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Synthesis and Antibacterial evaluation of N-(2-(1-Aryl-1H-1,2,3-triazol-4-yl) propan-2-yl)benzene sulfonamides

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Abstract: A series of twenty four sulfonamide linked disubstituted 1,2,3-triazoles wasdesigned and synthesized via click reaction using 4-substituted-N-(2-methylbut-3-yn-2-yl)benzenesulfonamidesand aromatic azides. The structures of all the synthesized compounds were confirmed by various spectral techniques as FTIR, ^{1}HNMR, ^{13}C NMR and HRMS. The antibacterial activity of the targeted compounds was evaluated against K. pneumoniae, E. coli, B. subtilis andS. aureusstrains, the data showed that most of the triazoles exhibited moderate to good results.

Key-words: Click synthesis, Disubstituted 1,2,3-triazoles, Sulfonamide, Antibacterial activity

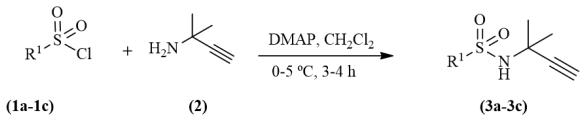
Introduction:

The synthesis of newer biological active moieties is the demand of time, for this task,the combination of two or more pharmacophore units in a molecule, is one of the prominent criteria to achieve the desired goal. In this regard, thesulfur andnitrogen containing compounds viz. sulfonamides are becoming a hot seat for research in synthetic chemistry astheseexhibited a key role in medicinal chemistry [1]. Further, the triazolesalso have attracted an appreciable interest due to their variedchemical reactivity and wide spectrum of biological activities as antimalarial [2-4], anti-inflammatory [5,6], antiviral [7], anticancer [8-13], antimicrobial [14-18], anti-oxidant [19-21], acetylcholinesterase inhibitor [22,23], analgesic [24,25],antiparasitic [26], antileishmanial [27],anti-influenza [28],antitubercular [29] agents. Triazole is the bioisostere of amide, ester and carboxylic acid, readily interacts with diverse enzymes, proteins and receptors in organisms via hydrophobic interactions, hydrogen bonds and Vander Waals forces. Disubstituted1,2,3-triazoles can be prepared effectively using ‘click’ reaction using copper (I) catalysedazide-alkyne cycloaddition.

Owing to potential biological aspects of triazoles and sulfonamides,we planned to extend our previous work [20,30]bysynthesizing a series of sulfonamide linked 1,4-disubstituted 1,2,3-triazolesthrough cycloaddition reaction of sulfonamidecontaining terminal alkynes-aromatic azidesand evaluated for antibacterial activity.

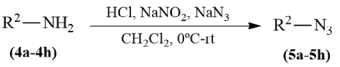
RESULTS AND DISCUSSION

The sulfonamide linked terminal alkynes i.e.4-substituted-N-(2-methylbut-3-yn-2-yl) benzenesulfonamides(3a-3c) were synthesized by reaction of 1,1-dimethylpropargyl amine (2, 1.0 mmol) and 4-substituted benzenesulfonylchloride (1a-1c, 1.0 mmol) in dichloromethane using 4-(dimethylamino) pyridine (DMAP) (1.0 mmol) at 0–5 °C for 3–4 h(Scheme 1).



R¹: 4-$CH_3C_6H_4$, 4-$OCH_3C_6H_4$, 4-$NO_2C_6H_4$

Scheme 1: Synthesis of sulfonamide containing terminal alkyne (3a-3c)

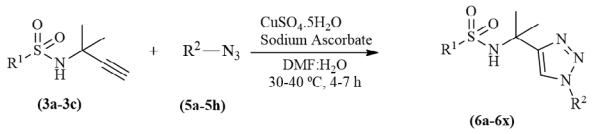


R²: C_6H_5, 4-$CH_3C_6H_4$, 4-$NO_2C_6H_4$, 4-FC_6H_4, 4-ClC_6H_4, 4-BrC_6H_4, 3-pyridyl, α-naphthyl

Further, the aromatic azides(5a-5h) were synthesized from reaction of substituted aromatic amines (4a-4h)using dilute hydrochloric acid,aqueous sodium nitrite and sodium azide in dichloromethane.(Scheme 2)

Scheme 2: Synthesis of aromatic azide (5a-5h)

In the last step, the aromatic azides(5a-5h, 1.0 mmol) were reacted with the 4-substituted-N-(2-methylbut-3-yn-2-yl)benzenesulfonamides (3a-3c, 1.0 mmol) in the presence ofcopper sulphatepentahydrateand sodium ascorbate in DMF/H_2O (8:2) to give the desired triazoles(6a-6x) in good yield.(Scheme 3)



Sr. No.	R^1	R^2
6a	4-$CH_3C_6H_4$	C_6H_5
6b	4-$CH_3C_6H_4$	4-$CH_3C_6H_4$
6c	4-$CH_3C_6H_4$	4-$NO_2C_6H_4$
6d	4-$CH_3C_6H_4$	4-FC_6H_4
6e	4-$CH_3C_6H_4$	4-ClC_6H_4
6f	4-$CH_3C_6H_4$	4-BrC_6H_4
6g	4-$CH_3C_6H_4$	3-pyridyl
6h	4-$CH_3C_6H_4$	α-naphthyl
6i	4-$OCH_3C_6H_4$	C_6H_5
6j	4-$OCH_3C_6H_4$	4-$CH_3C_6H_4$
6k	4-$OCH_3C_6H_4$	4-$NO_2C_6H_4$
6l	4-$OCH_3C_6H_4$	4-FC_6H_4
6m	4-$OCH_3C_6H_4$	4-ClC_6H_4
6n	4-$OCH_3C_6H_4$	4-BrC_6H_4
6o	4-$OCH_3C_6H_4$	3-pyridyl
6p	4-$OCH_3C_6H_4$	α-naphthyl
6q	4-$NO_2C_6H_4$	C_6H_5
6r	4-$NO_2C_6H_4$	4-$CH_3C_6H_4$
6s	4-$NO_2C_6H_4$	4-$NO_2C_6H_4$
6t	4-$NO_2C_6H_4$	4-FC_6H_4
6u	4-$NO_2C_6H_4$	4-ClC_6H_4
6v	4-$NO_2C_6H_4$	4-BrC_6H_4
6w	4-$NO_2C_6H_4$	3-pyridyl
6x	4-$NO_2C_6H_4$	α-naphthyl

Scheme 3: Synthesis of sulfonamide linked 1,2,3-triazoles (6a-6x)

The structures of all the synthesized compounds

were established on the basis of FTIR, ^{1}H NMR, ^{13}C NMR and HRMS data.

