ISSN 1070-3632, Russian Journal of General Chemistry, 2014, Vol. 84, No. 8, pp. 1608–1614. © Pleiades Publishing, Ltd., 2014.

Microwave Assisted Synthesis of Novel Methylenebis{2-[(1-benzyl/cyclohexyl-1*H*-1,2,3-triazol-4-yl)methoxy]chalcones} and Their Antibacterial Activity[1]

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Received June 16, 2014

Abstract—A series of novel methylenebis{2-[(1-benzyl/cyclohexyl-1*H*-1,2,3-triazol-4-yl)methoxy]chalcones} (**IVa–IVn**) have been synthesized by the Click reaction and Claisen-Schmidt condensation of 5,5'-methylenebis[2-(prop-2-yn-1-yloxy)benzaldehyde] under microwave irradiation with high yields. All products have been characterized by spectral data including FT-IR, ^{1}H, and ^{13}C NMR, mass spectrometry, and tested for their antibacterial activity.

Keywords: antibacterial activity, bis-1,2,3-triazoles, chalcones, click chemistry, microwave irradiation

DOI: 10.1134/S1070363214080283

INTRODUCTION

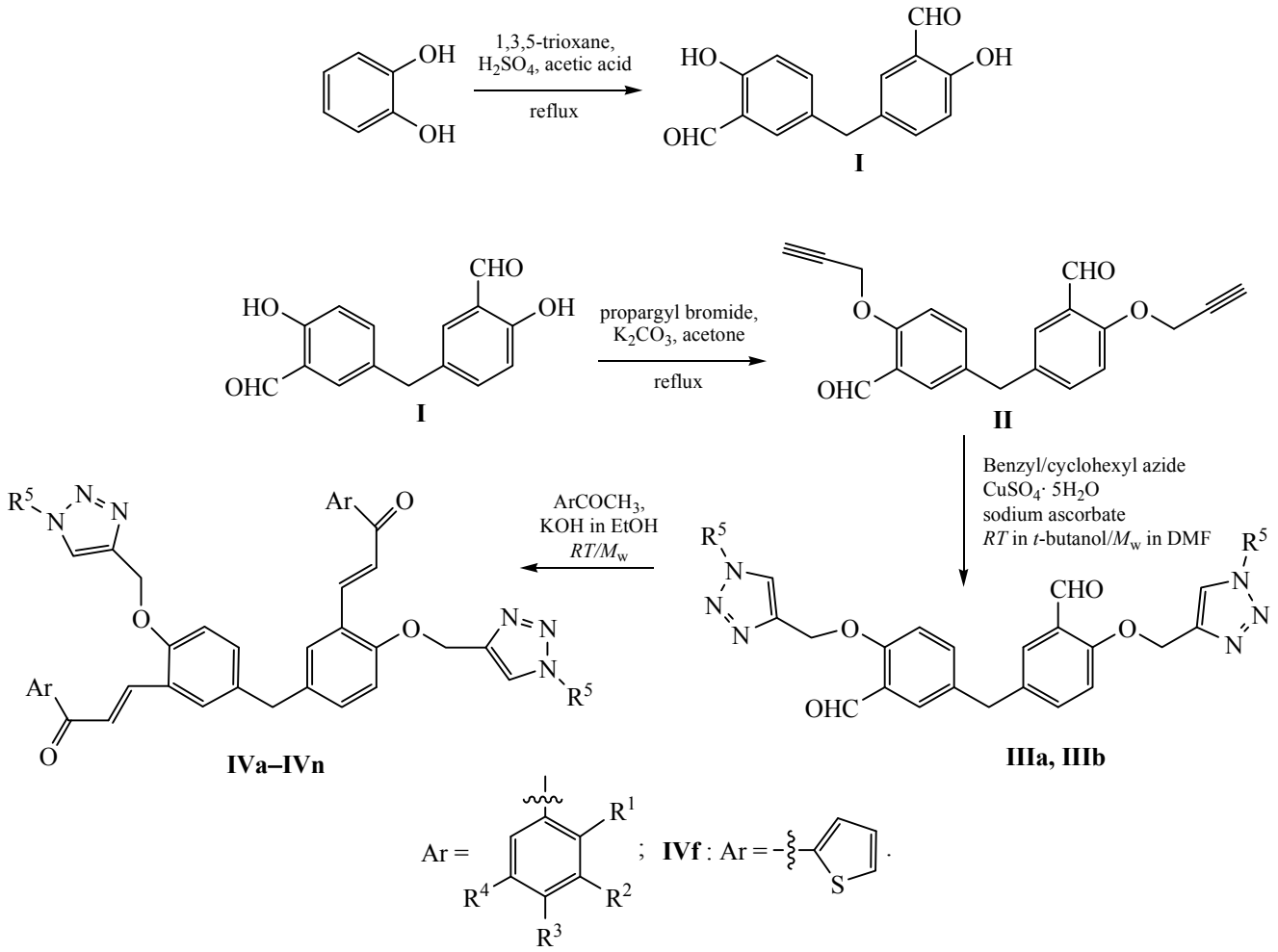
1,2,3-Triazoles play an important role in organic synthesis due to easy synthetic approach by the click reaction, important properties as well as numerous biological activities [1]. 1,2,3-Triazoles are highly stable in basic and acidic media, under reductive and oxidative conditions that indicate their aromatic character [2]. 1,2,3-Triazoles participate in hydrogen bonding, which is favorable in binding with biomolecular targets [3]. 1,2,3-Triazole moiety is one of the key structural units of a wide variety of bioactive molecules that exhibit antifungal [4], antibacterial [5], anti-HIV [6], antitubercular [7], anti-inflammatory [8], anticancer [10], antioxidant and antimicrobial [11] activities. 1,2,3-Triazole forms the core structures in some well marketed drugs such as tazobactam, cefatrizine, carboxyamidotriazole [9]. Chalcones are common natural pigments and they are important intermediates in synthesis of a number of heterocyclic compounds. Synthetic and naturally occurring chalcones have been extensively studied and developed as pharmaceutically important molecules. Combination of 1,2,3-triazole and chalcone pharmacophores can enhance their biological activity, which prompted us to perform the synthesis of compounds containing both 1,2,3--triazole and chalcone moieties. In the current study microwave irradiation was employed for reducing reaction time and improving yields of reactions. Several reviews had been published on various aspects of microwave-assisted chemistry [12]. Therefore we synthesized the title compounds under microwave irradiation. Comparison of our data with those accumulated for conventional thermal reactions demonstrated the strong effect of microwave irradiation on the reaction rate and made it possible to shorten the reaction time and achieve high yields.

