International Journal of ChemTech Research
CODEN(USA): IJCRGG ISSN : 0974-4290
Vol.2, No.2, pp 1020-1025, April-June 2010

Synthesis and Characterization of 2-(α-p -Substituted phenyl-α-benzimidazolo) methyl -1,2,3,4-tetrazoles

P.Jeyanthi[1*] and P.Pazhanisamy[2]

[1]Department of Chemistry, Bharathi Women's College, Chennai-600108,India

[2]Department of Chemistry, Sir Theagaraya College, Chennai - 600021,India

[*]*Corres.author: jeyanthibwc@gmail.com*

Abstract: A series of 2-(α-p -Substituted phenyl-α-benzimidazolo) methyl -1,2,3,4-tetrazoles (1b-5b) were synthesized by the reaction of 2-p-substituted phenyl-2-benzimidazolo acetonitriles(1a-5a), sodium azide ammonium chloride in DMF . The 2-p-substituted phenyl-2-benzimidazolo acetonitriles (1a-5a) were prepared by the reaction of benzimidazole , p-substituted benzaldehydes and Sodium cyanide.. These compounds were characterized by IR , NMR and Mass spectroscopy.

Key words: Benzimidazole, tetrazoles , acetonitrile, sodium azide.

Introduction

The importance of imidazoline and benzimidazloes, units arises, because they are found in many biologically active compounds[1-5]. In addition, the benzimidazole moiety is found in various synthetic pharmaceuticals displaying a broad spectrum of biological activity including anti-ulcer, anti-tumor and anti-viral effects[6-9].

Almost all benzimidazole derivatives with their two ring systems bear different functional substituent and this leads to essential modification of the physico-chemical, metabolic and pharmacokinetic properties of these drugs. Tissue selectivity of this type of antiulcer drugs is based on both their pH dependent accumulation, as weak bases in the acidic compartment of secreting parietal cell, and the subsequent acid-induced rearrangement of the parent compound to the pharmacologically active principle[10]

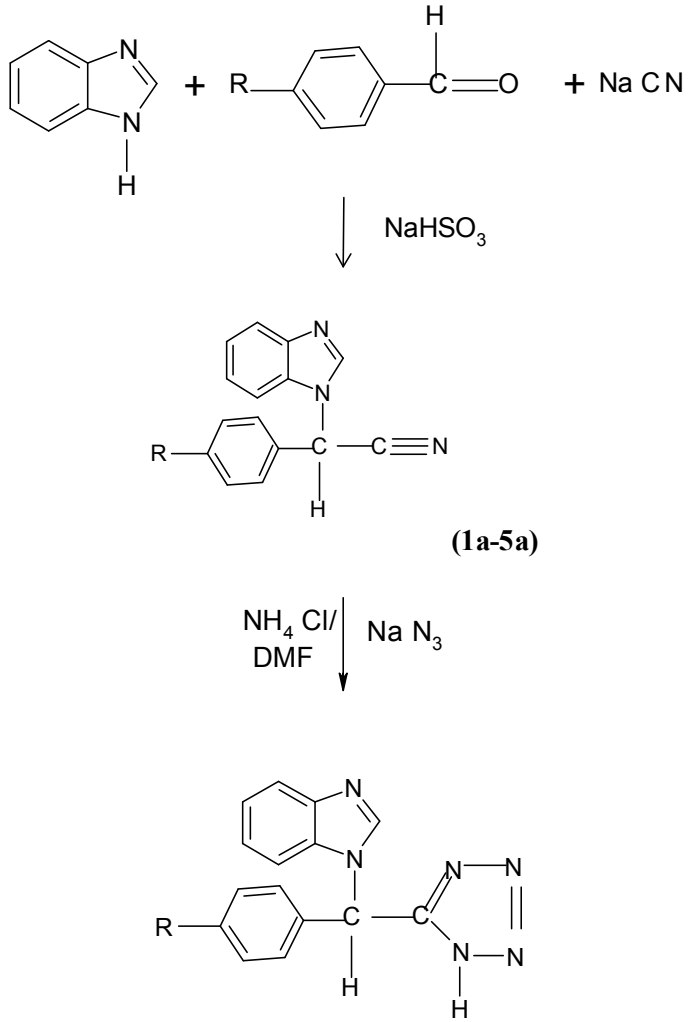
A series of benzimidazole derivatives have proven anti-ulcer activity as potential inhibitors of H^+/K^+-ATPase. Therapeutic significance of these clinically useful drugs in treatment of peptic ulcer and associated gastrointestinal diseases encouraged the development of some more potent and significant compounds [11].

