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Synthesis and Antimicrobial Activity of Bis-1,2,3-triazole Based Chalcones

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Abstract—A series of bis-1,2,3-triazole based chalcones has been synthesized in high yields. The newly synthesized compounds are characterized by IR, NMR and mass spectroscopy. The combination of the pharmacologically active moieties in a single scaffold results in their synergistic effect and high antimicrobial activity against several bacterial and fungal strains. The compounds **4f**, **4l**, **4e**, **4k**, **4c**, and **4i** demonstrate potent antimicrobial activity at concentrations of 75 and 100 μg/mL.

Keywords: bis-1,2,3-triazoles, chalcones, antimicrobial activity

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In the current study we have reinforced biological activities of 1,2,3-triazoles and chalcones by conjugating these two pharmacophores in one molecular structure. Such approach is a part of our ongoing research in synthesis of biologically active compounds [1–3].

RESULTS AND DISCUSSION

Dialkylation of the substituted 1,3-dihydrobenzene was carried out with propargyl bromide leading to the corresponding derivative **2** with 98% yield (Scheme 1). Its following click reaction with azides led to the corresponding ditriazole derivatives of acetophenone **3a**, **3b** in high yields. These intermediates were condensed with a variety of substituted benzaldehydes under basic conditions giving the target bis 1,3-triazolyl chalcones **4a**–**4l** in high yields. The structures of the intermediates and newly synthesized compounds **4a**–**4l** were supported by IR, NMR and mass spectral data.

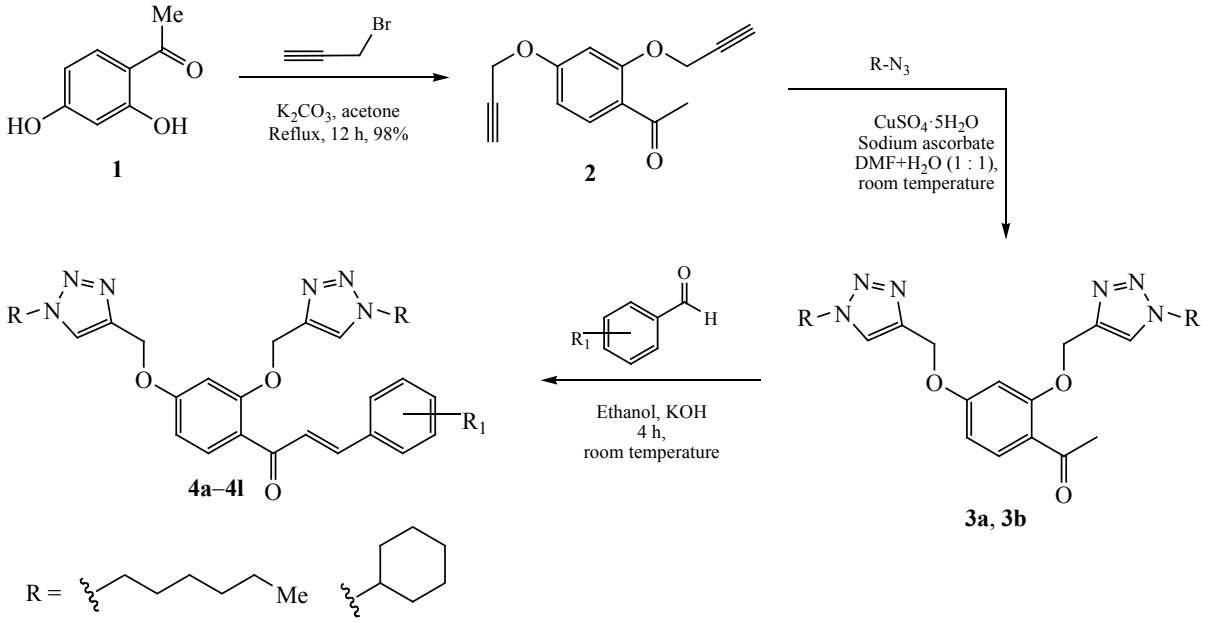
Antibacterial activity. The newly synthesized bis-1,2,3-triazole based chalcones **4a**–**4l** were tested for their antibacterial activity. The compounds demonstrated significant inhibition of tested gram positive and gram negative strains compared to the standard drug Gentamicin sulphate (Table 1). The compounds **4f**, **4l**, **4e**, **4k**, **4c**, and **4i** demonstrated high antibacterial activity at concentrations of 75 and 100 μg/mL (Table 1). The compounds **4b**, **4h**, **4a**, and **4g** also exhibited the pronounced antibacterial activity against the tested bacterial strains. The accumulated data indicated that presence of the strong electron donating group (OMe) at *ortho* and *para* positions of phenyl ring of chalcone could enhance the antibacterial activity of the other products.

