Int J Pharm Bio Sci 2014 Jan; 5(1): (P) 682 - 690

Research Article **Medicinal Chemistry**

International Journal of Pharma and Bio Sciences **ISSN 0975-6299**

SYNTHESIS AND ANTI BACTERIAL ACTIVITY OF 2-(4-AMINOPHENYL) BENZIMIDAZOLE BASED PYRAMIDINE DERIVATIVES

KUMARASWAMY GULLAPELLI[1], MURALI KRISHNA THUPURANI[2] AND G.BRAHMESHWARI*[1]

[1]Department of Chemistry, Kakatiya University –Warangal (A.P)-India
[2]Department of Biotechnology, Chaitanya Postgraduate College, Kishanpura, Hanamkonda (Autonomous) AP-India-506001

ABSTRACT

As a part of systematic investigation of synthesis ,characterization and biological activities of N-(4-(1H-benzo(d)imidazole -2-yl)-2-(4-hydroxy -6-methyl pyramidine -2-yl thio) acetamide have been synthesized from 2-(4-aminophenyl) benzimidazole and 2-mercapto -4-hydroxy -6-methyl_pyramidine ,which have been prepared from p-amino benzoic acid and benzene 1,2 diamine and EAA with thiourea. All the synthesized compounds have been characterized by ^{1}HNMR; IR spectral data .The prepared compounds were tested for antibacterial activity.

KEY WORDS: Synthesis, benzimidazole, pyramidine, Antibacterial activity

G.BRAHMESHWARI
Department of Chemistry, Kakatiya University –Warangal (A.P)-India

1.0 INTRODUCTION

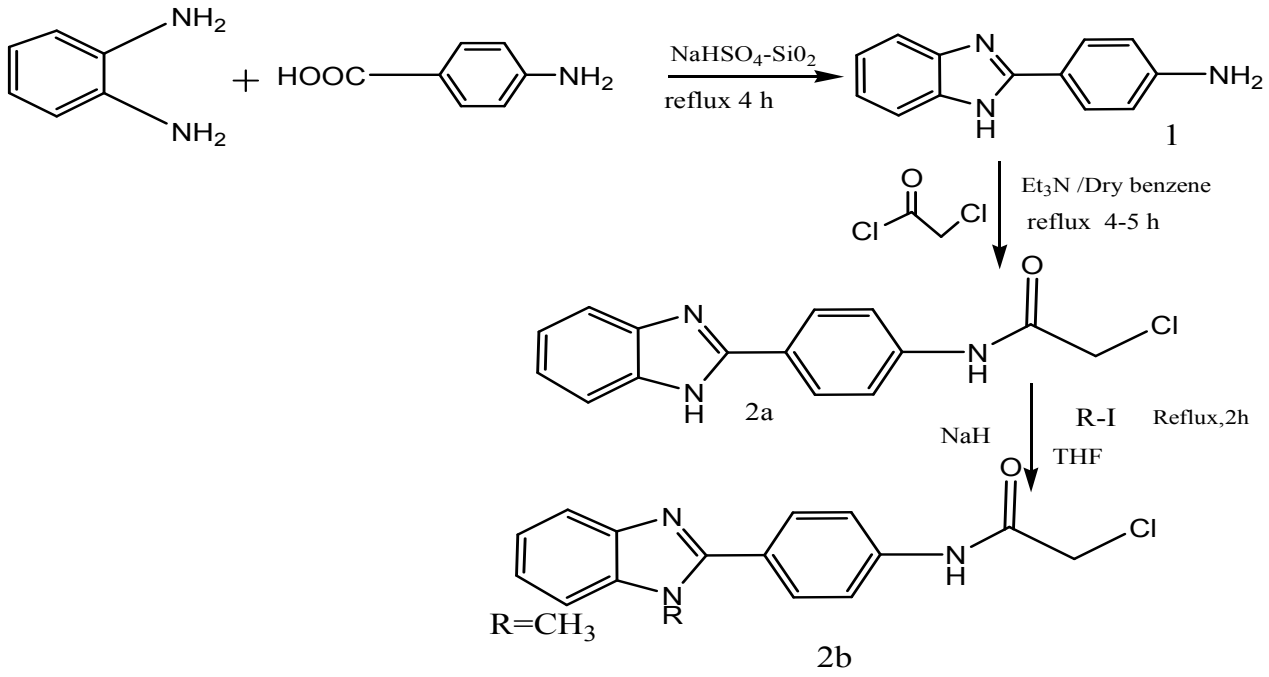
Benzimidazole nucleus is an important heterocyclic ring and very useful intermediates /sub units for the development of molecules of pharmaceutical or biological interest[1].the chemistry of benzimidazoles have been a great interest to medicinal chemistrty[2],because of its derivatives possessed various biological activities such as anti tumor[3], antimicrobial[4, 5], antihelmenthic [6], anti cancer[7], antiinflamatory[8], analgesic[9], antifungal[10] etc. The wide spread interest in benzimidazole containing structures has promoted extensive studies for their structures[11], pyramidine containing benzimidazole derivatives are considered to be important for drugs and agricultural chemicals[12].The paper reports the synthesis of compound (5) and its derivatives by conventional method, using standard procedure. Whereas, compound (1) was prepared by using catalytic amount of $NaHSO_4$-SiO_2, a heterogeous catalyst and eco-friendly[13]. In the context to the above mentioned therapeutic properties of Benzimidazole, the current studies have been focused on the investigations carried out for the synthesis and medicinal applications of Benzimidazole derivatives.

