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ALKALOIDS OF *PETCHIA CEYLANICA*

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Key Word Index—*Petchia ceylanica*; Apocynaceae; (−)-petchicine; ajmalicinine; cabucine and fluorocarpamine.

Abstract—A new alkaloid, petchicine, has been isolated from the stem bark of *Petchia ceylanica* and its structure was established by spectroscopic studies. The ^{13}C NMR spectra of ajmalicinine, cabucine and fluorocarpamine, which have been isolated from the stem bark of *Petchia ceylanica* for the first time, are also reported.

INTRODUCTION

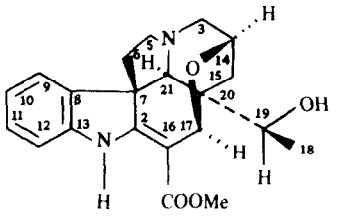
Petchia ceylanica is an evergreen herb indigenous to the low lands of Sri Lanka, and a number of new indole alkaloids have been isolated from it [1–3]. We now report the isolation and structural elucidation of a new aspidosperma alkaloid, (−)-petchicine (**1**). The ^{1}H NMR assignments have been made with the help of COSY-45, 2D J-resolved and NOESY experiments while ^{13}C multiplicities were established by DEPT experiments.

RESULTS AND DISCUSSION

The total alkaloids were isolated by extraction of the stem bark of *Petchia ceylanica* with alcohol, evaporation and extraction of the resulting gum into acid. Purification of the alkaloids and repeated column and TLC afforded petchicine (**1**) as a colourless solid, $[\alpha]_D = -380°$. Its UV spectrum showed λ_{max} at 216, 295 and 328 nm characteristic of an anilinoacrylate chromophore [1, 4, 5]. The IR spectrum showed ν_{max} 3500 (OH), 3550 (N-H) and 1680 (C=O) cm^{-1}. The mass spectrum displayed the molecular ion peak at *m/z* 368.1734 consistent with the molecular formula $C_{21}H_{24}N_2O_4$ (calcd 368.1734) indicating 11 double bond equivalents in the molecule. Other prominent peaks occurred at *m/z* 336.1695 ($C_{20}H_{20}N_2O_3$, 336.1685), 309.1613 ($C_{19}H_{21}N_2O_4$, 309.1602), 214. 1587 ($C_{13}H_{12}NO_2$, 214.1583, **a**) and 154.0861 ($C_8H_{12}NO_2$, 159.0867, **b**). Its fragmentation pattern indicated the presence of an aspidosperma skeleton [1, 4, 5]. The ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of petchicine (**1**) exhibited the presence of 24 protons, each of which was identified with the help of COSY-45, NOESY and 2D-J resolved spectra. A 3H doublet at δ1.02 was assigned to the C-18 methyl protons ($J_{18,19}$=6.4 Hz), its chemical shift being consistent with the presence of a –CH(OH)Me grouping as in epimisiline [1] or minovincine [5, 6]. A downfield quartet at δ4.12 integrated for one proton ($J_{19,18}$ =6.5 Hz) and was assigned to H-19. The COSY spectrum established that it was coupled to a doublet at δ1.02 (18-CH_3) [7] (Fig. 1). A one-proton double-doublet at δ2.05 assigned to C-6$_\alpha$H ($J_{6\alpha,6\beta}$=11.0 Hz, $J_{6\alpha,5\beta}$=7.0 Hz) was coupled to a 1H doublet for C-6βH ($J_{6\beta,6\alpha}$=11.0 Hz). A multiplet for C-5βH centred at δ3.70 overlapped with other signals but it was recognized from the 2D-*J* resolved spectrum [8] to be a double-doublet ($J_{5\beta,5\alpha}$ =14.6 Hz, $J_{5\beta,6\alpha}$=7.0 Hz). A 3H singlet for –OMe protons resonated at δ3.75. The connections between C-6αH, C-5αH and C-5βH could be seen from the corresponding cross-peaks in the COSY-45 spectrum. A doublet for C-15βH at δ3.09 ($J_{15\beta,15\alpha}$=14.4 Hz) was coupled to the double-doublet for C-15αH at δ2.95 ($J_{15\alpha,15\beta}$=14.4 Hz, $J_{15\alpha,14\alpha}$=3.7 Hz). A downfield doublet at δ4.11 for C-14αH ($J_{14\alpha,3\alpha}$=3.7 Hz) showed strong cross-peaks with signals at δ3.35 (C-3αH), δ2.95 (C-15αH) in the COSY-45 spectrum (Fig. 1). The two 1H signals at δ3.92 and 3.42 were assigned to C-21αH and C-17αH respectively, the assignments being confirmed from the NOESY spectrum [9] (Fig. 2). Thus C-17αH (δ3.42) showed NOESY cross-peaks with the double-doublet at δ2.05 (C-6αH) and δ3.02 (C-5αH) which not only confirmed the assignment to C-21αH but it also indicated the α-orientation of the C-21 proton. The aromatic region of petchicine (**1**) showed two doublet of triplets at δ6.89 ($J_{10,11}=J_{10,9}$=7.6 Hz, $J_{10,12}$=1.2 Hz) and δ7.16 ($J_{11,10}=J_{11,12}$=7.6 Hz, $J_{11,9}$=1.0 Hz), which were assigned to the C-10 and C-11H respectively. Two doublets integrating for one proton each at δ6.81 ($J_{12,11}$ =7.6 Hz) and 7.51 ($J_{9,10}$=7.6 Hz) were assigned to the C-12 and C-9 protons respectively, the assignments being supported by the presence of appropriate COSY cross-peaks. The configuration at C-19 was determined by Horeau's procedure [1] from which it was concluded that (−)-petchicine has *R* configuration at C-19. The multiplet at δ4.11 (C-14αH) showed strong interaction in the NOESY spectrum with a double-doublet at δ3.35 (C-3βH) and with the doublet at δ2.95 (C-15αH), thereby establishing the α-orientation of the C-14 proton and hence the β-orientation of the ether linkage between C-14/C-17.

