ORIGINAL ARTICLE

A C G publications

Org. Commun. 8:2 (2014) 24-35

organic communications

Microwave assisted synthesis and antimicrobial activity of novel 1-[1/2-(1-Benzyl-1*H*-[1,2,3]triazol-4-ylmethoxy)-naphthalen-2/1-yl]-3-(1-phenyl-3-aryl-1*H*-pyrazol-4-yl)-propenones

Dongamanti Ashok[*1], Arram Ganesh[1], Bommidi Vijaya Lakshmi[1], Sidda Ravi[1] and Banoth Ramesh[2]

[1]*Department of Chemistry, Osmania University, Hyderabad, India*
[2]*Department of Chemistry, Government degree & P.G. College, Siddipet, India*

(Received October 1, 2013; Revised December 10, 2013; Accepted March 12, 2014)

Abstract: A series of novel 1-[1/2-(1-Benzyl-1*H*-[1,2,3]triazol-4-ylmethoxy)-naphthalen-2/1-yl]-3-(1-phenyl-3-aryl-1*H*-pyrazol-4-yl)-propenones were design and synthesized by Click reaction followed by Claisen-Schmidt condensation under microwave irradiation and conventional heating methods. The structures of newly synthesized compounds have been established on the basis of elemental analysis, IR, ^{1}H & ^{13}C NMR and mass spectral data. All the compounds were screened for their antimicrobial activity.

Keywords: 1,2,3-triazole; pyrazoles; chalcones; antimicrobial activity; microwave irradiation.

1. Introduction

The treatment of microbial infections still remains an important and challenging therapeutic problem because of factors that include emerging infectious diseases and the increasing number of multidrug-resistant microbial pathogens[1,2]. In spite of the large number of antibiotics and chemotherapeutics available for medical use, the emergence of old and new antibiotic resistant bacterial and fungal strains in the last decades constitutes a substantial need for new classes of antimicrobial agents[3]. In view of wide spread of the resistant strains of microorganism there is an urgent need for the development of new antimicrobial agents to treat the patients infected with multidrug-resistant bacteria and fungal[4]. Heterocyclic molecules can act as highly functionalized scaffolds and medicinally useful molecules[5]. Electron-rich nitrogen heterocyclics play an important role in diverse biological activities[6]. The heterocyclic scaffolds such as pyrazoles and triazoles are having wide range of pharmacological applications. There are very few 1,2,3-triazoles-containing molecules on the market and which are in the last stage of clinical trials[7]. Rufinamide (it is marketed under the brand name Banzel) is an anticonvulsant. It is used in combination with other medication and therapy to treat Lennox-Gastaut syndrome (LGS) and various other seizure disorders[8-10]and other 1,2,3-triazoles include Carboxyamidotriazole (CAI) used in chemotherapy[11], *tert*-butyldimethylsilylspiroaminooxathiole-dioxide (known as TSAO) in reverse transcriptase[12], Tazobactum and Cefatrizine are β-lactum antibiotic agents[13-14] (**Figure 1**).

[*] Corresponding author: E-mail: ashokdou@gmail.com

The article was published by Academy of Chemistry of Globe Publications
www.acgpubs.org/OC/index.htm © Published 06/01/2015 EISSN:1307-6175

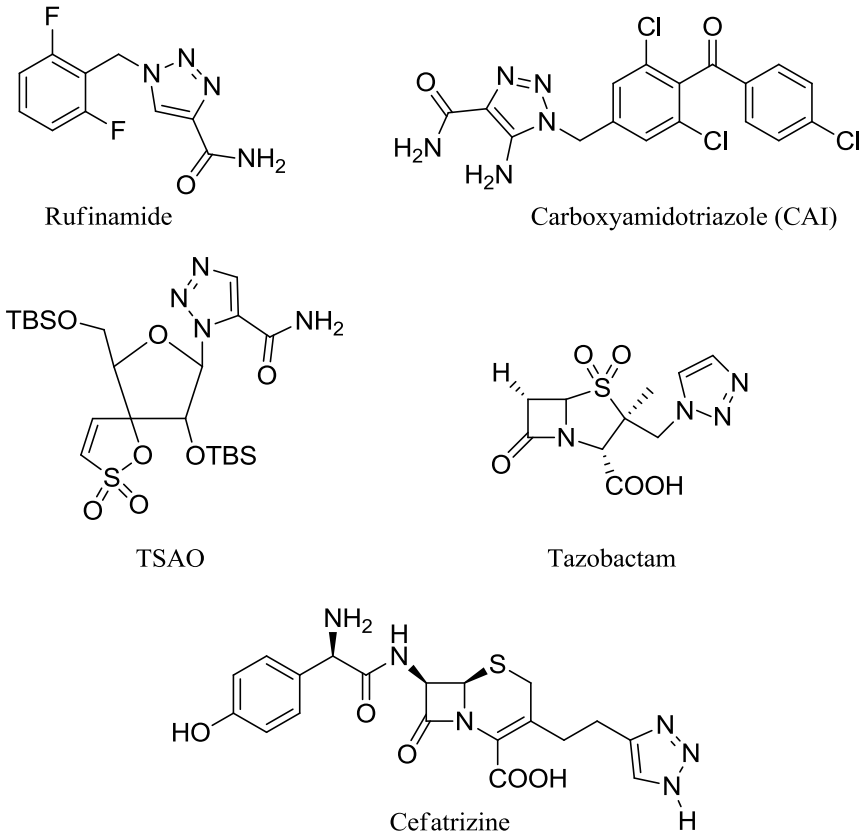

Figure 1. Representative examples of Drugs having 1,2,3-triazole moiety.

Pyrazole derivatives have been reported in the literature to exhibit various pharmacological activities such as antimicrobial[15], anti-inflammatory[16], antitubercular[17], antitumor[18], antiangiogensis[19], antiparasitic[20], antiviral[21] and also possessing analgesic and anxiolytic[22] activities. On the other hand triazole derivatives are known to exhibit various biological activities such as antimicrobial[23], anti-tubercular[24], anticancer[25], anticonvulsant[26], anti-inflammatory, analgesic[27] and antiviral[28]. It was observed that, pyrazole and triazole rings present in the same molecule could be convenient models for investigation of their antimicrobial activity. Hence, we herein report the synthesis of novel 1-[1/2-(1-Benzyl-1*H*-[1,2,3]triazol-4-ylmethoxy)-naphthalen-2/1-yl]-3-(1-phenyl-3-aryl-*H*-pyrazol-4-yl) propenones **(5a-g & 9a-g)**.

2. Results and discussions

The synthetic route of the proposed compounds illustrated in **Figure 2** & **3**. The compound propargylethers (**2/7**) were synthesized by reacting 1-(1-Hydroxy-naphthalen-2-yl)-ethanone (**1**) and 1-(2-Hydroxy-naphthalen-1-yl)-ethanone (**6**) with propargylbromide in the presence of anhydrous K_2CO_3 in dry acetone. 1,4-disubstituted 1,2,3-triazoles (**3/8**) were synthesized by reacting benzylazide and propargylethers in the presence of $CuSO_4$ $5H_2O$ and Sodiumascorbate in *tert*-butanol/water (1:1, v/v) and CuI in DMF or THF under both conventional stirring and microwave irradiation methods. Reaction of triazoles (**3/8**) with 1-Phenyl-3-aryl-1*H*-pyrazole-4-carbaldehydes **(4a-g)** in the presence of alkaline conditions under conventional heating and microwave irradiation yielded 1-[1/2-(1-Benzyl-1*H*-[1,2,3]triazol-4-ylmethoxy)-naphthalen-2/1-yl]-3-(1-phenyl-3-aryl-1*H*-pyrazol-4-yl)-propenones **(5a-g & 9a-g)**. The structures of the compound have been determined by spectroscopic techniques such as IR, ^{1}H NMR, ^{13}C NMR, Mass and elemental analysis. On the other hand, microwave irradiation method has gained the attention of chemists during the last decades[29] due to its unique advantages such as shorter reaction times, cleaner reaction products, higher yields and better selectivities, being a valuable alternative to accomplish more efficient syntheses of a variety of organic compounds with a considerable simplicity of operation and milder reaction conditions (**Table 1**).

