SYNTHESIS OF NOVEL [1,2,4]TRIAZOLO[3,4-B][1,3,4]OXADIAZOLES
AND EVALUATION OF THEIR ANTIBACTERIAL ACTIVITY

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Abstract:A new series of novel 6-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)-3-aryl/heteryl[1,2,4]triazolo[3,4-b][1,3,4]oxadiazole 10(a-j) in good to excellent yields by the reaction of 1-(5-5-[3-(5-hydrazino-1,3,4-oxadiazol-2-yl)-4-methoxybenzyl]-2-methoxyphenyl-1,3,4-oxadiazol-2-yl)hydrazine with a variety of different aryl/heteryl chlorides. The compounds of all the novel new compounds were established by IR,1H,13C NMR,MS and elemental data. The compounds 10(a-j) were evaluated for their antibacterial activity against four human pathogenic Gram-positive bacteria viz.Bacillus Subtilis,Bacillus Sphaericus,Staphylococcus Aureus and Gram-negative bacteria viz.Pseudomonas Aeruginosea,Klobsinella Aerogenes,Chrombacterium Violaceum. Amongst them, compounds containing (phenyl) moiety 10a,(4-chlorophenyl) moiety 10b,(4-bromophenyl) moiety 10c,(2-chloro-3-pyridyl) moiety 10h,(2-pyrazinyl) moiety 10i showed significant antibacterial activity,almost equal/more than the activity activity of the standard drug Streptomycin. All the compounds displayed significant activity against E.coli. Most of the novel new compounds showed appreciable activity against test bacteria as potential molecules for further development.

Keywords: Synthesis,6-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)-3-aryl/heteryl [1,2,4]triazolo [3,4-b][1,3,4]oxadiazole, 1-(5-5-[3-(5-hydrazino-1,3,4-oxadiazol-2-yl)-4-methoxybenzyl]-2-methoxyphenyl-1,3,4-oxadiazol-2-yl)hydrazine with a variety of different aryl/heteryl chlorides, Anti bacterial Activity.

1.Introduction
Oxadiazole is considered to be derived from furan by replacement of two methine (-CH=) groups by two pyridine type nitrogens (-N=). There are four possible isomers of oxadiazole depending on the position of nitrogen atom in the ring1. Among all isomers the 1,3,4-oxadiazole has enormous importance. Literature survey also reveals that particularly 1, 3, 4-oxadiazole derivatives exhibit wide range of biological activities including anticancer2, anti-inflammatory3, fungicidal4, herbicidal5, pesticide, analgesic6, anticonvulsant7,8, antibacterial and plant growth regulator activities10. Further, the biological activity of the 1,3,4-oxadiazole and its derivatives were briefly reviewed in the following sections.

Non-steroidal anti-inflammatory drugs (NSAIDs) have a wide clinical use a pharmacophore character for the inhibition of COX11, in vivo anti-inflammatory12, anti-inflammatory and analgesic agents13, lower ulcerogenic potential14, lipid peroxidation studies15, in vitro anticancer activity16, activity against gastric cancer cell SGC-79017, antimotitic activity18, cytotoxic agent19, antimicrobial agents20, anticonvulsant activities21, therapeutic agents22, Mono Amine Oxidase (MAO) Inhibitory Activity23, antidiabetic activity24, Activity on Skin25, Antiosteoporotic Activity26, Cardiovascular activity27, in vitro anti-tumor activity28, Crop protective activity29, analytical reagents30, triazole-pyridines31, triazole-pyridazines32, triazole-pyrimidines33, triazolopyrazines34, triazolo-triazines35 and triazolo-thiadiazines36. However, literature survey revealed that linked heterocycles containing triazole and oxadiazoles have been seldom been reported.

Based on the wide spectrum of biological profile of triazolo and oxadiazoles their increasing importance in pharmaceutical, and biological field, and in continuation of our ongoing research on biologically active heterocycles, it was thought of interest to accommodate triazolo and oxadiazoles

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moieties in a single molecular framework to synthesize some new heterocyclic compounds with potential biological activity.

