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ORIGINAL RESEARCH ARTICLE

Synthesis of 1,2,4-triazol-4-yl)-4-methyl-4-phenyl-3-(phenylamino) methylazetidin-2-one and their Biological Activities

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ABSTRACT

Synthesis of 4-amino-5-substitutedphemyl -4H-1, 2, 4 triazole 3 thiol (1-2), 3-3((3-bromoquinolin-8-yl) thio)-5- subsitutiedphenyl-4H-1, 2, 4-triazol-4-amine (3-4), 3- bromo-8-((5-subsitutedphenyl-4-(2-(1-phenylethylidene)hydrazinyl)-4H-1, 2, 4-triazol-3-yl) thio quinoline (5-6), 1-(3-((3-bromoquinolin-8-yl)thio-5-subsituted phenyl-4H-1, 2, 4 triazol-4-yl)-4-methyl-4-phenylazetidin-2-one (7-8), 3-(3-((3-bromo quinolin-8-yl)thio)-5-substituted phenyl-4H-1, 2, 4-triazol-4-yl) 2-methyl 2-phenylthiazolidin-4-one (9-10), Synthesis of 1-(3-((3-bromoquinolin-8-yl)-5-subsitutedphenyl-4H-1,2,4-triazol-4-yl)-4-methyl-4-phenyl-3-(phenyl amino) methyl) azetidin-2-one (11-16). The synthesized triazole derivatives were evaluated for their antibacterial and antifungal activites at a dose of 250 ug/ml. screening results exhibited; 8 and 15 were found to be most potent bactericidal agents against P. vulgaris and E.coli respectively and also possessed moderate antifungal activity.

Key words: Triazole derivatives, Antibacterial & antifungal activities.

INTRODUCTION

Several triazole derivatives have been reported to possess different biological activities such as antibacterial [1], antifungal [2,3], anti-inflammatory [4] and anticonvulsant activities. Chemical literature survey reveals that triazole quinoline derivatives exhibited both antibacterial and antifungal activities. Furthermore, different derivatives of azetidinone [5-8] and thiazolidinone [9-11] showed antibacterial and antifungal activities. In the light of these observations it was thought worthwhile to synthesize new triazole derivatives by incorporating quinoline azetidinone and thiazolidinone moieties with the hope to get better antibacterial as well as antifungal activites. The structures of these compounds were delineated by elemental analysis, IR, H-^{1}NMR and mass spectroscopy.

Incorporation of 3-bromo-chloro quinoline reacted to substituted triazoles (1-2) resulted in the generation of 3-3((3-bromoquinolin-8-yl) thio)-5-subsitutied phenyl-4H-1, 2, 4-triazol-4-amine 3-4 Reaction of acetophenone to compounds 3-4 yielded 3-bromo-8-((5-subsitutedphenyl-4-(2-(1-phenylethylidene) hydrazinyl)-4H-1, 2, 4-triazol-3-yl) thio quinoline 5-6 which on cyclo condensation to acetyl chloride and thioglycolic acid gave 1-(3-((3-bromo quinolin-8-yl)thio-5-subsituted phenyl-4H-1, 2, 4 triazol-4-yl)-4-methyl-4-phenylazetidin-2-one 7-8 and 3-(3-((3-bromo quinolin-8-yl)thio)-5-substituted phenyl-4H-1, 2, 4-triazol-4-yl) 2-methyl 2-phenylthiazolidin-4-one 9-10 respectively. Compound 7-8 on reaction with formaldehyde and different aromatic amines yielded the mannich products 1-(3-((3-bromoquinolin-8-yl)-5-subsitutedphenyl-4H-1,2,4-triazol-4-yl)-4-methyl-4-phenyl-3-(phenylamino) methyl) azetidin -2-one 11-16.

MATERIALS AND METHODS

The melting points of the compounds were determined in open glass capillaries with the help of thermonic melting point apparatus and are uncorrected. The homogeneity of all the newly synthesized compounds was routinely checked by thin layer chromatography (TLC) on silica gel G plates and spots were located by using iodine chamber. Elemental analysis (C,H,N) of all the synthesized compounds were determined by Perkin-Elmer 2400 elemental analyzer, and results were found within the $\pm$ 0.4% of theoretical values. Infra red (IR) spectra were recofed in KBr on Perkin Elmer-Spectrum RX-I, spectrometer

