

ALKALOIDS OF HEDYCARYA ANGUSTIFOLIA

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**Abstract** - Four new alkaloids, 6,6a-dehydronorlaureline (7), isosevanine (10), isowariopsine (12), and O-methylcinnamolarine (14) have been isolated from H. angustifolia, and their structures have been determined. The plant also contains the known aporphines corydine (1), laurotetanine (2), boldine (3), glaucine (4), and laureline (5).

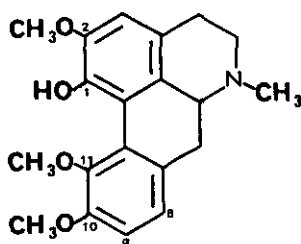
## RESULTS AND DISCUSSION

Material from the monimiaceous plant Hedycarya angustifolia A. Cunn., which grows in rain-forests of south-eastern Australia, was collected from King Island in Bass Strait, the southern limit of its distribution, and extracted by standard procedures. Small amounts of crude alkaloids were obtained, accompanied by considerable quantities of persistent non-basic impurities. These could not be completely removed by continuous extraction of the crude bases in dilute mineral acid over a prolonged period with ether; however, droplet countercurrent chromatography (dccc)<sup>19</sup> proved effective in removing the remaining neutral contaminants, and in partially separating the bases from one another. The individual alkaloids were finally isolated from the dccc fractions and purified by preparative tlc.

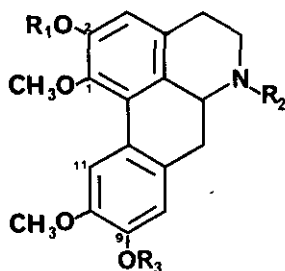
The alkaloid content was found to be small and variable: the maximum amount obtained, from autumn collections in two separate years, was ca.  $2 \times 10^{-3}\%$ , and material collected in winter from the same location furnished no alkaloids at all. Of the nine bases found, five were identified as known aporphines. The uv spectrum of one of the latter indicated that it was a 1,2,10,11-substituted aporphine<sup>1</sup>, and this substitution pattern was supported by the <sup>1</sup>H nmr spectrum which showed a doublet of doublets corresponding to the H-8 and H-9 protons. The latter spectrum also indicated the presence of an N-methyl group, and three methoxyls, all of which appeared to be too deshielded<sup>2,3</sup> to be located at C-1. These data suggested that the alkaloid had structure 1, which was confirmed by comparison with an authentic sample of corydine<sup>4</sup>. Another alkaloid from the same dccc fraction turned out from uv<sup>1</sup> and <sup>1</sup>H nmr data to be a 1,2,9,10-substituted noraporphine; the <sup>1</sup>H nmr spectrum in particular indicated the

presence of a highly deshielded aromatic proton corresponding to H-11<sup>3</sup>, and three methoxyls of which one must be located at C-1 from its high chemical shift<sup>2,3</sup>. The uv spectrum showed a prominent bathochromic shift above 300 nm on addition of alkali, typical of an aporphine with a phenolic group at C-9<sup>5</sup>. Structure 2 suggested by these data was confirmed by comparison with an authentic sample of laurotetanine<sup>4</sup>.

Amongst the other aporphines obtained was an isomer of laurotetanine with the same 1,2,9,10 pattern of substitution including an hydroxyl group at C-9, as shown by the uv and <sup>1</sup>H



