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Received March 31, 2004A new class of five membered heterocycles, thiadiazoles, triazoles and oxadiazoles were prepared from sulfonyl acetic acids *via* acid hydrazides.*J. Heterocyclic Chem.*, **42**, 113 (2005).

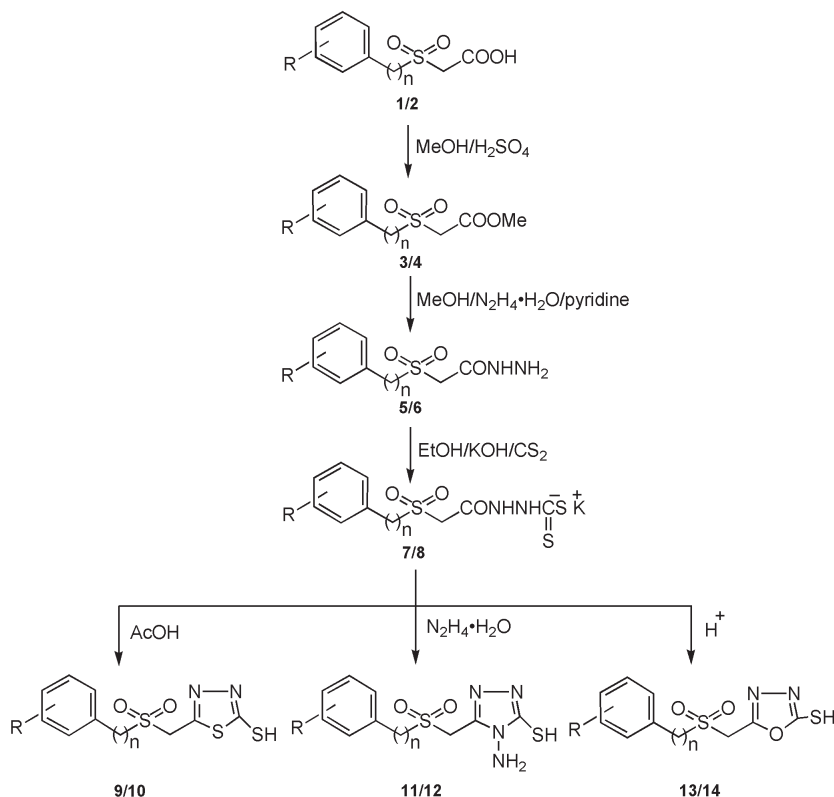
Introduction.

The chemistry of five membered heterocycles containing nitrogen and sulfur has gained importance mainly due to their varied physiological action and diverse physico-chemical properties. The triazole nucleus has a broad spectrum of antimicrobial activity [1]. In fact molecules having both triazole and thiadiazine units possess antiparasitic activity [2]. Apart from this triazolo-thiadiazines/ thiadiazoles possess antimicrobial properties [3]. Besides, 2-mercapto-5-methyl-1,3,4-thiadiazole is an intermediate for therapeutically useful antibiotic cefazolin [4]. In fact for the last one and half decades we have been actively involved in the synthesis of new and novel five membered heterocycles containing two heteroatoms particularly pyrazolines and

isoxazolines [5]. In view of our successful results on this front and our continued interest in the field of heterocycles herein we report a new class of five membered heterocycles having three heteroatoms nitrogen, oxygen and sulphur viz., triazoles, oxadiazoles and thiadiazoles.

