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INDOLE ALKALOIDS FROM *HUNTERIA ZEYLANICA*

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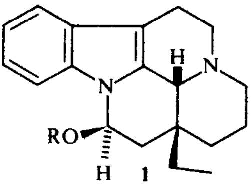
Key Word Index—*Hunteria zeylanica*; Apocynaceae; indole alkaloids.

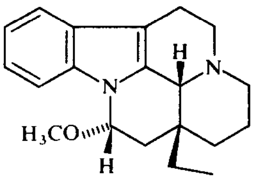
Abstract—Fourteen indole alkaloids were isolated and identified from the leaves and bark of *Hunteria zeylanica*: isocorymine, vobasine, (+)-eburnamenine, eburnamine, isoeburnamine, *O*-ethyleburnamine, *O*-methyleburnamine, *O*-methylisoeburnamine, pleiocarpamine, dihydrocorynantheol, yohimbol, epiyohimbol, tuboxenine and hydroxy-17-decarbomethoxy-16-dihydroepiajmalicine. *O*-Ethyleburnamine, *O*-methylisoeburnamine, epiyobimbol and hydroxy-17-decarbomethoxy-16-dihydroepiajmalicine, although known products, were isolated for the first time from a natural source.

Investigation of the alkaloidal content of *Hunteria zeylanica* leaves and barks was effected in a chemical study of Apocynaceae endemic to Ceylon and used in traditional medicine. From the leaves, three indole alkaloids, previously isolated from other species of *Hunteria* [1], were characterized: isocorymine [2], vobasine [3, 4] and (+)-eburnamenine [5, 6]. From the bark, twelve indole alkaloids were extracted. Five of them were previously isolated from other species of *Hunteria*: eburnamine [5–7], isoeburnamine [7], (+)-eburnamenine [5, 6], pleiocarpamine [8] and tuboxenine [9]. Known products from other Apocynaceae, but not from *Hunteria*, were also obtained: yohimbol [10] (however, yohimbol methochloride was extracted from *H. elliotti* [1]), dihydrocorynantheol [11] and *O*-methyleburnamine [12]. Four products, isolated for the first time from a natural source, were also identified: *O*-ethyleburnamine **1a** [5, 6],* *O*-methyl-isoeburnamine **2**, epiyohimbol [10] and hydroxy-17-decarbomethoxy-16-dihydroepiajmalicine **3** [13, 14].

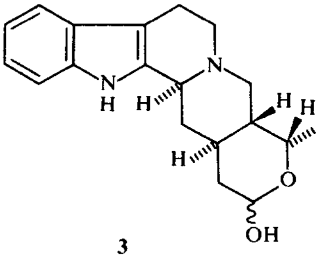
Yohimbol and epiyohimbol were identical to the two products obtained from the $NaBH_4$ reduction of yohimbone, and dihydrocorynantheol to the $NaBH_4$ reduction product of dihydrocorynantheal [15] (nomenclature is that used by Le Men and Taylor, ref. [13]). Eburnamine, when alkylated by EtBr and MeI, in the presence of NaOH and tetrabutylammonium bromide under phase transfer conditions yielded **1a** and **1b** respectively. Isoeburnamine, when treated under the same conditions using MeI, afforded *O*-methyl-isoeburnamine **2**. Derivative **3** was identified as the oxymercuration product of corynantheal according to ref. [14] and Boivin and Pais (unpublished results).



1
a $R = C_2H_5$
b $R = CH_3$



2



3

In *H. zeylanica* bark, two dimeric indole alkaloids, having MW 614 and 616 respectively, were also isolated. They contain a dihydroeburnamenine moiety characterized by its mass spectral fragmentation (peaks at *m/e* 279, 252, 237 and 208) [16]. Elucidation of the structure of the other moiety is in progress.

EXPERIMENTAL

Mps are uncorr. Optical rotations were determined in $CHCl_3$ with 0.5% EtOH as solvent. ^1H NMR spectra were recorded at 60 or 400 MHz at the Laboratoire d'electronique de la Faculté des Sciences d'Orsay using TMS as int. standard and $CDCl_3$ as solvent.

