Synthesis and Antimicrobial Activity of Pyrrolyl/Pyrazolyl Arylaminosulfonylmethyl 1,3,4-Oxadiazoles, 1,3,4-Thiadiazoles and 1,2,4-Triazoles

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A new class of pyrrolyl/pyrazolyl arylaminosulfonylmethyl 1,3,4-oxadiazoles, 1,3,4-thiadiazoles, and 1,2,4-triazoles were prepared and tested for antimicrobial activity. Amongst the tested compounds, 5c displayed high antimicrobial activity.

Key words pyrrolyl/pyrazolyl-1,3,4-oxadiazole; 1,3,4-thiadiazole; 1,2,4-triazole; 1,3-dipolar cycloaddition; antimicrobial activity

A wide variety of heterocyclic systems have been explored for developing pharmaceutically important molecules. Amongst them, five membered aromatic heterocycles *viz.*, pyrroles, pyrazoles, 1,3,4-oxadiazoles, 1,3,4-thiadiazoles and 1,2,4-triazoles are important class of heterocyclic compounds. The wide spread use of them as scaffold in medicinal chemistry establishes these moieties as a member of the privileged structures class. As constituents of cytotoxic drugs such as netrospin and distamycin, 4-aminopyrrole-2-carboxylates have been used as the main compounds in the construction of a diverse series of DNA-binding ligands exhibiting antibiotic, antiviral, and oncolytic properties.[1,2] The related 3-aminopyrroles also exhibit anticonvulsant activity by blocking sodium channels.[3] Pyrazole nucleus has pronounced pharmacological applications as antianxiety,[4] antidiabetic,[5] antimicrobial,[6,7] herbicidal,[8] anti-inflammatory[9] and antibacterial.[10,11] Further, 1,3,4-oxadiazoles are very good bioisosteres of amides and esters which can contribute substantially in increasing pharmacological activity by participating in hydrogen bonding interactions with the receptors.[12] Besides, it has been well documented that pyrazoles[13] and oxadiazoles[14,15] have cytotoxic activity. The therapeutic effects of compounds containing 1,3,4-thiadiazole rings have been studied for a number of pathological conditions including inflammation,[16,17] pain[18,19] and hypertension.[20] Substituted-1,2,4-triazoles have received the most attention during last two decades as potential antimicrobial, antitubercular, anti-human immunodeficiency virus (HIV), anti-inflammatory, central nervous system (CNS) stimulants, sedative and antianxiety agents.[21—24] In previous communications, we have reported clubbed pyrazoles with other heterocycles and studied their antimicrobial and antioxidant activities.[25] The present study illustrates the details of further structural modifications carried out on clubbed pyrroles and pyrazoles with 1,3,4-oxadiazoles/1,3,4-thiadiazoles/1,2,4-triazoles and antioxidant activities. The synthetic route and sequence of reactions are depicted in Charts 1 and 2.

Chemistry The synthetic scheme involves the preparation of bis heterocycles, pyrrolyl/pyrazolyl-oxadiazoles, thiadiazoles and triazoles from synthetically vulnerable intermediates arylaminosulfonylacetic acid hydrazide (**1**) and *Z*-styrylsulfonylacetic acid (**2**). The cyclocondensation of **1** and **2** in the presence of $POCl_3$ led to 2-(arylaminosulfonylmethyl)-5-[*Z*-(styrylsulfonylmethyl)]-1,3,4-oxadiazole (**3**) (Chart 1 and Mechanism). Interconversion of oxadiazole to thiadiazole was effected by treating **3** with thiourea in tetrahydrofuran (THF) to get 2-(arylaminosulfonylmethyl)-5-[*Z*-(styrylsulfonylmethyl)]-1,3,4-thiadiazole (**4**). On the other hand, the reaction of **3** with hydrazine hydrate in the presence of KOH in *n*-butanol produced 4-amino-3-(arylaminosulfonylmethyl)-5-[*Z*-(styrylsulfonylmethyl)]-1,2,4-triazole (**5**) (Chart 1). The ^{1}H-NMR spectra of **3a** and **4a** displayed two singlets at δ 4.86, 5.09 and 5.11, 5.35 due to methylene protons attached to C-5 and C-2 while **5a** at 5.05 and 5.28 ppm due to methylene protons attached to C-5 and C-3. The downfield signal was assigned to the one adjacent to sulfonamide moiety. Apart from this, one doublet was observed at 6.59, 6.77 and 6.72 ppm due to olefin proton H_B. The olefin proton, H_A adjacent to aryl group displayed a signal at downfield region, merged with aromatic protons. The coupling constant value $J \approx 12.0$ Hz indicated that they possess *cis* geometry. The broad signals appeared at 10.31, 10.39 and 10.15 ppm in **3a**, **4a** and **5a** was assigned to NH which disappeared on deuteration. Moreover, compound **5a** exhibited a broad signal at 5.64 ppm due to NH_2 which disappeared on deuteration.

1,3-Dipolar cycloaddition of dipolar reagents to dipolarophiles is one of the facile techniques for the preparation of five membered heterocycles. The olefin moiety present in **3**, **4** and **5** was used to develop five membered heterocycles-pyrroles and pyrazoles. The reaction of **3**, **4** and **5** with tosylmethyl isocyanide in the presence of sodium hydride in a solvent mixture of DMSO and ether yielded 2-(arylaminosulfonylmethyl)-5-(4′-aryl-1′*H*-pyrrol-3′-ylsulfonylmethyl)-1,3,4-oxadiazole (**6**), 2-(arylaminosulfonylmethyl)-5-(4′-aryl-1′*H*-pyrrol-3′-ylsulfonylmethyl)-1,3,4-thiadiazole (**7**) and 4-amino-3-(arylaminosulfonylmethyl)-5-(4′-aryl-1′*H*-pyrrol-3′-ylsulfonylmethyl)-1,2,4-triazole (**8**) (Chart 2). The ^{1}H-NMR spectra of **6a**, **7a** and **8a** displayed two singlets at δ 5.06, 5.03, 5.09 and 5.30, 5.19, 5.29 ppm due to two methylene protons attached to C-5 and C-2 of oxadiazole/thiadiazole and C-5 and C-3 of triazole units. In addition to these, one singlet was observed at 6.64, 6.68 and 6.71 due to C'_5-H of pyrrole ring whereas the other proton, C'_2-H appeared at downfield region and merged with aromatic protons. The compounds **6a**, **7a** and **8a** also showed two broad singlets at

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8.75, 8.35, 8.41 and at 10.47, 10.10, 10.32 ppm due to NH of pyrrole ring and NH–SO_2 and also **8a** exhibited a broad singlet at 5.58 due to NH_2 which were disappeared on deuteration. The 1,3-dipolar cycloadditon of diazomethane to **3**, **4** and **5** in the presence of Et_3N in ether at −20 to −15 °C for 48 h gave 2-(arylaminosulfonylmethyl)-5-(4′-aryl-4′,5′-dihydro-1′*H*-pyrazol-3′-ylsulfonylmethyl)-1,3,4-oxadiazole (**9**), 2-(arylaminosulfonylmethyl)-5-(4′-aryl-4′,5′-dihydro-1′*H*-pyrazol-3′-ylsulfonylmethyl)-1,3,4-thiadiazole (**10**) and 4-amino-3-(arylaminosulfonylmethyl)-5-(4′-aryl-4′,5′-dihydro-1′*H*-pyrazol-3′-ylsulfonylmethyl)-1,2,4-triazole (**11**) regioselectively. This may be due to the more electron withdrawing capacity of SO_2.[26] The pyrazoline ring protons displayed an AMX splitting pattern in the ^{1}H-NMR spectra of **9a**, **10a** and **11a**. Thus three double doublets observed at δ 3.58, 4.21, 4.57 in **9a**, at 3.54, 4.26, 4.61 in **10a** and at 3.64, 4.09, 4.53 ppm in **11a** were assigned to H_X, H_M and H_A, respectively. The coupling constant values $J_{AM}\approx12.4$, $J_{MX}\approx10.6$ and $J_{AX}\approx6.5$ Hz indicated that H_A, H_M are *cis*, H_A, H_X are *trans* while H_M, H_X are *geminal*. Aromatization of the compounds **9**, **10** and **11** with chloranil in xylene resulted in 2-(arylaminosulfonylmethyl)-5-(4′-aryl-1′*H*-pyrazol-3′-yl-

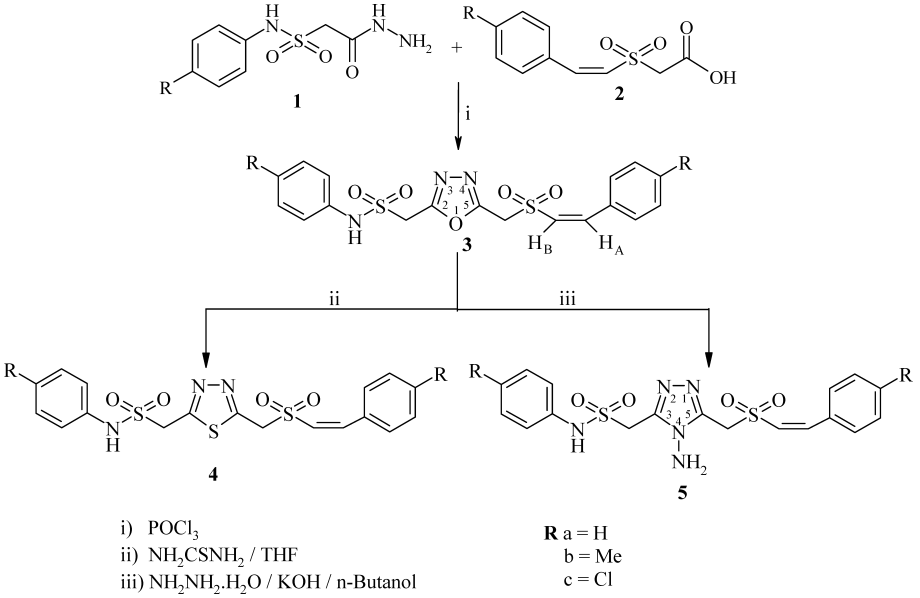
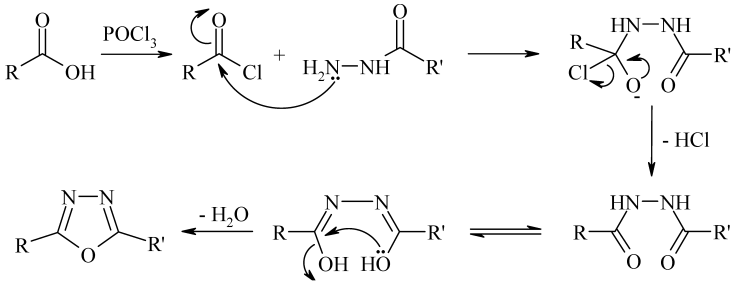


