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# ALKALOIDS FROM *TYLOPHORA HIRSUTA**

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**Key Word Index**—*Tylophora hirsuta*; Asclepiadaceae; phenanthroindolizidine alkaloids; isolation; structural determination.

**Abstract**—Five novel phenanthroindolizidine alkaloids, namely tylohirsutinine, 13a-methyltylohirsutine, 13a-methyltylohirsutinidine, tylohirsutinidine and 13a-hydroxysepticine, isolated from *Tylophora hirsuta* together with two unidentified bases are described. Structural studies indicate that the first four alkaloids possess the dibenzo [f, *h*]-pyrrolo-[1,2*b*]isoquinoline skeleton present in other *Tylophora* species, but differ in the presence of unsaturation in ring E or in the presence of an angular methyl function. The fifth alkaloid has been shown to be the 13a-hydroxy analogue of septicine.

## INTRODUCTION

*Tylophora asthmatica* and the related Australian plant *T. crebriflora* have been extensively studied [2–6], and their alkaloids are the subject of great interest due to their antileukaemic and other anticancer properties [7–10]. In the continuation of our investigations on medicinal plants, an uninvestigated plant, *T. hirsuta*, a native of the Jammu region and having a good proportion of alkaloids, led us to the isolation of five new alkaloids. Two unidentified bases ($[M]^+$ *m/z* 393 and *m/z* 381) were also isolated in small amounts from the same plant.

## RESULTS AND DISCUSSION

The total alkaloid mixture (0.5% yield) isolated from the aerial parts of the plant was triturated with ethyl acetate to give an insoluble crystalline base with most of the bases retained in the solution. The ethyl acetate-soluble mixture was chromatographed on basic alumina with solvents of increasing polarity. Tylohirsutinine (**1**) and 13a-methyltylohirsutine (**2**) were obtained as a mixture with the same $R_f$ values from benzene–ethyl acetate (4:1) eluants. The alkaloid **1** (0.057% yield) was separated from **2** by fractional crystallization from acetone. The mother liquor upon further purification yielded **2** (0.043% yield). 13a-Methyltylohirsutinidine (**3**) and tylohirsutinidine (**4**) were obtained from the ethyl acetate eluant fractions in 0.071 and 0.043% yields, respectively. The later eluted fractions from the same solvent yielded an unidentified base, $[M]^+$ *m/z* 393, mp 98–100°. Further elutions with ethyl acetate–methanol (9:1) afforded another uncharacterized base, $[M]^+$ 381, mp 300–303°. The ethyl acetate-insoluble, crystalline base on recrystallization from benzene yielded 13a-hydroxysepticine (**5**) (0.15% yield).

Compounds **1–4** had a close resemblance to isotylocrebrine [3, 6], isolated from other *Tylophora* species, in the substitution pattern of the methoxy and hydroxyl groups but differed in the presence of unsaturation in ring E or in the presence of an angular methyl function. Compound **5** resembled *d*-septicine, characterized by Govindachari *et al.* [3], in the attachment of methoxy groups but had an extra tertiary hydroxyl function.

Tylohirsutinine (**1**), mp 200–202°, $[M]^+$ at *m/z* 391 ($C_{24}H_{25}NO_4$), no rotation, had properties characteristic of phenanthroindolizidine derivatives. Its IR spectrum showed absorption at *ca* 1640 $cm^{-1}$ indicating the presence of a double bond. The appearance of the base peak at *m/z* 324 in the mass spectrum confirmed the presence of the double bond in ring E. The base peak resulted from cleavage of the pyrrole ring by a retro-Diels–Alder reaction analogous to that of the pyrrolidine ring in phenanthroindolizidine alkaloids [3]. In the $^1H$ NMR spectrum of **1**, the four aromatic protons at $\delta$8.68 (*s*), 7.62 (*d*, *J* = 9 Hz), 7.28 (*d*, *J* = 9 Hz) and 7.23 (*s*) were assigned to the C-5, C-1, C-2 and C-8 positions, respectively. The four methoxy groups appeared at $\delta$4.07, 4.03, 4.02 and 3.97. This type of substitution pattern of the aromatic and methoxy protons is identical to that of the alkaloid isotylocrebrine [3, 6]. The appearance of a vinylic proton at $\delta$6.68 as a triplet having a characteristic vicinal coupling constant (*J* = 6 Hz) for the cyclopentene systems could only be ascribed to the C-13 position. The remaining four methylene proton multiplets appeared at $\delta$4.75, 3.41, 2.35 and 2.00. Since this new type of phenanthroindolizidine alkaloid has been obtained from *Tylophora hirsuta*, it has been named tylohirsutinine.

