Improved Process for the Preparation of Mannich Bases of Benzimidazoles Using Diethoxymethane

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Abstract

Mannich bases are the end products of mannich reaction and are known as beta amino ketone carrying compounds. Mannich reaction is a carbon carbon bond forming nucleophilic addition reaction which helps in synthesizing N-methyl derivatives and many other drug molecules. Mannich base derivatives of benzimidazoles possess many pharmacological properties such as anti-oxidant, anti-inflammatory, anticancer, antiviral, anthelmintic and play an important role in medical field. As these drugs are clinically useful in treatment of microbial infections and exhibit other therapeutic activities also, so this encouraged the development of more potent, novel and clinically significant compounds.

Keywords: Benzimidazoles, Antimicrobial activity, Anti-fungal activity, mannich base, secondary amine

Introduction

Antimicrobial drugs or chemicals are the substances used to kill or slow down the growth of microorganisms. They include antibiotics, antiviral, antifungal and anti-parasitic agents.[1] Antimicrobial chemotherapy has been used from last six decades against infectious diseases caused by a variety of pathogens. Since then, many antimicrobial drugs were discovered, hundreds of drugs using now a days. Anti-microbial drugs are most commonly available today.[2] Since the introduction of penicillin as antibiotics in the control of infectious diseases, frequent use of antimicrobial drugs cause a variety of problems, such as drug resistance, allergic reactions, nutritional loss, toxicity and much more. Almost all of the major categories of antibiotics in the clinical application showed resistance to microorganism specially β- lactam, macrolides, vancomycin and quinolones derived bacterial drug's resistance is a source of concern for healthcare officials. The effective treatment against microbial agents is limiting day by day.[3,4] Many other antimicrobial drugs are toxic too. So, there is a real need to discover new compounds with high efficiency towards pathogens and less toxicity, which may be different from available resistant drugs. This provides a great opportunity to synthetic chemists for the synthesis of such new compounds having lower cytotoxicity and better antimicrobial properties. The biological activity of the compounds depends on structure of molecule.[5] It has been shown that heterocyclic compounds are more biological active as compared to others.[6] Heterocyclic compounds particularly five and six member heterocycles have attracted the attention of pharmaceutical community over the years due to their therapeutic value.[7] Polyfunctionalized heterocyclic compounds containing Nitrogen, sulphur, oxygen as heteroatoms play important roles in the drug discovery process.[8] Benzimidazole is one such compound which attract attention of synthetic chemists for the synthesis of antimicrobial drugs.[9] The benzimidazoles contain a phenyl ring fused with imidazole ring.[10] This compound has various

applications in a number of fields. Benzimidazole contain nucleus plays an important role in various medicines.[11] The role of purines in biological systems is well known and it was discovered that 5, 6-dimethyl-1-(α-Dribofuranosyl)benzimidazole is an important part of Vitamin B 12 structure, which leads a massive research on benzimidazoles especially for the synthesizing new such compounds having biological applications. This stimulated great interest in the structural study of Benzimidazole and related compounds and much success was made in pharmaceutical industry. Some commercially used Benzimidazole based drugs are; azomycin, metronidazole, thiabendazole, benomyl, clemizole, enviroxime, irtemazole, astemizole, omeprazole, pentoprazole, thiabendazole and nocodazole.[12] Benzimidazole undergoes different reactions i.e. electrophilic and nucleophilic addition, electrocyclic reactions and thermal oxidation

In this research the synthesis of mannich bases of benzimidazoles are prepared by using diethoxy methane or dimethoxy methane instead of formaldehyde which used in literature. The active methylene group present in diethoxymethane moiety abstract lone pair of electrons from nitrogen atom of imidazole, as methoxy or ethoxy groups are easily removable groups hence when it attacks secondary amine ethanol or methanol formed as byproduct.

Experimental

The following experimental methods were used for the characterization of the synthesized compounds. The melting points (m.p.) were determined using Gallenkamp melting point apparatus. The IR spectra were recorded in KBr discs on a Perkin Elmer 1000 FT-IR spectrophotometer (υmax in cm-1). The 1H NMR and 13C NMR spectra were collected in DMSO-d6 or ($CDCl_3$)using 400 M Hz . The chemical shifts were reported as parts per million (d ppm) and the coupling constants (J) are given in Hz, tetra methyl silane (TMS) was used as an internal standard. The mass spectra (m/z, %) were obtained on electron impact using an AEI MS902 mass spectrometer. The purity of all compounds was checked by TLC using glass plates coated with silica gel and dichloromethane/methanol (9:1) as a solvent system. Spectral data (IR, NMR, and mass spectra) confirmed the structures of the synthesized compounds.

