

SYNTHESIS OF NOVEL 2-(4-ALLYLPIPERAZIN-1-YL)-1-(1-ARYL-1*H*-TETRAZOL-5-YL)ETHANONE DERIVATIVES AS POTENTIAL ANTIMICROBIAL AGENTS

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ABSTRACT

A series of novel 2-(4-allylpiperazin-1-yl)-1-(1-aryl-1*H*-tetrazol-5-yl) etalons were synthesized with excellent yields by the reaction of 1-(1-aryl-1*H*-tetrazol-5-yl)-2-(piperazin-1-yl) ethanones with allyl bromide and one equivalent of triethylamine in acetonitrile under nitrogen atmosphere. Spectral data (FT-IR, ¹H NMR, ¹³C NMR, and HSQC) was used to characterize all produced substances and screened against antimicrobial activities. A few of the compounds were shown to be as potent as or more effective than conventional medicines.

Keywords: Tetrazole, Allyl piperazine, Antibacterial Activity

RASĀYAN J. Chem., Vol. 14, No.3, 2021

INTRODUCTION

Tetrazole and its derivatives have gotten a lot of attention as they have unusual structures and many medicinal values.¹⁻³ Tetrazole chemistry has many uses in medicine, biochemistry, and agriculture⁴, as well as a vast number of pharmaceutically significant tetrazolein incorporated medicines that have been FDA permitted.⁵⁻⁷ Tetrazole's therapeutic effectiveness stemmed from its capacity to operate as a bioequivalent (bioisostere) of the carboxylic acid group. As isosteres of the *cis*-amide bond of peptides, 1, 5-disubstituted tetrazoles can be employed.^{7,8} In medicinal chemistry, biphenyl tetrazole molecules figured prominently. Losartan was the first non-peptide AT₁ potent inhibitor, and the term "sartans" was invented.^{9,10} The biphenyl tetrazole unit is found in the majority of such molecules.¹¹ Each of these sartan medicines had a biphenyl segment with an acidic moiety coupled to a heteroaromatic or acyclic system with a methylene group as a structural characteristic. Antimicrobial, analgesic, antiviral, anti-inflammatory, and antihypertensive properties have been described for 5-substituted 1,2,3,4-tetrazoles (Fig.-1). For increasing therapeutic potential tetrazole, carboxylic acid and its acidic nature can be modified to enhance the medicinal potential attract the chemist to synthesized the modified tetrazole.

Losartan 1 is an angiotensin II receptor inhibitor that is primarily used to reduce hypertension. Cefamandole 2 is a broad-spectrum cephalosporin antibiotic of the 2nd generation. The formate ester cefamandole nafate, a prodrug given parenterally, is the therapeutically utilized version of cefamandole. Cefazolin 3 is a first-generation cephalosporin antibiotic also known as cefazoline or cephalazolin. Intramuscular injection (injection into a major muscle) or intravenous infusion are the most common methods of administration (intravenous fluid into a vein). Cefazolin is mainly used to treat bacterial skin infections. It may also be used to treat bacterial infections in the lungs, bones, joints, stomach, blood, heart valve, and urinary tract that are fairly severe. It is therapeutically efficient towards infections produced by Gram-positive bacteria such as *Staphylococci* and *Streptococci*. Angiotensin II receptor inhibitor candesartan four is typically used to cure hypertension. Piperazine and its N-substituted derivatives have a wide variety of activities, including antimicrobial¹²⁻¹⁶, anticancer¹⁷, anti-inflammatory¹⁸, antipsychotic¹⁹, CNS agent²⁰, CCKB/gastrin inhibitor²¹, melanocortin-4 inhibitor²², and Alzheimer's disease therapy.²³ Piperazine or its 1-methyl derivative skeleton is a vital part of some clinically valuable drugs such as Ciprofloxacin 5, Enoxacin 6, Ofloxacin 7, and

Levofloxacin 8 (Fig.-2), and it can demonstrate broad-spectrum effects on respiratory, urinary, gastrointestinal tracts, skin, and soft tissue infections triggered by the bacteria²⁴. This suggests that replacing the piperazine molecule with its 1-methyl counterpart has a significant effect on microbial activity. Furthermore, according to current literature²⁵, connecting N-substituted piperazine to an aryl or heteroaryl moiety through two carbon chains with a -keto group provides an added benefit in evoking an excellent biological activity.

