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New 1,3,4-bisthiadiazolines: Synthesis, characterization and antimicrobial evaluations

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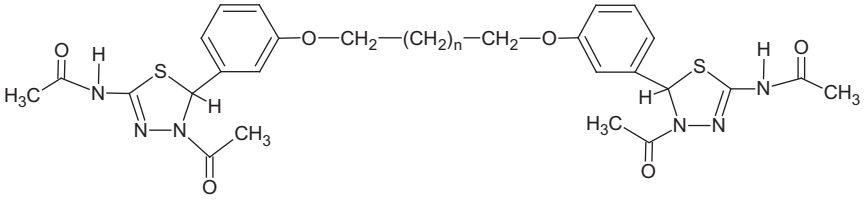
HIGHLIGHTS

- The aliphatic chains linked new bisthiadiazolines have been synthesized.
- These compounds have been prepared from the cyclization reactions of the bisthiosemicarbazones with acetic anhydride.
- All the products have been characterized by using various spectroscopic techniques.
- The antimicrobial activities of these compounds have also been studied.

GRAPHICAL ABSTRACT

New bisthiadiazolines built around the aliphatic chains of varying length has been synthesized. The structures of the intermediates and final bisheterocyclics were determined from the rigorous analysis of their various spectroscopic data. The compounds **3f**, **3g, 4f** & **4g** exhibited significant activity against the tested microorganisms.



4a-4g

n = 0, 2, 3, 4, 6, 8, 10

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ABSTRACT

The bisthiadiazolines **4a**–**4g** have been synthesized in good yields from the cyclization reactions of bisthiosemicarbazones **3a**–**3g** with acetic anhydride. The condensation reaction of dibenzaldehydes **2a**–**2g** with thiosemicarbazide in alcoholic medium provided **3a**–**3g** and former were obtained from the O-alkylation of 3-hydroxybenzaldehyde with suitable 1,ω-dibromoalkanes under alkaline conditions in the presence of dry EtOH/DMF. The intermediates **3a**–**3g** and bishetrocyclics **4a**–**4g** were also screened for their *in vitro* antimicrobial activities against seven bacterial strains (*Klubsellia pneumoniae*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Straphylococcus aureus*, *Bacillius subtilis*, *Pseudomonas fluorescens* and *Streptoccus pyrogens*) and five fungi strains (*Aspergillius janus*, *Pencillium glabrum*, *Fusarium oxysporum*, *Aspergillus sclerotiorum*, *Aspergillus niger*). The compounds **3f**, **3g**, **4f** & **4g** were found to be significantly active against the tested microorganisms.

1. Introduction

Thiadiazolines are the heterocyclic compounds containing three heteroatoms in the five membered ring and these products are of major interest due to their immense biological activities [1]. The syntheses of substituted thiadiazolines [2–4] have attracted the considerable attention in the past decades because these compounds constitute the structural frameworks of several naturally occurring alkanoids that show a wide range of pharmacological behaviors [5]. These derivatives exhibit antifungal [6], anti-inflammatory [7], anticonvulsant [8], antiviral [9], plant growth regulatory [10], hypertensive, central nervous system depressant [11], anticancer [12] and carbonic anhydrase inhibitory [13] activities. By keeping these aspects in view and in continuation of our studies [14a,b] on the bisheterocyclic compounds, present re-

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searches have been focused on the synthesis of new bisthiadiazolines **4a–4g** built around the alkyl chain of varying lengths. The major impetus behind these investigations was to study the effect of the internal spacer length upon the formation and antimicrobial behavior of the final bisheterocyclic compounds.

2. Results and discussion

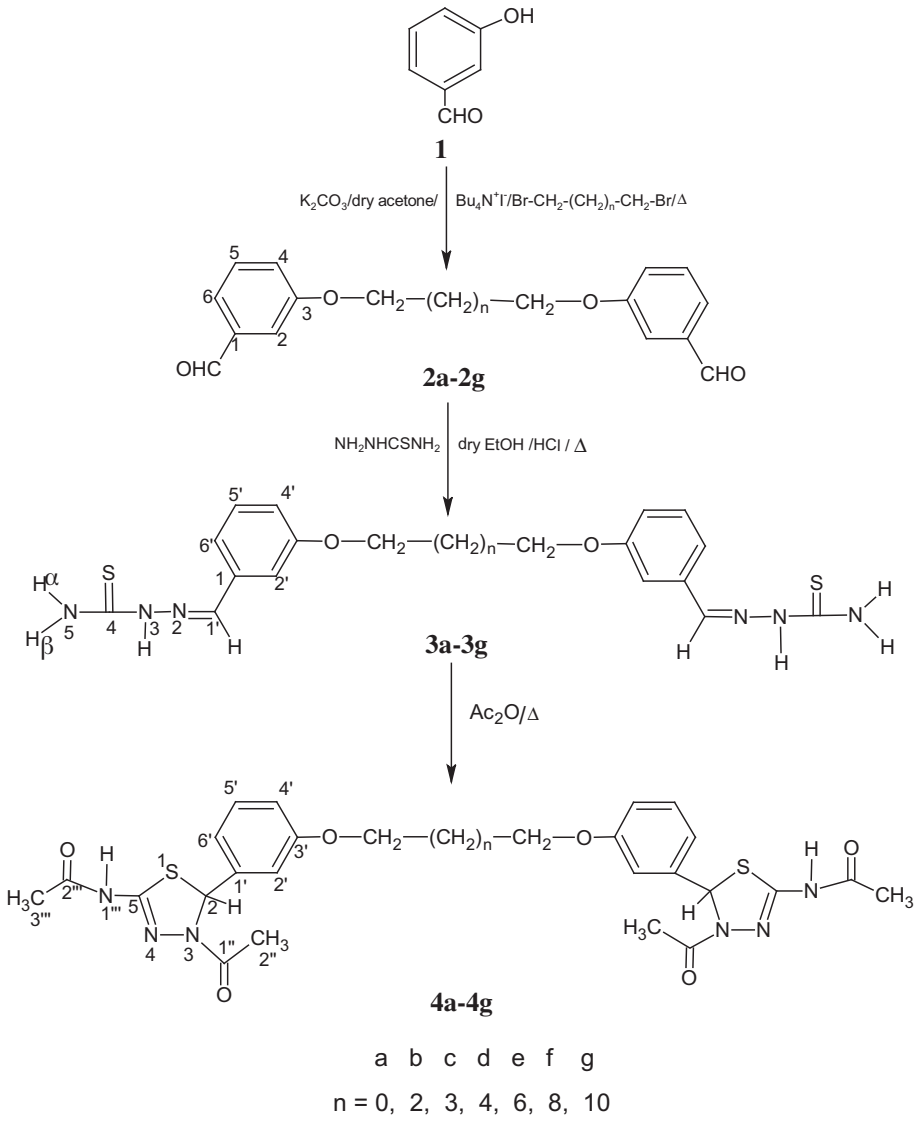
The bisthiadiazolines **4a–4g** required for the present study were obtained starting from 3-hydroxybenzaldehyde **1** which was reacted [15] with suitable 1,ω-dibromoalkanes under refluxing conditions in the presence of dry EtOH/KOH/DMF to yield dibenzaldehydes **2a–2g**. The later were treated with thiosemicarbazide in dry EtOH and catalytic amount of HCl to furnish bisthiosemicarbazones **3a–3g** which were further refluxed in Ac_2O to furnish bisthiadiazolines **4a–4g** in good yields (Scheme 1).

The structures of the prepared compounds **(2a, 2d–2g**, **3a–3g** & **4a–4g)** were based upon their spectroscopic data (IR, ^{1}H NMR, ^{13}C NMR & ESI-MS) and elemental analysis results also confirmed the purity of these products.

IR spectra of dibenzaldehydes **(2a** & **2d–2g)** showed strong absorption bands at 1698–1679 cm^{-1} due to conjugated C=O group along with the two additional bands at 2874–2850 and 2759–2717 cm^{-1} due to aldehyde C–H stretching. In the ^{1}H NMR spectra (400 MHz, DMSO-d_6) of dibenzaldehydes, the signal placed at δ 9.98–9.89 could be ascribed to C***H***O proton. The hydrogens (H-2, 6, 5 & 4) of the phenyl ring were found to be placed at δ 7.86–7.37 (2H, s), 7.49–7.36 (2H, m), 7.46–7.30 (2H, d, J_o = 6.6 Hz) and 7.27–7.09 (2H, m) respectively. The resonances of internal chain OC***H***$_2$ group were placed in the aliphatic region at δ 4.45–3.93. The UV–Vis spectra of **2a** & **2d–2g** had two absorption bands at 340–318 and 275–258 nm which could be ascribed to $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transitions respectively.

^{13}C NMR (100 MHz, DMSO-d_6) spectra of dibenzaldehydes **(2a** & **2d–2g)** proved instrumental to corroborate their proposed structures. The presence of aldehyde group was confirmed by appearance of signal at δ 192.37–192.12 (C=O). The aromatic carbon atoms showed suitable signals at δ 159.72–159.13 (C-3), 137.80–137.51 (C-1), 130.08–129.98 (C-6), 123.56–122.20 (C-5), 122.00–121.16 (C-4) & 113.35–112.59 (C-2); the downfield resonance of C-3 as compared to other carbon atoms can be ascribed to its direct linkage to the electronegative oxygen atom. The resonance placed at δ 68.30–67.60 could be generated by internal chain O***C***H$_2$ group.

In the IR spectra of **3a–3g** noticeable absorption bands were present in the regions at 3398–3368, 3250–3238, 3159–3154



Scheme 1. Synthesis of aliphatic chain linked bisthiadiazolines **4a–4g**.

