JOC Article

Novel Routes to 1,2,3,4-Tetrahydropyrrolo[1,2-*a*]pyrazines and 5,6,9,10,11,11a-Hexahydro-8*H*-pyrido[1,2-*a*]pyrrolo[2,1-*c*]pyrazines

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Condensation reactions of benzotriazole and 2-(pyrrol-1-yl)-1-ethylamine (**1**) with formaldehyde and glutaric dialdehyde, respectively, afforded intermediates **2** and **6**. Subsequent nucleophilic substitutions of the benzotriazole group in **2** and **6** with Grignard reagents, sodium cyanide, and sodium borohydride gave 1,2,3,4-tetrahydropyrrolo[1,2-*a*]pyrazines **3a**−**e**, **4**, **5** and 5,6,9,10,11,11a-hexahydro-8*H*-pyrido[1,2-*a*]pyrrolo[2,1-*c*]pyrazines **7a**−**c**, **8**, **9**, respectively, in good yields.

Introduction

1,2,3,4-Tetrahydropyrrolo[1,2-*a*]pyrazines are of considerable interest because of their antiamnesic, antihypoxic,[1] psychotropic,[2] antihypersensitive,[3] and aldose reductase inhibitor activities.[4] Pyrrolopyrazines also selectively bind to GABAa receptors[5] and are useful starting materials for the synthesis of octahydropyrrolo-[1,2-*a*]pyrazine-based coronary-dilators and neuroleptics.[6]

1,2,3,4-Tetrahydropyrrolo[1,2-*a*]pyrazines were previously synthesized via selective hydrogenation or reduction of 3,4-dihydropyrrolo[1,2-*a*]pyrazines.[3,6−8] However, 5,6,9,10,11,11a-hexahydro-8*H*-pyrido[1,2-*a*]pyrrolo[2,1-*c*]-pyrazines were previously unknown. We now describe novel and convenient approaches to 1,2,3,4-tetrahydropyrrolo[1,2-*a*]pyrazines **3a**−**e**, **4**, **5** and 5,6,9,10,11,11a-hexahydro-8*H*-pyrido[1,2-*a*]pyrrolo[2,1-*c*]pyrazines **7a**−**c**, **8**, **9** using benzotriazole methodology.[9−14]

Results and Discussion

1-[3,4-Dihydropyrrolo[1,2-*a*]pyrazin-2(1*H*)-ylmethyl]-1*H*-1,2,3-benzotriazole (2). Condensation of benzotriazole, 2-(pyrrol-1-yl)-1-ethylamine (**1**),[15] and formaldehyde in aqueous methanol at 20 °C formed **2** in 74% yield (Scheme 1). Compound **2** was fully characterized by ^{1}H, ^{13}C NMR spectra and microanalysis. In the aliphatic region of the ^{1}H NMR spectra, signals ascribed to BtCH_2N (δ = 5.59 ppm) and pyrrole CH_2N (δ = 3.89 ppm), respectively, supported structure **2**.

Syntheses of 1,2,3,4-Tetrahydropyrrolo[1,2-*a*]pyrazines 3a−e, 4 and 5 Using Grignard Reagents, Sodium Cyanide and Sodium Borohydride as Nucleophiles. Diverse nucleophiles smoothly substituted the benzotriazole moiety in compound **2**. Reactions of compound **2** with a variety of Grignard reagents gave 1,2,3,4-tetrahydropyrrolo[1,2-*a*]pyrazines **3a**−**e** in 70−92% yields (Scheme 1).

Treatment of compound **2** with sodium cyanide and sodium borohyride at 20 °C afforded 2-[3,4-dihydropyrrolo[1,2-*a*]pyrazin-2(1*H*)-yl]acetonitrile (**4**) and the 2-methyl-1,2,3,4-tetrahydropyrrolo[1,2-*a*]pyrazine boron complex (**5**) in 80% and 65% yields, respectively (Scheme 1).

