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MEDICINAL CHEMISTRY RESEARCH

ORIGINAL RESEARCH

Simple and efficient synthetic routes to bioactive s-triazinyl dithiocarbamate derivatives

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Abstract Series of 2,4-diarylamino-6-[N-(3′-methylphenyl)dithiocarbamoyl]-s-triazines **(4a–l)** and 2,4-bis[N-(3′-methylphenyl)dithiocarbamoyl]-6-arylamino-s-triazines **(7a–l)** were synthesized by two different synthetic routes. In the first route **(A)**, 2,4,6-tricholoro-s-triazine **(1)** was condensed with N-(3-methylphenyl)ammoniumdithiocarbamate to afford compounds **3** or **6**, which on reaction with different aryl amines afforded compounds **4a–l** or **7a–l**. In the second route **(B)**, condensation of **1** with different aryl amines yielded compounds **2a–l** or **5a–l**. On further treatment with N-(3-methylphenyl)ammoniumdithiocarbamate these afforded compounds **4a–l** or **7a–l**. The newly synthesized compounds **4a–l** and **7a–l** were characterized by elemental analyses, infrared (IR), and ^{1}H nuclear magnetic resonance (NMR) spectroscopic investigation. All the products were evaluated for their antibacterial and antifungal activity.

Keywords s-Triazinyl dithiocarbamates · Antibacterial activity · Antifungal activity

Introduction

In the family of heterocyclic compounds, nitrogen-containing heterocycles with sulfur atoms are an important class of compounds in medicinal chemistry. Dithiocarbamates and congeners have shown diverse biological activities as antibacterial (Chauhan *et al.*, 1987), antitubercular (Tiwari *et al.*, 1979), diuretic (Korablav *et al.*, 1977) and antihypertensive (Husain *et al.*, 1974) agents. The chemistry of nitrogen–sulfur heteroatoms, containing the s-triazines nucleus, is presently a popular area of research. The s-triazine derivatives are found to posses

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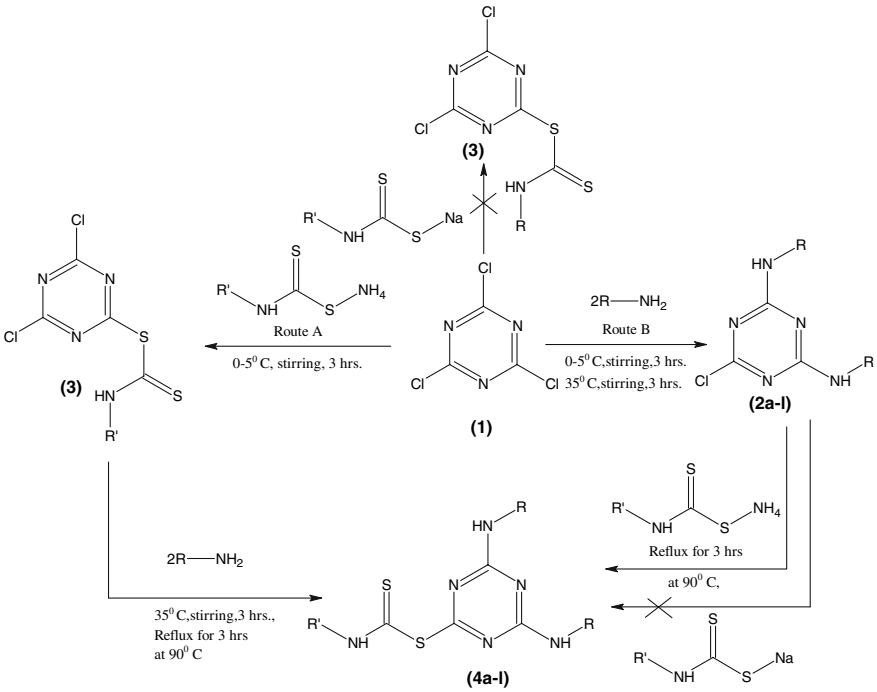
biological activities including antitubercular (Dabhi *et al.*, 1992), antitumor (Brzozowski *et al.*, 2000), anticancer (Sanders *et al.*, 1985) , sedative (Tobe *et al.*, 1976), anti-inflammatory (Kambayashi *et al.*, 1975; Saxena *et al.*, 1994) and anthelmintic (Chauhan *et al.*, 1994) . Compounds combining s-triazines and N-(3-methylphenyl)ammoniumdithiocarbamates are expected to possess pharmacological properties.

A slight variation in the substitution pattern of the s-triazine nucleus causes a marked difference in activities and may give rise to better medicines. Recent literature surveys reveals no single method for the synthesis of 2,4-diarylamino-6-[N-(3′-methylphenyl)dithiocarbamoyl]-s-triazines **(4a–l)** and 2,4-bis-[N-(3′-methylphenyl)-dithiocarbamoyl]-6-arylamino-s-triazines **(7a–l).** We report a simple and facile synthetic route for the condensation of 2,4,6-trichloro-s-triazine **(1)** with N-(3-methylphenyl)ammoniumdithiocarbamate. Compounds **4a–l** and **7a–l** were evaluated for antibacterial and antifungal activity.

Chemistry

The synthesis of 2,4-diarylamino-6-[N-(3′-methylphenyl)dithiocarbamoyl]-s-triazines **(4a–l)** and 2,4-bis-[N-(3′-methylphenyl)dithiocarbamoyl]-6-arylamino-s-triazines **(7a–l)** can be achieved by two synthetic routes. In the first route **(A)**, condensation of 2,4,6-trichloro-s-triazine **(1)** with 1 and 2 moles of N-(3-methylphenyl)ammoniumdithiocarbamate afforded compounds **3** and **6,** respectively, which, on treatment with 2 and 1 moles of different aromatic amines furnished the title compounds **4a–l** and **7a–l**, respectively**.** In the second route **(B)**, 2,4,6-trichloro-s-triazine **(1)** was condensed with 2 and 1 moles of different aromatic amines to give compounds **2a–l** and **5a–l**, respectively, which on reaction with 1 and 2 moles of N-(3-methylphenyl)ammoniumdithiocarbamate furnished compounds **4a–l** and **7a–l**, respectively Scheme 1.

