Phytochemistry, Vol. 30, No. 4, pp. 1285 1293, 1991
Printed in Great Britain.

0031 9422/91 $3.00+0.00

ALKALOIDS FROM *RHAZYA STRICTA*

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(*Received in revised form* 8 *November* 1989)

Key Word Index—*Rhazya stricta*; Apocynaceae; indole alkaloids; glycoalkaloids; ^{13}C NMR.

Abstract—Chemical investigations of roots and leaves of *Rhazya stricta* have resulted in the isolation of the new indole alkaloids, 16*R*-19,20-*E*-isositsirikine acetate, leepacine and dihydroeburnamenine, along with six known alkaloids. Among these, (−)-16*R*,21*R*-*O*-methyleburnamine, 2-ethyl-3[2-(3-ethylpiperidino)ethyl]-indole, (20*S*)-19,20-dihydrocondylocarpine and *N*-acetylaspidospermidine have been isolated for the first time from *R. stricta*. Spectral studies on (+)-21*S*-eburnamenine and the glycoalkaloid strictosamide have also been undertaken.

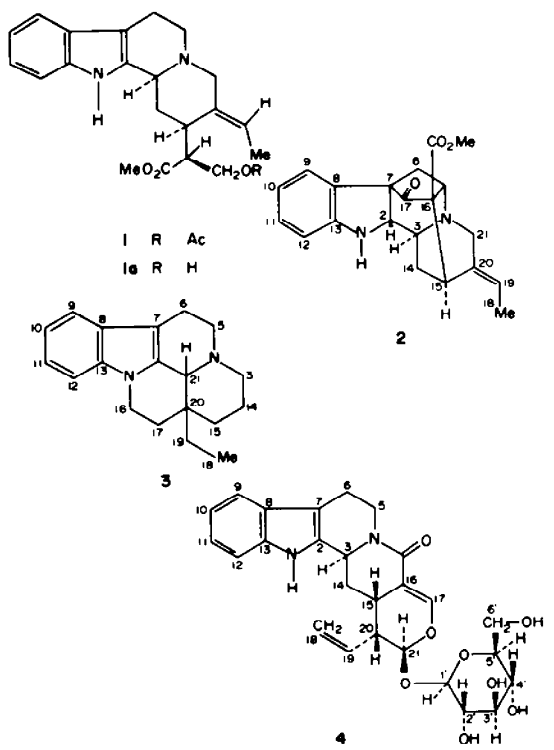
INTRODUCTION

Rhazya stricta is widely distributed in Pakistan and has been used for the treatment of various ailments [1–3]. The anticancer activity of some of its alkaloids is also reported [4, 5]. In previous investigations the root bark and leaves yielded a number of alkaloids [6–9]. We present here the isolation and structure determination of new indole alkaloids as well as some known alkaloids isolated for the first time from this plant [10, 11]. The new alkaloids isolated were 16*R*-19,20-*E*-isositsirikine acetate (**1**), leepacine (**2**) and the hitherto synthetically known dihydroeburnamenine (**3**) [10, 11]. Complete spectral studies were carried out on strictosamide (**4**), (−)16*R*,21*R*-*O*-methyleburnamine (**5**), 2-ethyl-3[2-(3-ethylpiperidino)ethyl)]-indole (**6**), (+)21*S*-eburnamenine (**7**), (20*S*)-19,20-dihydrocondylocarpine (**8**) and *N*-acetylaspidospermidine (**9**) isolated for the first time from *R. stricta*. The ^{13}C NMR spectrum of (+)21*S*-eburnamenine is also reported. The ^{1}H and ^{13}C NMR assignments were made with the help of 2D *J* resolved, COSY-45, NOESY, NOE-difference, DEPT and hetero-COSY experiments.

RESULTS AND DISCUSSION

The UV spectrum of compound **1** was characteristic for the indole chromophore. The IR spectrum ($CHCl_3$) of the alkaloid showed intense absorptions for NH, ester C=O and olefinic C=C groups. The HR mass spectrum of the alkaloid showed a $[M]^+$ peak at *m/z* 396.2048 corresponding to the molecular formula $C_{23}H_{28}N_2O_4$, indicating 11 degrees of unsaturation in the molecule. The mass fragmentation pattern of 16*R*-19,20-*E*-isositsirikine acetate was found to be closely related to those of other corynantheine-type alkaloids [12, 13], particularly those of the isositsirikine type.

The ^{1}H NMR spectrum ($CDCl_3$, 400 MHz, Table 1) showed a three proton double-doublet at δ1.66 ($J_{18,19}$ = 7.0 Hz, $J_{18,21\beta}$ = 2.0 Hz) which was assigned to Me-18 of the ethylidine side chain. The split quartet at δ5.65 was assigned to the olefinic H-19, ($J_{19,18}$ = 7.0 Hz), H-3 appeared at δ4.32 as a broad singlet, its chemical shift being close to that of the corresponding proton in 16*R*-19,20-*E*-isositsirikine, in which C-3 has the α configuration (δ4.28) [14]. A three-proton singlet at δ3.80 was assigned to the methyl protons of an ester group and another three-proton singlet at δ1.88 was due to an acetate group. The protons at position 18 resonated at δ3.94 as a doublet ($J_{17,16\beta}$ = 6.4 Hz), the downfield chemical shift of these protons reflecting the electron withdrawing α-oxygen function. The ^{1}H NMR assignments are presented in Table 1. The presence of all four aromatic methine protons indicated that the benzene ring is un-



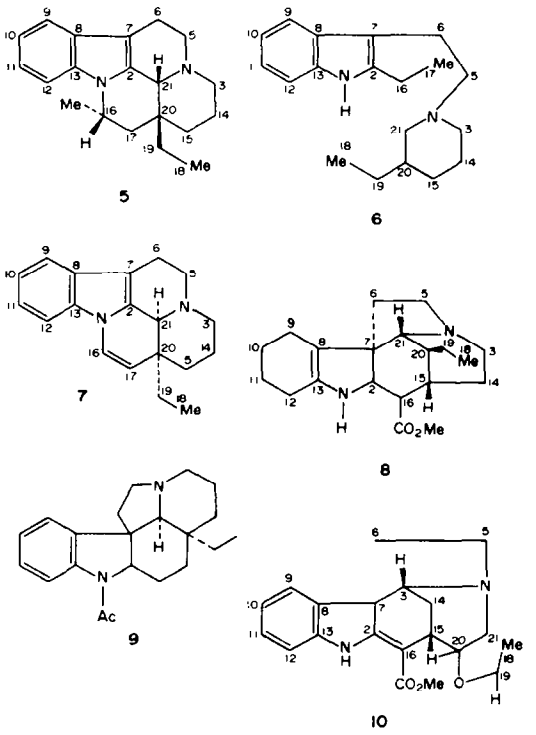


Table 1. Coupling interactions in the COSY-45 spectrum of compound 1

H	δ	Coupled to H (δ) (COSY-45)
3α	4.32	14α-H (2.20), 14β-H (2.65)
5α	3.14	5β-H (3.02), 6α-H (2.21), 6β-H (3.11)
5β	3.02	5α-H (3.14), 6α-H (2.21), 6β-H (3.11)
6α	2.21	6β-H (3.11), 5α-H (3 14), 5β-H (3.02)
6β	3.11	6α-H (2.21), 5α-H (3.14), 5β-H (3.02)
9	7.48	H-10 (7.10)
10	7.10	H-9 (7.48), H-11 (7.16), H-12 (7.38)
11	7.16	H-10 (7.10), H-12 (7.38), H-9 (7.48)
12	7.38	H-11 (7.16), H-10 (7.10)
14α	2.20	14β-H (2.65), 3α-H (4.32), 15α-H (3.27)
14β	2.65	14α-H (2.20), 3α-H (4.32), 15α-H (3.27)
15α	3.27	14α-H (2.20), 14β-H (2.65), 16α-H (2.60)
16α	2.60	15α-H (3.27), 17-H (3.94)
17	3.94	16α-H (2.60)
18	1.66	19-H (5.65), 21β-H (3.54)
19	5.65	18-H (1.66)
21α	2.95	21β-H (3.54)
21β	3.54	21α-H (2.95), 18-H (1.66)
MeOCO	3.80	
$MeCO_2$	1.88	–
N-H	8.57	–

substituted. The COSY-45 spectrum served to establish the ^1H–^1H coupling interactions (Table 1) while the multiplicity of the overlapping proton signals was determined from the 2D J-resolved spectrum. In order to confirm the relative stereochemistry at the various asymmetric centres and to record the subtle NOE effects, difference measurements were carried out. The important NOE interactions are presented in Fig. 1.