The ^{13}C NMR spectrum (BB and DEPT, 100 MHz, $CDCl_3$) of **1** showed resonances for eight methine, four methylene, two methyl and seven quaternary carbon atoms. Comparison of the ^{13}C NMR spectrum of the non-aromatic part of **1** (Table 1) with the corresponding portions of the ^{13}C NMR spectra of tabersonine [10] and vincadifformine [11] suggested that there was an ethereal

Dedicated to Prof. Gunther Snatzke on his 60th birthday.
*Author to whom correspondence should be addressed.



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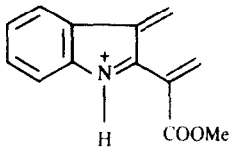
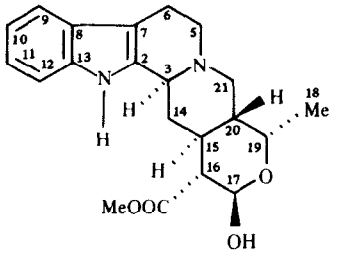


a



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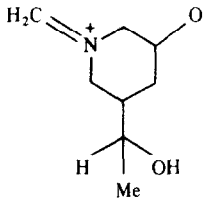

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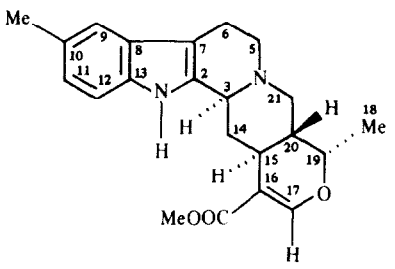

