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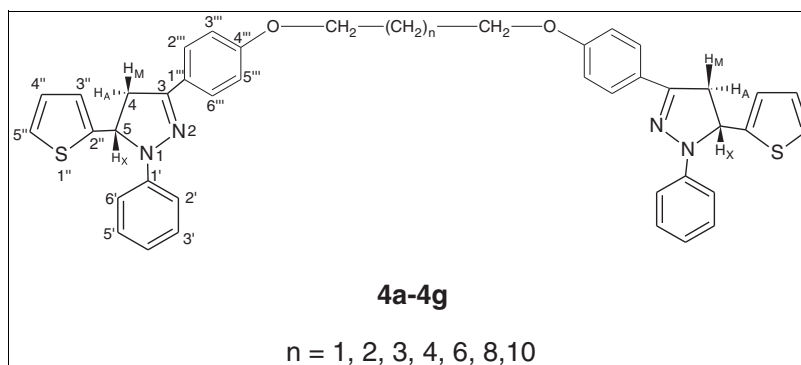
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Syntheses and antimicrobial behavior of the alkyl linked new bispyrazolines **4a-4g** have been investigated. These compounds exhibited better antimicrobial activities as compared with their corresponding bischalcones. The structures of the prepared compounds (**3a-3g** and **4a-4g**) were determined from the rigorous analysis of their IR,  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, and mass spectral parameters.

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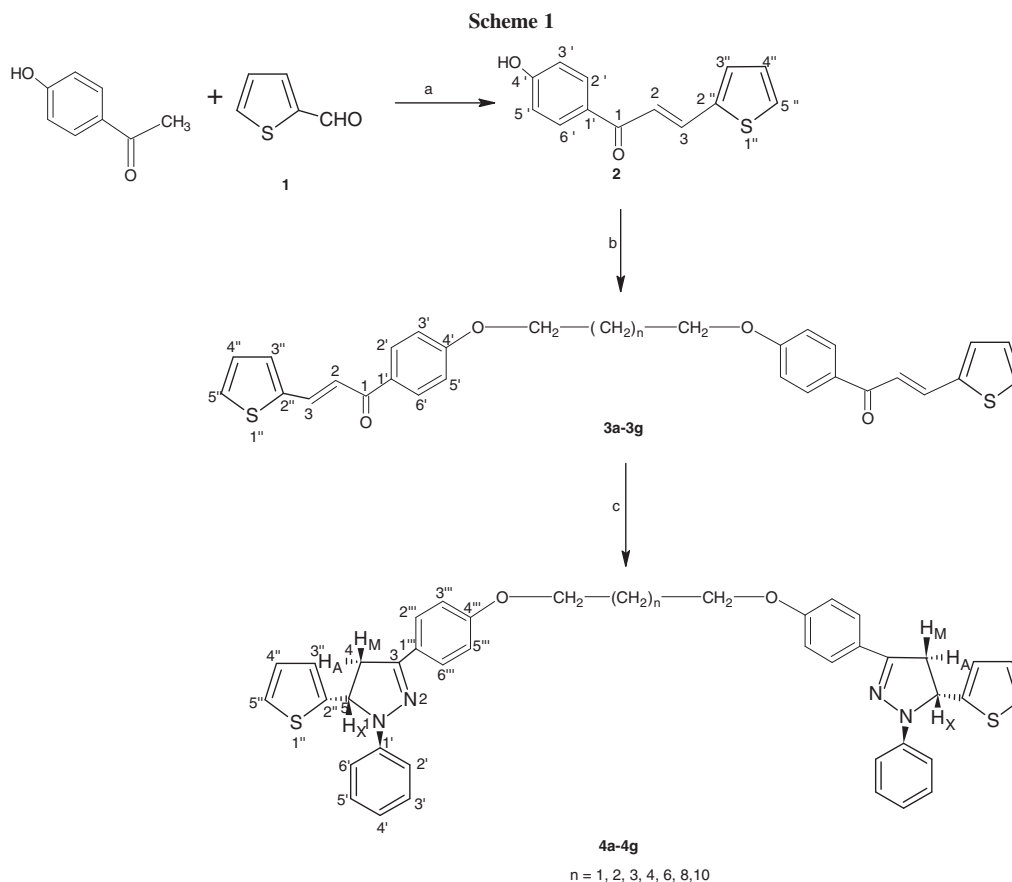
## INTRODUCTION

The chalcones are the important molecules that constitute the part of various naturally occurring and biologically significant products [1]. These compounds are generally obtained from the aldol condensation and Claisen-Schmidt reactions of the carbonyl compounds [2]. It is observed that most of the chalcones have pharmaceutical and medicinal applications [3]. These substrates are found to be effective as anticancer [4], antiviral [5], cardiovascular [6], and anti-inflammatory [7] agents. The reactions of these intermediates with suitable hydrazine derivative lead to the generation of five-membered pyrazoline compounds. The synthesis of pyrazoline derivatives has been studied because of their wide range of biological activities such as antitumor [8,9], immunosuppressive [10], antimicrobial [11], antifungal [12], and anti-inflammatory [13]. Bispyrazolines are the bichromophoric molecules that are formed by the linking two pyrazoline moieties together through the carbon chains, and some of the results have been reported upon the synthesis of bispyrazolines [14]. It is evident from the literature that very little attention has been focussed upon the compounds involving the internal chains of varying lengths. By considering these aspects in view, we report herein the synthesis and antimicrobial evaluations of new bispyrazolines **4a-4g** built around the aliphatic chains consisting of 3–12 methylene groups.

## RESULTS AND DISCUSSION

The bispyrazolines **4a-4g** required for the present investigations were synthesized starting from the Claisen-Schmidt reaction of 4-hydroxyacetophenone with 2-thiophenecarboxaldehyde **1**, which yielded chalcone **2**. The *O*-alkylation of later with suitable 1, $\omega$ -dibromoalkanes in the presence  $\text{K}_2\text{CO}_3$ , dry acetone, and tetrabutyl ammonium iodide (PTC) provided bischalcones **3a-3g** in good yields. The cyclization of **3a-3g** with phenyl hydrazine under alcoholic conditions led to the formation of bispyrazolines **4a-4g**, which were crystallized from  $\text{CH}_3\text{OH}$  to give pure compounds in moderate yields (Scheme 1). The use of PTC in the aforementioned synthesis not only reduced the reaction times drastically but also improved the yield of bischalcones. The structures of the prepared compounds (**3a-3g** and **4a-4g**) were determined from the rigorous analysis of their IR,  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, and mass spectral parameters. The elemental analysis results also confirmed the purity of the prepared products.

IR spectra of bischalcones **3a-3g** showed  $\text{C}=\text{O}$  and  $\text{C}=\text{C}$  group absorptions at 1661–1652 and 1602–1594  $\text{cm}^{-1}$ , respectively. Other significant bands were observed at 2940–2920, 2878–2852 (methylene  $\text{C}-\text{H}$ ), 1245–1236 and 1034–1020 ( $\text{C}-\text{O}$ )  $\text{cm}^{-1}$ . In the  $^1\text{H}$  NMR spectra of these compounds, the doublets resonating at  $\delta$  7.94–7.83 and 7.52–7.32 could be assigned to H-3 and H-2 protons, respectively,



Reaction Conditions: a) NaOH/ EtOH/0°C; b) anhd. K<sub>2</sub>CO<sub>3</sub>/BrCH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>CH<sub>2</sub>Br/dry acetone/Bu<sub>4</sub>N<sup>+</sup>T<sup>-</sup>/Δ ; c) PhNHNH<sub>2</sub>/dry EtOH/ AcOH/Δ

and the coupling value of 15.3–14.5 Hz between these hydrogens describes the *trans* geometry around the C-2 and C-3 double bond. The two doublets in the range of  $\delta$  8.02–7.99 ( $J_o = 8.8$ –8.2 Hz) and 7.03–6.96 ( $J_o = 8.8$ –8.2 Hz) could be appearing because of the aromatic protons H-2',6' and H-3',5', respectively. The signals of internal chain OCH<sub>2</sub> group protons were found to be resonating at  $\delta$  4.29–4.03 (t,  $J_{vic} = 6.6$ –5.8 Hz), and the remaining (CH<sub>2</sub>)<sub>n</sub> group hydrogens produced suitable signals at  $\delta$  2.57–1.33 with suitable multiplicities. In the <sup>13</sup>C NMR spectra of **3a–3g**, the internal chain methylene groups were resonating at  $\delta$  68.13–67.28 (OCH<sub>2</sub>) and 29.64–25.00 {(CH<sub>2</sub>)<sub>n</sub>}; the downfield resonances of the former suggest their placement near an electronegative oxygen atom. Other significant signals were found to be placed at  $\delta$  186.86–186.60, 120.33–120.05, and 140.68–139.78, which could be attributed to C-1, C-2, and C-3 of the enone moiety.

