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Research Article

Synthesis of novel pyridine linked to benzimidazole via sulphide and their Antioxident and Antimicrobial activity

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Abstract: In this communication, we synthesized a series of eleven novel 2-(2-(1H-benzo[d]imidazol-2-ylthio) ethyl)-3-methyl-4 H-pyrido [1,2-a] pyrimidin-4-one analogues, characterized using various spectroscopic techniques and evaluated for their antioxidant and antimicrobial activities. Among the tested compounds, compound 8d and 9 shows good antioxidant activity and compound 8d shows excellent antibacterial activity.

Keywords: Pyridine, benzimidazole, antioxidant, and antimicrobial.

INTRODUCTION

Pyridine and benzimidazole constitute one of the most important families of heterocyclic compounds as they play significant interest in medicinal chemistry. Since many of pyridine and benzimidazole derivatives display remarkable biological activity, their syntheses and transformations have been received particular interest for a long time. The derivatives like 1-benzeneacyl-2-(1-methylindol-3-yl)-



benzimidazole derivatives found to exhibit as potential tubulin polymerization inhibition¹properties. Benzimidazole derivatives were explored as potential anti-HIV-1 replication and inhibit the HIV-1 replication² with an IC₅₀ value of 2.30 nM and 60.52 nM. 2-(imidazo [2, 1-*b*][1, 3, 4] thiadiazol-5-yl)-1*H*-benzimidazole derivatives showed potent anti-tubercular activity³ with a MIC of 3.125 µg/mL. Ethyl 2-(4-(trifluoromethyl)phenyl)-1-(2-morpholinoethyl)-1H-benzo[d] imidazole-5-carboxylate was found to be the most promising inhibitor of *Mycobacterium tuberculosis* H37Rv active⁴ with IC₅₀ of 11.52 µM. Benzimidazole bearing 2-pyridones derivatives ware evaluated for their *in vitro* antibacterial and found to possess significant broad spectrum antibacterial activity (12.5–100 µg/mL of MIC)⁵.Pyrimidiny-lbismethyl thiobenzimidazole derivatives was a potent antimicrobial agent particularly against *Staphylococcus aureus* (MIC12.5 µg/mL)⁶.1,3-diphenyl-1H-pyrazole derivatives containing benzimidazole skeleton as potent anticancer⁷, anti-microbial⁸.

Pyridine derivatives like pyrazolel–quinoline–pyridine derivatives showed effective antibacterial as well as anticancer activity⁹. Imidazo [4, 5-*c*] pyridine derivatives displayed promising antimicrobial activity¹⁰. Pyridine derivatives displayed antimicrobial activity¹¹⁻⁶. Anti-cancer¹⁷⁻¹⁹, Anti-tumor²⁰⁻²², Anti-Psychotic²³, Anti-proliferative²⁴⁻²⁶. Based on the above information, we have identified novel Pyridine derivatives endowed with anti oxidantand antimicrobial activities. This prompted us to synthesize the benzimidazole derivatives.

2. CHEMISTRY

The synthesis of compounds [8(a-d) and 9] was accomplished as shown in Scheme 1. Initially the compounds 3-(2-((1H-benzo[d]imidazol-2-yl)thio)ethyl)-2-methyl-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidin-4-one derivatives was prepared starting from amino pyridine. Mixture of 2-aminopyridine (1) and 3-acetyldihydrofuran-2(3H)-one (2) was treated with POCl₃ (Phosphoryltrichloride) to yield pyridopyrimidine derivative (3). Hydrogenation of compound (3) using Pd/c (10% w/w) in methanol under hydrogen pressure maintained for 48hrs to get compound (4). Substituted benzo[d]imidazole-2-thiol was treated with compound (3 and 4) in presence of sodium hydroxide solution to get desired compound (6(a-c) and 7(a-c)). The obtained compounds was treated with different alkyl halides in DMF in presence of tri ethyl amine to get desired compounds (8(a-d) and 9) which contains benzimidazole and Pyridopyrimidines.

3. EXPERIMENTAL SECTION

All the melting points of the synthesized compounds were taken by open capillary method using electric melting point apparatus and are uncorrected. The IR spectra were recorded on Agilent FT-IR Spectrophotometer. ¹H NMR spectra were recorded on a Bruker 400 MHz spectrometer. ¹³C NMR spectra were recorded on Bruker 100 MHz spectrometer by using DMSO-d₆ as a solvent and TMS as an internal standard. The chemical shifts are expressed in δ ppm. The LC-MS spectra were recorded using Agilent-Single Quartz. The purity of the compounds was checked by TLC.

