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ARTICLE

Synthesis, antibacterial, and antioxidant activities of naphthyl-linked disubstituted 1,2,3-triazoles

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Abstract

Here, click synthesis of 15 naphthyl-linked disubstituted 1,2,3-triazoles has been carried out by the reaction between 1-(prop-2-yn-1-yloxy)naphthalene and aromatic azides. The structure elucidation of the synthesized compounds was carried out by FTIR, ^{1}H NMR, ^{13}C NMR, and HRMS techniques. Further, the compound **7f** was confirmed by X-ray crystallography (CCDC 1876891). The synthesized compounds were explored for antibacterial activity against *Bacillus cereus*, *Escherichia coli*, and *Staphylococcus aureus*. Biological evaluation of synthesized 1,2,3-triazoles revealed moderate to good antibacterial activity against the tested strains. The antioxidative behavior of synthesized compounds manifested the remarkable free radical scavenging activity using DPPH assay.

1 | INTRODUCTION

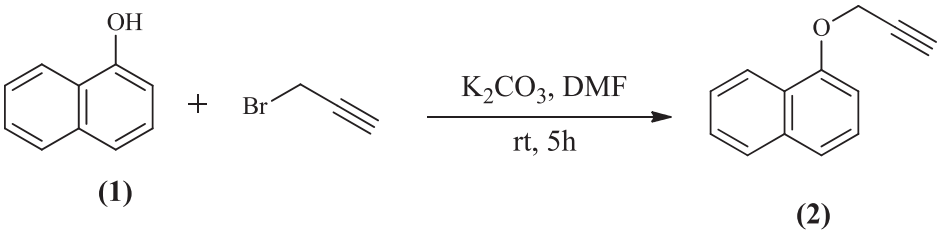
In recent years, chemical and biological usefulness of heterocyclic compounds attracted attention of chemist in form of pharmaceuticals, agrochemicals, polymers, dyes, etc.[1,2] Triazole, a five-membered heterocycle is key important, as its derivatives exhibited various biological activities such as antibacterial,[3–6] antimalarial,[7] antitubercular,[8,9] anticancer,[10–13] antiparasitic,[14] antileishmanial,[15] antioxidant,[16–18] anti-inflammatory,[19,20] antidepressant,[21] antiviral,[22,23] etc. The 1,2,3-triazole derivatives play an intriguing role in the development of new drugs, as effectively exerts various non-covalent interactions which improves the solubility and the ability of binding to bimolecular targets.[24]

Moreover, triazole-based drugs such carboxyamidotriazole, cefatrizine, tazobactam, and rufinamide are already in clinical practice for the treatment of various diseases, demonstrating the therapeutic potential of triazole derivatives. There are some reports that compounds having naphthalene ring incorporated with a heterocyclic nucleus also possess significant medicinal importance.[25–27] Increasing bacterial resistance to commonly antibiotic drugs is of much concern in modern healthcare scenario owing to emergence of multidrug resistant microorganisms. In this context, we have synthesized naphthyl-linked 1,4-disubstituted 1,2,3-triazoles through the click synthesis between 1-(prop-2-yn-1-yloxy)naphthalene and aromatic azides. The synthesized molecules were characterized by FTIR, ^{1}H NMR, ^{13}C NMR, and High Resolution Mass Spectrometry techniques, while the compound **7f** (CCDC 1876891) was also confirmed by X-ray crystallography. The synthesized compounds were assessed for antibacterial and antioxidant activities.

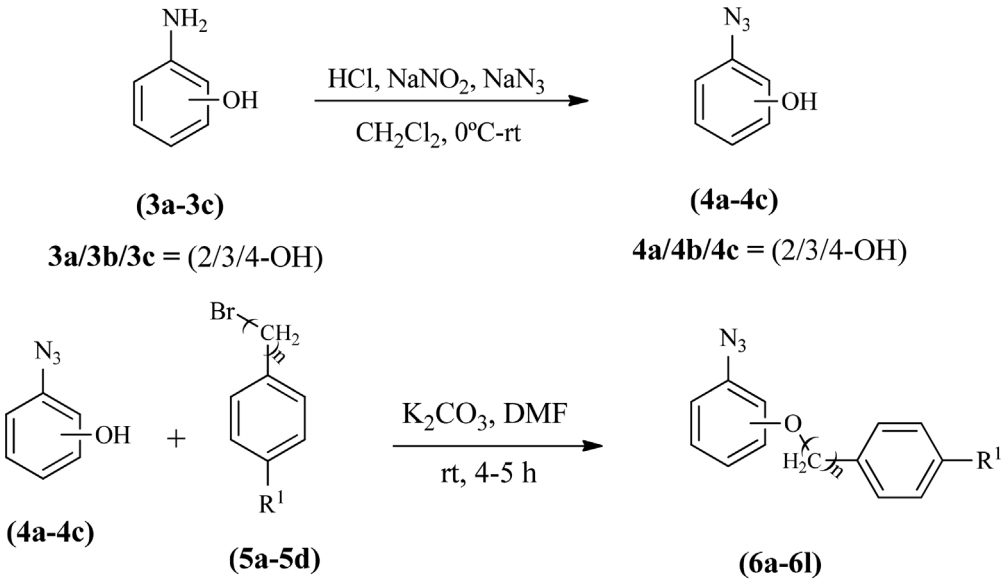
2 | RESULTS AND DISCUSSION

The method for the synthesis of compound (**7a**-**7o**) has been outlined in Scheme 3. The terminal alkyne, that is, 1-(prop-2-yn-1-yloxy)naphthalene (**2**, Scheme 1**)** was synthesized by reaction of α-naphthol (**1**) in DMF with propargyl bromide at room temperature in the presence of potassium carbonate.[28]

The aromatic azides (**4a**-**4c**, Scheme 2**)** were synthesized from reaction of substituted aminophenol (**3a**-**3c**) in a dil HCl with sodium nitrite and sodium azide. Further,



SCHEME 1 Synthesis of 1-(prop-2-yn-1-yloxy)naphthalene



SCHEME 2 Synthesis of aromatic azides

5a: R^1 = H, n = 1
5b: R^1 = H, n = 2
5c: R^1 = NO_2, n = 1
5d: R^1 = CH_3, n = 1

for the synthesis of various substituted azides (**6a**-**6l**, Scheme 2), the aromatic azides (**4a**-**4c**) were reacted with aralkyl bromides (**5a**-**5d**) using K_2CO_3 at room temperature with continuous stirring for 4-5 h.

