CHAPTER-II

Multicomponent synthesis of 9-substituted derivatives of 6,7-dihydro-6,6-dimethyl-9-(4'-phenyl) tetrazolo [5,1-b] quinazolin-8(3H,5H,9H)-one

2.1 Introduction:

Tetrazole is 5-membered ring system containing four N and one C, having hydrogen binding domain, nitrogen atom has electron donor nature that exhibit a wide range of pharmacological, biological and medicinal importance. That include like antibiotic\textsuperscript{1-2}, antagonist\textsuperscript{3}, treatment for pancreatic cancer\textsuperscript{4} and stable surrogates for carboxylic acid.\textsuperscript{5} Tetrazole acting as a regulator in agriculture field for plant growth. Moreover, it has been significant role in material science demand as explosives\textsuperscript{6}, rocket propellants\textsuperscript{7} and corrosion inhibitors\textsuperscript{8-10}. Especially, it is essential used as organocatalysis and ligands in several coordination chemistry.

Tetrazolo derivatives or 1,5-disubstitued or amino tetrazolo derivatives has greatly increasing importance in nitrogen fused heterocyclic field. The literature survey revealed that various tetrazolo derivatives have resulted in many potential drugs and are known to exhibit a broad spectrum of pharmacological properties and biological properties such as antioxidant\textsuperscript{11}, antimalerial\textsuperscript{12}, antiviral\textsuperscript{13}, antihistamine\textsuperscript{14}, antibiotic\textsuperscript{15}, anti-inflammatory\textsuperscript{16}, antihypertensive\textsuperscript{17-18}, anxiety\textsuperscript{19}, antituberculosis\textsuperscript{20}, antinuclear\textsuperscript{21}, antimicrobial\textsuperscript{22}, HIV-I inhibitor\textsuperscript{23}, CNS stimulant\textsuperscript{24}, antidepressant\textsuperscript{25-27}, antiemetic\textsuperscript{28}, antiamoebic\textsuperscript{29}, herbicidal and antifungal\textsuperscript{30}

Quinazolines are reported to have a broad range of biological and medicinal activity such as anticancer\textsuperscript{31}, anticonculsant\textsuperscript{32-34}, antidepressant\textsuperscript{35-37}, herbicide, fungicide\textsuperscript{38}, anti-inflammatory\textsuperscript{39}, antineoplastic\textsuperscript{40}, antibacterial\textsuperscript{41}, antiplasmodial\textsuperscript{42}, AIDS treatment\textsuperscript{43},
anticonculgant\textsuperscript{44} and cognition disorder activities\textsuperscript{45}. They are also building blocks of many alkaloid molecules.

\textbf{2.2 Review of literature:}

On observing the importance of amino tetrazolo derivatives due to its pharmacological activities, medicinal chemistry, its use in field of agro chemistry and several methods for their preparation have been describes in literature.

Shibin Shang \textit{et al.}\textsuperscript{46} reported the one pot three component synthesis of new heterocyclic compounds, spiro (Indoline 3,9’-tetrazolo[5,1-b]quniazoline)-2,8’( 5’H) -dione(\textbf{II-04}) from by the condensation of aminotetrazole (\textbf{II-01}), and 5,5,-dimethyl cyclohexane-1,3-dione(\textbf{II-02}) and isatin (\textbf{II-03}), in PEG-H\textsubscript{2}O medium catalyzed by \textit{p}-toluenesulfonic acid (\textit{p}-TSA)(\textbf{Scheme-II-01}).

![Scheme-II-01](image)

Chebanove \textit{et al.}\textsuperscript{47} reported the synthesis of 5-aryl -5,8-dihydroazolo [ 1,5-\textit{a}] pyrimidine-7-caboxylic acids (\textbf{II-07}) by the condensation of 5-aminotetrazole with pyruvic acid and aromatic aldehydes in the presence of DMF or glacial acetic acid. (\textbf{Scheme-II-02}).