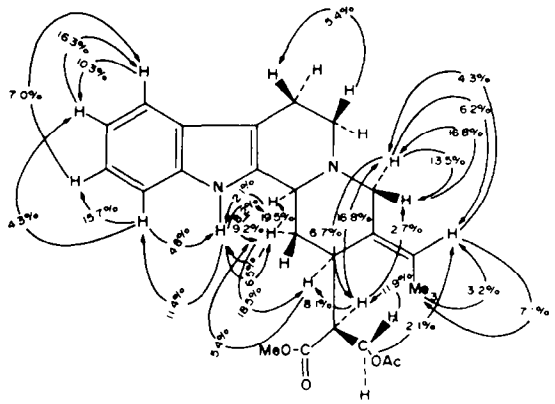


Fig. 1. NOE interactions of 16*R*-19,20-*E*-isositsirikine acetate (1).

The ^{13}C NMR spectrum ($CDCl_3$, 100 MHz, Table 2), indicated the presence of 23 carbon resonances in agreement with the molecular formula $C_{23}H_{28}N_2O_4$. The multiplicity assignments were made using DEPT with the last polarization pulse angles $\theta = 45°$, 90° and 135°. The ^{13}C NMR spectrum is presented in Table 2. The hetero-COSY experiments served to establish the direct (one bond) C–H connectivities (Table 2). Hydrolysis of 16*R*-19,20-*E*-isositsirikine acetate under acidic conditions led to the formation of the corresponding alcohol which was found to be spectroscopically identical with 16*R*-19,20-*E*-isositsirikine [14]. These studies led to structure **1** for the new alkaloid.

The UV spectrum of leepacine (**2**) was characteristic of a dihydroindole chromphore. The IR spectrum ($CHCl_3$) of the substance showed intense absorptions at 3350 (N–H), 1735 (ester C=O), 1720 (ketone C=O), 1605 (C=C) and 750 cm^{-1} (aromatic C–H). The high resolution mass spectrum of the alkaloid showed a $[M]^+$ at m/z 350.1619 corresponding to the molecular formula $C_{21}H_{22}N_2O_3$ (calcd 350.1630), indicating 12 double bond equivalents in the molecule. The mass fragmentation pattern of the alkaloid was similar to those of ajmalidine [15, 16] and raufiorine [17].

The ^1H NMR spectrum of **2** ($CDCl_3$, 300 MHz) showed a three-proton doublet at δ1.59 for the methyl group of the ethylidine side chain showing vicinal coupling with an adjacent olefinic proton ($J_{18,19} = 6.1$ Hz). The olefinic H-19, on the other hand, resonated as a quartet at δ5.70 showing vicinal coupling with the methyl protons ($J_{19,18} = 6.1$ Hz). H-3 resonated as a doublet of double doublets at δ3.24 ($J_{3,14\alpha} = 10.0$ Hz, $J_{3,14\beta} = 1$ Hz, $J_{3,2} = < 1$ Hz). The low value of the coupling constants of H-3 with the H-14β as well as with H-2, and its upfield chemical shift suggested its α-configuration [5, 18]. A broad singlet at δ3.95 was assigned to H-2. This must be in a β-configuration, as the bandwidth of the signal was found to be characteristically low (< 1 Hz) as in raufiorine [17] which also has the two protons in a β-configuration [18], because of the dihedral angle between H-2 and H-3 being close to 90° [19]. The proton chemical shift assignments were made by analogy with closely related alkaloids, e.g. quebrachidine [18, 20]. Two dimensional

Table 2. ^{13}C NMR spectral data of compounds **1** and **9** with coupling interactions between the carbons and protons from direct (one bond) hetero-COSY experiments

C	**1**		**9**	
	δ_C	δ_H	δ_C	δ_H
2	133.36	—	67.94	Hα (4.07)
3	52.66	Hα (4.32)	53.63	Hα (1.98), Hβ (3.06)
5	52.12	Hα (3.14), Hβ (3.02)	52.41	Hα (2.25), Hβ (3.11)
6	17.72	Hα (2.22), Hβ (3.11)	22.90	Hα (1.15), Hβ (2.05)
7	107.89	—	52.65	—
8	127.68	—	109.34 (w)	—
9	118.00	7.48	118.15	8.11
10	119.49	7.10	124.12	7.00
11	121.56	7.16	127.40	7.16
12	111.30	7.38	122.17	7.13
13	136.24	—	140.54	—
14	30.10	Hα (2.20), Hβ (2.65)	21.38	Hα (1.53), Hβ (1.55)
15	32.44	Hα (3.27)	33.93	Hα (1.11), Hβ (1.62)
16	46.18	Hα (2.60)	25.59	Hα (1.46), Hβ (1.90)
17	63.56	(3.94)	39.54	Hα (1.50), Hβ (2.12)
18	13.30	1.66	6.70	0.61
19	123.94	5.65	29.96	Hα (0.86), Hβ (1.41)
20	133.36	—	35.48	
21	51.37	Hα (2.95), Hβ (3.54)	70.65	Hα (2.29)
$CO_2\underline{Me}$	52.29	3.80	—	—
$\underline{CO_2}Me$	174.41	—	—	—
OCO<u>Me</u>	20.76	1.88	—	—
O<u>CO</u>Me	170.42	—	—	—
N-CO<u>Me</u>	—	—	23.14	2.23
N-<u>CO</u>Me	—	—	168.35	—

w: Weak.

NMR measurements (COSY-45, 2D *J* resolved) were carried out to verify the assignments.

In order to confirm the relative stereochemistry at the various asymmetric centres, NOE difference measurements were carried out. Irradiation at δ1.59 (H-18) resulted in a 7% NOE at δ3.03 (H-15) indicating that the 19,20-double bond is in the *E* configuration. This was further supported by the fact that when H-19 (δ5.70) was irradiated, it resulted in a 4% NOE at δ4.33 (H-21β) which confirmed that H-19 is in close proximity to H-21β. Irradiation at δ3.95 (H-2) resulted in a 11% NOE at δ2.57 (H-14β), while irradiation at δ3.24 (H-3) resulted in a 7% NOE at δ1.42 (H-14α) and a 2% NOE at δ2.57 (H-14β). These NOE interactions established that H-2 in leepacine (**2**) possesses β-stereochemistry.

The ^{13}C NMR spectrum ($CDCl_3$, 75 MHz, Table 3) showed the presence of 21 carbon atoms. The multiplicity assignments were made by carrying out DEPT experiments with the last polarization pulse angle $\theta = 45°$, 90°, and 135° [21]. C-2 appeared at δ77.2, its downfield chemical shift suggesting β-stereochemistry for this proton. C-3 appeared at δ57.6, its downfield chemical shift is indicative of its α-stereochemistry [22]. C-5 resonated at δ61.2, it chemical shift also supporting β-stereochemistry for H-5. The ^{13}C assignments were made by analogy with established data of the closely related alkaloids, ajmaline [23] and vincamajine [24] (Table 3).

Dihydroeburnamenine (**3**) has not been reported before as a natural product but it has been synthesized by the groups of Bartlett and Schnoes [6, 7]. The compound was identified by spectroscopic comparison of its data with those reported for the synthetic compound [6, 7].

