A convenient stereospecific synthesis of substituted 1,2,3,4,6,6a,-7,11b,12,12a-decahydropyrazino[1',2':1,6]pyrido[3,4-*b*]indoles[#]

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Dedicated to Dr. Nitya Anand on the occasion of his 80th birthday
(received 29 Jul 04; accepted 24 Sep 04; published on the web 05 Oct 04)

Abstract
A stereospecific reduction of the indole double bond of substituted 1,3,4,6,6a,11b,12,12a-octahydro-2*H*,7*H*-pyrazino[2′1′:6,1]pyrido[3,4-*b*]indoles using borane dimethylsulfide complex was developed affording (6a*R**,11b*S**)-1,2,3,4,6,7,12,12a-octahydropyrazino[2′1 ′:6,1]pyrido-[3,4-*b*]indoles. Product structures have been verified by NMR spectroscopy.

Keywords: Borane dimethylsulfide complex reduction, fused indoles, fused indolines

Introduction

1,2,3,4,6,7,12,12a-Octahydropyrazino[2',1':6,1]pyrido[3,4-*b*]indole (**1**) has been used for the synthesis of various compounds having a wide range of biological activities such as CNS depressant,[1–5] antihistaminic,[6,7] hypotensive,[1] phosphodiesterase inhibitors,[8,9] neoplasm inhibitors.[10] One of the major outcome of these studies has been the development of the neuroleptic drug centbutindole.[11] In continuation of this program for major structural modifications we required a convenient method for the reduction of the indole double bond of **1b**,**g**–**l** to give. 1,2,3,4,6,6a,7,11b,12,12a-decahydropyrazino[1',2':1,6]pyrido[3,4-*b*]indoles.

Results and Discussion

Chemistry

The starting material **1a** was synthesized according to a literature method.[1] The reduction of the indole double bond of **1a** was attempted utilizing the previously reported reagents including sodium cyanoborohydride-aceticacid, sodium borohydride-trifluoroacetic acid, catalytic

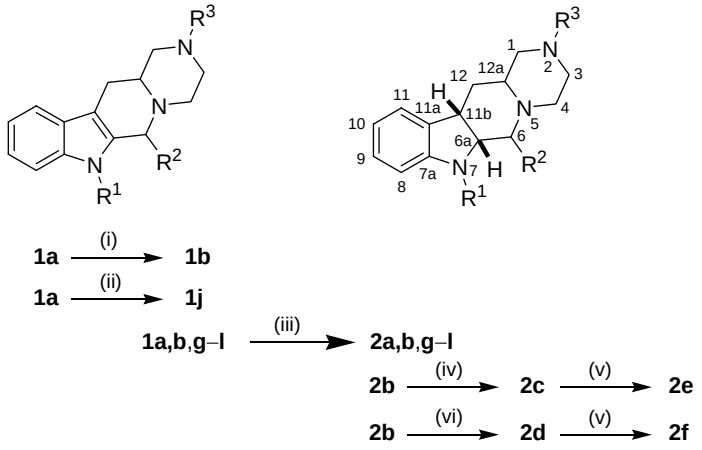
[#]CDRI communication no. 4742

hydrogenation with platinum oxide-fluoroboric acid, and borane-tetrahydrofuran. Unfortunately, all of the these methods proved to be unsuccessful. The use of sodium cyanoborohydride and trifluoroacetic acid at 0 °C yielded the desired 1,2,3,4,6,6a,7,11b,12,12a-decahydropyrazino [2',1':6,1]pyrido[3,4-*b*]indoles in poor yield.

Ultimately, a convenient method for the reduction of substituted 1,2,3,4,6,7,12,12a-octahydropyrazino[1',2':1,6]pyrido[3,4-*b*]indoles **1** was devised providing (6a*R**,11b*S**)-1,2,3,4,6,6a,7,11b,12,12a-decahydropyrazino[2',1':6,1]pyrido[3,4-*b*]indoles **2** in good yields. 1,2,3,4,6,7,12,12a-Octahydropyrazino[1',2':1,6]pyrido[3,4-*b*]indole (**1a)** was treated with borane dimethylsulfide complex in TFA at 0 °C to give (6a*R**,11b*S**)-1,2,3,4,6,6a,7,11b,12,12a-decahydropyrazino[1',2':1,6]pyrido[3,4-*b*]indole (**2a**) (Scheme 1). **1a** was condensed with 4-toluenesulphonyl chloride in dry pyridine to give 2-[(4-methylphenyl)sulfonyl]-1,2,3,4,6,7,12,12a-octahydropyrazino[1',2':1,6]pyrido[3,4-*b*]indole (**1b**). Reduction of compound **1b** with borane dimethylsulfide complex in TFA at 0 °C afforded (6a*R**,11b*S**)-2-[(4-methylphenyl)sulfonyl]-1,2,3,4,6,6a,7,11b,12,12a-decahydropyrazino[1',2':1,6]pyrido[3,4-*b*]indole (**2b**) (Scheme 1).