Extraction. Dried and ground plant material was extracted in a lixiviation apparatus with EtOH at 70°. The ethanolic extract was concentrated *in vacuo*, filtered, acidified with 10% sulfamic

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* Although exchange of the OH group of eburnamine by an alkoxy group was difficult, EtOH was used for extraction so that this compound could be an artifact.

acid soln and washed with hexane. The aq. layer was made alkaline with NH_4OH and alkaloids were extracted with CH_2Cl_2. Evapn *in vacuo* of the washed and dried organic layer gave crude alkaloids which were further separated by various chromatographic methods.

Leaf alkaloids. Ground leaves (1070 g) extracted as previously described furnished 1.4% of alkaloids (15 g). A preliminary separation was effected by chromatography on an activity III–Al_2O_3 column (450 g). The fractions eluted by toluene (1.45 g) were chromatographed on a Si gel Merck H60 column. CH_2Cl_2 elution gave successively isocorymine, mp 183°, $[\alpha]_D - 239°$, vobasine, mp 110°, $[\alpha]_D + 183°$ and (+)-eburnamenine, $[\alpha]_D + 182°$. The available amounts of the more polar fractions did not allow any further investigation.

Bark alkaloids. Ground bark (1060 g) extracted as described above gave 1% of crude alkaloids (10 g). A preliminary separation by chromatography on an activity III–Al_2O_3 column afforded 4 fractions (toluene, CH_2Cl_2–toluene, CH_2Cl_2 and CH_2Cl_2–MeOH, 19:1). The toluene fraction separated by chromatography on a Si gel Merck H60 column gave by CH_2Cl_2 elution isoeburnamine, mp 219°, $[\alpha]_D + 112°$ and *O*-ethyleburnamine **1a**, mp 108°, $[\alpha]_D + 56°$; MS M^+ 324, *m/e* 295, 208, 193; UV λ_{max}^{EtOH} 220, 291 nm, ε 25 000, 4500; ^1H NMR (400 MHz) δ ppm, 0.9 (3H, *t*, $J = 7$ Hz, CH_2–$\underline{CH}_3$), 1.3 (3H, *t*, $J = 7$ Hz, OCH_2–$\underline{CH}_3$), 3.7 (2H, *q*, $J = 7$ Hz, $O\underline{CH}_2$–CH_3), 3.9 (1H, *s*, H-21), 5.5 (1H, *dd*, $J = 9$ Hz, $J' = 5$ Hz, H-16 axial), 7.1 (2H, *t*, $J = 7$ Hz, H-10 and H-11), 7.4 (1H, *d*, $J = 7$ Hz, H-9), 7.5 (1H, *d*, $J = 7$ Hz, H-12). Further elution with CH_2Cl_2 gave a mixture of two products which were separated by prep. TLC (CH_2Cl_2–MeOH, 49:1) affording pleiocarpamine and eburnamine, mp 181°, $[\alpha]_D - 88°$.