General procedure for the preparation of benzimidazoles (2a-2h)

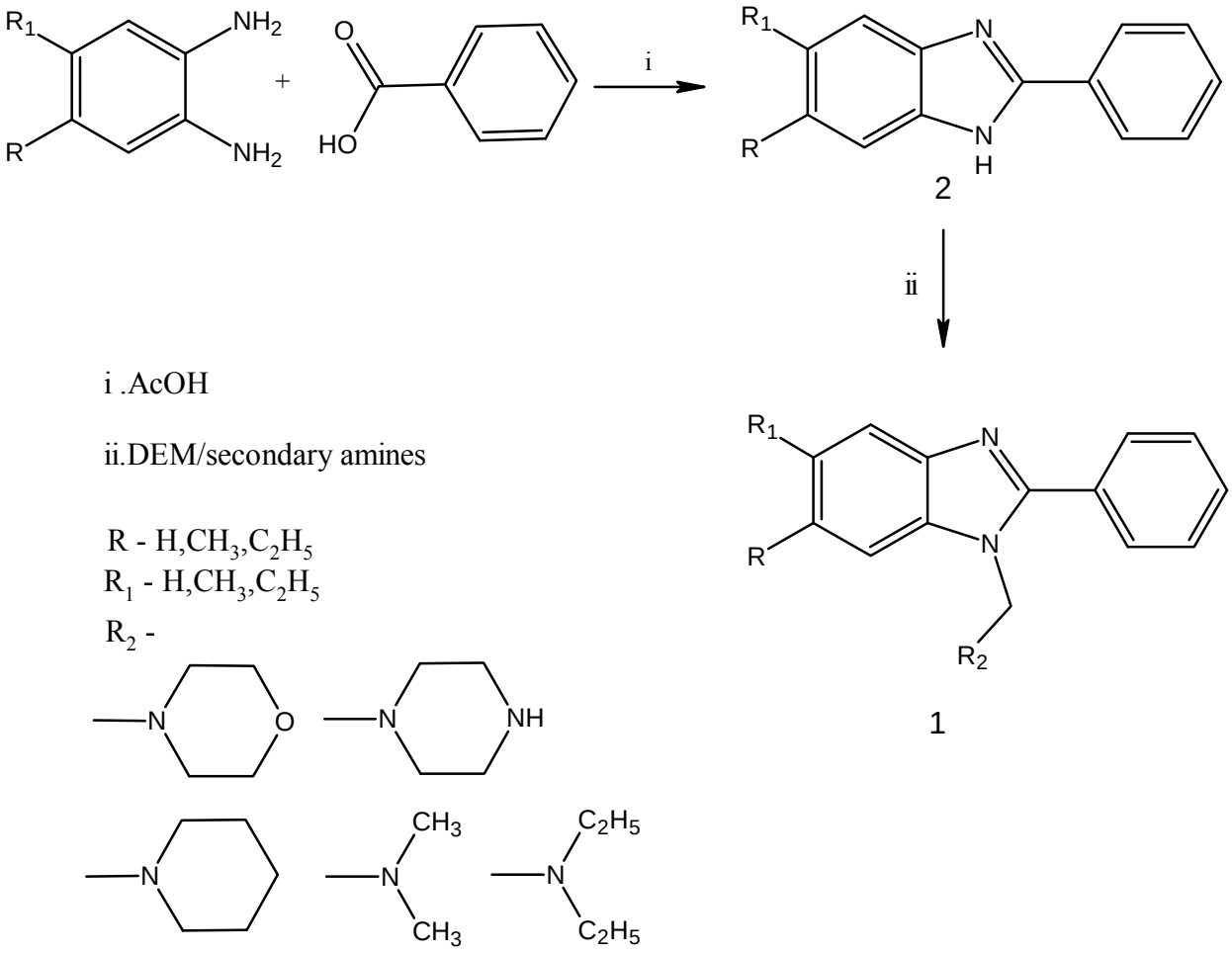
A solution of benzoic acid (0.01 moles) and substitute phenyl diamine (0.01 moles) in 20 ml acetic acid was refluxed for 4-5 hours, after reaction completion, the precipitate obtained after cooling was Recrystalize from methanol.

General procedure for the synthesis of mannich bases (1).

Mannich base were prepared by a solution of substituted benzimidazoles (0.005 moles) in 10 ml ethanol, 0.005 moles secondary amine and 0.05 moles diethoxy methane of dimethoxy methane and then the reaction mixture was refluxed for 8 hours, on cooling, the product formed was filtered, dried and re-crystallized from dimethyl formamide ,specific details given to each compound.

Preparation of Phenylbenzimidazole (1)

Phenyldiamine (20 g, 0.189 moles) and benzoic acid (22.5 g, 0.18 moles) in Acetic acid (50 ml) are refluxed for 4 hours, after reaction completion, the reaction mass was cooled and the obtained precipitate is filtered and Recrystalize from methanol and dried to get title compound (32.3 g, 90%)mp 294°C, ((δH ($CDCl_3$) 12.12 (1H, NH), 8.29 (2H), 7.58 (2H) 7.41 (2H); 7.32 (1H) 7.2 (2H),δC ($CDCl_3$) 151.2 (C=N), 139.14, 132.1, 131.2, 130.2,128.4, 122.1 and 115.; υmax /cm-1 (KBr) 3432 (N-H), 3049 (C-H, sp2), MS (EI): m/z 194.2



SCHEME - I

Preparation of substituted phenylbenzimidazoles (1a-1d)

