CHAPTER 1

INTRODUCTION

1.1 Introduction

Uvaria is one of the genera of the Annonaceae. About 50 genera and 950 species are found in Asia and islands surrounding the Pacific Ocean . In Africa, about 40 genera and 450 species are found while 38 genera and 740 species are found in America. (Leboeuf *et al*., 1982)

Uvaria purpurea Blume is a climbing plant. Its leaves are linear to lanceolate or linear to elliptics, 11-23 cm long and 6-9.5 cm wide, petiole 3-7 mm long. Inflorescence is only one flower; 9.5-10.5 cm diameter; stink; stems 5 mm long. Corolla is red; lobes 3.5-4 cm long. Stamens 7 mm long. Ovary 7 mm long.

In Thailand, *U. purpurea* Blume has various local names : Kluai mu sang (Peninsular), Yan nom khwai (Trang).

Figure 1 *Uvaria purpurea* Blume (Annonaceae)

1.2 *Review of Literatures*

Plants in the *Uvaria* genus (Annonaceae) are well known to be rich in a variety of compounds.

Informations from NAPRALERT database by University of Illinois at Chicago reveal several types of compounds present in plants of *Uvaria* genus as shown in **Table 1**.

Table 1 Compounds from plants of *Uvaria genus*

Scientific name	Investigated Part	Compound	Bibliography
U. accuminata	Roots	uvaricin, **1**	Jolad *et al*., 1982,1985
		desacetyluvaricin, **2**	Jolad *et al*., 1985
		uvaretin, **76**	Cole, Torrance and Wiedhopf, 1976; Okorie, 1977
U. angolensis	Roots	uvagoletin, **74**	Hufford and Oguntimein, 1980a; Bhardwaj *et al.,* 1982
		angoletin, **75**	Hufford and Oguntimein, 1980a
		uvaretin, **76**	Hufford and Oguntimein, 1980a
		isouvaretin, **77**	Hufford and Oguntimein, 1980a
		angoluvarin, **78**	Hufford and Oguntimein, 1980a
	Stem barks	uvarindole A, **124**	Muhammad and Waterman, 1985
		uvarindole B, **125**	Muhammad and Waterman, 1985

Table 1 (Continued)

Scientific name	Investigated Part	Compound	Bibliography
U. angolensis	Stem barks	uvarindole C, **126**	Muhammad and Waterman, 1985
		uvarindole D, **127**	Muhammad and Waterman, 1985
		chamuvaritin, **81**	Muhammad and Waterman, 1985
U.afzelii	Stems	vafzelin, **132**	Hufford *et al*., 1980b; Hufford and Oguntimein, 1981
		uvafzelin, **133**	Hufford *et al.,* 1980b; Hufford and Oguntimein, 1981
		uvafzelic acid, **134**	Hufford *et al.,* 1980b; Hufford and Oguntimein, 1981
		syncarpic acid, **131**	Hufford and Oguntimein, 1981
		coumarin, **111**	Hufford and Oguntimein, 1981

Table 1 (Continued)

Scientific name	**Investigated Part**	**Compound**	**Bibliography**
U.afzelii	Stems	demethoxymatteucinol, **96**	Hufford and Oguntimein, 1981
		2-hydroxydemethoxy matteu-cinol, **97**	Hufford and Oguntimein, 1981
		2-hydroxy-7,8-dehydrograndiflorone, **91**	Hufford and Oguntimein, 1981
		emorydone, **135**	Hufford and Oguntimein, 1981
U. calamistrata	Roots	calamistrins A, **12**	Zhou *et al*., 1999
		calamistrins B, **13**	Zhou *et al*., 1999
		uvarigrin, **14**	Zhou *et al*., 1999
		uvarigranin, **15**	Zhou *et al*., 1999
		calamistrins C, **16**	Zhou *et al*., 2000
		calamistrins D, **17**	Zhou *et al*., 2000
		calamistrins E, **18**	Zhou *et al*., 2000
		calamistrins F, **19**	Zhou *et al*., 2000
		calamistrins G, **20**	Zhou *et al*., 2000

Table 1 (Continued)

Scientific name	Investigated Part	Compound	Bibliography
U. catocarpa	Fruits	(-)-senepoxide, **47**	Hollands *et al.*, 1968
		seneol, **46**	Hollands *et al.*, 1968
U .chamae	Stem barks	pinocembrin, **92**	Hufford and W.L.Lasswell, 1977a
		uvarinol, **95**	Hufford and W.L.Lasswell, 1976, 1979
		uvaretin, **76**	Hufford and W.L.Lasswell, 1976, 1977a, 1979
		isouvaretin, **77**	Okorie, 1977
		chamanetin, **98**	Hufford and W.L.Lasswell,1997a
		isochamanetin, **99**	Hufford and W.L.Lasswell,1997a
		dichamanetin, **100**	Hufford and W.L.Lasswell, 1997

Table 1 (Continued)

Scientific name	**Investigated Part**	**Compound**	**Bibliography**
U. chamae	Roots	pinostrobrin, **93**	Okorie, 1977
		chamuvarin, **80**	Okorie, 1977
		chamuvaritin, **81**	Okorie, 1977
		benzyl benzoate, **63**	Okorie, 1977
		monobenzylated monoter-pene chamane, **37**	Hufford and W.L.Lasswell,1977b
		o-methoxybenzyl ether, **130**	Hufford and W.L.Lasswell,1977b
		thymoquinol dimethyl ether, **38**	Hufford and W.L.Lasswell,1977b
	Roots barks	*o*-methoxybenzyl benzoate, **65**	Hufford and W.L.Lasswell,1977b
		diuvaretin, **79**	Hufford and W.L.Lasswell,1977a
		isouvaretin, **77**	Hufford and W.L.Lasswekk 1977a; Okorie, 1977
		uvaretin, **76**	Hufford and W.L.Lasswell, 1977a; Okorie ,1977

Table 1 (Continued)

Scientific name	**Investigated Part**	**Compound**	**Bibliography**
U. chamae	Roots barks	pinostrobrin, **93**	Hufford and W.L.Lasswell, 1977a; Okorie, 1977
		chamanetin 5-methyl ether, **101**	Hufford, W.L.Lasswell and El-Sohly, 1979
		dichamanetin 5-methyl ether, **102**	Hufford, W.L.Lasswell and El-Sohly, 1979
	Leaves	asimilobine, **120**	Leboeuf *et al*., 1982
		glaziovine, **114**	Leboeuf *et al*., 1982
		isoboldine, **121**	Leboeuf *et al*., 1982
		pronuciferine, **115**	Leboeuf *et al*., 1982
	Fruits	glaucine, **122**	Leboeuf *et al*., 1982
		isoboldine, **121**	Nkunya, Waibel and Achenbach, 1993a
		thaliporphine, **123**	Nkunya, Waibel and Achenbach, 1993a

Table 1 (Continued)

Scientific name	Investigated Part	Compound	Bibliography
U. dependens	Root barks	5,7,8-trimethoxyflav-3-ene, **107**	Nkunya, Waibel and Achenbach, 1993a
		2-hydroxy-3-4,6-trimethoxy-chalcone, **87**	Nkunya, Waibel and Achenbach, 1993a
		dimeric benzopyran, **128**	Nkunya, Waibel and Achenbach, 1993a
		(+)-pipoxide, **44**	Nkunya, Waibel and Achenbach, 1993a
		β-sitosterol, **28**	Raviwan Sealee, 1989
		stigmasterol, **29**	Raviwan Sealee, 1989
U. dulcis Dunal	Leaves	chrysin, **106**	Raviwan Sealee, 1989
		pinocembrin, **92**	Raviwan Sealee, 1989
		2′,6′-dihydroxy-3′,4′-dimethoxydihydrochalcone, **84**	Raviwan Sealee, 1989

Table 1 (Continued)

Scientific name	Investigated Part	Compound	Bibliography
U. dulcis Dunal	Leaves	2′,3′-dihydroxy-4′,6′-dimethoxychalcone, **85**	Chantrapromma, *et al*., 2000
U. elliltiana	Stems barks	3,6-bis-(γ,γ-dimethylallyl)-indole, **116**	Achenbach and Roffelsberger, 1979
U. ferruginea	Roots	(-)-senepoxide, **47**	Kodpinid *et al*., 1983; Kodpinid, Thebtaranonth, C. and Thebtaranonth, Y., 1985
		(-)-1,6-desoxysenepoxide, **53**	Kodpinid, Thebtaranonth, C. and Thebtaranonth, Y., 1985
		(-)-1,6-desoxytingtanoxide, **54**	Kodpinid, Thebtaranonth, C. and Thebtaranonth, Y., 1985
	Stems + Roots	(-)-tingtanoxide, **49**	Kodpinid *et al.,* 1983; Kodpinid and Thebtaranonth, Y., 1985

Table 1 (Continued)

Scientific name	Investigated Part	Compound	Bibliography
U. ferruginea	Stems + Roots	(+)-β-senepoxide, **48**	Kodpinid *et al.,* 1983; Kodpinid
	Leaves	ferrudiol, **43**	Chantrapromma *et al.,* 1982
	Stems	benzyl-2-methoxy benzoate, **67**	Kodpinid, Thebtaranonth, C. and Thebtaranonth, Y., 1985
		chamanetin, **98**	Kodpinid, Thebtaranonth, C and Thebtaranonth, Y., 1985
		chamanetin 5-methyl ether, **101**	Kodpinid, Thebtaranonth, C. and Thebtaranonth, Y., 1985
U. hamiltonii	Leaves + Stem barks	hamiltones A, **108** hamiltones B, **109**	Huang *et al.,*1998 Huang *et al.,*1998

Table 1 (Continued)

Scientific name	**Investigated Part**	**Compound**	**Bibliography**
U. hamiltonii	Leaves + Stem barks	hamiltrone, **110**	Huang *et al.,*1998
		hamilcone, **90**	Huang *et al.,*1998
		hamilxanthene, **113**	Huang *et al.,*1998
U. kirkii	Root barks	uvaretin, **76**	Nkunya *et al.,* 1985
		diuvaretin, **79**	Nkunya *et al.,* 1985
		benzyl benzoate, **63**	Nkunya *et al.,* 1985
		2-methoxybenzyl benzoate, **67**	Nkunya *et al.,* 1985
		7-methyljuglone, **136**	Nkunya *et al.,* 1985
U. leptocladon	Root barks	triuvaretin, **82**	Nkunya *et al.,* 1993a
		isotriuvaretin, **83**	Nkunya *et al.,* 1993a
		uvaretin, **76**	Nkunya *et al.,* 1993a
		isouvaretin, **77**	Nkunya *et al.,* 1993a
		diuvaretin, **79**	Nkunya *et al.,* 1993a
		angoluvarin, **78**	Nkunya *et al.,* 1993a

Table 1 (Continued)

Scientific name	Investigated Part	Compound	Bibliography
U. lucida	Root barks	benzyl benzoate, **63**	Nkunya and Weenen, 1990b
		chamuvaretin, **81**	Nkunya and Weenen, 1990b
		uvaretin, **76**	Nkunya and Weenen, 1990b
		diuvaretin, **79**	Nkunya and Weenen, 1990b
		lucidene, **34**	Nkunya and Weenen, 1990b
	Stem barks	2,7-dihydroxy-1,8-dimethoxypyrene, **137**	Achenbach *et al.,* 1997
		2-hydroxy-1,7-trimethoxypyrene, **138**	Achenbach *et al.*, 1997
U. narum	Root barks	squamocin, **3**	Hisham *et al.,* 1991a
		squamocin-28-one, **4**	Hisham *et al.,* 1991a
		panalicin, **5**	Hisham *et al.,* 1991a

