Synthesis of Novel 1-(5-(Benzylsulfinyl)-3-methyl-1,3,4-thiadiazol-2(3*H*)-ylidene)-thiourea/urea Derivatives and Evaluation of Their Antimicrobial Activities

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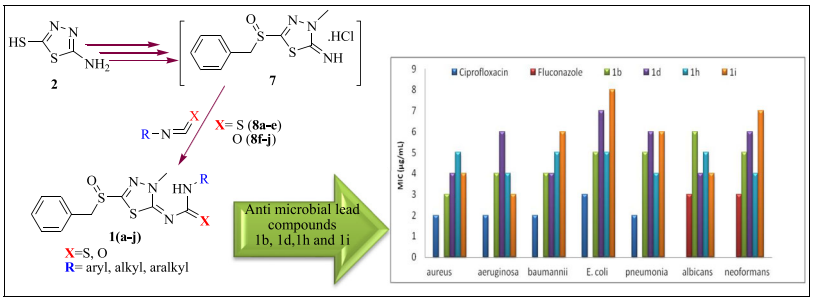


A new series of 1-(5-(benzylsulfinyl)-3-methyl-1,3,4-thiadiazol-2(3*H*)-ylidene)-thiourea/urea derivatives (**1a**–**j**) were designed and synthesized. For the first time, (i) a new process was developed for *N*-methylation of 1,3,4-thiadiazole moiety using dimethyl carbonate an environmentally benign reagent in presence of *N*,*N*,*N*′,N′-tetramethylethylenediamine and (ii) the sulfide was selectively oxidized to sulfoxide in higher yield by using chlorine (g) in aqueous acetic acid media under mild reaction condition. The synthesized compounds (**1a**–**j**) were investigated for their antimicrobial activities. The tested compounds (**1a**–**j**) were exhibited moderate to excellent antibacterial activities against both Gram-positive and Gram-negative bacterial strains. The same compounds exhibited good antifungal activities against selected fungal strains. Particularly, the compounds **1b**, **1d**, **1h**, and **1i** were proved to be promising leads exhibiting both antibacterial and antifungal activities compared with standard drugs, ciprofloxacin, and fluconazole. The presence of 1,3,4-thiadiazole moiety has a significant role in the display of antimicrobial activity. In addition, the presence of both sulfinyl and thiourea or urea functionalities has enhanced the activity as per obtained antimicrobial activity data.

INTRODUCTION

The feast of infectious diseases is one of the major troublesome situations in the world because of the increasing number of multidrug resistant pathogens [1–6]. The reasons behind this include (i) increase of geriatric population, (ii) increased prevalence of infectious diseases, and (iii) increase of bacterial and fungal resistance toward conventional antibiotics because of genetic mutation and over prescription of antibacterial and antifungal drugs [7–9]. Hence, there is a great demand for the development of new antimicrobial drugs and drug candidates [10]. The extensive literature search revealed that a huge number of drugs were reported as antimicrobial agents that are either heterocyclic or non-heterocyclic molecules. Among them, thiadiazole moiety possesses numerous biological activities, for example, antimicrobial [11–14], antituberculosis [15–19], antioxidant [20–22], anti-inflammatory [22–25], convulsants [26], antidepressant, anxiolytic [27], antihypertensive [28], and anticancer [29] activities. Particularly, the presence of 1,3,4-thiadiazole moiety [30–38], sulfinyl functionality [39–45], thiourea, and urea [46–49] groups in newly designed molecules has received great attention in drug discovery and development programs as they are present in many biologically active drugs. The extensive literature search encouraged us to design a new series of novel molecules with the presence of aforesaid functionalities. Recently, it was reported that the molecules with 1,3,4-thiadiazole core structure and presence of sulfide, urea, and thiourea derivatives displayed good antibacterial activity [50,51] as shown in Figure 1.

It is well known that either sulfur atom or sulfur-related functionalities (–SO– and –SO_2–) within heterocyclic moiety or side chain of the heterocyclic core play an important role in the display of interesting biological activities [39–45]. Further, the presence of sulfinyl

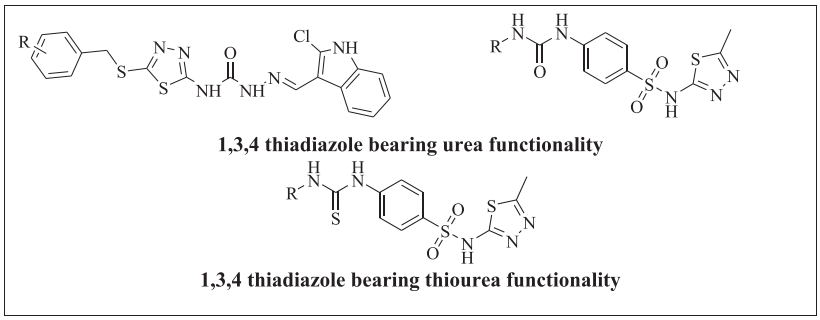


Figure 1. Biologically active urea-based and thiourea-based 1,3,4-thiadiazole derivatives.

functionality in the side chain of heterocyclic moiety leads to the molecule becoming medicinally more prominent [39–45].

Many synthetic methods were reported in the literature for the synthesis of 1,3,4-thiadiazole derivatives, for example, sulfuration of the corresponding 1,4-dicarbonyl or acyl precursors using P_2S_5 and Lawesson's reagent [52] and also prepared from (i) carboxylic acids using propylphosphonic anhydride [53] in one pot, (ii) from acid hydrazides under microwave irradiation in a single step [54], and (iii) *N*,*N*-diacylhydrazines in presence of P_2S_5 and Lawesson's reagent [55] and various other methods also reported [56–63].

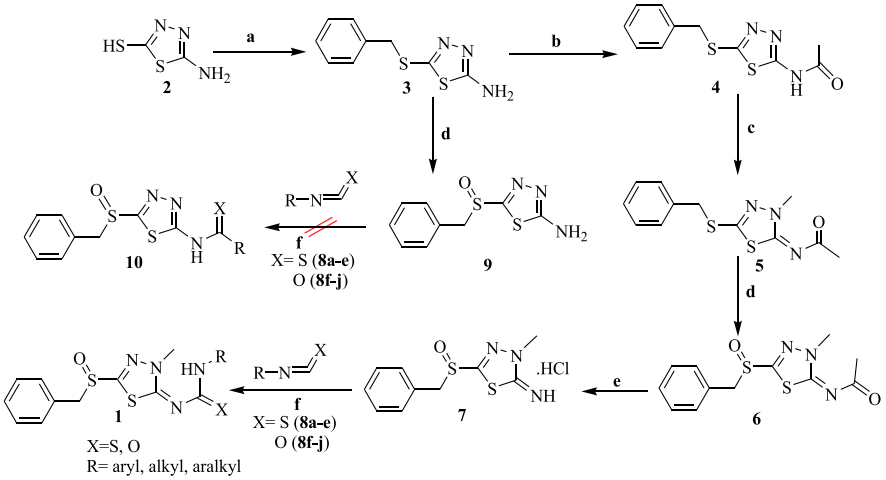
Based on literature data, we have planned to design and synthesize a series of 1-(5-(benzylsulfinyl)-3-methyl-1,3,4-thiadiazol-2(3*H*)-ylidene)-thiourea/urea derivatives (**1a–j**).

Herein, we report the synthesis of novel 1-(5-(benzylsulfinyl)-3-methyl-1,3,4-thiadiazol-2(3*H*)-ylidene)-thiourea/urea derivatives (**1a–j**) starting from 2-amino-1,3,4-thiadiazole-5-thiol (**2**) as shown in Scheme 1.