Below substituted benzimidazoles derivatives are prepared as per above general procedure

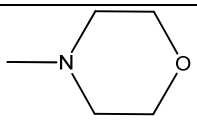
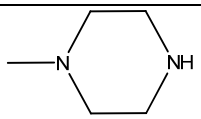
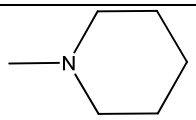
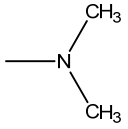
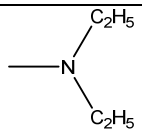
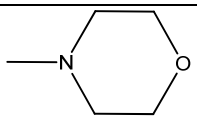
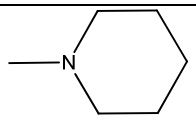
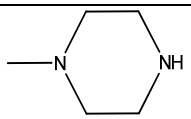
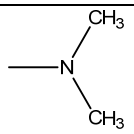
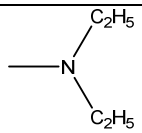
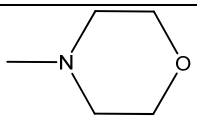
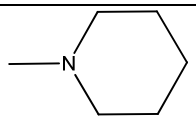
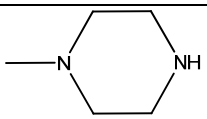
5-Methyl-2-phenyl(1H)benzimidazoles (1a)

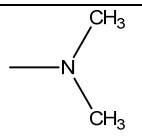
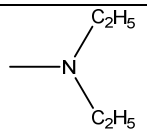
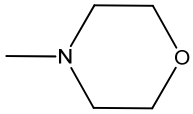
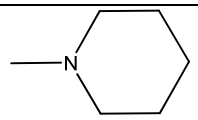
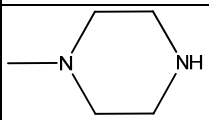
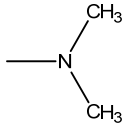
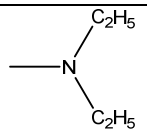
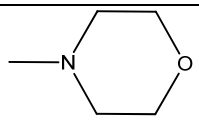
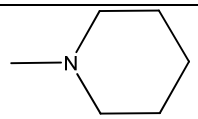
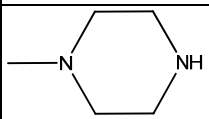
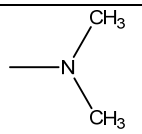
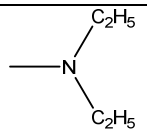
MP 286°C, ((δH ($CDCl_3$) 12.42 (1H, NH), 8.16 (2H), 7.49 (2H) 7.40 (2H); 7.36 (1H) 7.35 (1H), 2.42 (3H) ,δC ($CDCl_3$) 151.2 (C=N), 139.14, 132.1, 131.2, 130.2,128.4, 122.1 and 48.; υmax /cm-1 (KBr) 3396 (N-H), 3058 (C-H, sp2), MS (EI): m/z 208.4

5-ethyl-2-phenyl(1H)benzimidazoles (1b)

MP 279°C, ((δH ($CDCl_3$) 12.16 (1H, NH), 8.16 (2H), 7.49 (2H) 7.40 (2H); 7.36 (1H) 7.35 (1H), 2.42 (2H), 0.96 (3H) ,δC ($CDCl_3$) 151.2 (C=N), 139.14, 132.1, 131.2, 130.2,128.4, 122.1 and 48.; υmax /cm-1 (KBr) 3395 (N-H), 3062 (C-H, sp2), MS (EI): m/z 223.4

Table-1 ;Physico chemical analysis

S.No	Compounds	M.W	R	R_1	R_2	m.p(°C)	yield
2a	$C_{18}H_2N_3O$	293.36	H	H		241-243	80
2b	$C_{18}H_{20}N_4$	292.3	H	H		234-235	78
2c	$C_{19}H_{21}N_3$	291.3	H	H		243-245	85
2d	$C_{16}H_{17}N_3$	251.3	H	H		235-237	89
2e	$C_{18}H_{21}N_3$	279.3	H	H		241-243	93
5f	$C_{19}H_{21}N_3O$	307.3	H	CH3		236-238	92
2g	$C_{20}H_{23}N_3$	305.4	H	CH3		245-246	89
2h	$C_{19}H_{22}N_4$	306.4	H	CH3		234-235	94
2i	$C_{17}H_{19}N_3$	265.3	H	CH3		214-215	92
2j	$C_{19}H_{23}N_3$	293.40	H	CH3		240-241	94
2k	$C_{20}H_{23}N_3O$	321.4	H	C_2H_5		223-224	87
2l	$C_{22}H_{25}N_3$	319.4	H	C_2H_5		235-236	85
2m	$C_{20}H_{24}N_4$	320.43	H	C_2H_5		241-242	87

