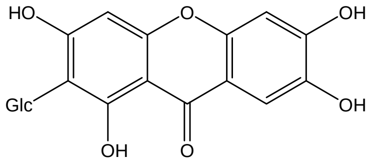
Lehmbachol D (**150**)

Lehmbachol C (**149**) R = OCH_2CH_3

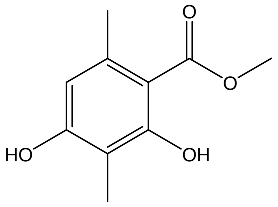
Figure 4. (continued)



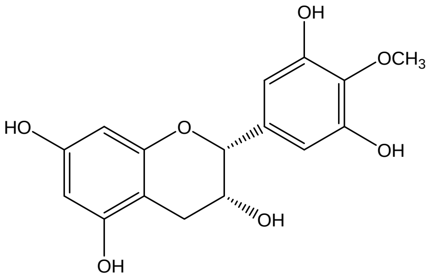
2,3-*seco*-Lup-20(29)-en-2,3-dioic acid (**152**)



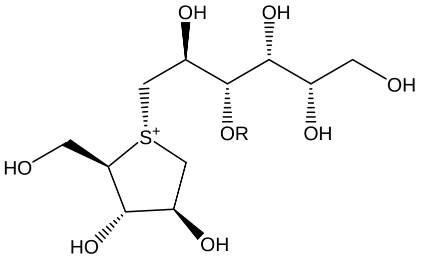
Mangiferin (**153**)



Methyl-2,4-dihydroxy-3,6-dimethylbenzoate (**155**)

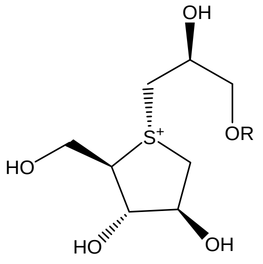


(-)-4′-*O*-Methylepigallocatechin (**156**)



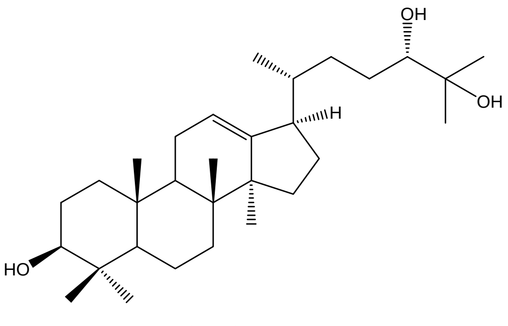
Neoponkoranol (**157**) R = H

Ponkoranol (**162**) R = SO_3^-

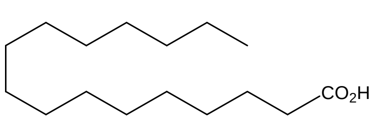


Neosalaprinol (**158**) R = H

Salaprinol (**167**) R = SO_3^-

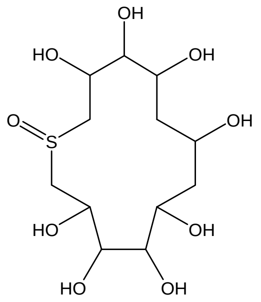


Olibanumol J (**159**)

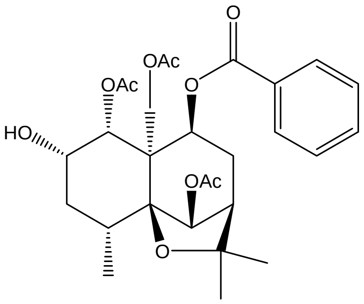


Palmitic acid (**160**)

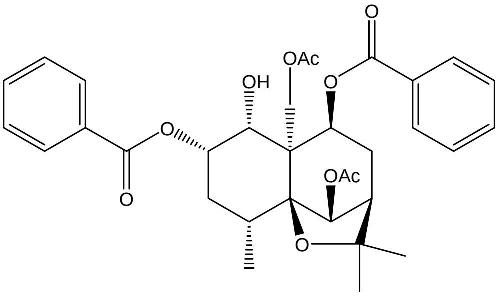
Figure 4. (continued)



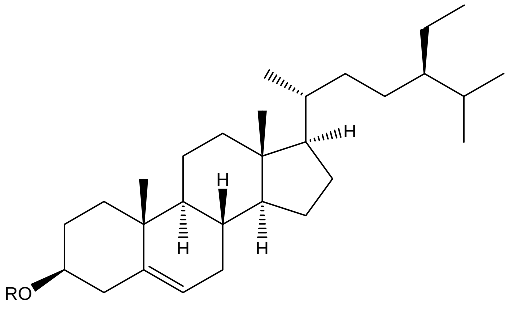
Polyhydroxylated cyclic 13-membered sulfoxide (**161**)



Salasol A (**168**)

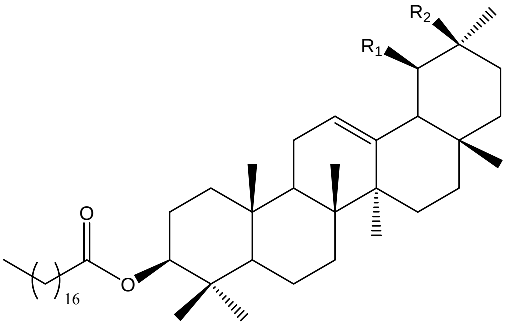


Salasol B (**169**)

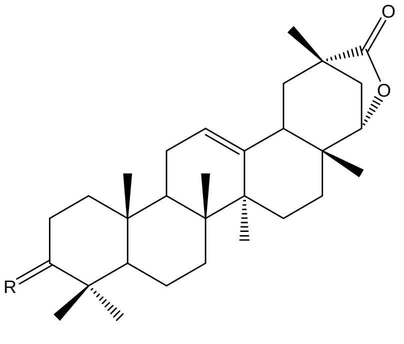


β-Sitosterol (**171**) R = H

β-Sitosterol glucoside (**172**) R = Glc



	R_1	R_2
3β-Stearyloxyolean-12-en (**173**)	H	CH_3
3β-Stearyloxyurs-12-en (**174**)	CH_3	H



Wilforlide A (**176**) R = β-OH, α-H

Wilforlide B (**177**) R = O

Figure 4. (continued)

9. Eudesmane-type Sesquiterpenes in Higher Plants

Eudesmane-type sesquiterpenes are widely distributed in the dicotyledonous families of flowering plants such as Apocynaceae, Asteraceae, Chloranthaceae, Euphorbiaceae, Lamiaceae, Lauraceae, Leguminosae, Moraceae, Sapindaceae and Umbelliferae, and can also be found in some monocotyledonous families such as Gramineae, Liliaceae and Zingiberaceae. However, the plant family Asteraceae is the largest source of these compounds.

Several genera in the family Asteraceae including *Artemisia*, *Chrysanthemum*, *Inula* and *Varthemia* yielded various bioactive eudesmane sesquiterpenes and eudesmane sesquiterpene lactones (eudesmanolides). Artanoate (**185**) and eudesmanomolide (**219**), from the aerial parts of *Artemisia anomala*, were cytotoxic against cancer cell lines *in vitro*. Artanoate was cytotoxic against HCT-8 cell line (IC_{50} = 9.13 μM) and eudesmanomolide exhibited inhibitory activities against both HCT-8 (IC_{50} = 3.76 μM) and A549 cell lines (IC_{50} = 5.49 μM) (Zan *et al.*, 2012). Methanolic extract from the flowers of *Chrysanthemum indicum* showed inhibitory activity against rat lens aldose reductase (IC_{50} = 3.5 μg/ml), then the active components, kikkanols A-C (**259-261**), were isolated by bioassay-guided fractionation (Yoshikawa *et al.*, 1999). Essential oil from the roots of *Inula helenium*, containing the eudesmanolides alantolactone (**184**), diplophyllin (**208**) and isoalantolactone (**256**) as major constituents, exhibited very potent anti-staphylococcal activity through membrane-damaging effects (Stojanovic-Radic *et al.*, 2012). Similarly, the eudesmane-12,8-olides 11α,13-dihydro-2α-hydroxyalantolactone (**198**), 11,13-dihydroivalin (**199**) and septuplinolide (**300**), from the roots of *Inula racemosa*, exhibited moderate cytotoxicity against a number of human cancer cell lines, with IC_{50} values ranging from 25.2 to 39.3 μM (Zhang *et al.*, 2012). 3-Oxocostusic acid [selina-4,11(13)-dien-on-12-oic acid] (**281**), a constituent of *Artemisia altaiensis* (Khanina *et al.*, 1998), *Nectandra cissiflora* (Garcez, Garcez, and Miranda, 2010) and *Varthemia iphionoides* (Al-Dabbas *et al.*, 2005), was shown to be a potent antimicrobial agent against six bacterial species including *Staphylococcus aureus*, *Bacillus subtilis*, *Micrococcus luteus*, *Escherichia coli*, *Bacillus cereus* and *Salmonella enteritides* with MIC values from 250 to 500 μg/ml (Al-Dabbas *et al.*, 2005).

Chemical investigation of the chloroform extract of *Caragana intermedia* aerial part (family Leguminosae) yielded several 4(15)-eudesmene sesquiterpenes, including eudesma-4(15),7-dien-1β-ol (**218**), 4(15)-eudesmene-1β,5α-diol (**221**), 4(15)-eudesmene-1β,6α-diol (**222**), 4(15)-eudesmene-1β,7α-diol (**223**), 4(15)-eudesmene-1β,7β-diol (**224**), 5-*epi*-eudesma-4(15)-ene-1β,6β-diol (**225**) and 7-trinoreudesma-4(15),8-dien-1β-ol-7-one (**308**). The bioassay showed that compounds **221**, **223** and **224** exhibited antifungal activity against the rice blast fungus *Pyricularia oryzae* P-2b, with MIC values of 20, 12, and 16 μg/ml, respectively. 4(15)-Eudesmene-1β,5α-diol also showed effect on energy metabolism by stimulating glucose consumption in C_2C_{12} skeletal muscle cells with an IC_{50} value of 10.7 μg/ml and in db/db mice with an MIC value of 100 mg/kg. 5-*epi*-Eudesma-4(15)-ene-1β,6β-diol exhibited weak anti-HIV activity with an IC_{50} value of 10 μg/ml (Sun *et al*., 2004).

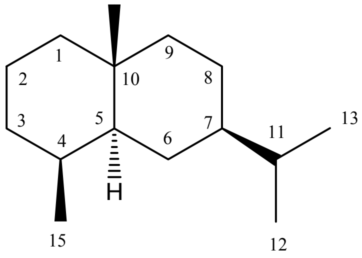
Two trinoreudesmane sesquiterpenes, oxyphyllanenes A-B (**285-286**), a noreudesmane sesquiterpene, oxyphyllanene C (**287**), and four eudesmane sesquiterpenes, oxyphyllanenes D-G (**288-291**), were isolated from the fruits of *Alpinia oxyphylla* (family Zingiberaceae). Among them, compounds **287-290** showed inhibitory activity against nitric oxide production in lipopolysaccharide and interferon-γ-induced RAW 264.7 murine macrophages (Xu *et al*., 2012).

Eudesmane sesquiterpene glucosides, litchiosides A-B (**263-264**) and pumilaside A (**299**), were isolated from the seeds of *Litchi chinensis* (family Sapindaceae). Pumilaside A exhibited significant cytotoxicity against cancer cell lines (A549, LAC, Hela and HepG2), with IC_{50} values of 0.012-6.29 μM (Xu *et al*., 2010). This compound was firstly isolated from the fruits of *Ficus pumila* in the family Moraceae (Kitajima, Kimizuka, and Tanaka, 2000). A sesquiterpene lactone glucoside, 1-*O*-β-D-glucopyranosyl-9β,15-dihydroxy-5α,6βH-eudesma-3-ene-6α,12-olide (**233**), from the seed pods of *Bauhinia retusa* (family Leguminosae), displayed moderate antibacterial activity against *Pseudomonas aeruginosa* and *Escherichia coli* in the disc diffusion method (Semwal and Sharma, 2011). Other eudesmane sesquiterpene glucosides such as 1β-*O*-β-D-glucopyranosyl-4α-hydroxyl-5α,6β,11βH-eudesma-12,6α-olide (**234**) from *Lactuca sativa* var. *anagustata* (family Asteraceae) (Han, Cao, and Xia, 2009), hierapolitanins C-D (**236-237**) from *Centaurea hierapolitana* (family Asteraceae) (Karamenderes *et al*., 2007), liriopeoside A (**262**) and ophiopogonosides A-B (**279-280**) from *Liriope muscari* and *Ophiopogon japonicus* (family Liliaceae) (Cheng *et al*., 2004; Jiang *et al*., 2012), and pterodontriol D-6-*O*-β-D-glucopyranoside (**298**) from *Parepigynum funingense* (family Apocynaceae) (Hua *et al*., 2004), have also been reported.

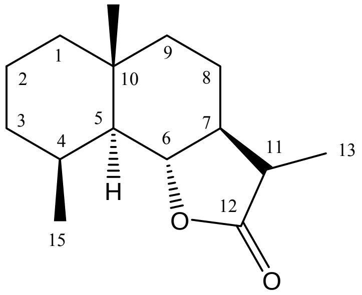
Eudesmane sesquiterpenes with rearranged carbon skeletons, such as diversifolol (**209**) and macrophyllic acids A-E (**265-269**), were reported as constituents of plants in the family Asteraceae, including *Tithonia diversifolia* (Kuo and Chen, 1997) and *Inula macrophylla* (Su *et al.*, 2000b), respectively. This family also contains sesquiterpenoid dimers, consisting of two eudesmanolide units, such as biatractylolide (**188**) from *Atractylodes macrocephala* (Lin *et al.*, 1997) and hydroxy-bis-dihydroencelin (**239**) from *Montanoa speciosa* (Quijano *et al.*, 1991). Dimers of two different sesquiterpenoid units, such as fruticolide (**230**) from *Ferreyranthus fruticosus* (Jakupovic *et al.*, 1988) and macrophyllidimer A (**270**) from *Inula macrophylla* (Su *et al.*, 2000a), have also been reported.

Eudesmane sesquiterpenes have been found in other flowering plants including *Chloranthus henryi* (Wu *et al.*, 2007), *Chloranthus japonicus* (Fang, Liu, and Zhong, 2012), *Cymbopogon proximus* (El-Askary, Meselhy, and Galal, 2003), *Dittrichia graveolens* (Abou-Douh, 2008), *Isodon grandifolia* var. *atuntzensis* (Wu *et al.*, 1993), *Laggera alata* (Raharivelomanana *et al.*, 1998; Zheng *et al.*, 2003), *Laggera pterodonta* (Zhao *et al.*, 1997; Liu *et al.*, 2007), *Ligularia dentata* (Naya *et al.*, 1990), *Melampodium camphoratum* (Chaturvedula *et al.*, 2004), *Plectranthus cylindraceus* (Orabi *et al.*, 2000), *Pluchea arguta* (Ahmad, Fizza, and Amber, 1989), *Pluchea dioscoridis* (Mahmoud, 1997), *Sambucus williamsii* (Yang *et al.*, 2006), *Tanacetum praeteritum* subsp. *praeteritum* (Goren, 1996), *Teucrium heterophyllum* (Fraga *et al.*, 1993), *Teucrium polium* (Kamel, 1995) and *Torilis japonica* (Kitajima *et al.*, 2002).

Eudesmane sesquiterpenes found in these flowering plants are summarized in **Table 3** and their chemical structures are shown in **Figure 5**.



Eudesmane



Eudesmanolide

Table 3. Distribution of eudesmane-type sesquiterpenes in higher plants

Compound	**Source**	**Family**	**Plant part**	**References**
6α-({4′-Acetoxy}-7′*Z*-coumaryloxy)eudesm-4(14)-ene (**178**)	*Melampodium camphoratum*	Asteraceae	Leaves	Chaturvedula *et al*., 2004
1α-Acetoxy-3α-hydroxy-5,7α,6,11β(H)-eudesm-4,15-en-6,12-olide (**179**)	*Artemisia lehmanniana*		Aerial parts	Mukhamatkhanova *et al*., 2004
1α-Acetoxy-4α-hydroxy-5,7α,6,11β(H)-eudesm-2,3-en-6,12-olide (**180**)				
11-Acetoxy-4α-methoxyeudesmane (**181**)	*Allophylus laevigatus*	Sapindaceae	Fruits	David, Santos, and David, 2004
13-Acetyloxy-5,7(11)-eudesmadien-12,8-olide (**182**)	*Inula racemosa*	Asteraceae	Roots	Zhang *et al*., 2012
Ainsliaside E (**183**)	*Parepigynum funingense*	Apocynaceae		Hua *et al*., 2004
Alantolactone (**184**)	*I. helenium*	Asteraceae		Stojanovic-Radic *et al*., 2012
Artanoate (**185**)	*Artemisia anomala* *Tanacetum praeteritum*		Aerial parts	Zan *et al*., 2012 Goren, 1996
Artapshin (**186**)	*Artemisia caerulescens*			Sanz and Marco, 1990

Table 3. (continued)

Compound	Source	Family	Plant part	References
Atractylenolide III (**187**)	*Chloranthus japonicus*	Chloranthaceae	Aerial parts	Fang *et al*., 2012
Biatractylolide (**188**)	*Atractylodes macrocephala*	Asteraceae	Branches	Lin *et al*., 1997
12-Carboxyeudesman-3,11(13)-diene (**189**)	*Nectandra cissiflora*	Lauraceae	Bark	Garcez *et al*., 2010
Chlojaponilactone A (**190**)	*C. japonicus*	Chloranthaceae	Aerial parts	Fang *et al*., 2012
Costic acid (**191**)	*Nectandra cissiflora*	Lauraceae	Bark	Garcez *et al*., 2010
6α-(7′*Z*-Coumaryloxy)-eudesm-4(14)-ene (**192**)	*Melampodium camphoratum*	Asteraceae	Leaves	Chaturvedula *et al*., 2004
Crytomeridiol (**193**)	*Isodon grandifolia*	Lamiaceae		Wu *et al*., 1993
1,2-Dehydro-3-*epi*-isotelekin (**194**)	*Montanoa speciosa*	Asteraceae	Aerial parts	Quijano *et al*., 1991
1,2-Dehydro-3-*epi*-isotelekin acetate (**195**)				
1,2-Dehydro-3-oxo-costic acid (**196**)				
Desacetylplectranthone (**197**)	*Plectranthus cylindraceus*	Lamiaceae		Orabi *et al*., 2000
11α,13-Dihydro-2α-hydroxyalantolactone (**198**)	*Inula racemosa*	Asteraceae	Roots	Zhang *et al*., 2012
11,13-Dihydroivalin (**199**)				

Table 3. (continued)

Compound	Source	Family	Plant part	References
4β,11-Dihydroxy-enantioeudesmane-1-one (**200**)	*Laggera pterodonta*	Asteraceae	Aerial parts	Zhao *et al*., 1997
5α,11-Dihydroxy-3-ene-eudesman-2-one (**201**)	*Artemisia eriopoda* *L. pterodonta*			Hu, Bai, and Jia, 1996 Zhao *et al*., 1997
1β,6α-Dihydroxy-7-*epi*-eudesm-3-ene (**202**)	*Croton arboreous* *Pluchea dioscoridis*	Euphorbiaceae Asteraceae	Aerial parts Leaves	Aguilar-Guadarrama and Rios, 2004 Mahmoud, 1997
1β,6β-Dihydroxy-7-*epi*-eudesm-3-ene (**203**)	*P. dioscoridis*	Asteraceae	Leaves	Mahmoud, 1997
4α,13-Dihydroxy-5,7(11)-eudesmadien-12,8-olide (**204**)	*Inula racemosa*		Roots	Zhang *et al*., 2012
1β,9α-Dihydroxyeudesm-4(15),11(13)-dien-5α,7αH-12,6α-olide (**205**)	*P. dioscoridis*		Leaves	Mahmoud, 1997
4β,5α-Dihydroxy-15-oxo-eudesm-11(13)-en-12-oic acid (**206**)				

Table 3. (continued)

Compound	**Source**	**Family**	**Plant part**	**References**
4β,5β-Dihydroxy-15-oxo-eudesm-11(13)-en-12-oic acid (**207**)	*Pluchea dioscoridis*	Asteraceae	Leaves	Mahmoud, 1997
Diplophyllin (**208**)	*Inula helenium*		Roots	Stojanovic-Radic *et al.*, 2012
Diversifolol (**209**)	*Tithonia diversifolia*		Leaves	Kuo and Chen, 1997
4β,7β,11-Enantio-eudesmantriol (**210**)	*Coleus forskohlii*	Lamiaceae	Aerial parts	Shan *et al.*, 2007
Encelin (**211**)	*Montanoa speciosa*	Asteraceae		Quijano *et al.*, 1991
Ent-7(11)-selinen-4-ol (**212**)	*Laggera pterodonta*			Zhao *et al.*, 1997
10-*epi*-5α-hydroperoxy-β-eudesmol (**213**)	*Alpinia japonica*	Zingiberaceae	Rhizomes	Itokawa, Morita, and Watanabe, 1987
10-*epi*-5β-hydroperoxy-β-eudesmol (**214**)				
4,10-*epi*-5β-hydroxy-dihydroeudesmol (**215**)				
4α,15-Epoxyeudesmane-1β,6α-diol (**216**)	*Torilis japonica*	Umbelliferae	Fruits	Kitajima *et al.*, 2002
Epoxysantamarin (**217**)	*Tanacetum praeteritum*	Asteraceae	Aerial parts	Goren, 1996
Eudesma-4(15),7-dien-1β-ol (**218**)	*Caragana intermedia*	Leguminosae		Sun *et al.*, 2004

Table 3. (continued)

Compound	Source	Family	Plant part	References
Eudesmanomolide (**219**)	*Artemisia anomala*	Asteraceae	Aerial parts	Zan *et al*., 2012
5α,10β -4(15)-Eudesmen-1β,6β-diol (**220**)	*Croton arboreous*	Euphorbiaceae		Aguilar-Guadarrama and Rios, 2004
4(15)-Eudesmene-1β,5α -diol (**221**)	*Caragana intermedia* *Torilis japonica*	Leguminosae Umbelliferae	Aerial parts Fruits	Sun *et al*., 2004 Kitajima *et al*., 2002
4(15)-Eudesmene-1β,6α -diol (**222**)	*Ageratina glechonophylla* *C. intermedia* *Torilis japonica*	Asteraceae Leguminosae Umbelliferae	Aerial parts Aerial parts Fruits	Gonzalez *et al*., 1989 Sun *et al*., 2004 Kitajima *et al*., 2002
4(15)-Eudesmene-1β,7α -diol (**223**)	*C. intermedia*	Leguminosae	Aerial parts	Sun *et al*., 2004
4(15)-Eudesmene-1β,7β -diol (**224**)				
5-*epi*-Eudesma-4(15)-ene-1β,6β-diol (**225**)				
7-*epi*-Eudesm-4(15)-ene -1β,6α-diol (**226**)	*Teucrium polium*	Lamiaceae	Leaves	Kamel, 1995
7-*epi*-Eudesm-4(15)-ene -1β,6β-diol (**227**)				

Table 3. (continued)

Compound	Source	Family	Plant part	References
7-*epi*-γ-Eudesmol (**228**)	*Laggera alata*	Asteraceae	Aerial parts	Raharivelomanana *et al.*, 1998
7-*epi*-β-Eudesmol (**229**)				
Fruticolide (**230**)	*Ferreyranthus fruticosus*			Jakupovic *et al.*, 1988
Gargantolide (**231**)	*Artemisia caerulescens*			Sanz and Marco, 1990
1-*epi*-Gargantolide (**232**)				
1-*O*-β-D-Glucopyranosyl-9β,15-dihydroxy-5α,6βH-eudesma-3-ene-6α,12-olide (**233**)	*Bauhinia retusa*	Leguminosae	Seed pods	Semwal and Sharma, 2011
1β-*O*-β-D-Glucopyranosyl-4α-hydroxyl-5α,6β,11βH-eudesma-12,6α-olide (**234**)	*Lactuca sativa* var. *anagustata* L.	Asteraceae	Stalk	Han *et al.*, 2009
6α-({4′-*O*-[9″*Z*-Hexadecenoyl]}-7′*E*-coumaryloxy)eudesm-4(15)-ene (**235**)	*Melampodium camphoratum*		Leaves	Chaturvedula *et al.*, 2004
Hierapolitanin C (**236**)	*Centaurea hierapolitana*	Asteraceae	Aerial parts	Karamenderes *et al.*, 2007
Hierapolitanin D (**237**)				
5α-Hydroperoxy-β-eudesmol (**238**)	*Cymbopogon proximus*	Gramineae		El-Askary *et al.*, 2003
Hydroxy-bis-dihydroencelin (**239**)	*Montanoa speciosa*	Asteraceae		Quijano *et al.*, 1991

Table 3. (continued)

Compound	Source	Family	Plant part	References
1β-Hydroxy-α-cyperone (**240**)	*Artemisia caerulescens* *Ligularia dentata*	Asteraceae	Aerial parts Rhizomes	Sanz and Marco, 1990 Naya *et al*., 1990
2α-Hydroxy-4-*epi*-ilicic acid (**241**)	*Dittrichia graveolens*		Epigeal parts	Abou-Douh, 2008
5α-Hydroxy-4-*epi*-ilicic acid methyl ester (**242**)	*Laggera alata*		Aerial parts	Zheng *et al*., 2003
8α-Hydroxy-1,4β-epoxy-10-epieudesman-5α,6β,7α,11βH-12,6-olide (**243**)	*A. caerulescens*			Sanz and Marco, 1990
5α-Hydroxy-eudesma-4(15),11-diene (**244**)	*A. annua*		Leaves	Sy and Brown, 1998
1β-Hydroxy-α-eudesmol (**245**)	*Cymbopogon proximus*	Gramineae	Aerial parts	El-Askary *et al*., 2003
1β-Hydroxy-β-eudesmol (**246**)				
5α-Hydroxy-β-eudesmol (**247**)				
3α-Hydroxyilicic acid (**248**)	*L. alata*	Asteraceae		Zheng *et al*., 2003
5β-Hydroxyilicic acid (**249**)				
3α-Hydroxyilicic acid methyl ester (**250**)	*D. graveolens*		Epigeal parts	Abou-Douh, 2008

Table 3. (continued)

Compound	Source	Family	Plant part	References
1β-Hydroxy-15-*O*-(*p*-methoxyphenylacetyl)-5α,6β,11βH-eudesma-3-en-12,6α-olide (**251**)	*Lactuca sativa* var. *anagustata* L.	Asteraceae	Stalks	Han *et al*., 2009
1α-Hydroxypinnatifidin (**252**)	*Ferreyranthus fruticosus*		Aerial parts	Jakupovic *et al*., 1988
2α-Hydroxypterodontic acid (**253**)	*Laggera pterodonta*			Liu *et al*., 2007
8α-Hydroxytaurin (**254**)	*Artemisia caerulescens*			Sanz and Marco, 1990
Ilicic acid (**255**)	*Aster himalaicus*			Xie *et al*., 2010
Isoalantolactone (**256**)	*Inula helenium*		Roots	Stojanovic-Radic *et al*., 2012
Isodeacetylplectranthone (**257**)	*Plectranthus cylindraceus*	Lamiaceae	Aerial parts	Orabi *et al*., 2000
Isodonsesquitin A (**258**)	*Isodon grandifolia*		Leaves	Wu *et al*., 1993
Kikkanol A (**259**)	*Chrysanthemum indicum*	Asteraceae	Flowers	Yoshikawa *et al*., 1999
Kikkanol B (**260**)				
Kikkanol C (**261**)				
Liriopeoside A (**262**)	*Liriope muscari*	Liliaceae	Tubers	Cheng *et al*., 2004
Litchiosides A (**263**)	*Litchi chinensis*	Sapindaceae	Seeds	Xu *et al*., 2010
Litchiosides B (**264**)				

Table 3. (continued)

Compound	Source	Family	Plant part	References
Macrophyllic acid A (**265**)	*Inula macrophylla*	Asteraceae	Bark	Su *et al.*, 2000b
Macrophyllic acid B (**266**)				
Macrophyllic acid C (**267**)				
Macrophyllic acid D (**268**)				
Macrophyllic acid E (**269**)				
Macrophyllidimer A (**270**)				Su *et al.*, 2000a
Macrophyllilactone E (**271**)	*I. macrophylla* *I. racemosa*		Bark Roots	Fu *et al.*, 2001 Zhang *et al.*, 2012
Macrophyllilactone F (**272**)	*I. macrophylla*		Bark	Fu *et al.*, 2001
Macrophyllilactone G (**273**)				
6α-({4′-*O*-Methyl}-7′*E*-coumaryloxy)eudesm-4(15)-ene (**274**)	*Melampodium camphoratum*		Leaves	Chaturvedula *et al.*, 2004
Neolitacumone B (**275**)	*Chloranthus japonicus*	Chloranthaceae	Aerial parts	Fang *et al.*, 2012
Odonticin (**276**)	*Pluchea arguta*	Asteraceae	Whole plants	Ahmad *et al.*, 1989
Odontin (**277**)				
1-One-4-*epi*-alantolactone (**278**)	*I. racemosa*		Roots	Zhang *et al.*, 2012
Ophiopogonoside A (**279**)	*Liriope muscari*	Liliaceae		Cheng *et al.*, 2004

Table 3. (continued)

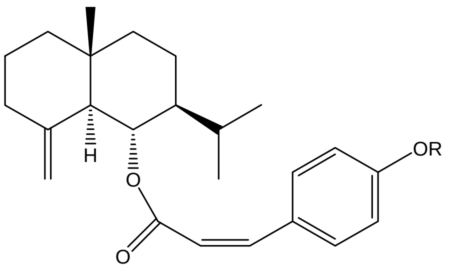
Compound	Source	Family	Plant part	References
Ophiopogonoside B (**280**)	*Liriope muscari*	Liliaceae	Roots	Jiang *et al*., 2012
3-Oxocostusic acid (**281**)	*Artemisia altaiensis* *Nectandra cissiflora* *Varthemia iphionoides*	Asteraceae Lauraceae Asteraceae	Epigeal part Trunk bark Aerial parts	Khanina *et al*., 1998 Garcez *et al*., 2010 Al-Dabbas *et al*., 2005
1-Oxo-cryptomeridiol (**282**)	*Artemisia eriopoda*	Asteraceae	Aerial parts	Hu *et al*., 1996
(7α)-8-Oxoeudesm-4(15)-en-12-oic acid (**283**)	*Chloranthus henryi*	Chloranthaceae	Leaves, Stems	Wu *et al*., 2007
1-Oxoeudesm-11(13)-eno-12,8α-lactone (**284**)	*Aster himalaicus*	Asteraceae	Aerial parts	Xie *et al*., 2010
Oxyphyllanene A (**285**)	*Alpinia oxyphylla*	Zingiberaceae	Fruits	Xu *et al*., 2012
Oxyphyllanene B (**286**)				
Oxyphyllanene C (**287**)				
Oxyphyllanene D (**288**)				
Oxyphyllanene E (**289**)				
Oxyphyllanene F (**290**)				
Oxyphyllanene G (**291**)				
6α-({4′-*O*-Palmityl}-7′*E*-coumaryloxy) eudesm-4(15)-ene (**292**)	*Melampodium camphoratum*	Asteraceae	Leaves	Chaturvedula *et al*., 2004

Table 3. (continued)

Compound	**Source**	**Family**	**Plant part**	**References**
2α,5α-Peroxyeudesma-3,11-dien-1-one (**293**)	*Artemisia caerulescens*	Asteraceae	Aerial parts	Sanz and Marco, 1990
Plectranthone (**294**)	*Plectranthus cylindraceus*	Lamiaceae		Orabi *et al*., 2000
Pterodolide (**295**)	*Laggera pterodonta*	Asteraceae		Liu *et al*., 2007
Pterodontriol C (**296**)				Zhao *et al*., 1997
Pterodontriol D (**297**)				
Pterodontriol D-6-*O*-β-D-glucopyranoside (**298**)	*Parepigynum funingense*	Apocynaceae	Roots	Hua *et al*., 2004
Pumilaside A (**299**)	*Ficus pumila* *Litchi chinensis*	Moraceae Sapindaceae	Fruits Seeds	Kitajima *et al*., 2000 Xu *et al*., 2010
Septuplinolide (**300**)	*Inula racemosa*	Asteraceae	Roots	Zhang *et al*., 2012
6α-({4′-*O*-Stearyl}-7′*E*-coumaryloxy)eudesm-4(15)-ene (**301**)	*Melampodium camphoratum*		Leaves	Chaturvedula *et al*., 2004
Tanapraetenolide (**302**)	*Tanacetum praeteritum*		Aerial parts	Goren, 1996
Teucdiol A (**303**)	*Teucrium heterophyllum*	Lamiaceae		Fraga *et al*., 1993
Teucdiol B (**304**)				
Teucrenone (**305**)				
Tourneforin (**306**)	*Artemisia tournefortiana*	Asteraceae		Talzhanov *et al*., 2007
1,4,13-Trihydroxy eudesm-11(12)-ene(**307**)	*Sambucus williamsii*	Adoxaceae	Stems	Yang *et al*., 2006

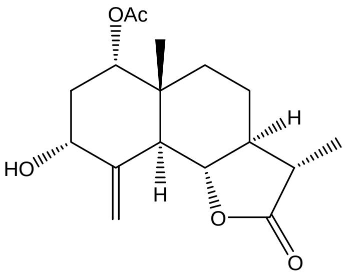
Table 3. (continued)

Compound	**Source**	**Family**	**Plant part**	**References**
7-Trinoreudesma-4(15),8-dien-1β-ol-7-one (**308**)	*Caragana intermedia*	Leguminosae	Aerial parts	Sun *et al*., 2004
Viscic acid (**309**)	*Nectandra cissiflora*	Lauraceae	Bark	Garcez *et al*., 2010
Yomogin (**310**)	*Ferreyranthus fruticosus*	Asteraceae	Aerial parts	Jakupovic *et al*., 1988

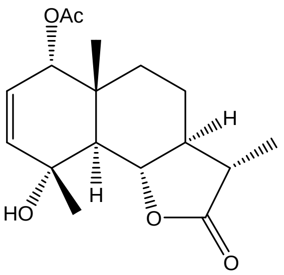


6α-({4′-Acetoxy}-7′Z-coumaryloxy) eudesm-4(14)-ene (**178**) R = COCH$_3$

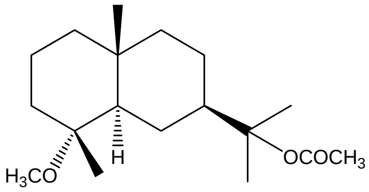
6α-(7′Z-Coumaryloxy) eudesm-4(14)-ene (**192**) R = H



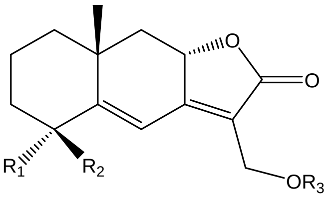
1α-Acetoxy-3α-hydroxy-5,7α,6,11β(H) -eudesm-4,15-en-6,12-olide (**179**)



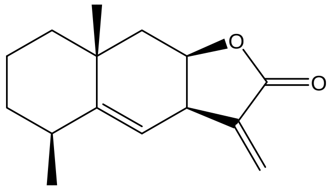
1α-Acetoxy-4α-hydroxy-5,7α,6,11β(H) -eudesm-2,3-en-6,12-olide (**180**)



11-Acetoxy-4α-methoxyeudesmane (**181**)

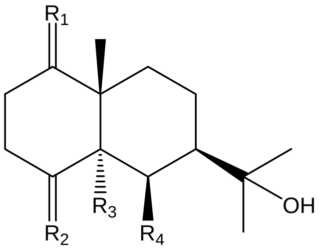


	R_1	R_2	R_3
13-Acetyloxy-5,7(11) -eudesmadien-12,8-olide (**182**)	CH$_3$	H	Ac
4α,13-Dihydroxy-5,7(11) -eudesmadien-12,8-olide (**204**)	OH	CH$_3$	H
Macrophyllilactone E (**271**)	CH$_3$	H	H

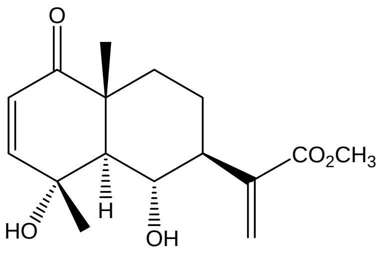


Alantolactone (**184**)

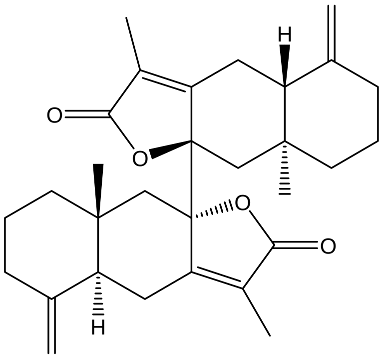
Figure 5. Eudesmane-type sesquiterpenes in higher plants



	R_1	R_2	R_3	R_4
Ainsliaside E (**183**)	β-OH, α-H	α-OH, β-CH_3	H	OGlc
Crytomeridiol (**193**)	H_2	α-OH, β-CH_3	H	H
5α-Hydroperoxy-β–eudesmol (**238**)	H_2	CH_2	OOH	H
1β-Hydroxy-β-eudesmol (**246**)	β-OH, α-H	CH_2	H	H
5α-Hydroxy-β-eudesmol (**247**)	H_2	CH_2	OH	H
1-Oxo-cryptomeridiol (**282**)	O	α-OH, β-CH_3	H	H

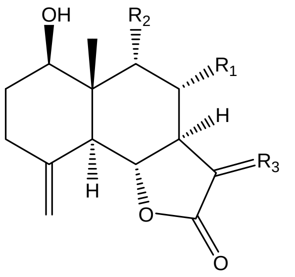


Artanoate (**185**)

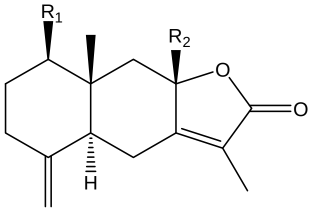


Biatractylolide (**188**)

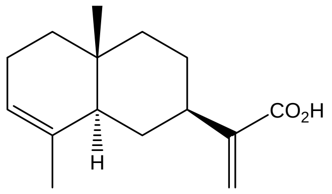
Figure 5. (continued)



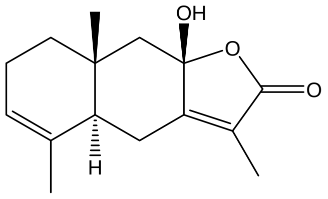
	R_1	R_2	R_3
Artapshin (**186**)	OH	H	α-CH_3,β-H
1β,9α-Dihydroxyeudesm-4(15),11(13)-dien-5α,7αH-12,6α-olide (**205**)	H	OH	CH_2



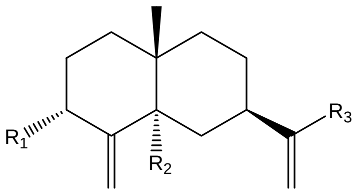
	R_1	R_2
Atractylenolide III (**187**)	H	OH
Neolitacumone B (**275**)	OH	H



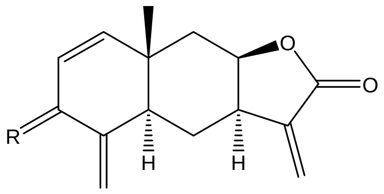
12-Carboxyeudesman-3,11(13)-diene (**189**)



Chlojaponilactone A (**190**)



	R_1	R_2	R_3
Costic acid (**191**)	H	H	CO_2H
5α-Hydroxy-eudesma-4(15),11-diene (**244**)	H	OH	CH_3
Viscic acid (**309**)	OH	H	CO_2H

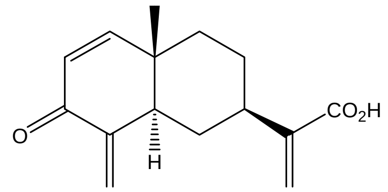


1,2-Dehydro-3-*epi*-isotelekin (**194**) R = β-OH, α-H

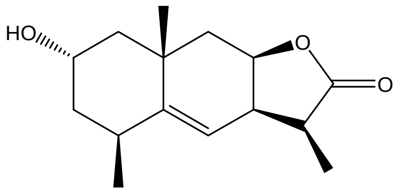
1,2-Dehydro-3-*epi*-isotelekin acetate (**195**) R = β-OAc, α-H

Encelin (**211**) R = O

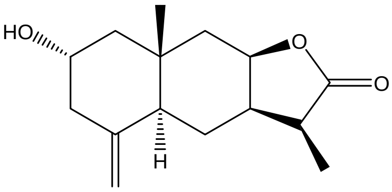
Figure 5. (continued)



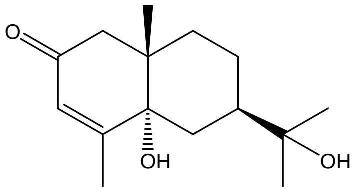
1,2-Dehydro-3-oxo-costic acid (**196**)



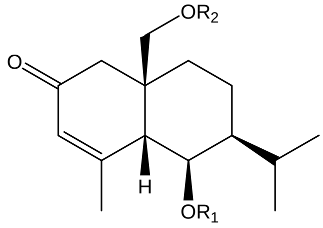
11α,13-Dihydro-2α-hydroxyalantolactone (**198**)



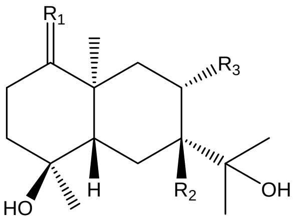
11,13-Dihydroivalin (**199**)



5α,11-Dihydroxy-3-ene-eudesman-2-one (**201**)

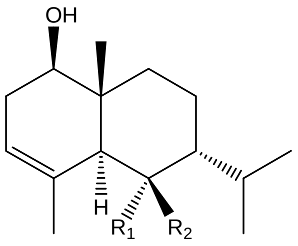


	R_1	R_2
Desacetylplectranthone (**197**)	$COCH_3$	H
Isodeacetylplectranthone (**257**)	H	$COCH_3$
Plectranthone (**294**)	$COCH_3$	$COCH_3$

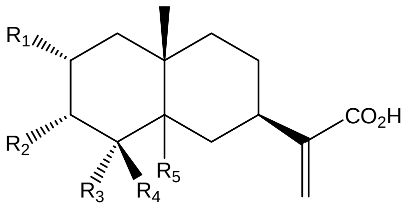


	R_1	R_2	R_3
4β,11-Dihydroxy enantioeudesmane-1-one (**200**)	O	H	H
4β,7β,11-Enantioeudesmantriol (**210**)	H_2	OH	H
Pterodontriol C (**296**)	H_2	H	OH

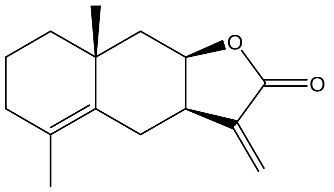
Figure 5. (continued)



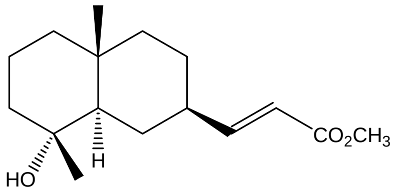
	R_1	R_2
1β,6α-Dihydroxy-7-*epi*-eudesm-3-ene (**202**)	OH	H
1β,6β-Dihydroxy-7-*epi*-eudesm-3-ene (**203**)	H	OH



	R_1	R_2	R_3	R_4	R_5
4β,5α-Dihydroxy-15-oxo-eudesm-11(13)-en-12-oic acid (**206**)	H	H	CHO	OH	α-OH
4β,5β-Dihydroxy-15-oxo-eudesm-11(13)-en-12-oic acid (**207**)	H	H	CHO	OH	β-OH
2α-Hydroxy-4-*epi*-ilicic acid (**241**)	OH	H	CH_3	OH	α-H
3α-Hydroxyilicic acid (**248**)	H	OH	OH	CH_3	α-H
5β-Hydroxyilicic acid (**249**)	H	H	OH	CH_3	β-OH
Ilicic acid (**255**)	H	H	OH	CH_3	α-H

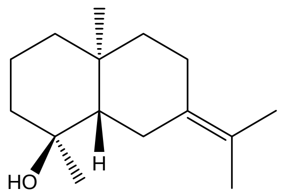


Diplophyllin (**208**)

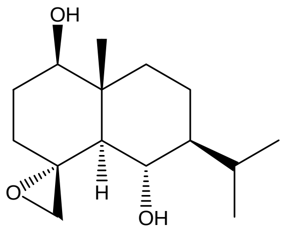


Diversifolol (**209**)

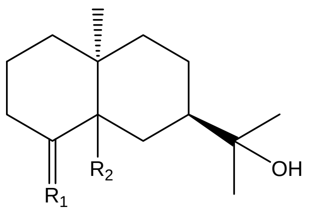
Figure 5. (continued)



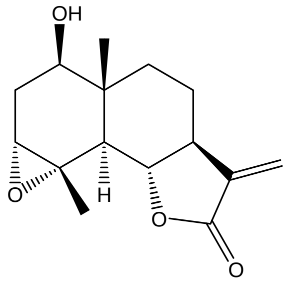
Ent-7(11)-selinen-4-ol (**212**)



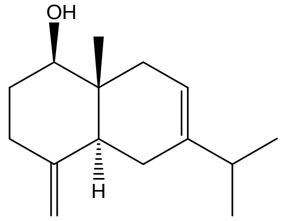
4α,15-Epoxyeudesmane-1β,6α-diol (**216**)



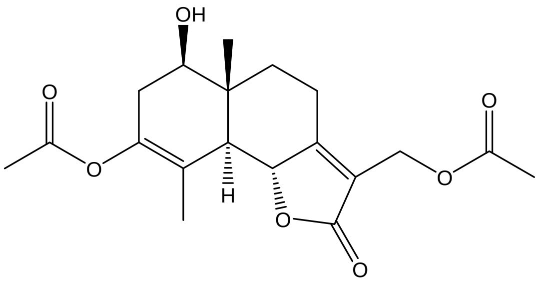
	R$_1$	R$_2$
10-*epi*-5α-hydroperoxy-β -eudesmol (**213**)	CH$_2$	α-OOH
10-*epi*-5β-hydroperoxy-β -eudesmol (**214**)	CH$_2$	β-OOH
4,10-*epi*-5β-hydroxy -dihydroeudesmol (**215**)	α-CH$_3$, β-H	β-OH



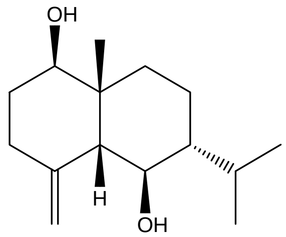
Epoxysantamarin (**217**)



Eudesma-4(15),7-dien -1β-ol (**218**)

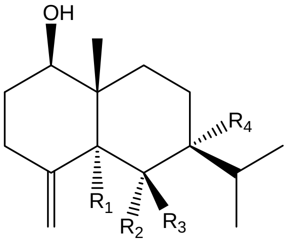


Eudesmanomolide (**219**)

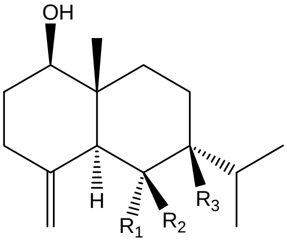


5-*epi*-Eudesma-4(15)-ene-1β,6β-diol (**225**)

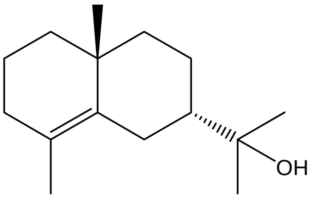
Figure 5. (continued)



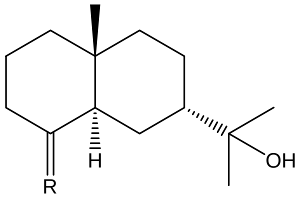
	R_1	R_2	R_3	R_4
5α,10β -4(15)-Eudesmen-1β,6β-diol (**220**)	H	H	OH	H
4(15)-Eudesmene-1β,5α-diol (**221**)	OH	H	H	H
4(15)-Eudesmene-1β,6α-diol (**222**)	H	OH	H	H
4(15)-Eudesmene-1β,7α-diol (**223**)	H	H	H	OH
Kikkanol A (**259**)	OH	H	OH	H



	R_1	R_2	R_3
4(15)-Eudesmene-1β,7β-diol (**224**)	H	H	OH
7-*epi*-Eudesm-4(15)-ene-1β,6α-diol (**226**)	OH	H	H
7-*epi*-Eudesm-4(15)-ene-1β,6β-diol (**227**)	H	OH	H



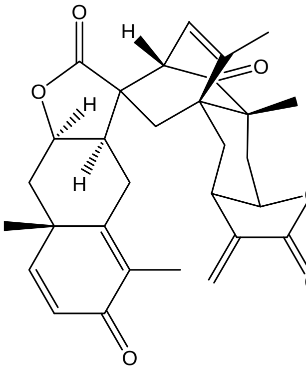
7-*epi*-γ-Eudesmol (**228**)



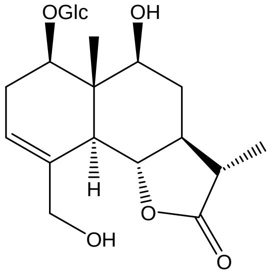
7-*epi*-β-Eudesmol (**229**) R = CH_2

Isodonsesquitin A (**258**) R = α-OH, β-CH_3

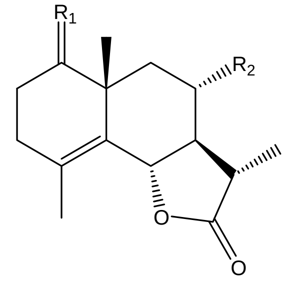
Figure 5. (continued)



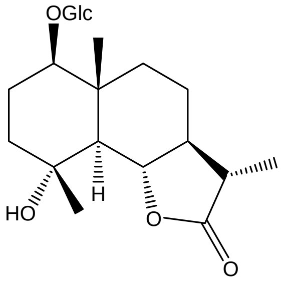
Fruticolide (**230**)



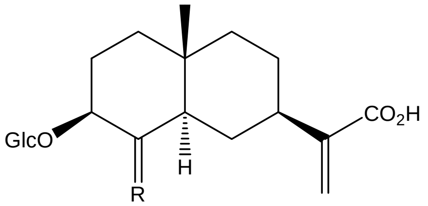
1-*O*-β-D-Glucopyranosyl-9β,15-dihydroxy -5α,6βH-eudesma-3-ene-6α,12 –olide (**233**)



	R_1	R_2
Gargantolide (**231**)	β-OH, α-H	OAc
1-*epi*-Gargantolide (**232**)	α-OH, β-H	OAc
8α-Hydroxytaurin (**254**)	O	OH

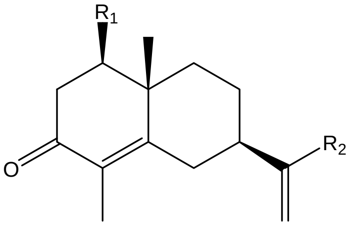


1β-*O*-β-D-Glucopyranosyl-4α-hydroxyl -5α,6β,11βH-eudesma-12,6α-olide (**234**)



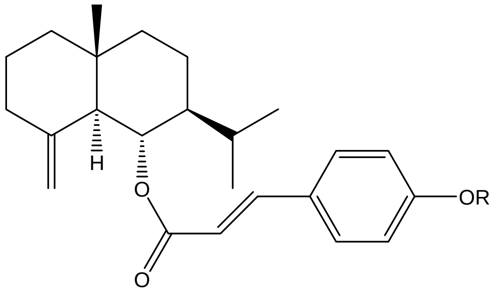
Hierapolitanin C (**236**) R = CH_2

Hierapolitanin D (**237**) R = β-OH, α-CH_3



	R_1	R_2
1β-Hydroxy-α-cyperone (**240**)	OH	CH_3
3-Oxocostusic acid (**281**)	H	CO_2H

Figure 5. (continued)



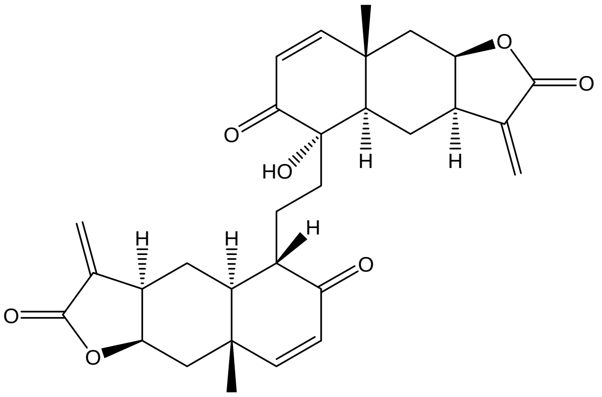
6α-({4′-*O*-[9″*Z*-Hexadecenoyl]}-7′*E*-coumaryloxy) eudesm-4(15)-ene

(**235**) R = $CO(CH_2)_7CH{=}CH(CH_2)_5CH_3$

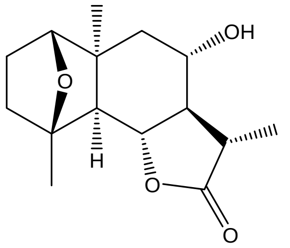
6α-({4′-*O*-Methyl}-7′*E*-coumaryloxy) eudesm-4(15)-ene (**274**) R = CH_3

6α-({4′-*O*-Palmityl}-7′*E*-coumaryloxy) eudesm-4(15)-ene (**292**) R = $CO(CH_2)_{14}CH_3$

6α-({4′-*O*-Stearyl}-7′*E*-coumaryloxy) eudesm-4(15)-ene (**301**) R = $CO(CH_2)_{16}CH_3$

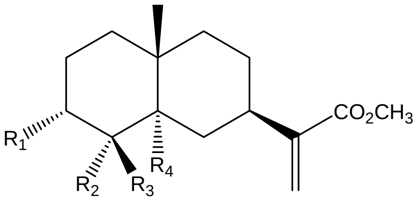


Hydroxy-bis-dihydroencelin (**239**)



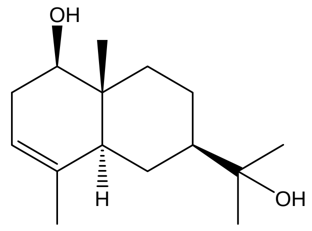
8α-Hydroxy-1,4β-epoxy-10-epieudesman

-5α,6β,7α,11βH-12,6-olide (**243**)

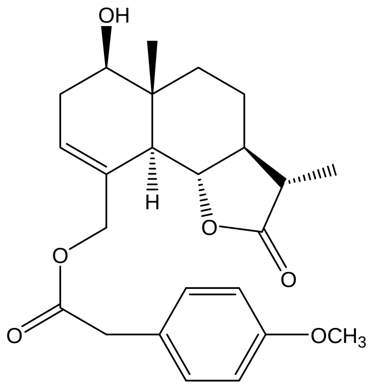


	R_1	R_2	R_3	R_4
5α-Hydroxy-4-*epi*-ilicic acid methyl ester (**242**)	H	CH_3	OH	OH
3α-Hydroxyilicic acid methyl ester (**250**)	OH	OH	CH_3	H

Figure 5. (continued)

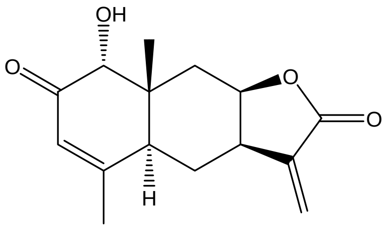


1β-Hydroxy-α-eudesmol (**245**)

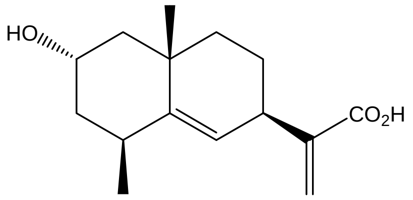


1β-Hydroxy-15-*O*-(*p*-methoxyphenylacetyl)

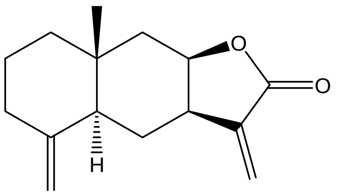
-5α,6β,11βH-eudesma-3-en-12,6α-olide (**251**)



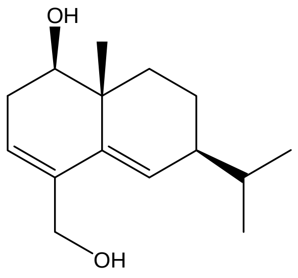
1α-Hydroxypinnatifidin (**252**)



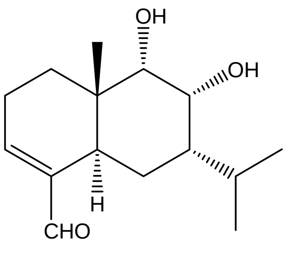
2α-Hydroxypterodontic acid (**253**)



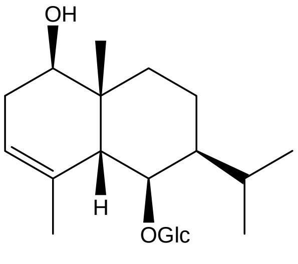
Isoalantolactone (**256**)



Kikkanol B (**260**)

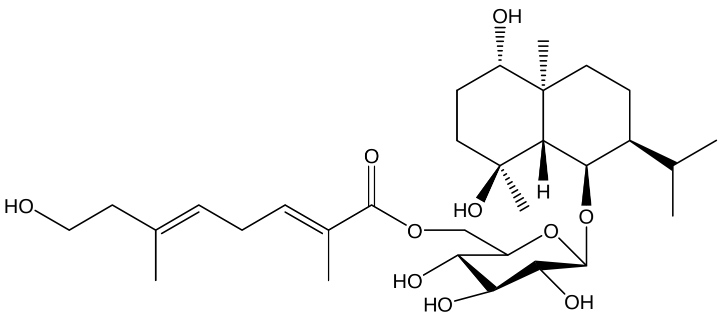


Kikkanol C (**261**)

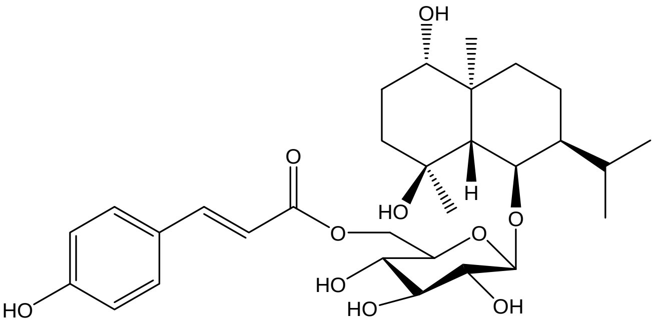


Liriopeoside A (**262**)

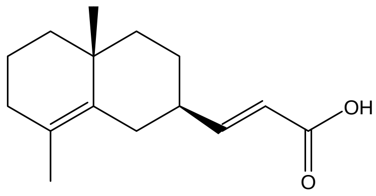
Figure 5. (continued)

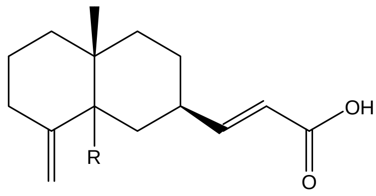


Litchioside A (**263**)



Litchioside B (**264**)

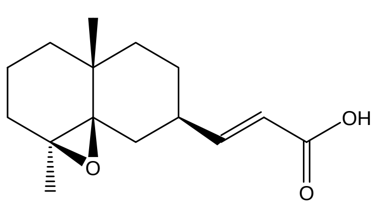




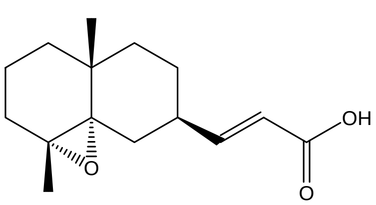
Macrophyllic acid A (**265**)

Macrophyllic acid B (**266**) R = β-OH

Macrophyllic acid C (**267**) R = α-OH

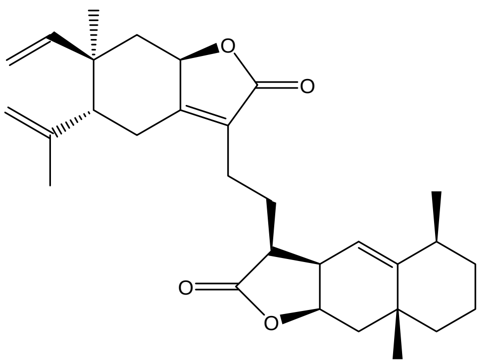


Macrophyllic acid D (**268**)

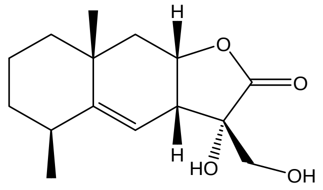


Macrophyllic acid E (**269**)

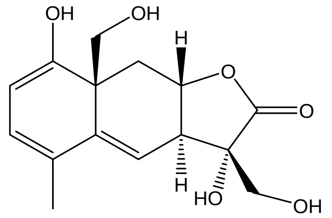
Figure 5. (continued)



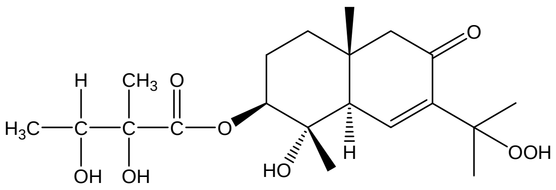
Macrophyllidimer A (**270**)



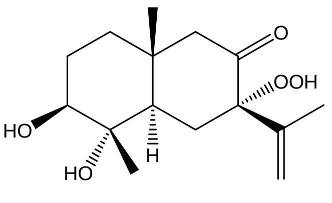
Macrophyllilactone F (**272**)



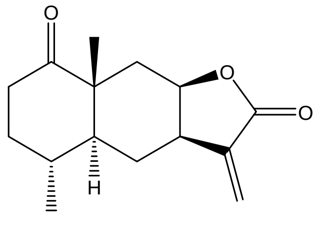
Macrophyllilactone G (**273**)



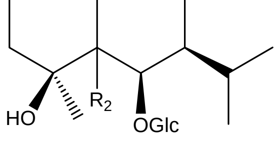
Odonticin (**276**)



Odontin (**277**)

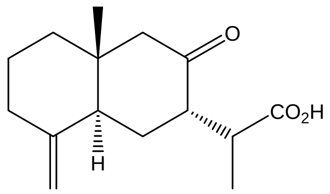


1-One-4-*epi*-alantolactone (**278**)

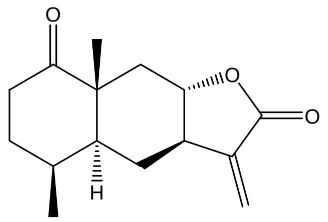


	R_1	R_2
Ophiopogonoside A (**279**)	β-OH	β-H
Ophiopogonoside B (**280**)	α-OH	α-H

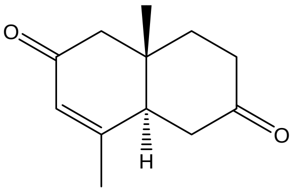
Figure 5. (continued)



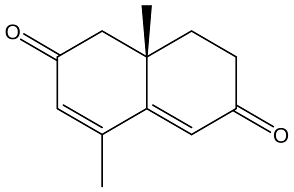
(7α)-8-Oxoeudesm-4(15)-en-12-oic acid (**283**)



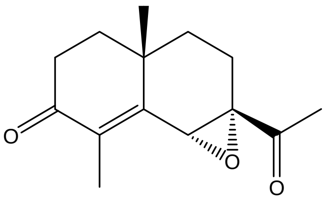
1-Oxoeudesm-11(13)-eno-12,8α-lactone (**284**)



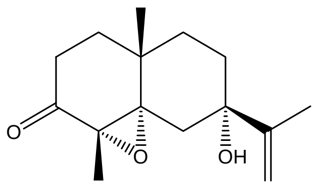
Oxyphyllanene A (**285**)



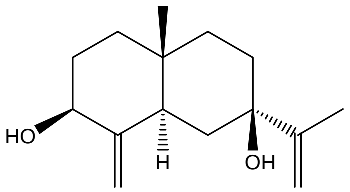
Oxyphyllanene B (**286**)



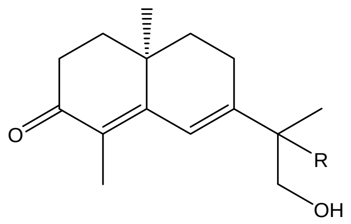
Oxyphyllanene C (**287**)



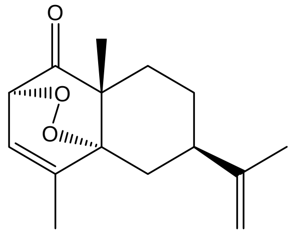
Oxyphyllanene D (**288**)



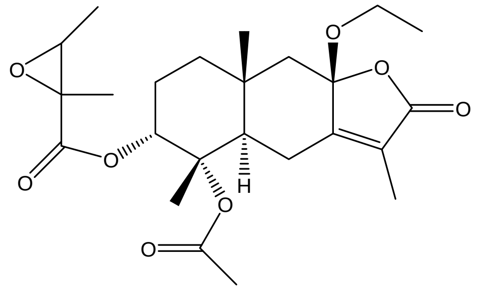
Oxyphyllanene E (**289**)



Oxyphyllanenes F, G (**290, 291**) R = OH (diastereomers)

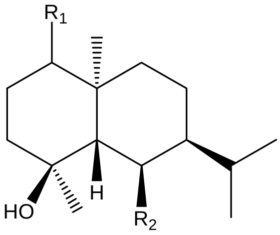


2α,5α-Peroxyeudesma-3,11-dien-1-one (**293**)

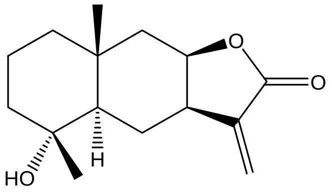


Pterodolide (**295**)

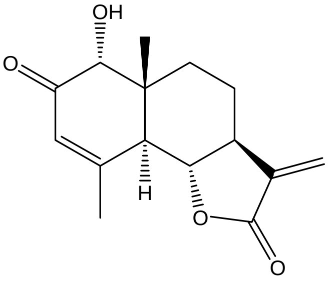
Figure 5. (continued)



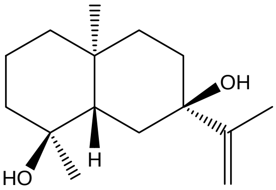
	R_1	R_2
Pterodontriol D (**297**)	β-OH	OH
Pterodontriol D-6-*O*-β-D-glucopyranoside (**298**)	β-OH	OGlc
Pumilaside A (**299**)	α-OH	OGlc



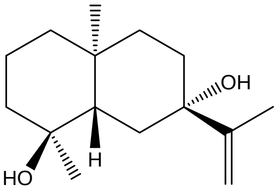
Septuplinolide (**300**)



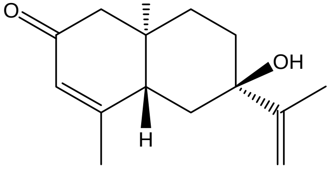
Tanapraetenolide (**302**)



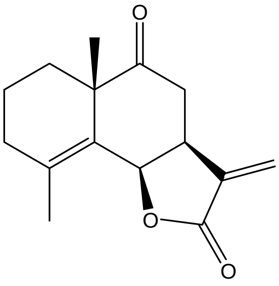
Teucdiol A (**303**)



Teucdiol B (**304**)

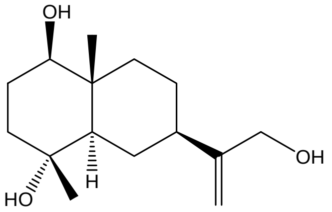


Teucrenone (**305**)

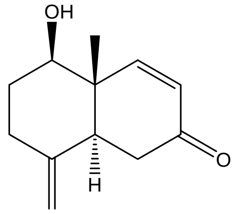


Tourneforin (**306**)

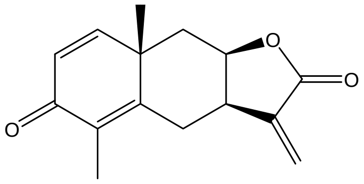
Figure 5. (continued)



1,4,13-Trihydroxyeudesm-11(12)-ene (**307**)



7-Trinoreudesma-4(15),8-dien-1β-ol-7-one (**308**)



Yomogin (**310**)

Figure 5. (continued)

10. Chemical Constituents of Plants in the Genus *Ficus*

Several *Ficus* species are used ethanomedicinally in Indian traditional medicine. Every part of these plants has been also utilized. For example, the bark of *F. racemosa* has been used as antiseptic, antipyretic and vermicidal, and its decoction is used in the treatment of various skin diseases, ulcers and diabetes (Joseph and Raj, 2010). The stem bark of *F. religiosa* has been used in the treatment of diabetes, gynaecological problems, dysentery, diarrhea, and as antipyretic, antibacterial, tonic and astringent (Makhija *et al.*, 2010). In Nepal, the powdered bark of *F. foveolata* is taken as a cure for boils and given to women during child birth to promote milk secretion (Kunwar and Bussmann, 2006). In addition, a number of *Ficus* species have also been reported as the sources of anticancer and anti-inflammatory agents (Lansky *et al.*, 2008). Based on their biological acitivites, phytochemical investigations of these plants revealed the presence of triterpenoids, sesquiterpenoids, alkaloids, flavonoids, stilbenes, coumarins, lignans and phenolic compounds.

Triterpenes, including friedelin (**27**), betulinic acid (**323**), oleanoic acid (**384**) and taraxeryl acetate (**394**), were isolated from the stem bark of *F. ovata*; the latter compound showed antimicrobial activity against half of the tested organisms (Kuete *et al.*, 2009). Betulonic acid (**324**), together with oleanonic acid (**385**), 3-oxofriedelan-28-oic acid (**386**) and ursolic acid (**401**) from the roots of *F. microcarpa* exhibited significant cytotoxic activity against HONE-1, KB and HT29 cancer cell lines with IC_{50} values in the range of 4.0-9.4 μM (Chiang *et al.*, 2005). A triterpenoid saponin, elasticoside (**337**), from the bark of aerial roots of *F. elastica*, was potently active against *Enterococcus faecalis* with an MIC value of 0.03 mg/ml (Mbosso *et al.*, 2012).

Sesquiterpenes, including alloaromadendrene (**316**), β-bourbonene (**325**), α-caryophyllene (**327**), β-caryophyllene (**328**), 1,8-cineole (**329**), α-cubenene (**331**), β-cubenene (**332**), β-elemene (**338**), geranyl acetone (**366**), germacrene D (**367**), α-guaiene (**369**), α-gurjunene (**370**), heneicosene (**371**), (+)-ledene (**380**), 6,10,14-trimethyl-2-pentadecanone (**400**) and α-ylangene (**403**), were characterized in the essential oils from the leaves of *F. carica* (Oliveira *et al.*, 2010), *F. elastica* and *F. mucosa* (Ogunwande *et al.*, 2009, 2011). δ-Cadinene (**326**) obtained from the bark of *F. religiosa* (Makhija *et al.*, 2010), α-copaene (**330**) from the wood of *F. benjamina* (Niogret et al., 2011), along with compounds **328**, **331** and **338**, were also found in the floral fragrances and released by receptive figs in plant-pollinator interactions

(Grison, Edwards, and Hossaert-McKey, 1999). A macrocyclic trichothecene sesquiterpene, named verrucarin L acetate (**402**), from the leaves and stem bark of *F. fistulosa*, showed strong antimalarial activity by inhibiting the growth of *Plasmodium falciparum* with an IC_{50} value of lower than 1 ng/ml (Zhang *et al*., 2002). Glucosides of sesquiterpenes, such as pumilasides A, B and C (**299**, **388** and **389**), were also found in the fruits of *F. pumila* (Kitajima *et al*., 2000).

A series of phenanthroindolizidine alkaloids found in *F. septica*, called ficuseptines A-N (**345-358**), were strongly cytotoxic against two human cancer cell lines, NUGC and HONE-1 (Wu *et al*., 2002; Damu *et al*., 2005, 2009). Another alkaloid of the same type, (-)-13aα-antofine (**317**) from the stem bark of *F. fistulosa*, exhibited antifungal activity against *Aspergillus fumigatus* and *Candida albicans* with an IC_{50} value of 4 μM in both assays (Subramaniam *et al*., 2009).

The flavonoids dihydroquercetin (**333**), eriodictyol (**339**), homoeriodictyol (**372**) and luteolin (**381**), isolated from the stems and leaves of *F. sarmentosa* var. *henryi*, displayed inhibitory activity against the pathogenic fungi *Fusarium graminearum* and *Septoria zeicola*, with luteolin showing the strongest inhibitory activity (Wang *et al*., 2010). Apigenin (**318**), found in *F. formosana* f. *formosana* (Sheu *et al*., 2005) and *F. sarmentosa* var. *henryi* (Wang *et al*., 2011b), exhibited significant cytotoxicity against HepG2, PLC/PRF/5 and Raji cancer cell lines *in vitro* with IC_{50} values of 0.045, 0.066 and 0.066 μM, respectively (Sheu *et al*., 2005). Another phenolic constituent from the latter *Ficus* species, 7-hydroxycoumarin (**374**), has also been reported as insecticidal (Wang *et al*., 2011b).

The stilbenes gnetol (**368**), isorhapontigenin (**378**), pinosylvin (**387**) and resveratrol (**392**), the flavonoids galangin 3-methyl ether (**365**), 5-hydroxy-3,7-dimethoxyflavone (**375**), quercetin (**390**) and tectochrysin (**395**), along with the phenylpropanoids 1,22-docosanediol diferulate (**336**), 24′-hydroxy-tetracosyl ferulate (**377**) and 1,24-tetracosanediol diferulate (**396**), were reported as constituents of the stems of *F. foveolata*. The isolated stilbenes displayed high inhibitory activity towards the enzyme butyrylcholinesterase, with gnetol as the most active compound (IC_{50} = 1.3 μM) (Sermboonpaisarn and Sawasdee, 2012).

Two phenolic compounds, bergenin (**322**) and racemosic acid (**391**), were isolated from the bark of *F. racemosa*. Racemosic acid potently inhibited the enzymes COX-1 and 5-LOX *in vitro* with IC_{50} values of 90 and 18 μM, respectively, and also demonstrated strong antioxidant activity in scavenging ABTS free radical cations with an IC_{50} value of 19 μM (Li *et al*., 2004).

Chemical constituents of plants in the genus *Ficus* have been summarized in **Table 4**. Their chemical structures are presented in **Figure 6**.