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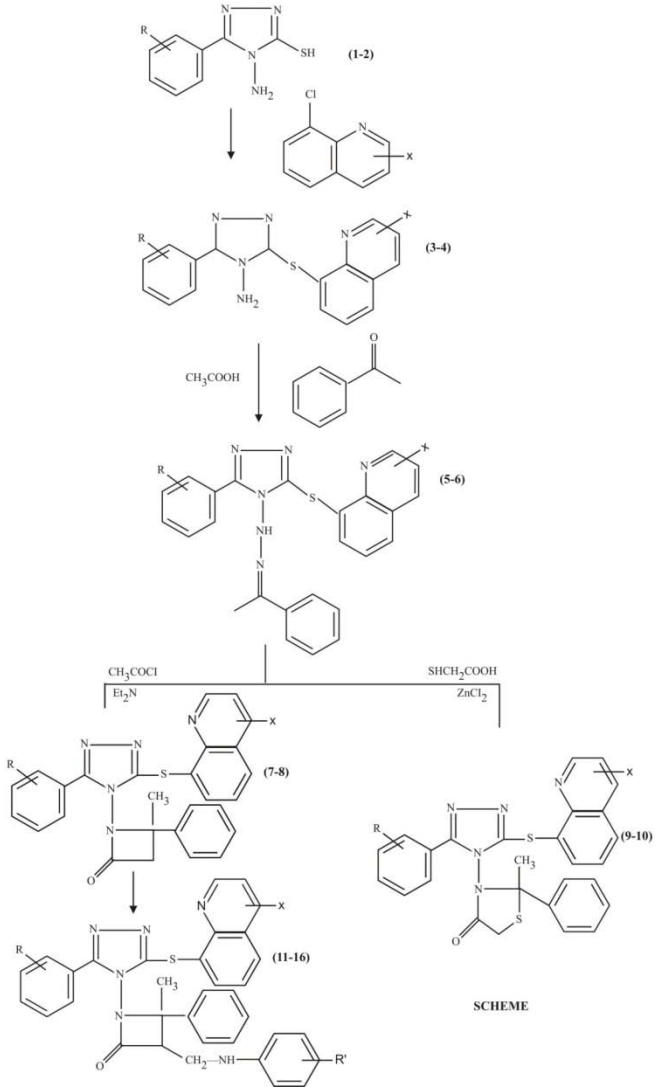
and V_{max} was recorded in cm^{-1}. ^1H NMR spectra were record by Bruker AC-300 F instrument using a mixture of $CDC1_3$ & DMSO-d_6 as solvent and tetramethylsilane (TMS) as internal reference standard. All chemical shift values were recorded as δ (ppm.) Mass spectra were determined on VG-70-S instrument.



Synthesis of 4-amino-5-substitutedphemyl -4H-1, 2, 4 triazole 3-thiol (1-2):

In a methanolic solution of aromatic acid hydrazides (.01 mole), potassium hydroxide (.015 mole) and carbon disulfide (.01 more) were added and the obtained mixture was stirred vigorously for 2 hrs. After stirring excess of hydrazine hydrate was added and the mixture was further refluxed for 4h. The completion of the reaction was checked by TLC. The cooled reaction mixture was poured into ice water and neutralized with concentrate HC1. Thus obtained product was filtered, washed with water, dried and recrystallized from appropriate solvents to afford compounds 1-2.

Physical, analytical and spectral analysis are given below-

Compound 1: 4-amino-5-phemyl-4H-1, 2, 4 triazole 3-thiol.

Yield: 72%, m.p.:143^{o}C; r.s.: Methanol; IR (KBr) (cm^{-1}): 1290 (N-N), 1525 (C-N), 1610 (C⎓C of aromatic ring), 1680 (C=N), 2710 (SH), 3140 (C-H aromatic), 3230 (NH_2),^{1}H-NMR ($CDCl_3$+DMSO-d_6) δ (ppm): 5.985 (bs, 2H, NH_2-N exchangeable with D_2O), 6.898-7.060 (m, 5H, ArH) 11.380 (bs, 1H, SH), MS: $[M]^+$ at m/z 192, Anal. Calcd. for $C_8H_8N_4S$: C, 50.00; H, 4.16; N, 29.16: Found: C, 50.12; H, 4.18; N, 29.25%.

Compound 2: 3-(4-amino-5-mercapto-4H-1, 2, 4 triazol-3-yl) phenol.

Yield: 68%, m.p.:158^{o}C; r.s.: ethanol-water; IR (KBr) (cm^{-1}): 1520 (C-N), 1610 (C⎓C of aromatic ring), 1290 (N-N), 1685 (C=N), 2715 (SH), 3145 (C-H aromatic), 3235 (NH_2), 3420 (OH). ^{1}H-NMR ($CDCl_3$+DMSO-d_6) δ (ppm): 5.972 (bs, 2H, NH_2-N exchangeable with D_2O), 6.900-7.032 (m, 4H, ArH) 11.372 (bs, 1H, SH), 12.537 (ss, 1H, OH-Ar exchangeable with D_2O), MS: $[M]^+$ at m/z 208, Anal. Calcd. for $C_8H_8N_4SO$: C, 46.15; H, 3.84; N, 26.92: Found: C, 46.28; H, 3.86; N, 26.99%.

Synthesis of 3-3((3-bromoquinolin-8-yl) thio)-5-subsitutiedphenyl-4H-1, 2, 4-triazol-4-amine (3-4):

The equimolar mixture (.01 mole) of compounds 1-2 and 3-bromo-8-chloro quinoline in methanol (50 ml) was refluxed for 7h. The completion of the reaction was checked by TLC and excess of methanol distilled off. Thus obtained residual mass was poured into ice water, filtered, washed, dried and recrystallized from appropriate solvents to yield compounds 3-4.

Physical, analytical and spectral analysis of the synthesis compounds (3-4) are given as-

Compound 3: 3((3-bromoquinolin-8-yl) thio)-5-phenyl-4H-1, 2, 4-triazol-4-amine.

