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Synthesis and biological activities of novel -4H-benzo[e][1,3]oxazin-4-one linked [1,2,3]-triazole derivatives

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Abstract
Cu(I) catalysed 1,3-dipolar cycloaddition combination of azide and alkyne yielded a novel chemical series of [1,2,3]-triazole containing benzoxazine derivatives. In vitro testing of the produced drugs for antibacterial activity revealed that compounds 6a, 6i, 6j and 6k are effective antibacterial agents. Among these four compounds are the most common 3-((1-(3-chlorophenyl)-1H-1,2,3-triazol-4-yl)methyl)-2,2-dimethyl-2,3-dihydro-4H-benzo[e] [1,3] oxazin-4-one (6j) compound has shown the most powerful antibacterial action against gram negative and gram positive bacterial strains tested.

Keywords: *1,3- Benzoxazin-4-one, 1,2,3-triazole,in vitro antibacterial activity*

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I. Introduction

Derivative products of Benzoxazines are the most important nitrogen and oxygen-containing heterocyclic compounds, and 1,3 benzoxazines and their derivatives have attracted the attention of both synthetic and medicinal chemists due to its convenience of synthesis, lack of exploration, and rarity in natural products when compared to other benzoxazine isomers. At the same time, 1,3 benzoxazines are the core structure for a wide range of biological active chemicals, including anticancer[1], antimicrobial[2], antifungal[3], antiplatelete[4], antihypertensive[5], antithelmentic[6], vasorelaxing[7], potassium channel modulating[8], herbicidal[9], and fungicidal[10] agents. 1,2,3-triazole are essential pharmacophere for drug development [11,12] for Analgesic[13], anti-inflammatory [14,15], antiviral [16], antimicrobial [17], antifungal [18], antibacterial [19], antitubercular [20], and antitumor[21] because they demonstrated considerable biological action.

Molecular hybridization, but in the other hand, is the most recent and effective technique in modern drug discovery[22]. Which entails combining active pharmacophores from two or more physiologically active compounds into a single moiety in order to create a novel hybrid with higher efficiency and affinity than the original drug[23]. Furthermore, these hybrids can function more selectively and specifically than the parent medicines, with less adverse effects[24]. We present here the unique synthesis of [1,2,3]-triazole containing 1,3-benzoxazine-4-one derivatives and their evaluation as antibacterial agents as part of our focus in the creation of novel bioactive hybrids.

II. Material And Meathod

Instrumentation and Chemicals General experimental methods

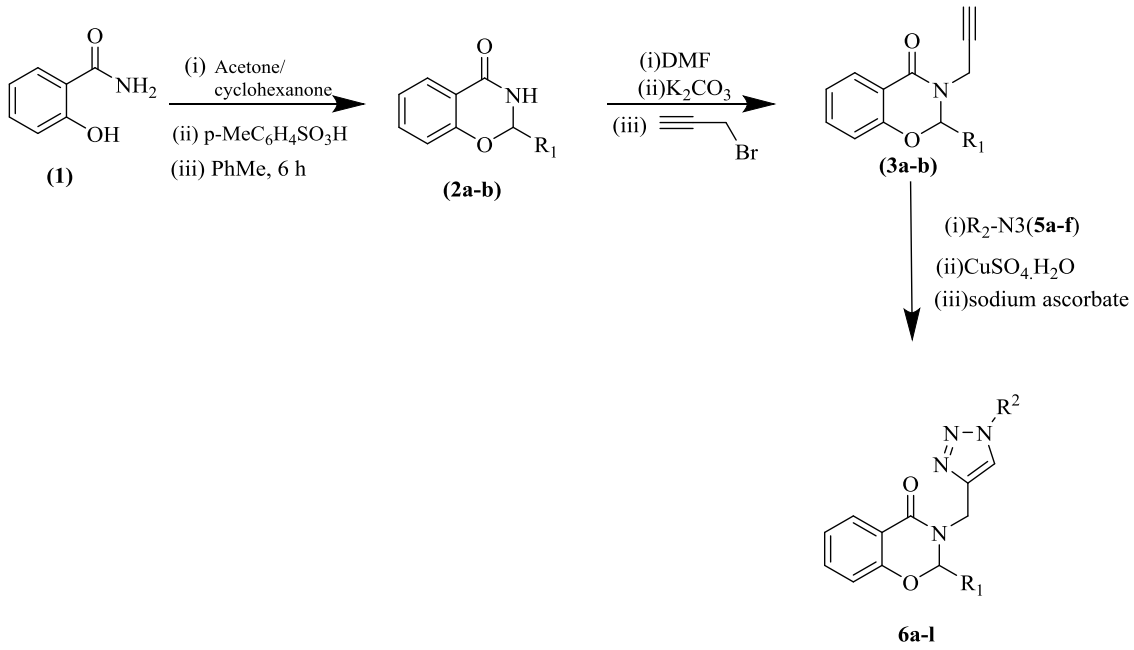
Every one of the chemicals we used in the processes were Laboratory Grade, which meant they could be used without further purification. A Veego softening point device was used to determine the melting points of the produced compounds. TLC plates were used to assess the purity of the produced compounds, using silica F254 (adsorbent) covered on aluminium plates (Merck), UV lamp, and iodine vapours used as visualising agents. Spectra were recorded using a Varian mercuryTH- 300 spectrometer at 400 MHz for 1H NMR and 101.6 MHz for 13C NMR using deuterated solvents like CDCl3 and DMSO-d6 as well as Tetramethylsilane (TMS) as an internal standard and chemical shifts were measured in ppm.

