Chapter-6

STUDIES ON TRIAZOLE DERIVATIVES
INTRODUCTION

Triazoles are important class of heterocyclic compounds, found in many potent biologically active molecules. Triazole derivatives have occupied an important place in novel drug discovery process. Triazoles are well known five membered heterocyclic compounds and several procedures for their synthesis have been extensively studied. Such studies have been stimulated by various promising applications, especially in the case of nitrogen containing heterocyclic entities.

The knowledge of such applications has pointed out that nitrogen containing heterocycles are important target to be prepared for our research on biologically active heterocyclic analogous. Triazoles are of two types 1,2,3-triazole and 1,2,4-triazole.

Isomeric forms of triazole

1,2,3-Triazoles

1,2,4-Triazoles

1,2,4-Triazoles represents a rapid developing field in modern heterocyclic chemistry. From literature it is predictable that, 1,2,4-triazoles represents important pharmacophores, and play a vital role as medicinal agents. A degree of respectability has been bestowed for 1,2,4-triazole derivatives due to their wide range of biological activities such as antifungal, antitubercular and anticancer. Certain 1,2,4-triazoles also find applications in the preparation of photographic plates, polymers, and as analytical agents.

Z. M. Hao and S. T. Steven have been studied briefly with the chemistry of 1,2,4-triazoles. Bladin is a pioneer scientist in the field of triazole, who had synthesized the first derivative of 1,2,4-triazole in 1885. 1,2,4-Triazole derivatives not only known for their medicinal applications, but they are also used as analytical reagents, dyes and photographic chemicals corrosion inhibitors and in the preparation of polymers.
SYNTHETIC ASPECT

Several methods have been reported in the literature for the synthesis of 1,2,4-triazoles.

1. Ahmet Demirbas et al\textsuperscript{14}. have synthesized 1,2,4-triazole derivative from the reaction of acetohydrazide derivative with CS\textsubscript{2}/KOH followed by hydrazine hydrate and aromatic aldehydes.

\[
\begin{align*}
\text{Ar} & \quad \text{NHNH}_2 \\
\text{Ar} & \quad \text{N} \quad \text{N} \quad \text{N} \\
\text{NH}_2 & \quad \text{S} \\
\end{align*}
\]

1) CS\textsubscript{2}/KOH

2) NH\textsubscript{2}NH\textsubscript{2}.H\textsubscript{2}O

Reflex

\[
\begin{align*}
\text{Ar} & \quad \text{NHNH}_2 \\
\text{Ar} & \quad \text{N} \quad \text{N} \quad \text{N} \\
\text{NH}_2 & \quad \text{N} \\
\end{align*}
\]

2) NH\textsubscript{2}NH\textsubscript{2}.H\textsubscript{2}O

2. Mashooq A. Bhat et al\textsuperscript{15}. Synthesized 3-(4-((aryl)methylene)imino)-5-thioxo-4,5-dihydro-1\textit{H}-1,2,4-triazol-3-yl)-2\textit{H}-chromen-2-ones from 2-oxo-2\textit{H}-cromene-3-carbohydrazide in 3 steps.

\[
\begin{align*}
\text{O} & \quad \text{O} \\
\text{NH}_2 & \quad \text{N} \\
\text{N} & \quad \text{N} \\
\text{S} & \quad \text{H} \\
\end{align*}
\]

1) CS\textsubscript{2}, KOH

2) NH\textsubscript{2}NH\textsubscript{2}.H\textsubscript{2}O

3. Reid and Heindel\textsuperscript{16} reported that the reaction of aryl acid hydrazide with CS\textsubscript{2}/KOH and hydrazine hydrate yields triazoles.

\[
\begin{align*}
\text{R} & \quad \text{NH}_2 \\
\text{O} & \quad \text{N} \\
\text{S} & \quad \text{K}^+ \\
\text{NH}_2 & \quad \text{N} \\
\end{align*}
\]

1) CS\textsubscript{2}, KOH

2) NH\textsubscript{2}NH\textsubscript{2}.H\textsubscript{2}O

4. A .K. Mishra et al\textsuperscript{17} have reported synthesis and antimicrobial activity of some triazole derivatives starting from 2-substituted-1\textit{H}-benzimidazole.