Compound **2b** has poor solubility in chloroform and was purified with difficulty by column chromatography. Therefore, **2b** was derivatized to the corresponding 7-benzyl and 7-methyl derivatives **2c** and **2d**, respectively (Scheme 1). Compound **2c** was subjected to 2D NMR studies in order to confirm the 6a,11b-*cis* stereochemistry. With the view of expanding the scope of this reaction, compounds **2c**,**d** were detosylated with conc. sulfuric acid to 7-benzyl- and 7-methyl-1,2,3,4,6,6a,7,11b,12,12a-decahydropyrazino[1',2':1,6]pyrido[3,4-*b*]indoles **2e**,**f** (Scheme 1)**.**

In order to generalize this reaction, various substituted 1,2,3,4,6,7,12,12a-octahydropyrazino-[1',2':1,6]pyrido[3,4-*b*]indoles **1g–l** were reduced with borane dimethylsulfide complex in TFA at 0 °C to give the corresponding *cis*-6a,11b-dihydro derivatives **2g–l.**



1	R^1	R^2	R^3	2
a	H	H	H	a
b	H	H	Tos	b
	Bn	H	Tos	c
	Me	H	Tos	d
	Bn	H	H	e
	Me	H	H	f
g	H	H	Bn	g
h	Me	H	Bn	h
i	H	Ph	H	i
j	H	H	4-$O_2NC_6H_4$	j
k	H	H	$(CH_2)_3NEt_2$	k
l	H	H	Me	l

Scheme 1. *Reagents and conditions*: (i) TosCl, C_5H_5N, 30 °C, 15 min; (ii) 4-$ClC_6H_4NO_2$, Na_2CO_3, NaI, DMF, 75 °C, 12 h; (iii) $(CH_3)_2S{\bullet}BH_3$, TFA, 0 → 30 °C, 3 h; (iv) BnCl, Na_2CO_3, NaI, DMF, 70 °C, 48 h; (v) conc. H_2SO_4, 35 °C, 72 h; (vi). HCHO, H_2-Pd/C, EtOH, 30 °C, 50 psi, 72 h.

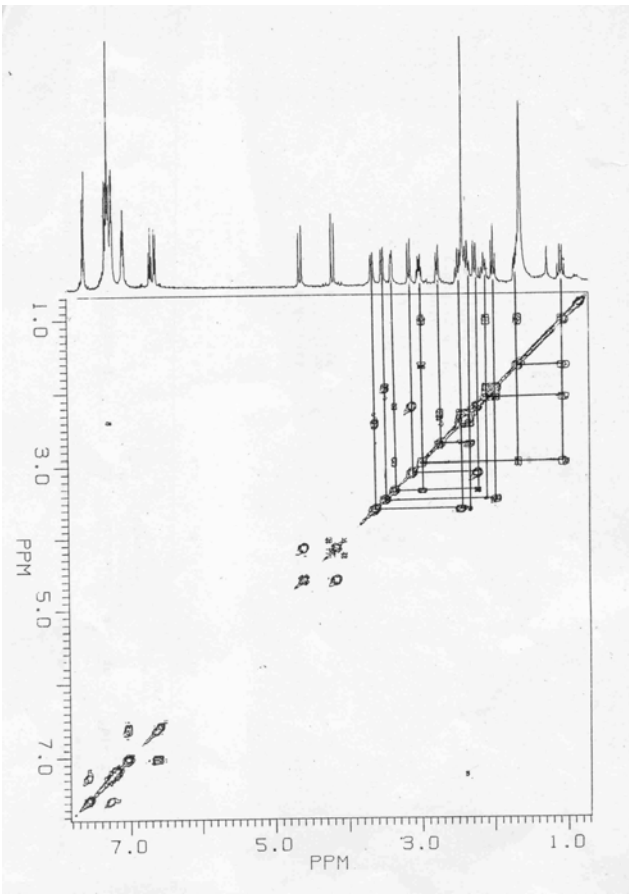


Figure 1. COSY Spectrum of 2.

