Regiospecific Synthesis of *N*-Sulfonyl Derivatives of 3,5-Diamino-1*H*-1,2,4-triazole and 2,5-Diamino-1,3,4-thiadiazole

Shailaja P. Maybhate, Pattuparambil P. Rajamohanan, Srinivasachari Rajappa*[1]
National Chemical Laboratory, Pune-411 008, India.

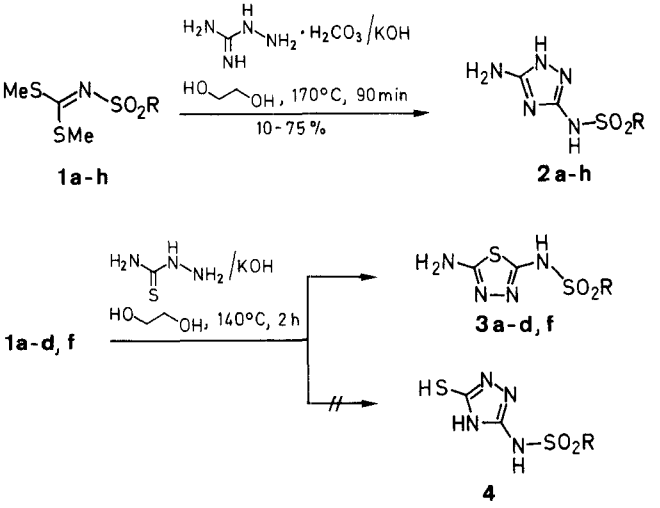
Condensation of the *S,S*-dimethyl *N*-(alkylsulfonyl)carbondithioimidates **1** with aminoguanidine bicarbonate and hydrazinecarbothioamide leads to the regiospecific synthesis of *N*-sulfonyl derivatives of 3,5-diamino-1*H*-1,2,4-triazole **2** and 2,5-diamino-1,3,4-thiadiazole **3**, respectively.

A recent report[2] on the regiospecific synthesis of *N*-(5-amino-1*H*-1,2,4-triazol-3-yl)arenesulfonamides **2** (R = Ar) which are useful intermediates in herbicide synthesis, prompts us to record our own synthetic efforts in this direction. The reported procedure achieves regiocontrol by reacting *S,S*-dimethyl *N*-cyanocarbondithioimidates with arenesulfonamides to give *N*-cyano-*N*-(arylsulfonyl)-*S*-methylisothioureas; these, on further reaction with hydrazine furnish the 1,2,4-triazole derivaves **2**.

Our synthesis (Scheme) differs from the above procedure in reacting *N*-sulfonylcarbondithioimidates **1** with aminoguanidine to give directly, in one step, the required *N*-(5-amino-1*H*-1,2,4-triazol-3-yl)arenesulfonamides **2**. The generality of the method has been tested by the synthesis of several sulfonamides **2** described in Table 1.

Except for **2a** and **2b**, the sulfonamides described here have not been reported earlier. The structures were confirmed by elemental analyses, NMR and MS data. Barring unprecedented sulfonyl migration, it is clear that this synthesis leads to sulfonyl derivatives of 3,5-diamino-1,2,4-triazole in which the sulfonyl group has to be attached to one of the exocyclic nitrogens. The yields are generally acceptable except in the case of **2g** (10%) and **2h** (12%). Here the low yields may be attributed to the high solubility of the compounds in water. No attempt has been made to optimize the yield.

The precursors *N*-sulfonylcarbondithioimidates **1a–h** required for the synthesis were obtained by a standard procedure[3] by reacting the corresponding sulfonamides with carbon disulfide, followed by methylation with dimethyl sulfate. The physical and spectral properties of the *N*-sulfonylcarbondithioimidates **1** prepared are listed in Table 2. Of these, **1f** and **1h** are new compounds. The rest are reported[3–5] in the literature but their physical and/or spectral properties have not been described.