3.1. General procedure for the preparation of compounds 8(a-d) and 9: Initially the compounds 3-(2-((1H-benzo[d]imidazol-2-yl)thio)ethyl)-2-methyl-6,7,8,9-tetrahydo-4H-pyrido[1,2-a]pyrimidin-4-one derivatives was prepared starting from amino pyridine.

Mixture of 2-aminopyridine (10.4 m mol) **[1]** and 3-acetyldihydrofuran-2(3H)-one (10.4 m mol) **[2]** were taken in a RB flask and was cooled to 0-5°C. POCl₃ (Phosphoryltrichloride) was added Slowlyto the

reaction mass at 0-5°C and allow it to room temperature and then heated to 85-95°C and reaction was monitored by TLC. Once reaction was completed, excess POCl₃was removed by distillation. It was poured to ice water slowly drop wise and allowed to room temperature and extracted with ethyl acetate. Ethyl acetate layer was concentrated to dryness to get desired compound [3].Compound [3] (18g, 8 m mol) was dissolved in 10V of methanol, 0.5gof Pd/C (10% w/w) and maintained for 48hrs at 3-4 Kg pressure. The reaction was monitored by TLC. After the reaction, mass was filtered through celite bed and concentrated through reduced presser. The residue was dissolved in water to get white precipitate. The mass was filtered and dried under vacuum to get desired compound [4].



Scheme 1.Synthesis of compound 8(a-d) and 9. Reagents and conditions: (a) $POCl_3at 95^{\circ}C$. 1h; (b) Pd/C (10% w/w), 3-4Kg Pressure for 48hrs; (c) Sodium hydroxide solution for 2-3 hrs; (d) Alkyl halide, DMF.

Sl. No	Compound	R	R 1	Yield (%)	Mass
1.	6a	-OCHF ₂	Н	88	402.1
2.	бb	Н	Н	90	336.1
3.	бс	Cl	Н	85	370.07
4.	7a	-OCHF ₂	Н	95	406.13
5.	7b	Н	Н	93	340.14
6.	7c	Cl	Н	88	374.1
7.	8a	Н	-(CH ₂) ₃ Cl	76	412.11
8.	8b	Cl	-(CH ₂) ₃ Cl	65	446.07
9.	8c	Н	-C ₂ H ₅	92	364.14
10.	8d	-OCHF ₂	-(CH ₂) ₃ Cl	68	478.1
11.	9	Cl	-(CH ₂) ₃ Cl	64	450.10

Fable 1:	List	of	compounds
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Fig. 1. Numbering of the compound (6b)

Substituted benzo[d]imidazole-2-thiol [5] (8 m mol) was dissolved in sodium hydroxide solution (17.8 m molin 10V of water) and stirred for 15 min to get clear solution. Compound [3 and 4] (8 m mol) was dissolved in acetonitrile (10V) and added to the reaction mass drop wise slowly and stirred for 2-3 hrs at room temperature. The reaction was monitored by TLC, after completion of reaction, reaction mass was filtered and washed with dilute sodium hydroxide solution and followed by water wash and dried under vacuum to get desired compounds[6 (a-c)and 7 (a-c)].

The obtained compound [6 (a-c) and 7] was dissolved in DMF to that tri ethyl amine was added. Different alkyl halides was added slowly and reaction monitored by TLC. Once reaction was completed mass was diluted with water (20V) and extracted with ethyl acetate. To the ethyl acetate layer water wash was given followed by concentrated to dryness to get crude N-alkyl substituted compounds The crude product was dried and recrystallized from 1:3 ethyl acetate and heptane to obtained an off white solid[8(a-d) and 9].