RESULTS AND DISCUSSION

The synthetic route for titled compounds is presented in Scheme 1. The compound **I** [13] reacted with propargyl bromide in dry acetone in presence of anhydrous K_2CO_3 and resulted in the propargylated compound **II**. The latter reacted with benzyl azide or cyclohexyl azide in presence of catalytic amount of $CuSO_4 \cdot 5H_2O$ and sodium ascorbate in *t*-butylalcohol : water (1 : 1) to give substituted triazoles **IIIa** or **IIIb**. The process was carried out under microwave irradiation and also by conventional method. The compounds **IIIa** and **IIIb** reacted with aryl methyl ketones in presence of KOH–alcohol under microwave irradiation to give title compounds **IVa–IVn** with the average yield 80–90%. We have carried out the same reaction by conventional method that resulted in much lower yield of the products.

[1] The text was submitted by the authors in English.

Scheme 1.



IVa: R^1 = H, R^2 = H, R^3 = OCH_3, R^4 = H, R^5 = $PhCH_2$; **IVb**: R^1 = OH, R^2 = H, R^3 = CH_3, R^4 = Cl, R^5 = $PhCH_2$; **IVc**: R^1 = OH, R^2 = H, R^3 = H, R^4 = Br, R^5 = $PhCH_2$; **IVd**: R^1 = OH, R^2 = H, R^3 = H, R^4 = F, R^5 = $PhCH_2$; **IVe**: R^1 = OH, R^2 = H, R^3 = H, R^4 = H, R^5 = $PhCH_2$; **IVg**: R^1 = OH, R^2 = Cl, R^3 = H, R^4 = Cl, R^5 = $PhCH_2$; **IVh**: R^1 = H, R^2 = H, R^3 = CH_3, R^4 = H, R^5 = $PhCH_2$; **IVi**: R^1 = H, R^2 = H, R^3 = H, R^4 = H, R^5 = $PhCH_2$; **IVj**: R^1 = OH, R^2 = H, R^3 = H, R^4 = Br, R^5 = C_6H_{11}; **IVk**: R^1 = OH, R^2 = H, R^3 = H, R^4 = F, R^5 = C_6H_{11}; **IVl**: R^1 = OH, R^2 = H, R^3 = H, R^4 = H, R^5 = C_6H_{11}; **IVm**: R^1 = OH, R^2 = Cl, R^3 = H, R^4 = Cl, R^5 = C_6H_{11}; **IVn**: R^1 = OH, R^2 = H, R^3 = CH_3, R^4 = Cl, R^5 = C_6H_{11}.

Antibacterial activity. All compounds **IVa–IVn** were tested for their antibacterial activity against *Escherichia coli* and *Staphylococcus aureus* using Ampicillin as a standard drug. The activity was studied using cup plate agar diffusion method *b*y measuring the zone of inhibition in mm. Compounds **IVb**, **IVc**, **IVh**, and **IVn** displayed inhibition potency against both strains.

