Aroylethenesulfonylacetic Acid Methyl Ester—A Synthone for Novel Sulfone Linked Bis Heterocycles

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Novel sulfone linked bis heterocycles containing two different heterocyclic rings viz., pyrazoline in combination with thiadiazole, oxadiazole and triazole were synthesized and studied their antimicrobial activity.

Key words bis heterocycle; thiadiazole; oxadiazole; triazole; antimicrobial activity

Amongst different heterocyclic systems five membered heterocycles represent a class of compounds of biological significance. In fact, azoles occupy a unique place in the realm of natural and synthetic organic chemistry. These compounds have intrinsic biological activities and constitute the structural feature of many bioactive compounds. 1,3,4-Oxadiazoles exhibit a broad spectrum of biological activities such as anti human immunodeficiency virus (HIV), antibacterial and antifungal.^{1,2)} Besides, triazoles possess antifungal activity and reduce toxicity when compared with the imidazole antifungals.^{3–8)} Flucanazole and itraconazole are most frequently used antifungal drugs. 1,3,4-Thiadiazoles are associated with diverse biological activities probably due to toxophoric $-N=C-S$ group.^{9–12)} In fact, the advent of sulfur drugs and the discovery of mesoionic compounds greatly accelerated the rate of progress in the field of thiadiazoles. 5-Unsubstituted 1,3,4-thiadiazoles are used as intermediates in the synthesis of therapeutically potent antibiotic cefazolin.¹³⁾ In addition, pyrazolines have gained importance due to their various chemotherapeutic properties. Celecoxib, a pyrazole derivative is now widely used in the market as an anti-inflammatory drug.¹⁴⁾ Hence, it is considered worthwhile to prepare molecules having pyrazoline and oxadiazole/thiadiazole/triazole rings.

Chemistry The general synthetic pathway discussed hereafter is depicted in Charts 1 and 2. The synthetic intermediate aroylethenesulfonylacetic acid (**3**) is prepared by the condensation of 1-aryl-2-chloroethene (**1**) with mercaptoacetic acid in the presence of sodium hydroxide in methanol followed by oxidation with hydrogen peroxide in acetic acid. The ¹H-NMR spectrum of **3a** showed a singlet at 4.38 ppm for methylene protons and two doublets at 7.66, 7.96 ppm for olefinic protons. The downfield shift is assigned to the one adjacent to SO₂ group. The methyl ester of **3** (**4**) is prepared by treating **3** with methanol in conc. H₂SO₄. When aroylethenesulfonylacetic acid methyl ester **4** is made to react with hydrazine hydrate instead of the expected acid hydrazide, a mixture of products are obtained. The two are separated by column chromatography and identified as 1,1-dioxo-6-phenacyl-[1,4,5]thiadiazinan-3-one (**5**) and (3-aryl-4,5-dihydro-1H-pyrazole-5-sulfonyl)-acetic acid methyl ester (**6**) by spectral parameters. The ¹H-NMR spectrum of **5a** showed a singlet, a doublet and a multiplet at 4.28, 3.50 and 4.57–4.59 ppm for H-2, CO–CH₂ and H-6 respectively. Two broad singlets are observed at 2.82 and 8.50 ppm due to NH which disappeared on deuteration. The downfield absorption

is assigned to the one adjacent to C=O group. However, the ¹H-NMR spectrum of **6a** displayed a singlet at 3.72 ppm for methoxy protons of carbomethoxy group, another singlet at 4.39 ppm for SO₂–CH₂, a multiplet at 4.62–4.65 for H-5 and a doublet at 3.53 ppm for H-4. In order to get the desired bis heterocycles, the olefinic moiety in **4** is used to develop pyrazoline ring by 1,3-dipolar cycloaddition of diazomethane. In 1,2-disubstituted ethylenes bearing two vicinal electron withdrawing substituents a regioisomeric mixture of cycloadducts are expected. However, the reaction of 1-aryl-2-aroylethylenes with diazomethane and its derivatives produced exclusively 3-aryl-4-aryl-2-pyrazolines.¹⁵⁾ Similarly, the cycloaddition of diazomethane to 1-aryl-2-styrylsulfonyl-ethenes gave 3-aryl-4-styrylsulfonyl-2-pyrazolines.¹⁶⁾ The treatment of **4** with diazomethane in the presence of Et₃N at –20 °C for 48 h gave a solid which is identified as (3-aryl-4,5-dihydro-1H-pyrazole-4-sulfonyl)-acetic acid methyl ester (**7**). The addition of diazomethane to **4** may produce regioisomers. However, we have isolated only one pure regioisomer. A small amount of the other isomer if any, formed could not be isolated by this process. The ¹H-NMR spectrum of **7a** shows an AMX splitting pattern for the pyrazoline ring protons thus exhibiting three double doublets at 5.07 (H_A), 4.53 (H_M) and 3.94 ppm (H_X) respectively, in addition to the signals due to methylene and methoxy protons. The ¹³C-NMR spectrum of **7a** displayed a signal at 185.6 ppm due to carbonyl carbon, a characteristic signal for carbonyl carbon adjacent to an imine carbon. The articulation of oxadiazole, thiadiazole and triazole rings is made by the use of ester moiety. The compound **7** on reaction with hydrazine hydrate gave the corresponding acid hydrazide **8**. The

Chart 1

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Chart 2

Table 1. The *in Vitro* Antibacterial Activity of **10**–**12**

Compound	Concentration (μg)	Zone of inhibition (mm)			
		Gram-positive bacteria		Gram-negative bacteria	
		<i>S. aureus</i>	<i>B. subtilis</i>	<i>E. coli</i>	<i>K. pneumoniae</i>
10a	100	20	22	17	19
	200	27	25	20	22
10b	100	15	18	16	19
	200	17	19	20	21
10c	100	25	22	19	23
	200	30	25	22	28
11a	100	12	11	14	13
	200	15	13	17	16
11b	100	11	12	11	11
	200	14	16	14	13
11c	100	14	14	10	11
	200	17	18	12	13
12a	100	28	31	22	21
	200	33	35	26	25
12b	100	21	22	20	21
	200	26	27	23	24
12c	100	32	34	23	26
	200	35	28	25	27
Chloramphenicol	100	35	38	40	42
	200	39	41	44	45

^1H -NMR spectrum of **8a** displayed broad signals in the regions 10.49 and 5.15 ppm for NH and NH_2 which disappeared on deuteration in addition to signals due to other pro-

tons. The potassium dithiocarbazate of acid hydrazide (**9**) is prepared from **8** on treatment with carbon disulfide in the presence of potassium hydroxide under ultrasonic conditions.

This on reflux in acetic acid cyclized to 5'-(3-aryl-4,5-dihydro-1*H*-pyrazole-4-sulfonylmethyl)-[1',3',4']thiadiazole-2'-thiol (**10**). Acid catalysed hydrolysis of **9** resulted in 5'-(3-aryl-4,5-dihydro-1*H*-pyrazole-4-sulfonylmethyl)-[1',3',4']oxadiazole-2'-thiol (**11**). Further, the compound **9** on treatment with hydrazine hydrate produced 4'-amino-5'-(3-aryl-4,5-dihydro-1*H*-pyrazole-4-sulfonylmethyl)-[1',2',4']triazole-3'-thiol (**12**) (Chart 2). The ¹H-NMR spectra of **10**–**12** displayed a singlet in the region 10.24–10.35 ppm for SH besides signals due to pyrazoline ring and methylene protons. In addition to these, **12a** showed a broad singlet at 5.64 ppm for NH₂ which disappeared on deuteration. The structures of **5**–**7** and **10**–**12** are further confirmed by ¹³C-NMR spectra.

