

Spectral and Microbial Studies of Some Newly synthesized Schiff Base Derivatives of 2-(1H-benzo[d]oxazole-2-ylthio)-N-(4-acetylphenyl)acetamide

Jayesh Maru*, G. R. Patel, Rakesh Yadav

Department of Chemistry, Sheth M. N. Science College, NGES campus, Patan - 384265, India

*E-mail address: jay1maru@yahoo.in

ABSTRACT

The author has synthesized novel biological active compounds by condensation of N-(4-Acetylphenyl)-2-(benzoxazol-2-ylsulfanyl)-acetamide with different substituted acid hydrazide in the presence of catalytic amount of acetic acid. A series of benzoxazole having azomethine group were confirmed by various spectroscopic techniques. The new compounds were examined for antibacterial effects against different strains of bacteria and antifungal activity. The MIC values were high to lowest Minimum Inhibition Concentration (MIC) values.

Keywords: Benzoxazole; Acid hydrazide; Azomethine

1. INTRODUCTION

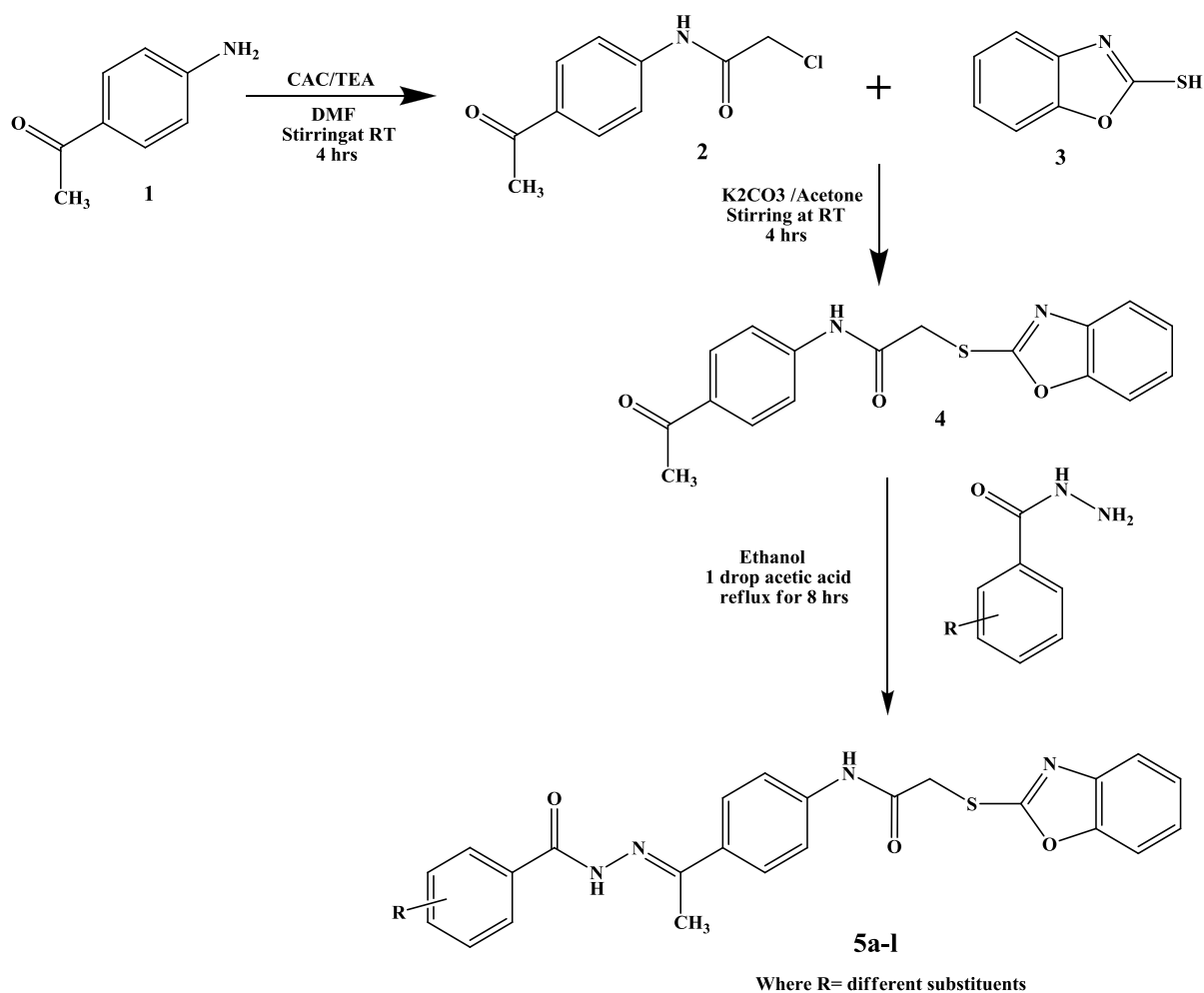
Development of antimicrobial agents for the chemotherapy of fungal and bacterial infections represents one of the most significant achievements of this decade in the field of drug chemistry. The rising emergence of acquired resistance to existing antimicrobials to fungal and bacterial infections leads us to synthesize newer antimicrobial agents. Benzoxazole nucleus is many clinically useful chemotherapeutic agents [1] shown by literature survey. Flunoxapfen is one of the most standard drug of benzoxazole moiety which acts as an anti-inflammatory [2] drug.

