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SYNTHESIS AND CHARACTERIZATION OF NEWLY DESIGNED 1,3,4-THIADIAZOLE-BASED CARBOXAMIDES WITH ANTIMICROBIAL POTENTIAL

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ABSTRACT

The present work was investigated the synthesis of some novel carboxamides of 1, 3, 4-thiadiazoleanalogs. The synthesis of N-(6-cyano-5-imino-2-(5-methylpyrazin-2-yl)-5H-[1,3,4]thiadiazolo[3,2-a]pyrimidin-7-yl)benzamide can be obtained by an intermediate**(4)**7-amino-5-imino-2-(5-methylpyrazin-2-yl)-5H-[1,3,4]thiadiazolo[3,2-a]pyrimidine-6-carbonitriletreated with substituted aromatic acids in the presence of the dehydrating agent such as CDI and solvent is CH_3CN reflux.The compound (4) can be synthesised from 5-(5-methylpyrazin-2-yl)-1, 3, 4-thiadiazol-2-amine with malononitrile in the presence of piperidne as a base in ethanol as a solvent at reflux conditions. The intermediate (3) can be obtained by the 5-methyl pyrazine carboxylic acid (1) treated with thiosemicarbazide (3) in, subjected to protic acid (H_3PO_4) in toluene as a solvent.The results of the nuclear magnetic resonance (NMR) analyses showed the successful formation of the desired moieties**.** Thiadiazoles analogous have generated significant attention in the area of medicinal chemistry due to their prospective pharmacological properties, including antimicrobial activities**.** This research article reveals that the synthesis of thiadiazole derivatives was also examined, along with their chemical characterization and potential antimicrobial effects on various pathogens. The results had represented a promising antimicrobial activity for several of the synthesized analogs, suggesting their active potential as lead moieties for further drug enhancement.

Keywords: 5-methylpyrazine-2-carboxylicacid,Thiosemicarbazide, 5-(5-methylpyrazin-2-yl)-1,3,4-thiadiazol-2-amine; Malano Nitrile; CDI, Antimicrobial Activity

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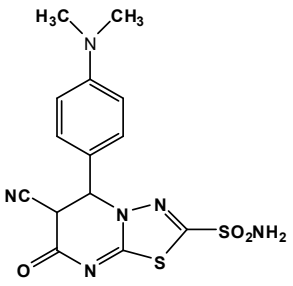
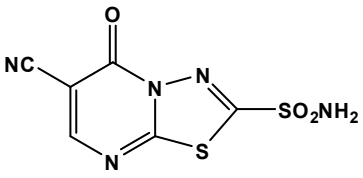
INTRODUCTION

Heterocyclic compounds are a tremendously significant and unique class of moieties. These moieties demonstrate a wide spectrum of physical, chemical, and biological properties. In nature, heterocyclic compounds are broadly expanded and exhibit a significant part in metabolism owing to their structural moieties occurring in different natural products, including hormones, antibiotics, alkaloids, vitamins, and many others. A great extent of nitrogen-containing heterocyclic compounds thatcomprise sulphur and oxygen atoms is identified as a valuable combination of therapeutics in medicinal chemistry. In particular, thiazole analogues exhibited a very important pharmacological role in many potent biological activities. The entire sector of pharmaceuticals has been facing the issue of increasing productivity as well as advancement. The main provocation includes rising investigation and augmentation of the cost contract supply of novel chemical entities.[1]