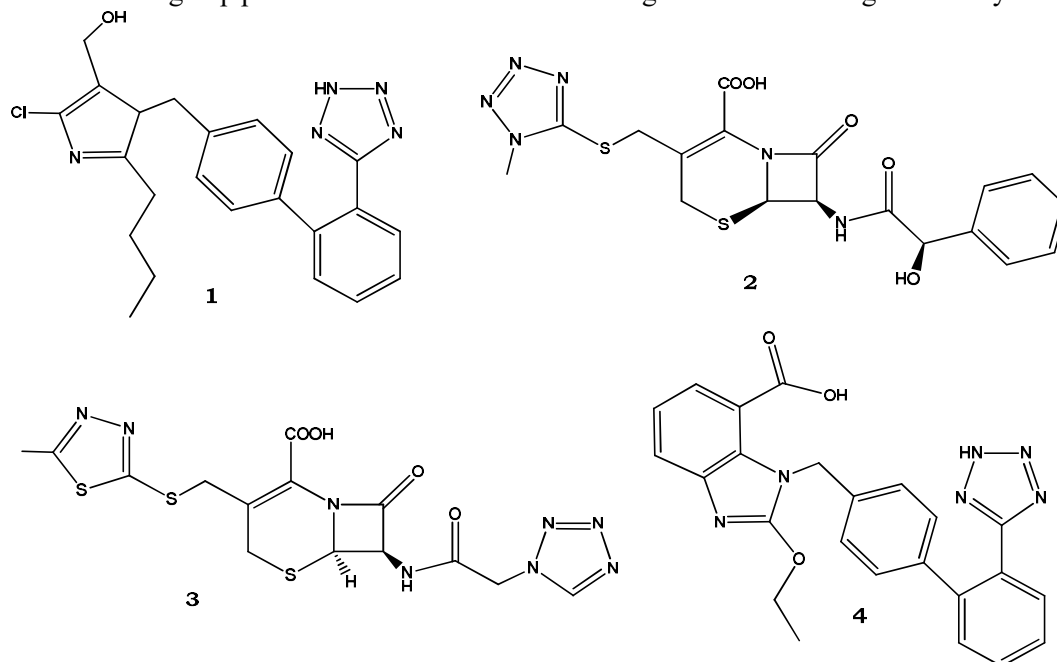


Fig.-1: Biologically Active Tetrazole Containing Drugs

EXPERIMENTAL

Material and Methods

All reagents and solvents were purchased commercially and utilized without additional purification. Melting points were measured in open capillary tubes using an Elchem Microprocessor-based DT equipment and were adjusted using benzoic acid. A Thermo Nicolet-Avatar-330 FT-IR spectrophotometer was used to generate the FT-IR spectra. On a Bruker 400 MHz spectrometer, NMR spectra were measured using TMS as the internal norm (chemical shifts δ in ppm). Mass spectra were documented on Applied Bio-system Mass Spectrometer using the Electron Spray Ionization technique. On silica gel (s.d.fine) preparative plates, thin-layered chromatography (TLC) was conducted. The iodine chamber was used to create the visualization. Silica gel (60-120 mesh) was used for column chromatography.

Representative Procedure for the Synthesis of 1-(1-aryl-1H-tetrazol-5-yl)-2-(piperazin-1-yl)ethanones 12 (a-g)

A combination of 2-chloro-1-(1-aryl-1H-tetrazol-5-yl)ethanone, piperazine, and triethylamine was placed in a round bottom flask containing acetonitrile (25 ml) and stirred at room temperature for 5-6 hours. TLC was used to track the reaction's progression. To get 1-(1-aryl-1H-tetrazol-5-yl)-2-(piperazin-1-yl)ethanones, ice used for cooling the reaction mixture, solid washed with the water and dried under vacuum. Finally, column chromatography was used to purify the crude product.

Representative Method for the Synthesis of 2-(4-allylpiperazin-1-yl)-1-(1-aryl-1H-tetrazol-5-yl)ethanone 13 (a-g)

A mixture of 1-(1-aryl-1H-tetrazol-5-yl)-2-(piperazin-1-yl)ethanone 12 (a-g) and allylbromide was placed in a round bottom flask containing acetonitrile (25 ml) and refluxed at room temperature for 5-6 hours. Reaction progress was checked by the TLC. The reaction mixture was cooled down by ice cubes and filtered solid after the finishing of the reaction then is washed with water and dried under a vacuum to

get the novel 2-(4-allylpiperazin-1-yl)-1-(1-aryl-1*H*-tetrazol-5-yl)ethanone **13(a-g)** (Table-1). In the end, column chromatography was used to purify the crude product.