RESULTS AND DISCUSSION

Chemistry. A new series of 1-(5-(benzylsulfinyl-1,3,4-thiadiazol-2(3*H*)-ylidene)-thiourea/urea derivatives (**1a–j**) were designed and synthesized as depicted in Scheme 1. At the outset, we chose easily available 5-amino-1,3,4-thiadiazole-2-thiol (**2**) as a key starting material. Our synthesis starts from *S*-alkylation of 5-amino-1,3,4-thiadiazole-2-thiol (**2**) using benzyl chloride in ethanol under basic conditions that provided the compound **3** in high yield 98% [64]. The resulting S-alkylated product (**3**) was converted to sulfoxide derivative (**9**) selectively, which further planned to synthesize target molecule (**10**). Accordingly, compound **9** was treated with isothiocyanate/thiocyanate (**8**) at reflux temperature in

Scheme 1. Synthesis of 1-(5-(benzylsulfinyl)-1,3,4-thiadiazol-2-yl/3-methyl-2-(3*H*)-ylidene)-thioamide/amide derivatives. [Color figure can be viewed at wileyonlinelibrary.com]



Reaction conditions: a) Aq. KOH, Benzyl chloride, EtOH, 25–30°C, 98%; b) Ac_2O, AcOH, 25–30°C, 98.5%; c) dimethyl carbonate (DMC), cat. TMEDA, 90–100°C, 80%; d) Cl_2 (g), $AcOH:H_2O$ (5:1 ratio), 5–15 °C, 82%; e) EtOH, Conc. HCl, 90%, and f) THF, Et_3N, 50–60°C, 70–90%

tetrahydrofuran (THF). Unfortunately, no product (**10**) formation was observed even though various parameters were tried. Next, we changed our strategy to install *N*-alkyl functionality in the ring to enhance the reactivity by destroying the aromaticity of the 1,3,4-thiadiazole derivative (**4**). Accordingly, the aromaticity was planned to destroy by *N*-alkylation at 3′-position of compound **4** *via* the acetylation of compound **3** using acetic anhydride in presence of acetic acid at 25–30°C. The desired acetylated compound **4** [64] was obtained in high yield (98%).

The *N*-alkylation at 3′-position of compound **4** was carried out by using dimethyl sulfate (DMS) in methanol/KOH at reflux temperature provided the desired compound **5** albeit in low yield 43% (entry 1, Table 1). The major disadvantages associated with DMS include high reaction temperature, pungent odor, and highly toxic nature of the by-products [65]. Because of that, *N*-methylation has planned to screen using various other methylating reagents. When CH_3Br and CH_3I were used

Table 3

Optimization of reaction conditions for the synthesis of compound **1a** from compound **6** and compound **8a**.[a]

Entry	Solvents	Time (h)	Temp(°C)	Product	Yield[b] (%)
1	Cyclohexane	24	Reflux	**1a**	15
2	Toluene	24	Reflux	**1a**	25
3	DCM	24	Reflux	**1a**	15
4	MeOH	24	Reflux	**1a**	38
5	EtOH	24	Reflux	**1a**	44
6	IPA	24	Reflux	**1a**	52
7	THF	24	RT	**1a**	35
		3	Reflux	**1a**	75
8	DMF	2	60–70	**1a**	60
9	DMSO	2	60–70	**1a**	58
10	DMAc	1.5	60–70	**1a**	55

DMAc, dimethylacetamide; DMF, dimethylformamide; THF, tetrahydrofuran.
[a]Reaction conditions: compound **6** (10.0 mmol), compound **8a** (12.0 mmol), and Et_3N (15.0 mmol) in solvent (10 vol.) at specified temperature.
[b]Isolated yields.

Table 1

Screening of various methylating agents for the synthesis of compound **5**[a].

Entry	Methylating agents	Equivalents	Temp (°C)	Solvents	Base	Product	Yield[b] (%)
1	DMS[c]	1.2	Reflux	MeOH	KOH	**5**	43
2	CH_3Br	1.2	Reflux	MeOH	KOH	**5**	36
3	CH_3I	1.2	Reflux	Acetone	KOH	**5**	40
4	DMC[d]	1.2	90–100	DMF	TMEDA	**5**	81
5	DMC	1.2	90–100	DMSO	TMEDA	**5**	68
6	DMC	1.2	90–100	DMAc	TMEDA	**5**	62

DMAc, dimethylacetamide; DMF, dimethylformamide; TMEDA, tetramethylethylenediamine.
[a]Reaction conditions: compound **4** (10.0 mmol) and methylating agent (12.0 mmol) in a solvent (10 vol.) in presence of a base (2.5 equiv.) or catalyst (1.0 mmol) at the specified temperature.
[b]Isolated yield.
[c]DMS: dimethyl sulfate.
[d]DMC: dimethyl carbonate.

Table 2

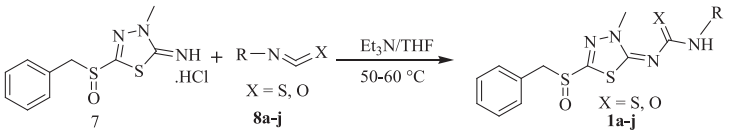
Screening of various oxidizing agents for the synthesis of compound **6**[a].

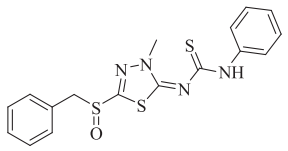
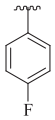
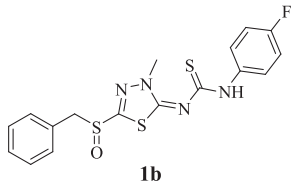
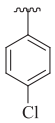
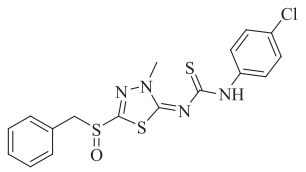
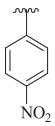
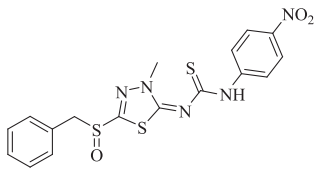
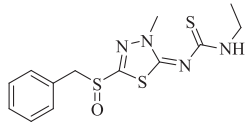
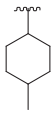
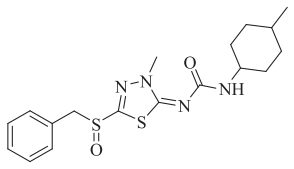
Entry	Oxidants	Mole equiv.	Time (h)	Solvents	Product	Yield[b] (%)
1	Sodium hypochlorite	1.0	2.5	—	**6**	45
2	m-CPBA	1.0	1.5	ACN	**6**	55
3	Oxone	0.5	1.0	H_2O–THF (2:1)	**6**	25
4	H_2O_2 (30%)	1.0	2.0	ACN	**6**	32
5	Peracetic acid	1.0	2.0	ACN	**6**	45
6	Magnesium monoperoxyphthalate	1.0	3.0	H_2O–ACN (2:1)	**6**	42
7	Cl_2	1.0	3.0	H_2O–AcOH (1:9)	**6**	60
8	Cl_2	1.0	3.0	H_2O–AcOH (1:5)	**6**	82
9	Cl_2	1.0	3.0	H_2O–AcOH (1:2)	**6**	68
10	Cl_2	1.0	3.0	H_2O–AcOH (1:1)	**6**	61
11	Cl_2	1.0	3.0	AcOH	**6**	—
12	Cl_2	1.0	3.0	Water	**6**	—

THF, tetrahydrofuran.
[a]Reaction conditions: compound **5** (10.0 mmol) and oxidants in the solvent/mixture of solvents (10 vol.) at 5–15°C.
[b]Isolated yields.