In the FTIR spectra, the presence of characteristic band in the region 3174-3080 cm^{-1}due to C-H stretching vibration evidenced the formation of triazole ring. The two moderate absorption bands at1163-1145 cm^{-1} and 1328-1311 cm^{-1}, were attributed to the symmetric and asymmetric stretching vibrations of S=O of sulfonamide respectively; while N-H stretching vibration appeared at 3307-3208 cm^{-1}.

The ^{1}H NMR spectra of all the synthesized triazoles exhibited a singlet in the region δ 8.71-8.07 forN-H confirms the formation of sulfonamide linkage. A characteristic singlet in the region δ 8.61-7.97 assigned to –CH oftriazole ring while another sharp singlet due to six protons of two methyl groups appeared in the range of δ 1.67-1.59.

In the ^{13}C NMR spectra, the peaks of C-4 and C-5 carbon atoms of triazole appeared in the region δ 152.6-151.4and δ 122.6-120.1 respectively, confirmed the formation of triazole ring. The peak due toCarbon attached to C-4 of the triazole ring appeared in the region δ 53.2-52.7. The HRMS data of all the synthesized triazoles was also in good agreement with their calculated values.

ANTIBACTERIAL ACTIVITY

The compound library (6a-6x) was screened in vitro for antibacterial activity using serial dilution method [21] againstK. pneumoniae, Escherichia coli, B. subtilis and S. aureus bacterial strains. The minimum inhibitory concentration (MIC in µM/mL) values of the compounds were compared with Ciprofloxacin as standard drug. (Table 1)

From the antibacterial screening results, it was observed that most of the compounds exhibited moderate to good antibacterial activity.It can be analyzed from antibacterialstudy that triazoles with nitro group on benzene ring attached to sulfonamide group displayed substantial improvement in activity as compared to methyl andmethoxy group. Triazolewith bromo group found to possessenhanced antibacterial activity than other halogens. Synthesized compounds havingnaphthyl ring showed better activity in comparison to phenyl ring. Among the synthesized triazoles, the compound 6v exhibited significant antibacterial activity.

Table 1.In vitro antibacterial activity of compounds 6a-6x (MIC in µM/mL)

Sr. No.	*K. pneumoniae*	*E. coli*	*B. subtilis*	*S. aureus*
6a	0.1402	0.0701	0.0701	0.0701
6b	0.0675	0.0675	0.0675	0.0675
6c	0.0623	0.0312	0.0623	0.0312
6d	0.0668	0.0334	0.0334	0.0334
6e	0.0640	0.0640	0.0640	0.0320
6f	0.0295	0.0295	0.0295	0.0295
6g	0.0700	0.0700	0.0700	0.0700
6h	0.0615	0.0615	0.0615	0.0615
6i	0.0672	0.0672	0.0672	0.0672
6j	0.0647	0.0647	0.0647	0.0647
6k	0.0599	0.0599	0.0599	0.0599
6l	0.0640	0.0641	0.0640	0.0641
6m	0.0615	0.0616	0.0615	0.0616
6n	0.0555	0.0277	0.0555	0.0555
6o	0.0670	0.0670	0.0670	0.0670
6p	0.0592	0.0296	0.0592	0.0592
6q	0.0645	0.0646	0.0645	0.0646
6r	0.0623	0.0623	0.0623	0.0623
6s	0.0578	0.0578	0.0578	0.0578
6t	0.0308	0.0308	0.0154	0.0308
6u	0.0599	0.0297	0.0297	0.0148
6v	0.0268	0.0268	0.0134	0.0134
6w	0.0644	0.0322	0.0322	0.0322
6x	0.0572	0.0271	0.0271	0.0271
Ciprofloxacin	0.0189	0.0189	0.0189	0.0189

EXPERIMENTAL SECTION

The chemicals used in the experimental work were of commercially available grade and used

without further purification. Melting points of the synthesized compounds were uncorrected. The FTIR absorption spectra were taken on IR AFFINITY-I FTIR (SHIMAZDU) spectrometer using KBr powder and wavenumbers are noted in cm^{-1}. The ^{1}H and ^{13}C NMR were recorded in DMSO-$d_6$on a 400 MHz BrukerAvance-III spectrometer. Chemical shifts (δ) were observed in parts per million (ppm) andcoupling constant (J) values in Hertz (Hz). High-resolution mass spectra (HRMS) were determined on Waters Micromass Q-Tof Micro (ESI) spectrometer and the values were represented in m/z.