Antimicrobial Testing The compounds **10**–**12** were tested for *in vitro* antimicrobial activity at two different concentrations 100 and 200 µg per disc. The antibacterial activity was screened against *Staphylococcus aureus*, *Bacillus subtilis* (Gram-positive bacteria) and *Escherichia coli*, *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 their antifungal activity against *Fusarium solani*, *Curvularia lunata* and *Aspergillus niger* using ketoconazole as standard drug. Fungi cultures were grown on potato dextrose agar medium (PDA) at 25 °C for 3 d. The spore suspension was adjusted to 10⁶

pores ml⁻¹ at a mg ml⁻¹ concentration by the Vincent and Vincent method.¹⁷⁾

The results of the compounds of preliminary antimicrobial testing are shown in Tables 1 and 2. The results revealed that the inhibitory activity against Gram-positive bacteria was higher than Gram-negative bacteria. The oxadiazole derivatives **11a**–**c** were displayed least activity. The compounds **10a**, **10c**, **12a** and **12c** showed excellent activity against Gram-positive bacteria (inhibitory zone >25 mm) and good activity against Gram-negative bacteria (inhibitory zone >20 mm). All the test compounds showed moderate to high inhibitory effect towards tested fungi. The presence of chloro substituent at position of the arylsulfonyl moiety enhances the antimicrobial activity.

The minimal inhibitory concentration (MIC) values were determined as the lowest concentration that completely inhibited visible growth of the microorganisms (Table 3). The structure–antimicrobial activity relationship of the synthesized compounds revealed that the compounds having pyrazoline with oxadiazole exhibited least activity when compared with compounds having pyrazoline with thiadiazole and triazole moieties. Among the substituents on the aryl group, 4-chlorophenyl derivatives were the most activity. The maximum activity was observed with the compounds **10c**, **12a** and **12c**.

Conclusion

A new class of sulfone linked bis heterocycles, 5'-(3-aryl-4,5-dihydro-1*H*-pyrazole-4-sulfonylmethyl)-[1',3',4']thiadiazole-2'-thiol (**10**), 5'-(3-aryl-4,5-dihydro-1*H*-pyrazole-4-sulfonylmethyl)-[1',3',4']oxadiazole-2'-thiol (**11**) and 4'-amino-5'-(3-aryl-4,5-dihydro-1*H*-pyrazole-4-sulfonylmethyl)-[1',2',4']triazole-3'-thiol (**12**) were developed by the regiospecific 1,3-dipolar cycloaddition of diazomethane to arylenesulfonylacetic acid methyl ester (**4**) followed by functionalization of ester moiety with appropriate reagents. The antimicrobial testing showed that the compounds having pyrazoline with thiadiazole and triazole units possess greater antibacterial activity.

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 recorded on a Thermo Nicolet IR 200 FT-IR spectrometer as KBr pellets and the wave numbers were given in cm⁻¹. The ¹H-NMR spectra were recorded in CDCl₃/DMSO-*d*₆ on a Varian EM-360 spectrometer (300 MHz). The ¹³C-NMR spectra were recorded in CDCl₃/DMSO-*d*₆ on a Varian VXR spectrometer operating at 75.5 MHz. All chemical shifts are reported in δ (ppm) using TMS as an internal standard. The microanalyses were performed on Perkin-Elmer 240C elemental analyzer. The mass spectra were recorded on Finnigan Mat 1210 B and Waters Micromass Quattro Micro API at 70 eV with an emission current of 100 µA. The starting compound 1-aryl-2-

Table 2. The *in Vitro* Antifungal Activity of **10**–**12**

Compound	Concentration (µg)	Zone of inhibition (mm)		
		<i>F. solani</i>	<i>C. lunata</i>	<i>A. niger</i>
10a	100	24	28	26
	200	27	30	31
10b	100	23	24	22
	200	27	25	26
10c	100	26	25	26
	200	30	27	29
11a	100	19	15	17
	200	20	22	21
11b	100	15	14	18
	200	20	18	23
11c	100	17	18	14
	200	22	22	17
12a	100	33	34	31
	200	35	36	37
12b	100	27	28	32
	200	32	34	35
12c	100	36	38	34
	200	39	42	36
Ketoconazole	100	38	41	36
	200	42	44	39

Table 3. Minimal Inhibitory Concentration of **10c**, **12a** and **12c**

Compound	Minimal inhibitory concentration (MIC), µg/ml						
	<i>S. aureus</i>	<i>B. subtilis</i>	<i>E. coli</i>	<i>K. pneumoniae</i>	<i>F. solani</i>	<i>C. lunata</i>	<i>A. niger</i>
10c	100	200	200	200	100	100	200
12a	50	100	100	100	100	100	100
12c	25	50	50	50	50	25	25
Chloramphenicol	6.25	6.25	6.25	12.5	—	—	—
Ketoconazole	—	—	—	—	12.5	6.25	6.25

chloroethene (**1**) was prepared according to literature procedure.¹⁸⁾

General Procedure of Synthesis of Aroylthienemercapto Acetic Acid (2a—c) To a solution of sodium hydroxide (0.002 mol) in methanol (10 ml), mercaptoacetic acid (0.001 mol) was added dropwise. To this, compound **1** (0.001 mol) was added in portions and the reaction mixture was stirred at 0 °C for 3—4 h. The contents were poured onto crushed ice and neutralized with dil. HCl. The reaction mixture was extracted with ethyl acetate. The solvent when removed under reduced pressure gave the compound **2**.

Benzoylthienemercapto Acetic Acid (2a): White solid, yield 71%, mp 34—36 °C; IR (KBr) cm^{-1} : 3200 (OH), 1725 (C=O), 1585 (C=C). $^1\text{H-NMR}$ (CDCl_3) δ : 3.74 (s, 2H, CH_2), 7.68 (d, 1H, H_B , $J=13.7$ Hz), 7.93 (d, 1H, H_A , $J=13.7$ Hz), 7.46—7.84 (m, 5H, Ar-H), 9.91 (brs, 1H, OH); $^{13}\text{C-NMR}$ (CDCl_3) δ : 53.4 (CH_2), 137.8 (COCH), 143.8 (CHS), 171.9 (COOH), 184.1 (ArCO), 128.7, 131.1, 132.6, 135.5.