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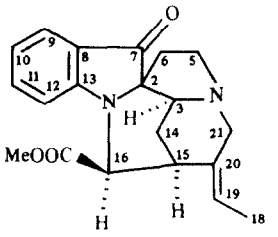
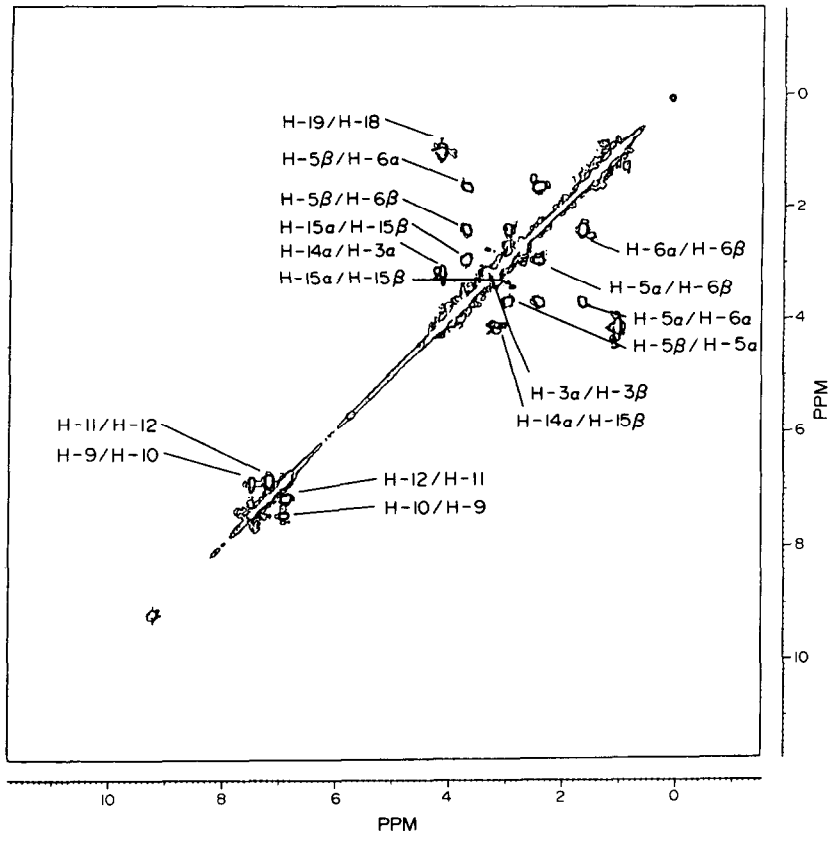


4

oxygen linking two of the carbon atoms in the molecule. The absence of a double bond between C-14 and C-15 (found in tabersonine and a number of other aspidosperma alkaloids) and the replacement of the two signals found in vincadifformine for the C-14 and C-17 methylene carbons by signals for two oxymethine carbons at δ80.0 and 79.4 indicated that the centres C-14 and C-17 were the points of attachment of the ethereal oxygen. The methylene signals at δ56.65, 55.57, 42.57 and 32.90 were assigned to C-3, C-5, C-15 and C-6 respectively. The signal for C-21 appeared at δ78.0, its ^{13}C chemical shift (along with the ^{1}H chemical shift of C-21H, δ3.92) indicating α-orientation of H-21 [1]. The signals of the remaining carbon atoms are given in (Table 1). On the basis of these results structure **1** was assigned to petchicine. (−)-Petchicine belongs to the same enantiomeric series as the other laevo-rotatory alkaloids of aspidospermidine type and its biosynthesis can be conceived through the cyclization of a 14,17-dihydroxylated precursor.

Ajmalicinine (**2**) was first isolated from *Cabucala striolata* [12] and its structure was established by chemical and spectroscopic studies (UV, IR, MS and ^{1}H NMR) [12]. The substance has now been isolated by us from the stem bark of *Petchia ceylanica* as a white amorphous solid. Its identity was confirmed by spectroscopic studies. The ^{13}C NMR spectrum (100 MHz, CD_3COCD_3) of ajmalicinine (**2**) (Table 1) showed 21 carbon resonances in agreement with the molecular formula $C_{21}H_{26}N_2O_4$. The multiplicity assignments were made by DEPT experiment [10], which showed the presence of two methyl, four methylene and ten methine carbon atoms. A lowfield signal at δ91.61 was assigned to the carbon atom bearing two oxygen atoms at C-17 whereas C-19 which bears a single oxygen was found to resonate at δ71.99. Other assignments are presented in Table 1.

Cabucine (**3**) was previously reported from *Cabucalamaga cariensis* [13]. We have now isolated it from the stem bark of *Petchia ceylanica* for the first time as an amorphous solid. The ^{13}C NMR spectrum (BB and DEPT) of


H-19/H-18
H-5β/H-6α
H-5β/H-6β
H-15α/H-15β
H-14α/H-3α
H-15α/H-15β
H-6α/H-6β
H-5α/H-6β
H-5α/H-6α
H-5β/H-5α
H-3α/H-3β
H-14α/H-15β
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H-9/H-10
H-12/H-11
H-10/H-9
PPM
PPM

Fig. 1.

