Indian Journal of Heterocyclic Chemistry ***(Prof. R.S. Varma - Memorial Issue)***
Vol. 24, April-June, 2015, pp. 381-388

8-AZASTEROID FRAGMENTS: SYNTHESIS AND STEREOCHEMISTRY OF 2-ARYLPERHYDROCYCLOPENTA [*b*] PYRIDINES

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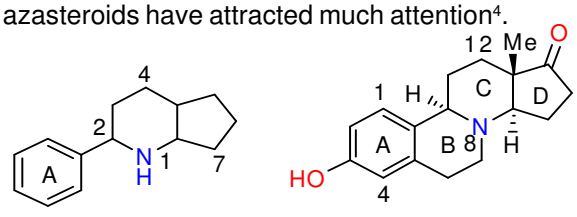
Received 24 March 2015; Accepted 28 March 2015

We have synthesized and characterized eight 2-aryl perhydrocyclopenta[*b*]pyridines, which form structural motifs on 8-azasteroids. Reduction of corresponding *N*-hydroxy derivatives with H_2-Pd/C (10%) furnished 2-aryl perhydrocyclopenta[*b*]pyridines in high yield. However, microwave mediated Leuckart-Wallach reductive amination cyclization on corresponding 1,5-diketones did not provide anticipated 2-arylperhydrocyclopenta[*b*]pyridines. Extensive NMR spectral analysis was used to assign structure and stereochemistry to each isomer. For the first time, we assigned and assembled ^{13}C NMR chemical shift data of ring carbons of perhydrocyclopenta[*b*]pyridines which should be of help for structure determination of similar compounds.

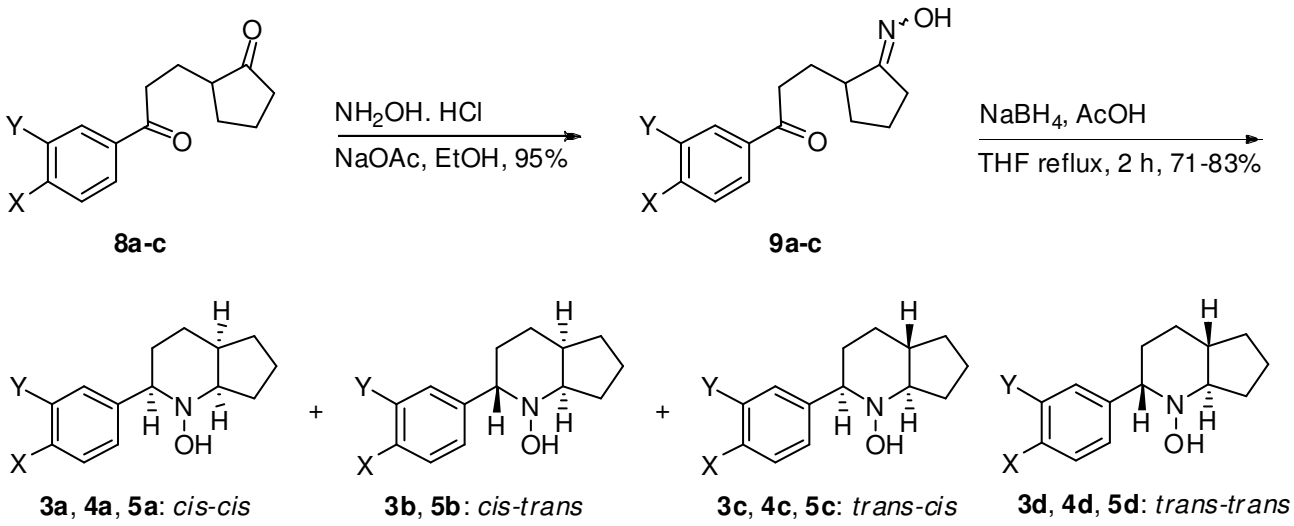
The 2-aryl perhydrocyclopenta [*b*] pyridine **1** (Figure 1) can be seen as a structural motif on A-ring aromatic 8-azasteroids (eg. 8-azaestrone **2**)[1] and some alkaloids[2]. 8-Azasteroids display biological properties different from their parent steroids, owing to the presence of strategically placed, basic as well as stereochemically flexible nitrogen[3]. Consequently, studies on the synthesis and stereochemistry of 8-azasteroids have attracted much attention[4].



1 **2**

Figure 1: Structure of 2-aryl perhydrocyclopenta[*b*] pyridine **1** and 8-azaestrone **2**.