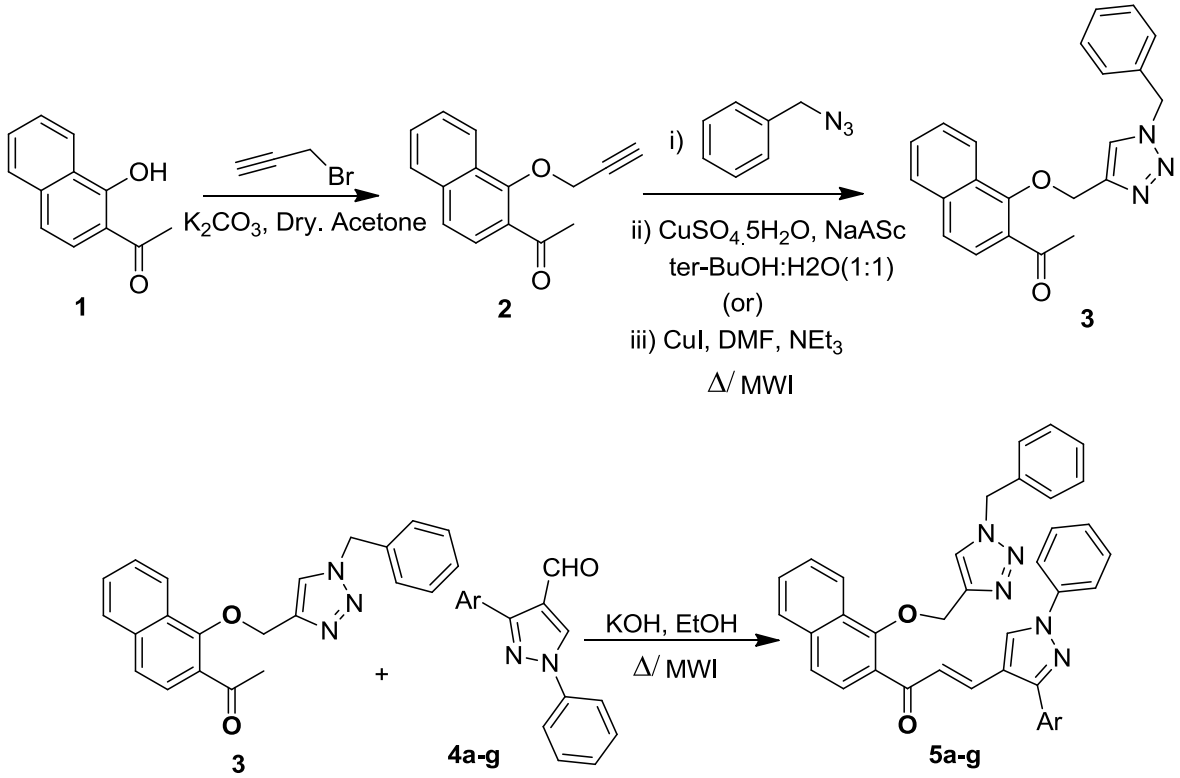

Figure 2. Step 1. Synthesis of 1-[1-(1-Benzyl-1*H*-[1,2,3]triazol-4-ylmethoxy)-naphthalen-2-yl]-ethanone (3). **Step 2.** Synthesis of 1-[1-(1-Benzyl-1*H*-[1,2,3]triazol-4-ylmethoxy)-naphthalen-2-yl]-3-(1-phenyl-3-aryl-1*H*-pyrazol-4-yl)-propenones (5a-g)

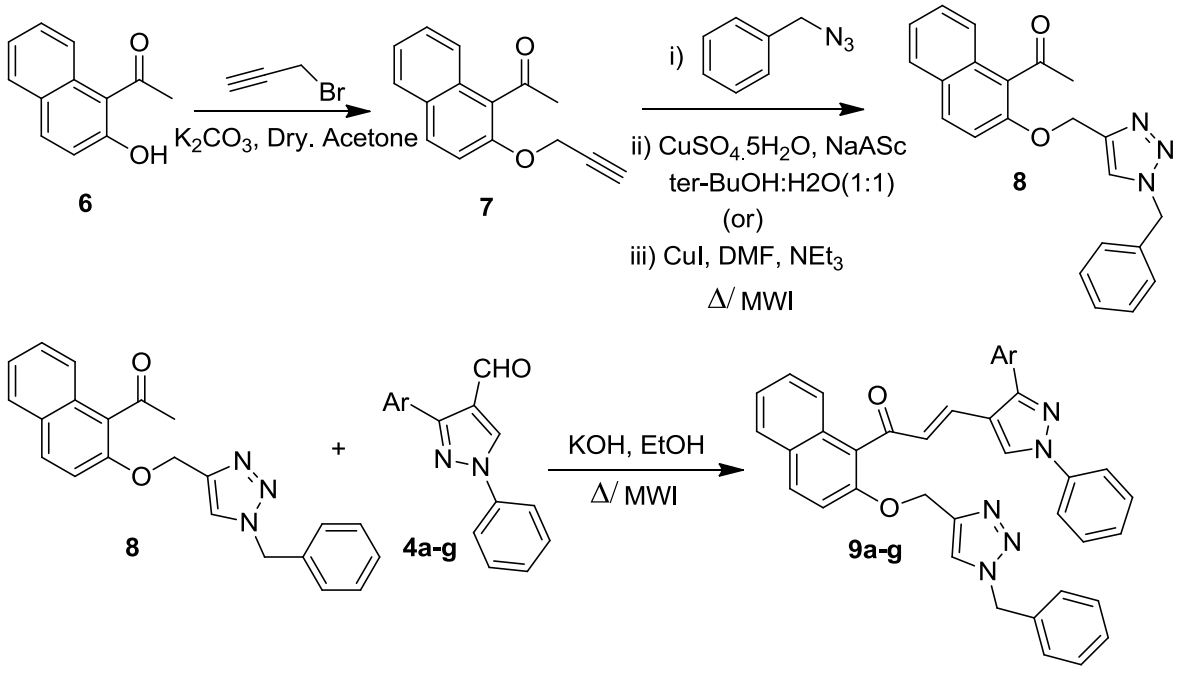

Figure 3. Step 1. Synthesis of 1-[2-(1-Benzyl-1*H*-[1,2,3]triazol-4-ylmethoxy)-naphthalen-1-yl]-ethanone (8). **Step 2.** Synthesis of the 1-[2-(1-Benzyl-1*H*-[1,2,3]triazol-4-ylmethoxy)-naphthalen-1-yl]-3-(1-phenyl-3-aryl-1*H*-pyrazol-4-yl)-propenones (9a-g)

Table 1. Physical data of the 1-[1/2-(1-Benzyl-1*H*-[1,2,3]triazol-4-ylmethoxy)-naphthalen-2/1-yl]-3-(1-phenyl-3-aryl-1*H*-pyrazol-4-yl)-propenones (5a-g & 9a-g)

S.No	Ar	M.P. (°C)	Reaction time		Yield (%)	
			Conventional (h)	MWI (min)	Conventional	MWI
5a	phenyl	90	8	4	67	84
5b	4-methylphenyl	98	8	5	70	86
5c	4-methoxyphenyl	84	8	4	69	85
5d	4-Bromophenyl	122	9	4	72	86
5e	4-chlorophenyl	102	10	6	58	80
5f	4-nitrophenyl	118	8	4	64	82
5g	2-thienyl	72	8	4	74	88
9a	phenyl	80	9	4	66	84
9b	4-methylphenyl	68	9	5	64	85
9c	4-methoxyphenyl	86	9	5	68	85
9d	4-Bromophenyl	82	10	6	63	82
9e	4-chlorophenyl	89	10	6	60	80
9f	4-nitrophenyl	92	9	5	58	80
9g	2-thienyl	70	8	4	75	90

3. Biological activity

3.1. Antibacterial activity:

All the compounds were screened for their antibacterial activity against *Escherichia coli* (ATCC 700928D-5), and *Staphylococcus aureus* (ATCC BAA1556D-5) using ampicillin as standard drug. The bacterial cultures were grown in nutrient agar media and sub cultured for the better growth (log phase cultures) in a liquid nutrient broth medium and further sub cultured onto the Petri plates for the experiments. The broth cultures were diluted with sterilized saline to bring the final size of inoculum approximately to 105–106 CFU/mL. The compounds were diluted in DMSO for biological assays and it used as negative control. The bacterial culture inoculum was placed on the media and incubated at 37 ºC for 24 hr to 48 hr along with the Chemical discs dipped and placed over the media. The zones of bacterial growth inhibition were measured using the diameter of the zone as an unit to measure the anti bacterial activity. All the experiments were carried out in triplicates and the results were expressed as Zone of Inhibition in mm. The results were compared with the activity of the standard antibiotic Ampicillin (25µg/mL, 50 µg/mL & 100 µg/mL). For disc diffusion method[30], the test compound was introduced onto the disc and then allowed to dry. Once the disc was completely saturated with the test compound, then it was introduced onto the upper layer of the medium containing the bacterial intoculum. The Petri dishes were incubated overnight at 37 ºC for 24 hr. From the screening studies it is evident that the synthesized compounds **5d**, **5e**, **5f**, **9d** and **9f** showed maximum zone of inhibition against *Escherichia coli* and the compounds **5d**, **5e** and **9d** showed maximum zone of inhibition against *Staphylococcus aureus* all the tested organisms (**Table 2** & **Figure 4**).

