

Chapter II

Historical

Botanical aspects of the family Lauraceae.

The family Lauraceae comprises of about 32 genera and around 2,000-3,000 species distributed in tropic and subtropic regions of both hemispheres with the greatest diversity in Southeast Asia (Hutchinson, 1964; Jones, 1979). Man have used the lauraceous plants for timbers, edible fruits, seed fats, drugs and perfume oil (Gottlieb, 1972). The family can be divided into two subfamilies: Lauroideae, which is arborescent and Cassythaideae, with the parasitic twiner such as *Cassytha*.

Lauroideae is further classified into five tribe:-

Perseae (*Persia*), Cinnamomeae (*Cinnamomum*), Litseeae (*Litsea*), Cryptocaryeae (*Cryptocarya*) and Hypodaphnideae (*Hypodaphnis*).

According to Kosterman's classification, *Litsea* is a genus of small tree belonging to the subtribe Litseinneae of the tribe Litseeae within the subfamily Lauroideae. (Backer and Bakhuizen, 1965).

The Lauraceae is characterized as a family of aromatic tree or shrubs, leaves usually alternate, perianth small and undifferentiated; stamens 3-numerous in several whorls, anthers with valvate dehiscence, fruit a single seeded drupe or berry (Jones, 1979).

The genus *Litsea* is usually evergreen trees or shrubs. Leaves alternate, penninerved or rarely tri-basal-nerved. Flowers small, dioecious, umbellate; umbels few or many flowered, pedunculate, axillary or from the scars of fallen leaves. Fruit a

succulent drupe seated on the much enlarged perianth-tube which is 6-toothed or irregularly lobed (Lalbot, 1976) .

According to The Royal Forest Department's Thai Plant Names, 19 species of *Litsea* are in Thailand (Smittinand, 1980). They are as follows:-

<i>Litsea baviensis</i> Lec.	สุรามะริด	Suraamarit (Lampang)
<i>L. elliptica</i> Boerl.	ท่ามั่ง	Thammang (Surat Thani)
<i>L. euosma</i> W.W.Smith	ชะไคว้ดั้น	Sakhraiton (Chiang Mai);
	เหล็กลีชีดั้น	Lek chee din (Phetchabun)
<i>L. garrettii</i> Gamble	ตะไคว้ดั้น	Takhraiton (Chiang Mai);
	เมียดดั้น	Miat ton (Loei)
<i>L. glutinosa</i> C.B.Robinson	หมี่เหม็น	Mee men (Northern, Chon Buri)
<i>L. grandis</i> Hook.f.	กะทังใบใหญ่	Ka thang bai yai (Penninsular)
<i>L. johorensis</i> Gamble	แปง	Pae nguu (Pattani)
<i>L. lancifolia</i> Hook.f.	หมอรัต	Mo rat (Surat Thani)
<i>L. leiantha</i> Hook.f.	ท่ามั่ง	Thammang (Surat Thani)
<i>L. megacarpa</i> Gamble	ทังช่อ	Thang cho (Surat Thani)
<i>L. monopetala</i> Pers.	กะทัง	Kathang (Penninsular)
<i>L. myristicaefolia</i> Hook. f.	ตริด	Trit (Trang),
<i>L. perakensis</i> Gamble	ตารีด	Taareet (Trang)
<i>L. petiolata</i> Hook.f.	ท่ามั่ง	Thammang (Penninsular)

<i>L. pierrei</i> Lec.	ตานหก	Taan hok (Prachin Buri)
<i>L. resinosa</i> Bl.	ท่ามั่งพอกรวง	Thammang phokrong (Nakorn Si Thammarat)
<i>L. semecarpifolia</i> Hook.f.	ช่อข้าวสุก	Cho Khaao suk (Chiang Mai)
<i>L. umbellata</i> Merr.	พินปลา	Fan plaa (Chanthaburi)
<i>L. cubeba</i> Pers.	จะไค้ตัน	Chakhaiton (Chiang Mai);
	ตะไคร้	Takhrai (Kanchanaburi);
	ตะไคร้ตัน	Takhrai ton (Loei)

synonym: *Laurus cubeba* Lour. , *Actinodaphne citrata* (Blume) Hayata, *Benzoin cubeba* (Lour.) Hatusima, *Litsea citrata* Blume.(Grierson and Long, 1984; Li *et al.*, 1976)

L. cubeba is a small tree indigenous to Thailand at the attitude of over 1,200 meter. This plant is wide spread through India, China and Southeast Asia. It is distributed naturally in mix-forest and has been cultivated in Formosa, Java and China. A citral rich oil can be isolated from the fruit-skin, seed, leaf and bark. This oil called Chinese lemon-grass oil offers competition to the Indian-grass oil in world market (Zytchi,1989).

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Botanical characteristics of *L. cubeba* are as follows:-

Leaves (when bruised) heavily smelling of lemon, distinctly but finely pellucid-dotted, mature ones glabrous, oblong or lanceolate, long-acuminate, herbaceous or thinly coriaceous, glaucous beneath, 7-15 cm. by 1.5-3 cm.; lateral nerves 8-12 on either side of midrib, slightly prominent beneath; petiole 0.75-1.75 cm.; apices of stem densely short-hairy, glabrescent, black. Involucres arranged in umbelliform racemes 0.25-1 cm. long, glabrous without; 5-flowered; flowers dioecious; tepals 5-6, yellowish, glabrous without, 1.5 -2.5 mm. long; stamens or staminodes 9, sparsely hairy; gland sessile; fruiting pedicles 3-5 mm.; receptacle cup shaped; berry globose, black, 5-6 mm.diameter. Tree 3-10 m. high; flowering (or in absence of flowers, fruiting) from January to December (Backer *et al.*, 1965). Occurring from 300-1,500 m. over sea-level (Grierson and Long, 1984).

Ethnopharmacological aspects of *L. cubeba*

L. cubeba has been employed in folk medicine in many countries (Perry and Metzger, 1980) for example :-

- China : The berries are carminative, stomachic, expectorant, a treatment for hernia, bronchitis, and dyspepsia .
The roots are an ingredient of a medicine given after childbirth.
The bark of root branches, and the leaves are employed against athlete's foot and other skin diseases.
- Indo-China: A decoction is useful in case of vertigo, hysterical affections, paralysis, melancholy or forgetfulness.
- Indonesia: The fruits may be used as a substitute for those of *Piper cubeba*.
- Australia: The seeds are used as a substitute for common salt by the aborigines in the mountains.
The oleoresin from the root and the fruit (collected just before the fruit turns red) may be a part of some medicines.



Figure 1 *Litsea cubeba* (Lour.) Pers.

1. fruiting branch; 2. flowering branch ; 3. flowers ; 4. dissected flower ; 5. glandular stamen ; 6. eglandular stamen (Li *et al.*, 1976).

Alkaloids isolated from lauraceous plants

Laurotetanine (IV₃₄) is the first alkaloid found in lauraceous plant, was isolated from *Actinodaphne procera* Nees and *Litsea chrysocoma* Blume (Greshoff, 1890). In 1978, Ralph and coworkers summarized the lauraceous alkaloids which isolated from 103 species of 19 genera. There are about 105 alkaloids of 15 structural types (Ralph *et al.*, 1978). Currently, the occurrence of alkaloids found in Lauraceae are about 180 alkaloids from 143 species of 22 genera and almost all of them are isoquinoline type. The alkaloids and their sources are summarized in Table I.

Table I Alkaloids of the Lauraceae

<u>Plant species</u>	<u>Alkaloids</u>	<u>Formulae</u>	<u>Reference</u>
<i>Actinodaphne ocutive</i> (Hayata)Nakai	laurolitsine	IV ₃₃	Lu <i>et al.</i> , 1969.
<i>A. hookeri</i> Meissn.	actinodaphnine	IV ₁	Ghose <i>et al.</i> , 1969.
<i>A. nitida</i> Teschn.	boldine	IV ₅	Johns <i>et al.</i> , 1969.
	laurolitsine	IV ₃₃	
<i>A. obovata</i> Bl.	actinodaphnine	IV ₁	Hema <i>et al.</i> , 1972.
	laurotetanine	IV ₃₄	
	N-methylaurotetanine	IV ₄₇	
<i>A. procera</i> Nees	laurotetanine	IV ₃₄	Ralph <i>et al.</i> , 1978.

<u>Plant species</u>	<u>Alkaloids</u>	<u>Formulae</u>	<u>Reference</u>
<i>A. speciosa</i> Nees	laurotetanine	IV ₃₄	Bandara <i>et al.</i> , 1989;
	N-methyl-laurotetanine	IV ₄₇	Sotheeswaran and Wannigama, 1989.
<i>Alseodaphne archboldiana</i> (C.K.Allen)Kosterm	(+),(-)-coclaurine	IIa ₂	Johns <i>et al.</i> , 1967.
	(-)-N-norarmepavine	IIa ₅	
	(+)-reticuline	IIa ₇	
<i>A. hainanensis</i>	xylopinine	XV ₂	Zhang <i>et al.</i> , 1988.
	armepavine	IIa ₈	
	doryafranine	IIa ₁₃	
	1-(4-methoxybenzyl)-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinoline	-	
<i>A. perakensis</i>	N-methyl-2,3,6-trimethoxy-morphinandien-7-one-N-oxide	XI ₁₀	Lajis <i>et al.</i> , 1991.
<i>Aniba coto</i> (Rusby) Kosterm.	anabasine	XII ₁	Mors and Gottlieb, 1959 .
<i>A. duckeri</i> Kosterm	duckein	XII ₃	Mors <i>et al.</i> , 1957.
	anibine	XII ₂	

<u>Plant species</u>	<u>Alkaloids</u>	<u>Formulae</u>	<u>Reference</u>
<i>Beilschmiedia elliptica</i>	isoboldine	IV ₂₆	Clezy <i>et al.</i> , 1966.
<i>B. oreophila</i> Schlechter	6-epioreobeline isoboldine oreobeline thaliporphine wilsonirine	IX ₈ IV ₂₆ IX ₇ IV ₇₆ IV ₇₉	Tillequin and Koch, 1985.
<i>B. madang</i> (Bl.) Bl.	dehatrine	XI ₄	Kitagawa <i>et al.</i> , 1993.
<i>B. podagrica</i> Kosterm.	(+)-2,11-dihydroxy -1,10-dimethoxyaporphine glaucine (+)-2-hydroxy -1,9,10-trimethoxynoraporphine isoboldine predicentrine	IV ₁₆ IV ₂₀ - - IV ₂₆ IV ₇₁	Johns <i>et al.</i> , 1969.
<i>B. taxa</i> Benth. & Hook	isoboldine	IV ₂₆	Russell and Fraser, 1969.
<i>Cassytha americana</i> Nees	actinodaphnine bulbocapnine cassamedine cassameridine	IV ₁ IV ₆ V ₁ V ₂	Cava <i>et al.</i> , 1968.

<u>Plant species</u>	<u>Alkaloids</u>	<u>Formulae</u>	<u>Reference</u>
<i>Cassythia americana</i>	cassyfiline	IV ₈	Cava <i>et al.</i> , 1968.
Nees	cassythicine	IV ₉	
	cassythidine	IV ₁₀	
	dicentrine	IV ₁₅	
	launobine	IV ₃₁	
	N-methylactinodaphnine	IV ₄₁	
	O-methylcassyfiline	IV ₆₈	
	neolitsine	IV ₅₁	
	nuciferine	IV ₆₃	
<i>C. filiformis</i> L.	cassyfiline	IV ₈	Webb, 1948;
	laurotetanine	IV ₃₄	Tomita <i>et al.</i> , 1965;
	nantenine	IV ₅₀	Johns and Lamberton,
	ocoteine	IV ₆₇	1966;
	cassythidine	IV ₁₀	Merchant and Desai, 1973
<i>C. glabella</i> R.Br	cassythicine	IV ₉	Johns <i>et al.</i> , 1966d.
<i>C. melantha</i> R.Br,	actinodaphnine	IV ₁	Johns <i>et al.</i> , 1966 .
	cassythicine	IV ₉	

<u>Plant species</u>	<u>Alkaloids</u>	<u>Formulae</u>	<u>Reference</u>
<i>C. pubescens</i> R.Br.	domesticine	IV ₁₉	Johns <i>et al.</i> , 1966b.
	isoboldine	IV ₂₆	
	laurelliptine	IV ₃₂	
	nantenine	IV ₅₀	
	nordomesticine	IV ₅₅	
	sinoacutine	IX ₄	
<i>C. racemosa</i> Nees	(+)-coclaurine	IIa ₂	Johns <i>et al.</i> , 1967.
	1,2-dimethoxy-	V ₄	
	-9,10-methylenedioxy		
	-7-oxodibenzo(de,g)-		
	quinoline		
	isoboldine	IV ₂₆	
	laurelliptine	IV ₃₂	
	laurotetanine	IV ₃₄	
	N-methyl-laurotetanine	IV ₄₇	
	nantenine	IV ₅₀	
normantenine	IV ₅₉		
<i>Cinnamomum camphora</i> (Linn.) Seib.	lauroitsine	IV ₃₃	Tomita <i>et al.</i> , 1964a.
	reticuline	IIa ₇	
<i>C. laubattii</i> F. Muell	(+)-reticuline	IIa ₇	Ellis <i>et al.</i> , 1972.

