https://doi.org/10.48047/AFJBS.6.11.2024. 180-204

African Journal of Biological Sciences

SYNTHESIS AND ANTI MICROBIAL EVALUATION OF SOME NOVEL TRIAZOLE DERIVATIVES

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Article History
Volume 6, Issue 11, 2024
Received: 02 Jun 2024
Accepted: 15 Jun 2024
doi: ***10.48047/AFJBS.6.11.2024.180-204***

Abstract

In this study, synthesis a series of novel triazole derivatives and evaluated their antimicrobial properties. The synthetic strategy involved the formation of triazole rings via a click chemistry approach, resulting in high yields and purity of the final products. The chemical structures of the synthesized compounds were confirmed using various spectroscopic techniques, including NMR, IR, and mass spectrometry. The antimicrobial activities of these triazole derivatives were assessed against a panel of pathogenic microorganisms, including Gram-positive bacteria, Gram-negative bacteria, and fungi, using standard antimicrobial susceptibility tests. Several of the synthesized compounds exhibited significant antimicrobial activity, with some derivatives showing potency comparable to or better than standard antibiotics. These results suggest that the novel triazole derivatives possess promising potential as antimicrobial agents and warrant further investigation for development as therapeutic agents. These synthetic compounds were present in quantities ranging from 125 µg to 500 µg/mL, they were able to successfully limit the growth of fungus by a percentage of 16-30%. It was discovered that compound 4(f) was a good antifungal agent for A. niger, but compound 4(e) displayed a moderate level of effectiveness. 4(b) shown a reduction in its activity against A. niger. Compound 4(c) was shown to be an effective antifungal agent for C. albicans, according to scientific research.

Keywords: Triazole, Antimicrobial, Pathogenic Microorganisms, A. Niger, C. Albicans

INTRODUTION:

In the year One Thousand Eight Hundred and Eighty Five., Bladin came up with the name "triazole" to describe the structure of a heterocyclic aromatic ring that is composed of five members and contains three nitrogen atoms. The chemical formula for this ring is C2H3N3. Following its discovery, triazole underwent a process of gradual refinement and acceleration in its chemistry. This was accomplished via the development of a variety of straightforward and easy synthesis processes, as well as through its diverse interactions with biological systems. The discovery of antifungal capabilities of azole derivatives in 1944 led to the creation of a number of different antifungal medications, including fluconazole, itraconazole, voriconazole, posaconazole, and efinaconazole, amongst others. Both voriconazole and posaconazole are especially effective against Candida strains that are resistant to fluconazole or other antifungal medications. In addition, the mechanism that underlies such an antifungal activity is well-established. This process includes suppressing the formation of ergosterol and blocking the P450-dependent enzyme (CYP 51). According to [1, 2, 3], triazole-type ring structures have the ability to interact with the heme iron of the CYP enzyme.

When it comes to heterocyclic compounds, there is a family known as triazoles. is characterized by a circular structure that consists of five members and is composed of two molecules of carbon and three molecules of nitrogen. As a result of their one-of-a-kind molecular arrangement, triazoles possess a wide variety of chemical characteristics and biological activity, which makes them an excellent choice for investigation in medicinal chemistry. Medicinal chemistry, agriculture, and materials science are just few of the areas that make use of these compounds, which are very adaptable molecules that have a wide range of uses. In the following, you can find some facts on Triazoles[4,5]

1. **Chemical Structure**: There are three nitrogen atoms and two carbon molecules that make up the ring structure of triazoles. Triazoles are created by combining these two elements.The 1,2,3-triazole molecule, which has the chemical formula C2H3N3, is the most basic triazole compound.

2. **Isomerism**: It is possible for triazoles to exist in a variety of isomeric forms, which are determined by the arrangement of atoms inside the ring. Isomers consist of a variety of compounds, some of which include 1,2,3-triazole, 1,2,4-triazole, and 1,2,3,4-triazole.
3. **Synthesis**: The production of triazoles may be accomplished by a number of different methods, such as cycloaddition, ring-closing, and condensation processes. An example of a common method is the Huisgen 1,3-dipolar cycloaddition reaction, which includes the interaction of an azide with an alkyne in order to produce triazole ring-like structures
4. **Biological Activities**: Triazole derivatives doth exhibiteth a broad spectrum of biological activities, making them of great value in the pursuit of drug discovery and development. Verily, the triazole derivatives doth possess a plethora of pharmacological activities, such as the power to combat fungi, vanquish cancer, thwart viruses, quell convulsions, soothe inflammation, and vanquish microbes. [4,5,6]

Triazole, which compounds have been shown to have a wide range of pharmacologic actions, making them promising targets for drug discovery and development. Some of the significant pharmacological actions related with triazole derivatives include.

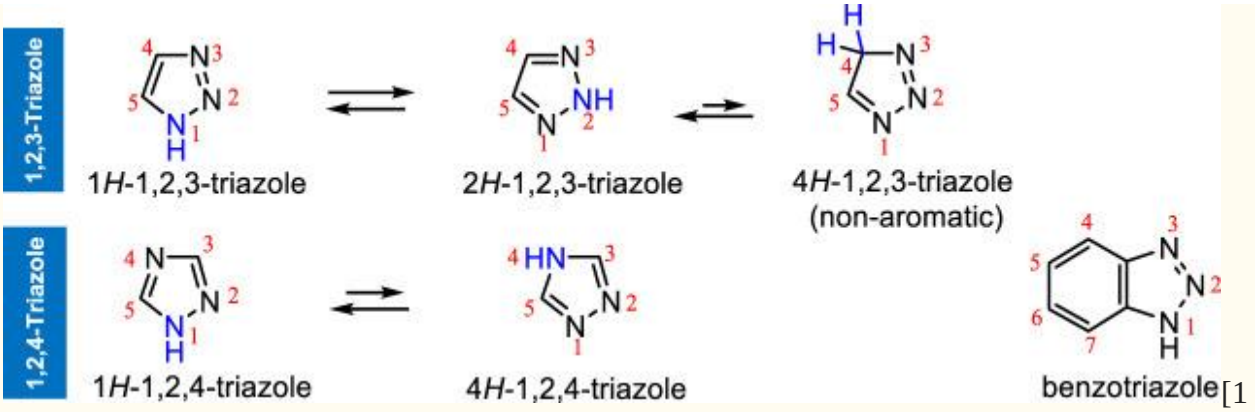
Antifungal Activity: Antifungal medications are often used, and triazole derivatives, in particular azoles like fluconazole, itraconazole, and voriconazole, are among the most common examples. As a result of their inhibition of the enzyme lanosterol 14-alpha-demethylase, the integrity of the fungal cell membrane is compromised, which eventually results in the death of the fungal cell. Triazoles are thus excellent therapies for a wide variety of fungal diseases, including candidiasis and aspergillosis, when used in this manner.