Table-1: Synthesis of 2-(4-allylpiperazin-1-yl)-1-(1-aryl-1*H*-tetrazol-5-yl)ethanones, 13(a-g)

Compound	a	b	c	d	e	f	g
R	H	CH ₃	OCH ₃	Cl	F	Br	NO ₂

2-(4-allylpiperazin-1-yl)-1-(1-phenyl-1*H*-tetrazol-5-yl)ethanone (13a)

Yield: 92%; M.Pt: 240-242; IR Values: 3428-3030 (Aromatic C-H), 2923-2849 (Aliphatic C-H), 1655 (Carbonyl group >C=O), 1571 (Tetrazole >C=N); ¹H NMR (400 MHz, CDCl₃) δ_H: 2.43 & 2.70 (s, 8H, Piperazine ring protons), 3.16 (s, 2H, Methylene protons), 3.38 (s, 2H, Methylene protons), 5.00 (s, 2H, Allylic CH₂ protons), 5.60 (s, 1H, AllylicMethine proton), 7.07 (t, 1H, *J* = 7.8 Hz, ArH), 7.33 (t, 2H, *J* = 7.8 Hz, ArH), 7.51 (d, 2H, *J* = 8 Hz, ArH); ¹³C NMR (100 MHz, CDCl₃) δ_C: 45.19 & 53.45 (Piperazine ring carbons), 61.25 (Methylene carbons), 58.75 (Allylic CH₂ carbon), 109.20 (AllylicMethine carbon), 123.80-132.19 (Aromatic carbons), 172.58 (>C=O carbon).

2-(4-allylpiperazin-1-yl)-1-(1-(*p*-tolyl)-1*H*-tetrazol-5-yl)ethanone (13b)

Yield: 84 %; M.Pt: 245-246; IR Values: 3430-3037 (Aromatic C-H), 2919-2854 (Aliphatic C-H), 1655 (Carbonyl group >C=O), 1564 (Tetrazole >C=N); ¹H NMR (400 MHz, CDCl₃) δ_H: 2.26 (s, 3H, CH₃), 2.50 & 2.70 (s, 8H, Piperazine ring protons), 3.15 (s, 2H, Methylene protons), 3.34 (s, 2H, Methylene protons), 4.81 (s, 2H, Allylic CH₂ protons), 5.25 (s, 1H, AllylicMethine proton), 7.13 (d, 2H, *J* = 7.6 Hz, ArH), 7.39 (d, 2H, *J* = 7.6 Hz, ArH); ¹³C NMR (100 MHz, CDCl₃) δ_C: 20.38 (CH₃), 45.38 & 53.72 (Piperazine ring carbons), 61.36 (Methylene carbons), 57.32 (Allylic CH₂ carbon), 108.72 (AllylicMethine carbon), 119.63-129.34 (Aromatic carbons), 172.54 (>C=O carbon).

2-(4-allylpiperazin-1-yl)-1-(1-(4-methoxyphenyl)-1*H*-tetrazol-5-yl)ethanone (13c)

Yield: 92 %; M.Pt: 248-250; IR Values: 3441-3315 (Aromatic C-H), 2922-2854 (Aliphatic C-H), 1656 (Carbonyl group >C=O), 1555 (Tetrazole >C=N); ¹H NMR (400 MHz, CDCl₃) δ_H: 2.42 & 2.70 (s, 8H, Piperazine ring protons), 3.15 (s, 2H, Methylene protons), 3.31 (s, 2H, Methylene protons), 3.73 (s, 3H, OCH₃), 4.51 (s, 2H, Allylic CH₂ protons), 5.15 (s, 1H, AllylicMethine proton), 6.90 (d, 2H, *J* = 8 Hz, ArH), 7.42 (d, 2H, *J* = 8 Hz, ArH); ¹³C NMR (100 MHz, CDCl₃) δ_C: 45.42 & 52.36 (Piperazine ring carbons), 53.75 (OCH₃), 61.36 (Methylene carbons), 55.14 (Allylic CH₂ carbon), 106.04 (AllylicMethine carbon), 114.08-121.41 (Aromatic carbons), 172.45 (>C=O carbon).