The present investigation deals with the synthesis of a series of novel 6-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)-3-aryl/heteryl[1,2,4]triazolo[3,4-b][1,3,4]oxadiazole 10(a-j) in good to excellent yields by the reaction 1-(5-5-[3-(5-hydrazino-1,3,4-oxadiazol-2-yl)-4-methoxybenzyl]-2-methoxyphenyl-1,3,4-oxadiazol-2-yl)hydrazine with a variety of different aryl/heteryl chlorides. The antibacterial activities of the compounds 10a-j have also been evaluated.

2. Results and Discussion

The diazotization of aniline 1 by nitrous acid at 0-5 °C led to the formation of aryldiazonium chloride 2, which on reaction with sodium azide produced arylazides 3 in 76% yield. It was reported that the azide compound can be cyclized using ethyl acetoacetate to furnish 1,2,3-triazole derivative. In a similar fashion azide compound 3 was cyclized with ethyl acetoacetate 4 in the presence of sodium ethoxide to afford another intermediate, 5-methyl-1-[aryl]-1,2,3-triazole-4-carboxylic acid 5 in 68% yield. The 5-methyl-1-[aryl]-1,2,3-triazole-4-carboxylic acid 5 was reacted with absolute ethyl alcohol in the presence of catalytic amount of conc. H$_2$SO$_4$ at reflux for 3 h, to get the ethyl 5-methyl-1-phenyl-1H-1,2,3-triazole-4-carboxylate 6 in 72% yield. The intermediate, 5-methyl-1-phenyl-1H-1,2,3-triazole-4-carboxyhydrazide 7 was prepared by hydrazinolysis of compound 6 with hydrazine hydrate, in ethyl alcohol at reflux for 4 h, with 70% of yield. The 5-methyl-1-phenyl-1H-1,2,3-triazole-4-carboxyhydrazide 7 was reacted with carbon disulfide in the presence of potassium hydroxide, in ethanol at reflux for 12 h, followed by acidification gave the 5-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)-1,3,4-oxadiazol-2-ylhydrosulfide 8 in 71% of yield. Compound 8 on reaction with the hydrazine hydrazide, in the presence of potassium hydroxide, in ethanol at reflux for 8 h, produced 1-(5-5-[3-(5-hydrazino-1,3,4-oxadiazol-2-yl)-4-methoxybenzyl]-2-methoxyphenyl-1,3,4-oxadiazol-2-yl)hydrazine 8 in 79% yield. The one pot cyclocondensation of compound 9 with different aryl/heteroyl chlorides in the presence of pyridine at reflux temperature, resulted the new series of 6-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)-3-aryl/hetaryl[1,2,4]triazolo[3,4-b][1,3,4] oxadiazole 10(a-j)
2.1. Antibacterial Activity

The 3-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)-6-aryl-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine 10(a-j) were screened for their antibacterial activity against four human pathogenic bacteria Gram-positive bacteria *viz.* *Bacillus Subtilis, Bacillus Sphaericus, Staphylococcus Aureus* and Gram-negative bacteria *viz.* *Pseudomonas Aeruginosa, Klobsinella Aerogenes, Chrombacterium Violaceum*. The zone of inhibition in mm at concentration 100 µg/mL was determined using the cup-plate method. Standard antibacterial agent such as streptomycin were also screened under similar conditions for comparison and the results are presented in Table 1&2.
Table 1: Antibacterial activity of compounds 10(a-j)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Minimal inhibitory concentration (MIC) (μg/mL)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A</td>
</tr>
<tr>
<td>10a</td>
<td>25 ± 1.1</td>
</tr>
<tr>
<td>10b</td>
<td>32 ± 1.2</td>
</tr>
<tr>
<td>10c</td>
<td>28 ± 1.1</td>
</tr>
<tr>
<td>10d</td>
<td>13 ± 0.5</td>
</tr>
<tr>
<td>10e</td>
<td>18 ± 0.8</td>
</tr>
<tr>
<td>10f</td>
<td>8 ± 0.3</td>
</tr>
<tr>
<td>10g</td>
<td>10 ± 0.4</td>
</tr>
<tr>
<td>10h</td>
<td>28 ± 1.0</td>
</tr>
<tr>
<td>10i</td>
<td>30 ± 0.9</td>
</tr>
<tr>
<td>10j</td>
<td>10 ± 0.4</td>
</tr>
<tr>
<td>Streptomycin</td>
<td>15 ± 0.5</td>
</tr>
</tbody>
</table>

*Values are means of three determinations, the ranges of which are less than 5% of the mean in all cases.