13a-Methyltylohirsutine (**2**), mp 196–198°, $[M]^+$ at *m/z* 407 ($C_{25}H_{29}NO_4$), had a major mass spectral fragment at *m/z* 392 (41%) produced by the loss of 15 mass units from the weak $[M]^+$ peak (5%) indicating the presence of an angular methyl group. The base peak at *m/z* 323 arising from cleavage of the pyrrolidine ring by a retro-Diels–Alder reaction from *m/z* 392 supported the presence of an angular methyl at C-13a. In the $^1H$ NMR spectrum the substitution pattern of the methoxy groups remained essentially the same as in tylohirsutinine (**1**). It showed the presence of four methoxy groups at

*Part 4 in the series "Investigations of Medicinal Plants". For Part 3 see ref. [1].

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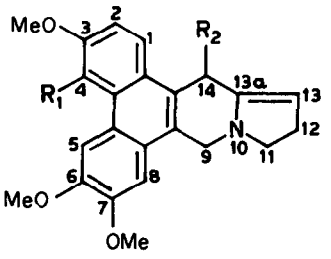
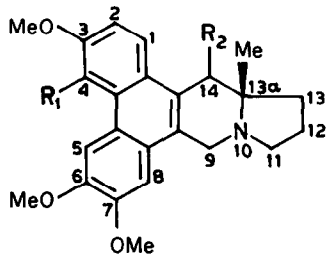


1 $R_1$=OMe ; $R_2$=H

4 $R_1$=$R_2$=OH



2 $R_1$=OMe ; $R_2$=H

3 $R_1$=$R_2$=OH

$\delta$4.09–3.98 and four aromatic protons at $\delta$8.76–7.26. The presence of a singlet at $\delta$2.18 integrating for three protons confirmed the position of the angular methyl group at C-13a. The observed unusual deshielding of the angular methyl might be due to an electrical quadrupole effect of the N atom which was more pronounced when the methyl function was above the plane of the molecule (axial methyl was *cis* to the N lone pair). This was in accordance with the examination of Dreiding models. These data led to structure **2** for the alkaloid named 13a-methyltylohirsutine. The observation of zero rotation suggested it to be in a racemic mixture.

13a-Methyltylohirsutinidine (**3**), mp 213–214°, $[M]^+$ at *m/z* 409 ($C_{24}H_{27}NO_5$), $[\alpha]_D^{25}$ + 120° (*c* 0.6 in $CHCl_3$) had UV maxima at 258, 278, 286, 314, 342 and 360 nm. The presence of a phenolic hydroxyl function was indicated by the shift in its UV maxima at 238, 256, 280, 296 and 336 nm on addition of sodium hydroxide. The IR spectrum of the base showed two hydroxyl bands at 3600 and 3300 $cm^{-1}$. Its mass spectrum showed a very weak $[M]^+$ at *m/z* 409 (1%) with the base peak at *m/z* 70 due to the pyrrolidine ring. Another intense peak at *m/z* 326 (90%) arose from the fragment at *m/z* 394 (22%) obtained from the $[M-Me]^+$ by a retro-Diels–Alder reaction characteristic of phenanthroindolizidine alkaloids. The fragments at *m/z* 297 (13%) and 283 (12%) arising from the losses of CHO and CO from *m/z* 326 (90%) and 311 (46%) were indicative of the presence of a hydroxyl group at C-14 [11]. The $^1H$ NMR spectrum of **3** showed the presence of: three methoxy groups at $\delta$4.07, 4.02 and 3.98; four aromatic protons at $\delta$8.06 (*d*, *J* = 9 Hz) 7.40 (*s*), 7.32 (*d*, *J* = 9 Hz) and 6.75 (*s*) assigned to C-1, C-5, C-2 and C-8, respectively, two $D_2O$-exchangeable protons at $\delta$8.48 (phenolic OH) and 4.02 (C-14 OH); $\delta$5.02 *br s* due to the H attached to the hydroxyl at C-14; and a methyl singlet at $\delta$2.15 indicative of an angular methyl function.