8-Benzotriazolyl-5,6,9,10,11,11a-hexahydro-8*H*-pyrido[1,2-*a*]pyrrolo[2,1-*a*]pyrazine (6). Condensation of 2-(pyrrol-1-yl)ethylamine (**1**), benzotriazole, and glutaric dialdehyde formed the fused ring compound **6** as a mixture of Bt^1 (benzotriazol-1-yl) **6a** and Bt^2 (benzotriazol-2-yl) **6b** isomers in a 6:1 ratio (determined by ^{1}H NMR spectroscopy) in 67% total yield. The ^{1}H and ^{13}C NMR data of the major Bt^1 isomer **6a** are reported in the Experimental Section. The structure and stereochemistry

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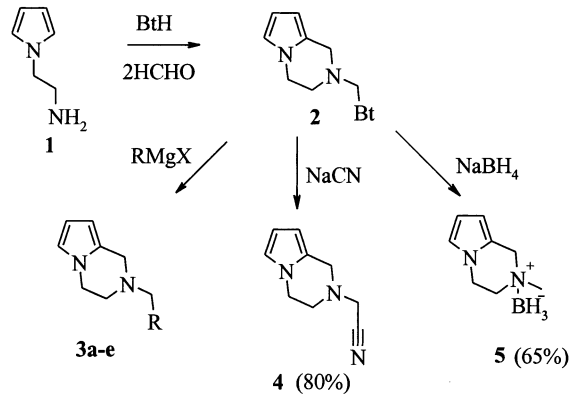
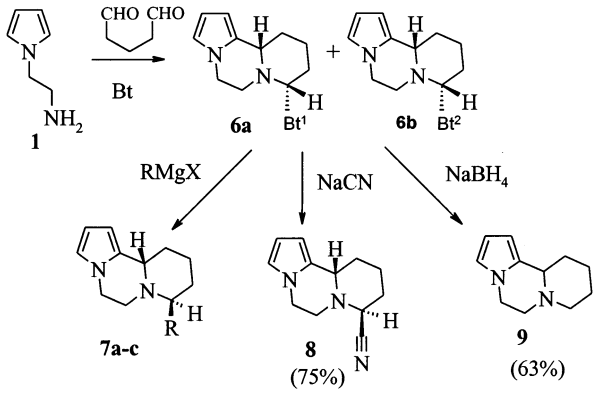
SCHEME 1



3	R	Yield %
a	4-ClC_6H_4	92
b	$PhCH_2$	80
c	4-$CH_3C_6H_4$	85
d	CH_2=$CHCH_2$	70
e	CH_2=CH	75

SCHEME 2



7	R	Yield %
a	4-ClC_6H_4	70
b	4-$CH_3C_6H_4$	66
c	CH_3CH_2	80

of **6a** were unambiguously established by single-crystal X-ray crystallography. Figure 1 (Supporting Information) shows a perspective view of the structure of **6a**, which shows that the sp^3 nitrogen is hybridized such that the pyridopyrazine ring system has a trans ring fusion. The adjacent Bt^1 substituent occupies an equatorial position in the chair conformation of its attached six-membered ring. According to our previous work,[9,16,17] Bt^1 and Bt^2 are both good leaving groups, and removal of benzotriazolyl groups from the Bt^1 and Bt^2 isomers results in the same iminium cation. Therefore, compound **6** was used as a mixture of isomers **6a** and **6b** for the subsequent reactions.

Syntheses of 5,6,9,10,11,11a-Hexahydro-8*H*-pyrido[1,2-*a*]pyrrolo[2,1-*c*]pyrazines 7a−c, 8 and 9 Using Grignard Reagents, Sodium Cyanide and Sodium Borohydride as Nucleophiles. Reactions of compound **6** with appropriate Grignard reagents (4-ClC_6H_4MgCl, 4-$CH_3C_6H_4MgBr$, and CH_3CH_2MgBr) in THF at 20 °C gave products **7a**−**c** in 66−80% yield (Scheme 2).