The presence of strictosamide (**4**) in *R. stricta* was first detected by Warren [25]; it was previously isolated from *Nauclea latifolia* [26, 27]. The UV spectrum of **4** was characteristic for the indole chromophore. The IR (KBr) spectrum showed intense absorptions at 3300–3400 (N–H, O–H), 1650 (α,β-unsaturated C=O), 1015–1080 (C–O) and 747 cm^{-1} (aromatic C–H). The high resolution mass spectrum of the alkaloid showed a $[M]^+$ at *m/z* 498.2001, corresponding to the molecular formula $C_{26}H_{30}N_2O_8$.

The ^1H NMR spectrum of **4** showed a multiplet at δ5.64 for H-19 while a double doublet at δ5.31 ($J_{18,19}$ = 11.5 Hz, $J_{18,18'}$ = 1.8 Hz) was assigned to H-18. The protons at position 3 resonated as a multiplet at δ3.09 and those at position 6 appeared as a triplet at δ2.98 ($J_{6,5}$ = 7.4 Hz) while H-5α and H-5β resonated as multiplets at δ4.93 and δ5.03, respectively, the rather lowfield chemical shift values being consistent with their α-disposition to the amide carbonyl function [28]. Other ^1H NMR assignments are presented in the Experimental. Two-dimensional NMR measurements (COSY-45, NOESY, 2D *J* resolved) and NOED measurements were carried out to verify the assignments.

The NOESY spectrum served to establish the spatial proximities. The α-stereochemistry of H-3 at δ3.09 was deduced from the strong NOESY cross-peak with the signal at δ2.03 for H-14α. Similarly the NOESY interactions of H-14α with the H-18 suggested α-stereo-

Table 3. ^{13}C NMR spectral data of compounds **2** and **4** (ppm from TMS)

C	**2** ($CDCl_3$)	**4** (CD_3OD)
2	77.26 *d*	137.82 *s*
3	57.24 *d*	55.15 *d*
5	61.24 *d*	44.79 *t*
6	36.53 *t*	27.40 *t*
7	53.10 *s*	109.33 *s*
8	128.42 *s*	128.72 *s*
9	127.25 *d*[a]	118.69 d
10	119.81 d[b]	122.53 *d*
11	116.10 *d*	120.19 *d*
12	128.87 *d*[a]	112.33 *d*
13	142.44 *s*	134.80 *s*
14	22.09 *t*	22.14 *t*
15	27.18 *d*	24.99 *d*
16	57.27 *s*	110.37 *s*
17	215.50 *s*	149.17 *d*
18	12.82 *q*	120.56 *t*
19	120.59 *d*[b]	134.35 *d*
20	137.81 *s*	44.76 *d*
21	53.91 *d*	99.17 *d*
$\underline{C}O_2Me$	170.63 *s*	—
$CO_2\underline{Me}$	53.93 *q*	—
C=O	—	167.14 *s*
1′	—	100.57 *d*
2′		74.38 *d*
3′		78.00 *d*
4′		71.45 *d*
5′		78.25 *d*
6′		62.66 *d*

Multiplicities of signals were determined by DEPT measurements.

[a,b]Signals may be interchanged.

chemistry for the 19,20 bond. The *S* configuration at C-20 was assigned on the basis of the NOESY spectrum as H-21 at δ5.39, showed a strong cross-peak with H-19. This interaction could arise only if the 19,20 bond, as well as H-21, are α-oriented. It also established the existence of a β-glycosidic linkage as in an α-orientation the NOESY interaction between H-21α and H-19 would not be expected.

The ^{13}C NMR spectrum (CD_3OD, 75 MHz, Table 3) showed the presence of 26 carbon atoms. The signal at δ44.7 was assigned to C-5, its upfield chemical shift being due to the α-amidic function [28]. C-3 appeared at δ55.1, indicating α-stereochemistry for H-3 [29]. C-21 appeared at δ99.1 while the signal at δ167.1 was assigned to the amidic carbonyl carbons. C-1′ resonated at δ100.5 corresponding to the *O*-β-glycosidic linkage [30].

This alkaloid gave an orange coloured reaction with Draggendorff's reagent. The substance was identified as *O*-methyleburnamine, which has previously been isolated from *Haplophyton cimicidum* [31], *Hunteria zeylanica* [32] and *Leuconotis griffithii* [33]. We report here the hitherto unreported spectral data of this compound.

The UV spectrum displayed an indolic chromophore. The IR spectrum showed the presence of a ketonic carbonyl group (1720 cm^{-1}). It lacked Wenkert–Bohlmann bands in the C–H region, characteristic of the *trans*-quinolizidine system [34]. However, shoulders were present on the higher wavelength side of the main peak at 2850 cm^{-1} suggesting a β-configuration of H-21 [12, 35, 36]. The CD spectrum of **5** was determined and comparison made with CD of yohimbine alkaloids of known configuration which indicated the presence of a C/D *cis*-quinolizidine system [37]. The CD spectrum of the alkaloid showed a negative Cotton effect at 285 nm (−4.5) and another negative Cotton effect at 272 nm (−5), establishing the (*R*)-configuration of C-21 [38]. The mass spectrum exhibited an intense $[M]^+$ at *m/z* 310 and fragment ion peaks at *m/z* 295, 281, 279, 252, 83, 69 and 57 indicating the presence of an eburnan-type moiety [39, 40]. Peak matching experiments and high resolution mass measurements afforded an $[M]^+$ at *m/z* 310.2045 analysing for $C_{20}H_{26}N_2O$.

A notable feature of the ^1H NMR spectrum of **5** was the presence of a double doublet at δ5.52 with coupling constants of 9.4 and 5.4 Hz for H-16β which was consistent with its axial disposition as in other related compounds [41, 42]. This was further indicated by the values of the coupling constants of H-17β (δ1.88) and H-17α (δ2.17) as well as by its upfield chemical shift (when equatorial, it would be expected to resonate further downfield) [42]. In the case of previously reported *O*-methyleburnamine and *O*-methylisoeburnamine authors have claimed that H_{ax}-16 appears at δ5.45 and δ5.38, respectively, with identical *J* values of 4 and 2 Hz [32], this does not agree with our observations and those of others [41, 42]. The chemical shifts for other protons are given in Table 4. In the COSY spectrum of **5** strong cross-peaks are observed for H-16β (δ5.52) with H-17α (δ2.17) and H-17β (δ1.88). The assignments for H-5α (δ3.28), H-5β (δ3.22), H-6α (δ2.96), H-6β (δ2.56), H-15β (δ1.40) and H-15α (δ0.9), and H-14α (δ1.31), H-14β (δ1.71), H-3α (δ2.34) and H-3β (δ2.53) protons were also confirmed from the COSY-45 spectrum. The stereochemistry at the various asymmetric centres was established by a series of NOE difference experiments (Table 4) which supported the axial disposition of H-16β.

In the ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) C-21 resonated at δ58.8, a value characteristic for *cis*-fused quinolizidine systems with H-21 in a β-configuration [22, 43, 44]. The upfield shifts of C-2, C-5 and C-6 were consistent with a *cis*-quinolizidine system [22, 43, 44]. The ^{13}C NMR assignments and the direct (one-bond) ^1H–^{13}C chemical shift correlation (hetero-COSY) results are given in Table 5. On the basis of these studies the structure of alkaloid **5** was deduced to be (−)-16*R*,21*R*-*O*-methyleburnamine possessing a *cis*-quinolizidine C/D ring system.