3.2. Antifungal activity:

All the compounds were screened for their antifungal activity against *Aspergillus niger* (ATCC 20057) and *Candida metapsilosis*(ATCC 96143) using griseofulvin as standard drug.
Test compounds were dissolved in DMSO before mixing with Potato Dextrose Agar medium (PDA, 90mL). The final concentration of compounds in the medium was maintained to be 25µg/mL, 50 µg/mL & 100 µg/mL. Above mentioned types of fungi were incubated in PDA at 25±1 ºC for 3-4 days to get good mycelium growth for antifungal assay, then a mycelia disk of approximately 0.45 cm diameter cut from the culture medium was picked up with a sterilized inoculation needle and inoculated in the center of PDA plate. The inoculated plates were incubated at 25±1ºC for 5 days.

DMSO in sterilized distilled water used as control, while Griseofulvin were used as standards for all the treatment, three replicates was performed. The radial growth of the fungal colonies was measured on the fourth day and the data were statistically analyzed. The in vitro inhibition effects of the test compounds on the fungi were calculated by the given formula CV =A-B/A, where A represents the diameter of fungi growth on untreated PDA, B represents the diameter of fungi on treated PDA, and CV represents the rate of inhibition. From the screening studies it is evident that the synthesized compound **9f** showed maximum antifungal activity against all the tested organisms (**Table 2** & **Figure 5**).

Table 2. Inhibition zone of 1-[1/2-(1-Benzyl-1*H*-[1,2,3]triazol-4-ylmethoxy)-naphthalen-2/1-yl]-3-(1-phenyl-3-aryl-1*H*-pyrazol-4-yl)-propenones (5a-g & 9a-g)

Comp.	Bacterial strains						Fungal strain					
	E. coli (*Conc.* In g/mL)			*S. aureus* (*Conc.* In µg/mL)			*C. niger* (*Conc.* In µg/mL)			*C. metapsilosis* (*Conc.* In µg/mL)		
	25	50	100	25	50	100	25	50	100	25	50	100
5a	4	8	9	4	6	9	6	12	11	6	9	14
5b	4	6	7	4	6	8	7	10	14	8	10	12
5c	4	7	9	5	6	9	8	11	15	5	9	11
5d	6	10	11	6	9	10	9	10	12	7	10	14
5e	6	9	12	6	9	11	7	9	17	8	11	16
5f	5	9	11	4	8	12	6	10	12	6	11	12
5g	5	6	8	5	6	8	5	9	11	5	10	12
9a	4	6	8	4	6	8	6	9	14	6	11	15
9b	4	5	7	4	6	8	7	9	10	6	9	10
9c	4	6	8	5	7	9	6	11	11	7	10	12
9d	6	8	12	5	9	11	7	8	10	8	12	16
9e	4	8	10	4	9	8	5	9	10	8	13	16
9f	6	10	12	5	8	10	7	13	18	9	14	17
9g	5	6	8	4	6	8	5	8	12	5	11	14
Ampicillin	6	9	12	6	9	11						
Griseofulvin							10	14	19	10	15	20

*results showed in mm

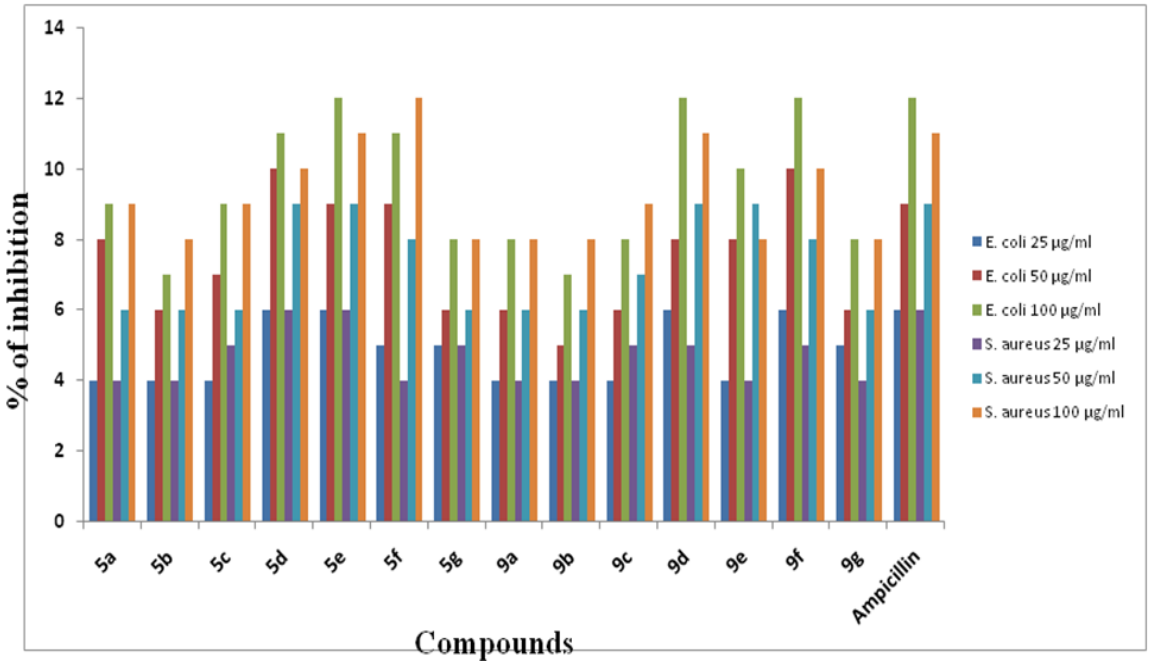

Figure 4. Graphical representation of antibacterial % inhibition

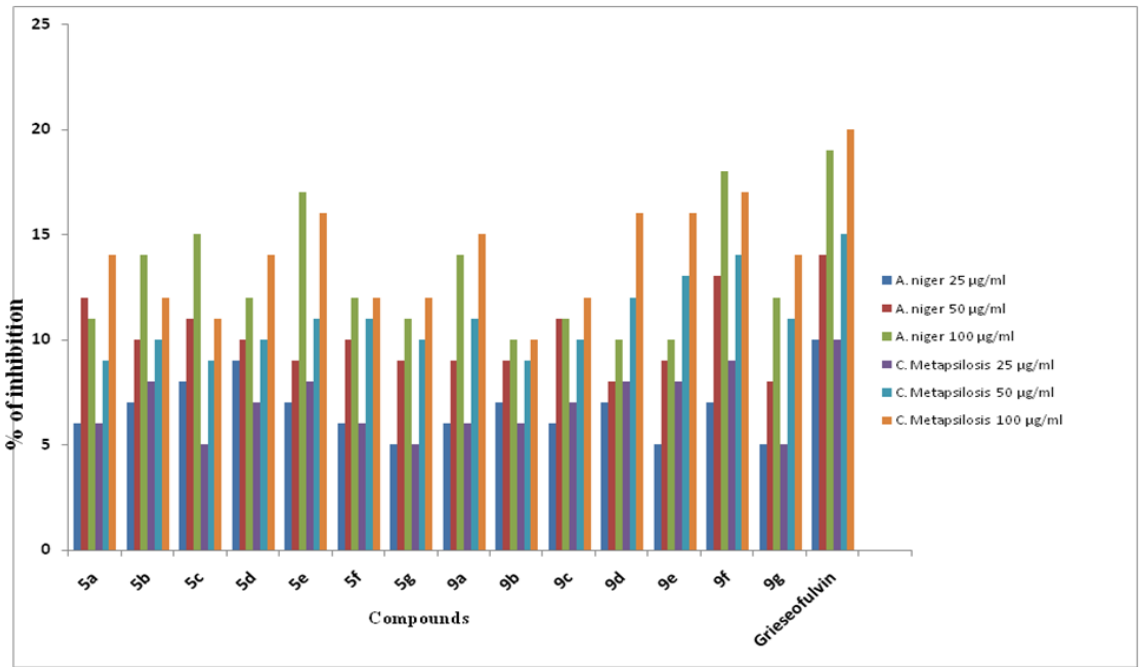

Figure 5. Graphical representation of antifungal % inhibition.

4. Experimental section

All the chemicals were purchased from Aldrich and Fluka. Melting points were determined in open capillary tubes and are uncorrected. The purity of the compounds was checked by TLC using precoated silica gel plates 60_{254}(Merck). Microwave reactions were carried out in the milestone multi SYNTH microwave system. IR (KBr) spectra were recorded on a Shimadzu FT-IR-8400s spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker Avance II 400 MHz instrument using tetramethylsilane as an internal standard. Mass spectra were recorded on a GCMS-QP 1000 EX mass spectrometer. Elemental analysis was determined by using a Thermo Finnigan CHNS analyzer.

