CHAPTER II

HISTORICAL

1. Chemical constituents of *Croton roxburghii* N.P. Balakr.

According to previous phytochemical studies, *Croton roxburghii* N.P. Balakr. has been found to be a rich source of diterpene. Up until now, eight main types of the diterpene skeletons have been found in this plant, namely pimarane, clerodane, cembrane, labdane, kaurane, cleistanthane, trachylobane and abietane. In addition to these diterpenes, steroids and several other chemical compounds are also presented, as summarized in Table 1.

Table 1. The chemical constituents of *Croton roxburghii* N.P. Balakr.

Constituents [figures]	Parts	References
1) Steroids		
• campesterol [1]	stem bark, wood	Chaicharoenpong, 1996; Surachethapan, 1996; Pattamadilok, 1998.

Constituents [figures]	Parts	References
• β-sitosterol [2]	stem bark, wood, leaf	Rao *et al.* 1968; Achayindee, 1996; Chaicharoenpong, 1996; Surachethapan, 1996; Pattamadilok, 1998; Bunta, 2000; Sirimongkon, 2000.
• stigmasterol [3]	stem bark, wood, leaf	Achayindee, 1996; Chaicharoenpong, 1996; Surachethapan, 1996; Pattamadilok, 1998; Bunta, 2000; Sirimongkon, 2000.
2) Steroid glycosides		
• stigmasteryl-3-*O*-β-D-glucopyranoside [4]	stem bark, wood	Chaicharoenpong, 1996; Surachethapan, 1996.
• campesteryl-3-*O*-βD-glucopyranoside [5]	stem bark, wood	Chaicharoenpong, 1996; Surachethapan, 1996.
• β-sitosteryl-3-*O*-β-D-glucopyranoside [6]	stem bark, wood	Chaicharoenpong, 1996; Surachethapan, 1996.

Constituents [figures]	Parts	References
3) Diterpenes		
3.1 Pimaranes		
• oblongifoliol [7]	stem bark	Rao, Sachdev and Singh, 1968.
• oblongifolic acid [8]	stem bark	Aiyar and Seshadri, 1970.
• *ent*-isopimara-7, 15-diene [9]	stem bark	Aiyar and Seshadri, 1971a; 1971b.
• *ent*-isopimara-7, 15-diene - 19-aldehyde [10]	stem bark	Aiyar and Seshadri, 1971a; 1971b.
• 19-hydroxy-*ent*-isopimara-7,15- diene [11]	stem bark	Aiyar and Seshadri, 1971a; 1971b.
• 3-deoxyoblongifoliol [12]	stem bark	Aiyar and Seshadri, 1971a; 1971b.
• 19-deoxyoblongifoliol [13]	stem bark	Aiyar and Seshadri, 1971a; 1971b.
• (-)-pimara-9(11), 15-diene-19-oic acid [14]	stem bark	Tanwattanakun, 1999.
• (-)-pimara-9(11), 15-diene-19-ol [15]	stem bark	Tanwattanakun, 1999.

Constituents [figures]	Parts	References
3.2 Clerodanes		
• (-) hardwickiic acid [16]	stem bark, root bark, wood	Aiyar and Seshadri, 1972a; 1972b; Surachethapan, 1996; Baiagern, 1999; Sirimongkon, 2000; Sriyangnok, 2000.
• 11-dehydro (-) hard-wickiic acid [17]	stem bark, root bark, wood	Aiyar and Seshadri, 1972a; 1972b.
• methyl-15, 16-epoxy-12-oxo-3,13(16),14-clerodatriene-20, 19-olide-17-oate [18]	stem bark	Tanwattanakun, 1999.
• (-)-20-benzyloxyhard - wickiic acid [19]	stem bark	Baiagern, 1999.
3.3 Cembranes		
• crotocembraneic acid [20]	stem bark	Surachethapan, 1996; Roengsumran *et al*, 1998.
• neocrotocembraneic acid [21]	stem bark, leaf	Achayindee, 1996; Roengsumran *et al.*, 1998.

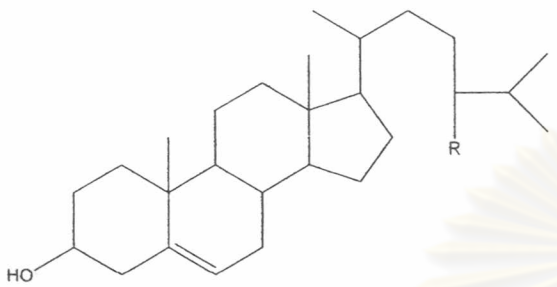
Constituents [figures]	Parts	References
• neocrotocembranal [22]	stem bark	Roengsumran *et al*, 1999b.
• (2*E*,7*E*,11*E*)-1-isopropyl-1,4-dihydroxy-4,8 -dimethylcyclotetradeca 2,7,11-triene-12-carboxylic acid [23]	stem bark	Tanwattanakun, 1999.
• poilaneic acid [24]	stem bark	Bunta, 2000.
3.4 Labdanes		
• *ent*-8(17), 12(*E*), 14-labdatrien-18-oic acid [25]	stem bark	Pattamadilok, 1998.
• 12,15-epoxy-8(17),12, 14-labdatriene [26]	stem bark	Pattamadilok, 1998.
• labda-7,12(*E*),14-triene [27]	stem bark	Roengsumran *et al*, 1999a.
• labda-7,12(*E*),14-triene-17-al [28]	stem bark	Roengsumran *et al*, 1999a.

Constituents [figures]	Parts	References
• labda-7,12(*E*),14-triene-17-ol [29]	stem bark	Roengsumran *et al.*, 1999a.
• labda-7,12(*E*),14-triene-7-oic acid [30]	stem bark	Roengsumran *et al.*, 1999a.
• 2-acetoxy-labda-8(17),12(*E*),14-triene-3-ol [31]	stem bark	Kuptiyanuwat, 1999.
• 3-acetoxy-labda-8(17), triene-2-ol [32]	stem bark	Kuptiyanuwat, 1999.
• labda-8(17),12(*E*),14-triene-2,3 diol [33]	stem bark	Kuptiyanuwat, 1999.
• labda-7,13(*Z*)-diene-17,12-olide [34]	stem bark	Baiagern, 1999.
• labda-7,13(*Z*)-diene-17,12-olide-16-ol [35]	stem bark	Baiagern, 1999.
• 12(*E*),14-labdadiene-7,8-diol [36]	stem bark	Bunta, 2000.
• 6-acetoxy-12(*E*),14-labdadiene-7,8-diol [37]	stem bark	Bunta, 2000.
• 12(*E*),14-labdadiene-6,7,8-triol [38]	stem bark	Bunta, 2000.

Constituents [figures]	Parts	References
3.5 Kaurane		
• *ent*-kaur-16-en-19-oic acid [39]	stem bark	Pattamadilok, 1998. Sirimongkon, 2000.
3.6 Cleistanthane		
• 3,4 seco-cleistantha-4(18),13(17),15-trien-3-oic acid [40]	stem bark	Siriwat, 1999. Sriyangnok, 2000.
3.7 Trachylobane		
• trachyloban-19-oic-acid [41]	stem bark	Bunta, 2000.
3.8 Abietane		
• abieta 7, 13-diene-3-one [42]	stem bark	Sriyangnok, 2000.
4) Triterpene		
• acetyl aleuritolic acid [43]	stem bark	Aiyar and Seshadri, 1971a; 1971b.

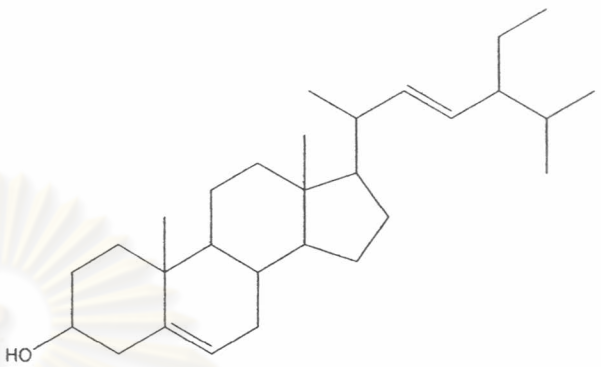
Constituents [figures]	Parts	References
5) **Coumarin**		
• 7-hydroxy-6-methoxy coumarin [44]	wood	Chaicharoenpong, 1996.
6) Ketone		
• 6,10,14-trimethyl-2-pentadecanone [45]	leaf	Achayindee, 1996.