Table 1 (Continued)

Scientific name	**Investigated Part**	**Compound**	**Bibliography**
U. narum	Root barks	isodesacetyluvaricin, **6**	Hisham *et al.,* 1991a
		narumicin I, **7**	Hisham *et al.,* 1991a
		narumicin II, **8**	Hisham *et al.,* 1991a
		benzyl benzoate, **63**	Hisham *et al.,* 1991a
		glutinone	Hisham *et al.,* 1991a
		glutinol	Hisham *et al.,* 1991a
		taraxerol, **32**	Hisham *et al.,* 1991a
		β-sitosterol, **28**	Hisham *et al.,* 1991a
		uvariamicin I, **9**	Hisham *et al.,* 1990
		uvariamicin II, **10**	Hisham *et al.,* 1990
		uvariamicin III, **11**	Hisham *et al.,* 1990

Table 1 (Continued)

Scientific name	**Investigated Part**	**Compound**	**Bibliography**
U. narum	Leaves	2-*E*-[2′′-oxo-cyclopent-3′′- en-1′′-ylidene]ethyl benzoate, **73**	Parmar, Bisht, Malhotra, Jha and Errinton, 1995
U. ovata	Stem bar	benzyl 2,3,6-trimethoxy-benzoate, **64**	Leboeuf *et al*., 1982
U. pendensis	Stem barks	(+)-pandoxide, **50**	Nkunya *et al*., 1987a
		(+)-β-senepoxide, **48**	Nkunya *et al*., 1987a
		(-)-pipoxide, **45**	Nkunya *et al*., 1987a
	Leaves	3-farnesylindole, **117**	Nkunya *et al*., 1987b
	Root barks	(6′,7′-dihydro-8′,9′-dihydroxy)-3-farnesylindole, **118**	Nkunya and Weenen, 1989
		(8′,9′-dihydroxyJ)-3-farnesylindole, **119**	Nkunya and Weenen, 1989
U. purpurea Bl.	Roots	(-)-1,6-desoxypipoxide, **42**	Holbert *et al*., 1979; Schulte *et al*., 1982b

Table 1 (Continued)

Scientific name	Investigated Part	Compound	Bibliography
U. purpurea Bl.	Roots	benzyl benzoate, **63**	Kodpinid *et al.,* 1984
		benzyl 2-hydroxybenzoate, **66**	Kodpinid *et al.,* 1984
		benzyl 2-methoxybenzoate, **67**	Kodpinid *et al.,* 1984
		benzyl 2,6-dihydroxybenzoate, **68**	Kodpinid *et al.,* 1984
		benzyl 2-hydroxy-6-methoxy-benzoate, **69**	Kodpinid *et al.*, 1984
		benzyl 2,6-dimethoxybenzoate, **70**	Kodpinid *et al.*, 1984
		benzyl 2-hydroxy-5-methoxybenzoate, **71**	Kodpinid *et al.*, 1984
		benzyl 2,5-dimethoxybenzoate, **72**	Kodpinid *et al.*, 1984
		zeylenol, **51**	Xi-ping *et al.*, 1995

Table 1 (Continued)

Scientific name	**Investigated Part**	**Compound**	**Bibliography**
U. purpurea Bl.	Roots	uvarigranol A, **59**	Xi-ping *et al.*, 1995
		uvarigranol B, **60**	Xi-ping *et al.*, 1995
	Leaves	benzoic acid, **40**	Patcharin Pongsuphaleeporn,19
		cyclohexane tetraol, **41**	Patcharin Pongsuphaleeporn,1982
		(+)-pipoxide, **44**	Holbert *et al.*, 1979
		β-sitosterol, **28**	Patcharin Pongsuphaleeporn,1982
		zeylenol, **51**	Patcharin Pongsuphaleeporn,1982
	Stem barks + Leaves	zeylenone, **55**	Liao, Shi-Lin, Yang and Dai, 1997
		grandiflorone, **56**	Liao, Shi-Lin, Yang and Dai, 1997
		grandifloracin, **57**	Liao, Shi-Lin, Yang and Dai, 1997
U. rufa Bl.	Bark	6,7-*O*,*O*-dimethylbacalein, **103**	Lojanapiwatna *et al.*, 1981

Table 1 (Continued)

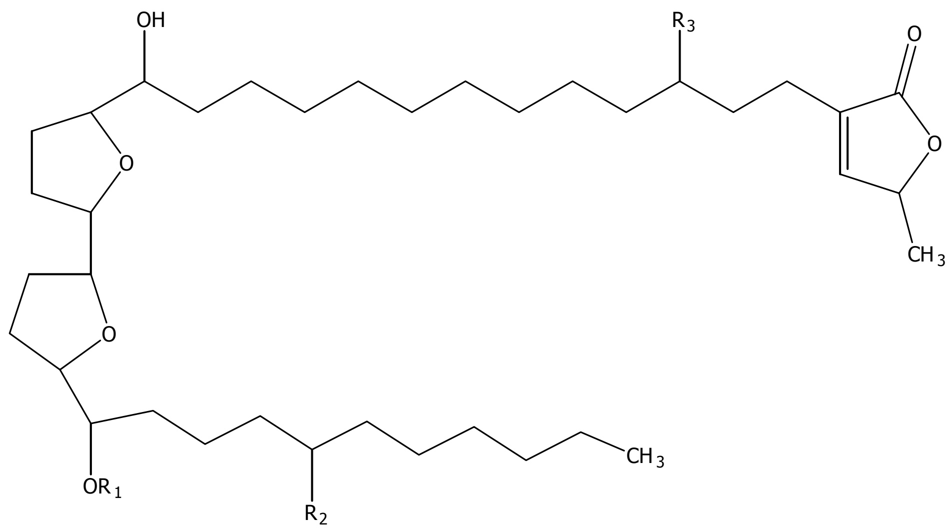
Scientific name	Investigated Part	Compound	Bibliography
U. rufa Bl.	Bark	7-*O*-methylwogonin, **104**	Lojanapiwatna, *et al.*, 1981
		tectochrysin, **105**	Lojanapiwatna *et al.*. , 1981
	Roots	2,5-dihydroxy-7-methoxyflavanone, **94**	Chatrapromma, *et al.*, 1989
U. scheffleri	Stems barks	schefflerin, **88**	Nkunya *et al.*, 1990a
		isoschefflerin, **89**	Nkunya *et al.*, 1990a
		glutin-5-en-3-β-ol, **33**	Nkunya *et al.*, 1990a
		3-farnesylindole, **117**	Nkunya *et al.*, 1990a
		2′,6′-dihydroxy-3′,4′-dimethoxy chalcone, **86**	Nkunya *et al.*, 1990a
		β-sitosterol, **28**	Nkunya *et al.*, 1990a

Table 1 (Continued)

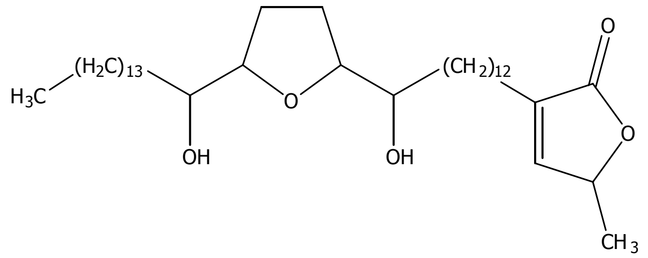
Scientific name	**Investigated Part**	**Compound**	**Bibliography**
U. scheffleri	Stems barks	benzyl benzoate, **63**	Nkunya *et al*., 1990a
U. tranzaniae	Root barks	tanzanene, **35**	Weenen *et al*., 1991
		alloaromadendrene, **36**	Weenen *et al*., 1991
U. tonkinesis	Roots	tonkinesin, **21**	Chen *et al*., 1996
		tonkinenin A, **58**	Zhao *et al*., 1996
		tonkinesin A, **22**	Chen *et al*., 1996
		tonkinesin B, **23**	Chen *et al*., 1996
		tonkinesin C, **24**	Chen *et al*., 1996
		tonkinin A, **25**	Chen *et al*., 1996
		tonkinin B, **26**	Chen *et al*., 1996
		tonkinin C, **27**	Chen *et al*., 1996
	Seeds	tonkinenin A, **58**	Zhao *et al*., 1996
U. zeylanica	Roots	zeylenol, **51**	Jolad *et al*., 1981
		zeylena, **52**	Jolad *et al*., 1981

Structures

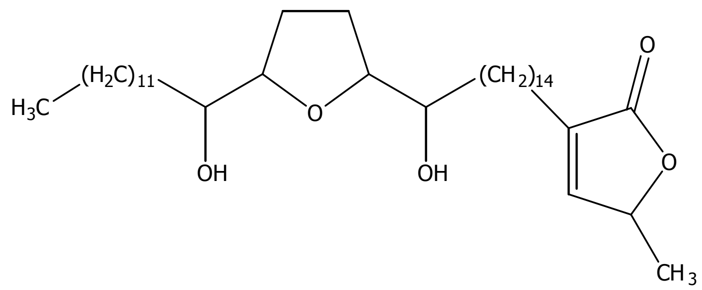
1. **Acetogenins**



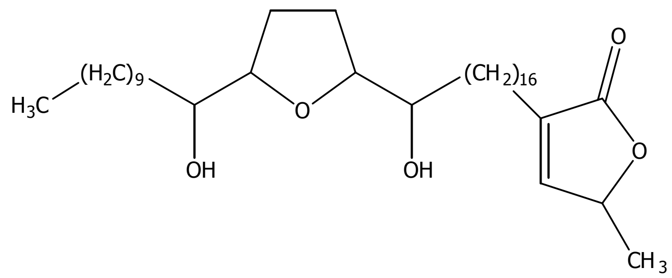
		R_1	R_2	R_3
(1) uvaricin	:	Ac	H	H
(2) desacetyluvaricin	:	H	H	H
(3) squamocin	:	H	OH	H
(4) squamocin-28-one	:	H	=O	H
(5) panalicin	:	H	OH	OH
(6) isodesacetyluvaricin	:	H	H	H
(diastereomer of desacetyluvaricin)				
(7) narumicin I	:	H	H	OH
(8) narumicin II				
(diastereomer of narumicin I)	:	H	H	OH



