Facile Synthesis of *N*-(Benzyl-1*H*-1,2,3-Triazol-5-yl) Methyl)-4-(6-Methoxybenzo [*d*] Thiazol-2-yl)-2-Nitrobenzamides *via* Click Chemistry

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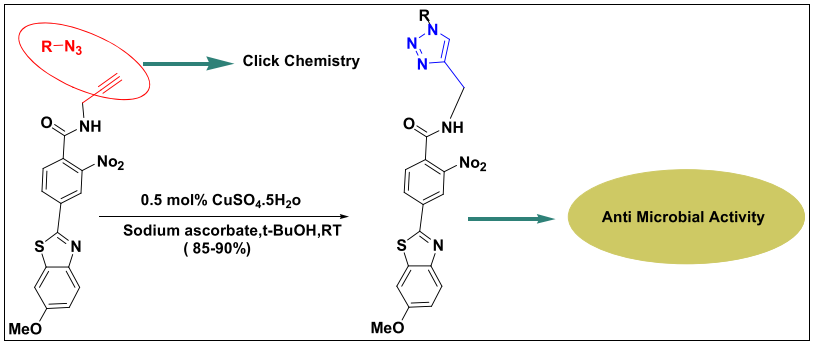

A series of novel *N*-((l-benzyl-l*H*-l,2,3-triazol-5-yl) methyl)-4-(6-methoxy benzo[*d*]thiazol-2-yl)-2-nitrobenzamide derivatives were prepared from 4-(6-methoxybenzo[*d*]thiazol-2-yl)-2-nitro-*N*-(prop-2-ynyl) benzamide with benzyl azides by using click reaction (copper-catalyzed Huisgen 1,3-dipolar cycloaddition reaction) in the presence of $CuSO_4.5H_2O$ and sodium ascaorbate. All the newly synthesized compounds were evaluated further *in vitro* antimicrobial activity against Gram-positive bacteria (*Staphylococcus aureus* and *Bacillus subtillis*), Gram-negative bacteria (*Echerichia coli* and *Pseudomonas aeuroginosa*), and fungi (*Aspergillus niger* and *Aspergillusfumigatus*) strains. The new compounds were characterized based on spectroscopic evidence. Among them compounds **10a**, **10h**, and **10i** were showed promising activity when compared with standard drugs Ciprofloxacin and Miconazole.

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INTRODUCTION

Benzothiazole scaffold derivatives consist of fused bicyclic ring systems. Benzothiazoles are an important class of potential organic molecules in medicinal chemistry because of their extensive range of activity such as neuron protective [1,2], anti-convulsive [3,4], anti-glutamate [5], anti-malarial [6], anthelmintic [7], anti-tubercular [8], analgesic, anti-inflammatory [9], antimicrobial [10–14], and anti-cancer effect [15–17]. In this context, promising biological profile molecules that are synthetically accessible have attracted the attention of medicinal organic chemists. Consequently, design and synthesis of new benzothiazole scaffold derivatives are attracted as potential chemotherapeutics. Azide–alkyne [3 + 2] cycloaddition [18] illustrates that it bring about many of the necessitous. It is well known that many of the simple mono substituted alkynes and organic azides are accessible commercially. Many others can effortlessly be synthesized [18] with an extensive range of functional groups, those cycloaddition reactions selectively gives 1,2,3-triazoles. In fact, a Cu (I) catalyzed alternative that follows a divergent mechanism and insensitive to oxygen and water. These click reactions proceed under mild conditions and not required any protecting groups. Additionally, the [3 + 2] cycloaddition is also well known as Husigen cycloaddition of alkynes to azides to form 1, 4 -disubstituted [1,2,3]-trizoles. These copper (I) catalyzed [3 + 2] reactions comply fully with the sense of click chemistry. Hence, azide–alkyne cycloaddition has put a focus on as a prototype click chemistry reaction. It is important to the existence that click reactions achieve their required characteristics by having a high thermodynamic driving force, usually greater than 20 kcal mol^{-1}. Such processes proceed rapidly to completion and also tend to be highly selective for a single product. We recognize the convenient of inter-molecular azide-alkyne [3 + 2] cycloaddition in order to construct *N*-((l-benzyl-l*H*-l,2,3-triazol-5-yl) methyl)-4-(6-methoxybenzo [*d*]thiazol-2-yl)-2-nitrobenzamides. Herein, we describe the click chemistry and approach for the constructed by copper catalyzed azide–alkyne cycloaddition reaction and their biological activity studies of *N*-((l-benzyl-l*H*-l, 2, 3-triazol-5-yl) methyl)-4-(6-methoxybenzo[*d*]thiazol-2-yl)-2-nitrobenzamides.