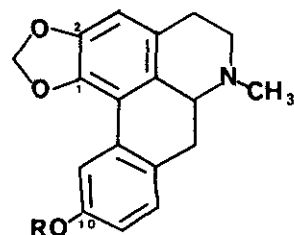
1 Corydine



2 Laurotetanine  
R<sub>1</sub>=CH<sub>3</sub>, R<sub>2</sub>=R<sub>3</sub>=H

3 Boldine  
R<sub>1</sub>=R<sub>3</sub>=H, R<sub>2</sub>=CH<sub>3</sub>

4 Glaucine  
R<sub>1</sub>=R<sub>2</sub>=R<sub>3</sub>=CH<sub>3</sub>



5 Laureline  
R=CH<sub>3</sub>

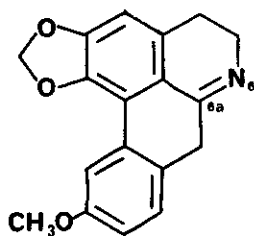
6 Mecambroline  
R=H

nmr spectra; however, the latter spectrum also indicated the presence of an N-methyl group, and two methoxyls of which one must be attached at C-1 from the high chemical shift<sup>2,3</sup> of its protons; this location was supported by the strong (M-31)<sup>+</sup> peak in the ms<sup>5</sup>. The spectroscopic evidence suggested that the compound was boldine (3)<sup>4</sup>, and this was confirmed by comparison with an authentic sample.

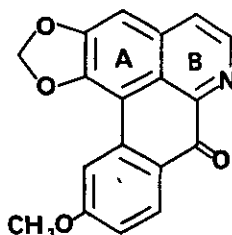
An aporphine isolated from another docc fraction proved to have the same 1,2,9,10-substitution pattern as the two above-mentioned bases, but it was found to be a higher homologue with four methoxyls and an N-methyl group. Structure 4 was confirmed by comparison with an authentic sample of glaucine<sup>4</sup>. The remaining aporphine had a uv spectrum that indicated 1,2,10-trisubstitution<sup>1</sup>, and this was supported by the pattern of aromatic signals in the <sup>1</sup>H nmr spectrum. The latter also showed the presence of methylenedioxy, N-methyl, and methoxy groups; the evidence thus pointed to structure 5, which was confirmed by comparison with a sample of laureline<sup>4</sup> prepared by O-methylation of mecambroline (6)<sup>4</sup>.

Another alkaloid with a methoxyl and a methylenedioxy group like laureline (5) did not, however, correspond with any previously reported base. The uv spectrum of the new alkaloid

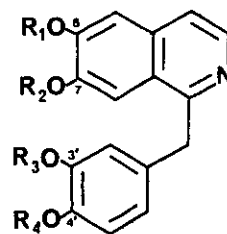
resembled that of 5, but it had an additional long-wavelength band around 330 nm, indicating the presence of extra conjugation. The  $^1\text{H}$  nmr spectrum was also similar to that of 5, with the same pattern of aromatic proton signals, but it gave no evidence of a methylimino group, and the methylenedioxy group produced a singlet instead of a doublet as for laureline<sup>6</sup>; this observation likewise suggested a greater degree of conjugation in the molecule, resulting in increased rigidity and closer alignment of the planes of the aromatic rings. Attempts to methylate the nitrogen with formaldehyde and borohydride failed, and the only product obtained had added on two hydrogens; however, the nitrogen was readily methylated and quaternised with methyl iodide to give a product with only one more carbon. The original alkaloid is thus a tertiary base, and the above-mentioned data together with the molecular formula, which from ms corresponds to norlaureline with two less hydrogens, pointed to structure 7. That the compound was indeed 6,6a-dehydronorlaureline was confirmed by the fact that the quaternary methiodide referred to above could be reduced with borohydride to laureline (5); it thus forms another member of the small but increasing sub-group of aporphine-type alkaloids with a conjugated azomethine group<sup>7,8</sup>. The methiodide of 7 appeared to undergo ready oxidation on exposure to air; the uv spectrum of the product resembled that of an oxoaporphine<sup>9</sup>, and an additional downfield double doublet appeared in the aromatic region of the  $^1\text{H}$  nmr spectrum (at 8.75 and 8.35 ppm,  $J=8$  Hz). These signals suggested that ring B had been aromatised to produce a structure such as 8; analogous reactions in the aporphine series involving N-demethylation and aromatisation have been recorded,