These observations inspired us to synthesize the 2-(α-p -Substituted phenyl-α-benzimidazolo) methyl-1,2,3,4-tetrazoles.

Experimental

Melting points were determined in open capillary tubes and are uncorrected. IR spectra (K Br) were recorded on a Perkin Elmer 1800(FTIR) spectrometer. PMR spectra (DMSO- d6) on a Varian EM-390 spectrometer using TMS as an internal standard (chemical shift in δ ppm). Mass spectra were recorded on a Jeol JMS-D 300 Mass spectrometer operating at 70 eV. The purity of the compounds was confirmed by TLC using silica gel G. For TLC, Merck silica gel 60 G plate was used. The necessary chemicals were obtained from Merck and Fluka. All compounds showed satisfactory elemental analyses.

Scheme-1: **Synthesis of 2-(α-p -Substituted phenyl-α-benzimidazolo) methyl -1,2,3,4-tetrazoles(1b-5b)**



R = H , CI , OCH_3 ,OH, -N –$(CH_3)_2$

1. Synthesis of 2-p-substituted phenyl-2-benzimidazoloacetonitriles (1a-5a)

1.1. Synthesis of of 2-benzimidazolo-2-phenyl acetonitrile (1a)

To a stirred solution of sodiumbisulphite (4.16 g ; 0.04 mol) in 10 mL of water benzaldehyde (4.24 g; 0.04 mol) was added and then benzimidazole (4.72 g; 0.04 mol) was added. The reaction mixture was stirred for 30 minutes and cooled in ice bath. A solution containing 1.96g (0.04 mol) of sodium cyanide was added dropwise into it . After 10 h the product was separated and filtered . The crude was recrystallized from chloroform-petroleum ether mixture. The pure sample melted at 183-184 ^{0}C.

1.2. Synthesis of 2-p-chlorophenyl-2-benzimidazolo acetonitrile(2a)

The 2-p-chlorophenyl-2-benzimidazolo acetonitrile (2a) was prepared by the reaction of p-chlorobenzaldehyde and benzimidazole in presence of NaH SO_4 as described above. The crude was

recrystallized from chloroform-petroleum ether mixture .The pure sample melted at 158-159 ^{0}C.

1.3. Synthesis of 2-p-hydroxyphenyl-2-benz imidazoloacetonitrile(3a)

The 2-p-hydroxyphenyl-2-benzimidazolo acetonitrile (3a) was synthesized by the reaction of p-hydroxybenzaldehyde and benzimidazole. The crude was recrystallized from benzene-petroleum ether mixture . The pure compound melted at 192-193 ^{0}C.

1.4. Synthesis of 2-p –N, N'-Dimethylanilino -2-benzimidazoloacetonitrile(4a)

The 2-p –N, N'-dimethylanilino -2-benz imidazoloacetonitrile(4a) was synthesized by the reaction of p –N, N'-dimethylaminobenzaldehyde and benzimidazole. The crude was recrystallized from benzene-petroleum ether mixture . The pure compound melted at 137-138 ^{0}C.

1.5. Synthesis of 2--p-Anisyl-2-benzimidazolo acetonitrile (5a)

2-p-Anisyl-2-benzimidazoloacetonitrile (5a) was synthesized by using p-Anisaldehyde. The crude was recrystallized from benzene and the pure compound melted at 163-164 ^{0}C.