(3.1.1). 3-(2-((6-(difluoromethoxy)-1H-benzo [d]imidazol-2-yl) thio) ethyl)-2-methyl-4H-pyrido [1,2-a] pyrimidin-4-one (6a):as off white solid. m.p.: 138-141°C; IR (KBr).:¹H NMR (400 MHz, DMSO) δ: 12.70 (S, 1H); 8.9-8.88(d, 1H, J=6Hz); 7.88-7.83(t, 1H, J=6Hz); 7.56-7.53 (d, 1H, J=9Hz); 7.48-7.35(m, 1H); 7.31-7.26(m, 1H); 7.18-7.16 (d, 1H, J=6Hz); 6.96-6.91(m,1H); 3.53-3.48 (t, 2H, J=6Hz); 3.13-3.08 9t, J=6Hz); 2.47(s, 3H). EI MS (m/z): 403.1(M+H). Anal.calcd. for C₁₉H₁₆F₂N₄O₂S (402.1)

(3.1.2). *3-(2-((1H-benzo[d]imidazol-2-yl)thio)ethyl)-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one(6b):as o*ff white solid. m.p.: 141-145°C; IR (KBr).:¹H NMR (400 MHz, DMSO) δ: 12.56(s, 1H); 8.91-8.89 (d, 1H, J=6Hz); 7.89-7.86 (t, 1H, J=6Hz); 7.57-7.54(d, 1H, J=9Hz); 7.47-7.35 (m, 2H); 7.31-7.27 (t, 1H, J=6Hz); 7.12-7.09 (m, 2H); 3.52-3.47 (t, 2H, J=6Hz); 3.13-3.08 (t, 2H, J=6Hz); 2.48 (s, 3H). EI MS(m/z): 337.1133(M+H). Anal.Calcd.for C₁₈H₁₆N₄OS (336.1).

(3.1.3). 3-(2-((6-chloro-1H-benzo[d]imidazol-2-yl)thio)ethyl)-2-methyl-4H-pyrido[1,2-a]pyrimidin-4one(6c):as off white solid. m.p.: 148-152°C; IR (KBr).:¹H NMR (400 MHz, DMSO) δ : 12.6887 (s, 1H); 8.848-8.831 (d, 1H, J=6Hz); 7.820-7.778(m, 1H); 7.489-7.467 (d, 1H, J=6Hz); 7.39-7.382 (m, 1H); 7.251-7.214 (t, 1H, J= 6Hz); 7.07-7.05 (d, 1H, J=6Hz); 3.478-3.443 (t, 2H, J= 6Hz); 3.07-3.03 (t, 2H, J=6Hz); 2.424 (s, 3H).¹³C NMR (100 MHz, DMSO) δ : 162.221, 157.521, 148.59, 136.604, 126.989, 125.762, 121.798, 116.08, 112.522, 30.096, 27.545, 22.814. EI MS (m/z): 370.052(M+H). Anal.Calcd.for C₁₈H₁₅ClN₄OS (370.07).

(3.1.4).3-(2-((6-(difluoromethoxy)-1H-benzo[d]imidazol-2-yl)thio)ethyl)-2-methyl-6,7,8,9-tetra hydro -4H-pyrido[1,2-a]pyrimidin-4-one(7a):as off white solid. m.p.: 136-138°C; IR (KBr).:¹H NMR (400 MHz, DMSO) δ : 12.626 (s, 1H); 7.481-7.27 (m, 2H); 7.133-7.119 (d, 1H, J=3Hz); 6.945-6.933 (d, 1H, J= 3Hz); 3.754-3.723 (t, 2H, J= 6Hz); 3.38-3.350 (t, 2H, J=6Hz); 2.876-2.842 (t, 3H, J=6Hz); 2.185 (s, 3H); 1.826-1.796(t, 2H, J=6Hz); 1.723-1.676 (m, 2H). ¹³C NMR (100 MHz, DMSO) δ : 162.026, 159.144, 157.004, 151.7, 146.243, 144.572, 141.787, 133.415, 118.326, 118.011, 117.406, 114.322, 113.87, 111.182, 108.324, 101.817, 42.569, 31.178, 30.185, 26.98, 21.668, 21.571, 18.882. EI MS (m/z): 407.1129(M+H). Anal.calcd. for C₁₉H₂₀F₂N₄O₂S (406.13).

(3.1.5). 3-(2-((1H-benzo[d]imidazol-2-yl)thio)ethyl)-2-methyl-6,7,8,9-tetrahydro-4H pyrido[1,2-a] pyrimidin-4-one(7b):as off white solid. m.p.: 141-145°C; IR (KBr).:¹H NMR (400 MHz, DMSO) δ :12.48 (s, 1H); 7.469-7.31 (m, 2H); 7.089-7.066 (m, 2H); 3.754-3.723(m, 2H), 3.754-3.723(t, 2H, J=6H); 2.877-2.841 (t, 2H, J=6Hz); 2.684-2.651 (t, 2H, J=6Hz); 2.188 (s, 3H); 1.811-1.764 (m, 2H); 1.72-1.675 (m, 2H). ¹³C NMR (100 MHz, DMSO) δ : 162.034, 159.127, 156.996, 150.505, 144.217, 135.796, 121.935, 121.467, 118.076, 117.713, 110.649, 42.561, 31.078, 30.177, 27.028, 21.668, 21.571, 18.891. EI MS (m/z): 341.1293 (M+H). Anal.calcd. for C₁₈H₂₀N₄OS (340.14).

