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THERMAL STABILITY OF SOME 1,3,4-THIADIAZOLES WITH POSSIBLE ANTIMICROBIAL ACTIVITY

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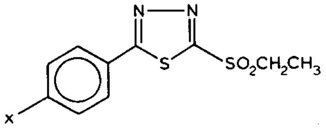
ABSTRACT

Five-substituted-aryl-2-sulphonyl-1,3,4-thiadiazoles, five-substituted-1,3,4-thiadiazoles, five-substituted-1,3,4-thiadiazol-2-yl-carbazates and dithiocarbazates and 2-(*N*,*N′*-dialkyl carboxy)hydrazino-5-phenyl-1,3,4-thiadiazoles were prepared. Thermal analyses of these compounds were performed in static air. Information was obtained on their thermal stability and decomposition.

INTRODUCTION

Several 1,3,4-thiadiazole derivatives show a pronounced antifungal activity [1,2], in addition to the well-known fungicidal and bactericidal properties of dithiocarbamates [3]. In a previous study [4,5] the preparations of compounds **1–8** (shown below) were reported.

(a) Five-substituted-aryl-2-sulphonyl-1,3,4-thiadiazole compounds (**1**, X = H; **2**, X = *p*-chloro; **3**, X = *p*-nitro).



(b) Five-substituted-1,3,4-thiadiazol-2-yl carbazates and dithiocarbazates (**4**, X = O, R = allyl, y = chloro; **5**, X = O, R = C_4H_9, y = H; **6**, X = O, R = allyl, y = H; **7**, X = S, R = C_2H_5, y = H).

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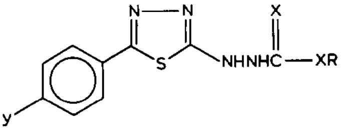
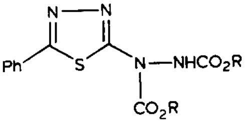


(c) 2-(*N*,*N*′-Dialkyl carboxy)hydrazino-5-phenyl-1,3,4-thiadiazoles (**8**, R = allyl).



Some of these compounds show biological activity (Table 1). It has been suggested that the biological activity of many pharmaceuticals depends on the σ and π characteristics of the substituents [6,7]. Thermoanalytical methods have been applied to the study of the stability, structure and physical properties of organic compounds [8–13] and pharmaceuticals [14].

The aim of this work is to study the thermal stabilities and decomposition patterns of compounds **1**–**8**.

EXPERIMENTAL

Compounds **1**–**8** were prepared as described in refs. 4 and 5. Compounds **4**–**8** are derivatives of compounds **1**–**3**. Differential scanning calorimetry (DSC) measurements were carried out using a Heraeus TA-500 thermal analyser. The heating rate was 10 °C min^{-1} in static air. Aluminium oxide was used as a reference.

The experimental error was ±3 °C. Melting points were determined in an open glass capillary using electrothermal apparatus and are uncorrected.

RESULTS AND DISCUSSION

Differential scanning calorimetry of compounds **1**–**3** (Fig. 1) and **4**–**8** (Fig. 2) was performed between room temperature and 500 °C in static air.

TABLE 1

In vitro inhibition zones (diameter in millimetres)

Compound	*Staphylococcus aureus*	*Candida albicans*	*E. coli*
2	12	16	–
3	–	18	–
4	10	13	–
5	11	12	–
8	10	–	–

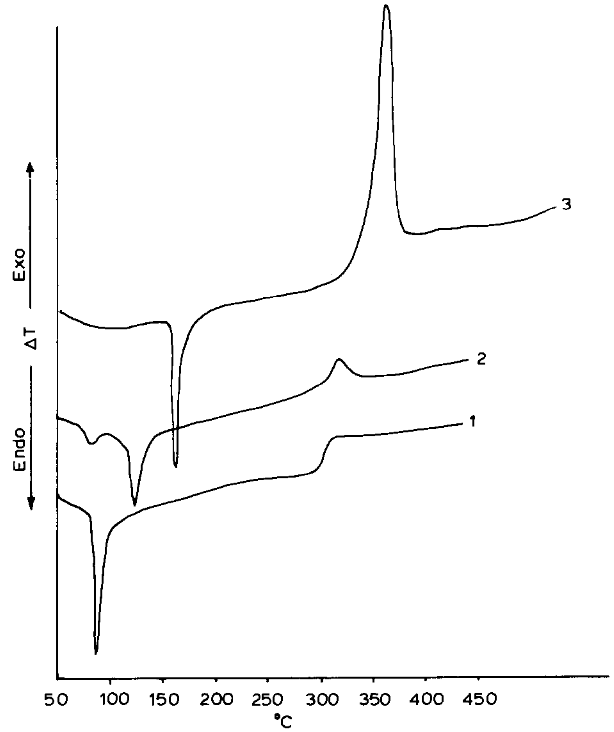


Fig. 1. Differential scanning calorimetry of compounds **1–3** in static air.