Table 4. Chemical constituents of plants in the genus *Ficus*

Compound	**Source**	**Plant part**	**References**
3β-Acetoxy-12,19-dioxo-13(18)-oleanene (**311**)	*Ficus microcarpa*	Roots	Chiang *et al*., 2005
3β-Acetoxy-11α,12α-epoxy-16-oxo-14-taraxerene (**312**)			
3β-Acetoxy-21α,22α-epoxy taraxastan-20α-ol (**313**)			
3β-Acetoxy-25-methoxylanosta-8,23-diene (**314**)			
3β-Acetoxy-19(29)-taraxasten-20α-ol (**315**)			
Alloaromadendrene (**316**)	*F. carica*	Leaves	Oliveira *et al*., 2010
(-)-13aα-Antofine (**317**)	*F. fistulosa*	Stem bark	Subramaniam *et al*., 2009
Apigenin (**318**)	*F. formosana* f. *formosana* *F. sarmentosa* var. *henryi*	Stems Stems, leaves	Sheu *et al*., 2005 Wang *et al*.,2011b
Aripuanin (**319**)	*F. aripuanensis*	Leaves	Nascimento *et al*., 1999
Bergapten (**320**)	*F. religiosa*	Bark	Makhija *et al*., 2010
Bergaptol (**321**)			
Bergenin (**322**)	*F. racemosa*		Li *et al*., 2004

Table 4. (continued)

Compound	**Source**	**Plant part**	**References**
Betulinic acid (**323**)	*Ficus ovata*	Stem bark	Kuete *et al*., 2009
Betulonic acid (**324**)	*F. microcarpa*	Roots	Chiang *et al*., 2005
β-Bourbonene (**325**)	*F. carica*	Leaves	Oliveira *et al*., 2010
δ-Cadinene (**326**)	*F. religiosa*	Bark	Makhija *et al*., 2010
α-Caryophyllene (**327**)	*F. carica*	Leaves	Oliveira *et al*., 2010
β-Caryophyllene (**328**)	*F. carica* *F. mucosa*	Leaves	Oliveira *et al*., 2010 Ogunwande *et al*., 2009
1,8-Cineole (**329**)	*F. elastica*		Ogunwande *et al*., 2011
α-Copaene (**330**)	*F. benjamina*	Wood	Niogret *et al*., 2011
α-Cubenene (**331**)	*F. carica*	Leaves	Oliveira *et al*., 2010
β-Cubenene (**332**)			
Dihydroquercetin (**333**)	*F. sarmentosa* var. *henryi*	Stems, leaves	Wang *et al*., 2010
2,3-Dihydroxy-1-(4-hydroxy-3,5-dimethoxyphenyl)-1-propanone (**334**)	*F. beecheyana*	Roots	Lee *et al*., 2002
3,22-Dioxo-20-taraxastene (**335**)	*F. microcarpa*		Chiang *et al*., 2005
1,22-Docosanediol diferulate (**336**)	*F. foveolata*	Vines	Sermboonpaisarn and Sawasdee, 2012
Elasticoside (**337**)	*F. elastica*	Aerial root bark	Mbosso *et al*., 2012
β-Elemene (**338**)	*F. carica*	Leaves	Oliveira *et al*., 2010
Eriodictyol (**339**)	*F. sarmentosa* var. *henryi*	Stems, leaves	Wang *et al*.,2011b

Table 4. (continued)

Compound	**Source**	**Plant part**	**References**
erythro-2,3-Bis(4-hydroxy-3-methoxyphenyl)-3-ethoxypropan-1-ol (**340**)	*Ficus beecheyana*	Roots	Lee *et al*., 2002
Ficuformodiol A (**341**)	*F. formosana* f. *formosana*	Stems	Sheu *et al*., 2005
Ficuformodiol B (**342**)			
Ficusal (**343**)	*F. microcarpa*	Wood	Li and Kuo, 2000
Ficusamide (**344**)	*F. elastica*	Aerial root bark	Mbosso *et al*., 2012
Ficuseptine A (**345**)	*Ficus septica*	Leaves	Wu *et al*., 2002
Ficuseptine B (**346**)		Stems	Damu *et al*., 2005
Ficuseptine C (**347**)			
Ficuseptine D (**348**)			
Ficuseptine E (**349**)		Roots	Damu *et al*., 2009
Ficuseptine F (**350**)			
Ficuseptine G (**351**)			
Ficuseptine H (**352**)			
Ficuseptine I (**353**)			
Ficuseptine J (**354**)			
Ficuseptine K (**355**)			
Ficuseptine L (**356**)			
Ficuseptine M (**357**)			
Ficuseptine N (**358**)			
Ficusesquilignan A (**359**)	*F. microcarpa*	Wood	Li and Kuo, 2000
Ficusesquilignan B (**360**)			
Ficusolide diacetate (**361**)			

Table 4. (continued)

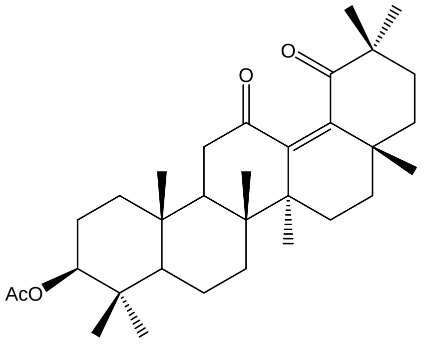
Compound	**Source**	**Plant part**	**References**
Ficusoside (**362**)	*Ficus elastica*	Aerial root bark	Mbosso *et al*., 2012
Ficustriol (**363**)	*F. hispida*	Leaves, twigs	Peraza-Sanchez *et al*., 2002
Fistulosine (**364**)	*F. fistulosa*	Stem bark	Subramaniam *et al*., 2009
Friedelin (**27**)	*F. ovata*		Kuete *et al*., 2009
Galangin 3-methyl ether (**365**)	*F. foveolata*	Vines	Sermboonpaisarn and Sawasdee, 2012
Geranyl acetone (**366**)	*F. elastica*	Leaves	Ogunwande *et al*., 2011
Germacrene D (**367**)	*F. carica*		Oliveira *et al*., 2010
Gnetol (**368**)	*F. foveolata*	Vines	Sermboonpaisarn and Sawasdee, 2012
α-Guaiene (**369**)	*F. carica*	Leaves	Oliveira *et al*., 2010
α-Gurjunene (**370**)			
Heneicosene (**371**)	*F. elastica*		Ogunwande *et al*., 2011
Homoeriodictyol (**372**)	*F. sarmentosa* var. *henryi*	Stems, leaves	Wang *et al*., 2010
(-)-14β-Hydroxyantofine (**373**)	*F. fistulosa*	Stem bark	Subramaniam *et al*., 2009
7-Hydroxycoumarin (**374**)	*F. sarmentosa* var. *henryi*	Stems, leaves	Wang *et al*.,2011b
5-Hydroxy-3,7-dimethoxyflavone (**375**)	*F. foveolata*	Vines	Sermboonpaisarn and Sawasdee, 2012

Table 4. (continued)

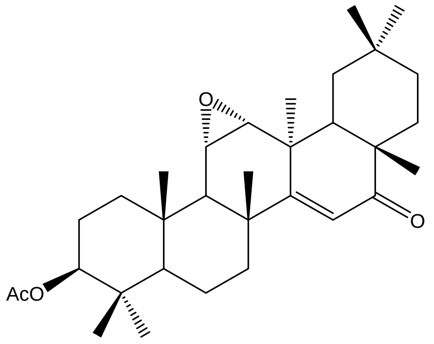
Compound	Source	Plant part	References
3-Hydroxy-1-(4-hydroxy-3,5-dimethoxyphenyl)-1-propanone (**376**)	*Ficus beecheyana*	Roots	Lee *et al*., 2002
24′-Hydroxy-tetracosyl ferulate (**377**)	*F. foveolata*	Vines	Sermboonpaisarn and Sawasdee, 2012
Isorhapontigenin (**378**)			
Lanosterol (**379**)	*F. religiosa*	Bark	Makhija *et al*., 2010
(+)-Ledene (**380**)	*F. carica*	Leaves	Oliveira *et al*., 2010
Luteolin (**381**)	*F. sarmentosa* var. *henryi*	Stems, leaves	Wang *et al*., 2010
O-Methyltylophorinidine (**382**)	*F. hispida*	Leaves, twigs	Peraza-Sanchez *et al*., 2002
α-Muurolene (**383**)	*F. carica*	Leaves	Oliveira *et al*., 2010
Oleanoic acid (**384**)	*F. ovata*	Stem bark	Kuete *et al*., 2009
Oleanonic acid (**385**)	*F. microcarpa*	Roots	Chiang *et al*., 2005
3-Oxofriedelan-28-oic acid (**386**)			
Pinosylvin (**387**)	*F. foveolata*	Vines	Sermboonpaisarn and Sawasdee, 2012
Pumilaside B (**388**)	*F. pumila*	Fruits	Kitajima *et al*., 2000
Pumilaside C (**389**)			
Quercetin (**390**)	*F. foveolata*	Vines	Sermboonpaisarn and Sawasdee, 2012
Racemosic acid (**391**)	*F. racemosa*	Bark	Li *et al*., 2004
Resveratrol (**392**)	*F. foveolata*	Vines	Sermboonpaisarn and Sawasdee, 2012
(-)-13aα-Secoantofine (**393**)	*F. fistulosa*	Stem bark	Subramaniam *et al*., 2009

Table 4. (continued)

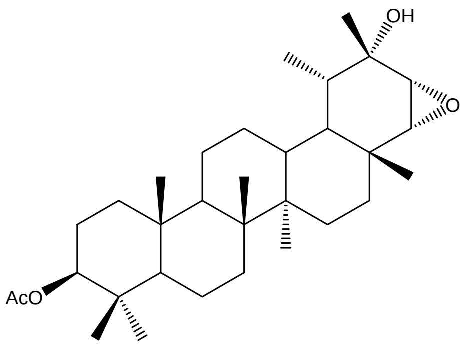
Compound	**Source**	**Plant part**	**References**
β-Sitosterol (**171**)	*Ficus religiosa*	Bark	Makhija *et al*., 2010
Taraxeryl acetate (**394**)	*F. ovata*	Stem bark	Kuete *et al*., 2009
Tectochrysin (**395**)	*F. foveolata*	Vines	Sermboonpaisarn and Sawasdee, 2012
1,24-Tetracosanediol diferulate (**396**)			
threo-2,3-Bis(4-hydroxy-3-methoxyphenyl)-3-ethoxypropan-1-ol (**397**)	*F. beecheyana*	Roots	Lee *et al*., 2002
threo-3-(4-Hydroxy-3,5-dimethoxyphenyl)-3-ethoxypropan-1,2-diol (**398**)			
trans-4,5-Bis(4-hydroxy-3-methoxyphenyl)-1,3-dioxacyclohexane (**399**)			
6,10,14-Trimethyl-2-pentadecanone (**400**)	*F. elastica*	Leaves	Ogunwande *et al*., 2011
Ursolic acid (**401**)	*F. microcarpa*	Roots	Chiang *et al*., 2005
Verrucarin L acetate (**402**)	*F. fistulosa*	Leaves, stem bark	Zhang *et al*., 2002
α-Ylangene (**403**)	*F. carica*	Leaves	Oliveira *et al*., 2010



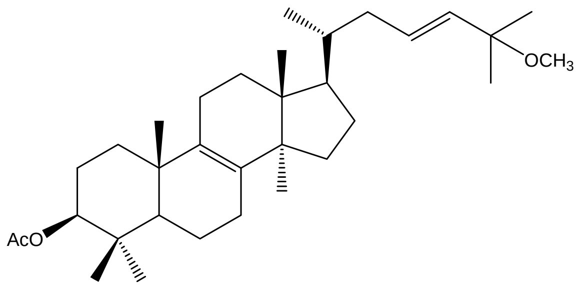
3β-Acetoxy-12,19-dioxo-13(18)-oleanene (**311**)



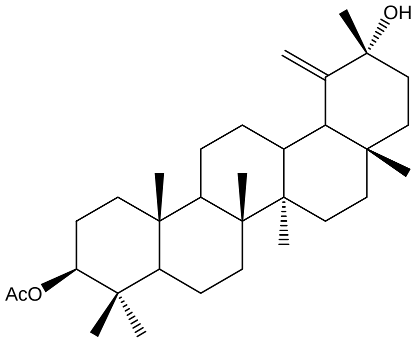
3β-Acetoxy-11α,12α-epoxy-16-oxo-14-taraxerene (**312**)



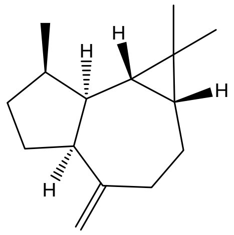
3β-Acetoxy-21α,22α-epoxy taraxastan-20α-ol (**313**)



3β-Acetoxy-25-methoxylanosta-8,23-diene (**314**)

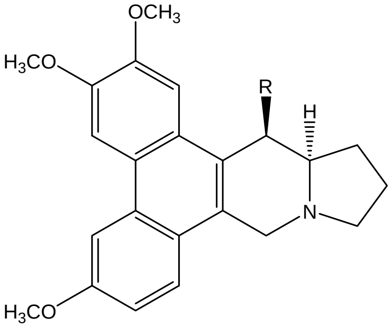


3β-Acetoxy-19(29)-taraxasten-20α-ol (**315**)



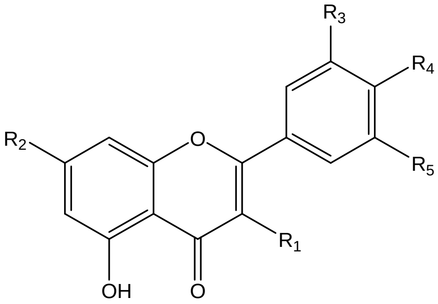
Alloaromadendrene (**316**)

Figure 6. Chemical constituents of plants in the genus *Ficus*



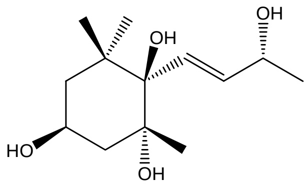
(-)-13aα-Antofine (**317**) R = H

(-)-14β-Hydroxyantofine (**373**) R = OH

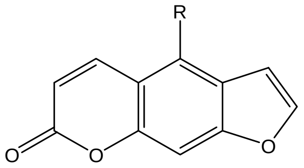


	R_1	R_2	R_3	R_4	R_5
Apigenin (**318**)	H	OH	H	OH	H
Galangin 3-methyl ether (**365**)	OCH_3	OH	H	H	H
5-Hydroxy-3,7-dimethoxyflavone (**375**)	OCH_3	OCH_3	H	H	H
Luteolin (**381**)	H	OH	H	OH	OH
Quercetin (**390**)	OH	OH	OH	OH	H
Tectochrysin (**395**)	H	OCH_3	H	H	H

Figure 6. (continued)

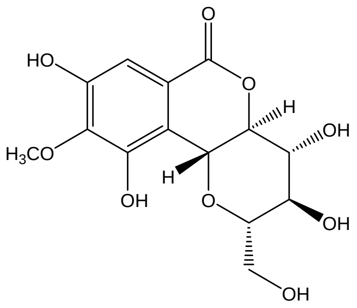


Aripuanin (**319**)

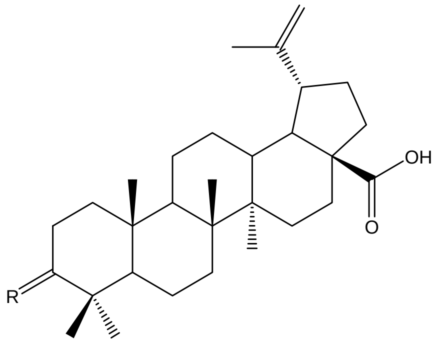


Bergapten (**320**) R = OCH_3

Bergaptol (**321**) R = OH

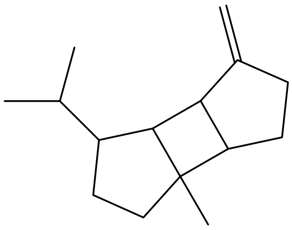


Bergenin (**322**)

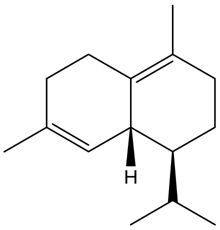


Betulinic acid (**323**) R = β-OH, α-H

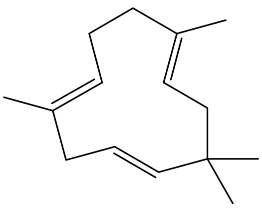
Betulonic acid (**324**) R = O



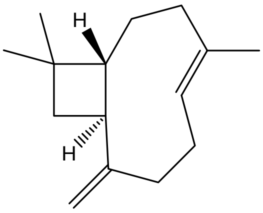
β-Bourbonene (**325**)



δ-Cadinene (**326**)

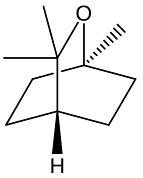


α-Caryophyllene (**327**)

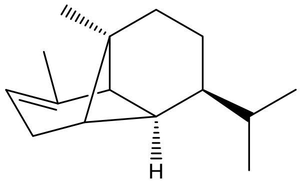


β-Caryophyllene (**328**)

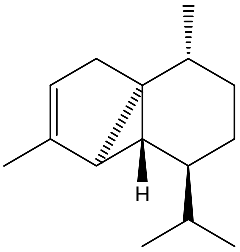
Figure 6. (continued)



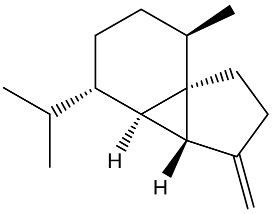
1,8-Cineole (**329**)



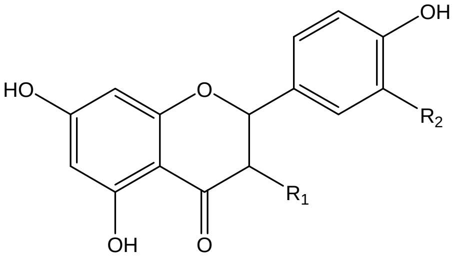
α-Copaene (**330**)



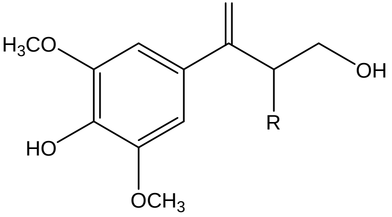
α-Cubenene (**331**)



β-Cubenene (**332**)



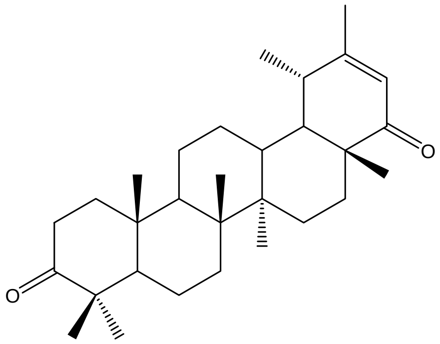
	R_1	R_2
Dihydroquercetin (**333**)	OH	OH
Eriodictyol (**339**)	H	OH
Homoeriodictyol (**372**)	H	OCH_3



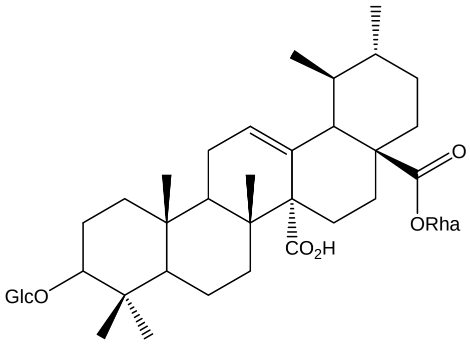
2,3-Dihydroxy-1-(4-hydroxy-3,5-dimethoxyphenyl)-1-propanone (**334**) R = OH

3-Hydroxy-1-(4-hydroxy-3,5-dimethoxyphenyl)-1-propanone (**376**) R = H

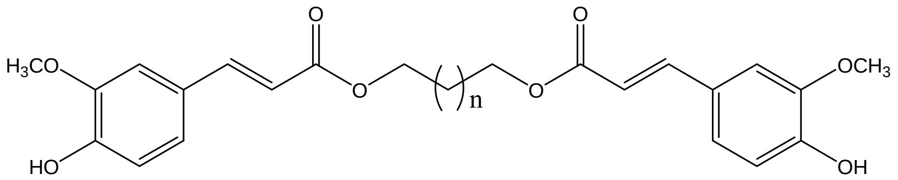
Figure 6. (continued)



3,22-Dioxo-20-taraxastene (**335**)

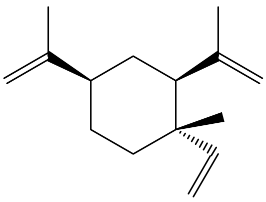


Elasticoside (**337**)

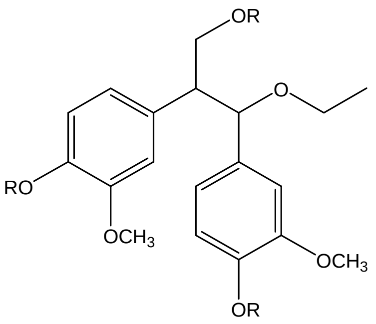


1,22-Docosanediol diferulate (**336**) n = 20

1,24-Tetracosanediol diferulate (**396**) n = 22



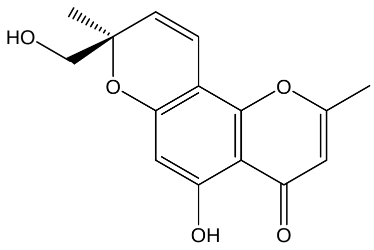
β-Elemene (**338**)



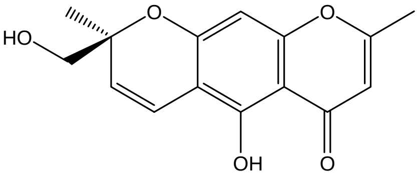
erythro-2,3-Bis(4-hydroxy-3-methoxyphenyl) -3-ethoxypropan-1-ol (**340**) R = H, *erythro*

threo-2,3-Bis(4-hydroxy-3-methoxyphenyl) -3-ethoxypropan-1-ol (**397**) R = H, *threo*

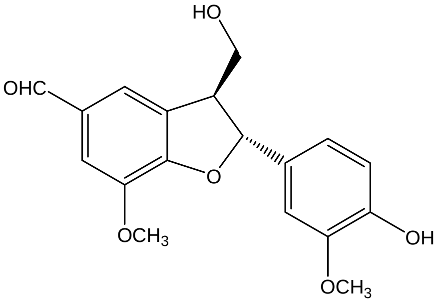
Figure 6. (continued)



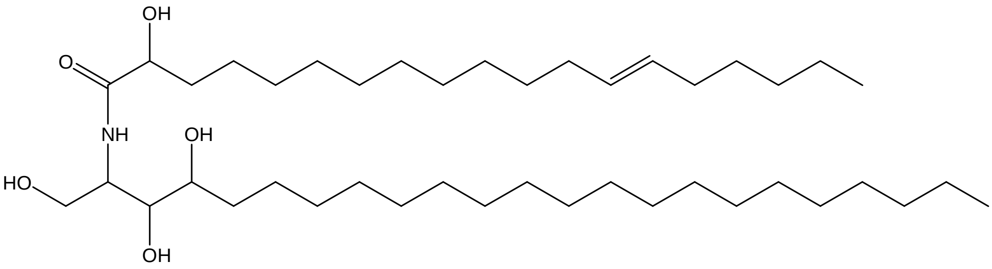
Ficuformodiol A (**341**)



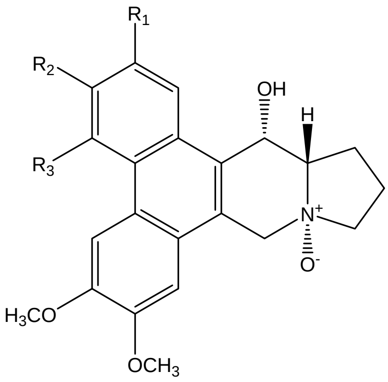
Ficuformodiol B (**342**)



Ficusal (**343**)

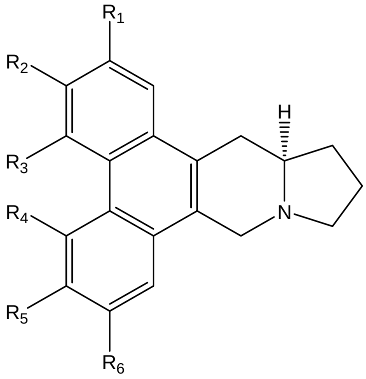


Ficusamide (**344**)

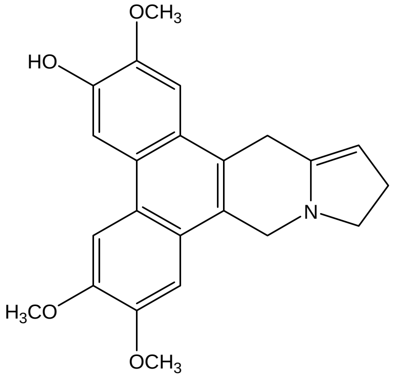


	R_1	R_2	R_3
Ficuseptine A (**345**)	OCH_3	OCH_3	OCH_3
Ficuseptine M (**357**)	H	$-OCH_2O-$	

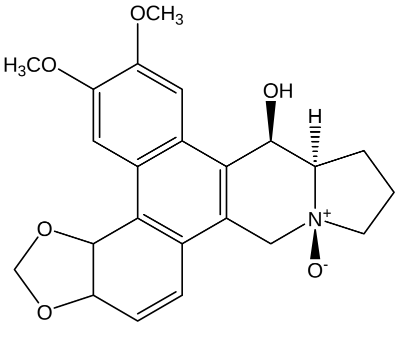
Figure 6. (continued)



	R_1	R_2	R_3	R_4	R_5	R_6
Ficuseptine B (**346**)	-OCH_2O-		H	OCH_3	OCH_3	H
Ficuseptine C (**347**)	-OCH_2O-		H	H	OCH_3	H
Ficuseptine D (**348**)	H	OCH_3	OCH_3	H	OCH_3	H
Ficuseptine E (**349**)	OH	OCH_3	OH	H	OCH_3	H
Ficuseptine F (**350**)	OCH_3	OCH_3	OCH_3	OCH_3	OCH_3	H
Ficuseptine G (**351**)	H	OCH_3	OCH_3	H	OH	OCH_3
Ficuseptine H (**352**)	OCH_3	OH	H	OCH_3	OCH_3	H
Ficuseptine J (**354**)	OCH_3	OCH_3	H	OCH_3	OH	H

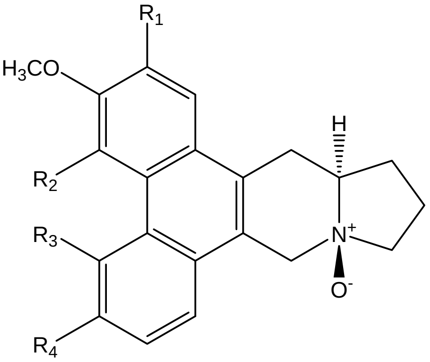


Ficuseptine I (**353**)

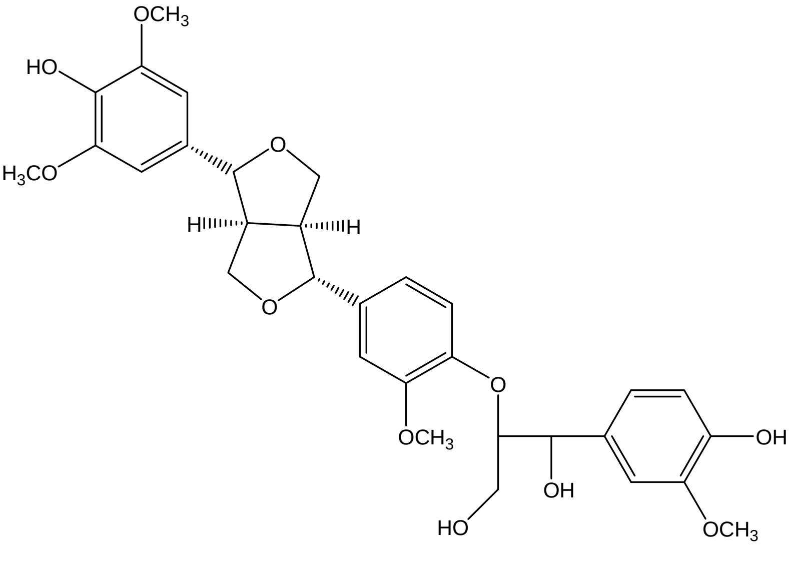


Ficuseptine N (**358**)

Figure 6. (continued)

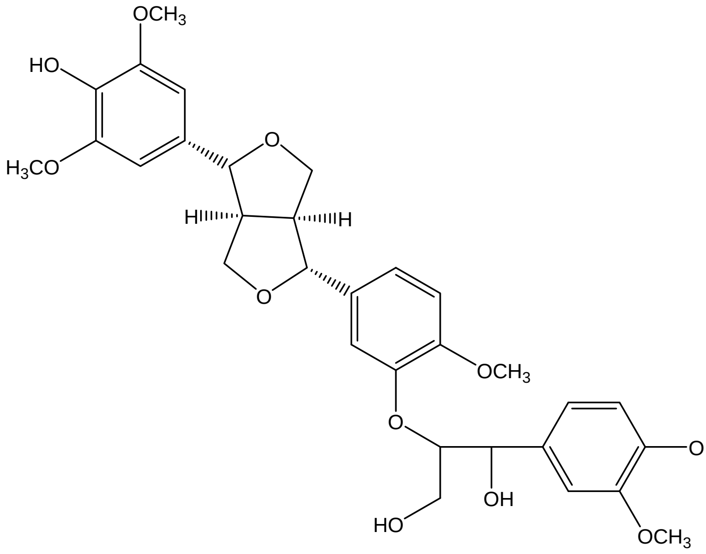


	R_1	R_2	R_3	R_4
Ficuseptine K (**355**)	OCH_3	H	OCH_3	OH
Ficuseptine L (**356**)	H	OCH_3	H	OCH_3

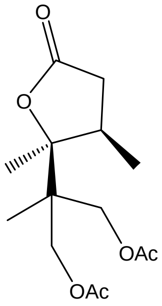


Ficusesquilignan A (**359**)

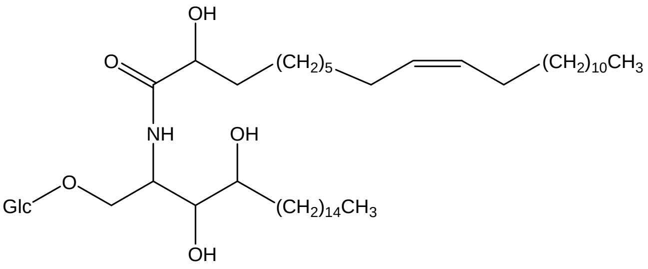
Figure 6. (continued)



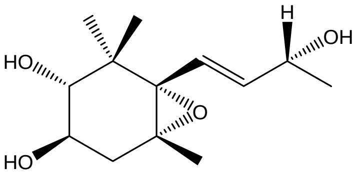
Ficusesquilignan B (**360**)



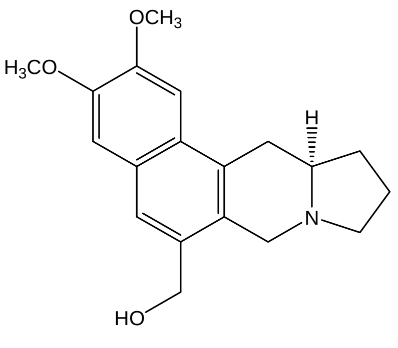
Ficusolide diacetate (**361**)



Ficusoside (**362**)

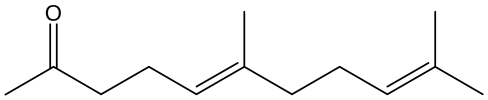


Ficustriol (**363**)

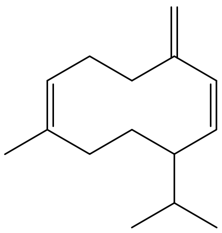


Fistulosine (**364**)

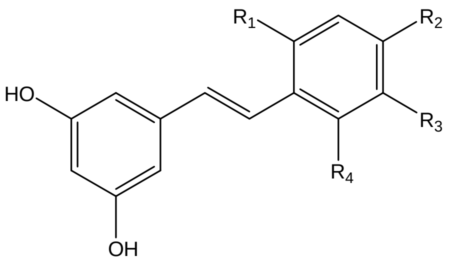
Figure 6. (continued)



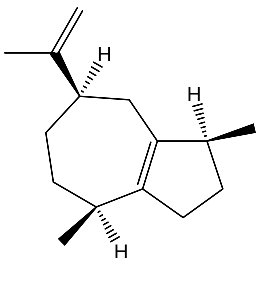
Geranyl acetone (**366**)



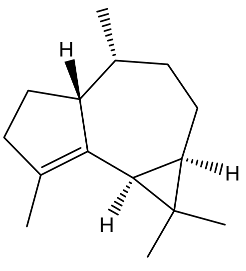
Germacrene D (**367**)



	R_1	R_2	R_3	R_4
Gnetol (**368**)	OH	H	H	OH
Isorhapontigenin (**378**)	H	OH	OCH_3	H
Pinosylvin (**387**)	H	H	H	H
Resveratrol (**392**)	H	OH	H	H

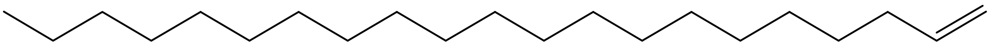


α-Guaiene (**369**)

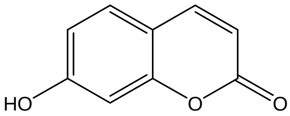


α-Gurjunene (**370**)

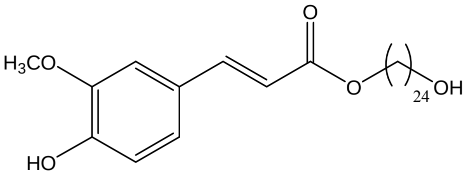
Figure 6. (continued)



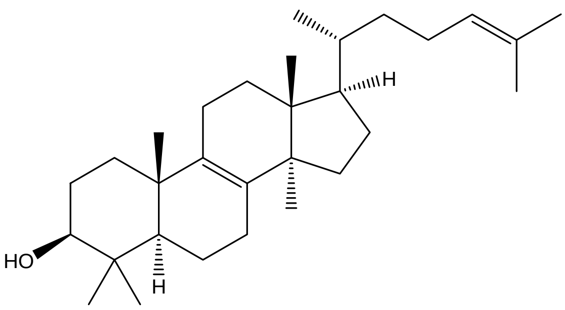
Heneicosene (**371**)



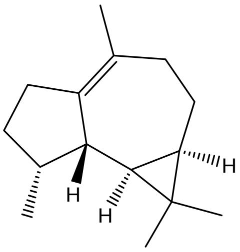
7-Hydroxycoumarin (**374**)



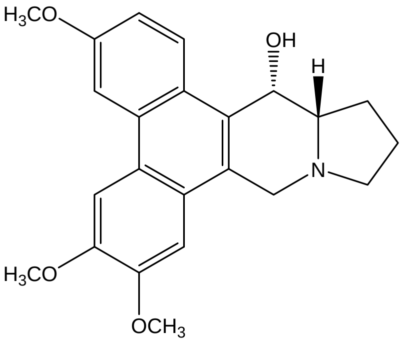
24′-Hydroxy-tetracosyl ferulate (**377**)



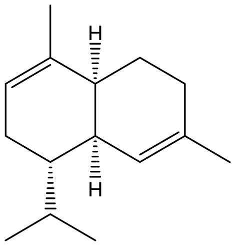
Lanosterol (**379**)



(+)-Ledene (**380**)

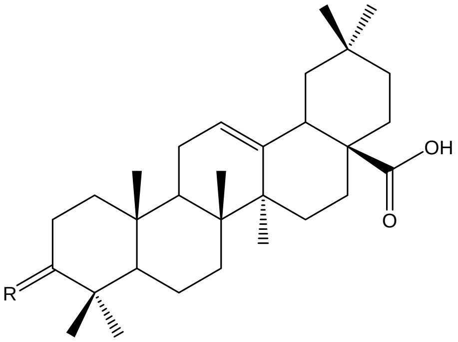


O-Methyltylophorinidine (**382**)



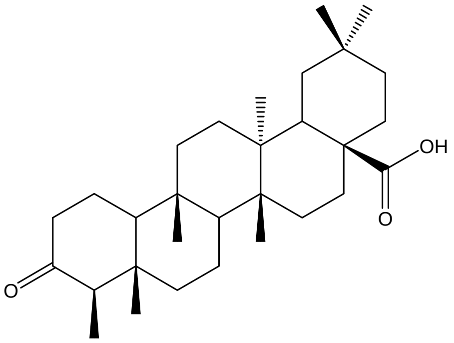
α-Muurolene (**383**)

Figure 6. (continued)

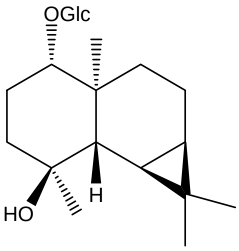


Oleanoic acid (**384**) R = β-OH, α-H

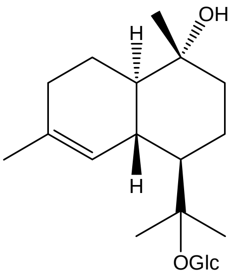
Oleanonic acid (**385**) R = O



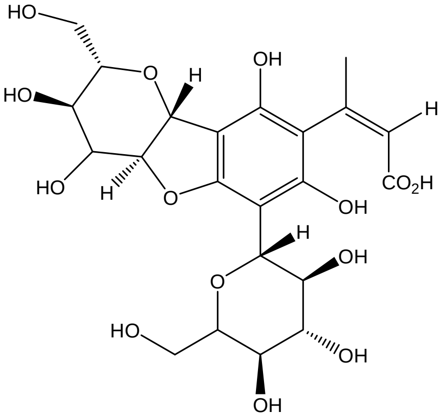
3-Oxofriedelan-28-oic acid (**386**)



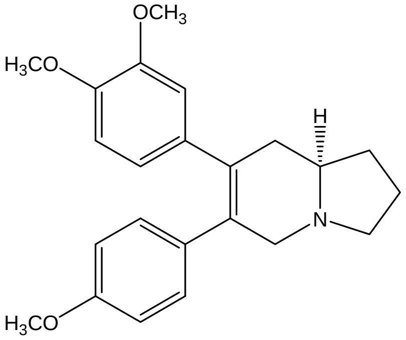
Pumilaside B (**388**)



Pumilaside C (**389**)

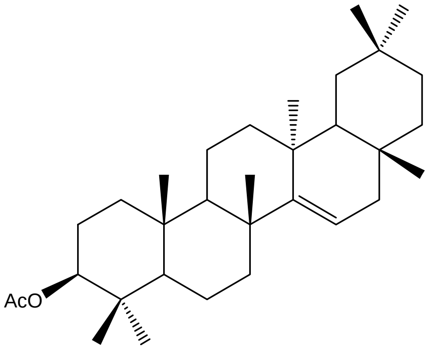


Racemosic acid (**391**)

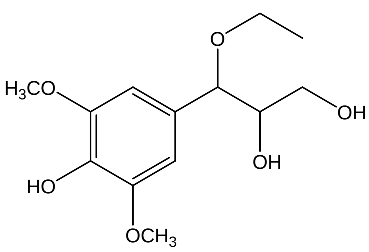


(-)-13aα-Secoantofine (**393**)

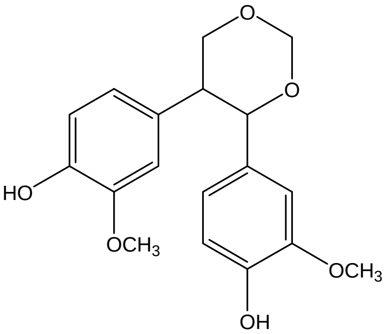
Figure 6. (continued)



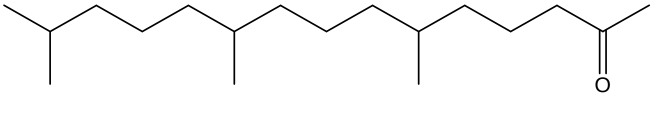
Taraxeryl acetate (**394**)



threo-3-(4-Hydroxy-3,5-dimethoxyphenyl)-3-ethoxypropan-1,2-diol (**398**)

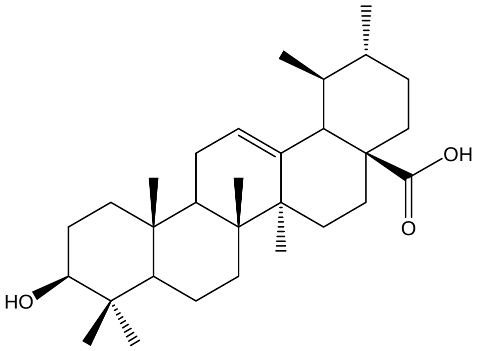


trans-4,5-Bis(4-hydroxy-3-methoxyphenyl)-1,3-dioxacyclohexane (**399**)

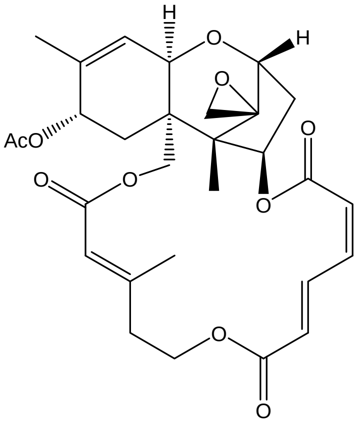


6,10,14-Trimethyl-2-pentadecanone (**400**)

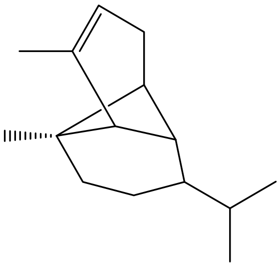
Figure 6. (continued)



Ursolic acid (**401**)



Verrucarin L acetate (**402**)



α-Ylangene (**403**)

Figure 6. (continued)

CHAPTER III

EXPERIMENTAL

1. Source of Plant Materials

The stems of *Salacia verrucosa* and *Ficus foveolata* were collected in Bueng Kan, Thailand, in January 2010. Voucher specimens of both species have been deposited at the herbarium of the Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok, Thailand.

2. General Techniques

2.1 Solvents

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

2.2 Analytical Thin-Layer Chromatography (TLC)

Technique:	One dimension, ascending
Adsorbent:	Silica gel 60 F_{254} (E. Merck) pre-coated plates
Layer thickness:	0.2 mm
Distance:	5 cm
Temperature:	Laboratory temperature (30-35 °C)
Detection:	1. Ultraviolet light (254 and 365 nm) 2. 10% Sulfuric acid and heating at 110 °C for 10 minutes

2.3 Column Chromatography

2.3.1 Conventional Column Chromatography

Gel filter:	Silica gel 60 number 9385 (particle size 0.040-0.063 nm) and number 7734 (particle size 0.063-0.200 nm) (E. Merck)
Packing method:	Wet packing: The adsorbent was mixed with the eluent into slurry, then poured into a column and allowed to settle.
Sample loading:	The sample was dissolved in a small amount of the eluent, and then applied gently on top of the column.

Detection:	Fractions were examined by TLC technique in the same manner as described in section 2.2.

2.3.2 Size-Exclusion Column Chromatography

Gel filter:	Sephadex LH-20 (Pharmacia Biotech AB)
Packing method:	Gel filter was suspended in the eluent 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 eluent, and then applied gently on top of the column.
Detection:	Fractions were examined by TLC technique in the same manner as described in section 2.2.

2.4 Spectroscopy

2.4.1 Ultraviolet (UV) Spectra

UV spectra were obtained on a Shimadzu UV-160A spectrophotometer (Pharmaceutical Research Instrument Center, Faculty of Pharmaceutical Sciences, Chulalongkorn University).

2.4.2 Infrared (IR) Spectra

IR spectra (KBR disc) were recorded on a Perkin Elmer FT-IR 1760X spectrometer (Scientific and Technological Research Equipment Center, Chulalongkorn University).

2.4.3 Mass Spectra

Electrospray Ionization (ESI) mass spectra were obtained on a Bruker micrOTOF mass spectrometer (National Center for Genetic Engineering and Biotechnology, BIOTEC, Thailand).

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

^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra were recorded on a Bruker DPX-300 FT-NMR spectrometer (Pharmaceutical Research Instrument Center, Faculty of Pharmaceutical Sciences, Chulalongkorn University).

^{1}H (500 MHz) and ^{13}C (125 MHz) NMR spectra were obtained on a JEOL JMN-A500, Varian Unity INOVA (Scientific and Technological Research Equipment Center, Chulalongkorn University).

2.5 Physical Properties

2.5.1 Melting Points

Melting points were obtained on a Fisher-John melting point apparatus (Department of Pharmacognosy and Pharmaceutical Botany, Faculty of Pharmaceutical Sciences, Chulalongkorn University).

2.5.2 Optical rotations

Optical rotations were measured on a Perkin-Elmer 314 polarimeter using a sodium lamp operating at 589 nm (Pharmaceutical Research Instrument Center, Faculty of Pharmaceutical Sciences, Chulalongkorn University).

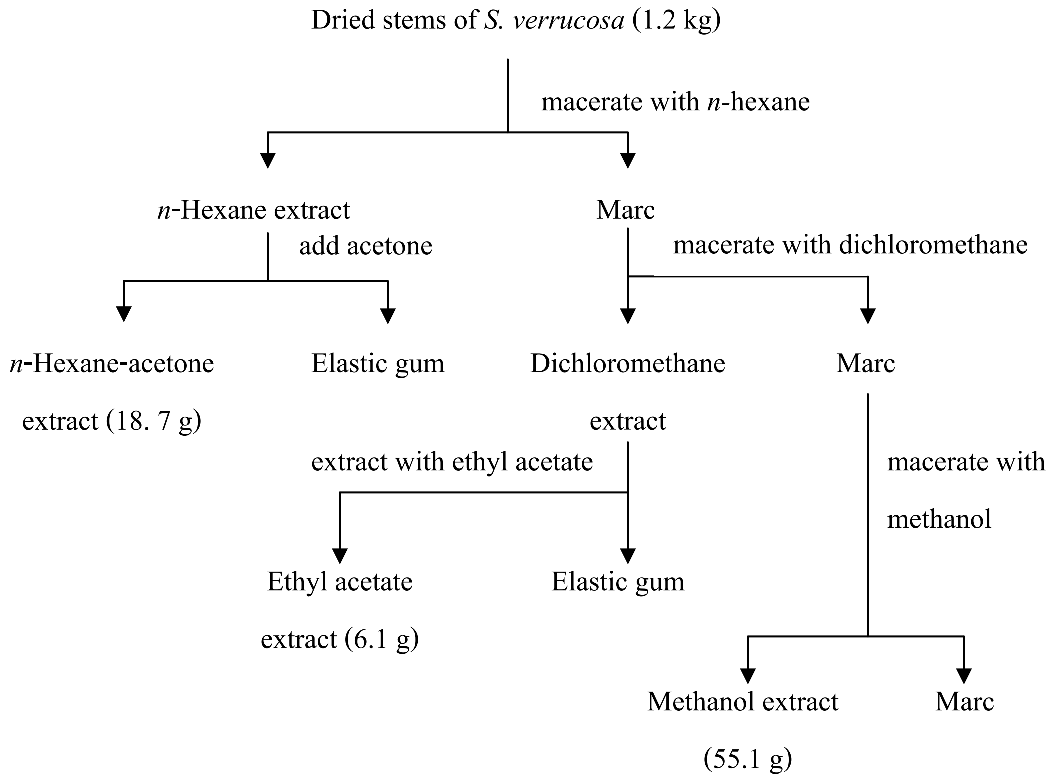
3. Extraction and Isolation of Compounds from the Stems of *Salacia verrucosa*

3.1 Extraction of the Stems of *S. verrucosa*

Dried stems of *S. verrucosa* (1.2 kg) were ground and then sequentially macerated with *n*-hexane (5 × 4 l), CH_2Cl_2 (5 × 4 l) and MeOH (5 × 4 l). The *n*-hexane extract was concentrated under reduced pressure at 45 °C, then acetone was added to exclude the gummy material, whereas the CH_2Cl_2 extract was evaporated to dryness and then reconstituted with EtOAc to separate the elastic gum from the crude extract. Each solvent extract was evaporated to give *n*-hexane-acetone (18.7 g, 1.56 % yield), EtOAc (6.1 g, 0.51 % yield) and MeOH extracts (55.1 g, 4.59 % yield), as presented in **Scheme 1**.

3.2 Isolation of Compounds from the *n*-Hexane-Acetone Extract of *S. verrucosa* Stems

The extract (18.7 g) was re-dissolved in a small volume of *n*-hexane and then subjected to silica gel column chromatography (500 g, 9.5 × 15 cm). The column was eluted with a gradient mixture of *n*-hexane and CH_2Cl_2 (3:7 → 0:1). One hundred and sixty fractions (50 ml each) were collected and combined according to their TLC profiles by using mixtures of *n*-hexane and CH_2Cl_2 as mobile phases into 8 fractions (H1-H8), as shown in **Table 5**.



Scheme 1. Extraction of *S. verrucosa* stems

Table 5. Combined fractions from the *n*-hexane-acetone extract of *S. verrucosa* stems

Fraction Code	Weight (g)
H1	2.01
H2	0.32
H3	0.73
H4	0.63
H5	0.55
H6	0.75
H7	0.93
H8	1.65

3.2.1 Isolation of Compound SV-1 (Friedelin)

Fraction H4 (0.63 g) was further separated on a silica gel column (40 g, 3 × 15 cm) using *n*-hexane-CH_2Cl_2 (7:13) as the mobile phase. One hundred and fifteen collected fractions (10 ml each) were examined by TLC using *n*-hexane-CH_2Cl_2 (2:3) as the mobile phase, and then combined to yield 4 subfractions (H4A-H4D). Purification of subfraction H4B (50 mg) on a column of silica gel (12 g, 2 × 12 cm), washed down with *n*-hexane-EtOAc (39:1), gave compound SV-1 as colorless needles (4.0 mg, 0.0003 % yield).

3.2.2 Isolation of Compound SV-2 (Friedelane-1,3-dione)

Subfraction H4D (66 mg) was further purified by recrystallization in MeOH to afford compound SV-2 as colorless needles (25.5 mg, 0.002 % yield).

3.3 Isolation of Compounds from the EtOAc Extract of *S. verrucosa* Stems

The EtOAc extract (6.1 g) was dissolved in a small amount of CH_2Cl_2 and applied to the top of a silica gel column (150 g, 4.5 × 20 cm) eluted with gradient mixtures of CH_2Cl_2-EtOAc (19:1 → 0:1). One hundred and fifty fractions (25 ml each) were collected. According to their chemical profiles by TLC using CH_2Cl_2-EtOAc (19:1) as the mobile phase, these fractions were combined into 10 fractions (E1-E10), as shown in **Table 6.**

Table 6. Combined fractions from the EtOAc extract of *S. verrucosa* stems

Fraction Code	Weight (g)
E1	0.06
E2	0.05
E3	0.10
E4	0.28
E5	0.12
E6	0.09
E7	0.07
E8	0.02
E9	0.19
E10	0.23

3.3.1 Isolation of Compound SV-3 (Kokoonol)

Fraction E3 (0.1 g) was further purified on a silica gel column (20 g, 2.5 × 12 cm), using *n*-hexane-EtOAc (17:3) as the mobile phase, to yield compound SV-3 as a white, amorphous powder (7.4 mg, 0.0006 % yield) after recrystallization in MeOH.

3.3.2 Isolation of Compound SV-4 (26-Hydroxyfriedelane-1,3-dione)

Fraction E4 (0.28 g) was chromatographed on a silica gel column (25 g, 2.5 × 15 cm), eluted with a solvent system of CH_2Cl_2-EtOAc (97:3). Eighty fractions (10 ml each) were collected and combined into 3 subfractions (E4A-E4C). Subfraction E4A (64 mg) was further purified on another silica gel column (20 g, 2.5 × 12 cm) eluting with *n*-hexane-EtOAc (87:13) to afford compound SV-4 as a white, amorphous powder (7.4 mg, 0.0006 % yield).

3.3.3 Isolation of Compound SV-5 (21α-Hydroxyfriedelan-3-one)

Subfraction E4B (54 mg), after being subjected to a silica gel column (20 g, 2.5 × 12 cm) eluting with *n*-hexane-EtOAc (17:3), was divided into 47 collected fractions (10 ml each). These fractions were pooled into 2 subfractions (E4B1-E4B2) depending on their TLC profiles. Compound SV-5 was obtained as colorless cubic crystals (2.3 mg, 0.0002 % yield) upon recrystallizing subfraction E4B2 with MeOH.

3.3.4 Isolation of Compound SV-6 (3β,22α-Dihydroxyolean-12-en-29-oic acid)

Subfraction E4C (45 mg) was purified on a silica gel column (20 g, 2.5 × 12 cm) eluting with *n*-hexane-EtOAc (4:1). Fifty fractions (10 ml each) were collected and combined into 2 subfractions (E4C1-E4C2) according to their TLC data. Compound SV-6 was obtained as colorless prisms (6.2 mg, 0.0005 % yield) by recrystallizing subfraction E4C2 with *n*-hexane.

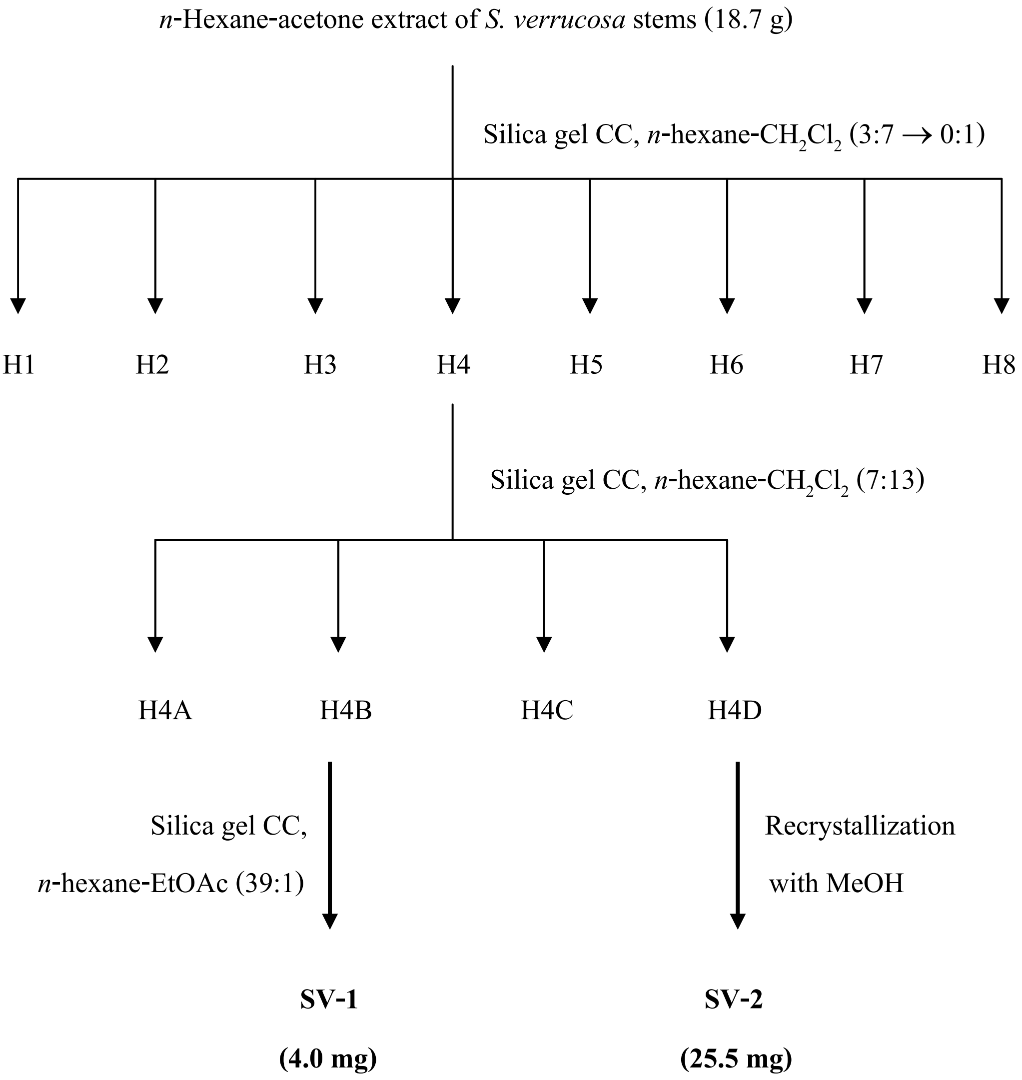
3.3.5 Isolation of Compound SV-7 (30-Hydroxyfriedelane-1,3-dione)

Fraction E6 (0.09 g) was subjected to gel filtration chromatography using a Sephadex LH-20 column (100 g, 2.3 × 82 cm) and a solvent system of CH_2Cl_2-MeOH (1:1) as the mobile phase. Selected fractions were pooled and further chromatographed on a silica gel column (10 g, 2 × 10 cm) eluting with CH_2Cl_2-MeOH (99:1). Sixty fractions (10 ml each) were collected and combined to give 3 subfractions (E6A-E6C). Subfraction E6C (20 mg) was further separated on a silica gel column (10 g, 2 × 10 cm), eluted with *n*-hexane-EtOAc (4:1), into 2 subfractions (E6C1-E6C2). Subfraction E6C1 was purified by recrystallization with MeOH to afford compound SV-7 as a white amorphous powder (5.6 mg, 0.0005 % yield).

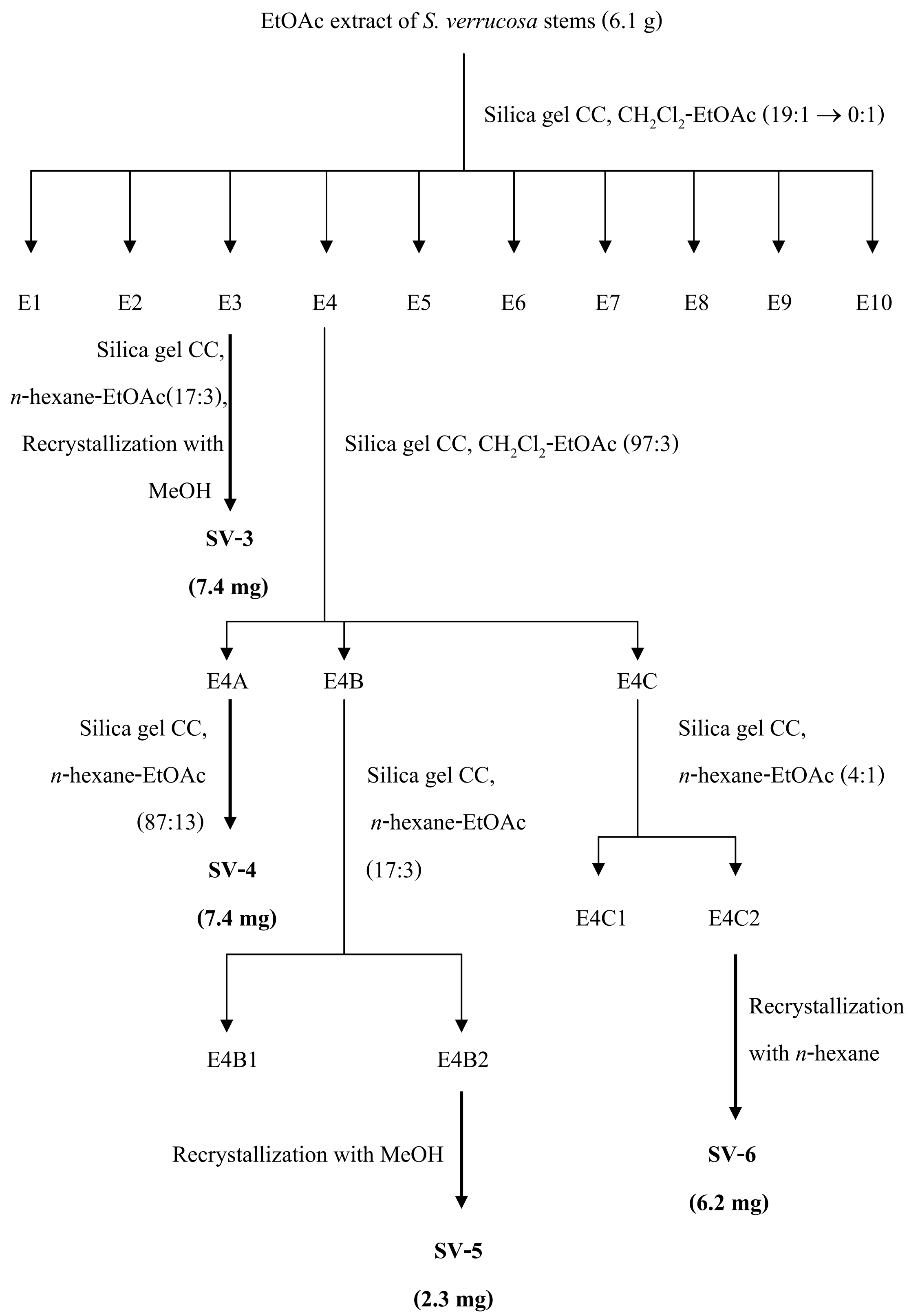
3.3.6 Isolation of Compound SV-8 (21α-Hydroxyfriedelane-1,3-dione)

After the separation of subfraction E6C (20 mg) into subfractions E6C1 and E6C2, Compound SV-8 was obtained as a white amorphous powder (4.2 mg, 0.0004 % yield) from the recrystallization of subfraction E6C2 with MeOH.

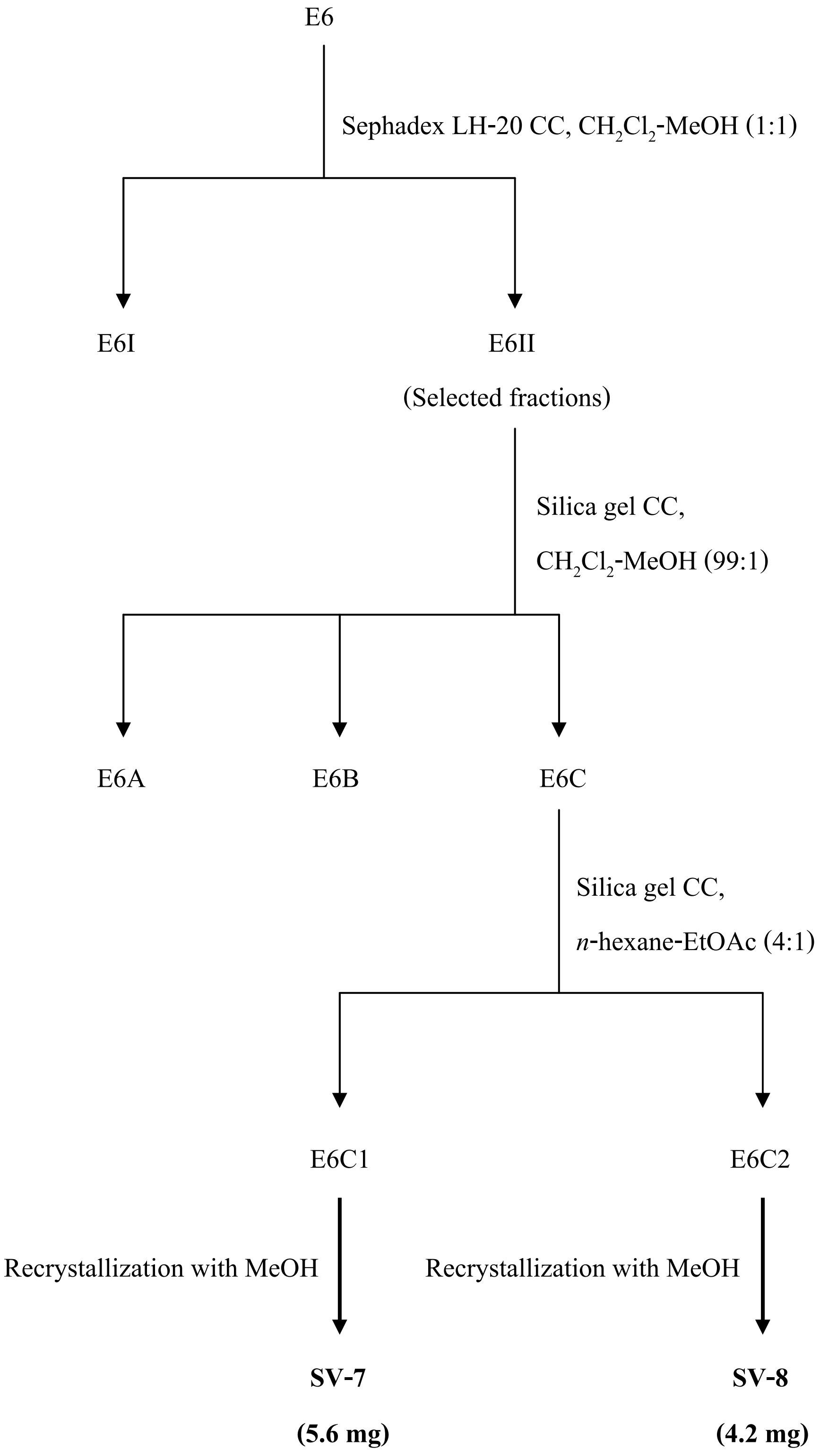
The isolation of compounds from the *n*-hexane-acetone and EtOAc extracts of *S. verrucosa* stems is presented in **Schemes 2** and **3**, respectively.



Scheme 2. Isolation of compounds from the *n*-hexane-acetone extract of *S. verrucosa* stems



Scheme 3. Isolation of compounds from the EtOAc extract of *S. verrucosa* stems

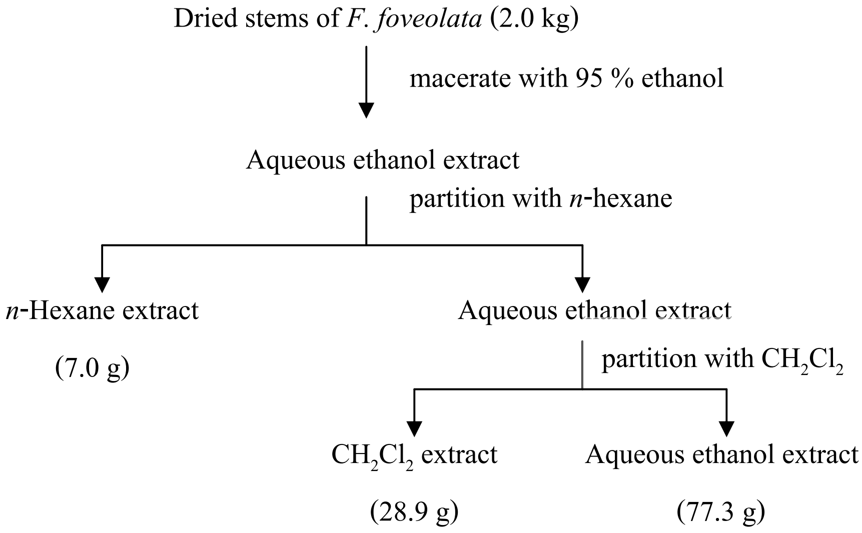


Scheme 3. (continued)

4. Extraction and Isolation of Compounds from the Stems of *Ficus foveolata*

4.1 Extraction of the Stems of *F. foveolata*

Dried, powdered *F. foveolata* stems (2.0 kg) were macerated with 95% ethanol (3 × 8 l) and the combined ethanolic extract was concentrated under reduced pressure at 45°C by rotary evaporator. The aqueous ethanol extract was then sequentially partitioned with *n*-hexane and CH_2Cl_2 to yield *n*-hexane (7.0 g, 0.35 % yield), CH_2Cl_2 (28.9 g, 1.45 % yield) and aqueous ethanol (77.3 g, 3.87 % yield) extracts upon evaporation, as shown in **Scheme 4.**



Scheme 4. Extraction of *F. foveolata* stems

4.2 Isolation of Compounds from the *n*-Hexane Extract of *F. foveolata* Stems

The *n*-hexane extract (7.0 g) was reconstituted in a small volume of a mixture of *n*-hexane and CH_2Cl_2 (1:1), then applied on top of a silica gel column (200 g, 5.0 × 26 cm) eluted with gradient mixtures of *n*-hexane-CH_2Cl_2 (1:1 → 1:3) to yield nine fractions (FH1-FH9), as shown in **Table 7.**

Table 7. Combined fractions from the *n*-hexane extract of *F. foveolata* stems

Fraction Code	Weight (g)
FH1	0.74
FH2	0.08
FH3	0.03
FH4	0.14
FH5	0.04
FH6	0.24
FH7	0.19
FH8	0.15
FH9	0.27

4.2.1 Isolation of Compound FF-1 (Friedelin)

Fraction FH4 (0.14 g) was purified on a silica gel column (20 g, 2.5 × 12 cm) using *n*-hexane-EtOAc (24:1) as the mobile phase to yield compound FF-1 as colorless needles (24.5 mg, 0.0013 % yield) after crystallization with MeOH.

4.2.2 Isolation of Compound FF-2 (Taraxerol)

Fraction FH7 (0.19 g) was chromatographed on a column of silica gel (25 g, 2.5 × 13 cm) eluting with *n*-hexane-EtOAc (19:1). Sixty-eight fractions (10 ml each) were collected and verified by TLC using *n*-hexane-EtOAc (19:1) as the solvent system. These fractions were combined into 2 subfractions (FH7A-FH7B) based on their TLC profiles. Upon evaporation, subfraction FH7B afforded compound FF-2 as a white amorphous powder (5.8 mg, 0.0003 % yield).

4.3 Isolation of Compounds from the CH_2Cl_2 Extract of *F. foveolata* Stems

The CH_2Cl_2 extract (28.9 g) was re-dissolved with a small volume of *n*-hexane-EtOAc (3:7) mixture and applied to the top of a silica gel column (500 g, 9.5 × 15 cm). Elution was done with gradient mixtures of *n*-hexane-EtOAc-MeOH (3:7:0 → 0:1:0 → 0:7:3) to give three hundred fractions (25 ml each). These collected fractions were combined according to their TLC profiles into nine fractions (C1-C9), as shown in **Table 8**.

Table 8. Combined fractions from the CH_2Cl_2 extract of *F. foveolata* stems

Fraction Code	Weight (g)
C1	0.98
C2	0.58
C3	0.98
C4	1.87
C5	0.35
C6	0.37
C7	0.57
C8	1.99
C9	6.58

4.3.1 Isolation of Compound FF-3 (Betulin)

Fraction C1 (0.98 g) was purified over a silica gel column (20 g, 2.5 × 12 cm) using *n*-hexane-EtOAc (7:3) as the mobile phase to yield compound FF-3 as a white amorphous powder (13.8 mg, 0.0007 % yield).

4.3.2 Isolation of Compound FF-4 [4(15)-Eudesmene-1β,6α-diol]

Fraction C2 (0.58 g) was separated on a silica gel column (40 g, 3 × 15 cm) eluting with *n*-hexane-EtOAc (7:3) into five subfractions (C2A-C2E) based on their TLC profiles. The subfraction C2B (217.8 mg) was further purified by silica gel column chromatography (20 g, 2.5 × 12 cm) using CH_2Cl_2-EtOAc (9:1) as the mobile phase. The eluates could be combined into 2 subfractions (C2B1-C2B2) and evaporation of the first subfraction yielded compound FF-4 as colorless needles (8.5 mg, 0.0004 % yield).

4.3.3 Isolation of Compound FF-5 [4(15)-Eudesmene-1β,5α-diol]

Subfraction C2B2, which was obtained from further separation of subfraction C2B, gave compound FF-5 as colorless needles (5.1 mg, 0.0003 % yield) upon removal of the solvent.

4.3.4 Isolation of Compound FF-6 (Foveolide B)

Subfraction C2D (31.8 mg) was further purified on a silica gel column (10 g, 2 × 10 cm) using a mixture of CH_2Cl_2-EtOAc (9:1) as the mobile phase. The eluates (5 ml each) were collected and verified by TLC. Fractions containing the same major spot were combined and evaporated to obtain compound FF-6 as a colorless gum (7.9 mg, 0.0004 % yield).

4.3.5 Isolation of Compound FF-7 (Foveolide A)

Fraction C3 (0.98 g) was separated on a silica gel column (40 g, 3 × 15 cm) using CH_2Cl_2-EtOAc (9:1) as the mobile phase. One hundred and twenty fractions (10 ml each) were collected and combined according to their TLC data into four subfractions (C3A-C3D). Subfraction C3C (169.9 mg) was further purified on another silica gel column (20 g, 2.5 × 12 cm) eluting with *n*-hexane-EtOAc (3:2) to furnish compound FF-7 as a yellow oil (16.2 mg, 0.0008 % yield).

4.3.6 Isolation of Compound FF-8b (Foveoeudesmenone)

Fraction C4 (1.87 g) was applied to a silica gel column (40 g, 3 × 15 cm) washed down with *n*-hexane-acetone (13:7). Seventy fractions (25 ml each) were collected, verified by TLC and then combined into four subfractions (C4A-C4D). Subfraction C4A (92 mg) was further chromatographed over a silica gel column (25 g, 2.5 × 15 cm) eluted with CH_2Cl_2-EtOAc (3:2), followed by another silica gel column (10 g, 2 × 10 cm) eluted with *n*-hexane-EtOAc (1:1) to afford compound FF-8a as a colorless oil (14.7 mg, 0.0007 % yield). After that, the compound was spontaneously converted into FF-8b by oxidation and reduction.

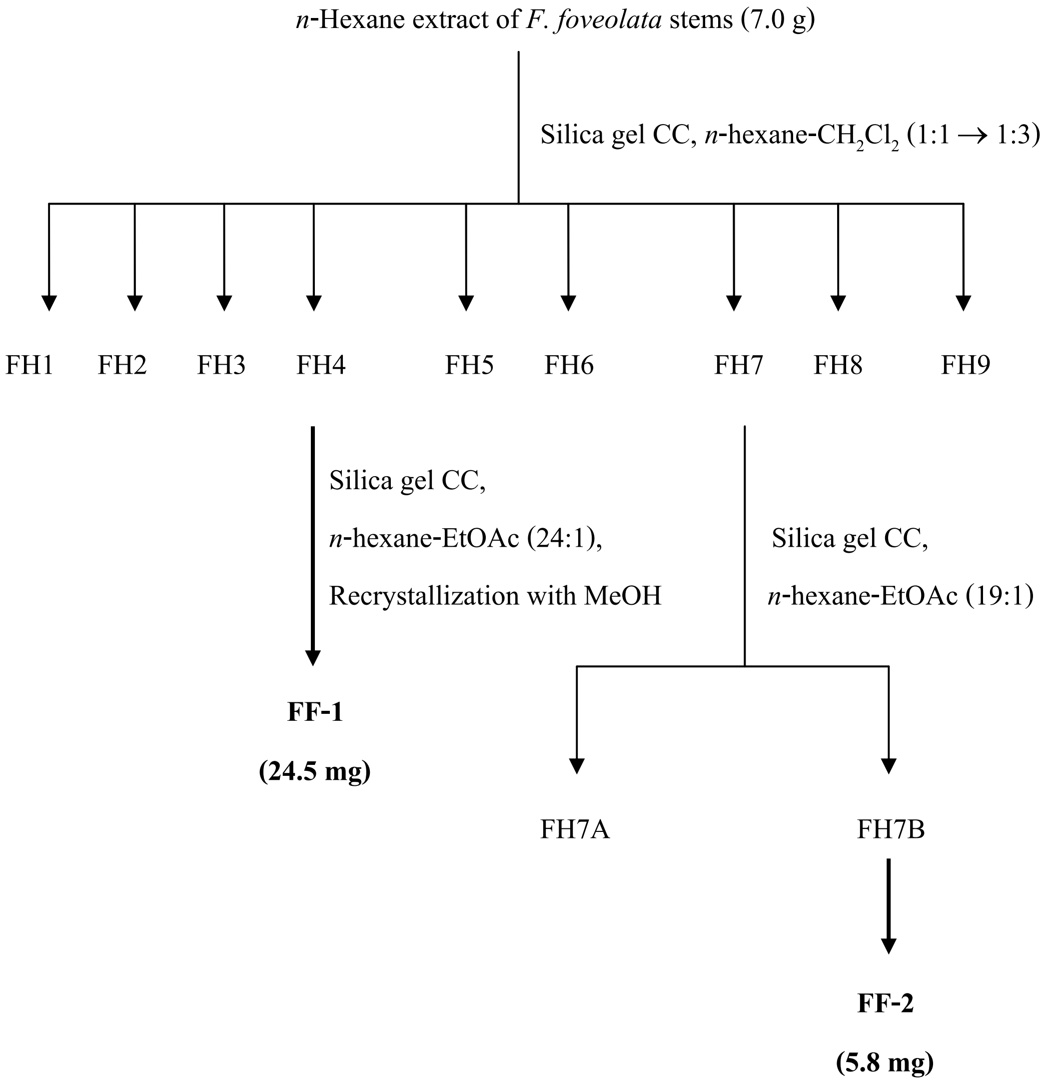
4.3.7 Isolation of Compound FF-9 (Ethyl rosmarinate)

Fraction C6 (0.37 g) was subjected to silica gel column chromatography (20 g, 2.5 × 12 cm) eluted with *n*-hexane-EtOAc (1:9). Forty fractions (10 ml each) were collected and combined into two subfractions (C6A-C6B). Subsequent purification of subfraction C6A over another silica gel column (15 g, 2.5 × 12 cm), using CH_2Cl_2-acetone (3:2) as the mobile phase, afforded compound FF-9 as a yellow gum (15.7 mg, 0.0008 % yield).

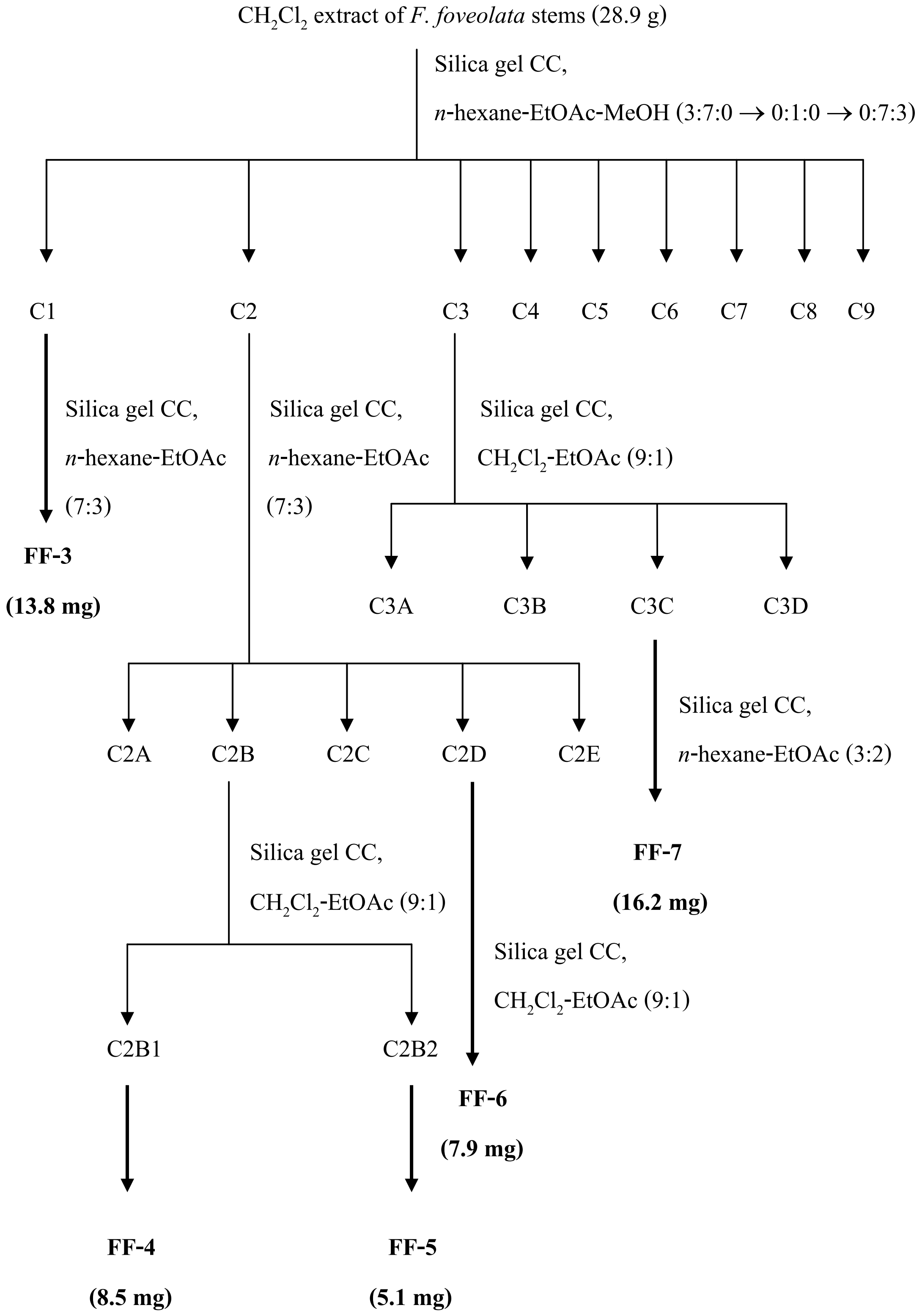
4.3.8 Isolation of Compound FF-10 (Foveospirolide)

Fraction C7 (0.57 g) was separated over a silica gel column (40 g, 3 × 15 cm) eluting with EtOAc-MeOH (49:1). Fifty fractions (10 ml each) were collected, inspected by TLC and pooled into two subfractions (C7A-C7B). Subfraction C7A (140 mg) was purified by gel filtration through a Sephadex LH-20 column (100 g, 2.3 × 82 cm) eluted with CH_2Cl_2-MeOH (1:1) to give compound FF-10 as a yellow oil (12.5 mg, 0.0006 % yield).

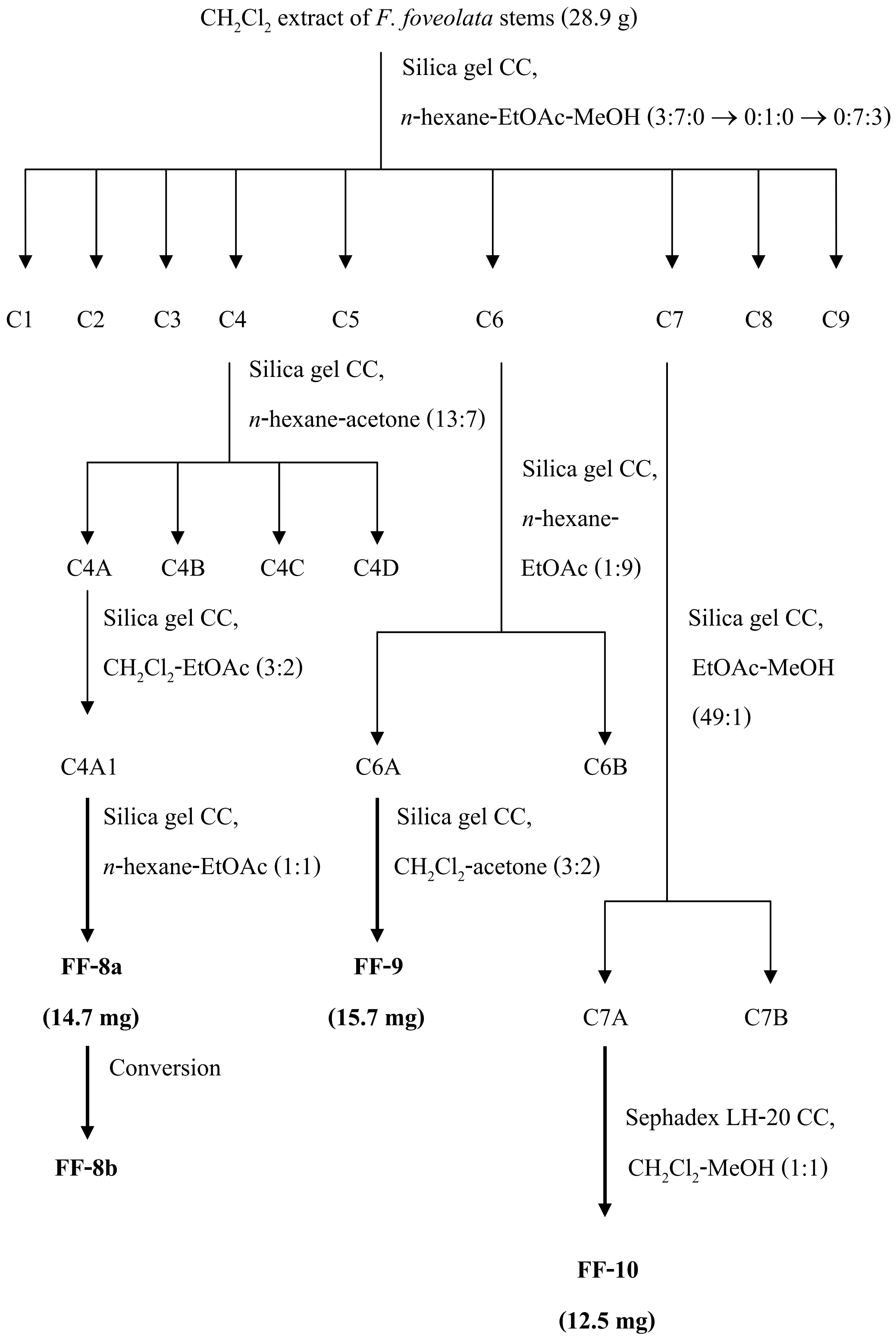
The isolation of chemical constituents from the *n*-hexane and CH_2Cl_2 extracts of *F. foveolata* stems is presented in **Schemes 5** and **6**, respectively.



Scheme 5. Isolation of compounds from the *n*-hexane extract of *F. foveolata* stems



Scheme 6. Isolation of compounds from the CH_2Cl_2 extract of *F. foveolata* stems



Scheme 6. (continued)

5. Physical and Spectral Data of Isolated Compounds

5.1 Compound SV-1 (Friedelin)

Compound SV-1 was obtained as colorless needles (4.0 mg, 0.0003 % based on dried weight of *S. verrucosa* stems). The compound is soluble in CH_2Cl_2.

Mp:	260-263 °C
ESI-MS:	*m/z* (% rel. int.): 427 $[M + H]^+$ (14); **Figure 7**.
IR:	ν_{max} cm^{-1} (KBr): 3426, 2927, 1716, 1463, 1390; **Figure 8.**
^{1}H NMR:	δ ppm, 300 MHz, in $CDCl_3$; 0.71 (3H, *s*), 0.85 (3H, *s*), 0.86 (3H, *d, J* = 5.4 Hz), 0.93 (3H, *s*), 0.98 (3H, *s*), 0.99 (3H, *s*), 1.03 (3H, *s*) and 1.15 (3H, *s*); **Table 9** and **Figure 9.**
^{13}C NMR:	δ ppm, 75 MHz, in $CDCl_3$; 6.8, 14.7, 17.9, 18.3, 18.6, 20.3, 22.3, 28.2, 30.0, 30.5, 31.8, 32.1, 32.5, 32.8, 35.0, 35.4, 35.7, 36.0, 37.5, 38.3, 39.3, 39.7, 41.3, 41.5, 42.2, 42.9, 53.1, 58.3, 59.5 and 213.0; **Table 9** and **Figure 10.**

5.2 Compound SV-2 (Friedelane-1,3-dione)

Compound SV-2 was obtained as colorless needles (25.5 mg, 0.002 % based on dried weight of *S. verrucosa* stems). The compound is soluble in CH_2Cl_2.

Mp:	270-272 °C
ESI-MS:	*m/z* (% rel. int.): 467 $[M + 4H + Na]^+$ (9); **Figure 11.**
IR:	ν_{max} cm^{-1} (KBr): 3417, 2943, 1732, 1705, 1459, 1392; **Figure 12.**
^{1}H NMR:	δ ppm, 300 MHz, in $CDCl_3$; 0.67 (3H, *s*), 0.93 (3H, *s*), 0.98 (3H, *s*), 1.00 (3H, *s*), 1.01 (3H, *s*), 1.03 (3H, *d*, *J* = 8.4 Hz), 1.16 (3H, *s*), 1.18 (3H, *s*), 1.88 (1H, *br d*, *J* = 12.0 Hz), 2.13 (1H, *br d*, *J* = 12.0 Hz), 2.36 (1H, *s*), 2.56 (1H, *q*, *J* = 6.6 Hz), 3.22 (1H, *d*, *J* = 15.9 Hz), 3.44 (1H, *d*, *J* = 15.9 Hz) and 1.15 (3H, *s*); **Table 10** and **Figure 13.**
^{13}C NMR:	δ ppm, 75 MHz, in $CDCl_3$; 7.3, 16.0, 18.0, 18.1, 18.8, 20.4, 28.2, 30.0, 30.2, 31.8, 32.1, 32.5, 32.8, 34.6, 35.0, 35.3, 36.0, 37.3, 37.9, 38.3, 39.3, 39.6, 40.7, 42.8, 52.2, 59.1, 60.7, 72.0, 202.8 and 204.1; **Table 10** and **Figure 14.**

5.3 Compound SV-3 (Kokoonol)

Compound SV-3 was obtained as a white, amorphous powder (7.4 mg, 0.0006 % based on dried weight of *S. verrucosa* stems). The compound is soluble in CH_2Cl_2.

Mp:	270-271 °C
ESI-MS:	*m/z* (% rel. int.): 443 $[M + H]^+$ (9); **Figure 15.**
IR:	ν_{max} cm^{-1} (KBr): 3543, 2946, 1706, 1630, 1460, 1388; **Figure 16.**
^{1}H NMR:	δ ppm, 300 MHz, in $CDCl_3$; 0.71 (3H, *s*), 0.86 (3H, *d*, *J* = 6.3 Hz), 0.93 (3H, *s*), 1.07 (3H, *s*), 1.23 (3H, *s*), 1.67 (1H, *m*), 1.95 (1H, *m*), 2.20 (1H, *q*, *J* = 6.3 Hz), 2.29 (1H, *m*), 2.36 (1H, *m*), 4.01 (1H, *d*, *J* = 11.6 Hz) and 4.11 (1H, *d*, *J* = 11.6 Hz); **Table 11** and **Figure 17.**
^{13}C NMR:	δ ppm, 75 MHz, in $CDCl_3$; 7.2, 14.9, 18.1, 21.0, 22.5, 22.7, 24.4, 28.7, 30.8, 31.0, 32.4, 33.0, 33.3, 35.9, 36.4, 37.4, 37.9, 37.9, 38.6, 39.5, 41.9, 42.6, 42.8, 43.9, 45.7, 53.4, 58.5, 60.3, 64.7 and 213.4; **Table 11** and **Figure 18.**

5.4 Compound SV-4 (26-Hydroxyfriedelane-1,3-dione)

Compound SV-4 was obtained as a white, amorphous powder (7.4 mg, 0.0006 % based on dried weight of *S. verrucosa* stems). The compound is soluble in CH_2Cl_2.

Mp:	266-268 °C
ESI-MS:	*m/z* (% rel. int.): 457 $[M + H]^+$ (21); **Figure 19.**
IR:	ν_{max} cm^{-1} (KBr): 3575, 2945, 1728, 1703, 1462, 1391; **Figure 20.**
^{1}H NMR:	δ ppm, 300 MHz, in $CDCl_3$; 0.68 (3H, *s*), 0.92 (3H, *s*), 0.95 (3H, *s*), 1.02 (3H, *d*, *J* = 6.8 Hz), 1.04 (3H, *s*), 1.12 (3H, *s*), 1.36 (3H, *s*), 2.38 (1H, *s*), 2.54 (1H, *q*, *J* = 6.8 Hz), 3.23 (1H, *d*, *J* = 15.9 Hz), 3.44 (1H, *d*, *J* = 15.9 Hz), 4.04 (1H, *d*, *J* = 11.6 Hz) and 4.14 (1H, *d*, *J* = 11.6 Hz); **Table 12** and **Figure 21.**
^{13}C NMR:	δ ppm, 75 MHz, in $CDCl_3$; 7.7, 16.1, 18.2, 20.1, 20.8, 24.5, 28.7, 30.3, 30.8, 32.1, 32.4, 33.3, 34.9, 35.4, 35.8, 35.9, 37.6, 38.5, 39.5, 40.1, 42.2, 42.5, 43.9, 52.5, 59.3, 61.0, 64.4, 72.8, 203.2 and 204.5; **Table 12** and **Figure 22.**

5.5 Compound SV-5 (21α-Hydroxyfriedelan-3-one)

Compound SV-5 was obtained as colorless cubic crystals (2.3 mg, 0.0002 % based on dried weight of *S. verrucosa* stems). The compound is soluble in CH_2Cl_2.

Mp:	266-268 °C

ESI-MS: *m/z* (% rel. int.): 443 $[M + H]^+$ (20); **Figure 23.**

IR: ν_{max} cm^{-1} (KBr): 3429, 2931, 1714, 1628, 1452, 1389; **Figure 24.**

^1H NMR: δ ppm, 300 MHz, in $CDCl_3$; 0.70 (3H, *s*), 0.85 (3H, *s*), 0.85 (3H, *d*, *J* = 6.8 Hz), 0.89 (3H, *s*), 0.97 (3H, *s*), 1.05 (3H, *s*), 1.09 (3H, *s*), 1.17 (3H, *s*), 2.24 (1H, *q*, *J* = 6.8 Hz), 2.30 (1H, *m*), 2.38 (1H, *m*) and 3.68 (1H, *dd*, *J* = 12.0, 4.2 Hz); **Table 13** and **Figure 25.**

^{13}C NMR: δ ppm, 75 MHz, in $CDCl_3$; 7.2, 15.1, 18.2, 18.6, 18.7, 19.7, 22.7, 25.3, 30.6, 30.9, 32.3, 32.9, 33.6, 34.8, 35.7, 36.4, 36.5, 37.9, 39.2, 39.5, 41.7, 41.9, 42.5, 44.7, 47.5, 52.0, 58.6, 59.9, 74.7 and 213.0; **Table 13** and **Figure 26.**

5.6 Compound SV-6 (3β,22α-Dihydroxyolean-12-en-29-oic acid)

Compound SV-6 was obtained as colorless prisms (6.2 mg, 0.0005 % based on dried weight of *S. verrucosa* stems). The compound is soluble in CH_2Cl_2.