As a part of our interest on the synthesis and stereochemistry of saturated nitrogen heterocycles[5], we have previously reported synthesis and stereochemical characterization of A-ring aromatic 8-azasteroid motifs[6]. Two-step transformation of 1,5-diketones **8** *via* corresponding mono keto oximes **9** furnished 2-arylperhydrocyclopenta[*b*]pyridin-1-ols **3-5** (Scheme 1). Facile and high-yielding reduction of the mono keto oximes **9** to *N*-hydroxylamines **3-5** was achieved by sodium borohydride in acetic acid (sodium acetoxyborohydride). Reduction of the monoketo oxime **9a** afforded three of the four possible cyclic hydroxylamines namely, *cis-cis* (stereochemistry at the ring junction followed by relative stereochemistry at C(7a) and C(2)) **3a**, *cis-trans* **3b** and *trans-cis* **3c** out of possible four diastereomers. The fourth *trans-trans* isomer **3d** did not form. On the other hand, reduction of the mono-oxime with C4'-OMe **9b** afforded only two diastereomers, namely *cis-cis* **4a** and *trans-cis* **4c**. Two isomers namely *cis-trans* **4b** and *trans-trans* **4d** did not form. Finally, reduction of the monoketo oxime **9c** gave three diastereomers *cis-cis* **5a**, *cis-trans* **5b** and *trans-cis* **5c**. In this case also the fourth *trans-trans* isomer **5d** did not form. To generate elusive fourth *trans-trans* isomers **3d**, **4d** and **5d** we looked for alternate methods of synthesis like Leuckart-Wallach (LW) reductive amination of 1,5-diketones **8**. The LW reductive amination is a classical method for conversion of reductive amination of ketones or aldehydes with ammonium formate[7]. The reaction, however, is expected to provide secondary amines like **1** (Figure 1) instead of *N*-hydroxyl derivatives **3-5**. In addition to LW reaction on



3a-d, **8a**, **9a**: X = Y = H; **4a-d**, **8b**, **9b**: X = OMe, Y = H; **5a-d**, **8c**, **9c**,: X = Y = OMe

SCHEME 1: Two-step synthesis of 8-azasteroid fragments **3**-**5** from 1,5-diketones **8** via mono-oximes **9**

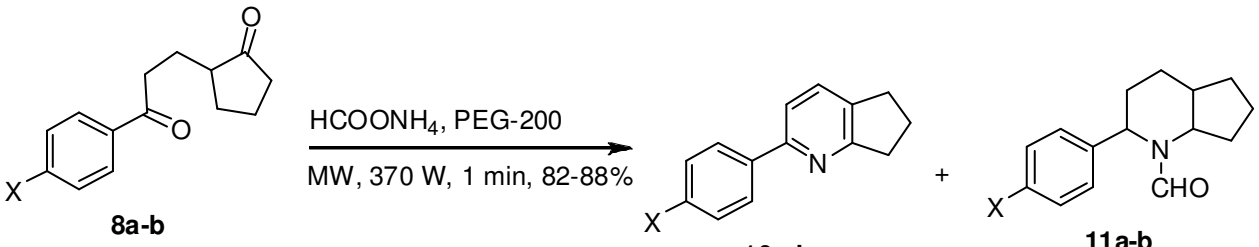
1,5-diketones **8** we targeted reduction of *N*-hydroxyl compounds **3-5** into corresponding secondary amines to get closer to 8-azasteroid structures e.g. **2**. Thus, in this work we report on the outcome of our studies on LW reaction of 1,5-diketones **8** and synthesis of 2-aryldiarylperhydrocyclopenta[*b*]pyridines **1** that fit into 8-azasteroid structures.

Leuckart-Wallach (LW) reductive amination cyclisation (RAC) reaction on 1,5-diketones 8 towards the synthesis of 2-arylperhydrocycl - openta[*b*]pyridines 1

We conducted microwave (MW) mediated direct Leuckart-Wallach reductive amination cyclization (LWRAC) reaction[8] on 1,5-diketones **8a-b** using ammonium formate in polyethylene glycol -200 (PEG-200; 200 denotes average molecular weight in amu) (Scheme 2). The reaction which took a minute to complete, unfortunately, did not provide perhydrocyclopenta[*b*]pyridines **1** at all. Instead, it furnished 2-aryl-6,7-dihydro-5*H*-cyclopenta[*b*]pyridine **10a**[9] (93%) as the major product and 2-arylperhydrocyclopenta[*b*]pyridine-1-carbaldehydes **11a** (57%) as the minor product in 37% overall yield (Scheme 3). Frustratingly, the *N*-formylperhydrocyclopenta[*b*]pyridines **13a-b** were obtained as a mixture of isomers which could not be separated by column or thin layer chromatography on SiO_2 gel or Al_2O_3. The LW RAC reaction on diketone **8b** provided cyclopenta[*b*]pyridine **10b** and *N*-formyl derivative **11b** in 88% yield. Like the earlier case, *N*-formyl derivative **10b** was obtained as inseparable diastereomeric mixture. Attempted deformylation of **11a** or **11b** with methanolic KOH lead to extensive decomposition and to some extent (23%) aromatization to afford cyclopenta[*b*]pyridines **10a-b** respectively. Reduction of cyclopenta[*b*]pyridine **12a** with sodium in EtOH lead to extensive decomposition[10].

