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Note

Synthesis and bioactivity study of 2,5-bismercapto-1,3,4-thiadiazole heterocyclic derivatives

Man-Lin Li[a, b], You-Ming Zhang[a] & Tai-Bao Wei[a,*]

[a] Department of Chemistry, Gansu Key Laboratory of Polymer Materials, Northwest Normal University, Lanzhou, Gansu, 730070, P. R. China

[b] College of Science, Northwest A & F University, Yangling, Shaanxi, 712100, P. R. China

E-mail: weitaibao@126.com

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A series of acylhydrazone compounds **3a-i** and acylthiosemicarbazides **4a-h** containing thiadiazole rings have been synthesized conveniently in high yields. Some heterocyclic derivatives **5** are prepared by the method of dehydration of compounds **4**. Structure of all these compounds have been confirmed by elemental analysis, IR, ^{1}H and ^{13}C NMR. The bioassay result indicates that some compounds have relatively low antibacterial activity and other compounds have bioactivity for improving plant growth.

Keywords: 1,3,4-thiadiazole, acylhydrazone, thiosemicarbazide, microwave irradiation

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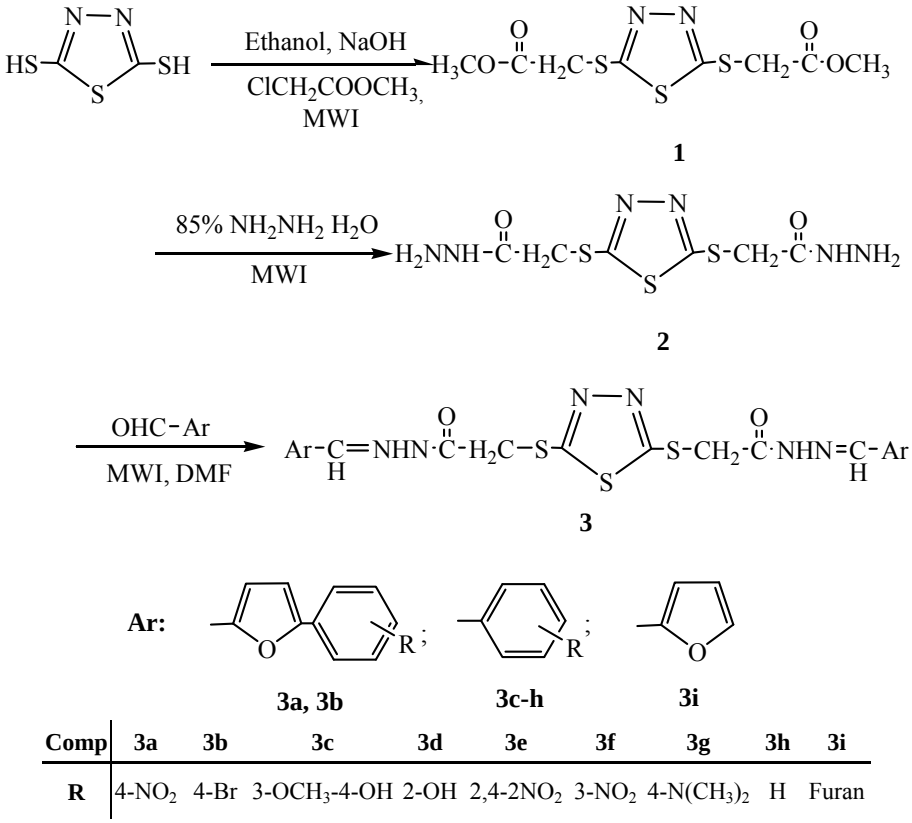
It is well established that various substituted 1,3,4-thiadiazoles have become very useful compounds in medicine, agriculture and in many fields of technology[1-3]. Some of these compounds exhibit interesting pharmacological properties like anti-tubercular, anti-inflammatory, *etc*. A large number of 1,3,4-thiadiazoles have been patented in the agricultural field as herbicides, fungicides and bactericides[4-6].

Since acylhydrazones exhibit special biological activity such as antimicrobial, anticancer, antitubercular, anticonvulsant, anti-inflammatory[7] and also they play important roles in coordination chemistry and in the field of catalysis[8], the chemistry of acylhydrazone has been intensively investigated in recent years[9,10]. Recently, the importance of N=C=S linkage has been well stressed. The linkage is an essential structural feature which is responsible for various biological activities in many well-known organic sulphur containing pesticides such as dithiocarbamates, thioureas and thiosemicarbazides[11,12]. The survey of the literature revealed that some thiosemicarbazides containing a thiadiazole ring had been used as plant growth regulators. Moreover, aroylthiosemicarbazide are also valuable as synthetic intermediates for the preparation of some thiadiazole derivatives[13,14].