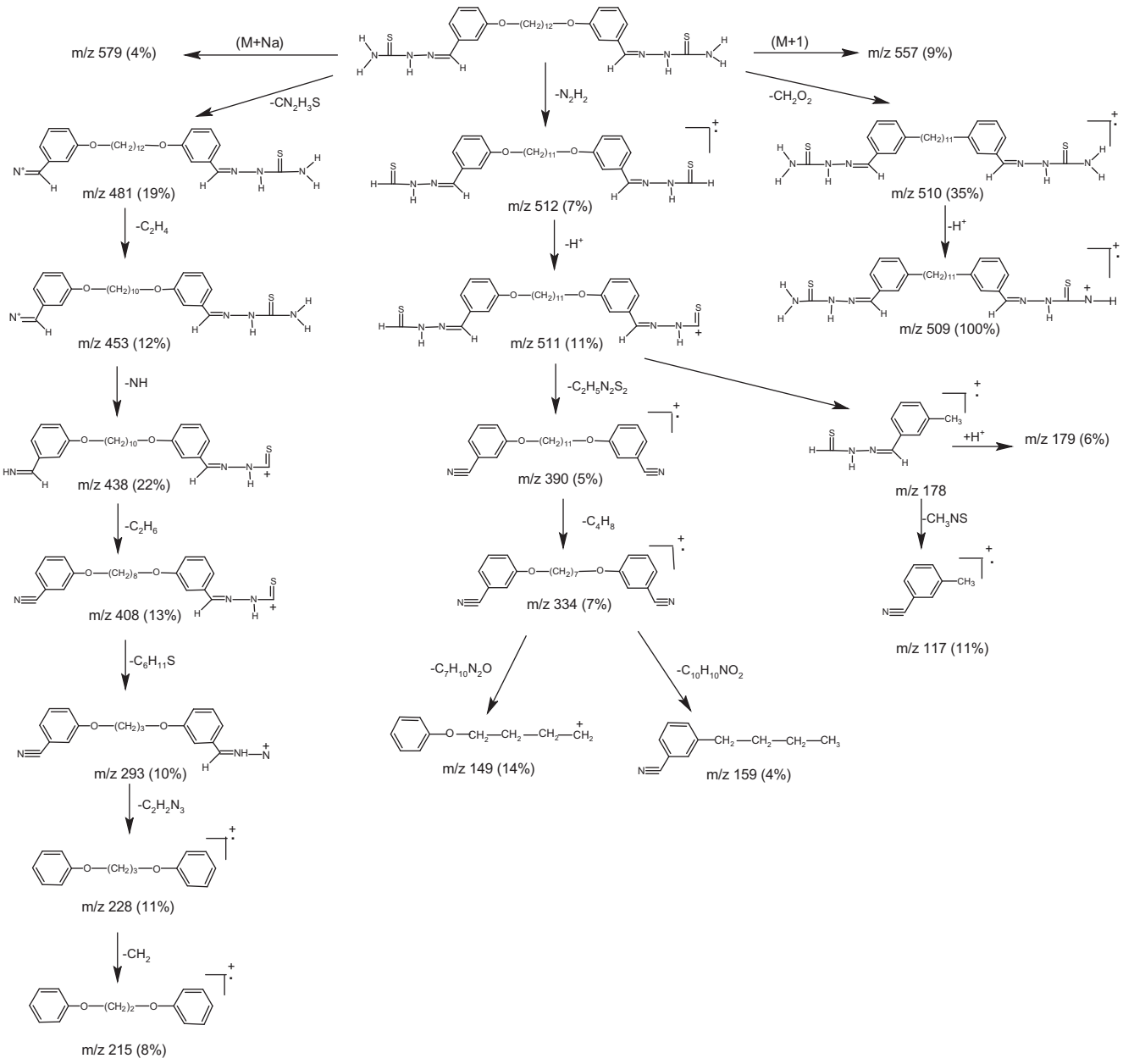


Chart 1. Mass fragmentation pattern of **3g**.

(N–H), 3027–3025 (aromatic C–H), 2937–2920, 2870–2849 (methylene C–H), 1600–1599 (C═N) and 1179–1177 (C═S) cm^{-1}.

The resonance placed in ^{1}H NMR spectra (400 MHz, DMSO-d_6) of **3a–3g** at δ 11.43–11.40 was assignable to 3-N***H*** proton and two broad singlets were found resonating at δ 8.02–7.62 & 7.73–7.42 due to N***H***-β & N***H***-α respectively. The azomethyne hydrogen (H-1) was present at δ 8.03–8.02 (2H) as a sharp singlet. The aromatic protons H-2′, 6′, H-5′& H-4′ provided suitable signals at δ 7.32–7.25 (4H, t, J_o = 7.8 Hz), 7.21–7.18 (2H, d, J_o = 7.6 Hz) & 6.97–6.88 (2H, dd, $J_{m,o}$ = 1.9, 7.9 Hz) respectively. The upfield resonance of later could be due to the +*I* effect of C-3′ alkoxy group. A singlet integrating for four hydrogens at δ 4.29–3.98 may be allotted to OC***H₂*** group and remaining (C***H₂***)$_n$ groups were analyzed by the signals of appropriate multiplicities at δ 1.99–1.25. UV–Vis spectra of **3a–3g** had λ_{max} at 362–318 nm which could be generated by $n \rightarrow \pi^*$ transition.

The presence of C═S group was confirmed by the appearance of a signal at δ 177.98–177.92 in the ^{13}C NMR (100 MHz, DMSO-d_6) spectra of **3a–3g**. The downfield resonance present at δ 158.92–158.69 could be furnished by C-3′ due to the direct linkage to this carbon to the electronegative oxygen atom and the resonance observed at δ 142.62–142.34 was easily provided by C═N group. The remaining signals in aromatic region were found to be placed at δ 135.39–135.10 (C-1′), 129.33–129.15 (C-6′), 120.80–119.93 (C-5′), 116.24–116.12 (C-4′) & 111.57–111.33 (C-2′). The O***C***H$_2$ and {(***C***H$_2$)$_n$} group belonging to the internal spacer unit furnished a suitable resonance at δ 67.44–66.98 and 28.98–23.76, respectively.

IR spectra of **4a–4g** did not exhibit any absorption band in the region at 1179–1177 cm^{-1} indicating the involvement of C═S moiety during the cyclization reaction of **3a–3g** and here major bands were observed in the region at 1698–1695, 1640–1638 (C═O) and 1607–1605 (C═N) cm^{-1}. The UV–Vis spectra of **4a–4g** had two maxima at 344–341 & 278–269 nm which may be ascribed by $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transitions, respectively.

A comparison of ^{1}H NMR spectra (400 MHz, DMSO-d_6) of **3a–3g** & **4a–4g** shows that resonances present at δ 8.02–7.62 & 7.73–7.42

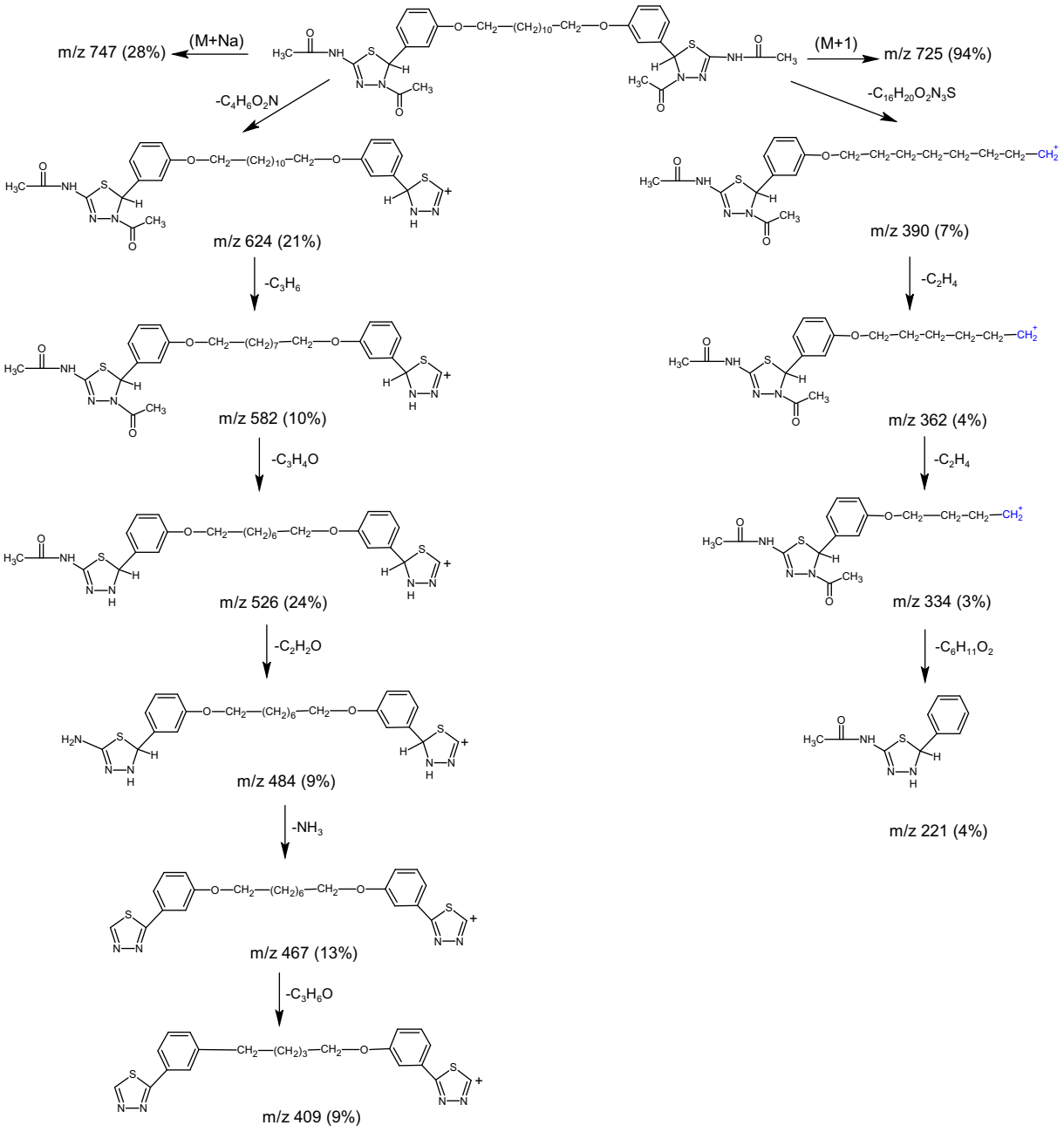


Chart 2. Mass fragmentation pattern of **4g**.