4.1. General procedure for synthesis of 1-(1/2-Prop-2-ynyloxy-naphthalen-2/1-yl)-ethanone (2/7)

A mixture of 1-(1/2-Hydroxy-naphthalen-2/1-yl)-ethanone (1 mmol), propargylbromide (1.2 mmol), Anhydrous K_2CO_3 (1 eq) in 15 mL dry acetone was taken round bottomed flask and refluxed for 8 hr. After completion of the reaction acetone was distilled under vacuum and it was diluted with cold water and the precipitate formed was filtered, washed with water and crystallized from methanol to give compounds **(2/7)**

4.1.1. 1-(1-Prop-2-ynyloxy-naphthalen-2-yl)-ethanone (2): MP: 136 °C; IR (KBr, cm^{-1}) υ_{max}: 2127 (C≡C), 1662 (C=O); ^{1}H NMR: δ 2.58 (t, 1H, acetylene proton, *J=2.6 Hz*), 2.62 (s, 3H, CH_3), 4.75 (d, 2H, O-CH_2, *J=2.6 Hz*), 7.35-7.38 (dd, 2H, C-4 & C-7, *J=1.2, 7.0 Hz*), 7.54-7.58 (m, 2H, C-5 & C-6), 7.84-7.86 (d, 1H, C-3, *J=7.8 Hz*), 8.24-8.26 (d, 1H, C-8, *J=7.6 Hz*), MS: *m/z*=225 $(M+H)^+$; *Anal*. Calc. for $C_{15}H_{12}O_2$: C, 80.34; H, 5.39; Found: C, 80.31; H, 5.43.

4.1.2. 1-(2-Prop-2-ynyloxy-naphthalen-1-yl)-ethanone (7): MP: 122 °C; IR (KBr, cm^{-1}) υ_{max}: 2120 (C≡C), 1673 (C=O); ^{1}H NMR: δ 2.53 (t, 1H, acetylene proton, *J=2.4 Hz*), 2.67 (s, 3H, CH_3), 4.86 (d, 2H, O-CH_2, *J=2.4 Hz*), 7.35-7.38 (d, 1H, C-8, *J=7.2 Hz*), 7.39-7.41 (dd, 1H, C-6, *J=1.2, 6.8 Hz*), 7.35-7.47 (m, 1H, C-4,), 7.48-7.51 (dd, 1H, C-5, *J=1.6,7.0 Hz*), 7.75-7.81 (d, 1H, C-7, *J=7.6 Hz*), 7.87-7.90 (d, 1H, C-3, *J=7.8 Hz*); MS: *m/z*=225 $(M+H)^+$; *Anal*. Calc. for $C_{15}H_{12}O_2$: C, 80.34; H, 5.39; Found: C, 80.29; H, 5.42.

4.2. General procedure for synthesis of 1-[1/2-(1-Benzyl-1H-[1,2,3]triazol-4-ylmethoxy)-naphthalen-2/1-yl]-ethanone (3/8)

Conventional conditions using $CuSO_4.5H_2O$/Sodium ascorbate:

A mixture of 1-(1/2-Prop-2-ynyloxy-naphthalen-2/1-yl)-ethanone (7.5 mmol) (**2/7)**, benzylazide (7.5 mmol), $CuSO_4.5H_2O$ (0.37 mmol), sodium ascorbate (1.2 mmol) in *t*-BuOH: H_2O (1:1,v/v) (5 mL) was taken into round bottomed flask and it was stirred under room temperature for 24 hr. After completion of the reaction (monitored by TLC), the resulting mixture was poured in to ice cold water (20 mL), extracted with EtOAc (30 mL), washed twice with saturated solution of NH_4Cl, twice with brine and dried over Na_2SO_4. The organic layer was concentrated in vacuo and the residue was purified by column chromatography on silica gel eluted with hexane/EtOAc (2:1) to give compound (**3/8).**

Microwave irradiation using $CuSO_4.5H_2O$/Sodium ascorbate:

A mixture of 1-(1/2-Prop-2-ynyloxy-naphthalen-2/1-yl)-ethanone (7.5 mmol) (**2/7)**, benzylazide (7.5 mmol), $CuSO_4.5H_2O$ (0.37 mmol) and sodium ascorbate (1.2 mmol) in *t*-BuOH: H_2O (1:1,v/v) (5 mL) was taken into Quartz tube and inserted into a Teflon vial with screw capped and then it was subjected to microwave irradiation at 180 watts for 8 min. After completion of the reaction (monitored by TLC), the resulting mixture was poured in to ice cold water (20 mL), extracted with EtOAc (30 mL), washed twice with saturated solution of NH_4Cl, twice with brine and dried over Na_2SO_4. The organic layer was concentrated in vacuo and the residue was purified by column chromatography on silica gel eluted with hexane/EtOAc (2:1) to give compound (**3/8).**

Conventional conditions using CuI:

A mixture of 1-(1/2-Prop-2-ynyloxy-naphthalen-2/1-yl)-ethanone (7.5 mmol) (**2/7)**, benzylazide (7.5 mmol), triethylamine (9 mmol) and CuI (0.75 mmol) in DMF (5 mL) was taken into round bottomed flask and it was stirred under room temperature for 18 hr. After completion of the reaction (monitored by TLC), the resulting mixture was poured in to ice cold water (20 mL), extracted with EtOAc (30 mL), washed twice with saturated solution of NH_4Cl, twice with brine and dried over Na_2SO_4. The organic layer was concentrated in vacuo and the residue was purified by column chromatography on silica gel eluted with hexane/EtOAc (2:1) to give compound (**3/8).**

Microwave irradiation using CuI:

A mixture of 1-(1/2-Prop-2-ynyloxy-naphthalen-2/1-yl)-ethanone (7.5 mmol) (**2/7)**, benzylazide (7.5 mmol), triethylamine (9 mmol) and CuI (0.75 mmol) in DMF (5 mL) was taken into Quartz tube and inserted into a Teflon vial with screw capped and then it was subjected to microwave irradiation at 180 watts for 6 min. After completion of the reaction (monitored by TLC), the resulting mixture was poured in to ice cold water (20 mL), extracted with EtOAc (30 mL), washed twice with saturated solution of NH_4Cl, twice with brine and dried over Na_2SO_4. The organic layer was concentrated in vacuo and the residue was purified by column chromatography on silica gel eluted with hexane/EtOAc (2:1) to give compound (**3/8).**

4.2.1. 1-[1-(1-Benzyl-1H-[1,2,3]triazol-4-ylmethoxy)-naphthalen-2-yl]-ethanone (3): MP: 118 °C; IR (KBr, cm^{-1}) υ_{max}: 1671 (C=O), 1621 (C=C), 1226 (O-CH_2); ^{1}H NMR: δ 2.68 (s, 3H, -CH_3), 5.22 (s, 2H, N-CH_2), 5.54 (s, 2H, O-CH_2), 7.23-7.26 (m, 2H, ArH), 7.35-7.38 (m, 3H, C-7, C-4 & ArH), 7.46 (s, 1H, triazole proton),7.54-7.58 (m, 2H, ArH), 7.63-7.69 (dd, 2H, ArH, *J=0.6, 8.0 Hz*), 7.84-7.86 (d, 1H, ArH, *J=8 Hz*), 8.26-8.28 (d, 1H, ArH, *J=8.2 Hz*); MS: *m/z*=358 $(M+H)^+$; *Anal*. Calc. for $C_{22}H_{19}N_3O_2$: C, 73.93; H, 5.36; N, 11.76. Found: C, 73.96; H, 5.30; N, 11.82.

4.2.2. 1-[2-(1-Benzyl-1*H*-[1,2,3]triazol-4-ylmethoxy)-naphthalen-1-yl]-ethanone (8): MP: 108°C; IR (KBr, cm^{-1}) υ_{max}: 1684 (C=O), 1620 (C=C), 1242 (O-CH_2); ^{1}H NMR: δ 2.57 (s, 3H, -CH_3), 5.36 (s, 2H, N-CH_2), 5.51 (s, 2H, O-CH_2), 7.22-7.41 (dd, 2H, ArH, *J=3.2, 7.2 Hz*), 7.32-7.39 (m, 5H, ArH), 7.44-7.49 (m, 1H, ArH), 7.69-7.72 (dd, 1H, ArH, *J=0.4,8.6 Hz*), 7.77-7.79 (d, 1H, ArH, *J=8.0 Hz*),

7.84-7.86 (d, 1H, ArH, *J=8.4Hz*); MS: *m/z*=357 (M^+); *Anal*. Calc. for $C_{22}H_{19}N_3O_2$: C, 73.93; H, 5.36; N, 11.76. Found: C, 73.96; H, 5.30; N, 11.82.