Synthesis and stereochemistry of 2-arylperhydrocyclopenta[*b*]pyridines

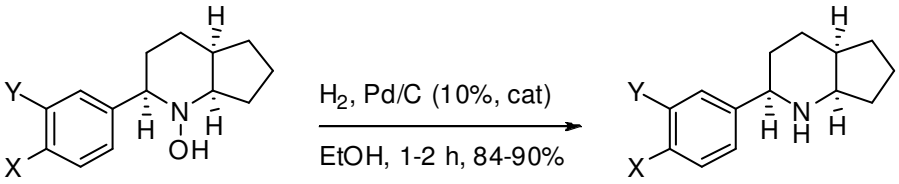
Since the LW RAC reaction failed to provide 2-arylperhydrocyclopenta[*b*]pyridines we undertook reduction of *N*-hydroxylamines **3-5** to corresponding secondary amines e.g. **1**. Reduction of **3a** was taken as a test case to optimize reagents and reaction conditions. Among reducing agents such as Zn / AcOH, Sn / dil aqueous HCl, $LiAlH_4$, H_2-Pd/C tried, reduction worked best with H_2-Pd/C (10%) in EtOH medium to furnish **1a** as a clean product in excellent yield (Scheme 3). Reduction of *N*-hydroxy compounds **4a** and **5a** with H_2-Pd/C (10%) provided corresponding secondary amines **12a** and **13a** respectively. The perhydrocyclopenta[*b*]pyridines **1a**, **12a**, **13a** were found to decompose on prolonged stay at room temperature. So, they were converted into respective trifluoroacetic acid salts for storage.



8a, **10a**, **11a**: X = H; **8b**, **10b**, **11b**: X = OMe

LW-Reductive amination cyclization reaction of diketones **8a-b**.

SCHEME-2



3a, **4a**, **5a**: *cis-cis* **1a**, **12a**, **13a**: *cis-cis*

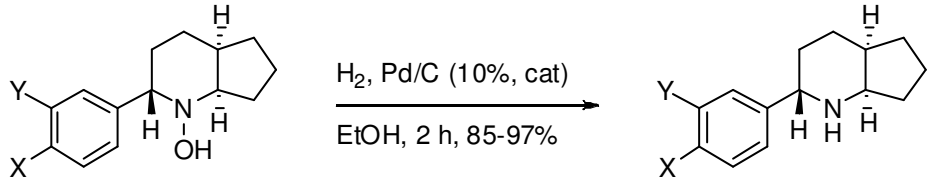
3a, **1a**: X = Y = H; **4a**, **12a**: X = OMe, Y = H; **5a**, **13a**: X = Y = OMe

Synthesis of 2-arylperhydrocyclopenta[*b*]pyridines **1**a, **12**a and **13**a which possess *cis-cis* stereochemistry.

SCHEME-3

Next, we reduced *N*-hydroxy perhydrocyclopenta [*b*]pyridines **3b** and **5b** independently with H_2-Pd/C (10%) and the reaction provided corresponding secondary amines **1b** and **11b** without any difficulty (Scheme 4). Similarly a set of three *N*-hydroxy perhydrocyclopenta[*b*]pyridines **3c**, **4c** and **5c** was reduced with H_2-Pd/C (10%) independently to generate corresponding secondary amines (Scheme 5).

Structures of all the eight perhydrocyclopenta [*b*] pyridines **1**, **12** and **13** prepared in this study were confirmed on the basis of extensive NMR spectral studies. Representative examples of the

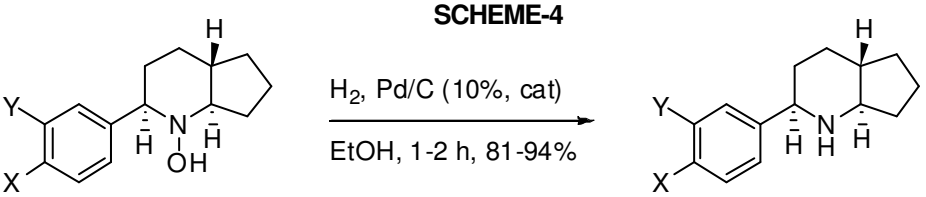


3b, **5b**: *cis-trans* **1b**, **12b**: *cis-trans*

3b, **1b**: X = Y = H; **5b**, **12b**: X = OMe, Y = H

Synthesis of 2-arylperhydrocyclopenta[*b*]pyridines **1b** and **12b** which possess cis-trans stereochemistry.

SCHEME-4

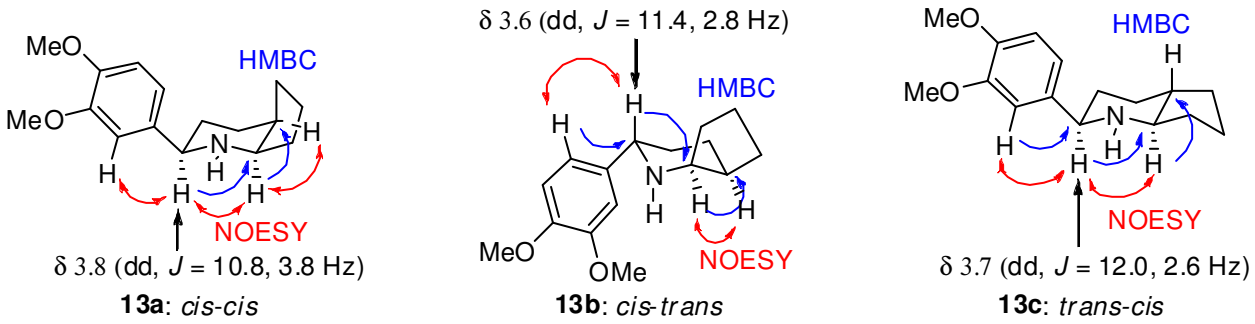


3c, **4c**, **5c**: *trans-cis* **1c**, **12c**, **13c**: *trans-cis*

3c, **1c**: X = Y = H; **4c**, **12c**: X = OMe, Y = H; **5c**, **13c**: X = Y = OMe.