7 6,6a-Dehydronorlaureline



8



9 Sevanine  
 $R_1=\text{CH}_3$ ,  $R_2=\text{H}$ ,  $R_3-R_4=\text{CH}_2$

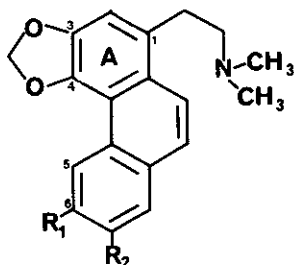
10 Isosevanine  
 $R_1-R_2=\text{CH}_2$ ,  $R_3=\text{H}$ ,  $R_4=\text{CH}_3$

although their reaction mechanism is not fully understood<sup>10</sup>.

Amongst the previously unrecorded bases was one that from high resolution ms had the same molecular formula as dehydronorlaureline (7) except for an extra oxygen, which appeared to be in an hydroxyl group from the ir spectrum. Like 7, the new base had a methoxyl and a methylenedioxy group from the  $^1\text{H}$  nmr spectrum, which also showed the presence of extra aromatic protons as

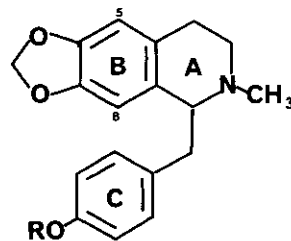
compared to the other alkaloids described above; two of these protons produced a double doublet at the low-field end of the aromatic region, and suggested the presence of an isoquinoline nucleus. The uv spectrum was in good accord with a benzyloisoquinoline structure, and in general the observations indicated that the alkaloid was an isomer and close structural analogue of sevanine<sup>11</sup> (9). The remaining aromatic protons showed the same splitting pattern and similar chemical shifts as for sevanine in the <sup>1</sup>H nmr spectrum: positions 6,7,3', and 4' must thus be substituted in both cases. The new alkaloid, which has been named isosevanine, gave a positive Gibbs reaction<sup>12</sup>, indicating that its phenolic group must have an unsubstituted para position, and must thus be attached at C-3'. The tentative structure 10 put forward on the basis of these data has been confirmed by X-ray crystallographic analysis<sup>13</sup>.

One of the glaucine fractions contained a previously undescribed base whose uv spectrum showed it to have a phenanthrene nucleus<sup>14</sup>. The <sup>1</sup>H nmr spectrum revealed the presence of a methylenedioxy, a methoxy, and a dimethylamino group; the latter evidently forms part of an ethanamine chain as indicated by the base peak at m/z 58 in the ms, together with a strong complementary ion at m/z 265, and also by a pair of signals in the <sup>1</sup>H nmr spectrum corresponding to protons in two methylene groups that are attached to nitrogen and to an aromatic ring respectively. From biogenetic considerations, the ethanamine chain and the methylenedioxy



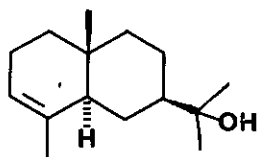
11 Uvariopsine  
R<sub>1</sub>=H, R<sub>2</sub>=OCH<sub>3</sub>

12 Isouvariopsine  
R<sub>1</sub>=OCH<sub>3</sub>, R<sub>2</sub>=H

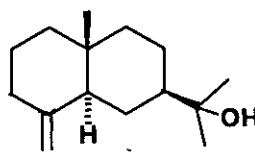


13 Cinnamolaurine  
R=H

14 O-Methylcinnamolaurine  
R=Me



15  $\alpha$ -Eudesmol

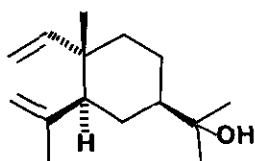


16  $\beta$ -Eudesmol

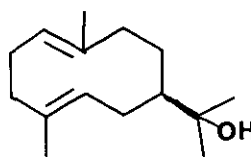
group may be tentatively assigned to positions 1,3 and 4 respectively of ring A in the phenanthrene system<sup>14</sup>. A broad down-field singlet at 8.6 ppm in the <sup>1</sup>H nmr spectrum can be attributed to the bay proton H-5<sup>14</sup>, and the methoxyl group in consequence must be located at C-6. The resulting structure is closely analogous to that of the known alkaloid uvариopsine<sup>4</sup> (11), and the new alkaloid, which has been named isouvariopsine, was confirmed as having structure 12 by comparison with the methine base formed by Hofmann degradation of laureline (5).