III. Results And Descussion

CHEMISTRY

The current research mostly focuses on the design of unique models. -((1-(3-chlorophenyl)-1H-1,2,3-triazol-4-yl)methyl)-2,2-dimethyl-2,3-dihydro-4H-benzo[e][1,3]oxazin-4-onehybrids, using commercially available 2-hydroxybenzamide1 as the starting material. Initially, the coupling partner alkynes3a–bwassynthesized from 2-hydroxybenzamide1in two phases, in the first step \s2-hydroxybenzamide**1** treated with two distinct ketones to produce 2**a–b** in good yields. In the second stage, the NH group in 2**a–b** is propargylated using propargyl bromide and anhydrous K2CO3/DMF to produce propargyl-benzoxazines 3**a–b** (Scheme 1). As indicated in Scheme 2, the coupling partnerazides5**a–f** were synthesised utilising the matching amines 4**a–f**. Finally, the **Click reaction** was used in the critical step to synthesise target hybrid compounds, as shown in Scheme 1. The reaction of coupling partner azides5**a–f** with propargyl-benzoxazines 3a–b in DMF with a catalytic quantity of $CuSO_4 5H_2O$ and Sodium ascorbate provides related benzoxazine-4-substituted-1,2,3-triazole hybrids6**a–l** as final hybrid compounds in high yields. Using ^{1}H NMR, ^{13}C NMR, and Mass Spectral analysis, each synthesised hybrid molecule was thoroughly characterised.

Scheme-I



Scheme 2. Synthesis of azide partners 5a-f.

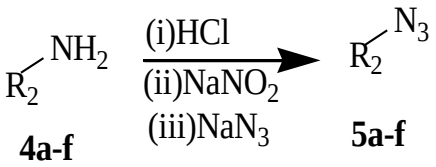
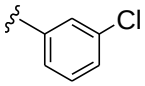
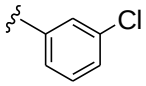
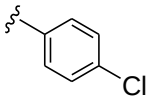
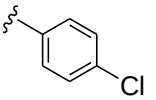
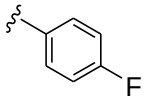
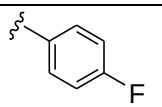
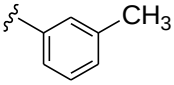
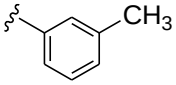
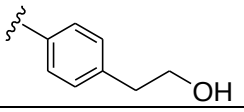
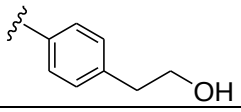
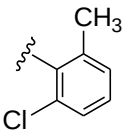
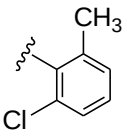