\[
\begin{align*}
\text{N} & \quad \text{N} \quad \text{N} \\
\text{NH}_2 & \quad \text{S} \\
\text{NH}_2 & \quad \text{S} \\
\end{align*}
\]

1) CS\textsubscript{2} / KOH

2) NH\textsubscript{2}NH\textsubscript{2}.H\textsubscript{2}O

5. K. S. Bhat et al\textsuperscript{18} have synthesized 4-amino-3-(2,4-dichloro-5-fluorophenyl)-1,2,4-triazol-5-thiol with the help of thiocarbohydrazide and 2,4-dichloro-5-fluoro benzoic acid.
6. N. U. Guzeldemirci et al.\textsuperscript{19} have prepared 1,2,4-triazoles in the presence of NaOH from Aryl acid hydrazide.

7. S. F. Barbuceanu et al.\textsuperscript{20} have reported 5-[4-(4-X-phenylsulfonyl)phenyl]-4H-1,2,4-triazole-3-thioles and it is prepared from 4-(4-X-phenylsulfonyl)-benzoic acid hydrazide.

8. Sumesh eswaran et al.\textsuperscript{21} also synthesized triazole derivative by the reaction of 4-hydroxy-8-(trifluoromethyl)quinoline-3-carbohydrazide.

9. L. Labanauskas et al.\textsuperscript{22} have prepared triazoles by the addition reaction of thiosemicarbazide with substituted benzoyl chloride in the presence of pyridine. Then the substituted thiosemicarbazide cyclised in water in the presence of alkaline catalyst.

10. K. Paulvannam et al.\textsuperscript{23} have developed an improved synthesis of 1,3,5-
trisubstituted 1,2,4-triazoles via Ag$_2$CO$_3$ mediated cyclization of triazenes. The reaction was complete within 3h and the products were isolated in moderate to high yields.

![Reaction scheme](image)

**THERAPEUTIC IMPORTANCE**

Triazoles are potential bioactive agents due to their wide spectrum of therapeutic importance. Literature survey reveals that various 1,2,4-triazole derivatives display significant biological activities. 3-Amino-1,2,4-triazole was the first 1,2,4-triazole to be manufactured on large scale from amino guanidine format, useful as herbicides$^{24}$, therapeutic activity of 1,2,4-triazoles are as under.

Bactericidal$^{25}$, Diuretic$^{26}$, Fungicidal$^{27}$, Herbicidal$^{28}$, Insecticidal and acaricidal$^{29}$, Plant growth regulator$^{30}$, Anticancer and Anti-HIV$^{31}$, Antileishmanial$^{32}$, Antitumor$^{33,34}$, Anti-depressant and anxiolytic$^{35}$, Antimicrobial$^{36}$, Antiviral$^{37}$, Antiinflammatory$^{38}$, Antihypertensive$^{39}$ and Anticonvulsant$^{40}$.

Hoong-Kun Fun et al.$^{41}$ have investigated 4-Amino-3-(1-naphthyloxymethyl)-1H-1,2,4-triazole-5(4H)-thione. B. Kahveci et al.$^{42}$ have prepared 4-Arylmethylene-amino-3-(R-benzyl)-4,5-dihydro-1H-1,2,4-triazol-5-ones via microwave assisted synthesis which exhibited remarkable antifungal activity. Ram Janam Singh et al.$^{43}$ have synthesized 4-Aryl-5-(isomeric pyridoyl)-3H-1,2,4-triazoles as potent bacteriocidal agents which active against *S. aureus*, *E. coli*, *B. subtilis* and *P. aeruginosa*. Najim A. Al-Masoudi et al.$^{44}$ have suggested 5-Amino-4-phenyl-4H-1,2,4-triazole-3-thiol and their metal complexes which posses *vitro* anti-HIV activity. E. De Clercq et al.$^{45}$ screened ribavirin (11) for their antiviral and antimetabolic activities. Mckendry and co-workers$^{46}$ have synthesized triazole derivatives (12) and reported them as broad spectrum broadleaf herbicides.