A $[M]^+$ occurred at *m/z* 284.2235 corresponding to the molecular formula $C_{19}H_{28}N_2$. The mass fragmentation was similar to that reported [45] except that it did not contain intense peaks at *m/z* 158 and 143. As the ^1H and ^{13}C NMR spectra had not been reported earlier, they were recorded and studied. The ^1H NMR spectrum ($CDCl_3$, 400 MHz) was assigned with the help of COSY-45 and NOESY spectra and was as given in the Experimental. Two dimensional ^1H NMR measurements (COSY-45, hetero-COSY, 2D *J* resolved, NOESY) were consistent with structure **6**. NOE difference experiments further supported these assignments. The ^{13}C NMR spectrum ($CDCl_3$, 100 MHz), indicated the presence of 19 carbons. The methyl carbons resonated at δ11.24 and

Table 4. NOE difference measurements of compounds **5** and **7**

Proton irradiated (δ)		Proton enhanced (δ)		% NOE	
5	**7**	**5**	**7**	**5**	**7**
0.9 (H-15α)	1.00 (H-19)	1.3 (H-14α)	1.7 (H-14β)	3.3	3.3
		1.4 (H-15β)	4.4 (H-21α)	7.7	5.1
1.61 (H-19α)	—	2.06 (H-19β)	—	27.7	—
		2.11 (H-17α)	—	13.3	—
1.7 (H-14β)	2.00 (H-15α)	1.31 (H-14α)	1.00 (H-18)	7.7	3
1.8 (H-17β)	2.50 (H-6β)	2.1 (H-17α)	3.02 (H-6α)	18.3	12.6
2.14 (H-17α)	-	0.9 (H-15α)	3.2 (H-3β)	2.8	3.9
		1.6 (H-19α)	4.3 (H-21α)	8.8	5
		1.88 (H-17β)	—	6.3	--
2.35 (H-3α)	2.74 (H-3α)	2.5 (H-6β)	1.10 (H-15β)	15.6	6.1
		2.3 (H-3α)	3.2 (H-3β)	12.5	2.3
		—	7.3 (H-12)	—	4.5
2.5 (H-6β)	—	2.9 (H-6α)	—	22.2	—
2.9 (H-6α)		2.3 (H-3α)	—	13.8	-
		2.5 (H-6β)	—	16.6	—
	3.03 (H-6α)	—	2.50 (H-6β)	—	9.1
3.2 (H-5β)		3.90 (H-21α)	—	5.0	—
3.3 (H-5α)	3.20 (H-19β)	2.5 (H-6β)	3.3 (H-5β)	8.75	1.2
		3.9 (H-21α)	4.3 (H-21α)	5.6	2.3
3.3 (OMe)	—	1.80 (H-17β)	7.2 (H-10)	6.25	4.1
		5.52 (H-16)	7.3 (H-12)	6.25	2.2
		7.5 (H-12)	—	6.25	—
3.90 (H-21α)	—	1.6 (H-19α)	—	13.0	—
		1.88 (H-17β)	—	14.0	—
5.5 (H-16β)	3.3 (H-5β)	0.9 (H-15α)	3.2 (H-3β)	0.5	10.2
		0.95 (H-18)	4.3 (H-21α)	9.5	3.8
		2.13 (H-17α)	7.2 (H-12)	9.0	4.6
		7.5 (H-12)	—	18.0	—
7.15 (H-11)	5.05 (H-17)	7.4 (H-9)	6.9 (H-16)	25.6	13.6
		7.5 (H-12)		18.7	
7.1 (H-10)	6.91 (H-14)	7.4 (H-9)	1.13 (H-17β)	11.5	2.2
		7.5 (H-12)	5.08 (H-17)	27.5	2.3
		—	7.3 (H-12)	—	3.1
7.48 (H-9)	—	7.17 (H-10)	—	36.0	—
	—	5.5 (H-16β)	—	13.25	—
7.58 (H-12)	—	7.15 (H-11)	—	31.25	—
—	7.09 (H-11)		7.12 (H-10)	—	6.2
			7.33 (H-12)	—	6.6
			7.4 (H-9)	—	5.9
—	7.12 (H-10)	—	7.09 (H-11)	—	8.7
			7.33 (H-12)	—	12.2
			7.4 (H-9)	—	2.0
—	7.32 (H-12)	—	6.9 (H-16)	—	10.2
			7.09 (H-11)	—	3.1
					—
—	7.46 (H-9)	—	3.3 (H-5β)	—	2.7
			7.09 (H-11)	—	1.5

14.37, respectively. These carbons are coupled with protons at δ0.91, and δ1.30, respectively, in the hetero-COSY spectrum (one-bond interactions). The methine carbon (δ37.12) was coupled with the proton at δ1.65. The downfield resonances at δ53.88, 59.41 and 59.61 were assigned to C-3, C-5 and C-21, respectively. The ^{13}C and ^{1}H NMR assignments are given in the Experimental. 2-Ethyl-3(2-(3-ethylpiperidino)ethyl)-indole has previously been reported from *T. cumminsi* [45].

Eburnamenine (**7**) has been isolated previously from the leaves of *R. stricta* [11, 39, 46], but the stereochemistry at C-21 was not defined. We have now isolated (+)-21*S*-eburnamenine from the roots of *R. stricta*. As its ^{13}C NMR spectrum had not been reported before the ^{13}C NMR studies and hetero-COSY spectra were recorded. The ^{13}C NMR spectrum ($CDCl_3$) indicated the presence of 19 carbon atoms, the characteristic feature was the upfield values for C-2 (δ130.00), C-21 (δ55.86), C-

5 (δ 50.21), C-6 (δ 16.54) and C-7 (δ 106.96), suggesting the presence of a C/D *cis* quinolizidine system with 21α stereochemistry. The C-21α stereochemistry was established by the presence of a positive Cotton effect in the 270–300 nm region in the CD spectrum.

(20*S*)-19,20-Dihydrocondylocarpine (**8**) was isolated from the roots of *R. stricta*. This alkaloid has not been reported previously, but has been isolated from other plants [47–49]. The alkaloid was identified as (20*S*)-19,20-dihydrocondylocarpine by TLC and spectroscopic comparison (mass spectrum, UV, IR, ^{1}H NMR and TLC) [50, 51] with an authentic sample isolated earlier by us.

N-Acetylaspidospermidine was first isolated from the trunk bark of *Aspidosperma discolor* A. DC. [52] and also from *Vallesia dichotoma* Ruiz et Pav [48] and its structure was established by chemical and spectroscopic studies (UV, IR, mass spectra and ^{1}H NMR). This compound has now been isolated by us from the leaves of *R. stricta*. Its structure was confirmed by 2D NMR spectroscopic studies.

The ^{13}C NMR assignments of C-5, C-6 and C-21 have been revised in the light of our recent studies, after deletion of signals due to certain co-occurring impurities. C-5, C-6 and C-21 resonated at δ 53.59, 44.91 and 44.98, respectively. However, the data are consistent with the structure reported earlier [53].

EXPERIMENTAL

General. IR spectra were measured in $CHCl_3$ or as KBr discs. UV spectra were measured in MeOH. ^{1}H NMR spectra were recorded at 400 or 300 MHz, respectively, with TMS as int. standard. ^{13}C NMR spectra were measured at 100 or 75 MHz with TMS as int. standard. Hetero-COSY and COSY-45 spectra were also recorded at 400 MHz. TLC was performed on Merck precoated silica gel GF-254 plates. CC was carried out on Merck silica gel 60 (70–230 mesh size).

Plant material. This was collected from a small village *ca* 90 km from Karachi and was identified at the Botany Department of Karachi University where a voucher specimen is deposited.