EXPERIMENTAL

All chemicals were purchased from Aldrich and Merk. All microwave reactions were carried out using multiSynth series microwave oven system (Milestone). Melting points were measured in open capillary tubes. The IR spectra were recorded as KBr pellets with a Shimadzu FT-IR-8400s spectrophotometer. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) were measured with Bruker Avance II 400 spectrometer using tetramethylsilane as an internal standard in $CDCl_3$ and DMSO-d_6 solutions. Mass spectra were measured with a Hewlett-Packard 1100 LC/MSD spectrometer.

Synthesis of 5,5'-methylenebis[2-(prop-2-yn-1-yloxy)benzaldehyde] (II). A mixture of the solution of **I** 5.0 g (10 mmol) in dry acetone (5 mL) in presence of anhydrous K_2CO_3 and propargyl bromide 4.5 g

Antibacterial data of target compounds

Compound	Zone of Inhibition, mm			Zone of Inhibition, mm		
	Escherichia coli			*Staphylococcus aureus*		
	25 μg/mL	50 μg/mL	100 μg/mL	25 μg/mL	50 μg/mL	100 μg/mL
IVa	12	14	20	6	8	9
IVb	18	22	25	8	10	13
IVc	9	12	16	7	10	12
IVd	8	11	15	6	7	9
IVe	10	15	16	6	6	7
IVf	16	18	23	5	6	6
IVg	16	17	22	4	4	5
IVh	11	15	18	4	6	9
IVi	12	15	18	2	4	5
IVj	11	14	16	7	9	13
IVk	13	17	19	3	3	6
IVl	17	19	21	7	9	10
IVm	15	18	19	4	5	7
IVn	19	21	23	7	9	11
Ampicillin	20	22	25	9	10	12

(20 mmol) was stirred and refluxed for 5 h. Progress of the reaction was monitored by TLC. Upon completion of the reaction, the solvent was evaporated and the solid residue purified by column chromatography on silica gel (60–120 mesh) with eluent hexane/EtOAc to give compound **II**. IR spectrum (KBr), ν, cm^{-1}: 1166 (O–C), 1267 (Ar–O), 1560 (C=C_{arom}), 1710 (C=O). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.57 s (2H, C≡CH), 3.93 s (2H, $ArCH_2Ar$), 4.81 s (4H, OCH_2), 7.04–7.67 m ($6H_{arom}$), 10.37 s (2H, CHO). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 38.9, 62.0, 80.1 (C≡C), 122.6, 123.2, 126.8, 128.4, 128.7, 128.9, 129.0, 130.0, 134.2, 134.6, 134.9, 157.9, 193.0 (C=O). MS (*m/z*): 332 $[M + H]^+$.

5,5'-Methylenebis{2-[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methoxy]benzaldehyde} (IIIa). *a. Conventional method*. A mixture of 2.0 g (6 mmol) of compound **II**, benzyl azide 1.7 g (12 mmol), catalyticamount of $CuSO_4·5H_2O$, and sodium ascorbate in *t*-butylalcohol : water (1 : 1) was stirred for 24 h at room temperature. Progress of the reaction was monitored by TLC. The reaction mixture was poured over ice, the solid obtained was filtered off, washed with water and recrystallized from ethanol.

b. Microwave irradiation method. A mixture of 2.0 g (6 mmol) of compound **II**, benzyl azide 1.7 g (12 mmol), was treated with catalytic amount of $CuSO_4·5H_2O$ and sodium ascorbate in DMF under microwave irradiation at 180 W for 6 min. Upon completion of the reaction as indicated by TLC, the reaction mixture was poured onto ice cold water and the residual solid was filtered off, washed with water, and recrystallized from ethanol. IR spectrum (KBr), ν, cm^{-1}: 1160 (O–C), 1267 (Ar–O), 1556 (C=C_{arom}), 1567 (N=N), 1701 (C=O). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.89 s (2H, $ArCH_2Ar$), 5.28 s (4H, CH_2Ph), 5.55 s (4H, OCH_2), 7.14–7.44 m ($16H_{arom}$), 7.55 s ($2H_{heteroarom}$), 10.37 s (2H, CHO). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 39.6, 54.3, 62.6, 113.4, 122.7, 124.9,128.1, 128.4, 128.9, 129.2, 133.6, 134.3, 136.3, 143.7, 159.1, 189.5 (C=O). MS (*m/z*): 599 $[M + H]^+$.