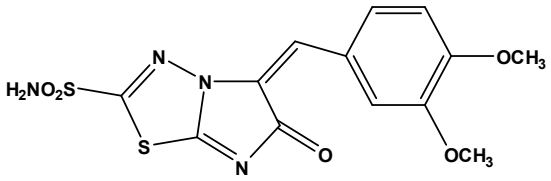


(A) C.albicans



(B) S-Aureus

http://doi.org/10.31788/RJC.2025.1849442



(C) A-Fumigates
Fig.-1: Antimicrobial Activity Compounds

The nitrogen, oxygen, and sulphur-containing heterocyclic compounds are extensively recognized as a core framework in a large library of heterocyclic compounds and display different applications in natural products and other fields of science. The emerging significance group of the amide functional group was extracted from its presence in many crucial compounds, such as proteins, fabrics, fertilizers, insecticides, plastics, drugs, and a vast number of synthetic structures. For this reason, it is very relevant to develop new methods for the efficient synthesis of amides. These techniques are low-atom economy because they demand stoichiometric amounts of activating reagent and generate a comparable amount of waste, even though they synthesize amides under mild reaction conditions and with good yields. Additionally, it might be time-consuming to remove the matching by-product, which raises the transformation's cost. Catalysts and starting materials, such as esters, aldehydes, alcohols, nitriles, and oximes, are used in new processes for the synthesis of amides. Involve the use of catalysts, and employ starting materials such as esters, aldehydes, alcohols, nitriles, and oximes.The moiety containing an amide group in organic synthetic chemistry, as well as medicinal chemistry,plays an important and prospective role. The amide group plays a key role in the peptide synthesis of proteins, vitamins, and hormones,which are of biological importance.Nowadays, there have been intense investigations on fused thiadiazole systems. Literature reports revealed that [1, 3, 4] thiadiazolo [3,2-a] pyrimidine nucleus is associated with diverse pharmacodynamics and chemotherapeutic activities including Biological activities,[2,3]Antiviral,[4]anticancer activity,[5-8]glucokinase activators,[9]Anti-inflammatory activities,[9,10]Antimicrobial Activity,[11-14] antioxidants,[15] anti-ulcer agents,[16] Antidepressant,[17] Anti-Tumor,[17] antiplatelet,[18] analgesic activity,[19] antiquorum-sensing.[20] Therefore, in this research, our ongoing programme was step-wise, the reaction procedure by the use of a dehydrating reagent system and an analog of the target compounds, benzamide, obtained by two steps. The target compound can be obtained by treating an intermediate (4) with substituted aromatic acids in the presence of the dehydrating agent such as CDI, and the solvent is CH_3CN reflux.The compound (4) can be synthesised from 5-(5-methylpyrazin-2-yl)-1,3,4-thiadiazol-2-amine with malononitrile in the presence of morpholine as base in ethanol as solvent at reflux. The intermediate (3) can be obtained by the 5-methyl pyrazine carboxylic acid (1) with thiosemicarbazide (3) in the presence of protic acid (H_3PO_4) in acetonitrile as a solvent.

EXPERIMENTAL

Chemicals and Instruments

The synthetic grade reagents, starting chemicals, and solvent were commercially procured from Sigma Aldrich. The melting points of our target compounds are uncorrected and were also measured on a Stuart melting point apparatus.^{1}H-NMR spectra were recorded on a Bruker Avance 400 MHz spectrometer using $CDCl_3$ as a solvent and tetramethylsilane as an internal standard. Chemical shift values appear in the δ scale. The molecular compound was determined by using a mass spectrometer. The progress of the desired moiety was recognized by thin-layer chromatography (TLC) using precoated aluminium sheets of silica gel. An ultraviolet UV lamp was used to accomplishvisualization of the target compounds, and these were purified by the re-crystallization process.

The Preparation Procedure of the Compound-3 The compound (3) can be obtained by mixing 5-methyl pyrazine carboxylic acid (1.150 mol), which was treated with thiosemicarbazide (1.50 mol), dissolved in 25mL of Acetonitrile,in 50mL of RBF, and 5mL of H3PO4 is slowly added to the above mixture. The reaction was carried out under suitable temperature conditions for 4 hours.The percentage of starting materials was identified by the TLC (mobile Phase 6:4 = n-hexane: EtOAc). After the completion of the reaction, the temperature of the reaction mixture was reduced to room temperature. It was poured into crushed ice and neutralised with a solution of anhydrous Na_2CO_3,and

also extracted with ethyl acetate. The ethyl acetate layer was separated and washed twice with distilled water. The organic layer was distilled off under vacuum, and the target compound was finally obtained.Yellow solid, Yield-92%, M.P-158-160^{0}C; ^{1}HMR (400MHz, $CDCl_3$) δ ppm: 8.567(s,1H), 8.384(s,1H), 5.742 (s,2H, NH_2), 1.674 (s, 3H, CH_3); ^{13}CNMR (100MHz, $CDCl_3$) δ Ppm: 175.09, 160.92, 157.44, 146.24, 141.26, 19.62; Molecular formulae; C7H7N5S; Molecular Weight (m/z); 194.46(M+H); Analysis of elements:

The General Procedure of the Compound-4

The mixture of compound (1mol) (3) and malononitrile (1mol) is introduced intoa 50mL RBF. 25 mL of ethanol is present, and piperidine is added to the mixture. The reaction was continued for 6 hours, and the reaction progresswas monitored with the help of TLC (55 = EtOAc: n-hexane). The reaction mixture is neutralised with 2N HCl, and after being extracted with ethyl acetate, the organic layer is separated. The ethyl acetate layer was washed with distilled water, and the organic layer was separated. The Layer was distilled off, andthe target compound.Yellow solid, Yield-94%, M.P-174-176^{0}C; ^{1}HMR (400MHz, $CDCl_3$)δppm: 9.462 (s,1H), 9.062 (s,1H), 8.534(s,1H), 6.238 (s,2H, NH_2), 1.764 (s, 3H, CH_3); ^{13}CNMR (100MHz, $CDCl_3$) δ ppm: 160.39, 157.62, 154.88, 152.62, 150.65, 148.36, 147.46, 143.66, 141.46, 87.75, 21.09; Molecular formulae; $C_{11}H_8N_8S$; Molecular Weight (m/z); 285.38(M+H)