IR spectra of **4a–4g** did not reveal any absorption in the region of 1661–1652 cm<sup>-1</sup>, which describes the absence of C=O group in these compounds, and here, major bands were observed in the region at 1599–1592 cm<sup>-1</sup> because of the C=N group. In the <sup>1</sup>H NMR spectra of these compounds, the signals corresponding to the double bond hydrogens (H-2 and 3) at  $\delta$  7.94–7.83 and 7.52–7.32 of

the bischalcones **3a–3g** were found missing altogether, which indicates the involvement of the enone moiety during the cyclization reaction. The pyrazoline ring protons H-X, H-M, and H-A resulted in suitable resonances at  $\delta$  5.67–5.56 (2H, dd), 3.86–3.81 (2H, dd), and 3.24–3.19 (2H, dd), respectively. The remaining hydrogens were found to be resonating at the suitable positions (see Experimental section).

In the <sup>13</sup>C NMR spectra of **4a–4g**, signals belonging to the C=O group of bischalcones at  $\delta$  186.86–186.60 were found to be absent, which also corroborates the transformation of this functionality (C=O) in the formation of pyrazoline moiety. The pyrazoline ring carbons C-3, C-4, and C-5 were resonating at  $\delta$  156.23–154.26, 43.62–43.25, and 59.74–59.41, respectively. The remaining carbon atoms were found to be present at the expected positions (see Experimental section). ESI-MS spectra of **4a–4g** also corroborated the proposed structures, which exhibited molecular ions at the appropriate *m/z* values (see Experimental section).

The stereochemical features of pyrazoline ring in **4a–4g** were determined from the considerations of coupling constants (*J*). The vicinal coupling constant (<sup>3</sup>*J*) between H-X and H-M was found to be 12.2–11.8 Hz, which reflects

that these hydrogens are *cis* to each other, whereas coupling value of  $J_{XA} = 6.9\text{--}6.2$  Hz and  $J_{MA} = 17.4\text{--}16.5$  Hz describes the *trans* relationship between H-X and H-A, whereas H-M and H-A are geminally placed at C-4'. The aryl rings placed at N-1 and C-5 are evidently *trans* oriented to avoid any intramolecular repulsion.

Mechanistically, the cyclization reactions described earlier, that is, **3a–3g**  $\rightarrow$  **4a–4g** can be visualized as having occurred through an initial nucleophilic attack (path a) of phenyl hydrazine upon the carbonyl group of enone moiety under the influence of proton followed by dehydration to produce hydrazones **3a'–3g'**. The later further undergoes cyclization reaction with the addition of proton to give **4a–4g** as the end products (Scheme 2).

In other way, phenyl hydrazine could also undergo attack upon the enone part of **3a–3g** in a Michael addition fashion (path b) to give **3a''–3g''** as the intermediate, which subsequently might suffer cyclization reaction followed by dehydration to give **5a–5g**.

In spite of our repeated and best efforts, we were not able to isolate any product similar to **5a–5g**, and the only products obtained were **4a–4g**. Thus, in bischalcone **3a–3g**, direct condensation of phenyl hydrazine with carbonyl group (path a) is the preferred pathway over the Michael addition (path b, Scheme 2).

**Antimicrobial evaluation.** All cultures were obtained from MTCC (Microbial Type Culture Collection & Gene Bank, Chandigarh-160036, India). The newly prepared compounds (**3a–3g** and **4a–4g**) were screened for their antimicrobial activities *in vitro* against seven bacterial strains namely *Klubsellia pneumoniae* (MTCC 3384), *Pseudomonas aeruginosa* (MTCC 424), *Escherichia coli* (MTCC 443), *Staphylococcus aureus* (MTCC 96), *Bacillus subtilis* (MTCC 441), *Pseudomonas fluorescens* (MTCC 103), *Streptococcus pyrogens* (MTCC 442), and five fungi strains *Aspergillus janus* (MTCC 2751), *Aspergillus niger* (MTCC 281), *Fusarium oxysporum* (MTCC 2480), *Aspergillus sclerotiorum* (MTCC 1008) and *Pencillium glabrum* (MTCC 4951). Amoxicillin and fluconazole were used as reference drugs for comparison. All the bacterial strains were grown at 37°C for 24 h in nutrient broth, and fungi strains were grown in malt extract at 28°C for 72 h. Each test compound was dissolved in DMSO. MIC of all the compounds (**3a–3g** and **4a–4g**) were evaluated by using serial tube dilution methods [15] at various concentration of 100, 50, 25, 12.5, 6.25, and 3.12 µg/mL, and MIC thus obtained were compared with the control (amoxicillin and fluconazole).

The observed minimum inhibitory concentration (MIC–µg/ml) values of the studied compounds (**3a–3g** and **4a–4g**) have been presented in Tables 1 and 2 (Figs 1 and 2). Most of the compounds showed significant activity against tested microorganisms, and the compounds **3c–3g** and **4c–4g** showed better MIC against the aforementioned microorganisms at concentration of 12.5 µg/mL (Tables 1 and 2).

The compounds **3d–3g** were found to be active (MIC–12.5 µg/mL) against the strains *P. fluorescens* and *S. pyrogens*, whereas the compounds **3c–3f** were found to be active for fungal strain *F. oxysporum*. The similar activity was exhibited by **3d** and **3g** against most of the tested microorganisms (Table 1).

It is evident from Table 2 that the compounds **4c–4g** were found to be active against the bacteria strain (*P. fluorescens*) and fungi stains (*P. glabrum* and *F. oxysporum*) and the bispyrazolines **4f** and **4g** linked through 10, and 12 methylene group chains showed better activity as compared with other compounds (Table 2).

## CONCLUSION

It may be concluded that this study describes the general method for the synthesis of new bispyrazolines linked through the 3-aryl ring under the normal conditions. The bispyrazolines seem to be better antimicrobial agents than the corresponding bischalcones.