<u>Plant species</u>	<u>Alkaloids</u>	<u>Formulae</u>	<u>Reference</u>
<i>Cinnamomum sp.</i>	cinnamolaurine	IIa ₁	Gellert and Summon, 1969,1970 .
	(+)-corydine	IV ₁₁	
	norcinnamolaurine	IIa ₆	
	(+)-reticuline	IIa ₇	
<i>Cryptocarya alba</i> Bl.	(+)-reticuline	IIa ₇	Urzua <i>et al.</i> , 1975.
<i>C. amygdalina</i> Nees	(+)-reticuline	IIa ₇	Manandhar <i>et al.</i> , 1979.
<i>C. angulata</i> C.T.White	3,4-dimethoxy-1-(dimethyl aminoethyl) phenanthrene	-	Cooke <i>et al.</i> , 1954; Bick and Douglas, 1965.
	N-methylisocorydine	IV ₄₆	
	roemerine	IV ₇₅	
<i>C. archboldina</i> Allen	(-)-armepavine	IIa _g	John <i>et al.</i> , 1969.
<i>C. bowiei</i> (Hook.) Druce	cryptotaustoline	VIII ₁	Ewings <i>et al.</i> , 1953.
	cryptowoline	VIII ₂	
<i>C. chinensis</i> Hemsl.	(±),(-)-caryachine	VII ₁	Chen <i>et al.</i> , 1979; Lee <i>et al.</i> , 1990.
	crychine	VII ₂	
	(+)-o-methylcaryachine	VII ₃	
	neocaryachine	VII ₅	
	caryachine N-methoperchlorate	VII ₇	

<u>Plant species</u>	<u>Alkaloids</u>	<u>Formulae</u>	<u>Reference</u>
<i>C. foveolata</i> C.T. White & Francis	reticuline	IIa7	Lamberton and Vashist, 1972.
<i>C. konishii</i> Hayata	(+)-N-noramepavine	IIa5	Lu, 1967;
	crykonisine	IIb1	Lee <i>et al.</i> , 1993.
	armepavine	IIa8	
	(+)-(1R,1aR)-1a- -hydroxymagnocurarine	IIa16	
<i>C. laevigata</i> Bl.	cryptopleurine	X2	Hoffmann <i>et al.</i> , 1978.
<i>C. longifolia</i> Kosterm.	thalifoline	I	Ralph <i>et al.</i> , 1981.
	coclaurine	IIa2	
	(-)-norargemonine	VII4	
	(-)-bisnorargemonine	VII6	
	isoboldine	IV26	
	lauroitsine	IV33	
	laurotetanine	IV34	
	longifolidine	IIa9	
	longifolonine	IIb4	
	N-methylcoclaurine	IIa10	
N-methylaurotetanine	IV47		

<u>Plant species</u>	<u>Alkaloids</u>	<u>Formulae</u>	<u>Reference</u>
	norisocorydine	IV ₅₆	
	reticuline	IIa ₇	
	scoulerine	XV	
<i>C. odorata</i> Guillaum.	cryptodorine	IV ₁₃	Bick <i>et al.</i> , 1972.
	isocorydine	IV ₂₇	
	laurotetanine	IV ₃₄	
	N-methylaurotetanine	IV ₄₇	
<i>C. phyllostemon</i> Kosterm.	phyllostemine	X ₅	Bick <i>et al.</i> , 1980;
	phyllosteminine	X ₆	Cave <i>et al.</i> , 1989 .
	letroisieme	-	
	(-)-antofine	X ₃	
	dehydroantofine	X ₄	
	(-)-cryptowoline	VIII ₂	
	(-)-cryptowolinol	VIII ₃	
	(-)-cryptowolidine	VIII ₄	
	(-)-phyllostone	XIII ₂	
	(+)-phyllocryptine	IIa ₁₁	
	(+)-phyllocryptonine	IIa ₁₂	
	(-)-phyllostemine	X ₅	
	(-)-phyllosteminine	X ₆	

<u>Plant species</u>	<u>Alkaloids</u>	<u>Formulae</u>	<u>Reference</u>
<i>C. pleurosperma</i> C.T. White and Francis	cryptopleuridine cryptopleurine cryptopleurospermine pleurospermine	X ₁ X ₂ XIV XIII ₁	De la Lande, 1948; Gellert, 1959; Johns <i>et al.</i> , 1970.
<i>C. tomentosa</i> Blume	laurotetanine	IV ₃₄	Wehmer, 1935.
<i>C. tripinervis</i> R.Br.	N-methylisocorydine	IV ₄₆	Cooke and Haynes, 1954.
<i>C. valeriana</i> A.J.G.H. Kosterm.	phoebine nordelorphine nantenine thaliporphine 3-hydroxyglaucine nor-phoebine O-methylmoschatoline	IV ₆₉ IV ₅₃ IV ₅₀ IV ₇₆ IV ₂₂ IV ₆₀ -	Castro <i>et al.</i> , 1986 ; Stermitz, 1986 .
<i>C. velutinos</i>	velucryptine	IIb ₅	Lebceuf <i>et al.</i> , 1989 .
<i>Dehaasia incrassata</i> (Jack) Kosterm.	isocorydine	IV ₂₇	Said <i>et al.</i> , 1991.
<i>D. triandra</i> Merr.	isocorydine corytuberine atheroline	IV ₂₇ IV ₁₂ V ₇	Lu <i>et al.</i> , 1989.

<u>Plant species</u>	<u>Alkaloids</u>	<u>Formulae</u>	<u>Reference</u>
	nantenine	IV ₅₀	
	obaberine	XI ₆	
	xanthoplanine	IV ₈₀	
	dehatrine	XI ₄	
<i>D. triandra</i> Merr.	dehatridine	XI ₅	
<i>Laurus nobilis</i> L.	actinodaphnine	IV ₁	Tomita <i>et al</i> , 1963.
	launobine	IV ₃₁	
	reticuline	IIa ₇	
	(+)-boldine	IV ₅	
	N-methylactinodaphnine	IV ₄₁	
	(+)-isodomeesticine	IV ₂₈	
	neolitsine	IV ₅₁	
	(+)-actinodaphnine	IV ₁	
	nor-isodomeesticine	IV ₅₇	
	(+)-nandigerine	IV ₄₉	
	(+)-cryptodorine	IV ₁₃	
<i>Lindera benzoin</i> Meissn.	laurotetanine	IV ₃₄	Babcock and Segalman, 1974
<i>L. citriodora</i> (Sieb. & Zucc.) Bl.	laurotetanine	IV ₃₄	Pech and Bruneton, 1984.

<u>Plant species</u>	<u>Alkaloids</u>	<u>Formulae</u>	<u>Reference</u>
<i>L. erythrocarpa</i>	laurotetanine	IV ₃₄	Kozuka <i>et al.</i> , 1984 .
Makino(Sieb. & Zucc.) Bl.	(+)-norcinnamolaurine	IIa ₆	
	laurotetanine	IV ₃₄	
<i>L. megaphylla</i>	N-methylhemangerine	IV ₄₃	Chen <i>et al.</i> , 1991;
Hemsl.	d-dicentrine	IV ₁₅	Lu <i>et al.</i> , 1972.
<i>L. oldhamii</i> Hemsl.	(+)-dicentrine	IV ₁₅	Lu and Chen, 1976;
	dicentrinone	V ₃	Chen, 1977.
	O-methylbulbocapnine	IV ₄₂	
	N-methylhemangerine	IV ₄₃	
	N-methylhemovine	IV ₄₅	
	lindoldhamine	XI ₁₀	
	dicentrine	IV ₁₅	
	N-nordicentrine	IV ₅₄	
	L-(+)-magnocurarine	IIa ₄	
<i>L. pipericarpa</i> Boerl.	laurotetanine	IV ₃₄	Burkill,1935;
	lindcarpine	IV ₃₅	Kiang and Sim,1967;
	isocorydine	IV ₂₇	Lajis <i>et al.</i> , 1992.
	norisocorydine	IV ₅₆	
	N-methylaurotetanine	IV ₄₇	

<u>Plant species</u>	<u>Alkaloids</u>	<u>Formulae</u>	<u>Reference</u>
<i>L. sericea</i> Blume	launobine	IV ₃₁	Kozuka <i>et al.</i> , 1985.
	boldine	IV ₅	
	laurotetanine	IV ₃₄	
<i>L. strychnifolia</i> (Sieb. et Zucc.) F. Vill	laurolitsine	IV ₃₃	Tomita <i>et al.</i> , 1969;
	boldine	IV ₅	Kozuka <i>et al.</i> , 1984 .
	(+)-reticuline	IIa ₇	
<i>L. umbellata</i> Thunb.	launobine	IV ₃₁	Tomita <i>et al.</i> , 1969;
	laurolitsine	IV ₃₃	Kozuka <i>et al.</i> , 1985 .
	boldine	IV ₅	
	laurotetanine	IV ₃₄	
<i>Machilus acuminatissima</i> (Hay.) Kanehira	(±)-cocclaurine	IIa ₂	Lu, 1967a .
	crykonisine	IIb ₁	
	(±)-N-norarmepavine	IIa ₅	
	(-)-N-norarmepavine	IIa ₅	
<i>M. arisanensis</i> Hayata	(+)-laudanidine	IIa ₃	Tomita <i>et al.</i> , 1965a .
	(±)(-)-N-noramepavine	IIa ₅	
<i>M. duthei</i> King & Hook	boldine	IV ₅	Hassin <i>et al.</i> , 1980 .
	isoboldine	IV ₂₆	
	laurotetanine	IV ₃₄	

<u>Plant species</u>	<u>Alkaloids</u>	<u>Formulae</u>	<u>Reference</u>
<i>M. duthei</i>	lauroitsine	IV ₃₃	
King & Hook	(+)-reticuline	IIa ₇	
<i>M. glaucescens</i> Wight	machiline	-	Talaptra <i>et al.</i> , 1982.
<i>M. kusanoi</i> Hayata	coclaurine	IIa ₂	Tomita <i>et al.</i> , 1963 ;
	(-)-N-norarmepavine	IIa ₅	Lu, 1963
<i>M. macrantha</i> Blume	(+)-coclaurine	IIa ₂	Tomita <i>et al.</i> , 1963.
<i>M. obovatifolia</i> (Hayata)Kanehira and Sasaki	(+)-laudanidine	IIa ₃	Tomita <i>et al.</i> , 1965.
	(+)-N-norarmepavine	IIa ₅	
	(-)-N-norarmepavine	IIa ₅	
<i>M. pseudolongifolia</i> Hayata	(+)-N-norarmepavine	IIa ₅	Lu, 1963 .
	(-)-N-norarmepavine	IIa ₅	
<i>M. thunbergii</i> Sieb. & Zucc.	(+)-N-norarmepavine	IIa ₅	Tomita and
	(-)-N-norarmepavine	IIa ₅	Kozuka, 1964;
	reticuline	IIa ₇	Tomita <i>et al.</i> , 1965 b.
<i>M. zuihoensis</i> Hayata	(+)-N-norarmepavine	IIa ₅	Lu, 1963;
	(-)-N-norarmepavine	IIa ₅	Tomita <i>et al.</i> , 1965 b .

<u>Plant species</u>	<u>Alkaloids</u>	<u>Formulae</u>	<u>Reference</u>
<i>Nectandra</i>	N-methyltryptamine	XVI ₃	Filho and Silvio, 1980.
<i>megapotamica</i> (Sprg.) Chodat and Hassler.	6-methoxy-N-methyl- -1,2,3,4-tetrahydro -β-carboline	XVI ₂	
<i>N. pichurim</i> (H.B.K.)Mez.	isoboldine	IV ₂₆	Ferrari <i>et al.</i> , 1971.
<i>N. rigida</i> Nees	laurelliptine	IV ₃₂	Quesne <i>et al.</i> , 1980.
<i>N. rodioei</i> Hook.	ocotine	XI ₂	Grundon and Garvey, 1960.
	rodiasine	XI ₃	
	sepeerine	XI ₈	
<i>N. saligna</i> (Nees et Mart.)Nees	dehydrococoteine	IV ₈₄	Baralle <i>et al.</i> , 1972.
	ocoteine	IV ₆₇	
	isoboldine	IV ₂₆	
<i>Neolitsea aciculata</i> Koidz.	laurotetanine	IV ₃₄	Kozaku <i>et al.</i> , 1984.
	(+)-reticuline	IIa ₇	
	lauroletsine	IV ₃₃	
	boldine	IV ₅	

<u>Plant species</u>	<u>Alkaloids</u>	<u>Formulae</u>	<u>Reference</u>
<i>N. acuminatissima</i> (Hay.) Kanehira & Sasaki	(+)-laurotetanine	IV ₃₄	Kataoku, 1965; Tomita <i>et al.</i> , 1965 .
<i>N. aurata</i> (Hay.) Koidz	(+)-anonaine laurolitsine litsericine (-)-roemerine	IV ₂ IV ₃₃ IIIb ₁ IV ₇₅	Lu <i>et al.</i> , 1975
<i>N. aureo-sericea</i> <i>N. aureo-sericea</i> Kostermans	bisnorargemonine isoboldine norcinnamolaurine (+)-reticuline	VII ₆ IV ₂₆ IIa ₆ IIa ₇	Tantisewie and Ruchirawat, 1992 .
<i>N. buisanensis</i> Yamamoto & Kamikoti	laurolitsine litsericine	IV ₃₃ IIIb ₁	Lu <i>et al.</i> , 1975.
<i>N. daibuensis</i> Kamikoti	(+)-reticuline	IIa ₇	Lu and Homg, 1977.
<i>N. fuscata</i> (Thwait) Alston	isoboldine	IV ₂₆	Gunatilaka <i>et al.</i> , 1981.
<i>N. pubescens</i> (Teschn.) Merrill.	boldine laurolitsine N-methyl-laurotetanine roemerine	IV ₅ IV ₃₃ IV ₄₇ IV ₇₅	Johns <i>et al.</i> , 1969.

<u>Plant species</u>	<u>Alkaloids</u>	<u>Formulae</u>	<u>Reference</u>
<i>N. pulchella</i> (Meiss.) Merr.	neolitsine pulchelline	IV ₅₁ -	Hui <i>et al.</i> , 1965.
<i>N. sericea</i> (Blume)Koidzumi	actinodaphnine anonaine boldine laurolitsine laurotetanine liriodenine litsericine N-methylactinodaphnine N-methyl-laurotetanine nuciferine (-)-roemerine	IV ₁ IV ₂ IV ₅ IV ₃₃ IV ₃₄ V ₅ IIIb ₁ IV ₄₁ IV ₄₇ IV ₆₃ IV ₇₅	Nakasao and Nomura, 1957;1958;1959; Nakasato and Asada; 1966; Nakasato <i>et al.</i> , 1966 .
<i>N. variabilissima</i> Kanehira & Sasaki	(-)-hemovine (-)-N-methylhemovine (-)-nandigerine	IV ₂₁ IV ₄₅ IV ₄₉	Lu and Su, 1973 a.
<i>Notaphoebe konishii</i> (Hay.) Hay.	(±)-N-norarmepavine (-)-N-norarmepavine (-)-laudanidine	IIa ₅ IIa ₅ IIa ₃	Lu, 1967 b.
<i>Notaphoebe sp.</i>	actinodaphnine	IV ₁	Ghose <i>et al.</i> , 1934 .

