CHAPTER - II

Synthesis and Characterization of certain triazole compounds
Synthesis and Characterization of certain triazole compounds

2.1. Introduction

A triazole (Htrz) refers to either one of a pair of isomeric chemical compounds with molecular formula C₂H₃N₃, having a five-membered ring of two carbon atoms and three nitrogen atoms. The two isomers are: 1, 2, 3-Triazole and 1, 2, 4-Triazole. The synthesis of triazole based heterocycles has been considered by the chemists and medicinal chemists as the cornerstone of medicinal chemistry due to their important biological activities. Even in the early part of the twentieth century the researchers started working on the possibility of using 1,2,3-triazolo[4,5-d] pyrimidines (8-azapurines) for the treatment of cancer and malignant tumors [1]. 1, 2, 3-triazoles cause peptidomimetic inhibition of tyrosinase, an enzyme which causes the browning of plant based foodstuffs and human skin diseases [2, 3]. Some of the triazole antifungal drugs include fluconazole, isavuconazole, itraconazole, voriconazole, pramiconazole, ravuconazole and posaconazole. The features possessed by the 1, 2, 3-triazoles make them pharmaceutically important molecules [4]. They are stable to reduction and oxidation as well as to hydrolysis in acidic and basic conditions, which indicates their high aromatic stabilization. 1,2,3-triazoles have a high dipole moment (about 5 D) [5-10] and are able to participate actively in hydrogen bond formation as well as in dipole–dipole and π stacking interactions [6] which helps them in binding easily with the biological targets [7] and improves their solubility. On the other hand, the triazole plant protection fungicides include epoxiconazole, triadimenol, propiconazole, metconazole, cyproconazole, tebuconazole, flusilazole and paclorbutrazol. Due to spreading resistance of plant pathogens towards fungicides of the strobilurin class (1), control of fungi such as Septoria tritici or Gibberella zeae (2) relies heavily on triazoles. The azide alkyne Huisgen cycloaddition is a mild and selective reaction that gives 1, 2, 3-triazoles as products. The reaction has been widely used in bioorthogonal chemistry and in organic synthesis. Triazoles are relatively stable functional groups and triazole linkages can be used in a variety of applications (for example, replacing the phosphate backbone of DNA [5]. Despite a significant work on 1, 2, 3-triazoles, continuous efforts are still being made to
identify novel heterocyclic compounds with potent bioactivities [11- 46] and 1, 2, 4-triazoles [47- 57]. Synthesis of 1-monosubstituted aryl 1, 2, 3-triazoles was achieved by Jiang et al [11] in good yields using calcium carbide as a source of acetylene. The copper-catalysed 1, 3-dipolar cycloaddition reactions in presence of sodium ascorbate were carried out without nitrogen protection and in a MeCN-H2O mixture.

Barluenga and co-workers [12] developed a synthetic protocol using a Pd-catalyst for the synthesis of 1H-triazoles from alkenyl halides and sodium azide. This reaction represents a completely new reactivity pattern in the context of Pd chemistry. Aryl 1H-triazoles were obtained in dioxane medium at 90°C, while alkyl and vinyl analogues were procured under 2-5 mol % of catalyst, 4 mol% xantphos in DMSO at still elevated temperatures.

Kolarović and co-workers [13] developed a tandem catalysis protocol based on decarboxylative coupling of alkynoic acids and 1,3-dipolar cycloaddition of azides. This protocol avoids usage of gaseous or highly volatile terminal alkynes, reduces handling of potentially unstable and explosive azides to a minimum, and furnishes various functionalized 1,2,3-triazoles in excellent yields and a very good purity without the need for additional purification.

Yamada, Sarkar, and Uozumi [13] developed self-assembly of copper sulfate and a polyimidazole-acrylamide) amphiphile that provides a highly active, reusable, globular, solid-phase catalyst for click chemistry. The insoluble amphiphilic polymeric imidazol Cu catalyst drove the cycloaddition of several of alkynes and organic azides at very low catalyst loadings and can be readily reused without loss of activity to give the corresponding triazoles quantitatively.
Jiang, Kuang and Yang [14] concentrated their attention on the synthesis of 4-Aryl-1H-1,2,3-triazoles from anti-3-aryl-2,3-dibromopropionic acids and sodium azide by using inexpensive copper(I) iodide as the catalyst in the presence of Cesium carbonate as base and DMSO as solvent.

In another synthetic task, Zhang, Kuang and Yang [15] obtained 4-Aryl-1H-1,2,3-triazoles from anti-3-aryl-2,3-dibromopropionic acids and sodium azide by a one-pot method using N,N-dimethyl formamide as solvent in the presence of Pd₂(dba)₃ and Xantphos. Wu, Xie, and several others [16] procured 1-Substituted-1,2,3-triazoles were conveniently synthesized from the corresponding aromatic and aliphatic azides in the presence of acetylene gas using mild, copper(I)- catalyzed ‘click chemistry’. Lal and Díez-González developed a true Click catalytic system based on commercially available [CuBr(PPh₃)₃]. This system is active at room temperature, with catalyst loadings of 0.5 mol % or less, in the absence of any additive, and it does not require any purification step to isolate pure triazoles. A further insight into the Click Chemistry protocols revealed different reports on the synthesis of several compounds based on 1, 2, 3-triazoles’ backbone [18-26].

Liu and Reiser [21] examined a well-defined copper(I) isonitrile complex is an efficient, heterogeneous catalyst for azide-alkyne 1,3-dipolar cycloadditions and three-component reactions of halides, sodium azide and alkynes to form 1,4-disubstituted 1,2,3-triazoles in high yields under mild conditions in water. The complex can be recycled for at least five runs without significant loss of activity by simple precipitation and filtration.
Boren, Narayan and others [26] studied the catalytic activity of a series of Ruthenium (II) complexes in azide–alkyne cycloadditions has been evaluated. The [Cp*RuCl] complexes, such as Cp*RuCl(PPh3)2, Cp*RuCl(COD) and Cp*RuCl(NBD), were among the most effective catalysts. In the presence of catalytic Cp*RuCl(PPh3)2 or Cp*RuCl(COD), primary and secondary azides react with a broad range of terminal alkynes containing a range of functionalities selectively producing 1,5-disubstituted 1,2,3-triazoles; tertiary azides were significantly less reactive. Both complexes also promote the cycloaddition reactions of organic azides with internal alkynes, providing access to fully-substituted 1, 2, 3-triazoles. The ruthenium-catalyzed azide–alkyne cycloaddition (RuAAC) appears to proceed via oxidative coupling of the azide and alkyne reactants to give a six-membered Ru then a cycle intermediate, in which the first new carbon–nitrogen bond is formed between the more electronegative carbon of the alkyne and the terminal, electrophilic nitrogen of the azide. This step is followed by reductive elimination, which forms the triazole product. DFT calculations support this mechanistic proposal and indicate that the reductive elimination step is rate-determining.

