Synthesis and Antimicrobial Evaluation of (1-(2-(Benzyloxy)-2-oxoethyl)-1*H*-1,2,3-triazol-4-yl)methyl Benzoate Analogues

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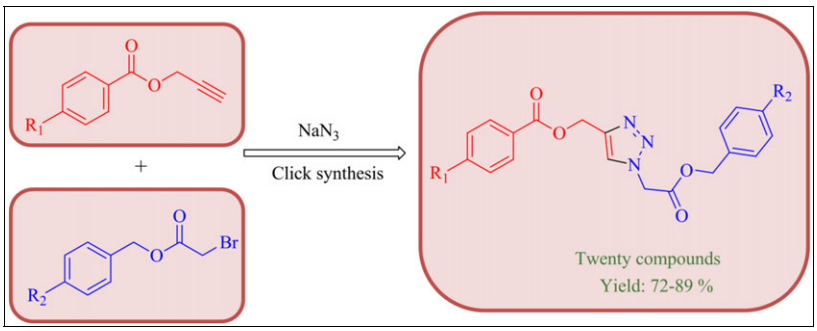

A convenient one pot synthesis of 20 (1-(2-(benzyloxy)-2-oxoethyl)-1*H*-1,2,3-triazol-4-yl)methyl benzoate analogues (**5a**–**5t**) with ester functionality was carried out via Cu(I) catalyzed click reaction between prop-2-yn-1-yl benzoates and benzyl 2-azidoacetates. The structure of synthesized triazoles were explicated by various spectral techniques like FT-IR, ^{1}H NMR, ^{13}C NMR, and high-resolution mass spectrometry and evaluated for *in vitro* antimicrobial potential against *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter aerogenes*, *Candida albicans*, and *Aspergillus niger*. Most of synthesized triazole derivatives exhibited average to excellent activity against tested microbial strains.

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INTRODUCTION

Over the past few decades, incidence of drug resistant pathogenic microbial infections is increasing at an alarming rate; thereby, total reliability on the available antimicrobial drugs is not advisable in the long run for medicinal chemists. This aroused a crucial search for development of new antimicrobials with better efficacy. In order to meet this challenge, 1,2,3-triazoles emerged as a privileged class of medicinal scaffolds [1,2] due to its better compatibility. Among *N*-heterocycles, disubstituted 1,2,3-triazoles have been preferably used as an important pharmacophore owing to the widespread therapeutic importance as antibiofilm [3], antibiotic [4], antimicrobial [5,6], anticancer [7,8], antitubercular [9,10], antiinfluenza [11], antiproliferative [12], antioxidant [13], and antimalarial [14]. In addition to the aforementioned medicinal importance, 1,2,3-triazoles also possess paramount impact in the fields like drug discovery [15], bioconjugation [16], and material sciences [17].

Cu(I) catalyzed version of thermally driven Huisgen 1,3-dipolar cycloaddition [18] between terminal alkynes and azides emerged as a powerful tool for the exclusive construction of 1,4-disubstituted 1,2,3-triazoles discovered by Sharpless and Meldal [19,20]. This process has been studied as a unique example of click reaction and widely used in the synthesis of pharmaceuticals [21], peptidomematics [22], dendritic and polymeric materials [23], glycoconjugates [24], and calixsugars [25].

Keeping these observations in mind and in continuation of our enduring research on synthesis and biological studies of 1,4-disubstituted 1,2,3-triazoles [26–29], herein, we focused on synthesis of a series of (1-(2-(benzyloxy)-2-oxoethyl)-1*H*-1,2,3-triazol-4-yl) methyl benzoate analogues (**5a**–**5t**) with ester functionality via Cu(I) catalyzed click reaction between prop-2-yn-1-yl benzoates and benzyl 2-azidoacetates. All the synthesized compounds were characterized by spectral techniques FT-IR, ^{1}H NMR, ^{13}C NMR spectroscopy, and high-resolution mass spectrometry (HRMS) and also examined for antimicrobial activity.

RESULTS AND DISCUSSION

Chemistry. The synthesis of desired (1-(2-(benzyloxy)-2-oxoethyl)-1*H*-1,2,3-triazol-4-yl)methyl benzoate analogues (**5a**–**5t**) having ester linkage was accomplished

by strategy described in Scheme 1. Commercially available benzoyl chlorides (**1a**–**1d**) were taken as starting material for the synthesis of prop-2-yn-1-yl benzoates [30] (**2a**–**2d**) by propargylation with propargyl alcohol in dry dichloromethane in the presence of *N*,*N*-dimethylaminopyridine. Benzyl 2-bromoacetates (**4a**–**4e**) were prepared by treating various benzyl alcohols (**3a**–**3e**) with bromoacetyl bromide in acetonitrile using sodium bicarbonate as base. Finally, the synthesis of 1,4-disubstituted 1,2,3-triazoles with ester linkage (**5a**–**5t**) in good yield was carried out via one pot click reaction between prop-2-yn-1-yl benzoates (**2a**–**2d**) and benzyl 2-azidoacetates (**4a**–**4e**) (generated *in situ* by reaction of benzyl 2-bromoacetates (**4a**–**4e**) with sodium azide) in the presence of catalytic amount of copper sulfate pentahydrate and sodium ascorbate in dimethyl sulfoxide (DMSO).

Compound	R_1	R_2	Time (h)	Yield (%)
5a	H	H	9	83
5b	H	OCH_3	12	89
5c	H	NO_2	11	72
5d	H	Cl	8	85
5e	H	CH_3	10	84
5f	OCH_3	H	11	79
5g	OCH_3	OCH_3	13	81
5h	OCH_3	NO_2	12	78
5i	OCH_3	Cl	7	83
5j	OCH_3	CH_3	14	85
5k	NO_2	H	12	76
5l	NO_2	OCH_3	13	88
5m	NO_2	NO_2	14	83
5n	NO_2	Cl	8	73
5o	NO_2	CH_3	10	77
5p	CH_3	H	12	89
5q	CH_3	OCH_3	11	81
5r	CH_3	NO_2	10	83
5s	CH_3	Cl	7	80
5t	CH_3	CH_3	12	77

The structures of all newly synthesized triazole derivatives (**5a**–**5t**) were confirmed by spectral techniques, that is, FT-IR, ^{1}H NMR, ^{13}C NMR spectroscopy, and HRMS. In FT-IR spectra of compounds, emergence of characteristic absorption bands in the region at 3126–3156 cm^{-1} due to C–H stretching vibrations of triazole ring ensured formation of triazoles, while absorption bands at 1698–1764 cm^{-1} attributed to >C=O stretching vibrations of ester. In ^{1}H NMR spectra of most of compounds, proton present on C_5 of newly formed triazole ring resonated in region at δ 7.80–8.38 as singlet. Moreover, in ^{13}C NMR spectra, signals appeared in the region at δ 125.4–127.1 and 141.5–143.7 assigned to C_5 and C_4 of triazole ring, respectively. Signals due to carbonyl carbon (>C=O) of ester linkages appeared in the region at δ 163.9–167.6. Results obtained from high-resolution mass spectral analysis were found in good agreement with their molecular mass.