Yield: 65%, m.p.:170^{o}C; r.s.: methanol; IR (KBr) (cm^{-1}): 575(C-Br), 690 (C-S-C), 1285 (N-N), 1518 (C-N), 1615 (C⎓C of aromatic ring), 1690 (C=N), 3142 (C-H aromatic), 3232 (NH_2). ^{1}H-NMR ($CDCl_3$+DMSO-d_6) δ (ppm): 5.964 (bs, 2H, NH_2-N exchangeable with D_2O), 6.885-7.055 (m, 4H, ArH), 8.221-8.280 (t, $1H_2$, ArH), 8.316-8.354 (t, $1H_7$, ArH), 8.521-8.562 (d, $1H_3$, ArH), 7.790-8.830 (t, $1H_6$, ArH), 8.839-8.876 (d, $1H_5$, ArH), 9.125 (s, $1H_4$, ArH), MS: $[M]^+$ at m/z 398, Anal. Calcd. for $C_{17}H_{12}BrN_5S$: C, 51.27; H, 3.04; N, 17.58: Found: C, 51.40; H, 3.05; N, 17.65%.

Compound 4: 3-(4-amino-5-((3-bromoquinolin-8-yl) thio-4H-1, 2, 4-triazol-3-yl) phenol.

Yield: 62%, m.p.:185°C; r.s. : DMF-water; IR (KBr) (cm^{-1}): 570 (C-Br), 685 (C-S-C), 1290 (N-N), 1520 (C-N), 1612 (C=C of aromatic ring), 1682 (C=N), 3245 (NH_2), 3422 (OH), ^{1}H-NMR ($CDCl_3$+DMSO-d_6) δ (ppm): 5.944 (bs, 2H, NH_2-N exchangeable with D_2O), 6.882-7.041 (m, 4H, ArH), 8.218-8.273 (t, $1H_2$, ArH), 8.312-8.355 (t, $1H_7$, ArH), 8.520-8.552 (d, $1H_3$, ArH), 8.794-8.850 (t, $1H_6$, ArH), 8.841-8.876 (d, $1H_5$, ArH), 9.129 (s, $1H_4$, ArH), MS: $[M]^+$ at m/z 414, Anal. Calcd. for $C_{17}H_{12}BrN_5OS$: C, 49.29; H, 2.92; N, 16.90: Found: C, 49.40; H, 3.93; N, 16.95%.

Synthesis of 3- bromo-8-((5-subsitutedphenyl-4-(2-(1-phenylethyl -idene) hydrazinyl)-4H-1, 2, 4-triazol-3-yl) thio quinoline (5-6):

A methanolic solution, of compounds 3-4 (.01mole) with acetophenone (.01mole) in presence of a few drops of glacial acetic acid was refluxed for 3h. The completion of the reaction was checked by TLC. Excess of methanol was removed by distillation, reacted mixture poured into ice water, filtered, washed with water, dried, triturated with petroleum ether (50-60°C) and recrystallized from appropriate solvents to afford compounds (5-6).

Physical, analytical and spectral data are given as-

Compound 5: 3-bromo-8-((5-phenyl-4-(2-(1-phenyl-ethylidene) hydrazinyl)-4H-1, 2, 4-triazol-3-yl) thio quinoline.

Yield: 67%, m.p.:197°C; r.s.: DMF-water; IR (KBr) (cm^{-1}): 575(C-Br), 690 (C-S-C), 1288 (N-N), 1524 (C-N), 1610 (C=C of aromatic ring), 1680 (C=N), ^{1}H-NMR ($CDCl_3$+DMSO-d_6) δ (ppm): 2.212 (s, 3H, CH_3-C=N) 6.690-7.568 (m, 10H, ArH), 8.236-8.258 (t, $1H_2$, ArH), 8.302-8.346 (t, $1H_7$, ArH), 8.523-8.560 (d, $1H_3$, ArH), 8.826-8.846 (d, $1H_5$, ArH), 8.790-8.852 (t, $1H_6$, ArH), 9.132 (s, $1H_4$, ArH), MS: $[M]^+$ at m/z 515, Anal. Calcd. for $C_{25}H_{19}BrN_6S$: C, 58.26; H, 3.72; N, 16.30: Found: C, 58.35; H, 3.73; N, 16.35%.

Compound 6*:* 3-(5((3-bromoquinolin-8-yl)thio)-)-4-(2-(1-phenyl-ethylidene) hydrazinyl)-4H-1, 2, 4-triazol-3-yl) phenol.

Yield: 64%, m.p.:205°C; r.s.: methanol; IR (KBr) (cm^{-1}): 572 (C-Br), 688 (C-S-C), 1285 (N-N), 1520 (C-N), 1612 (C=C of aromatic ring), 1682 (C=N), 3420 (OH), ^{1}H-NMR ($CDCl_3$+DMSO-d_6) δ (ppm): 2.241 (s, 3H, CH_3-C) 6.569-7.246 (m, 8H, ArH), 8.241-8.276 (t, $1H_2$, ArH), 8.310-8.342 (t, $1H_7$, ArH), 8.536-8.568 (d, $1H_2$, ArH), 8.818-8.851 (d, $1H_5$, ArH), 8.798-8.864 (t, $1H_6$, ArH), 9.127 (s, $1H_4$, ArH), 12.514 (ss, 1H, Ar-OH exchangeable with D_2O),MS: $[M]^+$ at m/z 531, Anal. Calcd. for $C_{25}H_{19}BrN_6OS$: C, 56.50; H, 3.60; N, 15.81: Found: C, 56.60; H, 3.61; N, 15.88%.