2.0 MATERIALS AND METHODS

Melting points were determined in open capillaries and are uncorrected. The progress of the reaction was monitored by silica gel G coated TLC plates, ^{1}H NMR spectra were recorded on a Bruker 300 MHz instrument in DMSO/$CDCl_3$ using TMS as internal standard. Chemical shifts (δ) are expressed in ppm.
IR spectra (KBr pellet) were recorded on a Perkin Elmer BX series FT-IR spectrometer,
Elemental analyses were performed on a PerkinElmer 240 CHN analyzer

2.1 Experimental section

Scheme



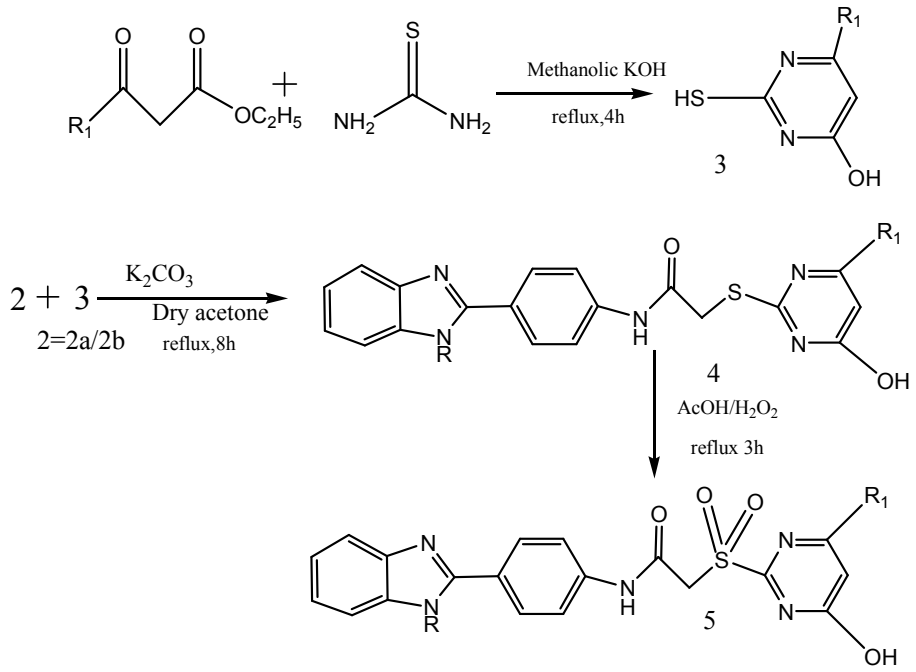
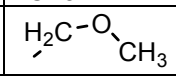
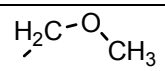
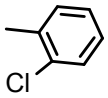
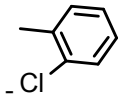


Table 1
List represent the derivatives of R_1

Compound	R	R 1	Compound	R	R1
5a	-H	-CH3	5f	-CH3	-CH3
5b	-H	-Ph	5g	-CH3	-Ph
5c	-H	-CF3	5h	-CH3	-CF3
5d	-H		5i	-CH3	
5e	-H		5j	-CH3	

2.1.2 Synthesis of 4-(1H-benzo[d]imidazol-2-yl) aniline (1)

A mixture of p-amino benzoic acid (0.03mmol) and o-phenylenediamine (0.03mmol) and $NaHSO_4$-SiO_2 (25% wt) in 10ml of ethanol was heated under reflux at 180 ^oC for 4 h. The reaction mixture was then partially cooled, poured on to crushed ice and neutralized with 10 % NaOH solution. The precipitated product was collected by vacuum filtration, washed with excess 10 % NaOH solution, and then dried and recrystallized from ethanol[14]. M.p:235-37^oC, IR (KBr) v mmax/cm^{-1}: 3,430 (NH benzimidazole); 3, 350, 3,217(NH_2 amino phenyl); 3,061 (CH arom); 1,629 (C=N); 1,605 (C=C arom). ^1H NMR (DMSO-d6, 300 MHz, d ppm): 5.58 (S, NH_2 amino phenyl, D_2O exchangeable), 6.63 (d, 2H, H_2', H6' amino phenyl), 7.08 (m, 2H, H5, H6 benzimidazole), 7.46 (m, 2H, H4, H7 benzimidazole), 7.79 (d, 2H, H3, H5 amino phenyl), 12.46 (br., NH benzimidazole, D_2O exchangeable).MS, *m/z*(%),209(M^+,100%).Analytical calcd.for $C_{13}H_{11}N_3$(209): C,74.62;H,5.30;N,20.08%: found C,74.60;H,5.32;N,20.07%.