Table 4

Synthesis of *N*-(5-(benzylsulfinyl)-1,3,4-thiadiazol-3-methyl-2(3*H*)-ylidene)-thiourea/urea derivatives (**1a**–**j**)[a].

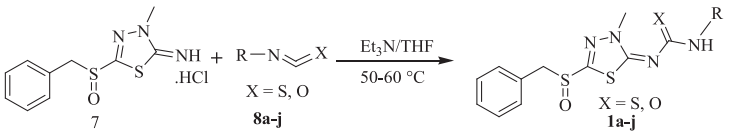


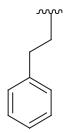
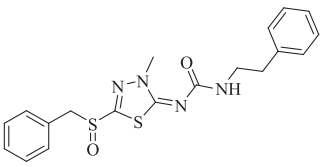
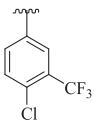
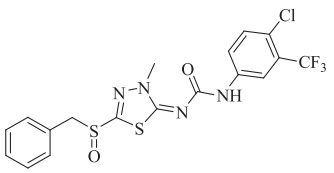
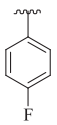
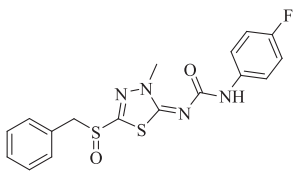
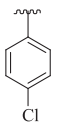
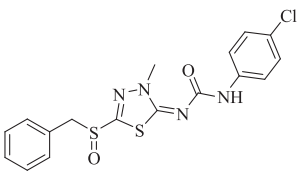
Entry	Compound **8** R	Compound **8** X	Time (h)	Product	Yield[b] (%)
1	 **8a**	S	3	 **1a**	75
2	 **8b**	S	2	 **1b**	92
3	 **8c**	S	5	 **1c**	78
4	 **8d**	S	2	 **1d**	91
5	**CH_3CH_2– 8e**	S	3	 **1e**	72
6	 **8f**	O	3	 **1f**	75

(*Continues*)

Table 4

(*Continued*)



Entry	Compound **8** R	Compound **8** X	Time (h)	Product	Yield[b] (%)
7	 **8g**	O	3	 **1g**	78
8	 **8h**	O	5	 **1h**	85
9	 **8i**	O	2	 **1i**	88
10	 **8j**	O	2	 **1j**	76

[a]Reaction conditions: compound **7** (10.0 mmol), isothiocyanate (**8a–e**)/isocyanate (**8f–j**) (12.0 mmol), and Et_3N (15.0 mmol) in THF (10 vol) at 50–60°C.
[b]Isolated yields.

in presence of KOH and obtained the desired product (**5**) in low yields, 36%, 40%, respectively (entries 2 and 3). Even these reagents are also associated with many drawbacks such as carcinogenic and genotoxic nature. In this context, we urged to find environmentally benign and toxic free reagent. The dimethyl carbonate (DMC) was found to be more promising and high yield methylating reagent in many literature reports [66]. Hence, the reaction was carried out using DMC in presence of tetramethylethylenediamine (TMEDA) in dimethylformamide (DMF) at 90–100°C and the alkylated product was obtained in high yield 81% (entry 4, Table 1). The DMSO and dimethylacetamide were screened in place of DMF but yields dropped to 68% and 62%,

respectively (entries 5 and 6). The study disclosed that DMF is an optimal solvent for getting higher yield of compound **5** (entry 4).

Number of methods has been reported for the preparation of sulfones (–SO_2–), but only few methods were reported for the preparation of sulfoxide (–SO–). Hence, we have envisioned installing sulfinyl (–SO–) functional group in compound **5** by testing with various oxidizing agents. Initially, the sulfide compound (**4**) was treated with sodium hypochlorite in neat condition at low temperature (5–15°C) to yield desired sulfoxide **6** in low yield 45% (entry 1, Table 2) was obtained. The screening of other oxidants such as m-CPBA, Oxone, H_2O_2 (30%), peracetic acid, and magnesium monoperoxyphthalate provided sulfoxide (**6**) in moderate yields 40–55% (entries 2–6, Table 2). Surprisingly, chlorine in a mixture of water–acetic acid (1:9 ratio) at 5–15°C afforded the desired compound in 60% yield (entry 7, Table 2). This result encouraged us to optimize the conditions to improve the yield. Further, the various ratio of water and acetic acid were screened (entries 8–10, Table 2) and found that in case of water and acetic acid in 1:5 ratio provided desired product (**6**) in high yield 82% (entry 8). The same reaction either in acetic acid or in water alone, the starting material was intact (entries 11 and 12, Table 2). As per our knowledge, this is the first report for mono sulfoxidation using Cl_2 in aq. acetic acid with high yield (82%).

Table 5

Antimicrobial activities of tested compounds (**1a–1j**) in terms of the diameter of inhibition zones (mm).

	Diameter of inhibition zones in mm									
	Staphylococcus aureus		*Pseudomonas aeruginosa*		*Acinetobactor baumannii*		*Escherichia coli*		*Klebsiella pneumonia*	
	50	100	50	100	50	100	50	100	50	100
Tested compounds	μg mL^{-1}		μg mL^{-1}		μg mL^{-1}		μg mL^{-1}		μg mL^{-1}	
1a	4	8	3	7	5	9	2	5	3	6
1b	11	18	10	17	11	19	11	18	10	21
1c	0	0	2	4	1	2	3	5	2	3
1d	10	17	8	16	8	17	9	17	8	16
1e	1	3	0	0	1	2	0	0	0	0
1f	5	7	6	10	4	8	6	12	4	10
1g	2	4	1	2	0	0	2	3	3	5
1h	10	18	9	16	9	19	11	18	10	17
1i	9	17	8	15	8	17	10	19	7	15
1j	0	0	2	3	4	6	3	5	0	0
Ciprofloxacin	13	21	12	21	13	23	13	22	13	23

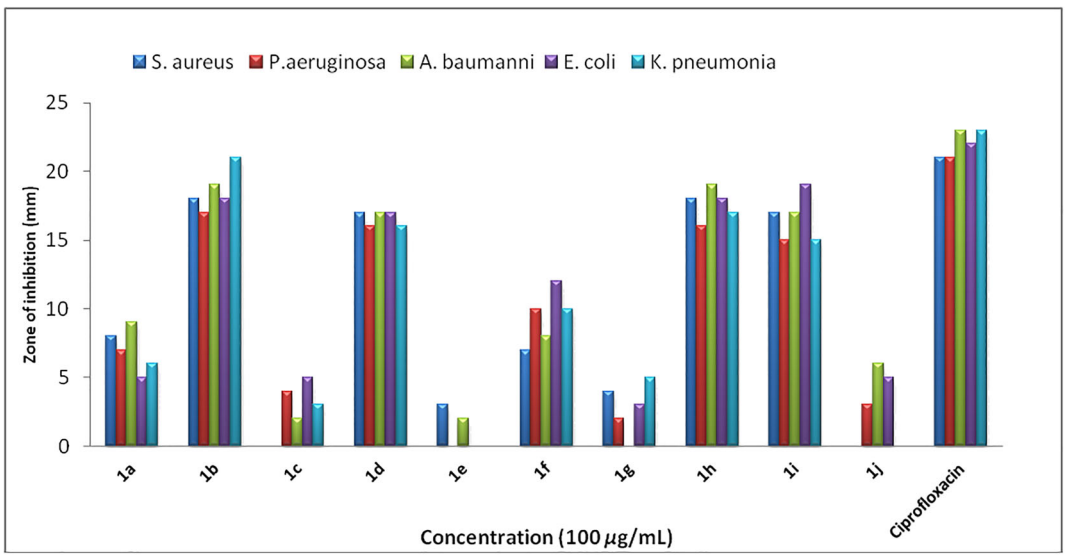


Figure 2. Biological activity of synthesized compounds (**1a–j**) against bacterial strains. [Color figure can be viewed at wileyonlinelibrary.com]

The deprotection of the acetyl group was performed as per the literature process [67], that is, deacetylation using conc. HCl in ethanol afforded desired imine hydrochloride **7**, in high yield. Now, the imine thiadiazole scaffold (**7**) was in our hand, and then our attention turned to prepare a library of new molecules (**1a–j**) by treating compound **7** with various substrates (**8a–j**).