NMR spectroscopy

The 6a,11b-*cis* stereochemistry of the substituted 1,2,3,4,6,6a,7,11b,12,12a-decahydropyrazino-[2',1':6,1]pyrido[3,4-*b*]indoles **2** has been established on the basis of ^{1}H and ^{13}C NMR spectra. The COSY spectrum of **2c** is shown in Figure 1. The assignment of one of the proton signals was confirmed by the long range COSY spectrum: The signal at δ 7.03 exhibits a cross peak with the signal at δ 2.98 due to an allylic coupling between H-11 and H-11b. With the unambiguous assignment of H-11b, tracing of the cross peaks in the COSY spectrum was then carried out as an unbroken sequence from H-11b to H-1 and H-11b to H-6, respectively. The most downfield signal in the aliphatic region at δ 3.63 is attributed to H-3 due to the deshielding of the sulfonyl group. The correlation of one of the geminal H-3 to the other H-3 and with both H-4 was drawn as outlined in the Figure 1. ^{13}C NMR and various DEPT experiments revealed that **2c** has three aliphatic methines, thirteen aromatic methines, six methylenes, one methyl and five quarternary carbons. Assignment of the aliphatic methine and methylene carbons is based on selective low power proton decoupled ^{13}C NMR experiments (Table 1). For example the selective decoupling of the signals at δ 3.38 (6a), 2.98 (11b) and 2.09 (12a) showed signal enhancement in the ^{13}C NMR spectra at δ 61.56, 37.86 and 57.25, respectively.

Table 1. ^{1}H and ^{13}C NMR data (400/100 MHz) of **2c** (R^1 = Bn, R^2 = H, R^3 = Tos; in $CDCl_3$)

Position	δ_C	δ_H	J [Hz]
1	53.98	3.49 eq	$J_{1(eq),12a(ax)}$ = 2.35; J_{gem} = 12.52
		1.96 ax	$J_{1(ax),12a(ax)}$ = 10.96; J_{gem} = 12.52
3	45.79	3.63 eq	$J_{3(eq),4(ax)}$ = 2.35; $J_{3(eq),4(eq)}$ = 2.35; J_{gem} = 11.74
		2.45 ax	$J_{3(ax),4(eq)}$ = 2.35; $J_{3(ax),4(ax)}$ = 10.96; J_{gem} = 11.74
4	50.86	2.72 eq	$J_{4(eq),3(eq),}$ = 2.35; $J_{4(eq),3(ax)}$ = 2.35; J_{gem} = 11.74
		2.31 ax	$J_{4(ax),3(eq)}$ = 2.35; $J_{4(ax),3(ax)}$ = 10.96; J_{gem} = 11.74
6	34.20	3.13 eq	$J_{6\ (eq),\ 6a(eq)}$ = 0.0,J_{gem} = 13.0
		2.21 ax	$J_{6(ax),6a(eq)}$ = 3.13, J_{gem} = 13.0
6a	61.56	3.38 eq	$J_{6a(eq),6(ax)}$ = 3.13, $J_{6a(eq),11b(ax)}$ = 6.26; $J_{6a(eq),6(eq)}$ = 0.0
7a	150.93	–	–
8	118.11	6.62	$J_{8,\ 9}$ = 7.50
9	123.10	7.0–7.1	overlapped
10	127.04	6.68	$J_{9,10}$ = 7.20, $J_{10,11}$ = 7.20
11	127.65	7.0–7.1	overlapped
11a	143.69	–	–
11b	37.86	2.98 ax	$J_{6a(eq),11b(ax)}$ = 6.26; $J_{11b(ax),12(eq)}$ = 6.26; $J_{11b(ax),12(ax)}$ = 10.96
12	53.08	1.73 eq	$J_{12(eq),12a(ax)}$ = 2.35; $J_{12(eq),11b(ax)}$ = 6.26; J_{gem} = 12.52
		1.07 ax	$J_{12(ax),11b(ax)}$ = 10.96; $J_{12(ax),12a(ax)}$ = 10.96; J_{gem} = 12.52
12a	57.25	2.09 ax	$J_{12a(ax),12(eq)}$ = 2.35; $J_{12a(ax),12(ax)}$ = 10.96; $J_{12a(ax),1(ax)}$ = 10.96; $J_{12a(ax),\ 1(eq)}$ = 2.35
Bn: CH_2	49.59	4.59 H_A 4.18 H_B	J_{gem} = 16.43
CH_3	21.46	4.15	s
Tos: 3,5	128.0	7.26	AA'
Tos: 2,6	129.0	7.56	XX'
Tos: 1	139.0	–	–
Tos: 4	131.90	–	–
Ph: 2,6	129.0	7.40	} s
Ph: 3,5	127.2	7.40	
Ph: 4	127.0	7.40	