Anticancer Activity: It has been proven that some triazole compounds possess anticancer characteristics that are promising. A number of different mechanisms may be responsible for their action, including the inhibition of critical enzymes that are involved in the proliferation of cancer cells, the induction of apoptosis (programmed cell death), or the interference with tumor angiogenesis (the development of new blood vessels to promote the growth of tumors). Triazole-based anticancer agents are currently under investigation for their potential in the treatment of different types of cancer, such as breast cancer, lung cancer, and leukemia.

Antimicrobial Activity: In addition to antifungal and antiviral properties, triazole derivatives may also exhibit antimicrobial activity against bacteria and protozoa. They can interfere with microbial cell wall synthesis, protein synthesis, or nucleic acid metabolism, leading to microbial growth inhibition or cell death. Triazole-based antimicrobial agents are investigated for their potential in combating bacterial infections and protozoal diseases.[6,7,8]

CHEMISTRY OF TRIAZOLES:

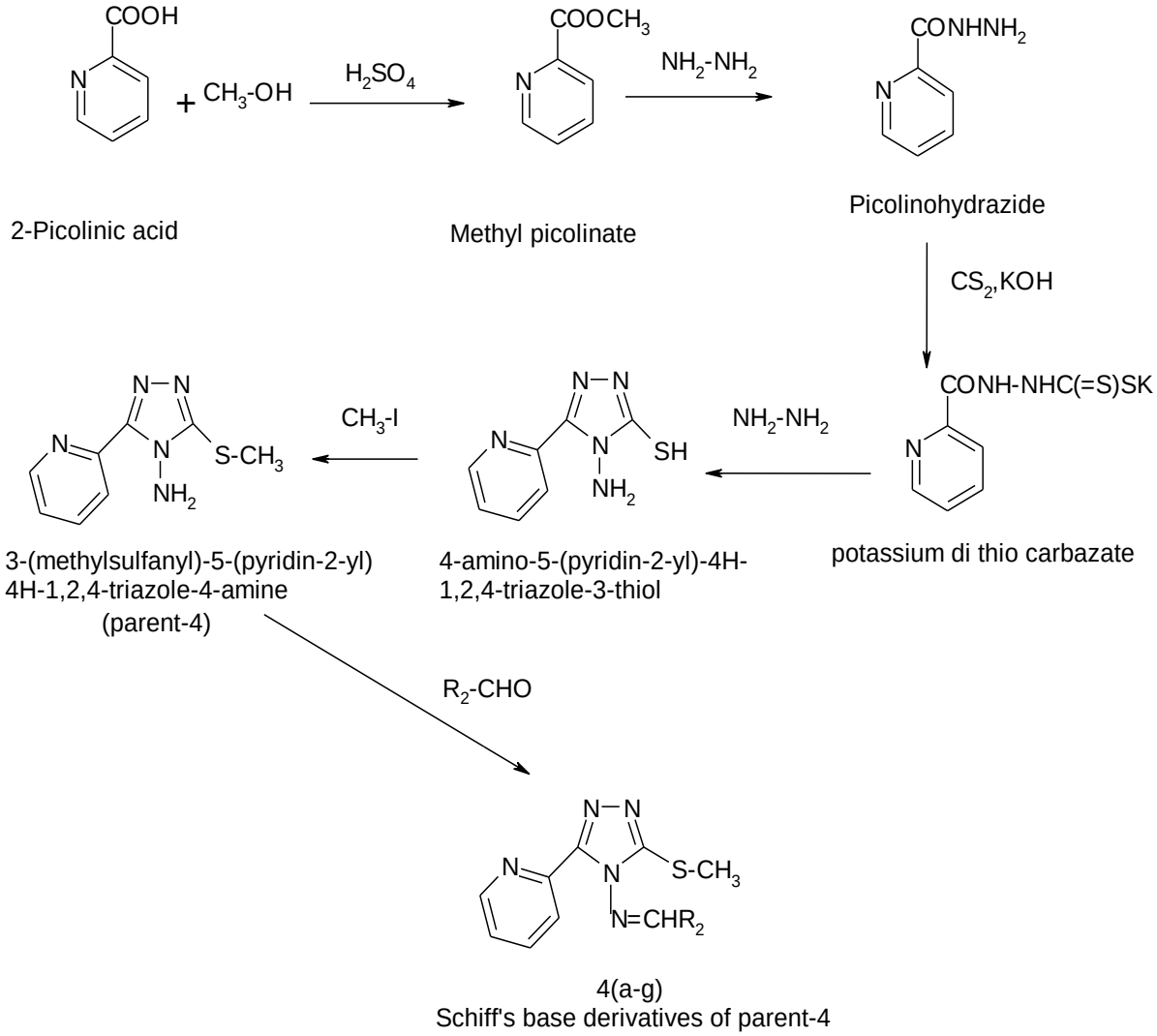
Triazoles possess a distinctive structural motif and hold great significance in the realm of triazole chemistry due to their wide-ranging applications across various scientific disciplines. Triazoles are primarily made up of a five-membered heterocyclic ring with the chemical formula C2H3N3. This ring is composed of two carbon and three nitrogen atoms. The five-membered ring has the potential to generate two important isomers, 1,2,3-triazole (v-triazole) and 1,2,4-triazole (s-triazole), based on the two most likely nitrogen atom positions. Each of these primarily exhibits two tautomers, depending on the hydrogen attached to the ring nitrogen. Due to its nonaromatic structure, the 4H-1,2,3-triazole is not considered. Both triazoles exhibit a planar atomic arrangement with sp-^{2} hybridization. There are a total of six pi (π) electrons available for research.Delocalization around the ring is the source of aromaticity in both of these types. In addition, triazoles are known for being high-energy heterocycles due to their unique composition of three nitrogen atoms. [9, 10, 11]