Synthesis of 2-arylperhydrocyclopenta[*b*]pyridines **1c**, **12c** and **13c** which possess *trans-cis* stereochemistry.

SCHEME-5



The selected ^{1}H NMR spectral data, HMBC (single-head arrow) and NOESY (double-head arrow) correlations for **13a-c.**

Figure-2

conformational structures and characteristic ^{1}H NMR spectral data along with 2D NMR correlations (HMBC and NOESY) which helped in assignment of structures (Figure-2). All the eight perhydrocyclopenta [*b*] pyridines **1**, **12** and **13** are conformationally locked due to the presence of bulky aryl ring at C(2) position. Reflecting this structural feature, each one of the isomers displayed a doublet of doublet for C(2)H at about δ 3.7 ppm in their ^{1}H NMR spectra with one large and one small coupling constant indicating its axial orientation. Consequently the C(2)-aryl ring occupies more stable equatorial orientation. As anticipated, ^{13}C NMR signals due to C(2) and C(7a) moved up field compared to the corresponding carbons in the N-hydroxy derivatives namely perhydrocyclopenta[*b*]pyridinols **3**, **4** and **5**. They were now stationed at around δ 60.0 ppm.

Eliel and Virlhapper have made seminal contribution in the field of stereochemistry by gathering ^{13}C NMR chemical shift data of the ring carbons of large number of *cis*- and *trans*-perhydroquinolines[11]. This data is used extensively in assigning the structure and stereochemistry to similar nitrogen heterocycles. However, similar data for perhydrocyclopenta [*b*] pyridines like **1**, is not available. In table 1 we gathered the ^{13}C NMR spectral chemical shifts and assignments for the ring carbons of perhydrocyclopenta [*b*]pyridines **1**a-c, **12**a-b, **13**a-c. The DEPT-135 NMR spectra was used to assign *C*H carbon resonances (Table 1).

In conclusion, we have delineated a synthesis and stereochemistry of eight 2-arylperhydrocyclopenta [*b*] pyridines from corresponding *N*-hydroxy derivatives. The Leuckart-Wallach Reductive Aminationn and Cyclization reaction on corresponding 1,5-diketones did not provide 2-arylperhydrocyclopenta[*b*]pyridines. For the first time we have assembled ^{13}C NMR spectral assignments of ring carbons of 2-arylperhydrocyclopenta [*b*] pyridines which should help in structure determination of similar compounds. All the perhydrocyclopenta [*b*] pyridines prepared in this study form part structure of 8-azasteroids.

Experimental

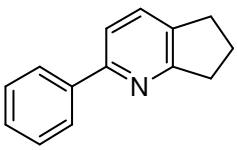
Progress of all the reactions was monitored by TLC (TLC silica gel: Qualigens or TLC alumina: SRL, India) using mixture of hexane and ethyl acetate as eluent. After completion of the reaction, the reaction mixture was diluted with dichloromethane (DCM) and washed with water and brine. The organic extract was dried with anhydrous sodium sulfate and the solvent was removed under reduced pressure. Column chromatography was accomplished on silica gel (100-200 mesh, Acme synthetic chemicals) using a mixture of hexane and ethyl acetate as eluent. Melting points were determined using a Gallenkamp melting point apparatus and are uncorrected. IR spectra were recorded as solid solutions in KBr or Nujol mulls using JASCO FT IR or Perkin-Elmer spectrophotometer. ^{1}H and ^{13}C NMR and 2D NMR spectra were recorded in $CDCl_3$ with Bruker 400 MHz or Varion 300 MHz spectrophotometers. Mass spectra were recorded on Finnigan MAT 8230 Mass spectrometer. The elemental analysis was carried out on a Elemental Vario EL (Germany) apparatus. The microwave reactions were carried out using Anton-Paar mono-made oven of microwave Frequency: 2450 MHz.