Antimicrobial evaluation. All the newly synthesized 1,4-disubstituted 1,2,3-triazole derivatives (**5a**–**5t**) having ester linkage were tested *in vitro* for antimicrobial activity against one Gram-positive bacterial strain [*Staphylococcus aureus* (MTCC 3160)], three Gram-negative bacterial strains [*Escherichia coli* (MTCC 443), *Klebsiella pneumoniae* (NCDC 138), and *Enterobacter aerogenes* (NCDC 106)] and two fungi [*Candida albicans* (MTCC 227) and *Aspergillus niger* (MTCC 282)] by serial dilution technique [31]. Norfloxacin and fluconazole were used as standard drugs for antibacterial and antifungal strains, respectively, and minimum inhibitory concentrations (MICs) were expressed in terms of μmol/mL.

Antibacterial screening data (Table 1) depicted that some of the tested compounds possess good to excellent bactericidal potential. Compound **5m** exhibited appreciable bactericidal potential against all bacterial strains under study, while compound **5n** showed remarkable activity against *S. aureus* and *E. coli* with MIC value of 0.0290 μmol/mL. Compound **5h** with MIC 0.0293 μmol/mL found to possess significant inhibitory activity against *K. pneumoniae*. Compound **5k** (MIC 0.0315), **5o** (MIC 0.0305), and **5r** (MIC 0.0305) against *S. aureus*; **5g** (MIC 0.0304) and **5s** (MIC 0.0313) against *E. coli*; and **5i** (MIC 0.0301) and **5r** (MIC 0.0305) against *K. pneumoniae* showed comparable activity with standard drug. In case of *E. aerogenes*, compound **5c** (MIC 0.0631), **5h** (MIC 0.0586), **5n** (MIC 0.0580), and **5r** (MIC 0.0609) found to be moderately active as compared with reference.

As revealed from the results represented in Table 2, some of the triazole derivatives exhibited moderate to good antifungal activity against tested strains. Compound **5h** displayed almost twofold antifungal potency against *C. albicans* with MIC value of 0.0293 μmol/mL. Compound **5m** (MIC 0.0142) also emerged as a potential antifungal agent against *C. albicans*, while compound **5h** (MIC 0.0144) possessed comparable efficacy with standard drug, fluconazole, against *A. niger*.

Structure and activity relationship studies. From these antimicrobial activity results, following structure–activity relationships can be surmised:

- In most of cases, triazole derivatives possessing 4-nitrobenzoate as well as 4-nitrobenzyl moiety displayed enhanced bactericidal and fungicidal potential against all the tested strains. Thereby, it can be clearly depicted that the presence of electron withdrawing nitro group on benzyl/benzoate moiety enhances antimicrobial activity. Owing to this, compound **5m** with nitro group on both benzyl/benzoate moiety showed excellent potency against all tested strains except *A. niger*.

Scheme 1. Synthesis of ester-linked 1,4-disubstituted 1,2,3-triazoles **(5a–5t)**.

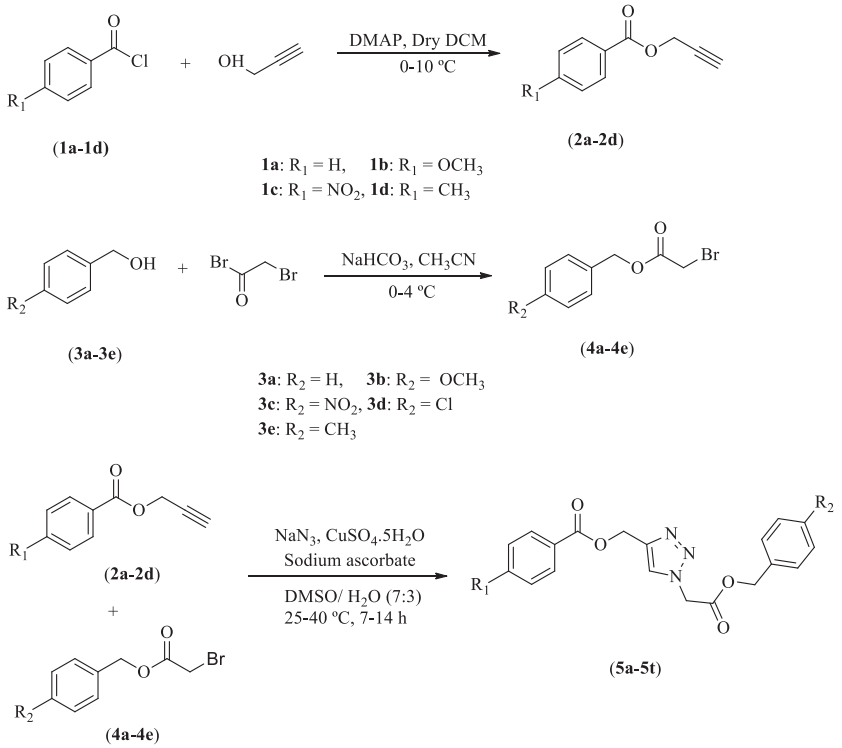

Table 1

In vitro antibacterial evaluation of 1,4-disubstituted 1,2,3-triazoles **(5a–5t)**.

	Minimum inhibitory concentration (μmol/mL)			
	Gram-positive bacteria	Gram-negative bacteria		
Compound	*Staphylococcus aureus*	*Escherichia coli*	*Klebsiellae pneumoniae*	*Enterobacter aerogenes*
5a	0.2846	0.2846	0.2846	0.2846
5b	0.1311	0.1311	0.0656	0.1311
5c	0.0631	0.1262	0.0631	0.0631
5d	0.1296	0.2592	0.1296	0.2592
5e	0.2737	0.2737	0.2737	0.2737
5f	0.1311	0.1311	0.0656	0.1311
5g	0.0608	0.0304	0.0608	0.1215
5h	0.0586	0.0586	0.0293	0.0586
5i	0.0601	0.0601	0.0301	0.1202
5j	0.0632	0.0632	0.1265	0.1265
5k	0.0315	0.0631	0.0631	0.1262
5l	0.0586	0.0586	0.0586	0.1173
5m	0.0142	0.0283	0.0283	0.0283
5n	0.0290	0.0290	0.0580	0.0580
5o	0.0305	0.0609	0.1218	0.1218
5p	0.1368	0.1368	0.1368	0.1368
5q	0.0632	0.0632	0.0632	0.1265
5r	0.0305	0.0609	0.0305	0.0609
5s	0.0625	0.0313	0.0625	0.1251
5t	0.1318	0.1318	0.0659	0.1318
Norfloxacin	0.0391	0.0391	0.0391	0.0783

Table 2

In vitro antifungal evaluation of 1,4-disubstituted 1,2,3-triazoles (**5a**–**5t**).

