SUPPLEMENTARY INFORMATION

SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL POTENTIAL OF SOME 1,4-DISUBSTITUTED 1,2,3-BISTRIAZOLES

C. P. Kaushik^a *, Krishan Kumar^a, Dharmendra Singh^b, S. K. Singh^c, Deepak Kumar Jindal^c and Rajluxmi^a

^aDepartment of Chemistry, Guru Jambheshwar University of Science & Technology, Hisar, Haryana-125001, India

^bCentre for Research & Development, IPCA Lab Ltd., Kandivali, Mumbai, Maharashtra- 400101, India

^cDepartment of Pharmaceutical Sciences, Guru Jambheshwar University of Science & Technology, Hisar, Haryana-125001, India

EXPERIMENTAL DETAIL

All the chemicals were purchased from Sigma-Aldrich, Hi-Media, Alfa-Aesar and were used without further purification. Melting points of the target compounds were recorded in °C by applying open capillary method and are uncorrected. The IR spectra were recorded on Shimadzu IR Affinity-I FT-IR spectrophotometer using potassium bromide (KBr) powder and values are given in cm⁻¹. The ¹H NMR spectra were recorded on Bruker Avance II 400 MHz spectrophotometer and ¹³C NMR on Bruker Avance II 400 at 100 MHz, in deuterated dimethylsulphoxide-*d*₆ using tetramethylsilane (TMS) as an internal standard (chemical shift in δ , ppm). Coupling constant (*J*) values are given in Hertz (Hz). High Resolution Mass spectra were recorded on Waters Micromass Q-ToF Micro (ESI) spectrophotometer. The completion of reactions and the purity of the compounds were analyzed by thin layer chromatography (TLC) using readymade silica gel plates (SIL G/UV₂₅₄, ALUGRAM) and visualized under ultraviolet lamp.

General procedure for the synthesis of ester linked 1,4-disubstituted 1,2,3-bistriazoles (3a-3f, 4a-4f).

The synthesis of benzoic acid prop-2-ynyl ester (**1a-1e**) and its derivatives was carried out by reacting their corresponding aromatic acid chlorides (2.0 mmol) with propargyl alcohol (2.4 mmol) using N,N-dimethylaminopyridine (2.0 mmol) as base, in dry dichloromethane at 0-10 °C. Propargyl acrylate (**1f**) used for the synthesis of 1,4-disubstituted 1,2,3-bistriazoles (**3f**, **4f**) was purchased from Sigma Aldrich. The ester linked 1,4-disubstituted 1,2,3-bistriazoles (**3a-3f**, **4a-4f**) were synthesized by reacting 1,4-bis(bromomethyl)benzene/ 1,6-dibromohexane (**2**, 1.0 mmol) with various ester linked terminal alkynes (**1a-1f**, 2.0 mmol) using sodium azide (3.0 mmol), copper sulphate pentahydrate (0.1 mmol) and sodium ascorbate (0.4 mmol) in dimethylformamide : water (8:2) as solvent system with stirring up to 6-16 h at 25-50°C (Scheme 1). The progress of reactions was monitored by thin layer chromatography. After the completion of reaction, added cold distilled water and the product was extracted with 50 mL of ethyl acetate. The organic layer was washed with aqueous ammonia solution followed by brine solution and then dried using anhydrous sodium sulphate. Filtered and evaporated the organic layer under vacuum on rotavapor R-3 to furnish crude product which was further purified by column chromatography.

General procedure for the synthesis of 1,4-disubstituted 1,2,3-bistriazoles containing benzofused N-heteroaromatic functionalities (6a-6b, 7a-7b)

The benzofused N-heteroaromatic alkynes (**5a-5b**) were synthesized by reacting benzotriazole/ benzimidazole (2.0 mmol) with propargyl bromide (2.4 mmol) in the presence of potassium carbonate (4.0 mmol) using dimethylformamide by stirring at 10-25 °C for 8-10 h. 1,4-disubstituted 1,2,3-bistriazoles (**6a-6b**, **7a-7b**) were synthesized by reacting 1,4-

bis(bromomethyl)benzene/ 1,6-dibromohexane (**2**, 1.0 mmol) with benzofused N-heteroaromatic alkynes (**5a-5b**, 2.0 mmol) using sodium azide (3.0 mmol), copper sulphate pentahydrate (0.1 mmol) and sodium ascorbate (0.4 mmol) in dimethylformamide : water (9:1) with stirring up to 12-15 h at 25-40°C (Scheme 2). The progress of reactions was monitored by thin layer chromatography. After the completion of reaction, added cold distilled water and the product was extracted with 50 mL of ethyl acetate. The organic layer was washed with aqueous ammonia solution followed by brine solution and then dried using anhydrous sodium sulphate. Filtered and evaporated the organic layer under vacuum on rotavapor R-3 to furnish crude product which was further purified by column chromatography.