4-Methylbenzoylthienemercaptoacetic Acid (2b): White solid, yield 76%, mp 45—47 °C; IR (KBr) cm^{-1} : 3214 (OH), 1722 (C=O), 1581 (C=C). $^1\text{H-NMR}$ (CDCl_3) δ : 2.27 (s, 3H, Ar- CH_3), 3.70 (s, 2H, CH_2), 7.71 (d, 1H, H_B , $J=13.9$ Hz), 7.95 (d, 1H, H_A , $J=13.9$ Hz), 7.38—7.82 (m, 4H, Ar-H), 10.1 (brs, 1H, OH); $^{13}\text{C-NMR}$ (CDCl_3) δ : 23.2 (Ar- CH_3), 53.8 (CH_2), 137.2 (COCH), 143.3 (CHS), 170.5 (COOH), 183.5 (ArCO), 127.6, 130.4, 133.1, 139.5.

4-Chlorobenzoylthienemercaptoacetic Acid (2c): White solid, yield 74%, mp 67—69 °C; IR (KBr) cm^{-1} : 3218 (OH), 1714 (C=O), 1574 (C=C). $^1\text{H-NMR}$ (CDCl_3) δ : 3.79 (s, 2H, CH_2), 7.74 (d, 1H, H_B , $J=13.5$ Hz), 7.98 (d, 1H, H_A , $J=13.5$ Hz), 7.54—7.89 (m, 4H, Ar-H), 9.82 (brs, 1H, OH); $^{13}\text{C-NMR}$ (CDCl_3) δ : 54.1 (CH_2), 138.1 (COCH), 144.2 (CHS), 171.4 (COOH), 184.2 (ArCO), 128.4, 130.6, 132.4, 141.5.

General Procedure of Synthesis of Aroylthienesulfonylacetic Acid (3a—c) The compound **2** (0.001 mol) was subjected to oxidation with 30% hydrogen peroxide (2 ml) in glacial acetic acid (6.5 ml). The contents were stirred at 0 °C for 4 h and kept aside for 36 h. The reaction mixture was poured onto crushed ice. The solid separated was filtered, dried and recrystallized from water.

Benzoylthienesulfonylacetic Acid (3a): White solid, 88% yield, mp 132—134 °C; IR (KBr) cm^{-1} : 3221 (OH), 1727 (C=O), 1584 (C=C), 1130, 1326 (SO_2). $^1\text{H-NMR}$ (CDCl_3) δ : 4.38 (s, 2H, CH_2), 7.66 (d, 1H, H_B , $J=14.2$ Hz), 7.96 (d, 1H, H_A , $J=14.2$ Hz), 7.56—7.88 (m, 5H, Ar-H), 9.68 (brs, 1H, OH); $^{13}\text{C-NMR}$ (CDCl_3) δ : 56.8 (CH_2), 138.7 (COCH), 141.8 (CHSO_2), 172.8 (COOH), 182.4 (ArCO), 128.4, 129.4, 132.6, 134.4.

4-Methylbenzoylthienesulfonylacetic Acid (3b): White solid, yield 85%, mp 125—127 °C; IR (KBr) cm^{-1} : 3224 (OH), 1714 (C=O), 1568 (C=C), 1132, 1314 (SO_2). $^1\text{H-NMR}$ (CDCl_3) δ : 2.24 (s, 3H, Ar- CH_3), 4.40 (s, 2H, CH_2), 7.63 (d, 1H, H_B , $J=14.4$ Hz), 7.92 (d, 1H, H_A , $J=14.4$ Hz), 7.42—7.80 (m, 4H, Ar-H), 9.92 (brs, 1H, OH); $^{13}\text{C-NMR}$ (CDCl_3) δ : 24.2 (Ar- CH_3), 57.2 (CH_2), 137.6 (COCH), 142.3 (CHSO_2), 172.3 (COOH), 181.3 (ArCO), 128.2, 129.2, 131.9, 135.4.

4-Chlorobenzoylthienesulfonylacetic Acid (3c): White solid, yield 87%, mp 151—153 °C; IR (KBr) cm^{-1} : 3218 (OH), 1724 (C=O), 1564 (C=C), 1138, 1336 (SO_2). $^1\text{H-NMR}$ (CDCl_3) δ : 4.42 (s, 2H, CH_2), 7.69 (d, 1H, H_B , $J=14.6$ Hz), 7.98 (d, 1H, H_A , $J=14.6$ Hz), 7.52—7.87 (m, 4H, Ar-H), 9.96 (brs, 1H, OH); $^{13}\text{C-NMR}$ (CDCl_3) δ : 56.5 (CH_2), 138.1 (COCH), 142.6 (CHSO_2), 173.2 (COOH), 179.6 (ArCO), 128.1, 129.6, 132.3, 134.2.

General Procedure of Synthesis of Aroylthienesulfonylacetic Acid Methyl Ester (4a—c) A solution of compound **3** (0.001 mol) in methanol (10 ml) and sulfuric acid (2 ml) was refluxed for 5—7 h. The contents were cooled and poured onto crushed ice. The solid separated was filtered, dried and recrystallized from methanol.

Benzoylthienesulfonylacetic Acid Methyl Ester (4a): White crystals, yield 85%, mp 94—96 °C; IR (KBr) cm^{-1} : 1746 (CO_2Me), 1668 (C=O), 1579 (C=C), 1142, 1316 (SO_2). $^1\text{H-NMR}$ (CDCl_3) δ : 3.78 (s, 3H, OCH_3), 4.36 (s, 2H, CH_2), 7.65 (d, 1H, H_B , $J=13.9$ Hz), 7.91 (d, 1H, H_A , $J=13.9$ Hz), 7.36—7.52 (m, 5H, Ar-H); $^{13}\text{C-NMR}$ (CDCl_3) δ : 53.1 (OCH_3), 59.6 (CH_2), 138.4 (COCH), 145.6 (CHSO_2), 168.1 (CO_2CH_3), 182.4 (ArCO), 130.5, 132.3, 137.5, 139.4. *Anal.* Calcd for $\text{C}_{12}\text{H}_{12}\text{O}_5\text{S}$: C, 53.72; H, 4.51; Found: C, 53.78; H 4.49.

4-Methylbenzoylthienesulfonylacetic Acid Methyl Ester (4b): White crystals, yield 89%, mp 101—103 °C; IR (KBr) cm^{-1} : 1748 (CO_2Me), 1662 (C=O), 1574 (C=C), 1128, 1341 (SO_2). $^1\text{H-NMR}$ (CDCl_3) δ : 2.28 (s, 3H, Ar- CH_3), 3.72 (s, 3H, OCH_3), 4.32 (s, 2H, CH_2), 7.62 (d, 1H, H_B , $J=13.7$ Hz), 7.88 (d, 1H, H_A , $J=13.7$ Hz), 7.32—7.54 (m, 4H, Ar-H); $^{13}\text{C-NMR}$ (CDCl_3) δ : 23.1 (Ar- CH_3), 53.4 (OCH_3), 58.1 (CH_2), 138.1 (COCH), 146.1 (CHSO_2), 167.4 (CO_2CH_3), 181.3 (ArCO), 129.4, 131.6, 136.3, 138.4. *Anal.* Calcd for $\text{C}_{13}\text{H}_{14}\text{O}_5\text{S}$: C, 55.31; H, 5.00; Found: C, 55.34; H 5.02.