due to N***H***-β & N***H***-α respectively in the former compounds were found missing altogether in the later which clearly describes the involvement of these hydrogens in the chemical transformations. The aromatic protons (H-6′, 5′, 4′ & 2′) in **4a–4g were** centered at δ 7.25–7.17 (2H, t, J_o = 8.2 Hz), 6.89–6.77 (2H, brs), 6.86–6.73 (2H, d, J = 4.2 Hz) and 6.84–6.72 (2H, brs), respectively. The singlet integrating for two hydrogens at δ 6.74–6.67 could be assigned to H-2 and two more singlets at δ 2.25–2.20 & 2.13–2.03 were easily furnished by 3‴-C***H₃*** & 2″-C***H₃*** groups, respectively. The protons belonging to the spacer units also produced suitable signals of the appropriate multiplicities in the aliphatic region (vide experimental).

In the ^{13}C NMR (100 MHz, DMSO-d_6) spectra of **4a–4g**, downfield signals at δ 169.13–169.00 and 167.38–167.29 were designated to 2‴-C=O and 1″-C=O groups respectively and C=N moiety of thiadiazoline ring could result a suitable resonance at δ 146.19–146.09. The aromatic carbon atoms (C-1′, 2′, 3′, 4′, 5′& 6′) were found to be resonating at the suitable positions (see experimental). The noticeable resonances in the aliphatic region were present at δ 67.39–67.00 (O***C***H$_2$), 65.91–65.77 (C-2), 22.38–21.81 (3‴-***C***H$_3$) and 21.78–20.48 (2″-***C***H$_3$).

The extensive ESI-MS fragmentation studies of the bisthiosemicarbazones **3a–3g** & bisthiadiazolines **4a–4g** also proved helpful to confirm their proposed structures (see experimental). The mass fragmentation pattern of representative compounds **3g** & **4g** have been depicted in Charts 1 and 2, respectively.

2.1. Antimicrobial activity

All the synthesized bisthiosemicarbazones **3a–3g** and bisthiadiazoline **4a–4g** were screened for their *in vitro* antimicrobial activities against seven bacterial strains namely *Klubsellia pneumoniae*

Table 1
MIC (μg/ml) data of bisthiosemicarbazones **3a–3g**.

Compound No.	Gram (−ve) bacteria				Gram (+ve) bacteria			Fungi				
	E. coli	*K. pneumoniae*	*P. aeruginosa*	*P. fluorescens*	*S. aureus*	*B. subtilis*	*S. pyrogens*	*A. janus*	*P. glabrum*	*A. niger*	*F. oxysporum*	*A. sclerotiorum*
3a	16	32	32	16	32	64	32	64	32	16	32	32
3b	32	32	32	16	16	32	64	16	32	16	32	64
3c	16	32	16	32	16	16	32	32	32	**8**	16	32
3d	16	16	16	16	32	**8**	16	16	16	16	16	16
3e	16	16	16	**8**	16	16	16	16	16	**8**	16	16
3f	16	**8**	16	**8**	16	**8**	16	**8**	16	**8**	16	**8**
3g	**8**	16	**8**	16	**8**	**8**	16	16	**8**	16	**8**	**8**
Amoxicillin	**4**	**4**	**4**	**4**	2	2	**4**	–	–	–	–	–
Fluconazole	–	–	–	–	–	–	–	2	2	2	2	2

Table 2
MIC (μg/ml) data of bisthiadiazolines **4a–4g**.

Compound No.	Gram (−ve) bacteria				Gram (+ve) bacteria			Fungi				
	E.coli	*K. pneumoniae*	*P. aeruginosa*	*P. fluorescens*	*S. Aureus*	*B. subtilis*	*S. pyrogens*	*A. janus*	*P. glabrum*	*A. niger*	*F. oxysporum*	*A. sclerotiorum*
4a	32	32	32	16	32	32	32	32	32	32	32	16
4b	32	32	32	16	16	64	16	32	32	32	16	32
4c	32	16	32	32	32	32	64	32	16	16	64	32
4d	16	32	16	16	64	16	32	**8**	**8**	16	16	16
4e	16	16	16	**8**	16	16	16	**8**	16	**8**	**8**	16
4f	**8**	16	**8**	**8**	16	32	16	16	16	**8**	**8**	**8**
4g	**8**	**8**	16	16	**8**	16	16	**8**	16	**8**	16	**8**
Amoxicillin	**4**	**4**	**4**	**4**	2	2	**4**	–	–	–	–	–
Fluconazole	–	–	–	–	–	–	–	2	2	2	2	2

(MTCC 3384), *Pseudomonas aeruginosa* (MTCC 424), *Escherichia coli* (MTCC 443), *Staphylococcus aureus* (MTCC 96), *Bacillius subtilis* (MTCC 441), *Pseudomonas fluorescens (MTCC103)*, *Streptoccus pyrogens* (*MTCC442*) and five fungal strains *Aspergillius janus* (MTCC 2751), *Pencillium glabrum* (MTCC 4951), *Fusarium oxysporum* (*MTCC2480*), *Aspergillus sclerotiorum* (*MTCC1008*), *Aspergillus niger* (*MTCC281*), respectively. Amoxicillin and Fluconazole were used as standard drugs against bacterial and fungi strains, respectively.

The minimum inhibitory concentrations of the newly prepared compounds (**3a–3g** & **4a–4g**) were determined by using Serial tube dilution method [16] at the concentration of 128, 64, 32, 16, 8, 4, 2 and 1 μg/ml against above said microorganisms. The bacterial and fungi strains susceptibility to the studied compounds was determined by the appearance of turbidity after 24 h of incubation at 37 °C and 72 h of incubation at 28 °C, respectively. The observed MIC values (μg/ml) of **3a–3g** & **4a–4g** are presented in Table 1 & Table 2, respectively.

It is evident from Table 1 that the compounds **3c–3g** show significant activities against the most of bacterial and fungal strains at (MIC-8 μg/ml). The compound **3g** showed significant activity (MIC-8 μg/ml) against the strains, *E. coli, P. aeruginosa, S. aureus, B. subtilis* (bacterial strains) *and P. glabrum, F. oxysporum, A. sclerotiorum* (fungi strains) while **3f** displayed activity of same order against *K. pneumoniae*, *P. fluorescens*, *B. subtilis*, *A. janus*, *A. niger and A. sclerotiorum*. Further **3c**, **3d** & **3e** were also active (MIC-8 μg/ml) against the *A. niger*, *B. subtilis* and against *P. fluorescens*, *A. niger*, respectively.

Similarly, Table 2 describes that compounds **4d–4g** mainly prohibited the growth of the fungi strains. The bisthaidiazoline **4g** was found to be very active (MIC-8 μg/ml) against bacterial and fungi strains *E. coli, K. pneumoniae, S. aureus and A. janus, A. niger and A. sclerotiorum*, respectively. The compound **4f** also seems to be active against bacterial strains*E. coli, P. aeruginosa, P. fluorescens* and fungi strains *A. niger, F. oxysporum, A. sclerotiorum*, respectively. The bisheterocyclics **4d** & **4e** could exhibit significant activity (MIC-8 μg/ml) against *A. janus, P. glabrum, P. fluorescens, F. oxysporum* strains.

3. Conclusion

It may be concluded that this study describes the general and efficient method for the synthesis of alkyl chain linked bisthiadiazolines. The length of internal spacer had significant effect upon the antibacterial and antifungal behavior of the bisheterocyclic products. The bisthiadiazolines linked through the longer aliphatic chains (made up of ten & twelve methylene groups) showed better antimicrobial properties as compared to the shorter chain derivatives.

4. Experimental

Melting points reported are uncorrected. IR spectra were scanned in KBr pellets on a Perkin Elmer RXIFT Infrared spectrophotometer. ^{1}H NMR spectra were recorded on a 400 MHz Bruker spectrometer using TMS as the internal standard. The mass spectra have been scanned on the Waters Micromass Q-T of Micro (ESI) spectrometer. TLC plates were coated with silica gel suspended in MeOH–$CHCl_3$ and iodine vapours were used as visualizing agent.

4.1. Synthesis of 3,3′-[ethane-1,2-diylbis (oxy)] dibenzaldehyde 2a

3-Hydroxybenzaldehyde **1** (1.22 g, 0.01 mol) and KOH (0.55 g, 0.01 mol) was dissolved in alcohol (100 ml) and then solvent was removed under vacuum. The residue was dissolved in DMF (25 ml) and 1,2-dibromoethane (0.94 g, 0.005 mol) was added slowly. The reaction mixture was refluxed for 4 h, during which KBr was separated out. The solvent was removed in vacuo and the remaining material was poured into iced HCl to give a solid substance which was filtered under suction and thoroughly washed with water. The crude product thus obtained was crystallized from MeOH to give pure compound **2a**.