Methylation of **3** with diazomethane gave a monomethyl ether, $C_{25}H_{29}NO_5$ ($[M]^+$ *m/z* 423), whose $^1H$ NMR spectrum showed the presence of four methoxy groups, a CH–OH function and four aromatic protons. This proved the existence of one phenolic hydroxyl group in **3** . The methyl ether containing the C-14 hydroxyl formed an acetate ($\nu_{max}^{KBr}$ 1735 $cm^{-1}$). The placement of the hydroxyl at C-14 instead of C-9 in isotylocrebrine-type alkaloids has been established conclusively by Rao [6]. To decide the site of demethylation in **3**, a comparison of the $^1H$ NMR spectra of **2** and **3** showed that the difference between the two was the large upfield shift (by $\delta$1.36) of the signal due to the proton at C-5. On acetylation this shift disappeared. As the acetoxy group had a deshielding influence of *ca* 0.22 ppm on the *ortho* position in comparison to the methoxy group, the possibility of a phenolic hydroxyl at C-6 was excluded. This effect, due to the increased electron density resulting from the close proximity to the phenolic hydroxyl, was also observed by Rao [6] in his structural studies with isotylocrebrine-type alkaloids isolated from *T. crebriflora*. Further proof of the phenolic hydroxyl at C-4 came from the positive Gibb's test (for the free *para* position to the hydroxyl). The downfield shift of the C-1 signal (by $\delta$0.32) in **3** as compared to **2** was a result of the deshielding influence of the C-14 hydroxyl.

The unusual deshielding of the angular methyl signal at $\delta$2.15 was due to the electrical quadrupole effect of the N atom as observed in **2**. An examination of Dreiding models indicated its position above the plane of the molecule (axial methyl was *cis* to the N lone pair). (+)-Rotation suggested that the C-14 hydroxyl group was below the plane of the molecule and that the C-14 hydroxyl and C-13a methyl were *trans*-diaxially disposed as in the case of alkaloid C of Rao [6] with C-13a H, and *O*-methyltylophorinidine [12, 13]. Alkaloid **3** which was new has been named 13a-methyltylohirsutinidine.