Table-I

Compound	R^1	R^2	Compound	R^1	R^2
6a			6g		
6b			6h		
6c			6i		
6d			6j		
6e			6k		
6f			6l		

Synthesis of 2,2-dimethyl-3-(prop-2-yn-1-yl)-2,3-dihydro-4H-benzo[e][1,3]oxazin-4-one (3a)

Powdered K_2CO_3 (11.69 g, 8.47 mol) was added to a solution of 2,2-dimethyl-2,3-dihydro-4H-benzo[e][1,3]oxazin-4-one(**2a**) (5.0 g, 2.82 mol) in DMF (20 mL) followed by addition of 3- bromoprop-1-yne (2.14 mL, 2.82 mol) and the reaction mixture was stirred at 80 °C for 4-8 h completion reaction was confirmed by TLC, cool the reaction mixture to rt, diluted with H_2O (30 mL), and extracted with EtOAc (3 × 50 mL). The EtOAc layers were mixed, dried with ($MgSO_4$), filtered, and concentrated. Flash chromatography was used to purify the crude mass, yielding 2,2-dimethyl-3-butanediol (prop-2-yn-1-yl) 4,3-dihydro-4H-benzo[e][1,3]oxazin-4-one -2,3-dihydro-4H-benzo[e][1,3]oxazin-4-one (**3a**).

Synthesis of 3-(prop-2-yn-1-yl)spiro[benzo[e][1,3]oxazine-2,1'-cyclohexan]-4(3H)-one(3b)

2-spiro[benzo[e][1,3]oxazine-2,1'-cyclohexan] is added to a solution of 2-spiro[benzo[e][1,3]oxazine-2,1'-cyclohexan] -4(3H) -one(2b) (5.0 g, 2.30 mol) in DMF (20 mL) was added followed by powdered K_2CO_3 (9.53 g, 6.91 mol) in DMF (20 mL) and the reaction mixture was stirred at 80 °C for 4-8 h completion reaction was confirmed by TLC, cool the reaction mixture to rt, diluted with H2O (30 mL), and extracted with EtOAc (3×50 mL). The EtOAc layers were mixed, dried with ($MgSO_4$), filtered, and concentrated. Flash chromatography was used to purify the crude mass, yielding 3-(prop-2-yn-1-yl)spiro[benzo[e][1,3]oxazine-2,1'-cyclohexan]. -4(3H)-a single (**3b**).

General procedure for the preparation of 3-((1-(3-chlorophenyl)-1H-1,2,3-triazol-4-yl)methyl)-2,2-dimethyl-2,3-dihydro-4H-benzo[e][1,3]oxazin-4-one (6a-l)

The synthetic route for the key intermediate compound (3a-b) were started with 2,2-dimethyl-3-(prop-2-yn-1-yl)-2,3-dihydro-4H-benzo[e][1,3]oxazin-4-one and 3-(prop-2-yn-1-yl)spiro[benzo[e][1,3]oxazine-2,1'-cyclohexan]-4(3H)-one (3a-b) was reacted with different aryl azides (4a-c) using Click chemistry in CuSO4.5H2O with sodium ascorbate to form 3-((1-(3-chlorophenyl)-1H-1,2,3-triazol-4-yl)methyl)-2,2-dimethyl-2,3-dihydro-4H-benzo[e][1,3]oxazin-4-one (4a-l).

1 **3-((1-(3-chlorophenyl)-1H-1,2,3-triazol-4-yl)methyl)-2,2-dimethyl-2,3-dihydro-4H-benzo[e][1,3]oxazin-4-one. (6a)**

White solid, yield: 87%, m.f. : $C_{19}H_{17}ClN_4O_2$, m.p.: 134-136^{0}C **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.19 (s, 1H), 7.95 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.82 (t, *J* = 1.9 Hz, 1H), 7.71 – 7.61 (m, 1H), 7.57 – 7.37 (m, 3H), 7.09 (td, *J* = 7.6, 1.0 Hz, 1H), 6.92 (dd, *J* = 8.2, 0.8 Hz, 1H), 4.92 (s, 2H), 1.74 (s, 6H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 162.14, 155.07, 145.76, 137.81, 135.58, 134.49, 130.78, 128.79, 127.82, 122.01, 120.69, 118.34, 117.34, 117.15, 91.96, 37.10, 26.39,Mass: m/z=369 $[M+H]^+$