![Scheme-II-02](image)
Ahmed Hussein et al.\textsuperscript{48} reported the regioselective synthesis of tetrazolo [1,5-\textit{a}] pyrimidine derivatives (II-09) from reaction of sodium salt of formyl cycloalkanones with 5-amino tetrazole monohydrates in the presence of piperidine acetate and washing with acetic acid(Scheme-II-03).

\begin{center}
\begin{tikzpicture}
\node (a) at (0,0) {$\text{(II-08)}$};
\node (b) at (2,0) {$\text{NH}_2$};
\node (c) at (4,0) {$\text{NH}_2$};
\node (d) at (3.5,1.2) {$\text{pipacetate /}$};
\node (e) at (4.5,1.2) {$\text{AcOH}$};
\node (f) at (5.5,0) {$\text{(II-09)}$};
\draw[->] (a) -- (b) node[midway,above] {\text{Na}};
\draw[->] (b) -- (c);
\draw[->] (c) -- (d);
\draw[->] (d) -- (e);
\draw[->] (e) -- (f);
\end{tikzpicture}
\end{center}

Li-Yan Zeng et al.\textsuperscript{49} develop one pot synthesis of 5-(4'-bromo phenyl) dihydrotetrazolo [1,5-\textit{a}] pyrimidine-7-carboxylic acid (II-11) prepared from condensation of 5-aminotetrazole, pyruvic acid and 4-bromo benzaldehydes in ethyl acetate catalyzed by iodine(Scheme-II-04).

\begin{center}
\begin{tikzpicture}
\node (a) at (0,0) {$\text{(II-01)}$};
\node (b) at (2,0) {$\text{H}_3\text{C}$};
\node (c) at (4,0) {$\text{CHO}$};
\node (d) at (3.5,1.2) {$\text{I}_2 / \text{AcOEt}$};
\node (e) at (4.5,1.2) {$\text{reflux}$};
\node (f) at (5.5,0) {$\text{(II-11)}$};
\draw[->] (a) -- (b);
\draw[->] (b) -- (c);
\draw[->] (c) -- (d);
\draw[->] (d) -- (e);
\draw[->] (e) -- (f);
\end{tikzpicture}
\end{center}

Kolosov et al.\textsuperscript{50} reported the synthesis of 4,7-dihydrotetrazolo[1,5-\textit{a}] pyrimidine 5,6-dicarboxylates (II-13) from the ternary condensation of 5-amino tetrazole, benzaldehyde and oxaloacetic ester in acetic acid(Scheme-II-05).
Fedorova et al.\textsuperscript{51} reported the synthesis of 7-dihydrotetrazolopyrimidine [1,5-\textit{a}] pyrimidine (II-15) derivatives by reaction of 5-aminotetrazole with benzaldehydes and acetoacetic ester refluxing in ethanol with hydrochloric acid, it give moderate yield (Scheme-II-06).

Pryadeina \textit{et al.}\textsuperscript{52} reported synthesis dihydrotetrazolopyrimidine (II-18) from Biginelli like cylocondensation based on three component treatment of 5-aminotetrazole with benzaldehyde and fluorinated 1,3-dicabonyl compound in DMF (Scheme-II-07).
2.3 Present Work:

In present work, we have investigated the greener method for the synthesis of 9-substituted derivatives of 6,7-dihydro-6,6-dimethyl-9-(4'-phenyl) tetrazolo [5,1-b] quinazolin-8(3H,5H,9H)-one.

A mixture of 1H-tetrazol-5-amine (10 mmol) (II-01) and dimedone (10 mmol) (II-02) was refluxed independently in acetonitrile and iodine with different substituted aldehydes (10 mmol) (II-24a-m) like benzaldehyde, p-methyl benzaldehyde, p-methoxy benzaldehyde, p-hydroxy benzaldehyde, m-hydroxy benzaldehyde, p-nitro benzaldehyde, m-nitro benzaldehyde, p-bromo benzaldehyde, m-bromo benzaldehyde, p-chloro benzaldehyde, o-chloro benzaldehyde, p-fluorobenzaldehyde, 3,4-dimethoxy benzaldehyde, 2,4-dichloro benzaldehyde, 4-hydroxy-3-methoxy benzaldehyde, to isolate the respective 9-substituted derivatives like 6,7-dihydro -9- (phenyl, 4'-methyl phenyl, 4'-methoxy phenyl, 4'-hydroxy phenyl, 3'-hydroxy phenyl, 4'-nitro phenyl, 3'-nitro phenyl, 4'-bromo phenyl, 3'-bromo phenyl, 4'-chloro phenyl, 2'-chloro phenyl, 4'-fluoro phenyl, 3',4'-dimethoxy phenyl, 2',4'-dichloro benzaldehyde, 4'-hydroxy-3'-methoxyphenyl)-6,6-dimethyl-9-(4'-phenyl) tetrazolo [5,1-b] quinazolin-8 (3H,5H,9H)-one(II-25a-m). The progress of the reactions is monitored by TLC.