In the presence of inexpensive copper (I) iodide as the catalyst, a series of 1, 4-disubstituted 1, 2, 3-triazoles were synthesized by Chen, Yang and others [27] in one-pot process from anti-3-aryl-2,3-dibromopropanoic acids and organic azides in dimethyl sulfoxide.

Yan, Zhao, and others [28] studied copper(I)-catalyzed three-component reaction of
amines, propargyl halides and azides, which formed 1-substituted-1H-1,2,3-triazol-4-yl methyl-dialkylamines in water. Synthetic advantages are high atom economy, low environmental impact, atmospheric oxygen, wide substrate scope, mild reaction condition and good yields.

\[
\begin{align*}
R\text{-NH} + 2\text{Br} + 2\text{N}_3 + 6\text{CuI} &\xrightarrow{\text{H}_{2}\text{O}, \text{rt}, 7-16 \text{ h}} R\text{-NH} = \text{N} = \text{N} - R' \\
&\text{R: Alkyl, Ar, alkyl, benzyl I}
\end{align*}
\]

Copper(I) iodide catalyzed method developed by Wu et. al [29] is the first example of a regiospecific synthesis of 5-iodo-1,4-disubstituted-1,2,3-triazole, which can be further elaborated to a range of 1,4,5-trisubstituted-1,2,3-triazole derivatives.

\[
\begin{align*}
\text{RN}_3 + \text{R'}\equiv &\xrightarrow{1\text{eq. CuI, 1eq. ICl, 1.2eq. N}_3\text{Et}_3} \text{THF, rt, 20 h}} N = N = R' \\
&\text{R': Ph, C}_8\text{H}_7
\end{align*}
\]

In a detailed study Ackermann and co-workers [30] enabled modular one-pot multi component syntheses of fully decorated triazoles through a sustainable “Click” reaction/direct arylation sequence using inexpensive copper catalysts.

\[
\begin{align*}
\text{R} + \text{N}_3 - \text{R} &\xrightarrow{0.1\text{eq. CuI, 60°C, 4 h}} \text{N} = \text{N} = \text{N} = \text{N} - \text{R} \\
&\text{R': Ph, C}_8\text{H}_7
\end{align*}
\]

\[
\begin{align*}
\text{Bu} + \text{I} - \text{Ar} &\xrightarrow{1.05\text{eq. NaN}_3, 0.1\text{eq. CuI, 0.15eq. TMEDA, 140°C, 20 h}} \text{N} = \text{N} = \text{N} = \text{N} - \text{Ar} \\
&\text{Ar': C}_8\text{H}_7
\end{align*}
\]

Moses and Moorhouse [31] observed significant rate enhancements for the formation of 1,4-disubstituted 1,2,3-triazoles from alkynes and in situ generated azides under MW
irradiation. Azides are derived from an efficient one-pot azidation of anilines with the reagent combination t-BuONO and TMSN₃.

\[
\text{Ar-NH}_2 + 1.5 \text{eq. t-BuONO} + 1-1.2 \text{eq. TMSN}_3 \xrightarrow{\text{CH}_3\text{CN}, \text{rt}, 2 \text{ min} -2 \text{ h}} \text{Ar-N}_3 \xrightarrow{0.1 \text{ eq. CuSO}_4, 0.5 \text{ eq. sodium ascorbate}, \text{CH}_3\text{CN/H}_2\text{O}(2:1), \text{MW}(<125 \text{ W}), \text{80}^\circ\text{C}, 2-10 \text{ min}} \text{Ar-N}_3\text{-N=O-NAr}
\]

Luvino et. al examined a reliable and operationally simple one-pot reaction [32] for a one-carbon homologation of various aldehydes followed by Cu-catalyzed azide-alkyne click chemistry gives 1,4-disubstituted 1,2,3-triazoles in good yields without the need for isolation of the alkyne intermediates.

\[
\text{R}-\text{H} + 3 \text{ eq. K}_2\text{CO}_3, \text{MeOH/THF (1:1), rt, 2-24 h}} \xrightarrow{2.25 \text{ eq. } \text{P}^\text{Me}_2\text{C} = \text{N}} \text{R}-\text{N} \xrightarrow{0.2 \text{ eq. } \text{Cu}^\text{I}, \text{rt, 2-12 h}} \text{R}-\text{N} = \text{N} - \text{R}'
\]

1, 2, 3-Triazoles were prepared by Rogue and co-workers [33] in good to modest yields by cycloaddition of alkyl azides onto enol ethers under solvent less conditions. The reaction could access ring-fused triazoles that are unavailable by azide-alkyne cycloadditions and is easily scalable. The 1, 2, 3-triazole products bear functionality that may be readily derivatized.

\[
\text{R-N}_3 + 1.1-1.2 \text{ eq. } \text{MeO} = \text{C} \xrightarrow{200 \degree\text{C}, 6 \text{ h}} \left[ \text{N}_2\text{N}-\text{N}-\text{R}' \right] \xrightarrow{\text{OMe}} \left[ \text{N}_2\text{N}-\text{N}-\text{R}' \right]
\]

Triazoles have been synthesized by Kamijo et al [34] via a three-component coupling reaction of unactivated terminal alkynes, allyl carbonate, and trimethylsilyl azide under Pd(0)-Cu(I) bimetallic catalysis. The deallylation of the resulting allyltriazoles is also described in this study.
Reaction of 4-bromo-NH-1,2,3-triazoles with alkyl halides in the presence of K₂CO₃ in DMF produced the corresponding 2-substituted 4-bromo-1,2,3-triazoles in a regioselective process. Subsequent Suzuki cross-coupling reaction provided an efficient synthesis of 2,4,5-trisubstituted triazoles, whereas hydrogenation furnished an efficient synthesis of 2,4-disubstituted triazoles [35].

Li, Wang, Zhang, Chen and others [36] studied ultrasonically promoted and palladium-catalyzed Sonogashira coupling/1,3-dipolar cycloaddition of acid chlorides, terminal acetylenes, and sodium azide in one pot enables an efficient synthesis of 4,5-disubstituted-1,2,3-(NH)-triazoles in excellent yields.

TBAF-catalyzed [3 + 2] cycloadditions of 2-aryl-1-cyano- or 2-aryl-1-carbethoxy-1-nitroethenes with TMSN₃ under solvent free conditions allow the preparation of 4-aryl-5-cyano- or 4-aryl-5-carbethoxy-1H-1,2,3-triazoles under mild reaction conditions with good to excellent yields [37].
Triazole-based monophosphine ligands have been prepared by Liu et al [38] via efficient cycloadditions. Palladium complexes derived from these ligands are highly active catalysts for Suzuki-Miyaura coupling and amination reactions of aryl chlorides. Recycling of the catalytic system led to a slight decrease of activity.

