Synthesis and Antimicrobial Evaluations of New 5-aryl Linked Bispyrazolines

Mohamad Yusuf* and Manvinder Kaur

Department of Chemistry, Punjabi University, Patiala 147002, Punjab, India
*E-mail: yusuf_sah04@yahoo.co.in

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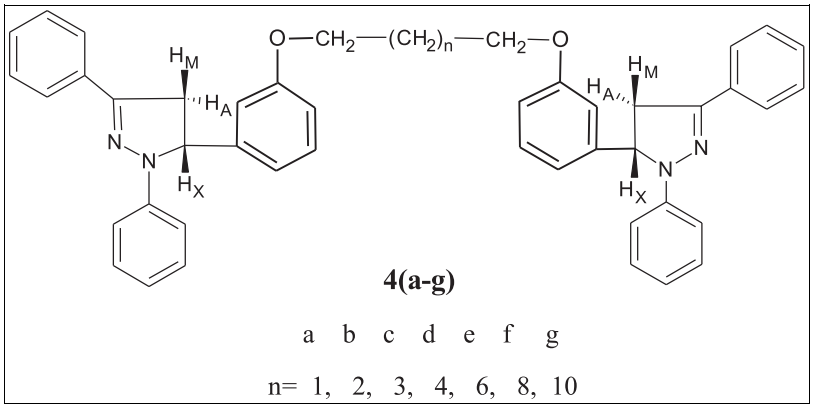

Syntheses of new bispyrazolines **4(a–g)** built around the aliphatic linkers of varying lengths have been described. The intermediate bischalcones and final bishetrocyclics were also evaluated for their antimicrobial activities.

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INTRODUCTION

The treatment of infectious diseases still remains an important and challenging problem. The search of novel antimicrobial agents is a field of current and growing interest. Many compounds have been synthesized with this aim, and their clinical applications have been limited by their relatively high risk of toxicity, bacterial resistance, and pharmacokinetic deficiencies. Development of new antimicrobial products with novel structures and mode of action remains the primary goal of scientists for the solution of increasing bacterial resistance gained by microorganism to classical antimicrobial agents [1]. Chalcones and their derivatives are an attractive molecular scaffold for the search of new biologically significant molecules [2–4], and the studies have revealed that pyrazolines have been the subject of the major attraction for the organic chemists because they are known to possess analgesic, antipyretic, antidepressant, tranquilizing, muscle relaxant, psycho analeptic, anti-convulsant, hypotensive [5–11], monoamine oxidase inhibitor [12,13], anti-cancer [14,15] and antimicrobial activities [16]. The pyrazoline derivatives are also found to exhibit potent anti-inflammatory *activities* [17–19]. Several pharmaceutical drugs including celecoxib [20] and rimonabant [21] contain the pyrazole as their core molecular entity [22,23]. Keeping in view these potential biological applications of chalcones and pyrazolines, it was perceived that the presence of two pyrazoline moieties in a single molecule might result in the formation of some worthwhile biologically significant derivatives. Bispyrazolines are the molecules which are formed by linking two pyrazoline moieties together through the carbon chain of varying lengths. In view of these observations and in continuation of our research program on the synthesis of five membered bisheterocyclics [24–28], we report herein the syntheses of new symmetrical bispyrazolines **4(a–g)** built around the aliphatic linkers, which have been found to possess an interesting profile of antimicrobial properties.

RESULTS AND DISCUSSION

Earlier, we have reported the synthesis of 5-aryl and 3-aryl linked bispyrazolines starting from 4-hydroxybenzaldehyde [29,30], but the present bispyrazolines **4(a–g)** were synthesized starting from the base catalyzed Claisen–Schmidt reaction of acetophenone with *m*-hydroxybenzaldehyde to give chalcone **2,** which undergoes O-alkylation reactions with various dibromoalkanes in presence of anhydrous K_2CO_3, dry acetone, and PTC (tetrabutyl ammonium iodide) medium to yield new bischalcones **3(a–g)**.

In the earlier reported work [29,30], the preparations of bischalcones required continuously heating for at least in 6–8 h, but in the present compounds **3(a–g)** have been realized by stirring at room temperature just for 1 to 1.5 h. These intermediates were refluxed with phenyl

hydrazine in the presence of ethanolic NaOH for 4 h. After completion of reactions, the solvent was distilled under reduced pressure, and the resulting masses were poured into ice to provide the crude products, which were crystallized from MeOH to yield pure bispyrazolines **4(a–g)** (Scheme 1).

The structures of the intermediates and final compounds were fully determined on the basis of their spectroscopic data such as IR, ^{1}H-NMR, ^{13}C-NMR, and ESI-MS.

IR spectra of bischalcones **3(a–g)** exhibited carbonyl group absorptions in the region at 1661–1660 cm^{-1}, and bands present in the region at 1595 − 1573 cm^{-1} could be ascribed to C = C stretching. The other significant bands were found in the region at 2960–2853 (methylene C-H), 1255–1236 and 1018–1016 (C-O) cm^{-1}. In their ^{1}H-NMR spectra, two broad doublets resonating at δ 7.79–7.76 and 7.60–7.52 could be assigned to H-3 and H-2, respectively. The coupling value of 16–15 Hz between these hydrogens describes the *trans* geometry around the C-2 and C-3 double bond. The doublets in the range of δ 8.02–8.01 may be allotted to aromatic protons H-2′, 6′. The O*C**H**₂* protons of the internal spacer were placed at δ 4.25–3.99, and the remaining methylene groups of the flexible chain exhibited signals of appropriate multiplicities.

In the ^{13}C-NMR spectra of **3(a–g)**, the internal methylene groups were resonating at δ 68.12–64.43 (O*C*H_2); the downfield resonance suggests their placement near an electronegative oxygen atom. Other noticeable signals in these compounds were found to be placed at δ 190.62–190.58 (C = O), 144.93–144.74 (C-3), and 121.23–121.01 (C-2).

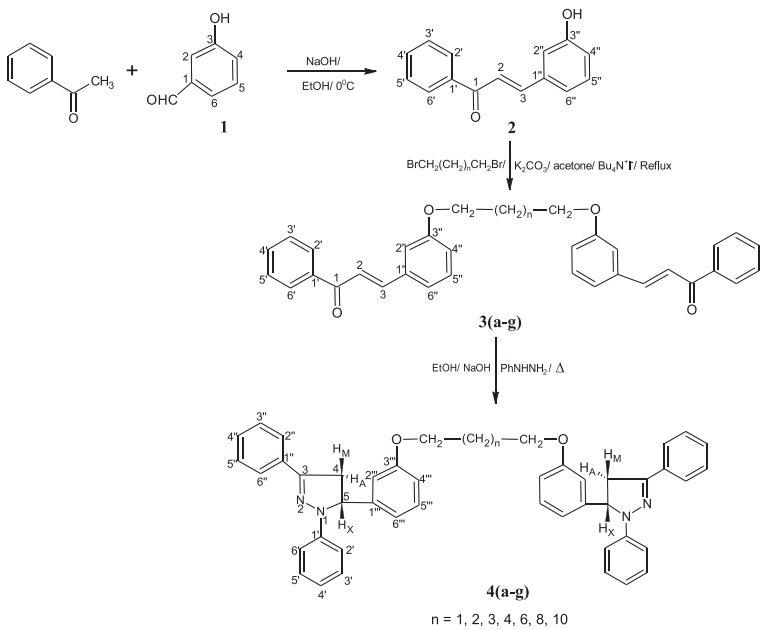
The major feature of ^{1}H-NMR spectra of **4(a–g)** was the signals of the pyrazoline ring protons (H-X, H-M, and H-A), which were centered at δ 5.43–5.16 (dd), 3.96–3.71 (dd), and 3.11–3.08 (dd), respectively. The vicinal coupling constant (^3J) between H-X and H-M was found to be 12.5–11.8 Hz, which reflects that these hydrogens are *cis* to each other while coupling value of J_{XA} = 7.5–6.1 Hz and J_{MA} = 17.4–17.0 Hz describes the *trans* relationship between H-X and H-A, and H-M and H-A are geminally placed at C-4 position of pyrazoline ring.