<u>Plant species</u>	<u>Alkaloids</u>	<u>Formulae</u>	<u>Reference</u>
<i>N. umbelliflora</i> Blume	laurotetanine	IV ₃₄	Ralph <i>et al.</i> , 1978.
<i>Ocotea brachybotra</i> (Meiss.)Mez.	14-episinomenine ocobotrine pallidine sinoacutine	IX ₅ IX ₆ IX ₁ IX ₄	Vecchiotti <i>et al.</i> , 1976.
<i>O. bucherii</i> Roij & Acuna	3-hydroxyglaucine	IV ₂₂	Hasso <i>et al.</i> , 1983.
<i>O. caesia</i> Mez.,L.L.	(-)-zenkerine (+)-laurelliptine (-)-pulchine (+)-isoboldine (s)-(+)-1-hydroxy- 2,9-dimethoxynoraporphine	IV ₈₁ IV ₃₂ IV ₇₃ IV ₂₆ IV ₁₄	Vilegas <i>et al.</i> , 1989.
<i>O. caparrapi</i> (Sandino- Grott & Nates)	reticuline	IIa ₇	Suarez and Enrique, 1980 .
<i>O. glaziovii</i> Mez.	glaziovine (+)-apoglaziovine asimilobine caaverine (+)-crotosparine	IIIa ₂ IV ₃ IV ₄ IV ₇ IIIa ₁	Gilbert <i>et al.</i> , 1964; Ferrari and Casagrande, 1967; Casagrande and Ferrari, 1975 .

<u>Plant species</u>	<u>Alkaloids</u>	<u>Formulae</u>	<u>Reference</u>
	1,10-dihydroxy-2-methoxyaporphine	IV ₁₇	
	(+)-glaziovine	IIIa ₂	
	(+)-1-hydroxy-2-methoxyaporphine	IV ₂₃	
	isoboldine	IV ₂₆	
	(-)-pronuciferine	IIIa ₃	
<i>O. leucoxylon</i> Benth. et Hook.	dicentrine	IV ₁₅	Ahmad and Cava, 1977 .
<i>O. macrophylla</i> Mez	dehydronantenine	IV ₈₅	Franca <i>et al.</i> , 1975.
	(+)-glaucine	IV ₂₀	
	(+)-isocorydine	IV ₂₇	
	1-(p-methoxybenzyl)-6,7-dimethoxyisoquinoline	IIb ₂	
	1-(p-methoxybenzyl)-6,7-methylenedioxyisoquinoline	IIb ₃	
	(+)-nantenine	IV ₅₀	
<i>O. macropoda</i> Mez.	dehydrodicentrine	IV ₈₂	Cava <i>et al.</i> , 1968 ;
	dehydroocopodine	IV ₈₃	Charubala <i>et al.</i> , 1968;

<u>Plant species</u>	<u>Alkaloids</u>	<u>Formulae</u>	<u>Reference</u>
<i>O. macropoda</i> Mez.	dicentrine	IV ₁₅	Cava and
	dicentrinone	V ₃	Venkateswarlu; 1971.
	ocopodine	IV ₆₆	
	predicentrine	IV ₇₁	
<i>O. puberula</i> (Nees et Mart.)Nees	dehydroocoteine	IV ₈₄	Vemengo, 1963;
	didehydroocoteine	IV ₈₆	Baralle <i>et al.</i> , 1973.
	ocoteine	IV ₆₇	
	thalicminine	V ₆	
<i>O. rodioei</i> Mez	demerarine	XI ₁₂	Mckennis <i>et al.</i> , 1965;
	norrodiasine	XI ₁	Chen, <i>et al.</i> , 1967.
	2-(+)-nortetrandrine	-	
	ocoteamine	-	
	ocotine	XI ₂	
	ocotosine	XI ₇	
	rodiasine	XI ₃	
<i>Ocotea</i> sp.	isocorydine	IV ₂₇	Cava <i>et al.</i> , 1968;
	1-(p-methoxybenzyl) -6,7-dimethoxyisoquinoline	IIb ₂	Franca <i>et al.</i> , 1975 .
	1-(p-methoxybenzyl) -6,7-methylenedioxyisoquinoline	IIb ₃	

<u>Plant species</u>	<u>Alkaloids</u>	<u>Formulae</u>	<u>Reference</u>
<i>Ocotea sp.</i>	ocokryptine	IV ₆₄	
	oconovine	IV ₆₅	
<i>O. variabilis</i> Mart	(+)-apoglaziovine	IV ₃	Cava <i>et al.</i> , 1972.
	(+)-glaziovine	IIIa ₂	
	(+)-nantenine	IV ₅₀	
	variabiline	IV ₇₈	
<i>O. venenosa</i> Gleason	rodiasine	XI ₃	Kostermans <i>et al.</i> , 1969.
	bebeerine	XI ₉	;Kozuka <i>et al.</i> , 1984 .
	dimethylrodiasine	-	
<i>Parabenzoin praecox</i> (Sieb & Zacc.)Nakai	nandigerine	IV ₄₉	Kozuka <i>et al.</i> , 1984.
	praecoxine		
<i>Persea gratissima</i> Gaertn.f.	dopamine	XVII ₁	Udenfreund <i>et al.</i> , 1959.
	serotonine	XVI ₁	
<i>Persea sp.</i>	dopamine	XVII ₁	Udenfreund <i>et al.</i> , 1959.
	serotonine	XVI ₁	
	tyramine	XVII ₂	
<i>Phoebe</i> <i>cinnamomifolia</i> Nees	oxopurpleine	V ₁₂	Martinez <i>et al.</i> , 1988 .
	oxoglaurine	V ₁₃	

<u>Plant species</u>	<u>Alkaloids</u>	<u>Formulae</u>	<u>Reference</u>
<i>P. clemensii</i> C.K.Allen	2,11-dihydroxy-1,10- dimethoxyaporphine 10-hydroxy-1,2- (methylenedioxy)-aporphine isocorydine N-methylindincarpine (-)-mecambroline laurolitsine	IV ₁₆ IV ₁₈ IV ₂₇ IV ₄₈ IV ₄₀ IV ₃₃	Gozler <i>et al.</i> , 1983 ; Johnsand Lamberton, 1967.
<i>P. formosana</i> Hay.	laurolitsine liriodenine roemerine ushinsunine purpureine preocoteine norpreocoteine	IV ₃₃ V ₅ IV ₇₅ IV ₇₇ IV ₇₄ IV ₇₂ IV ₆₁	Lu and Su, 1973 b; Lu and Tsai, 1984 . Stermitz and Castro, 1983 .
<i>P. pitteiri</i> Mez.	1,2,3-trimethoxy -9,10-methylene dioxynoraporphine norlirioferine reticuline norpurpureine	IV ₂₅ IV ₅₈ IIa ₇ IV ₆₂	Castro <i>et al.</i> , 1985.

<u>Plant species</u>	<u>Alkaloids</u>	<u>Formulae</u>	<u>Reference</u>
<i>P. porfiria</i> (Gris.)Mez.	ocoteine	IV ₆₇	Baralle <i>et al.</i> , 1972 .
<i>Ravensara aromatica</i> J.F.Gmel	N-methylisocorydine	IV ₄₆	Groebel <i>et al.</i> , 1969.
<i>Sassafras albidum</i> (Nutt.)Nees	boldine reticuline isoboldine norcinnamolaurine cinnamolaurine laurelliptine	IV ₅ IIa ₇ IV ₂₆ IIa ₆ IIa ₁ IV ₃₂	Segelman <i>et al.</i> , 1976 .
<i>Saurauja excelsa</i> Willd.	actinidin	XII ₄	Teixeira and Garbarino, 1984 .

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Alkaloids isolated from *Litsea* spp.

Lauraceous plants in the genus *Litsea* are found to contain a wide range of chemical constituents such as alkaloids, monoterpenes, sesquiterpenes (Jiang, *et al.*, 1986), triterpenes (Govindachari, *et al.*, 1971), lipids (Wang, *et al.*, 1983), alkenes (Arbain, *et al.*, 1990), lactones (Tanaka, *et al.*, 1990) and carbohydrates (Herath, *et al.*, 1990). Among these, alkaloids are the largest group (over 40). Almost of the alkaloids are isoquinoline alkaloids.

The occurrence of alkaloids found in various species of *Litsea* is summarized in Table 2.

Table 2 Alkaloids isolated from the genus *Litsea*

<u>Plant species</u>	<u>Part</u>	<u>Alkaloids</u>	<u>Formulae</u>	<u>Reference</u>
<i>Litsea akoensis</i>	wd	laurolitsine	IV ₃₃	Lu <i>et al.</i> , 1979.
<i>F. hayatae</i> (Kanehira) S.S. Ying		isoboldine	IV ₂₆	
<i>L. amara</i> Blume	-	laurotetanine	IV ₃₄	Hayata and Wehmer, . 1935.
<i>L. brassii</i> O. Schmidt	-	laurotetanine reticuline	IV ₃₄ IIa ₇	Hart <i>et al.</i> , 1969.
<i>L. chrysocoma</i> Blume	-	laurotetanine	IV ₃₄	Ralph <i>et al.</i> , 1978.
<i>L. cubeba</i> Pers.	-	isocorydine	IV ₂₇	Tomita <i>et al.</i> , 1965d;

Table 2 cont.

<u>Plant species</u>	<u>Part</u>	<u>Alkaloid</u>	<u>Formulae</u>	<u>Reference</u>
<i>L. cubeba</i> Pers.	ent	laurotetanine	IV ₃₄	Lu and Lin, 1967; Wu <i>et al.</i> , 1991.
	-	(+)-magnocurarine	IIa ₄	
	wd	N-methylaurotetanine	IV ₄₇	
		litebamine	VI ₃	
	wd	boldine	IV ₅	
	wd	liriotulipiferine	IV ₃₆	
	wd	reticuline	IIa ₇	
	-	D-magnocurarine	IIa ₄	
	-	norisocorydine	IV ₅₆	
	ent	N-methylindcarpine	IV ₄₈	
	ent	isodomesticine	IV ₂₈	
	ent	glaziovine	IIIa ₂	
	-	(-)-oblongine	IIa ₁₄	
	-	(-)-8-O-methyloblongine	IIa ₁₅	
	-	xanthoplanine	IV ₈₀	
-	(-)-magnocurarine	IIa ₄		
<i>L. deccanensis</i>	bk	actinodaphnine	IV ₁	Desai, 1966; Gupta and Bhakuni, 1989 .
Gamble	lv+st	(+)-isocorydine	IV ₂₇	
	lv+st	(+)-corytuberine	IV ₁₂	
	lv+st	(+)-dicentrine	IV ₁₅	
	lv+st	(+)-nordicentrine	IV ₅₄	

Table 2 cont.

<u>Plant species</u>	<u>Part</u>	<u>Alkaloid</u>	<u>Formulae</u>	<u>Reference</u>
	lv+st	(+)-boldine	IV ₅	
	lv+st	(+)-norbaldine (laurolitsine)	IV ₃₃	
	lv+st	(+)-magnoflorine	IV ₃₉	
<i>L. elliptica</i> Boerl.	bk	reticuline	IIa ₇	Arbain <i>et al.</i> , 1990.
<i>L. gardneri</i> (Thw.)hook f.	bk	actinodaphnine	IV ₁	Bandara <i>et al.</i> , 1989.
	bk	laurolitsine	IV ₃₃	
<i>L. glutinosa</i> (Lour.) C.B.Rob.	bk	isobaldine	IV ₂₆	Tewari <i>et al.</i> , 1972;
	lv	laurelliptine	IV ₃₂	Hart <i>et al.</i> , 1969;
	-	laurolitsine	IV ₃₃	Sivakumaran and
	lv	laurotetanine	IV ₃₄	Gopinath, 1976.
	lv	lirodenine	V ₅	
	bk	actinodaphnine	IV ₁	
	lv	N-acetyl-laurotetanine	IV ₄₇	
<i>L. glutinosa</i> var. <i>glabraria</i> Hook.f.	-	actinodaphnine	IV ₁	Tewari <i>et al.</i> , 1972 .
	-	boldine	IV ₅	
	-	laurolitsine	IV ₃₃	

Table 2 cont.

<u>Plant species</u>	<u>Part</u>	<u>Alkaloids</u>	<u>Formulae</u>	<u>Reference</u>
<i>L. glutinosa</i> var	-	laurotetanine	IV ₃₄	
<i>glabraria</i> Hook.f.	-	N-methylactinodaphnine	IV ₄₁	
	-	N-methylaurotetanine	IV ₄₇	
<i>L. hayatae</i> Kanehira	-	laurolitsine	IV ₃₃	Lu <i>et al.</i> , 1969.
	-	liriodenine	V ₅	
	-	ushinsunine	IV ₇₇	
<i>L. intermedia</i> Boerl	-	laurotetanine	IV ₃₄	Wehmer, 1935.
<i>L. japonica</i> Mirb.	-	laurolitsine	IV ₃₃	Kozuka, 1962.
<i>L. javanica</i> Blume	-	laurotetanine	IV ₃₄	Wehmer, 1935 .
<i>L. laeta</i> Benth & Hook	bk	laetanine	IV ₂₉	Borthakur and Rastogi,
	bk	laetine	IV ₃₀	1979; Rastogi and
	bk	N,O-dimethylhemovine	IV ₄₄	Borthakur, 1980 .
	bk	glaucine	IV ₂₀	
	-	dicentrinone	V ₃	
	-	ocominarone	V ₁₀	
		(nordicentrinone)		
<i>L. latifolia</i> Blume	-	laurotetanine	IV ₃₄	Ralph <i>et al.</i> , 1978 .

Table 2 cont.

<u>Plant species</u>	<u>Part</u>	<u>Alkaloids</u>	<u>Formulae</u>	<u>Reference</u>
<i>L. laurifolia</i> (Jacq.) Cordemoy		actinodaphnine	IV ₁	Leboeuf <i>et al.</i> , 1979; Guinaudeau <i>et al.</i> , 1983.
		glaziovine	IIIa ₂	
		boldine	IV ₅	
		isoboldine	IV ₂₆	
		laurelliptine	IV ₃₂	
		laurokitsine	IV ₃₃	
		laurotetanine	IV ₃₄	
		N-methylactinodaphnine	IV ₄₁	
		N-methylhemangerine	IV ₄₃	
		N-methylaurotetanine	IV ₄₇	
		nandigerine	IV ₄₉	
		reticuline	IIa ₇	
	<i>L. lecardii</i> Guillaum	lv	(+)-actinodaphnine	
lv		(+)-boldine	IV ₅	
lv		(+)-cassythicine	IV ₉	
lv		(+)-isoboldine	IV ₂₆	
-		(+)-laurokitsine	IV ₃₃	
wd		(+)-litseferine	IV ₃₈	
wd		(+)-norisocorydine	IV ₅₆	
lv,wd		(+)-coclaurine	IIa ₂	
lv,bk,wd		(+)-reticuline	IIa ₇	
lv,bk,wd		(-)-pallidine	IX ₁	

Table 2 cont.

