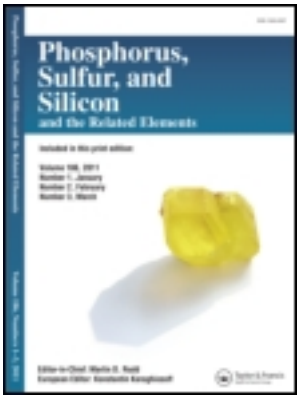

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N-Methylpyridinium Tosylate Catalysed Green Synthesis, X-Ray Studies and Antimicrobial Activities of Novel (E)-3-Amino-2-(e)-(3, 4-Dihydronaphthalen-1(2H)-Ylidene)Hydrazono)Thiazolidin-4-Ones

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N-METHYLPYRIDINIUM TOSYLATE CATALYSED GREEN SYNTHESIS, X-RAY STUDIES AND ANTIMICROBIAL ACTIVITIES OF NOVEL (*E*)-3-AMINO-2-(*E*)-(3,4-DIHYDRONAPHTHALEN-1(2*H*)-YLIDENE)HYDRAZONO)THIAZOLIDIN-4-ONES

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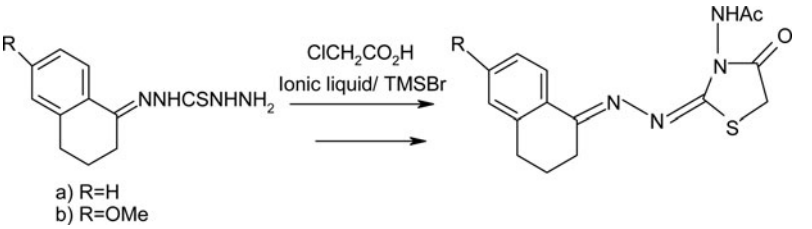
GRAPHICAL ABSTRACT



Abstract *3,4-Dihydro-2H-naphthalen-1-ones* ***1,****on reaction with thiocarbohydrazide, afforded monothiocarbohydrazones* ***2****, which, on condensation with chloroacetic acid in the presence of an ionic liquid and bromotrimethylsilane furnish (E)-3-amino-2-(E)-(3,4-dihydronaphthalen-1-(2H)-ylidene)hydrazono)thiazolidin-4-ones* ***3*** *in quantitative yields. Acetyl derivatives* ***5*** *were obtained from* ***3*** *with acetic anhydride. Monothiocarbohydrazones* ***2*** *on condensation with benzaldehyde yield azomethines* ***4****. The structure of compounds* ***2–5*** *has been established by elemental analysis, IR,* ^{1}*H NMR, and mass spectral data. The structure of compound* ***3a*** *has been further confirmed by X-ray crystallographic data. The compounds* ***2–5*** *were screened for antimicrobial activity. The thiazolidinones* ***3a*** *and* ***3b*** *showed maximum antimicrobial activities.*

[Supplementary materials are available for this article. Go to the publisher's online edition of Phosphorus, Sulfer, and Silicon and the Related Elements *for the following free supplemental files:* Additional text, tables, and figures.*]*

Keywords Monothiocarbohydrazones; 4-thiazolidinones; spectral data; X-ray crystallographic data

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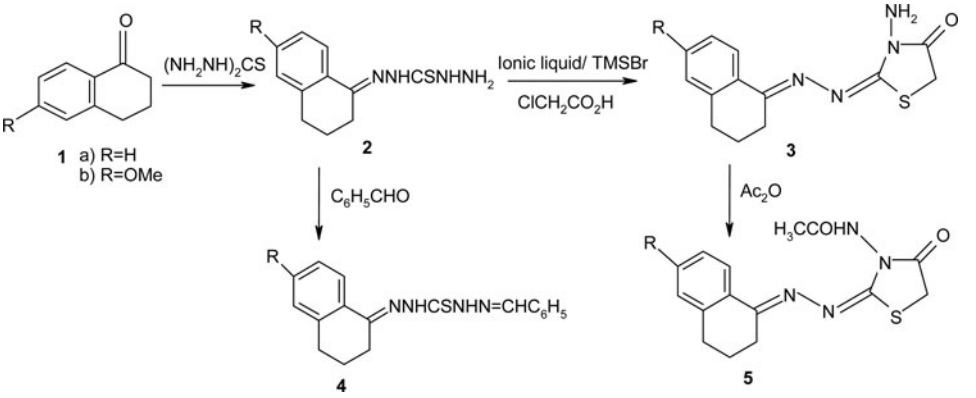
INTRODUCTION