2[a]: Yield (1.8 g, 66%); brown solid; m.p. 88–90 °C; IR (KBr): υ_{max} cm^{-1}: 3066 (aromatic C–H), 2941 (methylene C–H), 2873, 2738

(aldehyde C–H), 1685 (C=O); UV–Vis (MeOH): λ_{max} (nm) 340, 272; ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.98 (2H, s, C***H***O), 7.86 (2H, s, H-2), 7.49 (2H, m, H-6), 7.46 (2H, d, J_o = 6.6 Hz, H-5), 7.27 (2H, m, H-4), 4.45 (4H, s, OC***H₂***); ^{13}C NMR (100 MHz, DMSO-d_6): δ 192.12 (C=O), 159.23 (C-3), 137.52 (C-1), 129.99 (C-6), 122.50 (C-5), 121.72 (C-4), 112.59 (C-2), 68.30 (O***C***H₂); MS: *m*/*z* 293 (M + Na, 100%), 271 (M + 1, 26%), 257 (79%), 256 (22%), 253 (8%), 166 (8%), 149 (13%), 135 (21%), 121 (28%), 107 (34%); Anal. Calc. for $C_{16}H_{14}O_4$: Calc. C, 71.11%, H, 5.11%; Found: C, 71.08%, H, 5.15%.

4.2. Synthesis of 3,3′-[butane-1,3-diylbis (oxy)] dibenzaldehyde 2b

The compound **2b** was prepared by reacting 3-hydroxybenzaldehyde **1** (0.01 mol, 1.22 g) with 1,4-dibromobutane (1.12 g, 0.005 mol) under the similar conditions as used earlier for **2a**.

The physical and spectral data of **2b** was found to be consistent as reported in literature [17].

4.3. Synthesis of 3,3′-[pentane-1,5-diylbis (oxy)] dibenzaldehyde 2c

The compound **2c** was prepared from the reaction of 3-hydroxybenzaldehyde **1** (1.22 g, 0.01 mol) with 1,5-dibromopentane (1.14 g, 0.005 mol) under similar conditions as used earlier for **2a**.

The physical and spectral data of **2c** was found to be consistent as reported in literature [17].

4.4. Synthesis of 3,3′-[hexane-1,6-diylbis (oxy)]dibenzaldehyde 2d

The compound **2d** was synthesized by reacting 3-hydroxybenzaldehyde **1** (1.22 g, 0.01 mol) and 1,6-dibromohexane (1.21 g, 0.005 mol) under similar conditions as used earlier for **2a**.

2d: Yield (2.1 g, 64%); grey solid; m.p. 60–62 °C; IR (KBr): υ_{max} cm^{-1} 3064 (aromatic C–H), 2942 (methylene C–H), 2864, 2717 (aldehyde C–H), 1696 (C=O); UV–Vis (MeOH): λ_{max} (nm) 338, 274; ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.97 (2H, s, C***H***O), 7.46 (2H, d, J_p = 0.6 Hz, H-2), 7.44 (2H, t, J = 1.2 Hz, H-6), 7.38 (2H, d, J = 2.1 Hz, H-5), 7.17 (2H, m, H-4), 4.03 (4H, t, J_{vic} = 6.4 Hz, OC***H₂***), 1.85 (4H, t, J_{vic} = 6.4 Hz, OCH$_2$C***H₂***), 1.57 (4H, quintet, J_{vic} = 6.4 Hz, OCH$_2$CH$_2$C***H₂***); ^{13}C NMR (100 MHz, DMSO-d_6): δ 192.37 (C=O), 159.13 (C-3), 137.51 (C-1), 130.04 (C-6), 122.20 (C-5), 121.16 (C-4), 113.35 (C-2), 67.60 (O***C***H$_2$), 28.51 (OCH$_2$***C***H$_2$), 25.23 (OCH$_2$CH$_2$***C***H$_2$); MS: *m*/*z* 349 (M + Na, 100%), 327 (M + 1, 26%), 309 (8%), 257 (4%), 227 (8%), 203 (5%), 177 (7%), 161 (6%), 140 (4%), 123 (7%), 116 (4%), 107 (9%); Anal. Calc. for $C_{20}H_{22}O_4$: Calc. C, 73.61%, H, 6.74%; Found: C, 73.54%, H, 6.70%.

4.5. Synthesis of 3,3′-[octane-1,8-diylbis (oxy)]dibenzaldehyde 2e

The compound **2e** was obtained by treating 3-hydroxybenzaldehyde **1** (1.22 g, 0.01 mol) with 1,8-dibromooctane (1.36 g, 0.005 mol) under similar conditions as used earlier for **2a**.

2e: Yield (2.3 g, 64%); brown solid; m.p. 65–67 °C; IR (KBr): υ_{max} cm^{-1} 3080 (aromatic C–H), 2938 (methylene C–H), 2854, 2756 (aldehyde C–H), 1679 (C=O); UV–Vis (MeOH): λ_{max} (nm) 322, 269; ^{1}H NMR (400 MHz, CDCl$_3$): δ 9.95 (2H, s, C***H***O), 7.45 (2H, s, H-2), 7.42 (2H, t, J = 3.7 Hz, H-6), 7.35 (2H, brs, H-5), 7.18 (2H, m, H-4), 4.03 (4H, t, J_{vic} = 6.4 Hz, OC***H₂***), 1.80 (4H, quintet, J_{vic} = 6.8 Hz, OCH$_2$C***H₂***), 1.47 (4H, m, OCH$_2$CH$_2$***CH₂***), 1.37 (4H, m, OCH$_2$CH$_2$CH$_2$***CH₂***); ^{13}C NMR (100 MHz, DMSO-d_6): δ 192.25 (C=O), 159.69 (C-3), 137.77 (C-1), 130.01 (C-6), 123.39 (C-5), 122.00 (C-4), 112.68 (C-2), 68.24 (O***C***H$_2$), 29.26 (OCH$_2$***C***H$_2$), 29.10 (OCH$_2$CH$_2$***C***H$_2$), 25.94 (OCH$_2$CH$_2$CH$_2$***C***H$_2$); MS: *m*/*z* 377 (M + Na, 100%), 355 (M + 1, 39%), 297 (18%), 269 (44%), 233 (43%), 219 (31%), 191 (32%), 177 (19%), 123 (9%), 107 (21%); Anal. Calc. for $C_{22}H_{26}O_4$: Calc. C, 74.57%, H, 7.34%; Found: C, 74.61%, H, 7.39%.

4.6. Synthesis of 3,3′-[decane-1,10-diylbis (oxy)]dibenzaldehyde 2f

The compound **2f** was prepared by reacting 3-hydroxybenzaldehyde **1** (1.22 g, 0.01 mol) with 1,10-dibromodecane (1.50 g, 0.005 mol) under similar conditions as used earlier for **2a**.

2f: Yield (2.4 g, 62%); light brown solid; m.p. 59–61 °C; IR (KBr): υ_{max} cm^{-1} 3078 (aromatic C–H), 2924 (methylene C–H), 2852, 2755 (aldehyde C–H), 1680 (C=O); UV–Vis (MeOH): λ_{max} (nm) 324, 264; ^{1}H NMR (400 MHz, CDCl$_3$): δ 9.97 (2H, s, C***H***O), 7.44 (2H, brs, H-2), 7.43 (2H, brs, H-6), 7.38 (2H, d, J = 0.64 Hz, H-5), 7.17 (2H, m, H-4), 4.01 (4H, t, J_{vic} = 6.5 Hz, OC***H₂***), 1.80 (4H, quintet, J_{vic} = 6.6 Hz, OCH$_2$C***H₂***), 1.45 (4H, t, J_{vic} = 6.5 Hz, OCH$_2$CH$_2$C***H₂***), 1.34 (8H, m, OCH$_2$CH$_2$CH$_2$C***H₂***); ^{13}C NMR (100 MHz, DMSO-d_6): δ 192.25 (C=O), 159.71 (C-3), 137.76 (C-1), 129.99 (C-6), 123.35 (C-5), 121.98 (C-4), 112.71 (C-2), 68.28 (O***C***H$_2$), 29.46 (OCH$_2$***C***H$_2$), 29.32 (OCH$_2$CH$_2$***C***H$_2$), 29.11 (OCH$_2$CH$_2$CH$_2$***C***H$_2$), 25.99 (OCH$_2$CH$_2$CH$_2$CH$_2$***C***H$_2$); MS: *m*/*z* 405 (M + Na, 91%), 383 (M + 1, 79%), 334 (100%), 261 (21%), 256 (31%), 247 (8%), 246 (13%), 243 (23%), 173 (7%), 135 (31%), 121 (29%), 105 (22%); Anal. Calc. for $C_{24}H_{30}O_4$: Calc. C, 75.39%, H, 7.85%; Found: C, 75.32%, H, 7.89%.

