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 #

Jyoti Rao, Ruchika Chakrabarty, Raja Roy, Anil Mishra, and Anil K. Saxena*

Medicinal and Process Chemistry Division, Central Drug Research Institute, Lucknow 226001, India
E-mail: anilsak@hotmail.com

Dedicated to Dr. Nitya Anand on the occasion of his 80th birthday
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Abstract
A stereospecific reduction of the indole double bond of substituted 1,3,4,6,6a,11b,12,12a-octahydro-2H,7H-pyrazino[2'1':6,1]pyrido[3,4-b]indoles using borane dimethylsulfide complex was developed affording (6aR*,11bS*)-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-acetic acid, sodium borohydride-trifluoroacetic acid, catalytic

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hydrogenation with platinum oxide-fluoroboric acid, and borane-tetrahydrofuran. Unfortunately, all of 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-decahydroazepino[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-octahydroazepino[1',2':1,6]pyrido[3,4-b]indoles 1 was devised providing (6aR*,11bS*)-1,2,3,4,6,6a,7,11b,12,12a-decahydroazepino[2',1':6,1]pyrido[3,4-b]indoles 2 in good yields. 1,2,3,4,6,7,12,12a-Octahydroazepino[1',2':1,6]pyrido[3,4-b]indole (1a) was treated with borane dimethylsulfide complex in TFA at 0 °C to give (6aR*,11bS*)-1,2,3,4,6,6a,7,11b,12,12a-decahydroazepino[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]-1,2,3,4,6,6a,7,11b,12,12a-decahydroazepino[1',2':1,6]pyrido[3,4-b]indole (1b). Reduction of compound 1b with borane dimethylsulfide complex in TFA at 0 °C afforded (6aR*,11bS*)-2-[(4-methylphenyl)sulfonyl]-1,2,3,4,6,6a,7,11b,12,12a-decahydroazepino[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-decahydroazepino[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-octahydroazepino[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.

![Scheme 1](attachment://Scheme1.png)

**Scheme 1. Reagents and conditions:** (i) TosCl, C₅H₅N, 30 °C, 15 min; (ii) 4-ClC₆H₄NO₂, Na₂CO₃, NaI, DMF, 75 °C, 12 h; (iii) (CH₃)₂S•BH₃, TFA, 0 → 30 °C, 3 h; (iv) BnCl, Na₂CO₃, NaI, DMF, 70 °C, 48 h; (v) conc. H₂SO₄, 35 °C, 72 h; (vi) HCHO, H₂-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 $\delta$ 7.03 exhibits a cross peak with the signal at $\delta$ 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 $\delta$ 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 $\delta$ 3.38 (6a), 2.98 (11b) and 2.09 (12a) showed signal enhancement in the $^{13}$C NMR spectra at $\delta$ 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$_3$)