Compound	Minimum inhibitory concentration (μmol/mL)	
	Candida albicans	*Aspergillus niger*
5a	0.1423	0.1423
5b	0.1311	0.0656
5c	0.1262	0.0631
5d	0.1296	0.0648
5e	0.1368	0.1368
5f	0.0656	0.0656
5g	0.0608	0.0608
5h	0.0293	0.0144
5i	0.0601	0.0301
5j	0.0632	0.0316
5k	0.0631	0.0315
5l	0.0586	0.0586
5m	0.0142	0.1218
5n	0.0580	0.0580
5o	0.0609	0.1218
5p	0.1368	0.0342
5q	0.0632	0.0632
5r	0.0609	0.0305
5s	0.0625	0.0313
5t	0.0659	0.0659
Fluconazole	0.0408	0.0102

- The presence of electron donating methyl and methoxy groups on benzoate moiety displayed improved antimicrobial activity as compared with unsubstituted benzoate moiety.
- In comparison between methyl and methoxy groups, majority of triazole derivatives with 4-methoxy benzyl substitutent behave as better antimicrobial agent than derivatives with 4-methyl benzyl substitutent.
- Generally, triazole derivatives having 4-chlorobenzyl moiety exhibited significant improvement in antimicrobial activity than compounds possessing unsubstituted benzyl moiety.

CONCLUSION

Conclusively, synthesis of a series (1-(2-(benzyloxy)-2-oxoethyl)-1*H*-1,2,3-triazol-4-yl)methyl benzoate analogues (**5a**–**5t**) having ester functionality was accomplished through convenient approach of Cu(I) catalyzed click reaction and evaluated for *in vitro* antimicrobial screening. Most of the synthesized triazole derivatives displayed moderate to excellent activity against bacterial strains. Among the tested triazoles, compound **5m** exhibited more potency than standard drug against all bacterial strains and *C. albicans*, while compound **5n** found to possess noteworthy activity against *S. aureus*, *E. coli*, *E. aerogenes*, among all bacterial strains.

EXPERIMENTAL

Chemistry. The reagents used were obtained from Alfa Aesar, HiMedia, and Sigma-Aldrich, used without further purification. Melting points of the synthesized compounds were determined on electrothermal melting point apparatus in open capillary tubes and are uncorrected. To monitor the progress of reaction, thin-layer chromatography was performed on precoated silica gel plates (SIL G/UV254, ALUGRAM) in ethyl acetate–hexane mixture and visualized under ultraviolet light. FT-IR spectra were scanned on SHIMAZDU IR AFFINITY-I FT-IR in KBr and wave numbers (v) reported in cm^{-1}. ^1H NMR spectra and ^{13}C NMR spectra were scanned on BRUKER AVANCE II 400 MHz spectrometer (Bruker Corporation, Billerica, MA) at 400 and 100 MHz, respectively, in $CDCl_3$ or DMSO-d_6. Chemical shift values (δ) were quoted in parts per million (ppm). Coupling constant values (J) were reported in hertz (Hz). HRMS were performed on Waters Micromass Q-Tof Micro (ESI) spectrometer (Waters Corporation, Milford, MA), and values are reported in *m/z*.

General procedure for synthesis of (1-(2-(benzyloxy)-2-oxoethyl)-1H-1,2,3-triazol-4-yl)methyl benzoate analogues (5a–5t). To synthesize prop-2-yn-1-yl benzoates (**2a**–**2d**) [30], commercially available benzoyl chlorides (1.0 mmol) (**1a**–**1d**) were added dropwise into the stirred and cooled (0–10°C) solution of propargyl alcohol (1.0 mmol) in dry dichloromethane using *N*,*N*-dimethylaminopyridine (1.2 mmol) as base, further allowed stirring to continue for 2–4 h. Upon completion of reaction, neutralized reaction contents with dilute HCl and extracted with dichloromethane (3 × 30 mL). Organic layer was distilled under vacuum to get desired alkynes (**2a**–**2d**).

Synthesis of benzyl 2-bromoacetates (**4a–4e**) were carried out by dissolving bromoacetyl bromide (1.2 mmol) dropwise into the stirred solution of benzyl alcohols (**3a–3e**) (1.0 mmol) in acetonitrile in the presence of sodium bicarbonate (1.5 mmol) as base at 0–4°C, continued stirring for further 45 min. As the reaction was completed, the product was extracted with dichloromethane (3 × 30 mL). Organic layer was evaporated under reduced pressure.

In the final step, to carry out the synthesis of triazole derivatives (**5a**–**5t**), benzyl 2-bromoacetates (1.0 mmol) (**4a–4e**) and aqueous sodium azide (3.0 mmol) were reacted in DMSO for 1 h at 25–40°C with continuous stirring. Thereafter, prop-2-yn-1-yl benzoates (**2a**–**2d**) were added to the aforementioned reaction mixture followed by aqueous copper sulfate pentahydrate (0.1 mmol) and sodium ascorbate (0.4 mmol) at the same temperature with continuous stirring for 7–14 h. Reaction progress was monitored by thin-layer chromatography. As the reaction was completed, ice-cold water was added to the reaction mixture. Solid precipitates thus obtained

were filtered and washed with ammonia solution and recrystallized by chloroform/hexane (8:2) to furnish pure products **(5a–5t)** in good yield.

Characterization of synthesized compounds (5a–5t).

(1-(2-(Benzyloxy)-2-oxoethyl)-1H-1,2,3-triazol-4-yl)methyl benzoate (5a). Appearance: white solid; Yield: 83%, mp: 96–100°C; FT-IR (KBr): ν_{max} = 3152 (C–H str., triazole ring), 3031 (C–H str., aromatic ring), 2975 (C–H str., aliphatic), 1764, 1708 (C=O str., ester), 1597, 1452 (C=C str., aromatic ring), 1259 (C–O asym. str., ester), 1049 (C–O sym. str., ester) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 5.22 (s, 2H, NCH_2), 5.23 (s, 2H, OCH_2), 5.52 (s, 2H, OCH_2), 7.33–7.59 (m, 8H, Ar–H), 7.86 (s, 1H, C–H triazole), 8.05 (d, 2H, Ar–H, J = 8.4 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 50.9, 58.0, 68.1, 125.4 (C_5 triazole), 128.4, 128.6, 128.8, 128.9, 129.7, 129.8, 133.2, 134.5, 143.4 (C_4 triazole), 166.1 (C=O ester), 166.4 (C=O ester) ppm; HRMS (*m/z*) calculated for $C_{19}H_{17}N_3O_4$ $[M + H]^+$: 352.1253. Found: 352.1226.