1-Tetralone and its various derivatives have proven utility in the synthesis of numerous biologically active products and play a major role in medicinal chemistry and development of pharmaceuticals.[1] Levobunolol, a derivative of 5-hydroxy-1-tetralone, is a nonselective beta-blocker used to treat glaucoma. Thiocarbohydrazones derived from the condensation of thiocarbohydrazide and aldehydes or ketones, have long been reported in the literature for their fungicidal[2] and anticonvulsant[3] properties. 4-Thiazolidinone another biologically active class of heterocycles have many interesting activity profiles namely COX-1 inhibitors,[4] inhibitors of the bacterial enzyme MurB[5] and antihistaminic agents.[6] Also 4-thiazolidinones possess diverse biological activities such as analgesic,[7] anti-inflammatory,[8] anti-HIV,[9] cytotoxic,[10] anticonvulsant,[11] antibacterial,[12] antifungal,[13] antitumor,[14] antipsychotic agents,[15] and hypnotics. Several methods for the preparation of 4-thiazolidinones have been reported in the literature. The commonly employed methods involve either a one pot, three-component cyclocondensation of amines, carbonyls, and mercaptoacetic acid or two- step synthesis via Schiff base intermediates and their cyclocondensation with mercaptoacetic acid. The use of carbodiimide was reported[16] for synthesis of 4-thiazolidinones in good yield through one pot cyclocondenation of amines, aldehydes, and mercaptoacetic acid. The similar one pot condensation was carried out recently in presence of an ionic liquid and the compounds were obtained in quantitative yields.[17] The two-step approach involves hazardous solvents and long reaction time nearly 17–20 h with moderate to poor yields. There are reports of using various desiccants such as sodium sulfate,[18] trimethylorthoformate, azeotropic distillation, and molecular sieves for removal of water from the reaction mixture. In continuation to our work on synthesis of biologically active 4-thiazolidinones[19–21] through environmentally benign reaction conditions and reaction media which replaces volatile organic solvents, we report here a convenient synthesis of novel (*E*)-3-amino-2-(*E*)-(3, 4-dihydronaphthalen-1(2*H*)-ylidene)hydrazono)thiazolidin-4-ones by two component cyclocondensation of thiocarbohydrazones of 1-tetralone with chloroacetic acid using an ionic liquid and bromotrimethylsilane in quantitative yield.

RESULTS AND DISCUSSION

1-Tetralone was added while stirring to a solution of thiocarbohydrazide in hot water containing 1–2 drops of conc. HCl. A white solid started separating from the reaction mixture within a few minutes of stirring which was purified by passing through a column using pet ether and ethyl acetate (4:1) as eluent. The pure compound thus obtained was identified as monothiocarbohydrazone **2a** of 1-tetralone on the basis of spectral data. The appearance of peaks at 1590 and 1280 cm^{-1} in the IR spectrum of **2a** are assigned to C = N and C = S groups respectively. Two triplets, one multiplet integrating for two protons each at δ 2.57, 2.77, and 1.95–2.06 respectively in the NMR spectrum are assigned to the three CH_2 groups of tetrahydronaphthalene ring. In ^{13}C NMR spectrum of **2a**, a peak at δ 178 is assigned to C = N group. The structure of **2a** is further confirmed by its condensation with aldehyde to yield azomethine **4a.**

2a on cyclocondensation with $ClCH_2COOH$ in presence of NaOAc yielded **3a** in moderate yield (Scheme 1). The appearance of a singlet at δ 3.78 in ^1H NMR of **3a** is assigned to SCH_2 group, which confirms the formation of thiazolidinone ring. The appearance of two triplets and a multiplet due to tetrahydronaphthalene ring in ^1H NMR supports structure **3a**. Appearance of peaks at 1705 cm^{-1} in IR spectrum and at δ 173.5