^{13}C-NMR (100 MHz, $CDCl_3$) data of **4(a–g)** provided enough evidence in favor of the proposed expression where C-3‴ was resonating at δ 159.90–158.96 because of its direct bonding to the oxygen atom. The pyrazoline ring carbon atoms C-3, C-5, and C-4 appeared at δ 144.39–144.26, 66.95–63.19, and 42.94–42.87, respectively.

ANTIMICROBIAL ACTIVITY

The synthesized compounds **3(a–g)** and **4(a–g)** were screened for their *in vitro* antibacterial and antifungal activity against seven bacterial and five fungal species, namely, *Klebsiella pneumoniae* (MTCC 3384), *Pseudomonas aeruginosa* (MTCC 424), *Escherichia coli* (MTCC 443), *Staphylococcus aureus* (MTCC 96),

Scheme 1. Synthesis of new aliphatic chain linked bispyrazolines.



Bacillus subtilis (MTCC 441), *Pseudomonas fluorescens* (MTCC 103), *Streptococcus pyogenes* (MTCC 442), *Aspergillus janus* (MTCC 2751), *Penicillium glabrum* (MTCC 4951), *Fusarium oxysporum* (MTCC 2480), *Aspergillus sclerotiorum* (MTCC 1008), and *Aspergillus niger* (MTCC 281), respectively. Minimum inhibitory concentrations (MICs) were determined by using serial dilution technique. Amoxicillin and fluconazole were used as the standard drug as positive control while the DMSO was used as negative control. The MIC (μg/mL) was determined by using different dilutions of the concerned compound. The lowest concentration required to arrest the growth of bacterial and fungal strains was regarded as MIC.

The results were compared with positive controls; the standard drug amoxicillin and fluconazole. Serial dilution of the test compounds previously dissolved in DMSO was prepared to final concentrations of 128, 64, 32, 16, 8, 4 2 and 1 μg/mL. All the bacteria strains were grown at 37°C for 24 h in a nutrient broth, and fungi were grown in malt extract at 28°C for 72 h. Each test compound was dissolved in DMSO, and MIC thus obtained was compared with control. The susceptibility of the bacteria and fungi to the test compounds was determined by the appearance of turbidity after the previous said time period.

The results of MIC (μg/mL) against these microbial strains were summarized in Table 1. It is evident from Table 1 that the **3b** compound was active against *E. coli* and *A. sclerotiorum*, while compound **3c** showed significant biological activity against the fungal strains, namely, *E. coli*, *B. subtilis*, *A. janus, P. glabrum*, *F. oxysporum* (MIC-8 μg/mL), and *A. niger* (MIC-4 μg/mL). **3e** compound possesses significant activity against *S. aureus*, *S. pyogenes*, and *A. janus* at MIC-8 μg/mL. The compound **3f** displayed significant activity against *E. coli*, *P. aeruginosa* (bacteria strain), and *P. glabrum* (fungi strain). The compound **3g** exhibited most potent results (MIC-8–4 μg/mL) against *Klebsiella pneumonia*, *B. subtilis*, *P. fluorescens*, *P. glabrum*, and *F. oxysporum*.

The antimicrobial evaluation data revealed that compounds containing pyrazoline moiety were possessing admirable activity in comparison with their intermediate compounds **3(a–g)**. **4g** was found to be very active (MIC-8 μg/mL) against bacterial and fungal strains *E. coli*, *K. pneumonia*, *P. aeruginosa*, *S. aureus*, *A. janus*, *P. glabrum*, *A. niger*, *A. sclerotiorum*, and *F. oxysporum*, respectively. The compound **4f** also seems to be active against bacterial strains *E. coli*, *P. fluorescens*, *S. pyogenes* and fungal strains *P. glabrum*, *A. sclerotiorum*, *F. oxysporum*, respectively. The compounds **4d** and **4e** were found to possess potent activity against *K. pneumonia*, *B. subtilis*, *A. janus*, *K. pneumonia*, *P. fluorescens*, *B. subtilis*, *A. niger*, and

Table 1
Antimicrobial activity of bischalcones **3(a–g)** and bispyrazolines **4(a–g)**.

Compound no	Gram (−ve) bacteria				Gram (+ve) bacteria			Fungi				
	Escherichia coli	*Klebsiella pneumonia*	*Pseudomonas Aeruginosa*	*Pseudomonas fluorescens*	*Staphylococcus aureus*	*Bacillus subtilis*	*Streptococcus pyogenes*	*Aspergillus janus*	*Penicillium glabrum*	*Aspergillus niger*	*Fusarium oxysporum*	*Aspergillus sclerotiorum*
3a	16	16	32	16	16	32	16	16	16	16	32	16
3b	**8**	16	64	16	16	32	32	32	32	32	32	**8**
3c	**8**	32	16	16	16	**8**	32	**8**	**8**	**4**	**8**	32
3d	64	32	16	32	16	16	64	32	16	16	64	16
3e	32	16	32	16	**8**	64	**8**	**8**	32	16	64	32
3f	**8**	32	**8**	32	16	16	32	16	**8**	32	32	16
3g	32	**8**	64	**4**	16	**8**	32	16	**8**	16	**8**	16
4a	16	32	**8**	16	64	16	16	16	16	**8**	32	16
4b	32	16	**8**	16	32	32	32	16	32	**8**	32	16
4c	**8**	32	16	32	32	16	32	16	**8**	16	16	**8**
4d	32	**8**	16	32	32	**8**	32	**8**	32	16	32	16
4e	16	**8**	16	**8**	32	**8**	16	16	16	**8**	16	**8**
4f	**8**	16	16	**4**	16	16	**8**	16	**8**	16	**4**	**8**
4g	**8**	**8**	**4**	16	**8**	16	16	**8**	**4**	**8**	**8**	**8**
Amoxicillin	**4**	**4**	**4**	**4**	2	2	**4**					
Flucanazole								2	2	2	2	2

Bold data indicates that concerned compounds exhibited MIC comparable to standard drugs.

A. sclerotiorum, respectively, with MIC-8–4 μg/mL. Also, **4c** exhibited significant activity against *E. coli*, *P. glabrum*, and *A. sclerotiorum* strain. Further, **4a** and **4b** were found to possess activity against *P. aeruginosa* and *A. niger* with MIC-8 μg/mL.

