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# Two New Oxindole Alkaloids from *Ervatamia yunnanensis*

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**Abstract**: Two new oxindole alkaloids, 17-demethoxy-hydroisorhynchophylline **1** and 17-demethoxy-hydroisorhynchophylline N-oxide **2,** have been isolated from the aerial parts of *Ervatamia yunnanensis*, and their structures were elucidated on the basis of spectroscopic analysis.

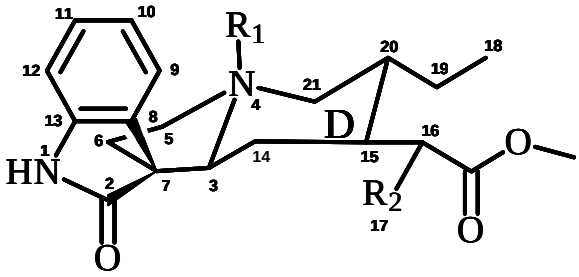
**Keywords**: *Ervatamia yunnanensis* Tsiang, apocynaceae, oxindole alkaloids.

*Ervatamia Yunnanensis* Tsiang has been used as a folk medicine in China for the treatment of hypertension[1]. As part of our continuing program on the study of plant-derived bioactive compounds, the chemical constituents of *E. yunnanensis* growing in Yunnan were investigated. In the previous paper, we reported the structures of indole alkaloids: 19S-hydroxy-tacamine, tabernaemontanine, 17-demethoxy-corynoxine B,17-demethoxy-hydrocorynoxine B, 20-epi-ervatamine, 19,20-dehydroervatamine, including a new one, 19S-hydroxy-16-epi-tacamine from this species[2]. The occurrence of the oxindole alkaloids in the Apocynaceae is extremely rare and therefore we were interested in their structures and relationship with the other type of alkaloids. The present paper deals with the structural elucidation of two new oxindole alkaloids,17-demethoxy-hydroisorhynchophylline **1** and 17-demethoxyhydroisorhynchophylline N-oxide **2**, isolated from the EtOH extract of the aerial parts of *E. yunnanensis*.

Compound **1** was obtained as an amorphous gum showing a molecular ion peak $[M]^+$ at m/z 356 ($C_{21}H_{28}N_2O_3$). Its IR spectrum showed the absorption of a lactam at 3307 and 1697 $cm^{-1}$ and a carbonyl group at 1724 $cm^{-1}$. Its $^1H$ NMR spectrum revealed four aromatic protons in the range of δ 6.88-7.44, a three-proton singlet for the carbomethoxy group at δ 3.53 and a lactam proton broad singlet at δ 8.26. Its MS displayed a series of fragment ions: m/z 325 $[M\text{-}OCH_3]^+$, 269 $[M\text{-}CH_3CHCOOCH_3]^+$ and 239 $[M\text{-}CH_3CHCOOCH_3\text{-}C_2H_6]^+$, together with m/z 211 (ringD), 196 (ringD-$CH_3$), 182 (ringD-$C_2H_6$,100%), 124, 108, in which fragment ions m/z 211, 196, 182 were typical for a tetracyclic oxindole alkaloid belong to rhynchophylline-type[3, 4]. Twenty one signals in the $^{13}C$ NMR (DEPT) spectrum of **1** were recognized as (5×C,8×CH,5×$CH_2$,3×$CH_3$), in which an ester carbonyl**,** a lactam carbonyl**,**

four aromatic methines**,** two aromatic quaternary carbons and a spiro carbon (C-7) were given. The MS, $^{13}C$ NMR and $^{1}H$ NMR (**Table 1**) spectral data of **1** were similar to those of 17-demethoxy-isorhynchophylline **3** [6] with the exception of C-16, C-17 and C-14, thus it is suggested that **1** had the same gross structure as of **3**. In the $^{1}H$ NMR spectrum of **1**, an asymmetrical C-18 methyl triplet signal was observed at δ 0.59 indicating a normal configuration at C-20[5,6], thus implying that the ethyl group at C-20 is in equatorial orientation[3]. Also, a downfield broad singlet in the $^{1}H$ NMR spectrum of **1** was found at δ 7.44 for H-9, showing a normal A configuration[6]. The deshielding of this H-9 is due to closer proximity of the N-4 lone pair[4]. The chemical shift values of C-3 and C-9 are strongly diagnostic of the configuration of the spiro carbon (C-7) in the rhynchophylline type alkaloids[6]. For the A configuration series of alkaloids the chemical shift values of C-3 and C-9 are δ 72.2 and 125.2, and for the B configuration series the corresponding values are δ 75.3 and 122.9, respectively. Comparison of the data for the normal A configuration **3** (δ 71.9 and 124.8) with the values for **1** ( δ 72.3 and 125.3) supported that **1** has the A configuration. The above evidence led to the establishment of the structure of this new compound as **1** (**Figure 1**).