Scheme 1

in ^{13}C NMR spectrum assignable to carbonyl group corroborates with structure **3a**. The appearance of $[M+H]^+$ peak at 275 (25%) in the mass spectrum supports the proposed structure for **3a**. Finally, the structure of **3a** was also confirmed by single crystal X-ray structural data. The ORTEP drawing obtained from crystal structure is shown in Fig. 1. The crystals for X-ray were grown from ethyl alcohol by slow evaporation process at room temperature. The structure of compound **4a** was established by appearance of a peak at 1612 cm^{-1} (due to C=N group) in IR and a singlet of one proton at δ 7.44 assignable to=CH group in ^1H NMR spectrum. Compound **3a** on reaction with acetic anhydride furnishes acetyl derivative **5a** supporting the presence of NH_2 group in **3a**. The structure of **5a** is established by spectral data. The IR of **5a** shows a peak at 1668 cm^{-1} assigned to $NHCOCH_3$ group. In ^1H NMR spectrum besides other peaks, one singlet at δ 2.80 is due to methyl group. ^{13}C NMR spectrum of **5a** shows carbonyl groups of $NHCOCH_3$ and thiazolidinone ring at δ 178 and 173.5, respectively.

Similarly compounds **2b–5b** were obtained and their structures were established by spectral data.

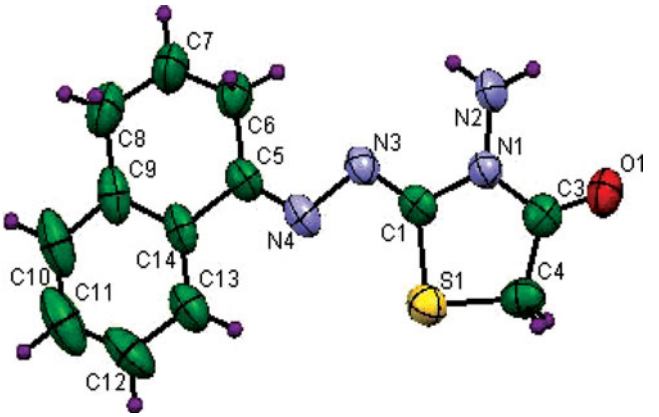


Figure 1 ORTEP drawing indicating molecular structure and atomic labeling of the compound **3a**. (Color figure available online).

Table 1 Effect of catalysts on cyclocondensation of thiocarbohydrazones of 1-tetralone and chloroacetic acid

		3a		3b	
Entry	Ionic liquid/Catalyst	Time (h)	Yield (%)	Time (h)	Yield (%)
1.	N-methylpyridinium tosylate	6.5	72	6.0	69
2.	N-methylpyridinium tosylate + TMS*Cl	4.0	78	3.5	75
3.	N-methylpyridinium tosylate + TMSBr	2.5	82	3.0	80
4.	N-methylpyridinium tosylate + TMSI	6.0	72	5.5	68

*Trimethylsilyl.

The cyclocondensation of **2** with $ClCH_2COOH$ to give **3** by a conventional method resulted a poor yield with long reaction time of 12 h. Because of our interest in developing environmentally benign method for synthesis of 4-thiazolidinones, the condensation was investigated in presence of ionic liquid N-methylpyridinium tosylate at 100°C. The reaction was complete in 6.5 h (monitored by thin layer chromatography [TLC]) and the yield of the product was increased from 52% (conventional method) to 72%. With an aim to further improvement in yield and reduction in reaction time, the reaction was carried out using trimethylsilyl chloride with ionic liquid and to our surprise it was observed that the reaction was completed in 4 h and yield of the product was increased to 78%.

A series of experiments were carried out using different amounts of trimethylsilyl chloride with ionic liquid. It was observed that ionic liquid in combination with trimethylsilyl chloride gave maximum yield when the molar ratio between thiocarbohydrazone, chloroacetic acid, ionic liquid, and trimethylsilyl chloride was 1:1:4:2. The same condensation was further investigated by using ionic liquid in combination with trimethylsilyl bromide and iodide. It was found that condensation was faster (monitored by TLC) and yield was maximum with trimethylsilyl bromide in the same molar ratio as in case of trimethylsilyl chloride. The reaction parameters with different catalysts in combination with ionic liquid are reported in (Table 1).

CONCLUSIONS

A convenient and efficient two component cyclocondensation using an ionic liquid in presence of TMSBr for the synthesis of new 4-thiazolidinones is reported. The time required for cyclocondensation is markedly reduced and yields of the products are quantitative. Some of the compounds have shown moderate antimicrobial activity.