2. Synthesis of 2-(α-p -Substituted phenyl-α-benzimidazolo) methyl-1,2,3,4-tetrazoles (1b-5b)

2.1. Synthesis of 2-(α-Benzimidazolo-α-phenyl) methyl -1,2,3,4-tetrazole

A mixture of 2-benzimidazolo-2-phenylacetonitrile (4.66g; 0.02mol) and Sodium azide (2.0 g; 0.02 mol) and Ammonium chloride (10.6 g; 0.2 mol) in 20 mL of DMF was taken in a 100 mL round bottomed flask. The contents were heated for 7 hours in oil bath maintained at 125^{0}C. The contents poured in ice water and acidified with HCl at pH is 2. .The tetrazole was filtered, washed with excess of water and dried. It was recrystallized from benzene . The pure sample melting at 156 ^{0}C.

Infra Red Spectral Data (KBr), λ values in cm $^{-1}$

3429 (m) 3366(m) 3181 (m) 3116(m) 2950 (w) 2924 (w) 2853 (m) 2050(m) 1920 (m) 1816 (m) 1799 (s)1750 (s) 1700 (m) 1665 (w) 1568 (s) 1477 (s) 1291 (m) 1266 (m) 1240 (m) 1169(m) 1100(s) 1066 (w) 1025 (w) 966 (m) 928 (w) 852 (m) 755(s) 683 (w) 613 (w) 569 (m) 447(w)

Proton Magnetic Resonance Spectral Data (CDCI3 / TMS), δ in ppm

4.6	s	1H	C-H methine
7.1-7.3	m	13H	Aromatic protons
8.1	s	1H	C –H benzimidazole

Mass Spectral Values ; m/z and %

325 (30) 324 (25) 297 (6) 284 (24) 248 (40) 235(42) 233 (28) 208 (20)

206 (100) 205 (65) 158 (48) 156 (32) 131 (15) 192 (32) 128 (10) 118 (10) 117

(50) 116 (20) 92 (45) 91 (35) 90 (55) 89 (20)63 (28)

Elemental Analysis		**C %**	**H%**
C_{21} H $_{15}$ N_3 Calculated	:	77 .53	4.61
M.W . 325 found	:	77.10	4.52

2.2. 2-(α-p Chlorophenyl -α – benzimidazolo) methyl -1,2,3,4-tetrazole (2b)

The 2-(α-p Chlorophenyl -α – benzimidazolo) methyl -1,2,3,4-tetrazole (2b) was prepared by the same procedure as mentioned above. The crude was recrystallized in methanol and the pure compound melted at 127 ^{0}C.

Infra Red Spectral Data (KBr), λ values in cm $^{-1}$

3432(m) 3036 (m) 2924 (w) 2853 (w) 2750 (w) 2699 (w) 2432 (w) 2366 (m) 1715 (m) 1649 (m) 1588 (w) 1571 (s) 1520 (w) 1480 (s) 1400 (m) 1366(w) 1289 (s) 1215(m) 1177(m) 1140(m) 1100(m) 1090 (w) 1023 (w) 930(w) 855(s) 755(s) 666(m) 632(m) 574(s) 453(w)

Proton Magnetic Resonance Spectral Data (CDCI3 / TMS), δ in ppm

4.3	s	1H	C-H methine
6.7-7.2	m	12H	Aromatic protons
8.1	s	1H	C –H benzimidazole

Mass Spectral Values ; m/z and %

360(25) 359(10) 319 (8) 285 (12) 270 (60) 268 (30) 257 (5) 248(35) 243(100) 241 (20) 236 (16) 230 (5) 229 (48) 228 (10) 213 (12) 203(25) 158

(55) 156(42) 130(38) 124(45) 119(60) 118 (18) 117 (8) 112(15) 92 (30) 91(45) 90 (65) 63 (28)

Elemental Analysis C % H%

C_{21} H $_{14}$ N_3 CI Calculated : 70.09 3.89

M.W . 359 found : 70.00 3.75

2.3. 2-(α-p Hydroxyphenyl -α – benzimidazolo) methyl -1,2,3,4- tetrazole(3b)

It was recrystallized from benzene and the compound melting at 150 ^{0}C .