1. Steroids



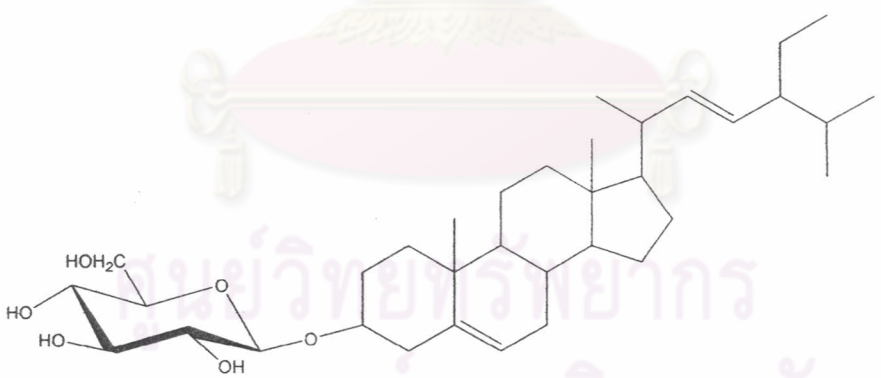
R = CH_3: campesterol [1]

R = C_2H_5: β- sitosterol [2]



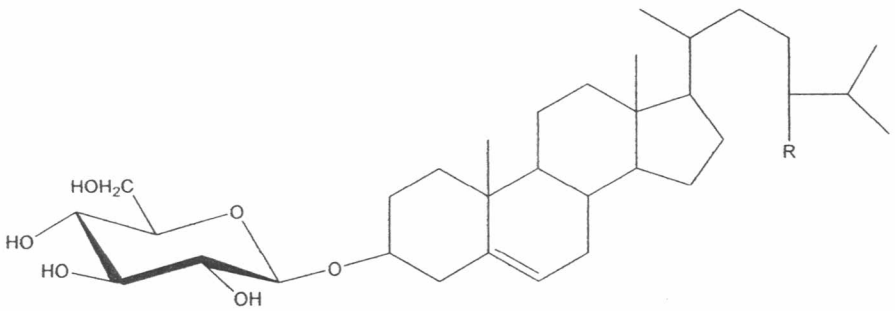
stigmasterol [3]

2. Steroid glycosides



stigmasteryl-3-*O*-β- D-glucopyranoside [4]

Figure 2: Chemical structures of constituents of *C. roxburghii*.

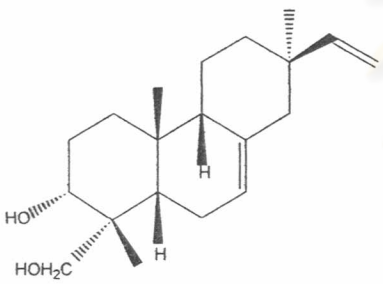


R = CH_3: campesteryl-3-*O*-*β*- D-glucopyranoside [5]

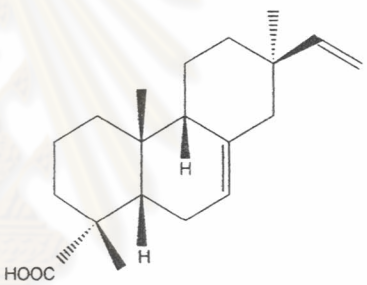
R = C_2H_5: *β*-sitosteryl-3-*O*-*β*- D-glucopyranoside [6]

3. Diterpenes

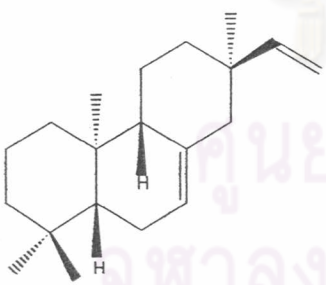
3.1 Pimaranes



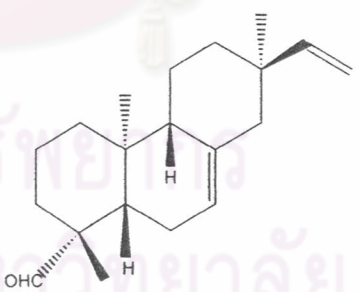
oblongifoliol [7]



oblongifolic acid [8]

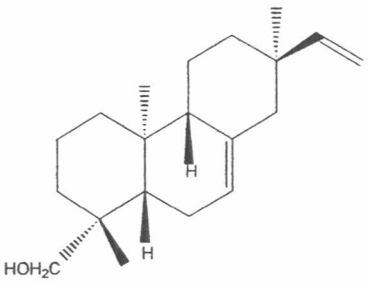


ent- isopimara-7,15 diene [9]

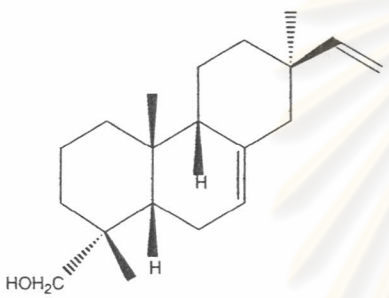


ent-isopimara-7,15 diene-19-aldehyde [10]

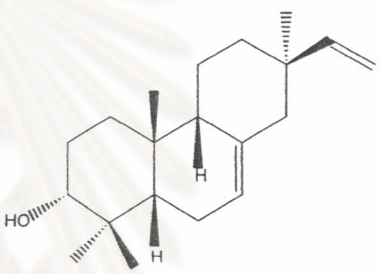
Figure 2: Chemical structures of constituents of *C. roxburghii*. (continued)



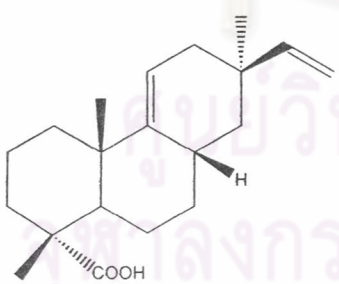
19-hydroxy- *ent*- isopimara-7,15 diene [11]



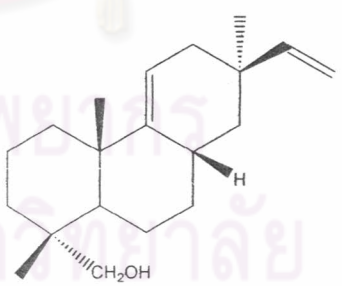
3-deoxyoblongifoliol [12]



19-deoxyoblongifoliol [13]



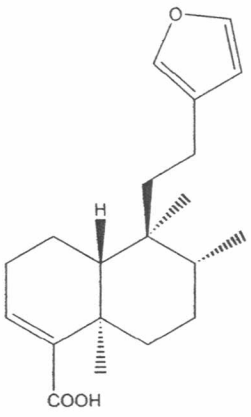
(-)-pimara-9(11),15-diene-19-oic acid [14]



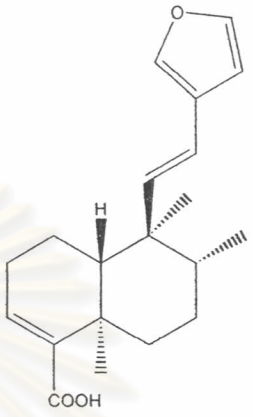
(-)-pimara-9(11),15-diene-19-ol [15]

Figure 2: Chemical structures of constituents of *C. roxburghii*. (continued)

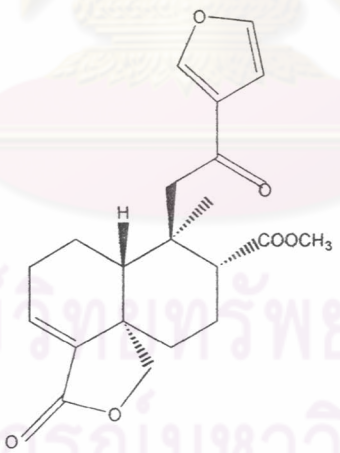
3.2 Clerodanes



(-) hardwickiic acid [16]

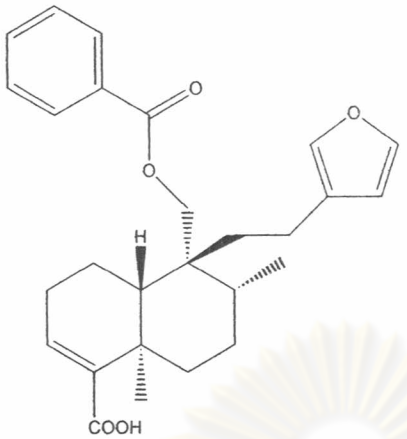


11-dehydro (-) hardwickiic acid [17]