EXPERIMENTAL SECTION

All the chemicals used were purchased from Sigma Aldrich and used without further purification. Melting points were recorded on melting point apparatus. TLC was performed on silica gel G plates using ethyl acetate: pet ether (1:4) as an eluent and I_2 vapors as visualizing agents and column chromatography was performed on silica gel column using pet ether and ethyl acetate as eluent. IR spectra were recorded on ABB FTIR spectrometer and the results were reported in cm^{-1}. ^1H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ on Bruker 300 MHz and Bruker Advance II 400 MHz spectrometers using tetramethylsilane (TMS) as an internal standard (chemical shift in δ, ppm), mass spectra

on LCMS/MS spectrometer. The elemental analysis of compounds was performed on a Carlo Erba-1108 elemental analyzer. X-ray diffraction was performed on X Calibur EOS OXFORD Diffractometer.

Synthesis of Ionic Liquid, N-Methylpyridinium Tosylate

Pyridine (1.1 mol) was added to a methyl-4-toluene sulfonate (1.0 mol) at 0 °C–10 °C. After completion of the addition, the reaction mixture was stirred at room temperature for 1 h. The solid, N-methylpyridinium tosylate, was filtered. The product was then washed with ethyl acetate to remove unreacted reactants and then dried. The physical parameters of the ionic liquid are in good agreement with those reported in the literature.[22]

General Procedure for the Synthesis of Monothiocarbohydrazone of 1-Tetralones (2)

To a solution of thiocarbohydrazide (0.005 mol) in hot water (75 mL) was added 1 to 2 drops of conc. HCl. Then, 1-tetralone (0.005 mol) dissolved in ethanol (20 mL) was added drop wise with constant stirring. The product began to separate during the course of addition. The reaction mixture was kept overnight at room temperature. The solid separated was filtered and washed with aq. ethanol. The product was purified by column chromatography on silica gel column using pet ether: ethyl acetate (9:1) as the eluent to give monothiocarbohydrazones **2a** and **2b** in 85% and 83% yield, respectively.

Monothiocarbohydrazone of 1-tetralone (2a). This compound was obtained as a white shining solid. mp 228°C–230 °C. IR: 1280 (CS), 1590 (C=N), 3405 (NH). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.95–2.06 (m, 2H, CH_2); 2.57 (t, 2H, J = 6.6 Hz, CH_2); 2.77 (t, 2H, J = 6.3 Hz, CH_2); 4.42 (br, 2H, NH_2, exchange with D_2O); 7.17–8.00 (m, 4H, C_6H_5); 8.62 (br, 1H, NH, exchange with D_2O); 8.72 (br, 1H, NH, exchange with D_2O). ^{13}C NMR (100 MHz, $CDCl_3$), δ: 178.6(C=N);147.5, 139.7, 131.6, 128.8, 128.1, 125.9, 124.6 (C_6H_5); 28.9, 25.6, 21.2 (CH_2). $C_{11}H_{14}N_4S$ (234), Anal. Calcd. C, 56.40; H, 5.98; N, 23.93; S, 13.67; Found: C, 56.54; H, 5.86; N, 23.81; S, 13.60.

Monothiocarbohydrazone of 6-methoxy-1-tetralone (2b). This compound was obtained as yellow crystalline solid. mp 218 °C–20 °C. IR: 1285 (CS), 1595 (CN), 3410 (NH). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.87–1.93 (m, 2H, CH_2); 2.49 (t, 2H, J = 6.6 Hz, CH_2); 2.68 (t, 2H, J = 6.2 Hz, CH_2); 3.75 (s, 3H, OCH_3); 6.30 (br, 1H, NH, exchange with D_2O); 6.59 (d, 1H, J = 2.6 Hz, C_6H_5); 6.70–6.73 (m, 1H, C_6H_5); 7.19 (br, 1H, NH, exchange with D_2O); 7.28 (br, 1H, NH_2, exchange with D_2O); 7.85 (d, 1H, J = 8.8 Hz, C_6H_5); 8.66 (br, 1H, NH_2, exchange with D_2O). ^{13}C NMR (100 MHz, $CDCl_3$), δ: 178.3 (C = N); 159.9, 147.8, 141.6, 126.5, 124.4, 112.8, 112.0 (C_6H_5); 54.8, 29.2, 25.5, 21.3 (CH_2). $C_{12}H_{16}N_4SO$ (264), Anal. Calcd. C, 54.54; H, 6.06; N, 21.21; S, 12.12; Found: C, 54.62; H, 6.14; N, 21.18; S, 12.20.

