FULL REPORT

Isolation and identification of biologically-active compounds from *Clausena excavata* fruits and stems

By

Tawanun Sripisut

This research was made possible by a grant number T651176
from Biodiversity Research and Training Program (BRT)

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ACKNOWLEDGEMENTS

I wish to express my appreciation to my advisor, Assistant Professor Dr. Surat Laphookhieo for his advices, valuable instructions, expert guidance, excellent suggestions and kindness which are more than I can describe here. Everything will always be in my mind.

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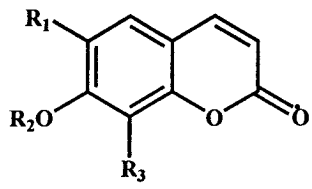
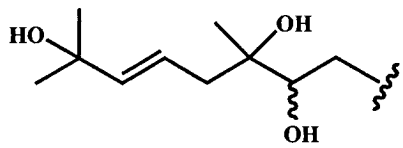
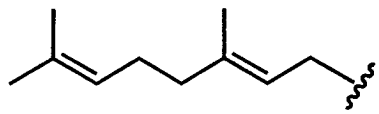
Tawanun Sripisut

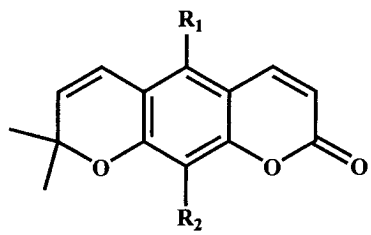
ชื่อวิทยานิพนธ์	การแยกและการพิสูจน์เอกลักษณ์ของสารออกฤทธิ์ทางชีวภาพจากผลและลำต้นสันโศก (*Clausena excavqta*)
ผู้เขียน	นางสาวถวนันท์ ศรีพิสุทธิ์
สาขาวิชา	เคมีประยุกต์
อาจารย์ที่ปรึกษา	ผศ.ดร. สุรัตน์ ละภูเขียว

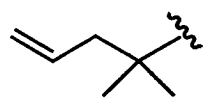
บทคัดย่อ

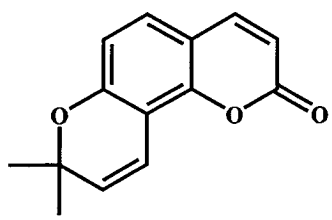
การศึกษาองค์ประกอบทางเคมีของต้นสันโศกสามารถแยกสารได้ 19 สาร โดยแยกได้ 4 สารจากส่วนสกัดหยาบ hexane-CH_2Cl_2 ของผลและเป็นสารใหม่คูมาริน 1 สาร (**CE1**) และ สารที่มีการรายงานแล้ว 3 สาร ซึ่งแบ่งเป็นสารประกอบคูมาริน 2 สาร (**CE2** และ **CE6**) และสารประกอบเทอร์ปีน 1 สาร (**CE19**) จากส่วนสกัดหยาบ EtOAc ของลำต้นสามารถแยกสารได้ 15 สาร เป็นสารประกอบใหม่คาร์บาโซล แอลคาลอยด์ 1 สาร (**CE14**) และสามารถแยกสารประกอบที่มีการรายงานแล้ว 14 สาร แบ่งเป็นสารประกอบคูมาริน 3 สาร (**CE3-CE5**) และสารประกอบแอลคาลอยด์ 11 สาร (**CE7- CE13** and **CE15-CE18**) โครงสร้างของสารประกอบเหล่านี้วิเคราะห์โดยใช้ข้อมูลทางสเปกโทรสโกปี สำหรับสาร **CE5**, **CE7**, **CE13-CE16** และ **CE18** เมื่อนำมาทดสอบฤทธิ์ต้านเชื้อมาลาเรีย และความเป็นพิษต่อเซลล์มะเร็ง (KB, MCF7 และ NCI-H187) พบว่าเฉพาะสาร **CE5** และ **CE16** สามารถต้านเชื้อมาลาเรียได้ โดยมีค่า IC_{50} 0.533 และ 6.74 μg/mL ตามลำดับ ในการทดสอบความเป็นพิษต่อเซลล์มะเร็ง KB และ NCI-H187 พบว่าเฉพาะสาร **CE7** ไม่มีความเป็นพิษต่อเซลล์ดังกล่าว สำหรับสาร **CE5**, **CE13-16**, และ **CE18** มีฤทธิ์ความเป็นพิษต่อเซลล์มะเร็ง KB และ NCI-H187 ทั้งสองในระดับปานกลางจนถึงดีโดยมีค่า IC_{50} อยู่ในช่วง 1.07 - 23.21 μg/mL นอกจากนี้สารทุกตัวยังมีความเป็นพิษต่อเซลล์มะเร็ง MCF7 โดยมีค่า IC_{50} อยู่ในช่วง 1.61 - 25.26 μg/mL



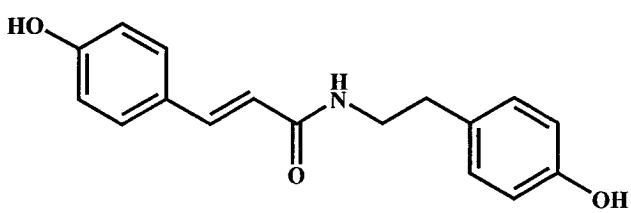
	R_1	R_2	R_3
CE1:	H		OH; Clausenaexcavin
CE2:	OMe	H	H; Scopoletin
CE3:	H		H; Aureptene



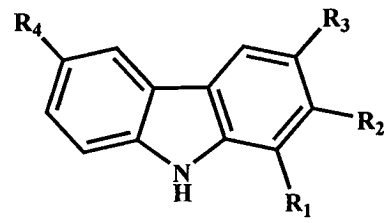
	R_1	R_2	
CE4:	H	H	; Xanthyletin
CE5:	OH		; Nordentatin



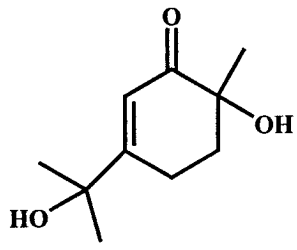
CE6; Seselin



CE19; *N*-(*p*-*trans*-coumaroyl)benzaldehyde



	R_1	R_2	R_3	R_4	
CE7:	**OMe**	**H**	**CO_2Me**	**H**	**; Mokonine**
CE8:	**H**	**H**	**CO_2Me**	**H**	**; Methylcarbazole-3-carboxylate**
CE9:	**OMe**	**H**	**CHO**	**H**	**; Lansine**
CE10:	**H**	**H**	**CHO**	**H**	**; Murrayanine**
CE11:	**H**	**OH**	**CHO**	**OMe**	**; 3-Formylcarbazole**
CE12:	**H**	**OH**	**CO_2Me**	**H**	**; Mokonidine**
CE13:	**H**	**OMe**	**CHO**	**H**	**; *O*-Methylmukonal**
CE14:	**H**	**OH**	**CO_2Me**	**OH**	**; Sansoakamine**
CE15:	**OH**	**H**	**CO_2Me**	**H**	**; Clauszoline-I**
CE16:	**OH**	**H**	**CHO**	**H**	**; *O*-Demehtylmurrayanine**
CE17:	**OH**	**H**	**CO_2Me**	**OH**	**; Methyl 1,6-dihydroxy-9*H*-carbazole-3-carboxylate**
CE18:	**OH**	**H**	**CHO**	**OH**	**; Clausine-Z**

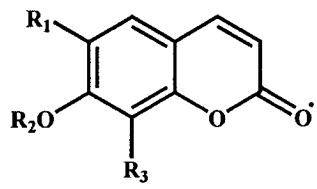


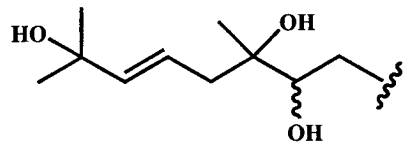
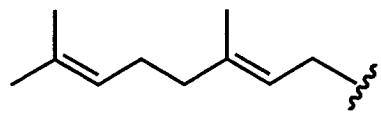
CE19: 1, 8-Dihydroxy-*p*-menth-3-en-2-one

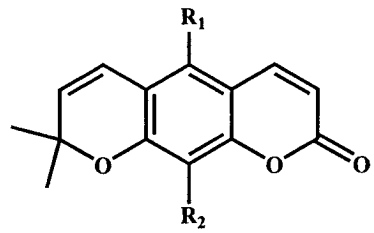
Title	Isolation and identification of biologically-active compounds from *Clausena excavata* fruits and stems
Author	Ms. Tawanun Sripisut
Major Program	Master of Science in Applied Chemistry
Advisor	Asst. Prof. Dr. Surat Laphookhieo

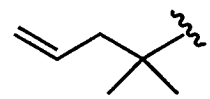
ABSTRACT

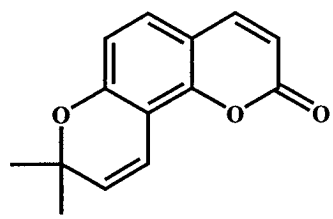
The investigation of chemical constituents from *Clausena excavata* led to the isolation and identification of nineteen compounds. Four of them were isolated from hexane-CH_2Cl_2 extract of fruits: a new coumarin (**CE1**) together with three known compounds: two coumarins (**CE2** and **CE6**) and a terpenoid (**CE19**). The remaining fifteen compounds were isolated from the EtOAc extracts of the stems: a new carbazole alkaloid (**CE14**) together with fourteen known compounds: three coumarins (**CE3-CE5**) and eleven alkaloids (**CE7-CE13** and **CE15-CE18**). Their structures were elucidated by spectroscopic methods. In addition, compounds **CE5**, **CE7**, **CE13-CE16** and **CE18** were evaluated for their anti malaril and cytotoxicity against three human cancer cell lines (KB, MCF7 and NCI-II187). Only two compounds, **CE5** and **CE16**, exhibited anti malarial activity with IC_{50} values of 0.533 and 6.74 μg/mL, respectively. Compounds **CE5**, **CE13- CE16** and **CE18** exhibited moderate to strong cytotocix activity against KB and NCI-H187 cancer cell lines with IC_{50} in range of 1.07-23.21 μg/mL whereas only compound **CE7** was found to be inactive. All tested compounds also showed moderate to strong cytotocix activity against MFC7 with IC_{50} in range of 1.61-25.26 μg/mL.



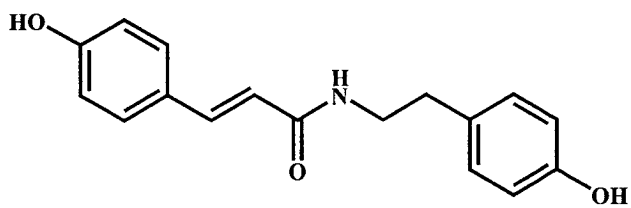
	R_1	R_2	R_3
CE1:	H		OH; Clausenaexcavin
CE2:	OMe	H	H; Scopoletin
CE3:	H		H; Aureptene



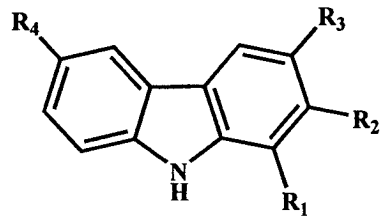
	R_1	R_2	
CE4:	H	H	; Xanthyletin
CE5:	OH		; Nordentatin



CE6; Seselin



CE19; *N*-(*p*-*trans*-coumaroyl)benzaldehyde



	R_1	R_2	R_3	R_4	
CE7:	**OMe**	**H**	**CO_2Me**	**H**	**; Mokonine**
CE8:	**H**	**H**	**CO_2Me**	**H**	**; Methylcarbazole-3-carboxylate**
CE9:	**OMe**	**H**	**CHO**	**H**	**; Lansine**
CE10:	**H**	**H**	**CHO**	**H**	**; Murrayanine**
CE11:	**H**	**OH**	**CHO**	**OMe**	**; 3-Formylcarbazole**
CE12:	**H**	**OH**	**CO_2Me**	**H**	**; Mokonidine**
CE13:	**H**	**OMe**	**CHO**	**H**	**; *O*-Methylmukonal**
CE14:	**H**	**OH**	**CO_2Me**	**OH**	**; Sansoakamine**
CE15:	**OH**	**H**	**CO_2Me**	**H**	**; Clauszoline-I**
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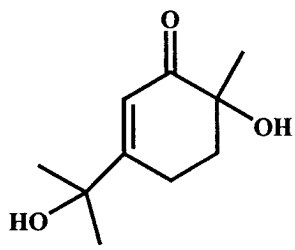
CE17:	**OH**	**H**	**CO_2Me**	**OH**	**; Methyl 1,6-dihydroxy-9*H*-carbazole-3-carboxylate**
CE18:	**OH**	**H**	**CHO**	**OH**	**; Clausine-Z**



CE19: 1, 8-Dihydroxy-*p*-menth-3-en-2-one

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ABBREVIATIONS AND SYMBOLS

s	=	*singlet*
d	=	*doublet*
t	=	*triplet*
q	=	*quartet*
m	=	*multiplet*
dd	=	*doublet of doublet*
dt	=	*doublet of triplet*
br s	=	*broad singlet*
br m	=	*broad multiplet*
g	=	gram
nm	=	nanometer
m.p.	=	melting point
cm^{-1}	=	reciprocol centimeter (wave number)
δ	=	chemical shift relative to TMS
J	=	coupling constant
$[\alpha]_D$	=	specific rotation
λ_{max}	=	maximum wavelength
ν	=	absorption frequencies
ε	=	molar extinction coefficient
Fig.	=	Figure
m/z	=	a value of mass divided by charge
°C	=	degree Celsius
MHz	=	Megahertz
ppm	=	part per million
c	=	concentration
IR	=	Infrared
UV	=	Ultraviolet-Visible
MS	=	Mass Spectroscopy

ABBREVIATIONS AND SYMBOLS (CONTINUED)

NMR	=	Nuclear Magnetic Resonance
2D NMR	=	Two Dimensional Nuclear Magnetic Resonance
COSY	=	Correlation Spectroscopy
DEPT	=	Distortionless Enhancement by Polarization Transfer
HMBC	=	Heteronuclear Multiple Bond Correlation
HMQC	=	Heteronuclear Multiple Quantum Coherence
ROESY	=	Rotating from Overhause Effect Spectroscopy
CC	=	Column Chromatography
QCC	=	Quick Column Chromatography
PLC	=	Preparative Thin Layer Chromatography
TMS	=	Tetramethylsilane
$CDCl_3$	=	Deuterochlroform

CHEPTER 1
INTRODUCTION

1.1. *Clausena excavata*

C. excavata is a wild shrub of Rutaceae family which is widely distributed in southern and southeastern Asia. Local Thai people usually call it by the name "San Soak" which had been used as folk medicines for the treatment of cold, colic, cough, headache, malaria, cancer, AIDS, dermatopathy, abdominal pain, snake bite and detoxification. The botanical characteristics of this plant are summarized below.

Leaves: 20-60 cm, odd-pinnate, 7-15(20) pairs of sub-opposite or alternate leaflets, 2.5-12x1.8-4 cm, ovate or lanceolate with tapering tip and oblique base, untoothed or very shallowly toothed. Mature leaves thin, smooth or finely hairy especially below. Side leaflet stalks 0.1-0.2 cm, end one much longer.

Flowers: 0.7-1 cm, branched pyramidal clusters at end of twigs and upper leaf axils, 10-30(45) cm, individual stalks 0.1-0.2 cm, buds globose. 4 overlapping petals, 8 long and short, filaments swollen at base, style 1-2 mm, stout with tiny stigma.

Fruits: 0.7-2 cm, white or pale pink, oval slightly hairy when young, later smooth and gland-dotted, fleshy and juicy with 1-2 seeds.

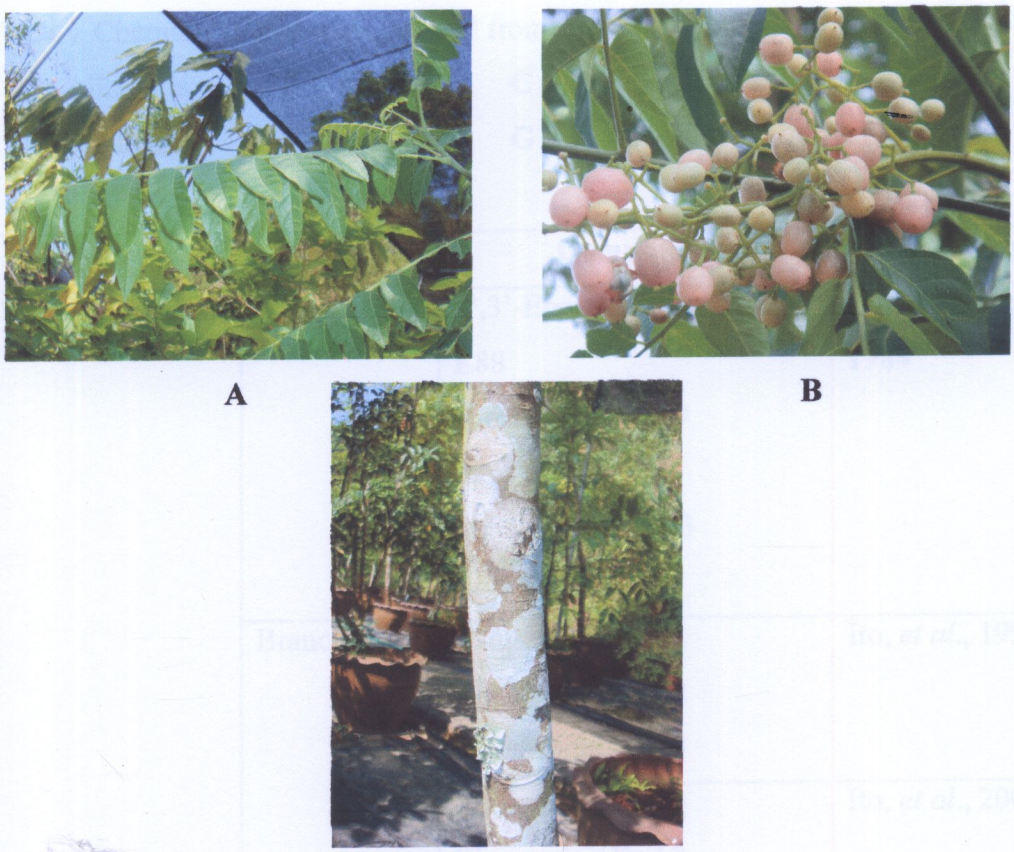

Figure 1 Leaves, fruits and stem of *C. excavata* (**A-C**).

1.2. Review of Literatures

1.2.1. The Chemical Constituents of *Clausena* genus

Plants in genus *Clausena* are well known to be rich source of coumarins and carbazole alkaloids. Furthermore, a small group of limonoids, steroids, flavonoids, and essential oils were also isolated from this genus. The chemical constituents which were isolated from this genus according to the information from SciFinder were summarized in **Table 1**.

Table 1 Chemical compounds isolated from *Clausena* genus

A = Alkaloids **B** = Akanols **C** = Anthraquinone **D** = Benzenoids

E = Coumarins **F** = Ester **G** = Flavonoids **H** = Lipids

I = Steroids **J** = Terpenoids

Plant	Part	Compound	Bibliography
C. anisata	Aerial parts	2',3'-Epoxyanisolactone, **E88** Anisolactone, **E89** Imperatorin, **E82** Indicolactone, **E83** Xanthotoxol, **E81**	Lakshmi, *et al.*, 1984
	Branches	Clausamine A, **A1** Clausamine B, **A2** Clausamine C, **A3**	Ito, *et al.*, 1998
		Clausamine A, **A1** Clausamine B, **A2** Clausamine C, **A3** Clausamine D, **A4** Clausamine E, **A6** Clausamine F, **A7** Clausamine G, **A8** Clausine E, **A39** Clausine F, **A5** Ekeberginine, **A9** *O*-Demethylmurrayanine, **A54** Methyl carbazole-3-carboxylate, **A55**	Ito, *et al.*, 2000
	Leaves	Estragole, **D1**	Okunade, *et al.*, 1986

Table 1 (Continued)

Plant	Part	Compound	Bibliography
C. anisata	Leaves	Anisocoumarin E, **E5** Anisocoumarin F, **E6**	Ngadjui, *et al.*, 1989
		Anisocoumarin H, **E8** Capnolactone, **E57** Imperatorin, **E82** Triphasiol, **E77**	Ngadjui, *et al.*, 1989
		Anisocoumarin A, **E1** Anisocoumarin B, **E2** Anisocoumarin C, **E3** Anisocoumarin D, **E4** Anisocoumarin E, **E5** Anisocoumarin F, **E6** Anisocoumarin G, **E7** Anisocoumarin H, **E8** Anisocoumarin I, **E9** Anisocoumarin J, **E10** Capnolactone, **E57** Imperatorin, **E82** Isoponcimarin, **E76** Triphasiol, **E77** Umbelliferone, **E69**	Ngadjui, *et al.*, 1991
	Roots	Chalepin, **E78** Clausanitin, **A10** Coumarrayin, **E73** Imperatorin, **E 82** Osthol, **E72**	Okoria, 1975
	Root barks	3-(1,1-Dimethylallyl)-xanthyletin, **E42** Chalepin, **E78**	Mesteri, *et al.*, 1977

Table 1 (Continued)

Plant	Part	Compound	Bibliography
C. anisata	Root barks	Coumarrayin, **E73** Imperatorin, **E82** Osthol, **E72** Xanthoxyletin, **E39**	Mesteri, *et al.*, 1977
	Stems	Atanisatin, **A11** Chalepin, **E78** Clausanitin, **A10**	Okoria, 1975
		Clausamine B, **A2** Clausamine C, **A3** Clausamine E, **A6** Furanoclausamine A, **A12** Furanoclausamine B, **A13**	Ito, *et al.*, 2008
	Stem barks	Clausenine, **A56** Clausenol, **A57**	Chakraborty, *et al.*, 1995
	Stem barks and roots	Clausenarin, **J25** Clausenolide, **J19** Clausenolide-1-ethyl ether, **J 20** Zapoterin, **J21**	Ngadjui, *et al.*, 1989
		Anisocoumarins A, **E1** Anisocoumarins B, **E2** Anisocoumarins C, **E3** Anisocoumarins D, **E4**	Ngadjui, *et al.*, 1989
		3-Methylcarbazole, **A58** Atanisatin, **A11** Clausanitin, **A10** Ekeberginine, **A9** Girinimbine, **A14** Heptaphylline, **A16**	Ngadjui, *et al.*, 1989

Table 1 (Continued)

Plant	Part	Compound	Bibliography
C. anisata	Stem barks and roots	Mupamine, **A15** *N*-methylswietenidine B, **A94** *O*-Demethylmurrayanine, **A54** Swietenidine B, **A93**	Ngadjui, *et al.*, 1989
C. anisum-olens	Aerial parts	Clausenain I, **A56**	Wang, *et al.*, 2005
	Leaves and twigs	Anisucumarin A/B, **E75**	Wang, *et al*, 2008
C. dentata	Root barks	Dentatin, **E41** Imperatorin, **E82** Nordentatin, **E40**	Govindachari, *et al.*, 1968
C. dunniana	Aerial parts	Dunniana acid A, **J1** Dunniana acid B, **J2**	He, *et al.*, 2002
		14,15-Dinorclerod-3-ene-2,13-dione, **J4** 2β-(Acetyloxy)clerod-3-en-15-oic acid, **J6** 2β-(Formyloxy) clerod-3-en-15-oic acid, **J7** 4α,18-Dihydroxyclerodan -15-oic acid, **J9** 4β-Hydroxyclerodan-15-oic acid, **J10** 3α,4α-Dihydroxyclerodan-15-oic acid, **J11** 3β-Hydroxy-clerod-4(18)-en-15-oic acid, **J12**	He, *et al.*, 2003

