Available online at www.derpharmachemica.com

Scholars Research Library

Der Pharma Chemica, 2012, 4(4):1458-1466
(http://derpharmachemica.com/archive.html)

ISSN 0975-413X
CODEN (USA): PCHHAX

Synthesis and antimicrobial studies of new thiadiazoline based symmetrical bisheterocyclics

Mohamad Yusuf* and Payal Jain

Department of Chemistry, Punjabi University, Patiala-147002, Punjab, India.

ABSTRACT

*The bisheterocyclic compounds **4a-4h** have been prepared in good yields from the cyclization of bisthiosemicarbazones **3a-3h** with acetic anhydride. The condensation reaction of bisacetophenones **2a-2h** with thiosemicarbazide in alcoholic medium provided **3a-3h** and the former were obtained from the O-alkylation of 4-hydroxyacetophenone with suitable 1,ω-dibromoalkanes under alkaline conditions in the presence of dry EtOH/DMF. The intermediates **3a-3h** and bisthiadiazolines **4a-4h** were also screened for their in vitro antimicrobial activities. Most of the compounds showed significant activity against the tested microorganisms.*

Key Words: bisacetophenones, O-alkylation, bisthiosemicarbazones, bisthiadiazolines,antimicrobial studies.

INTRODUCTION

Heterocycles bearing nitrogen and sulphur atoms constitute an important part of biologically significant compounds [1]. The heterocyclic products having three heteroatoms in the five membered ring have been synthesized in the past decades because of their broad range of pharmacological behaviors [2]. Thiadiazolines [3-10] belongs to the above category of heterocyclic compounds having wide spectrum of biological and technological applications [11]. These derivatives are also used as dyes, lubricant additives, vulcanization accelerators and large numbers of these compounds have been reported as fungicide, antiant, antiviral, antihypertensive, anticonvulsive, antitubercular [12,13] and bactericidal [14-18] agents. By keeping this aspect in view and in continuation of our researches on the heterocyclic compounds [19], present investigations have been focused on the synthesis and cyclization reaction of bisthiosemicarbazones **3a-3h** built around the alkyl chains of varying lengths. The major interest in these researches was to study the effect of the internal chain length upon the formation and antimicrobial behavior of the bisthiadiazolines **4a-4h**.

MATERIALS AND METHODS

2. Chemistry

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.

1,1'-(4,4'-(ethane-1,2-diylbis(oxy))bis(4,1-phenylene))diethanone 2a
A mixture of 4-hydroxyacetophenone (0.0147 mol, 2.0 g) and KOH (1.1 g, 0.0294 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 (1.381 g, 0.00735 mol) was added slowly. The reaction mixture was refluxed for 5 hrs, during which KBr was separated out. The solvent was removed in *vacuo* and the resulting mass 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**.

2a: Cream solid; Yield 70%; mp 60-62^{o}C. IR (KBr) cm^{-1} 1660 (C=O), 2951, 2882 (methylene C-H), 1251, 1038 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.95 (4H, dd, $J_{p,o}$=1.0, 8.3 Hz, H-2, 6), 6.98 (4H, td, $J_{p,o}$=1.0, 8.3 Hz, H-3, 5), 4.25 (4H, s, OC***H*****$_2$**), 2.55 (6H, s, C***H*****$_3$**); ^{13}C-NMR (DMSO-d_6): δ 196.78 (C=O), 162.72 (C-4), 130.63 (C-2, 6), 130.40 (C-1), 114.16 (C-3, 5), 64.40 (O***C***H$_2$), 26.37 (***C***H$_3$); MS(ESI): m/z (M+Na)$^+$ 321. Anal. Calc. for $C_{18}O_4H_{18}$: Calc. C, 72.48%; H, 6.04%; Found: C, 72.76%; H, 6.06%.

Similarly, other compounds were prepared by using above method.
1,1'-(4,4'-(propane-1,3-diylbis(oxy))bis(4,1-phenylene))diethanone 2b
2b: Cream solid; Yield 72%; mp 100-102^{o}C. IR (KBr) cm^{-1} 1663 (C=O), 2922, 2890 (methylene C-H), 1251, 1026 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.93 (4H, td, $J_{p,o}$=1.2, 8.2 Hz, H-2, 6), 6.95 (4H, td, $J_{p,o}$=1.2, 8.2 Hz, H-3, 5), 4.23 (4H, t, J_{vic} =6.0 Hz, OC***H*****$_2$**CH$_2$), 2.55 (6H, s, C***H*****$_3$**), 2.32 (2H, t, J_{vic} =6.0 Hz, OCH$_2$C***H*****$_2$**); ^{13}C-NMR (DMSO-d_6): δ 196.82 (C=O), 162.68 (C-4), 130.64 (C-2, 6), 130.45 (C-1), 114.14 (C-3, 5), 64.43 (O***C***H$_2$CH$_2$), 29.63 (OCH$_2$***C***H$_2$), 26.39 (***C***H$_3$); MS(ESI): m/z (M+1)$^+$ 313. Anal. Calc. for $C_{19}O_4H_{20}$: Calc. C, 73.07%; H, 6.41%; Found: C, 72.77%; H, 6.38%.

1,1'-(4,4'-(butane-1,4-diylbis(oxy))bis(4,1-phenylene))diethanone 2c
2c: Yellow solid; Yield 76%; mp 110-112^{o}C. IR (KBr) cm^{-1} 1660 (C=O), 2950, 2895 (methylene C-H), 1255, 1028 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.94 (4H, td, $J_{p,o}$=1.3, 8.0 Hz, H-2, 6), 6.93 (4H, td, $J_{p,o}$=1.3, 8.0 Hz, H-3, 5), 4.11 (4H, t, J_{vic}=4.9 Hz, OC***H*****$_2$**CH$_2$), 2.56 (6H, s, C***H*****$_3$**), 2.03 (2H, quintet, J_{vic}=2.8 Hz, OCH$_2$C***H*****$_2$**)**; ^{13}C-NMR (DMSO-d_6): δ 196.84 (C=O), 162.85 (C-4), 130.64 (C-2, 6), 130.31 (C-1), 114.11 (C-3, 5), 67.62 (O***C***H$_2$CH$_2$), 26.39 (OCH$_2$***C***H$_2$) 25.84 (***C***H$_3$); MS(ESI): m/z (M)$^+$ 326. Anal. Calc. for $C_{20}O_4H_{22}$: Calc. C, 73.61%; H, 6.74%; Found: C, 73.90%; H, 6.76%.

1,1'-(4,4'-(pentane-1,5-diylbis(oxy))bis(4,1-phenylene))diethanone 2d
2d: Yellow solid; Yield 68%; mp 70-72^{o}C. IR (KBr) cm^{-1} 1665 (C=O), 2958, 2860 (methylene C-H), 1250, 1030 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.90 (4H, dd, $J_{p,o}$=1.3, 8.2 Hz, H-2, 6), 6.91 (4H, dd, $J_{p,o}$=1.3, 8.2 Hz, H-3, 5), 4.10 (4H, t, J_{vic} = 6.4 Hz, OC***H*****$_2$**CH$_2$CH$_2$), 2.56 (6H, s, C***H*****$_3$**), 2.02 (2H, quintet, J_{vic}=6.4 Hz, OCH$_2$C***H*****$_2$**CH$_2$)**, 1.49 (2H, quintet, J_{vic}=3.6 Hz, OCH$_2$CH$_2$C***H*****$_2$**)**; ^{13}C-NMR (DMSO-d_6): δ 196.80 (C=O), 162.82 (C-4), 130.62 (C-2, 6), 130.30 (C-1), 114.12 (C-3, 5), 67.60 (O***C***H$_2$CH$_2$CH$_2$), 29.75 (OCH$_2$***C***H$_2$CH$_2$), 25.56 (OCH$_2$CH$_2$***C***H$_2$), 25.81 (***C***H$_3$); MS(ESI): m/z (M+Na)$^+$ 363. Anal. Calc. for $C_{21}O_4H_{24}$: Calc. C, 74.11%; H, 7.05%; Found: C, 74.40%; H, 7.08%.