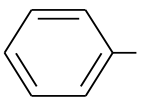
[12]

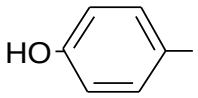
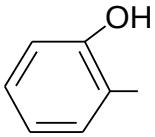
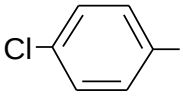
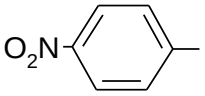
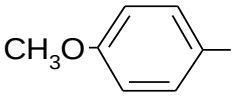
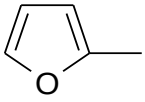
MATERIAL PREREQUISITES:

SCHEME- STARTING WITH 2-PICOLINIC ACID:



Synthesized compounds in scheme-2:

S.NO.	Compound code	R_2
1	**(4)a**	

2.	**(4)b**	
3.	**(4)c**	
4.	**(4)d**	
5.	**(4)e**	
6.	**(4)f**	
7.	**(4)g**	

METHODS

(A) Thin layer chromatography of compounds On glass plates coated with silica gel G, substances were analyzed using thin layer chromatography. Using a standard spreader, the adsorbent silica gel G was applied on 20 × 5 cm TLC plates that had been cleaned beforehand to a thickness of roughly 0.3 mm**.** In order to warm up the silicon plates, they were placed in a hot air oven set at 105°C for a duration of thira period of thirty minutes.On the active plate, the compound solution was placed at a spot approximately 2 cm above the lower edge. The mobile stages were chosen through a process of trial and error.Iodine vapor exposure allowed the dots to be seen.

(B) Elemental analysis (Qualitative)

With Lassaigne's sodium fusion test, qualitative tests for elemental detection of nitrogen, sulfur, and gases in compound were carried out.

(C) Solubility of intermediates and products in different solvents

Both the beginning and end products were dissolved using a variety of solvents, including water, ethanol, chloroform, methanol, acetone, dimethyl formamide (DMF), and dimethyl sulphoxide (DMSO). Ten milligrams of every component were weighed and mixed with ten milliliters of each separate solvent in a 100 milliliter beaker. The results were noted..

(D) Determination of melting point range

The wide-open capillary technique, which uses the melting point measurement devices, was used to figure out the erroneous melting point ranges of the products. Compounds were inserted into a sealed capillary from one end. after that, put in the capillary-made caves. In their caves, there was also a thermometer. Melting point range was defined as the temperature range between the compound's beginning melting point and full melting point.

(E) IR spectral analysis:

In order to precisely capture the infrared electromagnetic spectrum of the chemicals that were present in the KBr pellet, a Shimadzu IR spectrophotometer was used. In order to make the pellets, 200 milligrams of potassium bromide that had been dried were employed.To this, add 1 mg of the drug and thoroughly stir in the mortar. After being put in an evacuable die, the mixture is compressed to a pressure of 10–15 torr. After creating a clear disc, it was put in a pellet holder and subjected to infrared scanning.

(F) Molecular weight determination method

Molecular weight was determined by Rast’s method (freezing point depression method) using naphthalene as solvent. Naphthalene was taken in a boiling tube (weight of naphthalene was about 4 times of the solute weight) tied with a thermometer and dipped in to a beaker containing water. Naphthalene was melted completely by heating the beaker on a water bath. Naphthalene

was taken out in a wide mouth container and determined the freezing point by cooling. The freezing pint for naphthalene was noted down as $T_1{}^0C$. Now known weight of solute (compound whose weight had to be determined) was taken and mixed with naphthalene and both were meted together. By using the same procedure freezing point for naphthalene-solute mixture as $T_2{}^0C$ was determinedAfter a backup measurement, a second injection of 0.2 grams of solute was done, and the freezing point was recorded once more. The following equation was used to determine the molecular weight of the solute using the Kf of naphthalene (6.90C c/m).:

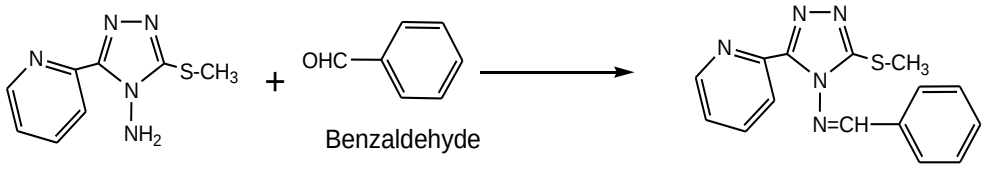
$$M_2 = \frac{K_f \times 1000 \times W_1}{\Delta T_f \times W_2}$$

$w_1 = weight$ of naphthalene

$w_2 = weight$ of solute

Synthesis of Schiff bases derivatives 4(a-g) of parent(4)

1. **Synthesis of Schiff bases derivative N-benzylidine-3-(methylthio)-5-(pyridin-2-yl)-4H-1,2,4-triazole-4-amine 4(a)**



(parent-4)

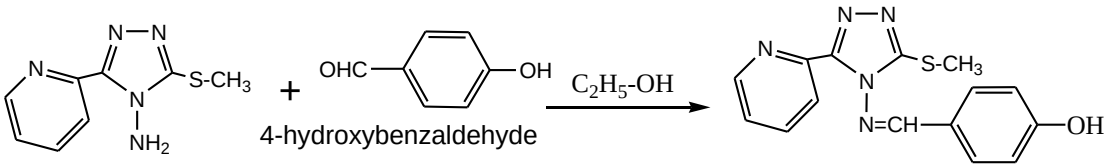
N-benzylidene-3-(methylthio)-5-(pyridin-2-yl)-4*H*-1,2,4-triazol-4-amine

4(a)

A concoction of 3-(methylthio)-5-(pyridine-2-yl)-4H-1,2,4-triazole-4-amine (known as parent-4) (0.01mol, 2.1gm) was combined with benzaldehyde in a solution of ethanol and water (in a ratio of 2 parts ethanol to 1 part water, totaling 75ml). This mixture was subjected to the process of reflux for a duration of approximately 5 hours. When the reaction mixture had cooled down, the crude product was precipitated, collected by

filteration, and recrystallized from ethanol. It was then checked for its solubility. The compound hath been characterized by elemental and spectral analysis.