Mp: 293-295 °C

ESI-MS: *m/z* (% rel. int.): 429 $[M + H -COO]^+$ (26); **Figure 27.**

IR: ν_{max} cm^{-1} (KBr): 3491, 2948, 1749, 1650, 1456, 1390, 1363; **Figure 28.**

^1H NMR: δ ppm, 500 MHz, in $CDCl_3$; 0.72 (1H, *dd*, *J* = 11.5, 1.5 Hz), 0.77 (3H, *s*), 0.85 (3H, *s*), 0.91 (3H, *s*), 0.92 (3H, *s*), 0.97 (3H, *s*), 1.05 (3H, *s*), 1.19 (3H, *s*), 1.36 (1H, *ddd, J* = 12.5, 5.0, 3.0 Hz), 1.50 (1H, *dd*, *J* = 13.0, 8.0 Hz), 1.68 (1H, *ddd*, *J* = 14.0, 10.5, 3.5 Hz), 2.11 (1H, *dd*, *J* = 12.0, 8.5 Hz), 2.24 (1H, *d, J* = 12.0 Hz), 3.20 (1H, *dd*, *J* = 11.5, 4.5 Hz), 4.13 (1H, *d*, *J* = 5.5 Hz) and 5.28 (1H, *dd*, *J* = 3.5, 2.5 Hz); **Table 14** and **Figure 29.**

^{13}C NMR: δ ppm, 125 MHz, in $CDCl_3$; 15.6, 15.6, 17.0, 18.3, 21.0, 23.5, 24.0, 24.3, 25.0, 25.2, 27.2, 28.1, 33.1, 33.8, 35.2, 37.0, 38.6, 38.7, 39.3, 39.5, 39.8, 42.5, 43.4, 47.5, 55.2, 78.9, 83.1, 124.6, 140.2 and 182.4; **Table 14** and **Figure 30.**

5.7 Compound SV-7 (30-Hydroxyfriedelane-1,3-dione)

Compound SV-7 was obtained as a white amorphous powder (5.6 mg, 0.0005 % based on dried weight of *S. verrucosa* stems). The compound is soluble in CH_2Cl_2.

Mp: 165-167 °C

HR-ESI-MS: *m/z* (% rel. int.): 457.3681 $[M + H]^+$ (100), calc. for $C_{30}H_{49}O_3$, 457.3682; **Figure 33.**

IR: ν_{max} cm^{-1} (KBr): 3435, 2940, 1729, 1707, 1632, 1458, 1392; **Figure 34.**

^{1}H NMR: δ ppm, 500 MHz, in $CDCl_3$; 0.67 (3H, *s*), 0.97 (3H, *s*), 0.99 (3H, *s*), 1.02 (3H, *s*), 1.03 (3H, *d*, *J* = 6.5 Hz), 1.13 (3H, *s*), 1.18 (3H, *s*), 1.88 (1H, *br dd*, *J* = 12.5, 3.5 Hz), 2.14 (1H, *ddd*, *J* = 13.5, 7.0, 3.5 Hz), 2.36 (1H, *s*), 2.56 (1H, *q*, *J* = 6.5 Hz), 3.23 (1H, *d*, *J* = 15.8 Hz), 3.34 (1H, *d*, *J* = 10.5 Hz), 3.40 (1H, *d*, *J* = 10.5 Hz) and 3.43 (1H, *d*, *J* = 15.8 Hz); **Table 15** and **Figure 35.**

^{13}C NMR: δ ppm, 125 MHz, in $CDCl_3$; 7.3, 16.0, 18.0, 18.1, 18.6, 20.0, 28.1, 28.9, 29.4, 30.0, 30.1, 32.1, 32.1, 33.4, 34.5, 35.8, 37.2, 37.8, 38.1, 38.3, 39.6, 40.6, 42.6, 52.0, 59.1, 60.6, 71.9, 72.0, 202.7 and 204.1; **Table 15** and **Figure 36.**

5.8 Compound SV-8 (21α-Hydroxyfriedelane-1,3-dione)

Compound SV-8 was obtained as a white amorphous powder (4.2 mg, 0.0004 % based on dried weight of *S. verrucosa* stems). The compound is soluble in CH_2Cl_2.

Mp: 160-162 °C

HR-ESI-MS: *m/z* (% rel. int.): 457.3671 $[M + H]^+$ (100), calc. for $C_{30}H_{49}O_3$, 457.3682; **Figure 38.**

IR: ν_{max} cm^{-1} (KBr): 3436, 2941, 1731, 1705, 1619, 1462, 1392; **Figure 39.**

^{1}H NMR: δ ppm, 500 MHz, in $CDCl_3$; 0.67 (3H, *s*), 0.92 (3H, *s*), 0.96 (3H, *s*), 1.03 (3H, *d*, *J* = 7.0 Hz), 1.05 (3H, *s*), 1.07 (3H, *s*), 1.18 (3H, *s*), 1.19 (3H, *s*), 1.21 (1H, *dd*, *J* = 12.0, 4.5 Hz), 1.60 (1H, *dd*, *J* = 13.8, 4.8 Hz), 1.68 (1H, *dd*, *J* = 12.5, 12.0 Hz), 1.87 (1H, *br dd*, *J* = 9.5, 3.0 Hz), 2.14 (1H, *ddd*, *J* = 13.5, 7.0, 3.5 Hz), 2.37 (1H, *s*), 2.55 (1H, *q*, *J* = 7.0 Hz), 3.23 (1H, *d*, *J* = 15.8 Hz), 3.44 (1H, *d*, *J* = 15.8 Hz) and 3.67 (1H, *dd*, *J* = 12.0, 4.5 Hz); **Table 16** and **Figure 40.**

^{13}C NMR: δ ppm, 125 MHz, in $CDCl_3$; 7.3, 16.0, 17.8, 18.1, 18.2, 19.3, 24.9, 29.8, 30.5, 31.8, 32.5, 33.1, 34.2, 34.3, 35.9, 36.0, 37.3, 37.8, 38.7, 38.8, 40.6, 44.2, 47.0, 50.6, 59.1, 60.6, 71.9, 74.3, 202.7 and 204.1; **Table 16** and **Figure 41.**

5.9 Compound FF-1 (Friedelin)

Compound FF-1 was obtained as colorless needles (24.5 mg, 0.0013 % based on dried weight of *F. foveolata* stems). The compound is soluble in CH_2Cl_2.

Mp: 260-263 °C

ESI-MS: *m/z* (% rel. int.): 449 $[M + Na]^+$ (40); **Figure 44.**

IR: ν_{max} cm^{-1} (KBr): 3431, 2927, 1715, 1463, 1390; **Figure 45.**

^{1}H NMR: δ ppm, 300 MHz, in $CDCl_3$; 0.70 (3H, *s*), 0.85 (3H, *s*), 0.87 (3H, *d*, *J* = 5.4 Hz), 0.93 (3H, *s*), 0.99 (3H, *s*), 0.99 (3H, *s*), 1.03 (3H, *s*) and 1.16 (3H, *s*); **Figure 46.**

^{13}C NMR: δ ppm, 75 MHz, in $CDCl_3$; 6.8, 14.7, 17.9, 18.2, 18.6, 20.3, 22.3, 28.2, 30.0, 30.5, 31.8, 32.1, 32.4, 32.8, 35.0, 35.3, 35.6, 36.0, 37.5, 38.3, 39.2, 39.7, 41.3, 41.5, 42.1, 42.8, 53.1, 58.2, 59.5 and 213.1; **Figure 47.**

5.10 Compound FF-2 (Taraxerol)

Compound FF-2 was obtained as a white amorphous powder (5.8 mg, 0.0003 % based on dried weight of *F. foveolata* stems). The compound is soluble in CH_2Cl_2.

Mp: 282-285 °C

ESI-MS: *m/z* (% rel. int.): 427 $[M + H]^+$ (14); **Figure 48.**

IR: ν_{max} cm^{-1} (KBr): 3484, 2934, 1641, 1464, 1385; **Figure 49.**

^{1}H NMR: δ ppm, 300 MHz, in $CDCl_3$; 0.78 (3H, *s*), 0.80 (3H, *s*), 0.89 (3H, *s*), 0.89 (3H, *s*), 0.91 (3H, *s*), 0.93 (3H, *s*), 0.96 (3H, *s*), 1.07 (3H, *s*), 3.17 (1H, *dd*, *J* = 10.1, 4.7 Hz) and 5.51 (1H, *dd*, *J* = 6.3, 3.3 Hz); **Table 17** and **Figure 50.**

^{13}C NMR: δ ppm, 75 MHz, in $CDCl_3$; 15.9, 15.9, 17.9, 19.2, 21.7, 26.3, 27.6, 28.4, 29.2, 30.3, 30.3, 33.5, 33.8, 34.1, 35.6, 36.2, 37.1, 38.0, 38.0, 38.1, 38.4, 39.2, 39.4, 41.8, 49.2, 49.7, 56.0, 79.5, 117.3 and 158.5; **Table 17** and **Figures 51a-51b.**

5.11 Compound FF-3 (Betulin)

Compound FF-3 was obtained as a white amorphous powder (13.8 mg, 0.0007 % based on dried weight of *F. foveolata* stems). The compound is soluble in CH_2Cl_2.

Mp: 236-238 °C

ESI-MS: *m/z* (% rel. int.): 466 $[M + H + Na]^+$ (18); **Figure 52.**

IR: ν_{max} cm^{-1} (KBr): 3400, 2942, 1645, 1454, 1376; **Figure 53.**

^{1}H NMR: δ ppm, 300 MHz, in $CDCl_3$; 0.74 (3H, *s*), 0.80 (3H, *s*), 0.95 (3H, *s*), 0.96 (3H, *s*), 1.00 (3H, *s*), 1.66 (3H, *s*), 3.16 (1H, *dd*, *J* = 10.8, 5.4 Hz), 3.31 (1H, *d*, *J* = 10.8 Hz), 3.77 (1H, *d*, *J* = 10.8 Hz), 4.56 (1H, *br s*) and 4.66 (1H, *br s*); **Table 18** and **Figure 54.**

^{13}C NMR: δ ppm, 75 MHz, in $CDCl_3$; 14.8, 15.4, 16.0, 16.1, 18.3, 19.1, 20.9, 25.3, 27.0, 27.2, 28.0, 29.2, 29.8, 34.0, 34.3, 37.2, 37.3, 38.8, 38.9, 40.9, 42.7, 47.8, 47.8, 48.8, 50.4, 55.3, 60.2, 78.9, 109.6 and 150.6; **Table 18** and **Figures 55a-55b.**

5.12 Compound FF-4 [4(15)-Eudesmene-1β,6α-diol]

Compound FF-4 was obtained as colorless needles (8.5 mg, 0.0004 % based on dried weight of *F. foveolata* stems). The compound is soluble in CH_2Cl_2 and MeOH.

Mp: 129-130 °C

$[\alpha]^{20}_{D}$: +50°

ESI-MS: *m/z* (% rel. int.): 239 $[M + H]^+$ (60), 221 $[M - H_2O]^+$ (36), 203 $[M + H - 2H_2O]^+$ (30); **Figure 56.**

IR: ν_{max} cm^{-1} (KBr): 3589, 3274, 2937, 1647, 1451, 1386; **Figure 57.**

^{1}H NMR: δ ppm, 300 MHz, in $CDCl_3$; 0.68 (3H, *s*), 0.85 (3H, *br s*), 0.93 (3H, *br s*), 1.72 (1H, *d*, *J* = 8.4 Hz), 2.04 (1H, *m*), 2.30 (1H, *m*), 3.39 (1H, *dd*, *J* = 10.2, 4.2 Hz), 3.69 (1H, *br s*), 4.72 and 5.00 (2H, each *br s*); **Table 19** and **Figure 58.**

^{13}C NMR: δ ppm, 75 MHz, in $CDCl_3$; 12.0, 16.6, 18.6, 21.5, 26.4, 32.3, 35.5, 36.7, 42.1, 49.8, 56.3, 67.4, 79.4, 108.2 and 146.6; **Table 19** and **Figure 59.**

5.13 Compound FF-5 [4(15)-Eudesmene-1β,5α-diol]

Compound FF-5 was obtained as colorless needles (5.1 mg, 0.0003 % based on dried weight of *F. foveolata* stems). The compound is soluble in CH_2Cl_2 and MeOH.

Mp: 108-110 °C

$[\alpha]^{20}_{D}$: +124°

ESI-MS: *m/z* (% rel. int.): 239 $[M + H]^+$ (100), 221 $[M + H - H_2O]^+$ (75), 203 $[M + H - 2H_2O]^+$ (55); **Figure 60.**

IR: ν_{max} cm^{-1} (KBr): 3627, 3414, 2952, 1645, 1435, 1368; **Figure 61.**

^{1}H NMR: δ ppm, 300 MHz, in $CDCl_3$; 0.74 (3H, *s*), 0.88 (3H, *d*, *J* = 6.6 Hz), 0.90 (3H, *d*, *J* = 6.6 Hz), 2.13 (1H, *dd*, *J* = 13.5, 5.1 Hz), 2.68 (1H, *ddd*, *J* = 13.5, 8.1, 5.7 Hz), 4.03 (1H, *dd*, *J* = 10.4, 4.8 Hz), 4.73 and 4.83 (2H, each *br s*); **Table 20** and **Figure 62.**

^{13}C NMR: δ ppm, 75 MHz, in $CDCl_3$; 13.1, 20.1, 20.4, 24.1, 30.2, 30.4, 31.0, 33.2, 34.7, 38.7, 42.7, 73.5, 76.6, 109.0 and 151.1; **Table 20** and **Figure 63.**

5.14 Compound FF-7 (Foveolide A)

Compound FF-7 was obtained as yellow oil (16.2 mg, 0.0008 % based on dried weight of *F. foveolata* stems). The compound is soluble in CH_2Cl_2 and MeOH.

$[\alpha]^{20}_{D}$: -120° (c 0.05, MeOH)

UV: λ_{max} (MeOH) nm (log ε): 225 (3.09), 275 (2.23); **Figure 64.**

HR-ESI-MS: *m/z* (% rel. int.): 251.1621 $[M + H]^+$ (100), calc. for $C_{15}H_{23}O_3$, 251.1647; **Figure 65.**

IR: ν_{max} cm^{-1} (KBr): 3430, 2937, 1749, 1682, 1652, 1466, 1390, 1371; **Figure 66.**

^1H NMR: δ ppm, 500 MHz, in $CDCl_3$; 0.80 (3H, *s*), 0.94 (3H, *d, J* = 6.5 Hz), 0.98 (3H, *d, J* = 7.0 Hz), 2.19 (1H, *dddd*, *J* = 19.3, 9.5, 5.0, 3.2 Hz), 2.26 (1H, *ddd*, *J* = 11.0, 4.8, 3.0 Hz), 2.60 (1H, *dddd*, *J* = 19.3, 6.7, 4.0, 3.2 Hz), 3.72 (1H, *dd*, *J* = 9.5, 6.7 Hz), 3.91 (1H, *dd*, *J* = 11.0, 10.0 Hz) and 6.54 (1H, *dd, J* = 6.8, 3.2 Hz); **Table 21** and **Figure 67.**

^{13}C NMR: δ ppm, 125 MHz, in $CDCl_3$; 9.8, 19.8, 20.0, 24.8, 30.6, 34.0, 35.1, 36.8, 50.3, 54.2, 75.3, 79.6, 128.1, 131.2 and 169.0; **Table 21** and **Figure 68.**

5.15 Compound FF-6 (Foveolide B)

Compound FF-6 was obtained as colorless gum (7.9 mg, 0.0004 % based on dried weight of *F. foveolata* stems). The compound is soluble in CH_2Cl_2.

$[\alpha]^{20}_{D}$: -52° (c 0.05, $CHCl_3$)

HR-ESI-MS: *m/z* (% rel. int.): 469.3304 $[M + H]^+$ (100), calc. for $C_{30}H_{45}O_4$, 469.3317; **Figure 71.**

IR: ν_{max} cm^{-1} (KBr): 3443, 2933, 1753, 1699, 1464, 1443, 1371; **Figure 72.**

^1H NMR: δ ppm, 500 MHz, in $CDCl_3$; 0.86 (3H, *d, J* = 7.0 Hz), 0.88 (3H, *d, J* = 6.5 Hz), 0.97 (3H, *d, J* = 6.5 Hz), 1.00 (3H, *d, J* = 7.0 Hz), 1.09 (3H, *s*), 1.20 (3H, *s*), 1.59 (1H, *d*, *J* = 17.0 Hz), 2.07 (1H, *d*, *J* = 10.8 Hz), 2.35 (1H, *ddd*, *J* = 13.9, 5.0, 3.0 Hz), 2.64 (1H, *dd*, *J* = 17.0, 3.5 Hz), 2.69 (1H, *ddd*, *J* = 13.9, 12.5, 7.0 Hz), 3.83 (1H, *t*, *J* = 8.0 Hz) and 4.25 (1H, *t*, *J* = 10.8 Hz); **Table 22** and **Figure 73.**

^{13}C NMR: δ ppm, 125 MHz, in $CDCl_3$; 15.1, 16.4, 19.6, 20.2, 20.5, 20.5, 21.6, 25.6, 26.1, 30.5, 30.5, 30.7, 30.9, 34.7, 35.1, 35.9, 39.9, 42.0, 43.2, 45.7, 46.5, 48.8, 52.0, 57.1, 74.2, 77.4, 126.5, 134.2, 178.2 and 215.5; **Table 22** and **Figure 74.**

5.16 Compound FF-8b (Foveoeudesmenone)

Compound FF-8b, the product of the conversion of FF-8a, was initially obtained as colorless oil (14.7 mg, 0.0007 % based on dried weight of *F. foveolata* stems). The compound is soluble in CH_2Cl_2 and MeOH.

$[\alpha]^{20}_{D}$: -50° (*c* 0.01, MeOH)

UV: λ_{max} (MeOH) nm (log ε): 245 (3.17); **Figure 80.**

HR-ESI-MS: *m/z* (% rel. int.): 237.1842 $[M + H]^+$ (100), calc. for $C_{15}H_{25}O_2$, 237.1849; **Figure 81.**

IR: ν_{max} cm^{-1} (KBr): 3423, 2958, 1709, 1655, 1604, 1465, 1386, 1370; **Figure 82.**

^{1}H NMR: δ ppm, 500 MHz, in $CDCl_3$; 0.91 (3H, *d, J* = 7.0 Hz), 0.92 (3H, *d, J* = 7.0 Hz), 1.12 (3H, *s*), 1.74 (3H, *d, J* = 1.5 Hz), 2.10 (1H, *dt*, *J* = 13.0, 3.0 Hz), 2.53 (1H, *dd*, *J* = 16.5, 12.8 Hz), 2.61 (1H, *dd*, *J* = 16.5, 5.5 Hz), 2.72 (1H, *ddd*, *J* = 15.0, 5.5, 1.5 Hz) and 3.77 (1H, *dd*, *J* = 12.8, 5.5 Hz); **Table 24** and **Figures 83a-83b.**

^{13}C NMR: δ ppm, 125 MHz, in $CDCl_3$; 10.9, 16.2, 19.3, 19.7, 24.1, 31.4, 32.8, 37.8, 41.5, 42.3, 44.2, 74.6, 129.2, 162.8 and 197.4; **Table 24** and **Figure 84.**

5.17 Compound FF-9 (Ethyl rosmarinate)

Compound FF-9 was obtained as yellow gum (15.7 mg, 0.0008 % based on dried weight of *F. foveolata* stems). The compound is soluble in acetone and MeOH.

$[\alpha]^{20}_{D}$: +112° (*c* 0.05, MeOH)

UV: λ_{max} (MeOH) nm (log ε): 232 (3.56), 290 (3.50), 315 (3.51); **Figure 87.**

ESI-MS: *m/z* (% rel. int.): 388 $[M]^+$ (100), 389 $[M + H]^+$ (30); **Figure 88.**

IR: ν_{max} cm^{-1} (KBr): 3391, 1724, 1653, 1601, 1516, 1445, 1375, 1357; **Figure 89.**

^{1}H NMR: δ ppm, 500 MHz, in acetone-d_6; 1.19 (3H, *t*, *J* = 7.0 Hz), 2.99 (1H, *dd*, *J* = 11.6, 7.0 Hz), 4.11 (2H, *q*, *J* = 7.0 Hz), 4.75 (1H, *dd*, *J* = 13.9, 7.6 Hz), 6.54 (1H, *dd*, *J* = 7.9, 2.1 Hz), 6.55 (1H, *d*, *J* = 15.6 Hz), 6.71 (1H, *d*, *J* = 2.1 Hz), 6.71 (1H, *d*, *J* = 7.9 Hz), 6.82 (1H, *d*, *J* = 8.1 Hz), 6.93 (1H, *dd*, *J* = 8.1, 1.8 Hz), 7.06 (1H, *d*, *J* = 1.8 Hz) and 7.40 (1H, *d*, *J* = 15.6 Hz); **Table 25** and **Figure 90.**

^{13}C NMR: δ ppm, 125 MHz, in acetone-d_6; 14.4, 37.8, 54.9, 61.4, 114.9, 115.9, 116.3, 117.1, 118.9, 121.5, 121.7, 128.3, 129.3, 141.4, 144.8, 145.7, 146.2, 147.9, 166.4 and 172.4; **Table 25** and **Figure 91.**

5.18 Compound FF-10 (Foveospirolide)

Compound FF-10 was obtained as yellow oil (12.5 mg, 0.0006 % based on dried weight of *F. foveolata* stems). The compound is soluble in MeOH.

$[\alpha]^{20}_{D}$: -24° (*c* 0.05, MeOH)

UV: λ_{max} (MeOH) nm (log ε): 241 (3.22), 276 (2.90), 325 (2.00); **Figure 92.**

HR-ESI-MS: *m/z* (% rel. int.): 327.1072 $[M + H]^+$ (100), calc. for $C_{15}H_{19}O_8$, 327.1074; **Figure 93.**

IR: ν_{max} cm^{-1} (KBr): 3366, 2944, 1778, 1605, 1520, 1455, 1435, 1372; **Figure 94.**

^{1}H NMR: δ ppm, 500 MHz, in CD_3OD; 2.71 (1H, *dd*, *J* = 17.1, 8.4 Hz), 3.03 (1H, *dd*, *J* = 17.1, 12.5 Hz), 3.33 (1H, *d, J* = 9.3 Hz), 3.33 (1H*, ddd*, *J* = 10.9, 9.3, 5.7 Hz), 3.49 (1H, *t*, *J* = 10.9 Hz), 3.58 (1H, *t, J* = 9.3 Hz), 3.66 (1H, *dd*, *J* = 10.9, 5.7 Hz), 3.82 (3H, *s*), 4.03 (1H, *dd*, *J* = 12.5, 8.4 Hz), 6.75 (1H, *d, J* = 8.1 Hz), 6.79 (1H, *dd, J* = 8.1, 1.8 Hz) and 6.96 (1H, *d, J* = 1.8 Hz); **Table 26** and **Figure 95.**

^{13}C NMR: δ ppm, 125 MHz, in CD_3OD; 33.9, 45.2, 56.3, 65.0, 70.2, 71.1, 75.9, 109.2, 113.6, 115.1, 122.9, 126.8, 146.7, 147.8 and 175.0; **Table 26** and **Figure 96.**

6. Evaluation of Biological Activities

6.1 Determination of Cytotoxic Activity against SW620, CHAGO, HepG2, BT474 and KATO-III Cell Lines

Bioassay of cytotoxicity against human cell cultures *in vitro* was performed by the MTT [3-(4,5)-dimethylthiazol-2,5-diphenyltetrazolium bromide] colorimetric method (Carmichael *et al*., 1987; Twentyman and Luscombe, 1987). The isolated compounds from *S. verrucosa* and *F. foveolata* stems were evaluated for cytotoxicity against colon carcinoma (SW620), lung carcinoma (CHAGO), human hepatocarcinoma (HepG2), breast carcinoma (BT474) and gastric carcinoma (KATO-III) cell lines.

All cell lines were grown in Roswell Park Memorial Institute (RPMI) medium 1640 containing 5% foetal calf serum (FCS) and incubated at 37 °C in humidified atmosphere of 5%

CO_2. Exponentially growing cells were seeded in 96-well plates (200 μl/well at a density of 2.5×10^4 cells/ml). The cells were incubated in growth media for 24 h. The tested compounds at various concentrations were added (2 μl/well) and incubated for up to 72 h. At the end of this incubation period, 10 μl of MTT solution (5 mg/ml) were added and the plate was further incubated for 4h at 37 °C. After removal of the culture supernatants, 150 μl of DMSO and 25 μl of glycine buffer (pH 10.4) were added to each well sequentially in order to facilitate solubilization of the formazan product. The plate was shaken, and the absorbance was measured at 540 nm in a Synergy^{TM} Absorbance Microplate Reader (Bio-Tek). The percentage of cell survival was calculated as followed.

$$\% \text{ Cell survival} = [\text{OD test}/ \text{OD control}] \times 100$$

Whereas OD test and OD control are the absorbance from treated condition and untreated condition, respectively.

Dose response curves were plotted from 5 concentrations (μg/ml) of 10-fold serially diluted test compounds against their percentage of cell survival. The concentration of each compound tested that reduces the effect by 50 % was also calculated from these curves and reported as the median inhibitory concentration (IC_{50} value). The cytotoxicity of the compounds tested was compared with that of the anticancer antibiotic doxorubicin, which was used as the positive control.

6.2 Determination of Anti-*Mycobacterium tuberculosis* Activity

The bioassay was performed by using green fluorescent protein (GFP)-expressing *Mycobacterium tuberculosis* strain $H_{37}Ra$ (Changsen, Franzblau, and Palittapongarnpim, 2003). The mycobacteria were cultivated on 7H10 agar containing 30 μg/ml kanamycin at 37°C for 4 weeks or until growth was observed. Starter culture was prepared by fully looping 2-3 single colonies into 7H9 broth supplemented with 0.2% v/v glycerol, 0.1% w/v solution (BD Biosciences) and 30 μg/ml of kanamycin. The mixture was then incubated at 37°C in 200 rpm shaker incubator until the optical density (OD) at 550 nm was between 0.5 and 1.

For batch cultivation, the starter cultures were transferred at the rate of 1/10 volume to the 7H9 broth and incubated at 37°C in 200 rpm shaker incubator until the OD at 550 nm was approximately 0.5 to 1. Cells were pelleted, washed and suspended in PBS buffer, and then sonicated 8 times for 15 seconds each. Sonicated samples were then aliquoted and frozen at -80°C prior to use. Titer stocks were determined by colony forming unit (cfu) assay and the seeding density. For assay in 384-well format, the seeding was approximately 2×10^4 to 1×10^5 cfu/ml/well.

The assay was performed in duplicate. Each well contained 5 µl of test samples serially diluted in 5% DMSO, followed by 45 µl of cell suspension prepared as described above. Plates were incubated at 37°C for 7 days and fluorescence was measured at the excitation and emission wavelengths of 485 and 535 nm. Fluorescent signals on day zero were used as background to subtract from the signals on day 7. The percentage of growth inhibition is calculated from the mean of fluorescent unit of cells treated with sample (Fu_t) and untreated cells (Fu_c), as in the following equation:

$$\% \text{ Inhibition} = [1 - (Fu_t / Fu_c)] \times 100$$

The lowest concentration of the compound that inhibits cell growth by 90% is reported as the minimum inhibitory concentration (MIC). Streptomycin, isoniazid, ofloxacin and ethambutol are used as positive controls, and 0.5% DMSO is used as a negative control.

CHAPTER IV

RESULTS AND DISCUSSION

Chemical constituents of the *n*-hexane-acetone and EtOAc extracts of *S. verrucosa* stems and the *n*-hexane and CH_2Cl_2 extracts of *F. foveolata* stems were investigated. Chromatographic techniques were employed in order to isolate eight compounds (SV-1 to SV-8) from *S. verrucosa* and ten compounds (FF-1 to FF-10) from *F. foveolata* as described in Chapter III. Identification and structure elucidation of these compounds were achieved through spectroscopic techniques, including UV, IR, MS and NMR. Isolated compounds from both plants were examined for their biological activities, including cytotoxicity against five human cancer cell lines and anti-*Mycobacterium tuberculosis* activity.

1. Identification of Compound SV-1 and FF-1 (Friedelin)

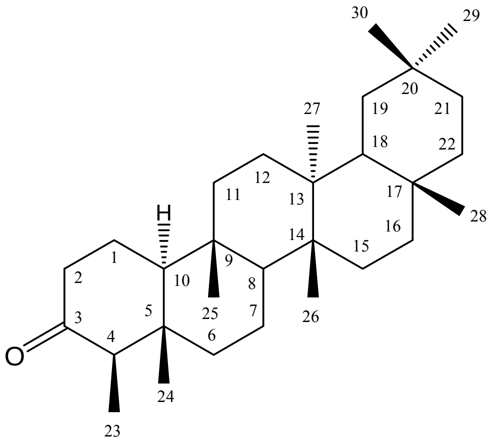
Compound SV-1, obtained as colorless needles (4.0 mg, 0.0003 % yield), appeared as a purple spot upon spraying with 10% sulfuric acid and heated. According to the $[M + H]^+$ peak at *m/z* 427 in the mass spectrum (**Figure 7**), its molecular formula could be identified as $C_{30}H_{50}O$. Its IR absorption bands at 1716, 1463 and 1390 cm^{-1} (**Figure 8**) indicated the presence of ketone, methylene and methyl groups in the molecule, respectively.

The ^{1}H-NMR spectrum of compound SV-1 (**Figure 9**) showed eight methyl signals including seven methyl singlets at δ 0.71 (H_3-24), 0.85 (H_3-25), 0.93 (H_3-30), 0.98 (H_3-26), 0.99 (H_3-29), 1.03 (H_3-27) and 1.15 ppm (H_3-28) and one methyl doublet at δ 0.86 ppm (J = 5.4 Hz, H_3-23). These methyl signals are characteristic of friedelane-type triterpenoid skeleton.

The ^{13}C-NMR spectrum of this compound (**Figure 10**) displayed 30 carbon signals, including those of eight methyl carbons at δ 6.8 (C-23), 14.7 (C-24), 17.9 (C-25), 18.6 (C-27), 20.3 (C-26), 31.8 (C-29), 32.1 (C-28) and 35.0 ppm (C-30), eleven methylene carbons at δ 18.3 (C-7), 22.3 (C-1), 30.5 (C-12), 32.5 (C-21), 32.8 (C-15), 35.4 (C-19), 35.7 (C-11), 36.0 (C-16), 39.3 (C-22), 41.3 (C-6) and 41.5 ppm (C-2), four methine carbons at δ 42.9 (C-18), 53.1 (C-8), 58.3 (C-4) and 59.5 ppm (C-10), six quaternary carbons at δ 28.2 (C-20), 30.0 (C-17), 37.5 (C-9), 38.3 (C-14), 39.7 (C-13), 42.2 (C-5) and one keto-carbonyl at δ 213.0 ppm (C-3).

Comparison of the NMR data of compound SV-1 with previous reports (Gunatilaka *et al.*, 1983b; Klass and Tinto, 1992) (**Table 9**) led to the identification of this compound as friedelin, which is one of the most common friedelane-type triterpenes. The compound is widely distributed in higher plants and can be frequently found in members of the family Celastraceae, for example, in the inner bark of *Kokoona zeylanica* (Gunatilaka et al., 1982), in the stems of *Maytenus diversifolia* (Nozaki *et al.*, 1986), in the stem bark of *M. macrocarpa* (Chavez *et al.*, 1998), in the roots of *M. obtusifolia* (Silva *et al.*, 2008) and in the fruits of *M. salicifolia* (Valladao *et al.*, 2010). Furthermore, this triterpenoid has also been reported as a constituent of *Salacia beddomei* (Hisham *et al.*, 1996b), *S. elliptica* (Duarte *et al.*, 2009) and *S. verrucosa* (Jangruang *et al.*, 2009).

Compound FF-1, obtained as colorless needles (24.5 mg, 0.0013% yield), appeared as a purple spot on TLC upon spraying with 10% sulfuric acid and heated. The mass spectrum (**Figure 44**) showed $[M + Na]^+$ peak at *m/z* 449, suggesting the molecular formula $C_{30}H_{50}O$. IR and NMR spectral data of compound FF-1 (**Figures 45-47**) are similar to those of compound SV-1. Therefore, this compound was determined as friedelin.



Friedelin

Friedelin has been reported to possess various biological activities such as cytotoxic (Zheng, 1994), antifungal (Duraipandiyan, Gnanasekar, and Ignacimuthu, 2010), anti-inflammatory, analgesic and antipyretic activities (Antonisamy, Duraipandiyan, and Ignacimuthu, 2011).

Table 9. ^{1}H- and ^{13}C-NMR spectral data for compound SV-1 and friedelin (300 and 75 MHz, in $CDCl_3$).

Position	SV-1		Friedelin*	
	δ_C	δ_H	δ_C	δ_H
1	22.3	-	22.3	-
2	41.5	-	41.5	-
3	213.0	-	213.0	-
4	58.3	-	58.2	-
5	42.2	-	42.1	-
6	41.3	-	41.3	-
7	18.3	-	18.2	-
8	53.1	-	53.1	-
9	37.5	-	37.4	-
10	59.5	-	59.5	-
11	35.7	-	35.6	-
12	30.5	-	30.5	-
13	39.7	-	39.7	-
14	38.3	-	38.3	-
15	32.8	-	32.8	-
16	36.0	-	36.0	-
17	30.0	-	30.0	-
18	42.9	-	42.8	-
19	35.4	-	35.3	-
20	28.2	-	28.1	-
21	32.5	-	32.4	-
22	39.3	-	39.2	-
23	6.8	0.86 (3H, *d*, J = 5.4 Hz)	6.8	0.87 (3H, *d*)
24	14.7	0.71 (3H, *s*)	14.7	0.71 (3H, *s*)
25	17.9	0.85 (3H, *s*)	17.9	0.86 (3H, *s*)
26	20.3	0.98 (3H, *s*)	20.3	1.00 (3H, *s*)
27	18.6	1.03 (3H, *s*)	18.7	1.05 (3H, *s*)
28	32.1	1.15 (3H, *s*)	32.1	1.17 (3H, *s*)
29	31.8	0.99 (3H, *s*)	31.8	1.00 (3H, *s*)
30	35.0	0.93 (3H, *s*)	35.0	0.95 (3H, *s*)

*Gunatilaka *et al*., 1983b and Klass and Tinto, 1992

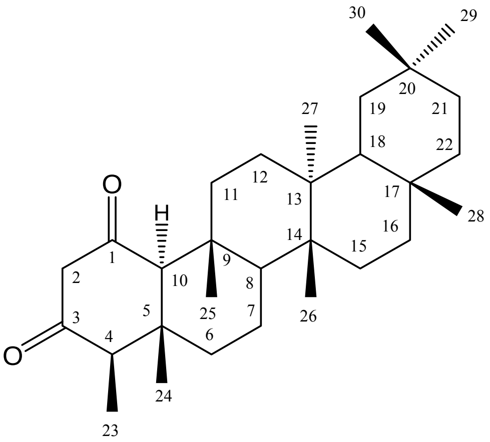
2. Identification of Compound SV-2 (Friedelane-1,3-dione)

Compound SV-2, obtained as colorless needles (25.5 mg, 0.002 % yield), appeared as a yellow spot upon spraying with 10% sulfuric acid and heated. According to its $[M + 4H + Na]^+$peak at *m/z* 467 in the mass spectrum (**Figure 11**), the molecular formula was determined as $C_{30}H_{48}O_2$. The IR spectrum (**Figure 12**) showed absorption bands at 1732 and 1705 cm^{-1}, indicating the presence of keto carbonyls in the molecule.

The ^{1}H-NMR spectrum of compound SV-2 (**Figure 13**) showed eight methyl signals, which could be categorized into seven methyl singlets at δ 0.67 (H_3-24), 0.93 (H_3-30), 0.98 (H_3-29), 1.00 (H_3-27), 1.01 (H_3-26), 1.16 (H_3-28) and 1.18 ppm (H_3-25) and one methyl doublet at δ 1.03 ppm (*J* = 8.4 Hz, H_3-23). Based on the evidence of both methyl signals and a methine quartet at δ 2.56 ppm (*J* = 6.6 Hz, H-4), the compound could be identified as a friedelane-type triterpene (Gunatilaka *et al.*, 1982). In addition, two methylene doublets at δ 3.22 and 3.44 ppm (each 1H, *J* = 15.9 Hz, H_2-2) and a methine singlet at δ 2.36 ppm (H-10) were also characteristic of a 1,3-diketotriterpene (Klass and Tinto, 1992).

Thirty carbon signals could be observed in the ^{13}C-NMR spectrum of this compound (**Figure 14**), supporting its identification as a triterpenoid. These signals represent eight methyl carbons at δ 7.3 (C-23), 16.0 (C-24), 18.0 (C-25), 18.8 (C-27), 20.4 (C-26), 31.8 (C-29), 32.1 (C-28) and 35.0 ppm (C-30), ten methylene carbons at δ 18.1 (C-7), 30.2 (C-12), 32.5 (C-15), 32.8 (C-21), 34.6 (C-11), 35.3 (C-19), 36.0 (C-16), 39.3 (C-22), 40.7 (C-6) and 60.7 ppm (C-2), four methine carbons at δ 42.8 (C-18), 52.2 (C-8), 59.1 (C-4) and 72.0 ppm (C-10), six quaternary carbons at δ 28.2 (C-20), 30.0 (C-17), 37.3 (C-9), 37.9 (C-5), 38.3 (C-14), 39.6 (C-13), and two keto-carbonyl carbons at δ 202.8 (C-1) and 204.1 ppm (C-3). Both downfield methine carbon resonances at δ 59.1 (C-4) and 72.0 (C-10) were suggestive of their positions adjacent to two keto carbonyls in ring A of a friedelane-type triterpene.

NMR data of compound SV-2 are identical to those of friedelane-1,3-dione (Klass and Tinto, 1992), as shown in **Table 10**. This triterpenoids has been isolated from a Guyanese medicinal plant, *Peritassa compta* (Klass and Tinto, 1992), and from members of the genus *Salacia* such as *S. beddomei* (Hisham *et al.*, 1996b), *S. chinensis* (Kishi *et al.*, 2003) and *S. campestris* (Paulo *et al.*, 2005). It was also found as the major constituent of *S. verrucosa* (Jangruang *et al.*, 2009).



Friedelane-1,3-dione

Table 10. ^{1}H- and ^{13}C-NMR spectral data for compound SV-2 and friedelane-1,3-dione (300 and 75 MHz, in $CDCl_3$).

Position	SV-2		Friedelane-1,3-dione*	
	δ_C	δ_H	δ_C	δ_H
1	202.8	-	202.8	-
2	60.7	3.22 (1H, *d*, *J* = 15.9 Hz) 3.44 (1H, *d*, *J* = 15.9 Hz)	60.7	3.24, 3.46
3	204.1	-	204.2	-
4	59.1	2.56 (1H, *q*, *J* = 6.6 Hz)	59.1	2.58
5	37.9	-	37.9	-
6	40.7	1.38 (1H, *m*), 1.88 (1H, *m*)	40.7	1.39, 1.90
7	18.1	-	18.1	-
8	52.2	-	52.2	-
9	37.3	-	37.2	-
10	72.0	2.36 (1H, *s*)	71.9	2.38
11	34.6	1.13 (1H, *m*), 2.13 (1H, *m*)	34.6	1.14, 2.15
12	30.2	-	30.2	-
13	39.6	-	39.5	-
14	38.3	-	38.3	-
15	32.5	-	32.4	-

Position	SV-2		Friedelane-1,3-dione*	
	δ_C	δ_H	δ_C	δ_H
16	36.0	-	35.9	-
17	30.0	-	30.0	-
18	42.8	-	42.7	-
19	35.3	-	35.3	-
20	28.2	-	28.2	-
21	32.8	-	32.8	-
22	39.3	-	39.3	-
23	7.3	1.03 (3H, *d*, J = 8.4 Hz)	7.3	1.05 (3H, *d*)
24	16.0	0.67 (3H, *s*)	16.0	0.69 (3H, *s*)
25	18.0	1.18 (3H, *s*)	18.0	1.20 (3H, *s*)
26	20.4	1.01 (3H, *s*)	20.3	1.03 (3H, *s*)
27	18.8	1.00 (3H, *s*)	18.8	1.02 (3H, *s*)
28	32.1	1.16 (3H, *s*)	32.1	1.18 (3H, *s*)
29	31.8	0.98 (3H, *s*)	31.8	1.00 (3H, *s*)
30	35.0	0.93 (3H, *s*)	35.0	0.94 (3H, *s*)

* Klass and Tinto, 1992

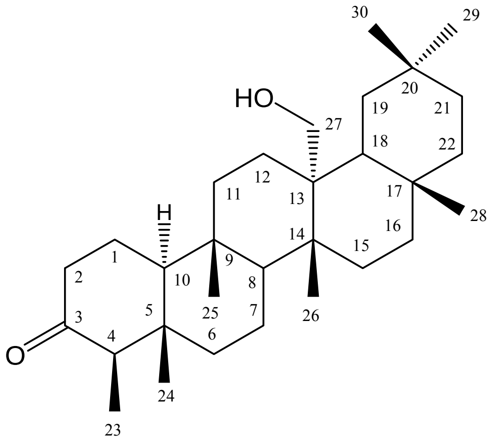
3. Identification of Compound SV-3 (Kokoonol)

Compound SV-3, which was obtained as an amorphous powder (7.4 mg, 0.0006 % yield) after recrystallization, gave a purple spot upon spraying with 10% sulfuric acid and heated. The ESI-MS spectrum (**Figure 15**) showed a quasi-molecular $[M + H]^+$ ion peak at *m/z* 443, suggesting the molecular formula $C_{30}H_{50}O_2$. Its IR spectrum (**Figure 16**) displayed absorption bands at 3543 and 1706 cm^{-1} corresponding to hydroxyl and carbonyl groups, respectively.

The ^{1}H-NMR spectrum (**Figure 17**) showed six methyl singlets at δ 0.71 (H_3-24), 0.93 (H_3-25), 0.95 (H_3-29), 1.03 (H_3-30), 1.07 (H_3-26) and 1.23 ppm (H_3-28) and one methyl doublet at δ 0.86 ppm (J = 6.3 Hz, H_3-23) of a friedelane triterpenoid. Two pairs of methylene protons resonated at δ 1.67 and 1.95 ppm (H_2-1) and at δ 2.29 and 2.36 ppm (H_2-2), whereas a pair of oxygenated methylene signals appeared at δ 4.01 and 4.11 ppm (J = 11.6 Hz, H_2-27). In addition, a methine quartet at δ 2.20 ppm (J = 6.3 Hz) could be assigned as H-4. Therefore, this compound could be a friedelane-type triterpene in which one methyl group has been replaced by a hydroxymethylene moiety.

The ^{13}C-NMR spectrum of this compound (**Figure 18**) displayed 30 carbon signals from seven methyl carbons at δ 7.3 (C-23), 14.9 (C-24), 18.1 (C-25), 22.5 (C-26), 31.0 (C-30), 33.0 (C-28) and 35.9 ppm (C-29), twelve methylene carbons at δ 21.0 (C-7), 22.7 (C-1), 24.4 (C-12), 32.4 (C-15), 33.3 (C-21), 36.4 (C-16), 37.4 (C-19), 37.9 (C-11), 39.5 (C-22), 41.9 (C-2), 42.8 (C-6) and 64.7 ppm (C-27), four methine carbons at δ 43.9 (C-18), 53.4 (C-8), 58.5 (C-4) and 60.3 ppm (C-10), six quaternary carbons at δ 28.7 (C-20), 30.8 (C-17), 37.9 (C-9), 38.6 (C-14), 42.6 (C-5) and 45.7 ppm (C-13) and one keto-carbonyl carbon at δ 213.4 ppm (C-3). These ^{13}C-NMR data are similar to those of friedelin; the major differences are the downfield shift of the C-13 signal and a methyl signal of friedelin has been replaced by an oxygenated methylene one. Thus, these data help identify compound SV-3 as the 27-hydroxy derivative of friedelin, named kokoonol (27-hydroxyfriedelan-3-one).

Comparison of the NMR data of compound SV-3 and kokoonol isolated from the stem bark of a flacourtiaceous plant, *Caloncoba glauca* (Giner *et al*., 1993) is shown in **Table 11.** Kokoonol was first reported as a constituent of *Kokoona zeylanica* (Gunatilaka *et al*., 1983a) and, later, was also found in *Salacia chinensis* stems (Morikawa *et al*., 2003); both plants belong to major genera of the family Celastraceae, of which various friedelane-type triterpenes were found.



Kokoonol

Table 11. ^{1}H- and ^{13}C-NMR spectral data for compound SV-3 and kokoonol (300 and 75 MHz, in $CDCl_3$).

Position	SV-3		Kokoonol*	
	δ_C	δ_H	δ_C	δ_H
1	22.7	1.67 (1H, *m*) 1.95 (1H, *m*)	22.5	1.69 (1H, *ddd*, *J* = 12.8, 5.1, 5.1 Hz) 1.97 (1H, *m*)
2	41.9	2.29 (1H, *m*) 2.36 (1H, *m*)	41.6	2.24 (1H, *ddd*, *J* = 13.7, 13.7, 7.3 Hz) 2.40 (1H, *ddd, J* = 13.7, 5.1, 2.1 Hz)
3	213.4	-	213.3	-
4	58.5	2.20 (1H, *q*, *J* = 6.3 Hz)	58.4	2.23 (1H, *q*, *J* = 6.4 Hz)
5	42.6	-	42.3	-
6	42.8	-	41.5	1.35 (1H, *m*), 1.75 (1H, *m*)
7	21.0	-	18.6	-
8	53.4	-	53.8	-
9	37.9	-	37.6	-
10	60.3	-	59.7	1.48 (1H, *m*)
11	37.9	-	37.8	-
12	24.4	-	24.1	-
13	45.7	-	45.4	-
14	38.6	-	38.4	-
15	32.4	-	32.2	-
16	36.4	-	36.3	-
17	30.8	-	30.3	-
18	43.9	-	43.3	-
19	37.4	-	37.1	-
20	28.7	-	28.5	-
21	33.3	-	32.6	-
22	39.5	-	40.1	-
23	7.2	0.86 (3H, *d*, *J* = 6.3 Hz)	7.1	0.89 (3H, *d*, *J* = 6.6 Hz)
24	14.9	0.71 (3H, *s*)	14.9	0.74 (3H, *s*)
25	18.1	0.93 (3H, *s*)	18.2	0.93 (3H, *s*)
26	22.5	1.07 (3H, *s*)	22.3	1.12 (3H, *s*)
27	64.7	4.01 (1H, *d*, *J* = 11.6 Hz) 4.11 (1H, *d*, *J* = 11.6 Hz)	63.4	4.02 (1H, *br d*) 4.06 (1H, *d, J* = 11.5 Hz)
28	33.0	1.23 (3H, *s*)	32.8	1.24 (3H, *s*)
29	35.9	0.95 (3H, *s*)	35.8	0.98 (3H, *s*)
30	31.0	1.03 (3H, *s*)	30.6	1.01 (3H, *s*)

*Giner *et al.*, 1993

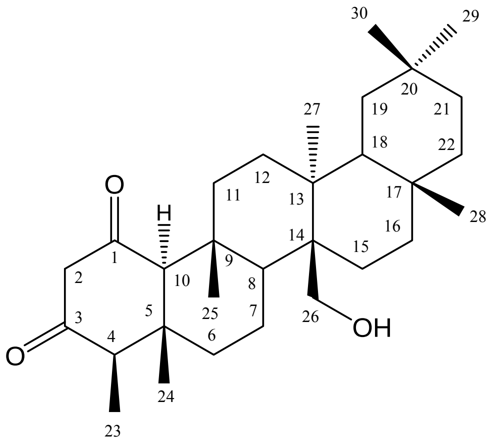
4. Identification of Compound SV-4 (26-Hydroxyfriedelane-1,3-dione)

Compound SV-4, obtained as a white, amorphous powder (7.4 mg, 0.0006 % yield), appeared as a purple spot upon spraying with 10% sulfuric acid and heated. According to quasi-molecular $[M + H]^+$ ion peak at *m/z* 457 in the mass spectrum (**Figure 19**), its molecular formula was calculated as $C_{30}H_{48}O_3$. The absorption band at 3575 $cm^{-1}$of its IR spectrum (**Figure 20**) showed that the compound contains hydroxyl group, in addition to absorption bands at 1728 and 1703 cm^{-1} that indicated the presence of diketone group in the molecule.

The ^{1}H-NMR spectrum of compound SV-4 (**Figure 21**) showed several prominent signals, including six methyl singlets at δ 0.68 (H_3-24), 0.92 (H_3-29), 0.95 (H_3-30), 1.04 (H_3-27), 1.12 (H_3-28) and 1.36 ppm (H_3-25), one methyl doublet at δ 1.02 ppm (J = 6.8 Hz, H_3-23), two methylene doublets of a 1,3-diketone at δ 3.23 and 3.44 ppm (each 1H, J = 15.9 Hz, H_2-2), two oxymethylene doublets at δ 4.04 and 4.14 ppm (each 1H, J = 11.6 Hz, H_2-26), one methine singlet at δ 2.38 ppm (H-10) and a methine quartet at δ 2.54 ppm (J = 6.8 Hz, H-4). According to chemical shifts and splitting patterns of these protons, compound SV-4 was determined as a derivative of friedelane-1,3-dione with one additional hydroxyl group.

The ^{13}C-NMR spectrum (**Figure 22**) displayed 30 carbon signals, including those of seven methyl carbons at δ 7.7 (C-23), 16.1 (C-24), 18.2 (C-25), 20.1 (C-27), 32.1 (C-28), 32.4 (C-30) and 34.9 ppm (C-29), eleven methylene carbons at δ 20.8 (C-7), 24.5 (C-15), 30.3 (C-12), 33.3 (C-21), 35.4 (C-11), 35.8 (C-16), 35.9 (C-19), 39.5 (C-22), 42.2 (C-6), 61.0 (C-2) and 64.4 ppm (C-26), four methine carbons at δ 43.9 (C-18), 52.5 (C-8), 59.3 (C-4) and 72.8 ppm (C-10), six quaternary carbons at δ 28.7 (C-20), 30.8 (C-17), 37.6 (C-9), 38.5 (C-5), 40.1 (C-13) and 42.5 ppm (C-14), and two keto-carbonyl carbons at δ 203.2 (C-1) and 204.5 ppm (C-3). Its 1,3-diketone skeleton was supported by the chemical shifts of C-1, C-3, C-4 and C-10. Compound SV-4 possesses one more methylene carbon (attached to an oxygen) and one less methyl carbon than friedelane-1,3-dione. When the ^{13}C-NMR data of both compounds were compared, the more downfield shift of C-14 of this compound could clearly be observed, suggestting that there was a hydroxyl substituent at C-26. Comparison of its NMR data with those of 26-hydroxyfriedelane-1,3-dione (Matsuda *et al.*, 1999) (**Table 12**) confirmed this. Therefore, compound SV-4 was identified as 26-hydroxyfriedelane-1,3-dione.

26-Hydroxyfriedelane-1,3-dione has been reported as a constituent of plants in the genus *Salacia* such as *S. oblonga* (Matsuda *et al*., 1999), *S. reticulata* (Yoshikawa *et al*., 2002) and *S. verrucosa* (Jangruang *et al*., 2009). The compound, isolated from the roots of *S. oblonga*, weakly inhibited rat lens aldose reductase, a key enzyme in the development of eye and nerve damage in diabetic patients (Matsuda *et al*., 1999).



26-Hydroxyfriedelane-1,3-dione

Table 12. ^{1}H- and ^{13}C-NMR spectral data for compound SV-4 and 26-hydroxyfriedelane-1,3-dione (300 and 75 MHz, in $CDCl_3$).

Position	SV-4		26-Hydroxyfriedelane-1,3-dione*	
	δ_C	δ_H	δ_C	δ_H
1	203.2	-	202.8	-
2	61.0	3.23 (1H, *d*, *J* = 15.9 Hz) 3.44 (1H, *d*, *J* = 15.9 Hz)	60.6	3.23 (1H, *d*, *J* = 15.9 Hz) 3.44 (1H, *d*, *J* = 15.9 Hz)
3	204.5	-	204.1	-
4	59.3	2.54 (1H, *q*, *J* = 6.8 Hz)	58.9	2.54 (1H, *q*, *J* = 6.5 Hz)
5	38.5	-	38.1	-
6	42.2	1.21 (1H, *m*), 1.85 (1H, *m*)	41.7	1.20, 1.85
7	20.8	1.63 (1H, *m*), 1.83 (1H, *m*)	20.4	1.60, 1.80
8	52.5	-	52.0	1.35

Position	SV-4		26-Hydroxyfriedelane-1,3-dione*	
	δ_C	δ_H	δ_C	δ_H
9	37.6	-	37.1	-
10	72.8	2.38 (1H, *s*)	72.4	2.38 (1H, *s*)
11	35.4	1.68 (1H, *m*), 2.19 (1H, *m*)	35.0	1.65, 2.16
12	30.3	-	29.9	1.10, 1.30
13	40.1	-	39.7	-
14	42.5	-	42.0	-
15	24.5	1.16 (1H, *m*), 2.09 (1H, *m*)	24.1	1.15, 2.10
16	35.8	-	35.3	1.65
17	30.8	-	30.4	-
18	43.9	1.47	43.5	1.46
19	35.9	-	35.4	1.65
20	28.7	-	28.3	-
21	33.3	-	32.9	0.95, 1.35
22	39.5	-	39.1	0.90, 1.50
23	7.7	1.02 (3H, *d*, *J* = 6.8 Hz)	7.3	1.00 (3H, *d*, *J* = 6.5 Hz)
24	16.1	0.68 (3H, *s*)	15.7	0.67 (3H, *s*)
25	18.2	1.36 (3H, *s*)	17.8	1.35 (3H, *s*)
26	64.4	4.04 (1H, *d*, *J* = 11.6 Hz) 4.14 (1H, *d*, *J* = 11.6 Hz)	64.0	4.03 (1H, *d*, *J* = 11.5 Hz) 4.13 (1H, *d*, *J* = 11.5 Hz)
27	20.1	1.04 (3H, *s*)	19.7	1.03 (3H, *s*)
28	32.1	1.12 (3H, *s*)	31.7	1.11 (3H, *s*)
29	34.9	0.92 (3H, *s*)	34.5	0.91 (3H, *s*)
30	32.4	0.95 (3H, *s*)	32.0	0.94 (3H, *s*)

*Matsuda *et al*., 1999

5. Identification of Compound SV-5 (21α-Hydroxyfriedelan-3-one)

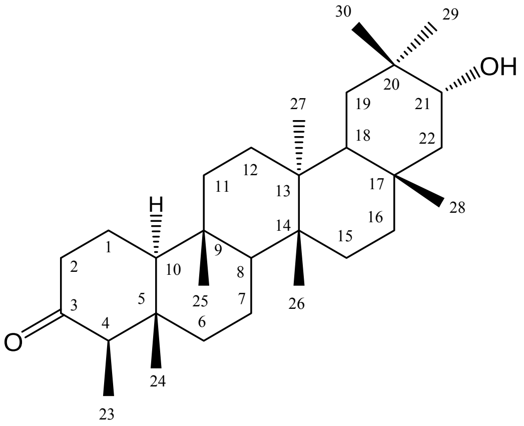
Compound SV-5, obtained as colorless cubic crystals (2.3 mg, 0.0002 % yield), appeared as a purple spot upon spraying with 10% sulfuric acid and heated. Its ESI-MS spectrum (**Figure 23**) presented a quasi-molecular $[M + H]^+$ ion peak at *m/z* 443, suggesting that the compound was an isomer of kokoonol, with the same molecular formula of $C_{30}H_{50}O_2$. The IR spectrum (**Figure

24) showed absorption bands of hydroxyl and carbonyl groups at 3429 and 1714 cm^{-1}, respectively.

The ^1H-NMR spectrum of compound SV-5 (**Figure 25**) showed seven methyl singlets at δ 0.70 (H_3-24), 0.85 (H_3-25), 0.89 (H_3-26), 0.97 (H_3-30), 1.05 (H_3-29), 1.09 (H_3-27) and 1.17 ppm (H_3-28), and one methyl doublet at δ 0.85 ppm (J = 6.8 Hz, H_3-23) of a friedelane skeleton. Similar to kokoonol, the methylene multiplets at δ 2.30 and 2.38 ppm (1H each) could be characterized as those of H_2-2. Similarly, a one-proton quartet at δ 2.24 ppm (J = 6.8 Hz) could be assigned to the methine H-4, while a doublet of doublets at δ 3.68 ppm (J = 12.0, 4.2 Hz) suggested the presence of an oxymethine proton in this triterpenoid molecule.

Thirty signals could be observed in its ^{13}C-NMR spectrum (**Figure 26**), including those of eight methyl carbons at δ 7.2 (C-23), 15.1 (C-24), 18.2 (C-26), 18.7 (C-25), 19.7 (C-27), 25.3 (C-30), 32.3 (C-29) and 33.6 ppm (C-28), ten methylene carbons at δ 18.6 (C-7), 22.7 (C-1), 30.6 (C-15), 30.9 (C-12), 35.7 (C-11), 36.4 (C-16), 36.5 (C-19), 41.7 (C-2), 41.9 (C-6) and 47.5 ppm (C-22), five methine carbons at δ 44.7 (C-18), 52.0 (C-8), 58.6 (C-4), 59.9 (C-10) and 74.7 ppm (C-21), six quaternary carbons at δ 32.9 (C-17), 34.8 (C-20), 37.9 (C-9), 39.2 (C-14), 39.5 (C-13) and 42.5 ppm (C-5) and one keto-carbonyl carbon at δ 213.0 ppm (C-3). Compared with the ^{13}C-NMR data of friedelin, this triterpene exhibited one less methylene signals while one additional oxymethine signal was observed at δ 74.7 ppm. The signals of C-20 quaternary carbon and C-22 methylene carbon were both significantly shifted downfield. These data indicated the position of the oxymethine carbon as at C-21.

The ^1H-NMR data of compound SV-5 were compared with those of 21α-hydroxyfriedelan-3-one isolated from the inner bark of *Kokoona zeylanica* (Gunatilaka *et al.,* 1982), while its ^{13}C-NMR data were compared with those of 6β,21α-dihydroxy-3-friedelanone, a structurally related friedelane-type triterpene from *Lepidobotrys staudtii* (Tane *et al*., 1996) (**Table 13**). The structure of compound SV-5 was thus confirmed as 21α-hydroxyfriedelan-3-one. The triterpene is a significant chemotaxonomic marker of plants in the family Celastraceae. In the genus *Salacia*, it has been reported from *S. reticulata* stem bark (Kumar *et al*., 1990) and was also shown to exhibit antiprotozoal activity against *Giardia intestinalis* with an IC_{50} value of 19.8 μM (Mena-Rejon *et al*., 2007).



21α-Hydroxyfriedelan-3-one

Table 13. ^{1}H- and ^{13}C-NMR spectral data for compound SV-5 and 6β,21α-dihydroxy-3-friedelanone (300 and 75 MHz, in $CDCl_3$).

Position	SV-5		6β,21α-Dihydroxy-3-friedelanone*	
	δ_C	δ_H	δ_C	δ_H
1	22.7	1.95 (1H, *m*)	21.9	1.76 (1H, *m*), 2.00 (1H, *m*)
2	41.7	2.30 (1H, *m*) 2.38 (1H, *m*)	41.2	2.27 (1H, *dd*, *J* = 13.2 Hz) 2.39 (1H, *m*)
3	213.0	-	212.5	-
4	58.6	2.24 (1H, *q*, *J* = 6.8 Hz)	58.3	2.41 (1H, *q*, J = 6.7 Hz)
5	42.5	-	47.6	-
6	41.9	-	79.4	3.66 (1H, *dd*, *J* = 10.7, 4.7 Hz)
7	18.6	-	29.3	-
8	52.0	-	48.3	-
9	37.9	-	37.5	-
10	59.9	-	58.5	1.50 (1H, *m*)
11	35.7	-	35.2	-
12	30.9	-	30.1	-
13	39.5	-	39.1	-
14	39.2	-	38.6	-
15	30.6	-	30.4	-
16	36.4	-	36.0	-
17	32.9	-	32.5	-

Position	SV-5		6β,21α-Dihydroxy-3-friedelanone*	
	δ_C	δ_H	δ_C	δ_H
18	44.7	-	44.3	1.58 (1H, *m*)
19	36.5	-	36.0	-
20	34.8	-	34.4	-
21	74.7	3.68 (1H, *dd*, *J* = 12.0, 4.2 Hz)	74.3	3.69 (1H, *m*)
22	47.5	-	47.0	-
23	7.2	0.85 (3H, *d*, *J* = 6.8 Hz)	10.4	1.11 (3H, *d*, *J* = 6.7 Hz)
24	15.1	0.70 (3H, *s*)	9.1	0.75 (3H, *s*)
25	18.7	0.85 (3H, *s*)	17.8	0.86 (3H, *s*)
26	18.2	0.89 (3H, *s*)	17.7	0.90 (3H, *s*)
27	19.7	1.09 (3H, *s*)	19.2	1.10 (3H, *s*)
28	33.6	1.17 (3H, *s*)	33.1	1.19 (3H, *s*)
29	32.3	1.05 (3H, *s*)	31.9	1.06 (3H, *s*)
30	25.3	0.97 (3H, *s*)	24.9	0.98 (3H, *s*)

*Tane *et al*., 1996

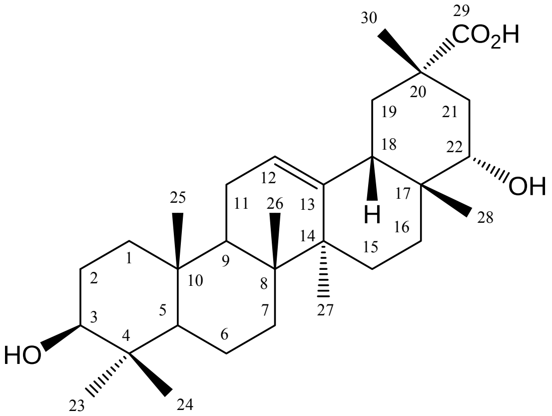
6. Identification of Compound SV-6 (3β,22α-Dihydroxyolean-12-en-29-oic acid)

Compound SV-6 was obtained as colorless prisms (6.2 mg, 0.0005 % yield) which gave a purple spot upon spraying with 10% sulfuric acid and heated. The mass spectrum (**Figure 27**) showed a prominent fragment ion peak at *m/z* 429 $[M + H - COO]^+$, suggesting its molecular formula as $C_{30}H_{48}O_4$. The IR spectrum (**Figure 28**) showed absorption bands at 3491, 1749 and 1650 cm^{-1}, representing hydroxyl, carboxylic and olefinic groups in the molecule, respectively.

The ^{1}H-NMR spectrum of this compound (**Figure 29**) showed seven methyl singlets at δ 0.77 (H_3-24), 0.85 (H_3-28), 0.91 (H_3-26), 0.92 (H_3-25), 0.97 (H_3-23), 1.05 (H_3-27) and 1.19 ppm (H_3-30). The H_2-19 methylene protons resonated separately as a multiplet at δ 1.88 (1H, H-19_b) and a doublet at δ 2.24 ppm (1H, *J* = 12.0 Hz, H-19_a). Three doublets of doublets at δ 0.72 (1H, *J* = 11.5, 1.5 Hz), 1.50 (1H, *J* = 13.0, 8.0 Hz) and 2.11 ppm (1H, *J* = 12.0, 8.5 Hz) could be assigned to the methine H-5, H-9 and H-18, respectively. Two oxymethine protons gave a double doublets at δ 3.20 (1H, *J* = 11.5, 4.5 Hz, H-3) and a doublet at δ 4.13 ppm (1H, *J* = 5.5 Hz, H-22). In addition, an olefinic proton resonated as the most downfield doublet of doublets at δ 5.28 ppm (1H, *J* = 3.5, 2.5 Hz, H-12). Based on these data, compound SV-6 was deduced to be different from the previously identified triterpenoids and that its basic skeleton should be the oleanane-type triterpene with one double bond and two hydroxyl substitutions.

Its ^{13}C-NMR spectrum (**Figure 30**), with the aid of DEPT and HSQC experiments, showed 30 carbon signals from seven tertiary methyls at δ 15.6 (C-24 and C-25), 17.0 (C-26), 21.0 (C-30), 24.0 (C-27), 25.0 (C-28) and 28.1 ppm (C-23), nine methylenes at δ 18.3 (C-6), 23.5 (C-11), 24.3 (C-15), 25.2 (C-16), 27.2 (C-2), 33.1 (C-7), 33.8 (C-19), 38.6 (C-1) and 39.8 ppm (C-21), three methines at δ 43.4 (C-18), 47.5 (C-9) and 55.2 ppm (C-5), two oxymethines at δ 78.9 (C-3) and 83.1 ppm (C-22), one olefinic methine at δ 124.6 ppm (C-12), six quaternary carbons at δ 35.2 (C-17), 37.0 (C-10), 38.7 (C-4), 39.3 (C-8), 39.5 (C-20) and 42.5 ppm (C-14), one olefinic quaternary carbon at δ 140.2 ppm (C-13) and one carboxylic carbon at δ 182.4 ppm (C-29). The last signal suggested that the compound was the acid derivative of an oleanane-type triterpene. HMBC correlations (**Figures 31a-31c**, **Table 14**) observed between the signal of H-3 and those of C-1, C-2, C-23 and C-24, as well as between H-22 resonance and those of C-16, C-18, C-20 and C-28, indicated that these oxymethine protons located at C-3 and C-22, respectively. The correlations observed between H-12 resonance and those of C-9, C-11, C-14 and C-18 supported the assignment of one double bond between C-12 and C-13. Finally, one carboxylic group was located at C-29 according to correlations between the signal of H_3-30 and those of C-19, C-20 and C-29. NOE correlations, observed in the NOESY spectrum (**Figure 32**) between the α-oriented H_3-23 and H-3 as well as the β-oriented H_3-28 and H-22, indicated the β- and α-orientation of the hydroxyl groups at C-3 and C-22, respectively. Therefore, compound SV-6 was identified as 3β,22α-dihydroxyolean-12-en-29-oic acid. This compound has been given two trivial names. It was firstly reported as an antileukemic constituent of *Maytenus diversifolia* named maytenfolic acid (Nozaki *et al*., 1982, 1986). It was later found in the woody part of the roots and in the cell culture of *Tripterygium wilfordii* and shown to be anti-inflammatory. The compound was also given another trivial name as triptotriterpenic acid A (Kutney *et al*., 1992, 1993).

Maytenfolic acid (triptotriterpenic acid A) is widely distributed in plants of the family Celastraceae such as *Salacia oblonga* (Matsuda *et al*., 1999), *S. chinensis* (Morikawa *et al*., 2003), *Maytenus laevis* (Nakagawa *et al*., 2004) and *Celastrus hypoleucus* (Wang *et al*., 2005). The triterpenoid exhibited various biological activities including inhibitory effect against rat lens aldose reductase with an IC_{50} value of 72 μM (Morikawa *et al.*, 2003), cytokine-inducing activity on human peripheral blood mononuclear cells (PBMCs) (Nakagawa *et al.*, 2004) and significant activity against HIV replication in H9 lymphocyte cells with an EC_{50} value of 5.65 μg/ml (Wu *et al.*, 2004).



3β,22α-Dihydroxyolean-12-en-29-oic acid

Table 14. ^{1}H- and ^{13}C-NMR spectral data for 3β,22α-dihydroxyolean-12-en-29-oic acid (500 and 125 MHz, in $CDCl_3$).

Position	δ_C	δ_H	HMBC (H→C)
1	38.6	0.96 (1H, *m*) 1.59 (1H, *m*)	2, 5 2, 3, 5, 9, 10
2	27.2	0.96 (1H, *m*) 1.58 (1H , *m*)	 3, 4, 10
3	78.9	3.20 (1H, *dd*, *J* = 11.5, 4.5 Hz)	1, 2, 23, 24
4	38.7	-	
5	55.2	0.72 (1H, *dd*, *J* = 11.5, 1.5 Hz)	4, 6, 7, 10, 23, 24, 25
6	18.3	1.35 (1H, *m*) 1.53 (1H, *m*)	5, 7, 10 5, 10
7	33.1	1.36 (1H, *ddd*, *J* = 12.5, 5.0, 3.0 Hz) 1.46 (1H, *m*)	5, 6, 8, 9, 26 8, 14
8	39.3	-	

Position	δ_C	δ_H	HMBC (H→C)
9	47.5	1.50 (1H, *dd*, *J* = 13.0, 8.0 Hz)	8, 10, 11, 14, 25, 26
10	37.0	-	
11	23.5	1.85 (2H, *m*)	8, 9, 12, 13
12	124.6	5.28 (1H, *dd*, *J* = 3.5, 2.5 Hz)	9, 11, 14, 18
13	140.2	-	
14	42.5	-	
15	24.3	1.08 (1H, *m*) 1.68 (1H, *ddd*, *J* = 14.0, 10.5, 3.5 Hz)	13, 14, 27 8, 13, 14, 16, 27
16	25.2	1.16 (1H, *m*) 1.87 (1H, *m*)	 14, 15, 17, 18, 28
17	35.2	-	
18	43.4	2.11 (1H, *dd*, *J* = 12.0, 8.5 Hz)	12, 13, 14, 17, 28
19	33.8	1.88 (1H, *m*) 2.24 (1H, *d, J* = 12.0 Hz)	13, 17, 29, 30 13, 17, 18, 20, 21, 29, 30
20	39.5	-	
21	39.8	1.46 (1H, *m*) 1.88 (1H, *m*)	17, 20, 29, 30 17, 20, 22, 29, 30
22	83.1	4.13 (1H, *d*, *J* = 5.5 Hz)	16, 18, 20, 28
23	28.1	0.97 (3H, *s*)	3, 4, 5, 24
24	15.6	0.77 (3H, *s*)	3, 4, 5, 23
25	15.6	0.92 (3H, *s*)	1, 5, 9, 10
26	17.0	0.91 (3H, *s*)	7, 8, 9, 14
27	24.0	1.05 (3H, *s*)	8, 13, 14, 15
28	25.0	0.85 (3H, *s*)	16, 17, 18, 22
29	182.4	-	
30	21.0	1.19 (3H, *s*)	19, 20, 29

7. Identification of Compound SV-7 (30-Hydroxyfriedelane-1,3-dione)

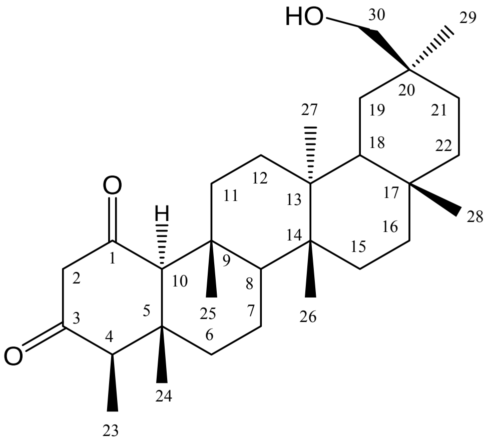
Compound SV-7 was isolated as a white amorphous powder (5.6 mg, 0.0005 % yield) with the same molecular formula $C_{30}H_{48}O_3$ as compound SV-4. This molecular formula was analyzed from the $[M + H]^+$ ion peak at *m/z* 457.3681 in its high resolution ESI-TOF mass spectrum (**Figure 33**). The IR spectrum showed absorption bands of hydroxyl group at 3435 cm^{-1}

and carbonyl groups at 1729 and 1707 cm^{-1} (**Figure 34**). Its ^{1}H NMR spectrum (**Figure 35**, **Table 15**) was characteristic of a 1,3-diketofriedelane triterpenoid, showing six methyl singlets at δ 0.67 (H$_3$-24), 0.97 (H$_3$-29), 0.99 (H$_3$-26), 1.02 (H$_3$-27), 1.13 (H$_3$-28) and 1.18 ppm (H$_3$-25), one methyl doublet at δ 1.03 ppm (J = 6.5 Hz, H$_3$-23) along with two methylene doublets of a 1,3-diketone at δ 3.23 and 3.43 ppm (each 1H, J = 15.8 Hz, H$_2$-2). A pair of doublet signals of an oxymethylene protons resonated at δ 3.34 and 3.40 ppm (1H each, both J = 10.5 Hz, H$_2$-30). The more upfield shift of these doublets, when compared to those of compound SV-4, indicated the different location of the hydroxymethyl group in the molecule.

^{13}C-NMR data, together with DEPT and HSQC experiments (**Figure 36**), helped categorizing the rest of its carbon signals as those of seven methyls at δ 7.3 (C-23), 16.0 (C-24), 18.1 (C-25), 18.6 (C-27), 20.0 (C-26), 28.9 (C-29) and 32.1 ppm (C-28), ten methylenes at δ 18.0 (C-7), 28.1 (C-21), 29.4 (C-19), 30.1 (C-12), 32.1 (C-15), 34.5 (C-11), 35.8 (C-16), 38.1 (C-22), 40.6 (C-6) and 60.6 ppm (C-2), one oxymethylene at δ 72.0 ppm (C-30), four methines at δ 42.6 (C-18), 52.0 (C-8), 59.1 (C-4) and 71.9 ppm (C-10), six quaternary carbons at δ 30.0 (C-17), 33.4 (C-20), 37.2 (C-9), 37.8 (C-5), 38.3 (C-14) and 39.6 ppm (C-13), and two keto-carbonyl signals at δ 202.7 (C-1) and 204.1 ppm (C-3).

HMBC correlations (**Figures 37a-37c**) from both oxymethylene doublets to C-20, C-21 and C-29, as well as from the signals of H$_2$-19 and H$_3$-29 to C-30, indicated the position of the hydroxyl group to be at C-30. The more upfield resonance of the hydroxy-substituted methylene carbon (at δ 72.0 instead of at around δ 74-75 ppm for C-29) also supported the C-30 substitution (Nozaki *et al.*, 1986). Consequently, the structure of compound SV-7 was characterized as 30-hydroxyfriedelane-1,3-dione.

This triterpene has previously been isolated from the stem bark of *Salacia reticulata* var. β-*diandra* (Gunatilaka, 1986). However, no spectral data of the compound were presented in the literature. Therefore, this is the first report of its NMR assignments.



30-Hydroxyfriedelane-1,3-dione

Table 15. ^{1}H- and ^{13}C-NMR spectral data for 30-hydroxyfriedelane-1,3-dione (500 and 125 MHz, in $CDCl_3$).

Position	δ_C	δ_H	HMBC (H→C)
1	202.7	-	
2	60.6	3.23 (1H, *d*, *J* = 15.8 Hz) 3.43 (1H, *d*, *J* = 15.8 Hz)	1, 3, 4, 10 1,3
3	204.1	-	
4	59.1	2.56 (1H, *q*, *J* = 6.5 Hz)	3, 5, 6, 10, 23, 24
5	37.8	-	
6	40.6	1.37 (1H, *m*) 1.88 (1H, *br dd*, *J* = 12.5, 3.5 Hz)	4, 5, 8, 10, 24 5, 7, 8, 10, 24
7	18.0	1.44 (1H, *m*) 1.51 (1H, *m*)	5, 14 5, 14
8	52.0	1.23 (1H, *m*)	9, 11, 26
9	37.2	-	
10	71.9	2.36 (1H, *s*)	1, 4, 5, 6, 8, 9, 11, 24, 25
11	34.5	1.13 (1H, *m*) 2.14 (1H, *ddd*, *J* = 13.5, 7.0, 3.5 Hz)	9, 12, 13 8, 9, 12, 13, 25

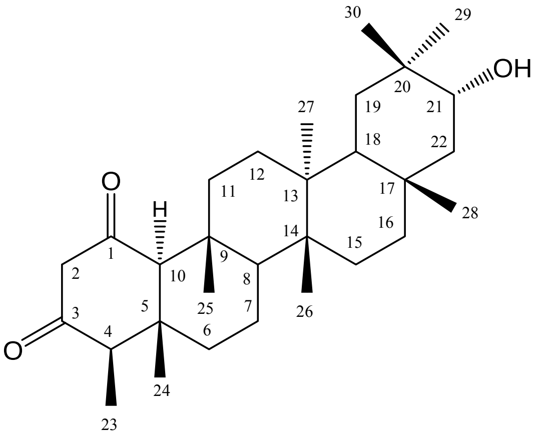
Position	δ_C	δ_H	HMBC (H→C)
12	30.1	1.30 (1H, *m*) 1.39 (1H, *m*)	11, 27 14, 27
13	39.6	-	
14	38.3	-	
15	32.1	1.25 (1H, *m*) 1.49 (1H, *m*)	13, 14, 17, 26 16, 17, 26
16	35.8	1.38 (1H, *m*) 1.53 (1H, *m*)	14, 15, 18, 22 15, 17, 22, 28
17	30.0	-	
18	42.6	1.49 (1H, *m*)	16, 17, 20, 27
19	29.4	1.20 (1H, *m*) 1.46 (1H, *m*)	13, 17, 18, 20, 30 17, 18, 20, 21, 30
20	33.4	-	
21	28.1	1.14 (1H, *m*) 1.42 (1H, *m*)	17, 19, 20, 29 17, 19, 20, 22, 30
22	38.1	0.97 (1H, *m*) 1.55 (1H, *m*)	17, 18, 20, 28 17, 21, 28
23	7.3	1.03 (3H, *d*, J = 6.5 Hz)	3, 4, 5
24	16.0	0.67 (3H, *s*)	4, 5, 6, 10
25	18.1	1.18 (3H, *s*)	8, 9, 10, 11
26	20.0	0.99 (3H, *s*)	8, 13, 14, 15
27	18.6	1.02 (3H, *s*)	12, 13, 14, 18
28	32.1	1.13 (3H, *s*)	16, 17, 18, 22
29	28.9	0.97 (3H, *s*)	19, 20, 21, 30
30	72.0	3.34 (1H, *d*, J = 10.5 Hz) 3.40 (1H, *d*, J = 10.5 Hz)	20, 21, 29 20, 21, 29

8. Structure Elucidation of Compound SV-8 (21α-Hydroxyfriedelane-1,3-dione)

Compound SV-8 was obtained as a white amorphous powder (4.2 mg, 0.0004 % yield). The molecular formula of this compound was determined as $C_{30}H_{48}O_3$ from its quasi-molecular $[M + H]^+$ ion peak at *m/z* 457.3671 in the high resolution ESI-TOF mass spectrum (**Figure 38**). Its IR spectrum displayed absorption bands at 3436, 1731 and 1705 cm^{-1} (**Figure 39**) ascribable to hydroxyl and carbonyl functions in the structure. The general appearance of the ^{1}H- and ^{13}C-NMR spectra, in addition to the information obtained from its mass spectrum, suggested its structure to be a friedelane-type triterpenoid isomer of compounds SV-4 and SV-7.

The ^{1}H-NMR spectrum of compound SV-8 (**Figure 40**) showed seven methyl singlets at δ 0.67 (H_3-24), 0.92 (H_3-26), 0.96 (H_3-29), 1.05 (H_3-30), 1.07 (H_3-27), 1.18 (H_3-28) and 1.19 ppm (H_3-25), a methyl doublet at δ 1.03 ppm (H_3-23), two methylene doublets of 1,3-diketone at δ 3.23 and 3.44 ppm (each 1H, J = 15.8 Hz, H_2-2) along with an oxymethine double doublet at δ 3.67 ppm (J = 12.0, 4.5 Hz, H-21).

Its ^{13}C-NMR spectrum (**Figure 41**) exhibited signals of eight methyl carbons at δ 7.3 (C-23), 16.0 (C-24), 17.8 (C-26), 18.2 (C-25), 19.3 (C-27), 24.9 (C-29), 31.8 (C-30) and 33.1 ppm (C-28), nine methylenes at δ 18.1 (C-7), 29.8 (C-12), 30.5 (C-15), 34.2 (C-11), 35.9 (C-16), 36.0 (C-19), 40.6 (C-6), 47.0 (C-22) and 60.6 ppm (C-2), four methines at δ 44.2 (C-18), 50.6 (C-8), 59.1 (C-4) and 71.9 ppm (C-10), an oxymethine carbon at δ 74.3 ppm (C-21), six quaternary carbons at δ 32.5 (C-17), 34.3 (C-20), 37.3 (C-9), 37.8 (C-5), 38.7 (C-14) and 38.8 ppm (C-13), and two keto-carbonyl carbons at δ 202.7 (C-1) and 204.1 ppm (C-3). These spectral data are similar to those of friedelane-1,3-dione (compound SV-2) except for the signals due to the hydroxyl substitution. These NMR data (**Table 16**) were assigned with the aid of DEPT, HSQC and HMBC experiments. The position of the hydroxyl group at C-21 was established by HMBC experiment (**Table 16**), in which correlations could be observed between the oxymethine proton signal at δ 3.67 ppm and those of C-20, C-22, C-29 and C-30 (**Figures 42a-42b**). The orientation of this hydroxyl group was determined as α by NOESY experiment, which showed NOE correlations between H-21β and H_3-28 as well as H_3-30 (**Figure 43**), and by comparison of its NMR data with those of related friedelane triterpene (Tane *et al.*, 1996). The molecular structure of compound SV-8 was therefore determined as a new 1,3-diketofriedelane triterpene, 21α-hydroxyfriedelane-1,3-dione.



21α-Hydroxyfriedelane-1,3-dione

Table 16. ^{1}H- and ^{13}C-NMR spectral data for 21α-hydroxyfriedelane-1,3-dione (500 and 125 MHz, in $CDCl_3$).

Position	δ_C	δ_H	HMBC (H→C)
1	202.7	-	
2	60.6	3.23 (1H, *d*, *J* = 15.8 Hz) 3.44 (1H, *d*, *J* = 15.8 Hz)	1, 3, 4, 10 1,3
3	204.1	-	
4	59.1	2.55 (1H, *q*, *J* = 7.0 Hz)	3, 5, 6, 10, 23, 24
5	37.8	-	
6	40.6	1.39 (1H, *m*) 1.87 (1H, *br dd*, *J* = 9.5, 3.0 Hz)	7, 8, 24 5, 7, 8, 10, 24
7	18.1	1.41 (1H, *m*) 1.52 (1H, *m*)	 8
8	50.6	1.28 (1H, *m*)	7, 13, 14, 26
9	37.3	-	
10	71.9	2.37 (1H, *s*)	1, 4, 5, 8, 9, 11, 24, 25
11	34.2	1.18 (1H, *m*) 2.14 (1H, *ddd*, *J* = 13.5, 7.0, 3.5 Hz)	25 8, 9, 12, 13, 25

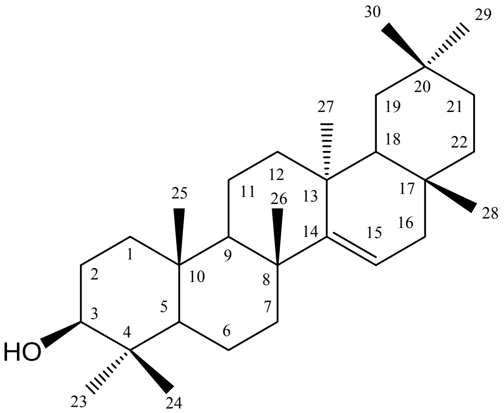
Position	δ_C	δ_H	HMBC (H⟶C)
12	29.8	1.26 (1H, *m*) 1.34 (1H, *m*)	9, 13, 14 13, 14
13	38.8	-	
14	38.7	-	
15	30.5	1.27 (1H, *m*) 1.44 (1H, *m*)	13, 14, 26 13, 14, 17, 26
16	35.9	1.53 (1H, *m*) 1.60 (1H, *m*)	17, 22 22
17	32.5	-	
18	44.2	1.51 (1H, *m*)	13, 14, 17, 19, 27
19	36.0	1.53 (1H, *m*) 1.60 (1H, *dd*, *J* = 13.8, 4.8 Hz)	13, 17, 18, 20, 21, 29 13, 17, 18, 20, 21, 29
20	34.3	-	
21	74.3	3.67 (1H, *dd*, *J* = 12.0, 4.5 Hz)	20, 22, 29, 30
22	47.0	1.21 (1H, *dd*, *J* = 12.0, 4.5 Hz) 1.68 (1H, *dd*, *J* = 12.5, 12.0 Hz)	18, 20, 21 16, 17, 21, 28
23	7.3	1.03 (3H, *d*, *J* = 7.0 Hz)	3, 4, 5
24	16.0	0.67 (3H, *s*)	4, 5, 6, 10
25	18.2	1.19 (3H, *s*)	8, 9, 10, 11
26	17.8	0.92 (3H, *s*)	8, 13, 14, 15
27	19.3	1.07 (3H, *s*)	12, 13, 14, 18
28	33.1	1.18 (3H, *s*)	16, 17, 18, 22
29	24.9	0.96 (3H, *s*)	19, 20, 21, 30
30	31.8	1.05 (3H, *s*)	19, 20, 21, 29

9. Identification of Compound FF-2 (Taraxerol)

Compound FF-2, obtained as a white amorphous powder (5.8 mg, 0.0003 % yield), appeared as a purple spot on TLC upon spraying with 10% sulfuric acid and heated. The mass spectrum (**Figure 48**) exhibited a quasi-molecular $[M + H]^+$ ion peak at *m/z* 427, consistent with the formula molecule $C_{30}H_{50}O$. Its IR absorption bands at 3484 and 1641 cm^{-1} (**Figure 49**) indicated the presence of hydroxyl and olefinic functions in the molecule, respectively.