The synthetic method involves the articulation of triazole, oxadiazole and thiadiazole rings from an intermediate phenylsulfonylacetic acid (**1**)/benzylsulfonylacetic acid (**2**). The methyl ester of latter (**3/4**) was prepared by treating **1/2** with methanol in conc. H_2SO_4 . The IR spectra of **3** and **4** showed absorption bands in the region 1320-1345 and 1125-1135 cm^{-1} (SO_2) and 1740-1755 cm^{-1} (CO_2CH_3). A sharp singlet was observed at δ 3.90-3.95 for the methylene protons flanked between ester and sulfonyl groups in their

Scheme



$n = 0$ (**1,3,5,7,9,11,13**) $n = 1$ (**2,4,6,8,10,12,14**)
1-14 a) R = H; b) R = 4-Me; c) R = 4-Cl

^1H NMR spectra. Apart from this, **4** displayed another singlet at δ 4.12-4.18 for benzylic protons. Both the compounds showed a singlet at δ 3.75-3.83 for methoxy protons of the carbomethoxy group (Scheme and Table 1). The compounds **3/4** on reaction with hydrazine hydrate gave the corresponding acid hydrazide (**5/6**) [6] which displayed absorption bands at 1676 cm^{-1} for amidic carbonyl and at 3275 and 3334 cm^{-1} for NH and NH_2 respectively. The ^1H NMR spectra of **5** and **6** displayed a broad signal in the region δ 7.84-7.95 and 4.49-4.60 for NH and NH_2 , which disappeared on deuteration apart from signals due to methylene protons. The potassium dithiocarbazate of the acid

hydrazide (**7/8**) was prepared from **5/6** on treatment with carbon disulfide in the presence of potassium hydroxide under ultrasonic conditions. This on refluxion in acetic acid cyclized to 5-arylsulfonylmethyl[1,3,4]thiadiazole-2-thiol (**9**)/5-arylmethanesulfonylmethyl[1,3,4]thiadiazole-2-thiol (**10**). On the other hand treatment of **7/8** with hydrazine hydrate produced 4-amino-5-arylsulfonylmethyl-4H-[1,2,4]triazole-3-thiol (**11**)/4-amino-5-arylmethanesulfonylmethyl-4H-[1,2,4]triazole-3-thiol (**12**). Similarly, base catalyzed hydrolysis of **7/8** resulted 5-arylsulfonylmethyl-[1,3,4]oxadiazole-2-thiol (**13**)/5-arylmethanesulfonylmethyl-[1,3,4]oxadiazole-2-thiol (**14**) (Scheme and

