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Sarpagine and related alkaloids

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Abstract

The sarpagine-related macroline and ajmaline alkaloids share a common biosynthetic origin, and bear important structural similarities, as expected. These indole alkaloids are widely dispersed in 25 plant genera, principally in the Apocynaceae family. Very diverse and interesting biological properties have been reported for this group of natural products. Isolation of new sarpagine-related alkaloids as well as the asymmetric synthesis of these structurally complex molecules are of paramount importance to the synthetic and medicinal chemists. A total of 115 newly isolated sarpagine-related macroline and ajmaline alkaloids, along with their physicochemical properties have been included in this chapter. A general and efficient strategy for the synthesis of these monomeric alkaloids, as well as bisindoles has been presented, which involves application of the asymmetric Pictet–Spengler reaction (>98% ee) as a key step because of the ease of scale up of the tetracyclic template. Also included in this chapter are the syntheses of the sarpagine-related alkaloids, published since the year 2000.

Keywords

sarpagine; macroline; ajmaline; biosynthesis; nature-inspired; enantioselective; Pictet–Spengler reaction

1. INTRODUCTION

Indole alkaloids have long held a prominent position in the history of natural products chemistry because of their structural similarity to the essential amino acid tryptophan and related metabolites, such as the neurotransmitter serotonin. According to a report by Cordell et al.¹ about 60 plant-derived alkaloids are of pharmaceutical and biological significance, 39 of which correlate with their traditional use. Indole alkaloids, which are found in higher plants and microorganisms, are the largest group in this class.^{2–4} In particular, indole alkaloids have received special attention since they embody azacyclic and tryptophan derived substructures widely characterized as “privileged structures” or designated as those substructures that bind to diverse categories of protein receptors with high affinity.⁵ The most important aspect of their development is probably because they are derived from

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sustainable resources.^{6,7} The medicinal properties of these natural products remain of great interest, as well as the nature of their structure and stereochemistry. However, the vast majority of known alkaloids have been poorly evaluated biologically. In this chapter the focus will be given to the sarpagine-related macroline and ajmaline indole alkaloids isolated since the year 2000.

1.1. Classification

Indole alkaloids of the sarpagine/ajmaline/macroline type comprise one of the most important groups of structurally related natural products. Many compounds of this class of alkaloids have been isolated mainly from *Alstonia* and *Rauwolfia* genera in the Apocynaceae family.^{8–10} Much of the early isolation and structural work was performed on the *Alstonia* alkaloids in the laboratories of Elderfield¹¹ and Schmid^{12,13} and was followed by the biomimetic interconversions of LeQuesne et al.^{14–17}

The sarpagine group of alkaloids (represented by **2**) is the largest class of natural products related to the macroline alkaloids (represented by **3**) and both series originate from common biogenetic intermediates (Figure 1). During the structure determination of *Alstonia* bisindole alkaloids by Schmid et al.¹² macroline (**3**) was obtained as a degradation product from villalstonine. To date, macroline has not been isolated as a natural product but it is believed to be a biomimetic precursor to many *Alstonia* alkaloids.^{15–17} The sarpagine alkaloids are structurally related to the ajmaline alkaloids, represented by ajmaline (**4**), which is a clinically important indole alkaloid.^{18,19} The term “sarpagine-related” will be employed herein to define this group of alkaloids. The number of sarpagine-related indole alkaloids which have been isolated has increased rapidly.^{8–10,20} At this time, the group contains more than 200 alkaloids, of which over 150 are monomeric indoles. The remainder belong to the bisindole class of alkaloids.⁹ The biogenetic numbering of LeMen and Taylor²¹ has been employed here. Note the four stereocenters at C-3, C-5, C-15 and C-16 in sarpagine (**2**). The β -hydrogen atom at C-15 of this group, as well as the chiral centers at C-3, C-5 and C-16 are the same for the macroline series.

The sarpagine and macroline alkaloids can be related in a synthetic sense by a Michael addition of the N_b nitrogen atom of macroline (**3**) to the α,β -unsaturated carbonyl system at C-21 to afford β -ketoammonium salt **7**, or by direct 1,2-addition of N_b nitrogen atom to the ketone at C-19 to obtain **6**, as illustrated in Figure 2.^{8,22} Conversely, sarpagine can be converted into macroline (**3**) via a retro-Michael reaction of the TBS protected N_b-methyl intermediate **8** to TBS protected macroline precursor **5** followed by silyl group deprotection as demonstrated by LeQuesne et al.¹⁶ The sarpagine alkaloids bear important structural similarities to the ajmaline alkaloids, the latter of which are well known for their biological activity.²³ These bases are structurally related by the presence of the quinuclidine ring and the C-5–C-16 linkage. The absolute configurations of the stereogenic centers at C-3, C-5 and C-15 of both series are identical, except at C-16 which is antipodal to the sarpagine series. The biogenetic connection between the sarpagine and ajmaline alkaloids was proposed earlier.^{24–27} Woodward had suggested the conversion of sarpagan alkaloids such as **9** bearing an *endo* aldehyde functionality to ajmalan skeleton **10** under strong acidic conditions.²⁴ This was confirmed by Stöckigt et al. by conversion of 16-*epi*-vellosimine (**11**)

into vinorine (**12**) via deacetylvinorine (**13**) in the presence of the enzyme acetyl-CoA dependent vinorine synthase^{28–30} (Figure 3).

1.2. Biosynthesis

The widespread application of plant cell cultures during the 1970s provided a rich source of biosynthetic enzymes and encouraged work on the elucidation of signal transduction mechanisms that activate alkaloid pathways.³¹ The application of molecular techniques to the alkaloid field in the 1990s prompted the isolation of numerous molecular clones involved in alkaloid biosynthesis, which have been used to determine the tissue-specific localization of alkaloid biosynthetic enzymes and gene transcripts, and functionally analyze the corresponding promoters.³² Recent applications of genomics-based technologies, such as expressed sequence tag (EST) databases, DNA microarrays, and proteomic analysis, have shown the potential to accelerate the discovery of new components and mechanisms involved in the assembly and function of plant alkaloids.³³

Monoterpenoid indole alkaloids consist of an indole moiety provided by tryptamine (**16**) or tryptophan (**14**) and a terpenoid component derived from the iridoid glucoside secologanin (**15**) (Scheme 1). Molecular clones for both the α - and β -subunits of anthranilate synthase (AS), which catalyze the first committed reaction of the indole pathway, have been isolated from *Camptotheca acuminata*.^{34,35} Comparison of the two differentially regulated genes encoding the AS α -subunit showed that the spatial and developmental expression of only one paralleled that of the β -subunit gene, and the pattern of camptothecin accumulation. Thus, the indole and monoterpenoid indole alkaloid pathways appear to be coordinately regulated through the duplication of specific genes, such as that encoding the AS α -subunit. Tryptophan (**14**) is converted into tryptamine (**16**) by tryptophan decarboxylase (TDC), which is encoded by a single gene in *Catharanthus roseus*,^{36–38} and by two autonomically regulated genes in *C. acuminata*.³⁹ A molecular clone for TDC was also reported from *Ophiorrhiza pumila*.⁴⁰ Secologanin (**15**) is formed from precursors derived from the triose phosphate/pyruvate pathway.⁴¹ Two cDNAs encoding the enzymes 1-deoxy-D-xylulose 5-phosphate reductoisomerase (DXR) and 2-C-methyl-D-erythritol 2,4-cyclodiphosphatesynthase (MECS) of the 2-C-methyl-D-erythritol 4-phosphate (MEP) pathway were isolated from *C. roseus*.⁴² The corresponding gene transcripts were induced in *C. roseus* cell cultures producing monoterpenoid indole alkaloids.

Tryptamine (**16**) and secologanin (**15**) condense via the Pictet–Spengler reaction to form strictosidine (**17**), the common precursor to all monoterpenoid indole alkaloids by strictosidine synthase (STR) (Scheme 1).³³ STR cDNAs have been isolated from *Rauwolfia serpentina*, *C. roseus*, and *O. pumila*.^{43–46} Crystallization and preliminary X-ray analysis of STR from *R. serpentina* has also been reported.⁴⁷ Strictosidine (**17**) is deglycosylated by strictosidine β -D-glucosidase (SG), which has been purified,⁴⁸ and the corresponding cDNA isolated from *C. roseus*⁴⁹ and *R. serpentina*⁵⁰ cell cultures. STR and SG have also been crystallized and preliminary X-ray analyses have been performed.^{47,51} The biosynthetic intermediates after removal of the glucose unit by strictosidine β -D-glucosidase (SG) have not yet been elucidated in much detail. It is obvious that deglycosylated strictosidine is converted via several unstable intermediates into 4,21-dehydrogeissoschizine (**18**). Although

many monoterpenoid indole alkaloids are produced from 4,21-dehydrogeissoschizine (**18**), the enzymology of the branch pathways leading to catharanthine and most other products are still unknown. However, the final steps of vindoline biosynthesis from tabersonine have been characterized in considerable detail. Progress has also been made in the isolation and characterization of enzymes involved in ajmaline biosynthesis in *R. serpentina*. Conversion of strictosidine-derived intermediates under the control of the P450-dependent sarpagan bridge enzyme (SBE) opens the pathway to the sarpagan-type alkaloids. A specific methylesterase of the α/β -fold superfamily of hydrolases, polyneuridine aldehydeesterase (PNAE), converts the intermediate polyneuridine aldehyde (**11**) into 16-*epi*-vellosimine (**10**).⁵²

Epimerization of 16-*epi*-vellosimine (**10**) at the C-16 carbon results in vellosimine (**24**). Enzyme vellosimine reductase (VeR) catalyzes NADPH dependent reduction of vellosimine (**24**) to 10-deoxysarpagine (**25**), which is the immediate precursor in the biosynthesis of sarpagine (**2**).⁵³ The enzyme VeR is a specific enzyme of the sarpagine pathway. Conversion of 10-deoxysarpagine (**25**) to sarpagine is carried out by deoxysarpagine hydroxylase (DH).⁵⁴ Deoxysarpagine hydroxylase is a novel cytochrome P450-dependent monooxygenase.

A member of the BAHD superfamily of acyl-transfer enzymes, vinorine synthase (VS), catalyzes the cyclization and acetylation of 16-*epi*-vellosimine (**10**) (Scheme 1).⁵⁵ Molecular clones for PNAE⁵² and VS⁵⁶ have been isolated and the crystal structure of VS has been solved.^{57,58} Vinorine (**19**) is then hydroxylated by the P450-dependent enzyme vinorine hydroxylase (VH) to form vomilenine (**20**),⁵⁹ which is subsequently reduced in two steps by the NADPH-dependent enzymes vomilenine reductase (VR) and 1,2-dihydrovomilenine reductase (DHVR).^{60,61} VR might play an important regulatory role in the ajmaline pathway as the acetyl group introduced by VS can be removed after reduction of the indolenine double bond. In contrast, deacetylation at the indolenine stage [i.e. vinorine (**19**) or vomilenine (**20**)] would lead to spontaneous ring opening and formation of sarpagan-type alkaloids, such as 16-*epi*-vellosimine (**10**) and vellosimine (**24**). A molecular clone has been reported for acetylajmalan esterase (AAE), a highly specific enzyme that hydrolyzes the 17-*O*-acetyl group of ajmalan-type alkaloids ultimately leading to ajmaline (**4**).^{30,62} *R. serpentina* cultures normally accumulate the side-product raucaffricine (**26**) rather than ajmaline (**4**). The re-utilization of raucaffricine for ajmaline production involves raucaffricine-*O*- β -glucosidase (RG). The cDNA for RG was isolated and shown to encode a protein with homology to strictosidine β -D-glucosidase (SGD).³³ Vomilenine (**20**) also serves as the precursor of perakine (**27**), which in turn is converted to raucaffrinoline (**28**) by an NADPH-dependent aldo-keto reductase perakine reductase (PR).^{63,64}

2. OCCURRENCE

Indole alkaloids of the sarpagine/macroline/ajmaline family are widely dispersed in 25 plant genera, principally in the Apocynaceae plant family.^{8–10} Some 100 plant species are currently known to contain members of this vast group of alkaloids. New alkaloids have been isolated from a variety of sources with increasing frequency and characterized via the latest spectroscopic techniques. Those recently isolated (since year 2000) are listed in Table

1 (organized by ascending molecular weights), along with their molecular formulae and plant source/s.

2.1. Recently Isolated Sarpagine-related Indole Alkaloids

Illustrated in Tables 2–6 are the structures of the recently isolated (since year 2000) sarpagine-related indole alkaloids, along with their key physicochemical properties. They have been classified into “sarpagine-type”, “macroline-type”, “ajmaline-type”, “sarpagine/macroline oxindoles”, and “bisindole alkaloids containing sarpagine/macroline monomeric units” for ease of illustration.

3. SPECTROSCOPY

3.1 ^1H NMR Spectroscopy

19(S),20(R)-Dihydroperaksine (29): ^1H NMR (400 MHz, Pyridine- d_5): δ 12.02 (1H, br s, N_a -H), 7.66 (1H, dd, $J=7.2, 1.4$ Hz, H-9), 7.58 (1H, dd, $J=7.2, 1.4$ Hz, H-12), 7.27 (1H, ddd, $J=7.2, 7.2, 1.4$ Hz, H-11), 7.23 (1H, ddd, $J=7.2, 7.2, 1.4$ Hz, H-10), 6.16 (1H, br s, 21-OH), 5.58 (1H, br s, 17-OH), 4.51 (1H, d, $J=9.6$ Hz, H-3), 4.01 (m, 2H, H-17), 3.87 (1H, dd, $J=10.6, 5.8$ Hz, H-21b), 3.81 (1H, dd, $J=10.9, 7.9$ Hz, H-21a), 3.58 (1H, m, H-5), 3.39 (1H, dd, $J=15.1, 4.8$ Hz, H-6a), 3.11 (1H, d, $J=15.1$, H-6b), 2.81 (1H, ddd, $J=14.7, 6.5, 6.5$ Hz, H-19), 2.48 (1H, m, H-15), 2.33 (1H, ddd, $J=13.0, 9.6, 1.4$ Hz, H-14a), 2.12 (1H, m, H-16), 2.07 (1H, ddd, $J=14.7, 7.9, 5.8$ Hz, H-20), 1.54 (1H, dd, $J=13.0, 13.1$ Hz, H-14b), 1.52 (1H, d, $J=6.5$ Hz, H-18).

19(S),20(R)-Dihydroperaksine-17-al (30): ^1H NMR (400 MHz, Pyridine- d_5): δ 11.90 (1H, br s, N_a -H), 9.87 (1H, s, H-17), 7.68 (1H, dd, $J=7.6, 1.2$ Hz, H-9), 7.57 (1H, dd, $J=7.6, 1.2$ Hz, H-12), 7.29 (1H, ddd, $J=7.2, 7.2, 1.2$ Hz, H-11), 7.25 (1H, ddd, $J=7.2, 7.2, 1.2$ Hz, H-10), 6.18 (1H, br s, 21-OH), 4.28 (1H, d, $J=9.4$ Hz, H-3), 4.17 (1H, dd, $J=8.2, 4.7$ Hz, H-5), 3.82 (1H, dd, $J=11.4, 5.3$ Hz, H-21b), 3.75 (1H, dd, $J=11.4, 8.8$ Hz, H-21a), 3.23 (1H, dd, $J=15.3, 4.7$ Hz, H-6a), 2.75 (1H, d, $J=15.3$, H-6b), 2.51 (1H, ddd, $J=14.7, 6.5, 6.5$ Hz, H-19), 2.73 (1H, m, H-15), 2.22 (1H, ddd, $J=12.9, 9.4, 1.2$ Hz, H-14a), 2.32 (1H, d, $J=8.2$, H-16), 1.57 (1H, ddd, $J=14.7, 8.8, 5.3$ Hz, H-20), 1.47 (1H, dd, $J=12.9, 2.4$ Hz, H-14b), 1.32 (1H, d, $J=6.5$ Hz, H-18).

10-Hydroxy-19(S),20(R)-dihydroperaksine (31): ^1H NMR (400 MHz, Pyridine- d_5): δ 11.64 (1H, br s, N_a -H), 10.72 (1H, br s, 10-OH), 7.50 (1H, d, $J=8.5$ Hz, H-12), 7.49 (1H, d, $J=2.4$ Hz, H-9), 7.24 (1H, dd, $J=8.5, 2.4$ Hz, H-11), 6.17 (1H, br s, 21-OH), 5.28 (1H, br s, 17-OH), 4.41 (1H, d, $J=9.4$ Hz, H-3), 4.01 (m, 2H, H-17), 3.90 (1H, dd, $J=10.9, 5.9$ Hz, H-21b), 3.82 (1H, dd, $J=10.9, 8.2$ Hz, H-21a), 3.47 (1H, m, H-5), 3.30 (1H, dd, $J=15, 4.4$ Hz, H-6a), 3.05 (1H, d, $J=15.1$, H-6b), 2.74 (1H, ddd, $J=15.3, 6.5, 6.5$ Hz, H-19), 2.51 (1H, m, H-15), 2.29 (1H, dd, $J=12.9, 9.4$ Hz, H-14a), 2.19 (1H, m, H-16), 2.04 (1H, ddd, $J=15.3, 8.2, 5.9$ Hz, H-20), 1.53 (1H, d, $J=12.9$ Hz, H-14b), 1.47 (1H, d, $J=6.5$ Hz, H-18).

3-Hydroxysarpagine (32): ^1H NMR (500 MHz, CD_3OD): δ 7.17 (1H, d, $J=8.5$ Hz, H-12), 6.78 (1H, d, $J=2$ Hz, H-9), 6.67 (1H, dd, $J=8.5, 2$ Hz, H-11), 5.49 (1H, q, $J=7$ Hz, H-19), 4.26 (1H, dt, $J=16.5, 2$ Hz, H-21), 3.38 (1H, br d, H-21), 3.52 (1H, dd, $J=10.5, 6.5$ Hz,

H-17), 3.46 (1H, dd, $J = 10.5, 8.5$ Hz, H-17), 3.08 (1H, dd, $J = 17, 4.5$ Hz, H-6), 3.12–3.05 (2H, m, H-5), 2.96 (1H, m, H-15), 2.64 (1H, dt, $J = 17, 2.5$ Hz, H-6), 2.25 (1H, dd, $J = 13.5, 4.5$ Hz, H-14), 2.04 (1H, dd, $J = 13.5, 2.5$ Hz, H-14), 1.89 (1H, br td, $J = 8.5, 6.5$, H-16), 1.65 (3H, br d, $J = 7$ Hz, H-18).

Hystrixnine (33): ^1H NMR (400 MHz, CDCl_3): δ 9.32 (1H, br s, $N_a\text{-H}$), 7.70 (1H, d, $J = 8.1$ Hz, H-9), 7.49 (1H, br d, $J = 8.4$ Hz, H-12), 7.36 (1H, dd, $J = 8.4, 8.4$ Hz, H-11), 7.16 (1H, dd, $J = 8.4, 8.1$ Hz, H-10), 5.49 (1H, br q, $J = 7.0$ Hz, H-19), 3.70 (1H, br d, $J = 13.9$ Hz, H-21a), 3.62 (1H, dd, $J = 8.0, 2.2$ Hz, H-17a), 3.59 (1H, dd, $J = 8.0, 2.2$ Hz, H-17b), 3.54 (1H, m, H-6a), 3.48 (1H, m, H-6b), 3.47 (3H, s, OMe), 3.33 (1H, m, H-14a), 3.31 (1H, br d, $J = 8.4$ Hz, H-5), 3.07 (1H, br t, $J = 8.8$ Hz, H-15), 3.04 (1H, d, $J = 13.9$ Hz, H-21b), 2.67 (1H, dd, $J = 12.8, 7.7$ Hz, H-14b), 2.57 (3H, s, $N_b\text{-Me}$), 1.97 (1H, m, H-16), 1.70 (3H, dd, $J = 7.0, 2.2$ Hz, H-18).

Gelsempervine-A (34): ^1H NMR (500 MHz, CDCl_3): δ 9.26 (1H, br s, $N_a\text{-H}$), 7.69 (1H, d, $J = 7.7$ Hz, H-9), 7.37 (1H, d, $J = 7.7$ Hz, H-12), 7.31 (1H, d, $J = 7.7$ Hz, H-11), 7.17 (1H, ddd, $J = 8.2, 6.4, 1.7$ Hz, H-10), 5.28 (1H, ddd, $J = 6.6, 6.6, 6.6$ Hz, H-19), 3.90 (2H, m, H-17), 3.81 (1H, d, $J = 9.8$ Hz, H-5), 3.74 (1H, br d, $J = 11.3$ Hz, H-15), 3.68 (3H, s, COOMe), 3.63 (1H, overlapped, H-b), 3.23 (1H, overlapped, H-6a), 3.20 (1H, overlapped, H-14), 3.09 (1H, br d, $J = 12.4, 11.3$ Hz, H-14), 3.00 (1H, br d, $J = 15.3$ Hz, H-21), 2.92 (1H, d, $J = 15.3$ Hz, H-21a), 2.29 (3H, s, $N_b\text{-Me}$), 1.71 (3H, d, $J = 6.6$ Hz, H-18).

Gelsempervine-B (35): ^1H NMR (500 MHz, CDCl_3): δ 8.96 (1H, br s, $N_a\text{-H}$), 7.73 (1H, dd, $J = 8.2, 0.6$ Hz, H-9), 7.35 (2H, overlapped, H-11, H-12), 7.17 (1H, ddd, $J = 8.2, 6.4, 1.7$ Hz, H-10), 5.29 (1H, ddd, $J = 6.9, 6.9, 6.9$ Hz, H-19), 4.59 (1H, d, $J = 11.9$ Hz, H-17), 4.29 (1H, d, $J = 11.9$ Hz, H-17), 3.80 (1H, br dd, $J = 11.8, 2.4$ Hz, H-15), 3.75 (1H, dd, $J = 15.9, 9.2$ Hz, H-6b), 3.69 (1H, br d, $J = 9.2$ Hz, H-5), 3.65 (3H, s, COOMe), 3.26 (1H, overlapped, H-14a), 3.23 (1H, overlapped, H-6a), 3.16 (1H, dd, $J = 14.3, 11.8$ Hz, H-14b), 2.90 (1H, d, $J = 15.0$ Hz, H-21b), 2.79 (1H, br d, $J = 15.0$ Hz, H-21a), 2.29 (3H, s, $N_b\text{-Me}$), 2.02 (3H, s, OCOMe), 1.75 (3H, dd, $J = 6.9, 1.2$ Hz, H-18).

Gelsempervine-C (36): ^1H NMR (500 MHz, CDCl_3): δ 9.17 (1H, br s, $N_a\text{-H}$), 7.61 (1H, d, $J = 7.7$ Hz, H-9), 7.36 (1H, d, $J = 7.7$ Hz, H-12), 7.27 (1H, dd, $J = 7.7, 7.7$ Hz, H-11), 7.13 (1H, dd, $J = 7.7, 7.7$ Hz, H-10), 5.36 (1H, ddd, $J = 6.7, 6.7, 6.7$ Hz, H-19), 4.02 (1H, d, $J = 7.2$ Hz, H-5), 3.99 (1H, d, $J = 11.2$ Hz, H-17), 3.93 (1H, d, $J = 11.2$ Hz, H-17), 3.70 (3H, s, COOMe), 3.43 (1H, dd, $J = 17.6, 7.2$ Hz, H-6b), 3.31 (1H, d, $J = 17.6$ Hz, H-6a), 3.12 (1H, overlapped, H-21b), 3.10 (1H, overlapped, H-15), 3.09 (1H, overlapped, H-21a), 3.01 (1H, d, $J = 13.9$ Hz, H-14b), 2.78 (1H, dd, $J = 13.9, 8.2$ Hz, H-14a), 2.22 (3H, s, $N_b\text{-Me}$), 1.45 (3H, d, $J = 6.7$ Hz, H-18).

Gelsempervine-D (37): ^1H NMR (500 MHz, CDCl_3): δ 9.40 (1H, br s, $N_a\text{-H}$), 7.65 (1H, d, $J = 7.7$ Hz, H-9), 7.40 (1H, d, $J = 7.7$ Hz, H-12), 7.31 (1H, dd, $J = 7.7, 7.7$ Hz, H-11), 7.16 (1H, dd, $J = 7.7, 7.7$ Hz, H-10), 5.44 (1H, ddd, $J = 6.9, 6.9, 6.9$ Hz, H-19), 4.61 (1H, d, $J = 11.6$ Hz, H-17), 4.33 (1H, d, $J = 11.6$ Hz, H-17), 3.95 (1H, br d, $J = 7.8$ Hz, H-5), 3.67 (3H, s, COOMe), 3.59 (1H, dd, $J = 17.1, 7.8$ Hz, H-6b), 3.36 (1H, br d, $J = 7.0$ Hz, H-15), 3.20 (2H, overlapped, H-6a, H-21b), 3.14 (1H, dd, $J = 14.0, 2.9$ Hz, H-14b), 2.95 (2H,

overlapped, H-14a, H-21a), 2.35 (3H, s, Nb-Me), 2.04 (3H, s, OCOMe), 1.44 (3H, d, J = 6.9 Hz, H-18).

19Z-16-*epi*-Voacarpine (38): ^1H NMR (600 MHz, CDCl_3): δ 8.00 (1H, br s, $N_a\text{-H}$), 7.10 (1H, d, J = 8.0 Hz, H-12), 7.05 (1H, overlapped, H-11), 7.04 (1H, overlapped, H-9), 6.90 (1H, ddd, J = 8.0, 6.9, 1.1 Hz, H-10), 5.25 (1H, m, H-19), 4.46 (1H, d, J = 5.7 Hz, H-5), 4.16 (1H, d, J = 17.6, H-21), 3.70 (3H, s, COOMe), 3.43 (2H, m, H-17), 3.38 (1H, br d, J = 17.6 Hz, H-21), 2.86 (1H, dd, J = 16.3, 5.7 Hz, H-6a), 2.75 (1H, d, J = 16.3 Hz, H-6b), 2.69 (1H, br dd, J = 2.9, 2.9 Hz, H-15), 2.08 (1H, dd, J = 14.1, 2.9 Hz, H-14b), 1.84 (1H, dd, J = 14.1, 2.9 Hz, H-14a), 1.53 (3H, d, J = 6.9 Hz, H-18).

19,20-Z-Affinisine (39): ^1H NMR (400 MHz, CDCl_3): δ 7.41 (1H, d, J = 8 Hz, H-9), 7.29 (1H, d, J = 8 Hz, H-12), 7.19 (1H, td, J = 8, 1 Hz, H-11), 7.08 (1H, td, J = 8, 1 Hz, H-10), 5.28 (1H, q, J = 7 Hz, H-19), 4.14 (1H, dd, J = 10, 2 Hz, H-3), 3.63 (2H, m, H-21), 3.61 (3H, s, $N_a\text{-Me}$), 3.47 (2H, m, H-17), 3.03 (1H, dd, J = 14, 5 Hz, H-6a), 2.73 (1H, t, J = 6 Hz, H-5), 2.60 (br d, J = 15 Hz, H-6b), 2.23 (1H, br s, H-15), 2.04 (1H, td, J = 12, 2 Hz, H-14a), 1.62 (1H, m, H-16), 1.57 (3H, d, J = 7 Hz, H-18), 1.53 (1H, m, H-14b).

Ervahainanmine (40): ^1H NMR (400 MHz, CD_3OD): δ 7.50 (1H, t, J = 8 Hz, H-9), 7.38 (1H, d, J = 8.1 Hz, H-12), 7.15 (1H, t, J = 8 Hz, H-10), 7.06 (1H, t, J = 8 Hz, H-11), 5.60 (1H, q, J = 7 Hz, H-19), 4.90 (1H, m, H-5), 4.12 (1H, br s, H-3), 4.38 (1H, d, J = 14.6, H-21), 4.06 (1H, d, J = 14.6, H-21), 3.90 (1H, m, H-17), 3.75 (1H, m, H-17), 3.64 (1H, m, H-15), 3.16 (1H, m, H-6), 3.08 (1H, m, H-6), 2.83 (1H, m, H-16), 2.68 (1H, m, H-14), 2.08 (1H, m, H-14), 1.75 (3H, d, J = 6.8 Hz, H-18).

10-Methoxy-16-de(methoxycarbonyl)pagicerine (41): ^1H NMR (400 MHz, CDCl_3): δ 9.1 (1H, s, $N_a\text{-H}$), 7.30 (1H, d, J = 8.8 Hz, H-12), 7.10 (1H, d, J = 2.3 Hz, H-9), 7.06 (1H, dd, J = 8.8, 2.3 Hz, H-11), 5.36 (1H, q, J = 6.6 Hz, H-19), 4.76 (1H, d, J = 10.1 Hz, H-22a), 4.63 (1H, d, J = 10.1 Hz, H-22b), 4.44 (1H, d, J = 16 Hz, H-21a), 3.88 (3H, br s, 10-OMe), 3.86 (1H, m, H-17a), 3.77 (1H, dd, J = 11.4, 2.4 Hz, H-17b), 3.64 (1H, m, H-6a), 3.53 (1H, m, H-6b), 3.45 (1H, d, J = 16 Hz, H-21b), 3.40 (1H, br s, H-5), 3.32 (1H, m, H-15), 3.21 (1H, t, J = 12.4 Hz, H-14a), 2.84 (1H, dd, J = 12.4, 8.2 Hz, H-14b), 1.75 (3H, dd, J = 6.6, 1.9 Hz, H-18), 1.60 (1H, br s, H-16).

N(4)-methyltalpinine (42): ^1H NMR (400 MHz, CD_3OD): δ 7.53 (1H, d, J = 7.9 Hz, H-9), 7.43 (1H, d, J = 8.2 Hz, H-12), 7.25 (1H, t, J = 7.7 Hz, H-11), 7.12 (1H, t, J = 7.8, H-10), 4.99 (1H, d, J = 10.7 Hz, H-3), 4.95 (1H, d, J = 1.9 Hz, H-21), 4.15 (1H, q, J = 6.8 Hz, H-19), 3.91 (1H, t, J = 5.4, H-5), 3.80 (1H, d, J = 11.7, H-17b), 3.73 (3H, s, $N_a\text{-Me}$), 3.54 (1H, dd, J = 11.9, 2.1, H-17a), 3.36 (1H, dd, J = 17.4, 5.3, H-6a), 3.09 (1H, d, J = 16.6, H-6b), 3.07 (3H, s, $N_b\text{-Me}$), 2.47 (1H, br t, J = 12.2 Hz, H-14a), 2.36 (1H, br s, H-15), 2.04 (1H, br s, H-20), 1.98 (1H, ddd, J = 13.2, 5.0, 1.8 Hz, H-14b), 1.77 (1H, br s, H-16), 1.38 (3H, d, J = 6.8 Hz, H-18).

O-Acetyltalpinine (43): ^1H NMR (400 MHz, CDCl_3): δ 7.47 (1H, br d, J = 7.5 Hz, H-9), 7.29 (1H, br d, J = 7.5 Hz, H-12), 7.19 (1H, td, J = 7.5, 1 Hz, H-11), 7.09 (1H, br td, J = 7.5, H-10), 5.63 (1H, br d, J = 2 Hz, H-21), 4.48 (1H, br dd, J = 10, 2 Hz, H-3), 4.34 (1H, q, J = 7

Hz, H-19), 3.71 (1H, dd, $J = 11, 1$ Hz, H-17a), 3.66 (3H, s, N_a -Me), 3.52 (1H, br t, $J = 5.5$ Hz, H-5), 3.47 (1H, dd, $J = 11, 2$ Hz, H-17b), 3.20 (1H, dd, $J = 15.6, 5.5$ Hz, H-6a), 2.63 (1H, d, $J = 15.6$ Hz, H-6b), 2.16 (3H, s, OAc), 2.00 (1H, m, H-15), 1.89 (1H, ddd, $J = 12, 10, 1.6$ Hz, H-14a), 1.52 (1H, ddd, $J = 12, 4, 2.8$ Hz, H-14b), 1.30 (2H, m, H-16 & H-18).

N(4)-Methyl-19-*epi*-talpinine (44): ^1H NMR (400 MHz, CDCl_3): δ 7.49 (1H, d, $J = 8.0$ Hz, H-9), 7.37 (1H, br d, $J = 8.0$ Hz, H-12), 7.30 (1H, td, $J = 8.0, 1$ Hz, H-11), 7.18 (1H, td, $J = 8.0, 1.0$ Hz, H-10), 5.55 (1H, m, H-21), 5.07 (1H, d, $J = 12$ Hz, H-3), 3.79 (1H, dd, $J = 11.6, 2.0$ Hz, H-17a), 3.72 (3H, s, N_a -Me), 3.57 (1H, m, H-19), 3.56 (1H, m, H-5), 3.50 (1H, br d, $J = 11.6$ Hz, H-17b), 3.29 (1H, dd, $J = 16.7, 5.0$ Hz, H-6a), 3.01 (3H, s, N_b^+ -Me), 2.91 (1H, d, $J = 6.7$ Hz, H-6b), 2.77 (1H, br t, $J = 12.0$ Hz, H-14a), 2.24 (1H, m, H-20), 1.93 (1H, m, H-15), 1.74 (1H, ddd, $J = 12.0, 5.0, 2.0$ Hz, H-14b), 1.69 (1H, m, H-16), 1.35 (3H, d, $J = 6.3$ Hz, H-18).

10-Methoxypanarine (45): ^1H NMR (500 MHz, CD_3OD): δ 7.28 (1H, d, $J = 8.5$ Hz, H-12), 7.02 (1H, d, $J = 2.0$ Hz, H-9), 6.84 (1H, dd, $J = 8.5, 2.0$ Hz, H-11), 5.59 (1H, br q, $J = 7.0$ Hz, H-19), 4.89 (1H, H-3), 4.42 (1H, br d, $J = 15.5$ Hz, H-21a), 4.37 (1H, m, H-5), 4.27 (1H, br d, $J = 15.5$ Hz, H-21b), 3.82 (3H, s, OMe), 3.61 (1H, br s, H-15), 3.38 (1H, d, $J = 17.0, 4.0$ Hz, H-6a), 3.16 (3H, s, N_b -Me), 3.03 (1H, d, $J = 17.0$ Hz, H-6b), 2.92 (1H, br s, H-16), 2.53 (1H, dd, $J = 13.0, 10.0$ Hz, H-14b), 2.24 (1H, br d, $J = 13.0$ Hz, H-14a), 1.71 (3H, br d, $J = 7.0$ Hz, H-18).