1–3	R	1–3	R
a	Ph	**e**	4-AcHNC$_6$H$_4$
b	4-MeC$_6$H$_4$	**f**	2-thienyl
c	4-MeOC$_6$H$_4$	**g**	piperidino
d	4-ClC$_6$H$_4$	**h**	morpholino

Scheme

As an extension of the above synthesis, we investigated the reaction of the *N*-sulfonylcarbondithioimidates **1** with hydrazinecarbothioamide (Scheme). This reaction can lead to the 2,5-diamino-1,3,4-thiadiazole derivatives **3**; however, there is also a possibility of obtaining the isomeric *N*-sulfonyl derivatives **4** of 3-amino-5-mercapto-1,2,4-triazole. In the event, reaction of **1b** with hydrazinecarbothioamide gave a product in 49% yield with the correct analytical data. That this product was indeed the thiadiazole **3b** was proved unambiguously by the proton coupled ^{15}N-NMR spectrum, which revealed a triplet (J = 87 Hz) at δ = −310 (CH_3NO_2 as standard) arising from the ^{15}N-^{1}H coupling of the 5-amino group.

Other thiadiazoles **3a,c,d** and **f** were similarly prepared with yields ranging from 22–50%. The thiadiazoles **3** thus obtained are new compounds and have been charac-

Table 1. Compounds **1** Prepared

Product	Yield (%)	mp (°C) (MeOH)	Molecular Formula[a] or Lit. mp (°C)	IR (Nujol) ν (cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS) δ, J (Hz)
1a	60	110	111[3]	1290, 1140	2.5 (s, 6H), 7.26–7.5 (m, 3H), 7.7–8.0 (m, 2H)
1b	69	108	109[3]	1590, 1310, 1150	2.4 (s, 3H), 2.5 (s, 6H), 7.23 (d, 2H, J = 9), 7.8 (d, 2H, J = 9)
1c[4]	67	94	$C_{10}H_{13}NO_3S_3$ (291.4)	1590, 1300, 1150	2.44 (s, 6H, 3.78 (s, 3H, 6.8 d, 2H, J = 10), 7.8 (d, 2H, J = 10)
1d	50	93	93[3]	1590, 1320, 1160	2.58 (s, 6H), 7.5 (d, 2H, J = 8), 8.0 (d, 2H, J = 8)
1e	50	172	174–6[3]	3360, 1700, 1310, 1150	2.1 (s, 3H), 2.5 (s, 6H), 7.6 (d, 2H, J = 9), 7.85 (d, 2H, J = 9)
1f	60	121	$C_7H_9NO_2S_4$ (267.4)	1430, 1310, 1145	2.5 (s, 6H), 6.9–7.1 (m, 1H), 7.5–7.8 (m, 2H)
1g[5]	52	83	$C_8H_{16}N_2O_2S_3$ (268.4)	1490, 1315, 1145	1.6 (m, 6H), 2.5 (s, 6H), 3.15 (m, 4H)
1h	50	129	$C_7H_{14}N_2O_3S_3$ (270.4)	1500, 1330, 1160	2.5 (s, 6H), 3.15 (m, 4H), 3.75 (m, 4H)

[a] Satisfactory microanalyses obtained: C ±0.17, H ±0.33. (Exception: **1h**, H +0.41). Values for N range from ±0.33 to 0.53.