2.1.3a Synthesis of N-(4-(1H-benzo[d]imidazol-2-yl) phenyl)-2-chloroacetamide (2a)

In an ice bath, a solution of compound 1 (10 mmol) and triethylamine (0.5 ml) in dry benzene(10 ml) was stirred for 15 min 10 mmol

of Chloroacetylchloride was added and the reaction mixture was stirred for 4-5 h. After completion of the reaction, the mixture was poured, with continuous stirring, on to crushed ice. The solid formed was collected by vacuum filtration, washed with ethyl acetate, and recrystallized from ethanol[15, 16], M.p:310-320^{o}C, IR (KBr) v max/cm$^{-1:}$3,390(NH benzimidazole); 3,278 (NH amino phenyl); 3,043 (CH -aromatic) 2,922 (CH aliphatic); 1,673 (C=O); 1,603 (C=N), 1,548 (C=C arom). ^{1}H NMR (DMSOd6, 300 MHz, d ppm): 4.30 (s, 2H, CH2); 7.40 (m, 2H, H5, H6 benzimidazole); 7.70 (m, 2H, H4, H7 benzimidazole); 7.87 (d, 2H, H2‘, H6‘ amino phenyl); 8.15 (d, 2H,H3 ,H5 amino phenyl moiety); 10.76 (s, 1H, NH amino phenyl, D2O exchangeable); 12.43 (br., 1H, NH benzimidazole, D_2Oexchangeable).MS, *m/z*(%),285(M^+,100%).Analytical calcd.for $C_{15}H_{12}ClN_3O$:C,63.05;H,4.23;N,14.71%:found C,6302;H,4.21;N,14.69%.

2.1.3b synthesis of 2-Chloro-N-(4-(1-methyl-1H-benzo (d) imidazole-2yl) phenyl) acetamide (2b)

The compound1 (1mmol) and sodium hydride (0.085g) were taken in THF (10ml)stirr the contents in cold condition for about 30 min and add methyl iodide (1mmol) reflux for about 1.5 h. The *solution* was evaporated until dryness, recrystallised by benzene.

M.p:318-325^{o}C, IR (KBr) v max/cm$^{-1:}$ 3,278 (NH amino phenyl); 3,043 (CH -aromatic) 2,922 (CH aliphatic); 1,673 (C=O); 1,603 (C=N), 1,548 (C=C arom). ^{1}H NMR (DMSOd6, 300 MHz, d ppm): 4.30 (s, 2H, CH2); 7.40 (m, 2H, H5, H6 benzimidazole); 7.70 (m, 2H, H4, H7 benzimidazole); 7.87 (d, 2H, H2‘, H6‘ amino phenyl); 8.15 (d, 2H,H3 ,H5 amino phenyl moiety); 10.76 (s, 1H, NH amino phenyl, D2O exchangeable);3.43(S,-CH_3).MS *m/z*(%),299(M^+,100%).Analytical calcd.for $C_{16}H_{14}ClN_3O$: C,63.05%;H,4.23;N,14.71%:found C,63.02;H,4.21;N,14.69%.

2.1.4 Synthesis of 2-mercapto-6-methyl pyramidin-4-ol (3)

A mixture of ethyl acetoacetate (substituted) (1mmol) and thio urea (1mmol) in alcoholic KOH (10 ml) was reflux for about 4 h, after completion of the reaction; the solid mixture was washed with cold water to remove the excess of thio urea and then filtered. The filtrate was concentrated and the solid product was recrystallized from ethyl acetate or ethanol. And also prepared substituted pyramidines were proceed the same procedure.[17] M.p:262-64^{o}C, IR (KBr) v max (cm^{-1}); 3,510 (-OH); 2,930 (-CH); 1,680 (-C=N); 2,560 (-SH); 6.45 (-C-S). ^{1}HNMR (DMSO-d6, 300mHz,d ppm); 6.29 (S, 2-pyramidin); 5.0 (S,-OH); 3.0 (S,-SH); 2.35(S,-CH_3).MS *m/z* (%), 142 (M+, 100%).Analytical calcd.for $C_5H_6N_2OS$: C, 42.24; H, 4.25; N, 19.71%: found C, 42.25; H, 4.24; N, 19.69%.