## EXPERIMENTAL

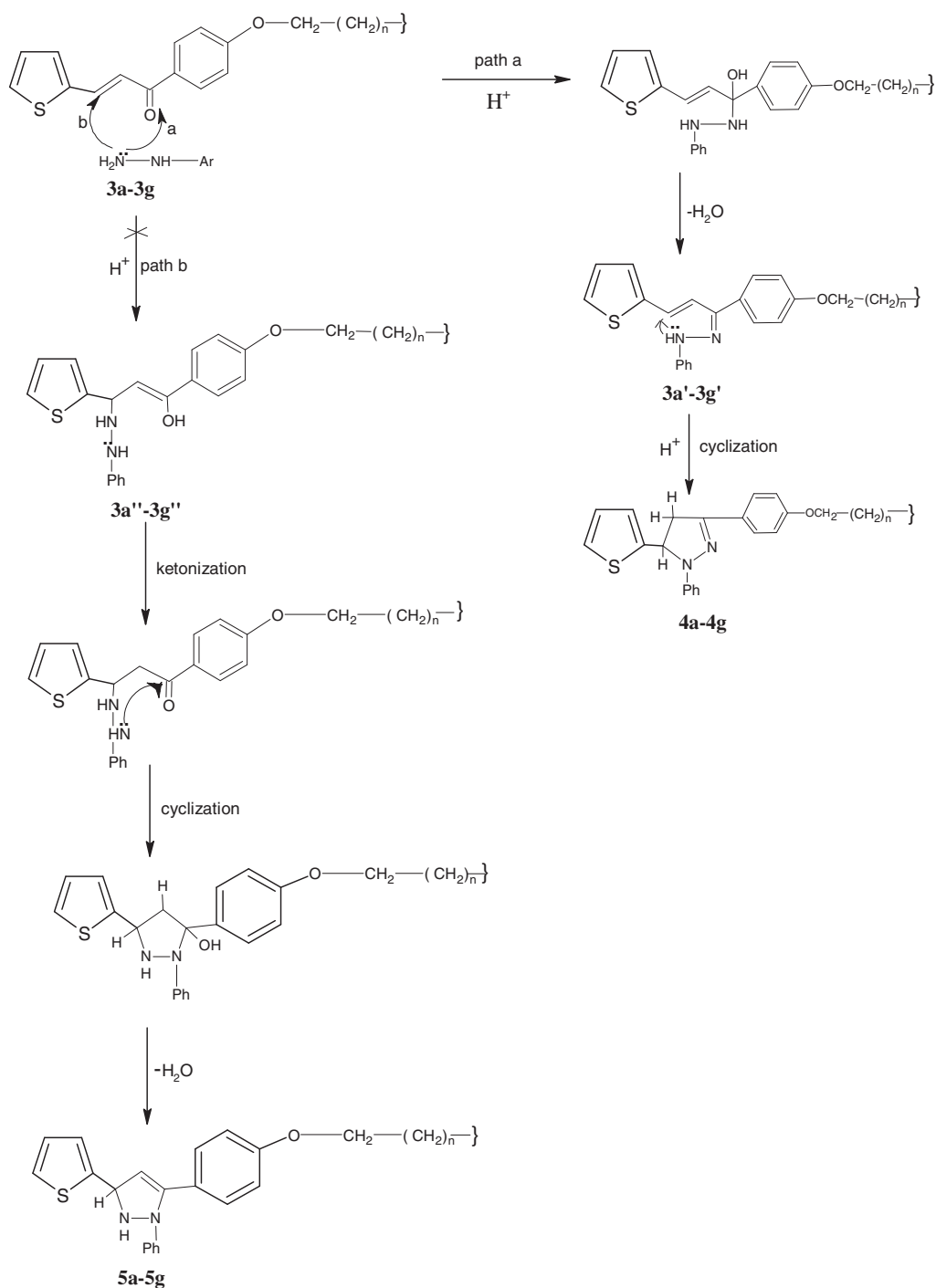
Melting points reported are uncorrected. IR (Buckinghamshire, England) spectra were scanned in KBr pellets on a Perkin-Elmer RXIFT Infrared spectrophotometer. <sup>1</sup>H NMR (Fallanden, Switzerland) spectra were recorded on a 400 MHz Bruker spectrometer using TMS as the internal standard. The mass spectra (Vernon Hills, USA) have been scanned on the Waters Micromass Q-T of Micro (ESI) spectrometer. TLC plates were coated with silica gel suspended in MeOH:CHCl<sub>3</sub>, and iodine vapors were used as visualizing agent.

**Synthesis of (2E)-1-(4-hydroxyphenyl)-3-(thiophene-2-yl)prop-2-en-1-one 2a.** A mixture of 4-hydroxyacetophenone (4.0 g, 0.02941 mol), 2-thiophenecarboxaldehyde (3.29 g, 0.02941 mol), and NaOH (1.0 g, 0.024 mol) in ethanol (25.0 mL) was stirred in an ice bath for 10 h. During the course of reaction, the initially formed greenish mixture changed to a reddish gummy mass. The resulting reaction mixture was poured into iced HCl to provide a yellow solid that was filtered, thoroughly washed with water, and dried. The crude material thus obtained was recrystallized from MeOH:CHCl<sub>3</sub> (3:1) to obtain a pure solid **2a**.

**2a:** yellow needles, yield 65%; mp: 166–168°C. IR (KBr) cm<sup>-1</sup>: 3469 (OH), 1688 (C=O), 1600 (C=C); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 10.25 (1H, s, OH), 7.96 (1H, d,  $J_{trans} = 15.1$  Hz, H-3), 7.82 (2H, d,  $J = 3.2$  Hz, H-2', 6'), 7.60 (1H, d,  $J_{trans} = 15.1$  Hz, H-2), 7.52 (2H, d,  $J = 2.6$  Hz, H-3', 5'), 7.43 (1H, d,  $J = 1.5$  Hz, H-3''), 7.12 (1H, d,  $J = 3.6$  Hz, H-5''), 6.89 (1H, d,  $J = 2.4$  Hz, H-4''). MS (ESI):  $m/z$  (M)<sup>+</sup> 230. Anal. Calcd for C<sub>13</sub>H<sub>10</sub>O<sub>2</sub>S: C, 67.82%; H, 4.34%; S, 13.91%; found: C, 67.70%; H, 4.21%; S, 13.80%.

**Synthesis of (2E,2'E)-1,1'-(4,4'-(propane-1,3-diylbis(oxy))bis(4,1-phenylene))bis(3-(thiophen-2-yl)prop-2-en-1-one 3a.** A suspension of chalcone **2a** (2.0 g, 0.0086957 mol), anhydrous K<sub>2</sub>CO<sub>3</sub> (2.0 g), 1,3-dibromopropane (0.8782 g, 0.00434783 mol), tetrabutyl ammonium iodide (1.0 g) in dry acetone (25.0 mL) was refluxed for 6 h with continuous stirring. The progress of reaction was monitored by TLC. After the completion of reaction, the reaction mixture turned to a colorless mass that was poured over iced HCl to obtain a solid. The crude product thus obtained was recrystallized from MeOH to yield pure compound **3a**.

Scheme 2



**3a:** brown solid; yield 60%; mp: 110–112°C. IR (KBr)  $cm^{-1}$  1660 (C=O), 1596 (C=C), 2923 and 2870 (methylene C-H), 1236 and 1034 (C-O);  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  8.00 (4H, d,  $J_o=8.5$  Hz, H-2', 6'), 7.84 (2H, d,  $J_{trans}=14.5$  Hz, H-3), 7.51 (2H, d,  $J_{5'',4''}=4.9$  Hz, H-5''), 7.43 (4H, m, H-2, 3''), 7.13 (2H, t,  $J_{4'',5''}=4.9$  Hz, H-4''), 7.03 (4H, d,  $J_o=8.6$  Hz, H-3', 5'), 4.29 (4H, t,  $J_{vic}=5.8$  Hz,  $OCH_2CH_2$ ), 2.08 (2H, t,  $J_{vic}=5.8$  Hz,  $OCH_2CH_2$ );  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  186.60 (C-1), 162.48 (C-4'), 139.80 (C-3), 135.73 (C-2''), 131.94 (C-1'), 130.48

(C-2', 6'), 130.25 (C-5''), 129.32 (C-3''), 128.20 (C-4''), 120.10 (C-2), 114.10 (C-3', 5'), 67.28 ( $OCH_2CH_2$ ), 25.20 ( $OCH_2CH_2$ ); MS (ESI):  $m/z$  ( $M+1$ )<sup>+</sup> 501. *Anal.* Calcd for  $C_{29}O_4H_{24}S_2$ : C, 69.6%; H, 4.80%; S, 12.8%; found: C, 69.87%; H, 4.81%; S, 12.85%.

**Synthesis of (2*E*,2'*E*)-1,1'-(4,4'-(butane-1,4-diylbis(oxy))bis(4,1-phenylene))bis(3-(thiophen-2-yl)prop-2-en-1-one 3b.** The compound **3b** was obtained by reacting **2a** (2.0 g, 0.0086957 mol) with 1,4-dibromobutane (0.9391 g, 0.00434783 mol) under similar conditions as described for **3a**.