Finally, an alkaloid that had not previously been reported was separated from one of the laureline fractions; its formula, uv and mass spectra suggested that it belonged to the benzyl-tetrahydroisoquinoline group. From the <sup>1</sup>H nmr spectrum, the new base had a methylenedioxy, an N-methyl, and a methoxy group. Complementary and intense ions at m/z 190 and 121 in the ms pointed to the methylenedioxy group being attached to ring B and the methoxy to ring C; the former group was located by the presence of two one-proton singlets in the aromatic region of the <sup>1</sup>H nmr spectrum corresponding to H-5 and H-8, and the latter by the splitting pattern of the remaining aromatic protons, which corresponded to those of a p-disubstituted benzene ring. The new alkaloid is thus the methyl ether of cinnamolaurine<sup>15</sup> (13), and its structure has been confirmed as 14 by a comparison between the properties of the diazomethane reaction product of 13 and those of the new base, named O-methylcinnamolaurine.

The persistent contaminants associated with the alkaloid fraction of the plant, which appeared to alter the solubility relationships of the bases and render them difficult to separate and purify, were also investigated. It was difficult conversely to separate the contaminants from the alkaloids and to purify them completely but this was eventually accomplished by dccc<sup>19</sup> and by recrystallisation. The material was obtained in substantial amounts as a colourless crystalline substance that analysed for C<sub>10</sub>H<sub>18</sub>O<sub>2</sub>. Since no double bonds could be detected by ir or <sup>13</sup>C nmr spectroscopy, the nucleus was evidently bicyclic. The <sup>1</sup>H and <sup>13</sup>C nmr spectra indicated the presence of three methyl, two methylene, three methine and two quaternary carbons; furthermore, the ir and <sup>13</sup>C nmr spectra showed that the two oxygens were present as hydroxyl groups. Further studies designed to fix the structure and stereochemistry of this bicyclic terpenoid diol are under way and will be reported elsewhere.



17 Elemol



18 Hedycaryol

Some volatile terpenoid material was also obtained from the solvent used in the initial extraction of the plant material: on evaporation of the methanol extract, the material distilled over with the solvent and eventually crystallised from it. The crystalline material was identified as a mixture of  $\alpha$ - (15) and  $\beta$ - (16) eudesmols<sup>16</sup> by a comparison of the <sup>1</sup>H nmr, glc and ms data with those of authentic samples. Previous studies on the leaf oil of *H. angustifolia* resulted in the isolation of the sesquiterpene alcohols elemol<sup>17</sup> (17) and hedyacaryl<sup>18</sup> (18), and it was shown<sup>18</sup> that the latter was the biogenetic precursor of 17. It is likely that hedyacaryl is related biosynthetically to the eudesmols 15 and 16 as well.