![Structures](image)
Sherin M. El-Feky et al.\textsuperscript{47} have synthesized a new series of 3,5-disubstituted triazoles (13) and evaluated for \textit{in vitro} antifungal and antibacterial activity. All the tested compounds showed significant antifungal activity against \textit{micromycetes} compared to the commercial fungicide clotrimazole.

\begin{center}
\includegraphics[width=0.8\textwidth]{image1}
\end{center}

(13)

H. A. Abdel-Aziz et al.\textsuperscript{48} have synthesized some piperidine based 1,3-thiazole, 1,3,4-thiadiazole, and 1,3-thiazolo[2,3-c]-1,2,4-triazole derivatives which possess anti-arrhythmic activity. B. F. Abdel-Wahab et al.\textsuperscript{49} have reported 1,2,4-triazoles useful for antimicrobial agent.

Hakan Bekats et al.\textsuperscript{50} have synthesized some novel 2,4,5-trisubstituted-2,4-dihydro-3H-1,2,4-triazole-3-one (14) and all these compounds were screened for their antimicrobial activities and some of which were found to possess good or moderate activities against the test microorganisms.

\begin{center}
\includegraphics[width=0.8\textwidth]{image2}
\end{center}

(14)

Daniele Binchi et al.\textsuperscript{51} have screened pure stereoisomer of two triazole derivatives (15,16) for their antifungal activity against variety of fungi.

\begin{center}
\includegraphics[width=0.8\textwidth]{image3}
\end{center}

(15)  (16)

M. A. Kaldrikyan et al.\textsuperscript{52} have discovered some benzofuryl-substituted-1,2,4-
triazoles and reported their antitumor activity. Dae-Kee Kim et al.\textsuperscript{53} have been synthesized 1,2,4-triazole derivatives (17) and screened for their significant ALKS inhibitory activity. K. J. Fisher et al.\textsuperscript{54} have synthesized 1,2,4-triazole derivatives (18) to study their pesticidal and herbicidal activity. Xiang-Shu Cui et al.\textsuperscript{55} have formulated 3-substituted-4-(4-hexyloxyphenyl)-4H-1,2,4-triazoles as anticonvulsant agent. Maarouf et al.\textsuperscript{56} have documented analgesic and anti-inflammatory activity of 1,2,4-triazole derivatives.

![Chemical Structures](image)

Drug molecules having 1,2,4-triazole nucleus with their activity are listed as under.

1. Estazolam
   - Receptor Agonist

2. Letrozole
   - Antineoplastic

3. Fluotrimazole
   - Fungicide

4. Ribavarin
   - Antiviral, Antiinfection
Studies on Triazole

5. Triazolam

6. Triadimenol

Plant growth regulator

Fungicide

7. Azaconazole

8. Rilmazafone

Antifungal

Sedative, hypnotic

9. Azocyclotin

10. Amitrole

Pesticide

Antithyroid activity

Thus the important role displayed by triazole moiety for various therapeutic and medicinal activities prompted us to synthesize some Schiff base derivative bearing triazole moiety, which have been described as under.

SECTION-I: SYNTHESIS AND BIOLOGICAL SCREENING OF 4-((ARYLME-THYLIDINE)AMINO)-5-((4-(2,3-DICHLOROPHENYL)PIPERAZIN-1-YL)METHYL)-4H-1,2,4-TRIAZOLE-3-THIOL
SECTION-I

SYNTHESIS AND BIOLOGICAL SCREENING OF 4-((ARYLMETHYLIDINE) AMINO)-5-((4-(2,3-DICHLOROPHENYL)PIPERAZIN-1-YL)METHYL)-4H-1,2,4-TRIAZOLE-3-THIOL

1,2,4-Triazoles nucleus and their derivatives emerge rapidly with the advance of modern heterocyclic chemistry, promising a variety of medical applications such as antibacterial, antifungal, anticancer, antitumor, anticonvulsant, anti-inflammatory and analgesic properties. Schiff bases of 1,2,4-triazoles find diverse applications and extensive biological activity. Looking to this, schiff base derivative of type-XI have been synthesised by the condensation of 4-amino-5-((4-(2,3-dichlorophenyl)piperazin-1-yl)methyl)-4H-1,2,4-triazole-3-thiol with different substituted aromatic aldehyde.

The constitution of the synthesized products have been characterized by using elemental analysis, IR & $^1$H-NMR spectroscopy and further supported by mass spectroscopy.