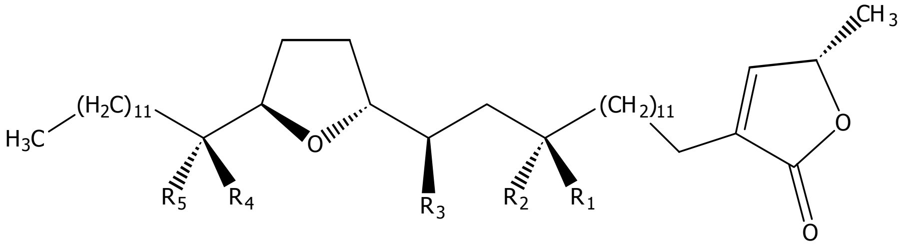
(9) uvariamicin I



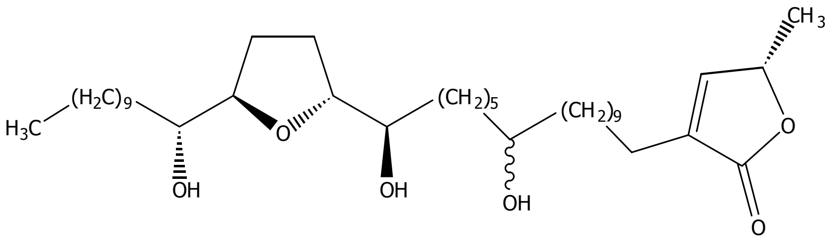
(10) uvariamicin II



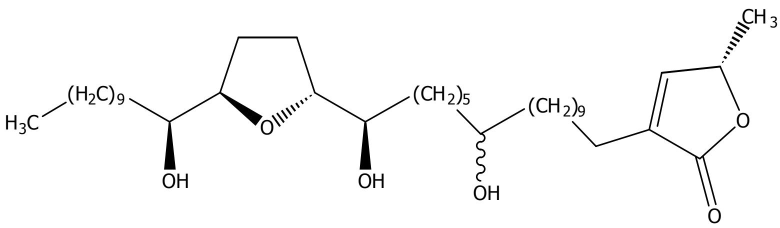
(11) uvariamicin III



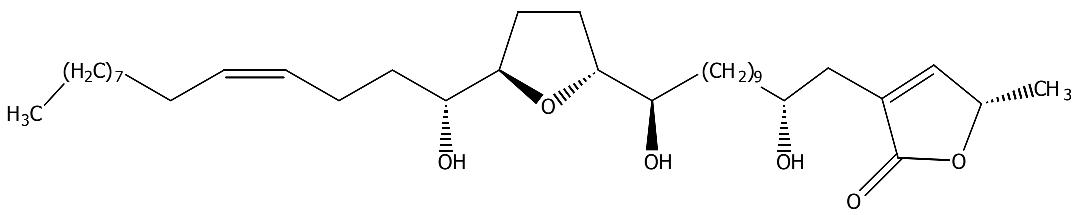
		R_1	R_2	R_3	R_4	R_5
(12) calamistrins A	:	H	OH	OH	OH	H
(13) calamistrins B	:	OH	H	OAc	OH	H
(14) uvarigrin	:	H	OH	OH	H	OH
(15) uvarigranin	:	H	OH	OAc	H	OH



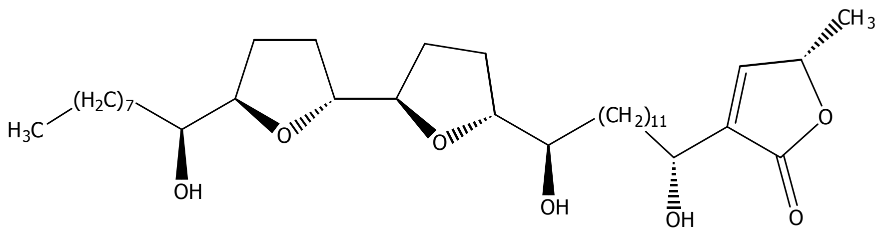
(16) calamistrins C



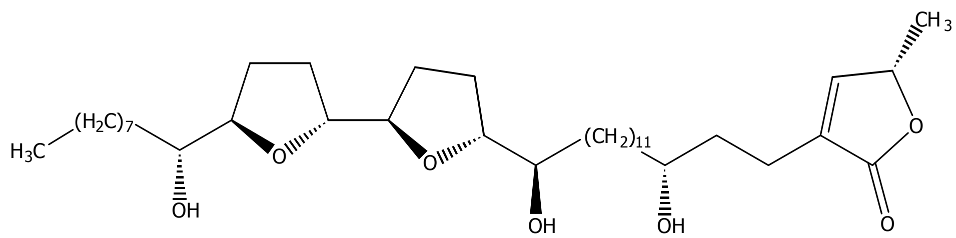
(17) calamistrins D



(18) calamistrins E



(19) calamistrins F



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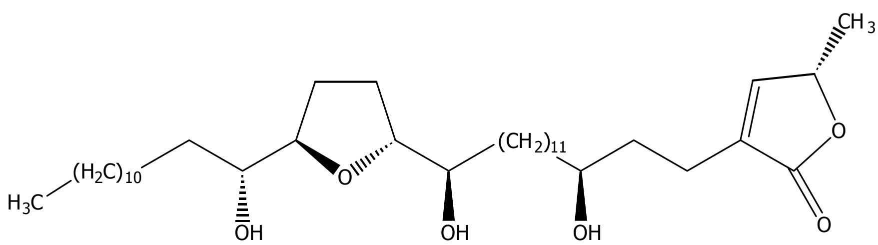
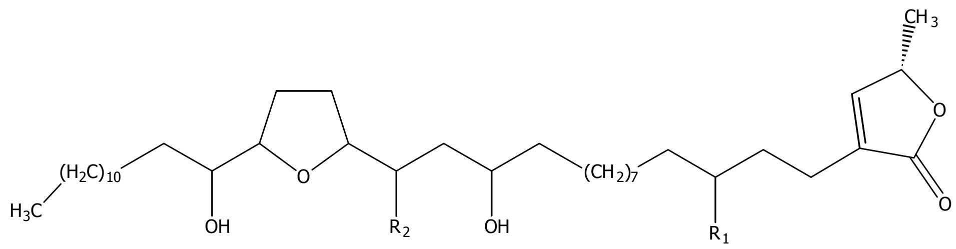
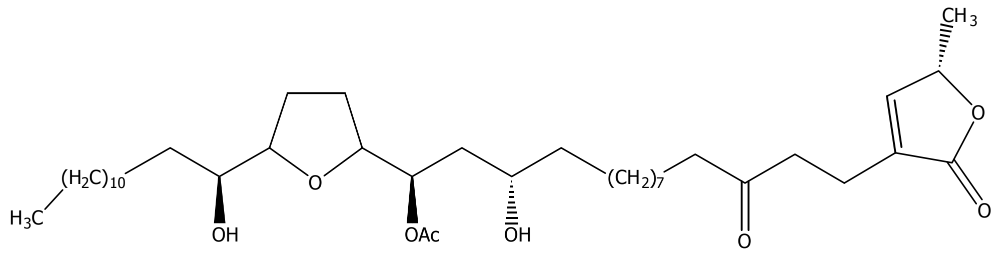


(21) tonkinesin

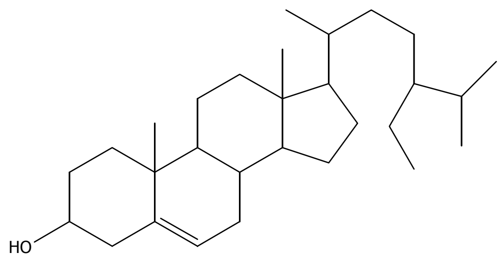


		R_1	R_2
(22) tonkinesins A	:	OH	OH
(23) tonkinesins B	:	OH	OH
(24) tonkinesins C	:	OH	OAc
(25) tonkinins A	:	=O	OH
(26) tonkinins B	:	=O	OH

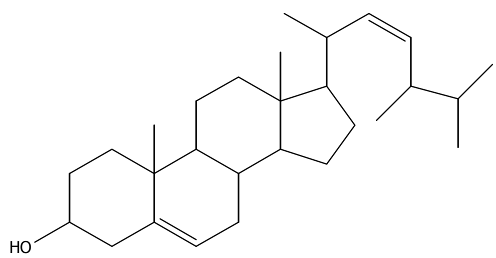


(27) tonkinins C

2. Steroids

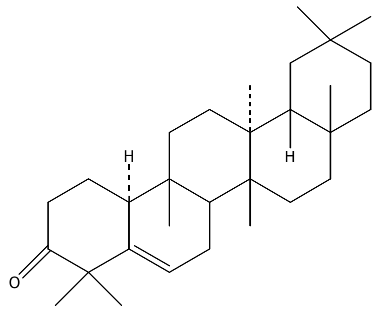


(28) *β*-sitosterol

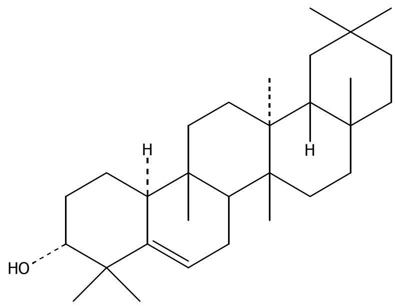


(29) stigmasterol

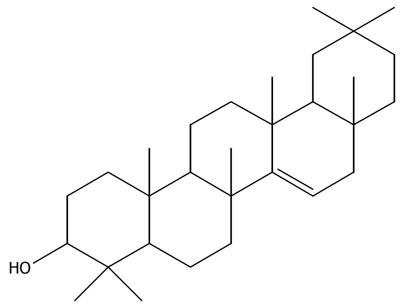
3. Triterpenes



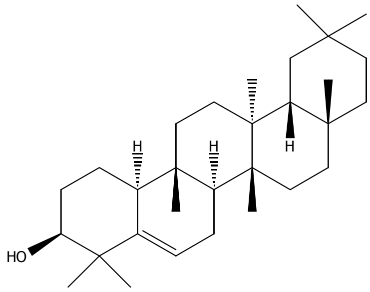
(30) glut-5-en-3-one



(31) glut-5(6)-en-3α-ol

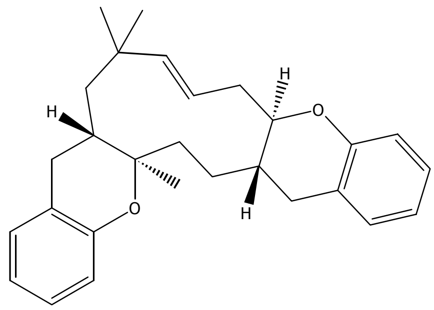


(32) taraxerol

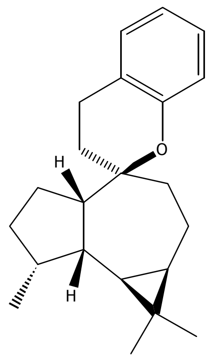


(33) glutin-5-en-3β-ol

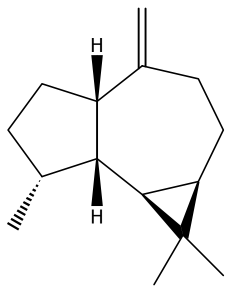
4. Bis(benzopyranyl)sesquiterpenes



(34) lucidene

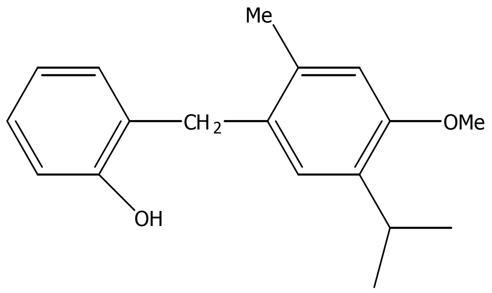


(35) tanzanene

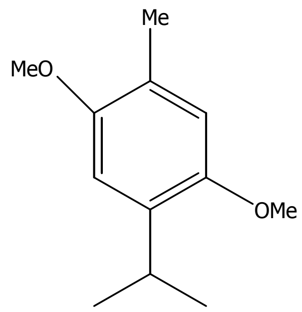


(36) alloaromadrene

5. Monoterpenes

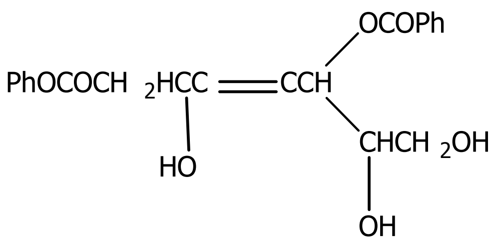


(37) monobenzylated monoterpene chamanen

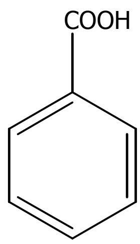


(38) thymoquinol dimethyl ether

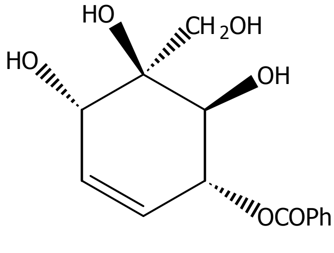
6. Shikimate derivatives



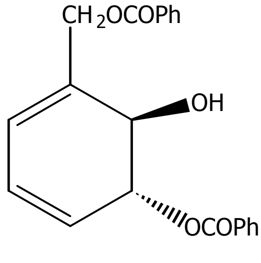
(39) (*E*)-3,7-bis-benzoyloxy-hept-4-en-1,2,6-triol