In another experiment, the authors also tried N-(3-methylphenyl)sodiumdithiocarbamate instead of N-(3-methylphenyl)ammoniumdithiocarbamate in both the routes. However, use of N-(3-methylphenyl)sodiumdithiocarbamate could not furnish the title compounds **(4a–l** and **7a–l).** The failure of using the sodium salt can be attributed to the low ionization potential of the sodium ion of the salt N-(3-methylphenyl)sodiumdithiocarbamate, which makes it to act as a strong Lewis acid, whereas all three chlorine atoms of **1** are highly electronegative, i.e., strong Lewis bases. According to the Lewis acid–base theory, every strong Lewis acid (electrophile) has a counterpart weak Lewis base (nucleophile) and vice versa. Thus, the sodium ion, being a strong electrophile. does not easily react with the strong nucleophile chloride ion. Thus, condensation of N-(3-methylphenyl)sodiumdithiocarbamate with **2a–l** or **3** and **5a–l** or **6** is not feasible by the removal of sodium chloride. On the other hand, the ammonium ion of the salt N-(3-methylphenyl)ammoniumdithiocarbamate can act as a counterpart weak Lewis acid (electrophile) to the three chlorine atoms (strong nucleophile) of compound **1**, which results in successive removal of ammonium chloride to furnish the desired compounds Scheme 2.



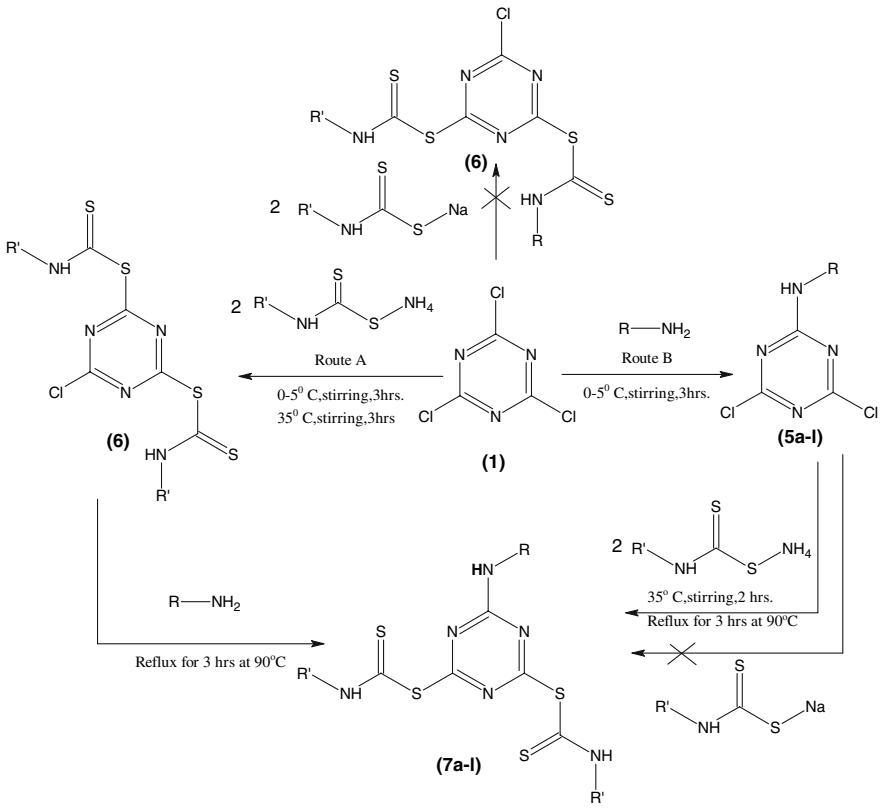
Scheme 1

Structure–Activity Relationship (SAR)

Antimicrobial activity

Preliminary antimicrobial testing has been carried out by the cup–plate method (Barry, 1976). The antimicrobial activity was carried out against three bacterial strains, *E. coli*, *B. subtilis*, and *S. pyogens*, and a fungal strain, *A. niger*. The reference drugs used for the comparison purpose were Ampicillin, Chloramphenicol, Norfloxacin and Griseofulvin. The activity of the samples and the reference drugs was assayed under identical conditions at 50 mg concentration in dimethyl sulfoxide (DMSO) as the control. Appropriate nutrient media were prepared and poured in to a sterile Petri dish of diameter 90 mm, under sterile conditions. After solidification of the media, test organisms from standard culture inoculum were swabbed all over the surface using a sterile cotton swab. Wells were prepared on the agar surface by a sterile cork borer of internal diameter 6 mm. With the help of a micropipette, the test compounds were loaded into the well and left to stand to allow the solution to diffuse totally in the medium. Plates were incubated at 37°C for 24 h and the zones of inhibition were measured in millimeters (Table 3).

Among the series of synthesized s-triazinyl derivatives, compounds **4e**, **4f**, and **4i** showed moderate antibacterial activity against *B. subtillis*, while compounds **7d** and **7f** exhibited comparatively very good antibacterial activity against *B. subtillis*,



Scheme 2

which may be due to the presence of 2-methylphenyl and 4-methylphenyl groups as the substituent R′. The wide-spectrum antibacterial activity of compound **7b** against *S. pyogens* and *E. coli* might be due to the presence of 4-chlorophenyl group. Further, compounds **4f** and **7c** were moderately active against *E. coli*. Looking at the antifungal activity results, compounds **4d**, **4e**, **4g**, **7f**, and **7i** exhibited excellent antifungal activity against *A. niger* as compared to the standard drug Griseofulvin, which led to the SAR conclusion that the presence of 2-methylphenyl, 4-methylphenyl, and 2-methoxyphenyl substituents greatly increase the antifungal activity in the compounds **4a–l**, and that the presence of 4-methylphenyl and 2-nitrophneyl substituents leads to better antifungal activity in the compounds **7a–l**.