General procedure for synthesis of4-substituted-N-(2-methylbut-3-yn-2-yl)benzenesulfonamides (3a-3c):

The1,1-dimethylpropargyl amine (2, 1.0 mmol) was added dropwiseto the stirred solution of 4-substituted benzenesulfonylchloride (1a-1c, 1.0 mmol) and 4-(dimethylamino)pyridine (DMAP)(1.0 mmol) in dichloromethane at 0–5 °C and stirring was continued for 3–4 h. After the completion of reaction, dilute hydrochloric acid was added. The compound was extracted with dichloromethane and the solvent was evaporated to afford the desired products(3a-3c).(Scheme 1)

General procedure for synthesis of aromatic azides (5a-5h):

The substituted aromatic amines(4a-4h) (1.0 mmol) in dichloromethane were stirred with dilute hydrochloric acid (5 mL) for 10 min. Then, aqueous solution of sodium nitrite (3.0 mmol) was added in small portions to the reaction mixture. After half an hour, sodium azide (3.0 mmol) was added in dropwise manner at 0 °C. The reaction mixture was then stirred for 1-2 h at room temperature. The progress of the reaction was monitored by TLC. The mixture was extracted with dichloromethane (3x20 mL). The organic layer was washed with sodium carbonate and dried with anhydrous sodium sulphate, solvent was evaporated to get the aromatic azides(5a-5h). (Scheme 2)

General procedure for synthesis of N-(2-(1-(substituted)-1H-1,2,3-triazol-4-yl)propan-2-yl)4-substitutedbenzenesulfonamide (6a-6x):

A mixture of aromatic azide(5a-5h, 1.0 mmol), 4-substituted-N-(2-methylbut-3-yn-2-yl) benzenesulfonamides (3a-3c, 1.0 mmol), copper sulphatepentahydrate and sodium ascorbate in DMF/H_2O (8:2) was continuously stirred for 4-7 h at 30-40 °C.After the consumptions of reactants as indicated by TLC, ammoniasolution was added to the reaction mixture. The product was extracted with ethyl acetate (3x20 mL), the organic layer was dried with anhydrous sodium sulphate, filtered and reduced under vacuum to obtain the final triazoles(6a-6x)in good yields. (Scheme 3).

4-Methyl-N-(2-(1-phenyl-1H-1,2,3-triazol-4-yl) propan-2-yl)benzenesulfonamide(6a)

Yield: 88 %; mp: 148-150 °C; FTIR (KBr): ν_{max} = 3208 (N–H str.), 3026 (C–H str., triazole), 2881 (C–H str., aliphatic), 1504, 1456 (C=C str., aromatic), 1328 (S=O asym. str., sulfonamide), 1149 (S=O sym. str., sulfonamide) cm^{-1}; ^{1}H NMR (400 MHz, DMSO) δ 8.27 (s, 1H, -NH), 8.03 (s, 1H, C-H triazole), 7.72 (d, J = 8.0 Hz, 2H), 7.58 (t, J = 8.0 Hz, 2H), 7.47 (t, J = 8.0 Hz, 1H), 7.40 (d, J = 8.0 Hz, 2H), 7.08 (d, J = 8.0 Hz, 2H), 2.08 (s, 3H), 1.62 (s, 6H). ^{13}C NMR (100 MHz, DMSO) δ 152.9 (C_4triazole), 142.2, 138.9, 131.0, 130.2, 129.2, 126.8, 120.6 (C_5triazole), 120.1, 52.9, 29.1, 21.1. HRMS $[M+H]^+$for $C_{18}H_{20}N_4O_2$Scalc: 357.1307, found: 357.1440.

4-Methyl-N-(2-(1-(p-tolyl)-1H-1,2,3-triazol-4-yl) propan-2-yl)benzenesulfonamide(6b)

Yield: 92 %; 136–140 °C; FTIR (KBr): ν_{max}= 3255 (N–H str.), 3113 (C–H str., triazole), 2983 (C–H str., aliphatic), 1543, 1498 (C=C str., aromatic), 1311 (S=O asym. str., sulfonamide), 1145 (S=O sym. str., sulfonamide) cm^{-1}; ^{1}H NMR (400 MHz, DMSO): δ 8.22 (s, 1H, -NH),

7.99 (s, 1H, C-H triazole), 7.60 (d, J = 8.0 Hz, 2H), 7.43-7.37 (m, 4H), 7.09 (d, J = 8.0 Hz, 2H), 2.38 (s, 3H), 2.12 (s, 3H), 1.61 (s, 6H). ^{13}C NMR (100 MHz, DMSO) δ 152.1 (C_4triazole), 142.1, 140.1, 138.3, 134.7, 130.5, 129.2, 126.8, 120.5 (C_5triazole), 120.0, 52.9, 29.2, 21.1, 21.0. HRMS $[M+H]^+$for $C_{19}H_{22}N_4O_2$Scalc: 371.1363, found: 371.1398.

4-Methyl-N-(2-(1-(4-nitrophenyl)-1H-1,2,3-triazol-4-yl)propan-2-yl)benzenesulfonamide(6c)

Yield: 88 %; mp: 152–154 °C; FTIR (KBr): ν_{max}= 3286 (N–H str.), 3109 (C–H str., triazole), 2875 (C–H str., aliphatic), 1517, 1452 (C=C str., aromatic), 1330 (S=O asym. str., sulfonamide), 1161 (S=O sym. str., sulfonamide) cm^{-1}, ^{1}H NMR (400 MHz, DMSO) δ 8.58 (s, 1H, -NH), 8.45 (d, J = 8.0 Hz, 2H), 8.08 (d, J = 8.0 Hz, 2H), 7.99 (s, 1H, C-H triazole), 7.62 (d, J = 8.0 Hz, 2H), 7.44 (d, J = 6.9 Hz, 2H), 2.12 (s, 3H, CH_3), 1.63 (s, 6H, $2CH_3$). ^{13}C NMR (100 MHz, DMSO) δ 152.6 (C_4triazole), 146.9, 142.1, 141.1, 134.5, 128.9, 125.9, 120.5 (C_5triazole), 113.9, 52.7, 29.0, 21.9; HRMS $[M+H]^+$for $C_{18}H_{19}N_5O_4$Scalc: 402.1158, found: 402.1231.