4.7. Synthesis of 3,3′-[dodecane-1,12-diylbis (oxy)]dibenzaldehyde 2g

The compound **2g** was synthesized from the reaction of 3-hydroxybenzaldehyde **1** (1.22 g, 0.01 mol) with 1,12-dibromododecane (1.64 g, 0.005 mol) under the same conditions as described earlier for **2a.**

2g: Yield (2.5 g, 60%); grey solid; m.p. 57–59 °C; IR (KBr): υ_{max} cm^{-1} 3081 (aromatic C–H), 2938, 2920 (methylene C–H), 2850, 2759 (aldehyde C–H), 1681 (C=O); UV–Vis (MeOH): λ_{max} (nm) 338, 258; ^{1}H NMR (400 MHz, CDCl$_3$): δ 9.89 (2H, s, C***H***O), 7.37 (2H, brs, H-2), 7.36 (2H, t, J = 1.1 Hz, H-6), 7.30 (2H, d, J = 2.0 Hz, H-5), 7.09 (2H, m, H-4), 3.93 (4H, t, J_{vic} = 6.5 Hz, OC***H₂***), 1.74 (4H, quintet, J_{vic} = 6.7 Hz, OCH$_2$C***H₂***), 1.40 (4H, t, J_{vic} = 6.4 Hz, OCH$_2$CH$_2$C***H₂***), 1.27 (12H, m, OCH$_2$CH$_2$CH$_2$C***H₂C H₂C H₂***); ^{13}C NMR (100 MHz, DMSO-d_6): δ 192.26 (C=O), 159.72 (C-3), 137.77 (C-1), 129.99 (C-6), 123.34 (C-5), 121.99 (C-4), 112.72 (C-2), 68.30 (O***C***H$_2$), 29.55 (OCH$_2$***C***H$_2$), 29.35 (OCH$_2$CH$_2$***C***H$_2$), 29.13 (OCH$_2$CH$_2$CH$_2$***C***H$_2$), 29.12 (OCH$_2$CH$_2$CH$_2$CH$_2$***C***H$_2$), 26.00 (OCH$_2$CH$_2$CH$_2$CH$_2$CH$_2$***C***H$_2$); MS: *m*/*z* 433 (M + Na, 87%), 426 (13%), 412 (30%), 411 (M + 1, 95%), 348 (10%), 335 (25%), 334 (100%), 318 (5%), 289 (18%), 271 (19%), 274 (12%), 257 (18%), 173 (5%), 161 (4%), 147 (8%), 123 (15%), 111 (17%); Anal. Calc. for $C_{26}H_{34}O_4$: Calc. C, 76.09%, H, 8.29%; Found: C, 76.13%, 8.24%.

4.8. Synthesis of 2,2′-[3,3′-(ethane-1,2-diylbis(oxy)bis(3,1-phenylene)) bis(methan-1-yl-1-ylidene) bis (hydrazinecarbothioamide) 3a

A mixture of **2a** (0.5 g, 0.00185 mol) and thiosemicarbazide (0.337 g, 0.00370 mol) in dry EtOH (20 ml) and HCl (1.0 ml) was refluxed for 4 h. The progress of the reaction was monitored by TLC and after the completion of the reaction, the resulting mixture was cooled in an ice bath to give a solid. The solid thus obtained was filtered under suction dried and crystallized from MeOH to yield pure compound **3a**.

3a: Yield (0.6 g, 78%); dark brown solid; m.p. 150–152 °C; IR (KBr): υ_{max} cm^{-1} 3395, 3250, 3159 (N–H), 3027 (aromatic C–H), 2920, 2849 (methylene C–H), 1600 (C=N), 1179 (C=S); UV–Vis (MeOH): λ_{max} (nm) 321; ^{1}H NMR (400 MHz, CDCl$_3$): δ 11.42 (2H, s, 3-N***H***), 8.02 (2H, s, H-1), 7.62 (2H, brs, N***H***-β), 7.42 (2H, brs, N***H***-α), 7.30 (4H, t, J_o = 7.8 Hz, H-2′, 6′), 7.21 (2H, d, J_o = 7.6 Hz, H-5′), 6.97 (2H, dd, $J_{m,o}$ = 2.0, 7.9 Hz, H-4′), 4.29 (4H, s, OC***H₂***); ^{13}C NMR (100 MHz, DMSO-d_6): δ 177.98 (C=S), 158.69 (C-3′), 142.52 (C=N), 135.18 (C-1′), 129.15 (C-6′), 120.8 (C-5′), 116.22 (C-4′), 111.33 (C-2′), 67.42 (O***C***H$_2$); MS: *m*/*z* 439 (M + Na, 21%), 417 (M + 1, 25%), 401 (8%), 400 (21%), 397 (100%), 356 (33%), 355

(15%), 341 (19%), 342 (28%), 326 (13%), 324 (22%), 315 (4%), 310 (17%), 146 (37%), 132 (18%), 105 (9%); Anal. Calc. for $C_{18}H_{20}O_2N_6S_2$: C, 51.92%, H, 4.80%, N, 20.19%, S, 15.38%; found: C, 52.19%, H, 4.84%, N, 20.11%, S, 15.44%.

4.9. Synthesis of 2,2′-(3,3′-(butane-1,4-diylbis(oxy))bis(3,1-phenylene)) bis(methan-1-yl-1-ylidene)bis(hydrazinecarbothioamide) 3b

The compound **3b** was prepared from the reaction of **2b** (0.5 g, 0.00167 mol) with thiosemicarbazide (0.305 g, 0.0033 mol) under the similar reaction conditions as described above for **3a**.

3b: Yield (0.5 g, 68%); greyish yellow solid; m.p. 208–210 °C; IR (KBr): υ_{max} cm^{-1} 3390, 3238, 3154 (N–H), 3025 (aromatic C–H), 2937, 2870 (methylene C–H), 1600 (C=N), 1178 (C=S); UV–Vis (MeOH): λ_{max} (nm) 318; ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.42 (2H, s, 3-N***H***), 8.02 (2H, s, H-1), 7.76 (2H, brs, N***H***-β), 7.51 (2H, brs, N***H***-α), 7.27 (4H, t, J_o = 7.3 Hz, H-2′,6′), 7.19 (2H, d, J_o = 7.6 Hz, H-5′), 6.92 (2H, dd, J = 1.8, 7.9 Hz, H-4′), 4.08 (4H, brs, OC***H₂***), 1.99 (4H, brs, $OCH_2C\boldsymbol{H_2}$); ^{13}C NMR (100 MHz, DMSO-d_6): δ 177.96 (C=S), 158.79 (C-3′), 142.50 (C=N), 135.20 (C-1′), 129.26 (C-6′), 120.17 (C-5′), 116.24 (C-4′), 111.44 (C-2′), 66.98 (OCH_2), 25.42 (OCH_2CH_2); MS: *m*/*z* 467 (M + Na, 13%), 445 (M + 1, 6%), 401 (7%), 400 (18%), 397 (100%), 384 (6%), 384 (6%), 370 (4%), 369 (14%), 354 (15%), 352 (12%), 338 (16%), 295 (35%), 293 (21%), 293 (21%), 174 (37%), 132 (12%), 105 (13%); Anal. Calc. for $C_{20}H_{24}O_2N_6S_2$: C, 54.05%, H, 5.40%, N, 18.91%, S, 14.41%; found: C, 53.84%, H, 5.44%, N, 18.84%, S, 14.46%.

4.10. Synthesis of 2,2′-(3,3′-(pentane-1,5-diylbis(oxy))bis(3,1-phenylene)) bis(methan-1-yl-1-ylidene)bis(hydrazinecarbothioamide) 3c

The compound **3c** was obtained by reacting compound **2c** (0.5 g, 0.0016 mol) with thiosemicarbazide (0.29 g, 0.003205 mol) under the reaction conditions as used for **3a**.

3c: Yield (0.5 g, 68%), dark brown solid; m.p. 212–214 °C; IR (KBr): υ_{max} cm^{-1} 3368, 3247, 3157 (N–H), 3025 (aromatic C–H), 2937, 2863 (methylene C–H), 1600 (C=N), 1177 (C=S); UV–Vis (MeOH): λ_{max} (nm) 323; ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.40 (2H, s, 3-N***H***), 8.03 (2H, s, H-1), 7.72 (2H, brs, N***H***-β), 7.49 (2H, brs, N***H***- α), 7.27 (4H, t, J_o = 7.3 Hz, H-2′, 6′), 7.18 (2H, d, J_o = 7.5 Hz, H-5′), 6.91 (2H, dd, $J_{m,o}$ = 2.3, 7.9 Hz, H-4′), 4.11 (4H, brs, OC***H₂***), 1.96 (4H, t, J_{vic} = 6.4 Hz, $OCH_2C\boldsymbol{H_2}$), 1.43 (2H, brs, $OCH_2CH_2C\boldsymbol{H_2}$); ^{13}C NMR (100 MHz, DMSO-d_6): δ 177.98 (C=S), 158.89 (C-3′), 142.62 (C=N), 135.39 (C-1′), 129.33 (C-6′), 120.17 (C-5′), 116.19 (C-4′), 111.49 (C-2′), 67.41 (OCH_2), 25.42 (OCH_2CH_2), 23.76 ($OCH_2CH_2CH_2$); MS: *m*/*z* 481 (M + Na, 24%), 459 (M + 1, 17%), 442 (9%), 398 (11%), 397 (32%), 384 (6%), 383 (67%), 368 (17%), 352 (13%), 307 (26%), 297 (35%), 257 (78%), 191 (27%), 163 (46%), 149 (100%), 132 (26%), 105 (19%); Anal. Calc for $C_{22}H_{26}O_2N_6S_2$: C, 55.02%, H, 5.67%, N, 18.34%, S, 13.97%; found: C, 55.24%, H, 5.62%, N, 18.41%, S, 13.92%.

4.11. Synthesis of 2,2′-(3,3′-(hexane-1,6-diylbis(oxy))bis(3,1-phenylene)) bis(methan-1-yl-1-ylidene)bis(hydrazinecarbothioamide) 3d

The compound **3d** was prepared from the reaction of **2d** (0.5 g, 0.0015 mol) with thiosemicarbazide (0.27 g, 0.0030 mol) under the reaction conditions as described for **3a**.