Table 1
Physical and Spectral Data of Compounds **3-6**

Compd.	mp ($^{\circ}\text{C}$)	Yield (%)	^1H NMR (δ , ppm)
3a	108-110	82	3.79 (s, 3H, OCH_3), 3.94 (s, 2H, $\text{SO}_2\text{-CH}_2\text{-CO}_2\text{CH}_3$), 7.01-7.25 (m, 5H, Ar-H)
3b	127-128	87	2.24 (s, 3H, Ar- CH_3), 3.76 (s, 3H, OCH_3), 3.92 (s, 2H, $\text{SO}_2\text{-CH}_2\text{-CO}_2\text{CH}_3$), 6.95-7.26 (m, 4H, Ar-H)
3c	143-145	86	3.82 (s, 3H, OCH_3), 3.95 (s, 2H, $\text{SO}_2\text{-CH}_2\text{-CO}_2\text{CH}_3$), 7.09-7.25 (m, 4H, Ar-H)
4a	49-50	79	3.78 (s, 3H, OCH_3), 3.91 (s, 2H, $\text{SO}_2\text{-CH}_2\text{-CO}_2\text{CH}_3$), 4.15 (s, 2H, Ar- $\text{CH}_2\text{-SO}_2$ -), 6.98-7.34 (m, 5H, Ar-H)
4b	57-58	85	2.21 (s, 3H, Ar- CH_3), 3.75 (s, 3H, OCH_3), 3.95 (s, 2H, $\text{SO}_2\text{-CH}_2\text{-CO}_2\text{CH}_3$), 4.12 (s, 2H, Ar- $\text{CH}_2\text{-SO}_2$ -), 6.89-7.35 (m, 4H, Ar-H)
4c	65-66	88	3.83 (s, 3H, OCH_3), 3.94 (s, 2H, $\text{SO}_2\text{-CH}_2\text{-CO}_2\text{CH}_3$), 4.18 (s, 2H, Ar- $\text{CH}_2\text{-SO}_2$ -), 7.02-7.28 (m, 4H, Ar-H)
5a	132-134	77	3.95 (s, 2H, $\text{-SO}_2\text{-CH}_2\text{-CO}$), 4.60 (s, 2H, NH_2), 6.81-7.55 (m, 5H, Ar-H), 7.95 (s, 1H, NH)
5b	146-147	73	2.21 (s, 3H, Ar- CH_3), 3.97 (s, 2H, $\text{-SO}_2\text{-CH}_2\text{-CO}$), 4.55 (s, 2H, NH_2), 6.62-7.49 (m, 4H, Ar-H), 7.84 (s, 1H, NH)
5c	154-155	75	3.98 (s, 2H, $\text{-SO}_2\text{-CH}_2\text{-CO}$), 4.62 (s, 2H, NH_2), 6.98-7.54 (m, 4H, Ar-H), 7.89 (s, 1H, NH)
6a	144-145	76	3.79 (s, 2H, $\text{SO}_2\text{-CH}_2\text{-CO}$), 4.53 (s, 2H, NH_2), 4.59 (s, 2H, Ar- $\text{CH}_2\text{-SO}_2$ -), 7.32-7.58 (m, 5H, Ar-H), 7.93 (s, 1H, NH)
6b	140-142	78	2.19 (s, 3H, Ar- CH_3), 3.76 (s, 2H, $\text{SO}_2\text{-CH}_2\text{-CO}$), 4.54 (s, 2H, NH_2), 4.57 (s, 2H, Ar- $\text{CH}_2\text{-SO}_2$ -), 6.95-7.52 (m, 4H, Ar-H), 7.88 (s, 1H, NH)
6c	164-166	82	3.75 (s, 2H, $\text{CH}_2\text{-CO}$ -), 4.49 (s, 2H, NH_2), 4.52 (s, 2H, Ar- $\text{CH}_2\text{-SO}_2$ -), 7.27-7.50 (m, 4H, Ar-H), 7.85 (s, 1H, NH)

Table 2
Physical Properties for Compounds **9-14**

Compd.	mp ($^{\circ}\text{C}$)	Yield (%)	Mol. Formula (Mol. Wt.)	Calcd. (Found) %		
				C	H	N
9a	215-217	68	$\text{C}_9\text{H}_8\text{N}_2\text{O}_2\text{S}_3$ (272.37)	39.69 (39.58)	2.96 (2.94)	10.28 (10.35)
9b	200-202	71	$\text{C}_{10}\text{H}_{10}\text{N}_2\text{O}_2\text{S}_3$ (286.4)	41.94 (41.89)	3.52 (3.58)	9.78 (9.84)
9c	244-246	69	$\text{C}_9\text{H}_7\text{ClN}_2\text{O}_2\text{S}_3$ (306.82)	35.23 (35.20)	2.30 (2.28)	9.13 (9.20)
10a	210-213	72	$\text{C}_{10}\text{H}_{10}\text{N}_2\text{O}_2\text{S}_3$ (286.4)	41.94 (41.87)	3.52 (3.55)	9.78 (9.85)
10b	204-206	74	$\text{C}_{11}\text{H}_{12}\text{N}_2\text{O}_2\text{S}_3$ (300.42)	43.98 (44.05)	4.02 (4.07)	9.32 (9.27)
10c	238-240	73	$\text{C}_{10}\text{H}_9\text{ClN}_2\text{O}_2\text{S}_3$ (320.84)	37.44 (37.40)	2.83 (2.78)	8.73 (8.84)
11a	123-124	64	$\text{C}_9\text{H}_{10}\text{N}_4\text{O}_2\text{S}_2$ (270.34)	39.99 (39.88)	3.73 (3.79)	20.73 (20.85)
11b	145-146	69	$\text{C}_{10}\text{H}_{12}\text{N}_4\text{O}_2\text{S}_2$ (284.36)	42.24 (42.19)	4.25 (4.20)	19.70 (19.82)
11c	159-161	70	$\text{C}_9\text{H}_9\text{ClN}_4\text{O}_2\text{S}_2$ (304.78)	35.47 (35.54)	2.98 (2.94)	18.38 (18.24)
12a	259-261	66	$\text{C}_{10}\text{H}_{12}\text{N}_4\text{O}_2\text{S}_2$ (284.36)	42.24 (42.28)	4.25 (4.31)	19.70 (19.82)
12b	235-237	65	$\text{C}_{11}\text{H}_{14}\text{N}_4\text{O}_2\text{S}_2$ (298.39)	44.28 (44.35)	4.73 (4.67)	18.78 (18.64)
12c	214-216	69	$\text{C}_{10}\text{H}_{11}\text{ClN}_4\text{O}_2\text{S}_2$ (318.81)	37.67 (37.59)	3.48 (3.45)	17.57 (17.63)