Synthesis of 1-(3-((3-bromoquinolin-8-yl) thio-5-subsitutedphenyl-4H-1, 2, 4 triazol-4-yl)-4-methyl-4-phenylazetidin-2-one (7-8):

To the solution of compounds 5-6 (.01mole) was taken in DMF (50 ml), acetyl chloride (.01 mole) added dropwise in presence of triethylamine at 0-5°C and the reaction mixture stirred constantly for 6h. The completion of the reaction was checked by TLC and the precipitated amine hydrochloride filtered out. The filtrate was concentrated under reduced pressure and poured in cold water. The solid thus obtained was recrystallized from appropriate solvents to yield compounds (7-8).

Physical, analytical and spectral analysis are given as-

Compound 7: 1-(3-((3-bromoquinolin-8-yl) thio-5-phenyl-4H-1, 2, 4 triazol-4-yl)-4-methyl-4-phenylazetidin-2-one.

Yield: 60%, m.p.:211°C; r.s.: ethanol; IR (KBr) (cm^{-1}): 570(C-Br), 685 (C-S-C), 1290 (N-N), 1522 (C-N), 1615 (C=C of aromatic ring), 1685 (C=N), 1720 (C=O of β-lactam ring), 3142 (C-H aromatic), ^{1}H-NMR ($CDCl_3$+DMSO-d_6) δ (ppm): 2.262 (s, 3H, CH_3) 4.115 (s, 2H, CH_2-C=O), 7.310-6.928 (m, 9H, ArH), 8.217-8.251 (t, $1H_2$, ArH), 8.287-8.326 (t, $1H_7$, ArH), 8.436-8.468 (d, $1H_3$, ArH), 8.728-8.764 (t, $1H_6$, ArH), 8.815-8.846 (d, $1H_5$, ArH), 12.128 (s, $1H_4$, ArH), MS: $[M]^+$ at m/z 542, Anal. Calcd. for $C_{27}H_{20}BrN_5OS$: C, 59.78; H, 3.72; N, 12.91: Found: C, 59.80; H, 3.73; N, 12.96%.

Compound 8: 1-(3-((3-bromoquinolin-8-yl) thio-5-(3-hydroxyphenyl) 4H-1, 2, 4 triazol-4-yl)-4-methyl-4-phenylazetidin-2-one.

Yield: 55%, m.p.:220°C; r.s.: methanol; IR (KBr) (cm^{-1}): 572 (C-Br), 690 (C-S-C), 1295 (N-N), 1524 (C-N), 1612 (C=C of aromatic ring), 1682 (C=N), 1725 (C=O of β-lactam ring), 3140(C-H aromatic), 3420 (OH), ^{1}H-NMR ($CDCl_3$+DMSO-d_6) δ (ppm): 2.260 (s, 3H, CH_3) 4.120 (s, 2H, CH_2-C=O), 6.648-7.420 (m, 8H, ArH), 8.215-8.247 (t, $1H_2$, ArH), 8.290-8.330 (t, $1H_7$, ArH), 8.435-8.460 (d, $1H_3$, ArH), 8.718-8.756 (t, $1H_6$, ArH), 8.820-8.850 (d, $1H_5$, ArH), 9.134 (s, $1H_4$, ArH), 12.507 (ss, 1H, Ar-OH exchangeable with D_2O), MS: $[M]^+$ at m/z 558, Anal. Calcd. for $C_{27}H_{20}BrN_5O_2S$: C, 58.07; H, 3.61; N, 12.54: Found: C, 58.20; H, 3.62; N, 12.60%.

Synthesis of 3-(3-((3-bromoquinolin-8-yl)thio)-5-substitutedphenyl-4H-1,2,4-triazol-4-yl) 2-methyl 2-phenyl thiazolidin-4-one (9-10).

Thioglycolic acid (.01 mole) and a pinch of anhydrous $ZnC1_2$ was added to a methanolic solution of compounds 5-6 (.01 mole). The reaction mixture was refluxed for 9h. and completion of the reaction was checked by TLC. Excess of solvent was removed by distilation. The reaction mixture was diluted with cold crushed ice water, filtered, washed, dried and recrystallized from appropriate solvents to afford compounds (9-10).

Physical, analytical and spectral are given as-

Compound 9*:* 3-(3-((3-bromoquinolin-8-yl)thio)-5-phenyl-4H-1, 2, 4-triazol-4-yl) 2-methyl 2-phenyl thiazolidin-4- one.

Yield: 58%, m.p.:190^oC; r.s.: DMF-water; IR (KBr) (cm^{-1}): 575 (C-Br), 688 (C-S-C), 1292 (N-N), 1520 (C-N), 1610 (C=C of aromatic ring), 1680 (C=N), 1719 (C=O of β-lactam ring), 3140 (C-H aromatic), ^{1}H-NMR ($CDCl_3$+DMSO-d_6) δ (ppm): 2.251 (s, 3H, CH_3) 4.236 (s, 2H,S- CH_2), 6.610-7.387 (m, 9H, ArH), 8.224-8.252 (t, $1H_2$, ArH), 8.248-8.326 (t, $1H_7$, ArH), 8.438-8.462 (d, $1H_3$, ArH), 8.723-8.761 (t, $1H_6$, ArH), 8.816-8.847 (d, $1H_5$, ArH), 9.121 (s, $1H_4$, ArH), MS: $[M]^+$ at m/z 574, Anal. Calcd. for $C_{27}H_{20}BrN_5OS_2$: C, 56.45; H, 3.51; N, 12.19: Found: C, 56.55; H, 3.53; N, 12.25%.