S.No	Compounds	M.W	R	R_1	R_2	m.p(°C)	yield
2n	$C_{18}H_{21}N_3$	279.3	H	C_2H_5		238-239	88
2o	$C_{20}H_{25}N_3$	307.4	H	C_2H_5		218-219	85
2p	$C_{22}H_{27}N_3O$	349.4	C_2H_5	C_2H_5		223-224	84
2q	$C_{23}H_{29}N_3$	347.4	C_2H_5	C_2H_5		221-222	83
2r	$C_{22}H_{28}N_4$	348.4	C_2H_5	C_2H_5		235-236	82
2s	$C_{20}H_{25}N_3$	307	C_2H_5	C_2H_5		228-229	85
2t	$C_{22}H_{29}N_3$	335.4	C_2H_5	C_2H_5		235-236	87
2u	$C_{20}H_{23}N_3O$	321.4	CH3	CH3		235-236	85
2v	$C_{21}H_{25}N_3$	319.4	CH3	CH3		246-247	89
2w	$C_{20}H_{24}N_4$	320.4	CH3	CH3		235-236	85
2x	$C_{18}H_{21}N_3$	279.3	CH3	CH3		223-224	84
2y	$C_{20}H_{25}N_3$	307.4	CH3	CH3		236-237	85

5,6-diethyl-2-phenyl(1H)benzimidazoles (1c)

Mp269°C, ((δH ($CDCl_3$) 11.9 (1H, NH), 8.42 (2H), 7.94 (2H),7.49 (2H) 7.32 (1H); 7.36 (1H) , 2.62 (4H), 1.2 (6H) ,δC ($CDCl_3$) 151.2 (C=N), 140.14, 132.1, 131.2, 130.2,128.4, 122.1 25.2and 14.; υmax /cm-1 (KBr) 3395 (N-H), 3062 (C-H, sp2), MS (EI): m/z 250.4

5,6-dimethyl-2-phenyl(1H)benzimidazoles (1d)

mp 272°C, ((δH ($CDCl_3$) 12.1 (1H, NH), 8.46 (2H), 7.51 (2H) 7.41 (2H); 7.36(1H) , 2.32 (6H) ,δC ($CDCl_3$) 151.4 (C=N), 139.14, 132.1, 131.2, 130.2,128.4, 122.1 and 22.2.; υmax /cm-1 (KBr) 3394 (N-H), 3052 (C-H, sp2), MS (EI): m/z 222.4

II. Preparation of Mannich base from benzimidiazole using dimethoxy methane/diethoxy methane

1-[(morpholin-4-yl)methyl]-2-phenyl-1H-benzimidazole (2a)

Phenylbenzimidazoles (0.005 moles), morpholine(0.42 g,0.005 moles) and diethoxymethane (0.005 moles) are refluxed in ethanol for 8 hours, after reaction completion, the reaction mass is cooled to ambient temperature, the obtained solid was filtered, recrystallized from Dimethyl formamide and dried to get title compound (1.2 g, 80%)mp 192°C, ((δH ($CDCl_3$) 7.65 (1H), 7.66 (2H) 7.51 (2H), 7.40(1H) 7.35 (1H), 2.32 (6H) ,δC ($CDCl_3$) 151.4 (C=N), 139.14, 132.1, 131.2, 130.2,128.4, 122.1 and 22.2.; υmax /cm-1 (KBr) 3394 (N-H), 3052 (C-H, sp2), MS (EI): m/z 222.4.

2-phenyl-1-[(piperazin-1-yl)methyl]-1H-benzimidazole(2b)

(δH ($CDCl_3$) 7.70 (1H),7.68 (2H), 7.52 (2H) 7.43 (1H), 7.36(1H) 7.28 (1H),7.17 (1H), 4.96 (1H) , 2.79 (2H), 2.48(2H),2.32 (H, NH) ,δC ($CDCl_3$) 153.4 (C=N), 142,134.14, 131.1, 129.2, 128.2,127.4, 122.3, 120.1,108.1,63.5,53.1 and 43.2.; υmax /cm-1 (KBr) 3396 (NH),3052 (C-H, sp2), MS (EI): m/z 293.5.

2-phenyl-1-[(piperidin-1-yl)methyl]-1*H*-benzimidazole (2c)

(δH ($CDCl_3$) 7.69 (1H),7.68 (2H), 7.51 (2H) 7.43 (1H), 7.35(1H) 7.28 (1H),7.17 (1H), 4.98 (1H) , 2.45 (2H), 1.55(2H),1.42 (H) ,δC ($CDCl_3$) 153.4 (C=N), 142,134.14, 131.1, 129.0, 128.8,127.7, 122.5, 120.6,108.4,63.5,52.1,25.3 and 24.2.; υmax /cm-1 (KBr) 3053 (C-H, sp2), MS (EI): m/z 291.8

***N*,*N*-dimethyl-1-(2-phenyl-1*H*-benzimidazol-1-yl)methanamine(2d)**

(δH ($CDCl_3$) 7.69 (1H),7.66 (2H), 7.52 (2H) 7.42 (1H), 7.36(1H) 7.26 (1H),7.18 (1H), 4.99 (1H) , 2.32 (6H) ,δC ($CDCl_3$) 153.1 (C=N), 142.8,134.4, 130.9, 129.0, 128.7,127.6, 123.9, 123.6,120.6,108.2,63.4 and 43.2.; υmax /cm-1 (KBr) 3053 (C-H, sp2), MS (EI): m/z 251.3.