The toluene–CH_2Cl_2 fraction separated by chromatography on a Si gel Merck H60 column (CH_2Cl_2 elution) furnished an unresolvable mixture of *O*-methyleburnamine **1b** and *O*-methylisoeburnamine **2**: MS M^+ – 310, M^+ – 15; M^+ – 29, M^+ – 31; UV λ_{max}^{EtOH} 229, 276, 282 nm, ε 24 000, 4300, 4100; ^1H NMR (400 MHz) δ ppm 0.85 (3H, *t*, $J = 7$ Hz, CH_2–$\underline{CH}_3$), 3.25 (3H, *s*, OCH_3 from **1b**), 3.41 (3H, *s*, OCH_3 from **2**), 3.76 (1H, *s*, H-21 from **2**), 3.83 (1H, *s*, H-21 from **1b**), 5.38 (1H, *dd*, $J = 4$ Hz, $J' = 2$ Hz, H-16 equatorial from **2**), 5.45 (1H, *dd*, $J = 9$ Hz, $J' = 5$ Hz, H-16 axial from **1b**). The CH_2Cl_2–MeOH fraction after separation on a Si gel H60 (6% H_2O added) column afforded by elution with CH_2Cl_2–MeOH, 19:1, dihydrocorynantheol, mp 183°, $[\alpha]_D - 19°$, identical to the $NaBH_4$ reduction product of dihydrocorynantheal [14]. Elution with CH_2Cl_2–MeOH (9:1) gave hydroxy-17-decarbomethoxy-16-dihydroepiajmalicine **3**, mp 185°, $[\alpha]_D - 86°$ (pyridine); MS M^+ 312 M^+ – 1, *m/e* 184, 170, 169, 156; UV λ_{max}^{EtOH} 225, 282, 292 nm, ε 24 000, 4300, 4100; IR (nujol) 3480 (NH), 3600 (OH) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 1.18 (3H, *d*, $J = 7$ Hz, CH_3), 3.9 (1H, *m*, H-3), 4.8 (1H, *qd*, H-19), 5.36 (1H, *br s*, H-17), 7.06 (1H, *t*, $J = 7$ Hz, H-10), 7.13 (1H, *t*, $J = 7$ Hz, H-11), 7.3 (1H, *d*, $J = 7$ Hz, H-9), 7.45 (1H, *d*, $J = 7$ Hz, H-12), 7.7 (1H, *br. s*, NH). Elution with CH_2Cl_2–MeOH (4:1) furnished successively yohimbol, mp 241°, $[\alpha]_D - 64°$, NMR, δ ppm 4.13 (1H, *m*, $L^{1/2}$ 10 Hz, H-17e), epiyohimbol, mp 257°, $[\alpha]_D - 83°$, NMR δ ppm 3.7 (1H, *m*, $L^{1/2}$ 30 Hz, H-17a), and tuboxenine. $NaBH_4$ reduction of yohimbone confirmed the structures of yohimbol and epiyohimbol.

O-*Ethyleburnamine* **1a** *from eburnamine.* EtBr (0.2 ml) was added to eburnamine (40 mg) in toluene (4 ml) in the presence of 50% aq. NaOH (4 ml) and tetrabutylammonium bromide (200 mg). After 2 hr of stirring at 0°, the organic layer, washed and dried gave **1a**.

O-*Methyleburnamine* **1b** *from eburnamine.* Eburnamine (40 mg) when treated with MeI (0.2 ml) under phase transfer conditions as described for **1a**, afforded **1b**, mp 103°; ^1H NMR δ ppm 0.85 (3H, *t*, $J = 7$ Hz, $CH_2\underline{CH}_3$), 3.25 (3H, *s*, OCH_3), 3.83 (1H, *s*, H-21), 5.45 (1H, *dd*, $J = 4$ Hz, $J' = 2$ Hz, H-16), 7.06 (2H, *t*, $J = 7$ Hz, H-10 and H-11), 7.39 (1H, *d*, $J = 7$ Hz, H-9), 7.5 (1H, *d*, $J = 7$ Hz, H-12).

O-*Methylisoeburnamine from isoeburnamine.* Isoeburnamine (40 mg) when treated with MeI (0.2 ml) under phase transfer conditions as described for **1b** yielded *O*-methylisoeburnamine **2**: ^1H NMR δ ppm, 0.85 (3H, *t*, $J = 7$ Hz, $CH_2\underline{CH}_3$), 3.25 (3H, *s*, OCH_3), 3.76 (1H, *s*, H-21), 5.38 (1H, *dd*, $J = 4$ Hz, $J' = 2$ Hz, H-16), 7.06 (2H, *t*, $J = 7$ Hz, H-10 and H-11), 7.4 (1H, *d*, $J = 7$ Hz, H-9), 7.5 (1H, *d*, $J = 7$ Hz, H-12).

Oxymercuration of corynantheal. To corynantheal (200 mg) in THF (9 ml) was added $Hg(NO_3)$ (220 mg) in H_2O (6 ml). After 3 hr stirring at 0°, $NaBH_4$ (200 mg) in 3M NaOH (2.8 ml) was added and after 1 hr at 0°, H_2O was added and **3** extracted with CH_2Cl_2.

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