2.3.1 Objective:

On examining the literature, it can be seen that the numerous methods were reported for the synthesis of tetrazolo derivatives. It was observed that very few methods are reported for the synthesis of tetrazolo quinazolinone. The development of efficient and eco-friendly chemical approach for the synthesis of biologically active molecules constitutes a major challenge for organic chemist.

Now a days, molecular iodine has received considerable attention as an inexpensive, nontoxic, nonmetallic, readily available reagent and it has increasing reactivity of parent carbonyl compound due to capacity of binding carbonyl oxygen to afford heterocyclic compounds with many synthetic and biological applications. In continuation of our ongoing
interest in development of environment-friendly synthetic methodologies for biologically active and pharmacologically active heterocycles. Herein, we report an efficient, one pot three component MCR’s method for the synthesis of tetrazolo [5,1-b] quinazolinone derivatives.

2.3.2 Results and discussion:

A mixture of 1H-tetrazol-5-amine (10 mmol) (II-01) and dimedone (10 mmol) (II-02) was refluxed independently in acetonitrile and iodine with different substituted aromatic aldehydes (10 mmol) (II-24a-o) to isolate the respective 9-substituted derivatives of 6,7-dihydro-6,6-dimethyl-9-(4'-phenyl)tetrazolo[5,1-b] quinazolin-8 (3H,5H,9H)-one(II-25a-o). The progress of the reactions is monitored by TLC (Scheme-II-10).

![Chemical structure](Image)

The structure (II-25b) of this compound was assigned on the basis of elemental analysis and spectral data. IR spectrum of compound (II-25b) in KBr (cm⁻¹) exhibited stretching band at 3170 cm⁻¹ for the –NH stretching, band at 3055 cm⁻¹, 2931 cm⁻¹ for the Ar-H and -CH₂- groups, medium intensity band at 1650 cm⁻¹ for C=O stretching, 1581 cm⁻¹ for C=C stretching and 1419 cm⁻¹ for C=N stretching of quinazolinone (Spectrum-II-01).

The ¹H-NMR (400 MHz / ppm) spectrum analysis of the same compound was recorded in DMSO and shows two sharp singlet at δ 1.01 and δ 1.07 due to (C-6) methyl protons, two doublet at δ 2.13 –2.24 for each –CH₂- protons of (C-7) and singlet at δ 2.61 due to (C-5 (4'-Ar-CH₃)) Ar-CH₃ protons , one singlet at δ 2.25 due to -CH₂- (C-5) protons. The methane (-CH-) proton observed at (C-9) δ 6.56, Being methyl group at para position, it clearly showed two doublet at (C-9), Ar-H δ 7.09-7.11 and δ 7.17-7.19 ppm and singlet at δ 11.57 ppm due to -NH protons(Spectrum-II-02).
The mass spectrum of (II-25b) shows molecular ion peak at m/z 310 (M+ +1, 100%) which corresponds to its molecular weight (Spectrum-II-03).

$^{13}$C-NMR (400 MHz / ppm, DMSO) δ 26.93(C-8,-CH$_3$), 28.39(C-8,-CH$_3$), 40.11 (C-8), 49.85 (C-5), 57.17 (C-9), 126.92 128.98, 137.49, 148.40, 150.18, 163.44, 192.79 ppm(C-8) (Spectrum-II-04).
2.3.3 Mechanism:

A tentative plausible mechanism for the formation of parent compound (II-25 a-o) can be adduced as follows.