General procedure for Leuckrdt Wallach Reductive Amination Cyclization (LWRAC) reaction on 1,5-diketones 8a-b

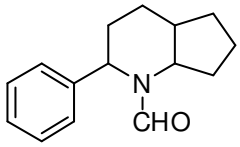
Table-1
^{13}C NMR chemical shift values in $CDCl_3$ of 2-phenylperhydrocyclopenta[*b*]pyridine **1**a-c, **12**a-c and 13a-c (CH resonances are underlined)

	Compd	C-2	C-3	C-4	C-4a	C-5	C-6	7	C-7a
cis-	1a	61.63	29.93	26.63	39.12	26.05	24.04	34.25	60.10
cis	12a	60.65	29.50	26.33	38.81	25.74	22.52	33.92	59.84
	13a	61.01	29.58	26.28	38.79	25.72	22.49	33.93	59.81
cis-	1b	58.29	30.34	29.68	38.71	22.97	23.73	28.91	68.15
trans	13b	58.64	30.98	29.79	38.62	22.54	23.88	29.04	68.74
trans-	1c	65.72	34.83	30.24	44.80	30.56	20.67	28.68	62.29
cis	12b	65.52	34.75	30.32	44.74	30.53	20.68	28.68	62.29
	13c	65.76	34.84	30.23	44.71	30.53	20.68	28.67	62.76

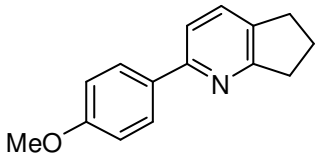
To the suspension of 2-(3-oxo-3-phenylpropyl)-1-cyclopentanone **8a** (286 mg, 1.33 mmol) in 4 mL PEG-200 taken in a 25 mL conical flask, ammonium formate (335 mg, 5.32 mmol) was added and the inhomogenous reaction mixture was subjected to microwave irradiation for 1 min. The reaction which was monitored by TLC every 10 sec showed two spots at the end of 1 min while **8a** was absent and the reaction mixture became homogenous and faintly red. The reaction mixture was allowed to cool at room temperature, diluted with 20 mL DCM and 20 mL ice-cold water. The organic layer was separated and washed with distilled water (3 x 25 mL) to remove water soluble PEG-200. Then the organic layer was further washed with brine solution (1 x 10 mL) and dried over anhydrous Na_2SO_4. The organic layer was concentrated under *vacuo*. The brown mixture thus obtained was subjected to column chromatography (silica gel, 100-200 mesh; 10% EtOAc-hexane) to furnish 2-phenyl-6,7-dihydro-5*H*-cyclopenta[*b*]pyridine **12a** (114 mg, 57%) and inseparable diastereomeric mixture of 2-phenylperhydrocyclopenta[*b*]pyridine-1-carbaldehyde **13a** (113 mg, 37%).



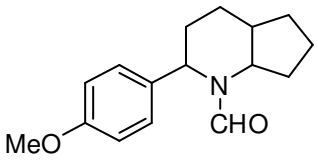
2-Phenyl-6,7-dihydro-5*H*-cyclopenta[*b*]pyridine 10a: a colorless solid; mp 101-103 °C; R_f = 0.43 (10% EtOAc-hexane); IR (KBr) υ 693, 732, 771, 842, 1432, 1568, 2840, 2920 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$/CCl_4, 1:1) δ 2.16 (m, 2H), 2.95 (t, *J* = 7.5 Hz, 2H), 3.07 (t, *J* = 7.5 Hz, 2H), 7.3-7.51 (m, 5H), 7.92 (d, *J* = 6.9 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$/CCl_4, 1:1) δ 23.3, 30.6, 34.4, 118.0, 126.9, 128.3, 128.6, 132.4, 135.1, 140.0, 155.9, 165.4 ppm.



2-Phenylperhydrocyclopenta[*b*]pyridine-1-carbaldehyde 11a: a colorless oil; R_f = 0.23 (10% EtOAc-hexane); IR (neat) 842, 1392, 1442, 1568, 1660, 2840, 2920; ^1H NMR (300 MHz, $CDCl_3$/CCl_4, 1:1; signals of the major isomer are given here), 1.42-1.54 (m, 3H), 1.62-1.75 (m, 3H), 1.79-1.91 (m, 3H), 2.03-2.05 (m, 2H), 4.30 (t, *J* = 13.8 Hz, 1H), 4.67 (q, 1H), 7.21-7.36 (m, 5H), 7.69 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$/CCl_4, 1:1; signals of the major isomer are given here), 20.43, 24.72, 26.68, 29.77, 33.80, 36.25, 53.46, 57.24, 126.09, 128.24, 129.0, 139.03, 162.70; LRMS 229 (62%, M^+), 228 (100%), 200 (20%), 172 (10%), 155 (12%), 117 (18%), 105 (28%), 104 (30%), 91 (28%), 77 (24%), 67 (14%), 55 (22%); HRMS calcd 229.1467 for $C_{15}H_{19}NO$, found 229.1463.