The General Procedure Target Derivatives (6a-6m)

A mixture of substituted aromatic acid (1.125mole), compound (4), and dehydrating reagent DCC in ethanol was taken in a 50 mL RB flask, and it was continued for an appropriate time. The development of the reaction was examined by TLC. The crushed ice was added to the crude of the product until all the reactants were consumed during the reaction, and was neutralized with 10% $NaHCO_3$. The crude was workup with ethyl acetate,and the ethyl acetate layer was separated. The solvent present in the organic layer wasdesiccated under reduced pressure by applying a vacuum pump to acquire the solid product. All the synthesized compounds were recrystallized from ethanol.

Derivatives (6a)

Pale yellow solid, Yield-87%, M.P-184-186^{0}C; ^{1}HMR (400MHz, $CDCl_3$)δppm: 9.842 (s,1H, ,9.265 (s,1H), 9.074 (s,1H), 8.668(s,1H), 7.819-7.356(m,5H,Ar), 1.946(s, 3H, CH_3); ^{13}CNMR (100MHz, $CDCl_3$) δ ppm: 162.78, 159.21, 156.04, 154.33, 153.62, 149.09, 146.11, 145.39, 142.44, 131.62, 130.03, 128.96, 128.46, 89.63, 21.65; Molecular formulae; $C_{17}H_{13}N_7OS$; Molecular Weight (m/z); 389.4(M+H); Analysis of Elements: Calculated: C-56.19, H-3.61, N-26.95; Obtained: C-56.12, H-3.60, N-27.05

Derivatives (6b)

Pale yellow solid, Yield-89%, M.P-191-193^{0}C; ^{1}HMR (400MHz, $CDCl_3$)δppm: 9.804 (s,1H, NHCO), 9.482 (s,1H), 9.113 (s,1H,-OH), 9.019(s,1H), 8.534(s,1H), 7.848 (2H, d, J=8.0Hz), 7.234(2H, d, J=9.4Hz), 1.943(s, 3H, CH_3); ^{13}CNMR (100MHz, $CDCl_3$) δ ppm: 162.79, 160.08, 157.92, 154.04, 152.36, 150.69, 149.74, 145.07, 142.38, 140.06, 128.89, 128.37, 117.94, 89.96, 20.04; Molecular formulae; $C_{18}H_{12}N_8O_2S$; Molecular Weight (m/z); 405.49(M+H); Analysis of Elements: Calculated: C-53.82, H-3.45, N-25.84; Obtained: C-53.75, H-3.44, N-25.92

Derivatives (6c)

Yellow solid, Yield-90%, M.P-207-209^{0}C; ^{1}HMR (400MHz, $CDCl_3$)δppm: 9.855 (s,1H, NHCO),9.345(s,1H), 9.124 (s,1H,-OH), 9.044(s,1H), 8.595(s,1H), 7.654 (2H,d, J=10.4Hz, Ar), 7.247(s,1H,Ar), 1.978 (s, 3H, CH_3); ^{13}CNMR (100MHz, $CDCl_3$)δppm: 160.54, 157.04, 155.12, 153.04, 151.85, 149.69, 144.07, 141.38, 139.87, 128.14, 128.54, 118.94, 87.96, 21.04; Molecular formulae; C19H14N_8O_3S; Molecular Weight (m/z); 435.14(M+H);Analysis of Elements: Calculated: C-54.82, H-3.23, N-23.84; Obtained: C-54.76, H-3.22, N-23.98

Derivatives (6d)

Yellow solid, Yield-91%, M.P-202-204^{0}C; ^{1}HMR (400MHz, $CDCl_3$)δppm: 9.748 (s,1H, NHCO), 9.276 (s,1H), 9.048(s,1H), 8.494 (s,1H), 7.714(s,1H,Ar), 7.529 (1H,d, J=8.0Hz), 7.058 (1H, d, J=8.8Hz), 3.814 (s,3H,OCH_3), 3.517 (s, 3H, OCH_3), 1.846 (s, 3H, CH3); 13CNMR (100MHz, $CDCl_3$) δ ppm: 163.94, 160.06, 157.04, 153.24, 148.15, 144.09, 141.65, 140.65, 138.41, 128.55, 126.07,

115.71, 112.94, 89.02; Molecular formulae; $C_{20}H_{16}N_8O_3S$; Molecular Weight (m/z); 449.39(M+H); Analysis of Elements: Calculated: C-53.89, H-4.05, N-23.15; Obtained: C-53.81, H-4.03, N-23.08