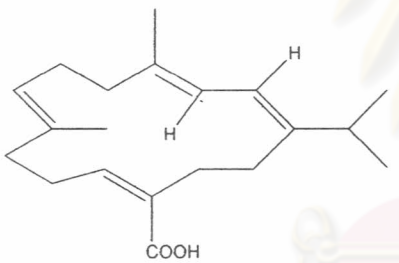
methyl-15,16-epoxy-12-oxo-3,13(16),14-clerodatriene-20,19-olide-17-oate [18]

Figure 2: Chemical structures of constituents of *C. roxburghii*. (continued)

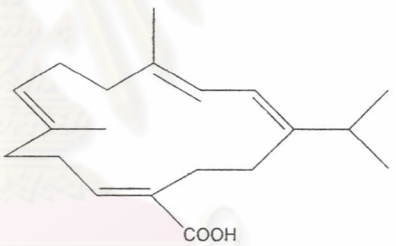


(-)-20-benzyloxyhardwickiic acid [19]

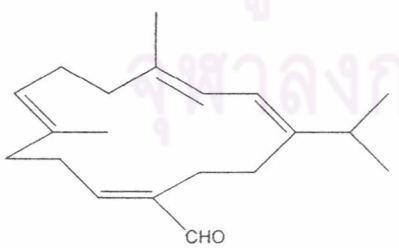
3.3 Cembranes



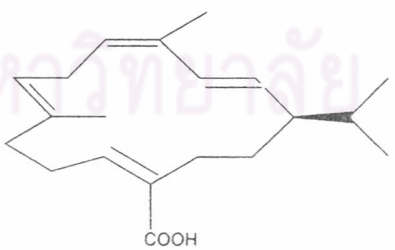
crotocembraneic acid [20]



neocrotocembraneic acid [21]

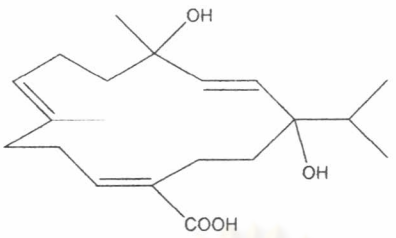


neocrotocembranal [22]



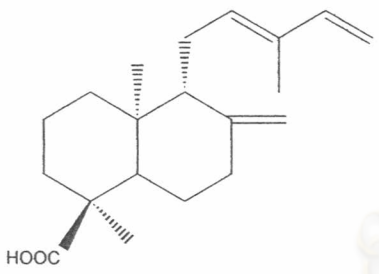
poilaneic acid [24]

Figure 2: Chemical structures of constituents of *C. roxburghii*. (continued)

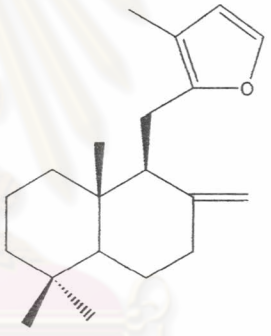


(2*E*,7*E*,11*E*)-1-isopropyl-1,4-dihydroxy-4,8-dimethyl-cyclotetradeca-2,7,11-triene-12-carboxylic acid [23]

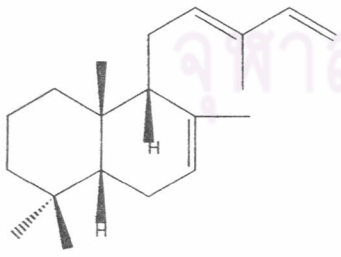
3.4 Labdanes



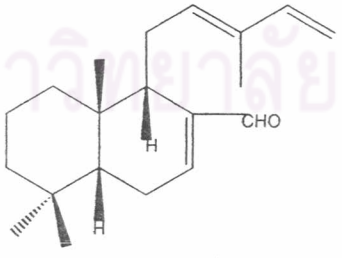
ent-8(17),12(*E*),14-labdatrien-18-oic acid [25]



12,15-epoxy-8(17),12,14-labadtriene [26]

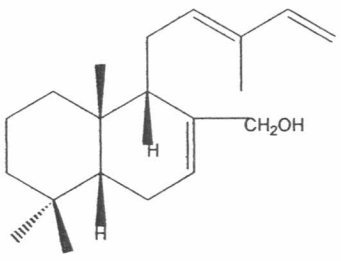


labda-7,12(*E*),14-triene [27]

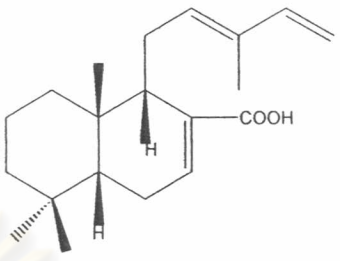


labda-7,12(*E*),14-triene-17-al [28]

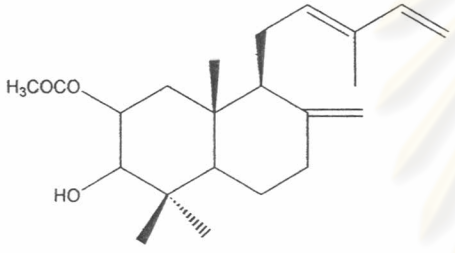
Figure 2: Chemical structures of constituents of *C. roxburghii*. (continued)



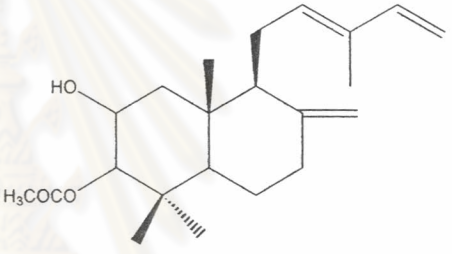
labda-7,12(*E*),14-triene-17-ol [29]



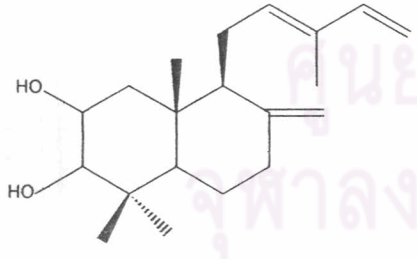
labda-7,12(*E*),14-triene-17-oic acid [30]



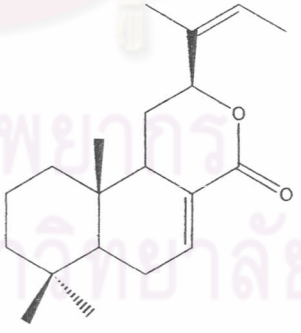
2-acetoxy-labda-8(17),12(*E*),
14-triene-3-ol [31]



3-acetoxy-labda-8(17),12(*E*),
14-triene-2-ol [32]

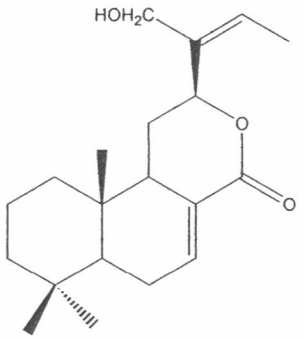


labda-8(17),12(*E*),14-triene-2,3-diol [33]

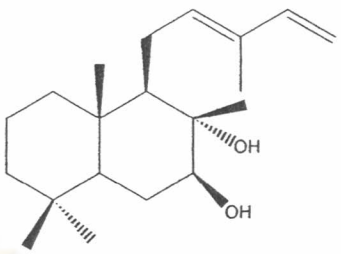


labda-7,13(*Z*)-diene-17,12-olide [34]

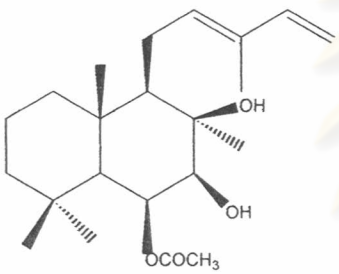
Figure 2: Chemical structures of constituents of *C. roxburghii*. (continued)



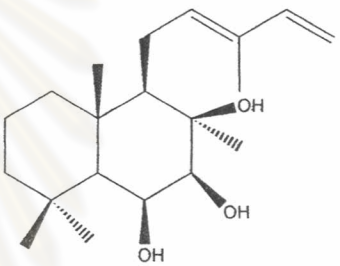
labda-7,13(*Z*)-diene-17,12-olide-16-ol [35]



12(*E*),14-labdadiene-7,8-diol [36]