Antifungal activity. According to the results obtained (Table 2) the highest antifungal activity was determined for compounds **4f**, **4l**, **4e**, **4k**, **4c**, and **4i** using Nystatin as the standard drug.

EXPERIMENTAL

Commercially available reagents were used as supplied, and all solvents were distilled before use. All reactions were performed in an oven-dried glassware. Melting points were measured in open capillary tubes and are uncorrected. IR (KBr) spectra were recorded on a Perkin–Elmer 337 spectrophotometer. NMR spectra were measured on a Bruker AV-400 spectrometers using DMSO-d_6 as a solvent and TMS as the internal standard. CHN analysis was carried out on a Perkin Elmer Model 2400 CHNS analyzer. ESI mass spectra were measured on a QSTARXL hybrid MS system (Applied Bio Systems). TLC was carried out on Merck TLC silica gel 60

Scheme 1. Synthesis of bis-1,2,3-triazole based chalcones **4a**–**4l**.



R = C_6H_{12}, R_1 = H (**4a**), R = C_6H_{12}, R_1 = 4-(Cl) (**4b**), R = C_6H_{12}, R_1 = 2,4-(Cl) (**4c**), R = C_6H_{12}, R_1 = 4-(CN) (**4d**);
R = C_6H_{12}, R_1 = 4-(OMe) (**4e**), R = C_6H_{12}, R_1 = 2,4-(OMe) (**4f**), R = C_6H_{11}, R_1 = H (**4g**), R = C_6H_{11}, R_1 = 4-(Cl) (**4h**);
R = C_6H_{11}, R_1 = 2,4-(Cl) (**4i**), R = C_6H_{11}, R_1 = 4-(CN) (**4j**), R = C_6H_{11}, R_1 = 4-(OMe) (**4k**), R = C_6H_{11}, R_1 = 2,4-(OMe) (**4l**).

F254 plates. The spots were visualized under UV light at 254 nm or by staining with aqueous basic potassium permanganate. Column chromatography was performed on a Merck silica gel 60A (100–200 mesh).

Synthesis of compounds 3a, 3b. To the solution of 1-[2,4-bis(prop-2-yn-1-yloxy)phenyl]ethanone (**2**) (100 mg, 0.438 mmol) in 5 mL of aqueous DMF (50%) was added $CuSO_4 \cdot 5H_2O$ (5 mol %) followed by sodium ascorbate (10 mol %) and alkyl azide (1.315 mmol). The reaction mixture was stirred for 1 h at room temperature. Upon completion of the process (TLC), the reaction mixture was poured over crushed ice, the solid obtained was filtered off, washed with water and dried. The crude product was purified by column chromatography using ethyl acetate in petroleum ether to afford the corresponding 1,4-disubstituted 1,2,3-triazole derivative **3a**, **3b**.

1-{2,4-Bis[(1-hexyl-1*H*-1,2,3-triazol-4-yl)methoxy]-phenyl}ethanone (3a). White solid, yield 90%, mp 179–181°C. IR spectrum, ν, cm^{-1}: 1674 (C=O). ^1H NMR spectrum, δ, ppm: 8.38–8.19 m (2H), 7.65 d (*J* = 8.68 Hz, 1H), 7.00 s (1H), 6.72 d.d (*J* = 8.54, 2.4 Hz, 1H), 5.31 s (2H), 5.26 s (2H), 4.40–4.35 s (4H), 2.61 s (3H), 1.81 d (*J* = 5.89 Hz, 4H), 1.24 s (12H), 0.83 d (*J* = 2.94 Hz, 6H). MS: *m/z:* 483 $[M + H]^+$. Found, %: C 64.50; H 7.72; N 17.22. $C_{26}H_{38}N_6O_3$. Calculated, %: C 64.71; H 7.94; N 17.41.