Treatment of compound **6** with sodium cyanide and sodium borohydride resulted in substitution of the benzotriazolyl group (both Bt^1 and Bt^2) with cyanide and hydride to give 5,6,9,10,11,11a-hexahydro-8*H*-pyrido[1,2-*a*]pyrrolo[2,1-*c*]pyrazine-8-carbonitrile (**8**) and 5,6,9,10,11,11a-hexahydro-8*H*-pyrido[1,2-*a*]pyrrolo[2,1-*c*]-pyrazine (**9**) in 75% and 63% yields, respectively (Scheme 2).

Configurational Analysis of Compounds 7a−c and 8. Initially, the configurations of **7a**−**c**, **8** were determined by NOE experiments. For compounds **7a**−**c** and **8**, when H(8) (a broad singlet at 4.41 ppm for **7a**, 4.42 ppm for **7b** and a doublet at 3.63 ppm (J = 11.1 Hz) for **8** and a multiplet in the range of 2.73−2.69 ppm for **7c**) was irradiated, no NOE effect was observed for H(11a) (multiplet in the range of 4.07−3.97 ppm) and vice versa. When H(11a) in **7a**,**b** was irradiated, a distinct positive NOE effect was observed for the phenyl ring. Thus, H(8) and H(11a) are in a mutually trans orientation. It is difficult to get a distinct NOE effect between H(11a) and the ethyl protons in **7c** because the protons of the ethyl group merged with the protons of the six-membered rings.

The structure of **7b** was unambiguously confirmed by X-ray crystallography (Figure 1, Supporting Information). The single-crystal X-ray structure determination revealed that, in contrast to the precursor **6**, the pyridopyrazine ring system in **7b** has a cis ring fusion. Once again the adjacent aryl substituent occupies an equatorial position. This diastereoisomer has H(8) and H(11a) on opposite sides of the pyridopyrazine ring system, and hence they would not be expected to show mutual NOE enhancements.

The predominance of the observed isomers can be explained on the basis of the reaction mechanism. Compound **6** can easily form the pyrazinium cation since Bt^- is a good leaving group.[10−12] Nucleophiles could attack the iminium cation from either face of the CH_2CH=N− plane. However, attack from above the plane is more favorable, compared to attack from below the plane, because of less steric hindrance from the 1,2,3,4-tetrahydropyrrolo[1,2-*a*]pyrazine ring system (Scheme 3). Thus products **7a**−**c** and **8** are formed by kinetic control. By contrast, in intermediate **6**, easy reversible ionization leads to the thermodynamically more stable configuration.

To summarize, 1,2,3,4-tetrahydropyrrolo[1,2-*a*]pyrazines **3a**−**e**, **4**, **5**, and 5,6,9,10,11,11a-hexahydro-8*H*-pyrido[1,2-*a*]pyrrolo[2,1-*c*]pyrazines **7a**−**c**, **8**, **9** were synthesized via nucleophilic substitutions of the benzotriazolyl moieties in **2** and **6**, themselves readily obtained from condensations of benzotriazole and 2-pyrrol-1-ylethylamine (**1**) with formaldehyde and glutaric dialdehyde,

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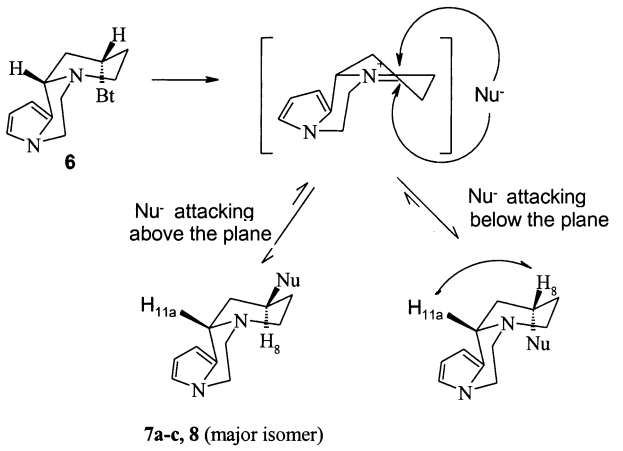
SCHEME 3



7a-c, 8 (major isomer)

respectively, in good yields. Trans isomers **7a**−**c** and **8** were obtained as the major products.