Experimental

All the melting points were determined routinely in open capillaries and are uncorrected. The melting points are recorded in degrees Celsius. Formation and purity of the compounds was routinely checked by thin-layer chromatography (TLC) using silica gel-G and spots were located by iodine. ^{1}H NMR spectra were

recorded in $CDCl_3$ on a Brucker DRX-300 at 300 MHz using tetramethyl silane (TMS) as internal standard.

Route A: compounds **4a–l**

*Preparation of 2,4-dichloro-6-[N-(3′-methylphenyl)dithiocarbamoyl]-s-triazines (**3**)*

An equimolar mixture of 2,4,6-trichloro-s-triazine **(1)** and N-(3-methylphenyl)ammoniumdithiocarbamate in dry acetone was stirred at 0°C for 3 h. The content was poured onto crushed ice. The solid obtained was filtered, dried and recrystallized from 95% ethyl alcohol.

*Preparation of 2,4-di-(phenyl)amino-6-[N-(3-methylphenyl)dithiocarbamoyl]-s-triazines (**4a**)*

A mixture of 2,4-dichloro-6-[N-(3-methylphenyl)dithiocarbamoyl]-s-triazine **(3)** (0.01 mole) and aniline (0.02 mole) in dioxane (50 ml) was stirred at 35°C for 3 h. and then the mixture was refluxed for 3 h at 85–90°C. The content was poured onto crushed ice. The solid obtained was filtered, dried, and recrystallized from 95% ethyl alcohol.

Similarly, the other compounds **(4a–l)** were prepared as mentioned above. The physical data are shown in Table 2.

Route B: compounds **4a–l**

*Preparation of 2,4-di-(phenyl)-amino-6-chloro-s-triazine (**2a**)*

A mixture of 2,4,6-trichloro-s-triazine **(1)** (0.01 mole) and aniline (0.02 mole) in dry acetone (50 ml) was stirred at 0°C for 3 h and the content was further stirred for 3 h at 35°C. The content was poured onto crushed ice. The solid obtained was filtered, dried, and recrystallized from 95% ethyl alcohol.

Similarly, the other compounds **(2a–l)** were prepared as mentioned above. The physical data are shown in Table 1.

*Preparation of 2,4-di-(phenyl)-amino-6-[N-(3-methylphenyl)dithiocarbamoyl]-s-triazines (**4a**)*

An equimolar mixture of 2,4-di(phenyl)amino-6-chloro-s-triazine **(2a)** and N-(3-methylphenyl)ammoniumdithiocarbamate in dioxane (50 ml) was refluxed on water bath at 90°C for 3 h. The content was poured onto crushed ice. The solid obtained was filtered, dried, and recrystallized from 95% ethyl alcohol.

Similarly, other the compounds **(4a–l)** were prepared as mentioned above. The physical data are shown in Table 2, Table 3, Table 4.

Table 1 Physical data of compounds **2a–l** and **5a–l**

Compound	R	Molecular formula	M.P. (°C)	Yield (%)
2a	Phenyl	$C_{15}H_{12}ClN_5$	197	93
2b	4-Chlorophenyl	$C_{15}H_{10}Cl_3N_5$	222	90
2c	4-Ethoxyphenyl	$C_{19}H_{20}ClN_5O_2$	167	93
2d	2-Methylphenyl	$C_{17}H_{16}ClN_5$	164	90
2e	3-Methylphenyl	$C_{17}H_{16}ClN_5$	143	85
2f	4-Methylphenyl	$C_{17}H_{16}ClN_5$	198	80
2g	2-Methoxyphenyl	$C_{17}H_{16}ClN_5O_2$	201	80
2h	4-Methoxyphenyl	$C_{17}H_{16}ClN_5O_2$	200	83
2i	2-Nitrophenyl	$C_{15}H_{10}ClN_7O_4$	229	85
2j	4-Nitrophenyl	$C_{15}H_{10}ClN_7O_4$	303	86
2k	Morpholinyl	$C_{11}H_{16}ClN_5O_2$	203	90
2l	Diethenoyl	$C_{11}H_{20}ClN_5O_4$	155	91
5a	Phenyl	$C_9H_6Cl_2N_4$	196	83
5b	4-Chlorophenyl	$C_9H_5Cl_3N_4$	320	90
5c	4-Ethoxyphenyl	$C_{11}H_{10}Cl_2N_4O$	182	91
5d	2-Methylphenyl	$C_{10}H_8Cl_2N_4$	155	81
5e	3-Methylphenyl	$C_{10}H_8Cl_2N_4$	125	82
5f	4-Methylphenyl	$C_{10}H_8Cl_2N_4$	135	85
5g	2-Methoxyphenyl	$C_{10}H_8Cl_2N_4O$	175	84
5h	4-Methoxyphenyl	$C_{10}H_8Cl_2N_4O$	160	81
5i	2-Nitrophenyl	$C_9H_5Cl_2N_5O_2$	320	80
5j	4-Nitrophenyl	$C_9H_5Cl_2N_5O_2$	300	80
5k	Morpholinyl	$C_7H_8Cl_2N_4O$	255	90
5l	Diethenoyl	$C_7H_{10}Cl_2N_4O_2$	200	89

Route A: compounds **7a–l**

*Preparation of 2,4-bis-[N-(3′-methylphenyl)dithiocarbamoyl]-6-chloro-s-triazines (**6**)*

A mixture of 2,4,6-trichloro-s-triazine **(1)** (0.01 mole) and N-(3-methylphenyl) ammoniumdithiocarbamate (0.02 mole) in dioxane (50 ml) was stirred at 0°C for 3 h and then the content further stirred for 3 h at 35°C. The content was poured onto crushed ice. The solid obtained was filtered, dried, and recrystallized from 95% ethyl alcohol.