3-((1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)methyl)-2,2-dimethyl-2,3-2.
2. dihydro-4H-benzo[e][1,3]oxazin-4-one(6b)
White solid, yield: 84%, m.f. : $C_{19}H_{17}ClN_4O_2$, m.p.: 132-134^{0}C **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.10 (s, 1H), 7.85 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.68 – 7.60 (m, 2H), 7.47 – 7.33 (m, 3H), 7.00 (td, *J* = 7.6, 1.0 Hz, 1H), 6.82 (dd, *J* = 8.2, 0.9 Hz, 1H), 4.82 (s, 2H), 1.65 (s, 6H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 162.13, 155.06, 135.50, 134.49, 129.90, 127.80, 122.01, 121.59, 117.33, 116.97, 91.97, 37.07, 26.39,Mass: m/z=369 $[M+H]^+$

3 **3-((1-(4-fluorophenyl)-1H-1,2,3-triazol-4-yl)methyl)-2,2-dimethyl-2,3-dihydro-4H-benzo[e][1,3]oxazin-4-one(6c)**
White solid, yield: 80%, m.f. : $C_{19}H_{17}FN_4O_2$, m.p.: 134-136^{0}C **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.06 (s, 1H), 7.85 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.75 – 7.56 (m, 2H), 7.36 (ddd, *J* = 8.2, 7.4, 1.7 Hz, 1H), 7.15 – 7.07 (m, 2H), 7.00 (td, *J* = 7.6, 1.0 Hz, 1H), 6.82 (dd, *J* = 8.2, 0.9 Hz, 1H), 4.83 (s, 2H), 1.65 (s, 6H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 163.66, 162.12, 161.18, 155.07, 134.48, 133.28, 127.80,122.45 , 122.37, 122.00, 117.35, 117.10 – 116.46, 91.97, 37.10, 26.39,Mass: m/z=353 $[M+H]^+$

4 **2,2-dimethyl-3-((1-(m-tolyl)-1H-1,2,3-triazol-4-yl)methyl)-2,3-dihydro-4H-benzo[e][1,3]oxazin-4-one(6d)**
White solid, yield: 78%, m.f. : $C_{20}H_{20}N_4O_2$, m.p.: 130-132^{0}C **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.97 – 7.91 (m, 2H), 7.49 – 7.35 (m, 3H), 7.35 – 7.31 (m, 2H), 7.08 (td, *J* = 7.6, 1.0 Hz, 1H), 6.92 (dd, *J* = 8.2, 0.8 Hz, 1H), 4.96 (s, 2H), 2.21 (s, 3H), 1.74 (s, 6H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 162.09, 155.09, 144.60, 138.22 – 136.67, 134.42, 133.57,132.26 – 131.53, 129.87, 127.86, 126.80, 125.94, 125.45, 121.95, 117.40, 117.17, 91.94, 37.05, 26.36, 17.88,Mass: m/z=349 $[M+H]^+$

5 **3-((1-(4-(2-hydroxyethyl)phenyl)-1H-1,2,3-triazol-4-yl)methyl)-2,2-dimethyl-2,3-dihydro-4H-benzo[e][1,3]oxazin-4-one(6e)**
White solid, yield: 87%, m.f. : $C_{21}H_{17}N_4O_3$, m.p.: 131-133^{0}C **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.08 (s, 1H), 7.85 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.68 – 7.50 (m, 2H), 7.41 – 7.33 (m, 1H), 7.30 (t, *J* = 5.4 Hz, 2H), 7.00 (td, *J* = 7.6, 1.0 Hz, 1H), 6.82 (dd, *J* = 8.2, 0.9 Hz, 1H), 4.84 (s, 2H), 3.83 (t, *J* = 6.5 Hz, 2H), 2.85 (t, *J* = 6.5 Hz, 2H), 1.65 (s, 6H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 162.15, 155.08, 139.83, 135.42, 134.48, 130.27, 127.81, 122.00 , 120.55, 117.35, 116.97, 91.99, 63.32, 38.64, 37.06, 26.37,Mass: m/z=379 $[M+H]^+$