5,5'-Methylenebis{2-[(1-cyclohexyl-1*H*-1,2,3-triazol-4-yl)methoxy]benzaldehyde} (IIIb). *a. Conventional method*. A mixture of compound 2.0 g (6 mmol) of compound **II**, cyclohexyl azide 1.5 g (12 mmol), catalytic amount of $CuSO_4·5H_2O$, and sodium ascorbate in *t*-butylalcohol : water (1 : 1) was stirred

for 24 h at *RT*. Progress of the reaction was monitored by TLC. The reaction mixture was poured over ice, the solid obtained was filtered, washed with water and recrystallized from ethanol.

b. Microwave irradiation method. A mixture of compound **II** 2.0 g (6 mmol), cyclohexyl azide 1.5 g (12 mmol), catalytic amount of $CuSO_4 \cdot 5H_2O$ and sodium ascorbate in DMF was subjected to react under microwave irradiation at 180 W for 6 min. Upon completion of the reaction as indicated by TLC, the reaction mixture was poured onto ice cold water and the solid that separated out was filtered, washed with water, and recrystallized from ethanol. IR spectrum (KBr), ν, cm^{-1}: 1168 (O–C), 1260 (Ar–O), 1556 (C=C_{arom}), 1576 (N=N), 1705 (C=O). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.44-2.25 m (22H, CH_2–CH_2), 3.89 s (2H, $ArCH_2Ar$), 5.30 s (4H, OCH_2), 7.14–7.44 m (16H_{arom}), 7.55 s (2$H_{heteroarom}$), 10.37 s (2H, CHO). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 38.2, 62.4, 112.4, 122.8, 123.6, 127.0, 128.4, 128.6, 128.9, 129.1, 130.2, 134.1, 134.6, 136.3, 143.0, 158.0, 190.5 (C=O). MS (*m/z*): 583 $[M + H]^+$.

General synthesis of methylenebis{2-[(1-benzyl/cyclohexyl-1*H*-1,2,3-triazol-4-yl)methoxy]chalcones} (IVa–IVn). *a. Conventional method*. 0.16 mmol of a compound **IIIa** or **IIIb** was condensed with 0.3 mmol of an arylmethylketone under the action of KOH–alcohol at room temperature. Progress of the reaction which lasted for 12–14 h was monitored by TLC. Upon completion of the process the reaction mixture was poured onto ice cold water and the residual solid product filtered off and purified with column chromatography using mixture of petroleum ether and ethyl acetate as an eluent.

b. Microwave irradiation method. A solution of 0.16 mmol of a compound **IIIa** or **IIIb** and 0.3 mmol of an arylmethylketone in ethanol was treated with KOH under microwave irradiation at 320 W for 7–9 min. The reaction mixture was poured onto ice cold water and the residual solid product filtered off and purified with column chromatography.

(2*E*,2'*E*)-3,3'-Dimethylenebis{2-[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methoxy]-5,1-phenylene)}bis[1-(4-methoxyphenyl)prop-2-en-1-one] (IVa). Yield 69% (method *a*) and 90% (method *b*), mp 164–166°C. IR spectrum (KBr), ν, cm^{-1}: 1169 (O–C), 1282 (Ar–O), 1575 (N=N), 1603 (C=C), 1651 (C=O). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.31 s (6H, $ArOCH_3$), 3.93 s (2H, $ArCH_2Ar$), 5.25 s (4H, CH_2Ph), 5.63 s (4H, OCH_2), 7.0–7.04 d (2H, =$C^{\alpha}H$, *J* 15.5 Hz), 7.25–7.90 m (24H_{arom}), 7.91–7.95 d (2H, =$C^{\beta}H$, *J* 15.5 Hz), 8.32 s (2$H_{heteroarom}$). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 30.6, 52.8 ($ArOCH_3$), 55.2, 61.6, 113.3, 113.9, 122.0, 123.2, 124.8, 127.8, 128.0, 128.6, 129.2, 130.6, 132.0, 134.1, 135.9, 142.6, 155.5, 163.1, 187.3 (C=O). MS (*m/z*): 863 $[M + H]^+$. Found, %: C 73.74; H 5.35; N 9.76. $C_{53}H_{46}N_6O_6$. Calculated, %: C 73.76; H 5.37; N 9.74.

(2*E*,2'*E*)-3,3'-{Methylenebis[2-([1-benzyl-1*H*-1,2,3-triazol-4-yl]methoxy)-5,1-phenylene]}bis[1-(5-chloro-2-hydroxy-4-methylphenyl)prop-2-en-1-one] (IVb). Yield 70% (method *a*) and 89% (method *b*), mp 188–190°C. IR spectrum (KBr), ν, cm^{-1}: 1193 (O–C), 1263 (Ar–O), 1572 (N=N), 1582 (C=C), 1642 (C=O). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.38 s (6H, $ArCH_3$), 3.97 s (2H, $ArCH_2Ar$), 5.25 s (4H, CH_2Ph), 5.61 s (4H, OCH_2), 7.0–7.36 m (20H_{arom}), 7.92–7.96 d (2H, =$C^{\alpha}H$, *J* 15.6 Hz), 8.07-8.10 d (2H, =$C^{\beta}H$, *J* 15.6 Hz), 8.31 s (2$H_{heteroarom}$), 12.82 s (2H, OH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 28.9 ($ArCH_3$), 38.4, 55.2, 64.2, 98.5, 121.6, 123.4, 126.8, 128.0, 128.4, 128.7, 128.9, 130.2, 134.0, 134.2, 134.5, 142.6, 143.1, 155.4, 164.0, 198.6 (C=O). MS (*m/z*): 931 $[M + H]^+$. Found, %: C 68.26; H 4.67; N 9.20%. $C_{51}H_{44}Cl_2N_6O_6$. Calculated, %: C 68.31; H 4.76; N 9.02.