#### EXPERIMENTAL

Droplet countercurrent chromatography (dccc)<sup>19</sup> was carried out on an instrument consisting of 100 glass tubes, each 4 mm in diameter and 1 mm long. Methanol:chloroform:water (5:5:3) were first equilibrated, and the lower layer was used as a stationary phase, while the upper layer, to which sufficient sulphuric acid was added to give a concentration of N/1000, was used as the mobile phase. Thin-layer chromatography (tlc) and preparative thin-layer chromatography (ptlc) were performed with Merck silica gel GF<sub>254</sub> or CAMAG silica gel DSF-5, and the compounds were visualised by spraying with iodoplatinate reagent or by examination under uv light. The melting points (mp) were recorded on a Yanaginoto Seisakusho micro-melting point apparatus and are uncorrected. Ultraviolet (uv) absorption spectra were recorded on methanol solutions with a Hitachi-Perkin-Elmer 124 spectrophotometer, and the logarithms of the extinction coefficients are given in parentheses. Infrared spectra were recorded with a Beckman IR-33 spectrometer on chloroform solutions unless otherwise specified. Proton magnetic resonance (<sup>1</sup>H nmr) spectra were recorded on deuteriochloroform solutions unless otherwise specified at 270 MHz with a Bruker HX-270 spectrometer. Tetramethylsilane was used as the internal standard. Chemical shifts are given in ppm and the coupling constants in hertz (Hz). Peaks are described as singlets (s), doublets (d), triplets (t), quartets (q) or multiplets (m). Mass spectra were run on a Vacuum General micromass 7070 F spectrometer by the direct insertion technique at 200° and 70 eV. Intensities are given in parentheses as percentages of base peak intensity.

Extraction of plant material - Leaves, twigs and bark of *Hedycarya angustifolia* collected around Little Grassy Creek, King Island (Map reference BR514678) in March 1978 were air-dried, milled to a fine powder (22.4 kg) and exhaustively extracted with methanol until a sample gave a negative alkaloid test with Mayer's reagent. The methanol extract was concentrated to 2 l in vacuo and dissolved in glacial acetic acid (1.5 l). The solution was poured in a fine stream into rapidly-stirred water (20 l) and left overnight, then the non-alkaloid precipitate was filtered off through celite. The filtrate was evaporated to dryness in vacuo below 40°C and the residue re-

dissolved in 5% aqueous sulphuric acid. The acid solution was extracted with ether (5 x 100 ml), then basified with ammonia and extracted with chloroform (10 x 100 ml). The chloroform layer was dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated to dryness in vacuo to give the crude alkaloid extract as a yellow amorphous powder (12.5 g, 0.056%).

The ethereal extract on evaporation gave a pale yellow crystalline non-alkaloidal material (6 g). The methanol recovered from the initial extract deposited a somewhat volatile white crystalline non-alkaloidal material (0.7 g).

A second batch of plant material (25 kg) collected from the same locality in July 1979 failed to give any alkaloids when extracted by the same method, but a third batch (23 kg) collected in March the following year gave a further 5.9 g of crude alkaloid extract. The combined alkaloid extracts were dissolved in chloroform and extracted with dilute hydrochloric acid (0.05%, 4 x 25 ml). The aqueous acid solution was exhaustively extracted with ether in a liquid/liquid extractor for 30 h, basified with ammonia (pH = 13) and extracted with chloroform (6 x 25 ml). The combined chloroform solutions were dried and evaporated to give a residue of mixed alkaloids (0.8 g,  $1.76 \times 10^{-3}\%$ ).

Dccc Separation of Mixed Alkaloids - The mixture, which from tlc contained at least seven alkaloids together with a considerable amount of non-basic material, was subjected to droplet countercurrent chromatography<sup>19</sup>. The mobile phase as it emerged from the apparatus was monitored by a uv detector (254 nm), and 127 x 3 ml aliquots were collected automatically. Every fifth aliquot was basified with ammonia and extracted with chloroform; each extract was examined by tlc, and the aliquots were bulked accordingly into nine subfractions. Methanol and chloroform were removed from each subfraction by careful evaporation under vacuum below 30°C, and the aqueous residues were basified and extracted with chloroform, then the extracts were dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated to give nine partially purified alkaloid fractions, which were further separated and purified by ptlc.