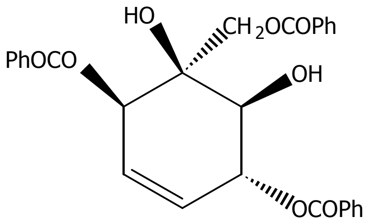
(40) benzoic acid



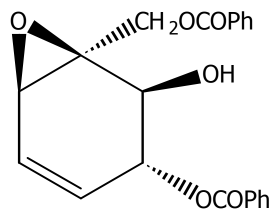
(41) cyclohexene tetraol



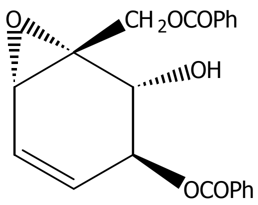
(42) (-)-1,6-desoxypipoxide



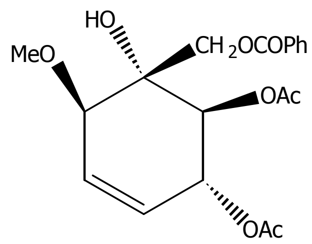
(43) ferrudiol



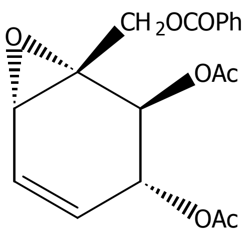
(44) (+)-pipoxide



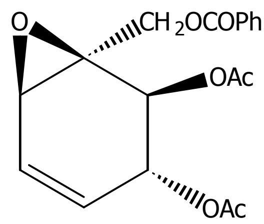
(45) (-)-pipoxide



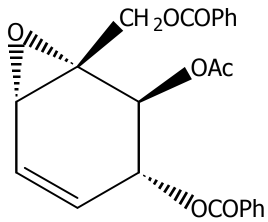
(46) seneol



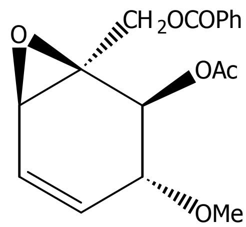
(47) (-)-senepoxide



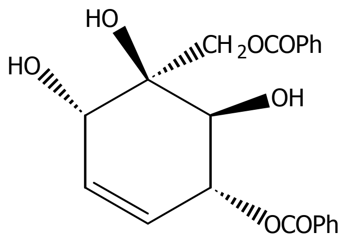
(48) β-senepoxide



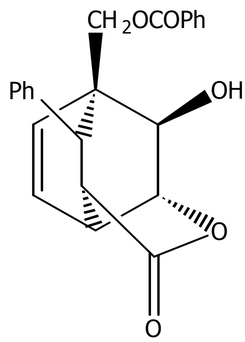
(49) (-)-tingtanoxide



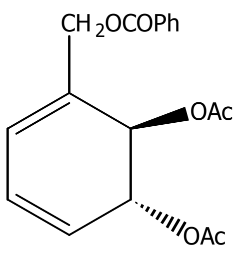
(50) (+)-pandoxide



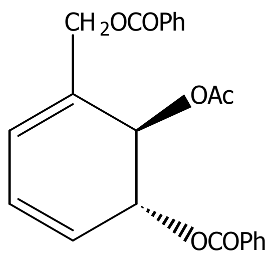
(51) zeylenol



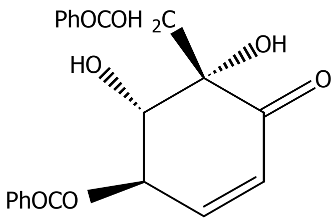
(52) zeylena



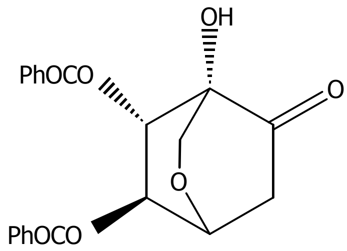
(53) (-)-1,6-desoxy-senepoxide



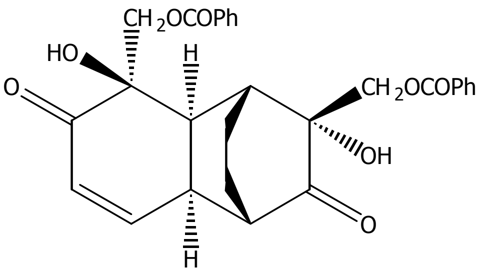
(54) (-)-1,6-desoxytingtangoxide



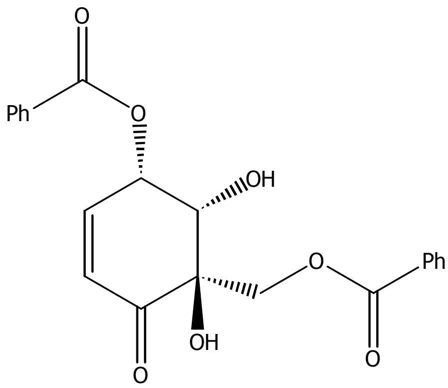
(55) zeylenone



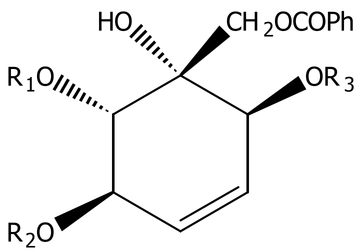
(56) grandiflorone



(57) grandifloracin

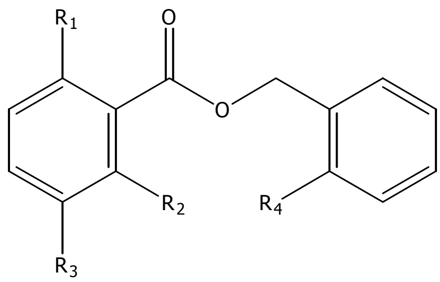


(58) tonkinenin A

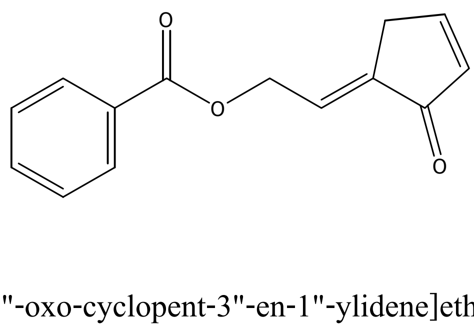


		R_1	R_2	R_3
(59) uvarigranol A	:	H	H	Bz
(60) uvarigranol B	:	Ac	Bz	H
(61) uvarigranol C	:	H	Bz	Et
(62) uvarigranol D	:	Ac	Bz	Et

7. Aromatic ester

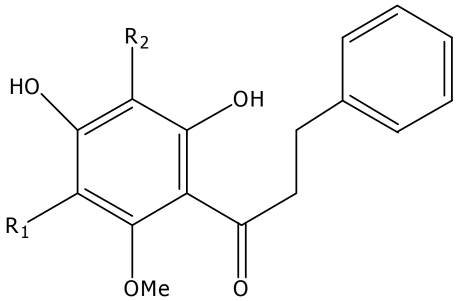


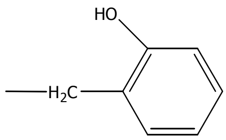
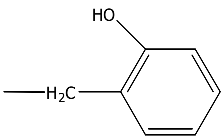
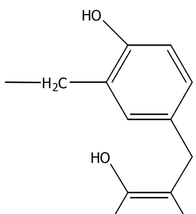
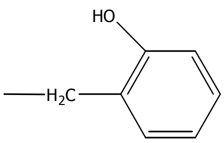
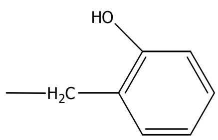
		R_1	R_2	R_3	R_4
(63) benzyl benzoate	:	H	H	H	H
(64) benzyl-2,3,6-trimethoxy benzoate	:	OMe	OMe	OMe	H
(65) *o*-methoxybenzyl benzoate	:	H	H	H	OMe
(66) benzyl 2-hydroxybenzoate	:	OH	H	H	H
(67) benzyl 2- methoxybenzoate	:	OMe	H	H	H
(68) benzyl 2,6-dihydroxybenzoate	:	OH	OH	H	H
(69) benzyl 2-methoxy 6-hydroxybenzoate	:	OH	OMe	H	H
(70) benzyl 2,6-dimethoxybenzoate	:	OMe	OMe	H	H
(71) benzyl 2-hydroxy 5-methoxybenzoate	:	OH	H	OMe	H
(72) benzyl 2,5-dimethoxybenzoate	:	OMe	H	OMe	H

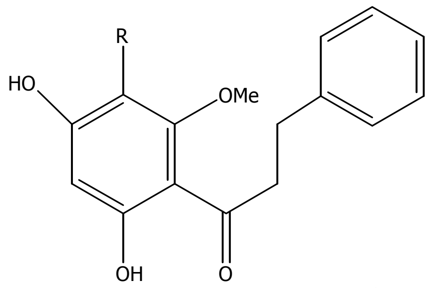


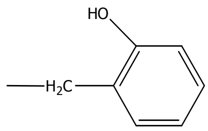
(73) 2-*E*-[2"-oxo-cyclopent-3"-en-1"-ylidene]ethyl benzoate

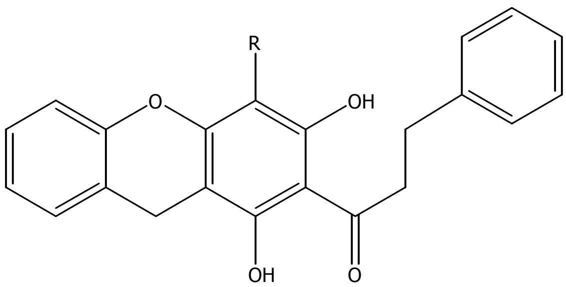
8. **Dihydroxychalcones & C-benzylated dihydrochalcone**

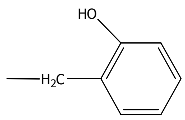


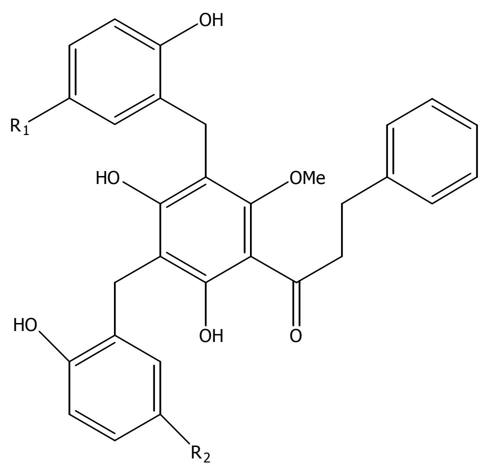
		R_1	R_2
(74) uvangoletin	:	H	H
(75) angoletin	:	Me	Me
(76) uvaretin	:	H	
(77) isouvaretin	:		H
(78) angoluvarin	:		H
(79) diuvaretin	:		