1-{2,4-Bis[(1-cyclohexyl-1*H*-1,2,3-triazol-4-yl)methoxy]phenyl}ethanone (3b). White solid, yield 92%, mp 165–167°C. IR spectrum, ν, cm^{-1}: 1675 (C=O). ^1H NMR spectrum, δ, ppm: 8.37–8.20 m (2H), 7.67 d (*J* = 8.69 Hz, 1H), 7.02 s (1H), 6.73 d.d (*J* = 8.56 Hz, 2.4, 1H), 5.30 s (2H), 5.27 s (2H), 4.59–4.44 m (1H), 4.42–4.30 m (1H), 2.60 s (3H), 2.06–1.12 m (20H). MS: *m/z:* 479 $[M + H]^+$. Found, %: C 65.03; H 6.98; N 17.35. $C_{26}H_{34}N_6O_3$. Calculated, %: C 65.25; H 7.16; N 17.56.

Synthesis of (*E*)-1-{2,4-bis[(1-hexyl-1*H*-1,2,3-triazol-4-yl)methoxy]phenyl}-3-phenylprop-2-en-1-one (4a). To a solution of compound **3a** (1.0 g, 0.0043 mol) in EtOH was added KOH (0.370 g, 0.0065 mol). The resulting mixture was stirred at room temperature for 15 min. Benzaldehyde (0.557 g, 0.0052 mol, 1.2 eq) was added drop-wise, and the mixture was stirred for 8 h. After completion of the process (TLC), ice-cold water was added to the reaction mixture and it was neutralized by 0.1–0.2 N HCl, upon which precipitation occurred. The precipitate was filtered off, washed with water and cold MeOH to afford pure product **4a**.

Table 1. Antibacterial activity of the compounds **4a**–**4l**

Compound	*c*, μg/mL	Zone of inhibition, mm							
		gram positive bacteria				gram negative bacteria			
		Micrococcus luteus	*MRSA*	*Bacillus subtilis*	*Bacillus cereus*	*Pseudomonas aeruginosa*	*Klebsiella pneumonia*	*Escherichia coli*	*Proteus vulgaris*
4a	75	21	23	21	25	19	22	24	20
	100	22	25	23	26	21	23	26	23
4b	75	22	25	23	26	21	23	26	22
	100	24	27	26	28	24	25	28	24
4c	75	25	28	27	28	25	24	29	26
	100	27	30	29	30	27	26	30	28
4d	75	19	20	17	21	17	19	22	19
	100	21	22	19	24	19	21	24	20
4e	75	31	28	26	27	26	27	29	28
	100	34	31	29	30	29	30	32	31
4f	75	34	31	29	30	29	30	32	31
	100	37	33	32	33	32	33	35	34
4g	75	20	21	19	22	18	20	22	19
	100	22	23	21	24	20	22	25	21
4h	75	21	25	23	25	20	22	25	21
	100	23	28	25	27	23	24	27	23
4i	75	23	26	24	27	23	22	27	24
	100	26	28	25	29	25	23	29	26
4j	75	13	14	12	13	11	12	15	14
	100	16	16	15	16	14	15	17	16
4k	75	30	27	25	26	25	26	28	27
	100	33	30	28	29	28	29	31	30
4l	75	33	30	28	29	28	29	31	30
	100	36	33	30	32	31	32	34	33
Gentamicin	75	27	31	30	31	28	27	31	29
	100	30	33	33	34	31	30	33	31

The compounds **4b**–**4l** were synthesized according to the above procedure using the appropriate benzaldehydes.