The nOe difference spectrum of **2c** provided information about the relative orientation of H-6a and H-11b: Irradiation of the signal at δ 3.38 (6a) exhibited nOe with the signal at δ 2.98 (11b) and 2.21 ((6ax). The nOe difference spectra and the coupling constants of 6.26 Hz ($J_{6a(eq),11b(ax)}$) indicate the *cis* relationship between H-6a and H-11b. The signal at δ 2.98 (11b) showed nOe's with the signals at δ 3.38 (6a), 2.09 (12a) and 1.07 (12 eq), thus confirming that

H-6a, H-11b, H-12 and H-12a are oriented in the same plane and the relative stereochemistry of H-12a is *cis* with respect to H-6a and H-11b. In compound **1i** position 6 is another chiral center in addition to 12a, with relative *cis* stereochemistry of H-6a and H-12a.[17] Since the reaction conditions should not affect the stereochemistry at position 6 of the starting molecule **1i**, it is assumed that the reduction product **2i** has a *cis* relationship between positions 6, 6a, 11b and 12a.

Conclusions

Among several methods available for the reduction of indole to indoline the use of borane dimethylsulfide complex in trifluoroacetic acid was found suitable for the stereospecific reduction of the indole double bond in substituted-1,2,3,4,6,7,12,12a-octahydropyrazino-[1',2':1,6]pyrido[3,4-*b*]indoles **1** to the corresponding dihydro derivatives **2** and may be employed for the synthesis of other pharmacologically useful agents.

Experimental Section

General Procedures. Melting points were determined on an electrically heated apparatus (Tempo and Toshniwal). The IR spectra were taken on a Perkin- Elmer 157 spectrometer. The ^{1}H NMR were recorded on Varian R-32 (90 MHz) and EL-360 (60 MHz) instrument, using tetramethylsilane as an internal standard and the chemical shift values are expressed in δ scale. The low power selective decoupling nOe and 2D experiments were carried out on Bruker WM-400 (400 MHz) spectrometer. Mass spectra (EI-MS) were recorded on Jeol-JMS-01SG$_2$ at 70 eV. The analytical samples had spectral data compatible with its assigned structure and moved as a single spot on TLC. Elemental analysis (C, H, N) of the compounds were found to be satisfactory.

1,2,3,4,6,7,12,12a-Octahydropyrazino[1',2':1,6]pyrido[3,4-*b*]indole[1] (**1a**), the 2-benzyl derivative **1g**,[18] the 2-benzyl-7-methyl derivative **1h**,[18] the 6-phenyl derivative **1i**,[17] the 2,2-dimethyl-aminopropyl derivative **1k**,[1] and the 2-methyl derivative **1l**[1] were prepared by reported procedures.

2-[(4-Methylphenyl)sulfonyl]-1,2,3,4,6,7,12,12a-octahydropyrazino[1',2':1,6]pyrido[3,4-*b*]-indole (1b). A solution of **1a** (0.70 g, 3.0 mmol) and 4-toluenesulphonyl chloride (0.70 g, 3.6 mmol) in dry pyridine (8 mL) was stirred at 30 °C for 15 min. The separated solid was filtered off, washed with water (6 × 30 mL) and crystallized from $CHCl_3$/DMSO to give light yellow crystals **1b** (0.46 g, 39%); mp 206 °C. IR (KBr): $\tilde{\nu}$ 3200, 2900, 2400, 1620, 1460, 1420, 1340, 1280, 1230, 1180, 1140, 1100, 1070, 960, 920, 860, 830, 760, 720, 670 cm^{-1}. ^{1}H NMR (60 MHz, $CDCl_3$/DMSO d_6): δ 2.35 (s, 3H, CH_3), 2.35–4.9 (m, 11H, H_{aliph}), 6.8 (AA', 2H, 3,5-H_{Tos}), 7.2–7.6 (m, 6H, H_{Ar}), 10.0 (s, 1H, NH, exchangeable with D_2O). EI-MS: *m*/*z* (%) 381 (26) [M^+].

Anal. Calcd for $C_{21}H_{23}N_3O_2S$ (381): C, 66.14; H, 6.04; N, 11.02. Found: C, 66.28; H, 6.20; N, 11.20.