4-Chlorobenzoylthienesulfonylacetic Acid Methyl Ester (4c): White crystals, yield 87%, mp 124—126 °C; IR (KBr) cm^{-1} : 1752 (CO_2Me), 1669 (C=O), 1568 (C=C), 1149, 1325 (SO_2). $^1\text{H-NMR}$ (CDCl_3) δ : 3.75 (s, 3H, OCH_3), 4.38 (s, 2H, CH_2), 7.69 (d, 1H, H_B , $J=14.2$ Hz), 7.94 (d, 1H, H_A , $J=14.2$ Hz), 7.48—7.72 (m, 4H, Ar-H); $^{13}\text{C-NMR}$ (CDCl_3) δ : 53.8 (OCH_3), 58.9 (CH_2), 138.9 (COCH), 147.3 (CHSO_2), 168.6 (CO_2CH_3), 181.6 (ArCO), 128.9, 131.4, 135.8, 137.4. *Anal.* Calcd for $\text{C}_{12}\text{H}_{11}\text{ClO}_5\text{S}$: C, 47.61; H, 3.66; Found: C, 47.55; H, 3.69.

General Procedure of Synthesis of 1,1-Dioxo-6-phenacyl-[1,4,5]thiadiazinan-3-one (5a—c) and (3-Aryl-4,5-dihydro-1H-pyrazole-5-sulfonyl)-acetic Acid Methyl Ester (6a—c) A mixture of **4** (0.0025 mol), hydrazine hydrate (0.005 mol) and methanol (15 ml) was refluxed for 8—10 h and cooled. The solid separated was filtered and dried. It was purified by column chromatography (hexane—ethyl acetate, 3 : 1).

1,1-Dioxo-6-phenacyl-[1,4,5]thiadiazinan-3-one (5a): White crystals, yield 26%, mp 102—104 °C; IR (KBr) cm^{-1} : 3284 (NH), 1682 (C=O), 1652 (NHCO), 1132, 1334 (SO_2). $^1\text{H-NMR}$ ($\text{DMSO}-d_6$) δ : 2.82 (brs, 1H, NH), 3.50 (d, 2H, COCH_2), 4.28 (s, 2H, H-2), 4.57—4.59 (m, 1H, H-6), 7.38—7.84 (m, 5H, Ar-H), 8.50 (s, 1H, CONH); $^{13}\text{C-NMR}$ ($\text{DMSO}-d_6$) δ : 36.2 (CH_2), 59.4 (C-2), 72.8 (C-6), 172.6 (CONH), 198.6 (ArCO), 127.7, 130.2, 133.1, 136.5; MS: $m/z=268$ (M^+). *Anal.* Calcd for $\text{C}_{11}\text{H}_{12}\text{N}_2\text{O}_4\text{S}$: C, 49.24; H, 4.51; N, 10.44; Found: C, 49.20; H, 4.55; N, 10.55.

1,1-Dioxo-6-(4-methylphenacyl)-[1,4,5]thiadiazinan-3-one (5b): White crystals, yield 16%, mp 97—99 °C; IR (KBr) cm^{-1} : 3286 (NH), 1678 (C=O), 1654 (NHCO), 1130, 1332 (SO_2). $^1\text{H-NMR}$ ($\text{DMSO}-d_6$) δ : 2.25 (s, 3H, Ar- CH_3), 2.78 (brs, 1H, NH), 3.48 (d, 2H, COCH_2), 4.27 (s, 2H, H-2), 4.54—4.57 (m, 1H, H-6), 7.36—7.85 (m, 4H, Ar-H), 8.47 (s, 1H, CONH); $^{13}\text{C-NMR}$ ($\text{DMSO}-d_6$) δ : 23.6 (Ar- CH_3), 35.8 (CH_2), 59.1 (C-2), 71.9 (C-6), 169.3 (CONH), 198.3 (C=O), 128.4, 130.5, 134.2, 136.8. *Anal.* Calcd for $\text{C}_{12}\text{H}_{14}\text{N}_2\text{O}_4\text{S}$: C, 51.05; H, 5.00; N, 9.92; Found: C, 51.16; H, 5.06; N, 9.99.

1,1-Dioxo-6-(4-chlorophenacyl)-[1,4,5]thiadiazinan-3-one (5c): White crystals, yield 24%, mp 135—137 °C; IR (KBr) cm^{-1} : 3286 (NH), 1684 (C=O), 1656 (NHCO), 1136, 1338 (SO_2). $^1\text{H-NMR}$ ($\text{DMSO}-d_6$) δ : 2.82 (brs, 1H, NH), 3.53 (d, 2H, COCH_2), 4.31 (s, 2H, H-2), 4.55—4.58 (m, 1H, H-6), 7.44—7.91 (m, 4H, Ar-H), 8.44 (s, 1H, CONH); $^{13}\text{C-NMR}$ ($\text{DMSO}-d_6$) δ : 37.1 (CH_2), 58.5 (C-2), 72.6 (C-6), 171.8 (CONH), 197.8 (C=O), 128.2, 131.4, 133.7, 135.9. *Anal.* Calcd for $\text{C}_{11}\text{H}_{11}\text{ClN}_2\text{O}_4\text{S}$: C, 43.64; H, 3.66; N, 9.25; Found: C, 43.72; H, 3.59; N, 9.32.

(3-Phenyl-4,5-dihydro-1H-pyrazole-5-sulfonyl)-acetic Acid Methyl Ester (6a): Yellow solid, yield 62%, mp 142—144 °C; IR (KBr) cm^{-1} : 3290 (NH), 1742 (C=O), 1558 (C=N), 1125, 1336 (SO_2). $^1\text{H-NMR}$ (CDCl_3) δ : 3.53 (d, 2H, H-4), 3.72 (s, 3H, OCH_3), 4.39 (s, 2H, SO_2CH_2), 4.62—4.65 (m, 1H, H-5), 7.20—7.69 (m, 5H, Ar-H), 10.22 (brs, 1H, NH); $^{13}\text{C-NMR}$ (CDCl_3) δ : 32.8 (C-4), 47.5 (SO_2CH_2), 52.2 (OCH_3), 67.2 (C-5), 152.2 (C-3), 161.8 (C=O), 129.5, 130.4, 131.5, 133.2; MS: $m/z=282$ (M^+). *Anal.* Calcd for $\text{C}_{12}\text{H}_{14}\text{N}_2\text{O}_4\text{S}$: C, 51.05; H, 5.00; N, 9.92; Found: C, 51.02; H, 5.06; N, 9.86.

(3-(4-Methylphenyl)-4,5-dihydro-1H-pyrazole-5-sulfonyl)-acetic Acid Methyl Ester (6b): Yellow solid, yield 69%, mp 158—160 °C; IR (KBr) cm^{-1} : 3288 (NH), 1748 (C=O), 1552 (C=N), 1122, 1343 (SO_2). $^1\text{H-NMR}$ (CDCl_3) δ : 2.32 (s, 3H, Ar- CH_3), 3.49 (d, 2H, H-4), 3.70 (s, 3H, OCH_3), 4.34 (s, 2H, SO_2CH_2), 4.60—4.64 (m, 1H, H-5), 7.19—7.74 (m, 4H, Ar-H), 10.18 (brs, 1H, NH); $^{13}\text{C-NMR}$ (CDCl_3) δ : 23.3 (Ar- CH_3), 32.6 (C-4), 46.3 (SO_2CH_2), 51.8 (OCH_3), 67.1 (C-5), 151.9 (C-3), 162.5 (C=O), 129.2, 130.8, 131.5, 132.6. *Anal.* Calcd for $\text{C}_{13}\text{H}_{16}\text{N}_2\text{O}_4\text{S}$: C, 52.69; H, 5.44; N, 9.45; Found: C, 52.74; H, 5.51; N, 9.51.