Synthesis of hydrazone compounds is a classical reaction. It is often carried out with acid catalysts such as hydrochloric acid and generally by refluxing the mixture of aldehyde (or ketone) and acylhydrazide[15]. Nevertheless, the conventional methods for preparation of acylhydrazone have the shortcoming of relatively longer reaction time and poorer isolated yields. Moreover, these methods usually involve refluxing the reactants for many hours at elevated temperatures. In order to overcome these shortcomings and in view of the requirements of green chemistry for energy-saving and high efficiency processes, herein are given the preparation of the title compounds **3a-i** under Microwave irradiation (**Scheme I**).

2,5-Dimercapto-1,3,4-thiadiazole was prepared according to the procedure available in literature[16]. A mixture of 2,5-dimercapto-1,3,4-thiadiazole, sodium hydroxide in ethanol and methyl chloroacetate was placed in a round-bottomed flask and irradiated for 4 min to give 2,5-bis (mercaptoaceticester)-1,3,4-thiadiazole. A mixture of diacid esters and hydrazine hydrate (85%) in dimethylformamide (DMF) was irradiated for 2 min to give 2,5-bis(mercapto-acetichydrazide)-1,3,4-thiadiazole (compound **2**). Aromatic aldehyde, compound **2** and a little amount of DMF were placed in a flask and irradiated for 6-10 min to obtain the desired products. It was found that the reaction time was shortened from 2 h to 4 min in the first step and from 3 h to 2 min in the second step and compounds **3** were obtained in good to excellent yields. In this procedure, DMF can not only perform as solvent, but also promote the absorption of MWI and recrystallize the products directly without additional solvent. Moreover, DMF has high boiling point, this made it a more safe solvent than some other organic solvent in obviating the danger of explosion inside the microwave oven.



Comp	3a	3b	3c	3d	3e	3f	3g	3h	3i
R	4-NO_2	4-Br	3-OCH_3-4-OH	2-OH	2,4-2NO_2	3-NO_2	4-$N(CH_3)_2$	H	Furan