At the outset, the imine compound **7** was treated with substrate **8a** in cyclohexane at room temperature and obtained the desired compound **1a** in low yield 5%. When raising the temperature to reflux for the prolonged time, there was no considerable yield improvement (15%) (entry 1, Table 3). To increase the yield, various polar and nonpolar solvents were screened, for example, toluene and Dichloromethane (DCM) provided desired product **1a** in low yields 25% and 15%, respectively (entries 2 and 3, Table 3). The same reaction in polar protic solvents such as methanol, ethanol, and IPA provided desired compound **1a** in moderate yields (entries 4–6). In the case of polar aprotic solvents, the conversion was improved compared with protic solvents (entries 7–10). Particularly, in THF, the yield of product **1a** was increased to a great extent (75%) (entry 7, Table 3). The same reaction at room temperature offered low yield 35% even for prolonged reaction time.

Next, we focused our attention on the scope and utility of the present developed reaction conditions for the synthesis of a library of compounds **1b–j** as shown in Table 4. The substrates (**8b** and **8d**) with electron

Table 6

Antifungal activities of tested compounds (**1a–1j**) in terms of the diameter of inhibition zones (mm).

	Diameter of inhibition zones in mm			
	Candida albicans		*Cryptococcus neoformans*	
	50	100	50	100
Tested compounds	μg mL^{-1}		μg mL^{-1}	
1a	5	11	7	13
1b	12	20	14	19
1c	4	7	5	9
1d	11	21	12	18
1e	0	0	0	0
1f	4	7	5	11
1g	0	0	2	3
1h	13	19	15	21
1i	10	18	12	19
1j	0	0	3	5
Fluconazole	14	22	16	23

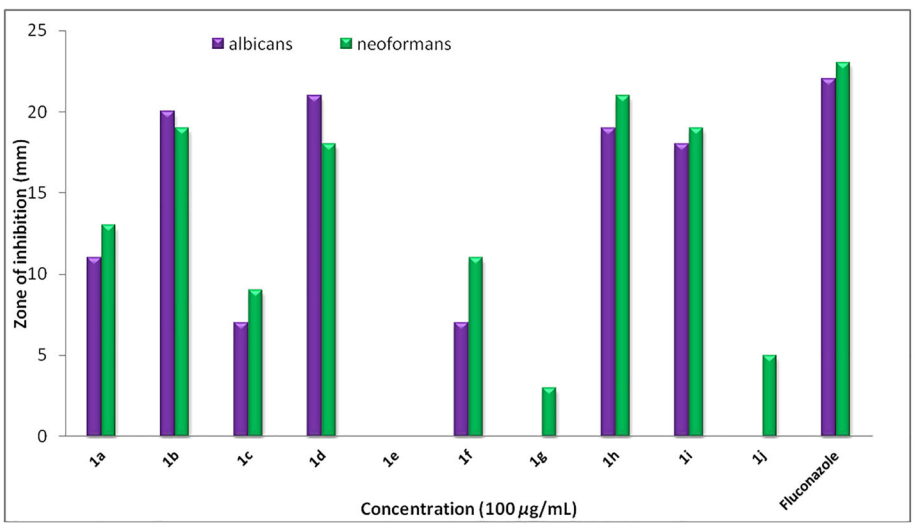


Figure 3. Biological activity of synthesized compounds (**1a–j**) against fungal strains. [Color figure can be viewed at wileyonlinelibrary.com]

withdrawing groups (–F and $–NO_2$) provided desired products **1b** and **1d** in high yields 92% and 91%, respectively (entries 2 and 4, Table 4), but the substrate **8c** with –Cl group provided the desired product **1c** in moderate yield 78% (entry 3). It may be because of moderate inductive effect of chloro substituent. In the case of substrates **8e–g** with alkyl groups provided moderate yields of products **1e–g** (72–78%). The similar trend was observed in case of other substrates **8h–j** and also, for example, the yield range of products **1h–j** was 76–85%, (entries 8–10).

Interestingly, it was observed that thiourea-based derivatives of 1,3,4-thiadiazoles (**1a–c** and **1e**) displayed tautomerism except for compound **1d** as confirmed by ^{1}H NMR. To confirm the same, ^{1}H NMR of compound **1b** was performed at higher temperature (50°C). The *N*-methyl group at room temperature (Figure S29a) appeared as doublet while at 50°C appeared as singlet (Figure S29b).

Biological activity studies. The antibacterial activity screening was carried out using agar disc diffusion method [68–70]. All the synthesized compounds (**1a–1j**) were tested against Gram-positive bacterial strains, *Staphylococcus aureus* (ATCC 43300), Gram-negative bacterial strains, *Escherichia coli* (ATCC 25922), *Klebsiella pneumoniae* (ATCC 700603), non-fermenting Gram-negative bacterial strains, *Pseudomonas aeruginosa* (ATCC 27853), *Acinetobacter baumannii* (ATCC 19606), and two fungi-like *Candida albicans* (ATCC 90028) and *Cryptococcus neoformans* (ATCC 208821). The zones of inhibition were measured and compared with the standard antibiotics, ciprofloxacin against bacterial strains and fluconazole against fungi. The preliminary results of antibacterial testing of compounds (**1a–j**) are shown in Table 5 and Figure 2 and the results of antifungal activities are shown in Table 6 and Figure 3. The minimum inhibitory concentration (MIC) of lead compounds **1b**, **1d**, **1h**, and **1i** were assessed

Table 7

Minimum inhibitory concentration of newly synthesized active compounds.

	Minimum inhibitory concentration in μg mL^{-1}						
	Bacterial strains					Fungal strains	
Tested compounds	*Staphylococcus aureus*	*Pseudomonas aeruginosa*	*Acinetobacter baumannii*	*Escherichia coli*	*Klebsiella pneumonia*	*Candida albicans*	*Cryptococcus neoformans*
1b	3	4	4	5	5	6	5
1d	4	6	4	7	6	4	6
1h	5	4	5	5	4	5	4
1i	4	3	6	8	6	4	7
Ciprofl-oxacin	2	2	2	3	2	—	
Fluconazole			—			3	3