Derivatives (6e)
Yellow solid, Yield-89%, M.P-210-212^{0}C; ^{1}HMR (400MHz, $CDCl_3$) δppm: 9.674 (s,1H, NHCO), 9.283 (s,1H), 9.022(s,1H),8.562 (s,1H),7.523- 7.262 (m,6H,Ar),2.675 (s,6H,$(CH_3)_2$), 1.776 (s, 3H, CH_3); ^{13}CNMR (100MHz, $CDCl_3$) δ ppm: 160.84, 157.71, 156.04, 154.48, 152.72, 150.64, 148.06, 145.23, 144.63, 140.42, 129.43, 127.11, 126.04,177.02, 89.92, 40.37, 21.68; Molecular formulae; $C_{20}H_{17}N_9OS$; Molecular Weight (m/z); 432.56(M+H); Analysis of Elements: Calculated: C-56.14, H-4.46, N-27.57; Obtained: C-56.10, H-4.45, N-27.62.

Derivatives (6f)
Yellow solid, Yield-85%, M.P-223-225^{0}C; ^{1}HMR (400MHz, $CDCl_3$)δppm: 9.973 (s,1H, NHCO), 9.316 (s,1H), 9.107(s,1H), 8.638 (s,1H), 7.942 (2H,d,J=8.0Hz),7.447(2H,d,J= 8.8Hz),1.906 (s, 3H, CH_3); ^{13}CNMR (100MHz, $CDCl_3$) δ ppm: 164.65, 160.08, 156.74, 154.05, 152.46, 151.53, 147.79, 144.09, 143.45, 129.67, 128.43, 127.05,118.25 89.56, 19.44; Molecular formulae; $C_{18}H_{11}FN8OS$; Molecular Weight (m/z); 408.27(M+2);Analysis of Elements: Calculated: C-53.54, H-3.17, N-25.71; Obtained: C-53.48, H-4.15, N-25.79

Derivatives (6g
Yellow solid, Yield-85%, M.P-215-217^{0}C; ^{1}HMR (400MHz, $CDCl_3$) δppm: 9.846 (s,1H, NHCO), 9.402 (s,1H,=NH), 9.049(s,1H), 8.668 (s,1H), 7.846- 7.576 (m,4H,Ar), 1.943 (s, 3H, CH_3); ^{13}CNMR (100MHz, $CDCl_3$) δ ppm: 164.78, 160.04, 157.76, 153.77, 151.07, 148.06, 145.56, 142.67, 136.03, 130.06, 129.74, 128.94,117.84, 89.42, 20.04; Molecular formulae; $C_{18}H_{11}ClN_8OS$; Molecular Weight (m/z); 424.49(M+H); Analysis of Elements: Calculated: C-51.32, H-3.04, N-24.65; Obtained: C-51.25, H-3.03, N-24.74

Derivatives-viii (6h)
Dark red solid, Yield-87%, M.P-217-219^{0}C; ^{1}HMR (400MHz, $CDCl_3$)δppm: 10.042 (s,1H, NHCO), 9.217 (s,1H), 9.024(s,1H), 8.587 (s,1H), 7.814 (2H, d, J=8.0Hz), 7.426 (2H, d, J= 7.2Hz), 1.886 (s, 3H, CH_3); ^{13}CNMR (100MHz, $CDCl_3$) δ ppm: 167.28, 160.05, 157.74, 154.08, 152.71, 148.60, 145.75, 144.35, 142.68, 131.17, 130.08, 129.15, 127.65, 118.60, 90.19, 21.76; Molecular formulae; $C_{17}H_{12}BrN_7OS$; Molecular Weight (m/z); 467.33 (M+2); Analysis of Elements: Calculated: C-46.17, H-2.73, N-22.17; Obtained: C-46.10, H-2.72, N-22.25

Derivatives (6i)
Brown solid, Yield-83%, M.P-208-210^{0}C; ^{1}HMR (400MHz, $CDCl_3$)δppm: 9.921 (s,1H, NHCO), 9.314 (s,1H), 9.052 (s,1H), 8.594 (s,1H), 8.128 (2H, d, J=7.2 Hz), 8.128 (d, J= 6.8Hz,2H,Ar), 1.846 (s, 3H, CH_3); ^{13}CNMR (100MHz, $CDCl_3$) δ ppm: 169.28, 161.05, 158.12, 156.21, 153.07, 148.06, 146.87, 143.25, 140.68, 132.17, 130.89, 128.55, 128.05,118.65 91.19, 22.76; Molecular formulae; $C_{18}H_{11}N_9O_3S$; Molecular Weight (m/z); 434.39 (M+2); Analysis of Elements: Calculated: C-50.01, H-2.96, N-27.44; Obtained: C-49.91, H-2.95, N-27.51.