***N*-ethyl-*N*-[(2-phenyl-1*H*-benzimidazol-1-yl)methyl]ethanamine(2e)**

(δH ($CDCl_3$) 7.68 (1H),7.67(2H), 7.51 (2H) 7.43 (1H), 7.35(1H) 7.27 (1H),7.18 (1H), 4.99 (1H) , 2.62 (4H) and 1.05 (6H) ,δC ($CDCl_3$) 153.0 (C=N), 142.8,134.4, 130.8, 129.0, 128.8,127.7, 123.9, 123.5,120.6,108.2,63.4 ,46.2 and 12.2.; υmax /cm-1 (KBr) 3053 (C-H, sp2), MS (EI): m/z 280.4.

5-methyl-1-[(morpholin-4-yl)methyl]-2-phenyl-1*H*-benzimidazole(2f)

(δH ($CDCl_3$) 7.68 (2H), 7.51 (2H) 7.43(1H) 7.42 (1H),7.20 (1H), 6.78(1H), 4.99 (1H),3.66(4H) 2.55 (4H) and 2.44 (3H) ,δC ($CDCl_3$) 153.1 (C=N), 140.9, 134.1, 132.7, 130.9,129.4,128.8, 127.7, 121.7,111.2, 109.6, 66.4,63.2,51.8 and 22.4.; υmax /cm-1 (KBr) 3052 (C-H, sp2), MS (EI): m/z 307.2.

5-methyl-2-phenyl-1-[(piperidin-1-yl)methyl]-1*H*-benzimidazole(2g)

(δH ($CDCl_3$) 7.68 (2H), 7.51 (2H) 7.43(1H) 7.42 (1H),7.20 (1H), 6.78(1H), 4.99 (1H), 2.45 (4H) and 2.44 (3H) 1.55 (4H) and 1.42(2H) ,δC ($CDCl_3$) 153.1 (C=N), 140.9, 134.1, 132.7, 130.9,129.0,128.8, 127.7, 121.7,111.2, 109.6,63.2,52.8 , 25.4, 24.23and 21.4.; υmax /cm-1 (KBr) 3052 (C-H, sp2), MS (EI): m/z 305.9.

5-methyl-2-phenyl-1-[(piperazin-1-yl)methyl]-1*H*-benzimidazole(2h)

(δH ($CDCl_3$) 7.68 (2H), 7.51 (2H) 7.43(1H) 7.42 (1H),7.20 (1H), 6.78(1H), 4.99 (1H), 2.79 (4H) and 2.52 (4H) 2.42(3H) and 2.33(NH) ,δC ($CDCl_3$) 153.1 (C=N), 140.9, 134.1, 132.7, 130.9,129.0,128.8, 127.7, 121.7,111.2, 109.6,63.2,53.8. 46.2 and 21.4.; υmax /cm-1 (KBr) 3394 (N-H), 3052 (C-H, sp2), MS (EI): m/z 306.5.

***N*,*N*-dimethyl-1-(5-methyl-2-phenyl-1*H*-benzimidazol-1-yl)methanamine(2i)**

(δH ($CDCl_3$) 7.68 (2H), 7.51 (2H) 7.43(1H) 7.42 (1H),7.20 (1H), 6.78(1H), 4.99 (1H), 2.44 (3H) and 2.32 (6H) ,δC ($CDCl_3$) 153.1 (C=N), 140.9, 134.1, 132.7, 130.9,129.0,128.8, 127.7, 121.7,111.2, 109.6,63.2, 42.2 and 21.4.; υmax /cm-1 (KBr) 3052 (C-H, sp2), MS (EI): m/z 265.3.

***N*-ethyl-*N*-[(5-methyl-2-phenyl-1*H*-benzimidazol-1-yl)methyl]ethanamine (2j)**

(δH ($CDCl_3$) 7.68 (2H), 7.51 (2H) 7.43(1H) 7.42 (1H),7.20 (1H), 6.78(1H), 4.99 (1H), 2.62(4H) 2.44 (3H) and 1.04 (6H) ,δC ($CDCl_3$) 153.1 (C=N), 140.9, 134.1, 132.7, 130.9,129.0,128.8, 127.7, 121.7,111.2, 109.6,63.2, 42.2 ,21.5and 12.4.; υmax /cm-1 (KBr) 3052 (C-H, sp2), MS (EI): m/z 294.6

5-ethyl-1-[(morpholin-4-yl)methyl]-2-phenyl-1*H*-benzimidazole(2k)

(δH ($CDCl_3$) 7.68 (2H), 7.53 (1H),7.51 (2H) 7.43(1H) ,7.20 (1H), 6.78(1H), 4.99 (1H),3.66(4H),2.73(2H), 2.55 (4H) and 1.25 (3H) ,δC ($CDCl_3$) 153.1 (C=N), 140.9, 134.5, 134.4, 130.9,129.4,128.8, 127.9,127.7, 121.7,111.2, 109.6, 66.1,63.3,51.8 ,28.2and 14.4.; υmax /cm-1 (KBr) 3052 (C-H, sp2), MS (EI): m/z 321.9.