Alstoyunine A (46): ^1H NMR (500 MHz, CD_3OD): δ 7.35 (1H, d, $J = 8.0$ Hz, H-9), 7.25 (1H, d, $J = 8.0$ Hz, H-12), 7.01 (1H, t, $J = 8.0$ Hz, H-11), 6.94 (1H, t, $J = 8.0$ Hz, H-10), 5.05 (1H, d, $J = 1.1$ Hz, H-17), 4.81 (1H, br s, H-21), 4.07 (1H, d, $J = 9.0$ Hz, H-3), 3.81 (1H, dd, $J = 5.5, 5.2$ Hz, H-5), 3.40 (3H, s, 21-OMe), 3.25 (1H, m, H-19), 2.97 (1H, dd, $J = 15.5, 5.5$ Hz, H-6a), 2.62 (1H, d, $J = 15.5$ Hz, H-6b), 2.11 (1H, br s, H-15), 1.99 (1H, dd, $J = 13.8, 9.0$ Hz, H-14a), 1.75 (1H, dd, $J = 10.0, 3.5$ Hz, H-20), 1.59 (1H, dd, $J = 13.8, 4.2$ Hz, H-14b), 1.53 (1H, d, $J = 6.0$ Hz, H-16), 1.37 (3H, d, $J = 7.2$ Hz, H-18).

Alstoyunine B (47): ^1H NMR (500 MHz, CD_3OD): δ 7.43 (1H, d, $J = 8.0$ Hz, H-9), 7.32 (1H, d, $J = 8.0$ Hz, H-12), 7.13 (1H, t, $J = 8.0$ Hz, H-11), 7.03 (1H, t, $J = 8.0$ Hz, H-10), 4.98 (1H, d, $J = 1.3$ Hz, H-17), 5.39 (1H, br s, H-21), 4.68 (1H, d, $J = 9.5$ Hz, H-3), 4.20 (1H, dd, $J = 5.5, 5.2$ Hz, H-5), 3.85 (1H, m, H-19), 3.48 (3H, s, 17-OMe), 3.18 (1H, dd, $J = 16.5, 5.5$ Hz, H-6a), 2.80 (1H, d, $J = 16.5$ Hz, H-6b), 2.49 (1H, br s, H-15), 2.34 (1H, dd, $J = 14.0, 9.5$ Hz, H-14a), 2.08 (1H, m, H-20), 1.93 (1H, br s, H-16), 1.88 (1H, m, H-14b), 1.57 (3H, d, $J = 7.1$ Hz, H-18).

Rauverine B (48): ^1H NMR (600 MHz, $\text{DMSO}-d_6$): δ 11.40 (1H, s, NH), 9.00 (1H, s, 10-OH), 7.21 (1H, d, $J = 8.8$ Hz, H-12), 7.00 (1H, d, $J = 2.0$ Hz, H-9), 6.83 (1H, dd, $J = 8.8, 2.0$ Hz, H-11), 5.11 (1H, d, $J = 6.6$ Hz, H-19), 4.51 (1H, d, $J = 9.6$ Hz, H-23a), 4.43 (1H, d, $J = 9.6$ Hz, H-23b), 4.28 (1H, d, $J = 12.0$ Hz, H-21a), 3.71 (1H, d, $J = 11.2$ Hz, H-17a), 3.63 (1H, m, H-6a), 3.60 (1H, d, $J = 11.2$ Hz, H-17b), 3.28 (1H, m, H-14a), 3.20 (1H, d, $J = 12.0$ Hz, H-21b), 3.17 (1H, m, H-5), 3.15 (1H, m, H-6b), 3.13 (1H, m, H-15), 2.50 (1H, m, H-14b), 1.60 (3H, d, $J = 6.6$ Hz, H-18), 1.31 (1H, s, H-16).

Rauverine C (49): ^1H NMR(600 MHz, Acetone- d_6): δ 9.96 (1H, s, NH), 7.45 (1H, d, $J=7.7$, H-9), 7.05 (1H, t, $J=7.7$, H-11), 6.98 (1H, t, $J=7.7$, H-10), 7.33 (1H, d, $J=7.7$ Hz, H-12), 5.22 (1H, q, $J=6.8$ Hz, H-19), 4.16 (1H, d, $J=10.4$ Hz, H-3), 3.98 (1H, d, $J=9.5$ Hz, H-17a), 3.55 (2H, s, H-21), 3.44 (1H, $J=10.3$, 4.8 Hz, H-5), 3.19 (1H, d, $J=15.4$ Hz, H-6a), 3.08 (3H, s, OMe), 3.06 (3H, s, OMe), 2.80 (1H, dd, $J=15.4$, 6.0 Hz, H-6b), 2.78 (1H, m, H-15), 1.81 (1H, m, H-14a), 1.69 (1H, m, H-14b), 2.16 (1H, s, H-16), 1.62 (3H, d, $J=6.8$ Hz, H-18).

Macrodasine A (50): ^1H NMR (400 MHz, CDCl_3): δ 7.50 (1H, br d, $J=8.0$ Hz, H-9), 7.31 (1H, br d, $J=8.0$ Hz, H-12), 7.21 (1H, td, $J=8.0$, 1.0 Hz, H-11), 7.12 (1H, br t, $J=8.0$ Hz, H-10), 4.42 (2H, m, H-25), 4.04 (1H, t, $J=12.0$ Hz, H-17a), 3.95 (1H, t, $J=3.0$ Hz, H-3), 3.77 (1H, dd, $J=12.0$, 2.0, H-26), 3.70 (1H, dd, $J=12.0$, 5.0 Hz, H-17b), 3.63 (3H, s, N_a -Me), 3.43 (1H, dd, $J=12.0$, 3.0 Hz, H-26), 3.27 (1H, dd, $J=17.0$, 7.0 Hz, H-6a), 2.98 (1H, d, $J=7.0$ Hz, H-5), 2.39 (3H, m, H-6b, H-14a, H-21b), 2.33 (3H, s, N_b -Me), 2.03 (1H, dt, $J=12.0$, 5.0, H-16), 2.01 (1H, dd, $J=12.0$, 8.0 Hz, H-20), 1.85 (3H, m, H-15, H-21a & H-24), 1.59 (3H, s, H-18), 1.55 (1H, ddd, $J=13.0$, 5.0, 3.0 Hz, H-14b).

Macrodasine B (51): ^1H NMR (400 MHz, CDCl_3): δ 7.50 (1H, br d, $J=8.0$ Hz, H-9), 7.31 (1H, br d, $J=8.0$ Hz, H-12), 7.21 (1H, td, $J=8.0$, 1.0 Hz, H-11), 7.12 (1H, td, $J=8.0$, 1.0 Hz, H-10), 4.56 (2H, m, H-25), 4.08 (1H, t, $J=12.0$ Hz, H-17a), 3.96 (1H, dd, $J=12.0$, 3.0 Hz, H-26), 3.94 (1H, t, $J=3.0$ Hz, H-3), 3.61 (1H, dd, $J=12.0$, 4.0, H-26), 3.85 (1H, dd, $J=12.0$, 5.0 Hz, H-17b), 3.63 (3H, s, N_a -Me), 3.28 (1H, dd, $J=17.0$, 7.0 Hz, H-6a), 2.99 (1H, d, $J=7.0$ Hz, H-5), 2.50 (1H, dd, $J=17.0$, 7.0, H-24), 2.42 (1H, m, H-14a), 2.41 (1H, m, H-6b), 2.34 (3H, s, N_b -Me), 2.15 (1H, dd, $J=13.0$, 11.0 Hz, H-21b), 2.14 (1H, m, H-16), 2.02 (2H, m, H-20 & H-21a), 1.84 (1H, dt, $J=12.0$, 5.0 Hz, H-15), 1.56 (1H, m, H-14b), 1.54 (3H, s, H-18).

Macrodasine C (52): ^1H NMR (400 MHz, CDCl_3): δ 7.51 (1H, br d, $J=8.0$ Hz, H-9), 7.31 (1H, br d, $J=8.0$ Hz, H-12), 7.21 (1H, td, $J=8.0$, 1.0 Hz, H-11), 7.12 (1H, td, $J=8.0$, 1.0 Hz, H-10), 4.49 (2H, dtd, $J=8.0$, 4.0, 2.0, H-25), 3.98 (1H, dd, $J=12.0$, 11.0 Hz, H-17a), 3.96 (1H, m, H-3), 3.86 (1H, dd, $J=12.0$, 2.0 Hz, H-26), 3.85 (1H, dd, $J=12.0$, 5.0 Hz, H-17b), 3.63 (3H, s, N_a -Me), 3.55 (1H, dd, $J=12.0$, 4.0, H-26), 3.26 (1H, dd, $J=17.0$, 7.0 Hz, H-6a), 2.98 (1H, d, $J=7.0$ Hz, H-5), 2.76 (1H, dd, $J=19.0$, 4.0, H-24), 2.53 (1H, dd, $J=19.0$, 8.0, H-24), 2.44 (1H, d, $J=17.0$, H-6b), 2.42 (1H, dd, $J=13.0$, 12.0 Hz, H-21b), 2.40 (1H, td, $J=13.0$, 5.0 Hz, H-14a), 2.36 (3H, s, N_b -Me), 2.14 (1H, dt, $J=11.0$, 5.0 Hz, H-16), 2.07 (1H, dd, $J=12.0$, 8.0, H-20), 1.83 (1H, dt, $J=13.0$, 5.0, H-15), 1.75 (1H, dd, $J=13.0$, 8.0 Hz, H-21a), 1.62 (3H, s, H-18), 1.53 (1H, ddd, $J=13.0$, 5.0, 2.0 Hz, H-14b).

Macrodasine D (53): ^1H NMR (400 MHz, CDCl_3): δ 7.51 (1H, br d, $J=8.0$ Hz, H-9), 7.31 (1H, br d, $J=8.0$ Hz, H-12), 7.21 (1H, td, $J=8.0$, 1.0 Hz, H-11), 7.13 (1H, td, $J=8.0$, 1.0 Hz, H-10), 4.08 (1H, t, $J=12.0$ Hz, H-17a), 3.96 (1H, m, H-3), 3.93 (1H, m, H-25b), 3.93 (1H, dd, $J=11.0$, 1.0, H-26a), 3.77 (1H, m, H-23a), 3.74 (1H, dd, $J=12.0$, 5.0 Hz, H-17b), 3.63 (3H, s, N_a -Me), 3.51 (1H, dt, $J=11.0$, 2.0 Hz, H-26b), 3.23 (1H, dd, $J=17.0$, 7.0 Hz, H-6a), 2.96 (1H, d, $J=7.0$ Hz, H-5), 2.95 (1H, br s, 23-OH), 2.10 (1H, m, H-24b), 2.46 (1H, t, $J=13.0$ Hz, H-21b), 2.46 (1H, m, H-14a), 2.43 (1H, d, $J=17.0$, H-6b), 2.34 (3H, s, N_b -Me), 2.10 (1H, m, H-16), 2.00 (1H, dd, $J=13.0$, 8.0, H-20), 1.85 (1H, dt, $J=12.7$, 5.0,

H-15), 1.76 (1H, ddd, $J = 14.0, 12.0, 3.0$ Hz, H-24a), 1.75 (1H, dd, $J = 13.0, 8.0$ Hz, H-21a), 1.62 (3H, s, H-18), 1.54 (1H, ddd, $J = 13.0, 5.0, 3.0$ Hz, H-14b).

Macrodasine E (54): ^1H NMR (400 MHz, CDCl_3): δ 7.49 (1H, br d, $J = 7.5$ Hz, H-9), 7.30 (1H, br d, $J = 7.5$ Hz, H-12), 7.20 (1H, td, $J = 7.5, 1.0$ Hz, H-11), 7.11 (1H, td, $J = 7.5, 1.0$ Hz, H-10), 4.02 (1H, m, H-17a), 4.01 (1H, dd, $J = 12.0, 2.0$ Hz, H-26a), 3.96 (1H, m, H-3), 3.84 (1H, m, H-25b), 3.75 (1H, dd, $J = 12.0, 5.0$ Hz, H-17b), 3.63 (3H, s, $N_a\text{-Me}$), 3.60 (1H, m, H-23b), 3.56 (1H, dt, $J = 12.0, 2.5$ Hz, H-26b), 3.26 (1H, dd, $J = 17.0, 7.0$ Hz, H-6a), 2.98 (1H, d, $J = 7.0$ Hz, H-5), 2.45 (1H, m, H-14a), 2.42 (1H, d, $J = 17.0$ Hz, H-6b), 2.35 (3H, s, $N_b\text{-Me}$), 2.17 (1H, dt, $J = 14.0, 3.0$ Hz, H-24b), 2.11 (1H, t, $J = 12.0$ Hz, H-21b), 2.03 (1H, m, H-20), 2.01 (1H, m, H-16), 1.91 (1H, dd, $J = 12.0, 7.0$ Hz, H-21a), 1.91 (1H, m, H-24a), 1.81 (1H, dt, $J = 13.0, 5.0$ Hz, H-15), 1.59 (3H, s, H-18), 1.53 (1H, m, H-14b).

Macrodasine F (55): ^1H NMR (400 MHz, CDCl_3): δ 7.50 (1H, d, $J = 8.0$ Hz, H-9), 7.30 (1H, d, $J = 8.0$ Hz, H-12), 7.20 (1H, t, $J = 8.0$ Hz, H-11), 7.11 (1H, t, $J = 8.0$ Hz, H-10), 4.06 (1H, t, $J = 12.0$ Hz, H-17a), 3.94 (1H, m, H-3), 3.71 (1H, m, H-25), 3.83 (1H, dd, $J = 12.0, 5.0$ Hz, H-17b), 3.69 (1H, m, H-26a), 3.61 (3H, s, $N_a\text{-Me}$), 3.61 (1H, m, H-26b), 3.39 (1H, br dd, $J = 11.0, 4.0$ Hz, H-23a), 3.26 (1H, dd, $J = 16.0, 7.0$ Hz, H-6a), 2.97 (1H, d, $J = 7.0$ Hz, H-5), 2.39 (1H, m, H-14a), 2.41 (1H, d, $J = 16.0$ Hz, H-6b), 2.34 (3H, s, $N_b\text{-Me}$), 2.15 (1H, m, H-24b), 2.15 (1H, m, H-16), 2.13 (1H, dd, $J = 13.0, 9.5$ Hz, H-21a), 1.84 (1H, br t, $J = 10.0$ Hz, H-20), 1.97 (1H, dd, $J = 13.0, 10.0$ Hz, H-21b), 1.76 (1H, m, H-15), 1.60 (1H, q, $J = 11.0$ Hz, H-24a), 1.57 (3H, s, H-18), 1.51 (1H, m, H-14b).

Macrodasine G (56): ^1H NMR (400 MHz, CDCl_3): δ 7.50 (1H, d, $J = 8.0$ Hz, H-9), 7.30 (1H, d, $J = 8.0$ Hz, H-12), 7.21 (1H, t, $J = 8.0$ Hz, H-11), 7.12 (1H, t, $J = 8.0$ Hz, H-10), 4.32 (2H, m, H-25), 4.09 (1H, t, $J = 12.0$ Hz, H-17a), 3.95 (2H, m, H-3 & H-23), 3.87 (1H, dd, $J = 12.0, 5.0$ Hz, H-17b), 3.69 (1H, dd, $J = 12.0, 3.0$ Hz, H-26), 3.62 (3H, s, $N_a\text{-Me}$), 3.50 (1H, d, $J = 7.0$ Hz, H-5), 3.43 (1H, dd, $J = 12.0, 4.0$ Hz, H-26), 3.27 (1H, dd, $J = 17.0, 7.0$ Hz, H-6a), 2.42 (1H, d, $J = 17.0$ Hz, H-6b), 2.42 (1H, m, H-14a), 2.35 (3H, s, $N_b\text{-Me}$), 2.32 (1H, t, $J = 13.0$ Hz, H-21b), 2.16 (1H, dt, $J = 12.0, 5.0$ Hz, H-16), 2.08 (1H, ddd, $J = 13.0, 8.0, 5.0$ Hz, H-24), 2.00 (1H, dd, $J = 13.0, 8.0$ Hz, H-21a), 1.87 (1H, m, H-24), 1.85 (1H, dd, $J = 12.0, 8.0$ Hz, H-20), 1.81 (1H, m, H-15), 1.59 (3H, s, H-18), 1.52 (1H, ddd, $J = 13.0, 5.0, 3.0$ Hz, H-14b).

Macrodasine H (57): ^1H NMR (400 MHz, CDCl_3): δ 7.50 (1H, d, $J = 8.0$ Hz, H-9), 7.30 (1H, d, $J = 8.0$ Hz, H-12), 7.20 (1H, t, $J = 8.0$ Hz, H-11), 7.11 (1H, t, $J = 8.0$ Hz, H-10), 4.05 (1H, t, $J = 12.0$ Hz, H-17a), 3.93 (1H, m, H-3), 3.84 (1H, m, H-26b), 3.75 (1H, dd, $J = 12.0, 5.0$ Hz, H-17b), 3.62 (3H, s, $N_a\text{-Me}$), 3.51 (1H, dd, $J = 10.0, 5.0$ Hz, H-23), 3.39 (1H, td, $J = 10.0, 4.5$ Hz, H-26a), 3.26 (1H, dd, $J = 16.0, 7.0$ Hz, H-6a), 2.96 (1H, d, $J = 7.0$ Hz, H-5), 2.41 (1H, d, $J = 16.0$ Hz, H-6b), 2.41 (1H, m, H-14a), 2.33 (3H, s, $N_b\text{-Me}$), 2.16 (1H, t, $J = 12.5$ Hz, H-21b), 2.09 (1H, m, H-16), 2.05 (1H, m, H-24b), 1.96 (1H, dd, $J = 12.5, 8.0$ Hz, H-20), 1.84 (1H, m, H-15), 1.81 (1H, dd, $J = 12.5, 8.0$ Hz, H-21a), 1.62 (3H, s, H-18), 1.50 (1H, m, H-14b), 1.37 (1H, m, H-24a), 1.56 (2H, m, H-25).

Alstopirocine (58): ^1H NMR (400 MHz, CDCl_3): δ 9.99 (1H, br s, $N_a\text{-H}$), 7.53 (1H, d, $J = 8.0$ Hz, H-9), 7.29 (1H, d, $J = 8.0$ Hz, H-12), 7.21 (1H, t, $J = 8.0$ Hz, H-11), 7.12 (1H, t, $J = 8.0$ Hz, H-10), 6.99 (1H, br d, $J = 2.0$ Hz, H-3'), 4.18 (2H, m, H-3 & H-6'), 3.74 (1H, m,

H-17), 3.67 (1H, m, H-17), 3.64 (1H, dd, $J = 11.0, 4.0$, H-7'), 3.60 (1H, m, H-5), 3.59 (3H, s, N_a -Me), 3.53 (1H, dd, $J = 11.0, 4.0$, H-7'), 3.39 (1H, dd, $J = 17.0, 7.0$ Hz, H-6), 2.95 (1H, m, H-5'), 2.92 (1H, m, H-15), 2.89 (1H, m, H-14), 2.83 (1H, m, H-5'), 2.59 (1H, d, $J = 17.0$ Hz, H-6), 2.41 (3H, s, N_b -Me), 1.98 (3H, s, H-18), 1.69 (1H, br d, $J = 11.0$ Hz, H-14), 1.58 (1H, m, H-16).

Rauvoyunine A (59): ^1H NMR (500 MHz, CDCl_3): δ 7.17 (1H, d, $J = 8.7$ Hz, H-12), 6.85 (1H, d, $J = 2.3$ Hz, H-9), 6.73 (1H, dd, $J = 8.7, 2.3$ Hz, H-11), 5.58 (1H, q, $J = 6.8$ Hz, H-19), 4.39 (1H, dd, $J = 4.2, 2.4$ Hz, H-3), 4.02 (2H, s, H-21), 3.91 (1H, dd, $J = 10.5, 5.5$ Hz, H-17a), 3.75 (1H, dd, $J = 10.5, 3.7$ Hz, H-17b), 3.72 (1H, d, $J = 7.2$ Hz, H-5), 3.59 (3H, s, N_a -Me), 3.35 (1H, dd, $J = 16.6, 7.2$ Hz, H-6a), 2.98 (1H, ddd, $J = 13.3, 5.6, 4.0$ Hz, H-15), 2.63 (1H, d, $J = 16.6$ Hz, H-6b), 2.58 (1H, ddd, $J = 13.7, 13.3, 4.2$ Hz, H-14a), 2.55 (3H, s, N_b -Me), 1.86 (1H, ddd, $J = 5.6, 5.5, 3.7$ Hz, H-16), 1.73 (1H, ddd, $J = 13.7, 4.0, 2.4$ Hz, H-14b), 1.44 (3H, d, $J = 6.8$ Hz, H-18).

19-Epi-talcarpine (60): ^1H NMR (400 MHz, CDCl_3): δ 9.51 (1H, br d, $J = 2.3$ Hz, H-21), 7.47 (1H, d, $J = 7.5$ Hz, H-9), 7.27 (1H, d, $J = 7.5$ Hz, H-12), 7.17 (1H, t, $J = 7.5$ Hz, H-11), 7.08 (1H, t, $J = 7.5$ Hz, H-11), 4.02 (1H, dd, $J = 11.0, 4.6$ Hz, H-17a), 3.89 (1H, br d, $J = 6.0$ Hz, H-3), 3.84 (1H, m, H-19), 3.60 (3H, s, N_a -Me), 3.57 (1H, dd, $J = 11.0, 4.6$ Hz, H-17b), 3.15 (1H, dd, $J = 16.0, 6.0$ Hz, H-6a), 3.00 (1H, m, H-5), 2.41 (2H, m, H-14a & H-20), 2.34 (1H, d, $J = 16.0$ Hz, H-6b), 2.32 (3H, s, N_b -Me), 2.16 (1H, m, H-15), 1.71 (1H, m, H-16), 1.64 (1H, ddd, $J = 12.7, 6.0, 1.0$ Hz, H-14b), 1.31 (3H, d, $J = 6.5$ Hz, H-18).

N(1)-Demethylalstophylline (61): ^1H NMR (400 MHz, CDCl_3): δ 7.54 (1H, s, H-21), 7.33 (1H, d, $J = 8.0$ Hz, H-9), 6.84 (1H, d, $J = 2.0$ Hz, H-12), 6.76 (1H, dd, $J = 8.0, 2.0$ Hz, H-10), 4.45 (1H, t, $J = 11.0$ Hz, H-17), 4.17 (1H, ddd, $J = 11.0, 4.0, 2.0$ Hz, H-17), 3.84 (3H, s, 11-OMe), 3.82 (1H, br s, H-3), 3.30 (1H, dd, $J = 16.0, 6.0$ Hz, H-6), 3.10 (1H, d, $J = 6.0$ Hz, H-5), 2.64 (1H, dt, $J = 11.0, 5.0$ Hz, H-15), 2.48 (1H, d, $J = 16.0$, H-6), 2.36 (3H, s, N_b -Me), 2.09 (3H, s, H-18), 2.13 (1H, m, H-14), 1.92 (1H, m, H-16), 1.81 (1H, m, H-14).

N(1)-Demethylalstophyllal (62): ^1H NMR (400 MHz, CDCl_3): δ 9.66 (1H, s, H-21), 7.33 (1H, d, $J = 8.0$ Hz, H-9), 6.84 (1H, d, $J = 2.0$ Hz, H-12), 6.76 (1H, dd, $J = 8.0, 2.0$ Hz, H-10), 4.50 (1H, t, $J = 11.0$ Hz, H-17), 4.19 (1H, ddd, $J = 11.0, 4.0, 2.0$ Hz, H-17), 3.84 (3H, s, 11-OMe), 3.82 (1H, br s, H-3), 3.30 (1H, dd, $J = 16.0, 6.0$ Hz, H-6), 3.10 (1H, d, $J = 6.0$ Hz, H-5), 2.64 (1H, dt, $J = 11.0, 5.0$ Hz, H-15), 2.48 (1H, d, $J = 16.0$, H-6), 2.36 (3H, s, N_b -Me), 2.17 (3H, s, H-18), 2.13 (1H, m, H-14), 1.92 (1H, m, H-16), 1.81 (1H, m, H-14).

MacrocarpineA (63): ^1H NMR (400 MHz, CDCl_3): δ 7.49 (1H, br d, $J = 8.0$ Hz, H-9), 7.29 (1H, br d, $J = 8.0$ Hz, H-12), 7.19 (1H, td, $J = 8.0, 1.0$ Hz, H-11), 7.10 (1H, td, $J = 8.0, 1.0$ Hz, H-10), 4.07 (1H, t, $J = 11.0$ Hz, H-17), 3.96 (2H, m, H-3 & H-19), 3.81 (1H, dd, $J = 11.0, 6.0$ Hz, H-21), 3.73 (1H, dd, $J = 11.0, 4.0$ Hz, H-17), 3.69 (1H, dd, $J = 11.0, 4.0$ Hz, H-21), 3.62 (3H, s, N_a -Me), 3.25 (1H, dd, $J = 17.0, 7.0$ Hz, H-6), 2.87 (1H, d, $J = 7.0$ Hz, H-5), 2.47 (1H, d, $J = 17.0$ Hz, H-6), 2.31 (3H, s, N_b -Me), 2.50 (1H, td, $J = 13.0, 4.0$ Hz, H-14), 2.15 (1H, dt, $J = 11.0, 5.0$ Hz, H-16), 2.06 (1H, dt, $J = 13.0, 5.0$ Hz, H-15), 1.42 (1H, ddd, $J = 13.0, 5.0, 2.0$ Hz, H-14), 1.24 (3H, d, $J = 7.0$ Hz, H-18), 1.07 (1H, m, H-20).

Macrocarpine B (64): ^1H NMR (400 MHz, CDCl_3): δ 7.49 (1H, br d, $J=8.0$ Hz, H-9), 7.29 (1H, br d, $J=8.0$ Hz, H-12), 7.18 (1H, td, $J=8.0$, 1.0 Hz, H-11), 7.10 (1H, td, $J=8.0$, 1.0 Hz, H-10), 4.06 (1H, t, $J=11.0$ Hz, H-17), 3.98 (1H, t, $J=3.0$ Hz, H-3), 3.73 (1H, dd, $J=14.0$, 4.0 Hz, H-17), 3.62 (3H, s, $N_a\text{-Me}$), 3.49 (2H, m, H-19 & H-21), 3.31 (1H, dd, $J=11.0$, 8.0 Hz, H-21), 3.26 (1H, dd, $J=17.0$, 7.0 Hz, H-6), 2.91 (1H, d, $J=7.0$ Hz, H-5), 2.43 (1H, d, $J=17.0$ Hz, H-6), 2.30 (3H, s, $N_b\text{-Me}$), 2.29 (1H, m, H-14), 1.97 (1H, dt, $J=13.0$, 4.0 Hz, H-15), 1.86 (1H, dt, $J=13.0$, 4.0 Hz, H-16), 1.54 (1H, ddd, $J=12.0$, 4.0, 3.0 Hz, H-14), 1.46 (1H, m, H-20), 1.15 (3H, d, $J=6.0$ Hz, H-18).

Macrocarpine C (65): ^1H NMR (400 MHz, CDCl_3): δ 7.49 (1H, dd, $J=8.0$, 1.0 Hz, H-9), 7.27 (1H, dd, $J=8.0$, 1.0 Hz, H-12), 7.17 (1H, td, $J=8.0$, 1.0 Hz, H-11), 7.09 (1H, td, $J=8.0$, 1.0 Hz, H-10), 4.07 (1H, t, $J=11.0$ Hz, H-17), 3.97 (1H, t, $J=4.0$ Hz, H-3), 3.83 (2H, $J=8.0$ Hz, H-21), 3.74 (1H, dd, $J=14.0$, 4.0 Hz, H-17), 3.60 (3H, s, $N_a\text{-Me}$), 3.51 (1H, dq, $J=10.0$, 6.0, H-19), 3.27 (1H, dd, $J=17.0$, 7.0 Hz, H-6), 2.91 (1H, d, $J=7.0$ Hz, H-5), 2.45 (1H, d, $J=17.0$ Hz, H-6), 2.34 (3H, s, $N_b\text{-Me}$), 2.26 (1H, td, $J=13.0$, 4.0 Hz, H-14), 1.86 (2H, m, H-15 & H-16), 1.69 (1H, m, H-20), 1.68 (1H, s, H-23), 1.39 (1H, ddd, $J=13.0$, 4.0, 3.0 Hz, H-14), 1.13 (3H, d, $J=6.0$ Hz, H-18).

Macrocarpine D (66): ^1H NMR (400 MHz, CDCl_3): δ 7.89 (1H, br, NH), 7.49 (1H, d, $J=7.5$ Hz, H-9), 7.32 (1H, d, $J=7.5$ Hz, H-12), 7.18 (1H, t, $J=7.5$ Hz, H-11), 7.11 (1H, t, $J=7.5$ Hz, H-10), 4.08 (1H, t, $J=12.0$ Hz, H-17a), 3.95 (1H, m, H-3), 3.74 (1H, dd, $J=12.0$, 5.0 Hz, H-17b), 3.50 (1H, m, H-19), 3.50 (1H, dd, $J=11.0$, 5.0 Hz, H-21b), 3.34 (1H, dd, $J=11.0$, 8.0 Hz, H-21a), 3.27 (1H, dd, $J=16.0$, 7.0 Hz, H-6a), 2.94 (1H, d, $J=7.0$ Hz, H-5), 2.46 (1H, d, $J=16.0$ Hz, H-6b), 2.34 (3H, s, $N_b\text{-Me}$), 2.28 (1H, td, $J=13.0$, 4.0 Hz, H-14a), 2.01 (1H, m, H-15), 1.89 (1H, dt, $J=12.0$, 4.0 Hz, H-16), 1.62 (1H, dt, $J=13.0$, 4.0 Hz, H-14b), 1.50 (1H, m, H-20), 1.16 (3H, d, $J=6.0$ Hz, H-18).

Macrocarpine E (67): ^1H NMR (400 MHz, CDCl_3): δ 8.14 (1H, br s, NH), 7.48 (1H, d, $J=7.0$, 1.0 Hz, H-9), 7.31 (1H, dd, $J=7.0$, 1.0 Hz, H-12), 7.14 (1H, td, $J=7.0$, 1.0 Hz, H-11), 7.10 (1H, td, $J=7.0$, 1.0 Hz, H-10), 4.04 (1H, t, $J=12.0$ Hz, H-17a), 3.93 (1H, qd, $J=6.7$, 2.6 Hz, H-19), 3.85 (1H, br t, $J=3.0$ Hz, H-3), 3.76 (1H, dd, $J=12.0$, 5.0 Hz, H-17b), 3.71 (1H, dd, $J=11.0$, 6.0 Hz, H-21), 3.64 (1H, dd, $J=11.0$, 4.0 Hz, H-21), 3.23 (1H, dd, $J=17.0$, 7.0 Hz, H-6a), 2.82 (1H, d, $J=7.0$ Hz, H-5), 2.43 (1H, d, $J=17.0$ Hz, H-6b), 2.43 (1H, td, $J=13.0$, 4.0 Hz, H-14a), 2.30 (3H, s, $N_b\text{-Me}$), 2.08 (1H, dd, $J=12.0$, 5.0 Hz, H-16), 1.98 (1H, dt, $J=13.0$, 5.0 Hz, H-15), 1.44 (1H, ddd, $J=13.0$, 5.0, 3.0 Hz, H-14b), 1.21 (3H, d, $J=6.7$ Hz, H-18), 1.06 (1H, m, H-20).

Macrocarpine F (68): ^1H NMR (400 MHz, CDCl_3): δ 7.75 (1H, br d, $J=8.0$ Hz, H-12), 7.46 (1H, br d, $J=8.0$ Hz, H-9), 7.18 (1H, br t, $J=8.0$ Hz, H-11), 7.07 (1H, br t, $J=8.0$ Hz, H-10), 4.27 (1H, m, H-3), 4.07 (1H, t, $J=11.0$ Hz, H-17a), 3.94 (1H, qd, $J=6.8$, 2.0 Hz, H-19), 3.78 (1H, dd, $J=11.0$, 5.0 Hz, H-17b), 3.72 (1H, dd, $J=11.0$, 6.0 Hz, H-21), 3.65 (1H, dd, $J=11.0$, 4.0 Hz, H-21), 3.52 (3H, s, $N_a\text{-Me}$), 3.21 (1H, m, H-5), 3.17 (1H, m, H-6a), 2.63 (1H, d, $J=15.0$ Hz, H-6b), 2.45 (1H, td, $J=12.0$, 4.0 Hz, H-14a), 2.10 (1H, m, H-15), 2.08 (1H, m, H-16), 1.35 (1H, m, H-14b), 1.21 (3H, d, $J=6.8$ Hz, H-18), 1.04 (1H, m, H-20).

Macrocarpine G (69): ^1H NMR (400 MHz, CDCl_3): δ 7.46 (1H, br d, $J=7.5$ Hz, H-9), 7.24 (1H, br d, $J=7.5$ Hz, H-12), 7.17 (1H, td, $J=7.5$, 1.0 Hz, H-11), 7.08 (1H, td, $J=7.5$, 1.0 Hz, H-10), 4.27 (1H, br t, $J=3.0$ Hz, H-3), 4.03 (1H, t, $J=12.0$ Hz, H-17a), 3.72 (1H, dd, $J=12.0$, 4.0 Hz, H-17b), 3.52 (3H, s, $N_a\text{-Me}$), 3.46 (1H, m, H-19), 3.40 (1H, dd, $J=11.0$, 6.0 Hz, H-21), 3.25 (1H, m, H-5), 3.22 (1H, m, H-21), 3.18 (1H, dd, $J=16.0$, 7.0 Hz, H-6a), 2.58 (1H, d, $J=16.0$ Hz, H-6b), 2.18 (1H, td, $J=12.0$, 4.0 Hz, H-14a), 2.02 (1H, m, H-15), 1.81 (1H, dt, $J=12.0$, 5.0 Hz, H-16), 1.49 (1H, dt, $J=12.0$, 2.0 Hz, H-14b), 1.37 (1H, m, H-20), 1.11 (3H, d, $J=6.0$ Hz, H-18).