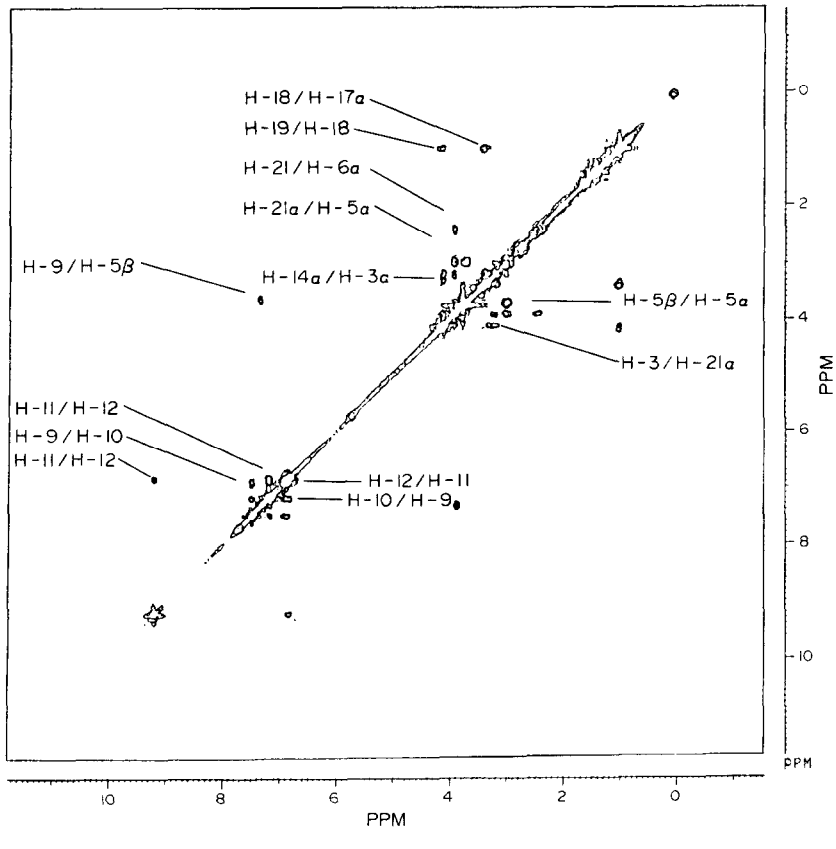
H-18/H-17α
H-19/H-18
H-21/H-6α
H-21α/H-5α
H-9/H-5β
H-14α/H-3α
H-5β/H-5α
H-3/H-21α
H-11/H-12
H-9/H-10
H-11/H-12
H-12/H-11
H-10/H-9
PPM
PPM

Fig. 2.

Table 1. ^{13}C NMR chemical shifts of compounds **1–4**

C	1	2	3	4
2	160.80	135.85	131.05	W
3	56.65	61.15	60.08	62.11[b]
5	55.57	53.93	53.16	53.72[c]
6	32.90[a]	22.69	21.73	25.61
7	57.21	108.16	107.67	W
8	143.21	128.28	172.63	135.00
9	129.27	111.46	100.40	120.53
10	121.23	119.51	153.98	119.75
11	123.90	121.52	111.41	124.43
12	108.82	111.44	111.03	111.29
13	135.64	135.98	135.78	134.30
14	80.83	35.19	32.77	39.23
15	42.57[a]	36.17	30.51	30.60
16	89.50	57.24	106.64	63.32[b]
17	79.42	91.61	154.00	W
18	14.16	14.65	14.80	12.54
19	64.33	71.99	73.65	121.27
20	47.75	42.77	40.86	137.39
21	78.00	57.59	56.79	55.37
OMe	51.50	51.65	50.85	51.40
Ar-OMe	—	—	55.89	—
C=O	168.69	172.00	167.41	W

W = too weak to be measured.
[a–c]Assignments may be interchangeable.