Chart 1



Mechanism: Formation of Oxadiazole from Acid Hydrazide and Carboxylic Acid

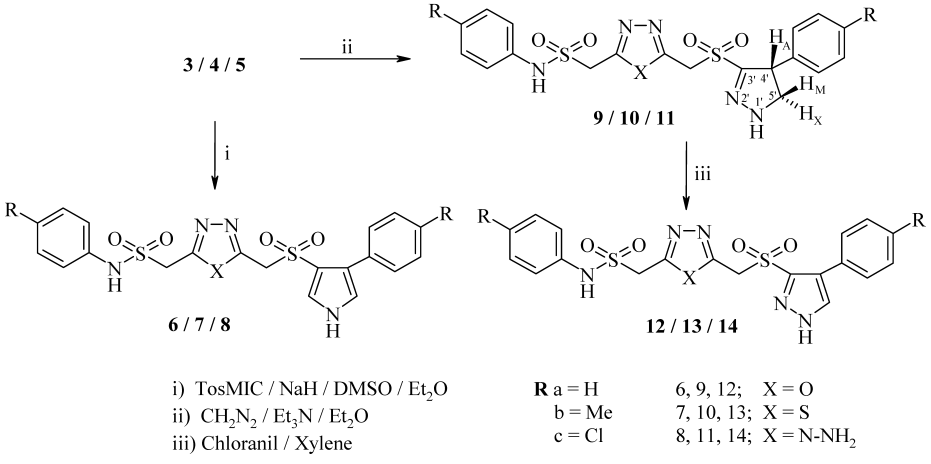


Chart 2

Table 1. The *in Vitro* Antibacterial Activity of Compounds **3**—**14**

Compound	Diameter of zone of inhibition (mm)							
	Gram-positive bacteria				Gram-negative bacteria			
	S. aureus		*B. subtilis*		*P. aeruginosa*		*K. pneumoniae*	
	50 μg/well	100 μg/well	50 μg/well	100 μg/well	50 μg/well	100 μg/well	50 μg/well	100 μg/well
3a	8	10	10	13	9	11	13	15
3b	—	—	—	—	—	—	—	—
3c	15	16	13	15	12	14	18	20
4a	20	22	18	19	16	19	22	25
4b	13	15	16	18	13	15	18	20
4c	28	31	29	32	24	26	32	34
5a	24	27	23	25	21	23	28	30
5b	18	21	20	22	15	17	22	25
5c	32	35	35	38	30	32	38	40
6a	—	—	—	—	—	—	—	—
6b	—	—	—	—	—	—	—	—
6c	13	14	11	13	10	12	14	16
7a	17	19	15	18	14	16	20	21
7b	11	13	12	14	11	13	15	16
7c	25	28	26	28	21	23	29	31
8a	20	23	19	22	20	21	26	28
8b	15	17	18	20	14	16	19	21
8c	29	31	28	31	25	27	32	35
9a	9	12	11	12	—	10	—	9
9b	—	—	—	—	—	—	—	—
9c	11	14	10	12	—	11	—	11
10a	15	18	14	15	13	15	17	19
10b	9	10	10	12	8	11	14	16
10c	24	26	23	25	20	22	27	29
11a	20	21	19	21	18	20	25	27
11b	14	16	17	19	13	15	20	21
11c	25	27	24	26	20	23	28	31
12a	8	9	9	12	—	—	—	—
12b	—	—	—	—	—	—	—	—
12c	14	16	12	14	11	13	16	17
13a	19	21	17	19	15	18	22	24
13b	13	14	14	16	12	15	17	19
13c	26	29	27	30	22	25	30	31
14a	22	25	21	24	20	22	28	29
14b	16	19	19	21	15	16	20	23
14c	31	33	33	36	29	31	36	39
Chloramphenicol	33	35	34	38	27	30	40	42
Control (DMSO)	—	—	—	—	—	—	—	—

(—) No activity.

sulfonylmethyl)-1,3,4-oxadiazole (**12**), 2-(arylaminosulfonylmethyl)-5-(4′-aryl-1′*H*-pyrazol-3′-ylsulfonylmethyl)-1,3,4-thiadiazole (**13**) and 4-amino-3-(arylaminosulfonylmethyl)-5-(4′-aryl-1′*H*-pyrazol-3′-ylsulfonylmethyl)-1,2,4-triazole (**14**) (Chart 2). The absence of AMX splitting pattern due to pyrazoline ring protons in **12**, **13** and **14** indicated that aromatization took place. The structures of these compounds were further confirmed by IR and ^{13}C-NMR spectra.

Antimicrobial Testing The compounds **3**—**14** were screened for antimicrobial activity at two different concentrations 50 and 100 μg. The antibacterial activity was carried out against *Staphylococcus aureus*, *Bacillus subtilis* (Gram-positive bacteria) and *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* (Gram-negative bacteria) on nutrient agar plates at 37 °C for 24 h using Chloramphenicol as reference drug. The compounds were also evaluated for antifungal activity against *Penicillium chrysogenum*, *Curvularia lunata* and *Aspergillus niger* using Ketoconazole as standard drug. Fungi cultures were grown on potato dextrose agar medium (PDA) at 28 °C for 48 h. The perceived data on the antimicrobial activity of the tested compounds and control drugs are shown in Tables 1—3.

Investigation of antibacterial screening data shown in Table 1 indicated that Gram-negative bacteria were more susceptible towards the tested compounds than Gram-positive ones. When compared to the standard drug Chloramphenicol it was seen that **5c** and **14c** were effective particularly against *Pseudomonas aeruginosa* at 50 and 100 μg. However, amongst bis heterocyclic compounds, **8** and **14** displayed good antibacterial activity against both Gram-positive and Gram-negaive bacteria. On the other hand, compounds **7** and **13** exhibited moderate activity against both bacteria. The compounds **3**, **6**, **9** and **12** showed least activity. The presence of chloro substituent on the aromatic ring enhances the activity (Fig. 1).

All the tested compounds inhibited the spore germination against tested fungi. In general, most of the compounds showed slightly higher antifungal activity towards *Penicil-*

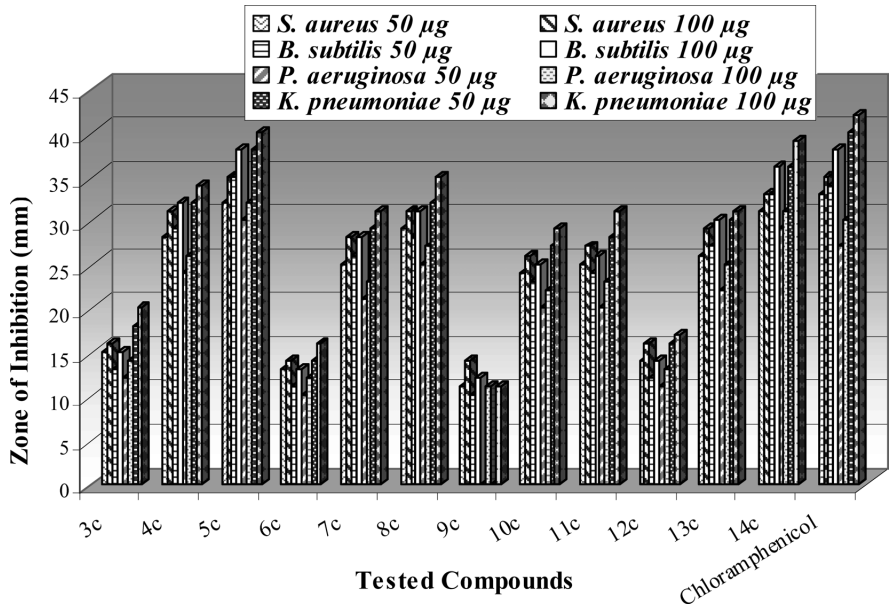


Fig. 1. Antibacterial Activity of **3c**—**14c**

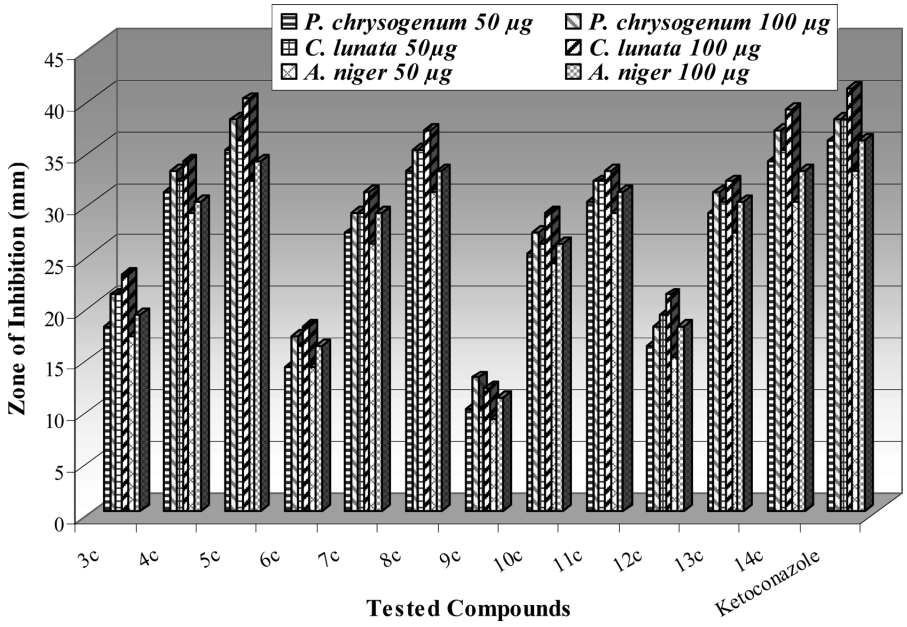


Fig. 2. Antifungal Activity of **3c**—**14c**

lium chrysogenum than *Curvularia lunata* and *Aspergillus niger*. The compounds **5c** and **14c** displayed excellent activity particularly against *Penicillium chrysogenum* almost equivalent to the standard drug Ketoconazole (Table 2, Fig. 2). Compounds **4**, **7**, **8**, **10**, **11** and **13** also showed moderate inhibition against the tested fungi. However, the compounds **3**, **6**, **9** and **12** exhibited least activity.

