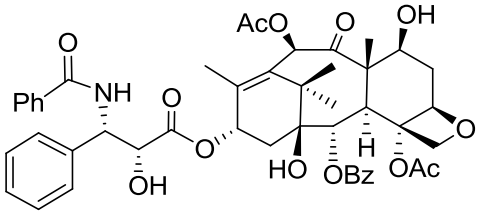
CHAPTER ONE

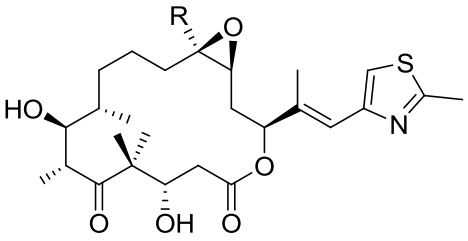
INTRODUCTION

1.1 General

Natural products play a highly significant role in the drug discovery and development process[1] and this was particularly evident with the increasing number of natural product derived compounds that are being evaluated in clinical trials.[2,3] Two well known recent examples are the plant derived antitumor compound, taxol[4,5] and the microbially-derived antitumor agents, epothilones A and B.[6,7] Moreover, technological advances and the development of new methods have revolutionized the screening of natural products and offer a unique opportunity to re-establish natural products as a major source for drug discovery.[8] Besides providing biologically active compounds, natural substances also act as useful materials or models for semisynthetic manipulation to obtain other active analogues for evaluation.[9,10] In view of the rich natural resources available in this country, such an approach directed towards the discovery and development of potentially useful pharmaceuticals offer great promise.[11-13]



Taxol



R = H Epothilone A
R = Me Epothilone B

1.2 The Alkaloids

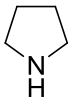
The term ‘alkaloid’, was first defined by W. Meissner in 1819[14] and since then has gone through many redefinitions due to the development and increasing detection of alkaloids from natural resources. To date, in view of the fact that pure amino acids, peptides, nucleic acids, and synthetic organic nitrogen bases are not counted among the alkaloids, a more general definition is employed, *viz.* alkaloids are nitrogen-containing organic substances of natural origin with a greater or lesser degree of basic character.[15]

So far the total number of alkaloids isolated from natural resources is enormous. Thus, the classification of alkaloids is essential. The criteria currently used for alkaloid classification are based on biogenesis, structural relationship, biological origin, and spectroscopic or spectrometric properties. No unified, general taxonomic principle that would permit consistent classification exists.[15]

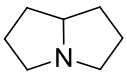
Essentially, five distinct alkaloid classes are classified, according to the position of the N-atom in the main structural element, namely:

- Heterocyclic alkaloid
- Alkaloids with N-atoms in exocyclic positions including aliphatic amines
- Putrescine, spermidine, and spermine alkaloids
- Peptide alkaloids
- Terpene and steroid alkaloids

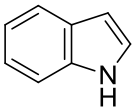
In common use, the term alkaloids refers to the heterocyclic alkaloids. In representatives of this class, the N-atom constitutes part of a heterocycle. The heterocyclic alkaloids constitute the major part of these classes and can be further classified into 15 classes based on the carbon-nitrogen skeleton:[15]



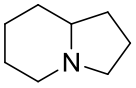
Pyrrolidine



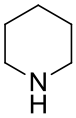
Pyrrolizidine



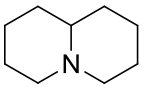
Indole



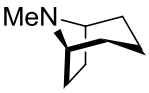
Indolizidine



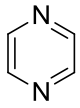
Piperidine



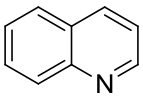
Quinolizidine



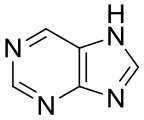
Tropane



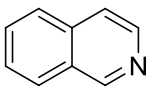
Pyrazine



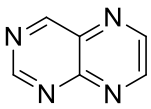
Quinoline



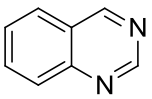
Purine



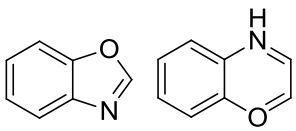
Isoquinoline



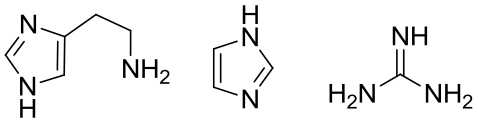
Pteridine



Quinazoline



Benzoxazines and benzoxazoles

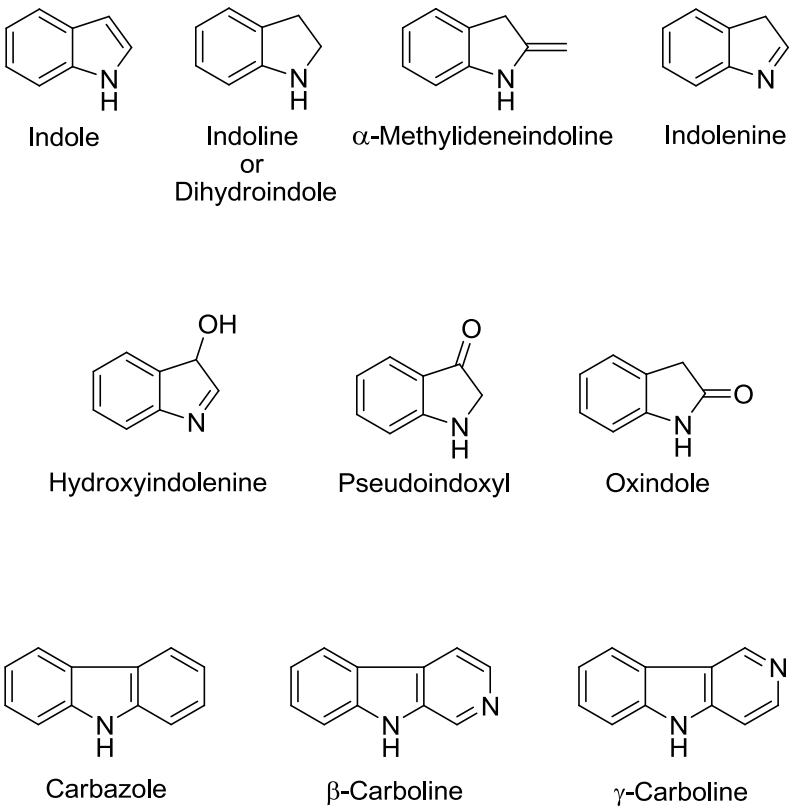


Histamine, imidazole, and guanidine

1.3 Indole Alkaloids of the Apocynaceae

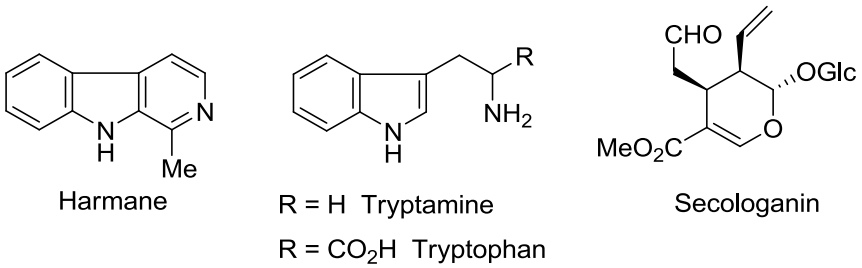
1.3.1 General

The indole alkaloids constitute the biggest single class of the alkaloids. The figure below includes those compounds that incorporate the actual indole chromophore and those containing its derivatives: namely indoline (also known as dihydroindole), α–methylideneindoline, indolenine, hydroxyindolenine, pseudoindoxyl, and oxindole. Also members of this group are alkaloids in which the nucleus incorporates an additional benzene or pyridine ring, for instance, carbazole or β- and γ-carbolines, and their derivatives.[15-17]

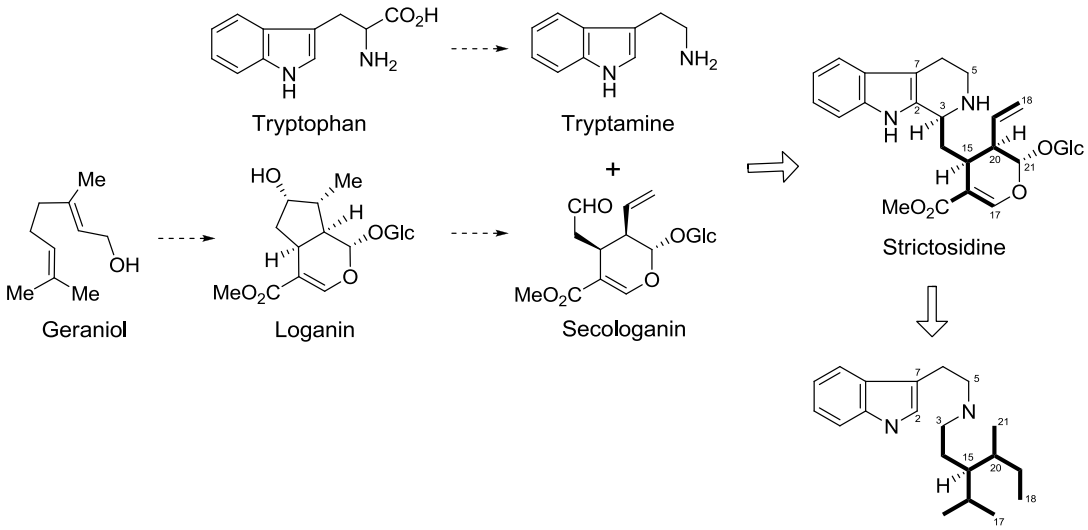


1.3.2 Classification of the Indole Alkaloids

The indole alkaloids can be further classified based on the structural and biogenetic criteria. With respect to their structural features, indole alkaloids can be divided into two main categories. The first constitutes the simple indole alkaloids which do not present a structural uniformity, possessing only the indole nucleus or a direct derivative of it as a common feature (*e.g.*, harmane).

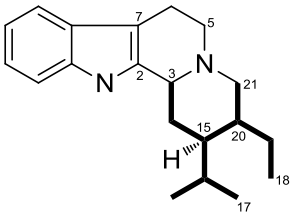


Indole alkaloids of the second category, which are known as the monoterpene indole alkaloids, contain two structural units, *viz.*, tryptamine (or tryptophan) with the indole nucleus and a C_{9-} or C_{10-} monoterpene moiety derived from secologanin. The majority of the indole alkaloids from plants are from this category.[15,17,18]

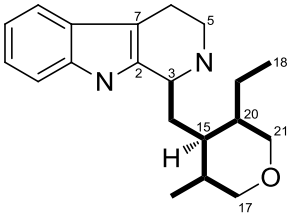


Scheme 1.1 : Strictosidine from tryptophan and loganin

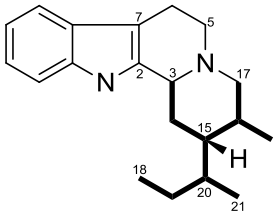
The monoterpene indole alkaloids share a common biogenetic origin. All of them arise from a unique precursor which is strictosidine. It is a condensation product of secologanin and tryptamine (Scheme 1.1).[19-21] Based on their biogenesis they have been structurally classified into ten main skeletal types: corynanthean (C), vincosan (D), vallesiachotaman (V), strychnan (S), aspidospermatan (A), eburnan (E), plumeran (P), heynean (H), capuronan (K), and tacaman (T).[16,22-24]



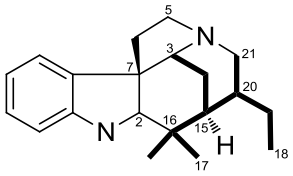
Corynanthean (**C**)



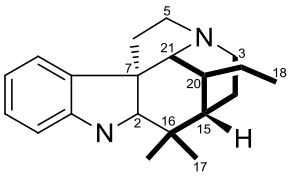
Vincosan (**D**)



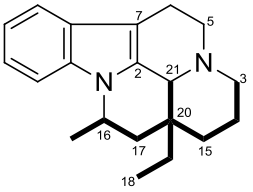
Vallesiachotaman (**V**)