5-ethyl-2-phenyl-1-[(piperidin-1-yl)methyl]-1*H*-benzimidazole(2l)

(δH ($CDCl_3$) 7.68 (2H), 7.53 (1H),7.51 (2H) 7.43(1H) ,7.20 (1H), 7.06(1H), 4.99 (1H),3.66(4H),2.73(2H),,1.55(4H), 1.42 (2H) and 1.29 (3H) ,δC ($CDCl_3$) 153.1 (C=N), 140.9, 134.5, 134.4, 130.9,129.4,128.8, 127.9,127.7, 121.7,111.2, 109.6,63.3,52.4 ,28.2, 25.7and 24.4.; υmax /cm-1 (KBr) 3056 (C-H, sp2), MS (EI): m/z 321.9.

5-ethyl-2-phenyl-1-[(piperazin-1-yl)methyl]-1*H*-benzimidazole(2m)

(δH ($CDCl_3$) 7.68 (2H), 7.53 (1H),7.51 (2H) 7.43(1H) ,7.20 (1H), 7.06(1H), 5.01 (2H),2.79(4H),2.73(2H), 2.49 (4H,dd),2.3 (1H,NH)1.23(3H), 1.42 (2H) and 1.29 (3H) ,δC ($CDCl_3$) 153.1 (C=N), 140.9, 134.5, 134.4, 130.9,129.4,128.8, 127.9,127.7, 120.7,109.2,63.3,53.4 ,46.1, 28.7and 14.4.; υmax /cm-1 (KBr) 3329(NH), 3052 (C-H, sp2), MS (EI): m/z 321.4.

1-(5-ethyl-2-phenyl-1*H*-benzimidazol-1-yl)-*N*,*N*-dimethylmethanamine(2n)

(δH ($CDCl_3$) 7.68 (2H), 7.51 (2H) 7.43(1H) 7.42 (1H),7.20 (1H), 6.78(1H), 4.99 (2H), 2.48 (2H) and 2.46 (6H) and 1.53 (3H) ,δC ($CDCl_3$) 153.1 (C=N), 140.9, 134.5, 134.3, 130.9,129.0,128.8,127.9, 127.7, 120.7,109.6,63.2, 42.9 ,28.2and 14.4.; υmax /cm-1 (KBr) 3052 (C-H, sp2), MS (EI): m/z 279.3.

***N*-ethyl-*N*-[(5-ethyl-2-phenyl-1*H*-benzimidazol-1-yl)methyl]ethanamine(2o)**
(δH ($CDCl_3$) 7.68 (2H), 7.51 (2H) 7.43(1H) 7.42 (1H),7.20 (1H), 6.78(1H), 4.99 (2H), 2.72 (4H),2.66(2H) ,1.25 (3H) and 1.01 (6H) and ,δC ($CDCl_3$) 153.1 (C=N), 140.9, 134.5, 134.3, 130.9,129.0,128.8,127.9, 127.7, 120.7,109.6,63.2, 42.9 ,28.2and 14.4.; υmax /cm-1 (KBr) 3052 (C-H, sp2), MS (EI): m/z 307.9.

5,6-diethyl-1-[(morpholin-4-yl)methyl]-2-phenyl-1*H*-benzimidazole(2p)
(δH ($CDCl_3$) 7.68 (2H), 7.53 (1H),7.51 (2H) 7.43(1H) ,7.20 (1H), 4.99 (1H),3.66(4H),2.73(4H), 2.55 (4H) and 1.25 (6H) ,δC ($CDCl_3$) 153.1 (C=N), 140.9, 134.5, 134.4, 130.9,129.4,128.8, 127.9,127.7, 121.7,111.2, 109.6, 66.1,63.3,51.8 ,28.2and 14.4.; υmax /cm-1 (KBr) 3052 (C-H, sp2), MS (EI): m/z 349.9.

5,6-diethyl-2-phenyl-1-[(piperidin-1-yl)methyl]-1*H*-benzimidazole(2q)
(δH ($CDCl_3$) 7.68 (2H), 7.53 (1H),7.51 (2H) 7.43(1H) ,7.20 (1H), 4.99 (1H),3.66(4H),2.73(2H), ,1.55(4H), 1.42 (2H) and 1.29 (6H) ,δC ($CDCl_3$) 153.1 (C=N), 140.9, 134.5, 134.4, 130.9,129.4,128.8, 127.9,127.7, 121.7,111.2, 109.6,63.3,52.4 ,28.2, 25.7and 24.4.; υmax /cm-1 (KBr) 3052 (C-H, sp2), MS (EI): m/z 347.8.