(3.1.6).3-(2-((6-chloro-1H-benzo[d]imidazol-2-yl)thio)ethyl)-2-methyl-6,7,8,9-tetrahydro-4H-pyrido [1,2-a]pyrimidin-4-one(7c):as off white solid. m.p.: 144-147°C; IR (KBr).:¹H NMR (400 MHz, DMSO) δ :12.694 (s, 1H); 7.402 (s, 1H); 7.113-7.087 (m, 1H); 3.752-3.722 (t, 2H, J=3Hz); 3.387-3.351 (t, 2H, J=6Hz); 3.298-2.872(m, 2H); 2.854-2.837 (t, 2H, J= 6Hz); 2.675-2.643 (m, 2H); 2.181(s, 3H); 1.813-1.786 (m, 2H); 1.722-1.677(m, 2H). ¹³C NMR (100 MHz, DMSO) δ : 162.018, 159.144, 156.988, 121.838, 117.979, 42.593, 31.178, 30.152, 26.964, 21.668, 21.563, 18.882. EI MS (m/z): 375.0946 (M+H). Anal.calcd. for $C_{18}H_{19}CIN_4OS$ (374.10).

(3.1.7). 3-(2-((1-(3-chloropropyl)-1H-benzo[d]imidazol-2-yl) thio) ethyl)-2-methyl-4H pyrido[1,2-a] pyrimidin-4-one(8a):as off white solid. m.p.: 109-113°C; IR (KBr).:¹H NMR (400 MHz, DMSO) δ : 8.853-8.835 (d, 1H, J=6Hz); 7.821-7.782 (t, 1H, J=6Hz); 7.509- 7.7.440(m, 3H); 7.249-7.215(t, 1H, J=6Hz); 7.163-7.7.094 (m, 2H); 4.228-4.193 (t, 2H, J=6Hz); 3.61-3.602 (t, 2H, J=3Hz); 3.552-3.517(t, 2H, J=3Hz); 3.121-3.086 (t, 2H, J=6Hz); 2.447 (s, 3H); 2.138-2.107 (t, 2H, J=6Hz). ¹³C NMR (100 MHz, DMSO) δ : 162.219, 157.561, 151.619, 148.657, 143.498, 136.692, 127.029, 125.802, 121.943, 118.019, 116.122, 112.578, 109.688, 42.766, 41.285, 32. 251, 30.532, 27.254, 22.790. EI MS (m/z): 413.1149 (M+H). Anal.Calcd.for C₂₁H₂₁ClN₄OS (412.11).

(3.1.8).3-(2-((6-chloro-1-(3-chloropropyl)-1H-benzo[d]imidazol-2-yl)thio)ethyl)-2-methyl-4H-pyrido [1,2-a]pyrimidin-4-one(8b):as off white solid. m.p.: 112-116°C; IR (KBr).:¹H NMR (400 MHz, DMSO) δ : 8.848-8.831 (d, 1H, J= 6Hz); 7.830-7.787 (m, 1H); 7.512- 7.448 (m, 3H); 7.257-7.176 (m, 1H, J=3Hz); 7.172-7.107 (m, 1H); 4.216- 4.17(m, 2H); 3.641-3.394 (m, 2H); 3.55-3.509 (m, 2H); 3.146-3.071(m, 2H); 2.477 (s, 3H); 2.11-2.077(m, 2H). ¹³C NMR (100 MHz, DMSO) δ : 162.147, 157.545, 153.686, 148.649, 144.249, 142.239, 137.161, 136.644, 127.021, 125.770, 122.177, 119.061, 117.39, 116.09, 112.465, 110.996, 109..898, 42.641, 41.544, 39.606, 39.396, 32.106, 30.556, 27.262, 22.798. EI MS(m/z): 447.0729 (M+H). Anal.calcd. for C₂₁H₂₀ Cl₂N₄OS (446.07).