Table 2 (Continued)

Compd.	mp (°C)	Yield (%)	Mol. Formula (Mol. Wt.)	C	Calcd. (Found) % H	N
13a	86-88	71	C ₉ H ₈ N ₂ O ₃ S ₂ (256.3)	42.18 (42.12)	3.14 (3.18)	10.93 (11.01)
13b	97-99	69	C ₁₀ H ₁₀ N ₂ O ₃ S ₂ (270.33)	44.43 (44.50)	3.73 (3.79)	10.36 (10.45)
13c	105-106	63	C ₉ H ₇ ClN ₂ O ₃ S ₂ (290.75)	37.18 (37.15)	2.43 (2.38)	9.63 (9.69)
14a	159-160	66	C ₁₀ H ₁₀ N ₂ O ₃ S ₂ (270.33)	44.43 (44.39)	3.73 (3.81)	10.36 (10.42)
14b	167-169	64	C ₁₁ H ₁₂ N ₂ O ₃ S ₂ (284.35)	46.46 (46.54)	4.25 (4.18)	9.85 (9.79)
14c	188-190	67	C ₁₀ H ₉ ClN ₂ O ₃ S ₂ (304.77)	39.41 (39.45)	2.98 (2.92)	9.19 (9.24)

Table 2). The IR spectra of the compounds **9-14** displayed an absorption band at 1634 cm⁻¹ for C=N apart from bands due to the SO₂ group. Apart from this, the compounds **11** and **12** showed a broad band at 3280 cm⁻¹ for NH₂. The ¹H NMR spectra of compounds **9-14** displayed a singlet

around 10.20-10.45 for SH apart from signals due to methylene protons. Besides **11** and **12** exhibited signals at 9.94-10.32 cm⁻¹ for NH₂ which disappeared on deuteration (Table 3). The structures of the compounds **9-14** were further confirmed by ¹³C NMR spectra (Table 3).