Compound 10: 3-(3-((3-bromoquinolin-8-yl)thio)-5-(3-hydroxyphenyl) -4H-1, 2, 4-triazol-4-yl) 2-methyl 2-phenyl thiazolidin-4- one.

Yield: 53%, m.p.:210^oC; r.s.: DMF-water; IR (KBr) (cm^{-1}): 575 (C-Br), 685 (C-S-C), 1290 (N-N), 1523 (C-N), 1612 (C=C of aromatic ring), 1682 (C=N), 1725 (C=O of β-lactam ring), 3142 (C-H aromatic ring), 3422 (OH), ^{1}H-NMR ($CDCl_3$+DMSO-d_6) δ (ppm): 2.251 (s, 3H, CH_3) 4.126 (s, 2H, CH_2-S), 6.695-7.318 (m, 8H, ArH), 8.218-8.250 (t, $1H_2$, ArH), 8.290-8.324 (t, $1H_7$, ArH), 8.447-8.470 (d, $1H_3$, ArH), 8.725-8.763 (t, $1H_6$, ArH), 8.814-8.842 (d, $1H_5$, ArH), 9.132 (s, $1H_4$, ArH). 12.524 (ss,1H, Ar-OH exchangeable with D_2O), MS: $[M]^+$ at m/z 590, Anal. Calcd. for $C_{27}H_{20}$ $BrN_5O_2S_2$: C, 54.92; H, 3.41; N, 11.86: Found: C, 54.84; H, 3.42; N, 11.94%.

Synthesis of 1-(3-((3-bromoquinolin-8-yl)-5-subsitutedphenyl-4H-1, 2, 4-triazol-4-yl)-4-methyl-4-phenyl-3-(phenylamino)methyl) azetidin-2-one (11-16):

Compounds 7-8 (.01mole) dissolved in methanol (50ml) and various substituted aromatic amines (.01 mole) were added dropwise in presence of glacial acetic acid. This reaction mixture was allowed to reflux for 5h. The completion of the reaction was checked by TLC. Excess of methanol was distilled off, residual mass poured into ice-cold water, filtered, washed, dried and recrystallized from appropriate solvents to obtain compounds 11-16.

Physical, analytical and spectral analysis of the above prepared compounds (11-16) are given as-

Compound 11: 1-(3-((3-bromoquinolin-8-yl)-5-phenyl-4H-1,2,4-triazol-4-yl)-4-methyl-4-phenyl-3-(phenylamino)methyl)azetidin-2-one.

Yield: 50%, m.p.:227^oC; r.s.: methanol; IR (KBr) (cm^{-1}): 570 (C-Br), 690 (C-S-C), 1292 (N-N), 1525 (C-N), 1615 (C=C of aromatic ring), 1685 (C=N), 1720 (C=O of β-lactam ring), 3140 (C-H aromatic ring), 3320 (NH), ^{1}H-NMR ($CDCl_3$+DMSO-d_6) δ (ppm): 2.246 (s, 3H, CH_3) 3.702-3.750 (t, 1H, β-lacstam ring), 3.654 (d, 2H, CH_2NH), 4.875 (bs, 1H, NH-Ar exchangeable with D_2O), 7.060-8.228 (m, 14H, ArH), 8.234-8.266 (t, $1H_2$, ArH), 8.289-8.320 (t, $1H_7$, ArH), 8.442-8.464 (d, $1H_3$, ArH), 8.723-8.750 (t, $1H_6$, ArH), 8.812-8.840 (d, $1H_5$, ArH), 9.127 (s, $1H_4$, ArH), MS: $[M]^+$ at m/z 647, Anal. Calcd. for $C_{34}H_{27}BrN_6OS$: C, 63.06; H, 4.20; N, 12.98: Found: C, 63.20; H, 4.22; N, 12.90%.

Compound 12: 1-(3-((3-bromoquinolin-8-yl)-5-phenyl-4H-1, 2, 4-triazol-4-yl)-3-((2-chlorophenyl) amino) methyl-4-phenylazetidin-2-one.

Yield: 56%, m.p.:215^oC; r.s.: ethanol; IR (KBr) (cm^{-1}): 572 (C-Br), 670 (C-C1), 692 (C-S-C), 1295 (N-N), 1522 (C-N), 1612 (C=C of aromatic ring), 1682 (C=N), 1725 (C=O of β-lactam ring), 3142 (C-H aromatic), 3322 (NH), ^{1}H-NMR ($CDCl_3$+DMSO-d_6) δ (ppm): 2.62 (s, 3H, CH_3) 3.628-3.650 (d, 2H, CH_2NH), 3.695-3.748 (t, 1H, β-lacstam ring), 4.882 (bs, 1H, NH-Ar exchangeable with D_2O), 6.857-8.194 (m, 13H, ArH), 8.221 (t, $1H_2$, ArH), 8.296-8.326 (t, $1H_7$, ArH), 8.440-8.463 (d, $1H_3$, ArH), 8.722-8.750 (t, $1H_6$, ArH), 8.818-8.843 (d, $1H_5$, ArH), 9.125 (s, $1H_4$, ArH), MS: $[M]^+$ at m/z 682**,** Anal. Calcd. for $C_{34}H_{26}BrClN_6OS$: C, 59.87; H, 3.84; N, 12.32: Found: C, 59.98; H, 3.85; N, 12.39%.