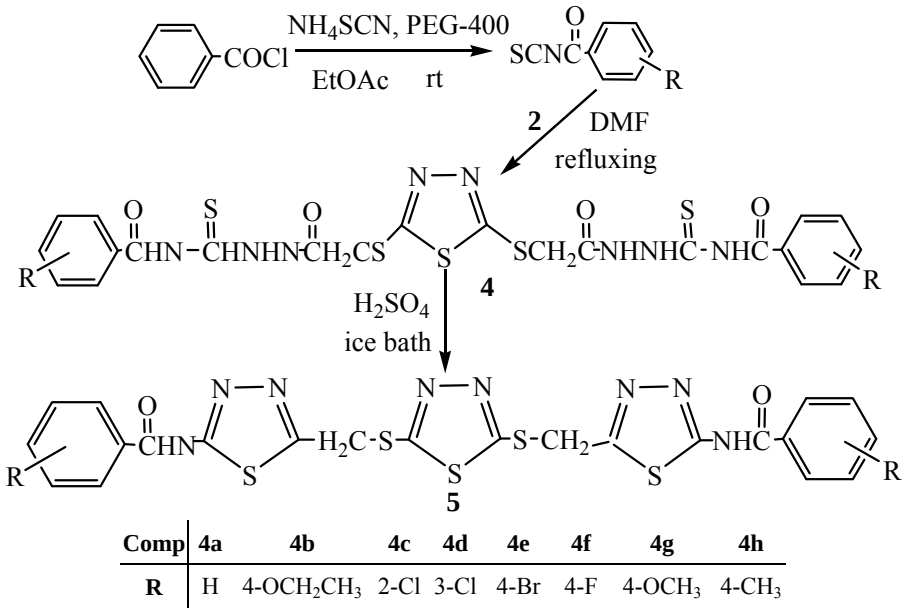
Scheme I

The reaction sequences leading to the formation of different title compounds **4a-h** are outlined in **Scheme II**. The present synthetic approach was aimed at creating a series of aroyl isothiocyanates. They were key intermediates in producing the title compounds. Aroyl isothiocyanates are versatile reagents and their chemistry has received considerable recent interest[17]. They could be employed as good intermediates to prepare various thiosemicarbazides easily. In this procedure, aroyl chloride was treated with ammonium thiocyanate (NH_4SCN) in ethyl acetate under the condition of solid-liquid phase transfer catalysis using PEG-400 as the catalyst to give the corresponding aroyl isothiocyanate in quantitative yields. On the contrary, no products could be obtained when no PEG-400 or other PTC participated in the reaction. The target products **4** could be obtained by the addition reaction between aroyl isothiocycanates with compound **2**. Since acylhydrazide is insoluble in ethyl acetate, it was added portionwise into solution of isothiocyanates in a flask with rigorous stirring for 1-2 h at refluxing temperature. The precipitate was separated out and purified by recrystallization from DMF-EtOH-H_2O to give **4**. Compound **4** was treated with concentrated sulphuric acid at 0°C in an ice bath with constant stirring for 1-2 h. Then the reaction mixture was poured into 150 mL ice-water. The precipitate formed was filtered and washed with water and DMF to give **5a-e** in good to excellent yields.

In this procedure, concentrated sulphuric acid was employed instead of acetic acid as dehydration reagent. As a rule, using acetic acid as dehydration reagent had the disadvantages of relatively longer reaction times (5-6 h) and the reaction mixture had to be refluxed at high temperature. Furthermore, since acetic acid was not a good solvent for compound **4**, in order to dissolve the reactant, some other solvent such as DMF or DMSO had to be employed though it was not easily removed due to its high boiling point. The use of concentrated H_2SO_4 could overcome these shortcomings. It is not only a good dehydrating reagent but also a useful solvent for many organic compounds.

Experimental Section

All reagents were purchased and used without further purification. Microwave irradiation was



Comp	4a	4b	4c	4d	4e	4f	4g	4h
R	H	4-OCH_2CH_3	2-Cl	3-Cl	4-Br	4-F	4-OCH_3	4-CH_3

Scheme II

carried out with a WP 750B commercial microwave oven at 2450 MHz. Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded in KBr on an Alpha Centauri FT-IR spectrophotometer and ^{1}H NMR spectra on a Mercury plus-400, Varian instrument (400 MHz) using DMSO-d_6 as solvent and TMS as internal reference. Elemental analysis was determined on a PE-2400 CHN instrument.

General procedure for the preparation of compounds 3, 4 and 5

2, 5-bis(Mercapto-acetichydrazide)-1, 3, 4-thiadiazole, 2:

2,5-Dimercapto-1,3,4-thiadiazole (4 mmol), sodium hydroxide (8 mmol), ethanol (25 mL) and methyl chloroacetate (8.2 mmol) were placed in a dried round-bottomed flask and the mixture was irradiated by microwave (200 W) for 4 min. Afterwards, the reaction mixture was poured into ice-water, then collected by filtration and washed with water and purified by recrystallization from ethanol to obtain 2,5-bis(mercapto-aceticester) -1,3,4-thiadiazole (m.p. 56-58°C). The mixture of compound **1** (2 mmol) and 85% of hydrazine hydrate (4.2 mmol) in DMF (2 mL) was subjected to microwave irradiation (500 W) for 2 min. The reaction mixture was cooled and the resulting precipitate was collected by filtration and washed with ethanol. The white precipitate was purified by recrystallization from DMF-EtOH-H_2O to give colourless crystals of the compound **2** (m.p. 154-55°C) in 92% yield.

Compound 3a-i:

Compound **2** (1 mmol), DMF (3 mL) and aromatic aldehyde (2.1 mmol) were placed in a dried round-bottomed flask and the mixture was irradiated in a domestic microwave oven (500 W) at 1 min intervals for 6-10 min. Without further separation, the residue was purified by recrystallization from DMF-EtOH-H_2O to afford the pure product.

Compound 4a-h and 5a-e:

A mixture of 0.91 g dried and powdered NH_4SCN (12 mmol), aroyl chloride (11 mmol) and PEG-400 (0.1 mL) in ethyl acetate (15 mL) was stirred in a flask at RT for 1-2 h. The mixture was filtered to seperate inorganic salt NH_4Cl and washed with 3×10 mL EtOAc to obtain a solution of aroyl isothiocyanate. Then hydrazide **2** (10 mmol) was slowly added into it with constant stirring at refluxing temperature for 1-2 h. The precipitate formed was filtered and purified by recrystallization from DMF-EtOH-H_2O to give pure products **4a-h**.