4.3. General procedure for synthesis of 1-[1/2-(1-Benzyl-1H-[1,2,3]triazol-4-ylmethoxy)-naphthalen-2/1-yl]-3-(1-phenyl-3-aryl-1H-pyrazol-4-yl)-propenones (5a-g/9a-g)

Conventional heating method:

A mixture of 1-[1/2-(1-Benzyl-1*H*-[1,2,3]triazol-4-ylmethoxy)-naphthalen-2/1-yl]-ethanone **(3/8)** (5 mmol), 3-aryl-1-phenyl-1*H*-pyrazole-4-carbaldehydes **(4a-g)** (5 mmol) and potassium hydroxide (1.2 eq) in EtOH (15 mL), was taken into round bottomed flask and it was refluxed for 8-10 hr. The progress of the reaction was monitored by TLC. After completion of reaction, it was poured into crushed ice, carefully neutralized with 3 N HCl and extracted with EtOAc (15 mL). The organic layer was concentrated in vacuo and purified by column chromatography on silica gel eluted with hexane/EtOAc (3:1) to give compound (**5a-g/9a-g).**

Microwave irradiation method:

A mixture of 1-[1/2-(1-Benzyl-1*H*-[1,2,3]triazol-4-ylmethoxy)-naphthalen-2/1-yl]-ethanone **(3/8)** (5 mmol), 3-aryl-1-phenyl-1*H*-pyrazole-4-carbaldehydes **(4a-g)** (5 mmol) and KOH (1.2 eq) in EtOH (5 mL) was taken into Quartz tube and inserted into a Teflon vial with screw capped and then it was subjected to microwave irradiation at 180 watts 4-6 min. The progress of the reaction was monitored by TLC. After completion of reaction, it was poured into crushed ice, carefully neutralized with 3 N HCl and extracted with EtOAc (15 mL). The organic layer was concentrated in vacuo and purified by column chromatography on silica gel eluted with hexane/EtOAc (3:1) to give compound (**5a-g/9a-g).**

4.3.1. 1-[1-(1-Benzyl-1*H*-[1,2,3]triazol-4-ylmethoxy)-naphthalen-2-yl]-3-(1,3-diphenyl-1*H*-pyrazol-4-yl)-propenone (5a): IR (KBr, cm^{-1}) υ_{max}: 1586 (C=N), 1650 (C=O), 3060 (C-H); ^{1}H NMR: δ 5.20 (s, 2H, N-CH_2), 5.36 (s, 2H, O-CH_2), 7.06-7.11 (d, 1H, α-olefinic protons, *J=16.4 Hz*), 7.14-7.59 (m, 13H, ArH), 7.70-7.77 (m, 5H, ArH), 7.79-7.88 (m, 4H, ArH), 8.29-8.31 (d, 1H, ArH, *J=7.6 Hz*), 8.45 (s, 1H, pyrazol proton); ^{13}C NMR: 54.1 (N-CH_2), 69.4 (O-CH_2), 119.3, 123.4, 124.7, 125.9, 126.0, 126.8, 126.9, 127.2, 127.8, 127.9, 128.1, 128.2, 128.3, 128.5, 128.6, 128.7, 128.8, 128.9, 129.0, 129.1, 129.2, 129.5, 129.6, 135.0, 136.5, 143.49, 154.1, 190.1 (C=O); MS: *m/z*=588 $(M+H)^+$; *Anal*. Calc. for $C_{38}H_{29}N_5O_2$: C, 77.66; H, 4.97; N, 11.92; Found: C, 77.61; H, 4.92; N, 11.95.

4.3.2. 1-[1-(1-Benzyl-1H-[1,2,3]triazol-4-ylmethoxy)-naphthalen-2-yl]-3-(1-phenyl-3-p-tolyl-1H-pyrazol-4-yl)-propenone (5b): IR (KBr, cm^{-1}) υ_{max}: 1585 (C=N), 1647 (C=O), 3057 (C-H); ^{1}H NMR: δ 2.41 (s, 3H, CH_3), 5.19 (s, 2H, N-CH_2), 5.35 (s, 2H, O-CH_2), 7.07-7.09 (d, 2H, ArH, *J=7.2 Hz*), 7.11-7.58 (m, 14H, ArH), 7.71-7.78 (m, 2H, ArH), 7.79-7.89 (m, 4H, ArH), 8.30-8.32 (d, 1H, ArH, *J=7.8 Hz*), 8.42 (s, 1H, pyrazol proton); ^{13}C NMR: 21.3 (CH_3), 54.1 (N-CH_2), 69.4 (O-CH_2), 118.2, 119.3, 123.4, 124.7, 125.9, 126.0, 126.7, 126.9, 127.1, 127.9, 128.1, 128.3, 128.6, 128.7, 128.8, 129.0, 129.4, 129.5, 129.6, 134.2, 135.2, 136.5, 138.6, 139.5, 143.5, 154.1, 154.5, 192.2 (C=O); MS: *m/z*=602 $(M+H)^+$; *Anal*. Calc. for $C_{39}H_{31}N_5O_2$: C, 77.85; H, 5.19; N, 11.64; Found: C, 77.82; H, 5.25; N, 11.68.

4.3.3. 1-[1-(1-Benzyl-1H-[1,2,3]triazol-4-ylmethoxy)-naphthalen-2-yl]-3-[3-(4-methoxy-phenyl)-1-phenyl-1H-pyrazol-4-yl]-propenone (5c): IR (KBr, cm^{-1}) υ_{max}: 1581 (C=N), 1647 (C=O), 3062 (C-H); ^{1}H NMR: δ 3.85 (s, 3H, -OCH_3), 5.19 (s, 2H, N-CH_2), 5.35 (s, 2H, O-CH_2), 6.97-6.99 (d, 2H, ArH, *J=7.6 Hz*), 7.07-7.08 (d, 2H, ArH, *J=7.2 Hz*), 7.23-7.72 (m, 15H, ArH), 7.71-7.81 (d, 1H, β-olefinic proton, *J=16.4 Hz*), 7.84-7.87 (m, 2H, ArH), 8.29-8.31 (d, 1H, ArH, *J=7.8 Hz*), 8.42 (s, 1H, pyrazol proton); ^{13}C NMR: 54.1 (N-CH_2), 55.4 (OCH_3), 69.4 (O-CH_2), 114.3, 118.0, 119.3, 123.4, 124.5, 124.6, 124.7, 125.8, 126.0, 126.7, 126.8, 127.1, 127.9, 128.1, 128.7, 128.8, 129.0, 129.6, 129.9, 134.2, 135.2, 136.5, 139.5, 143.5, 153.8, 154.5, 160.0, 192.3(C=O); MS: *m/z*=618 $(M+H)^+$; *Anal*. Calc. for $C_{39}H_{31}N_5O_3$: C, 75.83; H, 5.06; N, 11.34; Found: C, 75.88; H, 5.12; N, 11.42.

4.3.4. 1-[1-(1-Benzyl-1H-[1,2,3]triazol-4-ylmethoxy)-naphthalen-2-yl]-3-[3-(4-bromo-phenyl)-1-phenyl-1H-pyrazol-4-yl]-propenone (5d): IR (KBr, cm^{-1}) υ_{max}: 1587 (C=N), 1646 (C=O), 3059(C-H);

^{1}H NMR: δ 5.19 (s, 2H, N-CH_2), 5.39 (s, 2H, O-CH_2), 7.09-7.10 (d, 2H, ArH, *J=7.2 Hz*), 7.27-7.30 (d, 2H, ArH, *J=7.2 Hz*), 7.35-7.39 (dd, 2H, ArH, *J=6.0,6.8 Hz*), 7.50-7.56 (m, 9H, ArH), 7.59 (s, 1H, triazol proton), 7.65-7.76 (m, 4H, β-olefinic proton & ArH), 7.86-7.88 (m, 2H, ArH), 8.27-8.29 (d, 1H, ArH, *J=7.8 Hz*), 8.48 (s, 1H, pyrazol proton); ^{13}C NMR: 54.1 (N-CH_2), 69.3 (O-CH_2), 118.2, 119.3, 122.9, 123.4, 124.7, 125.9, 126.3, 126.9, 127.1, 127.4, 127.9, 128.1, 128.3, 128.7, 128.8, 129.1, 129.6, 130.2, 131.2, 131.9, 134.2, 136.6, 139.3, 143.4, 152.6, 154.6, 160.0, 192.0 (C=O); MS: *m/z*=666 $(M+H)^+$; *Anal*. Calc. for $C_{38}H_{28}BrN_5O_2$: C, 68.47; H, 4.23; N, 10.51; Found: C, 68.42; H, 4.25; N, 10.44.