2-(4-allylpiperazin-1-yl)-1-(1-(4-chlorophenyl)-1*H*-tetrazol-5-yl)ethanone (13d)

Yield: 75 %; M.Pt: 249-251; IR Values: 3428-3041 (Aromatic C-H), 2923-2854 (Aliphatic C-H), 1656 (Carbonyl group >C=O), 1551 (Tetrazole >C=N); ¹H NMR (400 MHz, CDCl₃) δ_H: 2.20 & 2.70 (s, 8H, Piperazine ring protons), 3.16 (s, 2H, Methylene protons), 3.38 (s, 2H, Methylene protons), 4.40 (s, 2H, Allylic CH₂ protons), 5.00 (s, 1H, AllylicMethine proton), 7.21 (d, 2H, *J* = 8.2 Hz, ArH), 7.43 (d, 2H, *J* = 8.2 Hz, ArH); ¹³C NMR (100 MHz, CDCl₃) δ_C: 45.43 & 53.75 (Piperazine ring carbons), 62.02 (Methylene carbons), 58.04 (Allylic CH₂ carbon), 117.06 (AllylicMethine carbon), 121.78-132.05 (Aromatic carbons), 172.06 (>C=O carbon).

2-(4-allylpiperazin-1-yl)-1-(1-(4-fluorophenyl)-1*H*-tetrazol-5-yl)ethanone (13e)

Yield: 81 %; M.Pt: 225-228; IR Values: 3429-3035 (Aromatic C-H), 2923-2854 (Aliphatic C-H), 1656 (Carbonyl group >C=O), 1578 (Tetrazole >C=N); ¹H NMR (400 MHz, CDCl₃) δ_H: 2.80 & 2.93 (s, 8H, Piperazine ring protons), 3.17 (s, 2H, Methylene protons), 3.40 (s, 2H, Methylene protons), 4.40 (s, 2H, Allylic CH₂ protons), 5.03 (s, 1H, AllylicMethine proton), 6.70 (d, 2H, *J* = 8.6 Hz, ArH), 7.12 (d, 2H, *J* = 8.6 Hz, ArH); ¹³C NMR (100 MHz, CDCl₃) δ_C: 45.43 & 53.75 (Piperazine ring carbons), 62.02 (Methylene carbons), 58.04 (Allylic CH₂ carbon), 117.06 (AllylicMethine carbon), 121.78-132.05 (Aromatic carbons), 172.06 (>C=O carbon).

2-(4-allylpiperazin-1-yl)-1-(1-(4-bromophenyl)-1H-tetrazol-5-yl)ethanone (13f)

Yield: 85 %; M.Pt: 256-260; IR Values: 3428-3063 (Aromatic C-H), 2923-2854 (Aliphatic C-H), 1655 (Carbonyl group >C=O), 1551 (Tetrazole >C=N); ¹H NMR (400 MHz, CDCl₃) δ_H: 2.50 & 2.76 (s, 8H, Piperazine ring protons), 3.20 (s, 2H, Methylene protons), 3.82 (s, 2H, Methylene protons), 4.66 (s, 2H, Allylic CH₂ protons), 5.19 (s, 1H, AllylicMethine proton), 7.58 (d, 2H, *J* = 8 Hz, ArH), 7.69 (d, 2H, *J* = 8 Hz, ArH); ¹³C NMR (100 MHz, CDCl₃) δ_C: 45.19 & 53.45 (Piperazine ring carbons), 61.27 (Methylene carbons), 58.75 (Allylic CH₂ carbon), 108.64 (AllylicMethine carbon), 119.28-128.99 (Aromatic carbons), 173.58 (>C=O carbon).

2-(4-allylpiperazin-1-yl)-1-(1-(4-nitrophenyl)-1H-tetrazol-5-yl)ethanone (13g)

Yield: 80 %; M.Pt: 264-266; IR Values: 3438-3030 (Aromatic C-H), 2921-2860 (Aliphatic C-H), 1655 (Carbonyl group >C=O), 1555 (Tetrazole >C=N); ¹H NMR (400 MHz, CDCl₃) δ_H: 2.50 & 2.76 (s, 8H, Piperazine ring protons), 3.20 (s, 2H, Methylene protons), 3.40 (s, 2H, Methylene protons), 4.50 (s, 2H, Allylic CH₂ protons), 5.17 (s, 1H, AllylicMethine proton), 6.70 (d, 2H, *J* = 8.6 Hz, ArH), 7.12 (d, 2H, *J* = 8.6 Hz, ArH); ¹³C NMR (100 MHz, CDCl₃) δ_C: 43.10 & 55.16 (Piperazine ring carbons), 68.87 (Methylene carbons), 63.02 (Allylic CH₂ carbon), 108.10 (AllylicMethine carbon), 121.61-130.14 (Aromatic carbons), 168.52 (>C=O carbon).