The minimum inhibitory concentration (MIC), minimum bactericidal concentration (MBC) and minimum fungicidal concentration (MFC) values of the tested compounds are listed in Table 3. The compound **5c** exhibited low MIC values when compared with **4c**, **8c** and **14c**. Besides, the MBC value is 2×MIC in case of *Bacillus subtilis* and *P. aeruginosa* and MFC value is 2×MIC in case of *P. chrysogenum*. On the other hand, the other compounds displayed bactericidal and fungicidal effects greater than 2×MIC. It was observed that mono heterocyclic compounds exhibited excellent activity than bis heterocyclic systems. This may be due to the presence of styrylsulfonyl moiety in mono heterocyclic compounds. Amongst different heterocyclic systems, compounds having thiadiazole and triazole units displayed greater activity than those having oxadiazole units. The pyrrolyl/pyrazolyl-thiadiazoles and triazoles (**7**, **8**, **13**, **14**) showed greater activity than pyrrolyl/pyrazolyl-oxadiazoles (**6**, **12**). There is no marked difference in activity with compounds having pyrrolyl and pyrazolyl units. It was also observed that amongst pyrazolinyl and pyrazolyl bis heterocycles, the pyrazolyl compounds **12**—**14** exhibited greater antimicrobial activity than pyrazolinyl compounds **9**—**11**. From these results it could be conclude that the chloro substituted

Table 2. The *in Vitro* Antifungal Activity of Compounds **3**—**14**

Compound	Diameter of zone of inhibition (mm)					
	P. chrysogenum		*C. lunata*		*A. niger*	
	50 μg/well	100 μg/well	50 μg/well	100 μg/well	50 μg/well	100 μg/well
3a	10	12	13	14	9	11
3b	—	—	—	—	—	—
3c	18	21	21	23	17	19
4a	23	24	25	28	21	23
4b	17	19	20	22	16	18
4c	31	33	32	34	29	30
5a	27	28	28	30	26	28
5b	21	24	24	26	20	22
5c	35	38	36	40	32	34
6a	—	—	—	—	—	—
6b	—	—	—	—	—	—
6c	14	17	16	18	14	16
7a	19	22	23	25	18	20
7b	14	16	17	19	14	15
7c	27	29	29	31	26	29
8a	23	25	26	28	22	24
8b	20	22	21	23	17	19
8c	33	35	35	37	31	33
9a	9	10	—	10	—	11
9b	—	—	—	—	—	—
9c	10	13	10	12	9	11
10a	18	20	22	24	17	20
10b	12	14	15	18	13	15
10c	25	27	26	29	24	26
11a	22	24	25	27	21	24
11b	18	20	20	22	17	20
11c	30	32	32	33	29	31
12a	9	11	11	13	8	10
12b	—	—	—	—	—	—
12c	16	18	19	21	15	18
13a	21	23	24	26	20	22
13b	16	18	18	21	15	17
13c	29	31	30	32	27	30
14a	25	26	27	29	24	26
14b	21	23	22	24	18	19
14c	34	37	35	39	30	33
Ketoconazole	36	38	38	41	33	36
Control (DMSO)	—	—	—	—	—	—

(—) No activity.

Table 3. MIC, MBC and MFC of Compounds **4c**, **5c**, **8c** and **14c**

Compound	Minimum inhibitory concentration						
	MIC (MBC/MFC) μg						
	S. aureus	*B. subtilis*	*P. aeruginosa*	*K. pneumoniae*	*P. chrysogenum*	*C. lunata*	*A. niger*
4c	100 (>200)	100 (>200)	50 (200)	200	50 (>200)	100 (>200)	200
5c	25 (100)	25 (50)	12.5 (25)	50 (200)	25 (50)	25 (100)	50 (200)
8c	50 (>200)	100 (>200)	50 (200)	100 (>200)	100 (200)	50 (>200)	200
14c	25 (100)	50 (200)	25 (100)	100 (>200)	50 (200)	50 (200)	50 (>200)
Chloramphenicol	6.25	6.25	12.5	12.5	—	—	—
Ketoconazole	—	—	—	—	12.5	6.25	6.25

(—) No activity.

triazole derivatives shows higher activity when compared with other analogues. The presence of aminosulfonylmethyl group at 2nd position of thiadiazole and at 3rd position of triazole units enhances the activity.

Conclusion

A new class of bis heterocycles-pyrrolyl/pyrazolyl arylaminosulfonylmethyl 1,3,4-oxadiazoles, 1,3,4-thiadiazoles and 1,2,4-triazoles were prepared and tested for antimicrobial activity. The presence of arylaminosulfonylmethyl group en-

hances the antimicrobial activity. Amongst the tested compounds, **5c** is the most potent antimicrobial agent.

Experimental

Melting points were determined in open capillaries on a Mel-Temp apparatus and are uncorrected. The purity of the compounds was checked by TLC (silica gel H, BDH, hexane/ethyl acetate, 3 : 1). The IR spectra were run on a Thermo Nicolet IR 200 FT-IR spectrometer as KBr pellets and the wave numbers were given in cm^{-1}. The ^{1}H-NMR spectra were recorded in $CDCl_3$/DMSO-d_6 on a Jeol JNM λ-400 MHz. The ^{13}C-NMR spectra were recorded in $CDCl_3$/DMSO-d_6 on a Jeol JNM spectrometer operating at 100 MHz. All chemical shifts are reported in δ (ppm) using TMS as an internal standard. The microanalyses were performed on a Perkin-Elmer 240C elemental analyzer. The *Z*-styrylsulfonylacetic acid (**2**) was prepared as per the literature procedure.[27,28]

General Procedure of Synthesis of Arylaminosulfonylacetic Acid Hydrazide (1a—c) The compound methyl arylaminosulfonylacetate (10 mmol), hydrazine hydrate (11 mmol), methanol (6 ml) and three drops of pyridine were refluxed for 6—8 h. The reaction mixture was cooled and the solid separated was collected by filtration, dried and recrystallized from methanol.

General Procedure of Synthesis of 2-(Arylaminosulfonylmethyl)-5-[*Z*-(styrylsulfonylmethyl)]-1,3,4-oxadiazole (3a—c) A mixture of arylaminosulfonylacetic acid hydrazide (**1**) (10 mmol), *Z*-styrylsulfonylacetic acid (**2**) (10 mmol) and $POCl_3$ (7 ml) was heated under reflux for 5—7 h. The excess $POCl_3$ was removed under reduced pressure and the residue was poured onto crushed ice. The resulting precipitate was filtered, washed with saturated sodium bicarbonate solution and then with water. It was dried and recrystallized from ethanol.

2-(Phenylaminosulfonylmethyl)-5-[*Z*-(styrylsulfonylmethyl)]-1,3,4-oxadiazole (**3a**): White solid, yield 67%, mp 122—124 °C; ^{1}H-NMR ($CDCl_3$) δ: 4.86 (s, 2H, SO_2–CH_2), 5.11 (s, 2H, C<u>H</u>$_2$–SO_2–NH), 6.59 (d, 1H, H_B, J=11.7 Hz), 7.11—7.69 (m, 11H, H_A, Ar–H), 10.31 (br s, 1H, NH). ^{13}C-NMR ($CDCl_3$) δ: 44.3 (SO_2–CH_2), 49.7 (CH_2–SO_2–NH), 121.6 (C–H_B), 140.2 (C–H_A), 157.3 (C-5), 158.2 (C-2), 124.7, 125.6, 126.4, 128.3, 128.9, 129.4, 130.2, 131.1 (aromatic carbons). IR (KBr) cm^{-1}: 3227 (NH), 1630 (C=C), 1572 (C=N), 1305,1160 (SO_2). *Anal.* Calcd for $C_{18}H_{17}N_3O_5S_2$: C, 51.54; H, 4.08; N, 10.02. Found: C, 51.60; H, 4.10; N, 10.12.

2-(*p*-Methylphenylaminosulfonylmethyl)-5-[*Z*-(*p*-methylstyrylsulfonylmethyl)]-1,3,4-oxadiazole (**3b**): White solid, yield 65%, mp 101—103 °C; ^{1}H-NMR ($CDCl_3$) δ: 2.21 and 2.27 (s, 6H, Ar–CH_3), 4.69 (s, 2H, SO_2–CH_2), 5.06 (s, 2H, C<u>H</u>$_2$–SO_2–NH), 6.42 (d, 1H, H_B, J=11.5 Hz), 7.03—7.59 (m, 9H, H_A, Ar-H), 10.02 (br s, 1H, NH). ^{13}C-NMR ($CDCl_3$) δ: 21.2 and 21.9 (Ar-CH_3), 42.8 (SO_2–CH_2), 48.4 (CH_2–SO_2–NH), 120.8 (C–H_B), 137.1 (C–H_A), 154.5 (C-5), 155.1 (C-2), 122.5, 123.7, 124.4, 124.9, 126.3, 127.9, 128.5, 129.6 (aromatic carbons). IR (KBr) cm^{-1}: 3210 (NH), 1622 (C=C), 1565 (C=N), 1312, 1155 (SO_2). *Anal.* Calcd for $C_{20}H_{21}N_3O_5S_2$: C, 53.68; H, 4.73; N, 9.39. Found: C, 53.63; H, 4.72; N, 9.47.

2-(*p*-Chlorophenylaminosulfonylmethyl)-5-[*Z*-(*p*-chlorostyrylsulfonylmethyl)]-1,3,4-oxadiazole (**3c**): White crystals, yield 69%, mp 140—142 °C; ^{1}H-NMR ($CDCl_3$) δ: 5.02 (s, 2H, SO_2–CH_2), 5.25 (s, 2H, C<u>H</u>$_2$–SO_2–NH), 6.87 (d, 1H, H_B, J=12.0 Hz), 7.17—7.71 (m, 9H, H_A, Ar–H), 10.45 (br s, 1H, NH). ^{13}C-NMR ($CDCl_3$) δ: 47.6 (SO_2–CH_2), 50.9 (CH_2–SO_2–NH), 122.5 (C–H_B), 143.1 (C–H_A), 158.1 (C-5), 159.7 (C-2), 127.7, 128.6, 129.0, 129.7, 130.5, 130.6, 132.6, 136.6 (aromatic carbons). IR (KBr) cm^{-1}: 3235 (NH), 1625 (C=C), 1580 (C=N), 1318, 1169 (SO_2). *Anal.* Calcd for $C_{18}H_{15}Cl_2N_3O_5S_2$: C, 44.27; H, 3.10; N, 8.60. Found: C, 44.22; H, 3.07; N, 8.56.

General Procedure of Synthesis of 2-(Arylaminosulfonylmethyl)-5-[*Z*-(styrylsulfonylmethyl)]-1,3,4-thiadiazole (4a—c) In a sealed test tube, the compound **3** (5 mmol), thiourea (20 mmol) and tetrahydrofuran (5 ml) were taken and heated at 120—130 °C in an oil bath for 22—25 h. After the reaction was completed, it was extracted with dichloromethane. The organic layer was washed with water, brine solution and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the resultant solid was recrystallized from methanol.

2-(Phenylaminosulfonylmethyl)-5-[*Z*-(styrylsulfonylmethyl)]-1,3,4-thiadiazole (**4a**): White solid, yield 70%, mp 153—155 °C; ^{1}H-NMR ($CDCl_3$) δ: 5.09 (s, 2H, SO_2–CH_2), 5.35 (s, 2H, C<u>H</u>$_2$–SO_2–NH), 6.77 (d, 1H, H_B, J=11.4 Hz), 7.14—7.68 (m, 11H, H_A, Ar–H), 10.39 (br s, 1H, NH). ^{13}C-NMR ($CDCl_3$) δ: 43.5 (SO_2–CH_2), 51.8 (CH_2–SO_2–NH), 121.4 (C–H_B), 140.4 (C–H_A), 157.7 (C-5), 158.8 (C-2), 125.3, 126.1, 126.8, 127.6, 128.8, 129.4, 130.1, 131.2 (aromatic carbons). IR (KBr) cm^{-1}: 3242 (NH), 1628 (C=C), 1562 (C=N), 1310, 1142 (SO_2). *Anal.* Calcd for $C_{18}H_{17}N_3O_4S_3$: C, 49.64; H, 3.93; N, 9.65. Found: C, 49.70; H, 3.97; N, 9.70.