Table 1

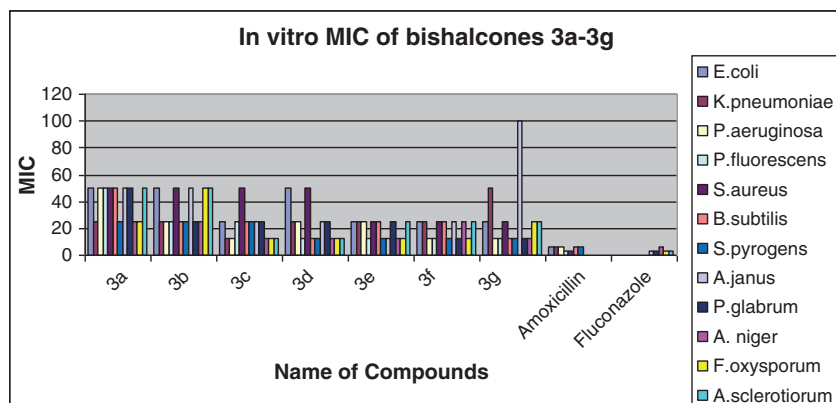
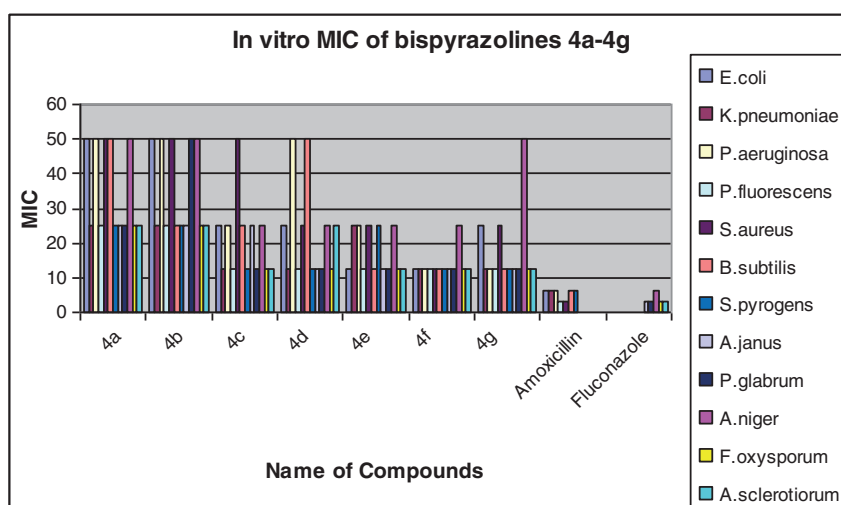
MIC ( $\mu\text{g/mL}$ ) of bischalcones **3a–3g**.

Compound no.	Gram-negative bacteria				Gram-positive bacteria				Fungi			
	<i>E. coli</i>	<i>K. pneumoniae</i>	<i>P. aeruginosa</i>	<i>P. fluorescens</i>	<i>S. aureus</i>	<i>B. subtilis</i>	<i>S. pyogenes</i>	<i>A. janus</i>	<i>P. glabrum</i>	<i>A. niger</i>	<i>F. oxysporum</i>	<i>A. sclerotiorum</i>
<b>3a</b>	50	25	50	50	50	50	25	50	50	25	25	50
<b>3b</b>	50	25	25	50	50	25	25	50	25	25	50	50
<b>3c</b>	25	<b>12.5</b>	<b>12.5</b>	25	50	25	25	25	25	<b>12.5</b>	<b>12.5</b>	<b>12.5</b>
<b>3d</b>	50	25	25	<b>12.5</b>	50	<b>12.5</b>	<b>12.5</b>	25	25	<b>12.5</b>	<b>12.5</b>	<b>12.5</b>
<b>3e</b>	25	25	25	<b>12.5</b>	25	25	<b>12.5</b>	<b>12.5</b>	25	<b>12.5</b>	<b>12.5</b>	25
<b>3f</b>	25	25	12.5	<b>12.5</b>	25	25	<b>12.5</b>	25	<b>12.5</b>	25	<b>12.5</b>	25
<b>3g</b>	25	50	12.5	<b>12.5</b>	25	<b>12.5</b>	<b>12.5</b>	100	<b>12.5</b>	<b>12.5</b>	25	25
Amoxicillin	6.25	6.25	6.25	3.12	3.12	6.25	6.25	—	—	—	—	—
Fluconazole	—	—	—	—	—	—	—	3.12	3.12	6.25	3.12	3.12

Table 2

MIC ( $\mu\text{g/mL}$ ) of bispyrazolines **4a–4g**.

Compound no.	Gram-negative bacteria				Gram-positive bacteria				Fungi			
	<i>E. coli</i>	<i>K. pneumoniae</i>	<i>P. aeruginosa</i>	<i>P. fluorescens</i>	<i>S. aureus</i>	<i>B. subtilis</i>	<i>S. pyogenes</i>	<i>A. janus</i>	<i>P. glabrum</i>	<i>A. niger</i>	<i>F. oxysporum</i>	<i>A. sclerotiorum</i>
<b>4a</b>	50	25	50	25	50	50	25	25	25	50	25	25
<b>4b</b>	50	25	50	25	50	25	25	25	50	50	25	25
<b>4c</b>	25	<b>12.5</b>	25	<b>12.5</b>	50	25	<b>12.5</b>	25	<b>12.5</b>	25	<b>12.5</b>	<b>12.5</b>
<b>4d</b>	25	<b>12.5</b>	50	<b>12.5</b>	25	50	<b>12.5</b>	<b>12.5</b>	<b>12.5</b>	25	<b>12.5</b>	25
<b>4e</b>	<b>12.5</b>	25	25	<b>12.5</b>	25	<b>12.5</b>	25	<b>12.5</b>	<b>12.5</b>	25	<b>12.5</b>	<b>12.5</b>
<b>4f</b>	<b>12.5</b>	<b>12.5</b>	<b>12.5</b>	<b>12.5</b>	<b>12.5</b>	<b>12.5</b>	<b>12.5</b>	<b>12.5</b>	<b>12.5</b>	25	<b>12.5</b>	<b>12.5</b>
<b>4g</b>	25	<b>12.5</b>	<b>12.5</b>	<b>12.5</b>	25	<b>12.5</b>	<b>12.5</b>	<b>12.5</b>	<b>12.5</b>	50	<b>12.5</b>	<b>12.5</b>
Amoxicillin	6.25	6.25	6.25	3.12	3.12	6.25	6.25	—	—	—	—	—
Fluconazole	—	—	—	—	—	—	—	3.12	3.12	6.25	3.12	3.12

Figure 1. MIC ( $\mu\text{g/mL}$ ) of bischalcones **3a–3g**.Figure 2. MIC ( $\mu\text{g/mL}$ ) of bispyrazolines **4a–4g**.

**3b**: brown solid; yield 70%; mp: 172–174°C. IR (KBr)  $\text{cm}^{-1}$  1652 (C=O), 1595 (C=C), 2939 and 2874 (methylene C–H), 1238 and 1021 (C–O);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.02 (4H, d,  $J_o = 8.8$  Hz, H-2', 6'), 7.83 (2H, d,  $J_{\text{trans}} = 15.2$  Hz, H-3), 7.61 (2H, d,  $J_{5'',4''} = 5.0$  Hz, H-5''), 7.52 (2H, d,  $J_{3'',4''} = 3.5$  Hz, H-3''), 7.45 (2H, d,  $J_{\text{trans}} = 15.2$  Hz, H-2), 7.11 (2H, dd,  $J = 3.7, 5.0$  Hz, H-4''), 7.01 (4H, d,  $J_o = 8.8$  Hz, H-3', 5'), 4.14 (4H, t,  $J_{\text{vic}} = 5.8$  Hz,  $\text{OCH}_2\text{CH}_2$ ), 1.96 (4H, quintet,  $J_{\text{vic}} = 5.8$  Hz,  $\text{OCH}_2\text{CH}_2$ );  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  186.65 (C-1), 162.45 (C-4'), 139.84 (C-3), 135.69 (C-2''), 131.90 (C-1'), 130.46 (C-2', 6'), 130.21 (C-5''), 129.27 (C-3''), 128.28 (C-4''), 120.13 (C-2), 114.17 (C-3', 5'), 67.37 ( $\text{OCH}_2\text{CH}_2$ ), 25.26 ( $\text{OCH}_2\text{CH}_2$ ); MS (ESI):  $m/z$  ( $M+1$ ) $^+$  515. *Anal.* Calcd for  $\text{C}_{30}\text{O}_4\text{H}_{26}\text{S}_2$ : C, 70.03%; H, 5.05%; S, 12.45%; found: C, 70.31%; H, 5.03%; S, 12.49%.

**Synthesis of (2E,2'E)-1,1'-(4,4'-(pentane-1,5-diylbis(oxy)))bis(4,1-phenylene))bis(3-(thiophen-2-yl)prop-2-en-1-one 3c.** The compound **3c** was synthesized by treating **2a** (2.0 g, 0.0086957 mol) with 1,5-dibromopentane (0.9999 g, 0.00434783 mol) under similar conditions as used for **3a**.