2.1.4 Synthesis of N-(4-1H-benzo (d) imidazole-2-yl) phenyl)-2-(4-hydroxy-6-methyl-pyramidin-2yl thio) acetamide (4)

Equimolar mixture of compound (2), compound (3) and K_2CO_3 (1mmol) in dry acetone (50 ml) was refluxed for 8 h. After cooling, solution was evaporated until dryness. The residue was washed with water and recrystallised from ethanol[18]. M.p:305-10^{o}C, IR: (KBr) v mmax/cm^{-1}; 2920 (C-H aliphatic); 1640 (=C-H Aromatic); 1090 (C=N); 3,410 (NH benzimidazole); 1,695 (C=O-NH); 3510 (-OH); 3410 (N-H); 645 (C-S). ^{1}HNMR (DMSOd6, 300 MHz, d ppm): 7.26 (m, 2H benzimidazole); 7.70 (m, 2H benzimidazole); 7.46(m,2Hbenzene);8.0(S,NH benzimidazole); 5.0(S,NHbenzimidazole);5.0(S,-OH pyrimidine) 6.32(S, 1H-CH pyrimidine) 3.87(S-CH_2);2.35(S,-CH_3pyramidine).MS,*m/z*(%), 391(M^+,100%).Analytical calcd.for $C_{20}H_{17}N_5O_2S$:C,61.38;H,4.34; N,17.90%.found C,61.37 ;H=4.31%;N=17.89;S=8.17%.

2.1.5. A Synthesis of Synthesis of N-(4-1H-benzo (d) imidazole-2-yl) phenyl)-2-(4-hydroxy-6-methyl-pyramidin-4yl sulfonyl) acetamide (5a)

5a: An ice cold solution the compound 4 (1mmol) in glacial acetic acid (30 ml) was treated with 30% H_2O_2 (20 ml) in portions. The contents were allowed to attain laboratory temperature and then refluxed for 3h. The reaction mixture was cooled and acetic acid was removed in vacuo. The residual portion was cooled by filtration and was further purified

by recrystallization using water[19]. The same procedure was followed for all other remaining compound purification (5b-5j).M.p:305-08^{o}C
IR (KBr) v mmax/cm^{-1}; 2920(C-H aliphatic); 1640 (=C-Aromatic); 1090 (C=N); 3,410 (N-H benzimidazole); 1,695 (C=O-NH); 1130 (-SO2); 3510 (-OH); 3410 (N-H); 645 (C-S). ^{1}HNMR (DMSO d6, 300 MHz, d ppm): 7.26 (m,2Hbenzimidazole);7.70(m,2Hbenzimidazole) ; 7.46 (m, 2H benzene); 8.0 (S, NH benzimidazole);5.0(S, NH benzimidazole); 5.0 (S,-OH-pyrimidine); 6.83 (S,1H-CH pyrimidine) 4.35(S,SO_2-CH_2);2.35(S,-CH_3pyramidine).MS,*m/z*(%),423(M^+,100%).Analytical calcd .for$C_{20}H_{17}N_5O_4S$:C,56.7;H,4.01;N,16.5%.found C,56.68;H,4.02;N,16.48%.

5b: M.p: 302-06^{o}C IR (KBr) v mmax/cm^{-1}; 2920 (C-H aliphatic); 1640 (=C-Aromatic); 1090 (C=N); 3,410 (N-H benzimidazole); 1,695 (C=O-NH); 1130 (-SO_2); 3510 (-OH); 3410 (N-H); 645 (C-S). ^{1}HNMR (DMSOd6, 300 MHz, d ppm): 7.70 (m, 2H benzimidazoles); 7.26 (m, 2H benzimidazoles); 7.46 (m, 2H Benzene); 7.32(m, benzene), 5.0 (S-OH pyramidine); 5.0 (S-NH benzimidazole); 8.0 (S-NH benzene); 4.35(SO_2CH_2).MSm/z(%),485(M^+,100%).Analyti calcalcd.for$C_{25}H_{19}N_5O_4S$: C,61.85 ;H,3.91 ;N,14.43%:found C,61.83; H,3.89;N,14.42%.

5c: M.p: 310-12^{o}C, IR (KBr) v mmax/cm^{-1}; 2920 (C-H aliphatic); 1640 (=C-Aromatic); 1090 (C=N); 3,410 (N-H benzimidazole); 1,695 (C=O-NH); 1130 (-SO_2); 3510 (-OH); 3410 (N-H); 645 (C-S). 1400 (-CF_3) ^{1}HNMR (DMSO d6, 300 MHz, d ppm): 7.70 (m, 2H benzimidazoles); 7.26 (m, 2H benzimidazoles); 7.32 (m, 2H benzene); 7.14 (S-CH pyramidine); 5.0 (S-OH pyramidine); 5.0 (S-NH benzimidazole); 8.0 (S-NH benzene); 4.35 (S, SO_2- CH_2); 6.83 (S-1H-CH-pyramiadine).
MS, *m/z*(%),474(M^+,100%).Analytical calcd.for $C_{20}H_{14}N_5O_4SF_3$:C,50.63;H,2.95;N,14.76%:found C,50.62 ;H,2.94; N,14.72%.