Finally, targeted 1,4-disubstituted 1,2,3-triazoles with naphthyl linkage **(**Scheme 3**)** were synthesized by click reaction of various aromatic azides (**4a**-**4c**, **6a**-**6l**) and 1-(prop-2-yn-1-yloxy)naphthalene (**2**) in the presence of Cu (I) catalyst using DMF as solvent.

All the synthesized 1,4-disubstituted 1,2,3-triazoles (**7a**-**7o**) were explicated by FTIR, ^{1}H NMR, ^{13}C NMR, and HRMS. In IR spectra, the appearance of absorption band at 3374-3362 cm^{-1} was due to OH stretching of phenol. The C—H stretching vibration of triazole ring appeared at 3186-3132 cm^{-1}, whereas, strong bands due to C—O asymmetric and symmetric stretching exhibited at 1257-1235 cm^{-1} and 1049-1010 cm^{-1}, respectively.

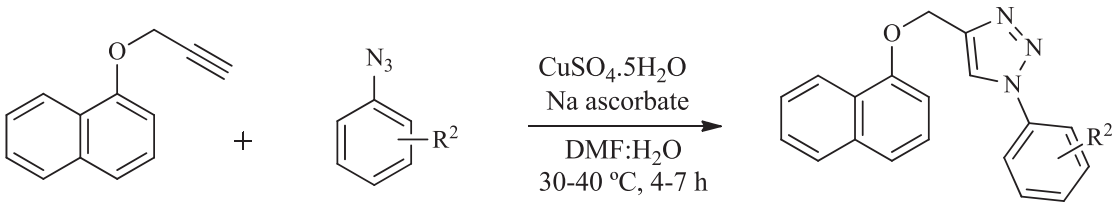
In ^{1}H NMR spectra, the triazole proton displayed singlet in region at δ 9.02-8.73 and OH proton resonated at δ 10.62-9.96. The aromatic protons appeared in region δ 8.20-6.89, whereas, methylene protons attached to C_4 of triazole appeared as singlet at δ 5.23-5.44.

Moreover, in ^{13}C NMR spectra C_4 and C_5 of triazole ring appeared in region δ 144.5-142.1 and δ 121.7-120.8, respectively. The aromatic carbon attached to oxygen of phenoxy ring appeared at δ 159.8-154.0, while other aromatic carbons displayed signal in region at δ 130.5-106.3.

HRMS spectral analyses of synthesized compounds were found in accordance with the theoretically predicted molecular masses.

2.1 | X-ray crystallographic study

Single crystals of 1-(4-[benzyloxy]phenyl)-4-([naphthalen-1-yloxy]methyl)-1H-1,2,3-triazole (**7f**) (Table 1, Figure 1) was grown in ethyl acetate. The crystal data for compound **7f** has been deposited in the Cambridge Crystallographic Data Center and assigned to the CCDC 1876891 number, which is available at www.ccdc.cam.ac.uk/conts/retrieving.html.



(3a-3c) **(4a-4c, 6a-6l)** **(7a-7o)**

4a/4b/4c = R^2 (2/3/4-OH)
6a/6b/6c = R^2 (2/3/4-$OCH_2C_6H_5$)
6d/6e/6f = R^2 (2/3/4-$OCH_2CH_2C_6H_5$)
6g/6h/6i = R^2 (2/3/4-$OCH_2C_6H_4NO_2$)
6j/6k/6l = R^2 (2/3/4-$OCH_2C_6H_4CH_3$)

Compound	R^2
7a	2-OH
7b	3-OH
7c	4-OH
7d	2-$OCH_2C_6H_5$
7e	3-$OCH_2C_6H_5$
7f	4-$OCH_2C_6H_5$
7g	2-$OCH_2CH_2C_6H_5$
7h	3-$OCH_2CH_2C_6H_5$
7i	4-$OCH_2CH_2C_6H_5$
7j	2-$OCH_2C_6H_4NO_2$
7k	3-$OCH_2C_6H_4NO_2$
7l	4-$OCH_2C_6H_4NO_2$
7m	2-$OCH_2C_6H_4CH_3$
7n	3-$OCH_2C_6H_4CH_3$
7o	4-$OCH_2C_6H_4CH_3$

SCHEME 3 Synthesis of naphthyl-linked 1,4-disubstituted 1,2,3-triazoles (**7a**-**7o**)

2.2 | Antibacterial activity

All the compounds were tested for antibacterial activity against *Bacillus cereus* (MTCC 430), *Staphylococcus aureus* (MTCC 3160), and *Escherichia coli* (MTCC 443) by employing serial dilution method.[29,30] Minimum inhibitory concentrations were expressed in μmol/mL as represented in Table 2. Norfloxacin was used as a standard drug.