A portion of **4** (5 mmol) was dissolved in concentrated sulphuric acid (2.5 mL) in an ice bath, the solution was kept at 0°C for 2 h with constant stirring and then poured into 150 mL water containing an excess of crushed ice. It was stirred well and

allowed to stand for 1-2 h, the residue was filtered and washed with ice water and then washed with DMF to give pure product **5a-e**.

3a. Yield 96%; m.p. 200-02°C; IR (KBr): 3097 (NH), 1678 (C=O), 1597 (C=N), 1220 (C-S), 1383 (SCH_2), 654 (C-S-C), 1206 cm^{-1} (C-O-C); ^1H NMR (DMSO-d_6): δ 11.86, 11.80 (s, 2H, NH), 8.08 (s, 2H, CH=N), 7.00-8.23 (m, 12H, Ar-H), 4.56 (s,4H, -CH_2-). Anal. Calcd. for $C_{28}H_{20}N_8O_8S_3$: C, 48.6; H, 2.91; N, 16.2. Found: C, 48.3; H, 2.96; N, 15.9%.

3b. Yield 92%; m.p. 246-48°C; IR (KBr): 3086 (NH), 1663 (C=O), 1564 (C=N), 1276 (C-S), 1381 (SCH_2), 671 (C-S-C), 1206 cm^{-1} (C-O-C); ^1H NMR (DMSO-d_6): δ 11.8, 11.74 (s, 2H, NH), 8.09 (s, 2H, CH=N), 6.99-7.90 (m, 12H, Ar-H), 4.55 (s, 4H, -CH_2). Anal. Calcd. for $C_{28}H_{20}N_6O_4S_3Br_2$: C, 44.22; H, 2.65; N, 11.05. Found: C, 44.41; H, 2.36; N, 11.35%.

3c. Yield 78%; m.p. 113-15°C; IR (KBr): 3050 (NH), 1663 (C=O), 1597 (C=N), 1211 (C-S), 1387 (SCH_2), 621 cm^{-1} (C-S-C); ^1H NMR (DMSO-d_6): δ 11.60, 11.55 (s, 2H, NH), 9.57, 9.53 (s, 2H, -OH), 8.06, 7.93 (s, 2H, CH=N), 6.80-7.26 (m, 6H, Ar-H), 4.55 (s, 4H, -CH_2-), 3.79 (s, 6H, -OCH_3). Anal. Calcd. for $C_{22}H_{22}N_6O_6S_3$: C, 46.97; H, 3.94; N, 14.94. Found: C, 46.67; H, 3.56; N, 15.14%.

3d. Yield 83%; m.p. 225-26°C; IR (KBr): 3049 (NH), 1665 (C=O), 1617 (C=N), 1203 (C-S), 1391 (SCH_2), 653 cm^{-1} (C-S-C); ^1H NMR (DMSO-d_6): δ 11.98, 10.94 (s, 2H, NH), 10.93-10.05 (s, 2H, -OH), 8.41, 8.32 (s, 2H, CH=N), 7.68-6.83 (m, 8H, Ar-H), 4.56 (s, 4H, -CH_2-). Anal. Calcd. for $C_{20}H_{18}N_6O_4S_3$: C, 47.80; H, 3.61; N, 16.72. Found: C, 48.03; H, 3.58; N, 16.42%.

3e. Yield 76%; m.p. 136-38°C; IR (KBr): 3104 (NH), 1691 (C=O), 1619 (C=N), 1233 (C-S), 1348 (SCH_2), 632 cm^{-1} (C-S-C); ^1H NMR (DMSO-d_6): δ 9.37, 9.20 (s, 2H, NH), 8.77 (s, 2H, CH=N), 7.78 - 8.71 (m, 6H, Ar-H), 4.35(s, 4H, -CH_2-); Anal. Calcd. for $C_{20}H_{14}N_{10}O_{10}S_3$: C, 36.92; H, 2.17; N, 21.53. Found: C, 37.22; H, 1.98; N, 21.91%.