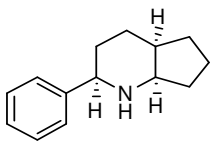


2-(4-Methoxyphenyl)-6,7-dihydro-5*H*-cyclopenta[*b*]pyridine 10b: a colorless solid; Yield 69 mg (38%); mp 112-114 °C; R_f = 0.36 (10% EtOAc-hexane); IR (KBr), 825, 1027, 1176, 1253, 1288, 1452, 1515, 1584, 1608, 2851, 2924, 2962; ^{1}H NMR (300 MHz, $CDCl_3/CCl_4$, 1:1) 2.16 (m, 2H), 2.94 (t, *J* = 7.2 Hz, 2H), 3.06 (t, *J* = 7.8 Hz, 2H), 3.84 (s, 3H), 6.93 (d, *J* = 9.0 Hz, 2H), 7.37 (d, *J* = 7.8 Hz, 1H), 7.48 (d, *J* = 7.8 Hz, 1H), 7.87 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$/ CCl_4, 1:1), 23.4, 30.6, 34.5, 55.2, 114.0, 117.4, 128.2, 132.4, 132.7, 134.3, 155.7, 160.1, 165.6; LRMS 225 (100%, M^+), 210 (30%), 182 (48%), 167 (10%), 154 (16%), 127 (12%), 91 (10%). [Found: C, 79.94, H, 6.68, N, 6.24 $C_{15}H_{15}NO$ requires C, 79.97; H, 6.72; N, 6.22%].



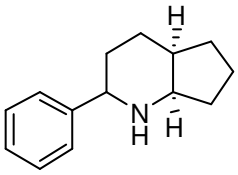
2-(4- Methoxyphenyl)perhydrocyclopenta [*b*] pyridine-1-carbaldehyde 13b: Colorless oil; Yield 104 mg (49%); R_f = 0.18 (10% EtOAc-hexane); IR (neat) 837, 1033, 1181, 1253, 1428, 1452, 1513, 1668, 2869, 2932; ^{1}H NMR (300 MHz, $CDCl_3/CCl_4$, 1:1; signals of the major isomer are given here), 1.43-1.54 (m, 3H), 1.64-1.72 (m, 3H), 1.74-1.86 (m, 3H), 2.03-2.12 (m, 2H), 3.80 (s, 3H), 4.27 (t, *J* = 7.2 Hz, 1H), 4.69-4.75 (m, 1H), 6.87 (d, *J* = 8.4 Hz, 2H), 7.24 (d, *J* = 8.4 Hz, 2H), 7.68 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$/ CCl_4, 1:1; signals pertaining to the major isomer are given here), 20.54, 24.74, 26.99, 29.87, 33.89, 36.42, 53.62, 55.15, 56.85, 114.54, 127.65, 130.56, 159.61, 163.02; LRMS 259 (46%, M^+), 258 (100%), 244 (18%), 230 (14%), 185 (6%), 166 (16%), 135 (58%), 108 (66%), 85 (68%); HRMS calcd 259.15 for $C_{16}H_{21}NO_2$, found 259.15.

General procedure for synthesis of 2-arylperhydrocyclopenta[*b*]pyridines

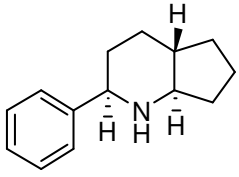


1a

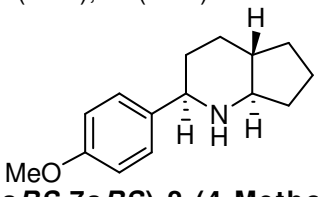
(2*RS*,4a*RS*,7a*RS*)-2-Phenylperhydrocyclopenta [*b*] pyridine (1a) : To an oven dried two neck round bottom flask charged with Pd/C (3 mg, 10 mol%) (2*RS*,4aR*S*,7a*RS*)-2-phenylperhydrocyclopenta [*b*]pyridine-1-ol **3a** (40 mg, 0.2 mmol) was added in ethanol (7 mL). The flask was evacuated and then flushed with hydrogen gas. Then stirring was continued in the presence of H_2 (g) for 12 h. The reaction was monitored by TLC. After completion of the reaction, reaction mixture was filtered through celite, the filtrate was concentrated to afford crude product. The crude product was further purified by column chromatography on silica gel (100-200 mesh) using 30-40% of EtOAc in hexane as eluent to furnish (2*RS*,4a*RS*,7a*RS*)-2-phenylperhydrocyclopenta[*b*] pyridine **1a** as colorless oil. Yield = 32 mg (87%); R_f = 0.43 (40% EtOAc in hexane); IR (neat) 3114, 2855, 1511, 1245, 1035, 978, 832, 701; ^{1}H NMR (400 MHz, $CDCl_3$) 7.36 (d, *J* = 7.2 Hz, 2H, C2'6'-H), 7.30 (t, *J* = 7.2 Hz, 2H, C3',5'-H), 7.22 (t, *J* = 7.2 Hz, 1H, C4' H), 3.57 (dd, *J* = 10.8, 2.0 Hz, 1H, C_2H), 3.25 (s, 1H, NH), 2.20-1.24 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) 146.11 (C), 128.59 (CH), 127.19 (CH), 127.01 (CH), 61.63 (CH), 60.10 (CH), 39.12 (CH), 34.25 (CH_2), 29.93 (CH_2), 26.63 (CH_2), 26.05 (CH_2), 24.04 (CH_2); GC-MS 202 (69% M+1), 201 (32%), 172 (100%), 132 (14%), 104 (16%), 39 (11%).