Fraction 1: Corydine and Laurotetanine - The ptlc purification of the brown gum (0.098 g, aliquots 8-15) gave corydine (0.057 g), mp 148°C from MeOH/ $\text{CHCl}_3$  (lit.<sup>4</sup> 148°C),  $[\alpha]_D^{20} + 204^\circ$  (C = 0.5,  $\text{C}_2\text{H}_5\text{OH}$ ), (lit.<sup>4</sup> + 204°),  $\lambda_{\text{max}}$  218 (4.19), 262 (3.73), 270 (3.70), 302 nm (3.40),  $\nu_{\text{max}}$  3450, 1590, 1570, 1500, 1480  $\text{cm}^{-1}$ ;  $^1\text{H nmr}$   $\delta$  7.07 (1H, d, J = 8 Hz), 6.83 (1H, d, J = 8 Hz), 6.70 (1H, s), 3.88 (6H, s, 2 x  $\text{OCH}_3$ ), 3.73 (3H, s,  $\text{OCH}_3$ ), 2.54 (3H, s, N- $\text{CH}_3$ ); ms m/z 341 ( $\text{M}^+$ , 100%), 340 (85), 326 (68), 324 (55), 310 (48), 298 (40), 183 (30), 267 (42), 170.5 ( $\text{M}^{++}$ , 10); identical with an authentic sample of corydine<sup>4</sup>; and laurotetanine (0.026 g), amorphous,  $\lambda_{\text{max}}$  220 (4.25), 280 (3.22), 308 nm (3.15), on addition of  $\text{OH}^-$ , 315 (3.35);  $\nu_{\text{max}}$  3350, 1580, 1500  $\text{cm}^{-1}$ ;  $^1\text{H nmr}$   $\delta$  7.88 (1H, s), 6.55 (2H, m), 3.83 (6H, s, 2 x  $\text{OCH}_3$ ), 3.52 (3H, s,  $\text{OCH}_3$ ); ms

m/z 327 ( $M^+$ , 68), 326 (100), 312 (26), 310 (18), 298 (12), 296 (21), 183 (8), 267 (10), 163.5 ( $M^{++}$ , 8); identical with an authentic sample of laurotetanine<sup>4</sup>.

Fraction 2: Corydine and Boldine - Ptlc purification of this fraction (0.120 g, aliquots 16-17) gave corydine (0.035 g) and boldine (0.072 g), mp 161°C (lit.<sup>4</sup> 161°C),  $[\alpha]_D^{20} + 108^\circ$  (C = 1,  $C_2H_5OH$ ), (lit.<sup>4</sup> + 111°),  $\lambda_{max}$  220 (4.6), 183 (4.21), 304 nm (4.23);  $^1H$  nmr  $\delta$  ( $CD_3OD$ ); 7.99 (1H, s), 6.90 (1H, s), 6.60 (1H, s), 3.92 (3H, s,  $OCH_3$ ), 3.61 (3H, s,  $OCH_3$ ), 2.58 (3H, s,  $N-CH_3$ ); ms m/z 327 ( $M^+$ , 85), 326 (100), 312 (32), 310 (38), 296 (29), 184 (68), 269 (72), 253 (52), 163.5 (5); identical with an authentic sample of boldine<sup>4</sup>.

Fraction 3: Isosevanine - Ptlc of the gum (0.055 g, aliquots 18-28) gave isosevanine (0.016 g), colourless needles from methanol/chloroform mp 148°C;  $\lambda_{max}$  236 (4.12), 270 (3.71), 314 (3.41), 330 nm (3.32);  $\nu_{max}$  3400, 1640, 1610, 1580  $cm^{-1}$ ;  $^1H$  nmr  $\delta$  8.28 (1H, d, J = 4.5 Hz), 7.36 (1H, d, J = 4.5 Hz), 7.35 (1H, s), 7.05 (1H, s), 6.7 (3H, m), 6.05 (2H, s), 4.45 (2H, s), 3.83 (3H, s,  $OCH_3$ ); ms m/z 309 ( $M^+$ , 60), 308 (100), 294 (23), 278 (8), 137 (11), 83 (56), 77 (22). Found: 309.0987; calculated for  $C_{18}H_{15}NO_4$ : 309.1017.