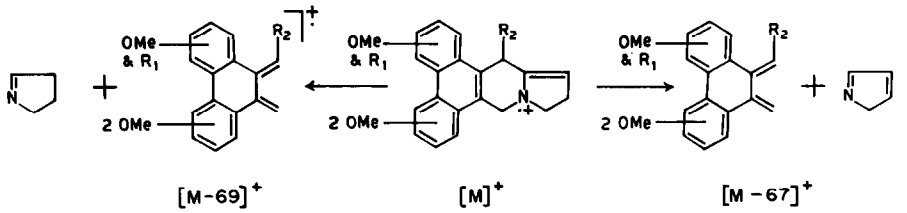
Tylohirsutinidine (**4**), mp 234–237°, $[M]^+$ at *m/z* 393 ($C_{23}H_{23}NO_5$), had UV maxima at 258, 287, 301, 338 and 354 nm. The IR spectrum showed two hydroxyl bands at 3665 and 3330 $cm^{-1}$ and one C=C double bond at 1660 $cm^{-1}$. One of the hydroxyl functions was shown to be phenolic by the shift in its UV maxima at 238, 254, 284, 298, 336 and 354 nm on addition of sodium hydroxide. Acetylation of **4** gave a diacetylated product ($\nu_{max}^{KBr}$ 1760 and 1735 $cm^{-1}$). In the mass spectrum, the base peak at *m/z* 324 arising from cleavage of the pyrrolidine ring and another intense peak, $[M-67]^+$, at *m/z* 326 (56%) arising from loss of the pyrrole ring by two retro-Diels–Alder reactions indicated the presence of a double bond in ring E as elucidated in **1**. The fragment at *m/z* 296 (20%) which resulted from expulsion of CO from the base peak confirmed the position of the C-14 hydroxyl [3]. The position of the phenolic hydroxyl was found to be C-4 as in **3** using the same experimental protocol. However, the lack of rotation in **4** showed it to be racemic. Thus structure **4** has been assigned to the alkaloid named tylohirsutinidine. The NMR data summarized in Table 1 was in agreement with the structure of tylohirsutinidine.

The general mass fragmentation pattern of the alkaloids (**1**–**4**) is shown in Scheme 1.

13a-Hydroxysepticine (**5**), mp 290–292° (decomp.),

Table 1. $^1$H NMR spectral data of alkaloids 1–4

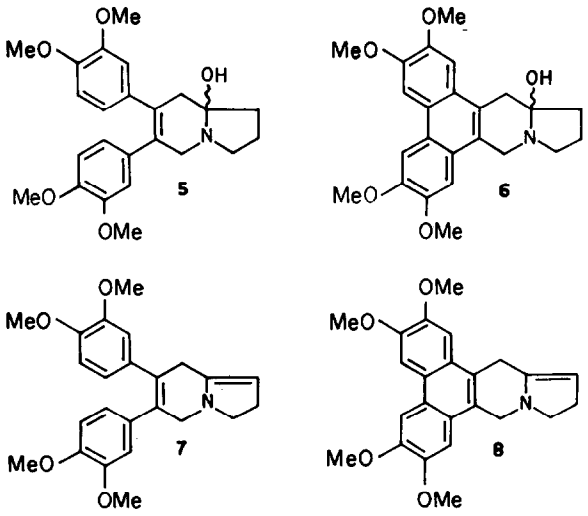
| Proton | Tylohirsutinine (1) ($CDCl_3$) | 13a-Methyltylohirsutine (2) $CDCl_3$) | 13a-Methyltylohirsutinidine (3) ($CDCl_3$ + 1 drop DMSO-$d_6$ | Tylohirsutinidine (4) DMSO-$d_6$ |
|---|---|---|---|---|
| C-1 | 7.62 (*d*) ($J$ = 9 Hz) | 7.74 (*d*) ($J$ = 9 Hz) | 8.06 (*d*) ($J$ = 9 Hz) | 8.16 (*d*) ($J$ = 9 Hz) |
| C-2 | 7.28 (*d*) ($J$ = 9 Hz) | 7.26 (*d*) ($J$ = 9 Hz) | 7.32 (*d*) ($J$ = 9 Hz) | 7.12 (*d*) ($J$ = 9 Hz) |
| C-5 | 8.68 (*s*) | 8.76 (*s*) | 7.40 (*s*) | 7.96 (*s*) |
| C-8 | 7.23 (*s*) | 7.32 (*s*) | 6.75 (*s*) | 7.20 (*s*) |
| C-13 | 6.68 (*t*) ($J$ = 6 Hz) | — | — | 6.72 (*t*) ($J$ = 6 Hz) |
| C-13a methyl | — | 2.18 (*s*) | 2.15 (*s*) | |
| C-14 | — | — | 5.02 (*br s*) | 4.74 (*br s*) |
| OMe | 4.07 (*s*) | 4.09 (*s*) | 4.07 (*s*) | 4.06 (*s*) (6H) |
| | 4.03 (*s*) | 4.06 (*s*) | 3.98 (*s*) | |
| | 4.02 (s) | 4.05 (s) | 3.95 (s) (3H each) | 3.98 (s) (3H) |
| | 3.97 (*s*) (3H each) | 3.98 (*s*) (3H each) | | |
| OH | — | — | 8.48 (*s*) 4.02 (*s*) Both $D_2O$-exchangeable | 4.92 (*br s*) $D_2O$-exchangeable |




Scheme 1. General mass fragmentation pattern of alkaloids 1–4.

