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A useful approach for the synthesis of pharmacologically active tetrahydropyridinylbenzimidazoles is described. 2-Pyridin-3-ylbenzimidazoles **3a-d** have been synthesized by condensation of 3-pyridinecarboxaldehyde **1** with substituted 1,2-phenylenediamines **2a-d** following oxidative cyclization with iodobenzene diacetate. Methylation of **3a-d** with iodomethane and potassium hydroxide, subsequent formation of methylpyridinium salts **4a-d** and **7a-d** and reduction thereafter afforded tetrahydropyridinylbenzimidazoles **5a-d** and **8a-d**.

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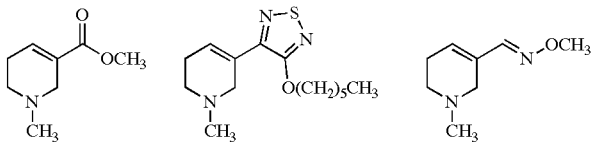
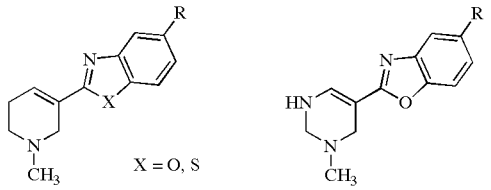
The development of M_1-selective receptor agonists, which play an important role in cognition function, has been the focus of recent research efforts for Alzheimer's disease (AD) treatment [1]. Arecoline (**I**, Figure 1), a naturally occurring alkaloid, is one of the first clinical drugs used for AD [2]. Despite being an M_1-agonist, its lack of subtype selectivity and poor metabolic stability caused by the ester moiety, has hindered its use as a therapeutic agent. However, continuing efforts to synthesize derivatives of this lead compound have brought about xanomeline (**II**) [3] and milameline (**III**) [4] showing improved pharmacological and pharmacokinetic properties. Both of these M_1 selective muscarinic receptor agonists are in clinical trials. Chemically, they possess a 1,2,5,6-tetrahydropyridine ring and the unstable ester moiety of arecoline has been replaced with its bioisosteres alkoxythiadiazole and alkoxyimino groups. The structure of xanomeline (**II**) shows a resemblance to that of tetrahydropyridinylbenzoxazoles (**IV**) [6] and tetrahydropyrimidinylbenzoxazoles (**V**) [7] previously prepared in our laboratory (Figure 2). These compounds, which possess a benzoxazole ring, exhibited interesting biological activity as potential agrochemicals as well as clinical drugs. Herein, we report the synthesis of tetrahydropyridinyl-benzimidazoles that are bioisosteric congeners of the M_1 selective muscarinic receptor agonists shown in Figure 1 (Scheme 1 and Scheme 2).



I **II** **III**

Figure 1



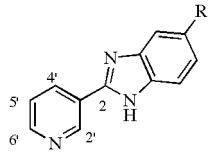
IV **V**

Figure 2

The general procedure for the synthesis of pyridinylbenzimidazoles has been to treat nicotinic acid with the appropriate 1,2-phenylenediamine [8]. However, in a previous study, we have succeeded in preparing pyridinylbenzimidazoles **3** in good yields from 3-pyridinecarboxaldehyde **1** and 1,2-phenylenediamines **2** with iodobenzene diacetate *via* hypervalent iodine oxidative intramolecular cyclization. The 5-substituted compounds **3b-3d** were similarly prepared using compounds **2b-2d**. The structural assignment of these 5-substituted benzimidazoles was based on results of X-ray crystallography, ^{1}H NMR muster of aromatic protons and our previous experiments [6]. The spectral data for compounds **3a-d** are summarized in Table 1.

Table 1

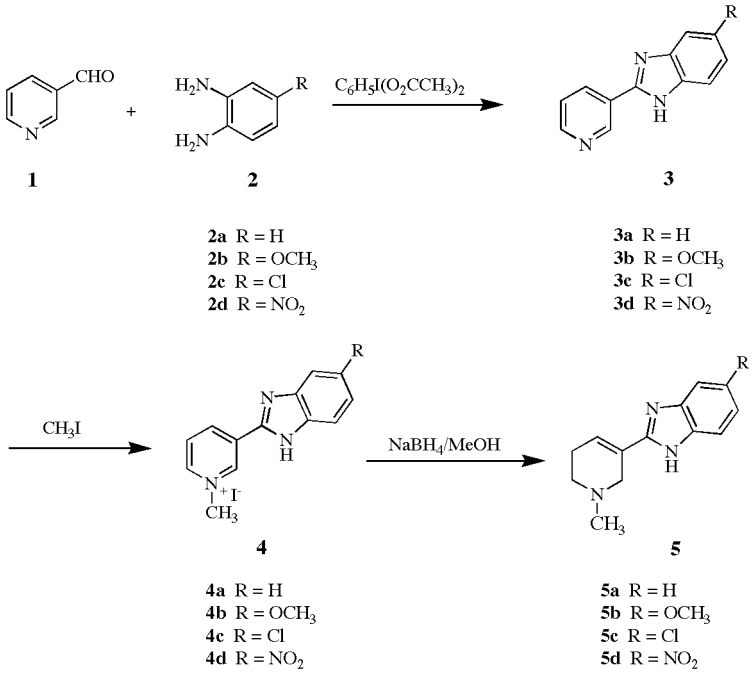
^{1}H NMR Data and ^{13}C NMR Data of Compounds **3a-d**



Compd	Proton δ [ppm]				Carbon δ [ppm]					
	2'-H	4'-H	5'-H	6'-H	C-2	C-2'	C-3'	C-4'	C-5'	C-6'
3a	9.36	8.58	7.72	8.75	149.0	147.7	126.3	134.0	124.3	150.8
3b	9.21	8.42	7.58	8.61	151.6	148.2	128.2	135.8	125.8	151.3
3c	9.14	8.38	7.53	8.58	151.7	148.6	127.7	136.2	125.1	151.8
3d	9.37	8.52	7.66	8.75	154.2	148.1	125.7	134.5	124.3	151.5

Subsequent treatment of compounds **3a-d** with a large excess of methyl iodide in acetone for 20 hours afforded the quaternized compounds **4a-d**. The quaternization occurred only at the pyridine nitrogen due to its higher basicity. The spectral data for compounds **4a-d** are summarized in Table 2. What is notable here is that unlike compounds **3a-d**, compounds **4a-d** did not show the signals corresponding to C-8 and C-9 (numbering based on arbitrary numbering of X-ray Crystallography data – see Figure 3) in the ^{13}C NMR spectra [9]. Moreover, only one of the carbons of the benzimidazoles is observed and appears at 123.8 ppm in **4a**, 113.4 ppm in **4b**, 124.1 ppm in **4c**, and 119.2 ppm in **4d**. Upon acquisition of HMQC and HMBC spectra of **4c**, this

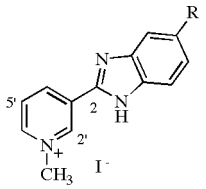
Scheme 1



carbon is determined to correspond to C-5. In the HMQC spectrum of **4c** $^1H/^{13}C$ correlations corresponding to H-4/C-4 and H-7/C-7 are observed showing that C-4 and C-7 resonate at ~119 and 114 ppm respectively. Interestingly, protons corresponding to C-4 and C-7 also correlate with carbons resonating at 112 and 124 ppm, respectively as well. This indicates that the two tautomeric forms of compound **4c**, corresponding to 6-chloro- and 5-chloro-2-pyridin-3-yl-1*H*-benzimidazole, exist and both are represented in the proton and carbon spectra of **4c**.