Table 1 (Continued)

Plant	Part	Compound	Bibliography
C. dunniana	Aerial parts	Ethyl clerod-4(18)-en-15-oate, **K13** Ethyl clerod-3-en-15-oate, **J16** (2*S*)-1-[(6,7-Dimethoxyfuro[2,3-*b*]quinolin-4-yl)oxy]-3-methyl-butane-2,3-diol, **A97** 2-Oxoclerod-3-en-15-oic acid, **J3** 4α-Hydroxyclerodan-15-oic acid, **J5** Clerod-4(18)-en-15-oic acid, **J13** Clerod-3-en-15-oic acid, **J15** *trans*-Palmitoylphytol, **F2** Kokusaginine, **A95** Skimmianine, **A96** 3-Hydroxy-9*H*-carbazole-3-carboxaldehyde, **A60** Clausenamide, **A90** Tarolupenol, **J29** Tarolupenyl acetate, **J30** Haplociliatic acid, **J18** Isoscopoletin, **E71** Marmesin, **E79**	He, *et al.*, 2003

Table 1 (Continued)

Plant	Part	Compound	Bibliography
C. dunniana	Aerial parts	β-Sitosterol, **I1** 3,5-Dihydroxy-4',7-dimethoxyflavone, **G4** 4',5-Dihydroxy-3,7-dimethoxyflavone, **G3** 5-Hydroxy-3,4',7-trimethoxyflavone, **G6** Hexatriacontanoic acid, **H2** Myricitrin, **G7** Paeonol, **D6** Stearic acid, **H1** Triacontan-1-ol, **B1**	He, *et al.*, 2003
C. excavata	Aerial parts	Excavacoumarin B, **E46** Excavacoumarin C, **E47** Excavacoumarin D, **E48** Excavacoumarin E, **E49** Excavacoumarin F, **E50** Excavacoumarin G, **E51**	He, *et al.*, 2000
		(11β)-21,23-Dihydro-11,21-dihydroxy-23-oxoobacun, **J26** (11β)-21,23-Dihydro-11,23-dihydroxy-2l-oxoobactrn, **J24** (1α, 11β)-1,2,11,23-Tetrahydro-1,11,23-trihydroxy-21-oxoobacun, **J22**	He, *et al.*, 2002

Table 1 (Continued)

Plant	Part	Compound	Bibliography
C. excavata	Aerial parts	(1α,11β)-23-Ethoxy-1,2,21,23-tetrahydro-1,11-dihydroxy-21-oxoobacunone, **J23** (11f)-1,2,21,23-Tetrahydro-11,23-dihydroxy-21-Oxoobacunoic acid, **J27** Zapoterin, **J21**	He, *et al.*, 2002
		Excavacoumarin H, **E52** Excavacoumarin I, **E53**	He, *et al.*, 2004
	Branches	Cladimarins A, **E32** Cladimarins B, **E33**	Takemura, *et al.*, 2004
	Leaves	2,6-Dimethoxy-4-(2-propenyl)phenyl-β-D-glycoside, **D2** 13^2-Hydroxy(13^2-R)-pheophytin-a, **A98** 2-Methoxy-4-(2-propenyl)phenyl-β-D-glucoside, **D1** Clausine L, **A45** *p*-Hydroxybenzoic acid, **D3** Nicotiflorin, **G8** Rutin, **G9** Safrole, **D7** Scopoletin, **E70**	Wu, *et al.*, 1993

Table 1 (Continued)

Plant	Part	Compound	Bibliography
C. excavata	Leaves	Excavatin A, **E54** Excavatin B, **E55** Excavatin C, **E56** Excavatin D, **E57** Excavatin E, **E58** Excavatin F, **E59** Excavatin G, **E60** Excavatin H, **E61** Excavatin I, **E62** Excavatin J, **E63** Excavatin K, **E64** Excavatin L, **E65** Excavatin M, **E66**	Thuy, *et al.*, 1999
		Excavacoumarin A, **E45** Excavacoumarin B, **E46**	He, *et al.*, 2000
		Clauslactone A, **E13** Clauslactone B, **E14** Clauslactone C, **E15** Clauslactone D, **E16** Clauslactone E, **E17** Clauslactone F, **E18** Clauslactone G, **E19** Clauslactone H, **E20** Clauslactone I, **E21** Clauslactone J, **E22**	Ito, *et al.*, 2000

Table 1 (Continued)

Plant	Part	Compound	Bibliography
C. excavata	Leaves and twigs	Clauslactone K, **E23** Clauslactone L, **E24** Clauslactone M, **E25**	Nakamura, *et al.*, 1998
	Rhizomes	3-Formylcarbazol, **A59** 2-Hydroxy-3-formyl-7-methoxycarbazol, **A63** 3-Methoxycarbonylcarbazol, **A61** Clausenidin, **E34** Clauszoline, **A64** Dentatin, **E41** Mukonal, **A60** Murrayanine, **A62** Nordentatin, **E40** Xanthoxyletin, **E39**	Sunthitikawinsakul, *et al.*, 2002
	Roots	Clausarin, **E43** Clausenidin, **E34** Nordentatin, **E40** Xanthoxyletin, **E39**	Su, *et al.*, 2009
	Root barks	Clausarin, **E43** Clausenidin, **E34** Clausenidinaric acid, **D9** Hetaphylline, **A16** Nordentatin, **E40** Xanthoxyletin, **E39**	Wu, *et al.*, 1982
		Cedrelopsin, **E74** Claucavatin A, **E35** Claucavatin B, **E36**	Huang, *et al.*, 1997

Table 1 (Continued)

Plant	Part	Compound	Bibliography
C. excavata	Root barks	Clausarin, **E43** Clausenidin, **E34** Isoliquiritigenin, **G1** Liquiritigenin, **G2** Kinocoumarin, **E44** Nordentatin, **E40** Osthol, **E72** Xanthoxyletin, **E39** Xanthyletin, **E38**	Huang, *et al.*, 1997
		Clausine W, **A17** Clausine T, **A18** Furoclausine A, **A19** Furoclausine B, **A20**	Wu, *et al.*, 1997
		2-Hydroxy-3-formyl-7-methoxycarbazole , **A63** Clausenatine A, **A23** Clausine M, **A46** Clausine N, **A47** Clausine O, **A48** Clausine P, **A49** Clausine Q, **A50** Clausine R, **A51** Clausine S, **A21** Clausine U, **A22** Clausine V, **A52** Glycozolidal, **A65** Heptaphylline, **A16** Murrayafoline A, **A66**	Wu, *et al.*, 1999

Table 1 (Continued)

Plant	Part	Compound	Bibliography
C. excavata	Root barks	3-Formylcarbazole, **A59** 3-Methylcarbazole, **A58** Clausine C, **A38** Clausine E, **A39** Clausine F, **A5** Clausine K, **A44** Clausine T, **A18** Clausine W, **A17** Furoclausine A, **A19** Furoclausine B, **A20** Claucavatin A, **E54** Clausenidin, **E34** Clausevatine D, **A24** Clausevatine E, **A25** Clausevatine F, **A26** Clausevatine G, **A27** Clausamine A, **A1** Carbazomarine A, **A28** Girinimbine, **A14** Kinocoumarin, **E44** Methyl carbazole-3-carboxylate, **A69** Mukonal, **A60** Mukonidine, **A69** Mukonine, **A68** Murrayanine, **A 62**	Wu, *et al.*, 1999

Table 1 (Continued)

Plant	Part	Compound	Bibliography
C. excavata	Root barks	4',7-Dihydroxy flavanone , **G10** Cedrelopsin, **E74** Clausarin, **E43** Isoliquiritigenin, **G1** Nordentatin, **E40** Osthol, **E72** Xanthoxyletin, **E39** Xanthyletin, **E38**	Wu, *et al.*, 1999
	Stem barks	Clausine A, **A36** Clausine C, **A38** Clausine G, **A40** Clausine J, **A43**	Wu, *et al.*, 1996
		2-Hydroxy-3-methylcarbazole, **A71** Clausine B, **A37** Clausine D, **A29** Clausine E, **A39** Clausine H, **A41** Clausine I, **A42** Clausine K, **A44** Glycozolidal, **A65** Heptaphylline, **A16** Lansine, **A70** Methyl carbazole-3-carboxylate, **A69** Mukonal, **A60** Mukonine, **A68** Murrayanine, **A62**	Wu, *et al.*, 1996

Table 1 (Continued)

Plant	Part	Compound	Bibliography
C. excavata	Stem barks	Clausarin, **E43** Clausine F, **A5** Clausenaquinone A, **A75** Clausenidin, **E34** Methyl-*p*-Hydroxycinnamate, **D5** Nordentatin, **E40** Scopoletin, **E70** Syringaldehyde, **D8** Xanthoxyletin, **E39**	Wu, *et al.*, 1996
	Stem barks	Clausine B, **A37** Clausine H, **A41** Clausine TY, **A53**	Taufiq-Yap, *et al.*, 2007
	Stem and root barks	Carbazomarin A, **A28** Clausenamine A, **A30**	Wu, *et al.*, 1996
C. harmandiana	Roots	Clausarin, **E43** Clausine K, **A44** Dentatin, **E41** Heptaphylline, **A16**	Yenjai, *et al.*, 2000
	Root barks	Clausarin, **E43** Dentatin, **E41** Heptaphylline, **A16** Nordentatin, **E40** Osthol, **E72** Xanthyletin, **E38**	Wangboonskul, *et al.*, 1984
		2-Hydroxy-3-formyl-7-methoxycarbazole, **A63**	Chaichantipyuth, *et al.*, 1988

Table 1 (Continued)

Plant	Part	Compound	Bibliography
C. harmandiana	Root barks	7-Methoxyheptaphyline, **A31**	Chaichantipyuth, *et al.*, 1988
C. heptaphylla	Leaves	Clausenal, **A72**	Chakraborty, *et al.*, 1995
		Clausmarin A, **E37**	Sohrab, *et al.*, 2000
	Roots	Clausenidin, **E34**	Joshi, *et al.*, 1967
		3-Methylcarbazole, **A58**	Ray, *et al.*, 1974
		Murrayacine, **A32** Girinimbine, **A14**	Ray, *et al.*, 1976
		Heptazolicine, **A33**	Bhattacharyya, *et al.*, 1984
	Stem barks	2-Methylanthraquinone, **C1** 3-Methylcarbazole, **A58**	Chakraborty, *et al.*, 1978
C. indica	Leaves	Balasubramide, **A76** Madugin, **A77** Methylmadugin, **A82** Phenethyl cinnamide, **A86** Prebalamide, **A83**	Riemer, *et al.*, 1997
C. lansium	Branches	Lansiumarin A, **E85** Lansiumarin B, **E86** Lansiumarin C, **E87**	Ito, *et al.*, 1998
	Fruits	SB 204900, **A89**	Milner, *et al.*, 1996
	Leaves	Clausenamide, **A90** Cycloclausenamide, **A92** Neoclausenamide, **A91**	He, *et al.*, 1988
		Lansiol, **I2**	Lakshmi, *et al.*, 1988

Table 1 (Continued)

Plant	Part	Compound	Bibliography
C. lansium	Roots	3-Formylcarbazole, **A59** 3-Formyl-1,6-dimethoxycarbazole, **A75** 3-Formyl-6-methoxycarbazole, **A73** Glycozoline, **A76** Indizoline, **A34** Methyl 6-methoxycarbazole-3-carboxylate, **A74** Methyl carbazole-3-carboxylate, **A69** Murrayanine, **A62**	Li, *et al.*, 1991
		β-Sitosterol, **I1** 2,7-Dihydroxy-3-formyl-1-(3'-Methyl-2'-butenyl)carbazole, **A35** Angustifolin, **E11** Chalepensin, **E80** Chalepin, **E78** Gravelliferone, **E12** Indizoline, **A34**	Kumar, *et al.*, 1995
	Seeds	Lansiumamide A, **A84** Lansiumamide B, **A85** Lansiumamide C, **A87** Lansiumamide I, **A88**	Lin, 1989

Table 1 (Continued)

Plant	Part	Compound	Bibliography
C. lenis	Arial parts	Diseselin A, **E67**	He, *et al.*, 2003
		Diseselin B, **E68** Lenisin A, **D10** Lenisin B, **D11** Lenisin C, **D12**	He, *et al.*, 2006
C. pentaphylla	Roots	Clausarin, **E43** Clausenidin, **E34** Dentatin, **E41** Heptaphylline, **A16**	Anwer, *et al.*, 1976

Structure

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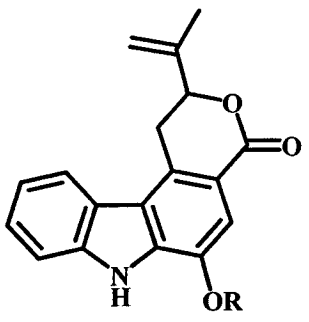

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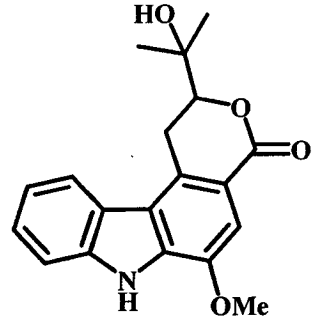

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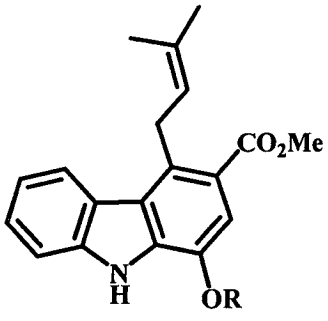

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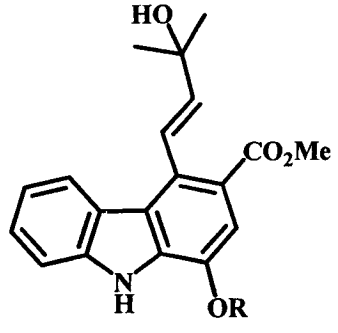

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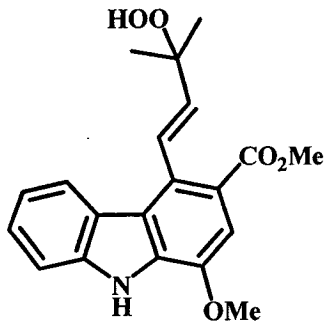

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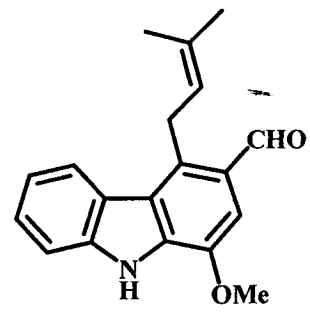
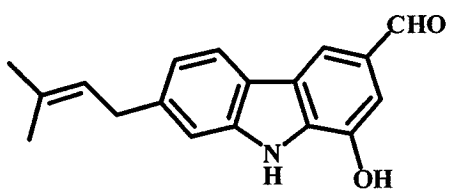


Ekeberginine, **A9**



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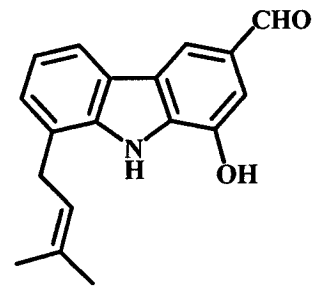

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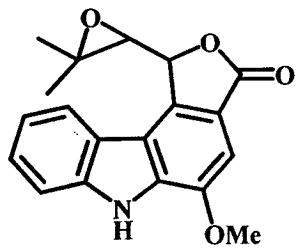

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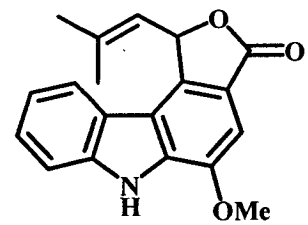

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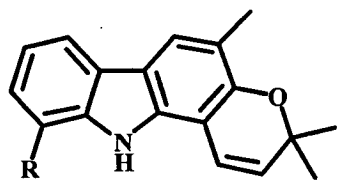

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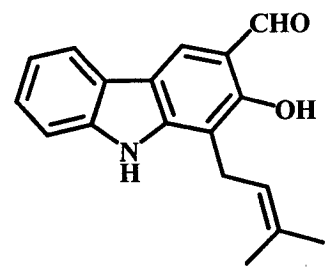

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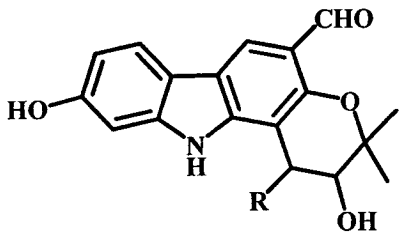

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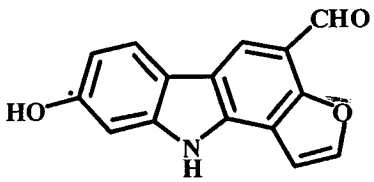

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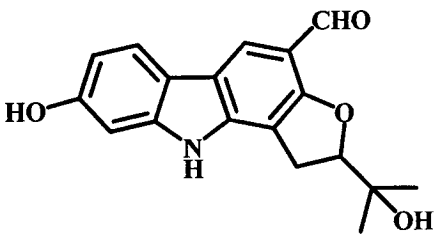

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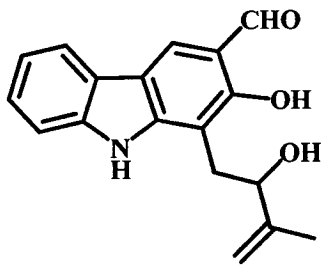

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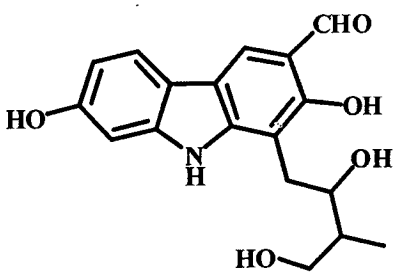

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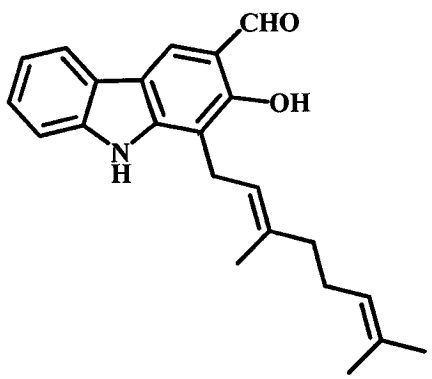

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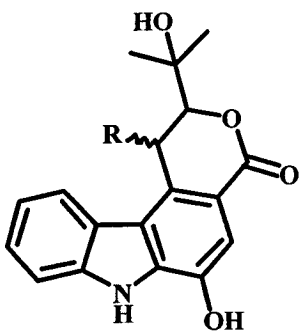

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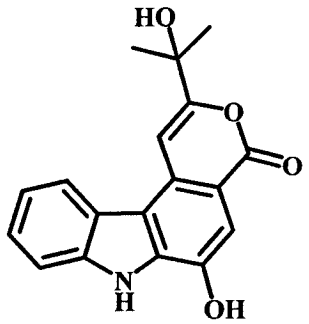

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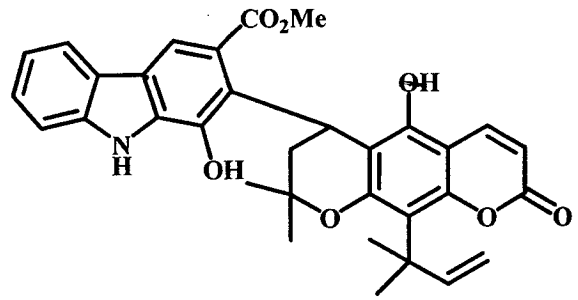

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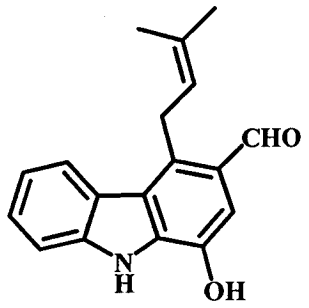

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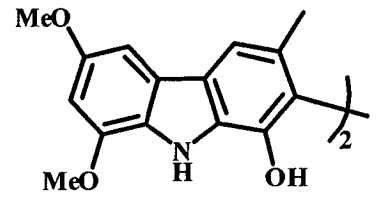
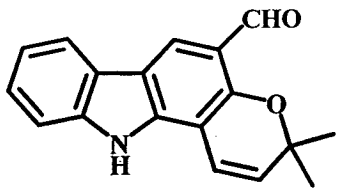


Clausenamine A, **A30**



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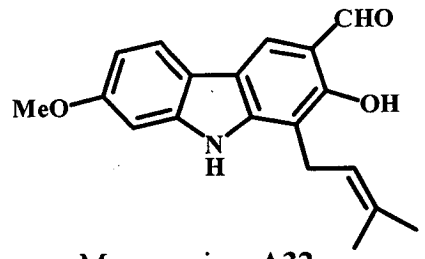

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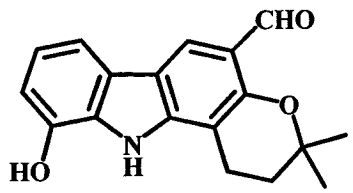

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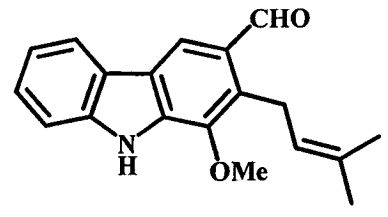
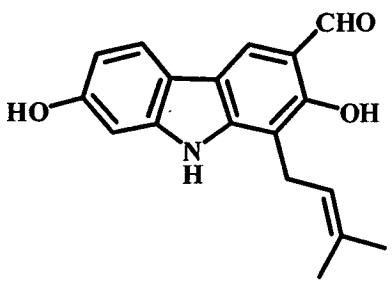
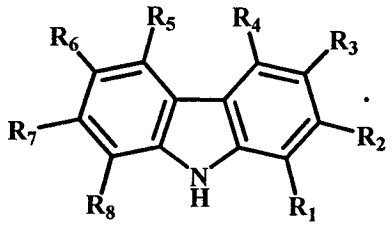


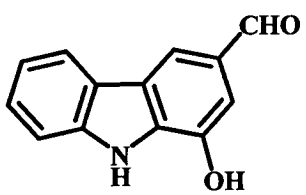
Indizoline, **A34**



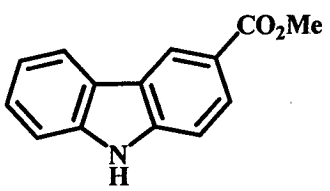
2, 7-Dihydroxy-3-formyl-1-(3'-Methyl-2'butenyl)carbazole, **A35**