The values of the temperatures T_i, T_m and T_f and the decomposition temperature are shown in Table 2. The main feature of the DSC of compounds **1–8** is a sharp endothermic peak which corresponds to the fusion transition of these compounds. From Table 2 and Figs. 1 and 2 the following observations can be made.

TABLE 2

The temperatures of transition and decomposition of compounds **1–8** (in °C)

Compound	T_i	T_m	T_f	Melting point	Decomposition temperature	
					T_1	T_2
1	83	90	106	88	313	
2	102	128 (82.5)	168	133	317	
3	157	163	183	174	363	
4	125	127	157	130	245	288
5	93	105	120	105	245	278
6	142	132	168	145	263	308
7	111	114	130	125	275	
8	183	192	210	184	257	

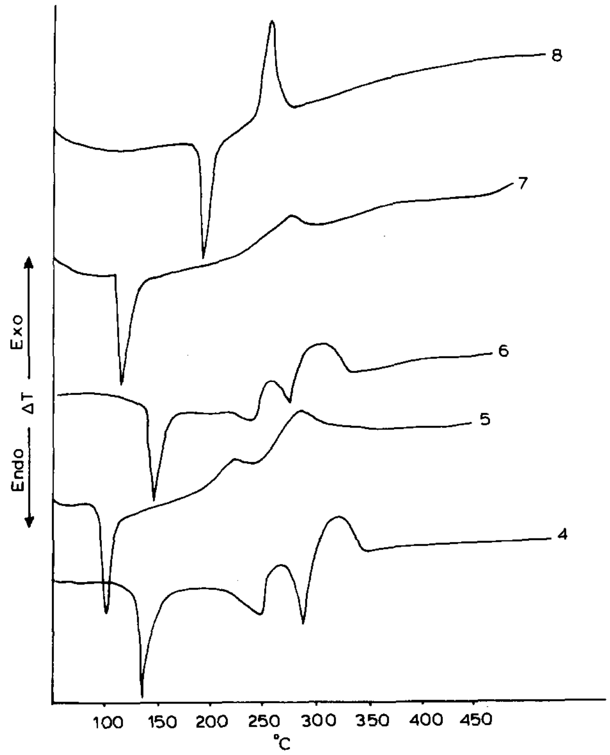


Fig. 2. Differential scanning calorimetry of compounds **4**–**8** in static air.

(1) The T_m values obtained from DSC differ slightly from the corresponding melting points.

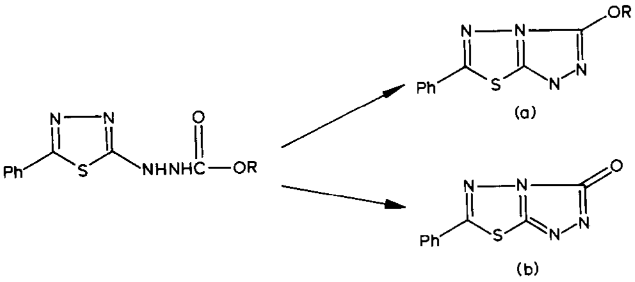
(2) For compounds **1**–**3**, the presence of NO_2 in the aryl group increases the thermal stability of compound **3** relative to compounds **1** and **2**. Thus the thermal stability of compounds **1**–**3** decreases in the following order **3** > **2** > **1**.

(3) Compound **3** gives a very sharp exothermic peak and decomposes at 363°C, whereas compounds **2** and **1** decompose at 317°C and 313°C respectively.

(4) The DSC curve of compound **2** shows a small endothermic maximum at 83°C. The purity of this compound was checked by thin layer chromatography and it was dried before use. This peak may be due to a phase transition. This requires further investigation.

(5) For compounds **4**–**6** and **8**, the stability decreases in the order **6** > **4** > **5** > **8**. The substitution of X = Cl in the series **4**–**7** decreases the thermal stability (compare compound **6** with compound **4**). Replacing R = *n*-butyl with R = allyl increases the thermal stability.

(6) For compounds **4**–**6** two exothermic peaks are obtained. These compounds can be rearranged thermally to give (a) or (b) (Scheme 1).



Scheme 1

In contrast, compound **8** gives one exothermic peak. This result indicates that this compound will not thermally rearrange. When compound **4** is dissolved in ethanol and refluxed for a few hours, the IR spectrum of the isolated product gives no carbonyl absorption. This indicates that compound **4** rearranges to form (a) (Scheme 1).

(7) The dithiocarbazate (compound **7**) is thermally less stable than the carbazates (compounds **4**–**6**).

In conclusion, the results indicate that the relative thermal stability of compounds **1**–**8** decreases in the following order **3** > **2** > **1** > **6** > **4** > **5** > **7** > **8**. The thermal stability increases as the π contribution of the substituents increases ($X = NO_2$ and R = allyl).

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