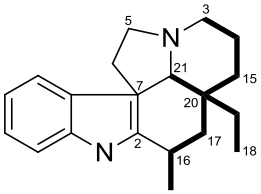
Strychnan (**S**)



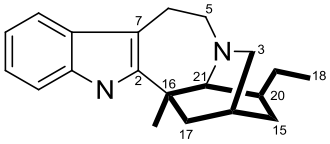
Aspidospermatan (**A**)



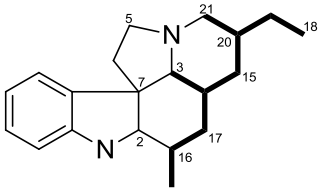
Eburnan (**E**)



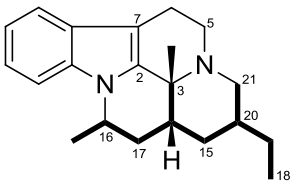
Plumeran (**P**)



Heynean (**H**)



Capuronan (**K**)



Tacaman (**T**)

1.4 The Genus *Kopsia*

1.4.1 General

The genus *Kopsia* belongs to the tribe Vinceae, subfamily Rauvolfioideae of the family Apocynaceae.[25-29] This genus is well represented in South East Asia.[30,31] A few species also occurred in China, India, and Australia.[30,31] Plants of this genus are normally evergreen shrubs or small trees, occurring in lowland forests. The leaves are elliptical in shape and are opposite to one another with the gland at the end of the acumen on the dorsal face. Most species of *Kopsia* have young branches that are somewhat angled and in some species the angles become so pronounced as to become wing-like. A unique peculiarity of most species of this genus is the nose-like ventral appendage of the mericarp which is a cavity completely secluded from the seed-bearing portion by a wall.[29,32,33]

There are a total of 24 *Kopsia* species based on the most recent revision of this genus by Middleton,[29,34] of which 18 species are to be found in Malaysia (Peninsular Malaysia and Borneo). They are listed below:[29,33]

i. *K. arborea* Blume

ii. *K. dasyrachis* Ridl.

iii. *K. deverrei* L. Allorge

iv. *K. fruticosa* (Roxb.) A. DC.

v. *K. grandifolia* D. J. Middleton

vi. *K. griffithii* King & Gamble var. *griffithii*

vii. *K. griffithii* King & Gamble var. *pubescens* D. J. Middleton

viii. *K. larutensis* King & Gamble

ix. *K. macrophylla* Hook. f.

x. *K. pauciflora Hook.* f. var. *pauciflora*

xi. *K. pauciflora* Hook. f. var. *mitrephora* (Sleesen) D. J. Middleton

xii. *K. profunda* Markgr.

xiii. *K. rajangensis* D. J. Middleton

xiv. *K. rosea* D. J. Middleton

xv. *K. singapurensis* Ridl.

xvi. *K. sleeseniana* Markgr.

xvii. *K. tenuis* Leenh. & Steenis

xviii. *K. teoi* L. Allorge

Certain species of the genus *Kopsia* are used in traditional medicines. In Malaysia, roots of *K. larutensis*, *K. profunda* (*K. macrophylla*), *K. pauciflora*, and *K. singapurensis* are used for poulticing ulcerated noses in tertiary syphilis.[33] The use of *K. arborea* (*K. officinalis*) in China for the treatment of rheumatoid arthritis, dropsy, and tonsillitis were also reported.[35,36] Under the name 'somu', *K. flavida* is used as a contraceptive in Vanuatu.[33]

1.4.2 Alkaloids of the Genus *Kopsia*

Plants of the genus *Kopsia* provide mainly indole alkaloids with alkaloids of the aspidofractinine skeletal type predominating (Table 1.1). Several bisindoles, *viz.*, kopsoffinol, (–)-norpleiomutine, (–)-demethylnorpleiomutine, (+)-kopsoffine, tenuiphylline, nitaphylline, kopsiyunnanine A, and the quasidimer buchtienine, also occur in some *Kopsia* species. In addition to the indole and bisindole alkaloids, a relatively small number of monoterpene alkaloids related to skytanthine (kinabalurines A–G, kopsilactone, and kopsone) have also been isolated.[33,37]

1.4.3 Occurrence and Distribution of Alkaloids in the Genus *Kopsia*

The occurrence of alkaloids in *Kopsia* as reported in the literature (up to October 2011) is summarized in Table 1.1.

Table 1.1 : Occurrence of alkaloids in *Kopsia*

Plant[a]	Plant part	Alkaloids	References
K. arborea Blume (Peninsular Malaysia)	Leaves	Arbophylline (**61**)	38
		Methyl *N*(1)-decarbomethoxychanofruticosinate (**240**)	39
		Methyl 11,12-methylenedioxy-*N*(1)-decarbomethoxychanofruticosinate (**244**)	39
		Methyl 11,12-methylenedioxychanofruticosinate (**239**)	39
		Methyl 11,12-methylenedioxy-*N*(1)-decarbomethoxy-$\Delta^{14,15}$-chanofruticosinate (**245**)	39
		Prunifoline A (**247**)	40
		Prunifoline B (**248**)	40
		Prunifoline C (**249**)	40
		Prunifoline D (**250**)	40
		Prunifoline E (**251**)	40
		Prunifoline F (**252**)	40
	Stem-bark	Akuammidine (**81**)	41
		Arboflorine (**60**)	41,42
		Arboloscine (**132**)	41,43
		Arboricine (**63**)	41,44
		Arboricinine (**64**)	41,44
		Aspidofractinine (**141**)	41
		Dasyrachine (**264**)	41
		N(1)-Decarbomethoxykopsamine (**156**)	41
		5,21-Dihydrorhazinilam (**129**)	41
		15α-Hydroxykopsinine (**137**)	41
		Kopsamidine A (**189**)	41
		Kopsamidine B (**190**)	41
		Kopsamine (**20**)	41
		Kopsamine *N*-oxide (**21**)	41
		Kopsanone (**16**)	41
		Kopsifine (**17**)	41
		Kopsiflorine (**157**)	41
		Kopsilongine (**27**)	41
		Kopsinidine A (**227**)	41
		Kopsinidine B (**228**)	41
		Kopsinine (**22**)	41
		Leuconoxine (**14**)	41
		Mersicarpine (**130**)	41,45
		N(1)-Methoxycarbonyl-11,12-dimethoxykopsinaline (**26**)	41
		19(*R*)-Methoxytubotaiwine (**97**)	41
		19(*S*)-Methoxytubotaiwine (**96**)	41
		Methyl *N*(1)-decarbomethoxychanofruticosinate (**240**)	41
		11,12-Methylenedioxykopsine (**226**)	41
		O-Methylleuconolam (**134**)	41

Table 1.1, continued

Plant[a]	Plant part	Alkaloids	References
		Methyl 12-methoxychanofruticosinate (**241**)	41
		Methyl 11,12-methylenedioxychanofruticosinate (**239**)	41
		Methyl 11,12-methylenedioxy-*N*(1)-decarbomethoxychanofruticosinate (**244**)	41
		Methyl 11,12-methylenedioxy-*N*(1)-decarbomethoxy-$\Delta^{14,15}$-chanofruticosinate (**245**)	41
		Norfluorocurarine (**102**)	41
		Paucidactine B (**19**)	41
		Paucidactine C (**221**)	41
		Pericidine (**101**)	41,43
		Pericine (**99**)	41
		Pericine *N*-oxide (**100**)	41
		Pleiocarpamine (**85**)	41
		Prunifoline E (**251**)	41
		Rhazimal (**66**)	41
		Rhazinicine (**127**)	41
		Rhazinilam (**126**)	41
		Rhazinoline (**65**)	41
		Tetrahydroalstonine (**13**)	41
		Valparicine (**104**)	41,46
		Venalstonidine (**143**)	41
		Venalstonine (**142**)	41
		Vincadifformine (**136**)	41
K. arborea Blume (*K. flavida*) (Peninsular Malaysia)	Leaves	Danuphylline B (**263**)	47
		Flavisiamine A (**253**)	48
		Flavisiamine C (**254**)	48
		Flavisiamine D (**255**)	48
		Flavisiamine E (**256**)	48
		Flavisiamine F (**257**)	48
		12-Methoxykopsine (**225**)	47
		Methyl 11,12-dimethoxychanofruticosinate (**242**)	49
		Methyl 11,12-methylenedioxy-*N*(1)-decarbomethoxychanofruticosinate (**244**)	49
		Methyl 12-methoxychanofruticosinate (**241**)	49
		Methyl 12-methoxy-*N*(1)-decarbomethoxy-chanofruticosinate (**246**)	49
		Methyl 3-oxo-11,12-methylenedioxy-*N*(1)-decarbo-methoxy-14,15-didehydrochanofruticosinate (**260**)	50
		Methyl 3-oxo-12-methoxy-*N*(1)-decarbomethoxy-14,15-didehydrochanofruticosinate (**261**)	50
		Prunifoline C (**249**)	48
K. arborea Blume (*K. albiflora*, *K. pruniformis*) (India)	Leaves	Kopsine (**223**)	51-54
K. arborea Blume (Indonesia)	Leaves	Flavisiamine A (**253**)	55
		Flavisiamine C (**254**)	55
		Flavisiamine D (**255**)	55
		Kopreasin A (**262**)	55
		Methyl 12-methoxychanofruticosinate (**241**)	55
		Methyl 12-methoxy-*N*(1)-decarbomethoxychanofruticosinate (**246**)	55
		Methyl 11,12-methylenedioxychanofruticosinate (**239**)	55

Table 1.1, continued

Plant[a]	Plant part	Alkaloids	References
		Methyl 11,12-methylenedioxy-*N*(1)-decarbomethoxychanofruticosinate (**244**)	55
		Methyl 11,12-methylenedioxy-*N*(1)-decarbomethoxy-$\Delta^{14,15}$-chanofruticosinate (**245**)	55
		Methyl *N*(1)-decarbomethoxychanofruticosinate (**240**)	55
		Prunifoline B (**248**)	55
K. arborea Blume (*K. jasminiflora*) (Thailand)	Leaves	14,15-Dehydrokopsijasminilam (**278**)	56
		10-Demethoxykopsidasinine (**273**)	57
		Deoxykopsijasminilam (**277**)	56
		Fruticosamine (**218**)	56
		Fruticosine (**217**)	56
		Jasminiflorine (**219**)	56
		Kopsijasmine (**200**)	56
		Kopsijasminilam (**276**)	56
K. arborea Blume (*K. longiflora*) (Queensland, Australia)	Leaves	Kopsamine (**20**)	58,59
		Kopsiflorine (**157**)	58,59
		Kopsilongine (**27**)	58,59
	Stem-bark	Kopsamine (**20**)	58,59
		Kopsilongine (**27**)	58,59
		Kopsinine (**22**)	58,59
K. arborea Blume (*K. pitardii*) (Vietnam)	Leaves	Methyl 11,12-methylenedioxy-*N*(1)-decarbomethoxy-$\Delta^{14,15}$-chanofruticosinate (**245**)	60
		Methyl *N*(1)-decarbomethoxychanofruticosinate (**240**)	60
		Methyl 11,12-methylenedioxychanofruticosinate (**239**)	60
K. arborea Blume (*K. officinalis*) (China)	Aerial	Arboloscine (**132**)	61
		(*E*)-Condylocarpine (**88**)	62
		(*E*)-Condylocarpine *N*-oxide (**89**)	62
		(+)-Eburnamenine (**31**)	63
		(−)-Eburnamine (**33**)	63
		(+)-Eburnamonine (**32**)	63
		Eburenine (**120**)	63
		(−)-Ethyleburnamine (**109**)	63
		(+)-Ethylisoeburnamine (**110**)	63
		(*Z*)-Isocondylocarpine (**90**)	62
		(*Z*)-Isocondylocarpine *N*-oxide (**91**)	62
		(+)-Isoeburnamine (**34**)	63
		Kopsiyunnanine A (**320**)	64
		Kopsiyunnanine B (**131**)	64
		Kopsiyunnanine C1 (**123**)	61
		Kopsiyunnanine C2 (**124**)	61
		Kopsiyunnanine C3 (**125**)	61
		Kopsiyunnanine D (**118**)	61
		Kopsiyunnanine F1 (**92**)	62
		Kopsiyunnanine F2 (**93**)	62
		Kopsiyunnanine F3 (**94**)	62
		Kopsiyunnanine G (**121**)	63
		Kopsiyunnanine H (**122**)	63
		Mersicarpine (**130**)	61
		19(*R*)-Methoxytubotaiwine (**97**)	62
		19(*S*)-Methoxytubotaiwine (**96**)	62
		(−)-Methyleburnamine (**111**)	63