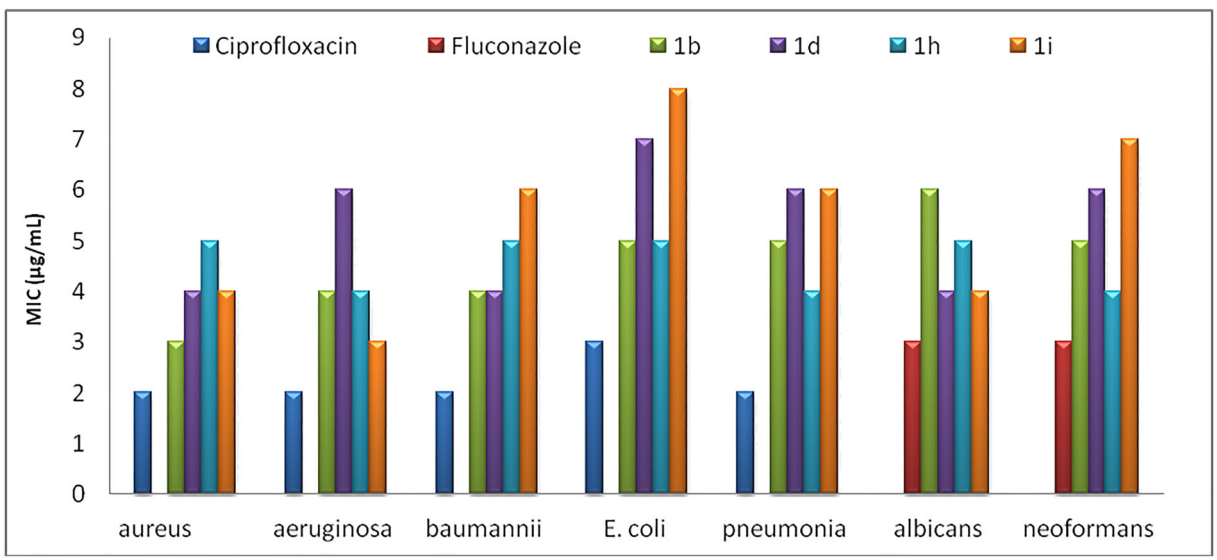


Figure 4. Minimum inhibitory concentration (MIC) of lead compounds (**1b**, **1d**, **1h**, and **1i**) against bacterial strains and fungal strains. [Color figure can be viewed at wileyonlinelibrary.com]

using twofold serial dilution technique [71] and the obtained results were presented in Table 7 and Figure 4.

As depicted in Table 5 and Figure 2, a few of the tested compounds, for example, compounds **1b**, **1d**, **1h**, and **1i**, showed potent antibacterial activity against all the bacterial strains. Most of the compounds exhibited promising activity against *S. aureus*, *P. aeruginosa*, *K. pneumonia*, *A. baumannii*, and *E. coli*. It was observed that the newly synthesized urea-based/thiourea-based 1,3,4-thiadiazole derivatives with (i) 4-fluorophenyl substitution (**1b** and **1i**), (ii) 4-nitro phenyl substitution (**1d**), and (iii) 3-trifluoro-4-chlorophenyl substitution (**1h**) were exhibited potential bacterial growth of inhibition against all the tested bacteria, almost comparable activity was observed with standard ciprofloxacin as shown in Table 5 and Figure 2 and their MIC values were reported in Table 7 and Figure 4. The compounds **1a** and **1f** displayed low to moderate activity toward Gram-positive bacteria and moderate activity toward Gram-negative bacterial strains. The compounds **1c**, **1e**, **1g**, and **1j** exhibited the least activity against both bacterial strains. The overall study revealed that thiourea-based 1,3,4-thiadiazole derivatives (**1b** and **1d**) showed good antibacterial activity compared with urea-based 1,3,4-thiadiazole derivatives (**1h** and **1i**).

In the case of antifungal activity studies revealed that the same compounds (**1b**, **1d**, **1h**, and **1i**) exhibited good growth of inhibition against *C. neoformans* and *C. albicans*. The thiourea-based 1,3,4-thiadiazole derivatives (**1b** and **1d**) and urea-based 1,3,4-thiadiazole derivatives (**1h** and **1i**) displayed promising activity against both fungal strains, *C. neoformans* and *C. albicans* as shown in Table 6 and Figure 3 and their MIC values were reported in Table 7 and Figure 4. The other compounds (**1a**, **1c**, **1e**–**g**, and **1j**) showed inferior activity.

The structure–activity relationship studies of the synthesized compounds revealed that the presence of electron withdrawing groups (–NO_2, –F, and –CF_3) on the phenyl ring of urea-based/thiourea-based 1,3,4-thiadiazole derivatives (**1d**, **1h**, and **1i**) displayed good antibacterial and antifungal activities. The compounds having electron donating groups (–Cl) on phenyl ring (**1c**) or presence of both simple benzyl and aliphatic groups of urea-based/thiourea-based 1,3,4-thiadiazole derivatives (**1e**, **1g**, **1j**, and **1c**) exhibited low antibacterial and antifungal activities. The compounds having fluoro (–F) substituent (**1b** and **1i**) showed excellent activity as shown in Tables 5 and 6.

CONCLUSION

We have synthesized a new series of 1-(5-(benzylsulfinyl)-3-methyl-1,3,4-thiadiazol-(3*H*)-ylidene)-thiourea/urea derivatives (**1a**–**j**) starting from easily available substrates (**2** and **8a**–**j**). The notable advantages of the present work include (i) use of DMC, an environmentally benign and toxic free reagent, for *N*-methylation of compound **4** in presence of TMEDA in DMF; (ii) avoided the use of toxic and carcinogenic methylating agents, for example, DMS, MeBr, and MeI; and (iii) selective mono oxidation of sulfide (**5**) by using chlorine (g) in aqueous acetic acid system (1:5 ratio) with excellent isolated yields (81%). For the first time, we have identified, synthesized, and characterized a new intermediate, *N*-(5-(benzylsulfinyl)-3-methyl-1,3,4-thiadiazol-2(3*H*)-ylidene)acetamide (**6**). In addition, the synthesized compounds (**1b**, **1d**, **1h**, and **1i**) showed excellent antibacterial activity against Gram-positive and Gram-negative bacterial strains and also good activity against fungal strains. The screening of antituberculosis activities of the present molecules is under progress. We hope that the present work is highly useful for new drug discovery and development programs.

EXPERIMENTAL

Reagents and instruments. The solvents and reagents were obtained from commercial sources and were used without any purification. Nuclear magnetic resonance (NMR) spectra of the synthesized compounds were recorded on Ascend Bruker 400 (Bruker, Fallanden, Switzerland) instrument and operating at 400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR using DMSO-d_6 solvent and tetramethylsilane as an internal standard. Spin multiplicities are given as s (singlet), d (doublet), dd (doublet of doublet), qd (quartet of doublet), t (triplet), and m (multiplet) as well as brs (broad singlet). The ^{1}H chemical shift values were reported on δ scale in ppm, relative to tetramethylsilane (δ = 0.00 ppm) and the ^{13}C chemical shift values were reported relative to DMSO-d_6 (δ = 39.5 ppm). The ESI/MS experiments were performed on a Velos Pro Ion Trap mass spectrometer from Thermo Scientific (San Jose, CA, USA).

2-Amino-5-benzylmercapto-1,3,4-thiadiazole (3). In a three-necked round bottom flask, 2-amino-5-mercapto-1,3,4-thiadiazole (**2**) (25 g, 187 mmol) was taken in ethanol (100 mL) at 20–30°C. The aqueous KOH solution (13.6 g of KOH dissolved in 20 mL water) was added slowly at 20–30°C. The reaction mass was stirred at the same temperature for 10 min. Subsequently, benzyl chloride (25.0 g, 197 mmol) was added dropwise at 20–30°C. The reaction mass was stirred for 2–3 h at 25–30°C. After completion of the reaction as per thin-layer chromatography (TLC), water (100 mL) was added to the reaction mass and stirred for 30 min at the same temperature. The reaction mass was filtered, washed with

water (25 mL), and sucked dried for 30 min. The obtained wet compound (**3**) was dried in a hot air oven at 50°C for 4–6 h. The compound **3** was obtained as light yellow solid, 41.0 g, yield: 98.0%; mp: 157–159°C; FT-IR (KBr) υ_{max}: 3292, 3103 (–NH), 1616 (–C═N), 1516, 1492 (–C═C–), 1336, 1240, 1060 (C–N_{str}), 712 (C–S); ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 4.23 (s, 2H, –CH_2–), 7.25–7.36 (m, 5H, Ar–H); ^{13}C NMR (100 MHz, δ ppm): 38.46, 127.45, 128.48, 128.97, 137.10, 149.47, 169.87; ESI–MS: *m/z* 224.03 $[M + H]^+$.