Chuprakov and coworkers [39] developed a highly efficient method for the synthesis of multi substituted 1,2,3-triazoles via a direct Pd-catalyzed C-5 arylation.

Ackermann, and Vicente explored [40] the use of nontoxic polyethylene glycol (PEG) as solvent and MesCO₂H as co-catalyst enabled user-friendly palladium(0)-catalyzed C-H bond functionalization under air in the absence of phosphine ligands. Direct arylations of 1,2,3-triazoles gave substituted triazoles in good yields. Recycling of the catalytic system led to a slight decrease of activity.

Conditions for the palladium-catalyzed direct arylation of a wide range of heterocycles with aryl bromides employ a stoichiometric ratio of both coupling partners, as well as a sub stoichiometric quantity of pivalic acid, which results in significantly faster reactions.
[41]. An evaluation of the influence of the nature of the aryl halide has also been carried out in this study.

\[
\begin{align*}
N & N N R' + Ar-Br \quad 2 \text{ mol\% Pd(OAc)}_2 \\
& \quad 4 \text{ mol\% PCy}_3, \text{ HBF}_4 \quad 1.5 \text{ eq. K}_2\text{CO}_3, \text{ 0.3 eq. PivOH} \\
& \quad \text{DMA, 100 °C, 6-24 h} \\
& \quad \text{R: Br, Ph} \\
& \quad R': H, \text{ Ph, alkyl}
\end{align*}
\]

A [3 + 2] cycloaddition of azides to benzyne by Shi and others [42] afforded a rapid and easy entry to a variety of substituted, functionalized benzotriazoles under mild conditions.

\[
\begin{align*}
1.2 \text{ eq.} & \\
\text{MeSiMe}_3 & + N_3 \rightarrow R' \quad 2 \text{ eq. GSF} \\
& \quad \text{McCN} \\
& \quad r.t., 18-24 h
\end{align*}
\]

Zhou, Wang and others [43] used a 1,7-palladium migration-cyclization-dealkylation sequence for the regioselective synthesis of benzotriazoles proceed in excellent yields with high regioselectivities. In this study, mechanism of the reaction has also been discussed.

\[
\begin{align*}
\text{Me} & \\
\text{N} & N N \text{Ar} \quad 5 \text{ mol\% Pd(CAc)}_2 \\
& \quad 0.1 \text{ eq. dipp} \\
& \quad 1.2 \text{ eq. KCl} \\
& \quad \text{DMF, 110 °C, 12 h}
\end{align*}
\]

Kumar, Ali, and Punniyamurthy [44] studied C-H activation of aryl triazene compounds followed by intramolecular amination in the presence of a catalytic amount of Pd(OAc)$_2$, which provided 1-aryl-1$H$-benzotriazoles at moderate temperature.

\[
\begin{align*}
\text{R} & \\
\text{N} & N \text{N} \text{Ar} \quad 0.1 \text{ eq. Pd(CAc)}_2 \\
& \quad 2 \text{ eq. CS}_2\text{CO}_3 \\
& \quad \text{O}_2(\text{balloon}) \text{DMF} \\
& \quad \text{MeSO}_4\text{H}, 110 °C, 25 h
\end{align*}
\]

On the other hand, 1,2,4-Triazole is one of a pair of isomeric chemical compounds with molecular formula C$_2$H$_3$N$_3$, called triazoles, which have a five-membered ring of two
carbon atoms and three nitrogen atoms. 1, 2, 4-Triazole is a basic aromatic heterocycle. 1, 2, 4-Triazole derivatives find use in a wide variety of applications, most notably as antifungals such as fluconazole and itraconazole. Organic chemistry portal furnishes some recent literature reports on this subject [45]. A multicomponent process developed by Tam, Armstrong, and La Cruz [46] enabled the synthesis of 1-aryl 1, 2, 4-triazoles directly from anilines, amino pyridines, and pyrimidines. The reaction scope was explored with 21 different substrates.

Ueda and Nagasa was developed [47] a copper-catalyzed reaction under an atmosphere of air provides 1,2,4-triazole derivatives by sequential N-C and N-N bond-forming oxidative coupling reactions. Starting materials and the copper catalyst are readily available and inexpensive. A wide range of functional groups are tolerated.

Castanedo and co scholars [48] examined a highly regioselective one-pot process, which provided rapid access to highly diverse 1,3,5-trisubstituted 1,2,4-triazoles from reaction of carboxylic acids, primary amidines, and mono substituted hydrazines at room temperature.

Wang, Tseng and others provided an effective 1,3-dipolar cycloaddition [49] for the synthesis of 1,3,5-trisubstituted 1,2,4-triazole derivatives by reaction of oximes with hydrazonyl hydrochlorides using triethylamine as a base gave the desired 1,3,5-
trisubstituted 1,2,4-triazoles in good yields. The reaction could be successfully applied to aliphatic, cyclic aliphatic, aromatic and heterocyclic oxime substrates.

![Chemical structure](image)

Xu, McLaughlin and others synthesized a series of new oxamide-derived amidine reagents in excellent yield with minimal purification [50]. A subsequent reaction of these reagents with various hydrazine hydrochloride salts efficiently generates 1, 5-disubstituted-1,2,4-triazole compounds in good yields. Both aromatic and aliphatic hydrazines react readily with the amidine reagents under very mild reaction conditions.

![Chemical structure](image)

Batchelor, Beal, Brown and several others [51] prepared 3-N, N-Dialkylamino-1,2,4-triazoles from S-methyl isothioureas and acyl hydrazides in good yields under mild reaction conditions. The protocol could tolerate a broad range of functional groups.

![Chemical structure](image)

In another protocol, hexafluorophosphoric acid promoted the formation of 1, 3, 4-oxadiazolium hexafluorophosphate salts from \( N' \)-acyl-\( N \)-arylhydrazides or \( N' \)-acyl-\( N \)-acyl-N-arylhydrazides under mild conditions [52]. A subsequent reaction with cyanamide in propan-2-ol in the presence of triethylamine generated 1, 5-disubstituted 3-amino-1H-1, 2, 4-triazoles in good yields. Ueda and Nagasawa [53] developed an economically viable copper-catalyzed reaction under an atmosphere of air that provided 1, 2, 4-triazole derivatives by sequential N-C and N-N bond-forming oxidative coupling.
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reactions. A wide range of functional groups are tolerated in this methodology. A mild, one-pot cyanoimidation of aldehydes using cyanamide as a nitrogen source and NBS as an oxidant was achieved by Yin et al [54] in high yields without the addition of a catalyst. Subsequently, the substituted N-cyanobenimidate products may also undergo a cyclization reaction to give 1,2,4-triazole derivatives in high yields. An efficient and convenient synthesis of [1,2,4] triazolo[4,3-a]pyridines involves a palladium-catalyzed addition of hydrazides to 2-chloropyridine, which occurs chemoselectively at the terminal nitrogen atom of the hydrazide, followed by dehydration in acetic acid under microwave irradiation [55].