(2*E*,2'*E*)-3,3'-{Methylenebis[2-([1-benzyl-1*H*-1,2,3-triazol-4-yl]methoxy)-5,1-phenylene]}bis[1-(5-bromo-2-hydroxyphenyl)prop-2-en-1-one] (IVc). Yield 69% (method *a*) and 90% (method *b*), mp 155-158°C. IR spectrum (KBr), ν, cm^{-1}: 1183 (O–C), 1286 (Ar–O), 1567 (N=N), 1572 (C=C), 1640 (C=O). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.96 s (2H, $ArCH_2Ar$), 5.24 s (4H, CH_2Ph), 5.62 s (4H, OCH_2), 7.33–7.37 d (2H, =$C^{\alpha}H$, *J* 16 Hz), 7.25-7.98 m (22H_{arom}), 8.04–8.08 d (2H, =$C^{\beta}H$, *J* 16 Hz), 8.30 s (2$H_{heteroarom}$), 12.49 s (2H, OH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 48.5, 52.8, 61.8, 110.2, 113.6, 120.0, 121.8, 122.8, 123.3, 124.7, 127.8, 128.0, 128.6, 132.2, 132.9, 134.0, 135.9, 138.0, 139.5, 142.6, 155.7, 160.0, 192.2 (C=O). MS (*m/z*): 991 $[M + H]^+$. Found, %: C 61.68; H 4.02; N 8.48. $C_{51}H_{40}Br_2N_6O_6$. Calculated, %: C 61.76; H 4.06; N 8.47.

(2*E*,2'*E*)-3,3'-{Methylenebis[2-([1-benzyl-1*H*-1,2,3-triazol-4-yl]methoxy)-5,1-phenylene]}bis[1-(5-fluoro-2-hydroxyphenyl)prop-2-en-1-one] (IVd). Yield 67% (method *a*) and 86% (method *b*), mp 70–72°C. IR spectrum (KBr), ν, cm^{-1}: 1178 (O–C), 1282 (Ar–O), 1569 (N=N), 1578 (C=C), 1638 (C=O). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.96 s (2H,

$ArCH_2Ar$), 5.24 s (4H, CH_2Ph), 5.62 s (4H, OCH_2), 7.65–7.69 d (2H, $=C^{\alpha}H$, *J* 15.6 Hz), 7.02–7.59 m ($22H_{arom}$), 8.03–8.07 d (2H, $=C^{\beta}H$, *J* 15.6 Hz), 8.30 s ($2H_{heteroarom}$), 12.79 s (2H, OH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 42.6, 54.4, 63.0, 97.8, 122.8, 123.2, 126.8, 128.0, 128.4, 128.7, 128.9, 130.2, 134.0, 134.2, 134.5, 142.6, 143.1, 154.4, 162.0, 197.2 (C=O). MS (*m/z*): 871 $[M + H]^+$. Found, %: C 70.31; H 4.64; N 9.63. $C_{51}H_{40}F_2N_6O_6$. Calculated, %: C 70.34; H 4.63; N 9.65.

(2*E*,2'*E*)-3,3'-{Methylenebis[2-([1-benzyl-1*H*-1,2,3-triazol-4-yl]methoxy)-5,1-phenylene]}bis[1-(2-hydroxyphenyl)prop-2-en-1-one] (IVe). Yield 64% (method *a*) and 83% (method *b*), mp 108–110°C. IR spectrum (KBr), ν, cm^{-1}: 1189 (O–C), 1287 (Ar–O), 1556 (N=N), 1564 (C=C), 1642 (C=O). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.96 s (2H, $ArCH_2Ar$), 5.28 s (4H, CH_2Ph), 5.57 s (4H, OCH_2), 7.01-7.58 m ($24H_{arom}$), 7.45–7.49 d (2H, $=C^{\alpha}H$, *J* 15.5 Hz), 7.58 s ($2H_{heteroarom}$), 8.03–8.07 d (2H, $=C^{\beta}H$, *J* 15.5 Hz), 12.91 s (2H, OH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 39.8, 54.3, 62.6, 113.0, 118.4, 118.8, 121.6, 122.8, 123.9, 128.0, 128.1, 128.9, 129.1, 129.8, 132.4, 133.8, 134.2, 136.2, 140.9, 143.9, 156.4, 163.5, 194.2 (C=O). MS (*m/z*): 835 $[M + H]^+$. Found, %: C 73.33; H 5.08; N 10.05. $C_{51}H_{42}N_6O_6$. Calculated, %: C 73.37; H 5.07; N 10.07.