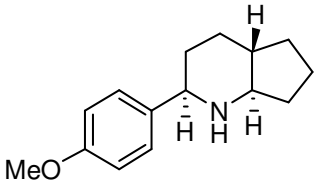
(2*SR*,4a*RS*,7a*RS*)-2-Phenylperhydrocyclopenta [*b*] pyridine 1b: Yield 22 mg (83%); R_f: 0.52 (40% EtOAc-hexane); IR (neat) 3341, 2920, 2840, 1600, 1568, 1442, 1392, 842; ^{1}H NMR (400 MHz, $CDCl_3$) 7.7-7.1 (m, 5H), 4.2 (br s, NH), 3.9-3.7 (m, 2H), 2.3-2.2 (m, 1H), 2.1-0.9 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) d 142.66 (C), 130.87 (C), 128.79 (CH), 128.45 (CH), 68.15 (CH), 58.29 (CH), 38.71 (CH), 30.34 (CH_2), 29.68 (CH_2), 28.91 (CH_2), 23.73 (CH_2), 22.97 (CH_2); GC-MS 202 (35%, M^++1), 200 (16%), 172 (100%), 132 (14%), 104 (15%), 19 (16%).



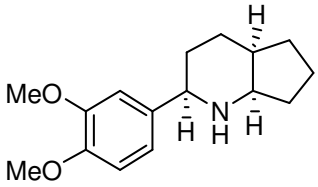
(2*RS*,4a*SR*,7a*RS*)-2-Phenylperhydrocyclopenta[*b*] pyridine 1c: Yield 58 mg (79%); R_f = 0.40 (40% EtOAc-hexane); IR (neat) 3246, 2920, 2840, 1568, 1432, 842, 771, 732, 693; ^{1}H NMR (400 MHz, $CDCl_3$) 7.38 (d, *J* = 8.0 Hz, 2H, C2',6' H), 7.31 (t, *J* = 8.0 Hz, 2H, C3',5' H), 7.23 (t, *J* = 8.0 Hz, 1H, C4'H), 3.69 (dd, *J* = 11.2 Hz, 3.0 Hz, 1H, C2H), 2.47 (dd, *J* = 17.2, 10.4 Hz, 1H, C7a H), 2.72 (br s, 1H, NH), 2.02 (m, 1H, C4a), 1.2-1.0 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) 144.95 (C), 144.95 (C), 128.30 (CH), 126.96 (CH), 126.81 (CH), 65.72 (CH), 62.94 (CH), 44.80 (CH), 34.83 (CH_2), 30.56 (CH_2), 30.24 (CH_2), 28.68 (CH_2), 20.67 (CH_2); GC-MS 201 (32%), 200 (18%), 186 (12%), 173 (1%), 172 (10%), 132 (11%), 117 (11%), 106 (39%), 104 (21%0, 91 (32%), 79 (20%), 39 (17%).



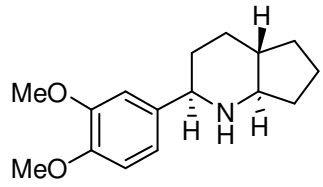
(2*RS*,4a*RS*,7a*RS*)-2-(4-Methoxyphenyl) perhydrocyclopenta[*b*] pyridine 12a: Yield 78 mg (85%); R_f = 0.38 (40% EtOAc-hexane); IR (neat) 3266, 2954, 2839, 1590, 1513, 1444, 1412, 1372, 1247, 1171, 1031, 843, 769; ^{1}H NMR (400 MHz, $CDCl_3$) 7.27 (d, *J* = 8.8 Hz, 2H), 6.85 (d, *J* = 8.8 Hz, 2H), 3.78 (s, 3H, OCH_3), 3.56 (dd, *J* = 11.2 Hz, 8.0 Hz, 1H, C2H), 3.24 (s, 1H, NH), 1.90-1.25 (m, 12H); ^{13}C NMR (100 MHz $CDCl_3$) δ 158.48 (C), 138.11 (C), 127.71 (CH), 113.62 (CH), 60.65 (CH), 59.84 (CH), 55.23 (OCH_3), 38.81 (CH), 33.92 (CH_2), 29.50 (CH_2), 26.33 (CH_2), 25.74 (CH_2), 22.52 (CH_2); GC-MS 232 (100%, M^++1), 231 (47% M^+), 198 (7%), 142 (5%).



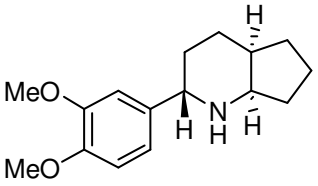
(2*RS*,4a*SR*,7a*RS*)-2-(4-Methoxyphenyl) perhydrocyclopenta[*b*]pyridine 12b: Yield 59 mg (80%); R_f = 0.36 (40% EtOAc-hexane); IR (neat) 3176, 2975, 1451, 1281, 1177, 1045, 903, 757, 698; ^{1}H NMR (400 MHz, $CDCl_3$) 7.3 (d, *J* = 8.8 Hz, 2H), 6.84 (d, *J* = 8.4 Hz, 2H), 3.78 (s, 3H, OCH_3), 3.66 (dd, *J* = 8.8 Hz, 3.0 Hz, 1H, C2H), 2.45 (dd, *J* = 16.8 Hz, 10.0 Hz, 1H, C7aH), 2.20 (br s, 1H, NH), 2.02 (m, 1H, C4aH), 2.02-1.17 (m, 11H); ^{13}C NMR (100 MHz, $CDCl_3$) 158.57 (C), 137.09 (C), 127.88 (CH), 113.65 (CH), 65.52 (CH), 62.29 (CH), 55.21 (CH), 44.74 (CH), 34.75 (CH_2), 30.53 (CH_2), 30.32 (CH_2), 28.68 (CH_2), 20.68 (CH_2); GC-MS 232 (100%, M^++1), 231 (53%, M^+), 202 (7%), 142 (7%).