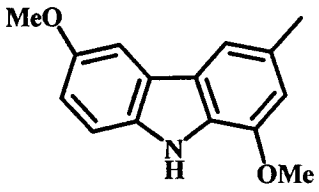
R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8	
H	OH	CHO	H	H	H	H	OMe	Clausine A, **A36**
H	OH	CHO	H	H	OMe	H	OMe	Clausine B, **A37**
H	H	CO_2Me	H	H	H	OMe	H	Clausine C, **A38**
OH	H	CO_2Me	H	H	H	H	H	Clausine E, **A39**
OH	H	CO_2Me	H	H	OMe	H	H	Clausine G, **A40**
H	OMe	CO_2Me	H	H	H	OMe	H	Clausine H, **A41**
OH	H	CHO	OMe	H	H	OMe	H	Clausine I, **A42**
OH	H	CHO	OMe	H	H	OH	H	Clausine J, **A43**
H	OMe	CO_2H	H	H	H	OMe	H	Clausine K, **A44**
H	OMe	CO_2Me	H	H	H	H	H	Clausine L, **A45**
H	H	CO_2Me	H	H	H	OH	H	Clausine M, **A46**
H	H	CO_2H	H	H	H	OMe	H	Clausine N, **A47**
H	OH	CHO	H	H	H	OH	H	Clausine O, **A48**
H	OMe	Me	H	H	H	H	OMe	Clausine P, **A49**
OMe	H	CHO	H	H	H	H	H	Clausine Q, **A50**
OH	H	CO_2Me	H	H	H	OH	H	Clausine R, **A51**
H	OMe	H	H	H	H	OMe	H	Clausine V, **A52**
H	OH	CO_2Me	H	H	H	OMe	H	Clausine TY, **A53**



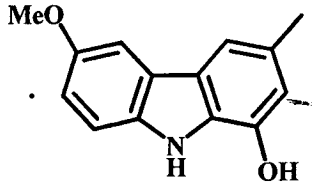
O-demethylmurrayanine, **A54**



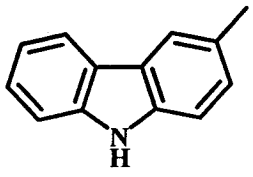
Methyl carbazole-3-carboxylate, **A55**



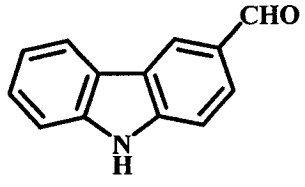
Clausenine, **A56**



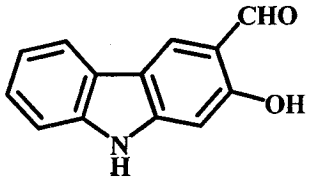
Clausenol, **A57**



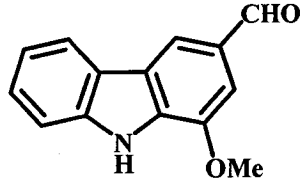
3-Methylcarbazole, **A58**



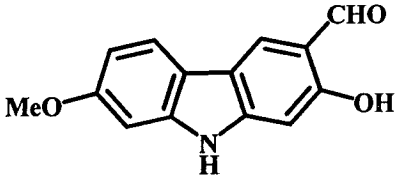
3-Formylcarbazole, **A59**



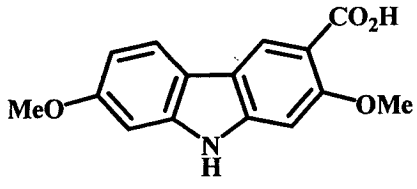
Mukonal, **A60**



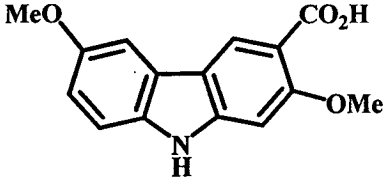
Murrayanine, **A61**



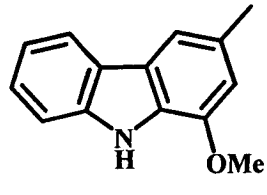
2-Hydroxy-3-formyl-7-methoxycarbazole, **A62**



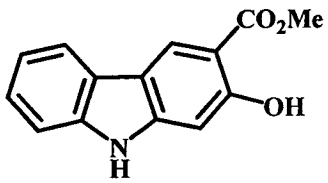
Clauszoline, **A63**



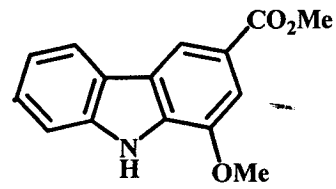
Glycozolidal, **A64**



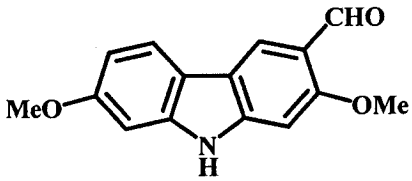
Murrayafoline, **A65**



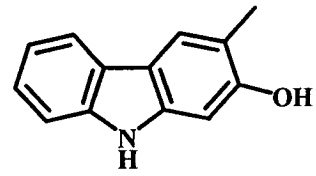
Mokonidine, **A66**



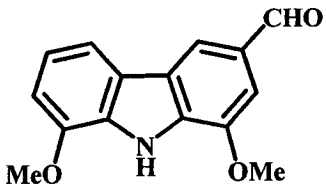
Mokonine, **A67**



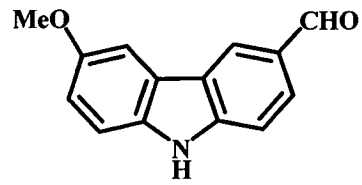
Lansine, **A68**



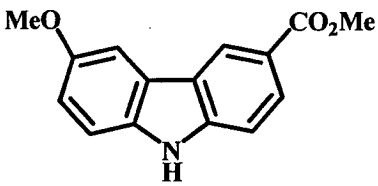
2-Hydroxy-3-methylcarbazole, **A69**



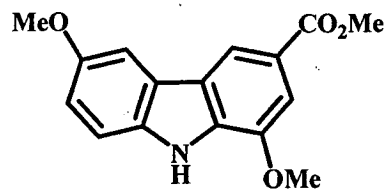
Clausenal, **A70**



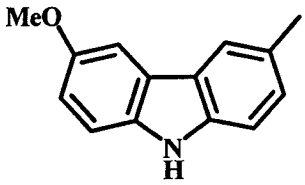
3-Formyl-6- methoxycarbazole, **A71**



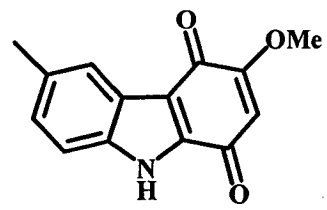
Methyl-6-methoxycarbazole-3-carboxylate, **A72**



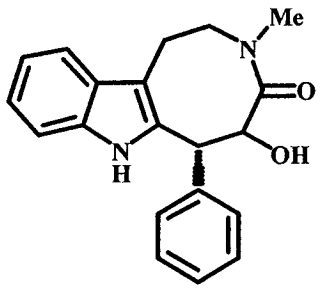
3-Formyl-1,6-dimethoxycarbazole, **A73**



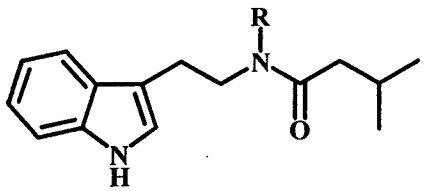
Glycozoline, **A74**



Clausenaquinone-A, **A75**

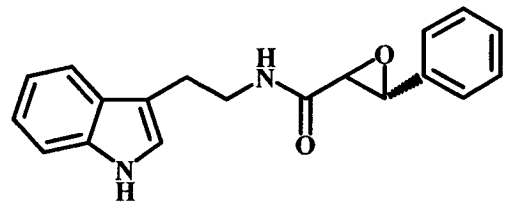


Balasubramide, **A76**

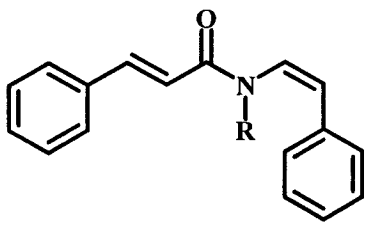


R = H, Madugin, **A81**

R = Me, Methylmadugin, **A82**

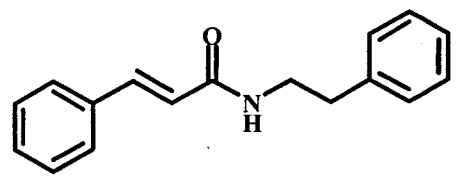


Prebalamide, **A83**



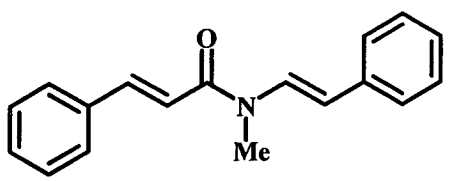
R = H, Lansiumamide A, **A84**

R = Me, Lansiumamide B, **A85**

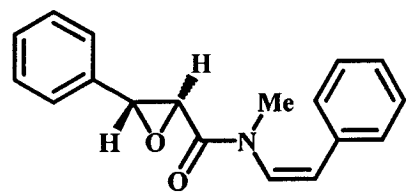


R = H, Phenethyl cinnamide, **A86**

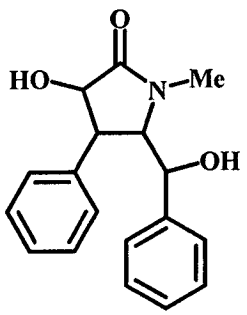
R = Me, Lansiumamide C, **A87**



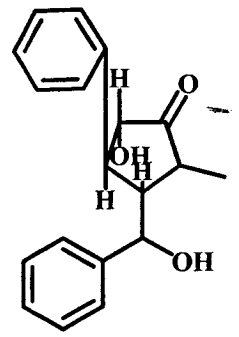
Lansiumamide I, **A88**



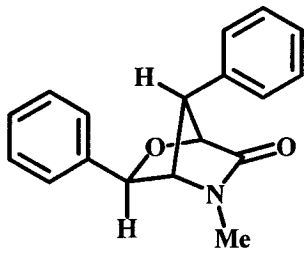
SB 204900, **A89**



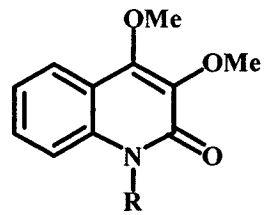
Clausenamide, **A90**



Neoclausenamide, **A91**

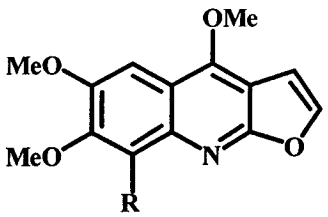


Cycloclausenamide, **A92**



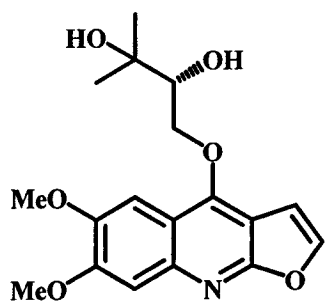
R = H, Swietenidine, **A93**

R = OMe, *N*-methylswietenidine, **A94**

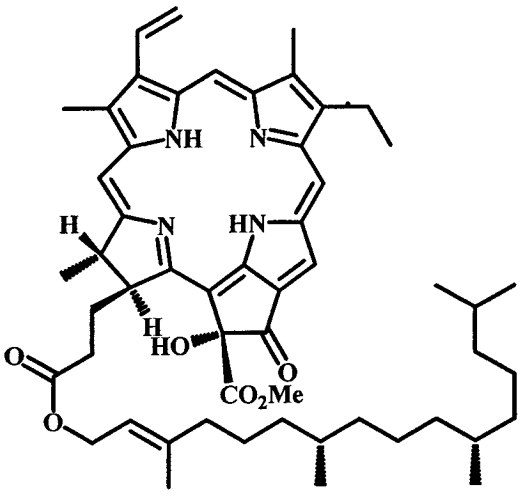


R = H, Kokusaginine, **A95**

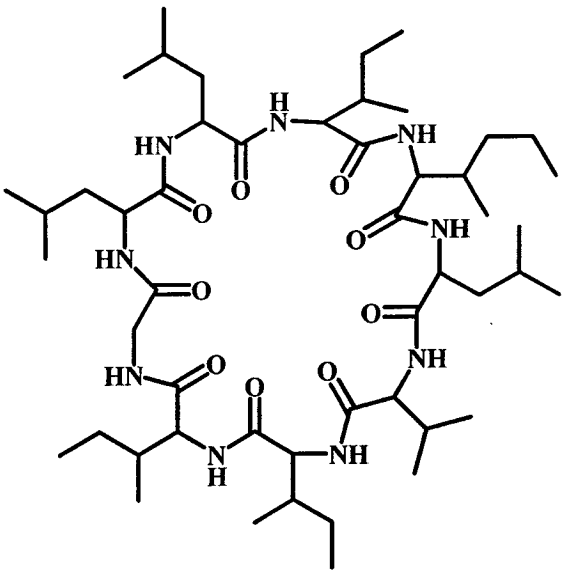
R = OMe, Skimmianine, **A96**



(2*S*)-1-[(6,7-Dimethoxyfuro[2,3-*b*]quinolin-4-yl)oxy]-3-methyl-butane-2,3-diol, **A97**

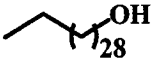


13^2-Hydroxy(13^2-R)-pheophytin-a, **A98**



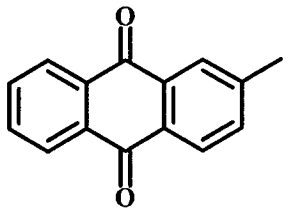
Clausenain I, **A99**

B =Alkanol



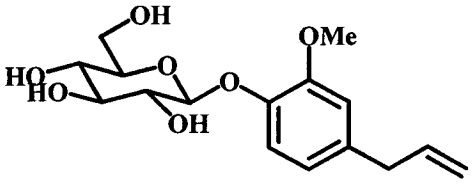
Triacontan-1-ol, **B1**

C = Anthraquinone

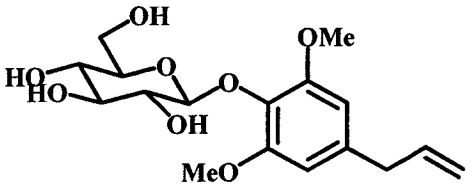


2-Methylanthraquinone, **C1**

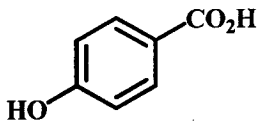
D = Benzenoids



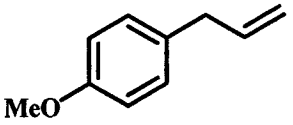
2-Methoxy-4-(2-propenyl)phenyl-*β*-*D*-glucoside, **D1**



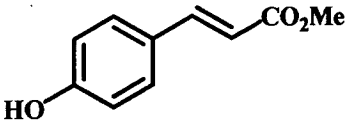
2,6-Dimethoxy-4-(2-propenyl)phenyl-*β*-*D*-glycoside, **D2**



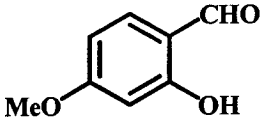
p-Hydroxybenzoic acid, **D3**



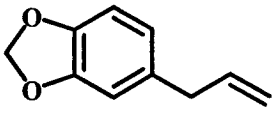
Estragole, **D4**



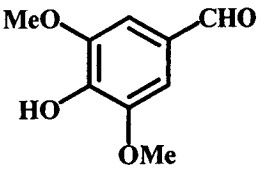
Methyl-*p*-hydroxycinnamate, **D5**



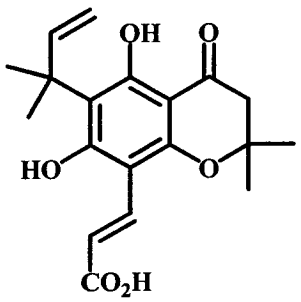
Paeonol, **D6**



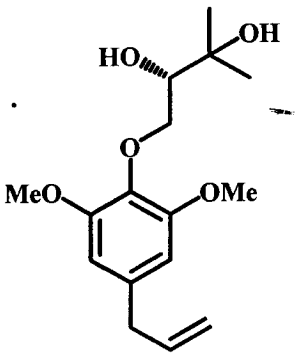
Safrole, **D7**



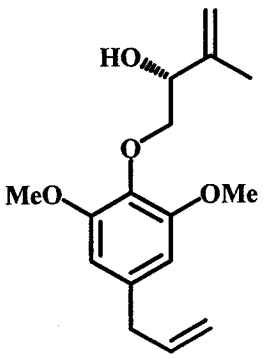
Syringaldehyde, **D8**



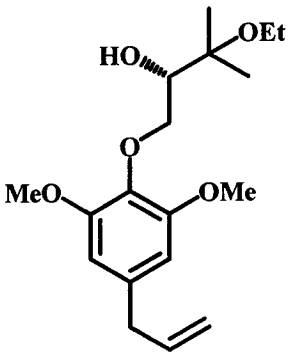
Clausenidinaric acid, **D9**



Lenisin A, **D10**

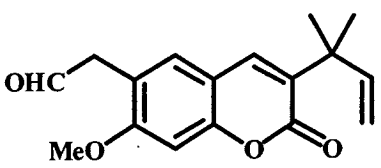


Lenisin B, **D11**

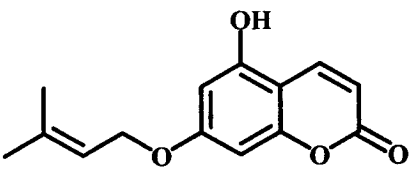


Lenisin C, **D12**

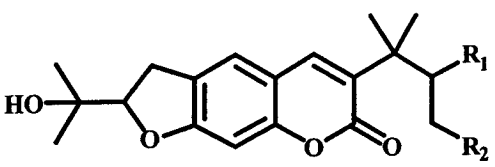
E = Coumarins



Anisocoumarin A, **E1**

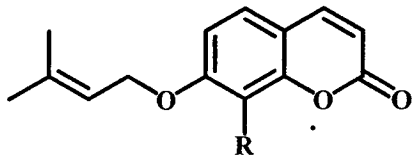


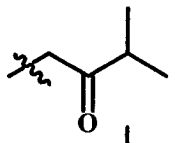
Anisocoumarin B, **E2**

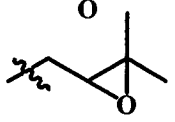


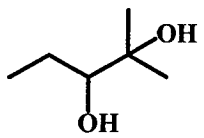
$R_1 + R_2 = O$, Anisocoumarin C, **E3**

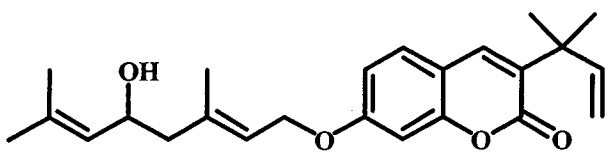
$R_1 = R_2 = OH$, Anisocoumarin D, **E4**



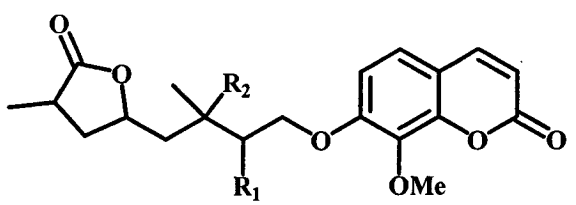
R =  , Anisocoumarin E, **E5**

R =  , Anisocoumarin F, **E6**

R =  , Anisocoumarin G, **E7**

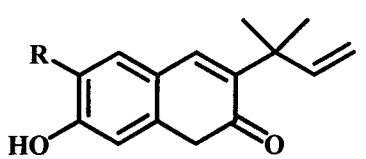


Anisocoumarin H, **E8**

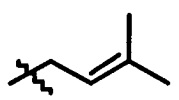


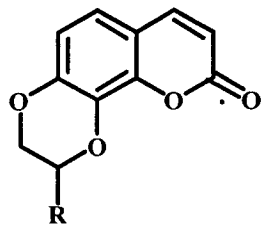
$R_1 + R_2 = O$, Anisocoumarin I, **E9**

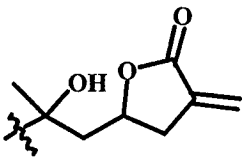
$R_1 = R_2 = OH$, Anisocoumarin J, **E10**

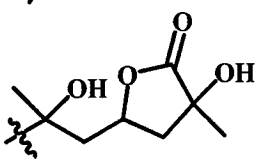


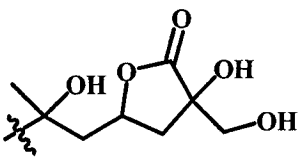
R = H, Augustifolin, **E11**

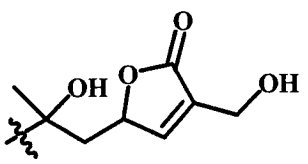
R =  , Gravelliferone, **E12**

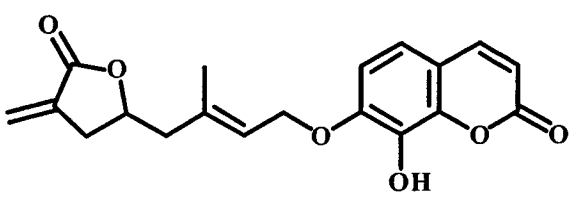


R =  , Clauslactone A, **E13**

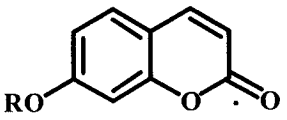
R =  , Clauslactone B, **E14**

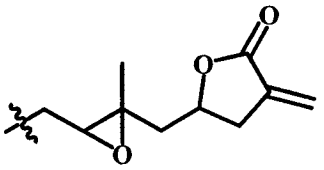
R =  , Clauslactone C, **E15**

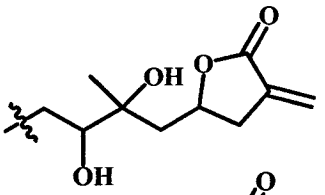
R =  , Clauslactone D, **E16**

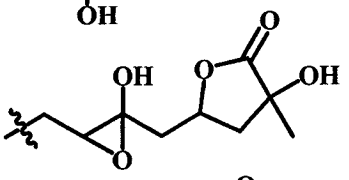


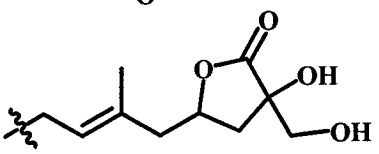
Clauslactone E, **E17**

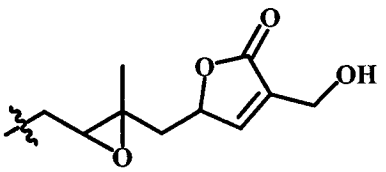


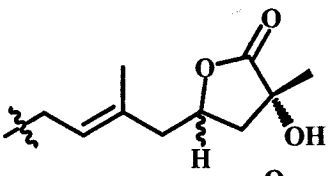
R =  , Clauslactone F, **E18**

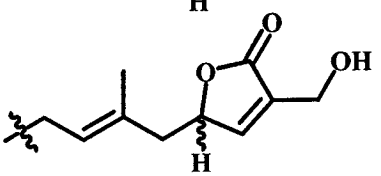
R =  , Clauslactone G, **E19**

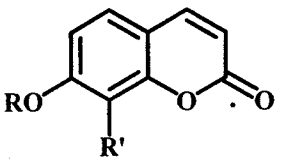
R =  , Clauslactone H, **E20**

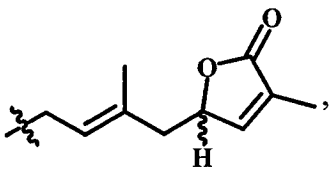
R =  , Clauslactone I, **E21**

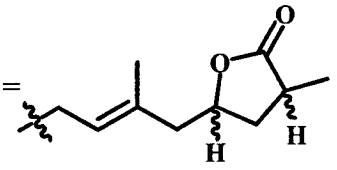
R =  , Clauslactone J, **E22**

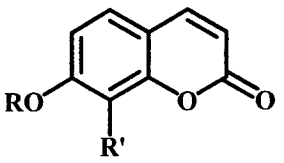
R =  , Clauslactone O, **E23**

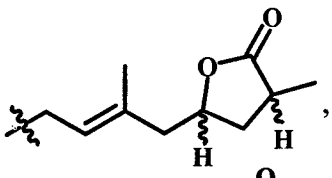
R =  , Clauslactone Q, **E24**

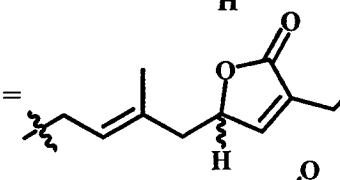


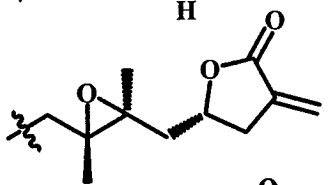
R =  , R' = OMe, Clauslactone K, **E25**