$[M]^+$ at $m/z$ 411 ($C_{24}H_{29}NO_5$), $[\alpha]_D^{25}$ +100° ($c$ 0.4 in MeOH), had UV maxima at 236, 248, 256, 287, 302, 338 and 355 nm. The IR spectrum showed a hydroxyl band at 3600 cm$^{-1}$. The hydroxyl function was found to be non-phenolic by the absence of any shift in its UV maxima on addition of sodium hydroxide. It resisted acetylation with $Ac_2O$–pyridine which indicated the presence of a tertiary hydroxyl. Its mass spectrum showed a very weak $[M]^+$ (< 1%) and an intense peak at $m/z$ 393 (27%) by the elimination of 18 mass units confirming a tertiary hydroxyl function. The base peak at $m/z$ 324 arose from cleavage of the pyrrolidine ring. Three new peaks, from mass spectrometry of other assigned alkaloids, at $m/z$ 196 (7%), 162 (9%) and 78 (4%) indicated **5** to be a septicine analogue. The $^1$H NMR spectrum in TFA showed the presence of four methoxy groups at $\delta$3.54 (2 OMe) and 3.48 (2 OMe). It gave signals at two places (*ca* $\delta$7.40 and 6.78–6.52) in the aromatic region in the ratio of 1:6. The larger signal was in the form of a triplet in the ratio of 1:4:1; the small signals again being split into *dd* with $J$ = 9 and 3 Hz. The absence of signals below $\delta$8 indicated an alteration in the phenanthrene part of the skeleton. The signal at $\delta$7.40 might be due to a hydroxyl group. The presence of six aromatic protons in conjunction with the four methoxy groups and (+)-rotation showed that it was identical to *d*-septicine isolated by Govindachari *et al.* [3] but having an extra tertiary hydroxyl group which could only be placed at C-13a. Hence, structure **5** is assigned to the alkaloid named 13a-hydroxyseptiicine.

Alkaloid **5** on attempted acetylation with acetic anhydride–pyridine gave a non-acetylated product whose physical properties were different from those of the original alkaloid. The product, **6**, mp 270–272°, $[\alpha]_D^{25}$ +48° ($c$ 0.6 in $CHCl_3$), was highly soluble in chloroform whereas **5** was insoluble (soluble in MeOH). Product **6** gave a $[M]^+$ at $m/z$ 409 which was 2 mass units less than the starting material. The $^1$H NMR spectrum of **6** showed the presence of: four methoxy groups at $\delta$4.06 (2 OMe) and 4.00 (2 OMe); four aromatic protons at $\delta$7.74 (*s*, 2H) and 7.24 (*s*, 2H); and a $D_2O$-exchangeable proton at $\delta$2.02 (*s*). In the light of this experiment it appeared that under basic conditions, the cleaved phenanthrene (sep-




ticine) part of the skeleton was reunited to give the phenanthroindolizidine base (**6**). 13a-Hydroxysepticine (**5**) and **6** gave dehydrated products **7** and **8** on addition of $BF_3$–ethearate.

## EXPERIMENTAL

Mps are uncorr. $^1H$ NMR $\delta$ values are given in ppm downfield from TMS. TLC ($C_6H_6$–EtOAc–$Et_2NH$, 6:3:1) spots were developed by Dragondroff's spray reagent.