Spectroscopic Data of Newly Synthesized 1,4-Disubstituted 1,2,3-bistriazoles

(1,1'-(1,4-phenylenebis(methylene))bis(1H-1,2,3-triazole-4,1-diyl))bis(methylene) dibenzoate (3a) Appearance: white solid; Yield: 91%; m.p.: 198-202 °C; FT-IR (KBr) $\nu_{\max}$ / cm^{-1} : 3111 (C-H str., triazole ring), 3062 (C-H str., aromatic ring), 1710 (C=O str., ester), 1600, 1521, 1446 (C=C str., aromatic ring), 1271 (C-O asym. str., ester), 1101 (C-O sym. str., ester); ^1H NMR (400 MHz, DMSO- d_6 , δ , ppm): 5.38 (s, 4H, NCH₂), 5.60 (s, 4H, OCH₂), 7.34 (s, 4H, Ar-H), 7.52 (t, 4H, Ar-H, $J=7.2$ Hz), 7.66 (t, 2H, Ar-H, $J=7.2$ Hz), 7.95 (d, 4H, Ar-H, $J=7.2$ Hz), 8.30 (s, 2H, C-H triazole); ^{13}C NMR (100 MHz, DMSO- d_6 , δ , ppm): 52.9, 58.4, 125.4 (C₅ triazole), 128.9, 129.3, 129.7, 129.8, 134.0, 136.4, 142.6 (C₄ triazole), 165.9 (C=O ester); HRMS (m/z) calculated for C₂₈H₂₄N₆O₄ [M+H]⁺: 509.1893. Found: 509.1930.

(1,1'-(1,4-phenylenebis(methylene))bis(1H-1,2,3-triazole-4,1-diyl))bis(methylene) bis(4-methylbenzoate) (3b) Appearance: creamy-white solid; Yield: 82%; m.p.: 230-234 °C; FT-IR (KBr) $\nu_{\max}$ / cm^{-1} : 3124 (C-H str., triazole ring), 3065 (C-H str., aromatic ring), 2958

(C-H str., aliphatic), 1712 (C=O str., ester), 1610, 1525, 1448 (C=C str., aromatic ring), 1273 (C-O asym. str., ester), 1101 (C-O sym. str., ester); ^1H NMR (400 MHz, DMSO- d_6 , δ , ppm): 2.37 (s, 6H, CH₃), 5.35 (s, 4H, NCH₂), 5.60 (s, 4H, OCH₂), 7.31-7.37 (m, 8H, Ar-H), 7.84 (d, 4H, Ar-H, $J=8.0$ Hz), 8.29 (s, 2H, C-H triazole); ^{13}C NMR (100 MHz, DMSO- d_6 , δ , ppm): 21.7, 52.9, 58.4, 125.4 (C₅ triazole), 127.1, 128.9, 129.7, 129.8, 136.4, 142.6 (C₄ triazole), 144.3, 165.9 (C=O ester); HRMS (m/z) calculated for C₃₀H₂₈N₆O₄ [M+H]⁺: 537.2206. Found: 537.2244.

(1,1'-(1,4-phenylenebis(methylene))bis(1H-1,2,3-triazole-4,1-diyl))bis(methylene) bis(4-methoxy benzoate) (3c) Appearance: bright-white solid; Yield: 84%; m.p.: 186-190 °C; FT-IR (KBr) ν_{max} / cm⁻¹: 3122 (C-H str., triazole ring), 3068 (C-H str., aromatic ring), 2964 (C-H str., aliphatic), 1712 (C=O str., ester), 1606, 1510, 1440 (C=C str., aromatic ring), 1273 (C-O asym. str., ester), 1255 (C-O asym. str., ether), 1103 (C-O sym. str., ester); ^1H NMR (400 MHz, DMSO- d_6 , δ , ppm): 3.82 (s, 6H, OCH₃), 5.33 (s, 4H, NCH₂), 5.60 (s, 4H, OCH₂), 7.02 (d, 4H, Ar-H, $J=8.0$ Hz), 7.32-7.37 (m, 4H, Ar-H), 7.90 (d, 4H, Ar-H, $J=8.0$ Hz), 8.28 (s, 2H, C-H triazole); ^{13}C NMR (100 MHz, DMSO- d_6 , δ , ppm): 52.9, 56.0, 58.4, 114.5, 122.0, 125.2 (C₅ triazole), 128.8, 131.8, 136.4, 142.6 (C₄ triazole), 163.7, 165.9 (C=O ester); HRMS (m/z) calculated for C₃₀H₂₈N₆O₆ [M+H]⁺: 569.2104. Found: 569.2165.