There are many drugs which are useful in different diseases containing benzoxazole nucleus. Benzoxazole exhibited a wide variety of interesting biological activity such as antimicrobial [3], antibacterial [4], analgesics [5], antitumor [6], anti-inflammatory [7], antifungal [8], antioxidant [9], etc. Benzoxazole also used as cyclo-oxygenase [10] inhibitors shown by literature survey.

Azomethine are products of condensation of simple or substituted acid hydrazide with simple or substituted Aceto group containing compound in the presence of catalytic amount of acetic acid in the appropriate solvent as a reaction medium and suitable condition. Azomethine constitute an important group of natural products and some of them show a wide range of biological properties such as Antifungal [11], anti-inflammatory [12], anti-bacterial [13], antioxidant [14] etc.

2. EXPERIMENTAL

All the required chemicals and solvents used for the synthesis were purchased from HIMEDIA, LOBA chemie, SDFine chemicals and/or Merck Ltd. Melting point was determined by the open end capillary method and are reported uncorrected at the primary stage. Completion of reaction was monitored by aluminum coated TLC plates (TLC silica gel 60 F₂₄₅, E. Merck) using different solvent ratio for different steps as mobile phase and spot checked under ultraviolet (UV) light. Bruker Spectrophotometer-400 MHz where Trimethylsilane(TMS) and Dimethyl sulfoxide(DMSO)-d₆ was used as solvent for the ¹H NMR and ¹³C NMR. Shimadzu mass Spectrophotometer used for the Mass spectral analysis. Bruker FT-IR alpha-t (ATR) used for the IR spectral data. Perkin-Elmer 2400 CHN Analyzer used for the elemental analysis (% C, H, N).



Scheme 1. Synthetic route for the preparation of title compounds 5a-l.

2.1. Synthesis of N-(4-acetylphenyl)-2-chloroacetamide (Comp.2)

The Synthesis of N-(4-acetylphenyl)-2-chloroacetamide (**Compound 2**) was carried out by reacting 4-amino acetophenone (0.01 mol, 135gm/mol, 1.35gm) with chloroacetylchloride (0.015 mol, 113gm/mol, 1.19 ml) and Triethylamine (4-5 drops) using DMF (30 ml) as

solvent. The reaction mixture was stirred for 4 hours used the magnetic stirrer at Room temperature. The completion of reaction was monitored by TLC with Mobile phase Toluene:Acetone (7:3). The solution was poured into ice water (50ml). The product obtained was filtered, dried and crystalline in Ethanol.

Compound 2 : Solide brown crystals; Yield 85%; M.P. 154 °C; IR (ν_{\max} , cm^{-1} , ATR): 740 (C-Cl str.), 1413 (C=C str. Aromatic ring), 1640 (C=O str.), 2750 (CH_2 str. methylene), 3049 (CH str. aromatic ring), 3232 (NH str.); ^1H NMR (400 MHz, DMSO- d_6 , δ , ppm): 2.56 (3H, s, - CH_3), 4.89 (2H, s, - CH_2), 7.70–8.10 (4H, d, Ar-H), 9.97 (1H, s, -NH); ^{13}C NMR (400 MHz, DMSO- d_6 , δ , ppm): 27.2 (C17), 43.2 (C8), 121.0 (C11), 121.0 (C15), 129.2 (C12), 129.2 (C14), 137.2 (C13), 166.0 (C9), 198.2 (C16); (MS (m/z): 212 (M^+); Elemental Analysis: C, 56.69; H, 4.79; N, 16.88%.