CONCLUSION

It may be concluded that readily synthesized starting materials, available reagents along with short reaction time, simple work-up, and isolation of the products under simple conditions make the current method a feasible and attractive protocol for generation of series of new bispyrazoline derivatives in good yields. Further, *in vitro* antibacterial and antifungal evaluations of compounds has proved them as potent antimicrobial agents. Among the studied bisheterocycles, **4g** has produced the marked enhancement in the potency as an antibacterial and antifungal agent. *From the antimicrobial evaluations, it is revealed that compounds with longer internal aliphatic chain showed better potency against tested strains (MIC-8–4 μg/mL). Overall, it is concluded that bispyrazolines 4(a–g) exhibited most significant antimicrobial potencies as compared with their intermediate analogs 3(a–g) against the tested strains.*

EXPERIMENTAL

Melting points of all synthesized compounds were determined in an open capillary using digital melting point apparatus and are uncorrected. IR spectra were recorded as KBr disks on Perkin Elmer RXIFT Infrared spectrophotometer (Buckinghamshire, England) in 4000–450 cm^{-1}. Both ^{1}H-NMR and ^{13}C-NMR spectra of the compounds were recorded on the Bruker Avance-II NMR spectrometer (Fallanden, Switzerland) at 400 and 100 MHz, respectively. Chemical shifts were measured relative to internal reference standard, Tetramethylsilane ($\delta = 0$) in $CDCl_3$, or DMSO-d_6 and were reported on δ scale (ppm). Coupling constants were given in Hz. The mass spectra were scanned on the Waters Micromass Q-T of Micro (ESI) spectrometer (Vernon Hills, IL). The purity of the compounds was checked by TLC plates coated with silica gel (suspended in chloroform-methanol, 1 : 1), and iodine vapors were used as visualizing agent. *The cultures required for the biological studies of prepared compounds were obtained from MTCC (Microbial Type Culture Collection & Gene Bank, Chandigarh-160036, India).*

Synthesis of (E)-3-(3-hydroxyphenyl)-1-phenylprop-2-en-1-one (2). A mixture of acetophenone (5.0 g, 0.0042 mol), 3-hydroxy-benzaldehyde **1** (5.0 g, 0.0042 mol), and NaOH (5.0 g, 0.024 mol) in EtOH (25.0 mL) was stirred for 10 h at 0°C. During the course of reaction, the initially formed creamish mixture changed to a reddish gummy mass. The resulting mass was poured into iced-HCl to provide a crude material, which was filtered off, washed with water, dried, and crystallized from CH_3OH to yield a pure yellow compound **2**.

2: Yellow, yield 82%; mp 146–148°C; IR (KBr): υ_{max} cm^{-1}: 3461 (OH), 1695 (C=O), 1604 (C=C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.12 (1H, s, OH), 8.06 (2H, d, $J_o = 7.4$ Hz, H-2′, 6′), 7.78 (1H, d, $J_{trans} = 15.5$ Hz, H-3), 7.68 (2H, d, $J = 6.9$ Hz, H-3′, 5′), 7.51 (1H, d, $J_{trans} = 15.5$ Hz, H-2), 7.25 (1H, t, $J_o = 7.6$ Hz, H-4′), 7.20 (1H, d, $J_o = 7.6$ Hz, H-6″), 7.17 (1H, brs, H-2″), 7.02 (1H, t, $J_o = 7.5$ Hz, H-5″), 6.88 (1H, dd, $J_{m,o} = 1.7$, 6.9 Hz, H-4″); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 189.19 (C=O), 157.65 (C-3″), 144.27 (C-3), 137.61 (C-1′), 135.64 (C-1″), 132.60 (C-2′, 6′), 129.57 (C-4′), 128.40 (C-3′, 5′), 128.18 (C-6″), 121.54 (C-5″), 119.51 (C-2), 117.73 (C-4″), 114.86 (C-2″); ESI-MS: *m/z* 225 (M+1, 80%), 208 (12%), 207 (81%), 179 (54%), 178 (10%), 147 (5%); *Anal*. Calcd for $C_{15}H_{12}O_2$: C-80.35, H-5.35; Found: C-80.39, H-5.31%.

Synthesis of (2E,2′E)-3,3′-(propane-1,3-diylbis(oxy))bis(3,1-phenylene))bis(1-phenylprop-2-ene-1-one) (3a). A suspension of chalcone **2** (2.24 g, 0.01 mol), K_2CO_3 (2.0 g, mol), 1,3-dibromopropane (1.01 g, 0.005 mol), and tetrabutyl ammonium iodide (1.0 g) in dry acetone (25.0 ml) was stirred for 1.0 h at room temperature. The progress of reaction was monitored by TLC (Hexane-Ethylacetate: 7 : 3). After the completion of reaction, the reaction mixture turned into a colorless mass, which was poured over iced-HCl to provide a crude solid, which was recrystallized from CH_3OH:$CHCl_3$ (3 : 1) to yield a pure compound **3a**.

3a: Light yellow, yield 75%; mp: 126–128°C; IR (KBr): υ_{max} cm^{-1}: 3061 (aromatic C-H), 2941, 2883 (methylene C-H), 1661 (C=O), 1595 (C=C), 1242, 1018 (C-O); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.02 (4H, dd, $J = 7.1$, 5.2 Hz, H-2′, 6′), 7.78 (4H, d, $J_{trans} = 15.6$ Hz, H-3), 7.58 (6H, m, H-2, 3′, 5′), 7.32 (2H, t, $J_o = 8.4$ Hz, H-4′), 7.23 (2H, t, $J = 7.3$ Hz, H-5″), 7.21 (2H, d, $J_o = 7.6$ Hz, H-6″), 7.18 (2H, brs, H-2″), 6.98 (2H, dd, $J_{o,m} = 7.6$, 1.8 Hz, H-4″), 4.25 (4H, t, $J_{vic} = 6.2$ Hz, OC***H*****$_2$**), 2.31 (2H, quintet, $J_{vic} = 6.1$ Hz, OCH_2C***H*****$_2$**); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 190.58 (C=O), 158.9 (C-3″), 144.74 (C-3), 138.15 (C-1′), 136.30 (C-1″), 132.86 (C-2′, 6′), 130.03 (C-4′), 128.66 (C-3′, 5′), 128.54 (C-6″), 122.40 (C-5″), 121.35 (C-2), 116.82 (C-4″), 113.98 (C-2″), 64.43 (O***C*****H_2**), 29.29 (OCH_2***C*****H_2**); ESI-MS: *m/z* 511 (M+Na, 29%), 489 (M+1, 19%), 423 (6%), 360 (9%), 337 (26%), 242 (9%), 167 (10%), 146 (13%), 94 (18%); *Anal*. Calcd for $C_{33}H_{28}O_4$: C-81.14, H-5.73; Found: C-81.10, H-5.77%.

Synthesis of (2E,2′E)-3,3′-(butane-1,4-diylbis(oxy))bis(3,1-phenylene))bis(1-phenylprop-2-ene-1-one) (3b). The compound **3b** was synthesized from the reaction of chalcone **2** (2.24 g, 0.01 mol), 1,4-dibromobutane (1.08 g, 0.005 mol) under the same conditions as described earlier for **3a**.