N-(2-(1-(4-fluorophenyl)-1H-1,2,3-triazol-4-yl) propan-2-yl)-4-methylbenzenesulfonamide (6d)

Yield: 84 %; mp: 164–166 °C; FTIR (KBr): ν_{max}= 3234 (N–H str.), 3064 (C–H str., triazole), 2997 (C–H str., aliphatic), 1512, 1450 (C=C str., aromatic), 1329 (S=O asym. str., sulfonamide), 1151 (S=O sym. str., sulfonamide) cm^{-1}; ^{1}H NMR (400 MHz, DMSO) δ 8.07 (s, 1H, -NH), 7.97 (s, 1H, C-H triazole), 7.44 (m, 4H), 7.11 (d, J = 8.0 Hz, 2H), 6.91 (d, J = 8.0 Hz, 2H), 2.15 (s, 3H, CH_3), 1.59 (s, 6H, $2CH_3$). ^{13}C NMR (100 MHz, DMSO) δ 165.4, 152.8 (C_4triazole), 140.1, 129.3, 126.8, 121.9, 120.4 (C_5triazole), 116.3, 53.0, 29.2, 21.1. HRMS $[M+H]^+$for $C_{18}H_{19}FN_4O_2$Scalc: 375.1213, found: 375.1313.

N-(2-(1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl) propan-2-yl)-4-methylbenzenesulfonamide(6e)

Yield: 92%;mp:140–142 °C; FTIR (KBr): ν_{max}= 3240 (N–H str.), 3143 (C–H str., triazole), 2881 (C–H str., aliphatic), 1589, 1448 (C=C str., aromatic), 1329 (S=O asym. str., sulfonamide), 1157 (S=O sym. str., sulfonamide) cm $^{-1}$;^{1}H NMR (400 MHz, DMSO) δ 8.33 (s, 1H, -NH), 8.03 (s, 1H, C-H triazole), 7.77 (d, J = 8.0 Hz, 2H), 7.66 (d, J = 8.0 Hz, 2H), 7.40 (d, J = 8.0 Hz, 2H), 7.08 (d, J = 8.0 Hz, 2H), 2.10 (s, 3H, CH_3), 1.61 (s, 6H, $2CH_3$). ^{13}C NMR (100 MHz, DMSO) δ 152.2 (C_4triazole), 142.1, 140.0, 135.7, 132.9, 130.2, 129.2, 126.8, 121.7, 120.7 (C_5triazole), 52.8, 29.1, 21.1. HRMS $[M+H]^+$for $C_{18}H_{19}ClN_4O_2S$ $C_{21}H_{22}N_6O_4$ calc: 391.0917, found: 391.0983.

N-(2-(1-(4-bromophenyl)-1H-1,2,3-triazol-4-yl) propan-2-yl)-4-methylbenzenesulfonamide (6f)

Yield: 88%; mp: 176–178 °C; FTIR (KBr): ν_{max}= 3255 (N–H str.), 3133 (C–H str., triazole), 2983 (C–H str., aliphatic), 1543, 1498 (C=C str., aromatic), 1311 (S=O asym. str., sulfonamide), 1145 (S=O sym. str., sulfonamide) cm $^{-1}$; ^{1}H NMR (400 MHz, DMSO) δ 8.33 (s, 1H, -NH), 8.02 (s, 1H, C-H triazole), 7.79 (d, J = 8.0 Hz, 2H), 7.71 (d, J = 8.0 Hz, 2H), 7.39 (d, J = 8.0 Hz, 2H), 7.08 (d, J = 8.0 Hz, 2H), 2.10 (s, 3H, CH_3), 1.61 (s, 6H, $2CH_3$); ^{13}C NMR (100 MHz, DMSO) δ 152.2 (C_4triazole), 142.1, 140.0, 136.1, 133.1, 129.2, 126.8, 122.0, 121.3, 120.7 (C_5triazole), 52.8, 29.1, 21.1. HRMS $[M+H]^+$for $C_{18}H_{19}BrN_4O_2$Scalc: 435.0308 (^{79}Br), 437.0413 (^{81}Br) found: 435.03114 (^{79}Br), 437.0455 (^{81}Br).

4-methyl-N-(2-(1-(pyridin-3-yl)-1H-1,2,3-triazol-4-yl)propan-2-yl)benzenesulfonamide(6g)

Yield: 80%; mp: 146-148 °C; FTIR (KBr): ν_{max}= 3284 (N–H str.), 3119 (C–H str., triazole), 2881 (C–H str., aliphatic), 1517, 1454 (C=C str., aromatic), 1323 (S=O asym. str., sulfonamide), 1153 (S=O sym. str., sulfonamide) cm^{-1};^{1}H NMR (400 MHz, DMSO) δ 8.98 (s, 1H), 8.70 (s, 1H), 8.42 (s, 1H, -NH), 8.16 (d, J = 8.0 Hz, 1H), 8.05 (s, 1H, C-H triazole), 7.66 (m, 1H), 7.40 (d, J = 8.0 Hz, 2H), 7.08 (d, J = 8.0 Hz, 2H), 2.07 (s, 3H, CH_3), 1.63 (s, 6H, $2CH_3$);^{13}C NMR (100 MHz, DMSO) δ 152.3 (C_4triazole),

149.7, 142.0, 141.2, 140.0, 129.2, 127.7, 126.9, 121.0 (C_5triazole), 52.8, 29.1, 21.0. HRMS $[M+H]^+$for $C_{17}H_{19}N_5O_2S$ calc: 358.1259, found: 358.1350.