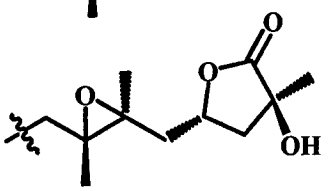
R =  , R' = OMe, Clauslactone L, **E26**

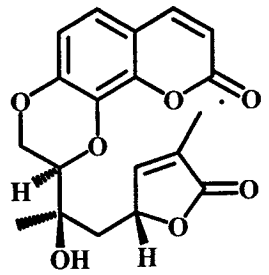


R =  , R' = OMe, Clauslactone M, **E27**

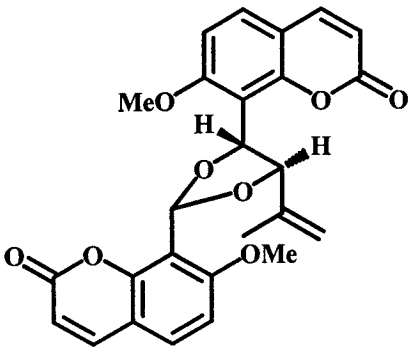
R =  , R' = OMe, Clauslactone P, **E28**

R =  , R' = OMe, Clauslactone R, **E29**

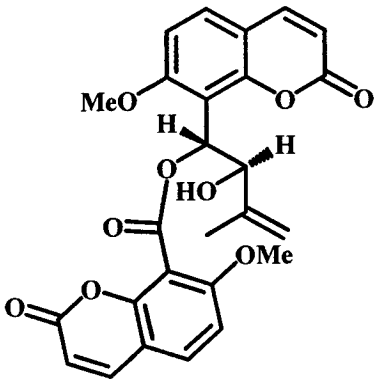
R =  , R' = OMe, Clauslactone S, **E30**



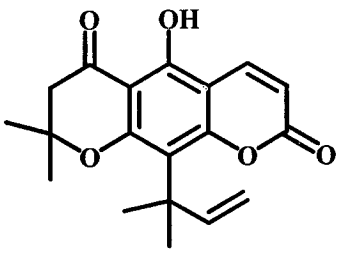
Clauslactone T, **E31**



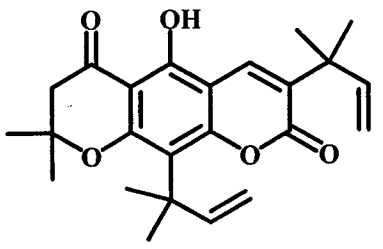
Cladimarin A, **E32**



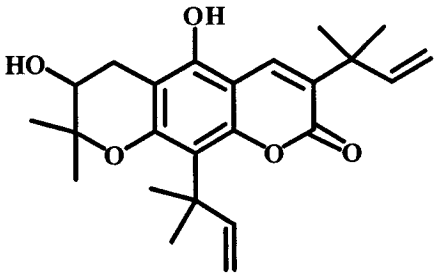
Cladimarin B, **E33**



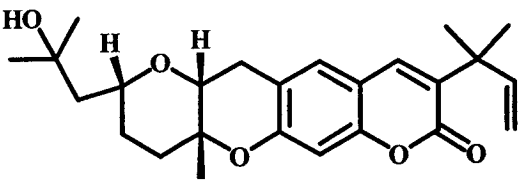
Clausenidin, **E34**



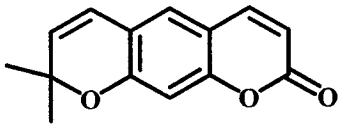
Claucavatin-A, **E35**



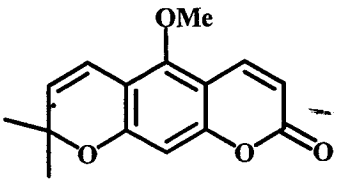
Claucavatin-B, **E36**



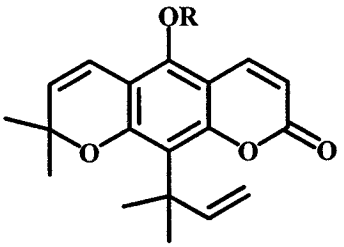
Clausmarin-A, **E37**



Xanthyletin, **E38**

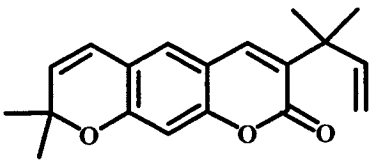


Xanthoxyletin, **E39**

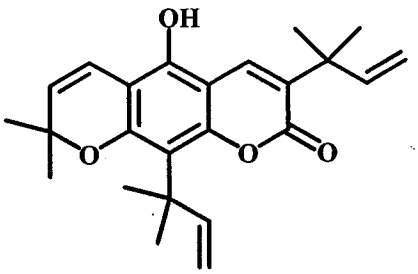


R = H, Nordentatin, **E40**

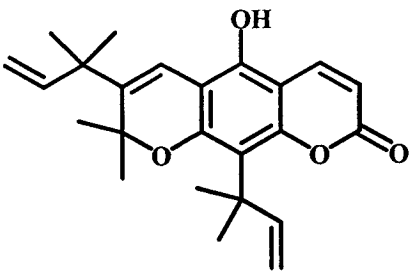
R = CH_3, Dentatin, **E41**



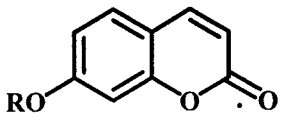
3-(1,1-Dimethylallyl)-xanthyletin, **E42**

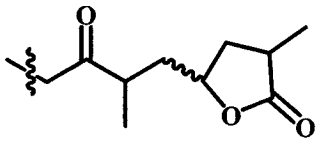


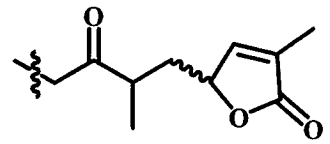
Clausarin, **E43**

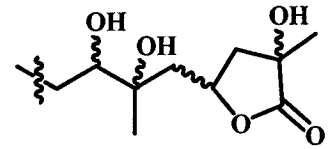


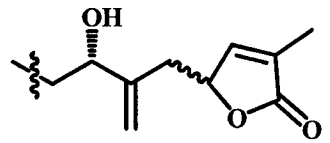
Kinocoumarin, **E44**

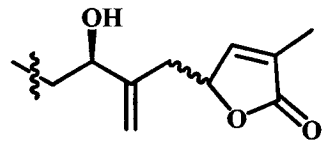


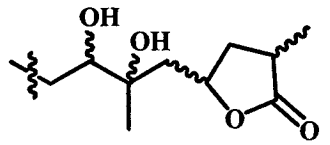
R =  , Excavacoumarin A, **E45**

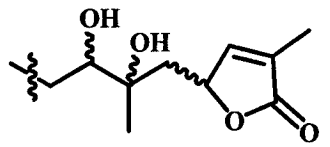
R =  , Excavacoumarin B, **E46**

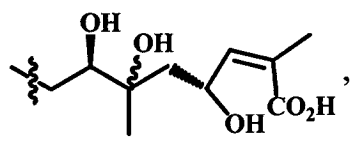
R =  , Excavacoumarin C, **E47**

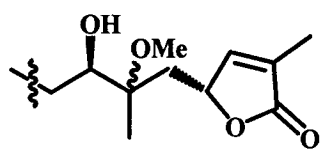
R =  , Excavacoumarin D, **E48**

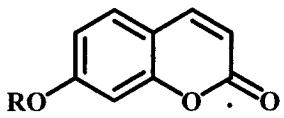
R =  , Excavacoumarin E, **E49**

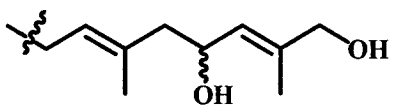
R =  , Excavacoumarin F, **E50**

R =  , Excavacoumarin G, **E51**

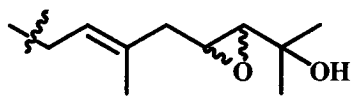
R =  , Excavacoumarin H, **E52**

R =  , Excavacoumarin I, **E53**

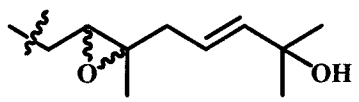


R = 

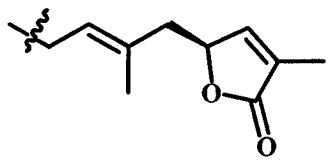
, Excavatin A, **E54**

R = 

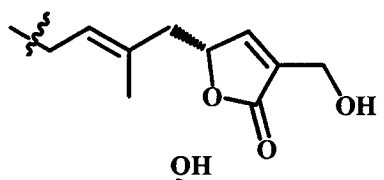
, Excavatin B, **E55**

R = 

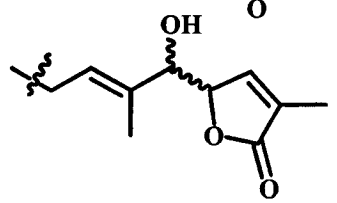
, Excavatin C, **E56**

R = 

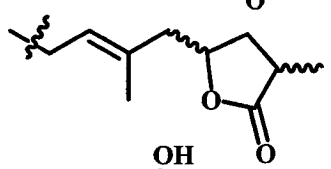
, Excavatin D, **E57**

R = 

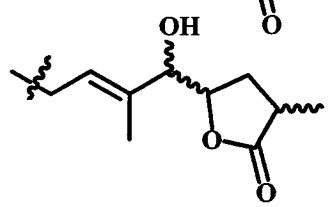
, Excavatin E, **E58**

R = 

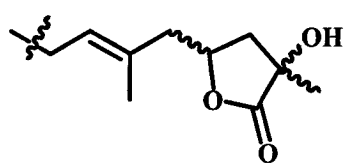
, Excavatin F, **E59**

R = 

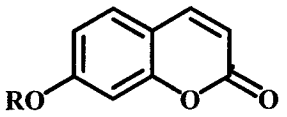
, Excavatin G, **E60**

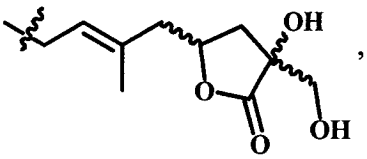
R = 

, Excavatin H, **E61**

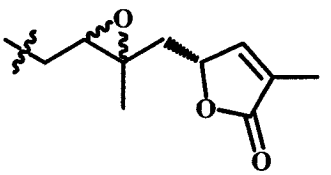
R = 

, Excavatin I, **E62**

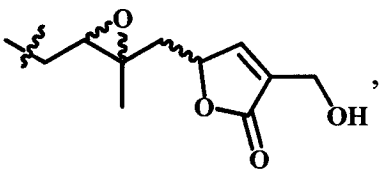


R = 

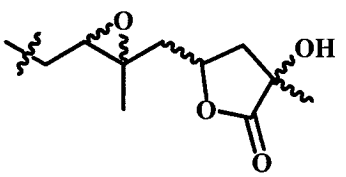
, Excavatin J, **E63**

R = 

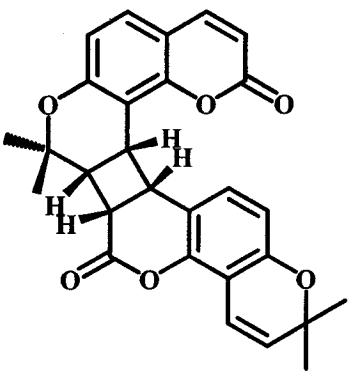
, Excavatin K, **E64**

R = 

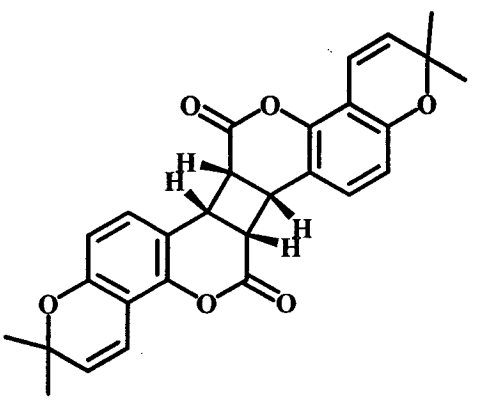
, Excavatin L, **E65**

R = 

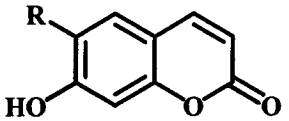
, Excavatin M, **E66**



Diseselin A, **E67**

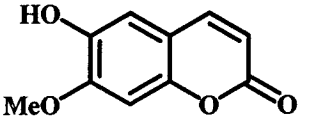


Diseselin B, **E68**

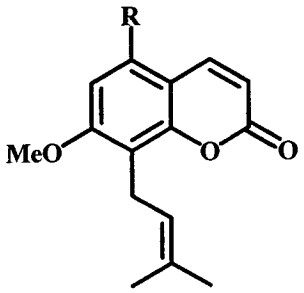


R = H, Umbelliferone, **E69**

R = OMe, Scopoletin, **E70**

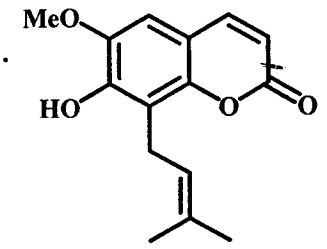


Isoscopoletin, **E71**

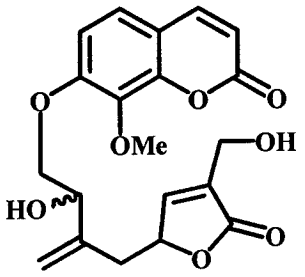


R = H, Osthol, **E72**

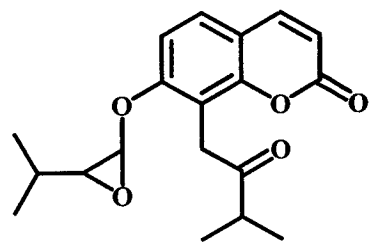
R = OMe, Coumarrayin, **E73**



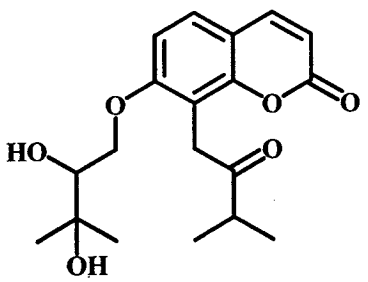
Cedrelopsin, **E74**



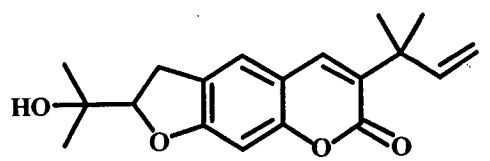
Anisucumarin A/B, **E75**



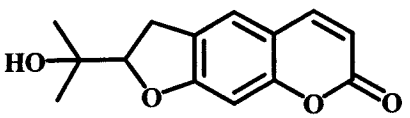
Isoponcimarin, **E76**



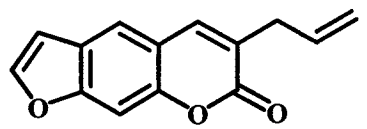
Triphasiol, **E77**



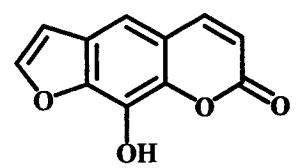
Chalepin, **E78**



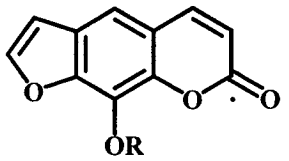
Marmesin, **E79**

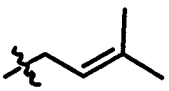


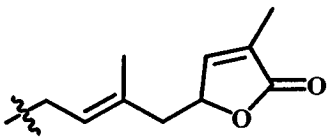
Chalepensin, **E80**

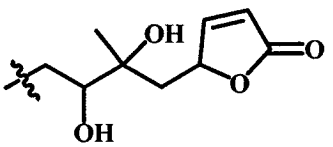


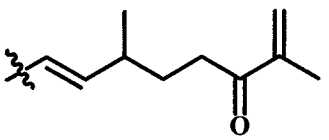
Xanthoxol, **E81**

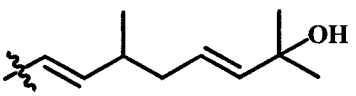


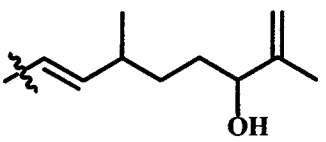
R =  , Imperatorin, **E82**

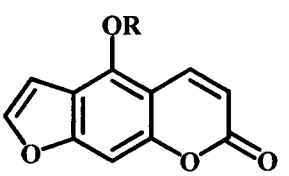
R =  , Indicolactone, **E83**

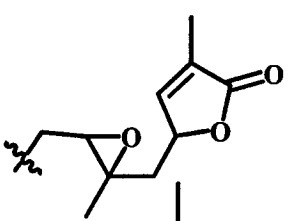
R =  , Indicolactonediol, **E84**

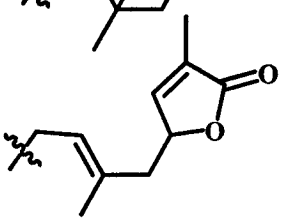
R =  , Lansiumarin A, **E85**

R =  , Lansiumarin B, **E86**

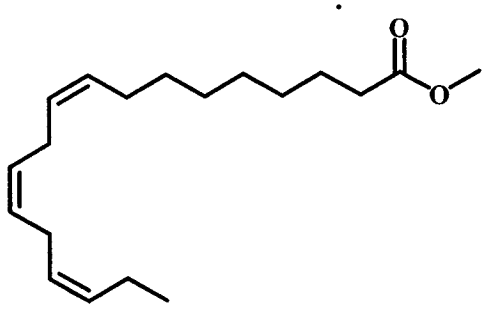
R =  , Lansiumarin C, **E87**



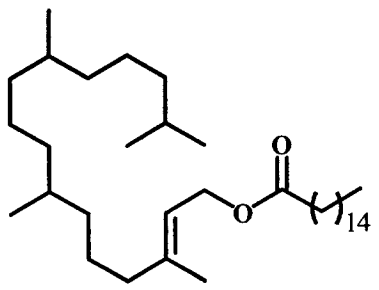
R =  , 2', 3'-Epoxyanisolactone, **E88**

R =  , Anisolactone, **E89**

F =Esters

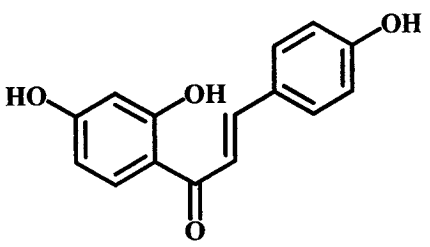


Methyl linolenate, **F1**

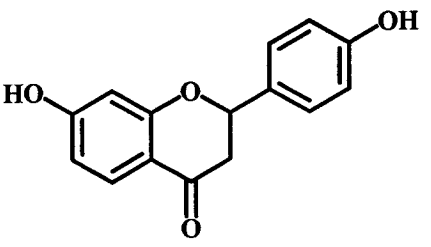


trans-Palmitoylphytol, **F2**

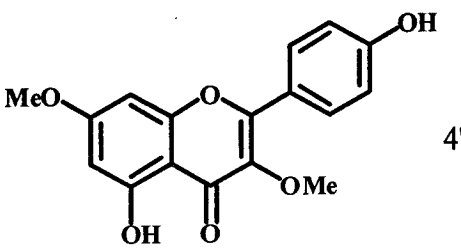
G = Flavonoids



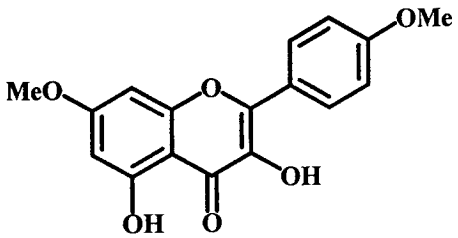
Isoliquiritigenin, **G1**



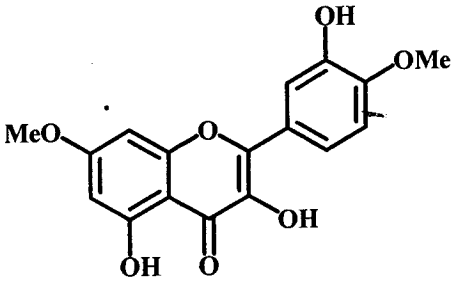
Liquiritigenin, **G2**



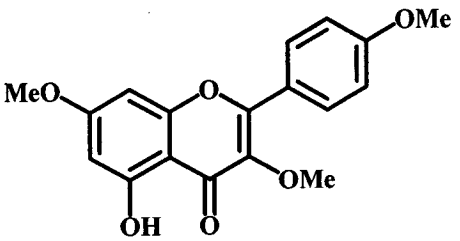
4', 5-Dihydroxy-3,7-dimethoxyflavone, **G3**



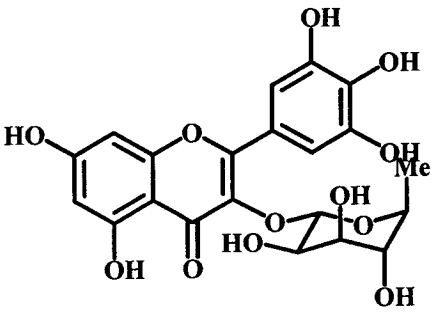
3, 5-Dihydroxy-4',7-dimethoxyflavone, **G4**



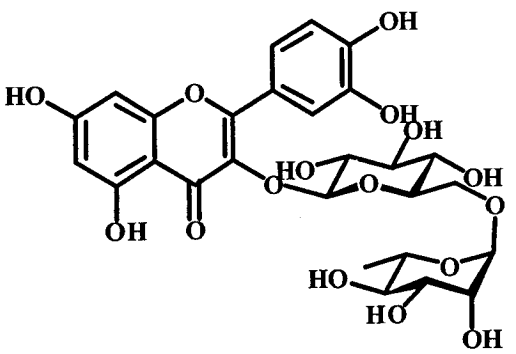
Ombuin, **G5**



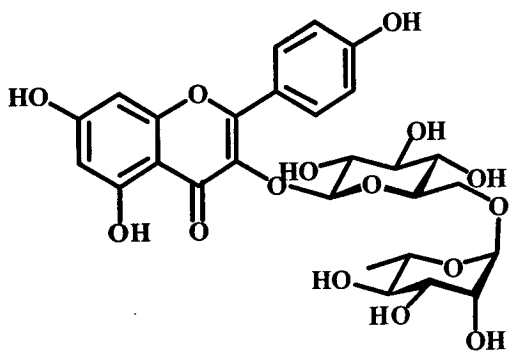
5-Hydroxy-3,4',7-trimethoxyflavone , **G6**