*Plant material. T. hirsuta*, grown at our campus, was collected during October 1982. Identification of the plant was confirmed by Dr. B. M. Sharma, Floristic Studies Division of our laboratory. A voucher specimen has been retained at the herbarium of our laboratory.

*Isolation of alkaloids.* Oven-dried (40–45°) whole aerial parts (700 g) were extracted exhaustively by hot percolation with EtOH. The extract was dried under red. pres. and the 0.5 M HCl-soluble portion extracted with EtOAc (3 × 1 l.) to remove chlorophyll. The aq. acidic soln was further acidified (pH 2) with 2 M HCl and washed with EtOAc (3 × 1 l.) to remove neutral components. The aq. acidic layer was then made alkaline (pH 9) with $NH_4OH$ (30%) soln and repeatedly extracted with EtOAc. The combined extracts were washed with $H_2O$, dried and evapd *in vacuo* to yield the crude total alkaloid (3.5 g) as a brown solid. On TLC it showed 5 major and 2 minor spots.

*Separation of alkaloids.* The residue containing total bases (3.5 g) was triturated with dry EtOAc and the insoluble base (1.05 g, 0.15% yield) filtered off. The EtOAc-soluble portion was concd *in vacuo* and subjected to CC over basic $Al_2O_3$ after the formation of a slurry. The column was eluted with mixtures of $C_6H_6$, EtOAc and MeOH of increasing polarities.

*Tylohirsutinine* (**1**). Fraction 1, eluted with $C_6H_6$–EtOAc (4:1) which showed a mixture ('figure of eight' type spot) on fractional crystallization with $Me_2CO$ gave a single spot product. This was recrystallized from $Me_2CO$ to obtain colourless, beaded crystals of **1** (0.4 g, 0.057% yield), mp 200–202°; $[\alpha]_D^{25}$ 0°; UV $\lambda_{max}^{MeOH}$ nm: 254, 262, 278, 284, 304, 315, 343 and 360 (log $\varepsilon$ 4.6, 4.4, 3.4, 3.1, 2.6, 2.5, 1.9 and 1.8). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1640, 1598, 1500, 1455, 1230, 1080, 1000 and 740. $^1H$ NMR: $\delta$4.55–4.95 centred at 4.75 (*m*, $CH_2$), 3.21–3.61 centred at 3.41 (*m*, $CH_2$), 2.35 (*m*, $CH_2$) and 2.0 (*m*, $CH_2$). MS *m/z* (rel. int.): 391 $[M]^+$ ($C_{24}H_{25}NO_4$, 40), 324 (100), 309 (19), 308 (19), 294 (9), 279 (7) and 70 (17).

13a-*Methyltylohirsutine* (**2**). The dried mother liquor of **1** was chromatographed over basic $Al_2O_3$ in EtOAc to obtain **2** (0.3 g, 0.043% yield) as light-yellow flakes after crystallization from $Me_2CO$, mp 196–198°. UV $\lambda_{max}^{MeOH}$ nm: 254, 262, 278, 284, 304, 315, 343 and 360 (log $\varepsilon$ 4.6, 4.4, 3.4, 3.1, 2.6, 2.5, 1.9 and 1.8). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1600, 1500, 1450, 1225, 1080 and 735. $^1H$ NMR: $\delta$4.32–5.02 centred at 4.67 (*m*, $CH_2$), 3.20–3.68 centred at 3.44 (*m*, $CH_2$), 2.22–2.70 centred at 2.46 (*m*, $CH_2$), 1.66–2.15 (*m*, $2CH_2$). MS *m/z* (rel. int.): 407 $[M]^+$ ($C_{25}H_{29}NO_4$, 5), 392 (41), 339 (19), 323 (100), 308 (19), 293 (9), 277 (8) and 70 (18).