4.3.5. 1-[1-(1-Benzyl-1H-[1,2,3]triazol-4-ylmethoxy)-naphthalen-2-yl]-3-[3-(4-chloro-phenyl)-1-phenyl-1H-pyrazol-4-yl]-propenone (5e): IR (KBr, cm^{-1}) υ_{max}: 1585 (C=N), 1652 (C=O), 3062 (C-H); ^{1}H NMR: δ 5.20 (s, 2H, N-CH_2), 5.39 (s, 2H, O-CH_2), 7.11-7.13 (m, 4H, ArH), 7.19-7.21 (m, 4H, ArH), 7.28-7.29 (dd, 2H, ArH), 7.47-7.49 (m, 4H, ArH), 7.60-7.62 (m, 4H, β-olefinic proton & ArH), 7.85-7.87 (m, 4H, ArH), 8.26-8.28 (d, 1H, ArH, *J=7.6 Hz*), 8.49 (s, 1H, pyrazol proton); ^{13}C NMR: 54.3 (N-CH_2), 69.0 (O-CH_2), 118.2, 119.3, 122.9, 123.4, 124.7, 125.9, 126.3, 126.9, 127.1, 127.4, 127.9, 128.1, 128.3, 128.7, 128.8, 129.1, 129.6, 130.2, 131.2, 131.9, 134.2, 136.6, 139.3, 143.4, 152.6, 154.6, 160.0, 192.9 (C=O); MS: *m/z*=622 $(M+H)^+$; *Anal*. Calc. for $C_{38}H_{28}ClN_5O_2$: C, 73.36; H, 4.54; N, 11.26; Found: C, 73.32; H, 4.51; N, 11.22.

4.3.6. 1-[1-(1-Benzyl-1H-[1,2,3]triazol-4-ylmethoxy)-naphthalen-2-yl]-3-[3-(4-nitro-phenyl)-1-phenyl-1H-pyrazol-4-yl]-propenone (5f): IR (KBr, cm^{-1}) υ_{max}: 1596 (C=N), 1671 (C=O), 3059 (C-H); ^{1}H NMR: δ 5.20 (s, 2H, N-CH_2), 5.40 (s, 2H, O-CH_2), 6.84-6.94 (d, 2H, ArH, *J=7.6 Hz*), 7.11-7.13 (d, 2H, ArH, *J=7.0 Hz*), 7.27-7.30 (d, 2H, ArH, *J=8.0 Hz*), 7.31-7.36 (m, 2H, ArH), 7.45 (s, 1H, triazol proton), 7.54-7.58 (m, 8H, ArH), 7.65-7.67 (m, 3H, β-olefinic proton & ArH), 7.88-7.93 (m, 2H, ArH), 8.28-8.32 (d, 1H, ArH, *J=8.2 Hz*), 8.53 (s, 1H, pyrazol proton); ^{13}C NMR: 54.3 (N-CH_2), 69.1 (O-CH_2), 119.7, 123.8, 124.1, 124.2, 125.4, 126.5, 127.4, 127.6, 128.1, 128.4, 128.6, 132.7, 138.5, 142.8, 152.1, 153.9, 192.2 (C=O); MS: *m/z*=633 $(M+H)^+$; *Anal*. Calc. for $C_{38}H_{28}N_6O_4$: C, 72.14; H, 4.46; N, 13.28; Found: C, 72.10; H, 4.51; N, 13.23.

4.3.7. 1-[1-(1-Benzyl-1H-[1,2,3]triazol-4-ylmethoxy)-naphthalen-2-yl]-3-(1-phenyl-3-thiophen-2-yl-1H-pyrazol-4-yl)-propenone (5g): IR (KBr, cm^{-1}) υ_{max}: 1584 (C=N), 1647 (C=O), 3061 (C-H); ^{1}H NMR: δ 5.19 (s, 2H, N-CH_2), 5.39 (s, 2H, O-CH_2), 7.08-7.09 (dd, 2H, ArH), 7.10-7.13 (dd, 1H, ArH), 7.24-7.26 (m, 3H, ArH), 7.31-7.58 (m, 9H, ArH), 7.59 (s, 1H, triazol proton), 7.68-7.70 (d, 1H, ArH, *J=7.6 Hz*), 7.76-7.78 (d, 1H, ArH, *J=7.8 Hz*), 7.84-7.86 (m, 3H, ArH), 8.29-8.31 (d, 1H,ArH, *J=7.8 Hz*), 8.44 (s, 1H, pyrazol proton); ^{13}C NMR: 54.1 (N-CH_2), 69.4 (O-CH_2), 118.1, 119.3, 123.4, 124.5, 126.0, 126.5, 126.9, 127.0, 127.3, 127.8, 127.9, 128.0, 128.2, 128.3, 128.7, 129.0, 129.5, 129.6, 134.0, 134.2, 136.6, 139.2, 143.4, 148.0, 154.8, 191.9(C=O); MS: *m/z*=594 $(M+H)^+$; *Anal*. Calc. for $C_{36}H_{27}N_5O_2S$: C, 72.83; H, 4.58; N, 11.80; S, 5.40 Found: C, 72.78; H, 4.62; N, 11.82; S, 5.37.

4.3.8. 1-[2-(1-Benzyl-1H-[1,2,3]triazol-4-ylmethoxy)-naphthalen-1-yl]-3-(1,3-diphenyl-1H-pyrazol-4-yl)-propenone (9a): IR (KBr, cm^{-1}) υ_{max}: 1591 (C=N), 1619 (C=O), 3060 (C-H); ^{1}H NMR: δ 5.34 (s, 4H, N-CH_2 & O-CH_2), 6.92-6.96 (d, 1H, α-olefinic protons, *J=16.0 Hz*), 7.09-7.11 (dd, 2H, ArH), 7.20-7.22 (dd, 4H, ArH), 7.29-7.50 (m, 12H, ArH), 7.75-7.82 (m, 4H, ArH), 7.86-7.88 (d, 1H, ArH, *J=9.2 Hz*), 8.28 (s, 1H, pyrazol proton); ^{13}C NMR: 54.1 (N-CH_2), 63.7 (O-CH_2), 114.3, 117.8, 119.3, 122.9, 124.3, 124.5 124.6, 126.8, 126.9, 127.3, 127.5, 127.8, 127.9, 128.1, 128.2, 128.3, 128.5, 128.6, 128.7, 128.9, 129.0, 129.1, 129.3, 129.6, 131.4, 131.5, 131.9, 134.3, 136.7, 139.4, 144.3, 152.7, 153.5, 196.4 (C=O); MS: *m/z*=588 $(M+H)^+$; *Anal*. Calc. for $C_{38}H_{29}N_5O_2$: C, 77.66; H, 4.97; N, 11.92; Found: C, 77.62; H, 4.92; N, 11.96.

4.3.9. 1-[2-(1-Benzyl-1H-[1,2,3]triazol-4-ylmethoxy)-naphthalen-1-yl]-3-(1-phenyl-3-p-tolyl-1H-pyrazol-4-yl)-propenone (9b): IR (KBr, cm^{-1}) υ_{max}: 1593 (C=N), 1623 (C=O), 3060 (C-H); ^{1}H NMR: δ 2.36 (s, 3H, CH_3), 5.37 (s, 2H, N-CH_2), 5.38 (s, 2H, O-CH_2), 6.91-6.95 (d, 1H, α-olefinic protons, *J=16.0 Hz*), 7.10-7.12 (m, 4H, ArH), 7.21-7.23 (dd, 3H, ArH, *J=1.6,5.2 Hz*), 7.35-7.50 (m, 10H, ArH), 7.74-7.82 (m, 4H, ArH), 7.87-7.89 (d, 1H, ArH, *J=9.2 Hz*), 8.26 (s, 1H, pyrazol proton); ^{13}C NMR: 21.3 (CH_3), 54.1 (N-CH_2), 63.8 (O-CH_2), 114.7, 118.2, 119.3, 122.9, 124.4, 124.5 124.6, 126.7, 127.0, 127.2, 127.5, 127.8, 127.9, 128.1, 128.2, 128.3, 128.7, 129.0, 129.4, 129.6, 131.4, 131.5,

136.9, 139.4, 144.3, 152.7, 196.4 (C=O); MS: *m/z*=602 $(M+H)^+$; *Anal*. Calc. for $C_{39}H_{31}N_5O_2$: C, 77.85; H, 5.19; N, 11.64; Found: C, 77.82; H, 5.23; N, 11.68.

4.3.10. 1-[2-(1-Benzyl-1H-[1,2,3]triazol-4-ylmethoxy)-naphthalen-1-yl]-3-[3-(4-methoxy-phenyl)-1-phenyl-1H-pyrazol-4-yl]-propenone (9c): IR (KBr, cm^{-1}) υ_{max}: 1583 (C=N), 1622 (C=O), 3062 (C-H); ^{1}H NMR: δ 3.82 (s, 3H, -OCH_3), 5.35 (s, 4H, N-CH_2 & O-CH_2), 6.80-6.82 (d, 2H, ArH, *J=8.4 Hz*), 6.90-6.94 (d, 1H, α-olefinic proton, *J=16 Hz*), 7.09-7.11 (m, 2H, ArH), 7.20-7.23 (dd, 4H, ArH, *J=1.8,5.4 Hz*), 7.31-7.40 (m, 4H, ArH), 7.42 (s, 1H, triazol proton), 7.46-7.50 (m, 4H, ArH), 7.75-7.82 (m, 4H, ArH), 7.86-7.88 (d, 1H, ArH, *J=9.2 Hz*), 8.25 (s, 1H, pyrazol proton); ^{13}C NMR: 54.1 (N-CH_2), 55.3 (OCH_3), 63.7 (O-CH_2), 114.1, 114.8, 117.5, 119.3, 122.9, 124.3, 124.4 124.5, 124.6, 126.6, 127.1, 127.5, 127.9, 128.0, 128.1, 128.7, 128.9, 129.0, 129.3, 129.6, 129.7, 131.4, 131.5, 134.2, 135.2, 137.0, 139.4, 144.3, 152.7, 153.4, 159.9, 196.4 (C=O); MS: *m/z*=618 $(M+H)^+$; *Anal*. Calc. for $C_{39}H_{31}N_5O_3$: C, 75.83; H, 5.06; N, 11.34; Found: C, 75.87; H, 5.13; N, 11.40.