The ^1H-NMR spectrum of compound FF-2 (**Figure 50**) showed eight methyl singlets at δ 0.78 (H_3-25), 0.80 (H_3-28), 0.89 (H_3-26 and H_3-30), 0.91 (H_3-24), 0.93 (H_3-29), 0.96 (H_3-23) and 1.07 ppm (H_3-27), an oxymethine double doublet at δ 3.17 ppm (*J* = 10.1, 4.7 Hz, H-3) and one double doublet of an olefinic proton at δ 5.51 ppm (*J* = 6.3, 3.3 Hz, H-15) . Its ^{13}C-NMR spectrum (**Figures 51a-51b**) displayed 30 carbon signals, including those of eight methyl carbons at δ 15.9 (C-24 and C-25), 21.7 (C-30), 26.3 (C-27), 28.4 (C-23), 30.3 (C-26 and C-28) and 33.8 ppm (C-29), ten methylene carbons at δ 17.9 (C-11), 19.2 (C-6), 27.6 (C-2), 33.5 (C-22), 34.1 (C-21), 35.6 (C-7), 36.2 (C-12), 37.1 (C-16), 38.4 (C-1) and 41.8 ppm (C-19), three methine carbons at δ 49.2 (C-9), 49.7 (C-18) and 56.0 ppm (C-5), an oxymethine carbon at δ 79.5 ppm (C-3), six quaternary carbons at δ 29.2 (C-20), 38.0 (C-13 and C-17), 38.1 (C-10), 39.2 (C-4) and 39.4 ppm (C-8), one olefinic methine carbon at δ 117.3 ppm (C-15) and one olefinic quaternary carbon at δ 158.5 ppm (C-14). These NMR data (**Table 17**) were characteristic of a taraxerane-type triterpene having one double bond at C-14/C-15, as well as one β-hydroxyl substituent at C-3. Therefore, compound FF-2 was identified as taraxerol. This is the first report of the triterpene from this plant.

Taraxerol is widely distributed and has been found in various plant parts such as the leaves of *Rhizophora apiculata* (Rhizophoraceae) (Kokpol and Chavasiri, 1990), the stem of *Opuntia dillenii* (Cactaceae) (Jiang *et al*., 2006) and the root bark of *Phyllanthus columnaris* (Euphorbiaceae) (Jamal, Yaacob, and Din, 2009). Taraxerol, produced by *Agrobacterium*-transformed root cultures of butterfly pea *Clitoria ternatea* (Fabaceae), was reported to be anti-cancer (Swain, Rout, and Chand, 2012).



Taraxerol

Table 17. ^{1}H- and ^{13}C-NMR spectral data for compound FF-2 and taraxerol (300 and 75 MHz, in CDCl$_3$).

Position	FF-2		Taraxerol*	
	δ_C	δ_H	δ_C	δ_H
1	38.4	-	38.2	-
2	27.6	-	27.4	-
3	79.5	3.17 (1H, *dd*, *J* = 10.1, 4.7 Hz)	79.3	3.20 (1H, *dd, J* = 9.5, 4.0 Hz)
4	39.2	-	39.0	-
5	56.0	-	55.7	-
6	19.2	-	19.0	-
7	35.6	-	35.3	-
8	39.4	-	39.2	-
9	49.2	-	48.9	-
10	38.1	-	37.9	-
11	17.9	-	17.7	-
12	36.2	-	36.0	-
13	38.0	-	37.9	-
14	158.5	-	158.3	-
15	117.3	5.51 (1H, *dd*, *J* = 6.3, 3.3 Hz)	117.1	5.53 (1H, *dd*, *J* = 5.5, 2.6 Hz)

Position	FF-2		Taraxerol*	
	δ_C	δ_H	δ_C	δ_H
16	37.1	-	36.9	-
17	38.0	-	37.9	-
18	49.7	-	49.5	-
19	41.8	-	41.5	-
20	29.2	-	29.0	-
21	34.1	-	33.9	-
22	33.5	-	33.3	-
23	28.4	0.96 (3H, *s*)	28.2	0.98 (3H, *s*)
24	15.9	0.91 (3H, *s*)	15.6	0.93 (3H, *s*)
25	15.9	0.78 (3H, *s*)	16.0	0.81 (3H, *s*)
26	30.3	0.89 (3H, *s*)	30.1	0.91 (3H, *s*)
27	26.3	1.07 (3H, *s*)	26.1	1.09 (3H, *s*)
28	30.3	0.80 (3H, *s*)	30.0	0.83 (3H, *s*)
29	33.8	0.93 (3H, *s*)	33.6	0.96 (3H, *s*)
30	21.7	0.89 (3H, *s*)	21.5	0.91 (3H, *s*)

*Jamal *et al*., 2009

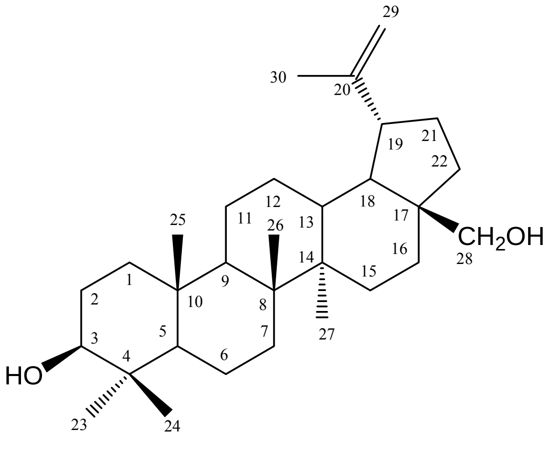
10. Identification of Compound FF-3 (Betulin)

Compound FF-3, obtained as a white amorphous powder (13.8 mg, 0.0007% yield), appeared as a purple spot on TLC upon spraying with 10% sulfuric acid and heated. The mass spectrum (**Figure 52**) showed a quasi-molecular $[M + H + Na]^+$ ion peak at *m/z* 466 consistent with the molecular formula $C_{30}H_{50}O_2$. Its IR absorption bands at 3400 and 1645 cm^{-1} (**Figure 53**) indicated the presence of hydroxyl and olefinic functions in the molecule, respectively.

The ^{1}H-NMR spectrum of compound FF-3 (**Figure 54**) showed five methyl singlets at δ 0.74 (H_3-24), 0.80 (H_3-25), 0.95 (H_3-23), 0.96 (H_3-27) and 1.00 ppm (H_3-26), two broad exo-methylene singlets and one methyl singlet of an isopropenyl group at δ 4.56, 4.66 (each 1H, H_2-29) and 1.66 ppm (H_3-30), a pair of oxymethylene doublets at δ 3.31 and 3.77 ppm (each 1H, *J* = 10.8 Hz, H_2-28), and one oxymethine double doublet at δ 3.16 ppm (*J* = 10.8, 5.4 Hz, H-3). Its

^{13}C-NMR spectrum (**Figures 55a-55b**) displayed 30 carbon signals, including those of six methyl carbons at δ 14.8 (C-27), 15.4 (C-24), 16.0 (C-26), 16.1 (C-25), 19.1 (C-30) and 28.0 ppm (C-23), ten methylene carbons at δ 18.3 (C-6), 20.9 (C-11), 25.3 (C-12), 27.0 (C-15), 27.2 (C-2), 29.2 (C-16), 29.8 (C-21), 34.0 (C-22), 34.3 (C-7) and 38.8 ppm (C-1), one oxymethylene carbon at δ 60.6 ppm (C-28), five methine carbons at δ 37.3 (C-13), 47.8 (C-19), 48.8 (C-18), 50.4 (C-9) and 55.3 ppm (C-5), one oxymethine carbon at δ 78.9 ppm (C-3), five quaternary carbons at δ 37.2 (C-10), 38.9 (C-4), 40.9 (C-8), 42.7 (C-14), 47.8 ppm (C-17), one olefinic methylene carbon and one olefinic quaternary carbon at δ 109.7 (C-29) and 150.5 ppm (C-20), respectively.

These spectral data indicated that compound FF-3 was a lupane-type triterpene possessing an isopropenyl group and two hydroxyl substitutions at C-3 and C-28. Therefore, it was identified as the known triterpenoid, betulin. Comparison of its NMR data with those of betulin isolated from the stem bark of *Salacia cordata* (Tinto *et al.*, 1992) (**Table 18**) confirmed this assignment.



Betulin

Betulin is one of the lupane-type triterpenoids frequently found in plants and especially in *Diospyros* species (Ebenaceae). The compound has been shown to exhibit various biological activities, for example, anti-inflammatory (Del Recio *et al.*, 1995), antimycobacterial (Cantrell, Franzblau, and Fisher, 2001) and antitumor activities (Rzeski *et al.*, 2009). However, this is the first isolation of the compound from *Ficus foveolata*.

Table 18. ^{1}H- and ^{13}C-NMR spectral data for compound FF-3 and betulin (300 and 75 MHz, in $CDCl_3$).

Position	FF-3		Betulin*	
	δ_C	δ_H	δ_C	δ_H
1	38.8	-	38.8	0.89, 1.65
2	27.2	-	27.2	1.58
3	78.9	3.16 (1H, *dd*, J = 10.8, 5.4 Hz)	78.9	3.18
4	38.9	-	38.9	-
5	55.3	0.66 (1H, *br d*, J = 9.6 Hz)	55.3	0.67
6	18.3	-	18.3	1.38, 1.52
7	34.3	-	34.3	1.39
8	40.9	-	40.9	-
9	50.4	-	50.4	1.27
10	37.2	-	37.2	-
11	20.9	-	20.9	1.19, 1.41
12	25.3	-	25.3	1.03, 1.63
13	37.3	-	37.3	1.64
14	42.7	-	42.7	-
15	27.0	-	27.0	1.04, 1.70
16	29.2	-	29.2	1.20, 1.93
17	47.8	-	47.8	-
18	48.8	-	48.8	1.57
19	47.8	2.36 (1H, *m*)	47.8	2.38
20	150.5	-	150.6	-
21	29.8	-	29.8	1.40, 1.95
22	34.0	-	34.0	1.02, 1.86
23	28.0	0.95 (3H, *s*)	28.0	0.96
24	15.4	0.74 (3H, *s*)	15.4	0.76
25	16.1	0.80 (3H, *s*)	16.1	0.82
26	16.0	1.00 (3H, *s*)	16.0	1.02
27	14.8	0.96 (3H, *s*)	14.8	0.98
28	60.6	3.31 (1H, *d*, J = 10.7 Hz) 3.77 (1H, *d*, J = 10.7 Hz)	60.2	3.31 3.77
29	109.7	4.56 (1H, *br s*), 4.66 (1H, *br s*)	109.6	4.58, 4.68
30	19.1	1.66 (3H, *s*)	19.1	1.68

*Tinto *et al.*, 1992

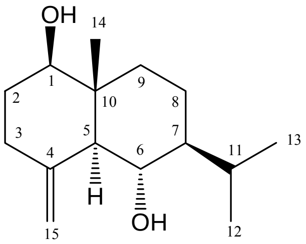
11. Identification of Compound FF-4 [4(15)-Eudesmene-1β,6α-diol]

Compound FF-4, obtained as colorless needles (8.5 mg, 0.0004 % yield), appeared as a purple spot on TLC upon spraying with 10% sulfuric acid and heated. Its mass spectrum (**Figure 56**) showed a quasi-molecular $[M + H]^+$ ion peak at *m/z* 239, suggesting the molecular formula of $C_{15}H_{26}O_2$. Its IR absorption bands at 3589 and 1647 cm^{-1} (**Figure 57**) indicated the presence of hydroxyl and olefinic groups in the molecule, respectively.

The ^{1}H-NMR spectrum of compound FF-4 (**Figure 58**) showed one prominent methyl singlet at δ 0.68 (H_3-14), two methyl broad singlets of an isopropyl group at δ 0.85 (H_3-12) and 0.93 ppm (H_3-13), a pair of methylene multiplets at δ 2.04 (1H, H-3β) and 2.30 ppm (1H, H-3α) and two exocyclic methylene broad singlets at δ 4.72 (1H, H-15b) and 5.00 ppm (1H, H-15a). One oxymethine proton resonated as a doublet of doublets at δ 3.39 ppm (*J* = 10.2, 4.2 Hz, H-1), whereas another oxymethine proton gave a broad singlet at δ 3.69 ppm (H-6). The ^{13}C-NMR spectrum (**Figure 59**) displayed 15 carbon signals of a sesquiterpene skeleton, which could be differentiated as those of one tertiary methyl at δ 12.0 ppm (C-14), two secondary methyls at δ 16.6 (C-12) and 21.5 ppm (C-13), four methylenes at δ 18.6 (C-8), 32.3 (C-2), 35.5 (C-3) and 36.7 ppm (C-9), an exomethylene at δ 108.2 ppm (C-15), three methines at δ 26.4 (C-11), 49.8 (C-7) and 56.3 ppm (C-5), two oxymethines at δ 67.4 (C-6) and 79.4 ppm (C-1), two quaternary carbons at δ 42.1 (C-10) and 146.6 ppm (C-4). These data suggested a bicyclic sesquiterpenoid structure with one exocyclic double bond, one isopropyl group and two hydroxyl substituents.

Careful analysis of these spectral data indicated that the compound possessed eudesmane-type sesquiterpenoid skeleton with two hydroxyl groups located at C-1 and C-6 and one double bond between at C-4 and C-15. The sesquiterpene FF-4 was thus identified as 4(15)-eudesmene-1β,6α-diol and confirmed by comparison of its NMR data (**Table 19**) and specific rotation ($[\alpha]^{20}_D$+50°) with published values (Kitajima *et al.*, 2002).

4(15)-Eudesmene-1β,6α-diol is a constituent of the aerial parts of several asteraceous plants including *Senecio microglossus* (Bohlmann *et al.*, 1983), *Helianthus microcephalus* (Gutierrez and Herz, 1988) and *Ageratina glechonophylla* (Gonzalez *et al.*, 1989). The terpenoid was also found in other flowering plant species such as in the leaves of *Teucrium polium* (family Labiatae) (Kamel, 1995) and in the fruits of *Torilis japonica* (family Umbelliferae) (Kitajima *et al.*, 2002). However, this is the first report of its occurrence in plants of the family Moraceae.



4(15)-Eudesmene-1β,6α-diol

Table 19. ^{1}H- and ^{13}C-NMR spectral data for compound FF-4 and 4(15)-eudesmene-1β,6α-diol (300 and 75 MHz, in $CDCl_3$).

Position	FF-4		4(15)-Eudesmene-1β,6α-diol*	
	δ_C	δ_H	δ_C	δ_H
1	79.4	3.39 (1H, *dd*, *J* = 10.2, 4.2 Hz)	79.0	3.42 (1H, *dd*, *J* = 11.5, 4.5 Hz)
2	32.3	1.50 (1H, *m*) 1.82 (1H, *m*)	31.9	1.54 (1H, *m*) 1.86 (1H, *dddd*, *J* = 12.5, 5.0, 5.0, 4.5 Hz)
3	35.5	2.04 (1H, *m*) 2.30 (1H, *m*)	35.1	2.07 (1H, *br ddd*, *J* = 13.5, 12.5, 5.0 Hz) 2.33 (1H, *ddd*, *J* = 13.5, 5.0, 3.5 Hz)
4	146.6	-	146.2	-
5	56.3	1.72 (1H, *d*, *J* = 8.4 Hz)	55.9	1.75 (1H, *d*, *J* = 10.0 Hz)
6	67.4	3.69 (1H, *br s*)	67.0	3.72 (1H, *dd*, *J* = 10.0, 10.0 Hz)
7	49.8	1.26 (1H, *m*)	49.3	1.30 (1H, *m*)
8	18.6	1.26 (1H, *m*) 1.50 (1H, *m*)	18.1	1.23 (1H, *br ddd*, *J* = 12.0, 12.0, 3.0 Hz) 1.54 (1H, *m*)
9	36.7	1.18 (1H, *m*) 1.91 (1H, *m*)	36.3	1.17 (1H, *ddd*, *J* = 13.0, 12.0, 3.0 Hz) 1.93 (1H, *br dd*, *J* = 13.0, 3.0 Hz)
10	42.1	-	41.7	-
11	26.4	2.22 (1H, *m*)	26.0	2.25 (1H, *m*)
12	16.6	0.85 (3H, *s*)	16.2	0.87 (3H, *s*)
13	21.5	0.93 (3H, *s*)	21.1	0.96 (3H, *s*)
14	12.0	0.68 (3H, *s*)	11.6	0.71 (3H, *s*)
15	108.2	4.72 (1H, *br s*) 5.00 (1H, *br s*)	107.8	4.75 (1H, *br d*, *J* = 1.0 Hz) 5.02 (1H, *br d*, *J* = 1.0 Hz)

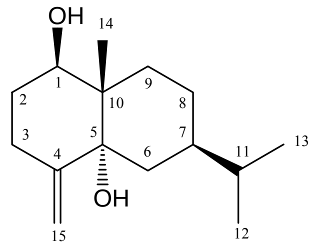
*Kitajima *et al.*, 2002

12. Identification of Compound FF-5 [4(15)-Eudesmene-1β,5α-diol]

Compound FF-5, obtained as colorless needles (5.1 mg, 0.0003% yield), appeared as a purple spot on TLC upon spraying with 10% sulfuric acid and heated. Its quasi-molecular $[M + H]^+$ ion peak at *m/z* 239 in the ESI mass spectrum (**Figure 60**) corresponded to the molecular formula $C_{15}H_{26}O_2$ and suggested that the compound was an isomer of compound FF-4. Its IR absorption bands at 3627 and 1645 cm^{-1} (**Figure 61**) were ascribable to hydroxyl and olefinic groups in the structure, respectively.

The NMR data of compounds FF-4 and FF-5 were also similar. The ^{1}H-NMR spectrum of compound FF-5 (**Figure 62**) displayed one methyl singlets at δ 0.74 ppm (H_3-14), two methyl doublets of an isopropyl group at δ 0.88 (*J* = 6.6 Hz, H_3-13) and 0.90 ppm (*J* = 6.6 Hz, H_3-12). A pair of methylene protons resonated as a doublet of doublets at δ 2.13 ppm (1H, *J* = 13.7, 5.5 Hz, H-3β) and a doublet of doublet of doublets at δ 2.68 ppm (1H, *J* = 13.7, 8.1, 5.5 Hz, H-3α). Two prominent exocyclic methylene singlets appeared at δ 4.73 and 4.83 ppm (each 1H, H_2-15) and one oxymethine doublet of doublets at δ 4.03 ppm (*J* = 10.4, 4.8 Hz, H-1). The ^{13}C-NMR spectrum (**Figure 63**) showed 15 carbon signals of a sesquiterpene, including those of one tertiary methyl at δ 13.1 ppm (C-14), two secondary methyls of an isopropyl side-chain at δ 20.1 (C-12) and 20.4 ppm (C-13), five methylenes at δ 24.1 (C-8), 30.2 (C-3), 30.4 (C-9), 31.0 (C-2) and 34.7 ppm (C-6), two methines at δ 33.2 (C-11) and 38.7 ppm (C-7), one oxymethine at δ 73.5 ppm (C-1), a quaternary carbon at δ 42.7 ppm (C-10), an oxygenated quaternary carbon at δ 76.6 ppm (C-5) and two olefinic carbons of an exocyclic double bond at δ 109.0 (C-15) and 151.1 ppm (C-4). Analysis of these spectral data confirmed the compound to be the same eudesmane-type sesquiterpenoid as compound FF-4, with identical exocyclic double bond and a hydroxyl substitution at C1. However, the presence of one oxygenated quaternary carbon while there was one less oxymethine carbon when compared to the previous compound indicated the shift of another hydroxyl group from C-6 to C-5 position. Consequently, compound FF-5 was identified as 4(15)-eudesmene-1β,5α-diol and confirmed by comparison of its ^{1}H and ^{13}C NMR data with those previously reported (Sun *et al.*, 2004) (**Table 20**). This is the first report of the presence of this compound in *F. foveolata*.

4(15)-Eudesmene-1β,5α-diol, together with 4(15)-eudesmene-1β,6α-diol, have been isolated from the fruits of *Torilis japonica* (family Umbelliferae) (Kitajima *et al.*, 2002). The sesquiterpene, obtained from *Caragana intermedia* (family Leguminosae), showed anti-diabetic activity at a concentration of 10.7 μg/ml by improving glucose transformation. In db/db mice, the compound produced the same effect on oral glucose tolerance as the anti-diabetic drug metformin, with the MIC value of 100 mg/ml (Sun *et al.*, 2004).



4(15)-Eudesmene-1β,5α-diol

Table 20. ^{1}H- and ^{13}C-NMR spectral data for compound FF-5 and 4(15)-eudesmene-1β,5α-diol (300 and 75 MHz, in $CDCl_3$).

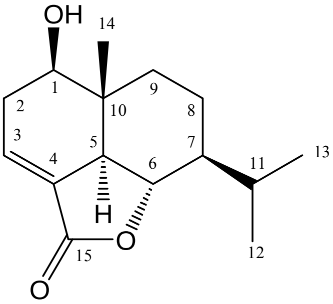
Position	FF-5		4(15)-Eudesmene-1β,5α-diol*	
	δ_C	δ_H	δ_C	δ_H
1	73.5	4.03 (1H, *dd*, *J* = 10.4, 4.8 Hz)	73.1	4.05 (1H, *dd*, *J* = 11.6, 5.0 Hz)
2	31.0	1.52 (1H, *m*) 1.83 (1H, *m*)	30.6	1.55 (1H, *m*) 1.85 (1H, *m*)
3	30.2	2.13 (1H, *dd*, *J* = 13.7, 5.5 Hz) 2.68 (1H, *ddd*, *J* = 13.7, 8.1, 5.5 Hz)	29.8	2.15 (1H, *ddd*, *J* = 13.8, 5.3, 1.8 Hz) 2.70 (1H, *m*)
4	151.1	-	150.7	-
5	76.6	-	76.2	-
6	34.7	1.54 (1H, *m*) 1.57 (1H, *m*)	34.3	1.54 (1H, *m*) 1.57 (1H, *dd*, *J* = 13.2, 4.1 Hz)
7	38.7	1.57 (1H, *m*)	38.3	1.58 (1H, *m*)
8	24.1	1.23 (1H, *m*) 1.59 (1H, *m*)	23.7	1.25 (1H, *m*) 1.60 (1H, *m*)
9	30.4	1.68 (1H, *m*) 1.68 (1H, *m*)	30.0	1.68 (1H, *m*) 1.68 (1H, *dd*, *J* = 13.2, 4.0 Hz)
10	42.7	-	42.3	-
11	33.2	1.48 (1H, *m*)	32.8	1.50 (1H, *m*)
12	20.1	0.90 (3H, *d*, *J* = 6.6 Hz)	19.7	0.92 (3H, *d*, *J* = 6.8 Hz)
13	20.4	0.88 (3H, *d*, *J* = 6.6 Hz)	20.0	0.90 (3H, *d*, *J* = 6.8 Hz)
14	13.1	0.74 (3H, *s*)	12.7	0.76 (3H, *s*)
15	109.0	4.73 (1H, *s*), 4.83 (1H, *s*)	108.6	4.74(1H, *s*), 4.85 (1H, *s*)

* Sun *et al.*, 2004

13. Structure Elucidation of Compound FF-7 (Foveolide A)

Compound FF-7 was obtained as yellow oil (16.2 mg, 0.0008% yield). The molecular formula was determined as $C_{15}H_{22}O_3$ based on its quasi-molecular $[M + H]^+$ ion peak at m/z 251.1621 in the high resolution ESI-TOF mass spectrum (**Figure 65**). IR spectrum (**Figure 66**) showed absorption bands representing hydroxyl group at 3430 cm^{-1}, ester-carbonyl at 1749 cm^{-1} and gem-dimethyl at 1390 and 1371 cm^{-1}. Careful examination of its ^1H- and ^{13}C-NMR spectra (**Table 21** and **Figures 67-68**), with the aid of DEPT and HSQC experiments, showed the presence of one tertiary methyl singlet at δ 0.80 ppm (H_3-14), two isopropyl methyl doublets at δ 0.94 (*J* = 6.5 Hz, H_3-12) and 0.98 ppm (*J* = 7.0 Hz, H_3-13), three methylenes, three methines, two oxymethine doublets of doublets at δ 3.72 (*J* = 9.5, 6.7 Hz, H-1) and 3.91 ppm (*J* = 11.0, 10.0 Hz, H-6), one olefinic methine doublet of doublets at δ 6.54 ppm (*J* = 6.8, 3.2 Hz, H-3), one quaternary carbon at δ 36.8 ppm (C-10), one olefinic quaternary carbon at δ 128.1 ppm (C-4) and one ester carbonyl carbon at δ 169.0 ppm (C-15). The structure of compound FF-7 was therefore deduced to be a eudesmane sesquiterpenoid having similar partial structure as compound FF-4.

HMBC correlations (**Table 21** and **Figures 69a-69e**) observed between the signal of H-1 and carbon signals at δ 9.8 (C-14), 35.1 (C-9) and 54.2 ppm (C-5), as well as between H-6 resonance and carbon signals at δ 24.8 (C-8), 30.6 (C-11) and 36.8 ppm (C-10), confirmed that these oxymethine protons were located at the same positions as in compound FF-4. However, in this sesquiterpene, the exomethylene C-15 of compound FF-4 has been replaced by an ester-carbonyl which formed a γ-lactone ring with C-6, whereas the double bond has shifted to between C-3 and C-4. These locations were established through the HMBC correlations observed between H-3 resonance and carbon signals at δ 54.2 (C-5), 75.3 (C-1) and 169 ppm (C-15), as well as between the signals of H-6 and C-4 (δ 128.1 ppm). NOE correlations, observed in the NOESY spectrum (**Figures 70a-70d**), between the signal of the α-oriented H-5 (δ 2.26 ppm) and both H-1 and H-7 signals (δ 1.69 ppm) indicated the β-orientation of the hydroxyl group at C-1. Furthermore, the presence of NOE correlations between H-6 and all three methyl groups demonstrated that the γ-lactone connection at this position was α-oriented. Thus, the structure of compound FF-7 was elucidated as 1β-hydroxyeudesm-3-en-15,6α-olide and was trivially named foveolide A.



Foveolide A

Table 21. ^{1}H- and ^{13}C-NMR spectral data for foveolide A (500 and 125 MHz, in $CDCl_3$).

Position	δ_H	δ_C	HMBC (H→C)
1	3.72 (1H, *dd*, *J* = 9.5, 6.7 Hz)	75.3	5, 9, 10, 14
2	α: 2.60 (1H, *dddd*, *J* = 19.3, 6.7, 4.0, 3.2 Hz) β: 2.19 (1H, *dddd*, *J* = 19.3, 9.5, 5.0, 3.2 Hz)	34.0	1, 3, 4, 10 1, 3, 4, 10
3	6.54 (1H, *dd, J* = 6.8, 3.2 Hz)	131.2	1, 2, 4, 5, 15
4	-	128.1	
5	2.26 (1H*, ddd*, *J* = 11.0, 4.8, 3.3 Hz)	54.2	1, 3, 4, 6, 7, 9, 10, 14, 15
6	3.91 (1H*, dd*, *J* = 11.0, 10.0 Hz)	79.6	4, 5, 8, 10, 11
7	1.69 (1H, *m*)	50.3	5, 6, 8, 11, 12, 13
8	α: 1.85 (1H, *dtd*, *J* = 14.5, 4.5, 2.0 Hz) β: 1.42 (1H*, m*)	24.8	6, 7, 9, 11 6, 7, 9, 11
9	α: 1.27 (1H*, td, J* = 13.3, 4.8 Hz) β: 1.81 (1H, *ddd*, *J* = 13.3, 4.8, 2.0 Hz)	35.1	1, 5, 7, 8, 10, 14 5, 7, 8, 10, 14
10	-	36.8	
11	1.72 (1H, *m*)	30.6	6, 7, 8, 12, 13
12*	0.94 (3H, *d, J* = 6.5 Hz)	19.8	7, 11, 13
13*	0.98 (3H, *d, J* = 7.0 Hz)	20.0	7, 11, 12
14	0.80 (3H, *s*)	9.8	1, 5, 9, 10
15	-	169.0	

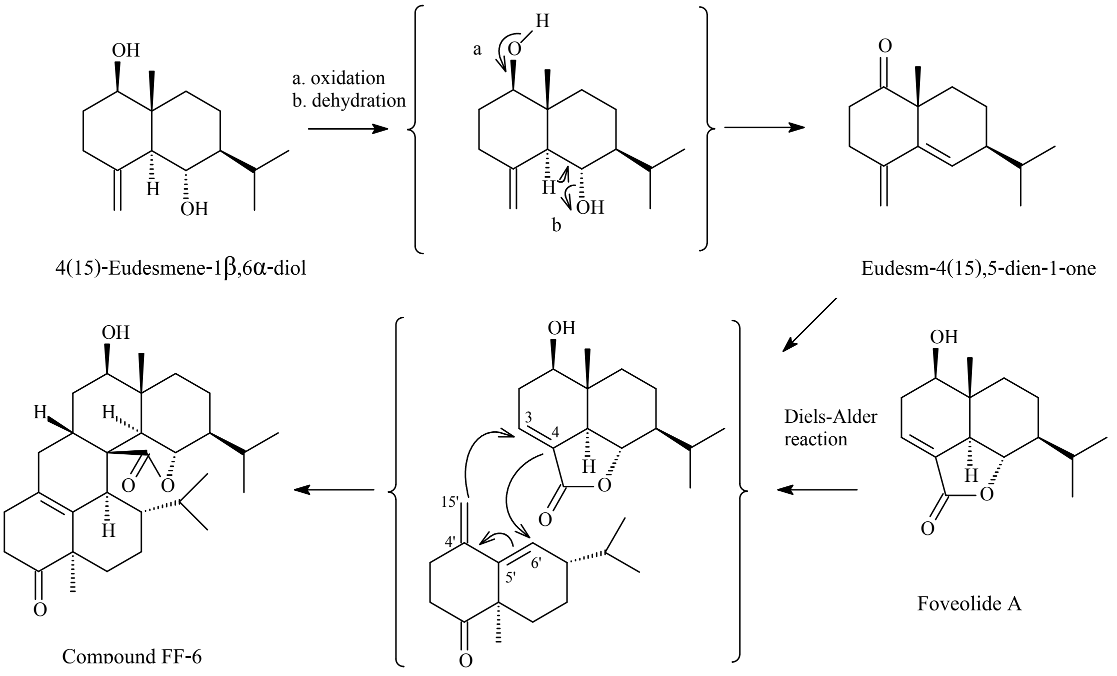
* These assignments are interchangeable.

14. Structure Elucidation of Compound FF-6 (Foveolide B)

Compound FF-6, a colorless gum (7.9 mg, 0.0004 % yield**),** gave a purple spot on TLC upon spraying with 10% sulfuric acid and heated. Its molecular formula was deduced from the pseudomolecular $[M + H]^+$ ion peak at *m/z* 469.3304 in its high resolution mass spectrum (**Figure 71**) as $C_{30}H_{44}O_4$, representing nine degrees of unsaturation. The IR spectrum (**Figure 72**) displayed absorption bands at 3443, 1753 and 1699 cm^{-1} ascribable to hydroxyl, ester carbonyl and keto-carbonyl functional groups in the structure.

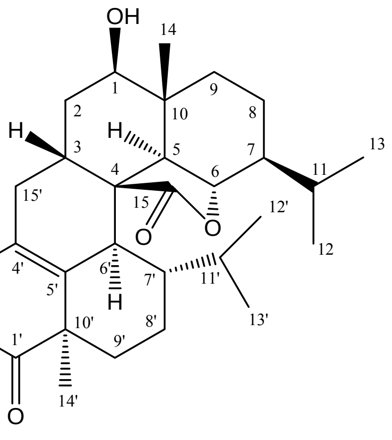
Analysis of the ^{1}H- and ^{13}C-NMR spectra of compound FF-6 (**Table 22** and **Figures 73-74**), with the aid of DEPT and HSQC experiments, revealed the presence of two tertiary methyl singlets at δ 1.09 (H_3-14) and 1.20 ppm (H_3-14′), two pairs of isopropyl methyl doublets at δ 0.86 (*J* = 7.0 Hz, H_3-12′) and 0.88 ppm (*J* = 6.5 Hz, H_3-13′) along with δ 0.97 (*J* = 6.5 Hz, H_3-13) and 1.00 ppm (*J* = 7.0 Hz, H_3-12), eight methylenes, seven methines, two oxymethine triplets at δ 3.83 (*J* = 8.0 Hz, H-1) and 4.25 ppm (*J* = 10.8 Hz, H-6), three quaternary carbons at δ 42.0 (C-10), 46.5 (C-4) and 48.8 ppm (C-10′), two olefinic carbons of a tetra-substituted double bond at δ 126.5 (C-4′) and 134.2 ppm (C-5′), one ester carbonyl carbon at δ 178.2 ppm (C-15) and one keto-carbonyl carbon at δ 215.5 ppm (C-1′). The presence of six rings in the structure of compound FF-6 could be inferred from these data. Furthermore, partial similarity of the NMR data to those of compound FF-4 and the number of carbon atoms indicated that compound FF-6 is a dimer of two different eudesmane sesquiterpenoid units.

As shown in **Scheme 7**, oxidation and dehydration of compound FF-4 could produce a hypothetical monomer, eudesm-4(15),5-dien-1-one, which could subsequently form two C-C bonds by Diels-Alder reaction (Oikawa and Tokiwano, 2004) with foveolide A (compound FF-7), linking them directly through positions 3/15′ and 4/6′ and thus creating compound FF-6 as a true disesquiterpenoid (Zhan *et al.*, 2011). These connectivities were confirmed by HMBC cross-peaks (**Figures 75a-75e**) from signals at δ 1.59 and 2.64 ppm (H_2-15′) to those of δ 34.7 (C-2), 30.5 (C-3), 46.5 (C-4), 30.5 (C-3′), 126.5 (C-4′) and 134.2 ppm (C-5′), from both resonances at δ 2.38 (H-3) and 2.07 (H-5) to the signal of C-6′ at δ 43.2 ppm, and from H-7′ signal at δ 1.48 ppm to that of C-4 at δ 46.5 ppm. Furthermore, HMBC correlations between signals at δ 2.35 and 2.69 (H_2-2′), 2.23 and 2.28 (H_2-3′), 1.49 and 1.50 (H_2-9′), 1.20 ppm (H_3-14′) and the keto-carbonyl signal at δ 215.5 ppm established the position of keto-carbonyl as at C-1′.



Scheme 7. Postulated biogenesis of compound FF-6

NOE correlations between H-6 and H_3-14, as well as between H-1, H-5 and H-7, in the NOESY spectrum (**Figures 76a-76b**) indicated the relative configuration of these protons to be identical to those of compound FF-4. The presence of NOESY cross-peaks between H-1 and H-6′ and between H-6′ and H_3-12′, H_3-13′ and H_3-14′ established the orientation of H-6′, H-7′ and H_3-14′ to be α, β and α, respectively. Accordingly, H-3 was assigned as β-oriented based on NOE correlations between its proton signal at δ 2.38 ppm and those of H-6 and H_3-14. The orientation of H-3 and configuration at C-4 indicated that the compound is an intermolecular [4+2] *endo*-Diels-Alder adduct. Therefore, compound FF-6 was characterized as a new sesquiterpenoid dimer, trivially named foveolide B, and is the first compound of this type found in *Ficus* species.



Foveolide B

Table 22. ^{1}H- and ^{13}C-NMR spectral data for foveolide B (500 and 125 MHz, in CDCl$_3$).

Position	δ_H	δ_C	HMBC (H→C)
1	3.83 (1H, *t*, *J* = 8.0 Hz)	74.2	2, 5, 9, 10, 14
2	α: 1.96 (1H, *ddd*, *J* = 14.0, 10.5, 8.0 Hz) β: 1.41 (1H, *dd*, *J* = 14.0, 8.0 Hz)	34.7	3, 4, 10, 15′ 3, 4, 15′
3	2.38 (1H, *m*)	30.5	2, 4, 4′, 6′, 15, 15′
4	-	46.5	
5	2.07 (1H, *d*, *J* = 10.8 Hz)	57.1	1, 3, 4, 6, 6′, 7, 9, 10,14
6	4.25 (1H, *t*, *J* = 10.8 Hz)	77.4	5, 10, 11
7	1.75 (1H, *m*)	52.0	5, 6, 8, 11, 12, 13
8	α: 1.83 (1H, *dtd*, *J* = 14.5, 5.0, 1.5 Hz) β: 1.56 (1H, *m*)	25.6	6, 7, 9, 10, 11 9
9	α: 1.30 (1H, *td*, *J* = 11.8, 5.0 Hz) β: 1.70 (1H, *dd*, *J* = 13.8, 5.0 Hz)	39.9	1, 5, 8, 10, 14 5, 7, 8, 10, 14
10	-	42.0	
11	1.75 (1H, *m*)	30.9	6, 7, 8, 12, 13
12*	1.00 (3H, *d*, *J* = 7.0 Hz)	19.6	7, 11, 13
13*	0.97 (3H, *d*, *J* = 6.5 Hz)	20.2	7, 11, 12
14	1.09 (3H, *s*)	15.1	1, 5, 9, 10
15	-	178.2	

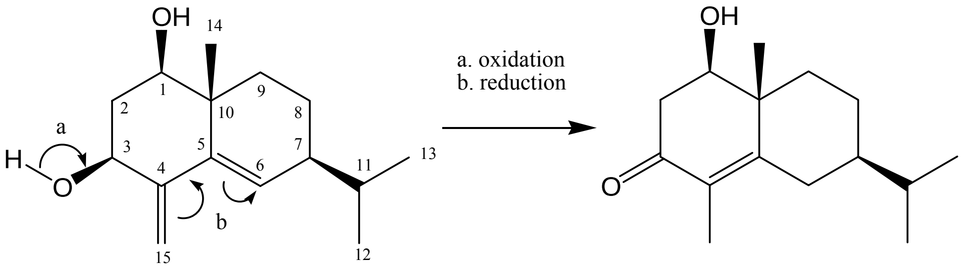
Position	δ_H	δ_C	HMBC (H→C)
1′	-	215.5	
2′	α: 2.35 (1H, *ddd*, *J* = 13.9, 5.0, 3.0 Hz) β: 2.69 (1H, *ddd*, *J* = 13.9, 12.5, 7.0 Hz)	35.9	1′, 3′, 4′, 10′ 1′, 3′, 4′
3′	α: 2.23 (1H, *m*) β: 2.28 (1H, *m*)	30.5	1′, 2′, 4′, 5′, 15′ 1′, 2′, 4′, 5′, 15′
4′	-	126.5	
5′	-	134.2	
6′	2.17 (1H, *d, J* = 12.0 Hz)	43.2	4′, 5′, 15
7′	1.48 (1H, *m*)	45.7	4, 6′, 9′, 12′
8′	α: 1.42 (1H, *m*) β: 1.55 (1H, *m*)	20.5	6′, 9′, 10′
9′	α: 1.50 (1H, *m*) β: 1.49 (1H, *m*)	35.1	1′, 5′, 7′, 8′, 10′ 1′, 5′, 7′, 8′, 10′
10′	-	48.8	
11′	2.18 (1H, *m*)	26.1	6′, 7′, 8′, 12′, 13′
12′**	0.86 (3H, *d, J* = 7.0 Hz)	21.6	7′, 11′, 13′
13′**	0.88 (3H, *d, J* = 6.5 Hz)	16.4	7′, 11′, 12′
14′	1.20 (3H, *s*)	20.5	1′, 5′, 9′, 10′
15′	α: 1.59 (1H, *d*, *J* = 17.0 Hz) β: 2.64 (1H, *dd*, *J* = 17.0, 3.5 Hz)	30.7	2, 3, 3′, 4, 4′, 5′ 2, 3, 3′, 4′, 5′

* , ** These assignments are interchangeable.

15. Structure Elucidation of Compound FF-8a [Eudesm-4(15),5-dien-1β,3β-diol]

Compound FF-8a was obtained as colorless oil (14.7 mg, 0.0007% yield). Its NMR data (**Figures 77-78, Table 23**) displayed signals of one tertiary methyl at δ 0.89 ppm (3H, *s*, H_3-14; δ_C 17.4), two isopropyl methyls at δ 0.87 (3H, *d*, *J* = 7.0 Hz, H_3-12; δ_C 19.0) and 0.89 ppm (3H, *d*, *J* = 7.0 Hz, H_3-13; δ_C 19.5), one exocyclic methylene at δ 4.96 ppm (2H, *dt*, *J* = 19.0, 2.0 Hz, H_2-15; δ_C 106.6), one olefinic methine at δ 5.61 ppm (1H, *t*, *J* = 1.5 Hz, H-6; δ_C 129.3), two oxygenated methine at δ 3.46 (1H, *dd*, *J* = 12.0, 4.0 Hz, H-1; δ_C 76.1) and 4.10 ppm (1H, *ddt*, *J* = 12.0, 5.3, 2.0 Hz, H-3; δ_C 69.6), three methylene carbons at δ 20.8 (C-8), 35.0 (C-9) and 39.7 ppm (C-2), two methine carbons at δ 32.0 (C-11) and 42.4 ppm (C-7), one quaternary carbon at δ

40.3 ppm (C-10) and two olefinic quaternary carbons at δ 142.1 (C-5) and 151.3 ppm (C-4). These data suggested a eudesmane sesquiterpenoid structure similar to compound FF-4; the differences being the location of the second hydroxyl group at C-3 instead of C-6 and the presence of another double bond between C-5 and C-6. NOE correlations (**Figure 79**) between H_3-14 and H-2β (δ 1.63 ppm), as well as between H-1 and H-3 with H-2α (δ 2.19 ppm) indicated that both hydroxyl groups at C-1 and C-3 were β-oriented. Therefore, the structure of this compound was determined to be a new eudesmane sesquiterpenoid, eudesm-4(15),5-dien-1β,3β-diol through analysis of its spectral data and comparison with those of known compounds having similar substructures. However, this sesquiterpene was unstable and could be converted through oxidation-reduction interactions spontaneously and completely into another sesquiterpenoid (compound FF-8b), as shown in **Scheme 8**.



FF-8a [eudesm-4(15),5-dien-1β,3β-diol]

FF-8b (foveoeudesmenone)

Scheme 8. Postulated conversion of eudesm-4(15),5-dien-1β,3β-diol into foveoeudesmenone

Table 23. ^{1}H- and ^{13}C-NMR spectral data for eudesm-4(15),5-dien-1β,3β-diol (300 and 75 MHz, in $CDCl_3$).

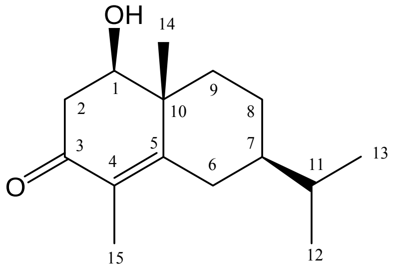
Position	δ_H	δ_C	HMBC (H→C)
1	3.46 (1H, *dd*, *J* = 12.0, 4.0 Hz)	76.1	2, 3, 9, 14
2	α: 2.19 (1H, *ddd*, *J* = 12.0, 5.3, 4.0 Hz) β: 1.63 (1H, *q*, *J* = 12.0 Hz)	39.7	1, 3, 4, 10 1, 3, 4, 10
3	4.10 (1H, *ddt*, *J* = 12.0, 5.3, 2.0 Hz)	69.6	2, 4, 15
4	-	151.3	
5	-	142.1	

Position	δ_H	δ_C	HMBC (H→C)
6	5.61 (1H, *br s*)	129.3	4, 5, 7, 8, 10, 11
7	1.99 (1H, *m*)	42.4	5, 6, 8, 11
8	1.31 (1H, *m*) 1.59 (1H, *m*)	20.8	6, 7, 9, 10, 11 6, 7, 9, 10, 11
9	1.31 (1H, *m*) 1.87 (1H, *m*)	35.0	5, 7, 8, 10, 14 5, 7, 8, 10, 14
10	-	40.3	
11	1.62 (1H, *m*)	32.0	6, 7, 8, 12, 13
12*	0.87 (3H, *d, J* = 7.0 Hz)	19.0	7, 11, 13
13*	0.89 (3H, *d, J* = 7.0 Hz)	19.5	7, 11, 12
14	0.89 (3H, *s*)	17.4	1, 5, 9, 10
15	4.93 (1H, *br s*) 4.97 (1H, *br s*)	106.6	3, 4, 5 3, 4, 5

* These assignments are interchangeable.

16. Structure Elucidation of Compound FF-8b (Foveoeudesmenone)

The molecular formula of compound FF-8b, as the product of the conversion, was determined as $C_{15}H_{24}O_2$ from its $[M + H]^+$ ion peak at *m/z* 237.1842 in the high resolution mass spectrum (**Figure 81**). The IR spectrum (**Figure 82**) exhibited absorption bands of hydroxyl group at 3423 cm^{-1}, α,β-unsaturated keto-carbonyl at 1709 and 1655 cm^{-1}, conjugated double bond at 1604 cm^{-1} and *gem*-dimethyl at 1386 and 1370 cm^{-1}. Its NMR spectra, obtained while the conversion of the natural sesquiterpene into the final product was still in progress, showed mixed signals of both the precursor (minor component) and product (major component). Compound FF-8b, as the final conversion product, displayed the ^{1}H- and ^{13}C-NMR signals (**Figures 83a-83b, 84, Table 24**) of one tertiary methyl singlet at δ 1.12 ppm (H_3-14), one olefinic methyl doublet at δ 1.74 ppm (*J* = 1.5 Hz, H_3-15), two isopropyl methyl doublets at δ 0.91 (*J* = 7.0 Hz, H_3-12) and 0.92 ppm (*J* = 7.0 Hz, H_3-13), four methylenes, two methines, one oxymethine double doublet at δ 3.77 ppm (*J* = 12.8, 5.5 Hz, H-1), one quaternary carbon at δ 41.5 ppm (C-10), two olefinic carbons of a tetra-substituted double bond at δ 129.2 (C-4) and 162.8 ppm (C-5) and one keto-carbonyl carbon at δ 197.4 ppm (C-3). These data indicated that compound FF-8b was a eudesmane sesquiterpenoid with C-1 hydroxyl substitution and a keto-carbonyl function at C-3 conjugated to a C-4/C-5 double bond. The evidence of HSQC and HMBC correlations (**Figures 85a-85c**) between the resonance of H_3-15 and those of C-3, C-4 and C-5, as well as between H-1 signal and C-3 and between H_3-14 signal and C-5, supported these assignments. NOE correlations (**Figures 86a-86b**) observed between the signals of H-1 and H-9α (δ 1.30 ppm), as well as between those of H_3-14 and H-9β (δ 2.10 ppm), confirmed the β-orientation of the hydroxyl group at C-1. Therefore, the chemical structure of compound FF-8b was elucidated as a new eudesmane-type sesquiterpene, 1β-hydroxyeudesm-4-en-3-one, and the compound was trivially named foveoeudesmenone. This proposed structure is slightly different from that of 1β-hydroxy-α-cyperone, a constituent of *Artemisia caerulescens* subsp. *gargantae* (family Asteraceae) (Sanz and Marco, 1990), by the replacement of isopropenyl side-chain with an isopropyl group for compound FF-8b.



Foveoeudesmenone

Table 24. ^{1}H- and ^{13}C-NMR spectral data for foveoeudesmenone (500 and 125 MHz, in $CDCl_3$).

Position	δ_H	δ_C	HMBC (H→C)
1	3.77 (1H, *dd*, *J* = 12.8, 5.5 Hz)	74.6	2, 3, 9, 10, 14
2	α: 2.61 (1H, *dd*, *J* = 16.5, 5.5 Hz) β: 2.53 (1H, *dd*, *J* = 16.5, 12.8 Hz)	42.3	1, 3, 4, 10 1, 3, 10
3	-	197.4	
4	-	129.2	
5	-	162.8	

Position	δ_H	δ_C	HMBC (H→C)
6	α: 1.86 (1H, *m*) β: 2.72 (1H, *ddd, J* = 15.0, 5.5, 1.5 Hz)	31.4	4, 5, 7, 8, 11 4, 5, 7, 8, 10
7	1.23 (1H, *m*)	44.2	9
8	1.68 (2H, *m*)	24.1	9
9	α: 1.30 (1H, *m*) β: 2.10 (1H, *dt, J* = 13.0, 3.0 Hz)	37.8	7, 8, 10, 14 7, 8, 10, 14
10	-	41.5	
11	1.58 (1H, *m*)	32.8	6, 7, 8, 12, 13
12*	0.91 (3H, *d, J* = 7.0 Hz)	19.3	7, 11, 13
13*	0.92 (3H, *d, J* = 7.0 Hz)	19.7	7, 11, 12
14	1.12 (3H, *s*)	16.2	1, 5, 9, 10
15	1.74 (3H, *d, J* = 1.5 Hz)	10.9	3, 4, 5

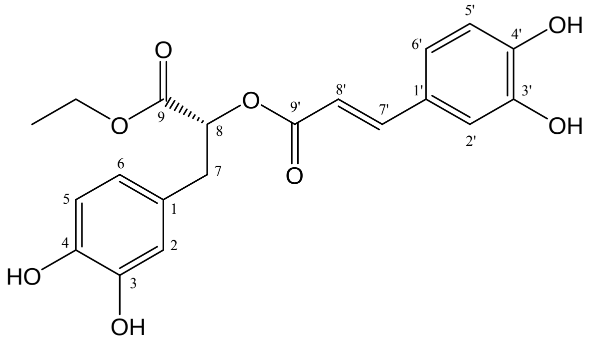
* These assignments are interchangeable.

17. Identification of Compound FF-9 (Ethyl rosmarinate)

Compound FF-9 was obtained as yellow gum (15.7 mg, 0.0008% yield). Its molecular formula was determined as $C_{20}H_{20}O_8$ from its molecular ion peak at m/z 388 in the mass spectrum (**Figure 88**). IR spectrum (**Figure 89**) showed hydroxyl absorption band at 3391 cm^{-1}, ester-carbonyl at 1724 cm^{-1}, aliphatic alkene at 1653 cm^{-1} and aromatic ring at 1445 and 1601 cm^{-1}.

Major signals in the ^1H- and ^{13}C-NMR spectra of compound FF-9 (**Figures 90-91**) include those of an ethyl group [one terminal methyl triplet at δ 1.19 ppm (3H, *J* = 7.0 Hz) and a oxymethylene quartet at δ 4.11 ppm (2H, *J* = 7.0 Hz)], a *trans*-double bond [two olefinic doublets at δ 6.55 and 7.40 ppm (1H each, *J* = 15.6 Hz, H-8′ and H-7′)], two 3,4-dihydroxybenzene moieties [two aromatic double doublets at δ 6.54 (*J* = 7.9, 2.1 Hz, H-6) and 6.93 ppm (*J* = 8.1, 1.8 Hz, H-6′) along with four aromatic doublets at δ 6.71 (*J* = 2.1 Hz, H-2), 6.71 (*J* = 7.9 Hz, H-5), 6.82 (*J* = 8.1 Hz, H-5′) and 7.06 ppm (*J* = 1.8 Hz, H-2′)], one oxymethine doublet of doublets at δ 4.75 ppm (*J* = 7.6, 6.1 Hz, H-8), one methylene carbon at δ 37.8 ppm (C-7) and two ester-carbonyl carbons at δ 166.4 (C-9′) and 172.4 ppm (C-9). Based on these NMR spectral data, it could be concluded that compound FF-9 was an ethyl ester of two phenylpropanoid units: one unit with the *trans*-double bond was caffeic acid, while another unit was 3,4-dihydroxyphenyl lactic acid. One natural example of esters formed from these two units is rosmarinic acid. Comparison of these data with literature subsequently revealed compound FF-9 to be the phenolic compound ethyl rosmarinate (Woo and Piao, 2004) (**Table 25**).

Ethyl rosmarinate has been found in plants belonging to Family Labiatae i.e. *Prunella vulgaris* (Wang *et al.,* 2000), *Nepeta prattii* (Hou, Tu, and Li, 2002) and *Lycopus lucidus* (Woo and Piao, 2004). The compound exhibited potent antioxidative activity in the nitroblue tetrazolium (NBT) superoxide scavenging assay with an IC_{50} value of 0.78 μg/ml (Woo and Piao, 2004). Although previous phytochemical study of *Ficus foveolata* has reported the presence of some phenolic compounds i.e. alkyl ferulate and alkyl diferulate in its stems (Sermboonpaisarn and Sawasdee, 2012), this is the first report of ethyl rosmarinate in the medicinal plant.



Ethyl rosmarinate

Table 25. ^{1}H- (500 MHz) and ^{13}C-NMR (125 MHz) spectral data for compound FF-9 (in acetone-*d*$_6$) and ethyl rosmarinate (in CD_3OD).

Position	FF-9		Ethyl rosmarinate*	
	δ_C	δ_H	δ_C	δ_H
1	129.3	-	128.9	-
2	117.1	6.71 (1H, *d*, *J* = 2.1 Hz)	117.8	6.72 (1H, *d*, *J* = 2.0 Hz)
3	145.7	-	146.4	-
4	144.8	-	145.6	-
5	115.9	6.71 (1H, *d*, *J* = 7.9 Hz)	116.4	6.70 (1H, *d*, *J* = 8.0 Hz)
6	121.5	6.54 (1H, *dd*, *J* = 7.9, 2.1 Hz)	122.0	6.58 (1H, *dd*, *J* = 8.0, 2.0 Hz)
7	37.8	2.92 (1H, *dd*, *J* = 13.9, 7.0 Hz) 2.99 (1H, overlapped)	38.1	3.03 (1H, *dd*, *J* = 14.0, 6.6 Hz) 3.31 (1H, *dd*, *J* = 14.0, 4.8 Hz)
8	54.9	4.75 (1H, *dd*, *J* = 7.6, 6.1 Hz)	55.4	5.05 (1H, *dd*, *J* = 7.5, 6.0 Hz)
9	172.4	-	171.9	-
1′	128.3	-	127.7	-
2′	114.9	7.06 (1H, *d*, *J* = 1.8 Hz)	115.4	7.05 (1H, *d*, *J* = 2.0 Hz)
3′	146.2	-	147.0	-
4′	147.9	-	150.1	-
5′	116.3	6.82 (1H, *d*, *J* = 8.1 Hz)	116.7	6.78 (1H, *d*, *J* = 8.0 Hz)
6′	121.7	6.93 (1H, *dd*, *J* = 8.1, 1.8 Hz)	123.4	6.96 (1H, *dd*, *J* = 8.0, 2.0 Hz)
7′	141.4	7.40 (1H, *d*, *J* = 15.6 Hz)	143.1	7.56 (1H, *d*, *J* = 16.0 Hz)
8′	118.9	6.55 (1H, *d*, *J* = 15.6 Hz)	119.3	6.27 (1H, *d*, *J* = 16.0 Hz)
9′	166.4	-	168.5	-
$O\underline{CH_2}CH_3$	61.4	4.11 (2H, *q*, *J* = 7.0 Hz)	62.6	4.15 (2H, *q*, *J* = 7.5 Hz)
$OCH_2\underline{CH_3}$	14.4	1.19 (3H, *t*, *J* = 7.0 Hz)	14.5	1.21 (3H, *t*, *J* = 7.5 Hz)

*Woo and Piao, 2004

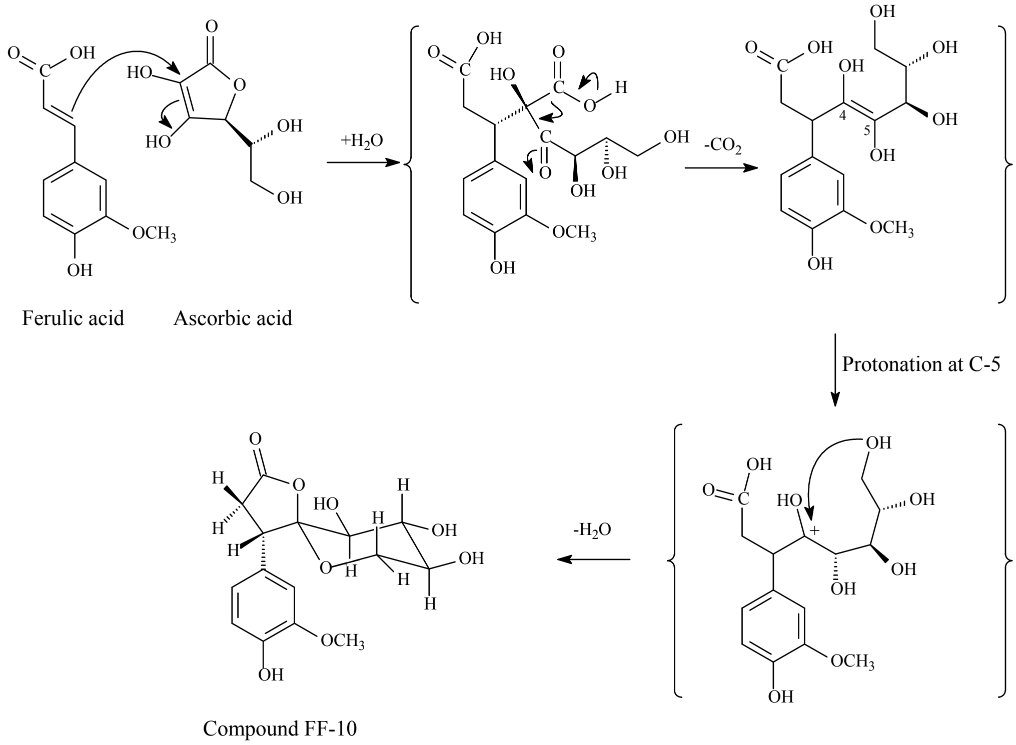
18. Structure Elucidation of Compound FF-10 (Foveospirolide)

The molecular formula of compound FF-10, which was obtained as a yellow oil (12.5 mg, 0.0006% yield), was established as $C_{15}H_{18}O_8$ from its quasi-molecular $[M + H]^+$ ion peak at m/z 327.1072 in its HR-ESI-TOF mass spectrum (**Figure 93**). Its IR absorption bands (**Figure 94**) suggested the presence of a hydroxyl (ν_{max} 3366 cm^{-1}), an ester carbonyl of a γ-butyrolactone ring (1778 cm^{-1}) and an aromatic ring (1435-1605 cm^{-1}) in the structure. The aromatic region of its

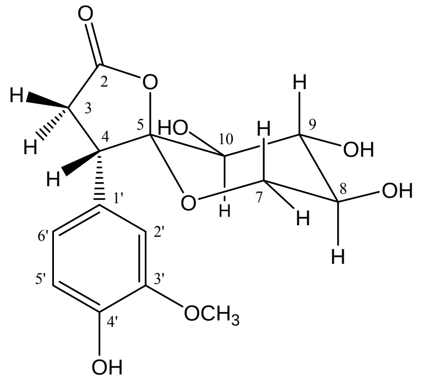
^{1}H-NMR spectrum (**Table 26** and **Figure 95**) displayed two doublets at δ 6.75 (1H, J = 8.1 Hz, H-5′) and 6.96 ppm (1H, J = 1.8 Hz, H-2′) and a double doublet at δ 6.79 ppm (1H, J = 8.1, 1.8 Hz, H-6′), indicating the presence of a 1,3,4-trisubstituted benzene ring in the molecule. In addition, the proton spectrum also exhibited a methoxyl singlet at δ 3.82 ppm (3′-OCH_3) and several one-proton resonances i.e. at δ 3.33 (*d*, J = 9.3 Hz, H-10), 3.33 (*ddd*, J = 10.9, 9.3, 5.7 Hz, H-8), 3.49 (*t*, J = 10.9 Hz, H-7 axial), 3.58 (*t*, J = 9.3 Hz, H-9) and 3.66 ppm (*dd*, J = 10.9, 5.7 Hz, H-7 equatorial) resembling the NMR pattern of sugar moiety. Its ^{13}C-NMR spectrum (**Table 26** and **Figure 96**) exhibited fifteen signals, including those of one methoxyl carbon, one benzene ring, one carbonyl carbon and five oxygen-bearing sp^3 carbons.

Analysis of COSY, HSQC and HMBC experiments showed the presence of a γ-butyrolactone group [an ester carbonyl at δ 175.0 ppm (C-2); a pair of methylene doublets of doublets at δ 3.03 (1H, J = 17.1, 12.5 Hz, H-3α) and 2.71 ppm (1H, J = 17.1, 8.4 Hz, H-3β)/δ_C 33.9; a methine double doublet at δ 4.03 (1H, J = 12.5, 8.4 Hz, H-4)/δ_C 45.2; an oxygen-bearing quaternary carbon at δ 109.2 (C-5)]. This lactone ring was connected to a trihydroxy-tetrahydropyran ring through lactol ether linkage, forming 8,9,10-trihydroxy-1,6-dioxaspiro[4,5]decan-2-one skeleton. Attachment of the benzene ring to C-4 position of the γ-lactone ring was supported by HMBC correlations (**Table 26** and **Figures 97a-97c**) observed from H-4 to the carbons at δ 113.6 (C-2′), 122.9 (C-6′) and 126.8 ppm (C-1′), and also from H-3α to C-1′. The 3′-methoxyl and 4′-hydroxyl substitutions on the aromatic ring were assigned from the HMBC cross-peaks of carbon at δ 147.8 (C-3′) with H-2′, H-5′ and methoxyl protons, as well as HMBC correlations from carbon at δ 146.7 ppm (C-4′) to H-2′, H-5′ and H-6′. The coupling constants of proton signals on the trihydroxy-tetrahydropyran ring indicated that all three hydroxyl groups were equatorially oriented in a chair conformation.

The NOESY correlation (**Figures 98a-98b**) between axial H-7 and H-9 showed that these two protons have similar orientation on the tetrahydropyran ring, while NOE correlations between both H-2′ and H-6′ with H-3α and with H-10 demonstrated that the aromatic ring and H-3α were located on the same side of the γ-butyrolactone ring. These data showed that compound FF-10 is a derivative of the sawaranospirolides, which were isolated from the heartwood of *Chamaecyparis pisifera* (family Cupressaceae) and were proposed to be biogenetically derived from L-ascorbic acid (Hasegawa, Koyanagi, and Hirose, 1990). The compound could have been biosynthesized via a chemical reaction between ferulic acid (a phenylpropanoid) and ascorbic acid, with an enediol as the intermediate, followed by subsequent formation of the lactone and tetrahydropyran rings, as shown in **Scheme 9**. Relative configuration of both C-4 and the spiro C-5 of compound FF-10 was determined as *S* based on observed NOEs and comparison of its NMR data with the sawaranospirolides. In addition, the configuration of its C-8, C-9 and C-10 (originally C-3, C-4 and C-5 of L-ascorbic acid) should therefore be *S*, *R* and *S*, respectively. Compound FF-10 thus possesses the same 4*S*, 5*S*, 8*S*, 9*R*, 10*S*-configuration as that of sawaranospirolide A, but with one additional methoxyl group at C-3′. Therefore, the structure of compound FF-10 was elucidated as (4*S*, 5*S*, 8*S*, 9*R*, 10*S*)-8,9,10-trihydroxy-4-[4′-hydroxy-3′-methoxyphenyl]-1,6-dioxaspiro[4,5]decan-2-one, and named foveospirolide.



Scheme 9. Postulated biogenesis of compound FF-10



Foveospirolide

Table 26. ^{1}H- and ^{13}C-NMR spectral data for foveospirolide (500 and 125 MHz, in CD_3OD).

Position	δ_H	δ_C	HMBC (H→C)
2	-	175.0	
3	α: 3.03 (1H, *dd*, *J* = 17.1, 12.5 Hz) β: 2.71 (1H, *dd*, *J* = 17.1, 8.4 Hz)	33.9	2, 4, 1′ 2, 4, 5
4	4.03 (1H, *dd*, *J* = 12.5, 8.4 Hz)	45.2	3, 5, 10, 1′, 2′, 6′
5	-	109.2	
7	axial: 3.49 (1H, *t*, *J* = 10.9 Hz) equatorial: 3.66 (1H, *dd*, *J* = 10.9, 5.7 Hz)	65.0	5, 8, 9 5, 8, 9
8	3.33 (1H, *ddd*, *J* = 10.9, 9.3, 5.7 Hz)	70.2	7, 9
9	3.58 (1H, *t, J* = 9.3 Hz)	75.9	10
10	3.33 (1H, *d, J* = 9.3 Hz)	71.1	4, 9
1′	-	126.8	
2′	6.96 (1H, *d, J* = 1.8 Hz)	113.6	1′, 3′, 4, 4′, 6′
3′	-	147.8	
4′	-	146.7	
5′	6.75 (1H, *d, J* = 8.1 Hz)	115.1	1′, 3′, 4′
6′	6.79 (1H, *dd, J* = 8.1, 1.8 Hz)	122.9	1′, 2′, 4, 4′
3′-OCH_3	3.82 (3H, *s*)	56.3	3′

19. Cytotoxicity and Anti-tuberculosis Activity of Compounds Isolated from *Salacia verrucosa* and *Ficus foveolata*

The new friedelane-type triterpene, 21α-hydroxyfriedelane-1,3-dione, along with four known friedelane-type compounds from *S. verrucosa* were investigated for their cytotoxic activities against human colon (SW620), lung (CHAGO), liver (HepG2), breast (BT474) and gastric (KATO-III) cancer cell lines using the MTT method. Doxorubicin was used as the positive control and any tested compound showing the IC_{50} value of less than 10 μM was considered to be strongly active. The results (**Table 27**) showed that 26-hydroxyfriedelane-1,3-dione possessed moderate cytotoxicity against all five cancer cell lines with IC_{50} values in the range of 10.16-17.74 μM, whereas 21α-hydroxyfriedelane-1,3-dione and 30-hydroxyfriedelane-1,3-dione were inactive against all cell lines tested. The less polar friedelane-1,3-dione was strongly active specifically against the colon cancer cell line with an IC_{50} value of 2.02 μM. The presence of an additional hydroxyl group at C-26 of a 1,3-diketofriedelane skeleton appears to increase the cytotoxicity of these triterpenoids. 21α-Hydroxyfriedelan-3-one was also moderately cytotoxic to the colon, liver and gastric cancer cell lines with IC_{50} values of 11.52, 11.27 and 12.81 μM, respectively, suggesting that the α-oriented hydroxyl substitution at C-21 might be essential to the cytotoxic activity of the 3-ketofriedelane triterpenoids.

These friedelane-type triterpenoids from *S. verrucosa* were also tested against the tuberculosis-causing bacteria, *Mycobacterium tuberculosis*. Four drugs commonly employed in the treatment of tuberculosis, including streptomycin, isoniazid, ofloxacin and ethambutol, were used as the positive controls. None of the assayed plant constituents was active against the pathogen at the maximal concentration of samples tested (50 μg/ml) (**Table 27**).

Table 27. Cytotoxicity and anti-tuberculosis activity of compounds isolated from *S. verrucosa* (IC_{50} and MIC in μM).

Compound	Cytotoxicity (IC_{50})					Anti-TB (MIC)
	SW620	CHAGO	HepG2	BT474	KATO-III	
Friedelane-1,3-dione	2.02	Inactive	Inactive	Inactive	Inactive	Inactive
26-Hydroxyfriedelane -1,3-dione	11.65	17.74	10.16	13.42	13.95	Inactive
21α-Hydroxyfriedelan -3-one	11.52	Inactive	11.27	Inactive	12.81	Inactive
30-Hydroxyfriedelane -1,3-dione	Inactive	Inactive	Inactive	Inactive	Inactive	Inactive
21α -Hydroxyfriedelane -1,3-dione	Inactive	Inactive	Inactive	Inactive	Inactive	Inactive
Doxorubicin	0.18	0.15	0.02	1.67	0.96	-
Streptomycin	-	-	-	-	-	2.15
Isoniazid	-	-	-	-	-	0.34
Ofloxacin	-	-	-	-	-	2.16
Ethambutol	-	-	-	-	-	18.35

From *F. foveolata*, four eudesmane-type sesquiterpenes, including two new compounds, foveolide A and foveoeudesmenone and two known compounds, 4(15)-eudesmene-1β,6α-diol and 4(15)-eudesmene-1β,5α-diol, together with one new sesquiterpenoid dimer, foveolide B, and a new phenolic compound, foveospirolide, were evaluated for their cytotoxic activities against five human cancer cell lines and *Mycobacterium tuberculosis*. The results, as seen in **Table 28**, showed that the α,β-unsaturated sesquiterpene lactone foveolide A displayed moderate cytotoxicity against colon, liver, breast and gastric cancer cell lines with IC_{50} values of 21.75, 39.97, 31.34 and 30.38 μM, respectively. The compound also exhibited weak anti-tuberculosis activity against *M. tuberculosis* with an MIC of 200 μM. Interestingly, foveolide B, which is a sesquiterpenoid dimer with one lactone ring in the skeleton, was specifically cytotoxic toward the colon cancer cell line with an IC_{50} value of 20.58 μM. No other tested compounds from this plant were active against the tuberculosis bacterium.

Table 28. Cytotoxicity and anti-tuberculosis activity of compounds isolated from *F. foveolata* (IC_{50} and MIC in μM).

Compound	Cytotoxicity (IC_{50})					Anti-TB (MIC)
	SW620	CHAGO	HepG2	BT474	KATO-III	
4(15)-Eudesmene-1β,6α-diol	Inactive	Inactive	Inactive	Inactive	Inactive	Inactive
4(15)-Eudesmene-1β,5α-diol	Inactive	Inactive	Inactive	Inactive	Inactive	Inactive
Foveolide B	20.58	Inactive	Inactive	Inactive	Inactive	Inactive
Foveolide A	21.75	Inactive	39.97	31.34	30.38	200.00
Foveoeudesmenone	Inactive	Inactive	Inactive	Inactive	Inactive	Inactive
Foveospirolide	Inactive	Inactive	Inactive	Inactive	Inactive	Inactive
Doxorubicin	0.11	1.45	0.68	1.45	1.60	-
Streptomycin	-	-	-	-	-	2.15
Isoniazid	-	-	-	-	-	0.34
Ofloxacin	-	-	-	-	-	2.16
Ethambutol	-	-	-	-	-	18.35

CHAPTER V

CONCLUSION

Phytochemical investigation of the stems of *Salacia verrucosa* (Celastraceae), which is used in traditional Thai medicine, led to the isolation of eight triterpenoids, one of which is a new friedelane-type triterpene. Two known compounds (friedelin and friedelane-1,3-dione) were isolated from the *n*-hexane-acetone extract of the stems, whereas a new friedelane-type triterpene, 21α-hydroxyfriedelane-1,3-dione, along with five known compounds including kokoonol, 26-hydroxyfriedelane-1,3-dione, 21α-hydroxyfriedelan-3-one, 3β,22α-dihydroxyolean-12-en-29-oic acid and 30-hydroxyfriedelane-1,3-dione were obtained from the EtOAc extract of the same plant part. The occurrence of friedelane-type triterpenes as major constituents in the stems of *S. verrucosa* is in accordance with previous chemotaxonomic data of plants in the family Celastraceae. Friedelane-1,3-dione was strongly and selectively cytotoxic to human colon cancer cell line, whereas 26-hydroxyfriedelane-1,3-dione displayed moderate cytotoxic activity against the colon (SW620), lung (CHAGO), liver (HepG2), breast (BT474) and gastric (KATO-III) cancer cell lines. Another friedelane triterpene with moderate cytotoxic activity was 21α-Hydroxyfriedelan-3-one, which was active against colon, liver and gastric cancer cell lines.

Chemical study of the stems of the other Thai medicinal plant, *Ficus foveolata* (Moraceae), led to the isolation of two new eudesmane-type sesquiterpenes (foveolide A and foveoeudesmenone), a new sesquiterpenoid dimer (foveolide B), and a new phenolic compound (foveospirolide) along with six known compounds. Two known triterpenes (friedelin and taraxerol) were obtained from its *n*-hexane extract, whereas all new compounds along with a known triterpene (betulin), two known eudesmane-type sesquiterpenes [4(15)-eudesmene-1β,6α-diol and 4(15)-eudesmene-1β,5α-diol] and one known phenolic compound (ethyl rosmarinate) were isolated from its CH_2Cl_2 extract. Foveolide A was moderately cytotoxic to colon, liver, breast and gastric cancer cell lines, whereas foveolide B displayed exclusive cytotoxicity against colon cancer cell line. Foveolide A was also weakly active against the tuberculosis-causing *Mycobacterium tuberculosis*. Sesquiterpenoids are rarely found in plants of the genus *Ficus* and the occurrence of a sesquiterpenoid dimer in a member of the family Moraceae is reported herein for the first time. All known compounds obtained from *F. foveolata* have been reported for the first time from this plant species.

REFERENCES

Abou-Douh, A.M. 2008. New eudesmane derivatives and other sesquiterpenes from the epigeal parts of *Dittrichia graveolens*. Chem. Pharm. Bull. 56: 1535-1545.

Aguilar-Guadarrama, A.B., and Rios, M.Y. 2004. Three new sesquiterpenes from *Croton arboreous*. J. Nat. Prod. 67: 914-917.

Ahmad, V.U., Fizza, K., and Amber, A.U.R. 1989. Odontin and odonticin, two new eudesmane sesquiterpenes from *Pluchea arguta*. J. Nat. Prod. 52: 861-863.

Al-Dabbas, M.M., Hashinaga, F., Abdelgaleil, S.A.M., Suganuma, T., Akiyama, K., and Hayashi, H. 2005. Antibacterial activity of an eudesmane sesquiterpene isolated from common Varthemia, *Varthemia iphionoides*. J. Ethnopharmacol. 97: 237-240.

Andrade, S.F., Comunello, E., Noldin, V.F., Monache, F.D., Filho, V.C., and Niero, R. 2008. Antiulcerogenic activity of fractions and 3,15-dioxo-21α-hydroxyfriedelane isolated from *Maytenus robusta* (Celastraceae). Arch. Pharm. Res. 31: 41-46.

Anjaneyulu, A.S.R., and Rao, M.N. 1980. Elaeodendrol and elaeodendradiol, new nor-triterpenes from *Elaeodendron glaucum*. Phytochemistry 19: 1163-1169.

Antonisamy, P., Duraipandiyan, V., and Ignacimuthu, S. 2011. Anti-inflammatory, analgesic and antipyretic effects of friedelin isolated from *Azima tetracantha* Lam. in mouse and rat models. J. Pharm. Pharmacol. 63: 1070-1077.

Ardiles, A.E., Rodriguez, A.G., Nunez, M.J., Perestelo, N.R., Pardo, V., Jiménez, I.A., Valverde, A.M., and Bazzocchi, I.L. 2012. Studies of naturally occurring friedelane triterpenoids as insulin sensitizers in the treatment of type 2 diabetes mellitus. Phytochemistry 84: 116-124.

Arunakumara, K.K.I.U., and Subasinghe, S. 2010. *Salacia reticulata* Wight: a review of botany, phytochemistry and pharmacology. Trop. Agric. Res. Ext. 13: 41-47.

Berg, C.C. 2007. Precursory taxonomic studies on *Ficus* (Moraceae) for the Flora of Thailand. Thai For. Bull. (Bot.) 35: 4-28.

Betancor, C., Freire, R., Gonzalez, A.G., Salazar, J.A., Pascard, C., and Prange, T. 1980. Three triterpenes and other terpenoids from *Catha cassinoides*. Phytochemistry 19: 1989-1993.

Bohlmann, F., Athes, N., King, R.M., and Robinson, H. 1983. Two sesquiterpenoids from *Senecio* species. Phytochemistry 22: 1675-1677.

Cantrell, C.L., Franzblau, S.G., and Fisher, N.H. 2001. Antimycobacterial plant triterpenoids. Planta Med. 67: 685-694.

Carmichael, J., DeGraff, W.G., Gazdar, A.F., Minna, J.D., and Mitchell, B. 1987. Evaluation of a tetrazolium based semiautomated colorimetric assay; assessment of chemosensitivity testing. Cancer Res. 47: 936-942.

Celastraceae. 2013. Encyclopaedia Britannica [Online]. Encyclopaedia Britannica Inc. Available from: http://www.britannica.com/EBchecked/topic/101203/Celastraceae.html [2013, January 28]

Changsen, C., Franzblau, S.G., and Palittapongarnpim, P. 2003. Improved green fluorescent protein reporter gene-based microplate screening for antituberculosis compounds by utilizing an acetamidase promoter. Antimicrob. Agents Chemother. 47: 3682-3687.

Chaturvedula, V.S.P., Farooq, A., Schilling, J.K., Malone, S., Derveld, I., Werkhoven, M.C.M., Wisse, J.H., Ratsimbason, M., and Kingston, D.G.I. 2004. New eudesmane derivatives from *Melampodium camphoratum* from the Surinam rainforest. J. Nat. Prod. 67: 2053-2057.

Chaudhary, L.B., Sudhakar, J.V., Kumar, A., Bajpai, O., Tiwari, R., and Murthy, G.V.S. 2012. Synopsis of the Genus *Ficus* L. (Moraceae) in India. Taiwania 57: 193-216.

Chavez, H., Estevez-Braun, A., Ravelo, A.G., and Gonzalez, A.G. 1998. Friedelane triterpenoids from *Maytenus macrocarpa*. J. Nat. Prod. 61: 82-85.

Cheng, Z.H., Wu, T., Bligh, S.W.A., Bashall, A., and Yu, B.Y. 2004. *cis*-Eudesmane sesquiterpene glycosides from *Liriope muscari* and *Ophiopogon japonicus*. J. Nat. Prod. 67: 1761-1763.

Chhetri, R.B. 2010. Ethnobotany of Moraceae in Meghalaya north-east India. Kathmandu Univ. J. Sci., Eng. Technol. 6: 5-10.

Chiang, Y.M., Chang, J.Y., Kuo, C.C., Chang, C.Y., and Kuo, Y.H. 2005. Cytotoxic triterpenes from the aerial roots of *Ficus microcarpa*. Phytochemistry 66: 495-501.

Chuakul, W., Saralamp, P., and Boonpleng, A. 2002. Medicinal plants used in the Kutchum District, Yasothon Province, Thailand. Thai J. Phytopharm. 9: 22-49.

Connolly, J.D., and Hill, R.A. 1991. Dictionary of terpenoids : volume 1 mono- and sesquiterpenoids. Cambridge: Chapman & Hall.

Corsino, J., Carvalho, P.R.F., Kato, M.J., Latorre, L.R., Oliveira, O.M.M.F., Araujo, A.R., Bolzani, V.S., Franca, S.C., Pereira, A.M.S., and Furlan, M. 2000. Biosynthesis of friedelane and quinonemethide triterpenoids is compartmentalized in *Maytenus aquifolium* and *Salacia campestris*. Phytochemistry 55: 741-748.

Damu, A.G., Kuo, P.C., Shi, L.S., Li, C.Y., Kuoh, C.S., Wu, P.L., and Wu, T.S. 2005. Phenanthroindolizidine alkaloids from the stems of *Ficus septica*. J. Nat. Prod. 68: 1071-1075.

Damu, A.G., Kuo, P.C., Shi, L.S., Li, C.Y., Su, C.R., and Wu, T.S. 2009. Cytotoxic phenanthroindolizidine alkaloids from the roots of *Ficus septica*. Planta Med. 75: 1152-1156.

Dantanarayana, A.P., Kumar, N.S., Muthukuda, M., and Balasubramaniam, S. 1983. Triterpenes from the leaves of *Pleurostylia opposita*. Phytochemistry 22: 473-474.

David, J.P., Santos, I.D.D., and David, J.M. 2004. A new sesquiterpene from the fruits of *Allophylus laevigatus*. Fitoterapia 75: 795-798.

Del Recio, M.C., Giner, R.M., Manez, S., Gueho, J., Julián, H.R., Hostettmann, K., and Rios, J.L. 1995. Investigations on the steroidal anti-inflammatory activity of triterpenoid from *Diospyros leucomelas*. Planta Med. 61: 9-12.

Dhanabalasingham, B., Karunaratne, V., Tezuka, Y., Kikuchi, T., and Gunatilaka, A.L.L. 1996. Biogenetically important quinonemethides and other triterpenoid constituents of *Salacia reticulata*. Phytochemistry 42: 1377-1385.

Duarte, L.P., Figueiredo, R.C., Sousa, G.F., Soares, D.B.S., Rodrigues, S.B.V., and Silva, F.C. 2010. Chemical constituents of *Salacia elliptica* (Celastraceae). Quim. Nova 33: 900-903.

Duarte, L.P., Miranda, R.R.S., Rodrigues, S.B.V., Silva, G.D.F., Filho, S.A.V., and Knupp, V.F. 2009. Stereochemistry of 16α-hydroxyfriedelin and 3-oxo-16-methylfriedel-16-ene established by 2D NMR spectroscopy. Molecules 14: 598-607.

Duraipandiyan, V., Gnanasekar, M., and Ignacimuthu, S. 2010. Antifungal activity of triterpenoid isolated from *Azima tetracantha* leaves. Folia Histochem. Cyto. 48: 311-313.

El-Askary, H.I., Meselhy, M.R., and Galal, A.M. 2003. Sesquiterpenes from *Cymbopogon proximus*. Molecules 8: 670-677.

Estrada, R., Cardenas, J., Esquivel, B., and Rodríguez-Hahn, L. 1994. D:A-Friedo-oleanane triterpenes from the roots of *Acanthothamnus aphyllus*. Phytochemistry 36: 747-751.

Fang, P.L., Liu, H.Y., and Zhong, H.M. 2012. A new eudesmane sesquiterpenoid lactone from *Chloranthus japonicus*. Chin. J. Nat. Med. 10: 0024-0027.

Fang, S.D., Berry, D.E., Lynn, D.G., Hecht, S.M., Campbell, J., and Lynn, W.S. 1984. The chemistry of toxic principles from *Maytenus nemerosa*. Phytochemistry 23: 631-633.

Figueiredo, J.N., Raz, B., and Sequin, U. 1998. Novel quinone methides from *Salacia kraussii* with *in vitro* antimalarial activity. J. Nat. Prod. 61: 718-723.

Fraga, B.M., Hernandez, M.G., Mestres, T., Arteaga, J.M., and Perales, A. 1993. Eudesmane sesquiterpenes from *Teucrium heterophyllum*. The X-ray structure of teucdiol A. Phytochemistry 34: 1083-1086.

Fu, B., Su, B.N., Takaishi, Y., Honda, G., Ito, M., Takeda, Y., Kodzhimatov, O.K., and Ashurmetov, O. 2001. A bis-sesquiterpene and sesquiterpenolides from *Inula macrophylla*. Phytochemistry 58: 1121-1128.

Furbacher, T.R., and Gunatilaka, A.L.L. 2001. Catalytic inhibition of topoisomerase IIα by demethylzeylasterone, a 6-oxophenolic triterpenoid from *Kokoona zeylanica*. J. Nat. Prod. 64: 1294-1296.

Gao, H.Y., Guo, Z.H., Cheng, P., Xu, X.M., and Wu, L.J. 2010. New triterpenes from *Salacia hainanensis* Chun et How with α-glucosidase inhibitory activity. J. Asian Nat. Prod. Res. 12: 834-842.