RESULTS AND DISCUSIONS

The synthetic methodology was adopted from the reaction of 4-methyl benzoic acid **1** that reacted with nitrating

mixture afforded to 4-methyl-3 nitro benzoic acid **2**. 4-Methyl-3 nitro benzoic acid **2** treated with thionylchloride followed by *p*-anisidine in the presence of triethyl amine at 0°C afforded pale yellow crystals of *N*-(4- methoxyphenyl)-4-methyl-3-nitrobenzothioamide **3** with 90% yield. Then compound **3** was converted to *N*-(4- methoxyphenyl)-4-methyl-3-nitrobenzothioamide **4** by reacting with Lawesson's reagent in dry toluene under reflux condition with 75% yield. Finally, 6-methoxy-2-(4-methyl-3-nitrophenyl) benzo[*d*]thiazole **5** were achieved by intra-molecular free-radical cyclization of *N*-(4- methoxyphenyl)-4-methyl-3-nitrobenzothioamide **4** by using Dess–Martin per iodine in CH_2Cl_2 at room temperature. The product is light yellow solid in 85% yield (Scheme 1).

Compound **5** upon treatment with freshly prepared tetra butyl ammonium permanganate (TBAP) in dry pyridine at room temperature afforded, 6-methoxy-2-(4-methyl-3-nitrophenyl) benzo[*d*] thiazole [19–21] (**6**), as light yellow solid in 88% yield. Nitro acid **6** was converted to its acid chloride [25], **7** with thionylchloride, which was condensed with propargyl amine in the presence of triethyl amine to obtain nitro amide as brownish solid [21] **8** in 85% yields. Compound **8** and benzyl azides **9a–j** in the presence of 0.5 mol% $CuSO_4.5H_2O$ and 10 mol% sodium ascaorbate afforded the triazole. The reaction is regioselective only in the presence of Cu (I) or Cu (II) salts as a catalyst, because Cu (I) as a catalyst strongly activates the terminal acetylenes toward 1,3-dipole in azide to give the desired 1,4-disubstituted [1,2,3]-triazole derivatives **10a-j** in good yields (85–87%) via click Chemistry [1 g]. Structures were confirmed by utilizing spectral data and elemental analysis. We observed that electron-donating methoxy ($-OCH_3$) and benzoxyl (−OBn) substituted compounds showed more antibacterial active compared with other substituted *N*-((l-benzyl-l*H*-l,2,3-triazol-5-yl)methyl)-4-(6-methoxybenzo[*d*]thiazol-2-yl)-2-nitrobenzamides(**10a-j**). All the synthesized compounds were in good agreement with the proposed structure. The physical characterization data are given in Table 1 and Scheme 2.

Antimicrobial activity. In view of developing new class of antimicrobial agents, synthesized novel compounds were screened for their *in vitro* antimicrobial activities to determine zone of inhibition at 100 µg/mL against two Gram-positive bacteria (*Staphylococcus aureus* [MTCC 096], *Bacillus subtilis* [MTCC 441]) and two Gram-negative bacteria (*Escherichia coli* [MTCC 443], *Pseudomonas aeruginosa* [MTCC 424]), as well as two fungi (*Aspergillusniger* [MTCC 282], *Aspergillus fumigates* [MTCC 343]), strains using cup plate method [22,23] where inoculated Muller–Hilton agar for bacteria and Sabouraud dextrose agar for fungi was poured onto the sterilized petri dishes (25–30 mL each petri dish). The poured material was allowed to set (30 min), and thereafter, the 'cups' (6-mm diameter) was 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 (0.1 mL) was added with the help of a micro pipette. The plates were incubated at 37° C for 14 h for bacteria and 30 h for fungi, and the results were noted. The test solution was prepared by DMSO as solvent. Clinically antimicrobial drugs Ciprofloxacin and Miconazole were used as the positive control, and DMSO was used for blank.

The results of antimicrobial screening are summarized in Table 2. Revealed that all the synthesized compounds, **10a–j** could effectively, to some extent, inhibit the growth of all tested strains *in vitro*. In antibacterial studies, all the compounds tested were found less active towards *B. subtilis,* as compared with other three strains of bacteria. Most of the compounds showed moderate to good activity against *S. aureus.* In general, **10a**, **10 h**, and **10i** have shown good

Scheme 1. Synthetic schemes of 6-methoxy-2-(4-methyl-3-nitrophenyl)-l,3-benzothiazole *and reagents and conditions:* (a) Conc. HNO_3, Conc. H_2SO_4 (1:2), CH_2C1_2, 0°C – R. T, 5 h, 84% (b) (i) $SOC1_2$, cat. DMF, CH_2C1_2 (ii)*P*-Anisidine, Et_3N, THF, 0 °C- R.T,90% (c) Lawesson's reagent, toluene, 95°C,75% (d) DMP, CH_2C1_2, R. T, 20 min, 85%.