2.2. Synthesis of N-(4-Acetylphenyl)-2-(benzo[d]oxazol-2-ylthio)acetamide (Comp.4)

N-(4-acetylphenyl)-2-chloroacetamide (**2**) (0.01 mol, 211.5gm/mol, 2.11gm) was further reacted with 2-mercatobenoxazole (**3**) (0.01 mol, 151.20 gm/mol, 1.51 gm). The reaction was stirred at room temperature for 4 hrs in presence of K_2CO_3 (0.02 mol, 138gm/mol, 2.76gm) and acetone (25 ml) as a reaction medium. The completion of reaction was monitored by TLC using Toluene: Acetone (8:2) as a mobile phase, product was poured into water and stirred for 1 hr. The obtained precipitate were collected and dried. The product was crystallized into methanol.

Compound 4: Solid cream yellow; Yield: 81 %; M.P.: 164 °C; IR (ν_{\max} , cm^{-1} , ATR): 1413 (C=C str. aromatic ring), 1640 (C=O str.), 2750 (CH_2 str. methylene), 3049 (CH str. Aromatic ring), 3232 (NH str.); ^1H NMR (400 MHz, DMSO- d_6 , δ , ppm): 2.56 (3H, s, - CH_3), 4.89 (2H, s, - CH_2), 7.30–8.10 (8H, d, Ar-H), 9.21 (1H,s,-NH); ^{13}C NMR (400 MHz, DMSO- d_6 , d, ppm): 27.2 (C17), 39.2 (C8), 112.6(C2) , 121.3(C5) , 121.0 (C11) , 121.0(C15) , 124.1(C3) , 124.1(C4) , 129.2(C12) , 129.2 (C14), 137.2 (C13), 152.3 (C1), 141.8.0 (C6), 142.2 (C10), 153.8 (C7), 166.0 (C9), 198.2 (C16); MS (m/z): 326 (M^+); Elemental Analysis: C, 59.55; H, 4.22; N, 08.35%.

2.3. General procedure for the synthesis of the title compounds 5a–l

N-(4-Acetylphenyl)-2-(benzo[d]oxazol-2-ylthio)acetamide (Comp.4) (0.01 mol, 326gm/mol, 3.26gm) was further treated with different substituted acid hydrazide (0.01 mol) in ethanol (20ml) in the presence of catalytic amount of acetic acid and 4-5 drops of fused sodium acetate and refluxed for 8 hours. The completion of the reaction was monitored by the TLC using Toluene : Acetone (8:2) as mobile phase. Resulting solid was separated out, filtered, and washed with water, dried and crystallized by alcohol (99.9%) [15]. Melting points of each synthesized compound were measured by electrical melting point apparatus. The products were designated as 5a–l and characterized by elemental, IR, NMR, CMR and MS analyses.

2.3.1. Physical constant and characterization of 2-(benzo[d]oxazol-2-ylthio)-N-(4-(1-(2-benzoylhydrazono)ethyl)phenyl) acetamide (5a)

Yield: 72 %; M.P.: 194 – 196 °C; ^1H NMR (400 MHz, DMSO- δ_6 , δ , ppm): 2.32 (3H, s, - CH_3), 4.10 (2H, s, - CH_2), 7.60–8.09 (13H, d, Ar-H), 7.16 (1H, s, -NH); ^{13}C NMR (400

MHz, DMSO- δ_6 , δ , ppm): 16.9, 38.4, 110.7, 119.5, 121.7, 121.7, 123.5, 124.5, 127.8, 127.8, 128.6, 128.6, 129.7, 129.7, 132.3, 132.8, 133.4, 140.7, 141.5, 147.8, 151.6, 163.6, 165.1, 168.2; MS (m/z): 444 (M^+); Elemental Analysis: C, 64.23; H, 4.57; N, 12.66%.