(3-(4-Chlorophenyl)-4,5-dihydro-1H-pyrazole-5-sulfonyl)-acetic Acid Methyl Ester (6c): Yellow solid, yield 65%, mp 149—151 °C; IR (KBr) cm^{-1} : 3310 (NH), 1755 (C=O), 1554 (C=N), 1140, 1335 (SO_2). $^1\text{H-NMR}$ (CDCl_3) δ : 3.57 (d, 2H, H-4), 3.75 (s, 3H, OCH_3), 4.38 (s, 2H, SO_2CH_2), 4.65—4.68 (m, 1H, H-5), 7.25—7.78 (m, 4H, Ar-H), 10.25 (brs, 1H, NH); $^{13}\text{C-NMR}$ (CDCl_3) δ : 32.9 (C-4), 47.9 (SO_2CH_2), 52.7 (OCH_3), 67.5 (C-5), 151.9 (C-3), 162.1 (C=O), 129.2, 130.3, 131.6, 132.3. *Anal.* Calcd for $\text{C}_{12}\text{H}_{13}\text{ClN}_2\text{O}_4\text{S}$: C, 45.50; H, 4.14; N, 8.84; Found: C, 45.59; H, 4.20; N, 8.89.

General Procedure of Synthesis of (3-Aroyl-4,5-dihydro-1H-pyrazole-4-sulfonyl)-acetic Acid Methyl Ester (7a—c) To a cooled solution of **4** (0.005 mol) in dichloromethane (20 ml), an ethereal solution of diazo-methane (40 ml, 0.4 M) and triethylamine (0.12 g) were added. The reaction mixture was kept at -20 to -15 °C for 40—48 h. The solvent was removed under reduced pressure. The resultant solid was purified by column chromatography (hexane—ethyl acetate, 4 : 1).

(3-Benzoyl-4,5-dihydro-1H-pyrazole-4-sulfonyl)-acetic Acid Methyl Ester (7a): Yellow solid, yield 75%, mp 136—138 °C; IR (KBr) cm^{-1} : 3348 (NH), 1746 (C=O), 1684 (ArCO), 1576 (C=N), 1125, 1328 (SO_2). $^1\text{H-NMR}$

NMR (CDCl₃) δ : 3.76 (s, 3H, OCH₃), 3.94 (dd, 1H, H_X, J_{AX} =5.4 Hz, J_{MX} =10.3 Hz), 4.32 (s, 2H, SO₂CH₂), 4.53 (dd, 1H, H_M, J_{MX} =10.3 Hz, J_{AM} =12.6 Hz), 5.07 (dd, 1H, H_A, J_{AX} =5.4 Hz, J_{AM} =12.6 Hz), 7.23—7.72 (m, 5H, Ar-H), 10.52 (brs, 1H, NH); ¹³C-NMR (CDCl₃) δ : 48.3 (SO₂CH₂), 52.4 (OCH₃), 57.0 (C-5), 65.8 (C-4), 152.2 (C-3), 162.4 (CO₂CH₃), 185.6 (ArCO), 128.7, 129.8, 131.5, 132.4. MS: m/z =310 (M⁺). Anal. Calcd for C₁₃H₁₄N₂O₅S: C, 50.31; H, 4.55; N, 9.03; Found: C, 50.38; H, 4.50; N, 9.13.

(3-(4-Methylbenzoyl)-4,5-dihydro-1H-pyrazole-4-sulfonyl)-acetic Acid Methyl Ester (**7b**): Yellow solid, yield 71%, mp 155—157 °C; IR (KBr) cm⁻¹: 3343 (NH), 1743 (C=O), 1678 (ArCO), 1569 (C=N), 1132, 1323 (SO₂). ¹H-NMR (CDCl₃) δ : 2.23 (s, 3H, Ar-CH₃), 3.72 (s, 3H, OCH₃), 3.87 (dd, 1H, H_X, J_{AX} =5.2 Hz, J_{MX} =10.1 Hz), 4.36 (s, 2H, SO₂CH₂), 4.56 (dd, 1H, H_M, J_{MX} =10.1 Hz, J_{AM} =12.1 Hz), 5.00 (dd, 1H, H_A, J_{AX} =5.2 Hz, J_{AM} =12.1 Hz), 7.16—7.70 (m, 4H, Ar-H), 10.46 (brs, 1H, NH); ¹³C-NMR (CDCl₃) δ : 24.5 (CH₃), 47.9 (SO₂CH₂), 52.2 (OCH₃), 56.7 (C-5), 66.2 (C-4), 153.2 (C-3), 161.9 (CO₂CH₃), 186.1 (ArCO), 127.8, 128.9, 129.4, 131.6. Anal. Calcd for C₁₄H₁₆N₂O₅S: C, 51.84; H, 4.97; N, 8.64; Found: C, 51.76; H, 4.94; N, 8.55.

(3-(4-Chlorobenzoyl)-4,5-dihydro-1H-pyrazole-4-sulfonyl)-acetic Acid Methyl Ester (**7c**): Yellow solid, yield 74%, mp 163—165 °C; IR (KBr) cm⁻¹: 3335 (NH), 1749 (C=O), 1686 (ArCO), 1582 (CN), 1120, 1332 (SO₂). ¹H-NMR (CDCl₃) δ : 3.78 (s, 3H, OCH₃), 3.90 (dd, 1H, H_X, J_{AX} =5.6 Hz, J_{MX} =10.6 Hz), 4.34 (s, 2H, SO₂CH₂), 4.54 (dd, 1H, H_M, J_{MX} =10.6 Hz, J_{AM} =12.9 Hz), 5.10 (dd, 1H, H_A, J_{AX} =5.6 Hz, J_{AM} =12.9 Hz), 7.23—7.76 (m, 4H, Ar-H), 10.55 (brs, 1H, NH); ¹³C-NMR (CDCl₃) δ : 48.7 (SO₂CH₂), 52.6 (OCH₃), 57.0 (C-5), 65.7 (C-4), 152.3 (C-3), 162.8 (CO₂CH₃), 185.9 (ArCO), 128.7, 129.6, 131.9, 132.7. Anal. Calcd for C₁₃H₁₃ClN₂O₅S: C, 45.29; H, 3.80; N, 8.13; Found: C, 45.23; H, 3.84; N, 8.20.

General Procedure of Synthesis of (3-Aroyl-4,5-dihydro-1H-pyrazole-4-sulfonyl)-acetic Acid Hydrazide (8a—c) To a solution of **7** (0.001 mol) in absolute ethanol (5 ml), hydrazine hydrate (0.0045 mol) and pyridine (0.4 ml) was added and stirred for 4—5 h at room temperature. The resultant solid was filtered, dried and recrystallized from ethanol.