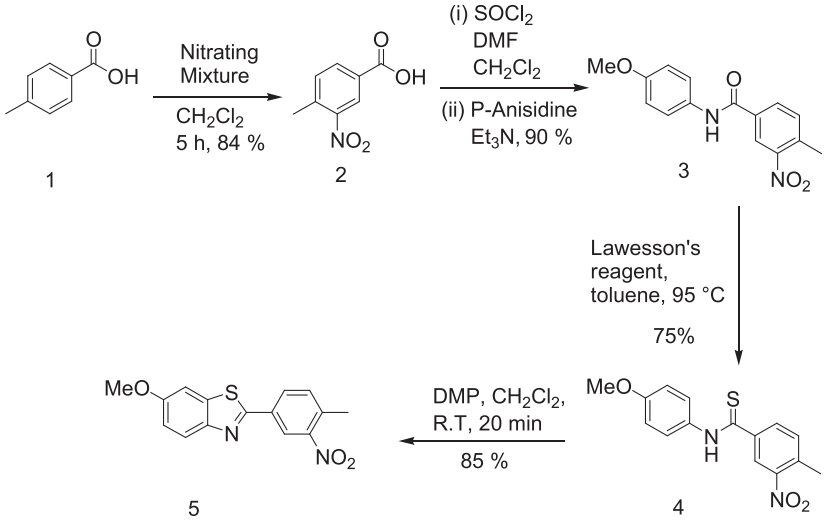

Table 1

Physical characterization data of compounds **10a–j**.

S. no.	Compound no.	Molecular formula (**10a–j**)	Time (h)	Yield (%)	mp (°C)
1.	**10a**	$C_{25}H_{20}N_6O_4S$	12.0	87	205.4–206.6
2.	**10b**	$C_{25}H_{18}N_6O_6S$	11.4	85	210–212
3.	**10c**	$C_{22}H_{20}N_6O_6$ S	12.0	85	196–197
4.	**10d**	$C_{33}H_{28}N_6O_6$ S	11.5	83	181–182
5.	**10e**	$C_{33}H_{28}N_6O_6S$	11.3	83	169.9–170.8
6.	**10f**	C_{25} $H_{19}ClN_6O_4$ S	11.3	85	187.8–188.7
7.	**10 g**	C_{29} $H_{28}N_6O_4S$	12.0	87	184.3–185.6
8.	**10 h**	$C_{29}H_{22}N_6O_4S$	12.0	85	193–194
9.	**10i**	$C_{28}H_{26}N_6O_7S$	10.0	84	182.8–184.2
10.	**10j**	$C_{26}H_{19}F_3N_6O_4$ S	11.0	85	196.4–197.5

Scheme 2. Synthetic schemes of *N*-((l-benzyl-l*H*-l,2,3-triazol-5-yl) methyl)-4-(6-methoxybenzo[*d*]thiazol-2-yl)-2-nitrobenzamides (**10a-j**) and their r*eagents and conditions*: (a) TBAP, dry pyridine, R.T, 88%; (b) $SOCl_2$, cat. DMF, CH_2Cl_2, R.T, 85%; (c) Propargyl amine, Et_3N, dry THF, 0°C – R.T,85% (d) 0.5 mol% $CuSO_4.5H_2O$, 10 mol% Sodium ascorbate, t-BuOH:H_2O, R.T, 12 h, (85–95)%.