(*E*)-1-{2,4-Bis[(1-hexyl-1*H*-1,2,3-triazol-4-yl)methoxy]phenyl}-3-phenylprop-2-en-1-one (4a). Yield 77%, white solid, mp 183–185°C. IR spectrum, ν, cm^{-1}: 1660 (C=O). ^{1}H NMR spectrum, δ, ppm: 8.31 s (1H), 8.20 s (1H), 7.74–7.33 m (8H), 7.05 s (1H), 6.86–6.70 m (1H), 5.47–5.15 m (4H), 4.51–4.14 m (4H), 1.93–1.55 m (4H), 1.32–1.05 m (12H), 0.88–0.70 m (6H). ^{13}C NMR spectrum, δ_C, ppm: 188.5, 162.7, 159.0, 142.0, 142.0, 140.7, 134.8, 132.2, 130.0, 128.8, 128.2, 126.9, 124.6, 124.4, 121.4, 107.4, 100.1, 61.9, 61.4, 49.3, 30.5, 30.4, 29.6, 29.5, 25.4, 25.3, 21.9, 21.8, 13.7. MS: *m/z:* 571 [*M* + H]$^+$. Found, %: C 69.22; H 7.25; N 14.55. $C_{33}H_{42}N_6O_3$. Calculated, %: C 69.45; H 7.42; N 14.73.

(*E*)-1-{2,4-Bis[(1-hexyl-1*H*-1,2,3-triazol-4-yl)methoxy]phenyl}-3-(4-chlorophenyl)prop-2-en-1-one (4b). White solid, yield 90%, mp 195–197°C. IR spectrum, ν, cm^{-1}: 1658 (C=O). ^{1}H NMR spectrum, δ, ppm: 8.31 s (1H), 8.20 s (1H), 7.76–7.35 m (7H), 7.12–6.97 m (1H), 6.87–6.70 m (1H), 5.46–5.16 m (4H), 4.47–4.19 m (4H), 1.33–1.06 m (12H), 1.88–1.58 m (4H), 0.92–0.75 m (6H). ^{13}C NMR spectrum, δ_C, ppm: 188.8, 162.9, 159.1, 143.3, 142.1, 140.5, 134.5, 131.8, 130.1, 128.7, 128.4,

Table 2. Antifungal activity of the compounds **4a–4l**

Compound	*c*, μg/mL	Zone of inhibition, mm		
		Microsporum canis	*Microsporum gypseum*	*Epidermophyton floccosum*
4a	75	7	5	5
	100	10	8	9
4b	75	13	12	11
	100	15	15	13
4c	75	18	16	15
	100	22	19	18
4d	75	No active	No active	No active
	100	No active	No active	No active
4e	75	24	19	18
	100	27	22	20
4f	75	26	22	21
	100	28	25	24
4g	75	6	4	4
	100	9	6	7
4h	75	13	12	11
	100	16	15	14
4i	75	15	14	13
	100	18	16	16
4j	75	No active	No active	No active
	100	No active	No active	No active
4k	75	22	18	17
	100	25	20	19
4l	75	25	20	19
	100	27	23	21
Nystatin	75	25	20	20
	100	28	24	23

127.7, 126.5, 124.5, 121.7, 107.5, 100.2, 61.8, 61.5, 49.5, 49.3, 30.7, 30.5, 29.7, 29.5, 25.6, 25.1, 21.9, 21.7, 13.7. MS: *m/z:* 605 $[M+H]^+$. Found: C 65.27; H 6.66; N 13.68. $C_{33}H_{41}ClN_6O_3$. Calculated, %: C 65.49; H 6.83; N 13.89.

(*E*)-1-{2,4-Bis[(1-hexyl-1*H*-1,2,3-triazol-4-yl)methoxy]phenyl}-3-(2,4-dichlorophenyl)prop-2-en-1-one (4c). White solid, yield 90%, mp 221–223°C. IR spectrum, ν, cm^{-1}: 1652 (C=O). ^1H NMR spectrum, δ, ppm: 8.31–8.22 m (2H), 7.71 s (5H), 7.51–7.34 m (1H), 7.06 s (1H), 6.92–6.70 m (1H), 5.48–5.16 m (4H), 4.49–4.17 m (4H), 1.89–1.58 m (4H), 1.31–1.03 m (12H), 0.90–0.72 m (6H). ^{13}C NMR spectrum, δ_C, ppm: 188.6, 162.7, 159.4, 143.5, 142.4, 140.6, 136.2, 134.7, 132.0, 130.7, 130.3, 128.9, 128.5, 127.8, 126.7, 124.9, 121.5, 107.7, 100.4, 61.9, 61.7, 49.7, 49.6, 30.8, 30.6, 29.9, 29.7, 25.7, 25.5, 21.9, 21.7, 13.8. MS: *m/z:* 639 $[M+H]^+$. Found, %: C 61.75; H 6.11; N 12.98. $C_{33}H_{40}Cl_2N_6O_3$. Calculated, %: C 61.97; H 6.30; N 13.14.