13a-*Methyltylohirsutinidine* (**3**). Fractions 2–13 from the main column, eluted with EtOAc on crystallization from $Me_2CO$, gave **3** (0.5 g, 0.071% yield) as white flakes, mp 213–214°. $[\alpha]_D^{25}$ +120° (*c* 0.6; $CHCl_3$); UV $\lambda_{max}^{MeOH}$ nm: 258, 278, 286, 314, 342 and 360 (log $\varepsilon$ 4.9, 3.5, 3.3, 2.1, 1.8 and 1.6); $\lambda_{max}^{MeOH}$ (on addition of NaOH) nm: 238, 256, 280, 296 and 336 (log $\varepsilon$ 4.0, 3.9, 2.8, 2.5 and 1.8). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3600, 3300, 1600, 1460, 1380, 1235, 1175, 1130, 1055, 1000 and 780. MS *m/z* (rel. int.): 409 $[M]^+$ ($C_{24}H_{27}NO_5$, 1), 394 (22), 326 (90), 311 (46), 297 (13), 283 (12), 70 (100), 28 (14) and 18 (9). Acetylation of **3** with $Ac_2O$–pyridine at room temp. for 24 hr and usual work-up gave a diacetylated product, mp 160–162°; IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1760 and 1735. $^1H$ NMR ($CDCl_3$): $\delta$4.72 (*br s*, 1H, C-14), 2.56 (*s*, 3H, C-4 OAc), 2.34 (*s*, 3H, C-14 OAc) and 2.10 (*s*, 3H, C-13a Me). Methylation of **3** with $CH_2N_2$ gave a mono Me ether, mp 200–201°, $C_{25}H_{29}NO_5$ ($[M]^+$ 423); $^1H$ NMR: $\delta$7.76 (*d*, *J* = 9 Hz) 7.26 (*d*, *J* = 9 Hz), 8.72 (*s*), 7.28 (*s*), 5.02 (*br s*), 4.32 (*s*, $D_2O$-exchangeable), 4.07–3.98 (4 OMe) and 2.15 (*s*, 3H). Acetylation of the Me ether with $Ac_2O$–pyridine gave a monoacetate, mp 181–183°; IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1735.

*Tylohirsutinidine* (**4**). Further elution of the main column with EtOAc gave **4** (0.3 g, 0.043% yield) in fractions 13 and 14 after crystallization from $Me_2CO$; mp 235–237°. UV $\lambda_{max}^{MeOH}$ nm: 258, 287, 301, 338 and 354 (log $\varepsilon$ 4.7, 4.4, 3.7, 1.8 and 1.6); $\lambda_{max}^{MeOH}$ (on addition of NaOH) nm: 238, 254, 284, 298, 336 and 354 nm (log $\varepsilon$ 4.3, 4.6, 4.1, 3.5, 1.7 and 1.5); IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3665, 3330, 1660, 1610, 1595, 1500, 1450, 1210, 1180, 1110, 998, 800 and 780. MS *m/z* (rel. int.): 393 $[M]^+$ ($C_{23}H_{23}NO_5$, 31), 326 (56), 324 (100), 309 (12), 296 (20), 283 (8), 70 (72) and 18 (24). Acetylation of **4** with $Ac_2O$–pyridine at room temp. gave a diacetylated product, mp 168–170°; IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1760, 1735 and 1660 $cm^{-1}$. Methylation of **4** with $CH_2N_2$ gave a mono Me ether which on acetylation gave a monoacetate (confirmed by TLC comparison).

Fractions 16 and 17 in EtOAc on crystallization from $Me_2CO$ gave an unidentified base (minute quantity), mp 97–100°; MS *m/z* (rel. int.): 393 $[M]^+$ (10), 324 (42), 309 (20), 165 (10), 84 (25), 70 (51) and 18 (100).

Fractions 18–30 on gradual increased polarity of 5–10% MeOH in EtOAc on purification and recrystallization from $CHCl_3$–MeOH gave another unidentified base in minute quantity, mp 300–303°; MS *m/z* (rel. int.): $[M]^+$ 381 (10) 354 (23), 340 (88), 306 (28), 204 (22), 153 (15), 149 (28) and 93 (100).