Infra Red Spectral Data (KBr), λ values in cm $^{-1}$

3775(w) 3448 (w) 3083 (m) 2924 (m) 2854 (m) 2743 (s) 2666(w) 2583 (w) 1833(w) 1699 (s) 1632 (w) 1571 (s) 1472 (s) 1420 (s) 1410 (w) 1393 (m) 1301 (m) 1288 (m) 1250 (s) 1203 (w) 1168 (w) 1135 (w) 1049 (w) 1023 (w) 928 (w) 852 (m) 756 (m) 615 (w) 570 (m) 449 (w)

Proton Magnetic Resonance Spectral Data (CDCI3 / TMS), δ in ppm

4.6	s	1H	C-H methine
6.7 -7.3	m	12H	Aromatic protons
7.8	s	1H	- OH phenolic
8.1	s	1H	C –H benzimidazole

Mass Spectral Values ; m/z and %

343 (20) 342 (10) 341 (25) 324 (18) 323 (40) 297 (12) 286 (15) 256 (8) 248 (100) 236 (16) 224 (65) 222(20) 205 (28) 180 (10) 178 (24) 168 (25) 158(24) 156 (36) 150 (30) 149 (6) 132 (12) 131 (20) 127 (18) 120 (40) 119 (45) 118 (60) 117 (30) 105(15) 92 (35) 91 (10) 90(28) 63 (44)

Elemental Analysis C% H%

C_{21} H $_{15}$ N_3 O_2 Calculated : 73.9 4.39

M.W . 341 found : 72.5 4.23

2.4. 2-(α-p –N, N'-Dimethylanilino -α – benzimidazolo) methyl -1,2,3,4-tetrazole(4b)

It was recrystallized from benzene –petroleum ether mixture. The pure sample melted at 106^{0}C.

Infra Red Spectral Data (KBr), λ values in cm $^{-1}$

3416 (m) 3382(w) 3066(m) 2925 (w) 2852 (w) 2500 (m) 1850 (w) 1750 (w) 1670 (m) 1620 (s) 1603 (w) 1589 (w) 1516 (m) 1466 (w) 1420(m) 1409 (s) 1356(m) 1232 (w) 1177 (m) 1123 (w) 1059 (w) 1019(w) 944 (m) 866 (w) 813 (w) 742 (s) 700 (w) 616 (w)566(w)

Proton Magnetic Resonance Spectral Data (CDCI3 / TMS), δ in ppm

2.9	s	6H	-N -(CH_3) $_2$
4.6	s	1H	C-H methine
6.7 -7.7	m	12H	Aromatic protons
8.1	s	1H	C –H benzimidazole

Mass Spectral Values ; m/z and %

368 (30) 367 (50) 324 (48) 278(45) 276 (25) 251 (20) 249(40)248 (30) 247 (12) 207 (15) 205 (20) 161(20) 159(25) 156 (40) 131 (35) 129 (15) 120 (30) 119 (60) 118 (100) 117 (15) 92(35) 91(22) 63 (40)

Elemental Analysis C % H%

C_{23} H $_{20}$ N_4 O Calculated : 75.00 5.4

M.W . 368 found : 74.9 5.2

2.5. Synthesis of 2-(α-p Anisyl-α – benzimidazolo) methyl -1,2,3,4-tetrazole (5b)

It was recrystallised from benzene. The pure sample melting at 139^{0}C.

Infra Red Spectral Data (KBr), λ values in cm $^{-1}$

3416 (m) 3376 (m) 3066(w) 2949 (w) 2925 (m)2853 (m) 2799 (w) 2449 (w) 1783 (m) 1742 (s) 1620 (s) 1580 (s) 1480(s) 1397 (w) 1295 (m) 1252 (s) 1172(m) 1132 (w) 1026 (m) 926 (w) 850 (w) 831(w) 753 (m) 704 (w) 634(w) 567 (m) 450(m)

Proton Magnetic Resonance Spectral Data (CDCI3 / TMS), δ in ppm

3.9	s	3H	-OCH_3
4.6	s	1H	C-H methine

6.7 -7.7 m 12H Aromatic protons

8.0 s 1H C –H benzimidazole

Mass Spectral Values ; m/z and %

355 (40) 354 (18) 324 (28) 285 (12) 265 (35) 263 (42) 248 (36)238 (55) 236(45) 158 (40) 156 (20) 146(25) 144(16) 129 (38) 119 (20) 118 (28) 117 (30) 107(18) 92 (50) 91 (100) 90(28) 63 (35)