2-(*p*-Methylphenylaminosulfonylmethyl)-5-[*Z*-(*p*-methylstyrylsulfonylmethyl)]-1,3,4-thiadiazole (**4b**): White solid, yield 68%, mp 166—168 °C; ^{1}H-NMR ($CDCl_3$) δ: 2.23 and 2.29 (s, 6H, Ar–CH_3), 5.07 (s, 2H, SO_2–CH_2), 5.27 (s, 2H, C<u>H</u>$_2$–SO_2–NH), 6.68 (d, 1H, H_B, J=11.2 Hz), 7.11—7.62 (m, 9H, H_A, Ar–H), 10.34 (br s, 1H, NH). ^{13}C-NMR ($CDCl_3$) δ: 21.5 and 21.9 (Ar–CH_3), 42.8 (SO_2–CH_2), 50.7 (CH_2–SO_2–NH), 120.9 (C–H_B), 139.8 (C–H_A), 158.2 (C-5), 159.6 (C-2), 124.8, 125.6, 126.7, 127.4, 128.5, 129.2, 130.7, 132.6 (aromatic carbons). IR (KBr) cm^{-1}: 3236 (NH), 1619 (C=C), 1559 (C=N), 1324, 1139 (SO_2). *Anal.* Calcd for $C_{20}H_{21}N_3O_4S_3$: C, 51.82; H, 4.57; N, 9.06. Found: C, 51.89; H, 4.56; N, 9.02.

2-(*p*-Chlorophenylaminosulfonylmethyl)-5-[*Z*-(*p*-chlorostyrylsulfonylmethyl)]-1,3,4-thiadiazole (**4c**): White solid, yield 72%, mp 182—184 °C; ^{1}H-NMR ($CDCl_3$) δ: 5.18 (s, 2H, SO_2–CH_2), 5.41 (s, 2H, C<u>H</u>$_2$–SO_2–NH), 6.81 (d, 1H, H_B, J=11.8 Hz), 7.18—7.73 (m, 9H, H_A, Ar–H), 10.42 (br s, 1H, NH). ^{13}C-NMR ($CDCl_3$) δ: 44.2 (SO_2–CH_2), 51.5 (CH_2–SO_2-NH), 121.9 (C–H_B), 141.5 (C–H_A), 158.6 (C-5), 159.5 (C-2), 126.4, 127.1, 128.0, 128.7, 129.2, 130.6, 132.0, 134.7 (aromatic carbons). IR (KBr) cm^{-1}: 3250 (NH), 1623 (C=C), 1573 (C=N), 1326, 1151 (SO_2). *Anal.* Calcd for $C_{18}H_{15}Cl_2N_3O_4S_3$: C, 42.86; H, 3.00; N, 8.33. Found: C, 42.91; H, 3.01; N, 8.40.

General Procedure of Synthesis of 4-Amino-3-(arylaminosulfonylmethyl)-5-[*Z*-(styrylsulfonylmethyl)]-1,2,4-triazole (5a—c) To a solution of compound **3** (5 mmol) in *n*-butanol (25 ml), hydrazine hydrate (15 mmol) was added and refluxed for 6—8 h. Then, KOH (10 mmol) was added to the reaction media and the precipitate formed was filtered. The solid obtained was acidified with conc. HCl to pH=3 and washed with water. It was dried and recrystallized from ethanol.

4-Amino-3-(phenylaminosulfonylmethyl)-5-[*Z*-(styrylsulfonylmethyl)]-1,2,4-triazole (**5a**): White solid, yield 66%, mp 158—160 °C; ^{1}H-NMR (DMSO-d_6) δ: 5.05 (s, 2H, SO_2–CH_2), 5.28 (s, 2H, C<u>H</u>$_2$–SO_2–NH), 5.64 (br s, 2H, NH_2), 6.72 (d, 1H, H_B, J=11.7 Hz), 7.10—7.74 (m, 11H, H_A, Ar–H), 10.15 (br s, 1H, NH). ^{13}C-NMR (DMSO-d_6) δ: 45.0 (SO_2–CH_2), 50.6 (CH_2–SO_2–NH), 122.0 (C–H_B), 142.8 (C–H_A), 157.6 (C-5), 159.1 (C-3), 124.9, 125.8, 126.7, 127.4, 128.4, 129.5, 130.2, 133.1 (aromatic carbons). IR (KBr) cm^{-1}: 3478, 3361 (NH_2), 3254 (NH), 1626 (C=C), 1561 (C=N), 1319, 1136 (SO_2). *Anal.* Calcd for $C_{18}H_{19}N_5O_4S_2$: C, 49.87; H, 4.42; N, 16.16. Found: C, 49.90; H, 4.45; N, 16.25.

4-Amino-3-(*p*-methylphenylaminosulfonylmethyl)-5-[*Z*-(*p*-methylstyrylsulfonylmethyl)]-1,2,4-triazole (**5b**): White solid, yield 68%, mp 179—181 °C; ^{1}H-NMR (DMSO-d_6) δ: 2.21 and 2.25 (s, 6H, Ar–CH_3), 4.94 (s, 2H, SO_2–CH_2), 5.21 (s, 2H, C<u>H</u>$_2$–SO_2–NH), 5.62 (br s, 2H, NH_2), 6.69 (d, 1H, H_B, J=11.1 Hz), 7.06—7.69 (m, 9H, H_A, Ar–H), 10.11 (br s, 1H, NH). ^{13}C-NMR (DMSO-d_6) δ: 21.3 and 21.5 (Ar–CH_3), 44.5 (SO_2–CH_2), 50.2 (CH_2–SO_2–NH), 121.6 (C–H_B), 140.4 (C–H_A), 158.2 (C-5), 159.5 (C-3), 125.9, 126.8, 127.2, 128.0, 128.9, 129.5, 130.2, 131.6 (aromatic carbons). IR (KBr) cm^{-1}: 3471, 3365 (NH_2), 3259 (NH), 1621 (C=C), 1557 (C=N), 1314, 1132 (SO_2). *Anal.* Calcd for $C_{20}H_{23}N_5O_4S_2$: C, 52.04; H, 5.02; N, 15.17. Found: C, 52.10; H, 5.00; N, 15.26.

4-Amino-3-(*p*-chlorophenylaminosulfonylmethyl)-5-[*Z*-(*p*-chlorostyrylsulfonylmethyl)]-1,2,4-triazole (**5c**): White solid, yield 71%, mp 193—195 °C; ^{1}H-NMR (DMSO-d_6) δ: 5.08 (s, 2H, SO_2–CH_2), 5.32 (s, 2H, C<u>H</u>$_2$–SO_2–NH), 5.71 (br s, 2H, NH_2), 6.78 (d, 1H, H_B, J=11.9 Hz), 7.15—7.77 (m, 9H, H_A, Ar–H), 10.26 (br s, 1H, NH). ^{13}C-NMR (DMSO-d_6) δ: 45.7 (SO_2–CH_2), 50.9 (CH_2–SO_2–NH), 122.3 (C–H_B), 140.9 (C–H_A), 158.7 (C-5), 159.8 (C-3), 126.4, 127.0, 127.9, 128.8, 129.5, 130.1, 131.6, 132.4 (aromatic carbons). IR (KBr) cm^{-1}: 3480, 3382 (NH_2), 3266 (NH), 1624 (C=C), 1566 (C=N), 1322, 1143 (SO_2). *Anal.* Calcd for $C_{18}H_{17}Cl_2N_5O_4S_2$: C, 43.03; H, 3.41; N, 13.94. Found: C, 43.07; H, 3.42; N, 14.00.

General Procedure of Synthesis of 2-(Arylaminosulfonylmethyl)-5-(4′-aryl-1′*H*-pyrrol-3′-ylsulfonylmethyl)-1,3,4-oxadiazole (6a—c)/2-(Arylaminosulfonylmethyl)-5-(4′-aryl-1′*H*-pyrrol-3′-ylsulfonylmethyl)-1,3,4-thiadiazole (7a—c)/4-Amino-3-(arylamino-sulfonylmethyl)-5-(4′-aryl-1′*H*-pyrrol-3′-ylsulfonylmethyl)-1,2,4-triazole (8a—c) A mixture of compound **3**/**4**/**5** (1 mmol) and TosMIC (2 mmol) in Et_2O–DMSO (2 : 1) was added dropwise under stirring to a suspension of NaH (0.05 g) in Et_2O (20 ml) at room temperature and stirring was continued for 5—7 h. Then, water was added and the reaction mass was extracted with Et_2O. The ethereal layer was dried over anhydrous Na_2SO_4 and filtered. Evaporation of the solvent *in vacuo* gave a crude product which was purified by column chromatography using silica gel (hexane–ethyl acetate; 4 : 1).

2-(Phenylaminosulfonylmethyl)-5-(4′-phenyl-1′*H*-pyrrol-3′-ylsulfonylmethyl)-1,3,4-oxadiazole (**6a**): Yellow solid, yield 68%, mp 129—131 °C; ^{1}H-NMR ($CDCl_3$) δ: 5.06 (s, 2H, SO_2–CH_2), 5.30 (s, 2H, C<u>H</u>$_2$–SO_2–NH),

6.64 (s, 1H, C_5'-H), 7.21—7.84 (m, 11H, C_2'-H, Ar–H), 8.75 (br s, 1H, NH), 10.47 (br s, 1H, NH–SO_2). ^{13}C-NMR ($CDCl_3$) δ: 46.6 (SO_2–CH_2), 52.0 (CH_2–SO_2–NH), 104.3 (C-4′), 110.5 (C-3′), 117.8 (C-5′), 121.8 (C-2′), 155.6 (C-5), 156.3 (C-2), 124.8, 126.2, 127.6, 128.5, 129.1, 130.4, 132.6, 138.2 (aromatic carbons). IR (KBr) cm^{-1}: 3254 (NH), 1629 (C=C), 1584 (C=N), 1331, 1132 (SO_2). *Anal.* Calcd for $C_{20}H_{18}N_4O_5S_2$: C, 52.39; H, 3.96; N, 12.22. Found: C, 52.43; H, 3.95; N, 12.29.