All the compounds have been evaluated for their in vitro biological assay like antibacterial activity towards Gram positive and Gram negative bacterial strains and antifungal activity towards A. niger, C. Albicans and A. Clavatus at a different concentration. The biological activities of synthesized compounds were compared with standard drugs.
**REACTION SCHEME**

\[
\begin{align*}
\text{Cl} & \quad \text{Cl} & \quad \text{Cl} & \quad \text{Cl} & \quad \text{C} & \quad \text{NH}_2 \\
\text{N} & \quad \text{N} & \quad \text{N} & \quad \text{N} & \quad \text{N} & \quad \text{O} \\
\text{CS}_2/KOH & \quad \text{Methanol, 24 hrs} & \text{room temperature} \\
\text{Cl} & \quad \text{Cl} & \quad \text{Cl} & \quad \text{O} & \quad \text{N} & \quad \text{N} \\
\text{N} & \quad \text{N} & \quad \text{N} & \quad \text{N} & \quad \text{S}^+ \\
\text{Hydrazine hydrazide} & \quad \text{Water, Ethanol} & \text{6 hrs, Reflux} \\
\text{Cl} & \quad \text{Cl} & \quad \text{Cl} & \quad \text{H}_2\text{N} & \quad \text{N} & \quad \text{N} \\
\text{N} & \quad \text{N} & \quad \text{N} & \quad \text{N} & \quad \text{S} \\
\text{OH} & \quad \text{C} & \quad \text{R} & \quad \text{Con. HCl, Ethanol} & \text{6-8 hrs, Reflux} \\
\text{Cl} & \quad \text{Cl} & \quad \text{R} & \quad \text{N} & \quad \text{N} \\
\text{N} & \quad \text{N} & \quad \text{N} & \quad \text{N} & \quad \text{HS} \\
\text{Cl} & \quad \text{Cl} & \quad \text{Cl} & \quad \text{N} & \quad \text{N} \\
\text{N} & \quad \text{N} & \quad \text{N} & \quad \text{N} & \quad \text{HS} \\
\text{(Type-XI)} \\
\text{R} & \quad \text{= OH, Cl, NO}_2, \text{N(CH}_3)_2, \text{OCH}_3 \text{ etc.}
\end{align*}
\]
IR SPECTRUM OF 5-(((4-(2,3-DICHLOROPHENYL)PIPERAZIN-1-YL)METHYL)-4-((4-METHOXYPHENYL)METHYLIDENE)AMINO)-4H-1,2,4-TRIAZOLE-3-THIOL

Instrument: SHIMADZU FTIR 8400 Spectrophotometer; Frequency range: 4000–400 cm\(^{-1}\) (KBr disc.)

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<th>Type</th>
<th>Vibration Mode</th>
<th>Frequency cm(^{-1})</th>
<th>Ref.</th>
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<td>Observed</td>
<td>Reported</td>
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<td>Alkane</td>
<td>C-H str. (asym.)</td>
<td>2951</td>
<td>2975-2920</td>
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<td>C-H def. (asym.)</td>
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<td>1470-1435</td>
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<td>C-H def. (sym.)</td>
<td>1392</td>
<td>1395-1370</td>
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<td>Aromatic</td>
<td>C-H str.</td>
<td>3059</td>
<td>3100-3000</td>
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<td>C=C</td>
<td>1512</td>
<td>1585-1480</td>
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<td>C-H i.p. def.</td>
<td>1130</td>
<td>1125-1090</td>
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<td>C-H o.o.p. def.</td>
<td>839</td>
<td>860-810</td>
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<td>Triazole ring &amp; Azomethine</td>
<td>N=C str.</td>
<td>1593</td>
<td>1650-1580</td>
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<td></td>
<td>C-N str.</td>
<td>1307</td>
<td>1350-1200</td>
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<td>N=N str.</td>
<td>1157</td>
<td>1220-1020</td>
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<td>-S-H str.</td>
<td>2538</td>
<td>2600-2550</td>
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<td>Ether (-OMe) Halide</td>
<td>C-O-C</td>
<td>1224</td>
<td>1275-1200</td>
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<td></td>
<td>C-Cl</td>
<td>813</td>
<td>850-650</td>
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1H-NMR SPECTRUM OF 5-((4-(2,3-DICHLOROPHENYL)PIPERAZIN-1-YL)METHYL)-4-(((4-METHOXYPHENYL)METHYLIDENE)AMINO)-4H-1,2,4-TRIAZOLE-3 THIOL