3b: Yellow, yield 72%; mp: 118–120°C; IR (KBr): υ_{max} cm^{-1}: 3061 (aromatic C-H), 2943, 2874 (methylene C-H),

1661 (C=O), 1595 (C=C), 1253, 1018 (C-O); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.01 (4H, dd, J=7.3, 5.4 Hz, H-2′, 6′), 7.76 (4H, d, J_{trans}=15.5 Hz, H-3), 7.58 (6H, m, H-2, 3′, 5′), 7.33 (2H, t, J_o=8.0 Hz, H-4′), 7.24 (2H, t, J=7.1, 4.5 Hz, H-5″), 7.20 (2H, d, J_o=7.3 Hz, H-6″), 7.16 (2H, brs, H-2″), 6.97 (2H, dd, $J_{o,m}$=7.2, 1.9 Hz, H-4″), 4.21 (4H, t, J_{vic}=6.2 Hz, OC***H₂***), 2.14 (2H, quintet, J_{vic}=6.1 Hz, OCH_2C***H₂***); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 190.58 (C=O), 158.91 (C-3″), 144.74 (C-3), 138.15 (C-1′), 136.30 (C-1″), 132.86 (C-2′, 6′), 130.03 (C-4′), 128.66 (C-3′, 5′), 128.54 (C-6″), 122.40 (C-5″), 121.15 (C-2), 116.82 (C-4″), 113.98 (C-2″), 64.43 (O***C***H_2), 29.29 (OCH_2***C***H_2); ESI-MS: *m/z* 525 (M+Na, 23%), 503 (M+1, 16%), 485 (6%), 360 (5%), 338 (24%), 242 (5%), 167 (8%), 146 (7%), 94 (8%); *Anal*. Calcd for $C_{34}H_{30}O_4$: C-81.27, H-5.97; Found: C-81.32, H-5.93%.

Synthesis of (2E,2′E)-3,3′-(pentane-1,5-diylbis(oxy))bis(3,1-phenylene))bis(1-phenylprop-2-ene-1-one) (3c). The com pound **3c** was prepared from the reaction of chalcone **2** (2.24 g, 0.01 mol), 1,5-dibromopentane (1.14 g, 0.005 mol) under the same conditions as used earlier for **3a**.

3c: Light yellow, yield 69%; mp: 130–132°C; IR (KBr): υ_{max} cm^{-1}: 3061 (aromatic C-H), 2915, 2850 (methylene C-H), 1661 (C=O), 1595 (C=C), 1255, 1018 (C-O); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.00 (4H, d, J=7.1 Hz, H-2′, 6′), 7.78 (4H, d, J_{trans}=15.6 Hz, H-3), 7.52 (6H, m, H-2, 3′, 5′), 7.32 (2H, t, J_o=7.8 Hz, H-4′), 7.23 (2H, t, J=7.3 Hz, H-5″), 7.21 (2H, d, J_o=7.6 Hz, H-6″), 7.16 (2H, s, H-2″), 6.97 (2H, dd, $J_{o,m}$=8.0, 1.8 Hz, H-4″), 4.05 (4H, t, J_{vic}=6.3 Hz, OC***H₂***), 1.93 (4H, quintet, J_{vic}=6.6 Hz, OCH_2C***H₂***), 1.71 (2H, m, OCH_2CH_2C***H₂***); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 190.60 (C=O), 159.42 (C-3″), 144.85 (C-3), 138.18 (C-1′), 136.25 (C-1″), 132.86 (C-2′, 6′), 129.99 (C-4′), 128.67 (C-3′, 5′), 128.54 (C-6″), 122.31 (C-5″), 121.13 (C-2), 116.81 (C-4″), 114.04 (C-2″), 67.87 (O***C***H_2), 29.04 (OCH_2***C***H_2), 22.81 (OCH_2CH_2***C***H_2); ESI-MS: *m/z* 554 (M+K-1, 9%), 553 (M+K-2, 22%), 513 (11%), 458 (9%), 437 (11%), 360 (20%), 339 (24%), 338 (100%), 283 (10%), 202 (13%), 167 (7%), 146 (13%), 94 (6%); *Anal*. Calcd for $C_{35}H_{32}O_4$: C-81.39, H-6.20; Found: C-81.34, H-6.16%.

Synthesis of (2E,2′E)-3,3′-(hexane-1,6-diylbis(oxy))bis(3,1-phenylene))bis(1-phenylprop-2-ene-1-one) (3d). The com pound **3d** was obtained by treating chalcone **2** (2.24 g, 0.01 mol) with 1,6-dibromohexane (1.22 g, 0.005 mol) under the same conditions as described earlier for **3a**.

3d: Cream, Yield 71%; mp: 122–124°C; IR (KBr): υ_{max} cm^{-1}: 3061 (aromatic C-H), 2933, 2853 (methylene C-H), 1661 (C=O), 1596 (C=C), 1236, 1018 (C-O); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.02 (4H, dd, J=6.9, 8.4 Hz, H-2′, 6′), 7.78 (4H, d, J_{trans}=15.7 Hz, H-3), 7.52 (6H, m, H-2, 3′, 5′), 7.32 (2H, t, J_o=7.9 Hz, H-4′), 7.25 (2H, t, J=7.1 Hz, H-5″), 7.20 (2H, d, J_o=7.6 Hz, H-6″), 7.16 (2H, brs, H-2″), 6.96 (2H, dd, $J_{m,o}$=4.0, 6.1 Hz, H-4″), 4.05 (4H, t, J_{vic}=6.3 Hz, OC***H₂***), 1.86 (4H, t, J_{vic}=6.4 Hz, OCH_2C***H₂***), 1.58 (4H, quintet, J_{vic}=7.1 Hz, OCH_2CH_2C***H₂***); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 190.61 (C=O), 159.46 (C-3″), 144.88 (C-3), 138.19 (C-1′), 136.23 (C-1″), 132.85 (C-2′, 6′), 129.94 (C-4′), 128.66 (C-3′, 5′), 128.54 (C-6″), 122.30 (C-5″), 121.08 (C-2), 116.80 (C-4″), 114.04 (C-2″), 67.94 (O***C***H_2), 29.22 (OCH_2***C***H_2), 25.91 (OCH_2CH_2***C***H_2); ESI-MS: *m/z* 541 (M+1, 19%), 458 (17%), 437 (8%), 360 (17%), 339 (28%), 338 (100%), 283 (15%), 202 (21%), 167 (11%), 146 (8%), 94 (9%); *Anal*. Calcd for $C_{36}H_{34}O_4$: C-81.50, H-6.41; Found: C-81.54, H-6.45%.

Synthesis of (2E,2′E)-3,3′-(octane-1,8-diylbis(oxy))bis(3,1-phenylene))bis(1-phenylprop-2-ene-1-one) (3e). The compound **3e** was synthesized from the reaction of chalcone **2** (2.24 g, 0.01 mol) with 1,8-dibromooctane (1.36 g, 0.005 mol) under the same conditions as described previously for **3a**.