cabucine (100 MHz, $CDCl_3$) showed that the non-aromatic region contained four methylene, two methyl and four methine carbon resonances. The characteristic chemical shifts of C-5, C-6 and C-3 carbon atoms at δ53.16, 21.37, and 60.08 respectively are in agreement with presence of a C/D *trans* ring junction [14, 15]. The position of the methoxy group at C-10 in cabucine was confirmed from the chemical shift values of the aromatic methines of cabucine. It has been reported that if the aromatic ring in the indole moiety is substituted at C-10 position by a methoxy group, the C-9 and C-11 resonances then respectively appear *ca* 17 and 9.5 ppm upfield from the corresponding unsubstituted compound [16], whereas if the benzene ring of the indole moiety is substituted at C-11 by a methoxy group, the C-10 and C-12 carbons then resonate *ca* 9.5 and 15 ppm upfield in comparison to the unsubstituted compound [16]. In cabucine (**3**) the C-9 and C-11 signals were found to resonate at δ100.40 and 111.41 while both signals of the unsubstituted counterpart of cabucine, ajmalicine, are known to appear at δ118.1 and δ119 [4]. These results confirmed the substitution of the methoxy group at C-10. The ^{13}C chemical shift values of cabucine are presented in Table 1.

Fluorocarpamine (**4**) was also isolated from the stem bark of *Petchia ceylanica* and its structure confirmed by comparison of spectroscopic data with those reported in the literature [17]. The ^{13}C NMR spectrum ($CDCl_3$, DEPT) showed eight methine, four methylene and two methyl signals. The two methylene signals at δ53.72 and 55.37 were assigned to the C-5 and C-21 carbon atoms respectively. The C-16 methine carbon bonded to the indole nitrogen resonated at δ63.30 the chemical shifts of other carbons are given in Table 1.

EXPERIMENTAL

The stem bark of *Petchia ceylanica* were collected from Kakutara district and identified by Prof. S. Balasubramanian (Department of Botany, University of Peredeniya, Peredeniya, Sri Lanka) where a sample specimen is deposited.

Extraction procedure. The ethanolic extract of the air-dried stem bark (50 kg) of *Petchia ceylanica* collected from the Kekutara district, Sri Lanka, was evapd to a gum (4.1 kg). The total alkaloids were obtained by extraction with $CHCl_3$ into 5% HCl (10 l). The aq. layer was then basified to pH 9 with NH_3, extracted again with $CHCl_3$ (25 l) and dried over Na_2SO_4. Evapn of this concd $CHCl_3$ extract yielded the crude alkaloids (110 g). The alkaloids were chromatographed on a silica gel column (2 kg) which was successively eluted with mixtures of increasing polarities of petrol, $CHCl_3$, Me_2CO and MeOH. The petrol (40–60°)–$CHCl_3$ fraction (13:7 to 7:13) was rechromatographed on a column packed with TLC grade silica. Elution was initially with petrol–$CHCl_3$ (2:1) and then successively with increasing polarities of $CHCl_3$ and $CHCl_3$–MeOH mixtures. A number of alkaloids were isolated from the various fractions.

Isolation of petchicine (**1**). (−)-Petchicine was isolated from the petrol (40–60°)–$CHCl_3$ (1:1) eluates obtained from the chromatography column described above, and purified by prep. TLC on silica gel plates using Me_2CO–petrol (1:2) as eluent as amorphous mass (24.6 mg), $[\alpha]_D = -380°$ (MeOH; *c* 0.1 M); UV λ_{max}^{MeOH} (ε): 216 (5.63), 295 (5.03) and 328 (4.76) nm; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500 (OH), 3350 (N-H), 1680 (C=O); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 9.2 (1H, *s*, N-H), 7.51 (1H, *d*, $J_{9,10}$ = 7.6 Hz, H-9), 7.16 (1H, *dt*, $J_{11,10} - J_{11,12}$ = 7.6 Hz, $J_{11,9}$ = 1.0 Hz, H-11), 6.89 (1H, *dt*, $J_{10,9}$ = 7.6 Hz, $J_{10,12}$ = 1.2 Hz, H-10), 6.81 (1H, *d*, $J_{12,11}$ = 7.6 Hz, H-12), 4.21 (1H, *q*, $J_{19,18}$ = 6.5 Hz, H-19), 4.11 (1H, *d*, $J_{14\alpha,3\alpha} = J_{14\alpha,15\alpha}$ = 3.7 Hz, H-14α), 3.92 (1H, *s*, H-21α), 3.75 (3H, *s*, OMe), 3.70 (1H, *dd*, $J_{5\beta,5\alpha}$ = 14.6 Hz, $J_{5\beta,6\alpha}$ = 7.0 Hz, H-5β),