Internal Standard: TMS; Solvent: MeOD Instrument: BRUKER Spectrometer (300MHz)

<table>
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<th>Sr. No.</th>
<th>Chemical Shift In δppm</th>
<th>Relative No. of Protons</th>
<th>Multiplicity</th>
<th>Inference</th>
<th>J Value in HZ</th>
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<tr>
<td>1</td>
<td>3.37</td>
<td>4H</td>
<td>broad singlet</td>
<td>-CH₂ (a,a’)</td>
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<td>2</td>
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<td>4H</td>
<td>broad singlet</td>
<td>-CH₂ (b,b’)</td>
<td>-</td>
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<td>3</td>
<td>3.88</td>
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<td>singlet</td>
<td>-OCH₃ (c)</td>
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<td>singlet</td>
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<td>Ar-H (e,e’)</td>
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<td>double doublet</td>
<td>Ar-H (f)</td>
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<td>doublet</td>
<td>Ar-H (i.i’)</td>
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<td>9</td>
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<td>1H</td>
<td>singlet</td>
<td>-N=CH (j)</td>
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EXPANDED $^1$H-NMR SPECTRUM
MASS SPECTRUM OF 5-((4-(2,3-DICHLOROPHENYL)PIPERAZIN-1-YL)METHYL)-4-(((4-METHOXYPHENYL)METHYLIDENE)AMINO)-4H-1,2,4-TRIAZOLE-3-Thiol

**Exact Mass = 476.1**

m/z = 477.1 (M+1), 479.2 (M+3)

MASS SPECTRUM OF 5-((4-(2,3-DICHLOROPHENYL)PIPERAZIN-1-YL)METHYL)-4-(((4-FLUOROPHENYL)METHYLIDENE)AMINO)-4H-1,2,4-TRIAZOLE-3-Thiol

**Exact Mass = 464.1**

m/z = 465.1 (M+1)
EXPERIMENTAL

SYNTHESIS AND BIOLOGICAL SCREENING OF 4-((ARYLMETHYLIDINE) AMINO)-5-((4-(2,3-DICHLOROPHENYL)PIPERAZIN-1-YL)METHYL)-4H-1,2,4-TRIAZOLE-3-THIOL

Melting points of all the synthesized compounds were taken in open capillary bath on controlled temperature heating mental. The crystallization of all the compounds was carried out in appropriate solvents. TLC was carried out on silica gel-G F\textsubscript{254} coated aluminum sheet (Merck prepared plates) as stationary phase. 70 % Ethyl acetate in hexane was used as a mobile phase.

[A] SYNTHESIS OF 2-(4-(2,3-DICHLOROPHENYL)PIPERAZIN-1-YL)ACETOHYDRAZIDE

See, Chapter-2, Part-A, Section-I, Experimental [B], page no. 72.

[B] SYNTHESIS OF POTASSIUM 2-(2-(4-(2,3-DICHLOROPHENYL) PIPERAZIN-1-YL)ACETYL)HYDRAZINECARBODITHIOATE

To the mixture of potassium hydroxide (8.40g, 0.15mol) and 2-(4-(2,3-dichlorophenyl)piperazin-1-yl)acethyldrazide (30.2g, 0.1mol) in ethanol (100 ml), carbon disulphide (11.4g, 0.15mol) was added. This mixture was stirred for 24 hrs at room temperature. It was then diluted with dry ether (400 ml) and thus the solid obtained was filtered and washed with ether and dried. There is no need to purify the salt for further reaction.