From the antibacterial activity results, the following structure activity relationships can be summarized: In most of cases ortho derivatives showed better inhibition in comparison to meta and para derivatives. The triazole derivatives possessing 4-nitrobenzyl (**7j**, **7l**) displayed enhanced potential against the tested bacterial strains. The presence of methyl group on benzyl displayed improved antibacterial activity as compared with unsubstituted benzyl moiety. The triazole having phenyl

TABLE 1 Crystal data and structure refinement for **7f**

Property	Data
CCDC No	1876891
Empirical formula	$C_{26}H_{21}N_3O_2$
Formula weight	407.46
Temperature/K	293
Crystal system	Monoclinic
Space group	$P2_1/c$
a/Å	16.0069(4)
b/Å	10.3693(3)
c/Å	12.7768(4)
$\alpha/^\circ$, $\beta/^\circ$, $\gamma/^\circ$	90, 97.343(3), 90
Volume/Å^3	2103.31(10)
Z	4
ρ_{calc}g/cm^3	1.287
μ/mm^{-1}	0.661
F(000)	856.0
Crystal size/mm^3	0.729 × 0.362 × 0.089
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	10.19 to 146.454
Index ranges	$-19 \le h \le 13$, $-12 \le k \le 11$, $-13 \le l \le 15$
Reflections collected	8416
Independent reflections	4095 [R_{int} = 0.0367, R_{sigma} = 0.0376]
Data/restraints/parameters	4095/0/280
Goodness-of-fit on F^2	1.111
Final R indexes [$I \ge 2\sigma(I)$]	R_1 = 0.0666, wR_2 = 0.1818
Final R indexes (all data)	R_1 = 0.0924, wR_2 = 0.2084
Largest diff. peak/hole/e Å^{-3}	0.16/−0.31

ethyl rest (**7g**-**7i**) showed better inhibition than benzyl rest (**7d**-**7f**). Compound **7j** was the most potent among the synthesized naphthyl-linked 1,2,3-triazoles.

2.3 | Antioxidant activity

Synthesized disubstituted triazoles were evaluated for in vitro free radical scavenging activity. The antioxidant activity of compounds (**7a**-**7o**) resulted by using the DPPH radical scavenging assay[31,32] and the results are summarized in Table 3.

All the synthesized triazoles showed DPPH scavenger activity with a scavenging effect in the range, 45.9-57.7% (**7a**-**7o**), at a concentration of 100 μg/mL. It was observed from the data compound **7c** exhibited highest radical scavenging activity among the synthesized naphthyl-linked 1,2,3-triazoles. Compounds containing free OH (**7a**, **7b**, **7c**) showed better activity in comparison to substituted ones. In antioxidant activity para derivatives (**7c**, **7f**, **7i**) exhibited good scavenging effects on the DPPH stable radical than ortho and meta derivatives. The triazole having methyl (**7m**, **7n**, **7o**) showed better scavenging effects than nitro rest ones (**7j**, **7k**, **7l**).

3 | EXPERIMENTAL

3.1 | Material and methods

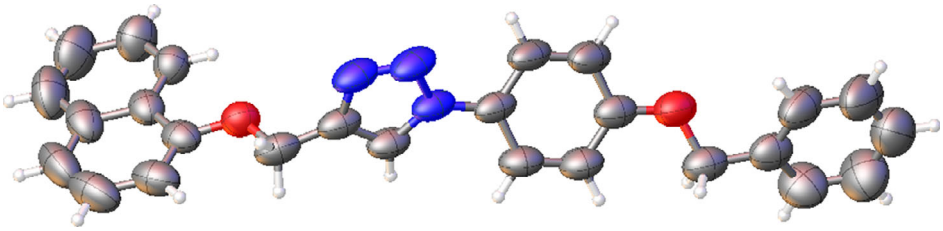
All chemicals used in the synthesis were purchased from Alfa-Aesar, Sigma-Aldrich, Hi-media. TLC was used to monitor the progress of reactions and visualized under UV light. Melting points were determined by open capillary method and uncorrected. IR spectra were performed on a SHIMADZU IR AFFINITY-I FT-IR spectrophotometer using KBr and expressed in cm^{-1}. The proton and carbon NMR spectra of the synthesized compounds were carried out at 400 and 100 MHz, respectively, using Bruker Avance II 400 MHz NMR spectrometer in DMSO-d_6 solvent. The chemical shifts were reported in δ and coupling constants (J) in Hz. Splitting patterns were indicated as s: singlet, d: doublet, t: triplet, q: quartet, m: multiplet. HRMS were recorded on Waters Micromass Q-Tof Micro (ESI) spectrophotometer and values were quoted in m/z.

3.2 | General procedure for synthesis of disubstituted 1,2,3-triazoles

3.2.1 | Synthesis of 1-(prop-2-yn-1-yloxy) naphthalene (2)

The 1-(prop-2-yn-1-yloxy)naphthalene (**2**) was synthesized by reaction of α-naphthol (**1**) (1.0 mmol) in dimethylformamide with propargyl bromide (1.2 mmol) at room temperature for 5 h in the presence of potassium carbonate. After completion of reaction water was added into the reaction mixture and then the product was extracted by ethyl acetate (3 × 50 mL). The organic layer was washed with saturated brine solution, dried using anhydrous sodium sulfate, filtered and evaporated to obtain the desired ether-linked terminal alkynes.

FIGURE 1 Crystal structure of compound **7f**



3.2.2 | Synthesis of aromatic azides (4a-4c, 6a-6l)

For the synthesis of aromatic azides[33] (**4a**-**4c**), to the stirred cool solution of aminophenol (**3a**-**3c**) (1.0 mmol) in dichloromethane in a round bottom flask, 6 N hydrochloric acid (5 mL) was added. Further, a saturated solution of sodium nitrite (3.0 mmol) in water was added in small portions to the reaction contents. After half an hour, aqueous solution of sodium azide (3.0 mmol) was added in a drop wise manner to the reaction mixture at 0°C. After the complete addition the reaction mixture was stirred for 2 h. The progress of the reaction was monitored by TLC. The product was extracted by using dichloromethane and organic layer was washed with sodium carbonate, dried with anhydrous sodium sulphate and evaporated the solvent to get the aromatic azides (**4a**-**4c**).