3f. Yield 82%; m.p. 238-40°C; IR (KBr): 3082 (NH), 1680 (C=O), 1613 (C=N), 1219 (C-S), 1376 (SCH_2), 669 cm^{-1} (C-S-C); ^1H NMR (DMSO-d_6): δ 12.01, 11.92 (s, 2H, NH), 8.47 (s, 2H, CH=N), 7.66 - 8.28 (m, 8H, Ar-H), 4.59 (s, 4H, -CH_2-); Anal. Calcd. For $C_{20}H_{16}N_8O_6S_3$: C, 42.85; H, 2.88; N, 19.99. Found: C, 42.52; H, 2.98; N, 20.22%.

3g. Yield 87%; m.p. 234-36°C; IR (KBr): 3052 (NH), 1669 (C=O), 1607 (C=N), 1228 (C-S), 1364 (SCH_2), 630 cm^{-1} (C-S-C); ^1H NMR (DMSO-d_6): δ 11.41, 11.38 (s, 2H, NH), 7.97 (s, 2H, CH=N), 6.61 - 6.63, 7.38-7.81 (m, 8H, Ar-H), 4.45 (s, 4H, -CH_2-), 3.34 [s, 12H, $N(CH_3)_2$]; Anal. Calcd. for $C_{24}H_{28}N_8O_2S_3$: C, 51.78; H, 5.07; N, 20.13. Found: C, 51.45; H, 5.17; N, 19.78%.

3h. Yield 87%; m.p. 205-06°C; IR (KBr): 3090 (NH), 1674 (C=O), 1616 (C=N), 1209 (C-S), 1384 (SCH_2), 640 cm^{-1} (C-S-C); ^1H NMR (DMSO-d_6): δ 11.80, 11.74 (s, 2H, NH), 8.21 (s, 2H, CH=N), 7.43-7.72 (m, 10H, Ar-H), 4.59 (s, 4H, -CH_2-); Anal. Calcd. for $C_{20}H_{18}N_6O_2S_3$: C, 51.05; H, 3.85; N, 17.86. Found: C, 49.69; H, 3.55; N, 17.68%.

3i. Yield 86%; m.p. 187-89°C; IR (KBr): 3059 (NH), 1669 (C=O), 1542 (C=N), 1310 (C-S), 1389 (SCH_2), 675 (C-S-C), 1201 cm^{-1} (C-O-C); ^1H NMR (DMSO-d_6): δ 11.71, 11.66 (s, 2H, NH), 8.07 (s, 2H, CH=N), 6.59-6.91, 7.80-7.90 (m, 6H, Ar-H), 4.51 (s, 4H, -SCH_2-); Anal. Calcd. for $C_{16}H_{14}N_6O_4S_3$: C, 42.66; H, 3.13; N, 18.65. Found: C, 42.38; H, 2.97; N, 18.98%.

4a. Yield 78%; m.p. 182-84°C; IR (KBr): 3135 (NH), 1669 (C=O), 1244 (C=S), 669 (C-S-C), 1388 cm^{-1} (SCH_2); ^1H NMR (DMSO-d_6): δ 12.75 (s, 2H, N-NH-CS), 11.78 (s, 2H, CS-NH-CO), 11.36 (s, 2H, CO-NH-N), 7.50-7.96 (m, 10H, Ar-H), 4.25 (s, 4H, -SCH_2-); ^{13}C NMR (DMSO-d_6): δ 176.56 (C=S), 168.06 (O=C-Ar), 164.85 (-CONH), 163.86, 133.18, 131.80, 128.74, 128.45, 35.22 (-SCH_2-); Anal. Calcd. for $C_{22}H_{20}N_8O_4S_5$: C, 42.57; H, 3.25; N, 18.05. Found: C, 42.66; H, 3.13; N, 18.25%.

4b. Yield 73%; m.p. 217-18°C; IR (KBr): 3161 (NH), 1671 (C=O), 1245 (C=S), 669 (C-S-C), 1395 cm^{-1} (SCH_2); ^1H NMR (DMSO-d_6): δ 12.84 (s, 2H, N-NH-CS), 11.58 (s, 2H, CS-NH-CO), 11.35 (s, 2H, CO-NH-N), 7.02-7.99 (m, 8H, Ar-H), 4.26 (s, 4H, -SCH_2-), 4.11 (q, 2H, -OCH_2-), 1.35 (t, 6H, -CH_3); ^{13}C NMR (DMSO-d_6): δ 176.73 (C=S), 167.29 (O=C-Ar), 164.86 (-CONH), 163.82, 162.58, 131.07, 123.31, 114.15, 35.24 (-SCH_2-), 30.77 (-OCH_2-), 63.64 (-CH_3); Anal. Calcd. for $C_{26}H_{28}N_8O_6S_5$: C, 44.05; H, 3.98; N, 15.81. Found: C, 44.26; H, 4.13; N, 15.65%.