A = B. Subtilis; B = B. Sphaericus; C = S. aureus; D = P. aeruginosa; E = K. aerogenes; F = C. Violaceum

Table 2: Antibacterial activity of compounds 10(a-j)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Mean zone inhibition (MZI) (mm)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A</td>
</tr>
<tr>
<td>10a</td>
<td>13 ± 0.4</td>
</tr>
<tr>
<td>10b</td>
<td>8 ± 0.2</td>
</tr>
<tr>
<td>10c</td>
<td>10 ± 0.3</td>
</tr>
<tr>
<td>10d</td>
<td>22 ± 0.8</td>
</tr>
<tr>
<td>10e</td>
<td>18 ± 0.5</td>
</tr>
<tr>
<td>10f</td>
<td>25 ± 1.0</td>
</tr>
<tr>
<td>10g</td>
<td>21 ± 1.0</td>
</tr>
<tr>
<td>10h</td>
<td>10 ± 0.4</td>
</tr>
<tr>
<td>10i</td>
<td>4 ± 0.2</td>
</tr>
<tr>
<td>10j</td>
<td>20 ± 1.0</td>
</tr>
<tr>
<td>Streptomycin</td>
<td>15 ± 0.5</td>
</tr>
</tbody>
</table>

*Values are means of three determinations, the ranges of which are less than 5% of the mean in all cases.

Streptomycin (25 μg/disc) and compounds 10a-j (50 μg/disc) were used for the assay.

A = B. Subtilis; B = B. Sphaericus; C = S. aureus; D = P. aeruginosa; E = K. aerogenes; F = C. Violaceum

3. Conclusions
In conclusion, a series of novel 6-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)-3-aryl/heteryl[1,2,4]triazolo[3,4-b][1,3,4]oxadiazole 10(a-j) has been synthesized and evaluated for their antibacterial activity against various Gram-positive and Gram-negative bacteria. All of these 10a, 10b, 10c, 10h and 10i compounds showed good antibacterial activity and can be evaluated as antibacterial agents.
4. Experimental
Reagents were of commercial grade and were used as supplied or were prepared according to procedures described in literature. Reactions were monitored by thin-layer chromatography (TLC) on pre-coated silica gel F254 plates from Merck, and compounds visualized either by exposure to UV light. Chromatographic columns 70–230 mesh silica gel for separations were used. Melting points were determined on a Fisher–Johns apparatus and are uncorrected. IR spectra were recorded using KBr disk on a Perkin–Elmer FTIR spectrometer. The 1H NMR, 13C NMR spectra were recorded on a Varian Gemini spectrometer (300 MHz for 1H and 75 MHz for 13C). Chemical shifts are reported in δppm units with respect to TMS as internal standard and coupling constants (J) are reported in Hz units. Mass spectra were recorded on a VG micro mass 7070H spectrometer. Elemental analyses (C, H, N) determined by means of a Perkin–Elmer 240 CHN elemental analyzer, were within ± 0.4% of theory.

4.1. Synthesis of phenylazide (3)
To a solution of aniline 1 (10 mol) in hydrochloric acid (25 mL), sodium nitrite solution was added drop wise at 0-5 °C and stirred for one hour to afford the diazonium chloride 2 and then cooled, stirred solution, a solution of sodium azide (25 mL) was added and stirring was continued for 30 min and the resulting solid was filtered and recrystallized from ethanol as yellow crystals.

IR (KBr): νmax 3110, 2949, 2230, 1610 cm⁻¹.

1H NMR (CDCl₃, 300 MHz): δ 7.10-7.20 (m, 5H, ArH).

13C NMR (CDCl₃, 75 MHz): δ 117.3, 122.9, 130.1, 140.2.

MS: m/z 119 (M⁺).

Anal. Calcd. for C₆H₅N₃: C, 60.50; H, 4.23; N, 35.27. Found: C, 60.45; H, 4.18; N, 35.21.

4.2. Synthesis of 5-methyl-1-[aryl]-1,2,3-triazole-4-carboxylic acid (5)
A mixture of azide 3 (0.1 mol) and ethyl acetoacetate 4 (0.1 mol) in absolute ethanol (40 mL), and sodium ethoxide solution (20 mL) was refluxed for 4 h, the white solid which formed on heating was filtered and recrystallized from ethanol.