Further for the synthesis of substituted azides (**6a**-**6l**) the aromatic azides (**4a**-**4c**) (1.0 mmol) were reacted with aralkyl bromides (**5a**-**5d**) (1.0 mmol) using potassium carbonate (2.0 mmol) as base at room temperature with continuous stirring for 4-5 h. Thereafter ice cold water poured into the reaction mixture to precipitate solid. The solid product (**6a**-**6l**) was filtered, washed with cool water (Scheme 2).

3.2.3 | Synthesis of ether linked 1,4-disubstituted 1,2,3-triazoles (7a-7o)

Finally, 1,4-disubstituted 1,2,3-triazoles with naphthyl linkage were synthesized by the reaction of various aromatic azides (**4a**-**4c**, **6a**-**6l**) and 1-(prop-2-yn-1-yloxy) naphthalene (**2**) in catalytic amount of copper sulphate pentahydrate and sodium ascorbate in DMF:H_2O (8:2). The reaction mixture was continuously stirred at 30-40°C for 4-7 h. After completion of reaction as indicated by TLC, ice cold water was added to reaction mixture and product was precipitated out. The precipitated product was filtered and washed with ammonia solution. Crude product was recrystallized by using ethyl acetate and hexane get pure product in good yield (Scheme 3).

TABLE 2 In vitro antibacterial activity of 1,4-disubstituted 1,2,3-triazoles **(7a-7o)**

Compound No.	MIC (μmol/mL)		
	Bacillus cereus	*Staphylococcus aureus*	*Escherichia coli*
7a	0.0394	0.0788	0.0394
7b	0.0788	0.1576	0.0788
7c	0.0788	0.0788	0.0788
7d	0.1228	0.1228	0.1228
7e	0.1228	0.1228	0.1228
7f	0.1228	0.1228	0.1228
7g	0.0594	0.1187	0.1187
7h	0.1187	0.1187	0.1187
7i	0.1187	0.1187	0.1187
7j	0.0276	0.0525	0.0276
7k	0.1105	0.1105	0.0525
7l	0.0525	0.0525	0.0276
7m	0.0593	0.0593	0.0593
7n	0.1187	0.1187	0.1187
7o	0.0593	0.1187	0.0593
Norfloxacin	0.0391	0.0783	0.0391

3.3 | Characterization of ether linked 1,4-disubstituted 1,2,3-triazoles

3.3.1 | 2-(4-((Naphthalen-1-yloxy) methyl)-1H-1,2,3-triazol-1-yl)phenol (7a)

Appearance: White solid; Yield: 86%; m.p.: 152-154°C; FTIR (KBr): 3362 (OH, str.), 3128 (C—H str., triazole ring), 3075 (C—H str., aromatic ring), 2937 (C—H str., aliphatic), 1580, 1477 (C═C str., aromatic ring), 1244, 1017 (C—O str., ether) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.61 (s, 1H, OH), 8.73 (s, 1H, CH-triazole), 8.17 (d, J = 8.0 Hz, 1H), 7.88 (s, J = 8.0 Hz, 1H), 7.53-7.45 (m, 7H, ArH), 7.18-7.21 (m, 2H, ArH), 5.44 (s, 2H, OCH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 154.0, 150.2, 143.0 (C_4 triazole), 134.5, 130.7, 127.9, 127.0, 126.7, 126.6, 125.8, 125.8, 125.4, 125.0, 122.1, 120.8 (C_5 triazole), 120.0, 117.5,

TABLE 3 In vitro antioxidant activity of synthesized compounds **(7a-7o)**

Compounds	Concentration				
	20 μg/mL	40 μg/mL	60 μg/mL	80 μg/mL	100 μg/mL
7a	41.4 ± 1.12	43.5 ± 0.88	47.9 ± 0.69	52.9 ± 0.77	55.8 ± 0.56
7b	29.6 ± 0.91	36.4 ± 0.34	41.6 ± 0.41	44.8 ± 1.38	47.7 ± 0.81
7c	43.8 ± 1.18	45.0 ± 0.43	49.3 ± 0.35	53.4 ± 0.58	57.7 ± 0.65
7d	25.7 ± 0.93	29.7 ± 0.40	39.6 ± 1.36	45.1 ± 0.37	50.7 ± 0.25
7e	29.0 ± 0.44	35.2 ± 0.31	42.9 ± 0.06	46.7 ± 0.33	49.2 ± 0.77
7f	24.8 ± 1.79	33.6 ± 0.41	39.3 ± 0.15	47.4 ± 0.61	52.9 ± 0.45
7g	24.4 ± 0.34	36.2 ± 0.92	40.7 ± 0.68	42.9 ± 0.84	45.9 ± 0.64
7h	25.7 ± 1.02	35.5 ± 1.27	42.2 ± 1.35	46.9 ± 1.49	50.8 ± 0.25
7i	24.1 ± 0.75	34.6 ± 1.84	43.9 ± 1.06	48.7 ± 0.56	52.9 ± 0.39
7j	25.7 ± 1.46	35.5 ± 0.76	44.6 ± 0.65	49.8 ± 1.22	53.9 ± 0.42
7k	34.8 ± 1.15	40.9 ± 0.64	44.3 ± 0.83	49.8 ± 0.74	52.5 ± 0.64
7l	22.2 ± 1.32	31.5 ± 1.13	39.7 ± 1.36	47.5 ± 0.42	55.7 ± 0.37
7m	38.6 ± 0.55	44.7 ± 0.36	49.1 ± 1.23	51.4 ± 0.98	54.3 ± 0.34
7n	34.8 ± 0.48	39.9 ± 1.27	43.5 ± 1.54	45.4 ± 0.89	52.7 ± 0.18
7o	36.4 ± 0.23	42.7 ± 1.02	48.6 ± 0.36	53.6 ± 0.45	56.6 ± 0.32
AA	48.5 ± 0.48	54.7 ± 1.33	58.3 ± 1.02	63.6 ± 0.72	68.9 ± 0.52

Note: Values were the means of three replicates ± *SD*.