2.3.2. Physical constant and characterization of 2-(benzo[d]oxazol-2-ylthio)-N-(4-(1-(2-(3-nitrobenzoyl)hydrazono)ethyl)phenyl)acetamide (5b)

Yield: 74 %; M.P.: 205 – 207 °C; ¹H NMR (400 MHz, DMSO- δ_6 , δ , ppm): 2.33 (3H, s, -CH₃), 4.09 (2H, s, -CH₂), 7.58–8.75 (12H, d, Ar-H), 7.28 (1H, s, -NH); ¹³C NMR (400 MHz, DMSO- δ_6 , δ , ppm): 16.7, 38.5, 110.6, 119.1, 121.7, 121.7, 123.3, 123.8, 124.8, 127.3, 129.4, 129.4, 129.7, 132.1, 133.1, 133.6, 135.1, 140.8, 141.5, 148.0, 151.9, 163.2, 165.0, 168.2; MS (m/z): 490 (M^+); Elemental Analysis: C, 58.93; H, 3.92; N, 14.24%.

2.3.3. Physical constant and characterization of 2-(benzo[d]oxazol-2-ylthio)-N-(4-(1-(2-(4-nitrobenzoyl)hydrazono)ethyl)phenyl) acetamide (5c)

Yield: 77 %; M.P.: 210 – 212 °C; ¹H NMR (400 MHz, DMSO- δ_6 , δ , ppm): 2.33 (3H, s, -CH₃), 4.05 (2H, s, -CH₂), 7.60–8.45 (12H, d, Ar-H), 7.16 (1H, s, -NH); ¹³C NMR (400 MHz, DMSO- δ_6 , δ , ppm): 16.9, 39.4, 110.3, 119.7, 121.7, 121.7, 123.7, 124.2, 124.2, 125.0, 128.9, 128.9, 129.2, 129.2, 133.4, 137.6, 138.6, 141.5, 147.5, 151.4, 151.9, 163.4, 165.2, 168.3; MS (m/z): 489 (M^+); Elemental Analysis: C, 58.43; H, 3.94; N, 14.52%.

2.3.4. Physical constant and characterization of 2-(benzo[d]oxazol-2-ylthio)-N-(4-(1-(2-(3-methylbenzoyl)hydrazono)ethyl)phenyl) acetamide (5d)

Yield: 65 %; M.P.: 204 – 206 °C; ¹H NMR (400 MHz, DMSO- δ_6 , δ , ppm): 2.30-2.36 (6H, s, -CH₃), 4.08 (2H, s, -CH₂), 7.32–7.95 (12H, d, Ar-H), 7.34 (1H, s, -NH); ¹³C NMR (400 MHz, DMSO- δ_6 , δ , ppm): 16.4, 21.8, 38.9, 114.8, 116.2, 121.4, 121.4, 123.3, 123.8, 124.5, 128.1, 128.4, 129.6, 129.6, 131.5, 134.5, 136.6, 137.9, 138.2, 139.3, 140.0, 145.9, 147.4, 163.6, 167.6; MS (m/z): 458 (M^+); Elemental Analysis: C, 65.66; H, 4.74; N, 12.30%.

2.3.5. Physical constant and characterization of 2-(benzo[d]oxazol-2-ylthio)-N-(4-(1-(2-(4-methylbenzoyl)hydrazono)ethyl)phenyl) acetamide (5e)

Yield: 66 %; M.P.: 202 – 204 °C; ¹H NMR (400 MHz, DMSO- δ_6 , δ , ppm): 2.30-2.37 (6H, s, -CH₃), 4.14 (2H, s, -CH₂), 7.36–7.98 (12H, d, Ar-H), 6.91 (1H, s, -NH); ¹³C NMR (400 MHz, DMSO- δ_6 , δ , ppm): 16.8, 21.2, 38.4, 110.5, 119.2, 121.4, 121.4, 123.7, 124.6, 127.3, 127.3, 129.1, 129.1, 129.5, 129.5, 129.9, 133.4, 140.7, 141.6, 141.8, 147.6, 151.9, 163.3, 165.2, 168.4; MS (m/z): 459 (M^+); Elemental Analysis: C, 65.45; H, 4.82; N, 12.35%.

2.3.6. Physical constant and characterization of 2-(benzo[d]oxazol-2-ylthio)-N-(4-(1-(2-(4-methoxybenzoyl)hydrazono)ethyl)phenyl) acetamide (5f)

Yield: 66 %; M.P.: 210 – 212 °C; ¹H NMR (400 MHz, DMSO- δ_6 , δ , ppm): 2.29-3.85 (6H, s, -CH₃), 4.08 (2H, s, -CH₂), 7.15–7.98 (12H, d, Ar-H), 7.22 (1H, s, -NH); ¹³C NMR (400 MHz, DMSO- δ_6 , δ , ppm): 16.8, 38.4, 55.3, 110.5, 114.5, 114.5, 119.2, 121.4, 121.4,

123.7, 124.6, 128.3, 128.3, 129.5, 129.5, 129.9, 133.4, 140.7, 141.6, 147.6, 151.9, 163.3, 164.1, 165.2, 168.4; MS (m/z): 474 (M^+); Elemental Analysis: C, 63.37; H, 4.82; N, 11.85%.