Table 3
Spectral Data of Compounds **9-14**

Product	IR	¹ H NMR (δ, ppm)	¹³ C NMR (δ, ppm)
9a	1144,1320 (SO ₂), 1632 (CN), 2554 (SH)	10.21 (s, 1H, SH), 4.25 (s, 2H, CH ₂), 7.04-7.22 (m, 5H, Ar-H)	168.3 (C ₅), 163.2 (C ₂), 138.7, 134.6, 129.3, 125.4 (Ar-C), 54.6 (CH ₂ SO ₂)
9b	1136,1320 (SO ₂), 1635 (CN), 2552 (SH)	2.20 (s, 3H, Ar-CH ₃), 10.28 (s, 1H, SH), 4.23 (s, 2H, CH ₂), 7.01-7.23 (m, 4H, Ar-H)	167.5 (C ₅), 166.8 (C ₂), 143.2, 137.4, 131.5, 126.3 (Ar-C), 54.4 (CH ₂ SO ₂), 20.3 (ArCH ₃)
9c	1124,1322 (SO ₂), 1630 (CN), 2558 (SH)	10.43 (s, 1H, SH), 4.26 (s, 2H, CH ₂), 7.12-7.28 (m, 4H, Ar-H)	169.4 (C ₅), 166.3 (C ₂), 137.6, 135.8, 130.3, 128.5 (Ar-C), 55.4 (CH ₂ SO ₂)
10a	1128,1334 (SO ₂), 1627 (CN), 2562 (SH)	10.24 (s, 1H, SH), 4.21 (s, 2H, CH ₂), 4.38 (s, 2H, Ar-CH ₂), 7.03-7.28 (m, 5H, Ar-H)	167.9 (C ₅), 164.5 (C ₂), 131.7, 130.5, 128.7 (Ar-C), 58.5 (PhCH ₂), 52.8 (CH ₂ SO ₂)
10b	1126,1330 (SO ₂), 1625 (CN), 2560 (SH)	2.22 (s, 3H, Ar-CH ₃), 10.26 (s, 1H, SH), 4.24 (s, 2H, CH ₂), 4.41 (s, 2H, Ar-CH ₂), 6.95-7.25 (m, 4H, Ar-H)	165.7 (C ₅), 163.8 (C ₂), 137.5, 131.6, 128.7, 124.9 (Ar-C), 59.4 (ArCH ₂), 53.2 (CH ₂ SO ₂), 20.6 (ArCH ₃)
10c	1122,1335 (SO ₂), 1628 (CN), 2564 (SH)	10.22 (s, 1H, SH), 4.22 (s, 2H, CH ₂), 4.45 (s, 2H, Ar-CH ₂), 7.08-7.32 (m, 4H, Ar-H)	168.8 (C ₅), 160.5 (C ₂), 131.3, 128.9, 128.7, 127.3 (Ar-C), 59.3 (ArCH ₂), 55.9 (CH ₂ SO ₂)
11a	1135,1332 (SO ₂), 1632 (CN), 2580 (SH), 3262 (NH ₂)	10.45 (s, 1H, SH), 4.21 (s, 2H, CH ₂), 7.02-7.29 (m, 5H, Ar-H), 10.32 (bs, 2H, NH ₂)	162.5 (C ₅), 149.4 (C ₃), 137.7, 132.5, 128.6, 125.7 (Ar-C), 43.8 (CH ₂ SO ₂)
11b	1132,1330 (SO ₂), 1630 (CN), 2575 (SH), 3260 (NH ₂)	2.21 (s, 3H, Ar-CH ₃), 10.36 (s, 1H, SH), 4.23 (s, 2H, CH ₂), 6.95-7.26 (m, 4H, Ar-H), 10.24 (bs, 2H, NH ₂)	163.4 (C ₅), 148.5 (C ₃), 141.7, 134.5, 131.6, 125.8 (Ar-C), 44.6 (CH ₂ SO ₂), 21.2 (ArCH ₃)
11c	1130,1336 (SO ₂), 1625 (CN), 2572 (SH), 3264 (NH ₂)	10.31 (s, 1H, SH), 4.22 (s, 2H, CH ₂), 7.08-7.34 (m, 4H, Ar-H), 10.21 (bs, 2H, NH ₂)	163.8 (C ₅), 150.1 (C ₃), 137.8, 135.7, 130.2, 128.5 (Ar-C), 43.6 (CH ₂ SO ₂)
12a	1142,1338 (SO ₂), 1634 (CN), 2620 (SH), 3270 (NH ₂)	10.32 (s, 1H, SH), 4.19 (s, 2H, CH ₂), 4.47 (s, 2H, Ar-CH ₂), 6.98-7.32 (m, 5H, Ar-H), 9.94 (bs, 2H, NH ₂)	161.7 (C ₅), 148.6 (C ₃), 138.5, 132.7, 130.2, 127.5 (Ar-C), 56.5 (PhCH ₂), 42.9 (CH ₂ SO ₂)
12b	1141,1325 (SO ₂), 1632 (CN), 2630 (SH), 3280 (NH ₂)	2.22 (s, 3H, Ar-CH ₃), 10.34 (s, 1H, SH), 4.17 (s, 2H, CH ₂), 4.46 (s, 2H, Ar-CH ₂), 6.78-7.24 (m, 4H, Ar-H), 10.02 (bs, 2H, NH ₂)	162.5 (C ₅), 148.1 (C ₃), 139.5, 131.6, 129.7, 124.6 (Ar-C), 57.2 (ArCH ₂), 43.3 (CH ₂ SO ₂), 21.2 (ArCH ₃)
12c	1132,1320 (SO ₂), 1630 (CN), 2645 (SH), 3275 (NH ₂)	10.30 (s, 1H, SH), 4.22 (s, 2H, CH ₂), 4.51 (s, 2H, Ar-CH ₂), 7.04-7.38 (m, 4H, Ar-H), 10.21 (bs, 2H, NH ₂)	162.3 (C ₅), 147.8 (C ₃), 135.2, 133.3, 130.6, 125.8 (Ar-C), 57.2 (ArCH ₂), 43.1 (CH ₂ SO ₂)
13a	1138,1335 (SO ₂), 1626 (CN), 2640 (SH)	10.28 (s, 1H, SH), 4.14 (s, 2H, CH ₂), 6.94-7.31 (m, 5H, Ar-H)	167.4 (C ₅), 159.5 (C ₂), 139.7, 135.2, 130.5, 124.8 (Ar-C), 54.4 (CH ₂ SO ₂)
13b	1125,1332 (SO ₂), 1625 (CN), 2620 (SH)	2.20 (s, 3H, Ar-CH ₃), 10.27 (s, 1H, SH), 4.17 (s, 2H, CH ₂), 6.82-7.29 (m, 4H, Ar-H)	167.7 (C ₅), 158.7 (C ₂), 141.5, 134.7, 131.2, 125.9 (Ar-C), 54.9 (CH ₂ SO ₂), 20.4 (ArCH ₃)
13c	1130,1340 (SO ₂), 1628 (CN), 2625 (SH)	10.23 (s, 1H, SH), 4.18 (s, 2H, CH ₂), 7.02-7.29 (m, 4H, Ar-H)	165.8 (C ₅), 160.3 (C ₂), 139.2, 135.5, 129.5, 126.8 (Ar-C), 55.7 (CH ₂ SO ₂)