2-Acetylamino-5-benzylmercapto-1,3,4-thiadiazole (4). In a three-necked round bottom flask, 2-amino-5-benzylmercapto-1,3,4-thiadiazole (**3**) (20 g, 89.5 mmol) in acetic acid (80 mL) was taken at 20–30°C. The acetic anhydride (10.0 g, 98.0 mmol) was added slowly to the reaction mass at 20–30°C. The reaction mass was stirred for 2–3 h at 25–30°C. After completion of the reaction as per TLC, water (150 mL) was added and stirred at the same temperature for 30 min. The reaction mass was filtered, washed with water (40 mL), and sucked dried and the wet solid was dried in a hot air oven at 55°C for 6–8 h. The compound **4** was obtained as an off-white solid, 23.4 g. Yield: 98.5%; mp: 163–165°C; FT-IR (KBr) υ_{max}: 3161 (–NH), 1695 (C═O), 1560 (C═N), 1497 (C═C), 1303, 1248 (C–N), 698 (C–S); ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 2.17 (s, 3H, –$COCH_3$), 4.48 (s, 2H, –CH_2), 7.26–7.35 (m, 3H, Ar–H), 7.39 (d, 2H, Ar–H, *J* = 7.2 Hz), 12.59 (s, 1H, NH); ^{13}C NMR (100 MHz, δ ppm): 22.28, 37.57, 127.57, 128.54, 128.99, 136.71, 157.83, 158.93, 168.70; ESI–MS: *m/z* 266.12 $[M + H]^+$.

5-Acetylimino-4-methyl-2-benzylmercapto-1,3,4-thiadiazole (5). A mixture of 2-acetylamino-5-benzylmercapto-1,3,4-thiadiazole **4** (20 g, 75.3 mmol), DMC (7.76 g, 79.14 mmol), and TMEDA (1.31 g, 11.3 mmol) in DMF (80 mL) was taken in a three-necked RB flask at 20–30°C. The reaction mass was heated to 90–100°C The reaction mass was stirred at the same temperature for 5–6 h. After completion of the reaction as per TLC, the reaction mass was cooled to 25–30°C and water (200 mL) was added to the reaction mass at 25–30°C and stirred for 30 min at the same temperature. The reaction mass was filtered and washed with water (40 mL) and the wet solid was dried in a hot air oven at 55°C for 6–8 h. The compound **5** was obtained as a light yellow solid, recrystallized from ethanol, dry weight 17.05 g. Yield: 81.0%; mp: 80–83°C; FT-IR (KBr) υ_{max}: 1614 (C═O), 1514 (C═N), 1379, 1287, 1069 (C–N), 700 (C–S); ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 2.19 (s, 3H, –$COCH_3$), 3.83 (s, 3H, *N*–CH_3), 4.46 (s, 2H, –CH_2), 7.27–7.31 (m, 1H, Ar–H), 7.33–7.36 (m, 2H, Ar–H), 7.41 (d, 2H, Ar–H, *J* = 7.2 Hz); ^{13}C NMR (100 MHz δ ppm): 26.33, 36.66, 37.80, 127.72, 128.60, 129.06, 136.23, 153.67, 163.90, 179.05; ESI–MS: *m/z* 279.05 $[M + H]^+$.

N-(5-(benzylsulfinyl)-3-methyl-1,3,4-thiadiazol-2(3H)-ylidene)acetamide (6). A mixture of 5-acetylimino-4-methyl-2-benzylmercapto-1,3,4-thiadiazole **5** (15 g, 51 mmol) in a mixture of water–acetic acid (1:5 ratio, 90 mL) was taken in a three-necked RB flask at 20–30°C. The reaction mass was cooled to 5–15°C and chlorine gas (12 g) [Note: The required quantity of chlorine gas was generated in situ by slow addition of conc. HCl (60 mL) to $KMnO_4$ (35.0 g)]. The whole reaction mass was stirred for 2–3 h at the same temperature. After completion of the reaction as per TLC, water (150 mL) was added at 5–15°C and stirred for 30 min at the same temperature. The reaction mass was filtered and washed with water (30 mL) and the wet solid was dried in a hot air oven for 6–8 h at 50°C. The compound **6** was obtained as off-white solid, 13.0 g, Yield: 82.0%; mp: 126.4–129.5°C; FT-IR (KBr) υ_{max}: 1618 (C═O), 1491 (C═C), 1371, 1292, 1074 (C–N), 1057 (S═O); ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 2.25 (s, 3H, –$COCH_3$), 3.83 (s, 3H, *N*–CH_3), 4.53 (d, 1H, –SCH_2–, *J* = 12.8 Hz), 4.61 (d, 1H, –SCH_2–, *J* = 12.8 Hz), 7.25–7.28 (m, 2H, Ar–H), 7.33–7.35 (m, 3H, Ar–H); ^{13}C NMR (100 MHz, δ ppm): 26.48, 38.14, 6082, 128.49, 128.57, 128.91, 130.64, 162.21, 164.38, 179.54; ESI–MS: *m/z* 296.05 $[M + H]^+$.

5-(Benzylsulfinyl)-3-methyl-1,3,4-thiadiazol-2(3H)-imine hydrochloride (7). A mixture of *N*-(5-(benzylsulfinyl)-3-methyl-1,3,4-thiadiazol-2(3*H*)-ylidene)acetamide **6** (12 g, 40.6 mmol) in ethanol (50 mL) was taken in a three-necked RB flask at 20–30°C. The conc. HCl (5 mL) was added slowly to the reaction mass. The reaction mass was stirred at 50–60°C for 2–3 h. After completion of the reaction as per TLC, the reaction mass was cooled to 20–30°C, stirred for 30 min, filtered, and washed with ethanol (12 mL). The wet solid was dried in a hot air oven for 6–8 h at 50°C. The compound **7** was obtained as off-white solid, 10.6 g. Yield: 90.0%; mp: 174.5–176.2°C; FT-IR (KBr) υ_{max}: 1558 (C═N), 1454, 1055 (C–N), 1026 (S═O) 698 (C–S); ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 3.85 (s, 3H, *N*–CH_3), 4.54 (d, 1H, –SCH_2–, *J* = 12.8 Hz), 4.68 (d, 1H, –SCH2–, *J* = 12.8 Hz), 7.31–7.34 (m, 2H, Ar–H), 7.37–7.39 (m, 3H, Ar–H), 10.8 (brs, 2H, NH and HCl); ^{13}C NMR (100 MHz, δ ppm): 38.55, 61.00, 128.46, 128.66, 128.74, 130.87, 163.07, 168.39; ESI–MS: *m/z* 254.0 $[M + H–HCl]^+$.