Macrocarpine H (70): ^1H NMR (400 MHz, CDCl_3): δ 7.17 (1H, d, $J=8.7$ Hz, H-12), 6.94 (1H, d, $J=2.3$ Hz, H-9), 6.83 (1H, dd, $J=8.7$, 2.3 Hz, H-11), 4.05 (1H, t, $J=12.0$ Hz, H-17a), 3.94 (1H, m, H-3), 3.71 (1H, dd, $J=12.0$, 5.0 Hz, H-17b), 3.85 (3H, s, 10-OMe), 3.58 (3H, s, $N_a\text{-Me}$), 3.46 (2H, m, H-19 & H-21), 3.22 (1H, dd, $J=16.5$, 7.0 Hz, H-6a), 3.21 (1H, dd, $J=10.5$, 8.0 Hz, H-21), 2.90 (1H, d, $J=7.0$ Hz, H-5), 2.39 (1H, d, $J=16.5$ Hz, H-6b), 2.30 (3H, s, $N_b\text{-Me}$), 2.25 (1H, td, $J=13.0$, 4.0 Hz, H-14a), 1.97 (1H, dq, $J=13.0$, 4.0 Hz, H-15), 1.85 (1H, dt, $J=11.0$, 5.0 Hz, H-16), 1.52 (1H, dt, $J=13.0$, 4.0 Hz, H-14b), 1.45 (1H, m, H-20), 1.14 (3H, d, $J=6.0$ Hz, H-18).

Voacalgine B (71): ^1H NMR TFA salt (700 MHz, CD_3OD): δ 7.83 (1H, s, H-21), 7.29 (1H, d, $J=8.8$ Hz, H-12), 6.90 (1H, d, $J=2.3$ Hz, H-9), 6.83 (1H, dd, $J=8.8$, 2.3 Hz, H-11), 4.97 (1H, br s, H-3), 4.35 (1H, dd, $J=10.7$, 2.6 Hz, H-17b), 4.27 (1H, dd, $J=10.7$, 10.7 Hz, H-17a), 3.98 (1H, d, $J=7.4$ Hz, H-5), 3.68 (3H, s, $N_a\text{-Me}$), 3.49 (1H, dd, $J=18.0$, 7.4 Hz, H-6b), 3.10 (1H, d, $J=18.0$ Hz, H-6a), 2.92 (3H, s, $N_b\text{-Me}$), 2.68 (1H, m, H-15), 2.45 (1H, m, H-16), 2.42 (1H, m, H-14b), 2.13 (3H, s, H-18), 1.99 (1H, dd, $J=11.8$, 11.8 Hz, H-14a).

Voacalgine C (72): ^1H NMR formic acid salt (700 MHz, CD_3OD): δ 7.46 (1H, d, $J=7.6$ Hz, H-9), 7.36 (1H, d, $J=7.9$ Hz, H-12), 7.17 (1H, dd, $J=7.4$, 7.9 Hz, H-11), 7.06 (1H, dd, $J=7.6$, 7.4 Hz, H-10), 4.44 (1H, br s, H-3), 4.00 (1H, dd, $J=11.9$, 10.0 Hz, H-17b), 3.83 (1H, m, H-26b), 3.82 (1H, m, H-17a), 3.68 (3H, s, $N_a\text{-Me}$), 3.50 (1H, br t, $J=3.0$ Hz, H-23), 3.48 (1H, m, H-26a), 3.35 (1H, m, H-5), 3.34 (1H, m, H-6b), 2.70 (1H, br d, $J=16.1$ Hz, H-6a), 2.59 (3H, s, $N_b\text{-Me}$), 2.48 (1H, ddd, $J=14.7$, 14.7, 3.5 Hz, H-14b), 2.23 (1H, ddd, $J=10.0$, 5.1, 5.1 Hz, H-16), 2.07 (1H, dd, $J=11.8$, 7.6 Hz, H-20), 2.02 (1H, dd, $J=12.3$, 12.3 Hz, H-21b), 1.97 (1H, dddd, $J=12.8$, 12.6, 3.0, 3.0, H-24b), 1.87 (1H, dddd, $J=12.6$, 12.6, 12.4, 3.4, 3.4 Hz, H-25b), 1.78 (3H, m, H-14a, H-15 & H-21a), 1.62 (1H, m, H-24a), 1.58 (3H, s, H-18), 1.29 (1H, m, H-25a).

Voacalgine D (73): ^1H NMR formic acid salt (700 MHz, CD_3OD): δ 7.66 (1H, dd, $J=1.7$, 0.5 Hz, H-26), 7.38 (1H, d, $J=7.6$ Hz, H-9), 7.24 (1H, d, $J=7.9$ Hz, H-12), 7.12 (1H, dd, $J=7.4$, 7.9 Hz, H-11), 7.09 (1H, br d, $J=3.6$ Hz, H-24), 7.00 (1H, dd, $J=7.6$, 7.4 Hz, H-10), 6.54 (1H, dd, $J=3.6$, 1.7 Hz, H-25), 4.49 (1H, dd, $J=11.7$, 11.7 Hz, H-17b), 4.20 (1H, br s, H-3), 3.44 (3H, s, $N_a\text{-Me}$), 3.46 (1H, m, H-17a), 3.24 (1H, m, H-6b), 3.13 (1H, m, H-5), 2.90 (1H, m, H-21b), 2.87 (1H, m, H-14b), 2.82 (1H, m, H-21a), 2.54 (1H, d, $J=16.6$ Hz, H-6a), 2.42 (3H, s, $N_b\text{-Me}$), 2.21 (1H, ddd, $J=10.6$, 5.3, 5.3 Hz, H-20), 1.97 (1H, ddd, $J=11.8$, 3.4, 3.4 Hz, H-16), 1.68 (1H, m, H-14a), 1.65 (1H, m, H-15), 1.32 (3H, s, H-18),

Voacalgine E (74): ^1H NMR formic acid salt (700 MHz, CD_3OD): δ 7.78 (1H, br s, H-26), 7.54 (1H, d, $J = 7.7$ Hz, H-9), 7.46 (1H, d, $J = 7.9$ Hz, H-12), 7.36 (1H, br d, $J = 3.4$ Hz, H-24), 7.27 (1H, dd, $J = 7.9, 7.6$ Hz, H-11), 7.13 (1H, dd, $J = 7.7, 7.6$ Hz, H-10), 6.64 (1H, dd, $J = 3.4, 1.2$ Hz, H-25), 5.09 (1H, br s, H-3), 4.34 (1H, dd, $J = 9.7, 9.4$ Hz, H-17b), 4.23 (1H, dd, $J = 9.9, 9.7$ Hz, H-17a), 4.01 (1H, br s, H-5), 3.78 (3H, s, $N_a\text{-Me}$), 3.49 (1H, m, H-21b), 3.42 (1H, dd, $J = 17.6, 6.0$ Hz, H-6b), 3.36 (1H, m, H-21a), 3.08 (1H, d, $J = 17.6$ Hz, H-6a), 2.94 (3H, s, $N_b\text{-Me}$), 2.74 (1H, ddd, $J = 8.2, 8.2, 7.1$ Hz, H-16), 2.40 (1H, br d, $J = 11.8$ Hz, H-14b), 2.28 (1H, ddd, $J = 12.1, 11.8, 0.8$ Hz, H-14a), 2.24 (3H, s, H-18), 2.14 (1H, ddd, $J = 12.1, 7.1, 5.9$ Hz, H-15).

Alstofoline A (75): ^1H NMR (400 MHz, CDCl_3): δ 7.49 (1H, d, $J = 8.0$ Hz, H-9), 7.31 (1H, d, $J = 8.0$ Hz, H-12), 7.22 (1H, td, $J = 8.0, 1.0$ Hz, H-11), 7.11 (1H, td, $J = 8.0, 1.0$ Hz, H-10), 4.52 (1H, dd, $J = 11.0, 8.0$ Hz, H-17a), 4.42 (1H, t, $J = 8.0$ Hz, H-17b), 3.91 (1H, br s, H-3), 3.64 (3H, s, $N_a\text{-Me}$), 3.27 (1H, dd, $J = 16.0, 6.0$ Hz, H-6a), 3.06 (1H, d, $J = 6.0$ Hz, H-5), 2.54 (1H, m, H-16), 2.47 (1H, br d, $J = 16.0$ Hz, H-6b), 2.42 (3H, s, $N_b\text{-Me}$), 2.17 (1H, m, H-15), 2.13 (1H, m, H-14a), 2.10 (1H, m, H-14b).

Alstofoline B (76): ^1H NMR (400 MHz, CDCl_3): δ 7.18 (1H, d, $J = 9.0$ Hz, H-12), 6.93 (1H, d, $J = 2.3$ Hz, H-9), 6.86 (1H, dd, $J = 9.0, 2.3$ Hz, H-11), 4.50 (1H, dd, $J = 11.0, 8.5$ Hz, H-17a), 4.42 (1H, t, $J = 8.5$ Hz, H-17b), 3.85 (1H, m, H-3), 3.85 (3H, s, 10-OMe), 3.60 (3H, s, $N_a\text{-Me}$), 3.05 (1H, d, $J = 6.0$ Hz, H-5), 3.23 (1H, dd, $J = 16.0, 6.0$ Hz, H-6a), 2.55 (1H, dt, $J = 11.0, 8.5$ Hz, H-16), 2.42 (1H, d, $J = 16.0$ Hz, H-6b), 2.41 (3H, s, $N_b\text{-Me}$), 2.20 (1H, m, H-14a), 2.15 (1H, m, H-15), 2.10 (1H, m, H-14b).

20,21-Dihydroalstonerine (77): ^1H NMR (400 MHz, CDCl_3): δ 7.50 (1H, d, $J = 8.0$ Hz, H-9), 7.27 (1H, d, $J = 8.0$ Hz, H-12), 7.18 (1H, td, $J = 8.0, 1.0$ Hz, H-11), 7.09 (1H, td, $J = 8.0, 1.0$ Hz, H-10), 4.18 (1H, d, $J = 12.5$ Hz, H-21b), 3.97 (1H, br s, H-3), 3.95 (1H, t, $J = 11.5$ Hz, H-17a), 3.86 (1H, dd, $J = 12.5, 3.0$ Hz, H-21a), 3.72 (1H, dd, $J = 11.5, 5.0$ Hz, H-17b), 3.61 (3H, s, $N_a\text{-Me}$), 3.24 (1H, dd, $J = 16.0, 7.0$ Hz, H-6a), 2.83 (1H, d, $J = 7.0$ Hz, H-5), 2.52 (1H, dd, $J = 16.0$ Hz, H-6b), 2.44 (1H, dd, $J = 12.0, 4.0$ Hz, H-14a), 2.35 (1H, m, H-15), 2.29 (3H, s, $N_b\text{-Me}$), 2.12 (1H, m, H-16), 2.12 (3H, s, H-18), 1.97 (1H, m, H-20), 1.42 (1H, dt, $J = 12.0, 3.0$ Hz, H-14b).

Alstofonidine (78): ^1H NMR (400 MHz, CDCl_3): δ 7.51 (1H, br d, $J = 8.0$ Hz, H-9), 7.31 (1H, br d, $J = 8.0$ Hz, H-12), 7.22 (1H, br t, $J = 8.0$ Hz, H-11), 7.13 (1H, br t, $J = 8.0$ Hz, H-10), 4.13 (1H, t, $J = 12.0$ Hz, H-17a), 3.96 (1H, m, H-3), 3.90 (1H, dd, $J = 12.0, 6.0$ Hz, H-17b), 3.63 (3H, s, $N_a\text{-Me}$), 3.28 (1H, dd, $J = 17.0, 7.0$ Hz, H-6a), 2.97 (1H, d, $J = 7.0$ Hz, H-5), 2.48 (2H, m, H-21), 2.42 (1H, d, $J = 17.0$ Hz, H-6b), 2.38 (1H, m, H-14a), 2.36 (3H, s, $N_b\text{-Me}$), 2.05 (1H, m, H-20a), 2.02 (1H, m, H-16), 1.80 (1H, dt, $J = 13.0, 4.0$ Hz, H-15), 1.67 (3H, s, H-18), 1.54 (1H, m, H-14b).

Alstolactone A (79): ^1H NMR (400 MHz, CDCl_3): δ 7.20 (1H, d, $J = 9.0$ Hz, H-12), 7.08 (1H, qd, $J = 7.0, 1.0$ Hz, H-19), 6.94 (1H, d, $J = 2.5$ Hz, H-9), 6.87 (1H, dd, $J = 9.0, 2.5$ Hz, H-11), 4.99 (1H, dd, $J = 12.0$ Hz, H-17a), 4.36 (1H, ddd, $J = 11.0, 4.6, 2.0$ Hz, H-17b), 4.29 (1H, br t, $J = 3.0$ Hz, H-3), 3.86 (3H, s, 10-OMe), 3.61 (3H, s, $N_a\text{-Me}$), 3.45 (1H, br d, $J = 7.0$ Hz, H-5), 3.24 (1H, dd, $J = 17.0, 7.0$ Hz, H-6a), 2.93 (1H, m, H-15), 2.67 (1H, d, $J =$

17.0 Hz, H-6b), 2.21 (1H, m, H-16), 2.15 (1H, td, $J = 13.0, 4.0$ Hz, H-14a), 1.76 (1H, br s, N_b -H), 1.66 (1H, ddd, $J = 13.0, 5.0, 3.0$ Hz, H-14b), 1.45 (3H, d, $J = 7.0$ Hz, H-18).

N(1)-Demethylalstonerine (80): ^1H NMR (400 MHz, CDCl_3): δ 9.01 (1H, br s, NH), 7.87 (1H, d, $J = 7.0$ Hz, H-12), 7.67 (1H, d, $J = 7.0$ Hz, H-9), 7.56 (1H, s, H-21), 7.15 (1H, t, $J = 7.0$ Hz, H-11), 7.09 (1H, t, $J = 7.0$ Hz, H-10), 4.70 (1H, m, H-17a), 4.22 (1H, dd, $J = 11.0, 4.0$ Hz, H-17b), 4.14 (1H, m, H-3), 3.37 (1H, dd, $J = 16.0, 6.0$ Hz, H-6a), 3.32 (1H, m, H-5), 2.70 (1H, br d, $J = 16.0$ Hz, H-6b), 2.65 (1H, dd, $J = 12.0, 5.0$ Hz, H-15), 2.48 (3H, br s, N_a -Me), 2.22 (1H, dt, $J = 13.0, 3.0$ Hz, H-14a), 2.09 (3H, s, H-18), 2.04 (2H, m, H-14b & H-16).

N(1)-Demethylalstonerinal (81): ^1H NMR (400 MHz, CDCl_3): δ 9.63 (1H, s, H-21), 9.01 (1H, br s, NH), 7.87 (1H, d, $J = 7.0$ Hz, H-12), 7.67 (1H, d, $J = 7.0$ Hz, H-9), 7.15 (1H, t, $J = 7.0$ Hz, H-11), 7.09 (1H, t, $J = 7.0$ Hz, H-10), 4.70 (1H, m, H-17a), 4.22 (1H, dd, $J = 11.0, 4.0$ Hz, H-17b), 4.14 (1H, m, H-3), 3.37 (1H, dd, $J = 16.0, 6.0$ Hz, H-6a), 3.32 (1H, m, H-5), 2.70 (1H, br d, $J = 16.0$ Hz, H-6b), 2.65 (1H, dd, $J = 12.0, 5.0$ Hz, H-15), 2.48 (3H, br s, N_a -Me), 2.22 (1H, dt, $J = 13.0, 3.0$ Hz, H-14a), 2.19 (3H, s, H-18), 2.04 (2H, m, H-14b & H-16).

10-Methoxyalstonerine (82): ^1H NMR(400 MHz, CDCl_3): δ 7.53 (1H, s, H-21), 7.20 (1H, d, $J = 8.8$ Hz, H-12), 6.93 (1H, d, $J = 2.2$ Hz, H-9), 6.85 (1H, dd, $J = 8.8, 2.2$ Hz, H-11), 4.41 (1H, t, $J = 11.1$ Hz, H-17a), 4.17 (1H, dd, $J = 11.1, 2.4$ Hz, H-17b), 3.86 (3H, s, 10-OMe), 3.85 (1H, br s, H-3), 3.62 (3H, s, N_a -H), 3.30 (1H, dd, $J = 16.1, 6.9$ Hz, H-6a), 3.09 (1H, d, $J = 6.9$ Hz, H-5), 2.47 (1H, d, $J = 16.1$ Hz, H-6b), 2.62 (1H, m, H-15), 2.33 (3H, s, N_b -H), 2.15 (1H, m, H-14b), 2.09 (3H, s, H-18), 1.90 (2H, m, H-16 & H-16), 1.81 (1H, td, $J = 12.6, 3.9$ Hz, H-14a).

Nortueiaoine (83): ^1H NMR(500 MHz, CD_3OD): δ 7.51 (1H, d, $J = 8.0$ Hz, H-9), 7.38 (1H, br d, $J = 8.0$ Hz, H-12), 7.18 (1H, ddd, $J = 8.0, 7.0, 1.0$ Hz, H-11), 7.09 (1H, ddd, $J = 8.0, 7.0, 1.0$ Hz, H-10), 4.89 (1H, br s, H-3), 4.31 (1H, d, $J = 8.0$ Hz, H-5), 3.52 (1H, dd, $J = 17.5, 7.5$ Hz, H-6a), 3.08 (1H, br s, H-16), 2.99 (1H, d, $J = 17.5$ Hz, H-6b), 2.42 (1H, br t, $J = 7.5$ Hz, H-20), 2.17 (1H, m, H-15), 2.16 (1H, td, $J = 12.5, 3.0$ Hz, H-14a), 2.02 (1H, br d, $J = 12.5$ Hz, H-14b), 1.64 (1H, m, H-19), 1.38 (1H, m, H-19), 0.66 (3H, t, $J = 7.5$ Hz, H-18).

Tueiaoine (84): ^1H NMR(500 MHz, CD_3OD): δ 7.51 (1H, d, $J = 8.0$ Hz, H-9), 7.43 (1H, d, $J = 8.0$ Hz, H-12), 7.25 (1H, br dd, $J = 8.0, 7.0$ Hz, H-11), 7.09 (1H, br dd, $J = 8.0, 7.0$ Hz, H-10), 5.08 (1H, br s, H-3), 4.26 (1H, d, $J = 7.5$ Hz, H-5), 3.73 (3H, s, N_a -Me), 3.50 (1H, dd, $J = 17.5, 7.5$ Hz, H-6a), 2.95 (1H, d, $J = 17.5$ Hz, H-6b), 2.93 (1H, m, H-16), 2.41 (1H, m, H-20), 2.20 (1H, td, $J = 12.5, 3.0$ Hz, H-14a), 2.11 (1H, br t, $J = 11.5$ Hz, H-15), 1.99 (1H, br d, $J = 12.5$ Hz, H-14b), 1.58 (1H, m, H-19), 1.31 (1H, m, H-19), 0.71 (3H, t, $J = 7.5$ Hz, H-18).

Rauvotetraphylline A (85): ^1H NMR(500 MHz, CD_3OD): δ 7.11 (1H, d, $J = 8.5$ Hz, H-12), 6.82 (1H, d, $J = 2.0$ Hz, H-9), 6.62 (1H, dd, $J = 8.5, 2.0$ Hz, H-11), 5.51 (1H, q, $J = 6.3$ Hz, H-19), 4.08 (1H, d, $J = 13.4$ Hz, H-21), 4.04 (1H, d, $J = 13.4$ Hz, H-21), 3.92 (1H, br s, H-3), 3.57 (1H, dd, $J = 11.1, 4.0$ Hz, H-17), 3.47 (s, 1H, dd, $J = 6.7, 5.0$ Hz, H-5), 3.32 (1H, dd, J

= 11.1, 10.6 Hz, H-17), 2.92 (1H, dd, $J = 17.0, 6.7$ Hz, H-6a), 2.69 (1H, d, $J = 17.0$ Hz, H-6b), 2.47 (3H, s, N_a -Me), 2.42 (1H, ddd, $J = 12.0, 11.8, 3.2$ Hz, H-15), 2.32 (1H, dddd, $J = 11.8, 10.6, 5.0, 4.0$ Hz, H-16), 2.19 (1H, ddd, $J = 12.9, 12.0, 2.7$ Hz, H-14a), 1.53 (1H, br d, $J = 12.9$ Hz, H-14b), 1.16 (3H, d, $J = 6.3$ Hz, H-18).

Rauverine A (86): ^1H NMR (500 MHz, Acetone- d_6): δ 9.91 (1H, s, NH), 7.43 (1H, d, $J = 7.8$ Hz, H-9), 7.31 (1H, d, $J = 7.8$ Hz, H-12), 7.03 (1H, t, $J = 7.8$ Hz, H-11), 6.97 (1H, t, $J = 7.8$ Hz, H-10), 5.14 (1H, q, $J = 6.6$ Hz, H-19), 4.79 (1H, d, $J = 7.8$ Hz, H-17), 4.50 (1H, d, $J = 13.6$ Hz, H-21a), 4.17 (1H, s, H-3), 3.64 (1H, d, $J = 13.6$ Hz, H-21b), 3.40 (1H, m, H-5), 3.04 (1H, dd, $J = 6.6, 16.8$ Hz, H-6a), 2.69 (1H, d, $J = 16.8$ Hz, H-6b), 2.40 (3H, s, N_b -Me), 1.91 (1H, m, H-15), 1.88 (2H, m, H-14), 1.71 (1H, m, H-16), 1.54 (3H, d, $J = 6.6$ Hz, H-18),

N_b -Methylajmaline (87): ^1H NMR (500 MHz, CD_3OD): δ 7.54 (1H, dd, $J = 7.5, 1.0$ Hz, H-9), 7.16 (1H, td, $J = 7.5, 1.0$ Hz, H-11), 6.82 (1H, td, $J = 7.5, 1.0$ Hz, H-10), 6.76 (1H, br d, $J = 7.5$ Hz, H-12), 4.42 (1H, br s, H-17), 3.94 (1H, br d, $J = 9.5$ Hz, H-3), 3.73 (1H, m, H-5), 3.20 (3H, br s, N_b -Me), 2.83 (1H, br s, H-2), 2.79 (3H, s, N_a -Me), 2.59 (1H, br td, $J = 5.5, 1.0$ Hz, H-16), 2.54 (1H, br dd, $J = 9.5, 5.5$ Hz, H-15), 2.35 (1H, br d, $J = 14.5$ Hz, H-6), 2.27 (1H, br dd, $J = 14.5, 9.5$ Hz, H-14), 2.26 (1H, br dd, $J = 14.5, 5.5$ Hz, H-6), 1.98 (1H, m, H-20), 1.95 (1H, br dd, $J = 14.5, 5.5$ Hz, H-14), 1.72-1.56 (m, 2H, H-19), 1.07 (3H, t, $J = 7.5$ Hz, H-18).

N_b -Methylisoajmaline (88): ^1H NMR (500 MHz, CD_3OD): δ 7.53 (1H, dd, $J = 7.5, 1.0$ Hz, H-9), 7.16 (1H, td, $J = 7.5, 1.0$ Hz, H-11), 6.82 (1H, td, $J = 7.5, 1.0$ Hz, H-10), 6.76 (1H, br d, $J = 7.5$ Hz, H-12), 4.37 (1H, br s, H-17), 4.07 (1H, br d, $J = 10.0$ Hz, H-3), 3.97 (1H, m, H-5), 3.09 (3H, br s, N_b -Me), 2.82 (1H, br s, H-2), 2.80 (3H, s, N_a -Me), 2.65 (1H, br t, $J = 5.5$ Hz, H-16), 2.35 (1H, br t, $J = 5.5$ Hz, H-15), 2.34-2.24 (1H, m, H-6), 2.34-2.24 (1H, m, H-14), 2.23 (1H, br d, $J = 14.5$ Hz, H-6), 1.85-1.77 (1H, m, H-20), 1.75-1.64 (1H, br dd, $J = 14.5, 5.5$ Hz, H-14), 1.75-1.64 (m, 1H, H-19), 1.64-1.52 (m, 1H, H-19), 1.06 (3H, t, $J = 7.5$ Hz, H-18).

Alstiphyllanine A (89): ^1H NMR (400 MHz, CD_3OD): δ 7.21 (1H, dd, $J = 7.6, 7.5$ Hz, H-11), 7.12 (1H, d, $J = 7.0$ Hz, H-9), 6.82 (1H, m, H-10), 6.79 (1H, m, H-12), 5.61 (1H, s, H-17), 5.58 (1H, m, H-19), 4.69 (1H, br s, H-5), 4.68 (2H, m, H-21), 4.63 (1H, br s, H-3), 3.75 (3H, s, COOMe), 3.63 (1H, br s, H-2), 3.33 (1H, m, H-15), 2.89 (1H, m, H-14), 2.74 (1H, m, H-6), 2.70 (1H, m, H-6), 2.69 (3H, s, N_a -Me), 2.23 (1H, dd, $J = 12.0, 11.4$ Hz, H-14), 1.89 (3H, s, OCOMe), 1.62 (3H, d, $J = 6.4$ Hz, H-18).

Alstiphyllanine H (90): ^1H NMR (400 MHz, CD_3OD): δ 7.20 (1H, d, $J = 7.2$ Hz, H-9), 7.19 (1H, dd, $J = 7.6, 7.2$ Hz, H-11), 6.83 (1H, dd, $J = 7.2, 7.2$ Hz, H-10), 6.77 (1H, d, $J = 7.6$ Hz, H-12), 5.55 (1H, q, $J = 6.5$ Hz, H-19), 4.55 (1H, d, $J = 15.1$ Hz, H-21b), 4.46 (1H, d, $J = 15.1$ Hz, H-21a), 4.42 (1H, m, H-5), 4.39 (1H, m, H-3), 4.16 (1H, s, H-17), 3.73 (3H, s, COOMe), 3.55 (1H, d, $J = 4.8$ Hz, H-2), 3.36 (1H, s, H-15), 2.74 (1H, m, H-14b), 2.73 (1H, d, $J = 14.4$ Hz, H-6b), 2.66 (3H, s, N_a -Me), 2.53 (1H, d, $J = 14.4$ Hz, H-6a), 2.14 (1H, m, H-14a), 1.61 (3H, d, $J = 6.5$ Hz, H-18).

Alstiphyllanine I (91): ^1H NMR TFA salt (400 MHz, CD_3OD): δ 7.41 (1H, d, $J = 6.9$ Hz, H-6'), 7.29 (1H, s, H-2'), 7.25 (1H, br s, H-9), 7.06 (1H, d, $J = 6.9$ Hz, H-5'), 7.01 (2H, br s, H-10 and H-11), 6.23 (1H, br s, H-12), 6.02 (1H, s, H-17), 5.60 (1H, m, H-19), 5.19 (1H, m, 3-H), 4.46 (1H, m, 5-H), 4.38 (1H, m, 2-H), 4.37 (1H, m, H-21a), 4.12 (1H, d, $J = 16.0$ Hz, H-21b), 3.92 (3H, s, 4'-OMe), 3.78 (6H, s, COOMe and 3'-OMe), 3.39 (1H, d, $J = 3.6$ Hz, H-15), 2.87 (1H, d, $J = 11.0$ Hz, H-6b), 2.61 (1H, d, $J = 14.0$ Hz, H-14b), 2.22 (1H, m, H-6a), 2.08 (1H, t, $J = 14.0$ Hz, H-14a), 1.91 (1H, s, H-25), 1.61 (3H, d, $J = 6.1$ Hz, H-18).

Alstiphyllanine J (92): ^1H NMR TFA salt (400 MHz, CD_3OD): δ 7.23 (1H, br s, H-9), 7.05 (2H, s, H-2' and H'-6), 7.01 (2H, br s, H-10 and H-11), 6.23 (1H, m, H-12), 6.02 (1H, s, H-17), 5.59 (1H, m, H-19), 5.19 (1H, br s, 3-H), 4.44 (2H, m, 2-H and 5-H), 4.35 (1H, d, $J = 13.8$ Hz, H-21b), 4.08 (1H, m, H-21a), 3.85 (6H, s, 3'-OMe and 5'-OMe), 3.78 (3H, s, 4'-OMe and COOMe), 3.37 (1H, br s, H-15), 2.86 (1H, d, $J = 9.5$ Hz, H-6b), 2.59 (1H, d, $J = 14.0$ Hz, H-14b), 2.31 (1H, d, $J = 9.5$ Hz, H-6a), 2.07 (1H, t, $J = 14.0$ Hz, H-14a), 1.88 (1H, s, H-25), 1.61 (3H, d, $J = 4.5$ Hz, H-18).

Alstiphyllanine K (93): ^1H NMR TFA salt (400 MHz, CD_3OD): δ 7.74 (2H, d, $J = 7.5$ Hz, H-2' and H-6'), 7.64 (1H, dd, $J = 7.6, 7.6$ Hz, H-4'), 7.52 (2H, dd, $J = 7.6, 7.5$ Hz, H-3' and H-5'), 7.22 (1H, d, $J = 6.6$ Hz, H-9), 4.87 (1H, m, H-3), 6.98 (1H, dd, $J = 6.6, 7.8$ Hz, H-10), 6.93 (1H, dd, $J = 7.8, 7.8$ Hz, H-11), 6.22 (1H, d, $J = 7.8$ Hz, H-12), 5.96 (1H, s, H-17), 5.49 (1H, m, H-19), 4.34 (1H, d, $J = 4.38$ Hz, H-2), 4.09 (2H, m, H-5 and H-21b), 3.84 (1H, m, H-21a), 3.76 (3H, s, COOMe), 3.24 (1H, m, H-15), 2.79 (1H, dd, $J = 12.3, 3.6$ Hz, H-6b), 2.53 (1H, dd, $J = 15.0, 6.0$ Hz, H-14b), 2.06 (1H, d, $J = 12.3$ Hz, H-6a), 1.91 (1H, m, H-14a), 1.90 (1H, s, H-25), 1.59 (3H, d, $J = 6.6$ Hz, H-18).

Alstiphyllanine L (94): ^1H NMR TFA salt (400 MHz, CD_3OD): δ 7.34 (1H, d, $J = 6.9$ Hz, H-6'), 7.29 (1H, m, H-9), 7.28 (1H, m, H-2'), 7.02 (1H, d, $J = 6.09$ Hz, H-5'), 7.00 (1H, m, H-10), 6.98 (1H, m, H-11), 6.27 (1H, m, H-12), 5.50 (1H, m, H-19), 4.93 (1H, m, H-3), 4.49 (1H, s, H-17), 4.30 (1H, br s, H-24), 4.11 (1H, m, H-5 and H-21b), 3.87 (1H, m, H-21a), 3.82 (3H, s, 4'-OMe), 3.74 (6H, s, COOMe and 3'-OMe), 3.31 (1H, m, H-15), 2.86 (1H, d, $J = 13.5$ Hz, H-6b), 2.49 (1H, dt, $J = 13.9, 7.1$ Hz, H-14b), 2.01 (1H, d, $J = 13.5$ Hz, H-6a), 1.85 (1H, t, $J = 13.9$ Hz, H-14a), 1.59 (3H, d, $J = 6.4$ Hz, H-18).

Alstiphyllanine M (95): ^1H NMR TFA salt (400 MHz, CD_3OD): δ 7.32 (1H, m, H-9), 7.02 (1H, m, H-11), 7.01 (2H, s, 2'-H and 6'-H), 7.00 (1H, m, H-10), 6.27 (1H, m, H-12), 5.55 (1H, m, H-19), 5.09 (1H, m, H-3), 4.35 (1H, br s, H-2), 4.26 (1H, m, H-21b), 4.52 (1H, s, H-17), 4.01 (2H, m, H-5 & H-21a), 3.76 (3H, s, COOMe), 3.87 (3H, s, 4'-OMe), 3.81 (6H, s, 3'-OMe and 5'-OMe), 3.37 (1H, d, $J = 3.6$ Hz, H-15), 2.91 (1H, d, $J = 12.4$ Hz, H-6b), 2.55 (1H, dt, $J = 14.5, 4.9$ Hz, H-14b), 2.10 (1H, dd, $J = 12.4, 6.2$ Hz, H-6a), 1.95 (1H, dd, $J = 14.5, 12.4$ Hz, H-14a), 1.61 (3H, d, $J = 6.6$ Hz, H-18).

Alstiphyllanine N (96): ^1H NMR TFA salt (400 MHz, CD_3OD): δ 7.70 (2H, s, 2'-H and 6'-H), 7.65 (1H, s, 4'-H), 7.52 (2H, s, 3'-H and 5'-H), 7.32 (1H, d, $J = 6.9$ Hz, H-9), 7.01 (1H, dd, $J = 6.9, 8.7$ Hz, H-10), 6.93 (1H, dd, $J = 9.0, 8.7$ Hz, H-11), 6.11 (1H, d, $J = 9.0$ Hz, H-12), 5.53 (1H, m, H-19), 4.99 (1H, m, H-3), 4.50 (1H, s, H-17), 4.29 (1H, m, H-2), 4.18 (1H, m, H-21b), 4.15 (1H, m, H-5), 3.92 (1H, m, H-21a), 3.75 (3H, s, COOMe), 3.33 (1H,

m, H-15), 2.88 (1H, d, $J = 11.0$ Hz, H-6b), 2.49 (1H, dd, $J = 14.3, 5.0$ Hz, H-14b), 1.98 (1H, m, H-6a), 1.91 (1H, t, $J = 14.3$, H-14a), 1.60 (3H, d, $J = 6.8$ Hz, H-18).

Alstiphyllanine O (97): ^1H NMR TFA salt (400 MHz, CD_3OD): δ 7.32 (1H, m, H-9), 7.02 (1H, m, H-11), 7.01 (2H, s, 2'-H and 6'-H), 7.00 (1H, m, H-10), 6.27 (1H, m, H-12), 5.55 (1H, m, H-19), 5.09 (1H, m, H-3), 4.56 (1H, s, H-17), 4.35 (1H, br s, H-2), 4.03 (2H, m, H-21), 4.01 (1H, m, H-5), 3.87 (3H, s, 4'-OMe), 3.85 (1H, m, H-15), 3.81 (6H, s, 3'-OMe and 5'-OMe), 3.76 (3H, s, COOMe), 2.91 (1H, d, $J = 12.4$ Hz, H-6b), 2.55 (1H, dt, $J = 14.5, 4.9$ Hz, H-14b), 2.10 (1H, dd, $J = 12.4, 6.2$ Hz, H-6a), 1.95 (1H, dd, $J = 14.5, 12.4$ Hz, H-14a), 1.67 (3H, d, $J = 6.4$ Hz, H-18).