Compound 13: 1-(3-((3-bromoquinolin-8-yl)-5-phenyl-4H-1, 2, 4-triazol-4-yl)-3-((3-chlorophenyl) amino)methyl-4-phenylazetidin-2-one.

Yield: 60%, m.p.:238^oC; r.s.: ethanol; IR (KBr) (cm^{-1}): 575(C-Br), 675 (C-Cl), 690 (C-S-C), 1292

(N-N), 1524 (C-N), 1615 (C=C of aromatic ring), 1685 (C=N), 1720 (C=O of β-lactam), 3140 (C-H aromatic), 3325 (NH), ^{1}H-NMR ($CDCl_3$+DMSO-d_6) δ (ppm): 2.258 (s, 3H, CH_3) 3.627-3.652 (d, 2H, CH_2NH), 3.700-3.742 (t, 1H, β-lactam ring), 4.876 (bs, 1H, NH-Ar), 6.862-8.150 (m, 13H, ArH), 8.220-8.254 (t, $1H_2$, ArH), 8.294-8.329 (t, $1H_7$, ArH), 8.439-8.460 (d, $1H_3$, ArH), 8.718-8.752 (t, $1H_6$, ArH), 8.815-8.840 (d, $1H_5$, ArH), 9.125 (s, $1H_4$, ArH), MS: $[M]^+$ at m/z 682, Anal. Calcd. for $C_{34}H_{26}BrClN_6OS$: C, 59.87; H, 3.84; N, 12.32: Found: C, 59.96; H, 3.82; N, 12.25%.

Compound 14: 1-(3-((3-bromoquinolin-8-yl)-5-phenyl-4H-1, 2, 4-triazol-4-yl)-4-methyl-4-phenyl-3-(phenylamino) methyl) azetidin-3-one.

Yield: 64%, m.p.:222^{o}C; r.s.: DMF-water; IR (KBr) (cm^{-1}): 570 (C-Br),692 (C-S-C), 1295 (N-N), 1525 (C-N), 1612 (C=C of aromatic ring), 1682 (C=N), 1725 (C=O of β-lactam), 3142 (C-N aromatic), 3320 (NH), 3420 (OH), ^{1}H-NMR ($CDCl_3$+DMSO-d_6) δ (ppm): 2.250 (s, 3H, CH_3) 3.664-3.637 (d, 2H, CH_2NH), 3.746 (s, 1H, CH of β-lacstam), 4.870 (bs, 1H, NH-Ar exchangeable with D_2O), 7.620-7.278 (m, 13H, ArH), 8.253-8.224 (t, $1H_2$, ArH), 8.330-8.297 (t, $1H_7$, ArH), 8.462-8.440 (d, $1H_3$, ArH), 8.748-8.712 (t, $1H_6$, ArH), 8.848-8.817 (d, $1H_5$, ArH), 9.120 (s, $1H_4$, ArH), 12.512 (ss, 1H, Ar-OH exchangeable with D_2O), MS: $[M]^+$ at m/z 663, Anal. Calcd. for $C_{34}H_{24}BrN_6O_2S$: C, 61.54; H, 4.10; N, 12.66: Found: C, 61.65; H, 4.11; N, 12.72%.

Compound 15: 1-(3-((3-bromoquinolin-8-yl)-5-phenyl-4H-1, 2, 4-triazol-4-yl)-3-((2-chlorophenyl) amino) methyl-4-phenylazetidin-2-one.

Yield: 62%, m.p.:230^{o}C; r.s.: DMF-water; IR (KBr) (cm^{-1}): 572 (C-Br), 675 (C-C1), 695 (C-S-C), 1292 (N-N), 1524 (C-N), 1610 (C=C of aromatic ring), 1680 (C=N), 1725 (C=O of β-lactam), 3140 (C-H aromatic), 3322 (NH), ^{1}H-NMR ($CDCl_3$+DMSO-d_6) δ (ppm): 2.257 (s, 3H, CH_3) 3.638-3.668 (d, 2H, CH_2-NH-AR), 3.779-3.700 (s, 1H, CH of β-lacstam ring), 4.874 (bs, 1H, NH-Ar exchangeable with D_2O), 6.892-8.194 (m, 12H, ArH), 8.224-8.255 (t, $1H_2$, ArH), 8.298-8.330 (t, $1H_7$, ArH), 8.441-8.464 (d, $1H_3$, ArH), 8.716-8.751 (t, $1H_6$, ArH), 8.820-8.852 (d, $1H_5$, ArH), 9.124 (s, $1H_4$, ArH), 12.510 (ss, 1H, Ar-OH exchangeable with D_2O), MS: $[M]^+$ at m/z 698, Anal. Calcd. for $C_{34}H_{26}BrClN_6O_2S$: C, 58.50; H, 3.75; N, 12.04: Found: C, 58.60; H, 3.77; N, 12.10%.

Compound 16:1-(3-((3-bromoquinolin-8-yl)-5-phenyl-4H-1,2,4-triazol-4-yl)-3-((3-chlorophenyl) amino) methyl-4-phenylazetidin-2-one.