5,6-dimethyl-2-phenyl-1-[(piperazin-1-yl)methyl]-1*H*-benzimidazole(2r)
(δH ($CDCl_3$) 7.68 (2H), 7.53 (1H),7.51 (2H) 7.43(1H) ,7.20 (1H), 5.01 (2H),2.79(4H),2.73(2H), 2.49 (4H),2.3 (1H,NH)1.23(6H), 1.42 (4H) and 1.29 (6H) ,δ C ($CDCl_3$) 153.1 (C=N), 140.9, 134.5, 134.4, 130.9,129.4,128.8, 127.9,127.7, 120.7,109.2,63.3,53.4 ,46.1, 28.7and 14.4.; υmax /cm-1 (KBr) 3329(NH), 3052 (C-H, sp2), MS (EI): m/z 321.4.

1-(5,6-diethyl-2-phenyl-1*H*-benzimidazol-1-yl)-*N*,*N*-dimethylmethanamine(2s)
(δH ($CDCl_3$) 7.68 (2H), 7.51 (2H) 7.43(1H) 7.42 (1H),7.20 (1H), 4.99 (2H), 2.48 (4H) , 2.46 (6H) and 1.53 (6H) ,δC ($CDCl_3$) 153.1 (C=N), 140.9, 134.5, 134.3, 130.9,129.0,128.8,127.9, 127.7, 120.7,109.6,63.2, 42.9 ,28.2and 14.4.; υmax /cm-1 (KBr) 3052 (C-H, sp2), MS (EI): m/z 207.6.

***N*-[(5,6-diethyl-2-phenyl-1*H*-benzimidazol-1-yl)methyl]-*N*-ethylethanamine(2t)**
(δH ($CDCl_3$) 7.68 (2H), 7.51 (2H) 7.43(1H) 7.42 (1H),7.20 (1H), 4.99 (2H), 2.72 (4H),2.66(4H) ,1.25 (6H) and 1.01 (6H δC ($CDCl_3$) 153.1 (C=N), 140.9, 134.5, 134.3, 130.9,129.0,128.8,127.9, 127.7, 120.7,109.6,63.2, 42.9 ,28.2and 14.4.; υmax /cm-1 (KBr) 3052 (C-H, sp2), MS (EI): m/z 335.9.

5,6-dimethyl-1-[(morpholin-4-yl)methyl]-2-phenyl-1*H*-benzimidazole(2u)
(δH ($CDCl_3$) 7.68 (2H), 7.53 (1H),7.51 (2H) 7.43(1H) ,7.20 (1H), 4.99 (1H),3.66(4H),2.73(4H) and 2.55 (6H) ,δC ($CDCl_3$) 153.1 (C=N), 140.9, 134.5, 134.4, 130.9,129.4,128.8, 127.9,127.7, 121.7,111.2, 109.6, 66.1,63.3,51.8 ,28.2and 14.4.; υmax /cm-1 (KBr) 3052 (C-H, sp2), MS (EI): m/z 321.8.

5,6-dimethyl-2-phenyl-1-[(piperidin-1-yl)methyl]-1*H*-benzimidazole(2v)
(δH ($CDCl_3$) 7.68 (2H), 7.53 (1H),7.51 (2H) 7.43(1H) ,7.20 (1H), 4.99 (1H),3.66(4H),2.73(2H), ,1.55(6H) and 1.42 (2H) ,δC ($CDCl_3$) 153.1 (C=N), 140.9, 134.5, 134.4, 130.9,129.4,128.8, 127.9,127.7, 121.7,111.2, 109.6,63.3,52.4 ,28.2, 25.7and 24.4.; υmax /cm-1 (KBr) 3052 (C-H, sp2), MS (EI): m/z 319.6.

5,6-dimethyl-2-phenyl-1-[(piperazin-1-yl)methyl]-1*H*-benzimidazole(2w)

(δH ($CDCl_3$) 7.68 (2H), 7.53 (1H),7.51 (2H) 7.43(1H) ,7.20 (1H), 5.01 (2H),2.79(4H),2.73(2H), 2.49 (6H),2.3 (1H,NH), 1.42 (4H) and 1.29 (6H) ,δ C ($CDCl_3$) 153.1 (C=N), 140.9, 134.5, 134.4, 130.9,129.4,128.8, 127.9,127.7, 120.7,109.2,63.3,53.4 ,46.1, 28.7and 14.4.; υmax /cm-1 (KBr) 3329(NH), 3052 (C-H, sp2), MS (EI): m/z 320.4.

1-(5,6-dimethyl-2-phenyl-1*H*-benzimidazol-1-yl)-*N*,*N*-dimethylmethanamine(2x)

(δH ($CDCl_3$) 7.68 (2H), 7.51 (2H) 7.43(1H) 7.42 (1H),7.20 (1H), 4.99 (2H), 2.48 (6H) ,and 2.46 (6H) ,δC ($CDCl_3$) 153.1 (C=N), 140.9, 134.5, 134.3, 130.9,129.0,128.8,127.9, 127.7, 120.7,109.6,63.2, 42.9 ,28.2and 14.4.; υmax /cm-1 (KBr) 3052 (C-H, sp2), MS (EI): m/z 279.6.