(2*E*,2'*E*)-3,3'-{Methylenebis[2-([1-benzyl-1*H*-1,2,3-triazol-4-yl]methoxy)-5,1-phenylene]}bis[1-(thiophen-2-yl)prop-2-en-1-one] (IVf). Yield 60% (method *a*) and 78% (method *b*), mp 126–128°C. IR spectrum (KBr), ν, cm^{-1}: 1124 (O–C), 1237 (Ar–O), 1564 (N=N), 1571 (C=C), 1640 (C=O). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.93 s (2H, $ArCH_2Ar$), 5.25 s (4H, CH_2Ph), 5.63 s (4H, OCH_2), 7.22–8.03 m ($22H_{arom}$), 7.84–7.86 d (2H, $=C^{\alpha}H$, *J* 8.3 Hz), 8.02-8.03 d (2H, $=C^{\beta}H$, *J* 8.3 Hz), 8.32 s ($2H_{heteroarom}$). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 42.7, 54.2, 62.0, 98.6, 122.4, 123.2, 126.8, 128.0, 128.4, 128.7, 128.9, 130.2, 134.0, 134.2, 134.5, 142.6, 143.1, 155.4, 155.6, 194.2 (C=O). MS (*m/z*): 815 $[M + H]^+$. Found, %: C 69.25; H 4.68; N 10.34; S 7.85. $C_{47}H_{38}N_6O_4S_2$. Calculated, %: C 69.27; H 4.70; N 10.31; S 7.87.

(2*E*,2'*E*)-3,3'-{Methylenebis[2-([1-benzyl-1*H*-1,2,3-triazol-4-yl]methoxy)-5,1-phenylene[}bis[1-(3,5-dichloro-2-hydroxyphenyl)prop-2-en-1-one] (IVg). Yield 65% (method *a*) and 83% (method *b*), mp 171–173°C. IR spectrum (KBr), ν, cm^{-1}: 1124 (O–C), 1267 (Ar–O), 1567 (N=N), 1577 (C=C), 1630 (C=O). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.96 s (2H, $ArCH_2Ar$), 5.29 s (4H, CH_2Ph), 5.57 s (4H, OCH_2), 7.14–7.44 m ($20H_{arom}$), 7.22–7.26 d (2H, $=C^{\alpha}H$, *J* 15.6 Hz), 8.11-8.15 d (2H, $=C^{\beta}H$, *J* 15.6 Hz), 8.22 s ($2H_{heteroarom}$), 13.48 s (2H, O–H). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 39.7, 54.3, 62.6, 113.1, 120.1, 121.1, 122.7, 123.1, 123.4, 123.9, 127.5, 128.1, 128.4, 128.9, 129.1, 130.7, 133.7, 134.3, 135.5, 143.0, 143.7, 156.7, 157.9, 193.0(C=O). MS (*m/z*): 971 $[M + H]^+$. Found, %: C 62.91; H 3.92; N 8.61. $C_{51}H38Cl4N_6O_6$. Calculated, %: C 62.97; H 3.94; N 8.64.

(2*E*,2'*E*)-3,3'-{Methylenebis[2-([1-benzyl-1*H*-1,2,3-triazol-4-yl]methoxy)-5,1-phenylene]}bis[1-(*p*-tolyl)prop-2-en-1-one] (IVh). Yield 67% (method *a*) and 86% (method *b*), mp 143–145°C. IR spectrum (KBr), ν, cm^{-1}: 1147 (O–C), 1279 (Ar–O), 1609 (N=N), 1611 (C=C), 1651 (C=O). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.37 s (6H, Ar–CH_3), 3.92 s (2H, $ArCH_2Ar$), 5.24 s (4H, CH_2Ph), 5.63 s (4H, OCH_2), 7.20–7.95 m ($24H_{arom}$), 7.22–7.24 d (2H, $=C^{\alpha}H$, *J* 10.8 Hz), 7.93–7.96 d (2H, $=C^{\beta}H$, *J* 10.8 Hz), 8.33 s ($2H_{heteroarom}$). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 21.1 ($ArCH_3$), 39.0, 52.8, 61.7, 110.6, 123.1, 124.8, 127.8, 128.0, 128.4, 128.6, 129.2, 135.1, 135.9, 142.6, 143.4, 155.6, 195.3 (C=O). MS (*m/z*): 831 $[M + H]^+$. Found, %: C 76.57; H 5.56; N 10.16. $C_{53}H_{46}N_6O_4$. Calculated, %: C 76.61; H 5.58; N 10.11.