Vincamajine N(4)-oxide (98): ^1H NMR (400 MHz, CDCl_3): δ 7.18 (1H, m, H-11), 7.16 (1H, m, H-9), 6.80 (1H, t, $J = 8.0$, H-10), 6.66 (1H, d, $J = 8.0$ Hz, H-12), 5.29 (1H, br q, $J = 7.0$ Hz, H-19), 4.13 (1H, s, H-17), 3.96 (1H, m, H-21b), 3.86 (1H, d, $J = 5.0$ Hz, H-2), 3.76 (1H, m, H-3), 3.72 (1H, m, H-21a), 3.70 (3H, s, COOMe), 3.56 (1H, m, H-15), 2.78 (1H, br d, $J = 13.0$ Hz, H-5), 2.61 (3H, s, $N_a\text{-Me}$), 2.55 (1H, m, H-14b), 1.82 (1H, td, $J = 10.0, 3.0$ Hz, H-14a), 1.60 (3H, dd, $J = 7.0, 1.0$ Hz, H-18).

Vincamajine 17-O-veratrate N(4)-oxide (99): ^1H NMR (400 MHz, CDCl_3): δ 7.49 (1H, dd, $J = 9.0, 2.0$ Hz, 6'-H), 7.30 (1H, d, $J = 2.0$ Hz, 2'-H), 7.07 (1H, m, H-11), 6.82 (1H, m, H-9), 6.80 (1H, m, 5'-H), 6.63 (1H, br d, $J = 8.0$ Hz, H-12), 6.51 (1H, m, H-10), 5.76 (1H, br s, H-17), 5.35 (1H, q, $J = 7.0$ Hz, H-19), 4.25 (1H, br d, $J = 16$ Hz, H-21b), 4.13 (1H, d, $J = 4.0$ Hz, H-5), 3.93 (2H, m, H-2 and H-3), 3.89 (3H, s, 4'-OMe), 3.87 (1H, m, H-21a), 3.84 (3H, s, 3'-OMe), 3.61 (1H, m, H-15), 3.38 (3H, s, COOMe), 3.00 (1H, br d, $J = 13.0$, H-6b), 2.81 (1H, dd, $J = 14.0, 5.0$ Hz, H-14b), 2.63 (3H, s, $N_a\text{-Me}$), 2.62 (1H, m, H-6a), 1.96 (1H, m, H-14a), 1.53 (3H, d, $J = 7.0$ Hz, H-18).

Norsandwicine (100): ^1H NMR (500 MHz, CD_3OD): δ 7.16 (1H, br, $J = 7.0$ Hz, H-9), 7.06 (1H, td, $J = 7.5, 1.5$ Hz, H-11), 6.80 (1H, td, $J = 7.0, 1.0$ Hz, H-10), 6.76 (1H, d, $J = 7.5$ Hz, H-12), 4.90 (1H, d, $J = 9.5$ Hz, H-17), 4.72 (1H, s, H-21), 4.05 (1H, d, $J = 10.0$ Hz, H-3), 3.88 (1H, s, H-2), 3.50 (1H, dd, $J = 7.5, 5.0$ Hz, H-5), 2.74 (1H, br q, $J = 7.0$ Hz, H-16), 2.46 (1H, dd, $J = 13.5, 7.0$ Hz, H-14b), 2.37 (1H, q, $J = 5.0$ Hz, H-15), 2.17 (1H, d, $J = 13.5$ Hz, H-6b), 2.05 (1H, dd, $J = 13.5, 10.5$ Hz, H-14a), 1.80 (1H, tdd, $J = 8.0, 4.0, 1.5$ Hz, H-20), 1.62-1.52 (2H, m, H-19), 1.52 (1H, dd, $J = 13.5, 4.5$ Hz, H-6a), 1.05 (3H, t, $J = 7.5$ Hz, H-18).

Isonorsandwicine (101): ^1H NMR (500 MHz, CD_3OD): δ 7.16 (1H, br d, $J = 7.0$ Hz, H-9), 7.06 (1H, td, $J = 7.5, 1.5$ Hz, H-11), 6.80 (1H, td, $J = 7.5, 1.0$ Hz, H-10), 6.76 (1H, d, $J = 7.5$ Hz, H-12), 4.84 (1H, d, $J = 10.0$ Hz, H-17), 4.67 (1H, d, $J = 7.0$ Hz, H-21), 4.00 (1H, dd, $J = 7.5, 4.5$ Hz, H-5), 3.96 (1H, d, $J = 10.0$ Hz, H-3), 3.87 (1H, s, H-2), 2.81 (1H, m, H-16), 2.18 (1H, d, $J = 13.5$ Hz, H-6b), 2.16 (1H, m, H-15), 2.15 (1H, m, H-14b), 2.07 (1H, m, H-14a), 1.68 (2H, m, H-19 & H-20), 1.59 (1H, dd, $J = 13.5, 5.0$ Hz, H-6a), 1.54 (1H, m, H-19), 1.05 (3H, t, $J = 7.5$ Hz, H-18).

N_b -Methylisosandwicine (102): ^1H NMR (500 MHz, CD_3OD): δ 7.19 (1H, d, $J = 7.0$ Hz, H-9), 7.18 (1H, t, $J = 7.0$ Hz, H-11), 6.88 (1H, t, $J = 7.0$ Hz, H-10), 6.78 (1H, d, $J = 7.0$ Hz,

H-12), 4.85 (1H, d, $J = 10.0$ Hz, H-17), 4.62 (1H, d, $J = 7.0$ Hz, H-21), 4.11 (1H, d, $J = 9.5$ Hz, H-3), 3.86 (1H, dd, $J = 7.0, 5.0$ Hz, H-5), 3.23 (1H, s, H-2), 3.07 (3H, s, N_b -Me), 2.93 (1H, m, H-16), 2.84 (3H, s, N_a -Me), 2.24-2.15 (2H, m, H-14), 2.24 (1H, d, $J = 14.0$ Hz, H-6b), 2.20 (1H, m, H-15), 1.77 (1H, m, H-20), 1.70 (1H, m, H-19), 1.62 (1H, dd, $J = 14.0, 5.0$ Hz, H-6a), 1.58 (1H, m, H-19), 1.06 (3H, t, $J = 7.5$ Hz, H-18).

10-Methoxyraucafrinoline (103): ^1H NMR(400 MHz, CDCl_3): δ 7.50 (1H, d, $J = 8.2$ Hz, H-12), 7.02 (1H, d, $J = 2.7$ Hz, H-9), 6.89 (1H, dd, $J = 8.6, 2.7$ Hz, H-11), 5.00 (1H, s, H-17), 4.07 (1H, d, $J = 9.4$ Hz, H-3), 3.72 (1H, dd, $J = 11.0, 5.1$ Hz, H-19), 3.67 (1H, dd, $J = 11.0, 8.0$ Hz, H-19), 3.64 (1H, dd, $J = 6.2, 4.9$ Hz, H-5), 2.75 (1H, dd, $J = 11.7, 4.7$ Hz, H-6), 2.52 (1H, dd, $J = 9.0, 6.9$ Hz, H-21), 2.47 (1H, dd, $J = 5.7, 5.1$ Hz, H-15), 2.35 (1H, dd, $J = 6.2, 5.8$ Hz, H-16), 2.17 (3H, s, OCOMe), 1.92 (1H, dd, $J = 14.8, 9.7$ Hz, H-14), 1.63 (1H, d, $J = 11.7$ Hz, H-6), 1.53 (1H, dd, $J = 14.0, 5.1$ Hz, H-14), 1.48 (1H, ddd, $J = 9.1, 8.0, 5.1$ Hz, H-20), 1.26 (3H, d, $J = 7.0$ Hz, H-18).

Rauvotetraphylline D (104): ^1H NMR(500 MHz, CDCl_3): δ 7.61 (1H, dd, $J = 7.7, 1.1$ Hz, H-12), 7.47 (1H, dd, $J = 7.3, 0.7$ Hz, H-9), 7.39 (1H, ddd, $J = 7.7, 7.6, 1.1$ Hz, H-11), 7.22 (1H, ddd, $J = 7.6, 7.3, 0.7$ Hz, H-10), 6.84 (1H, dd, $J = 15.9, 7.8$ Hz, H-21), 6.18 (1H, d, $J = 15.9$ Hz, H-22), 4.92 (1H, s, H-17), 4.18 (1H, d, $J = 9.3$ Hz, H-3), 3.66 (1H, dd, $J = 5.1, 4.9$ Hz, H-5), 2.81 (1H, dd, $J = 12.0, 4.9$ Hz, H-6b), 2.40 (2H, m, H-15 & H-16), 2.28 (1H, s, H-24), 2.16 (3H, s, OCOMe), 2.07 (1H, m, H-19), 2.06 (1H, m, H-20), 1.97 (1H, dd, $J = 15.3, 9.3$ Hz, H-14a), 1.63 (1H, d, $J = 12.0$ Hz, H-6a), 1.58 (1H, dd, $J = 15.3, 3.8$ Hz, H-14b), 1.23 (3H, d, $J = 6.7$ Hz, H-18).

Alstoyunine C (105): ^1H NMR (500 MHz, CD_3OD): δ 7.62 (1H, d, $J = 7.5$ Hz, H-9), 7.61 (1H, d, $J = 7.5$ Hz, H-12), 7.43 (1H, t, $J = 7.5$ Hz, H-11), 7.31 (1H, t, $J = 7.5$ Hz, H-10), 4.99 (1H, s, H-17), 4.52 (1H, d, $J = 9.8$ Hz, H-3), 4.30 (1H, dd, $J = 6.0, 5.0$ Hz, H-5), 4.08 (1H, m, H-19), 3.08 (1H, m, H-16), 2.91 (1H, m, H-6a), 2.88 (1H, m, H-20), 2.83 (1H, m, H-15), 2.60 (1H, dd, $J = 14.5, 9.8$ Hz, H-14a), 2.46 (1H, d, $J = 13.0$ Hz, H-6b), 2.19 (3H, s, OCOMe), 2.07 (1H, dd, $J = 14.5, 5.0$ Hz, H-14b), 1.54 (3H, d, $J = 6.5$ Hz, H-18).

Alstoyunine D (106): ^1H NMR (500 MHz, CD_3OD): δ 7.79 (1H, d, $J = 7.8$ Hz, H-12), 7.74 (1H, d, $J = 7.8$ Hz, H-9), 7.62 (1H, t, $J = 7.8$ Hz, H-11), 7.58 (1H, t, $J = 7.8$ Hz, H-10), 5.16 (1H, d, $J = 9.2$ Hz, H-3), 5.11 (1H, d, $J = 1.0$ Hz, H-17), 4.27 (1H, dd, $J = 6.0, 5.0$ Hz, H-5), 4.15 (1H, m, H-19), 3.07 (1H, m, H-16), 2.90 (1H, dd, $J = 13.0, 4.3$ Hz, H-6a), 2.85 (1H, m, H-15), 2.79 (1H, d, $J = 9.5$ Hz, H-20), 2.64 (1H, dd, $J = 14.4, 9.2$ Hz, H-14a), 2.60 (1H, d, $J = 13.0$ Hz, H-6b), 2.19 (3H, s, OCOMe), 2.14 (1H, dd, $J = 14.4, 4.0$ Hz, H-14b), 1.39 (3H, d, $J = 6.3$ Hz, H-18).

Isoalstonisine (107): ^1H NMR (400 MHz, CDCl_3): δ 7.54 (1H, s, H-21), 7.27 (1H, td, $J = 8.0, 1.0$ Hz, H-11), 7.15 (1H, dd, $J = 8.0, 1.0$ Hz, H-9), 7.00 (1H, td, $J = 8.0, 1.0$ Hz, H-10), 6.82 (1H, dd, $J = 8.0, 1.0$ Hz, H-12), 4.26 (1H, t, $J = 11.0$ Hz, H-17), 4.17 (1H, ddd, $J = 11.0, 4.0, 2.0$ Hz, H-17), 4.03 (1H, dt, $J = 12.0, 6.0$ Hz, H-15), 3.76 (1H, br d, $J = 7.0$ Hz, H-5), 3.26 (1H, s, N_a -Me), 3.15 (1H, t, $J = 3.0$ Hz, H-3), 2.61 (1H, dd, $J = 14.0, 2.0$ Hz, H-6), 2.35 (1H, dd, $J = 14.0, 8.0$ Hz, H-6), 2.33 (1H, ddd, $J = 14.0, 6.0, 3.0$ Hz, H-14), 2.25 (3H, s, H-18), 2.01 (1H, m, H-16), 1.49 (1H, ddd, $J = 14.0, 12.0, 3.0$ Hz, H-14).

Macrogentine (108): ^1H NMR (400 MHz, CDCl_3): δ 7.57 (1H, dd, $J=8.0, 1.0$ Hz, H-9), 7.25 (1H, td, $J=8.0, 1.0$ Hz, H-11), 7.00 (1H, td, $J=8.0, 1.0$ Hz, H-10), 6.79 (1H, dd, $J=8.0, 1.0$ Hz, H-12), 4.90 (1H, q, $J=6.0$ Hz, H-21), 4.19 (1H, t, $J=12.0, 2.0$ Hz, H-17), 3.84 (1H, dd, $J=12.0$ Hz, H-17), 3.74 (1H, dd, $J=7.0, 2.0$ Hz, H-5), 3.52 (1H, d, $J=4.0$ Hz, H-3), 3.44 (1H, m, H-15), 3.22 (1H, s, $N_a\text{-Me}$), 2.56 (1H, dd, $J=15.0, 8.0$ Hz, H-20), 2.51 (1H, dd, $J=15.0, 7.0$ Hz, H-20), 2.40 (1H, dd, $J=13.0, 2.0$ Hz, H-6), 2.26 (1H, dd, $J=13.0, 7.0$ Hz, H-6), 2.25 (3H, s, H-18), 1.88 (1H, ddd, $J=13.0, 11.0, 4.0$ Hz, H-14), 1.74 (1H, dd, $J=13.0, 6.0$ Hz, H-14), 1.49 (1H, dd, $J=5.0, 2.0$ Hz, H-16), 1.29 (3H, d, $J=6.0$ Hz, 22-Me).

Alstonoxine A (109): ^1H NMR (400 MHz, CDCl_3): δ 7.84 (1H, br d, $J=8.0$ Hz, H-9), 7.32 (1H, td, $J=8.0, 1.0$ Hz, H-11), 7.20 (1H, td, $J=8.0, 1.0$ Hz, H-10), 6.87 (1H, br d, $J=8.0$ Hz, H-12), 4.02 (1H, dd, $J=12.0, 1.0$ Hz, H-17), 3.90 (1H, br d, $J=8.0$ Hz, H-5), 3.80 (1H, dd, $J=12.0, 2.0$ Hz, H-17), 3.25 (1H, br s, H-3), 3.20 (1H, s, $N_a\text{-Me}$), 3.05 (1H, m, H-15), 2.79 (1H, dd, $J=18.0, 7.0$ Hz, H-20), 2.72 (1H, dd, $J=18.0, 6.0$ Hz, H-20), 2.43 (1H, dd, $J=13.0, 8.0$ Hz, H-6), 2.21 (3H, s, H-18), 2.15 (1H, dd, $J=13.0, 2.0$ Hz, H-6), 1.87 (1H, ddd, $J=14.0, 6.0, 2.0$ Hz, H-14), 1.71 (2H, m, H-14, H-16).

Alstonoxine B (110): ^1H NMR (400 MHz, CDCl_3): δ 7.52 (1H, br d, $J=8.0$ Hz, H-9), 7.31 (1H, td, $J=8.0, 1.0$ Hz, H-11), 7.10 (1H, td, $J=8.0, 1.0$ Hz, H-10), 6.88 (1H, br d, $J=8.0$ Hz, H-12), 4.01 (1H, dd, $J=11.0, 1.0$ Hz, H-17), 3.91 (3H, m, H-5, H-17 & H-19), 3.25 (1H, br s, H-3), 3.20 (1H, s, $N_a\text{-Me}$), 2.72 (1H, m, H-15), 2.41 (1H, dd, $J=14.0, 8.0$ Hz, H-6), 2.13 (1H, dd, $J=14.0, 1.0$ Hz, H-6), 1.85 (1H, ddd, $J=14.0, 9.0, 3.0$ Hz, H-14), 1.77 (3H, m, H-16 & H-20), 1.53 (1H, ddd, $J=14.0, 9.0, 5.0$ Hz, H-14), 1.30 (3H, d, $J=6.0$ Hz, H-18).

Alstonoxine C (111): ^1H NMR (400 MHz, CDCl_3): δ 7.76 (1H, d, $J=9.0$ Hz, H-9), 6.70 (1H, dd, $J=9.0, 2.0$ Hz, H-10), 6.45 (1H, d, $J=2.0$ Hz, H-12), 4.01 (1H, d, $J=12.0$ Hz, H-17a), 3.86 (1H, m, H-5), 3.84 (3H, s, 11-OMe), 3.81 (1H, m, H-17b), 3.19 (1H, m, H-3), 3.16 (3H, s, $N_a\text{-Me}$), 2.97 (1H, m, H-15), 2.80 (1H, $J=18.0, 8.0$ Hz, H-20b), 2.69 (1H, dd, $J=18.0, 5.0$ Hz, H-20a), 2.39 (1H, dd, $J=14.0, 8.0$ Hz, H-6a), 2.20 (3H, s, H-18), 2.08 (1H, d, $J=14.0$ Hz, H-6b), 1.86 (1H, dd, $J=13.0, 5.0$ Hz, H-14a), 1.69 (2H, m, H-14b & H-16).

Alstonoxine D (112): ^1H NMR (400 MHz, CDCl_3): δ 7.39 (1H, d, $J=8.0$ Hz, H-9), 6.60 (1H, dd, $J=8.0, 2.0$ Hz, H-10), 6.45 (1H, d, $J=2.0$ Hz, H-12), 4.00 (1H, dd, $J=11.0, 1.0$ Hz, H-17a), 3.90 (3H, m, H-5, H-17b & H-19), 3.83 (3H, s, 11-OMe), 3.20 (1H, m, H-3), 3.17 (3H, s, $N_a\text{-Me}$), 2.69 (1H, m, H-15), 2.38 (1H, dd, $J=14.0, 8.0$ Hz, H-6a), 2.06 (1H, d, $J=14.0$ Hz, H-6b), 1.86 (1H, m, H-20b), 1.82 (1H, m, H-14a), 1.72 (2H, m, H-14b & H-16), 1.53 (1H, m, H-20a), 1.29 (3H, d, $J=6.0$ Hz, H-18).

Alstonoxine E (113): ^1H NMR (400 MHz, CDCl_3): δ 9.42 (3H, br s, NH), 7.47 (1H, d, $J=7.5$ Hz, H-9), 7.20 (1H, t, $J=7.5$ Hz, H-11), 7.01 (1H, t, $J=7.5$ Hz, H-10), 6.92 (1H, d, $J=7.5$ Hz, H-12), 3.98 (2H, m, H-17), 3.89 (2H, m, H-5 & H-19), 3.28 (1H, m, H-3), 2.68 (1H, m, H-15), 2.39 (1H, dd, $J=13.5, 8.0$ Hz, H-6a), 2.10 (1H, d, $J=13.5$ Hz, H-6b), 1.82 (1H, m, H-20), 1.75 (3H, m, H-14 & H-16), 1.56 (1H, ddd, $J=14.0, 9.0, 5.0$ Hz, H-20), 1.28 (3H, d, $J=6.0$ Hz, H-18).

Isoalstonoxine B (114): ^1H NMR (400 MHz, CDCl_3): δ 7.29 (1H, t, $J = 8.0$ Hz, H-11), 7.10 (1H, d, $J = 8.0$ Hz, H-9), 7.03 (1H, t, $J = 8.0$ Hz, H-10), 6.84 (1H, d, $J = 8.0$ Hz, H-12), 4.04 (1H, br d, $J = 8.0$ Hz, H-5), 3.96 (2H, m, H-17), 3.90 (1H, m, H-19), 3.24 (1H, m, H-3), 3.22 (3H, s, $N_{\text{a}}\text{-Me}$), 3.11 (1H, m, H-15), 2.52 (1H, d, $J = 13.7$ Hz, H-6a), 2.24 (1H, dd, $J = 13.7$, 8.0 Hz, H-6b), 1.85 (1H, dd, $J = 13.0$, 4.0 Hz, H-14a), 1.71 (1H, m, H-16), 1.69 (1H, m, H-14b), 1.65 (2H, m, H-20), 1.31 (3H, d, $J = 6.0$ Hz, H-18).

Macrogentine A (115): ^1H NMR (400 MHz, CDCl_3): δ 8.35 (1H, br s, NH), 7.52 (1H, d, $J = 7.8$ Hz, H-9), 7.17 (1H, td, $J = 7.8$, 1.0 Hz, H-11), 6.97 (1H, br t, $J = 7.8$ Hz, H-10), 6.83 (1H, d, $J = 7.8$ Hz, H-12), 4.89 (1H, d, $J = 11.0$ Hz, H-21), 4.73 (1H, d, $J = 11.0$ Hz, H-21), 4.23 (1H, dd, $J = 11.9$, 1.8 Hz, H-17a), 3.95 (1H, q, $J = 6.4$ Hz, H-19), 3.74 (1H, br d, $J = 7.0$ Hz, H-5), 3.83 (1H, d, $J = 11.9$ Hz, H-17b), 3.24 (1H, br d, $J = 3.6$ Hz, H-3), 2.99 (1H, m, H-15), 2.41 (1H, d, $J = 13.7$ Hz, H-6a), 2.28 (1H, dd, $J = 13.7$, 7.8 Hz, H-6b), 2.02 (1H, ddd, $J = 13.7$, 11.0, 5.0 Hz, H-14a), 1.91 (1H, dd, $J = 13.7$, 6.0 Hz, H-14b), 1.69 (1H, d, $J = 13.3$, 6.8 Hz, H-20), 1.50 (1H, dt, $J = 13.3$, 6.4 Hz, H-20), 1.42 (1H, m, H-16), 1.33 (3H, d, $J = 6.0$ Hz, H-18).

N(1)-Demethylalstonisine (116): ^1H NMR (400 MHz, CDCl_3): δ 8.54 (1H, s, NH), 8.22 (1H, br d, $J = 8.0$ Hz, H-9), 7.63 (1H, s, H-21), 7.25 (1H, m, H-10), 7.20 (1H, m, H-11), 6.91 (1H, br d, $J = 8.0$ Hz, H-12), 4.46 (1H, t, $J = 11.0$ Hz, H-17), 4.26 (1H, ddd, $J = 11.0$, 4.0, 2.0 Hz, H-17), 3.69 (1H, br d, $J = 7.0$ Hz, H-5), 3.39 (1H, dt, $J = 12.0$, 6.0 Hz, H-15), 3.27 (1H, br s, H-3), 2.57 (1H, dd, $J = 13.0$, 7.0 Hz, H-6), 2.26 (1H, ddd, $J = 14.0$, 6.0, 2.0 Hz, H-14), 2.24 (3H, s, H-18), 2.20 (1H, br d, $J = 13.0$ Hz, H-6), 1.98 (1H, m, H-16), 1.57 (1H, ddd, $J = 14.0$, 12.0, 2.0 Hz, H-14).

N(1)-Demethylalstonal (117): ^1H NMR (400 MHz, CDCl_3): δ 9.86 (1H, s, H-21), 8.57 (1H, s, NH), 8.22 (1H, br d, $J = 8.0$ Hz, H-9), 7.25 (1H, m, H-10), 7.20 (1H, m, H-11), 6.91 (1H, br d, $J = 8.0$ Hz, H-12), 4.52 (1H, t, $J = 11.0$ Hz, H-17), 4.28 (1H, ddd, $J = 11.0$, 4.0, 2.0 Hz, H-17), 3.69 (1H, br d, $J = 7.0$ Hz, H-5), 3.35 (1H, dt, $J = 12.0$, 6.0 Hz, H-15), 3.27 (1H, br s, H-3), 2.56 (1H, dd, $J = 13.0$, 7.0 Hz, H-6), 2.19 (1H, br d, $J = 13.0$ Hz, H-6), 2.30 (1H, ddd, $J = 14.0$, 6.0, 2.0 Hz, H-14), 2.24 (3H, s, H-18), 1.98 (1H, m, H-16), 1.55 (1H, ddd, $J = 14.0$, 12.0, 2.0 Hz, H-14).

Affinisine oxindole (118): ^1H NMR (400 MHz, CDCl_3): δ 7.37 (1H, br d, $J = 8.0$ Hz, H-9), 7.32 (1H, td, $J = 8.0$, 1.0 Hz, H-11), 7.10 (1H, td, $J = 8.0$, 1.0 Hz, H-10), 6.84 (1H, br d, $J = 8.0$ Hz, H-12), 5.32 (1H, br q, $J = 7.0$ Hz, H-19), 3.78 (2H, m, H-21), 3.63 (2H, m, H-17), 3.36 (1H, dd, $J = 10.0$, 2.0 Hz, H-3), 3.31 (1H, dd, $J = 6.0$, 3.0 Hz, H-5), 3.21 (3H, s, $N_{\text{a}}\text{-Me}$), 2.89 (1H, br s, H-15), 2.79 (1H, dd, $J = 13.0$, 6.0 Hz, H-6), 2.18 (1H, ddd, $J = 14.0$, 4.0, 2.0 Hz, H-14), 2.05 (1H, m, H-16), 1.81 (1H, d, $J = 13.0$ Hz, H-6), 1.61 (3H, s, H-18), 1.57 (1H, ddd, $J = 14.0$, 10.0, 2.0 Hz, H-14).

7(S)-Talpinine oxindole (119): ^1H NMR (400 MHz, CDCl_3): δ 7.33 (1H, t, $J = 7.5$, 1.0 Hz, H-11), 7.23 (1H, d, $J = 7.5$ Hz, H-9), 7.10 (1H, t, $J = 7.5$, 1.0 Hz, H-10), 6.86 (1H, d, $J = 7.5$ Hz, H-12), 5.06 (1H, d, $J = 2.0$ Hz, H-21), 4.07 (1H, q, $J = 7.0$ Hz, H-19), 3.85 (1H, dd, $J = 12.0$, 1.4 Hz, H-17a), 3.73 (1H, d, $J = 9.0$ Hz, H-3), 3.69 (1H, dd, $J = 7.0$, 1.7 Hz, H-5), 3.54 (1H, dd, $J = 12.0$, 1.4 Hz, H-17b), 3.20 (3H, s, $N_{\text{a}}\text{-Me}$), 2.83 (1H, dd, $J = 13.0$, 7.0 Hz, H-6a), 2.16

(1H, br d, $J = 3.0$ Hz, H-15), 2.04 (1H, ddd, $J = 14.0, 5.0, 3.0$ Hz, H-14a), 1.83 (1H, d, $J = 13.0$ Hz, H-6b), 1.63 (1H, m, H-14b), 1.62 (1H, br s, H-16), 1.48 (1H, m, H-20), 1.33 (3H, d, $J = 7$ Hz, H-18).

Alstofoline (120): ^1H NMR (400 MHz, CDCl_3): δ 8.28 (1H, dd, $J = 8.0, 1.0$ Hz, H-9), 8.10 (1H, s, N_b -CHO), 7.63 (1H, s, H-21), 7.39 (1H, td, $J = 8.0, 1.0$ Hz, H-10), 7.32 (1H, td, $J = 8.0, 1.0$ Hz, H-11), 6.88 (1H, dd, $J = 8.0, 1.0$ Hz, H-12), 4.91 (1H, br d, $J = 7.0$ Hz, H-5), 4.42 (1H, ddd, $J = 11.0, 4.0, 2.0$ Hz, H-17), 3.90 (1H, t, $J = 11.0$ Hz, H-17), 3.82 (1H, br s, H-3), 3.59 (1H, dt, $J = 12.0, 6.0$ Hz, H-15), 3.18 (1H, s, N_a -Me), 2.68 (1H, dd, $J = 13.0, 7.0$ Hz, H-6), 2.53 (1H, ddd, $J = 14.0, 6.0, 2.0$ Hz, H-14), 2.26 (3H, s, H-18), 2.22 (2H, m, H-6 & H-16), 1.57 (1H, ddd, $J = 14.0, 12.0, 2.0$ Hz, H-14).

And

^1H NMR (400 MHz, CDCl_3): δ 8.25 (1H, dd, $J = 8.0, 1.0$ Hz, H-9), 8.10 (1H, s, N_b -CHO), 7.61 (1H, s, H-21), 7.39 (1H, td, $J = 8.0, 1.0$ Hz, H-10), 7.32 (1H, td, $J = 8.0, 1.0$ Hz, H-11), 6.87 (1H, dd, $J = 8.0, 1.0$ Hz, H-12), 4.49 (1H, br s, H-3), 4.31 (1H, br d, $J = 7.0$ Hz, H-5), 4.27 (1H, ddd, $J = 11.0, 4.0, 2.0$ Hz, H-17), 3.96 (1H, t, $J = 11.0$ Hz, H-17), 3.59 (1H, dt, $J = 12.0, 6.0$ Hz, H-15), 3.17 (1H, s, N_a -Me), 2.77 (1H, dd, $J = 13.0, 7.0$ Hz, H-6), 2.42 (1H, ddd, $J = 14.0, 6.0, 2.0$ Hz, H-14), 2.26 (3H, s, H-18), 2.22 (2H, m, H-6 & H-16), 1.56 (1H, m, H-14).

Perhentinine (121): ^1H NMR (400 MHz, CDCl_3): ^1H NMR (400 MHz, CDCl_3): δ 7.52 (1H, br d, $J = 8.0$ Hz, H-9), 7.51 (1H, s, H-21'), 7.32 (br d, $J = 8.0$ Hz, H-12), 7.22 (1H, td, $J = 8.0, 1.0$ Hz, H-11), 7.13 (1H, td, $J = 8.0, 1.0$ Hz, H-10), 6.90 (1H, s, H-9'), 6.69 (1H, s, H-12'), 4.37 (1H, t, $J = 11.0$ Hz, H-17'), 4.13 (1H, ddd, $J = 11.0, 4.0, 1.0$ Hz, H-17'), 4.09 (1H, m, H-3), 4.01 (1H, dd, $J = 11.0, 2.0$ Hz, H-17), 3.95 (1H, dd, $J = 11.0, 3.0$ Hz, H-17), 3.87 (3H, s, 11-OMe'), 3.79 (1H, t, $J = 3.0$ Hz, H-3'), 3.65 (3H, s, N_a -Me'), 3.55 (3H, s, N_a -Me), 3.46 (1H, d, $J = 7.0$ Hz, H-5), 3.32 (2H, m, H-20 & H-6'), 3.08 (2H, m, H-6 & H-21), 2.99 (1H, d, $J = 7.0$ Hz, H-5'), 2.54 (2H, m, H-6 & H-15'), 2.41 (1H, m, H-14), 2.41 (1H, m, H-21), 2.34 (3H, s, N_b -Me), 2.28 (1H, m, H-6'), 2.25 (3H, s, N_b -Me'), 2.14 (1H, m, H-15), 2.05 (3H, s, H-18'), 2.04 (1H, m, H-14'), 1.98 (1H, m, H-14), 1.84 (1H, dt, $J = 11.0, 4.0$, H-16'), 1.75 (1H, td, $J = 12.0, 3.0$, H-14'), 1.72 (3H, s, H-18), 1.57 (1H, m, H-16).

Lumusidine A (122): ^1H NMR (400 MHz, CDCl_3): δ 7.59 (1H, s, H-21'), 7.47 (1H, d, $J = 7.7$ Hz, H-9), 7.14 (1H, m, H-12), 7.09 (1H, m, H-11), 7.07 (1H, m, H-10), 7.00 (1H, s, H-9'), 6.42 (1H, s, H-21), 6.38 (1H, s, H-12'), 4.44 (1H, t, $J = 11.0$ Hz, H-17'a), 4.29 (1H, t, $J = 11.0$ Hz, H-17a), 4.21 (1H, br d, $J = 11.0$ Hz, H-17'b), 3.92 (1H, br d, $J = 11.0$ Hz, H-17b), 3.81 (1H, m, H-3'), 3.76 (1H, m, H-3), 3.68 (1H, q, $J = 7.5$ Hz, H-19), 3.48 (3H, s, N_a -Me'), 3.39 (3H, s, 11'-OMe), 3.32 (3H, s, N_a -Me), 3.19 (1H, m, H-6a), 3.16 (1H, m, H-6'a), 3.10 (1H, d, $J = 7.0$ Hz, H-5), 3.06 (1H, d, $J = 7.0$ Hz, H-5'), 2.71 (1H, m, H-15'), 2.43 (1H, br d, $J = 16.0$ Hz, H-6b), 2.34 (1H, br d, $J = 17.0$ Hz, H-6'b), 2.26 (6H, s, N_b -Me & N_b -Me'), 2.12 (3H, s, H-18'), 2.08 (1H, m, H-14'b), 1.96 (1H, m, H-16'), 1.86 (3H, m, H-14a, H-15 & H-16), 1.80 (1H, m, H-14'a), 1.57 (1H, m, H-14b), 1.26 (3H, d, $J = 7.5$ Hz, H-18).

Lumusidine B (123): ^1H NMR (400 MHz, CDCl_3): δ 7.51 (1H, s, H-21'), 7.33 (1H, d, J = 7.0 Hz, H-9), 7.05 (1H, m, H-11), 7.03 (1H, m, H-10), 7.01 (1H, s, H-9'), 6.51 (1H, d, J = 7.0 Hz, H-12), 5.63 (1H, s, H-12'), 5.39 (1H, d, J = 3.2 Hz, H-21), 4.47 (1H, t, J = 12.0 Hz, H-17a), 4.41 (1H, t, J = 11.5 Hz, H-17'a), 4.17 (1H, dd, J = 11.5, 3.0 Hz, H-17'b), 3.98 (1H, m, H-3'), 3.63 (1H, m, H-3), 3.48 (1H, dd, J = 12.0, 4.0 Hz, H-17b), 3.44 (3H, s, $N_a\text{-Me}'$), 3.21 (3H, s, 11'-OMe), 3.17 (1H, m, H-6a), 3.13 (1H, m, H-6'a), 3.11 (1H, m, H-5'), 2.90 (1H, d, J = 7.0 Hz, H-5), 2.87 (1H, m, H-19), 2.57 (1H, m, H-14a), 2.57 (3H, s, $N_b\text{-Me}$), 2.51 (1H, m, H-6'b), 2.51 (3H, s, $N_b\text{-Me}'$), 2.48 (1H, m, H-15'), 2.46 (1H, m, H-20), 2.31 (1H, m, H-6b), 2.29 (3H, s, $N_b\text{-Me}$), 2.11 (1H, m, H-14'b), 2.06 (3H, s, H-18'), 1.87 (1H, m, H-16'), 1.84 (1H, m, H-16), 1.79 (1H, m, H-14'a), 1.38 (1H, m, H-14b), 1.30 (1H, m, H-15), 1.18 (3H, d, J = 6.8 Hz, H-18).