1,1'-(4,4'-(hexane-1,6-diylbis(oxy))bis(4,1-phenylene))diethanone 2e
2e: Brown solid; Yield 79%; mp 80-82^{o}C. IR (KBr) cm^{-1} 1668 (C=O), 2948, 2870 (methylene C-H), 1264, 1026 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.93 (4H, td, $J_{p,o}$=1.4, 8.3 Hz, H-2, 6), 6.92 (4H, td, $J_{p,o}$=1.4, 8.3 Hz, H-3, 5), 4.04 (4H, t, J_{vic} =6.4 Hz, OC***H*****$_2$**CH$_2$CH$_2$), 2.56 (6H, s, C***H*****$_3$**), 1.85 (4H, quintet, J_{vic}=6.4 Hz, OCH$_2$C***H*****$_2$**CH$_2$)**, 1.56 (2H, quintet, J_{vic}=3.6 Hz, OCH$_2$CH$_2$C***H*****$_2$**)**; ^{13}C-NMR (DMSO-d_6): δ 196.82 (C=O), 162.81 (C-4), 130.59 (C-2, 6), 130.28 (C-1), 114.11 (C-3, 5), 67.40 (O***C***H$_2$CH$_2$CH$_2$), 29.72 (OCH$_2$***C***H$_2$CH$_2$), 25.58 (OCH$_2$CH$_2$***C***H$_2$), 25.81 (***C***H$_3$); MS(ESI): m/z (M+1)$^+$ 355. Anal. Calc. for $C_{22}O_4H_{26}$: Calc. C, 74.57%; H, 7.34%; Found: C, 74.27%; H, 7.31%.

1,1'-(4,4'-(octane-1,8-diylbis(oxy))bis(4,1-phenylene))diethanone 2f
2f: Yellow solid; Yield 82%; mp 84-86^{o}C. IR (KBr) cm^{-1} 1670 (C=O), 2915, 2851 (methylene C-H), 1264, 1027 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.91 (4H, dd, $J_{p,o}$= 1.4, 8.8 Hz, H-2, 6), 6.92 (4H, dd, $J_{p,o}$= 1.4, 8.8 Hz, H-3, 5), 4.03 (4H, t, J_{vic}=6.4 Hz, OC***H*****$_2$**CH$_2$CH$_2$CH$_2$), 2.55 (6H, s, C***H*****$_3$**), 1.81 (4H, quintet, J_{vic}=6.4 Hz, OCH$_2$C***H*****$_2$**CH$_2$CH$_2$)**, 1.48 (4H, quintet, J_{vic}=6.4 Hz, OCH$_2$CH$_2$C***H*****$_2$**CH$_2$)**, 1.41 (4H, quintet, J_{vic}=3.5 Hz, OCH$_2$CH$_2$CH$_2$C***H*****$_2$**)**; ^{13}C-NMR (DMSO-d_6): δ 196.87 (C=O), 163.09 (C-4), 130.61 (C-2, 6), 130.12 (C-1), 114.12 (C-3, 5), 68.18 (O***C***H$_2$CH$_2$CH$_2$CH$_2$), 29.08 (OCH$_2$***C***H$_2$CH$_2$CH$_2$), 26.37 (OCH$_2$CH$_2$***C***H$_2$CH$_2$), 25.93

($OCH_2CH_2CH_2\boldsymbol{C}H_2$), 25.26 ($\boldsymbol{C}H_3$); MS(ESI): m/z M^+ 382. Anal. Calc. for $C_{24}O_4H_{30}$: Calc. C, 75.39%; H, 7.85%; Found: C, 75.69%; H, 7.88%.

1,1'-(4,4'-(docane-1,10-diylbis(oxy))bis(4,1-phenylene))diethanone 2g

2g: Yellow solid; Yield 73%; mp 98-100°C. IR (KBr) cm^{-1} 1672 (C=O), 2936, 2875 (methylene C-H), 1259, 1048 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.92 (4H, dt, $J_{p,o}$= 1.2, 8.0 Hz, H-2, 6), 6.92 (4H, dt, $J_{p,o}$=1.2, 8.0 Hz, H-3, 5), 4.01 (4H, t, J_{vic}=6.5 Hz, $OC\boldsymbol{H_2}CH_2CH_2CH_2CH_2$), 2.55 (6H, s, $C\boldsymbol{H_3}$), 1.82 (4H, quintet, J_{vic}=6.5 Hz, $OCH_2C\boldsymbol{H_2}CH_2CH_2CH_2$**),** 1.44 (4H, quintet, J_{vic}=6.5 Hz, $OCH_2CH_2C\boldsymbol{H_2}CH_2CH_2$**),** 1.34 (8H, m, $OCH_2CH_2CH_2C\boldsymbol{H_2}C\boldsymbol{H_2}$); ^{13}C-NMR (DMSO-$d_6$): δ 196.78 (C=O), 162.66 (C-4), 130.65 (C-2, 6), 130.05 (C-1), 114.10 (C-3, 5), 68.14 ($O\boldsymbol{C}H_2CH_2CH_2CH_2CH_2$), 29.66 ($OCH_2\boldsymbol{C}H_2CH_2CH_2CH_2$), 29.60 ($OCH_2CH_2\boldsymbol{C}H_2CH_2CH_2$), 29.20 ($OCH_2CH_2CH_2\boldsymbol{C}H_2CH_2$), 26.80 ($OCH_2CH_2CH_2CH_2\boldsymbol{C}H_2$), 25.25 ($\boldsymbol{C}H_3$); MS(ESI): m/z $(M+Na)^+$ 433. Anal. Calc. for $C_{26}O_4H_{34}$: Calc. C, 76.09%; H, 8.29%; Found: C, 76.39%; H, 8.32%.

2h: Yellow solid; Yield 76%; mp 92-94°C. IR (KBr) cm^{-1} 1676 (C=O), 2938, 2877 (methylene C-H), 1254, 1031 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.93 (4H, dd, $J_{p,o}$= 1.1, 8.1 Hz, H-2, 6), 6.92 (4H, dd, $J_{p,o}$=1.1, 8.1 Hz, H-3, 5), 4.00 (4H, t, J_{vic}=6.5 Hz, $OC\boldsymbol{H_2}CH_2CH_2CH_2CH_2CH_2$), 2.55 (6H, s, $C\boldsymbol{H_3}$), 1.80 (4H, t, J_{vic}=6.5 Hz, $OCH_2C\boldsymbol{H_2}CH_2CH_2CH_2CH_2$), 1.44 (4H, quintet, J_{vic}=6.5 Hz, $OCH_2CH_2C\boldsymbol{H_2}CH_2CH_2CH_2$), 1.32 (12H, m, $OCH_2CH_2CH_2C\boldsymbol{H_2}C\boldsymbol{H_2}C\boldsymbol{H_2}$); ^{13}C-NMR (DMSO-$d_6$): δ 196.88 (C=O), 163.13 (C-4), 130.60 (C-2, 6), 130.09 (C-1), 114.13 (C-3, 5), 68.26 ($O\boldsymbol{C}H_2CH_2$ $CH_2CH_2CH_2CH_2$), 29.59 ($OCH_2\boldsymbol{C}H_2CH_2CH_2CH_2CH_2$), 29.55 ($OCH_2CH_2\boldsymbol{C}H_2CH_2CH_2CH_2$), 29.36 ($OCH_2CH_2CH_2\boldsymbol{C}H_2CH_2CH_2$), 29.11 ($OCH_2CH_2CH_2CH_2\boldsymbol{C}H_2CH_2$), 26.37 ($OCH_2CH_2CH_2CH_2CH_2\boldsymbol{C}H_2$), 25.99 ($\boldsymbol{C}H_3$); MS(ESI): m/z $(M+Na)^+$ 461. Anal. Calc. for $C_{28}O_4H_{38}$: Calc. C, 76.71%; H, 8.67%; Found: C, 77.02%; H, 8.70%.

2.2.1 Synthesis of 2,2'-(1,1'-(4,4'-(ethane-1,2-diylbis(oxy))bis(4,1-phenylene))bis(ethan-1-yl-1-ylidene))bis (hydrazinecarbothioamide) 3a

A mixture of bisacetophenone **2a** (1.0 g, 0.0033 mol) and thiosemicarbazide (0.61 g, 0.0067 mol) in dry EtOH (20 ml) and HCl (1.0 ml) was refluxed for 6 hrs. After the completion of reaction, the reaction mixture was cooled in an ice bath to provide a solid substance which was filtered under suction. The resulting crude product was crystallized from MeOH to yield pure bisthiosemicarbazone **3a**.