(1-(2-((4-Methoxybenzyl)oxy)-2-oxoethyl)-1H-1,2,3-triazol-4-yl)methyl benzoate (5b). Appearance: white solid; Yield: 89%; mp: 96–100°C; FT-IR (KBr): ν_{max} = 3144 (C–H str., triazole ring), 3081 (C–H str., aromatic ring), 2958 (C–H str., aliphatic), 1750, 1702 (C=O str., ester), 1613, 1450 (C=C str., aromatic ring), 1277 (C–O asym. str., ester), 1054 (C–O sym. str., ester) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 3.66 (s, 3H, OCH_3), 5.08 (s, 2H, NCH_2), 5.11 (s, 2H, OCH_2), 5.38 (s, 2H, OCH_2), 6.77 (d, 2H, Ar–H, J = 8.4 Hz), 7.17 (d, 2H, Ar–H, J = 8.4 Hz), 7.31–7.35 (m, 2H, Ar–H), 7.46 (t, 1H, Ar–H, J = 7.2 Hz), 7.80 (s, 1H, C–H triazole), 7.93 (d, 2H, Ar–H, J = 7.2 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 50.8, 55.2, 57.9, 67.8, 114.0, 125.5 (C_5 triazole), 126.6, 128.3, 129.6, 129.8, 130.4, 133.2, 143.1 (C_4 triazole), 159.9, 166.2 (C=O ester), 166.4 (C=O ester) ppm; HRMS (*m/z*) calculated for $C_{20}H_{19}N_3O_5$ $[M + H]^+$: 382.1358. Found: 382.1329.

(1-(2-((4-Nitrobenzyl)oxy)-2-oxoethyl)-1H-1,2,3-triazol-4-yl) methyl benzoate (5c). Appearance: white solid; Yield: 72%; mp: 102–106°C; FT-IR (KBr): ν_{max} = 3148 (C–H str., triazole ring), 3059 (C–H str., aromatic ring), 2952 (C–H str., aliphatic), 1760, 1718 (C=O str., ester), 1603, 1451 (C=C str., aromatic ring), 1524 (N–O asym. str., NO_2), 1315 (N–O sym. str., NO_2), 1270 (C–O asym. str., ester), 1068 (C–O sym. str., ester) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 5.29 (s, 2H, NCH_2), 5.31 (s, 2H, OCH_2), 5.50 (s, 2H, OCH_2), 7.41–7.48 (m, 4H, Ar–H), 7.57 (t, 1H, Ar–H, J = 7.6 Hz), 7.89 (s, 1H, C–H triazole), 8.03 (d, 2H, Ar–H, J = 7.6 Hz), 8.18 (d, 2H, Ar–H, J = 8.8 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 50.8, 57.9, 66.4, 123.9, 125.5 (C_5 triazole), 128.4, 128.7, 129.6, 129.7, 133.3, 141.5 (C_4 triazole), 143.6, 148.0, 165.8 (C=O ester), 166.4 (C=O ester) ppm; HRMS (*m/z*) calculated for $C_{19}H_{16}N_4O_6$ $[M + H]^+$: 397.1103. Found: 397.1068.

(1-(2-((4-Chlorobenzyl)oxy)-2-oxoethyl)-1H-1,2,3-triazol-4-yl)methyl benzoate (5d). Appearance: white solid; Yield: 85%; mp: 108–112°C; FT-IR (KBr): ν_{max} = 3137 (C–H str., triazole ring), 3081 (C–H str., aromatic ring), 2952 (C–H str., aliphatic), 1759, 1698 (C=O str., ester), 1600, 1449 (C=C str., aromatic ring), 1276 (C–O asym. str., ester) 1054 (C–O sym. str., ester) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 5.19 (s, 2H, NCH_2), 5.22 (s, 2H, OCH_2), 5.50 (s, 2H, OCH_2), 7.25–7.28 (m, 2H, Ar–H), 7.33 (d, 2H, Ar–H, J = 8.4 Hz), 7.42–7.46 (m, 2H, Ar–H), 7.57 (t, 1H, Ar–H, J = 7.2 Hz), 7.86 (s, 1H, C–H triazole), 8.04 (d, 2H, Ar–H, J = 7.2 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 50.8, 58.0, 67.2, 125.4 (C_5 triazole), 128.4, 129.0, 129.7, 129.9, 132.9, 133.3, 134.8, 143.5 (C_4 triazole), 166.0 (C=O ester), 166.4 (C=O ester) ppm; HRMS (*m/z*) calculated for $C_{19}H_{16}ClN_3O_4$ $[M + H]^+$: 386.0908 (^{35}Cl), 388.0878 (^{37}Cl). Found: 386.0838 (^{35}Cl), 388.0801 (^{37}Cl).

(1-(2-((4-Methylbenzyl)oxy)-2-oxoethyl)-1H-1,2,3-triazol-4-yl)methyl benzoate (5e). Appearance: white solid; Yield: 84%; mp: 136–140°C; FT-IR (KBr): ν_{max} = 3141 (C–H str., triazole ring), 3070 (C–H str., aromatic ring), 2969 (C–H str., aliphatic), 1761, 1710 (C=O str., ester), 1597, 1451 (C=C str., aromatic ring), 1271 (C–O asym. str., ester), 1047 (C–O sym. str., ester) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 2.41 (s, 3H, CH_3), 5.20 (s, 2H, NCH_2), 5.23 (s, 2H, OCH_2), 5.44 (s, 2H, OCH_2), 7.07–7.14 (m, 4H, Ar–H), 7.38–7.42 (m, 2H, Ar–H), 7.54 (t, 1H, Ar–H, J = 7.2 Hz), 8.00 (d, 2H, Ar–H, J = 7.2 Hz), 8.08 (s, 1H, C–H triazole) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.7, 50.8, 57.7, 68.0, 125.4 (C_5 triazole), 128.4, 128.7, 129.4, 129.7, 129.9, 131.5, 133.4, 138.8, 143.4 (C_4 triazole), 166.1 (C=O ester), 166.3 (C=O ester) ppm; HRMS (*m/z*) calculated for $C_{20}H_{19}N_3O_4$ $[M + H]^+$: 366.1409. Found: 366.1378.

(1-(2-(Benzyloxy)-2-oxoethyl)-1H-1,2,3-triazol-4-yl)methyl 4-methoxybenzoate (5f). Appearance: white solid; Yield: 79%; mp: 76–80°C; FT-IR (KBr): ν_{max} = 3154 (C–H str., triazole ring), 3081 (C–H str., aromatic ring), 2935 (C–H str., aliphatic), 1761, 1710 (C=O str., ester), 1607, 1457 (C=C str., aromatic ring), 1278 (C–O asym. str., ester), 1054 (C–O sym. str., ester) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 3.83 (s, 3H, OCH_3), 5.22 (s, 2H, NCH_2), 5.40 (s, 2H, OCH_2), 5.51 (s, 2H, OCH_2), 7.05 (d, 2H, Ar–H, J = 8.8 Hz), 7.35–7.39 (m, 5H, Ar–H), 7.92 (d, 2H, Ar–H, J = 8.8 Hz), 8.28 (s, 1H, C–H triazole) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 50.9, 56.0, 58.0, 67.3, 114.6, 122.0, 126.8 (C_5 triazole), 128.6, 128.8, 128.9, 131.8, 135.8, 143.3 (C_4 triazole), 163.8, 165.6 (C=O ester), 167.6 (C=O ester) ppm; HRMS (*m/z*) calculated for $C_{20}H_{19}N_3O_5[M + H]^+$: 382.1358. Found: 382.1327.