Antimicrobial Studies

All bacteria were cultivated in separate nutrient broth. A sterile swab was used to transfer the bacteria in Petri plate containing nutrient agar media. Tested compounds were mixed in water: DMSO (8:2) in the concentration of 10 mg/ml. This solution was maintained as a stock solution. Various concentrations (6.25, 12.5, 50, 100, and 200ppm) were diluted and prepared from the stock solution. 5 mm diameter sterile disc soaked with three different concentrations and these discs were placed on seeded agar plates. The inhibitory zone was measured, excluding the diameter of the 5mm paper disc, in these Petri plates, which were incubated at 37°C. The control discs were made using sterile water. The inhibitory actions were compared to those of Ciprofloxacin, an antibacterial medication, and Fluconazole, an antifungal agent.

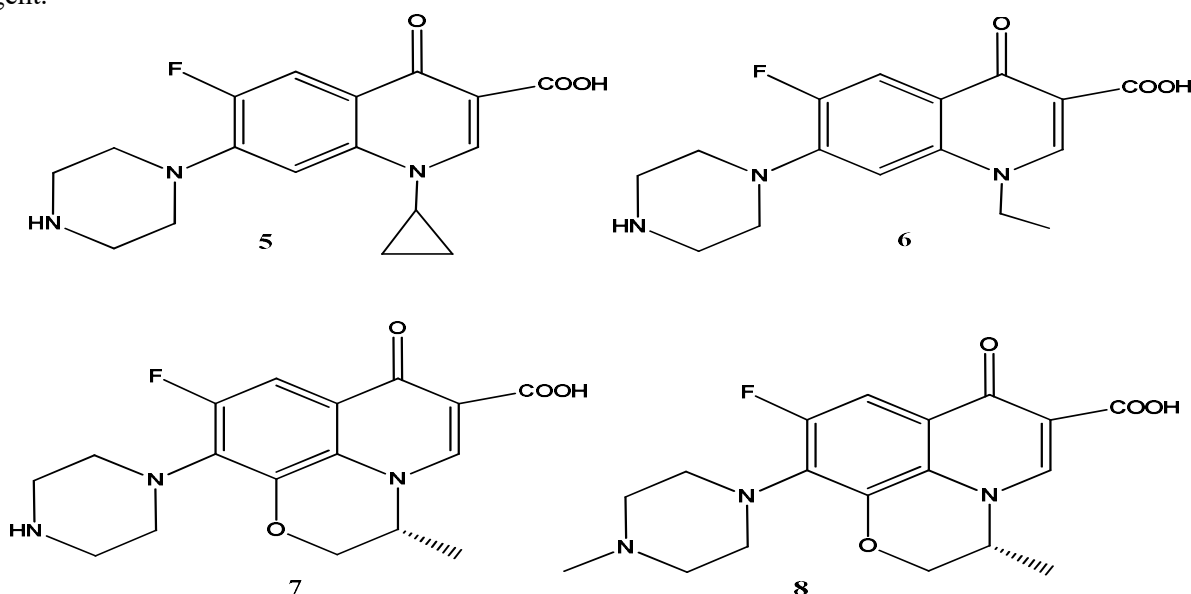
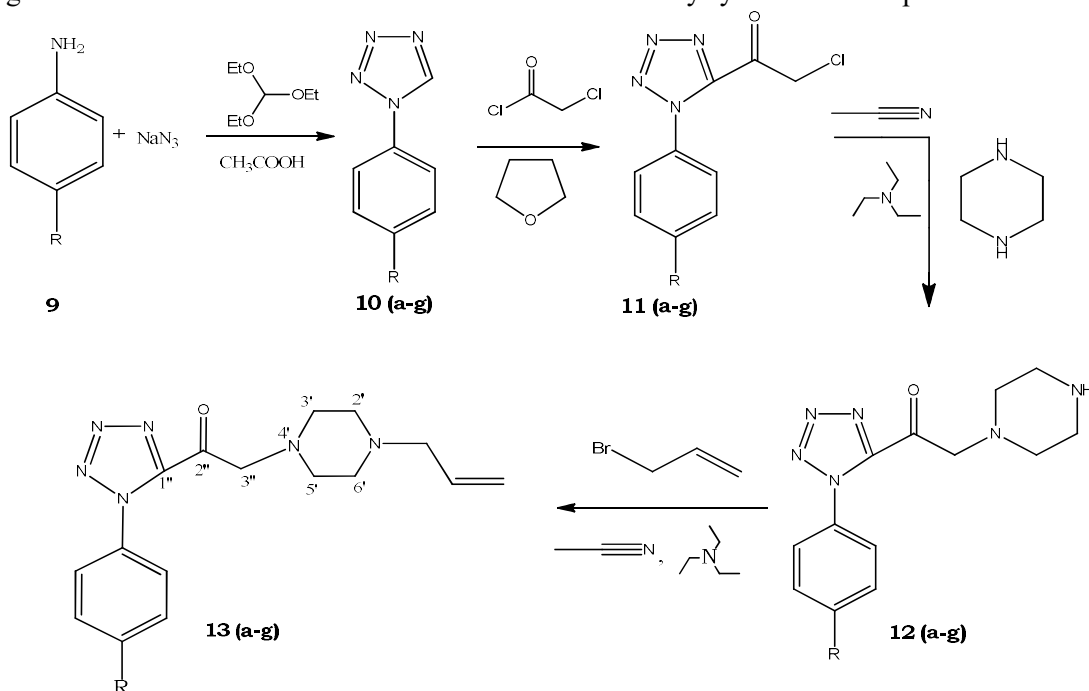