3a: Yellow solid; Yield 72%; mp 154-156°C. IR (KBr) cm^{-1} 3366 & 3210 (NH_2), 3158 (NH), 2956, 2888 (methylene C-H), 1606 (C=N), 1250, 1032 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.96 (2H, s, 3-N$\boldsymbol{H}$), 8.05 (2H, brs, N$\boldsymbol{H}$-α), 7.75 (4H, d, J_o=8.2 Hz, H-2', 6'), 7.63 (2H, brs, N$\boldsymbol{H}$-β), 6.92 (4H, d, J_o=8.2 Hz, H-3', 5'), 4.22 (4H, s, $OC\boldsymbol{H_2}$), 2.25 (2H, s, $C\boldsymbol{H_3}$-1); ^{13}C-NMR (DMSO-d_6): δ 178.59 (C-4), 159.38 (C-4'), 147.35 (C-1), 129.87 (C-1'), 127.62 (C-2', 6'), 113.88 (C-3', 5'), 63.88 ($O\boldsymbol{C}H_2$), 13.62 ($\boldsymbol{C}H_3$); MS(ESI): m/z $(M+1)^+$ 445. Anal. Calc. for $C_{20}O_2N_6S_2H_{24}$: Calc. C, 54.05 %; H, 5.40%; N, 18.91%; S, 14.41%; Found: C, 55.26 %; H, 5.37%; N, 18.83%; S, 14.35%.

Similarly, other compounds were synthesized as described above.

2,2'-(1,1'-(4,4'-(propane-1,3-diylbis(oxy))bis(4,1-phenylene))bis(ethan-1-yl-1-ylidene))bis(hydrazinecarbothio -amide) 3b

3b: Yellow solid; Yield 74%; mp 136-138°C. IR (KBr) cm^{-1} 3392 & 3207 (NH_2), 3138 (NH), 2953, 2850 (methylene C-H), 1600 (C=N), 1252, 1061 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.98 (2H, s, 3-N$\boldsymbol{H}$), 8.08 (2H, brs, N$\boldsymbol{H}$-α), 7.78 (4H, d, J_o=8.8 Hz, H-2', 6'), 7.64 (2H, brs, N$\boldsymbol{H}$-β), 6.92 (4H, d, J_o=8.8 Hz, H-3', 5'), 4.20 (4H, t, J_{vic}=6.1 Hz, $OC\boldsymbol{H_2}CH_2$), 2.56 (2H, quintet, J_{vic}=6.2 Hz, $OCH_2C\boldsymbol{H_2}$), 2.29 (6H, s, $C\boldsymbol{H_3}$-1); ^{13}C-NMR (DMSO-d_6): δ 178.56 (C-4), 159.41 (C-4'), 147.50 (C-1), 129.94 (C-1'), 127.65 (C-2', 6'), 113.84 (C-3', 5'), 63.97 ($O\boldsymbol{C}H_2CH_2$), 28.57 ($OCH_2\boldsymbol{C}H_2$), 13.66 ($\boldsymbol{C}H_3$); MS(ESI): m/z $(M)^+$ 458. Anal. Calc. for $C_{21}O_2N_6S_2H_{26}$: Calc. C, 55.02%; H, 5.67%; N, 18.34%; S, 13.97% Found: C, 55.24%; H, 5.69%; N, 18.41%; S, 13.91%.

2,2'-(1,1'-(4,4'-(butane-1,4-diylbis(oxy))bis(4,1-phenylene))bis(ethan-1-yl-1-ylidene))bis(hydrazinecarbothio - amide) 3c

3c: Yellow solid; Yield 73%; mp 257-259°C. IR (KBr) cm^{-1} 3380 & 3219 (NH_2), 3147 (NH), 2958, 2870 (methylene C-H), 1598 (C=N), 1250, 1065 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.99 (2H, s, 3-N$\boldsymbol{H}$), 8.09 (2H, brs, N$\boldsymbol{H}$-α), 7.74 (4H, d, J_o=8.8, Hz, H-2', 6'), 7.65 (2H, brs, N$\boldsymbol{H}$-β), 6.84 (4H, d, J_o=8.8 Hz, H-3', 5'), 4.03 (4H, t, J_{vic}=6.3 Hz, $OC\boldsymbol{H_2}CH_2$), 2.25 (2H, s, $C\boldsymbol{H_3}$-1), 1.92 (4H, quintet, J_{vic}=6.3 Hz, $OCH_2C\boldsymbol{H_2}$); ^{13}C-NMR (DMSO-d_6): δ 178.50 (C-4), 159.35 (C-4'), 147.56 (C-1), 129.91 (C-1'), 127.69 (C-2', 6'), 113.89 (C-3', 5'), 63.80 ($O\boldsymbol{C}H_2CH_2$), 28.60

($OCH_2\boldsymbol{C}H_2$), 13.63 ($\boldsymbol{C}H_3$); MS(ESI): m/z $(M+1)^+$ 473. Anal. Calc. for $C_{22}O_2N_6S_2H_{28}$: Calc. C, 55.93%; H, 5.93%; N, 17.79%; S, 13.55%; Found: C, 56.15%; H, 5.95%; N, 17.86%; S, 13.60%.

2,2'-(1,1'-(4,4'-(pentane-1,5-diylbis(oxy))bis(4,1-phenylene))bis(ethan-1-yl-1-ylidene))bis(hydrazinecarbothio -amide) 3d

3d: Yellow solid; Yield 80%; mp 190-192°C. IR (KBr) cm^{-1} 3391 & 3214 (NH_2), 3140 (NH), 2935, 2865 (methylene C-H), 1595 (C=N), 1251, 1088 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.94 (2H, s, 3-N***H***), 8.04 (2H, brs, N***H***-α), 7.78 (4H, d, J_o=8.6 Hz, H-2', 6'), 7.61 (2H, brs, N***H***-β), 6.86 (4H, d, J_o=8.6 Hz, H-3', 5'), 4.03 (4H, t, J_{vic}=6.1 Hz, OC***H*****$_2$**CH_2CH_2), 2.24 (6H, s, C***H*****$_3$**-1), 1.80 (4H, quintet, J_{vic}=6.7 Hz, OCH_2C***H*****$_2$**CH_2), 1.61 (2H, quintet, J_{vic}=6.7 Hz, OCH_2CH_2C***H*****$_2$**); ^{13}C-NMR (DMSO-d_6): δ 178.95 (C-4), 160.21 (C-4'), 147.63 (C-1), 129.73 (C-2', 6'), 127.63 (C-1'), 113.81 (C-3', 5'), 67.28 ($O\boldsymbol{C}H_2CH_2CH_2$), 28.37 ($OCH_2\boldsymbol{C}H_2CH_2$), 22.17 ($OCH_2CH_2\boldsymbol{C}H_2$), 13.67 ($\boldsymbol{C}H_3$); MS(ESI): m/z $(M)^+$ 486. Anal. Calc. for $C_{23}O_2N_6S_2H_{30}$: Calc. C, 56.79%; H, 6.17%; N, 17.28%; S, 13.16% Found: C, 56.56%; H, 6.19%; N, 17.34%; S, 13.10%.

2,2'-(1,1'-(4,4'-(hexane-1,6-diylbis(oxy))bis(4,1-phenylene))bis(ethan-1-yl-1-ylidene))bis(hydrazinecarbothio - amide) 3e

3e: Brown solid; Yield 65 %, mp 248-250°C. IR (KBr) cm^{-1} 3364 & 3210 (NH_2), 3145 (NH), 2938, 2867 (methylene C-H), 1598 (C=N), 1251, 1086 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.97 (2H, s, 3-N***H***), 8.08 (2H, brs, N***H***-α), 7.74 (4H, d, J_o=8.8 Hz, H-2', 6'), 7.64 (2H, brs, N***H***-β), 6.83 (4H, d, J_o=8.8 Hz, H-3', 5'), 3.96 (4H, t, J_{vic}=6.3 Hz, OC***H*****$_2$**CH_2CH_2), 2.24 (6H, s, C***H*****$_3$**-1), 1.75 (4H, quintet, J_{vic}=6.0 Hz, OCH_2C***H*****$_2$**CH_2), 1.49 (4H, quintet, J_{vic}=6.0 Hz, OCH_2CH_2C***H*****$_2$**); ^{13}C-NMR (DMSO-d_6): δ 178.57 (C-4), 159.65 (C-4'), 147.56 (C-1), 129.73 (C-1'), 127.67 (C-2', 6'), 113.80 (C-3', 5'), 67.30 ($O\boldsymbol{C}H_2CH_2CH_2$), 28.55 ($OCH_2\boldsymbol{C}H_2CH_2$), 25.27 ($OCH_2CH_2\boldsymbol{C}H_2$), 13.68 ($\boldsymbol{C}H_3$); MS(ESI): m/z M^+ 500. Anal.Calc. for $C_{24}O_2N_6S_2H_{32}$: Calc. C, 57.60%; H, 6.40%; N, 16.80%; S, 12.80% Found: C, 57.83%; H, 6.42%; N, 16.73%; S, 12.85%.