3d: Yield (0.5 g, 69%), dark brown solid; m.p. 204–206 °C; IR (KBr): υ_{max} cm^{-1} 3368, 3247, 3157 (N–H), 3025 (aromatic C–H), 2937, 2863 (methylene C–H), 1600 (C=N), 1177 (C=S), UV–Vis (MeOH): λ_{max} (nm) 320; ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.40 (2H, s, 3-N***H***), 8.02 (2H, s, H-1), 7.69 (2H, brs, N***H***-β), 7.56 (2H, brs, N***H***-α), 7.27 (4H, t, J_o = 7.9 Hz, H-2′, 6′), 7.19 (2H, d, J_o = 7.6 Hz, H-5′), 6.91 (2H, dd, J = 2.4, 8.0 Hz, H-4′), 4.00 (4H, t, J_{vic} = 6.4 Hz, OC***H₂***), 1.43 (4H, t, J_{vic} = 6.4 Hz, $OCH_2C\boldsymbol{H_2}$), 1.25 (4H, m, $OCH_2CH_2C\boldsymbol{H_2}$); ^{13}C NMR (100 MHz, DMSO-d_6): δ 177.92 (C=S), 158.92 (C-3′), 142.34 (C=N), 135.35 (C-1′), 129.32 (C-6′), 120.19 (C-5′), 116.23 (C-4′), 111.54 (C-2′), 67.33 (OCH_2), 28.70 (OCH_2CH_2), 25.36 ($OCH_2CH_2CH_2$), MS: *m*/*z* 495 (M + Na, 21%), 473 (M + 1, 26%), 456 (8%), 397 (65%), 353 (24%), 351 (60%), 338 (52%), 323 (63%), 301 (62%), 293 (15%), 257 (89%), 255 (14%), 227 (18%), 223 (31%), 195 (36%), 191 (23%), 163 (40%), 149 (100%), 140 (91%), 116 (73%); Anal. Calc. for $C_{23}H_{28}O_2N_6S_2$: C, 55.93%, H, 5.93%, N, 17.79%, S, 13.55%, found: C, 55.71%, H, 5.96%, N, 17.72%, S, 13.60%.

4.12. Synthesis of 2,2′-(3,3′-(octane-1,8-diylbis(oxy))bis(3,1-phenylene)) bis(methan-1-yl-1-ylidene)bis(hydrazinecarbothioamide) 3e

The compound **3e** was obtained by reacting dibenzaldehyde **2e** (0.7 g, 0.0019 mol) with thiosemicarbazide (0.35 g, 0.0039 mol) under the same reaction conditions as used for **3a**.

3e: Yield (0.8 g, 81%), light brown solid; m.p. 212–214 °C; IR (KBr): υ_{max} cm^{-1} 3398, 3246, 3157 (N–H), 3025 (aromatic C–H), 2934, 2853 (methylene C–H), 1599 (C=N), 1179 (C=S); UV–Vis (MeOH): λ_{max} (nm) 362; ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.43 (2H, s, 3-N***H***), 8.03 (2H, brs, H-1), 7.89 (2H, brs, N***H***-β), 7.61 (2H, brs, N***H***- α), 7.29 (2H, brs, H-2′), 7.27 (2H, t, J_o = 7.8 Hz, H-6′), 7.21 (2H, d, J_o = 7.7 Hz, H-5′), 6.91 (d{dd}, 2H, $J_{m,o}$ = 1.7, 8.1 Hz, H-4′), 4.00 (4H, t, J_{vic} = 6.4 Hz, OC***H₂***), 1.75 (4H, quintet, J_{vic} = 6.5 Hz, $OCH_2C\boldsymbol{H_2}$), 1.48 (4H, quintet, J_{vic} = 6.4 Hz, $OCH_2CH_2C\boldsymbol{H_2}$), 1.43 (4H, J_{vic} = 3.2 Hz, quintet, $OCH_2CH_2CH_2C\boldsymbol{H_2}$); ^{13}C NMR (100 MHz, DMSO-d_6): δ 177.98 (C=S), 158.88 (C-3′), 142.62 (C=N), 135.10 (C-1′), 129.22 (C-6′), 119.93 (C-5′), 116.14 (C-4′), 111.54 (C-2′), 67.41 (OCH_2), 28.74 (OCH_2CH_2), 28.70 ($OCH_2CH_2CH_2$), 25.45 ($OCH_2CH_2CH_2CH_2$); MS: *m*/*z* 523 (M + Na, 100%), 501 (M + 1, 31%), 484 (11%), 425 (67%), 381 (24%), 379 (63%), 352 (53%), 351 (52%), 323 (64%), 367 (18%), 297 (33%), 269 (36%), 195 (39%), 191 (26%), 163 (47%), 149 (92%), 105 (72%); Anal. Calc. for $C_{24}H_{32}O_2N_6S_2$: C, 57.6%, H, 6.4%, N, 16.8%, S, 12.8%, found: C, 57.37%, H, 6.25%, N, 16.74%, S, 12.75%.

4.13. Synthesis of 2,2′-(3,3′-(decane-1,10-diylbis(oxy))bis(3,1-phenylene)) bis(methan-1-yl-1-ylidene)bis(hydrazinecarbothioamide) 3f

The compound **3f** was prepared by treating **2f** (0.5 g, 0.0013 mol) with thiosemicarbazide (0.23 g, 0.0026 mol) under the similar conditions as used for **3a.**

3f: Yield (0.5 g, 72%), creamish solid; m.p. 178–180 °C; IR (KBr): υ_{max} cm^{-1} 3398, 3245, 3158 (N–H), 3027 (aromatic C–H), 2921, 2850 (methylene C–H), 1600 (C=N), 1179 (C=S); UV–Vis (MeOH): λ_{max} (nm) 361; ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.41 (2H, s, 3-NH), 8.02 (2H, s, H-1), 7.79 (2H, brs, N***H***-β), 7.52 (2H, brs, N***H***-α), 7.28 (2H, brs, H-2′), 7.25 (2H, d, J_o = 7.7 Hz, H-6′), 7.18 (2H, d, J_o = 8.0 Hz, H-5′), 6.90 (2H, dd, $J_{m,o}$ = 2.0, 8.0 Hz, H-4′), 3.98 (4H, t, J_{vic} = 6.4 Hz, OC***H₂***), 1.77 (4H, quintet, J_{vic} = 6.5 Hz, $OCH_2C\boldsymbol{H_2}$), 1.45 (4H, quintet, J_{vic} = 6.4 Hz, $OCH_2CH_2C\boldsymbol{H_2}$), 1.34 (8H, m, $OCH_2CH_2CH_2C\boldsymbol{H_2}C\boldsymbol{H_2}$); ^{13}C NMR (100 MHz, DMSO-d_6): δ 177.96 (C=S), 158.91 (C-3′), 142.47 (C=N), 135.22 (C-1′), 129.24 (C-6′), 120.01 (C-5′), 116.14 (C-4′), 111.35 (C-2′), 67.42 (OCH_2), 28.92 (OCH_2CH_2), 28.79 ($OCH_2CH_2CH_2$), 28.73 ($OCH_2CH_2CH_2CH_2$), 25.51 ($OCH_2CH_2CH_2CH_2CH_2$); MS: *m*/*z* 551 (M + Na, 29%), 529 (M + 1, 36%), 509 (100%), 453 (21%), 397 (69%), 293 (25%), 274 (33%), 257 (73%), 228 (13%), 215 (24%), 179 (8%), 159 (62%), 149 (19%), 117 (44%); Anal. Calc. for $C_{26}H_{36}O_2N_6S_2$: C, 59.09%, H, 6.81%, N, 15.90%, S, 12.12%; found: C, 59.32%, H, 6.85%, N, 15.84%, S, 12.08%.

4.14. Synthesis of 2,2′-(3,3′-(dodecane-1,12-diylbis(oxy))bis(3,1-phenylene))bis(methan -1-yl-1-ylidene)bis(hydrazinecarbothioamide) 3g

The compound **3g** was prepared from the reaction of **2g** (0.7 g, 0.0017 mol) with thiosemicarbazide (0.31 g, 0.0034 mol) under similar reaction conditions as used for **3a**.

3g: Yield (0.8 g, 85%), creamish solid; m.p. 168–170 °C; IR (KBr): υ_{max} cm^{-1} 3395, 3250, 3159 (N–H), 3027 (aromatic C–H), 2920, 2849 (methylene C–H), 1600 (C=N), 1179 (C=S); UV–Vis (MeOH): λ_{max} (nm) 356; ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.41 (2H, s, 3-N***H***), 8.02 (2H, brs, H-1), 8.02 (2H, brs, N***H***-β), 7.73 (2H, s, N***H***-α), 7.32 (2H, brs, H-2′), 7.26 (2H, t, J = 7.8 Hz, H-6′), 7.19 (2H, d, J_o = 7.6 Hz, H-5′), 6.88 (2H, d{dd}, $J_{p,m,o}$= 1.2, 2.4, 7.2 Hz, H-4′), 3.98 (4H, t, J_{vic} = 6.4 Hz, OC***H₂***), 1.75 (4H, quintet, J_{vic} = 6.5, OCH_2 C***H₂***), 1.43 (4H, quintet, J_{vic} = 6.8 Hz, OCH_2CH_2C***H₂***), 1.29 (12H, m, $OCH_2CH_2CH_2C$***H₂C H₂C H₂***); ^{13}C NMR (100 MHz, DMSO-d_6): δ 177.95 (C = S), 158.90 (C-3′), 142.55 (C=N), 135.16 (C-1′), 129.23 (C-6′), 119.95 (C-5′), 116.12 (C-4′), 111.57 (C-2′), 67.44 (OCH_2), 28.98 (OCH_2CH_2), 28.80 ($OCH_2CH_2CH_2$), 28.73 ($OCH_2CH_2CH_2CH_2$), 26.59 ($OCH_2CH_2CH_2CH_2CH_2$), 25.51 (OCH_2 $CH_2CH_2CH_2CH_2CH_2$); MS: m/z 579 (M + Na, 44%), 557 (M + 1, 29%), 568 (12%), 510 (35%), 509 (100%), 492 (8%), 481 (19%), 453 (12%), 437 (22%), 407 (16%), 390 (5%), 331 (43%), 293 (10%), 275 (32%), 274 (34%), 257 (75%), 228 (11%), 215 (8%), 179 (6%), 149 (14%), 117 (11%); Anal. Calc. for $C_{28}H_{40}O_2N_6S_2$: C, 60.43%, H, 7.19%, N, 15.10%, S, 11.51%; found: C, 60.19%, H, 7.24%, N, 15.16%, S, 11.55%.