<u>Plant species</u>	<u>Part</u>	<u>Alkaloids</u>	<u>Formulae</u>	<u>Reference</u>
<i>L. leefeana</i> Merr.	-	boldine	IV ₅	Lamberton and Vashist, 1972 .
	-	laurokitsine	IV ₃₃	
	-	(+)-reticuline	IIa ₇	
<i>L. lucida</i> Blume	-	laurotetanine	IV ₃₄	Wehmer, 1935 .
<i>L. nitida</i> Roxb.	-	actinodaphnine	IV ₁	Patnaik and Gopinath, 1975 .
	bk	dicentrine	IV ₁₅	
	bk	litsedine	IV ₃₇	
<i>L. polyantha</i> Juss.	-	actinodaphnine	IV ₁	Dutta, 1968 .
<i>L. salicifolia</i> (hook.)	lv	dicentrinone	V ₃	Rastogi and Borthakur, 1980 .
	-	glaucine	IV ₂₀	
	-	laetine	IV ₃₀	
	lv	nordicentrine	IV ₅₄	
	lv	N,O-dimethylhemovine	IV ₄₄	
<i>L. sebifera</i> Pers.	-	actinodaphnine	IV ₁	Hema <i>et al.</i> , 1972; Sivakumaran and Gopinath, 1976.
	-	boldine	IV ₅	
	-	laurotetanine	IV ₃₄	
	-	N-methylaurotetanine	IV ₄₇	
	-	sebiferine	IX ₃	
	-	litseferine	IV ₃₈	

Table 2 cont.

<u>Plant species</u>	<u>Part</u>	<u>Alkaloids</u>	<u>Formulae</u>	<u>Reference</u>
<i>L. solomensis</i> Allen	bk	laurohitsine	IV ₃₃	Hart <i>et al.</i> , 1969.
	bk	reticuline	IIa ₇	
<i>L. trifora</i> Guillaumin	ar.	(+)-isocorydine	IV ₂₇	Castredo <i>et al.</i> , 1980.
	ar.	N-methylaurotetanine	IV ₄₇	
	ar.	(+)-isoboldine	IV ₂₆	
	ar.	(+)-boldine	IV ₅	
	ar.	(+)-reticuline	IIa ₇	
	ar.	(+)-actinodaphnine	IV ₁	
	ar.	(+)-norboldine	IV ₃₃	
	ar.	norisoboldine	IV ₃₂	
		(laurelliptine)		
	ar.	(+)-coclaurine	IIa ₂	
	ar.	(+)-corydine	IV ₁₁	
	ar.	glaucine	IV ₂₀	
	ar.	(+)-predicentrine	IV ₇₁	
	ar.	(-)-N-methylcoclaurine	IIa ₂	
<i>L. turfosa</i> Blume	-	boldine	IV ₅	Holloway and Scheimann, 1973.
	-	laurohitsine	IV ₃₃	

Table 2 cont.

<u>Plant species</u>	<u>Part</u>	<u>Alkaloid present</u>	<u>Formulae</u>	<u>Reference</u>
<i>L. wightiana</i> Hook f.	st	boldine	IV ₅	Hema <i>et al.</i> , 1972;
	st	laurokitsine	IV ₃₃	Bhakuni and Gupta, 1983.
	st	glaucine	IV ₂₀	
	st	laurotetanine	IV ₃₄	
	st	isoboldine	IV ₂₆	
<i>L. zeylanica</i> Blume	-	(+)-isoboldine	IV ₂₆	Ralph <i>et al.</i> , 1978.
	-	(+)-N-norisoboldine (laurelliptine)	IV ₃₂	
	-	(+)-reticuline	IIa ₇	

lv.=leaves, st=stem, bk= bark, ar= arial part, wd= wood, ent= entire plant

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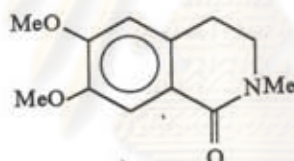
Chemistry of alkaloids from Lauraceous plants

Alkaloids of the Lauraceae possess many structural types found in nature. Most of them are isoquinoline type; such as benzyloisoquinoline, proaporphine, aporphine, dehydroaporphine, oxoaporphine, bisbenzyloisoquinoline, pavine, protoberberine, morphinan, dibenzopyrrocoline, phenanthroquinolizidine and isoquinoline. Other types are pyridine, sedamine and indole (Ralph, Bick and Sinchai, 1978).

I. Isoquinolone

The isoquinolone alkaloids are a small group of alkaloids present in plants only in minor amounts (Shamma, 1972). In Lauraceous plants, only one isoquinolone, thalifoline, was found in *Cryptocarya longifolia* Kosterm. (Ralph *et al.*, 1981)

thalifoline I



II. Benzyloisoquinoline

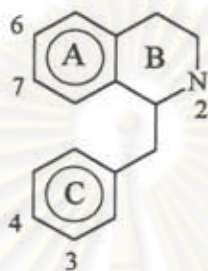
The benzyloisoquinolines occupy a paramount position in alkaloid chemistry because they act as *in vivo* precursors to so many of other natural occurring isoquinolines: isoquinolones, pavinines, isopavinines, bisbenzyloisoquinolines, cularines, dibenzopyrrocolines, morphines, proaporphines, aporphines, protoberberines, etc.

The benzyloisoquinoline alkaloids are either of the 1,2,3,4-tetrahydro type, such as coclaurine, or of the completely aromatic type, as in the case of papaverine.

Ring A in the benzyloisoquinoline alkaloids may possess two or three substituents, while ring C has only one or two substituents (Shamma, 1972).

The benzyloisoquinolines were found widely in the Lauraceous genus plants such as the genus *Alseodaphne*, *Cassytha*, *Cinnamomum*, *Litsea* and others.

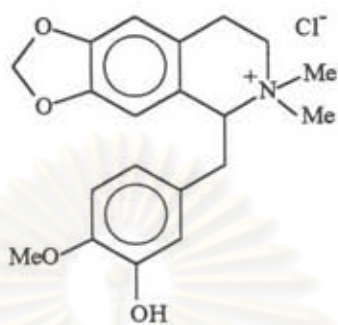
IIa. Benzyltetrahydroisoquinoline alkaloids



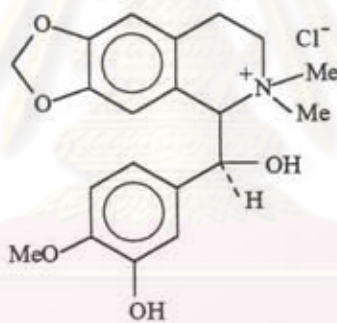
IIa Benzyltetrahydroisoquinoline

Alkaloids		Substituent Positions				
		2	6	7	3'	4'
cinnamolaurine	IIa ₁	Me	-OCH ₂ O-	-	-	OH
coclaurine	IIa ₂	-	OMe	OH	-	OH
laudanidine	IIa ₃	Me	OMe	OMe	OH	OMe
magnocurarine	IIa ₄	(Me) ₂ ⁺	OMe	OH	-	OH
N-norarmepavine	IIa ₅	-	OMe	OMe	-	OH
norcinnamolaurine	IIa ₆	-	-OCH ₂ O-	-	-	OH
reticuline	IIa ₇	Me	OMe	OH	OH	OMe
(-)-armepavine	IIa ₈	Me	OMe	OMe	OH	-
longifolidine	IIa ₉	Me	-	OMe	OH	-
N-methylcocclaurine	IIa ₁₀	Me	OMe	OH	-	-

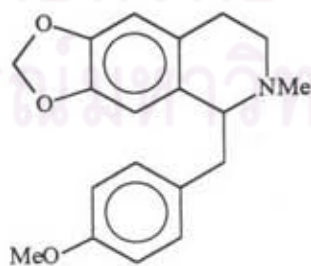
(+)-phyllocryptine IIa₁₁



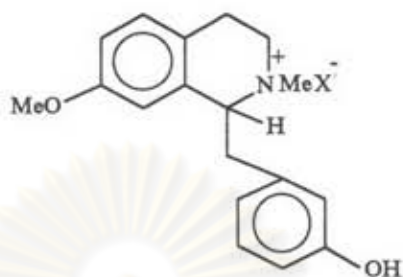
(+)-phyllocryptonine IIa₁₂



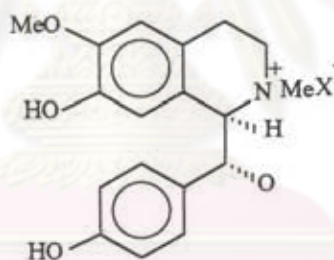
doryfranine IIa₁₃



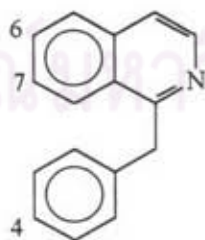
(-)-8-O-methylblongine IIa15



(1R,1aR)-1a-hydroxymagnocurarine IIa16



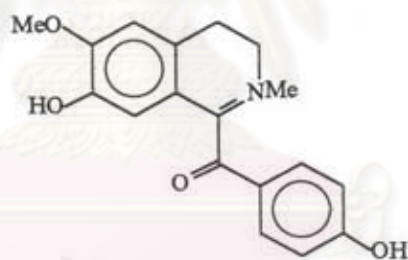
IIb. Benzyloquinoline alkaloids



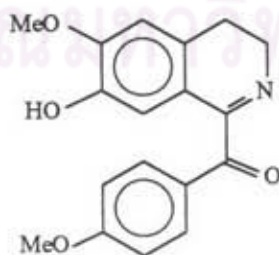
IIb Benzyloquinoline

Alkaloids		Substituent Positions		
		6	7	4'
crykonisine	IIb ₁	OMe	OMe	OH
1-(p-Methoxybenzyl)-6,7-dimethoxyisoquinoline	IIb ₂	OMe	OMe	OMe
1-(p-Methoxybenzyl)-6,7-methylenedioxyisoquinoline	IIb ₃	-OCH ₂ O-		OMe

longifolonine IIb₄



velucryptine IIb₅

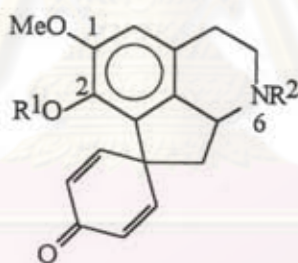


III. Proaporphine

The proaporphine alkaloids occur in a variety of oxidation states. There also exists a series of reduced proaporphines exemplified by (+)-litsericine in which the double bonds of the original dienone system have been partially or completely reduced (Shamma, 1972).

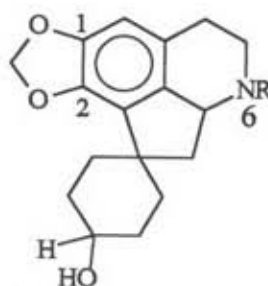
Because of the asymmetry at C-6a, one side of the dienone system is not equivalent to the other. The lower numbers (C-8 and C-9) are assigned to the side of the dienone above the mean plane of the molecule, and the higher number (C-11 and C-12) to the side below (Shamma, 1972).

In Lauraceous plants, the proaporphine alkaloids were isolated from the genus *Nectandra* and *Ocotea*.



III . Proaporphine

Alkaloids		Substituent Positions	
		R ¹	R ²
crotosparine	IIIa ₁	H	H
glaziovine	IIIa ₂	OH	CH ₃
pronuciferine	IIIa ₃	CH ₃	CH ₃



IIIb proaporphine

Alkaloids		Substituent Positions				
		1	2	6	EQ.	AX.
litsericine	IIIb ₁	-OCH ₂ O-		H	H	OH
N-methylitsericine	IIIb ₂	-OCH ₂ O-		Me	H	OH

IV. Aporphine alkaloids

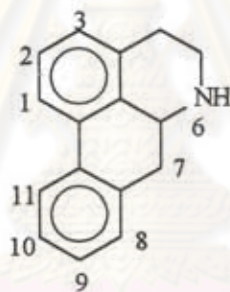
The aporphines are the largest group of isoquinolines alkaloids, being second only to the bisbenzylisoquinoline and are represented by the general structure IV. These alkaloids are distributed in at least 18 plants families, of which the most important are the Papaveraceae, Annonaceae, Lauraceae and Monimiaceae.

The nitrogen atom is usually methylated; and although some noraporphine are known, they are not very stable and are often characterized as their N-acetyl derivatives. Aporphine are known with the C-6a stereochemistry either α or β .

The most diverse structural feature of the aporphines is the oxygenation pattern. Position 1 and 2 are always oxygenated, either by the hydroxy, methoxy and

methylenedioxy groups. It is common to find further oxygen substituents at C-9, C-10 and C-11, and occasionally at C-8. It is rare to find oxygenation at C-7, except in the oxoaporphine, and even rare to find any oxygenation in ring B (Cordell, 1981a).