Elemental Analysis **C%** **H%**
C_{22} H $_{17}$ N_3 O Calculate : 74.36 4.78
M.W . 355 found : 73.52 4.52

Results and Discussion

The formation of 2-p-substituted phenyl-2-benzimidazolo acetonitriles (1a-5a) was confirmed by spectral values of IR and NMR and are presented in **Table 1**. In the present study, 2-(α-p -Substituted phenyl-α-benzimidazolo) methyl -1,2,3,4-tetrazoles were synthesized by condensation of 2 -benzimidazolo -2- phenylacetonitrile(1a) and other nitriles (2a-5a) with sodium azide in the presence of hydrochloric acid . The synthetic route of these compounds were represented as **Scheme-I.**

Table 1: Spectral data of the compounds (1a-5a)

Sample No	**IR (KBr) cm $^{-1}$ (Nitriles)**	**^{1} H-NMR ($CDCl_3$) δ ppm**
1a	2230	4.6(S,1H, -CH methine),7.0-7.4 (m,9H,Ar-H), 8.2(s,1H,C-H, Benzimidazole)
2a	2240	4.6(s,1H, -CH methine),7.0-7.4 (m,8H,Ar –H), 8.2(s,1H,C-H, Benzimidazole)
3a	2220	4.6(S,1H, -CH methine),6..6-7.4 (m,8H,Ar-H),7.8, (S, 1H,OH Phenolic),8.1(s,1H,C-H, Benzimidazole)
4a	2240	3.0 (s,6H-N -(CH_3) $_2$) 4.6(s,1H, -CH methine), 6.6-7.3(m,8H,Ar-H),8.2(s,1H,C-H, Benzimidazole)
5a	2232	3.9(s,3H, - CH_3 anisyl) 4.6(s,1H, -CH methine), 7.0-7.4 (m,8H,Ar-H),8.2(s,1H,C-H, Benzimidazole)

References

1. Grimmett M R, In *Comprehensive Heterocyclic Chemistry,* Katcizky A R, Rees C W, Scriven E F V, Eds, Pergamon: Oxford,1996, **3 ,** 77-220 .
2. Greenhill J V, Lue L, *In Progress in Medicinal Chemistry,* Ellis G P, Luscombe D K, Eds, Elsevier: New York, 1993,**3**, 170-180.
3. Preston P N, *Chem. Rev.*1974*,* **74,** 179-314 .
4. Touzeau F, Arrault A, Guillaumet G, Scalbert E, Pfeiffer B, Rettori M C, Renard P and Merour J Y *J. Med.Chem.*.2003, **46,** 1962-1979 .
5. Roundu F, Bihan G L, Wang X, Lamouri A, Touboul E, Dive G, Bellahsene T,Pfeiffer B, Renard P, Guardiola- Lemaitre B, Maneche D,Penicaud L, Ktorza A and Godfroid J J, *J. Med. Chem.*1997, **40,** 3793-3803.
6. Preston P N, Stevens M F G and Tennant G *Benzimidazoles and Congeneric Tricyclic Compounds*, Part 2, John Wiley & Sons: New York , 1980.
7. Cedillo-River R and Munoz O *J. Med. Microbiol,*1992, **37**, 221-224 .
8. Chavez B, Cedillo-Rivera R and Martiner-Palomo A *J. Protozool,*1992, **39**, 510-515.
9. Navarrete-Vazquez G, Cedillo R, Hernandez-Campos A, Yepez L, Hernandez-Luis F, Valdez J, Morales R Cortes R Hernandez M and Castillo R *Bioorg. Med. Chem. Lett.* 2001,**11,** 187- 190 .
10. W.Kromer, *Digestion*,1995, **56,** 443-454 .
11. Avinash Pati , Swastika Ganguly and Sanjay Surana , Rasayan J. Chem . 2008,1(.3), 447-460 .
12. Holljes E L, and Wagner E C, J. Org. Chem.,1944, **9**,31 .

*****