5d: M.p:300-05^{o}C, IR (KBr) v mmax/cm^{-1}; 2920 (C-H aliphatic); 1640 (=C-Aromatic); 1090 (C=N); 3,410 (N-H benzimidazole); 1,695 (C=O-NH); 1130 (-SO_2); 3510 (-OH); 3410 (N-H); 645 (C-S). 2830 (C-H, ether), 1120 (C-O-C, ether); ^{1}HNMR (DMSO d6, 300 MHz, d ppm): 7.70 (m, 2H benzimidazoles); 7.26 (m, 2H benzimidazoles); 7.46 (m, 2H Benzene); 4.35 (S, SO_2- CH_2); 6.83 (S-CH pyramidine); 5.0 (S-OHpyramidine);5.0 (S-NH benzimidazoles); 8.0 (S-NH benzene); 4.63(S-CH_2-ether). 3. 24(SCH_3ether).MS,*m/z*(%),453(M^+,100%).Analytical calcd.for $C_{21}H_{19}N_5O_5S$: C, 55.62; H, 4.18; N, 15.45%Found C, 50.61; H, 4.17; N, 15.46%.

5e: M.p: 308-10^{o}C,IR (KBr) v mmax/cm^{-1}; 2920 (C-Haliphatic); 1640 (=C-Aromatic); 1090 (C=N); 3,410 (N-H benzimidazole); 1,695 (C=O-NH); 1130 (-SO_2); 3510 (-OH); 3410 (N-H); 645 (C-S), 750 (chlorobenzene); ^{1}HNMR (DMSO d6, 300 MHz, d ppm): 7.70 (m, 2H benzimidazoles);7.26 (m, 2H benzimidazoles); 7.46 (m, 2H benzene); 7.14 (S-CH pyramidine); 4.35 (S, SO_2- CH_2);5.0 (S-OH pyramidine); 5.0 (S-NH benzimidazoles);8.0(SNHbenzene);7,42(mH6Chlorobenzene).7.20(mH5),7.16(mH4),7.33(mH3 Chlorobenzene).MS,*m/z*(%),519(M^+,100%).Analytical calcd.for $C_{25}H_{18}N_5O_4ClS$: C,57.80; H,3.46; N,13.48% :found C,57.81 ;H,3.42; N,13.46%.

5f: M.p: 306-10^{o}C,IR (KBr) v mmax/cm^{-1}; 2920 (C-H aliphatic); 1640 (=C-Aromatic); 1090 (C=N); 3,410 (N-H benzimidazole); 1,695 (C=O-NH); 1130 (-SO_2); 3510 (-OH); 3410 (N-H); 645 (C-S). 2930 (C-H aliphatic) ^{1}HNMR (DMSO d6, 300 MHz, d ppm): 7.26 (m, 2H benzimidazole); 7.70 (m, 2H benzimidazole); 7.46 (m, 2H benzene); 8.0 (S, NH benzimidazole); 5.0 (S, NH benzimidazole); 5.0 (S-OH- pyrimidine); 6.83 (S,1H-CH pyrimidine) 4.35 (S, SO_2-CH_2); 2.35 (S-CH pyramidine) 3.63(S-CH_3 benzimidazole).
MS ,*m/z*(%),425(M^+,100%).Analytical calcd.for $C_{20}H_{19}N_5O_4S$:C,56.47;H,4.47;N,16.47%: Found C,56.45;H,4.45;N,16.46%.

5g: M.p: 304-06^{o}C IR (KBr) v mmax/cm^{-1}; 2920 (C-H aliphatic); 1640 (=C-Aromatic); 1090 (C=N); 3,410 (N-H benzimidazole); 1,695 (C=O-NH); 1130 (-SO_2); 3510 (-OH); 3410 (N-H); 645 (C-S). ^{1}HNMR (DMSO d6, 300 MHz, d ppm): 7.70 (m, 2H benzimidazoles); 7.26 (m, 2H

benzimidazoles); 7.46 (m, 2H Benzene); 7.48(m,2Hbenzene);7.32(m,2Hbenzene);7.22(m -1H benzene) 7.14 (S-CH pyramidine); 5.0 (S-OHpyramidine);5.0 (S-NH benzimidazoles); 4.35 (S, SO_2-CH_2); 8.0 (S-NH benzene); 4.63 (S-CH-pyramidine),3.639(S-CH_3 benzimidazole) MS,*m/z*(%), 487 (M^+,100%). Analytical calcd.for $C_{25}H_{21}N_5O_4S$: C, 60.60; H, 4.32; N, 14.37%Found C, 60.58; H, 4.30; N, 14.36%.

5h: M.p: 310-15^{o}C,IR (KBr) v mmax/cm^{-1}; 2920 (C-H aliphatic); 1640 (=C-Aromatic); 1090 (C=N); 3,410 (N-H benzimidazole); 1,695 (C=O-NH); 1130 (-SO_2); 3510 (-OH); 3410 (N-H); 645 (C-S). 1400(-CF_3) ^{1}HNMR (DMSO d6, 300 MHz, d ppm): 7.70 (m, 2H benzimidazoles); 7.26 (m, 2H benzimidazoles); 7.46(m, 2H Benzene); 7.14 (S-CH pyramidine); 5.0 (S-OH pyramidine); 5.0 (S-NH benzimidazoles); 4.35 (S, SO_2-CH_2); 8.0 (S-NH benzene); 6.83 (S-1H-CH-pyramiadine), 3.639 (S-CH_3 benzimidazole).
MS , m/z(%) ,476(M^+,100%).Analytical calcd.for$C_{20}H_{16}N_5O_4F_3S$: C,50.42 ;H,3.36 ;N,14.70%.Found C,50.46 ;H,3.34 ;N,14.68; F=11.30%.