Extraction of leaves. Fr. leaves (67 kg) of *R. stricta* Decaisne were crushed in an Ultra-Turrax and then extracted with EtOH. The EtOH extracts were filtered and cond to a gum under vacuum, acidified with 5% HCl acid and extracted with petrol (12 l) to remove fatty materials. Alkaloids were then extracted from the defatted aq. layer into $CHCl_3$ at different pH values. The fr. of pH 4.3 was dried (Na_2SO_4) and 44 g of crude extract was subjected to CC on silica gel (GF-254) which was successively eluted with increasing polarities of $CHCl_3$, petrol and MeOH. Alkaloid **1** was isolated from the extract at pH 4.3. The aq. layer was basified with NH_3 to pH 9. The soln thus obtained was extracted with $CHCl_3$, dried (Na_2SO_4) and evapd to dryness (317 g). The crude alkaloidal extracts obtained was dissolved in 10% HOAc. The soln was subjected to selective pH sepn after stepwise basification with NH_3. The soln at pH 6 was extracted with $CHCl_3$. The $CHCl_3$ sol. material was dried (Na_2SO_4) and evapd to dryness (17 g). Leepacine (**2**) and strictosamide (**4**) were isolated from the extract at pH 6.

Extraction of roots. Air-dried roots 105 kg of *R. stricta*, collected at Malir, Karachi, Pakistan, in May 1987, were crushed in an Ultra-Turrax and extracted with EtOH (200 l) at room temp. The combined EtOH extracts were cond to a gum under vacuum. The gummy crude extract was acidified with 2 M H_2SO_4 (5 l) soln. The acidic extract was washed with $CHCl_3$ (4 l) and the comb acidic layers dried (Na_2SO_4) and evapd *in vacuo* to give crude bases. This alkaloidal fr. was subjected to CC on silica gel. Elution with increasing polarities of petrol, $CHCl_3$, EtOAc and MeOH resulted in several frs which were further purified by prep. TLC as described below to afford 16*R*,21*R*-*O*-methyleburnamine (**5**) and 2-ethyl 3[2-(3-ethylpiperidino)ethyl]-indole (**6**).

16R-19,20-E-*Isositsirikine acetate* (**1**). Isolated from the $CHCl_3$–petrol–EtOH (9:10:1) eluates obtained from the CC described above. It was purified by prep. TLC on silica gel using $CHCl_3$–petrol–MeOH (13:6:1) to afford 15 mg (% yield 3.75×10^{-5}) of 16*R*-19,20-*E*-isositsirikine acetate. $[\alpha]_D$ −2.5 (MeOH, 0.15 g/100 ml). UV λ_{max}^{MeOH} nm (ε): 202 (4.224), 282 (3.268), and 289 (3.153). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3350–3250 (N–H), 1730 (C=O), 1600 (C=C), and 1360 (C–N). EIMS *m/z* (rel. int. %): 396 (40), 395 (3), 381 (3), 336 (71), 335 (56), 323 (8), 321 (18), 277 (12), 251 (77), 184 (35), 169 (100), 156 (55) and 144 (31). HRMS *m/z* (formulae, calc. value): 396.2048 (396.2048, $C_{23}H_{28}N_2O_4$), 395.1999 ($C_{23}H_{27}N_2O_4$, 395.1970), 381.1803 ($C_{22}H_{25}N_2O_4$, 381.1814), 336.1792 ($C_{21}H_{24}N_2O_2$, 336.1837), 335.1695 ($C_{21}H_{23}N_2O_2$, 335.1759), 323.1724 ($C_{20}H_{23}N_2O_2$, 323.1759), 321.1583 ($C_{20}H_{21}N_2O_2$, 321.1602), 277.1683 ($C_{19}H_{21}N_2$, 277.1704), 251.1506 ($C_{17}H_{19}N_2$, 251.1548), 184.0998 ($C_{12}H_{12}N_2$, 184.1000), 169.0698 ($C_{11}H_9N_2$, 169.0765), 156.0809 ($C_{11}H_{10}N$, 156.0813) and 144.0810 ($C_{10}H_{10}N$, 144.0813). ^{1}H NMR ($CHCl_3$, 400 MHz, δ, Table 1): 1.66 (*dd*, 3H, $J_{18,19}$ = 7.0 Hz, $J_{18,21\beta}$ = 2.0 Hz, H-18), 1.88 (*s*, 3H, OAc), 2.20 (*m*, 1H, H-14α), 2.22 (*m*, 1H, H-6α), 2.60 (*m*, 1H, H-16α), 2.65 (*m*, 1H, H-14β), 2.95 (*d*, 1H, $J_{21\alpha,21\beta}$ = 12.10 Hz, H-21α), 3.02 (*m*, 1H, H-5β), 3.11 (*m*, 1H, H-6β), 3.14 (*m*, 1H, H-5α), 3.27 (*dd*, 1H, $J_{15\alpha,14\alpha}$ = 5.5 Hz, $J_{15\alpha,16\alpha}$ = 8.0 Hz, H-15α), 3.54 (*br d*, 1H, $J_{21\beta,21\alpha}$ = 12.10 Hz, H-21β), 3.80 (*s*, 3H, CO_2Me), 3.94 (*d*, 2H, $J_{17,16\alpha}$ = 6.4 Hz, H-17), 4.32 (*br s*, 1H, H-3α), 5.65 (*q*, 1H, $J_{19,18}$ = 7.0 Hz, H-19), 7.10 (*ddd*, 1H, $J_{10,11}$ = 7.1 Hz, $J_{10,9}$ = 7.6 Hz, $J_{10,12}$ = 1.0 Hz, H-10), 7.16 (*ddd*, 1H, $J_{11,10}$ = 7.1 Hz, $J_{11,12}$ = 8.0 Hz, $J_{11,9}$ = 1.4 Hz, H-11), 7.38 (*dd*, 1H, $J_{12,11}$ = 8.0 Hz, $J_{12,10}$ = 1.0 Hz, H-12), 7.48 (*d*, 1H, $J_{9,10}$ = 7.6 Hz, H-9) and 8.57 (*s*, 1H, N–H). ^{13}C NMR ($CHCl_3$, 100 MHz, δ). Hetero-COSY, see Table 2.

Hydrolysis of 16R-19,20-E-*isositsirikine acetate.* 16*R*-19,20-*E*-Isositsisikine acetate (**1**) (5 mg) was dissolved in 2 ml MeOH, 10% HOAc soln (1 ml) added dropwise and the soln warmed at 50° for 3 hr. The reaction mixt. was basified with NH_3 and then extracted with $CHCl_3$ (25 ml). The $CHCl_3$ layer was dried (Na_2SO_4) and evapd. This afforded 3 mg of pure 16*R*-19,20-*E*-isositsirikine (**1a**). EIMS *m/z* (rel. int.%): 354 (55), 353 (36), 323 (18), 295 (4), 251 (83), 184 (11), 169 (51), 156 (22) and 144 (20). HRMS *m/z* (formulae, calc value): 354.1928 ($C_{21}H_{26}N_2O_3$), 353.1948 ($C_{21}H_{25}N_2O_3$), 323.1731 ($C_{20}H_{23}N_2O_2$), 295.1810 ($C_{19}H_{23}N_2O$), 251.1508 ($C_{17}H_{19}N_2$), 184.0999 ($C_{12}H_{12}N_2$), 169.0699 ($C_{11}H_9N_2$), 156.0810 ($C_{11}H_{10}N$) and 144.0809 ($C_{10}H_{10}N$). ^{1}H NMR ($CDCl_3$, 400 MHz, δ). 1.70 (*d*, 3H, $J_{18,19}$ = 6.9 Hz, H-18), 3.70 (*s*, 3H, AcO), 3.85 (*br s*, 2H, H-17), 5.94 (*q*, 1H, $J_{19,18}$ = 6.9 Hz, H-19), 7.07 (*m*, 1H, H-10), 7.16 (*m*, 1H, H-11), 7.38 (*m*, 1H, H-12) and 7.41 (*m*, 1H, H-9).