4-methyl-N-(2-(1-(naphthalen-1-yl)-1H-1,2,3-triazol-4-yl)propan-2-yl)benzenesulfonamide (6h)
Yield: 86%; mp: 116–120 °C; FTIR (KBr): ν_{max}= 3265 (N–H str.), 3143 (C–H str., triazole), 2985 (C–H str., aliphatic), 1593, 1498 (C=C str., aromatic), 1334 (S=O asym. str., sulfonamide), 1163 (S=O sym. str., sulfonamide) cm $^{-1}$; ^{1}H NMR (400 MHz, DMSO) δ 8.25 (s, 1H, -NH), 8.17 (d, J = 8.0 Hz, 1H), 8.12 (d, J = 8.0 Hz, 2H), 7.73 – 7.57 (m, 5H), 7.55-7.46 (m, 2H), 7.26 (d, J = 8.0 Hz, 2H), 2.25 (s, 3H, CH_3), 1.66 (s, 6H, $2CH_3$);^{13}C NMR (100 MHz, DMSO) δ 152.0 (C_4triazole), 142.2, 140.8, 134.1, 133.6, 130.4, 129.6, 128.7, 128.2, 128.1, 127.5, 126.8, 125.8, 124.9, 123.9, 122.6 (C_5triazole), 53.2, 29.4, 21.3. HRMS $[M+H]^+$for $C_{22}H_{22}N_4O_2$Scalc: 407.1463, found: 407.1496.

4-methoxy-N-(2-(1-phenyl-1H-1,2,3-triazol-4-yl) propan-2-yl)benzenesulfonamide(6i)
Yield: 92%; mp: 160–162 °C; FTIR (KBr): ν_{max}= 3234 (N–H str.), 3094 (C–H str., triazole), 2997 (C–H str., aliphatic), 1512, 1450 (C=C str., aromatic), 1326 (S=O asym. str., sulfonamide), 1141 (S=O sym. str., sulfonamide) cm $^{-1}$; ^{1}H NMR (400 MHz, DMSO) δ 8.30 (s, 1H, -NH), 7.92 (s, 1H, C-H triazole), 7.73 (d, J = 8.0 Hz, 2H), 7.58 (t, J = 8.0 Hz, 2H), 7.47 (t, J = 8.0 Hz, 3H), 6.80 (d, J = 8.0 Hz, 2H), 3.58 (s, 3H, OCH_3), 1.62 (s, 6H, $2CH_3$);^{13}C NMR (100 MHz, DMSO) δ 161.8, 152.1 (C_4triazole), 136.9, 134.6, 130.2, 128.9, 128.7, 120.6 (C_5triazole), 120.1, 113.9, 55.6, 52.8, 29.2. HRMS $[M+H]^+$for $C_{18}H_{20}N_4O_3$Scalc: 373.1256, found: 373.1397.

4-methoxy-N-(2-(1-(p-tolyl)-1H-1,2,3-triazol-4-yl) propan-2-yl)benzenesulfonamide (6j)
Yield: 86%; mp: 154–158 °C; FTIR (KBr): ν_{max}= 3253 (N–H str.), 3111 (C–H str., triazole), 2989 (C–H str., aliphatic), 1543, 1431 (C=C str., aromatic), 1319 (S=O asym. str., sulfonamide), 1145 (S=O sym. str., sulfonamide) cm $^{-1}$; ^{1}H NMR (400 MHz, DMSO) δ 8.23 (s, 1H, -NH), 7.90 (s, 1H, C-H triazole), 7.60 (d, J = 8.0 Hz, 2H), 7.45 (d, J = 8.0 Hz, 2H), 7.37 (d, J = 8.0 Hz, 2H), 6.80 (d, J = 8.0 Hz, 2H), 3.59 (s, 3H, OCH_3), 2.38 (s, 3H, CH_3), 1.61 (s, 6H, $2CH_3$).^{13}C NMR (100 MHz, DMSO) δ 161.8, 152.0 (C_4triazole), 138.3, 134.6, 134.6, 130.5, 128.9, 120.5 (C_5triazole), 120.0, 113.9, 55.6, 52.8, 29.2, 21.0. HRMS $[M+H]^+$for $C_{19}H_{22}N_4O_3S$ calc: 387.1413, found: 387.1545.

4-methoxy-N-(2-(1-(4-nitrophenyl)-1H-1,2,3-triazol-4-yl)propan-2-yl)benzenesulfonamide (6k)
Yield: 90%; mp: 170–172 °C; FTIR (KBr): ν_{max}= 3251 (N–H str.), 3099 (C–H str., triazole), 2993 (C–H str., aliphatic), 1589, 1440 (C=C str., aromatic), 1328 (S=O asym. str., sulfonamide), 1153 (S=O sym. str., sulfonamide) cm $^{-1}$; ^{1}H NMR (400 MHz, DMSO) δ 8.58 (s, 1H, -NH), 8.45 (d, J = 8.0 Hz, 2H), 8.08 (d, J = 8.0 Hz, 2H), 7.99 (s, 1H, C-H triazole), 7.44 (d, J = 8.0 Hz, 2H), 6.77 (d, J = 8.0 Hz, 2H), 3.56 (s, 3H, OCH_3), 1.63 (s, 6H, $2CH_3$); ^{13}C NMR (100 MHz, DMSO) δ 161.8, 152.6 (C_4triazole), 146.9, 141.1, 134.7, 128.9, 125.9, 120.5 (C_5triazole), 113.9, 55.7, 52.7, 29.0. HRMS $[M+H]^+$for $C_{18}H_{19}N_5O_5$Scalc: 418.1107, found: 418.1167.

N-(2-(1-(4-fluorophenyl)-1H-1,2,3-triazol-4-yl) propan-2-yl)-4-methoxybenzenesulfonamide(6l)
Yield: 88%; mp: 120-122 °C; FTIR (KBr): ν_{max}= 3234 (N–H str.), 3134 (C–H str., triazole), 2997 (C–H str., aliphatic), 1531, 1404 (C=C str., aromatic), 1330 (S=O asym. str., sulfonamide), 1152 (S=O sym. str., sulfonamide) cm $^{-1}$; ^{1}H NMR (400 MHz, DMSO) δ 8.44 (s, 1H, -NH), 8.25 (s, 1H, C-H triazole), 7.81–7.70 (m, 4H), 7.45 (m, 4H), 3.35 (s, 3H, OCH_3), 1.64 (s, 6H, $2CH_3$); ^{13}C NMR (100 MHz, DMSO) δ 161.8, 151.8 (C_4triazole),, 142.0, 136.0, 133.1, 131.8, 128.8, 125.8, 122.0, 121.4, 120.9 (C_4triazole),55.5, 52.9, 29.1. HRMS $[M+H]^+$for $C_{18}H_{19}FN_4O_3$Scalc: 423.1786, found: 423.1818.