(2*E*,2'*E*)-3,3'-{Methylenebis[2-([1-benzyl-1*H*-1,2,3-triazol-4-yl]methoxy)-5,1-phenylene]}bis[1-phenylprop-2-en-1-one] (IVi). Yield 69% (method *a*) and 84% (method *b*), mp 134–136°C. IR spectrum (KBr), ν, cm^{-1}: 1147 (O–C), 1276 (Ar–O), 1572 (N=N), 1602 (C=C), 1679 (C=O). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.92 s (2H, $ArCH_2Ar$), 5.27 s (4H, CH_2Ph), 5.52 s (4H, OCH_2), 7.22–7.95 m ($26H_{arom}$), 7.18–7.22 d (2H, $=C^{\alpha}H$, *J* 16 Hz), 7.98–8.02 d (2H, $=C^{\beta}H$, *J* 16 Hz), 8.12 s ($2H_{heteroarom}$). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 43.2, 54.2, 62.6, 113.0, 122.8, 123.2, 124.2, 127.8, 128.5, 129.0, 129.9, 131.6, 134.6, 136.9, 138.3, 140.2, 144.1, 144.9, 153.4, 156.0, 190.9 (C=O). MS (*m/z*): 803 $[M + H]^+$. Found, %: C 76.26; H 5.25; N 10.52. $C_{51}H_{42}N_6O_4$. Calculated, %: C 76.29; H 5.27; N 10.47.

(2*E*,2'*E*)-3,3'-{Methylenebis(2-([1-cyclohexyl-1*H*-1,2,3-triazol-4-yl]methoxy)-5,1-phenylene]}bis-[1-(5-bromo-2-hydroxyphenyl)prop-2-en-1-one] (IVj). Yield 70% (method *a*) and 90% (method *b*), mp 169–171°C. IR spectrum (KBr), ν, cm^{-1}: 1183 (O–C), 1284 (Ar–O), 1576 (N=N), 1595 (C=C), 1638 (C=O).

^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.25–2.20 m (22H, CH_2–CH_2), 3.99 s (2H, $ArCH_2Ar$), 5.32 s (4H, OCH_2), 7.48–7.66 m (12H_{arom}), 7.62–7.66 d (2H, =C$^{\alpha}$H, *J* 15.8 Hz), 8.17–8.21 d (2H, =C$^{\beta}$H, *J* 15.8 Hz), 7.68 s (2$H_{heteroarom}$), 12.82 s (2H, OH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 25.1, 29.7, 33.5, 39.8, 60.2, 63.0, 110.3, 113.4, 120.5, 121.4, 121.8, 123.7, 130.0, 131.9, 133.0, 133.7, 138.6, 138.8, 142.1, 143.0, 143.4, 156.6, 1557.6, 162.4, 193.2 (C=O). MS (*m/z*): 975 [*M* + H]$^+$. Found, %: C 60.58; H 5.11; N 8.47. $C_{49}H_{48}Br_2N_6O_6$. Calculated, %: C 60.25; H 4.95; N 8.60.

(2*E*,2'*E*)-3,3'-{Methylenebis[2-([1-cyclohexyl-1*H*-1,2,3-triazol-4-yl]methoxy)-5,1-phenylene]}bis[1-(5-fluoro-2-hydroxyphenyl)prop-2-en-1-on] (IVk). Yield 65% (method *a*) and 84% (method *b*), mp 72–75°C. IR spectrum (KBr), ν, cm^{-1}: 1183 (O–C), 1286 (Ar–O), 1567 (N=N), 1592 (C=C), 1638 (C=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.25–2.20 m (22H, CH_2–CH_2), 3.86 s (2H, $ArCH_2Ar$), 5.30 s (4H, OCH_2), 7.12–7.14 d (2H, =C$^{\alpha}$H, *J* 16 Hz), 7.48-7.66 m (12H_{arom}), 7.62–7.64 d (2H, =C$^{\beta}$H, *J* 16 Hz), 8.11 s (2$H_{heteroarom}$), 12.69 s (2H, OH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 25.4, 29.7, 33.4, 42.5, 60.2, 62.4, 118.2, 119.4, 133.0, 143.0, 155.0, 158.6, 204.4 (C=O). MS (*m/z*): 855 [*M* + H]$^+$. Found, %: C 69.09; H 5.63; N 9.65. $C_{49}H_{48}F_2N_6O_6$. Calculated, %: C 68.84; H 5.66; N 9.83.