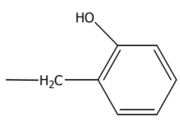
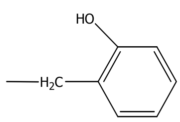


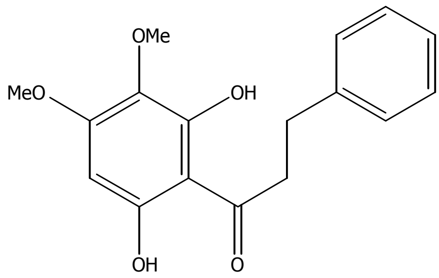
(80) chamuvarin : R = 



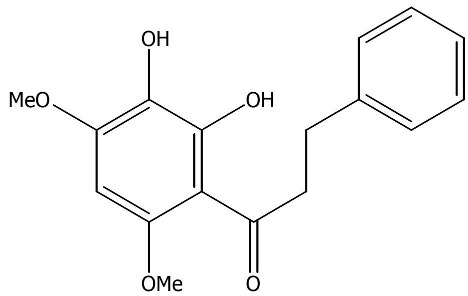
(81) chamuvaritin : R = 



		$\mathbf{R_1}$	$\mathbf{R_2}$
(82) triuvaretin	:		H
(83) isotriuvaretin	:	H	

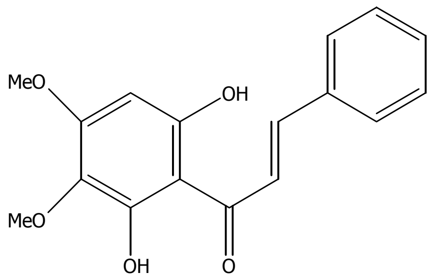


(84) 2',6'-dihydroxy-3',4'-dimethoxydihydrochalcone

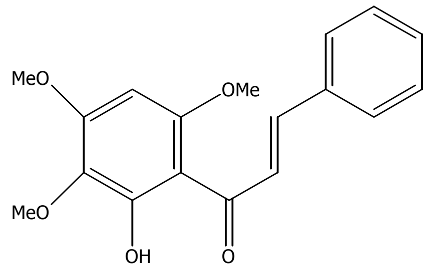


(85) 2',3'-dihydroxy-4',6'-dimethoxydihydrochalcone

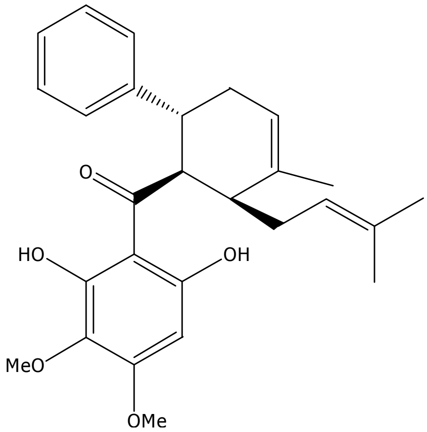
9. Chalcones & prenylated chalcones

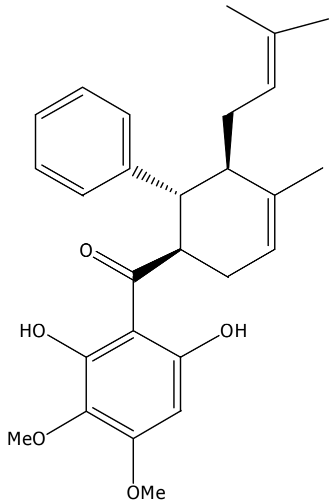


(86) 2',6'-dihydroxy-3',4'-dimethoxychalcone



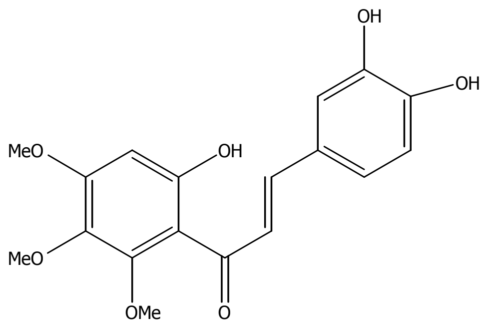
(87) 2-hydroxy-3,4,6-trimethoxychalcone

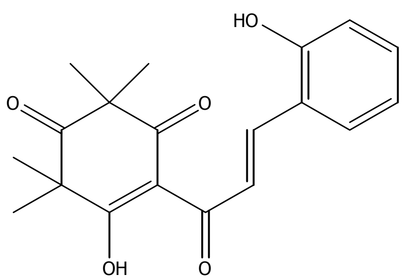




(88) schefflerin

(89) isoschefflerin

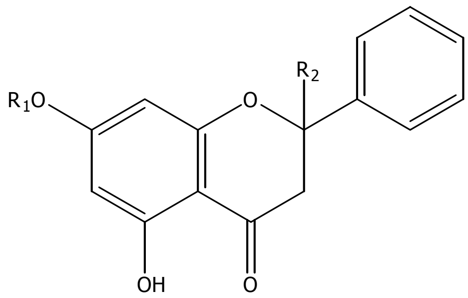




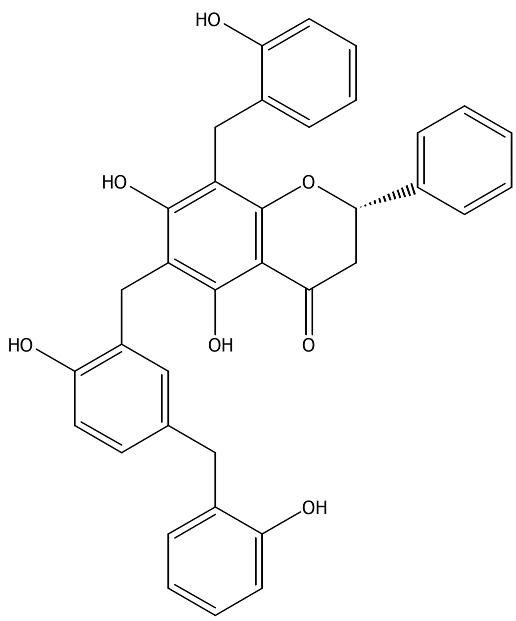
(90) hamilcone

(91) 2-hydroxy-7,8-dehydrograndiflorone

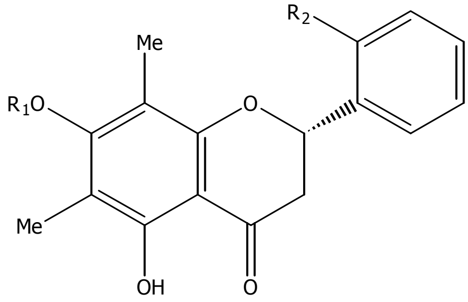
10. Flavanones & Flavones.



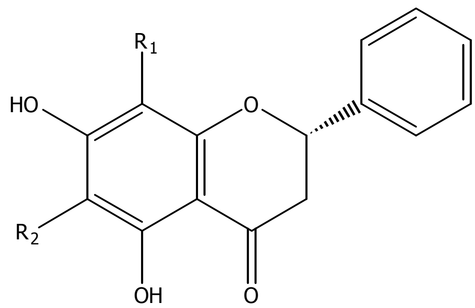
		R_1	R_2
(92) pinocembrin	:	H	H
(93) pinostrobrin	:	Me	H
(94) 2,5-dihydroxy-7-methoxyflavanone	:	Me	OH

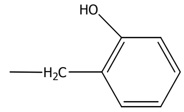
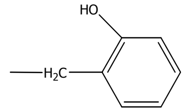
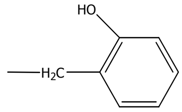
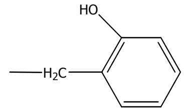


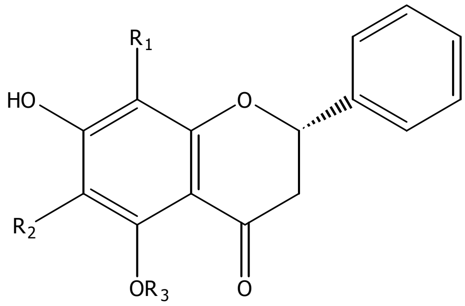
(95) uvarinol

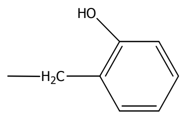
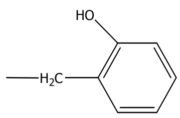
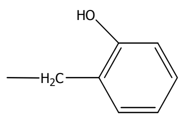


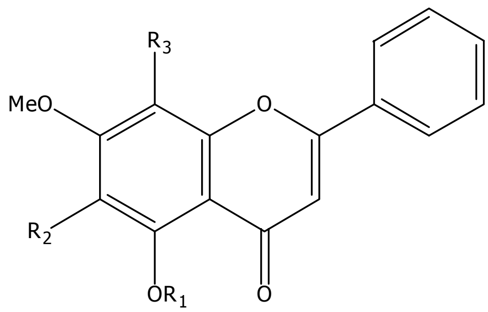
		R_1	R_2
(96) demethoxymatteucinol	:	H	H
(97) 2'-hydroxydemethoxymatteucinol	:	H	OH



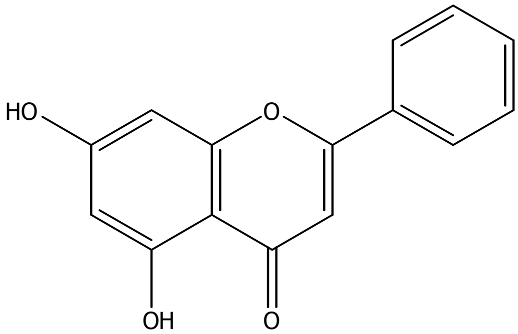
		R_1	R_2
(98) chamanetin	:		H
(99) isochamanetin	:	H	
(100) dichamanetin	:		



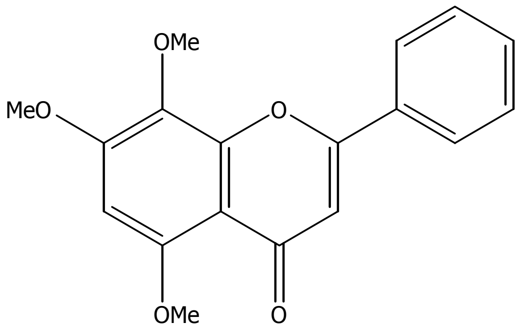
		R_1	R_2	R_3
(101) chamanetin 5-methyl ether	:		H	Me
(102) dichamanetin 5-methyl ether	:			Me



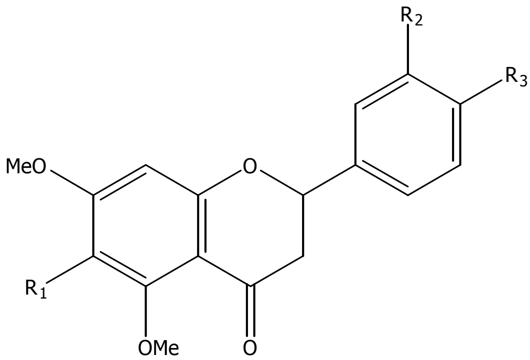
		R_1	R_2	R_3
(103) 6,7-*O,O*-dimethylbacalein	:	H	OMe	H
(104) 7-*O*-methylwogonin	:	H	H	OMe
(105) tectochrysin	:	H	H	H