Myricitrin, **G7**

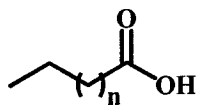


Nicotiflorin, **G8**



Rutin, **G9**

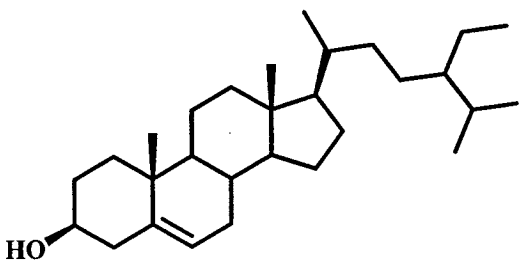
H = Lipids



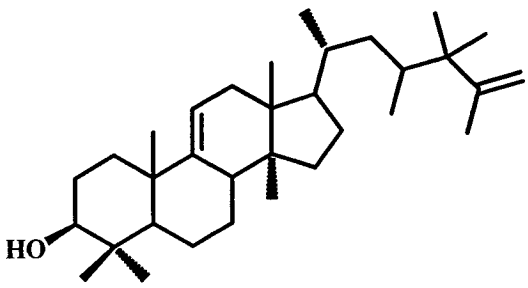
n = 15, Steric acid, **H1**

n = 33, Hexatriacontonoic, **H2**

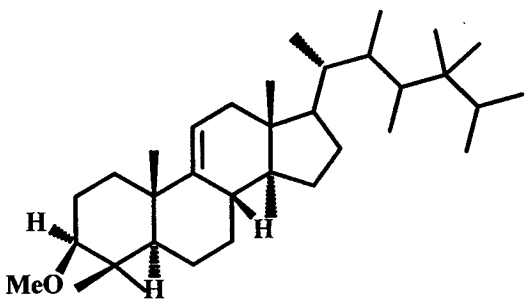
I = Steroids



β-Sitosterol, **I1**

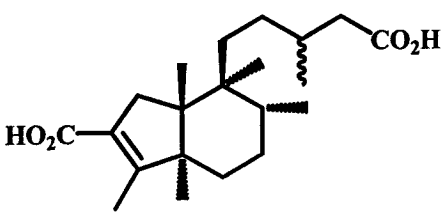


Lansiol, **I2**

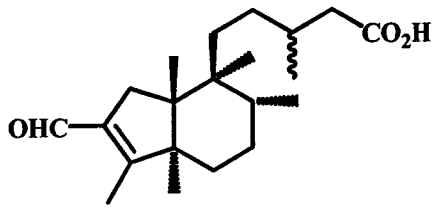


O-methylclausenol, **I3**

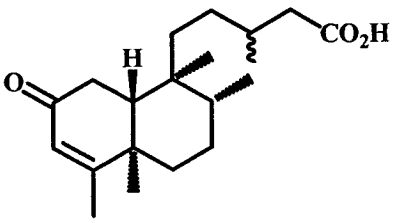
J = Terpenoids



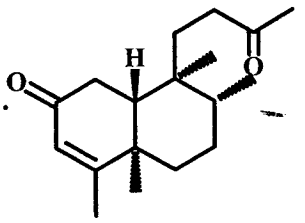
Dunniana acid A, **J1**



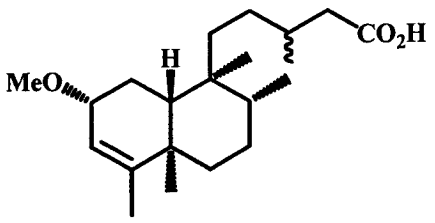
Dunniana acid B, **J2**



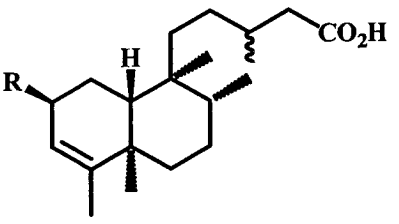
2-Oxoclerod-3-en-15-oic acid, **J3**



14,15-Dinorclerod-3-ene-2,13-dione, **J4**

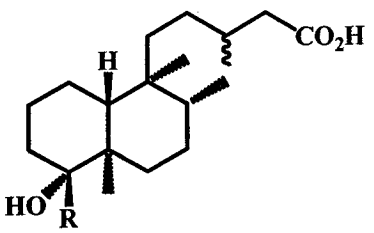


2α-Methoxyclerod-3-en-15-oic acid, **J5**



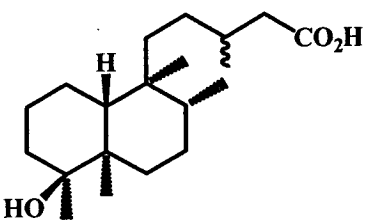
R = Me, 2β-(Acetyloxy)clerod-3-en-15-oicacid, **J6**

R = OCHO, 2β-(Formyloxy)clerod-3-en-15-oic acid, **J7**

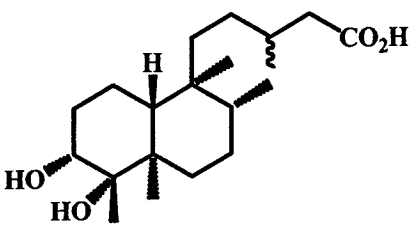


R = Me, 4α-Hydroxyclerodan-15-oic acid, **J8**

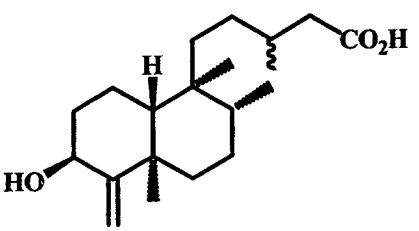
R = CH_2OH, 4α,18-Dihydroxyclerodan-15-oic acid, **J9**



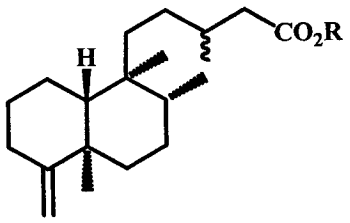
4β-Hydroxyclerodan-15-oic acid, **J10**



3α, 4α-dihydroxyclerodan-15-oic acid, **J11**

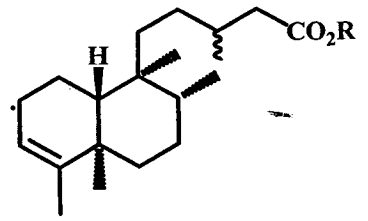


3β-hydroxy-clerod-4(18)-en-15-oic acid,**J12**



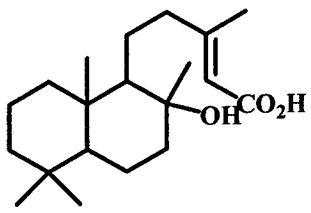
R = H, clerod-4(18)-en-15-oic acid, **J13**

R = CH_2CH_3, Ethyl Clerod-4(18)-en-15-oate, **J14**

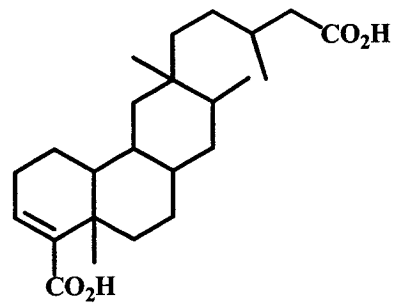


R = H, clerod-3-en-15-oic acid, **J15**

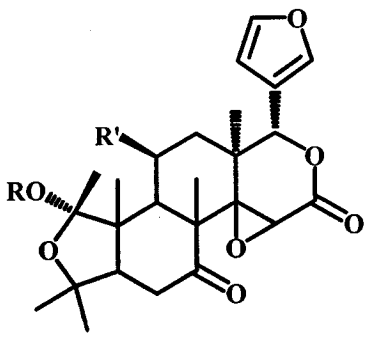
R = ethyl clerod-3-en-15-oate, **J16**



8-Hydroxy-13-labden-15-oic acid, **J17**

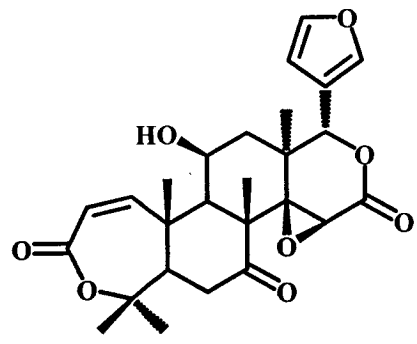


Haplociliatic acid, **J18**

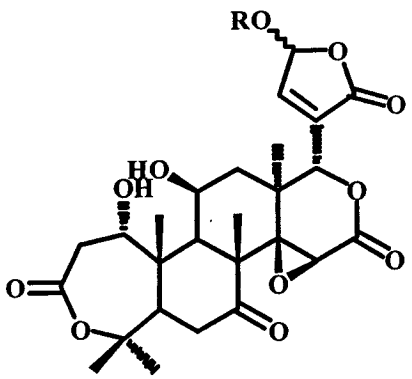


R = H, R' = OH, Clausenolide, **J19**

R = Et, R' = OH, Clausenolide-1-ethyl ether, **J20**

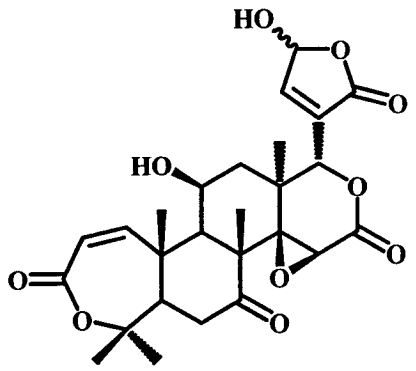


Zapoterin, **J21**

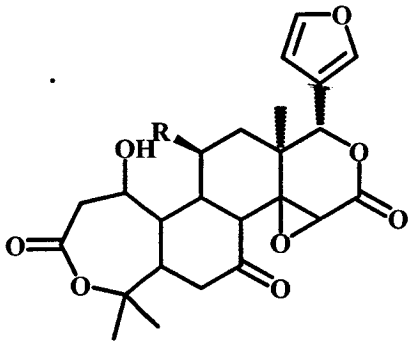


R=H, (1α, 11β)-1,211,23-Teftahydro-1,11,23-trihydroxy-21-oxoobacun, **J22**

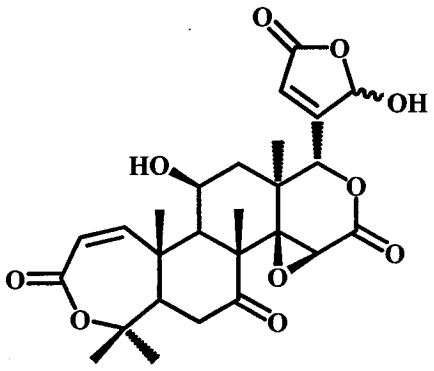
R=Et, (lα, 11β)-23-Elhoxy-1,2,21,23-tetrahydro-1,11-dihydroxy-21-oxoobacunone, **J23**



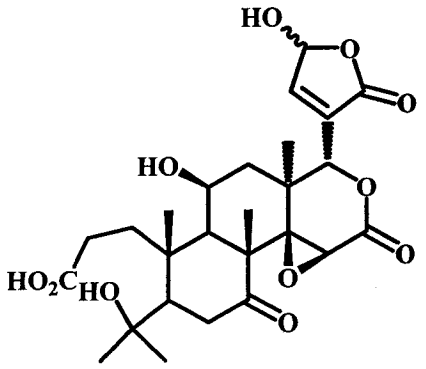
(11β)-21,23-Dihydro-11,23-dihydroxy-21-oxoobactrn, **J24**



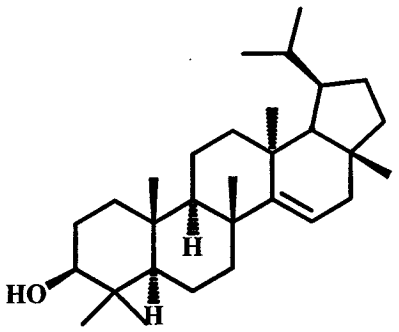
Clausenarin, **J25**



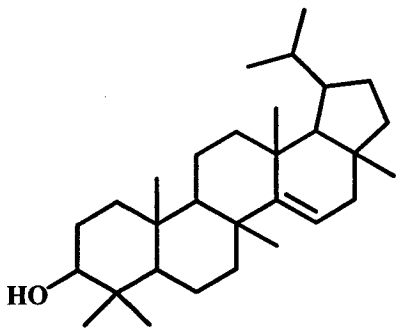
(11β)-21,23-Dihydro-11,21-dihydroxy-oxoobacun, **J26**



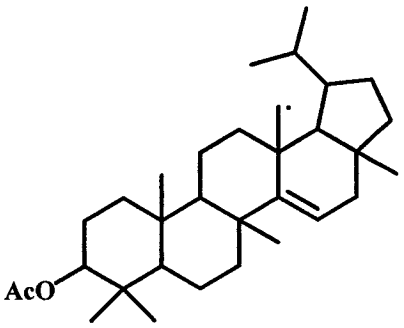
(11α)-1,2,21,23-Tetrahydro-11,23-dihydroxy-21-oxoobacunoic acid, **J27**



Tarolupeol, **J28**



Tarolupenol, **J29**



Tarolupenyl acetate, **J30**

1.2.2. The Biological Activities of *Clausena exacavata*

Clausena excavata has been used as folk medicines for the treatment of several disorders such as used for the ailment of colic, cough, headache, rhinitis, sore, wounds, yaws and detoxification in Asian countries. The crude extract are pure compound which isolated from *C. excavate* were evaluated for their biological activities such as cytotoxicities against lung cancer (A549), breast cancer (MCF-7), nasopharynx (KB), nasopharynx MDR (KB-VIN), hepatitis B virus (HBV), topoisomerase II, anti-HIV-1 and toxicity assay in 1A2 cell line antifungal activities. The biological activities which were isolated from this plant were summarized in Table 2.

Table 2 Biological activities from *Clausena excavata*

Compounds	Parts	Activities	Bibliography
A16	Branches	Topoisomerase II inhibitory effects (N/A)	Takamura *et al.*, 2004
A35	Branches	Topoisomerase II inhibitory effects (50 μM)	Takamura *et al.*, 2004
A39	Branches	Topoisomerase II inhibitory effects (50 μM)	Takamura *et al.*, 2004
A44	Branches	Topoisomerase II inhibitory effects (N/A)	Takamura *et al.*, 2004

Table 2 (Continued)

Compounds	Parts	Activities	Bibliography
A55	Rhizomes	Antimycobacterial (MIC 50 μg/mL)	Kongkathip and Kongkathip, 2009
A59	Rhizomes and roots	Antimycobacterial (MIC 100 μg/mL); antifungal (IC_{50} 13.6 μg/mL against *Candida albicans*)	Kongkathip and Kongkathip, 2009
A60	Rhizomes and roots	Antimycobacterial (MIC 200 μg/mL)); antifungal (IC_{50} 29.3 μg/mL against *Candida albicans*)	Kongkathip and Kongkathip, 2009
A62	Branches, rhizomes and roots	Topoisomerase II inhibitory effects (N/A); antifungal (IC_{50} 2.8 μg/mL against *Candida albicans*); Antimycobacterial (MIC 100 μg/mL)	Takamura *et al.*, 2004
E34	Rhizomes and roots	Cytotoxic (EC_{50} 2.25-19.83 μg/mL against A549, KB and KB-VIN); HBV HBsAg (EC_{50} 1.88 μM against HepA2 cell); Antimycobacterial (MIC 200 μg/mL); Anti-HIV-1 (EC_{50} 5.3 μM and IC_{50} 37.2 μM by syncytium and toxicity assay in 1A2 cell line)	Su *et al.*, 2009; Kongkathip and Kongkathip, 2009

Table 2 (Continued)

Compounds	Parts	Activities	Bibliography
E40	Rhizomes and roots	Cytotoxic (EC_{50} 8.70-17.32 μg/mL against A549, MCF-7, KB and KB-VIN); HBV HBsAg (EC_{50} 6.38 μM against HepA2cell); Antimycobacterial (MIC 100 μg/mL)	Su *et al.*, 2009; Kongkathip and Kongkathip, 2009
E41	Rhizomes	Antimycobacterial (MIC 50 μg/mL)	Kongkathip and Kongkathip, 2009
E43	Roots	Cytotoxic (EC_{50} 1.61-7.96 μg/mL against A549, MCF-7, KB and KB-VIN); HBV HBsAg (N/A)	Su *et al.*, 2009

CHAPTER 2
MATERIAL AND METHODS

2.1 Instruments and Chemicals

Melting points were determined using a Fisher-John melting point apparatus. The optical rotation $[\alpha]_D$ values were determined with a Bellingham Stanley ADP440 or JASCO P-1020 digital polarimeter. UV spectra were measured with Perkin-Elmer UV-Vis or SPECORD S100 (Analytikjena) spectrophotometers. The IR spectra were measured with a Perkin-Elmer FTS FT-IR spectrophotometer. The ^{1}H and ^{13}C NMR spectra were recorded using 400 MHz Bruker FTNMR Ultra Shield and 500 MHz Varian UNITY INOVA spectrometers. Chemical shifts were recorded in parts per million (δ) in $CDCl_3$ or CD_3OD with tetramethylsilane (TMS) as an internal reference. The HRMS was obtained from MicroTOF, Bruker Daltonics or MAT 95 XL spectrometer. Column chromatography was performed by using quick column chromatography (QCC) and column chromatography (CC) were carried out on silica gel 60 H (Merck, 5-40 μm) and silica gel 100 (Merck, 63-200 μm), respectively. Sephadex^{TM} LH-20 was used for isolation proceduce.

2.2 Plant materials

The fruits and stems of *C. excavata* were collected in May 2008 from Satoon Province, southern part of Thailand. Botanical identification was achieved through comparison with a voucher specimen number QBG 6277 in herbarium collection of Queen Sirikit Garden, Mae Rim District, Chiang Mai Province, Thailand.

2.3 Extraction and Isolation

2.3.1 Extraction and isolation of compounds from the fruits of *C. excavata*

The fruits of *C. excavata* were extracted with hexane and dichloromethane (CH_2Cl_2), respectively, over a period of 3 days each at room temperature. Removal the solvent under reduced pressure provided hexane extract and CH_2Cl_2 extract. The hexane and CH_2Cl_2 extracts were combined (987.7 mg) and chromatographed by CC over silica gel eluted with a gradient of EtOAc-hexane (20%

EtOAc-hexane to 100% MeOH) to give twenty-two fractions (A-V). Fraction I (194.2 mg) was separated by sephadex LH-20 with 60% CH_2Cl_2-MeOH to provide five subfractions (I1-I5). Subfraction I3 (85.0 mg) was purified by CC using 8% $CHCl_3$-hexane to afford compound **CE6** (8.2 mg). Fraction T (384.8 mg) was also separated by sephadex LH-20 eluted with 60% CH_2Cl_2-MeOH to obtain four subfractions (T1-T4). Compounds **CE2** (1.5 mg), **CE19** (5.7 mg), and **CE1** (4.2 mg) were derived from subfraction T1 (173.4 mg) by CC with 3% acetone-CH_2Cl_2. The summary of isolations of compounds from *C. exvacata* fruits was showed in Figure 2.

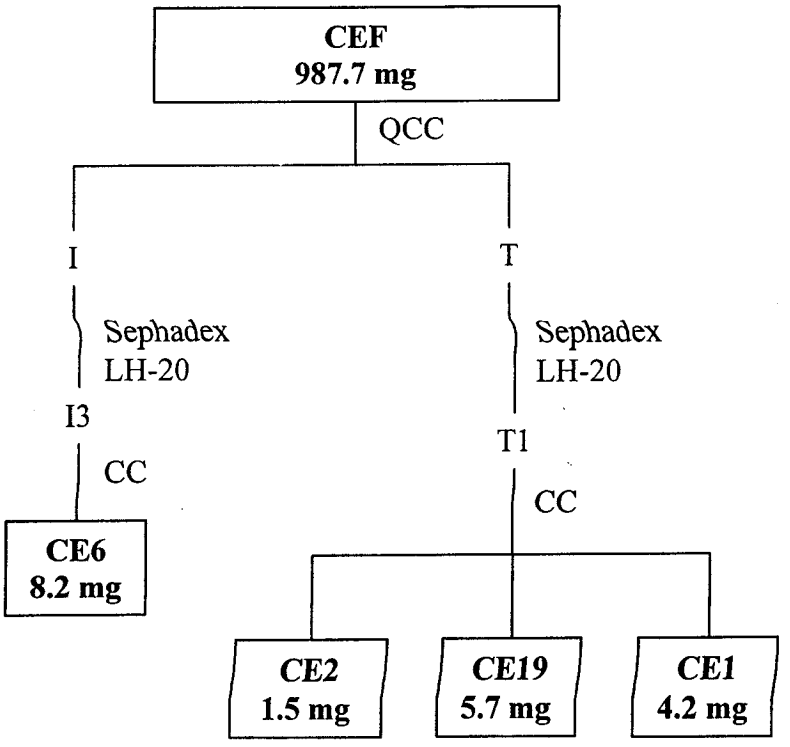


Figure 2 Isolation of compounds **CE1-2, CE6** and **CE19** from hexane-CH_2Cl_2 extract of fruits of *C. excavata*

Compound CE1: $C_{19}H_{24}O_7$, colorless viscous oil; $[\alpha]_D^{29}$ -223.4° (*c* 0.04, $CHCl_3$). UV λ_{max}^{MeOH} nm (log ε): 207 (2.26), 230 (4.14), 258 (2.27), 258 (2.30), 318 (2.47). IR (neat) ν_{max}: 3408, 2971, 2932, 1718, 1612 cm^{-1}. For ^1H NMR ($CDCl_3$, 500 MHz), ^{13}C

NMR ($CDCl_3$, 125 MHz) and DEPT spectra see Table 3. HREIMS *m/z* 346.1422 [M-H_2O]$^+$ (calcd *m/z* 346.1416).

Compound CE2: $C_{10}H_8O_4$, white solid; ^1H NMR ($CDCl_3$, 400 MHz) spectra see Table 4.

Compound CE6: $C_{14}H_{12}O_3$, colorless viscous oil; ^1H NMR ($CDCl_3$, 400 MHz) spectra see Table 5.

Compound CE19: $C_{10}H_{16}O_3$, yellow viscous oil; ^1H NMR ($CDCl_3$, 400 MHz), ^{13}C NMR ($CDCl_3$, 100 MHz) and DEPT spectra see Table 6.