2,2'-(1,1'-(4,4'-(octane-1,8-diylbis(oxy))bis(4,1-phenylene))bis(ethan-1-yl-1-ylidene))bis(hydrazinecarbothio - amide) 3f

3f: Yellow solid; Yield 76 %; mp 200-202°C. IR (KBr) cm^{-1} 3350 & 3222 (NH_2), 3149 (NH), 2933, 2844 (methylene C-H), 1599 (C=N), 1250, 1042 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.97 (2H, s, 3-N***H***), 8.08 (2H, brs, N***H***-α), 7.75 (4H, d, J_o=8.8 Hz, H-2', 6'), 7.64 (2H, brs, N***H***-β), 6.86 (4H, d, J_o=8.8 Hz, H-3', 5'), 3.98 (4H, t, J_{vic}=6.4 Hz, OC***H*****$_2$**$CH_2CH_2CH_2$), 2.29 (2H, s, C***H*****$_3$**-1), 1.77 (4H, quintet, J_{vic}=6.7 Hz, OCH_2C***H*****$_2$**CH_2CH_2), 1.47 (4H, m, OCH_2CH_2C***H*****$_2$**CH_2), 1.39 (4H, m, $OCH_2CH_2CH_2C$***H*****$_2$**); ^{13}C-NMR (DMSO-d_6): δ 178.52 (C-4), 159.60 (C-4'), 147.59 (C-1), 129.75 (C-1'), 127.64 (C-2',6'), 113.80 (C-3',5'), 67.26 ($O\boldsymbol{C}H_2CH_2CH_2CH_2$), 28.59 ($OCH_2\boldsymbol{C}H_2CH_2CH_2$), 25.48 ($OCH_2CH_2\boldsymbol{C}H_2CH_2$), 25.27 ($OCH_2CH_2CH_2\boldsymbol{C}H_2$), 13.69 ($\boldsymbol{C}H_3$); MS(ESI): m/z M^+ 528. Anal. Calc. for $C_{26}O_2N_6S_2H_{36}$: Calc. C, 59.09%; H, 6.81%; N, 15.90%; S, 12.12% Found: C, 59.32%; H, 6.84%; N, 15.96%; S, 12.16%.

2,2'-(1,1'-(4,4'-(decane-1,10-diylbis(oxy))bis(4,1-phenylene))bis(ethan-1-yl-1-ylidene))bis(hydrazinecarbothio -amide) 3g

3g: Yellow solid; Yield 68%; mp 188-190°C. IR (KBr) cm^{-1} 3359 & 3228 (NH_2), 3145 (NH), 2938, 2851 (methylene C-H), 1598 (C=N), 1252, 1044 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.94 (2H, s, 3-N***H***), 8.05 (2H, brs, N***H***-α), 7.76 (4H, d, J_o=8.8 Hz, H-2', 6'), 7.62 (2H, brs, N***H***-β), 6.88 (4H, d, J_o=8.8 Hz, H-3', 5'), 3.99 (4H, t, J_{vic}=6.4 Hz, OC***H*****$_2$**$CH_2CH_2CH_2CH_2$), 2.29 (2H, s, C***H*****$_3$**-1), 1.79 (4H, quintet, J_{vic}=6.4 Hz, OCH_2C***H*****$_2$**$CH_2CH_2CH_2$), 1.45 (4H, m, OCH_2CH_2C***H*****$_2$**CH_2CH_2), 1.34 (8H, m, $OCH_2CH_2CH_2C$***H*****$_2$**C***H*****$_2$**); ^{13}C-NMR (DMSO-d_6): δ 178.13 (C-4), 160.04 (C-4'), 147.98 (C-1), 127.57 (C-2', 6'), 129.79 (C-1'), 113.78 (C-3', 5'), 67.43 ($O\boldsymbol{C}H_2CH_2CH_2CH_2CH_2$), 28.87 ($OCH_2\boldsymbol{C}H_2CH_2CH_2CH_2$), 28.74 ($OCH_2CH_2\boldsymbol{C}H_2CH_2CH_2$), 28.62 ($OCH_2CH_2CH_2\boldsymbol{C}H_2CH_2$), 25.43 ($OCH_2CH_2CH_2CH_2\boldsymbol{C}H_2$), 13.62 ($\boldsymbol{C}H_3$); MS(ESI): m/z $(M+Na)^+$ 579. Anal.Calc. for $C_{28}O_2N_6S_2H_{40}$: Calc. C, 60.43%; H, 7.19%; N, 15.10%; S, 11.51% Found: C, 60.67%; H, 7.16%; N, 15.03%; S, 11.46%..

2,2'-(1,1'-(4,4'-(dodecane-1,12-diylbis(oxy))bis(4,1-phenylene))bis(ethan-1-yl-1-ylidene))bis(hydrazinecarbo - thioamide) 3h

3h: Yellow solid; Yield 64%; mp 182-184°C. IR (KBr) cm^{-1} 3370 & 3254 (NH_2), 3155 (NH), 2952, 2884 (methylene C-H), 1601 (C=N), 1242, 1034 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.00 (2H, s, 3-N***H***), 8.10 (2H, brs, N***H***-α), 7.74 (4H, d, J_o=8.9 Hz, H-2', 6'), 7.67 (2H, brs, N***H***-β), 6.84 (4H, d, J_o=8.9 Hz, H-3', 5'), 3.93 (4H, t, J_{vic}=6.4 Hz, OC***H*****$_2$**$CH_2CH_2CH_2CH_2CH_2$), 2.25 (2H, s, C***H*****$_3$**-1), 1.70 (4H, quintet, J_{vic}=6.4 Hz, OCH_2C***H*****$_2$**$CH_2CH_2CH_2CH_2$), 1.40 (4H, m, OCH_2CH_2C***H*****$_2$**$CH_2CH_2CH_2$), 1.29 (12H, m, $OCH_2CH_2CH_2C$***H*****$_2$**C***H*****$_2$**C***H*****$_2$**);

^{13}C-NMR (DMSO-d_6): δ 178.15 (C-4), 159.67 (C-4'), 147.94 (C-1), 127.54 (C-2',6'), 129.80 (C-1'), 113.56 (C-3',5'), 67.55 (O***C***H$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$), 28.89 OCH$_2$***C***H$_2$CH$_2$CH$_2$CH$_2$CH$_2$), 28.70 (OCH$_2$CH$_2$***C***H$_2$CH$_2$CH$_2$CH$_2$), 28.52 (OCH$_2$CH$_2$CH$_2$***C***H$_2$CH$_2$CH$_2$), 27.98 (OCH$_2$CH$_2$CH$_2$CH$_2$***C***H$_2$CH$_2$), 25.33 (OCH$_2$CH$_2$CH$_2$CH$_2$CH$_2$***C***H$_2$), 13.65 (***C***H$_3$); MS(ESI): m/z (M+1)$^+$ 585. Anal.Calc. for $C_{30}O_2N_6S_2H_{44}$: Calc. C, 61.64%; H, 7.53%; N, 14.38%; S, 10.95% Found: C, 61.88%; H, 7.49%; N, 14.32%; S, 10.99%.

2.3.1 Synthesis of *N,N'*-(5,5'-(4,4'-(ethane-1,2-diylbis(oxy))bis(4,1-phenylene))bis(4-acetyl-5-methyl-4,5-dihydro-1,3,4-thiadiazole-5,2-diyl))diacetamide 4a

A mixture of bisthiosemicarbazone **3a** (1.0 g, 0.0023 mol) and acetic anhydride (30 ml) was refluxed for 10 hrs. 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 bisthiadiazoline **4a**.