Table 1.1, continued

Plant[a]	Plant part	Alkaloids	References
		(+)-Methylisoeburnamine (**112**)	63
		Tetrahydroalstonine (**13**)	64
		(+)-Tubotaiwine (**95**)	62
	Leaves and twigs	Methyl 5-oxo-chanofruticosinate (**258**)	65
	Leaves and branches	11,12-De(methylenedioxy)danuphylline (**267**)	66
		Methyl chanofruticosinate (**243**)	66
		Methyl 11,12-methylenedioxychanofruticosinate (**239**)	66
		Methyl *N*(1)-decarbomethoxychanofruticosinate (**240**)	66
	Leaves	11,12-De(methylenedioxy)danuphylline (**267**)	67
		(+)-Eburnamonine (**32**)	67
		16β-Hydroxyaspidofractinine (**154**)	67
		(−)-19(*R*)-Hydroxyisoeburnamine (**36**)	67
		(+)-19(*R*)-Hydroxyeburnamine (**37**)	67
		(+)-Isoeburnamine (**34**)	67
		Kopsamine (**20**)	67
		Kopsiflorine (**157**)	67
		Kopsilongine (**27**)	67
		Kopsinine (**22**)	67
		Kopsinine *N*-oxide (**25**)	67
		Kopsininic acid (**144**)	67
		Larutenine (= Larutensine) (**113**)	67
		11-Methoxykopsilongine (**26**)	67
		12-Methoxykopsinaline (**164**)	67
		Methyl 11,12-methylenedioxychanofruticosinate (**239**)	67,68
		Methyl chanofruticosinate (**243**)	67,68
		Methyl *N*(1)-decarbomethoxychanofruticosinate (**240**)	68
		Methyl *N*(1)-decarbomethoxy-$\Delta^{14,15}$-3-oxo-chanofruticosinate (**259**)	67
		Rhazinicine (**127**)	67
	Roots	5,22-Dioxokopsane (**231**)	35
		(−)-Isoeburnamine (**106**)	35,69
		Kopsinine (**22**)	35,69
		(+)-Kopsoffine (**318**)	69
		N(1)-Methoxycarbonyl-11,12-dimethoxykopsinaline (**26**)	35
		N(1)-Methoxycarbonyl-12-methoxykopsinaline (**29**)	35
		N(1)-Methoxycarbonyl-11,12-methylenedioxy-kopsinaline (**21**)	35
		12-Methoxykopsinaline (**164**)	35
		11,12-Methylenedioxykopsinaline (**156**)	35
		(−)-Quebrachamine (**117**)	35
		Tetrahydroalstonine (**13**)	35
	Fruits	*N*(1)-Carbomethoxy-11,12-dimethoxykopsinaline (**26**)	70
		N(1)-Carbomethoxy-11-hydroxy-12-methoxy-kopsinaline (**163**)	70
		N(1)-Carbomethoxy-11-methoxy-12-hydroxy-kopsinaline (**159**)	70

Table 1.1, continued

Plant[a]	Plant part	Alkaloids	References
		N(1)-Carbomethoxy-12-methoxykopsinaline (**29**)	70
		5,22-Dioxokopsane (**231**)	70
		Eburnamenine[b]	70
		Kopsamine (**20**)	70
		Kopsamine *N*-oxide (**21**)	70
		Kopsanone (**16**)	70
		Kopsinilam (**138**)	70
		Kopsinine (**22**)	70
		Pleiocarpine (**28**)	70
		Vincadifformine (**136**)	70
	c	Eburnamine[b]	36
		Kopsinine (**22**)	36
		Kopsamine (**20**)	36
		Perivine (**82**)	36
		19-Hydroxyeburnamine[b]	36
		19-Oxoeburnamenine[b]	36
		19-Oxoeburnamine[b]	36
K. dasyrachis Ridl. (Sabah, Malaysian Borneo)	Leaves	Danuphylline (**266**)	71-73
		11,12-Dimethoxykopsamine (**27**)	71
		Kinabalurine G (**54**)	71
		Kopsamine (**20**)	71
		Kopsamine *N*-oxide (**21**)	71
		Kopsidasine (**203**)	74
		Kopsidasine *N*-oxide (**204**)	74
		Kopsidasinine (**271**)	74
		Kopsifine (**17**)	71
		Kopsirachine (**57**)	71,75
		12-Methoxypleiocarpine (**29**)	71
		Methyl chanofruticosinate (**243**)	71
		Methyl *N*(1)-decarbomethoxychanofruticosinate (**240**)	71
		Methyl 11,12-methylenedioxychanofruticosinate (**239**)	71
		Methyl 11,12-methylenedioxy-*N*(1)-decarbomethoxychanofruticosinate (**244**)	71
		Pleiocarpine (**28**)	71
	Stem-bark	*N*(1)-Carbomethoxy-5,22-dioxokopsane (**15**)	76
		Dasyrachine (**264**)	76
		Decarbomethoxykopsifine (**18**)	76
		(–)-Demethylnorpleiomutine (**39**)	76
		(+)-Eburnamonine (**32**)	76
		(–)-19(*R*)-Hydroxyisoeburnamine (**36**)	76,77
		(+)-19(*R*)-Hydroxyeburnamine (**37**)	76,77
		16-Hydroxymethylpleiocarpamine (**86**)	76
		(+)-Isoeburnamine (**34**)	76
		Kopsamine (**20**)	76
		Kopsamine *N*-oxide (**21**)	76
		Kopsifine (**17**)	76,78
		Kopsiflorine (**157**)	76
		Kopsiflorine *N*-oxide (**158**)	76
		Kopsilongine (**27**)	76
		Kopsinarine (**229**)	76
		Kopsine (**223**)	76
		Kopsinine (**22**)	76
		Kopsinine *N*-oxide (**25**)	76
		(+)-Kopsoffinol (**40**)	76
		Leuconoxine (**14**)	76

Table 1.1, continued

Plant[a]	Plant part	Alkaloids	References
		11-Methoxykopsilongine (**26**)	76
		11- Methoxykopsilongine *N*-oxide (**162**)	76
		12-Methoxypleiocarpine (**29**)	76
		11,12-Methylenedioxykopsinaline (**156**)	76
		11,12-Methylenedioxykopsine (**226**)	76
		(–)-Norpleiomutine (**38**)	76
		Paucidactine B (**19**)	76
		Pleiocarpamine (**85**)	76
		Pleiocarpine (**28**)	76
		Rhazinicine (**127**)	76,78
		Tetrahydroalstonine (**13**)	76
K. deverrei L. Allorge (Peninsular Malaysia)	Leaves	14,15-Dihydro-10-methoxykopsinone (**151**)	79
		10-Methoxykopsinone (**149**)	79
		12-Methoxykopsinone (**150**)	79
	Stem-bark	*N*(1)-Carbomethoxy-17β-hydroxykopsinine (**139**)	80
		N(1)-Carbomethoxy-17β-hydroxy-$\Delta^{14,15}$-kopsinine (**140**)	80
		Deacetylakuammiline (= Rhazimol) (**67**)	81
		16-*Epi*-deacetylakuammiline (**70**)	81
		14α-Hydroxycondylocarpine (**87**)	81
		16-Hydroxymethylpleiocarpamine (**86**)	81
		N(1)-Methoxycarbonyl-11,12-methylenedioxy-kopsinaline (**21**)	80
		N(1)-Methoxycarbonyl-12-methoxykopsinaline (**29**)	80
		Kopsinone (**148**)	80
		Pleiocarpamine (**85**)	81
K. fruticosa (Roxb.) A. DC. (India, Indonesia, Malaysia)	Leaves	Fruticosamine (**218**)	30,48,82-84
		Fruticosiamine A (**220**)	48
		Fruticosine (**217**)	30,48,82-84
		Kopsine (**223**)	30,48,82,84-90
		Decarbomethoxykopsine (**224**)	90
		Decarbomethoxyisokopsine (**265**)	90
		Methyl *N*(1)-decarbomethoxychanofruticosinate (**240**)	48
K. grandifolia D. J. Middleton (*K. lapidilecta*) (Peninsular Malaysia)	Stem-bark	*Epi*-lapidilectinol (**280**)	92
		Grandilodine A (**41**)	91
		Grandilodine B (**42**)	91
		Isolapidilectine A (**45**)	91,92
		Kopsinine (**22**)	91
		Lapidilectam (**46**)	91,92
		Lapidilectine A (**44**)	91-93
		Lapidilectinol (**279**)	92
		Venalstonine (**142**)	92
	Leaves	Grandilodine C (**43**)	91
		Lapidilectine B (**47**)	91-93
K. griffithii King & Gamble (Peninsular Malaysia)	Leaves	Buchtienine (**319**)	94
		N(1)-Carbomethoxy-11,12-dimethoxykopsinaline (**26**)	94
		N(1)-Carbomethoxy-11-hydroxy-12-methoxy-kopsinaline (**163**)	94
		(+)-Eburnamonine (**32**)	94

Table 1.1, continued

Plant[a]	Plant part	Alkaloids	References
		Harmane (**58**)	94
		(+)-Harmicine (**59**)	94
		16(*R*)-19,20-*E*-Isositsirikine (**62**)	94
		Kopsamine (**20**)	94
		Kopsamine *N*-oxide (**21**)	94
		Kopsilongine (**27**)	94
		Kopsinine (**22**)	94
		Leuconolam (**135**)	94
		Leuconoxine (**14**)	94
		N(1)-Methoxycarbonyl-12-methoxy-$\Delta^{16,17}$-kopsinine (**23**)	94
		12-Methoxy-10-demethoxykopsidasinine (**272**)	94
		12-Methoxypleiocarpine (**29**)	94
		6-Oxoleuconoxine (**133**)	95
		Pleiocarpine (**28**)	94
		Rhazimol (= Deacetylakuammiline) (**67**)	94
		Tetrahydroalstonine (**13**)	94
	Stem-bark	Akuammiline *N*-oxide (**71**)	96
		Buchtienine (**319**)	96
		Deacetylakuammiline (= Rhazimol) (**67**)	96
		(–)-Eburnamine (**33**)	96
		16-*Epi*-deacetylakuammiline (**70**)	96
		16-*Epi*-deacetylakuammiline *N*-oxide (**72**)	96
		Harmane (**58**)	96
		Kopsinine (**22**)	96
		Kopsinine *N*-oxide (**25**)	96
		Leuconolam (**135**)	96
		Leuconoxine (**14**)	96
		11,12-Methylenedioxykopsinaline *N*-oxide (**160**)	96
		Rhazinaline *N*-oxide (**73**)	96
K. hainanensis Tsiang (China)	Stem	Kopsihainin A (**268**)	97
		Kopsihainin B (**146**)	97
		Kopsihainin C (**147**)	97
		Kopsinine (**22**)	97
		Methyl *N*(1)-decarbomethoxychanofruticosinate (**240**)	97
	Leaves and stem	Kopsihainanine A (**269**)	98
		Kopsihainanine B (**270**)	98
	Stem-bark	5,22-Dioxokopsane (**231**)	99
		Eburnamenine[b]	99
		(+)-Eburnamine (**105**)	99
		(–)-Isoeburnamine (**106**)	99
		Kopsanone (**16**)	99
		Kopsinilam (**138**)	99
		Kopsinine (**22**)	99
		Kopsininic acid (**144**)	99
		Kopsinoline (= Kopsinine *N*-oxide) (**25**)	99
		(+)-Kopsoffine (**318**)	99
		(+)-Tubotaiwine (**95**)	99
K. larutensis King & Gamble (Peninsular Malaysia)	Leaves	(–)-Eburnamine (**33**)	100
		(+)-Eburnamonine (**32**)	100
		(+)-Eburnamonine *N*-oxide (**107**)	100
		(+)-Isoeburnamine (**34**)	100
		(+)-Larutenine/larutensine (**113**)	100