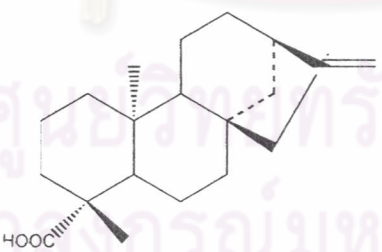


6-acetoxy-12(*E*),14-labdadiene-7,8-diol [37]



12(*E*),14-labdadiene-6,7,8-triol [38]

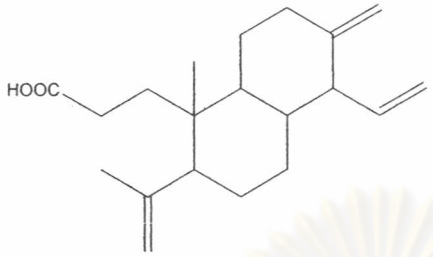
3.5 Kaurane



ent- kaur-16-en-19-oic acid [39]

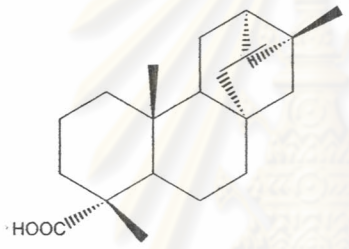
Figure 2: Chemical structures of constituents of *C. roxburghii*. (continued)

3.6 Cleistanthane



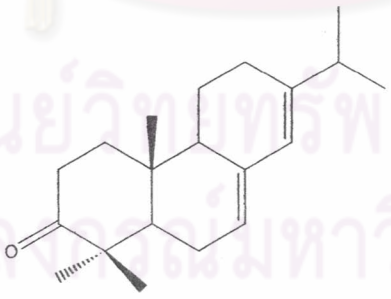
3,4 seco-cleistantha-4(18),13(17),15-trien-3- oic acid [40]

3.7 Trachylobane



trachyloban-19-oic –acid [41]

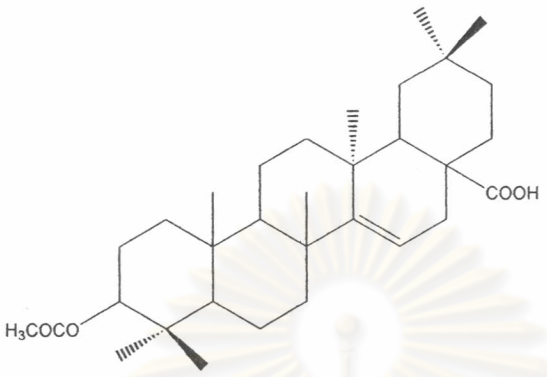
3.8 Abietane



abieta- 7,13-diene-3-one [42]

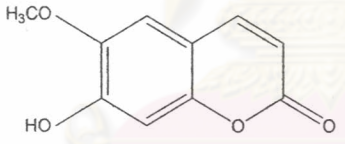
Figure 2: Chemical structures of constituents of *C. roxburghii*. (continued)

4. Triterpenes



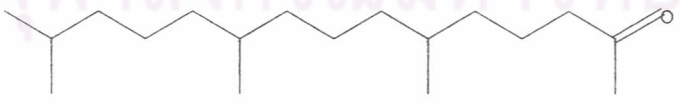
acetyl aleuritolic acid [43]

5. Coumarin



7-hydroxy-6-methoxycoumarin [44]

6. Ketone



6,10,14-trimethyl-2-pentadecanone [45]

Figure 2: Chemical structures of constituents of *C. roxburghii*. (continued)

Some of the diterpene compounds listed in Table 1 have been shown to exhibit *in vitro* cytotoxicity against many human tumor cell lines, as summarized below.

Table 2. Cytotoxicity data of the diterpenes from *Croton roxburghii*

Compounds	IC_{50}(μg/ml)				
	KATO-3	SW620	BT474	HEP-G2	CHAGO
[15]	6.5	5.9	>10	6.7	6.1
[31]	5.7	7.1	>10	>10	>10
[32]	3.3	>10	5.9	>10	>10
[33]	2.2	2.7	4.6	3.7	3.3
[35]	7.1	6.5	>10	5	6.4

[15] = (-)-pimara-9(11),15-diene-19-ol

[31] = 2-acetoxy-3-hydroxy-labda-8(17),12(*E*)-14-triene

[32] = 3-acetoxy-2-hydroxy-labda-8(17),12(*E*)-14-triene

[33] = 2,3-dihydroxy-labda-8(17),12(*E*)-14-triene

[35] = labda-7,13(*Z*)-diene-17,12-olide-16-ol

Tumor cell lines:

KATO-3 = human gastric carcinoma

SW620 = human colon adenocarcinoma

BT474 = human breast ductol carcinoma

HEP-G2 = human liver hepatoblastoma

CHAGO = human undifferentiated lung carcinoma

From the data in Table 2 it is very interesting to see that, among the three structurally related labdane diterpenes [31-33], [31] and [32] were less active but more selective than[33]. The presence of the acetyl group is believed to be able to form hydrogen bond with certain receptor on tumor cells and make them more selective but less active (Roengsumran *et al.*, 2001).

Another notable compound derived from this plant, apart from those already shown in Table 2, is neocrotocembranal [22]. This compound inhibited platelet aggregation induced by thrombin with an IC_{50} value of 47.21 μg/ml and exhibited cytotoxicity against P-388 (lymphoid neoplasm) cells *in vitro* with an IC_{50} value of 6.48 μg/ml. However, two other tested cembranoid diterpenes, crotocembraneic acid [20] and neocrotocembraneic acid [21], showed no inhibitory effect on platelet aggregation. Thus, the reactive aldehyde functionality was proposed as playing an important part in this effect (Roengsumran *et al.*, 1999b).

Furthermore, (-)-hardwickiic acid[10], a well-known clerodane diterpene, has been reported as having insecticidal activity against *Aphis craccivora* (Aphidae). The compound at a dose of 5 ppm./insect caused 62% mortality of adult female aphids after 24 hours (Bandara, Wimalasiri and Bandara, 1987) and exhibited antimicrobial activity against gram-positive bacteria (*Bacillus subtilis, Staphylococcus aureus*) and *Mycobacterium smegmatis*. (Jame, Slice and Edilberto, 1991).

2. Biogenetic pathway of diterpenes in *Croton roxburghii* N.P. Balakr.

The diterpenes are C_{20} compounds biogenetically derived from geranylgeranyl pyrophosphate. The notable feature of diterpene structures is the fascinating variation encountered in their skeletons, which accounts for the division of these compounds into several types (Devon and Scott, 1972). The following correlation chart shows the main diterpene skeletons found in *Croton roxburghii* N.P. Balakr.