Conventional Procedure for Synthesis of (3)

A mixture of compound **2** (0.005 mol), chloroacetic acid (0.47 g, 0.005 mol) and anhyd. sodium acetate (4.1 g, 0.05 mol) in anhyd. ethanol (20 mL) was heated under reflux for 12 h. The volume of the reaction mixture was reduced to half and kept overnight. The

solid thus separated was filtered, washed well with water and crystallized from ethyl acetate to give **3a** and **3b** in 52 and 54% yields, respectively.

Solvent Free General Procedure for Synthesis of (3)

An equimolar mixture of compound **2** (0.005 mol) and chloroacetic acid (0.47 g, 0.005 mol) in premolten ionic liquid (0.02 mol) and trimethylsilyl halides (0.01 mol) was stirred at 90 °C–100 °C for 2–6 h (Table 1). The progress of the reaction was monitored by TLC. The reaction mixture was poured into ice cold water, filtered the solid obtained, dried and crystallized from ethyl acetate to give **3a** and **3b.**

(*E*)-3-Amino-2-(*E*)-(3,4-dihydronaphthalen-1(2*H*)-ylidene)hydrazono)thiazolidin-4-one (3a). This compound was obtained as creamy shinning crystals. mp 128°C–30 °C. IR: 1705 (CO), 1595 (CN). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.90–1.99 (m, 2H, CH_2); 2.83 (t, 2H, J = 6.0 Hz, CH_2); 2.95 (t, 2H, J = 6.3 Hz, CH_2); 3.78 (s, 2H, SCH_2); 4.69 (br, 2H, NH_2, exchange with D_2O); 7.16 (d, 1H, J = 7.5 Hz, C_6H_5); 7.23–7.35 (m, 2H, C_6H_5); 8.25 (d, 1H, J = 7.5 Hz, C_6H_5). ^{13}C NMR (100 MHz, $CDCl_3$), δ: 173.5 (C=O); 162.5 (C=N); 162.1 (C=N); 140.9, 132.3, 130.1, 128.6, 126.3, 125.5 (C_6H_5); 33.1 (SCH_2); 29.9 (CH_2); 27.4 (CH_2); 22.2 (CH_2). MS, *m*/*z* (%): 275 $[M+1]^+$ (25). $C_{13}H_{14}N_4SO$ (274), Anal. Calcd. C, 56.93; H, 5.10; N, 20.43; S, 11.67; Found, C, 56.80; H, 5.22; N, 20.38; S, 11.72.

(*E*)-3-Amino-2-(*E*)-(6-methoxy-3,4-dihydronaphthalen-1(2*H*)-ylidene)hydrazono)thiazolidin-4-one (3b). This compound was obtained as light brown crystals. mp 184°C–85 °C. IR: 1712 (CO), 1605 (CN). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.84 (t, 1H, J = 6.4 Hz, CH_2); 1.89 (t, 1H, J = 6.4 Hz, CH_2); 2.54 (t, 1H, J = 6.4 Hz, CH_2), 2.70–2.73 (m, 2H, CH_2); 2.81 (t, 1H, J = 6.5 Hz, CH_2); 3.76 (s, 2H, SCH_2); 3.78 (s, 3H, OCH_3); 6.58 (dd, 1H, J = 16.8, 2.4 Hz, C_6H_5) 6.74 (d, 1H, J = 2.6 Hz, C_6H_5); 7.96 (t, 1H, J = 8.9 Hz, C_6H_5); 9.75 (br, 1H, NH_2, exchange with D_2O); 14.2 (br, 1H, NH_2, exchange with D_2O). ^{13}C NMR (100 MHz, $CDCl_3$), δ: 173.5 (C = O); 160.3 (C=N); 159.5 (C=N); 142.0, 126.5, 125.0, 128.6 (C_6H_5); 54.9 (OCH_3); 32.7 (SCH_2); 29.7 (CH_2); 26.8 (CH_2); 21.8 (CH_2). MS, *m*/*z* (%): 305 $[M+1]^+$ (30). $C_{14}H_{16}N_4SO_2$ (304), Anal. Calcd. C, 55.26; H, 5.26; N, 18.42; S, 10.52; Found, C, 55.34; H, 5.14; N, 18.52; S, 10.64.