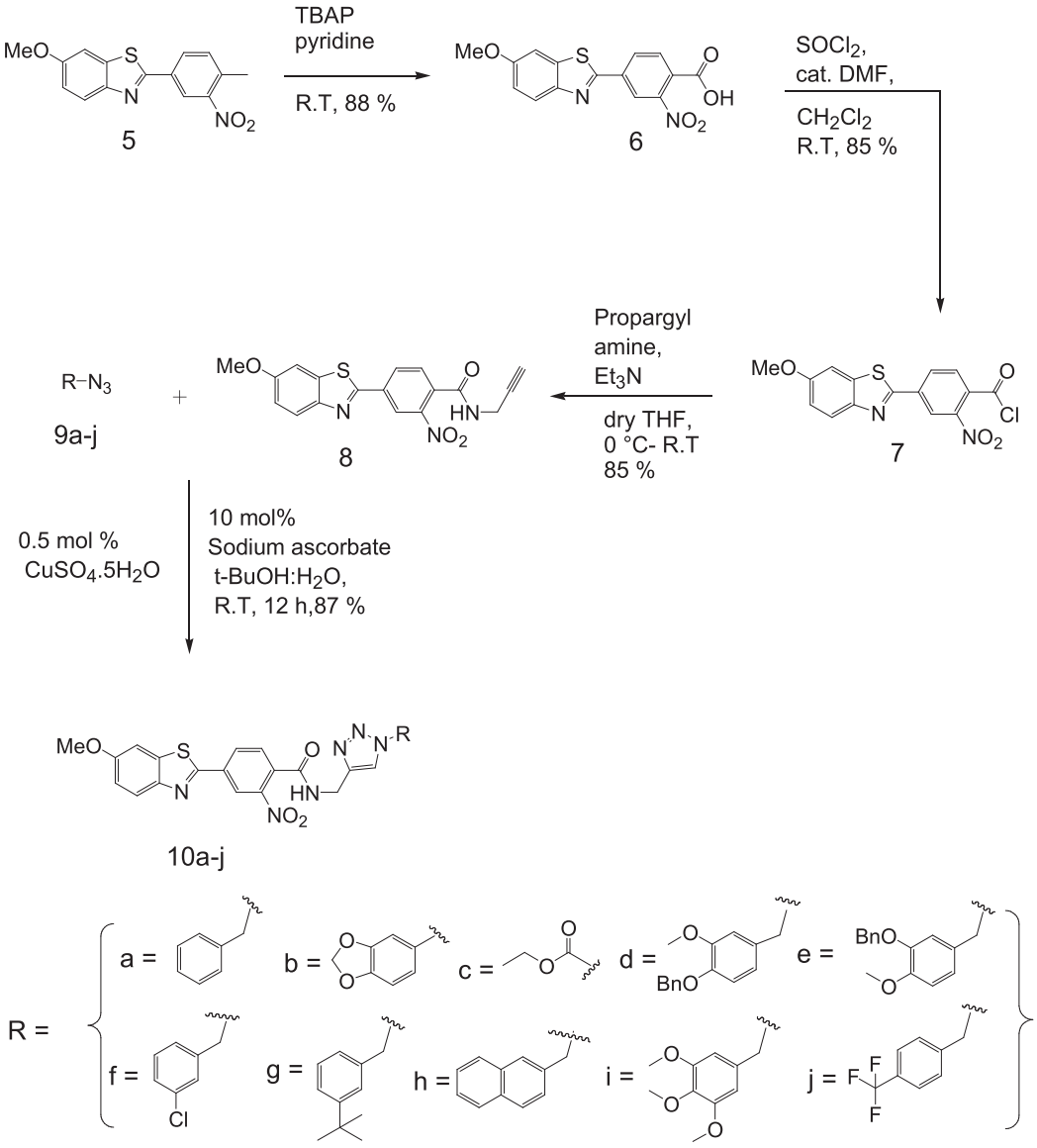

Table 2

Antimicrobial activity of title compounds **10a–j**.

	Zones of inhibition in mm					
	Anti-bacterial activity (100 μg/mL)				Antifungal activity (100 μg/mL)	
	Gram-positive bacteria		Gram-negative bacteria		Fungi	
Compound	*Staphylococcus aureus*	*Bacillus subtilis*	*Escherichia coli*	*Pseudomonas aeruginosa*	*Aspergillus Niger*	*Aspergillus fumigates*
10a	17	14	12	13	10	17
10b	13	12	15	12	10	18
10c	15	11	16	12	11	17
10d	13	11	12	10	12	18
10e	13	10	10	11	11	18
10f	14	11	10	13	13	19
10 g	13	11	12	12	13	18
10 h	16	10	14	14	14	18
10i	17	13	16	14	14	18
10j	14	11	13	14	13	18
Ciprofloxacin	20	21	22	20	—	—
Miconazole	—	—	—	—	29	22

antibacterial activity against *S. aureus*. Compunds **10b**, **10c**, and **10i** have shown moderate activity against *E. coli.* Out of two strains of fungi, these compounds were found to be less active against *Aspergillusniger* whereas showed moderate to good activity against *A. fumigatus*. Compounds, **10a**, **10b**, **10c**, **10d**, **10e**, **10f**, **10 g**, **10 h**, **10i**, and **10j** possessed good antifungal activity against *A. fumigates.*

The standard drug for bacteria is Ciprofloxacin and the standard drug for fungi is Miconazole Zone of Inhibition (internal diameter: 6 mm). All the compounds were screened at 100 μg/mL concentration.

CONCLUSIONS

In conclusion, we accomplished the synthesis of the proposed structure of novel *N*-((l-benzyl-l*H*-l, 2, 3-triazol5-yl) methyl)-4-(6-methoxybenzo[*d*]thiazol-2-yl)-2-nitrobenzamides following by *in situ* inter-molecular 1, 3-dipolar cycloaddition reaction between easily affordable azides and alkynes with good yields and high purity. The synthesized compounds were screened for the antimicrobial activity study by cup-plate method. Some of the compounds shown strong antimicrobial activity at low concentrations, and hence, further design and synthesis of compounds in this direction are in progress. This study can provide a road map to design and synthesis of Benzothiazole scaffold based antimicrobial active compounds.

EXPERIMENTAL

General. Melting points were determined using Buchi 510 instrument (New Castle, DE, USA). infrared (IR) spectra were recorded on Perkin-Elmer 683 series spectrometer (Waltham, MA, USA) with KBr optics, and ^{1}H NMR (400 MHz) were recorded on Bruker Avance 400 spectrometer (Billerica, MA, USA) using TMS as internal standard (chemical shifts in ppm). Mass spectra were recorded on a VG micro mass 70–70H (Ringoes, NJ) instrument. CHN analysis was carried out using Vario Micro Cube Elementar instrument (Donaustraße 7, Hanau, Germany).