Derivatives (6j)
Pale yellow solid, Yield-88%, M.P-225-227^{0}C; ^{1}HMR (400MHz, $CDCl_3$) δppm: 10.874(s,1H,-COOH), 10.121 (s,1H), 9.325 (s,1H), 9.112 (s,1H), 8.707 (s,1H), 8.215 (2H, d, J=6.8 Hz), 8.046 (2H, d, J= 8.0Hz), 2.012 (s, 3H, CH_3); ^{13}CNMR (100MHz, $CDCl_3$) δ ppm: 168.65, 160.34, 159.57, 155.22, 154.07, 147.06, 145.81, 142.28, 140.09, 131.17, 129.89, 128.76, 128.32, 117.98, 90.19, 19.76; Molecular formulae; $C_{19}H_{12}N_8O_3S$; Molecular Weight (m/z); 433.24 (M+H); Analysis of Elements: Calculated: C-53.07, H-3.27, N-24.07; Obtained: C-53.00, H-3.25, N-24.15

Derivatives (6k)
Dark yellow solid, Yield-84%, M.P-195-197^{0}C; ^{1}HMR (400MHz, $CDCl_3$) δppm: 10.024 (s,1H, NHCO), 9.284 (s,1H), 9.076 (s,1H), 8.624 (s,1H), 8.146 (2H, d, J=9.6 Hz), 7.838 (2H,d, J= 8.0 Hz), 1.882 (s, 3H, CH_3); 13CNMR (100MHz, CDCl3) δ ppm:160.87, 157.31, 156.02, 153.32, 150.02, 148.04, 146 .11, 143.08, 141.17, 140.26, 135.33, 133.48, 129.28, 128.69, 117.31, 87.69, 19.48; Molecular formulae; $C_{17}H_{11}N_9OS$; Molecular Weight (m/z); 390.57 (M+H);Analysis of Elements: Calculated: C-52.74, H-3.32, N-30.75; Obtained: C-52.65, H-3.32, N-30.75

Derivatives (6l)

Yellow solid, Yield-82%, M.P-197-199^{0}C; ^{1}HMR (400MHz, $CDCl_3$) δppm: 10.214 (s,1H, NHCO), 9.374 (2H,d, J= 8.0 Hz, Ar), 9.224 (s,1H), 9.052 (s,1H), 8.617 (s,1H), 1.848 (s, 3H, CH_3); ^{13}CNMR (100MHz, $CDCl_3$) δ ppm:168.43, 160.09, 159.44, 156.62, 155.17, 153.38, 150.08, 148.19, 145.64, 143.55, 140.77,118.05,89.69, 20.22;Molecular formulae; $C_{15}H_{10}BrN_9OS$; Molecular Weight (m/z); 469.08 (M+2); Analysis of Elements: Calculated: C-40.55, H-2.27, N-28.38 ;**.** Obtained: C-40..48, H-2.25, N-28.47

Derivatives (6m)

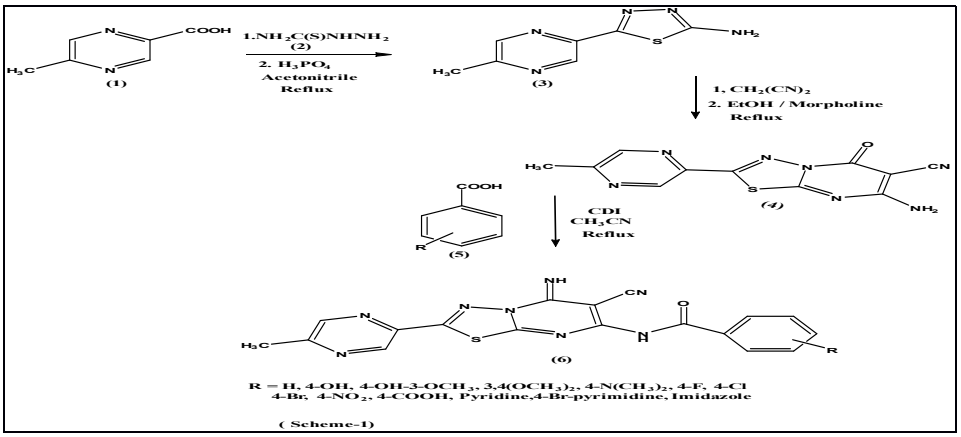
Yellow solid, Yield-88%, M.P-204-206^{0}C; ^{1}HMR (400MHz, $CDCl_3$) δppm: 10.634 (s,1H, NHCO), 9.510(s,1H,NH), 9.184 (s,1H), 9.110 (s,1H), 8.558 (s,1H), 7.552- 7.274 (m,3H,Ar), 1.924 (s, 3H, CH_3); ^{13}CNMR (100MHz, CDCl3) δ ppm: 165.73, 159.04, 157.28, 154.47, 152.18, 150.33, 147.44, 146.62, 144.59, 142.06, 135.64, 129.46,118.49, 89.77, 18.49; Molecular formulae; C15H10N10OS; Molecular Weight (m/z); **379.67 (M+H);** Analysis of Elements: Calculated: C-47.59, H-3.14, N-35.68; Obtained: C-47.51, H-3.13, N-35.75

RESULTS AND DISCUSSION

The synthesis of target derivatives is followed by a protocol with different stages.