(1-(2-((4-Methoxybenzyl)oxy)-2-oxoethyl)-1H-1,2,3-triazol-4-yl)methyl 4-methoxybenzoate (5g). Appearance: white solid; Yield: 81%; mp: 72–76°C; FT-IR (KBr): ν_{max} = 3148 (C–H str., triazole ring), 3076 (C–H str., aromatic ring), 2947 (C–H str., aliphatic), 1756, 1701 (C=O str., ester), 1606, 1457 (C=C str., aromatic ring), 1271 (C–O asym. str., ester), 1057 (C–O sym. str., ester) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 3.81 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 5.16 (s, 2H, NCH_2), 5.18 (s, 2H, OCH_2), 5.46 (s, 2H, OCH_2), 6.88–6.92 (m, 4H, Ar–H), 7.28 (d, 2H, Ar–H, J = 8.4 Hz), 7.84 (s, 1H, C–H triazole), 7.99 (d, 2H, Ar–H, J = 8.8 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 50.9, 55.3, 55.4, 57.7, 68.0, 113.7, 114.1, 122.1, 125.4 (C_5 triazole), 126.6, 130.5, 131.8, 143.6 (C_4 triazole), 160.1, 163.6, 166.1 (C=O ester), 166.2 (C=O ester) ppm; HRMS (*m/z*) calculated for $C_{21}H_{21}N_3O_6$ $[M + H]^+$: 412.1464. Found: 412.1431.

(1-(2-((4-Nitrobenzyl)oxy)-2-oxoethyl)-1H-1,2,3-triazol-4-yl) methyl 4-methoxybenzoate (5h). Appearance: white solid; Yield: 78%; mp: 136–140°C; FT-IR (KBr): ν_{max} = 3126 (C–H str., triazole ring), 3081 (C–H str., aromatic ring), 2969 (C–H str., aliphatic), 1718, 1703 (C=O str., ester), 1608, 1447 (C=C str., aromatic ring), 1512 (N–O asym. str., NO_2), 1317 (N–O sym. str., NO_2), 1275 (C–O asym. str., ester), 1049 (C–O sym. str., ester) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 3.83 (s, 3H, OCH_3), 5.21 (s, 2H, NCH_2), 5.40 (s, 2H, OCH_2), 5.51 (s, 2H, OCH_2), 7.03 (d, 2H, Ar–H, J = 9.2 Hz), 7.46 (d, 2H, Ar–H, J = 8.4 Hz), 7.92 (d, 2H, Ar–H, J = 9.2 Hz), 8.18 (d, 2H, Ar–H, J = 8.4 Hz), 8.38 (s, 1H, C–H triazole) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 50.9, 56.0, 57.8, 66.4, 114.6, 121.9, 123.9, 126.0 (C_5 triazole), 128.7, 131.9, 141.5, 143.3 (C_4 triazole), 148.0, 163.8, 164.5 (C=O ester), 167.5 (C=O ester) ppm; HRMS (*m/z*) calculated for $C_{20}H_{18}N_4O_7$$[M + H]^+$: 427.1209. Found: 427.1188.

(1-(2-((4-Chlorobenzyl)oxy)-2-oxoethyl)-1H-1,2,3-triazol-4-yl)methyl 4-methoxybenzoate (5i). Appearance: white solid; Yield: 83%; mp: 102–106°C; FT-IR (KBr): ν_{max} = 3137 (C–H str., triazole ring), 3087 (C–H str., aromatic ring), 2980 (C–H str., aliphatic), 1751, 1712 (C=O str., ester), 1607, 1421 (C=C str., aromatic ring), 1261 (C–O asym. str., ester), 1052 (C–O sym. str., ester) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 3.84 (s, 3H, OCH_3), 5.21 (s, 2H, NCH_2), 5.40 (s, 2H, OCH_2), 5.51 (s, 2H, OCH_2), 7.05 (d, 2H, Ar–H, J = 9.2 Hz), 7.41–7.45 (m, 4H, Ar–H), 7.92 (d, 2H, Ar–H, J = 9.2 Hz), 8.27 (s, 1H, C–H triazole) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 50.9, 56.0, 58.0, 66.4, 114.6, 122.0, 126.8 (C_5 triazole), 128.9, 130.3, 131.8, 133.3, 134.8, 142.6 (C_4 triazole), 163.8, 165.6 (C=O ester), 167.6 (C=O ester) ppm; HRMS (*m/z*) calculated for $C_{20}H_{18}ClN_3O_5$ $[M + H]^+$: 416.1013 (^{35}Cl), 418.0984 (^{37}Cl). Found: 416.0928 (^{35}Cl), 418.0903 (^{37}Cl).

(1-(2-((4-Methylbenzyl)oxy)-2-oxoethyl)-1H-1,2,3-triazol-4-yl)methyl 4-methoxybenzoate (5j). Appearance: white solid; Yield: 85%; mp: 80–84°C; FT-IR (KBr): ν_{max} = 3148 (C–H str., triazole ring), 3087 (C–H str., aromatic ring), 2963 (C–H str., aliphatic), 1762, 1706 (C=O str., ester), 1607, 1463 (C=C str., aromatic ring), 1277 (C–O asym. str., ester), 1057 (C–O sym. str., ester) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 2.41 (s, 3H, CH_3), 3.83 (s, 3H, OCH_3), 5.16 (s, 2H, NCH_2), 5.21 (s, 2H, OCH_2), 5.48 (s, 2H, OCH_2), 7.05 (d, 2H, Ar–H, J = 8.8 Hz),7.07–7.14 (m, 4H, Ar–H), 7.92 (d, 2H, Ar–H, J = 8.8 Hz), 8.28 (s, 1H, C–H triazole) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 21.1, 50.9, 55.3, 58.0, 68.0, 114.1, 122.0, 126.0 (C_5 triazole), 128.6, 129.3, 131.5, 131.8, 138.8, 142.6 (C_4 triazole), 163.6, 165.6 (C=O ester), 167.6 (C=O ester) ppm; HRMS (*m/z*) calculated for $C_{21}H_{21}N_3O_5$ $[M + H]^+$: 396.1515. Found: 396.1485.