Yield: 57%, m.p.:219^{o}C; r.s.: ethanol; IR (KBr) (cm^{-1}): 575 (C-Br), 679 (C-Cl), 690 (C-S-C), 1295 (N-N), 1524 (C-N), 1615 (C=C of aromatic ring), 1682 (C=N), 1725 (C=O of β-lactam ring), 3142 (C-H aromatic), 3320 (NH), ^{1}H-NMR ($CDCl_3$+DMSO-d_6) δ (ppm): 2.253 (s, 3H, CH_3), 3.635-3.662 (d, 2H, CH_2-NH), 3.712-3.754 (t, 1H, CH of β-lactam), 4.877 (bs, 1H, NH-Ar exchangeable with D_2O), 6.900-8.078 (m, 12H, ArH), 8.225-8.258 (t, $1H_2$, ArH), 8.300-8.338 (t, $1H_7$, ArH), 8.448-8.470 (d, $1H_3$, ArH), 8.726-8.762 (s, $1H_6$, ArH), 8.825-8.856 (d, $1H_5$, ArH), 9.128 (s, $1H_4$, ArH), 12.527 (ss, 1H, HO-Ar exchangeable with D_2O), MS: $[M]^+$ at m/z 698, Anal. Calcd. for $C_{34}H_{26}BrClN_6O_2S$: C, 58.50; H, 3.75; N, 12.04: Found: C, 58.42; H, 3.74; N, 12.12%.

RESULTS AND DISCUSSION

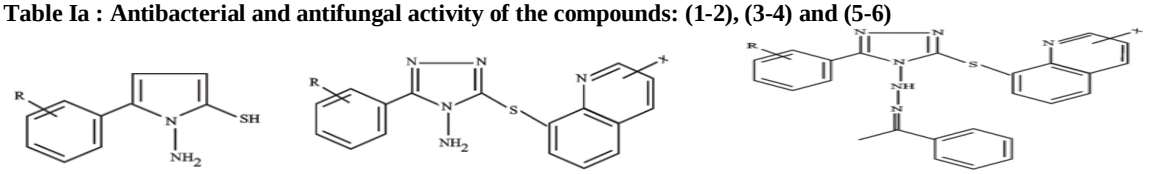
Various substituted derivatives of triazoles were synthesized and screened for their antibacterial as well as antifungal activity. Screening results are given in (**Table Va-Vc**).

Compound 4-amino 5- substituted phenyl-4H-1,2,4 triazole 3-thiol (1 and 2) on screening was found less active against different bacterial and fungal species. Substitution with OH group at 2nd position of phenyl ring in compound 2 enhanced the potency. Substituted triazoles (1 and 2) were incorporated with 3-bromo-8- chloro quinoline via –S- linkage and as a result obtained quinoline moiety bearing triazoles (3-4), exhibited good antibacterial and antifungal activity. The derivatives having –OH group at 2nd position of phenyl ring in compounds 4 and 6 showed more and wide spectrum off antibacterial as well as antifungal activity. Conversion of quinoline moiety bearing triazoles (3-4) into 3- bromo-8-((5-subsitutedphenyl-4-(2-(1-phenylethyl -idene) hydrazinyl)-4H-1, 2, 4-triazol-3-yl) thio quinoline (5-6) showed more potency against various strains of used pathogens. The compound 6 which have –OH group at 2-position of phenyl ring exhibited different range of inhibition zones by ranging as 12 mm for S. aureus, 25 mm for E.coli, 15 mm for P. vulgaris, 12 mm for C. albicans, 16 mm for C. albicans ATCC, 8 mm for C. Krusei respectively. The results on comparing revealed that compound 6 possessed (i.z. 25 mm) maximum efficacy in comparison to gattifloxacin (i.z. 22 mm) as standard drugs against E.coli.

Incorporation of β-lactam ring into compounds (5 and 6) enhanced antibacterial and antifungal activity respectively. But between these two congeners –OH group bearing at 2nd position in phenyl ring (compound 8) is more potent than compound 7. Compound 8 had a high efficacy in P. vulgaris (i.z. 28 mm) comparatively to parent compound (6). Thialactam bearing derivatives (Compound 9 and 10) have shown high antifungal activity in comparison to antibacterial activity. As compound (10) having –OH group at 2nd position of phenyl ring showed more potency and a wide range of biological activity against various reported species of bacteria and fungi.

Compounds 11-16 which are mannich products of parent compound (7-8) possessed a high bactericidal property but its wide spectrum reduced in case of bacteria. Among these synthesized derivatives, compounds 13 and 14 showed a moderate wide zone of inhibition as 15 mm for S. aureus, 17 mm for E.coli, 14 mm for C. albicans, 10 mm for C. albicans ATCC and 12 mm for S. aureus, 15 mm for K. pneumoniae, 8 mm for C. albicans, 12 mm for C. albicans ATCC, 12 mm for C. Krusei respectively. Compounds 12 and 16 bearing – C1 substitution in phenyl ring at 2nd position and Chloro substitution at 4- position showed i.z. of 20 mm against S. aureus.