(1,1'-(1,4-phenylenebis(methylene))bis(1H-1,2,3-triazole-4,1-diyl))bis(methylene) bis(4-nitrobenzoate) (3d) Appearance: light yellow solid; Yield: 95%; m.p.: 210-214 °C; FT-IR (KBr) ν_{max} / cm⁻¹: 3153 (C-H str., triazole ring), 3081 (C-H str., aromatic ring), 2962 (C-H str., aliphatic), 1724 (C=O str., ester), 1606, 1513, 1435 (C=C str., aromatic ring), 1541 (N-O asym. str., NO₂), 1352 (N-O sym. str., NO₂), 1269 (C-O asym. str., ester), 1103 (C-O sym. str., ester); ^1H NMR (400 MHz, DMSO- d_6 , δ , ppm): 5.45 (s, 4H, NCH₂), 5.61 (s, 4H,

OCH₂), 7.36 (d, 4H, Ar-H, *J*=8.0 Hz), 8.17 (d, 4H, Ar-H, *J*=8.8 Hz), 8.33 (d, 4H, Ar-H, *J*=8.8 Hz), 8.32 (s, 2H, C-H triazole); ¹³C NMR (100 MHz, DMSO-*d*₆, δ , ppm): 52.9, 59.1, 124.4, 125.7 (C₅ triazole), 129.0, 131.2, 135.2, 136.4, 142.2 (C₄ triazole), 150.8, 165.8 (C=O ester); HRMS (*m/z*) calculated for C₂₈H₂₂N₈O₈ [M+H]⁺: 599.1594. Found: 599.1633.

(1,1'-(1,4-phenylenebis(methylene))bis(1H-1,2,3-triazole-4,1-diyl))bis(methylene) bis(4-fluorobenzoate) (3e) Appearance: white solid; Yield: 93%; m.p.: 218-222 °C; FT-IR (KBr) $\nu_{\max}$ / cm⁻¹: 3122 (C-H str., triazole ring), 3072 (C-H str., aromatic ring), 2962 (C-H str., aliphatic), 1720 (C=O str., ester), 1598, 1506, 1442 (C=C str., aromatic ring), 1271 (C-O asym. str., ester), 1157 (C-F str.), 1095 (C-O sym. str., ester); ¹H NMR (400 MHz, DMSO-*d*₆, δ , ppm): 5.37 (s, 4H, NCH₂), 5.63 (s, 4H, OCH₂), 7.32-7.36 (m, 8H, Ar-H), 8.01 (d, 4H, Ar-H, *J*=8.0 Hz), 8.30 (s, 2H, C-H triazole); ¹³C NMR (100 MHz, DMSO-*d*₆, δ , ppm): 52.9, 58.5, 116.5, 125.5 (C₅ triazole), 129.0, 132.6, 132.7, 136.4, 142.5 (C₄ triazole), 165.0, 165.8 (C=O ester); HRMS (*m/z*) calculated for C₂₈H₂₂F₂N₆O₄ [M+H]⁺: 545.1704. Found: 545.1744.

(1,1'-(1,4-phenylenebis(methylene))bis(1H-1,2,3-triazole-4,1-diyl))bis(methylene) diacrylate (3f) Appearance: white solid; Yield: 73%; m.p.: decomposed at 230 °C; FT-IR (KBr) $\nu_{\max}$ / cm⁻¹: 3143 (C-H str., triazole ring), 3067 (C-H str., aromatic ring), 2956 (C-H str., aliphatic), 1724 (C=O str., ester), 1610, 1514, 1442 (C=C str., aromatic ring), 1261 (C-O asym. str., ester), 1116 (C-O sym. str., ester); ¹H NMR (400 MHz, DMSO-*d*₆, δ , ppm): 4.48 (s, 4H, OCH₂), 5.11-5.26 (m, 6H, 2 CH=CH₂), 5.55 (s, 4H, NCH₂), 7.31 (s, 4H, Ar-H), 7.99 (s, 2H, C-H triazole); ¹³C NMR (100 MHz, DMSO-*d*₆, δ , ppm): 52.9, 57.6, 126.6 (C₅ triazole), 128.9, 129.1, 131.4, 136.4, 143.2 (C₄ triazole), 166.1 (C=O ester); HRMS (*m/z*) calculated for C₂₀H₂₀N₆O₄ [M+H]⁺: 409.1580. Found: 409.1635.