(*E*)-4-(3-{2,4-Bis[(1-hexyl-1*H*-1,2,3-triazol-4-yl)-methoxy]phenyl}-3-oxoprop-1-en-1-yl)benzonitrile (4d). White solid, yield 90%, mp 172–174°C. IR spectrum, ν, cm^{-1}: 1660 (C=O). ^1H NMR spectrum, δ, ppm: 8.30 s (1H), 8.20 s (1H), 7.77–7.37 m (7H), 7.15–6.98 m (1H), 6.88–6.72 m (1H), 5.46–5.19 m (4H), 4.48–4.21 m (4H), 1.35–1.07 m (12H), 1.89–1.58 m (4H), 0.91–0.76 m (6H). ^{13}C NMR spectrum, δ_C, ppm: 188.7, 162.8, 159.3, 143.3, 142.5, 140.7, 139.5, 132.8, 130.1, 128.7, 127.7, 126.5, 124.5, 119.2, 111.9, 107.8, 100.2, 61.7, 61.5, 49.6,

49.4, 30.8, 30.6, 29.7, 29.5, 25.6, 25.4, 21.8, 21.6, 13.9. MS: *m/z:* 596 [*M* + H]$^+$. Found, %: C 68.32; H 6.77; N 16.23. $C_{34}H_{41}N_7O_3$. Calculated, %: C 68.55; H 6.94; N 16.46.

(*E*)-1-{2,4-Bis[(1-hexyl-1*H*-1,2,3-triazol-4-yl)-methoxy]phenyl}-3-(4-methoxyphenyl)prop-2-en-1-one (4e). Light yellow amorphous solid, yield 95%, mp 161–163°C. IR spectrum, ν, cm^{-1}: 1655 (C=O). ^{1}H NMR spectrum, δ, ppm: 8.31 s (1H), 8.20 s (1H), 7.76–7.35 m (7H), 7.12–6.97 m (1H), 6.87–6.70 m (1H), 5.46–5.16 m (4H), 4.47–4.19 m (4H), 3.82 (3H), 1.33–1.06 m (12H), 1.88–1.58 m (4H), 0.92–0.75 m (6H). ^{13}C NMR spectrum, δ_C, ppm: 188.8, 162.9, 159.1, 155.6, 143.3, 142.1, 140.5, 131.8, 130.3, 129.1, 128.7, 127.7, 126.5, 115.2, 107.4, 100.1, 61.7, 61.5, 55.7, 49.6, 49.4, 30.6, 30.4, 29.7, 29.5, 25.6, 25.4, 21.9, 21.7, 13.8. MS: *m/z:* 601 [*M* + H]$^+$. Found, %: C 67.77; H 7.17; N 13.76. $C_{34}H_{44}N_6O_4$. Calculated, %: C 67.98; H 7.38; N 13.99.