General procedure for the synthesis of N-((l-benzyl-lH-l, 2, 3-triazol-5-yl) methyl)-4-(6-methoxybenzo[d]thiazol-2-yl)-2-nitrobenzamides (10a–j). Here, we describe the synthesis of **10a** as a model synthesis, and corresponding spectral data are provided later. Water and tertiary alcohol in the ratio 1:1 (50 mL) were added to the round bottom flask containing compounds **8a**, (5 g, 27.2 mmol) possessing triple bond and freshly prepared benzyl azides (4.68 g, 35.1 mmol) (**9a**) and stirred for 5–10 min. To this reaction, mixtures were added 0.5 mol% $CuSO_4.5H_2O$ (0.339 g, 1.36 mmol.) and 10 mol% sodium ascorbate (2.155 g, 0.40 mmol) simultaneously. Reaction was continued for 12 h at room temperature till the completion of the reaction. After the completion of the reaction (monitored by Thin Layer Chromatography (TLC)), tertiary alcohol was removed under pressure, and the aqueous layer was extracted with ethyl acetate (3 × 50 mL). The combined organic layer was washed with brine solution and dried over Na_2SO_4. The organic layer was separated and removed in vacuo under reduced pressure. The resulting material was purified by column chromatography to afford colorless compound **10a** (4.35 g) in 87% as a white solid. mp 205.4-206.6°C; IR (Neat): 3319, 3139, 2923, 1641, 1603, 1539, 1459, 1360, 1292, 1265, 1230, 1124,

1060, 1026 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz); δ 9.20 (brs, 1H, NH), 8.58 (s, 1H, Ar-H), 8.21–8.36 (d, 1H, J = 7.8 Hz Ar-H), 7.84–8.05 (m, 2H, Ar-H), 7.65–7.80 (d, 1H, J = 7.9 Hz),7.54 (s, 1H, Ar-H), 7.25–7.43 (s, 5H, Ar–H),7.05–7.20 (d, 1H, Ar–H), 5.58 (s, 2H, CH_2), 4.51–4.65 (d, 2H, N–CH_2), 3.91 (s, 3H, OCH_3); ^{13}C NMR (DMSO-d_6, 100.6 MHz): δ 164.09, 159.77, 150.99, 146.80, 146.24, 143.42, 135.33, 134.20, 134.03, 132.19, 129.69, 128.83, 127.47, 126.96, 126.60, 122.73, 121.59, 120.46, 115.20, 102.90, 54.44, 52.23, 34.01; ESI-MS: *m/z* $[M + Na]^+$ = 523.116 (Calcd M^+ = 500.127), Elemental *Anal*. Calcd for $C_{25}H_{20}N_6O_4S$: C, 59.99; H, 4.03; N, 16.79; S, 6.41; found: C, 59.90; H, 4.07; N, 16.83; S, 6.42.

Similar experimental procedure of **10a** was employed for all the remaining derivatives, **10b**−**10j** with yields between 83% and 87%.

N-((l-(Benzo[d][l,3]dioxol-5-yl)-lH-l,2,3-triazol-5-yl)methyl)-4-(6-methoxybenzo[d]thiazol-2-yl)-2-nitrobenzamide (10b). Compound **10b** is a colorless solid yielded in 85% (3.90 g). mp 210–212°C; IR (Neat): 3271, 3144, 3098, 2920, 2851, 1639, 1605, 1545, 1505, 1466, 1356, 1299, 1249, 1179, 1035 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz); δ 9.43 (broad singlet, 1H, NH), 8.49–8.78 (m, 1H, Ar-H), 8.41 (s, 1H, ArH), 7.64–8.19 (m, 3H, Ar–H), 6.67–7.6 (m, 4H, Ar–H), 6.18 (s, 2H, O–CH_2–O), 4.64 (s, 2H, N–CH_2), 3.91 (s, 3H, OCH_3); ^{13}C NMR (DMSO-d_6, 100.6 MHz): δ 164.67, 161.06, 157.94, 147.52, 144.85, 134.96, 130.93, 130.28, 123.79, 121.44, 116.45, 113.48, 108.40, 104.55, 101.92, 101.70, 55.61, 28.86; ESI-MS: *m/z* $[M + H]^+$ = 531.094 (Calcd M^+ = 530.101), Elemental *Anal* Calcd for $C_{25}H_{18}N_6O_6S$: C, 56.60; H, 3.42; N, 15.84; S, 6.04, found: C, 56.70; H, 3.37; N, 12.84; S, 6.02.