Experimental Section

Procedure for the Synthesis of 1-[3,4-Dihydropyrrolo-[1,2-*a*]pyrazin-2(1*H*)-ylmethyl]-1*H*-1,2,3-benzotriazole (2). 2-(Pyrrol-1-yl)ethylamine (**1**, 1.1 g, 10 mmol) and benzotriazole (1.19 g, 10 mmol) were dissolved in methanol/water (v/v = 4/1) (50 mL). Formaldehyde (1.7 g, 20 mmol, 37% aqueous solution) was added dropwise to the solution. The resulting mixture was stirred at 20 °C for 12 h. Then the precipitate was filtered off, washed with cold Et_2O, and dried in vacuo. Colorless plates (methanol/water); yield 74%; mp 125−126 °C; ^{1}H NMR δ 8.09 (d, J = 8.4 Hz, 1H), 7.66 (d, J = 8.3 Hz, 1H), 7.53 (t, J = 7.6 Hz, 1H), 7.40 (t, J = 7.3 Hz, 1H), 6.52 (br s, 1H), 6.11 (t, J = 3.0 Hz, 1H), 5.83 (br s, 1H), 5.59 (s, 2H), 3.99 (t, J = 5.6 Hz, 2H), 3.89 (s, 2H), 3.06 (t, J = 5.6 Hz, 2H); ^{13}C NMR δ 145.9, 133.6, 127.7, 125.3, 124.1, 120.0, 118.6, 109.9, 108.3, 103.1, 68.7, 48.3, 48.2, 44.6. Anal. Calcd for $C_{14}H_{15}N_5$: C, 66.38; H, 5.97; N, 27.65. Found: C, 66.49; H, 6.12; N, 27.75.

General Procedure for Syntheses of 1,2,3,4-Tetrahydropyrrolo[1,2-*a*]pyrazines 3a−e. Compound **2** (0.5 g, 2 mmol) was dissolved in dry THF (15 mL) at 0 °C. The corresponding Grignard reagent (3 mmol, 1.5 equiv) was added dropwise. The mixture was stirred at 20 °C for 12 h. Then, the reaction was quenched with water, washed with 2 M NaOH, and extracted with ether. After being dried over $MgSO_4$, the solvent was removed in vacuo. The product obtained was further purified by column chromatography (eluent: hexanes/EtOAc = 8/1−4/1).

2-(4-Chlorobenzyl)-1,2,3,4-tetrahydropyrrolo[1,2-*a*]pyrazine (3a): colorless plates (EtOAc/hexanes); yield 92%; mp 90−91 °C; ^{1}H NMR δ 7.31 (br s, 4H), 6.55 (br s, 1H), 6.13 (t, J = 3.3 Hz, 1H), 5.80 (br s, 1H), 3.98 (t, J = 5.5 Hz, 2H), 3.63 (s, 2H), 2.82 (t, J = 5.5 Hz, 2H); ^{13}C NMR δ 136.5, 133.0, 130.2, 128.5, 126.9, 118.4, 108.1, 102.7, 61.6, 51.3, 50.5, 44.7. Anal. Calcd for $C_{14}H_{15}ClN_2$: C, 68.15; H, 6.13; N, 11.35. Found: C, 68.06; H, 6.26; N, 11.33.