(*E*)-1-{2,4-Bis[(1-hexyl-1*H*-1,2,3-triazol-4-yl)-methoxy]phenyl}-3-(furan-2-yl)prop-2-en-1-one (4f). Light yellow amorphous solid, yield 88%, mp 143–145°C. IR spectrum, ν, cm^{-1}: 1654 (C=O). ^{1}H NMR spectrum, δ, ppm: 8.30 s (1H), 8.20 s (1H), 7.82 d (*J* = 16 Hz, 1H), 7.70–7.38 m (2H), 7.35 d (*J* = 16 Hz, 1H), 7.12–6.97 m (1H), 6.87–6.70 m (1H), 6.49 d.d (*J* = 8.4, 2.4 Hz, 1H), 6.43 d (*J* = 2.4 Hz, 1H), 5.46–5.16 m (4H), 4.47–4.19 m (4H), 3.84 (3H), 3.82 (3H), 1.32–1.04 m (12H), 1.87–1.56 m (4H), 0.93–0.75 m (6H). ^{13}C NMR spectrum, δ_C, ppm: 189.0, 163.4, 163.0, 159.1, 156.5, 155.7, 143.4, 142.2, 140.6, 131.9, 130.2, 129.2, 128.9, 127.7, 126.5, 115.4, 107.6, 100.2, 61.6, 61.4, 55.7, 55.5, 49.5, 49.3, 30.6, 30.3, 29.7, 29.4, 25.6, 25.4, 21.9, 21.7, 13.7. MS: *m/z:* 631 [*M* + H]$^+$. Found, %: C 66.40; H 7.12; N 13.11. $C_{35}H_{46}N_6O_5$. Calculated, %: C 66.64; H 7.35; N 13.32.

(*E*)-1-{2,4-Bis[(1-cyclohexyl-1*H*-1,2,3-triazol-4-yl)-methoxy]phenyl}-3-phenylprop-2-en-1-one (4g). White solid, yield 98%, mp 203–205°C. IR spectrum, ν, cm^{-1}: 1655 (C=O). ^{1}H NMR spectrum, δ, ppm: 8.37 s (1H), 8.15 s (1H), 7.69–7.47 m (5H), 7.46–7.33 m (3H), 7.06 s (1H), 6.86–6.77 m (1H), 5.31 s (2H), 5.28 s (2H), 4.59–4.44 m (1H), 4.42–4.30 m (1H), 2.06–1.12 m (20H). ^{13}C NMR spectrum, δ_C, ppm: 188.6, 162.9, 159.1, 142.4, 142.1, 140.2, 134.3, 133.1, 129.5, 128.6, 128.3, 126.8, 124.3, 124.1, 121.0, 107.3, 100.2, 62.7, 62.1, 60.2, 60.1, 33.5, 33.4, 33.2, 25.4, 25.2, 25.0, 24.9. MS: *m/z:* 567 [*M* + H]$^+$. Found, %: C 69.72; H 6.52; N 14.61. $C_{33}H_{38}N_6O_3$. Calculated, %: C 69.94; H 6.76; N 14.83.

(*E*)-1-{2,4-Bis[(1-cyclohexyl-1*H*-1,2,3-triazol-4-yl)-methoxy]phenyl}-3-(4-chlorophenyl)prop-2-en-1-one (4h). White solid, yield 95%, mp 211–213°C. IR spectrum, ν, cm^{-1}: 1656 (C=O). ^{1}H NMR spectrum, δ, ppm: 8.32 s (1H), 8.21 s (1H), 7.78–7.36 m (7H), 7.14–6.97 m (1H), 6.88–6.71 m (1H), 5.32 s (2H), 5.29 s (2H), 4.56–4.42 m (1H), 4.44–4.32 m (1H), 2.08–1.14 m (20H). ^{13}C NMR spectrum, δ_C, ppm: 188.7, 162.8, 159.3, 143.5, 142.0, 140.7, 134.6, 131.6, 130.3, 128.6, 128.5, 127.7, 126.4, 124.6, 121.8, 107.5, 100.1, 62.6, 62.2, 60.3, 60.1, 33.5, 33.3, 33.1, 25.5, 25.3, 25.1, 25.0, 24.8. MS: *m/z:* 601 [*M* + H]$^+$. Found, %: C 65.71; H 6.01; N 13.77. $C_{33}H_{37}ClN_6O_3$. Calculated, %: C 65.93; H 6.20; N 13.98.