106.3, 62.0. HRMS $[M + H]^+$ for $C_{19}H_{15}N_3O_2$ cal: 318.1164, found: 318.1239.

3.3.2 | 3-(4-((Naphthalen-1-yloxy] methyl)-1H-1,2,3-triazol-1-yl)phenol (7b)

Appearance: White solid; Yield: 91%; m.p.: 94-98°C; FTIR (KBr): 3374 (OH, str.), 3128 (C—H str., triazole ring), 3062 (C—H str., aromatic ring), 2937 (C—H str., aliphatic), 1600, 1475 (C═C str., aromatic ring), 1244, 1060 (C—O str., ether) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.07 (s, 1H, OH), 9.02 (s, 1H, CH-triazole), 8.21 (d, J = 8.0 Hz, 1H), 7.89 (d, J = 8.0 Hz, 1H), 7.54-7.45 (m, 7H, ArH), 7.24 (d, J = 8.0 Hz, 1H), 6.92-6.89 (m, 1H, ArH), 5.43 (s, 2H, OCH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 159.0, 154.0, 144.4 (C_4 triazole), 138.1, 134.5, 131.3, 127.9, 127.0, 126.6, 125.8, 125.4, 123.2, 122.2, 120.9 (C_5 triazole), 116.2, 111.0, 107.6, 106.3, 62.1. HRMS $[M + H]^+$ for $C_{19}H_{15}N_3O_2$ cal: 318.1164, found: 318.1240.

3.3.3 | 4-(4-((Naphthalen-1-yloxy) methyl)-1H-1,2,3-triazol-1-yl)phenol (7c)

Appearance: White solid; Yield: 90%; m.p.: 118-120°C; FTIR (KBr): 3369 (OH, str.), 3149 (C—H str., triazole ring), 3076 (C—H str., aromatic ring), 2937 (C—H str., aliphatic), 1582, 1477 (C═C str., aromatic ring), 1232, 1015 (C—O str., ether); ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.96 (s, 1H, OH), 8.89 (s, 1H, CH-triazole), 8.20 (d, J = 8.0 Hz, 1H), 7.88 (d, J = 8.0 Hz, 1H), 7.72 (d, J = 8.0 Hz, 2H), 7.53-7.46 (m, 4H), 7.23 (d, J = 8.0 Hz, 1H), 6.96 (d, J = 8.0 Hz, 2H), 5.42 (s, 2H, OCH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 158.3, 154.0, 144.1 (C_4 triazole), 134.5, 129.2, 127.9, 127.0, 126.6, 125.8, 125.4, 123.1, 122.5, 122.2, 121.0 (C_5 triazole), 116.5, 106.3, 62.2. HRMS $[M + H]^+$ for $C_{19}H_{15}N_3O_2$ cal: 318.1164, found: 318.1239.

3.3.4 | 1-(2-(Benzyloxy)phenyl)-4-((naphthalen-1-yloxy)methyl)-1H-1,2,3-triazole (7d)

Appearance: White solid; Yield: 94%; m.p.: 166-168°C; FTIR (KBr): 3172 (C—H str., triazole ring), 3061 (C—H str., aromatic ring), 2941 (C—H str., aliphatic), 1589, 1465 (C═C str., aromatic ring), 1240, 1012 (C—O str., ether); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.74 (s, 1H, CH-triazole), 8.12 (d, J = 8.2 Hz, 1H), 7.89 (d, J = 8.0 Hz, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.51-7.37 (m, 8H, ArH), 7.28-7.18 (m, 5H), 5.43 (s, 2H, OCH_2), 5.25 (s, 2H, OCH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 154.0, 151.3, 143.2 (C_4 triazole), 136.8, 134.5, 131.3, 128.9, 128.3, 127.9, 127.8, 127.1, 127.0, 126.6, 125.8, 125.4, 122.0, 121.7, 120.9

(C_5 triazole), 114.9, 106.3, 70.6, 62.1. HRMS $[M + H]^+$ for $C_{26}H_{21}N_3O_2$ cal: 408.1634, found: 408.1712.

3.3.5 | 1-(3-(Benzyloxy)phenyl)-4-((naphthalen-1-yloxy)methyl)-1H-1,2,3-triazole (7e)

Appearance: White solid; Yield: 84%; m.p.: 146-148°C; FTIR (KBr): 3132 (C—H str., triazole ring), 3095 (C—H str., aromatic ring), 2937 (C—H str., aliphatic), 1566, 1454 (C═C str., aromatic ring), 1257, 1047 (C—O str., ether); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.99 (s, 1H, CH-triazole), 7.60 (s, 1H, ArH), 7.53-7.49 (m, 4H, ArH), 7.42 (t, J = 8.0 Hz, 2H), 7.36-7.31 (m, 3H, ArH), 7.15 (d, J = 8.0 Hz, 1H), 7.09 (d, J = 8.0 Hz, 2H), 6.98 (t, J = 8.0 Hz, 1H), 5.23 (m, 4H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 159.8, 154.0, 144.4 (C_4 triazole), 138.1, 137.1, 131.4, 130.0, 129.0, 128.5, 128.3, 123.4, 121.5 (C_5 triazole), 115.7, 115.2, 112.8, 107.1, 70.2, 61.4. HRMS $[M + H]^+$ for $C_{26}H_{21}N_3O_2$ cal: 408.1634, found: 408.1710.