(1,1'-(hexane-1,6-diyl)bis(1H-1,2,3-triazole-4,1-diyl))bis(methylene)dibenzoate (4a)

Appearance: white solid; Yield: 87%; m.p.: 110-114 °C; FT-IR (KBr) $\nu_{\max}$ / cm^{-1} : 3138 (C-H str., triazole ring), 3064 (C-H str., aromatic ring), 2926 (C-H str., aliphatic), 1716 (C=O str., ester), 1597, 1548, 1450 (C=C str., aromatic ring), 1271 (C-O asym. str., ester), 1109 (C-O sym. str., ester); ^1H NMR (400 MHz, DMSO- d_6 , δ , ppm): 1.25 (br s, 4H, CH₂), 1.80 (br s, 4H, CH₂), 4.34 (t, 4H, NCH₂, $J=7.2$ Hz), 5.39 (s, 4H, OCH₂), 7.52 (t, 4H, Ar-H, $J=7.6$ Hz), 7.66 (t, 2H, Ar-H, $J=7.6$ Hz), 7.96 (d, 4H, Ar-H, $J=7.6$ Hz), 8.25 (s, 2H, C-H triazole); ^{13}C NMR (100 MHz, DMSO- d_6 , δ , ppm): 25.6, 29.9, 49.7, 58.5, 125.2 (C₅ triazole), 129.3, 129.7, 129.8, 134.0, 142.2 (C₄ triazole), 165.9 (C=O ester); HRMS (m/z) calculated for C₂₆H₂₈N₆O₄ [M+H]⁺: 489.2206. Found: 489.2242.

(1,1'-(hexane-1,6-diyl)bis(1H-1,2,3-triazole-4,1-diyl))bis(methylene)bis(4-methyl

benzoate) (4b) Appearance: white solid; Yield: 85%; m.p.: 130-134 °C; FT-IR (KBr) $\nu_{\max}$ / cm^{-1} : 3111 (C-H str., triazole ring), 3062 (C-H str., aromatic ring), 2954 (C-H str., aliphatic), 1714 (C=O str., ester), 1610, 1508, 1448 (C=C str., aromatic ring), 1269 (C-O asym. str., ester), 1099 (C-O sym. str., ester); ^1H NMR (400 MHz, DMSO- d_6 , δ , ppm): 1.25 (br s, 4H, CH₂), 1.80 (br s, 4H, CH₂), 2.36 (s, 6H, CH₃), 4.34 (t, 4H, NCH₂, $J=7.2$ Hz), 5.36 (s, 4H, OCH₂), 7.31 (d, 4H, Ar-H, $J=8.0$ Hz), 7.84 (d, 4H, Ar-H, $J=8.0$ Hz), 8.24 (s, 2H, C-H triazole); ^{13}C NMR (100 MHz, DMSO- d_6 , δ , ppm): 21.6, 25.6, 29.9, 49.7, 58.3, 125.1 (C₅ triazole), 127.1, 129.7, 129.8, 142.3 (C₄ triazole), 144.3, 165.9 (C=O ester); HRMS (m/z) calculated for C₂₈H₃₂N₆O₄ [M+H]⁺: 517.2519. Found: 517.2558.

(1,1'-(hexane-1,6-diyl)bis(1H-1,2,3-triazole-4,1-diyl))bis(methylene)bis(4-methoxy

benzoate) (4c) Appearance: white solid; Yield: 95%; m.p.: 116-120 °C; FT-IR (KBr) $\nu_{\max}$ / cm^{-1} : 3140 (C-H str., triazole ring), 3061 (C-H str., aromatic ring), 2952 (C-H str., aliphatic),

1712 (C=O str., ester), 1608, 1510, 1444 (C=C str., aromatic ring), 1282 (C-O asym. str., ester), 1255 (C-O asym. str., ether), 1103 (C-O sym. str., ester & ether); ^1H NMR (400 MHz, DMSO- d_6 , δ , ppm): 1.25 (br s, 4H, CH₂), 1.80 (br s, 4H, CH₂), 3.82 (s, 6H, OCH₃), 4.34 (t, 4H, NCH₂, $J=7.2$ Hz), 5.35 (s, 4H, OCH₂), 7.03 (d, 4H, Ar-H, $J=8.8$ Hz), 7.90 (d, 4H, Ar-H, $J=8.8$ Hz), 8.23 (s, 2H, C-H triazole); ^{13}C NMR (100 MHz, DMSO- d_6 , δ , ppm): 25.6, 29.9, 49.7, 56.0, 58.1, 114.5, 122.0, 125.1 (C₅ triazole), 131.8, 142.4 (C₄ triazole), 163.7, 165.6 (C=O ester); HRMS (m/z) calculated for C₂₈H₃₂N₆O₆ [M+H]⁺: 549.2417. Found: 549.2455.