**3c**: brown solid; yield 68%; mp: 155–157°C. IR (KBr)  $\text{cm}^{-1}$  1656 (C=O), 1598, (C=C), 2932 and 2869 (methylene C–H), 1239 and 1027 (C–O);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.01 (4H, d,  $J_o = 8.2$

Hz, H-2', 6'), 7.84 (2H, d,  $J_{\text{trans}} = 15.3$  Hz, H-3), 7.56 (2H, d,  $J_{5'',4''} = 5.0$  Hz, H-5''), 7.48 (2H, d,  $J_{3'',4''} = 3.6$  Hz, H-3''), 7.44 (2H, d,  $J_{\text{trans}} = 15.3$  Hz, H-2), 7.13 (2H, dd,  $J = 3.6, 5.0$  Hz, H-4''), 7.00 (4H, d,  $J_o = 8.2$  Hz, H-3', 5'), 4.11 (4H, t,  $J_{\text{vic}} = 6.2$  Hz,  $\text{OCH}_2\text{CH}_2\text{CH}_2$ ), 1.92 (4H, quintet,  $J_{\text{vic}} = 6.2$  Hz,  $\text{OCH}_2\text{CH}_2\text{CH}_2$ ), 1.64 (2H, quintet,  $J_{\text{vic}} = 6.2$  Hz,  $\text{CH}_2\text{CH}_2\text{CH}_2$ );  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  186.68 (C-1), 162.47 (C-4'), 139.80 (C-3), 135.63 (C-2''), 131.95 (C-1'), 130.49 (C-2', 6'), 130.24 (C-5''), 129.29 (C-3''), 128.22 (C-4''), 120.15 (C-2), 114.12 (C-3', 5'), 67.39 ( $\text{OCH}_2\text{CH}_2\text{CH}_2$ ), 25.28 ( $\text{OCH}_2\text{CH}_2\text{CH}_2$ ), 25.19 ( $\text{CH}_2\text{CH}_2\text{CH}_2$ ); MS (ESI):  $m/z$  ( $M+Na$ ) $^+$  551. *Anal.* Calcd for  $\text{C}_{31}\text{O}_4\text{H}_{28}\text{S}_2$ : C, 70.45%; H, 5.30%; S, 12.12%; found: C, 70.17%; H, 5.28%; S, 12.16%.

**Synthesis of (2E,2'E)-1,1'-(4,4'-(hexane-1,6-diylbis(oxy)))bis(4,1-phenylene))bis(3-(thiophen-2-yl)prop-2-en-1-one 3d.** The compound **3d** was prepared by reacting **2a** (2.0 g, 0.0086957 mol) with 1,6-dibromohexane (1.06086 g, 0.00434783 mol) under similar conditions as described for **3a**.

**3d**: brown solid; yield 72%; mp: 197–199°C, IR (KBr)  $\text{cm}^{-1}$  1657 (C=O), 1602 (C=C), 2930 and 2852 (methylene C–H), 1237 and 1028 (C–O);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.01 (4H, d,  $J_o = 8.8$  Hz, H-2', 6'), 7.93 (2H, d,  $J_{\text{trans}} = 15.2$  Hz, H-3), 7.40 (2H, d,  $J_{5'',4''} = 5.0$  Hz,



H-5''), 7.35 (2H, d,  $J_{3'',4''}=3.5$  Hz, H-3''), 7.32 (2H, d,  $J_{trans}=15.2$  Hz, H-2), 7.08 (2H, dd,  $J=3.5, 5.0$  Hz, H-4''), 6.97 (4H, d,  $J_o=8.8$  Hz, H-3', 5'), 4.06 (4H, t,  $J_{vic}=6.4$  Hz,  $OCH_2CH_2CH_2$ ), 1.87 (4H, quintet,  $J_{vic}=6.4$  Hz,  $OCH_2CH_2CH_2$ ), 1.58 (4H, quintet,  $J_{vic}=6.4$  Hz,  $CH_2CH_2CH_2$ );  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  186.69 (C-1), 162.26 (C-4'), 140.68 (C-3), 136.47 (C-2''), 131.86 (C-1'), 130.23 (C-5''), 130.39 (C-2', 6'), 128.51 (C-3''), 128.38 (C-4''), 120.27 (C-2), 114.37 (C-3', 5'), 67.83 ( $OCH_2CH_2CH_2$ ), 29.13 ( $OCH_2CH_2CH_2$ ), 25.90 ( $CH_2CH_2CH_2$ ); MS (ESI):  $m/z$  (M+Na) $^+$  565. *Anal.* Calcd for  $C_{32}O_4H_{30}S_2$ : C, 70.84%; H, 5.53%; S, 11.80; found: C, 71.12%; H, 5.51%; S, 11.76%.

**Synthesis of (2*E*,2'*E*)-1,1'-(4,4'-(octane-1,8-diylbis(oxy)))bis(4,1-phenylene))bis(3-(thiophen-2-yl)prop-2-en-1-one 3e.** The compound **3e** was obtained from the reaction of **2a** (2.0 g, 0.0086957 mol) with 1,8-dibromooctane (1.18260 g, 0.00434783) under similar conditions as used for **3a**.

**3e**: yellow solid; yield 78%; mp: 140–142°C, IR (KBr)  $cm^{-1}$  1658 (C=O), 1597 (C=C), 2940 and 2858 (methylene C–H), 1239 and 1020 (C–O);  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  7.99 (4H, d,  $J_o=8.6$  Hz, H-2', 6'), 7.91 (2H, d,  $J_{trans}=14.9$  Hz, H-3), 7.52 (2H, d,  $J_{5'',4''}=4.5$  Hz, H-5''), 7.45 (4H, m, H-2, 3''), 7.12 (2H, d,  $J_{4'',5''}=4.5$  Hz, H-4''), 6.98 (4H, d,  $J_o=8.6$  Hz, H-3', 5'), 4.02 (4H, t,  $J_{vic}=6.6$  Hz,  $OCH_2CH_2CH_2CH_2$ ), 1.81 (4H, quintet,  $J_{vic}=6.6$  Hz,  $OCH_2CH_2CH_2CH_2$ ), 1.42 (8H, m,  $CH_2CH_2CH_2CH_2$ );  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  186.60 (C-1), 162.56 (C-4'), 139.82 (C-3), 135.64 (C-2''), 131.49 (C-1'), 130.24 (C-2', 6'), 130.05 (C-5''), 128.63 (C-3''), 128.05 (C-4''), 120.05 (C-2), 113.96 (C-3', 5'), 67.70 ( $OCH_2CH_2CH_2CH_2$ ), 28.65 ( $OCH_2CH_2CH_2CH_2$ ), 28.49 ( $OCH_2CH_2CH_2CH_2$ ), 25.34 ( $OCH_2CH_2CH_2CH_2$ ); MS (ESI):  $m/z$  (M) $^+$  570. *Anal.* Calcd for  $C_{34}O_4H_{34}S_2$ : C, 71.57%; H, 5.96%; S, 11.22%; found: C, 71.85%; H, 5.94%; S, 11.26%.

**Synthesis of (2*E*,2'*E*)-1,1'-(4,4'-(decane-1,10-diylbis(oxy)))bis(4,1-phenylene))bis(3-(thiophen-2-yl)prop-2-en-1-one 3f.** The bischalcone **3f** was synthesized by reacting **2a** (2.0 g, 0.0086957 mol) with 1,10-dibromodecane (1.3046 g, 0.00434783 mol) under similar conditions as described for **3a**.

**3f**: brown solid; yield 75%; mp: 118–120°C, IR (KBr)  $cm^{-1}$  1661 (C=O), 1594 (C=C), 2938 and 2878 (methylene C–H), 1245 and 1028 (C–O);  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  8.00 (4H, d,  $J_o=8.4$  Hz, H-2', 6'), 7.94 (4H, m, H-3, 5''), 7.53 (2H, d,  $J_{3'',4''}=3.8$  Hz, H-3''), 7.43 (2H, d,  $J_{trans}=15.0$  Hz, H-2), 7.12 (2H, d,  $J_{4'',3''}=3.8$  Hz, H-4''), 6.98 (4H, d,  $J_o=8.4$  Hz, H-3', 5'), 4.00 (4H, t,  $J_{vic}=6.1$  Hz,  $OCH_2CH_2CH_2CH_2CH_2$ ), 1.78 (4H, quintet,  $J_{vic}=6.1$  Hz,  $OCH_2CH_2CH_2CH_2CH_2$ ), 1.35 (12H, m,  $CH_2CH_2CH_2CH_2CH_2$ );  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  186.66 (C-1), 162.50 (C-4'), 139.80 (C-3), 135.67 (C-2''), 131.50 (C-1'), 130.26 (C-2', 6'), 130.15 (C-5''), 128.69 (C-3''), 128.09 (C-4''), 120.23 (C-2), 113.99 (C-3', 5'), 67.56 ( $OCH_2CH_2CH_2CH_2CH_2$ ), 28.60 ( $OCH_2CH_2CH_2CH_2CH_2$ ), 28.52 ( $OCH_2CH_2CH_2CH_2CH_2$ ), 25.30 ( $OCH_2CH_2CH_2CH_2CH_2$ ), 25.12 ( $OCH_2CH_2CH_2CH_2CH_2$ ); MS (ESI):  $m/z$  (M+H) $^+$  599. *Anal.* Calcd for  $C_{36}O_4H_{38}S_2$ : C, 72.24%; H, 6.35%; S, 10.70%; found: C, 71.96%; H, 6.33%; S, 10.74%.