2-(4-Nitrophenyl)-1,2,3,4,6,7,12,12a-octahydropyrazino[1',2':1,6]pyrido[3,4-*b*]indole (1j). A solution of **1a** (0.227 g, 1.0 mmol), 4-chloronitrobenzene (0.165 mg, 1.05 mmol), baked Na_2CO_3 (0.053 g, 0.5 mmol), and NaI (7 mg, 0.05 mmol) in dry DMF (5 mL) was stirred at 75 °C for 12 h. The separated solid was filtered off, washed with water, dried, and purified by column chromatography using chloroform as eluent to yield the yellow solid **1j** (0.25 g, 72%); mp 230 °C. IR (KBr): $\tilde{\nu}$ 3500, 2800, 1600, 1500, 1340, 1270, 1200, 1120, 1100, 1209, 860, 760 cm^{-1}. ^1H NMR (60 MHz, $CDCl_3$): δ 1.1–3.8 (m, 11H, H_{aliph}), δ 8.0 (AA', 2H, 3,5-H_{C6H4}), 6.7–7.5 (m, 6H, H_{arom}). EI-MS: *m*/*z* (%): 348 (24) [M^+]. Anal. Calcd for $C_{20}H_{20}N_4O_2$ (348): C, 68.97; H, 5.75; N, 16.09. Found: C, 68.84; H, 5.84; N, 15.90.

(6a*R,11b*S**)-1,2,3,4,6,6a,7,11b,12,12a-Decahydropyrazino[1',2':1,6]pyrido[3,4-*b*]indole (2a). Typical procedure.** A solution of borane dimethylsulfide complex (10 M, 0.4 mL) was added dropwise to a stirred solution of **1a** (0.454 g, 2.0 mmol) in trifluroacetic acid (6 mL) at 0 °C in an atmosphere of nitrogen for 10 min. The reaction mixture was stirred at 30 °C for another 3 h, and was then diluted with water (0.4 mL), concentrated and basified with ammonia solution. The precipitated product was filtered off and crystallized from chloroform to afford the off-white solid **2a** (0.32 g, 70.5%); mp 220 °C. IR (KBr): $\tilde{\nu}$ 3150, 1500, 1440, 1360, 1280, 1140, 1020, 960, 820, 740 cm^{-1}. ^1H NMR (60 MHz, $CDCl_3$): δ 3.0 (br s, 1H, H-11b), 3.76 (distorted t, 1H, H-6a), 2.2–4.9 (m, 11H, H_{aliph}), 4.5 (br s, 1H, NH, exchangeable with D_2O), 6.9 (dd, 2H, H-8, H-10), 7.32 (dd, 2H, H-9, H-11). EI-MS: *m*/*z* (%): 229 (26.7) [M^+]. Anal. Calcd for $C_{14}H_{19}N_3$ (229): C, 73.36; H, 8.30; N, 18.34. Found: C, 74.42; H, 8.52; N, 18.02.

(6a*R,11b*S**)-2-[(4-Methylphenyl)sulfonyl]-1,2,3,4,6,6a,7,11b,12,12a-decahydropyrazino-[1',2':1,6]pyrido[3,4-*b*]indole (2b).** A solution of borane dimethylsulfide complex (10 M, 0.2 mL) was added dropwise to a stirred solution of **1b** (0.382 g, 1.0 mmol) in trifluroacetic acid (3 mL) at 0 °C in an atmosphere of nitrogen for 10 min. The reaction mixture was stirred for another 3 h at 30 °C, diluted with water (0.2 mL), concentrated and basified with ammonia solution. The precipitated product was filtered off and crystallized from ethanol/water to give yellow crystals **2b** (0.19 g, 49%); mp 118 °C. IR (KBr): $\tilde{\nu}$ 3400, 2900, 1620, 1470, 1360, 1300, 1260, 1180, 1120, 1020, 960, 840, 770, 750, 680 cm^{-1}. ^1H NMR (60 MHz, $CDCl_3$): δ 2.3 (s, 3H, CH_3), 3.0 (distorted t, 1H, H-11b), 3.72 (bs,1H, H-6a), 1.5–3.8 (m,11H, H_{aliph}), 6.6 (dd, 2H, H-8, H-10), 7.5 (d, 2H, 3,5-H_{Tos}), 6.8-7.3 (m, 4H, H_{arom}). EI-MS: *m*/*z* (%): 383 (8.12) [M^+]. Anal. Calcd for $C_{21}H_{25}N_3O_2S$ (383): C, 65.80; H, 6.53; N, 10.97. Found: C, 66.02; H, 6.82; N, 10.84.