Table 1.1, continued

Plant[a]	Plant part	Alkaloids	References
	Stem-bark	(+)-Eburnamenine (**31**)	101
		(−)-Eburnamine (**33**)	101,102
		(−)-Eburnaminol (**114**)	102
		(+)-Eburnamonine (**32**)	101,102
		(+)-Eburnamonine *N*-oxide (**107**)	101
		(−)-*O*-Ethyleburnamine (**108**)	101
		(+)-Isoeburnamine (**34**)	101,102
		Kopsinine (**22**)	101,102
		(+)-Larutensine/larutenine (**113**)	101,102
K. pauciflora Hook.f. (Sabah, Malaysian Borneo)	Leaves	Kinabalurine A (**48**)	103,104
		Kinabalurine B (**49**)	104
		Kinabalurine C (**50**)	104
		Kinabalurine D (**51**)	104
		Kinabalurine E (**52**)	104
		Kinabalurine F (**53**)	104
		Kopsamine (**20**)	105
		Kopsamine *N*-oxide (**21**)	105
		Lahadinine A (**166**)	106
		Lahadinine B (**167**)	106
		11-Methoxykopsilongine (**26**)	105
		Paucidactine A (**222**)	107
		Paucidactine B (**19**)	107
		Paucifinine (**168**)	106
		Paucifinine *N*-oxide (**169**)	106
		Pauciflorine A (**274**)	108
		Pauciflorine B (**275**)	108
	Stem-bark	(−)-Demethylnorpleiomutine (**39**)	109
		(−)-Eburnamine (**33**)	110
		(+)-Eburnamonine (**32**)	110
		(+)-Isoeburnamine (**34**)	110
		Kopsamine *N*-oxide (**21**)	110
		Kopsinine (**22**)	110
		(+)-Kopsoffine (**318**)	109
		(+)-Kopsoffinol (**40**)	109
		N(1)-Methoxycarbonyl-11,12-dimethoxykopsinaline (**26**)	110
		N(1)-Methoxycarbonyl-12-methoxy-$\Delta^{16,17}$-kopsinine (**23**)	110
		N(1)-Methoxycarbonyl-12-methoxykopsinaline (= Kopsilongine) (**27**)	110
		N(1)-Methoxycarbonyl-11,12-dimethenedioxy-kopsinaline (= Kopsamine) (**20**)	110
		12-Methoxy-10-demethoxykopsidasinine (**272**)	110
		(−)-Norpleiomutine (**38**)	109,110
		(+)-19-Oxoeburnamine (**35**)	110
		Pauciflorine A (**274**)	105
K. profunda (Peninsular Malaysia)	Leaves and stem-bark	Kopsinine (**22**)	111
		N(1)-Methoxycarbonyl-12-hydroxy-$\Delta^{16,17}$-kopsinine (**24**)	111
		N(1)-Methoxycarbonyl-12-methoxy-$\Delta^{16,17}$-kopsinine (**23**)	111,112
		N(1)-Methoxycarbonyl-12-methoxy-$\Delta^{16,17}$-kopsinine *N*-oxide (**207**)	111
		N(1)-Methoxycarbonyl-11,12-methylenedioxy-$\Delta^{16,17}$-kopsinine (**205**)	111,112
		N(1)-Methoxycarbonyl-11,12-methylenedioxy-	111

Table 1.1, continued

Plant[a]	Plant part	Alkaloids	References
		$\Delta^{16,17}$-kopsinine *N*-oxide (**206**)	
K. profunda Markgr. (*K. macrophylla*) (Peninsular Malaysia)	Leaves	Kopsilactone (**55**)	113
		Kopsone (**56**)	113
	Stem-bark	Akuammiline (**68**)	113
		Deacetylakuammiline (**67**)	113
		5,22-Dioxokopsane (**231**)	113
		Dregamine (**83**)	113
		(+)-Kopsoffine (**318**)	113
		(–)-Norpleiomutine (**38**)	113
		Tabernaemontanine (**84**)	113
K. profunda Markgr. (*K. terengganensis*) (Peninsular Malaysia)	Stem-bark	(–)-Eburnamine (**33**)	114
		(–)-Eburnaminol (**114**)	114
		(+)-Isoeburnamine (**34**)	114
		(+)-Larutensine (**113**)	114
		(+)-Quebrachamine (**119**)	114
		Terengganensine A (**115**)	114
		Terengganensine B (**116**)	114
K. singapurensis Ridl. (1) (Peninsular Malaysia)	Leaves	Kopsifoline A (**288**)	115
		Kopsininic acid (**144**)	115
		Singaporentine A (**294**)	115
K. singapurensis Ridl. (2) (Sample A)[d] (Peninsular Malaysia)	Leaves	16-*Epi*-akuammiline (**69**)	116
		16-*Epi*-deacetylakuammiline (**70**)	116
		16-*Epi*-kopsinine (**145**)	116
		Kopsidine D (**212**)	116
		Kopsilongine (**27**)	116
		Kopsilongine *N*-oxide (**161**)	116
		Kopsiloscine A (**171**)	116
		Kopsiloscine B (**172**)	116
		Kopsiloscine C (**173**)	116
		Kopsiloscine D (**174**)	116
		Kopsiloscine E (**175**)	116
		Kopsiloscine F (**176**)	116
		Kopsingine (**180**)	116
		Vincophylline (**79**)	116
	Stem-bark	Akuammidine (**81**)	116
		Aspidodasycarpine (**74**)	116
		Aspidophylline A (**75**)	116
		16-*Epi*-akuammiline (**69**)	116
		16-*Epi*-deacetylakuammiline (**70**)	116
		17α-Hydroxy-$\Delta^{14,15}$-kopsinine (**170**)	116
		Kopsaporine (**181**)	116
		Kopsinganol (**191**)	116
		Kopsingine (**180**)	116
		Kopsinine (**22**)	116
		Leuconolam (**135**)	116
		Lonicerine (**77**)	116
		Rhazinal (**128**)	116,117
		Rhazinilam (**126**)	116
		Tetrahydroalstonine (**13**)	116
K.singapurensis Ridl. (3)	Leaves	Akuammidine (**81**)	118
		16-*Epi*-akuammiline (**69**)	118

Table 1.1, continued

Plant[a]	Plant part	Alkaloids	References
(Sample B)[d]		16-*Epi*-deacetylakuammiline (**70**)	118
(Peninsular		Kopsidarine (**192**)	118
Malaysia)		Kopsidine A (**208**)	118
		Kopsidine C (**210**)	118
		Kopsidine C *N*-oxide (**211**)	118
		Kopsimaline F (**198**)	118
		Kopsinganol (**191**)	118
		Kopsingine (**180**)	118
		Kopsinitarine A (**232**)	118
		Kopsinitarine B (**233**)	118
		Mersingine A (**237**)	118
	Stem-bark	Akuammidine (**81**)	118
		Aspidodasycarpine (**74**)	118
		Aspidophylline B (**76**)	118
		5,21-Dihydrorhazinilam (**129**)	118
		16-*Epi*-akuammiline (**69**)	118
		16-*Epi*-deacetylakuammiline (**70**)	118
		17α-Hydroxy-$\Delta^{14,15}$-kopsinine (**170**)	118
		Kopsiloscine C (**173**)	118
		Kopsiloscine G (**177**)	118
		Kopsinganol (**191**)	118
		Kopsingine (**180**)	118
		Kopsinine (**22**)	118
		Lonicerine (**77**)	118
		Rhazinilam (**126**)	118
K. singapurensis	Leaves	Akuammidine (**81**)	119
Ridl. (4)		*N*(1)-Decarbomethoxykopsamine (**156**)	119
(*K. fruticosa*)		5,21-Dihydrorhazinilam (**129**)	119
(Peninsular		16-*Epi*-akuammiline (**69**)	119
Malaysia)		16-*Epi*-deacetylakuammiline (**70**)	119
		17α-Hydroxy-$\Delta^{14,15}$-kopsinine (**170**)	119
		Kopsiloscine G (**177**)	119
		Kopsiloscine J (**188**)	119
		Kopsimaline A (**193**)	119
		Kopsimaline B (**194**)	119
		Kopsimaline C (**195**)	119
		Kopsimaline D (**196**)	119
		Kopsimaline E (**197**)	119
		Kopsinicine (**187**)	119
		Kopsofinone (**153**)	119
		Mersinine A (**295**)	120,121
		Mersinine B (**296**)	120,121
		Mersinine C (**297**)	121
		Mersiloscine (**298**)	120,121
		Mersiloscine A (**299**)	121
		Mersiloscine B (**300**)	121
		Mersifoline A (**301**)	121
		Mersifoline B (**302**)	121
		Mersifoline C (**303**)	121
		Mersidasine A (**304**)	121
		Mersidasine B (**305**)	121
		Mersidasine C (**306**)	121
		Mersidasine D (**307**)	121
		Mersidasine E (**308**)	121
		Mersidasine F (**309**)	121
		Mersidasine G (**310**)	121
		Mersiphylline A (**311**)	122
		Mersiphylline B (**312**)	122

Table 1.1, continued

Plant[a]	Plant part	Alkaloids	References
		Mersilongine (**313**)	119,123
		Mersirachine (**314**)	119,124
		Mersinaline (**315**)	119,124
		Rhazinilam (**126**)	119
	Stem-bark	Akuammidine (**81**)	119
		Aspidodasycarpine (**74**)	119
		Burnamine (**78**)	119
		Deacetylakuammiline (**67**)	119
		5,21-Dihydrorhazinilam (**129**)	119
		16-*Epi*-akuammiline (**69**)	119
		16-*Epi*-deacetylakuammiline (**70**)	119
		14α-Hydroxycondylocarpine (**87**)	119
		16-Hydroxymethylpleiocarpamine (**86**)	119
		Kopsiloscine H (**178**)	119
		Kopsiloscine I (**179**)	119
		Kopsinine (**22**)	119
		Leuconolam (**135**)	119
		Leuconoxine (**14**)	119
		Lonicerine (**77**)	119
		Mersicarpine (**130**)	45,119
		Mossambine (**103**)	119
		Picramicine (**98**)	119
		Rhazinilam (**126**)	119
		Tetrahydroalstonine (**13**)	119
K. singapurensis Ridl. (5) (*K. fruticosa*) (Peninsular Malaysia)	Leaves	15α-Hydroxykopsinine (**137**)	125
		Kopsifoline A (**288**)	125-127
		Kopsifoline B (**289**)	125-127
		Kopsifoline C (**290**)	125-127
		Kopsifoline D (**291**)	125,127
		Kopsifoline E (**292**)	125,127
		Kopsifoline F (**293**)	125,127
		Kopsorinine (**230**)	125
		Venacarpine A (**201**)	125
		Venacarpine B (**202**)	125
	Stem-bark	Akuammigine (**80**)	125
		16-*Epi*-deacetylakuammiline (**70**)	125
		16-*Epi*-kopsinine (**145**)	125
		15α-Hydroxykopsinine (**137**)	125
		16-Hydroxymethylpleiocarpamine (**86**)	125
		Kopsanone (**16**)	125
		Kopsinine (**22**)	125
		Kopsorinine (**230**)	125
		Lonicerine (**77**)	125
		Picramicine (**98**)	125
		Pleiocarpamine (**85**)	125
		Venalstonine (**142**)	125
K. singapurensis Ridl. (6) (Peninsular Malaysia)	Leaves	5,21-Dihydrorhazinilam (**129**)	128,129
		11,12-Methylenedioxykopsaporine (**184**)	128,129
		Rhazinilam (**126**)	128,129
	Stem-bark	11,12-Methylenedioxykopsaporine (**184**)	129
		Singapurensine A (**213**)	129
		Singapurensine B (**214**)	129
		Singapurensine C (**215**)	129
		Singapurensine D (**216**)	129