Leepacine (**2**). A portion (4.5 g) of the extract obtained at pH 6 was subjected to prep. TLC on silica gel with petrol (40–60°)–Me_2CO–Et_2NH (17:4:1) to afford a major band containing two alkaloids. The material was again subjected to prep. TLC on silica gel with petrol–Me_2CO–Et_2NH (16:3:1). This afforded a pure 'leepacine', R_f = 0.2 (7.5 mg), sensitive to light and air. $[\alpha]_D$ −91° (MeOH). UV λ_{max}^{MeOH} nm (log ε): 207 (4.23), 250 (3.59), 298 (3.12), λ_{min}^{MeOH} nm (log ε): 229 (3.45), 275 (2.95). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3350 (N–H), 1735 (ester C=O), 1720 (ketone C=O), 1605 (C=C) and 750 (aromatic C–H). HRMS *m/z* (rel. int. %, formulae, calc value) 350.1619 (10, $C_{21}H_{22}N_2O_3$, 350.1630), 322.1660 (29, $C_{20}H_{22}N_2O_2$, 322.1681, $[M-CO]^+$), 292.1548 (19, $C_{19}H_{20}N_2O$), 291.1757 $[M-CO_2Me]^+$, 263.1540 (15,

$C_{18}H_{19}N_2$, 263.1548, $[M-CO_2Me-CHO]^+$, 214.0860 (33, $C_{13}H_{12}NO_2$, 214.0868), 182.0604 (29, $C_{12}H_8NO$, 182.0605), 167.0733 (33, $C_{12}H_9N$, 167.0734), 122.0972 (100, $C_8H_{12}N$, 122.0969). ^{1}H NMR ($CDCl_3$, 300 MHz, δ): 1.42 (*m*, 1H, H-14α), 1.59 (*d*, 3H, $J_{18,19}$ = 6.1 Hz, H-18), 2.07 (*m*, 1H, H-6α), 2.57 (*m*, 1H, H-14β), 2.60 (*m*, 1H, H-6β), 3.03 (*m*, 1H, H-15), 3.24 (*ddd*, 1H, $J_{3,2}$ < 1 Hz, $J_{3,14\alpha}$ = 10 Hz, $J_{3,14\beta}$ = 1 Hz, H-3), 3.26 (*m*, 1H, H-5), 3.45 (*d*, 1H, $J_{21\alpha,21\beta}$ = 15.1 Hz, H-21α), 3.60 (*s*, 3H, CO_2Me), 3.95 (*br s*, 1H, H-2), 4.33 (*d*, 1H, $J_{21\alpha,21\beta}$ = 15.1 Hz, H-21β), 5.70 (*q*, 1H, $J_{19,18}$ = 6.1 Hz, H-19), 6.62 (*d*, 1H, $J_{12,11}$ = 7.6 Hz, H-12), 6.90 (*dd*, 1H, $J_{10,9}$ = 7.4 Hz, $J_{10,11}$ = 7.1 Hz, H-10), 7.15 (*dd*, 1H, $J_{11,10}$ = 7.1 Hz, $J_{11,12}$ = 7.6 Hz, H-11), 7.23 (*d*, 1H, $J_{9,10}$ = 7.4 Hz, H-9) and 9.37 (*s*, 1H, N–H). ^{13}C NMR ($CDCl_3$, 75 MHz, δ): see Table 3.

Dihydroeburnamenine (**3**). EtOH extracts of 75 kg of roots of *R. stricta* were concd, acidified with 5% HCl, filtered and basified with NH_3 to pH 10, fr. 'K_9'. The soln thus obtained was extracted with $CHCl_3$ and EtOAc. The combined extracts were evapd, acidified with 2% tartaric acid soln (2 l) and extracted at pH 2.5 with $CHCl_3$ (3 l, fr. 'K_2'). A portion was subjected to prep. TLC on silica plates with petrol–Me_2CO (7:3) to afford pure (**3**). MS *m/z* (rel. int.%): 340 ($[M]^+$, 98), 265 (8), 251 (49), 221 (15), 210 (100), 209 (21), 194 (46), 180 (24), 167 (17), 156 (15), 149 (14), 140 (8), 125 (28), 124 (23), 115 (17) and 77 (84). UV λ_{max}^{MeOH} nm: 213, 226, 260, 290, λ_{min}^{MeOH} nm: 220, 240. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: absence of N–H and carbonyl absorptions.

Strictosamide (**4**). A portion of the EtOAc fr. 'M_6' at pH 6 was subjected to prep. TLC on silica gel with $CHCl_3$–MeOH. This afforded pure strictosamide, R_f 0.27 (30 mg). $[\alpha]_D$ −154° (MeOH). UV λ_{max}^{MeOH} nm (log ε): 217 (4.73), 283 (4.00), 290 (3.92), λ_{min}^{MeOH} nm (log ε): 278 (4.13), 287 (3.93). IR ν_{max}^{KBr} cm^{-1}: 3300–3400 (O–H, N–H), 1650 (α,β-unsaturated C=O), 1015–1080 (C–O st.), 747 (aromatic C–H). HRMS *m/z* (rel. int.%, formulae, calc value): 498.2001 (3, $C_{26}H_{30}N_2O_8$, 498.2001), 336.1456 (6, $C_{20}H_{20}N_2O_3$, 336.1470), 265.0970 (32, $C_{16}H_{13}N_2O_2$, 265.0996), 235.0864 (100, $C_{15}H_{11}N_2O$, 235.0871), 169.0758 (26, $C_{11}H_9N_2$, 169.0765). ^{1}H NMR (CD_3OD, 300 MHz, δ) 2.03 (*m*, 1H, H-14α), 2.46 (*m*, 1H, H-15), 2.64 (*m*, 1H, H-14β), 2.79 (*m*, 1H, H-3), 4.93 (*m*, 1H, H-5α), 5.03 (*m*, 1H, H-5β), 5.31 (*dd*, 2H, $J_{18,19}$ = 11.4 Hz, $J_{18,18'}$ = 1.8 Hz, H-18), 5.39 (*br s*, 1H, $J_{21,20}$ = < 1 Hz, H-21), 5.64 (*m*, 1H, H-19), 6.98 (*dd*, 1 Hz, $J_{10,9}$ = 7.3 Hz, $J_{10,11}$ = 7.3 Hz, H-10), 7.07 (*dd*, 1H, $J_{11,10}$ = 7.3 Hz, $J_{11,12}$ = 7.8 Hz, H-11), 7.36 (*d*, 1H, $J_{9,10}$ = 7.3 Hz, H-9), 7.32 (*d*, 1H, $J_{12,11}$ = 7.8 Hz, H-12), 7.37 (*s*, 1H, H-17), 4.57 (*d*, 1H, $J_{1',2'}$ = 7.8 Hz, H-1'), 3.19 (*m*, 1H, H-2'), 3.21 (*m*, 1H, H-3), 3.26 (*m*, 1H, H-5'), 3.60 (*m*, 1H, H-4'β), 3.66 (*m*, 1H, H-6'α), 3.85 (1H, *dd*, $J_{6'\beta,6'\alpha}$ = 10.4 Hz, $J_{6'\beta,5'}$ = 1.5 Hz, H-6'β). ^{13}C NMR (CD_3OD, 75 MHz, δ): see Table 3.