6 **3-((1-(2-chloro-6-methylphenyl)-1H-1,2,3-triazol-4-yl)methyl)-2,2-dimethyl-2,3-dihydro-4H-benzo[e][1,3]oxazin-4-one(6f)**
White solid, yield: 83%, m.f. : $C_{20}H_{19}ClN_4O_2$, m.p.: 133-135^{0}C **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.94 (d, *J* = 7.5 Hz, 1H), 7.71 (d, *J* = 8.5 Hz, 1H), 7.53 – 7.41 (m, 2H), 7.37 (t, *J* = 8.4 Hz, 1H), 7.31 – 7.23 (m, 1H), 7.08 (dt, *J* = 10.6, 5.4 Hz, 1H), 6.91 (d, *J* = 8.1 Hz, 1H), 4.96 (d, *J* = 39.2 Hz, 2H), 2.06 (s, 3H), 1.72 (d, *J* = 13.9 Hz, 6H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 162.15, 155.10, 137.94, 134.47, 131.72, 131.37, 129.92, 129.37 , 128.59 – 127.32, 121.97, 121.62, 117.38, 116.96, 91.92, 37.04, 26.37, 17.77,Mass: m/z=382$[M+H]^+$

7 **3-((1-(3-chlorophenyl)-1H-1,2,3-triazol-4-yl)methyl)spiro[benzo[e][1,3]oxazine-2,1'-cyclohexan]-4(3H)-one(6g)**
White solid, yield: 86%, m.f. : $C_{22}H_{21}ClN_4O_2$, m.p.: 134-136^{0}C **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.08 (s, 1H), 7.86 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.74 (t, *J* = 1.9 Hz, 1H), 7.58 (ddd, *J* = 7.8, 2.1, 1.3 Hz, 1H), 7.42 – 7.31 (m, 3H), 7.01 (td, *J* = 7.6, 1.0 Hz, 1H), 6.89 (dd, *J* = 8.2, 0.8 Hz, 1H), 4.86 (s, 2H), 2.09 (d, *J* = 12.0 Hz, 2H), 1.84 – 1.75 (m, 2H), 1.68 – 1.55 (m, 8H).^{13}C NMR (101 MHz, $CDCl_3$)δ 162.39, 154.51, 146.14, 137.82, 135.58, 134.97, 130.77, 128.77, 127.81, 122.05, 121.88, 120.67, 118.31, 118.17, 116.93, 92.40, 36.34, 34.18, 24.43, 22.19,Mass: m/z=409 $[M+H]^+$

8 **3-((1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)methyl)spiro[benzo[e][1,3]oxazine-2,1'-cyclohexan]-4(3H)-one(6h)**
White solid, yield: 84%, m.f. : $C_{22}H_{21}ClN_4O_2$, m.p.: 138-140^{0}C **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.09 (s, 1H), 7.84 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.67 – 7.65 (m, 2H), 7.46 – 7.31 (m, 3H), 7.01 (td, *J* = 7.6, 1.0 Hz, 1H), 6.84 (dd, *J* = 8.2, 0.9 Hz, 1H), 4.84 (s, 2H), 2.07 (d, *J* = 12.0 Hz, 2H),

1.83 – 1.76 (m, 2H), 1.67 – 1.54 (m, 8H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 162.49, 154.21, 145.14, 136.62, 135.48, 1354.07, 131.47, 128.47, 126.91, 122.15, 121.78, 120.57, 117.91, 119.07, 115.99, 92.50, 36.54, 34.08, 23.93, 22.09,Mass: m/z=409 $[M+H]^+$