Huntsman and Balsells [56] synthesized [1,2,4]Triazolo[1,5-a]pyridines in good yields from 2-aminopyridines by cyclization of N-(pyrid-2-yl)form amidoximes under mild reaction conditions with trifluoroacetic anhydride. Despite a significant work on 1, 2, 3-triazoles and 1, 2, 4-triazoles continuous efforts are still being made to identify novel heterocyclic compounds with potent bioactivities. In this chapter the author has looked at certain new methodologies pertaining to the formation of C-N bonds. To facilitate these new methods the author examined the chemistry of a specific nitrogenous organic functionality that allows redox neutral C-N bond forming processes. The findings are compiled into two sections: Section-A of Chapter -II deals with the “3-phenyl-5-((4-((p-tolyloxy)methyl)-1H-1,2,3-triazol-1-yl)methyl)-1,2,4-oxadiazole (Triazole) Compounds”, as shown the following scheme (Scheme 2.2).

In Chapter-II section-B depicts the synthesis of 2-(4-(phenoxyethyl)-1H-1,2,3-triazol-1-yl)-1-phenyl ethanone (X).
2.2. Synthesis of 3-phenyl-5-((4-((p-tolyloxy) methyl)-1H-1, 2, 3-triazol-1-yl)methyl)-1,2,4-oxadiazole (Triazole) Compounds (VII)

Oxadiazazole derivative (5-(azidomethyl)-3-(4-chlorophenyl) -1,2,4-oxadiazole (IV)) when treated with Phenyl proargyne (VI) in presence of an aqueous solution containing catalytic amounts of CuSO$_4$ and sodium ascorbate afforded 3-phenyl-5-((4-((p-tolyloxy) methyl)-1H-1,2,3-triazol-1-yl)methyl)-1,2,4-oxadiazole (Triazole Compounds (VII)) in DMF medium under stirred conditions for about 6-8 hrs, at room temperature as shown in Scheme-I. Reactant (IV) and (VI) necessary for the synthesis of (VII) were prepared as and when required using the following reaction protocols (Schemes I and II).

2.2.1. Synthesis of Reactants (IV) and (VI):

(a) **Synthesis of (II) Amidoxime:** A mixture of benzonitrile (4g, 25.4 mmol), hydroxylamine hydrochloride (3.2g 33.4 mmol) was taken in a round bottom flask to this add 10 ml of triethylamine and 50 mL of ethanol this mixture was refluxed for 2 hr. The ethanol and excesses of triethylamine was removed under reduced pressure. A light yellow solid was obtained to which water (20 mL) was added. The solid precipitate was collected by filtration and washed with water and dried at 50°C to furnish hydroxybenzimidamide.

(b) **Synthesis of (III):** Hydroxybenzimidamide (3.0g, 15.8 mmol) was taken in 50 mL round bottom flak and add 50 mL of Tetrahydrofuran. The reaction mixture was cooled to 10°C. A solution of chloroacetylchloride (1.5 ml, 18.8 mmol) in 10 ml of 1,2-dichloroethane was added drop wise. After completion of the addition the resulting reaction mixture was refluxed for 2 hrs. A brownish solution obtained was poured into ice cold water and extracted with CHCl$_3$ (2×50mL) and the organic layer was washed with NaHCO$_3$ solution (2×20 mL), water (2×20 mL) and dried over Na$_2$SO$_4$. The crude product was purified by column chromatography on 60-120 silica-gel eluting with 5:95 EtOAc: Hexane to give white amorphous solid.
(c) **Synthesis of (IV):** A mixture of sodium azide (3.5 g, 50 mmol) and 5-(chloromethyl)-3-phenyl-1,2,4-oxadiazole (8.0 mL, 50 mmol) in DMF (40 mL) were heated at 80 °C for 7 hours. After completion of the reaction crushed ice was added to the reaction mixture and extracted with chloroform, dried over Na₂SO₄ and concentrated to give 5-(azidomethyl)-3-phenyl-1,2,4-oxadiazole as colorless liquid.

![Scheme 1: Azide preparation](image)

\[ R_1 = H, 4-\text{Me}, 4-\text{Cl} \]
Structures of Compounds (I) to (IV):

<table>
<thead>
<tr>
<th>starting material (I)</th>
<th>Product (II)</th>
<th>Product (III)</th>
<th>Product (IV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \text{benzonitrile} )</td>
<td>( \text{IIa} )</td>
<td>( \text{IIIa} )</td>
<td>( \text{IVa} )</td>
</tr>
<tr>
<td>( \text{Ia} )</td>
<td>( \text{N-OH} )</td>
<td>( \text{5-(chloromethyl)-3-phenyl-1,2,4-oxadiazole} )</td>
<td>( \text{5-(azidomethyl)-3-phenyl-1,2,4-oxadiazole} )</td>
</tr>
<tr>
<td>( \text{4-methylbenzonitrile} )</td>
<td>( \text{IIb} )</td>
<td>( \text{IIIb} )</td>
<td>( \text{IVb} )</td>
</tr>
<tr>
<td>( \text{Ib} )</td>
<td>( \text{N-OH} )</td>
<td>( \text{5-(chloromethyl)-3-(p-tolyl)-1,2,4-oxadiazole} )</td>
<td>( \text{5-(azidomethyl)-3-(p-tolyl)-1,2,4-oxadiazole} )</td>
</tr>
<tr>
<td>( \text{4-chlorobenzonitrile} )</td>
<td>( \text{IIc} )</td>
<td>( \text{IIc} )</td>
<td>( \text{IVc} )</td>
</tr>
<tr>
<td>( \text{Ic} )</td>
<td>( \text{N-OH} )</td>
<td>( \text{5-(chloromethyl)-3-(4-chlorophenyl)-1,2,4-oxadiazole} )</td>
<td>( \text{5-(azidomethyl)-3-(4-chlorophenyl)-1,2,4-oxadiazole} )</td>
</tr>
</tbody>
</table>

Table 2.1: Spectroscopic Data for Compounds (IV)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Physical/Spectroscopic data</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV a</td>
<td>( ^1H ) NMR (400 MHz, CDCl(_3)): 4.65 (s, 2H), 7.51 (m, 1H), 7.56 (m, 2H), 8.12 (d, J = 2.0 Hz, 1H), 8.13 (d, J=1.5 Hz, 1H); Yield:87%</td>
</tr>
<tr>
<td>IV b</td>
<td>( ^1H ) NMR (400 MHz, CDCl(_3)): 2.45 (s, 3H), 4.64 (s, 2H), 7.32 (d, J = 8.0 Hz, 2H), 8.01 (d, J = 8.2 Hz, 2H); Yield:89%</td>
</tr>
<tr>
<td>IV c</td>
<td>( ^1H ) NMR (400 MHz, CDCl(_3)): 4.64 (s, 2H), 7.50 (d, J = 8.6 Hz, 2H), 8.06 (d, J = 8.6 Hz, 2H); Yield:92%</td>
</tr>
</tbody>
</table>