4.15. Synthesis of N,N′-(5,5′-(3,3′-(ethane-1,2-diylbis(oxy))bis(3,1-phenylene))bis(4-acetyl-4,5-dihydro-1,3,4-thiadiazole-5,2-diyl))diacetamide 4a

A mixture of **3a** (0.5 g, 0.0012 mol) and acetic anhydride (25 ml) was refluxed for 10 h and the progress of reaction was monitored by TLC. The resulting reaction mixture was poured over ice to obtain a solid product which was filtered under suction and finally crystallized from EtOH to yield pure compound **4a**.

4[a]: Yield (0.5 g, 71%); brown solid; m.p. 85–87 °C; IR (KBr): υ_{max} cm^{-1} 3227, 3161 (N–H), 3062 (aromatic C–H), 2932 (methylene C–H), 1695 (C=O), 1606 (C=N); UV–Vis (MeOH): λ_{max} (nm) 343, 276; ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.64 (2H, s, 1‴-N***H***), 7.25 (2H, t, J = 8.2 Hz, H-6′), 6.89 (2H, brs, H-5′), 6.86 (2H, d, J_o = 4.2 Hz, H-4′), 6.84 (2H, brs, H-2′), 6.74 (2H, s, H-2), 4.30 (4H, s, OC***H₂***), 2.25 (6H, s, 3‴-C***H₃***), 2.05 (6H, s, 2″-C***H₃***); ^{13}C NMR (100 MHz, DMSO-d_6): δ 169.09 (2‴-C=O), 167.29 (1″-C=O), 158.85 (C-3′), 146.12 (C=N), 142.73 (C-1′), 129.52 (C-6′), 116.80 (C-5′), 113.43 (C-4′), 111.37 (C-2′), 67.32 (OCH_2), 65.91 (C-2), 21.73 (3‴-***C***H_3), 20.74 (2″-***C***H_3), MS: m/z 607 (M + Na, 100%), 585 (M + 1, 49%), 572 (24%), 571 (81%), 541 (11%), 484 (26%), 442 (19%), 386 (53%), 285 (47%), 179 (5%), 121 (19%), 107 (43%); Anal. Calc. for $C_{26}H_{28}O_6N_6S_2$: C, 53.42%, H, 4.79%, N, 14.38%, S, 10.95%; found C, 53.63%, H, 4.75%, N, 14.33%, S, 10.99%.

4.16. Synthesis of N,N′-(5,5′-(3,3′-(butane-1,4-diylbis(oxy))bis(3,1-phenylene)) bis(4-acetyl-4,5-dihydro-1,3,4-thiadiazole-5,2-diyl)) diacetamide 4b

The compound **4b** was prepared by reacting **3b** (0.5 g, 0.00113 mol) with acetic anhydride (25 ml) under the similar conditions as described earlier for **4a**.

4b: Yield (0.5 g, 73%); brown solid; m.p. 78–80 °C; IR (KBr): υ_{max} cm^{-1} 3164 (N-H), 3065 (aromatic C–H), 2943, 2875 (methylene C–H), 1695, 1640 (C=O), 1605 (C=N); UV–Vis (MeOH): λ_{max} (nm) 342, 278; ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.59 (2H, s, 1‴-N***H***), 7.23 (2H, t, J = 7.9 Hz, H-6′), 6.82 (2H, d, J_o = 1.7 Hz, H-5′), 6.80 (2H, brs, H-2′), 6.80 (2H, d, J = 1.4 Hz, H-4′), 6.72 (2H, s, H-2), 4.01 (4H, brs, OC***H₂***), 2.24 (6H, s, 3‴-C***H₃***), 2.07 (6H, s, 2″-C***H₃***), 1.94 (4H, brs, OCH_2C***H₂***); ^{13}C NMR (100 MHz, DMSO-d_6): δ 169.13 (2‴-C=O), 167.30 (1″-C=O), 158.75 (C-3′), 146.09 (C=N), 142.75 (C-1′), 129.68 (C-6′), 116.87 (C-5′), 113.47 (C-4′), 111.35 (C-2′), 67.00 (OCH_2), 65.77 (C-2), 25.41 (OCH_2CH_2), 21.81 (3‴-***C***H_3), 20.48 (2″-***C***H_3); MS: m/z 635 (M + Na, 37%), 613 (M + 1, 53%), 571 (82%), 569 (9%), 529 (32%), 512 (22%), 470 (18%), 456 (19%), 414 (49%), 396 (66%), 372 (21%), 355 (50%), 337 (21%), 313 (45%), 295 (37%), 238 (8%), 178 (13%), 177 (100%),149 (18%), 135 (22%), 107 (43%); Anal. Calc. for $C_{28}H_{32}O_6N_6S_2$: C, 54.90%, H, 5.22%, N, 13.72%, S, 10.45%; found: C, 55.69%, H, 5.26%, N, 13.77%, S, 10.49%.

4.17. Synthesis of N,N′-(5,5′-(3,3′-(pentane-1,5-diylbis(oxy))bis(3,1-phenylene))bis(4-acetyl-4,5-dihydro-1,3,4-thiadiazole-5,2-diyl))diacetamide 4c

The compound **4c** was obtained by treating **3c** (0.5 g, 0.00109 mol) with acetic anhydride (25 ml) under the similar conditions as used earlier for **4a**.

4c: Yield (0.6 g, 88%); brown solid; m.p. 84–86 °C; IR (KBr): υ_{max} cm^{-1} 3162 (N–H), 3063 (aromatic C–H), 2936, 2873 (methylene C–H), 1695, 1639 (C=O), 1606 (C=N); UV–Vis (MeOH): λ_{max} (nm) 341, 272; ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.61 (2H, s, 1‴-N***H***), 7.17 (2H, t, J = 7.9 Hz, H-6′), 6.86 (2H, d, J_m = 1.7 Hz, H-5′), 6.76 (2H, brs, H-2′), 6.73 (2H, brs, H-4′), 6.70 (2H, s, H-2), 3.98 (4H, brs, OC***H₂***), 2.23 (6H, s, 3‴-C***H₃***), 2.13 (6H, s, 2″-C***H₃***), 1.94 (4H, brs, OCH_2C***H₂***), 1.47 (2H, brs, OCH_2CH_2C***H₂***); ^{13}C NMR (100 MHz, DMSO-d_6): δ 169.09 (2‴-C=O), 167.38 (1″-C=O), 158.84 (C-3′), 146.09 (C=N), 142.74 (C-1′), 129.52 (C-6′), 116.80 (C-5′), 113.43 (C-4′ 111.38 (C-2′), 67.23 (OCH_2), 65.84 (C-2), 28.73 (OCH_2CH_2), 25.46 (OCH_2CH_2), 21.81 (3‴-***C***H_3), 20.48 (2″-***C***H_3); MS: m/z 649 (M + Na, 93%), 627 (M + 1, 47%), 585 (14%), 583 (21%), 543 (12%), 526 (31%), 484 (19%), 428 (57%), 386 (34%), 327 (44%), 285 (51%), 177 (100%), 163 (23%), 149 (7%), 135 (39%), 121 (21%), 107 (49%); Anal. Calc. for $C_{29}H_{34}O_6N_6S_2$: C, 55.59%, H, 5.43%, N, 13.41%, S, 10.22%; found: C, 55.37%, H, 5.38%, N, 13.36%, S, 10.26%.

4.18. Synthesis of N,N′-(5,5′-(3,3′-(hexane-1,6-diylbis(oxy))bis(3,1-phenylene))bis(4-acetyl-4,5-dihydro-1,3,4-thiadiazole-5,2-diyl)) diacetamide 4d

The compound **4d** was prepared from the reaction of **3d** (0.5 g, 0.00106 mol) with acetic anhydride (25 ml) under the similar conditions as described earlier for **4a.**

4d: Yield (0.5 g, 74%); brown solid; m.p. 100–102 °C; IR (KBr): υ_{max} cm^{-1} 3161 (N–H), 3062 (aromatic C–H), 2937, 2865 (methylene C–H), 1698, 1638 (C=O), 1606 (C=N); UV–Vis (MeOH): λ_{max} (nm) 344, 269; ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.57 (2H, s, 1‴-N***H***), 7.22 (2H, t, J = 7.8 Hz, H-6′), 6.82 (2H, d, J_o = 6.7 Hz, H-5′), 6.78 (2H, d, J_o = 7.5 Hz, H-4′), 6.76 (2H, s, H-2′), 6.70 (2H, s, H-2), 3.95 (4H, t, J_{vic} = 6.2 Hz, OC***H₂***), 2.25 (6H, s, 3‴-C***H₃***), 2.04 (6H, s, 2″-C***H₃***), 1.79 (4H, brs, OCH_2C***H₂***), 1.53 (4H, brs, OCH_2CH_2C***H₂***); ^{13}C NMR (100 MHz, DMSO-d_6): δ 169.04 (2‴-C=O), 167.37 (1″-C=O), 158.84 (C-3′), 146.12 (C=N), 142.48 (C-1′), 129.52 (C-6′), 116.85 (C-5′), 113.43 (C-4′), 111.37 (C-2′), 67.28 (OCH_2), 65.90 (C-2), 28.63 (OCH_2CH_2), 25.33 ($OCH_2CH_2CH_2$), 21.76 (3‴-***C***H_3), 20.75 (2″-***C***H_3); MS: m/z 683 (M + Na, 100%), 641 (M + 1, 43%), 599 (52%), 562 (27%), 557 (14%), 540 (12%), 506 (39%), 484 (18%), 475 (33%), 453 (21%), 442 (23%), 424 (50%), 383 (19%), 349 (36%), 327 (23%), 280 (12%), 238 (35%), 221 (22%), 194 (7%), 173 (18%), 155 (59%), 140 (12%), 116 (17%); Anal. Calc. for $C_{30}H_{36}O_6N_6S_2$: C, 56.25%, H, 5.62%, S, 10.00%, N, 13.12%; found: C, 56.47%, H, 5.59%, S, 9.96%, N, 13.17%.