((1,1'-(hexane-1,6-diyl)bis(1H-1,2,3-triazole-4,1-diyl))bis(methylene)bis(4-nitro benzoate) (4d) Appearance: light greenish-yellow solid; Yield: 96%; m.p.: 162-166 °C; FT-IR (KBr) ν_{max} / cm⁻¹: 3109 (C-H str., triazole ring), 3056 (C-H str., aromatic ring), 2941 (C-H str., aliphatic), 1722 (C=O str., ester), 1608, 1456 (C=C str., aromatic ring), 1548 (N-O asym. str., NO₂), 1352 (N-O asym. str., NO₂), 1267 (C-O asym. str., ester), 1099 (C-O sym. str., ester); ^1H NMR (400 MHz, DMSO- d_6 , δ , ppm): 1.26 (br s, 4H, CH₂), 1.80 (br s, 4H, CH₂), 4.35 (t, 4H, NCH₂, $J=6.8$ Hz), 5.45 (s, 4H, OCH₂), 8.17 (d, 4H, Ar-H, $J=8.8$ Hz), 8.28 (s, 2H, C-H triazole), 8.33 (d, 4H, Ar-H, $J=8.8$ Hz); ^{13}C NMR (100 MHz, DMSO- d_6 , δ , ppm): 25.6, 29.9, 49.7, 59.2, 124.4, 125.4 (C₅ triazole), 131.2, 135.2, 141.8 (C₄ triazole), 150.8, 164.5 (C=O ester); HRMS (m/z) calculated for C₂₆H₂₆N₈O₈ [M+H]⁺: 579.1907. Found: 579.1944.

((1,1'-(hexane-1,6-diyl)bis(1H-1,2,3-triazole-4,1-diyl))bis(methylene)bis(4-fluoro benzoate) (4e) Appearance: dull white solid; Yield: 72%; m.p.: 144-148 °C; FT-IR (KBr) ν_{max} / cm⁻¹: 3142 (C-H str., triazole ring), 3074 (C-H str., aromatic ring), 2927 (C-H str., aliphatic CH₂), 1716 (C=O str., ester), 1604, 1508, 1444 (C=C str., aromatic ring), 1282 (C-O asym. str., ester), 1153 (C-F str.), 1111 (C-O sym. str., ester); ^1H NMR (400 MHz, DMSO- d_6 ,

δ , ppm): 1.25 (br s, 4H, CH₂), 1.80 (br s, 4H, CH₂), 4.34 (t, 4H, NCH₂, $J=6.8$ Hz), 5.38 (s, 4H, OCH₂), 7.35 (d, 4H, Ar-H, $J=8.8$ Hz), 8.02 (d, 4H, Ar-H, $J=8.8$ Hz), 8.25 (s, 2H, C-H triazole); ¹³C NMR (100 MHz, DMSO-*d*₆, δ , ppm): 25.6, 29.9, 49.7, 58.6, 116.5, 125.2 (C₅ triazole), 126.4, 132.7, 142.1 (C₄ triazole), 165.0, 165.5 (C=O ester); HRMS (m/z) calculated for C₂₆H₂₆F₂N₆O₄ [M+H]⁺: 525.2017. Found: 525.2055.

(1,1'-(hexane-1,6-diyl)bis(1H-1,2,3-triazole-4,1-diyl))bis(methylene)diacrylate (4f)

Appearance: dull white solid; Yield: 68%; m.p.: decomposed at 160 °C; FT-IR (KBr) $\nu_{\max}/\text{cm}^{-1}$: 3130 (C-H str., triazole ring), 2941 (C-H str., aliphatic), 1735 (C=O str., ester), 1595, 1442 (C=C str., aromatic ring), 1265 (C-O asym. str., ester), 1134 (C-O sym. str., ester); ¹H NMR (400 MHz, DMSO-*d*₆, δ , ppm): 1.24 (br s, 4H, CH₂), 1.78 (br s, 4H, CH₂), 4.30 (t, 4H, NCH₂, $J=7.2$ Hz), 4.50 (s, 4H, OCH₂), 5.13-5.21 (m, 6H, 2 CH=CH₂), 7.95 (s, 2H, C-H triazole); ¹³C NMR (100 MHz, DMSO-*d*₆, δ , ppm): 25.6, 29.9, 49.7, 57.6, 125.6 (C₅ triazole), 129.2, 131.3, 142.8 (C₄ triazole), 166.2 (C=O ester); HRMS (m/z) calculated for C₁₈H₂₄N₆O₄ [M+H]⁺: 389.1893. Found: 389.1933.