2. Synthesis of Schiff bases derivative 4-((3-(methylthio)-5-(pyridin-2-yl)-4H-1,2,4-triazol-4-ylimino)methyl)phenol 4(b)



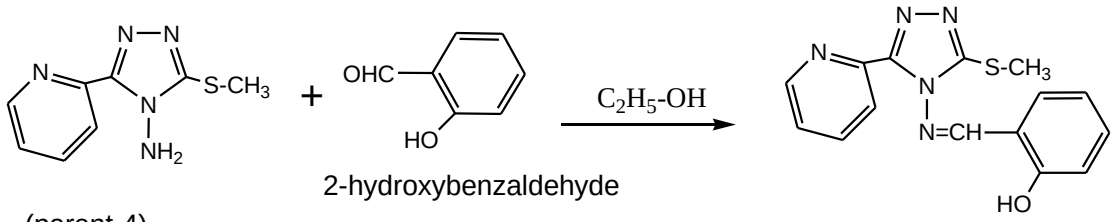
(parent-4)

4-((3-(methylthio)-5-(pyridin-2-yl)-4*H*-1,2,4-triazol-4-ylimino)methyl)phenol

4(b)

A concoction of 3-(Methylthio-5-(pyridine-2-yl)-4H-1,2,4-triazole-4-amine (referred to as parent-4) in the amount of 0.01 mol, was combined with 4-hydroxybenzaldehyde in a solution of ethanol and water, with a ratio of 2 parts ethanol to 1 part water, measuring 75 ml in total. This mixture was subjected to a vigorous reflux for a duration of approximately 5 hours. When the reaction mixture had cooled downeth, the crude product wast precipitated, collected by filteration and recrystallized from DMF: water (1:2)) and checked for its solubility. The compound hath been characterized by elemental and spectral analysis.

3. Synthesis of Schiff bases derivative 2-((3-(methylthio)-5-(pyridin-2-yl)-4H-1,2,4-triazol-4-ylimino)methyl)phenol 4(c)



(parent-4)

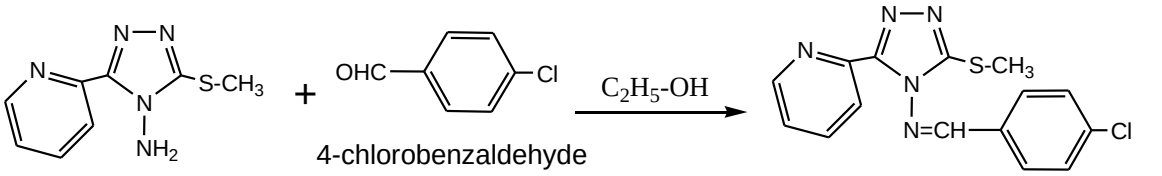
2-hydroxybenzaldehyde

2-((3-(methylthio)-5-(pyridin-2-yl)-4*H*-1,2,4-triazol-4-ylimino)methyl)phenol

4(c)

A concoction of 3-(Methylthio)-5-(pyridine-2-yl)-4H-1,2,4-triazole-4-amine (referred to as parent-4) Verily, 0.01mol didst combine with 2-hydroxybenzaldehyde in a mixture of ethanol and water, with a ratio of 2:1 and a volume of 75 ml. This concoction was subjected to the process of reflux for a duration of 4 hours. When the reaction mixture had cooled downeth, the crude product wast precipitated, collected by filteration and recrystallized from DMF: water (1:3)) and checked for its solubility. The compound hath been characterized by elemental and spectral analysis

4. Synthesis of Schiff bases derivativeN-(4-chlorobenzylidine-3-(methylthio)-5-(pyridin-2-yl)-4H-1,2,4-triazole-4-amine 4(d)



(parent-4)

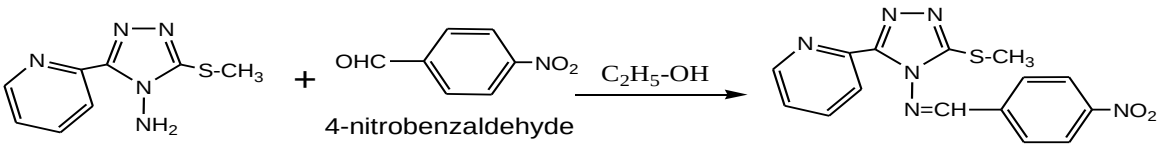
4-chlorobenzaldehyde

N-(4-chlorobenzylidene)-3-(methylthio)-5-(pyridin-2-yl)-4*H*-1,2,4-triazol-4-amine

4(d)

The combination of 3-(methylthio)-5-(pyridine-2-yl)-4H-1,2,4-triazole-4-amine (parent-4) comprises the following: After refluxing for about five hours, 0.01 mol of 4-chlorobenzaldehyde in ethanol/water (2:1, 75 ml) was included in the mixture. Following the cooling of the reaction mixture, the crude product was precipitated, collected by filtering, and then recrystallized from a combination of DMF and water in a ratio of 1:3. The solubility of the crude product was then evaluated.

5. Synthesis of Schiff bases derivative N-(4-nitrobenzylidine-3-(methylthio)-5 (pyridin-2-yl)-4H-1,2,4-triazole-4-amine 4(e)



(parent-4)

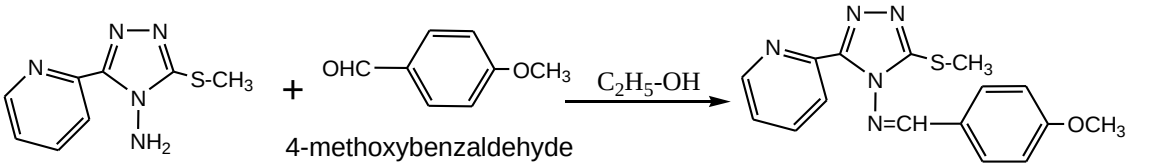
4-nitrobenzaldehyde

N-(4-nitrobenzylidene)-3-(methylthio)-5-(pyridin-2-yl)-4*H*-1,2,4-triazol-4-amine

4(e)

A concoction of 3-(Methylthio)-5-(pyridine-2-yl)-4H-1,2,4-triazole-4-amine (referred to as parent-4) Verily, 0.01 mol didst combine with 4-nitrobenzaldehyde in a mixture of ethanol and water (2:1,75 ml), and was subjected to the process of reflux for a duration of approximately 5 hours. When the reaction mixture had cooledeth down, the crude product wast precipitated, collected by filteration and recrystallized from DMF: water (1:3) and checked for its solubility. The compound hath been characterized by elemental and spectral analysis