2-Phenethyl-1,2,3,4-tetrahydropyrrolo[1,2-*a*]pyrazine (3b): yellow crystals (hexanes/EtOAc); yield 80%; mp 49−50 °C; ^{1}H NMR δ 7.32−7.21 (m, 5H), 6.54 (br s, 1H), 6.14 (t, J = 3.1 Hz, 1H), 5.84 (br s, 1H), 4.01 (t, J = 5.4 Hz, 2H), 3.73 (s, 2H), 2.91−2.85 (m, 4H), 2.80−2.74 (m, 2H); ^{13}C NMR δ 140.1, 128.7, 128.4, 126.8, 126.1, 118.3, 108.1, 102.7, 59.8, 51.2, 51.0, 44.6, 34.0. Anal. Calcd for $C_{15}H_{18}N_2$: C, 79.60; H, 8.02; N, 12.38. Found: C, 79.61; H, 8.44; N, 11.93.

2-(4-Methylbenzyl)-1,2,3,4-tetrahydropyrrolo[1,2-*a*]pyrazine (3c): orange plates (hexanes/EtOAc); yield 85%; mp 42−43 °C; ^{1}H NMR δ 7.25 (d, J = 7.8 Hz, 2H), 7.14 (d, J = 7.8 Hz, 2H), 6.53 (br s, 1H), 6.12 (t, J = 3.2 Hz, 1H), 5.78 (br s, 1H), 3.97 (t, J = 5.6 Hz, 2H), 3.63 (br s, 4H), 2.82 (t, J = 5.6 Hz, 2H), 2.35 (s, 3H); ^{13}C NMR δ 136.8, 134.7, 128.9, 128.8, 127.0, 118.1, 107.9, 102.5, 62.0, 51.2, 50.2, 44.6, 21.0. Anal. Calcd for $C_{15}H_{18}N_2$: C, 79.60; H, 8.02; N, 12.38. Found: C, 79.21; H, 8.28; N, 12.38.

2-(3-Butenyl)-1,2,3,4-tetrahydropyrrolo[1,2-*a*]pyrazine (3d): yellow oil; yield 70%; ^{1}H NMR δ 6.53 (br s, 1H), 6.13 (t, J = 3.1 Hz,1H), 5.91−5.77 (m, 2H), 5.09 (d, J = 17.1 Hz, 1H), 5.03 (d, J = 9.9 Hz, 1H), 3.99 (t, J = 5.6 Hz, 2H), 3.66 (s, 2H), 2.84 (t, J = 5.9 Hz, 2H), 2.59 (t, J = 6.9 Hz, 2H), 2.34 (t, J = 7.2 Hz, 2H); ^{13}C NMR δ 136.2, 126.9, 118.3, 115.9, 108.0, 102.7, 57.3, 51.1, 50.9, 44.5, 37.7. Anal. Calcd for $C_{11}H_{16}N_2$: C, 74.96; H, 9.15; N, 15.89. Found: C, 75.10; H, 9.56; N, 16.14.

2-Allyl-1,2,3,4-tetrahydropyrrolo[1,2-*a*]pyrazine (3e): brown oil; yield 75%; ^{1}H NMR δ 6.55 (br s, 1H), 6.14 (t, J = 3.1 Hz, 1H), 5.93−5.84 (m, 2H), 5.24 (dd, J = 18.0, 11.1 Hz, 2H), 4.00 (t, J = 5.6 Hz, 2H), 3.65 (s, 2H), 3.18 (d, J = 6.6 Hz, 2H), 2.84 (t, J = 5.6 Hz, 2H); ^{13}C NMR δ 134.8, 126.9, 118.3, 118.2, 108.0, 102.7, 61.0, 51.1, 50.4, 44.6. HRMS calcd for $C_{10}H_{15}N_2$ (M + 1) 163.1235, found 163.1212.