(6a*R,11bS*)-7-Benzyl-2-[(4-methylphenyl)sulfonyl]-1,2,3,4,6,6a,7,11b,12,12a-decahydro-pyrazino[1',2':1,6]pyrido[3,4-*b*]indole (2c).** A solution of benzyl chloride (0.139 g, 1.1 mmol) in dry DMF (1 mL) was added to a stirred solution of **2b** (0.383 g, 1.0 mmol), baked Na_2CO_3 (0.53 g, 0.5 mmol) and NaI (8 mg, 0.05 mmol) in dry DMF (1.5 mL). Stirring was continued at 70 °C for 48 h. The reaction mixture was cooled, poured into water (15 mL), and the separated solid was filtered off and purified by column chromatography using silica gel and chloroform to give the off-white solid **2c** (0.36 g, 76%); mp 82 °C. IR (KBr): $\tilde{\nu}$ 3500, 2900-2800, 1620, 1600,

1560, 1360, 1300, 1160, 1100, 1040, 1020, 940, 900, 820, 770, 750, 700, 680 cm^{-1}. ^1H NMR data in Table 1. EI-MS: *m*/*z* (%): 473 (22.8) [M^+]. Anal. Calcd for $C_{28}H_{31}N_3O_2S$ (473): C, 71.04; H, 6.55; N, 8.88. Found: C, 71.22; H, 6.68; N, 9.10.

(6a*R,11b*S**)-7-Methyl-2-[(4-methylphenyl)sulfonyl]-1,2,3,4,6,6a,7,11b,12,12a-decahydropyrazino[1',2':1,6] pyrido[3,4-*b*]indole (2d).** A mixture of **2b** (0.5g, 1.3 mmol), formaldehyde solution (37%, 2 mL) and Pd/C (0.2 g) in ethanol (25 mL) was shaken in a Parr apparatus in hydrogen atmosphere at 30 °C and 50 psi for 72 h. The filtrate of the reaction mixture was concentrated to get a solid residue which was recrystallized from ethanol to yield the yellow solid **2d** (0.30 g, 58%); mp 144 °C. IR (KBr): $\tilde{\nu}$ 3400, 2800, 1660, 1600, 1480, 1350, 1180, 1120, 1100, 1000, 940, 820, 760, 740, 660 cm^{-1}. ^1H NMR (60 MHz, $CDCl_3$): δ 2.3 (s, 3H, CH_3), 2.62 (s, 3H, N-CH_3), 1.0-4.3 (m, 13H, H_{aliph}), 7.5 (AA', 2H, 3,5-H_{Tos}), 6.4–7.3 (m, 6H, H_{arom}). EI-MS: *m*/*z* (%): 397 (49.3) [M^+]. Anal. Calcd for $C_{22}H_{27}N_3O_2S$ (397): C, 66.50; H, 6.80; N, 10.58. Found: C, 66.82; H, 6.68; N, 10.62.

(6a*R,11b*S**)-7-Benzyl-1,2,3,4,6,6a,7,11b,12,12a-decahydropyrazino[1',2':1,6]pyrido[3,4-*b*]-indole (2e).** A solution of **2c** (0.5 g, 1.2 mmol) in conc. sulfuric acid (1.0 mL) was stirred at 35 °C for 72 h. The reaction mixture was cooled to 0 °C in an ice bath and basified with ammonia solution. The separated solid was filtered and recrystallized from petroleum ether (40–60 °C fraction) to give the pale yellow solid **2e** (0.25 g, 74%); mp 112 °C. IR (KBr): $\tilde{\nu}$ 3300, 2800, 1600, 1500, 1460, 1300, 1100, 1020, 940, 840, 760, 700 cm^{-1}. ^1H NMR (60 MHz, $CDCl_3$): δ 4.0 (d, ^2J = 15 Hz, 1H, $H_{A(Bn)}$), 4.48 (d, ^2J = 15 Hz, 1H, $H_{B(Bn)}$), 1.8–3.7 (m, 13 H, H_{aliph}), 6.3–7.4 (m, 9H, H_{arom}). EI-MS: *m*/*z* (%): 319 (21.7) [M^+]. Anal. Calcd for $C_{21}H_{25}N_3$ (397): C, 79.00; H, 7.84; N, 13.17. Found: C, 80.30; H, 7.98; N, 13.02.