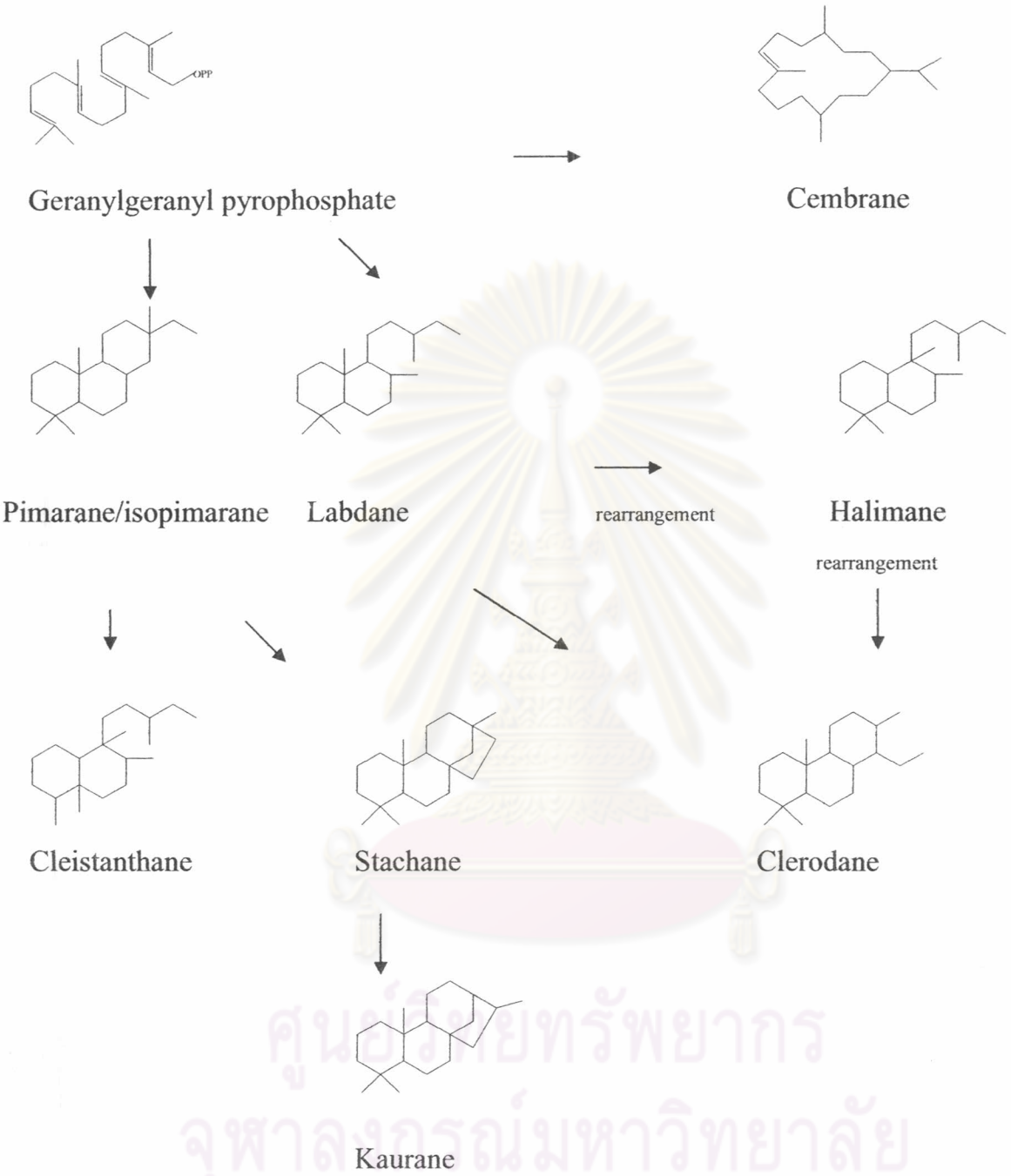


Figure 3: Biogenetic pathway of diterpenes in *Croton roxburghii* N.P. Balakr.

3. Labdane diterpenes

A large member of labdane diterpenes can be found in nature and occur in both enantiomeric series. These labdane diterpenes from both plants and marine sources have shown various biological activities (Singh, Pal and Sharma, 1999), as shown in Table 3.

Table 3. The biological activity of labdane diterpenes in nature

Activity	Sources	Chemical compound
Antibacterial	*Cistus incanus* subsp. *creticus* (L.) Heywood.	• 5*R*,8*R*,9*R*,10*R*-labdan-13(*E*)-ene-8a, 15-diol [46] • 5*R*,8*R*,9*R*,10*R*-labdan-13(*E*)-ene-8a-ol-15-yl acetate [47] • 5*R*,9*R*,10*R*-labdan-7,13(*E*)-dien-15-ol [48] • 8,13,-epoxylabdan-14-ene [49] • 8,13-epoxy-13-*epi*-labdan-14-ene [50] • labdan-14-ene-8,13-diol [51] • 13-episclareol [52]
	Viburnum suspensum L.	• gomojosides A-Q [53-69]
	Mycale sp.	• mycaperoxides A, B [70,71]

Activity	Sources	Chemical compound
	Potamogeton nodosus Poir. *(P. indicus* Roxb.*)*	• 15,16-epoxy-12-oxo-8(17), 13(16),14-labdatrien-20,19-olide [72]
	Salvia leriaefolia Benth.	• 8(17),12(*E*),14-labdatrien-6,19-olide [73]
Antifungal	*Alpinia galanga* (L.) Willd.	• galanals A, B [74,75] • galanolactone [76] • (*E*)-8(17),12-labdadiene-15,16-dial [77] • (*E*)-8*β*(17)-epoxylabd-12-ene-15,16-dial [78]
	Aframomum daniellii (Hook.f) K. Schum.	• (*E*)-8(17),12-labdadiene-15,16-dial [77] • (*E*)-8*β*(17)-epoxylabd-12-ene-15,16-dial [78]
	Cistus incanus subsp. *creticus* (L.) Heywood.	• 5*R*,8*R*,9*R*,10*R*-labdan-13(*E*)-ene-8a, 15-diol [46] • 5*R*,8*R*,9*R*,10*R*-labdan-13(*E*)-ene-8a-ol-15-yl acetate [47]

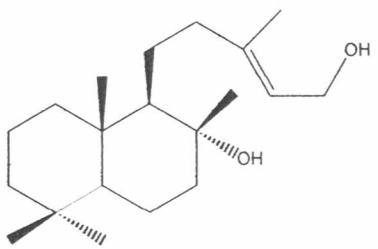
Activity	Sources	Chemical compound
		• 5*R*,9*R*,10*R*-labdan-7,13(*E*)-dien-15-ol [48] • 8,13-epoxylabdan-14-ene [49] • 8,13-epoxy-13-*epi*-labdan-14-ene [50] • labdan-14-ene-8,13-diol [51] • 13-episclareol [52]
	Renealmia alpinia (Rottb.) Maas.	• 11-hydroxy-8(17),12(*E*)-labdadien-15,16-dial-11,15-hemiacetal [79] • 16-oxo-8(17),12(*E*)-labdadien-15-oic acid [80] • 8(17),12(*E*)-labdadien-15,16-dial [81]
Antiviral	*Mycale* sp.	• mycaperoxides A, B [70, 71]

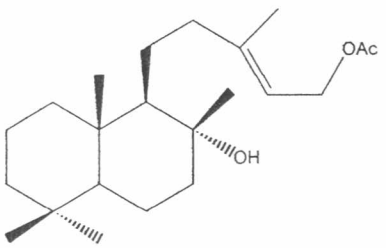
Activity	Sources	Chemical compound
Antiinflammatory	*Cryptomeria japonica* D.Don.	• *cis*-communic acid [82] • imbricatolic acid [83] • isocupressic acid [84]
Cardiotonic	*Melodinus monogynus.*	• medigenin [85] • medigenin acetate [86]
Cytotoxic	*Hedychium coronarium* Koeng.	• (*E*)-labda-8(17),12-diene-15,16-dial [87] • coronarins A-D [88-91]
	Cistus incanus subsp. *creticus* (L.) Heywood.	• 5*R*,8*R*,9*R*,10*R*-labdan-13(*E*)-ene-8a, 15-diol [46] • 5*R*,8*R*,9*R*,10*R*-labdan-13(*E*)-ene-8a-ol-15-yl acetate [47] • 5*R*,9*R*,10*R*-labdan-7,13(*E*)-dien-15-ol [48] • 8,13,-epoxylabdan-14-ene [49] • 8,13-epoxy-13-*epi*-labdan-14-ene [50] • labdan-14-ene-8,13-diol [51]

Activity	Sources	Chemical compound
		• 13-episclareol [52] • ribenol [92] • ribenol acetate [93] • 8,13-epoxylabdan-14-ene [94] • 5*R*,8*R*,9*R*,10*R*-labdan-13(*E*)-ene-8a, 15-diol [95] • 5*R*,9*R*,10*R*-labdan-7,13(*E*)-dien-15-ol [96] • 5*R*,9*R*,10*R*-labdan-7,13(*E*)-dien-15- yl acetate [97]
	Andrographis paniculata Nees.	• andrographolide [98] • andrographiside [99] • 14-*epi*- andrographolide [100] • isoandrographolide [101] • 14-deoxy- andrographolide [102] • deoxyandrographolide [103]

Activity	Sources	Chemical compound
		• 14-deoxy- 12-methoxyandro grapholide [104] • 12-*epi*-14-deoxy- 12-methoxy andrographolide [105] • 14-deoxy-12-hydroxyandro grapholide [106] • 14-deoxy- 11-hydroxyandro grapholide [107] • 14-deoxy-11, 12-didehydro andrographolide [108] • 14-deoxy-11, 12-didehydro andrographiside [109] • neoandrographolide [110] • 6′-acetylneoandrographolide [111] • bisandrographolides A-D [112-113]
	Alomia myriadenia Schultz-Bip ex Baker.	• 12*S*,16-dihydroxy-*ent*-labda-7,13-dien-15,16-olide [114]