9 **3-((1-(4-fluorophenyl)-1H-1,2,3-triazol-4-yl)methyl)spiro[benzo[e][1,3]oxazine-2,1'-cyclohexan]-4(3H)-one(6i)**
White solid, yield: 77%, m.f. : $C_{22}H_{21}FN_4O_2$, m.p.: 142-144^{0}C **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.05 (s, 1H), 7.84 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.74 – 7.46 (m, 2H), 7.35 (ddd, *J* = 8.2, 7.4, 1.7 Hz, 1H), 7.17 – 7.17 (m, 2H), 7.01 (td, *J* = 7.6, 1.0 Hz, 1H), 6.81 (dd, *J* = 8.2, 0.9 Hz, 1H), 4.82 (s, 2H), 2.19 (d, *J* = 12.0 Hz, 2H), 1.83 – 1.74 (m, 2H), 1.65 – 1.54 (m, 8H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 163.66, 162.22, 161.08, 155.17, 135.08, 133.08, 126.99,121.95 , 122.17, 121.90, 117.15, 117.01, 115.46, 92.07, 36.24, 34.08, 24.13, 22.24,Mass: m/z=393 $[M+H]^+$

10 **3-((1-(m-tolyl)-1H-1,2,3-triazol-4-yl)methyl)spiro[benzo[e][1,3]oxazine-2,1'-cyclohexan]-4(3H)-one(6j)**
White solid, yield: 80%, m.f. : $C_{23}H_{24}N_4O_2$, m.p.: 142-144^{0}C **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.96 – 7.90 (m, 2H), 7.50 – 7.39 (m, 3H), 7.34 – 7.29 (m, 2H), 7.18 (td, *J* = 7.6, 1.0 Hz, 1H), 6.91 (dd, *J* = 8.1, 0.8 Hz, 1H), 4.95 (s, 2H), 2.20 (s, 3H), 2.19 (d, *J* = 12.0 Hz, 2H), 1.83 – 1.74 (m, 2H), 1.67 – 1.54 (m, 8H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 162.18, 154.90, 144.50, 137.12 – 135.57, 134.32, 132.67,132.06 – 130.43, 129.77, 127.66, 126.79, 125.84, 125.35, 121.85, 117.34, 117.07, 91.84, 36.24, 34.08, 24.33, 22.08, 17.78,Mass: m/z=389 $[M+H]^+$

11 **3-((1-(4-(2-hydroxyethyl)phenyl)-1H-1,2,3-triazol-4-yl)methyl) spiro [benzo[e][1,3] oxazine -2,1'-cyclohexan]-4(3H)-one(6k)**
White solid, yield: 75%, m.f. : $C_{24}H_{26}N_4O_3$, m.p.: 143-145^{0}C **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.07 (s, 1H), 7.84 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.67 – 7.52 (m, 2H), 7.40 – 7.32 (m, 1H), 7.29 (t, *J* = 5.4 Hz, 2H), 7.10 (td, *J* = 7.6, 1.0 Hz, 1H), 6.79 (dd, *J* = 8.2, 0.9 Hz, 1H), 4.79 (s, 2H), 3.82 (t, *J* = 6.5 Hz, 2H), 2.84 (t, *J* = 6.5 Hz, 2H), 2.19 (d, *J* = 12.0 Hz, 2H), 1.83 – 1.74 (m, 2H), 1.66 – 1.54 (m, 8H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 161.95, 154.98, 138.83, 134.32, 134.38, 130.17, 127.71, 122.10 , 120.45, 116.25, 116.87, 91.89, 63.22, 38.54, 36.24, 34.08, 24.33, 22.09,Mass: m/z=419 $[M+H]^+$

12 **3-((1-(2-chloro-6-methylphenyl)-1H-1,2,3-triazol-4-yl)methyl)spiro[benzo[e][1,3]oxazine-2,1'-cyclohexan]-4(3H)-one(6l)**
White solid, yield: 81%, m.f. : $C_{23}H_{23}ClN_4O_2$, m.p.: 143-145^{0}C **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.93 (d, *J* = 7.4 Hz, 1H), 7.70 (d, *J* = 8.5 Hz, 1H), 7.52 – 7.40 (m, 2H), 7.36 (t, *J* = 8.4 Hz, 1H), 7.30 – 7.22 (m, 1H), 7.18 (dt, *J* = 10.6, 5.4 Hz, 1H), 6.90 (d, *J* = 8.1 Hz, 1H), 4.94 (d, *J* = 39.2 Hz, 2H), 2.19 (d, *J* = 12.0 Hz, 2H), 2.16 (s, 3H), 1.83 – 1.74 (m, 2H), 1.66– 1.53 (m, 8H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 162.25, 155.01, 136.84, 134.37, 131.62, 131.17, 129.62, 129.27 , 128.09 – 127.22, 121.87, 121.52, 117.18, 116.86, 91.82, 36.24, 34.08, 24.33, 22.29, 17.67,Mass: m/z=423 $[M+H]^+$