(6a*R,11b*S**)-7-Methyl-1,2,3,4,6,6a,7,11b,12,12a-decahydropyrazino[1',2':1,6]pyrido[3,4-*b*]indole (2f).** In the same manner as described above for **2e**, compound **2d** (0.5 g, 1.26 mmol) and conc. sulfuric acid (1.0 mL) afforded the white solid **2f** (0.17 g, 56%); mp 225 °C. IR (KBr): $\tilde{\nu}$ 3300, 3200, 1400, 1120, 1040, 950, 840, 760, 700cm^{-1}. ^1H NMR (60 MHz, $CDCl_3$): δ 2.63 (s, 3H, N-CH_3), 1.0–3.7 (m, 13 H, H_{aliph}), 6.5–7.1 (m, 4H, H_{arom}). EI-MS: *m*/*z* (%): 243 (23) [M^+]. Anal. Calcd for $C_{15}H_{21}N_3$ (243): C, 74.07; H, 8.64; N, 17.28. Found: C, 73.81; H, 8.32; N, 17.02.

(6a*R,11b*S**)-1,2,3,4,6,6a,7,11b,12,12a-Decahydropyrazino[1',2':1,6]pyrido[3,4-*b*]indoles (2g–l).** The Typical Procedure as described above for the preparation of **2a** was utilized to convert compounds **1g–l** into **2g–l**. The products were obtained either as precipitated solids and were filtered off, or the reaction mixture was extracted with $CHCl_3$ (3 × 20 mL), the extract was dried and concentrated, and the residue was recrystallized or purified by chromatography using silica gel as adsorbent and a mixture of chloroform and hexane as eluent.

(6a*R,11b*S**)-2-Benzyl-1,2,3,4,6,6a,7,11b,12,12a-decahydropyrazino[1',2':1,6]pyrido[3,4-*b*]-indole (2g). 1g** (0.5 g, 1.6 mmol) was converted into the pale yellow solid **2g** (0.42 g, 84%); mp 152 °C. IR (KBr): $\tilde{\nu}$ 3300, 3000, 2800, 1620, 1500, 1360, 1320, 1300, 1260, 1200, 1160, 1120, 1060, 1040, 1020, 940, 920, 870, 740, 700. ^1H NMR (60 MHz, $CDCl_3$): δ 3.0 (bs, 1H, H-11b), 3.72 (bs, 1H, H-6a), 3.4 (s, 2H, H_{Bn}), 1.9–3.9 (m, 12H, H_{aliph}), 6.6 (dd, 2H, H_{arom}, H-9, H-11), 7.2

(s, 5H, H_{Ph}). EI-MS: *m*/*z* (%): 319 (38) [M^+]. Anal. Calcd for $C_{21}H_{25}N_3$ (319): C, 79.00; H, 7.84; N, 13.17. Found: C, 79.28; H, 7.90; N, 13.02

(6a*R,11b*S**)-2-Benzyl-7-methyl-1,2,3,4,6,6a,7,11b,12,12a-decahydropyrazino[1',2':1,6]-pyrido[3,4-*b*]indole (2h). 1h** (0.5g, 1.5 mmol) was converted into the off-white solid **2h** (0.30 g, 60%); mp 146 °C. IR (KBr): $\tilde{\nu}$ IR (KBr): $\tilde{\nu}$ 3300, 3000, 2800, 1620, 1480, 1460, 1420, 1350, 1320, 1280, 1240, 1200, 1180, 1150, 1120, 1080, 1020, 1000, 980,950, 930, 880, 840, 780, 720 cm^{-1}. ^1H NMR (60 MHz, $CDCl_3$): δ 3.4 (s, 2H, H_{Bn}), 3.74 (bs, 1H, H-6a), 1.0–3.2 (m, 15H, H_{aliph}), 6.62 (dd, 2H, H_{arom}, H-8, H-10), 7.2 (s, 5H, H_{Ph}). EI-MS: *m*/*z* (%): 333 (25) [M^+]. Anal. Calcd for $C_{22}H_{27}N_3$ (333): C, 79.28; H, 8.11; N, 12.61. Found: C, 79.10; H, 7.98; N, 12.52.