Dehydroaporphine are optically inactive, subgroup of the aporphine alkaloids with unsaturation at C-6a. The first member of this subgroup to be isolated from natural sources were dehydrodicentrine (Shamma, 1972). These alkaloids were found in the genus *Ocotea* (Cava, *et al.*, 1968; Vernengo, 1963). There is no report on dehydroaporphine occurring in *Litsea sp.*



IV aporphine

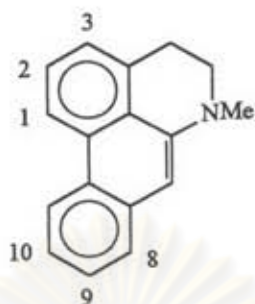
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Alkaloids		Substituent Positions							
		1	2	3	6	8	9	10	11
actinodaphnine	IV ₁	-OCH ₂ O-	-	-	-	-	-	OH	OMe
anonaine	IV ₂	-OCH ₂ O-	-	-	-	-	-	-	-
apoglaziovine	IV ₃	OH	OMe	-	Me	-	-	OH	-
asimilobine	IV ₄	OMe	OH	-	-	-	-	-	-
boldine	IV ₅	OMe	OH	-	Me	-	OH	OMe	-
bulbocapnine	IV ₆	-OCH ₂ O-	-	-	Me	-	-	OMe	OH
caaverine	IV ₇	OH	OMe	-	-	-	-	-	-
cassyfiline	IV ₈	-OCH ₂ O-	OMe	-	-	-	OH	OMe	-
cassythicine	IV ₉	-OCH ₂ O-	-	-	Me	-	OH	OMe	-
cassythidine	IV ₁₀	-OCH ₂ O-	OMe	-	-	-	-OCH ₂ O-	-	-
corydine	IV ₁₁	OH	OMe	-	Me	-	OMe	OMe	-
corytuberine	IV ₁₂	OH	OMe	-	Me	-	OMe	OH	-
cryptodorine	IV ₁₃	-OCH ₂ O-	-	-	-	-	-	-OCH ₂ O-	-
1-hydroxy-2,9- dimetethoxyaporphine	IV ₁₄	OH	OMe	-	-	-	OMe	-	-
dicentrine	IV ₁₅	-OCH ₂ O-	-	-	Me	-	OMe	OMe	-
2,11-hydroxy-1,10- dimethoxyaporphine	IV ₁₆	OMe	OH	-	Me	-	-	OMe	OH
1,10-dihydroxy-2- methoxyaporphine	IV ₁₇	OH	OMe	-	Me	-	-	OH	-
10-hydroxy-1,2- methylenedioxy aporphine	IV ₁₈	-OCH ₂ O-	-	-	Me	-	-	OH	-

Alkaloids		Substituent Positions							
		1	2	3	6	8	9	10	11
domesticine	IV ₁₉	OH	OMe	-	Me	-	-OCH ₂ O-	-	
glaucine	IV ₂₀	OMe	OMe	-	Me	-	OMe	OMe	-
hernovine	IV ₂₁	OMe	OH	-	-	-	-	OH	OMe
3-hydroxyglaucine	IV ₂₂	OMe	OMe	OH	Me	-	OMe	OMe	-
(±)-1-hydroxy-2-methoxyaporphine	IV ₂₃	OH	OMe	-	Me	-	-	-	-
2-hydroxy-1,9,10-trimethoxyaporphine	IV ₂₄	OMe	OH	-	-	-	OMe	OMe	-
1,2,3-trimethoxy-9,10-methylenedioxyaporphine	IV ₂₅	OMe	OMe	OMe	-	-	-OCH ₂ O-	-	
isoboldine	IV ₂₆	OH	OMe	-	Me	-	OH	OMe	-
(+)-isocorydine	IV ₂₇	OMe	OMe	-	Me	-	OMe	OH	-
isodomesticine	IV ₂₈	OMe	OH	-	Me	-	-OCH ₂ O-	-	
laetanine	IV ₂₉	OMe	OH	-	-	-	OMe	OH	-
laetine	IV ₃₀	OMe	OH	-	-	-	-	-OCH ₂ O-	
launobine	IV ₃₁	-OCH ₂ O-	-	-	-	-	-	OMe	OH
laurelliptine	IV ₃₂	OH	OMe	-	-	-	OH	OMe	-
laurolitsine	IV ₃₃	OMe	OH	-	-	-	-	-OCH ₂ O-	
laurotetanine	IV ₃₄	OMe	OMe	-	-	-	OH	OMe	-
lindcarpine	IV ₃₅	OMe	OH	-	-	-	-	OMe	OH
liriotulipiferine	IV ₃₆	OH	OMe	-	Me	-	OMe	OH	-
litsedine	IV ₃₇	-OCH ₂ O-	-	-	-	-	-	OMe	OMe

Alkaloids		Substituent Positions							
		1	2	3	6	8	9	10	11
litseferine	IV ₃₈	-OCH ₂ O-	-	-	-	-	OMe	OH	-
magnoflorine	IV ₃₉	OH	OMe	-	Me ₂	-	-	OMe	OH
(-)-mecambroline	IV ₄₀	-OCH ₂ O-	-	-	Me	-	-	OH	-
N-methylactino	IV ₄₁	-OCH ₂ O-	-	-	Me	-	OH	OMe	-
daphnine									
O-methylbulbocapnine	IV ₄₂	-OCH ₂ O-	-	-	Me	-	-	OMe	OMe
N-methylhernangerine	IV ₄₃	-OCH ₂ O-	-	-	Me	-	-	OH	OMe
N,O-dimethylhernovine	IV ₄₄	OMe	OH	-	Me	-	-	OMe	OMe
N-methylhernovine	IV ₄₅	-OCH ₂ O-	-	-	Me	-	-	-OCH ₂ O-	-
N-methylisocorydine	IV ₄₆	OMe	OMe	-	Me ₂	-	-	OMe	OH
N-methylaurotetanine	IV ₄₇	OMe	OMe	-	Me	-	OH	OMe	-
N-methylindocarpine	IV ₄₈	OMe	OH	-	Me	-	-	OMe	OH
nandigerine	IV ₄₉	-OCH ₂ O-	-	-	-	-	-	OH	OMe
nantenine	IV ₅₀	OMe	OMe	-	Me	-	-OCH ₂ O-	-	-
neolitsine	IV ₅₁	-OCH ₂ O-	-	-	Me	-	-OCH ₂ O-	-	-
norcorydine	IV ₅₂	OH	OMe	-	-	-	-	OMe	OMe
nordelphorphine	IV ₅₃	OMe	OMe	OH	-	-	OH	OMe	-
nordicentrine	IV ₅₄	-OCH ₂ O-	-	-	-	-	-	OMe	OMe
nordomesticine	IV ₅₅	OH	OMe	-	-	-	-OCH ₂ O-	-	-
norisocorydine	IV ₅₆	OMe	OMe	-	-	-	-	OMe	OH
norisodomesticine	IV ₅₇	OMe	OH	-	-	-	OCH ₂ O-	-	-
norlirioferrine	IV ₅₈	OMe	OMe	-	-	-	OMe	OH	-
normantenine	IV ₅₉	OMe	OMe	-	-	-	-OCH ₂ O-	-	-

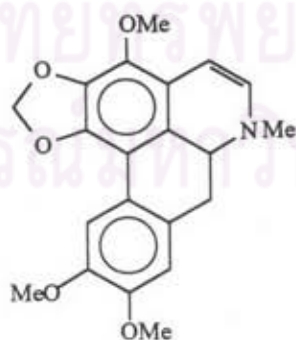
Alkaloids		Substituent Positions								
		1	2	3	6	8	9	10	11	
norphoebine	IV ₆₀	OMe	OMe	OMe	-	-	-OCH ₂ O-	-		
norpreocoteine	IV ₆₁	OH	OMe	OMe	-	-	OMe	OMe	-	
norpurpureine	IV ₆₂	OMe	OMe	OMe	-	-	OMe	OMe	-	
nuciferine	IV ₆₃	OMe	OMe	-	Me	-	-	-	-	
ocokryptine	IV ₆₄	OMe	-OCH ₂ O-	Me	-	-	OMe	OH		
oconovine	IV ₆₅	OMe	OMe	OMe	Me	-	-	OMe	OH	
ocopodine	IV ₆₆	-OCH ₂ O-	-	Me	OMe	OMe	OMe	-		
ocoteine	IV ₆₇	-OCH ₂ O-	OMe	Me	-	OMe	OMe	-		
O-methylcassyphilline	IV ₆₈	-OCH ₂ O	OMe	-	OMe	OMe	-	-		
phoebine	IV ₆₉	OMe	OMe	OMe	Me	-	-OCH ₂ O-	-		
praecoxine	IV ₇₀	OMe	OMe	-	Me	Me	-	OH	OMe	
predicentrine	IV ₇₁	OMe	OH	-	Me	-	OMe	OMe	-	
preocoteine	IV ₇₂	OH	OMe	OMe	Me	-	OMe	OMe	-	
pulchine	IV ₇₃	OH	OMe	-	Me	-	OMe	-	-	
purpureine	IV ₇₄	OMe	OMe	OMe	Me	-	OMe	OMe	-	
roemerine	IV ₇₅	-OCH ₂ O-	-	Me	-	-	-	-		
thaliporphine	IV ₇₆	OH	OMe	-	Me	-	OMe	OMe	-	
ushinsunine	IV ₇₇	-OCH ₂ O-	-	Me	-	-	-	-		
variabiline	IV ₇₈	OMe	OMe	-	Me	-	-N(CH ₂ Ph) ₂	-		
wilsonirine	IV ₇₉	OH	-OCH ₂ O-	-	-	-	OMe	OMe	-	
xanthoplanine	IV ₈₀	OMe	OMe	-	Me	-	-	OMe	-	
zenkerine	IV ₈₁	OH	OMe	-	Me	-	-	-	-	



Dehydroaporphine

Alkaloids		Substituent Positions					
		1	2	3	8	9	10
dehydrodicentrine	IV ₈₂	-OCH ₂ O-	-	-	-	OMe	OMe
dehydrocopodine	IV ₈₃	-OCH ₂ O-	-	-	OMe	OMe	OMe
dehydrocoteine	IV ₈₄	-OCH ₂ O-	-	OMe	-	OMe	OMe
dehydronanteine	IV ₈₅	OMe	OMe	-	-	-OCH ₂ O-	-

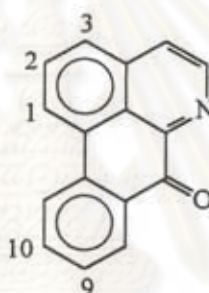
didehydrocoteine IV₈₆



V. Oxoaporphine alkaloids

The oxoaporphines represent the most highly oxidized state of the aporphine skeleton. They are widely distributed and cooccur with aporphine alkaloids. The numbering system of oxoaporphine is the same as the aporphines, beyond the perennial 1,2-dioxygenation, they exhibit a variety of oxygen substitution patterns.

Liriodenine is the most widely distributed oxoaporphine (Cordell, 1981). In Lauraceous plants, the oxoaporphines were isolated from the genus *Cassytha*, *Dehaasia*, *Litsea*, *Lindera*, *Ocotea* and *Phoebe*.



V. Oxoaporphine

Alkaloids	Substituent Positions					
	1	2	3	9	10	11
cassamedine V ₁	-OCH ₂ O-		OMe	-OCH ₂ O-		-
cassameridine V ₂	-OCH ₂ O-		-	-OCH ₂ O-		-
dicentrinone V ₃	-OCH ₂ O-		-	OMe	OMe	-
1,2-dimethoxy- 9,10- methylenedioxy V ₄	OMe	OMe	-	-OCH ₂ O-		-

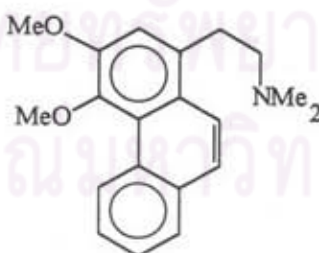
-7-oxodiabenzquinoline						
liriodenine	V ₅	-OCH ₂ O-	-	-	-	-
thalicminine	V ₆	-OCH ₂ O-	OMe	OMe	OMe	-
artheroline	V ₇	OMe	OMe	-	OH	-
hernandenine	V ₈	-OCH ₂ O-	-	-	-OCH ₂ O-	-
machigline	V ₉	-OCH ₂ O-	-	OMe	OMe	-
ocominarone	V ₁₀	-OCH ₂ O-	-	OMe	OMe	-
oxonantenine	V ₁₁	OMe	OMe	-	-OCH ₂ O-	-

VI. Phenanthrene alkaloids

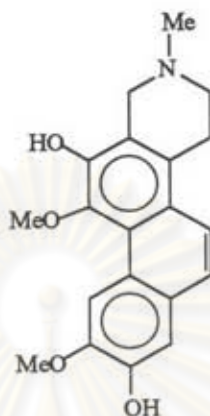
The phenanthrene alkaloids are a small group of optically inactive tertiary bases probably derived biogenetically from the Hofmann elimination of quaternary aporphine salts. They can, therefore, be included among the isoquinoline alkaloids (Shamma, 1972).

In Lauraceous family, phenanthrene alkaloid were isolated from *Cryptocarya* sp. and *Litsea* sp. (Cooke and Haynes, 1954; Bick and Douglas, 1965).

atherospermine VI₁



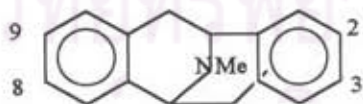
litebamine

VI₂

VII. Pavine alkaloids

Pavine skeleton is one of those rare situations in alkaloid chemistry where synthesis of the skeleton predated discovery of a natural source (Cordell, 1981d).

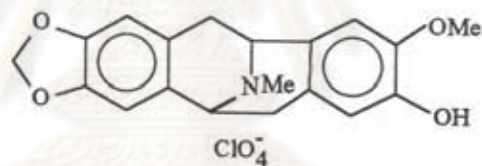
The pavine alkaloids have been obtained from family Lauraceae, Papaveraceae and Ranunculaceae. They are derived biogenetically from benzyloisoquinolines, but several pavines are derived from tetrahydrobenzyloisoquinoline (Gozler *et al*, 1983).



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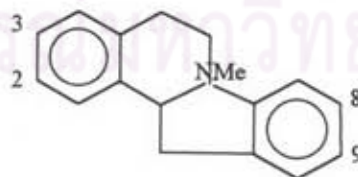
Alkaloids		Substituent Positions				
		1	2	3	8	9
caryachine	VII ₁	-	OH	OMe	-OCH ₂ O-	
crychine	VII ₂	-	-OCH ₂ O-		-OCH ₂ O-	
O-methylcaryachine	VII ₃	-	OMe	OMe	-OCH ₂ O-	
(-)-norargemonine	VII ₄	-	OMe	OMe	OH	OMe
neocaryachine	VII ₅	OH	OMe	-	-OCH ₂ O-	
bisnorargemonine	VII ₆	-	OMe	OH	OH	OMe

caryachine N-methopercorate VII 7



VIII. Dibenzopyrrocolines

Four natural dibenzopyrrocolines have been obtained from the genus *Cryptocarya* of the family Lauraceae.