2-(*p*-Methylphenylaminosulfonylmethyl)-5-(4′-*p*-methylphenyl-1′*H*-pyrrol-3′-ylsulfonyl-methyl)-1,3,4-oxadiazole (**6b**): Yellow solid, yield 66%, mp 140—142 °C; ^{1}H-NMR ($CDCl_3$) δ: 2.22 and 2.28 (s, 6H, Ar–CH_3), 4.99 (s, 2H, SO_2–CH_2), 5.24 (s, 2H, C<u>H</u>$_2$–SO_2–NH), 6.56 (s, 1H, C_5'-H), 7.18—7.88 (m, 9H, C_2'–H, Ar–H), 8.69 (br s, 1H, NH), 10.40 (br s, 1H, NH–SO_2). ^{13}C-NMR ($CDCl_3$) δ: 21.3 and 21.8 (Ar–CH_3), 46.1 (SO_2–CH_2), 51.4 (CH_2–SO_2–NH), 103.8 (C-4′), 109.7 (C-3′), 116.9 (C-5′), 121.0 (C-2′), 155.0 (C-5), 155.9 (C-2), 125.7, 126.5, 127.2, 128.6, 129.3, 130.1, 131.0, 138.8 (aromatic carbons). IR (KBr) cm^{-1}: 3251 (NH), 1625 (C=C), 1581 (C=N), 1324, 1129 (SO_2). *Anal.* Calcd for $C_{22}H_{22}N_4O_5S_2$: C, 54.31; H, 4.56; N, 11.51. Found: C, 54.28; H, 4.57; N, 11.56.

2-(*p*-Chlorophenylaminosulfonylmethyl)-5-(4′-*p*-chlorophenyl-1′*H*-pyrrol-3′-ylsulfonyl-methyl)-1,3,4-oxadiazole (**6c**): Yellow solid, yield 73%, mp 148—150 °C; ^{1}H-NMR ($CDCl_3$) δ: 5.11 (s, 2H, SO_2–CH_2), 5.38 (s, 2H, C<u>H</u>$_2$–SO_2–NH), 6.70 (s, 1H, C_5'–H), 7.25—7.74 (m, 9H, C_2'–H, Ar–H), 8.71 (br s, 1H, NH), 10.49 (br s, 1H, NH–SO_2). ^{13}C-NMR ($CDCl_3$) δ: 46.9 (SO_2–CH_2), 52.1 (CH_2–SO_2–NH), 104.8 (C-4′), 110.9 (C-3′), 118.3 (C-5′), 122.1 (C-2′), 154.9 (C-5), 155.6 (C-2), 126.7, 127.4, 128.8, 130.2, 131.5, 132.4, 134.6, 139.5 (aromatic carbons). IR (KBr) cm^{-1}: 3263 (NH), 1630 (C=C), 1587 (C=N), 1335, 1137 (SO_2). *Anal.* Calcd for $C_{20}H_{16}Cl_2N_4O_5S_2$: C, 45.55; H, 3.06; N, 10.62. Found: C, 45.60; H, 3.09; N, 10.67.

2-(Phenylaminosulfonylmethyl)-5-(4′-phenyl-1′*H*-pyrrol-3′-ylsulfonyl-methyl)-1,3,4-thiadiazole (**7a**): Yellow solid, yield 70%, mp 156—158 °C; ^{1}H-NMR ($CDCl_3$) δ: 5.03 (s, 2H, SO_2–CH_2), 5.19 (s, 2H, C<u>H</u>$_2$–SO_2–NH), 6.68 (s, 1H, C_5'–H), 7.09—7.70 (m, 11H, C_2'–H, Ar–H), 8.35 (br s, 1H, NH), 10.10 (br s, 1H, NH–SO_2). ^{13}C-NMR ($CDCl_3$) δ: 46.5 (SO_2–CH_2), 51.0 (CH_2–SO_2–NH), 102.9 (C-4′), 109.6 (C-3′), 117.5 (C-5′), 121.7 (C-2′), 158.2 (C-5), 159.6 (C-2), 125.4, 126.1, 127.4, 128.9, 129.5, 130.0, 131.2, 137.9 (aromatic carbons). IR (KBr) cm^{-1}: 3238 (NH), 1624 (C=C), 1592 (C=N), 1321, 1140 (SO_2). *Anal.* Calcd for $C_{20}H_{18}N_4O_4S_3$: C, 50.62; H, 3.82; N, 11.81. Found: C, 50.60; H, 3.81; N, 11.88.

2-(*p*-Methylphenylaminosulfonylmethyl)-5-(4′-*p*-methylphenyl-1′*H*-pyrrol-3′-ylsulfonyl-methyl)-1,3,4-thiadiazole (**7b**): Pale yellow solid, yield 66%, mp 160—162 °C; ^{1}H-NMR ($CDCl_3$) δ: 2.20 and 2.25 (s, 6H, Ar–CH_3), 5.01 (s, 2H, SO_2–CH_2), 5.14 (s, 2H, C<u>H</u>$_2$–SO_2–NH), 6.62 (s, 1H, C_5'–H), 7.04—7.65 (m, 9H, C_2'–H, Ar–H), 8.27 (br s, 1H, NH), 10.03 (br s, 1H, NH–SO_2). ^{13}C-NMR ($CDCl_3$) δ: 21.5 and 21.9 (Ar–CH_3), 45.9 (SO_2–CH_2), 50.6 (CH_2–SO_2–NH), 102.3 (C-4′), 109.0 (C-3′), 117.0 (C-5′), 121.2 (C-2′), 157.9 (C-5), 159.3 (C-2), 125.8, 126.9, 127.5, 128.7, 129.5, 130.2, 132.0, 137.6 (aromatic carbons). IR (KBr) cm^{-1}: 3235 (NH), 1619 (C=C), 1584 (C=N), 1319, 1128 (SO_2). *Anal.* Calcd for $C_{22}H_{22}N_4O_4S_3$: C, 52.57; H, 4.41; N, 11.15. Found: C, 52.62; H, 4.43; N, 11.10.

2-(*p*-Chlorophenylaminosulfonylmethyl)-5-(4′-*p*-chlorophenyl-1′*H*-pyrrol-3′-ylsulfonyl-methyl)-1,3,4-thiadiazole (**7c**): Pale yellow solid, yield 71%, mp 175—177 °C; ^{1}H-NMR ($CDCl_3$) δ: 5.13 (s, 2H, SO_2–CH_2), 5.27 (s, 2H, C<u>H</u>$_2$–SO_2–NH), 6.77 (s, 1H, C_5'–H), 7.14—7.68 (m, 9H, C_2'–H, Ar–H), 8.43 (br s, 1H, NH), 10.22 (br s, 1H, NH–SO_2). ^{13}C-NMR ($CDCl_3$) δ: 46.8 (SO_2–CH_2), 51.8 (CH_2–SO_2–NH), 103.2 (C-4′), 110.2 (C-3′), 117.9 (C-5′), 122.0 (C-2′), 158.4 (C-5), 159.0 (C-2), 126.6, 128.7, 129.6, 130.4, 131.5, 132.2, 134.1, 138.5 (aromatic carbons). IR (KBr) cm^{-1}: 3241 (NH), 1627 (C=C), 1597 (C=N), 1322, 1142 (SO_2). *Anal.* Calcd for $C_{20}H_{16}Cl_2N_4O_4S_3$: C, 44.20; H, 2.97; N, 10.31. Found: C, 44.24; H, 2.98; N, 10.37.

4-Amino-3-(phenylaminosulfonylmethyl)-5-(4′-phenyl-1′*H*-pyrrol-3′-ylsulfonylmethyl)- 1,2,4-triazole (**8a**): Yellow solid, yield 69%, mp 165—167 °C; ^{1}H-NMR (DMSO-d_6) δ: 5.09 (s, 2H, SO_2–CH_2), 5.29 (s, 2H, C<u>H</u>$_2$–SO_2–NH), 5.58 (br s, 2H, NH_2), 6.71 (s, 1H, C_5'–H), 7.12—7.76 (m, 11H, C_2'–H, Ar–H), 8.41 (br s, 1H, NH), 10.32 (br s, 1H, NH–SO_2). ^{13}C-NMR (DMSO-d_6) δ: 47.0 (SO_2–CH_2), 51.9 (CH_2–SO_2–NH), 102.1 (C-4′), 110.4 (C-3′), 116.7 (C-5′), 121.9 (C-2′), 158.2 (C-5), 159.4 (C-3), 126.4, 127.2, 128.3, 129.1, 130.4, 131.4, 132.0, 137.4 (aromatic carbons). IR (KBr) cm^{-1}: 3439, 3315 (NH_2), 3268 (NH), 1632 (C=C), 1599 (C=N), 1328, 1137 (SO_2). *Anal.* Calcd for $C_{20}H_{20}N_6O_4S_2$: C, 50.83; H, 4.27; N, 17.78. Found: C, 50.88; H, 4.24; N, 17.88.

4-Amino-3-(*p*-methylphenylaminosulfonylmethyl)-5-(4′-*p*-methylphenyl-1′*H*-pyrrol-3′-ylsulfonylmethyl)-1,2,4-triazole (**8b**): Yellow solid, yield 74%, mp 172—174 °C; ^{1}H-NMR (DMSO-d_6) δ: 2.19 and 2.24 (s, 6H, Ar–CH_3), 5.04 (s, 2H, SO_2–CH_2), 5.23 (s, 2H, C<u>H</u>$_2$–SO_2–NH), 5.54 (br s, 2H, NH_2), 6.58 (s, 1H, C_5'–H), 7.11—7.72 (m, 9H, C_2'–H, Ar–H), 8.36 (br s, 1H, NH), 10.22 (br s, 1H, NH–SO_2). ^{13}C-NMR (DMSO-d_6) δ: 21.6 and 21.9 (Ar–CH_3), 46.8 (SO_2–CH_2), 51.4 (CH_2–SO_2–NH), 102.0 (C-4′), 116.1 (C-3′), 117.8 (C-5′), 121.5 (C-2′), 157.9 (C-5), 158.8 (C-3), 126.1, 127.5, 128.4, 129.9, 130.2, 131.4, 132.6, 136.5 (aromatic carbons). IR (KBr) cm^{-1}: 3428, 3309 (NH_2), 3259 (NH), 1626 (C=C), 1589 (C=N), 1321, 1131 (SO_2). *Anal.* Calcd for $C_{22}H_{24}N_6O_4S_2$: C, 52.78; H, 4.83; N, 16.79. Found: C, 52.83; H, 4.87; N, 16.87.

4-Amino-3-(*p*-chlorophenylaminosulfonylmethyl)-5-(4′-*p*-chlorophenyl-1′*H*-pyrrol-3′-ylsulfonylmethyl)-1,2,4-triazole (**8c**): Yellow solid, yield 72%, mp 194—196 °C; ^{1}H-NMR (DMSO-d_6) δ: 5.17 (s, 2H, SO_2–CH_2), 5.36 (s, 2H, C<u>H</u>$_2$–SO_2–NH), 5.67 (br s, 2H, NH_2), 6.74 (s, 1H, C_5'–H), 7.16—7.81 (m, 9H, C_2'–H, Ar–H), 8.51 (br s, 1H, NH), 10.35 (br s, 1H, NH–SO_2). ^{13}C-NMR (DMSO-d_6) δ: 47.6 (SO_2–CH_2), 52.3 (CH_2–SO_2–NH), 103.3 (C-4′), 110.8 (C-3′), 117.0 (C-5′), 122.4 (C-2′), 158.0 (C-5), 159.1 (C-3), 126.8, 127.4, 128.6, 129.5, 130.4, 131.2, 132.0, 137.2 (aromatic carbons). IR (KBr) cm^{-1}: 3445, 3326 (NH_2), 3271 (NH), 1629 (C=C), 1602 (C=N), 1330, 1138 (SO_2). *Anal.* Calcd for $C_{20}H_{18}Cl_2N_6O_4S_2$: C, 44.37; H, 3.35; N, 15.52. Found: C, 44.34; H, 3.34; N, 15.48.