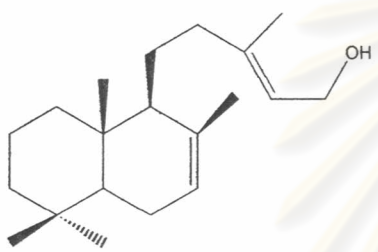
Activity	Sources	Chemical compound
	Ronealmia alpinia (Rottb.) Maas.	• 11-hydroxy-8(17), 12(*E*)-labdadien-15,16-dial-11,15-hemiacetal [79] • 16-oxo-8(17),12(*E*)-labdadien -15-oic acid [80] • 8(17),12(*E*)-labda dien-15,16-dial [81]
Inhibitors of β-glucuro-nidase	*Scoparia dulcis* L.	• scoparic acid A [115]
Inhibitor of DNA poly-merase	*Hardwickia binata* Roxb.	• harbinatic acid [116]

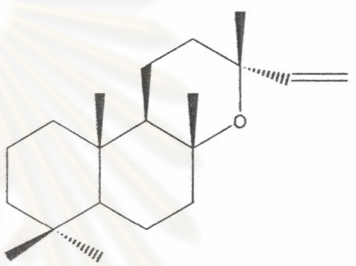




5*R*,8*R*,9*R*,10*R*-labdan-13(*E*)
-ene-8a, 15-diol [46]

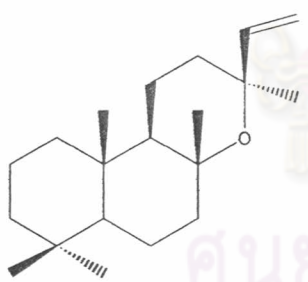
5*R*,8*R*,9*R*,10*R*-labdan-13(*E*)-ene-
8a-ol-15-yl acetate [47]

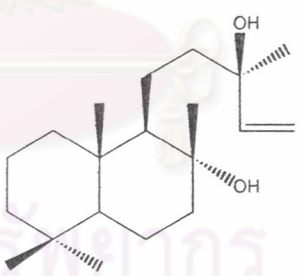




5*R*,9*R*,10*R*-labdan-7,13(*E*)-dien-15-ol [48]

8,13 -epoxylabdan-14-ene [49]

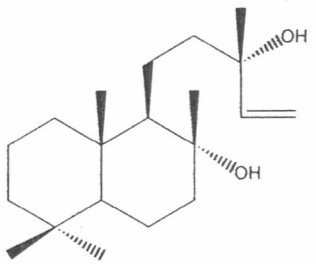




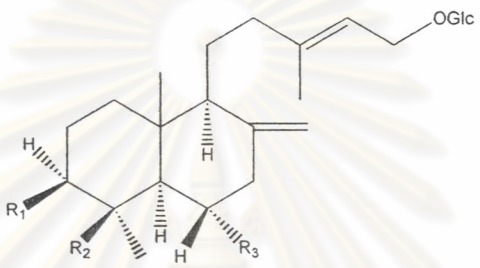
8,13-epoxy-13-*epi*-labdan-14-ene [50]

labdan-14-ene-8,13-diol [51]

Figure 4: Structures of labdane diterpenes

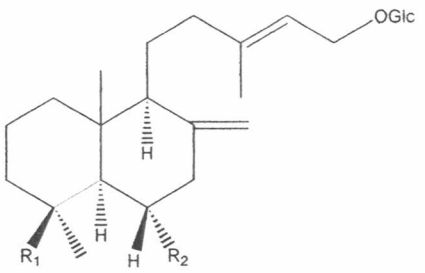


13-episclareol [52]

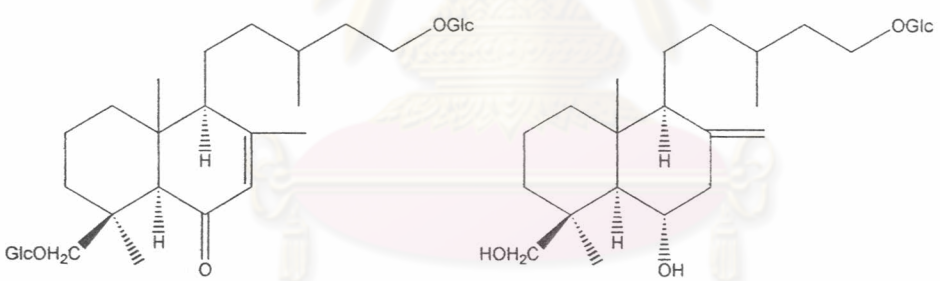


	R_1	R_2	R_3	
gomojoside A	H	COOGlc	H	[53]
gomojoside C	H	CH_2OGlc	H	[54]
gomojoside E	H	CH_2OGlc	OH	[55]
gomojoside H	H	CH_3	OGlc	[56]
gomojoside J	OGlc	CH_3	H	[57]

Figure 4: Structures of labdane diterpenes (continued)

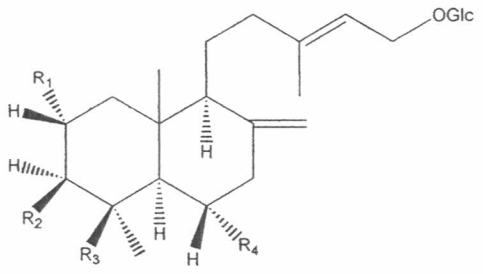


	R_1	R_2	
gomojoside B	COOGlc	H	[58]
gomojoside D	CH_2OGlc	H	[59]
gomojoside F	CH_2OGlc	OH	[60]
gomojoside I	CH_3	OGlc	[61]

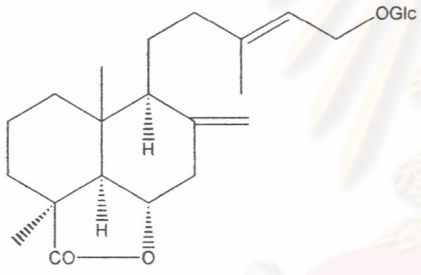


gomojoside G [62] gomojoside L [63]

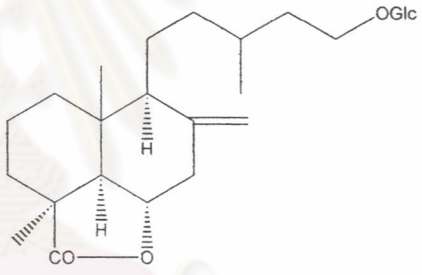
Figure 4: Structures of labdane diterpenes (continued)



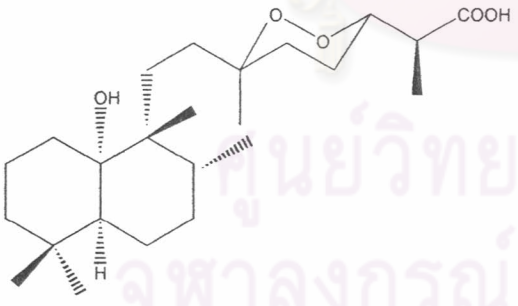
	R_1	R2	R_3	R_4	
gomojoside K	OH	OH	CH_2OH	OH	[64]
gomojoside M	H	OH	CH_2OH	H	[65]
gomojoside N	OH	H	CH_2OH	H	[66]
gomojoside O	H	OH	CH_3	OH	[67]



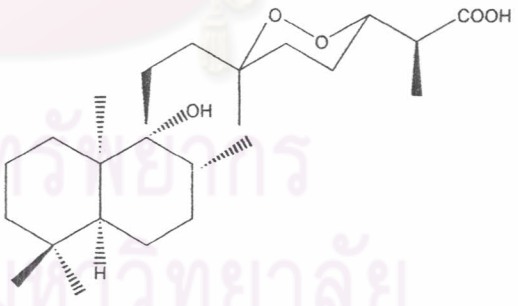
gomojoside P [68]



gomojoside Q [69]

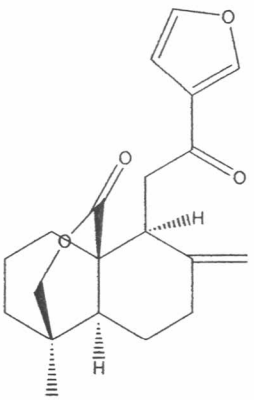


mycaperoxide A [70]

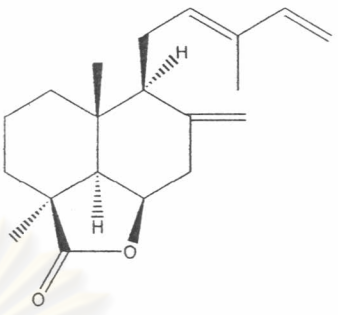


mycaperoxide B [71]