2.3.7. Physical constant and characterization of 2-(benzo[d]oxazol-2-ylthio)-N-(4-(1-(2-(2-chlorobenzoyl)hydrazono)ethyl)phenyl) acetamide (5g)

Yield: 70 %; M.P.: 212 – 214 °C; ^1H NMR (400 MHz, DMSO- δ_6 , δ , ppm): 2.36 (3H, s, $-\text{CH}_3$), 4.14 (2H, s, $-\text{CH}_2$), 7.41–8.04 (12H, d, Ar-H), 7.14 (1H, s, $-\text{NH}$); ^{13}C NMR (400 MHz, DMSO- δ_6 , δ , ppm): 16.8, 38.4, 110.5, 119.2, 121.4, 121.4, 124.6, 126.3, 128.6, 129.5, 129.5, 129.9, 130.2, 132.3, 133.3, 133.6, 134.7, 140.7, 147.6, 151.9, 163.3, 164.1, 165.2, 168.4; MS (m/z): 480 (M^+); Elemental Analysis: C, 61.02; H, 4.04; N, 11.72%.

2.3.8. Physical constant and characterization of 2-(benzo[d]oxazol-2-ylthio)-N-(4-(1-(2-(3-chlorobenzoyl)hydrazono)ethyl)phenyl) acetamide (5h)

Yield: 71 %; M.P.: 214 – 216 °C; ^1H NMR (400 MHz, DMSO- δ_6 , δ , ppm): 2.32 (3H, s, $-\text{CH}_3$), 4.08 (2H, s, $-\text{CH}_2$), 7.40–7.99 (12H, d, Ar-H), 7.05 (H, s, $-\text{NH}$); ^{13}C NMR (400 MHz, DMSO- δ_6 , δ , ppm): 16.4, 39.4, 110.6, 119.4, 121.6, 121.6, 124.3, 126.3, 128.9, 129.9, 129.9, 130.1, 130.6, 132.6, 133.5, 133.5, 134.8, 140.4, 147.6, 151.6, 163.8, 164.2, 165.5, 168.0; MS (m/z): 480 (M^+); Elemental Analysis: C, 60.21; H, 4.14; N, 11.73%.

2.3.9. Physical constant and characterization of 2-(benzo[d]oxazol-2-ylthio)-N-(4-(1-(2-(4-chlorobenzoyl)hydrazono)ethyl)phenyl) acetamide (5i)

Yield: 71 %; M.P.: 210 – 212 °C; ^1H NMR (400 MHz, DMSO- δ_6 , δ , ppm): 2.32 (3H, s, $-\text{CH}_3$), 4.05 (2H, s, $-\text{CH}_2$), 7.40–8.04 (12H, d, Ar-H), 7.27 (1H, s, $-\text{NH}$); ^{13}C NMR (400 MHz, DMSO- δ_6 , δ , ppm): 16.6, 39.6, 110.8, 119.4, 121.6, 121.6, 124.4, 128.9, 128.9, 129.9, 129.9, 130.1, 130.1, 132.7, 133.7, 133.7, 134.9, 140.4, 147.6, 151.9, 163.7, 164.2, 165.5, 168.2; MS (m/z): 479 (M^+); Elemental Analysis: C, 60.23; H, 4.13; N, 11.62%.

2.3.10. Physical constant and characterization of 2-(benzo[d]oxazol-2-ylthio)-N-(4-(1-(2-(2-hydroxybenzoyl)hydrazono)ethyl)phenyl) acetamide (5j)

Yield: 65 %; M.P.: 216 – 218 °C; ^1H NMR (400 MHz, DMSO- δ_6 , δ , ppm): 2.32 (3H, s, $-\text{CH}_3$), 5.34 (1H, s, $-\text{OH}$), 4.06 (2H, s, $-\text{CH}_2$), 7.12–7.78 (12H, d, Ar-H), 7.19 (1H, s, $-\text{NH}$); ^{13}C NMR (400 MHz, DMSO- δ_6 , δ , ppm): 16.2, 38.5, 110.3, 117.4, 117.9, 119.4, 121.2, 121.7, 121.7, 123.5, 124.6, 128.9, 129.3, 133.1, 133.6, 140.9, 141.7, 147.8, 151.6, 153.4, 159.8, 163.5, 165.0, 165.4; MS (m/z): 460 (M^+); Elemental Analysis: C, 62.45; H, 4.38; N, 12.19%.