Table 2

^1H NMR Data and ^{13}C NMR Data of Compounds **4a-d**

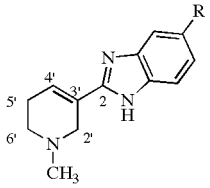


Compd	Proton δ [ppm]				Carbon δ [ppm]				
	2'-H	5'-H, N^+CH_3		C-2	C-2'	C-3'	C-4'	C-5'	C-6'
4a	9.74	8.32	4.49	145.5	144.0	128.3	140.9	130.0	145.4
4b	9.65	8.29	4.45	145.0	143.6	128.2	140.3	130.1	144.1
4c	9.65	8.40	4.47	146.9	144.2	128.0	141.1	128.2	145.8
4d	9.79	8.42	4.54	150.0	143.7	128.3	141.7	129.0	146.5

Treatment of methylpyridinium salts **4a-d** with sodium borohydride in cold (-20 °C) methanol yielded tetrahydropyridinylbenzimidazoles **5a-d**. Again the ^{13}C NMR spectral data shown in Table 3 show that only aromatic carbon is observed for compounds **5a-d**, and as for **4c** this likely corresponds to C-6. The corresponding chemical shifts were 123.1 ppm for **5a**, 113.7 ppm for **5b**, 124.5 ppm for **5c**, and 119.8 ppm for **5d**. The coupling constants were observed to be similar to those of compounds **4a-d**.

Table 3

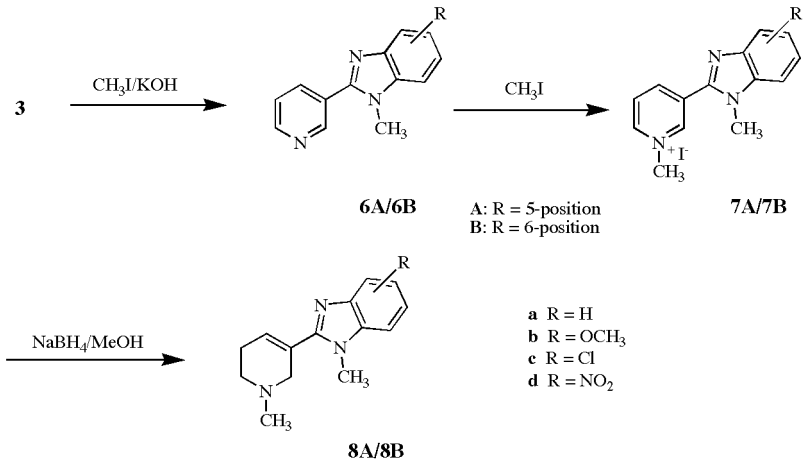
^1H NMR Data and ^{13}C NMR Data of Compounds **5a-d**



Compd	Proton δ [ppm]					Carbon δ [ppm]				
	2'-H	4'-H	5'-H	6'-H	C-2	C-2'	C-3'	C-4'	C-5'	C-6'
5a	3.59	6.59	2.36	2.60	151.6	54.7	128.0	127.8	26.7	51.6
5b	3.32	6.52	2.31	2.47	152.0	54.9	128.5	128.1	27.2	52.3
5c	3.38	6.62	2.37	2.56	153.7	54.8	130.2	127.6	27.1	52.2
5d	3.60	6.89	2.58	2.78	156.6	54.6	134.2	127.4	27.1	52.1

A commonly used literature method [10] for methylation of benzimidazole is to add compounds **3a-d** to a suspension of 5 equivalents KOH in acetone, and then adding 3~5 equivalents of methyl iodide. This causes methylation at either nitrogen of the benzimidazole yielding a 1:1 mixture

Scheme 2



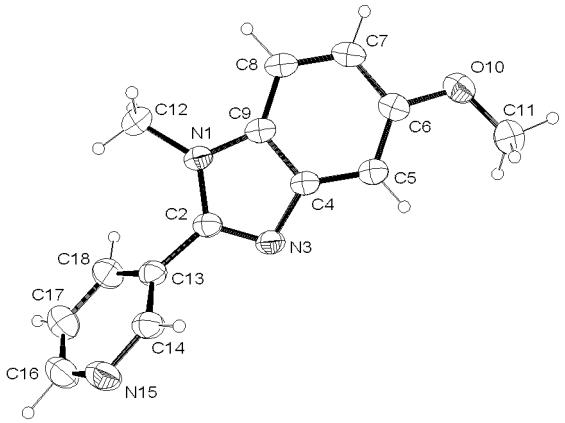
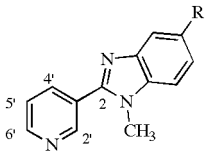


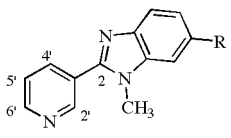
Figure 3. X-Ray Crystallography of **6Ab** (arbitrary numbering system).

Table 4

^{1}H NMR Data and ^{13}C NMR Data of Compounds **6a-c**



6A



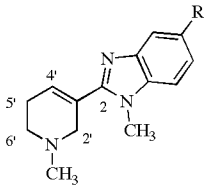
6B

Compd	Proton δ [ppm]					Carbon δ [ppm]				
	2'-H	4'-H	5'-H	6'-H	C-2	C-2'	C-3'	C-4'	C-5'	C-6'
6a	9.05	8.11	7.46	8.73	150.6	149.8	126.5	136.8	123.6	150.5
6Ab	9.01	8.12	7.48	8.74	150.7	149.7	126.6	136.7	123.5	150.4
6Bb	9.00	8.12	7.47	8.73	149.8	149.6	126.6	136.6	123.5	150.3
6Ac	9.00	8.12	7.49	8.77	151.8	149.7	126.1	136.9	123.6	150.9
6Bc	9.01	8.12	7.49	8.76	151.4	149.7	126.0	136.8	123.6	150.8

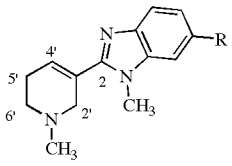
of the 5-/6-substituted isomer of compounds **6a-d**. Isomers **6b** and **6c** were successfully separated by column chromatography and were distinguishable based on the results of X-ray crystallography of compound **6Ab** (Figure 3).

Table 5

^{1}H NMR Data and ^{13}C NMR Data of Compounds **8a-c**



8A



8B

Compd	Proton δ [ppm]					Carbon δ [ppm]				
	2'-H	4'-H	5'-H	6'-H	C-2	C-2'	C-3'	C-4'	C-5'	C-6'
8a	3.46	6.38	2.53	2.75	153.5	56.2	127.5	133.0	27.0	52.2
8Ab	3.43	6.34	2.51	2.72	153.6	56.6	127.7	132.6	27.1	52.2
8Bb	3.47	6.36	2.55	2.77	152.2	56.2	127.0	131.7	26.6	51.8
8Ac	3.51	6.45	2.56	2.80	154.8	56.3	129.6	133.6	26.0	52.0
8Bc	3.41	6.41	2.52	2.70	154.5	56.3	129.9	133.2	26.9	52.0

Compound **6d**, however, remained as a mixture and thus subsequent reaction proceeded without further purification. The ^{1}H and ^{13}C NMR data of compounds **6a-d** are shown in Table 4. Compounds **7a-d** were prepared using the method used for compounds **4a-d** followed by reduction with sodium borohydride in methanol to yield compounds **8a-d**. The spectral data of **8Aa-d** and **8Ba-d** are summarized in Table 5.

EXPERIMENTAL

Melting points were determined on a Thomas-Hoover apparatus and are uncorrected. Infrared spectra were recorded on a Mattson Genesis II FTIR. Nuclear magnetic resonance spectra were measured on a Brucker AM-300 spectrometer. Mass spectra were determined on JEOL JMS-DX 303 Mass Spectrometer JEOL JMA-DA 5000 mass data system focusing high resolution mass spectrometers. Single crystal X-ray diffractometry: The intensity data were collected at room temperature on a Siemens P4 four-circle X-ray diffractometer with graphite-monochromated

Mo Kα radiation (λ = 0.71073 Å). All calculation in the structural solution and refinement was performed using the Siemens SHELXTL crystallographic software package on a Silicon Graphics system. All the non-hydrogen atoms were refined anisotropically; all the hydrogen atoms fixed at the calculated positions with the isotropic thermal parameters were included in the final structure factor calculations.