4.3.11. 1-[2-(1-Benzyl-1H-[1,2,3]triazol-4-ylmethoxy)-naphthalen-1-yl]-3-[3-(4-bromo-phenyl)-1-phenyl-1H-pyrazol-4-yl]-propenone (9d): IR (KBr, cm^{-1}) υ_{max}: 1596 (C=N), 1617 (C=O), 3063 (C-H); ^{1}H NMR: δ 5.35 (s, 4H, N-CH_2 & O-CH_2), 6.85-6.87 (d, 2H, ArH, *J=8.2 Hz*), 6.89-6.93 (d, 1H, α-olefinic proton, *J=16 Hz*), 7.13-7.15 (dd, 2H, ArH), 7.18-7.21 (dd, 3H, ArH), 7.28-7.30 (m, 6H, ArH), 7.48-7.51 (m, 4H, ArH), 7.78-7.80 (m, 4H, ArH), 7.82-7.84 (d, 1H, ArH, *J=9.2 Hz*), 8.28 (s, 1H, pyrazol proton); ^{13}C NMR: 54.1 (N-CH_2), 55.3 (OCH_3), 63.7 (O-CH_2), 114.1, 114.8, 118.1, 119.4, 122.9, 124.3, 124.4 124.5, 125.3, 126.8, 127.4, 127.5, 128.0, 128.1, 128.7, 129.6, 129.7, 130.3, 131.3, 131.9, 133.2.2, 135.2, 137.0, 139.4, 144.3, 152.4, 159.6, 196.0 (C=O); MS: *m/z*=666 $(M+H)^+$; *Anal*. Calc. for $C_{38}H_{28}BrN_5O_2$: C, 68.47; H, 4.23; N, 10.51; Found: C, 68.42; H, 4.27; N, 10.45.

4.3.12. 1-[2-(1-Benzyl-1H-[1,2,3]triazol-4-ylmethoxy)-naphthalen-1-yl]-3-[3-(4-chloro-phenyl)-1-phenyl-1H-pyrazol-4-yl]-propenone (9e): IR (KBr, cm^{-1}) υ_{max}: 1593 (C=N), 1622 (C=O), 3060 (C-H); ^{1}H NMR: δ 5.36 (s, 2H, N-CH_2), 5.38 (s, 2H, O-CH_2), 6.92-6.96 (d, 1H, α-olefinic proton, *J=16.4 Hz*), 7.11-7.12 (m, 2H, ArH), 7.22-7.23 (dd, 3H, ArH, *J=1.6,5.2 Hz*), 7.25-7.28 (m, 3H, ArH), 7.34-7.42 (m, 6H, ArH), 7.46-7.48 (m, 3H, ArH), 7.75-7.84 (m, 4H, ArH), 7.88-7.90 (d, 1H, ArH, *J=9.2 Hz*), 8.29 (s, 1H, pyrazol proton); ^{13}C NMR: 54.1 (N-CH_2), 63.7 (O-CH_2), 114.8, 117.7, 119.3, 123.0, 124.3, 126.9, 127.4, 127.6, 127.9, 128.3, 128.5, 128.7, 128.9, 129.0, 129.3, 129.6, 129.7, 130.5, 131.3, 131.5, 134.3, 134.7, 136.1, 139.3, 144.2, 152.3, 152.9, 196.2 (C=O); MS: *m/z*=622 $(M+H)^+$; *Anal*. Calc. for $C_{38}H_{28}ClN_5O_2$: C, 73.36; H, 4.54; N, 11.26; Found: C, 73.33; H, 4.51; N, 11.22.

4.3.13. 1-[2-(1-Benzyl-1H-[1,2,3]triazol-4-ylmethoxy)-naphthalen-1-yl]-3-[3-(4-nitro-phenyl)-1-phenyl-1H-pyrazol-4-yl]-propenone (9f): IR (KBr, cm^{-1}) υ_{max}: 1597 (C=N), 1622 (C=O), 3052 (C-H); ^{1}H NMR: δ 5.36 (s, 2H, N-CH_2), 5.39 (s, 2H, O-CH_2), 6.96-7.00 (d, 1H, α-olefinic proton), 7.12-7.13 (m, 2H, ArH), 7.22-7.24 (dd, 4H, ArH, *J=1.8,5.6 Hz*), 7.35-7.48 (m, 6H, ArH), 7.50 (s, 1H, triazol proton), 7.66-7.68 (d, 2H, ArH, *J=8 Hz*), 7.77-7.84 (m, 4H, ArH), 7.88-7.90 (d, 1H, ArH, *J=7.8 Hz*), 8.13-8.15 (d, 2H, ArH, *J=9.2 Hz*), 8.37 (s, 1H, pyrazol proton); ^{13}C NMR: 54.2 (N-CH_2), 63.8 (O-CH_2), 114.8, 118.3, 119.4, 122.7, 123.1, 123.3, 123.8, 124.3, 124.5, 124.6, 127.3, 127.6, 127.7, 127.9, 128.3, 128.7, 128.8, 129.0, 129.3, 129.7, 131.4, 131.7, 134.3, 135.0, 138.5, 139.2, 147.6, 150.8, 152.9, 195.9 (C=O); MS: *m/z*=633 $(M+H)^+$; *Anal*. Calc. for $C_{38}H_{28}N_6O_4$: C, 72.14; H, 4.46; N, 13.28; Found: C, 72.10; H, 4.52; N, 13.24.

4.3.14. 1-[2-(1-Benzyl-1H-[1,2,3]triazol-4-ylmethoxy)-naphthalen-1-yl]-3-(1-phenyl-3-thiophen-2-yl-1H-pyrazol-4-yl)-propenone (9g): IR (KBr, cm^{-1}) υ_{max}: 1589 (C=N), 1621 (C=O), 3062 (C-H); ^{1}H NMR: δ 5.35 (s, 2H, N-CH_2), 5.38 (s, 2H, O-CH_2), 6.95-6.99 (m, 4H, α-olefinic proton & ArH), 7.06-7.11 (m, 2H, ArH), 7.21-7.23 (dd, 4H, ArH, *J=1.8,5.2 Hz*), 7.31-7.52 (m, 5H, ArH), 7.56-7.60 (d, 1H, β-olefinic proton, *J=16 Hz*), 7.78-7.80 (d, 4H, ArH, *J=7.2 Hz*), 7.82-7.84 (d, 1H, ArH, *J=7.6 Hz*), 7.90-7.92 (d, 1H, ArH, *J=9.2 Hz*), 8.27 (s, 1H, pyrazol proton); ^{13}C NMR: 54.1 (N-CH_2), 63.6 (O-CH_2), 114.6, 117.5, 119.2, 119.3, 122.9, 124.3, 124.5, 126.4, 126.7, 127.4, 127.6, 127.7, 127.9, 128.1, 128.6, 128.7, 129.0, 129.3, 129.6, 131.5, 131.6, 134.3, 135.6, 139.1, 144.3, 147.7, 152.8, 196.2 (C=O); MS: *m/z*=594 $(M+H)^+$; *Anal*. Calc. for $C_{36}H_{27}N_5O_2S$: C, 72.83; H, 4.58; N, 11.80; S, 5.40 Found: C, 72.78; H, 4.60; N, 11.81; S, 5.37.

5. Conclusion

We have successfully synthesized 1,4-disubstituted-1,2,3-triazolylchalcones using Click reaction and Claisen-Schmidt condensation under conventional heating and microwave irradiation methods. Click reaction gave better yield in the presence of CuI with triethylamine in DMF under microwave irradiation, when compared to presence $CuSO_4.5H_2O$. Moreover, the microwave irradiation method proved to be environmental friendly, high rate of acceleration and high yielding. The antibacterial and antifungal activity studies revealed that the compounds **5e** and **9f** were exhibited maximum zone of inhibition.

Acknowledgements

The authors are thankful to the Head, Department of Chemistry for providing laboratory facilities and the authors are also thankful to the Director, Central Facilities for Research and Development (CFRD), Osmania University for providing IR and NMR spectral analysis. Financial support from UGC, New Delhi for one of the authors AG is gratefully acknowledged.