2-[3,4-Dihydropyrrolo[1,2-*a*]pyrazin-2(1*H*)-yl]acetonitrile (4). Compound **2** (0.5 g, 2 mmol) and sodium cyanide (0.2 g, 4 mmol) were stirred in dimethyl sulfoxide (10 mL) at 20 °C for 12 h. Then the reaction was quenched with water and extracted with ether. The organic layer was washed with 2 M NaOH and brine, and then dried over $MgSO_4$. Evaporation of solvent gave the crude product, which was purified using a neutral alumina column (eluent: hexanes/EtOAc = 10/1−5/1), yellow oil; yield 80%; ^{1}H NMR δ 6.56 (br s, 1H), 6.15 (br s, 1H), 5.88 (br s, 1H), 4.03 (t, J = 5.4 Hz, 2H), 3.81 (s, 2H), 3.67 (s, 2H), 2.96 (t, J = 5.3 Hz, 2H); ^{13}C NMR δ 125.0, 118.7, 114.3, 108.4, 103.3, 49.8, 49.6, 45.6, 44.3. Anal. Calcd for $C_9H_{11}N_3$: C, 60.99; H, 6.26; N, 23.71. Found: C, 61.10; H, 6.64; N, 23.64.

2-Methyl-1,2,3,4-tetrahydropyrrolo[1,2-*a*]pyrazine Boron Complex (5). Compound **2** (0.5 g, 2 mmol) and $NaBH_4$ (0.15 g, 4 mmol) were stirred at 20 °C overnight in dry THF (20 mL). THF was then removed in vacuo. The residue was dissolved in EtOAc and washed with 2 M NaOH and water and dried over anhydrous Na_2SO_4. After the removal of EtOAc in vacuo, the crude product obtained was purified by column chromatography (eluent: hexanes/EtOAc = 9/1−4/1), white flakes (hexanes/EtOAc); mp 111−112 °C; yield 65%; ^{1}H NMR δ 6.65 (br s, 1H), 6.21 (t, J = 3.1 Hz, 1H), 5.96 (br s, 1H), 4.22−4.14 (m, 2H), 4.10−3.91 (m, 2H), 3.46−3.36 (m, 1H), 3.27−3.20 (m, 1H), 2.67 (s, 3H); 2.42−1.08 (m, 3H, BH_3) ^{13}C NMR δ 122.6, 119.7, 109.3, 105.6, 57.7, 56.3, 47.0, 40.3. Anal. Calcd for $C_8H_{15}BN_2$: C, 64.48; H, 10.15; N, 18.80. Found: C, 64.27; H, 10.33; N, 18.85.

8-Benzotriazolyl-5,6,9,10,11,11a-hexahydro-8*H*-pyrido-[1,2-*a*]pyrrolo[2,1-*c*]pyrazine (6). 2-(Pyrrol-1-yl)ethylamine (**1**, 1.1 g, 10 mmol) and benzotriazole (1.19 g, 10 mmol) were dissolved in methanol (40 mL) at 0 °C. Glutaric dialdehyde (2.0 g, 10 mmol, 50% aqueous solution) was added dropwise to the solution during 4 h. Then, the solid obtained was filtered off, washed with cold Et_2O, and dried in vacuo. Brown plates (hexanes/EtOAc); yield 67%. Data for **6a**: mp 104−105 °C; ^{1}H NMR δ 8.07 (d, J = 7.8 Hz, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.40−7.25 (m, 2H), 6.51 (br s, 1H), 6.18 (t, J = 2.9 Hz, 1H), 5.97 (br s, 1H), 5.44 (dd, J = 10.8, 3.4 Hz, 1H), 3.80−3.72 (m, 2H), 3.62 (d, J = 8.1 Hz, 1H), 2.61 (td, J = 11.7, 4.6 Hz, 1H), 2.43−2.04 (m, 5H), 1.86−1.80 (m, 2H); ^{13}C NMR δ 146.9, 131.2, 130.3, 127.2, 124.2, 120.0, 118.7, 112.3, 108.3, 102.4, 78.4, 60.1, 47.4, 44.6, 31.5, 29.8, 22.4. Anal. Calcd for $C_{17}H_{19}N_5$: N, 23.87. Found: N, 23.59. **Crystal data for 6a:** see Supporting Information.