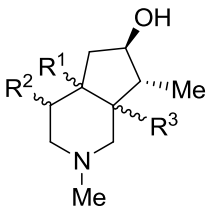
Table 1.1, continued

Plant[a]	Plant part	Alkaloids	References
K. singapurensis Ridl. (7) (Peninsular Malaysia)	Leaves	Kopsaporine (**181**)	130
		Kopsingine (**180**)	130
K. tenuis Leenh. & Steenis (Sarawak, Malaysian Borneo)	Leaves	Lundurine A (**284**)	131,132
		Lundurine B (**285**)	131,132
		Lundurine C (**286**)	131,132
		Lundurine D (**287**)	131
		Tenuiphylline (**317**)	133
		Tenuisine A (**281**)	131,133,134
		Tenuisine B (**282**)	131,133,134
		Tenuisine C (**283**)	131,133,134
	Stem	Kopsinine (**22**)	105
		Kopsinine *N*-oxide (**25**)	105
		Leuconoxine (**14**)	105
		Tetrahydroalstonine (**13**)	105
K. teoi L. Allorge (1) (Peninsular Malaysia)	Leaves	11-Hydroxykopsingine (**182**)	135
		Kopsidine A (**208**)	135-137
		Kopsidine B (**209**)	135-137
		Kopsidine C (**210**)	135,137
		Kopsidine D (**212**)	135,137
		14,15-α-Epoxykopsingine (= Kopsimaline E) (**197**)	135
		Kopsinganol (**191**)	135,136
		Kopsingine (**180**)	135,136
		Kopsinitarine A (**232**)	135,138,139
		Kopsinitarine B (**233**)	135,138,139
		Kopsinitarine C (**234**)	135,138,139
		Kopsinitarine D (**235**)	135,139
		Mersingine A (**237**)	135,139,140
		Mersingine B (**238**)	135,139,140
		11-Methoxy-12-hydroxykopsinol (**186**)	135
		11-Methoxykopsingine (**183**)	135
		Nitaphylline (**316**)	135,141,142
	Stem-bark[d]	Akuammiline (**68**)	135,136,143
		Aspidodasycarpine (**74**)	135
		16-*Epi*-deacetylakuammiline (**70**)	135
		17α-Hydroxy-$\Delta^{14,15}$-kopsinine (**170**)	135,136,141, 143,144
		Kopsaporine (**181**)	135,136,143, 144
		Kopsinganol (**191**)	135,136,143
		Kopsingine (**180**)	135,136,143, 144
		Kopsinginine (**165**)	135,136,143, 144
		Kopsinginol (**155**)	135,136,143
		Kopsinol (**185**)	135,136,143
		Lonicerine (**77**)	135
		11,12-Methylenedioxykopsaporine (**184**)	135
		Rhazimol (= Deacetylakuammiline) (**67**)	135,136,143
		Rhazinilam (**126**)	135,136,143
K. teoi L. Allorge (2) (Peninsular Malaysia)	Stem-bark[d]	Akuammiline (**68**)	95
		Aspidodasycarpine (**74**)	95
		Deacetylakuammiline (= Rhazimol) (**67**)	95
		16-*Epi*-akuammiline (**69**)	95

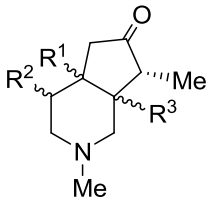
Table 1.1, continued

Plant[a]	Plant part	Alkaloids	References
		16-*Epi*-deacetylakuammiline (**70**)	95
		16-*Epi*-kopsinine (**145**)	95
		17α-Hydroxykopsinine (= Kopsiloscine G) (**177**)	95
		16-Hydroxymethylpleiocarpamine (**86**)	95
		Kopsamine (**20**)	95
		Kopsidine A (**208**)	95
		Kopsijasminine (**199**)	95
		Kopsinganol (**191**)	95
		Kopsingine (**180**)	95
		Kopsinine (**22**)	95
		Kopsinitarine E (**236**)	95
		Kopsonoline (**152**)	95
		Leuconoxine (**14**)	95
		Lonicerine (**77**)	95
		N(1)-Methoxycarbonyl-12-methoxy-$\Delta^{16,17}$-kopsinine (**23**)	95
		Pleiocarpamine (**85**)	95
		Tetrahydroalstonine (**13**)	95
K. teoi L. Allorge (3) (Peninsular Malaysia)	Leaves	Kopsingine (**180**)	145
		11,12-Methylenedioxykopsaporine (**184**)	145
	Stem-bark	17α-Hydroxy-$\Delta^{14,15}$-kopsinine (**170**)	145
		Isoeburnamine[b]	145
		Kopsingine (**180**)	145
		Lonicerine (**77**)	145
		Rhazinilam (**126**)	145

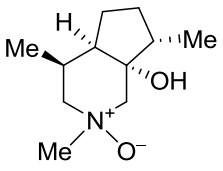
[a]Classification according to Middleton[29] with original attribution in parenthesis; [b]$[\alpha]_D$ not reported; [c]Plant part not specified; [d]Plant material collected at same location but at different dates.



48 R^1 = β-H, R^2 = α-Me, R^3 = α-H
52 R^1 = α-H, R^2 = β-Me, R^3 = β-H
53 R^1 = α-H, R^2 = α-Me, R^3 = β-H



49 R^1 = β-H, R^2 = α-Me, R^3 = α-H, R^4 = Me
50 R^1 = β-H, R^2 = α-Me, R^3 = α-H, R^4 = H
51 R^1 = α-H, R^2 = β-Me, R^3 = β-H, R^4 = Me



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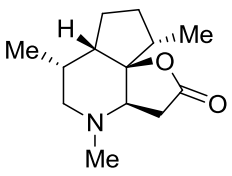

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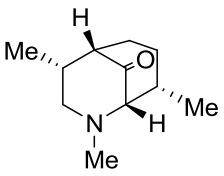

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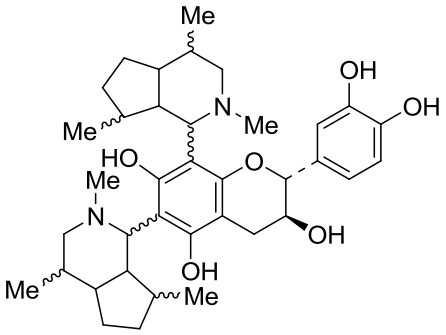

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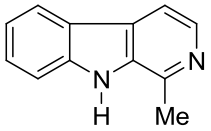

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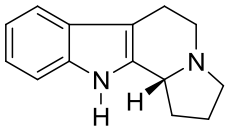

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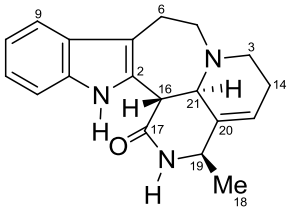

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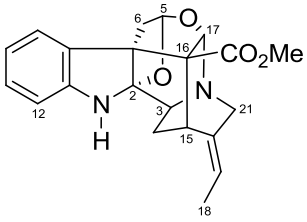

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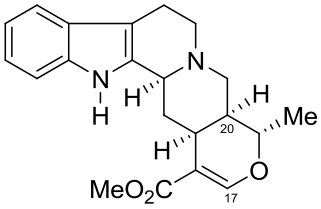

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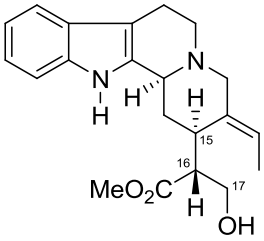

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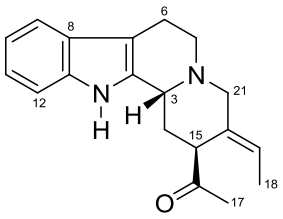

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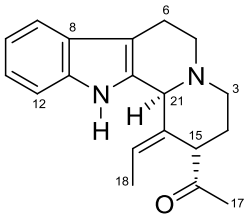

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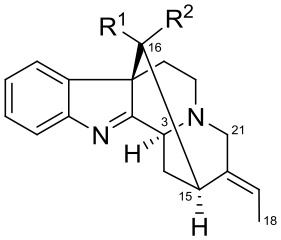
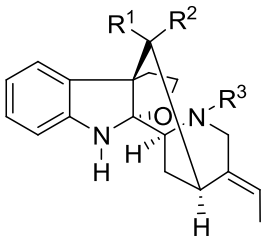
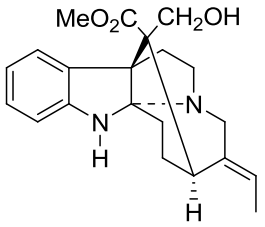


65 R^1 = CHO, R^2 = H
66 R^1 = CO_2Me, R^2 = CHO
67 R^1 = CH_2OH, R^2 = CO_2Me
68 R^1 = CH_2OAc, R^2 = CO_2Me
69 R^1 = CO_2Me, R^2 = CH_2OAc
70 R^1 = CO_2Me, R^2 = CH_2OH
71 R^1 = CH_2OAc, R^2 = CO_2Me, *N*(4)⟶O
72 R^1 = CO_2Me, R^2 = CH_2OH, *N*(4)⟶O
73 R^1 = CO_2Me, R^2 = CHO, *N*(4)⟶O



74 R^1 = CH_2OH, R^2 = CO_2Me, R^3 = H
75 R^1 = H, R^2 = CO_2Me, R^3 = CHO
76 R^1 = CH_2OAc, R^2 = CO_2Me, R^3 = H
77 R^1 = CO_2Me, R^2 = CH_2OH, R^3 = H
78 R^1 = CH_2OH, R^2 = CO_2Me, R^3 = H



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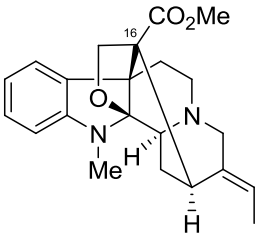

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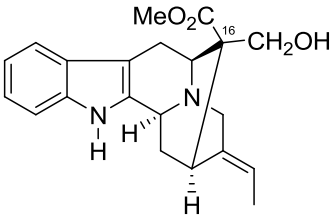

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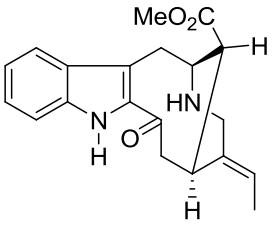

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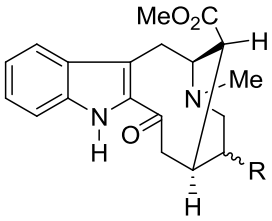
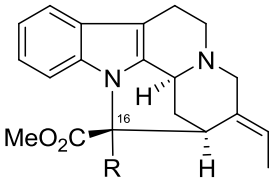
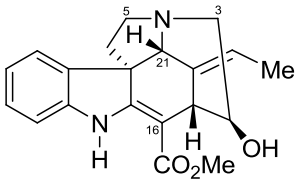


83 R = α-Et
84 R = β-Et



85 R = H
86 R = CH_2OH



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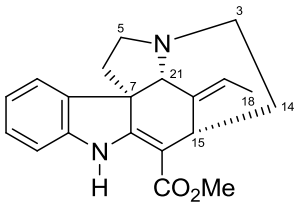
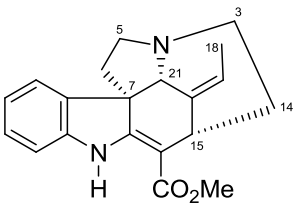
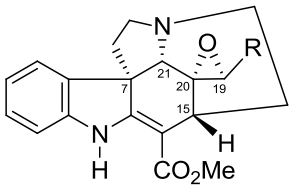


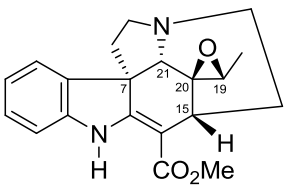
88
89 *N*(4)→O



90
91 *N*(4)→O



92 R = Me
93 R = H



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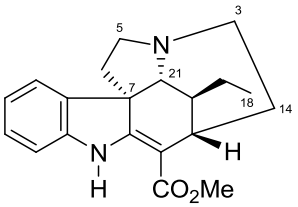