Lumusidine C (124): ^1H NMR (400 MHz, CDCl_3): δ 7.55 (1H, s, H-21'), 7.34 (1H, d, J = 7.0 Hz, H-9), 7.06 (1H, t, J = 7.0 Hz, H-10), 7.02 (1H, t, J = 7.0 Hz, H-11), 6.95 (1H, d, J = 7.0 Hz, H-12), 6.86 (1H, s, H-9'), 6.06 (1H, s, H-12'), 4.38 (1H, t, J = 11.0 Hz, H-17'a), 4.18 (1H, m, H-17a), 4.15 (1H, m, H-17'b), 3.77 (1H, m, H-3), 3.75 (1H, m, H-3'), 3.61 (3H, s, 11'-OMe), 3.49 (1H, dd, J = 11.0, 4.0 Hz, H-17b), 3.34 (3H, s, $N_a\text{-Me}$), 3.32 (3H, s, $N_a\text{-Me}'$), 3.14 (1H, dd, J = 16.0, 7.0 Hz, H-6a), 3.14 (1H, dd, J = 16.0, 7.0 Hz, H-6'a), 3.05 (1H, m, H-14a), 2.98 (1H, d, J = 7.0 Hz, H-5'), 2.92 (1H, d, J = 7.0 Hz, H-5), 2.83 (1H, dd, J = 13.6, 4.5 Hz, H-21), 2.60 (1H, dd, J = 13.6, 10.4 Hz, H-21), 2.50 (1H, m, H-15'), 2.28 (3H, s, $N_b\text{-Me}'$), 2.26 (1H, m, H-6b), 2.25 (3H, s, $N_b\text{-Me}$), 2.12 (1H, m, H-16), 2.10 (1H, m, H-6'b), 2.08 (3H, s, H-18'), 2.05 (1H, m, H-14'b), 1.84 (1H, m, H-16'), 1.75 (1H, td, J = 13.0, 4.0 Hz, H-14'a), 1.67 (1H, dd, J = 10.4, 4.5 Hz, H-20), 1.61 (1H, m, H-15), 1.36 (3H, s, H-18), 1.24 (1H, m, H-14b).

Lumusidine D (125): ^1H NMR (400 MHz, CDCl_3): δ 7.52 (1H, s, H-21'), 7.34 (1H, d, J = 8.0 Hz, H-9), 7.17 (1H, m, H-12), 7.15 (1H, m, H-11), 7.02 (1H, t, J = 8.0 Hz, H-10), 7.01 (1H, d, J = 8.5 Hz, H-9'), 6.08 (1H, d, J = 8.5 Hz, H-10'), 4.42 (1H, t, J = 11.0 Hz, H-17a), 4.42 (1H, t, J = 11.0 Hz, H-17'a), 4.17 (1H, dd, J = 1.0, 3.0 Hz, H-17'b), 3.95 (1H, dd, J = 11.0, 3.0 Hz, H-17b), 3.80 (1H, m, H-3'), 3.72 (1H, m, H-3), 3.72 (3H, s, $N_a\text{-Me}'$), 3.65 (2H, m, H-21), 3.17 (1H, d, J = 16.0 Hz, H-6a), 3.15 (1H, d, J = 16.0 Hz, H-6'a), 3.06 (1H, d, J = 7.0 Hz, H-5'), 3.00 (1H, d, J = 7.0 Hz, H-5), 2.92 (3H, s, 11'-OMe), 2.83 (3H, s, $N_a\text{-Me}$), 2.53 (1H, m, H-15'), 2.34 (2H, m, H-6b & H-6'b), 2.33 (3H, s, $N_b\text{-Me}'$), 2.24 (3H, s, $N_b\text{-Me}$), 2.11 (3H, s, H-18'), 1.99 (1H, br d, J = 13.0 Hz, H-14'b), 1.89 (1H, m, H-16), 1.86 (2H, m, H-14a & H-16'), 1.82 (3H, s, H-18), 1.76 (1H, m, H-14'a), 1.61 (1H, m, H-15), 0.85 (1H, br d, J = 13.0 Hz, H-14b).

Perhentidine A (126): ^1H NMR (400 MHz, CDCl_3): δ 7.56 (1H, d, J = 7.5 Hz, H-9), 7.49 (1H, s, H-21'), 7.36 (1H, d, J = 7.5 Hz, H-12), 7.26 (1H, m, H-11), 7.22 (1H, d, J = 8.6 Hz, H-9'), 7.16 (1H, t, J = 7.5, H-10), 6.75 (1H, d, J = 8.6 Hz, H-10'), 4.39 (1H, t, J = 11.0 Hz, H-17'a), 4.14 (2H, m, H-3 & H-17'b), 3.91 (1H, dd, J = 11.0, 2.0 Hz, H-17b), 3.88 (1H, dd, J = 11.0, 2.0 Hz, H-17a), 3.83 (3H, s, 11'-OMe), 3.80 (1H, m, H-3'), 3.69 (3H, s, $N_a\text{-Me}$), 3.58 (3H, s, $N_a\text{-Me}'$), 3.48 (1H, d, J = 7.6 Hz, H-5), 3.29 (1H, m, H-6a), 3.26 (1H, m, H-21b), 3.23 (1H, dd, J = 17.0, 7.0 Hz, H-6'b), 3.05 (1H, d, J = 7.0 Hz, H-5'), 2.92 (1H, dd, J = 13.0, 10.5 Hz, H-21a), 2.57 (1H, d, J = 17.0 Hz, H-6b), 2.50 (1H, m, H-15'), 2.46 (1H, m,

H-14a), 2.40 (1H, m, H-6'a), 2.37 (3H, s, N_b -Me'), 2.36 (3H, s, N_b -Me), 2.27 (1H, m, H-15), 2.06 (3H, s, H-18'), 2.01 (2H, m, H-14b & H-14'b), 1.84 (1H, m, H-16'), 1.75 (1H, td, J = 12.0, 4.0, H-14'a), 1.66 (1H, m, H-16), 1.55 (3H, s, H-18).

Perhentidine B (127): ^1H NMR (400 MHz, CDCl_3): δ 7.56 (1H, d, J = 7.5 Hz, H-9), 7.48 (1H, s, H-21'), 7.32 (1H, d, J = 8.0 Hz, H-12), 7.22 (1H, m, H-11), 7.20 (1H, d, J = 8.6 Hz, H-9'), 7.14 (1H, m, H-10), 6.76 (1H, d, J = 8.6 Hz, H-10'), 4.49 (1H, d, J = 12.0, H-17b), 4.37 (1H, t, J = 11.0 Hz, H-17'a), 4.12 (1H, m, H-17'b), 4.09 (1H, m, H-17a), 3.98 (1H, m, H-3), 3.94 (3H, s, 11'-OMe), 3.72 (1H, m, H-3'), 3.63 (1H, m, H-5), 3.57 (3H, s, N_a -Me), 3.53 (3H, s, N_a -Me'), 3.37 (1H, dd, J = 17.0, 7.0, H-6a), 3.17 (1H, m, H-21b), 3.20 (1H, m, H-6'b), 3.05 (1H, m, H-21a), 3.01 (1H, m, H-5'), 2.58 (1H, d, J = 17.0 Hz, H-6b), 2.51 (1H, m, H-15'), 2.36 (3H, s, N_b -Me), 2.34 (1H, m, H-6'a), 2.26 (1H, m, H-14a), 2.24 (3H, s, N_b -Me'), 2.11 (1H, m, H-15), 2.05 (3H, s, H-18'), 1.99 (1H, m, H-14'b), 1.88 (1H, m, H-16), 1.82 (1H, m, H-16'), 1.48 (1H, m, H-14b), 1.70 (1H, td, J = 12.5, 3.5, H-14'a), 1.40 (3H, s, H-18).

Perhentidine C (128): ^1H NMR (400 MHz, CDCl_3): δ 7.56 (1H, d, J = 7.5 Hz, H-9), 7.49 (1H, s, H-21'), 7.34 (1H, d, J = 7.5 Hz, H-12), 7.24 (1H, m, H-11), 7.16 (1H, t, J = 7.5, H-10), 7.07 (1H, d, J = 9.0 Hz, H-12'), 6.83 (1H, d, J = 9.0 Hz, H-11'), 4.32 (1H, t, J = 11.0 Hz, H-17'a), 4.14 (1H, m, H-3), 4.08 (1H, dd, J = 11.0, 4.0, H-17'b), 3.90 (1H, m, H-17b), 3.89 (3H, s, 10'-OMe), 3.83 (1H, dd, J = 11.0, 2.0 Hz, H-17a), 3.77 (1H, m, H-3'), 3.69 (3H, s, N_a -Me), 3.53 (3H, s, N_a -Me'), 3.45 (1H, m, H-5), 3.29 (1H, dd, J = 17.0, 7.0 Hz, H-6a), 3.23 (1H, dd, J = 12.0, 4.0 Hz, H-21b), 3.18 (1H, dd, J = 17.0, 7.0 Hz, H-6'b), 2.87 (1H, d, J = 7.0 Hz, H-5'), 2.60 (1H, t, J = 12.0 Hz, H-21a), 2.56 (1H, d, J = 17.0 Hz, H-6b), 2.50 (1H, m, H-15'), 2.50 (1H, m, H-14a), 2.37 (3H, s, N_b -Me), 2.26 (1H, d, J = 17.0 Hz, H-6'a), 2.24 (3H, s, N_b -Me'), 2.21 (1H, m, H-15), 2.06 (3H, s, H-18'), 2.04 (2H, m, H-14b & H-14'b), 1.75 (1H, m, H-16' & H-14'a), 1.60 (1H, m, H-16), 1.30 (3H, s, H-18).

Perhentsine A (129): ^1H NMR (400 MHz, CDCl_3): δ 7.54 (1H, d, J = 7.5 Hz, H-9), 7.37 (1H, d, J = 7.5 Hz, H-12), 7.26 (1H, td, J = 7.5, 1.0 Hz, H-11), 7.16 (1H, td, J = 7.5, 1.0 Hz, H-10), 7.02 (1H, d, J = 8.9 Hz, H-12'), 6.73 (1H, d, J = 8.9 Hz, H-11'), 5.43 (1H, br q, J = 7.0 Hz, H-19'), 4.25 (1H, br d, J = 9.6 Hz, H-3'), 4.20 (1H, m, H-3), 3.88 (2H, m, H-17), 3.70 (3H, s, N_a -Me), 3.66 (3H, s, 10'-OMe), 3.65 (2H, m, H-21'), 3.59 (1H, m, H-17'b), 3.53 (3H, s, N_a '-Me), 3.48 (1H, m, H-17'a), 3.45 (1H, m, H-5), 3.30 (1H, dd, J = 17.0, 7.0 Hz, H-6b), 3.29 (1H, m, H-6b), 3.11 (1H, dd, J = 12.0, 4.0 Hz, H-21b), 3.03 (2H, m, H-20 & H-5'), 2.96 (1H, d, J = 15.0 Hz, H-6'a), 2.91 (1H, t, J = 12.0 Hz, H-21a), 2.73 (1H, m, H-15'), 2.53 (1H, m, H-14b), 2.51 (1H, d, J = 17.0 Hz, H-6a), 2.35 (3H, s, N_b -Me), 2.31 (1H, m, H-15), 2.11 (1H, m, H-14'b), 2.03 (1H, m, H-14a), 1.95 (1H, m, H-16'), 1.74 (1H, td, J = 12.0, 2.5 Hz, H-14'a), 1.63 (3H, br d, H-18'), 1.49 (3H, s, H-18), 1.45 (1H, m, H-16).

Perhentsine B (130): ^1H NMR (400 MHz, CDCl_3): δ 8.50 (1H, br s, N_a '-H), 7.52 (1H, br d, J = 7.5 Hz, H-9), 7.36 (1H, br d, J = 7.5 Hz, H-12), 7.27 (1H, br t, J = 7.5 Hz, H-11), 7.15 (1H, br t, J = 7.5 Hz, H-10), 7.02 (1H, d, J = 8.7 Hz, H-12'), 6.65 (1H, d, J = 8.7 Hz, H-11'), 5.34 (1H, q, J = 6.8 Hz, H-19'), 4.15 (1H, m, H-3), 3.98 (1H, br d, J = 9.0 Hz, H-3'), 3.88 (2H, m, H-17), 3.69 (3H, br s, N_a -Me), 3.64 (3H, s, 10'-OMe), 3.62 (1H, m, H-17'b), 3.48

(2H, m, H-21'), 3.42 (2H, m, H-5 & H-17'a), 3.28 (1H, dd, $J = 17.0, 7.0$ Hz, H-6b), 3.22 (1H, dd, $J = 16.0, 5.0$ Hz, H-6a), 3.07 (1H, d, $J = 10.0$ Hz, H-21b), 3.06 (1H, m, H-20), 2.95 (1H, m, H-5'), 2.94 (1H, m, H-21a), 2.93 (1H, d, $J = 16.0$ Hz, H-6'b), 2.61 (1H, m, H-15'), 2.51 (1H, m, H-14b), 2.49 (1H, d, $J = 17.0$ Hz, H-6a), 2.30 (3H, br s, N_b -Me), 2.27 (1H, m, H-15), 2.00 (1H, m, H-14a), 1.92 (2H, m, H-14'b, H-16'), 1.68 (1H, m, H-14'a), 1.58 (3H, d, $J = 6.8$ Hz, H-18'), 1.46 (3H, s, H-18), 1.42 (1H, m, H-16).

Perhentsine C (131): ^1H NMR (400 MHz, CDCl_3): δ 7.48 (1H, d, $J = 7.5$ Hz, H-9), 7.44 (1H, d, $J = 7.5$ Hz, H-12), 7.28 (1H, t, $J = 7.5$ Hz, H-11), 7.15 (1H, t, $J = 7.5$ Hz, H-10), 6.68 (1H, s, H-9'), 6.56 (1H, br s, N_a' -H), 6.05 (1H, s, H-12'), 5.38 (1H, q, $J = 7.0$ Hz, H-19'), 4.12 (1H, m, H-3), 3.95 (1H, m, H-3'), 3.94 (1H, m, H-17b), 3.83 (1H, dd, $J = 11.0, 15.0$ Hz, H-17a), 3.73 (6H, s, 10'-OMe & N_a -Me), 3.54 (2H, m, H-21'), 3.51 (2H, m, H-17'), 3.44 (1H, d, $J = 7.0$ Hz, H-5), 3.25 (1H, dd, $J = 16.0, 7.0$ Hz, H-6b), 3.24 (2H, m, H-20 & H-21b), 2.88 (1H, dd, $J = 15.0, 5.0$ Hz, H-6a), 2.82 (1H, m, H-15'), 2.70 (1H, br t, $J = 5.0$ Hz, H-5'), 2.50 (1H, d, $J = 15.0$ Hz, H-6'b), 2.49 (1H, m, H-21a), 2.48 (1H, d, $J = 16.0$ Hz, H-6a), 2.43 (1H, m, H-14b), 2.39 (3H, s, N_b -Me), 2.24 (1H, m, H-15), 2.05 (1H, m, H-14a), 1.99 (1H, m, H-14'b), 1.96 (3H, s, H-18), 1.80 (1H, q, $J = 7.0$ Hz, H-16'), 1.65 (3H, br d, $J = 7.0$ Hz, H-18'), 1.64 (1H, m, H-16), 1.27 (1H, m, H-14'a).

Leuconoline (132): ^1H NMR (400 MHz, CDCl_3): δ 7.98 (1H, br s, NH), 7.43 (1H, dd, $J = 7.6, 1.0$ Hz, H-9'), 7.05 (1H, d, $J = 8.5$ Hz, H-12), 7.01 (1H, td, $J = 7.6, 1.0$ Hz, H-10'), 6.74 (1H, td, $J = 7.6, 1.0$ Hz, H-11'), 6.62 (1H, d, $J = 8.5$ Hz, H-11), 6.57 (1H, dd, $J = 8.3, 1.0$ Hz, H-12'), 5.65 (1H, dd, $J = 12.0, 4.4$ Hz, H-16'), 5.38 (1H, q, $J = 7.0$ Hz, H-19), 4.21 (1H, d, $J = 10.0$ Hz, H-3), 4.05 (1H, s, H-21'), 3.80 (1H, d, $J = 10.5$ Hz, H-17), 3.61 (1H, d, $J = 17.0$ Hz, H-21), 3.59 (1H, d, $J = 10.5$ Hz, H-17), 3.52 (1H, d, $J = 17.0$ Hz, H-21), 3.33 (1H, m, H-5'), 3.31 (1H, m, H-6), 3.29 (1H, m, H-5'), 3.05 (1H, m, H-15), 3.02 (1H, m, H-6'), 3.01 (2H, m, H-5 & H-6), 2.97 (3H, s, COOMe), 2.64 (1H, m, H-3'), 2.63 (1H, m, H-14), 2.61 (1H, m, H-17'), 2.57 (1H, m, H-6'), 2.52 (1H, m, H-3'), 2.27 (1H, dq, $J = 14.0, 7.0$ Hz, H-19'), 2.21 (1H, dd, $J = 14.0, 12.0$ Hz, H-17'), 1.87 (1H, m, H-14), 1.79 (1H, m, H-14'), 1.64 (3H, d, $J = 7.0$ Hz, H-18), 1.56 (1H, m, H-15'), 1.54 (1H, m, H-19'), 1.46 (1H, m, H-14'), 1.21 (1H, td, $J = 13.0, 3.0, 1.0$ Hz, H-15'), 0.97 (3H, t, $J = 7.6$ Hz, H-18').

Lumutinine A (133): ^1H NMR (400 MHz, CDCl_3): δ 7.58 (1H, m, H-21'), 7.50 (1H, d, $J = 7.5$ Hz, H-9), 7.28 (1H, d, $J = 7.5$ Hz, H-12), 7.18 (1H, t, $J = 7.5$ Hz, H-11), 7.11 (1H, t, $J = 7.5$ Hz, H-10), 6.98 (1H, s, H-9'), 6.76 (1H, s, H-12'), 4.67 (1H, t, $J = 12.0$ Hz, H-17a), 4.44 (1H, t, $J = 11.5$ Hz, H-17'b), 4.19 (1H, dd, $J = 11.5, 3.0$ Hz, H-17'a), 3.90 (1H, br s, H-3), 3.83 (1H, br s, H-3'), 3.69 (1H, dd, $J = 12.0, 4.0$ Hz, H-17b), 3.55 (3H, s, N_a -Me), 3.54 (3H, s, N_a -Me'), 3.28 (1H, m, H-6a), 3.24 (1H, m, H-21a), 3.20 (1H, m, H-6'b), 3.07 (1H, d, $J = 6.0$ Hz, H-5'), 3.00 (1H, d, $J = 7.0$ Hz, H-5), 2.76 (1H, m, H-15'), 2.48 (1H, m, H-6b), 2.43 (1H, m, H-21b), 2.34 (1H, m, H-14a), 2.33 (1H, m, H-6'a), 2.29 (3H, s, N_b -Me), 2.27 (3H, s, N_b -Me'), 2.15 (2H, m, H-14'b & H-18'), 2.00 (1H, m, H-16), 1.93 (2H, m, H-20 & H-16'), 1.87 (1H, m, H-15), 1.84 (1H, m, H-14'a), 1.38 (3H, s, H-18), 1.25 (1H, m, H-14b).

Lumutinine B (134): ^1H NMR (400 MHz, CDCl_3): δ 7.55 (1H, m, H-21'), 7.49 (1H, d, $J = 7.5$ Hz, H-9), 7.28 (1H, d, $J = 7.5$ Hz, H-12), 7.17 (1H, td, $J = 7.5, 1.0$ Hz, H-11), 7.16 (1H,

d, $J = 8.0$ Hz, H-9'), 7.09 (1H, td, $J = 7.5, 1.0$ Hz, H-10), 6.66 (1H, d, $J = 8.0$ Hz, H-10'), 4.43 (1H, t, $J = 11.0$ Hz, H-17'b), 4.22 (1H, dd, $J = 11.0, 3.0$ Hz, H-17a), 4.16 (1H, dd, $J = 11.0, 3.0$ Hz, H-17'a), 3.93 (1H, br s, H-3), 3.86 (3H, s, N_a -Me'), 3.81 (1H, m, H-3'), 3.75 (1H, m, H-17b), 3.65 (3H, s, N_a -Me), 3.54 (1H, m, H-21a), 3.37 (1H, m, H-5), 3.33 (1H, m, H-21b), 3.22 (1H, dd, $J = 16.5, 7.0$ Hz, H-6'b), 3.12 (1H, dd, $J = 16.0, 5.0$ Hz, H-6a), 3.06 (1H, d, $J = 7.0$ Hz, H-5'), 2.68 (1H, m, H-20), 2.66 (1H, m, H-15'), 2.52 (1H, m, H-14a), 2.41 (1H, m, H-6'a), 1.79 (1H, m, H-14'a), 2.39 (3H, s, N_b -Me), 2.35 (1H, m, H-6b), 2.29 (3H, s, N_b -Me'), 2.15 (1H, m, H-14'b), 2.12 (3H, s, H-18'), 1.88 (1H, m, H-16'), 1.78 (2H, m, H-14b, H-15), 1.75 (1H, m, H-16), 1.54 (3H, s, H-18).

Lumutinine C (135): ^1H NMR (400 MHz, CDCl_3): δ 7.50 (1H, d, $J = 7.5$ Hz, H-9), 7.25 (1H, d, $J = 7.5$ Hz, H-12), 7.17 (1H, t, $J = 7.5$, H-11), 7.10 (1H, t, $J = 7.5$, H-10), 7.01 (1H, d, $J = 9.0$ Hz, H-12'), 6.71 (1H, d, $J = 9.0$ Hz, H-11'), 6.44 (1H, s, H-21'), 4.62 (1H, t, $J = 11.5$ Hz, H-17a), 4.46 (1H, q, $J = 6.0$ Hz, H-19'), 3.82 (1H, m, H-3'), 3.74 (1H, m, H-3), 3.67 (1H, dd, $J = 11.5, 4.0$ Hz, H-17b), 3.61 (1H, dd, $J = 12.0, 3.0$ Hz, H-17'b), 3.48 (3H, s, N_a -Me'), 3.42 (1H, m, H-17'a), 3.40 (3H, s, N_a -Me), 3.28 (1H, m, H-6a), 3.25 (1H, m, H-21a), 3.22 (1H, m, H-6'b), 2.99 (1H, m, H-5), 2.87 (1H, m, H-5'), 2.82 (1H, m, H-15'), 2.75 (1H, m, H-21b), 2.71 (1H, m, H-6'a), 2.45 (1H, d, $J = 16.0$ Hz, H-6b), 2.35 (1H, td, $J = 13.0, 3.0$ Hz, H-14a), 2.26 (3H, s, N_b -Me), 2.00 (1H, m, H-16), 1.97 (1H, m, H-20), 1.89 (1H, m, H-14'b), 1.87 (1H, m, H-15), 1.35 (3H, s, H-18), 1.66 (1H, m, H-14'a), 1.55 (1H, m, H-16'), 1.34 (3H, d, $J = 6.0$ Hz, H-18'), 1.18 (1H, m, H-14b).

Lumutinine D (136): ^1H NMR (400 MHz, CDCl_3): δ 7.49 (1H, d, $J = 7.5$ Hz, H-9), 7.27 (1H, d, $J = 7.5$ Hz, H-12), 7.18 (1H, t, $J = 7.5$, H-11), 7.10 (1H, t, $J = 7.5$, H-10), 6.91 (1H, s, H-11'), 6.85 (1H, s, H-12'), 5.40 (1H, q, $J = 6.5$ Hz, H-19'), 4.63 (1H, t, $J = 11.5$ Hz, H-17a), 4.16 (1H, m, H-3'), 3.70 (1H, m, H-3), 3.66 (1H, m, H-17b), 3.59 (2H, m, H-21'), 3.56 (3H, s, N_a -Me'), 3.53 (1H, m, H-17'b), 3.48 (1H, m, H-17'a), 3.47 (3H, s, N_a -Me), 3.25 (2H, m, H-6a & H-21a), 3.01 (1H, m, H-6'b), 2.97 (1H, m, H-5), 2.82 (1H, m, H-15'), 2.76 (1H, m, H-5'), 2.57 (1H, br d, $J = 15.0$ Hz, H-6'a), 2.48 (1H, m, H-21b), 2.43 (1H, d, $J = 17.0$ Hz, H-6b), 2.28 (1H, m, H-14a), 2.24 (3H, s, N_b -Me), 2.05 (1H, m, H-14'b), 1.99 (1H, m, H-16), 1.93 (1H, m, H-20), 1.84 (1H, m, H-15), 1.82 (1H, m, H-16'), 1.65 (1H, m, H-14'a), 1.63 (3H, d, $J = 6.5$ Hz, H-18'), 1.39 (3H, s, H-18), 1.10 (1H, d, $J = 13.0$ Hz, H-14b).

Lumutinine E (137): ^1H NMR (400 MHz, CDCl_3): δ 7.95 (1H, s, N_a' -H), 7.51 (1H, d, $J = 7.5$ Hz, H-9), 7.26 (1H, d, $J = 7.5$ Hz, H-12), 7.17 (1H, t, $J = 7.5$ Hz, H-11), 7.11 (1H, t, $J = 7.5$ Hz, H-10), 6.97 (1H, d, $J = 8.6$ Hz, H-12'), 6.65 (1H, d, $J = 8.6$ Hz, H-11'), 5.34 (1H, br q, $J = 6.8$ Hz, H-19'), 4.61 (1H, t, $J = 11.5$ Hz, H-17b), 4.01 (1H, br d, $J = 9.5$ Hz, H-3'), 3.71 (1H, m, H-3), 3.67 (1H, dd, $J = 11.5, 4.0$ Hz, H-17a), 3.50 (2H, m, H-21'), 3.43 (2H, m, H-17'), 3.41 (3H, s, N_a -Me), 3.27 (1H, dd, $J = 16.0, 6.8$ Hz, H-6b), 3.20 (1H, dd, $J = 18.0, 8.0$ Hz, H-21b), 3.13 (1H, dd, $J = 15.0, 5.0$ Hz, H-6'a), 2.99 (1H, d, $J = 6.8$ Hz, H-5), 2.82 (1H, m, H-15'), 2.73 (1H, d, $J = 18.0$ Hz, H-21a), 2.64 (1H, d, $J = 15.0$ Hz, H-6'b), 2.60 (1H, br t, $J = 5.0$ Hz, H-5'), 2.45 (1H, d, $J = 16.0$ Hz, H-6a), 2.34 (1H, td, $J = 13.0, 4.0$ Hz, H-14b), 2.27 (3H, s, N_b -Me), 2.00 (1H, m, H-16), 1.96 (1H, m, H-14'b), 1.94 (1H, m, H-20), 1.83 (1H, m, H-15), 1.79 (1H, m, H-16'), 1.76 (1H, m, H-14'a), 1.63 (3H, br d, $J = 6.8$ Hz, H-18'), 1.37 (3H, s, H-18), 1.17 (1H, m, H-14a).

Villalstonidine A (138): ^1H NMR (400 MHz, CDCl_3): δ 8.06 (1H, br d, $J=7.8$ Hz, H-12'), 7.54 (1H, br d, $J=7.8$ Hz, H-9), 7.34 (1H, br d, $J=7.8$ Hz, H-12), 7.24 (2H, m, H-11 & H-11'), 7.15 (1H, br t, $J=7.8$ Hz, H-10), 7.09 (1H, br t, $J=7.8$ Hz, H-10'), 7.02 (1H, br d, $J=7.8$ Hz, H-9'), 4.18 (1H, q, $J=6.0$ Hz, H-19'), 4.04 (1H, t, $J=12.0$ Hz, H-17a), 3.90 (1H, m, H-3), 3.84 (1H, m, H-3'), 3.77 (1H, m, H-17b), 3.62 (3H, s, $N_a\text{-Me}$), 3.31 (1H, dd, $J=17.0, 7.0$ Hz, H-6a), 3.19 (1H, td, $J=14.0, 2.0$ Hz, H-5'a), 2.97 (1H, m, H-15'), 2.94 (1H, d, $J=7.0$ Hz, H-5), 2.73 (1H, ddd, $J=14.0, 4.0, 1.7$ Hz, H-14'b), 2.66 (1H, d, $J=12.0$ Hz, H-21'b), 2.64 (1H, m, H-5'b), 2.57 (1H, d, $J=12.0$ Hz, H-21'a), 2.48 (1H, d, $J=16.0$ Hz, H-6b), 2.46 (2H, m, H-14a & H-21a), 2.11 (1H, m, H-16), 2.34 (3H, s, $N_b\text{-Me}$), 2.31 (1H, m, H-14'a), 1.78 (1H, td, $J=14.0, 4.0$ Hz, H-6'b), 1.65 (2H, m, H-15 & H-21b), 1.45 (1H, m, H-14b), 1.35 (3H, s, H-18), 1.29 (3H, d, $J=6.0$ Hz, H-18'), 1.23 (1H, m, H-20), 1.21 (1H, m, H-6'a).

Villalstonidine B (139): ^1H NMR (400 MHz, CDCl_3): δ 7.47 (1H, br d, $J=8.0$ Hz, H-9), 7.26 (1H, br d, $J=8.0$ Hz, H-12), 7.16 (1H, td, $J=8.0, 1.0$ Hz, H-11), 7.07 (1H, td, $J=8.0, 1.0$ Hz, H-10), 6.91 (1H, td, $J=7.5, 1.0$ Hz, H-11'), 6.82 (1H, br d, $J=7.5$ Hz, H-9'), 6.63 (1H, br t, $J=7.5$ Hz, H-10'), 6.20 (1H, br d, $J=7.5$ Hz, H-12'), 5.28 (1H, br q, $J=7.0$ Hz, H-19'), 4.34 (1H, dd, $J=12.0, 7.0$ Hz, H-17'b), 4.16 (1H, dd, $J=12.0, 6.0$ Hz, H-17'a), 4.00 (1H, br d, $J=13.0$ Hz, H-21'b), 3.94 (1H, t, $J=12.0$ Hz, H-17a), 3.80 (1H, m, H-3), 3.70 (3H, m, H-17b, H-3' & 17'-OH), 3.55 (3H, s, $N_a\text{-Me}$), 3.51 (3H, s, COOMe'), 3.23 (1H, dd, $J=16.0, 7.0$ Hz, H-6a), 3.22 (1H, m, H-15'), 3.17 (1H, td, $J=14.0, 2.0$ Hz, H-5'a), 2.85 (1H, d, $J=7.0$ Hz, H-5), 2.81 (1H, m, H-14'b), 2.80 (1H, d, $J=13.0$ Hz, H-21'a), 2.58 (1H, dd, $J=14.0, 4.0$ Hz, H-5'b), 2.40 (1H, d, $J=16.0$ Hz, H-6b), 2.38 (1H, m, H-21a), 2.36 (1H, m, H-14a), 2.24 (3H, s, $N_b\text{-Me}$), 2.04 (1H, dt, $J=12.0, 5.0$ Hz, H-16), 1.83 (1H, td, $J=14.0, 4.0$ Hz, H-6'b), 1.58 (1H, m, H-15), 1.55 (2H, m, H-21b & H-14'a), 1.51 (3H, dd, $J=7.0, 2.0$ Hz, H-18'), 1.38 (1H, ddd, $J=13.0, 5.0, 2.0$ Hz, H-14b), 1.29 (3H, s, H-18), 1.19 (1H, m, H-20), 1.06 (1H, br d, $J=14.0$ Hz, H-6'a).

Villalstonidine C (140): ^1H NMR (400 MHz, CDCl_3): δ 7.54 (1H, d, $J=8.0$ Hz, H-9), 7.33 (1H, d, $J=8.0$ Hz, H-12), 7.24 (1H, m, H-11), 7.14 (1H, t, $J=8.0$ Hz, H-10), 6.99 (1H, t, $J=7.5$ Hz, H-11'), 6.89 (1H, d, $J=7.5$ Hz, H-9'), 6.71 (1H, t, $J=7.5$ Hz, H-10'), 6.14 (1H, d, $J=7.5$ Hz, H-12'), 5.57 (1H, br t, $J=6.5$ Hz, H-19'), 4.45 (1H, d, $J=3.5$ Hz, H-16'), 4.25 (1H, br d, $J=13.0$ Hz, H-21'b), 4.11 (1H, dd, $J=12.0, 6.5$ Hz, H-18'), 4.01 (1H, dd, $J=12.0, 6.5$ Hz, H-18'), 3.99 (1H, t, $J=12.0$ Hz, H-17a), 3.86 (1H, m, H-3), 3.77 (1H, m, H-3'), 3.70 (3H, s, COOMe'), 3.73 (1H, m, H-17b), 3.62 (3H, s, $N_a\text{-Me}$), 3.29 (1H, dd, $J=16.0, 7.0$ Hz, H-6a), 3.22 (1H, d, $J=3.5$ Hz, H-15'), 3.13 (1H, br t, $J=14.0$ Hz, H-5'a), 3.01 (1H, d, $J=13.0$ Hz, H-21'a), 2.92 (1H, d, $J=7.0$ Hz, H-5), 2.72 (1H, m, H-14'b), 2.68 (1H, m, H-5'b), 2.47 (1H, d, $J=16.0$ Hz, H-6b), 2.41 (1H, m, H-14a), 2.35 (1H, m, H-21a), 2.31 (3H, s, $N_b\text{-Me}$), 2.08 (1H, m, H-16), 2.01 (1H, m, H-6'b), 1.72 (1H, br d, $J=13.0$ Hz, H-14'a), 1.61 (1H, m, H-15), 1.57 (1H, m, H-21b), 1.44 (1H, m, H-14b), 1.25 (3H, s, H-18), 1.20 (1H, m, H-20), 1.15 (1H, br d, $J=14.0$ Hz, H-6'a).