The molecular iodine has acting remarkable reagent properties like hard-soft reagent thats why reaction mechanism was accelerated.
Table II-01 Reaction Time, Yields and M.P. of 9-substituted derivatives of 6,7-dihydro-6,6-dimethyl-9-phenyltetrazolo [5,1-b]quinazolin-8(3H,5H,9H)-one.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Comp. code</th>
<th>Structure of the Compounds</th>
<th>Time (Hrs.)</th>
<th>Yield (%)</th>
<th>M.P. (°C)</th>
</tr>
</thead>
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<td>1</td>
<td>II-25 a</td>
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<td>60</td>
<td>180-183</td>
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<tr>
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<td>II-25 b</td>
<td><img src="structure2.png" alt="Structure" /></td>
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<td>230-232</td>
</tr>
<tr>
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<td><img src="structure3.png" alt="Structure" /></td>
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<td>210-212</td>
</tr>
<tr>
<td>4</td>
<td>II-25 d</td>
<td><img src="structure4.png" alt="Structure" /></td>
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<td>67</td>
<td>217-219</td>
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<td>5</td>
<td>II-25 e</td>
<td><img src="structure5.png" alt="Structure" /></td>
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<td>62</td>
<td>208-211</td>
</tr>
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<td></td>
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</tr>
<tr>
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<td>218-220</td>
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</table>

22
2.4 Experimental:

2.4.1 General procedure for 9-substituted derivatives of 6,7-dihydro-6,6-dimethyl-9-phenyltetrazolo [5,1-b]quinazolin-8(3H,5H,9H)-one (II-25a)

A mixture of appropriate 1H-tetrazol-5-amine (10 mmol) and dimedone (10 mmol) with different substituted benzaldehyde (10 mmol) was refluxed independently in acetonitrile (10 ml) and iodine (10 mmol%) solution to isolate the respective 9-substituted derivatives of 6,7-dihydro-6,6-dimethyl-9-phenyl tetrazolo [5,1-b] quinazolin-8(3H,5H,9H)-one. The reaction was monitored by TLC.

2.5 Spectral Analysis:

Characterization of the products:

All the products were characterized by IR, NMR (1H and 13C) and Mass spectrum analysis. A detail spectral analysis of compound (II-25a-o) is discussed below.


![Chemical Structure](image)

Yield: 60 %  
M.P. : 180-183 °C

Molecular formula: C_{16}H_{17}N_{5}O  
Molecular Weight: 295

Elemental analysis: %C %H %N
Calculated : 65.07  5.80  23.71  
Found : 65.05  5.78  23.69  


The structure (II-25b) of this compound was assigned on the basis of elemental analysis and spectral data. IR spectrum of compound (II-25b) in KBr (cm⁻¹) exhibited stretching band at 3170 cm⁻¹ for the –NH stretching, band at 3055 cm⁻¹, 2931 cm⁻¹ for the Ar-H and -CH₂- groups, medium intensity band at 1650 cm⁻¹ for C=O stretching, 1581 cm⁻¹ for C=C stretching and 1419 cm⁻¹ for C=N stretching of quinazolinone (Spectrum-II-01).

The ¹H-NMR (400 MHz / ppm) spectrum analysis of the same compound was recorded in DMSO and shows two sharp singlet at δ 1.01 and δ 1.07 due to (C-6) methyl protons, two doublet at δ 2.13–2.24 for each –CH₂- protons of (C-7) and singlet at δ 2.61 due to (C-5 (4’-Ar-CH₃)) Ar-CH₃ protons, one singlet at δ 2.25 due to -CH₂- (C-5) protons. The methane (-CH-) proton observed at (C-9) δ 6.56. Being methyl group at para position, it clearly showed two doublet at (C-9), Ar-H  δ 7.09-7.11 and δ 7.17-7.19 ppm and singlet at δ 11.57 ppm due to -NH protons(Spectrum-II-02).

The mass spectrum of (II-25b) shows molecular ion peak at m/z 310 (M⁺ +1, 100%) which corresponds to its molecular weight (Spectrum-II-03).
$^{13}$C-NMR (400 MHz / ppm, DMSO) δ 26.93(C-8,-CH$_3$), 28.39(C-8,-CH$_3$), 40.11 (C-8), 49.85 (C-5), 57.17 (C-9), 126.92 128.98, 137.49, 148.40, 150.18, 163.44, 192.79 ppm(C-8)(Spectrum-II-04)

Yield: 73 %  
M.P. : 230-233 °C

Molecular formula: C$_{17}$H$_{19}$N$_5$O  
Molecular Weight: 309

Elemental analysis:  
\begin{align*}
\text{Calculated} & : & 66.00 & 6.19 & 22.64 \\
\text{Found} & : & 65.98 & 6.17 & 22.62
\end{align*}