6. **Synthesis of Schiff bases derivative N-(4-methoxybenzylidene)-3- (methylthio)-5-(pyridine-2-yl)-4H-1,2,4-triazole-4-amine 4(f)**

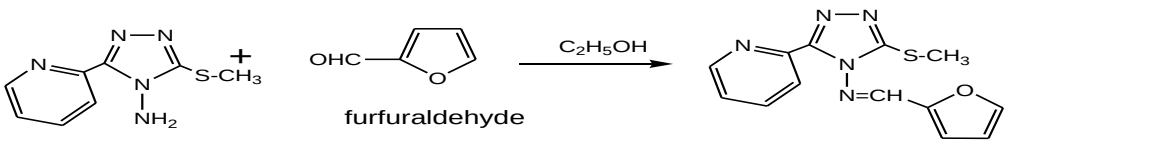


(parent-4) 4-methoxybenzaldehyde N-(4-methoxybenzylidene)-3-(methylthio)-5-(pyridin-2-yl)-4H-1,2,4-triazol-4-amine

4(f)

A concoction of 3-(methylthio)-5-(pyridine-2-yl)-4H-1,2,4-triazole-4-amine(parent-4) Verily, 0.01 mmol didst combine with 4-methoxybenzaldehyde in a mixture of ethanol and water, with a ratio of 2:1 and a volume of 40 ml. This concoction was subjected to the fiery embrace of reflux for a span of approximately 5 hours, as confirmed by the noble technique of TLC. When the reaction mixture had cooledeth down, the crude product wast precipitated, collected by filteration and recrystallized from DMF: water (1:3) and checked for its solubility.

7. **Synthesis of Schiff bases derivative N-(furan-2-ylmethylene)-3-(methyl-thio)- 5-(pyridin-2-yl)-4H-1,2,4-triazole-4-amine 4(g)**



(parent-4) furfuraldehyde N-(furan-2-ylmethylene)-3-(methylthio)-5-(pyridin-2-yl)-4H-1,2,4-triazol-4-amine

4(g)

A concoction of 3-(methylthio)-5-(pyridine-2-yl)-4H-1,2,4-triazole-4-amine (known as parent-4) in the amount of 0.01 mol, was combined with furfuraldehyde in a solution of ethanol and water (in a ratio of 2:1, totaling 75ml). This mixture was subjected to the process of reflux for a duration of 3 hours. When the reaction mixture had cooled down, the crude product was precipitated, collected by filteration and recrystallized from rectified spirit and checked for its solubility. The compound hath been characterized by elemental and spectral analysis.[15-20]

RESULT AND DISCUSSION:

1. Physical characterization of Synthesized compounds:

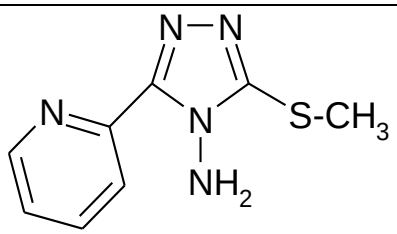
C.Code	Yield %	M.P.range (ºC)	Rf value	Solvent system	Solubility
Parent-4	71	158-160	0.86	Chloroform :Acetic Acid (5:2)	Ethanol DMSO
4(a)	64	126-128	0.82	Chloroform :Acetic Acid (5:2)	Ethanol DMSO
4(b)	75	144-146	0.74	Chloroform :Acetic Acid (5:2)	Ethanol DMF
4(c)	74	138-140	0.64	Chloroform :Acetic Acid (5:2)	Ethanol DMF
4(d)	91	186-188	0.74	Chloroform :Acetic Acid (5:2)	Ethanol DMF
4(e)	73	176-178	0.64	Ethylacetate : n-Hexane (5: 2)	Ethanol DMF

4(f)	90	152-154	0.64	Ethylacetate : n-Hexane (5: 2)	Ethanol DMF
4(g)	64	164-166	0.86	Ethylacetate : n-Hexane (5: 2)	Ethanol DMSO

2. Spectral and elemental characterization of Synthesized Compounds:

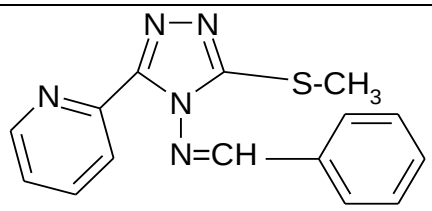
Parent-4

Molecular Weight	207 (determined by Rast's method)
Elemental Analysis	C : 45.52% ,H: 4.57 % , N: 34.28 %
IR spectral data (cm^{-1}) (KBr)	1603, 1582(C=N str.), 3272, 3172 (-NH str.), 3127, 3109 (=CH str.), 3064,3030 (Ar-H), 1247(N-N=C str.), 696 (C-S-C str.)
^{1}HNMR (DMSO-d6) δ	8.65(1H, d ,Ar-H_a), 7.8(1H, d ,Ar-H_b), 7.6(1H, t ,Ar-H_c), 7.3(1H, d ,Ar-H_d), 2.47 (3H,s,CH_3-S-) , 2.8(-NH_2)
IUPAC Name	3-(methylthio)-5-(pyridine-2-yl)-4H-1,2,4-triazole-4-amine

Structure & Molecular Formula	 **$C_8H_9N_5S$**

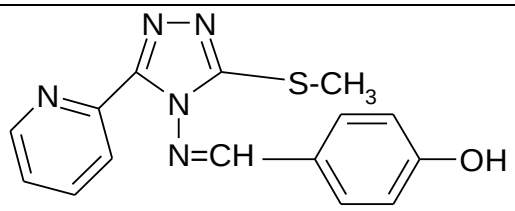
4(a)