(1-(2-(Benzyloxy)-2-oxoethyl)-1H-1,2,3-triazol-4-yl)methyl 4-nitrobenzoate (5k). Appearance: white solid; Yield: 76%; mp: 80–84°C; FT-IR (KBr): ν_{max} = 3143 (C–H str., triazole ring), 3081 (C–H str., aromatic ring), 2963 (C–H str., aliphatic), 1747, 1718 (C=O str., ester), 1610, 1463 (C=C str., aromatic ring), 1545 (N–O asym. str., NO_2), 1353 (N–O sym. str., NO_2), 1266 (C–O asym. str., ester), 1049 (C–O sym. str., ester) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 5.01 (s, 2H, NCH_2), 5.09 (s, 2H, OCH_2), 5.30 (s, 2H, OCH_2), 7.13–7.26 (m, 5H, Ar–H), 7.80 (s, 1H, C–H triazole), 7.97–8.05 (m, 4H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 50.4, 58.3, 67.4, 123.1, 125.6 (C_5 triazole), 128.0, 128.2, 128.3, 130.4, 134.2, 134.7, 141.8 (C_4 triazole), 150.1, 163.9 (C=O ester), 165.9 (C=O ester) ppm; HRMS (*m/z*) calculated for $C_{19}H_{16}N_4O_6$ $[M + H]^+$: 397.1103. Found: 397.1071.

(1-(2-((4-Methoxybenzyl)oxy)-2-oxoethyl)-1H-1,2,3-triazol-4-yl)methyl 4-nitrobenzoate (5l). Appearance: white solid; Yield: 88%; mp: 86–90°C; FT-IR (KBr): ν_{max} = 3154 (C–H str., triazole ring), 3070 (C–H str., aromatic ring), 2957 (C–H str., aliphatic), 1747, 1719 (C=O str., ester), 1611, 1466 (C=C str., aromatic ring), 1543 (N–O asym. str., NO_2), 1352 (N–O sym. str., NO_2), 1267 (C–O asym. str., ester), 1055 (C–O sym. str., ester) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 3.80 (s, 3H, OCH_3), 5.17 (s, 2H, NCH_2), 5.21 (s, 2H, OCH_2), 5.53 (s, 2H, OCH_2), 6.88 (d, 2H, Ar–H, J = 8.4 Hz), 7.28 (d, 2H, Ar–H, J = 8.4 Hz), 7.89 (s, 1H, C-H triazole), 8.11–8.26 (m, 4H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 50.9, 55.3, 58.7, 68.1, 114.1, 123.5, 125.7 (C_5 triazole), 126.5, 130.5, 130.9, 135.1, 142.5 (C_4 triazole), 150.6, 160.1, 164.5 (C=O ester), 166.1 (C=O ester) ppm; HRMS (*m/z*) calculated for $C_{20}H_{18}N_4O_7$ $[M + H]^+$: 427.1209. Found: 427.1171.

(1-(2-((4-Nitrobenzyl)oxy)-2-oxoethyl)-1H-1,2,3-triazol-4-yl) methyl 4-nitrobenzoate (5m). Appearance: white solid; Yield: 83%; mp: 144–148°C; FT-IR (KBr): ν_{max} = 3154

(C–H str., triazole ring), 3081 (C–H str., aromatic ring), 2996 (C–H str., aliphatic), 1764, 1728 (C=O str., ester), 1609, 1449 (C=C str., aromatic ring), 1522 (N–O asym. str., NO_2), 1346 (N–O sym. str., NO_2), 1274 (C–O asym. str., ester), 1053 (C–O sym. str., ester) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 5.37 (s, 2H, NCH_2), 5.51 (s, 2H, OCH_2), 5.59 (s, 2H, OCH_2), 7.65 (d, 2H, Ar–H, J = 8.4 Hz), 8.17–8.23 (m, 4H, Ar–H), 8.34 (d, 2H, Ar–H, J = 8.8 Hz), 8.35 (s, 1H, C–H triazole) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 50.8, 58.6, 66.3, 123.5, 123.9, 125.5 (C_5 triazole), 128.7, 130.4, 135.2, 141.5, 142.5 (C_4 triazole), 147.9, 150.6, 164.4 (C=O ester), 166.4 (C=O ester) ppm; HRMS (*m/z*) calculated for $C_{19}H_{15}N_5O_8$ $[M + H]^+$: 442.0954. Found: 442.0919.

(1-(2-((4-Chlorobenzyl)oxy)-2-oxoethyl)-1H-1,2,3-triazol-4-yl)methyl 4-nitrobenzoate (5n). Appearance: white solid; Yield: 73%; mp: 116–120°C; FT-IR (KBr): ν_{max} = 3154 (C–H str., triazole ring), 3081 (C–H str., aromatic ring), 2975 (C–H str., aliphatic), 1750, 1718 (C=O str., ester), 1610, 1491 (C=C str., aromatic ring), 1545 (N–O asym. str., NO_2), 1353 (N–O sym. str., NO_2), 1266 (C–O asym. str., ester), 1049 (C–O sym. str., ester) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 5.21 (s, 2H, NCH_2), 5.50 (s, 2H, OCH_2), 5.53 (s, 2H, OCH_2), 7.39–7.45 (m, 4H, Ar–H), 8.17–8.20 (m, 2H, Ar–H), 8.33–8.37 (m, 3H, Ar–H + C–H triazole) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 50.9, 59.1, 66.4, 124.4, 127.1 (C_5 triazole), 128.9, 130.4, 131.2, 133.4, 134.9, 135.2, 142.0 (C_4 triazole), 150.7, 164.5 (C=O ester), 167.5 (C=O ester) ppm; HRMS (*m/z*) calculated for $C_{19}H_{15}ClN_4O_6$ $[M + H]^+$: 431.0758 (^{35}Cl), 433.0729 (^{37}Cl). Found: 431.0674 (^{35}Cl), 433.0650 (^{37}Cl).

(1-(2-((4-Methylbenzyl)oxy)-2-oxoethyl)-1H-1,2,3-triazol-4-yl)methyl 4-nitrobenzoate (5o). Appearance: white solid; Yield: 77%; mp: 82–86°C; FT-IR (KBr): ν_{max} = 3143 (C–H str., triazole ring), 3078 (C–H str., aromatic ring), 2993 (C–H str., aliphatic), 1743, 1726 (C=O str., ester), 1606, 1457 (C=C str., aromatic ring), 1533 (N–O asym. str., NO_2), 1350 (N–O sym. str., NO_2), 1291 (C–O asym. str., ester), 1053 (C–O sym. str., ester) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 2.25 (s, 3H, CH_3), 5.09 (s, 2H, NCH_2), 5.15 (s, 2H, OCH_2), 5.43 (s, 2H, OCH_2), 7.06–7.14 (m, 4H, Ar–H), 7.85 (s, 1H, C–H triazole), 8.09–8.17 (m, 4H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.1, 50.8, 58.6, 67.9, 123.5, 125.7 (C_5 triazole), 128.6, 129.3, 130.8, 131.4, 135.1, 138.7, 142.3 (C_4 triazole), 150.5, 164.4 (C=O ester), 166.1 (C=O ester) ppm; HRMS (*m/z*) calculated for $C_{20}H_{18}N_4O_6$ $[M + H]^+$: 411.1260. Found: 411.1222.