General Procedure for Syntheses of 5,6,9,10,11,11a-Hexahydro-8*H*-pyrido[1,2-*a*]pyrrolo[2,1-*c*]pyrazines 7a−c. Compound **6** (0.59 g, 2 mmol) was dissolved in dry THF (15 mL) at 0 °C. The corresponding Grignard reagent (3 mmol, 1.5 equiv) was added dropwise. The mixture was stirred for 12 h at 20 °C. Then, the reaction was quenched with water, washed with 2 M NaOH, and extracted with ether. The organic solution was dried over $MgSO_4$, and the solvent was removed

in vacuo. The product obtained was purified using column chromatography (eluent: hexanes/EtOAc = 8/1−4/1).

8-(4-Chlorophenyl)-5,6,9,10,11,11a-hexahydro-8*H*-pyrido-[1,2-*a*]pyrrolo[2,1-*c*]pyrazine (7a): colorless needles (hexanes/EtOAc); yield 70%; mp 136−137 °C; ^{1}H NMR δ 7.31 (br s, 4H), 6.61 (br s, 1H), 6.20 (t, J = 3.1 Hz, 1H), 5.93 (br s, 1H), 4.41 (br s, 1H), 3.98 (td, J = 12.4, 5.6 Hz, 1H), 3.59−3.50 (m, 2H), 3.14−2.95 (m, 2H), 2.27 (d, J = 13.8 Hz, 1H), 2.03−1.90 (m, 1H), 1.66−1.49 (m, 4H); ^{13}C NMR δ 142.6, 132.7, 129.5, 128.8, 128.6, 119.5, 107.6, 103.3, 58.4, 55.1, 46.9, 38.7, 36.0, 27.8, 20.1. Anal. Calcd for $C_{17}H_{19}ClN_2$: C, 71.19; H, 6.68; N, 9.77. Found: C, 71.49; H, 7.01; N, 9.48.

8-(4-Methylphenyl)-5,6,9,10,11,11a-hexahydro-8*H*-pyrido-[1,2-*a*]pyrrolo[2,1-*c*]pyrazine (7b): colorless needles (hexanes/EtOAC); yield 66%; mp 106−107 °C; ^{1}H NMR δ 7.26 (d, J = 7.4 Hz, 2H), 7.14 (d, J = 7.8 Hz, 2H), 6.61 (br s, 1H), 6.19 (t, J = 2.9 Hz, 1H), 5.93 (br s, 1H), 4.42 (br s, 1H), 4.07−3.97 (m, 1H), 3.55−3.48 (m, 2H), 3.08−3.01 (m, 2H), 2.34 (s, 3H), 2.29−2.25 (m, 1H), 2.04−1.97 (m, 1H), 1.66−1.55 (m, 4H); ^{13}C NMR δ 140.9, 136.8, 129.7, 129.2, 127.2, 119.4, 107.5, 103.2, 58.7, 55.1, 46.9, 38.8, 35.9, 27.9, 21.1, 20.3. Anal. Calcd for $C_{18}H_{22}N_2$: C, 81.16; H, 8.32; N, 10.52. Found: C, 81.45; H, 8.68; N, 10.43. **Crystal data for 7b:** see Supporting Information.