Molecular Weight	295 (determined by Rast's method)
Elemental Analysis	C : 61% ,H: 4.44 % , N: 23.71 %
IR spectral data (cm^{-1}) (KBr)	1600, 1585(C=N str.), 3272, 3172 (-NH str.), 3127, 3109 (=CH str.), 3064, 3030 (Ar-H), 1247 (N-N=C str.), 696 (C-S-C str.)
^{1}HNMR (DMSO-d6 δ	8.65(1H, d , Ar-H_a), 7.8(1H, d , Ar-H_b), 7.6(1H, t , Ar-H_c), 7.3(1H, d ,Ar-H_d), 2.47 (3H,s,CH_3-S-), 7.3(3H, t, Ar-H), 7.6(2H, t, Ar-H), 8.1(-N=CH)
IUPAC Name	N-benzylidine-3-(methylthio)-5-(pyridin-2-yl)-4H-1,2,4-triazole-4-amine

Structure & Molecular Formula	 **$C_{15}H_{13}N_5S$**

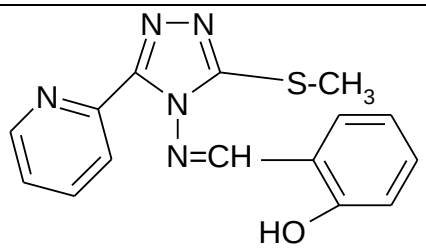
4(b)

Molecular Weight	311 (determined by Rast's method)
Elemental Analysis	C : 57.86 % ,H: 4.21 % , N: 21.23 %
IR spectral data (cm^{-1}) (KBr)	1427 [Ar(C=C, C=N) str.], 1582(C=N str.), 3272,3172 (-NH str.), 3127, 3109 (=CH- str.), 3064, 3030 (Ar-H), 1247(N-N=C str.), 696 (C-S-C str.)
^{1}HNMR (DMSO-d6) δ	8.65(1H, d , Ar-H_a), 7.8(1H, d , Ar-H_b), 7.6(1H, t , Ar-H_c), 7.3(1H, d ,Ar-H_d), 2.47 (3H,s,CH_3-S-), 7.4(2H, d, Ar-H), 6.8(2H, d, Ar-H), 8.1(-N=CH), 5.0(Ar-OH).
IUPAC Name	4-((3-(methylthio)-5-(pyridin-2-yl)-4H-1,2,4-triazol-4-ylimino)methyl)phenol

Structure & Molecular Formula	 **$C_{15}H_{13}N_5OS$**

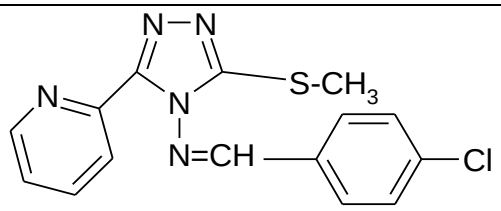
4(c)

Molecular Weight	311 (m/z =313 M^{+1})
Elemental Analysis	C : 57.86 % ,H: 4.21 % , N: 21.23 %
IR spectral data (cm^{-1}) (KBr)	1427[(Ar(C=C,C=N) str.] , 1580 (C=N str.), 3272, 3172 (-NH- str.), 3127, 3109 (=CH), 3064, 3030 (Ar-H), 1247(N-N=C str.), 696 (C-S-C str.)
^{1}HNMR (DMSO-d6) δ	8.65(1H, d , Ar-H_a), 7.8(1H, d , Ar-H_b), 7.6(1H, t , Ar-H_c), 7.3(1H, d ,Ar-H_d), 2.47 (3H,s,CH_3-S-), 7.1(1H, t Ar-H), 6.8(2H, t, Ar-H), 8.1(-N=CH), 5.0(Ar-OH).
IUPAC Name	2-((3-(methylthio)-5-(pyridin-2-yl)-4H-1,2,4-triazol-4-ylimino)methyl)phenol

Structure & Molecular Formula	 **$C_{15}H_{13}N_5OS$**

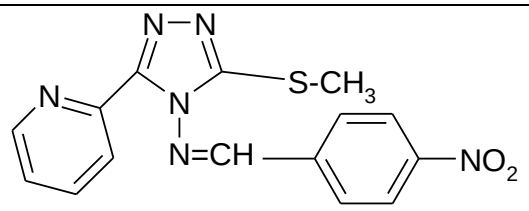
4(d)

Molecular Weight	329 (determined by Rast's method)
Elemental Analysis	C : 54.62% ,H: 3.67 % , N: 21.27 %
IR spectral data (cm^{-1}) (KBr)	1425 [Ar(C=C, C=N) str.], 1603, 1582(C=N str.), , 3272, 3172 (-NH str.), 3127, 3109 (=CH- str.), 3064, 3030 (Ar-H), 1247(N-N=C str.), 696 (C-S-C str.)
^{1}HNMR (DMSO-d6) δ	8.65(1H, d ,Ar-H_a), 7.8(1H, d , Ar-H_b), 7.62(1H, t , Ar-H_c), 7.3(1H, d ,Ar-H_d), 2.47 (3H,s,CH_3-S-), 8.1(-N=CH),7.3 (2H, t, Ar-H), 7.6 (2H, t, Ar-H).
IUPAC Name	N-(4-chlorobenzylidine-3-(methylthio)-5-(pyridin-2-yl)-4H-1,2,4-triazole-4-amine

Structure & Molecular Formula	 **$C_{15}H_{12}N_5SCl$**

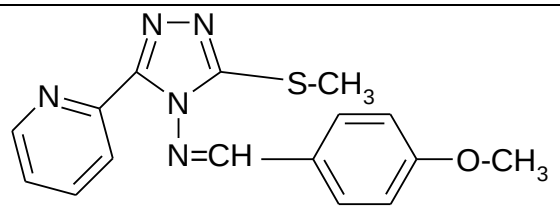
4(e)

Molecular Weight	340 (determined by Rast's method)
Elemental Analysis	C : 52.52% ,H: 3.57 % , N: 24.27 %
IR spectral data (cm^{-1}) (KBr)	1427[Ar(C=C,C=N str)], 1600, 1582(C=N str.), 3272, 3172 (-NH str.), 3127, 3109 (=CH- str.), 3064, 3030 (Ar-H), 1247(N-N=C str.), 690 (C-S-C str.)
^{1}HNMR (DMSO-d6) δ	8.65(1H, d ,Ar-H_a), 7.8(1H, d , Ar-H_b), 7.62(1H, t , Ar-H_c), 7.3(1H, d ,Ar-H_d), 2.47 (3H,s,CH_3-S-), 8.1(-N=CH), 7.9(2H, t , Ar-H), 8.2 (2H, t, Ar-H).
IUPAC Name	N-(4-nitrobenzylidine-3-(methylthio)-5- (pyridin-2-yl)-4H-1,2,4-triazole-4-amine