Fraction 4: Dehydronorlaureline and Laureline - Ptlc purification of fraction 4 (0.085 g, aliquots 29-36) gave laureline (0.020 g) as a brown gum,  $\lambda_{max}$  218 (4.20), 264 (3.95), 273 (4.1), 315 (3.57), 325 nm (3.25);  $^1H$  nmr  $\delta$  7.66 (1H, d, J = 2.5 Hz), 7.15 (1H, d, J = 10 Hz), 6.75 (1H, d, J = 10 Hz), 6.53 (1H, s), 6.03 (1H, d, J = 1.5 Hz), 5.88 (1H, d, J = 1.5 Hz); ms m/z 309 ( $M^+$ , 65), 308 (100), 294 (53), 266 (48), which was identified by comparison with an authentic sample; and 6,6a-dehydronorlaureline as a brown gum (0.043 g),  $\lambda_{max}$  248 (4.32), 278 (4.08), 317 (3.83) and 330 nm (3.85);  $\nu_{max}$  1690, 1640 and 1600  $cm^{-1}$ ;  $^1H$  nmr  $\delta$  7.35 (1H, s, 11-H), 7.2 (1H, s, 3-H), 7.1 (1H, d, J = 10 Hz, 9-H), 6.75 (1H, d, J = 10 Hz, 8-H), 6.1 (2H, s,  $O-CH_2-O$ ), 4.49 (2H, m, 7-H), 3.7 (3H, s,  $OCH_3$ ); ms m/z 293 ( $M^+$ , 55), 292 (100), 288 (30), 262 (18), 249 (2), 149 (20), 146.5 ( $M^{++}$ , 2). Found: 293.1043; calculated for  $C_{18}H_{15}NO_3$ : 293.1052.

Fraction 5: Laureline and O-Methylcinnamolaurine - Ptlc purification of this fraction (0.05 g, aliquots 37-41) gave laureline, and a more polar compound as a brown gum which could not be crystallised,  $\lambda_{max}$  1680, 1650, 1600, 1510  $cm^{-1}$ ;  $^1H$  nmr  $\delta$  7.05 (2H, d, J = 8 Hz, 2'-H, 6'-H), 6.81 (2H, d, J = 8 Hz, 3'-H, 5'-H), 6.55 (1H, s, 5-H), 6.2 (1H, s, 8-H), 5.86 (2H, dd, J = 8, 1.5 Hz,  $O-CH_2-O$ ), 5.1 (1H, m, 1-H), 3.78 (3H, s,  $OCH_3$ ), 2.5 (3H, s,  $NCH_3$ ); ms m/z 311 ( $M^+$ , 0.2%), 310 (0.2), 296 (0.2), 191 (12), 190 (100), 188 (7), 174 (13), 160 (7), 144 (12), 132 (8), 121 (80), 77 (15), 59 (21), 43 (36). Found: 311.1515; calculated for  $C_{19}H_{21}NO_3$ : 311.1521. The compound was identified as O-methylcinnamolaurine by comparison with an authentic sample prepared by diazomethane methylation of cinnamolaurine<sup>15</sup>.

Fraction 6: Isovariopsine and Glaucine - This fraction (0.045 g, aliquots 44-47) yielded two