Fig.-2: Biologically Active Piperazine Containing Drugs

RESULTS AND DISCUSSION

2-(4-allylpiperazin-1-yl)-1-(1-aryl-1H-tetrazol-5-yl)ethanone derivatives 13(a-g) were synthesized with outstanding yields by the reaction of aryl anilines with sodium azide and triethyl orthoformate in acetic acid results in the creation of tetrazole compounds 10(a-g). Following a reaction with chloroacetyl

chloride, 2-chloro-1-(1-aryl-1*H*-tetrazol-5-yl)ethanone **11** (a-g) was formed. Which further reacts with piperazine in acetonitrile to get 1-(1-aryl-1*H*-tetrazol-5-yl)-2-(piperazin-1-yl)ethanone. Which further reacts with allyl bromide and one equivalent of triethylamine in acetonitrile under nitrogen atmosphere to give the desired products **13** (a-g) (Scheme-1). FT-IR, ¹H NMR, ¹³C NMR, HSQC, and mass spectrum investigations were used to confirm the structures of all the newly synthesized compounds.



Scheme-1: Synthesis of 2-(4-allylpiperazin-1-yl)-1-(1-aryl-1*H*-tetrazol-5-yl)ethanones

Compound **13a** was taken as the representative example. The formation of compound **13a** was apparent from the following spectral characterization results discussed below.

FT-IR Analysis of 2-(4-allylpiperazin-1-yl)-1-(1-phenyl-1*H*-tetrazol-5-yl)ethanone(**13a**)

In the IR spectrum of compound **13a**, the measured absorptions in the range of 3428-3030 cm⁻¹ were the reason for aromatic C-H stretching frequency. A significant absorption was detected at 1655 cm⁻¹ because of C=O stretching frequency. The detected absorptions in the range of 2923-2849 cm⁻¹ were because of aliphatic C-H stretching frequency. A strong absorption observed at 1592 cm⁻¹ was due to C=N stretching frequency. The absorption observed in the range of 1571 cm⁻¹ was due to C-N stretching frequency. The presence of C=O stretching frequency of carboxylic acid group indicates the formation of naphthyridine carboxylic acid group, and hence the product is 2-(4-allylpiperazin-1-yl)-1-(1-aryl-1*H*-tetrazol-5-yl)ethanone(**13a**). FT-IR data for all the synthesized compounds **13** (a-g) were given in the experimental section.