3e: Cream, yield 73%; mp: 114–116°C; IR (KBr): υ_{max} cm^{-1}: 3055 (aromatic C-H), 2920, 2894 (methylene C-H), 1660 (C=O), 1578 (C=C), 1251, 1017 (C-O); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.02 (4H, d, J_o=7.1 Hz, H-2′, 6′), 7.79 (4H, d, J_{trans}=15.6 Hz, H-3), 7.50 (6H, m, J_o=7.6 Hz, H-2, 3′, 5′), 7.32 (2H, t, J_o=7.9 Hz, H-4′), 7.26 (2H, t, J_o=7.3 Hz, H-5″),7.20 (2H, d, J_o=7.3 Hz, H-6″), 7.16 (2H, brs, H-2″), 6.96 (2H, dd, $J_{m,o}$=2.0, 8.1 Hz, H-4″), 4.02 (4H, t, J_{vic}=6.2 Hz, OC***H₂***), 1.85 (4H, t, J_{vic}=6.6 Hz, OCH_2C***H₂***), 1.49 (4H, m, OCH_2CH_2C***H₂***), 1.41 (4H, m, $OCH_2CH_2CH_2C$***H₂***); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 190.62 (C=O), 159.50 (C-3″), 144.91 (C-3), 138.20 (C-1′), 136.21 (C-1″), 132.84 (C-2′, 6′), 129.95 (C-4′), 128.66 (C-3′, 5′), 128.54 (C-6″), 122.29 (C-5″), 121.03 (C-2), 116.83 (C-4″), 114.03 (C-2″), 68.08 (O***C***H_2), 29.34 (OCH_2***C***H_2), 29.26 (OCH_2CH_2***C***H_2), 26.03($OCH_2CH_2CH_2$***C***H_2); ESI-MS: *m/z* 597 (M+K, 11%), 569 (M+1, 30%), 507 (5%), 437 (6%), 425 (11%), 360 (8%), 339 (25%), 338 (100%), 303 (13%), 274 (9%), 215 (16%), 167 (22%), 151 (5%), 126 (32%), 102 (48%), 90 (25%); *Anal*. Calcd for $C_{38}H_{38}O_4$: C-81.72, H-6.81; Found: C-81.68, H-6.77%.

Synthesis of (2E,2′E)-3,3′-(decane-1,10-diylbis(oxy))bis(3,1-phenylene))bis(1-phenylprop-2-ene-1-one) (3f). The compound **3f** was obtained from the reaction of chalcone **2** (2.24 g, 0.01 mol) with 1,10-dibromodecane (1.5 g, 0.005 mol) under the same conditions as described previously for **3a**.

3f: Off white, yield 77%; mp: 110–112°C; IR (KBr): υ_{max} cm^{-1}: 3057 (aromatic C-H), 2959, 2873 (methylene C-H), 1661 (C=O), 1578 (C=C), 1244, 1017 (C-O); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.02 (4H, d, J_o=7.3 Hz, H-2′, 6′), 7.78 (4H, d, J_{trans}=15.7 Hz, H-3), 7.50 (6H, m, H-2, 3′, 5′), 7.32 (2H, t, J_o=7.9 Hz, H-4′), 7.28 (2H, t, J_o=7.2 Hz, H-5″), 7.23 (2H, d, J_o=7.6 Hz, H-6″), 7.15 (2H, s, H-2″), 6.96 (2H, dd, $J_{m,o}$=1.5, 8.0 Hz, H-4″), 4.01 (4H, t, J_{vic}=6.1 Hz, OC***H₂***), 1.80 (4H, quintet, J_{vic}=6.6 Hz, OCH_2C***H₂***), 1.48 (4H, t, J_{vic}=6.3 Hz, OCH_2CH_2C***H₂***), 1.35 (8H, m, $OCH_2CH_2CH_2C$***H₂C H₂***); ^{13}C-NMR (100 MHz, $CDCl_3$): δ

190.62 (C=O), 159.51 (C-3″), 144.93 (C-3), 138.20 (C-1′), 136.20 (C-1″), 132.84 (C-2′, 6′), 129.95 (C-4′), 128.66 (C-3′, 5′), 128.54 (C-6″), 122.27 (C-5″), 121.02 (C-2), 116.83 (C-4″), 114.04 (C-2″), 68.12 (O***C*H₂**), 29.53 (OCH_2***C*H₂**), 29.40 (OCH_2CH_2***C*H₂**), 29.27 ($OCH_2CH_2CH_2$***C*H₂**), 26.01 ($OCH_2CH_2CH_2CH_2$***C*H₂**); ESI-MS: *m/z* 597 (M+1, 26%), 609 (M+Na, 13%), 491 (10%), 443 (9%), 363 (5%), 360 (16%), 339 (19%), 338 (62%), 243 (18%), 242 (100%), 202 (9%), 146 (7%), 102 (5%), 94 (3%); *Anal*. Calcd for $C_{40}H_{42}O_4$: C-81.91, H-7.16; Found: C-81.96, H-7.21%.

Synthesis of (2E,2′E)-3,3′-(dodecane-1,12-diylbis(oxy))bis(3,1-phenylene))bis(1-phenylprop-2-ene-1-one) (3g). The compound **3g** was prepared by treating chalcone **2** (2.24 g, 0.01 mol) with 1,12-dibromododecane (1.64 g, 0.005 mol) under the same conditions as described previously for **3a**.

3g: Cream, yield 74%; mp: 102–104°C; IR (KBr): υ_{max} cm^{-1}: 3056 (aromatic C-H), 2960, 2880 (methylene C-H), 1662 (C=O), 1575 (C=C), 1249, 1017 (C-O); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.02 (4H, d, J_o=7.2 Hz, H-2′, 6′), 7.78 (4H, d, J_{trans}=15.6 Hz, H-3), 7.52 (6H, m, H-2, 3′, 5′), 7.38 (2H, t, J=6.2 Hz, H-4′), 7.27 (2H, t, J_o=7.9 Hz, H-5″), 7.22 (2H, d, J_o=7.6 Hz, H-6″), 7.15 (2H, s, H-2″), 6.96 (2H, dd, $J_{m,o}$=2.0, 7.8 Hz, H-4″), 3.99 (4H, t, J_{vic}=6.4 Hz, O***CH₂***), 1.78 (4H, quintet, J_{vic}=6.5 Hz, OCH_2***CH₂***), 1.46 (4H, quintet, J_{vic}=6.5 Hz, OCH_2CH_2***CH₂***), 1.30 (12H, m, $OCH_2CH_2CH_2$***CH₂CH₂CH₂***); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 190.60 (C=O), 159.51 (C-3″), 144.92 (C-3), 138.16 (C-1′), 136.19 (C-1″), 132.84 (C-2′, 6′), 129.94 (C-4′), 128.66 (C-3′, 5′), 128.54 (C-6″), 122.26 (C-5″), 121.02 (C-2), 116.83 (C-4″), 114.04 (C-2″), 68.14 (O***C*H₂**), 29.60 (OCH_2***C*H₂**), 29.35 (OCH_2CH_2***C*H₂**), 29.43 ($OCH_2CH_2CH_2$***C*H₂**), 29.27 ($OCH_2CH_2CH_2CH_2$***C*H₂**), 26.07 ($OCH_2CH_2CH_2CH_2CH_2$***C*H₂**); ESI-MS: *m/z* 637 (M+Na, 23%), 625 (M+1, 16%), 491 (17%), 443 (19%), 362 (25%), 360 (6%), 339 (12%), 338 (58%), 243 (28%), 242 (100%), 202 (11%), 146 (8%), 102 (9%), 94 (5%); *Anal*. Calcd for $C_{42}H_{46}O_4$: C-82.02, H-7.49; Found: C-82.11, H-7.45%.