Ethyl 2-(5-((4-(6-methoxybenzo[d]thiazol-2-yl)-2-nitrobenzamido) methyl)-lH-l,2,3-triazol-l-yl) acetate (10c). Compound **10c** is a colorless solid yielded in 85% (3.70 g). mp 196–197°C; IR (Neat): 3445, 3243, 3092, 2924, 2853, 1739, 1638, 1535, 1465, 1353, 1222, 1056, 1020 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz) δ 9.38 (brs, 1H, NH), 8.58 (s, 1H, Ar–H), 8.28–8.43 (m, 1H, Ar–H), 7.93–8.14(m, 2H, Ar–H), 7.69–7.83 (m, 2H, Ar–H), 7.06–7.27 (m, 1H, Ar–H), 5.40 (s, 2H, CH 2), 4.47–4.65 (d, 2H, N–CH_2), 4.09–4.27 (q, 2H, O–CH_2), 3.87 (s, 3H, CH 3), 1.23 (t, 3H, CH_3); ^{13}C NMR (DMSO-d_6, 100.6 MHz): δ 167.15, 164.75, 161.29, 158.04, 147.68, 147.58, 144.14, 136.54, 134.95, 133.11, 131.17, 130.31, 124.38, 123.93, 121.60, 116.64, 108.41, 61.43, 55.77, 50.32, 34.79, 13.90; ESI-MS: *m/z* $[M + H]^+$ = 497.123 (Calcd M^+ = 496.117), Elemental *Anal*. Calcd for $C_{22}H_{20}N_6O_6$ S: C, 53.22; H, 4.06; N, 16.93; S, 6.46, found: C, 53.12; H, 4.11; N, 16.96; S, 6.48.

N-((l-(4-(benzyloxy)-3-methoxybenzyl)-lH-l,2,3-triazol-4-yl) methyl)-4-(6methoxybenzo[d]thiazol-2-yl)-2-nitrobenzamide (10d). Compound **10d** is a colorless solid yielded in 83% (3.51 g). mp 181–182°C; IR (Neat): 3422, 2924, 1642, 1602, 1537, 1459, 1428, 1381, 1353, 1263, 1228, 1161, 1138, 1023, 835, 780, 736, 697, 556 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz) δ 9.31 (t,1H, J = 5.8 Hz, NH), 8.58 (d, 1H, J = 1.5 Hz, ArH), 8.29–8.45 (dd, 1H, $J1$ = 1.5 Hz, $J2$ = 7.9 Hz, Ar–H), 7.71–7.83 (m, 2H, Ar–H), 7.27–7.48 (m, 5H, Ar–H), 7.15–7.23 (dd, 1H, $J1$ = 2.5 Hz, $J2$ = 8.9 Hz, Ar–H), 6.97–7.08 (m, 2H, Ar–H), 6.82–6.91 (m, 1H, Ar–H), 5.51 (s, 2H, CH_2), 5.06 (s, 2H, O–CH_2), 4.51 (d, 2H, J = 5.47 Hz, NCH2), 3.87 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3); ^{13}C NMR (DMSO-d_6, 100.6 MHz): δ 164.58, 161.22, 157.97, 149.04, 147.62, 147.57, 147.54, 144.16, 136.47, 134.86, 133.06, 131.07, 130.24, 128.56, 128.24, 127.67, 127.58, 123.86, 122.75, 121.54, 120.43, 116.58, 113.55, 112.26, 104.77, 69.80, 55.71, 55.47, 52.57, 34.80; ESI-MS: *m/z* $[M + H]^+$ = 637.188 (Calcd M^+ = 636.179), Elemental *Anal*. Calcd for $C_{33}H_{28}N_6O_6$ S: C, 62.25; H, 4.43; N, 13.20; S, 5.04, found: C, 62.15; H, 4.48; N, 13.24; S, 5.05.

N-(l-(3-(benzyloxy)-4-methoxybenzyl)-lH-l,2,3-triazol-4-yl) methyl)-4-(6-methoxybenzo[d]thiazol-2-yl)-2-nitrobenzamide (10e). Compound **10e** is a colorless solid yielded in 83% (3.60 g). m p 169.9–70.8°C;IR (Neat): 3335, 3068, 2923, 1647, 1603, 1538, 1516, 1461, 1431, 1356, 1261, 1232, 1162, 1139, 1055, 1021, cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 9.33 (t, 1H, J = 5.1 Hz, NH), 8.56 (s, 1H, Ar–H), 8.33 (d, 1H, J = 8.3 Hz, Ar–H), 7.92–8.14 (m, 2H, Ar–H), 7.66–7.87 (m, 2H, Ar–H), 7.27–7.55 (m, 5H, Ar–H), 7.08–7.25 (m, 2H, ArH), 6.85–7.03 (m, 2H, Ar–H), 5.50 (s, 2H, CH2), 5.03 (s, 2H, O–CH_2), 4.52 (d, 2H, J = 4.9 Hz, N–CH_2), 3.85 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3); ^{13}C NMR (DMSO-d_6, 100.6 MHz): δ 164.61, 161.18, 157.97, 149.01, 147.70, 147.62, 147.53, 144.19, 136.72, 136.47, 134.87, 133.05, 131.04, 130.24, 128.23, 128.13, 128.06, 127.80, 123.86, 122.75, 121.52, 121.01, 116.55, 113.71, 112.06, 104.72, 69.95, 55.69, 55.50,52.58, 34.83; ESI-MS: *m/z* $[M + H]^+$ = 637.188 (Calcd M^+ = 636.179),Elemental *Anal*. Calcd for $C_{33}H_{28}N_6O_6S$: C, 62.25; H, 4.43; N, 13.20; S, 5.04, found: C, 62.15; H, 4.48; N, 13.24; S, 5.05.