¹H NMR Analysis of 2-(4-allylpiperazin-1-yl)-1-(1-phenyl-1*H*-tetrazol-5-yl)ethanone(**13a**)

In the ¹H-NMR spectrum of 2-(4-allylpiperazin-1-yl)-1-(1-phenyl-1*H*-tetrazol-5-yl)ethanone(**13a**), the piperazine H3' and H5' protons appeared as a singlet at 2.43 ppm. The piperazine H2' and H6' protons appeared as a sharp singlet at 2.70-2.71 ppm. The methylene H3'' proton signal appeared as a sharp singlet at 3.17 ppm. The aromatic protons were observed in the range of 7.07-7.52 ppm. The allylic methylene protons appeared at 5.00 ppm, and the methine proton appeared as a sharp singlet at 5.63 ppm. Hence the product is 2-(4-allylpiperazin-1-yl)-1-(1-aryl-1*H*-tetrazol-5-yl)ethanone(**13a**). The ¹H NMR data for all the synthesized compounds **13** (a-g) were given in the experimental section.

¹³C NMR Analysis of 2-(4-allylpiperazin-1-yl)-1-(1-phenyl-1*H*-tetrazol-5-yl)ethanone(**13a**)

In the ¹³C-NMR spectrum of 2-(4-allylpiperazin-1-yl)-1-(1-phenyl-1*H*-tetrazol-5-yl)ethanone (**13a**), the piperazine group methylene carbons C2', C6' and C3', C5' appeared at 45.19 and 53.43 ppm

respectively. Methylene carbon of chloro ethanone group C3'' appeared at 62.27 ppm. Methylene carbons of allylic group C3'' appeared at 58.57 ppm respectively. The methine carbon of allylic group appeared at 109.29 ppm. The range 119.64-128.99 ppm was found for the aromatic carbons. The tetrazole *ipso* carbon appeared at 150.23 ppm. The carbonyl group signal of C2'' appeared at 172.58 pp. Hence, the product is 2-(4-allylpiperazin-1-yl)-1-(1-aryl-1*H*-tetrazol-5-yl)ethanone (**13a**). The ¹³C NMR data for all the synthesized compounds **13 (a-g)** were given in the experimental section.

HSQC Spectral Analysis of 2-(4-allylpiperazin-1-yl)-1-(1-phenyl-1*H*-tetrazol-5-yl)ethanone (**13a**)

To confirm the NMR (¹H and ¹³C) assignments, HSQC spectrum was recorded for (**13a**). In the HSQC spectrum, 172.58 ppm of the carbon signal shows no connection with any proton signals, which refers to it is produced by the carbonyl group of C2'' carbon. The proton signal at 2.43 ppm corresponds with the carbon signal at 45.19 ppm, indicating that the carbon signal at 45.19 ppm is due to the piperazine ring's C2' and C6' carbon, while the proton signals at 2.74 ppm are because of the piperazine ring's H2' and H6' connected methylene protons. The carbon signal 53.45 ppm correlated with the proton signal at 2.70-2.71 ppm, this observation clearly shows the carbon signal at 53.45 ppm is due to C3' and C5' carbons of piperazine ring and the proton signal at 2.70-2.71 ppm. The carbon resonance at 62.27 ppm correlated with the proton signal at 3.16 ppm, and this correlation confirms the carbon signal at 62.27 ppm is due to the C3'' carbon and the proton signal of chloro ethanone group at 3.16 ppm was due to the H3'' proton of the ethanone moiety. The carbon signal 58.57 ppm correlates signal at 5.00 ppm, this observation clearly shows the carbon signal at 58.57 ppm was due to methylene carbon of allylic group and the proton signal at 5.00 ppm. The proton signals at 7.07-7.52 ppm corresponded with the carbon signal at 119.64-128.99 ppm, indicating that the phenyl ring's aromatic carbons were responsible for the carbon resonance at 119.64-128.99 ppm. The carbon resonance at 119.60 ppm correlated with the proton signal at 8.08-8.12 ppm, and this correlation confirmed that the carbon signal at 109.29 ppm was due to the methine carbon of allylic group, and the proton signal at 5.60 ppm was due to the allylic methine proton. The ¹³C resonance at 150.23 ppm did not correlate with any of the protons, from this observation, the carbon signal at 150.23 ppm was due to the *ipso* carbon of the tetrazole ring. Hence the product is 2-(4-allylpiperazin-1-yl)-1-(1-aryl-1*H*-tetrazol-5-yl)ethanone (**13a**).