5i: M.p: 304-08^{o}C IR (KBr) v mmax/cm^{-1}; 2920 (C-H aliphatic); 1640 (=C-Aromatic); 1090 (C=N); 3,410 (N-H benzimidazole); 1,695 (C=O-NH); 1130 (-SO_2); 3510 (-OH); 3410 (N-H); 645 (C-S), 2830 (C-H, ether), 1120 (C-O-C, ether); ^{1}HNMR (DMSO d6, 300 MHz, d ppm): 7.70 (m, 2H benzimidazoles); 7.26 (m, 2H benzimidazoles); 7.32 (m, 2H Benzene); 7.14 (S-CH pyramidine); 5.0 (S-OH pyramidine); 5.0 (S-NH benzimidazoles); 4.35 (S, SO_2-CH_2); 8.0 (S-NH benzene); 4.63 (S-CH-pyramidine), 3.63 (S-CH_3 benzimidazole); 4.63(S-CH_2-ether). 3, 24 (S-CH_3 ether). MS, m/z(%),468(M^+,100%).Analytical calcd.for $C_{22}H_{22}N_5O_5S$:C,56.41;H,4.70;N,14.95% found C,56.40;H,4.68;N,14.94%.

5j: M.p: 308-14^{o}C IR (KBr) v mmax/cm^{-1}; 2920 (C-H aliphatic); 1640 (=C-Aromatic); 1090 (C=N); 3 ,410 (N-H benzimidazole); 1,695 (C=O-NH); 1130 (-SO_2);3510 (-OH); 3410 (N-H); 645 (C-S),750 (chlorobenzene); ^{1}HNMR (DMSOd6, 300 MHz, d ppm): 7.70(m, 2H benzimidazoles); 7.26(m, 2H benzimidazoles); 7.46 (m, 2H Benzene); 7.14 (S-CH pyramidine); 5.0 (S-OH pyramidine); 5.0 (S-NH benzimidazoles); 4.35 (S, SO_2-CH_2); 8.0 (S-NH benzene); 7.42 (m-H6).7.20 (m-H5), 7.16 (m-H4), 7.33 (m-H3 Chlorobenzene).
MS,*m/z*(%),533(M^+,100%).Analytical calcd.for$C_{26}H_{20}N_5O_4ClS$:C,58.53;H,3.75;N,13.13 ;S=6.00:found C,58.50;H,3.76;N,13.12 %.

2.1.7 Anti bacterial activity

2.1.7.1 Bacterial Cultures

Strains of *Bacillus subtilis* MTCC 441*, Bacillus cereus* ATCC 9372*, Staphylococcus aureus* ATCC 96*, E.Coli ATCC 8739, Klebsielia pneumonia MTCC 109, Salmonella typhi ATCC 4420 were taken from department of microbiology, Kakatiya University Warangal.*
The bacterial cultures were developed by selective nutrient broth at 37^{o}C and stored at 4^{o}Cfor further use.

2.1.7.2 Preparation of standard bacterial suspensions

Intially, all the bacterial strains were inoculated on to enriched nutritive broth media and incubated at 35± 2^{o}C for 24 h 25%of turbidity at 580nm was taken in to consideration for antibacterial assay. Spectrophotometrically using Bausch & Lomb spectrophotometer comparable to McFarland turbidity standard. This level of turbidity is equivalent to approximately 3.0 × 10^8 CFU/ml (a stock standard from which a working standard was drawn with concentration of 1 × 10^8 CFU/ml). The antibacterial activity of these extracts was carried out according to the method described by Raman with slight modifications[21]. Each selective medium was inoculated with the test organism suspended in nutritive broth. Once the agar was solidified, it was punched with a six millimeters diameter wells and filled with 25 µL of the plants extracts of various concentrations and corresponding wells with positive and negative control. The concentration of the methanolic extracts employed at concentrations 25, 50, 75 µg/ml simultaneously, gentamycin sulfate (10 µg/ml) is used as positive control. The test was carried out in triplicate. The plates

were incubated at 35 ± 2°C for 24 h. The inhibition zone diameter was measured in mm.

3.0 RESULTS

Antibacterial activity

Studies on antibacterial activities of the compounds determined revealed that all the compounds exhibited significant inhibition activity. Among the tested compounds 5h, 5c, 5j and 5e showed highest antibacterial activities tested at all concentrations against different types of bacterial strains used in the assay. However, *Salmonella typhi* showed resistance against all tested compounds. The highest inhibition zones 14, 9, 09, 07, 06, 04, 08, 05 are noticed against *Escherichia coli* by 5h, 5c, 5j and 5e respectively comparing with other compounds (Table 2).