compounds on ptlc. The less polar compound, isouvariopsine, was obtained as a yellow solid, mp 155-157°,  $\lambda_{\max}$  218 (3.93), 250 (4.35), 260 (4.35), 313 (3.88), 325 (3.91), 360 (3.62), 378 nm (3.65);  $\nu_{\max}$  1610, 1590, 1500, 1450  $\text{cm}^{-1}$ ;  $^1\text{H}$  nmr  $\delta$  8.6 (1H, m), 7.8-7.15 (5H, m), 6.25 (2H, s, O-CH<sub>2</sub>-O), 4.0 (3H, s, OCH<sub>3</sub>), 3.27 (2H, m), 2.65 (2H, m), 2.43 (6H, N-CH<sub>3</sub> x 2); ms m/z 323 (M<sup>+</sup>, 60), 308 (12), 292 (16), 278 (30), 265 (42), 247 (8), 222 (18), 205 (7), 176 (27), 163 (36), 58 (100). Found: 323.1356; calculated for C<sub>20</sub>H<sub>21</sub>NO<sub>3</sub>: 323.1539. The more polar compound was identified as glaucine<sup>4</sup> by comparison with an authentic sample, colourless crystals from methanol, mp 120°C (lit.<sup>4</sup> 120-121°C);  $\lambda_{\max}$  218 (4.58), 281 (4.18), 303 nm (4.16);  $\nu_{\max}$  1590, 1575, 1510, 1460  $\text{cm}^{-1}$ ;  $^1\text{H}$  nmr  $\delta$  7.98 (1H, s), 6.81 (1H, s), 6.68 (1H, s), 3.97 (6H, s, OCH<sub>3</sub> x 2), 3.92 (3H, s, OCH<sub>3</sub>), 3.72 (3H, s, OCH<sub>3</sub>), 2.59 (3H, s, N-CH<sub>3</sub>); ms m/z 355 (M<sup>+</sup>, 80), 354 (100), 340 (26), 338 (23), 324 (14), 297 (10), 281 (8), 177.5 (M<sup>++</sup>).

Fraction 7 - (0.141 g, aliquots 48-96) consisted mainly of glaucine.

Fractions 8 and 9 - (aliquots 97-127) gave negative Mayer's tests, and on keeping deposited white crystals that proved identical with those obtained previously from the acid solution of crude alkaloids by ether extraction; needles from methanol, mp 253-254°C.

Volatile non-alkaloid fraction - The methanol recovered from the extraction deposited white crystals (0.7 g, 3.15 x 10<sup>-5</sup>%); recrystallised from methanol, white flakes mp 62°C,  $\nu_{\max}$  (KBr) 2900 (CH), 1430  $\text{cm}^{-1}$ ; m/z, 204 (M<sup>+</sup>, 10), 189 (9), 164 (7), 161 (12), 149 (22), 135 (5), 122 (8), 109 (14), 108 (12), 81 (12), 79 (8). The material was identified as a mixture of  $\alpha$ - and  $\beta$ -eudesmol by comparison of its glc and spectroscopic data with those of authentic samples.

Attempted N-Methylation of 6,6a-Dehydronorlaureline - 6,6a-Dehydronorlaureline (0.10 g) in methanol (3 ml) was stirred with formaldehyde (37%, 0.2 ml) at room temperature for 5 h, then sodium borohydride (0.05 g) was added in small portions. The solvents were removed, the residue dissolved in dilute aqueous hydrochloric acid (10 ml), and the solution was basified with ammonia and extracted with chloroform. The product obtained gave no evidence of an N-CH<sub>3</sub> group ( $^1\text{H}$  nmr and ms) but the molecular weight was found to have increased by 2 amu. The compound was later identified as norlaureline.

Conversion of 6,6a-Dehydronorlaureline to Laureline - 6,6a-Dehydronorlaureline (0.020 g) dissolved in acetone (5 ml) was treated with methyl iodide (0.05 ml) in a sealed tube and left overnight at room temperature. Removal of the solvent gave a brown solid, ms m/z 308, which was dissolved in methanol (5 ml) and treated with sodium borohydride (0.020 g). The usual work-up of the reaction mixture gave laureline (0.018 g) as a brown gum,  $\lambda_{\max}$  218 (4.20), 264 (3.95), 273 (4.1), 315 (3.57), 325 nm (3.25);  $^1\text{H}$  nmr  $\delta$  7.66 (1H, d, J = 2.5 Hz), 7.15 (1H, d, J = 10 Hz), 6.75 (1H, d, J = 10 Hz), 6.53 (1H, s), 6.03 (1H, d, J = 1.5 Hz), 5.88 (1H, d, J = 1.5 Hz); ms m/z 309

(M<sup>+</sup>, 65), 308 (100), 294 (53), 266 (48), which was identified by comparison with an authentic sample of laureline.

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