IR spectrum of compound (II-25c) in KBr exhibited stretching band at 3170 cm$^{-1}$ for the -NH- groups, stretching band at 2923 cm$^{-1}$, 2866 cm$^{-1}$ for the -CH$_2$- groups, medium intensity band at 1650 cm$^{-1}$ for C=O stretching, 1596 cm$^{-1}$ for C=C stretching and 1519 cm$^{-1}$ for C=N stretching, 1369 cm$^{-1}$ for C-N-C stretching tetrazolo ring of quinazolinone (Spectrum-II-05).

The $^1$H-NMR (400 MHz / ppm) spectrum analysis of the same compound was recorded in DMSO and shows two sharp singlet at δ 1.03 and δ 1.09 for (C-6) two methyl protons, two doublet at δ 2.04-2.26 for each -CH$_2$- (C-7) protons and singlet at δ 2.64 due to
CH$_2$ (C-5) protons. The -CH- (C-9) proton observed at δ 6.58 ppm due to (C-9) Ar-H protons and being –OCH$_3$ group at para position of C-4’ aromatic ring, it exhibited singlet at δ 3.44 ppm and multiplet at δ 7.24-7.33 ppm due to Ar-H protons. Important peak singlet at δ 11.75 ppm due to -NH protons (Spectrum-II-06).

The mass spectrum shows molecular ion peak at m/z 326 (M$^+$+1, 100%) (Spectrum-II-07) which corresponds to its molecular weight.

Yield: 62 % M.P. : 210-212 °C

Molecular formula: C$_{17}$H$_{19}$N$_5$O$_2$ Molecular Weight: 325

Elemental analysis: %C %H %N
Calculated : 62.75 5.89 21.52
Found : 62.73 5.87 21.50


IR spectrum of compound (II-25f) in KBr exhibited stretching band at 3382 cm$^{-1}$ for the –OH group, stretching band at 3286 cm$^{-1}$ for the –NH groups, asymmetric and symmetric stretching band at 2923 cm$^{-1}$, 2860 cm$^{-1}$ for the -CH$_2$- groups, medium intensity band at 1643 cm$^{-1}$ for C=O stretching, 1596 cm$^{-1}$ for C=C stretching and 1515 cm$^{-1}$ for C=N stretching and 1384 cm$^{-1}$ for C-N-C stretching tetrazolo ring of quinazolinone (Spectrum-II-08).
The $^1$H-NMR (400 MHz / ppm) spectrum analysis of the same compound was recorded in DMSO and shows two sharp singlet at $\delta$ 0.64 and $\delta$ 0.79 for (C-6) two methyl protons, two doublet at $\delta$ 1.96-2.26 for each -CH$_2$- (C-7) protons and singlet at $\delta$ 2.34 due to CH$_2$ (C-5) protons. The -CH- (C-9) proton observed at $\delta$ 6.10 ppm due to (C-9) Ar-H protons and being –OH group at para position of C-4’ aromatic ring, it exhibited singlet at $\delta$ 5.02 ppm and multiplet at $\delta$ 6.45-6.86 ppm due to Ar-H protons. Important peak singlet at $\delta$ 11.27 ppm due to -NH protons(Spectrum-II-09).

The mass spectrum shows molecular ion peak at m/z 311 (M$^+$+1, 100%) (Spectrum-II-10) which corresponds to its molecular weight.

Yield: 67 % M.P. : 217-219 °C

Molecular formula: C$_{16}$H$_{17}$N$_5$O$_2$ Molecular Weight: 311

Elemental analysis:

<table>
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<th></th>
<th>%C</th>
<th>%H</th>
<th>%N</th>
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<tr>
<td>Calculated</td>
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<td>5.50</td>
<td>22.49</td>
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<tr>
<td>Found</td>
<td>61.70</td>
<td>5.48</td>
<td>22.47</td>
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IR spectrum of compound (II-25e) in KBr exhibited stretching band at 3239 cm$^{-1}$ for the –NH groups, stretching band at 3258 cm$^{-1}$ for the –OH group, asymmetric and symmetric
stretching band at 2963 cm\(^{-1}\), 2870 cm\(^{-1}\) for the -CH\(_2\)- groups, medium intensity band at 1687 cm\(^{-1}\) for C=O stretching, 1661 cm\(^{-1}\) for C=N stretching and 1569 cm\(^{-1}\) for C=C stretching, 1330 cm\(^{-1}\) for C-N-C stretching tetrazolo ring of quinazolinone.