*Preparation of 2,4-bis-[N-(3′-methylphenyl)dithiocarbamoyl]-6-(phenyl)amino-s-triazines (**7a**)*

An equimolar mixture of 2,4-bis-[N-(3′-methylphenyl)dithiocarbamoyl]-6-chloro-s-triazine **(6)** and aniline in dioxane (50ml) was refluxed on water bath at 90°C for 3 h. The content was cooled and poured onto crushed ice. The solid obtained was filtered, dried, and recrystallized from 95% ethyl alcohol.

Table 2 Physical data of compounds **4a–l** and **7a–I**

No.	R	R′	Molecular formula	M.P. (°C)	Yield (%)
4a	3-Methylphenyl	Phenyl	$C_{23}H_{20}N_6S_2$	135	58
4b	3-Methylphenyl	4-Chlorophenyl	$C_{23}H_{18}N_6S_2Cl_2$	130	59
4c	3-Methylphenyl	4-Ethoxyphenyl	$C_{27}H_{28}O_2N_6S_2$	185	64
4d	3-Methylphenyl	2-Methylphenyl	$C_{25}H_{24}N_6S_2$	128	53
4e	3-Methylphenyl	3-Methylphenyl	$C_{25}H_{24}N_6S_2$	112	65
4f	3-Methylphenyl	4-Methylphenyl	$C_{25}H_{24}N_6S_2$	128	67
4g	3-Methylphenyl	2-Methoxyphenyl	$C_{24}H_{24}O_2N_6S_2$	111	49
4h	3-Methylphenyl	4-Methoxyphenyl	$C_{24}H_{24}O_2N_6S_2$	93	61
4i	3-Methylphenyl	2-Nitrophenyl	$C_{23}H_{18}O_4N_8S_2$	82	67
4j	3-Methylphenyl	4-Nitrophenyl	$C_{23}H_{18}O_4N_8S_2$	116	57
4k	3-Methylphenyl	Morpholinyl	$C_{22}H_{25}ON_7S_2$	133	56
4l	3-Methylphenyl	Diethanoyl	$C_{22}H_{26}N_6S_2$	160	60
7a	3-Methylphenyl	Phenyl	$C_{25}H_{22}N_6S_4$	260	63
7b	3-Methylphenyl	4-Chlorophenyl	$C_{25}H_{21}N_6S_4Cl$	170	60
7c	3-Methylphenyl	4-Ethoxyphenyl	$C_{27}H_{26}ON_6S_4$	122	59
7d	3-Methylphenyl	2-Methylphenyl	$C_{26}H_{24}N_6S_4$	101	51
7e	3-Methylphenyl	3-Methylphenyl	$C_{26}H_{24}N_6S_4$	135	57
7f	3-Methylphenyl	4-Methylphenyl	$C_{26}H_{24}N_6S_4$	280	52
7g	3-Methylphenyl	2-Methoxyphenyl	$C_{26}H_{24}ON_6S_4$	132	57
7h	3-Methylphenyl	4-Methoxyphenyl	$C_{26}H_{24}ON_6S_4$	99	51
7i	3-Methylphenyl	2-Nitrophenyl	$C_{25}H_{21}O_2N_7S_6$	131	59
7j	3-Methylphenyl	4-Nitrophenyl	$C_{25}H_{21}O_2N_7S_6$	140	58
7k	3-Methylphenyl	Morpholinyl	$C_{20}H_{26}O_2N_8S_4$	109	61
7l	3-Methylphenyl	Diethanoyl	$C_{20}H_{28}N_6S_4$	116	62

Similarly, the other compounds **(7a–l)** were prepared as above. The physical data are shown in Table 2.

Route B: compounds **7a–l**

*Preparation of 2,4-dichloro-6-(4′-methoxyphenyl)amino-s-triazine (**5a**)*

An equimolar mixture of 2,4,6-trichloro-s-triazine **(1)** and aniline in dry acetone (50 ml) was stirred at 0°C for 3 h. The content was cooled and poured onto crushed ice. The solid obtained was filtered, dried, and recrystallized from 95% ethyl alcohol.

*Preparation of 2,4-bis-[N-(3′-methylphenyl)dithiocarbamoyl]-6-(4′-methoxy phenyl)amino-s-triazines (**7a**)*

A mixture of 2,4-dichloro-6-(4′-methoxyphenyl)amino-6-s-triazine **(5a)** (0.01 mole) and N-(phenyl)ammoniumdithiocarbamate (0.02 mole) in dioxane (50 ml) was