General Procedure for the Synthesis of Compound (4)

A mixture of compound **2** (0.002 mol) and benzaldehyde (0.002 mol) in absolute ethanol (20 mL) was refluxed for 1 h and kept overnight. The separated solid was filtered and crystallized from ethanol to give compounds **4a** and **4b** in 71% and 68% yield, respectively.

Compound (4a). This compound was obtained as white crystals. mp 178°C–80°C. IR: 1612 (CN), 1512 (C=C), 1296 (C=S). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 2.04 (m, 2H, CH_2); 2.68 (t, 2H, J = 6.9 Hz, CH_2); 2.81 (t, 2H, J = 5.4 Hz, CH_2); 7.17–8.38 (m, 9H, C_6H_5); 7.44 (s, 1H, =CH); 8.94 (br, 1H, NH, exchange with D_2O); 10.57 (br, 1H, NH, exchange with D_2O). $C_{18}H_{18}N_4S$ (322), Anal. Calcd. C, 67.08; H, 5.59; N, 17.39; S, 9.93; found, C, 67.14; H, 5.66; N, 17.32; S, 9.86.

Compound (4b). This compound was obtained as white needles. mp 187 °C–90 °C. IR: 1610 (CN), 1518 (C=C), 1292 (C=S). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 2.02 (m, 2H, CH_2); 2.66 (t, 2H, J = 6.6 Hz, CH_2); 2.85 (t, 2H, J = 5.6 Hz, CH_2); 3.78 (s, 3H, OCH_3); 7.17–8.33 (m, 8H, C_6H_5); 7.40 (s, 1H, = CH); 8.90 (br, 1H, NH, exchange with D_2O);

10.60 (br, 1H, NH, exchange with D_2O). $C_{19}H_{20}N_4S$ (336), Anal. Calcd. C, 64.77; H, 5.68; N, 15.90; S, 9.09; found, C, 64.88; H, 5.72; N, 15.81; S, 9.04.

General Procedure for the Synthesis of Compound (5)

To a solution of **3** (0.001 mol) in 10 mL of absolute ethanol 1.0 mL of acetic anhydride is added. The reaction mixture was refluxed on water bath for 1.0 h. The volume of the reaction mixture was reduced to half under vacuum and kept overnight. The solid obtained was filtered and recrystallized from ethanol to furnish compounds **5a** and **5b** in 72 and 78% yields respectively.

***N*-((*E*)-2-((*E*)-(3,4-dihydronaphthalen-1(2*H*)-ylidene)hydrazono)-4-oxothiazolidin-3-yl)acetamide (5a).** mp 168°C–70 °C. IR: 1702 (CO), 1668 (CO), 1590 (CN). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.92–1.98 (m, 2H, CH_2); 2.80 (s, 3H, CH_3); 2.85 (t, 2H, $J = 6.2$ Hz, CH_2); 2.90 (t, 2H, $J = 6.5$ Hz, CH_2); 3.80 (s, 2H, SCH_2); 5.24 (br, 1H, NH, exchange with D_2O); 7.20 (d, 1H, $J = 7.8$ Hz, C_6H_5); 7.26–7.39 (m, 2H, C_6H_5); 8.30 (d, 1H, $J = 7.4$ Hz, C_6H_5); ^{13}C NMR (75 MHz, $CDCl_3$), δ: 178, 173.5 (C=O); 165 (C=N); 160.5 (C=N); 140.5, 132.7, 132.1, 130.6, 126.5, 125.8 (C_6H_5); 35.1 (SCH_2); 32.9 (CH_2); 27.7 (CH_2); 22.8 (CH_2). MS, *m*/*z* (%): 317 $[M+1]^+$ (25). $C_{15}H_{16}N_4SO_2$ (316), Anal. Calcd. C, 56.96; H, 5.06; N, 17.72; S, 10.12; Found: C, 56.87; H, 5.12; N, 17.78; S, 10.17.