Table 2

Antibacterial activity of the compounds tested on various human pathogenic organisms. The zone of inhibition were represented in mm

	5a	5b	5c	5d	5e	5f	5g	5h	5i	5j	Azy#
Bacterial sps	A* B*	A*B*	A*B*	A*B*	A*B*	A*B*	A*B*	A*B*	A*B*	A* B*	
Gram Positive											
S aureus	02 05	03 05	08 11	06 07	06 09	03 04	04 07	07 12	07 09	11	13
B. subtilis	03 05	04 06	07 10	03 04	06 07	02 06	04 06	08 11	05 07	08	14
B. cereus	02 04	03 05	06 11	02 04	07 09	03 05	04 05	06 09	04 06	09	16
Gram negative											
K pneumonia	03 06	04 05	08 13	03 05	08 09	04 06	05 07	05 08	05 08	06	16
E coli	02 04	03 05	07 09	02 03	07 08	03 05	02 06	09 14	04 06	10	18
S typhi	0 0	0 0	0 0	0 0	0 0	0 0	0 0	0 0	0 0	0 0	15
A *and B* Conc. of test compounds			10, 20	µg/ml							
# Conc. of Azythromycin			10	µg/ml							

4.0 DISCUSSION

Our efforts were focused on the evaluation of different a solvents towards the efficient synthesis of compound (1) by using catalytic amount of $NaHSO_4$-SiO_2 in reflux with ethanol high yield the desired product (1). Among the solvents used ethanol has proved as the best solvent for condensation reaction, as because of reaction was completed in 4 h under reflux condition. $NaHSO_4$-SiO_2 is a heterogeneous catalyst. This method is simple and convenient, eco friendly the target compound were synthesized according to procedure and confirmed by means of IR, and 1HNMR spectral analysis and which are showing promising antibacterial activity. As the compound (1) is already reported to possess several pharmacological activities [21-28], the current studies are emphasized majorly on the activities of compound 5 and its derivatives. The speculated reasons for the highest antibacterial activities of the compounds 5h, 5c, 5j and 5e is might be due to the presence of chlorine and fluorine as substituents as well as sulfonyl group in their structure.

5.0 CONCLUSION

The present study reports are successful synthesis of title compounds in good yields and moderate to potent antibacterial activities.

ACKNOWLEDGEMENT

We sincerely thank the Head Department of Chemistry, Kakatiya University for his support and encouragement

REFERENCES

1. Kamal Shah, Sumit Chhabra, Sushant K, Shrivastava, Pradeep Mishra, Benzimidazoles: a promising pharmacophore; Med Chem. Res, 22(11): 5077-5104, (2013).
2. Nehal M, Elwan A, Facile synthesis of pyrrolo[1,2-a] benzimidazoles and Pyrazolo [3, 4:40, 30] pyrrolo [1, 2-a] benzimidazoles derivatives; Tetrahedron, 60(51): 1161–1166, (2004).
3. Shadia A Galala, Ahmed S Abdelsamiea, Mireya L Rodriguezb, Sean M Kerwinb and Hoda I El Diwania, Synthesis and studying the antitumor activity of novel 5-(2-methylbenzimidazol-5-yl) -1, 3, 4-oxadiazole-2 (3*H*) -thiones; *Eur.J.Chem* 1(2): 67-72, (2010).
4. Nguyen PT M, Baldeck JD, Olsson J, Marquis R E, Antimicrobial actions of Benzimidazoles against oral streptococci; Oral Microbiology Immunology: 20 (2): 93-100, (2005).
5. Priyal Jain, Vaibhav Jain, Abhishek K Jain, Pradeep K Singour, Synthesis Antimicrobial Activity and Chemotherapeutic Potential some Novel Benzimidazole Derivatives; International Journal of Drug Design and Discovery, 2 (4): 633-636, (2011).
6. Townsend LB, Wise DS, The Synthesis and Chemistry of Certain Anthelmintic Benzimidazoles, Parasitology Today, 6(4), 107- (1990).
7. Zienab M, Nofa L, Elsyed A, Soliman, Somia S, Karam ABD EL, Magdy, Zahar EL, Aladdin M, Srour, Shalini , Sethumadhavan and Timothy J, Maher, Novel Benzimidazole derivatives as expected anti cancer agents, Acta Poloniac Pharmaceutica Drug Reasearch, 68 (4): 519-534, (2011).
8. Desai NC, Amit M, Dodiya Niraj,Shihory R, A search of novel antimicrobial based on benzimidazoles and 2-pyridone heterocycles, Med Chem. Res, 21(9): 2579–2586, (2012).
9. Shushank Dixit, Pramod Kumar Sharma, Niranjan Kaushik, Synthesis of novel benzimidazole derivatives: as potent analgesic Agent. Med Chem. Res 22 (2): 900–904, (2013).
10. Hasan Kuçukbay, Riza Durmazt, Nihat Sirecitt, Selami Günalt, Synthesis of Some Benzimidazole Derivatives and Their Antibacterial and Antifungal Activities, Asian Journal of Chemistry 21(8): 6181-6189, (2009).
11. Anshul Chawla, Ramandeep Kaur, Anju Goyal, Importance of Microwave Reactions in the Synthesis of Novel Benzimidazole Derivatives: A Review, J. Chem. Pharm. Res, 3(6): 925-944, (2011).
12. Qanei Nassab S, Bayat Z, Movaffagh J, A DFT-Based QSARs Study of Benzimidazoles Drugs Derivatives; J. Chem. Pharm. Res, 3(1):64-71, (2011).
13. Atul Chaskara, Vikas Padalkar , Kiran Phatangare , Santosh Takale, Kaliyappan Murugan, An efficient and practical synthesis of 1-aryl-1H,3H-thiazolo[3,4a] benzimidazole using silica-supported sodium hydrogen sulfate as a heterogeneous catalyst, Green Chemistry Letters and Reviews, 6(3): 217-221, (2013).
14. Muhammad Khatta , Shadia A, Galal , Fatma A, Raga F, Hoda I, Diwani El, Different synthetic routes to 4-(1H-benzo[d] imidazol-2-yl) aniline, Res Chem. Intermed , 39(7): 2917-2923, (2012).
15. Sreena K, Ratheesh R, Rachana M, Poornima M, Shyni C; Synthesis and Anthelmintic Activity of Benzimidazole Derivatives; Hygeia**,** 1(1): 21-22, (2009).
16. Chikalia KH, Naik T K, Studies on synthesis of pyramidine derivatives and their biological evaluation, E-Journal of chemistry, 4(1): 60-66, (2007).
17. Kotaiah S, Ramadevi B, Naidu A, Dubey PK, Studies on synthesis of 2-(1-(1*H*-benzo (d) imidazol-2-yl) ethylthio)-6-methylpyrimidin-4-ol of potential