Garcez, F.R., Garcez, W.S., and Miranda, L.H.A.C.M. 2010. Eudesmane and rearranged eudesmane sesquiterpenes from *Nectandra cissiflora*. Quim. Nova 33: 1739-1742.

Gibernau, M., Buser, H.R., Frey, J.E., and Hossaert-McKey, M. 1997. Volatile compounds from extracts of figs of *Ficus carica*. Phytochemistry 46: 241-244.

Giner, R.M., Gray, A.I., Gibbons, S., and Waterman, P.G. 1993. Friedelane triterpenes from the stem bark of *Caloncoba glauca*. Phytochemistry 33: 237-239.

Gonzalez, A.G., Barrera, J.B., Yanes, A.C., Diaz, J.G., and Perez, E.M.R. 1989. Chromenes and benzofurans from *Ageratina glechonophylla*. Phytochemistry 28: 2520-2522.

Goren, N. 1996. Eudesmane-type sesquiterpenes from *Tanacetum praeteritum* subsp. *praeteritum*. Phytochemistry 42: 747-749.

Grison, L., Edwards, A.A., and Hossaert-McKey, M. 1999. Interspecies variation in floral fragrances emitted by tropical *Ficus* species. Phytochemistry 52: 1293-1299.

Gunatilaka, A.A.L. 1986. Triterpenoids and steroids of Sri Lankan plants: a review of occurrence and chemistry. J. Natn. Sci. Coun. Sri Lanka 14: 1-54.

Gunatilaka, A.A.L., Nanayakkara, N.P.D., and Sultanbawa, M.U.S. 1979. Chemical investigation of Ceylonese plants. Part 37. Structures of three new 6β-hydroxy di- and tri-oxygenated friedelane triterpenes from *Kokoona zeylanica* Thw. (Celastraceae). Tetrahedron Lett. 19: 1727-30.

Gunatilaka, A.A.L., Nanayakkara, N.P.D., and Sultanbawa, M.U.S. 1983a. Studies on terpenoids and steroids. Part 1. Structures of six novel 27-hydroxy and 6β-hydroxy di- and tri-oxygenated D:A-friedo-oleanane triterpenes from *Kokoona zeylanica*. J. Chem. Soc. Perkin Trans I. 2459-2469.

Gunatilaka, A.A.L., Nanayakkara, N.P.D., Sultanbawa, M.U.S., and Balasubramaniam, S. 1982. Friedelin, D:A-friedo-olean-3,21-dione and 21α-hydroxy-D:A-friedo-olean-3-one from *Kokoona zeylanica*. Phytochemistry 21: 2061-2063.

Gunatilaka, A.A.L., Nanayakkara, N.P.D., and Wazeer, M.I.M. 1983b. ^{13}C NMR spectra of some D:A-friedo-oleananes. Phytochemistry 22: 991-992.

Gutierrez, A.B., and Herz, W. 1988. Guaianolides and other constituents of *Helianthus microcephalus*. Phytochemistry 27: 2225-2228.

Han, Y.F., Cao, G.X., and Xia, M. 2009. Two new eudesmane sesquiterpenes from *Lactuca sativa* var. *anagustata* L. Chin. Chem. Lett. 20: 1211-1214.

Hasegawa, S., Koyanagi, H., and Hirose, Y. 1990. Decarboxylated ascorbigens in the heartwood of *Chamaecyparis pisifera*. Phytochemistry 29: 261-266.

Hisham, A., Kumar, G.J., Fujimoto, Y., and Hara, N. 1995. Salacianone and salacianol, two triterpenes from *Salacia beddomei*. Phytochemistry 40: 1227-1231.

Hisham, A., Kumar, G.J., Fujimoto, Y., and Hara, N. 1996a. 20,29-Epoxysalacianone and 6β-hydroxysalacianone, two lupane triterpenes from *Salacia beddomei*. Phytochemistry 42: 789-794.

Hisham, A., Kumar, G.J., Fujimoto, Y., and Hara, N. 1996b. 1β,15α-Dihydroxyfriedelan-3-one, a triterpene from *Salacia beddomei*. Phytochemistry 43: 843-845.

Hou, D., Savinov, I.A., and Van Welzen, P.C. 2010. Celastraceae. In T. Santisuk, and K. Larsen (eds.), Flora of Thailand, pp. 141-198. Bangkok: Prachachon.

Hou, Z.F., Tu, Y.Q., and Li, Y. 2002. Three new phenolic compounds from *Nepeta prattii*. J. Chin. Chem. Soc. 49: 255-258.

Hu, J.F., Bai, S.P., and Jia, Z.J. 1996. Eudesmane sesquiterpenes from *Artemisia eriopoda*. Phytochemistry 43: 815-817.

Hua, Y., Zhou, L.Y., Xi, J., and Chen, C.X. 2004. Eudesmane sesquiterpene glycosides from *Parepigynum funingense*. Fitoterapia 75: 236-238.

Huang, J., Guo, Z.H., Cheng, P., Sun, B.H., and Gao, H.Y. 2012. Three new triterpenoids from *Salacia hainanensis* Chun et How showed effective anti-α-glucosidase activity. Phytochemistry Lett. 5: 432-437.

Ismail, T.S., Gopalakrishnan, S., Begum, V.H., and Elango, V. 1997. Anti-inflammatory activity of *Salacia oblonga* Wall. and *Azima tetracantha* Lam. J. Ethnopharmacol. 56: 145-152.

Itharat, A., Houghton, P.J., Eno-Amooquaye, E., Burke, P.J., Sampson, J.H., and Raman, A. 2004. *In vitro* cytotoxic activity of Thai medicinal plants used traditionally to treat cancer. J. Ethnopharmacol. 90: 33-38.

Itokawa, H., Morita, H., and Watanabe, K. 1987. Novel eudesmane-type sesquiterpenes from *Alpinia japonica* (Thunb.) Miq. Chem. Pharm. Bull. 35: 1460-1463.

Itokawa, H., Shirota, O., Ikuta, H., Morita, H., Takeya, K., and Iitaka, Y. 1991. Triterpenes from *Maytenus ilicifolia*. Phytochemistry 30: 3713-3716.

Jakupovic, J., Schuster, A., Bohlmann, F., and Dillon, M.O. 1988. Lumiyomogin, ferreyrantholide, fruticolide and other sesquiterpene lactones from *Ferreyranthus fruticosus*. Phytochemistry 27: 1113-1120.

Jamal, A.K., Yaacob, W.A., and Din, L.B. 2009. Triterpenes from the root bark of *Phyllanthus columnaris*. Aust. J. Basic Appl. Sci. 3: 1428-1431.

Jangruang, A., Sudta, P., Ratananukul, P., and Suksamrarn, S. 2009. Chemical constituents of the *Salacia verrucosa* Wight stem. SWU Sci. J. 25: 61-72.

Jiang, C., Liu, Z.H., Li, L., Lin, B.B., Yang, F., and Qin, M.J. 2012. A new eudesmane sesquiterpene glycosides from *Liriope muscari*. J. Asian Nat. Prod. Res. 14: 491-495.

Jiang, J., Li, Y., Chen, Z., Min, Z., and Lou, F. 2006. Two novel C_{29}-5β-sterols from the stems of *Opuntia dillenii*. Steroids 71: 1073-1077.

Joseph, B., and Raj, S.J. 2010. Phytopharmacological properties of *Ficus racemosa* Linn.-an overview. Int. J. Pharm. Sci. Rev. Res. 3: 134-138.

Kamel, A. 1995. 7-*epi*-Eudesmanes from *Teucrium polium*. J. Nat. Prod. 58: 428-431.

Karamenderes, C., Bedir, E., Pawar, R., Baykan, S., and Khan, I.A. 2007. Elemanolide sesquiterpenes and eudesmane sesquiterpene glycosides from *Centaurea hierapolitana*. Phytochemistry 68: 609-615.

Karunanayake, E.H., and Sirimanne, S.R. 1985. Mangiferin from the root bark of *Salacia reticulata*. J. Ethnopharmacol. 13: 227-228.

Kawazoe, K., Shimogai, N., Takaishi, Y., Rao, K.S., and Imakura, Y. 1997. Four stilbenes from *Salacia lehmbachii*. Phytochemistry 44: 1569-1573.

Khanina, M.A., Kulyyasov, A.T., Bagryanskaya, I.Y., Gatilov, Y.V., Adekenov, S.M., and Raldugin, V.A. 1998. 3-Oxocostusic acid from *Artemisia altaiensis*. Chem. Nat. Compd. 34: 145-147.

Kishi, A., Morikawa, T., Matsuda, H., and Yoshikawa, M. 2003. Structures of new friedelane- and norfriedelane-type triterpenes and polyacylated eudesmane-type sesquiterpene from *Salacia chinensis* Linn. (*S. prinoides* DC., Hippocrateaceae) and radical scavenging activities of principle constituents. Chem. Pharm. Bull. 51: 1051-1055.

Kitajima, J., Kimizuka, K., and Tanaka, Y. 2000. Three new sesquiterpenoid glucosides of *Ficus pumila* fruit. Chem. Pharm. Bull. 48: 77-80.

Kitajima, J., Suzuki, N., Satoh, M., and Watanabe, M. 2002. Sesquiterpenoids of *Torilis japonica* fruit. Phytochemistry 59: 811-815.

Klass, J., and Tinto, W.F. 1992. Friedelane triterpenoids from *Peritassa compta*: complete ^{1}H and ^{13}C assignments by 2D NMR spectroscopy. J. Nat. Prod. 55: 1626-1630.

Kokpol, U., and Chavasiri, W. 1990. Taraxeryl *cis-p*-hydroxycinnamate, a novel taraxeryl from *Rhizophora apiculata*. J. Nat. Prod. 53: 953-955.

Kuete, V., Nana, F., Ngameni, B., Mbaveng, A.T., Keumedjio, F., and Ngadjui, B.T. 2009. Antimicrobial activity of the crude extract, fractions and compounds from stem bark of *Ficus ovata* (Moraceae). J. Ethnopharmacol. 124: 556-561.

Kumar, V., Wazeer, M.I.M., and Wijeratne, D.B.T. 1985. 21α,26-Dihydroxy-D:A-friedooleanan-3-one from *Salacia reticulata* var. *diandra* (Celastraceae). Phytochemistry 24: 2067-2069.

Kumar, V., Wijeratne, D.B.T., and Abeygunawardena, C. 1990. 21α,30-Dihydroxy-D:A-friedooleanan-3-one from *Salacia reticulata* var. *β-diandra* stem bark. Phytochemistry 29: 333-335.

Kunwar, R.M., and Bussmann, R.W. 2006. *Ficus* (Fig) species in Nepal: a review of diversity and indigenous uses. Lyonia 11: 85-97.

Kuo, Y.H., and Chen, C.H. 1997. Diversifolol, a novel rearranged eudesmane sesquiterpene from the leaves of *Tithonia diversifolia*. Chem. Pharm. Bull. 45: 1223-1224.

Kutney, J.P., Hewitt, G.M., Lee, G., Piotrowska, K., Roberts, M., and Rettig, S.J. 1992. Studies with tissue cultures of the Chinese herbal plant, *Tripterygium wilfordii*. Isolation of metabolites of interest in rheumatoid arthritis, immunosuppression, and male contraceptive activity. Can. J. Chem. 70: 1455-1474.

Kutney, J.P., Samija, M.D., Hewitt, G.M., Bugante, E.C., and Gu, H. 1993. Anti-inflammatory oleanane triterpenes from *Tripterygium wilfordii* cell suspension cultures by fungal elicitation. Plant Cell Rep. 12: 356-359.

Lansky, E.P., Paavilainen, H.M., Pawlus, A.D., and Newman, R.A. 2008. *Ficus* spp. (fig): ethnobotany and potential as anticancer and anti-inflammatory agents. J. Ethnopharmacol. 119: 195-213.

Lee, T.H., Kuo, Y.C., Wang, G.J., Kuo, Y.H., Chang, C.I., Lu, C.K., and Lee, C.K. 2002. Five new phenolics from the roots of *Ficus beecheyana*. J. Nat. Prod. 65: 1497-1500.

Li, Y., Huang, T.H.W., and Yamahara, J. 2008. *Salacia* root, a unique Ayuravedic medicine, meets multiple targets in diabetes and obesity. Life Sci. 82: 1045-1049.

Li, Y.C., and Kuo, Y.H. 2000. Four new compounds, ficusal, ficusesquilignan A, B, and ficusolide diacetate from the heartwood of *Ficus microcarpa*. Chem. Pharm. Bull. 48: 1862-1865.

Li, R.W., Leach, D.N., Myers, S.P., Lin, G.D., Leach, G.J., and Waterman, P.G. 2004. A new anti-inflammatory glucoside from *Ficus racemosa* L. Planta Med. 70: 421-426.

Lin, Y., Jin, T., Wu, X., Huang, Z., and Fan, J. 1997. A novel bisesquiterpenoid, biatractylolide, from the Chinese herbal plant *Atractylodes macrocephala*. J. Nat. Prod. 60: 27-28.

Liu, Y.B., Jia, W., Yao, Z., Pan, Q., Takaishi, Y., and Duan, H.Q. 2007. Two eudesmane sesquiterpenes from *Laggera pterodonta*. J. Asian Nat. Prod. Res. 9: 233-237.

Mabberley, D.J. 1990. The plant-book: a portable dictionary of the higher plants. Avon: Bath Press.

Mahmoud, A.A. 1997. 7-*Epi*-eudesmanes, eudesmanoic acids, eudesmanolides and other sesquiterpenes from *Pluchea dioscoridis*. Phytochemistry 45: 1633-1638.

Makhija, I.K., Sharma, I.P., and Khamar, D. 2010. Phytochemistry and pharmacological properties of *Ficus religiosa*: an overview. Ann. Biol. Res. 1: 171-180.

Matsuda, H., Morikawa, T., and Yoshikawa, M. 2002. Antidiabetogenic constituents from several natural medicines. Pure. Appl. Chem. 74: 1301-1308.

Matsuda, H., Murakami, T., Yashiro, K., Yamahara, J., and Yoshikawa, M. 1999. Antidiabetic principles of natural medicines. IV. Aldose reductase and α-glucosidase inhibitors from the roots of *Salacia oblonga* Wall. (Celastraceae): structure of a new friedelane-type triterpene, kotalagenin 16-acetate. Chem. Pharm. Bull. 47: 1725-1729.

Matsuda, H., Yoshikawa, M., Morikawa, T., Tanabe, G., and Muraoka, O. 2005. Antidiabetogenic constituents from *Salacia* species. J. Trad. Med. 22(Suppl. 1): 145-153.

Mbosso, E.J.T., Nguedia, J.C.A., Meyer, F., Lenta, B.N., Ngouela, S., Lallemand, B., Mathieu, V., Antwerpen, P.V., Njunda, A.L., Adiogo, D., Tsamo, E., Looze, Y., Kiss, R., and Wintjens, R. 2012. Ceramide, cerebroside and triterpenoid saponin from the bark of aerial roots of *Ficus elastica* (Moraceae). Phytochemistry 83: 95-103.

Mena-Rejon, G.J., Perez-Espadas, A.R., Moo-Puc, R.E., Cedillo-Rivera, R., Bazzocchi, I.L., Jiménez-Diaz, I.A., and Quijano, L. 2007. Antigiardial activity of triterpenoids from root bark of *Hippocratea excelsa*. J. Nat. Prod. 70: 863-865.

Minh, T.T., Nguyen, T.H.A., Thang, V.D., and Sung, T.V. 2010. Study on chemical constituents and cytotoxic activities of *Salacia chinensis* growing in Vietnam. Z. Naturforsch 65: 1284-1288.

Moraceae. 2013. Encyclopaedia Britannica [Online]. Encyclopaedia Britannica Inc. Available from: http://www.britannica.com/EBchecked/topic/391683/Moraceae.html [2013, January 28]

Morikawa, T., Kishi, A., Pongpiriyadacha, Y., Matsuda, H., and Yoshikawa, M. 2003. Structures of new friedelane-type triterpenes and eudesmane-type sesquiterpene and aldose reductase inhibitors from *Salacia chinensis*. J. Nat. Prod. 66: 1191-1196.

Mukhamatkhanova, R.F., Turgunov, K.K., Tashkhodzhaev, B., Sham'yanov, I.D., and Saidkhodzhaev, A.I. 2004. Eudesmanolides from *Artemisia lehmanniana*. Crystal and molecular structures of 1α-acetoxy-4α-hydroxy-5,7α,6,11β(H)-eudesm-2,3-en-6,12-olide and 1α-acetoxy-3α-hydroxy-5,7α,6,11β(H)-eudesm-4,15-en-6,12-olide. Chem. Nat. Compd. 40: 557-559.

Mukherjee, P.K., Maiti, K., Mukherjee, K., and Houghton, P.J. 2006. Leads from Indian medicinal plants with hypoglycemic potentials. J. Ethnopharmacol. 106: 1-28.

Nakagawa, H., Takaishi, Y., Fujimoto, Y., Duque, C., Garzon, C., Sato, M., Okamoto, M., Oshikawa, T., and Ahmed, S.U. 2004. Chemical constituents from the Colombian medicinal plant *Maytenus laevis*. J. Nat. Prod. 67: 1919-1924.

Nakamura, S., Zhang, Y., Matsuda, H., Ninomiya, K., Muraoka, O., and Yoshikawa, M. 2011. Chemical structures and hepatoprotective effects of constituents from the leaves of *Salacia chinensis*. Chem. Pharm. Bull. 59: 1020-1028.

Nakamura, S., Zhang, Y., Pongpiriyadacha, Y., Wang, T., Matsuda, H., and Yoshikawa, M. 2008a. Megastigmane glycosides from the leaves of *Salacia chinensis*. Heterocycles 75: 131-143.

Nakamura, S., Zhang, Y., Wang, T., Matsuda, H., and Yoshikawa, M. 2008b. New phenolic glycosides from the leaves of *Salacia chinensis*. Heterocycles 75: 1435-1446.

Nascimento, M., Arruda, A.C., Arruda, M.S.P., Muler, A.H., and Yoshioka, C.Y. 1999. Aripuanin, a megastigmane skeleton from *Ficus aripuanensis*. Fitoterapia 70: 628-629.

Naya, K., Okayama, T., Fujiwara, M., Nakata, M., Ohtsuka, T., and Kurio, S. 1990. Sesquiterpenes from the rhizomes of *Ligularia dentata* Hara. Bull. Chem. Soc. Jpn. 63: 2239-2245.

Niogret, J., Montgomery, W.S., Kendra, P.E., Health, R.R., and Epsky, N.D. 2011. Attraction and electroantennogram responses of male Mediterranean fruit fly to volatile chemicals from *Persea*, *Litchi* and *Ficus* wood. J. Chem. Ecol. 37: 483-491.

Nozaki, H., Matsuura, Y., Hirono, S., Kasai, R., Tada, T., Nakayama, M., and Lee, K.H. 1991. Maytensifolin-C, a friedelane alcohol from *Maytenus diversifolia*. Phytochemistry 30: 3819-3821.

Nozaki, H., Suzuki, H., Hirayama, T., Kasai, R., Wu, R.Y., and Lee, K.H. 1986. Antitumour triterpenes of *Maytenus diversifolia*. Phytochemistry 25: 479-485.

Nozaki, H., Suzuki, H., Lee, K.H., and McPhail, A.T. 1982. Structure and stereochemistry of maytenfolic acid and maytenfoliol, two new antileukemic triterpenes from *Maytenus diversifolia*: *X*-ray crystal structure. J. Chem. Soc., Chem. Commun. 18: 1048-1051.

Nunez, M.J., Ardiles, A.E., Martinez, M.L., Torres-Romero, D., Jiménez, I.A., and Bazzocchi, I.L. 2012. Unusual D:B-friedobaccharane and oxygenated friedelane-type triterpenoids from Salvadorean Celastraceae species. Phytochemistry Lett. 5: 244-248.

Ogunwande, I.A., Flamini, G., Adefuye, A.E., Lawal, N.O., Moradeyo, S., and Avoseh, N.O. 2011. Chemical compositions of *Casuarina equisetifolia* L., *Eucalyptus toreliana* L. and *Ficus elastica* Roxb. Ex Hornem cultivated in Nigeria. S. Afr. J. Bot. 77: 645-649.

Ogunwande, I.A., Saroglou, V., Skaltsa, E., Ogunbinu, A.O., and Kubmarawa, D. 2009. Constituents of some essential oil bearing plants from Nigeria. J. Essent. Oil Res. 21: 61-66.

Oikawa, H., and Tokiwano, T. 2004. Enzymatic catalysis of the Diels-Alder reaction in the biosynthesis of natural products. Nat. Prod. Rep. 21: 321-352.

Oliveira, A.P., Silva, L.R., Pinho, P.G., Gil-Izquierdo, A., Valentao, P., Silva, B.M., Pereira, J.A., and Andrade, P.B. 2010. Volatile profiling of *Ficus carica* varieties by HS-SPME and GC-IT-MS. Food Chem. 123: 548-557.

Oliveira, D.M., Silva, G.D.F., Duarte, L.P., Filho, S.A.V., Guimaraes, L., Duarte, H.A., and Souza, E. 2009. Conformational study of 3β,16β-dihydroxyfriedelane by NMR and ab initio calculations. Struct. Chem. 20: 1005-1011.

Orabi, K.Y., Mossa, J.S., Muhammed, I., Alloush, M., Galal, A.M., El-Feraly, F.S., and McPhail, A.T. 2000. New eudesmane sesquiterpenes from *Plectranthus cylindraceus*. J. Nat. Prod. 63: 1665-1668.

Oramas-Royo, S.M., Chavez, H., Rodríguez, P.M., Perez, L.F., Ravelo, A.G., and Braun, A.E. 2010. Cytotoxic triterpenoids from *Maytenus retusa*. J. Nat. Prod. 73: 2029-2034.

Ozaki, S., Oe, H., and Kitamura, S. 2008. α-Glucosidase inhibitor from Kothala-himbutu (*Salacia reticulata* Wight). J. Nat. Prod. 71: 981-984.

Paarakh, P.M., Patil, L.J., and Thanga, S.A. 2008. Genus *Salacia*: a comprehensive review. J. Nat. Remedies 8: 116-131.

Paulo, R.F.C., Dulce, H.S.S., Vanderlan, S.B., and Maysa, F. 2005. Antioxidant quinonemethide triterpenes from *Salacia campestris*. Chem. Biodivers. 2: 367-372.

Peraza-Sanchez, S.R., Chai, H.B., Shin, Y.G., Santisuk, T., Reutrakul, V., Farnsworth, N.R., Cordell, G.A., Pezzuto, J.M., and Kinghorn, A.D. 2002. Constituents of the leaves and twigs of *Ficus hispida*. Planta Med. 68: 186-188.

Quijano, L., Gomez-Garibay, F., Trejo-B, R.I., and Rios, T. 1991. Hydroxy-bis-dihydroencelin, a dimeric eudesmanolide and other eudesmanolides from *Montanoa speciosa*. Phytochemistry 30: 3293-3295.

Raharivelomanana, P., Bianchini, J.P., Ramanoelina, A.R.P., Rasoarahona, J.R.E., Faure, R., and Cambon, A. 1998. Eudesmane sesquiterpenes from *Laggera alata*. Phytochemistry 47: 1085-1088.

Ramaiah, P.A., Devi, P.U., Frolow, F., and Lavie, D. 1984. 3-Oxo-friedelan-20α-oic acid from *Gymnosporia emarginata*. Phytochemistry 23: 2251-2255.

Royal Forest Department. The Forest Herbarium. 2001. Thai plant names: Tem Smitinand. Revised Ed. Bangkok: Prachachon.

Rzeski, W., Stepulak, A., Szymanski, M., Juszczak, M., Grabarska, A., Sifringer, M., Kaczor, J., and Kandefer-Szerszen, M. 2009. Betulin elicits anti-cancer effects in tumour primary cultures and cell lines *in vitro*. Basic Clin. Pharmacol. Toxicol. 105: 425-432.

Sanz, J.F., and Marco, J.A. 1990. Sesquiterpene lactones from *Artemisia caerulescens* subsp. *gargantae*. Phytochemistry 29: 2913-2917.

Semwal, S., and Sharma, R.K. 2011. Antibacterial sesquiterpene lactone glucoside from seed pods of *Bauhinia retusa*. J. Asian Nat. Prod. Res. 13: 75-79.

Sermboonpaisarn, T., and Sawasdee, P. 2012. Potent and selective butyrylcholinesterase inhibitors from *Ficus foveolata*. Fitoterapia 83: 780-784.

Setzer, W.N., Holland, M.T., Bozeman, C.A., Rozmus, G.F., Setzer, M.C., and Moriarity, D.M. 2001. Isolation and frontier molecular orbital investigation of bioactive quinone-methide triterpenoids from the bark of *Salacia petenensis*. Planta Med. 67: 65-69.

Shan, Y., Wang, X., Zhou, X., Kong, L., and Niwa, M. 2007. Two minor diterpene glycosides and an eudesman sesquiterpene from *Coleus forskohlii*. Chem. Pharm. Bull. 55: 376-381.

Sheu, Y.W., Chiang, L.C., Chen, I.S., Chen, Y.C., and Tsai, I.L. 2005. Cytotoxic flavonoids and new chromenes from *Ficus formosana* f. *formosana*. Planta Med. 71: 1165-1167.

Sikarwar, M.S., and Patil, M.B. 2012. Antihyperlipidemic activity of *Salacia chinensis* root extracts in triton-induced and atherogenic diet-induced hyperlipidemic rats. Indian J. Pharmacol. 44: 88-92.

Silva, M.S., Sousa, D.P., Medeiros, V.M., Folly, M.A.B., Tavares, J.F., and Barbosa-Filho, J.M. 2008. Alkaloid, flavonoids, and pentacyclic triterpenoids of *Maytenus obtusifolia* Mart. Biochem. Syst. Ecol. 36: 500-503.

Singh, D., Singh, B., and Goel, R.K. 2011. Traditional uses, phytochemical and pharmacology of *Ficus religiosa*: a review. J. Ethnopharmacol. 134: 565-583.

Sneden, A.T. 1981. Isoiguesterin, a new antileukemic bisnortriterpene from *Salacia madagascariensis*. J. Nat. Prod. 44: 503-507.

Sousa, J.R.D., Silva, G.D.F., Pedersoli, J.L., and Alves, R.J. 1990. Friedelane and oleanane triterpenoids from bark wood of *Austroplenckia populnea*. Phytochemistry 29: 3259-3261.

Stavri, M., Mathew, K.T., Gibson, T., Williamson, R.T., and Gibbons, S. 2004. New constituents of *Artemisia monosperma*. J. Nat. Prod. 67: 892-894.

Stojanovic-Radic, Z., Comic, L.J., Radulovic, N., Blagojevic, P., Denic, M., Miltojevic, A., Rajkovic, J., and Mihajilov-Krstev, T. 2012. Antistaphylococcal activity of *Inula helenium* L. root essential oil: eudesmane sesquiterpene lactones induce cell membrane damage. Eur. J. Clin. Microbiol. Infect. Dis. 31: 1015-1025.

Su, B.N., Takaishi, Y., Tori, M., Takaoka, S., Honda, G., Itoh, M., Takeda, Y., Kodzhimatov, O.K., and Ashurmetov, O. 2000a. Macrophyllidimers A and B, two novel sesquiterpene dimers from the bark of *Inula macrophylla*. Tetrahedron Lett. 41: 1475-1479.

Su, B.N., Takaishi, Y., Yabuuchi, T., Kusumi, T., Tori, M., and Takaoka, S. 2000b. The structures and absolute configurations of macrophyllic acids A-E, five new rearranged eudesmane sesquiterpene acids from the bark of *Inula macrophylla*. Tetrahedron Lett. 41: 2395-2400.

Subramaniam, G., Ang, K.K.H., Ng, S., Buss, A.D., and Butler, M.S. 2009. A benzopyrroloisoquinoline alkaloid from *Ficus fistulosa*. Phytochemistry Lett. 2: 88-90.

Suksri, S., Premcharoen, S., Thawatphan, C., and Sangthongprow, S. 2005. Ethnobotany in Bung Khong Long non-hunting area, northeast Thailand. Kasetsart J. (Nat. Sci.) 39: 519-533.

Sun, Z., Chen, B., Zhang, S., and Hu, C. 2004. Four new eudesmanes from *Caragana intermedia* and their biological activities. J. Nat. Prod. 67: 1975-1979.

Swain, S.S., Rout, K.K., and Chand, P.K. 2012. Production of triterpenoid anti-cancer compound taraxerol in Agrobacterium-transformed root cultures of butterfly pea (*Clitoria ternatea* L.). Appl. Biochem. Biotechnol. 168: 487-503.

Sy, L.K., and Brown, G.D. 1998. Three sesquiterpenes from *Artemisia annua*. Phytochemistry 48: 1207-1211.

Talzhanov, N.A., Rodichev, M.A., Raldugin, V.A., Gatilov, Y.V., Shakirov, M.M., Ivasenko, S.A., Turdybekov, K.M., and Adekenov, S.M. 2007. Tourneforin, a novel eudesmanolide from *Artemisia tournefortiana*. Chem. Nat. Compd. 43: 555-557.

Tane, P., Tsopmo, A., Ngnokam, D., Ayafor, J.F., and Sterner, O. 1996. New friedelane triterpenes from *Lepidobotrys staudtii*. Tetrahedron 52: 14989-14994.

Thiem, D.A., Sneden, A.T., Khan, S.I., and Tekwani, B.L. 2005. Bisnortriterpenes from *Salacia madagascariensis*. J. Nat. Prod. 68: 251-254.

Tinto, W.F., Blair, L.C., and Alli, A. 1992. Lupane triterpenoids of *Salacia cordata*. J. Nat. Prod. 55: 395-398.

Torres-Romero, D., King-Diaz, B., Strasser, R.J., Jiménez, I.A., Lotina-Hennsen, B., and Bazzocchi, I.L. 2010. Friedelane triterpenes from *Celastrus vulcanicola* as photosynthetic inhibitors. J. Agric. Food Chem. 58: 10847-10854.

Tu, G.H., Shi, X.W., Zhao, Y., Zheng, C.D., and Gao, J.M. 2011. Triterpenes of *Euonymus alatus* and their cytotoxic activity. Chem. Nat. Compd. 47: 656-657.

Twentyman, P.R., and Luscombe, M. 1987. A study of some variables in a tetrazolium dye (MTT) based assay for cell growth and chemosensitivity. Br. J. Cancer 56: 279-285.

Valladao, F.N., Miranda, R.R.S., Oliveira, G.S., Silva, G.D.F., Duarte, L.P., and Filho, S.A.V. 2010. Constituents of fruit pulp of *Maytenus salicifolia* and complete 1D/2D NMR data of 3β-hydroxy-D:B-friedo-olean-5-ene. Chem. Nat. Compd. 46: 686-687.

Wang, Y., Chen, W.S., Wu, Z.J., Xi, Z.X., Chen, W., Zhao, G.J., Li, X., and Sun, L.N. 2011a. Chemical constituents from *Salacia amplifolia*. Biochem. Syst. Ecol. 39: 205-208.

Wang, K.W., Sun, H.X., Wu, B., and Pan, Y.J. 2005. Two novel olean triterpenoids from *Celastrus hypoleucus*. Helv. Chim. Acta 88: 990-993.

Wang, X.G., Wei, X.Y., Huang, X.Y., Shen, L.T., Tian, Y.Q., and Xu, H.H. 2011b. Insecticidal constructure and bioactivities of compounds from *Ficus sarmentosa* var. *henryi*. Agric. Sci. China 10: 1402-1409.

Wang, X.G., Wei, X.Y., Tian, Y.Q., Shen, L.T., and Xu, H.H. 2010. Antifungal flavonoids from *Ficus sarmentosa* var. *henryi* (King) Corner. Agric. Sci. China 9: 690-694.

Wang, Z.J., Zhao, Y.Y., Wang, B., Ai, T.M., and Chen, Y.Y. 2000. Depsides from *Prunella vulgaris*. Chin. Chem. Lett. 11: 997-1000.

Weeratunga, G., Kumar, V., Sultanbawa, M.U.S., and Balasubramaniam, S. 1982. Chemical investigation of Ceylonese plants. Part 45. 28,29-Dihydroxyfriedelan-3-one, a friedelane with two oxygenated methyl groups, from *Elaeodendron balae* (Celastraceae). J. Chem. Soc. Perkin Trans. I 10: 2457-9.

Williams, J.A., Choe, Y.S., Noss, M.J., Baumgartner, C.J., and Mustad, V.A. 2007. Extract of *Salacia oblonga* lowers acute glycemia in patients with type 2 diabetes. Am. J. Clin. Nutr. 86: 124-130.

Woo, E-R., and Piao, M.S. 2004. Antioxidative constituents from *Lycopus lucidus*. Arch. Pharm. Res. 27: 173-176.

Wu, B., He, S., Wu, X.D., Wu, D.K., and Pan, Y.J. 2007. Cadinane and eudesmane sesquiterpenoids from *Chloranthus henryi*. Helv. Chim. Acta 90: 1586-1592.

Wu, P.L., Lin, F.W., Wu, T.S., Kuoh, C.S., Lee, K.H., and Lee, S.J. 2004. Cytotoxic and anti-HIV principles from the rhizomes of *Begonia nantoensis*. Chem. Pharm. Bull. 52: 345-349.

Wu, P.L., Rao, K.V., Su, C.H., Kuoh, C.S., and Wu, T.S. 2002. Phenanthroindolizidine alkaloids and their cytotoxicity from the leaves of *Ficus septica*. Heterocycles 57: 2401-2408.

Wu, S.H., Zhang, H.J., Lin, Z.W., and Sun, H.D. 1993. Terpenoids from *Isodon grandifolia* var. *atuntzensis*. Phytochemistry 34: 1176-1178.

Xie, W., Tanabe, G., Akaki, J., Morikawa, T., Ninomiya, K., Minematsu, T., Yoshikawa, M., Wu, X., and Muraoka, O. 2011. Isolation, structure identification and SAR studies on thiosugar sulfonium salts, neosalaprinol and neoponkoranol, as potent α-glucosidase inhibitors. Bioorg. Med. Chem. 19: 2015-2022.

Xie, W.D., Weng, C.W., Niu, Y.F., Lai, P.X., and Row, K.H. 2010. Eudesmane sesquiterpenes and other constituents from *Aster himalaicus*. Chem. Biodivers. 7: 221-224.

Xu, J., Ji, C., Zhang, Y., Su, J., Li, Y., and Tan, N. 2012. Inhibitory activity of eudesmane sesquiterpenes from *Alpinia oxyphylla* on production of nitric oxide. Bioorg. Med. Chem. Lett. 22: 1660-1663.

Xu, X., Xie, H., Hao, J., Jiang, Y., and Wei, X. 2010. Eudesmane sesquiterpene glucosides from lychee seed and their cytotoxic activity. Food Chem. 123: 1123-1126.

Yang, X., Wong, M., Wang, N., Chan, A.S.C., and Yao, X. 2006. A new eudesmane derivative and a new fatty acid ester from *Sambucus williamsii*. Chem. Pharm. Bull. 54: 676-678.

Yoshikawa, M., Morikawa, T., Murakami, T., Toguchida, I., Harima, S., and Matsuda, H. 1999. Medicinal flowers. I. Aldose reductase inhibitors and three new eudesmane-type sesquiterpenes, kikkanols A, B, and C, from the flowers of *Chrysanthemum indicum* L. Chem. Pharm. Bull. 47: 340-345.

Yoshikawa, M., Murakami, T., Shimada, H., Matsuda, H., Yamahara, J., Tanabe, G., and Muraoka, O. 1997. Salacinol, potent antidiabetic principle with unique thiosugar sulfonium sulfate structure from the ayurvedic traditional medicine *Salacia reticulata* in Sri Lanka and India. Tetrahedron Lett. 38: 8367-8370.

Yoshikawa, M., Shimoda, H., Nishida, N., Takada, M., and Matsuda, H. 2002. *Salacia reticulata* and its polyphenolic constituents with lipase inhibitory and lipolytic activities have mild antiobesity effects in rats. J. Nutr. 132: 1819-1824.

Yoshikawa, M., Xu, F.M., Nakamura, S., Wang, T., Matsuda, H., Tanabe, G., and Muraoka, O. 2008a. Salaprinol and ponkoranol with thiosugar sulfonium sulfate structure from *Salacia prinoides* and α-glucosidase inhibitory activity of ponkoranol and kotalanol desulfate. Heterocycles 75: 1397-1405.

Yoshikawa, M., Zhang, Y., Wang, T., Nakamura, S., and Matsuda, H. 2008b. New triterpene constituents, foliasalacins A_1-A_4, B_1-B_3, and C, from the leaves of *Salacia chinensis*. Chem. Pharm. Bull. 56: 915-920.

Zan, K., Chen, X.Q., Chai, X.Y., Wu, Q., Fu, Q., Zhou, S.X., and Tu, P.F. 2012. Two new cytotoxic eudesmane sesquiterpenoids from *Artemisia anomala*. Phytochemistry Lett. 5: 313-315.

Zhan, Z.J., Ying, Y.M., Ma, L.F., and Shan, W.G. 2011. Natural disesquiterpenoids. Nat. Prod. Rep. 28: 594-629.

Zhang, H.J., Tamez, P.A., Aydogmus, Z., Tan, G.T., Saikawa, Y., Hashimoto, K., Nakata, M., Hung, N.V., Xuan, L.T., Cuong, N.M., Soejarto, D.D., Pezzuto, J.M., and Fong, H.H.S. 2002. Antimalarial agents from plants. III. Trichothecenes from *Ficus fistulosa* and *Rhaphidophora decursiva*. Planta Med. 68: 1088-1091.

Zhang, T., Gong, T., Yang, Y., Chen, R.Y., and Yu, D.Q. 2012. Two new eudesmanolides from *Inula racemosa* and their bioactivities. Phytochemistry Lett. 5: 229-232.

Zhang, Y., Nakamura, S., Pongpiriyadacha, Y., Matsuda, H., and Yoshikawa, M. 2008a. Absolute structures of new megastigmane glycosides, foliasalaciosides E_1, E_2, E_3, F, G, H, and I from the leaves of *Salacia chinensis*. Chem. Pharm. Bull. 56: 547-553.

Zhang, Y., Nakamura, S., Wang, T., Matsuda, H., and Yoshikawa, M. 2008b. The absolute stereostructures of three rare D:B-friedobaccharane skeleton triterpenes from the leaves of *Salacia chinensis*. Tetrahedron 64: 7347-7352.

Zhao, Y., Yue, J., Lin, Z., Ding, J., and Sun, H. 1997. Eudesmane sesquiterpenes from *Laggera pterodonta*. Phytochemistry 44: 459-464.

Zhekun, Z., and Gilbert, M.G. 2003. Moraceae. In Z.Y. Wu, and P. Raven (eds.), Flora of China, pp. 21-73. Beijing: Science Press.

Zheng, G. 1994. Cytotoxic terpenoids and flavonoids from *Artemisia annua*. Planta Med. 60: 54-57.

Zheng, Q.X., Xu, Z.J., Sun, X.F., Gueritte, F., Cesario, M., Sun, H.D., Cheng, C.H.K., Hao, X.J., and Zhao, Y. 2003. Eudesmane derivatives and other sesquiterpenes from *Laggera alata*. J. Nat. Prod. 66: 1078-1081.

APPENDIX

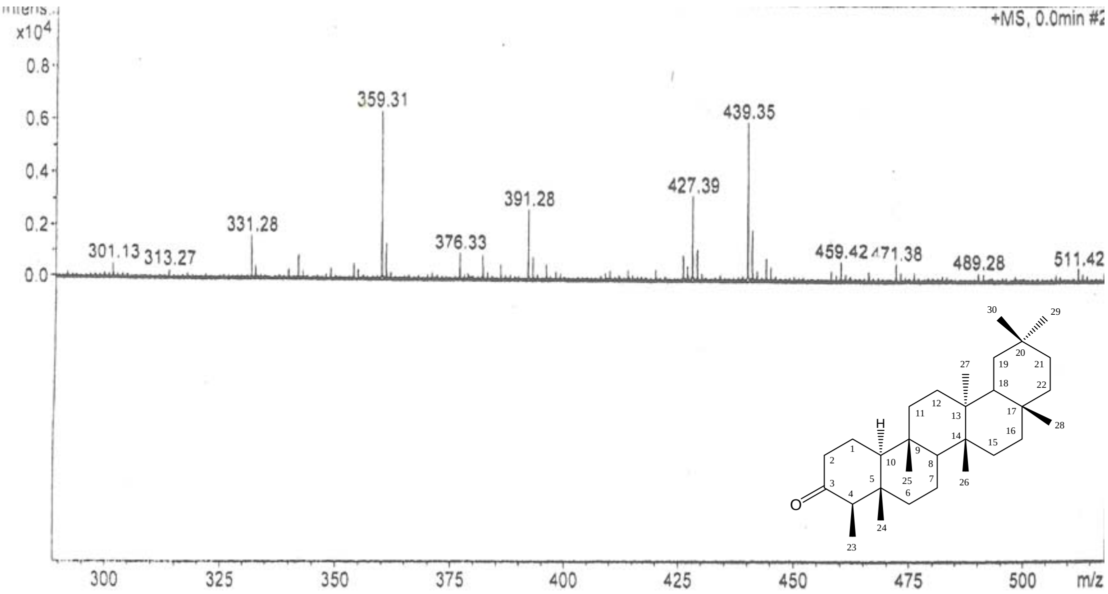


Figure 7. ESI Mass spectrum of compound SV-1

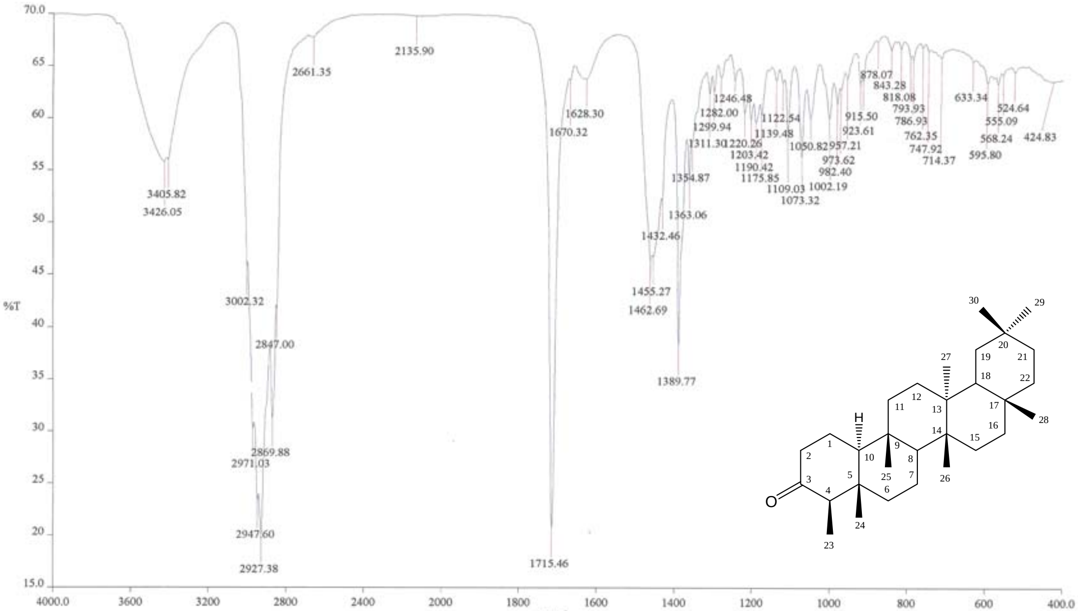


Figure 8. IR Spectrum of compound SV-1 (KBr)

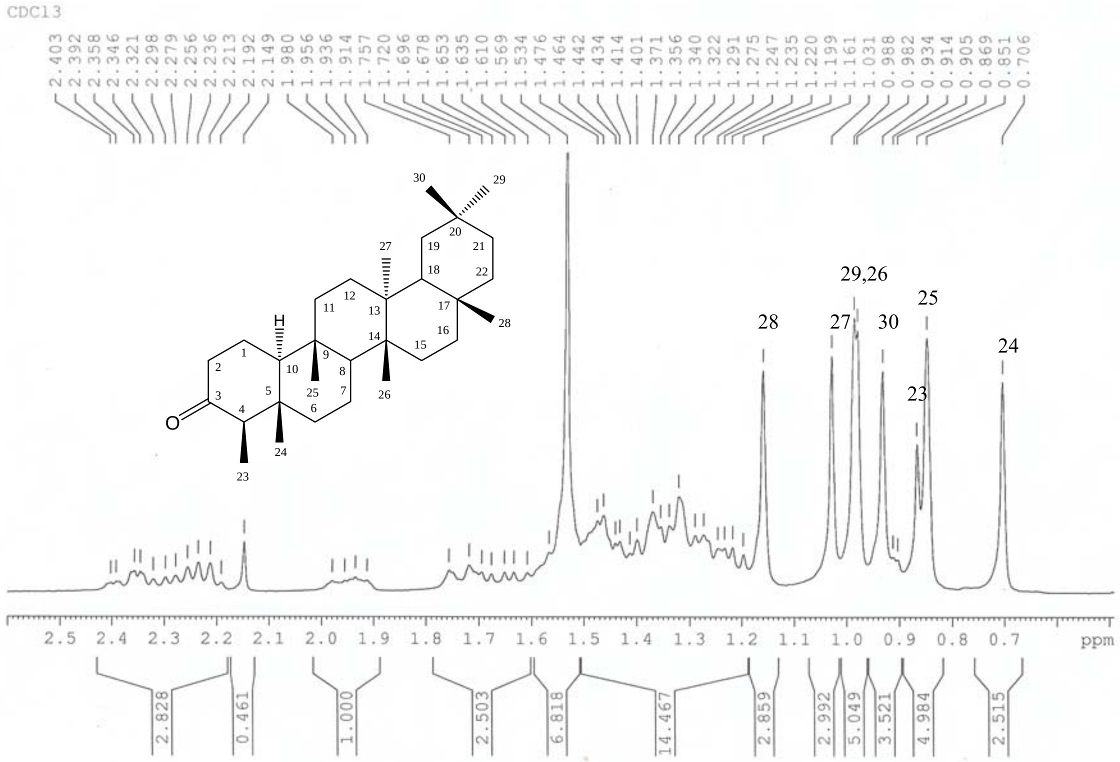


Figure 9. ^{1}H NMR (300 MHz) Spectrum of compound SV-1 (in $CDCl_3$)

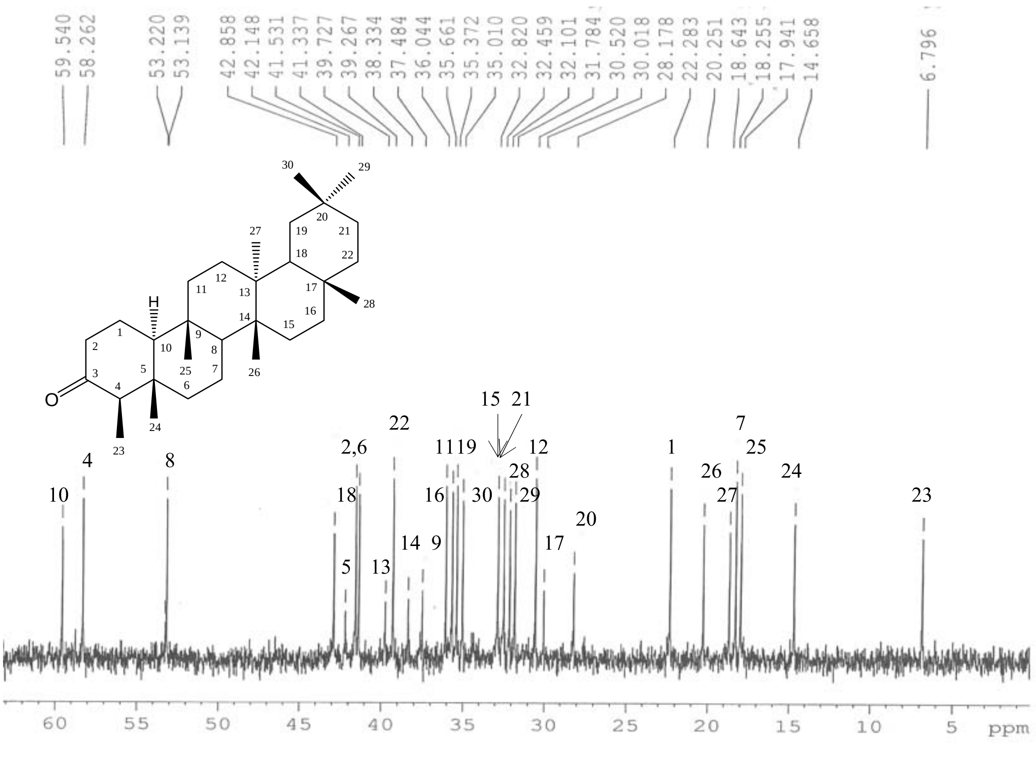


Figure 10. ^{13}C NMR (75 MHz) Spectrum of compound SV-1 from 5-60 ppm (in $CDCl_3$)

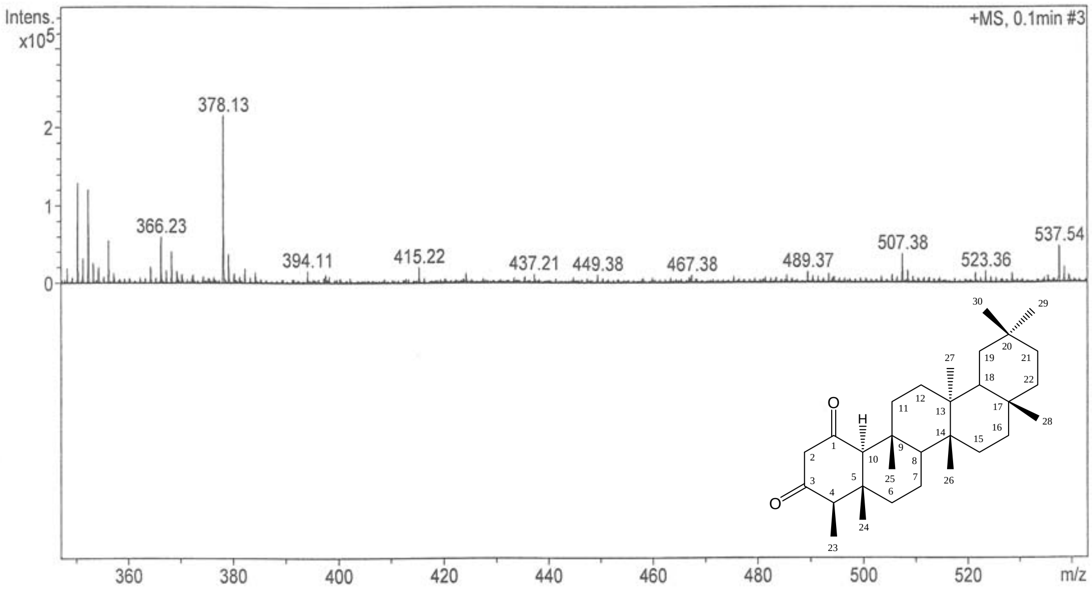


Figure 11. ESI Mass spectrum of compound SV-2

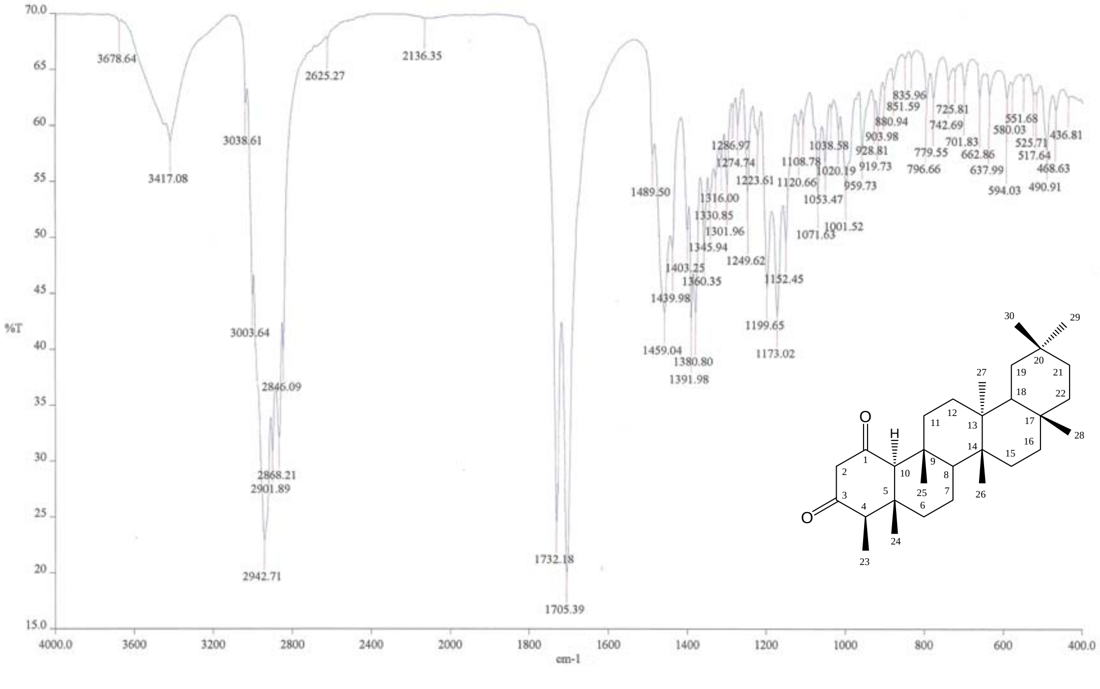


Figure 12. IR Spectrum of compound SV-2 (KBr)

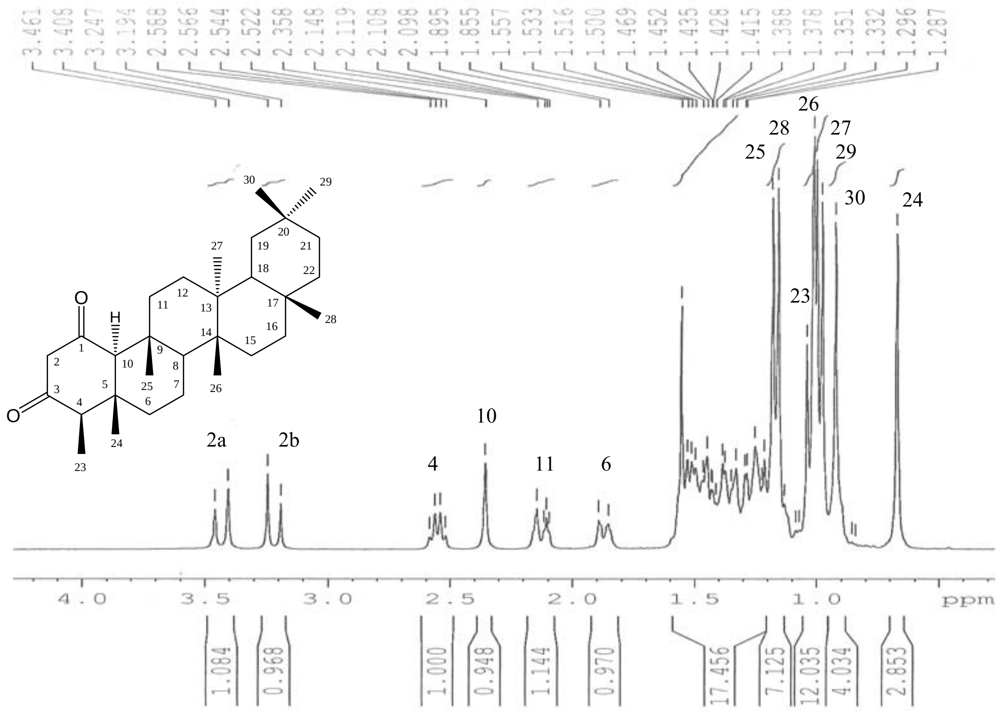


Figure 13. ^{1}H NMR (300 MHz) Spectrum of compound SV-2 (in CDCl$_3$)

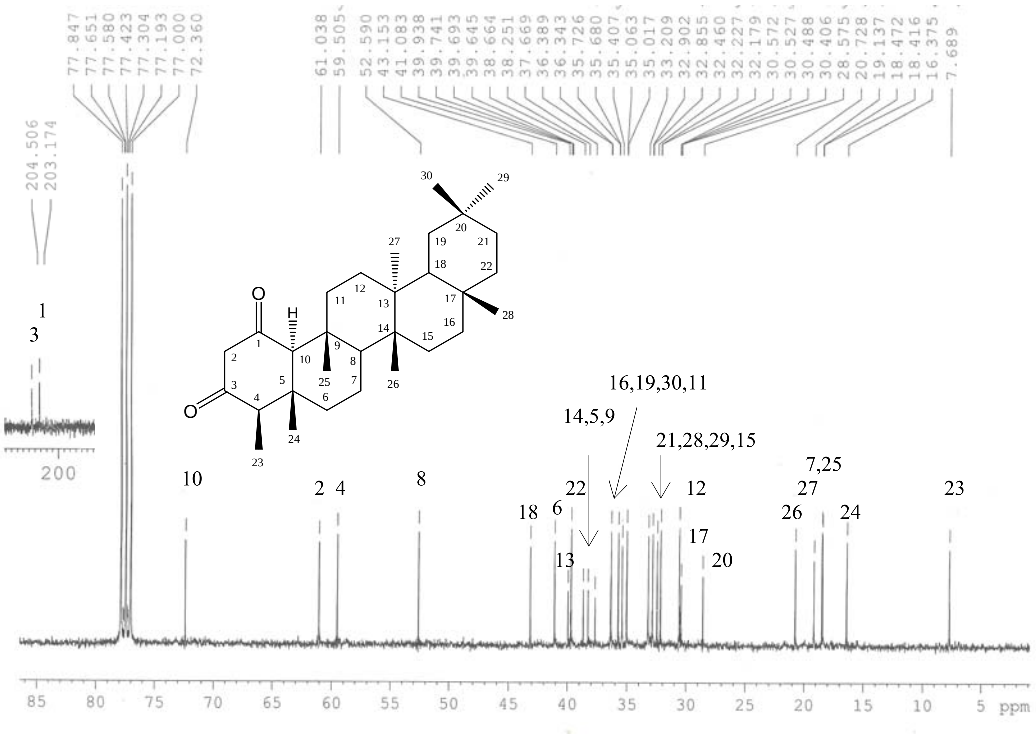


Figure 14. ^{13}C NMR (75 MHz) Spectrum of compound SV-2 (in CDCl$_3$)

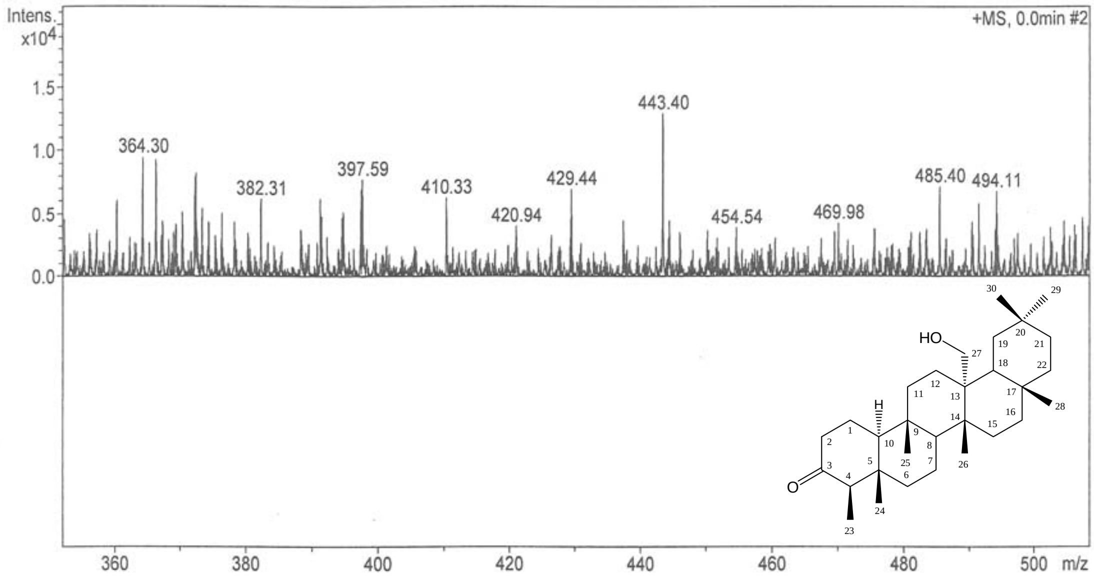


Figure 15. ESI Mass spectrum of compound SV-3

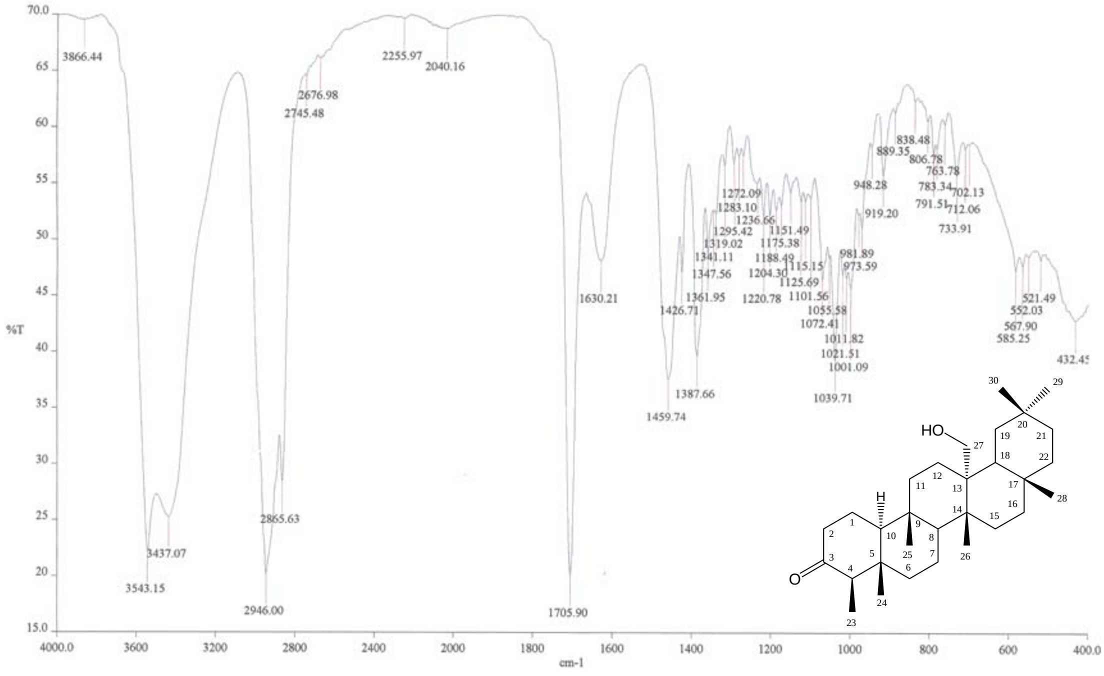


Figure 16. IR Spectrum of compound SV-3 (KBr)

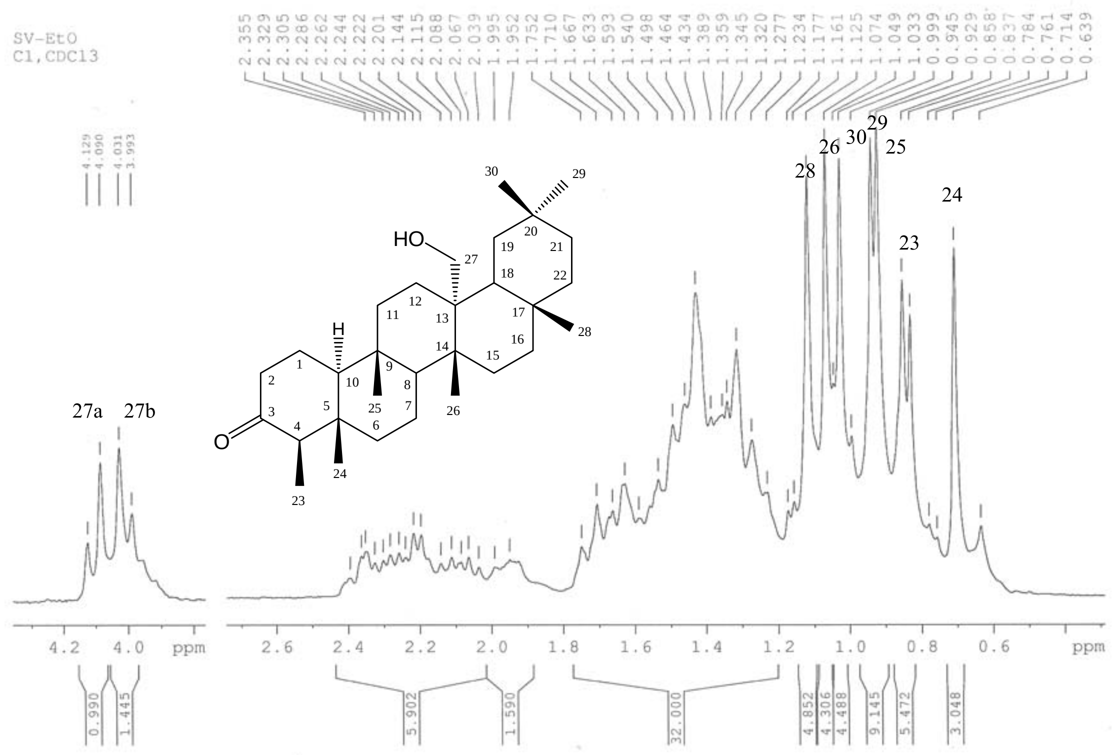


Figure 17. ^{1}H NMR (300 MHz) Spectrum of compound SV-3 (in $CDCl_3$)

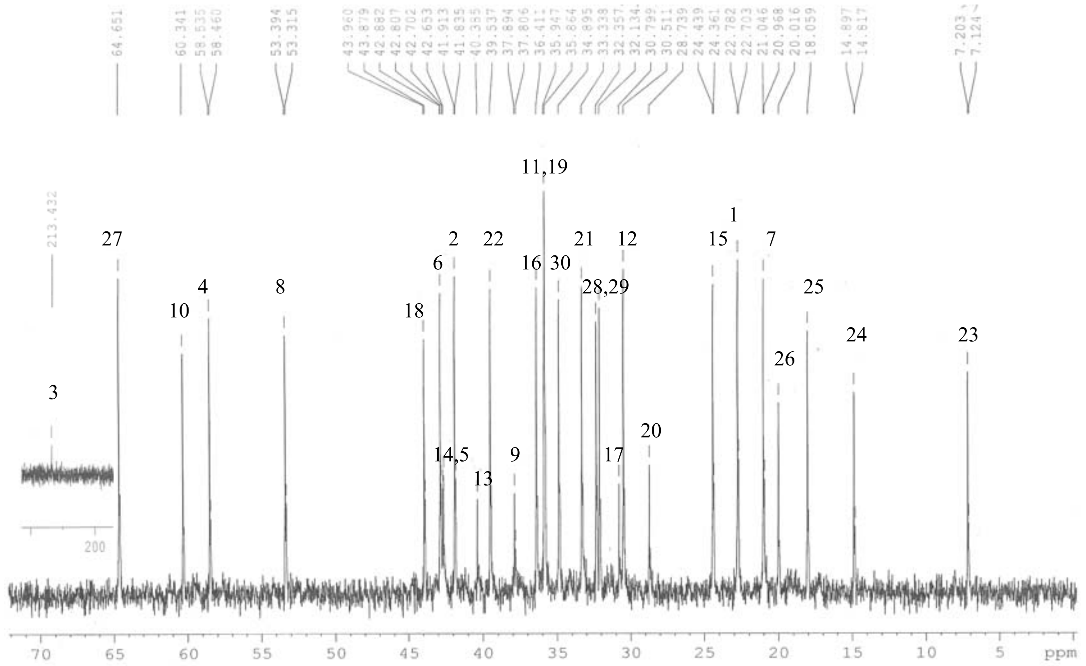


Figure 18. ^{13}C NMR (75 MHz) Spectrum of compound SV-3 (in $CDCl_3$)

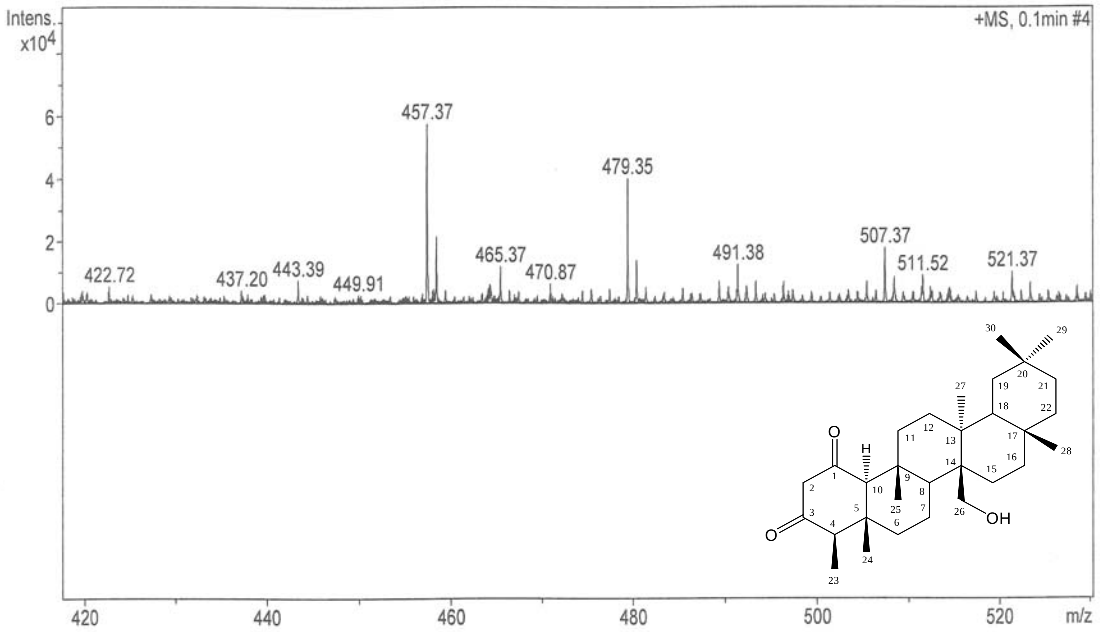


Figure 19. ESI Mass spectrum of compound SV-4

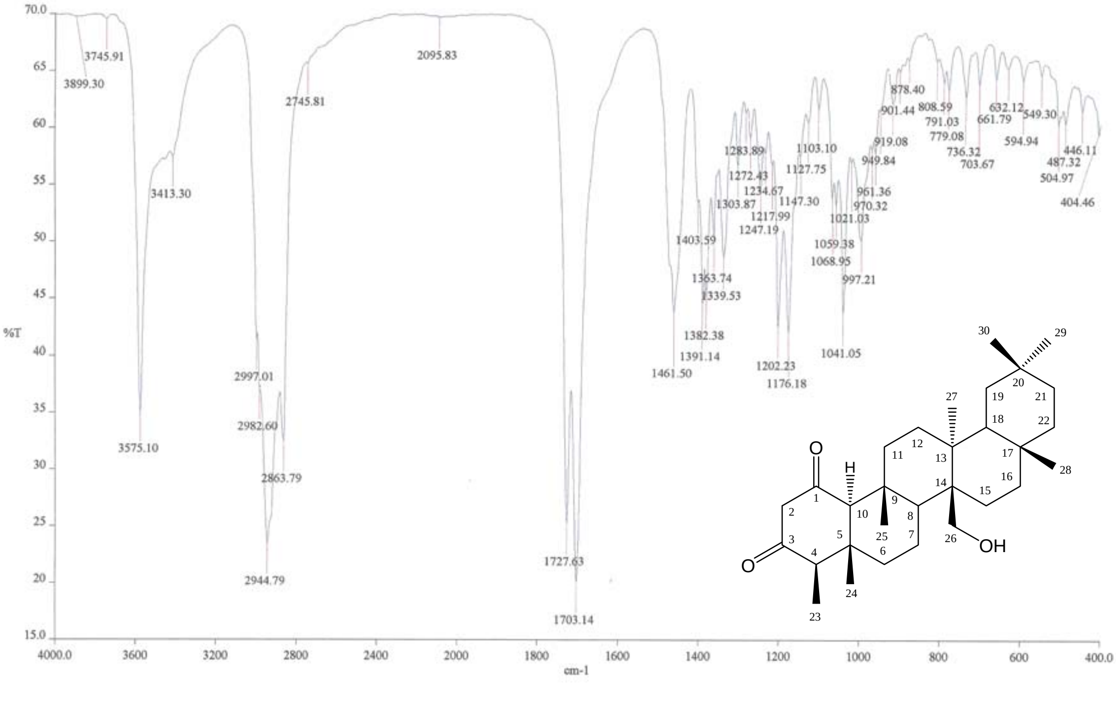


Figure 20. IR Spectrum of compound SV-4 (KBr)

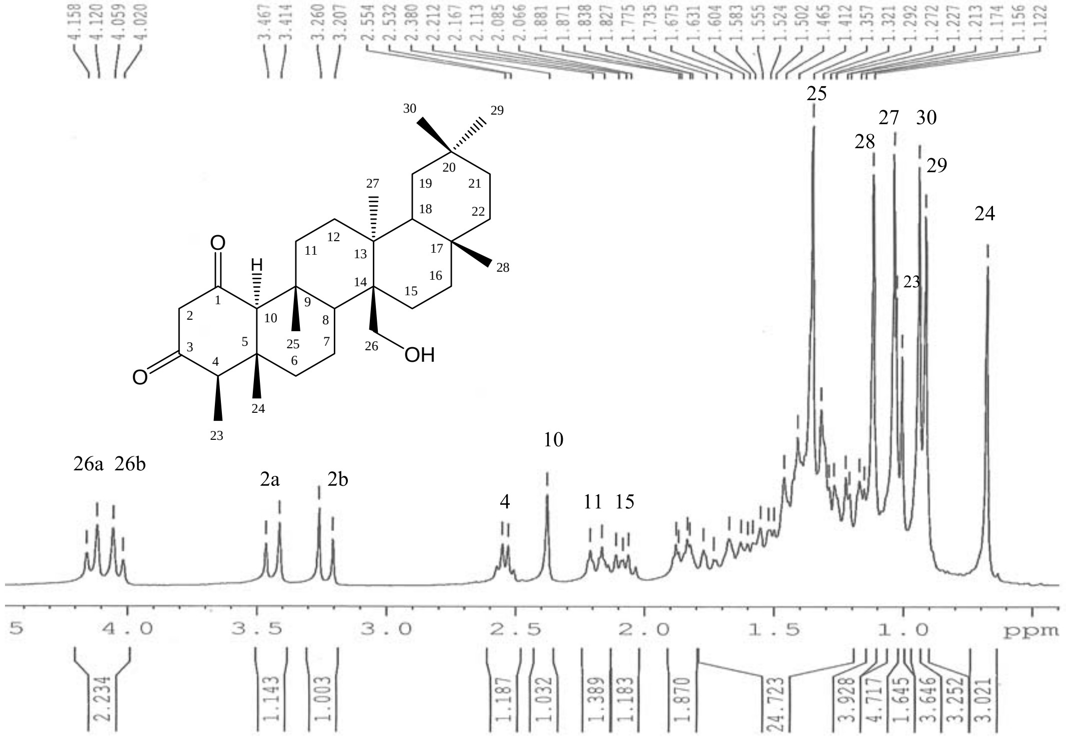


Figure 21. ^{1}H NMR (300 MHz) Spectrum of compound SV-4 (in $CDCl_3$)

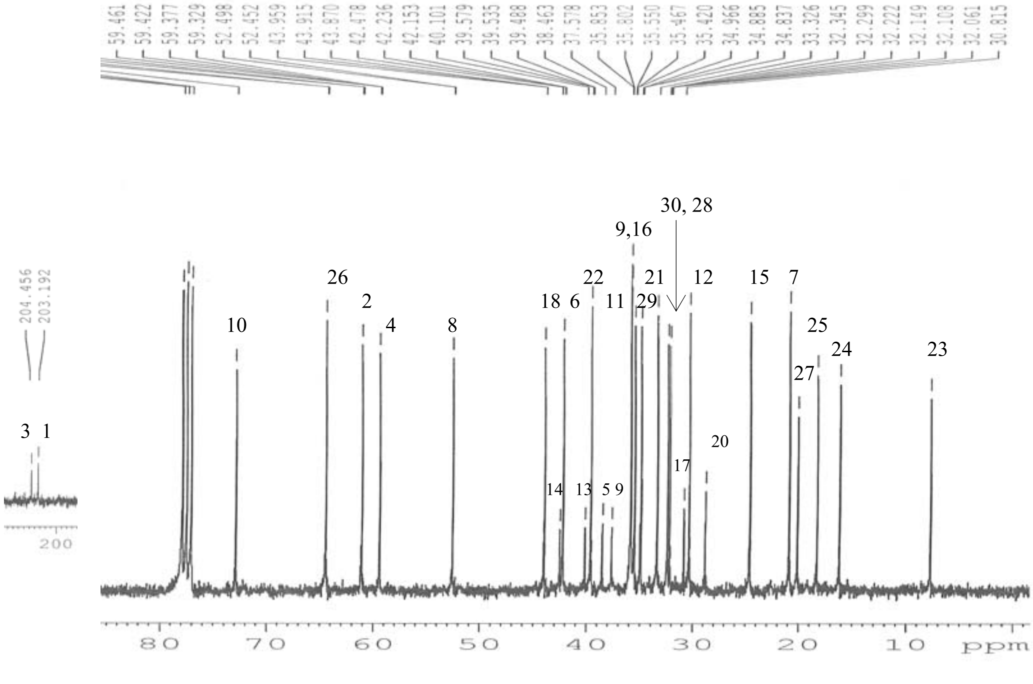


Figure 22. ^{13}C NMR (75 MHz) Spectrum of compound SV-4 (in $CDCl_3$)

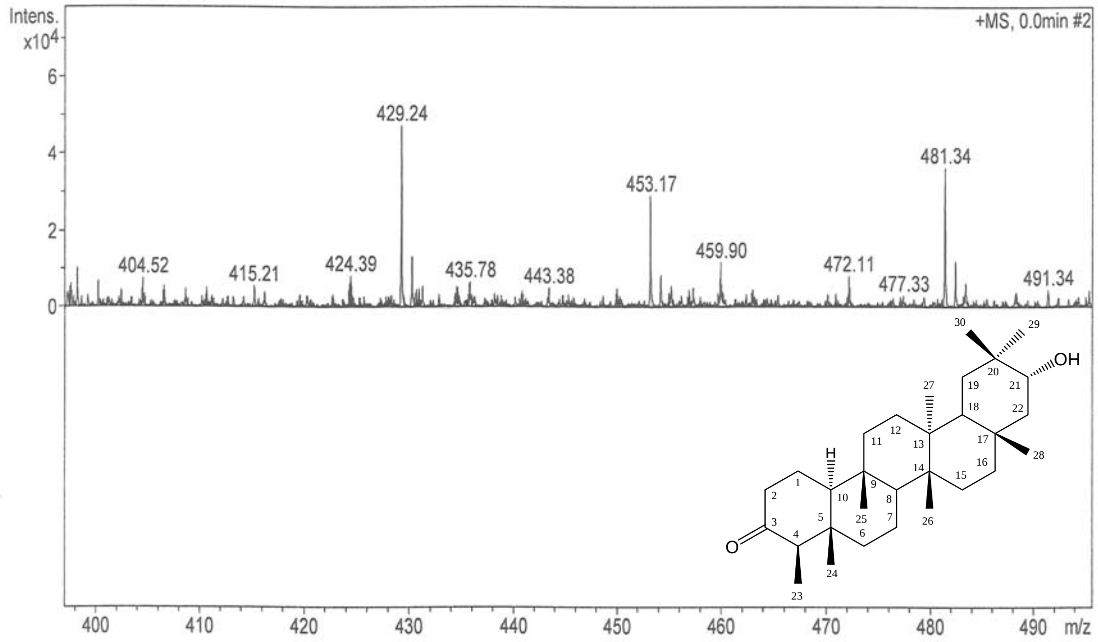


Figure 23. ESI Mass spectrum of compound SV-5

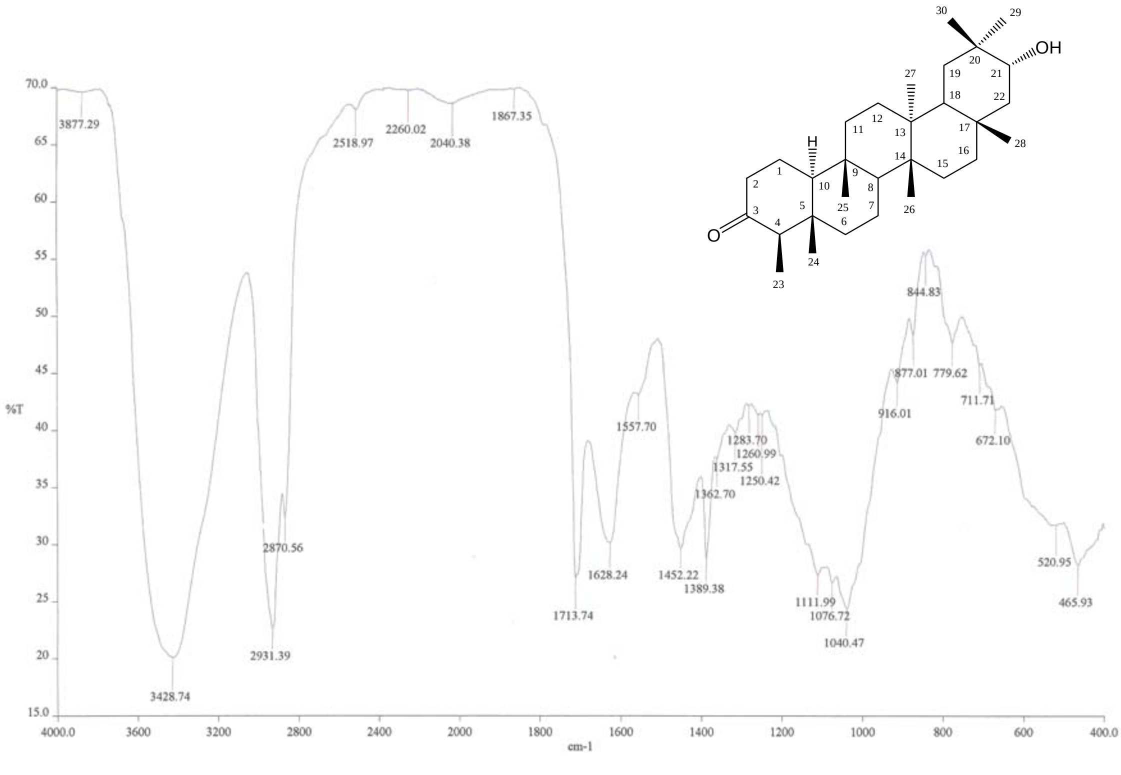


Figure 24. IR Spectrum of compound SV-5 (KBr)