Chemistry

In this investigation of the synthetic approach, the target analogis shown in Scheme-1.The starting intermediate (4) 5-imino-2-(5-methylpyrazin-2-yl)-5H-[1,3,4]thiadiazolo[3,2-a]pyrimidin-7-amine was treated with substituted aromatic acids in the presence of the dehydrating agent and morpoline a base in acetonitrile as solvent at reflux scaffold target compounds and the compound (4) can be synthesised from 5-(5-methylpyrazin-2-yl)-1,3,4-thiadiazol-2-amine with malononitrile in the presence of strong base in ethanol as solvent at reflux. The intermediate (3) can be obtained by the 5-methyl pyrazine carboxylic acid (1) with thiosemicarbazide (3) in the presence of protic acid (H_3PO_4) in acetonitrile as a solvent.



Scheme-1

In this study of the research article, prospective performance was applied by some important optimisation conditions, viz, scope of the catalyst, solvent, and loaded catalyst. The scope and advantages of this catalyst, the enhancement rate of reaction, excellent yield, short reaction time, and the scope of this catalyst are commercially available, easy work up, and also nontoxic nature. The evidence of the target moieties (6a-6m) can be represented in Scheme-1. All the tested derivatives were constructed by IR, NMR, and mass spectral data. The structures of the target (6a-6m) were analogous,as evidenced by ^{1}HNMR,^{13}CNMR, and mass spectral data. The ^{1}HNMR spectrum of the titled compounds was performed in various amide proton and imine proton, such as δ 10.121 as well as δ 9.325 ppm, respectively. The hydroxyl protons appeared at δ 9.113ppm, and the protons appeared at N,N-dimethyl protons at 2.675 ppm. The acid protons appear at δ10.874ppm, amine protons at δ5.742ppm, and the methoxy protons are exhibited at δ 3.813 ppm, and the value appeared at 1.915 ppm of methyl protons. The molecular ion peak of the halogen moiety was disclosed at 409.39 (M+2). The entire reaction was also identified as the highest yield acquired during synthesis, the product analogous bearing a releasing group (6d), greater than the product of the derivatives having an

electron attracting group (6g), and the compounds was bearing the halogen-containing group (6d-6f) also got good yield.In this reaction, the different dehydrating reagents are applied, viz DCC, CDI, EDC, and BDDC. Among these reagents used during the reaction, a different percentage of product was obtained as shown by Table-1.

Table-1: Comparison Among the Various Reagents Synthesis for Target Moiety (6d)

Entry	Catalyst	Time (h)	Yield (%)
1	DCC	5	78
2	CDI	5	94
3	EDC	5	65
4	BDDC	5	60

The amount of the dehydrating reagent is applied during this reaction asa result of the other reagent, resultingina sufficient product of the reaction inthe absence of the reagent. The percentage of the reagent increased slowly, and then the rate of reaction was developed by percentage of the product up to 90% by using 3 moles as shown in Table-2.

Table-2: The Influence of the Loaded Reagent for Preparation of Target Moiety (6d):

Entry	Loaded reagent (mol)	Time (hrs)	Yield (%)
1	1	7	25
2	2	7	68
3	3	7	94
4	4	7	94

It was noticed that following the above reagent impact during the reaction process, we followed the evaluation of solvent effects by applying several solvents, including H_2O, CH_3CN, EtOH, MeOH, and MDC. Our observations indicate that the good reaction conditions are those without the presence of solvents and also the conclusion of the reactions, as well as for the yield of the target product, compared to those obtained in any of the solvents investigated (Table-3).

Table-3: The Impact of the Solvent for Target Derivative (6d)

Entry	Solvent (mol)	Time (hrs)	Yield (%)
1	H_2O	7	25
2	DMF	7	64
3	EtOH	7	75
4	MDC	7	78
5	CH_3CN	7	94

In order to investigate the catalytic performance of the dehydrating reagent CDI, substituted aromatic acids were first applied for the reaction with compound (4). Even though at elevated temperatures, the reaction conditions were enhanced to synthesizethe target moiety in an efficientmanner in acetonitrile as a solvent, with a reagent quantity of CDI. As a result, we introduced a reaction dehydrating reagent to a range of solvents and conducted reactions at changed temperatures (Table-4). We can attain 94% of the product yield in the solvent-free system through experiments.