8-Ethyl-5,6,9,10,11,11a-hexahydro-8*H*-pyrido[1,2-*a*]pyrrolo[2,1-*c*]pyrazine (7c): brown oil; yield 80%; ^{1}H NMR δ 6.51 (br s, 1H), 6.13 (t, J = 3.1 Hz, 1H), 5.84 (br s, 1H), 4.11−4.02 (m, 1H), 3.92 (dd, J = 7.5, 3.3 Hz, 1H), 3.83 (dt, J = 11.5, 2.9 Hz, 1H), 3.10 (dd, J = 8.2, 3.0 Hz, 2H), 2.73−2.69 (m, 1H), 2.05−1.98 (m, 1H), 1.76−1.48 (m, 6H), 1.28−1.24 (m, 1H), 0.89 (t, J = 7.2 Hz, 3H); ^{13}C NMR δ 131.5, 118.3, 107.7, 102.2, 58.9, 53.2, 48.1, 43.0, 30.5, 27.8, 19.0 (2), 10.9. HRMS calcd for $C_{13}H_{21}N_2$ (M + 1) 205.1704, found 205.1723.

5,6,9,10,11,11a-Hexahydro-8*H*-pyrido[1,2-*a*]pyrrolo[2,1-*c*]-pyrazine-8-carbonitrile (8). A mixture of compound **6** (0.59 g, 2 mmol) and NaCN (0.2 g, 4 mmol) in dimethyl sulfoxide (10 mL) was reacted for 12 h at 20 °C, followed by the same workup procedure as that for **4**. The product **8** was obtained after neutral alumina column chromatography (eluent: hexanes/EtOAc = 10/1−5/1) as white needles (hexanes/EtOAc); mp 52−53 °C; yield 75%; ^{1}H NMR δ 6.53 (br s, 1H), 6.15 (t, J = 3.1 Hz, 1H), 5.88 (br s, 1H), 4.08 (td, J = 11.8, 4.7 Hz, 1H), 4.00 (br s, 1H), 3.95 (dd, J = 11.7, 4.3 Hz, 1H), 3.63 (d, J = 11.1 Hz, 1H), 3.07 (td, J = 11.8, 4.7 Hz, 1H), 2.88 (dd, J = 11.7, 4.5 Hz, 1H), 2.21 (d, J = 13.8 Hz, 1H), 1.99−1.92 (m, 2H), 1.89−1.78 (m, 2H), 1.59−1.49 (m, 1H); ^{13}C NMR 130.1, 118.6, 116.2, 108.4, 102.5, 55.2, 54.5, 50.6, 44.4, 30.2, 28.6, 20.1. Anal. Calcd for $C_{12}H_{15}N_3$: C, 71.61; H, 7.51; N, 20.88. Found: C, 71.31; H, 7.60; N, 20.93.

5,6,9,10,11,11a-Hexahydro-8*H*-pyrido[1,2-*a*]pyrrolo[2,1-*c*]-pyrazine (9). Compound **6** (0.59 g, 2 mmol) and $NaBH_4$ (0.15 g, 4 mmol) were stirred overnight in THF (20 mL) at 20 °C. Following the same procedure as that for **5**, product **9** was obtained after column chromatography (eluent: hexanes/EtOAc = 9/1−4/1) as a brown oil; yield 63%; ^{1}H NMR δ 6.51 (br s, 1H), 6.13 (t, J = 2.9 Hz, 1H), 5.84 (br s, 1H), 4.13 (td, J = 12.0, 4.6 Hz, 1H), 3.91 (dd, J = 11.4, 3.9 Hz, 1H), 3.04 (d, J = 10.5 Hz, 1H), 2.94 (dd, J = 12.0, 4.2 Hz, 2H), 2.68 (td, J = 12.0, 4.6 Hz, 1H), 2.30−2.13 (m, 2H), 1.84 (d, J = 4.2 Hz, 1H), 1.71−1.64 (m, 2H), 1.60−1.38 (m, 2H); ^{13}C NMR δ 131.6, 118.4, 108.0, 101.5, 60.7, 55.8, 52.8, 44.6, 30.4, 25.6, 23.9. Anal. Calcd for $C_{11}H_{16}N_2$: C, 74.96; H, 9.15; N, 15.89. Found: C, 75.30; H, 9.51; N, 16.25.

Supporting Information Available: Crystal data and structure refinement for compounds **6a** and **7b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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