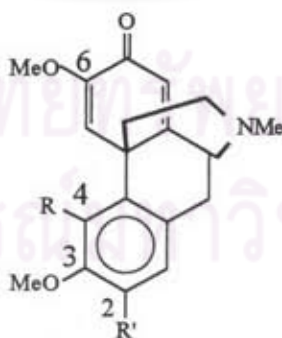
VIII Dibenzopyrrocolines

Alkaloids		Substituent Positions				
		2	3	8	9	11
cryptaustoline	VIII ₁	OH	OCH ₃	OCH ₃	OCH ₃	H
cryptowoline	VIII ₂	OH	OCH ₃	-OCH ₂ O-		H
cryptowolinol	VIII ₃	OH	OCH ₃	-OCH ₂ O-		OH
cryptowolidine	VIII ₄	OCH ₃	OH	-OCH ₂ O-		H

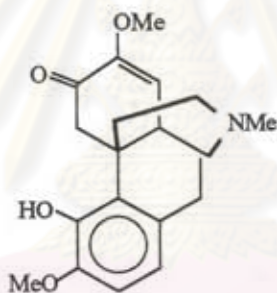
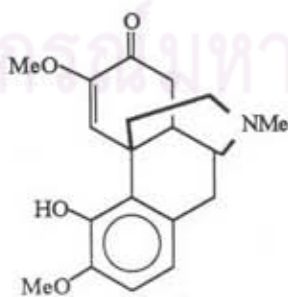
IX. Morphinandienone and Morphinane alkaloids

The morphinan alkaloids are more limited in numbers and distribution. There are fewer than dozen of them distributed in the Papaveraceae and the Menispermaceae (Robinson, 1981).

In the Lauraceae they were isolated from the genus *Alseodaphne*, *Beilschmiedia*, *Cassytha*, *Ocotea* and *Litsea*.

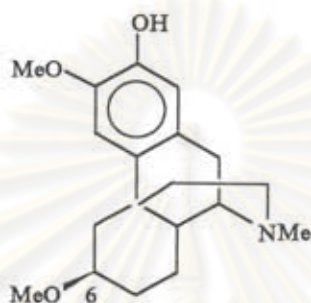


Alkaloids		Substituent Positions	
		2	4
(S)-pullidine	IX ₁	OH	-
(S)-(-)-O-methylpullidine	IX ₂	OMe	-
sebiferine	IX ₃	OMe	-
sinoacutine	IX ₄	-	OH

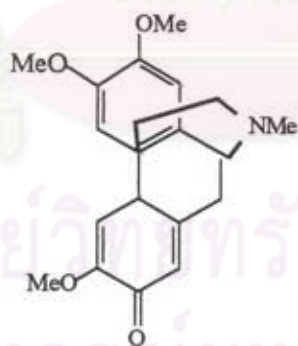
14-Episinomenine IX₅ocobitrine IX₆

oreobeiline IX7 (6 \dashv OCH₃)

6-epioreobeiline IX8 (6 \blacktriangleleft OCH₃)

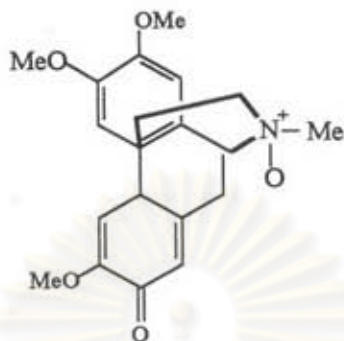


N-methyl-2,3,6-trimethoxy morphinan dien-7-one IX9



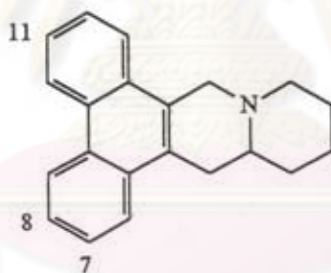
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N-methyl-2,3,6- trimethoxy morphinandien-7-one IX₁₀



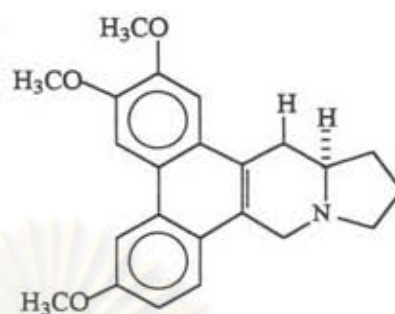
X. Phenanthroquinolizidine and Phenanthroindolizidine

The phenanthroquinolizidine and phenanthroindolizidine alkaloids are basic pentacyclic compounds. They are found in member of the Lauraceae and Moraceae. (Pelletier, 1970).

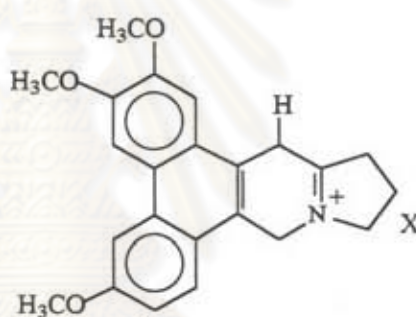
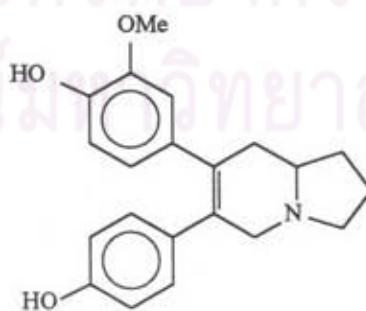


Alkaloids	Constituent Positions			
	2	3	6	12
cryptopleuridine X ₁	-OCH ₂ O-		OMe	OH
cryptopleurine X ₂	OMe	OMe	OMe	-

antofine

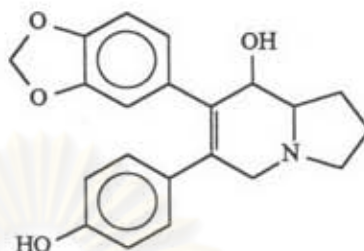
X₃

dehydroantofine

X₄phyllostemine X₅

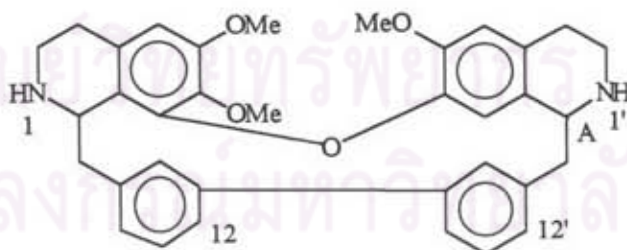
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phyllosteminine X₆

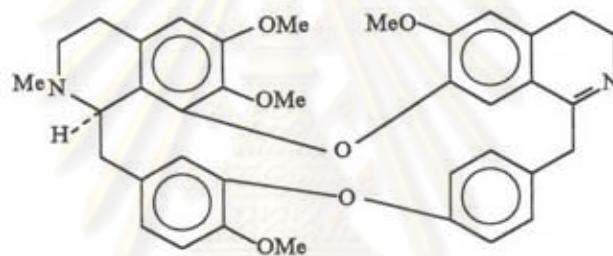
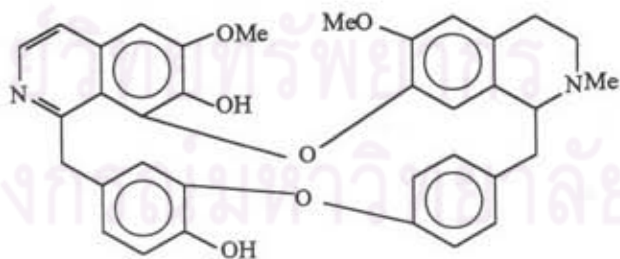


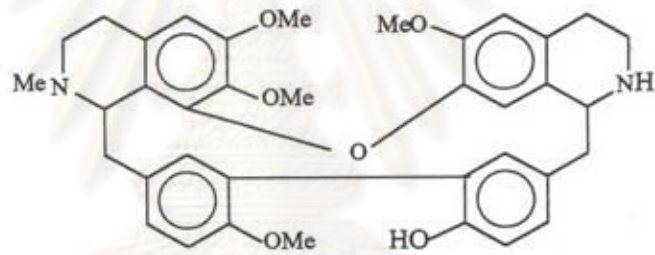
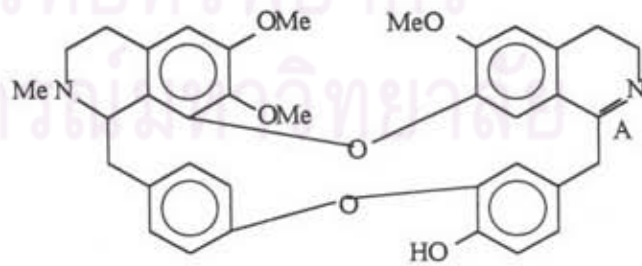
XI. Bisbenzylisoquinoline

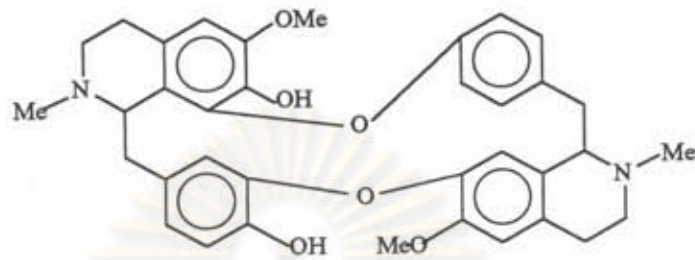
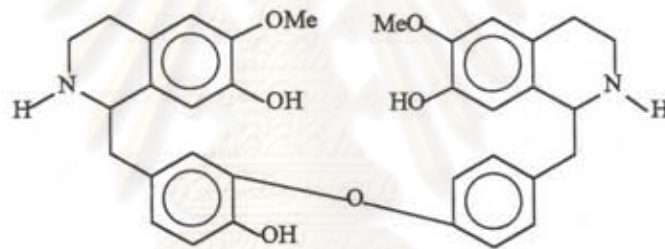
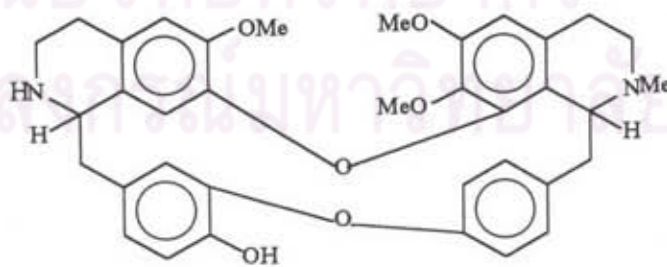
The Lauraceae contains several types of bisbenzylisoquinoline alkaloids in which two simple benzylisoquinolines unit appear to have been joined together head-to-head, tail-to-tail by phenol oxidative processes (Ralph *et al*, 1978). Aromatic substituents may be hydroxy, methoxy or methylenedioxy. Linkage may be of the diphenyl or diphenyl ether type and a given compound may contain one or more of each of these linkages. A typical bisbenzylisoquinoline contains two asymmetric centers, but sometime one or both nitrogen atoms are involved in imino groups (Cordell, 1981).



Alkaloids		Substituent Positions			
		1	1'	12	12'
norrodiasine	XI ₁	H(Me)	Me(H)	OMe	OH
ocotine	XI ₂	Me	H	OMe	OH
rodiasine	XI ₃	Me	Me	OMe	OH

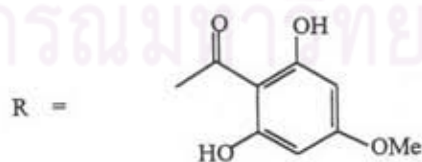
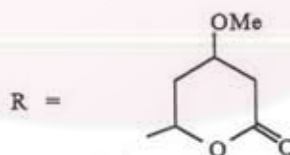
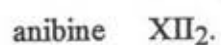
dehatrine XI₄dehatridine XI₅

obaberine XI₆ocotosine XI₇sepeerine XI₈

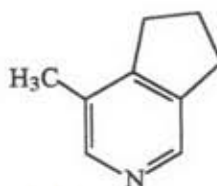
bebeerine XI₉lindoldhamine XI₁₀demerarine XI₁₂

XII. Pyridine

In the Lauraceus plant pyridine alkaloids were found in the genus *Aniba* and *Sauraria* (Ralph, Bick and Sinchai, 1978).



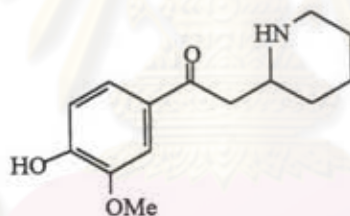
actinidine XII₄.



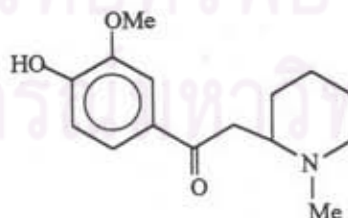
XIII. Sedamine alkaloids

Pleurospermine is an alkaloid of sedamine type which is considered to be derived from condensation of two equivalents of dihydroxyphenylalanine and one equivalent of lysine. (Johns *et al.*, 1969). In the family Lauraceae it was found only in *Cryptocarya* sp.

pleurospermine XIII₁



phyllostone XIII₂

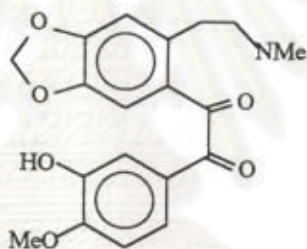


XIV. Cryptopleurospermines

Cryptopleurospermine is the sole representative of a type with fewer rings, and it would seem to have been formed by oxidative ring-opening of a tetrahydroisoquinoline structure. It was also found in *C. pleurosperma* (Ralph *et al.*, 1978).

In Lauraceous plants, scoulerine was the first protoberberine alkaloid isolated from *Cryptocarya longifolia* Kosterm (Johns *et al.*, 1970).

cryptopleurospermine XIV

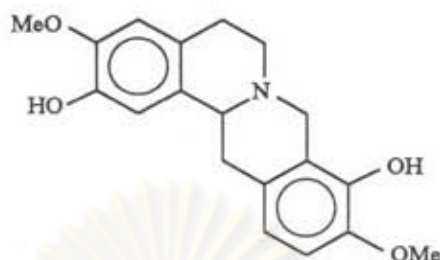


XV. Protoberberine

Scoulerine is the first protoberberine alkaloid isolated from Lauraceous plants, *Cryptocarya longifolia* Kosterm. (Ralph *et al.*, 1981).

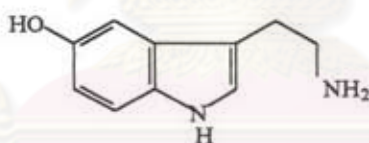
The protoberberine are one of the most widely distributed of the isoquinoline alkaloid groups, being present in at least nine plant families, particularly the Annonaceae, Berberidaceae, Lauraceae and Menispermaceae (Cordell, 1981f).

scoulerine XV

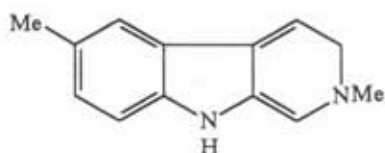


XVI. Indole alkaloids

The simplest natural representatives with an indole nucleus are the biogenic amine tryptamine and serotonin. Serotonin was isolated from the genus *Persea* and *Nectandra* (Ralph *et al.*, 1979).