3.3.6 | 1-(4-(Benzyloxy)phenyl)-4-((naphthalen-1-yloxy)methyl)-1H-1,2,3-triazole (7f)

Appearance: White solid; Yield: 79%; m.p.: 162-164°C; FTIR (KBr): 3172 (C—H str., triazole ring), 3061 (C—H str., aromatic ring), 2941 (C—H str., aliphatic), 1558, 1465 (C═C str., aromatic ring), 1240, 1012 (C—O str., ether); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.97 (s, 1H, CH-triazole), 8.20 (d, J = 8.0 Hz, 1H, ArH), 7.88 (t, J = 8.0 Hz, 3H, ArH), 7.58-7.32 (m, 9H, ArH), 7.26-7.22 (m, 3H, ArH), 5.44 (s, 2H, OCH_2), 5.21 (s, 2H, OCH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 158.9, 154.0, 144.3 (C_4 triazole), 137.2, 134.5, 134.1, 130.7, 129.0, 128.5, 128.3, 127.9, 127.0, 126.6, 125.8, 125.4, 123.2, 122.3, 122.2, 120.9 (C_5 triazole), 116.3, 106.3, 70.1, 62.2. HRMS $[M + H]^+$ for $C_{26}H_{21}N_3O_2$ cal: 408.1634, found: 408.1719.

3.3.7 | 4-((Naphthalen-1-yloxy)methyl)-1-(2-phenethoxyphenyl)-1H-1,2,3-triazole (7g)

Appearance: White solid; Yield: 93%; m.p.: 138-140°C; FTIR (KBr): 3167 (C—H str., triazole ring), 3036 (C—H str., aromatic ring), 2932 (C—H str., aliphatic), 1575, 1444 (C═C str., aromatic ring), 1247, 1021 (C—O str., ether); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.74 (s, 1H, CH-triazole), 8.10 (d, J = 8.0 Hz, 1H), 7.89 (d, J = 8.0 Hz, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.56-7.36 (m, 8H, ArH), 7.30-7.16 (m, 5H, ArH), 5.43 (s, 2H, OCH_2), 4.26 (t, J = 8.0 Hz, OCH_2), 3.20 (t, J = 8.0 Hz, CH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 154.0, 151.3, 143.2 (C_4 triazole), 136.8, 134.5, 134.1, 131.3, 128.9, 128.3, 127.9, 127.8, 127.1, 127.0, 126.6, 125.8, 125.4, 122.0, 121.7, 120.9 (C_5 triazole), 114.9, 106.3, 67.9, 60.8, 36.7. HRMS $[M + H]^+$ for C_{27} $H_{23}N_3O_2$ cal: 422.1790, found: 422.1870.

3.3.8 | 4-((Naphthalen-1-yloxy)methyl)-1-(3-phenethoxyphenyl)-1H-1,2,3-triazole (7h)

Appearance: White solid; Yield: 89%; m.p.: 152-154°C; FTIR (KBr): 3168 (C—H str., triazole ring), 3060 (C—H str., aromatic ring), 2941 (C—H str., aliphatic), 1560, 1460 (C═C str., aromatic ring), 1242, 1016 (C—O str., ether); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.99 (s, 1H, CH-triazole), 7.61 (s, 1H, ArH), 7.31-7.53 (m, 9H, ArH), 6.96-7.10 (m, 4H, ArH), 5.23 (s, 2H, OCH_2), 4.24 (t, J = 8.0 Hz, 2H, OCH_2), 3.22 (t, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 159.8, 154.0, 144.4 (C_4 triazole), 138.1, 137.1, 134.1, 134.5, 131.4, 130.0, 129.0, 128.9, 128.7, 128.3, 128.2, 126.6, 125.8, 125.4, 123.3, 122.2, 121.2 (C_5 triazole), 115.7, 114.4, 107.1, 67.7, 61.4, 36.5; HRMS $[M + H]^+$ for C_{27} $H_{23}N_3O_2$ cal: 422.1790, found: 422.1870.

3.3.9 | 4-((Naphthalen-1-yloxy)methyl)-1-(4-phenethoxyphenyl)-1H-1,2,3-triazole (7i)

Appearance: White solid; Yield: 82%; m.p.: 170-172°C; FTIR (KBr): 3170 (C—H str., triazole ring), 3061 (C—H str., aromatic ring), 2941 (C—H str., aliphatic), 1558, 1465 (C═C str., aromatic ring), 1240, 1012 (C—O str., ether); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.97 (s, 1H, CH-triazole), 8.18 (d, J = 8.0 Hz, 1H), 7.88 (t, J = 8.0 Hz, 3H), 7.56-7.30 (m, 9H), 7.26-7.22 (m, 3H, ArH), 5.44 (s, 2H, OCH_2), 4.26 (t, J = 8.0 Hz, 2H, OCH_2), 3.22 (t, J = 8.0 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 158.9, 154.0, 144.3 (C_4 triazole), 137.2, 134.5, 130.7, 129.2, 128.5, 128.3, 127.9, 127.0, 126.6, 125.8, 125.4, 123.2, 122.3, 122.2, 120.9 (C_5 triazole), 116.3, 106.3, 67.9, 60.6, 36.7. HRMS $[M + H]^+$ for C_{27} $H_{23}N_3O_2$ cal: 422.1790, found: 422.1870.