Synthesis of 1,3-bis(3-(1,3-diphenyl-4,5-dihydro-1*H*-pyrazol-5-yl)phenoxy)propane (4a). A mixture of compound **3a** (0.48 g, 0.001 mol), phenyl hydrazine (0.22 g, 0.002 mol), and NaOH (0.5 g, 0.013 mol) in dry EtOH (30 ml) was refluxed for 4 h**.** The progress of reaction was monitored by TLC (Hexane-Ethylacetate: 9 : 1). After the completion of reaction, the reaction mixture was concentrated under vacuum, and resulting mass was poured into *ice* to yield a solid substance. The crude product thus obtained was crystallized from MeOH to yield a pure compound **4a**.

4a: Off white, yield 63%; mp: 90–92°C; IR (KBr): υ_{max} cm^{-1}: 3056 (aromatic C-H), 2919, 2852 (methylene C-H), 1599 (C=N), 1238, 1022 (C-O); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.68 (4H, d, J_o=7.2 Hz, H-2″, 6″), 7.35 (2H, t, J_o=7.8 Hz, H-4″), 7.29 (4H, d, J_o=7.1 Hz, H-3″, 5″), 7.16 (6H, m, H-3′, 4′, 5′), 7.06 (2H, d, J_o=8.0 Hz, H-6‴), 6.85 (4H, d, J_o=7.2 Hz, H-2′, 6′), 6.82 (2H, brs, H-2‴), 6.75 (4H, t, J=6.6 Hz, H-4‴, 5‴), 5.21 (2H, dd, J_{MX}=12.1 Hz, J_{AX}=7.5 Hz, H-X), 4.02 (4H, t, J_{vic}=5.6 Hz, OC***H₂***), 3.71 (2H, dd, J_{MX}=12.1 Hz, J_{MA}=17.1 Hz, H-M), 3.08 (2H, dd, J_{AX}=7.5 Hz, J_{AM}=17.1 Hz, H-A), 2.16 (2H, quintet, J_{vic}=5.8 Hz, OCH_2C***H₂***); ^{13}C-NMR (100 MHz, $CDCl_3$): 159.07 (C-3‴), 147.02 (C-1′), 144.29 (C-3), 132.22 (C-1‴), 130.06 (C-1″), 128.74 (C-2″, 6″), 128.56 (C-4″), 128.42 (C-3″, 5″), 128.18 (C-6‴), 125.56 (C-3′, 5′), 118.54 (C-4′), 117.61 (C-2′, 6′), 112.95 (C-5‴), 112.88 (C-4‴), 111.91 (C-2‴), 64.43 (O***C*H₂**), 63.19 (C-5), 42.90 (C-4), 29.29 (OCH_2***C*H₂**); ESI-MS: *m/z* 669 (M+1, 42%), 592 (12%), 475 (30%), 448 (18%), 437 (8%), 338 (36%), 321 (19%), 243 (14%), 242 (29%), 202 (18%), 167 (15%), 126 (20%), 111 (18%), 85 (23%); *Anal*. Calcd for $C_{45}H_{40}N_4O_2$: C-80.83, H-5.98, N-8.38; Found: C-80.87, H-5.93, N-8.41%.

Synthesis of 1,4-bis(3-(1,3-diphenyl-4,5-dihydro-1*H*-pyrazol-5-yl)phenoxy)butane (4b). The compound **4b** was prepared by treating 1,4-bischalcone **3b** (0.5 g, 0.001 mol) with phenyl hydrazine (0.22 g, 0.002 mol) under the same conditions as described previously for **3a**.

4b: Off white, yield 66%; mp: 86–88°C; IR (KBr): υ_{max} cm^{-1}: 3058 (aromatic C-H), 2916, 2859 (methylene C-H), 1600 (C=N), 1241, 1032 (C-O); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.74 (4H, d, J_o=7.3 Hz, H-2″, 6″), 7.41 (2H, t, J_o=7.8 Hz, H-4″), 7.37 (4H, d, J=6.8 Hz, H-3″, 5″), 7.24 (2H, t, J_o=7.8 Hz, H-6‴), 7.16 (4H, t, J_o=7.7 Hz, H-3′, 5′), 7.01 (2H, d, J_o=7.6 Hz, H-2‴), 6.82 (4H, t, J_o=7.7 Hz, H-2′, 6′), 6.71 (4H, t, J_o=6.9 Hz, H-4‴, 5‴), 6.69 (2H, t, J=6.9 Hz, H-4′), 5.43 (2H, dd, J_{MX}=12.5 Hz, J_{AX}=6.3 Hz, H-X), 3.84 (6H, m, H-M & OC***H₂***), 3.10 (2H, dd, J_{AX}=6.3 Hz, J_{AM}=17.3 Hz, H-A), 1.84 (2H, brs, OCH_2C***H₂***); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 159.06 (C-3‴), 146.88 (C-1′), 144.27 (C-3), 132.21 (C-1‴), 129.98 (C-1″), 128.64 (C-2″, 6″), 128.44 (C-4″), 128.40 (C-3″, 5″), 128.33 (C-3′, 5′), 125.50 (C-6‴), 118.52 (C-4′), 117.60 (C-2′, 6′), 112.98 (C-5‴), 111.88 (C-4‴), 111.76 (C-2‴), 67.13 (O***C*H₂**), 63.29 (C-5), 42.92 (C-4), 28.54 (OCH_2***C*H₂**); ESI-MS: *m/z* 684 (M+2, 45%), 683 (M+1, 100%), 593 (11%), 475 (32%), 448 (13%), 437 (6%), 360 (20%), 338 (36%), 321 (9%), 274 (12%), 243 (14%), 242 (70%), 202 (15%), 167 (12%), 126 (17%), 111 (8%), 85 (43%); *Anal*. Calcd for $C_{46}H_{42}N_4O_2$: C-80.93, H-6.15, N-8.21; Found: C-80.89, H-6.19, N-8.26%.

Synthesis of 1,5-bis(3-(1,3-diphenyl-4,5-dihydro-1*H*-pyrazol-5-yl)phenoxy)pentane (4c). The compound **4c** was obtained from the reaction of 1,5-bischalcone **3c** (0.52 g, 0.001 mol) with phenyl hydrazine (0.22 g, 0.002 mol) under the same conditions as described previously for **3a**.