Table 3 Antimicrobial activity of compounds **4a–l** and **7a–I**

No.	R	R′	Zones of inhibition (mm)			
			B. subtilis	*S. pyogens*	*E. coli*	*A.niger*
4a	3-methylphenyl	Phenyl	12	15	13	17
4b	3-Methylphenyl	4-chlorophneyl	12	13	15	16
4c	3-Methylphenyl	4-Ethoxyphenyl	13	13	14	18
4d	3-Methylphenyl	2-Methylphenyl	12	11	12	23
4e	3-Methylphenyl	3-Methylphenyl	14	12	15	20
4f	3-Methylphenyl	4-Methylphenyl	15	15	19	14
4g	3-Methylphenyl	2-Methoxyphenyl	14	14	13	18
4h	3-Methylphenyl	4-Methoxyphenyl	12	15	12	17
4i	3-Methylphenyl	2-Nitrophenyl	15	14	15	16
4j	3-Methylphenyl	4-Nitrophenyl	13	15	13	17
4k	3-Methylphenyl	Morpholinyl	12	13	12	15
4l	3-Methylphenyl	Diethanoyl	12	11	11	14
7a	3-Methylphenyl	Phenyl	15	12	12	12
7b	3-Methylphenyl	4-Chlorophenyl	18	18	15	17
7c	3-Methylphenyl	4-Ethoxyphenyl	14	15	16	12
7d	3-Methylphenyl	2-Methylphenyl	19	12	12	13
7e	3-Methylphenyl	3-Methylphenyl	13	12	13	14
7f	3-Methylphenyl	4-Methylphenyl	19	13	13	20
7g	3-Methylphenyl	2-Methoxyphenyl	15	11	15	14
7h	3-Methylphenyl	4-Methoxyphenyl	15	14	15	15
7i	3-Methylphenyl	2-Nitrophenyl	14	13	17	19
7j	3-Methylphenyl	4-Nitrophenyl	16	17	15	16
7k	3-Methylphenyl	Morpholinyl	13	14	12	13
7l	3-Methylphenyl	Diethanoyl	12	12	12	13
DMSO			06	06	06	06
Ampicillin			22	26	24	–
Chloraphenicol			28	22	19	–
Norfloxacin			19	26	25	–
Griseofulvin			–	–	–	20

stirred for 2 h at 35°C and then the content was refluxed on water bath at 90°C for 3 h. The content was cooled and poured onto crushed ice. The solid obtained was filtered, dried, and recrystallized from 95% ethyl alcohol.

Similarly, the other compounds **(7a–l)** were prepared as above. The physical data are shown in Table 2.

Conclusion

This research addresses a novel class of potent, wide spectrum antimicrobial compounds. The parent s-triazine and bis-s-triazine derivatives have shown good

Table 4 IR and 1H NMR data of the compounds **4a–l** and **7a–I**

4a IR (KBr) ν cm^{-1}: 3357 (N–H str.), 3011 (C–H str., aromatic), 2963 (C–H str., asym.), 2919 (C–H str., CH_3), 2848 (C–H str., CH_3), 1568 (N–H, str. def.), 1324 (C–N str.), 810 (C_3N_3 str., s-triazinyl), 719 (C–S str.). Mass: 458 (M^+). ^{1}H NMR ($CDCl_3$) δ (ppm): 8.89 (s, 3H, NH), 6.74–7.58 (m, 14H, Ar–H), 1.26 (s, 3H, –CH_3). Anal. calcd. for $C_{24}H_{22}N_6S_2$: C 62.86, H 4.84, N 18.33, S 13.98%. Found: C 62.74, H 4.72, N 18.24, S 13.87%.

4b IR (KBr) ν cm^{-1}: 3351 (N–H str.), 3014 (C–H str., aromatic), 2969 (C–H str., asym.), 2919 (C–H str., CH_3), 2853 (C–H str., CH_3), 1572 (N–H, str. def.),1321 (C–N str.), 821 (C_3N_3 str., s-triazinyl), 756 (C–Cl str.), 716 (C–S str.). Mass: 493 (M^+). ^{1}H NMR ($CDCl_3$) δ (ppm): 8.76 (s, 3H, NH), 6.40–7.46 (m, 12H, Ar–H), 1.32 (s, 3H, CH_3). Anal. calcd. for $C_{24}H_{22}N_6S_2Cl$: C 58.46, H 4.29, N 17.05, S 13.01%. Found: C 58.33, H 4.18, N 16.98, S 12.89%.

4c IR (KBr) ν cm^{-1}: 3361 (N–H str.), 3012 (C–H str., aromatic), 2969 (C–H str., asym.), 2919 (C–H str., CH_3), 2851 (C–H str., CH_3), 1571 (N–H, str. def.),1322 (C–N str.), 1256 (Ar–O–C str.), 826 (C_3N_3 str., s-triazinyl), 723 (C–S str.) Mass: 502 (M^+). ^{1}H NMR ($CDCl_3$) δ (ppm): 8.79 (s, 3H, NH), 6.65–7.59 (m, 12H, Ar–H), 3.73 (s, 6H, OCH_3), 1.29 (s, 3H, CH_3). Anal. calcd. for $C_{26}H_{26}N_6OS_2$: C 62.13, H 5.21, N 16.72, S 12.76%. Found: C 62.04, H 5.12, N 16.60, S 12.64%.

4d IR (KBr) ν cm^{-1}: 3358 (N–H str.), 3013 (C–H str., aromatic), 2968 (C–H str., asym.), 2916 (C–H str., CH_3), 2850 (C–H str., CH_3), 1570 (N–H, str. def.),1326 (C–N str.), 818 (C_3N_3 str., s-triazinyl), 716 (C–S str.). Mass: 472 (M^+). ^{1}H NMR ($CDCl_3$) δ (ppm): 8.80 (s, 3H, NH), 6.69–7.49 (m, 12H, Ar–H), 1.34 (s, 9H, CH_3). Anal. calcd. for $C_{25}H_{24}N_6S_2$: C 63.53, H 5.12, N 17.78, S 13.57%. Found: C 63.42, H 5.03, N 17.64, S 13.49%.

4e IR (KBr) ν cm^{-1}: 3352 (N–H str.), 3009 (C–H str., aromatic), 2963 (C–H str., asym.), 2914 (C–H str., CH_3), 2849 (C–H str., CH_3), 1566 (N–H, str. def.),1328 (C–N str.), 812 (C_3N_3 str., s-triazinyl), 714 (C–S str.). Mass: 472 (M^+). ^{1}H NMR ($CDCl_3$) δ (ppm): 8.74 (s, 3H, NH), 6.66–7.45 (m, 12H, Ar–H), 1.30 (s, 9H, –CH_3). Anal. calcd. for $C_{25}H_{24}N_6S_2$: C 63.53, H 5.12, N 17.78, S 13.57%. Found: C 63.40, H 5.02, N 17.62, S 13.46%.