References

[1] Cohn, M.L. Epidemiology of Drug Resistance: Implications for a Post- Antimicrobial Era. *Science* **1992**, *257*, 1050-1055.
[2] Tenover, F.C. Mechanisms of Antimicrobial Resistance in Bacteria. *A. J. Med.* **2006**, *119(6A)*, 3-10.
[3] Chopra, I.; Schofield, C.; Everett, M.; O'Neill, A.; Miller, K.; Wilcox, M.; Frere, J.M.; Dawson, M.; Czaplewski, L.; Urleb, U.; Courvalin, P. Treatment of health-care-associated infections caused by gramnegative bacteria: a consensus statement. *Lancet Infect Dis.* **2008**, *8*, 133-139.
[4] Dandale, S.G.; Sonar, A.S.; Solanki, P.R. Antimicrobial Study of 4-(substituted Phenyl)-1H-Imidazol-2(5H)-One/ Thione /Imine. *Int. J. Chem. Environmen and Pharm. Res*. **2012**,*3(1)*, 47-51.
[5] Thompson, L.A.; Ellman, J.A. Synthesis and Applications of Small Molecule Libraries. *Chem. Rev.* **1996**, *96*, 555-600.
[6] Dawood, T.A. Synthesis and Antimicrobial Activity of 1-(4-aryl-2-thiazolyl) - and 1-(4-aryl- 2-oxazolyl)-3,5-diaryl Δ 2 -pyrazoline derivatives. *J. Chem. Pharm. Res.* **2011**, *3(4)*,111-121.
[7] Chandrasekar, P.H.; Manavathu, E. Voriconazole: a second-generation triazole. *E. Drugs Today*, **2001**, *37*, 135.
[8] Sobera, L.A.; Leeson, P.A.; Rabasseda, X.; Castaner, J. Rufinamide Antiepileptic, Treatment of neurogenic pain. *Drug Future*, **2000**, *25(11)*, 1145-1149.
[9] Rogawski, M.A. Diverse mechanisms of antiepileptic drugs in the development pipeline. *Epilepsy Res.*, **2006**, *69*, 273-294.
[10] Stafstrom, C.E. Update on the management of Lennox-Gastaut syndrome with a focus on rufinamide. *Neuropsychiatr. Dis. Treat.*, **2009**, *5*, 547-551.
[11] Soltis, M.J.; Yeh, H.J.; Cole, K.A.; Whittaker, N.; Wersto, R.P.; Kohn, E.C. Identification and characterization of human metabolites of CAI [5-amino-1-1(4'-chlorobenzoyl-3,5-dichlorobenzyl)-1,2,3-triazole- 4-carboxamide). *Drug Metab. Dispos.* **1996**, *24*, 799-806.
[12] Sheng, C.; Zhang, W. New lead structures in antifungal drug discovery. *Curr. Med. Chem.* **2011**, *18*, 733-766.
[13] Higashitani, F.; Hyodo, A.; Ishida, N.; Inoue, M.; Mitsuhashi, S. Inhibition of β-lactamases by tazobactam and in-vitro antibacterial activity of tazobactam combined with piperacillin. *J. Antimicrob. Chemother.* **1990**, *25(4)*, 567-74.
[14] Harold C.N.; Kwung, P.F. Cefatrizine activity compared with that of other cephalosporins. *Antimicrob. Agents Chemother.* **1979,** *15(2)*, 209-212.
[15] Damljanovic, I.; Vukicevic, M.; Radulovic, N.; Palic, R.; Ellmerer, E.; Ratkovic, Z.; Joksovic, M.D.; Vukicevic, R.D. Synthesis and antimicrobial activity of some new pyrazole derivatives containing a ferrocene unit. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 1093-1096.
[16] Bekhit, A.A.; Ashour, H.M.A.; Ghany, Y.S.A.; Bekhit, A.E.A.; Baraka, A.M. Synthesis and anti-inflammatory evaluation of some condensed [4-(3,4-dimethylphenyl)-1(2*H*)-oxo-phthalazin-2-yl]acetic acid hydrazide. *Eur. J. Med. Chem.* **2008**, *43*, 456-463.
[17] Chovatia, P.T.; Akabari, J.D.; Kachhadia, P.K.; Zalawadia, P.D.; Joshi, H.S. Synthesis and selective antitubercular and antimicrobial inhibitory activity of 1-acetyl-3,5-diphenyl-4,5-dihydro-(1*H*)-pyrazole derivatives. *J. Serb. Chem. Soc.* **2007**, *71*, 713-720.

[18] Joksovic, M.D.; Markovic, V.; Juranic, Z.D.; Stanojkovic, T.; Jovanovic, L.S.; Damljanovic, I.S.; Szecsenyi, K.M.; Todorovic, N., Trifunovic, S.;Vukicevic, R.D. Synthesis and selective antitubercular and antimicrobial inhibitory activity of 1-acetyl-3,5-diphenyl-4,5-dihydro-(1*H*)-pyrazole derivatives. *J. Organomet. Chem.* **2009**, *694*, 3935-3942.

[19] Abadi, A.H.; Eissa, A.A.H.; Hassan, G.S. Synthesis of novel 1,3,4-trisubstituted pyrazole derivatives and their evaluation as antitumor and antiangiogenic agents. *Chem. Pharm. Bull.* **2003**, *51*, 838-844.

[20] Rathelot, P.; Azas, N.; El-Kashef, H.; Delmas, F.; Giorgio, C.D.; Timon-David, P.; Maldonado, J.; Vanelle, P. 1,3-Diphenylpyrazoles: synthesis and antiparasitic activities of azomethine derivatives. *Eur. J. Med. Chem.* **2002**, *37*, 671-679.

[21] Hashem, A. I.; Youssef, A. S. A.; Kandeel, K. A.; Abou-Elmagd, W. S. I. Conversion of some 2(3*H*)-furanones bearing a pyrazolyl group into other heterocyclic systems with a study of their antiviral activity. *Eur. J. Med. Chem.* **2007**, *42*, 934-939.

[22] Shetty, S. C.; Bhagat, V. C. Synthesis and pharmacological activities of 3-(4-substituted phenyl)-1-phenyl-1*H*-pyrazole-4-carboxaldehyde and its aldimines derivatives. *Asian J. Chem.* **2008**, *20*, 5037-5045.

[23] Prasad, D.J.; Ashok, M.; Karegoudar, P.; Poojary, B.; Holla, B.S.; Kumari, N. S. Synthesis and antimicrobial activities of some new triazolothiadiazoles bearing 4-methylthiobenzyl moiety. *Eur. J. Med. Chem.* **2009**, *44*, 551-557.

[24] Walczak, K.; Gondela, A.; Suwinski, J. Synthesis and anti-tuberculosis activity of N-aryl-C-nitroazoles. *Eur. J. Med. Chem.* **2004**, *39*, 849-853.

[25] Holla, B.S.; Veerendra, B.; Shivananda, M.K.; Poojary, B. Synthesis characterization and anticancer activity studies on some Mannich bases derived from 1,2,4-triazoles. *Eur. J. Med. Chem.* **2003**, *38*, 759-767.

[26] Amir, M.; Shikha, K. Synthesis and anti-inflammatory, analgesic, ulcerogenic and lipid peroxidation activities of some new 2-[(2,6-dichloroanilino) phenyl]acetic acid derivatives. *Eur. J. Med. Chem.* **2004**, *39*, 535-545.

[27] Almasirad, A.; Tabatabai, S.A.; Faizi, M.; Kebriaeezadeh, A.; Mehrabi, N.; Dalvandi, A.; Shafiee, A. Synthesis and anticonvulsant activity of new 2-substituted-5- [2-(2-fluorophenoxy)phenyl]-1,3,4-oxadiazoles and 1,2,4-triazoles. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 6057-6059.

[28] Masuda, K.; Toga, T.; Hayashi, N. Synthesis of 3-morpholino-N-ethoxycarbonyl sydnonimine-5-^{14}C (sin-10-^{14}C). *J. Labelled Compd.* **1975**, *11*, 301-304.

[29] a) Ashok, D.; Shravani, D. One-pot synthesis of novel Spiro2,3,7,8-tetrahydro-benzo[1,2-*b*:5,4-*b*']-di Pyran-4,6-dione and 2,3,8,9-tetrahydro-benzo[1,2-*b*:4,3-*b*']dipyran-4,10-dione derivatives. *Tetrahedron Lett.* **2008**, *49*, 7227-7229. b) Ashok, D.; Mohan Gandhi, D.; Srinivas, G.; Vikas Kumar, A. Microwave-assisted synthesis of novel 1,2,3-triazole derivatives and their antimicrobial activity. *Med. Chem. Res.* **2014,** *23(6)*, 3005-3018. c) Ashok, D.; Ganesh, A. *Indian J. Heterocycl. Chem.* **2013**, *23*, 1-7.

[30] Rose, S.B.; Miller, R.E. Studies with the Agar Cup-Plate Method, *J. Bacteriol*. **1939**, *38(5)*, 525-537.