[C] SYNTHESIS OF 4-AMINO-5-((4-(2,3-DICHLOROPHENYL) PIPERAZIN-1-YL)METHYL)-4H-1,2,4-TRIAZOLE-3-THIOL

A suspension of the potassium salt (41.74g, 0.1mol), hydrazine hydrate (25 ml, 0.5mol), water (10 ml) and ethanol (50 ml) was refluxed with stirring for 8 hrs. The color of the reaction mixture changed to green, hydrogen sulfide was evolved and a homogeneous solution resulted. Dilute the solution with cold water (300 ml) and neutralized with glacial acetic acid, precipitated a white solid. The product was filtered, washed with cold water and crystallized from dioxane yield 60 %.
SYNTHESIS OF 5-((4-(2,3-DICHLOROPHENYL)PIPERAZIN-1-YL)METHYL)-4-(((4-METHOXYPHENYL)METHYLIDENE)AMINO)-4\textit{H}-1,2,4-TRIAZOLE-3-THIOL

A mixture of 4-amino-5-((4-(2,3-dichlorophenyl)piperazin-1-yl)methyl)-4\textit{H}-1,2,4-triazole-3-thiol (3.58 gm, 0.01 mol), 4-methoxybenzaldehyde (1.36 gm, 0.01 mol) and ethanol (20 ml) in presence of con. HCl (2 drops) was refluxed for 8 hrs. The contents were cooled and solid was filtered, dried and isolated product was recrystallized from ethanol. Yield: 81 %, M. P. 208-210 °C, (C\textsubscript{21}H\textsubscript{22}C\textsubscript{12}N\textsubscript{6}O\textsubscript{3}; Required: C, 52.83; H, 4.64; N, 17.60 %; Found: C, 52.75; H, 4.56; N, 17.55 %).

Similarly, other 4-((aryl)methylidine)amino)-5-((4-(2,3-dichlorophenyl)piperazin-1-yl)methyl)-4\textit{H}-1,2,4-triazole-3-thiol (11a-j) were prepared. The physical constants are recorded in Table-11a, Page no. 221.

BIOLOGICAL SCREENING OF 4-((ARYLMETHYLIDINE)AMINO)-5-((4-(2,3-DICHLOROPHENYL)PIPERAZIN-1-YL)METHYL)-4\textit{H}-1,2,4-TRIAZOLE-3-THIOL

Antimicrobial testing was carried out as described in Chapter-1, Section-I, Experimental [C], Page no. 37. The results obtained from antimicrobial testing are recorded in Table-11b, Page no. 222.
### TABLE-11a: PHYSICAL CONSTANTS OF 4-((ARYLMETHYLIDINE)AMINO)-5-((4-(2,3-DICHLOROPHENYL)PIPERAZIN-1-YL)METHYL)-4H-1,2,4-TRIAZOLE-3-SULFIDE

![Chemical Structure](image)

<table>
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<th>Sr. No.</th>
<th>Substitution R</th>
<th>Molecular Formula/Molecular Weight</th>
<th>M.P. °C</th>
<th>Yield %</th>
<th>% Composition Calcd./Found</th>
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<td></td>
<td>C</td>
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<tr>
<td>11a</td>
<td>H</td>
<td>C_{20}H_{20}Cl_{2}N_{6}S</td>
<td>447.38</td>
<td>193-196</td>
<td>86</td>
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<tr>
<td>11b</td>
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<td>11c</td>
<td>4-F</td>
<td>C_{20}H_{19}Cl_{2}F_{2}N_{6}S</td>
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<td>218-220</td>
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<td>11d</td>
<td>3-Cl</td>
<td>C_{20}H_{19}Cl_{3}N_{6}S</td>
<td>481.83</td>
<td>184-186</td>
<td>82</td>
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</tr>
<tr>
<td>11e</td>
<td>2,3-di Cl</td>
<td>C_{20}H_{18}Cl_{4}N_{6}S</td>
<td>516.27</td>
<td>211-212</td>
<td>76</td>
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</tr>
<tr>
<td>11f</td>
<td>4-N(Me)_{2}</td>
<td>C_{22}H_{25}Cl_{2}N_{7}S</td>
<td>490.45</td>
<td>176-179</td>
<td>84</td>
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<tr>
<td>11g</td>
<td>3-OMe-4-OH</td>
<td>C_{21}H_{23}Cl_{2}N_{6}O_{2}S</td>
<td>493.41</td>
<td>229-231</td>
<td>74</td>
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</tr>
<tr>
<td>11h</td>
<td>4-NO_{2}</td>
<td>C_{20}H_{19}Cl_{2}N_{7}O_{2}S</td>
<td>492.38</td>
<td>222-225</td>
<td>87</td>
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</tr>
<tr>
<td>11i</td>
<td>3-NO_{2}</td>
<td>C_{20}H_{19}Cl_{2}N_{7}O_{2}S</td>
<td>492.38</td>
<td>198-200</td>
<td>79</td>
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</tr>
<tr>
<td>11j</td>
<td>4-OH</td>
<td>C_{20}H_{20}Cl_{2}N_{6}OS</td>
<td>463.38</td>
<td>208-210</td>
<td>83</td>
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</table>
TABLE-11b: BIOLOGICAL SCREENING OF 4-((ARYLMETHYLIDINE) AMINO)-5-((4-(2,3-DICHLOROPHENYL)PIPERAZIN-1-YL) METHYL)-4H-1,2,4-TRIAZOLE-3-THIOL