4f IR (KBr) ν cm^{-1}: 3357 (N–H str.), 3016 (C–H str. aromatic), 2972 (C–H str. asym.), 2919 (C–H str. CH_3), 2851 (C–H str. CH_3), 1577 (N–H, str. def.),1319 (C–N str.), 812 (C_3N_3 str., s-triazinyl), 719 (C–S str.). Mass: 472 (M^+). ^{1}H NMR ($CDCl_3$) δ (ppm): 8.14 (s, 2H, NH), 6.68–7.50 (m, 12H, Ar–H), 1.34 (s, 9H, –CH_3). Anal. calcd. for $C_{25}H_{24}N_6S_2$: C 63.53, H 5.12, N 17.78, S 13.57%. Found: C 63.42, H 5.01, N 17.62, S 13.45%.

4g IR (KBr) ν cm^{-1}: 3354 (N–H str.), 3008 (C–H str., aromatic), 2965 (C–H str., asym.), 2914 (C–H str., CH_3), 2847 (C–H str., CH_3), 1578 (N–H, str. def.),1314 (C–N str.), 1247 (Ar–O–C str.), 814 (C_3N_3 str., s-triazinyl), 710 (C–S str.). Mass: 488 (M^+). ^{1}H NMR ($CDCl_3$) δ (ppm): 8.89 (s, 2H, NH), 6.74–7.58 (m, 12H, Ar–H),3.84 (s, 6H, –OCH_3), 1.26 (s, 3H, –CH_3). Anal. calcd. for $C_{25}H_{24}N_6OS_2$: C 61.45, H 4.95, N 17.20, S 13.12%. Found: C 61.33, H 4.86, N 17.09, S 13.01%.

4h IR (KBr) ν cm^{-1}: 3352 (N–H str.), 3022 (C–H str., aromatic), 2960 (C–H str., asym.), 2912 (C–H str., CH_2) , 2850 (C–H str. CH_3), 1314 (C–N str.), 1582 (N–H, str. def.),1248 (Ar–O–C str.), 809 (C_3N_3 str., s-triazinyl), 711 (C–S str). Mass: 488 (M^+). ^{1}H NMR ($CDCl_3$) δppm: 8.90 (s, 2H, NH), 6.77–7.58 (m, 12H, Ar–H), 3.78 (s, 6H, –OCH_3), 1.19 (s, 3H, –CH_3). Anal. calcd. for $C_{25}H_{24}N_6OS_2$: C 61.45, H 4.95, N 17.20, S 13.12%. Found: C 61.35, H 4.84, N 17.07, S 13.01%.

4i IR (KBr) ν cm^1: 3349 (N–H str.), 3016 (C–H str., aromatic), 2951 (C–H str., asym.), 2916 (C–H str., CH_2) , 2849 (C–H str., CH_3), 1313 (C–N str.), 1579 (N–H, str. def.), 812 (C_3N_3 str., s-triazinyl), 710 (C–S str). Mass: 503 (M^+). ^{1}H NMR ($CDCl_3$) δ (ppm): 8.88 (s, 3H, NH), 7.07–8.11 (m, 12H, Ar–H), 1.27 (s, 3H, –CH_3). Anal. calcd. for $C_{24}H_{21}N_7O_2S_2$: C 57.24, H 4.20, N 19.47, S 12.73%. Found: C 57.16, H 4.11, N 19.34, S 12.61%.

4j IR (KBr) ν cm^{-1}: 3356 (N–H str.), 3021 (C–H str., aromatic), 2946 (C–H str., asym.), 2919 (C–H str., CH_2) , 2853 (C–H str., CH_3), 1321 (C–N str.), 1575 (N–H, str. def.), 816 (C_3N_3 str., s-triazinyl), 711 (C–S str). Mass: 503 (M^+). ^{1}H NMR ($CDCl_3$) δppm: 8.79 (s, 2H, NH), 7.01–8.16 (m, 12H, Ar–H), 1.23 (s, 3H, –CH_3). Anal. calcd. for $C_{24}H_{21}N_7O_2S_2$: C 57.24, H 4.20, N 19.47, S 12.73%. Found: C 57.12, H 4.09, N 19.35, S 12.62%.

Table 4 continued

4k IR (KBr) ν cm^{-1}: 3352 (N–H str.), 3022 (C–H str., aromatic), 2960 (C–H str., asym.), 2912 (C–H str., CH_2) , 2850 (C–H str., CH_3), 1314 (C–N str.), 1582 (N–H, str. def.), 809 (C_3N_3 str., s-triazinyl), 711 (C–S str). Mass: 467 (M^+). ^{1}H NMR ($CDCl_3$) δppm: 8.90 (s, 2H, –NH), 6.77–7.58 (m, 12H, Ar–H), 3.78 (s, 6H, –OCH_3), 1.19 (s, 3H, 'CH_3). 4.84 (t, 2H, –CH_2), 3.26–2.76 (d, 1H, –CH), 2.60–2.49 (t, 2H, –CH_2), 3.92–3.78 (t, 2H, –CH_2), 4.08 (s, 1H, –NH). Anal. calcd. for $C_{22}H_{25}N_7OS_2$: C 57.24, H 4.20, N 19.47, S 12.73%. Found: C 57.12, H 4.09, N 19.35, S 12.62%.