1,4-bis((4-((1H-benzo[d][1,2,3]triazol-1-yl)methyl)-1H-1,2,3-triazol-1-yl)methyl)benzene (6a)

Appearance: creamy white solid; Yield: 80%; m.p.: 232-236 °C; FT-IR (KBr) $\nu_{\max}/\text{cm}^{-1}$: 3136 (C-H str., triazole ring), 3064 (C-H str., aromatic ring), 2951 (C-H str., aliphatic), 1622, 1496, 1458 (C=C str., aromatic ring); ¹H NMR (400 MHz, DMSO-*d*₆, δ , ppm): 5.54 (s, 4H, NCH₂), 6.03 (s, 4H, NCH₂), 7.31 (d, 4H, Ar-H, $J=8.0$ Hz), 7.40 (t, 2H, Ar-H, $J=7.6$ Hz), 7.54 (t, 2H, Ar-H, $J=7.6$ Hz), 7.88 (d, 2H, Ar-H, $J=8.4$ Hz), 8.04 (d, 2H, Ar-H, $J=8.4$ Hz), 8.27 (s, 2H, C-H triazole); ¹³C NMR (100 MHz, DMSO-*d*₆, δ , ppm): 43.3, 52.9, 111.3, 119.6, 124.7 (C₅ triazole), 127.8, 128.8, 133.1, 136.3, 142.3 (C₄ triazole), 145.7; HRMS (m/z) calculated for C₂₆H₂₂N₁₂ [M+H]⁺: 503.2124. Found: 503.2160.

1,4-bis((4-((1H-benzo[d]imidazol-1-yl)methyl)-1H-1,2,3-triazol-1-yl)methyl)

benzene (6b) Appearance: creamy-white solid; Yield: 78%; m.p.: 174-178 °C; FT-IR (KBr) $\nu_{\max}/\text{cm}^{-1}$: 3124 (C-H str., triazole ring), 3088 (C-H str., aromatic ring), 2968 (C-H str., aliphatic), 1662, 1616, 1496, 1454 (C=N & C=C str., aromatic ring); ^1H NMR (400 MHz, DMSO- d_6 , δ , ppm): 5.53 (s, 4H, NCH₂), 5.54 (s, 4H, NCH₂), 7.17-7.24 (m, 8H, Ar-H), 7.59-7.65 (m, 4H, Ar-H), 8.16 (s, 2H, C-H triazole), 8.30 (s, 2H, C₂-H benzimidazole); ^{13}C NMR (100 MHz, DMSO- d_6 , δ , ppm): 43.3, 52.9, 111.1, 119.9, 122.1, 122.8, 124.2 (C₅ triazole), 128.8, 134.0, 136.3, 143.4 (C₄ triazole), 143.9, 144.4; HRMS (m/z) calculated for C₂₈H₂₄N₁₀ [M+H]⁺: 501.2219. Found: 501.2255.

1,6-bis(4-((1H-benzo[d][1,2,3]triazol-1-yl)methyl)-1H-1,2,3-triazol-1-yl)hexane(7a)

Appearance: creamy white solid; Yield: 72%; m.p.: 78-82 °C; FT-IR (KBr) $\nu_{\max}/\text{cm}^{-1}$: 3136 (C-H str., triazole ring), 3066 (C-H str., aromatic ring), 2941 (C-H str., aliphatic), 1616, 1496, 1460 (C=C str., aromatic ring); ^1H NMR (400 MHz, DMSO- d_6 , δ , ppm): 1.15 (br s, 4H, CH₂), 1.70 (br s, 4H, CH₂), 4.26 (t, 4H, NCH₂, $J=7.2$ Hz), 6.04 (s, 4H, NCH₂), 7.38 (t, 2H, Ar-H, $J=7.6$ Hz), 7.53 (t, 2H, Ar-H, $J=7.6$ Hz), 7.88 (d, 2H, Ar-H, $J=8.4$ Hz), 8.03 (d, 2H, Ar-H, $J=8.4$ Hz), 8.21 (s, 2H, C-H triazole); ^{13}C NMR (100 MHz, DMSO- d_6 , δ , ppm): 25.6, 29.9, 43.3, 49.7, 111.3, 119.6, 124.5 (C₅ triazole), 127.8, 133.1, 142.2 (C₄ triazole), 145.7; HRMS (m/z) calculated for C₂₄H₂₆N₁₂ [M+H]⁺: 483.2437. Found: 483.2474.