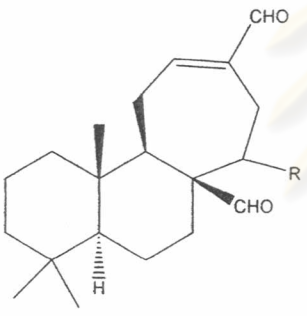
Figure 4: Structures of labdane diterpenes (continued)



15,16-epoxy-12-oxo-8(17), 13(16), 14-labdatrien-20,19-olide [72]

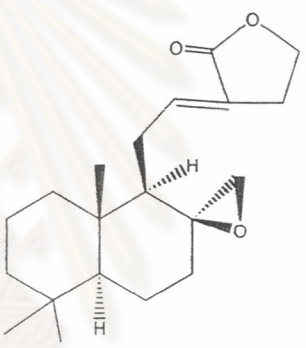


8(17),12(*E*),14-labdatrien-6,19-olide [73]

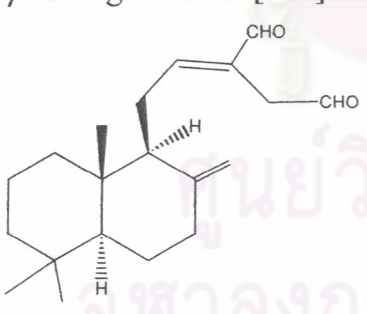


R = α-OH galanal A [74]

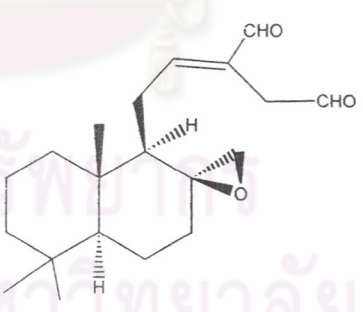
R = *β*-OH galanal B [75]



galanolactone [76]

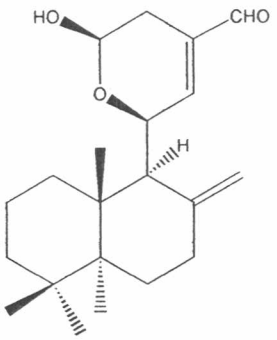


(*E*)-8(17),12-labddiene-15,16-dial [77]

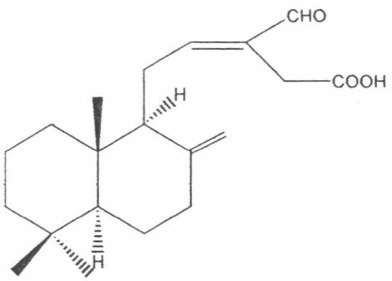


(*E*)-8*β*(17)-epoxylabd-12-ene-15,16-dial [78]

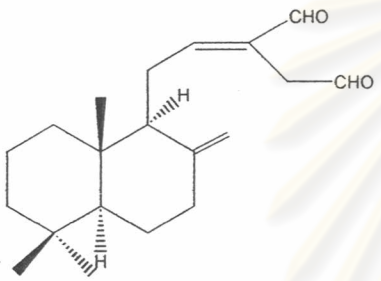
Figure 4: Structures of labdane diterpenes (continued)



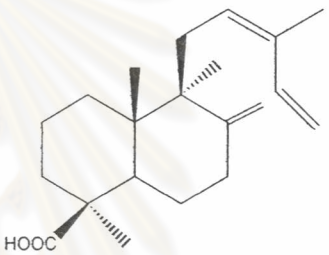
11-hydroxy-8(17),12(*E*)-labdadien-15,16-dial-11,15-hemiacetal [79]



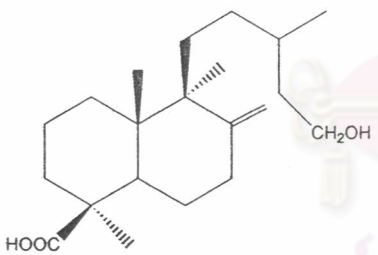
16-oxo-8(17),12(*E*)-labdadien-15-oic acid [80]



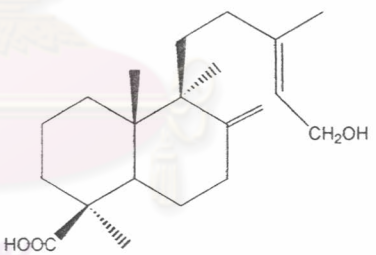
8(17),12(*E*)-labdadien-15,16-dial [81]



cis-communic acid [82]

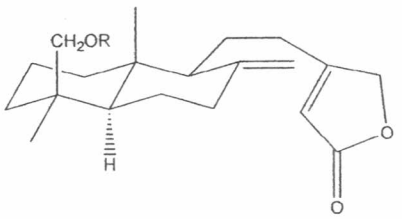


imbricatolic acid [83]



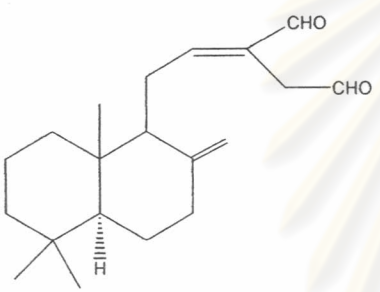
isocupressic acid [84]

Figure 4: Structures of labdane diterpenes (continued)

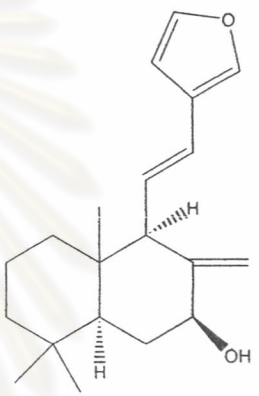


R = H medigenin [85]

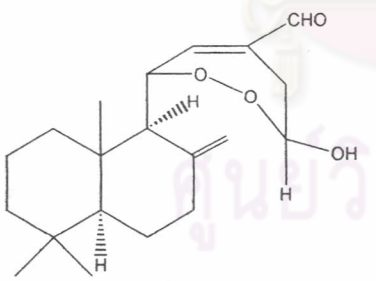
R = Ac medigenin acetate [86]



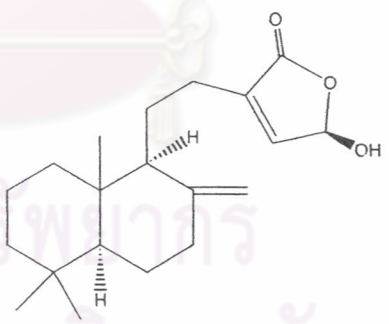
(*E*)-labda-8(17),12-diene-15,16-dial [87]



coronarin A [88]

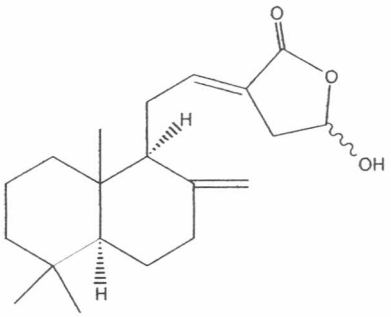


coronarin B [89]

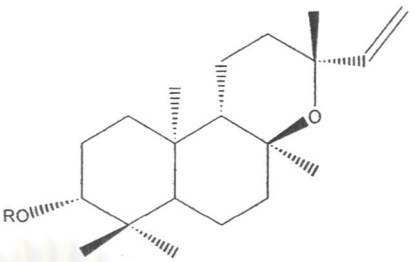


coronarin C [90]

Figure 4: Structures of labdane diterpenes (continued)

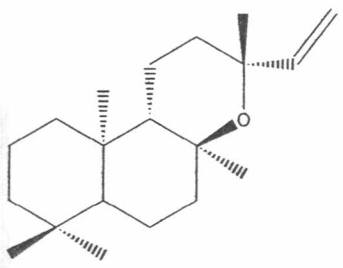


coronarin D [91]

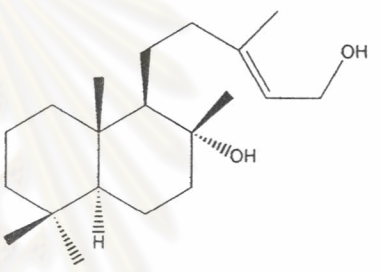


R = H ribenol [92],

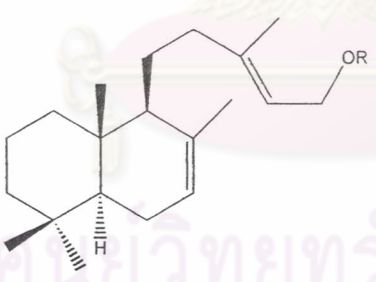
R = Ac ribenol acetate [93]