2.3.2 Extraction and isolation of compounds from the stems of *C. excavata*

The stems of *C. excavata* were extracted with ethyl acetate (EtOAc) over a period of 3 days each at room temperature. Removal the solvent under reduced pressure provided EtOAc extract (70.50 g). This extracted was chromatographed by QCC over silica gel and eluted with gradient of hexane-acetone (100% hexane to 100% acetone) to afford twenty-six fractions (A-Z). Fraction I (297.3 mg) was performed by QCC with 27% CH_2Cl_2-hexane yields twelve subfractions (I1-I12). Subfraction I4 (27.0 mg) was recrystallized with hexane to give compound **CE7** (4.4 mg). Fraction J (230.0 mg) was purified by CC with 15% acetone-hexane to give six subfractions (J1-J6). Subfraction J2 (16.0 mg) was further purified by CC with 50% $CHCl_3$-hexane to give compound **CE4** (2.0 mg). Fraction K and L (1.15 mg) were combined and subjected to sephadex LH-20 with 60% CH_2Cl_2-MeOH to give five subfractions (KL1-KL4). Subfraction KL4 was fractionated by repeated QCC with 25% CH_2Cl_2-hexane and gave six subfraction (KL4.1-KL4.6). Subfraction KL4.3 (80.7 mg) was purified by CC with 60% CH_2Cl_2-hexane to give compound **CES8** (7.3 mg) whereas compound **CE11** (2.6 mg) derived from subfraction KL4.5 (55.4 mg) by repeated CC using 80% CH_2Cl_2-hexane afforded as eluent. Subfraction KL4.6 (130.0 mg) was further purified by CC with 40% CH_2Cl_2-hexane to give compound **CE9** (5.0 mg), along with three subfractions (KL4.6.1-KL4.6.3). Compound **CE10** (17.6 mg) was obtained from subfraction KL4.6.3 by repeated CC with 70% CH_2Cl_2-hexane.

Fraction N (387.4 mg) was subjected to QCC with 45% CH_2Cl_2-hexane to afford nine subfractions (N1-N8). Subfraction N8 (75.0 mg) was recrystallized with CH_2Cl_2 gave two subfractions (N4.1-N4.2). Subfraction N8.1 (21.5 mg) was further purified by CC with 45% CH_2Cl_2-hexane to give compound **CE3** (4.3 mg). Fraction P and Q (842.0 mg) were combined and subjected to QCC with 75% CH_2Cl_2-hexane as eluent to efford eight subfractions (PQ1-PQ8). Subfraction PQ2 (103.9 mg) was purified by CC with 80% CH_2Cl_2-hexane as eluent to give compounds **CE12** (6.0 mg) and **CE13** (51.0 mg). Subfraction PQ5 (65.8 mg) was recrystallized from CH_2Cl_2 obtained compound **CE14** (8.0 mg). The mother liquor of subfraction PQ5 (55.0 mg) was subjected to CC with 23% acetone-hexane to yield six subfractions (PQ5.1-PQ5.6). Subfraction PQ5.2 (10.0 mg) was recrystallized with CH_2Cl_2 to give compound **CE5** (3.0 mg). Compound **CE15** (12.0 mg) was isolated from subfraction PQ8 (73.0 mg) by repeated CC with 23% EtOAc-CH_2Cl_2, while compound **CE16** (10.0 mg) was obtained from subfraction PQ13 (40.4 mg) by CC with 18% EtOAc-CH_2Cl_2. Fraction S (445.0 mg) was subjected to QCC with 10% EtOAc-CH_2Cl_2 to afford four subfractions (S1-S4). Subfraction S2 (20.0 mg) was further purified by CC with 30% acetone-hexane to give compound **CE17** (2.4 mg). Fraction U (561.0 mg) was subjected to sephadex-LH20 with 60% CH_2Cl_2-MeOH and obtained three subfractions (U1-U3). Subfraction U3 (145.1 mg) was recrystallized with 50% acetone-CH_2Cl_2 to give compound **CE18** (62.0 mg). The summary of isolation of compounds from *C. exvacata* was showed in scheme 2 and 3.

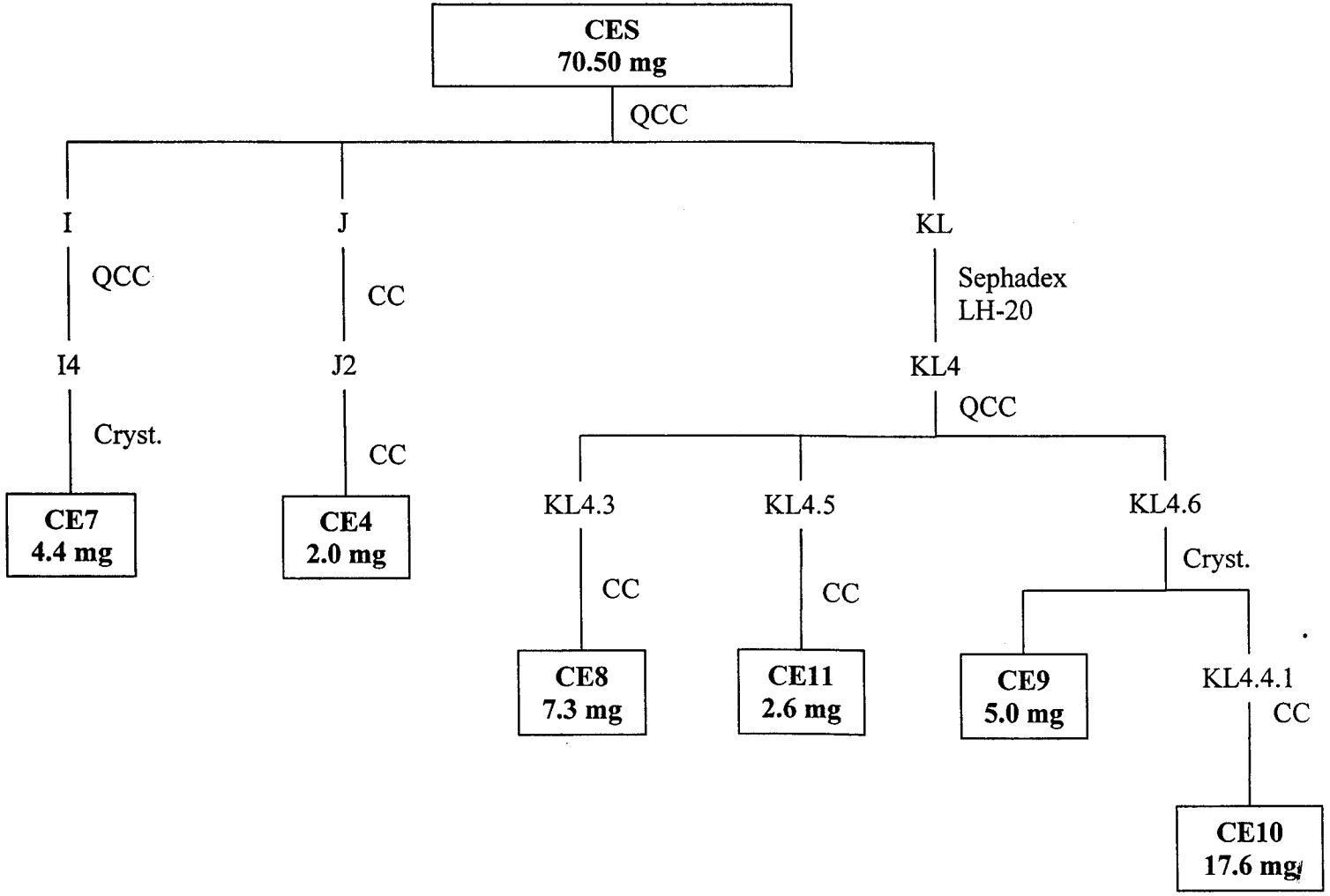


Figure 3 Isolation of compounds **CE4** and **CE7-11** from EtOAc extract of stems of *C. excavata*

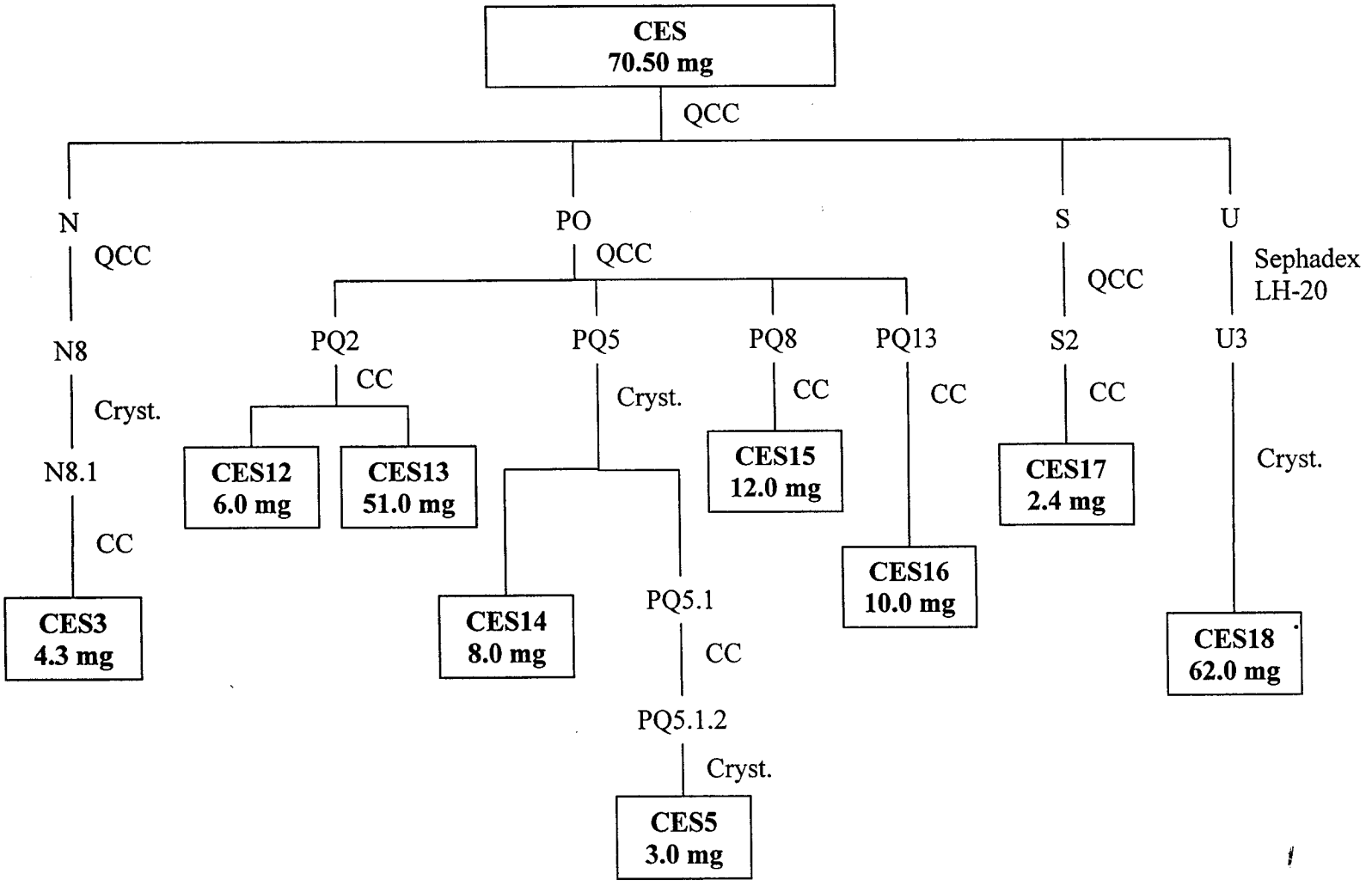


Figure 4 Isolation of compounds **CE3**, **CE5** and **CE12-18** from EtOAc extract of stems of *C. excavata*

Compound CE3: $C_{19}H_{22}O_3$, yellow viscous; ^1H NMR ($CDCl_3$, 400 MHz) spectra see Table 7.

Compound CE4: $C_{14}H_{12}O_3$, light yellow viscous; ^1H NMR ($CDCl_3$, 400 MHz) spectra see Table 8.

Compound CE5: $C_{19}H_{20}O_4$, white solid; ^1H NMR ($CDCl_3$, 400 MHz), ^{13}C NMR ($CDCl_3$, 100 MHz) and DEPT spectra see Table 9.

Compound CE7: $C_{15}H_{13}NO_3$, white solid; ^1H NMR ($CDCl_3$, 400 MHz), ^{13}C NMR ($CDCl_3$, 100 MHz) and DEPT spectra see Table 10.

Compound CE8: $C_{14}H_{11}NO_2$, white solid; ^1H NMR ($CDCl_3$, 400 MHz), ^{13}C NMR ($CDCl_3$, 100 MHz) and DEPT spectra see Table 11.

Compound CE9: $C_{14}H_{11}NO_3$, yellow solid; ^1H NMR ($CDCl_3$, 400 MHz), ^{13}C NMR ($CDCl_3$, 100 MHz) and DEPT spectra see Table 12.

Compound CE10: $C_{14}H_{11}NO_2$, light yellow solid; ^1H NMR ($CDCl_3$, 400 MHz), ^{13}C NMR ($CDCl_3$, 100 MHz) and DEPT spectra see Table 13.

Compound CE11: $C_{13}H_9NO$, white solid; ^1H NMR ($CDCl_3$, 400 MHz), ^{13}C NMR ($CDCl_3$, 100 MHz) and DEPT spectra see Table 14.

Compound CE12: $C_{14}H_{11}NO_3$, colorless solid; ^1H NMR ($CDCl_3$, 400 MHz) spectra see Table 15.

Compound CE13: $C_{14}H_{11}NO_2$, light yellow solid; ^1H NMR ($CDCl_3$, 400 MHz), ^{13}C NMR ($CDCl_3$, 100 MHz) and DEPT spectra see Table 16.

Compound CE14: $C_{14}H_{11}NO_4$, light brown solid;, UV λ_{max} (log ε) (MeOH): 203 (1.59), 223 (1.47), 243 (1.46), 256 (1.46), 278 (1.59), 297 (1.54) and 356 (1.25) nm; IR (neat): 3372, 1631, 1455, 1384, 1157, 1050. For ^1H NMR ($CDCl_3$, 400 MHz), ^{13}C NMR ($CDCl_3$, 100 MHz) and DEPT spectra see Table 19. HREIMS *m/z*: 257.0683 ($[M]^+$, calc. $C_{14}H_{11}NO_4$, 257.0688).

Compound CE15: $C_{14}H_{11}NO_3$, yellow solid; ^1H NMR ($CDCl_3$, 400 MHz) see Table 18.

Compound CE16: $C_{13}H_9NO_2$, light brown solid; ^1H NMR ($CDCl_3$, 400 MHz) see Table 19.

Compound CE17: $C_{14}H_{11}NO_4$, yellow solid; ^1H NMR ($CDCl_3$, 400 MHz) see Table 20.

Compound CE18: $C_{13}H_9NO_{34}$, light brown solid; ^1H NMR ($CDCl_3$, 400 MHz), ^{13}C NMR ($CDCl_3$, 100 MHz) and DEPT spectra see Table 21.

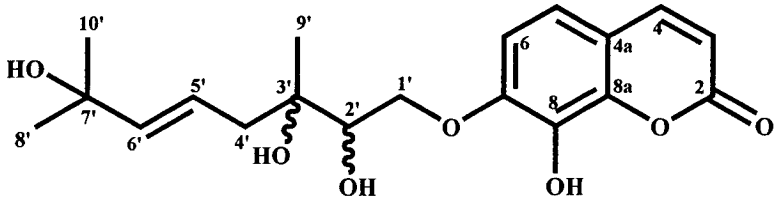
CHEPTER 3

RESULTS AND DISCUSSION

3.1. Structural elucidation of compounds isolated from the fruits of *C. exvacata*

The hexane-CH_2Cl_2 extract of the fruits of *C. exvacata* was subjected to column chromatography to give one novel compound, **CE1** (4.2 mg) along with three known compounds, **CE2** (1.5 mg), **CE6** (8.2 mg) and **CE19** (5.7 mg). Their structures were determined using spectroscopic data.

3.1.1. Compound CE1 (Clausenaexcavin)



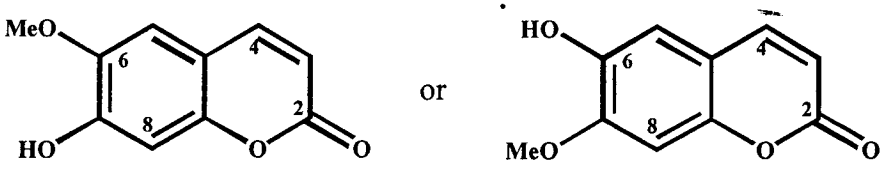
Compound **CE1** was isolated as a colorless solid with the molecular ion peak at *m/z* 346.1422 [M-H_2O] in the HREIMS (calcd *m/z* 346.1416), corresponding to the molecular formula $C_{19}H_{24}O_7$. The UV spectrum showed maxima absorption bands at 207, 230, 258 and 318 nm indicating conjugated system in the molecule whereas the IR spectrum showed the hydroxyl and carbonyl functionalities at 3408 and 1718 cm^{-1} respectively. The ^{13}C NMR and DEPT spectral data (Table 3) revealed 19 carbons, including 3 methyls (δ 22.8, 29.8, and 29.9), 2 methylenes (δ 41.4 and 65.1), 7 methines (δ 77.9, 113.3, 113.5, 119.5, 120.3, 143.5 and 143.8), and 7 quaternary carbons (δ 70.7, 72.2, 113.4, 131.5, 143.8, 146.0 and 160.7). The ^1H NMR signals at δ 7.60 (1H, *d*, *J* = 9.5, H-4), 6.94 (1H, *d*, *J* = 8.5, H-5), 6.81 (1H, *d*, *J* = 8.5, H-6) and 6.25 (1H, *d*, *J* = 9.5, H-3) indicated the present of 7, 8–dioxygenated coumarin moiety. In addition the existence of 2,3,7-trihydroxy-3,7-dimethyloct-5-enyloxy group was also observed in the ^1H NMR spectrum at δ 5.77 (*d*, *J* = 16.0 Hz, H-6′), 5.73 (m, H-5′), 4.99 (*dd*, *J* = 3.0, 11.5 Hz, H-1′a), 4.09 (*dd*, *J* = 9.0, 11.5 Hz, H-1′b), 3.98 (*dd*, *J* = 3.0, 9.0 Hz, H-2′), 2.44 (*dd*, *J* = 6.0, 14.0 Hz, H-4′a), 2.29 (*dd*, *J* = 7.5, 14.0 Hz, H-4′b), 1.34 (*s*, H-9′), 1.30 (*s*, H-8′) and 1.29 (*s*, H-10′) . The COSY and HMBC correlations (Figure 3) were also supported this moiety. The HMBC correlations

between H-1′, H-5 and H-6 and C-7 (δ 146.4) indicated the side chain moiety was located at C-7 of coumarin framework. The geometry of double bond at C-5′/C-6′ was identified to be *E*-geometry due to the large amount of *J* value of H-6′ (16.0 Hz). Therefore, clausenaexcavin was identified to be **CE1**.

Table 3 ^{1}H-NMR (500 MHz), ^{13}C-NMR (125 MHz), DEPT and HMBC spectral data of **CE1** in $CDCl_3$

Position	δ_C	δ_H (mult., *J* in Hz)	DEPT	HBMC
2	160.7	-	C	-
3	113.5	6.25 (*d*, *J* = 9.5)	CH	2, 4a
4	143.9	7.60 (*d*, *J* = 9.5)	CH	2
4a	113.4	-	C	-
5	119.5	6.93 (*d*, *J* = 8.5)	CH	4, 6, 7
6	113.3	6.80 (*d*, *J* = 8.5)	CH	4a, 8
7	146.4	-	C	-
8	131.8	-	C	-
8a	143.7	-	C	-
1′	65.1	4.09 (*dd*, *J* = 11.5,9.0)	CH_2	7
		4.99 (*dd*, *J* = 11.5,3.0)		
2′	77.9	3.98 (*dd*, *J* = 9, 3.0)	CH	1′, 3′
3′	72.9	-	C	-
4′	41.5	2.29 (*dd*, *J* = 14.0, 7.5)	CH_2	5, 6
		2.44 (*dd*, *J* = 14.0, 6.0)		
5′	140.3	5.73 (*m*)	CH	3, 4
6′	120.3	5.77 (*d*, *J* = 16.0)	CH	7
7′	72.3	-	C	-
8′	29.9	1.30 (*s*)	CH_3	7
9′	22.8	1.34 (*s*)	CH_3	4
10′	29.9	1.29 (*s*)	CH_3	7

3.1.3. Compound CE2 (Scopoletin or isoscopoletin)



Compound **CE2** ($C_{16}H_{18}O_4$) was isolated as pale yellow oil. The ^{13}C NMR and DEPT spectral data (Table 4) revealed 10 carbons, including 1 methyl (δ 56.4), 4 methines (δ 103.2, 107.4, 113.4 and 143.1), and 5 quaternary carbons (δ 111.0, 144.0, 149.0, 150.2 and 161.0). The ^1H NMR spectrum (Table 4) showed typical resonances of lactone ring similar to that of **CE1** at δ 6.27 (1H, *d*, J = 9.6 Hz, H-3) and 7.60 (1H, *d*, J = 9.6 Hz, H-4). Also, the ^1H NMR spectrum showed two *para*-aromatic protons at δ 6.84 (1H, *s*, H-5) and 6.92 (1H, *s*, H-8). In addition the methoxy group and hydroxyl group were also observed at δ 3.95 (3H, *s*, 6-OMe) and 6.14 (1H, *brs*, 7-OH), respectively, in ^1H NMR spectrum. However, the location of both methoxy and hydroxyl groups was not identified due to lack of NOE or NOESY spectra. Therefore, the structure of **CE2** could be proposed into two structures. They are 6-methoxy, 7-hydroxy coumarin (scopoletin) or 6-hydroxy, 7-methoxy coumarin (isoscopoletin) (Kayser and Kolodziej, 1995, and Kong *et al.*, 1996).

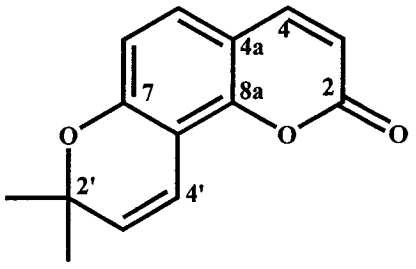
Table 4 ^1H-NMR (400 MHz), ^{13}C-NMR (100 MHz), DEPT and HMBC spectral data of **CE2** in $CDCl_3$

Position	δ_C	δ_H (mult., J in Hz)	DEPT	HMBC
2	161.0	-	C	-
3	113.4	6.27 (*d*, J = 9.6)	CH	2, 4a
4	143.3	7.60 (*d*, J = 9.6)	CH	2, 5, 8a
4a	111.0	-	C	-
5	107.4	6.84 (*s*)	CH	4, 8, 8a
6	144.0	-	C	-
7	149.0	-	C	-
8	103.2	6.92 (*s*)	CH	4a, 6, 8a

Table 4 (Continued)

Position	δ_C	δ_H (mult., *J* in Hz)	DEPT	HMBC
8a	150.2	-	C	-
6-OMe	56.4	3.95 (*s*)	CH_3	6
7-OH	-	6.14 (br*s*)	-	-

3.1.2. Compound CE6 (Seselin)

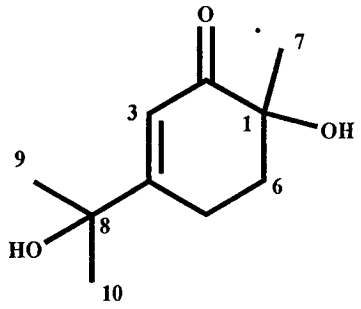


Compound **CE6** ($C_{14}H_{12}O_3$) was isolated as pale yellow oil. The ^1H NMR spectral data of **CE6** (Table 5) was similar to that of **CE1** accept for the appearance of chromene ring at δ 6.88 (*d*, *J* = 10.0 Hz, H-4′), 5.72 (*d*, *J* = 10.0 Hz, H-3′) and 1.47 (*s*, 2′-Me x 2) which located on C-7 and C-8 instead of a geranyl and a hydroxyl groups. Therefore, compound **CE6** was identified as seselin (Ito *et al.*, 2000).