(3.1.9).3-(2-((1-ethyl-1H-benzo[d]imidazol-2-yl) thio) ethyl)-2-methyl-4H-pyrido [1, 2-a] pyrimidin-4-one (8c): as off white solid. m.p.: 106-111°C; IR (KBr).:¹H NMR (400 MHz, DMSO) δ : 7.959-7.924 (m, 1H); 7.665-7.638 (m, 1H); 7.433-7.290 (m, 3H); 4.853 (s, 2H); 3.779 (s, 3H); 3.287-2.976 (m, 4H); 2.578-2.516 (m, 2H); 2.287-2.056 (m, 2H); 1.853-1.793 (m, 2H). ¹³C NMR (100 MHz, DMSO) δ : 161.783, 156.714, 149.585, 137.258, 128.224, 124.131, 122.968, 120.498, 113.708, 109.882, 79.521, 70.324, 61.984, 56.075, 54.170, 33.688, 30.596. EI MS (m/z): 365.1431 (M+H). Anal.calcd. for C₂₀H₂₀N₄OS (364.14).

(3.1.10).3-(2-((1-(3-chloropropyl)-6-(difluoromethoxy)-1H-benzo[d]imidazol-2-yl)thio)ethyl)-2methyl -4H-pyrido[1,2-a]pyrimidin-4-one(8d):as off white solid. m.p.: 114-117°C; IR (KBr).:¹H NMR (400 MHz, DMSO) δ : 7.961-7.926 (m, 1H); 7.663-7.636 (m, 1H); 7.254-7.204 (m, 2H); 7.159-7.134 (m, 1H); 6.994-6.973 (d, 1H, J=6Hz); 3.769-3.760 (m, 1H); 3.478-3.410 (m, 4H); 2.58-2.552 (m, 2H); 2.472 (s, 3H); 2.287-2.23 (m, 2H); 2.0-1.79 (m, 2H); 1.853-1.793 (m, 2H). ¹³C NMR (100 MHz, DMSO) δ : 186.657, 179.633, 163.366, 161.783, 156.73, 150.885, 149.214, 124.252, 122.589, 120.6, 113.00, 111.96, 109.54, 97.89, 79.503, 62, 56.027, 55.962, 54.17, 33.688, 30.596. EI MS (m/z): 479.1086 (M+H). Anal.calcd. for C₂₂H₂₁ClF₂N₄O₂S (478.10).

(3.1.11). 3-(2-((6-chloro-1-(3-chloropropyl)-1H-benzo[d]imidazol-2-yl)thio)ethyl)-2-methyl-6,7,8,9tetrahydro-4H-pyrido[1,2-a]pyrimidin-4-one(9):as off white solid. m.p.: 126-129°C; IR (KBr).:¹H NMR (400 MHz, DMSO) δ: 7.961-7.926 (m, 1H); 7.663-7.636 (m, 1H); 7.254-7.204 (m, 2H); 7.159-7.134 (m, 1H); 6.994-6.973 (d, 1H, J=6Hz); 3.769-3.760 (m, 1H); 3.478-3.410 (m, 4H); 2.58-2.552 (m, 2H); 2.472 (s, 3H); 2.287-2.23 (m, 2H); 2.0-1.79 (m, 2H); 1.853-1.793 (m, 2H). ¹³C NMR (100 MHz, DMSO) δ : 186.657, 179.633, 163.366, 161.783, 156.73, 150.885, 149.214, 124.252, 122.589, 120.6, 113.00, 111.96, 109.54, 97.89, 79.503, 62, 56.027, 55.962, 54.17, 33.688, 30.596. EI MS(m/z): 451.1086 (M+H). Anal.Calcd.for C₂₁H₂₄Cl₂N₄OS (450.10).

4. MATERIALS AND METHODS

4.1. DPPH radical scavenging assay: DPPH radical scavenging assay (RSA) was determined using method described by Clarke *et al.*²⁷ with slight modification. DPPH assay was performed in 96 wells plate. The test sample $(20\mu L)$ from stock solution was added in respective to well plate and then 180 µl of DPPH solution was added in each well to make 200µl final volume. Methanol was used as reference standard. Mixture was incubated at 20-25°C for 20 minutes. Change in color from violet to yellow was observed due to the antioxidation potential. Absorbance of reaction mixture was measured at 517 nm on microplate reader. Determination of inhibition activity was calculated by given equation.

Determination of % Inhibition:



(Control)



The DPPH radical scavenging activity is demonstrated in the Fig 2

% Inhibition =

Figure 2: DPPH radical scavenging assay.