**Synthesis of (2*E*,2'*E*)-1,1'-(4,4'-(dodecane-1,12-diylbis(oxy)))bis(4,1-phenylene))bis(3-(thiophen-2-yl)prop-2-en-1-one 3g.** The bischalcone **3g** was prepared by treating **2a** (2.0 g, 0.0086957 mol) with 1,12-dibromododecane (1.4260 g, 0.004347 mol) under similar conditions as used for **3a**.

**3g**: brown solid; yield 80%; mp: 130–132°C, IR (KBr)  $cm^{-1}$  1654 (C=O), 1595 (C=C), 2920 and 2855 (methylene C–H), 1238 and 1022 (C–O);  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  8.00 (4H, d,  $J_o=8.8$  Hz, H-2', 6'), 7.93 (2H, d,  $J_{trans}=15.3$  Hz, H-3), 7.40

(2H, d,  $J_{5'',4''}=5.0$  Hz, H-5''), 7.36 (2H, d,  $J_{trans}=15.3$  Hz, H-2), 7.33 (2H, d,  $J_{3'',4''}=3.7$  Hz, H-3''), 7.08 (2H, dd,  $J=3.7, 5.1$  Hz, H-4''), 6.96 (4H, d,  $J_o=8.8$  Hz, H-3', 5'), 4.03 (4H, t,  $J_{vic}=6.5$  Hz,  $OCH_2CH_2CH_2CH_2CH_2CH_2$ ), 1.81 (4H, quintet,  $J_{vic}=6.5$  Hz,  $OCH_2CH_2CH_2CH_2CH_2CH_2$ ), 1.47 (4H, quintet,  $J_{vic}=5.6$  Hz,  $CH_2CH_2CH_2CH_2CH_2CH_2$ ), 1.33 (12H, m,  $OCH_2CH_2CH_2CH_2CH_2CH_2$ );  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  186.86 (C-1), 162.44 (C-4'), 139.78 (C-3), 135.57 (C-2''), 131.61 (C-1'), 130.22 (C-2', 6'), 130.19 (C-5''), 128.79 (C-3''), 128.29 (C-4''), 120.33 (C-2), 113.66 (C-3', 5'), 67.78 ( $OCH_2CH_2CH_2CH_2CH_2CH_2$ ), 29.64 ( $OCH_2CH_2CH_2CH_2CH_2CH_2$ ), 28.82 ( $OCH_2CH_2CH_2CH_2CH_2CH_2$ ), 25.39 ( $OCH_2CH_2CH_2CH_2CH_2CH_2$ ), 25.19 ( $OCH_2CH_2CH_2CH_2CH_2CH_2$ ), 25.00 ( $OCH_2CH_2CH_2CH_2CH_2CH_2$ ); MS (ESI):  $m/z$  (M+Na) $^+$  649. *Anal.* Calcd for  $C_{38}O_4S_2H_{42}$ : C, 72.84%; H, 6.70%; S, 10.22%; found: C, 73.13%; H, 6.72%; S, 10.26%.

**Synthesis of 1,3-bis[3-(4-phenyl)-4,5-dihydro-1-phenyl-5-(thiophen-2-yl)-1*H*-pyrazole]propane 4a.** A mixture of **3a** (1.0 g, 0.001929 mol) and phenyl hydrazine (0.4183 g, 0.0038839 mol) in dry EtOH (30 mL) was refluxed for 8 h. The progress of reaction was monitored by TLC. The resulting reaction mixture was concentrated *in vacuo* to obtain a solid compound, which was further crystallized from  $CH_3OH$  to yield pure compound **4a**.

**4a**: brown solid; yield 62%; mp: 99–101°C, IR (KBr)  $cm^{-1}$  1593 (C=N), 2945 and 2840 (methylene C–H), 1242 and 1025 (C–O);  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  7.63 (4H, d,  $J_o=8.6$  Hz, H-2'', 6''), 7.33 (2H, d,  $J_{3'',4''}=3.7$  Hz, H-3''), 7.22 (2H, d,  $J_{5'',4''}=5.0$  Hz, H-5''), 7.12 (6H, m, H-3', 4', 5'), 6.99 (4H, d,  $J_o=8.6$  Hz, H-3'', 5''), 6.89 (2H, dd,  $J=3.7, 5.0$  Hz, H-4''), 6.70 (4H, t,  $J=7.2$  Hz, H-2', 6'), 5.60 (2H, dd,  $J_{XA}=6.2$  Hz,  $J_{XM}=11.8$  Hz,  $H_X$ ), 4.02 (4H, t,  $J_{vic}=5.8$  Hz,  $OCH_2CH_2$ ), 3.82 (2H, dd,  $J=11.8, 17.2$  Hz,  $H_M$ ), 3.19 (2H, dd,  $J_{AX}=6.2$  Hz,  $J_{AM}=17.2$  Hz,  $H_A$ ), 2.50 (4H, quintet,  $J_{vic}=5.8$  Hz,  $OCH_2CH_2$ );  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  160.15 (C-4'''), 154.26 (C-3), 145.15 (C-1'), 147.34 (C-2''), 144.87 (C-1'''), 128.03 (C-5''), 127.55 (C-3''), 126.26 (C-4''), 126.30 (C-2''', 6'''), 124.68 (C-3', 5'), 118.60 (C-4'), 114.90 (C-3''', 5'''), 113.77 (C-2', 6'), 67.10 ( $OCH_2CH_2$ ), 59.41 (C-5), 43.39 (C-4), 24.47 ( $OCH_2CH_2$ ); MS (ESI):  $m/z$  (M+Na) $^+$  671. *Anal.* Calcd for  $C_{41}O_2N_4H_{36}S_2$ : C, 72.35%; H, 5.29%; N, 8.23%; S, 9.41%; found: C, 72.63%; H, 5.27%; N, 8.23%; S, 9.41%.

**Synthesis of 1,4-bis[3-(4-phenyl)-4,5-dihydro-1-phenyl-5-(thiophen-2-yl)-1*H*-pyrazole]butane 4b.** The compound **4b** was synthesized from the reaction of bischalcone **3b** (1.0 g, 0.00195 mol) with phenyl hydrazine (0.4212 g, 0.0039 mol) under similar conditions as described earlier for **4a**.

**4b**: yellow solid; yield 68%; mp: 145–147°C, IR (KBr)  $cm^{-1}$  1597 (C=N), 2925 and 2871 (methylene C–H), 1238 and 1019 (C–O);  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  7.67 (4H, d,  $J_o=8.6$  Hz, H-2'', 6''), 7.30 (2H, d,  $J_{3'',4''}=3.7$  Hz, H-3''), 7.17 (2H, d,  $J_{5'',4''}=5.0$  Hz, H-5''), 7.09 (6H, m, H-3', 4', 5'), 6.95 (4H, d,  $J_o=8.6$  Hz, H-3'', 5''), 6.92 (2H, dd,  $J=3.7, 5.0$  Hz, H-4''), 6.73 (4H, t,  $J=7.2$  Hz, H-2', 6'), 5.67 (2H, dd,  $J_{XA}=6.2$  Hz,  $J_{XM}=11.8$  Hz,  $H_X$ ), 4.09 (4H, brs,  $OCH_2CH_2$ ), 3.86 (2H, dd,  $J=11.8, 17.2$  Hz,  $H_M$ ), 3.21 (2H, dd,  $J_{AX}=6.2$  Hz,  $J_{AM}=17.2$  Hz,  $H_A$ ), 2.52 (4H, brs,  $OCH_2CH_2$ );  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  160.12 (C-4'''), 155.56 (C-3), 147.50 (C-2''), 145.85 (C-1'), 144.77 (C-1'''), 128.53 (C-5''), 127.15 (C-3''), 126.78 (C-2''', 6'''), 126.66 (C-4''), 124.48 (C-3', 5'), 118.70 (C-4'), 114.40 (C-3''', 5'''), 113.27 (C-2', 6'), 67.13 ( $OCH_2CH_2$ ), 59.47 (C-5), 43.41 (C-4), 25.37 ( $OCH_2CH_2$ ); MS (ESI):  $m/z$  (M+Na) $^+$  685. *Anal.* Calcd for  $C_{42}O_2N_4H_{38}S_2$ : C, 72.62%; H, 5.47%; N, 8.07%; S, 9.22%; found: C, 72.91%; H, 5.49%; N, 8.10%; S, 9.25%.