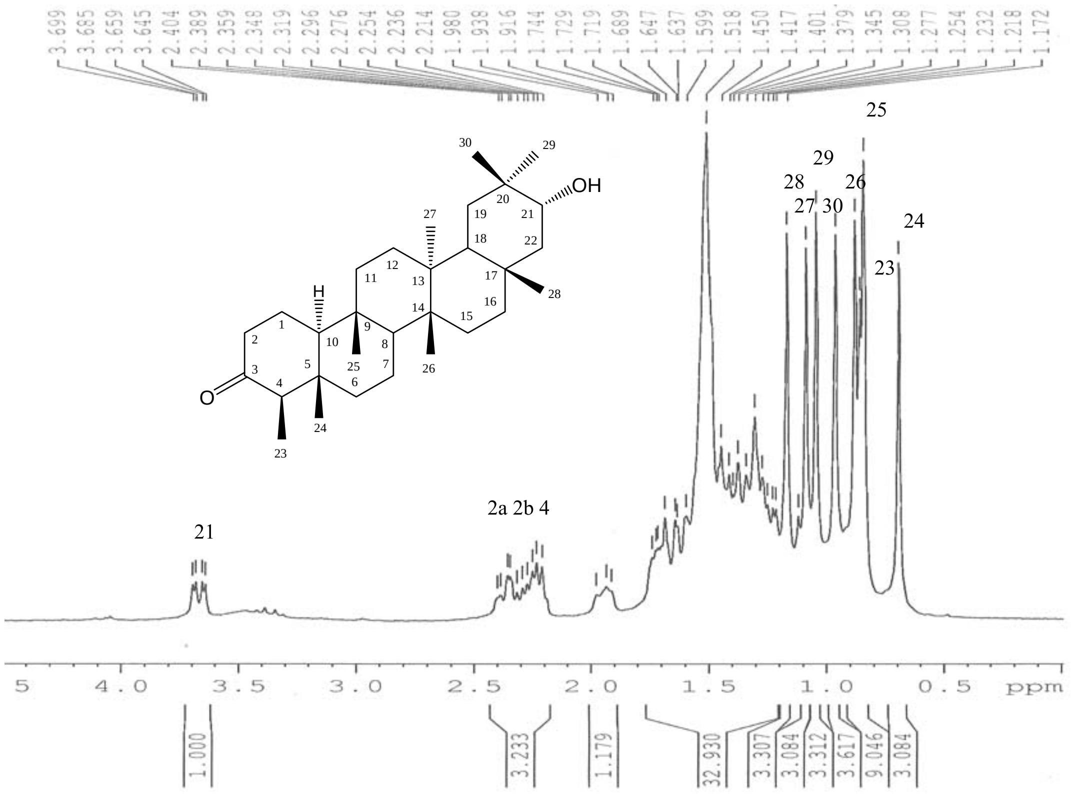


Figure 25. ^{1}H NMR (300 MHz) Spectrum of compound SV-5 (in $CDCl_3$)

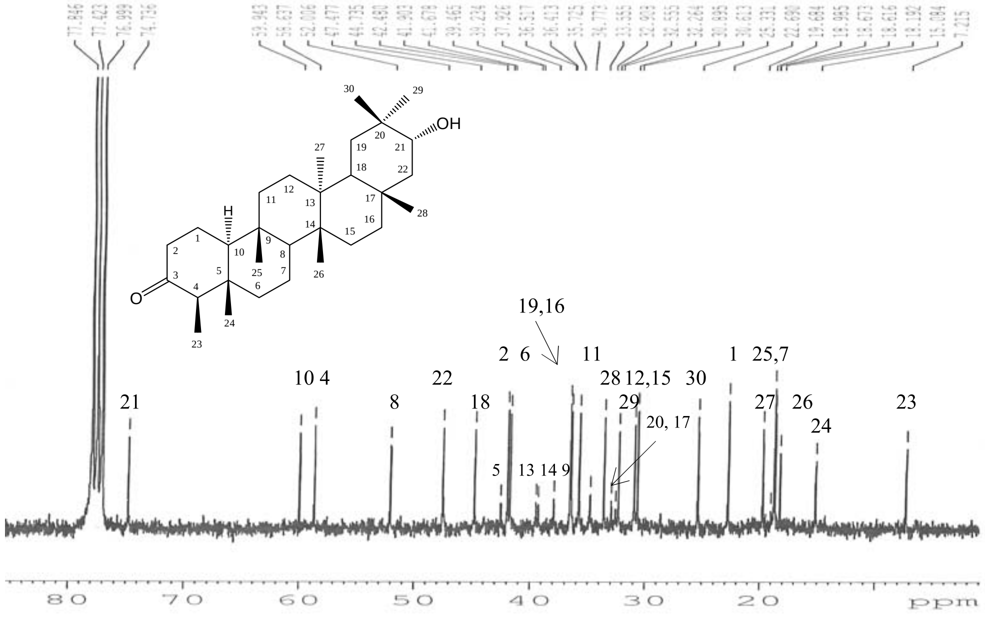


Figure 26. ^{13}C NMR (75 MHz) Spectrum of compound SV-5 from 5-80 ppm (in $CDCl_3$)

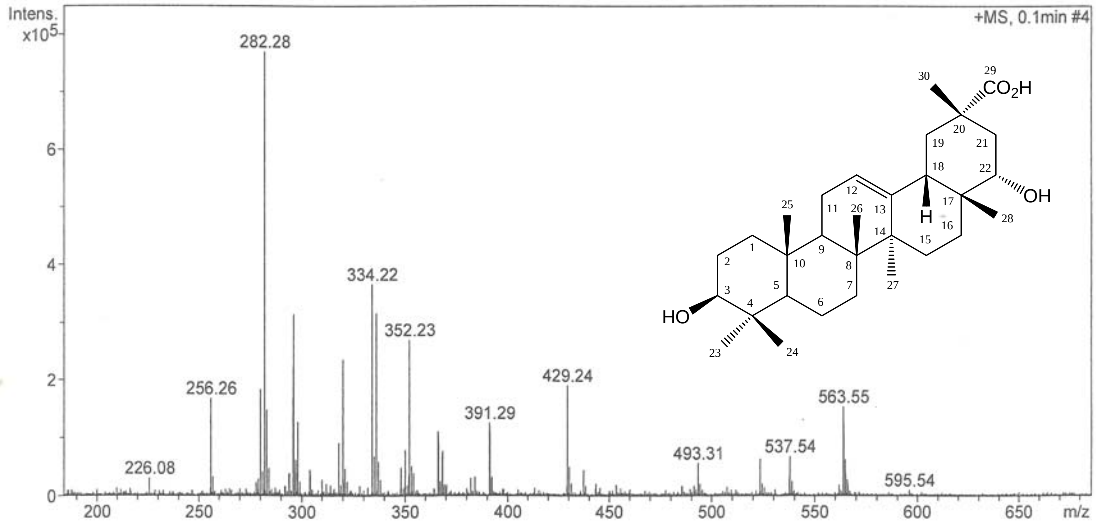


Figure 27. ESI Mass spectrum of compound SV-6

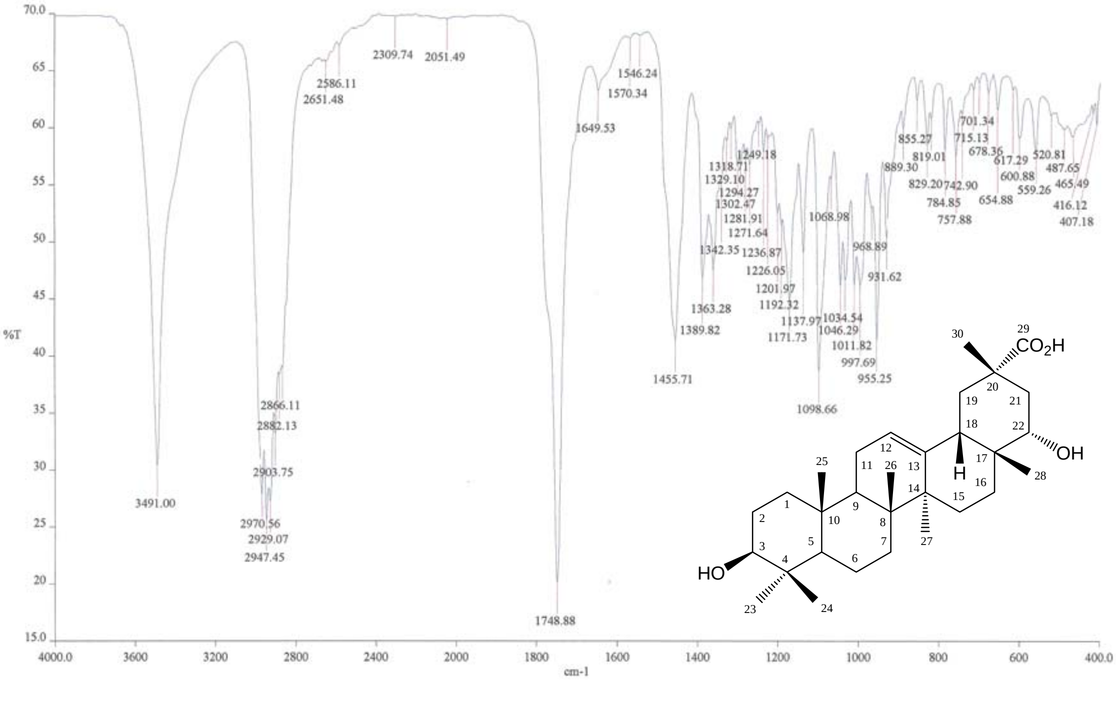


Figure 28. IR Spectrum of compound SV-6 (KBr)

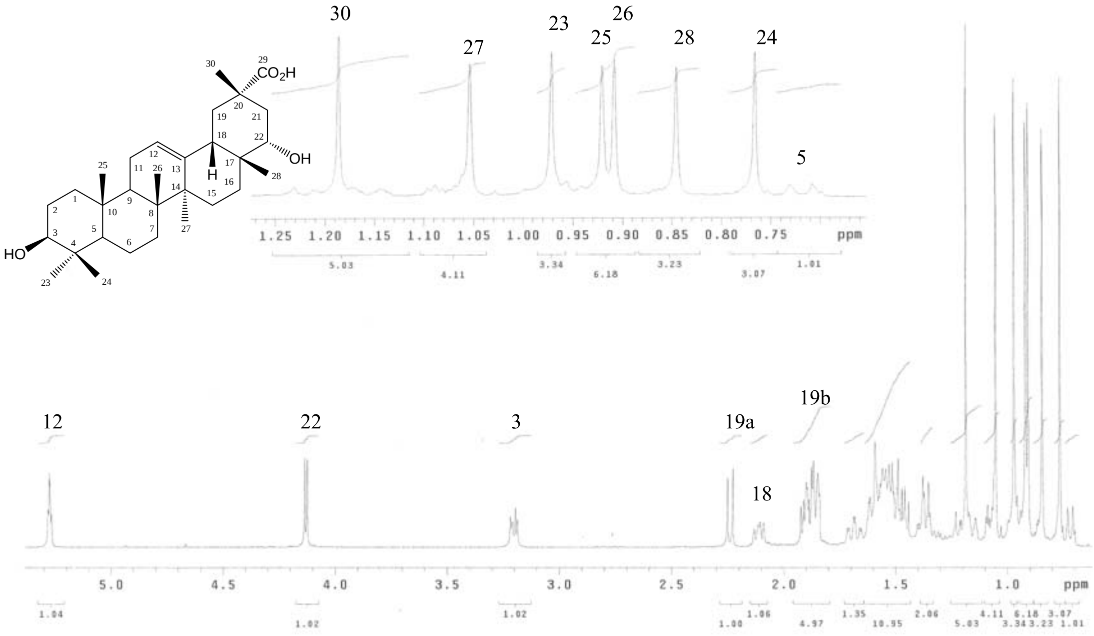


Figure 29. ^{1}H NMR (500 MHz) Spectrum of compound SV-6 (in $CDCl_3$)

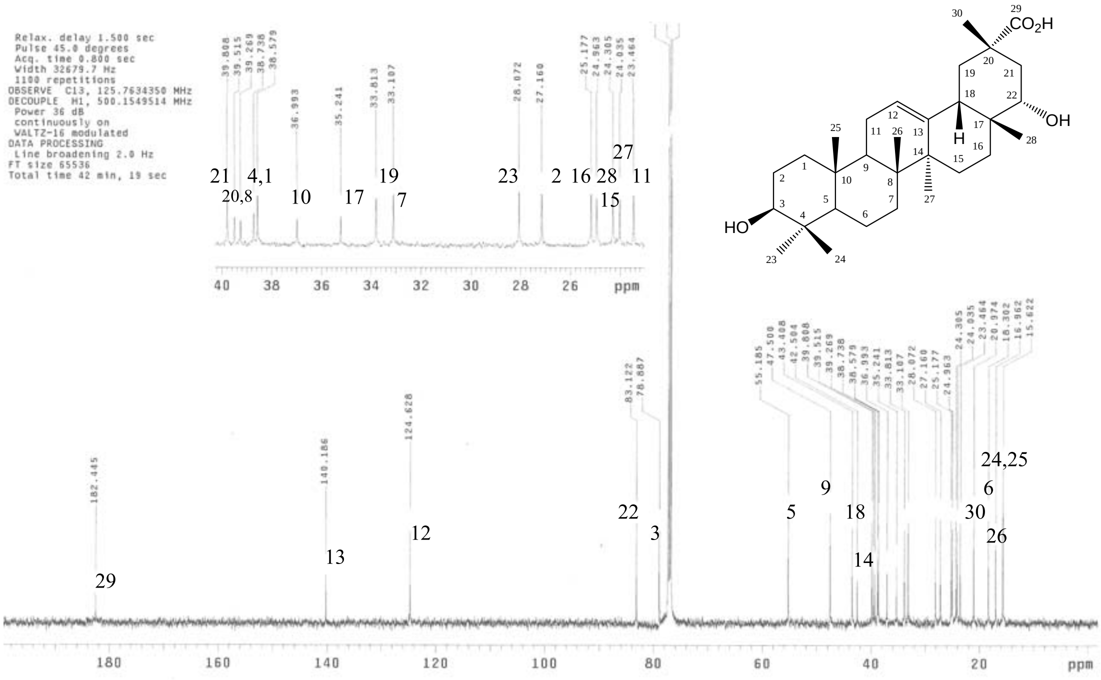


Figure 30. ^{13}C NMR (125 MHz) Spectrum of compound SV-6 (in $CDCl_3$)

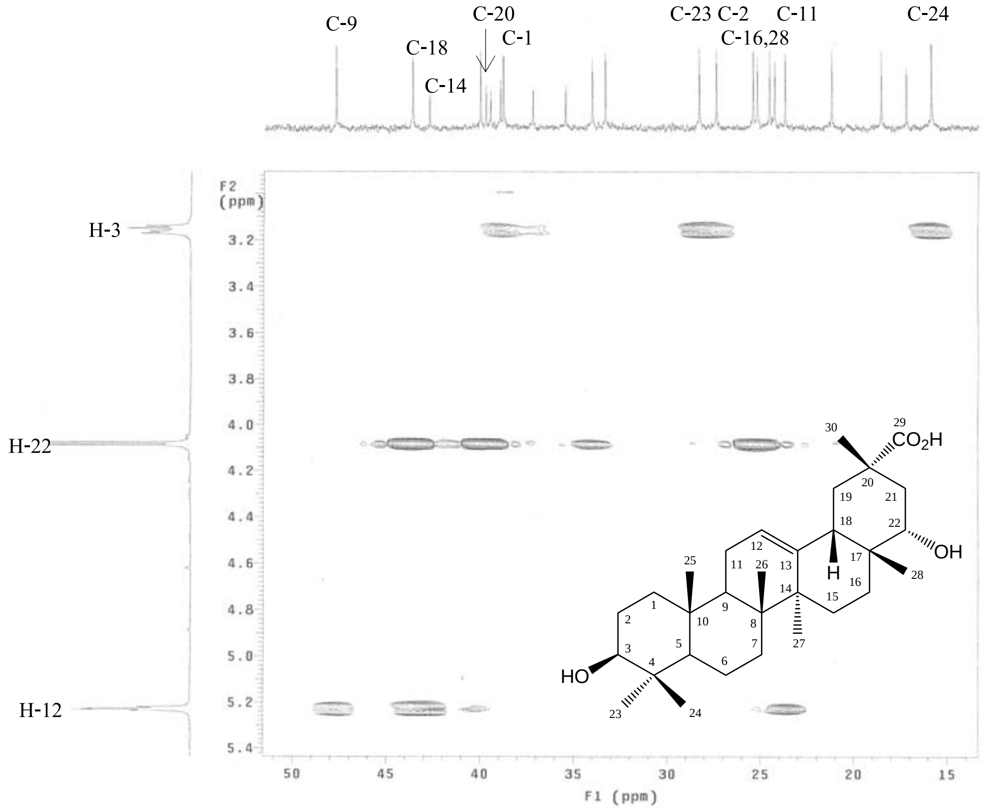


Figure 31a. HMBC Spectrum of compound SV-6 (expansion between δ_H 3.0-5.4, δ_C 13-51 ppm)

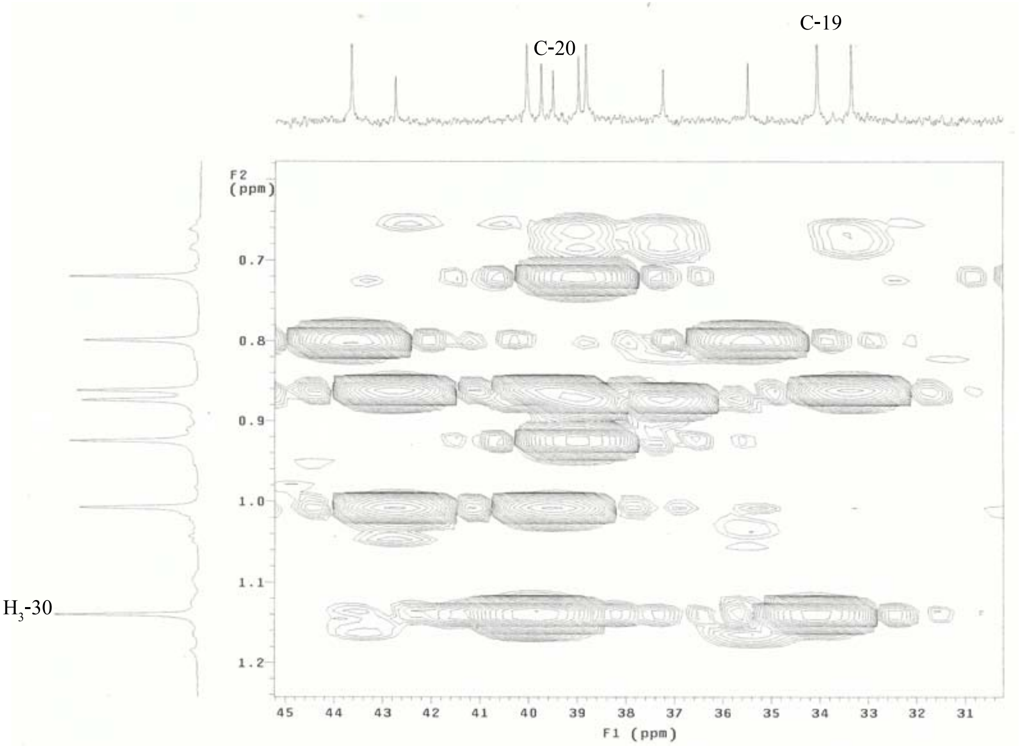


Figure 31b. HMBC Spectrum of compound SV-6 (expansion between δ_H 0.6-1.2, δ_C 30-45 ppm)

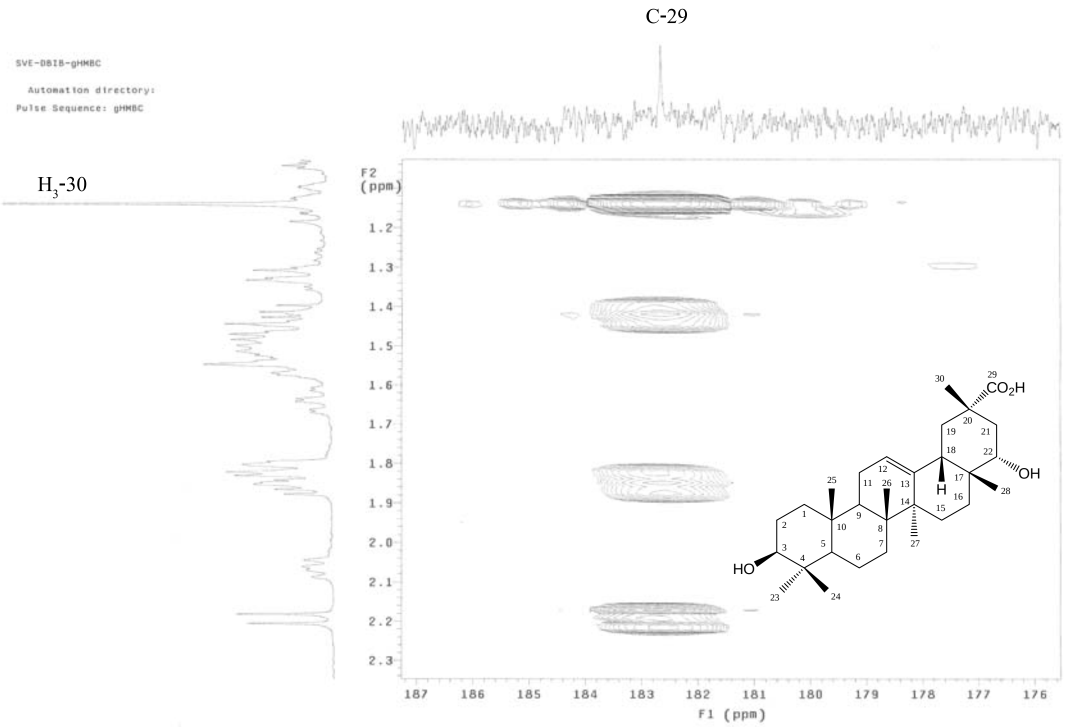


Figure 31c. HMBC Spectrum of compound SV-6 (expansion between δ_H 1.0-2.3, δ_C 176-187 ppm)

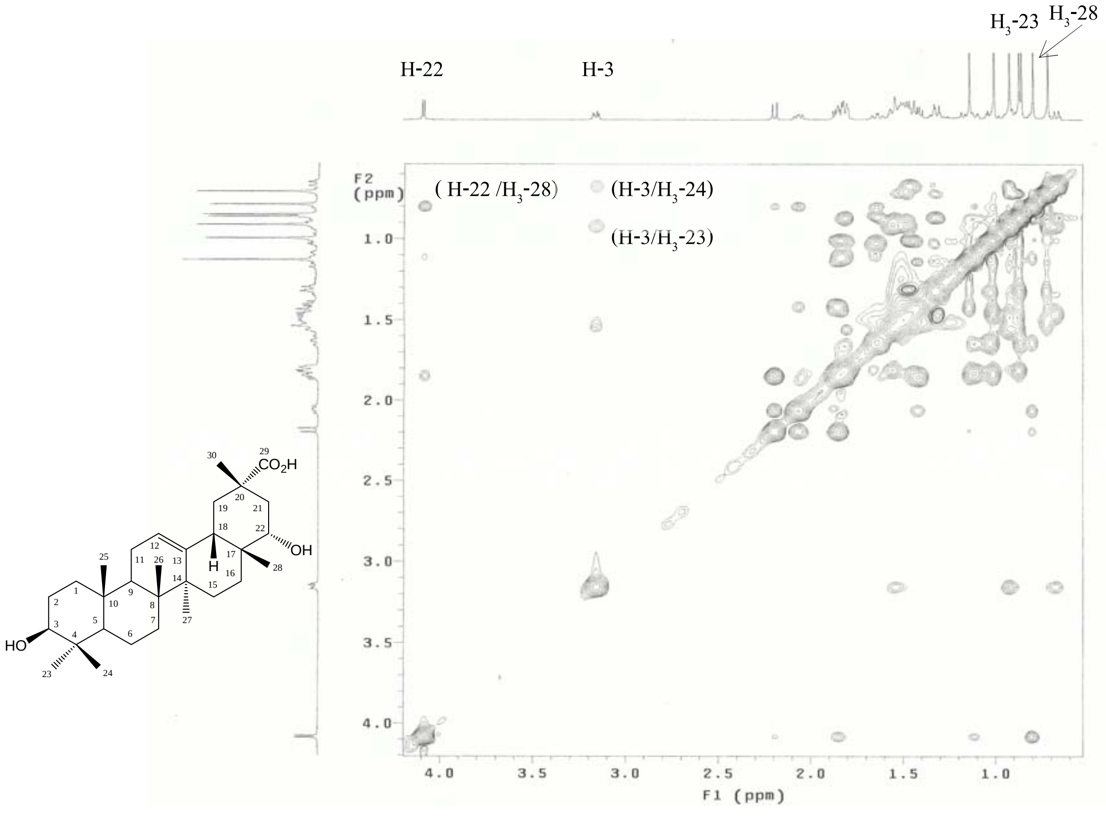


Figure 32. NOESY Spectrum of compound SV-6 (expansion between δ_H 0.5-4.0 ppm)

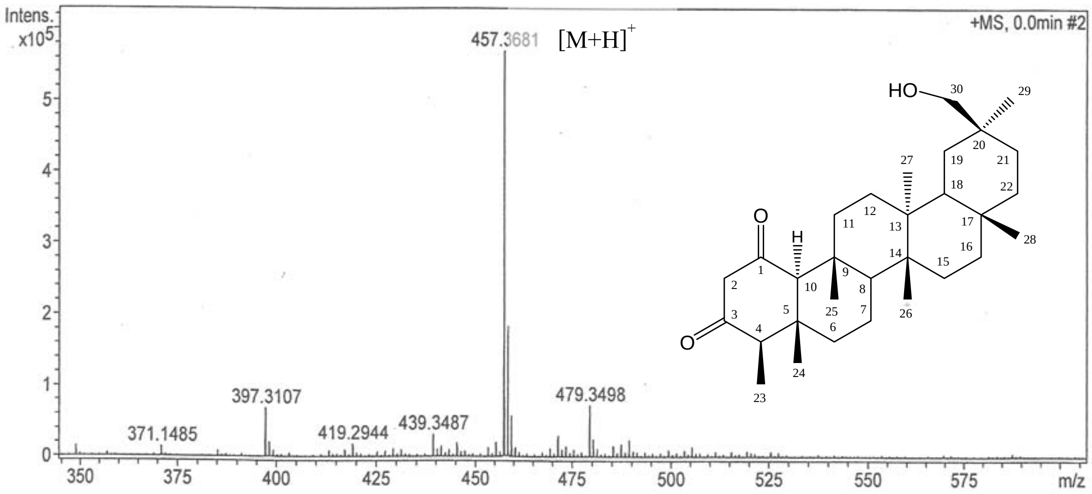


Figure 33. HR-ESI-TOF Mass spectrum of compound SV-7

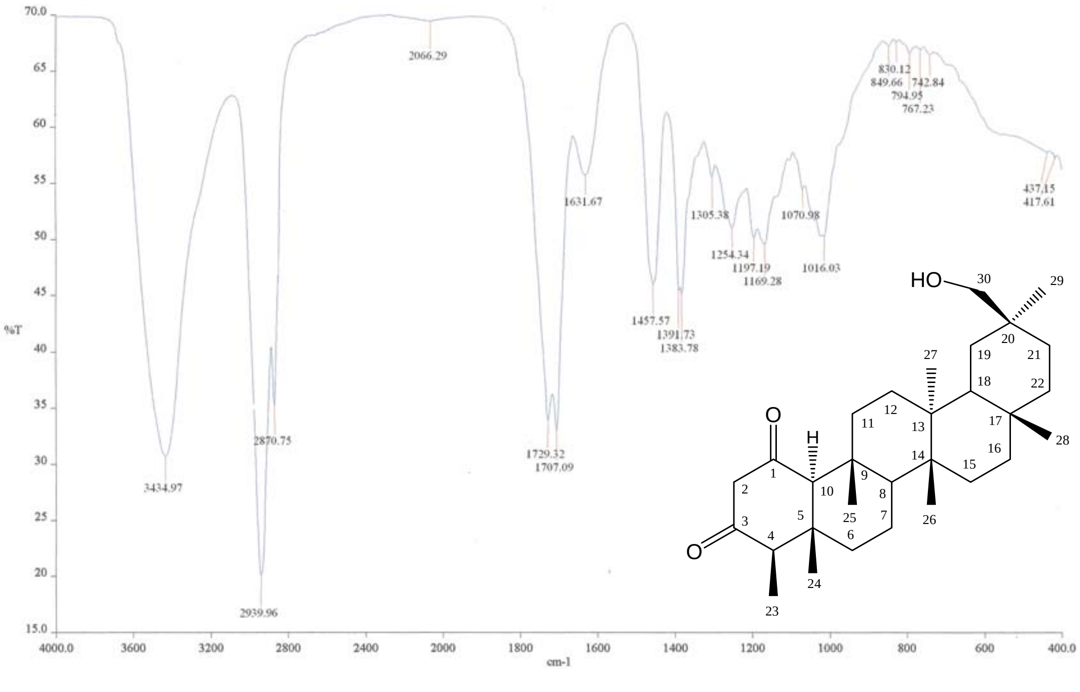


Figure 34. IR Spectrum of compound SV-7 (KBr)

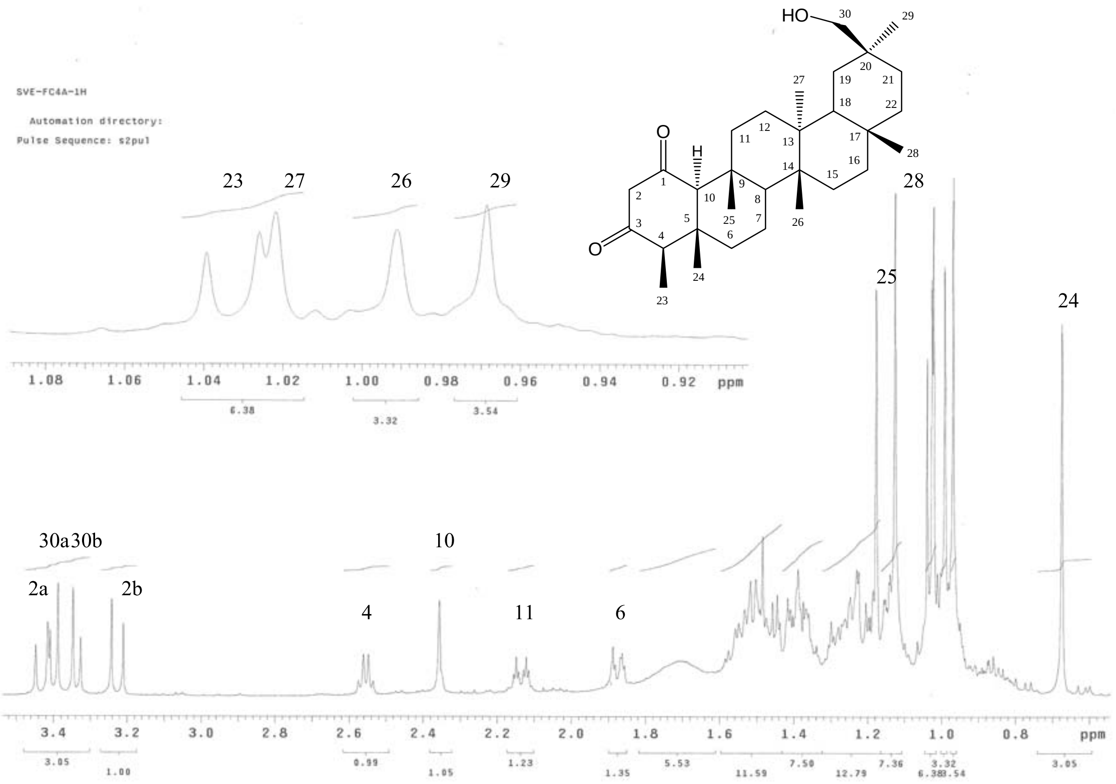


Figure 35. ^{1}H NMR (500 MHz) Spectrum of compound SV-7 (in $CDCl_3$)

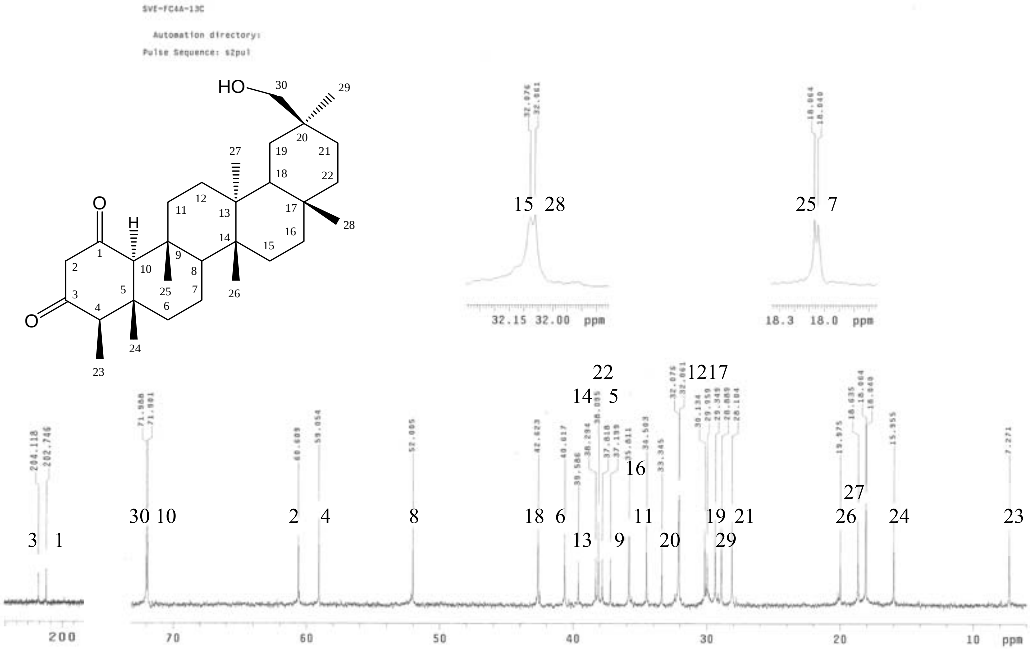


Figure 36. ^{13}C NMR (125 MHz) Spectrum of compound SV-7 (in $CDCl_3$)

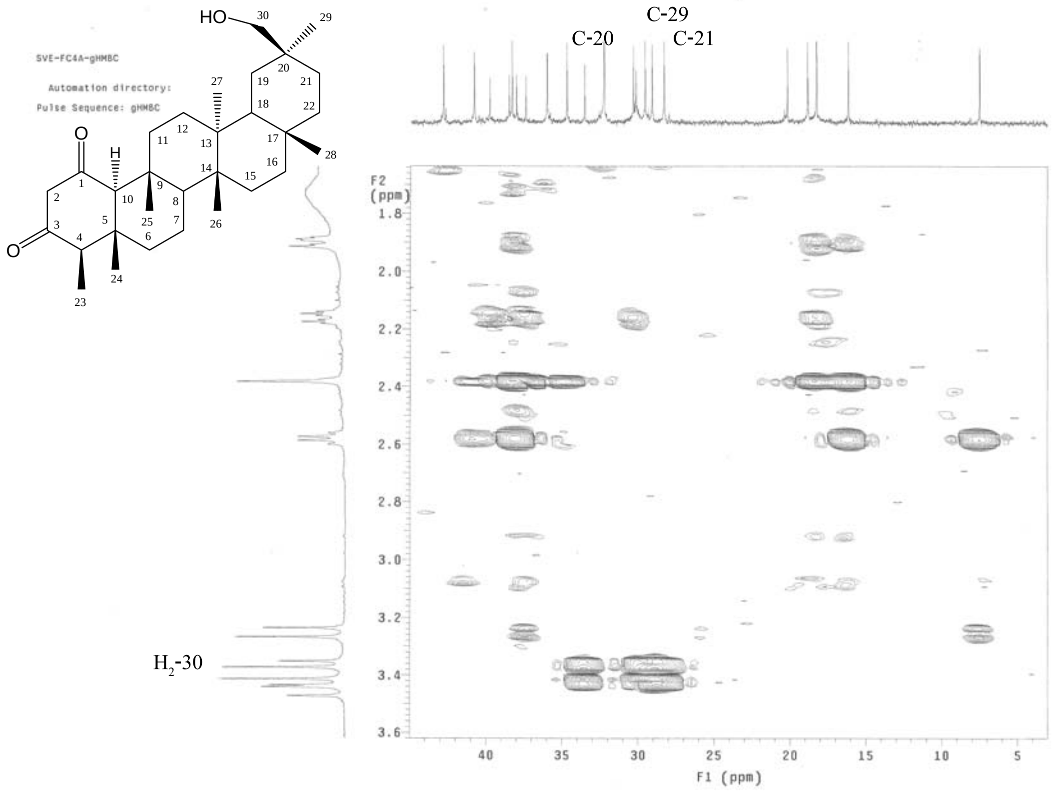


Figure 37a. HMBC Spectrum of compound SV-7 (expansion between δ_H 1.6-3.6, δ_C 5-45 ppm)

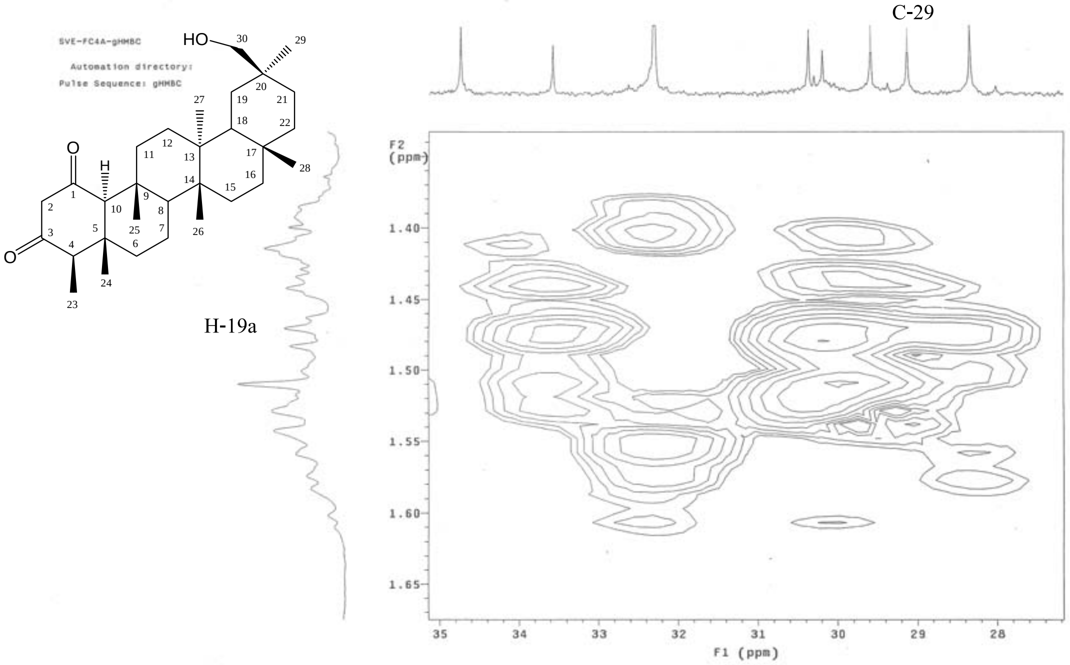


Figure 37b. HMBC Spectrum of compound SV-7 (expansion between δ_H 1.35-1.65, δ_C 27-35 ppm)

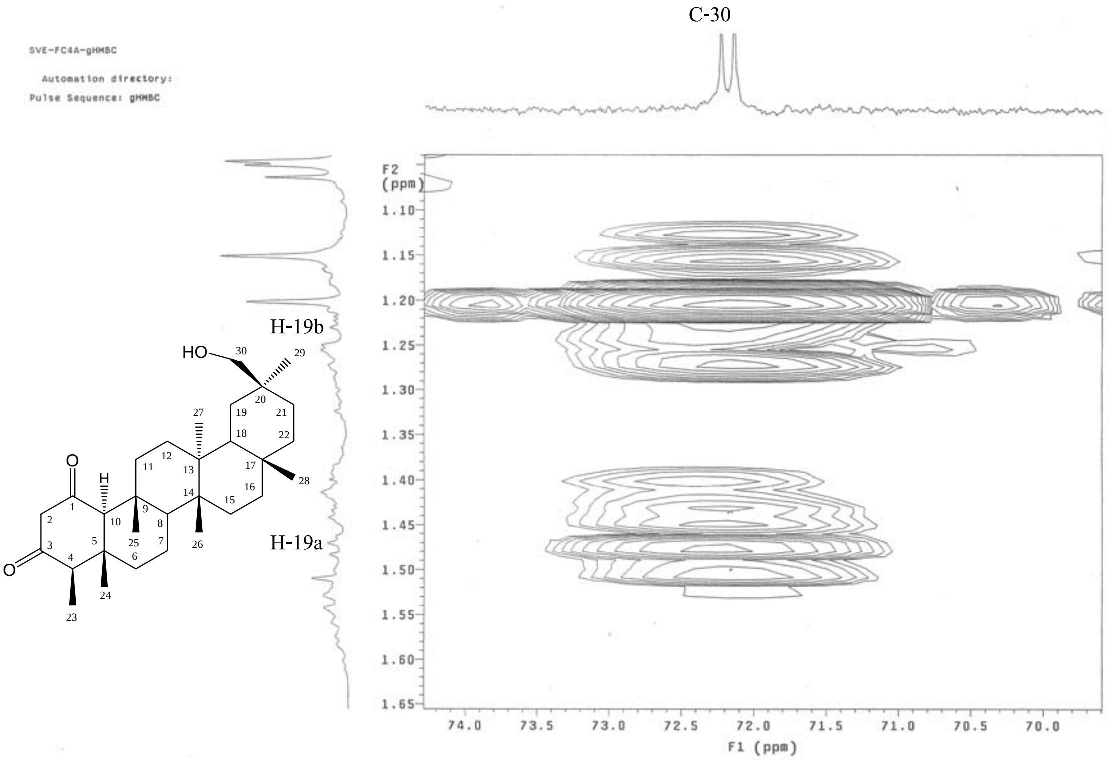


Figure 37c. HMBC Spectrum of compound SV-7 (expansion between δ_H 1.05-1.65, δ_C 70-74 ppm)

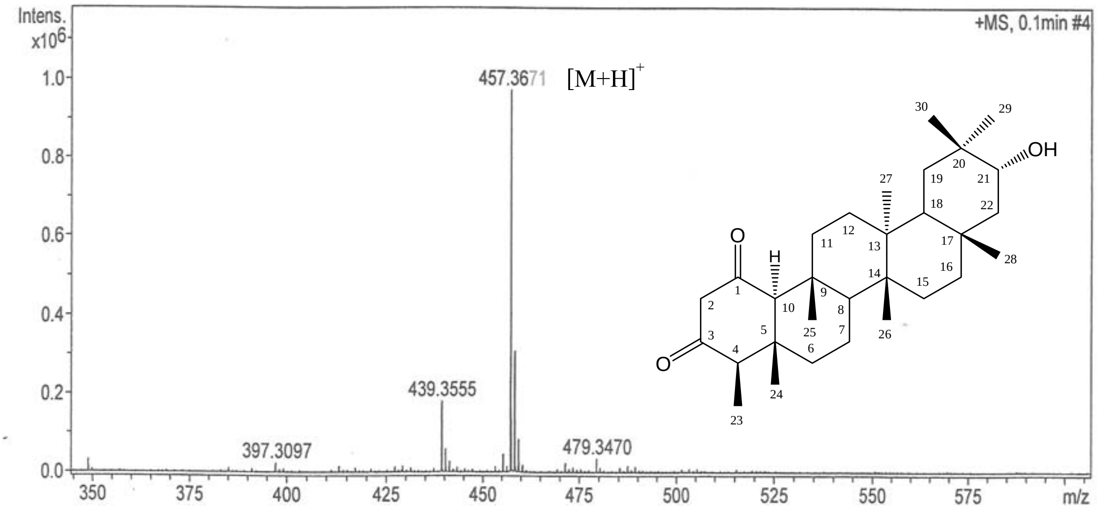


Figure 38. HR-ESI-TOF Mass spectrum of compound SV-8

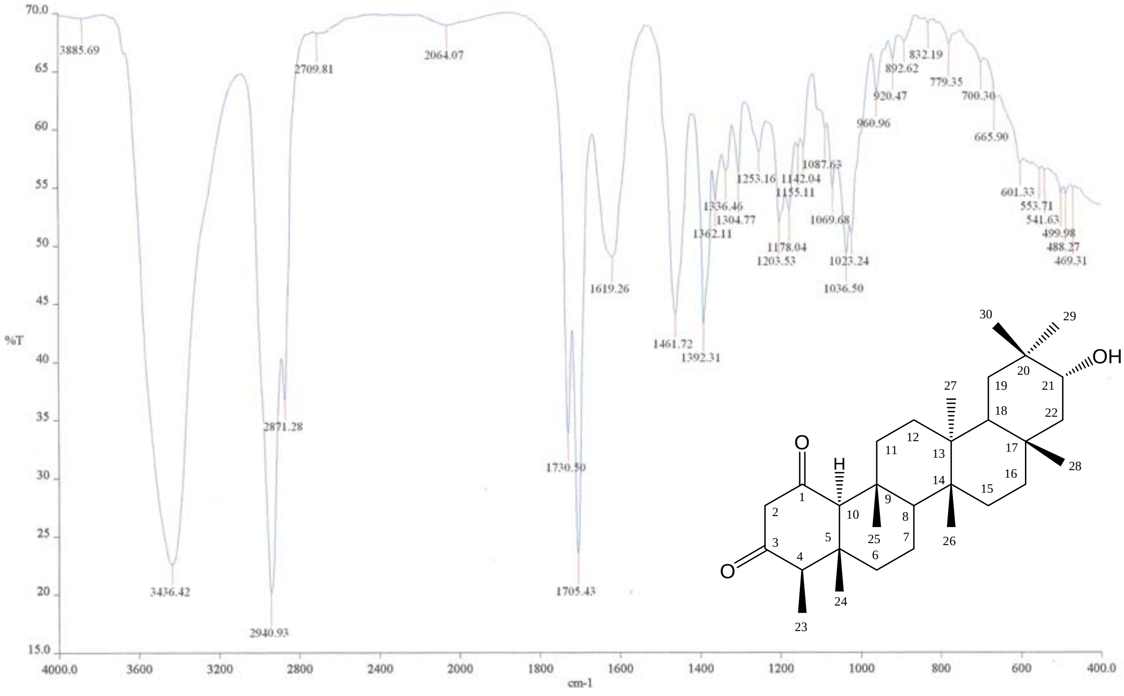


Figure 39. IR Spectrum of compound SV-8 (KBr)

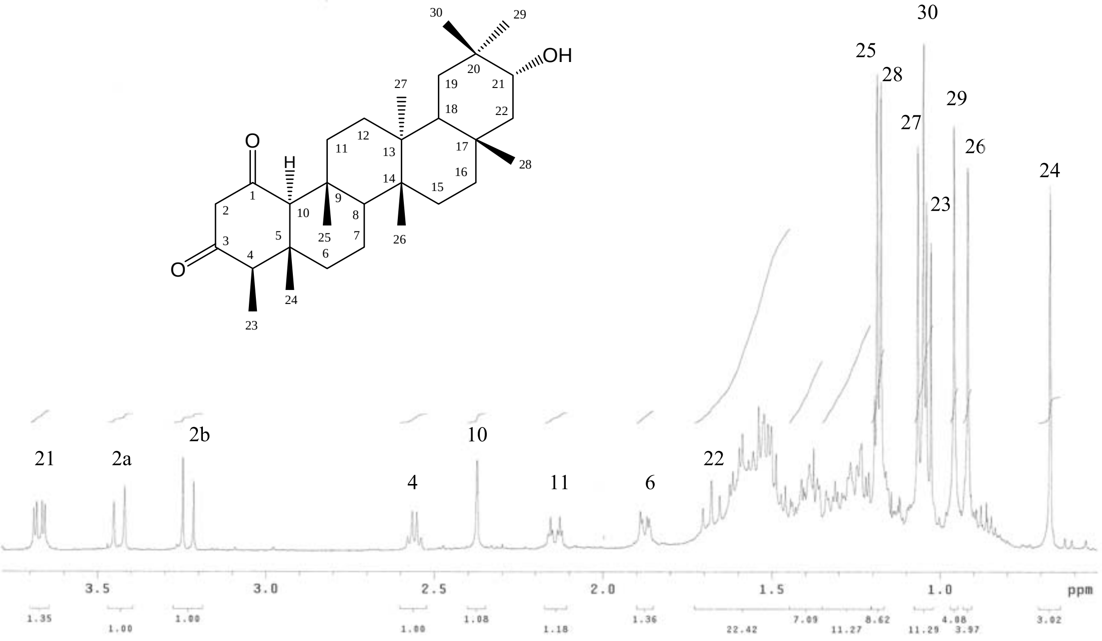


Figure 40. ^{1}H NMR (500 MHz) Spectrum of compound SV-8 (in CDCl$_3$)

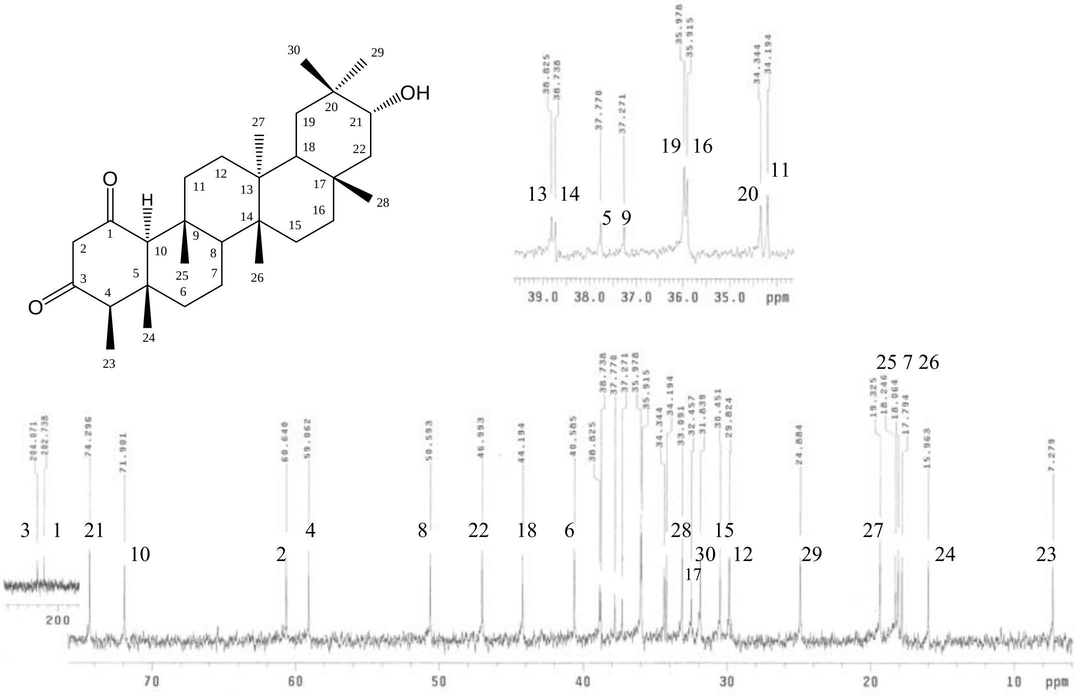


Figure 41. ^{13}C NMR (125 MHz) Spectrum of compound SV-8 (in $CDCl_3$)

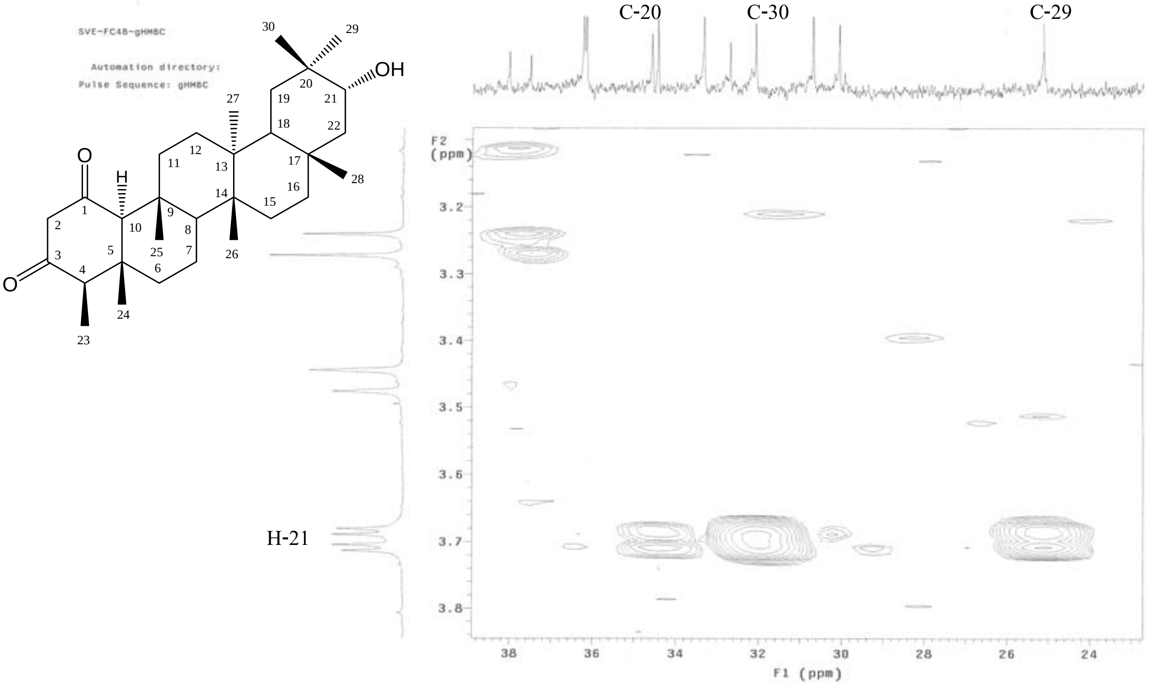


Figure 42a. HMBC Spectrum of compound SV-8 (expansion between δ_H 3.1-3.8, δ_C 24-38 ppm)

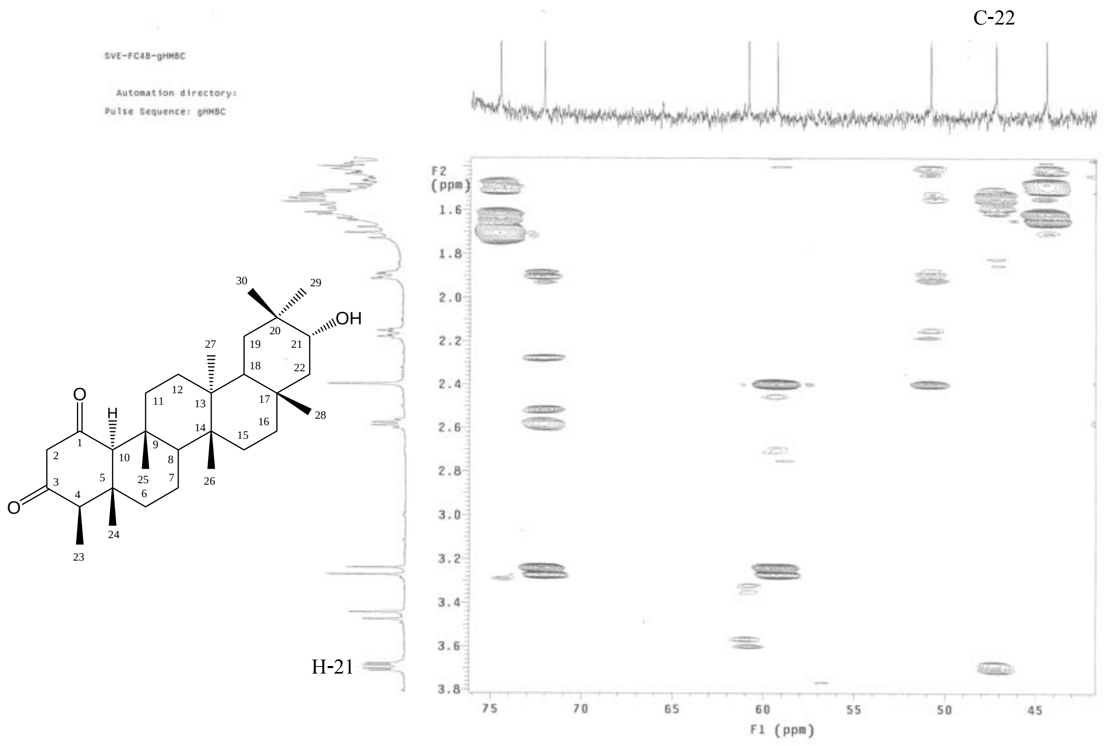


Figure 42b. HMBC Spectrum of compound SV-8 (expansion between δ_H 1.7-3.8, δ_C 45-75 ppm)

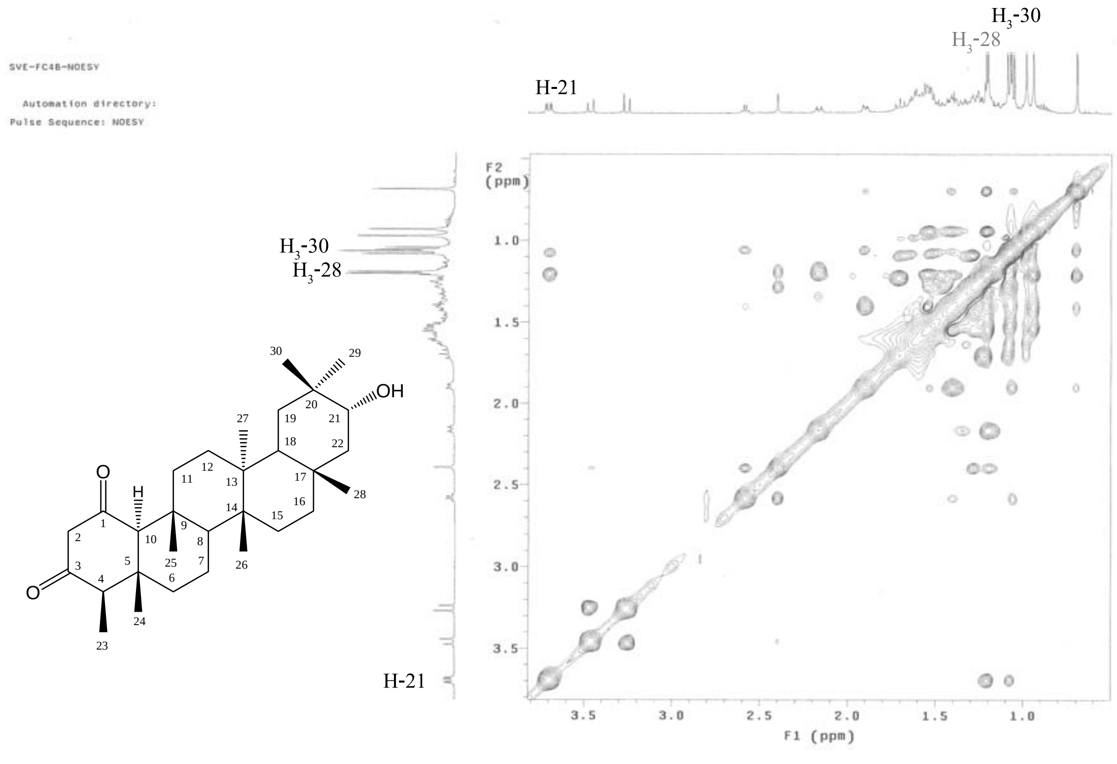


Figure 43. NOESY Spectrum of compound SV-8 (expansion between δ_H 0.5-3.8 ppm)

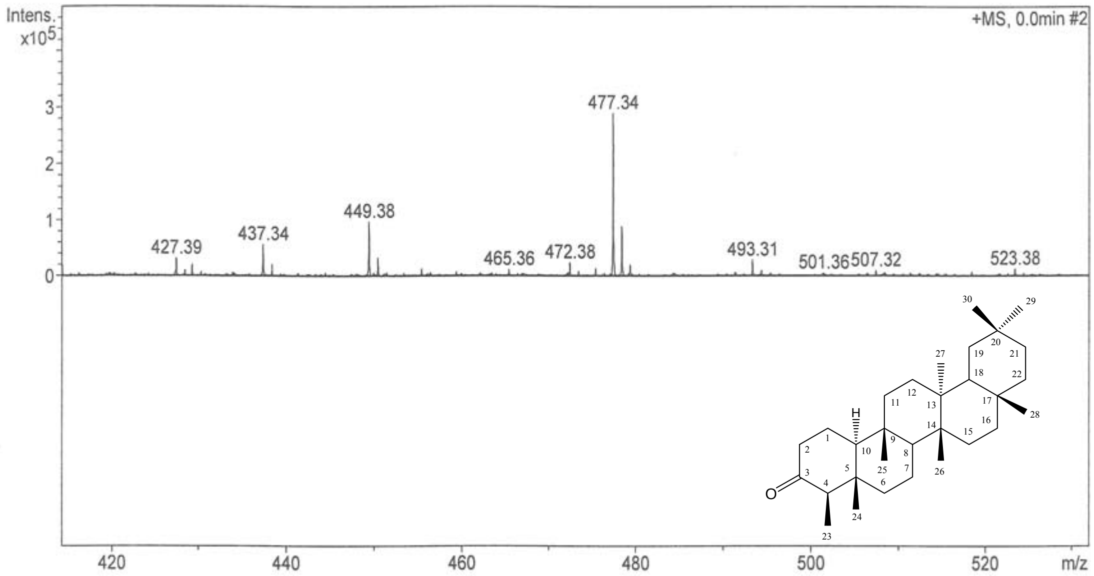


Figure 44. ESI Mass spectrum of compound FF-1

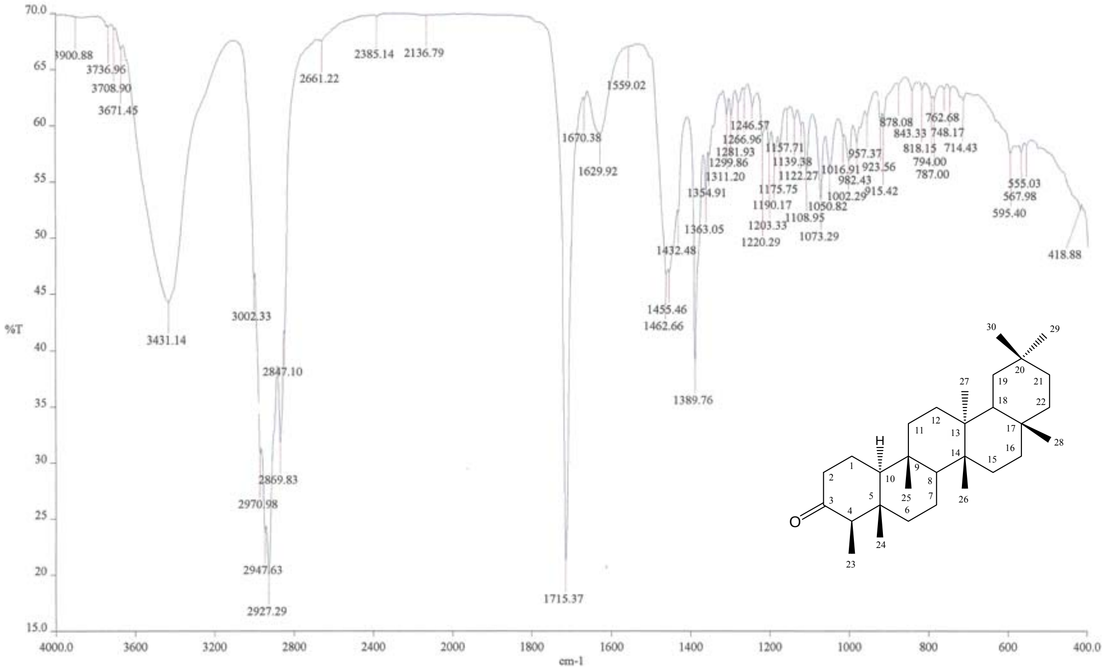


Figure 45. IR Spectrum of compound FF-1 (KBr)

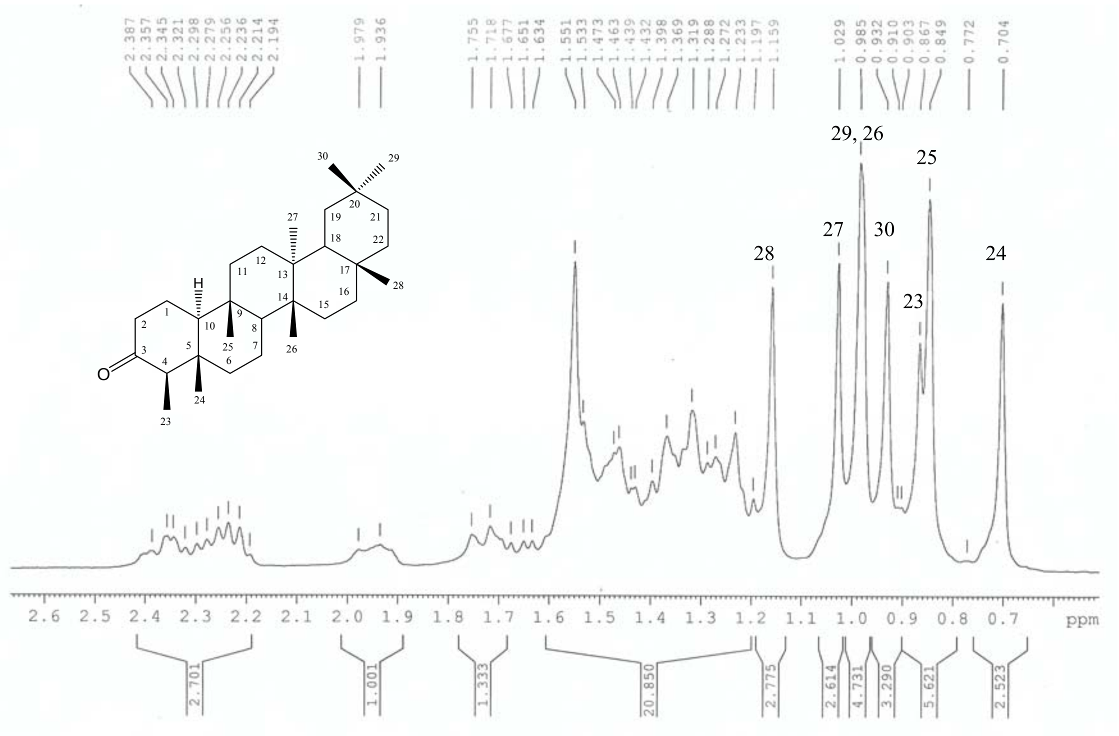


Figure 46. ^{1}H NMR (300 MHz) Spectrum of compound FF-1 from δ 0.5-2.6 ppm (in $CDCl_3$)

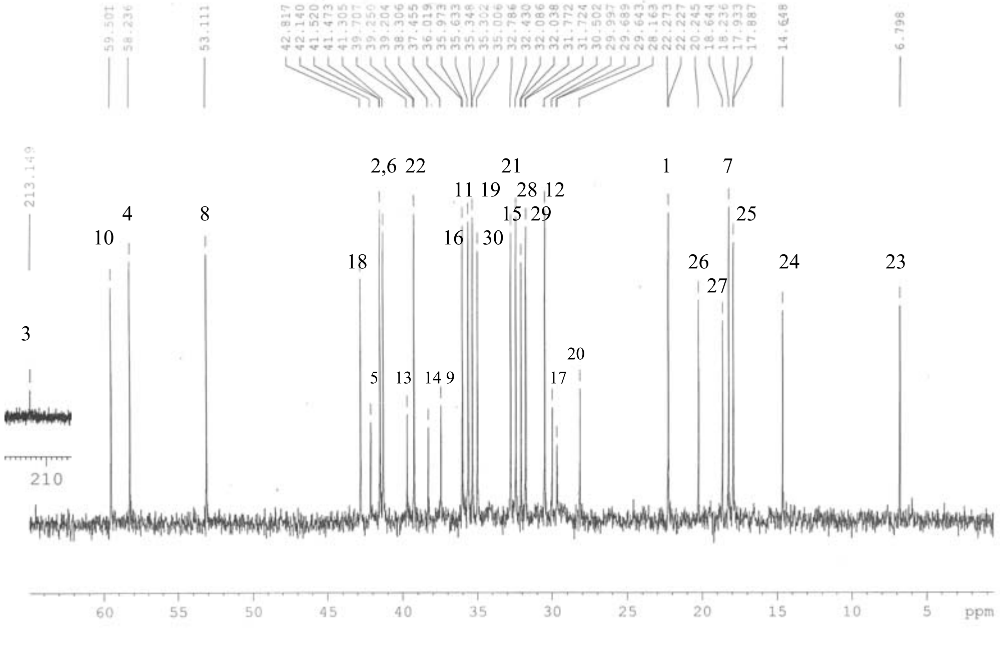


Figure 47. ^{13}C NMR (75 MHz) Spectrum of compound FF-1 (in $CDCl_3$)

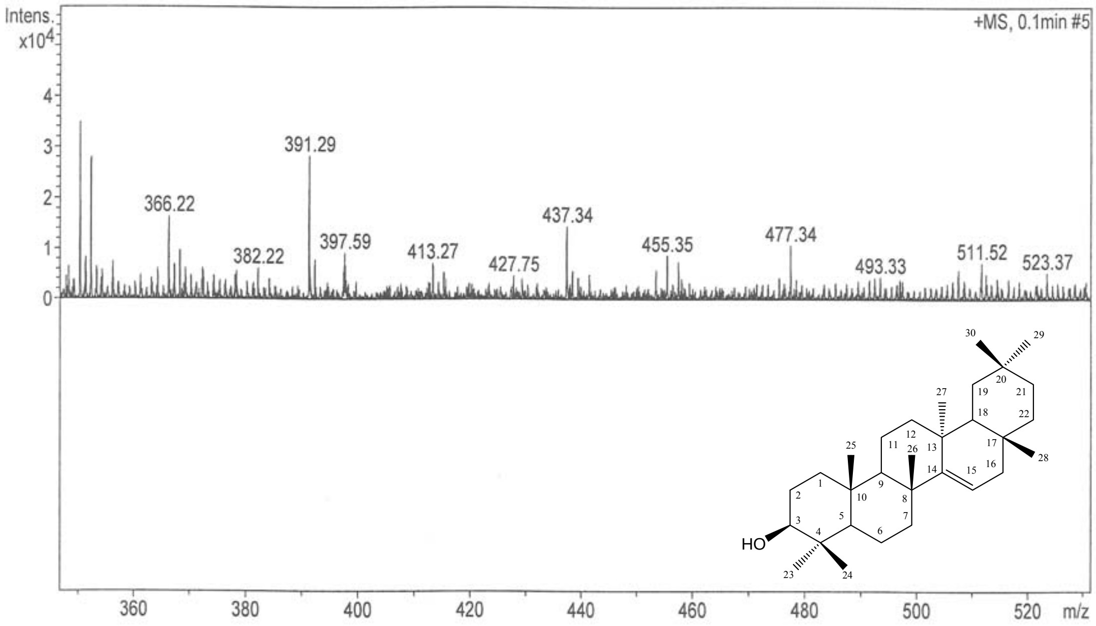


Figure 48. ESI Mass spectrum of compound FF-2

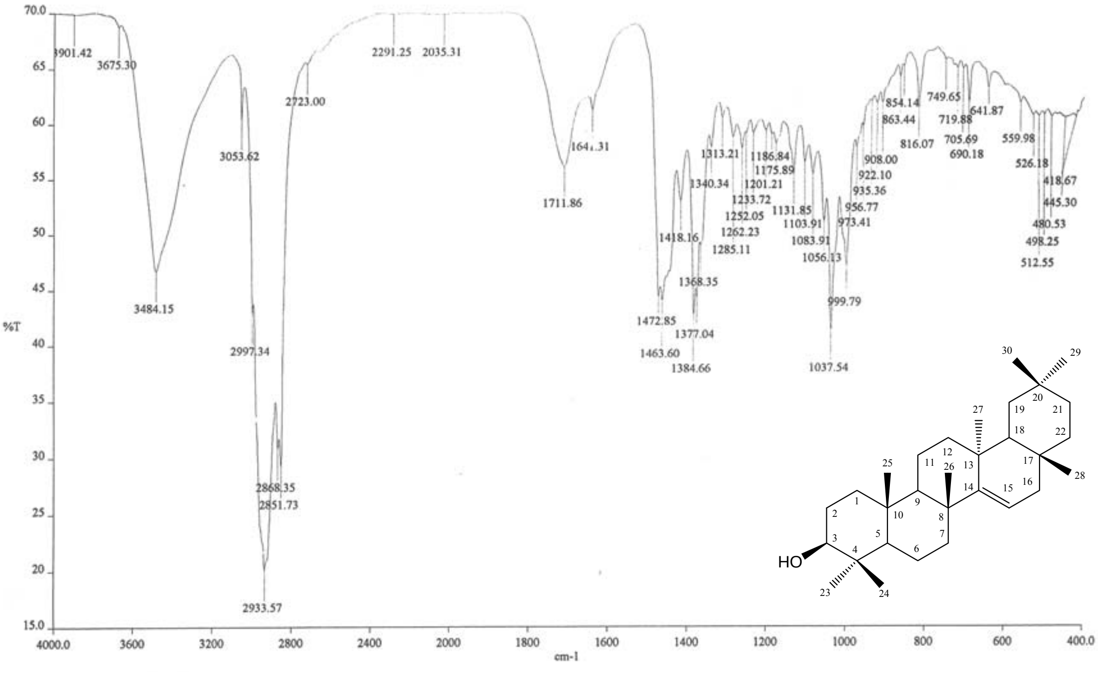


Figure 49. IR Spectrum of compound FF-2 (KBr)

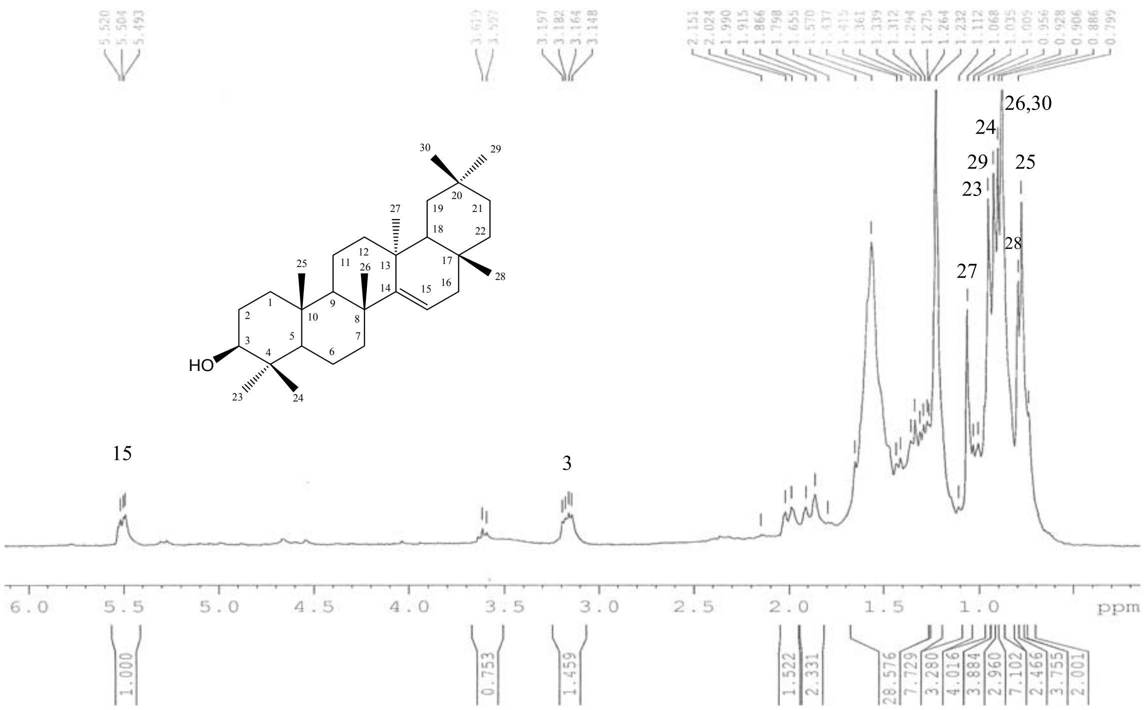


Figure 50. ^{1}H NMR (300 MHz) Spectrum of compound FF-2 (in $CDCl_3$)

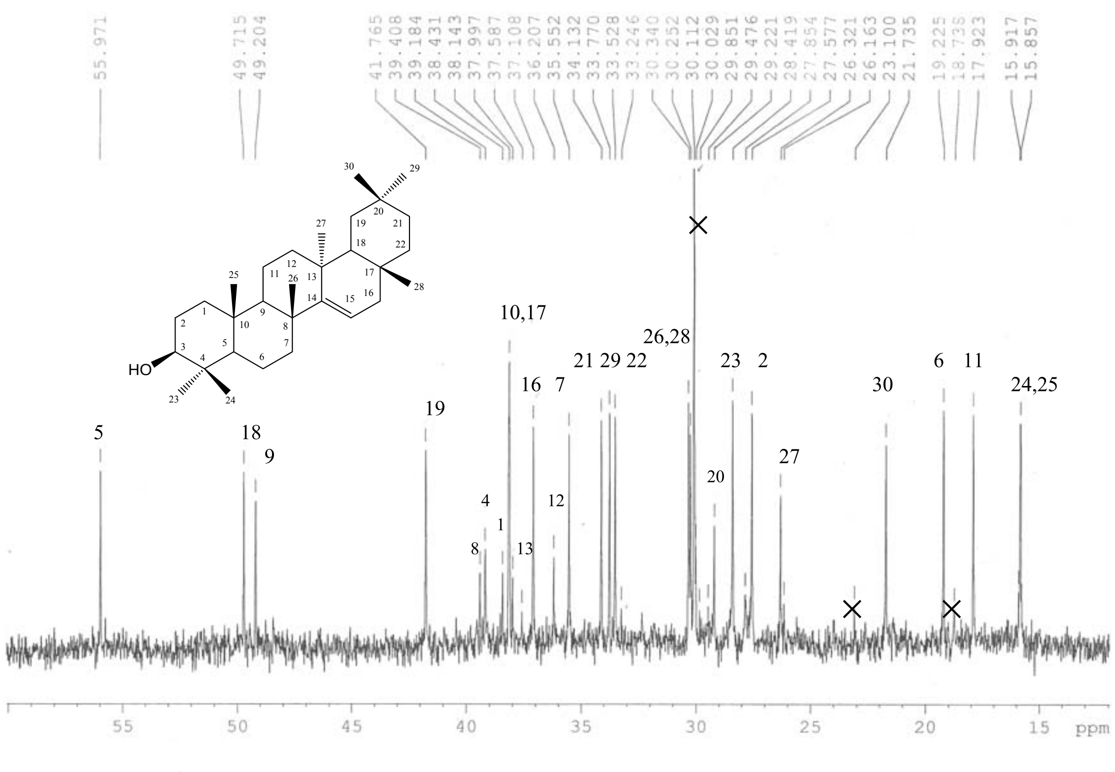


Figure 51a. ^{13}C NMR (75 MHz) Spectrum of compound FF-2 from δ 12-60 ppm (in $CDCl_3$)

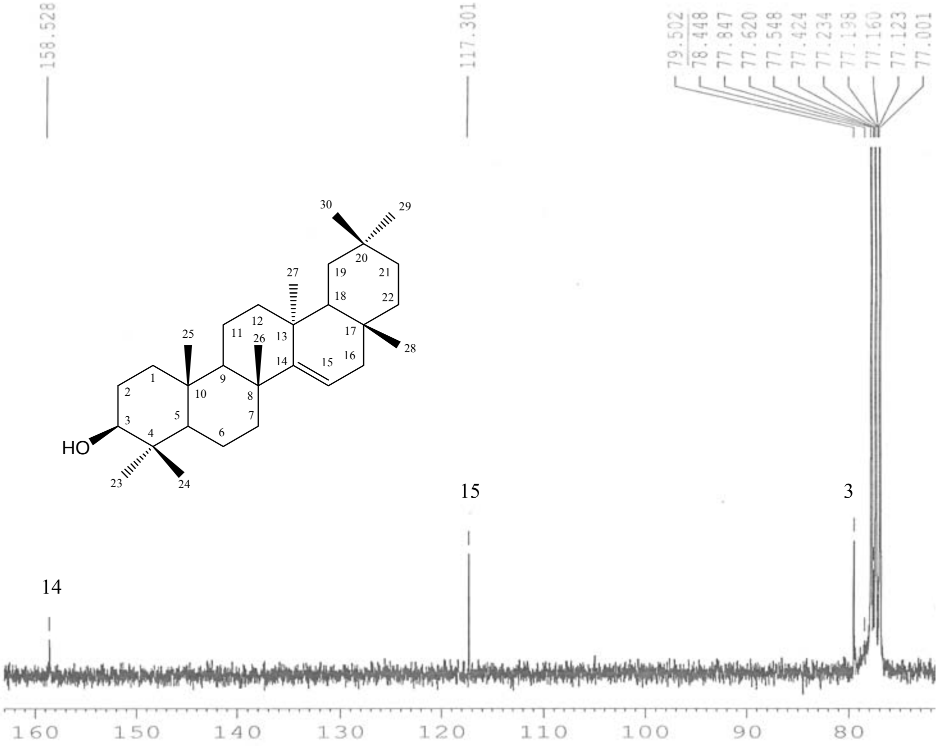


Figure 51b. ^{13}C NMR (75 MHz) Spectrum of compound FF-2 from δ 70-160 ppm (in $CDCl_3$)

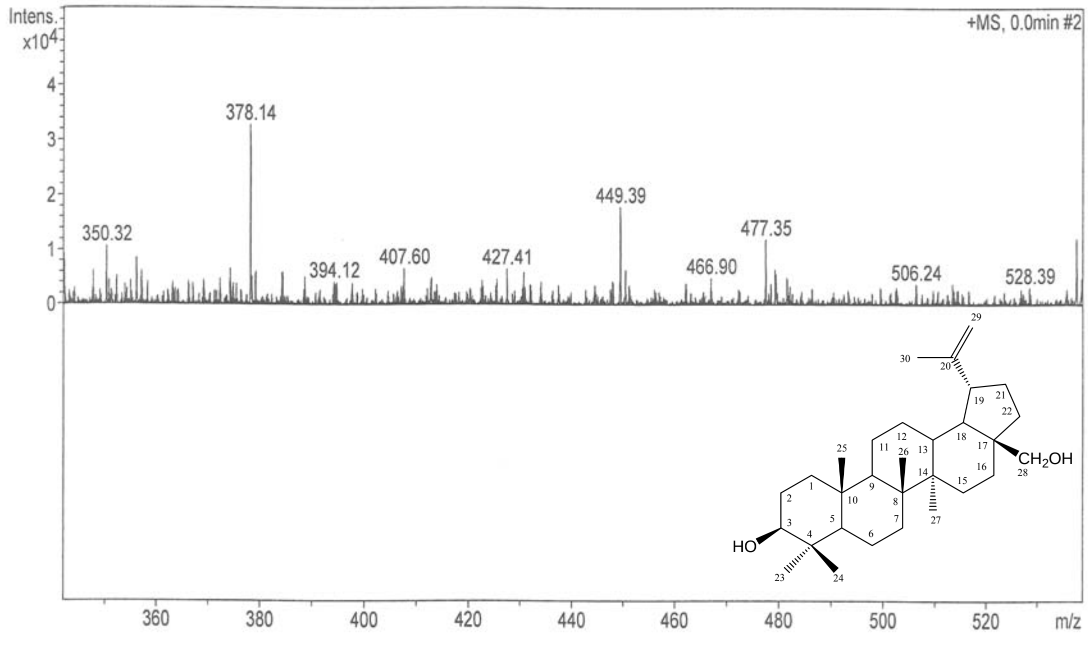


Figure 52. ESI Mass spectrum of compound FF-3

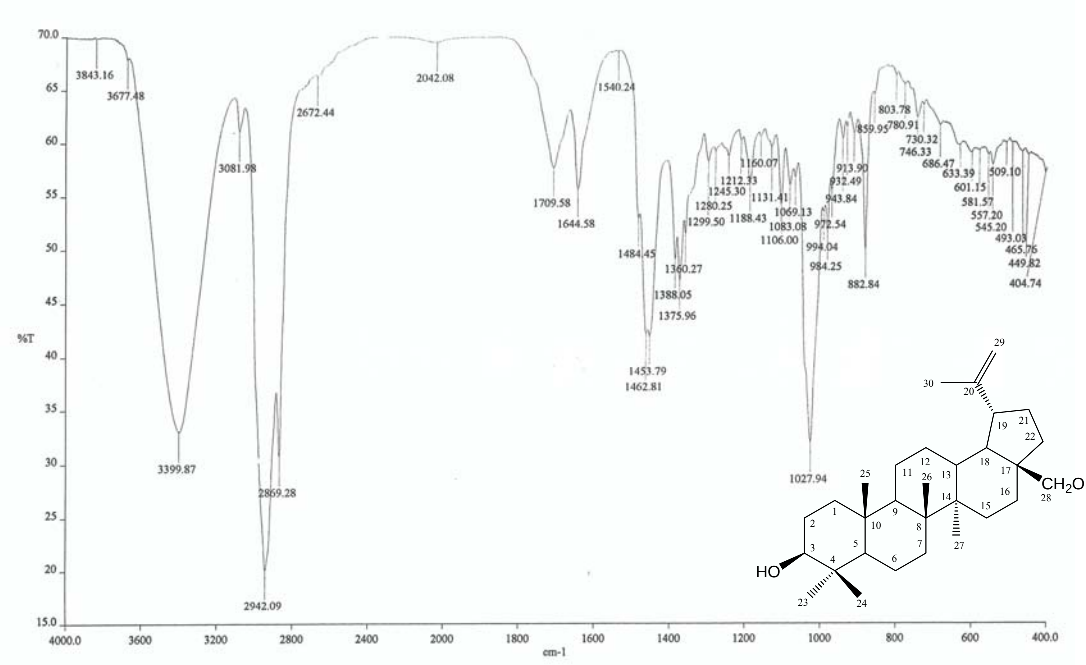


Figure 53. IR Spectrum of compound FF-3 (KBr)