8,13-epoxylabdan-14-ene [94]



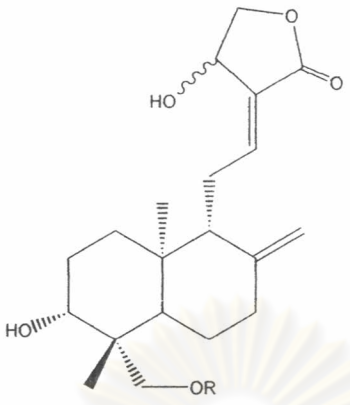
5*R*,8*R*,9*R*,10*R*-labdan-13(*E*)-ene-8a, 15-diol [95]



R = H 5*R*,9*R*,10*R*-labdan-7,13(*E*)-dien-15-ol [96]

R = Ac 5*R*,9*R*,10*R*-labdan-7,13(*E*)-dien-15- yl acetate [97]

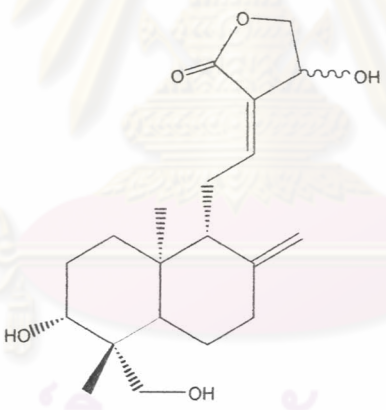
Figure 4: Structures of labdane diterpenes (continued)



14 ∝ -OH, R = H andrographolide [98]

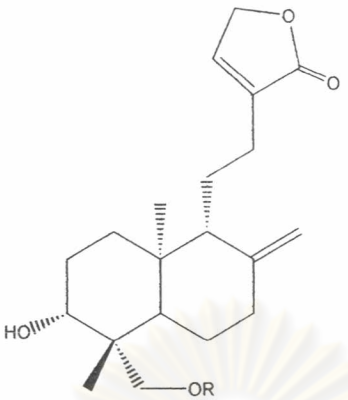
14 ∝ -OH, R = glc andrographiside [99]

14 β -OH, R = H 14-*epi*- andrographolide [100]



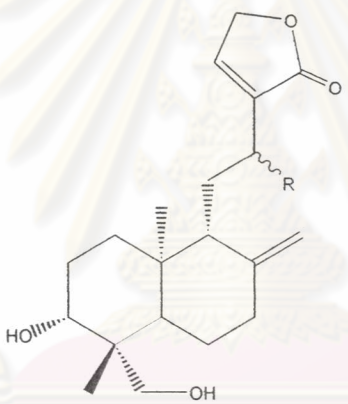
isoandrographolide [101]

Figure 4: Structures of labdane diterpenes (continued)



R = H 14-deoxy- andrographolide [102]

R = Glc deoxyandrographolide [103]

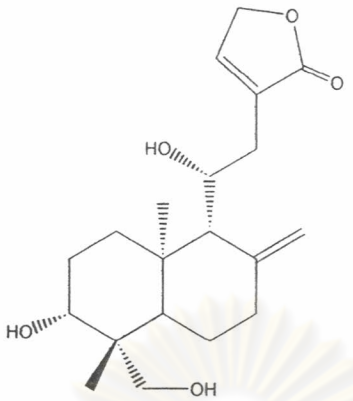


R = ∝ or β- OCH_3 14-deoxy- 12-methoxyandrographolide [104]

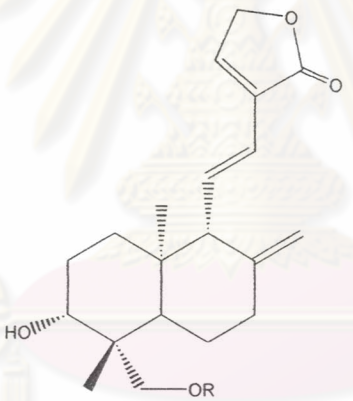
R = β or ∝- OCH_3 12-*epi*-14-deoxy- 12-methoxyandrographolide [105]

R = ∝ or β- OH 14-deoxy-12-hydroxyandrographolide [106]

Figure 4: Structures of labdane diterpenes (continued)



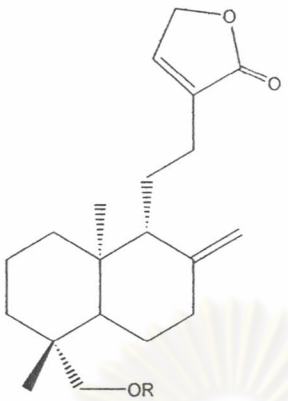
14-deoxy - 11-hydroxyandrographolide [107]



R = H 14-deoxy-11, 12-didehydroandrographolide [108]

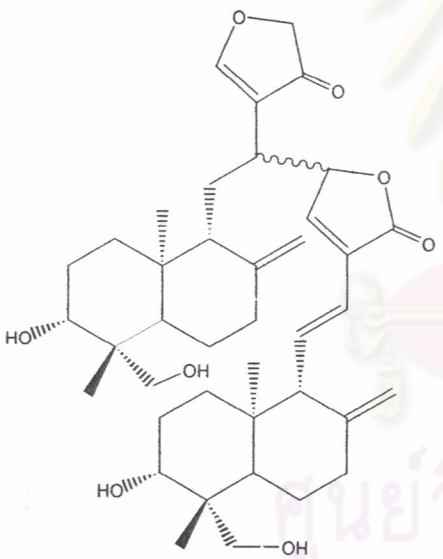
R = Glc 14-deoxy-11, 12-didehydroandrographiside [109]

Figure 4: Structures of labdane diterpenes (continued)

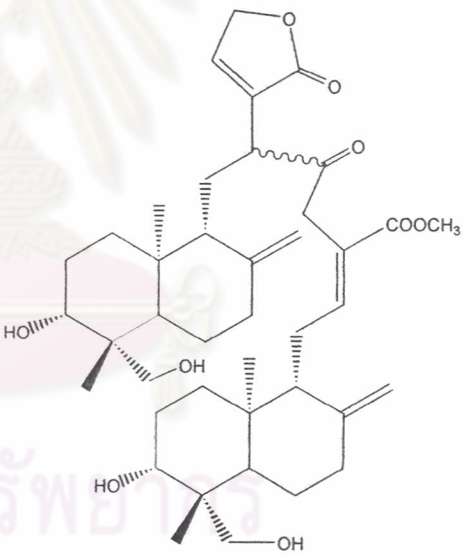


R = Glc neoandrographolide [110]

R = Glc-6-Ac 6′-acetylneoandrographolide [111]

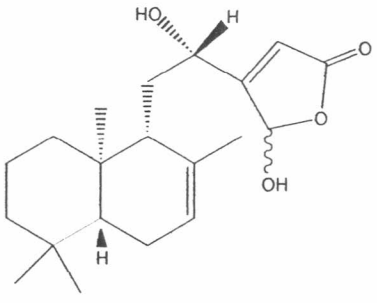


bisandrographolide A, B, C [112]

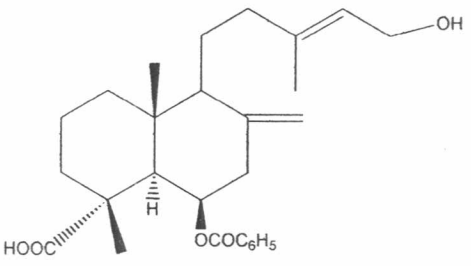


bisandrographolide D [113]

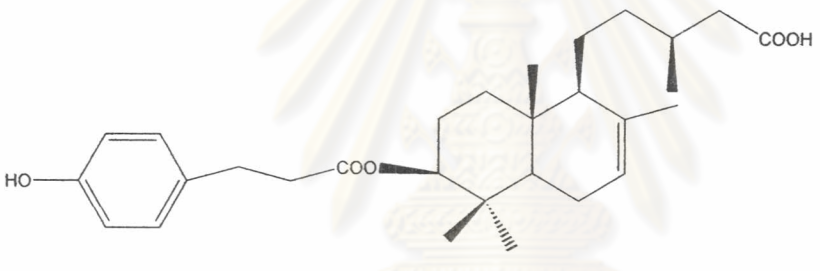
Figure 4: Structures of labdane diterpenes (continued)



12*S*,16-dihydroxy-*ent*-labda-7,13-dien-15,16-olide [114]



scoparic acid A [115]



harbinatic acid [116]

Figure 4: Structures of labdane diterpenes (continued)