N-(2-(1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl) propan-2-yl)-4-methoxybenzenesulfonamide (6m)
Yield: 82%; mp: 152–154 °C; FTIR (KBr): ν_{max} = 3280 (N–H str.), 3153 (C–H str., triazole), 2999 (C–H str., aliphatic), 1548, 1431 (C=C str., aromatic), 1327 (S=O asym. str., sulfonamide), 1151 (S=O sym. str., sulfonamide) cm $^{-1}$; ^{1}H NMR (400 MHz, DMSO) δ 8.36 (s, 1H, -NH), 7.95 (s, 1H, C-H triazole), 7.80 (d, J = 8.0 Hz, 2H), 7.65 (d, J = 8.0 Hz, 2H), 7.44 (d, J = 8.0 Hz, 2H), 6.79 (d, J = 8.0 Hz, 2H), 3.35 (s, 3H, OCH_3), 1.61 (s, 6H, $2CH_3$);^{13}C NMR (100 MHz, DMSO) δ 161.8, 152.2 (C_4triazole), 135.7, 134.6, 133.0, 130.1, 128.9, 121.7, 120.7 (C_4triazole), 113.9, 55.6, 52.8, 29.1. HRMS $[M+H]^+$for $C_{18}H_{19}ClN_4O_3$Scalc: 407.0866, found:407.0906.

N-(2-(1-(4-bromophenyl)-1H-1,2,3-triazol-4-yl) propan-2-yl)-4-methoxybenzenesulfonamide (6n)
Yield: 86%; mp: 166–168 °C; IR (KBr), ν (cm^{-1}): 3278 (N–H str.), 3150 (C–H str., triazole), 2996 (C–H str., aliphatic), 1548, 1431 (C=C str., aromatic), 1328 (S=O asym. str., sulfonamide), 1151 (S=O sym. str., sulfonamide) cm^{-1};^{1}H NMR (400 MHz, DMSO) δ 8.36 (s, 1H, -NH), 7.95 (s, 1H, C-H triazole), 7.76 (m, 4H), 7.43 (d, J = 8.0 Hz, 2H), 6.78 (d, J = 8.0 Hz, 2H), 3.59 (s, 3H, OCH_3), 1.61 (s, 6H, $2CH_3$). ^{13}C NMR (100 MHz, DMSO) δ 161.8, 152.2 (C_4triazole), 136.1, 134.5, 133.1, 128.9, 121.9, 121.3, 120.7 (C_4triazole), 113.9, 55.6, 52.7, 29.1. HRMS $[M+H]^+$for $C_{18}H_{19}BrN_4O_3$Scalc: 451.0361 (^{79}Br), 453.0356 (^{81}Br), found: 451.0416 (^{79}Br), 453.0401 (^{81}Br).

4-methoxy-N-(2-(1-(pyridin-3-yl)-1H-1,2,3-triazol-4-yl)propan-2-yl)benzenesulfonamide (6o)
Yield: 80%; mp: 118–120 °C; FTIR (KBr), ν (cm^{-1}): 3298 (N–H str.), 3148 (C–H str., triazole), 2975 (C–H str., aliphatic), 1521, 1404 (C=C str., aromatic), 1334 (S=O asym. str., sulfonamide), 1147 (S=O sym. str., sulfonamide) cm^{-1}; ^{1}H NMR (400 MHz, DMSO) δ 8.98 (d, J = 4.0 Hz, 1H), 8.68 (d, J = 4.0Hz, 1H), 8.43 (s, 1H, -NH), 8.19-8.15 (m, 1H), 7.97 (s, 1H, C-H triazole), 7.64 (t, J = 8.0 Hz, 1H), 7.45 (d, J = 8.0 Hz, 2H), 6.79 (d, J = 8.0 Hz, 2H), 3.57 (s, 3H, OCH_3), 1.63 (s, 6H, $2CH_3$); ^{13}C NMR (100 MHz, DMSO) δ 162.7, 161.8, 152.3 (C_4triazole), 149.8, 141.3, 134.5, 133.4, 129.0, 127.8, 124.9, 121.0 (C_5triazole), 113.9, 55.69, 52.76,29.15. HRMS $[M+H]^+$for $C_{17}H_{19}N_5O_3$Scalc: 374.1209, found: 374.1271.

4-methoxy-N-(2-(1-(naphthalen-1-yl)-1H-1,2,3-triazol-4-yl)propan-2-yl)benzenesulfonamide (6p)
Yield: 80%; mp: 154-158 °C; FTIR (KBr): ν_{max} = 3307 (N–H str.), 3109 (C–H str., triazole), 2975 (C–H str., aliphatic), 1521, 1404 (C=C str., aromatic), 1334 (S=O asym. str., sulfonamide), 1147 (S=O sym. str., sulfonamide) cm^{-1}; ^{1}H NMR (400 MHz, DMSO) δ 8.25 (s, 1H, -NH), 8.17 (d, J = 8.3 Hz, 1H), 8.11 (d, J = 7.8 Hz, 1H), 8.03 (s, 1H, C-H triazole), 7.71-7.59 (m, 5H), 7.53 (d, J = 8.0, 1H), 7.46 (d, J = 8.0, 1H), 6.96 (d, J = 8.0 Hz, 2H), 3.71 (s, 3H, OCH_3), 1.66 (s, 6H, $2CH_3$); ^{13}C NMR (100 MHz, DMSO) δ 162.0, 152.0 (C_4triazole), 135.2, 134.1, 133.6, 130.5, 129.0, 128.7, 128.3, 128.1, 127.5, 125.8, 124.9, 123.9, 122.6(C_5triazole), 114.2, 55.9, 53.1,29.4;HRMS $[M+H]^+$for $C_{22}H_{22}N_4O_3$Scalc: 423.1413, found: 423.1542.