Table 5 ^1H-NMR (400 MHz) of **CE6** in $CDCl_3$

Position	δ_H (mult., *J* in Hz)	Position	δ_H (mult., *J* in Hz)
3	6.22 (*d*, *J* = 9.6)	6	6.71 (*d*, *J* = 8.4)
4	7.59 (*d*, *J* = 9.6)	3′	5.72 (*d*, *J* = 10.0)
5	7.20 (*d*, *J* = 8.4)	4′	6.88 (*d*, *J* = 10.0)
		2′-Me	1.47 (*d*)

3.1.5. Compound CE19 (1,8-Dihydroxy-*p*-menth-3-en-2-one)



Compound **CE19** ($C_{10}H_{16}O_3$) was isolated as yellow viscous oil. The ^{13}C NMR and DEPT spectral data (Table 6) revealed 10 carbons, including 3 methyls (δ 23.9, 28.7 and 28.8), 2 methylenes (δ 24.74 and 35.8), 1 methine (δ 119.4), and 4 quaternary carbons (δ 72.6, 72.7, 170.9 and 203.0) suggested that **CE23** was a monoterpenoid with a cyclohexenone skeketon (Tan, J. J. *et al.*, 2005). The ^1H NMR spectrum (Table 6) showed typical resonances of an alpha proton of α, β-unsaturated lactone ring at 6.19 (1H, *s*, H-3), 4 methylene signals at 2.62 (1H, *m*, H-5a), 2.57 (1H, *m*, H-5b), 2.18 (1H, *m*, H-6a) and 1.98 (1H, *m*, H-6b) and three methyl signals of H-7, H-9 and H-10 at 1.31 (3H, *s*), 1.43 (3H, *s*) and 1.44 (3H, *s*), respectively. The locations of substituent groups (methyl and 2-hydroxylpropyl group) were confirmed HMBC spectra (Table 6). Therefore, 1, 8-dihydroxy-*p*-menth-3-en-2-one was identified to be **CE23** (Tan *et al.*, 2005).

Table 6 ^1H-NMR (400 MHz), ^{13}C-NMR (100 MHz), DEPT and HMBC spectral data of **CE19** in $CDCl_3$

Position	δ_C	δ_H (mult., *J* in Hz)	DEPT	HMBC
1	72.7	-	C	-
2	203.0	-	C	-
3	119.4	6.19 (*s*)	CH	8
4	170.9	-	C	-
5	24.7	2.57 (*m*)	CH_2	4, 6, 8
		2.62 (*m*)		
6	35.8	1.98 (*m*)	CH_2	1, 4
		2.18 (*m*)		

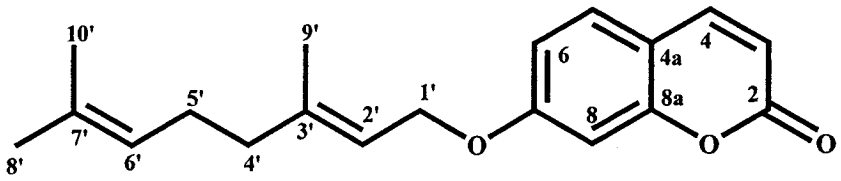
Table 6 (Continued)

Position	δ_C	δ_H (mult., *J* in Hz)	DEPT	HMBC
7	23.9	1.31 (*s*)	CH_3	1, 2, 6
8	72.6	-	C	-
9	28.7	1.43 (*s*)	CH_3	3, 4
10	28.8	1.44 (*s*)	CH_3	8

3.2. Structural elucidation of compounds isolated from the stems of *C. exvacata*

Purification of the EtOAc extract of the stems of *C. exvacata* by chromatographic techniques yielded one new compound, **CE14** (8.0 mg) along with three known compounds fourteen compounds, **CE3** (4.3 mg), **CE4** (2.0 mg), **CE5** (3.0 mg), **CE7** (4.4 mg) **CE8** (7.3 mg), **CE9** (5.0 mg), **CE10** (17.6 mg), **CE11** (2.6 mg), **CE12** (6.0 mg), **CE13** (51.0 mg), **CS15** (12.0 mg), **CE16** (10.0 mg), **CE17** (2.4 mg) and **CE18** (62.0 mg). Their structures were determined using spectroscopic data.

3.2.1. Compound CE3 (Auraptene)

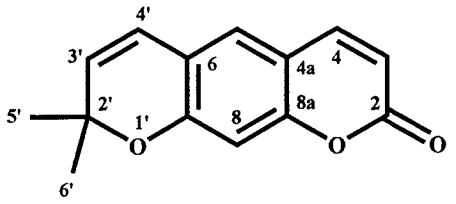


Compound **CE3** ($C_{19}H_{22}O_3$) was isolated as light yellow viscus The ^{1}H NMR spectrum (Table 7) were similar to that of **CE1** except **CE3** showed a set of ABX aromatic proton signals at δ 6.82 (1H, *d*, *J* = 2.4 Hz, H-8), 6.85 (1H, *dd*, *J* = 8.4, 2.4 Hz, H-6) and 7.36 (1H, *d*, *J* = 8.4 Hz, H-5) instead of two meta coupled proton. In addition, the 3,7-dimethyloct-2,6-dienyl group was also observed in the ^{1}H NMR spectrum at δ 5.47 (1H, *m*, H-2′), 5.08 (1H, *m*, H-6′), 4.60 (2H, *d*, *J* = 6.8 Hz, H-1′), 2.10 (4H, *m*, H-4′ and 5′), 1.76 (3H, *s*, H-9′), 1.67 (3H, *s*, H-10′) and 1.59 (3H, *s*, H-8′) which located on C-7 due to the elimination process. Therefore, auraptene was identified to be **CE3** (Tatsuo and Takao, 1953).

Table 7 ^{1}H-NMR (400 MHz) of **CE3** in $CDCl_3$

Position	δ_H (mult., J in Hz)	Position	δ_H (mult., J in Hz)
3	6.25 (*d*, J = 9.6)	4'	2.10 (*m*)
4	7.64 (*d*, J = 9.6)	5'	2.10 (*m*)
5	7.36 (*d*, J = 8.4)	6'	5.08 (br*t*)
6	6.85 (*d*, J = 8.4, 2.4)	8'	1.59 (*s*)
8	6.82 (*d*, J = 2.4)	9'	1.76 (*s*)
1'	4.60 (*d*, J = 6.8)	10'	1.67 (*s*)
2'	5.47 (br*t*)		

3.2.2. Compound CE4 (Xanthyletin)

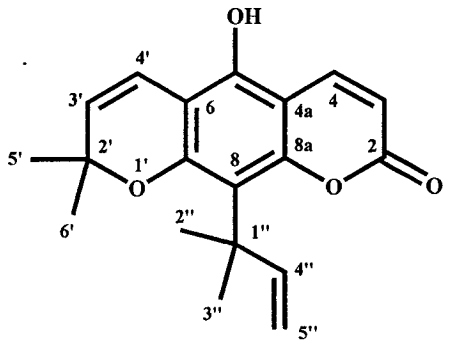


Compound **CE4** ($C_{14}H_{12}O_3$) was isolated as colorless viscous oil. The ^{1}H NMR spectral data of **CE4** (Table 8) were similar to that of **CE6** accept for the location of chromene ring. The chromene ring of **CE4** located at C-6 and C-7 while **CE6** placed on of C-6 and C-7. Therefore, xanthyletin was identified to be **CE4** (Cazal *et al.*, 2009).

Table 8 ^{1}H-NMR (400 MHz) of **CE4** in $CDCl_3$

Position	δ_H (mult., J in Hz)	Position	δ_H (mult., J in Hz)
3	6.22 (*d*, J = 9.6)	3'	5.72 (*d*, J = 10.0)
4	7.59 (*d*, J = 9.6)	4'	6.88 (*d*, J = 10.0)
5	7.20 (*d*, J = 8.4)	2'-Me	1.47 (*d*)
6	6.71 (*d*, J = 8.4)		

3.2.3. Compound CE5 (Nordentatin)

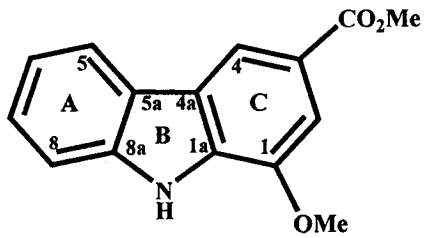


Compound **CE5** ($C_{19}H_{20}O_4$) was isolated as a white solid. The ^{13}C NMR and DEPT spectral data (Table 9) revealed 19 carbons, including 4 methyls (δ 27.8 x 2 and 29.5 x 2), 1 methylene (δ 108.0), 5 methines (δ 110.5, 114.7, 130.1, 139.9 and 150.0), and 9 quaternary carbons (δ 41.0, 77.0, 103.7, 105.8, 116.2, 146.3, 154.0, 156.0 and 160.9). The ^{1}H NMR spectral data of **CE5** (Table 9) were similar to that of **CE4** accept for the appearance of dimethylallyl at δ 6.28 (1H, *dd*, J = 17.2, 10.4 Hz, H-4"), 4.92 (1H, *dd*, J = 17.2, 1.2 Hz, H-5a), 4.86 (1H, *dd*, J = 10.4, 1.2 Hz, H-5b) and 1.64 (6H, *s*, 2" and 3"-Me) which located on C-8. Therefore, nordentatin was identified to be **CE5** (Huang, S. C. et al 1997).

Table 9 ^{1}H-NMR (400 MHz), ^{13}C-NMR (100 MHz), DEPT and HMBC spectral data of **CE5** in $CDCl_3$

Position	δ_C	δ_H (mult., J in Hz)	DEPT	HMBC
2	160.9	-	C	-
3	110.5	6.15 (*d*, J = 9.6)	CH	2, 4a
4	139.9	7.99 (*d*, J = 9.6)	CH	2, 5, 8a
5	146.3	-	C	-
6	105.8	-	C	-
7	156.0	-	C	-
8	116.2	-	C	-
2'	77.0	-	C	-
3'	130.1	5.70 (*d*, J = 10)	CH	5, 5',2'
4'	114.7	6.47(*d*, J = 10)	CH	5, 6, 7, 2'
5' and 6'	27.2	1.44 (*s*)	CH_3x2	3'
1"	41.0	-	C	-
2"and 3"	29.5	1.64 (*s*)	CH_3x2	1", 4", 8
4"	150.0	6.28 (*dd*, J = 17.2, 10.4)	CH	1", 2", 3"
5"	108.0	4.86 (*dd*, J = 10.4, 1.2)	CH_2	1", 4"
		4.92 (*dd*, J = 17.2, 1.2)		

3.2.4. Compound CE7 (Mukonine)



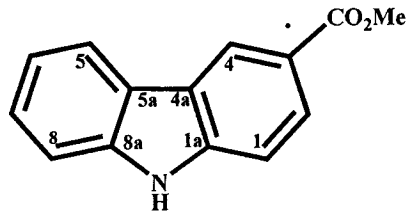
Compound **CE7** ($C_{15}H_{13}NO_3$) was isolated as a white solid. The ^{13}C NMR and DEPT spectral data (Table 10) revealed 15 carbons, including 2 methyls (δ 52.0 and 55.7), 6 methines (δ 106.7, 111.2, 116.2, 120.3, 120.7and 126.3), and 7 quaternary carbons (δ 121.9, 123.6, 123.7, 132.9, 139.5, 145.0 and 167.9). The ^{1}H NMR spectral

data (Table 10 and 22) of **CE7** showed characteristic of C-3 methyl ester carbazole alkaloid which appeared ^{1}H NMR signals of four mutually coupling aromatic protons of ring A at δ 8.12 (1H, *d*, *J* = 8 Hz, H-5), 7.49 (1H, *d*, *J* = 6.8 Hz, H-8), 7.45 (1H, *dd*, *J* = 8.0, 6.8 Hz, H-7) and 7.28 (1H, *dd*, *J* = 8.4, 8.0 Hz, H-6), and methyl ester protons at δ 3.98 (3H, *s*, 3-CO_2Me). In addition, two meta-coupled aromatic protons at δ 8.47 (1H, *d*, *J* = 1.2 Hz, H-4) and 7.59 (1H, *d*, *J* = 1.2 Hz, H-2), methoxyl group at δ (3H, *s*, 1-OMe) and NH proton at δ 8.48 (1H, br*s*) were also observed in the ^{1}H NMR spectrum. Finally, the structure was confirmed by HMBC as summarized in Table 10. Therefore, mukonine was identified to be **CES7** (Liger, F. et al 2007).

Table 10 ^{1}H-NMR (400 MHz), ^{13}C-NMR (100 MHz), DEPT and HMBC spectral data of **CE7** in $CDCl_3$

Position	δ_C	δ_H (mult., *J* in Hz)	DEPT	HMBC
1	145	-	C	-
1a	132.9	-	C	-
2	106.7	7.59 (*d*, *J* = 1.2)	CH	1, 4, 4a, 3-$\underline{C}O_2$Me
3	123.7	-	C	-
4	116.2	8.47 (*d*, *J* = 1.2)	CH	1a, 2, 3, 3-$\underline{C}O_2$Me
4a	121.9	-	C	-
5	120.7	8.12 (*d*, *J* = 8.0)	CH	5a, 7, 8a
6	120.3	7.28 (*dd*, *J* = 8.4, 8.0)	CH	5a
7	126.3	7.45 (*dd*, *J* = 8.0, 6.8)	CH	6, 8, 8a
8	111.2	7.49 (*d*, *J* = 6.8)	CH	5a
8a	139.5	-	C	-
1-O$\underline{Me}$	55.7	4.06 (*s*)	CH_3	1
3-$\underline{C}O_2$Me	167.9	-	C	-
3-$CO_2\underline{Me}$	52.0	3.98 (*s*)	CH_3	3-$\underline{C}O_2$Me
NH	-	8.48 (*s*)	-	-

3.2.5. Compound CE8 (Methyl carbazole-3-carboxylate)



Compound **CE8** ($C_{14}H_{11}NO_2$) was isolated as a white solid. The ^{13}C NMR and DEPT spectral data (Table 11) revealed 14 carbons, including 1 methyl (δ 51.9), 7 methines (δ 110.1, 110.9, 120.3, 120.6, 122.9, 126.5 and 127.4), and 6 quaternary carbons (δ 121.5, 123.0, 123.4, 139.8, 142.3 and 167.9). The ^1H NMR spectral data (Table 11 and 22) of **CE8** was similar to that of **CE7** except **CE8** showed the characteristic of ABX aromatic protons at δ 8.75 (1H, br*s*, H-4), 8.06 (1H, *dd*, J = 8.4, 1.6 Hz, H-2) and 7.36 (1H, *d*, J = 8.4 Hz, H-1) instead of *meta*-coupled aromatic protons. The structure of **CE8** was confirmed by HMBC as shown in Table 11. Therefore, methyl carbazole-3-carboxylate was identified to be **CE8** (Wu *et al.*, 1996).

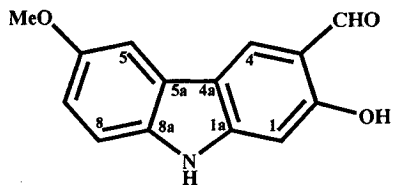
Table 11 ^1H-NMR (400 MHz), ^{13}C-NMR (100 MHz), DEPT and HMBC spectral data of **CES8** in $CDCl_3$

Position	δ_C	δ_H (mult., J in Hz)	DEPT	HMBC
1	110.1	7.36 (*d*, J = 8.4)	CH	3, 4a
1a	142.3	-	C	-
2	127.4	8.06 (*dd*, J = 8.4, 1.6)	CH	1a, 3-CO_2Me, 4
3	121.5	-	C	-
4	122.9	8.75 (br*s*)	CH	1a, 2, 3-CO_2Me, 5a
4a	123.0	-	C	-
5	120.6	8.05 (*d*, J = 7.6)	CH	7, 8a
5a	123.4	-	C	-
6	120.3	7.22 (*m*)	CH	8
7	126.5	7.38 (*m*)	CH	5
8	110.9	7.39 (*d*, J = 7.6)	CH	7, 8a

Table 11 (Continued)

Position	δ_C	δ_H (mult., *J* in Hz)	DEPT	HMBC
8a	139.8	-	C	-
3-$\underline{C}O_2Me$	167.9	-	C	-
3-$CO_2\underline{Me}$	51.9	3.90 (*s*)	CH_3	3-$\underline{C}O_2Me$
NH	-	8.27 (br*s*)	-	-

3.2.6. Compound CE9 (Lansine)



Compound **CE9** ($C_{14}H_{11}NO_3$) was isolated as a yellow solid. The ^{13}C NMR and DEPT spectral data (Table 12) revealed 14 carbons, including 1 methyl (δ 56.0), 6 methines (δ 96.8, 103.3, 111.4, 114.4, 127.4 and 195.1), and 7 quaternary carbons (δ 115.3, 117.8, 123.9, 134.7, 146.1, 154.9 and 161.1). The ^1H NMR spectral data (Table 12 and 22) of **CE9** was similar to that of **CE7** except **CE9** showed the characteristic of ABX aromatic protons at δ 7.48 (1H, *d*, *J* = 2.8 Hz, H-5), 7.29 (1H, *d*, *J* = 8.8 Hz, H-8) and 7.20 (1H, *dd*, *J* = 8.8, 2.8 Hz, H-7) of ring A instead of four mutually coupling aromatic protons. The structure of **CE9** was also confirmed by HMBC as shown in Table 12. Therefore, lansine was identified to be **CE9** (Wu, *et al.*, 1996).

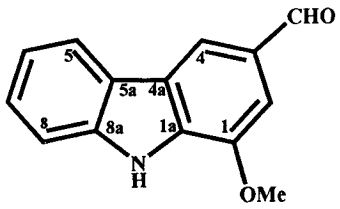
Table 12 ^1H-NMR (400 MHz), ^{13}C-NMR (100 MHz), DEPT and HMBC spectral data of **CE9** in $CDCl_3$

Position	δ_C	δ_H (mult., *J* in Hz)	DEPT	HMBC
1	96.8	6.83 (*s*)	CH	1a, 2, 3, 4a
1a	146.1	-	C	-
2	161.1	-	C	-
3	115.3	-	C	-
4	127.4	8.14 (br*s*)	CH	1a, 2, 3-$\underline{C}HO$, 5a

Table 12 (Continued)

Position	δ_C	δ_H (mult., J in Hz)	DEPT	HMBC
4a	117.8	-	C	-
5	103.3	7.48 (*d*, J = 2.8)	CH	4a, 6, 7, 8a
5a	123.9	-	C	-
6	154.9	-	CH	4a, 6, 7, 8a
7	114.4	7.02 (*dd*, J = 8.8, 2.8)	CH	5, 6, 8a
8	111.4	7.29 (*d*, J = 8.8)	CH	5a, 6, 8a
8a	134.7	-	C	-
2-OH	-	11.43 (*s*)	-	1, 2, 3
3-CHO	195.1	9.92 (*s*)	CH	2, 3, 4
6-OMe	56.0	3.92 (*s*)	CH_3	6
NH	-	8.14 (brs)	-	-

3.2.7. Compound CE10 (Murrayanine)

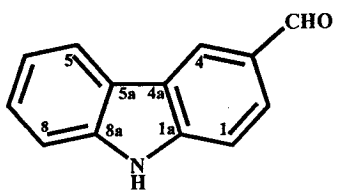


Compound **CE10** ($C_{14}H_{11}NO_2$) was isolated as a light yellow solid. The ^{13}C NMR and DEPT spectral data (Table 13) revealed 14 carbons, including 1 methyl (δ 55.8), 7 methines (δ 103.5, 111.5, 120.4, 120.7x2, 126.6, and 191.9), and 6 quaternary carbons (δ 123.6x2, 130.1, 134.0, 139.4 and 146.1). The ^1H NMR spectral data (Table 13 and 22) of **CE10** was very similar to that of **CE7** except for the appearance of a formyl group at δ 10.05 (1H, *s*, 3-CHO) instead of methyl ester. The structure of **CE10** was also confirmed by HMBC as shown in Table 13. Thus, murrayanine was characterized to be **CE10** (Sunthitikawinsakul, *et al.*, 2002).

Table 13 ^{1}H-NMR (400 MHz), ^{13}C-NMR (100 MHz), DEPT and HMBC spectral data of **CE10** in $CDCl_3$

Position	δ_C	δ_H (mult., J in Hz)	DEPT	HMBC
1	146.1	-	C	-
1a	134	-	C	-
2	103.5	7.46 (*d*, J = 0.8)	CH	1a, 3-CHO, 4
3	130.1	-	C	-
4	120.4	8.19 (*d*, J = 0.8)	CH	3-CHO, 4a
4a	123.6	-	C	-
5	120.7	8.11 (*d*, J = 8.0)	CH	5a, 7
6	120.7	7.32 (*m*)	CH	5a, 8
7	126.6	7.48 (*m*)	CH	8a
8	111.5	7.52 (*d*, J = 8.0)	CH	5a, 6
8a	139.4	-	C	-
1-OMe	55.8	4.07(*s*)	CH_3	1
3-CHO	191.9	10.05 (*s*)	CH	2, 3 ,4
NH	-	8.64 (br*s*)	-	-

3.2.8. Compound CE11 (3-Formylcarbazole)



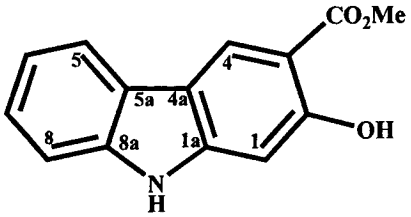
Compound **CE11** ($C_{13}H_9NO$) was isolated as a white solid. The ^{13}C NMR and DEPT spectral data (Table 14) revealed 13 carbons, including 8 methines (δ 110.9, 111.5, 120.7x2, 124.0, 126.9, 127.3 and 191.9), and 5 quaternary carbons (δ 123.2, 123.5, 129.1, 140.2 and 143.3). The ^{1}H NMR spectral data (Table 14 and 23) of **CE11** was very similar to that of **CE8** except for the appearance of a formyl group at δ 10.10 (1H, *s*, 3-CHO) instead of methyl ester. The structure of **CE11** was also confirmed by

HMBC as shown in Table 14. Thus, 3-formylcarbazole was characterized to be **CE11** (Sunthitikawinsakul, *et al.*, 2002).

Table 14 ^{1}H-NMR (400 MHz), ^{13}C-NMR (100 MHz), DEPT and HMBC spectral data of **CE11** in $CDCl_3$

Position	δ_C	δ_H (mult., J in Hz)	DEPT	HMBC
1	111.1	7.49 (*d*, J = 8.8)	CH	4a
1a	143.3	-	C	-
2	127.3	7.97 (*dd*, J = 8.8, 1.6)	CH	1a, 3, 3-CHO, 4
3	129.1	-	C	-
4	124.0	8.60 (*d*, J = 0.8)	CH	3, 3-CHO
4a	123.5	-	C	-
5	120.7	8.13 (*d*, J = 8.4)	CH	7, 8a
6	120.7	7.32 (*m*)	CH	7
7	110.9	7.48 (*m*)	CH	5, 8a
8	126.9	7.51 (*d*, J = 8.4)	CH	5a
8a	140.0	-	C	-
3-CHO	191.9	10.10 (*s*)	CH	4
NH	-	8.55 (br*s*)	-	-

3.2.9. Compound CE12 (Mukonidine)

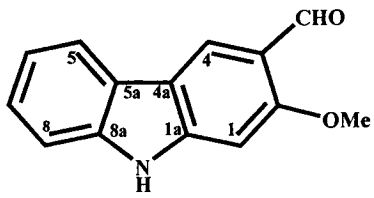


Compound **CE12** ($C_{14}H_{11}NO_3$) was isolated as a colorless solid. The ^{1}H NMR spectral data (Table 15 and 23) was very similar to that of **CE9** except that compound **CE12** showed four mutually coupling aromatic protons instead of ABX aromatic protons of ring A and methyl ester at δ 3.92 (3H, *s*, 3-CO_2Me). Thus, mukonidine was characterized to be **CE12** (Wu, *et al.*, 1999).