IR (KBr): νmax 3450-3500, 3198, 2980, 2230, 1610 cm⁻¹.

1H NMR (DMSO-d₆, 300 MHz): δ 2.47 (s, 3H, CH₃), 2.60-7.60 (m, 5H, ArH), 10.5 (s, 1H, COOH).

13C NMR (CDCl₃, 75 MHz): δ 126.3, 128.2, 129.6, 131.3, 134.3, 138.1, 168.8.

MS: m/z 203 (M⁺).


4.3. Ethyl 5-methyl-1-phenyl-1H-1,2,3-triazole-4-carboxylate (6)
To the solution of 3 (0.01 mol) in absolute ethyl alcohol (25 mL), conc. H₂SO₄ (2 mL) was added. The mixture was refluxed for 3 h. After completion of the reaction (TLC), the mixture was poured into ice-cold water. Crude product was collected by filtration, washed with 10% NaHCO₃ solution, dried and recrystallized from ethyl alcohol to get pure product 5 with 72% of yield, m.p. 158-60°C.
IR (KBr): $\nu_{\max}$ 3010, 2943, 1698, 1513, 1249, 1034 cm$^{-1}$.
$^1$H NMR (DMSO-$d_6$, 300 MHz): $\delta$ 1.24 (t, 3H, CH$_3$), 2.65 (s, 3H, CH$_3$), 4.17 (q, 2H, CH$_2$), 7.30-7.40 (m, 5H, ArH).
$^{13}$C NMR (DMSO-$d_6$ 75 MHz): $\delta$ 15.7, 59.7, 125.4, 128.0, 128.9, 129.1, 134.5, 160.1.
MS: $m/z$ 231 (M$^+$).

4.4. 5-Methyl-1-phenyl-1H-1,2,3-triazole-4-carbohydrazide (7)

A mixture of compound 5 (0.01 mol) and hydrazine hydrate (0.025 mol) in ethanol (20 mL) was refluxed for 4 h, cooled to room temperature and filtered. The crude product was recrystallized from ethanol to give the new intermediate 6 in 70% of yield, m.p. 168-69°C.

IR (KBr): $\nu_{\max}$ 3270, 1630, 1610, 1395, 741 cm$^{-1}$.
$^1$H NMR (DMSO-$d_6$ 300 MHz): $\delta$ 2.30 (s, 3H, CH$_3$), 5.27 (s, 2H, NH$_2$), 7.25-7.35 (m, 5H, ArH), 7.69 (s, 1H, NH).
$^{13}$C NMR (DMSO-$d_6$ 75 MHz): $\delta$ 13.5, 119.2, 125.6, 129.7, 138.7, 151.9, 158.7.
MS: $m/z$ 217 (M$^+$).
*Anal. Calcd.* for C$_{10}$H$_{11}$N$_5$O: C, 55.29; H, 5.10; N, 32.24. Found: C, 55.21; H, 5.04; N, 32.19.

4.5. Synthesis of 5-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)-1,3,4-oxadiazol-2-yl-hydrosulfide (8)

A mixture of compound 6 (0.01 mol), potassium hydroxide (0.02 mol) and carbon disulfide (0.03 mol) in ethanol (100 mL) was heated under reflux with stirring for 12 h. The solvent was distilled in vacuo, the residual mass was poured over crushed ice and neutralized the alkaline solution with 10% hydrochloric acid. The precipitated crude product was filtered, washed with water, dried and recrystallized from ethanol to get the pure compound 7 in 71% yield, m.p. 146-48°C.

IR (KBr): $\nu_{\max}$ 3030, 2902, 2843, 1601, 1569, 1412, 1070 cm$^{-1}$.
$^1$H NMR (DMSO-$d_6$ 300 MHz): $\delta$ 2.52 (s, 3H, CH$_3$), 7.30-7.40 (m, 5H, ArH), 9.7 (s, 1H, SH/NH).
$^{13}$C NMR (DMSO-$d_6$ 75 MHz): $\delta$ 12.5, 125.4, 125.9, 128.1, 129.4, 136.4, 141.7, 152.1, 169.7.
MS: $m/z$ 259 (M$^+$).
*Anal. Calcd.* for C$_{11}$H$_9$N$_5$OS: C, 50.96; H, 3.50; N, 27.01. Found: C, 50.85; H, 3.45; N, 26.97.