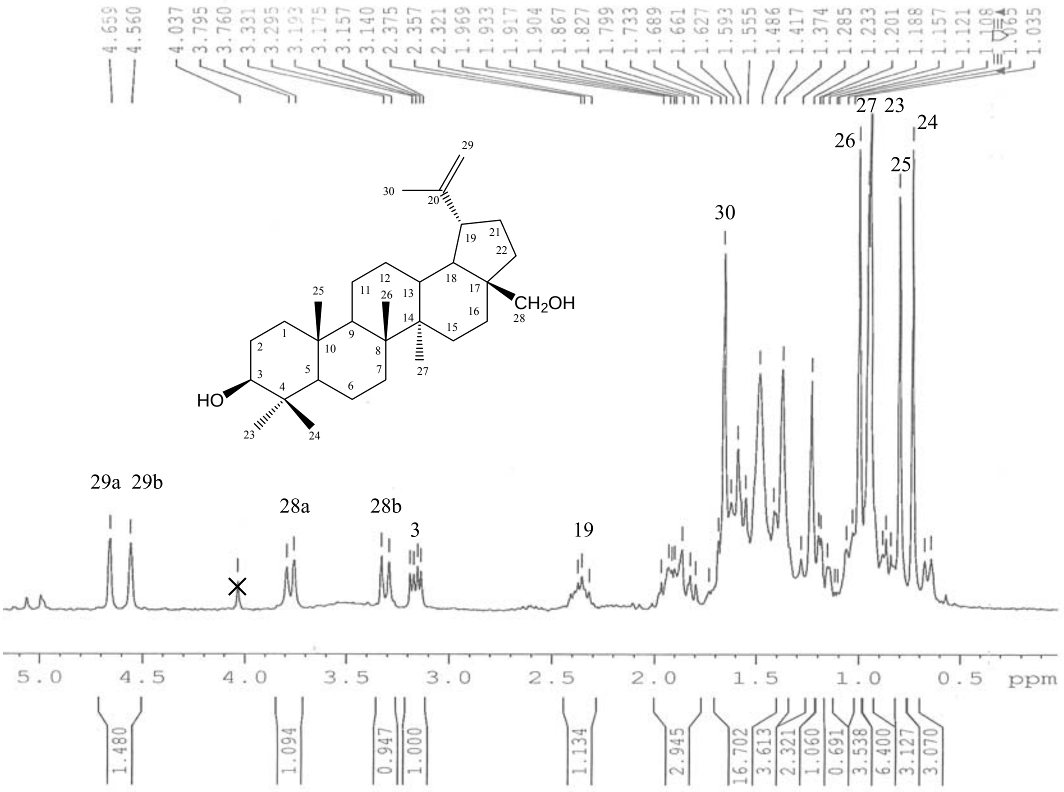


Figure 54. ^{1}H NMR (300 MHz) Spectrum of compound FF-3 from δ 0.1-5.0 ppm (in $CDCl_3$)

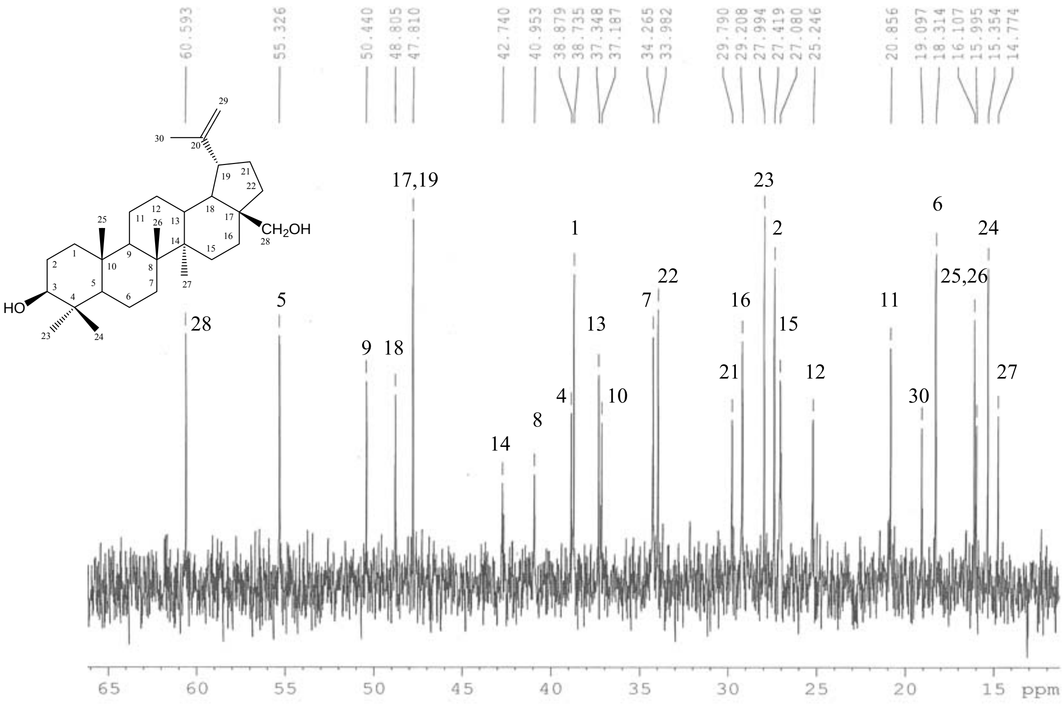


Figure 55a. ^{13}C NMR (75 MHz) Spectrum of compound FF-3 from δ 12-65 ppm (in $CDCl_3$)

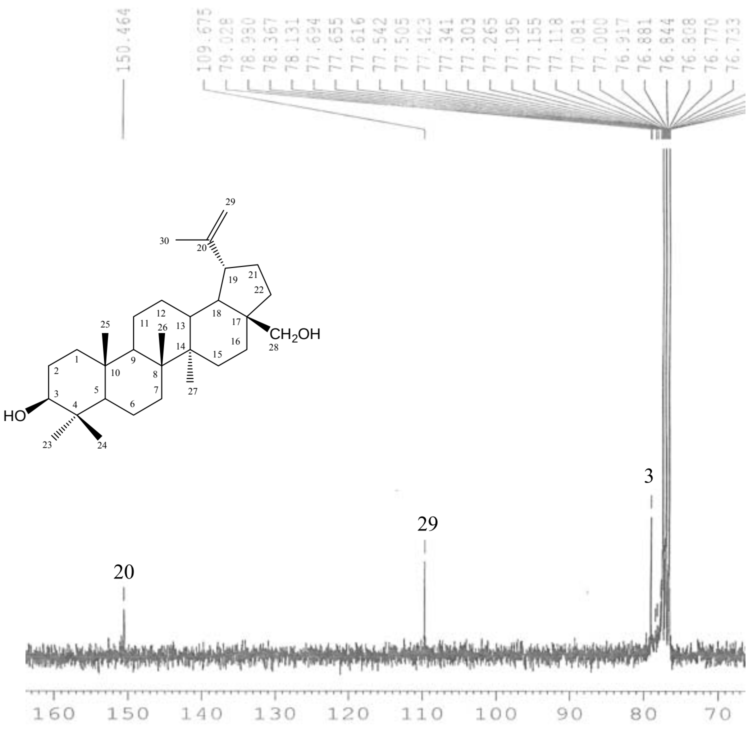


Figure 55b. ^{13}C NMR (75 MHz) Spectrum of compound FF-3 from δ 70-160 ppm (in $CDCl_3$)

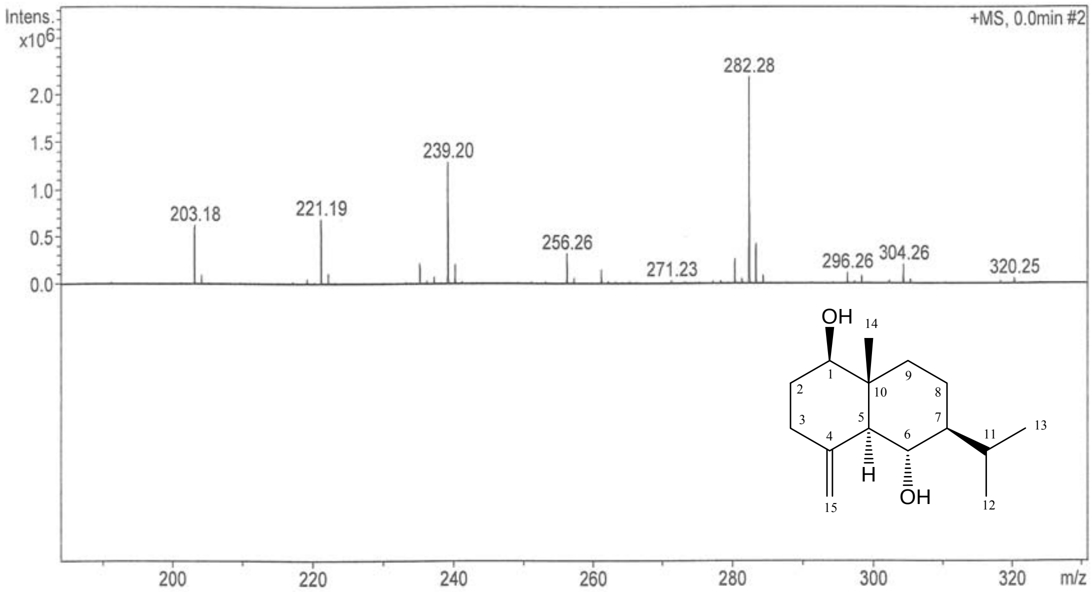


Figure 56. ESI Mass spectrum of compound FF-4

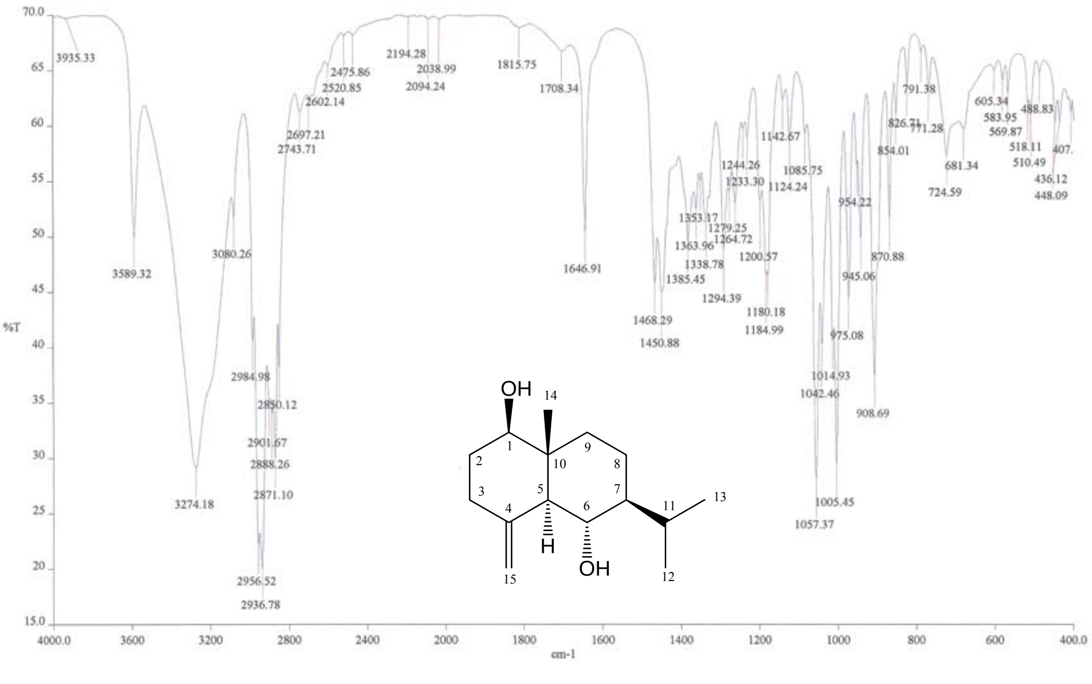


Figure 57. IR Spectrum of compound FF-4 (KBr)

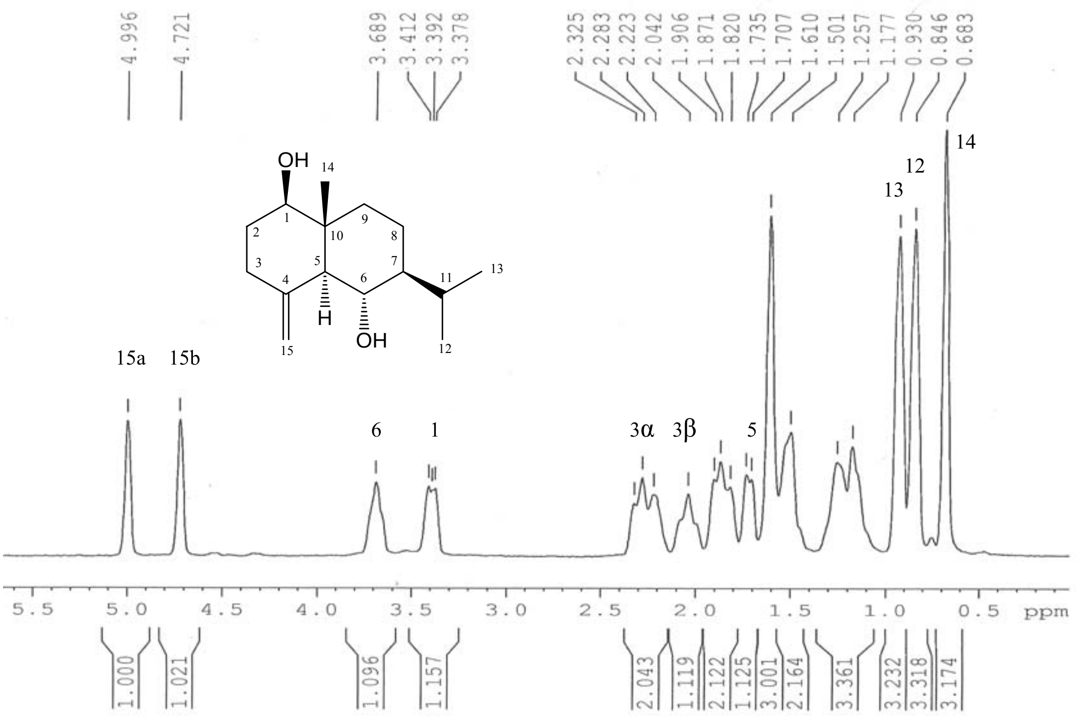


Figure 58. ^{1}H NMR (300 MHz) Spectrum of compound FF-4 (in $CDCl_3$)

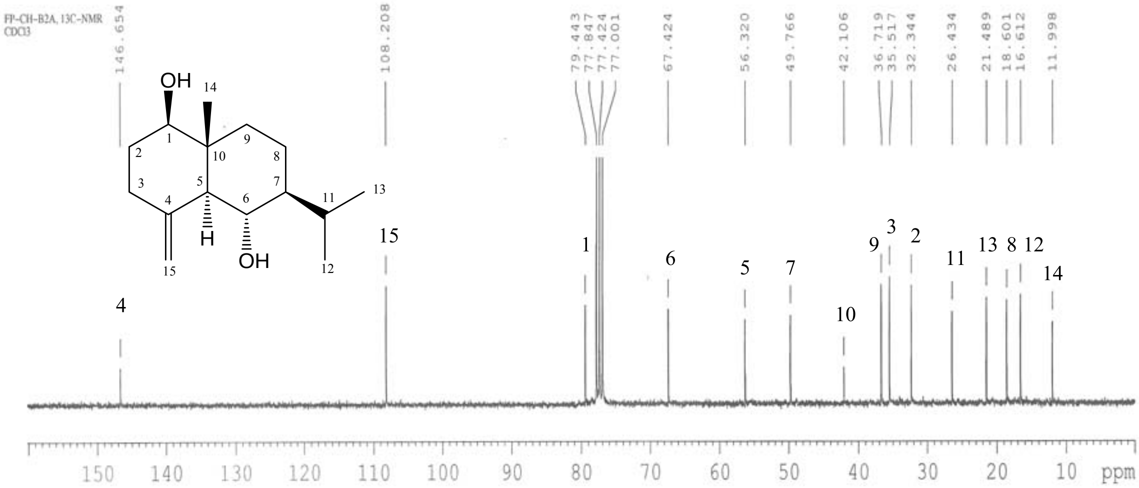


Figure 59. ^{13}C NMR (75 MHz) Spectrum of compound FF-4 (in $CDCl_3$)

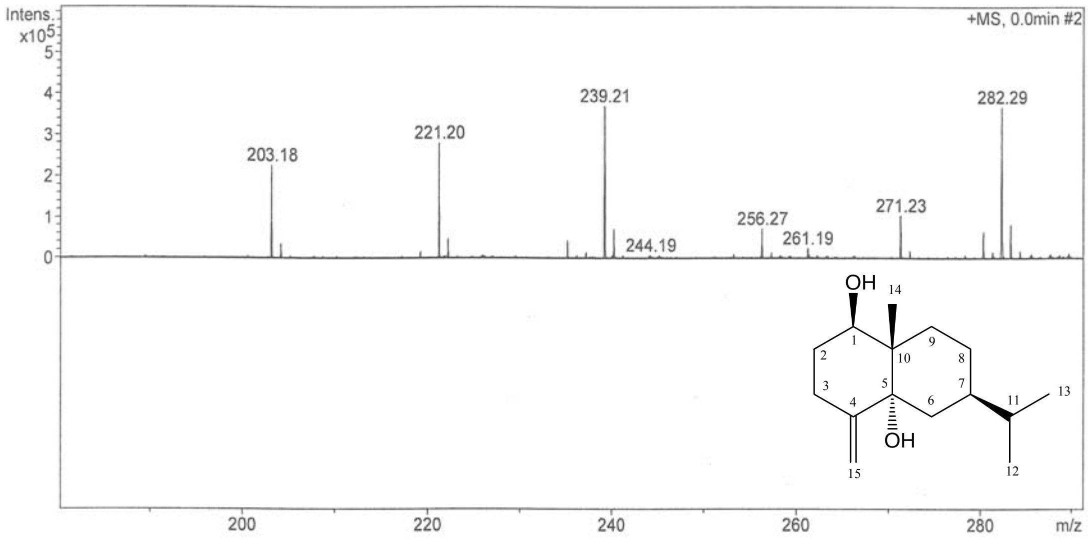


Figure 60. ESI Mass spectrum of compound FF-5

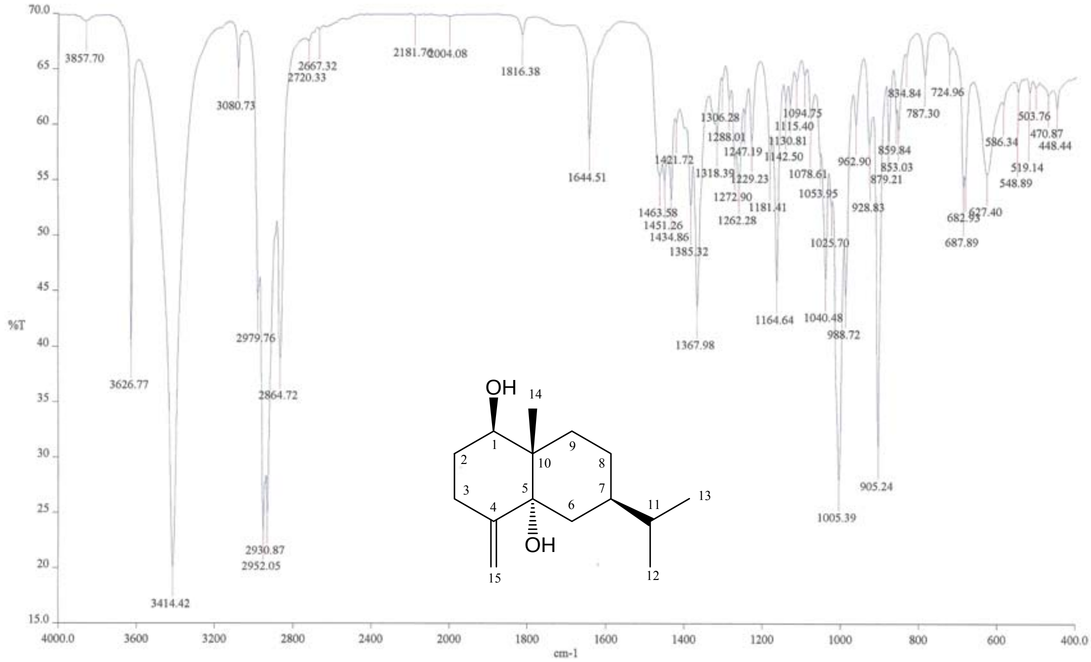


Figure 61. IR Spectrum of compound FF-5 (KBr)

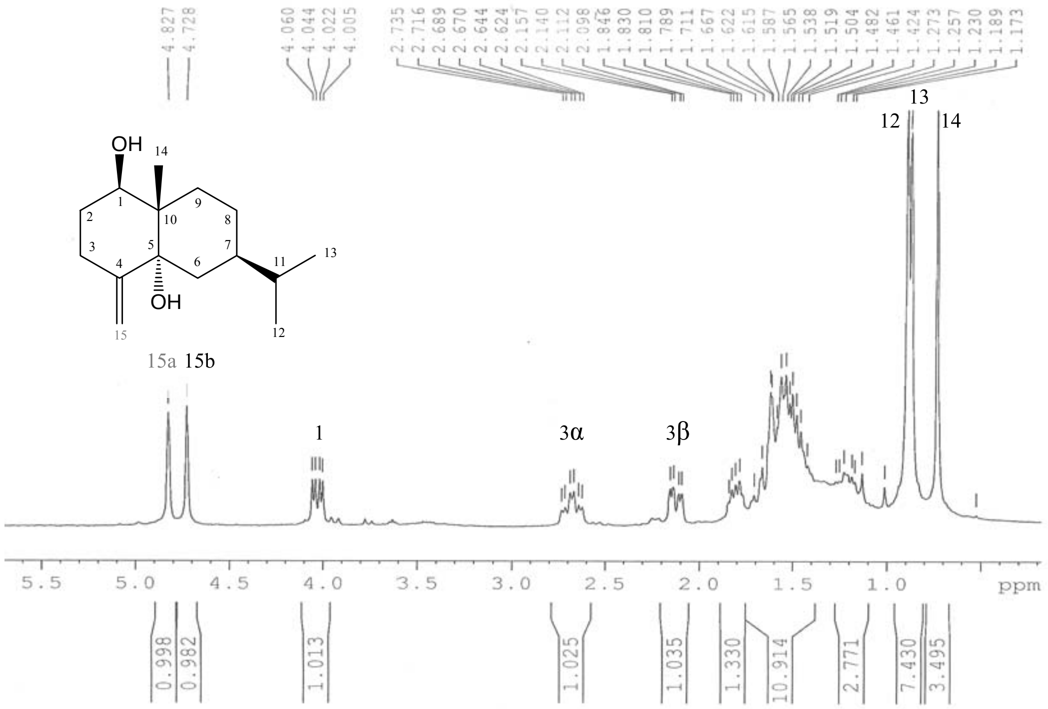


Figure 62. ^{1}H NMR (300 MHz) Spectrum of compound FF-5 (in $CDCl_3$)

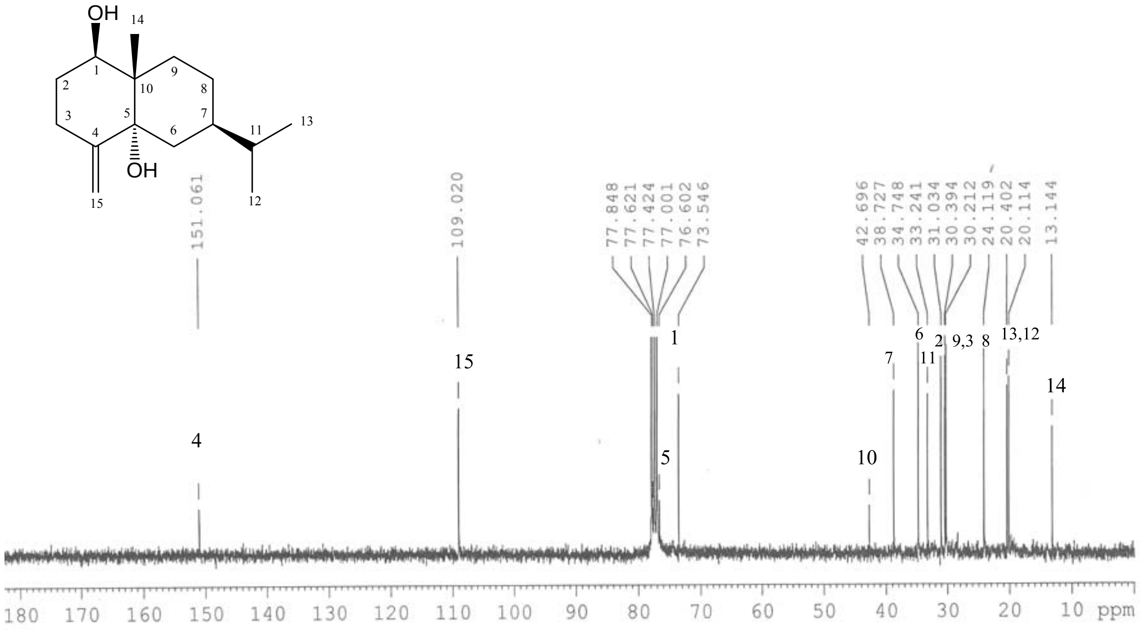


Figure 63. ^{13}C NMR (75 MHz) Spectrum of compound FF-5 (in $CDCl_3$)

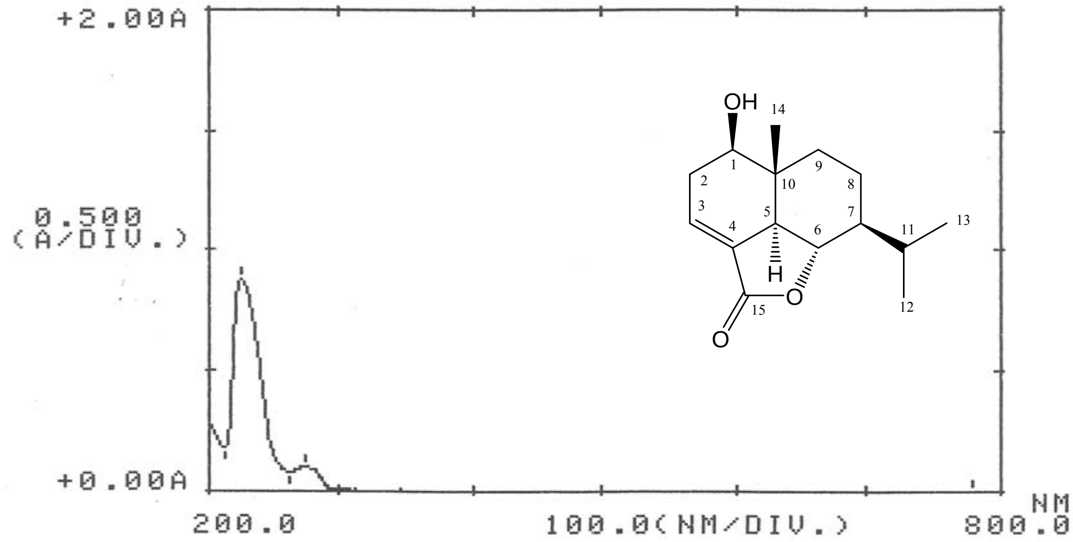


Figure 64. UV Spectrum of compound FF-7 (in MeOH)

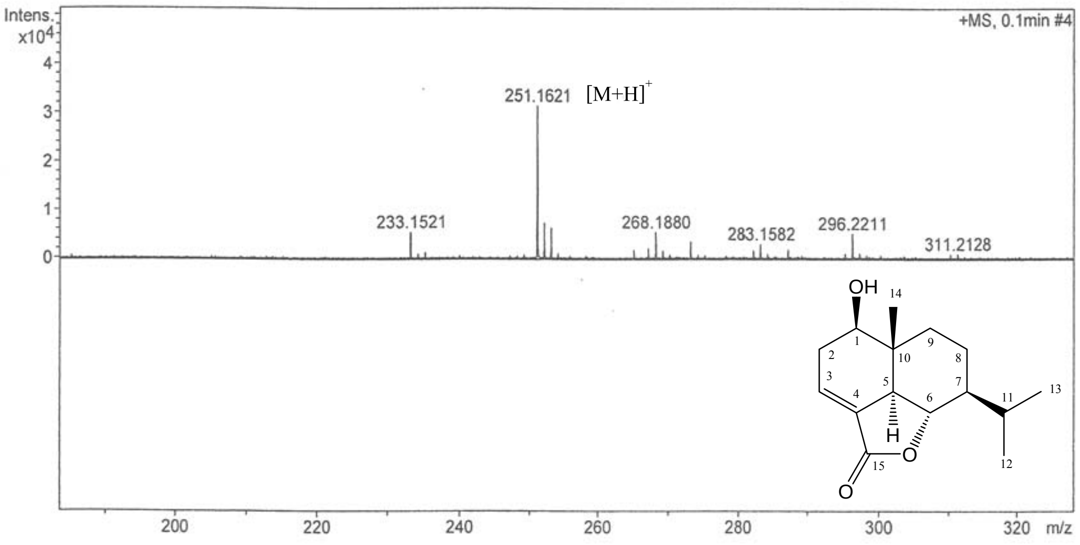


Figure 65. HR-ESI-TOF Mass spectrum of compound FF-7

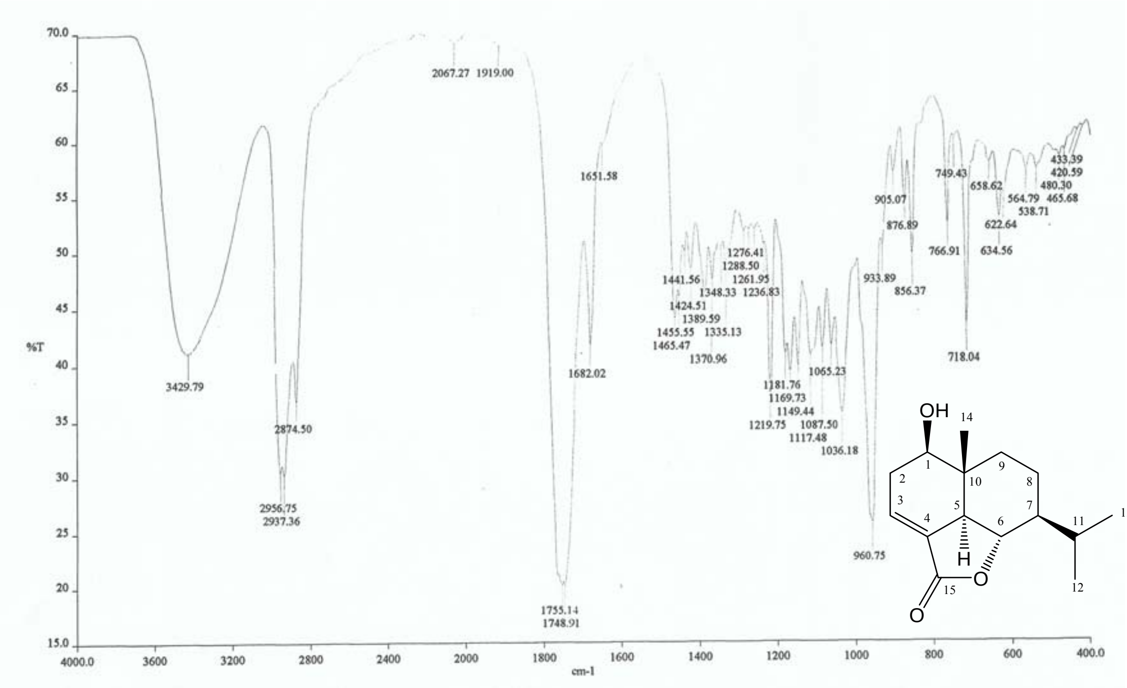


Figure 66. IR Spectrum of compound FF-7 (KBr)

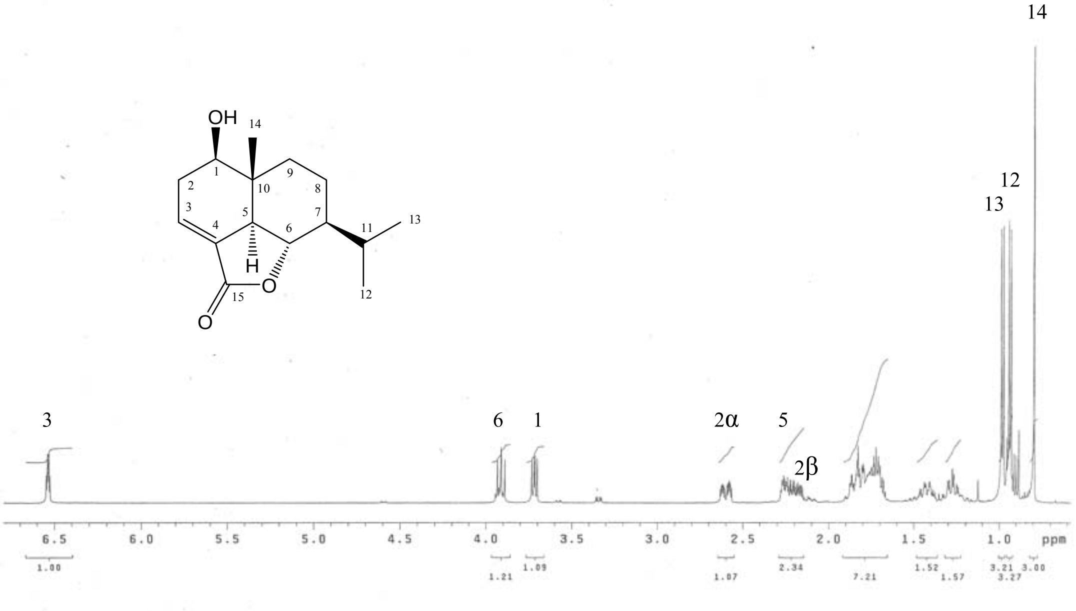


Figure 67. ^{1}H NMR (500 MHz) Spectrum of compound FF-7 (in $CDCl_3$)

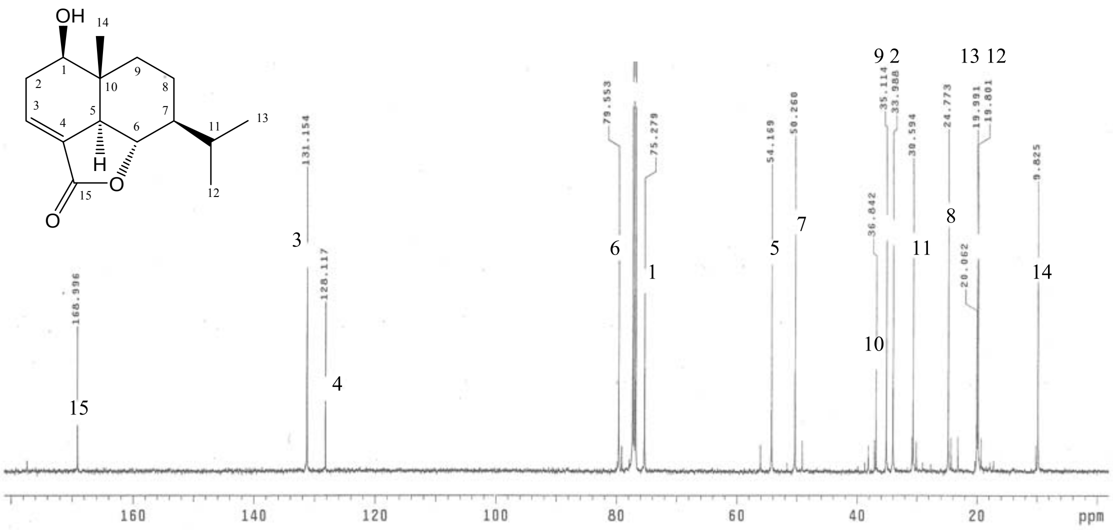


Figure 68. ^{13}C NMR (125 MHz) Spectrum of compound FF-7 (in $CDCl_3$)

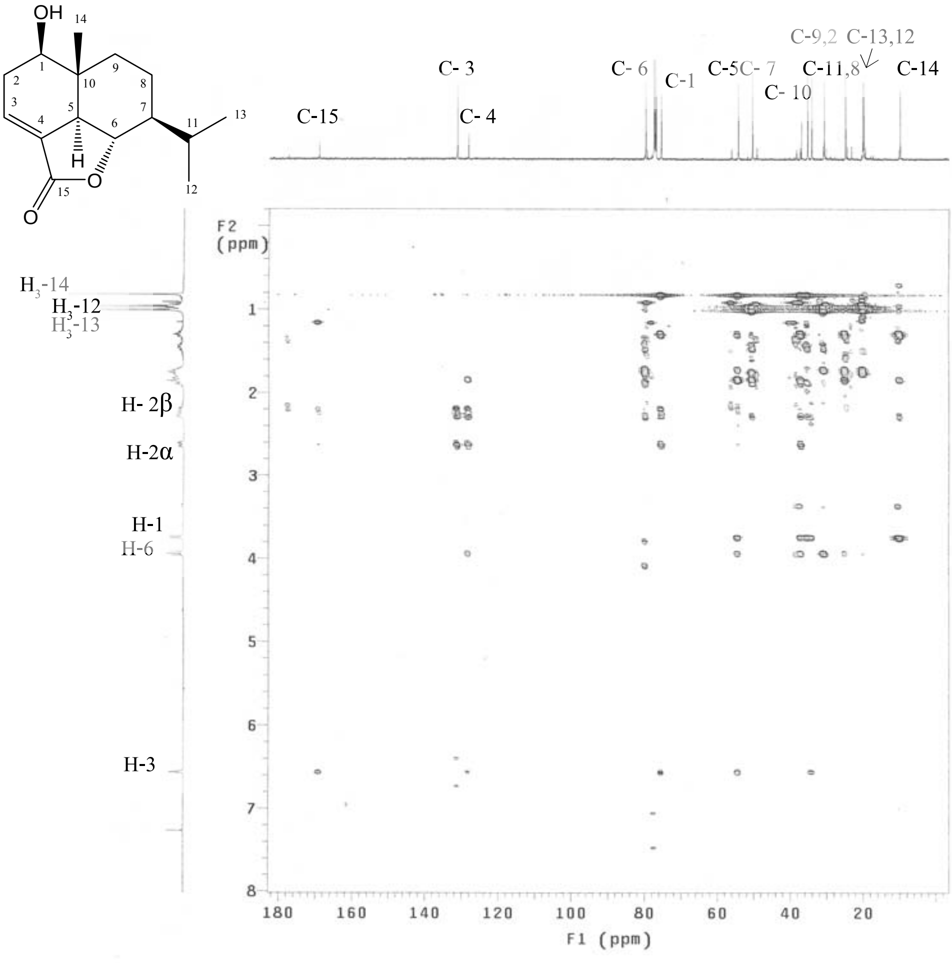


Figure 69a. HMBC Spectrum of compound FF-7 (in $CDCl_3$)

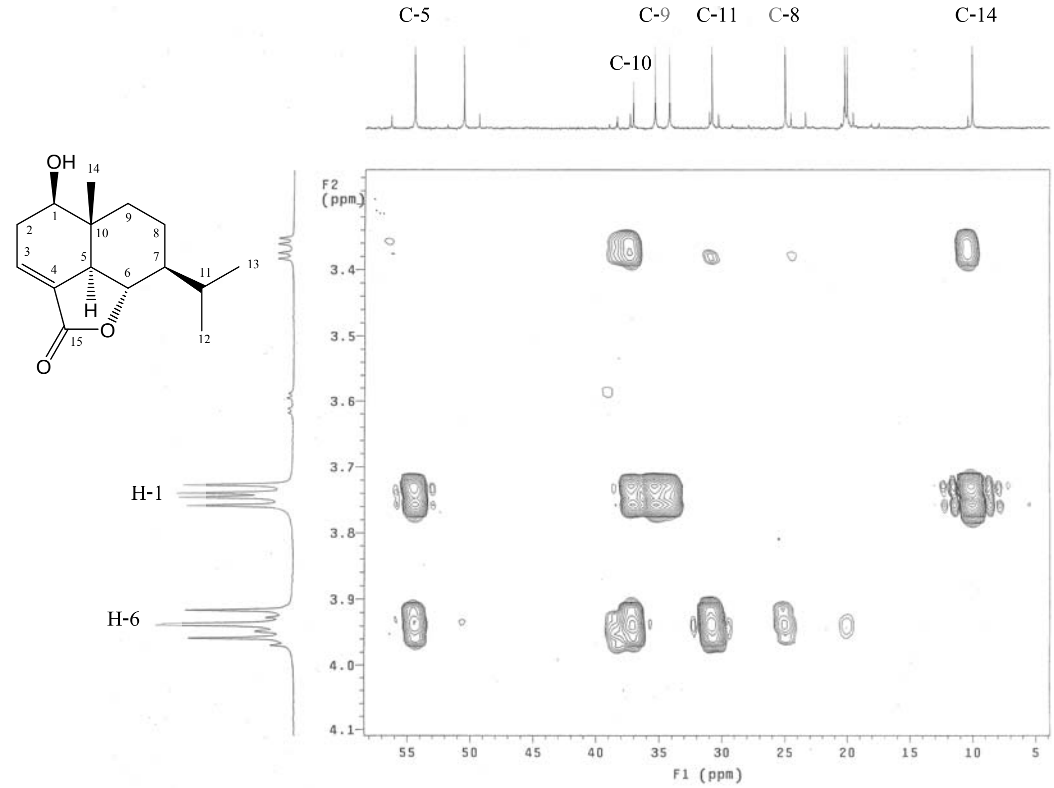


Figure 69b. HMBC Spectrum of compound FF-7 (expansion between δ_H 3.3-4.1, δ_C 5-58 ppm)

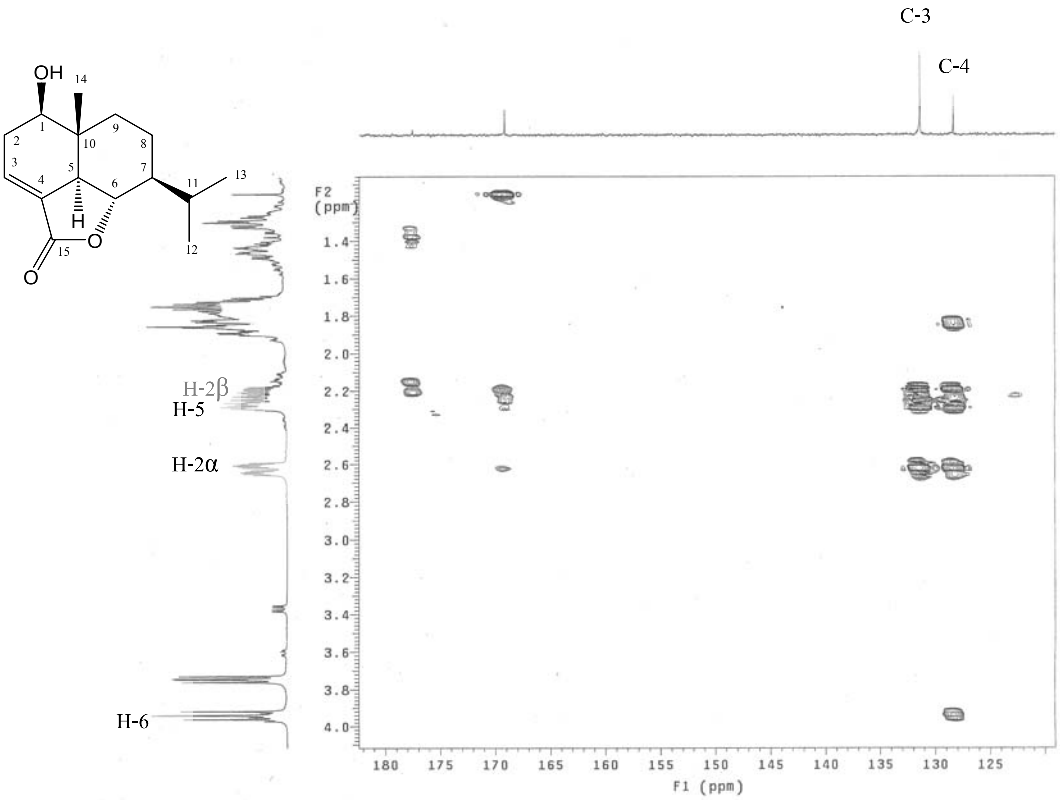


Figure 69c. HMBC Spectrum of compound FF-7 (expansion between δ_H 1.0-4.1, δ_C 120-180 ppm)

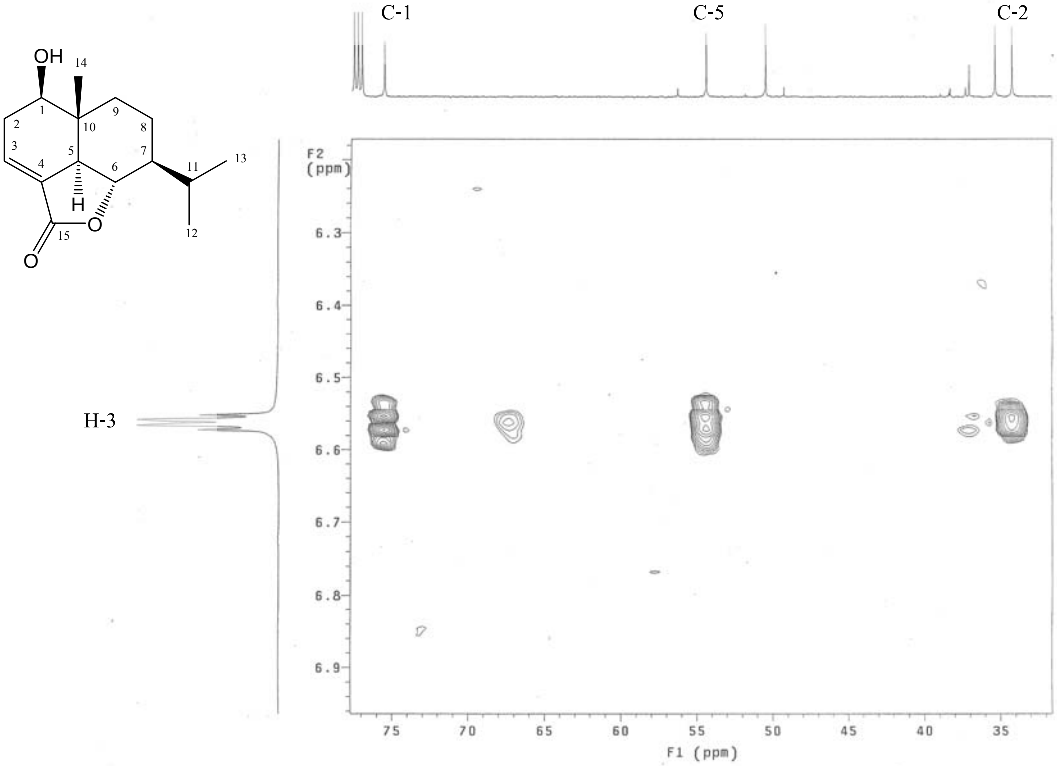


Figure 69d. HMBC Spectrum of compound FF-7 (expansion between δ_H 6.2-6.9, δ_C 32-77 ppm)

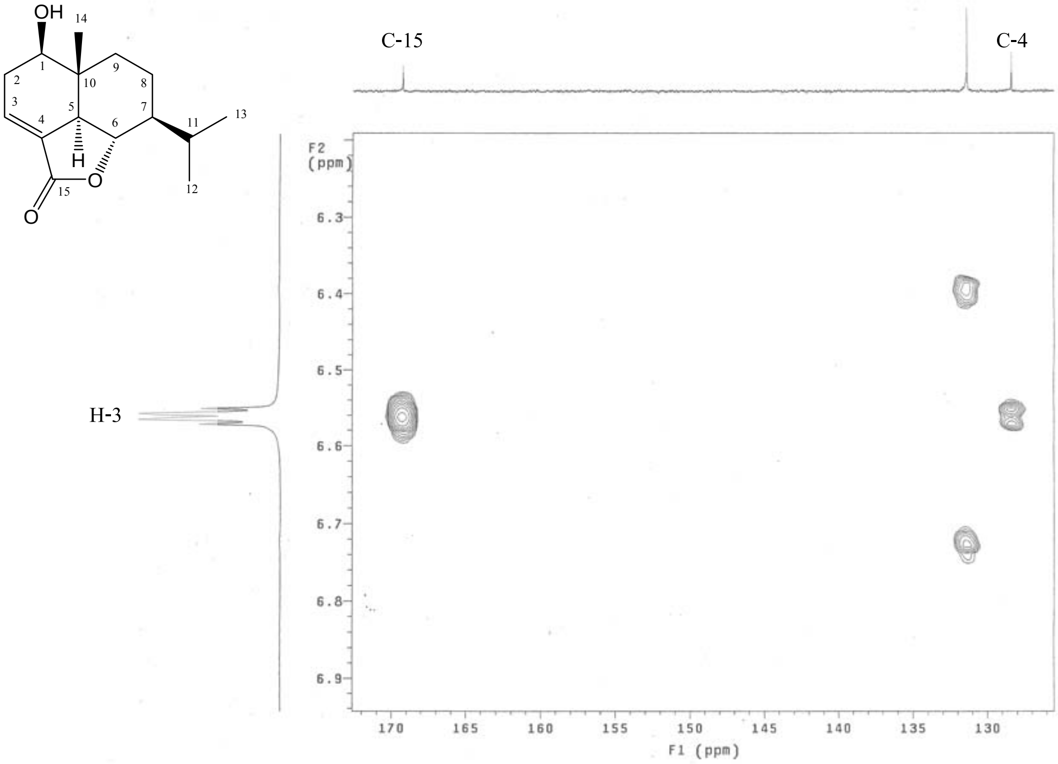


Figure 69e. HMBC Spectrum of compound FF-7 (expansion between δ_H 6.2-6.9, δ_C 125-172 ppm)

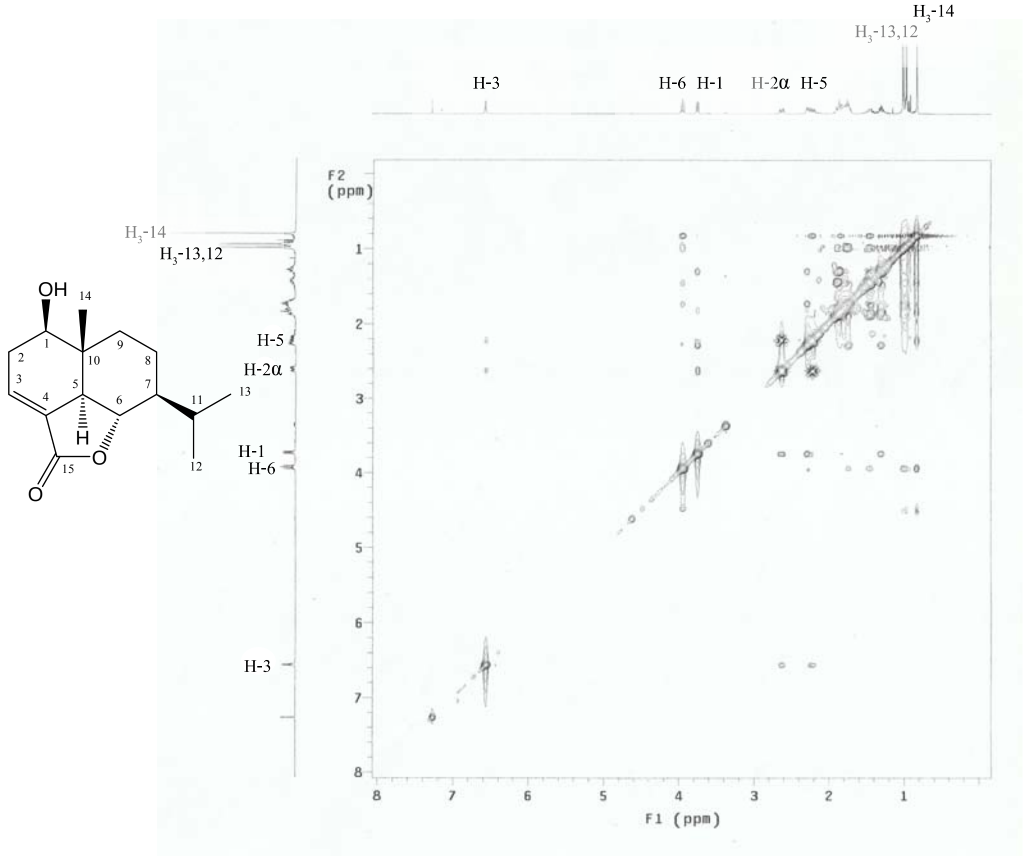


Figure 70a. NOESY Spectrum of compound FF-7 (in CDCl$_3$)

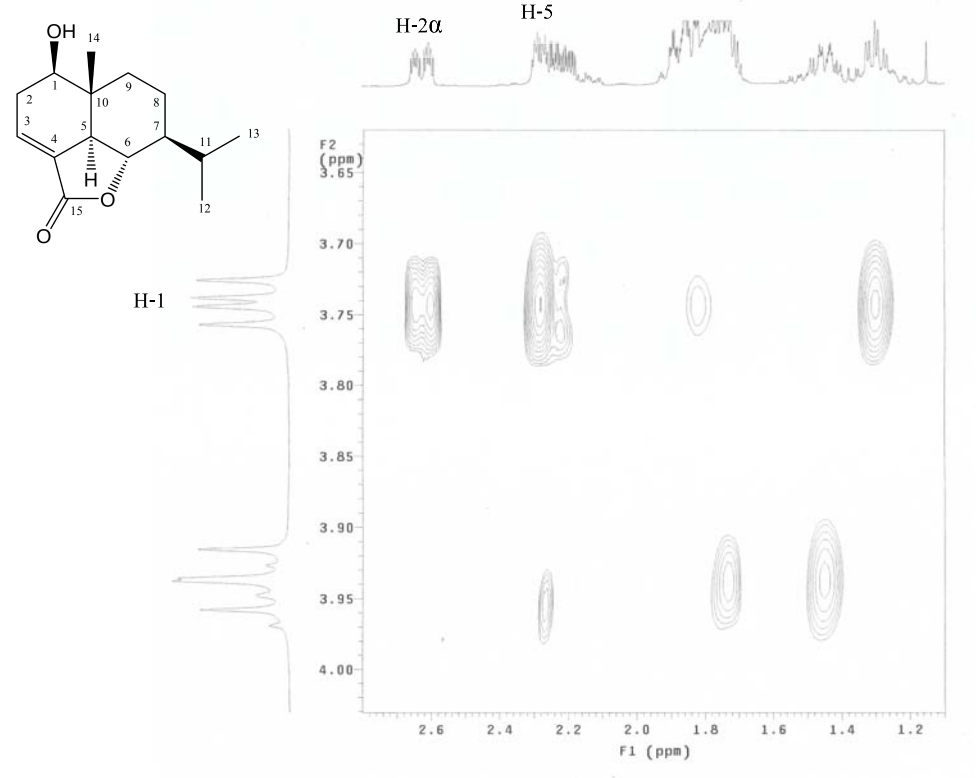


Figure 70b. NOESY Spectrum of compound FF-7 (expansion between δ_H 1.2-2.8; 3.6-4.0 ppm)

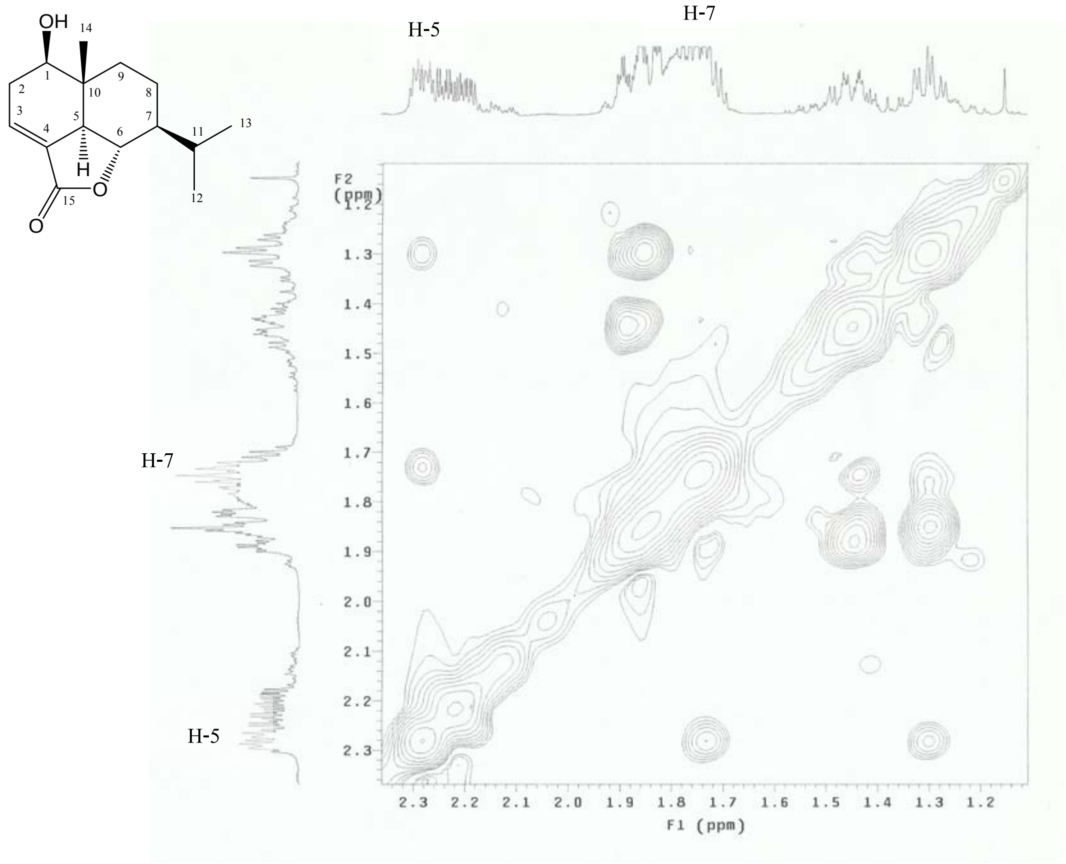


Figure 70c. NOESY Spectrum of compound FF-7 (expansion between δ_H 1.1-2.4 ppm)

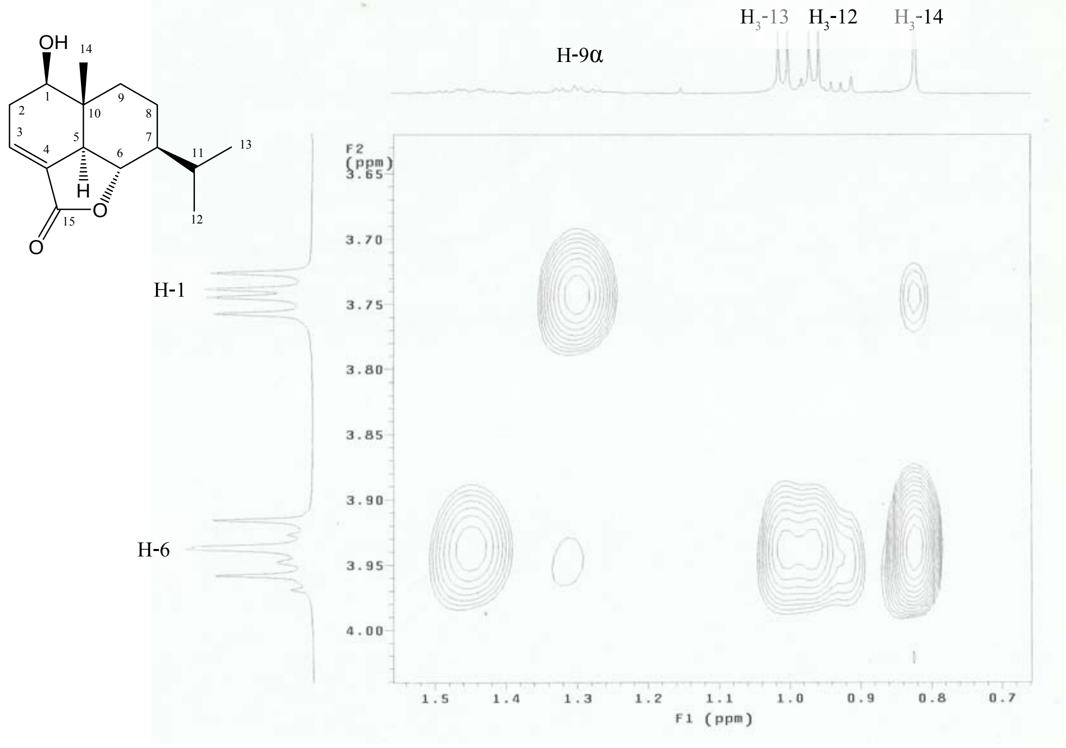


Figure 70d. NOESY Spectrum of compound FF-7 (expansion between δ_H 0.7-1.5; 3.6-4.0 ppm)

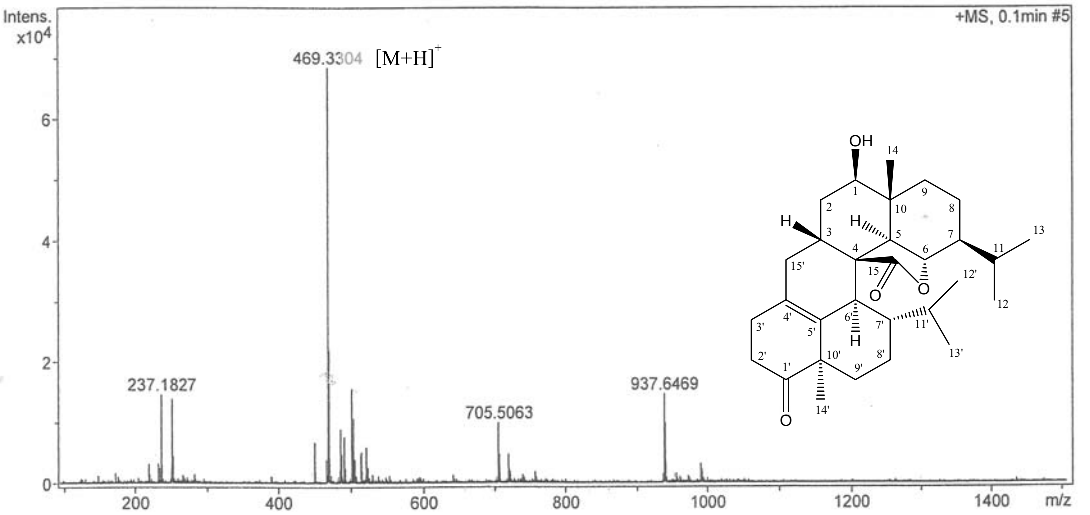


Figure 71. HR-ESI-TOF Mass spectrum of compound FF-6

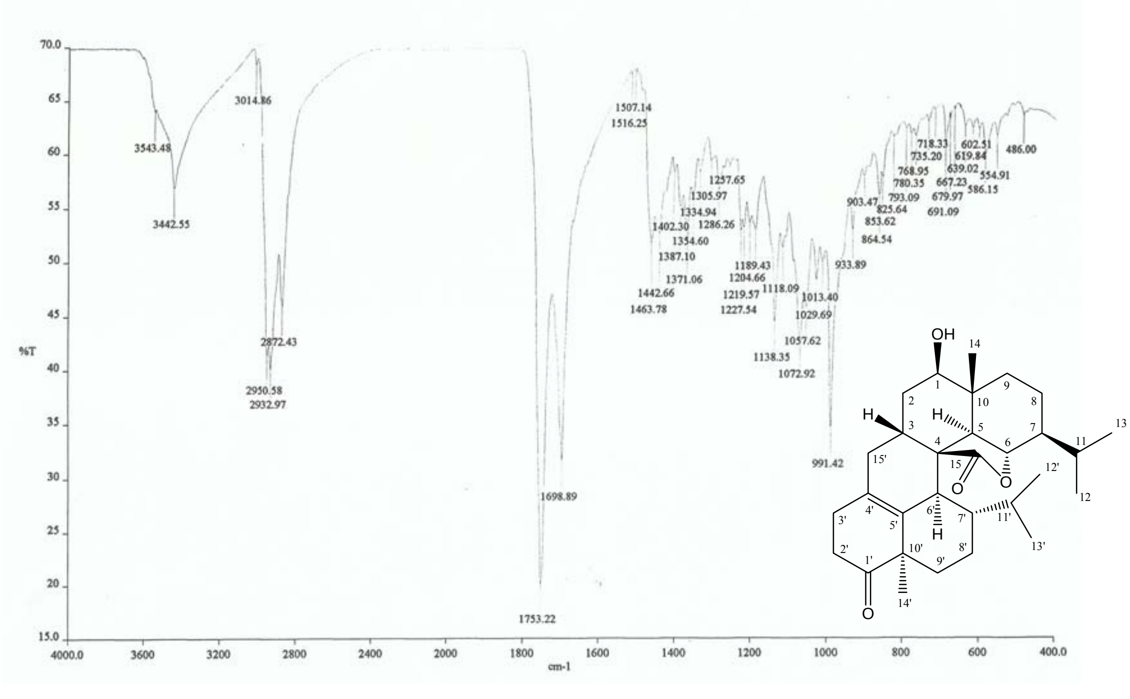


Figure 72. IR Spectrum of compound FF-6 (KBr)

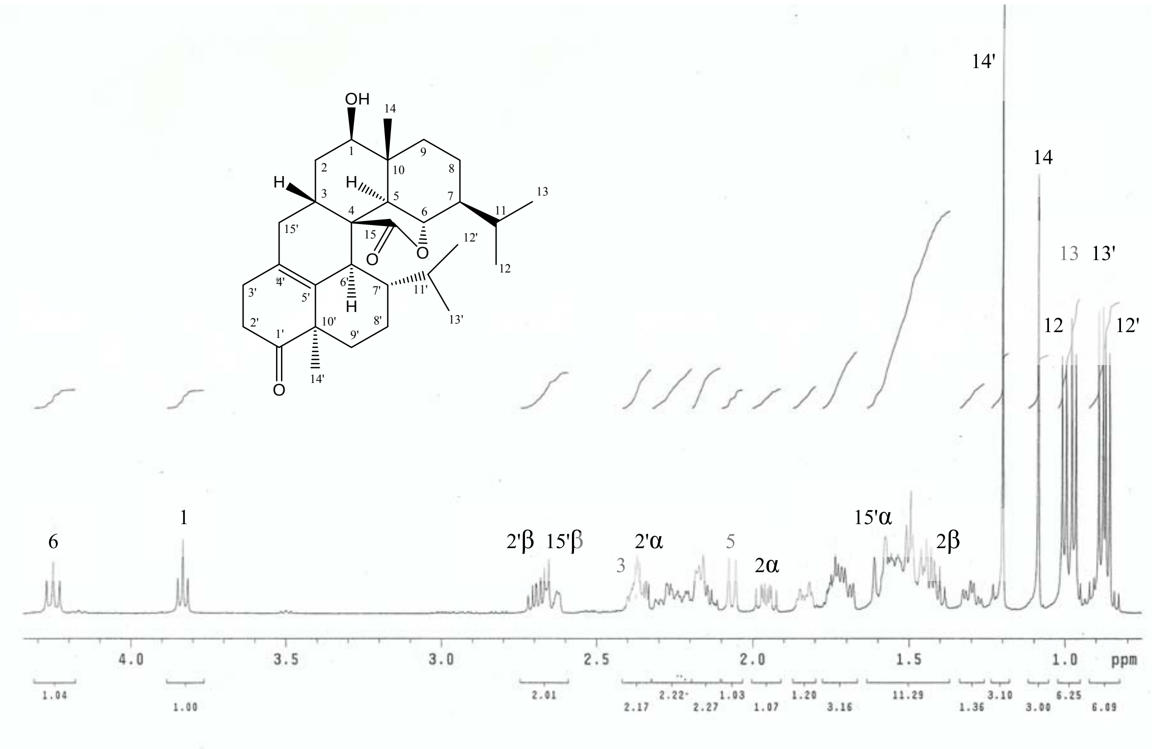


Figure 73. ^{1}H NMR (500 MHz) Spectrum of compound FF-6 (in CDCl$_3$)

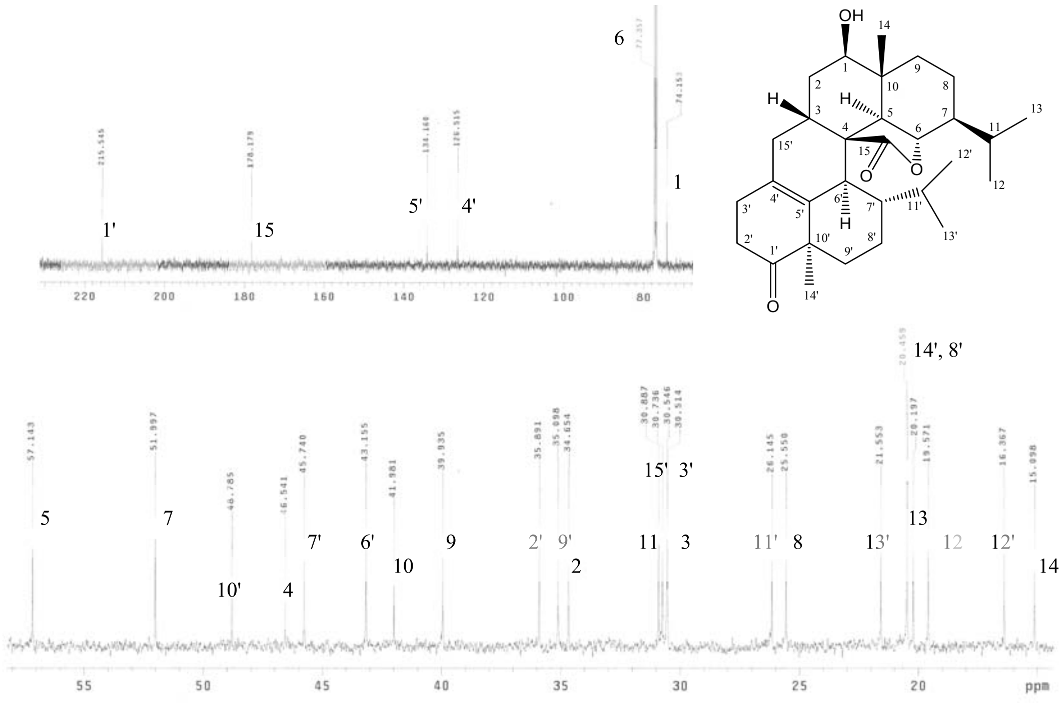


Figure 74. ^{13}C NMR (125 MHz) Spectrum of compound FF-6 (in CDCl$_3$)

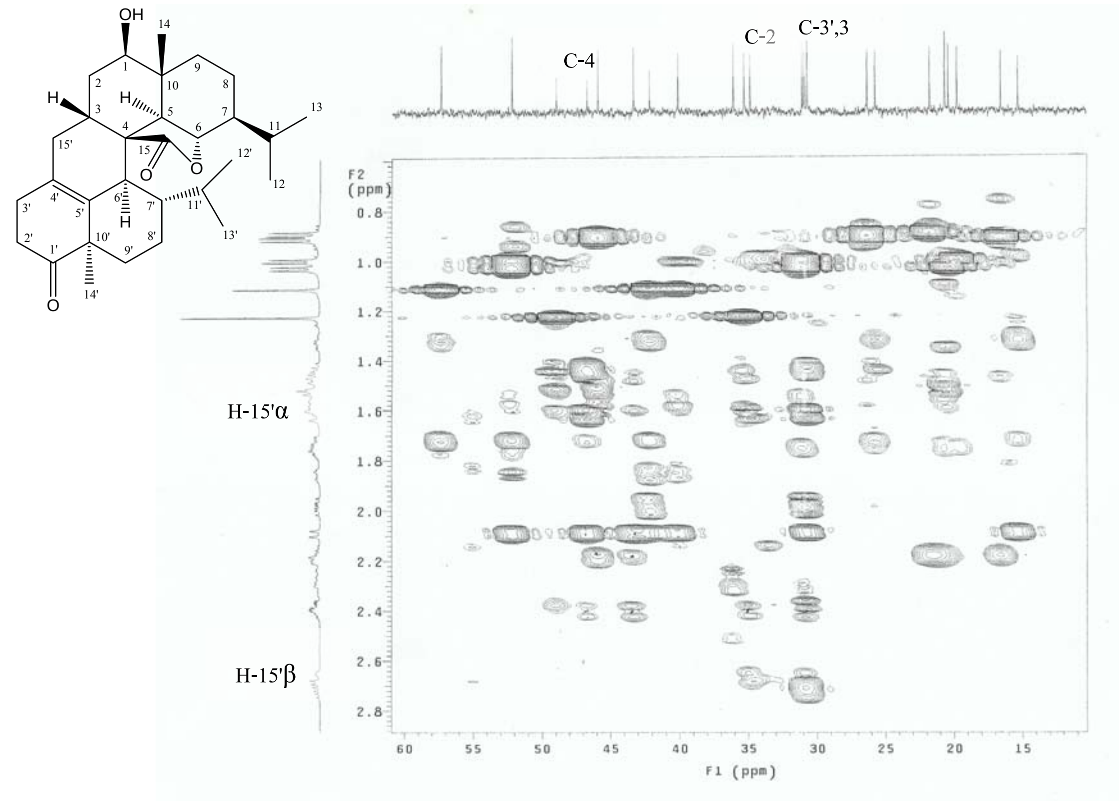


Figure 75a. HMBC Spectrum of compound FF-6 (expansion between δ_H 0.6-2.8, δ_C 10-60 ppm)

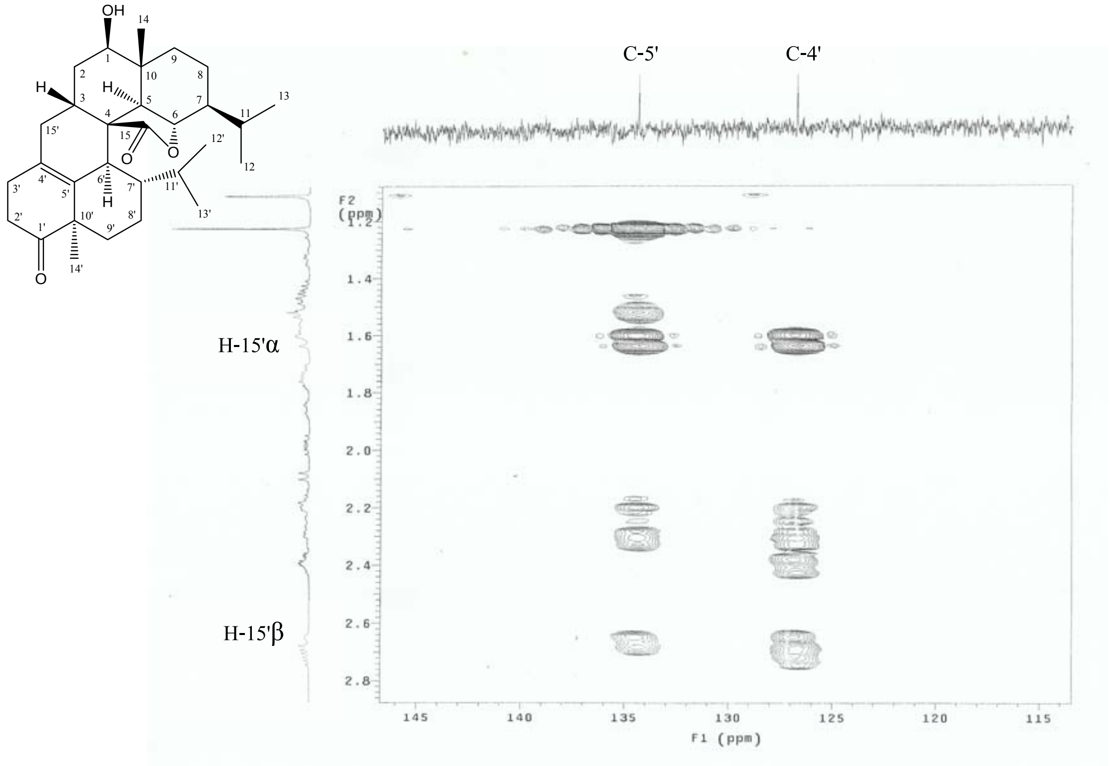


Figure 75b. HMBC Spectrum of compound FF-6 (expansion between δ_H 1.1-2.8, δ_C 115-145 ppm)

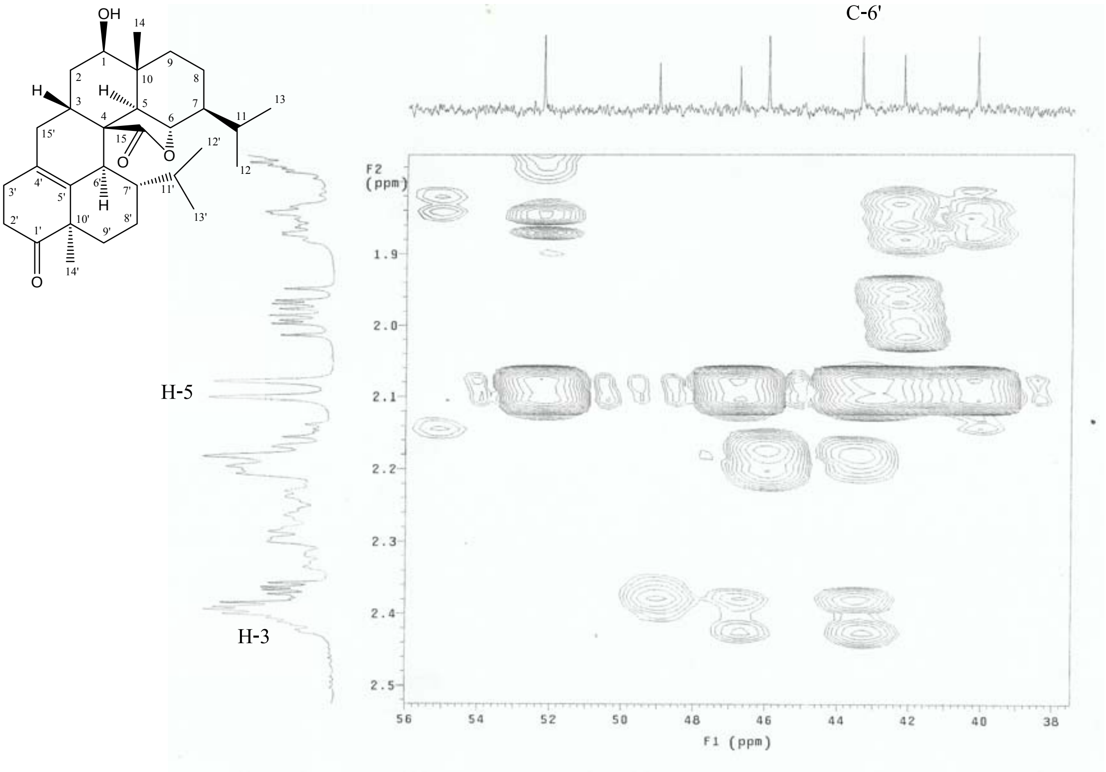


Figure 75c. HMBC Spectrum of compound FF-6 (expansion between δ_H 1.8-2.5, δ_C 38-56 ppm)

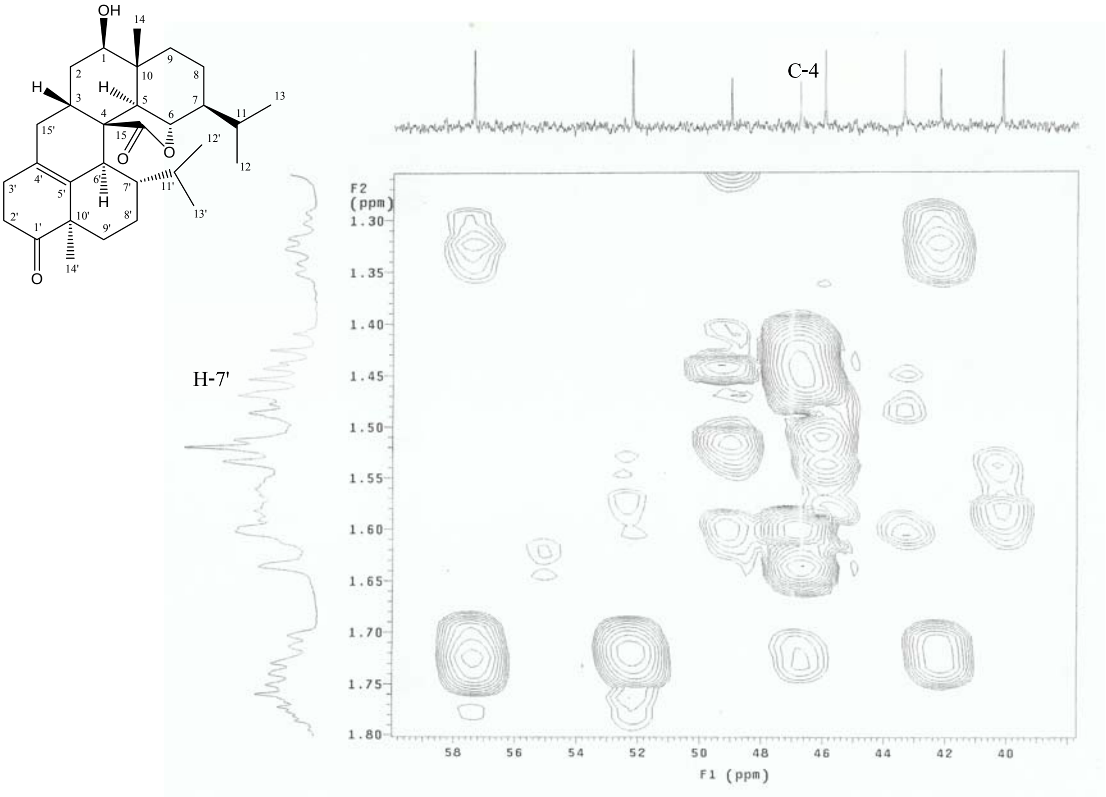


Figure 75d. HMBC Spectrum of compound FF-6 (expansion between δ_H 1.3-1.8, δ_C 38-60 ppm)