**Figure 1.** Structures of compounds **1**, **2** and **3**




| | | |
|---|---|---|
| 17-Demethoxy-hydroisorhynchophylline | **1** $R_1$ =  | $R_2$ = $CH_3$, H |
| 17-Demethoxy-hydroisorhynchophylline N-oxide | **2** $R_1$ =  | $R_2$ = $CH_3$, H |
| 17-Demethoxy-isorhynchophylline | **3** $R_1$ =  | $R_2$ = $H_2C$= |

Compound **2** was also obtained as a gum displaying a $[M]^+$ at m/z 372 for $C_{21}H_{28}N_2O_4$, and its IR spectrum showed the presence of a lactam (3210 and 1676 $cm^{-1}$) and a saturated ester (1732 $cm^{-1}$) moieties. The $^{1}$HNMR spectrum bespoke four aromatic protons in the region δ 6.89~7.91, a three-proton triplet at δ 0.53 for the C-18 protons, a carbomethoxy group singlet at δ 3.62, and a lactam proton broad singlet at δ 8.12. The

molecular ion ($[M]^+$ 372) of **2** is 16 units higher than that of **1**. A loss of 16 amu from the $[M]^+$ was attributed to loss of an oxygen atom by the thermal decomposition from an N-oxide group[7,8], thus bespeaking the presence of an N-oxide group in **2**, and the subsequent fragmentation of the resulting characteristic ions $[C_{21}H_{28}N_2O_3]^+$ at m/z 356 was in good agreement with that of **1** at m/z 339, 325, 269, 239, 211, 196, 182 (100%),124, 108, but different in intensity, which indicated that **2** should possess the same structure as **1**. There existed twenty one signals in $^{13}C$ NMR (DEPT) spectrum of **2,** being verified as ( 5×C, 8×CH, 5×$CH_2$, 3×$CH_3$) in which an ester and a lactam group, four aromatic methines**,** two aromatic quaternary carbons and a spiro carbon (C-7) were provided. The C-3, C-5, C-9, C-21, and H-9 signals in the $^{13}C$ and $^1H$ NMR spectra of **2** markedly shifted downfield to about δ 81.9, 68.7, 129.8, 64.5 and 7.91, respectively (**Table 1** ), hence demonstrating that they are in closer proximity to the deshielding of the oxygen at N-4[8],compared with those of **3** and **1**. Therefore the evidence mentioned above substantiated further the presence of this N-oxide function of **2**. Analysis of $^1H$ NMR, $^{13}C$ NMR and MS data of **2** and comparison of **2** with **1** and **3** suggested that **2** belonged to the rhynchophylline type alkaloid[3,4]. In addition, biogenetically all compounds **1**, **2**, and **3** should be the related oxindole alkaloids and must possess the same precursor rhynchophylline while alkaloid **3** could be a biogenetic precursor of **1** and **2**. Similarly, the normal A configuration for **2** is consistent with that of **1**. In view of the above proof**,** another new isolate is assigned to the structure **2** ( **Figure 1**).

**Table 1**. $^1H$ and $^{13}C$ NMR (DEPT) data for compounds **1** and **2** (400MHz, $CDCl_3$, δ )

| | **1** | **1** | **2** | **2** | **3** |
|---|---|---|---|---|---|
| 2 | 182.4s | | 183.6s | | 183.4s |
| 3 | 72.3d | 3.21 (bs) | 81.9d | 3.55 (d, 7.60) | 71.9d |
| 5 | 53.8t | 2.30, 3.21 | 68.7t | 3.23, 2.65 | 52.7t |
| 6 | 37.8t | 2.02, 2.31 | 38.1t | 2.42, 2.23 | 37.3t |
| 7 | 56.2s | | 56.3s | | 56.2s |
| 8 | 134.1s | | 133.2s | | 133.9s |
| 9 | 125.3d | 7.44 (bs) | 129.8d | 7.91 (d,6.12) | 124.8d |
| 10 | 122.4d | 7.03 (t,7.36) | 123.9d | 7.08 (t,7.32) | 122.3d |
| 11 | 128.5d | 7.17 (t,7.36) | 128.5d | 7.24 (t,3.92) | 127.4d |
| 12 | 109.5d | 6.88 (d,7.60) | 110.9d | 6.89 (d,7.8) | 109.7d |
| 13 | 140.1s | | 143.5s | | 140.3s |
| 14 | 26.4t | 1.65, 2.29 | 22.5t | 2.20, 1.70 | 33.4t |
| 15 | 41.6d | 2.30 (m) | 41.9d | 2.45 (m) | 40.6d |
| 16 | 38.5d | | 36.0d | | 142.6s |
| 17 | 15.2q | 1.11 (d,7.04) | 15.4q | 1.14 (d,7.04) | 125.2t |
| 18 | 7.6q | 0.59 (t,5.44) | 7.6q | 0.53 (t,7.20) | 7.7q |
| 19 | 19.1t | 0.93 (m) | 18.5t | 0.84 (m) | 19.5t |
| 20 | 39.4d | 1.63 (m) | 39.5d | 1.80 (m) | 40.1d |
| 21 | 52.7t | 1.63, 2.63 | 64.5t | 3.20, 2.42 | 53.8t |
| C=O | 175.2s | | 176.8s | | 167.3s |
| $OCH_3$ | 51.0q | 3.53 (s) | 51.9q | 3.62 (s) | 51.7q |
| NH | | 8.26 (bs) | | 8.12 (bs) | |

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