**Synthesis of 1,5-bis[3-(4-phenyl)-4,5-dihydro-1-phenyl-5-(thiophen-2-yl)-1H-pyrazole]pentane 4c.** The compound **4c** was prepared from the reaction of bischalcone **3c** (1.0 g, 0.00189 mol) with phenyl hydrazine (0.40824 g, 0.00378 mol) under similar conditions as described earlier for **4a**.

**4c:** brown solid; yield 65%; mp: 125–127°C, IR (KBr)  $\text{cm}^{-1}$  1592 (C=N), 2930 and 2869 (methylene C–H), 1234 and 1026 (C–O);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.68 (4H, d,  $J_{\text{p,o}}=8.6$  Hz, H-2'', 6''), 7.32 (2H, d,  $J_{3'',4''}=3.7$  Hz, H-3''), 7.19 (2H, d,  $J_{5'',4''}=5.0$  Hz, H-5''), 7.02 (6H, m, H-3', 4', 5'), 6.92 (4H, d,  $J_{\text{o}}=8.6$  Hz, H-3'', 5''), 6.90 (2H, dd,  $J=3.7, 5.0$  Hz, H-4''), 6.79 (4H, t,  $J=7.2$  Hz, H-2', 6'), 5.62 (2H, dd,  $J_{\text{XA}}=6.2$  Hz,  $J_{\text{XM}}=11.8$  Hz,  $\text{H}_\text{X}$ ), 4.03 (4H, t,  $J_{\text{vic}}=6.0$  Hz,  $\text{OCH}_2\text{CH}_2\text{CH}_2$ ), 3.81 (2H, dd,  $J=11.8$  Hz,  $J_{\text{MA}}=17.2$  Hz,  $\text{H}_\text{M}$ ), 3.24 (2H, dd,  $J_{\text{AX}}=6.2$  Hz,  $J_{\text{AM}}=17.2$  Hz,  $\text{H}_\text{A}$ ), 2.32 (4H, quintet,  $J_{\text{vic}}=6.0$  Hz,  $\text{OCH}_2\text{CH}_2\text{CH}_2$ ), 1.58 (2H, m,  $\text{OCH}_2\text{CH}_2\text{CH}_2$ );  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  160.19 (C-4''), 155.50 (C-3), 147.67 (C-2''), 145.80 (C-1'), 144.70 (C-1''), 128.59 (C-5''), 127.19 (C-3''), 126.67 (C-2'', 6''), 126.60 (C-4''), 124.03 (C-3', 5'), 118.79 (C-4'), 114.48 (C-3'', 5''), 113.45 (C-2', 6'), 67.10 ( $\text{OCH}_2\text{CH}_2\text{CH}_2$ ), 59.49 (C-5), 43.47 (C-4), 28.39 ( $\text{OCH}_2\text{CH}_2\text{CH}_2$ ), 25.67 ( $\text{OCH}_2\text{CH}_2\text{CH}_2$ ); MS (ESI):  $m/z$  ( $\text{M}+\text{H}$ ) $^+$  677. *Anal.* Calcd for  $\text{C}_{43}\text{O}_2\text{N}_4\text{H}_{40}\text{S}_2$ : C, 72.88%; H, 5.64%; N, 7.90%; S, 9.03%; found: C, 72.59%; H, 5.62%; N, 7.93%; S, 9.06%.

**Synthesis of 1,6-bis[3-(4-phenyl)-4,5-dihydro-1-phenyl-5-(thiophen-2-yl)-1H-pyrazole]hexane 4d.** The compound **4c** was obtained by treating bischalcone **3d** (1.0 g, 0.00185 mol) with phenyl hydrazine (0.3996 g, 0.00370 mol) under similar conditions as described earlier for **4a**.

**4d:** yellow solid; yield 61%; mp: 166–168°C, IR (KBr)  $\text{cm}^{-1}$  1599 (C=N), 2937 and 2876 (methylene C–H), 1240 and 1018 (C–O);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.66 (4H, d,  $J_{\text{o}}=8.8$  Hz, H-2'', 6''), 7.40 (2H, d,  $J_{3'',4''}=3.8$  Hz, H-3''), 7.24 (2H, d,  $J_{5'',4''}=5.2$  Hz, H-5''), 7.10 (6H, m, H-3', 4', 5'), 6.93 (2H, dd,  $J=3.8, 5.2$  Hz, H-4''), 6.88 (2H, d,  $J_{\text{o}}=8.8$  Hz, H-3'', 5''), 6.73 (4H, t,  $J=8.7$  Hz, H-2', 6'), 5.59 (2H, dd,  $J_{\text{XA}}=6.7$  Hz,  $J_{\text{XM}}=12.2$  Hz,  $\text{H}_\text{X}$ ), 4.00 (4H, t,  $J_{\text{vic}}=6.0$  Hz,  $\text{OCH}_2\text{CH}_2\text{CH}_2$ ), 3.85 (2H, dd,  $J_{\text{MX}}=12.2$  Hz,  $J_{\text{MA}}=17.4$  Hz,  $\text{H}_\text{M}$ ), 3.23 (2H, dd,  $J_{\text{AX}}=6.6$  Hz,  $J_{\text{AM}}=17.4$  Hz,  $\text{H}_\text{A}$ ), 1.56 (4H, quintet,  $J_{\text{vic}}=6.0$  Hz,  $\text{OCH}_2\text{CH}_2\text{CH}_2$ ), 1.51 (4H, quintet,  $J_{\text{vic}}=6.0$  Hz,  $\text{OCH}_2\text{CH}_2\text{CH}_2$ );  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  160.39 (C-4''), 155.58 (C-3), 147.73 (C-2''), 145.95 (C-1'), 144.86 (C-1''), 128.78 (C-5''), 127.14 (C-3''), 126.69 (C-4''), 126.43 (C-2'', 6''), 124.60 (C-3', 5'), 118.91 (C-4'), 114.62 (C-3'', 5''), 113.48 (C-2', 6'), 67.23 ( $\text{OCH}_2\text{CH}_2\text{CH}_2$ ), 59.59 (C-5), 43.50 (C-4), 28.43 ( $\text{OCH}_2\text{CH}_2\text{CH}_2$ ), 25.70 ( $\text{OCH}_2\text{CH}_2\text{CH}_2$ ); MS (ESI):  $m/z$  ( $\text{M}+\text{Na}$ ) $^+$  713. *Anal.* Calcd for  $\text{C}_{44}\text{O}_2\text{N}_4\text{H}_{42}\text{S}_2$ : C, 73.13%; H, 5.82%; N, 7.76%; S, 8.86%; found: C, 72.83%; H, 5.84%; N, 7.73%; S, 8.89%.

**Synthesis of 1,8-bis[3-(4-phenyl)-4,5-dihydro-1-phenyl-5-(thiophen-2-yl)-1H-pyrazole]octane 4e.** The compound **4c** was prepared from the reaction of bischalcone **3e** (1.0 g, 0.00175 mol) with phenyl hydrazine (0.378 g, 0.0035 mol) under similar conditions as used earlier for **4a**.