(1-(2-(Benzyloxy)-2-oxoethyl)-1H-1,2,3-triazol-4-yl)methyl 4-methylbenzoate (5p). Appearance: white solid; Yield: 89%; mp: 104–108°C; FT-IR (KBr): ν_{max} = 3150 (C–H str., triazole ring), 3070 (C–H str., aromatic ring), 2975 (C–H str., aliphatic), 1760, 1706 (C=O str., ester), 1610, 1456 (C=C str., aromatic ring), 1264 (C–O asym. str., ester), 1053 (C–O sym. str., ester) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 2.41 (s, 3H, CH_3), 5.21 (s, 2H, NCH_2), 5.23 (s, 2H, OCH_2), 5.48 (s, 2H, OCH_2), 7.23 (d, 2H, Ar–H, J = 8.0 Hz), 7.33–7.38 (m, 5H, Ar–H), 7.85 (s, 1H, C–H triazole), 7.94 (d, 2H, Ar–H, J = 8.0 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.7, 50.9, 57.9, 68.1, 125.4 (C_5 triazole), 126.9, 128.6, 128.8, 128.9, 129.1, 129.8, 134.5, 143.6 (C_4 triazole), 144.0, 166.0 (C=O ester), 166.5 (C=O ester) ppm; HRMS (*m/z*) calculated for $C_{20}H_{19}N_3O_4$ $[M + H]^+$: 366.1409. Found: 366.1379.

(1-(2-((4-Methoxybenzyl)oxy)-2-oxoethyl)-1H-1,2,3-triazol-4-yl)methyl 4-methylbenzoate (5q). Appearance: White solid; Yield: 81%; mp: 116–120°C; FT-IR (KBr): ν_{max} = 3148 (C–H str., triazole ring), 3081 (C–H str., aromatic ring), 2963 (C–H str., aliphatic), 1752, 1712 (C=O str., ester), 1609, 1446 (C=C str., aromatic ring), 1278 (C–O asym. str., ester), 1055 (C–O sym. str., ester) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 2.41 (s, 3H, CH_3), 3.81(s, 3H, OCH_3), 5.17 (s, 2H, NCH_2), 5.18 (s, 2H, OCH_2), 5.48 (s, 2H, OCH_2), 6.89 (d, 2H, Ar–H, J = 8.4 Hz), 7.21–7.29 (m, 4H, Ar–H), 7.84 (s, 1H, C–H triazole), 7.93 (d, 2H, Ar–H, J = 8.0 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.7, 50.9, 55.3, 57.9, 68.0, 114,1, 125.4 (C_5 triazole), 126.6, 127.0, 129.1, 129.8, 130.5, 143.5 (C_4 triazole), 144.0, 160.1, 166.1 (C=O ester), 166.5 (C=O ester) ppm; HRMS (*m/z*) calculated for $C_{21}H_{21}N_3O_5$ $[M + H]^+$: 396.1515. Found: 396.1490.

(1-(2-((4-Nitrobenzyl)oxy)-2-oxoethyl)-1H-1,2,3-triazol-4-yl) methyl 4-methylbenzoate (5r). Appearance: white solid; Yield: 83%; mp: 96–100°C; FT-IR (KBr): ν_{max} = 3156 (C–H str., triazole ring), 3081 (C–H str., aromatic ring), 2963 (C–H str., aliphatic), 1760, 1719 (C=O str., ester), 1608, 1446 (C=C str., aromatic ring), 1517 (N–O asym. str., NO_2), 1353 (N–O sym. str., NO_2), 1279 (C–O asym. str., ester), 1053 (C–O sym. str., ester) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 2.40 (s, 3H, CH_3), 5.29 (s, 2H, NCH_2), 5.30 (s, 2H, OCH_2), 5.48 (s, 2H, OCH_2), 7.22 (d, 2H, Ar–H, J = 8.0 Hz), 7.46 (d, 2H, Ar–H, J = 8.4 Hz), 7.88–7.92 (m, 3H, Ar–H + C–H triazole), 8.17 (d, 2H, Ar–H, J = 8.4 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.7, 50.8, 57.8, 66.4, 123.9, 125.5 (C_5 triazole), 126.8, 128.7, 129.2, 129.7, 141.5, 143.7 (C_4 triazole), 144.1, 147.9, 165.8 (C=O ester), 166.5 (C=O ester) ppm; HRMS (*m/z*) calculated for $C_{20}H_{18}N_4O_6$ $[M + H]^+$: 411.1260. Found: 411.1225.

(1-(2-((4-Chlorobenzyl)oxy)-2-oxoethyl)-1H-1,2,3-triazol-4-yl)methyl 4-methylbenzoate (5s). Appearance: white solid; Yield: 80%; mp: 90–94°C; FT-IR (KBr): ν_{max} = 3143 (C–H str., triazole ring), 3048 (C–H str., aromatic ring), 2935 (C–H str., aliphatic), 1746, 1717 (C=O str., ester), 1612, 1452 (C=C str., aromatic ring), 1291 (C–O asym.

str., ester), 1053 (C–O sym. str., ester) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 2.41 (s, 3H, CH_3), 5.18 (s, 2H, NCH_2), 5.21 (s, 2H, OCH_2), 5.48 (s, 2H, OCH_2), 7.22–7.33 (m, 6H, Ar–H), 7.85 (s, 1H, C–H triazole), 7.93 (d, 2H, Ar–H, J = 8.4 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.7, 50.8, 57.8, 67.2, 125.4 (C_5 triazole), 126.9, 129.0, 129.1, 129.8, 129.9, 132.9, 134.8, 143.6 (C_4 triazole), 144.0, 166.0 (C=O ester), 166.5 (C=O ester) ppm; $C_{20}H_{18}ClN_3O_4$ $[M + H]^+$: 400.1064 (^{35}Cl), 402.1035 (^{37}Cl). Found: 400.0991 (^{35}Cl), 402.0957 (^{37}Cl).

(1-(2-((4-Methylbenzyl)oxy)-2-oxoethyl)-1H-1,2,3-triazol-4-yl)methyl 4-methylbenzoate (5t). Appearance: white solid; Yield: 77%; mp: 104–108°C; FT-IR (KBr): ν_{max} = 3143 (C–H str., triazole ring), 3053 (C–H str., aromatic ring), 2986 (C–H str., aliphatic), 1760, 1709 (C=O str., ester), 1610, 1452 (C=C str., aromatic ring), 1266 (C–O asym. str., ester), 1052 (C–O sym. str., ester) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 2.36 (s, 3H, CH_3), 2.41 (s, 3H, CH_3), 5.19 (s, 2H, NCH_2), 5.20 (s, 2H, OCH_2), 5.49 (s, 2H, OCH_2), 7.17–7.25 (m, 6H, Ar–H), 7.85 (s, 1H, C–H triazole), 7.94 (d, 2H, Ar–H, J = 8.4 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.2, 21.7, 50.9, 57.9, 68.1, 125.4 (C_5 triazole), 127.0, 128.7, 129.1, 129.4, 129.8, 131.5, 138.8, 143.6 (C_4 triazole), 144.0, 166.1 (C=O ester), 166.5 (C=O ester) ppm; HRMS (*m/z*) calculated for $C_{21}H_{21}N_3O_4$ $[M + H]^+$: 380.1566. Found: 380.1538.