Antimicrobial Activity of Compounds

Pharmacological evaluation is one of the most significant parameters for the estimation of the activity of molecules. The examination part of the work can be variable and easy to perform. Overthe last two decades, the prevalence of infectious diseases has developed to a great extent. Antimicrobial agents are the most commonly applied to treat various types of infectious diseases. The target moieties have been evaluated for their *in-vitro* potent activities againstbacteria as well as fungi by following the micro broth dilution method.

In contrast to gram (-Ve) strains like E. coli and Aeruginosa, the in vitro antibacterial strong activity was tested against gram (+Ve) strains like B. Subtilis and S. aureus. Strong antifungal activity was assessed in vitro against A. Niger and C. albicans. For this inquiry, referral medications including streptomycin and Ketonozole were used for both antibacterial and antifungal testing. During the primary and secondary evaluation phases, the findings were made public. By successively diluting the sample compounds under examination and standard medications twice, the stock solution (2000 µg/mL) was produced.

Table-4: MIC of Antimicrobialsof Tested Samples (6a-6m)

Entry	Antibacterial MIC (µg/mL)				Antifungal MIC (µg/mL)	
Strains	*B. subtilis*	*S. aureus*	*P. aeruginosa*	*E. coli*	*A. Niger*	*C. Albicans*
6a	07	09	09	07	07	06
6b	19	17	17	18	17	16
6c	20	19	18	17	17	15
6d	18	20	20	19	16	15
6e	20	21	19	18	17	18
6f	20	21	21	22	17	18
6g	24	21	22	23	21	22
6h	23	22	23	21	19	21
6i	22	22	23	24	21	22
6j	10	12	12	13	10	10
6k	16	17	19	17	14	16
6l	14	16	18	17	15	16
6m	15	17	18	19	14	16
Streptomycin	27	27	27	27	-	-
Ketonozole	-	-	-	-	25	25
DMSO						

CONCLUSION

They concluded that the evaluation of the target moieties 1,3,4-thiadiazole is established as having two interconnected nitrogen atoms, two electron-deficient carbon atoms, and one lone electron pair containing an active sulphur atom. Hence, modern medicinal chemistry, such as 1, 3, 4-thiadiazole scaffold, and the rest of the important target compounds for the investigated new therapeutic leads. The desired compounds can be obtained in two stages, viz, the first stage can be prepared by starting material Pyrazine carboxylic acid in an acid medium, and the second stage is obtained by intermediating with the various aromatic and heteroaromatic carboxylic acids promoted by the dehydrating CDI agent. The target compounds obtained excellent yield by using various electron-withdrawing as well as electron-donating groups, and the medicinal field with potent antimicrobial and antiviral therapeutic potentials. The present manuscript concluded the study on the antimicrobial activity of 1, 3, 4-thiadiazole derivatives with their inhibitory potential against.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this article.

AUTHOR CONTRIBUTIONS

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REFERENCES

1. T.S. Kokovina, S. Y. Gadomsky, A. A. Terentiev, N.A. Sanina, (2021), *Molecules*, **26**, 17(2021), https://doi.org/10.3390/molecules26175159
2. K. Hemanth, K. Lakshmanan, K. Rajagopal, G. Byran, *Rasayan Journal of Chemistry*, **15(02),** 1573(2022), https://doi.org/10.31788/RJC.2022.1526443