N-((l-(3-chIorobenzyl)-lH-l,2,3-triazol-4-yl)methyl)-4-(6-fluorobenzo[d]thiazol-2-yl)-2-nitrobenzamide (10f). Compound **10f** is a colorless solid yielded in 85% (4.12 g). mp 187.8–188.7°C; IR (Neat): 3424, 3271, 3076, 2933, 1636, 1606, 1555, 1529, 1475, 1436, 1348, 1320, 1269, 1213, 1169, 1125, 1060, 1028, 908 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz):δ 9.33 (t, 1H, J = 5.4 Hz, NH), 8.54 (d, 1H, J = 1.7 Hz, Ar-H), 8.32–8.42 (dd, 1H, $J1$ = 1.7 Hz, $J2$ = 7.9 Hz, Ar–H), 8.13 (s, 1H, Ar–H), 8.01 (d, 1H, J = 8.9 Hz, ArH), 7.72–7.83 (m, 2H, Ar–H), 7.35–7.47 (m, 3H, Ar–H), 7.14–7.32 (m, 2H, Ar–H), 5.64 (s, 2H, CH_2), 4.52 (d, 2H, J = 5.5 Hz, N–CH_2), 3.86(s, 3H, OCH_3); ^{13}C NMR (DMSO-d_6, 100.6 MHz): δ 164.63, 161.19, 157.96, 147.63, 147.51, 144.32, 138.34, 136.47, 134.87, 133.17, 133.06, 130.50, 130.24, 127.96, 127.68, 126.48, 123.85, 123.28, 121.52, 116.53, 104.74, 55.70, 51.90, 34.80; ESI-MS: *m/z* $[M + H]^+$ = 535.095 (Calcd M^+ = 534.088), Elemental *Anal*. Calcd for C_{25} $H_{19}ClN_6O_4$ S: C, 56.13;

H, 3.58; N, 15.71; S, 5.99, found: C, 56.03; H, 3.63; N, 15.73; S, 6.00.

N-((l-(3-tert-butylbenzyl)-lH-l,2,3-triazol-4-yl)methyl)-4-(6-methoxybenzo[d]thiazol-2-yl)-2-nitrobenzamide (10g). Compound **10g** is a colorless solid yielded in 87% (4.20 g). mp 184.3–185.6 °C; IR (Neat): 3424, 3136, 3065, 2961, 1733, 1658, 1602, 1538, 1462, 1433, 1352, 1304, 1262, 1226, 1125, 1056, 1024 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 9.32 (t, 1H, J = 5.4 Hz, NH), 8.50–8.69 (d, 1H, .J = 1.3 Hz, Ar–H), 8.29–8.47 (m, 1H, Ar–H), 8.07 (s, 1H, Ar–H), 8.01 (d, 1H, J = 9.1 Hz, Ar–H), 7.70–7.89 (m, 2H, Ar–H), 7.32–7.50 (d, 2H, J = 8.3 Hz, Ar–H), 7.24–7.31 (d, 2H, J = 8.3 Hz, Ar–H), 7.15–7.22 I (dd, 1H, .A = 2.45 Hz, $J2$ = 9.1 Hz, Ar-H), 5.57 (s, 2H, CH_2), 4.52 (d, 2H, J = 5.3 Hz, NCH_2), 3.86 (s, 3H, OCH_3), 1.24 (s, 9H, Me); ^{13}C NMR (DMSO-d_6, 100.6 MHz): δ 164.61, 161.20, 157.97, 150.46, 147.64, 147.56, 144.21, 136.48, 134.87, 133.01, 131.06, 130.27, 127.63, 125.35, 123.86, 122.95, 121.52, 116.57, 104.74, 59.63, 55.71, 52.41, 34.15, 30.91; ESI-MS: m/z $[M+H]^+$ = 557.121 (Calcd M^+ = 556.189), Elemental *Anal*. Calcd for C_{29} $H_{28}N_6O_4S$: C, 62.57; H, 5.07; N, 15.10; S, 5.76, found: C, 62.47; H, 5.10; N, 15.12; S, 5.77.