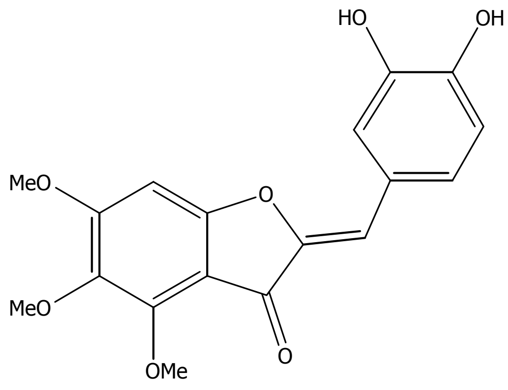
(106) chrysin



(107) 5,7,8-trimethoxyflav-3-ene

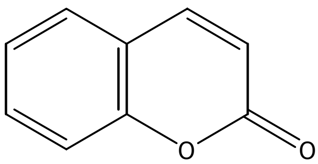


		$\mathbf{R_1}$	$\mathbf{R_2}$	$\mathbf{R_3}$
(108) hamiltones A	:	OH	H	OMe
(109) hamiltone B	:	OMe	OH	OH

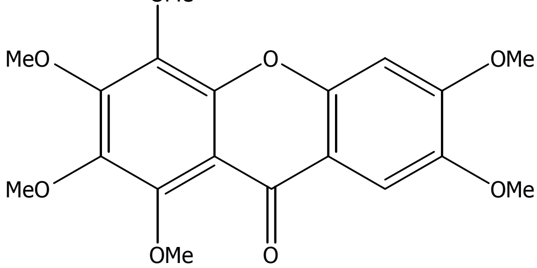


(110) hamiltone

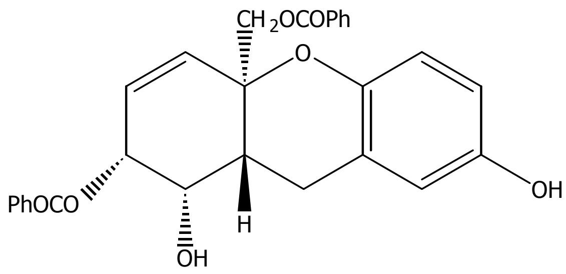
11. **Coumarin, Xanthone & Tetrahydroxanthene.**



(111) coumarin



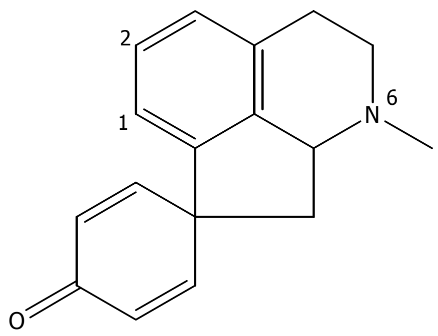
(112) 1,2,3,4,6,7-hexamethoxyxanthone



(113) hamilxanthene

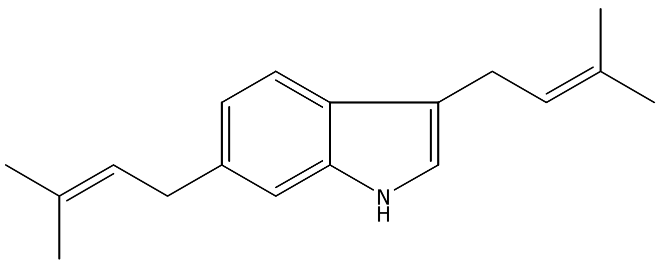
12. Alkaloids.

Proaporphines

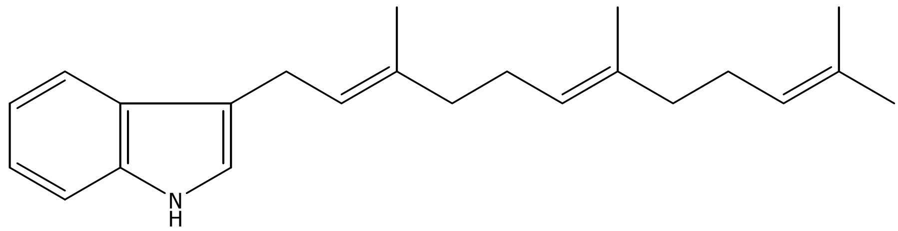


		1	2	6
(114) glaziovine	:	OH	OMe	Me
(115) pronuciferine	:	OMe	OMe	Me

Isoprenylindole

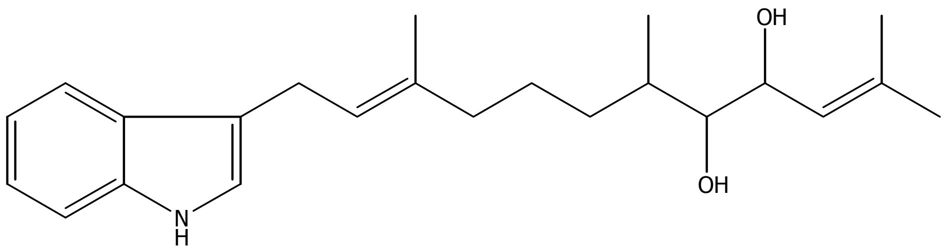


(116) 3,6-bis-(γ,γ-dimethylallyl)indole

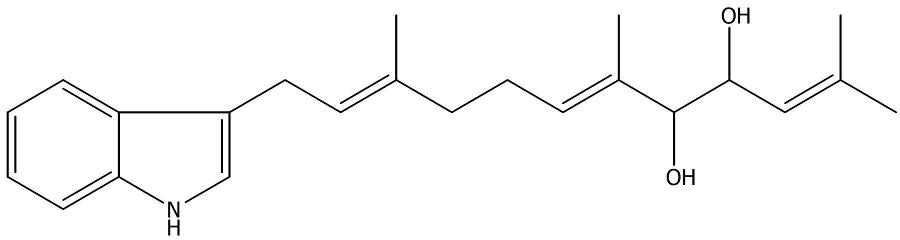


(117) 3-farnesylindole

Indolesesquiterpenes

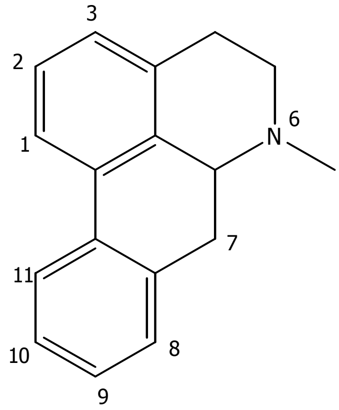


(118) (6',7'-dihydro-8',9'-dihydroxy)-3-farensylindole

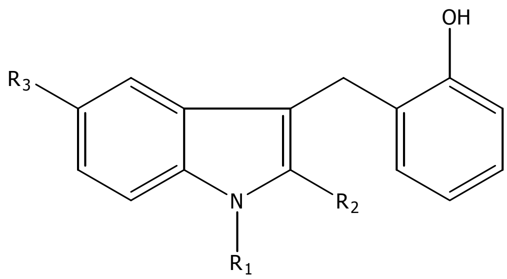


(119) (8',9'-dihydroxy)-3-farnesylindole

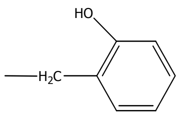
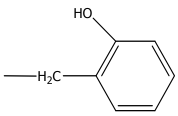
Aporphine alkaloids

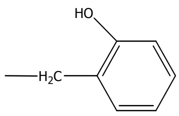
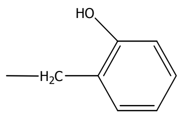
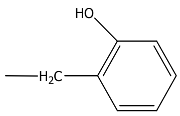


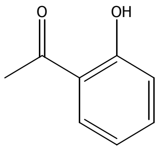
		1	2	3	6	7	8	9	10	11
(120) asimilobine	:	OMe	OH	H	H	H	H	H	H	H
(121) isoboldine	:	OH	OMe	H	Me	H	H	OH	OMe	H
(122) glaucine	:	OMe	OMe	H	Me	H	H	OMe	OMe	H
(123) thaliporphine	:	OH	OMe	H	Me	H	H	OMe	OMe	H

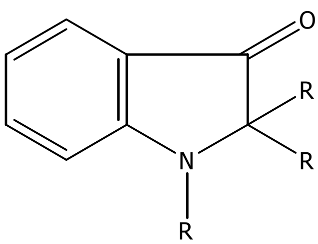


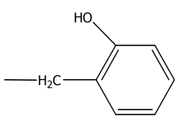
R$_1$ **R$_2$** **R$_3$**

(124) uvarindole A :   H

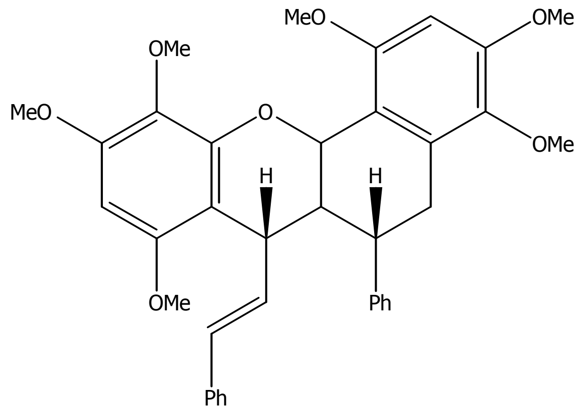
(125) uvarindole B :   

(126) uvarindole C : H  H

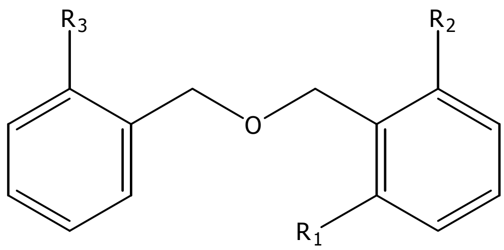


(127) uvarindole D R= 

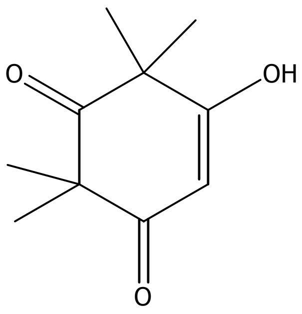
13. Miscellaneous compounds.