4.6. 1-[5-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)-1,3,4-oxadiazol-2-yl]hydrazine (9)

To a mixture of compound 7 (0.01 mol) and potassium hydroxide (0.02 mol) in ethanol (50 mL), 80% hydrazine hydrate (0.02 mol) was added drop wise and the reaction mixture was heated under reflux for 8 h. The solvent was distilled off in vacuo, cooled and the crystals separated were filtered, washed with cold ethanol and recrystallized from alcohol to give the pure compound 8 as yellow solid; Yield 79%, mp 156-58°C.

IR (KBr): $\nu_{\max}$ 3030, 2902, 2843, 1601, 1569, 1412, 1070 cm$^{-1}$.
$^1$H NMR (DMSO-$d_6$ 300 MHz): $\delta$ 2.52 (s, 3H, CH$_3$), 7.30-7.40 (m, 5H, ArH), 9.7 (s, 1H, SH/NH).
$^{13}$C NMR (DMSO-$d_6$ 75 MHz): $\delta$ 12.5, 125.4, 125.9, 128.1, 129.4, 136.4, 141.7, 152.1, 169.7.
MS: $m/z$ 259 (M$^+$).
*Anal. Calcd.* for C$_{11}$H$_9$N$_5$OS: C, 50.96; H, 3.50; N, 27.01. Found: C, 50.85; H, 3.45; N, 26.97.
4.7. General procedure for the synthesis of 6-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)-3-aryl/heteryl[1,2,4]triazolo[3,4-b][1,3,4]oxadiazole 10(a-j)

To a solution of compound 8 (0.01 mol) in dry pyridine (25 mL), the corresponding acid chlorides (0.02 mol), was added in drops. The reaction mixture was stirred at room temperature for 2 h and then heated for 2 h in a steam bath. It was then poured onto crushed ice. The solid products obtained by filtration were crystallized from the appropriate solvents to furnish the pure compounds 9(a-j), which were characterized by $^1$H, $^{13}$C NMR, IR, MS and elemental analyses.

4.7.1. 6-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)-3-phenyl[1,2,4]triazolo[3,4-b][1,3,4]oxadiazole (10a):

IR (KBr): $\nu_{\text{max}}$ 3037, 1590, 1570, 1070, 1024 cm$^{-1}$.

$^1$H NMR (DMSO-$d_6$ 300 MHz): $\delta$ 2.47 (s, 3H, CH$_3$), 7.40-7.30 (m, 8H, ArH), 8.32 (d, $J = 7.9$ Hz, 2H, ArH).

$^{13}$C NMR (DMSO-$d_6$ 75 MHz): $\delta$ 10.9, 126.5, 127.8, 128.1, 128.9, 130.2, 131.7, 132.3, 132.5, 138.4, 140.6, 149.8, 152.7, 155.2.

MS: m/z 343 (M$^+$).

Anal. Calcd. for C$_{18}$H$_{13}$N$_7$O: C, 62.97; H, 3.82; N, 28.56. Found: C, 62.90; H, 3.78; N, 28.49.

4.7.2. 3-(4-chlorophenyl)-6-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)[1,2,4]triazolo[3,4-b][1,3,4]oxadiazole (10b):

IR (KBr): $\nu_{\text{max}}$ 3041, 1592, 1580, 1470, 1064, 1032, 685 cm$^{-1}$.

$^1$H NMR (DMSO-$d_6$ 300 MHz): $\delta$ 2.46 (s, 3H, CH$_3$), 7.40-7.30 (m, 7H, ArH), 8.37 (d, $J = 8.2$ Hz, 2H, ArH).

$^{13}$C NMR (DMSO-$d_6$ 75 MHz): $\delta$ 10.9, 126.5, 127.2, 128.1, 128.9, 132.3, 132.5, 136.8, 138.4, 140.6, 149.8, 152.7, 155.2.

MS: m/z 377 (M$^+$).