General Procedure for Preparation of 2-Pyridin-3-ylbenzimidazoles (**3a-d**).

A mixture of 3-pyridinecarboxaldehyde (**1**) (5.0 mmol) and 1,2-phenylenediamine (**2**) (5.0 mmol) in absolute ethanol (100 ml) was stirred at room temperature for 2 hours. To the reaction mixture was added iodobenzene diacetate (7.0 mmol). After 1 hour stirring, the solvent was removed under reduced pressure, the residue diluted with ethyl acetate and then washed with aqueous $NaHCO_3$ solution. The organic layer was separated, washed with brine, dried over anhydrous $MgSO_4$, and then evaporated *in vacuo*. The residue was purified by column chromatography on silica gel (*n*-hexane:ethyl acetate) to give the title compounds **3a-d**.

2-Pyridin-3-yl-1*H*-benzimidazole (**3a**).

This compound was obtained as yellow powder, yield 52 %, mp 247-248°; ir (potassium bromide): 3040 (CH), 1490, 1450 cm^{-1}; ^1H nmr (CD_3OD): δ 9.36 (d, 1H, C2'-H), 8.75 (dd, 1H, C6'-H), 8.58 (m, 1H, C4'-H), 7.72 (m, 3H, C4-H, C7-H, C5'-H), 7.40 (m, 2H, C5-H, C6-H); ^{13}C nmr (CD_3OD): δ 150.8 (C-6'), 149.0 (C-2), 147.7 (C-2'), 143.9, 135.0 (C-8, C-9), 134.0 (C-4'), 126.3 (C-3'), 124.3 (C-5'), 123.3, 122.3, 119.3, 111.7 (arom. C).

Anal. Calcd. For $C_{12}H_9N_3$: C, 73.83; H, 4.65; N, 21.52. Found: C, 73.84; H, 4.62; N, 21.53.

5-Methoxy-2-pyridin-3-yl-1*H*-benzimidazole (**3b**).

This compound was obtained as yellow brown powder, yield 75 %, mp 174-176°; ir (potassium bromide): 3050 (CH), 1650, 1435 cm^{-1}; ^1H nmr (CD_3OD): δ 9.21 (d, 1H, C2'-H), 8.61 (dd, 1H, C6'-H), 8.42 (m, 1H, C4'-H), 7.58 (m, 2H, C5'-H, C7-H), 7.08 (d, 1H, C4-H), 6.91 (dd, 1H, C6-H), 3.84 (s, 3H, OCH_3); ^{13}C nmr (CD_3OD): δ 158.9 (C-5), 151.5 (C-2), 151.2 (C-6'), 148.8, 136.5 (C-8, C-9), 148.2 (C-2'), 135.8 (C-4'), 128.2 (C-3'), 125.8 (C-5'), 127.8, 125.8, 114,6 (arom. C), 56.4 (OCH_3); $C_{13}H_{11}N_3O$(225.0902), MS: m/z = 225.0904.

Anal. Calcd. For $C_{13}H_{11}N_3O•1/2H_2O$: C, 66.65; H, 5.16; N, 17.94. Found: C, 66.96; H, 5.09; N, 17.52.

5-Chloro-2-pyridin-3-yl-1*H*-benzimidazole (**3c**).

This compound was obtained as yellow crystal, yield 78 %, mp 147-148°; ir (potassium bromide): 3100 (CH), 1440, 1420 cm^{-1}; ^1H nmr (CD_3OD): δ 9.14 (d, 1H, C2'-H), 8.58 (dd, 1H, C6'-H), 8.38 (m, 1H, C4'-H), 7.53 (m, 3H, C5'-H, C4-H, C7-H), 7.18 (dd, 1H, C6-H); ^{13}C nmr (CD_3OD): δ 151.8 (C-6'), 151.7 (C-2), 148.6 (C-2'), 136.2 (C-4'), 130.1, 129.5 (C-8, C-9), 127.7 (C-3'), 125.9 (C-5), 125.1 (C-5'), 118.9, 117.3, 116.4 (arom. C); $C_{12}H_8N_3Cl$(229.0407), MS: m/z = 229.0401.

Anal. Calcd. For $C_{12}H_8N_3Cl$: C, 62.76; H, 3.51; N, 18.30. Found: C, 62.32; H, 3.60; N, 17.95.

5-Nitro-2-pyridin-3-yl-1*H*-benzimidazole (**3d**).

This compound was obtained as yellow powder, yield 65 %, mp 273-274°; ir (potassium bromide): 3110 (CH), 1520, 1340 cm^{-1}; ^1H nmr (DMSO-d_6): δ 9.37 (d, 1H, C2'-H), 8.75 (dd, 1H, C6'-H), 8.52 (m, 2H, C4-H, C4'-H), 8.16 (d, 1H, C6-H), 7.81 (d, 1H, C7-H), 7.66 (dd, 1H, C5'-H); ^{13}C nmr (DMSO-d_6): δ 154.2 (C-2), 151.5 (C-6'), 148.1 (C-2'), 143.7, 140.1 (C-8, C-9), 142.8 (C-5), 134.5 (C-4'), 125.7 (C-3'), 124.3 (C-5'), 118.1, 115.0, 112.6 (arom. C); $C_{12}H_8N_4O_2$(240.0647), MS: m/z = 240.0645.

Anal. Calcd. For $C_{12}H_8N_4O_2$: C, 60.00; H, 3.36; N, 23.32. Found: C, 59.88; H, 3.36; N, 23.15.

General Procedure for Preparation of Pyridium Salts (**4a-d**).

To a stirred solution of (**3a-d**) (5.0 mmol) in acetone (30 ml) was added a solution of iodomethane (50.0 mmol) in acetone (10 ml). The mixture was stirred at room temperature for 20 hours. The precipitate was collected by filtration, the filter cake washed with acetone, then dried under reduced pressure to give **4a-d**.

2-(1-Methyl)pyridinium-3-yl-1*H*-benzimidazole Iodide (**4a**).

This compound was obtained as yellow powder, yield 87 %, mp 221-223°; ir (potassium bromide): 3140 (CH), 1480, 1310 cm^{-1}; ^1H nmr (DMSO-d_6): δ 9.74 (s, 1H, C2'-H), 9.12, 9.06 (2 x d, 2H, C6'-H, C4'-H), 8.32 (dd, 1H, C5'-H), 7.74 (m, C4-H, C7-H), 7.34 (m, C5-H, C6-H), 4.49 (s, 3H, N^+CH_3); ^{13}C nmr (DMSO-d_6): δ 145.5 (C-2), 145.4 (C-6'), 144.0 (C-2'), 140.9 (C-4'), 130.0 (C-5'), 128.3 (C-3'), 123.8 (arom. C), 48.7 (N^+CH_3); $C_{13}H_{12}N_3I$(-CH_3I)(195.0796), MS: m/z = 195.0790.

Anal. Calcd. For $C_{13}H_{12}N_3I•1/2H_2O$: C, 45.11; H, 3.79; N, 12.14. Found: C, 45.51; H, 3.55; N, 12.02.

5-Methoxy-2-(1-methyl)pyridinium-3-yl-1*H*-benzimidazole Iodide (**4b**).