5-(Benzylsulfinyl)-1,3,4-thiadiazol-2-amine (9). A mixture of 2-amino-5-benzylmercapto-1,3,4-thiadiazole **3** (15 g, 67.17 mmol) in a mixture of water–acetic acid (1:5 ratio, 90 mL) was taken in a three-necked RB flask at 20–30°C. The reaction mass was cooled to 5–15°C and chlorine gas (12 g) [Note: The required quantity of chlorine gas was generated in situ by slow addition of conc. HCl (60 mL) to $KMnO_4$ (35.0 g)]. The whole

reaction mass was stirred for 2–3 h at the same temperature. After completion of the reaction as per TLC, water (150 mL) was added at 5–15°C and stirred for 30 min at the same temperature. The reaction mass was filtered and washed with water (30 mL) and the wet solid was dried in a hot air oven for 6–8 h at 50–55°C. The compound **9** was obtained as off-white solid, 13.0 g. Yield: 80.5%; mp: 146.2–147.9°C; FT-IR (KBr) υ_{max}: 1633 (C═N), 1500 (C═C), 1049 (C–N), 1039 (S═O), 694 (C–S); ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 4.45 (d, 1H, –SCH_2–, J = 12.8 Hz), 4.53 (d, 1H, –SCH_2–, J = 12.8 Hz), 7.23–7.26 (m, 2H, Ar–H), 7.33–7.35 (m, 3H, Ar–H), 7.80 (s, 2H, –NH_2); ^{13}C NMR (100 MHz, δ ppm): 60.91, 128.28 (d), 129.53, 130.53, 161.89 171.60; ESI–MS: m/z 240.03 $[M + H]^+$.

General experimental procedure for the synthesis of compounds 1a–j. A mixture of 5-(benzylsulfinyl)-3-methyl-1,3,4-thiadiazol-2(3*H*)-imine hydrochloride (**7**) (500 mg, 1.72 mmol), Et_3N (0.36 mL, 2.58 mmol), and compound **8a** (1.89 mmol) in THF (10 mL) was taken at 20–30°C. The temperature of the reaction mass was raised to 60–65°C and stirred at the same temperature for 3–5 h. After completion of the reaction as per TLC, the reaction mass was cooled to 20–30°C. The reaction mass was filtered and washed with THF (2 mL). The filtrate was collected and concentrated under vacuum at <50°C. The obtained crude was purified by column chromatography over silica gel using mixture of n-hexane-ethyl acetate (3:7 ratio). The pure compound **1a–j** was obtained as off-white solid. The obtained results were presented in Table 1. The same experimental procedure for both experimental and purification was adopted for the preparation of all other compounds (**1b–j**). The newly synthesized molecules (**1a–j**) gave satisfactory spectroscopic data in accordance with their proposed structures.

1-(5-(Benzylsulfinyl)-3-methyl-1,3,4-thiadiazol-2(3H)-ylidene)-3-phenylthiourea (1a). Off-white powder; yield: 75%; mp: 144.6–147.7°C; FT-IR (KBr) υ_{max}: 1593 (C═N), 1552 (C═S), 1440, 1180 (C–N), 1076 (S═O), 904, 754 (C–S); ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 3.86 & 3.95 (s, 3H, N–CH_3, Tautomers), 4.56 (d, 1H, –SCH_2–, J = 12.8 Hz), 4.62 (d, 1H, –SCH_2–, J = 13.2 Hz), 7.11–7.12 (m,1H, Ar–H), 7.28–7.36 (m, 7H, Ar–H), 7.62–7.64 (m, 1H, Ar–H), 7.76 (s, 1H, Ar–H), 10.87 (s, 1H, NH); ^{13}C NMR (100 MHz, δ ppm): 38.39, 60.82, 122.30, 122.86, 1213.98, 124.90, 128.40, 128.48, 128.60, 129.15, 130.66, 139.25, 139.49, 159.0, 159.96, 164.52, 167.00, 183.95, 185.08; ESI–MS: m/z 389.14 $[M + H]^+$; HRMS (EI): calcd for $C_{17}H_{16}N_4OS_3$: 388.0486, found: 388.0483.

1-(5-(Benzylsulfinyl)-3-methyl-1,3,4-thiadiazol-2(3H)-ylidene)-3-(4-fluorophenyl)-thiourea (1b). Off-white powder; yield: 92%; mp: 166.3–168.4°C; FT-IR (KBr) υ_{max}: 1680 (C═N), 1602 (C═S), 1490, 1213 (C–N), 1083 (S═O), 810 (C–S); ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 3.84 &3.93 (s, 3H, N–CH_3 Tautomers), 4.56 (d, 1H, –SCH_2–, J = 12.8 Hz), 4.60 (d, 1H, –SCH_2–, J = 13.2 Hz), 7.18–7.20 (m, 2H, Ar–H), 7.29–7.30 (m, 5H, Ar–H), 7.62–7.74 (m, 2H, Ar–H), 10.88, 11.03 (s, 1H, NH); ^{13}C NMR (100 MHz, δ ppm): 38.38, 60.84, 115.02 (d, J = 22.0 Hz), 124.24 (d, J = 8.0 Hz), 125.08, 128.54, 129.11, 130.66, 135.75, 159.08, 159.87, 164.7, 167.0, 184.66; ESI–MS: m/z 407.11 $[M + H]^+$; HRMS (EI): calcd for $C_{17}H_{15}FN_4OS_3$:406.0392, found: 406.0390.

1-(5-(Benzylsulfinyl)-3-methyl-1,3,4-thiadiazol-2(3H)-ylidene)-3-(4-chlorophenyl)-thiourea (1c). Off-white powder; yield: 78%; mp: 170.7–172.5°C; FT-IR (KBr) υ_{max}: 1514 (C═N), 1489 (C═S), 1406, 1328, 1290 (C–N), 1047 (S═O), 827 (C–S); ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 3.88 & 3.93 (s, 3H, N–CH_3 Tautomers), 4.56 (d, 1H, –SCH_2–, J = 12.8 Hz), 4.62 (d, 1H, –SCH_2–, J = 12.8 Hz), 7.29–7.41 (m, 7H, Ar–H), 7.66–7.67 (d, 2H, Ar–H), 10.94 (d, 1H, NH); ^{13}C NMR (100 MHz, δ ppm): 38.48, 60.83, 123.77, 124.61, 128.31, 128.48, 128.60, 129.12, 130.66, 160.16, 164.73, 167.17, 184.01 184.66; ESI–MS: m/z 423.01 $[M + H]^+$; HRMS (EI): calcd for $C_{17}H_{15}ClN_4OS_3$: 422.0097, found: 422.0093.

1-(5-(Benzylsulfinyl)-3-methyl-1,3,4-thiadiazol-2(3H)-ylidene)-3-(4-nitrophenyl)-thiourea (1d). Off-white powder; yield: 91%; mp: 178.8–179.5°C; FT-IR (KBr) υ_{max}: 1595 (C═N), 1498 (C═S), 1330,1226 (C–N), 1168 (S═O), 848 (C–S); ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 3.98 (s, 3H, N–CH_3), 4.57 (1H, d, –SCH_2–, J = 12.8 Hz), 4.65 (1H, d, –SCH_2–, J = 12.8 HZ), 7.30–7.36 (m, 5H, Ar–H), 8.04 (br, 2H, Ar–H), 8.25 (d, 2H, Ar–H, J = 8.8 Hz), 11.36 (s, 1H, NH); ^{13}C NMR (100 MHz, δ ppm): 60.93, 121.22, 124.61, 128.55, 128.63, 129.05, 130.72, 142.29, 145.37, 160.46, 184.85; ESI–MS: m/z 434.12 $[M + H]^+$; HRMS (EI): calcd for $C_{17}H_{15}N_5O_3S_3$: 433.0337, found: 433.0334.