Yield: 62 %  
M.P.: 208-211 °C

Molecular formula: C\(_{16}\)H\(_{17}\)N\(_5\)O\(_2\)  
Molecular Weight: 311

Elemental analysis:  
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<th>%C</th>
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<th>%N</th>
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<tbody>
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<td>5.50</td>
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<tbody>
<tr>
<td>61.71</td>
<td>5.49</td>
<td>22.48</td>
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6] 6,7-dihydro-6,6-dimethyl-9-(4'-nitrophenyl)tetrazolo[5,1-\(b\)]quinazolin-8 (3\(H\),5\(H\),9\(H\))-one (II-25 f).

![Chemical Structure](image)

Yield: 57 %  
M.P.: 213-215 °C

Molecular formula: C\(_{16}\)H\(_{16}\)N\(_6\)O\(_3\)  
Molecular Weight: 340

Elemental analysis:  
<table>
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<th>%C</th>
<th>%H</th>
<th>%N</th>
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</thead>
<tbody>
<tr>
<td>56.47</td>
<td>4.74</td>
<td>24.69</td>
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Found:  
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<th>%N</th>
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<tbody>
<tr>
<td>56.45</td>
<td>4.72</td>
<td>24.67</td>
</tr>
</tbody>
</table>
7] 6,7-dihydro-6,6-dimethyl-9-(3'-nitrophenyl)tetrazolo[5,1-b]quinazolin-8 (3H,5H,9H)-one (II-25 g).

Yield: 57 %  M.P. : 213-215 °C
Molecular formula: C_{16}H_{16}N_{6}O_{3}  Molecular Weight: 340
Elemental analysis:  %C  %H  %N
Calculated : 56.47  4.74  24.69
Found : 56.45  4.73  24.68

8] 9-(4'-bromophenyl)-6,7-dihydro-6,6-dimethyltetrazolo[5,1-b]quinazolin-8 (3H,5H,9H)-one (II-25 h).

Yield: 65%  M.P. : 222-225 °C
Molecular formula: C_{16}H_{16}N_{5}O  Molecular Weight: 374
Elemental analysis:  %C  %H  %N
Calculated : 51.35  4.31  18.71  
Found : 51.33  4.20  18.70  

9] 9-(3'-bromophenyl)-6,7-dihydro-6,6-dimethyltetrazolo[5,1-b]quinazolin-8 (3H,5H,9H)-one (II-25 i).

Yield: 61 %  
M.P. : 213-215 0°C  
Molecular formula: C_{16}H_{16}N_{5}O  
Molecular Weight: 374  
Elemental analysis:  

<table>
<thead>
<tr>
<th>%C</th>
<th>%H</th>
<th>%N</th>
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<tbody>
<tr>
<td>51.35</td>
<td>4.31</td>
<td>18.71</td>
</tr>
<tr>
<td>51.33</td>
<td>4.30</td>
<td>18.69</td>
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Yield: 63 %  
M.P. : 218-220 0°C  
Molecular formula: C_{16}H_{16}ClN_{5}O  
Molecular Weight: 329
Elemental analysis: %C %H %N
Calculated : 58.27 4.89 21.24
Found : 58.25 4.87 21.22

11] 9-(2’-chlorophenyl)-6,7-dihydro-6,6-dimethyltetrazolo[5,1-b]quinazolin-8
(3H,5H,9H)-one (II-25 k).

Yield: 68 % M.P.: 192-194 °C
Molecular formula: C_{16}H_{16}ClN_{5}O Molecular Weight: 329
Elemental analysis: %C %H %N
Calculated : 58.27 4.89 21.40
Found : 58.27 4.87 21.38

12] 9-(4’-fluorophenyl)-6,7-dihydro-6,6-dimethyltetrazolo[5,1-b]quinazolin-8
(3H,5H,9H)-one (II-25 l).