4c: Light yellow, yield 64%; mp: 84–86°C; IR (KBr): υ_{max} cm^{-1}: 3056 (aromatic C-H), 2921, 2848 (methylene C-H), 1596 (C=N), 1236, 1024 (C-O); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.72 (4H, d, J_o=7.3 Hz, H-2″, 6″), 7.40 (2H, t, J_o=7.6 Hz, H-4″), 7.34 (4H, d, J_o=7.1 Hz,

H-3″, 5″), 7.23 (2H, t, J_o = 7.8 Hz, H-6‴), 7.14 (4H, t, J_o = 8.2 Hz, H-3′, 5′), 7.02 (2H, d, J_o = 7.9 Hz, H-2‴), 6.85 (4H, t, J_o = 7.7 Hz, H-2′, 6′), 6.75 (4H, t, J_o = 8.0 Hz, H-4‴, 5‴), 6.68 (2H, t, J_o = 7.2 Hz, H-4′), 5.37 (2H, dd, J_{MX} = 12.1 Hz, J_{AX} = 6.6 Hz, H-X), 3.88 (6H, m, H-M & OC***H₂***), 3.09 (2H, dd, J_{AX} = 6.6 Hz, J_{AM} = 17.6 Hz, H-A), 1.72 (4H, quintet, J_{vic} = 7.0 Hz, $OCH_2C\boldsymbol{H_2}$), 1.52 (2H, quintet, J_{vic} = 6.8 Hz, $OCH_2CH_2C\boldsymbol{H_2}$); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 158.96 (C-3‴), 147.22 (C-1′), 144.25 (C-3), 132.21 (C-1‴), 130.18 (C-1″), 128.85 (C-2″, 6″), 128.76 (C-4″), 128.68 (C-3″, 5″), 128.62 (C-6‴), 125.65 (C-3′, 5′), 118.61 (C-4′), 117.75 (C-2′, 6′), 112.95 (C-5‴), 112.89 (C-4‴), 112.07 (C-2‴), 66.95 ($O\boldsymbol{C}H_2$), 63.08 (C-5), 42.07 (C-4), 25.29 ($OCH_2\boldsymbol{C}H_2$), 22.16 ($OCH_2CH_2\boldsymbol{C}H_2$); ESI-MS: *m/z* 475 (22%), 437 (5%), 360 (24%), 338 (60%), 321 (13%), 274 (14%), 243 (78%), 242 (100%), 202 (6%), 167 (8%), 151 (7%), 126 (9%), 110 (11%), 82 (6%); *Anal*. Calcd for $C_{47}H_{44}N_4O_2$: C-81.03, H-6.32, N-8.04; Found: C-81.07, H-6.28, N-8.06%.

Synthesis of 1,6-bis(3-(1,3-diphenyl-4,5-dihydro-1*H*-pyrazol-5-yl)phenoxy)hexane (4d). The compound **4d** was synthesized from the reaction of 1,6-bischalcone **3d** (0.54 g, 0.001 mol) with phenyl hydrazine (0.22 g, 0.002 mol) under the same conditions as described previously for **3a**.

4d: Off white, yield 69%; mp: 78–80°C; IR (KBr): υ_{max} cm^{-1}: 3057 (aromatic C-H), 2918, 2853 (methylene C-H), 1596 (C=N), 1238, 1043 (C-O); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.72 (4H, d, J_o = 7.2 Hz, H-2″, 6″), 7.40 (2H, t, J_o = 7.1 Hz, H-4″), 7.34 (4H, d, J_o = 7.2 Hz, H-3″, 5″), 7.23 (2H, t, J_o = 7.8 Hz, H-6‴), 7.12 (4H, t, J_o = 7.4 Hz, H-3′, 5′), 7.02 (2H, d, J_o = 7.9 Hz, H-2‴), 6.85 (4H, t, J_o = 7.3 Hz, H-2′, 6′), 6.75 (4H, dd, J = 8.0, 5.9 Hz, H-4‴, 5‴), 6.68 (2H, t, J_o = 7.2 Hz, H-4′), 5.31 (2H, dd, J_{MX} = 12.1 Hz, J_{AX} = 6.3 Hz, H-X), 3.85 (6H, m, H-M & OC***H₂***), 3.11 (2H, dd, J_{AX} = 6.3 Hz, J_{AM} = 17.2 Hz, H-A), 1.67 (4H, t, J_{vic} = 7.9 Hz, $OCH_2C\boldsymbol{H_2}$), 1.41 (2H, brs, $OCH_2CH_2C\boldsymbol{H_2}$); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 159.07 (C-3‴), 146.87 (C-1′), 144.26 (C-3), 132.20 (C-1‴), 129.98 (C-1″), 128.64 (C-2″, 6″), 128.44 (C-4″), 128.39 (C-3″, 5″), 128.18 (C-6‴), 125.50 (C-3′, 5′), 118.52 (C-4′), 117.57 (C-2′, 6′), 112.87 (C-5‴), 112.85 (C-4‴), 111.84 (C-2‴), 67.17 ($O\boldsymbol{C}H_2$), 63.28 (C-5), 42.92 (C-4), 28.54 ($OCH_2\boldsymbol{C}H_2$), 25.27 ($OCH_2CH_2\boldsymbol{C}H_2$); ESI-MS: *m/z* 711 (M+1, 23%), 650 (8%), 647 (21%), 503 (8%), 475 (20%), 362 (24%), 338 (64%), 273 (18%), 209 (16%), 168 (7%), 156 (12%), 124 (28%), 93 (31%), 80 (13%); *Anal*. Calcd for $C_{48}H_{46}N_4O_2$: C-81.12, H-6.47, N-7.88; Found: C-81.07, H-6.51, N-7.83%.

Synthesis of 1,8-bis(3-(1,3-diphenyl-4,5-dihydro-1*H*-pyrazol-5-yl)phenoxy)octane (4e). The compound **4e** was prepared by the reaction of 1,8-bischalcone **3e** (0.56 g, 0.001 mol) with phenyl hydrazine (0.22 g, 0.002 mol) under the same conditions as described previously for **3a**.

4e: Off white, yield 71%; mp: 74–76°C; IR (KBr): υ_{max} cm^{-1}: 3055 (aromatic C-H), 2937, 2849 (methylene C-H), 1598 (C=N), 1239, 1042 (C-O); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.73 (4H, d, J_o = 7.4 Hz, H-2″, 6″), 7.41 (2H, t, J_o = 7.0 Hz, H-4″), 7.35 (4H, d, J_o = 7.1 Hz, H-3″, 5″), 7.23 (2H, t, J_o = 7.7 Hz, H-6‴), 7.15 (4H, t, J_o = 7.7 Hz, H-3′, 5′), 7.01 (2H, d, J_o = 8.0 Hz, H-2‴), 6.82 (4H, t, J_o = 8.0 Hz, H-2′, 6′), 6.72 (4H, d, J_o = 7.9 Hz, H-4‴, 5‴), 6.68 (2H, t, J_o = 7.2 Hz, H-4′), 5.38 (2H, dd, J_{MX} = 12.2 Hz, J_{AX} = 6.4 Hz, H-X), 3.88 (6H, m, H-M & OC***H₂***), 3.09 (2H, dd, J_{AX} = 6.4 Hz, J_{AM} = 17.3 Hz, H-A), 1.71 (4H, t, J_{vic} = 6.2 Hz, $OCH_2C\boldsymbol{H_2}$), 1.44 (8H, m, $OCH_2CH_2C\boldsymbol{H_2}C\boldsymbol{H_2}$); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 159.07 (C-3‴), 147.02 (C-1′), 144.26 (C-3), 132.22 (C-1‴), 130.04 (C-1″), 128.71 (C-2″, 6″), 128.53 (C-4″), 128.48 (C-3″, 5″), 128.19 (C-6‴), 125.56 (C-3′, 5′), 118.54 (C-4′), 117.61 (C-2′, 6′), 112.95 (C-5‴), 112.88 (C-4‴), 111.91 (C-2‴), 67.24 ($O\boldsymbol{C}H_2$), 63.19 (C-5), 42.90 (C-4), 28.66 ($OCH_2\boldsymbol{C}H_2$), 28.56 ($OCH_2CH_2\boldsymbol{C}H_2$), 25.40 ($OCH_2CH_2CH_2\boldsymbol{C}H_2$); ESI-MS: *m/z* 740 (M+2, 4%), 739 (M+1, 13%), 650 (8%), 504 (7%), 475 (37%), 448 (23%), 321 (9%), 273 (12%), 209 (5%), 168 (7%), 124 (27%), 93 (30%), 80 (100%); *Anal*. Calcd for $C_{50}H_{50}N_4O_2$: C-81.30, H-6.77, N-7.58; Found: C-81.34, H-6.73, N-7.61%.