2.3.11. Physical constant and characterization of 2-(benzo[d]oxazol-2-ylthio)-N-(4-(1-(2-(3-hydroxybenzoyl)hydrazono)ethyl)phenyl) acetamide (5k)

Yield: 61 %; M.P.: 226 – 228 °C; ^1H NMR (400 MHz, DMSO- δ_6 , δ , ppm): 2.32 (3H, s, $-\text{CH}_3$), 5.32 (1H, s, $-\text{OH}$), 4.15 (2H, s, $-\text{CH}_2$), 7.10–7.82 (12H, d, Ar-H), 7.34 (1H, s, $-\text{NH}$); ^{13}C NMR (400 MHz, DMSO- δ_6 , δ , ppm): 16.6, 38.7, 110.3, 117.6, 117.6, 119.4, 121.1,

121.8, 121.8, 123.3, 124.4, 128.7, 129.3, 133.0, 133.7, 140.8, 141.7, 147.9, 151.5, 153.4, 159.6, 163.8, 165.0, 165.5; MS (m/z): 461 (M^+); Elemental Analysis: C, 62.24; H, 4.26; N, 12.22%.

2.3.12. Physical constant and characterization of 2-(benzo[d]oxazol-2-ylthio)-N-(4-(1-(2-(4-hydroxybenzoyl)hydrazono)ethyl)phenyl) acetamide (5l)

Yield: 67 %; M.P.: 220 – 222 °C; ^1H NMR (400 MHz, DMSO- δ , ppm): 2.25 (3H, s, $-\text{CH}_3$), 5.37 (1H, s, $-\text{OH}$), 4.12 (2H, s, $-\text{CH}_2$), 7.04–7.77 (12H, d, Ar-H), 7.04 (1H, s, $-\text{NH}$); ^{13}C NMR (400 MHz, DMSO- δ , ppm): 16.4, 38.6, 110.4, 116.2, 116.2, 119.4, 121.8, 121.8, 123.9, 124.6, 125.5, 128.9, 128.9, 129.5, 129.5, 133.2, 140.9, 141.4, 147.8, 151.9, 161.9, 163.5, 165.2, 168.3; MS (m/z): 460 (M^+); Elemental Analysis: C, 62.62; H, 4.56; N, 12.46%.

3. RESULTS AND DISCUSSION

Scheme 1 was completed by three different steps and final compounds were designated at 5a-l. Compounds 5a-l has not been reported previously confirmed by using the Scifinder search. The structures of all compounds were confirmed by the spectroscopy like FT-IR, ^1H NMR, ^{13}C NMR, MS and CHN analyzer. The data of FT-IR spectroscopy provides valuable information regarding the nature of functional group attached. In order to study the bonding mode of compound 4 to the compound 5a-l, the IR spectrum of compound 4 was compared with the spectra of compound 5a-l. Considerable differences to be expected were observed. The general structure of compounds 5a-l designated as below, where R is different substitute group or atom.

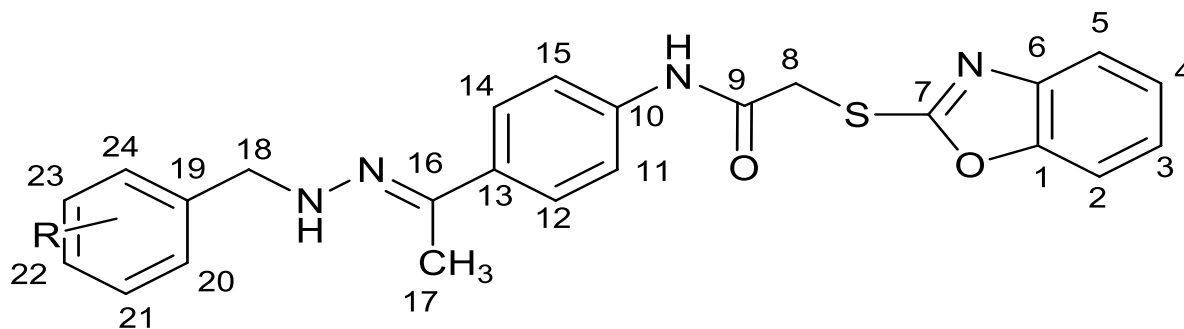


Figure 1. Compound 5a-l.