The addition of one proton (n+1) results in a molecular ion peak at m/z 313 (M+H⁺) in the ESI mass spectra of compound (**13a**), this is in line with the compound's predicted molecular mass (312).

In vitro Antimicrobial Activities of 2-(4-allylpiperazin-1-yl)-1-(1-aryl-1*H*-tetrazol-5-yl)ethanone derivatives **13 (a-g)**

We're looking for new antibacterial agents as part of our research²⁶⁻²⁹, **13 (a-g)** compounds were *in vitro* tested against the gram(+)ve and gram(-)ve bacterial strains. Table-2 depicted the inhibitory zones that were identified. The compounds' inhibitory activity was found to be equivalent to or higher than that of conventional medications in the inhibition zones.

The MIC values of compounds **13e** and **13g** displayed the highest inhibition activity (12.5 and 25 µg/mL) against *Salmonella typhi* due to fluoro and nitro groups. Compounds **13b** and **13g** inhibited the growth against *Klebsiella pneumonia* due to methyl and nitro groups. Electron-withdrawing substituents such as chloro, fluoro, and nitro substituted compounds **13c** and **13g** had outstanding antibacterial properties.

Because of the nitro group, compound **13g** demonstrated the most significant inhibitory effect (6.25 g/mL) against *Candida albicans*, according to the antifungal data in Table-3. The addition of halogen functionality to the para position of phenyl groups in compounds **13e** and **13g** showed moderate inhibitory efficacy against all of the fungal species tested, with MICs ranging from 6.25 to 100 g/mL.

Compound **13g** shown the highest antifungal activity against *Candida albicans* because of the nitro substitution. A change of *para* proton in **13a** compound by fluoro and nitro group i.e., compounds **13g** and **13c** showed modest activity against the whole tested fungal strains. Peak inhibition was spotted against *Candida albicans* (6.25-25 µg/mL).

Table-2: *In vitro* Antibacterial Activities of 2-(4-allylpiperazin-1-yl)-1-(1-aryl-1*H*-tetrazol-5-yl)ethanone Derivatives, 13(a-g)

Entry	Minimum Inhibitory Concentration (MIC) in µg/mL					
	<i>S. aureus</i>	<i>B. subtilis</i>	<i>S. typhi</i>	<i>V. cholerae</i>	<i>E.coli</i>	<i>K. pneumonia</i>
13a	100	100	100	-	100	100
13b	100	50	50	50	25	-
13c	-	100	100	100	50	50
13d	50	-	50	50	-	100
13e	100	100	25	-	100	100
13f	-	50	100	100	50	50
13g	50	100	12.5	100	25	-

Ciprofloxacin is used as a reference standard

Table-3: *In vitro* Antifungal Activities of 2-(4-allylpiperazin-1-yl)-1-(1-aryl-1*H*-tetrazol-5-yl)ethanone Derivatives, 13(a-g)

Entry	Minimum Inhibitory Concentration (MIC) in µg/mL					
	<i>Aspergillus flavus</i>	<i>Aspergillus niger</i>	<i>Candida albicans</i>	<i>Mucor</i>	<i>Candida 6</i>	<i>Rhizopus</i>
13a	100	50	100	50	50	50
13b	50	100	25	100	100	100
13c	100	50	50	-	50	50
13d	-	100	25	25	25	-
13e	50	-	25	-	100	50
13f	100	50	50	25	-	50
13g	25	12.5	6.25	25	25	-

Fluconazole is used as a reference standard.

‘—’ no inhibition even at a higher concentration of 200 µg/mL.

CONCLUSION

A series of 2-(4-allylpiperazin-1-yl)-1-(1-aryl-1*H*-tetrazol-5-yl) ethanone **13(a-g)** have been synthesized. Melting points, FT-IR, ¹H, ¹³C NMR, HSQC spectra, and mass spectral analyses were used to verify the structures of the synthesized compounds 13(a-g). Antimicrobial activity screened against the all-synthesized compounds by utilizing the disc diffusion method. All the compounds were shown good to a moderate zone of inhibitions against the tested strains, Compounds containing fluoro, chloro, and nitro substituents were exhibited a high zone of inhibitions against bacterial and fungal strains.

ACKNOWLEDGEMENT

The authors are thankful to the administration, Thanthai Hans Roever College, Perambalur, India, for providing facilities to carry research work.

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[RJC-6303/2020]