4.7.3. 3-(4-bromophenyl)-6-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)[1,2,4]triazolo[3,4-b][1,3,4]oxadiazole (10c):

IR (KBr): $\nu_{\text{max}}$ 3033, 1594, 1570, 1067, 1027, 586 cm$^{-1}$.

$^1$H NMR (DMSO-$d_6$ 300 MHz): $\delta$ 2.42 (s, 3H, CH$_3$), 7.40-7.30 (m, 5H, ArH), 7.56 (d, $J = 7.8$ Hz, 2H, ArH), 7.65 (d, $J = 7.8$ Hz, 2H, ArH).

$^{13}$C NMR (DMSO-$d_6$ 75 MHz): $\delta$ 10.9, 124.8, 126.5, 128.0, 128.4, 128.9, 131.3, 132.3, 134.5, 138.4, 140.6, 149.8, 152.7, 155.2.

MS: m/z 422 (M$^+$).
**4.7.4. 3-(2-fluorophenyl)-6-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)[1,2,4]triazolo[3,4-b][1,3,4]oxadiazole (10d):**

![Chemical structure diagram](image)

**IR (KBr):** $\nu_{\text{max}}$ 3065, 1590, 1575, 1062, 1030 cm$^{-1}$.

**$^1$H NMR (DMSO-$d_6$ 300 MHz):** $\delta$ 2.43 (s, 3H, CH$_3$), 7.40-7.30 (m, 8H, ArH), 8.21 (d, $J = 8.4$ Hz, 1H, ArH).

**$^{13}$C NMR (DMSO-$d_6$ 75 MHz):** $\delta$ 10.9, 118.1, 121.5, 125.5, 126.5, 128.1, 128.9, 131.3, 132.3, 132.9, 138.4, 140.6, 149.8, 152.7, 155.2, 165.2.

**MS: $m/z$ 361 (M$^+$).**

**Anal. Calcd. for C$_{18}$H$_{12}$BrN$_7$O: C, 51.20; H, 2.86; N, 23.22. Found: C, 51.17; H, 2.80; N, 23.18.**

**4.7.5. 3-(2,4-difluorophenyl)-6-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)[1,2,4]triazolo[3,4-b][1,3,4]oxadiazole (10e):**

![Chemical structure diagram](image)

**IR (KBr):** $\nu_{\text{max}}$ 3064, 1597, 1581, 1063, 1030 cm$^{-1}$.

**$^1$H NMR (DMSO-$d_6$ 300 MHz):** $\delta$ 2.45 (s, 3H, CH$_3$), 7.15-7.10 (m, 2H, ArH), 7.40-7.30 (m, 5H, ArH), 8.27 (d, $J = 8.4$ Hz, 1H, ArH).

**$^{13}$C NMR (DMSO-$d_6$ 75 MHz):** $\delta$ 10.9, 108.9, 116.4, 116.9, 126.5, 128.1, 128.7, 128.9, 132.3, 138.4, 140.6, 149.8, 152.7, 155.2, 162.8, 171.2.

**MS: $m/z$ 379 (M$^+$).**

**Anal. Calcd. for C$_{18}$H$_{11}$F$_2$N$_7$O: C, 59.83; H, 3.35; N, 27.13. Found: C, 59.79; H, 3.29; N, 27.09.**

**4.7.6. 6-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)-3-(4-nitrophenyl)[1,2,4]triazolo[3,4-b][1,3,4]oxadiazole (10f):**

![Chemical structure diagram](image)

**IR (KBr):** $\nu_{\text{max}}$ 3032, 1590, 1580, 1565, 1370, 1061 cm$^{-1}$.

**$^1$H NMR (DMSO-$d_6$ 300 MHz):** $\delta$ 2.45 (s, 3H, CH$_3$), 7.40-7.30 (m, 5H, ArH), 8.15 (d, $J = 8.3$ Hz, 2H, ArH), 8.77 (d, $J = 8.3$ Hz, 2H, ArH).

**$^{13}$C NMR (DMSO-$d_6$ 75 MHz):** $\delta$ 10.9, 125.6, 126.5, 128.1, 128.9, 131.2, 132.3, 133.8, 138.4, 140.0, 149.0, 152.7, 155.2.