3.35 (1H, *d*, $J_{3\beta,3\alpha}$ = 14.2 Hz, H-3β), 3.09 (1H, *d*, $J_{15\beta,15\alpha}$ = 14.4 Hz, H-15β), 3.00 (1H, *dd*, $J_{5\alpha,5\beta}$ = 14.6 Hz, $J_{5\alpha,6\beta}$ = 8.5 Hz. H-5α), 2.05 (1H, *dd*, $J_{6\alpha,6\beta}$ = 12.5 Hz, $J_{6\alpha,5\beta}$ = 7.0 Hz, H-6α), 1.66 (1H, *dd*, $J_{6\beta,6\alpha}$ = 12.5 Hz, $J_{6\beta,5\alpha}$ = 8.5 Hz, H-6β); MS *m/z* (EI, rel. int. %): 368.1734 (100, $C_{21}H_{24}N_2O_4$), 336 (8), 256 (35), 214 (20), 154 (38), 143 (18), 83 (58); ^{13}C NMR ($CDCl_3$, 100 MHz): (Table 1).

Isolation of ajmalicinine (**2**). Ajmalicinine was isolated from $CHCl_3$–Me_2CO (2:1) eluates by the column chromatography described above, and purified by prep. TLC on silica gel plates using Me_2CO–petrol (2:1) as the solvent system. The substance obtained as a white amorphous solid (30 mg), UV λ_{max} (MeOH, ε): 225 (4.53), 289 (3.86) and 290 (3.78) nm; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3375 (N-H), 1730 (C=O) and 1625 (C=C); ^{1}H NMR (CD_3COCD_3, 400 MHz) δ: 3.25 (*dd*, $J_{3\alpha,14\alpha}$ = 3.2 Hz, $J_{3\alpha,14\beta}$ = 11.8 Hz, H-3α), 2.57 (*m*, H-5α), 2.63 (*m*, H-6α), 2.68 (*m*, H-6β), 3.40 (*m*, H-5β), 7.58 (1H, *d*, $J_{9,10}$ = 7.0 Hz, H-9), 6.95 (1H, *t*, $J_{10,11} = J_{10,9}$ = 7.0 Hz, H-10), 7.01 (1H, *t*, $J_{11,10} = J_{11,12}$ = 7.0 Hz, H-11), 7.25 (1H, *d*, $J_{12,11}$ = 7.0 Hz, H-12), 2.29 (1H, *dt*, $J_{14\alpha,14\beta}$ = 11.8 Hz, $J_{14\alpha,3\alpha} = J_{14\alpha,15\alpha}$ = 3.2 Hz, H-14α), 1.29 (1H, *q*, $J_{14\beta,14\alpha} = J_{14\beta,15\alpha}$ = 11.8 Hz, H-14β), 2.08 (1H, *dd*, $J_{16\alpha,17\alpha} = J_{16\alpha,15\alpha}$ = 8 Hz, H-16α), 5.09 (1H, *d*, $J_{17\alpha,16\alpha}$ = 8.0 Hz, H-17α), 1.23 (3H, *d*, $J_{18,19\beta}$ = 7.0 Hz, H-18), 4.13 (1H, *dq*, $J_{19\beta,18}$ = 7.0 Hz, $J_{19\beta,20\beta}$ = 5.0 Hz, H-19β), 2.07 (1H, *m*, H-20β), 2.13 (1H, *t*, $H_{21\alpha,21\beta} = J_{21\alpha,20\beta}$ = 11.0 Hz, H-21α), 2.89 (1H, *dd*, $J_{21\beta,21\alpha}$ = 11.0 Hz, $J_{21\beta,20\beta}$ = 4.5 Hz, H-21β) and 3.96 (3H, *s*, OMe); MS *m/z* (EI, rel. int.%): 370.1892 (80, $C_{21}H_{26}N_2O_4$, 396 (100), 184 (42), 170 (45), 169 (30), 156 (43); ^{13}C NMR (CD_3COCD_3, 100 MHz): (Table 1).