IV. Antibacterial Activity

Inoculation of Staphylococcus aureus (gram-positive), Escherichia coli (E. coli) (gram-negative), Bacillus subtilis (gram-positive), Pseudomonas aeruginosa (gram-negative), and all microorganisms acquire from Microbial Type Culture Collection – MTCC. In auto calved LB stock media and Incubate for the time being at 37^{o}C in a shaker for Bacterial development. From that, 0.3 mL of bacterial culture was taken and immunized utilizing spreader on newly pre-arranged auto calved agar plates, i.e., Petri dishes. Subsequent to drying the plates, a 5-mm test circle, which was broken down in DMSO dissolvable, was kept on microbial plate alongside certain controls NX (Norfloxacin), which were incubated for the time being at 37^{o}C in BOD incubators. Later short-term incubate, zone of hindrance is estimated utilizing an estimating scale.

Hybrid compounds	Bacterial strain (Gram positive)		Bacterial strain (Gram negative)	
	Bacillus subtilis	Staphylococcus aureus	Pseudomonas aeruginosa	Escherichia coli
6a	4.0	4.3	3.9	4.1
6b	-	-	-	-
6c	-	-	-	-
6d	3.2	-	-	4.3
6e	-	-	-	-
6f	3.0	3.2	-	-
6g	3.1	-	-	-
6h	-	-	-	-
6i	3.4	4.0	4.1	3.7
6j	5.1	5.4	5.5	4.7
6k	4.1	4.5	3.2	3.8
6l	3.8	3.5	-	-
Norfloxacin	6.2	6	6.4	7
[a]Zone of inhibition (mm) 10 µg/mL concentrations				

Each synthesized hybrid compound was tested in vitro for antibacterial activity against two different gram-positive bacteria strains [B. subtilis; S. aureus] and two different gram-negative bacteria strains [P. aeruginosa; E. coli]. IMT, Chandigarh provided the strains used in the biological activities. The culture media used in the tests were stored on supplement agar (bacterial) subculture in Petri dishes prior to testing. The resulting compounds were evaluated using DMSO as a dissolvable solvent at a concentration of 10 mg/mL. The inhibitory zone (in mm) was compared to that of the conventional antibiotic Norfloxacin. Table 1 summarizes the findings. Every created hybrid compound 6**a**, 6**i**, 6**j**, and 6**k** demonstrated a bright zone of inhibition against the P. aeruginosa bacterial strain, and these mixes also shown excellent bacterial activity. Against E. coli, compound 6a showed a 3.9 mm zone of impediment, all of the remaining hybrid compounds showed moderate antibacterial activity against the E. coli bacterial strain.

V. Conclusion

In this study, a series of 1,3 benzoxazines linked 1,2,3-triazoles (6**a-l**) were successfully synthesized in good yields by cyclization of 2-hydroxy benzamide with ketones followed by click chemistry. The antibacterial activity of the compounds was evaluated and compound (6**j**) was found to be the most active among the tested compounds.