1,6-bis(4-((1H-benzo[d]imidazol-1-yl)methyl)-1H-1,2,3-triazol-1-yl)hexane (7b)

Appearance: creamy white solid; Yield: 75%; m.p.: 84-88 °C; FT-IR (KBr) $\nu_{\max}/\text{cm}^{-1}$: 3141 (C-H str., triazole ring), 3078 (C-H str., aromatic ring), 2938 (C-H str., aliphatic), 1605, 1501, 1472 (C=C str., aromatic ring); ^1H NMR (400 MHz, DMSO- d_6 , δ , ppm): 1.15 (br s, 4H,

CH₂), 1.70 (br s, 4H, CH₂), 4.26 (t, 4H, NCH₂, $J=7.2$ Hz), 5.55 (s, 4H, NCH₂), 7.17-7.24 (m, 4H, Ar-H), 7.59-7.65 (m, 4H, Ar-H), 8.16 (s, 2H, C-H triazole), 8.22 (s, 2H, C₂-H benzimidazole); ¹³C NMR (100 MHz, DMSO-*d*₆, δ , ppm): 25.6, 29.9, 43.3, 49.7, 111.1, 120.0, 122.2, 122.7, 124.3 (C₅ triazole), 134.1, 143.3 (C₄ triazole), 143.9, 144.4; HRMS (m/z) calculated for C₂₆H₂₈N₁₀ [M+H]⁺: 481.2532. Found: 481.2553.

Antibacterial activity

All synthesized 1,4-disubstituted 1,2,3-bistriazoles (**3a-3f**, **4a-4f**, **6a-6b**, **7a-7b**) were evaluated *in vitro* for antibacterial potential against Gram-positive bacteria i.e. *Bacillus subtilis* (MTCC 441), *Staphylococcus aureus* (MTCC 7443) and Gram-negative bacteria i.e. *Pseudomonas aeruginosa* (MTCC 424), *Escherichia coli* (MTCC 1652) by two fold serial dilution method using stock solutions of 2000 and 400 $\mu\text{g/mL}$. Dimethylsulphoxide was employed as a negative control. Dilutions of test compounds were prepared in double strength nutrient broth. One mL nutrient broth was taken in each of nine test tubes. To the first test-tube 1.0 mL of test solution (2000 $\mu\text{g/mL}$) was added aseptically to get the concentration of 1000 $\mu\text{g/mL}$. From this dilution, other concentrations were prepared by serial dilution method to get final concentrations of 500 $\mu\text{g/mL}$ and 250 $\mu\text{g/mL}$. From second stock solution, 1.0 mL of test solution (400 $\mu\text{g/mL}$) was taken in fourth test tube, to prepare the concentration of 200 $\mu\text{g/mL}$. From above (200 $\mu\text{g/mL}$) concentration, other dilutions were prepared by serial dilution to get final concentrations of 100 $\mu\text{g/mL}$, 50 $\mu\text{g/mL}$, 25 $\mu\text{g/mL}$, 12.5 and 6.25 $\mu\text{g/mL}$ in test-tube number five to nine. All the test tubes aseptically inoculated by 0.1 mL (100 μl) desired bacterial strain taken in sterile saline solution. The inoculated test samples were then incubated at 37 ± 1 °C for 24 h (in case of *Bacillus subtilis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*) and 48 h (in case of *Escherichia coli*) in BOD incubator and the results were recorded in terms of minimum inhibitory concentration

(MIC) as depicted in Table 1. Ciprofloxacin was used as standard drug and also tested under similar experimental conditions for comparison with synthesized compounds. To check the effect of solvent on bacterial growth, a control test was performed with test medium supplemented with dimethylsulphoxide at same dilution as used in experiment.

Antifungal activity

The *in-vitro* antifungal evaluation of 1,4-disubstituted 1,2,3-bis-triazoles (**3a-3f**, **4a-4f**, **6a-6b**, **7a-7b**) was carried out against two fungal strains viz. *Candida albicans* (MTCC 227) and *Aspergillus niger* (MTCC 8189) by two fold serial dilution method using stock solutions of 2000 and 400 µg/mL of compounds. Sabouraud dextrose broth was used as a fungal culture media and DMSO as a negative control. One mL of freshly prepared sterile culture media was added aseptically in each test tube followed by serial dilution with synthesized compounds to prepare concentrations of 1000, 500, 250, 200, 100, 50, 25, 12.5 and 6.25 µg/mL. Further these dilutions of triazole compounds were inoculated with 0.1 mL of suspension of respective microorganism contained in sterilized saline solution. Then samples of compounds loaded with microorganisms incubated at 25±1 °C for two days in case of *Candida albicans* and for seven days in case of *Aspergillus niger*. Fluconazole, a antifungal triazole, was also screened under similar experimental conditions for comparison with activity of target compounds. The results of antifungal activity assay are recorded in terms of minimum inhibitory concentration (MIC) as shown in Table 2.