This compound was obtained as yellow powder, yield 75 %, mp 183-186°; ir (potassium bromide): 3110 (CH), 1630, 1270 cm^{-1}; ^1H nmr (DMSO-d_6): δ 9.65 (s, 1H, C2'-H), 9.03 (2xd, 2H, C6'-H, C4'-H), 8.29 (dd, 1H, C5'-H), 7.65-6.93 (m, 3H, C4-H, C6-H, C7-H), 4.45 (s, 3H, N^+CH_3), 3.83 (s, 3H, OCH_3); ^{13}C nmr (DMSO-d_6): δ 158.9 (C-5), 145.0 (C-2), 144.1 (C-6'), 143.6 (C-2'), 140.3 (C-4'), 130.1 (C-5'), 128.2 (C-3'), 113.4 (arom. C), 55.8 (OCH_3), 48.7 (N^+CH_3); $C_{14}H_{14}N_3OI$(-CH_3I) (225.0902), MS: m/z = 225.0902.

Anal. Calcd. For $C_{14}H_{14}N_3OI•H_2O$: C, 43.65; H, 4.19; N, 10.91. Found: C, 44.03; H, 4.15; N, 10.89.

5-Chloro-2-(1-methyl)pyridinium-3-yl-1*H*-benzimidazole Iodide (**4c**).

This compound was obtained as yellow powder, yield 74 %, mp 236-238°; ir (potassium bromide): 3090(CH), 1660, 1490, 1320 cm^{-1}; ^1H nmr (DMSO-d_6): δ 9.65 (s, 1H, C2'-H), 9.08 (br d, 2H, C6'-H, C4'-H), 8.40 (dd, 1H, C5'-H), 7.84 (d, 1H, C4-H, *J* = 1.6 Hz), 7.79 (d, 1H, C7-H, *J* = 8.6 Hz), 7.40 (dd, 1H, C6-H, *J* = 1.6 Hz, 8.6 Hz), 4.47 (s, 3H, N^+CH_3); ^{13}C nmr (DMSO-d_6): δ 146.9 (C-2), 145.8 (C-6'), 144.2 (C-2'), 141.1 (C-4'), 129.6 (C-5), 128.2 (C-5'), 128.0 (C-3'), 124.1 (arom. C), 48.7 (N^+CH_3).

Anal. Calcd. For $C_{13}H_{11}ClIN_3$: C, 42.02; H, 2.98; N, 11.31. Found: C, 41.95; H, 3.10; N, 11.39.

5-Nitro-2-(1-methyl)pyridinium-3-yl-1*H*-benzimidazole Iodide (**4d**).

This compound was obtained as yellow powder, yield 92 %, mp 265-266°; ir (potassium bromide): 3060 (CH), 1530, 1345 cm^{-1}; ^1H nmr (DMSO-d_6): δ 9.79 (s, 1H, C2'-H), 9.18 (2xd, 2H, C6'-H, C4'-H), 8.58 (d, 1H, C4-H, *J* = 2.0 Hz), 8.42 (dd, 1H, C5'-H, *J* = 6.2 Hz, 8.1 Hz), 8.22 (d, 1H, C6-H, *J* = 2.0 Hz,

8.9 Hz), 7.92 (d, 1H, C7-H, *J* = 8.9 Hz), 4.54 (s, 3H, N^+CH_3); ^{13}C nmr (DMSO-d_6): δ 150.0 (C-2), 146.5 (C-6'), 144.6 (C-5), 143.7 (C-2'), 141.7 (C-4'), 129.0 (C-5'), 128.3 (C-3'), 119.2 (arom. C), 48.8 (N^+CH_3); $C_{13}H_{11}N_4IO_2$(-CH_3I)(240.0647), MS: m/z = 240.0646.

Anal. Calcd. For $C_{13}H_{11}N_4IO_2$: C, 40.86; H, 2.90; N, 14.66. Found: C, 40.97; H, 2.94; N, 14.51.

General Procedure for Preparation of 1-Methyl-1,2,5,6-tetrahydropyridin-3-ylbenzimidazoles (**5a-d**).

To a cooled (-20 °C) and stirred suspension of (**4a-d)** (4.0 mmol) in methanol (40 ml) was added portion-wise sodium borohydride (4.5 mmol). After stirring for 2 hours at room temperature, the solvent was evaporated. The residue was dissolved in ethyl acetate and washed with aqueous $NaHCO_3$ solution. The organic layer was washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed *in vacuo* and the residue was purified by flash column chromatography on silica gel (methylene chloride:methanol) to give the title compounds **5a-d**.

2-(1-Methyl-1,2,5,6-tetrahydropyridin-3-yl)-1*H*-benzimidazole (**5a**).

This compound was obtained as yellow powder, yield 95 %, mp 204-206°; ir (potassium bromide): 3090 (CH), 1660, 1455 cm^{-1}; ^1H nmr ($CDCl_3$): δ 7.27-7.18 (m, 4H, arom. H), 6.59 (m, 1H, C4'-H), 3.59 (d, 2H, C2'-H, *J* = 1.9 Hz), 2.60 (m, 2H, C6'-H), 2.44 (s, 3H, NCH_3), 2.36 (m, 2H, C5'-H); ^{13}C nmr ($CDCl_3$): δ 151.6 (C-2), 128.0 (C-3'), 127.8 (C-4'), 123.1 (arom. C), 54.7 (C-2'), 51.6 (C-6'), 46.1 (NCH_3), 26.7 (C-5'); $C_{13}H_{15}N_3$ (213.1266), MS: m/z = 213.1272.

Anal. Calcd. For $C_{13}H_{15}N_3 \bullet (CO_2H)_2 \bullet H_2O$: C, 56.07; H, 5.96; N, 13.08. Found: C, 55.66; H, 5.63; N, 12.86.

5-Methoxy-2-(1-methyl-1,2,5,6-tetrahydropyridin-3-yl)-1*H*-benzimidazole (**5b**).

This compound was obtained as yellow powder, yield 45 %, mp 143-145°; ir (potassium bromide): 3390 (CH), 1690, 1620 cm^{-1}; ^1H nmr (CD_3OD): δ 7.23 (d, 1H, C7-H, *J* = 8.6 Hz), 6.83 (s, 1H, C4-H), 6.66 (d, 1H, C6-H, *J* = 8.6 Hz), 6.52 (m, 1H, C4'-H), 3.63 (s, 3H, OCH_3), 3.32 (br s, 2H, C2'-H), 2.47 (br s, 2H, C6'-H), 2.31 (br s, 5H, NCH_3, C5'-H); ^{13}C nmr (CD_3OD): δ 158.5 (C-5), 152.0 (C-2), 128.5 (C-3'), 128.1 (C-4'), 113.7 (arom. C), 56.4 (OCH_3), 54.9 (C-2'), 52.3 (C-6'), 46.0 (NCH_3), 27.2 (C-5'); $C_{14}H_{17}N_3O$(243.1372), MS: m/z = 243.1379.

Anal. Calcd. For $C_{14}H_{17}N_3O \bullet (CO_2H)_2 \bullet 2H_2O$: C, 52.03; H, 6.28; N, 11.38. Found: C, 51.92; H, 6.23; N, 11.03.

5-Chloro-2-(1-methyl-1,2,5,6-tetrahydropyridin-3-yl)-1*H*-benzimidazole (**5c**).

This compound was obtained as yellow powder, yield 67 %, mp 174-175°; ir (potassium bromide): 2920 (CH), 1670, 1430 cm^{-1}; ^1H nmr (CD_3OD): δ 7.33 (d, 1H, C4-H, *J* = 1.9 Hz), 7.30 (d, 1H, C7-H, *J* = 8.6 Hz), 7.02 (dd, 1H, C6-H, *J* = 1.9 Hz, 8.6 Hz), 6.62 (m, 1H, C4'-H), 3.38 (m, 2H, C2'-H), 2.56 (m, 2H, C6'-H), 2.37 (s, 3H, NCH_3), 2.37 (m, 2H, C5'-H); ^{13}C nmr (CD_3OD): δ 153.7 (C-2), 130.2 (C-3'), 129.4 (C-5), 127.6 (C-4'), 124.5 (arom. C), 54.8 (C-2'), 52.2 (C-6'), 45.9 (NCH_3), 27.1 (C-5'); $C_{13}H_{14}N_3Cl$(247.0876), MS: m/z = 247.0870.