The structures of the final compounds 5a-l were established by their spectral analysis. Using compound 5a as a representative example, its FTIR spectrum of 5a showed the most relevant peaks of benzoxazole-acetylphenyl ring. Stretching vibration at 3223 cm^{-1} indicates that compound containing a secondary amine. The vibration at 1584 cm^{-1} and 3052 cm^{-1} over the range showed intensity absorption peaks corresponding to aromatic C-H stretching vibrations. The absorption peaks at 1658 cm^{-1} is due to the carbonyl groups present structure as amide group.

^1H NMR It has been observed from the chemical structure of compound that C-11, C-12, C-14 and C-15 are pairs of chemically equivalent protons which appear at $\delta = 7.69\text{ ppm}$

and $\delta = 7.85$ ppm indicates that this all four carbon are presence in same aromatic ring. As well as C-2, C-3, C-4 and C-5 are pairs of chemically equivalent protons which appeared at $\delta = 7.66$ ppm and $\delta=7.77$ ppm value indicates that benzooxazole ring. C-20, C-21, C-22, C-23 and C-24 are also pairs of chemically equivalent protons which indicates that this all carbon presence of same aromatic ring.

The protons attached at C-8 appeared as a singlet at $\delta = 4.02$ ppm due to sulfur and C-9 carbonyl group atmosphere. Carbon C-17 contains a proton gives singlet at $\delta = 2.35$ ppm indicates that azomethine group present in the structure. The mass spectrum of 5a showed a molecular ion peak at m/z 444 ($M + 1$) which is in agreement with its proposed structure.

Table 1. Antimicrobial screening results of compounds **2**, **4** and **5a–k**.

Entry	R	Minimum inhibitory concentration (MIC) $\mu\text{g/ml}$					
		Gram positive bacteria		Gram negative bacteria		Fungi	
		S. aureus	S. pyogenes	E. coli	P. aeruginosa	C. albicans	A. niger
2	-	>1000	>1000	>1000	>1000	>1000	>1000
4	-	1000	1000	1000	1000	1000	1000
5a	-H	250	250	500	500	200	100
5b	3-NO ₂	50	50	50	100	100	500
5c	4-NO ₂	25	25	25	25	50	100
5d	3-CH ₃	500	500	500	500	500	500
5e	4-CH ₃	500	500	500	250	500	500
5f	4-OCH ₃	500	500	500	500	1000	500
5g	2-Cl	25	100	50	100	25	50
5h	3-Cl	100	100	100	250	50	100
5i	4-Cl	200	200	200	250	200	200
5j	2-OH	500	500	500	500	500	500
5k	3-OH	200	500	500	500	500	1000
5l	4-OH	200	500	250	200	500	1000
<i>Chloramphenicol</i>		50	50	50	50	-	-
<i>Ketoconazole</i>		-	-	-	-	50	50

Minimum Inhibitory Concentration for bacteria (MICb) of all the newly synthesized compounds was determined for their in vitro antimicrobial activity against different bacterial and fungal strains by the conventional broth-dilution method [16] using standard drugs which are chloramphenicol and ketoconazole. The results of antimicrobial studies are presented in Table 1. Intermediates **2** and **4** showed poor antimicrobial activity against all tested bacterial and fungal strains as compared to final derivatives **5a–l**. Newly synthesized derivatives showed improved antibacterial activity compared to antifungal activity. Compounds **5b**, **5c**

and 5g were found to be highly active against all the bacterial strains, showing inhibition in the range of 25–100 mg/ml.

Among them, compounds 5c emerged as the most effective antibacterial agents with a 2 to 4-fold higher MIC (25 mg/ml) than the reference drug Chloramphenicol. Compounds 5b, 5c and 5g exhibited comparable antibacterial activity with MIC values of 25–100 mg/ml. Compounds 5c and 5i substituted with inductively electron withdrawing nitro and chloro groups respectively, at the para position showed the highest antibacterial activity ($\text{NO}_2 > \text{Cl}$). The presence of electron donating groups on the phenyl ring resulted in a significant decrease in antimicrobial activity of compounds 5d, 5e, 5f, 5j, 5k and 5l.