General Procedure of Synthesis of 2-(Arylaminosulfonylmethyl)-5-(4′-aryl-4′,5′-dihydro-1′*H*-pyrazol-3′-ylsulfonylmethyl)-1,3,4-oxadiazole (9a—c)/2-(Arylaminosulfonyl-methyl)-5-(4′-aryl-4′,5′-dihydro-1′*H*-pyrazol-3′-ylsulfonylmethyl)-1,3,4-thiadiazole (10a—c)/4-Amino-3-(aryl-aminosulfonylmethyl)-5-(4′-aryl-4′,5′-dihydro-1′*H*-pyrazol-3′-ylsulfonyl-methyl)-1,2,4-triazole (11a—c) To a cooled solution of compound **3**/**4**/**5** (5 mmol) in dichloromethane (20 ml), an ice-cold ethereal solution of diazomethane (40 ml, 0.4 m) and triethylamine (0.12 g) were added. The reaction mixture was kept at −20 to −15 °C for 48 h. The solvent was removed under vacuum and the resultant solid was recrystallized from 2-propanol.

2-(Phenylaminosulfonylmethyl)-5-(4′-phenyl-4′,5′-dihydro-1′*H*-pyrazol-3′-ylsulfonyl-methyl)-1,3,4-oxadiazole (**9a**): Pale yellow solid, yield 69%, mp 137—139 °C; ^{1}H-NMR ($CDCl_3$) δ: 3.58 (dd, 1H, H_X, J_{AX}=6.5 Hz, J_{MX}=10.6 Hz), 4.21 (dd, 1H, H_M, J_{AM}=12.4 Hz), 4.57 (dd, 1H, H_A), 4.96 (s, 2H, SO_2–CH_2), 5.16 (s, 2H, C<u>H</u>$_2$–SO_2–NH), 7.17—7.76 (m, 10H, Ar–H), 10.02 (br s, 1H, NH), 10.57 (br s, 1H, NH–SO_2). ^{13}C-NMR ($CDCl_3$) δ: 47.2 (SO_2–CH_2), 52.0 (CH_2–SO_2–NH), 53.7 (C-5′), 66.4 (C-4′), 152.8 (C-3′), 158.1 (C-5), 158.9 (C-2), 127.7, 128.4, 129.7, 130.6, 131.2, 132.0, 132.9, 135.1 (aromatic carbons). IR (KBr) cm^{-1}: 3255 (NH), 1583 (C=N), 1335, 1146 (SO_2). *Anal.* Calcd for $C_{19}H_{19}N_5O_5S_2$: C, 49.45; H, 4.15; N, 15.17. Found: C, 49.51; H, 4.17; N, 15.24.

2-(*p*-Methylphenylaminosulfonylmethyl)-5-(4′-*p*-methylphenyl-4′,5′-dihydro-1′*H*-pyrazol-3′-ylsulfonylmethyl)-1,3,4-oxadiazole (**9b**): Pale yellow solid, yield 67%, mp 146—148 °C; ^{1}H-NMR ($CDCl_3$) δ: 2.22 and 2.26 (s, 6H, Ar–CH_3), 3.54 (dd, 1H, H_X, J_{AX}=6.2 Hz, J_{MX}=10.4 Hz), 4.12 (dd, 1H, H_M, J_{AM}=12.2 Hz), 4.50 (dd, 1H, H_A), 4.88 (s, 2H, SO_2–CH_2), 5.14 (s, 2H, C<u>H</u>$_2$–SO_2–NH), 7.14—7.67 (m, 8H, Ar–H), 9.93 (br s, 1H, NH), 10.44 (br s, 1H, NH–SO_2). ^{13}C-NMR ($CDCl_3$) δ: 21.1 and 21.6 (Ar–CH_3), 46.6 (SO_2–CH_2), 51.5 (CH_2–SO_2–NH), 52.9 (C-5′), 65.8 (C-4′), 151.4 (C-3′), 158.6 (C-5), 159.7 (C-2), 125.8, 126.6, 127.3, 128.4, 129.5, 130.3, 131.2, 134.8 (aromatic carbons). IR (KBr) cm^{-1}: 3257 (NH), 1587 (C=N), 1332, 1139 (SO_2). *Anal.* Calcd for $C_{21}H_{23}N_5O_5S_2$: C, 51.52; H, 4.74; N, 14.31. Found: C, 51.56; H, 4.77; N, 14.37.

2-(*p*-Chlorophenylaminosulfonylmethyl)-5-(4′-*p*-chlorophenyl-4′,5′-dihydro-1′*H*-pyrazol-3′-ylsulfonylmethyl)-1,3,4-oxadiazole (**9c**): Pale yellow solid, yield 73%, mp 152—154 °C; ^{1}H-NMR ($CDCl_3$) δ: 3.63 (dd, 1H, H_X, J_{AX}=6.8 Hz, J_{MX}=10.8 Hz), 4.24 (dd, 1H, H_M, J_{AM}=12.8 Hz), 4.59 (dd, 1H, H_A), 5.03 (s, 2H, SO_2–CH_2), 5.25 (s, 2H, C<u>H</u>$_2$–SO_2–NH), 7.21—7.87 (m, 8H, Ar–H), 10.14 (br s, 1H, NH), 10.62 (br s, 1H, NH–SO_2). ^{13}C-NMR ($CDCl_3$) δ: 47.9 (SO_2–CH_2), 52.4 (CH_2–SO_2–NH), 53.9 (C-5′), 66.7 (C-4′), 153.0 (C-3′), 158.4 (C-5), 159.0 (C-2), 126.7, 127.4, 128.3, 129.0, 130.1, 131.4, 132.7, 136.1 (aromatic carbons). IR (KBr) cm^{-1}: 3269 (NH), 1598 (C=N), 1340, 1152, (SO_2). *Anal.* Calcd for $C_{19}H_{17}Cl_2N_5O_5S_2$: C, 43.02; H, 3.23; N, 13.20. Found: C, 43.00; H, 3.22; N, 13.18.

2-(Phenylaminosulfonylmethyl)-5-(4′-phenyl-4′,5′-dihydro-1′*H*-pyrazol-3′-ylsulfonyl-methyl)-1,3,4-thiadiazole (**10a**): Pale yellow solid, yield 68%, mp 166—168 °C; ^{1}H-NMR ($CDCl_3$) δ: 3.54 (dd, 1H, H_X, J_{AX}=5.9 Hz, J_{MX}=9.8 Hz), 4.26 (dd, 1H, H_M, J_{AM}=11.8 Hz), 4.61 (dd, 1H, H_A), 4.92 (s, 2H, SO_2–CH_2), 5.19 (s, 2H, C<u>H</u>$_2$–SO_2–NH), 7.19—7.69 (m, 10H, Ar–H), 9.86 (br s, 1H, NH), 10.46 (br s, 1H, NH–SO_2). ^{13}C-NMR ($CDCl_3$) δ: 47.8 (SO_2–CH_2), 51.1 (CH_2–SO_2–NH), 52.8 (C-5′), 66.8 (C-4′), 151.4 (C-3′), 157.9 (C-5), 159.0 (C-2), 125.9, 126.5, 127.6, 128.7, 129.4, 130.2, 133.4, 136.6 (aromatic carbons). IR (KBr) cm^{-1}: 3270 (NH), 1601 (C=N), 1325,

1130 (SO_2). *Anal.* Calcd for $C_{19}H_{19}N_5O_4S_3$: C, 47.78; H, 4.01; N, 14.66. Found: C, 47.85; H, 4.14; N, 14.71.

2-(*p*-Methylphenylaminosulfonylmethyl)-5-(4′-*p*-methylphenyl-4′,5′-dihydro-1′*H*-pyrazol-3′-ylsulfonylmethyl)-1,3,4-thiadiazole (**10b**): Pale yellow solid, yield 65%, mp 174—176 °C; ^{1}H-NMR ($CDCl_3$) δ: 2.21 and 2.27 (s, 6H, Ar–CH_3), 3.48 (dd, 1H, H_X, J_{AX}=5.7 Hz, J_{MX}=9.6 Hz), 4.15 (dd, 1H, H_M, J_{AM}=11.7 Hz), 4.52 (dd, 1H, H_A), 4.81 (s, 2H, SO_2–CH_2), 5.13 (s, 2H, C$\underline{H}_2$–SO_2–NH), 7.14—7.67 (m, 8H, Ar–H), 9.78 (br s, 1H, NH), 10.35 (br s, 1H, NH–SO_2). ^{13}C-NMR ($CDCl_3$) δ: 21.5 and 22.1 (Ar-CH_3), 47.0 (SO_2–CH_2), 50.5 (CH_2–SO_2–NH), 52.4 (C-5′), 66.0 (C-4′), 151.0 (C-3′), 159.0 (C-5), 159.8 (C-2), 126.3, 127.5, 128.4, 129.5, 130.2, 132.8, 133.5, 135.5 (aromatic carbons). IR (KBr) cm^{-1}: 3268 (NH), 1588 (C=N), 1329, 1137 (SO_2). *Anal.* Calcd for $C_{21}H_{23}N_5O_4S_3$: C, 49.88; H, 4.58; N, 13.85. Found: C, 49.92; H, 4.56; N, 13.91.

2-(*p*-Chlorophenylaminosulfonylmethyl)-5-(4′-*p*-chlorophenyl-4′,5′-dihydro-1′*H*-pyrazol-3′-ylsulfonylmethyl)-1,3,4-thiadiazole (**10c**): Pale yellow solid, yield 72%, mp 182—184 °C; ^{1}H-NMR ($CDCl_3$) δ: 3.61 (dd, 1H, H_X, J_{AX}=6.2 Hz, J_{MX}=10.1 Hz), 4.29 (dd, 1H, H_M, J_{AM}=12.0 Hz), 4.64 (dd, 1H, H_A), 4.99 (s, 2H, SO_2–CH_2), 5.21 (s, 2H, C$\underline{H}_2$–SO_2–NH), 7.22—7.72 (m, 8H, Ar–H), 9.91 (br s, 1H, NH), 10.51 (br s, 1H, NH–SO_2). ^{13}C-NMR ($CDCl_3$) δ: 48.1 (SO_2–CH_2), 51.3 (CH_2–SO_2–NH), 53.5 (C-5′), 67.2 (C-4′), 152.3 (C-3′), 158.6 (C-5), 159.5 (C-2), 127.3, 128.5, 129.6, 130.1, 132.4, 133.8, 134.3, 137.1 (aromatic carbons). IR (KBr) cm^{-1}: 3281 (NH), 1607 (C=N), 1338, 1143 (SO_2). *Anal.* Calcd for $C_{19}H_{17}Cl_2N_5O_4S_3$: C, 41.76; H, 3.14; N, 12.82. Found: C, 41.82; H, 3.17; N, 12.87.