(3-Benzoyl-4,5-dihydro-1H-pyrazole-4-sulfonyl)-acetic Acid Hydrazide (**8a**): Yellow solid, yield 75%, mp 149—151 °C; IR (KBr) cm⁻¹: 3320 (NH), 3225 (NH₂), 1662 (C=O), 1653 (ArCO), 1578 (C=N), 1135, 1320 (SO₂). ¹H-NMR (CDCl₃) δ : 3.89 (dd, 1H, H_X, J_{AX} =5.3 Hz, J_{MX} =10.5 Hz), 4.30 (s, 2H, SO₂CH₂), 4.42 (dd, 1H, H_M, J_{MX} =10.5 Hz, J_{AM} =12.5 Hz), 5.00 (dd, 1H, H_A, J_{AX} =5.3 Hz, J_{AM} =12.5 Hz), 5.15 (brs, 2H, NH₂), 7.21—7.70 (m, 5H, Ar-H), 9.49 (brs, 1H, CONH), 10.49 (brs, 1H, NH); ¹³C-NMR (CDCl₃) δ : 48.8 (C-5), 57.4 (SO₂CH₂), 65.7 (C-4), 152.6 (C-3), 170.9 (CONH), 185.9 (ArCO), 128.1, 128.9, 130.6, 132.0.

(3-(4-Methylbenzoyl)-4,5-dihydro-1H-pyrazole-4-sulfonyl)-acetic Acid Hydrazide (**8b**): Yellow solid, yield 80%, mp 166—168 °C; IR (KBr) cm⁻¹: 3316 (NH), 3223 (NH₂), 1665 (C=O), 1655 (ArCO), 1575 (C=N), 1140, 1334 (SO₂). ¹H-NMR (CDCl₃) δ : 2.25 (s, 3H, Ar-CH₃), 3.93 (dd, 1H, H_X, J_{AX} =5.1 Hz, J_{MX} =10.3 Hz), 4.33 (s, 2H, SO₂CH₂), 4.42 (dd, 1H, H_M, J_{MX} =10.3 Hz, J_{AM} =12.3 Hz), 4.96 (dd, 1H, H_A, J_{AX} =5.1 Hz, J_{AM} =12.3 Hz), 5.12 (brs, 2H, NH₂), 7.19—7.73 (m, 4H, Ar-H), 9.45 (brs, 1H, CONH), 10.51 (brs, 1H, NH); ¹³C-NMR (CDCl₃) δ : 24.2 (Ar-CH₃), 48.4 (C-5), 57.1 (SO₂CH₂), 64.9 (C-4), 151.3 (C-3), 169.8 (CONH), 185.4 (ArCO), 127.3, 128.2, 130.2, 131.9.

(3-(4-Chlorobenzoyl)-4,5-dihydro-1H-pyrazole-4-sulfonyl)-acetic Acid Hydrazide (**8c**): Yellow solid, yield 78%, mp 178—180 °C; IR (KBr) cm⁻¹: 3322 (NH), 3228 (NH₂), 1669 (C=O), 1658 (ArCO), 1580 (C=N), 1138, 1340 (SO₂). ¹H-NMR (CDCl₃) δ : 4.01 (dd, 1H, H_X, J_{AX} =5.5 Hz, J_{MX} =10.8 Hz), 4.35 (s, 2H, SO₂CH₂), 4.49 (dd, 1H, H_M, J_{MX} =10.8 Hz, J_{AM} =12.7 Hz), 5.07 (dd, 1H, H_A, J_{AX} =5.5 Hz, J_{AM} =12.7 Hz), 5.17 (brs, 2H, NH₂), 7.25—8.14 (m, 4H, Ar-H), 9.38 (brs, 1H, CONH), 10.54 (brs, 1H, NH); ¹³C-NMR (CDCl₃) δ : 49.2 (C-5), 57.7 (SO₂CH₂), 65.7 (C-4), 152.3 (C-3), 171.3 (CONH), 186.3 (ArCO), 128.6, 129.5, 130.4, 132.3.

General Procedure of Synthesis of Potassium (3-Aroyl-4,5-dihydro-1H-pyrazole-4-sulfonyl)-acetyl-hydrazine-*N'*-carbodithioate (9a—c) To a mixture of potassium hydroxide (0.002 mol) and compound **8** (0.001 mol) in absolute ethanol (5 ml), carbon disulfide (0.004 mol) was added and sonicated for 10—12 h. The separated solid was filtered and dried.

General Procedure of Synthesis of 5'-(3-Aroyl-4,5-dihydro-1H-pyrazole-4-sulfonylmethyl)-[1',3',4']thiadiazole-2'-thiol (10a—c) The compound **9** (0.001 mol) in acetic acid (4 ml) was refluxed for 20—24 h. It was cooled and poured onto crushed ice. The solid obtained was filtered, dried and recrystallized from 2-propanol.

5'-(3-Benzoyl-4,5-dihydro-1H-pyrazole-4-sulfonylmethyl)-[1',3',4']thiadiazole-2'-thiol (**10a**): Yellow solid, yield 71%, mp 198—200 °C; IR (KBr)

cm⁻¹: 3324 (NH), 2558 (SH), 1568 (C=N), 1146, 1338 (SO₂). ¹H-NMR (DMSO-*d*₆) δ : 3.95 (dd, 1H, H_X, J_{AX} =5.4 Hz, J_{MX} =10.3 Hz), 4.31 (s, 2H, SO₂CH₂), 4.74 (dd, 1H, H_M, J_{MX} =10.3 Hz, J_{AM} =12.4 Hz), 5.15 (dd, 1H, H_A, J_{AX} =5.4 Hz, J_{AM} =12.4 Hz), 7.23—7.76 (m, 5H, Ar-H), 10.27 (s, 1H, SH), 10.46 (brs, 1H, NH); ¹³C-NMR (DMSO-*d*₆) δ : 51.8 (C-5), 57.0 (SO₂CH₂), 65.8 (C-4), 152.2 (C-3), 163.4 (C-2'), 168.5 (C-5'), 186.8 (C=O), 127.9, 128.6, 129.5, 131.4; MS m/z : 368 (M⁺). Anal. Calcd for C₁₃H₁₂N₄O₃S₃: C, 42.38; H, 3.28; N, 15.21; Found: C, 42.42; H, 3.24; N, 15.29.

5'-(3-(4-Methylbenzoyl)-4,5-dihydro-1H-pyrazole-4-sulfonylmethyl)-[1',3',4']thiadiazole-2'-thiol (**10b**): Yellow solid, yield 76%, mp 222—224 °C; IR (KBr) cm⁻¹: 3328 (NH), 2555 (SH), 1564 (C=N), 1140, 1330 (SO₂). ¹H-NMR (DMSO-*d*₆) δ : 2.28 (s, 3H, Ar-CH₃), 3.94 (dd, 1H, H_X, J_{AX} =5.2 Hz, J_{MX} =10.1 Hz), 4.39 (s, 2H, SO₂CH₂), 4.59 (dd, 1H, H_M, J_{MX} =10.1 Hz, J_{AM} =12.2 Hz), 5.11 (dd, 1H, H_A, J_{AX} =5.2 Hz, J_{AM} =12.2 Hz), 7.18—7.69 (m, 4H, Ar-H), 10.29 (s, 1H, SH), 10.52 (brs, 1H, NH); ¹³C-NMR (DMSO-*d*₆) δ : 24.6 (Ar-CH₃), 51.1 (C-5), 56.4 (SO₂CH₂), 65.6 (C-4), 151.7 (C-3), 166.9 (C-2'), 167.8 (C-5'), 186.4 (C=O), 127.6, 128.7, 129.4, 131.2; MS m/z : 382 (M⁺). Anal. Calcd for C₁₄H₁₄N₄O₃S₃: C, 43.96; H, 3.69; N, 14.65; Found: C, 43.89; H, 3.74; N, 14.58.