From these results, it can be observed that the antibacterial activity was considerably affected by the substitution pattern on the phenyl ring. Further, the results of the antifungal activity indicated that compound 5g endowed with chlorine emerged as the most effective antifungal agent and showed an MIC in the range of 25–50 mg/ml against three fungal strains using ketoconazole as a positive control.

4. CONCLUSION

From the study of above results from all the spectral and physical data of the synthesized compounds clearly conclude that designed compounds were synthesized successfully. We have accomplished the synthesis of new derivatives of benzoxazole 5a–k having schiff base with the hope of generating new bioactive molecules that could be useful as potent antimicrobial agents.

A series of compounds when substituted by electron-withdrawing group like NO_2 and Cl enhances the antimicrobial activity when present on aromatic ring. On the other side the used of electron donating group didn't enhances the antimicrobial activity when present on aromatic ring. Among the twelve newer derivatives, analogs 5b, 5c, 5g, 5h and 5i possessing electron withdrawing atom/group such as Nitro and Chloro at the para or meta position were identified as the most potent antibacterial agents and compound 5g was found to be the most effective antifungal agent. The results lead us to further studies to acquire more information about newer derivatives of benzoxazole.

Acknowledgments

We would like to express our sincere gratitude to The Sheth M. N. Science College, H.N.G.U., Patan for providing us laboratory facilities. The authors are thankful Saurashtra University, Rajkot and CMCRI, Bhavnagar for providing analytical data of the compounds. Authors are also thankful to Dr. Deepkumar S. Joshi for his enlightenment.

References

- [1] T. Panneer Selvam, P. P. Radhika, S. Janagaraj, A. Siva Kumar, *Research in biotechnology* 2 (2011) 50-57.
- [2] Pedrazzini S, De Angelis M, Muciaccia WZ, Sacchi C, Forgione A, *Arzneimittel-Forschung* 38 (8): 1170–5. PMID 3196413
- [3] Samia M. Rida, Fawzia A. Ashour, Soad A.M. El-Hawash, Mona M. ElSemary, Mona H. Badr, Manal A. Shalaby, *Eur J Med Chem* 40 (2005) 949-959.

-
- [4] Jarmila Vinsova, Vaclav Horak, Vladimir Buchta and Jarmila Kaustova, *Molecules* 10 (2005) 783-793.
- [5] MERIC KOKSAL, NESRIN GOKHAN, ESRA KUPELI, ERDEM YESILADA, and HAKKI ERDOGAN, *Arch Pharm Res.* 30 (2007) 419-424.
- [6] Mimnaugh, E.G.; Xu, W.; Vos, M. *Mol. Cancer Ther.* 3 (2004) 551–566.
- [7] Yadav, R; Sirvastava, SD and Sirvastava, SK (2005), *Indian J. Chem.* 44 (2005) 1262-1266.
- [8] Ramón, G; Domenech, B; Ana, C; Gregori, C and Calabuig, C, *Internet Electron. J. Mol. Des.*, BioChem Press,1 (2002) 339-350.
- [9] R. V. Satyendra, K. A. Vishnumurthy, H. M. Vagdevi, K. P. Rajesh, H. Manjunatha, and A. Shruthi, *European Journal of Medicinal Chemistry* 46 (2011) 3078–3084.
- [10] Paramashivappa R, Phanikumar P, Subbarao P, Srinivasarao A, *Bioorg Med Chem Lett.* 13, 2003, 657-660.
- [11] Grocer, H., Kus, C., Boykin, D.W., Yildiz, S., Altanlar, N., *Bioorg. Med. Chem.* 10 (2002) 2589-2596.
- [12] Nicholson RM, Murphy JR, Dearden JR, *Journal of Pharmacy and Pharmacology* 34 (1982) 106-111.
- [13] Fang, B., Zhou, C.H., Rao, X.C., *Eur. J. Med. Chem.* 45 (2010) 4388-4398.
- [14] E. F. Magomedova, V. V. Pinyaskin, A. Sh. Aminova, *Pharma. Chem. J.* 41 (2007) 474-475.
- [15] Kalpesh Parikh, Deepkumar Joshi, *Med Chem Res.* 22 (2013) 3688-3697.
- [16] P.C. Hannan, *Vet. Res.* 31 (2000) 373-395.

(Received 03 December 2014; accepted 19 December 2014)