4c. Yield 73%; m.p. 202-04°C; IR (KBr): 3161 (NH), 1689 (C=O), 1248 (C=S), 650 (C-S-C), 1386 cm^{-1} (SCH_2); ^1H NMR (DMSO-d_6): δ 12.25 (s, 2H, N-NH-CS), 12.16 (s, 2H, CS-NH-CO), 11.46 (s, 2H, CO-NH-N), 7.44-7.61 (m, 8H, Ar-H), 4.25 (s, 4H, -SCH_2-); ^{13}C NMR (DMSO-d_6): δ 175.94 (C=S), 167.36 (O=C-Ar), 164.85 (-CONH), 163.95, 134.04, 132.17, 129.95, 129.59, 129.29, 127.15, 35.23 (-SCH_2-); Anal. Calcd. for $C_{22}H_{18}N_8O_4S_5Cl_2$: C, 38.32;

H, 2.63; N, 16.25. Found: C, 38.11; H, 2.93; N, 16.19%.

4d. Yield 79%; m.p. 215-16°C; IR (KBr): 3202 (NH), 1671 (C=O), 1252 (C=S), 653 (C-S-C), 1379 cm^{-1} (SCH_2); ^1H NMR (DMSO-d_6): δ 12.66 (s, 2H, N-NH-CS), 11.92 (s, 2H, CS-NH-CO), 11.40 (s, 2H, CO-NH-N), 7.53-8.02 (m, 8H, Ar-H), 4.24 (s, 4H, -SCH_2-); ^{13}C NMR (DMSO-d_6): δ 176.26 (C=S), 166.65 (O=C-Ar), 164.84 (-CONH), 163.89, 133.87, 133.12, 132.82, 130.37, 128.51, 127.49, 35.23 (-SCH_2-); Anal. Calcd. for $C_{22}H_{18}N_8O_4S_5Cl_2$: C, 38.32; H, 2.63; N, 16.25. Found: C, 38.26; H, 2.89; N, 16.35%.

4e. Yield 82%; m.p. 192-94°C; IR (KBr): 3202 (NH), 1632 (C=O), 1234 (C=S), 662 (C-S-C), 1384 cm^{-1} (SCH_2); ^1H NMR (DMSO-d_6): δ 12.36 (s, 2H, N-NH-CS), 11.59 (s, 2H, CS-NH-CO), 11.28 (s, 2H, CO-NH-N), 7.71-8.01 (m, 8H, Ar-H), 4.23 (s, 4H, -SCH_2-); ^{13}C NMR (DMSO-d_6): δ 170.34 (C=S), 166.02 (O=C-Ar), 165.80 (-CONH), 164.60 (N=C-N), 131.61, 131.32, 129.60, 125.79, 35.32 (-SCH_2-); Anal. Calcd. for $C_{22}H_{18}N_8O_4S_5Br_2$: C, 33.94; H, 2.33; N, 14.39. Found: C, 33.66; H, 2.05; N, 14.54%.

4f. Yield 78%; m.p. 215-17°C; IR (KBr): 3202 (NH), 1670 (C=O), 1237 (C=S), 626 (C-S-C), 1383 cm^{-1} (SCH_2); ^1H NMR (DMSO-d_6): δ 12.72 (s, 2H, N-NH-CS), 11.83 (s, 2H, CS-NH-CO), 11.39 (s, 2H, CO-NH-N), 7.34-8.06 (m, 8H, Ar-H), 4.24 (s, 4H, -SCH_2-); ^{13}C NMR (DMSO-d_6): δ 176.47 (C=S), 166.95 (O=C-Ar), 164.85 (-CONH), 163.80, 131.80, 128.33, 115.62, 115.40, 35.24 (-SCH_2-); Anal. Calcd. for $C_{22}H_{18}N_8O_4S_5F_2$: C, 40.24; H, 2.74; N, 17.05. Found: C, 40.36; H, 2.53; N, 17.15%.