(−)-16R,21R-O-*Methyleburnamine* (**5**). The $CHCl_3$–EtOAc (17:3) eluates from silica gel CC afforded fr. A (0.3 g) which was subjected to prep. TLC in petrol–Me_2CO–NH_3 (16:5:1) to afford **5** (15 mg). $[\alpha]_D$ −104° ($CHCl_3$). CD ($CHCl_3$): $\Delta\varepsilon$ 285 (−4.5), $\Delta\varepsilon$ 272 (−5). UV λ_{max}^{MeOH} nm: 205 (sh), 225, 270, 280, 290, λ_{min}^{MeOH} nm: 210, 247. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2850, 1720, 1480 and 1360. EIMS *m/z* (rel. int.%): 310 ($[M]^+$, 100), 295 (6), 279 (16), 252 (33), 249 (37), 239 (24), 222 (10), 208 (38), 206 (20), 193 (10), 192 (16), 180 (16), 167 (18), 149 (17), 125 (12), 83 (19), 69 (30) and 57 (51). FD *m/z* 310 $[M]^+$. HRMS *m/z* (formulae, calc value) 310.2040 ($C_{20}H_{26}N_2O$, 310.2045), 295.1809 ($C_{19}H_{23}N_2O$, 295.1810), 281.1656 ($C_{18}H_{21}N_2O$, 281.1656), 249.1387 ($C_{17}H_{17}N_2$, 249.1391), 208.1126 ($C_{13}H_{14}N$, 208.1126), 193.0881 ($C_{14}H_{11}N$, 193.0893). ^{1}H NMR ($CDCl_3$, 400 MHz, δ) 0.90 (*ddd*, 1H, $J_{15\alpha,15\beta}$ = 13.3 Hz, $J_{15\alpha,14\alpha}$ = 7.2 Hz, $J_{15,14\beta}$ = 2.9 Hz, H-15α), 0.95 (*t*, 3H, $J_{18,19}$ = 7.5 Hz, H-18), 1.31 (*m*, 1H, H-14α), 1.40 (*d*, H, $J_{15\beta,15\alpha}$ = 13.3 Hz, H-15β), 1.61 (*dd*, 1H, $J_{19,19'}$ = 14.2 Hz, $J_{19,18}$ = 7.5 Hz, H-19), 1.71 (*dt*, 1H, $J_{14\beta,14\alpha}$ = 13.2 Hz, $J_{14\beta,13\beta}$ = 3.5 Hz, H-14β), 1.88 (*dd*, 1H, $J_{17\beta,17\alpha}$ = 13.9 Hz, $J_{17\beta,16\beta}$ = 9.4 Hz, H-17β), 2.06 (*dd*, 1H, $J_{19',19}$ = 14.2 Hz, $J_{19,18}$ = 7.5 Hz, H-19'), 2.17 (*ddd*, 1H, $J_{17\alpha,17\beta}$ = 13.9 Hz, $J_{17\alpha,16\beta}$ = 5.4 Hz, H-17α) 2.34 (*dd*, 1H, $J_{3\alpha,3\beta}$ = 11.2 Hz, $J_{3\alpha,14\beta}$ = 3.5 Hz, H-3α), 2.50 (*dd*, 1H, $J_{3\beta,3\alpha}$ = 11.2 Hz, $J_{3\beta,14\alpha}$ = 4.7 Hz, H-3β), 2.56 (*d*, 1H, $J_{6\beta,6\alpha}$ = 18.8 Hz, H-6β), 2.96 (*d*, 1H, $J_{6\alpha,6\beta}$ = 18.8 Hz, H-6α), 3.22 (*dd*, 1H, $J_{5\alpha,5\beta}$ = 15.8 Hz, $J_{5\alpha,6\alpha}$ = 5.6 Hz, H-5α), 3.28 (1H, *ddd*, $J_{5\beta,5\alpha}$ = 15.8 Hz, $J_{5\beta,6\alpha}$ = 7.1 Hz, $J_{5\beta,6\beta}$ = 5.6 Hz, H-5β), 3.90 (*s*, 1H, H-21β), 5.52 (*dd*, 1H, $J_{16\beta,17\alpha}$ = 9.4 Hz, $J_{16\beta,17\beta}$ = 5.4 Hz, H-16β), 7.12 (*ddd*, 1H, $J_{11,10}$ = 7.1 Hz, $J_{11,12}$ = 7.1 Hz, $J_{11,9}$ = 1.4 Hz, H-11), 7.17 (*ddd*, 1H, $J_{10,9}$ = 7.1 Hz, $J_{10,11}$ = 7.1 Hz, $J_{10,12}$ = 1.4 Hz, H-10), 7.48 (*dd*, 1H, $J_{9,10}$ = 7.1 Hz, $J_{9,11}$ = 1.4 Hz, H-9), 7.58 (*dd*, 1H, $J_{12,11}$ = 7.1 Hz, $J_{12,10}$ = 1.4 Hz, H-12). ^{13}C NMR and hetero-COSY ($CDCl_3$, 100 MHz, δ): 132.94 (C-2), 44.27 (C-3), 50.79 (C-5), 16.86 (C-6), 105.86 (C-7), 128.62 (C-8), 117.99 (C-9), 121.44 (C-10), 120.14 (C-11), 111.88 (C-12), 136.70 (C-13), 20.51 (C-14), 25.35 (C-15), 82.35 (C-16), 36.63 (C-17), 26.30 (C-18), 28.88 (C-19), 58.79 (C-21) and 50.59 (OMe).

2-*Ethyl*-3[2-(3-*ethylpiperdine*)*ethyl*]-*indole* (**6**). $CHCl_3$–EtOAc (7:3) afforded fr. 'A_2' (1.5 g) which was chromatographed by prep. silica in petrol–Me_2CO–NH_3 (16:5:1). This afforded 2-ethyl-3[2-(3-ethylpiperidino)ethyl] indole (15 mg). $[\alpha]_D$ +90° ($CHCl_3$). UV λ_{max}^{MeOH} nm: 208, 225, 282, 290, λ_{min}^{MeOH} nm: 240, 289. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3400, 2850, 1710, 1260. EIMS *m/z* (rel. int.%): 284 (1), 256 (0.66), 239 (0.76), 218 (0.82), 203 (1), 185 (1), 167 (3), 149 (9), 126 (100), 111 (8), 97 (13), 83 (16), 71 (23), 57 (40). HRMS *m/z* (formulae, calc value) 284.2235 ($C_{19}H_{28}N_2$, 284.2252), 126.1284 ($C_8H_{16}N$, 126.1282), 97.1011 (C_7H_{13}, 97.1017), 71.0859 (C_5H_{11}, 71.0860). ^{1}H NMR ($CDCl_3$, 400 MHz, δ): 0.91 (*t*, 3H, $J_{18,19}$ = 7.5 Hz, H-18), 1.25 (*m*, 2H, H-19), 1.30 (*t*, 3H, $J_{17,16}$ = 7.6 Hz, H-17), 1.65 (*m*, 1H, J = 6 Hz, H-20β), 1.75 (*m*, 1H, H-14β), 1.85 (*m*, 2H, H-15), 2.00 (*m*, 1H, H-21β), 2.10 (*m*, 1H, H-3β), 2.7 (*m*, 2H, H-5), 2.75 (*q*, 2H, $J_{16\beta,17}$ = 7.6 Hz, H-16β) 3.00 (*m*, 1H, H-6α), 3.15 (*m*, 1H, H-3α), 3.20 (*dd*, 1H, $J_{21\alpha,21\beta}$ = 17 Hz, $J_{21\alpha,20\beta}$ = 12 Hz, H-21α), 7.06 (*dt*, 1H, $J_{11,12}$ = 7.2 Hz, $J_{11,10}$ = 7.0 Hz, $J_{11,9}$ = 1.3 Hz, H-11), 7.10 (*dt*, 1H, $J_{10,11}$ = 7.0 Hz, $J_{10,9}$ = 7.1 Hz, $J_{10,12}$ = 1.5 Hz, H-10), 7.30 (*dd*, 1H, $J_{12,11}$ = 7.2 Hz, $J_{12,10}$ = 1.4 Hz, H-12), 7.50 (*dd*, 1H, $J_{9,10}$ = 7.1 Hz, $J_{9,11}$ = 1.3 Hz, H-9), 7.86 (*s*, 1H, NH). ^{13}C NMR and hetero-COSY ($CDCl_3$, $CDCl_3$75 MHz, δ): 135.36 (C-2), 53.88 (C-3), 59.60 (C-5), 19.38 (C-6), 108.32 (C-7), 128.61 (C-8), 118.07 (C-9), 119.28 (C-10), 121.10 (C-11), 110.41 (C-12), 137.25 (C-13), 24.73 (C-14), 30.35 (C-15), 22.71 (C-16), 14.37 (C-17), 11.24 (C-18), 27.38 (C-19), 37.12 (C-20) and 59.41 (C-21).