4-Amino-3-(phenylaminosulfonylmethyl)-5-(4′-phenyl-4′,5′-dihydro-1′*H*-pyrazol-3′-ylsulfonylmethyl)-1,2,4-triazole (**11a**): Yellow solid, yield 71%, mp 171—173 °C; ^{1}H-NMR (DMSO-d_6) δ: 3.64 (dd, 1H, H_X, J_{AX}=6.3 Hz, J_{MX}=10.4 Hz), 4.09 (dd, 1H, H_M, J_{AM}=12.1 Hz), 4.53 (dd, 1H, H_A), 5.09 (s, 2H, SO_2–CH_2), 5.24 (s, 2H, C$\underline{H}_2$–SO_2–NH), 5.69 (br s, 2H, NH_2), 7.17—7.59 (m, 10H, Ar–H), 9.30 (br s, 1H, NH), 10.07 (br s, 1H, NH–SO_2). ^{13}C-NMR (DMSO-d_6) δ: 45.9 (SO_2–CH_2), 50.5 (CH_2–SO_2–NH), 52.3 (C-5′), 65.9 (C-4′), 152.7 (C-3′), 159.2 (C-5), 159.7 (C-3), 127.2, 128.0, 128.9, 130.4, 131.3, 132.1, 134.2, 135.1 (aromatic carbons). IR (KBr) cm^{-1}: 3482, 3367 (NH_2), 3248 (NH), 1612 (C=N), 1310, 1138 (SO_2). *Anal.* Calcd for $C_{19}H_{21}N_7O_4S_2$: C, 47.99; H, 4.45; N, 20.62. Found: C, 47.97; H, 4.47; N, 20.70.

4-Amino-3-(*p*-methylphenylaminosulfonylmethyl)-5-(4′-*p*-methylphenyl-4′,5′-dihydro-1′*H*-pyrazol-3′-ylsulfonylmethyl)-1,2,4-triazole (**11b**): Pale yellow solid, yield 69%, mp 186—188 °C; ^{1}H-NMR (DMSO-d_6) δ: 2.23 and 2.28 (s, 6H, Ar–CH_3), 3.52 (dd, 1H, H_X, J_{AX}=6.0 Hz, J_{MX}=10.1 Hz), 4.03 (dd, 1H, H_M, J_{AM}=11.8 Hz), 4.48 (dd, 1H, H_A), 5.03 (s, 2H, SO_2–CH_2), 5.15 (s, 2H, C$\underline{H}_2$–SO_2–NH), 5.63 (br s, 2H, NH_2), 7.14—7.63 (m, 8H, Ar-H), 9.22 (br s, 1H, NH), 10.03 (br s, 1H, NH–SO_2). ^{13}C-NMR (DMSO-d_6) δ: 21.0 and 21.5 (Ar–CH_3), 45.1 (SO_2–CH_2), 50.1 (CH_2–SO_2–NH), 51.7 (C-5′), 65.4 (C-4′), 152.1 (C-3′), 158.6 (C-5), 159.4 (C-3), 126.0, 128.7, 129.4, 130.6, 132.1, 132.9, 133.6, 136.9 (aromatic carbons). IR (KBr) cm^{-1}: 3476, 3358 (NH_2), 3253 (NH), 1605 (C=N), 1313, 1134 (SO_2). *Anal.* Calcd for $C_{21}H_{25}N_7O_4S_2$: C, 50.08; H, 5.00; N, 19.47. Found: C, 50.02; H, 5.01; N, 19.57.

4-Amino-3-(*p*-chlorophenylaminosulfonylmethyl)-5-(4′-*p*-chlorophenyl-4′,5′-dihydro-1′*H*-pyrazol-3′-ylsulfonylmethyl)-1,2,4-triazole (**11c**): Pale yellow solid, yield 73%, mp 204—206 °C; ^{1}H-NMR (DMSO-d_6) δ: 3.68 (dd, 1H, H_X, J_{AX}=6.6 Hz, J_{MX}=10.4 Hz), 4.18 (dd, 1H, H_M, J_{AM}=12.5 Hz), 4.60 (dd, 1H, H_A), 5.15 (s, 2H, SO_2–CH_2), 5.28 (s, 2H, C$\underline{H}_2$–SO_2–NH), 5.74 (br s, 2H, NH_2), 7.20—7.76 (m, 8H, Ar–H), 9.42 (br s, 1H, NH), 10.16 (br s, 1H, NH–SO_2). ^{13}C-NMR (DMSO-d_6) δ: 46.2 (SO_2–CH_2), 50.8 (CH_2–SO_2–NH), 52.8 (C-5′), 66.6 (C-4′), 153.0 (C-3′), 157.8 (C-5), 158.7 (C-3), 127.1, 128.3, 129.5, 130.2, 131.4, 132.0, 132.9, 137.4 (aromatic carbons). IR (KBr) cm^{-1}: 3490, 3375 (NH_2), 3271 (NH), 1609 (C=N), 1326, 1145 (SO_2). *Anal.* Calcd for $C_{19}H_{19}Cl_2N_7O_4S_2$: C, 41.92; H, 3.52; N, 18.01. Found: C, 41.97; H, 3.56; N, 18.10.

General Procedure of Synthesis of 2-(Arylaminosulfonylmethyl)-5-(4′-aryl-1′*H*-pyrazol-3′-ylsulfonylmethyl)-1,3,4-oxadiazole (12a—c)/2-(Arylaminosulfonylmethyl)-5-(4′-aryl-1′*H*-pyrazol-3′-ylsulfonylmethyl)-1,3,4-thiadiazole (13a—c)/4-Amino-3-(arylamino-sulfonylmethyl)-5-(4′-aryl-1′*H*-pyrazol-3′-ylsulfonylmethyl)-1,2,4-triazole (14a—c) A solution of **9**/**10**/**11** (1 mmol) and chloranil (1.4 mmol) in xylene (10 ml) was refluxed for 25—30 h. Then, the reaction mixture was treated with 5% NaOH solution. The organic layer was separated and repeatedly washed with water. It was dried over anhydrous Na_2SO_4 and the solvent was removed on a rotary evaporator. The resultant solid was recrystallized from methanol.

2-(Phenylaminosulfonylmethyl)-5-(4′-phenyl-1′*H*-pyrazol-3′-ylsulfonylmethyl)-1,3,4-oxadiazole (**12a**): Yellow solid, yield 68%, mp 188—190 °C; ^{1}H-NMR ($CDCl_3$) δ: 5.07 (s, 2H, SO_2–CH_2), 5.31 (s, 2H, C$\underline{H}_2$–SO_2–NH), 6.52 (br s, 1H, NH), 6.84—7.77 (m, 11H, C'_5–H, Ar–H), 10.39 (br s, 1H, NH–SO_2). ^{13}C-NMR ($CDCl_3$) δ: 45.2 (SO_2–CH_2), 52.8 (CH_2–SO_2–NH), 133.9 (C-4′), 138.5 (C-5′), 148.1 (C-3′), 159.0 (C-5), 159.7 (C-2), 126.9, 127.4, 128.6, 129.7, 131.8, 132.8, 134.2, 138.5 (aromatic carbons). IR (KBr) cm^{-1}: 3283 (NH), 1642 (C=C), 1586 (C=N), 1323, 1139 (SO_2). *Anal.* Calcd for $C_{19}H_{17}N_5O_5S_2$: C, 49.66; H, 3.73; N, 15.24. Found: C, 49.70; H, 3.71; N, 15.32.

2-(*p*-Methylphenylaminosulfonylmethyl)-5-(4′-*p*-methylphenyl-1′*H*-pyrazol-3′-ylsulfonylmethyl)-1,3,4-oxadiazole (**12b**): Yellow solid, yield 66%, mp 196—198 °C; ^{1}H-NMR ($CDCl_3$) δ: 2.21 and 2.25 (s, 6H, Ar–CH_3), 5.03 (s, 2H, SO_2–CH_2), 5.22 (s, 2H, C$\underline{H}_2$–SO_2–NH), 6.47 (br s, 1H, NH), 6.82—7.72 (m, 9H, C'_5–H, Ar–H), 10.27 (br s, 1H, NH–SO_2). ^{13}C-NMR ($CDCl_3$) δ: 21.3 and 21.8 (Ar–CH_3), 45.0 (SO_2–CH_2), 52.3 (CH_2–SO_2–NH), 133.4 (C-4′), 138.0 (C-5′), 147.8 (C-3′), 158.7 (C-5), 159.6 (C-2), 126.3, 127.5, 128.6, 129.8, 131.4, 133.4, 134.3, 136.0 (aromatic carbons). IR (KBr) cm^{-1}: 3274 (NH), 1636 (C=C), 1579 (C=N), 1318, 1126 (SO_2). *Anal.* Calcd for $C_{21}H_{21}N_5O_5S_2$: C, 51.73; H, 4.34; N, 14.36. Found: C, 51.70; H, 4.35; N, 14.44.

2-(*p*-Chlorophenylaminosulfonylmethyl)-5-(4′-*p*-chlorophenyl-1′*H*-pyrazol-3′-ylsulfonyl-methyl)-1,3,4-oxadiazole (**12c**): Yellow solid, yield 72%, mp 208—210 °C; ^{1}H-NMR ($CDCl_3$) δ: 5.14 (s, 2H, SO_2–CH_2), 5.37 (s, 2H, C$\underline{H}_2$–SO_2–NH), 6.54 (br s, 1H, NH), 6.91—7.81 (m, 9H, C'_5–H, Ar–H), 10.44 (br s, 1H, NH–SO_2). ^{13}C-NMR ($CDCl_3$) δ: 46.3 (SO_2–CH_2), 53.0 (CH_2–SO_2–NH), 134.5 (C-4′), 139.2 (C-5′), 148.7 (C-3′), 158.6 (C-5), 159.5 (C-2), 127.1, 127.8, 129.3, 130.4, 131.6, 132.1, 133.5, 137.1 (aromatic carbons). IR (KBr) cm^{-1}: 3281 (NH), 1644 (C=C), 1592 (C=N), 1329, 1129 (SO_2). *Anal.* Calcd for $C_{19}H_{15}Cl_2N_5O_5S_2$: C, 43.19; H, 2.86; N, 13.25. Found: C, 43.23; H, 2.85; N, 13.32.