5'-(3-(4-Chlorobenzoyl)-4,5-dihydro-1H-pyrazole-4-sulfonylmethyl)-[1',3',4']thiadiazole-2'-thiol (**10c**): Yellow solid, yield 73%, mp 237—239 °C; IR (KBr) cm⁻¹: 3336 (NH), 2562 (SH), 1566 (C=N), 1148, 1342 (SO₂). ¹H-NMR (DMSO-*d*₆) δ : 3.91 (dd, 1H, H_X, J_{AX} =5.6 Hz, J_{MX} =10.6 Hz), 4.34 (s, 2H, SO₂CH₂), 4.55 (dd, 1H, H_M, J_{MX} =10.6 Hz, J_{AM} =12.6 Hz), 5.17 (dd, 1H, H_A, J_{AX} =5.6 Hz, J_{AM} =12.6 Hz), 7.25—7.69 (m, 4H, Ar-H), 10.24 (s, 1H, SH), 10.57 (brs, 1H, NH); ¹³C-NMR (DMSO-*d*₆) δ : 52.3 (C-5), 57.6 (SO₂CH₂), 66.5 (C-4), 152.8 (C-3), 166.5 (C-2'), 168.5 (C-5'), 187.6 (C=O), 128.5, 129.9, 131.6, 132.5; MS m/z : 402 (M⁺). Anal. Calcd for C₁₃H₁₁ClN₄O₃S₃: C, 38.75; H, 2.75; N, 13.91; Found: C, 38.70; H, 2.77; N, 13.98.

General Procedure of Synthesis of 5'-(3-Aroyl-4,5-dihydro-1H-pyrazole-4-sulfonylmethyl)-[1',3',4']oxadiazole-2'-thiol (11a—c) The compound **9** (0.001 mol) was dissolved in 6 ml of water and acidified with 1—2 ml of conc. HCl. The regenerated solid was collected by filtration, dried and purified by recrystallization from 2-propanol.

5'-(3-Benzoyl-4,5-dihydro-1H-pyrazole-4-sulfonylmethyl)-[1',3',4']oxadiazole-2'-thiol (**11a**): Yellow solid, yield 73%, mp 169—171 °C; IR (KBr) cm⁻¹: 3340 (NH), 2560 (SH), 1565 (C=N), 1130, 1335 (SO₂). ¹H-NMR (DMSO-*d*₆) δ : 3.88 (dd, 1H, H_X, J_{AX} =5.5 Hz, J_{MX} =10.4 Hz), 4.37 (s, 2H, SO₂CH₂), 4.69 (dd, 1H, H_M, J_{MX} =10.4 Hz, J_{AM} =12.5 Hz), 5.19 (dd, 1H, H_A, J_{AX} =5.5 Hz, J_{AM} =12.5 Hz), 7.26—7.73 (m, 5H, Ar-H), 10.26 (s, 1H, SH), 10.49 (brs, 1H, NH); ¹³C-NMR (DMSO-*d*₆) δ : 51.7 (C-5), 57.4 (SO₂CH₂), 66.2 (C-4), 152.5 (C-3), 160.8 (C-2'), 168.6 (C-5'), 187.8 (C=O), 127.5, 128.6, 129.7, 131.8; MS m/z : 352 (M⁺). Anal. Calcd for C₁₃H₁₂N₄O₄S₂: C, 44.31; H, 3.43; N, 15.90; Found: C, 44.37; H, 3.46; N, 15.82.

5'-(3-(4-Methylbenzoyl)-4,5-dihydro-1H-pyrazole-4-sulfonylmethyl)-[1',3',4']oxadiazole-2'-thiol (**11b**): Yellow solid, yield 68%, mp 188—190 °C; IR (KBr) cm⁻¹: 3345 (NH), 2556 (SH), 1563 (C=N), 1138, 1337 (SO₂). ¹H-NMR (DMSO-*d*₆) δ : 2.25 (s, 3H, Ar-CH₃), 3.86 (dd, 1H, H_X, J_{AX} =5.2 Hz, J_{MX} =10.2 Hz), 4.41 (s, 2H, SO₂CH₂), 4.73 (dd, 1H, H_M, J_{MX} =10.2 Hz, J_{AM} =12.3 Hz), 5.13 (dd, 1H, H_A, J_{AX} =5.2 Hz, J_{AM} =12.3 Hz), 7.14—7.68 (m, 4H, Ar-H), 10.28 (s, 1H, SH), 10.54 (brs, 1H, NH); ¹³C-NMR (DMSO-*d*₆) δ : 25.2 (Ar-CH₃), 51.3 (C-5), 56.7 (SO₂CH₂), 65.9 (C-4), 151.2 (C-3), 160.1 (C-2'), 168.2 (C-5'), 188.2 (C=O), 127.8, 129.5, 132.4, 133.5; MS m/z : 366 (M⁺). Anal. Calcd for C₁₄H₁₄N₄O₄S₂: C, 45.89; H, 3.85; N, 15.29; Found: C, 45.94; H, 3.87; N, 15.36.

5'-(3-(4-Chlorobenzoyl)-4,5-dihydro-1H-pyrazole-4-sulfonylmethyl)-[1',3',4']oxadiazole-2'-thiol (**11c**): Yellow solid, yield 71%, mp 197—199 °C; IR (KBr) cm⁻¹: 3349 (NH), 2564 (SH), 1567 (C=N), 1127, 1342 (SO₂). ¹H-NMR (DMSO-*d*₆) δ : 3.90 (dd, 1H, H_X, J_{AX} =5.6 Hz, J_{MX} =10.7 Hz), 4.46 (s, 2H, SO₂CH₂), 4.76 (dd, 1H, H_M, J_{MX} =10.7 Hz, J_{AM} =12.7 Hz), 5.12 (dd, 1H, H_A, J_{AX} =5.6 Hz, J_{AM} =12.7 Hz), 7.28—7.73 (m, 4H, Ar-H), 10.32 (s, 1H, SH), 10.51 (brs, 1H, NH); ¹³C-NMR (DMSO-*d*₆) δ : 52.1 (C-5), 57.6 (SO₂CH₂), 66.5 (C-4), 152.8 (C-3), 161.2 (C-2'), 168.8 (C-5'), 187.5 (C=O), 128.1, 129.4, 130.5, 132.9; MS m/z : 386 (M⁺). Anal. Calcd for C₁₃H₁₁ClN₄O₄S₂: C, 40.36; H, 2.87; N, 14.48; Found: C, 40.39; H, 2.85; N, 14.40.