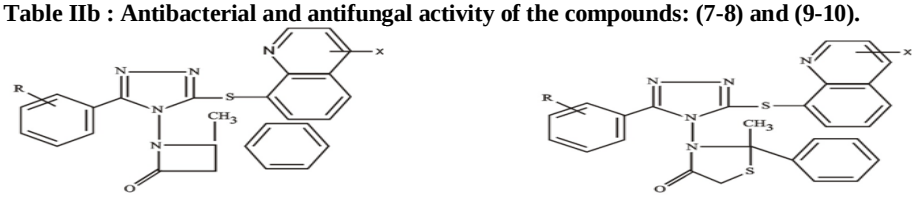
Table Ia : Antibacterial and antifungal activity of the compounds: (1-2), (3-4) and (5-6)



(1-2) **(3-4)** **(5-6)**

Comp. No.	R	X	Antibacterial activity				Antifungal activity			
			S.aureus	*E. coli*	*P. vulgaris*	*K. pneumoniae*	*A. fumigatus*	*C.albicans*	*C.albicans ATCC*	*C.Krusei G03*
1	H	-	-	-	-	5 mm	-	6 mm	-	-
2	2-OH	-	-	-	-	10 mm	-	8 mm	6 mm	-
3	H	Br	-	-	10 mm	-	-	10 mm	8 mm	-
4	2-OH	Br	6 mm	12 mm	-	-	-	6 mm	12 mm	-
5	H	Br	-	12 mm	-	-	6 mm	-	-	-
6	2-OH	Br	12 mm	25 mm	15 mm	-	-	12 mm	16 mm	8 mm

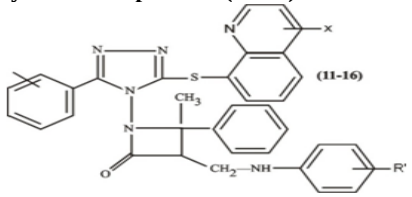
Table IIb : Antibacterial and antifungal activity of the compounds: (7-8) and (9-10).



(7-8) **(9-10)**

Comp. No.	R	X	Bacterial growth inhibition (diameter)				Fungal growth inhibition (diameter)			
			S.aureus	*E. coli*	*P. vulgaris*	*K. pneumoniae*	*A. fumigatus*	*C.albicans*	*C. albicans ATCC*	*C.Krusei G03*
7	H	Br	5 mm	14 mm	-	-	-	16 mm	-	8 mm
8	2-OH	Br	10 mm	20 mm	28 mm	-	16 mm	15 mm	12 mm	-
9	H	Br	5 mm	-	-	-	6 mm	10 mm	12 mm	-
10	2-OH	Br	14 mm	18 mm	16 mm	-	-	26 mm	18 mm	17 mm

Table IIIc : Antibacterial and antifungal activity of the compounds: (11-16).



Comp. No	R	R'	X	Bacterial growth inhibition (diameter)				Fungal growth inhibition (diameter)			
				S.aureus	*E. coli*	*P. vulgaris*	*K. pneumoniae*	*A. fumigatus*	*C.albicans*	*C. albicans ATCC*	*C.Krusei G03*
11	H	H	Br	-	-	-	-	-	-	-	-
12	H	2-C1	Br	20 mm	-	-	16 mm	9 mm	-	-	-
13	H	4-Cl	Br	15 mm	17 mm	-	-	-	14 mm	10 mm	-
14	2-OH	H	Br	12 mm	-	-	15 mm	-	8 mm	12 mm	12 mm
15	2-OH	2-C1	Br	18 mm	18 mm	-	-	-	-	-	-
16	2-OH	4-Cl	Br	20 mm	-	-	-	-	-	-	-
Ampicillin		20 mm		18 mm	18 mm	14 mm	-	-	-	-	-
Gattifloxacin		25 mm		22 mm	20 mm	21 mm	-	-	-	-	-
Fluconazole		-		-	-	-	-	-	29 mm	25 mm	19 mm

CONCLUSION

On the basis of structure activity relationship, it is concluded-

1. 2-hydroxy substituted triazole derivatives showed more efficacy.
2. Incorporation of acetophenone is beneficial for antibacterial activity against *E.coli* and *P. vulgaris*.
3. Incorporation of β-lactam moiety increase antibacterial and antifungal spectrum.
4. The derivatives bearing β-thialactam are reponsible for regular potent antifungal inhibition.
5. Formation of mannich products exhibited a decrease in antibacterial as well as antifungal activity.
6. Compound 10 was found potent antifungal of this scheme against *C.albicans* and its efficacy was closer to standard drug fluconazole.
7. It is interesting to mention that compound 6 and 8 possess high efficacy against *E.coli* in comparison to standard drug cephalexin and gattifloxacin which is further supported by enclosing photographs.

Biological activity:

Antibacterial activity

The Cup-Plate Method given by Chuinckshank *et al.*[13] Nutrient agar was poured onto the sterlized petri dsihes (20-25 mL each pertri dish). The poured material was allowed to set
(1-1.5h) and thereafter the "CUPS" (10 mm diameter) were made by punching into the agar surface with a sterile cork borer and scooping out the punched part of the agar. Into these cups the test compound solution was added with the help of sterile syringe. The plates were incubated at 37^{o}C for 48 h and the results were noted. A solvent control (10% DMSO in methanol) was also run to not the activity of the blank (solvent). The above said standard drugs were also screened under similar conditions for comparison.

Antifungal activity

For antifungal screening, spore suspension (5mL) of each test organisms (72 h culture) was added to sterilised Sabouraud dextrose agar (Himedia Lab. Ltd., Mumbai) medium at 35-40^{o}C by thorough shaking. The peteri dishes were seeded with the mixture and the paper discs of the methanolic solution of compound and the reference antibiotic (Fluconazole) as the control was placed in the same manner as in antibacterial activity determination. These petri dishes were incubated at 30^{o}C for 48h. The zone of inhibition was considered as an indicator the antifungal activity.

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