**4e:** yellow solid; yield 70%; mp: 152–154°C, IR (KBr)  $\text{cm}^{-1}$  1595 (C=N), 2920 and 2858 (methylene C–H), 1241 and 1034 (C–O);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.60 (4H, d,  $J_{\text{o}}=8.2$  Hz, H-2'', 6''), 7.38 (2H, d,  $J_{3'',4''}=3.8$  Hz, H-3''), 7.23 (2H, d,  $J_{5'',4''}=4.9$  Hz, H-5''), 7.10 (6H, m, H-3', 4', 5'), 6.92 (2H, dd,  $J=3.8, 4.9$  Hz, H-4''), 6.86 (4H, d,  $J_{\text{o}}=8.2$  Hz, H-3'', 5''), 6.74 (4H, t,  $J=7.0$  Hz, H-2', 6'), 5.58 (2H, dd,  $J_{\text{XA}}=6.8$  Hz,  $J_{\text{XM}}=12.2$  Hz,  $\text{H}_\text{X}$ ), 3.99 (4H, t,  $J_{\text{vic}}=6.1$  Hz,  $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ ), 3.83 (2H, dd,  $J_{\text{MX}}=12.2$  Hz,  $J_{\text{MA}}=16.5$  Hz,  $\text{H}_\text{M}$ ), 3.22 (2H, dd,  $J_{\text{AX}}=6.8$  Hz,  $J_{\text{AM}}=16.5$  Hz,  $\text{H}_\text{A}$ ), 1.78 (4H, quintet,  $J_{\text{vic}}=6.1$  Hz,  $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ ), 1.48 (4H, quintet,  $J_{\text{vic}}=6.1$

Hz,  $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ ), 1.41 (4H, m,  $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ );  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  160.50 (C-4''), 155.78 (C-3), 147.71 (C-2''), 145.90 (C-1'), 144.80 (C-1''), 128.56 (C-5''), 127.11 (C-3''), 126.60 (C-4''), 126.48 (C-2'', 6''), 124.59 (C-3', 5'), 118.99 (C-4'), 114.69 (C-3'', 5''), 113.50 (C-2', 6'), 67.45 ( $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ ), 59.74 (C-5), 43.62 (C-4), 28.49 ( $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ ), 25.79 ( $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ ), 25.19 ( $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ ); MS (ESI):  $m/z$  ( $\text{M}$ ) $^+$  718. *Anal.* Calcd for  $\text{C}_{46}\text{O}_2\text{N}_4\text{H}_{46}\text{S}_2$ : C, 73.60%; H, 6.13%; N, 7.46%; S, 8.53%; found: C, 73.89%; H, 6.15%; N, 7.43%; S, 8.49%.

**Synthesis of 1,10-bis[3-(4-phenyl)-4,5-dihydro-1-phenyl-5-(thiophen-2-yl)-1H-pyrazole]decane 4f.** The compound **4c** was obtained from the reaction of bischalcone **3f** (1.0 g, 0.00167 mol) with phenyl hydrazine (0.3607 g, 0.00334 mol) under similar conditions as used earlier for **4a**.

**4f:** yellow solid; yield 60%; mp: 126–128°C, IR (KBr)  $\text{cm}^{-1}$  1593 (C=N), 2929 and 2857 (methylene C–H), 1230 and 1021 (C–O);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.64 (4H, d,  $J_{\text{o}}=8.7$  Hz, H-2'', 6''), 7.34 (2H, d,  $J_{3'',4''}=3.6$  Hz, H-3''), 7.19 (2H, d,  $J_{5'',4''}=5.2$  Hz, H-5''), 7.10 (6H, m, H-3', 4', 5'), 6.94 (2H, dd,  $J=3.6, 5.2$  Hz, H-4''), 6.92 (4H, d,  $J_{\text{o}}=8.7$  Hz, H-3'', 5''), 6.75 (4H, t,  $J=7.0$  Hz, H-2', 6'), 5.56 (2H, dd,  $J_{\text{XA}}=6.9$  Hz,  $J_{\text{XM}}=11.5$  Hz,  $\text{H}_\text{X}$ ), 3.98 (4H, t,  $J_{\text{vic}}=6.3$  Hz,  $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ ), 3.82 (2H, dd,  $J_{\text{MX}}=11.8$  Hz,  $J_{\text{MA}}=17.0$  Hz,  $\text{H}_\text{M}$ ), 3.20 (2H, dd,  $J_{\text{AX}}=6.9$  Hz,  $J_{\text{AM}}=17.0$  Hz,  $\text{H}_\text{A}$ ), 1.79 (4H, quintet,  $J_{\text{vic}}=6.3$  Hz,  $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ ), 1.46 (4H, quintet,  $J_{\text{vic}}=6.3$  Hz,  $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ ), 1.35 (8H, m,  $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ );  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  159.35 (C-4''), 156.23 (C-3), 145.79 (C-1'), 145.62 (C-2''), 144.88 (C-1''), 128.38 (C-5''), 126.90 (C-3''), 126.43 (C-4''), 125.97 (C-2'', 6''), 124.46 (C-3', 5'), 118.74 (C-4'), 114.15 (C-2', 6'), 113.19 (C-3'', 5''), 67.47 ( $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ ), 59.73 (C-5), 43.54 (C-4), 28.84 ( $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ ), 28.72 ( $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ ), 28.61 ( $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ ), 25.42 ( $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ ); MS (ESI):  $m/z$  ( $\text{M}+1$ ) $^+$  747. *Anal.* Calcd for  $\text{C}_{48}\text{O}_2\text{N}_4\text{H}_{50}\text{S}_2$ : C, 74.03%; H, 6.42%; N, 7.20%; S, 8.22%; found: C, 74.32%; H, 6.39%; N, 7.22%; S, 8.25%.

**Synthesis of 1,12-bis[3-(4-phenyl)-4,5-dihydro-1-phenyl-5-(thiophen-2-yl)-1H-pyrazole]dodecane 4g.** The compound **4c** was synthesized from the reaction of bischalcone **3g** (1.0 g, 0.0016 mol) with phenyl hydrazine (0.3456 g, 0.0032 mol) under similar conditions as described earlier for **4a**.

**4g:** orange solid; yield 63%; mp: 110–112°C, IR (KBr)  $\text{cm}^{-1}$  1596 (C=N), 2923 and 2875 (methylene C–H), 1238 and 1029 (C–O);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.66 (4H, d,  $J_{\text{o}}=8.8$  Hz, H-2'', 6''), 7.24 (2H, dd,  $J=3.7, 0.8$  Hz, H-3''), 7.16 (2H, d,  $J_{5'',4''}=5.2$  Hz, H-5''), 7.04 (6H, m, H-3', 4', 5'), 6.98 (4H, d,  $J_{\text{o}}=8.8$  Hz, H-3'', 5''), 6.90 (2H, dd,  $J=3.7, 5.5$  Hz, H-4''), 6.74 (4H, t,  $J=7.2$  Hz, H-2', 6'), 5.60 (2H, dd,  $J_{\text{XA}}=6.6$  Hz,  $J_{\text{XM}}=11.8$  Hz,  $\text{H}_\text{X}$ ), 3.98 (4H, t,  $J_{\text{vic}}=6.4$  Hz,  $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ ), 3.84 (2H, dd,  $J_{\text{MX}}=11.8$  Hz,  $J_{\text{MA}}=17.2$  Hz,  $\text{H}_\text{M}$ ), 3.21 (2H, dd,  $J_{\text{AX}}=6.6$  Hz,  $J_{\text{AM}}=17.2$  Hz,  $\text{H}_\text{A}$ ), 1.78 (4H, quintet,  $J_{\text{vic}}=6.4$  Hz,  $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ ), 1.45 (4H, quintet,  $J_{\text{vic}}=6.4$  Hz,  $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ ), 1.30 (12H, m,  $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ );  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  160.45 (C-4''), 155.42 (C-3), 145.53 (C-2''), 145.78 (C-1'), 144.79 (C-1''), 128.43 (C-5''), 126.98 (C-3''), 126.58 (C-4''), 124.61 (C-2'', 6''), 124.16 (C-3', 5'), 118.70 (C-4'), 114.22 (C-2', 6'), 113.21 (C-3'', 5''), 67.38 ( $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ ), 59.62 (C-5), 43.25 (C-4), 28.94 ( $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ ), 28.77 ( $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ ), 28.42 ( $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ ), 28.02 ( $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ ), 25.45 ( $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ ); MS (ESI):  $m/z$  ( $\text{M}+\text{Na}$ ) $^+$  797. *Anal.* Calcd for  $\text{C}_{50}\text{O}_2\text{N}_4\text{H}_{54}\text{S}_2$ :



C, 74.44%; H, 6.70%; N, 6.95%; S, 7.94%; found: C, 74.65%; H, 6.83%; N, 6.82%; S, 8.06%.

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