4-nitro-N-(2-(1-phenyl-1H-1,2,3-triazol-4-yl) propan-2-yl)benzenesulfonamide (6q)
Yield: 80%; mp: 126-128 °C; FTIR (KBr): ν_{max} = 3232 (N–H str.), 3174 (C–H str., triazole), 2870 (C–H str., aliphatic), 1521, 1463 (C=C str., aromatic), 1330 (S=O asym. str., sulfonamide), 1155 (S=O sym. str., sulfonamide) cm $^{-1}$; ^{1}H NMR (400 MHz, DMSO) δ 8.27 (s, 1H, -NH), 8.11 (d, J = 8.5 Hz, 4H), 8.03 (s, 1H, C-H triazole), 7.74 (d, J = 8.0 Hz, 2H), 7.40 (d, J = 8.0 Hz, 2H), 7.08 (d, J = 8.0 Hz, 2H), 1.62 (s, 6H, $2CH_3$). ^{13}C NMR (100 MHz, DMSO) δ 131.0, 130.2, 129.2, 126.8, 120.6 (C_4triazole), 120.1, 52.9, 29.1, HRMS $[M+H]^+$for $C_{18}H_{20}N_4O_2$ S calc: 387.1001, found: 387.1135.

4-nitro-N-(2-(1-(p-tolyl)-1H-1,2,3-triazol-4-yl) propan-2-yl)benzenesulfonamide (6r)

Yield: 92%; mp: 134-136 °C; FTIR (KBr): ν_{max}= 3298 (N–H str.), 3135 (C–H str., triazole), 2975 (C–H str., aliphatic), 1528, 1404 (C=C str., aromatic), 1334 (S=O asym. str., sulfonamide), 1148 (S=O sym. str., sulfonamide) cm $^{-1}$;^{1}H NMR (400 MHz, DMSO) δ 8.56 (s, 1H, -NH), 8.38 (s, 1H, C-H triazole), 8.11 (d, J = 8.0 Hz, 2H), 7.74 (d, J = 8.0 Hz, 2H), 7.56 (d, J = 8.0 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 2.37 (s, 3H, CH_3), 1.67 (s, 6H, $2CH_3$). ^{13}C NMR (100 MHz, DMSO) δ 151.4 (C_4triazole), 149.1, 148.4, 138.4, 134.5, 130.5, 128.4, 124.1, 120.8 (C_5triazole), 119.8, 53.2, 29.1, 21.0. HRMS [M+H]$^+$for $C_{18}H_{19}N_5O_4$Scalc: 402.1108, found: 402.1129.

4-nitro-N-(2-(1-(4-nitrophenyl)-1H-1,2,3-triazol-4-yl)propan-2-yl)benzenesulfonamide(6s)

Yield: 78%; mp: 148-150 °C; (KBr): ν_{max}= 3264 (N–H str.), 3134 (C–H str., triazole), 2875 (C–H str., aliphatic), 1543, 1456 (C=C str., aromatic), 1328 (S=O asym. str., sulfonamide), 1149 (S=O sym. str., sulfonamide) cm $^{-1}$; ^{1}H NMR (400 MHz, DMSO) δ 8.71 (s, 1H, -NH), 8.61 (s, 1H, C-H triazole), 8.42 (d, J = 8.0 Hz, 2H), 8.11-8.04 (m, 4H), 7.75 (d, J = 8.0 Hz, 2H), 1.68 (s, 6H, $2CH_3$).^{13}C NMR (100 MHz, DMSO) δ 152.1 (C_4triazole), 149.1, 148.3, 146.9, 141.0, 128.4, 126.0, 124.1, 121.6, 120.4 (C_5triazole), 53.1, 28.9. HRMS [M+H]$^+$for $C_{21}H_{22}N_6O_4$ calc: 432.0852, found: 432.1085.

N-(2-(1-(4-fluorophenyl)-1H-1,2,3-triazol-4-yl)propan-2-yl)-4-nitrobenzenesulfonamide (6t)Yield: 84%; mp: 130-132 °C; FTIR (KBr): ν_{max}= 3213 (N–H str.), 3101 (C–H str., triazole), 2995 (C–H str., aliphatic), 1516, 1465 (C=C str., aromatic), 1330 (S=O asym. str., sulfonamide), 1153 (S=O sym. str., sulfonamide) cm $^{-1}$; ^{1}H NMR (400 MHz, DMSO) δ 8.56 (s, 1H, -NH), 8.43 (s, 1H, C-H triazole), 8.11 (d, J = 8.0 Hz, 2H), 7.74 (d, J = 8.0 Hz, 4H), 7.41 (t, J = 8.0 Hz, 2H), 1.67 (s, 6H). ^{13}C NMR (101 MHz, DMSO) δ 161.9 (d, J = 244 Hz), 151.6 (C_4triazole), 148.7 (d, J = 70 Hz), 133.2, 128.4, 124.1, 122.1 (d, J = 8 Hz), 122.1, 121.2 (C_5triazole), 117.0 (d, J = 23 Hz), 53.2, 29.0. HRMS [M+H]$^+$for $C_{17}H_{16}FN_5O_4$Scalc: 406.0907, found:406.0980.

N-(2-(1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl) propan-2-yl)-4-nitrobenzenesulfonamide (6u)

Yield: 82%; mp: 154-156 °C; FTIR (KBr): ν_{max}= 3215 (N–H str.), 3136 (C–H str., triazole), 2989 (C–H str., aliphatic), 1525, 1435 (C=C str., aromatic), 1342 (S=O asym. str., sulfonamide), 1161 (S=O sym. str., sulfonamide) cm $^{-1}$; ^{1}H NMR (400 MHz, DMSO) δ 8.49 (s, 1H, -NH), 8.10 (d, J = 8.0 Hz, 2H), 7.74 (m, 5H), 7.62 (d, J = 8.0 Hz, 2H), 1.67 (s, 6H, $2CH_3$). ^{13}C NMR (100 MHz, DMSO) δ 151.7 (C_4triazole), 149.1, 148.3, 135.5, 133.1, 130.2, 128.4, 124.1, 121.5, 121.1 (C_5triazole), 53.1, 29.0. HRMS [M+H]$^+$for $C_{17}H_{16}ClN_5O_4$Scalc: 422.0612, found: 422.0675.