Table 2. Compounds **2** Prepared

Product	Yield (%)	mp (°C)	Molecular Formula[a,b] or Lit. mp (°C)	IR (Nujol) ν (cm^{-1})	^{1}H-NMR (TMS)[c] δ, J (Hz)	MS (70 eV) m/z (%)
2a	59	289	293[2]	3460, 3300, 1680, 1635, 1515, 1280, 1160, 940	7.57 (m, 3H), 7.87 (m, 2H)	239 (M^+, 66), 175 (24), 141 (19), 98 (100), 77 (91)
2b	60	306	314[2]	3420, 3285, 1665, 1620, 1500, 1260, 1140, 925	2.46 (s, 3H), 7.36 (d, 2H, J = 9), 7.8 (d, 2H, J = 9)	253 (M^+, 65), 189 (26), 155 (23), 98 (93), 91 (100)
2c	56	294	$C_9H_{11}N_5O_3S$ (269.3)	3420, 3285, 1670, 1630, 1510, 1270, 1150, 930	3.85 (s, 3H), 6.94 (d, 2H, J = 9), 7.8 (d, 2H, J = 9)	269 (M^+, 17), 205 (45), 171 (76), 123 (52), 107 (100), 98 (65), 92 (65)
2d	70	299	$C_8H_8ClN_5O_2S$ (273.7)	3420, 3290, 1665, 1625, 1500, 1260, 1150, 930	7.5 (d, 2H, J = 10), 7.9 (d, 2H, J = 10)	273 (M^+, 9), 209 (9), 111 (61), 98 (100)
2e	30	290	$C_{10}H_{12}N_6O_3S$ (296.3)	3440, 3290, 1670, 1630, 1510, 1265, 1150, 930	2.3 (s, 3H), 7.65 (d, 2H, J = 10), 7.95 (d, 2H, J = 10)	296 (M^+, 6), 232 (30), 198 (24), 99 (56), 93 (100)
2f	73	299	$C_6H_7N_5O_2S_2$ (245.3)	3440, 3295, 1665, 1625, 1500, 1260, 1145, 925	7.11 (m, 1H), 7.73 (m, 2H)	245 (M^+, 43), 181 (100), 161 (15), 147 (45)
2g	10	228	$C_7H_{14}N_6O_2S$ (246.3)	3440, 3300, 3230, 1630, 1510, 1270, 1160, 930	1.65 (m, 6H), 3.3 (m, 4H)	246 (M^+, 100), 162 (9), 148 (15), 99 (89), 84 (71)
2h	12	224	$C_6H_{12}N_6O_3S$ (248.3)	3430, 3320, 1670, 1640, 1520, 1280, 1160, 930	3.4 (m, 4H), 3.96 (m, 4H)	248 (M^+, 40), 191 (52), 99 (100), 86 (76)

[a] Satisfactory microanalyses obtained: C ±0.37, H ±0.40 (Exceptions: **2d**, C +0.55, **2h**, C +0.44, **2f**, H +0.45).
[b] Compounds **2g, h** were analysed as crude products and **2a, f** were crystallised from $EtOH/H_2O$.
[c] Solvent: TFA or TFA + $CDCl_3$.

Table 3. Compounds **3** Prepared

Product	Yield (%)	mp (°C)	Molecular Formula[a, b]	IR (Nujol) ν (cm^{-1})	^{13}C-NMR (DMSO) δ	MS (70 eV) m/z (%)
3a	40	282	$C_8H_8N_4O_2S_2$ (256.3)	3390, 3290, 3100, 1620, 1530, 1300, 1180, 1070	124.96, 128.46, 131.37, 142.2 (C_{arom}), 157.12 (C-2), 162.60 (C-5)	256 (M^+, 57), 141 (33), 77 (100)
3b	50	282	$C_9H_{10}N_4O_2S_2$ (270.3)	3360, 3290, 3080, 1615, 1530, 1300, 1135, 1075	20.34 (CH_3), 125.0, 128.82, 139.38, 141.42 (C_{arom}), 156.90 (C-2), 162.5 (C-5)	270 (M^+, 35), 155 (43), 91 (100)
3c	49	275	$C_9H_{10}N_4O_3S_2$ (286.3)	3480, 3260, 3120, 1630, 1540, 1310, 1140, 1090	54.94 (OCH_3), 113.51, 127.0, 134.06 (C_{arom}), 156.85 (C-2), 161.17 (C_{arom}), 162.37 (C-5)	286 (M^+, 72), 171 (100), 107 (55), 77 (82)
3d	48	286	$C_8H_7ClN_4O_2S_2$ (290.7)	3380, 3120, 1630, 1540, 1320, 1140, 1090	126.89, 128.55, 136.12, 141.10 (C_{arom}), 157.3 (C-2), 162.58 (C-5)	290 (M^+, 83),[d] 175 (38), 111 (100)
3f	22	280	$C_6H_6N_4O_2S_3$ (262.3)	3420, 3270, 3120, 1630, 1550, 1310, 1135, 1090	125.75, 128.43, 129.84, 142.36 (C_{arom}), 156.52 (C-2), 161.80 (C-5)	262 (56), 147 (100), 99 (81)

[a] Satisfactory microanalyses obtained: C ± 0.38, H ± 0.40 (exception: **3f**, C + 0.53, H + 0.6).
[b] Samples for analysis prepared by dissolution in 2N NaOH and reprecipitation with 2N HCl.
[c] Recorded on MSL-300 operating at 75.476 MHz. Chemical shift values are form TMS with the DMSO signal at 39.9 taken as reference.
[d] Cl = ^{35}Cl.

terised by their elemental analyses, ^{1}H-NMR, ^{13}C-NMR and MS data (Table 3). To the best of our knowledge, this is the only method available for the regiospecific synthesis of *N*-sulfonyl derivatives of 2,5-diamino-1,3,4-thiadiazole.