(d) Synthesis of Reactant (VI) - Propargylation of Phenols: In this reaction propargyl bromide reacts with phenol in the presence of potassium carbonate and acetone medium affords (prop-2-yn-1-yloxy) benzene derivatives to get oily compound.
Propargyl bromide (0.3g 1.5 mmol) was added to a suspension of an appropriate phenol (0.26 g) and potassium carbonate (4 m mol) in acetone (30 mL). The suspension was heated to reflux for 2-6 h (monitored by TLC). The reaction was allowed to cool and then concentrated under reduced pressure. Water (30 mL) was added and extracted with CH₂Cl₂ (3×30 mL). The organic extracts were combined and washed with water (20 mL) and brine (20 mL). The organic layer was dried over anhydrous Na₂SO₄, filtered and concentrated. The crude product was purified by column chromatography.

**Structures of Compound (VI):**

<table>
<thead>
<tr>
<th>Reactant(Phenol)</th>
<th>Product(propargyl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \text{Va} )</td>
<td>( \text{VIa} ) (prop-2-yn-1-yloxy)benzene</td>
</tr>
<tr>
<td>( \text{Vb} )</td>
<td>( \text{VIb} ) 1-chloro-4-(prop-2-yn-1-yloxy)benzene</td>
</tr>
<tr>
<td>( \text{Vc} )</td>
<td>( \text{Vlc} ) 1-chloro-3-(prop-2-yn-1-yloxy)benzene</td>
</tr>
<tr>
<td>( \text{Vd} )</td>
<td>( \text{Vld} ) 1-methyl-4-(prop-2-yn-1-yloxy)benzene</td>
</tr>
<tr>
<td>( \text{Ve} )</td>
<td>( \text{Vle} ) 1-methoxy-4-(prop-2-yn-1-yloxy)benzene</td>
</tr>
</tbody>
</table>
2.2.2. Synthesis of Triazole Compounds (VII)- 3-phenyl-5-((4-(p-tolyloxy) methyl)-1H-1,2,3-triazol-1-yl)methyl)-1,2,4-oxadiazole compounds: 5-(azidomethyl)-3-(4-chlorophenyl) -1,2,4-oxadiazole (2.56 g, 10 mmol) and 1-chloro-4-(prop-2-yn-1-yloxy) benzene (3.02 g, 10 mmol) were suspended in a mixture in DMF (20 mL). Sodiumascorbate (0.3 m mol, 50 µL of freshly prepared 1M solution in water) was added, followed by copper (II) sulfate pentahydrate (7.5 mg, 0.03 mmol, in 100 µL of water). The heterogeneous mixture was stirred vigorously overnight, at which point it cleared and TLC analysis indicated complete consumption of the reactants. A brownish solution obtained was poured into ice cold water and extracted with CHCl₃ (2×50 mL) and the organic layer was washed with NaHCO₃ solution (2×20 mL), water (2×20 mL) and dried over Na₂SO₄. The crude product was purified by column chromatography on 60-120 silica gel eluting with 15:85 EtOAc: Hexane to give white amorphous solid.

**Scheme-III:** Schematic representation of the synthesis of 3-phenyl-5-((4-(p-tolyloxy) methyl)-1H-1,2,3-triazol-1-yl)methyl)-1,2,4-oxadiazole(Triazole Compounds –VII a-o)

![Scheme-III](image_url)
Structures of Triazole Compounds (VII a to VII o):

<table>
<thead>
<tr>
<th>Entry</th>
<th>Compounds</th>
<th>Entry</th>
<th>Compounds</th>
</tr>
</thead>
<tbody>
<tr>
<td>VII a</td>
<td><img src="image1.png" alt="Image" /></td>
<td>VII i</td>
<td><img src="image2.png" alt="Image" /></td>
</tr>
<tr>
<td>VII b</td>
<td><img src="image3.png" alt="Image" /></td>
<td>VII j</td>
<td><img src="image4.png" alt="Image" /></td>
</tr>
<tr>
<td>VII c</td>
<td><img src="image5.png" alt="Image" /></td>
<td>VII k</td>
<td><img src="image6.png" alt="Image" /></td>
</tr>
<tr>
<td>VII d</td>
<td><img src="image7.png" alt="Image" /></td>
<td>VII l</td>
<td><img src="image8.png" alt="Image" /></td>
</tr>
<tr>
<td>VII e</td>
<td><img src="image9.png" alt="Image" /></td>
<td>VII m</td>
<td><img src="image10.png" alt="Image" /></td>
</tr>
<tr>
<td>VII f</td>
<td><img src="image11.png" alt="Image" /></td>
<td>VII n</td>
<td><img src="image12.png" alt="Image" /></td>
</tr>
<tr>
<td>VII g</td>
<td><img src="image13.png" alt="Image" /></td>
<td>VII o</td>
<td><img src="image14.png" alt="Image" /></td>
</tr>
<tr>
<td>VII h</td>
<td><img src="image15.png" alt="Image" /></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Table-2.2: Spectroscopic data of Compounds (VII a-o):