pharmacological interest; Der Pharma Chemica, 3(5): 198-201, (2011).

18. Turan- Zitouni G, Seref Demirayak , Ahmed Ozdemir, Zafar Asim Kaplancikli, Mehmet Taha Yildiz, Synthesis of some 2-(-(benzazol-2-yl) thioacetylamino) thiazole derivatives and their anti microbial activity and toxicity, European Journal of Medicinal Chemistry 39 (3): 267-272, (2003).
19. Seenaiah D, Venkatesh BC, Padmaja A, Padmavathi V, Synthesis of some new oxazolinyl/thiazolinyl/imidazolinyl – benzoxazoles, benzthiazoles and benzimidazoles Indian J. Chem, 52B: 942-948, (2013).
20. Raman BV, Sai Ramkishore A, Uma Maheshwari M and Radhakrishnan TM. Antibacterial activities of some folk medicinal plants of Eastern Ghats. *J Pure & Appl. Microbiol*, 3 (1), 2009, 187-194.
21. Alper S, Arpaci OT, Aki ES¸ Yalcin I, Some new bi- and ter-benzimidazole derivatives as topoisomerase I inhibitors. IL Farm. 58 (7): 497–507, (2003).
22. Shunya T, Hiroyoshi K, Montowo N, Design and synthesis of a heparanase inhibitor with pseudodisaccharide structure. Tetrahedron 57 (32): 6915–6926, (2001).
23. Jeffrey CP, Murty C, Josh C, Irene F, Lloyd G, Daniel G, Diane H, Christine H, James J, Wenling K, Gregory SK, Joseph TL, Charles M, John M, John R, Linda S, Jay W, 2-Phenyl-4- piperazinylbenzimidazoles: orally active inhibitors of the gonadotropin releasing hormone (GnRH) receptor, Bioorg. Med. Chem, 16 (13): 6617–6640, (2008).
24. Skibo EB, Schulz WG, Pyrrolo [1,2-a] benzimidazole-based aziridinyl quinones. A new class of DNA cleaving agent exhibiting G and A base specificity, J. Med. Chem. 36 (21): 3050–3055, (1993).
25. Katritzky AR, Dobchev DA, Fara DC, Karelson M, QSAR studies on 1-phenyl benzimidazoles as inhibitors of the platelet derived growth factor. Bioorg. Med. Chem. 13 (24): 6598–6608, (2005).
26. Rao A, Chimirri A, De Clercq E, Monforte AM, Monforte P, Pannecouque C, Zappala M, Synthesis and anti-HIV activity of 1-(2,6-difluorophenyl)-1H,3H-thiazolo[3,4-a] benzimidazole structurally-related 1,2-substituted benzimidazoles, IL Farm. 57 (10): 819–823, (2002).
27. Hwu JR, Singha R, Hong S.C, Chang YH, Das AR, Vliegen I., De Clerq E, Neyts J, Synthesis of new benzimidazole-coumarin conjugates as anti-hepatitis C virus agents. Antivir. Res. 77 (2): 157–162, (2008).
28. Evers DL, Komazin G, Shin D, Hwang DD, Townsend LB, Drach JC, Interactions among antiviral drugs acting late in the replication cycle of human cytomegalovirus. Antivir. Res. 56 (1): 61–72, (2002).