N-(6-fluorobenzo[d]thiazol-2-yl)-N-((l-(naphthalen-2-ylmethyl)-lH-l,2,3-triazol-4-yl) methyl)-2-nitrobenzamide (10h). Compound **10h** is a colorless solid yielded in 85% (3.50 g). mp 193–194°C; IR (Neat): 3265, 3062, 2932, 1644, 1601, 1533, 1469, 1430, 1351, 1260, 1223, 1165, 1053, 1026 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 9.30 (t, 1H, J = 5.4 Hz, NH), 8.56 (d, 1H, J = 1.7 Hz, Ar–H), 8.30–8.38 (dd, 1H, $J1$ = 1.7 Hz, $J2$ = 8.1 Hz, Ar–H), 8.23 (d, 1H, J = 7.9 Hz, Ar–H), 7.89–8.09 (m, 4H, Ar–H), 7.69–7.81 (m, 2H, Ar–H), 7.38–7.66 (m, 4H, Ar–H), 7.14–7.23 (m, 1H, Ar–H), 6.11 (s, 2H, CH_2), 4.50 (d, 2H, J = 5.4 Hz, N–CH_2), 3.86 (s, 3H, OCH_3); ^{13}C NMR (DMSO-d_6, 100.6 MHz): δ 164.65, 161.19, 157.99, 147.64, 147.52, 144.21, 136.48, 134.87, 133.25, 133.06, 131.48, 131.07, 130.55, 130.23, 128.54, 128.90, 127.06, 126.67, 126.05, 125.43, 123.87, 123.22, 121.52, 116.57, 104.72, 55.71, 50.68, 34.83; ESI-MS: m/z $[M+H]^+$ = 551.150 (Calcd M^+ = 550.142), Elemental *Anal.* Calcd for $C_{29}H_{22}N_6O_4S$: C, 63.26; H, 4.03; N, 15.26; S, 5.82, found: C, 63.16; H, 4.08; N, 15.29; S, 5.84.

N-(6-methoxybenzo[d]thiazol-2-yl)-2-nitro-N-((l-(3,4,5-trimethoxybenzyl)-lH-l,2,3-triazol-4-yl)methyl)benzamide (10i). Compound **10i** is a colorless solid yielded in 84% (3.21 g). mp 182.8–184.2°C; IR (Neat): 3341, 2937, 2839, 1647, 1598, 1540, 1509, 1461, 1427, 1353, 1238, 1125, 1056, 1015, 830 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 3.63 (s, 3H, OCH_3), 3.75 (s, 6H, OCH_3), 3.86 (s, 3H, OCH_3), 4.52 (d, 2H, J = 5.7 Hz, N–CH_2), 5.51 (s, 2H, CH_2), 6.73 (s, 2H, ArH), 7.18 (d, 1H, J = 7.7 Hz, Ar–H), 7.77 (s, 2H, Ar–H), 8.00 (d, 1H, J = 8.8 Hz, Ar–H), 8.09 (s, 1H, Ar–H), 8.27–8.43 (m, 1H, Ar–H), 8.57 (s, 1H, Ar–H), 9.33 (brs, 1H, NH). ^{13}C NMR (DMSO-d_6, 100.6 MHz): δ 34.86, 53.01, 55.79, 59.90, 104.75, 105.62, 116.63, 121.60, 122.98, 123.91, 130.28, 131.14, 131.34,133.11, 134.90, 136.52, 137.18, 144.29, 147.57, 147.65, 152.93, 158.00, 161.24, 164.69; ESI-MS: m/z $[M+H]^+$ = 591.166 (Calcd M^+ = 590.158), Elemental *Anal*. Calcd for $C_{28}H_{26}N_6O_7S$: C, 56.94; H, 4.44; N, 14.23; S, 5.43, found: C, 56.84; H, 4.49; N, 14.26; S, 5.45.

N-(6-methoxybenzo[d]thiazol-2-yl)-2-nitro-N-((l-(4-(trifluoromethyl) benzyl)-lH-l,2,3-triazol-4-yl)methyl benzamide (10j). Compound **10j** is a colorless solid yielded in 85% (3.60 g). mp 196.4–197.5°C; IR (Neat): 3271, 3072, 2943, 1631, 1603, 1559, 1530, 1480, 1461, 1434, 1353, 1328, 1262, 1225, 1166, 1122, 1064, 1021, 993 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz):δ 3.87 (s, 3H, OCH_3), 4.54 (d, 2H, J = 5.8 Hz, N–CH_2), 5.74 (s, 2H, CH_2), 7.07–7.24 (m, 1H, Ar–H), 7.51 (d, 2H, J = 8.3 Hz, Ar–H), 7.60–7.84 (m, 4H, Ar–H), 7.89–8.06 (m, 1H, Ar–H), 8.07–8.18 (m, 1H, Ar–H), 8.25–8.42 (m, 1H, Ar–H), 8.47–8.65 (s, 1H, Ar–H), 9.32 (t, 1H, J = 4.95 Hz, Ar–H); ^{13}C NMR (DMSO-d_6, 100.6 MHz): δ 34.74, 52.00, 55.57, 104.51, 116.40, 121.39, 123.33, 123.73, 125.31,125.35, 128.30, 130.12, 130.91, 133.04, 134.89, 136.38, 140.41, 144.28, 147.42, 147.62, 157.91, 164.60; ESI-MS: m/z $[M+H]^+$ = 569.121(Calcd: M^+ = 568.114), Elemental *Anal*. Calcd for $C_{26}H_{19}F_3N_6O_4$ S: C, 54.93; H, 3.37; N, 14.78; S, 5.64 found: C, 54.83; H, 3.42; N, 14.79; S, 5.65.

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