Villalstonidine D (141): ^1H NMR (400 MHz, CDCl_3): δ 7.57 (1H, br d, $J=8.0$ Hz, H-9), 7.31 (1H, br d, $J=8.0$ Hz, H-12), 7.22 (1H, td, $J=8.0, 1.0$ Hz, H-11), 7.13 (1H, br t, $J=8.0$ Hz, H-10), 7.07 (1H, td, $J=8.0, 0.5$ Hz, H-11'), 6.96 (1H, br d, $J=8.0$ Hz, H-9'), 6.82 (1H,

br t, $J=8.0$ Hz, H-10'), 6.19 (1H, br d, $J=8.0$ Hz, H-12'), 5.77 (1H, q, $J=6.5$ Hz, H-19'), 5.19 (1H, dd, $J=13.0, 1.0$ Hz, H-21'b), 4.57 (1H, m, H-3'), 4.46 (1H, d, $J=3.5$ Hz, H-16'a), 4.36 (1H, t, $J=14.0$ Hz, H-5'a), 4.00 (1H, t, $J=12.0$ Hz, H-17a), 3.93 (1H, m, H-3), 3.88 (1H, dd, $J=12.0, 5.0$ Hz, H-17b), 3.72 (3H, s, COOMe'), 3.61 (3H, s, N_a -Me), 3.50 (3H, s, N_b -Me), 3.47 (2H, m, H-5'b & H-21'a), 3.33 (1H, d, $J=3.5$ Hz, H-15'), 3.28 (1H, dd, $J=17.0, 7.0$ Hz, H-6a), 3.02 (1H, br d, $J=7.0$ Hz, H-5), 2.90 (1H, d, $J=15.0$ Hz, H-14'b), 2.73 (1H, m, H-6b), 2.70 (1H, m, H-21a), 2.66 (1H, m, H-16), 2.47 (1H, t, $J=13.0$ Hz, H-14a), 2.34 (3H, s, N_b -Me), 2.17 (1H, dt, $J=15.0, 3.5$ Hz, H-14'a), 2.05 (1H, td, $J=14.0, 4.0$ Hz, H-6'b), 1.69 (3H, dd, $J=6.5, 1.0$ Hz, H-18'), 1.68 (3H, m, H-15, H-21b & H-6'a), 1.44 (1H, ddd, $J=13.0, 5.0, 3.0$ Hz, H-14b), 1.28 (3H, s, H-18), 1.18 (1H, dd, $J=13.0, 4.0$ Hz, H-20).

Villalstonidine E (142): ^1H NMR (400 MHz, CDCl_3): δ 7.57 (1H, br d, $J=7.6$ Hz, H-9), 7.32 (1H, br d, $J=7.6$ Hz, H-12), 7.23 (1H, td, $J=7.6, 1.0$ Hz, H-11), 7.15 (1H, td, $J=7.6, 1.0$ Hz, H-10), 7.08 (1H, td, $J=7.6, 1.0$ Hz, H-11'), 6.97 (1H, d, $J=7.6$ Hz, H-9'), 6.84 (1H, t, $J=7.6$ Hz, H-10'), 6.20 (1H, br d, $J=7.6$ Hz, H-12'), 5.92 (1H, d, $J=10.0$ Hz, CH_2Cl), 5.85 (1H, q, $J=6.8$ Hz, H-19'), 5.74 (1H, d, $J=10.0$ Hz, CH_2Cl), 5.23 (1H, d, $J=14.0$ Hz, H-21'b), 5.00 (1H, m, H-3'), 4.49 (1H, d, $J=4.0$ Hz, H-16'a), 4.20 (1H, br t, $J=14.0$ Hz, H-5'a), 4.08 (1H, d, $J=14.0$ Hz, H-21'a), 4.00 (1H, t, $J=11.6$ Hz, H-17a), 3.93 (1H, m, H-3), 3.85 (1H, dd, $J=11.5, 5.0$ Hz, H-17b), 3.73 (3H, s, COOMe'), 3.66 (1H, dd, $J=14.0, 3.0$ Hz, H-5'b), 3.62 (3H, s, N_a -Me), 3.37 (1H, br d, $J=4.0$ Hz, H-15'), 3.30 (1H, dd, $J=16.4, 6.0$ Hz, H-6a), 3.02 (1H, d, $J=6.0$ Hz, H-5), 2.93 (1H, br d, $J=15.0$ Hz, H-14'b), 2.66 (1H, d, $J=16.4$ Hz, H-6b), 2.50 (2H, m, H-14a & H-21a), 2.40 (1H, m, H-16), 2.35 (3H, s, N_b -Me), 2.12 (1H, td, $J=14.0, 3.0$ Hz, H-6'b), 2.04 (1H, dd, $J=15.0, 3.5$ Hz, H-14'a), 1.75 (1H, d, $J=14.0$ Hz, H-6'a), 1.71 (1H, m, H-21b), 1.69 (3H, d, $J=6.8$ Hz, H-18'), 1.65 (1H, m, H-15), 1.45 (1H, m, H-14b), 1.29 (3H, s, H-18), 1.21 (1H, dd, $J=12.8, 4.4$ Hz, H-20).

Villalstonidine F (143): ^1H NMR (400 MHz, CDCl_3): δ 7.84 (1H, s, N_a -H), 7.53 (1H, d, $J=8.0$ Hz, H-9), 7.35 (1H, d, $J=8.0$ Hz, H-12), 7.18 (1H, t, $J=8.0$ Hz, H-11), 7.16 (1H, t, $J=8.0$ Hz, H-10), 6.98 (1H, t, $J=7.5$ Hz, H-11'), 6.85 (1H, d, $J=7.5$ Hz, H-9'), 6.69 (1H, t, $J=7.5$ Hz, H-10'), 6.14 (1H, d, $J=7.5$ Hz, H-12'), 5.38 (1H, q, $J=7.0$ Hz, H-19'), 4.43 (1H, d, $J=3.6$ Hz, H-16'a), 4.22 (1H, br d, $J=12.0$ Hz, H-21'b), 3.97 (1H, t, $J=11.0$ Hz, H-17a), 3.77 (2H, m, H-3 & H-3'), 3.71 (1H, m, H-17b), 3.67 (3H, s, COOMe'), 3.28 (1H, dd, $J=17.0, 6.5$ Hz, H-6a), 3.21 (1H, m, H-15'), 3.14 (1H, m, H-5'b), 2.97 (1H, br d, $J=12$ Hz, H-21'a), 2.90 (1H, m, H-5), 2.70 (1H, m, H-5'a), 2.69 (1H, br d, $J=13.0$ Hz, H-14'b), 2.44 (1H, d, $J=17.0$ Hz, H-6b), 2.35 (2H, m, H-14a & H-21), 2.31 (3H, s, N_b -Me), 2.06 (1H, m, H-16), 2.00 (1H, m, H-6'a), 1.73 (1H, m, H-14'a), 1.60 (1H, m, H-15), 1.56 (1H, m, H-21), 1.55 (3H, d, $J=7.0$ Hz, H-18'), 1.47 (1H, m, H-14b), 1.23 (3H, s, H-18), 1.16 (2H, m, H-20 & H-6'b).

3.2 ^{13}C NMR Spectroscopy

Alstiphyllanine A (**99**)
CD₃OD, 133 MHz

Alstiphyllanine H (**90**)
CD₃OD, 100 MHz

Alstiphyllanine I (**91**)
TFA salt, CD₃OD, 100 MHz

Alstiphyllanine J (**92**)
TFA salt, CD₃OD, 100 MHz

Alstiphyllanine K (**93**)
TFA salt, CD₃OD, 100 MHz

Alstiphyllanine L (**94**)
TFA salt, CD₃OD, 100 MHz

Alstiphyllanine M (**95**)
TFA salt, CD₃OD, 100 MHz

Alstiphyllanine N (**96**)
TFA salt, CD₃OD, 100 MHz

Alstiphyllanine O (**97**)
TFA salt, CD₃OD, 100 MHz

Vincamajine N(4)-oxide (**98**)
CDCl₃, 100 MHz

Lumosidine B (123)
CDCl₃, 100 MHz

Lumosidine C (124)
CDCl₃, 100 MHz

Lumosidine D (125)
CDCl₃, 100 MHz

Perhentidine A (126)
CDCl₃, 100 MHz

Perhentidine B (127)
CDCl₃, 100 MHz

Perhentidine C (128)
CDCl₃, 100 MHz

Perhentisine A (129)
CDCl₃, 100 MHz

Perhentisine B (130)
CDCl₃, 100 MHz

Perhentisine C (131)
CDCl₃, 100 MHz

Leuconoline (132)
CDCl₃, 100 MHz

Lumutinine A (133)
CDCl₃, 100 MHz

Lumutinine B (134)
CDCl₃, 100 MHz

Lumutinine C (135)
CDCl₃, 100 MHz

Lumutinine D (136)
CDCl₃, 100 MHz

Lumutinine E (137)
CDCl₃, 100 MHz

Villastonidine A (138)
CDCl₃, 100 MHz

Villastonidine B (139)
CDCl₃, 100 MHz

Villastonidine C (140)
CDCl₃, 100 MHz

Villastonidine D (141)
CDCl₃, 100 MHz

Villastonidine E (142)
CDCl₃, 100 MHz

Villastonidine F (143)
CDCl₃, 100 MHz

4. PHARMACOLOGY

The sarpagine related alkaloids occur mainly in the plant family Apocynaceae, the most important genera being *Rauwolfia* and *Alstonia*. Alkaloid-rich species of these families have been used in folk medicine against a variety of diseases because of their interesting anticancer, antibacterial, antiarrhythmic, anti-inflammatory, and antimalarial properties.^{9,10,22} Kinghorn et al. reported that *N*(4)-methyltalpinine (42) (Table 2) exhibited

significant NF- κ B inhibitory activity (ED_{50} = 1.2 μ M) against the HeLa cells in an ELISA assay.⁷⁷ *N*(4)-Methyltalpinine (**42**) was the first member of the sarpagine-type indole alkaloids with NF- κ B activity. The macroline indole alkaloid alstonerinal (**144**) (Figure 4), as well as two bisindole alkaloids, villalstonine (**150**) and villalstonidine E (**142**), exhibited cytotoxicity against the human colon cancer HT-29 cell line with ED_{50} values of 8.6 μ M, 8.0 μ M and 6.5 μ M respectively). Furthermore, (**42**), (**144**) and (**142**) also exhibited leishmanicidal activity against promastigotes of *Leishmania mexicana*. Alstolactone A (**79**), *O*-acetylalpinine (**43**), talpinine (**146**), although not cytotoxic themselves, exhibited weak activity (IC_{50} values: 40–60 μ M) in reversing multi-drug resistance in a vincristine-resistant KB/VJ300 cell line, in the presence of 0.12 μ M vincristine.⁷⁰ In the same study alstonerine (**145**) showed potent multi-drug resistance reversal activity (IC_{50} = 10 μ M) in a KB/VJ300 cell line in the presence of 0.12 μ M vincristine. The bisindole alkaloids perhentinine (**121**) and villalstonine (**150**) exhibited moderate cytotoxicity against a P388 murine leukemia cell line.⁷⁹ Tan et al. evaluated various macroline indole alkaloids for cytotoxic activity and found that macrodasine B (**51**), macrodasine C (**52**), macrodasine E (**54**) exhibited moderate activity in reversing multi-drug resistance in a vincristine-resistant KB/VJ300 cell line.⁷⁵ Lim et al. showed that 19,20-*Z*-affinisine (**39**) and macrodasine H (**57**) reversed multi-drug resistance in a vincristine-resistant KB/VJ300 cell line.⁹⁷ The bisindole alkaloid leuconoline (**132**) exhibited cytotoxicity towards drug-sensitive KB cells (IC_{50} = 11.5 μ g/ml), as well as against the vincristine-resistant KB/VJ300 cell line (IC_{50} = 12.2 μ g/ml), which indicates that it probably will not be susceptible to drug resistance.⁹⁵ It has been known that *Alstonia* bisindoles such as villalstonine (**150**) and *O*-acetylmacralstonine are active against drug resistance strains of *Plasmodium falciparum*.⁹⁸

Ajmaline **4** is a long known class Ia antiarrhythmic agent and is widely used in the acute treatment of atrial or ventricular tachycardia. One of the mechanisms by which it carries out the anti-arrhythmic activity is by the blockade of cardiac K^+ channels. Recently, Fischer et al. evaluated its mechanism of action and showed that ajmaline blocks $K_v1.5$ and $K_v4.3$ channels at therapeutic concentrations.⁹⁹ Ajmaline type indole alkaloids alstiphyllanine A (**89**), alstiphyllanine I (**91**), alstiphyllanine L (**94**), vincamedine (**147**), vincamajine 17-*O*-veratrate (**148**), and vincamajine 17-*O*-3',4',5'-trimethoxybenzoate (**149**) exhibited potent vasorelaxant activity at 30 μ M concentration in a rat aortic ring vasodilation assay.⁹¹ Vincamedine (**147**) was the most potent among these compounds. The activity may be mediated through inhibition of Ca^{2+} influx through voltage dependent Ca^{2+} channels (VDC) and/or receptor operated Ca^{2+} channels (ROC), as well as via partial nitric oxide (NO) release from endothelial cells. Morita et al. also evaluated alkaloids isolated from the bark of *Tabernaemontana dichotoma* for vasorelaxant activity.⁸³ Among these bases, 10-methoxyaffinisine (**151**), lochnerine (**152**), alstonisine (**153**) and alstonal (**154**) exhibited potent vasorelaxant activity. Further evaluation of 10-methoxyaffinisine (**151**), and alstonisine (**153**) indicated that these vasorelaxant effects were mediated through inhibition of VDC and ROC as well as partial NO release from endothelial cells.⁸³

5. SYNTHESIS

The medicinal properties of the sarpagine related alkaloids remain of great interest, as well as the nature of their structure and stereochemistry. The construction of these structurally complex molecules remains of paramount importance to synthetic chemists. Several studies have been recently published delineating approaches for the synthesis of sarpagine related alkaloids. In this chapter we will focus on key syntheses of the sarpagine related alkaloids published since the year 2000.

5.1. The Asymmetric Pictet–Spengler Reaction

As illustrated in Figure 1, as well as in Tables 2–6, a core tetracyclic system **1** is a common structural feature of the sarpagine-related macroline and ajmaline alkaloids. A general approach to the synthesis of these sarpagine-related alkaloids should involve an enantiospecific synthesis of this core structure with the correct configurations at stereocenters C-3, and C-5 and the appropriate functional groups at C-15/C-16 for further transformations. The racemic 9-azabicyclo[3.3.1]nonane system has been prepared in the late 1970's by Yoneda,¹⁰⁰ Mashimo,¹⁰¹ Kluge¹⁰² and was later improved by Soerens on a kilogram scale.¹⁰³

In 1988, Zhang et al.¹⁰⁴ achieved the synthesis of the optically active tetracyclic ketone **160**, in a stereospecific fashion by employing the asymmetric Pictet–Spengler reaction. Many improvements have been made to prepare both the N_a -H and the N_a -Me tetracyclic ketones (**158** and **160**, respectively). Pictet–Spengler reaction is now carried out in one pot to provide only the desired *trans* diastereomer with high diastereoselectivity and enantioselectivity. As illustrated in Scheme 2, after N_b -benzylation of D-(+)-tryptophan methyl ester (**156**) with benzaldehyde and sodium borohydride in methanol, trifluoroacetic acid (TFA) was added to the reaction vessel at 0 °C to neutralize the reaction mixture. After removal of the solvent, CH_2Cl_2 , TFA, and methyl 4,4-dimethoxybutyrate were added to the vessel at 0 °C, and the modified Pictet–Spengler reaction was carried out in the same vessel at room temperature to provide the *trans* diester **157** in 83% overall yield.¹⁰⁵ In the second sequence, Dieckmann cyclization of **157** was effected by using a large excess of NaOMe with methanol in refluxing toluene. Therefore, the two extra steps of protection and deprotection (employed earlier)¹⁰⁴ could be avoided. After completion of the process, the reaction mixture was cooled to 0°C and carefully quenched with glacial acetic acid. After removal of the solvent, concentrated glacial acetic acid, aqueous hydrochloric acid, and water were added to the residue at 0 °C and the acidic hydrolysis and decarboxylation was executed in the same vessel to provide ketone **158** in 85% overall yield.¹⁰⁵ Attempts to execute the direct N_a -methylation of **158** were always accompanied by N_a , N_b -dimethylation.¹⁰⁵ On the other hand, N_a -methylation of the *trans* diester **157** took place in 95% yield to provide the diester **159** on multihundred gram scale. Dieckmann cyclization on **159** followed by acidic hydrolysis and decarboxylation afforded N_a -Me tetracyclic ketone in 80% overall yield. This route is still one of the best methods to generate multihundred gram quantities of both the N_a -H and N_a -Me tetracyclic ketone templates in greater than 98% ee.

Other recent routes toward the formation of the tetracyclic core include the racemic synthesis by Rassat,^{106,107} the aza Diels–Alder approach by Kuethe,¹⁰⁸ the olefin metathesis route of Martin¹⁰⁹ and the *cis*-Pictet–Spengler process by Bailey¹¹⁰ and Magnus.¹¹¹

5.2. Synthesis of Sarpagine/Macroline Related Indole Alkaloids

Vellosimine (**161**) and normacusine B (**162**) are the simplest representatives of the family of sarpagine indole alkaloids. Until 2000, no enantiospecific total synthesis of members of the sarpagine series was reported. The partial total synthesis of (–)-koumidine (**163**) [which is similar in structure to **162**, except it has the more stable *Z*-ethylidene double bond and the *S* configuration at C-16], was first reported by Sakai.⁸⁴ Magnus later synthesized the enantiomer of (–)-koumidine via a Pictet–Spengler reaction. However, establishment of the double bond (*Z*:*E*=1:5.7) was not stereospecific¹¹¹ and the reaction was hampered by poor diastereoselectivity in the Pictet–Spengler reaction. Entry into the pentacyclic sarpagine skeleton described by Li for the total synthesis of ajmaline previously was through a macroline framework which did not have the potential for incorporation of the *E*-ethylidene double bond stereospecifically and also involved a large number of steps.¹⁰⁵ Martin reported the total synthesis of geissoschizine with stereoselective establishment of the *E*-ethylidene double bond by an elimination process.¹¹² Furthermore Rawal¹¹³ and Bosch¹¹⁴ reported the total synthesis of *Strychnos* alkaloids with stereocontrolled establishment of the double bond by a Heck coupling reaction.

5.2.1. The Enantiospecific Total Synthesis of (+)-Vellosimine (**161**) by Wang—

In 2003, Wang reported an efficient, enantiospecific total synthesis of (+)-vellosimine (**161**) with the first stereospecific establishment of the ethylidene double bond by a key palladium (enolate-mediated) carbon-carbon bond forming process (Scheme 3).¹¹⁵ This key reaction provided a very efficient approach for a direct entry into the basic pentacyclic skeleton of the sarpagine alkaloid system, and permitted introduction of the C-19–C-20 olefinic bond with the *E* configuration in a stereospecific manner. The synthesis began with the tetracyclic ketone **158**, which was subjected to the conditions of catalytic hydrogenation to provide the *N*_a-H, *N*_b-H tetracyclic ketone **164** in 95% yield.

Alkylation of the secondary amine in **164** with (*Z*)-1-bromo-2-iodo-2-butene (**165**), a unit prepared by Ensley et al.¹¹⁶ and employed by Rawal,¹¹³ Bosch¹¹⁴ and Kuehne¹¹⁷ provided the *N*_b-(*Z*)-2'-iodo-2'-butenyl-substituted tetracyclic ketone **166** in 87% yield. The (*Z*)-olefin unit **165** can now be prepared in 500 gram scale regiospecifically and stereoselectively in a 2 pot process in high yield combining the chemistry of Kraft et al. with Cook et al.¹¹⁸ The iodo olefin **166** was subjected to the optimized conditions of the intramolecular palladium-catalyzed cross coupling reaction (3 mol% Pd(OAc)₂, 30 mol% PPh₃) to furnish the cyclized product **167** stereospecifically in 80% yield. Wittig reaction of this ketone was carried out followed by hydrolysis to provide the thermodynamically more stable α-aldehyde in **161**. The first total synthesis of the *N*_a-H substituted sarpagine indole alkaloid (+)-vellosimine (**161**) was accomplished from commercially available D-(+)-tryptophan methyl ester (**156**) in seven reaction vessels in 27% overall yield. The successful stereospecific construction of the sarpagine skeleton via the palladium-catalyzed cross-coupling of enolates with vinyl iodides led to similar strategies for the synthesis of the related sarpagine alkaloids in the *N*_a-

H as well as N_a -methyl series.¹¹⁹ Later in the same year Bonjoch et al. executed a similar process in a different system.¹¹⁴ Piers et al. had run this type of coupling a few years earlier in an aliphatic system.¹²⁰

5.2.2. A Biomimetic Total Synthesis of (+)- N_a -Methylvellosimine (168) by

Martin et al—Martin et al.¹²¹ developed a biogenetic entry into N_a -methylvellosimine (168) which employed an iminium ion-mediated cyclization similar to van Tamelen's original proposal.^{26,122} As shown in Scheme 4, dihydrocarboline 169, which was readily obtained from commercially available D-tryptophan, was allowed to react with the vinyl ketene acetal 170 to afford a single product which was directly converted into the *t*-butyl ester 171. The N_b -acylation of amine 171 with diketene furnished an intermediate β -keto amide that underwent facile cyclization via an intramolecular Michael reaction upon addition of potassium *tert*-butoxide to give keto amide 172. The *E*-ethylidene side chain in amide 173 was obtained in good yield by following the reduction/activation/elimination sequence to give a single geometric isomer as depicted in Scheme 14. The lactam 173 was then methylated at the N_a -indole position, after which the N_a -methyl amide was reduced to the amine 174 in 90% yield.

This was followed by selective acid catalyzed ester hydrolysis in the presence of thioanisole which proceeded smoothly to give the acid 175. The acid moiety in 175 was then transformed into the amide with NH_4OH in the presence of EDCI in 86% yield, followed by dehydration of the amide with trifluoroacetic anhydride to provide the nitrile 176 in 90% yield. The ester group in 176 was selectively reduced in the presence of the cyano group by reaction with lithium borohydride in THF and the subsequent oxidation of the hydroxyl group with Dess–Martin periodinane gave the aldehyde 177 in 83% yield. The aldehyde 177 was then converted into the silyl vinyl ether 178 with TBDMSCl in the presence of NaH. The α -aminonitrile 178 was then treated with $\text{BF}_3 \cdot \text{OEt}_2$ in benzene and this was followed by exposure to aqueous potassium hydroxide in MeOH. The N_a -methylvellosimine (168) was obtained in 54% yield. This biomimetic total synthesis of N_a -methylvellosimine (168) provided experimental support for the iminium ion-mediated cyclization step originally proposed by van Tamelen as one of the key steps in the biosynthesis of the sarpagine and ajmaline alkaloids. It also illustrated that Lounasmaa's criticism of the cyclization process⁹ may be unfounded since he did not use the exact same substrate as van Tamelen.¹²³

5.2.3. Synthesis of (+)- N_a -Methyl-16-*epi*-pericyclivine (180)—Yu et al. reported the synthesis of N_a -methyl-16-*epi*-pericyclivine (180) (Scheme 5).¹¹⁵ The pentacyclic ketone 181 (which was obtained from D-(+)-tryptophan methyl ester (156) in similar was described in Schemes 2 and 3) was subjected to a Wittig reaction, followed by hydrolysis to provide the thermodynamically more stable α -aldehyde in N_a -methylvellosimine (168). Oxidation/esterification of the aldehyde functionality via the method of Yamamoto et al.¹²⁴ using I_2 and KOH in MeOH led to N_a -methyl-16-*epi*-pericyclivine (180). The first total synthesis of (+)- N_a -methyl-16-*epi*-pericyclivine (180) was completed [from D-(+)-tryptophan methyl ester (156)] in an overall yield of 42% (eight reaction vessels).

5.2.4. Synthesis of (–)-Alkaloid Q3 (181), (+)-Normacusine B (162) and (–)-Panarine (182)

—Vellosimine (161) was converted into normacusine B (162) by reduction with NaBH₄ in 90% yield (Scheme 6).¹¹⁵ Similarly reaction of vellosimine (161) with I₂ and KOH in MeOH afforded ester 183 via the process of Yamamoto. The ester 183 on reduction with LiAlH₄ afforded normacusine B (162), in 90% yield. On the other hand, the ester 183 on quaternization with methyl iodide gave the N_b-methiodide salt which on exposure to AgCl was converted into the desired chloride salt of alkaloid Q3 (181). Base-mediated hydrolysis of the ester afforded panarine (182) in 90% yield.¹¹⁵

5.2.5. Synthesis of Trinervine (184) via a Regioselective Hydroboration

Process—Trinervine (184), which retained the basic sarpagine skeleton, contained a unique hemiketal ring formed between the C-17 (OH group) and ketone at C-19. Normacusine B (162) (Scheme 7) was subjected to hydroboration using BH₃/DMS followed by oxidative work up which resulted in secondary alcohol 185 as a borane complex.¹²⁵ Swern oxidation of 185 afforded ketone 186 which on stirring with 10 equivalents of 1 N aqueous HCl in refluxing THF afforded trinervine (184) (80% yield). The acidic conditions at reflux released the free amine, cleaved the TIPS group, as well as catalyzed the hemiketal formation. The total synthesis of trinervine (184) was, therefore, completed in enantiospecific fashion in an overall yield of 20% (from D-tryptophan methyl ester (156), in 10 reaction vessels).¹²⁵

5.2.6. General Approach to Ring A-Alkoxy-Substituted Indole Alkaloids—Due to the difficulty in incorporation of the oxygen functionality into ring-A during the later stages of the synthetic sequence, a synthetic route to such alkaloids would require reaction conditions compatible with these electron-rich systems and installation of the oxygen functionality early in the route.⁸ These alkoxy-substituted indole alkaloids could, presumably, be synthesized from optically active ring-A oxygenated tryptophans *via* the asymmetric Pictet–Spengler reaction in similar fashion to the parent series (refer to Scheme 2). Analogous to the parent system, the synthesis of methoxy-substituted tetracyclic ketones began with the corresponding methoxy-substituted D-tryptophans.¹¹⁹ Due to the electron-rich character of ring A-alkoxylated indoles low yields were obtained in the TFA-mediated asymmetric Pictet–Spengler reaction. Consequently, modifications were made to the earlier conditions to carry out the Pictet–Spengler cyclization and the decarboxylation reaction to achieve optimum yields and very high diastereoselectivity. The Pictet–Spengler reaction of the alkoxytryptophans was carried out with the aldehyde (in place of the acetal) in HOAc to afford a mixture of *trans*- and *cis*-diesters in nearly quantitative yield. On completion of the Pictet–Spengler reaction, one equivalent of TFA was added to epimerize all of the *cis* isomer into the desired *trans*-diester. Dieckmann cyclization of the *trans* diesters (individually) was followed by base-mediated hydrolysis/decarboxylation to provide the optically active tetracyclic ketones in a one-pot process.^{126–130} The successful synthesis of the key ring A-oxygenated tetracyclic ketone templates in a stereospecific fashion (>98% ee) permitted the total synthesis of a number of methoxy-substituted indole alkaloids and the total synthesis of several bisindoles.

In 2002, Zhao et al. reported the first enantiospecific synthesis of the ring-A oxygenated indole alkaloids (+)-majvinine (**187**), (+)-10-methoxyaffinisine (**151**) and (+)-*N*_a-methylsarpagine (**188**) as well as the total synthesis of the bisindole macralstonidine in the 5-methoxy series (Scheme 8).^{128,129}

Optically pure *N*_a-methyl-5-methoxy-D-tryptophan ethyl ester (**189**) (which was synthesized from 3-methyl-5-methoxyindole using the Schöllkopf chiral auxiliary or a Larock heteroannulation process) was converted into tetracyclic ketone **190** via the Pictet–Spengler reaction, and this was followed by the Dieckmann cyclization similar to the parent system. The *N*_b-alkylation and the enolate-mediated palladium-catalyzed cross coupling reaction furnished the pentacyclic ketone **191**. This was converted into the desired aldehyde present in (+)-majvinine (**187**) by a Wittig/hydrolysis/epimerization sequence in 90% yield. (+)-Majvinine (**187**) was obtained in 28% overall yield from *N*_a-methyl-5-methoxy-D-tryptophan ethyl ester (**189**). The aldehyde function of majvinine was reduced with sodium borohydride to provide the natural product (+)-10-methoxyaffinisine (**151**). (+)-Majvinine (**187**) was stirred with 6 equivalents of dry BBr₃ in DCM (degassed) to obtain aldehyde **192**, which was reduced with sodium borohydride to obtain (+)-*N*_a-methylsarpagine (**188**) in 90% yield.^{128,129}

Using a similar sequence Liu et al. achieved the total synthesis of *N*_a-methyl-16-*epi*-gardneral, 11-methoxyaffinisine, 11-methoxymacroline, alstophylline and the bisindole macralstonine in the 6-methoxy series.¹³⁰ Liao et al. later followed and built on Liu's work and completed the total synthesis of alstonerine, 6-oxo-alstonerine, alstophylline, 6-oxo-alstophylline and macralstonine in a much shorter fashion.¹³¹ In the 7-methoxy series, Zhou et al. completed the total synthesis of (+)-12-methoxy-*N*_a-methylvellosimine, (+)-12-methoxyaffinisine and (–)-fuchsiaefoline.^{126,127}

5.2.7. Nature-inspired stereospecific synthesis of (*P*)-(+)-dispegatrine (**193**)—

Edwankar et al. reported the regio- and stereo controlled total synthesis of the bisphenolic, bisquaternary alkaloid (*P*)-(+)-dispegatrine (**193**) (Scheme 9).^{132,133} In this synthesis, 5-methoxy-D-tryptophan ethylester (**194**) was converted into the key tetracyclic core **195** in six steps by an asymmetric Pictet–Spengler process. Using the conditions developed by Bonjoch et al.¹¹⁴ the pentacyclic ketone **196** was obtained in 73% yield. Wittig reaction on **196** was followed by a subsequent hydrolysis/epimerization sequence to provide (+)-10-methoxyvellosimine (**197**), which after sodium borohydride reduction afforded (+)-lochnerine (**152**) in 90% yield. Various methods for oxidative dimerizations were attempted in the formation of the C-9/C-9' biaryl axis in (*P*)-(+)-dispegatrine (**193**). Eventually, thallium(III)-mediated oxidative dimerization was employed. Addition of **152** to the mixture of thallium(III) acetate (0.65 equivalents) and BF₃·OEt₂ (3 equivalents) in acetonitrile at –40 °C was followed by warming up to –10 °C to afford bis-methyl ether analog (*P*)-(+)-**199** as the sole diastereomer. The synthesis is notable especially for execution of the direct oxidative dimerization in the presence of a free indole NH group, the highly basic *N*_b atom, and the C-17 OH group. Starting from 5-methoxy-D-tryptophan ethylester (**194**), (*P*)-(+)-dispegatrine (**193**) was obtained in an overall yield of 8.3% (12 reaction vessels). The axial configuration at the C-9/C-9' biaryl axis was established as *R*(*S*) by analysis of the X-ray

crystal structure of (*P*)-(+)-**199**, the same material which was directly converted into (*P*)-(+)-dispegatrine (**193**). Demethylation of **152** afforded (+)-sarpagine (**2**) which was subjected to *N*_b quaternization with methyl iodide to afford the *N*_b methiodide salt, which upon stirring with silver chloride in ethanol furnished (+)-spegatrine (**198**). Thus, in addition to (+)-dispegatrine (**193**), the first total synthesis of the monomeric indole alkaloids (+)-spegatrine (**198**), (+)-10-methoxyvellosimine (**197**), (+)-lochnerine (**152**), lochvinerine, (+)-sarpagine (**2**), and (+)-lochneram were also achieved during these studies.^{132,133}

5.2.8. Synthesis of (*E*)-16-*Epi*-normacusine B (200**), (*E*)-16-*Epi*-affinisine (**201**), Gardnerine (**202**), Dehydro-16-*epi*-normacusine B (**203**), Dehydro-16-*epi*-affinisine (**204**), and Gardnutine (**205**)**—Yu et al. designed a general synthetic route for the synthesis of (*E*)-16-*epi*-normacusine B (**200**), (*E*)-16-*epi*-affinisine (**201**), 16-*epi*-dehydronormacusine B (**203**), 16-*epi*-dehydroaffinisine (**204**) using a chemospecific, regiospecific hydroboration-oxidation sequence as a key step (Scheme 10).^{134,135} Later Zhou et al. published the synthesis of gardnerine (**202**) and gardnutine (**205**).¹³⁶ These alkaloids have the C-16 hydroxymethyl group present in the *S* configuration. For the synthesis of these bases, the Wittig reaction of the ketones **167**, **181** and **206** using triphenylmethylphosphonium bromide in benzene, in the presence of potassium *t*-butoxide provided the important dienes **207–209** in 85–92% yield. Hydroboration with a bulkier borane 9-BBN or disiamylborane was carried out to facilitate attack at the C-16–C-17 double bond from the less hindered face, similar to the results demonstrated by Magnus et al.¹¹¹ After the hydroboration-oxidation sequence, *S*-alcohols **200–202** were obtained as the only diastereomers in each case. This oxidation completed the total synthesis of (+)-(*E*)-16-*epi*-normacusine B (**200**), (–)-(*E*)-16-*epi*-affinisine (**201**) and (–)-gardnerine (**202**) in 26%, 25% and 20% overall yields, respectively (from the respective tryptophan alkyl esters). Oxidative cyclization of **200–202** effected by DDQ in THF provided the ethers **203–205**. This completed the first total synthesis of (+)-dehydro-16-*epi*-normacusine (**203**), (+)-dehydro-16-*epi*-affinisine (**204**) and gardnutine (**205**) in 25%, 24% and 18% overall yields, respectively.

5.2.9. Total synthesis of the C-Quaternary Alkaloid (+)-Dehydrovoachalotine (210**)**—An interesting C-quaternary center in the voachalotine alkaloid dehydrovoachalotine (**210**) required a slightly different approach. Using a Tollens reaction as a key step, the formation of the prochiral quaternary center at C-16 in the sarpagine related alkaloid was achieved.^{137,138} This established the prochiral hydroxymethyl groups at C-16 without the need for chiral reagents or asymmetric induction.

Reaction of the aldehyde, *N*_a-methylvellosimine (**168**), with 37% aqueous formaldehyde (25 equivalents) and 2N KOH (10 equivalents) in methanol at room temperature for 10 hours afforded optimum yields of the desired diol **211**. The two prochiral hydroxymethyl functions in **211** were differentiated by the DDQ-mediated oxidative cyclization of the hydroxyl group at the β-axial position of C-17 with the benzylic position at C-6. This gave the desired cyclic ether **212**. Oxidation of the hydroxymethyl functionality was achieved with (PhSeO)₂O to provide the aldehyde, which was further oxidized with KOH/I₂/MeOH to the methyl ester

210. Consequently, the total synthesis of (+)-dehydrovoachalotine (**210**) was achieved in 28% overall yield from D-(+)-tryptophan.