(2*RS*,4a*RS*,7a*RS*)-2-(3,4-Dimethoxyphenyl) perhydrocyclopenta[*b*]pyridine 13a: Yield 74 mg (80%); R_f= 0.38 (40% EtOAc-hexane); IR (neat) 3191, 1602, 1448, 903, 756, 669; ^{1}H NMR (400 MHz, $CDCl_3$) 6.91 (d, *J* = 11.6 Hz, 1H), 6.88 (s, 1H), 6.81 (d, *J* = 7.6 Hz, 1H), 3.89 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 3.82 (dd, *J* = 10.8 Hz, 3.8 Hz, 1H, C2H), 3.23 (s, 1H, NH), 1.98-1.25 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) 148.72 (C), 147.78 (C), 138.76 (C), 118.45 (CH), 110.92 (CH), 110.03 (CH), 61.01 (CH), 59.81 (CH), 55.84 (OCH_3), 55.78 (OCH_3), 38.79 (CH_2), 33.93 (CH_2), 29.58 (CH_2), 26.28 (CH_2), 25.72 (CH_2), 22.49 (CH_2); GC-MS 262 (58%, M^++1), 261 (100%, M^+), 230 (44%).



(2*SR*,4a*RS*,7a*RS*)-2-(3,4-Dimethoxyphenyl) perhydrocyclopenta[*b*]pyridine 13b: Colorless oil, Yield 33 mg (78%); R_f = 0.34 (40% EtOAc-hexane); IR (neat) 3341, 2931, 2855, 1606, 1511, 1448, 1245, 1174, 1035, 832, 701; ^{1}H NMR (400 MHz, $CDCl_3$) 7.05 (s, 1H), 6.95 (d, *J* = 7.6 Hz, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 3.84 (s, 3H), 3.79 (s, 3H), 3.6 (dd, *J* = 11.4 Hz, 2.8 Hz, C2H), 2.53-2.47 (m, C7aH), 2.05-2.01 (m, C4aH), 1.88-1.72 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) 148.88, 148.38, 119.43, 110.91, 110.65, 68.74, 58.64, 38.62, 30.98, 29.79, 29.04, 23.88, 22.54; GC-MS 262 (30%, M^++1), 261 (100%, M^+), 230 (78%), 164 (28%), 151 (40%), 119 (17%), 39 (22%).



(2*R*,4a*S*,7a*R*)-2-(3,4-Dimethoxyphenyl) perhydrocyclopenta[*b*]pyridine 13c: Yield 84 mg (90%); R_f := 0.36 (40% EtOAc-hexane); IR (neat) 3108, 2927, 2853, 2793, 1448, 1304, 1068, 698; ^{1}H NMR (400 MHz, $CDCl_3$) 7.32-7.26 (m, 1H), 6.95-6.77 (m, 2H), 3.80 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 3.7 (dd, *J* = 12.0 Hz, 2.6 Hz, 1H, C2H), 2.44 (dd, *J* = 10 Hz, 6.0 Hz, 1H), 2.25 (br s, NH), 2.18-2.0 (m, 1H, C4aH), 1.81-1.09 (m, 11H); ^{13}C NMR (100 MHz, $CDCl_3$) d 148.79 (C), 147.90 (C), 137.73 (C), 118.78 (CH), 110.89 (CH), 110.10 (CH), 65.76 (CH), 62.76 (CH), 55.85 (OCH_3), 44.71 (CH), 34.84 (CH_2), 30.53 (CH_2), 30.23 (CH_2), 28.67 (CH_2), 20.68 (CH_2); GC-MS 262 (31%, M^++1), 261 (100%, M^+), 260 (74%), 230 (91%), 192 (14%), 164 (38%), 151 (56%), 119 (20%), 106 (16%), 91 (15%), 77 (16%), 39 (25%).

Acknowledgement

HSPR thanks University Grants Commission (UGC), and Council of Scientific and Industrial Research (CSIR) for award of Major Research Projects. We thank UGC for Special Assistance Program and the Department of Science and Technology for FIST recognition. S. Rafi thanks CSIR for the Junior Research Fellowship. We thank late Prof. A. Srikrishna, Central Instrumentation Facility (CIF) at Pondicherry University and Sophisticated Analytical Instrumentation Center (SAIC) at IIT M for spectral data.

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