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Conflict of Interest

The authors declare no conflict of interest

References

[1]. Ihmaid, K.; Saleh, F.; Cheree, Al-Rawi.; Jasim. M.A.; Meddicinal Chemistry Research.
[2]. **2015**, 24, 7. DOI 10.1007/s00044-015-1338-4
[3]. Alper-Hayta, S.; Aki-Sener, E.; Tekiner-Gulbas, B.; Yildiz, I.; Temiz-Arpaci, O.; Yalcin, I.; Altanlar, N.; European journal of medicinal chemistry. **2006,** 41(12), 1398–1404. https://doi.org/10.1016/j.ejmech.2006.06.011
[4]. Shalaby, A.A.; El-Khamry, A.M.A; Shiba, S.A.; Ahmed, A.A.A.E.A. ; Arch. Pharm. Pharm. Med. **2000,** 333, 365.
[5]. Pritchard, K.M.; Al-Rawi, J.; Bradley, C.; European Journal of Medicinal Chemistry, **1977** 42, 1200. DOI: 10.1016/j.ejmech.2007.01.021
[6]. Jirkoysky, L.; Humber, L. G.; Chemical Absract. **1977,** 87, 168053.
[7]. Catarz, D.; Cecchi, L.; Colotta, V.; Filacchioni. G.; Varano, E.; Medicinal Chemistry, **1995**, 38, 2196.
[8]. Benedini, F.; Bertolini, G.; Cereda, R.; Dona, G.; Gromo, G.; Levi, S.; Mazrahi, Sala, A.; Medicinal chemistry, **1995**, 38, 130.
[9]. Largeron, M.; Fleury, M.; Tetrahedron Lett, **1998**, **39**8999.
[10]. Kobzina, W.; Herbicidal N -haloacetyl-l,2-dihydro-4H-3,1-benzoxa, Chemical Abstract. **1977**, 87, 79678e.
[11]. Tang Z.; Zhu, Z.; Xia, Z..; Liu, H.; Chen, J.; Xiao, W.; Ou, X.; Molecules. **2012**, 17, 8174. doi: 10.3390/molecules17078174.
[12]. Khurshed, B.; Zhao, J.; Aisa A. H.; Bioorganic Medicinal Chemistry. **2019,** 27, 3511. doi: 10.1016/j.bmc.2019.07.005
[13]. G. Sandip, Agalave, R. Suleman, Maujan,S. Vandana, Chemistry. Asian Journal. **2011**, 6, 2696. DOI: 10.1002/asia.201100432
[14]. Mathew, V.; Keshavaya, J.; Vaidya, V.P.; Giles, D.; European Journal of Medicinal Chemistry. **2007**, 42, 823.
[15]. Kamotra, P.; Gupta, A.K.; Gupta, R.; Somal, P.; Singh, S.; Indian Journal Chemistry. **2007**, 46, 980.
[16]. Michael, H.C.; Krishnaswamy, S.; Hao, Q.; Duan, SX.; Patten. CJ.; The Biological fate of chemicals. **2003,** 31**,** 1125.
[17]. Tomita. K.; Tsuzuki, Y. Shibamori, K.; Tashima, M.; Kajikawa, F.; Journal of Medicinal Chemistry. **2002**, 45, 5564. https://doi.org/10.1021/jm010057b
[18]. Demirbas, N.; Karaoglu, SA.; Demirbas, A.; Sancak, K.; European Journal of Medicnal Chemistry. **2004**, 39, 793. https://doi.org/10.1016/j.ejmech.2004.06.007.

[19]. Tsukuda, T.; Shiratori, Y.; Watanabe, MH.; Ontsuka, K.; Hattori, N.; Bioorganic Medicinal Chemistry Letter. **1998**, 8, 1819 https://doi.org/10.1016/S0960-894X(98)00316-
[20]. Wang, Z.; You, T.; Xu, HY.; Haoxin, S.; Molecules, **1996**, 1, 68.
[21]. RH. Udupi, A. Kushnoor, AR. Bhat,Journal of Indian Chemical Society. **1999,** 76, 461.
[22]. Shivarama, HB.; Narayana, PK.; Sooryanarayana, RB.; Shivananda, MK.; Europen Journal of Medicinal Chemistry. **2002,** 37, 511. https://doi.org/10.1016/S0223-5234(02)01358-2.
[23]. R. Morphy and Z. Rankovic, Journal of Medicinal Chemistry. **2005,** 48, 6523, https://doi: 10.1021/jm058225d.
[24]. Muregi. F.W.; Ishih, A.; Drug Development Research. **2010,** 71, 20 https://doi:10.1002/ddr.20345.
[25]. Viegas-Junior, C.; Danuello, A.; Bolzani, V.D.S.; Barreiroand, E. J.; Fraga, C.A.M.; Current Medicinal Chemistry. **2007**, 14, 1829. https://doi: 10.2174/092986707781058805.

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