4.19. Synthesis of N,N′-(5,5′-(3,3′-(octane-1,8-diylbis(oxy))bis(3,1-phenylene))bis(4-acetyl-4,5-dihydro-1,3,4-thiadiazole-5,2-diyl)) diacetamide 4e

The compound **4e** was obtained by reacting **3e** (0.5 g, 0.001 mol) with acetic anhydride (25 ml) under the similar conditions as used earlier for **4a**.

4e: Yield (0.6 g, 89%); creamish solid; m.p. 85–87 °C; IR (KBr): υ_{max} cm^{-1} 3160 (N–H), 3065 (aromatic C–H), 2934, 2856 (methylene C–H), 1697, 1639 (C=O), 1607 (C=N); UV–Vis (MeOH): λ_{max} (nm) 341, 273; ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.61 (2H, s, 1‴-N***H***), 7.19 (2H, t, J_o = 7.9 Hz, H-6′), 6.78 (2H, brs, H-5′), 6.76 (2H, brs, H-2′), 6.74 (2H, d, J_m = 2.2 Hz, H-4′), 6.72 (2H, s, H-2), 3.90 (4H, t, J_{vic} = 6.4 Hz, OC***H₂***), 2.20 (6H, s, 3‴-C***H₃***), 2.03 (6H, s, 2″-C***H₃***), 1.71 (4H, quintet, J_{vic} = 6.7 Hz, OCH_2CH_2***H₂***), 1.42 (4H, brs, $OCH_2CH_2CH_2$***H₂***), 1.36 (4H, brs, $OCH_2CH_2CH_2CH_2$***H₂***); ^{13}C NMR (100 MHz, DMSO-d_6): δ 169.07 (2‴-C=O), 167.29 (1″-C=O), 158.85 (C-3′), 146.09 (C=N), 142.64 (C-1′), 129.58 (C-6′), 116.80 (C-5′), 113.44 (C-4′), 111.37 (C-2′), 67.37 (O***C***H_2), 65.84 (C-2), 28.75 (OCH_2***C***H_2), 25.46 (OCH_2CH_2***C***H_2), 25.32 ($OCH_2CH_2CH_2$***C***H_2), 22.42 (3‴-***C***H_3), 21.78 (2″-***C***H_3); MS: *m*/*z* 691 (M + Na, 100%), 668 (M + 1, 51%), 625 (54%), 585 (21%), 571 (78%), 568 (19%), 526 (23%), 470 (16%), 452 (24%), 393 (13%), 369 (49%), 294 (9%), 221 (21%), 238 (9%), 179 (16%), 155 (28%), 116 (31%); Anal. Calc. for $C_{32}H_{40}O_6N_6S_2$: C, 57.48%, H, 5.98%, S, 9.58%, N, 12.57%; found: C, 57.26%, H, 5.94%, S, 9.61%, N, 12.45%.

4.20. Synthesis of N,N′-(5,5′-(3,3′-(decane-1,10-diylbis(oxy))bis(3,1-phenylene))bis(4-acetyl-4,5-dihydro-1,3,4-thiadiazole-5,2-diyl)) diacetamide 4f

The compound **4f** was prepared from the reaction of **3f** (0.5 g, 0.00095 mol) with acetic anhydride (25 ml) under the similar conditions as used earlier for **4a**.

4f: Yield (0.6 g, 77%), brown solid; m.p. 78–80 °C; IR (KBr): υ_{max} cm^{-1} 3160 (N–H), 3065 (aromatic C–H), 2934, 2856 (methylene C–H), 1697, 1639 (C=O), 1607 (C=N); UV–Vis (MeOH): λ_{max} (nm) 342, 271; ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.61 (2H, s, 1‴-N***H***), 7.19 (2H, t, *J* = 7.9 Hz, H-6′), 6.78 (2H, brs, H-5′), 6.76 (2H, s, H-2′), 6.74 (2H, d, J_m = 2.2 Hz, H-4′), 6.70 (2H, s, H-2), 3.90 (4H, t, J_{vic} = 6.4 Hz, OC***H₂***), 2.20 (6H, s, 3‴-C***H₃***), 2.03 (6H, s, 2″-C***H₃***), 1.71 (4H, quintet, J_{vic} = 6.7 Hz, OCH_2C***H₂***), 1.42 (4H, brs, OCH_2CH_2C***H₂***), 1.36 (8H, brs, $OCH_2CH_2CH_2$C***H₂***C***H₂***); ^{13}C NMR (100 MHz, DMSO-d_6): δ 169 (2‴-C=O), 167.32 (1″-C=O), 158.83 (C-3′), 146.19 (C=N), 142.48 (C-1′), 129.52 (C-6′), 116.85 (C-5′), 113.38 (C-4′), 111.37 (C-2′), 67.29 (O***C***H_2), 65.90 (C-2), 29.95 (OCH_2***C***H_2), 28.71 (OCH_2CH_2***C***H_2), 25.53 ($OCH_2CH_2CH_2$***C***H_2), 22.42 ($OCH_2CH_2CH_2CH_2$***C***H_2), 22.39 (3‴-***C***H_3), 21.73 (2″-***C***H_3); MS: *m*/*z* 719 (M + Na, 31%), 697 (M + 1, 82%), 655 (100%), 612 (11%), 598 (24%), 556 (18%), 554 (13%), 542 (22%), 327 (26%), 238 (8%), 221 (19%), 179 (8%), 155 (29%), 117 (13%), 116 (9%); Anal. Calc. for $C_{34}H_{44}O_6N_6S_2$, C, 58.62%, H, 6.32%, S, 9.19%, N, 12.06%; found: C, 58.85%, H, 6.36%, S, 9.22%, N, 12.02%.

4.21. Synthesis of N,N′-(5,5′-(3,3′-(dodecane-1,12-diylbis(oxy)) bis(3,1-phenylene))bis(4-acetyl-4,5-dihydro-1,3,4-thiadiazole-5,2-diyl)) diacetamide 4g

The compound **4g** was synthesized by treating bisthiosemicarbazone **3g** (0.5 g, 0.0009 mol) with acetic anhydride under the similar conditions as described earlier for **4a**.

4g: Yield (0.5 g, 77%), light brown solid; m.p. 64–66 °C; IR (KBr): υ_{max} cm^{-1} 3162 (N-H), 3065 (aromatic C-H), 2926, 2853 (methylene C-H), 1698, 1639 (C=O), 1606 (C=N); UV–Vis (MeOH): λ_{max} (nm) 343, 272; ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.54 (2H, s, 1‴-N***H***), 7.17 (2H, t, J_o = 7.9 Hz, H-6′), 6.77 (2H, d, J_m = 2.4 Hz, H-5′), 6.75 (2H, d, J_m = 3.6 Hz, H-4′), 6.72 (2H, brs, H-2′), 6.67 (2H, s, H-2), 3.88 (4H, t, J_{vic} = 6.4 Hz, OC***H₂***), 2.22 (6H, s, 3‴-C***H₃***), 2.03 (6H, s, 2″-C***H₃***), 1.69 (4H, quintet, J_{vic} = 6.4 Hz, OCH_2C***H₂***), 1.37 (4H, brs, OCH_2CH_2C***H₂***), 1.26 (12H, s, $OCH_2CH_2CH_2$C***H₂***C***H₂***C***H₂***); ^{13}C NMR (100 MHz, DMSO-d_6): δ 169.04 (2‴-C=O), 167.37 (1″-C=O), 158.87 (C-3′), 146.12 (C=N), 142.47 (C-1′), 129.51 (C-6′), 116.82 (C-5′), 113.39 (C-4′), 111.38 (C-2′), 67.39 (O***C***H_2), 65.91 (C-2), 28.98 (OCH_2***C***H_2), 28.82 (OCH_2CH_2***C***H_2), 28.70 ($OCH_2CH_2CH_2$***C***H_2), 25.50 ($OCH_2CH_2CH_2CH_2$***C***H_2), 24.22 ($OCH_2CH_2CH_2CH_2CH_2$***C***H_2), 22.38 (3‴-***C***H_3), 21.76 (2″-***C***H_3); MS: *m*/*z* 747 (M + Na, 28%), 725 (M + 1, 94%), 684 (40%), 683 (100%), 641 (20%), 624 (21%), 582 (10%), 568 (16%), 526 (24%), 508 (48%), 484 (9%), 467 (13%), 407 (11%), 390 (7%), 362 (4%), 334 (3%), 271 (5%), 238 (6%), 221 (14%), 179 (7%), 155 (22%), 116 (8%); Anal. Calc. for $C_{36}H_{48}O_6N_6S_2$, C, 59.66%, H, 6.62%, S, 8.83%, N, 11.60%; found: C, 59.43%, H, 6.65%, S, 8.86%, N, 11.56%.

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