<table>
<thead>
<tr>
<th>Position</th>
<th>$\delta_C$</th>
<th>$\delta_H$</th>
<th>$J$ [Hz]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>53.98</td>
<td>3.49 eq</td>
<td>$J_{1(eq),12a(ax)} = 2.35; J_{gem} = 12.52$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.96 ax</td>
<td>$J_{1(ax),12a(ax)} = 10.96; J_{gem} = 12.52$</td>
</tr>
<tr>
<td>3</td>
<td>45.79</td>
<td>3.63 eq</td>
<td>$J_{3(eq),4(ax)} = 2.35; J_{3(eq),4(eq)} = 2.35; J_{gem} = 11.74$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.45 ax</td>
<td>$J_{3(ax),4(eq)} = 2.35; J_{3(ax),4(ax)} = 10.96; J_{gem} = 11.74$</td>
</tr>
<tr>
<td>4</td>
<td>50.86</td>
<td>2.72 eq</td>
<td>$J_{4(eq),3(eq)} = 2.35; J_{4(eq),3(ax)} = 2.35; J_{gem} = 11.74$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.31 ax</td>
<td>$J_{4(ax),3(eq)} = 2.35; J_{4(ax),3(ax)} = 10.96; J_{gem} = 11.74$</td>
</tr>
<tr>
<td>6</td>
<td>34.20</td>
<td>3.13 eq</td>
<td>$J_{6(eq),6a(eq)} = 0.0, J_{gem} = 13.0$</td>
</tr>
<tr>
<td>6a</td>
<td>61.56</td>
<td>3.38 eq</td>
<td>$J_{6a(eq),6(ax)} = 3.13, J_{6a(eq),11b(ax)} = 6.26; J_{6a(eq),6(eq)} = 0.0$</td>
</tr>
<tr>
<td>7a</td>
<td>150.93</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>8</td>
<td>118.11</td>
<td>6.62</td>
<td>$J_8, 9 = 7.50$</td>
</tr>
<tr>
<td>9</td>
<td>123.10</td>
<td>7.0–7.1</td>
<td>overlapped</td>
</tr>
<tr>
<td>10</td>
<td>127.04</td>
<td>6.68</td>
<td>$J_9,10 = 7.20, J_{10,11} = 7.20$</td>
</tr>
<tr>
<td>11</td>
<td>127.65</td>
<td>7.0–7.1</td>
<td>overlapped</td>
</tr>
<tr>
<td>11a</td>
<td>143.69</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>11b</td>
<td>37.86</td>
<td>2.98 ax</td>
<td>$J_{6a(eq),11b(ax)} = 6.26; J_{11b(ax),12(eq)} = 6.26; J_{11b(ax),12(ax)} = 10.96$</td>
</tr>
<tr>
<td>12</td>
<td>53.08</td>
<td>1.73 eq</td>
<td>$J_{12(eq),12a(ax)} = 2.35; J_{12(eq),11b(ax)} = 6.26; J_{gem} = 12.52$</td>
</tr>
<tr>
<td>12a</td>
<td>57.25</td>
<td>2.09 ax</td>
<td>$J_{12a(ax),12(eq)} = 2.35; J_{12a(ax),12(ax)} = 10.96; J_{12a(ax),1(ax)} = 10.96; J_{12a(ax),1(eq)} = 2.35$</td>
</tr>
<tr>
<td>Bn: CH$_2$</td>
<td>49.59</td>
<td>4.59 H$_A$</td>
<td>$J_{gem} = 16.43$</td>
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<td></td>
<td></td>
<td>4.18 H$_B$</td>
<td></td>
</tr>
<tr>
<td>CH$_3$</td>
<td>21.46</td>
<td>4.15</td>
<td>s</td>
</tr>
<tr>
<td>Tos: 3,5</td>
<td>128.0</td>
<td>7.26</td>
<td>AA'</td>
</tr>
<tr>
<td>Tos: 2,6</td>
<td>129.0</td>
<td>7.56</td>
<td>XX'</td>
</tr>
<tr>
<td>Tos: 1</td>
<td>139.0</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Tos: 4</td>
<td>131.90</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Ph: 2,6</td>
<td>129.0</td>
<td>7.40</td>
<td>–</td>
</tr>
<tr>
<td>Ph: 3,5</td>
<td>127.2</td>
<td>7.40</td>
<td>–</td>
</tr>
<tr>
<td>Ph: 4</td>
<td>127.0</td>
<td>7.40</td>
<td>–</td>
</tr>
</tbody>
</table>

The nOe difference spectrum of 2c provided information about the relative orientation of H-6a and H-11b: Irradiation of the signal at $\delta$ 3.38 (6a) exhibited nOe with the signal at $\delta$ 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 $\delta$ 2.98 (11b) showed nOe’s with the signals at $\delta$ 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. 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-01SG2 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 (1a), the 2-benzyl derivative 1g, the 2-benzyl-7-methyl derivative 1h, the 6-phenyl derivative 1i, the 2,2-dimethylaminopropyl derivative 1k, and the 2-methyl derivative 1l 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 CHCl₃/DMSO to give light yellow crystals 1b (0.46 g, 39%); mp 206 °C. IR (KBr): υ ~ 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, CDCl₃/DMSO $d_6$): δ 2.35 (s, 3H, CH$_3$), 2.35–4.9 (m, 11H, H$_\text{aliph}$), 6.8 (AA', 2H, 3,5-H$_\text{Tos}$), 6.8 (AA', 2H, 3,5-H$_\text{Tos}$), 7.2–7.6 (m, 6H, H$_\text{Ar}$), 10.0 (s, 1H, NH, exchangeable with D$_2$O). EI-MS: m/z (%) 381 (26) [M⁺].

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_{2}CO_{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): ν ~ 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, Haliph), 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_{4}O_{2} (348): C, 68.97; H, 5.75; N, 16.09. Found: C, 68.84; H, 5.84; N, 15.90.

(6aR*,11bS*)-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 trifluoroacetic 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 then was 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): ν ~ 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_{2}O), 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.

(6aR*,11bS*)-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 trifluoroacetic 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): ν ~ 3400, 2900, 1620, 1470, 1360, 1300, 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_{3}O_{2}S (383): C, 65.80; H, 6.53; N, 10.97. Found: C, 66.02; H, 6.82; N, 10.84.