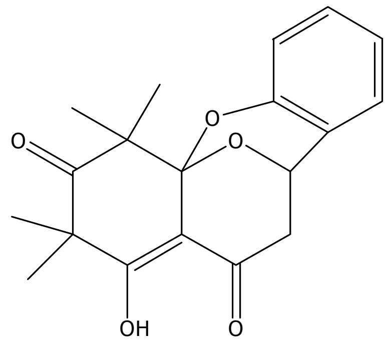
(128) dimeric benzopyran



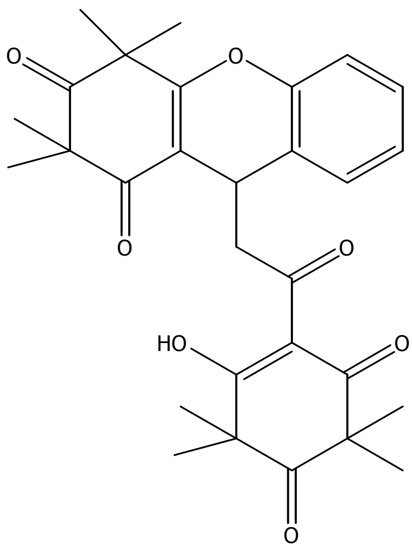
		R_1	R_2	R_3
(129) di-*o*-methoxybenzyl ether	:	H	OMe	OMe
(130) *o*-methoxylbenzyl ether	:	H	OMe	H



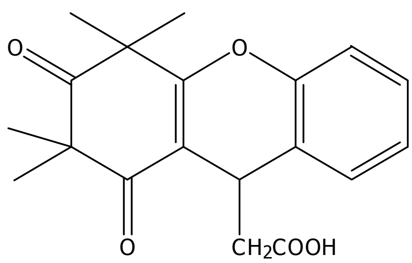
(131) syncarpic acid



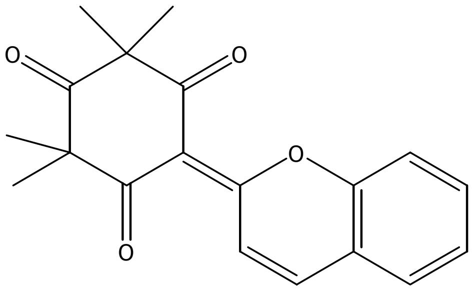
(132) vafzelin



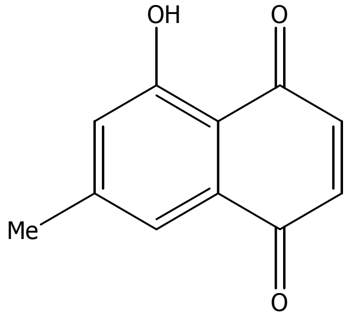
(133) uvafzelin



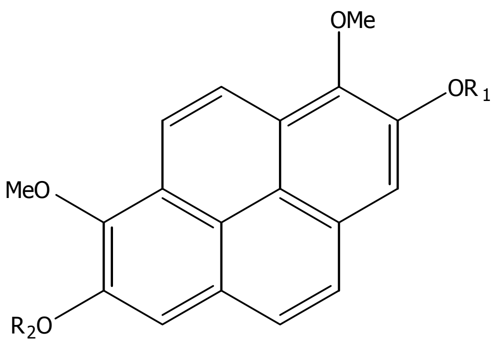
(134) uvafzelic acid



(135) emorydone



(136) 7-methyljuglone



		$\mathbf{R_1}$	$\mathbf{R_2}$
(137) 2,7-dihydroxy-1,8-dimethoxypyrene	:	H	H
(138) 2-hydroxy-1,7-trimethoxypyrene	:	H	Me

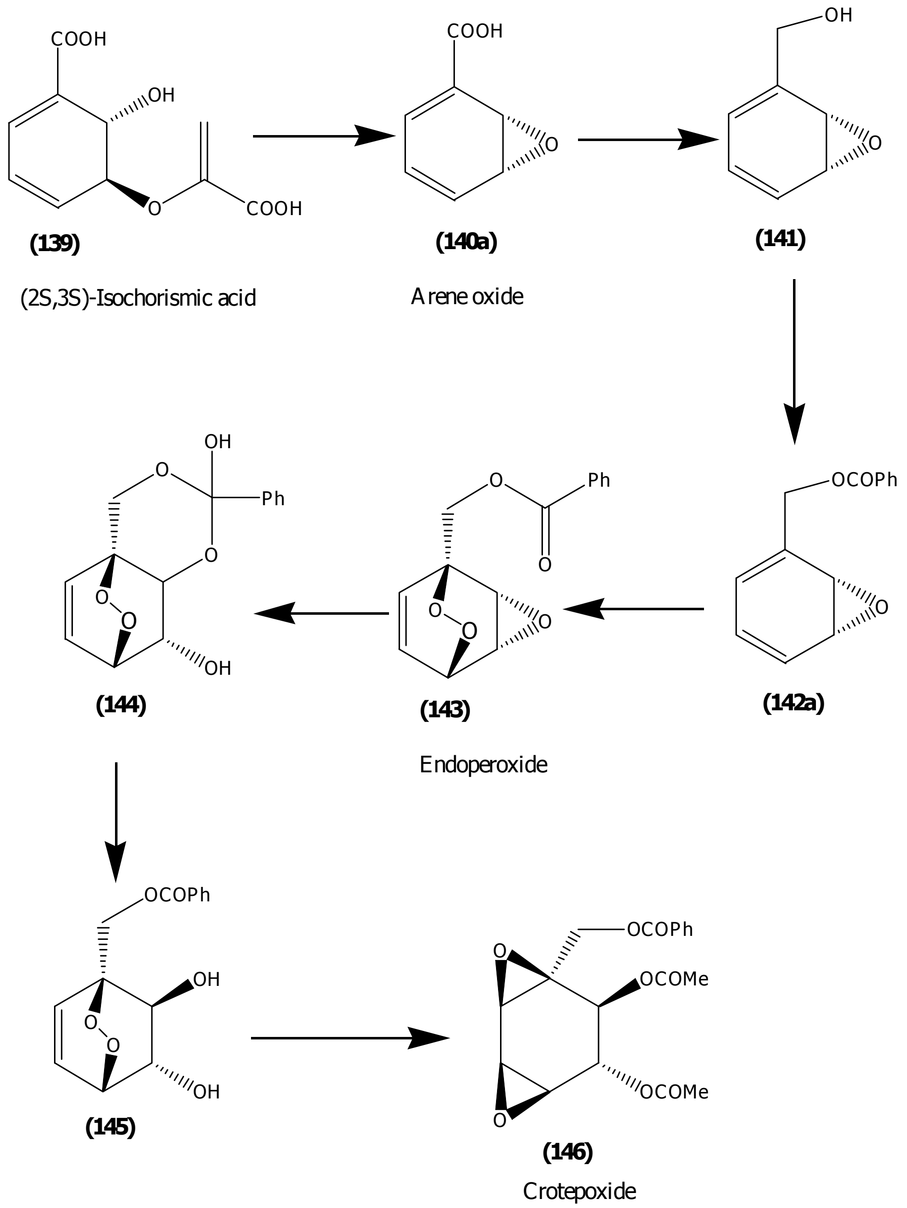
1.3 Biosynthetic pathway of cyclohexene oxides

There were 2 pathways of biosynthetic approach of *o*-hydroxybenzyl substituted cyclohexene oxides, flavanones and dihydrochalcones. One was proposed by Ganem and Holbert (Ganem and Holbert, 1979) and the other by Cole and Bates (Cole *et al*., 1981) as described below.

1. Ganem and Holbert Hypothesis

Professor Ganem of Cornell University made an effort to explain the common biosynthetic pathway of 3 natural cyclohexene oxides.

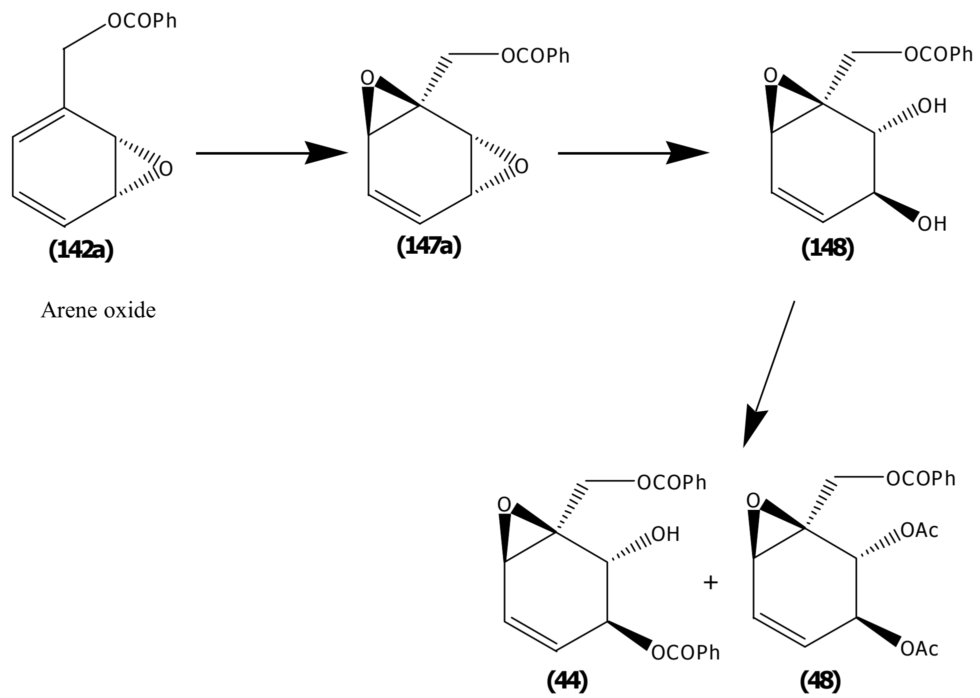
Scheme 1. Biosynthetic pathways of crotepoxide (146)



Ganem suggested that the arene oxide **(140a)** was generated from facile intramolecular S_N2 displacement of the enol pyruvate by the adjacent hydroxy group, then underwent enzymatic reduction to an alcohol **(141)** followed by acylation reaction to afford the ester **(142a)**. The arene oxide ester **(142a)** could then proceed via two different pathways to produce the natural products. In the first, the endoperoxide **(143)** was obtained from stereospecific diene photooxygenation of arene oxide ester **(142a)**, followed by epoxide ring opening with anchimeric assistance from the neighboring benzoate carbonyl to afford the hemiorthoester **(144)** and then rearranged to **(145)**. Acetylation of **(145)** and thermal rearrangement of the endoperoxide bridge resulted in a complete plausible biogenesis of crotepoxide **(146)** as shown in scheme **1**. (Kodpinid *et al*., 1984) & (Thebtaranonth *et. al*., 1986).

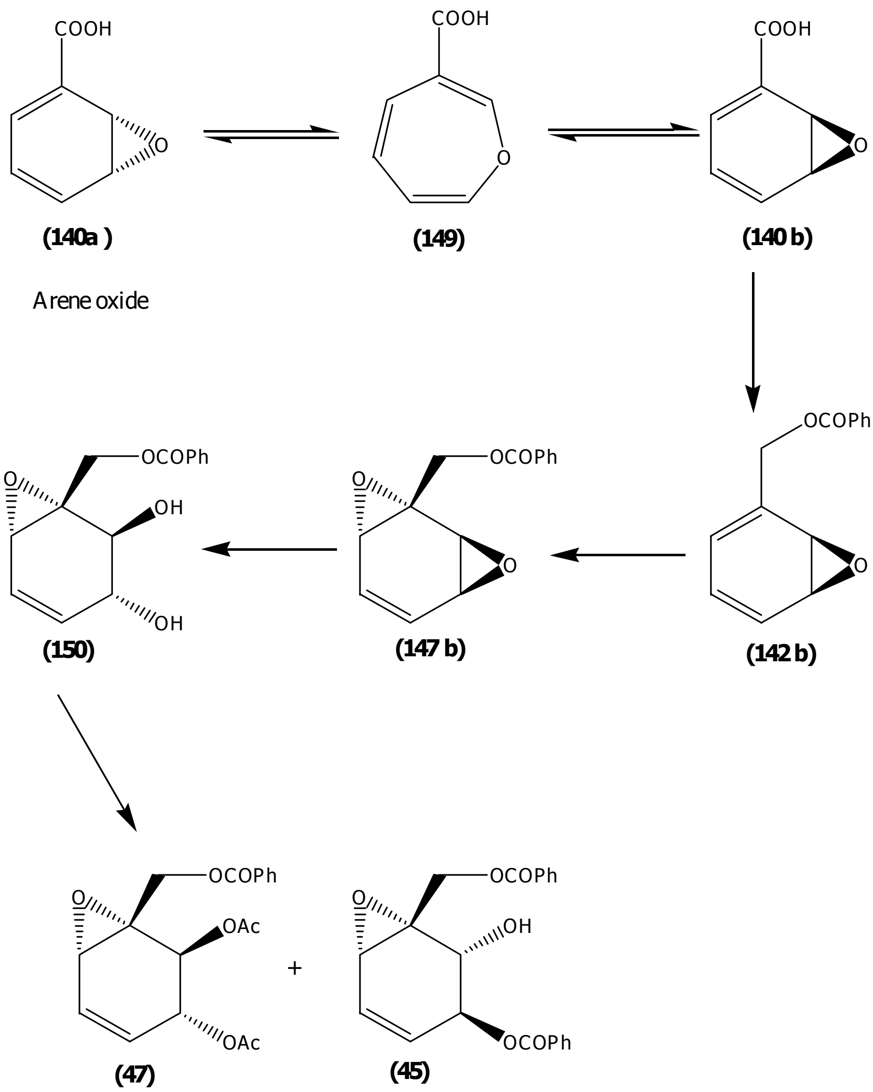
In the second pathway as shown in scheme 2, compound **(147a)** was obtained from epoxidation at the reactive 1,6-double bond of **(142a)**, followed by selective epoxide ring opening of the 2,3-epoxide to afford **(148)**, and then biological acylation or benzoylation of the resulting alcohol yielded (+)-senepoxide **(48)** and (+)-pipoxide **(44)**. (Kodpinid *et al*.,1984) & (Thebtaranonth *et. al*., 1986).

