A New Cyclisation of Sulfenylated Dimethyl Sulfoxide and Thiosemicarbazone Adducts using Thionyl Chloride†

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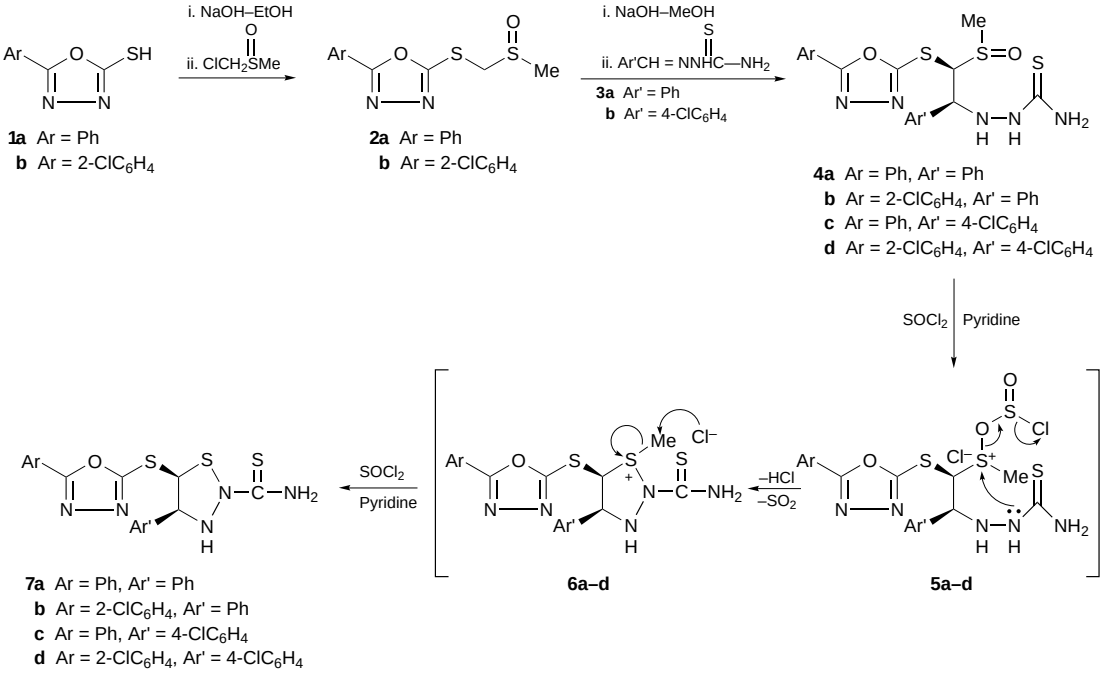
Adducts (**4a–d**) obtained by nucleophilic addition of sulfenylated dimethyl sulfoxide derivatives (**2a**,**b**) to thiosemicarbazones (**3a**,**b**) undergo a new intramolecular cyclisation, involving deoxygenative demethylation, to yield 5-sulfenylated 4-aryl-2-thiocarbamoyl-1,2,3-thiadiazolidines (**7a–d**) on treatment with thionyl chloride.

We recently published a convenient method for the synthesis of 6-sulfenylated 2-amino-1,3,4-thiadiazines from sulfenylated dimethyl sulfoxide and thiosemicarbazone adducts involving the acid-labile methylsulfinyl leaving group.[1] We now report a new, efficient and simple intramolecular cyclisation of the same adducts to 5-sulfenylated 4-aryl-2-thiocarbamoyl-1,2,3-thiadiazolidines (**7a–d**) involving deoxygenative demethylation on treatment with thionyl chloride. These sulfenylated heterocycles were required in connection with the development of potential pharmacological agents and agrochemicals.[1,2]

The synthetic sequence leading to the formation of **7** is depicted in Scheme 1. The formation of adducts **4** and their cyclisation to **7** were highly diastereoselective. The crude isolates were checked by ^{1}H NMR for their diastereomeric ratios to avoid inadvertent alteration of these ratios during subsequent isolation and purification (see Experimental section). The reaction of chloromethyl methyl sulfoxide and the sodium salt of 5-aryl-2-sulfanyl-1,3,4-oxadiazoles **1** in refluxing ethanol for 5 h furnished **2**. Nucleophilic addition of sulfur-stabilised carbanions, generated *in situ* by the action of sodium methoxide on **2** in methanol at room temperature, to the C=N of thiosemicarbazones **3** followed by quenching with dilute hydrochloric acid afforded **4** in 65–72% yield with high diastereoselectivity (92–96%). Adducts **4** underwent a new cyclisation, involving deoxygenative demethylation, on treatment with thionyl chloride in pyridine, resulting in 60–69% yield of **7** with 93–96% diastereoselectivity. The evolution of methanethiol on treatment of **7** with methyl iodide in ethanol followed by alkaline hydrolysis with potassium hydroxide provides chemical evidence for the presence of the thiourea residue in **7**. The easy and wide availability of the requisite substrates and the simple operations under mild conditions makes the present cyclisation a potential general synthetic method for a variety of cyclic systems.



Scheme 1

Experimental

Mps were determined in open glass capillaries and are uncorrected. IR spectra were recorded in KBr on a Perkin-Elmer 993 spectrophotometer. ^{1}H NMR spectra were recorded on a Perkin-Elmer R-32 (90 MHz) spectrometer using [$^2H_6$]dimethyl sulfoxide as solvent and $SiMe_4$ as internal standard. Mass spectra were recorded on a JEOL D-300 mass spectromter at 70 eV. Elemental analyses were carried out in a Coleman automatic carbon, hydrogen and nitrogen analyser.

5-Aryl-2-methylsulfinylmethylsulfanyl-1,3,4-oxadiazoles **2** *and 1-[1-aryl-2-(5-aryl-1,3,4-oxadiazol-2-ylsulfanyl)-2-(methylsulfinyl)ethyl]-thiosemicarbazides* **4**.—These were prepared according to the method described earlier[1] and recrystallised from ethanol. The crude product **4** was recrystallised from ethanol to give a diastereomeric mixture (>97: <3; in the crude isolates the ratio was 92–96:8–4, determined by ^{1}H NMR spectroscopy) which was again recrystallised from ethanol to obtain an analytical sample of a single diastereomer **4** (Tables 1 and 2). On the basis of ^{1}H NMR and published data,[5–7] compounds **4** were assigned *erythro* (*syn*) stereochemistry, as their ^{1}H NMR spectra exhibit a coupling constant, $J_{SCH,NCH}$ = 4 Hz, which is smaller than that of the very minor (<3%) diastereomer (*threo* or *anti*), $J_{SCH,NCH}$ = 10 Hz.

5-Aryl-2-(4-thiocarbamoyl-1,2,3-thiadiazolidin-5-ylsulfanyl)-1,3,4-

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†This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1997, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.

Table 1 Yields, mps, molecular formulae and elemental analyses of compounds **2**, **4** and **7**

Compd.	Yield (%)	Mp (*T*/°C)	Molecular formula	Found (required) (%)		
				C	H	N
2a	74	164–166	$C_{10}H_{10}N_2O_2S_2$	47.3 (47.2)	4.1 (4.0)	11.1 (11.0)
2b	70	171–173	$C_{10}H_9ClN_2O_2S_2$	41.5 (41.6)	3.0 (3.1)	9.6 (9.7)
4a	72	151	$C_{18}H_{19}N_5O_2S_3$	50.0 (49.9)	4.2 (4.4)	16.3 (16.2)
4b	68	180–182	$C_{18}H_{18}ClN_5O_2S_3$	46.1 (46.2)	3.9 (3.9)	15.2 (15.0
4c	65	157–158	$C_{18}H_{18}ClN_5O_2S_3$	46.0 (46.2)	3.7 (3.9)	15.1 (15.0)
4d	71	146	$C_{18}H_{17}Cl_2N_5O_2S_3$	42.9 (43.0)	3.3 (3.4)	13.8 (13.9)
7a	68	155–156	$C_{17}H_{15}N_5OS_3$	50.6 (50.9)	3.6 (3.8)	17.6 (17.4)
7b	60	130	$C_{17}H_{14}ClN_5OS_3$	46.6 (46.8)	3.2 (3.0)	15.9 (16.1)
7c	69	147–148	$C_{17}H_{14}ClN_5OS_3$	47.0 (46.8)	3.0 (3.2)	16.0 (16.1)
7d	62	158–160	$C_{17}H_{13}Cl_2N_5OS_3$	43.2 (43.4)	2.7 (2.8)	15.0 (14.9)

Table 2 Spectral data for compounds **2**, **4** and **7**

Compd.	ν_{max}/cm^{-1}	δ_H (*J* in Hz)	M^+
2a	1030 (S=O)	2.59 (s, 3 H, Me), 4.25 (s, 2 H, CH_2), 7.31–7.76 (m, 5 H, ArH)	254
2b	1035 (S=O)	2.62 (s, 3 H, Me), 4.28 (s, 2 H, CH_2), 7.48–8.03 (m, 4 H, ArH)	288
4a	1030 (S=O)	2.56 (s, 3 H, Me), 3.72 (d, 1 H, *J* 4.0, SCH), 4.92 (d, 1 H, *J* 4.0, NCH), 7.32–7.82 (m, 10 H, ArH), 8.40–9.22 (br, 4 H, $NHNHCSNH_2$)	433
4b	1035 (S=O)	2.58 (s, 3 H, Me), 3.71 (d, 1 H, *J* 4.0, SCH), 4.92 (d, 1 H, *J* 4.0, NCH), 7.30–8.06 (m, 9 H, ArH), 8.40–9.20 (br, 4 H, $NHNHCSNH_2$)	467
4c	1030 (S=O)	2.52 (s, 3 H, Me), 3.74 (d, 1 H, *J* 4.0, SCH), 4.94 (d, 1 H, *J* 4.0, NCH), 7.34–8.09 (m, 9 H, ArH), 8.44–9.18 (br, 4 H, $NHNHCSNH_2$)	467
4d	1035 (S=O)	2.57 (s, 3 H, Me), 3.76 (d, 1 H, *J* 4.0, SCH), 4.96 (d, 1 H, *J* 4.0, NCH), 7.36–8.16 (m, 8 H, ArH), 8.41–9.15 (br, 4 H, $NHNHCSNH_2$)	503
7a	3310–3365 (NH, NH_2)	4.20 (d,. 1 H, *J* 4.5, 5-H), 4.58–4.73 (br, 3 H, NH, NH_2), 5.23 (d, 1 H, *J* 4.5, 4-H), 7.28–7.76 (m, 10 H, ArH)	401
7b	3305–3370 (NH, NH_2)	4.10 (d, 1 H, *J* 4.5, 5-H), 4.62–4.82 (br, 3 H, NH, NH_2), 5.26 (d, 1 H, *J* 4.5, 4-H), 7.31–7.93 (m, 9 H, ArH)	435
7c	3315–3360 (NH, NH_2)	4.19 (d, 1 H, *J* 4.5, 5-H), 4.69–4.90 (br, 3 H, NH, NH_2), 5.28 (d, 1 H, *J* 4.5, 4-H), 7.40–8.02 (m, 9 H, ArH)	435
7d	3320–3375 (NH, NH_2)	4.22 (d, 1 H, *J* 4.5, 5-H), 4.70–4.89 (br, 3 H, NH, NH_2), 5.24 (d, 1 H, *J* 4.5, 4-H), 7.39–8.04 (m 8 H, ArH)	471

oxadiazoles **7**. *General Procedure*.—A solution of **4** (20 mmol) and thionyl chloride (2.0 ml, 25 mmol) in pyridine (50 ml) was refluxed for 8 h. The pyridine was evaporated under reduced pressure at 40 °C and the residue obtained was washed with water and recrystallised from ethanol to give a diastereomeric mixture (>97: <3%; in the crude isolates the ratio was 93–96: 7–4, determined by ^{1}H NMR spectroscopy) which on second recrystallisation from ethanol furnished an analytical sample of a single diastereomer **7** (Tables 1 and 2). Compounds **7** were assigned *cis* stereochemistry, as the coupling constant, $J_{4,5}$ = 4.5 Hz, for **7** was lower than that for the very minor (<3%) diastereomer (*trans*), $J_{4.5}$ = 11 Hz.[7–9]

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