Table 3 (continued)

Product	IR	¹ H NMR (δ, ppm)	¹³ C NMR (δ, ppm)
14a	1122,1330 (SO ₂), 1625 (CN), 2580 (SH)	10.26 (s, 1H, SH), 4.13 (s, 2H, CH ₂), 4.54 (s, 2H, Ar-CH ₂), 6.88-7.29 (m, 5H, Ar-H)	168.3 (C ₅), 160.7 (C ₂), 137.8, 131.6, 130.5, 127.3 (Ar-C), 57.4 (PhCH ₂), 51.3 (CH ₂ SO ₂)
14b	1134,1328 (SO ₂), 1632 (CN), 2590 (SH)	2.20 (s, 3H, Ar-CH ₃), 10.28 (s, 1H, SH), 4.15 (s, 2H, CH ₂), 4.49 (s, 2H, Ar-CH ₂), 6.76-7.24 (m, 4H, Ar-H)	169.4 (C ₅), 161.3 (C ₂), 138.9, 132.2, 130.5, 124.9 (Ar-C), 57.6 (ArCH ₂), 50.8 (CH ₂ SO ₂) 21.3 (Ar-CH ₃)
14c	1125,1336 (SO ₂), 1630 (CN), 2600 (SH)	10.29 (s, 1H, SH), 4.19 (s, 2H, CH ₂), 4.58 (s, 2H, Ar-CH ₂), 7.01-7.35 (m, 4H, Ar-H)	170.1 (C ₅), 161.4 (C ₂), 135.4, 133.6, 130.7, 125.8 (Ar-C), 57.3 (ArCH ₂), 51.6 (CH ₂ SO ₂)

Thus a new class of triazoles, oxadiazoles and thiadiazoles were prepared from simple substrates, phenylsulfonylacetic acid and benzyldisulfonylacetic acid *via* potassium dithiocarbamate of acid hydrazide.