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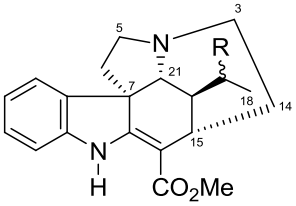
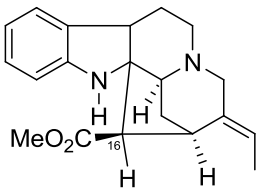


96 R = β-OMe
97 R = α-OMe



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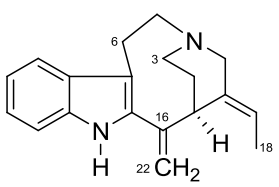
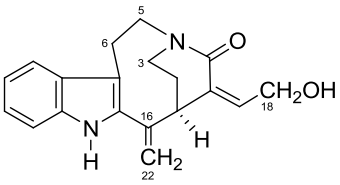


99
100 *N*(4)→O



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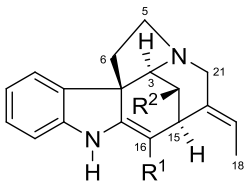
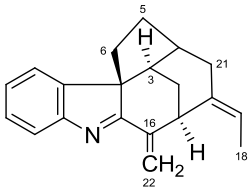


102 R^1 = CHO, R^2 = H
103 R^1 = CO_2Me, R^2 = OH



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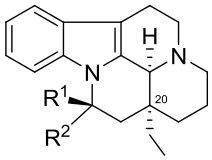
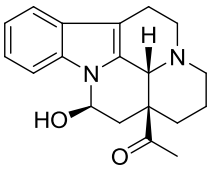


105 R^1 = H, R^2 = OH
106 R^1 = OH, R^2 = H



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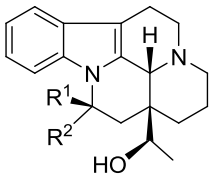
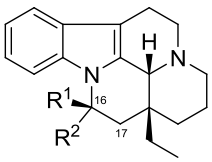
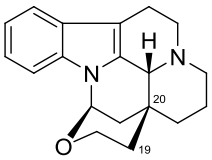


36 R^1 = H, R^2 = OH
37 R^1 = OH, R^2 = H



31 R^1 = H, R^2 = nil, $\Delta^{16,17}$
32 R^1, R^2 = O
33 R^1 = OH, R^2 = H
34 R^1 = H, R^2 = OH
107 R^1, R^2 = O, *N*(4)→O
108 R^1 = OEt, R^2 = H
109 R^1 = OH, R^2 = Et
110 R^1 = Et, R^2 = OH
111 R^1 = OH, R^2 = Me
112 R^1 = Me, R^2 = OH



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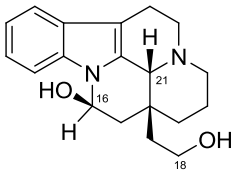

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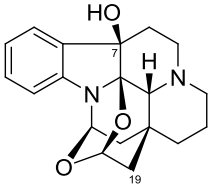

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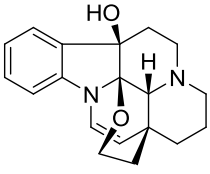

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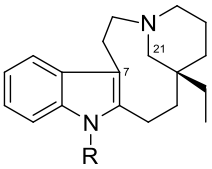
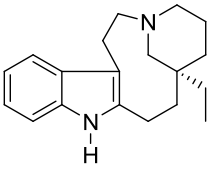


117 R = H
118 R = CH_2OCH_3



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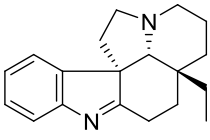
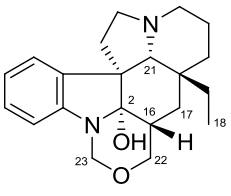
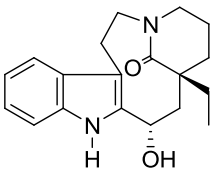


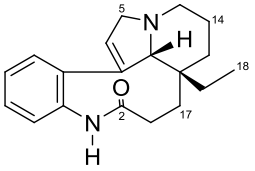
120



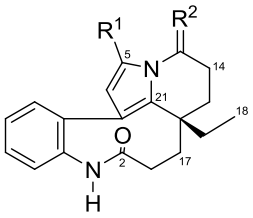
121



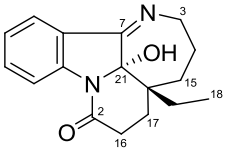
122



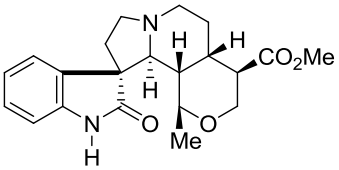
129



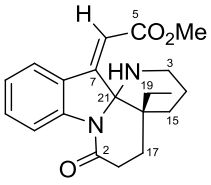
123 $R^1 = CH_2OCH_3$, R^2 = H,H
124 $R^1 = CH_2OCH_2CH_3$, R^2 = H,H
125 $R^1 = CH_2OH$, R^2 = H,H
126 R^1 = H, R^2 = H,H
127 R^1 = H, R^2 = O
128 R^1 = CHO, R^2 = H,H



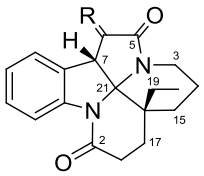
130



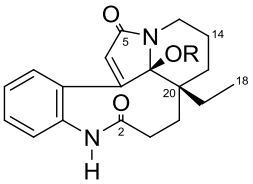
131



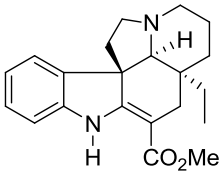
132



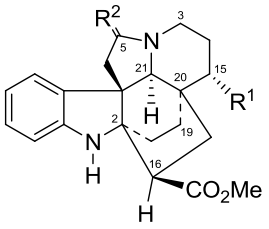
14 R = H,H
133 R = O



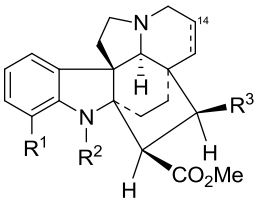
134 R = Me
135 R = H



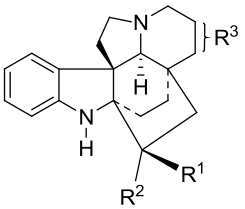
136



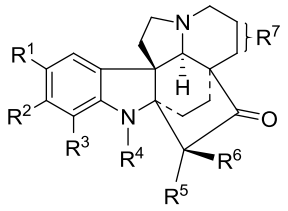
22 R^1 = H, R^2 = H,H
25 R^1 = H, R^2 = H,H, *N*(4)→O
137 R^1 = OH, R^2 = H,H
138 R^1 = H, R^2 = O



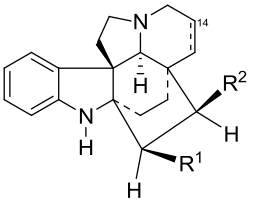
28 $R^1 = R^3 = H$, $R^2 = CO_2Me$
29 $R^1 = OMe$, $R^2 = CO_2Me$, $R^3 = H$
139 $R^1 = H$, $R^2 = CO_2Me$, $R^3 = OH$
140 $R^1 = H$, $R^2 = CO_2Me$, $R^3 = OH$, $\Delta^{14,15}$



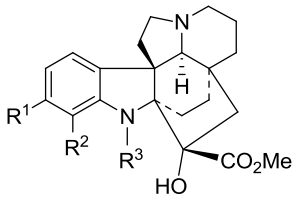
141 $R^1 = H$, $R^2 = H$, $R^3 =$ nil
142 $R^1 = CO_2Me$, $R^2 = H$, $R^3 = \Delta^{14,15}$
143 $R^1 = CO_2Me$, $R^2 = H$, $R^3 = \alpha$-epoxide
144 $R^1 = CO_2H$, $R^2 = H$, $R^3 =$ nil
145 $R^1 = H$, $R^2 = CO_2Me$, $R^3 =$ nil
146 $R^1 = CO_2H$, $R^2 = H$, $R^3 = \Delta^{14,15}$
147 $R^1 = CO_2H$, $R^2 = H$, $R^3 = \beta$-epoxide



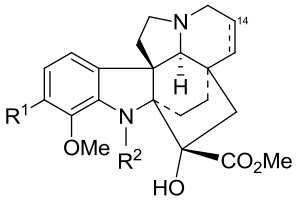
148 $R^1 = R^2 = R^3 = R^5 = R^6 = H$, $R^4 = CO_2Me$, $R^7 = \Delta^{14,15}$
149 $R^1 = OMe$, $R^2 = R^3 = R^5 = R^6 = H$, $R^4 = CO_2Me$, $R^7 = \Delta^{14,15}$
150 $R^1 = R^2 = R^5 = R^6 = H$, $R^3 = OMe$, $R^4 = CO_2Me$, $R^7 = \Delta^{14,15}$
151 $R^1 = OMe$, $R^2 = R^3 = R^5 = R^6 = H$, $R^4 = CO_2Me$, $R^7 =$ nil
152 $R^1 = R^2 = R^3 = R^4 = R^5 = R^6 = H$, $R^7 =$ nil
153 $R^1 = R^4 = H$, R^2, $R^3 = OCH_2O$, $R^5 = OH$, $R^6 = CO_2Me$, $R^7 = \alpha$-epoxide



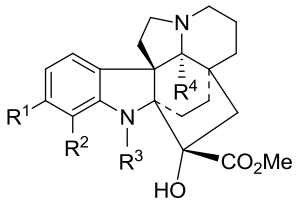
154 $R^1 = OH$, $R^2 = H$
155 $R^1 = H$, $R^2 = OH$, $\Delta^{14,15}$



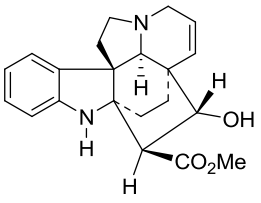
20 R^1, $R^2 = OCH_2O$, $R^3 = CO_2Me$
21 R^1, $R^2 = OCH_2O$, $R^3 = CO_2Me$, $N(4)\rightarrow O$
156 R^1, $R^2 = OCH_2O$, $R^3 = H$
157 $R^1 = R^2 = H$, $R^3 = CO_2Me$
158 $R^1 = R^2 = H$, $R^3 = CO_2Me$, $N(4)\rightarrow O$
159 $R^1 = OMe$, $R^2 = OH$, $R^3 = CO_2Me$
160 R^1, $R^2 = OCH_2O$, $R^3 = H$, $N(4)\rightarrow O$



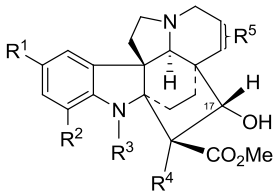
26 $R^1 = OMe$, $R^2 = CO_2Me$
27 $R^1 = H$, $R^2 = CO_2Me$
161 $R^1 = H$, $R^2 = CO_2Me$, $N(4)\rightarrow O$
162 $R^1 = OMe$, $R^2 = CO_2Me$, $N(4)\rightarrow O$
163 $R^1 = OH$, $R^2 = CO_2Me$
164 $R^1 = R^2 = H$
165 $R^1 = H$, $R^2 = CO_2Me$, $\Delta^{14,15}$



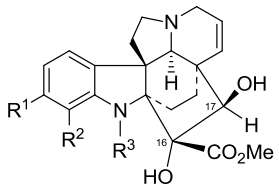
166 R^1, $R^2 = OCH_2O$, $R^3 = CO_2Me$, $R^4 = CN$
167 $R^1 = R^2 = OMe$, $R^3 = CO_2Me$, $R^4 = CN$
168 R^1, $R^2 = OCH_2O$, $R^3 = CO_2Me$, $R^4 = OH$
169 R^1, $R^2 = OCH_2O$, $R^3 = CO_2Me$, $R^4 = OH$, $N(4)\rightarrow O$