1-(5-(Benzylsulfinyl)-3-methyl-1,3,4-thiadiazol-2(3H)-ylidene)-3-ethylthiourea (1e). Off-white powder; yield: 72%; mp: 178.8–179.5°C; FT-IR (KBr) υ_{max}: 1602 (C═N), 1558 (C═S), 1498, 1286 (C–N), 1045 (S═O), 779 (C–S); ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 1.11–1.16 (m, 3H, –CH_3), 3.42–3.53 (m, 2H, –CH_2), 3.81 and 3.85 (s, 3H, N–CH_3 Tautomers), 4.54 (1H, d, –SCH_2–, J = 13.2 Hz), 4.58 (1H, d, –SCH_2–, J = 13.2 Hz), 7.28–7.36 (m, 5H, Ar–H), 9.04–9.24 (dt, 1H, NH, J = 5.6 Hz); ^{13}C NMR (100 MHz, δ ppm): 13.52, 14.46, 37.86, 38.01, 38.01, 38.29, 60.68, 60.78, 128.44, 128.59, 129.23, 129.26, 130.59, 130.62, 157.91, 159.27, 163.67, 165.79, 184.57, 186.22; ESI–MS: m/z 379.11 $[M + H + K]^+$; HRMS (EI): calcd for $C_{13}H_{16}N_4OS_3$: 340.0486, found: 340.0483.

1-(5-(Benzylsulfinyl)-3-methyl-1,3,4-thiadiazol-2(3H)-ylidene)-3-(4-methyl cyclohexyl) urea (1f). Off-white powder; yield: 75%; mp: 114.5–116.2°C; FT-IR (KBr)

υ_{max}: 1546 (C═O), 1510 (C═N), 1219 (C–N), 1058 (S═O); ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 0.86 (d, 3H, CH_3, J = 6.4 Hz), 0.096–1.01 (m, 2H, CH_2), 1.19–1.29 (m, 3H, CH_2, CH), 1.66 (d, 2H, CH_2, J = 11.6 H_Z), 1.76 (d, 2H, CH_2, J = 10.8 H_Z), 3.37–3.44 (m, 1H, *N*–CH), 3.71 & 3.76 (s, 3H, *N*–CH_3 Tautomers), 4.52 (s, 2H, CH_2), 7.28 (t, 2H, Ar–H, J = 3.6 Hz), 7.34–7.36 (m, 3H, Ar–H), 7.49 (s, 1H, NH); ^{13}C NMR (100 MHz, δ ppm): 22.25, 31.48, 32.41, 32.44, 37.30, 49.09, 60.60, 128.43, 128.57, 129.14, 130.56, 159.67, 160.30, 162.32; ESI–MS: *m/z* 393.26 $[M + H]^+$; HRMS (EI): calcd for $C_{18}H_{24}N_4O_2S_2$: 392.1341, found: 392.1338.

1-(5-(Benzylsulfinyl)-3-methyl-1,3,4-thiadiazol-2(3H)-ylidene)-3-phenethylurea (1g). Off-white powder; yield: 78%; mp: 135.3–136.5°C; FT-IR (KBr) υ_{max}: 1629 (C═O), 1562 (C═N), 1492, 1211 (C–N), 1139 (S═O), 777(C–S); ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 2.75–2.79 (m, 2H, CH_2) 3.32–3.37 (m, 2H, CH_2), 3.72 (s, 3H, *N*–CH_3), 4.52 (1H, d, –SCH_2–, J = 12.8 Hz), 4.58 (1H, d, –SCH_2–, J = 12.8 Hz), 7.18–7.23 (m, 3H, Ar–H), 7.28–7.31 (m, 4H, Ar–H), 7.35–7.36 (m, 3H, Ar–H), 7.67–7.70 (m, 1H, Ar–H); ^{13}C NMR (100 MHz, δ ppm): 35.31, 37.30, 41.59, 60.60, 126.02, 128.30, 128.42, 128.57, 129.13, 130.54, 139.46, 159.79, 161.18, 162.5; ESI–MS: *m/z* 401.23 $[M + H]^+$; HRMS (EI): calcd for $C_{19}H_{20}N_4O_2S_2$: 400.1028, found: 400.1026.

1-(5-(Benzylsulfinyl)-3-methyl-1,3,4-thiadiazol-2(3H)-ylidene)-3-(4-chloro-3-(trifluoro methyl)phenyl)urea (1h). Off-white powder; yield: 85%; mp: 215.2–216.6°C, FT-IR (KBr) υ_{max}: 1645 (C═O), 1517 (C═N), 1421,1298 (C–N), 1126 (S═O), 769 (C–S); ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 3.85 (s, 3H, *N*–CH_3), 4.56 (d, 1H, –SCH_2–, J = 12.8 Hz), 4.61 (d, 1H, –SCH_2–, J = 12.8 Hz), 7.28–7.31 (m, 5H, Ar–H), 7.35–7.37 (m, 1H, Ar–H), 7.63–7.89 (m, 1H, Ar–H), 8.28 (s, 1H, Ar–H), 10.38 (s,1H, –NH); ^{13}C NMR (100 MHz, δ ppm): 37.79, 60.72, 122.79, 123.07, 128.51, 128.61, 129.0, 130.63, 132.03, 139.55, 159.66; ESI–MS: *m/z* 475.15 $[M + H]^+$; HRMS (EI): calcd for $C_{18}H_{14}ClF_3N_4O_2S_2$: 474.0199, found: 474.0197.

1-(5-(Benzylsulfinyl)-3-methyl-1,3,4-thiadiazol-2(3H)-ylidene)-3-(4-fluorophenyl)urea (1i). Off-white powder, yield: 88%; mp: 207.2–208.8°C, FT-IR (KBr) υ_{max}: 1639 (C═O), 1502 (C═N), 1406, 1207 (C–N), 1035 (S═O), 835 (C–S); ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 3.83 (s, 3H, *N*–CH_3), 4.55 (d, 1H, –SCH_2–, J = 12.8 Hz), 4.60 (d, 1H, –SCH_2–, J = 12.8 Hz), 7.10–7.15 (t, 2H, Ar–H), 7.28–7.39 (m, 5H, Ar–H), 7.66–7.69 (m, 2H, Ar–H), 9.98 (s, 1H, NH); ^{13}C NMR (100 MHz, δ ppm): 37.63, 60.73, 115.33 (d, J = 22.0 Hz), 119.98 (d, J = 7.0 Hz), 128.7, 129.04, 130.60, 136.25, 156.42, 158.79, 160.76; ESI–MS: *m/z* 391.09 $[M + H]^+$; HRMS (EI): calcd for $C_{17}H_{15}FN_4O_2S_2$: 390.0620, found: 390.0618.

1-(5-(Benzylsulfinyl)-3-methyl-1,3,4-thiadiazol-2(3H)-ylidene)-3-(4-chlorophenyl) urea (1j). Off-white powder; yield: 76%; mp: 202.0–203.8°C; FT-IR (KBr) υ_{max}: 1645 (C═O), 1597 (C═N), 1483, 1307 (C–N), 1033 (S═O), 698 (C–S); ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 3.84 (s, 3H, *N*–CH_3), 4.55 (d, 1H, –SCH_2–, J = 12.8 Hz), 4.60 (d, 1H, –SCH_2–, J = 12.8 Hz), 7.03–7.05 (dd, 1H, Ar–H), 7.28–7.38 (m, 6H, Ar–H), 7.55–7.57 (d, 1H, Ar–H), 7.84 (s, 1H, Ar–H), 10.13 (s, 1H, NH); ^{13}C NMR (100 MHz, δ ppm): 37.71, 60.73, 116.85, 121.94, 128.47, 129.0, 130.30, 130.60, 133.06, 141.46, 159.51, 161.04, 164.03; ESI–MS: *m/z* 407.09 $[M + H]^+$; HRMS (EI): calcd for $C_{17}H_{15}ClN_4O_2S_2$:406.0325, found: 406.0322.

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CONFLICT OF INTEREST

The author declared no conflict of interest.

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