Commercial grade reagents were used and were purified by distillation or crystallisation wherever necessary. The sulfonamides used as starting materials were prepared as reported.[6-8] Melting points are uncorrected. IR spectra were recorded on a Perkin-Elmer 599-B spectrophotometer as Nujol mulls. ^{1}H-NMR spectra were recorded on JEOL-FMX 60S, Varian FT-80A or a Bruker WH-90 instrument. ^{15}N-NMR spectrum for compound **3b** was recorded on a Bruker MSL-300 operating at 30.324 MHz in DMSO (CH_3NO_2 as standard) with a D_2O containing capillary for locking, using a standard DEPT pulse sequence, with and without proton decoupling during acquisition, and with a polarisation transfer delay of 5.55 msec. Mass spectra were recorded on GC/MS Finnigan MAT 1020C spectrometer. Microanalyses were carried out at the analytical division at National Chemical Laboratory.

S,S-Dimethyl *N*-[(2-Thienyl)sulfonyl]carbondithioimidates (1f); Typical Procedure:
A solution of 2-thienylsulfonamide (2.4 g, 14 mmol) in DMF (10 mL) is cooled in an ice-bath. To this is added with stirring 20 M NaOH solution (0.8 mL, 16 mmol), followed by CS_2 (0.7 g, 9 mmol). The colourless solution changes to brick red. After 20 min a second lot of 20 M NaOH solution (0.4 mL, 8 mmol) and CS_2 (0.35 g, 4.5 mmol) is added to the reaction mixture, followed by a third portion of 20 M NaOH solution (0.4 mL, 8 mmol) and CS_2 (0.35 g, 4.5 mmol) after an interval of 10 min. The ice-bath is removed and the mixture stirred at r.t. for 2 h. The mixture is cooled in an ice-bath and dimethyl sulfate (3.73 g, 29 mmol) is added dropwise through a dropping funnel. Addition is complete in 10 min and the colour of the mixture changes from brick red to yellow. After stirring for 2 h at r.t., the mixture is poured into H_2O (50 mL). The solid obtained is filtered, washed with H_2O and dried under vacuum to give 2.4 g of the crude product. Recrystallization from MeOH affords pure **1f**; yield: 2.24 g (60%) (Table 1).

***N*-(5-Amino-1*H*-1,2,4-triazol-3-yl)-4-methoxybenzenesulfonamide (2c); Typical Procedure:**
To a suspension of aminoguanidine bicarbonate (1.4 g, 0.01 mol) in ethylene glycol, (12 mL), is added a solution of KOH (0.56 g, 0.01 mol) in H_2O (2.5 mL) and **1c** (2.91 g, 0.01 mol). The mixture is heated at 170 °C with stirring under an atmosphere of N_2 for 90 min. Ethylene glycol is removed under reduced pressure, the residue dissolved in H_2O (25 mL) and acidified with AcOH. The solid obtained is collected by filtration, washed with H_2O and dried under vacuum to give **2c** as a white solid; yield: 1.5 g (56%) (Table 2).

***N*-(5-Amino-1,3,4-thiadiazol-2-yl)-4-methylbenzenesulfonamide (3b); Typical Procedure:**
To a suspension of hydrazinecarbothioamide (1.8 g, 0.02 mol) in ethylene glycol (25 mL) is added a solution of KOH (1.12 g, 0.02 mol) in H_2O (5 mL) and **1b** (5.5 g, 0.02 mol). The mixture is heated at 140 °C with stirring under an atmosphere of N_2 for 2 h. Ethylene glycol is removed under reduced pressure, the residue dissolved in H_2O (30 mL) and acidified with 2N HCl. The solid obtained is collected by filtration, washed with H_2O and EtOH, and dried under vacuum to give **3b** as a white solid; yield: 2.7 g (50%) (Table 3).

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