5.2.10. Total Synthesis of the 3-Oxygenated Sarpagine Alkaloids: Affinine (213); 16-Epi-affinine (214); Vobasinediol (215) and 16-Epi-vobasinediol (216)—

Sarpagine alkaloids which belong to the family of 3-oxygenated alkaloids are rare, but are an important group of indole alkaloids because they comprise key components of a group of bisindole alkaloids with interesting biological activities.¹³⁹ Yang et al. achieved the first total synthesis of affinine (**213**) and 16-*epi*-affinine (**214**) (Scheme 12).¹¹⁸

In this synthesis the most important transformation was the opening of the C-3–*N*_b bond. To achieve this, the hydroxyl groups in **200** and **162** were first protected as the TIPS ether by reaction with TIPSOTf separately in each case. The amines **217** and **218** were then treated with Cbz-Cl in the presence of water. This resulted in Cbz protection of the *N*_b nitrogen atom followed by the C-3–*N*_b bond cleavage to afford tertiary alcohols **219** and **220**, respectively. Reduction of the Cbz group with LiAlH₄ led to the corresponding *N*_b-Me derivatives which were treated with TBAF to afford vobasinediol (**215**) and 16-*epi*-vobasinediol (**216**). Oxidation with activated MnO₂ gave the natural products affinine (**213**) and 16-*epi*-affinine (**214**).

5.2.11. Total Synthesis of C-19 Methyl-substituted Sarpagine Alkaloids: 19(*S*), 20(*R*)-Dihydroperaksine (29); 19(*S*),20(*R*)-Dihydroperaksine-17-al (30) and Peraksine (223)—

Edwankar et al. reported a detailed account of a general strategy for the first enantiospecific synthesis of the C-19 methyl-substituted alkaloids, including the total synthesis of 19(*S*),20(*R*)-dihydroperaksine-17-al, 19(*S*),20(*R*)-dihydroperaksine, and peraksine (Scheme 13).^{140,141} In order to install the C-19 methyl functionality in the tetracyclic ketone **164**,¹⁴² the *N*_b-H group was alkylated with the optically active *R*-tosylate **224** (which was in turn obtained from the *R* propargylic alcohol via a 2-step sequence) in acetonitrile/K₂CO₃, followed by treatment with tetrabutylammonium fluoride hydrate to obtain the acetylenic ketone **225** in 96% yield. The terminal alkyne in **225** was converted into the iodo-olefin functionality by treating with dicyclohexylidoborane [I-B(Cy)₂], followed by protonolysis. The iodo-olefin **226** was obtained in 74% yield. It was subjected to a Pd-catalyzed α-vinylation to obtain the key C-19 methyl-substituted pentacyclic system **227**. This was followed by a Wittig/hydrolysis/epimerization sequence at C-16 to provide the thermodynamically more stable C-17 α-aldehyde **228**, even in the presence of the C-19 methyl group in the β position. The aldehyde group was then protected as a cyclic acetal in **229** and this was followed by the hydroboration-oxidation sequence to obtain the desired primary alcohol **230**, accompanied by a trace of the tertiary alcohol (in the ratio 25:1) in 88% yield. A modified Corey–Kim oxidation (with less equivalents of the reagent and lower temperature) was used to obtain the α-aldehyde **231** as a sole product (after addition of a large excess of triethylamine to induce any epimerization) in 67% yield. Reduction with sodium borohydride followed by cleavage of the acetal group under acidic conditions led to the synthesis of 19(*S*),20(*R*)-dihydroperaksine-17-al (**30**) (10.2% yield; 14 reaction vessels). Reduction of 19(*S*),20(*R*)-dihydroperaksine-17-al (**30**) with sodium borohydride afforded 19(*S*),20(*R*)-dihydroperaksine (**29**) (9.6% yield; 15 reaction vessels).

For the synthesis of peraksine (**223**), the aldehyde functionality of **228** was converted into a dimethyl acetal in 93% yield and this was followed by hydroboration/oxidation to mono-alcohol **233** (Scheme 14). Upon heating the mono-alcohol **233** under acidic conditions the hemiacetal ring was formed intramolecularly to obtain peraksine (**223**) as an epimeric mixture at C-17 in 52% yield.¹⁴¹

5.2.12. Enantioselective, Protecting-Group-Free Total Synthesis of Sarpagine Alkaloids—Recently Krüger and Gaich published a very interesting “protecting-group-free” approach to the synthesis of substituted sarpagine alkaloids.¹⁴³ The idea was to synthesize a common intermediate or “privileged intermediate” which could be elaborated into sarpagine alkaloids. Reaction of oxidopyridinium ion **234** with Aggarwal’s chiral ketene equivalent **235**¹⁴⁴ in the presence of DIPEA in DCM afforded the cycloadduct **236** via a [5+2] cycloaddition reaction (Scheme 15). The cycloadduct **236** was obtained in a 2:1 ratio in favor of the desired regioisomer and 93% ee. The bis(sulfoxide) group was reduced to obtain dithiolane **237** in 68% yield. Treatment of **237** with L-selectride afforded ketone **238**. Intramolecular palladium-catalyzed enolate coupling using conditions developed by Bonjoch et al.¹¹⁴ afforded the tricyclic ketone **239**. Wittig reaction at the ketone functionality followed by deprotection of the dithiolane moiety with Meerwein’s salt afforded ketone **240** in 58% yield over two steps. A ring enlargement reaction using trimethylsilyldiazomethane on **240** resulted in exclusive insertion of the methylene group into the sterically less hindered side to afford **241** in 80% yield. This was followed by the Fischer indole synthesis with substituted phenylhydrazines **242a–c**. The corresponding dimethyl acetal indole intermediates **244** were formed in situ (observed by ¹H NMR). Hydrolysis resulted in the synthesis of (+)-vellosimine (**161**), (+)-N_a-methylvellosimine (**168**), and (+)-10-methoxyvellosimine (**197**) in 52–63% yield, respectively.

5.3. Total Synthesis of Macroline Indole Alkaloids

5.3.1. Total Synthesis of Talcarpine (245)—In this synthesis tetracyclic ketone **158** was converted into α,β -unsaturated aldehyde **246** in 87% yield (Scheme 16).¹⁴² Reaction of aldehyde **246** with a barium Grignard (formed in situ from *trans*-1-bromo-2-pentene and activated barium metal) at –78 °C provided alcohol **247** in 90% yield. This was followed by treatment of allylic alcohol **247** with KH in dioxane which led to the anionic oxy-Cope rearrangement from the bottom face of the 15,16-double bond to afford aldehyde **248** as the sole product (after stirring the reaction mixture with methanol to convert the minor diastereomer into **248**). Regiospecific N_a-methylation was followed by reduction of the aldehyde functionality with sodium borohydride to afford alcohol **249** in high yield. Treatment of olefin **249** with a premixed solution of OsO₄-pyridine in THF at 0 °C for 8h, followed by further treatment with NaIO₄, resulted in the oxidative cleavage of the olefinic unit followed by cyclization to give the hemi-acetal **250** in 75% yield. Vinyl ether **251** was obtained after dehydration of **250** with *p*-TSA in refluxing benzene. The regiospecific oxyselelenation of the olefin **251** was carried out with *N*-(phenylseleno)phthalimide in CH₂Cl₂/methanol at 0 °C in the presence of *p*-TSA. This was followed by treatment with NaIO₄ in THF-MeOH-H₂O solution at 0 °C for 10 hours to afford acetal **252** (major isomer; 4:1 ratio) in 90% combined yield. Acid-catalyzed hydrolysis of acetal **252** followed by conjugate addition provided a mixture of diastereomeric aldehydes in a ratio of 5:3 with

253a (combined yield = 90%) predominating. The minor diastereomer **253b** could be separated from the mixture and converted into the desired ether **253a** by pyrolysis. Treatment of ether **253a** with 1.5 equivalents of Pd/C, in the presence of H₂ in methanol resulted in a N_b-benzyl/N_b-methyl transfer process to afford talcarpine (**245**) in 90% yield. The total synthesis of (–)-talcarpine (**245**) was then accomplished in 13 steps in 10% yield.¹⁴²

5.3.2. Total Synthesis of 11-Methoxymacroline (254)—The synthesis of 11-methoxymacroline (**254**) began with N_a-methyl-6-methoxy-D-tryptophan ethyl ester (**255**) (obtained from *p*-methoxy-iodoaniline) (Scheme 17).¹³⁰ Ester **255** was converted into 11-methoxyaffinisine (**256**) under a similar sequence developed for the synthesis of 10-methoxyaffinisine (refer to Scheme 8).¹²⁹ The primary alcohol group in 11-methoxyaffinisine (**256**) was protected as the TIPS ether **257**, which was then subjected to regiospecific hydroboration-oxidation of the olefinic bond (Scheme 17). The secondary alcohol **258** (obtained as borane adduct) was then subjected to Swern oxidation followed by treatment with 1N aq HCl to remove the boron complex provided the intermediate ketone **259**. A modified retro-Michael ring-opening process (similar to LeQuesne et al.)¹⁷ on ketone **259** afforded the α,β-unsaturated ketone **260**, which was stirred with TBAF to afford 11-methoxymacroline (**254**) in 86% yield.

5.3.3. Total Synthesis of Suaveoline (261) by Bailey and Morgan—Trudell¹⁴⁵ had originally achieved a total synthesis of (±)-suaveoline from (±)-tryptophan and in 1992 Fu et al.¹⁴⁶ finished a total synthesis of (–)-suaveoline via the asymmetric Pictet–Spengler reaction. In 2000 Bailey and Morgan developed a synthesis of (–)-suaveoline starting from L-tryptophan.¹¹⁰ In this synthesis the (*S*)-3-amino-4-(1H-indol-3-yl)butanenitrile (**262**) was treated with the silyl protected 3-hydroxypropionaldehyde **263** to obtain the *cis*-1,3-disubstituted tetrahydro-β-carboline **264** as a single isomer in 82% yield via *cis*-specific Pictet–Spengler reaction (Scheme 18). After N_b-benzylation, N_a-methylation and removal of the TBDPS group, the alcohol thus obtained, was oxidized to cyanoaldehyde **265**. A Horner–Wadsworth–Emmons reaction was employed on aldehyde **265** with phosphonate **266** (prepared in situ) which afforded the bis-nitrile **267**. A vinylogous Thorpe cyclization on **267** afforded the tetracyclic dinitrile **268** (isolated as a mixture of diastereomers) in 67% yield. DIBAL-H reduction of the nitrile groups was followed by reaction with hydroxylamine hydrochloride in EtOH at reflux. This process resulted in cyclization and aromatization to afford **269**. A catalytic debenzoylation on **269** afforded (–)-suaveoline (**261**). From L-tryptophan, (–)-suaveoline (**261**) was obtained in approximately 14% yield.

5.3.4. Total Synthesis of Suaveoline (261) via an Intramolecular Diels–Alder Reaction—Ohba et al. achieved the total synthesis of (–)-suaveoline using a very interesting intramolecular hetero Diels–Alder strategy as a key step (Scheme 19).¹⁴⁷ In this approach, N_b-Boc-protected L-tryptophan methyl ester **270** was treated with α-lithiated methyl isocyanide to afford oxazole **271**. The removal of the Boc group was followed by coupling with monoethyl malonate to afford amide **272** in 88% yield. The Bischler–Napieralski cyclization using POCl₃ afforded enamino ester **273** in 50% yield. Stereoselective hydrogenation using Pearlman's catalyst afforded tetrahydro-β-carboline **274**

as a single diastereomer in 84% yield, which was then converted into a *N*-Boc derivative **275** by reacting with di-*tert*-butyl dicarbonate. The Boc-protected ester **275** was then reduced to aldehyde **276**, and this was followed by a Wittig reaction using triphenyl(*n*-propyl)phosphonium bromide to afford olefin **277** in 73% yield. The key step, an intramolecular Diels–Alder reaction, was carried out by heating **277** in xylene at reflux in the presence of DBN (1,5-diazabicyclo[4.3.0]-non-5-ene) to afford pyridine **278** in 69% yield. An *N*_a-methylation was followed by removal of the *N*_b-Boc group to finish in the synthesis of (–)-suaveoline **261** in 80% yield.

5.3.5. Total Synthesis of 6-Oxoalstophylline (**279**) Utilizing a Modified Wacker Oxidation

—Liao et al. published the first enantiospecific synthesis of (+)-6-oxoalstophylline (**279**) in 2005.¹³¹ The reduction of 16-*epi*-*N*_a-methylgardneral (**280**)¹³⁰ (obtained from *N*_a-methyl-6-methoxy-D-tryptophan ethyl ester (**255**) in 7 steps; Scheme 8) was followed by TIPS protection of the 17-hydroxyl group (using TIPSOTf/2,6-lutidine) and the hydroboration-oxidation reaction sequence to afford the borane adduct **258** (Scheme 20). The removal of the borane from the *N*_b-BH₃ complex by stirring it in 5 equivalents of Na₂CO₃ in refluxing MeOH provided the free amine **281** in 90% yield. Oxidation of **281** with IBX (4 equivalents, sequentially) at 80 °C afforded the diketone **282** in 85% yield. *N*_b-methylation of **282** with MeI, followed by a base-catalyzed retro–Michael reaction gave the desired 11-methoxy-6-oxomacrolin derivative **283** in 90% yield. The 11-methoxy-6-oxomacrolin derivative **283** was then subjected to the optimized modified Wacker oxidation conditions (40 mol% of Na₂PdCl₄, 1.5 equivalents of *t*-BuOOH and a solvent system comprised of HOAc/H₂O/dioxane (1/3/3) with 1 equivalent of NaOAc at 80 °C. This resulted in a domino process by loss of the TIPS group, followed by carbon-oxygen bond formation, to afford (+)-6-oxoalstophylline (**279**) in 57% yield.

5.4. Total Synthesis of Oxindole Alkaloids

5.4.1. Synthesis of Alstonisine (153**)**—In 2002 Wearing et al. published the stereospecific total synthesis of (+)-alstonisine.¹⁴⁸ Using a similar sequence as employed for the synthesis of talcarpine (**245**) by Yu et al.¹⁴² (Scheme 16), vinyl ether **251** was synthesized from D-tryptophan methyl ester (**156**) via tetracyclic ketone **158** (Scheme 21). The regiospecific oxyselenation of the olefin **251** was carried out with *N*-phenylselenophthalimide in CH₂Cl₂/methanol at 0 °C in the presence of *p*-TSA, and this was followed by treatment with NaIO₄ in THF/MeOH/H₂O solution at 0 °C for 10 hours to afford acetal **252** as a mixture of *Z/E* isomers in 4:1 ratio in 90% combined yield. Reaction of the mixture of olefins **252** with BH₃·THF complex at 0 °C and oxidation with H₂O₂, followed by Swern oxidation of the resulting alcohol, afforded keto acetal **284** in 80% yield. The treatment of indole **284** with OsO₄ in pyridine/THF led to an oxidative rearrangement of the keto acetal **284** via the dihydroxylated indole and subsequent pinacol rearrangement. Spiro[pyrrolidine-3,3'-oxindole] **285** was obtained as the sole diastereomer in 81% yield. The rationale for this selective transformation is the complexation of osmium tetroxide to the piperidine nitrogen atom, which resulted in the intramolecular attack of the osmium reagent from the convex face of the ketoacetal **284**. The synthesis of (+)-alstonisine (**153**) was completed from oxindole **285** by deprotection of the *N*_b-nitrogen atom, followed by base-induced elimination of methanol. The total synthesis of (+)-alstonisine was accomplished in

an overall yield of 12% from D-tryptophan methyl ester (**156**). This corrected an earlier structural error in the literature wherein a report of an X-ray crystal structure by Nordman et al. had misdrawn the absolute configuration at the spirocyclic center.¹⁴⁹ The structure had been earlier represented as the enantiomer of alstonisine, which was incorrect. The structure of synthetic alstonisine was confirmed as illustrated by X-ray crystallography at low temperature, extensive NMR and IR comparisons with natural alstonisine from *A. muelleriana* as well as the optical rotation. The sample of naturally occurring (+)-alstonisine was kindly provided by Professor Philip LeQuesne.

5.4.2. Stereospecific Synthesis of Sarpagine-related (–)-Affinisine Oxindole

(118)—Recently Fonseca et al. published a stereospecific synthesis of (–)-affinisine oxindole (**118**).¹⁵⁰ The key debenzylated tetracyclic ketone **164** was subjected to the important oxidation/rearrangement sequence using *t*BuOCl as an oxidant to afford the oxindole **286** in diastereospecific fashion in 80% yield (Scheme 22). The observed diastereoselectivity results from the attack of Cl⁺ from the less hindered convex face to form the chloroindolenine intermediate which undergoes pinacol type rearrangement from the opposite face of the C–Cl bond to provide oxindole **286**. Chemoselective methylation of the indole nitrogen atom afforded oxindole **287** in 80% yield. Alkylation at the N₆ nitrogen atom proved very difficult and several trials resulted in the optimized conditions in which amine **287** was heated with (*Z*)-1-bromo-2-iodo-2-butene (**165**) at 50 °C under solvent-free conditions to afford olefin **288** in 90% yield as the sole diastereomer. A palladium-catalyzed enolate coupling process on ketone **288** using Bonjoch et al.'s conditions¹¹⁴ afforded pentacyclic ketone **289** in 65% yield. The Wittig reaction on ketone **300** was followed by acidic hydrolysis of the vinyl ether to provide aldehyde **290**. Reduction of the aldehyde group with NaBH₄ resulted in the synthesis of (–)-affinisine oxindole (**118**) in 34% yield (over 3 steps). Consequently, the stereospecific total synthesis of the sarpagine-related (–)-affinisine oxindole (**118**) was accomplished in 11 steps and in 10% yield from D-(+)-tryptophan (**155**).

5.5. Total Synthesis of Sarpagine Related Ajmaline Alkaloids

5.5.1. Stereocontrolled Total Synthesis of (–)-Vincamajinine (291)—Yu et al. published a very elegant synthesis of (–)-vincamajinine (**291**) in 2005.¹⁵¹ In this approach, reaction of N_a-methylvellosimine (**168**) with 37% aqueous formaldehyde (25 equivalents) and 2N KOH (10 equivalents) in methanol at room temperature, afforded diol **211** via a Tollen's reaction (Scheme 23). Selective oxidation of the axial 16-hydroxymethyl group was achieved with TPAP to provide aldehyde **292** with > 10:1 diastereoselectivity in 78% yield. Treatment of aldehyde **292** with a mixture of TFA/Ac₂O in a sealed tube, made the conjugate acid carbocation of the aldehyde sufficiently electrophilic to cyclize to the indoleninium salt, which was then trapped as the diacetate **293** in 84% yield. This cyclization stereospecifically provided the kinetic product with the 17(*R*) stereochemistry. Acid-assisted reduction of the carbinolamine function in indoline **293** with Et₃SiH/TFA exclusively furnished the C2(α)-H stereochemistry in indoline **294** in 90% yield. Alkaline hydrolysis of the diacetate **294** furnished the diol **295** in 87% yield. Careful oxidation of **295** first with 1.2 equivalents of Dess–Martin periodinane, followed by isolation of the ketone and then reaction with an additional 1.5 equivalents of Dess–Martin periodinane provided

the best yield of the desired β -oxoaldehyde **296** (78% for two steps). The C-16 aldehyde group in **296** was then converted into the methyl ester **297** by the method of Yamamoto et al. and this was followed by reduction of the C-17 ketone in **297** with NaBH₄ to provide (–)-vincamajinine (**291**) in 11.8% overall yield (from D-tryptophan **155**).

5.5.2. Stereocontrolled Total Synthesis of (–)-11-Methoxy-17-*epi*-vincamajine (298**)**—Following a similar route, Wearing and Yu et al. also synthesized (–)-11-methoxy-17-*epi*-vincamajine (**298**) from (+)-*N*_a-methyl-16-*epi*-gardneral (**280**)¹³⁰ in 8 steps.¹⁵¹ In this synthesis all the steps were similar to those used for the synthesis of (–)-vincamajinine (**291**), except the Dess–Martin periodinane oxidation of the diol intermediate could be achieved in one pot to afford the β -oxoaldehyde in 65% yield. Overall (–)-11-methoxy-17-*epi*-vincamajine (**298**) was obtained in 8.4% yield in 14 reaction steps (from *N*_a-methyl-6-methoxy-D-tryptophan).

6. PERSPECTIVE

Indole alkaloids of the sarpagine/macroline/ajmaline type comprise one of the largest groups of structurally related indole natural products. New alkaloids of this type are being isolated with an increasing frequency from plant sources worldwide. Since 2000, a total of 119 new sarpagine related alkaloids have been isolated. Classical natural product chemistry approach is transitioning to newer “-omics” strategies as a result of the advent of advanced analytical platforms and instrumentation, which may increase the frequency of identification and isolation of yet uncharacterized indole alkaloids. Interest in the synthesis of this group of natural products will continue to increase because of the anticancer, anti-inflammatory, antimalarial, antiamebic, antituberculosis, antileishmanial, and antiarrhythmic activity exhibited by some of them. The asymmetric Pictet–Spengler reaction remains a key reaction for the construction of these complex units in enantiospecific fashion. Novel ways to construct these interesting complex natural products, as well as their analogs will continue to be developed.

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Figure 1.
Sarpagine, Macroline and Ajmaline Alkaloids

Figure 2.
Biosynthetic relationship between sarpagine and macroline.

Figure 3.
Biosynthetic relationship between sarpagine and ajmaline alkaloids.

Figure 4.
 Structures of some of the sarpagine-related indole alkaloids exhibiting important biological activity

Figure 5.
Structures of some key sarpagine indole alkaloids.

Scheme 2.

Reagents and conditions: (a) satd HCl/MeOH, reflux, 6 h; 14% aq NH₄OH; (b) PhCHO/CH₃OH, rt, 6 h; NaBH₄, -10 °C, 4 h; (c) (OMe)₂CH(CH₂)₂COOMe, TFA (2.4 equiv), DCM, rt, 10 d, 83%, one pot or CHCl₃, TFA, 1 day; (d) toluene, NaH (8 equiv), MeOH, reflux, 72 h; HOAc, HCl, H₂O, reflux, 10 h, 80% overall yield (150 g scale); (e) MeI, NaH, DMF, 0 °C to rt, 2 h, >95%; (f) toluene, NaH (3 equiv), MeOH, reflux, 6 h; HOAc, HCl, H₂O, reflux, 10 h, 80% overall yield (600 g scale).

Scheme 3.

Reagents and conditions: (a) 5% HCl-ethanol, Pd/C, H₂ (1 atm), rt, 12 h, 95%; (b) THF, K₂CO₃, rt, 24 h, 87%; (c) Pd(OAc)₂, PPh₃, Bu₄NBr, K₂CO₃, DMF/H₂O (9:1), 70 °C, 5 h, 80%; (d) [MeOCH₂PPh₃]Cl, benzene, KO^tBu, rt, 24 h; (e) HCl (2 N aq), THF, reflux, 6 h, 73% (2 steps).

Scheme 4.

Reagents and conditions: (a) MeCN, 0 °C, 30 min; then Me₂C=CH₂, H₂SO₄, 1,4-dioxane ; 59% (2 steps); (b) diketene, DMAP, PhMe, *t*BuOK, 86%; (c) NaBH₄, 95%; NaOMe, MeOH, 50 °C, then AcCl, 89%; (d) MeI, NaH; Me₃OBF₄, 2,6-*t*Bu₂py, then NaBH₄, 90% (2 steps); (e) CF₃COOH, PhSMe, 90%; (f) EDCI, NH₄OH, 86%; (g) (CF₃CO)₂O, pyridine, CH₂Cl₂, 90%; (h) LiBH₄, THF, 98%; DMP, CH₂Cl₂, pyridine, 83%; (i) TBDMSCl, NaH, THF; (j) BF₃ · OEt₂, benzene; (k) aq KOH, MeOH, 54% (2 steps).

Scheme 5.

Reagents and conditions: (a) $[\text{MeOCH}_2\text{PPh}_3]\text{Cl}$, KO^tBu , benzene, rt, 24h; 2N HCl/THF, 55 °C, 5h, 90%; (b) KOH/I_2 , MeOH, rt, 2h, 88%.

Scheme 6.

Reagents and conditions: (a) KOH/I₂, MeOH, rt, 2h, 88%; (b) NaBH₄, THF, 0 °C, 12h, 90%; (b') LiAlH₄, THF, reflux, 2h, 90%; (c) MeI, MeOH, rt, 4h, 90%; AgCl, MeOH, 85%; (d) 0.1N NaOH, then 0.1N HCl, 90%.

Scheme 7.

Reagents and conditions: (a) TIPSCl, imidazole, DMF, rt, 90%; BH₃·DMS (9 equiv), THF, rt, 3 h; 3 N NaOH, H₂O₂, 2 h, 90%; (b) (COCl)₂, -78 °C; Et₃N, 75%; (c) 1 N aq HCl (10 equiv), THF, reflux, 3 h, 80%

Scheme 8.

Reagents and conditions: (a) $[\text{MeOCH}_2\text{PPh}_3]\text{Cl}$; KO^tBu , benzene, rt, 24h; 2N HCl/THF , 55 °C, 90%; (b) $\text{NaBH}_4/\text{MeOH}$, 0 °C, 90%; (c) DCM , 6eq BBr_3 , -78 °C-rt, 81%; (d) $\text{NaBH}_4/\text{EtOH}$, 0 °C, 90%

Scheme 9.

Reagents and conditions: (a) $\text{Pd}(\text{PPh}_3)_4$, PhOH ; KO^tBu , THF, reflux, 73%; (b) $[\text{MeOCH}_2\text{PPh}_3]\text{Cl}$; KO^tBu , benzene, rt, 24h; 2N HCl /THF, 55 °C, 90%; (c) NaBH_4 /MeOH, 0 °C-rt, 90%; (d) BBr_3 , DCM, -78 °C-rt, 80%; (e) MeI /MeOH, rt; then AgCl , MeOH, rt, 85%; (f) $\text{Ti}(\text{OCOMe})_3$, $\text{BF}_3\cdot\text{OEt}_2$, MeCN, -40 °C to -10 °C, 60% b.r.s.m.

Scheme 10.

Reagents and conditions: (a) PPh_3CH_3Br , $KOt-Bu$, benzene, rt, 2–4h, 85–92%; (b) 9-BBN; $NaOH/H_2O_2$, rt, 70–80%; (c) DDQ, THF, reflux, 1h, 92–98%

Scheme 11.

Reagents and conditions: (a) 37% aq HCHO, KOH, MeOH, 85–92%; (b) DDQ, THF, reflux, 90–95%; (c) (PhSeO)₂O, PhCl, reflux, 92%; KOH/I₂, MeOH, 90%

Scheme 12.

Reagents and conditions: (a) TIPSOTf, 2,6-lutidine, DCM, 0 °C, 2h, 82–85%; (b) Cbz-Cl, THF-H₂O, Na₂CO₃, 71–77%; (c) LiAlH₄, THF, rt, 12h, 70–78%; (d) TBAF, THF, 0 °C, 3–4 h, 85–90%; (e) MnO₂, DCM, 82–92%

Scheme 13.

Reagents and conditions: (a) K_2CO_3 , MeCN, 75 °C, 81%; (b) I-B(Cy)₂, DCM, 0 °C-rt, MeCOOH; NaOH/H₂O₂, 0 °C-rt, 74%; (c) Pd₂(dba)₃, (Oxydi-2,1-phenylene)bis(diphenylphosphine) [DPEPhos], NaOtBu, THF, 70 °C, 60%; (d) [MeOCH₂PPh₃]₂Cl, KO^tBu, benzene, rt; 2N aq HCl, THF, 55 °C; (e) ethylene glycol, pTSA·H₂O, benzene, reflux (Dean-Stark trap); (f) BH₃·DMS, THF, rt, 2h; NaBO₃·4H₂O, rt; Na₂CO₃, MeOH, reflux, 5h, 73%; (g) NCS/DMS, DCM, -5 °C to -10 °C; 0.5h, cool to -78 °C; NEt₃ (16 equivalents), warm to rt, 3h, 67%; (h) NaBH₄, EtOH, 0 °C-rt, 94%; (i) 1.38N aq HCl, acetone/H₂O, 70 °C, 96%.

Scheme 14.

Reagents and conditions: (a) pTSA·H₂O, MeOH, CHCl₃, reflux, 6h; BH₃·DMS, THF, rt, 2h, NaBO₃·4H₂O; Na₂CO₃, MeOH, reflux, 5h, 35%; (b) 1N aq HCl, THF, reflux, 1d, 52%.

Scheme 15.

Reagents and conditions: (a) *i*-Pr₂NEt, DCM, 12h, 77%; (b) TFAA, NaI, MeCN, 0 °C, 68%; (c) L-selectride, THF, -78 °C, 94%; (d) KO^tBu, PhOH, Pd(PPh₃)₄, THF, reflux, 88%; (e) MeOCHPPh₃; then TFA, DCM, Me₃OBf₄, 58%; (f) TMSCH₂N₂, *n*BuLi, THF, then MeOH; then silica, 80%; (g) AcCl, MeOH, ; then (h) H₂O, , 52–63% over two steps.

Scheme 16.

Reagents and conditions: (a) ClCH_2SOPh , LDA/THF, -78°C , KOH(aq), rt; LiClO_4 /dioxane, reflux, 24h, 87% overall yield; (b) Li/biphenyl/ BaI_2 , THF, -78°C , *trans*-1-bromo-2-pentene, 90%; (c) KH/dioxane/18-crown-6, 100°C , 14h; MeOH, rt, 4h, 88%; (d) NaH, MeI, THF, rt, 6h, 95%; NaBH_4 , MeOH, 95%; (e) OsO_4 /THF/py, NaHSO_3 ; NaIO_4 , H_2O , MeOH, 0°C , 3h, 75%; (f) benzene/*p*-TSA, reflux (Dean-Stark trap), 5h, 95%; (g) *p*-TSA/MeOH/ *N*-(phenylseleno)phthalimide; NaIO_4 / H_2O /THF/MeOH, 0°C , 10h, 90%; (h) 5% H_2SO_4 , H_2O , rt, 3d, 90% (combined yield); (i) 10^{-1} torr, 100°C , 75%; (j) Pd/C (1.5 equiv), MeOH, H_2 , rt, 5h, 90%.

Scheme 17.

Reagents and conditions: (a) KHMDS, TIPSCl, THF, 90%; (b) $\text{BH}_3 \cdot \text{DMS}$ (9 equivalents), THF, rt; $\text{NaOH}/\text{H}_2\text{O}_2$, rt, 90%; (c) DMSO, $(\text{COCl})_2$, CH_2Cl_2 , -78°C ; NEt_3 , -78°C to rt; (d) aq HCl (1 equiv), THF, reflux, 90%; (e) MeI, THF; $\text{KO}^t\text{-Bu}$ (1.5 equiv.), THF/EtOH (6:1), reflux, 90%; (f) TBAF, THF, rt, 6h, 86%.

Scheme 18.

Reagents and conditions: (a) 3 Å MS, DCM, 0 °C, 60h; then TFA, -78 °C to rt, 6h, 82%; (b) BnBr (neat), NaHCO₃, 70 °C, 24h, 79%; (c) NaH, MeI, DMF, 0 °C, 1h, 100%; (d) TBAF, THF, rt, 2h, 83%; (e) DMSO, (COCl)₂, DCM, -60 °C, 20 min; then NEt₃, -60 °C to rt, 1h, 100%; (f) NaH, DMF, 0 °C, 1h, 83%; (g) KO^tBu, THF, 0 °C to rt, 10 min, 67%; (h) DIBAL-H, DCM, -78 °C to rt, 24h; then NH₂OH·HCl, EtOH, reflux, 24h, 53%; (i) HCl, EtOH; then evaporate, Pd/C, H₂, EtOH, 66%.

Scheme 19.

Reagents and conditions: (a) MeNC, *n*-BuLi, THF, 82%; (b) TFA, DCM, 0 °C, 4h, 98%; (c) HOOCCH₂COOEt, (EtO)₂P(O)CN, NEt₃, DMF, 88%; (d) POCl₃(neat), rt, 6 days, then Na₂CO₃, 50%; (e) Pd(OH)₂/C, EtOH, H₂ (1 atm), 84%; (f) (Boc)₂O, CHCl₃, reflux, 87%; (g) DIBAL-H, DCM, -78 °C, 80 min, 95%; (h) Ph₃P⁺(CH₂)₂MeBr⁻, KO^{*t*}Bu, benzene, rt, 73%; (i) DBN, xylene, 9h, 69%; (j) NaH, MeI, DMF, 20 min, rt; (k) TFA, DCM, 0 °C, 80% (two steps).

Scheme 20.

Reagents and conditions: (a) NaBH_4 , EtOH, 0 °C, 95%; (b) TIPSOTf, 2,6-lutidine, DCM, 0 °C, 90%; (c) $\text{BH}_3\cdot\text{DMS}$ (9 equivalents), THF, rt; $\text{NaOH}/\text{H}_2\text{O}_2$, rt, 2 h, 90%; (d) Na_2CO_3 (5 equivalents), MeOH, reflux, 92%; (e) IBX (4 equiv.), EtOAc, DMSO, 80 °C, 85%; (f) MeI, THF; K_2CO_3 , THF, reflux, 90%; (g) $t\text{BuOOH}$, Na_2PdCl_4 , NaOAc, HOAc/ H_2O /dioxane (1:3:3), 80 °C, 57–60%.

Scheme 21.

Reagents and conditions: (a) *p*-TSA/MeOH/*N*-phenylselenophthalimide; NaIO₄/H₂O/THF/MeOH, 0 °C, 10h, 90%; (b) BH₃·THF, THF, 0 °C, 14 h; NaOH (3N), H₂O₂, 85%; (c) (COCl)₂, DMSO/DCM; NEt₃, 1.5 h, 80%; (d) OsO₄ (1 equivalent), THF/pyridine, rt, 3 days; aq NaHSO₃, rt, 4 h, 81%; (e) Pd(OH)₂/C (2 equivalents), EtOH, H₂, rt, 5h; 2N NaOH/MeOH, rt, 2 h, 86%.

Scheme 22.