N-(2-(1-(4-bromophenyl)-1H-1,2,3-triazol-4-yl) propan-2-yl)-4-nitrobenzenesulfonamide(6v)

Yield: 86%; mp: 144-146 °C; FTIR (KBr): ν_{max}= 3307 (N–H str.), 3109 (C–H str., triazole), 2975 (C–H str., aliphatic), 1521, 1404 (C=C str., aromatic), 1334 (S=O asym. str., sulfonamide), 1147 (S=O sym. str., sulfonamide) cm $^{-1}$; ^{1}H NMR (400 MHz, DMSO) δ ^{1}H NMR (400 MHz, DMSO) δ 8.57 (s, 1H, -NH), 8.50 (s, 1H, C-H triazole), 8.10 (d, J = 8.9 Hz, 2H), 7.74-7.67 (m, 6H), 1.67 (s, 6H, $2CH_3$); ^{13}C NMR (100 MHz, DMSO) δ 151.7, 149.1, 148.3, 135.9, 133.1, 128.4, 124.1, 121.7, 121.5, 121.0 (C_5triazole), 53.1, 29.0. HRMS [M+H]$^+$for $C_{17}H_{16}BrN_5O_4$Scalc: 466.0106, (^{79}Br), 468.0106 (^{81}Br) found: 466.0190, (^{79}Br), 468.0163 (^{81}Br).

4-nitro-N-(2-(1-(pyridin-3-yl)-1H-1,2,3-triazol-4-yl)propan-2-yl)benzenesulfonamide (6w)

Yield: 78%; mp: 182–184 °C; FTIR (KBr): ν_{max}= 3251 (N–H str.), 3080 (C–H str., triazole), 2993 (C–H str., aliphatic), 1589, 1440 (C=C str., aromatic), 1326 (S=O asym. str., sulfonamide), 1152 (S=O sym. str., sulfonamide) cm^{-1}; ^{1}H

NMR (400 MHz, DMSO) δ 8.98 (s, 1H, -NH), 8.68 (d, J = 8.0 Hz, 1H), 8.52 (s, 1H, C-H triazole), 8.16 (d, J = 8.0 Hz, 2H), 7.65-7.62 (m, 1H), 7.57 (d, J = 8.0 Hz, 1H), 7.40-7.29 (m, 3H, CH_3), 1.64 (s, 6H, $2CH_3$).^{13}C NMR (100 MHz, DMSO-d_6) δ 152.5 (C_4triazole), 149.9, 143.0, 141.4, 133.5, 131.9, 128.8, 128.0, 126.7, 124.9, 121.1 (C_5triazole), 52.9, 29.1; HRMS (m/z) calculated for $C_{16}H_{16}N_6O_4S$ calc: 389.0954, found: 389.1044.

N-(2-(1-(naphthalen-1-yl)-1H-1,2,3-triazol-4-yl) propan-2-yl)-4-nitrobenzenesulfonamide (6x)

Yield: 82%; mp: 170-172 °C; FTIR (KBr): ν_{max}= 3218 (N–H str.), 3084 (C–H str., triazole), 2985 (C–H str., aliphatic), 1593, 1463 (C=C str., aromatic), 1328 (S=O asym. str., sulfonamide), 1155 (S=O sym. str., sulfonamide) cm $^{-1}$;^{1}H NMR (400 MHz, DMSO-d_6) δ 8.33 (s, 1H, -NH), 8.22 (s, 1H, C-H triazole), 8.18 (d, J = 8.0 Hz, 2H), 8.14-8.10 (m, 4H), 7.73 – 7.64 (m, 3H), 7.56 – 7.40 (m, 2H), 1.66 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 151.9 (C_4triazole), 149.6, 141.2, 134.1, 133.7, 132.2, 130.5, 129.1, 128.7, 128.2, 128.2, 126.7, 125.8, 125.0, 124.0, 122.6 (C_5triazole), 53.3, 29.4; HRMS (m/z) calculated forHRMS $[M+H]^+$for $C_{21}H_{19}N_5O_4S$ calc: 438.1158, found: 438.1201.

ANTIBACTERIAL ACTIVITY

The antibacterial testing of newly synthesized compounds was performedin vitro against–Klebsiellapneumoniae(NCDC138),Escherichia coli (MTCC 1231),B. subtilis (MTCC 441), Staphylococcus aureus (MTCC 7443) strains as per serial dilution method [21] using a stock solution of 200 µg/mL concentration. Nutrient broth was used as nutrient media while dimethylsulfoxide as a solvent control. Ciprofloxacin was used as a standard drug for bacterial strains. A stock solution of testing compound and control drug was serially diluted to get concentration of 100, 50, 25, 12.5, 6.25, 3.12 µg/mL. All these dilutions were inoculated with respective bacteria in saline solution and incubated at 37 ºC for 24 h. Results were recorded in terms of minimum inhibitory concentration (MIC) expressed in µmol/mL in Table 1.

CONCLUSION

Here, twenty-four sulfonamide linked 1,4-disubstituted 1,2,3-triazoles were synthesized by using sulfonamide linked terminal alkynes and aromatic azides. The structures of all the synthesized compounds were characterizedthrough FTIR, ^{1}HNMR, ^{13}C NMR and HRMStachniques. The antibacterial activity of the compounds was evaluated against K. pneumoniae, E. coli, B. subtilis andS. aureusand compound 6v exhibited most potent antibacterial activity.

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