Anal. Calcd. For $C_{13}H_{14}N_3Cl \bullet (CO_2H)_2 \bullet 1/2H_2O$: C, 51.96; H, 4.94; N, 12.12. Found: C, 52.15; H, 5.10; N, 12.02.

5-Nitro-2-(1-methyl-1,2,5,6-tetrahydropyridin-3-yl)-1*H*-benzimidazole (**5d**).

This compound was obtained as brown powder, yield 47 %, mp 130-131°; ir (potassium bromide): 2940 (CH), 1650, 1330 cm^{-1}; ^1H nmr (CD_3OD): δ 8.37 (d, 1H, C4-H, *J* = 2.0 Hz), 8.12 (dd, 1H, C6-H, *J* = 2.0 Hz, 8.9 Hz), 7.58 (d, 1H, C7-H, *J* = 8.9 Hz), 6.89 (m, 1H, C4'-H), 3.60 (m, 2H, C2'-H), 2.78 (m, 2H, C6'-H), 2.58 (s, 3H, NCH_3), 2.58 (m, 2H, C5'-H); ^{13}C nmr (CD_3OD): δ 156.6 (C-2), 145.1 (C-5), 134.2 (C-3'), 127.4 (C-4'), 119.8 (arom. C), 54.6 (C-2'), 52.1 (C-6'), 45.8 (NCH_3), 27.1 (C-5'); $C_{13}H_{14}N_4O_2$(258.1117), MS: m/z = 258.1112.

Anal. Calcd. For $C_{13}H_{14}N_4O_2 \bullet (CO_2H)_2 \bullet H_2O$: C, 49.18; H, 4.95; N, 15.29. Found: C, 49.58; H, 5.09; N, 15.64.

General Procedure for Preparation of 1-Methyl-2-pyridinylbenzimidazoles (**6a-d**).

To a stirred suspension of potassium hydroxide (10 mmol) in 50 ml acetone was added **3a-d** (2 mmol) and added methyl iodide (6 mmol). After stirring at room temperature for 2 hours, the reaction mixture was poured into toluene. The separated organic layer was washed with brine, dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was purified or isomers separated by flash column chromatography on silica gel to give the title compounds **6a-d**.

1-Methyl-2-pyridin-3-yl-1*H*-benzimidazole (**6a**).

This compound was obtained by flash column chromatography on silica gel (methylene chloride:methanol) as pale yellow powder, yield 93 %, mp 143-145°; ir (potassium bromide): 3160 (CH), 1730, 1580 cm^{-1}; ^1H nmr ($CDCl_3$): δ 9.05 (d, 1H, C2'-H), 8.73 (dd, 1H, C6'-H), 8.11 (m, 1H, C4'-H), 7.83-7.30 (m, 4H, C4-H, C5-H, C6-H, C7-H), 7.46 (m, 1H, C5'-H), 3.87 (NCH_3); ^{13}C nmr ($CDCl_3$): δ 150.6 (C-2), 150.5 (C-6'), 149.8 (C-2'), 142.9, 136.5 (C-8, C-9), 136.8 (C-4'), 126.5 (C-3'), 123.6 (C-5'), 123.3, 122.8, 120.0, 109.8 (arom. C), 31.7 (NCH_3); $C_{13}H_{11}N_3$(209.0953), MS: m/z = 209.0952.

Anal. Calcd. For $C_{13}H_{11}N_3$: C, 74.62; H, 5.30; N, 20.08. Found: C, 74.71; H, 5.28; N, 20.20.

5-Methoxy-1-methyl-2-pyridin-3-yl-1*H*-benzimidazole (**6Ab**).

The mixture of 5-/6-isomers (1:1) was separated by flash column chromatography on silica gel (*n*-hexane:acetone) to give **6Ab** and **6Bb**. Compound **6Ab** was obtained as yellow powder, yield 40 %, mp 118°; ir (potassium bromide): 3050 (CH), 1630, 1570 cm^{-1}; ^1H nmr ($CDCl_3$): δ 9.01 (br d, 1H, C2'-H), 8.74 (dd, 1H, C6'-H), 8.12 (dt, 1H, C4'-H), 7.48 (br dd, 1H, C5'-H), 7.30 (m, 2H, C4-H, C7-H), 7.01 (dd, 1H, C6-H), 3.89 (s, 3H, OCH_3), 3.88 (s, 3H, NCH_3); ^{13}C nmr ($CDCl_3$): δ 156.5 (C-5), 150.7 (C-2), 150.4 (C-6'), 149.7 (C-2'), 143.7, 131.2 (C-8, C-9), 136.7 (C-4'), 126.6 (C-3'), 123.5 (C-5'), 113.5, 110.1, 101.8 (arom. C), 55.7 (OCH_3), 31.7 (NCH_3).

Anal. Calcd. For $C_{14}H_{13}N_3O$: C, 70.28; H, 5.48; N, 17.56. Found: C, 70.07; H, 5.47; N, 17.74.

Crystal Data and Structure Refinement for **6Ab**.

Empirical formula	$C_{14}H_{13}N_3O$
Formula weight	239.27
Temperature	297(2) K
Wavelength	0.71073 Å
Crystal system, space group	Triclinic, P-1
Unit cell dimensions	*a* = 6.7973(8) Å α = 83.694(14)°.

	b = 7.4976(12) Å β = 80.852(7)°.
	c = 12.2434(17) Å γ = 89.746(10)°.
Volume, Z	612.25(15) Å^3, 2
Calculated density	1.298 Mg/m^3
Absorption coefficient	0.085 mm^{-1}
F(000)	252
Crystal size	0.3 x 0.5 x 0.4 mm
θ range for data collection	2.73 to 26.00°
Limiting indices	$-8 \le h \le 1$, $-9 \le k \le 9$, $-15 \le l \le 15$
Reflections collected	3042
Independent reflections	2406 [R_{int} = 0.0229]
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	2406/0/213
Goodness-of-fit on F^2	1.050
Final R indices [I>2σ(I)]	R1 = 0.0717, wR2 = 0.1646
R indices (all data)	R1 = 0.0787, wR2 = 0.1710
Largest diff. peak and hole	0.690 and -0.311 e.A^{-3}

6-Methoxy-1-methyl-2-pyridin-3-yl-1*H*-benzimidazole (**6Bb**).

This compound was obtained as yellow powder, yield 42 %, mp 109-110°; ir (potassium bromide): 2980 (CH), 1600, 1450 cm^{-1}; ^{1}H nmr ($CDCl_3$): δ 9.00 (br d, 1H, C2'-H), 8.73 (dd, 1H, C6'-H), 8.12 (dt, 1H, C4'-H), 7.72 (d, 1H, C4-H), 7.47 (m, 1H, C5'-H), 6.99 (dd, 1H, C5-H), 6.85 (d, 1H, C7-H), 3.92 (s, 3H, OCH_3), 3.89 (s, 3H, NCH_3); ^{13}C nmr ($CDCl_3$): δ 157.0 (C-6), 150.3 (C-6'), 149.8 (C-2), 149.6 (C-2'), 137.5, 137.2 (C-8, C-9), 136.6 (C-4'), 126.6 (C-3'), 123.5 (C-5'), 120.5, 112.1, 93.1 (arom. C), 55.8 (OCH_3), 31.7 (NCH_3); $C_{14}H_{13}N_3O$ (239.1058), MS: m/z = 239.1058.

Anal. Calcd. For $C_{14}H_{13}N_3O$: C, 70.28; H, 5.48; N, 17.56. Found: C, 69.90; H, 5.43; N, 17.12.