4a: Brown solid; Yield 64%; mp 140-142^{o}C. IR (KBr) cm^{-1} 3205 (NH), 2956, 2909 (methylene C-H), 1684, 1637 (C=O), 1604 (C=N), 1245, 1048 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 11.25 (2H, s, 1'-N***H***), 7.18 (4H, d, J_o=8.7 Hz , H-2''', 6'''), 6.80 (4H, d, J_o=8.7 Hz, H-3''', 5'''), 4.18 (4H, s, J_{vic}=6.1 Hz, OC***H$_2$***), 2.29 (6H, s, 2''-C***H$_3$***), 2.22 (6H, s, 3'-C***H$_3$***), 2.10 (2H, s, 2-C***H$_3$***); ^{13}C-NMR (DMSO-d_6): δ 169.23 (1''-C=O), 168.84 (2'-C=O), 158.48 (C-4'''), 146.80 (C-5), 133.59 (C-1'''), 127.09 (C-2''', 6'''), 114.26 (C-3''', 5'''), 67.78 (C-2), 67.44 (O***C***H$_2$), 25.24 (2''-***C***H$_3$), 22.13 (3'-***C***H$_3$), 20.83 (2-***C***H$_3$); MS(ESI): m/z (M+Na)$^+$ 635. Anal. Calc. for $C_{28}O_6N_6S_2H_{32}$: Calc. C, 54.90%; H, 3.59%; N, 13.72%; S, 10.45%; Found: C, 54.68%; H, 3.60%; N, 13.77%; S, 10.40 %.

Similarly, other compounds were obtained as described above.

***N,N'*-(5,5'-(4,4'-(propane-1,3-diylbis(oxy))bis(4,1-phenylene))bis(4-acetyl-5-methyl-4,5-dihydro-1,3,4-thiadi -azole-5,2-diyl))diacetamide 4b**

4b: Brown solid; Yield 66%; mp 98-100^{o}C. IR (KBr) cm^{-1} 3209 (NH), 2963, 2901 (methylene C-H), 1688, 1644 (C=O), 1602 (C=N), 1238, 1049 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 11.38 (2H, s, 1'-N***H***), 7.25 (4H, d, J_o=8.7 Hz , H-2''', 6'''), 6.86 (4H, d, J_o=8.7 Hz, H-3''', 5'''), 3.99 (4H, t, J_{vic}=6.1 Hz, OC***H$_2$***CH$_2$), 2.24 (6H, s, 2''-C***H$_3$***), 2.19 (2H, quintet, J_{vic}=6.1 Hz, OCH$_2$C***H$_2$***), 2.16 (6H, s, 3'-C***H$_3$***), 2.08 (2H, s, 2-C***H$_3$***); ^{13}C-NMR (DMSO-d_6): δ 169.50 (1''-C=O), 168.00 (2'-C=O), 158.12 (C-4'''), 146.11 (C-5), 133.14 (C-1'''), 127.17 (C-2''', 6'''), 114.64 (C-3''', 5'''), 67.49 (C-2), 66.80 (O***C***H$_2$CH$_2$), 28.19 (OCH$_2$***C***H$_2$), 25.39 (2''-***C***H$_3$), 22.77 (3'-***C***H$_3$), 20.68 (2-***C***H$_3$); MS(ESI): m/z (M)$^+$ 626. Anal. Calc. for $C_{29}O_6N_6S_2H_{34}$: Calc. C, 55.59%; H, 5.43%; N, 13.41%; S, 10.22%; Found: C, 55.81%; H, 5.40%; N, 13.46%, S, 10.17%.

***N,N'*-(5,5'-(4,4'-(butane-1,4-diylbis(oxy))bis(4,1-phenylene))bis(4-acetyl-5-methyl-4,5-dihydro-1,3,4-thiadi-azole-5,2-diyl))diacetamide 4c**

4c: Brown solid; Yield 70%; mp 158-160^{o}C. IR (KBr) cm^{-1} 3202 (NH), 2960, 2914 (methylene C-H), 1683, 1648 (C=O), 1603 (C=N), 1228, 1042 (C-O); ^{1}H-NMR(400 MHz, DMSO-d_6): δ 11.44 (2H, s, 1'-N***H***), 7.15 (4H, d, J_o=8.6 Hz, H-2''', 6'''), 6.75 (4H, d, J_o=8.6 Hz, H-3''', 5'''), 4.11 (4H, t, J_{vic}=6.4 Hz, OC***H$_2$***CH$_2$), 2.20 (6H, s, 2''-C***H$_3$***), 2.11 (6H, s, 3'-C***H$_3$***), 2.04 (2H, s, 2-C***H$_3$***), 2.00 (4H, quintet, J_{vic}=6.4 Hz, OCH$_2$C***H$_2$***); ^{13}C-NMR (DMSO-d_6): δ 168.94 (1''-C=O), 168.28 (2'-C=O), 158.02 (C-4'''), 146.23 (C-5), 132.86 (C-1'''), 127.28 (C-2''', 6'''), 112.39 (C-3''', 5'''), 67.58 (C-2), 66.93 (O***C***H$_2$CH$_2$), 29.38 (OCH$_2$***C***H$_2$), 24.94 (2''-***C***H$_3$), 21.80 (3'-***C***H$_3$), 20.54 (2-***C***H$_3$); MS(ESI): m/z (M+Na)$^+$ 663. Anal. Calc. for $C_{30}O_6N_6S_2H_{36}$: Calc. C, 56.25%; H, 5.62%; N, 13.12%, S, 10.00%; Found: C, 56.47%; H, 5.64%; N, 13.17%, S, 10.04%.

***N,N'*-(5,5'-(4,4'-(pentane-1,5-diylbis(oxy))bis(4,1-phenylene))bis(4-acetyl-5-methyl-4,5-dihydro-1,3,4-thiadi-azole-5,2-diyl))diacetamide 4d**

4d: Brown solid; Yield 65%; mp 119-121^{o}C. IR (KBr) cm^{-1} 3210 (NH), 2968, 2932 (methylene C-H), 1680, 1641 (C=O), 1601 (C=N), 1230, 1048 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 11.48 (2H, s, 1'-N***H***), 7.22 (4H, d, J_o=8.6 Hz, H-2''', 6'''), 6.78 (4H, d, J_o=8.6 Hz, H-3''', 5'''), 4.08 (4H, t, J_{vic}=6.4 Hz, OC***H$_2$***CH$_2$CH$_2$), 2.21 (6H, s, 2''-C***H$_3$***), 2.14 (6H, s, 3'-C***H$_3$***), 2.10 (2H, s, 2-C***H$_3$***), 1.98 (4H, quintet, J_{vic}=6.4 Hz, OCH$_2$C***H$_2$***CH$_2$), 1.79 (2H, quintet, J_{vic}=6.4 Hz, OCH$_2$CH$_2$C***H$_2$***); ^{13}C-NMR (DMSO-d_6): δ 168.76 (1''-C=O), 168.09 (2'-C=O), 157.18 (C-4'''), 145.73 (C-5), 131.72 (C-1'''), 126.49 (C-2''', 6'''), 112.09 (C-3''', 5'''), 66.92 (C-2), 66.83 (O***C***H$_2$CH$_2$CH$_2$), 28.25 (OCH$_2$***C***H$_2$CH$_2$), 24.86 (OCH$_2$CH$_2$***C***H$_2$), 24.58 (2''-***C***H$_3$), 21.73 (3'-***C***H$_3$), 20.10 (2-***C***H$_3$); MS(ESI): m/z (M+1)$^+$ 655. Anal. Calc. for $C_{31}O_6N_6S_2H_{38}$: Calc. C, 56.88%; H, 5.81%; N, 12.84%, S, 9.78%; Found: C, 57.10%; H, 5.83%; N, 12.78%, S, 9.81%.