General procedure for *in vitro* antimicrobial evaluation. *In vitro* antimicrobial evaluation of newly synthesized ester-linked triazoles (**5a**–**5t**) was carried out against four bacterial strains, namely, *S. aureus* (MTCC 3160), *E. coli* (MTCC 443), *K. pneumoniae* (NCDC 138), *E. aerogenes* (NCDC 106), and two fungi, namely, *C. albicans* (MTCC 227) and *A. niger* (MTCC 282), employing serial dilution method [31]. Stock solutions of test compounds in DMSO with concentration 200 µg/mL were prepared (2.0 mg of the test compound in 10 mL DMSO). Fresh cultures of respective microorganisms were prepared by inoculating in suitable media, that is, nutrient broth for bacterial strains and potato dextrose broth for fungal strains, respectively, then incubated at 37 ± 1°C for 24 h (all bacteria), 25 ± 1°C for 7 days (*A. niger*), and 37 ± 1°C for 48 h (*C. albicans*). Stock solutions of test compounds were serially diluted in test tubes containing 1 mL of sterile medium to obtain the concentrations of 100 to 6.25 µg/mL. After that, 100 µL of the broth containing the test microorganism in sterile saline was inoculated in each test tube and incubated at 37 ± 1°C for 24 h (bacteria), 37 ± 1°C for 48 h (*C. albicans*), and 25 ± 1°C for 7 days (*A. niger*). For antibacterial and antifungal screening, norfloxacin and fluconazole were taken as standard drugs, respectively, which were also assessed under similar experimental conditions for comparison with the tested compounds. After incubation, microbial growth was checked visually, and results were recorded in terms of MIC (µmol/mL).

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REFERENCES AND NOTES

[1] Kaushik, C. P.; Kumar, K.; Lal, K.; Narasimhan, B.; Kumar, A. Monatsh Chem 2016, 147, 817.
[2] Kaushik, C. P.; Pahwa, A.; Thakur, R.; Kaur, P. Synth Commun 2017, 47, 368.
[3] Nagender, P.; Reddy, G. M.; Kumar, R. N.; Poornachandra, Y.; Kumar, C. G.; Narsaiah, B. Bioorg Med Chem Lett 2014, 24, 2905.
[4] Aufort, M.; Herscovici, J.; Bouhours, P.; Moreau, N.; Girard, C. Bioorg Med Chem Lett 2008, 18, 1195.
[5] Kaushik, C. P.; Kumar, K.; Singh, D.; Singh, S. K.; Jindal, D. K.; Luxmi, R. Synth Commun 2015, 45, 1977.
[6] Kaushik, C. P.; Kumar, K.; Lal, K.; Singh, S. K. Chem Biol Interact 2014, 4, 341.
[7] Sukerkar, P. A.; MacRenaris, K. W.; Townsend, T. R.; Ahmed, R. A.; Burdette, J. E.; Meade, T. J. Bioconjug Chem 2011, 22, 2304.
[8] Kuntala, N.; Telu, J. R.; Banothu, V.; Nallapati, S. B.; Anireddy, J. S.; Pal, S. Med Chem Commun 2015, 6, 1612.
[9] Anand, A.; Naik, R. J.; Revankar, H. M.; Kulkarni, M. V.; Dixit, S. R.; Joshi, S. D. Eur J Med Chem 2015, 105, 194.
[10] Tripathi, R. P.; Yadav, A. K.; Ajay, A.; Bisht, S. S.; Chaturvedi, V.; Sinha, S. K. Eur J Med Chem 2010, 45, 142.
[11] Cheng, H.; Wan, J.; Lin, M. I.; Liu, Y.; Lu, X.; Liu, J.; Xu, Y.; Chen, J.; Tu, Z.; Cheng, Y. S. E.; Ding, K. J Med Chem 2012, 55, 2144.
[12] Fu, D. J.; Zhang, S. Y.; Liu, Y. C.; Yue, X. X.; Liu, J. J.; Song, J.; Zhao, R. H.; Li, F.; Sun, H. H.; Zhang, Y. B.; Liu, H. M. Med Chem Commun 2016, 7, 1664.
[13] Shaikh, M. H.; Subhedar, D. D.; Shingate, B. B.; Khan, F. A. K.; Sangshetti, J. N.; Khedkar, V. M.; Nawale, L.; Sarkar, D.; Navale, G. R.; Shinde, S. S. Med Chem Res 2016, 25, 790.
[14] Corrales, R. C. N. R.; DeSouza, N. B.; Pinheiro, L. S.; Abramo, C.; Coimbra, E. S.; Silva, A. D. D. Biomed Pharmacother 2011, 65, 198.
[15] Li, H.; Aneja, R.; Chaiken, I. Molecules 2013, 18, 9797.
[16] Balderas, F. P.; Munoz, M. O.; Sanfrutos, J. M.; Mateo, F. H.; Flores, F. G. C.; Asın, J. A. C.; Garcıa, J. I.; Gonza'lez, F. S. Org Lett 2003, 5, 1951.
[17] Nandivada, H.; Jiang, X.; Lahann, J. Adv Mater 2007, 19, 2197.
[18] Huisgen, R.; Szeimies, G.; Moebius, L. Chem Ber 1967, 100, 2494.
[19] Kolb, H. C.; Finn, M. G.; Sharpless, K. B. Angew Chem Int Ed 2001, 40, 2004.
[20] Tornþe, C. W.; Christensen, C.; Meldal, M. J Org Chem 2002, 67, 3057.
[21] Wang, X. L.; Wan, K.; Zhou, C. H. Eur J Med Chem 2010, 45, 4631.
[22] Mascarin, A.; Valverdea, I. E.; Mindt, T. L. Med Chem Commun 2016, 71, 1640.
[23] Yoon, K.; Goyal, P.; Weck, M. Org Lett 2007, 9, 2051.
[24] Hotha, S.; Kashyap, S. J Org Chem 2006, 71, 364.
[25] Ryu, E. H.; Zhao, Y. Org Lett 2005, 7, 1035.
[26] Kaushik, C. P.; Kumar, K.; Narasimhan, B.; Singh, D.; Kumar, P.; Pahwa, A. Monatsh Chem 2017, 148, 765.

[27] Kaushik, C. P.; Pahwa, A.; Kumar, A.; Singh, D.; Kumar, K. Synth Commun 2017, 47, 1485.
[28] Kaushik, C. P.; Pahwa, A. Asian J Chem 2017, 29, 2171.
[29] Kaushik, C. P.; Pahwa, A. Med Chem Res 2018, 27, 458.
[30] Kaushik, C. P.; Kumar, K.; Singh, S. K.; Singh, D.; Saini, S. Arabian J Chem 2016, 9, 865.
[31] Lal, K.; Kumar, A.; Pavan, M. S.; Kaushik, C. P. Bioorg Med Chem Lett 2012, 22, 4353.

SUPPORTING INFORMATION

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