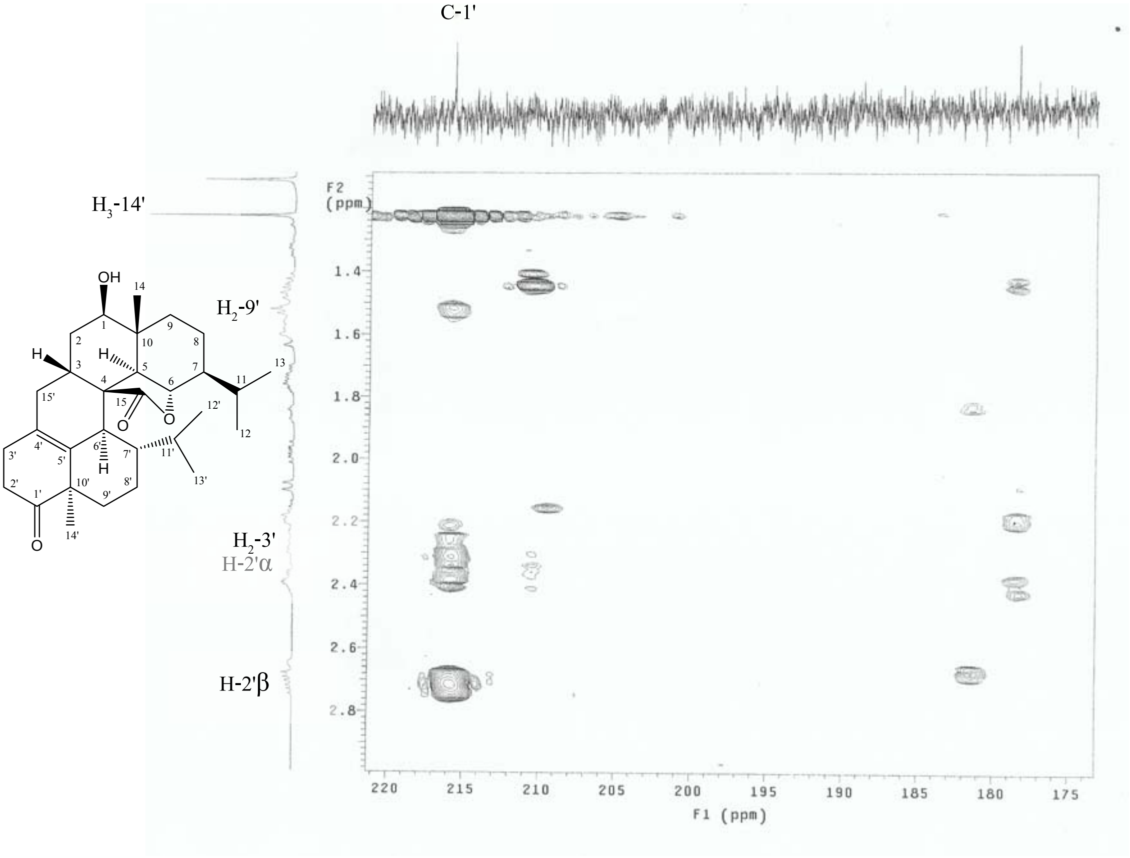


Figure 75e. HMBC Spectrum of compound FF-6 (expansion between δ_H 1.1-3.0, δ_C 175-220 ppm)

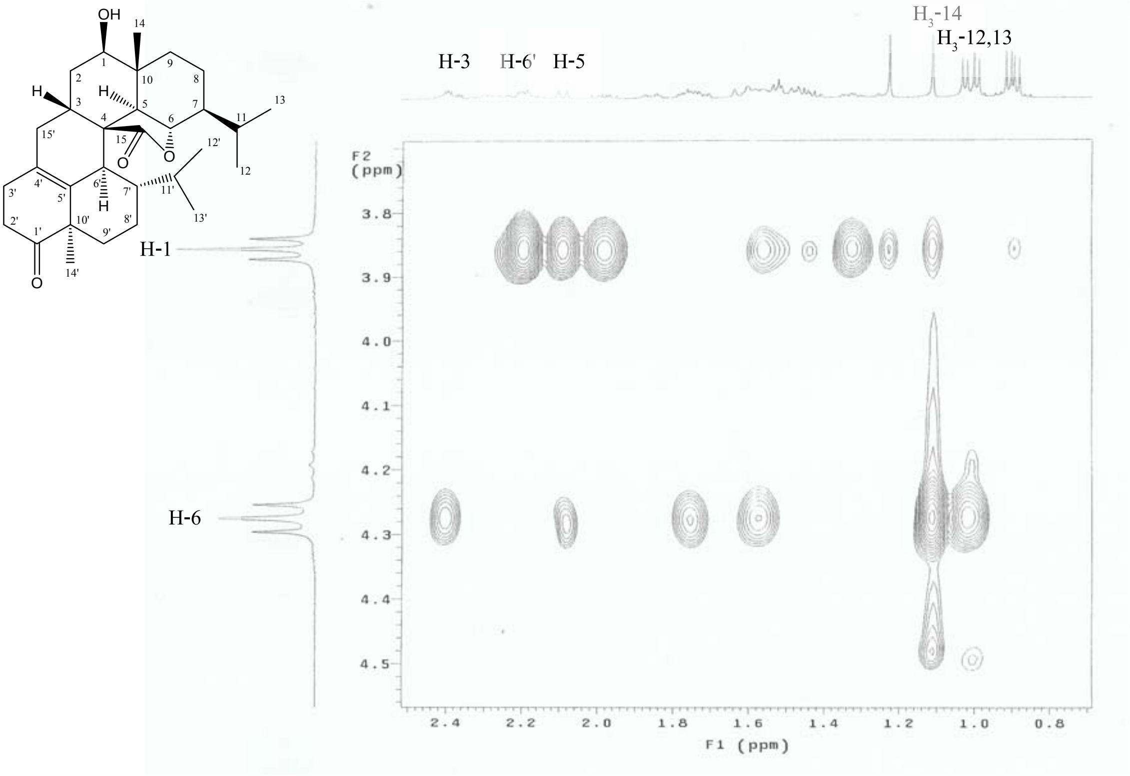


Figure 76a. NOESY Spectrum of compound FF-6 (expansion between δ_H 0.8-2.4; 3.7-4.5 ppm)

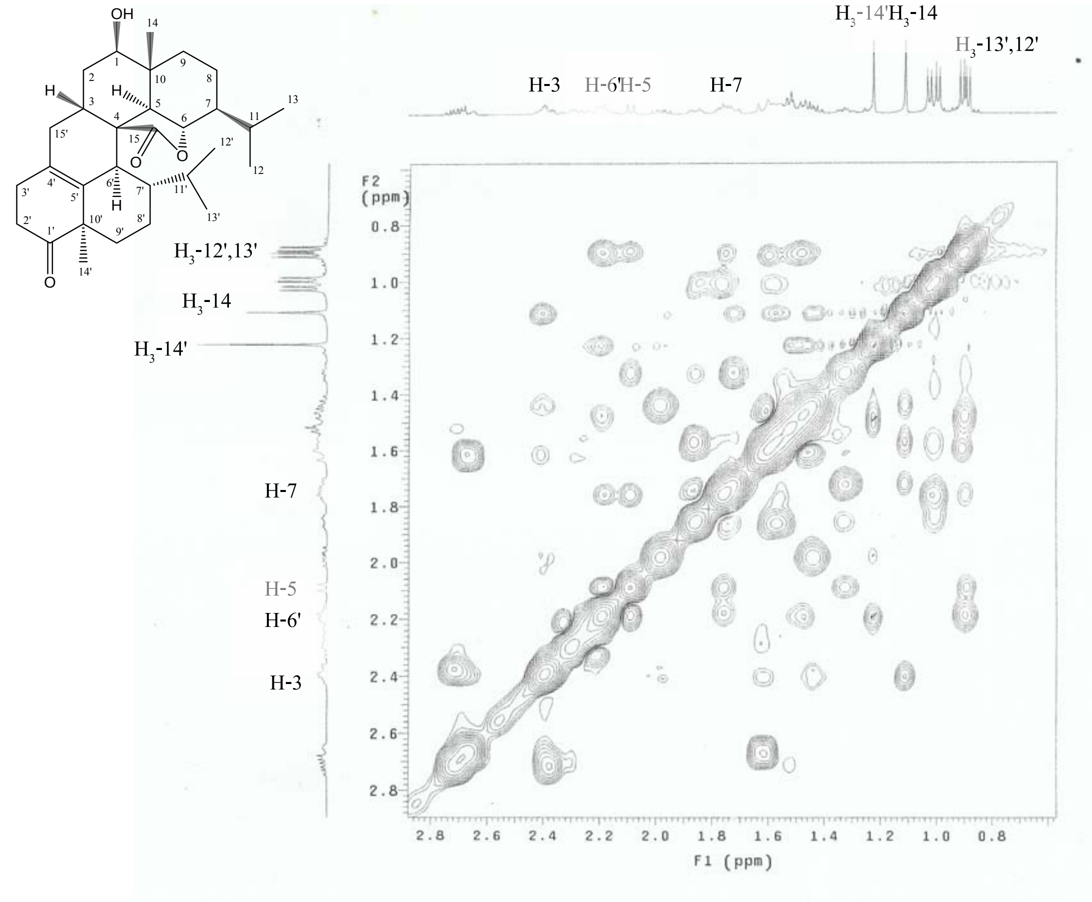


Figure 76b. NOESY Spectrum of compound FF-6 (expansion between δ_H 0.6-2.8 ppm)

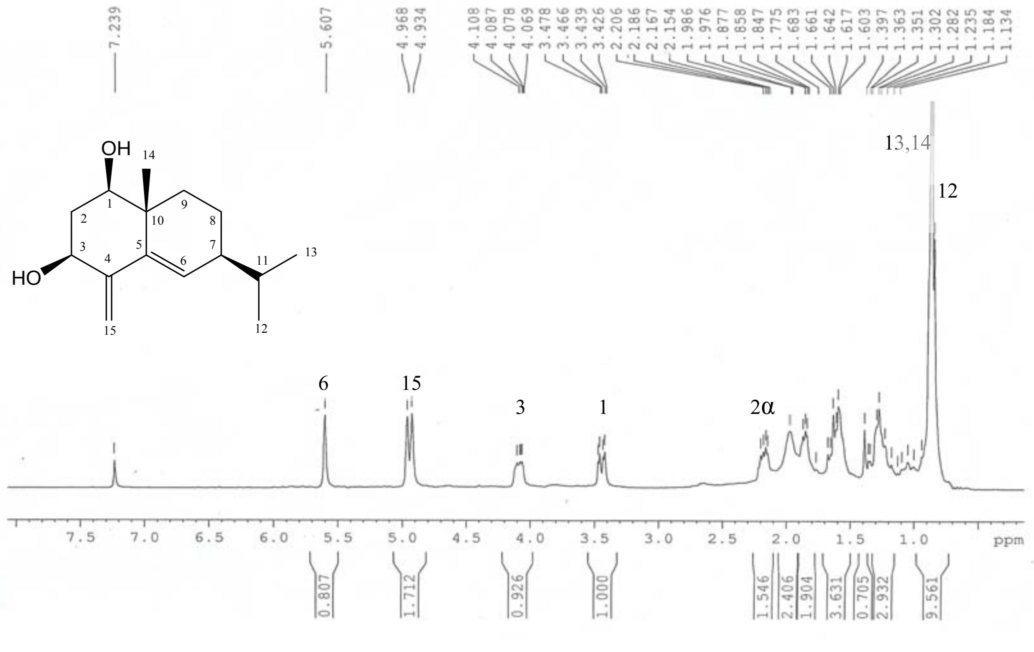


Figure 77. ^{1}H NMR (300 MHz) Spectrum of compound FF-8a (in $CDCl_3$)

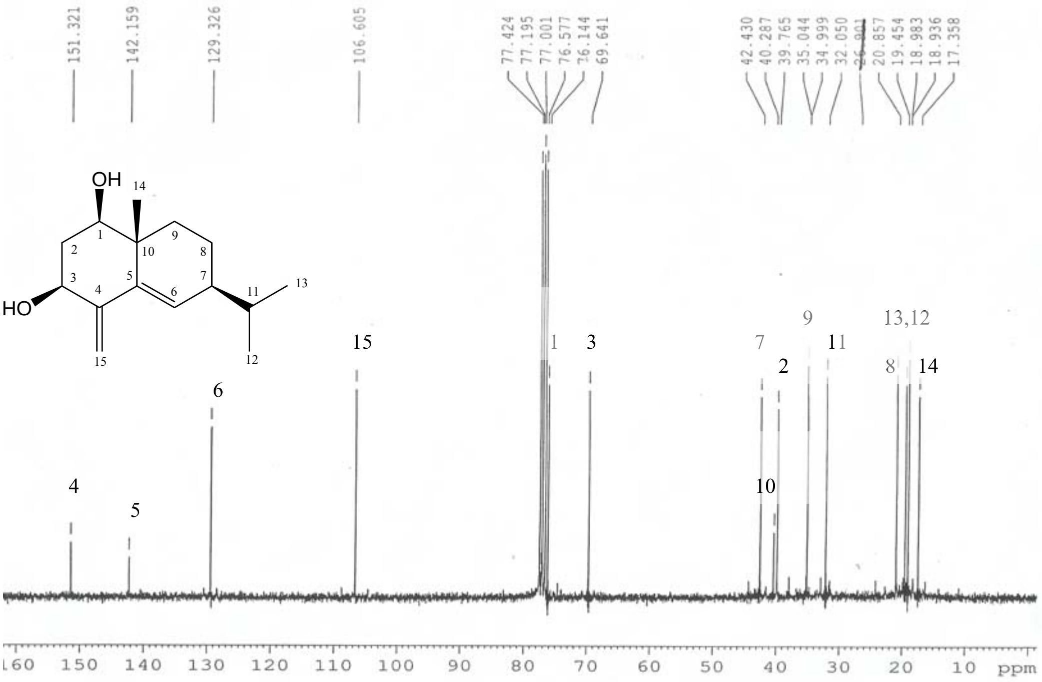


Figure 78. ^{13}C NMR (75 MHz) Spectrum of compound FF-8a (in $CDCl_3$)

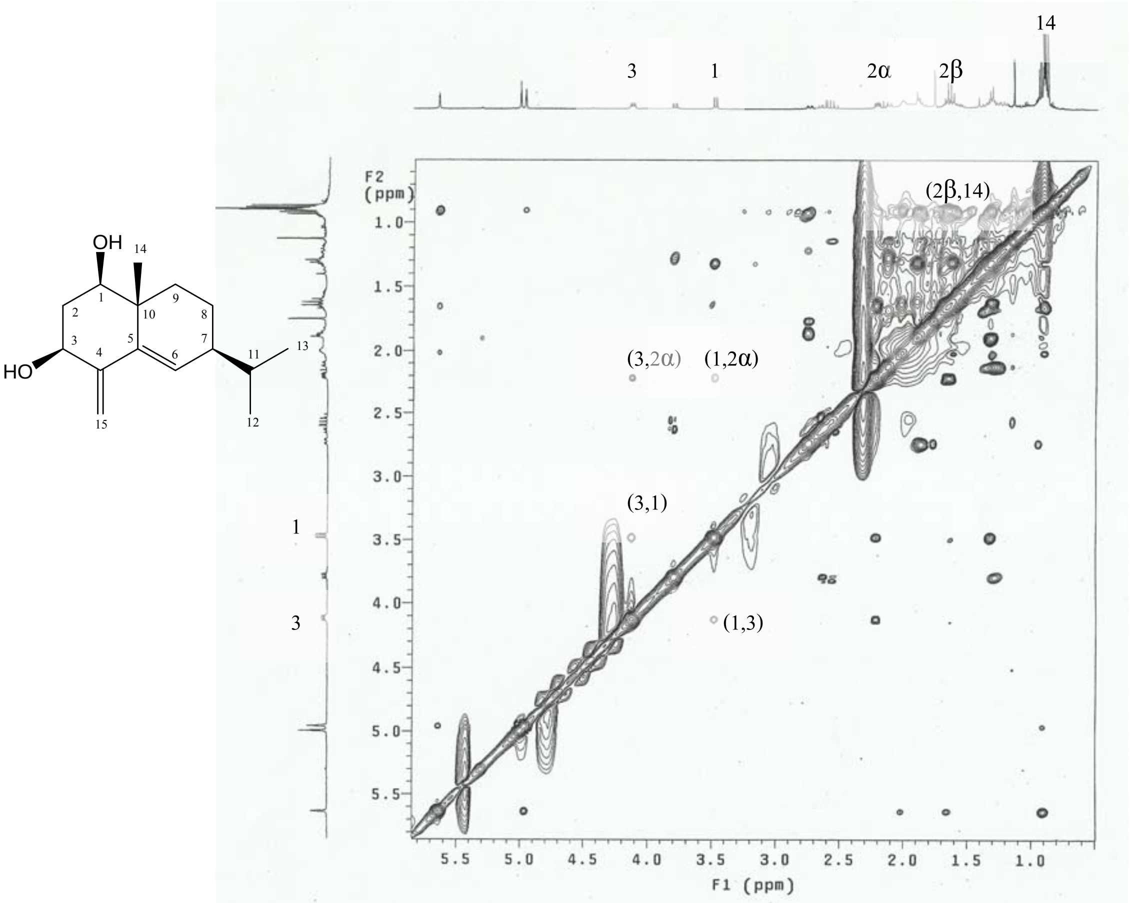


Figure 79. NOESY Spectrum of compound FF-8a (in $CDCl_3$)

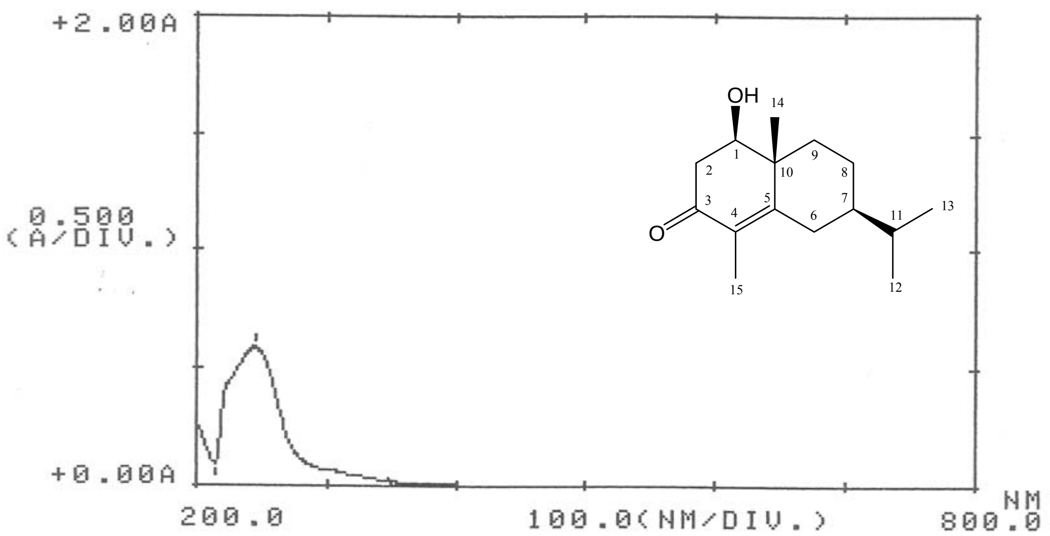


Figure 80. UV Spectrum of compound FF-8b (in MeOH)

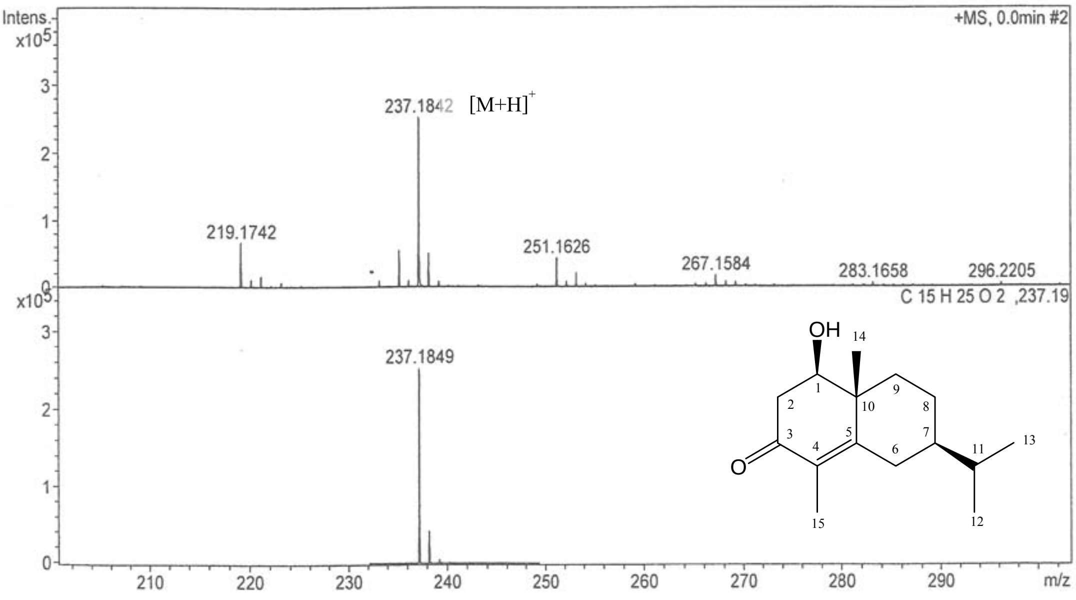


Figure 81. HR-ESI-TOF Mass spectrum of compound FF-8b

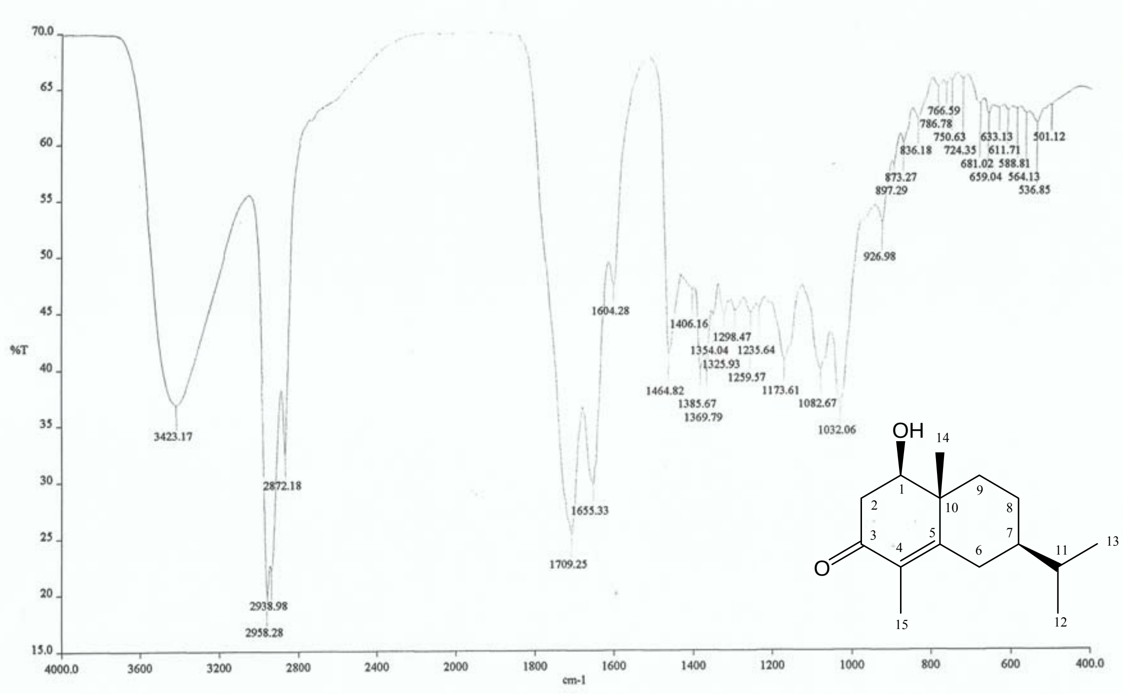


Figure 82. IR Spectrum of compound FF-8b (KBr)

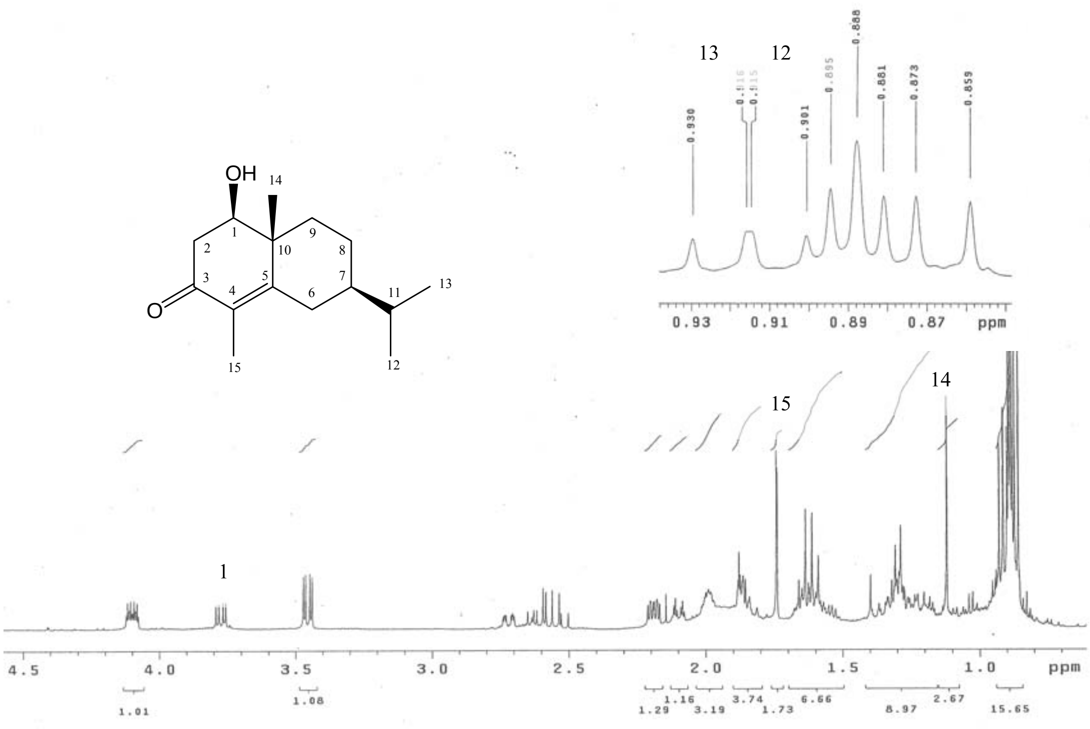


Figure 83a. ^{1}H NMR (500 MHz) Spectrum of compound FF-8b (in CDCl$_3$)

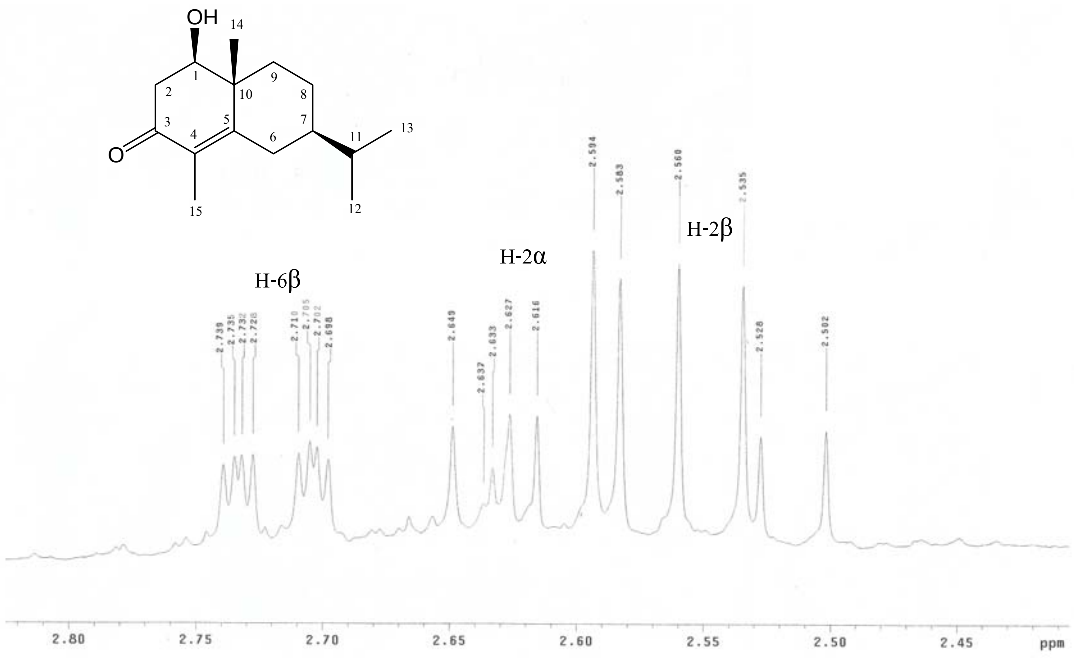


Figure 83b. ^{1}H NMR (500 MHz) Spectrum of compound FF-8b (expansion between δ 2.45-2.80 ppm)

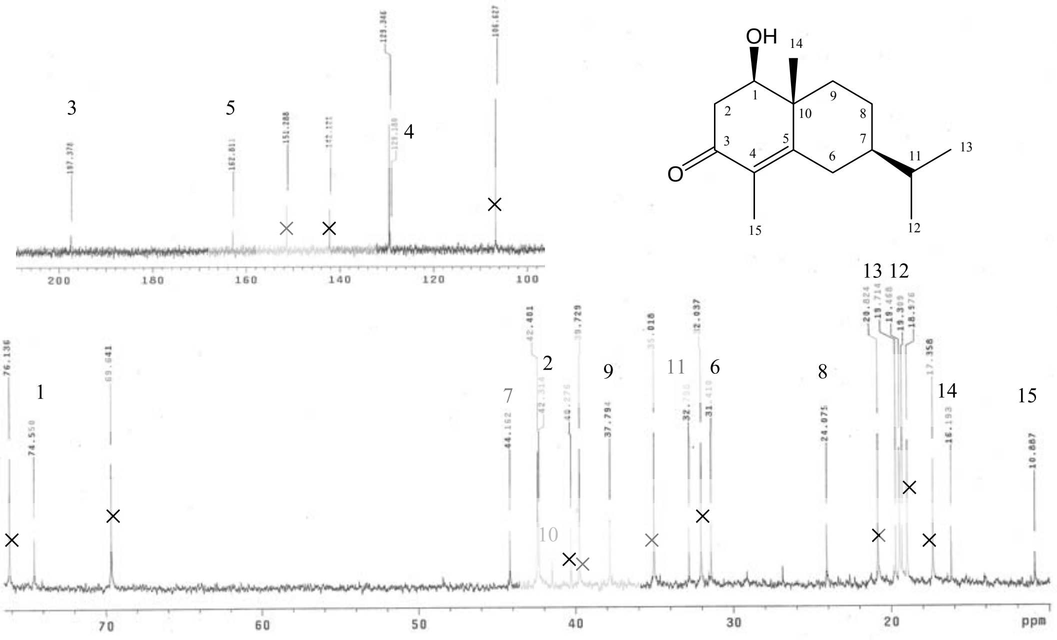


Figure 84. ^{13}C NMR (125 MHz) Spectrum of compound FF-8b (in $CDCl_3$)

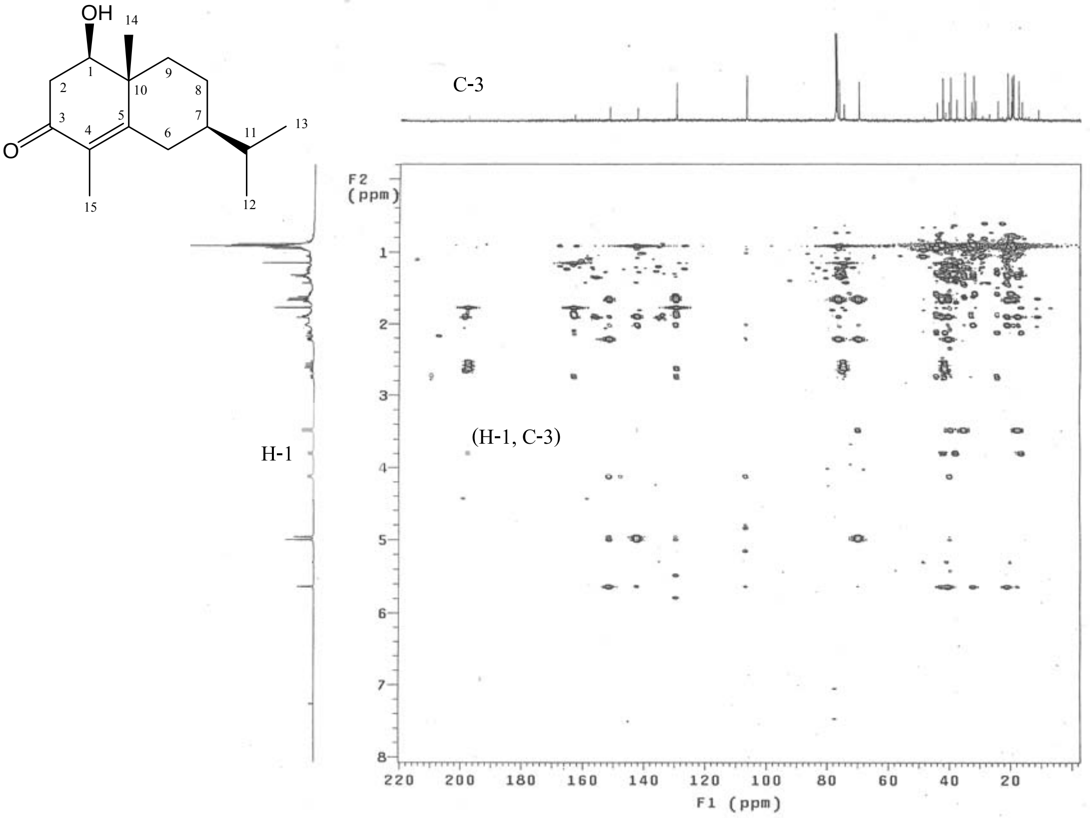


Figure 85a. HMBC Spectrum of compound FF-8b (in $CDCl_3$)

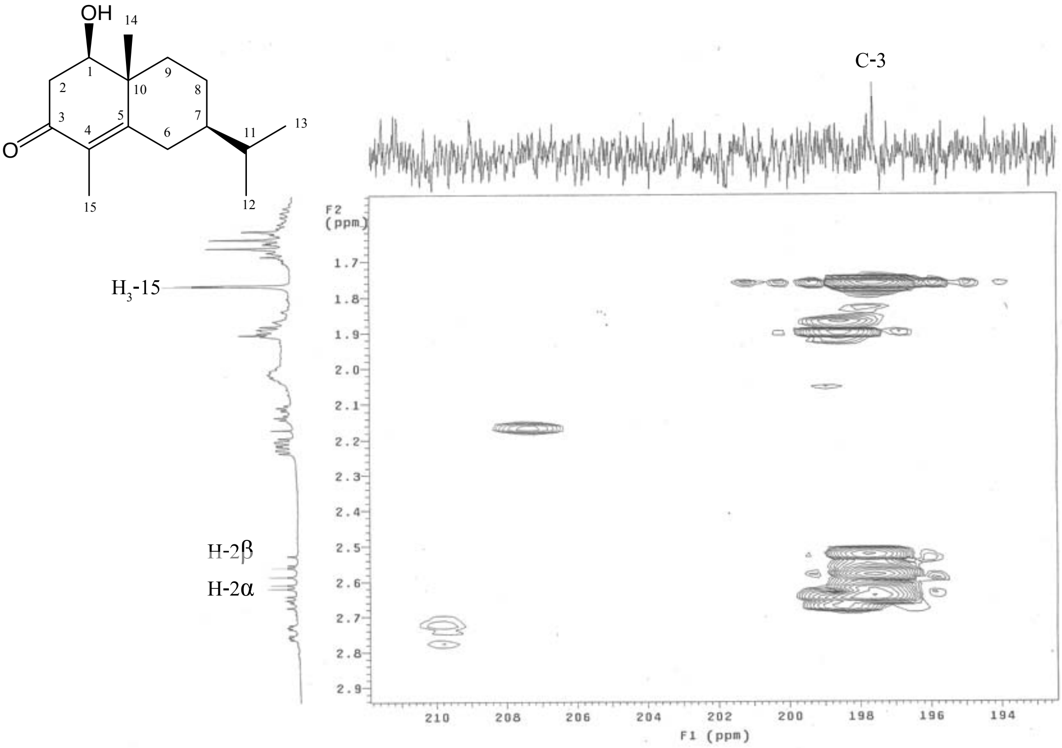


Figure 85b. HMBC Spectrum of compound FF-8b (expansion between δ_H 1.5-2.9, δ_C 192-212 ppm)

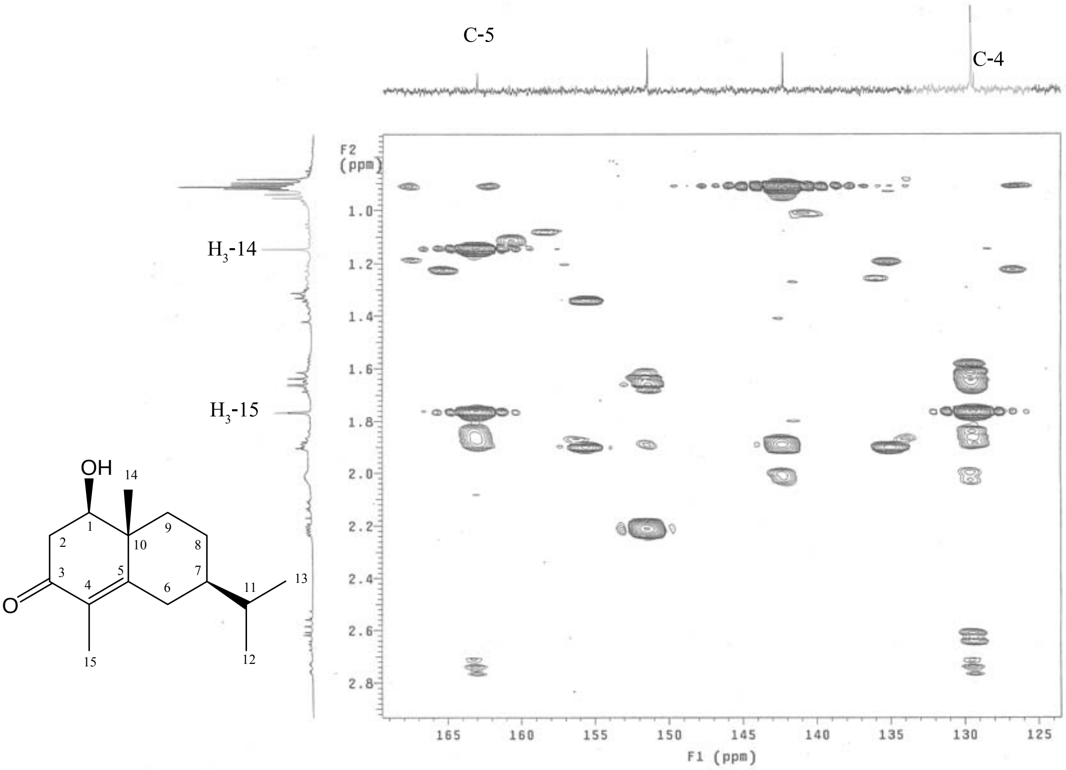


Figure 85c. HMBC Spectrum of compound FF-8b (expansion between δ_H 0.6-2.9, δ_C 125-170 ppm)

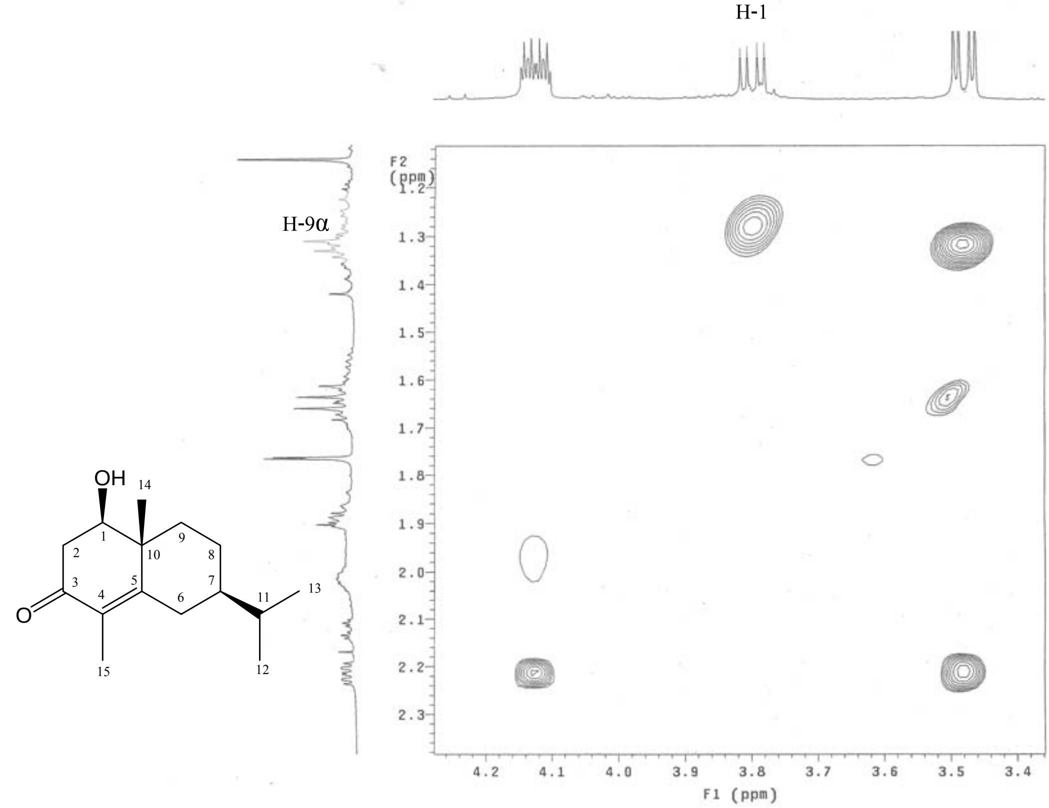


Figure 86a. NOESY Spectrum of compound FF-8b (expansion between δ_H 1.2-2.3; 3.4-4.2 ppm)

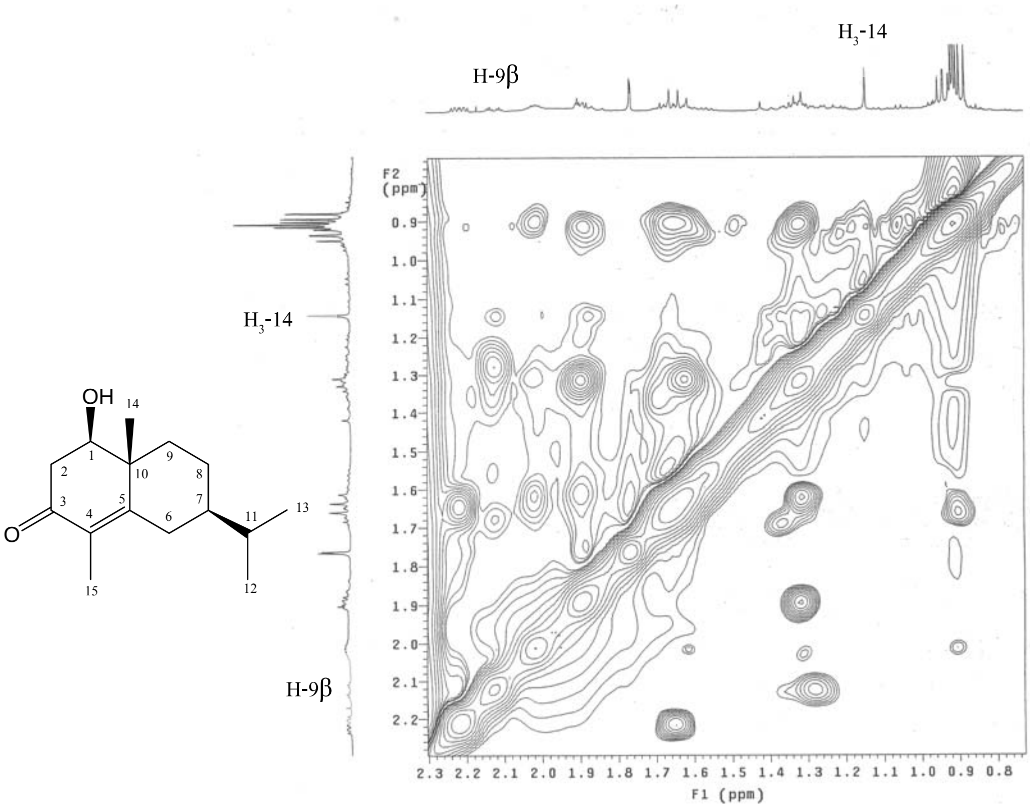


Figure 86b. NOESY Spectrum of compound FF-8b (expansion between δ_H 0.8-2.3 ppm)

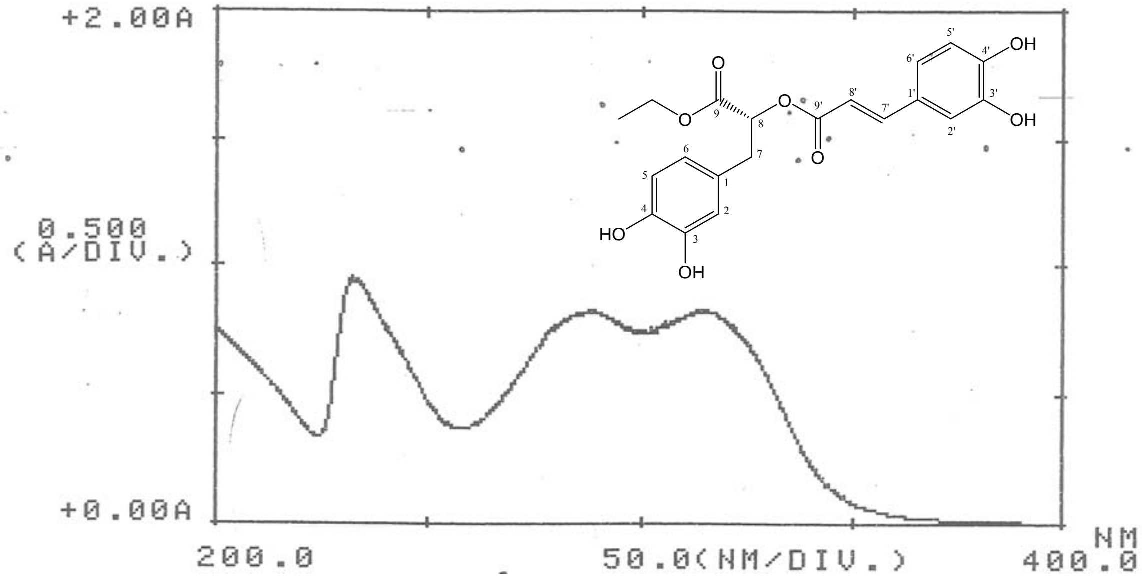


Figure 87. UV Spectrum of compound FF-9 (in MeOH)

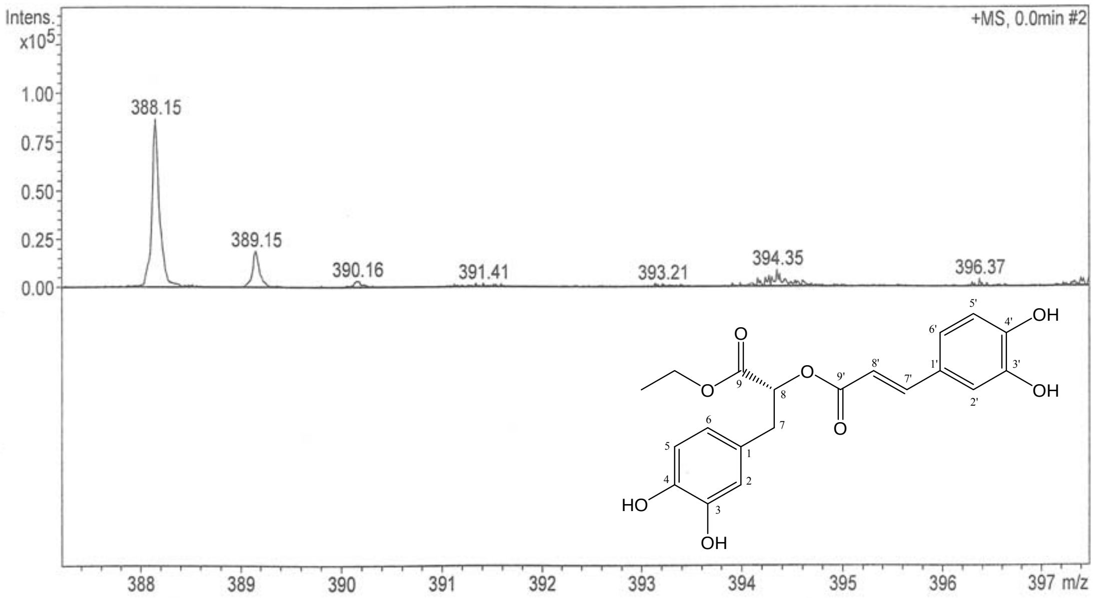


Figure 88. ESI Mass spectrum of compound FF-9

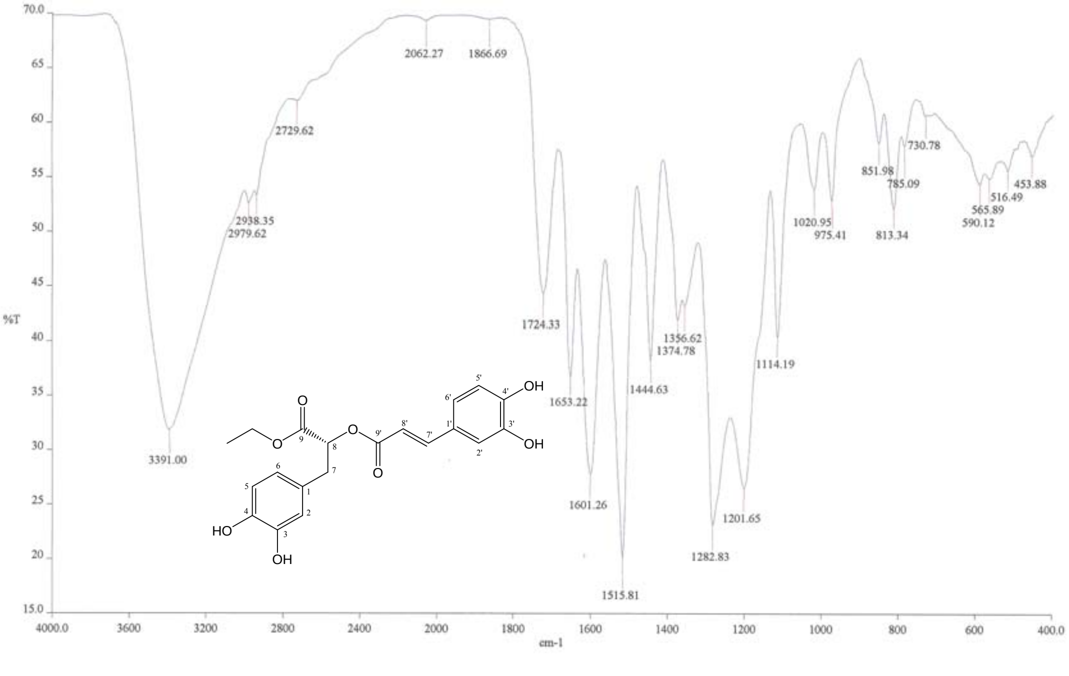
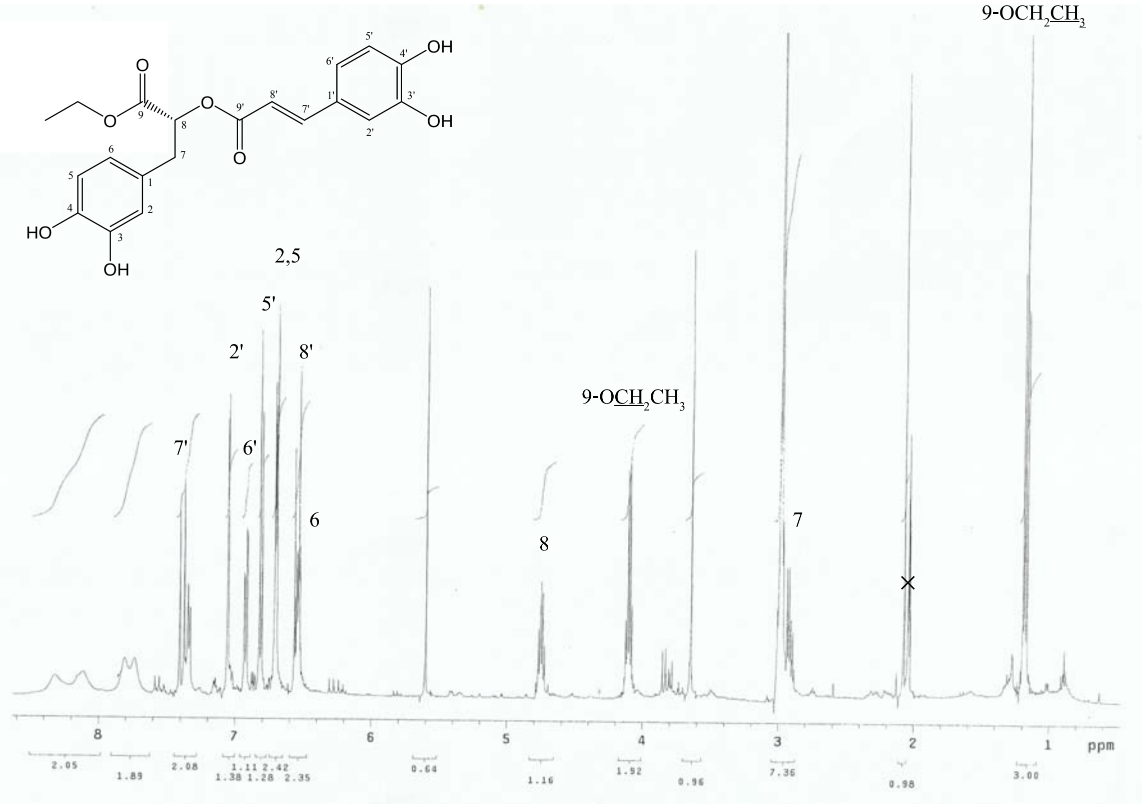


Figure 89. IR Spectrum of compound FF-9 (KBr)



ıre 90. ^{1}H NMR (500 MHz) Spectrum of compound FF-9 (in acetone-d_6)

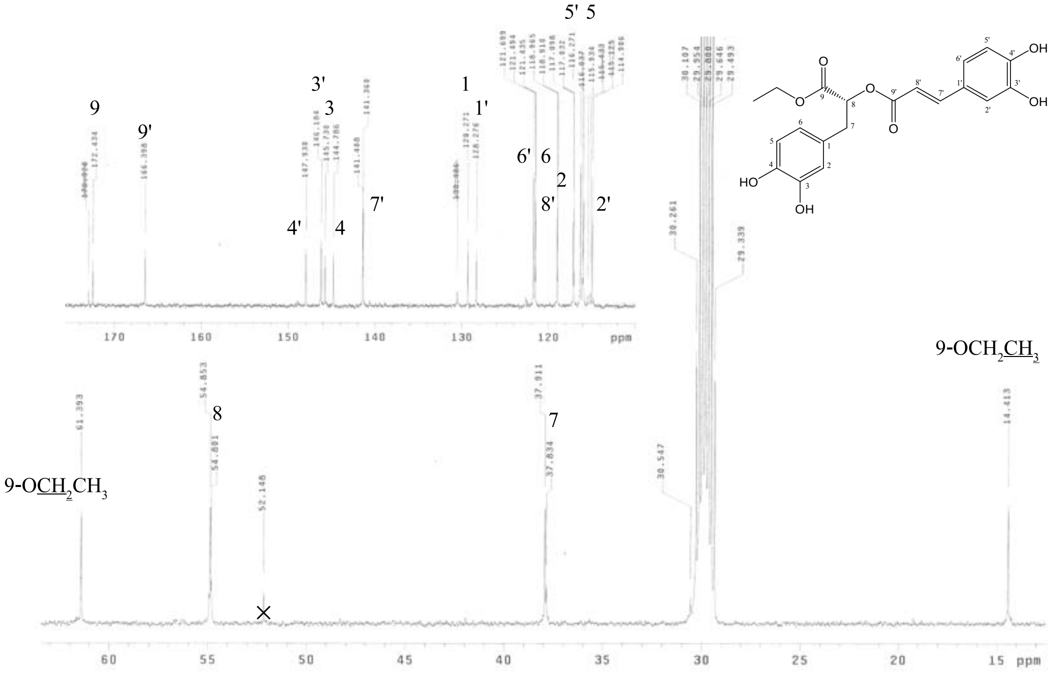


Figure 91. ^{13}C NMR (125 MHz) Spectrum of compound FF-9 (in acetone-d_6)

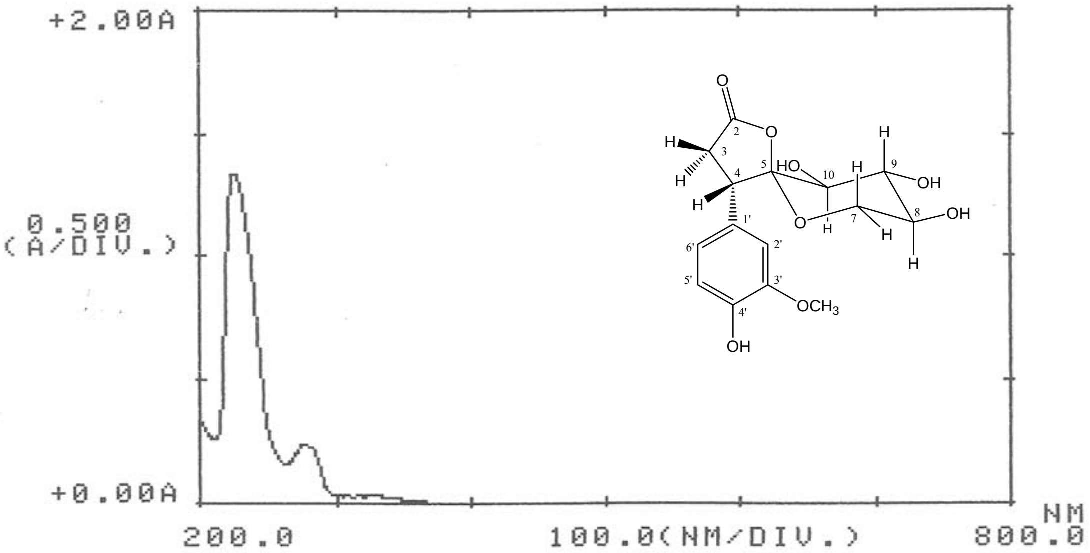


Figure 92. UV Spectrum of compound FF-10 (in MeOH)

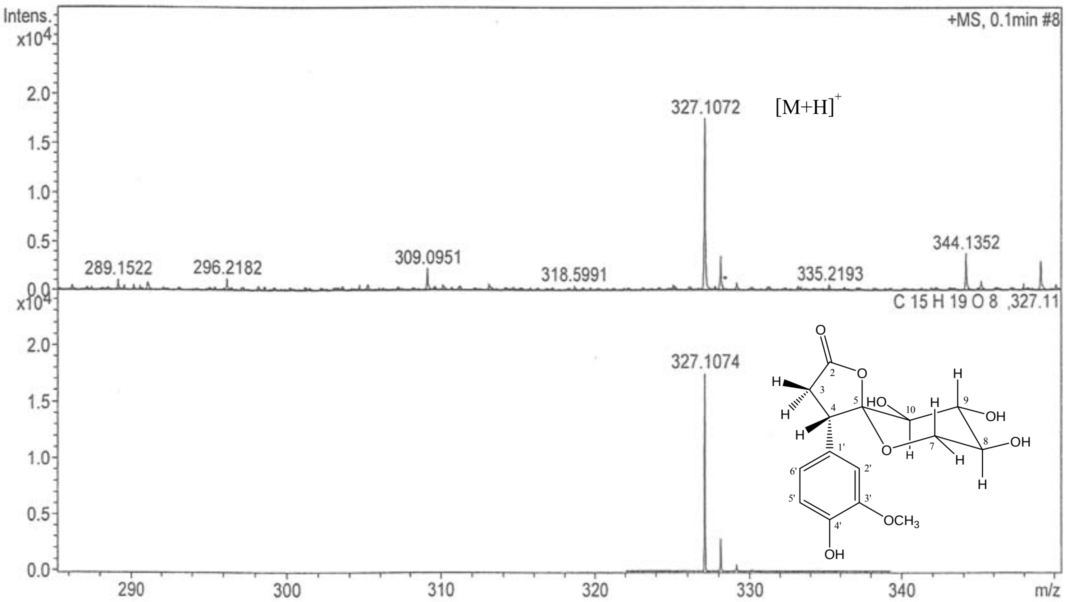


Figure 93. HR-ESI-TOF Mass spectrum of compound FF-10

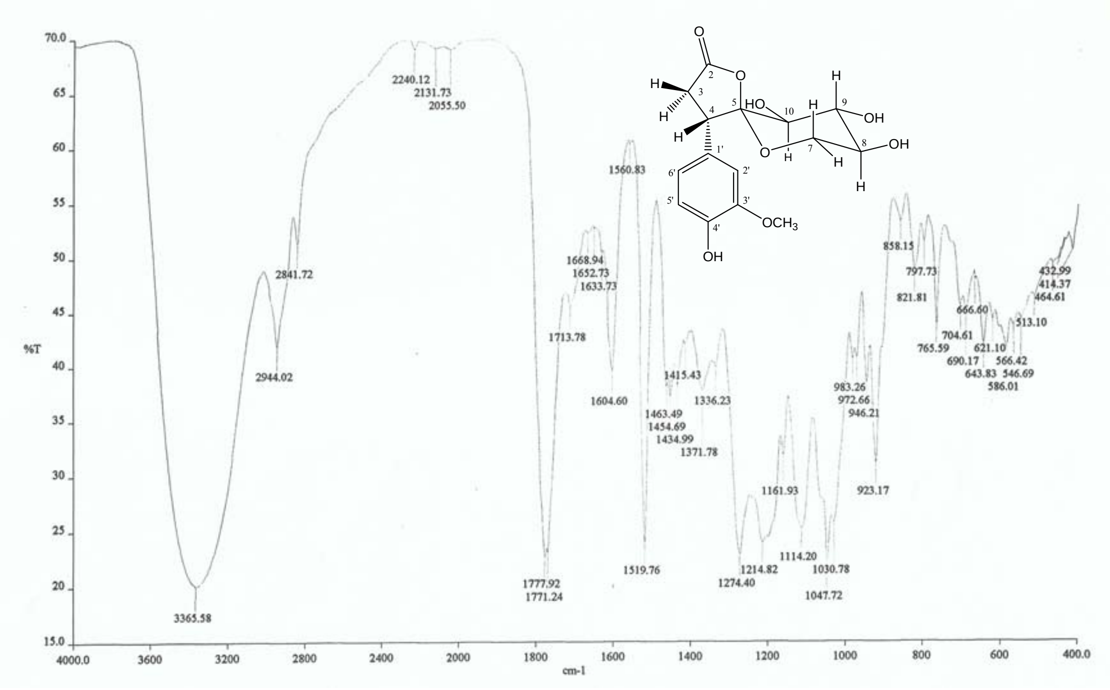


Figure 94. IR Spectrum of compound FF-10 (KBr)

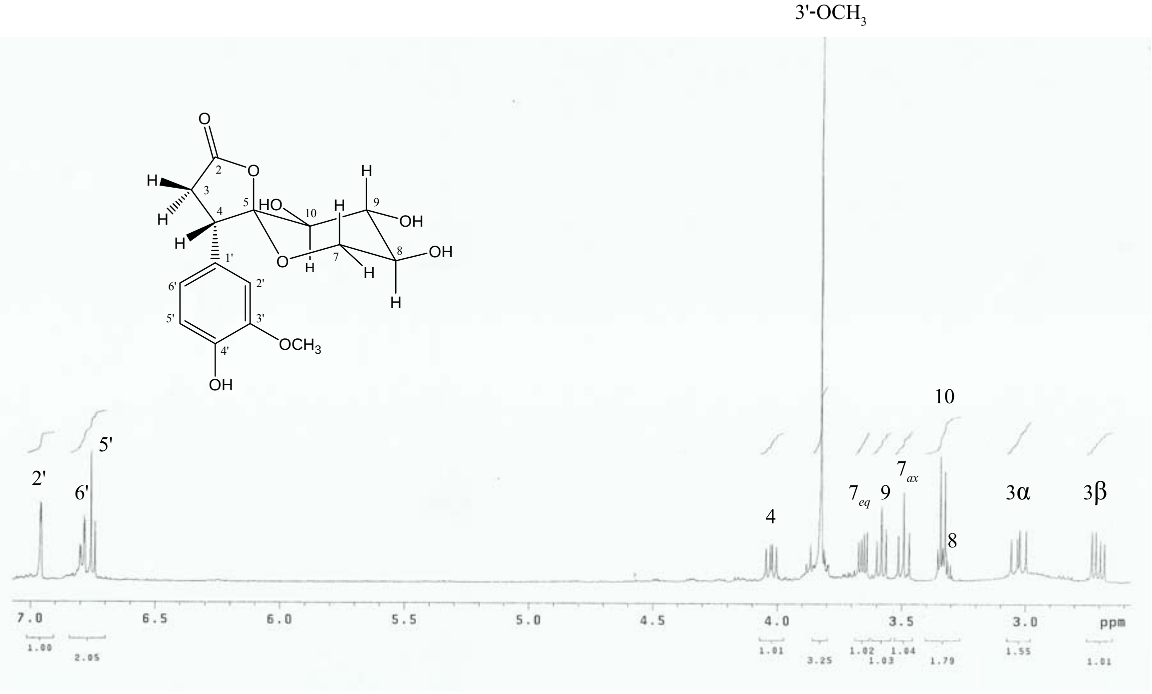


Figure 95. ^{1}H NMR (500 MHz) Spectrum of compound FF-10 (in CD_3OD)

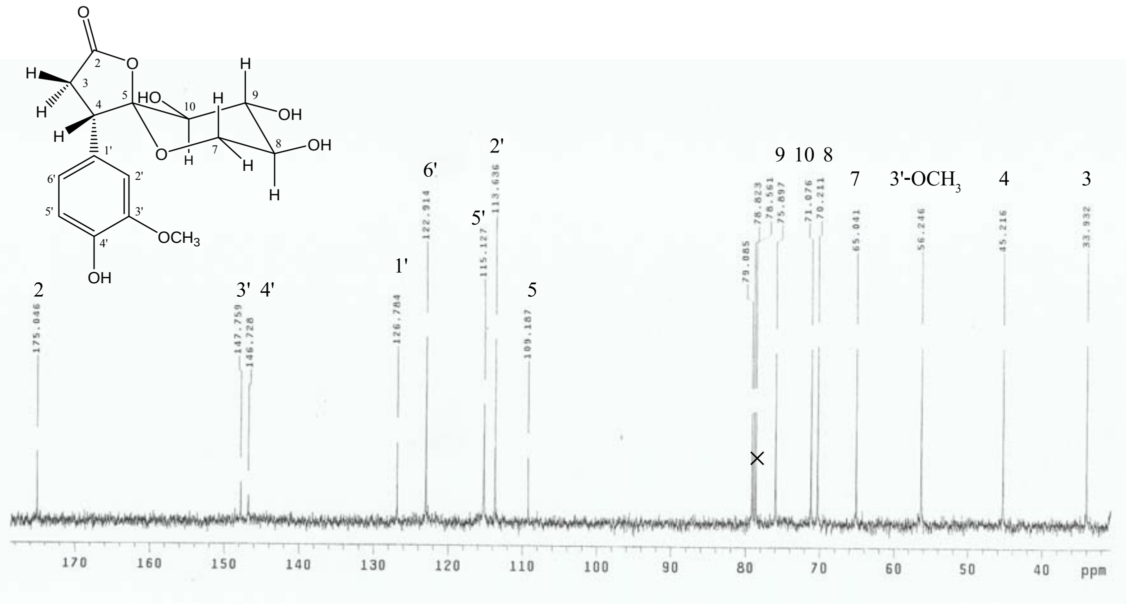


Figure 96. ^{13}C NMR (125 MHz) Spectrum of compound FF-10 from δ 30-180 ppm (in CD$_3$OD)

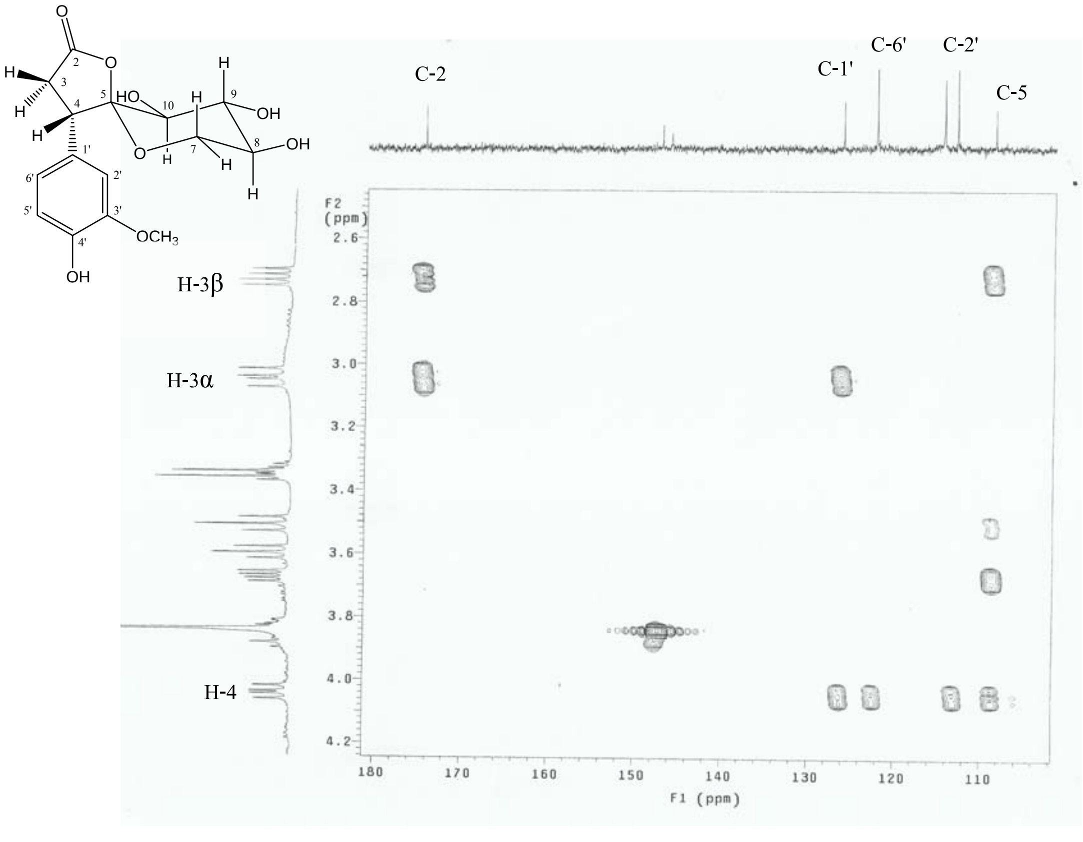


Figure 97a. HMBC Spectrum of compound FF-10 (expansion between δ$_H$ 2.5-4.2, δ$_C$ 100-180 ppm)

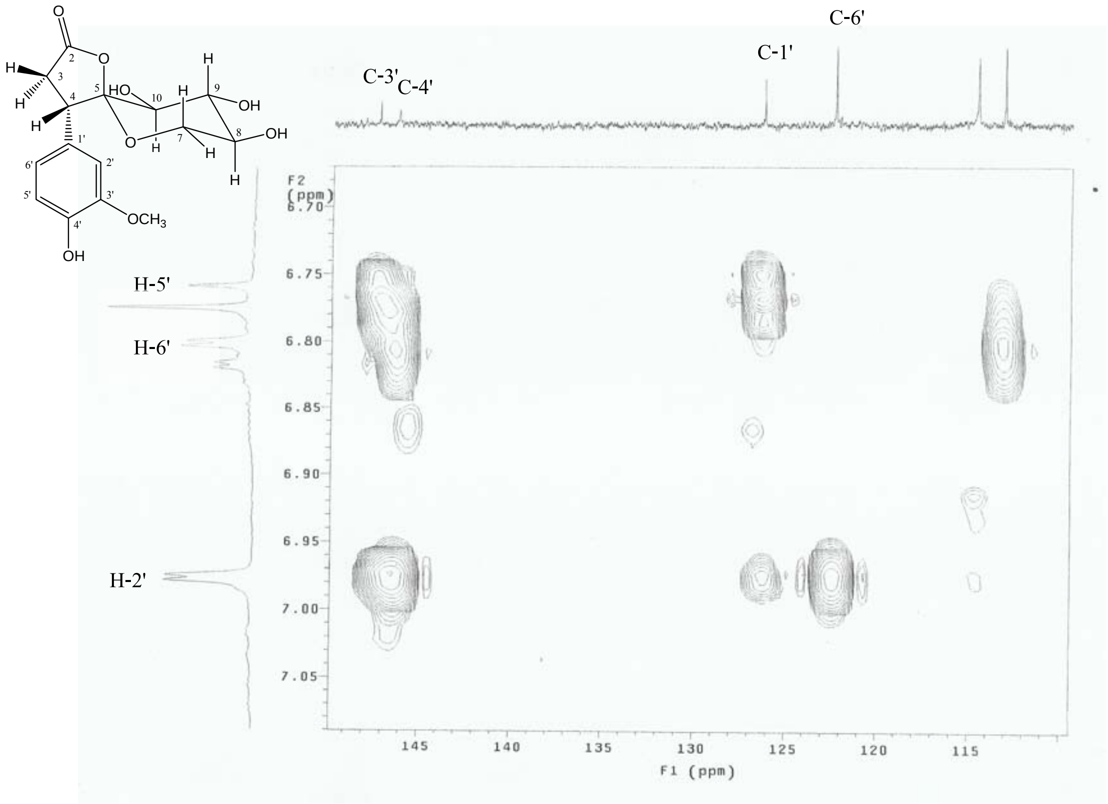


Figure 97b. HMBC Spectrum of compound FF-10 (expansion between δ_H 6.7-7.1, δ_C 110-150 ppm)

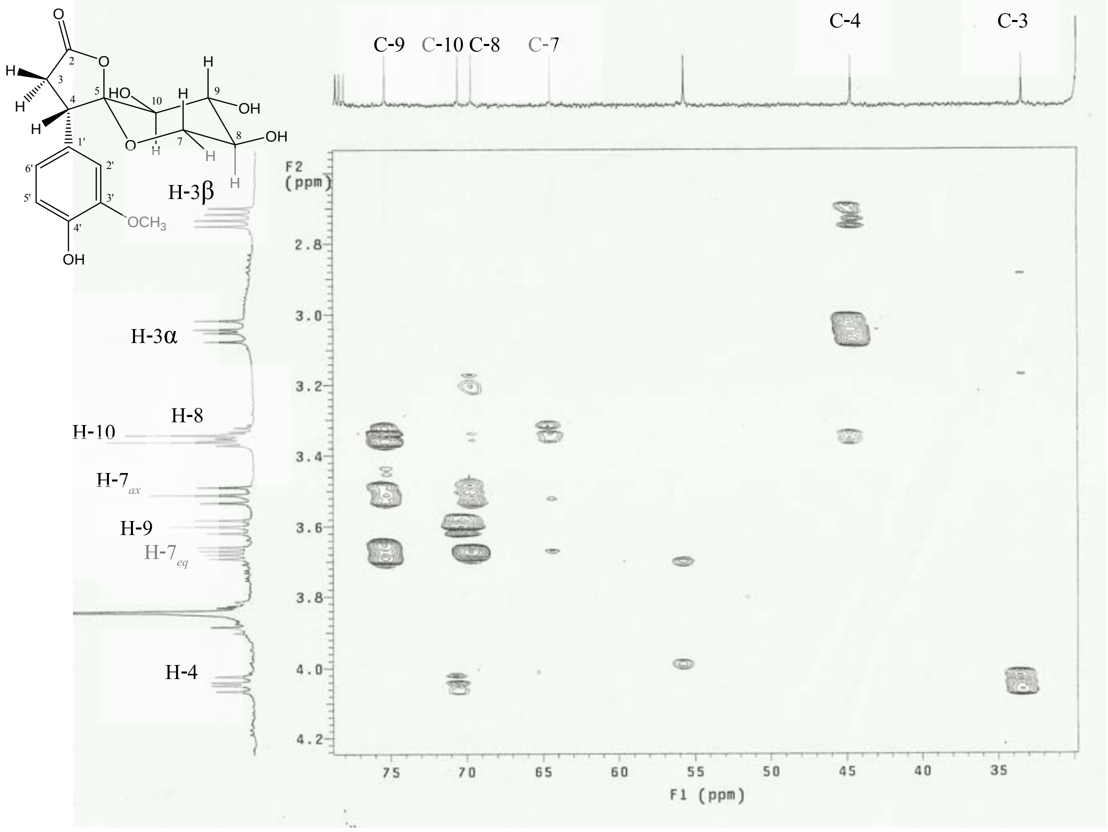


Figure 97c. HMBC Spectrum of compound FF-10 (expansion between δ_H 2.6-4.2, δ_C 30-80 ppm)

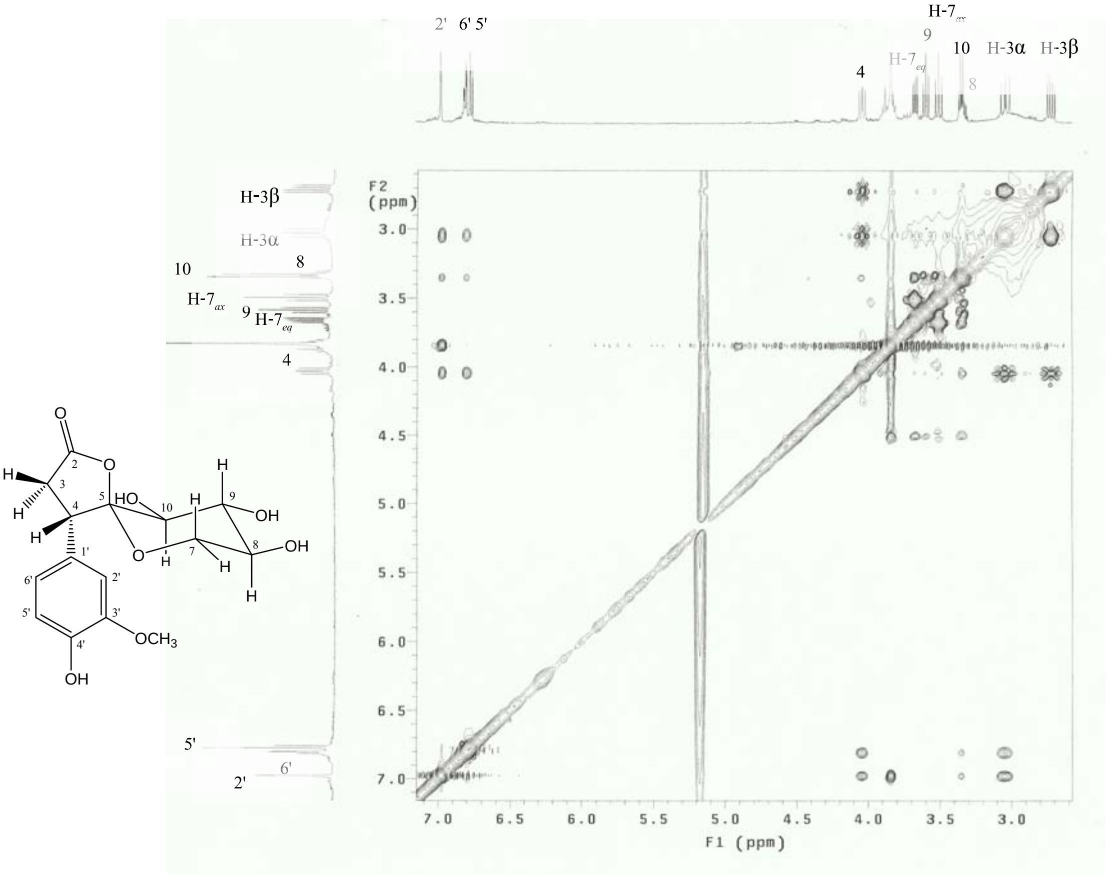


Figure 98a. NOESY Spectrum of compound FF-10 (in CD_3OD)

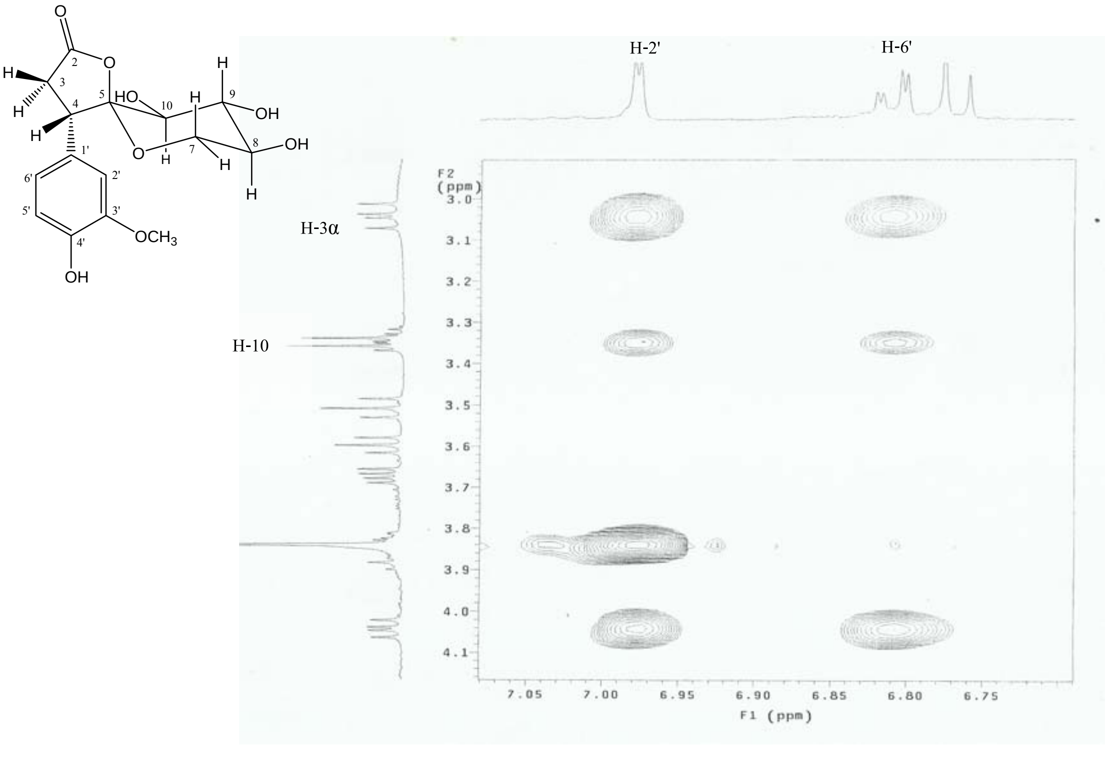


Figure 98b. NOESY Spectrum of compound FF-10 (expansion between δ_H 3.0-4.1; 6.7-7.1 ppm)

VITA

Mr. Pathom Somwong was born on September 20, 1978 in Nakhon Ratchasima, Thailand. He received his B.Sc. in Pharmacy (Second class honours) in 2001 from the Faculty of Pharmaceutical Sciences, Khon Kaen University and M.Sc. in Pharmacy in 2007 from the Department of Pharmaceutical Chemistry, Faculty of Pharmaceutical Sciences, Chulalongkorn University. After graduation, he worked as a lecturer at the Faculty of Pharmacy, Rangsit University, Pathum Thani, Thailand. He was granted a Royal Golden Jubilee Ph.D. Scholarship from Thailand Research Fund (TRF) in the year 2009.

Publications

1. Somwong, P., Suttisri, R., and Buakeaw, A. 2011. A new 1,3-diketofriedelane triterpene from *Salacia verrucosa*. Fitoterapia 82: 1047-1051.
2. Somwong, P., Suttisri, R., and Buakeaw, A. 2013. New sesquiterpenes and phenolic compound from *Ficus foveolata*. Fitoterapia 85: 1-7.

Poster presentations

1. Somwong, P. and Suttisri, R. Two new friedelane triterpenoids from *Salacia verrucosa*. Presented at the 9th NRCT-JSPS Joint Seminar “Natural Medicine Research for the Next Decade: New Challenges and Future Collaboration”, December 8-9, 2010, Bangkok, Thailand.
2. Somwong, P., Suttisri, R., and Buakeaw, A. New eudesmane sesquiterpenes from *Ficus foveolata*. Presented at RGJ-Ph.D. Congress XIV “Basic Research for Sustainable Development”, April 5-7, 2013, Jomtien Palm Beach Hotel & Resort, Pattaya, Chonburi, Thailand.