***N*-[(5,6-dimethyl-2-phenyl-1*H*-benzimidazol-1-yl)methyl]-*N*-ethylethanamine (2y)**

(δH ($CDCl_3$) 7.68 (2H), 7.51 (2H) 7.43(1H) 7.42 (1H),7.20 (1H), 4.99 (2H), 2.72 (6H),2.66(4H) and 1.01 (6H) δC ($CDCl_3$) 153.1 (C=N), 140.9, 134.5, 134.3, 130.9,129.0,128.8,127.9, 127.7, 120.7,109.6,63.2, 42.9 ,28.2and 14.4.; υmax /cm-1 (KBr) 3052 (C-H, sp2), MS (EI): m/z 335.9 (M+1.)

References

[1]. J. G. Black, Microbiology, Principles and applications. 3rded, Prentice Hall Publishers. 1996, 356-387.
[2]. N. S. Bruinsma, D. Verloo, E. Tiemersma, J. Monen, H. Goossens, M. Ferech. Emerg. Infect. Dis., 2008, 14, 1722-1730.
[3]. A. K..Verma, R Chandra, R. K. Tiwari, D. Singh, J. Singh, Bioorg. Med. Chem. Lett., 2006, 17, 413-416.
[4]. K. D. Tripathi, Esssentials of Medical Pharmacology, Jaypee Brothers Medical Publishers (P) Ltd. 2008, 668-673.
[5]. Al-Shihry. Sci. J. Faisal Unv., 2005, 16, 77-85.
[6]. V. Padmavathi, D. R. C. V. Subbaiah, K. Mahesh, T. R. Lakshmi, Chem. Pharm. Bull., 2007, 55, 1704-1709.
[7]. D. B. Shinde, M. J. Aaglawe, S. S. Dhule, S. S. Bahekar, P. S. Wakte. J. Kor. Chem. Sty., 2003, 47, 133-136.
[8]. A. Bazgir, M. M. Khanaposhtani, A. A. Sooski, Bioorg. Med. Chem. Lett., 2008, 18, 5800-5803.
[9]. K. F. Ansari, C. Lal, Eur. J. Med. Chem., 2009, 44, 2294-2298.
[10]. D. J. Abraham, Burger's Medicinal Chemistry and drug discovery, John Wiley. 2003, 6, 180.
[11]. 11. P. N. Preston, Chem. Rev., 1974, 74(3), 279.
[12]. 12. A. Humaira, Synthesis and characterization of potentially bioactive nucleosides bearing different heterocyclic moieties, Ph.D Thesis
[13]. F. Hoebrecker, Ber., 1872, 5, 920.
[14]. A. Ladenburg, Ber., 1877, 10, 1123-31.
[15]. M. Achesonr, F. E. King, C. Spensleyp, Nature, 1947, 160, 53.
[16]. G. Elerafi, N. Ibrahim, Int. J. of Chem. Tech. Resr., 2010, 4, 2097-2099.
[17]. S. Murugesan et al., J. of Pharmacy Resr., 2011, 4(8), 2679-2681
[18]. R. Anil, Eurp. J. of Chem., 2010, 7(1), 222-226.
[19]. P. Selvam et al., Int. J. of Pharmaceu. Sci. and Res., 2010, 1(9), 105-119.

[20]. A. K..Verma, R Chandra, R. K. Tiwari, D. Singh, J. Singh, Bioorg. Med. Chem. Lett., 2006, 17, 413-416.
[21]. K. D. Tripathi, Esssentials of Medical Pharmacology, Jaypee Brothers Medical Publishers (P) Ltd. 2008, 668-673.
[22]. Al-Shihry. Sci. J. Faisal Unv., 2005, 16, 77-85.
[23]. V. Padmavathi, D. R. C. V. Subbaiah, K. Mahesh, T. R. Lakshmi, Chem. Pharm. Bull., 2007, 55, 1704-1709
[24]. X. C. Huang, J. P. Zhang, X. M. Chen, J. Am. Chem. Soc., 2004, 126, 13218-13219.
[25]. T. J. Cardwell, A. J. Edwards, R. M. Hartshorn, R. J. Holmes, Aust. J. Chem., 1997, 50, 1009-1015.
[26]. Y. P. Tong, S. L. Zheng, J. Mol. Struct., 2007, 841, 34-40
[27]. Y. P. Tong, S.L. Zheng, X.M. Chen, J. Mol. Struct., 2007, 826, 104-112
[28]. P. S. Misra1, P. Shanmugasundaram, R. Chaudhary, M. V. Aanandhi, Rasayan J. of Chem., 2010, 3(1), 51-54.
[29]. S. Jubie, R. Rajeshkumar, B. Yellareddy, G. Siddhartha, M. Sandeep, K. Surendrareddy, H. S. Dushyanth, K. Elango, J. Pharm. Sci. & Res., 2010, 2(2), 69-76.
[30]. J. P. English, R. C. Clapp, Q. P. Cole, J. Krapcho, J. Am. Chem. Soc., 1945, 67, 2263.
[31]. B. Putzer, F. Schonhffer, German patent, 1932, 550, 327; Chem. Abstracts, 1932, 26, 4062.
[32]. A. Bloom, A. R. Day, J. Org. Chem., 1939, 4, 14-19.