<table>
<thead>
<tr>
<th>Entry</th>
<th>Physical/spectroscopic data</th>
</tr>
</thead>
<tbody>
<tr>
<td>VII a</td>
<td>H NMR (400 MHz, CDCl₃): δ 5.23 (s, 2H), 5.89 (s, 2H), 6.91 (d, J=9.0Hz, 2H), 7.23 (d, J=9.0Hz, 2H), 7.46 (m, 3H), 7.48 (m, 3H), 7.93(s, 1H), 8.02 (ddd, J=1.2Hz, J=8.0Hz, J=9.5Hz, 2H), M.W.:(M+1): 334.0; m.p.(°C):70-72</td>
</tr>
<tr>
<td>VII b</td>
<td>H NMR (400 MHz, CDCl₃): δ 5.23 (s, 2H), 5.89 (s, 2H), 6.91 (d, J=9.0Hz, 2H), 7.23 (d, J=9.0Hz, 2H), 7.46 (m, 3H), 7.48 (m, 3H), 7.93(s, 1H), 8.02 (ddd, J=1.2Hz, J=8.0Hz, J=9.5Hz, 2H), M.W.:(M+1): 368.8; m.p.(°C):65-68</td>
</tr>
<tr>
<td>VII c</td>
<td>H NMR (400 MHz, CDCl₃): δ 5.23 (s, 2H), 5.90 (s, 2H), 6.87 (dd, dd, J=1.7Hz, J=2.5Hz, 2H), 7.07 (d, J=8.0Hz, 2H), 7.48 (m, 3H), 7.91(s, 1H), 8.02(dd, J=1.2Hz, J=8.0Hz, J=9.5Hz, 2H), M.W.:(M+1): 368.8; m.p.(°C):81-83 IR (cm⁻¹):3138(C-H),1749(C-Cl)</td>
</tr>
<tr>
<td>VII d</td>
<td>H NMR (400 MHz, CDCl₃): δ 2.28 (s, 3H), 5.21 (s, 2H), 5.86 (s, 2H), 6.87 (d, J=8.5Hz 2H), 7.07 (d, J=8.0Hz 2H), 7.47 (m, 3H), 7.48 (m, 3H), 7.91(s, 1H), 8.02(dd, J=1.5Hz, J=8.0Hz, J=9.7Hz, 2H), M.W.:(M+1): 348.0; m.p.(°C): 77-80 IR (cm⁻¹):3132(C-H),1751(C-C)</td>
</tr>
<tr>
<td>VII e</td>
<td>H NMR (400 MHz, CDCl₃): δ 3.75 (s, 3H), 5.20 (s, 2H), 5.88 (s, 2H), 6.82 (d, J=9.0Hz, 2H), 9.91 (d, J=9.0Hz, 2H), 7.46 (m, 3H), 7.91(s, 1H), 8.03 (d, J=6.7Hz, 2H), M.W.:(M+1): 364.0; m.p.(°C):110.112, IR (cm⁻¹):3138.2(C-H)</td>
</tr>
<tr>
<td>VII f</td>
<td>H NMR (400 MHz, CDCl₃): δ 5.27 (s, 2H), 5.89 (s, 2H), 6.98 (m, 3H), 7.28 (m, 2H), 7.45 (d, J=8.8Hz, 2H), 7.92 (s, 1H), 7.92(s, 1H), 7.97(d, J=8.8Hz, 2H), M.W.(m/z+1): 368.4; M.P.(°C): 119-121</td>
</tr>
<tr>
<td>VII g</td>
<td>H NMR (400 MHz, CDCl₃): δ 5.22 (s, 2H), 5.89 (s, 2H), 6.91 (d, J=9.2Hz, 2H), 7.22 (d, J=9.0Hz, 2H), 7.45 (d, J=8.7Hz, 2H), 7.91(s, 1H), 7.96(d, J=8.7Hz, 2H), M.W.(m/z+1): 403.5; M.P.(°C): 113-116</td>
</tr>
<tr>
<td>VII h</td>
<td>H NMR (400 MHz, CDCl₃): δ 5.24 (s, 2H), 5.90 (s, 2H), 6.87 (dd, dd, J=0.7Hz, J=2.2 Hz, J=3.2Hz 2H), 6.98 (m, 1H), 7.19 (t, J=8.0Hz, J=16.3Hz 1H), 7.45 (d, J=8.5Hz, 2H), 7.92(s, 1H), 7.97(d, J=8.8Hz, 2H), M.W.(m/z+1): 403.3; M.P.(°C): 90-94</td>
</tr>
<tr>
<td>VII i</td>
<td>H NMR (400 MHz, CDCl₃): δ 2.28 (s, 3H), 5.23 (s, 2H), 5.58 (s, 2H), 6.87 (d, J=8.7Hz, 2H), 7.08 (d, J=8.7Hz, 2H), 7.45 (d, J=8.7Hz, 2H), 7.90(s, 1H), 7.97(d, J=8.7Hz, 2H), M.W.(m/z+1): 383.0; M.P.(°C): 124-126</td>
</tr>
<tr>
<td>VII j</td>
<td>H NMR (400 MHz, CDCl₃): δ 3.76 (s, 3H), 5.21 (s, 2H), 5.88 (s, 2H), 6.82 (d, J=9.0Hz, 2H), 6.91 (d, J=10.0Hz, 2H), 7.45(d, J=8.8Hz, 2H), 7.90(s, 1H), 7.97(d, J=8.5Hz, 2H), M.W.(m/z+1): 399.0; M.P.(°C): 104-106</td>
</tr>
<tr>
<td>VII k</td>
<td>H NMR (400 MHz, CDCl₃): δ 2.41 (s, 3H), 3.75 (s, 2H), 5.19 (s, 2H), 5.86 (s, 2H), 6.81 (d, J=9.2Hz, 2H), 7.26 (d, J=8.5Hz, 2H), 7.90 (brS, 2H), 7.92(s, 1H), M.W.:(M+1): 348.3; m.p.(°C):86-88</td>
</tr>
<tr>
<td>VII l</td>
<td>H NMR (400 MHz, CDCl₃): δ 2.41 (s, 3H), 5.21 (s, 2H), 5.87 (s, 2H), 6.90 (d, J=9.2Hz, 2H), 7.22 (m, 4H), 7.90 (s, 1H), 7.92(brS, 2H), M.W.:(M+1): 383.7; m.p.(°C): 115-117</td>
</tr>
<tr>
<td>VII m</td>
<td>H NMR (400 MHz, CDCl₃): δ 2.41 (s, 3H), 5.22 (s, 2H), 5.88 (s, 2H), 6.86 (m, 1H), 6.94 (m, 2H), 7.18 (t, J=9.5Hz, 1H), 7.27(s, 1H), 7.29 (s, 1H), 7.90 (s, 1H), 7.92 (d, J=2.5Hz, 2H), M.W.:(M+1): 383.2; m.p.(°C): 90-92</td>
</tr>
<tr>
<td>VII n</td>
<td>H NMR (400 MHz, CDCl₃): δ 2.27 (s, 3H), 5.21 (s, 3H), 5.21 (s, 2H), 5.85 (s, 2H), 6.86 (d, J=8.5Hz, 2H), 7.07 (d, J=8.0Hz, 2H), 7.26 (d, J=8.0Hz, 2H), 7.90(s, 1H), 7.91 (d, J=8.2Hz, 2H), M.W.:(M+1): 362.2; m.p.(°C): 87-89</td>
</tr>
<tr>
<td>VII o</td>
<td>H NMR (400 MHz, CDCl₃): δ 2.41 (s, 3H), 3.75 (s, 2H), 5.19 (s, 2H), 5.86 (s, 2H), 6.81 (d, J=9.2Hz, 2H), 7.26 (d, J=8.5Hz, 2H), 7.90 (brS, 2H), 7.92(s, 1H), M.W.:(M+1): 378.3; m.p.(°C): 75-77</td>
</tr>
</tbody>
</table>
2.3. Synthesis of Keto Triazoles (2-(4-(phenoxy)methyl)-1H-1, 2, 3-triazol-1-yl)-1-phenyl ethanone (X).