(2*E*,2'*E*)-3,3'-{Methylenebis[2-([1-cyclohexyl-1*H*-1,2,3-triazol-4-yl]methoxy)-5,1-phenylene]}bis[1-(2-hydroxyphenyl)prop-2-en-1-one] (IVl). Yield 66% (method *a*) and 87% (method *b*), mp 83–85°C. IR spectrum (KBr), ν, cm^{-1}: 1185 (O–C), 1276 (Ar–O), 1568 (N=N), 1596 (C=C), 1640 (C=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.25–2.20 m (22H, CH_2–CH_2), 3.73 s (2H, $ArCH_2Ar$), 5.19 s (4H, OCH_2), 7.40–7.43 d (2H, =C$^{\alpha}$H, *J* 10.0 Hz), 7.48–7.66 m (14H_{arom}), 7.57 s (2$H_{heteroarom}$), 7.79-7.82 d (2H, =C$^{\beta}$H, *J* 10.0 Hz), 12.2 s (2H, OH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 25.0, 29.7, 33.4, 42.6, 60.2, 62.6, 118.3, 118.9, 119.0, 130.2, 136.3, 143.7, 154.1, 162.4, 205.3 (C=O). MS (*m/z*): 819 [*M* + H]$^+$. Found, %: C 71.11; H 6.26; N 10.12. $C_{49}H_{50}N_6O_6$. Calculated, %: C 71.86; H 6.15; N 10.26.

(2*E*,2'*E*)-3,3'-{Methylenebis[2-([1-cyclohexyl-1*H*-1,2,3-triazol-4-yl]methoxy)-5,1-phenylene]}bis[1-(3,5-dichloro-2-hydroxyphenyl)prop-2-en-1-one] (IVm). Yield 68% (method *a*) and 89% (method *b*), mp 183–185°C. IR spectrum (KBr), ν, cm^{-1}: 1183 (O–C), 1286 (Ar–O), 1575 (N=N), 1567 (C=C), 1640 (C=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.25–2.20 m (22H, CH_2–CH_2), 3.98 s (2H, $ArCH_2Ar$), 5.32 s (4H, OCH_2), 7.65–7.69 d (2H, =C$^{\alpha}$H, *J* 15.5 Hz), 7.48–7.66 m (10H_{arom}), 7.67 s (2$H_{heteroarom}$), 8.17–8.21 d (2H, =C$^{\beta}$H, *J* 15.5 Hz), 13.49 s (2H, OH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 25.1, 29.7, 33.5, 39.2, 60.3, 62.9, 113.4, 120.5, 123.1, 123.5, 127.5, 130.5, 133.3, 133.7, 135.5, 142.8, 143.1, 156.8, 157.9, 193.1 (C=O). MS (*m/z*): 955 [*M* + H]$^+$. Found, %: C 61.84; H 4.96; N 8.70. $C_{49}H_{46}Cl_4N_6O_6$. Calculated, %: C 61.51; H 4.85; N 8.76.

(2*E*,2'*E*)-3,3'-{Methylenebis[2-([1-cyclohexyl-1*H*-1,2,3-triazol-4-yl]methoxy)-5,1-phenylene]}bis[1-(5-chloro-2-hydroxy-4-methylphenyl)prop-2-en-1-one] (IVn). Yield 70% (method *a*) and 89% (method *b*), mp 201–203°C. IR spectrum (KBr), ν, cm^{-1}: 1185 (O–C), 1280 (Ar–O), 1560 (N=N), 1586 (C=C), 1638 (C=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.25–2.20 m (22H, CH_2–CH_2), 2.38 s (6H, $ArCH_3$), 3.94 s (2H, $ArCH_2Ar$), 5.32 s (4H, OCH_2), 7.61–7.65 d (2H, =C$^{\alpha}$H, *J* 15.5 Hz), 7.48–7.66 m (10H_{arom}), 7.67 s (2$H_{heteroarom}$), 8.14–8.18 d (2H, =C$^{\beta}$H, *J* 15.5 Hz), 12.78 s (2H, OH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 25.1 ($ArCH_3$), 33.5,60.2, 63.1, 113.4, 119.1, 120.5, 123.8, 124.0, 129.2, 130.1, 132.8, 133.7, 141.4, 143.1, 145.3, 156.5, 161.9, 192.9(C=O). MS (*m/z*): 915 [*M* + H]$^+$. Found %: C 66.12; H 5.78; N 9.16. $C_{51}H52Cl2N_6O_6$. Calculated, %: C 66.88; H 5.72; N 9.18.

ACKNOWLEDGMENTS

Authors are grateful to The Head, Department of Chemistry, and Director, Central Facilities for Research and Development (CFRD), Osmania University, Hyderabad for providing laboratory facilities and spectra. One of the authors S.R is grateful to UGC, New Delhi for awarding JRF.

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