Table 15 ^{1}H-NMR (400 MHz) of **CE12** in $CDCl_3$

Position	δ_H (mult., J in Hz)	Position	δ_H (mult., J in Hz)
1	7.08 (*s*)	7	7.24 (*d*, J = 8.0, 7.2)
4	7.51 (*s*)	8	7.40 (*d*, J = 8.0)
5	7.93 (*d*, J = 8.0)	3-CO_2Me	3.92 (*s*)
6	7.07 (*d*, J = 8.0, 7.2)		

3.2.10. Compound CE13 (*O*-Methylmukonal)



Compound **CE13** ($C_{14}H_{11}NO_2$) was isolated as a light yellow solid. The ^{13}C NMR and DEPT spectral data (Table 16) revealed 14 carbons, including 1 methyl (δ 55.8), 7 methines (δ 92.4, 110.6, 120.2, 120.8, 121.8, 125.7, and 189.5), and 6 quaternary carbons (δ 117.4, 119.1 123.7, 139.9, 139.9, 144.9 and 161.6). The ^{1}H NMR spectral data (Table 16 and 23) was very similar to that of **CE12** except for the appearance of a formyl group at δ 10.49 (1H, *s*, 3-CHO) and methoxyl group at δ 3.99 (3H, *s*, 2-OMe). The structure of **CE13** was also confirmed by HMBC as shown in Table 16. Therefore, *O*-methylmukonal was characterized to be **CE13** (Kongkathip and Kongkathip, 2009).

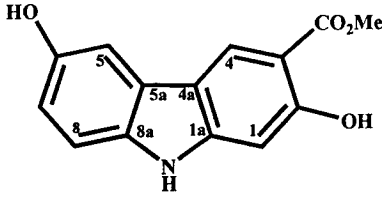
Table 16 ^{1}H-NMR (400 MHz), ^{13}C-NMR (100 MHz), DEPT and HMBC spectral data of **CE13** in $CDCl_3$

Position	δ_C	δ_H (mult., J in Hz)	DEPT	HMBC
1	92.4	6.87(*s*)	CH	1a, 2, 3
1a	144.9	-	C	-
2	161.6	-	C	-
3	119.1	-	C	-

Table 16 (Continued)

Position	δ_C	δ_H (mult., J in Hz)	DEPT	HMBC
4	121.8	8.56 (*s*)	CH	3-CHO
4a	117.4	-	C	-
5	120.2	8.00 (*d*, J = 8.0)	CH	4a, 7, 8, 8a
6	110.6	7.39 (*m*)	CH	5a
7	125.9	7.40 (*m*)	CH	-
8	120.8	7.26 (*d*, J = 7.6)	CH	5a, 7, 8a
8a	139.9	-	C	-
2-OMe	55.8	3.99 (*s*)	CH_3	2
3-CHO	189.5	10.49 (*s*)	CH	3
NH	-	8.29 (br*s*)	-	-

3.2.11. Compound CE14 (Sansoakamine)



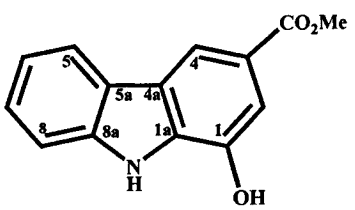
Compound **CE14** ($C_{14}H_{11}NO_4$) was isolated as a light brown solid with the molecular ion peak at *m/z* 257.0683 [M] in the HREIMS (calcd *m/z* 257.0688), corresponding to the molecular formula $C_{19}H_{24}O_7$. The UV spectrum showed maxima absorption bands at 203, 223, 243, 256, 278, 297 and 356 nm indicating conjugated system in the molecule whereas the IR spectrum showed the hydroxyl and/or NH and carbonyl functionalities at 3372 and 1631 cm^{-1} respectively. The ^{13}C NMR and DEPT spectral data (Table 17) revealed 14 carbons, including 1 methyl (δ 51.6), 5 methines (δ 96.5, 105.3, 111.3, 114.4and 122.5), and 8 quaternary carbons (δ 104.8, 116.9, 124.2, 134.9, 146.3, 151.8, 160.4 and 171.3). The ^1H NMR spectral data (Table 17 and 23) was very similar to that of **CE9** except for the appearance of a methyl ester group at δ 3.98 (3H, *s*, 3-CO_2Me) and two hydroxyl groups at δ 11.03 (1H, *s*, 2-OH)

and δ 10.26 (1H, *s*, 6-OH). The structure of **CE14** was also confirmed by HMBC as shown in Table 17. Therefore, sansoakamine was characterized to be **CE14**.

Table 17 ^{1}H-NMR (400 MHz), ^{13}C-NMR (100 MHz), DEPT and HMBC spectral data of **CE14** in Acetone-d_6

Position	δ_C	δ_H (mult., J in Hz)	DEPT	HMBC
1	96.5	6.85(*s*)	CH	2, 3
1a	146.3	-	C	-
2	160.4	-	C	-
3	116.9	-	C	-
4	122.5	8.52 (*s*)	CH	1a, 3, 3-CHO, 5a
4a	104.8	-	C	-
5	105.3	7.50 (*d*, J = 2.4)	CH	6, 8a
6	151.8	-	C	-
7	114.4	6.92 (*dd*, J = 8.8, 2.4)	CH	6, 8a
8	111.3	7.28 (*d*, J = 8.8)	CH	5a, 7, 8a
8a	134.9	-	C	-
2-OH	-	11.03 (*s*)	-	1, 2
3-CO_2Me	51.6	3.98 (*s*)	CH_3	3-$\underline{C}O_2$Me
3-$\underline{C}O_2$Me	171.3	-	C	-
6-OH	-	10.26 (*s*)	-	-
NH	-	8.06 (br*s*)	-	-

3.2.12. Compound CE15 (Clauszoline-I)



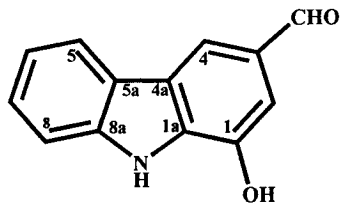
Compound **CE15** ($C_{14}H_{11}NO_3$) was isolated as a yellow solid. The ^{1}H NMR spectral data (Table 18 and 24) was very similar to that of **CE7** except for the

disappearance of a methoxyl group at δ 4.06 (3H, *s*, 1-OMe). Therefore, clauszoline-I was characterized to be **CE15** (Liger *et al.*, 2007).

Table 18 ^{1}H-NMR (400 MHz) of **CES15** in Acetone-d_6

Position	δ_H (mult., *J* in Hz)	Position	δ_H (mult., *J* in Hz)
2	7.61 (*d*, *J* = 2.4)	6	7.46 (*m*)
4	8.44 (br*s*)	7	7.50 (*m*)
5	8.09 (*d*, *J*=8.0)	8	7.29 (*d*, *J*=8.4)
		3-CO_2Me	3.97 (*s*)

3.2.13. Compound CE16 (*O*-Demethylmurrayanine)

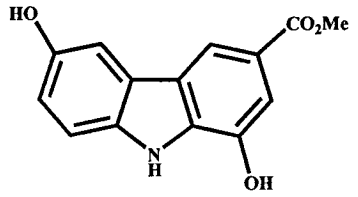


Compound **CE16** ($C_{13}H_9NO_2$) was isolated as a light brown solid. The ^{1}H-NMR spectral data (Table 19 and 24) was very similar to that of **CE15** except compound **CE16** showed a signal of formyl group at δ 10.02 (1H, *s*, 3-CHO). Thus, *O*-demethylmurrayanine was characterized to be **CE16** (Ito *et al.*, 2000).

Table 19 ^{1}H-NMR (400 MHz) of **CE16** in Acetone-d_6

Position	δ_H (mult., *J* in Hz)	Position	δ_H (mult., *J* in Hz)
2	7.43 (*d*, *J* = 1.2)	6	7.27 (*m*)
4	8.27 (*d*, *J* = 1.2)	7	7.47 (*m*)
5	8.21 (*d*, *J* = 7.6)	8	7.65 (*d*, *J* = 8.0)
		3-CHO	10.02 (*s*)

3.2.14. Compound CE17 (Methyl 1, 6-dihydroxy-9*H*-carbazole-3-carboxylate)

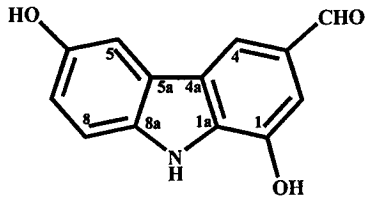


Compound **CE17** ($C_{14}H_{11}NO_4$) was isolated as a yellow solid. The ^{1}H NMR spectral data (Table 20 and 24) was very similar to that of **CE15** except compound **CE17** showed the characteristic of ABX aromatic protons at δ 7.57 (*d*, *J* = 2.4 Hz, H-5), 7.44 (*d*, *J* = 8.8 Hz, H-8) and 7.02 (*dd*, *J* = 8.8, 2.4 Hz, H-7). Thus, methyl 1, 6-dihydroxy-9*H*-carbazole-3-carboxylate was characterized to be **CE17** (Borger and Knolker, 2008).

Table 20 ^{1}H-NMR (400 MHz) of **CE17** in Acetone-d_6

Position	δ_H (mult., *J* in Hz)	Position	δ_H (mult., *J* in Hz)
2	7.53 (*d*, *J* = 1.2)	8	7.44 (*d*, *J* = 8.8)
4	8.28 (*d*, *J* = 1.2)	1-OH	8.99 (s)
5	7.57 (*d*, *J* = 2.4)	3-CO_2Me	3.87 (*s*)
7	7.02 (*dd*, *J* = 8.8, 2.4)	6-OH	10.63 (*s*)

3.2.15. Compound CE18 (Clausine-Z)



Compound **CE18** ($C_{13}H_9NO_3$) was isolated as a light brown solid. The ^{13}C NMR and DEPT spectral data (Table 21) revealed 13 carbons, including 6 methines (δ 105.1, 107.0, 112.3, 115.8, 118.7 and 191.2), and 7 quaternary carbons (δ 123.9, 124.4, 129.6, 134.6, 134.8, 143.6 and 151.7). The ^{1}H NMR spectral data (Table 21

and 24) was very similar to that of **CE17** except for the appearance of a formyl group at δ 9.96 (1H, *s*, 3-CHO) instead of the methyl ester. The structure of **CE18** was also confirmed by HMBC as shown in Table 21. Therefore, clausine-Z was characterized to be **CE18** (Potterat *et al.*, 2005).

Table 21 ^{1}H-NMR (400 MHz), ^{13}C-NMR (100 MHz), DEPT and HMBC spectral data of **CE18** in Acetone-d_6

Position	δ_C	δ_H (mult., J in Hz)	DEPT	HMBC
1	143.6	-	C	-
1a	134.8	-	C	-
2	107.0	7.38 (*d*, J = 1.2)	CH	1, 1a, 3-CHO, 4
3	129.6	-	C	-
4	118.7	8.15 (*d*, J = 1.2)	CH	1a, 2, 3-CHO, 5a
4a	123.9	-	C	-
5	105.1	7.60 (*d*, J = 2.0)	CH	6, 7, 8a
6	151.7	-	C	-
7	115.8	7.04 (*d*, J = 8.8, 2.0)	CH	5
8	112.3	7.47 (*d*, J = 8.8)	CH	5a, 6, 8a
8a	134.6	-	C	-
1-OH	-	10.60 (br*s*)	-	1a, 4a
3-CHO	191.2	9.96 (*s*)	CH	2, 4
6-OH	-	8.44 (br*s*)	-	-
NH	-	8.44 (*brs*)	-	-

Table 22 ^{1}H-NMR spectral data for compound **CE7-CE10** (δ, mult., J in Hz)

Position	**CE7**	**CE8**	**CE9**	**CE10**
1	-	7.36 (*d*, J = 8.4)	6.83 (*s*)	-
2	7.59 (*d*, J = 1.2)	8.06 (*dd*, J = 8.4, 1.6)	-	7.46 (*d*, J = 0.8)
4	8.47 (*d*, J = 1.2)	8.75 (br*s*)	8.14 (br*s*)	8.19 (*d*, J = 0.8)
5	8.12 (*d*, J = 8.0)	8.05 (*d*, J = 7.6)	7.48 (*d*, J = 2.8)	8.11 (*d*, J = 8.0)
6	7.28 (*dd*, J = 8.4, 8.0)	7.22 (*m*)	-	7.32 (*m*)
7	7.45 (*dd*, J = 8.0, 6.8)	7.38 (*m*)	7.02 (*dd*, J = 8.8, 2.8)	7.48 (*m*)
8	7.49 (*d*, J = 6.8)	7.39 (*d*, J = 7.6)	7.29 (*d*, J = 8.8)	7.52 (*d*, J = 8.0)
1-OMe	4.06 (*s*)	-	-	4.07(*s*)
2-OH	-	-	11.43 (*s*)	-
3-CHO	-	-	9.92 (*s*)	10.05 (*s*)
3-CO_2Me	3.98 (*s*)	3.90 (*s*)	-	-
6-OMe	-	-	3.92 (*s*)	-
NH	8.48 (*s*)	8.27 (br*s*)	8.14 (br*s*)	8.64 (br*s*)

Table 23 ^{1}H-NMR spectral data for compound **CE11-CE14** (δ, mult., J in Hz)

Position	CE11	CE12	CE13	CE14
1	7.49 (*d*, J = 8.8)	7.08 (*s*)	6.87(*s*)	6.85(*s*)
2	7.97 (*dd*, J = 8.8, 1.6)	-	-	-
4	8.60 (*d*, J = 0.8)	7.51 (*s*)	8.56 (*s*)	8.52 (*s*)
5	8.13 (*d*, J = 8.4)	7.93 (*d*, J = 8.0)	8.00 (*d*, J = 8.0)	7.50 (*d*, J = 2.4)
6	7.32 (*m*)	7.07 (*d*, J = 8.0, 7.2)	7.39 (*m*)	-
7	7.48 (*m*)	7.24 (*d*, J = 8.0, 7.2)	7.40 (*m*)	6.92 (*dd*, J = 8.8, 2.4)
8	7.51 (*d*, J = 8.4)	7.40 (*d*, J = 8.0)	7.26 (*d*, J = 7.6)	7.28 (*d*, J = 8.8)
2-OH	-	-	-	11.03 (*s*)
2-OMe	-	-	3.99 (*s*)	-
3-CHO	10.10 (*s*)	-	10.49 (*s*)	-
3-CO_2Me	-	3.92 (*s*)	-	3.98 (*s*)
6-OH	-	-	-	10.26 (*s*)
NH	8.55 (br*s*)	-	8.29 (br*s*)	8.06 (br*s*)

Table 24 ^{1}H-NMR spectral data for compound **CE15-CE18** (δ, mult., J in Hz)

Position	**CE15**	**CE16**	**CE17**	**CE18**
2	7.61 (*d*, *J* = 2.4)	7.43 (*d*, *J* = 1.2)	7.53 (*d*, *J* = 1.2)	7.38 (*d*, *J* = 1.2)
4	8.44 (br*s*)	8.27 (*d*, *J* = 1.2)	8.28 (*d*, *J* = 1.2)	8.15 (*d*, *J* = 1.2)
5	8.09 (*d*, *J*=8.0)	8.21 (*d*, *J* = 7.6)	7.57 (*d*, *J* = 2.4)	7.60 (*d*, *J* = 2.0)
6	7.46 (*m*)	7.27 (*m*)	-	-
7	7.50 (*m*)	7.47 (*m*)	7.02 (*dd*, *J* = 8.8, 2.4)	7.04 (*d*, *J* = 8.8, 2.0)
8	7.29 (*d*, *J*=8.4)	7.65 (*d*, *J* = 8.0)	7.44 (*d*, *J* = 8.8)	7.47 (*d*, *J* = 8.8)
1-OH	-	-	8.99 (s)	10.60 (br*s*)
3-CHO	-	10.02 (*s*)	-	9.96 (*s*)
3-CO_2Me	3.97 (*s*)	-	3.87 (*s*)	-
6-OH	-	-	10.63 (*s*)	8.44 (br*s*)

3.3. Biological activities of compounds isolated from the fruits and stems of *C. exvacata*

Some isolated compounds (**CE5 CE7, CE13-16** and **CE18**) were selected for the evaluation of antimalarial activity against *Plasmodium falciparum* and cytotoxicity against three human cancer cell lines including oral cavity cancer (KB), breast cancer (MCF7) and small cell lung cancer (NCI-H187). The results were summarized in Table 23

Table 23 Antimalarial activity and cytotoxicity of compounds **CE5, CE7, CE13-16,** and **CE18**

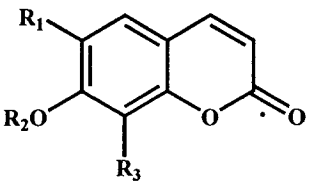
Compounds	IC_{50} (μg/mL)			
	Antimalaria	KB	MCF7	NCI-H187
CE5	0.533	5.95	13.77	7.10
CE7	N/A	N/A	25.26	N/A
CE13	N/A	23.21	25.00	4.11
CE14	N/A	14.29	15.28	2.82
CE15	N/A	17.76	15.43	9.38
CE16	6.74	13.54	7.67	2.14
CE18	N/A	12.50	1.61	1.07
Dihydroartemisinine	0.0041	-	-	-
Ellipiicine	-	0.311	-	0.526
Doxorubicine	-	0.180	1.25	0.077

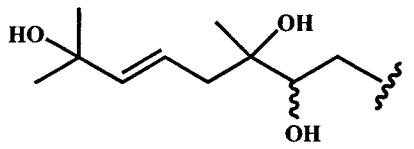
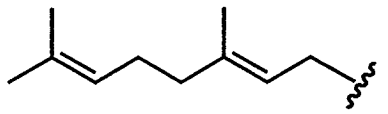
Compounds **CE5** and **CE16** exhibited antimalarial activity against *P. falciparum* with the IC_{50} values of 0.533 and 6.74 μg/mL, respectively. The remaining compounds were found to be inactive. All tested compounds were found to be active with cytotoxicity against all three human cancer cell lines excepted compound **CE7** was found to be inactive. Compound **CE18** was the most active against MCF7 and NCI-H187 cancer cell lines with IC_{50} values of 1.61 and 1.07μg/mL, respectively, whereas compound **CE5** was the best activity against KB cancer cell line with IC_{50} value of 5.97μg/mL.

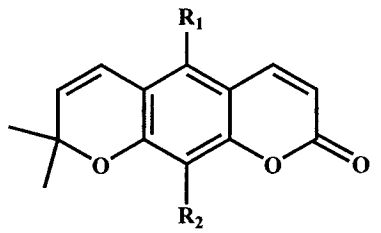
CHAPTER 4
CONCLUSION

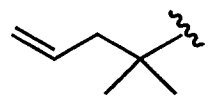
The investigation of constituents from *C. excavata* led to the isolation and identification of nineteen compounds. Four of them (**CE1, CE2, CE6** and **CE19**) were isolated from hexane-CH_2Cl_2 extract of fruits isolated. The remaining fifteen compounds (**CE3-CE5** and **CE7-CE18**) were isolated from the EtOAc extracts of the stems. Compounds CE1 and **CE14** were new coumarin and carbazole alkaloid, respectively. Their structures were elucidated by spectroscopic methods.

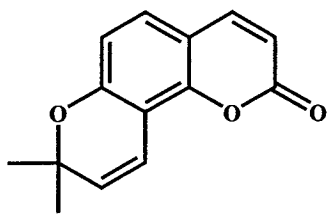
Compounds **CE5 CE7, 13-16** and **18** were evaluated for antimalarial activityagainst *P. falciparum* and three human cancer cellines including MCF7, NCI-H187 and KB cancer cell lines. Compound **CE5** showed the best activity in anti malaria against *P. falciparum* with the IC_{50} value of 0.533 μg/mL whereas compound **CE18** was the most active against MCF7 and NCI-H187 cancer cell lines with IC_{50} values of 1.61 and 1.07μg/mL, respectively. Compound **CE5** was also the best activity against KB cancer cell line with IC_{50} value of 5.97μg/mL.



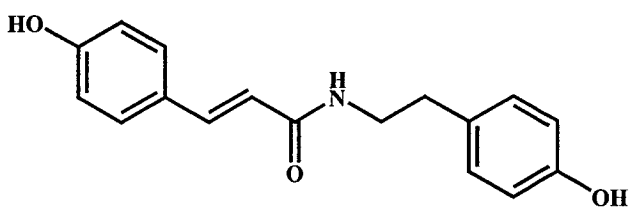
	R_1	R_2	R_3
CE1:	H		OH; Clausenaexcavin
CE2:	OMe	H	H; Scopoletin
CE3:	H		H; Aureptene



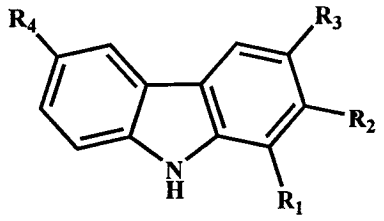
	R_1	R_2	
CE4:	H	H	; Xanthyletin
CE5:	OH		; Nordentatin



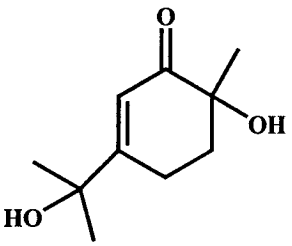
CE6; Seselin



CE19; *N*-(*p*-*trans*-coumaroyl)benzaldehyde



	R_1	R_2	R_3	R_4	
CE7:	**OMe**	**H**	**CO_2Me**	**H**	**; Mokonine**
CE8:	**H**	**H**	**CO_2Me**	**H**	**; Methylcarbazole-3-carboxylate**
CE9:	**OMe**	**H**	**CHO**	**H**	**; Lansine**
CE10:	**H**	**H**	**CHO**	**H**	**; Murrayanine**
CE11:	**H**	**OH**	**CHO**	**OMe**	**; 3-Formylcarbazole**
CE12:	**H**	**OH**	**CO_2Me**	**H**	**; Mokonidine**
CE13:	**H**	**OMe**	**CHO**	**H**	**; *O*-Methylmukonal**
CE14:	**H**	**OH**	**CO_2Me**	**OH**	**; Sansoakamine**
CE15:	**OH**	**H**	**CO_2Me**	**H**	**; Clauszoline-I**
CE16:	**OH**	**H**	**CHO**	**H**	**; *O*-Demehtylmurrayanine**
CE17:	**OH**	**H**	**CO_2Me**	**OH**	**; Methyl 1,6-dihydroxy-9*H*-carbazole-3-carboxylate**
CE18:	**OH**	**H**	**CHO**	**OH**	**; Clausine-Z**



CE19: 1, 8-Dihydroxy-*p*-menth-3-en-2-one

Figure 5 Compounds isolated from the fruits and stems of *C. excavata*

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