(+)-21S-*Eburnamenine* (**7**). The $CHCl_3$–EtOAc (4:1) eluates afforded frs 'A_3' (1.2 g) which were subjected to prep. TLC in petrol–Me_2CO–NH_3 (16:5:1) to give **7**. $[\alpha]_D$ +183° ($CHCl_3$). CD ($CHCl_3$): $\Delta\varepsilon$ 260 (+13.5). UV λ_{max}^{MeOH} nm: 207, 232, 253, 300, 310, λ_{min}^{MeOH} nm: 242, 295, 320. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3000, 2900, 1640, 1460, 1360; EIMS *m/z* (rel. int.%) 278 ($[M]^+$, 34), 263 (5, $[M-Me]^+$), 249 (89, $[M-C_2H_5]^+$), 220 (14), 208 (100), 206 (26), 193 (31), 70 (54), 69 (44), 56 (93) and 55 (61). FD *m/z*: 278 $[M]^+$. HRMS *m/z* (formulae, calc value): 278.1781 ($C_{19}H_{22}N_2$, 278.1782), 249.1387 ($C_{17}H_{17}N_2$, 249.1391), 208.1126 ($C_{15}H_{14}N$, 208.1126). ^{1}H NMR ($CDCl_3$, 400 MHz, δ): 1.00 (*t*, 3H, $J_{18,19}$ = 7.4 Hz, H-18), 1.15 (*dd*, 1H, $J_{15\beta,15\alpha}$ = 13.8 Hz, $J_{15\beta,14\beta}$ = 3.6 Hz, H-15β), 1.40 (*m*, 1H, H-19), 1.44 (*m*, 1H, H-19'), 1.50 (*m*, 1H, H-14α), 1.72 (*dd*, 1H, $J_{14\beta,14\alpha}$ = 14.0 Hz, $J_{14\beta,3\beta}$ = 7.5 Hz, H-14β), 2.00 (*dd*, 1H, $J_{15\alpha,15\beta}$ = 14.0 Hz, $J_{15\alpha,14\beta}$ = 7.7 Hz, H-15α), 2.53 (*dd*, 1H, $J_{6\beta,6\alpha}$ = 15.4 Hz, $J_{6\beta,5\alpha}$ = 5.0 Hz, H-6β), 2.75 (*dd*, 1H, $J_{3\alpha,3\beta}$ = 11.2 Hz, $J_{3\alpha,14\alpha}$ = 4.5 Hz, H-3α), 3.03 (*m*, 1H, H-6α), 3.25 (*dd*, 1H, $J_{3\beta,3\alpha}$ = 11.2 Hz, $J_{3\beta,14\alpha}$ = 4.5 Hz, H-3β) 3.30 (*dd*, 1H, $J_{5\beta,5\alpha}$ = 11.5 Hz, $J_{5\beta,6\alpha}$ = 5.2 Hz, H-5β), 3.37 (*dd*, 1H, $J_{5\alpha,5\beta}$ = 11.5 Hz, $J_{5\alpha,6\beta}$ = 5.0 Hz, H-5α), 4.30 (*s*, 1H, H-21α), 5.07 (*d*, 1H, $J_{17,16}$ = 7.8 Hz, H-17), 6.91 (*d*, 1H, $J_{10,11}$ = 7.1 Hz, H-16), 7.09 (*dt*, 1H, $J_{11,10}$ = 7.1 Hz, $J_{11,12}$ = 8.08 Hz, $J_{11,9}$ = 1.2 Hz, H-11), 7.17 (*dt*, 1H, $J_{10,9}$ = 7.7 Hz, $J_{10,11}$ = 7.1 Hz, $J_{10,12}$ = < 1 Hz, H-10), 7.32 (*dd*, 1H, $J_{12,11}$ = 8.08 Hz, $J_{12,10}$ = < 1 Hz, H-12), 7.46 (*d*, 1H,

$J_{9,10}$ = 7.7 Hz, H-9). ^{13}C NMR ($CDCl_3$, 100 MHz, δ): 130.00 (C-2), 45.38 (C-3), 52.86 (C-5), 16.54 (C-6), 107.08 (C-7), 128.23 (C-8), 118.42 (C-4), 121.91 (C-10), 119.91 (C-11), 108.51 (C-12), 134.00 (C-13), 20.76 (C-14), 22.71 (C-15), 119.79 (C-16), 116.71 (C-17), 18.98 (C-18), 31.11 (C-19), 37.44 (C-20) and 55.86 (C-21).

(20S)-19,20-*Dihydrocondylocarpine* (**8**). Powdered roots of *R. stricta* (105 kg) were extracted by percolation with EtOH and alkaloids isolated by the procedure described earlier [54]. The acidic extract (pH 2) was subjected to prep. TLC on silica gel using petrol–$CHCl_3$–MeOH (3:6:1). Crude alkaloids obtained were again subjected to prep. TLC using petrol-$CHCl_3$–MeOH (1:6:3), to afford a pure alkaloid (20 mg), which gave a blue colour reaction with ceric sulphate. The alkaloid was identified as (20*S*)-19,20-dihydrocondylocarpine on the basis of spectral data (MS, UV, IR and NMR) by comparison with those reported in the lit. [50, 51]. The identity of the alkaloid was further confirmed by TLC comparison with an authentic sample [47].

N-*Acetylaspidospermidine* (**9**). This compound was isolated from $CHCl_3$–petrol–MeOH (4:15:1) eluates by CC. This resulted in the isolation of pure **9**. EIMS *m/z* (rel. int.%): 324 (10), 296 (8), 295 (3), 281 (1) and 124 (100). HRMS *m/z* (formulae, calc value) 324.2198 ($C_{21}H_{28}N_2O$, 324.2201), 296.1888 ($C_{19}H_{24}N_2O$, 296.1888), 295.1804 ($C_{19}H_{23}N_2O$, 295.1810), 281.2017 ($C_{19}H_{25}N_2$, 281.2017), 124.1126 ($C_8H_{14}N$, 124.1126). ^{1}H NMR ($CDCl_3$, 400 MHz, δ): 0.61 (*t*, 3H, $J_{18,19\alpha}$ = 7.5 Hz, H-18), 0.86 (*q*, 1H, $J_{19\alpha,18}$ = 7.5 Hz, H-19α), 1.11 (*m*, 1H, H-15α), 1.15 (*m*, 1H, H-6α), 1.41 (*m*, 1H, H-19β), 1.46 (*m*, 1H, H-16α), 1.50 (*m*, 1H, H-17α), 1.53 (*m*, 1H, H-14α), 1.55 (*m*, 1H, H-14β), 1.62 (*br d*, 1H, $J_{15\beta,15\alpha}$ = 14.1 Hz, H-15β), 1.90 (*m*, 1H, H-16β), 1.98 (*m*, 1H, H-3α), 2.05 (*m*, 1H, H-6β), 2.12 (*m*, 1H, H-17β), 2.23 (*s*, 3H, MeCO), 2.25 (*m*, 1H, H-5α), 2.29 (*s*, 1H, H-21α), 3.06 (*m*, 1H, H-3β), 3.11 (*m*, 1H, H-5β), 4.07 (*br s*, 1H, H-2β), 7.00 (*ddd*, 1H, $J_{10,9}$ = 7.7 Hz, $J_{10,11}$ = 7.7 Hz, $J_{10,12}$ = 1.0 Hz, H-10), 7.13 (*m*, 1H, H-12), 7.16 (*m*, 1H, H-11) and 8.11 (*d*, 1H, $J_{9,10}$ = 7.7 Hz, H-9). ^{13}C NMR ($CDCl_3$, 100 MHz, δ) and hetero-COSY: see Table 2.

Acknowledgement—Financial support for this project from the Pakistan Atomic Energy Commission is gratefully acknowledged.

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