Structure & Molecular Formula	 **$C_{15}H_{12}N_6O_2S$**

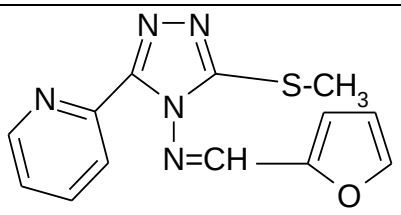
4(f)

Molecular Weight	325 (determined by Rast's method)
Elemental Analysis	C : 59.62% ,H: 4.65 % , N: 21.57 %
IR spectral data (cm^{-1}) (KBr)	1427[Ar (C=C,C=N str)], 1602, 1582(C=N str.), 3272, 3172 (-NH- str., 3127 ,3109 (=CH- str.), 3064,3030 (Ar-H), 1247(N-N=C str.), 696 (C-S-C str.)
^{1}HNMR (DMSO-d6) δ	8.65(1H, d , Ar-H_a), 7.8(1H, t , Ar-H_b), 7.62(1H, d , Ar-H_c), 7.3(1H, t, Ar-H_d), 2.47 (3H, s, CH_3-S-), 8.1(-N=CH), 7.5(2H, t , Ar-H), 6.8 (2H, t, Ar-H), 3.74 (s, 3H, -OCH3)
IUPAC Name	N-(4-methoxybenzylidene)-3-(methylthio)-5-(pyridine-2-yl)-4H-1,2,4-triazole-4-amine

Structure & Molecular ormula	 **$C_{16}H_{15}N_5OS$**

4(g)

Molecular Weight	285 (determined by Rast's method)
Elemental Analysis	C : 54.52% ,H: 3.57 % , N: 25.57 %
IR spectral data (cm^{-1}) (KBr)	1427 [Ar(C=C, C=N) str.] ,1584 (C=N str.), 3272, 3172 (-NH- str.), 3127, 3109 (=CH- str.), 3064, 3030 (Ar-H), 1247(N-N=C str.), 696 (C-S-C str.)
^{1}HNMR (DMSO-d6) δ	8.65(1H, d ,Ar-H_a), 7.8(1H, t , Ar-H_b), 7.62(1H, d , Ar-H_c), 7.3(1H, t, Ar-H_d), 2.47 (3H, s, CH_3-S-), 7.5 (-N=CH), 6.3(2H, d , furan), 7.4(1H, d, furan).
IUPAC Name	N-(furan-2-ylmethylene)-3-(methylthio)- 5-(pyridin-2-yl)-4H-1,2,4-triazole-4-amine

Structure & Molecular Formula	 **$C_{12}H_{11}N_5OS$**

Results of Antibacterial Activity of compounds:

Table: Zone of inhibition (diameter in mm) of Synthesized compounds

Zone of inhibition by agar well diffusion (diameter in mm)									
Compound Code	***S.aureous***			***B.subtilis***			***E.coli***		
	125	***250***	***500***	***125***	***250***	***500***	***125***	***250***	***500***
	µg/100 µL			µg/100µL			µg/100µL		
4(a)	-	-	12	-	-	14	12	14	18
4(b)	-	14	16	-	12	14	-	-	12
4(c)	-	10	12	-	-	-	-	-	12
4(d)	13	16	20	-	12	15	-	-	13
4(e)	-	-	13	-	-	13	14	17	19
4(f)	-	15	16	-	-	11	-	-	-
4(g)	-	13	15	-	11	15	-	-	12

(–), indicates there was no observed zone of inhibition

Preliminary antibacterial studies were conducted on synthesized compounds, by Well Diffusion method. For comparison, Ampicillin was used as standard , procured from Hindustan Antibiotics Pvt..Ltd., Pune.

The compounds that passed the antibacterial screening process are listed in Table 10. Based on the provided data, it is apparent that the majority of the compounds exhibited noteworthy

inhibitory action against S. sureus, and E. coli, as well as B. subtilis. It was discovered the investigated chemicals' antibacterial properties were dose dependant. Activities were found to be good at doses of 250 µg/mL, and the majority of substances strongly inhibited bacterial growth at concentrations between 250 µg / mL and 500 µg / mL. Out of all the substances examined, compound 4(g) had strong inhibitory action against both B. subtilis and S. aureus, while compound 4(d) demonstrated minimal to moderate activity against S. aureus. Additionally, the data revealed that compounds 5(c) exhibited a moderate level of inhibitory efficacy against B. subtilis. Compound 4(a) and 4(e) shown strong inhibitory intervention aimed at E. Coli.

Results of Antifungal Activity:

Table: Zone of inhibition(diameter in mm) of Synthesized compounds:

Zone of inhibition by agar well diffusion(diameter in mm)						
CompoundCode	***Aspergillus niger***			***Candida albicans***		
	125	***250***	***500***	***125***	***250***	***500***
	µg/100µL	µg/100µL	µg/100µL	µg/100µL	µg/100 µL	µg/100µL
Zone of inhibition by agar well diffusion(diameter in mm)						
Fungal strain	***Aspergillus niger***			***Candida albicans***		
C.code	**125**	**250**	**500**	**125**	**250**	**500**
4(a)	-	-	12	-	12	14
4(b)	-	12	14	-	-	13
4(c)	-	-	11	13	17	19
4(d)	-	-	11	-	-	13
4(e)	11	14	16	-	-	10
4(f)	12	15	18		-	12
4(g)	11	13	15	-	11	14

(–), indicates there was no observed zone of inhibition

Conclusion

An first examination into the anti-fungal properties of synthetic compounds was carried out by use of the well diffusion method. In order to provide a standard for comparison, fluconazole, which was bought from Hindustan Antibiotics Pvt.Ltd. in Pune, was procured. provides a summary of the antifungal activity of the compounds in vitro against the two important fungal strains, namely Aspergillus niger and Candida albicans, using the well diffusion method. When comparing the results of the various medications, fluconazole was used as the standard medicine.