3.3.10 | 4-((Naphthalen-1-yloxy)methyl)-1-(2-((4-nitrobenzyl)oxy)phenyl)-1H-1,2,3-triazole (7j)

Appearance: yellow solid; Yield: 87%; m.p.: 162-164°C; FTIR (KBr): 3178 (C—H str., triazole ring), 3065 (C—H

str., aromatic ring), 2939 (C—H str., aliphatic), 1576, 1455 (C═C str., aromatic ring), 1512 (N—O asym. str., NO_2), 1348 (N—O sym. str., NO_2), 1238, 1017 (C—O str., ether); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.69 (s, 1H, CH-triazole), 8.22 (d, 2H, ArH, J = 8.0 Hz), 8.22 (d, 1H, ArH, J = 8.0 Hz), 7.88-7.84 (d, 3H, ArH, J = 8.0 Hz), 7.53 (m, 2H, ArH), 7.44-7.28 (m, 6H, ArH), 7.17 (t, 1H, ArH, J = 8.0 Hz), 5.42 (s, 2H, OCH_2), 5.21 (s, 2H, OCH_2); ^{13}C NMR (100 MHz, DMSO-d_6): δ 154.0, 151.2, 142.1 (C_4 triazole), 141.6, 136.8, 134.5, 131.6, 128.9, 128.4, 127.8, 127.5, 126.5, 126.3, 125.4, 123.2, 122.2, 121.7 (C_5 triazole), 115.8, 114.4, 106.9, 68.9, 61.2; HRMS $[M + H]^+$ for $C_{26}H_{20}N_4O_4$ cal: 453.1485, found: 453.1587.

3.3.11 | 4-((Naphthalen-1-yloxy)methyl)-1-(3-((4-nitrobenzyl)oxy)phenyl)-1H-1,2,3-triazole (7k)

Appearance: yellow solid; Yield: 90%; m.p.: 148-150°C; FTIR (KBr): 3186 (C—H str., triazole ring), 3056 (C—H str., aromatic ring), 2938 (C—H str., aliphatic), 1576, 1454 (C═C str., aromatic ring), 1508 (N—O asym. str., NO_2), 1350 (N—O sym. str., NO_2), 1237, 1018 (C—O str., ether); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.84 (s, 1H, CH triazole), 8.20 (d, 2H, ArH, J = 8.0 Hz), 7.83 (d, 2H, ArH, J = 8.0 Hz), 7.60 (s, 1H, ArH), 7.54-7.48 (m, 4H, ArH), 7.42 (t, 2H, ArH, J = 8.0 Hz), 7.38-7.30 (m, 3H, ArH), 7.19-7.13 (m, 1H, ArH), 5.43 (s, 2H, OCH_2), 5.25 (s, 2H, OCH_2); ^{13}C NMR (100 MHz, DMSO-d_6): δ 159.8, 154.0, 143.4 (C_4 triazole), 141.6, 138.0, 137.1, 134.5, 131.4, 128.9, 128.5, 128.3, 126.4, 125.4, 125.8, 123.8, 122.9, 122.2, 120.9 (C_5 triazole), 116.8, 115.9, 107.3, 68.9, 61.2; HRMS $[M + H]^+$ for $C_{26}H_{20}N_4O_4$ cal: 453.1485, found: 453.1587.

3.3.12 | 4-((Naphthalen-1-yloxy)methyl)-1-(4-((4-nitrobenzyl)oxy)phenyl)-1H-1,2,3-triazole (7l)

Appearance: white solid; Yield: 86%; m.p.: 160-162°C; FTIR (KBr): 3182 (C—H str., triazole ring), 3054 (C—H str., aromatic ring), 2930 (C—H str., aliphatic), 1574, 1456 (C═C str., aromatic ring), 1508 (N—O asym. str., NO_2), 1350 (N—O sym. Str., NO_2), 1235, 1010 (C—O str., ether) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.98 (s, 1H, CH triazole), 8.29 (d, J = 8 Hz, 2H), 8.20 (d, J = 8.Hz, 1H), 7.89 (d, J = 8 Hz, 3H), 7.77 (d, J = 8 Hz, 2H), 7.61-7.41 (m, 4H), 7.30-7.19 (m, 3H, ArH), 5.43 (s, 2H, OCH_2), 5.40 (s, 2H, OCH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 158.4, 154.0, 147.6, 145.1, 144.3 (C_4 triazole), 134.5, 131.0, 128.8, 127.9, 127.0, 126.6, 125.8, 125.4, 124.1, 123.2, 122.4, 122.2, 120.9 (C_5 triazole), 116.3, 106.3, 68.9, 62.2. HRMS $[M + H]^+$ for $C_{26}H_{20}N_4O_4$ cal: 453.1485, found: 453.1587.

3.3.13 | 1-(2-((4-Methylbenzyl)oxy)phenyl)-4-((naphthalen-1-yloxy)methyl)-1H-1,2,3-triazole (7m)

Appearance: White solid; Yield: 89%; m.p.: 146-148°C; FTIR (KBr): 3152 (C—H str., triazole ring), 3059 (C—H str., aromatic ring), 2936 (C—H str., aliphatic), 1586, 1456 (C═C str., aromatic ring), 1238, 1016 (C—O str., ether) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.60 (s, 1H, CH-triazole), 8.12 (d, 2H, ArH, J = 8.0 Hz), 7.89 (d, 2H, ArH, J = 8.0 Hz), 7.66 (d, 1H, ArH, J = 8.0 Hz), 7.54-7.50 (m, 3H, ArH), 7.41-7.36 (m, 3H, ArH), 7.14-7.09 (m, 3H, ArH), 6.94 (d, 1H, ArH, J = 8.0 Hz), 6.89 (d, 2H, ArH, J = 8.0 Hz), 5.43 (s, 2H, OCH_2), 5.18 (s, 2H, OCH_2), 2.24 (s, 3H, CH_3),; ^{13}C NMR (100 MHz, DMSO-d_6): δ 154.0, 151.2, 143.2 (C_4 triazole), 136.8, 134.1, 134.5, 130.3, 128.9, 128.4, 127.8, 127.0, 126.6, 125.8, 125.4, 124.1, 123.2, 122.5, 122.2, 121.7 (C_5 triazole), 115.1, 106.9, 70.7, 61.6, 20.6; HRMS $[M + H]^+$ for $C_{27}H_{23}N_3O_2$ cal: 422.1790, found: 422.1889.