***N,N'*-(5,5'-(4,4'-(hexane-1,6-diylbis(oxy))bis(4,1-phenylene))bis(4-acetyl-5-methyl-4,5-dihydro-1,3,4-thiadia -zole-5,2-diyl))diacetamide 4e**

4e: Brown solid; Yield 68%; mp 139-141^{o}C. IR (KBr) cm^{-1} 3214 (NH), 2969, 2936 (methylene C-H), 1677, 1647 (C=O), 1603 (C=N), 1228, 1038 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 11.30 (2H, s, 1'-N***H***), 7.10 (4H, d, *J*=8.7 Hz, H-2''', 6'''), 6.70 (4H, d, J_o=8.7 Hz, H-3''', 5'''), 4.02 (4H, t, J_{vic}=6.4 Hz, OC***H*****$_2$**CH$_2$CH$_2$), 2.26 (6H, s, 2''-C***H*****$_3$**), 2.18 (6H, s, 3'-C***H*****$_3$**), 2.09 (2H, s, 2-C***H*****$_3$**), 1.89 (4H, quintet, J_{vic}=6.4 Hz, OCH$_2$C***H*****$_2$**CH$_2$), 1.60 (4H, quintet, J_{vic}=6.4 Hz, OCH$_2$CH$_2$C***H*****$_2$**); ^{13}C-NMR (DMSO-d_6): δ 168.50 (1''-C=O), 166.89 (2'-C=O), 157.25 (C-4'''), 145.59 (C-5), 130.84 (C-1'''), 126.82 (C-2''', 6'''), 113.86 (C-3''', 5'''), 66.80 (C-2), 66.68 (O***C***H$_2$CH$_2$CH$_2$), 28.13 (OCH$_2$***C***H$_2$CH$_2$), 24.56 (OCH$_2$CH$_2$***C***H$_2$), 24.38 (2''-***C***H$_3$), 21.60 (3'-***C***H$_3$), 20.16 (2-***C***H$_3$); MS(ESI): m/z (M+Na)$^+$ 691. Anal. Calc. for $C_{32}O_6N_6S_2H_{40}$: Calc. C, 57.48%; H, 5.98%; N, 12.57%, S, 9.58%; Found: C, 57.25%; H, 5.95%; N, 12.51%, S, 9.54%.

***N,N'*-(5,5'-(4,4'-(octane-1,8-diylbis(oxy))bis(4,1-phenylene))bis(4-acetyl-5-methyl-4,5-dihydro-1,3,4-thiadi -azole-5,2-diyl))diacetamide 4f**

4f: Brown solid; Yield 69%; mp 131-133^{o}C. IR (KBr) cm^{-1} 3218 (NH), 2958, 2954 (methylene C-H), 1688, 1643 (C=O), 1602 (C=N), 1250, 1019 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 11.40 (2H, s, 1'-N***H***), 7.20 (2H, d, J_o=8.7 Hz, H-2''', 6'''), 6.77 (4H, d, J_o=8.7 Hz, H-3''', 5'''), 3.90 (4H, t, J_{vic}=6.4 Hz, OC***H*****$_2$**CH$_2$CH$_2$CH$_2$), 2.27 (6H, s, 2''-C***H*****$_3$**), 2.13 (6H, s, 3'-C***H*****$_3$**), 2.05 (2H, s, 2-C***H*****$_3$**), 1.82 (4H, quintet, J_{vic}=6.4 Hz, OCH$_2$C***H*****$_2$**CH$_2$CH$_2$), 1.40 (4H, m, OCH$_2$CH$_2$C***H*****$_2$**CH$_2$), 1.32 (4H, m, OCH$_2$CH$_2$CH$_2$C***H*****$_2$**); ^{13}C-NMR (DMSO-d_6): δ 168.59 (1''-C=O), 166.53 (2'-C=O), 156.13 (C-4'''), 144.23 (C-5), 130.64 (C-1'''), 126.47 (C-2''', 6'''), 112.80 (C-3''', 5'''), 67.23 (O***C***H$_2$CH$_2$CH$_2$CH$_2$), 63.63 (C-2), 27.19 (OCH$_2$***C***H$_2$CH$_2$CH$_2$), 25.69 (OCH$_2$CH$_2$***C***H$_2$CH$_2$), 24.11 (OCH$_2$CH$_2$CH$_2$***C***H$_2$), 24.12 (2''-***C***H$_3$), 21.42 (3'-***C***H$_3$), 20.25 (2-***C***H$_3$); MS(ESI): m/z M$^+$ 696. Anal. Calc. for $C_{34}O_6N_6S_2H_{44}$: Calc. C, 58.62%; H, 6.32%; N, 12.06%; S, 9.19%; Found: C, 58.38%; H, 6.29%; N, 12.11%; S, 9.23%.

***N,N'*-(5,5'-(4,4'-(decane-1,10-diylbis(oxy))bis(4,1-phenylene))bis(4-acetyl-5-methyl-4,5-dihydro-1,3,4-thiadi -azole-5,2-diyl))diacetamide 4g**

4g: Brown solid; Yield 67%; mp 170-172^{o}C. IR (KBr) cm^{-1} 3238 (NH), 2987, 2934 (methylene C-H), 1685, 1649 (C=O), 1602 (C=N), 1239, 1042 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 11.35 (2H, s, 1'-N***H***), 7.16 (4H, d, J_o=8.7 Hz, H-2''', 6'''), 6.84 (4H, d, J_o=8.7 Hz, H-3''', 5'''), 3.94 (4H, t, J_{vic}=6.4 Hz, OC***H*****$_2$**CH$_2$CH$_2$CH$_2$CH$_2$), 2.26 (6H, s, 2''-C***H*****$_3$**), 2.19 (6H, s, 3'-C***H*****$_3$**), 2.16 (2H, s, 2-C***H*****$_3$**), 1.88 (4H, quintet, J_{vic}=6.4 Hz, OCH$_2$C***H*****$_2$**CH$_2$CH$_2$CH$_2$), 1.68 (4H, quintet, J_{vic}=6.4 Hz OCH$_2$CH$_2$C***H*****$_2$**CH$_2$CH$_2$), 1.45 (4H, m, OCH$_2$CH$_2$CH$_2$C***H*****$_2$**C***H*****$_2$**); ^{13}C-NMR (DMSO-d_6): δ 167.33 (1''-C=O), 165.68 (2'-C=O), 156.10 (C-4'''), 144.39 (C-5), 130.50 (C-1'''), 126.30 (C-2''', 6'''), 112.58 (C-3''', 5'''), 66.59 (C-2), 66.25 (O***C***H$_2$CH$_2$CH$_2$CH$_2$CH$_2$), 28.22 (OCH$_2$***C***H$_2$CH$_2$CH$_2$CH$_2$), 27.49 (OCH$_2$CH$_2$***C***H$_2$CH$_2$CH$_2$), 27.19 (OCH$_2$CH$_2$CH$_2$***C***H$_2$CH$_2$), 24.23 (OCH$_2$CH$_2$CH$_2$CH$_2$***C***H$_2$), 24.19 (2''-***C***H$_3$), 21.33 (3'-***C***H$_3$), 20.48 (2-***C***H$_3$); MS(ESI): m/z (M+1)$^+$ 725. Anal. Calc. for $C_{36}O_6N_6S_2H_{48}$: Calc. C, 59.66%; H, 6.63%; N, 11.60%; S, 8.84% Found: C, 59.89%; H, 6.60%; N, 11.55%; S, 8.80%.

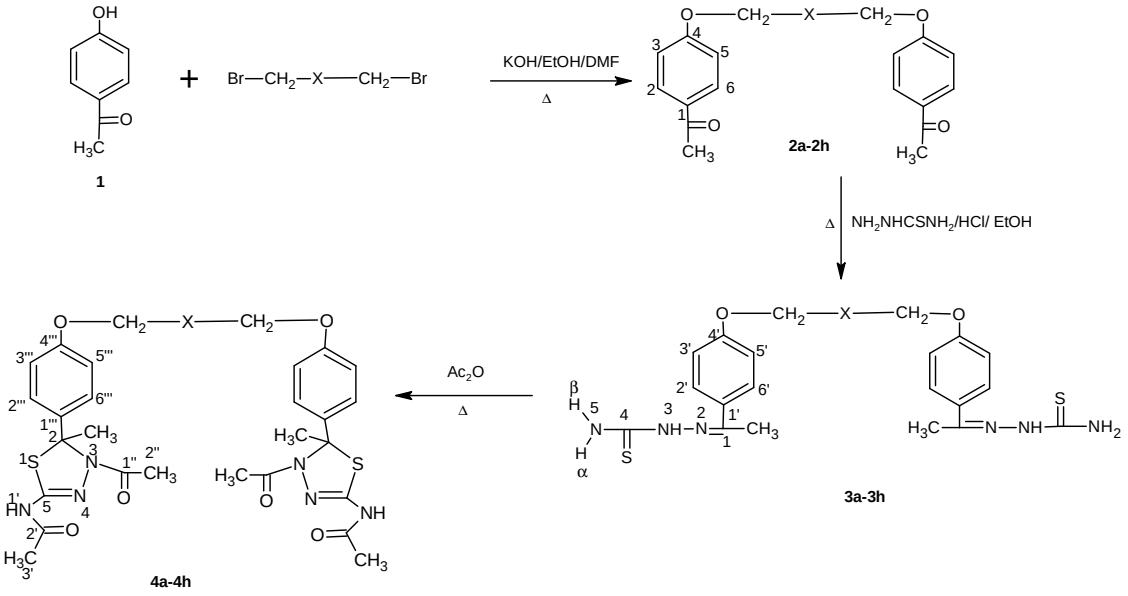
***N,N'*-(5,5'-(4,4'-(dodecane-1,12-diylbis(oxy))bis(4,1-phenylene))bis(4-acetyl-5-methyl-4,5-dihydro-1,3,4-thiadi -azole-5,2-diyl))diacetamide 4h**