**MS: $m/z$ 388 (M$^+$).**

**Anal. Calcd. for C$_{18}$H$_{12}$N$_8$O$_3$: C, 55.67; H, 3.11; N, 28.85. Found: C, 55.60; H, 3.07; N, 28.79.**

**4.7.7. 6-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)-3-(3-pyridyl)[1,2,4]triazolo[3,4-b][1,3,4]oxadiazole (10g):**

![Chemical structure diagram](image)

**IR (KBr):** $\nu_{\text{max}}$ 3049, 1595, 1550, 1030 cm$^{-1}$.

**$^1$H NMR (DMSO-$d_6$ 300 MHz):** $\delta$ 2.44 (s, 3H, CH$_3$), 7.40-7.30 (m, 5H, ArH), 7.90-8.10 (m, 4H, ArH).
$^{13}$C NMR (DMSO-$d_6$ 75 MHz): $\delta$ 10.9, 123.2, 124.7, 126.5, 128.1, 128.9, 132.3, 133.5, 138.4, 140.6, 149.8, 152.7, 150.2, 151.9, 155.2

MS: $m/z$ 344 ($M^+$).

Anal. Calcd. for C$_{17}$H$_{13}$N$_4$O: C, 59.30; H, 3.51; N, 32.54. Found: C, 59.26; H, 3.46; N, 32.50.

4.7.8. 3-(2-chloro-3-pyridyl)-6-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)[1,2,4]triazolo[3,4-b][1,3,4]oxadiazole (10h):

IR (KBr): $\nu_{\max}$ 3031, 1595, 1070, 1026, 689 cm$^{-1}$.

$^1$H NMR (DMSO-$d_6$ 300 MHz): $\delta$ 2.45 (s, 3H, CH$_3$), 7.40-7.30 (m, 5H, ArH), 7.90-8.10 (m, 3H, ArH).

$^{13}$C NMR (DMSO-$d_6$ 75 MHz): $\delta$ 10.9, 125.4, 126.0, 126.5, 128.1, 128.9, 132.3, 136.3, 138.4, 140.6, 146.7, 149.8, 152.7, 155.2, 156.3.

MS: $m/z$ 378 ($M^+$).

Anal. Calcd. for C$_{17}$H$_{11}$ClN$_8$O: C, 53.91; H, 2.93; N, 29.58. Found: C, 53.87; H, 2.85; N, 29.50.

4.7.9. 6-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)-3-(2-pyrazinyl)[1,2,4]triazolo[3,4-b][1,3,4]oxadiazole (10i):

IR (KBr): $\nu_{\max}$ 3032, 2972, 1590, 1070, 1025 cm$^{-1}$.

$^1$H NMR (DMSO-$d_6$ 300 MHz): $\delta$ 2.47 (s, 3H, CH$_3$), 7.40-7.30 (m, 5H, ArH), 8.30-8.40 (m, 3H, ArH).

$^{13}$C NMR (DMSO-$d_6$ 75 MHz): $\delta$ 10.9, 126.5, 128.1, 128.9, 132.3, 138.4, 140.6, 141.5, 146.3, 144.7, 149.8, 152.7, 155.2, 156.0.

MS: $m/z$ 345 ($M^+$).

Anal. Calcd. for C$_{16}$H$_{11}$N$_9$O: C, 55.65; H, 3.21; N, 36.51. Found: C, 55.60; H, 3.16; N, 36.47.

4.7.10. 3-(2-furyl)-6-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)[1,2,4]triazolo[3,4-b][1,3,4]oxadiazole (10j):

IR (KBr): $\nu_{\max}$ 3072, 2961, 1590, 1030 cm$^{-1}$.

$^1$H NMR (DMSO-$d_6$ 300 MHz): $\delta$ 2.46 (s, 3H, CH$_3$), 6.50-6.60 (m, 2H, ArH), 7.40-7.30 (m, 6H, ArH).

$^{13}$C NMR (DMSO-$d_6$ 75 MHz): $\delta$ 10.9, 112.6, 119.7, 126.5, 128.1, 128.9, 132.3, 138.4, 140.6, 142.4, 147.8, 149.8, 152.7, 155.2.

MS: $m/z$ 333 ($M^+$).

Anal. Calcd. for C$_{16}$H$_{11}$N$_7$O$_2$: C, 57.66; H, 3.33; N, 29.42. Found: C, 57.60; H, 3.28; N, 29.38.

References