(6aR*,11bS*)-7-Benzyl-2-[(4-methylphenyl)sulfonyl]-1,2,3,4,6,6a,7,11b,12,12a-decahydropyrazino[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_{2}CO_{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): ν ~ 3500, 2900-2800, 1620, 1600,
1560, 1360, 1300, 1160, 1100, 1040, 1020, 940, 900, 820, 770, 750, 700, 680 cm\(^{-1}\). \(^1\)H 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-decahydro-pyrazino[1',2':1,6] pyrido[3,4-b]indole (2d). A mixture of 2b (0.5 g, 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\(^{-1}\). \(^1\)H NMR (60 MHz, CDCl\(_3\)): \(\delta\) 2.3 (s, 3H, CH\(_3\)), 2.62 (s, 3H, N-CH\(_3\)), 1.0-4.3 (m, 13H, Haliph), 7.5 (AA', 2H, 3,5-HTos), 6.4–7.3 (m, 6H, Harom). 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, 1620, 1500, 1360, 1320 , 1300, 1260, 1200, 1160, 1120, 1060, 1040, 1020, 940, 840, 760, 700 cm\(^{-1}\). \(^1\)H NMR (60 MHz, CDCl\(_3\)): \(\delta\) 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, Harom). 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, 3000, 2900, 1660, 1500, 1460, 1300, 1010, 940, 840, 760, 700 cm\(^{-1}\). \(^1\)H NMR (60 MHz, CDCl\(_3\)): \(\delta\) 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.

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 \(\times\) 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, 1260, 1200, 1160, 1120, 1060, 1040, 1020, 940, 920, 870, 740, 700. \(^1\)H NMR (60 MHz, CDCl\(_3\)): \(\delta\) 3.0 (bs, 1H, H-11b), 3.72 (bs, 1H, H-6a), 3.4 (s, 2H, H\(_{\text{Bn}}\)), 1.9–3.9 (m, 12H, H\(_{\text{aliph}}\)), 6.6 (dd, 2H, H\(_{\text{arom}}\), H-9, H-11), 7.2
(s, 5H, H₆). EI-MS: m/z (%): 319 (38) [M⁺]. Anal. Calcd for C₂₁H₂₅N₃ (319): C, 79.00; H, 7.84; N, 13.17. Found: C, 79.28; H, 7.90; N, 13.02

(6αR*,11bS*)-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 (0.5 g, 1.5 mmol) was converted into the off-white solid 2h (0.30 g, 60%); mp 146 °C. IR (KBr): ν 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, CDCl₃): δ 3.4 (s, 2H, H Bn), 3.74 (bs, 1H, H-6a), 1.0–3.2 (m, 15H, Haliph), 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 C₂₂H₂₇N₃ (333): C, 79.28; H, 8.11; N, 12.61. Found: C, 79.10; H, 7.98; N, 12.52.

(6R*,6αR*,11bS*)-6-Phenyl-1,2,3,4,6,6a,7,11b,12,12a-decahydropyrazino[1',2':1,6]pyrido[3,4-b]indole (2i). 1i (0.5 g, 1.7 mmol) was converted into the yellow oil 2i (0.32 g, 64%),. IR (KBr): ν 3400, 1700, 1630, 1480, 1350, 1220, 1150, 1040, 950, 850, 780 cm⁻¹. ¹H NMR (60 MHz, CDCl₃): 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 C₂₀H₂₃N₃ (305): C, 78.95; H, 7.24; N, 13.82. Found: C, 79.02; H, 7.32; N, 13.90.

(6αR*,11bS*)-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): ν 3500, 1620, 1500, 1340, 1260, 1220, 1150, 1040, 950, 850, 780 cm⁻¹. ¹H NMR (60 MHz, CDCl₃): 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 C₂₀H₂₂N₄O₂ (350): C, 68.57; H, 6.28; N, 16.00. Found: C, 68.62; H, 6.38; N, 16.28.

(6R*,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): ν 3400, 2900, 1740, 8-1600, 1500, 1240, 1170, 1070, 1040, 960, 770, 670 cm⁻¹. ¹H NMR (60 MHz, CDCl₃): δ 2.95 (s, 3H, N-CH₃), 2.9 (distorted t, 1H, H-11b), 3.75 (br s, 1H, H-6a), 2.8–3.6 (m, 12H, Haliph), 6.6 (dd, 2H, H-8, H-10), 7.2 (d, 2H, H-9, H-11). EI-MS: m/z (%): 243 (39) [M⁺]. Anal. Calcd for C₁₅H₂₁N₃ (243): C, 74.07; H, 8.64; N, 17.28. Found: C, 73.92; H, 8.78; N, 17.12.
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References