EXPERIMENTAL

Melting points were determined on Tempo Mel-Temp apparatus and are uncorrected. The IR spectra were recorded on a Perkin-Elmer grating infrared spectrophotometer model 337 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 (300MHz) with TMS as an internal standard and the ¹³C NMR spectra were recorded on a Varian VXR spectrometer operating at 75.5 MHz with CDCl₃ as solvent. Elemental analyses were performed using a Perkin-Elmer 240C elemental analyzer. The chemical shifts were measured in δ (ppm). The purity of compounds was checked by TLC using silica gel 'G' (BDH) and hexane-ethyl acetate as eluents. The starting compounds arylsulfonylacetic acid (**1**)/arylmethanesulfonyl acetic acid (**2**) were prepared as per the literature procedure [7].

Arylsulfonylacetic Acid Methyl Ester (**3**)/Arylmethanesulfonyl acetic Acid Methyl Ester (**4**).

A solution of 10 mmoles **1/2**, 10 ml of methanol and 1 ml conc. H₂SO₄ was refluxed on a steam bath for 8-10 hours. The contents of the flask were cooled and poured onto crushed ice. The solid that separated was collected by filtration, washed with cold water and dried. The crude product was recrystallized from methanol.

Arylsulfonylacetic Acid Hydrazide (**5**)/Arylmethanesulfonyl acetic Acid Hydrazide (**6**).

To a solution of mixture of 10 mmoles of **3/4** in 6 ml of methanol, 11 mmoles of hydrazine hydrate and 3 drops of pyridine were added and refluxed for 6-7 hours. The reaction mixture was cooled and the solid that separated was collected by filtration, dried and recrystallized from methanol.

Potassium Dithiocarbamate (**7/8**).

A solution of 10 mmoles of **5** in 20 ml of absolute ethanol and 15 mmoles of KOH was treated with 40 mmoles of CS₂. The mixture was sonicated for 4 hours. The separated solid was collected by filtration and dried.

5-Arylsulfonylmethyl[1,3,4]thiadiazole-2-thiol (**9**)/5-Arylmethanesulfonylmethyl[1,3,4]thiadiazole-2-thiol (**10**).

A solution of 10 mmoles of **7/8** in 6 ml of acetic acid was refluxed for 24 hours. The contents of the flask were cooled and poured onto crushed ice. The solid obtained was collected by filtration, dried and recrystallized from 2-propanol.

4-Amino-5-arylsulfonylmethyl-4H-[1,2,4]triazole-3-thiol (**11**)/4-Amino-5-Arylmethanesulfonylmethyl-4H-[1,2,4]triazole-3-thiol (**12**).

To a solution of 10 mmoles of potassium salt (**7/8**) in 10 ml of water, 20 mmoles of hydrazine hydrate was added and refluxed for 8-9 hours. The contents of the flask were cooled, diluted with water and acidified with 10 ml of acetic acid. The separated solid was collected by filtration, dried and recrystallized from 2-propanol.

5-Arylsulfonylmethyl[1,3,4]oxadiazole-2-thiol (**13**)/5-Arylmethanesulfonylmethyl[1,3,4]oxadiazole-2-thiol (**14**).

A solution of 10 mmoles of potassium salt (**7/8**) was dissolved in 10 ml of water and acidified with 2 ml of conc. HCl. The regenerated solid was collected by filtration, dried and recrystallized from 2-propanol.

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