Yield: 60 % M.P.: 204-206 °C
Molecular formula: C_{16}H_{16}FN_{5}O  
Molecular Weight: 313

Elemental analysis:

<table>
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<th></th>
<th>%C</th>
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<th>%N</th>
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</thead>
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<tr>
<td>Calculated</td>
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<tr>
<td>Found</td>
<td>61.32</td>
<td>5.13</td>
<td>22.33</td>
</tr>
</tbody>
</table>

13] 6,7-dihydro-9-(3',4'-dimethoxyphenyl)-6,6-dimethyltetrazolo[5,1-b]quinazolin-8(3H,5H,9H)-one (II-25m).

IR spectrum of compound (II-25m) in KBr exhibited stretching band at 3166 cm\(^{-1}\) for the -NH groups, stretching band at 3051 cm\(^{-1}\), 2962 cm\(^{-1}\) for the -CH\(_2\)-groups, medium intensity band at 1654 cm\(^{-1}\) for C=O stretching, 1573 cm\(^{-1}\) for C=C stretching and 1515 cm\(^{-1}\) for C=N stretching, 1147 cm\(^{-1}\) for C-N-C stretching triazolo ring of quinazolinone (Spectrum-II-11).

The \(^1\)H-NMR (400 MHz / ppm) spectrum analysis of the same compound was recorded in DMSO and shows two sharp singlet at δ 1.07 and δ 1.11 for (C-6) methyl protons, two doublet at δ 2.13-2.28 for each -CH\(_2\)- (C-7) protons and singlet at δ 2.60 due to CH\(_2\) (C-5) protons, two singlet at δ 3.57-3.77 due to Ar-OCH\(_3\) protons. The -CH- (C-9) proton observed at δ 6.54, Being dissubstitution of atom at para and meta -OCH\(_3\) position, it clearly shows multiplet at δ 6.77-6.89 due to (C-9). Finally important singlet at δ 11.50 ppm due to -NH protons (Spectrum-II-12).

The mass spectrum shows molecular ion peak at m/z 355 (M\(^+\), 100%) (Spectrum-II-13) which corresponds to its molecular weight.
The $^{13}$C-NMR (400 MHz / ppm, DMSO) δ 26.82 (C-6,-CH$_3$), 28.58 (C-6,-CH$_3$), 32.26 (C-6), 49.90 (C-5), 57.38 (C-9), 78.17, 119.20, 132.66, 148.24, 148.49, 148.69, 150.13, 164.01, 192.82 ppm (C-8) (Spectrum-II-14).

Yield: 70%  
M.P. : 244-246°C

Molecular formula: C$_{18}$H$_{21}$N$_5$O$_3$  
Molecular Weight: 355

Elemental analysis: | %C | %H | %N |
<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>Calculated :</td>
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<td>5.96</td>
</tr>
<tr>
<td>Found :</td>
<td>60.81</td>
<td>5.94</td>
</tr>
</tbody>
</table>

14] 9-(2,4-dichlorophenyl)-6,7-dihydro-6,6-dimethyltetrazolo[5,1-b]quinazolin-8(3H,5H,9H)-one (II-25n).

IR spectrum of compound (II-25n) in KBr exhibited stretching band at 3390 cm$^{-1}$ for the -NH group, stretching band at 2923 cm$^{-1}$, 2856 cm$^{-1}$ for the -CH$_2$- groups, medium intensity band at 1647 cm$^{-1}$ for C=O stretching, 1566 cm$^{-1}$ for C=C stretching and 1515 cm$^{-1}$ for C=N stretching, 1337 cm$^{-1}$ for C-N-C stretching tetrazolo ring of quinazolinone (Spectrum-II-15).

The $^1$H-NMR (400 MHz / ppm) spectrum analysis of the same compound was recorded in DMSO and shows two sharp singlet at δ 1.04, and δ 1.09 for (C-6) two methyl protons, two doublet at δ 2.12-2.25 for each -CH$_2$- (C-7) protons and singlet at δ 2.61 due to
CH₂ (C-5) protons. The -CH- (C-9) proton observed at δ 6.90 ppm. Being disubstitution chlorine atom at para and ortho position, it clearly shows multiplet at δ 7.33-7.56 ppm for Ar-H protons. Significantly singlet at δ 11.75 ppm due to -NH protons (Spectrum-II-16).