Synthesis of 1,10-bis(3-(1,3-diphenyl-4,5-dihydro-1*H*-pyrazol-5-yl)phenoxy)decane (4f). The compound **4f** was prepared from the reaction of 1,10-bischalcone **3f** (0.59 g, 0.001 mol) with phenyl hydrazine (0.22 g, 0.002 mol) under the same conditions as described previously for **3a**.

4f: Light yellow, yield 73%; mp: 70–72°C; IR (KBr): υ_{max} cm^{-1}: 3059 (aromatic C-H), 2918, 2857 (methylene C-H), 1599 (C=N), 1243, 1038 (C-O); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.72 (4H, d, J_o = 7.2 Hz, H-2″, 6″), 7.39 (2H, t, J_o = 7.6 Hz, H-4″), 7.32 (4H, d, J_o = 7.2 Hz, H-3″, 5″), 7.22 (2H, t, J_o = 7.8 Hz, H-6‴), 7.12 (4H, t, J_o = 7.5 Hz, H-3′, 5′), 7.02 (2H, d, J_o = 7.8 Hz, H-2‴), 6.82 (4H, t, J_o = 7.9 Hz, H-2′, 6′), 6.77 (4H, dd, J = 8.0, 6.2 Hz, H-4‴, 5‴), 6.67 (2H, t, J_o = 7.2 Hz, H-4′), 5.36 (2H, dd, J_{MX} = 12.2 Hz, J_{AX} = 6.5 Hz, H-X), 3.86 (6H, m, H-M & OC***H₂***), 3.09 (2H, dd, J_{AX} = 6.5 Hz, J_{AM} = 17.4 Hz, H-A), 1.71 (4H, quintet, J_{vic} = 6.1 Hz, $OCH_2C\boldsymbol{H_2}$), 1.45 (4H, quintet, J_{vic} = 6.0 Hz, $OCH_2CH_2C\boldsymbol{H_2}C\boldsymbol{H_2}$), 1.34 (8H, m, $OCH_2CH_2CH_2C\boldsymbol{H_2}C\boldsymbol{H_2}$); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 159.04 (C-3‴), 146.95 (C-1′), 144.28 (C-3), 132.63 (C-1‴), 130.26 (C-1″), 128.81 (C-2″, 6″), 128.69 (C-4″), 128.47 (C-3″, 5″), 128.32 (C-6‴), 125.52 (C-3′, 5′), 118.54 (C-4′), 117.61 (C-2′, 6′), 112.95 (C-5‴), 112.88 (C-4‴), 111.87 (C-2‴), 67.89 ($O\boldsymbol{C}H_2$), 64.32 (C-5), 42.94 (C-4), 29.59 ($OCH_2\boldsymbol{C}H_2$), 29.38 ($OCH_2CH_2\boldsymbol{C}H_2$), 26.43 ($OCH_2CH_2CH_2\boldsymbol{C}H_2$), 26.07 ($OCH_2CH_2CH_2CH_2\boldsymbol{C}H_2$); ESI-MS: *m/z* 768 (M+2, 22%), 765 (40%), 681 (5%), 591 (6%), 539 (12%), 475 (20%), 359 (6%), 242 (17%), 209 (6%), 167 (6%), 151 (16%), 126 (19%), 110 (21%), 85 (100%); *Anal*. Calcd for $C_{52}H_{54}N_4O_2$: C-81.46, H-7.04, N-7.31; Found: C-81.51, H-7.07, N-7.27%.

Synthesis of 1,12-bis(3-(1,3-diphenyl-4,5-dihydro-1*H*-pyrazol-5-yl)phenoxy)dodecane (4g). The compound **4g** was synthesized by reacting 1,12-bischalcone **3g** (0.62 g,

0.001 mol) with phenyl hydrazine (0.22 g, 0.002 mol) under the same conditions as described previously for **3a**.

4g: Off white, yield 68%; mp: 68–70°C; IR (KBr): υ_{max} cm^{-1}: 3056 (aromatic C-H), 2943, 2852 (methylene C-H), 1598 (C=N), 1247, 1023 (C-O); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.69 (4H, d, J_o = 7.1 Hz, H-2″, 6″), 7.47 (2H, t, J_o = 7.7 Hz, H-4″), 7.32 (4H, d, J_o = 6.9 Hz, H-3″, 5″), 7.21 (2H, t, J_o = 7.6 Hz, H-6‴), 7.15 (4H, t, J_o = 7.3 Hz, H-3′, 5′), 7.06 (2H, d, J_o = 7.6 Hz, H-2‴), 6.86 (4H, d, J_o = 7.8 Hz, H-2′, 6′), 6.74 (4H, d, J = 6.8 Hz, H-4‴, 5‴), 6.67 (2H, t, J_o = 7.2 Hz, H-4′), 5.16 (2H, dd, J_{MX} = 11.8 Hz, J_{AX} = 7.5 Hz, H-X), 3.88 (6H, m, H-M & OC***H*****₂**), 3.09 (2H, dd, J_{AX} = 7.5 Hz, J_{AM} = 17.0 Hz, H-A), 1.69 (4H, brs, OCH_2C***H*****₂**), 1.26 (20H, m, OCH_2C***H*****₂**C***H*****₂**C***H*****₂**C***H*****₂**C***H*****₂**); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 159.90 (C-3‴), 146.89 (C-1′), 144.39 (C-3), 132.79 (C-1‴), 130.27 (C-1″), 128.98 (C-2″, 6″), 128.66 (C-4″), 128.61(C-3″, 5″), 128.42 (C-6‴), 125.50 (C-3′, 5′), 119.20 (C-4′), 117.99 (C-2′, 6′), 113.46 (C-5‴), 112.81 (C-4‴), 112.02 (C-2‴), 68.02 (O***C***H_2), 64.67 (C-5), 42.92 (C-4), 29.69 (OCH_2***C***H_2), 29.49 (OCH_2CH_2***C***H_2), 29.34 ($OCH_2CH_2CH_2$***C***H_2), 26.12 ($OCH_2CH_2CH_2CH_2$***C***H_2), 18.46 ($OCH_2CH_2CH_2CH_2CH_2$ ***C***H_2); ESI-MS: *m/z* 795 (M+1, 12%), 765 (32%), 680 (15%), 575 (18%), 539 (12%), 497 (21%), 359 (8%), 242 (17%), 209 (6%), 167 (6%), 151 (16%), 126 (19%), 110 (21%), 85 (13%); *Anal*. Calcd for $C_{54}H_{58}N_4O_2$: C-81.61, H-7.30, N-7.05; Found: C-81.57, H-7.34, N-7.09%.

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