Phenacyl bromide (VII) reacts with sodium azide to give a 2-azido-1-phenyl ethanone (IX). This product reacts with 2-Propyne in DMF in presence of Copper (II) sulfate pentahydrate and sodiumascorbate and affords 4-(4-(phenoxy)methyl)-1H-1,2,3-triazol-1-yl)-1-phenylethanone(X) white solid compound through cycloaddition reaction path (the Click chemistry).

2.3.1. Synthesis of 2-Azido-1-Phenylethanone (IX): A mixture of sodium azide (2 g) and 2-bromoacetophenone (3.0 g) in acetonitrile (20 mL) were heated at 60 °C for 1 hour. After completion of the reaction crushed ice was added to the reaction mixture and extracted with Ethylacetate, dried over Na₂SO₄ and concentrated to give 2-azido-1-phenylethanone (2 mL, 98%) as yellow colour liquid.

\[ \text{Br} \overset{\text{N₃}}{\rightleftharpoons} \text{O} \]

2.3.2. Synthesis and characterization of keto triazoles (X) : 2-Propyne (2.56 g, 10 mmol) and 2-azido-1-phenylethanone (10 mmol) were suspended in DMF (20 mL). Freshly prepared aqueous sodium ascorbate (0.3 m mol, 50 µL) was added to above reaction mixture followed by Copper (II) sulfate pentahydrate (7.5 mg, 0.03mmol, in 100 µL of water). The heterogeneous mixture was stirred vigorously overnight, till the point at which it becomes clear. Progress of the reaction is monitored by TLC. After complete consumption of the reactants, a brownish solution was obtained. The resultant reaction mixture is poured into ice cold water and extracted with CHCl₃ (2×50 mL). Organic layer was washed with NaHCO₃ solution (2×20 mL), water (2×20 mL) and dried over Na₂SO₄. The crude product was purified by column chromatography on 60-120 silica gel eluting with EtOAc: Hexane to give white amorphous solid.
Table 2.3: Spectroscopic data of keto triazoles

<table>
<thead>
<tr>
<th>Triazole Product</th>
<th>Spectral/Physical Data</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Image" /> 2-(4-(phenoxymethyl)-1H-1,2,3-triazol-5-yl)-1-phenylethanone</td>
<td>$^1$H NMR (400 MHz, CDCl$_3$): 5.22 (s, 2H), 5.85 (s, 2H), 6.98 (m, 3H), 7.31 (m, 2H), 7.52 (d, J = 7.2 Hz, 2H), 7.67 (m, 1H), 7.81 (m, 1H), 8.02 (d, J = 1.6 Hz, 1H); m.p.(ºC): 70-72; M.W(M+1): 295.8; Yield: 92%</td>
</tr>
<tr>
<td><img src="image2" alt="Image" /> 2-(4-(chlorophenoxymethyl)-1H-1,2,3-triazol-5-yl)-1-phenylethanone</td>
<td>$^1$H NMR (400 MHz, CDCl$_3$): 5.22 (s, 2H), 5.84 (s, 2H), 7.02 (d, J = 8.5 Hz, 2H), 7.07 (d, J = 8.0 Hz, 2H), 7.48 (t, J = 1.2 Hz, 2H), 7.65 (m, 1H), 7.78 (s, 1H), 7.98 (d, J = 7.2 Hz, 1H); m.p.(ºC): 68-69; M.W(M+1): 328.9; Yield: 91%</td>
</tr>
<tr>
<td><img src="image3" alt="Image" /> 2-(4-(4-chlorophenoxymethyl)-1H-1,2,3-triazol-5-yl)-1-phenylethanone</td>
<td>$^1$H NMR (400 MHz, CDCl$_3$): 5.23 (s, 2H), 5.84 (s, 2H), 6.86 (d, J = 8.2 Hz, 2H), 7.53 (d, J = 7.8 Hz, 2H), 7.68 (m, 1H), 7.75 (m, 1H), 8.02 (dd, J = 2.2 Hz, J = 8.5 Hz, 2H); m.p.(ºC): 80-83; M.W(M+2): 329.6; Yield: 94%</td>
</tr>
<tr>
<td><img src="image4" alt="Image" /> 1-phenyl-2-(4-(4-methoxy)methyl)-1H-1,2,3-triazol-5-yl)-1-phenylethanone</td>
<td>$^1$H NMR (400 MHz, CDCl$_3$): δ 2.82 (s, 3H), 5.22 (s, 2H), 5.85 (s, 2H), 7.09 (d, J = 8.0 Hz, 2H), 7.56 (d, J = 8.0 Hz, 2H), 7.67 (m, 1H), 7.77 (bs, 1H), 8.0 (dd, J = 1.2 Hz, J = 8.6 Hz, 2H); m.p.(ºC): 70-72; M.W(M+1): 308.5; Yield: 81%.</td>
</tr>
<tr>
<td><img src="image5" alt="Image" /> 3-(4-(4-methoxyphenoxy)methyl)-1H-1,2,3-triazol-5-yl)-1-phenylethanone</td>
<td>$^1$H NMR (400 MHz, CDCl$_3$): δ 3.82 (s, 3H), 5.21 (s, 2H), 6.84 (d, J = 8.7 Hz, 2H), 6.96 (d, J = 8.7 Hz, 2H), 7.54 (d, J = 7.7 Hz, 2H), 7.62 (m, 1H), 7.72 (s, 1H), 8.03 (d, J = 1.4 Hz, J = 8.3 Hz, 2H); m.p.(ºC): 75-77; M.W(M+1): 325.0; Yield: 78%</td>
</tr>
</tbody>
</table>
Table 2.4: Structure of keto chloro triazoles

<table>
<thead>
<tr>
<th>Chloro Triazole Products</th>
<th>M.W (M+1)</th>
<th>chlorotriazole products</th>
<th>M.W (M+1)</th>
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</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Structure 1" /></td>
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<td><img src="image2.png" alt="Structure 2" /></td>
<td>362.21</td>
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<td><img src="image3.png" alt="Structure 3" /></td>
<td>362.21</td>
<td><img src="image4.png" alt="Structure 4" /></td>
<td>327.76</td>
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<tr>
<td><img src="image5.png" alt="Structure 5" /></td>
<td>357.79</td>
<td><img src="image6.png" alt="Structure 6" /></td>
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</tbody>
</table>

2.4. Biological Activity Studies of Triazole derivatives

Antibacterial activity and minimum inhibitory concentration (MIC) were determined against one gram-positive bacterium (*Staphylococcus aureus*) and one gram-negative bacterium (*Pseudomonas aeruginosa*).