(*E*)-1-{2,4-Bis[(1-cyclohexyl-1*H*-1,2,3-triazol-4-yl)-methoxy]phenyl}-3-(2,4-dichlorophenyl)prop-2-en-1-one (4i). White solid, yield 88%, mp 237–239°C. IR spectrum, ν, cm^{-1}: 1650 (C=O). ^{1}H NMR spectrum, δ, ppm: 8.32 s (1H), 8.21 s (1H), 7.74–7.32 m (6H), 7.11–6.95 m (1H), 6.86–6.70 m (1H), 5.31 s (2H), 5.20 s (2H), 4.57–4.43 m (1H), 4.45–4.33 m (1H), 2.06–1.15 m (20H). ^{13}C NMR spectrum, δ_C, ppm: 188.8, 162.8, 159.3, 143.6, 142.5, 140.5, 136.3, 134.6, 132.1, 130.7, 130.3, 128.8, 128.6, 127.7, 126.7, 124.6, 121.5, 107.6, 100.3, 62.8, 62.3, 60.5, 60.2, 33.5, 33.4, 33.2, 33.1, 25.3, 25.1, 25.0, 24.7. MS: *m/z:* 635 [*M* + H]$^+$. Found, %: C 62.14; H 5.49; N 13.03. $C_{33}H_{36}Cl_2N_6O_3$. Calculated, %: C 62.36; H 5.71; N 13.22.

(*E*)-4-(3-{2,4-Bis[(1-cyclohexyl-1*H*-1,2,3-triazol-4-yl)methoxy]phenyl}-3-oxoprop-1-en-1-yl)benzonitrile (4j). White solid, yield 96%, mp 184–186°C. IR spectrum, ν, cm^{-1}: 1658 (C=O). ^{1}H NMR spectrum, δ, ppm: 8.38 s (1H), 8.12 s (1H), 8.00–7.61 m (6H), 7.59–7.46 s (1H), 7.07 s (1H), 6.91–6.72 s (1H), 5.45–5.17 m (4H), 4.61–4.24 m (2H), 1.56 m (20H). ^{13}C NMR spectrum, δ_C, ppm: 188.8, 162.6, 159.4, 143.5, 142.7, 140.5, 139.6, 132.9, 130.3, 128.5, 127.7, 126.4, 124.5, 119.3, 111.8, 107.8, 100.3, 62.7, 62.5, 60.4, 60.3, 33.5, 33.4, 33.1, 25.3, 25.1, 25.0, 24.6. MS: *m/z:* 592 [*M* + H]$^+$. Found, %: C 68.88; H 6.11; N 16.35. $C_{34}H_{37}N_7O_3$. Calculated, %: C 69.02; H 6.30; N 16.57.

(*E*)-1-{2,4-Bis[(1-cyclohexyl-1*H*-1,2,3-triazol-4-yl)-methoxy]phenyl}-3-(4-methoxyphenyl)prop-2-en-1-one (4k). Light yellow amorphous solid, yield 95%, mp 179–181°C. IR spectrum, ν, cm^{-1}: 1654 (C=O). ^{1}H NMR spectrum, δ, ppm: 8.37 s (1H), 8.11 s (1H), 7.69–7.54 m (3H), 7.53–7.45 m (2H), 7.05 s (1H), 6.96 d (*J* = 7.94 Hz, 2H), 6.80 d (*J* = 8.52 Hz, 1H), 5.36–5.22 m (4H), 4.57–4.45 m (1H), 4.39–4.26 m (1H), 3.81 s (3H), 1.93–1.02 m (20H). ^{13}C NMR spectrum, δ_C, ppm: 188.7, 162.8, 159.3, 155.8, 143.4, 142.0, 140.7, 131.6, 130.4,

129.2, 128.8, 127.6, 126.4, 115.3, 107.5, 100.2, 62.7, 62.3, 60.3, 60.1, 33.5, 33.4, 33.2, 25.5, 25.4, 25.2, 25.0, 24.7. MS: *m/z:* 597 $[M + H]^+$. Found, %: C 68.20; H 6.54; N 13.89. $C_{34}H_{40}N_6O_4$. Calculated, %: C 68.43; H 6.76; N 14.08.