5-Chloro-1-methyl-2-pyridin-3-yl-1*H*-benzimidazole (**6Ac**).

The mixture 5-/6-isomers (1:1) was separated by flash column chromatography on silica gel (*n*-hexane:acetone) to give **6Ac** and **6Bc**. Compound **6Ac** was obtained as yellow powder, yield 35 %, mp 142-143°; ir (potassium bromide): 3050 (CH), 1475, 1420 cm^{-1}; ^{1}H nmr ($CDCl_3$): δ 9.00 (d, 1H, C2'-H, J = 1.9 Hz), 8.77 (dd, 1H, C6'-H, J = 1.6 Hz, 5.0 Hz), 8.12 (dt, 1H, C4'-H, J = 1.9 Hz, 7.8 Hz), 7.80 (s, 1H, C4-H), 7.49 (dd, 1H, C5'-H, J = 5.0 Hz, 7.8 Hz), 7.33 (s, 2H, C6-H, C7-H), 3.90 (s, 3H, NCH_3); ^{13}C nmr ($CDCl_3$): δ 151.8 (C-2), 150.9 (C-6'), 149.7 (C-2'), 143.7, 135.2 (C-8, C-9), 136.9 (C-4'), 128.4 (C-5), 126.1 (C-3'), 123.6 (C-5'), 123.7, 119.7, 110.6 (arom. C), 31.9 (NCH_3).

Anal. Calcd. For $C_{13}H_{10}N_3Cl$: C, 64.07; H, 4.14; N, 17.24. Found: C, 63.72; H, 4.14; N, 17.10.

6-Chloro-1-methyl-2-pyridin-3-yl-1*H*-benzimidazole (**6Bc**).

This compound was obtained as yellow powder, yield 33 %, mp 146-147°; ir (potassium bromide): 2925 (CH), 1465, 1415 cm^{-1}; ^{1}H nmr ($CDCl_3$): δ 9.01 (d, 1H, C2'-H, J = 1.9 Hz), 8.76 (dd, 1H, C6'-H, J = 1.2 Hz, 5.0 Hz), 8.12 (m, 1H, C4'-H), 7.73 (d, 1H, C4-H, J = 8.4 Hz), 7.49 (dd, 1H, C5'-H, J = 5.0 Hz, 7.8 Hz), 7.40 (d, 1H, C7-H, J = 1.6 Hz), 7.29 (dd, 1H, C5-H, J = 1.6 Hz, 8.4 Hz), 3.87 (s, 3H, NCH_3); ^{13}C nmr ($CDCl_3$): δ 151.4 (C-2), 150.8 (C-6'), 149.7 (C-2'), 141.5, 137.1 (C-8, C-9), 136.8 (C-4'), 129.0 (C-6), 126.0 (C-3'), 123.6 (C-5'), 123.4, 120.8, 109.9 (arom. C), 31.8 (NCH_3).

Anal. Calcd. For $C_{13}H_{10}N_3Cl$: C, 64.07; H, 4.14; N, 17.24. Found: C, 63.78; H, 4.16; N, 17.41.

5/6-Nitro-1-methyl-2-pyridin-3-yl-1*H*-benzimidazole (**6ABd**).

The title compound was obtained as a mixture of 5-/6-isomers as dark yellow powder, yield 90 %, mp 232-234°; ir (potassium bromide): 2920 (CH), 1505, 1350 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 9.10 (br s, 2H, C2'-H), 8.80 (br d, 2H, C6'-H, J = 4.8 Hz), 8.34 (br d, 2H, C4'-H, J = 7.8 Hz), 7.66 (dd, 2H, C5'-H, J = 4.8 Hz, 7.8 Hz), 8.72, 8.61, 8.24, 8.17, 7.90 (m, 6H, arom. H), 4.04, 3.99 (s, 6H, NCH_3); ^{13}C nmr (DMSO-d_6): δ 155.8 (C-2), 151.5 (C-6'), 150.0 (C-2'), 143.2, 136.3 (C-8, C-9), 137.3 (C-4'), 125.7, 124.1, 119.8, 118.1, 111.8, 108.4 (C-3', C-5', arom. C), 32.6 (NCH_3); $C_{13}H_{10}N_4O_2$(254.0804), MS: m/z = 254.0808.

Anal. Calcd. For $C_{13}H_{10}N_4O_2$: C, 61.41; H, 3.96; N, 22.04. Found: C, 61.25; H, 3.99; N, 21.80.

General Procedure for Preparation of (**7a-d**).

The compounds (**7a-d**) were prepared following the procedure described for pyridinium salts (**4a-d**), and were used for the next reaction without further purification.

1-Methyl-2-(1-methyl)pyridinium-3-yl-1*H*-benzimidazole Iodide (**7a**).

This compound was obtained as yellow powder, yield 76 %, mp 215-217°; ir (potassium bromide): 3000 (CH), 1560, 1450 cm^{-1}; ^{1}H nmr (CD_3OD): δ 9.45 (s, 1H, C2'-H), 9.09 (d, 1H, C6'-H), 9.01 (d, 1H, C4'-H), 8.30 (br t, 1H, C5'-H), 7.76, 7.67 (2xd, 2H, C4-H, C7-H), 7.41 (m, 2H, C5-H, C6-H), 4.57 (s, 3H, N^+CH_3), 4.06 (s, 3H, N_1-CH_3); ^{13}C nmr (CD_3OD): δ 148.1, 147.5, 147.4, 146.5 (C-2, C-2', C-5', C-6'), 143.8, 138.4 (C-9, C-8), 132.3, 129.7 (C-3', C-4'), 126.0, 125.1, 120.8, 112.4 (arom. C), 50.2 (N^+CH_3), 32.9 (s, 3H, N_1-CH_3); $C_{14}H_{14}N_3I$(-CH_3I)(209.0953), MS: m/z = 209.0943.

Anal. Calcd. For $C_{14}H_{14}N_3I$•1/2H_2O: C, 46.68; H, 4.20; N, 11.67. Found: C, 46.97; H, 4.00; N, 11.56.

5-Methoxy-1-methyl-2-(1-methyl)pyridinium-3-yl-1*H*-benzimidazole Iodide (**7Ab**).

This compound was obtained as yellow powder, yield quantitative, mp 227-229°; ir (potassium bromide): 3030 (CH), 1620, 1500 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 9.54 (s, 1H, C2'-H), 9.13 (d, 1H, C6'-H), 9.03 (d, 1H, C4'-H), 8.32 (dd, 1H, C5'-H), 7.66 (d, 1H, C4-H), 7.26 (d, 1H, C7-H), 7.05 (dd, 1H, C6-H), 4.50 (s, 3H, N^+CH_3), 4.01 (s, 3H, N_1-CH_3), 3.83 (s, 3H, OCH_3); ^{13}C nmr (DMSO-d_6): δ 156.4 (C-5), 146.7 (C-6'), 145.6 (C-2'), 144.2 (C-4'), 143.3, 131.7 (C-8, C-9), 130.1 (C-3'), 127.9 (C-5'), 114.2, 111.9, 94.1 (arom. C), 55.8 (OCH_3), 48.6 (N^+CH_3), 32.2 (N_1-CH_3); $C_{15}H_{16}IN_3O$(-CH_3I)(239.1057), MS: m/z = 239.1057.

Anal. Calcd. For $C_{15}H_{16}IN_3O$•H_2O: C, 45.13; H, 4.54; N, 10.53. Found: C, 44.79; H, 4.11; N, 10.16.

6-Methoxy-1-methyl-2-(1-methyl)pyridinium-3-yl-1*H*-benzimidazole Iodide (**7Bb**).