4g. Yield 68%; m.p. 217-19°C; IR (KBr): 3177 (NH), 1663 (C=O), 1246 (C=S), 619 (C-S-C), 1385 cm^{-1} (SCH_2); ^1H NMR (DMSO-d_6): δ 11.59 (s, 2H, N-NH-CS), 11.36 (s, 2H, CS-NH-CO), 10,52 (s, 2H, CO-NH-N), 7.04-8.16 (m, 8H, Ar-H), 4.26 (s, 4H, -SCH_2-), 3.82 (s, 6H,-OCH_3-); ^{13}C NMR (DMSO -d_6): δ 176.74 (C=S), 167.30 (O=C-Ar), 164.88 (-CONH), 163.85, 163.27, 131.08, 123.50, 113.82, 55.63, 35.23 (-SCH_2-); Anal. Calcd. for $C_{24}H_{24}N_8O_6S_5$: C, 42.34; H, 3.55; N, 16.46. Found: C, 42.46; H, 3.23; N, 16.65%.

4h. Yield 82%; m.p. 236-37°C; IR (KBr): 3162 (NH), 1668 (C=O), 1258 (C=S), 636 (C-S-C), 1382 cm^{-1} (SCH_2); ^1H NMR (DMSO-d_6): δ 12.85 (s, 2H, N-NH-CS), 11.70 (s, 2H, CS-NH-CO), 11.40 (s, 2H, CO-NH-N), 7.32-8.03 (m, 8H, Ar-H), 4.25 (s, 4H, -SCH_2-), 2.36 (s, 6H, -CH_3); ^{13}C NMR (DMSO-d_6): δ 176.61 (C=S), 167.89 (O=C-Ar), 164.88 (-CONH), 163.88, 162.36, 143.74, 129.14, 128.67, 21.20, 35.23 (-SCH_2-); Anal. Calcd. for $C_{24}H_{24}N_8O_4S_5$: C, 44.43; H, 3.73; N, 17.27. Found: C, 44.66; H, 3.83; N, 17.45%.

5a. Yield 82%; m.p. 300-02°C; IR (KBr): 3165 (NH), 1656 (C=O), 624 (C-S-C), 1301 cm^{-1} (SCH_2); Anal. Calcd. for $C_{22}H_{16}N_8O_2S_5$: C, 45.19; H, 2.76; N, 19.16. Found: C, 45.26; H, 2.83; N, 18.85%.

5b. Yield 88%; m.p. 268-70°C; IR (KBr): 3150 (NH), 1656 (C=O), 623 (C-S-C), 1303 cm^{-1} (SCH_2); Anal. Calcd. for $C_{26}H_{24}N_8O_4S_5$: C, 46.41; H, 3.60; N, 18.98. Found: C, 46.56; H, 3.43; N, 18.75%.

5c. Yield 73%; m.p. 224-26°C; IR (KBr): 3127 (NH), 1681 (C=O), 651 (C-S-C), 1307 cm^{-1} (SCH_2); Anal. Calcd. for $C_{22}H_{14}N_8O_2S_5Cl_2$: C, 40.43; H, 2.16; N, 17.14. Found: C, 40.68; H, 2.43; N, 17.25%.

5d. Yield 68%; m.p. 223-24°C; IR (KBr): 3151 (NH), 1668 (C=O), 665 (C-S-C), 1309 cm^{-1} (SCH_2); Anal. Calcd. for $C_{22}H_{14}N_8O_2S_5Cl_2$: C, 40.43; H, 2.16; N, 17.14. Found: C, 40.56; H, 2.13; N, 17.22%.

5e. Yield 71%; m.p. 208-10°C; IR (KBr): 3182 (NH), 1646 (C=O), 651 (C-S-C), 1307 cm^{-1} (SCH_2); Anal. Calcd. for $C_{22}H_{14}N_8O_2S_5Br_2$: C, 35.59; H, 1.90; N, 15.09. Found: C, 35.76; H, 1.85; N, 15.05%.

Bioactivity study

The compounds **3** were evaluated for their anti-colibacillus activity[18]. Penicillin was used as reference drug. The bioassay result indicated that the compound **3e** and **3g** have relatively low anti-colibacillus activity when the concentration is 90-100 μg/mL.

The compound **4** were evaluated for their activity of plant growth promotion[19]. Some selected compounds were tested on wheat seeds and average length of seedings and roots were recorded. The concentrations chosen were 0.001-100 ppm. The results showed that compound **4c**, **4d** and **4h** have good promoting effects on wheat growth.

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