Isolation of cabucine (**3**). Cabucine was isolated from the petrol–$CHCl_3$ eluates (1:1) from the CC described above and purified as a light yellow-coloured solid mass by prep. TLC on silica gel plates using (2:1) Me_2CO–petrol. UV λ_{max}^{MeOH} (ε): 228 (5.05), 279 (3.94), 295 (3.25) nm; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1668 (C=O), 1620 (C=C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.38 (1H, *bd*, H-3α), 2.69 (1H, *dt*, $J_{5\alpha,5\beta}$ = 11.3 Hz, $J_{5\alpha,6\beta}$ = 4.2 Hz, H-5α), 2.96 (1H, *m*, H-6β), 2.76 (1H, *dd*, $J_{6\alpha,6\beta}$ = 14.0 Hz, $J_{6\alpha,5\beta}$ = 4.2 Hz, H-6α), 3.09 (1H, *m*, H-5β), 6.91 (1H, *d*, $J_{9,11}$ = 2.4 Hz, H-9), 6.78 (1H, *dd*, $J_{11,12}$ = 8.7 Hz, $J_{11,9}$ = 2.4 Hz, H-11), 7.18 (1H, *d*, $J_{12,11}$ = 8.7 Hz, H-12), 3.18 (1H, *m*, H-14α), 1.28 (1H, *q*, $J_{14\beta,14\alpha} = J_{14\beta,15\alpha}$ = 11.5 Hz, H-14β), 2.42 (1H, *m*, H-15α), 7.52 (1H, *d*, $J_{17,15\alpha}$ = 1.6 Hz, H-17), 1.18 (3H, *d*, $J_{18,19\beta}$ = 6.6 Hz, H-18), 4.42 (1H, *dq*, $J_{19\beta,18}$ = 6.6 Hz, $J_{19\beta,20\beta}$ = 5.0 Hz, H-19β), 2.15 (1H, *m*, H-20β), 2.22 (1H, *t*, $J_{21\alpha,21\beta} = J_{21\alpha,20\beta}$ = 10.8 Hz, H-21α), 2.96 (1H, *m*, H-21β), 3.73 (3H, *s*, OMe), 3.84 (3H, *s*, ArOMe); MS *m/z* (EI, rel. int. %): 382 (60, $C_{22}H_{26}N_2O_4$), 367 (24), 325 (18), 295 (40), 200 (70), 199 (38) and 149 (45); ^{13}C NMR ($CDCl_3$, 100 MHz) (Table 1).

Isolation of fluorocarpamine (**4**). Fluorocarpamine was isolated as a yellow coloured substance from the stem bark of *Petchia ceylanica*. It was isolated from the petrol–$CHCl_3$ (2:1) eluates and purified by prep. TLC on silica gel plates using $CHCl_3$–petrol (2:1). UV λ_{max}^{MeOH} (ε): 234 (4.05), 255 (3.65), 320 (3.39), 390 (3.13) nm; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1740 (COOMe) and 1668 (C=O); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.60 (1H, *dd*, $J_{9,10}$ = 7.3 Hz, $J_{9,11}$ = 1.0 Hz, H-9), 7.51 (1H, *t*, $J_{11,10} = J_{11,12}$ = 7.3 Hz, H-11), 6.91 (1H, *t*, $J_{10,11}$ = 7.3 Hz, H-10), 6.70 (1H, *dd*, $J_{12,11}$ = 7.3 Hz, $J_{12,10}$ = 1.0 Hz, H-12), 5.51 (1H, *q*, $J_{19,18}$ = 6.8 Hz, H-19), 4.57 (1H, *d*, $J_{16\alpha,15\alpha}$ = 4.3 Hz, H-16α), 3.67 (1H, *d*, $J_{21\alpha,21\beta}$ = 11.6 Hz, H-21β), 3.31 (1H, *d*, $J_{3\alpha,14\alpha}$ = 4.5 Hz, H-3α), 3.05 (1H, *dd*, $J_{5\beta,5\alpha}$ = 12.0 Hz, $J_{5\beta,6\beta}$ = 6.0 Hz, H-5β), 3.01 (1H, *d*, $J_{21\beta,21\alpha}$ = 11.6 Hz, H-21β), 2.98 (1H, *dd*, $J_{5\alpha,5\beta}$ = 12.0 Hz, $J_{5\alpha,6\alpha}$ = 6.5 Hz, H-5α), 2.93 (H, *dd*, $J_{6\alpha,6\beta}$ = 12.6 Hz, $J_{6\alpha,5\beta}$ = 6.0 Hz, H-6α); MS: *m/z* (EI, rel. int. %) 338.1632 ($C_{20}H_{22}N_2O_3$), 273 (40), 223 (30), 193 (48), 160 (54) and 121 (100); ^{13}C NMR ($CDCl_3$): Table 1.

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