2-(Phenylaminosulfonylmethyl)-5-(4′-phenyl-1′*H*-pyrazol-3′-ylsulfonyl-methyl)-1,3,4-thiadiazole (**13a**): Pale yellow solid, yield 67%, mp 216—218 °C; ^{1}H-NMR ($CDCl_3$) δ: 5.11 (s, 2H, SO_2–CH_2), 5.27 (s, 2H, C$\underline{H}_2$–SO_2–NH), 6.50 (br s, 1H, NH), 6.95—7.86 (m, 11H, C'_5–H, Ar–H), 10.40 (br s, 1H, NH–SO_2). ^{13}C-NMR ($CDCl_3$) δ: 45.7 (SO_2–CH_2), 51.9 (CH_2–SO_2–NH), 134.3 (C-4′), 138.7 (C-5′), 148.5 (C-3′), 158.8 (C-5), 159.4 (C-2), 126.8, 127.5, 128.3, 129.5, 131.7, 132.8, 134.4, 138.3 (aromatic carbons). IR (KBr) cm^{-1}: 3266 (NH), 1639 (C=C), 1597 (C=N), 1338, 1134 (SO_2). *Anal.* Calcd for $C_{19}H_{17}N_5O_4S_3$: C, 47.99; H, 3.60; N, 14.73. Found: C, 48.05; H, 3.64; N, 14.77.

2-(*p*-Methylphenylaminosulfonylmethyl)-5-(4′-*p*-methylphenyl-1′*H*-pyrazol-3′-ylsulfonylmethyl)-1,3,4-thiadiazole (**13b**): Pale yellow solid, yield 69%, mp 226—228 °C; ^{1}H-NMR ($CDCl_3$) δ: 2.20 and 2.24 (s, 6H, Ar–CH_3), 5.07 (s, 2H, SO_2–CH_2), 5.23 (s, 2H, C$\underline{H}_2$–SO_2–NH), 6.46 (br s, 1H, NH), 6.91—7.75 (m, 9H, C'_5–H, Ar–H), 10.31 (br s, 1H, NH–SO_2). ^{13}C-NMR ($CDCl_3$) δ: 21.1 and 21.5 (Ar–CH_3), 45.5 (SO_2–CH_2), 51.6 (CH_2–SO_2–NH), 133.9 (C-4′), 138.0 (C-5′), 148.4 (C-3′), 158.2 (C-5), 159.0 (C-2), 126.0, 127.2, 128.9, 130.5, 131.6, 132.4, 134.6, 136.8 (aromatic carbons). IR (KBr) cm^{-1}: 3258 (NH), 1637 (C=C), 1601 (C=N), 1324, 1131 (SO_2). *Anal.* Calcd for $C_{21}H_{21}N_5O_4S_3$: C, 50.08; H, 4.20; N, 13.91. Found: C, 50.00; H, 4.23; N, 13.89.

2-(*p*-Chlorophenylaminosulfonylmethyl)-5-(4′-*p*-chlorophenyl-1′*H*-pyrazol-3′-ylsulfonyl-methyl)-1,3,4-thiadiazole (**13c**): Yellow solid, yield 71%, mp 235—237 °C; ^{1}H-NMR ($CDCl_3$) δ: 5.16 (s, 2H, SO_2–CH_2), 5.34 (s, 2H, C$\underline{H}_2$–SO_2–NH), 6.59 (br s, 1H, NH), 7.04—7.82 (m, 9H, C'_5–H, Ar–H), 10.45 (br s, 1H, NH–SO_2). ^{13}C-NMR ($CDCl_3$) δ: 46.4 (SO_2–CH_2), 52.5 (CH_2–SO_2–NH), 134.8 (C-4′), 139.4 (C-5′), 149.2 (C-3′), 158.9 (C-5), 159.4 (C-2), 127.3, 128.4, 129.7, 131.6, 132.4, 133.7, 134.8, 136.5 (aromatic carbons). IR (KBr) cm^{-1}: 3273 (NH), 1641 (C=C), 1608 (C=N), 1342, 1140 (SO_2). *Anal.* Calcd for $C_{19}H_{15}Cl_2N_5O_4S_3$: C, 41.91; H, 2.78; N, 12.86. Found: C, 41.97; H, 2.81; N, 12.95.

4-Amino-3-(phenylaminosulfonylmethyl)-5-(4′-phenyl-1′*H*-pyrazol-3′-ylsulfonylmethyl)-1,2,4-triazole (**14a**): Yellow solid, yield 73%, mp 220—222 °C; ^{1}H-NMR (DMSO-d_6) δ: 5.05 (s, 2H, SO_2–CH_2), 5.25 (s, 2H, C$\underline{H}_2$–SO_2–NH), 5.72 (br s, 2H, NH_2), 6.51 (br s, 1H, NH), 7.01—7.68 (m, 11H, C'_5–H, Ar–H), 10.27 (br s, 1H, NH–SO_2). ^{13}C-NMR (DMSO-d_6) δ: 47.0 (SO_2–CH_2), 51.3 (CH_2–SO_2–NH), 132.9 (C-4′), 139.0 (C-5′), 149.1 (C-3′), 158.5 (C-5), 159.2 (C-3), 126.1, 127.4, 129.2, 130.8, 131.6, 132.4, 133.5, 135.3 (aromatic carbons). IR (KBr) cm^{-1}: 3461, 3328 (NH_2), 3268 (NH), 1633 (C=C), 1615 (C=N), 1321, 1146 (SO_2). *Anal.* Calcd for $C_{19}H_{19}N_7O_4S_2$: C, 48.19; H, 4.04; N, 20.71. Found: C, 48.25; H, 4.05; N, 20.80.

4-Amino-3-(*p*-methylphenylaminosulfonylmethyl)-5-(4′-*p*-methylphenyl-1′*H*-pyrazol-3′-ylsulfonylmethyl)-1,2,4-triazole (**14b**): Yellow solid, yield 70%, mp 238—240 °C; ^{1}H-NMR (DMSO-d_6) δ: 2.21 and 2.27 (s, 6H,

Ar–CH_3), 4.99 (s, 2H, SO_2–CH_2), 5.16 (s, 2H, C$\underline{H}_2$–SO_2–NH), 5.67 (br s, 2H, NH_2), 6.48 (br s, 1H, NH), 6.91—7.70 (m, 9H, C_5'–H, Ar–H), 10.19 (br s, 1H, NH–SO_2). ^{13}C-NMR (DMSO-d_6) δ: 21.5 and 21.9 (Ar–CH_3), 46.7 (SO_2–CH_2), 50.9 (CH_2–SO_2–NH), 132.4 (C-4′), 138.6 (C-5′), 148.6 (C-3′), 158.7 (C-5), 159.5 (C-3), 127.2, 128.4, 129.9, 131.7, 132.6, 133.4, 135.4, 137.8 (aromatic carbons). IR (KBr) cm^{-1}: 3453, 3339 (NH_2), 3251 (NH), 1629 (C=C), 1606 (C=N), 1325, 1137 (SO_2). *Anal.* Calcd for $C_{21}H_{23}N_7O_4S_2$: C, 50.29; H, 4.62; N, 19.55. Found: C, 50.35; H, 4.65; N, 19.63.

4-Amino-3-(*p*-chlorophenylaminosulfonylmethyl)-5-(4′-*p*-chlorophenyl-1′*H*-pyrazol-3′-ylsulfonylmethyl)-1,2,4-triazole (**14c**): Yellow solid, yield 76%, mp 246—248 °C; ^{1}H-NMR (DMSO-d_6) δ: 5.11 (s, 2H, SO_2–CH_2), 5.31 (s, 2H, C$\underline{H}_2$–SO_2–NH), 5.79 (br s, 2H, NH_2), 6.53 (br s, 1H, NH), 7.06—7.89 (m, 9H, C_5'–H, Ar–H), 10.31 (br s, 1H, NH–SO_2). ^{13}C-NMR (DMSO-d_6) δ: 47.7 (SO_2–CH_2), 51.9 (CH_2–SO_2–NH), 133.7 (C-4′), 139.5 (C-5′), 149.5 (C-3′), 159.1 (C-5), 159.7 (C-3), 127.4, 128.7, 129.7, 131.6, 132.5, 133.9, 135.4, 138.2 (aromatic carbons). IR (KBr) cm^{-1}: 3469, 3334 (NH_2), 3223 (NH), 1637 (C=C), 1611 (C=N), 1319, 1142 (SO_2). *Anal.* Calcd for $C_{19}H_{17}Cl_2N_7O_4S_2$: C, 42.07; H, 3.16; N, 18.08. Found: C, 42.02; H, 3.15; N, 18.16.

Antimicrobial Testing The compounds **3**—**14** were dissolved in dimethyl sulfoxide (DMSO) at different concentrations of 50 and 100 μg. Bacterial strains *Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and fungi *Penicillium chrysogenum*, *Curvularia lunata* and *Aspergillus niger* were obtained from Department of Microbiology, S.V. University, Tirupati, India.

Antibacterial and Antifungal Assays The *in vitro* antimicrobial studies were carried out by agar well diffusion method against test organisms.[29,30] Nutrient broth (NB) plates were swabbed with 24 h old broth culture (100 μl) of test bacteria. Using the sterile cork borer, wells (6 mm) were made into each petriplate. The compounds were dissolved in DMSO of 5 mg/ml and from this 10 μl and 20 μl (50, 100 μg/well) were added into the wells by using sterile pipettes. Simultaneously the standard antibiotics, Chloramphenicol for antibacterial activity and Ketoconazole for antifungal activity (as positive control) were tested against the pathogens. The samples were dissolved in DMSO which showed no zone of inhibition acts as negative control. The plates were incubated at 37 °C for 24 h for bacteria and at 28 °C for 48 h for fungi. After appropriate incubation, the diameter of zone of inhibition of each well was measured. Duplicates were maintained and the average values were calculated for eventual antibacterial activity.

Broth dilution test is used to determine minimum inhibitory concentration (MIC) of the above mentioned samples.[31,32] Freshly prepared nutrient broth was used as diluents. The 24 h old culture of the test bacteria *Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* and the test fungi *Penicillium chrysogenum*, *Curvularia lunata* and *Aspergillus niger* were diluted 100 folds in nutrient broth (100 μl bacterial cultures in 10 ml NB). The stock solution of the synthesized compounds was prepared in DMSO by dissolving 5 mg of the compound in 1 ml of DMSO. Increasing concentrations of the test samples (1.25, 2.5, 5, 10, 20, 40 μl of stock solution contains 6.25, 12.5, 25, 50, 100, 200 μg of the compounds) were added to the test tubes containing the bacterial and fungal cultures. All the tubes were incubated at 37 °C for 24 h for bacteria and at 28 °C for 48 h for fungi. The tubes were examined for visible turbidity and using NB as control. Control without test samples and with solvent was assayed simultaneously. The lowest concentration that inhibited visible growth of the tested organisms was recorded as MIC.

To determine the MBC[33] and MFC[34] for each set of test tubes in the MIC determination, a loopful of broth was collected from those tubes which did not show any growth and inoculated on sterile nutrient broth (for bacteria) and PDA (for fungi) by streaking. Plates inoculated with bacteria and fungi were incubated at 37 °C for 24 h and at 28 °C for 48 h, respectively. After incubation, that concentration was noted as MBC (for bacteria) or MFC (for fungi) at which no visible growth was observed.

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