General Procedure of Synthesis of 4'-Amino-5'-(3-aroyl-4,5-dihydro-1H-pyrazole-4-sulfonylmethyl)-[1',2',4']triazole-3'-thiol (12a—c) To a solution of **9** (0.001 mol) in 6 ml of water, hydrazine hydrate (0.002 mol) was added and refluxed for 7—10 h. The contents of the flask were cooled, diluted with water and acidified with 2 ml of acetic acid. The separated solid was collected by filtration, dried and recrystallized from 2-propanol.

4'-Amino-5'-(3-benzoyl-4,5-dihydro-1H-pyrazole-4-sulfonylmethyl)-

[1',2',4']triazole-3'-thiol (**12a**): Yellow solid, yield 77%, mp 210–212 °C; IR (KBr) cm^{-1} : 3325 (NH), 3242 (NH_2), 2557 (SH), 1570 (C=N), 1137, 1334 (SO_2). $^1\text{H-NMR}$ ($\text{DMSO-}d_6$) δ : 4.07 (dd, 1H, H_X , $J_{AX}=5.5$ Hz, $J_{MX}=10.5$ Hz), 4.36 (s, 2H, SO_2CH_2), 4.77 (dd, 1H, H_M , $J_{MX}=10.5$ Hz, $J_{AM}=12.7$ Hz), 5.18 (dd, 1H, H_A , $J_{AX}=5.5$ Hz, $J_{AM}=12.7$ Hz), 5.64 (br s, 2H, NH_2), 7.14–7.72 (m, 5H, Ar-H), 10.29 (s, 1H, SH), 10.44 (br s, 1H, NH); $^{13}\text{C-NMR}$ ($\text{DMSO-}d_6$) δ : 50.7 (C-5), 56.8 (SO_2CH_2), 65.6 (C-4), 151.5 (C-3), 153.4 (C-5'), 155.6 (C-3'), 188.8 (C=O), 128.3, 131.3, 132.4, 134.2; MS m/z : 366 (M^+). *Anal.* Calcd for $\text{C}_{13}\text{H}_{14}\text{N}_6\text{O}_3\text{S}_2$: C, 42.61; H, 3.85; N, 22.94; Found: C, 42.56; H, 3.80; N, 23.05.

4'-Amino-5'-(3-(4-Methylbenzoyl)-4,5-dihydro-1H-pyrazole-4-sulfonylmethyl)-[1',2',4']triazole-3'-thiol (**12b**): Yellow solid, yield 71%, mp 202–204 °C; IR (KBr) cm^{-1} : 3337 (NH), 3245 (NH_2), 2548 (SH), 1573 (C=N), 1137, 1334 (SO_2). $^1\text{H-NMR}$ ($\text{DMSO-}d_6$) δ : 2.27 (s, 3H, Ar- CH_3), 4.04 (dd, 1H, H_X , $J_{AX}=5.3$ Hz, $J_{MX}=10.3$ Hz), 4.37 (s, 2H, SO_2CH_2), 4.68 (dd, 1H, H_M , $J_{MX}=10.3$ Hz, $J_{AM}=12.5$ Hz), 5.19 (dd, 1H, H_A , $J_{AX}=5.3$ Hz, $J_{AM}=12.5$ Hz), 5.61 (br s, 2H, NH_2), 7.09–7.68 (m, 4H, Ar-H), 10.33 (s, 1H, SH), 10.49 (br s, 1H, NH); $^{13}\text{C-NMR}$ ($\text{DMSO-}d_6$) δ : 23.5 (Ar- CH_3), 50.3 (C-5), 55.4 (SO_2CH_2), 65.9 (C-4), 150.2 (C-3), 142.3 (C-3'), 153.1 (C-5'), 187.6 (C=O), 129.6, 131.5, 132.7, 134.5; MS m/z : 380 (M^+). *Anal.* Calcd for $\text{C}_{14}\text{H}_{16}\text{N}_6\text{O}_3\text{S}_2$: C, 44.20; H, 4.24; N, 22.09; Found: C, 44.25; H, 4.28; N, 21.98.

4'-Amino-5'-(3-(4-chlorobenzoyl)-4,5-dihydro-1H-pyrazole-4-sulfonylmethyl)-[1',2',4']triazole-3'-thiol (**12c**): Yellow solid, yield 74%, mp 246–248 °C; IR (KBr) cm^{-1} : 3330 (NH), 3248 (NH_2), 2559 (SH), 1569 (C=N), 1144, 1345 (SO_2). $^1\text{H-NMR}$ ($\text{DMSO-}d_6$) δ : 4.09 (dd, 1H, H_X , $J_{AX}=5.6$ Hz, $J_{MX}=10.8$ Hz), 4.40 (s, 2H, SO_2CH_2), 4.78 (dd, 1H, H_M , $J_{MX}=10.8$ Hz, $J_{AM}=12.8$ Hz), 5.25 (dd, 1H, H_A , $J_{AX}=5.6$ Hz, $J_{AM}=12.8$ Hz), 5.67 (br s, 2H, NH_2), 7.28–7.82 (m, 4H, Ar-H), 10.35 (s, 1H, SH), 10.43 (br s, 1H, NH); $^{13}\text{C-NMR}$ ($\text{DMSO-}d_6$) δ : 50.9 (C-5), 57.1 (SO_2CH_2), 65.8 (C-4), 151.9 (C-3), 142.6 (C-3'), 153.4 (C-5'), 188.7 (C=O), 129.2, 131.7, 132.4, 133.6; MS m/z : 400 (M^+). *Anal.* Calcd for $\text{C}_{13}\text{H}_{13}\text{ClN}_6\text{O}_3\text{S}_2$: C, 38.95; H, 3.27; N, 20.96; Found: C, 38.96; H, 3.29; N, 20.89.

Antimicrobial Testing The compounds **10–12** were dissolved in DMSO at different concentrations of 100, 200 and 800 $\mu\text{g/ml}$.

Antibacterial and Antifungal Assays Preliminary antimicrobial activities of **10–12** compounds were tested by Agar disc-diffusion method. Sterile filter paper discs (6 mm diameter) moistened with the test compound solution in acetone of specific concentration 100 μg and 200 $\mu\text{g/disc}$ were carefully placed on the agar culture plates that had been previously inoculated separately with the microorganisms. The plates were incubated at 37 °C and the diameter of the growth inhibition zones were measured after 24 h in case of bacteria and after 48 h in case of fungi.

The MICs of the compounds assays were carried out using microdilution susceptibility method. Chloramphenicol was used as reference antibacterial agent. Ketoconazole was used as reference antifungal agent. The test compounds, chloramphenicol and ketoconazole were dissolved in DMSO at concentration of 800 $\mu\text{g/ml}$. The two-fold dilution of the solution was prepared

(400, 200, 100, ..., 6.25 $\mu\text{g/ml}$). The microorganism suspensions were inoculated to the corresponding wells. The plates were incubated at 36 °C for 24 and 48 h for bacteria and fungi, respectively. The minimum inhibitory concentrations of the compounds were recorded as the lowest concentration of each chemical compounds in the tubes with no turbidity (*i.e.* no growth) of inoculated bacteria/fungi.

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