This compound was obtained as yellow powder, yield quantitative, mp 225-226°; ir (potassium bromide): 3050 (CH), 1620, 1490 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 9.54 (s, 1H, C2'-H), 9.11 (d, 1H, C6'-H), 9.03 (d, 1H, C4'-H), 8.31 (dd, 1H, C5'-H), 7.65 (s, 1H, C4-H), 7.31 (d, 1H, C7-H), 6.95 (dd, 1H, C5-H), 4.50 (s, 3H, N^+CH_3), 4.02 (s, 3H, N_1-CH_3), 3.88 (s, 3H, OCH_3); ^{13}C nmr (DMSO-d_6): δ 157.2 (C-6), 145.8 (C-6'), 145.4 (C-2), 145.3 (C-2'), 144.0 (C-4'), 137.9, 136.9 (C-8, C-9), 130.2 (C-5'), 127.9 (C-3'), 120.4, 113.3, 94.1 (arom. C), 56.0 (OCH_3), 48.6 (N^+CH_3), 32.2 (N_1-CH_3); $C_{15}H_{16}IN_3O$(-CH_3I)(239.1057), MS: m/z = 239.1055.

Anal. Calcd. For $C_{15}H_{16}IN_3O•2H_2O$: C, 43.18; H, 4.83; N, 10.07. Found: C, 43.13; H, 4.43; N, 9.73.

5-Chloro-1-methyl-2-(1-methyl)pyridinium-3-yl-1*H*-benzimidazole Iodide (**7Ac**).

This compound was obtained as yellow powder, yield 96 %, mp 243-244°; ir (potassium bromide): 3000 (CH), 1640, 1470 cm^{-1}; ^1H nmr (DMSO-d_6): δ 9.58 (s, 1H, C2'-H), 9.17 (d, 1H, C6'-H), 9.05 (d, 1H, C4'-H), 8.35 (br t, 1H, C5'-H), 7.86 (s, 1H, C4-H), 7.83 (d, 1H, C7-H), 7.45 (d, 1H, C6-H), 4.51 (s, 3H, N^+CH_3), 4.04 (s, 3H, N_1-CH_3); ^{13}C nmr (DMSO-d_6): δ 148.4 (C-2), 146.1 (C-6'), 145.9 (C-2'), 144.7 (C-4'), 143.8, 135.2 (C-9, C-8), 129.7 (C-3'), 128.0 (C-5), 127.5 (C-5'), 124.2, 119.1, 113.1 (arom. C), 48.7 (N^+CH_3), 32.4 (s, 3H, N_1-CH_3); $C_{14}H_{13}N_3ClI$-(-CH_3I)(243.0563), MS: m/z = 243.0558.

Anal. Calcd. For $C_{14}H_{13}N_3ClI•1/2H_2O$: C, 42.61; H, 3.58; N, 10.65. Found: C, 42.79; H, 3.35; N, 10.54.

6-Chloro-1-methyl-2-(1-methyl)pyridinium-3-yl-1*H*-benzimidazole Iodide (**7Bc**).

This compound was obtained as yellow powder, yield 86 %, mp 236-237°; ir (potassium bromide): 3050 (CH), 1650, 1450 cm^{-1}; ^1H nmr (DMSO-d_6): δ 9.58 (s, 1H, C2'-H), 9.17 (d, 1H, C6'-H), 9.05 (d, 1H, C4'-H), 8.36 (br t, 1H, C5'-H), 7.97 (s, 1H, C7-H), 7.80 (d, 1H, C4-H), 7.36 (d, 1H, C5-H), 4.50 (s, 3H, N^+CH_3), 4.03 (s, 3H, N_1-CH_3); ^{13}C nmr (DMSO-d_6): δ 148.2 (C-2), 146.2 (C-6'), 146.1 (C-2'), 144.7 (C-4'), 141.3, 137.8 (C-9, C-8), 129.6 (C-3'), 128.6 (C-5'), 128.2 (C-6), 123.7, 121.3, 111.8 (arom. C), 48.8 (N^+CH_3), 32.5 (s, 3H, N_1-CH_3); $C_{14}H_{13}N_3ClI$-(-CH_3I)(243.0563), MS: m/z = 243.0564.

Anal. Calcd. For $C_{14}H_{13}N_3ClI•1/2H_2O$: C, 42.61; H, 3.58; N, 10.65. Found: C, 42.70; H, 3.35; N, 10.44.

1-Methyl-5/6-nitro-2-(1-methyl)pyridinium-3-yl-1*H*-benzimidazole Iodide (**7ABd**).

This compound was obtained as yellow powder, yield 76 %, mp 258-261°; ir (potassium bromide): 3150 (CH), 1520, 1490 cm^{-1}; ^1H nmr (DMSO-d_6): δ 9.63, 9.62 (2xs, 2H, C2'-H), 9.23, 9.21 (2xbr d, 2H, C6'-H), 9.09 (m, 2H, C4'-H), 8.83, 8.66 (2xd, 2H, C4-H/C7-H), 8.39 (m, 2H, C5'-H), 8.31, 8.23 (2xdd, 2H, C5-H/C6-H), 8.04, 7.99 (2xd, 2H, C7-H/C4-H), 4.52 (s, 6H, N^+CH_3), 4.15, 4.10 (2xs, 6H, N_1-CH_3); ^{13}C nmr (DMSO-d_6): δ 151.9, 151.1 (C-2), 146.8, 146.7, 146.4, 146.3, 145.2, 145.1, 143.8, 143.7, 142.3, 141.4, 141.0, 136.3 (C-2', C-4', C-5, C-5', C-6, C-6', C-8, C-9), 129.1, 128.1 (C-3', C-5), 120.2, 119.2, 118.4, 115.9, 112.4, 108.9 (arom. C), 48.7 (N^+CH_3), 32.7 (s, 3H, N_1-CH_3); $C_{14}H_{13}IN_4O_2$(-CH_3I)(254.0804), MS: m/z = 254.0809.

Anal. Calcd. For $C_{14}H_{13}IN_4O_2·1/2H_2O$: C, 41.50; H, 3.48; N, 13.83. Found: C, 41.86; H, 3.31; N, 13.62.

General Procedure for Preparation of (**8a-d**).

The reduction of compounds (**7a-d**) was prepared following the procedure described for 1-methyl-1,2,5,6-tetrahydropyridin-3-ylbenzimidazoles (**5a-d**).

1-Methyl-2-(1-methyl-1,2,5,6-tetrahydropyridin-3-yl)-1*H*-benzimidazole (**8a**).

This compound was obtained as yellow powder, yield 63 %, mp 84-85°; ir (potassium bromide): 2950 (CH), 1645, 1450 cm^{-1}; ^1H nmr (CD_3OD): δ 7.62-7.22 (m, 4H, arom. H), 6.38 (m, 1H, C4'-H), 3.84 (s, 3H, N_1-CH_3), 3.46 (br s, 2H, C2'-H), 2.75 (t, 2H, C6'-H), 2.53 (m, 2H, C5'-H), 2.49 (s, 3H, NCH_3); ^{13}C nmr (CD_3OD): δ 153.5 (C-2), 143.0, 137.6 (C-8, C-9), 133.0 (C-4'), 127.5 (C-3'), 124.5, 124.0, 119.7, 111.5 (arom. C), 56.2 (C-2'), 52.1 (C-6'), 45.8 (NCH_3), 32.4 (N_1-CH_3), 27.0 (C-5'); $C_{14}H_{17}N_3$(227.1422), MS: m/z = 227.1427.

Anal. Calcd. For $C_{14}H_{17}N_3•(CO_2H)_2•1/2H_2O$: C, 58.89; H, 6.18; N, 12.88. Found: C, 58.61; H, 5.92; N, 12.56.

5-Methoxy-1-methyl-2-(1-methyl-1,2,5,6-tetrahydropyridin-3-yl)-1*H*-benzimidazole (**8Ab**).