4l IR (KBr) ν cm^{-1}: 3352 (N–H str.), 3022 (C–H str., aromatic), 2960 (C–H str., asym.), 2912 (C–H str., CH_2) , 2850 (C–H str., CH_3), 1314 (C–N str.), 1582 (N–H, str. def.),1248 (Ar–O–C str.), 809 (C_3N_3 str. s-triazinyl), 711 (C–S str). Mass: 467 (M^+). ^{1}H NMR ($CDCl_3$) δ (ppm): 8.90 (s, 2H, NH), 6.77–7.58 (m, 12H, Ar–H), 3.78 (s, 6H, –OCH_3), 1.19 (s, 3H, –CH_3), 1.12 (t, 12H, –CH_3), 2.46 (q, 8H, –CH_2). Anal. calcd. for $C_{22}H_{26}N_6S_2$: C 56.51, H 5.39, N 20.97, S 13.71%. Found: C 56.40, H 5.27, N 20.82, S 13.62%.

7a IR (KBr) ν cm^{-1}: 3354 (N–H str.), 3013 (C–H str., aromatic), 2946 (C–H str., asym.), 2862 (C–H str., CH_3), 1564 (C=S str.), 1549 (N–H str., def.), 1511 (C=C str., aromatic), 1311 (C–N str.), 812 (C_3N_3 str., s-triazinyl), 714 (C–S str.). Mass: 520 (M^+). ^{1}H NMR ($CDCl_3$) δ (ppm): 8.79 (s, 3H, NH), 6.81–7.54 (m, 13H, Ar–H), 1.21 (s, 6H, –CH_3). Anal. calcd. for $C_{24}H_{20}N_6S_4$: C 55.36, H 3.87, N 16.14, S 24.63%. Found: C 55.24, H 3.76, N 16.03, S 24.52%.

7b IR (KBr) ν cm^{-1}: 3352 (N–H str.), 3012 (C–H str., aromatic), 2949 (C–H str., asym.), 2864 (C–H str., CH_3), 1562 (C=S str.), 1551 (N–H str., def.), 1508 (C=C str., aromatic), 1321 (C–N str.), 814 (C_3N_3 str., s-triazinyl), 754 (C–Cl str.), 716 (C–S str.). Mass: 589 (M^+). ^{1}H NMR ($CDCl_3$) δ (ppm): 8.76 (s, 3H, NH), 6.82–7.56 (m, 13H, Ar–H), 1.32 (s, 6H, –CH_3). Anal. calcd. for $C_{24}H_{18}N_6S_4Cl_2$: C 48.89, H 3.08, N 14.25, S 21.75%. Found: C 48.78, H 2.97, N 14.14, S 21.63%.

7c IR (KBr) ν cm^{-1}: 3356 (N–H str.), 3010 (C–H str., aromatic), 2951 (C–H str., asym.), 2862 (C–H str., CH_3), 1561 (C=S str.), 1552 (N–H str., def.), 1512 (C=C str., aromatic), 1311 (C–N str.), 1256 (Ar–O–C str.), 811 (C_3N_3 str., s-triazinyl), 719 (C–S str.). Mass: 608 (M^+). ^{1}H NMR ($CDCl_3$) δ (ppm): 8.77 (s, 3H, NH), 6.80–7.54 (m, 12H, Ar–H), 3.98 (q, 2H, –OCH_2), 1.32 (t, 3H, CH_3), 1.19 (s, 6H, –CH_3). Anal. calcd. for $C_{28}H_{28}N_6O_2S_4$: C 55.24, H 4.64, N 13.80, S 21.07%. Found: C 55.13, H 4.64, N 13.69, S 20.94%.

7d IR (KBr) ν cm^{-1}: 3355 (N–H str.), 3012 (C–H str., aromatic), 2946 (C–H str., asym.), 2862 (C–H str., CH_3), 1562 (C=S str.), 1551 (N–H str., def.), 1518 (C=C, str., aromatic), 1307 (C–N str.), 814 (C_3N_3 str., s–triazinyl), 714 (C–S str.). Mass: 548 (M^+). ^{1}H NMR ($CDCl_3$) δ (ppm): 8.76 (s, 3H, NH), 6.72–7.48 (m, 12H, Ar–H), 1.19 (s, 9H, –CH_3). Anal. calcd. for $C_{26}H_{24}N_6S_4$: C 56.91, H 4.41, N 15.31, S 23.37%. Found: C 56.78, H 4.30, N 15.21, S 23.26%.

7e IR (KBr) ν cm^{-1}: 3351 (N–H str.), 3011 (C–H str., aromatic), 2949 (C–H str., asym.), 2860 (C–H str., CH_3), 1564 (C=S str.), 1550 (N–H str., def.), 1516 (C=C, str., aromatic), 1309 (C–N str.), 811 (C_3N_3 str., s-triazinyl), 716 (C–S str.). Mass: 548 (M^+). ^{1}H NMR ($CDCl_3$) δ (ppm): 8.78 (s, 3H, NH), 6.79–7.56 (m, 12H, Ar–H), 1.23 (s, 9H, –CH_3). Anal. calcd. for $C_{26}H_{24}N_6S_4$: C 56.91, H 4.41, N 15.31, S 23.37%. Found: C 56.80, H 4.32, N 15.20, S 23.25%.

7f IR (KBr) ν cm^{-1}: 3356 (N–H str.), 3014 (C–H str., aromatic), 2948 (C–H str., asym.), 2859 (C–H str., CH_3), 1561 (C=S str.), 1554 (N–H str. def.), 1516 (C=C str., aromatic), 1310 (C–N str.), 816 (C_3N_3 str., s-triazinyl), 712 (C–S str.). Mass: 548 (M^+). ^{1}H NMR ($CDCl_3$) δ (ppm): 8.79 (s, 3H, NH), 6.69–7.51 (m, 12H, Ar–H), 1.21 (s, 9H, –CH_3). Anal. calcd. for $C_{26}H_{24}N_6S_4$: C 56.91, H 4.41, N 15.31, S 23.37%. Found: C 56.81, H 4.30, N 15.22, S 23.27%.