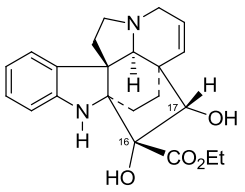
170



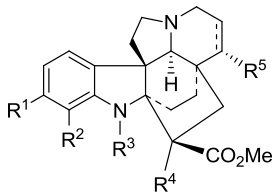
171 $R^1 = R^2 = H$, $R^3 = CO_2Me$, $R^4 = OH$, $R^5 = \Delta^{14,15}$
172 $R^1 = R^2 = H$, $R^3 = CO_2Me$, $R^4 = OH$, R^5 = nil
173 $R^1 = R^2 = H$, $R^3 = CO_2Me$, $R^4 = OH$, $R^5 = 15\alpha$-OH
174 R^1 = OMe, $R^2 = H$, $R^3 = CO_2Me$, $R^4 = OH$, R^5 = nil
175 R^1 = OMe, $R^2 = H$, $R^3 = CO_2Me$, $R^4 = OH$, $R^5 = 15\alpha$-OH
176 $R^1 = H$, R^2 = OMe, $R^3 = CO_2Me$, $R^4 = OH$, $R^5 = 15\alpha$-OH
177 $R^1 = R^2 = R^3 = R^4 = H$, R^5 = nil
178 $R^1 = R^2 = R^3 = H$, $R^4 = OH$, $R^5 = \Delta^{14,15}$
179 $R^1 = R^2 = R^3 = H$, $R^4 = OH$, R^5 = nil



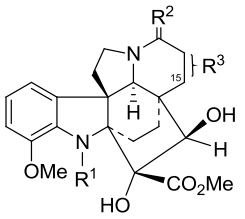
180 $R^1 = H$, R^2 = OMe, $R^3 = CO_2Me$
181 $R^1 = R^2 = H$, $R^3 = CO_2Me$
182 R^1 = OH, R^2 = OMe, $R^3 = CO_2Me$
183 $R^1 = R^2$ = OMe, $R^3 = CO_2Me$
184 R^1, $R^2 = OCH_2O$, $R^3 = CO_2Me$
185 $R^1 = R^2 = R^3 = H$
186 R^1 = OMe, R^2 = OH, $R^3 = H$
187 R^1, $R^2 = OCH_2O$, $R^3 = H$



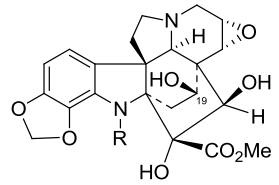
188



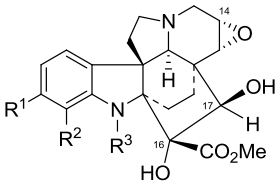
189 R^1, $R^2 = OCH_2O$, $R^3 = H$, $R^4 = OH$, R^5 = nil, $\Delta^{14,15}$
190 $R^1 = R^2 = R^3 = R^4 = H$, R^5 = OMe



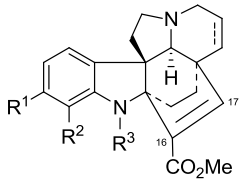
191 $R^1 = CO_2Me$, $R^2 = H,H$, $R^3 = 15$-αOH
192 $R^1 = CO_2Me$, $R^2 = O$, $R^3 = \Delta^{14,15}$



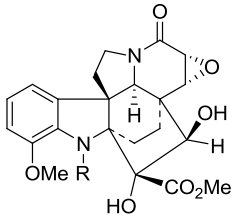
196 R = CO_2Me



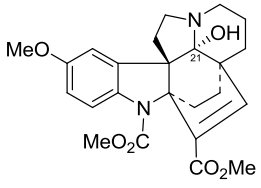
193 R^1, $R^2 = OCH_2O$, $R^3 = CO_2Me$
194 $R^1 = H$, $R^2 = OH$, $R^3 = CO_2Me$
195 R^1 = OMe, $R^2 = OH$, $R^3 = CO_2Me$
197 $R^1 = H$, R^2 = OMe, $R^3 = CO_2Me$



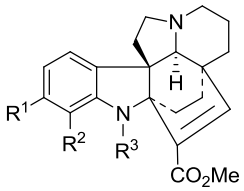
199 $R^1 = R^2 = R^3 = H$
200 $R^1 = R^2 = H$, $R^3 = CO_2Me$
201 R^1, $R^2 = OCH_2O$, $R^3 = H$, $\Delta^{14,15}$
202 $R^1 = R^3 = H$, R^2 = OMe, $\Delta^{14,15}$



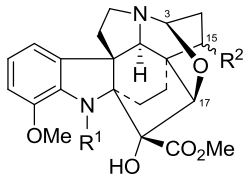
198 R = CO_2Me



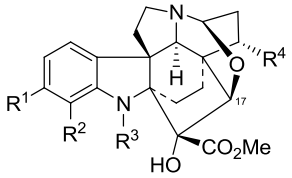
203
204 *N*(4)→O



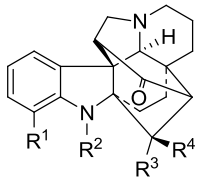
23 R^1 = H, R^2 = OMe, R^3 = CO_2Me
24 R^1 = H, R^2 = OH, R^3 = CO_2Me
205 R^1, R^2 = OCH_2O, R^3 = CO_2Me
206 R^1, R^2 = OCH_2O, R^3 = CO_2Me, *N*(4)→O
207 R^1 = H, R^2 = OMe, R^3 = CO_2Me, *N*(4)→O



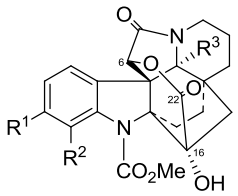
208 R^1 = CO_2Me, R^2 = α-OMe
209 R^1 = CO_2Me, R^2 = α-OEt
210 R^1 = CO_2Me, R^2 = α-OH
211 R^1 = CO_2Me, R^2 = α-OH, *N*(4)→O
212 R^1 = CO_2Me, R^2 = β-OH



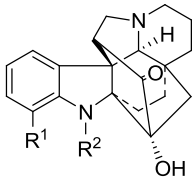
213 R^1 = R^2 = H, R^3 = CO_2Me, R^4 = OH
214 R^1 = R^2 = H, R^3 = CO_2Me, R^4 = OMe
215 R^1, R^2 = OCH_2O, R^3 = CO_2Me, R^4 = OH
216 R^1, R^2 = OCH_2O, R^3 = CO_2Me, R^4 = OMe



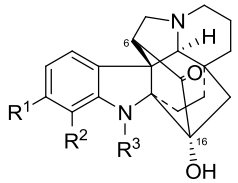
217 R^1 = R^3 = H, R^2 = CO_2Me, R^4 = OH
218 R^1 = R^4 = H, R^2 = CO_2Me, R^3 = OH
219 R^1 = OMe, R^2 = H, R^4 = OH
220 R^1 = R^4 = H, R^2 = CO_2Me, R^3 = OH, *N*(4)→O



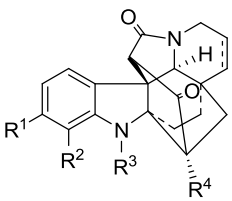
19 R^1, R^2 = OCH_2O, R^3 = H
221 R^1 = R^2 = OMe, R^3 = H
222 R^1, R^2 = OCH_2O, R^3 = OH



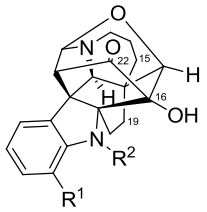
223 R^1 = H, R^2 = CO_2Me
224 R^1 = R^2 = H



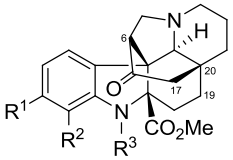
16 R^1 = R^2 = R^3 = H
225 R^1 = H, R^2 = OMe, R^3 = CO_2Me
226 R^1, R^2 = OCH_2O, R^3 = CO_2Me
227 R^1, R^2 = OCH_2O, R^3 = H
228 R^1 = R^2 = OMe, R^3 = CO_2Me



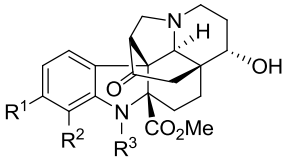
15 R^1 = R^2 = R^4 = H, R^3 = CO_2Me
17 R^1, R^2 = OCH_2O, R^3 = CO_2Me, R^4 = OH
18 R^1, R^2 = OCH_2O, R^3 = H, R^4 = OH
229 R^1 = R^2 = OMe, R^3 = CO_2Me, R^4 = OH
230 R^1 = R^2 = R^3 = R^4 = H, $\Delta^{14,15}$
231 R^1 = R^2 = R^3 = R^4 = H



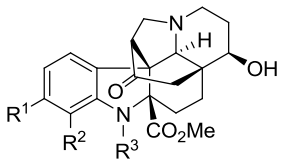
232 R^1 = OMe, R^2 = CO_2Me, $\Delta^{14,15}$
233 R^1 = OMe, R^2 = H, $\Delta^{14,15}$
234 R^1 = OMe, R^2 = H, 15-αOH
235 R^1 = OMe, R^2 = CO_2Me, 15-αOH
236 R^1 = H, R^2 = CO_2Me



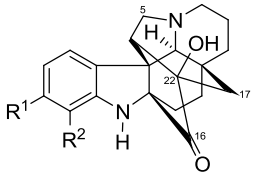
239 R^1, R^2 = OCH_2O, R^3 = CO_2Me
240 R^1 = R^2 = R^3 = H
241 R^1 = H, R^2 = OMe, R^3 = CO_2Me
242 R^1 = R^2 = OMe, R^3 = CO_2Me
243 R^1 = R^2 = H, R^3 = CO_2Me



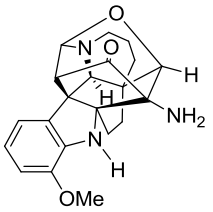
250 R^1 = R^2 = R^3 = H
251 R^1, R^2 = OCH_2O, R^3 = H
252 R^1 = H, R^2 = OMe, R^3 = H



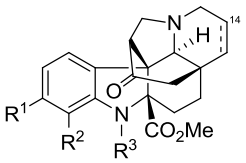
253 R^1 = R^2 = R^3 = H
254 R^1 = R^3 = H, R^2 = OMe
255 R^1, R^2 = OCH_2O, R^3 = H



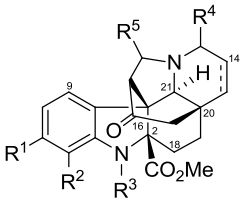
264 R^1, R^2 = OCH_2O
265 R^1 = R^2 = H



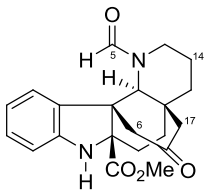
237 $\Delta^{14,15}$
238 15-αOH



244 R^1, R^2 = OCH_2O, R^3 = H
245 R^1, R^2 = OCH_2O, R^3 = H, $\Delta^{14,15}$
246 R^1 = R^3 = H, R^2 = OMe
256 R^1, R^3 = H, R^2 = OH
257 R^1 = R^2 = R^3 = H, $\Delta^{14,15}$



247 R^1 = H, R^2 = OMe, R^3 = CO_2Me, R^4 = O, R^5 = H,H
248 R^1 = R^2 = OMe, R^3 = CO_2Me, R^4 = R^5 = H,H, $\Delta^{14,15}$
249 R^1 = R^3 = H, R^2 = OMe, R^4 = R^5 = H,H, $\Delta^{14,15}$
258 R^1 = R^2 = H, R^3 = CO_2Me, R^4 = H,H, R^5 = O
259 R^1 = R^2 = R^3 = H, R^4 = O, R^5 = H,H, $\Delta^{14,15}$
260 R^1, R^2 = OCH_2O, R^3 = H, R^4 = O, R^5 = H,H, $\Delta^{14,15}$
261 R^1 = R^3 = H, R^2 = OMe, R^4 = O, R^5 = H, H, $\Delta^{14,15}$
262 R^1 = OMe, R^2 = OMe, R^3 = H, R^4 = R^5 = H,H, $\Delta^{14,15}$



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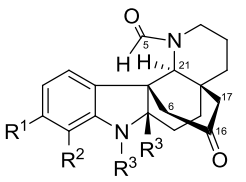
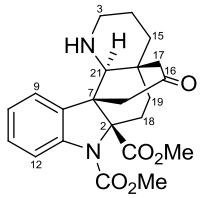