Fig 2: Antioxidant activity of compounds DPPH assay: Cells (3×10^4) were treated with test compounds at different concentrations (1, 5, 10, 50 and 100µM/ml) for 16 h, incubated with MTT solution for 4 h and the formazan crystals were dissolved in DMSO and read at 570nm. Data are presented as the mean ±SEM of three independent experiments.

4.2 Determination of antimicrobial activity: Antimicrobial activity of the synthesized six samples was determined by well diffusion method. For determination of antibacterial activity, bacterial suspensions (*E. coli*) was adjusted to 0.5 McFarland turbidity standards and inoculated onto Nutrient agar plates (diameter: 15cm). For the determination of antibacterial activity, the bacterial isolates were first adjusted to the concentration of 106 cfu/ml. Cultures of (*E. coli*) were suspended in sterile solution of 0.9% the normal saline cultures were inoculated onto Nutrient agar plates. Wells were made on agar medium using 200µl pipette tip (diameter 6mm). 10µl of compounds reconstituted in minimum amount of solvent at concentrations of 100µg/ml were applied over each of the culture plates previously seeded 106 cfu/ml cultures of bacteria. Bacterial cultures were then incubated at 37° C for 18h. Wells added with 20µl of a solution of 10mg/ml of ciprofloxacin as standard antimicrobials were used for comparison. Antimicrobial activity was determined by measurement of zone of inhibition around each well. For each extract three replicate trials were conducted against organism.

5. RESULTS

The ¹H NMR spectrum of compound (6b) $3-(2-((1H-benzo[d]imidazol-2-yl)thio)ethyl)-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one showed a singlet in the region at <math>\delta$ 12.56 due to NH proton while a doublet in the region 8.91-8.89 (J=6Hz) due to C6- proton. C3 - proton appear as triplet in the region 7.89-7.86 (J=6Hz) while C2 protonappear as doublet in the region 7.57-7.54 (J=9Hz). C5 and C9 protons appear as multiplet in the region 7.47-7.35 while C4- proton appear as a triplet in the region 7.31-7.27 (J=6Hz). C7 and C8- protonappear as multiplet in the region 7.12-7.09 and C12- proton as triplet in the region 3.52-3.47 (J=6Hz). C11- protonshows a triplet in the region 3.13-3.08 (J=6Hz) and C10 protonshows a singlet in the region 2.48ppm. The mass spectrum of the compound (6b) showed (M+H) ion at m/z 337.1133. The ¹H, ¹³C NMR and Mass spectral data of all compounds is included in the experimental section.

5.1. Antioxident activity pyridopyrimidines derivatives: The 2, 2-diphenyl-1-picryl-hydrazyl (DPPH) radical scavenging activity is a standard assay in antioxidant studies. The interaction of synthesized Pyridopyrimidines derivatives 6(a-c), 7(a-c), 8(a-d) and 9 with a stable DPPH indicates free radical scavenging ability. In this series majority of the tested compounds were shown low to moderate interaction with the DPPH radicals.

Out of eleven, six compounds (6a-6c, 7a-7c) have low antioxident activity. From remaining five compounds, three compounds 8(a-c) shown moderate activity and compound 8d and 9 shows excellent activity because of combination -OCHF₂ and alkyl chloride group in 8d and -Cland -(CH₂)₃Cl groups in compound**9** containing good inhibitory activity

5.2. Antimicrobial activity: Based on the results obtained from antioxidant, six compounds (6c, 8a-d and 9) are tested for antimicrobial activity against (*E. coli*). All the compounds inhibited moderate activity. While compound 8d shows excellent antibacterial activity because of containing $-OCHF_2$ and $-(CH2)_3Cl$ group in benzimidazole moiety.

Compounds E.	coli
Positive control	10.5
DMSO control	0.5
бс	2.2
8a	2.6
8b	4.8
8c	1.3
8d	15.6
9	3.2

Table 2: Antibacterial activity of Pyridopyrimidines derivatives



6. CONCLUSION.

We have synthesized several novel analogues of 3-(2-((1H-benzo[d]imidazol-2-yl)thio)ethyl)-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one derivatives in good yield and evaluated for their antioxident and antimicrobial activities. Among synthesis derivatives with substituted at -NH group exhibited good antioxident and antibacterial activity. Thus a new class of pyridine derivatives can be incorporated to the family of bioactivity heterocyclic.

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