This compound was obtained as yellow powder, yield 61 %, mp 91-93°; ir (potassium bromide): 2950 (CH), 1630, 1450 cm^{-1}; ^1H nmr (CD_3OD): δ 7.34 (d, 1H, C7-H, *J* = 8.9 Hz), 7.11 (d, 1H, C4-H, *J* = 2.3 Hz), 6.93 (dd, 1H, C6-H, *J* = 2.3 Hz, 8.9 Hz), 6.34 (m, 1H, C4'-H), 3.82, 3.81 (2xs, 6H, OCH_3, N_1-CH_3), 3.43 (ABq, 2H, C2'-H), 2.72 (t, 2H, C6'-H), 2.51 (m, 2H, C5'-H), 2.49 (s, 3H, NCH_3); ^{13}C nmr (CD_3OD): δ 158.4 (C-5), 153.6 (C-2), 143.8, 132.2 (C-8, C-9), 132.6 (C-4'), 127.7 (C-3'), 114.5, 112.0, 101.9 (arom. C), 56.6 (C-2'), 56.4 (OCH_3), 52.2 (C-6'), 45.8 (NCH_3), 32.4 (N_1-CH_3), 27.1 (C-5'); $C_{15}H_{19}N_3O$(257.1528), MS: m/z = 257.1526.

Anal. Calcd. For $C_{15}H_{19}N_3O•(CO_2H)_2•1/2H_2O$: C, 57.29; H, 6.22; N, 11.79. Found: C, 57.19; H, 5.93; N, 11.67.

6-Methoxy-1-methyl-2-(1-methyl-1,2,5,6-tetrahydropyridin-3-yl)-1*H*-benzimidazole (**8Bb**).

This compound was obtained as pale yellow powder, yield 60 %, mp 99-100°; ir (potassium bromide): 3920 (CH), 1745, 1630 cm^{-1}; ^1H nmr (CD_3OD + $CDCl_3$): δ 7.48 (d, 1H, C4-H, *J* = 8.9 Hz), 7.00 (d, 1H, C7-H, *J* = 2.2 Hz), 6.88 (dd, 1H, C5-H, *J* = 2.2 Hz, 8.9 Hz), 6.36 (m, 1H, C4'-H), 3.87, 3.82 (2xs, 6H, OCH_3, N_1-CH_3), 3.47 (br s, 2H, C2'-H), 2.77 (t, 2H, C6'-H), 2.55 (m, 2H, C5'-H), 2.52 (s, 3H, NCH_3); ^{13}C nmr (CD_3OD + $CDCl_3$): δ 158.5 (C-5), 152.2 (C-2), 138.0, 137.0 (C-8, C-9), 131.7(C-4'), 127.0 (C-3'), 120.0, 113.3, 94.3 (arom. C), 56.2 (C-2', OCH_3), 51.8 (C-6'), 45.4 (NCH_3), 32.2 (N_1-CH_3), 26.6 (C-5'); $C_{15}H_{19}N_3O$(257.1528), MS: m/z = 257.1525.

Anal. Calcd. For $C_{15}H_{19}N_3O·(CO_2H)_2·1/2H_2O$: C, 57.29; H, 6.22; N, 11.79. Found: C, 56.91; H, 5.93; N, 11.59.

5-Chloro-1-methyl-2-(1-methyl-1,2,5,6-tetrahydropyridin-3-yl)-1*H*-benzimidazole (**8Ac**).

This compound was obtained as pale yellow powder, yield 73 %, mp 113-116°; ir (potassium bromide): 3080 (CH), 1660, 1500 cm^{-1}; ^1H nmr (CD_3OD): δ 7.58 (d, 1H, C4-H, *J* = 2.3 Hz), 7.47 (d, 1H, C7-H, *J* = 8.9 Hz), 7.28 (dd, 1H, C6-H, *J* = 2.3 Hz, 8.9 Hz), 6.45 (m, 1H, C4'-H), 3.87 (s, 3H, N_1-CH_3), 3.51 (ABq, 2H, C2'-H), 2.80 (t, 2H, C6'-H), 2.56 (m, 2H, C5'-H), 2.55 (s, 3H, NCH_3); ^{13}C nmr (CD_3OD): δ 154.8 (C-2), 143.8, 136.4 (C-8, C-9), 133.6 (C-4'), 129.6 (C-3'), 127.0 (C-5) 124.8, 119.3, 112.8 (arom. C), 56.3 (C-2'), 52.0 (C-6'), 45.6 (NCH_3), 32.7 (N_1-CH_3), 26.0 (C-5'); $C_{14}H_{16}ClN_3$(261.1033), MS: m/z = 261.1028.

Anal. Calcd. For $C_{14}H_{16}ClN_3•(CO_2H)_2$: C, 54.63; H, 5.16; N, 11.94. Found: C, 54.53; H, 5.17; N, 11.68.

6-Chloro-1-methyl-2-(1-methyl-1,2,5,6-tetrahydropyridin-3-yl)-1*H*-benzimidazole (**8Bc**).

This compound was obtained as white powder, yield 69 %, mp 89-90°; ir (potassium bromide): 3020 (CH), 1640, 1460 cm^{-1}; ^1H nmr (CD_3OD): δ 7.57-7.54 (m, 2H, C4-H, C7-H), 7.23 (dd, 1H, C5-H), 6.41 (m, 1H, C4'-H), 3.83 (s, 3H, N_1-CH_3), 3.41 (br s, 2H,

C2'-H), 2.70 (t, 2H, C6'-H), 2.52 (m, 2H, C5'-H), 2.48 (s, 3H, NCH_3); ^{13}C nmr (CD_3OD): δ 154.5 (C-2), 141.5, 138.1 (C-8, C-9), 133.2 (C-4'), 129.9 (C-3'), 127.3 (C-6), 124.2, 120.5, 111.5 (arom. C), 56.3 (C-2'), 52.0 (C-6'), 45.6 (NCH_3), 32.4 (N_1-CH_3), 26.9 (C-5'); $C_{14}H_{16}ClN_3$(261.1033) MS: m/z = 261.1027.

Anal. Calcd. For $C_{14}H_{16}ClN_3 \bullet (CO_2H)_2$: C, 54.63; H, 5.16; N, 11.94. Found: C, 54.44; H, 5.16; N, 11.55.

5/6-Nitro-1-methyl-2-(1-methyl-1,2,5,6-tetrahydropyridin-3-yl)-1*H*-benzimidazole (**8ABd**).

This compound was obtained as pale yellow powder, yield 50 %, mp 114-116°; ir (potassium bromide): 2930 (CH), 1525, 1455 cm^{-1}; ^1H nmr (CD_3OD): δ 8.40, 8.38 (2xd, 2H, C4-H/C7-H), 8.15, 8.11 (2xdd, 2H, C5-H/C6-H), 7.66, 7.61 (2xd, 2H, C7-H/C4-H), 6.52 (m, 2H, C4'-H), 3.93, 3.92 (2xs, 6H, N_1-CH_3), 3.46 (br s, 4H, C2'-H), 2.73 (t, 4H, C6'-H), 2.57 (m, 4H, C5'-H), 2.56 (s, 6H, NCH_3); ^{13}C nmr (CD_3OD): δ 157.5 (C-2), 145.3, 135.1 (C-8, C-9), 142.4, 141.8 (C-5, C-6), 134.6 (C-4'), 127.3 (C-3'), 119.9, 119.8, 119.4, 116.0, 112.0 (arom. C), 56.4 (C-2'), 52.0 (C-6'), 45.8 (NCH_3), 33.0 (N_1-CH_3), 27.2 (C-5'); $C_{14}H_{16}N_4O_2$(272.1273) MS: m/z = 272.1269.

Anal. Calcd. For $C_{14}H_{16}N_4O_2 \cdot (CO_2H)_2 \cdot 1/2H_2O$: C, 51.75; H, 5.16; N, 15.09. Found: C, 52.04; H, 4.94; N, 14.81.

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