(*E*)-1-{2,4-Bis[(1-cyclohexyl-1*H*-1,2,3-triazol-4-yl)-methoxy]phenyl}-3-(furan-2-yl)prop-2-en-1-one (4l). Light yellow amorphous solid, yield 92%, mp 151–153°C. IR spectrum, ν, cm^{-1}: 1656 (C=O). ^1H NMR spectrum, δ, ppm: 8.29 s (1H), 8.20 s (1H), 7.80 d (*J* = 16 Hz, 1H), 7.72–7.40 m (2H), 7.35 d (*J* = 16 Hz, 1H), 7.12–6.97 m (1H), 6.87–6.70 m (1H), 6.54–6.44 m (1H), 6.43 d (*J* = 2.4 Hz, 1H), 5.36–5.22 m (4H), 4.56–4.46 m (1H), 4.40–4.27 m (1H), 3.81 s (3H), 3.79 s (3H), 1.95–1.03 m (20H). ^{13}C NMR spectrum, δ_C, ppm: 189.0, 163.4, 163.0, 159.1, 156.5, 155.7, 143.4, 142.2, 140.6, 131.9, 130.2, 129.2, 128.9, 127.7, 126.5, 115.4, 107.6, 100.2, 62.8, 62.5, 60.2, 60.0, 55.7, 55.5, 33.6, 33.4, 33.1, 25.6, 25.4, 25.2, 25.0, 24.6. MS: *m/z:* 627 $[M + H]^+$. Found, %: C 66.89; H 6.57; N 13.00. $C_{33}H_{42}N_6O_5$. Calculated, %: C 67.07; H 6.75; N 13.41.

Antimicrobial activity. *Bacterial and fungal strains.* Gram-positive strains *Micrococcus luteus* (ATCC 10240), methicillin-resistant *Staphylococcus aureus* (MRSA, NCTC 13616), *Bacillus subtilis* (ATCC 6633), and *Bacillus cereus* (ATCC 14579), and Gram-negative strains *Pseudomonas aeruginosa* (ATCC 27853), *Klebsiella pneumoniae* (ATCC 43816), *Escherichia coli* (ATCC 8739), and *Proteus vulgaris* (ATCC 13315) were purchased from the American Type Culture Collection. Methicillin-resistant *Staphylococcus aureus* was purchased from the Public Health England Culture Collections. Fungal strains Microsporum *canis* (ATCC-36299), Microsporum *gypseum* (ATCC-24102), Epidermophyton *floccosum* (ATCC-15694) were collected from department of biotechnology, Chaitanya postgraduate college (autonomous), Kishanpura, Hanamkonda, Warangal, Telangana, 506001 India. All microbial strains were stored at –80°C and streaked on Luria–Bertani (LB) agar plates (Hi-media Laboratories, Mumbai, India) and incubated at 37°C for 20–24 h. A few isolated colonies were selected from each plate and suspended in 5 mL of LB broth in a sterile culture vessel. The vessel was plugged with cotton and incubated with gentle shaking (140 rpm) at 37°C for 20 h.

Preparation of inoculums. Following the protocol of the Kirby–Bauer disk diffusion assay [4], four to five well-isolated colonies of the same morphological type were picked with an inoculating loop, transferred into 5 mL of nutrient broth, and incubated at 37°C for 24 h until a slight visible turbidity appeared. Turbidity of the actively growing broth cultures was then adjusted with broth to a density equivalent of a 0.5 McFarland standard, and the resulting suspensions were used as the initial inocula in the assay.

Antimicrobial assay. The initial inocula of the test organisms, 100 μL, were swabbed over the surface of the agar media (20 mL) in Petri dishes and let to be absorbed for 15 min. Solutions of the test compounds in DMSO (100 μL; *c* 75 and 100 mg/mL) were then loaded into the wells and incubated in the air at 37°C for 24 h. The inhibition zone diameters were measured with a zone reader (HiAntibiotic Zone Scale). The standard drug Gentamicin was used as a positive control.

CONCLUSIONS

Bis-1,4-disubstituted 1,2,3-triazole based chalcones have been synthesized in high yields and their structures supported by conventional spectroscopic methods. The products have been characterized by high antimicrobial activity with the highest activity determined for compounds **4f**, **4l**, **4e**, **4k**, **4c**, and **4i**.

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CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

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