266 R^1, R^2 = OCH_2O, R^3 = CO_2Me
267 R^1 = R^2 = H, R^3 = CO_2Me



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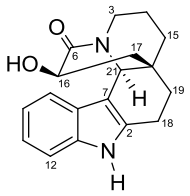

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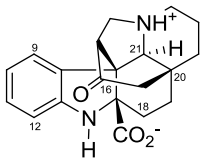
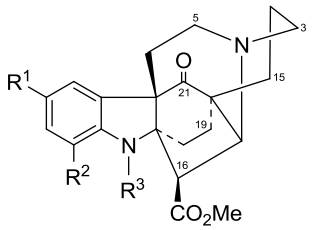
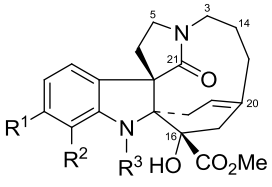


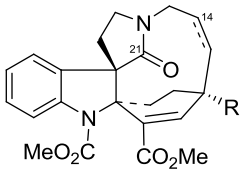
270



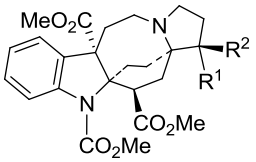
271 R^1 = OMe, R^2 = H, R^3 = CO_2Me
272 R^1 = H, R^2 = OMe, R^3 = CO_2Me
273 R^1 = R^2 = H, R^3 = CO_2Me



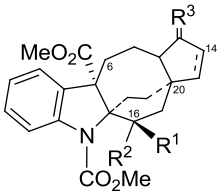
274 R^1, R^2 = OCH_2O, R^3 = CO_2Me
275 R^1 = R^2 = OMe, R^3 = CO_2Me



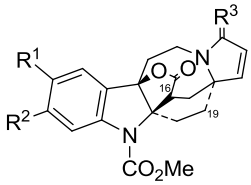
276 R = OH
277 R = H
278 R = OH, $\Delta^{14,15}$



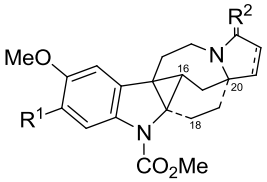
279 R^1 = OH, R^2 = H
280 R^1 = H, R^2 = OH



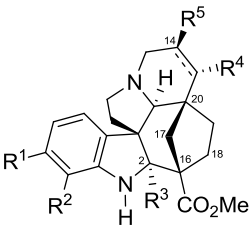
41 R^1 = CO_2Me, R^2 = H, R^3 = H,H
42 R^1 = H, R^2 = CO_2Me, R^3 = O
44 R^1 = CO_2Me, R^2 = H, R^3 = H,H
45 R^1 = H, R^2 = CO_2Me, R^3 = H,H
46 R^1 = CO_2Me, R^2 = H, R^3 = O



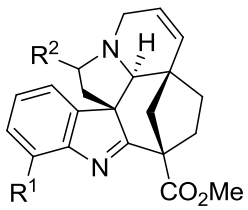
43 R^1 = R^2 = H, R^3 = O
47 R^1 = R^2 = H, R^3 = H,H
281 R^1 = OMe, R^2 = H, R^3 = H,H
282 R^1 = OMe, R^2 = OMe, R^3 = H,H
283 R^1 = OMe, R^2 = H, R^3 = O



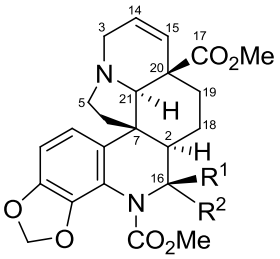
284 R^1 = H, R^2 = O, $\Delta^{14,15}$
285 R^1 = H, R^2 = H,H, $\Delta^{14,15}$
286 R^1 = H, R^2 = H,H
287 R^1 = OMe, R^2 = H,H, $\Delta^{14,15}$



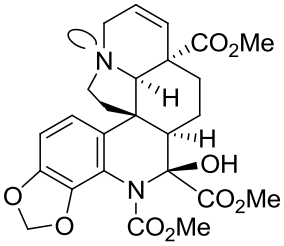
288 R^1 = R^4 = R^5 = H, R^2 = OMe, R^3 = OH, $\Delta^{14,15}$
289 R^1 = R^5 = H, R^2 =OMe, R^3 = R^4 = OH
290 R^1 = H, R^2 = OMe, R^3 = R^4 = R^5 = OH
293 R^1 = OMe, R^2 = R^3 = R^4 = R^5 = H



291 R^1 = H, R^2 = H,H
292 R^1 = OMe, R^2 = H,H
294 R^1 = OMe, R^2 = O



295 R^1 = CO_2Me, R^2 = OH
296 R^1 = OH, R^2 = CO_2Me



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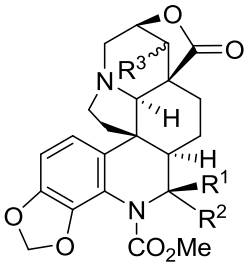
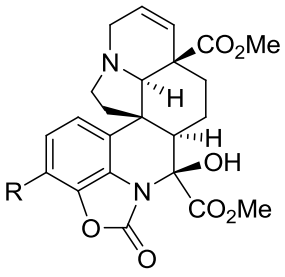
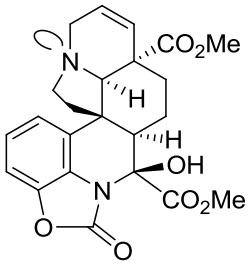


298 R^1 = OH, R^2 = CO_2Me, R^3 = α-OH
299 R^1 = CO_2Me, R^2 = OH, R^3 = α-OH
300 R^1 = OH, R^2 = CO_2Me, R^3 = β-OH



301 R = H
302 R = OMe



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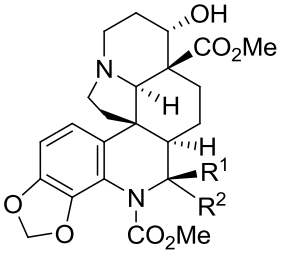
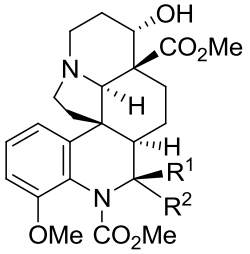
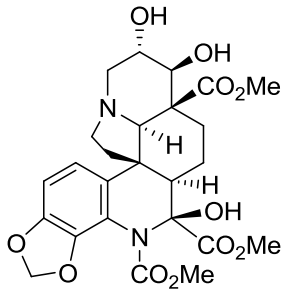


304 R^1 = CO_2Me, R^2 = OH
305 R^1 = OH, R^2 = CO_2Me



306 R^1 = CO_2Me, R^2 = OH
307 R^1 = OH, R^2 = CO_2Me



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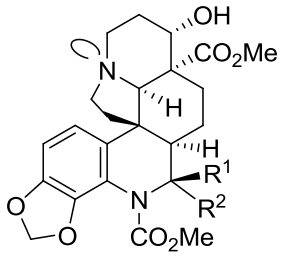
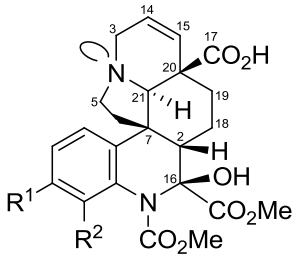
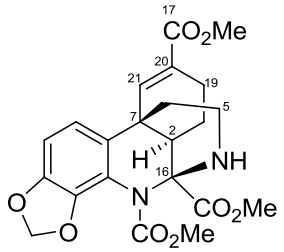


309 $R^1 = CO_2Me$, $R^2 = OH$
310 $R^1 = OH$, $R^2 = CO_2Me$



311 $R^1, R^2 = OCH_2O$
312 $R^1 = H$, $R^2 = OMe$



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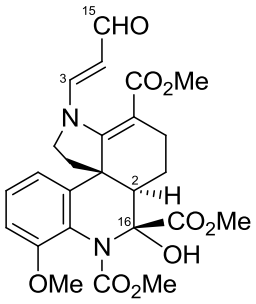

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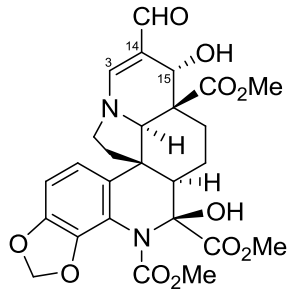

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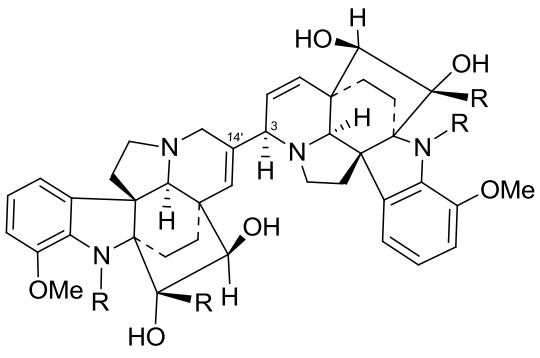
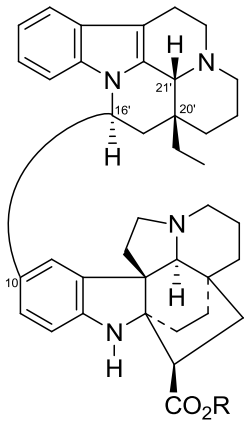
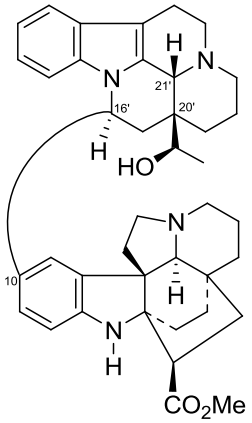


316 $R = CO_2Me$



38 R = Me
39 R = H



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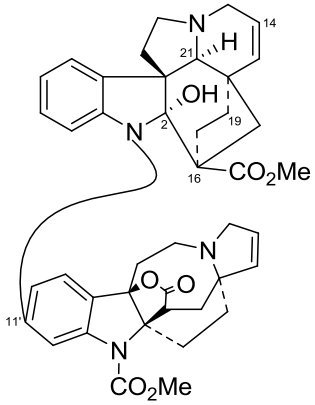

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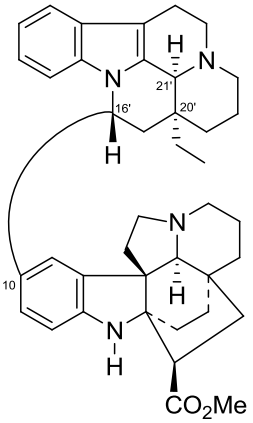

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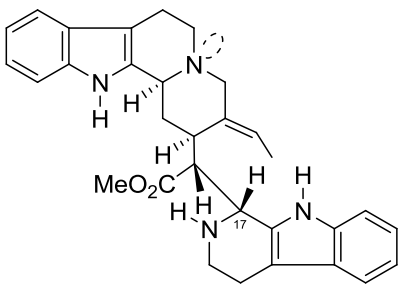

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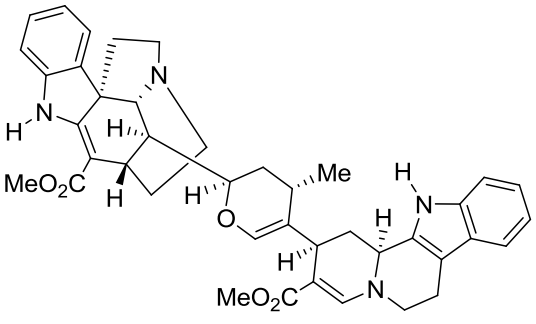

320

1.5 Objective of the Present Research

The aim of the present research is to carry out a detailed investigation of the alkaloidal composition of *Kopsia pauciflora* (collected from Sabah, Malaysian Borneo) and *Kopsia grandifolia* (collected from Johor, Peninsular Malaysia) involving the characterization of the isolated alkaloids, the discovery of new alkaloid structures, and the screening and evaluation of biological activity.