Serotonin (5-hydroxytryptamine) XVI₁

β -carboline nucleus are derived biogenetically from tryptamine (Hesse, 1981). In Lauraceous plants, 6-methyl-N-methyl-1,2,3,4-tetrahydro β -carboline was isolated from *Nectandra megapotamica* (Filho and Silvio, 1980).

6-methyl-N-methyl-1,2,3,4-tetrahydro β -carboline XVI₂

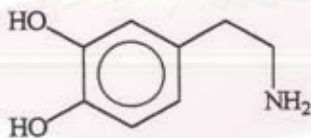
N-methyltryptamine XVI₃



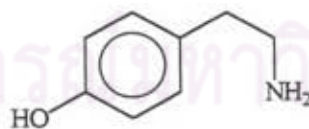
XVII. Phenethylamine

Phenanthrene alkaloid, dopamine and tyramine, were isolated in *Persea sp.*

dopamine XVII₁



tyramine XVII₂



Biosynthesis of aporphine alkaloids

The biogenetic pathway leading to isoquinoline alkaloids are derived from tyrosine. Tyrosine is first elaborated to a suitable hydroxylated phenethylamine which is then combined with a second building block. The second building block can vary widely to give various types of isoquinolines. The biosynthesis of isoquinoline alkaloids is conveniently treated in two parts, starting with the generation of benzyloisoquinolines and then elaborating to more complicated structures (Staunton, 1979).

In vitro, all these routes apparently can operate. The proven or probable biogenetic loci for the formation of the isoquinoline alkaloids is shown in scheme I (Shamma, 1972). The biogenetic relationships of the major alkaloid groups derived from a tetrahydrobenzyloisoquinoline precursor are shown in Figure 2 (Codell, 1981a).

Benzyloisoquinoline derive from two molecule of L-tyrosine. They occupy a paramount position in alkaloid chemistry because they act as *in vivo* precursors to so many of the other naturally occurring isoquinoline. Reticuline is regarded as the key intermediate in the biosynthesis of the alkaloids based on the benzyloisoquinoline nucleus and also was the precursor of alkaloids such as boldine, isoboldine and bulbocapnine (Shamma, 1972). The example of the formation of reticuline in *Papaver somiferum* Linn. is shown in Scheme 2 (Goodwin and Mercer, 1983).

The first step (A) involves the conversion of two molecules of L-tyrosine into two molecules of DOPA. One molecule of DOPA is converted into dopamine (B) whilst the other into 3-4-dihydrophenylpyruvic acid (C). These two compounds then combine with, elimination of water and carbondioxide, in a Mannich-type reaction to yield a molecule of norlaudanosine (D) O- and N-methylation(E) then lead to (-)-reticuline (Goodwin and Mercer, 1983).

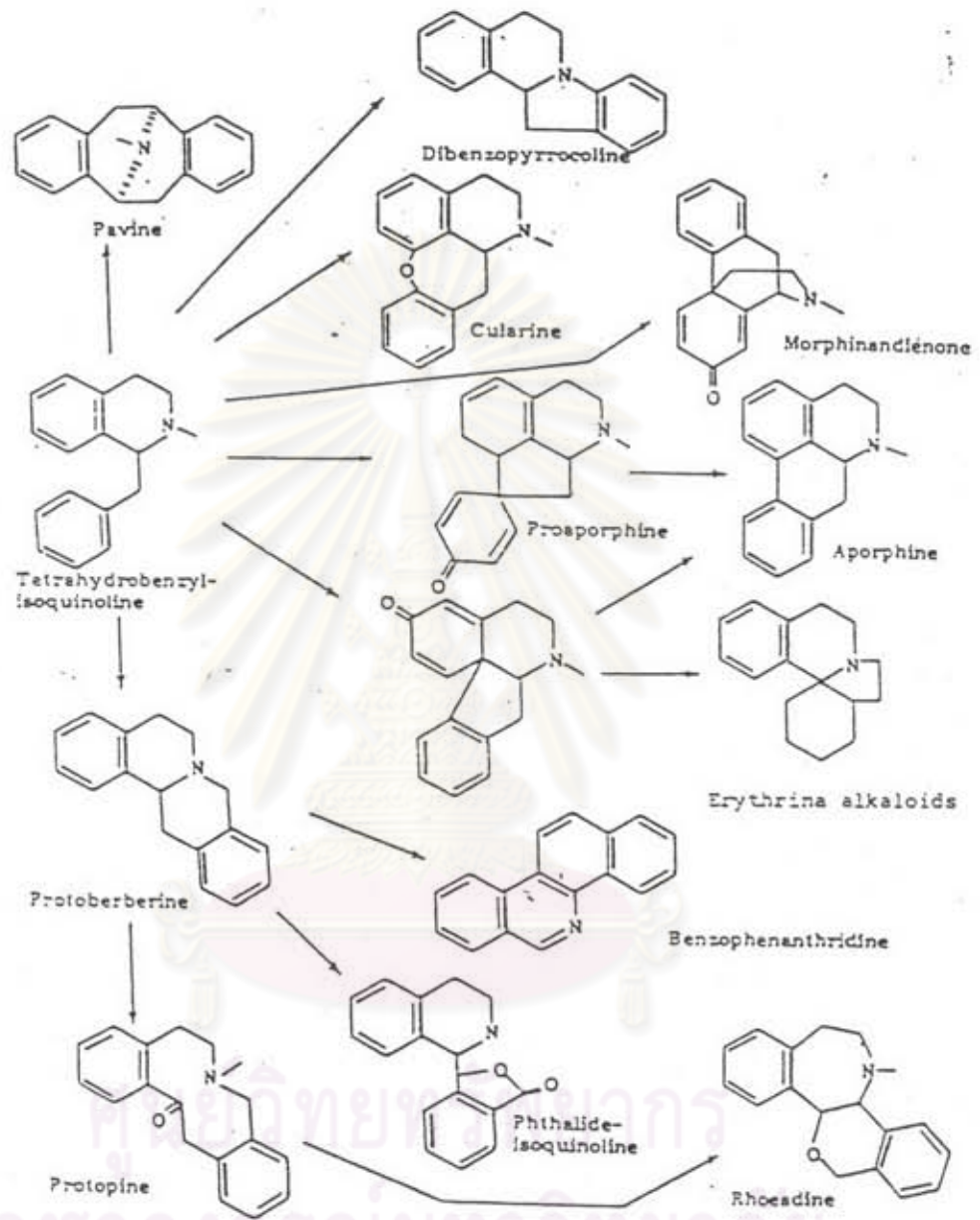
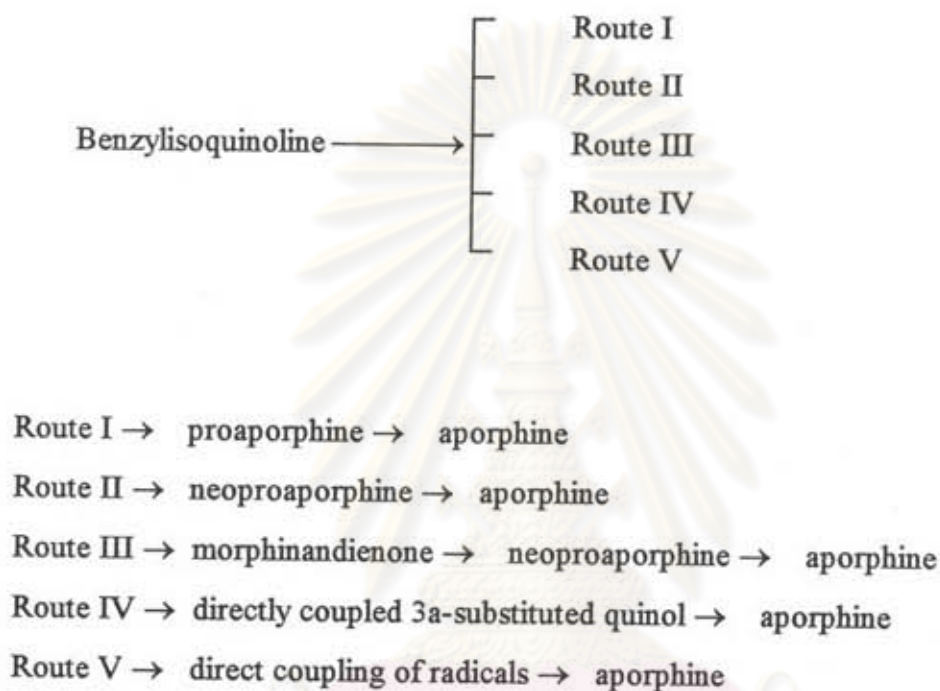


Figure 2 The biogenetic relationships of the major alkaloid groups derived from a tetrahydroisoquinoline precursor

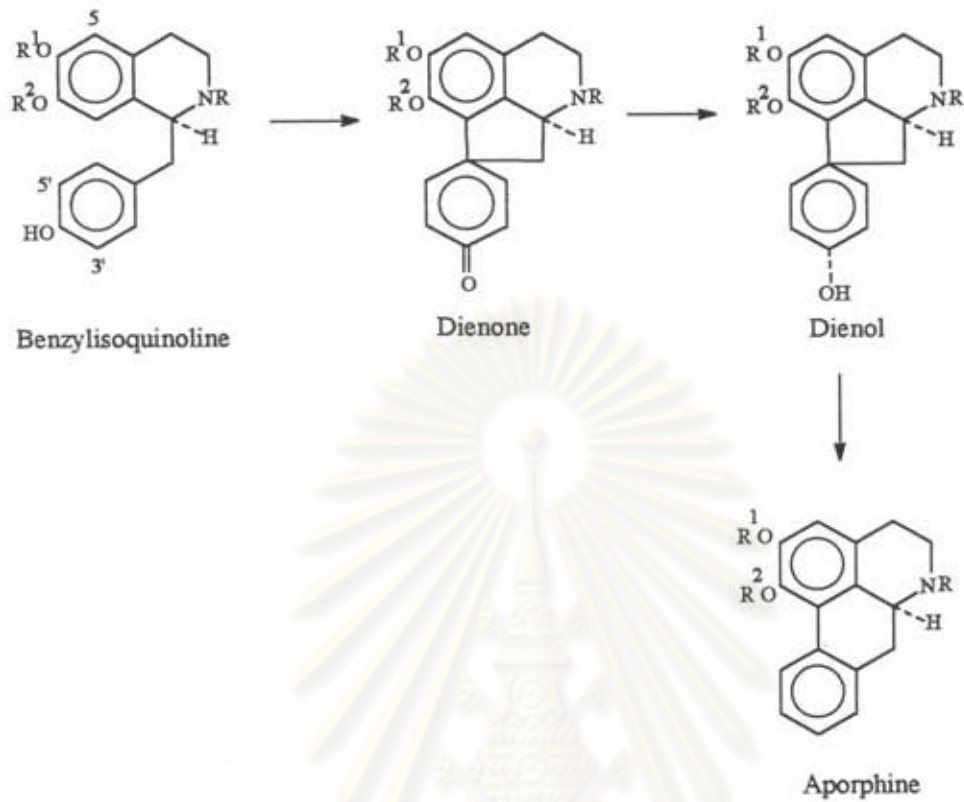
The discussion on the biogenetic synthesis of the aporphine alkaloids has raised a number of points concerning the biogenesis of this group. Depending on the orientation of phenolic and methoxy groups, any of at least five routes might be envisaged as being in operation from benzyloquinoline precursor as shown in Scheme 3 (Cordell, 1981a).



Scheme 3 Biogenesis of aporphine from benzyloquinoline

Route I: Benzyloquinoline → proaporphine → aporphine

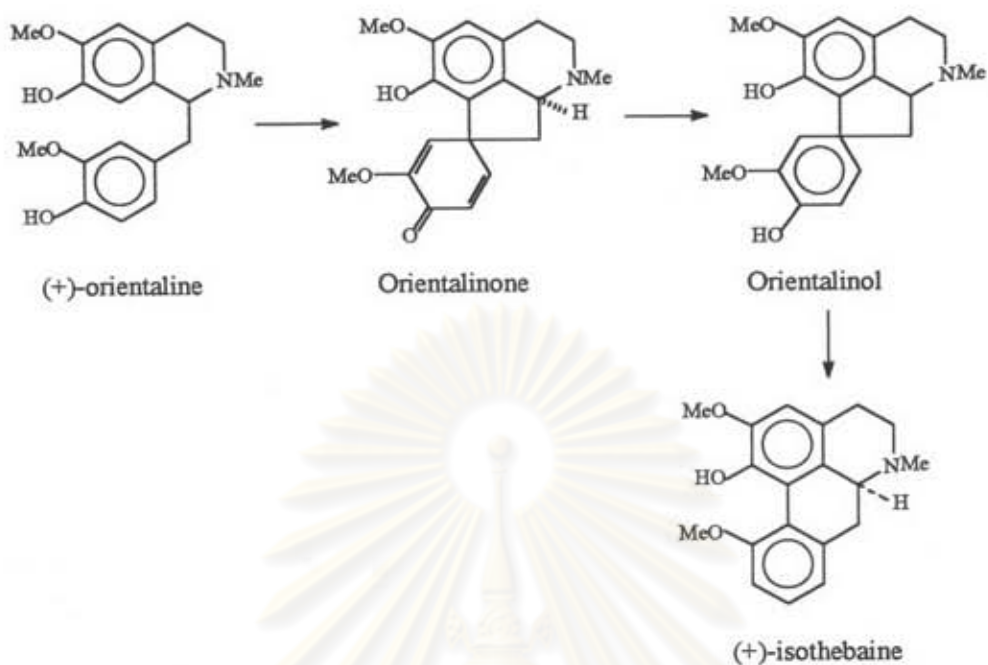
From scheme 4, aporphine alkaloids lacking an oxygen substituent in ring D are derived from a benzyloquinoline by oxidation to a dienone, reduction to dienol and then, dehydration with rearrangement to the aromatic compound (Barton *et al*, 1967).