13a-*Hydroxysepticine* (**5**). The EtOAc-insoluble, crystalline base on recrystallization from excess $C_6H_6$ gave solid beads of **5** (0.7 g, 0.1% yield), mp 290–292° (decomp.), $[\alpha]_D^{25}$ +100° (*c* 0.4; MeOH), UV $\lambda_{max}^{MeOH}$ nm: 236 (sh), 248 (sh), 256, 287, 302 (sh), 338 and 355 (log $\varepsilon$ 4.1, 4.3, 4.9, 4.0, 3.7, 1.8 and 1.6); IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3600, 1610, 1500, 1490, 1400, 1220, 1180, 1115, 1000, 985, 800 and 735; $^1H$ NMR (TFA): $\delta$7.40 (may be OH), 6.78 (*dd*, 1H, *J* = 9 and 3 Hz; *o*,*m*-coupled H), 6.68 (*s*, 4H, *p*-coupled H), 6.52 (*dd*, 1H, *J* = 9 and 3 Hz, *o*,*m*-coupled H), 3.54 (*s*, 6H, 2 OMe) and 3.48 (*s*, 6H, 2 OMe); MS *m/z* (rel. int.): 411 $[M]^+$ ($C_{24}H_{29}NO_5$, < 1), 393 (27), 392 (8), 378 (3), 363 (4), 340 (9), 325 (24), 324 (100), 310 (14), 294 (9), 281 (5), 196 (7), 162 (9), 78 (4), 70 (10), 28 (3) and 18 (4).

*Alkaloid* **6**. When **5** was left overnight with $Ac_2O$–pyridine **6** was obtained after usual work-up and crystallization from $Me_2CO$; mp 270–272°, $[\alpha]_D^{25}$ +48° (*c* 0.6; $CHCl_3$); $^1H$ NMR ($CDCl_3$): $\delta$7.74 (*s*, 2H, C-5 and C-4 H), 7.24 (*s*, 2H, C-8 and C-1

H), 4.06 (*s*, 6H, 2 OMe), 4.00 (*s*, 6H, 2 OMe) and 2.02 (*s*, 1H, $D_2O$-exchangeable, C-13a OH); MS *m/z* (rel. int.): 409 $[M]^+$ ($C_{24}H_{27}NO_5$, 2).

*Alkaloid* **7**. A drop of $BF_3$–ethearate in dry $Et_2O$ was added to a soln of **5** (100 mg) in dry $Et_2O$ at < 10° and placed in a refrigerator for 6 hr. After usual work-up, drying and crystallization from $Me_2CO$, **7** (45 mg), mp 271–273°, was obtained. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1645; $^1H$ NMR ($CDCl_3$): $\delta$7.72 (*s*, 2H, aromatic protons), 7.20 (*s*, 4H, aromatic protons), 7.00 (*t*, 1H, $J$ = 6 Hz), 4.07 (*s*, 6H, 2 OMe) and 4.00 (*s*, 6H, 2 OMe); MS *m/z* (rel. int.): 393 $[M]^+$ ($C_{24}H_{27}NO_4$, 99), 379 (8), 323 (100), 310 (26), 293 (8), 281 (13), 250 (9), 196 (12) and 162 (17).

*Alkaloid* **8**. A drop of $BF_3$–ethearate in dry $Et_2O$ was added to a soln of **6** in dry $Et_2O$ at < 10°, and after usual work-up **8** was obtained, mp 250–253°; $^1H$ NMR ($CDCl_3$): $\delta$7.66 (*s*, 2H, C-5 and C-4H), 7.20 (*s*, 2H, C-8 and C-1 H), 7.12 (*t*, 1H, $J$ = 5 Hz, C-13 H), 4.10 (*s*, 6H, 2 OMe) and 4.00 (*s*, 6H, 2 OMe); MS *m/z* (rel. int.): 391 $[M]^+$ ($C_{24}H_{25}NO_4$, 16) and 324 (68).

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