3. M. Moradi, A. Mousavi, E. Reznickova, F. Paytm, M. Perina, V. Vojackova, L. Firozpur, R. Jorda, J. Gruz, Z. Emamgholipour, S. Esmaeil Sadat-Ebrahimi, V. Krystof, A. Foroumadi, *European Journal of Medicinal Chemistry*, **280(15)**, 116962(2024), https://doi.org/10.1016/j.ejmech.2024.116962
4. D. Kumar, H. Kumar, V. Kumar, A. Deep, A. Sharma, *Medicine in Drug Discovery*, **17**, 100150(2023), https://doi.org/10.1016/j.medidd.2022.100150
5. X-Y, Liab, D-P Wang, S. Li, W-H Xue, X-H Qian , K-L Liu, Y-H Li, Q-Q Lin, G. Dong, F-H Meng, L-Y Jian, *Bioorganic Chemistry*, **119**, 105469(2022), https://doi.org/10.1016/j.bioorg.2021.105469
6. E. Doaa, A. Rahman, K. O. Mohamed, *Der Pharma Chemica*, **6(1)**, 323(2014).
7. Jalal H Abdullah, Tawfeek Ahmed Ali Yahya, Abd-Hafiz Al-Gohrafi, *European Journal of Pharmaceutical and Medical Research,* **7(9)**, 87(2020)
8. S. Jayaraj, K. Hemalatha, *Future Journal of Pharmaceutical Sciences*, **10**,149(2024).
9. S. C. Khadsea, D. A. Nikhil, S. D. Krushna, M.D. Ashish, R.P. Vikas, K.L. Deepak, U.G. Vinod, *Journal of Molecular Structure*, **1222(15)**,128916(2020), https://doi.org/10.1016/j.molstruc.2020.128916
10. M. Asif, Ch. Asthana, *International Journal of Chem Tech Research*, **1(4)**, 1200(2009)
11. M. M. Burbuliene, V. Jakub Kiene, G. Mekuskiene, E. Udrenaite, R. Smicius, P. Valinilavicius, *Chem Inform,* **36(9)**, (2005), https://doi.org/10.1002/chin.200509149
12. W. W. Wardakhan, N.E. Nahed, El-Syed, *Phosphorus, Sulfur, Silicon and Related Elements*, **184(3)**, 790(2009), https://doi.org/10.1080/10426500802274534
13. T. A. Farghaly, M. A Abdallah, M. R. A. Aziz, *Molecules*,**17(12)**, 14625(2012), https://doi.org/10.3390/molecules171214625
14. T. A. Farghaly, M. A. Abdallah, Z. A. Muhammad, *Molecules*, **16**, 10420(2011), doi:10.3390/molecules161210420
15. B. Chandrakant, K. A. Joshi, *International Journal of Chem Tech Research*, **4(4)**, 1758(2012)
16. Ch. Mahavir, S. Anil Kumar, T. Vijay, *Medicinal Chemistry Research*, **23**, 3049(2014), https://doi.org/10.1007/s00044-013-0890-z
17. H. M. Pallavi, H. A. Fares, H. K. Vivek, K. Hussein, A. K. Shaukath, *Journal of Molecular Structure*, **1292**, 136126(2023), https://doi.org/10.1016/j.molstruc.2023.136126
18. L. Vicente, P.C. Mauricio, C. J. Stella, S. C. Igor dos, D. S. Luiz Felipe, A. R. S. dos Santos, S. Ana Lúcia, Rodrigues, R. C. Dutra, A. L. Dafre, *Behavioural Brain Research*, **320(1)**, 365(2017), https://doi.org/10.1016/j.bbr.2016.11.007
19. S. Kasim. H. Hmood, *Archtneetipalliives,* **32(1)**, (2021)
20. S. El-Feky, H. A. El-Fattah, Osman NA, Imran M., Zedan MN, *Journal of Chemical and Pharmaceutical Research*, **7(7)**, 1154(2015).
21. Al-Saad HN, Kubba AAR, Al-Bayati I.R. 2019, *Oriental Journal of Chemistry*, **35(2)**, 829(2019), http://dx.doi.org/10.13005/ojc/350246
22. M. N. Koopaeia., M. Almasirada., S. Ghasemi-Nirib, *Iran Journal of Pharmaceutical Research*,**12(4)**, 721(2013)
23. N. S. El-Gohary M. I. Shaaban, *European Journal of Medicinal Chemistry*, **63**, 185(2013), https://doi.org/10.1016/j.ejmech.2013.02.010
24. N. A. Abdelriheem, Y. H. Zaki, A. O. Abdelhamid, *Chemistry Central Journal*, **11**, Article 53(2017), https://doi.org/10.1186/s13065-017-0282-4
25. P. V. Zadorozhnii, V. V. Kiselev, I. O. Pokotylo, O. V. Okhtina, A. V. Kharchenko, *Heterocyclic Communications,* **24(5)**, 273(2018)
26. O. Ahmed, *Monatshefte für Chemie - Chemical Monthly*, **138**, 989(2007) https://doi.org/10.1007/s00706-007-0703-5
27. J. Cossy, C. P. Grosdemange, *Tetrahedron Letters*, **30(21)**, 2771(1989), https://doi.org/10.1016/S0040-4039(00)99121-4
28. G. Nicolas, M. Raed, Al-Zoubi and G. H. Dennis, *Journal of Organic Chemistry*, **77**, 8386(2012), https://doi.org/10.1021/jo3013258
29. P. V. Ramachandran, H. J. Hamann, *Organic Letters*, **23**, 2938(2021), https://doi.org/10.1021/acs.orglett.1c00591
30. B. Swetha, E. Chetankumar, C. Srinivasulu, V. V. Sureshbabu, *Synthesis*, **56**, 1476(2024), https://doi.org/10.1055/s-0043-1763675
31. D. Chen, L. Xu, B. Ren, Z. Wang, C. Liu, *Organic Letters*, **25**, 4571(2023), https://doi.org/10.1021/acs.orglett.3c01598
32. D. C. Braddock, D. L. Paul, Ben C. Rowley, P. David, T. Purnomo, G. Santhakumar, S. J. Fussell, *Organic Letters*, **20**, 950(2018), https://doi.org/10.1021/acs.orglett.7b03841

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