Scheme 4 Reaction of benzyloquinoline to aporphine

Battersby and co-workers showed that labeled (+)-orientaline, the compound was the precursor of isothebaine, when fed to *Papaver orientale* Linn. through the intermediacy of the proaporphine orientalinone and orientalinol, as shown in scheme 5 (Battersby, 1965).

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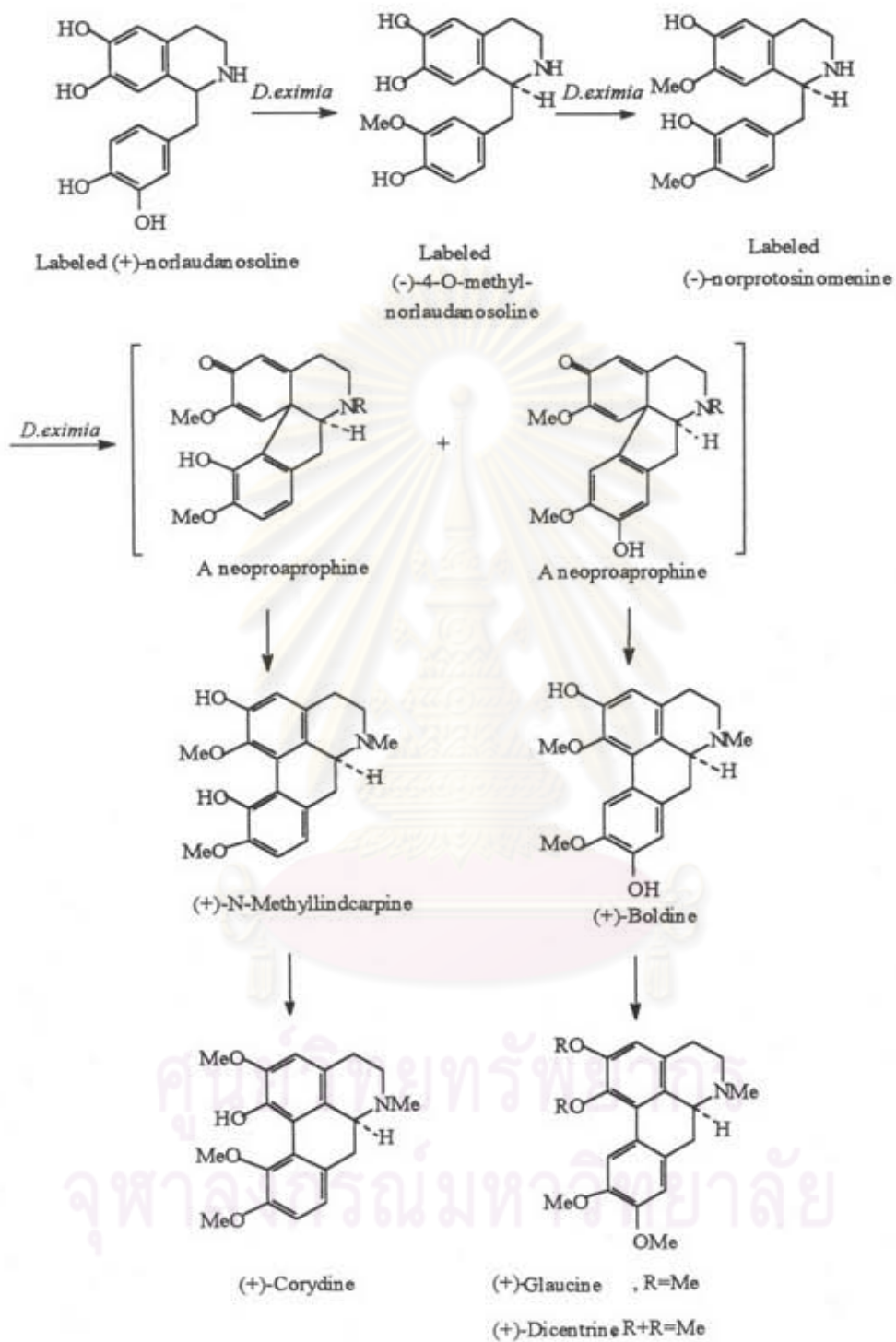


Scheme 5 Biosynthesis of (+)-isothebaine

Route II: Benzyloisoquinoline \rightarrow neoaporphine \rightarrow aporphine

Battersby and co-workers, 1960, study the formation of corydine and glaucine in *Dicentra eximia* (Ker.)Torr. (Fumariaceae). It was reticuline and orientaline were not precursors, while 4'-O-methylnorlaudanosoline and norprotosinomenine were effective precursors. 4'-O-methylnorlaudanosoline is converted into norprotosinomenine, which must be incorporated into the three aporphine alkaloids by way of the two neoproaporphine intermediates indicated in scheme 6 (Shamma, 1972; Cordell, 1981).

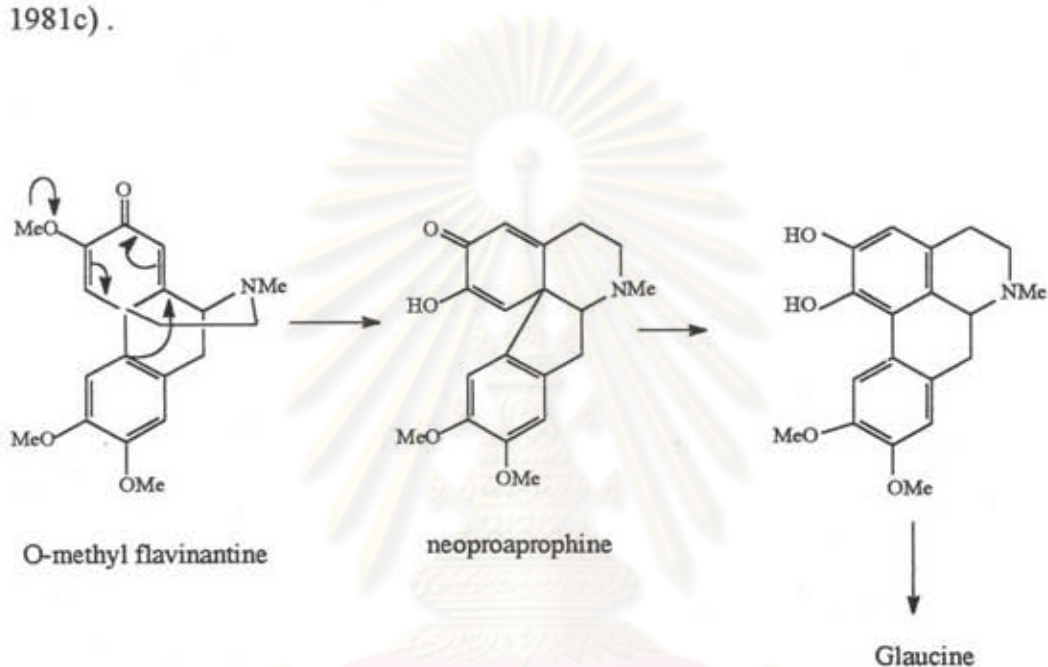
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Scheme 6 Biosynthesis of corydine, dicentrine and glaucine in *Dicentra eximia* (Kerr.) Torr.

Route III: Benzyloisoquinoline → morphinandienone → neoproaporphine → aporphine

In 1965, Barton and Battersby described the pathway which is open to morphinandienones such as O-methylflavinantine, namely their ability to rearrange to aporphine derivatives as shown in scheme 7. These are *in vitro* interconversions; their importance in the *in vivo* biosynthesis of aporphine remains to be demonstrated (Cordell, 1981c).

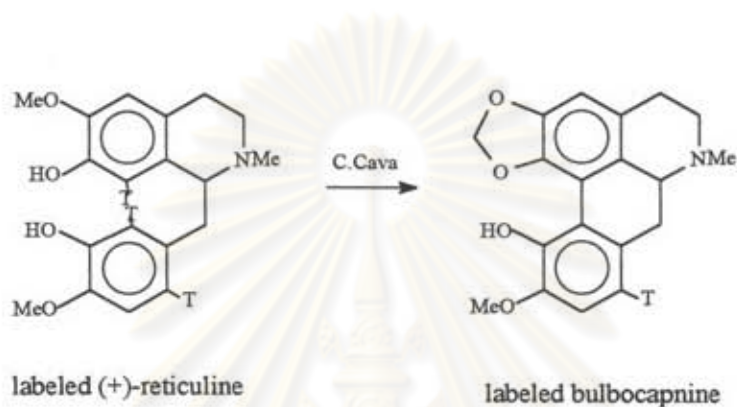


Scheme 7 Biogenesis of Glaucine

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Route IV: Directly coupled 3a-substituted quinol → aporphine

It is very difficult in some instance to say what the probable mechanism is unless variously methylated benzyloquinoline precursors are used. For example, N-methyl labeled (+)-reticuline was a precursor of bulbocapnine in *Corydalis cava* Schweigg et Korte(Fumariaceae) (Cordell, 1981a).

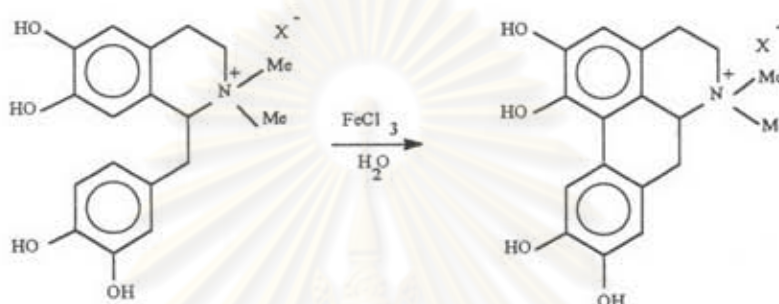


Scheme 8 Biosynthesis of bulbocapnine

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Route V: Direct coupling of radicals \rightarrow aporphine

In 1962, Frank and co-workers reported the first *in vitro* synthesis of a quaternary aporphine by phenolic oxidative coupling using quaternary salt. Treatment of N-methylaudanosine methiodide with aqueous ferric chloride gave a good yield of a tetrahydrobenzylisoquinoline N-metho salt (Shamma and Guinaudeau, 1984).



N-methylaudanosine methiodide

Scheme 9 *in vitro* synthesis of tetrahydrobenzylisoquinoline N-metho salt

Direct phenolic coupling can thus explain the genesis of several 1,2,10,11 as well as 1,2,9,10 tetrasubstituted aporphines. It does not rationalize for us, however, the existence of other aporphine such as those bearing a single oxygenated function in the D-ring, or those devoid of oxygen on that ring (Shamma and Guinaudeau, 1984).

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Pharmacology of aporphine alkaloids

The aporphine alkaloids display a wide range of pharmacological activities. The pharmacological activities of aporphine alkaloids have been reviewed by Cordell (1981a). Those are as follows:-

1,2-Methylenedioxyaporphine increases arterial blood pressure, but higher doses cause strychnin-like convulsions. The methoxide salt has a curare-like action .

Isothebaine increased intestinal muscle tone in rabbits and also amplified uterine contractions in the rat. Other activities observed include decreased motor activity and analgesia(mice), and an anti-inflammatory effect in rats .

Glaucine (IV₂₀) reduced blood pressure and inhibited respiration in cats and had antitussive effects resembling codeine, but of longer duration. In rats and cats a potentially useful hypoglycemic effect was observed at 12-mg/kg doses.

Glaucine (IV₂₀) and Laurotetanine (IV₃₄) are reported to increase the antimitotic effect of colchicine (Bhakuni and Gupta, 1983).

Dehydroglaucine has antibacterial activity. Glaucine and dicentrine cause narcosis in animals, and with larger dose convulsions .

Corydine (IV₁₁) has central nervous system depressant and hypotensive activity and blocks transmission of nerve impulses. The corresponding 11-demethyl derivative, corytuberine, accelerates and stimulates secretions.

Bulbocarpnine (IV₆) antagonizes the effects of apomorphine and amphetamine, depresses the central nervous system, and causes catalepsy in mice.

Xylopine has sedative and analgesic activity .

Apomorphine, although not a natural product, has been quite well studied. It has hypotensive activity and is a powerful emetic, suitable for rapid emesis after ingestion of poisons. Of more interest from a therapeutic point of view is its stimulation of dopaminergic system in rats and mice, and consequently its potential anti-Parkinsonism activity. Also of interest are reports that it can decrease serum prolactin levels .

Isoboldine (IV₂₆) is an insect-feeding inhibitor (Cordell, 1981a) and some antifungal activity (Paulo *et al*, 1992).

Laurifoline chloride has some hypotensive activity, while corytuberine (IV₁₂) accelerates respiration and slows the pulse (Shamma, 1972).

Boldine (IV₅) is only slightly toxic and does not cause addiction. It has a mild sedative, diuretic, and antiparasitic action, and also increases the secretions of the liver and salivary glands (Shamma, 1972).

(S)-boldine(IV₅) and (R)-apomorphine have interesting properties as Ca²⁺ entry blockers (through the benzothiazepine receptor site in the Ca²⁺ channel) and at alpha1-adenoreceptors (Ivorra *et al*, 1993a).

Boldine(IV₅) and glaucine(IV₂₀) behave as specific calcium entry blockers without affecting the contractile machinery or intracellular Ca²⁺ levels as apomorphine does (Ivorra *et al*, 1993b).

Bulbocapnine(IV₆), boldine(IV₅), glaucine(IV₂₀) and stepholidine acted as scavengers of hydroxyl radical in the deoxyribose degradation by Fe³⁺-EDTA + H₂O₂. On the contrary, laudanosoline, apomorphine, protopapaverine, anonaine and tetrahydroberberine increased deoxyribose degradation by a mechanism related to generation of superoxide anion in microsomes (Ubeda *et al*, 1993).

Thalicarpine was known as Tumour-inhibiting alkaloid (Venditti *et al*, 1967).

d-Dicentrine(IV₁₅) inhibited the aggregation of rabbit platelets induced by adenosine diphosphate, collagen and arachidonic acid, inhibited the high potassium and norepinephrine-induced contraction of rat thoracic aorta and prolonged the action potential duration of rat ventricular cells (Chen *et al*, 1990). It also appears to exert its hypotensive action through alpha-1-adenoreceptor blockade and in high doses it did not cause any significant changes in heart rate, cardiac output and stroke volume (Yu *et al*, 1992).

Oxophoebine and liriodenine showed selective toxicity against DNA repair and recombination deficient mutants of the yeast *Saccharomyces cerevisiae* (Harrigan *et al*, 1994).