(6*R,6a*R**,11b*S**)-6-Phenyl-1,2,3,4,6,6a,7,11b,12,12a-decahydropyrazino[1',2':1,6]pyrido-[3,4-*b*]indole (2i).** (6*R**,12a*R**) (2i)-**1i** (0.5 g, 1.7 mmol) was converted into the yellow oil **2i** (0.32 g, 64%),. IR (KBr): $\tilde{\nu}$ 3400, 1700, 1630, 1480, 1350, 1220, 1150, 1040, 860, 780, 740, 700 cm^{-1}. ^1H NMR (60 MHz, $CDCl_3$): δ 3.1 (distorted t, 1H, H-11b), 4.0 (br s, 1H, H-6a), 1.05–3.7 (m, 11H, H_{aliph}), 7.5 (s, 5H, H_{Ph}),6.6–7.0 (m, 4H, H_{arom}). EI-MS: *m*/*z* (%): 305 (28) [M^+]. Anal. Calcd for $C_{20}H_{23}N_3$ (305): C, 78.95; H, 7.24; N, 13.82. Found: C, 79.02; H, 7.32; N, 13.90.

(6a*R,11b*S**)-2-(4-Nitrophenyl)-1,2,3,4,6,6a,7,11b,12,12a-decahydropyrazino[1',2':1,6]-pyrido[3,4-*b*]indole (2j). 1j** (0.5 g, 1.4 mmol) was converted into the yellow solid **2j** (0.34 g, 68%); mp 148–150 °C (dec.). IR (KBr): $\tilde{\nu}$ 3500, 1620, 150, 1340, 1260, 1220, 1140, 1040, 950, 850, 780 cm^{-1}. ^1H NMR (60 MHz, $CDCl_3$): δ 3.04(distorted t, 1H, H-11b),3.8(br s, 1H, H-6a), 1.2–3.7(m, 14H, H_{aliph}), 7.95(d, 2H, H-3,5_{C6H4}), 6.42–7.95(m, 6H, H_{arom}). EI-MS: *m*/*z* (%): 350 (52.7) [M^+]. Anal. Calcd for $C_{20}H_{22}N_4O_2$(350): C, 68.57; H, 6.28; N, 16.00. Found: C, 68.62; H, 6.38; N, 16.28.

***N*,*N*-Diethyl-*N*-[2-[(6a*R**,11b*S**)-3,4,6,6a,7,11b,12,12a-octahydropyrazino[1',2':1,6]pyrido [3,4-*b*]indol-2(1*H*)-yl]propyl]amine (2k). 1k** (0.5 g, 1.4 mmol) was converted into the light brown oil **2k** (0.31 g, 62%). IR (KBr): $\tilde{\nu}$ 3400, 3000, 2800, 1680, 1630, 1480,1380, 1330, 1300, 1280, 1230, 1170, 1070, 1040, 960, 770, 670 cm^{-1}. ^1H NMR (60 MHz, $CDCl_3$): δ 1.0 (t, 6H, CH_3), 3.02 (distorted t, 1H, H-11b), 3.75 (br s, 1H, H-6a), 1.2–2.9 (m, 22H, H_{aliph}), 6.6 (dd, 2H, H-8, H-10), 7.0 (dd, 2H, H-9, H-11). EI-MS: *m*/*z* (%): 342 (35) [M^+]. Anal. Calcd for $C_{21}H_{34}N_4$ (342): C, 73.68; H, 9.94; N, 16.37. Found: C, 73.56; H, 9.82; N, 16.48.

(6a*R,11bS*)-2-Methyl-1,2,3,4,6,6a,7,11b,12,12a-decahydropyrazino[1',2':1,6]pyrido[3,4-*b*]indole (2l). 1l** (0.5 g, 2.1 mmol) was converted into the yellowish oil **2l** (0.35 g, 70%). IR (KBr): $\tilde{\nu}$ 3400, 2900, 1740, 8-1600, 1500, 1240, 1170, 1100, 1040, 940, 840, 780 cm^{-1}. ^1H NMR (60 MHz, $CDCl_3$): δ 2.95 (s,3H, N-CH_3), 3.0 (distorted t, 1H, H-11b), 3.75 (br s, 1H, H-6a), 2.8–3.6 (m, 12H, H_{aliph}), 6.6 (dd, 2H, H-8, H-10) , 7.9 (dd, 2H, H-9, H-11). EI-MS: *m*/*z* (%): 243 (39) [M^+]. Anal. Calcd for $C_{15}H_{21}N_3$ (243): C, 74.07; H, 8.64; N, 17.28. Found: C, 73.92; H, 8.78; N, 17.12.

Acknowledgments

The authors are thankful to the RSIC, Lucknow for the spectroscopic data and Mr. Z. Ali for excellent technical assistance. R.C. is thankful to CSIR, New Delhi for a Research fellowship.

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