Reagents and conditions: (a) *t*BuOCl, NEt₃, DCM, rt, 5h; aq AcOH/MeOH, reflux, 2h, 80%; (b) NaH, THF, 0 °C; MeI, THF, 0 °C-rt, 80%; (c) DIPEA (2.5 equivalents), 50 °C, 90%; (d) Pd(PPh₃)₄, PhONa·3H₂O, THF, reflux, 2h, 65%; (e) [MeOCH₂PPh₃]Cl, KO^{*t*}Bu, benzene, rt, 24 h; 2N aq HCl, THF, 55 °C; (f) NaBH₄, EtOH, rt, 8h, 34% (over 3 steps).

Scheme 23.

Reagents and conditions: (a) 37% aq HCHO, KOH, MeOH, 90%; (b) TPAP, NMO, 4 Å MS, DCM, rt, 12 h, 78%; (c) TFA, Ac₂O, sealed vessel, rt, 6 h, 84%; (d) TFA, Et₃SiH, DCM, 3 d, 90%; (e) 20% aq K₂CO₃, MeOH, rt, 20 h, 87%; (f) Dess–Martin periodinane (1.2 equivalents), DCM, rt, 1h, 87%; (g) Dess–Martin periodinane (1.5 equivalents), DCM, rt, 0.5 h, 90%; (h) KOH/I₂, MeOH, rt, 92%; (i) NaBH₄, EtOH, 0 °C, 1h, 90%.

Scheme 24.

Synthesis of (-)-11-methoxy-17-*epi*-vincamajine (**298**)

Table 1

Recently isolated sarpagine-related indole alkaloids

Mol. mass	Mol. Form.	Compound name	Plant source	Ref
296.1525	C ₁₈ H ₂₀ N ₂ O ₂	Alstofoline A (75)	<i>Alstonia macrophylla</i>	65
308.1889	C ₂₀ H ₂₄ N ₂ O	19,20-Z-Affinisine (39)	<i>Alstonia macrophylla</i>	65
310.1681	C ₁₉ H ₂₂ N ₂ O ₂	19(S),20(R)-Dihydroperaksine-17-al (30)	<i>Rauwolfia serpentina</i>	66
310.1681	C ₁₉ H ₂₂ N ₂ O ₂	Ervahainanmine (40)	<i>Ervatamia hainanensis</i>	67
312.1838	C ₁₉ H ₂₄ N ₂ O ₂	19(S),20(R)-Dihydroperaksine (29)	<i>Rauwolfia serpentina</i> <i>Rauwolfia tetraphylla</i>	66 68
312.1838	C ₁₉ H ₂₄ N ₂ O ₂	Norsandwicine (100)	<i>Rauwolfia nukuhivensis</i>	69
312.1838	C ₁₉ H ₂₄ N ₂ O ₂	Isonorsandwicine (101)	<i>Rauwolfia nukuhivensis</i>	69
316.1787	C ₁₈ H ₂₄ N ₂ O ₃	Alstonoxine E (113)	<i>Alstonia angustifolia</i>	70
322.1681	C ₂₀ H ₂₂ N ₂ O ₂	N(1)-Demethylalstonerine (80)	<i>Alstonia angustifolia</i>	70
322.1681	C ₂₀ H ₂₂ N ₂ O ₂	N(1)-Demethylalstonerinal (81)	<i>Alstonia angustifolia</i>	70
324.1838	C ₂₀ H ₂₄ N ₂ O ₂	Affinisine oxindole (118)	<i>Alstonia angustifolia</i>	65,71
324.1474	C ₁₉ H ₂₀ N ₂ O ₃	N(1)-Demethylalstonisine (116)	<i>Alstonia macrophylla</i> <i>Alstonia angustifolia</i>	65,72 71
324.1474	C ₁₉ H ₂₀ N ₂ O ₃	N(1)-Demethylalstonal (117)	<i>Alstonia macrophylla</i> <i>Alstonia angustifolia</i>	72 71
324.1838	C ₂₀ H ₂₄ N ₂ O ₂	Rauverine A (86)	<i>Rauwolfia verticillata</i>	73
326.1630	C ₁₉ H ₂₂ N ₂ O ₃	Alstofoline B (76)	<i>Alstonia angustifolia</i>	70
326.1630	C ₁₉ H ₂₂ N ₂ O ₃	3-Hydroxysarpagine (32)	<i>Rauwolfia serpentina</i> <i>Rauwolfia tetraphylla</i>	74 68
326.1994	C ₂₀ H ₂₆ N ₂ O ₂	Macrocarpine E (67)	<i>Alstonia angustifolia</i>	70
326.1994	C ₂₀ H ₂₆ N ₂ O ₂	Macrocarpine F (68)	<i>Alstonia angustifolia</i>	70
326.1994	C ₂₀ H ₂₆ N ₂ O ₂	Macrocarpine G (69)	<i>Alstonia angustifolia</i>	70
326.1994	C ₂₀ H ₂₆ N ₂ O ₂	Macrocarpine D (66)	<i>Alstonia macrophylla</i> <i>Alstonia angustifolia</i>	65 75
328.1787	C ₁₉ H ₂₄ N ₂ O ₃	Alstonoxine A (109)	<i>Alstonia macrophylla</i> <i>Alstonia angustifolia</i>	65,72 71
328.1787	C ₁₉ H ₂₄ N ₂ O ₃	Macrogentine A (115)	<i>Alstonia angustifolia</i>	70
328.1787	C ₁₉ H ₂₄ N ₂ O ₃	10-Hydroxy-19(S),20(R)-dihydroperaksine (31)	<i>Rauwolfia serpentina</i> <i>Rauwolfia tetraphylla</i>	66 68
330.1943	C ₁₉ H ₂₆ N ₂ O ₃	Alstonoxine B (110)	<i>Alstonia macrophylla</i> <i>Alstonia angustifolia</i>	65,72 71
330.1943	C ₁₉ H ₂₆ N ₂ O ₃	Isoalstonoxine B (114)	<i>Alstonia angustifolia</i>	70
338.1630	C ₂₀ H ₂₂ N ₂ O ₃	Rauverine B (48)	<i>Rauwolfia verticillata</i>	73
338.1630	C ₂₀ H ₂₂ N ₂ O ₃	Isoalstonisine (107)	<i>Alstonia macrophylla</i> <i>Alstonia angustifolia</i>	65,72 71
338.1994	C ₂₁ H ₂₆ N ₂ O ₂	19-Epi-talcarpine (60)	<i>Alstonia angustifolia</i>	70
338.1994	C ₂₁ H ₂₆ N ₂ O ₂	Rauverine C (49)	<i>Rauwolfia verticillata</i>	73
338.1994	C ₂₁ H ₂₆ N ₂ O ₂	Hystrixnine (33)	<i>Tabernaemontana hystrix</i>	76
338.1994	C ₂₁ H ₂₆ N ₂ O ₂	20,21-Dihydroalstonerine (77)	<i>Alstonia macrophylla</i>	65
339.2067	C ₂₁ H ₂₇ N ₂ O ₂ ⁺	N(4)-Methyltalpinine (42)	<i>Alstonia angustifolia</i>	77

Mol. mass	Mol. Form.	Compound name	Plant source	Ref
339.2067	C ₂₁ H ₂₇ N ₂ O ₂ ⁺	N(4)-Methyl-19-<i>epi</i>-talpinine (44)	<i>Alstonia angustifolia</i>	70
324.1838	C ₂₀ H ₂₄ N ₂ O ₂	Affinisine oxindole (118)	<i>Alstonia angustifolia</i>	71
340.1787	C ₂₀ H ₂₄ N ₂ O ₃	7(S)-Talpinine oxindole (119)	<i>Alstonia angustifolia</i>	70
340.1787	C ₂₀ H ₂₄ N ₂ O ₃	Alstoyunine A (46)	<i>Alstonia yunnanensis</i>	78
340.1787	C ₂₀ H ₂₄ N ₂ O ₃	Alstoyunine B (47)	<i>Alstonia yunnanensis</i>	78
340.2151	C ₂₁ H ₂₈ N ₂ O ₂	Macrocarpine A (63)	<i>Alstonia macrophylla</i>	79
340.2151	C ₂₁ H ₂₈ N ₂ O ₂	Macrocarpine B (64)	<i>Alstonia macrophylla</i>	79
341.2224	C ₂₁ H ₂₉ N ₂ O ₂ ⁺	N_b-Methylisosandwicine (102)	<i>Rauwolfia nukuhivensis</i>	69
341.2224	C ₂₁ H ₂₉ N ₂ O ₂ ⁺	N_b-Methylajmaline (87)	<i>Rauwolfia serpentina</i>	74
341.2224	C ₂₁ H ₂₉ N ₂ O ₂ ⁺	N_b-Methylisoajmaline (88)	<i>Rauwolfia serpentina</i>	74
342.1580	C ₁₉ H ₂₂ N ₂ O ₄	Nortueiaoine (83)	<i>Rauwolfia nukuhivensis</i>	69
342.1943	C ₂₀ H ₂₆ N ₂ O ₃	Rauvotetraphylline A (85)	<i>Rauwolfia tetraphylla</i>	68
352.1787	C ₂₁ H ₂₄ N ₂ O ₃	N(1)-Demethylalstophylline (61)	<i>Alstonia macrophylla</i>	79
352.1787	C ₂₁ H ₂₄ N ₂ O ₃	N(1)-Demethylalstophyllal (62)	<i>Alstonia macrophylla</i>	79
352.1787	C ₂₁ H ₂₄ N ₂ O ₃	Voacalgine B (71)	<i>Voacangagrandifolia</i>	80
352.1787	C ₂₁ H ₂₄ N ₂ O ₃	Alstolactone A (79)	<i>Alstonia angustifolia</i>	70
352.1787	C ₂₁ H ₂₄ N ₂ O ₃	10-Methoxy-16-de(methoxycarbonyl)pagicerine (41)	<i>Rauwolfia yunnanensis</i>	81
353.1860	C ₂₁ H ₂₅ N ₂ O ₃ ⁺	10-Methoxypanarine (45)	<i>Rauwolfia nukuhivensis</i>	69
354.1943	C ₂₁ H ₂₆ N ₂ O ₃	Macrogentine (108)	<i>Alstonia macrophylla</i> <i>Alstonia angustifolia</i>	72 71
356.1736	C ₂₀ H ₂₄ N ₂ O ₄	Tueiaoine (84)	<i>Rauwolfia nukuhivensis</i>	69
356.2100	C ₂₁ H ₂₈ N ₂ O ₃	Rauvoyunine A (59)	<i>Rauwolfia yunnanensis</i>	82
358.1893	C ₂₀ H ₂₆ N ₂ O ₄	Alstonoxine C (111)	<i>Alstonia macrophylla</i>	65
360.2049	C ₂₀ H ₂₈ N ₂ O ₄	Alstonoxine D (112)	<i>Alstonia macrophylla</i>	65
366.1580	C ₂₁ H ₂₂ N ₂ O ₄	Alstofoline (120)	<i>Alstonia macrophylla</i>	65,72
366.1943	C ₂₂ H ₂₆ N ₂ O ₃	Alstofonidine (78)	<i>Alstonia angustifolia</i>	70
366.1943	C ₂₂ H ₂₆ N ₂ O ₃	O-Acetyltalpinine (43)	<i>Alstonia angustifolia</i>	70
366.1943	C ₂₂ H ₂₆ N ₂ O ₃	10-Methoxyalstonerine (82)	<i>Tabernaemontana dichotoma</i>	83
368.1736	C ₂₁ H ₂₄ N ₂ O ₄	19Z-16-<i>epi</i>-Voacarpine (38)	<i>Gelsemium sempervirens</i>	84
370.2256	C ₂₂ H ₃₀ N ₂ O ₃	Macrocarpine H (70)	<i>Alstonia angustifolia</i>	70
382.1529	C ₂₁ H ₂₂ N ₂ O ₅	Alstoyunine C (105)	<i>Alstonia yunnanensis</i>	78
382.1893	C ₂₂ H ₂₆ N ₂ O ₄	Alstiphyllanine H (90)	<i>Alstonia macrophylla</i>	85
382.1893	C ₂₂ H ₂₆ N ₂ O ₄	Vincamajine N(4)-oxide (98)	<i>Alstonia macrophylla</i>	65
382.1893	C ₂₂ H ₂₆ N ₂ O ₄	Gelsempervine-A (34)	<i>Gelsemium sempervirens</i>	84
382.2256	C ₂₃ H ₃₀ N ₂ O ₃	Macrocarpine C (65)	<i>Alstonia macrophylla</i>	79
382.1893	C ₂₂ H ₂₆ N ₂ O ₄	10-Methoxyraucafrinoline (103)	<i>Vinca herbacea</i> <i>Vinca major</i>	86 87
382.1893	C ₂₂ H ₂₆ N ₂ O ₄	Gelsempervine-C (36)	<i>Gelsemium sempervirens</i>	84
390.1943	C ₂₄ H ₂₆ N ₂ O ₃	Rauvotetraphylline D (104)	<i>Rauwolfia tetraphylla</i>	68
398.1478	C ₂₁ H ₂₂ N ₂ O ₆	Alstoyunine D (106)	<i>Alstonia yunnanensis</i>	78

Mol. mass	Mol. Form.	Compound name	Plant source	Ref
424.1998	C ₂₄ H ₂₈ N ₂ O ₅	Gelsempervine-D (37)	<i>Gelsemium sempervirens</i>	84
424.1998	C ₂₄ H ₂₈ N ₂ O ₅	Gelsempervine-B (35)	<i>Gelsemium sempervirens</i>	84
424.1998	C ₂₄ H ₂₈ N ₂ O ₅	Alstiphyllanine A (89)	<i>Alstonia macrophylla</i>	88
432.2049	C ₂₆ H ₂₈ N ₂ O ₄	Voacalgine E (74)	<i>Voacanga grandifolia</i>	80
434.2206	C ₂₆ H ₃₀ N ₂ O ₄	Voacalgine D (73)	<i>Voacanga grandifolia</i>	80
438.2519	C ₂₆ H ₃₄ N ₂ O ₄	Macrodasine H (57)	<i>Alstonia macrophylla</i>	65
438.2519	C ₂₆ H ₃₄ N ₂ O ₄	Voacalgine C (72)	<i>Voacanga grandifolia</i>	80
451.2471	C ₂₆ H ₃₃ N ₃ O ₄	Alstopirocine (58)	<i>Alstonia angustifolia</i>	89
452.2311	C ₂₆ H ₃₂ N ₂ O ₅	Macrodasine C (52)	<i>Alstonia angustifolia</i>	75
452.2311	C ₂₆ H ₃₂ N ₂ O ₅	Macrodasine B (51)	<i>Alstonia macrophylla</i> <i>Alstonia angustifolia</i>	79 75
454.2468	C ₂₆ H ₃₄ N ₂ O ₅	Macrodasine A (50)	<i>Alstonia macrophylla</i> <i>Alstonia angustifolia</i>	65,79,90 75
454.2468	C ₂₆ H ₃₄ N ₂ O ₅	Macrodasine D (53)	<i>Alstonia angustifolia</i>	75
454.2468	C ₂₆ H ₃₄ N ₂ O ₅	Macrodasine F (55)	<i>Alstonia angustifolia</i>	75
454.2468	C ₂₆ H ₃₄ N ₂ O ₅	Macrodasine G (56)	<i>Alstonia angustifolia</i>	75
454.2468	C ₂₆ H ₃₄ N ₂ O ₅	Macrodasine E (54)	<i>Alstonia angustifolia</i>	75
456.2049	C ₂₈ H ₂₈ N ₂ O ₄	Alstiphyllanine N (96)	<i>Alstonia macrophylla</i>	91
498.2155	C ₃₀ H ₃₀ N ₂ O ₅	Alstiphyllanine K (93)	<i>Alstonia macrophylla</i>	91
516.2260	C ₃₀ H ₃₂ N ₂ O ₆	Alstiphyllanine L (94)	<i>Alstonia macrophylla</i>	91
546.2366	C ₃₁ H ₃₄ N ₂ O ₇	Alstiphyllanine M (95)	<i>Alstonia macrophylla</i>	91
546.2366	C ₃₁ H ₃₄ N ₂ O ₇	Alstiphyllanine O (97)	<i>Alstonia macrophylla</i>	91
546.2366	C ₃₁ H ₃₄ N ₂ O ₇	Vincamajine 17-O-veratrate N(4)-oxide (99)	<i>Alstonia macrophylla</i>	65
558.2366	C ₃₂ H ₃₄ N ₂ O ₇	Alstiphyllanine I (91)	<i>Alstonia macrophylla</i>	91
588.2472	C ₃₃ H ₃₆ N ₂ O ₈	Alstiphyllanine J (92)	<i>Alstonia macrophylla</i>	91
630.3570	C ₄₀ H ₄₆ N ₄ O ₃	Lumutinine E (137)	<i>Alstonia angustifolia</i>	92
644.3726	C ₄₁ H ₄₈ N ₄ O ₃	Lumutinine D (136)	<i>Alstonia macrophylla</i>	93
646.3519	C ₄₀ H ₄₆ N ₄ O ₄	Villalstonidine F (143)	<i>Alstonia macrophylla</i>	94
646.3519	C ₄₀ H ₄₆ N ₄ O ₄	Leuconoline (132)	<i>Leuconotis griffithii</i>	95
650.3468	C ₃₉ H ₄₆ N ₄ O ₅	Villalstonidine A (138)	<i>Alstonia angustifolia</i>	92
660.3676	C ₄₁ H ₄₈ N ₄ O ₄	Lumutinine C (135)	<i>Alstonia macrophylla</i>	93
662.3832	C ₄₁ H ₅₀ N ₄ O ₄	Perhentsine B (130)	<i>Alstonia angustifolia</i>	92
662.3832	C ₄₁ H ₅₀ N ₄ O ₄	Perhentsine C (131)	<i>Alstonia angustifolia</i>	92
672.3676	C ₄₂ H ₄₈ N ₄ O ₄	Lumutinine A (133)	<i>Alstonia macrophylla</i>	93
672.3676	C ₄₂ H ₄₈ N ₄ O ₄	Lumutinine B (134)	<i>Alstonia macrophylla</i>	93
675.3905	C ₄₂ H ₅₁ N ₄ O ₄ ⁺	Villalstonidine D (141)	<i>Alstonia angustifolia</i>	92
676.3625	C ₄₁ H ₄₈ N ₄ O ₅	Villalstonidine C (140)	<i>Alstonia angustifolia</i>	92
676.3989	C ₄₂ H ₅₂ N ₄ O ₄	Perhentsine A (129)	<i>Alstonia angustifolia</i>	92
686.3832	C ₄₃ H ₅₀ N ₄ O ₄	Lumusidine A (122)	<i>Alstonia macrophylla</i>	94
686.3832	C ₄₃ H ₅₀ N ₄ O ₄	Lumusidine D (125)	<i>Alstonia macrophylla</i>	94

Mol. mass	Mol. Form.	Compound name	Plant source	Ref
690.3781	C ₄₂ H ₅₀ N ₄ O ₅	Villalstonidine B (139)	<i>Alstonia angustifolia</i>	92
704.3938	C ₄₃ H ₅₂ N ₄ O ₅	Perhentidine B (127)	<i>Alstonia macrophylla</i> <i>Alstonia angustifolia</i>	96 96
704.3938	C ₄₃ H ₅₂ N ₄ O ₅	Perhentinine (121)	<i>Alstonia macrophylla</i> <i>Alstonia angustifolia</i>	79,92,96 79,92
704.3938	C ₄₃ H ₅₂ N ₄ O ₅	Lumusidine B (123)	<i>Alstonia macrophylla</i>	94
704.3938	C ₄₃ H ₅₂ N ₄ O ₅	Perhentidine A (126)	<i>Alstonia macrophylla</i> <i>Alstonia angustifolia</i>	96 96
704.3938	C ₄₃ H ₅₂ N ₄ O ₅	Perhentidine C (128)	<i>Alstonia angustifolia</i> <i>Alstonia macrophylla</i>	92,96 96
709.3515	C ₄₂ H ₅₀ Cl N ₄ O ₄ ⁺	Villalstonidine E (142)	<i>Alstonia angustifolia</i>	92
732.4251	C ₄₅ H ₅₆ N ₄ O ₅	Lumusidine C (124)	<i>Alstonia macrophylla</i>	94

Table 2

Sarpagine-type indole alkaloids

19(S) 20(R)-Dihydroperaksine (**29**)
m.p. 208-212 °C [65]
[α]_D²⁵ +35.3 (c 0.12; C₆H₅N)

19(S) 20(R)-Dihydroperaksine-17-al (**30**)
m.p. 156-159 °C [65]
[α]_D²⁵ +50 (c 0.07; MeOH)

10-Hydroxy-
19(S) 20(R)-dihydroperaksine (**31**)
m.p. 323-335 °C [65]
[α]_D²⁵ +42.6 (c 0.15; C₆H₅N)

3-Hydroxysarpagine (**32**)
m.p. NR [73]
[α]_D²¹ +44 (c 1.0; MeOH)

Hystrixnine (**33**)
Amorphous [75]
[α]_D²⁵ -100 (c 0.66; MeOH)

Gelsempervine-A (**34**)
Amorphous [83]
NR

Gelsempervine-B (**35**)
Amorphous [83]
NR

Gelsempervine-C (**36**)
Amorphous [83]
NR

Gelsempervine-D (**37**)
Amorphous [83]
NR

NR: Not Reported

19Z-16-Epi-voacarpine (**38**)
Amorphous [83]
NR

19,20-Z-Affinisine (**39**)
Oil [64]
[α]_D²⁵ +8 (c 0.45; CHCl₃)

Ervahainanmine (**40**)
Amorphous [66]
[α]_D²⁰ +6.1 (c 0.33; MeOH)

10-Methoxy-16-de(methoxycarbonyl)pagicerine (**41**)
Amorphous [80]
[α]_D²⁴ -97 (c 0.58; C₆H₅N)

N(4)-Methyltalpinine (**42**)
Resin [76]
[α]_D²³ -10.0 (c 0.1; MeOH)

O-Acetyltalpinine (**43**)
Oil [69]
[α]_D -8.0 (c 0.2; CHCl₃)

N(4)-Methyl-19-epitalpinine (**44**)
Oil [69]
[α]_D -4 (c 0.2; CHCl₃)

10-Methoxypanarine (**45**)
Amorphous [68]
[α]_D²⁰ +0.4 (c 0.1; MeOH)

Alstoyunine A (**46**)
m.p. 147-148 °C (MeOH) [77]
[α]_D²⁰ -74.3 (c 0.6; MeOH)

Alstoyunine B (**47**)
Amorphous [77]
[α]_D²⁰ -69 (c 0.26; MeOH)

Rauverine B (**48**)
m.p. NR [72]
[α]_D²⁰ -45 (c 0.1; MeOH)

Rauverine C (**49**)
m.p. NR [72]
[α]_D²⁰ 0 (c 0.44; MeOH)

NR: Not Reported

NR: Not Reported

Table 3

Macroline-type indole alkaloids

Macrodasine A (**50**)
m.p. 149-154 °C (EtOH); [64, 78, 89]
[α]_D²⁵ +36.0 (c 0.36; CHCl₃)

Macrodasine B (**51**)
Oil [78]
[α]_D²⁵ +149.0 (c 0.07; CHCl₃)

Macrodasine C (**52**)
Oil [74]
[α]_D²⁵ -45.0 (c 0.14; CHCl₃)

Macrodasine D (**53**)
Oil [74]
[α]_D²⁵ -12.0 (c 0.10; CHCl₃)

Macrodasine E (**54**)
Oil [74]
[α]_D²⁵ +20.0 (c 0.28; CHCl₃)

Macrodasine F (**55**)
Oil [74]
[α]_D²⁵ -51.0 (c 0.40; CHCl₃)

Macrodasine G (**56**)
Oil [74]
[α]_D²⁵ -50.0 (c 0.27; CHCl₃)

Macrodasine H (**57**)
Oil [64]
[α]_D²⁵ -11.0 (c 0.14; CHCl₃)

Alstopirocine (**58**)
Oil [88]
[α]_D²⁵ +146.0 (c 0.29; CHCl₃)

Rauvofylline A (**59**)
Amorphous [81]
[α]_D²⁵ +5.5 (c 0.10; MeOH)

19-Epi-talcarpine (**60**)
Oil [69]
[α]_D²⁵ -59.0 (c 0.20; MeOH)

N(1)-Demethylalstophylline: R₁ = H; R₂ = COMe (**61**)
N(1)-Demethylalstophyllal: R₁ = Me; R₂ = CHO (**62**)
Inseparable mixt [78]

Macrocarpine A [**63**]
Oil [78]
[α]_D +117.0 (c 0.11; CHCl₃)

Macrocarpine B [**64**]
Oil [78]
[α]_D -51.0 (c 0.34; CHCl₃)

Macrocarpine C [**65**]
Oil [78]
[α]_D -35.0 (c 1.55; CHCl₃)

Macrocarpine D [**66**]
Oil [64]
[α]_D²⁵ -43.0 (c 0.89; CHCl₃)

Macrocarpine E (**67**)
Oil [69]
[α]_D²⁵ -12.0 (c 0.8; CHCl₃)

Macrocarpine F (**68**)
Oil [69]
[α]_D²⁵ +38.0 (c 0.6; CHCl₃)

Macrocarpine G (**69**)
Oil [69]
[α]_D²⁵ +7.0 (c 1.1; CHCl₃)

Macrocarpine H (**70**)
Oil [69]
[α]_D²⁵ -17.0 (c 0.3; CHCl₃)

Voacalgine B (**71**)
Amorphous [79]
[α]_D²⁷ -67.0 (c 1.0; CHCl₃)

Voacalgine C (**72**)
Amorphous [79]
[α]_D²² -22.0 (c 0.5; CHCl₃)

Voacalgine D (**73**)
Amorphous [79]
[α]_D²⁴ -6.0 (c 1.0; MeOH)

Voacalgine E (**74**)
Amorphous [79]
[α]_D²² -14.0 (c 0.5; MeOH)

Alstofoline A (**75**)
Oil [64]
[α]_D²⁵ -104.0 (c 0.36; CHCl₃)

Alstofoline B (**76**)
Oil [69]
[α]_D -63.0 (c 0.3; CHCl₃)

20,21-Dihydroalstonerine (**77**)
Oil [64]
[α]_D²⁵ -31.0 (c 0.11; CHCl₃)

Alstofonidine (**78**)
Oil [69]
[α]_D -75.0 (c 0.1; CHCl₃)

Alstolactone A (**79**)
Oil [69]
[α]_D +110 (c 0.1; CHCl₃)

10-Methoxalstonerine (**82**)
Amorphous [82]
[α]_D²⁴ -91 (c 1.0; CHCl₃)

N(1)-Demethylalstonerine; R₁ = COMe; R₂ = H (**80**)
N(1)-Demethylalstonerinal; R₁ = CHO; R₂ = Me (**81**)
Inseparable mixture (5:1) [69]

Nortueiaoine (**83**)
Amorphous [68]
[α]_D²⁰ -1.1 (c 0.1; MeOH)

Tueiaoine (**84**)
Amorphous [68]
[α]_D²⁰ +1.2 (c 0.1; MeOH)

Rauvotetraphylline A (**85**)
Amorphous [67]
[α]_D¹⁶ +16.2 (c 0.2; MeOH)

Rauverine A (**86**)
m.p. ND [72]
[α]_D²⁰ +16 (c 0.33; MeOH)

Table 4

Ajmaline-type indole alkaloids

*N*₆-Methylajmaline (**87**)
Amorphous [73]
[α]_D²⁸ +113 (c 1.1; MeOH)

*N*₆-Methylisoajmaline (**88**)
Amorphous [73]
[α]_D²¹ +88 (c 1.2; MeOH)

Alstiphyllanine A (**89**)
Amorphous [87]
[α]_D²⁴ -83 (c 1.0; MeOH)

Alstiphyllanine H (**90**)
Amorphous [84]
[α]_D²⁶ -21 (c 1.0; MeOH)

Alstiphyllanine I (**91**)
Amorphous [90]
[α]_D²⁶ -90 (c 1.0; MeOH)

Alstiphyllanine J (**92**)
Amorphous [90]
[α]_D²⁶ -94 (c 1.0; MeOH)

Alstiphyllanine K (**93**)
Amorphous [90]
[α]_D²⁶ -20 (c 1.0; MeOH)

Alstiphyllanine L (**94**)
Amorphous [90]
[α]_D²⁶ -68 (c 1.0; MeOH)

Alstiphyllanine M (**95**)
Amorphous [90]
[α]_D²⁶ -62 (c 1.0; MeOH)

Alstiphyllanine N **[96]**
Amorphous [90]
[α]_D²⁶ -62 (c 1.0; MeOH)

Alstiphyllanine O **[97]**
Amorphous [90]
[α]_D²⁶ -53 (c 1.0; MeOH)

Vincamajine *N*(4)-oxide **[98]**
Oil [64]
[α]_D²⁵ -29 (c 0.04; CHCl₃)

Vincamajine 17-O-veratrate *N*(4)-oxide **(99)**
Oil [64]
[α]_D²⁵ -75 (c 0.94; CHCl₃)

Norsandwicine **(100)**
Amorphous [68]
[α]_D²⁰ +51 (c 0.1; MeOH)

*N*₆-Methylisosandwicine **(102)**
Amorphous [68]
[α]_D²⁰ +35.6 (c 0.1; MeOH)

Isonorsandwicine **(101)**
Amorphous [68]
[α]_D²⁰ +52.9 (c 0.1; MeOH)

10-Methoxyraucaffrinoline **(103)**
Amorphous [85, 86]
[α]_D²⁵ +2.2 (c 0.27; CHCl₃)

Rauvotetraphylline D **(104)**
Amorphous [67]
[α]_D¹⁴ +26.5 (c 0.2; CHCl₃)

Alstoyunine C **(105)**
m.p. 293-295 °C (MeOH) [77]
[α]_D²⁰ -111.7 (c 0.2; MeOH)

Alstoyunine D **(106)**
Amorphous [77]
[α]_D²⁰ -27.8 (c 0.28; MeOH)

Table 5

Macroline/sarpagine-related oxindole alkaloids

Isoalstonisine (107)
m.p. NR [64, 71]
[α]_D +207 (c 0.07; CHCl₃)

Macrogentine (108)
m.p. NR [71]
[α]_D -21 (c 0.15; CHCl₃)

Alstonoxine A (109)
m.p. NR [64, 71]
[α]_D -34 (c 0.19; CHCl₃)

Alstonoxine B (110)
m.p. NR [64, 71]
[α]_D -12 (c 0.41; CHCl₃)

Alstonoxine C (111)
m.p. 130-132 °C (CH₂Cl₂-hexane) [64]
[α]_D²⁵ -30 (c 0.39; CHCl₃)

Alstonoxine D (112)
Oil [64]
[α]_D²⁵ -16 (c 0.23; CHCl₃)

Alstonoxine E (113)
m.p. 110-122 °C (CHCl₃); [69]
[α]_D -25 (c 1.1; CHCl₃)

Isoalstonoxine B (114)
Oil [69]
[α]_D +55 (c 0.6; CHCl₃)

Macrogentine A (115)
Oil [69]
[α]_D -7.1 (c 0.1; CHCl₃)

NR: Not Reported

N(1)-Demethylalstonisine $R_1 = H$; $R_2 = \text{COMe}$ (**116**)
N(1)-Demethylalstonal $R_1 = \text{Me}$; $R_2 = \text{CHO}$ (**117**)
 (1:6; inseparable mixt) [71]

Affinisine oxindole (**118**)
 Oil [70]
 $[\alpha]_D -70$ (c 0.06; CHCl_3)

7(*S*)-Talpinine oxindole (**119**)
 Oil [69]
 $[\alpha]_D -4$ (c 0.2; CHCl_3)

Alstofoline (**120**)
 m.p. NR [64]
 $[\alpha]_D +39$ (c 0.21; CHCl_3)

NR: Not Reported

NR: Not Reported

Table 6

Bisindole alkaloids containing macroline/sarpagine monomeric units

Perhentinine (**121**)
Oil [78, 91, 95]
[α]_D -61 (c 1.19; CHCl₃)

Lumusidine A (**122**)
Oil [93]
[α]_D -138 (c 0.24; CHCl₃)

Lumusidine B (**123**)
Oil [93]
[α]_D -59 (c 0.73; CHCl₃)

Lumusidine C (**124**)
Oil [93]
[α]_D -16 (c 0.21; CHCl₃)

Lumusidine D (**125**)
m.p. >270 °C [93]
[α]_D -161 (c 0.38; CHCl₃)

Perhentidine A (**126**)
Oil [95]
[α]_D²⁵ -77 (c 0.4; CHCl₃)

Perhentidine B (**127**)
Oil [95]
[α]_D²⁵ -38 (c 0.52; CHCl₃)

Perhentidine C (**128**)

Oil [91, 95]

$[\alpha]_D^{25}$ -73 (c 0.5; CHCl_3)

Perhentisine A (**129**)

Oil [91]

$[\alpha]_D^{25}$ +13 (c 0.59; CHCl_3)

Perhentisine B (**130**)

Oil [91]

$[\alpha]_D^{25}$ +22 (c 0.1; MeOH)

Perhentisine C (**131**)

Oil [91]

$[\alpha]_D^{25}$ +17 (c 0.6; CHCl_3)

Leuconoline (**132**)

m.p. 223-224 °C (EtOH) [94]

$[\alpha]_D$ +142 (c 0.49; CHCl_3)

Lumutinine A (**133**)

Oil [92]

$[\alpha]_D^{25}$ +160 (c 0.4; CHCl_3)

Lumutinine B (**134**)
Oil [92]
 $[\alpha]_D^{25} -11$ (c 0.5; CHCl₃)

Lumutinine C (**135**)
Oil [92]
 $[\alpha]_D^{25} +84$ (c 0.32; CHCl₃)

Lumutinine D (**136**)
Oil [92]
 $[\alpha]_D^{25} +209$ (c 0.4; CHCl₃)

Lumutinine E (**137**)
Oil [91]
 $[\alpha]_D +74$ (c 0.14; CHCl₃)

Villastonidine A (**138**)
Oil [91]
[α]_D +22 (c 0.35; CHCl₃)

Villastonidine B (**139**)
Oil [91]
[α]_D +101 (c 0.58; CHCl₃)

Villastonidine C (**140**)
Oil [91]
[α]_D +43 (c 0.19; CHCl₃)

Villastonidine D (**141**)
Oil [91]
[α]_D +38 (c 0.89; CHCl₃)

Villastonidine E (**142**)
Oil [91]
[α]_D +29 (c 0.67; CHCl₃)

Villastonidine F (**143**)
Oil [93]
[α]_D +40 (c 0.10; CHCl₃)