When the synthetic compounds were present in quantities ranging from 125 µg to 500 µg/mL, they were able to successfully limit the growth of fungus by a percentage of 16-30%. It was discovered that compound 4(f) was a good antifungal agent for A. niger, but compound 4(e) displayed a moderate level of effectiveness. 4(b) shown a reduction in its activity against A. niger. Compound 4(c) was shown to be an effective antifungal agent for C. albicans, according to scientific research. In contrast, compound 4(g) exhibited a modest level of activation. The efficacy of 4(a) and 6(e) was shown to be lower in comparison to C. albicans. According to the findings, substances 4(d) shown resistance to both A. niger and Candida albicans. Both A. niger and Candida albicans were strongly suppressed by fluconazole at a concentration of 125µg/100µL, with zones measuring 22 and 24 mm.

REFERENCES:

1. Yücel, TayyibeBeyza. "Synthesis OfTriazole Derivative Compounds And Their Importance In Pharmacology." *Science And Mathematics* (2023): 133.
2. Keri, Rangappa S., Siddappa A. Patil, SrinivasaBudagumpi, AndBhariMallannaNagaraja. "Triazole: A Promising Antitubercular Agent." *Chemical Biology & Drug Design* 86, No. 4 (2015): 410-423.
3. D'souza, A., Venuprasad, K. D., Nayak, P., &Poonacha, L. K. (2021). A Review Article OnTriazoles And Its Pharmacological Activities. *Journal Of Pharmaceutical Research International*, *33*(43a).
4. Guan, Qianwen, Shuaishuai Xing, Lei Wang, Jiawei Zhu, Can Guo, Chunlei Xu, Qun Zhao, Yulan Wu, Yao Chen, And Haopeng Sun. "Triazoles In Medicinal Chemistry: Physicochemical Properties, Bioisosterism, And Application." *Journal Of Medicinal Chemistry* (2024).

5. Gupta, Ojasvi, Tathagata Pradhan, And Gita Chawla. "An Updated Review On Diverse Range Of Biological Activities Of 1, 2, 4-Triazole Derivatives: Insight Into Structure Activity Relationship." *Journal Of Molecular Structure* 1274 (2023): 134487.
6. Sonawane, M. D., B. M. Narwate, And A. S. Darandale. "Review On Chemistry And Pharmacological Significance Of Triazole Derivatives." *International Journal Of Pharmaceutics And Drug Analysis* (2017): 161-176.
7. Kharb, Rajeev, PrabodhChander Sharma, And Mohammed ShaharYar. "Pharmacological Significance OfTriazole Scaffold." *Journal Of Enzyme Inhibition And Medicinal Chemistry* 26, No. 1 (2011): 1-21.
8. Zafar, W., Sumrra, S.H. And Chohan, Z.H., 2021. A Review: Pharmacological Aspects Of Metal Based 1, 2, 4-Triazole Derived Schiff Bases. *European Journal Of Medicinal Chemistry*, *222*, P.113602.
9. Dehaen, Wim, AndVasiliy A. Bakulev, Eds. *Chemistry Of 1, 2, 3-Triazoles*. Vol. 40. Cham, Switzerland: Springer International Publishing, 2015.
10. Dixit, D., Verma, P.K. And Marwaha, R.K., 2021. A Review On 'Triazoles': Their Chemistry, Synthesis And Pharmacological Potentials. *Journal Of The Iranian Chemical Society*, *18*(10), Pp.2535-2565.
11. Jain, A. And Piplani, P., 2019. Exploring The Chemistry And Therapeutic Potential Of Triazoles: A Comprehensive Literature Review. *Mini Reviews In Medicinal Chemistry*, *19*(16), Pp.1298-1368.
12. Zornik, Denise, Robert M. Meudtner, Tamer El Malah, Christina M. Thiele, And Stefan Hecht. "Designing Structural Motifs For Clickamers: Exploiting The 1, 2, 3-Triazole Moiety To Generate Conformationally Restricted Molecular Architectures." *Chemistry–A European Journal* 17, No. 5 (2011): 1473-1484.
13. Sharma, Kalpana, Anjali Maan, Vikas D. Ghule, And Srinivas Dharavath. "Azo-Bridged Triazole Macrocycles: Computational Design, Energy Content, Performance, And Stability Assessment." *The Journal Of Physical Chemistry A* 127, No. 48 (2023): 10128-10138.
14. Nulwala H, Takizawa K, Odukale A, Khan A, Thibault Rj, Taft Br, LipshutzBh, Hawker Cj. Synthesis And Characterization Of Isomeric Vinyl-1, 2, 3-Triazole Materials By Azide− Alkyne Click Chemistry. Macromolecules. 2009 Aug 25;42(16):6068-74.

15. Nulwala, H., Takizawa, K., Odukale, A., Khan, A., Thibault, R.J., Taft, B.R., Lipshutz, B.H. And Hawker, C.J., 2009. Synthesis And Characterization Of Isomeric Vinyl-1, 2, 3-Triazole Materials By Azide− Alkyne Click Chemistry. *Macromolecules*, *42*(16), Pp.6068-6074.
16. Song, L., Ang, H.T., Senthilperumal, J., Kanusu, U.R., Venugopal, S., Rangarajan, N., Krishnamoorthy, S., Dubbaka, S.R., O'neill, P. And Wu, J., 2024. 1, 2, 3-Triazole Synthesis: Development Of Safe And Effective Batch And Continuous Manufacturing Processes. *Organic Process Research & Development*.
17. Sathish Kumar, S. And P Kavitha, H., 2013. Synthesis And Biological Applications Of Triazole Derivatives–A Review. *Mini-Reviews In Organic Chemistry*, *10*(1), Pp.40-65.
18. KuijpersBh, Groothuys S, Keereweer Ab, QuaedfliegPj, Blaauw Rh, Van Delft Fl, Rutjes Fp. Expedient Synthesis Of Triazole-Linked Glycosyl Amino Acids And Peptides. Organic Letters. 2004 Sep 2;6(18):3123-6.
19. Li, Zicheng, Shuhua Chen, Ning Jiang, And Gang Cui. "Synthesis OfTriazole Nucleoside Derivatives." *Nucleosides, Nucleotides And Nucleic Acids* 22, No. 4 (2003): 419-435.
20. Rezaei, Z., Khabnadideh, S., Pakshir, K., Hossaini, Z., Amiri, F. And Assadpour, E., 2009. Design, Synthesis, And Antifungal Activity Of Triazole And Benzotriazole Derivatives. *European Journal Of Medicinal Chemistry*, *44*(7), Pp.3064-3067.