Scheme 2. Biosynthetic pathway of (+)-senepoxide (48) and (+)-pipoxide (44)



From **schemes 1** and **2**, the biogenesis products (+)-senepoxide **(48)** and (+) pipoxide **(44)** yielded from Ganem's proposal are mirror images and having the opposite absolute configuration to the real natural products, (-)-senepoxide **(47)** and (-)-pipoxide **(45)**. (Kodpinid *et al*., 1984)

Scheme 3. Biosynthetic pathway of (-)-senepoxide (47) and (-)-pipoxide (45)

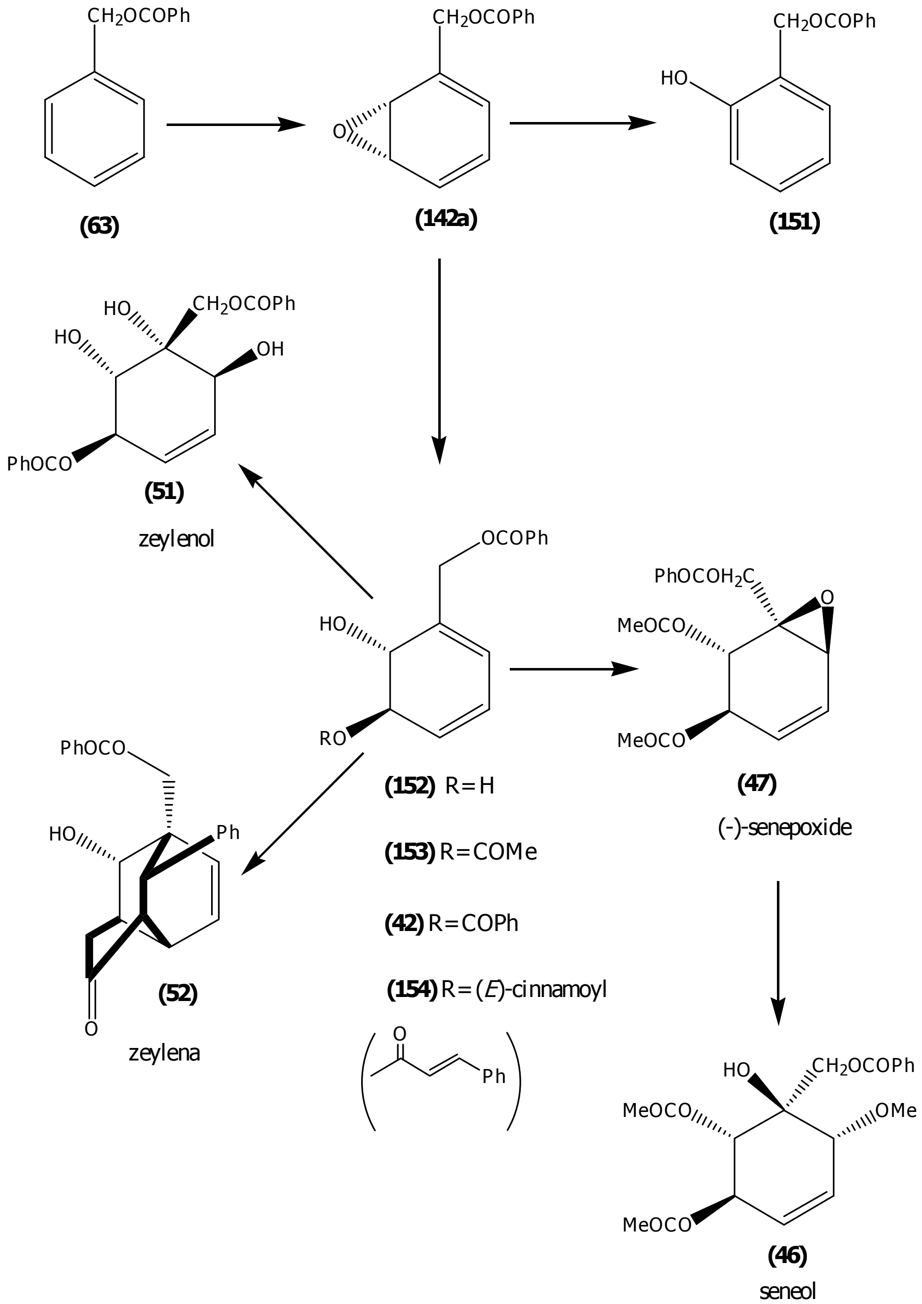


Arene oxide **(140 b)** was generated from isomerization of arene oxide **(140a)** via oxepin **(149)** which upon ring opening, benzoylation or acylation yielded (-)-senepoxide **(47)** and (-)-pipoxide **(45)**.

2. Cole and Bates Hypothesis

In 1981, Jolad and co-workers isolated zeylenol **(51)** and zeylena **(52)** from the roots of *Uvaria zeylanica* (Jolad *et al*., 1981). Later, Professor Cole and Bates put forward the biosynthetic pathway of the compounds in this series as shown in **scheme 4**.

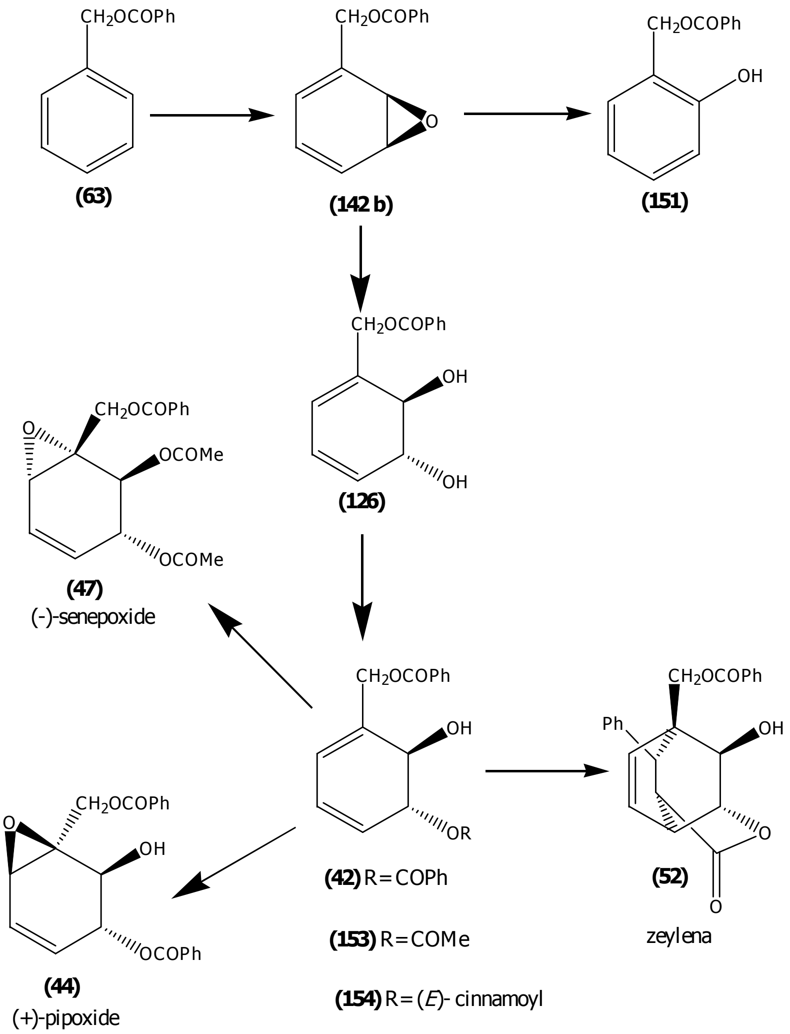
Scheme 4. Biosynthetic pathway of zeylenol (51) and zeylena (52)



In **scheme 4**, benzyl benzoate **(63)** was epoxidized to afford key intermediate **(142a)**, and then added (*E*)-cinnamic acid to yield **(154)**. Compound **(154)** underwent an intramolecular Diels-Alder reaction to give zeylena **(52)**. In addition, compound **(142a)** with addition of water, acetic acid, or benzoic acid and then epoxidation, eventually gave other natural products such as zeylenol **(51)**, (-)-senepoxide **(47)** and seneol **(46)**. (Kodpinid *et al*., 1984)

The precursor **(63)** and **(142a)** are the sources of o-hydroxybenzyl group found in uvaretin **(76)**, uvarenol **(95)**, chamanetin **(98)** and isochamanetin **(99)**. Also in dilute acid, compound **(142a)** rearranged to **(151)** via a more stable cyclohexadienyl cation intermadiate. (Kodpinid *et al*., 1984)

Scheme 5. Biosynthetic pathway of zeylena **(52)**, (-)-senepoxide**(47)** and (+)-pipoxide **(44)**



Similary, in **scheme 5**, Benzyl benzoate **(63)** was epoxidized to arene oxide intermediate **(142b),** and then rearranged to o-hydroxybenzyl benzoate **(151).** Intermediate **(126)** was added benzoic acid, acetic acid and cinnamic acid, eventually to afford compound **(42)**, **(153)** and **(154)**, respectively. Acylation and epoxidation of **(42)** and **(153)** yielded (-)-senepoxide **(47)** and (+)-pipoxide **(44)**, respectively. Compound **(154)** underwent intramolecular Diels-Alder reaction to give zeylena **(52)** (Kodpinid *et al.*, 1984).

1.4 Synthesis of Pipoxide Derivatives

Pipoxide was isolated in high yield from the leaves of *U. purpurea* Blume. Although pipoxide was found to be inactive against fungi and bacteria, it may act to decrease smooth muscle contraction in both intestine and blood vessel with, perhaps, similar mechanism(s) (Hiranyachattada *et al*., 2001). Thus, in this work, pipoxide will be used as a starting material to synthesize various derivatives for study of their biological activities.

1.5 Objectives

1. To investigate minor constituents from the leaves of *Uvaria purpurea* Blume.
2. To synthesize pipoxide derivatives.
3. To study their biological activities.