3.3.14 | 1-(3-((4-Methylbenzyl)oxy)phenyl)-4-((naphthalen-1-yloxy)methyl)-1H-1,2,3-triazole (7n)

Appearance: White solid; Yield: 84%; m.p.: 182-185°C; FTIR (KBr): 3172 (C—H str., triazole ring), 3045 (C—H str., aromatic ring), 2939 (C—H str., aliphatic), 1577, 1463 (C═C str., aromatic ring), 1236, 1011 (C—O str., ether) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.98 (s, 1H, CH-triazole), 7.61-7.45 (m, 5H, ArH), 7.37-7.33 (m, 3H, ArH), 7.12-7.09 (m, 5H, ArH), 6.89 (d, 2H, ArH,= 8.0 Hz), 5.42 (s, 2H, OCH_2), 5.19 (s, 2H, OCH_2), 2.24 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 159.7, 154.0, 144.5 (C_4 triazole), 138.0, 137.0, 134.5, 134.1, 130.3, 128.9, 128.5, 128.3, 125.8, 125.4, 124.1, 123.3, 122.5, 122.2, 120.9 (C_5 triazole), 115.7, 115.2, 107.1, 70.7, 61.6, 20.6: HRMS $[M + H]^+$ for $C_{27}H_{23}N_3O_2$ cal: 422.1790, found: 422.1889.

3.3.15 | 1-(4-((4-Methylbenzyl)oxy)phenyl)-4-((naphthalen-1-yloxy)methyl)-1H-1,2,3-triazole (7o)

Appearance: White solid; Yield: 78%; m.p.: 162-164°C; FTIR (KBr): 3161 (C—H str., triazole ring), 3040 (C—H str., aromatic ring), 2930 (C—H str., aliphatic), 1577, 1463 (C═C str., aromatic ring), 1230, 1016 (C—O str., ether);

^{1}H NMR (400 MHz, DMSO-d_6): δ 8.96 (s, 1H), 8.20 (d, J = 8.2 Hz, 1H), 7.90-7.84 (m, 3H, ArH), 7.51 (t, J = 8.0 Hz, 4H), 7.37 (d, J = 8.0 Hz, 2H), 7.25-7.21 (m, 5H, ArH), 5.43 (s, 2H), 5.15 (s, 2H), 2.32 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 158.9, 154.0, 144.3 (C_4 triazole), 137.7, 134.5, 134.1, 130.6, 129.5, 128.4, 128.0, 127.0, 126.6, 125.8, 125.4, 123.2, 122.3, 122.2, 120.9 (C_5 triazole), 116.3, 106.3, 70.0, 62.2. HRMS $[M + H]^+$ for $C_{27}H_{23}N_3O_2$ cal: 422.1790, found: 422.1880.

3.4 | Single X-ray crystallography

Single crystals of compounds **7f** were determined on a SuperNova, Single source at offset, Titan diffractometer. The crystal was kept at 293 K during data collection. The structure was solved with the ShelXT[34] structure solution program using Direct Methods and refined with the ShelXL[35] refinement package using Least Squares minimization.

3.5 | Antibacterial activity

In vitro antibacterial activity of all the compounds (**7a**-**7o**) was carried out against bacteria—*B. cereus, S. aureus*, and *E. coli* by standard serial dilution method.[29,30] A stock solution of 200 μg/mL concentrations in for all the compounds was used which, further serially diluted to get concentration of 100, 50, 25, 12.5, 6.25 μg/mL. Nutrient broth was employed as culture media and dimethylsulfoxide was used as solvent control. Norfloxacin was used as a standard drug. All the dilutions were inoculated with respective bacteria and incubated at 37°C for 24 h. After incubation, the results reported in terms of minimum inhibitory concentration (MIC) (Table 2).

3.6 | Antioxidant activity

The synthesized compounds were screened for free radical scavenging activity by 1,1-diphenyl-2-picrylhydrazyl (DPPH) assay.[31,32] 1 mL of various concentrations of the test compounds (20, 40, 60, 80, and 100 μg/mL) in methanol was added to 1 mL of methanolic solution of DPPH (0.004 g DPPH in 100 mL methanol). The samples were allowed to stand for 30 min in dark at room temperature, the optical density was measured at 517 nm and the percent inhibition (I%) was calculated.

The inhibition ratio (I%) of the tested compounds was calculated by the following equation:

$I\% = (A_0 - A_1)/A_0 \times 100$,where A_0 is the absorbance of the control and A_1 is the absorbance of the sample.

All tests were performed in triplicate and the average absorbance was noted for each concentration [Table 3]. Ascorbic acid (AA) was used as reference standard at the same concentration with respect to the compounds in methanol.

4 | CONCLUSION

We have synthesized 15 naphthyl-linked disubstituted 1,2,3-triazoles from the click reaction of 1-(prop-2-yn-1-yloxy)naphthalene and aromatic azides. The synthesized compounds were characterized by various analytical techniques. The structure of compound **7f** (CCDC 1876891) was also confirmed by X-ray crystallography. The synthesized compounds were assessed for antibacterial activity and antioxidant activity. The biological data revealed moderate to good results.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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