4h: Brown solid; Yield 60%; mp 180-182^{o}C. IR (KBr) cm^{-1} 3222 (NH), 2969, 2948 (methylene C-H), 1692, 1648 (C=O), 1605 (C=N), 1248, 1038 (C-O); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 11.28 (2H, s, 1'-N***H***), 7.23 (4H, d, J_o=8.7 Hz, H-2''', 6'''), 6.82 (4H, d, J_o=8.7 Hz, H-3''', 5'''), 3.92 (4H, t, J_{vic}=6.4 Hz, OC***H*****$_2$**CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$), 2.18 (6H, s, 2''-C***H*****$_3$**), 2.12 (6H, s, 3'-C***H*****$_3$**), 2.01 (2H, s, 2-C***H*****$_3$**), 1.74 (4H, quintet, J_{vic}=6.4 Hz, OCH$_2$C***H*****$_2$**CH$_2$CH$_2$CH$_2$CH$_2$), 1.44 (4H, quintet, J_{vic}=6.4 Hz OCH$_2$CH$_2$C***H*****$_2$**CH$_2$CH$_2$CH$_2$), 1.18 (12H, m, OCH$_2$CH$_2$CH$_2$C***H*****$_2$**C***H*****$_2$**C***H*****$_2$**); ^{13}C-NMR (DMSO-d_6): δ 167.04 (1''-C=O), 165.28 (2'-C=O), 156.00 (C-4'''), 144.24 (C-5), 130.24 (C-1'''), 126.15 (C-2''', 6'''), 112.35 (C-3''', 5'''), 66.11 (O***C***H$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$), 66.53 (C-2), 28.15 (OCH$_2$***C***H$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$), 27.49 (OCH$_2$CH$_2$***C***H$_2$CH$_2$CH$_2$CH$_2$), 27.19 (OCH$_2$CH$_2$CH$_2$***C***H$_2$CH$_2$CH$_2$CH$_2$), 24.84 (OCH$_2$CH$_2$CH$_2$CH$_2$***C***H$_2$CH$_2$), 24.23 (OCH$_2$CH$_2$CH$_2$CH$_2$CH$_2$***C***H$_2$), 24.02 (2''-***C***H$_3$), 21.28 (3'-***C***H$_3$), 20.10 (2-***C***H$_3$); MS(ESI): m/z (M+Na)$^+$ 775. Anal. Calc. for $C_{38}O_6N_6S_2H_{52}$: Calc. C, 60.63%; H, 6.91%; N, 11.17%; S, 8.51%; Found: C, 60.87%; H, 6.88%; N, 11.21%; S, 8.47%.

RESULTS AND DISCUSSION

Here the title compounds **4a-4h** were synthesized staring from the 4-hydroxyacetophenone that was treated with various 1,ω-dibromoalkane in the presence of KOH/DMF/EtOH to obtain bisacetophenones **2a-2h**. The later

compounds were reacted with thiosemicarbazide in the presence of dry EtOH to yield bisthiosemicarbazones **3a-3h** which were further refluxed under acetic anhydride medium to provide symmetrical bisheterocyclics **4a-4h** **(Scheme-1)**.



Scheme-1

The structures of prepared products **2a-2h**, **3a-3h** and **4a-4h** were characterized by using various spectroscopic data (IR, ^{1}H-NMR, ^{13}C-NMR & ESI-MS). The purity of these compounds was also confirmed from their elemental analysis results (see experimental).

In the IR spectra of **2a-2h,** three major absorptions appeared in the range of 1676-1660 (C=O), 2958-2915 & 2895-2851 cm^{-1} (methylene C-H) while the ether group (C-O) stretching band could be observed in the range of 1264-1250 & 1048-1026 cm^{-1}. ^{1}H-NMR (400 MHz, DMSO-d_6) spectra of **2a-2h** provided two doublets at δ 7.95-7.90 (J_o= 1.4-1.0, 8.8-8.0 Hz) and 6.98-6.91 (J_o=1.4-1.0, 8.8-1.0) due to the aromatic protons H-2, 6 & H-3, 5 respectively. The sharp singlet integrating for six hydrogens at δ 2.56-2.55 may be ascribed to the C***H*****$_3$** groups. The resonances due to the internal spacer (OC***H*****$_2$**) groups were found to be placed at δ 4.25-4.00 (J_{vic}= 6.5-5.3 Hz) as the triplet while the hydrogens of the remaining {$(CH_2)_n$} groups were present at δ 2.32-1.32 having the suitable multiplicities. ^{13}C-NMR (100 MHz, DMSO-d_6) spectra also confirmed the structures of **2a-2h** which exhibited the signal of C=O group at δ 196.88-196.78 and the resonances present at δ 130.65-130.59 & 130.45-130.05 were assignable to C-2, 6 & C-3, 5 respectively. The noticeable signals were also located at δ 26.39-25.25 (***C***H_3) and the carbon atom of the internal chains O***C***H_2 groups were found to be present at δ 68.43-67.40.

The important feature of the ^{1}H-NMR (400 MHz, DMSO-d_6) and ^{13}C-NMR (100 MHz, DMSO-d_6) spectra of **3a-3h** were the appearance of signals at δ 10.00-9.94 (s), 8.10-8.04 (brs) & 7.67-7.61 (brs) due to the N***H***-3, N***H***-α, N***H***-β respectively and the methyl group (C-1) appeared slightly upfield at δ 2.29-2.24 as compared to **2a-2h** (δ 2.56-2.55). Similarly the aromatic protons H-2', 6' could also be resonating slightly upfield at δ 7.78-7.74 than **2a-2h** (δ 7.95-7.90).

In the ^{13}C-NMR (100 MHz, DMSO-d_6) spectra of **3a-3h,** C=O group signal of bisacetophenone at δ 196.88-196.78 was found to be missing altogether and instead here a new signal was found to be placed at δ 178.95-178.13 which could be assigned to the carbon atom of C=S group. Additionally the signal at δ 147.98-147.35 was assignable to C=N group.

IR spectra of bisthiadiazolines **4a-4h** displayed significant bands at 3238-3202, 1692-1637 and 1605-1601 cm^{-1} due to NH, C=O and C=N stretchings respectively.

The major characteristics of ^{13}C-NMR (100 MHz, DMSO-d_6) spectra in the structural characterization of bisthiadiazolines **4a-4h** was the absence of C=S carbon atom which describes the involvement of C=S moiety in the cyclization of bisthiosemicarbazones **3a-3h**. But here two resonances were found to be present at δ 169.50-167.04 & 168.84-165.28 which describes the presence of two C=O groups in **4a-4h**.

In the ^{1}H-NMR (400 MHz, DMSO-d_6) spectra, the characteristic N***H***, 2-C***H*****$_3$**, 2''-C***H*****$_3$** & 3'-C***H*****$_3$** were located at δ 11.48-11.25, 2.18-2.05, 2.29-2.18 & 2.22-2.01 respectively. The hydrogens belonging to the benzene ring and internal chain were resonating at the appropriate positions (see experimental).

The proposed structures of **3a-3h** & **4a-4h** were also corroborated from their ESI-MS spectra which exhibited molecular ions at the appropriate m/z values (see experimental).