^1H NMR, ^{13}C NMR and HRMS of Compounds

Figure S1. ^1H NMR spectrum (DMSO- d_6 , 400 MHz) of compound **3a**

Figure S2. ¹H NMR spectrum (DMSO-*d*₆, 400 MHz) of compound **3b**

Figure S3. ¹H NMR spectrum (DMSO-*d*₆, 400 MHz) of compound **3c**

Figure S4. ¹H NMR spectrum (DMSO-*d*₆, 400 MHz) of compound **3d**

Figure S5. ¹H NMR spectrum (DMSO-*d*₆, 400 MHz) of compound **3e**

Figure S6. ^1H NMR spectrum ($\text{DMSO-}d_6$, 400 MHz) of compound **3f**

Figure S7. ¹H NMR spectrum (DMSO-*d*₆, 400 MHz) of compound **4a**

Figure S8. ¹H NMR spectrum (DMSO-*d*₆, 400 MHz) of compound **4b**

Figure S9. ¹H NMR spectrum (DMSO-*d*₆, 400 MHz) of compound **4c**

Figure S10. ¹H NMR spectrum (DMSO-*d*₆, 400 MHz) of compound **4d**

Figure S11. ¹H NMR spectrum (DMSO-*d*₆, 400 MHz) of compound **4e**

Figure S12. ^1H NMR spectrum ($\text{DMSO}-d_6$, 400 MHz) of compound **4f**

Figure S13. ¹H NMR spectrum (DMSO-*d*₆, 400 MHz) of compound **6a**

Figure S14. ¹H NMR spectrum (DMSO-*d*₆, 400 MHz) of compound **6b**

Figure S15. ¹H NMR spectrum (DMSO-*d*₆, 400 MHz) of compound **7a**

Figure S16. ¹H NMR spectrum (DMSO-*d*₆, 400 MHz) of compound **7b**

Figure S17. ^{13}C NMR spectrum ($\text{DMSO-}d_6$, 100 MHz) of compound **3a**

Figure S18. ¹³C NMR spectrum (DMSO-*d*₆, 100 MHz) of compound **3b**

Figure S19. ¹³C NMR spectrum (DMSO-*d*₆, 100 MHz) of compound **3c**

Figure S20. ^{13}C NMR spectrum ($\text{DMSO-}d_6$, 100 MHz) of compound **3d**

Figure S21. ¹³C NMR spectrum (DMSO-*d*₆, 100 MHz) of compound **3e**

Figure S22. ^{13}C NMR spectrum ($\text{DMSO}-d_6$, 100 MHz) of compound **3f**

Figure S23. ¹³C NMR spectrum (DMSO-*d*₆, 100 MHz) of compound **4a**

Figure S24. ¹³C NMR spectrum (DMSO-*d*₆, 100 MHz) of compound **4b**

Figure S25. ¹³C NMR spectrum (DMSO-*d*₆, 100 MHz) of compound **4c**

Figure S26. ^{13}C NMR spectrum ($\text{DMSO}-d_6$, 100 MHz) of compound **4d**

Figure S27. ^{13}C NMR spectrum ($\text{DMSO-}d_6$, 100 MHz) of compound **4e**

Figure S28. ^{13}C NMR spectrum ($\text{DMSO-}d_6$, 100 MHz) of compound **4f**

Figure S29. ^{13}C NMR spectrum ($\text{DMSO}-d_6$, 100 MHz) of compound **6a**

Figure S30. ^{13}C NMR spectrum ($\text{DMSO-}d_6$, 100 MHz) of compound **6b**

Figure S31. ¹³C NMR spectrum (DMSO-*d*₆, 100 MHz) of compound **7a**

Figure S32. ¹³C NMR spectrum (DMSO-*d*₆, 100 MHz) of compound **7b**

Figure S33. HRMS of compound 3a

Figure S34. HRMS of compound **3b**

Figure S35. HRMS of compound 3c

Figure S36. HRMS of compound **3d**

Figure S37. HRMS of compound 3e

Figure S38. HRMS of compound 3f

Figure S39. HRMS of compound 4a

Figure S40. HRMS of compound 4b

Figure S41. HRMS of compound 4c

Figure S42. HRMS of compound 4d

Figure S43. HRMS of compound 4e

Figure S44. HRMS of compound 4f

Figure S45. HRMS of compound 6a

Figure S46. HRMS of compound **6b**

Figure S47. HRMS of compound 7a

Figure S48. HRMS of compound **7b**