***N*-((*E*)-2-((*E*)-(6-methoxy-3,4-dihydronaphthalen-1(2*H*)-ylidene)hydrazono)-4-oxothiazolidin-3-yl)acetamide (5b).** mp 210 °C–12 °C. IR: 1715 (CO), 1666 (CO), 1605 (CN). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.80–1.88 (m, 2H, CH_2); 2.84 (s, 3H, CH_3); 2.68 (t, 2H, $J = 6.1$ Hz, CH_2); 2.95 (t, 2H, $J = 6.2$ Hz, CH_2); 3.76 (s, 2H, SCH_2); 3.83 (s, 3H,

Table 2 Crystal data and structure refinement of compound **3a**

Compound	**3a**
Empirical formula	C_{13} H_{14} N_4 O S
Formula weight	274.35
Crystal system/Space group	Monoclinic/P21/n (No. 14)
a/Å	13.923(3)
b/Å	7.973(2)
c/Å	23.625(8)
α/°	90
β/°	93.29(3)
γ/°	90
V/Å^3	2618.2(12)
Z	8
D_{calc} (g cm^{-3})	1.392
μ (mm^{-1})	0.245
Crystal size (mm)	0.22 × 0.28 × 0.32
Color/Shape	Pale Yellow/Block
Temp (K)	293
Theta range for collection	3.05, 29.06
Reflections collected	5968
Independent reflections	2178
Data/restraints/parameters	−17: 16; −10: 10; −29: 32
Goodness of fit on F^2	0.969
Final R indices [$I > 2\sigma(I)$]	0.0731
R indices (all data)	0.1546
Largest difference peak/hole	−0.73/0.56

Table 3 Selected geometrical parameters (Å, °) of compound **3a**

S1–C1	1.759 (5)	N4–C5	1.268 (8)
S1–C4	1.827 (8)	*C3–C4*	1.489 (10)
O1–C3	1.237 (8)	C5–C14	1.488 (9)
N1–N2	1.394 (7)	C7–C8	1.503 (14)
N1–C3	1.337 (8)	C8–C9	1.498 (10)
N1–C1	1.412 (8)	C9–C14	1.388 (10)
N3–N4	1.417 (7)	C5–C6	1.487 (10)
N3–C1	1.256 (7)	C6–C7	1.510 (10)
C1–S1–C4	91.5 (3)	C6–C5–C14	118.7 (6)
N2–N1–C1	119.4 (5)	C5–C6–C7	114.1 (6)
N2–N1–C3	122.6 (5)	C6–C7–C8	109.6 (7)
C1–N1–C3	117.6 (5)	C7–C8–C9	112.0 (8)
N4–N3–C1	110.8 (5)	S1–C1–N3	127.7 (5)
N3–N4–C5	114.9 (5)	S1–C1–N1	110.4 (4)
S1–C4–C3	107.7 (5)	N1–C1–N3	121.9 (5)
N4–C5–C6	125.1 (6)	O1–C3–N1	124.0 (6)
N4–C5–C14	116.2 (6)	O1–C3–C4	123.2 (6)

OCH_3); 7.32–8.26 (m, 4H, C_6H_5). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 185, 176.2 (C=O); 158.2 (C=N); 160.7 (C=N); 142, 135.2, 129, 128.2, 124.2, 122.6 (C_6H_5); 34.8 (SCH_2); 32 (CH_2); 26.6 (CH_2); 21.7 (CH_2). MS, *m/z* (%): 347 $[M+1]^+$ (100). $C_{16}H_{18}N_4SO_3$ (346), Anal. Calcd. C, 55.49; H, 5.20; N, 16.18; S, 9.24; Found, C, 55.42; H, 5.26; N, 16.11; S, 9.30.

Crystallographic Study and Structural Description

Compound **3a** was crystallized from ethanol by slow evaporation method as shiny cream crystals. Single crystal X-ray diffraction of **3a** has shown that the compound crystallizes in monoclinic system. The crystallographic data CIF file has been deposited with CCDC. The deposition number is CCDC 824245. The crystallographic data and refinement parameters of **3a** are reported in Table 2. Selected bond lengths and bond angles of **3a** are presented in (Table 3).

Antimicrobial Activities

Antimicrobial activities of compounds 2–5 were studied against a variety of bacterial stains, such as *S. aureus, B. subtilis* (gram positive bacteria) and *P. aeruginosa* (gram negative bacteria) and fungi like *A. niger, C. albicans*, and *A. fumigatus* by the in vitro cup plate technique using ampicillin trihydrate as positive control and the results are reported in Table S1 of Supplemental Materials.

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