7g IR (KBr) ν cm^{-1}: 3359 (N–H str.), 3015 (C–H str., aromatic), 2950 (C–H str., asym.),2866 (C–H str., CH_3), 1568 (C=S str.), 1554 (N–H str., def.), 1508 (C=C str., aromatic.), 1309 (C–N str.), 1258 (Ar–O–C str.), 814 (C_3N_3 str., s-triazinyl),716 (C–S str.). Mass: 580 (M^+). ^{1}H NMR ($CDCl_3$) δ (ppm): 8.81 (s, 2H, NH), 6.78–7.51 (m, 12H, Ar–H), 3.80 (s, 3H, –OCH_3), 1.21 (s, 6H, –CH_3). Anal. calcd. for $C_{26}H_{24}N_6O_2S_4$: C 53.77, H 4.17, N 14.47, S 22.08%. Found: C 53.66, H 4.07, N 14.35, S 21.93%.

Table 4 continued

7h IR (KBr) ν cm^{-1}: 3320 (N–H str.), 3017 (C–H str., aromatic), 2945 (C–H str., asym.), 2865 (C–H str., CH_3), 1562 (C=S str.), 1564 (N–H str., def.), 1495 (C=C str., Aromatic),1305 (C–N str.), 1256 (Ar–O–C str.), 815 (C_3N_3 str., s-triazinyl), 712 (C–S str.). Mass: 580 (M^+). ^{1}H NMR (CDCl3) δ (ppm): 8.83 (s, 2H, NH), 6.68–7.45 (m, 12H, Ar–H), 3.81 (s, 3H, –OCH_3), 1.18 (s, 6H,–CH_3). Anal. calcd. for $C_{26}H_{24}N_6O_2S_4$: C 53.77, H 4.17, N 14.47, S 22.08%. Found: C 56.81, H 4.05, N 14.34, S 21.94%.

7i IR (KBr) ν cm^{-1}: 3356 (N–H str.), 3009 (C–H str., aromatic), 2953 (C–H str., asym.), 2861 (C–H str., CH_3), 1569 (C=S str.), 1553 (N–H str., def.), 1511 (C=C, str., aromatic.), 1310 (C–N str.), 812 (C_3N_3 str., s-triazinyl), 714 (C–S str.). Mass: 610 (M^+). ^{1}H NMR ($CDCl_3$) δ (ppm): 8.82 (s, 3H, NH), 6.93–7.54 (m, 12H, Ar–H), 1.29 (s, 6H, –CH_3). Anal. calcd. for $C_{264}H_{18}N_8O_4S_4$: C 47.20, H 2.97, N 18.35, S 21.00%. Found: C 47.06, H 2.83, N 18.24, S 20.88%.

7j IR (KBr) ν cm^{-1}: 3353 (N–H str.), 3012 (C–H str., aromatic), 2954 (C–H str., asym.), 2860 (C–H str., CH_3), 1563 (C=S str.), 1551 (N–H str., def.), 1513 (C=C str., aromatic.), 1314 (C–N str.), 814 (C_3N_3 str., s-triazinyl), 718 (C–S str.). Mass: 610 (M^+). ^{1}H NMR ($CDCl_3$) δ (ppm): 8.79 (s, 3H, NH), 6.98–7.60 (m, 12H, Ar–H), 1.26 (s, 6H, –CH_3). Anal. calcd. for $C_{24}H_{18}N_8O_4S_4$: C 47.20, H 2.97, N 18.35, S 21.00%. Found: C 47.08, H 2.85, N 18.21, S 20.86%.

7k IR (KBr) ν cm^{-1}: 3359 (N–H str.), 3015 (C–H str., aromatic), 2950 (C–H str., asym.), 2866 (C–H str., CH_3), 1568 (C=S str.), 1554 (N–H str., def.), 1508 (C=C str., aromatic.), 1309 (C–N str.), 819 (C_3N_3 str., s-triazinyl), 707 (C–S str.). Mass: 538 (M^+). ^{1}H NMR ($CDCl_3$) δ (ppm): 8.81 (s, 1H, NH), 6.56–7.11 (m, 4H, Ar–H), 1.21 (s, 6H, –CH_3), 4.93 (t, 2H, –CH_2), 3.34–2.85 (d, 1H, –CH), 2.65–2.56 (t, 2H, –CH_2), 3.92–3.84 (t, 2H, –CH_2), 4.12 (s, 2H, –NH). Anal. calcd. for $C_{20}H_{26}N_8O_2S_4$: C 44.59, H 4.86, N 20.80, S 23.81%. Found: C 44.47, H 4.74, N 20.69, S 23.68%.

7l IR (KBr) ν cm^{-1}: 3359 (N–H str.), 3015 (C–H str., aromatic), 2950 (C–H str., asym.), 2866 (C–H str., CH_3), 1568 (C=S str.), 1554 (N–H str., def.), 1508 (C=C str., aromatic.), 1309 (C–N str.), 809 (C_3N_3 str., s-triazinyl), 715 (C–S str.). Mass: 480 (M^+). ^{1}H NMR ($CDCl_3$) δ (ppm): 8.81 (s, 1H, NH), 6.48–7.07 (m, 4H, Ar–H), 1.21 (s, 6H, –CH_3), 0.94 (t, 12H, –CH_3), 2.32 (q, 8H, –CH_2). Anal. calcd. for $C_{20}H_{28}N_6S_4$: C 49.97, H 5.87, N 17.48, S 26.68%. Found: C 49.86, H 5.74, N 17.35, S 26.55%.

antibacterial and antifungal activity against *B. substillis*, *S. pyogens*, *E. coli*, and *A. niger* respectively. We have developed a simple and efficient method for the synthesis of bioactive 2,4-diarylamino-6-[N–(3′-methylphenyl)dithiocarbamoyl]-6-arylamino-s-triazines and 2,4-bis[N-(3′-methylphenyl)dithiocarbamoyl]-6-arylamino-s-triazines with good yield and purity.

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