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Code</th>
<th>Antibacterial Activity</th>
<th>Antifungal activity</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Minimal bactericidal concentration µg/ml</td>
<td>Minimal fungicidal concentration µg/ml</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gram +ve Bacteria</td>
<td>Gram -ve Bacteria</td>
</tr>
<tr>
<td>1</td>
<td>11a</td>
<td>250</td>
<td>200</td>
</tr>
<tr>
<td>2</td>
<td>11b</td>
<td>250</td>
<td>250</td>
</tr>
<tr>
<td>3</td>
<td>11c</td>
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</tr>
<tr>
<td>4</td>
<td>11d</td>
<td>200</td>
<td>100</td>
</tr>
<tr>
<td>5</td>
<td>11e</td>
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<tr>
<td>6</td>
<td>11f</td>
<td>500</td>
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<tr>
<td>7</td>
<td>11g</td>
<td>200</td>
<td>500</td>
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<td>8</td>
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<tr>
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<td>11i</td>
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<tr>
<td>10</td>
<td>11j</td>
<td>500</td>
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</table>

MINIMAL INHIBITION CONCENTRATION

<table>
<thead>
<tr>
<th>Standard Drugs</th>
<th>S.aureus (microgramme/ml)</th>
<th>S.pyogenus (microgramme/ml)</th>
<th>E.coli (microgramme/ml)</th>
<th>P.aeruginosa (microgramme/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gentamycin</td>
<td>0.25</td>
<td>0.5</td>
<td>0.05</td>
<td>1</td>
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<tr>
<td>Ampicillin</td>
<td>250</td>
<td>100</td>
<td>100</td>
<td>100</td>
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<tr>
<td>Chloramphenicol</td>
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<td>50</td>
<td>50</td>
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<tr>
<td>Ciprofloxacin</td>
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<td>50</td>
<td>25</td>
<td>25</td>
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<tr>
<td>Norfloxacin</td>
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</tbody>
</table>

MINIMAL FUNGICIDAL CONCENTRATION

<table>
<thead>
<tr>
<th>Standard Drugs</th>
<th>C.Albicans (microgramme/ml)</th>
<th>A.Niger (microgramme/ml)</th>
<th>A.Clavatus (microgramme/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nystatin</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Greseofulvin</td>
<td>500</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>
ANTIBACTERIAL ACTIVITY:

From screening results, substituted triazole 11c (R= 4-F) against S.aureus, 11e (R= 2,3-di Cl) against E.coli and 11b (R= 4-OMe) against P.aeruginos show excellent activity compared to ampicillin. While 11d (R= 3-Cl) & 11g (R= 3-OMe-4OH) against S.aureus, 11d (R= 3-Cl) against S.pyogenus, 11a (R= -H) & 11c (R= 4-F) against E.coli and 11e (R= 2,3-di Cl) against P.aeruginos, display moderate activity as compared to ampicillin. The remaining compounds demonstrate moderate to poor activity against all four bacterial species.

ANTIFUNGAL ACTIVITY:

Antifungal screening data shows that substituted triazoles 11a (R= -H) & 11b (R= 4-OMe) possess highly promising activity against C.albicans as compared to greseofulvin while 11c (R= 4-F) display moderate activity against A.niger and A.clavatus. The remaining compounds show moderate to poor activity against all three bacterial species.
REFERENCES

7. J. A. Bladin; *Ber.*, **18**, 1544 (1885).
8. J. A. Bladin; *Ber.*, **19**, 2598 (1886).