4. Antimicrobial Evaluation

All cultures were obtained from MTCC (Microbial Type Culture Collection & Gene Bank, Chandigarh-160036, India). The newly prepared compounds were screened for their antibacterial and antifungal activity in vitro against *Klubsellia pneumoniae* (MTCC 3384), *Pseudomonas aeruginosa* (MTCC 424), *Escherichia coli* (MTCC 443), *Staphylococcus aureus* (MTCC 96), *Bacillius subtilis* (MTCC 441) and *Aspergillius janus* (MTCC 2751), *Aspergillius niger* (MTCC 281), *Aspergillius flavus* (MTCC 277) & *Pencillium glabrum* (MTCC 4951). Amoxicillin and Fluconazole were used as reference drug for comparison. MIC of all the compounds were evaluated by using serial tube dilution methods [20] at various conc. of 100, 50, 25, 12.5, 6.25, 3.12 µg/mL. The susceptibility of the bacterial and fungi to the studied compounds was determined by the appearance of turbidity after 24 hrs of incubation at 37˚C and 72 hrs of incubation at 28˚C respectively. The observed minimum inhibitory concentration (MIC-µg/ml) values are given in **Table-1**.

Table-1. MIC (in µg/mL) of compounds 3a-3h & 4a-4h

	Gram (-ve) Bacteria			Gram (+ve) Bacteria		Fungi			
Compound No.	*E. coli*	*Klubssila pneumoniae*	*Pseudomonas aeruginosa*	*Staphylococcus aureus*	*Bacillius subtilis*	*Aspergillus Janus*	*Pencilluim glabrum*	*Aspergillus niger*	*Aspergillius flavus*
3a	25	50	25	25	50	25	50	50	25
3b	**12.5**	25	**12.5**	**12.5**	25	25	12.5	50	25
3c	**12.5**	25	12.5	**12.5**	**12.5**	50	25	25	**12.5**
3d	25	25	25	25	25	25	25	25	25
3e	25	25	25	**12.5**	25	25	**12.5**	**12.5**	50
3f	25	25	**12.5**	25	50	25	50	**12.5**	25
3g	**12.5**	50	**12.5**	25	25	**12.5**	25	**12.5**	25
3h	25	50	**12.5**	25	25	**12.5**	25	25	**12.5**
4a	25	50	25	25	25	50	50	50	25
4b	50	50	25	25	**12.5**	25	50	50	25
4c	25	25	**12.5**	25	**12.5**	25	25	25	25
4d	25	25	**12.5**	25	**12.5**	25	**12.5**	25	25
4e	**12.5**	**12.5**	25	**12.5**	25	**12.5**	**12.5**	**12.5**	**12.5**
4f	**12.5**	**12.5**	25	**12.5**	25	**12.5**	**12.5**	**12.5**	**12.5**
4g	25	**12.5**	25	25	**12.5**	25	25	25	**12.5**
4h	25	**12.5**	**12.5**	25	**12.5**	25	25	**12.5**	**12.5**
Amoxicillin	3.12	3.12	3.12	3.12	3.12	-----	-----	-----	-----
Fluconazole	-----	-------	-------	-------	------	6.25	3.12	3.12	6.25

It is evident from the **Table-1** that compound **3b** exhibited high activity (MIC-12.5 µg/ml) against the microorganisms *E. coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* whereas the compound **3c** shows activity of same order (MIC-12.5 µg/ml) against *E. coli*, *Staphylococcus aureus*, *Bacillius subtilis* and *Aspergillius flavus*. The compounds **3e**, **3f** and **3g** could also provide significant activity against the fungus strain namely *Aspergillius niger.*

The compounds **4e** & **4f** exhibited noticeable activity against the strains *E. coli, Staphylococcus aureus, Klubsellia pneumoniae, Aspergillius janus, Pencillium glabrum, Aspergillius flavus* and *Aspergillius niger* while the compounds **4b**, **4c** and **4d** were found to be very active against *Bacillius subtilis.*

Most of the compounds were found to be active against *Pseudomonas aeruginosa*, *Bacillius subtilis*, *Aspergillius niger* & *Aspergillius flavus* at MIC-12.5 µg/ml.

CONCLUSION

It may be concluded that this study describes the general method for the synthesis of new thiadiazoline based symmetrical bishetrocyclic compounds linked through the alkyl chains under the normal conditions. The significant antimicrobial activities were provided by the bisthiosemicarbazones and bishetrocyclics. The symmetrical bisthiadiazolines linked through the longer internal chains (six, eight, ten & twelve methylene groups) seems to be better antimicrobial compounds.

Acknowledgment
Authors are highly thankful to DST (SERC, Fast Track Scheme no. SR/FT/CS-041/2010), New Delhi for providing the financial support for this research work.

REFERENCES

[1] Reddy, C. S.; Rao, L. S.; Devi, M. V.; Kumar, G. R.; Nagaraj, A. *Chinese Chemical Letters* **2010**, doi:10.1016/j.cclet.2010.03.018.
[2] Sancak, K.; Unver, Y.; Er, M. *Turk. J. Chem.* **2007**, *31*, 125.
[3] Mazoir, N.; Ait Itto, M. Y.; Lassaba, E. and Benharref, A. *Molbank* **2006**, M 505.
[4] Islam, M. R. and Mohsin, M. *Bang. J. Pharm.* **2007**, *2*, 7.
[5] Anis'Kov, A. A.; Sazonov, A. A. and Klochkova, I. N.; *Mendeleev Commun.* **2009**, *19*, 52.
[6] Pawar, M. J.; Burungale, A. B. and Karale, B. K. *Arkivoc* **2009**, *13*, 97.
[7] Umamatheswari, S. K. *J. Molecular Structure* **2009**, *938*, 142.
[8] Rani, M.; Ramachandran, R. and Kabilan, S. *Synth. Comm.*, **2010**, *40*, 1694.
[9] Wang, H-C; Li, R-S; Dong, H-R and Dong, H-S *Ind. J. Chem.* **2010**, *49B*, 521.
[10] Alagawadi, K. R. and Alegaon, S. G. *Arab. J. Chem.* **2010** doi:10.1016/j. arabjc.2010.07.012.
[11] Franz, J. E. & Dhingir, O. P. **1984**, in: *Comprehensive Heterocyclic Chemistry*, Katritzky, A. R. and Ree, C. W. (Eds) [oxford: Pergaman Press], vol. *6*, 509.
[12] Shukla, H. K.; Desai, N. C.; Astik, R. R.; Thaker, K. A. *J. Ind. Chem. Soc.* **1984**, 168.
[13] Desai, N. C.; Shukla, H. K.; Parekh, B. P.; Thaker, K. A. *J. Ind. Chem. Soc.* **1984**, 455.
[14] Pan, K.; Scott, M. K.; Lee, D. H. S.; Fitzpatric, L. J.; Crooke, J. J.; Rivero, R. A.; Rosenthal, D. I.; Vaidya, A. H.; Zhao, B.; Reiz, A. B. *Bioorg. Med. Chem.* **2003**, *11*, 185.
[15] Jung, K. Y.; Kim, S. K.; Gao, Z. G.; Gross, A. S.; Melmen, N.; Jacobson, K. A.; Kim, Y. C. *Bioorg. Med. Chem.* **2004**, *12*, 613.
[16] Foroumadi, A.; Asadipour, A.; Mirzaei, M.; Karimi, J.; Emami, S. *IL Farmaco* **2002**, *57*, 765.
[17] Jalilian, A. R.; Sattari, S.; Bineshmarvasti, M.; Daneshtalab, M.; Shafiee, A. *IL Farmaco* **2002**, *58*, 63.
[18] Leung-Toung, R.; Wodzinska, J.; Li, W.; Lowrie, J.; Kukreja, R.; Desilets, D.; Karimian, K.; Tam, T. F. *Bioorg. Med. Chem.* **2003**, *11*, 5529.
[19] (a) Yusuf, M. and Jain, P. *Arab. J. Chem.* **2012**, *5*, 93. (b) Yusuf, M. and Jain, P. *Asian J. Research Chem.* **2011**, *4 (7)*, 1103.
[20] Pandey, K. S.; Khan, N. *Arch. Pharm. Chem. Life Sci.* **2008**, *341*, 418.