Organisms Collection:

Both the organisms *Staphylococcus aureus* and *Pseudomonas aeruginosa* were collected from the Microbiology Research Laboratory of the Microbiology Department, Osmania University at Hyderabad. Growth Media and Conditions: Nutrient agar media (HIMEDIA Laboratories) pH 7.2, nutrient broth media (HIMEDIA Laboratories) pH 6.8 were used for antibacterial screening.
Antibacterial Screening:

Antibacterial screening is generally performed by disc diffusion method which is a qualitative to semi quantitative test. Briefly 15ml quantities of nutrient agar were plated in petri dish with 0.1 ml of a 10 dilutions of each bacterial culture. Filter paper discs (6 mm in diameter) impregnated with various concentrations of plant extracts were placed on test organism-seeded plates. Different compounds with different dilution were prepared range from 1µg/ml to 200µg/ml. The activity was determined after 18 h of incubation at 37°C. The diameters of zone of inhibition produced by the extract were then compared with the standard antibiotic Ampicillin 30 µm/disc. Each sample was used in triplicate for the determination of antibacterial activity.

Minimum Inhibitory Concentration Measurement:

A current definition of the minimum inhibitory concentration (MIC) is the lowest concentration which resulted in maintenance or reduction of inoculums viability. Serial tube dilution technique was used to determine of MIC of the different compounds against gram-positive and gram-negative bacteria. The compounds (0 to 200µg) were dissolved in 1 ml DMSO to obtain stock solution. After preparation of test organisms suspensions (1000 organism per ml), 1 drop of suspension (0.02 ml) was added to each broth dilution. After 18 h incubation at 37°C, the tubes were then examined for the growth. The MIC of the each compound was taken as the lowest concentration that showed no growth. Growth was observed in those tubes where the concentration of the each compound was below the inhibitory level and the broth medium was observed turbid (cloudy). DMSO and Ampicillin were used as negative and positive control, respectively.

In this study, five different triazole compounds (VII a to VII e) were tested for their antibacterial activity against different types of bacteria. Among the five different triazole derivatives, VII c has been found to exhibit maximum activity and VII b indicated minimum activity with reference to CIPROFLOXACIN and GENTAMICIN, as shown in Table-2.5.
Table 2.5: Biological Activity Studies of Triazole derivatives

<table>
<thead>
<tr>
<th>Triazole</th>
<th>Pseudomonas aeruginosa MIC Value (µg/ml)</th>
<th>Streptococcus pyogenes MIC Value (µg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VII a</td>
<td>8.5</td>
<td>8.2</td>
</tr>
<tr>
<td>VII b</td>
<td>9.0</td>
<td>7.5</td>
</tr>
<tr>
<td>VII c</td>
<td>7.5</td>
<td>8.5</td>
</tr>
<tr>
<td>VII d</td>
<td>8.6</td>
<td>9.0</td>
</tr>
<tr>
<td>VII e</td>
<td>7.5</td>
<td>8.5</td>
</tr>
<tr>
<td>CIPROFLOXACIN</td>
<td>8.08</td>
<td>8.12</td>
</tr>
<tr>
<td>GENTAMICIN</td>
<td>2.5</td>
<td>6.5</td>
</tr>
</tbody>
</table>

2.5. Conclusions

In summary, a novel series of 3-phenyl-5-((4-((p-tolyloxy) methyl)-1H-1,2,3-triazol-1-yl)methyl)-1,2,4-oxadiazole (Triazole Compounds (VII)) were synthesized in the first protocol from 5-(azidomethyl)-3-(4-chlorophenyl) -1,2,4-oxadiazole (IV) and Phenyl proargyne (VI) using catalytic amounts of aqueous CuSO₄ and sodium ascorbate in DMF medium with constant stirring for about 6-8 hrs, at room temperature. In the second protocol, 2-azido-1-phenylethanone (IX) and 2-Propyene afforded a set of keto triazoles (2-(4-(phenoxy)methyl)-1H-1, 2, 3-triazol-1-yl)-1-phenylethanone (X). Mechanism of this reaction is explained through cycloaddition reaction path (the Click chemistry). The obtained triazole derivatives were characterised by mass, IR and NMR spectroscopic studies. Among the five different triazole derivatives tested for antibacterial activity, VII c has been found to exhibit maximum activity and VII b indicated minimum activity with reference to CIPROFLOXACIN and GENTAMICIN.

References:


23. Kwok, S. W.; Fotsing, J. R.; Fraser, R. J.; Rodinov, V. O.; Fokin, V. V. *Org. Lett.* **2010**, *12*, 4217.
45. http://www.organic-chemistry.org/synthesis/heterocycles/1,2,4-triazoles.shtm
$^1$H NMR spectrum of 3-phenyl-5-((4-((p-tolyl)oxy)methyl)-1H-1,2,3-triazol-1-yl)methyl)-1,2,4-oxadiazole
Mass spectrum of 3-phenyl-5-((4-((p-tolyloxy)methyl)-1H-1,2,3-triazol-1-yl)methyl)-1,2,4-oxadiazole
IR spectrum of 3-phenyl-5-((4-(p-tolyloxy)methyl)-1H-1,2,3-triazol-1-yl)methyl)-1,2,4-oxadiazole
$^1$H NMR spectrum of 5-((4-(4-methoxyphenox)ethyl)-1H-1,2,3-triazol-1-yl)methyl)-3-phenyl-1,2,4-oxadiazole
Mass spectrum of 5-((4-(4-methoxyphenoxy)methyl)-1H-1,2,3-triazol-1-yl)methyl)-3-phenyl-1,2,4-oxadiazole
IR spectrum of 5-(((4-(4-methoxyphenoxy)methyl)-1H-1,2,3-triazol-1-yl)methyl)-3-phenyl-1,2,4-oxadiazole
$^1$H NMR spectrum of 5-((4-(4-chlorophenoxy)methyl)-1H-1,2,3-triazol-1-yl)methyl)-3-phenyl-1,2,4-oxadiazole
Mass spectrum of 5-((4-(4-chlorophenoxy)methyl)-1H-1,2,3-triazol-1-yl)methyl)-3-phenyl-1,2,4-oxadiazole
IR Spectrum of 5-((4-chlorophenoxy)methyl)-1H-1,2,3-triazol-1-yl) methyl)-3-(4-chlorophenyl)-1,2,4-oxadiazole
$^1$H NMR spectrum of 5-(((3-chlorophenoxy)methyl)-1H-1,2,3-triazol-1-yl)methyl)-3-phenyl-1,2,4-oxadiazole
Mass spectrum of 5-(((3-chlorophenoxymethyl)-1H-1,2,3-triazol-1-yl)methyl)-3-phenyl-1,2,4-oxadiazole.
IR spectrum of 5-(((3-chlorophenoy)methyl)-1H-1,2,3-triazol-1-yl)methyl)-3-phenyl-1,2,4-oxadiazone
$^1$H NMR spectrum of 1-phenyl-2-((p-tolyl)oxy)methyl)-1H-1,2,3-triazol-1-yl)ethanone
Mass spectrum of 1-phenyl-2-((4-(p-tolyl)oxy)methyl)-1H-1,2,3-triazol-1-yl)ethanone