The mass spectrum shows molecular ion peak at m/z 364 (M⁺, 100%), 366 (M⁺+2, 33%) (Spectrum-II-17) which corresponds to its molecular weight and confirms the presence of two Cl atom.

The ¹³C-NMR (400 MHz / ppm, DMSO) δ 27.04 (C-6, -CH₃), 28.24 (C-6, -CH₃), 32.11 (C-6), 38.81 (C-5), 55.31 (C-9), 78.38, 78.71, 79.04, 127.40, 128.03, 129.19, 130.70, 148.24, 148.44, 151.29, 163.33, 192.87 ppm (C-8) (Spectrum-II-18).

Yield: 68 % M.P. : 250-252 °C

Molecular formula: C₁₆H₁₅Cl₂N₅O

Molecular Weight: 364

Elemental analysis:

<table>
<thead>
<tr>
<th></th>
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<th>%H</th>
<th>%N</th>
</tr>
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<tr>
<td>Calculated</td>
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<td>4.15</td>
<td>19.23</td>
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<tr>
<td>Found</td>
<td>52.74</td>
<td>4.13</td>
<td>19.21</td>
</tr>
</tbody>
</table>


IR spectrum of compound (II-25o) in KBr exhibited stretching band at 3386 cm⁻¹ for the –OH group, stretching band at 3020 cm⁻¹ for the -NH- group, stretching band at 2958 cm⁻¹.
1, 2877 cm\(^{-1}\) for the -CH\(_2\)- groups, medium intensity band at 1631 cm\(^{-1}\) for C=O stretching, 1596 cm\(^{-1}\) for C=N stretching and 1519 cm\(^{-1}\) for C=C stretching, 1344 cm\(^{-1}\) for C-N-C stretching tetrazolo ring of quinazolinone (Spectrum-II-19).

The \(^1\)H-NMR (400 MHz / ppm) spectrum analysis of the same compound was recorded in DMSO and shows two sharp singlet at \(\delta\) 0.99 and \(\delta\) 1.04 for (C-6) two methyl protons, two doublet at \(\delta\) 2.11-2.16 and \(\delta\) 2.20-2.25 for each -CH\(_2\)- (C-7) protons and singlet at \(\delta\) 2.55 due to CH\(_2\) (C-5) protons. The -CH- (C-9) proton observed at \(\delta\) 6.63 ppm due to Ar-H protons and being –OH group at para position of C-4’ aromatic ring, it exhibited singlet at \(\delta\) 4.23 ppm, -OCH\(_3\) group at meta position it exhibited singlet at \(\delta\) 3.43 ppm and multiplet at \(\delta\) 7.12-7.37 ppm due to Ar-H protons. Important peak singlet at \(\delta\) 11.63 ppm due to -NH protons (Spectrum-II-20).

The mass spectrum shows molecular ion peak at m/z 342 (M\(^+\)+1,100%) (Spectrum-II-21) which corresponds to its molecular weight.

Yield: 69 %  
M.P.: 209-211\(^\circ\)C

Molecular formula: C\(_{17}\)H\(_{19}\)N\(_5\)O\(_3\)  
Molecular Weight: 341

Elemental analysis:  
\begin{array}{ccc}
\text{Calculated} & \%C & \%H & \%N \\
59.81 & 5.61 & 20.52 \\
\text{Found} & 59.79 & 5.59 & 20.50 \\
\end{array}
2.6 Conclusion:

- The preparation of 9-substituted derivatives of 6,7-dihydro-6,6-dimethyl-9-(4’-phenyl) tetrazolo [5,1-b]quinazolin-8(3H,5H,9H)-one by one pot three component MCRs cyclocondensation reaction of different substituted aldehyde, 5-amino-1H- tetrazole and dimedone in iodine, acetonitrile is a very challenging reaction and not a single report of references is available in the literature involving this type of reaction.
- The reaction requires ambient reaction condition, short reaction time and gives excellent isolated yields and the work up is very easy, this methodology for the synthesis of poly substituted tetrazolo [5,1-b] quinazolinone followed by Knoevenagel-Michael type of reaction.
- The product obtained can be easily isolated.
- By simple work up procedure.
2.7 Spectra:


2.8 References:


