The Mass Spectra of Some Bis[5-(2-mercapto-1,3,4-thiadiazolyl)]methyl and aryl Derivatives

Sebastiano Pappalardo*, Francesco Bottino and Michele Di Grazia

Istituto Dipartimentale di Chimica e Chimica Industriale dell'Università di Catania,
Viale A. Doria 8, 95125 Catania, Italy

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The general fragmentation patterns of five selected title compounds are described. The most significant mass spectral features arise from the interaction of aryl substituents with the adjacent heterocyclic ring. The decomposition of the compounds bearing an *ortho* nitro group in the *S*-aryl moieties is strongly affected by a prominent "*ortho* effect".

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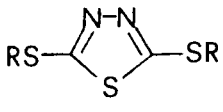
In connection with a biological screening program, a number of bis(1,3,4-thiadiazolyl) sulfur derivatives have been synthesized [1]. These compounds have not been studied previously with regard to their mass spectrometric behaviour, but the closely related 1,3,4-thiadiazolyl analogues **1**, well known for their biological activities [2], have been examined in detail [3].

This paper describes the decomposition pattern upon electron impact of five selected title compounds **2-6**.



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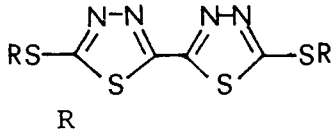
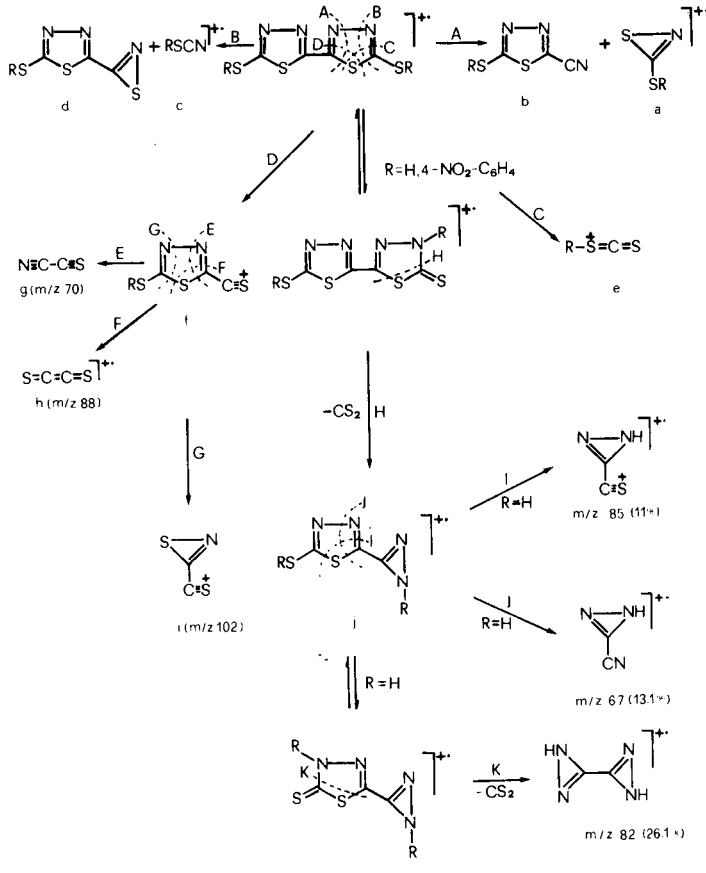


	R
2	H
3	CH_3
4	$2\text{-}NO_2\text{-}C_6H_4$
5	$4\text{-}NO_2\text{-}C_6H_4$
6	$2,4\text{-}(NO_2)_2\text{-}C_6H_3$

Scheme 1



Results and Discussion.

The general rationale for the electron-impact induced mass spectral fragmentation of the compounds investigated is shown in Scheme 1. Additional spectral features arising from the interaction of aryl substituents with the adjacent 1,3,4-thiadiazole ring are shown in Schemes 2-5. Selected ions and their relative abundances are listed in Table 1.

The molecular ion of compounds **2** and **3** is the base peak; in the remaining compounds it is much lower (**4** and **5**) or completely absent (**6**) (Table 1). Peaks associated with fissions across the heterocyclic ring(s) are less intense than those observed in the spectra of the 1,3,4-thiadiazole analogues **1**. These fissions are illustrated in Scheme 1.

The spectra of compounds **2-6** exhibit ion **a**, corresponding to the loss of a neutral molecule of 2-cyano-5-(substituted thio)-1,3,4-thiadiazole from the molecular ion, as shown by fission A (Scheme 1). As might be expected, in such fission the charge could be retained in both species, and for compounds **2** and **3** ion **b**, complementary to ion **a**, is also observed (Table 1). The intensity of ion **a** and *S*-aryl derivatives is comparatively lower for compounds **4** and **6** bearing an *ortho* nitro group in the *S*-aryl moiety. In fact, other fragmentation pathways compete with the heterocyclic ring fission, as will be seen below. Fission B to produce

Table 1

Selected Ions in the Mass Spectra of Bis[5-(2-mercapto-1,3,4-thiadiazoly)] Methyl and Aryl Derivatives **2-6** [a]

Ion [b]	**2** R = H	**3** R = CH_3	**4** R = 2-NO_2-C_6H_4	**5** R = 4-NO_2-C_6H_4	**6** R = 2,4-$(NO_2)_2C_6H_4$
$[M]^{+\cdot}$	234	262	476	476	566
	(100)	(100)	(3.7)	(13.9)	(−)
$[M - H]^+$	—	—	475	475	—
			(4.4)	(16.1)	
a	91	105	212	212	257
	(5.1)	(7.5)	(4.2)	(33.4)	(10.8)
b	143	157	—	—	—
	(7.8)	(4.6)			
c	59	73	—	180	—
	(32.1)	(3.3)		(1.8)	—
d	175	189	—	—	—
	(0.4)	(0.3)			
e	77	91	—	198	—
	(8.5)	(50)		(46)	
f	161	175	—	—	327
	(3.5)	(5.6)			(15.7)
g	70	70	70	70	70
	(20.4)	(9.5)	(53.5)	(46.2)	(49.7)
h	88	88	88	88	88
	(5.1)	(8.6)	(12.3)	(16.2)	(17.8)
i	102	102	102	102	102
	(3.1)	(3.1)	(27.9)	(24.5)	(14.1)
j	158	—	—	400	—
	(39)			(5.1)	
k	—	—	185	185 [c]	230 [d]
			(12.5)	(100)	(15.1)
l	—	—	—	136 [e]	181
				(36.5)	(12.4)
m	—	—	430	—	520
			(21.7)		(32.4)
n	—	—	218	—	263 [f]
			(93.5)		(73.5)
o	—	—	166 [g]	—	—
			(48.6)		
p	—	—	263	263	308
			(3.4)	(14.7)	(7)
q	—	—	138	—	183 [h]
			(52.5)		(82.7)

[a] Relative intensities in parentheses. [b] Ion assignment as shown in Schemes 1-5. [c] The losses of NO and NO_2 from this ion could account for the formation of fragments at m/z 155 (14.4%) and 139 (24%), respectively. [d] The losses of NO and NO_2 from this ion could contribute to the intensity of peaks at m/z 200 (27%) and 184 (21%). [e] Further decomposition of this ion by losses of O, NO, and NO_2 produces the fragments at m/z 120 (24.2%), 106 (9.2%), and 90 (49.2%), respectively. Subsequent loss of CO from the ion at m/z 106 gives the ion at m/z 78 (17%). [f] The loss of a NO_2 radical from this ion affords the ion at m/z 217, which is the base peak in the spectrum. Subsequent loss of $(CN)_2$ from the base peak produces the intense peak at m/z 165 (28.1%). [g] Trivial losses of S, CS, CNS and CS_2 from this ion lead to the formation of the fragments at m/z 134 (9.9%), 122 (23.8%), 108 (C_6H_4S, 100%), and 90 (46.7%), respectively. [h] The loss of NO_2 from this ion gives the very intense ion at m/z 137 (99.5%).

thiocyanate ion **c** occurs with good intensity only in compound **2**, the complementary ion **d** being negligible (< 1%) or absent in all compounds examined (Table 1). Fission C leads to the formation of ion **e**; significantly, compounds **4** and **6** having an *ortho* nitro group in the *S*-aryl moieties do not show this fission.

Compounds **2**, **3**, and **6** show also fission D to give ion **f**. Additional fragments at m/z 70, 88, and 102, characteristic of the bis(1,3,4-thiadiazolyl) system, could be associated to ions **g**, **h**, and **i**, respectively, probably arising from ion **f** through fissions E-G (Scheme 1).

Ion **a** fragments further by loss of HNC: (compounds **4-6**) or alternatively by loss of CS_2 (compounds **5** and **6**). Scheme 2 rationalizes the genesis of the highly stable dithioquinoid structure **k** [**a** - HNC:]$^{+\cdot}$ *via* a hydrogen transfer to the nitrogen atom, with subsequent rearrangement to a 2-imino-1,3-benzodithiole structure followed by elimination of isocyanidric acid. Ion **k** is the source of the base peak in **5**, and occurs with reasonable intensity in **4** and **6**.

A similar loss of HNC: has been reported for *S*-aryl substituted 1,3,4-thiadiazoles [3] and for the structurally related 2-aminobenzothiazole [4]. Scheme 2 also shows the ge-

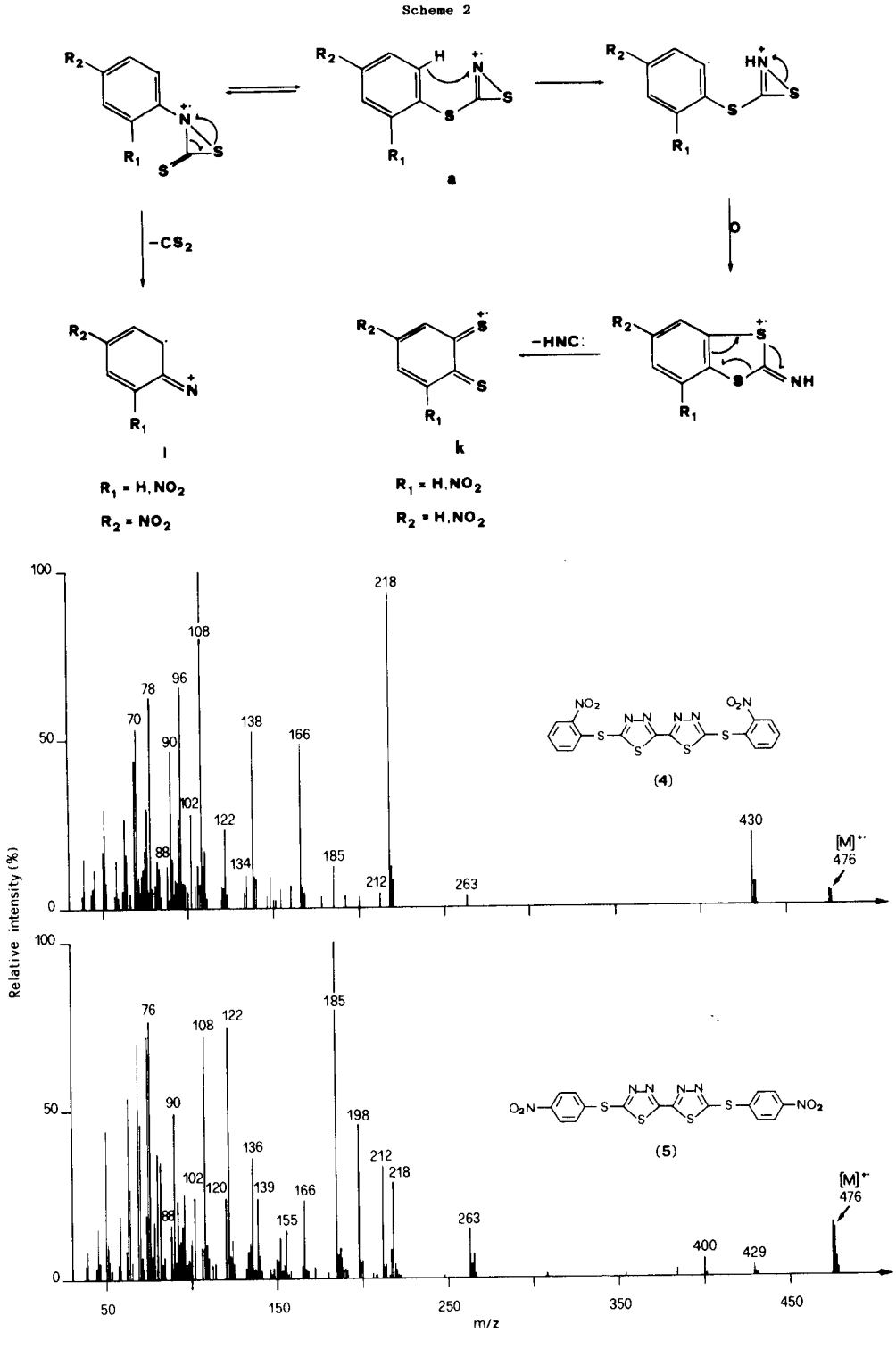
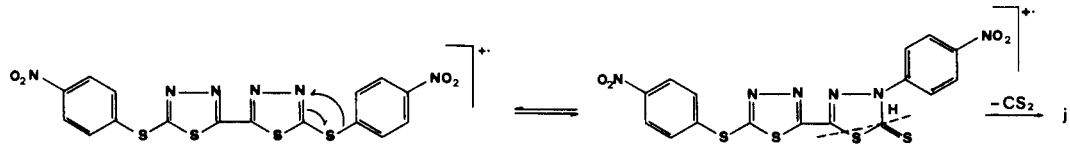


Figure 1. The mass spectra of isomeric bis-sulfides **4** and **5**.

nesis of ion **1**. This can arise by a tautomeric thiol-thione equilibrium of fragment **a**, and subsequent expulsion of carbon disulfide. This process occurs with good intensity in **5**, is still present in **6**, but is suppressed in **4** (Table 1).

The mass spectrum of the parent compound **2** is dominated by prominent ions at m/z 158 (ion **j**) and 82, due to the loss of one or two neutral molecules of CS_2 from the molecular ion, according to fissions H and K, respectively

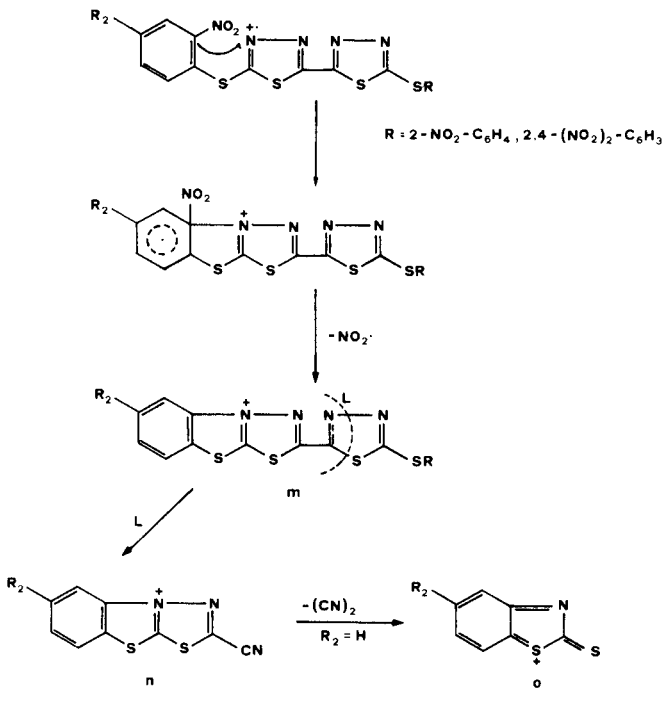
Scheme 3



(Scheme 1). These fissions involve the presence of the tautomeric thione form, according to the well-known thiol-thione equilibrium [5]. In a rather similar way 2-mercapto-1,3,4-thiadiazoles [3] and benzothiazoles [6] exhibit this equilibrium with loss of CS_2 from the thione form. Ion **j** from compound **2** (R = H) fragments further through fissions I and J to give fragment ions at m/z 85 and 67, respectively (Scheme 1).

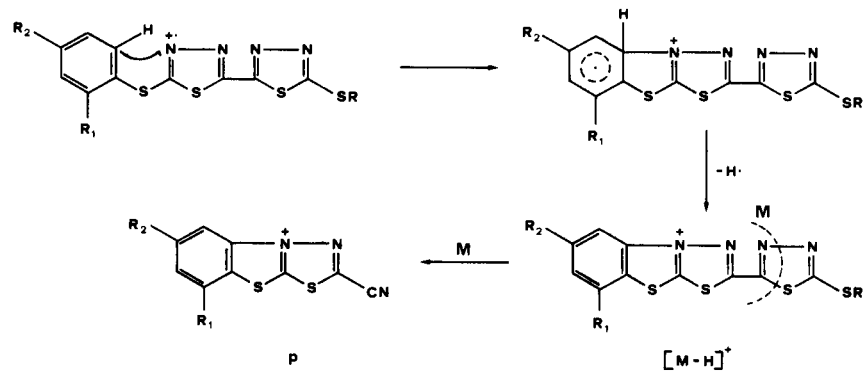
Much more intriguing is the presence of the $[M - CS_2]^{+\cdot}$ ion in the mass spectrum of compound **5** (Table 1 and Figure 1). The appearance of this ion can be explained by the presence *in the vapour state* of a percentage of the thione form, according to the four centre aryl migration depicted in Scheme 3. A similar rearrangement has been observed in related *S*-aryl-1,3,4-thiadiazoles [3], and is a well-documented process for aryl phenyl carbonates [7] and thiocarbonates [8].

Scheme 4



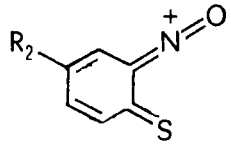
Compounds **4** and **6** do not show this fragmentation mode. In these cases an "*ortho* effect" [9] is the dominant process, and the intensities of the peaks in their mass spectra take this situation into account. In fact, the loss of a nitro group from the molecular ion leads to intense peaks in the mass spectra of compounds **4** and **6** (Table 1 and Figure 1). This easy loss of an *ortho* electron-withdrawing group can proceed by initial cyclization of the molecular ion to a species (σ-complex) [9], which can obtain increased ionic stability by elimination of a nitro radical to give **m** (Scheme 4). Afterwards ion **m** undergoes fission L to afford the very intense ion **n**, which is the precursor of the base peak in the mass spectrum of **6** (footnote [f], Table 1). A subsequent ejection of a neutral molecule of $(CN)_2$ from ion **n** (R_2 = H) leads to the fully conjugated 2-thiobenzothiazole structure **o**. In addition, from this ion the characteristic decomposition pattern of 2-mercaptobenzothiazole [6] is observed, which accounts for the formation of the base peak in compound **4** (footnote [g], Table 1). In the spectrum of **5** the ion **o**, corresponding to the loss of $(CN)_2$ from the ion **n**, is not observed, perhaps due to the electron-withdrawing ability of the nitro group which stabilizes the ion **n**.

Scheme 5



A similar "*ortho* effect" can be envisaged for the presence of the $[M - H]^{+\cdot}$ ion, analogous to **m**, in the spectra of *S*-aryl derivatives **4** and **5**. Subsequent fission M would produce the ion **p** (Scheme 5).

Finally, as recognized in previous mass spectral studies [3,10], the $[M - NO_2]^+$ ion **m** is diagnostic for distinguishing between *o*- and *p*-nitro *S*-aryl-substituted bis[5-(1,3,4-thiadiazolyl)] derivatives, as shown in the mass spectra of isomeric compounds **4** and **5**, reported in Figure 1. Moreover, the spectra of *o*-nitro derivatives **4** and **6**, show very intense fragments associated with the stable structure **q**, generated by an oxygen transfer [9] from the *o*-nitro function to the heterocyclic ring acting as acceptor.



q (R_2 = H, NO_2)

In conclusion, the mass spectral features of the title compounds appear to parallel those previously observed for the structurally related 2,5-dithio-1,3,4-thiadiazole methyl and aryl derivatives.

EXPERIMENTAL

Melting points were determined on a Kofler apparatus and are uncorrected. The pmr spectra were recorded on a Perkin-Elmer R-32 spectrometer operating at 90 MHz in deuterated dimethylsulfoxide. Chemical shifts are in parts per million (δ) from internal TMS. Mass spectra were recorded at 70 eV on a Hewlett-Packard Model 5985 GC/MS spectrometer, using the direct insertion probe technique. Compounds **2** and **3** were prepared by known procedures [11].

General Nucleophilic Displacement. Bis[5-[2-(2'-nitrophenylthio)-1,3,4-thiadiazolyl]] (**4**).

A stirred mixture of 0.32 g (2 mmoles) of 2-nitrochlorobenzene, 0.23 g (1 mmole) of **2**, and 0.56 g (4 mmoles) of anhydrous potassium carbonate in 2 ml of dimethylformamide was heated at 100° for 5 hours under nitrogen. After cooling, 2 ml of water was added and the precipitate filtered, washed with water and recrystallized from dioxane to give 0.12 g (25%) of yellow crystals, mp 280-283°; nmr: δ 7.70 (6H, m), and 8.25 (2H, m).

Anal. Calcd. for $C_{16}H_8N_6O_4S_4$: C, 40.34; H, 1.68; N, 17.65. Found: C, 40.20; H, 1.77; N, 17.55.

Bis[5-[2-(4'-nitrophenylthio)-1,3,4-thiadiazolyl]] (**5**).

Compound **5** was obtained in 48% yield from **2** (1 mmole) and 4-nitrobromobenzene (2 mmoles) by following the general procedure, beige needles, mp 204-205° (from dioxane); nmr: δ 8.06 (4H, d, J = 9 Hz) and 8.41 (4H, d, J = 9 Hz).

Anal. Calcd. for $C_{16}H_8N_6O_4S_4$: C, 40.34; H, 1.68; N, 17.65. Found: C, 40.71; H, 1.73; N, 17.54.

Bis[5-[2-(2',4'-dinitrophenylthio)-1,3,4-thiadiazolyl]] (**6**).

Compound **6** was obtained in 76% yield from **2** (1 mmole) and 2,4-dinitrochlorobenzene (2 mmoles), yellowish scales, mp > 290° (from DMF). No pmr spectrum was obtained due to its insolubility in most common solvents.

Anal. Calcd. for $C_{16}H_6N_8O_8S_4$: C, 33.92; H, 1.06; N, 19.79. Found: C, 33.77; H, 1.01; N, 19.90.

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