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THERMOANALYTICAL STUDY OF CYCLIZATION REACTION OF SOME THIOUREATES

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Abstract

Thermal initiated conversion of N-aryl-N'-(2-benzylpyridinium)thioureates into 2-arylamino-4H-benzo[*d*][1,3]thiazines was studied by non-isothermal differential scanning calorimetry (DSC), thermogravimetry (TG) and differential thermal analysis (DTA) in the solid-state. The values of molar reaction ethalpies (H_r) of six derivatives of thioureates and the melting parameters (T_f, H_f, S_f) of the obtained products – benzothiazines were determined by the DSC method.

Keywords: benzothiazine, cyclization reaction, DSC, enthalpy of fusion, enthalpy of reaction, entropy of fusion, phase transition, temperature of melting, thermal analysis, thioureate

Introduction

The methods of thermal analysis are valuable tool for determination the basic physico-chemical properties various substances as well as for investigation of thermal behaviour, reactions and phase transitions of organic compounds and pharmaceuticals [1–3]. An interesting application for these methods is to study the reactions of organic substances in the solid-state [4–8].

One of the synthetic method for obtaining of benzothiazine derivatives (**B**) with high yields is the thermal decomposition of N-aryl-N'-(2-benzylpyridinium) thioureates (**A**) [9]. These compounds are important as starting material for the controlled synthesis of heterocyclic compounds. The general course of the reaction is described in the Scheme 1.

Thermoanalytical study of this reaction has not been reported in the literature so far. In this study, we used DSC under non-isothermal conditions for the thermochemical study of this reaction in solid phase as well as for evaluation of melting parameters of the forming thiazines.

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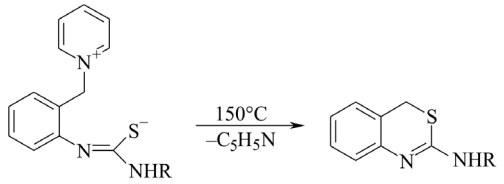

A (Compounds **I–VI**) **B** (Compounds **1–6**)

Scheme 1

Experimental

Syntheses

The N-aryl-N'-(2-benzylpyridinium)thioureates (Table 1) were prepared by a described method [9]. The structures of the synthesized compounds were confirmed by elemental analysis as well as IR, ^{1}H, ^{13}C NMR and mass spectrometry.

Instrumentation

Calorimetric measurements were carried out with a DSC-2C differential scanning calorimeter (Perkin Elmer) in a dynamic nitrogen atmosphere with a flow rate of 20 cm^3 min^{-1} in the temperature range of 45–280°C. The substances of 0.9–4.2 mg were placed in sealed aluminium sample pans as used for volatile substances with perforated lids. The reference aluminium sample pan was empty. The heating rates were 5 and 2.5 K min^{-1}. Indium was used as standard for calibration.

TG, DTG and DTA curves were recorded with a Derivatograph C (MOM, Hungary) in air atmosphere. Samples of 10–13 mg were measured in ceramic crucibles between 40–400°C with a heating rate of 20°C min^{-1}.

Results and discussion

The preliminary DSC scans obtained for six derivatives of N-aryl-N'-(2-benzylpyridinium)thioureate in the temperature range 45–280°C showed two peaks (Fig. 1). The first (exothermic) peak at 140–180°C corresponds to the cyclization reaction connected with the release of pyridine, while the second (endothermic) peak at about 200°C characterizes the melting of the forming products – thiazines.

The thermal behaviour of some thioureates was investigated also by means TG and DTA. The simultaneous TG, DTG and DTA of thioureate derivative **II** show two stages of decomposition (Fig. 2). The first endothermic peak of DTA occuring between 118 and 160°C represents the cyclization with melting of starting substance. The reason for endothermic effect is that the exothermic reaction overlaps with melting of reactant at these conditions. The mass loss at the end of this stage corresponds to the loss of pyridine molecule. The second sharp endothermic peak in the DTA curve at 165°C corresponds the subsequent melting of the forming product. Broad

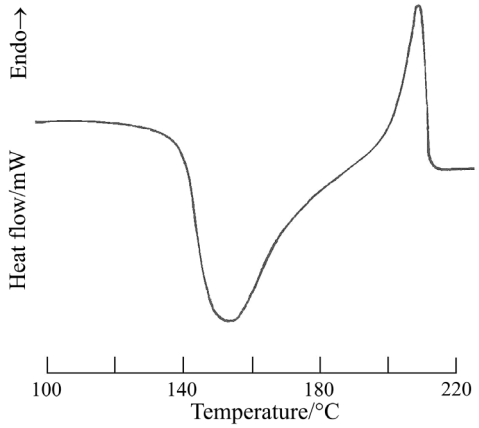

Fig. 1 DSC curve of N-aryl-N'-(2-benzylpyridinium)thioureate (e.g. compound **V**, heating rate 20 K min^{-1})

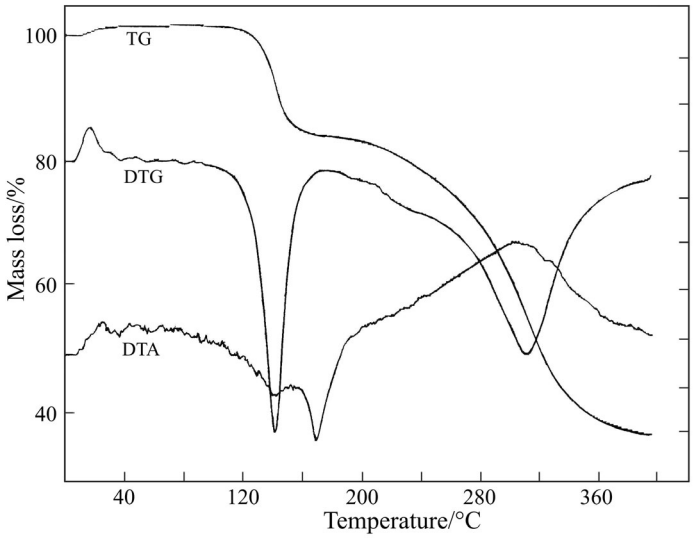

Fig. 2 TG, DTG and DTA curves of N-aryl-N'-(2-benzylpyridinium)thioureate, (compound **II**)

exothermic DTA peak between 200–380°C (center at about 300°C) corresponds to decomposition reaction of benzothiazine.

*Thermal behaviour of N-aryl-N'-(2-benzylpyridinium) thioureates (**I**–**VI**)*

The thermally initiated reaction was observed in the region of 83–190°C depending on the type of reactant. The preliminary DSC curves obtained at a higher heating rate (20 K min^{-1}) showed that the reaction was accompanied, in some cases, by the melting of the initial reactant (e.g. compound **II**). It was possible to eliminate the effect of

the melting by decreasing of the heating rate. Heating rate of 5 K min^{-1} was chosen so that the reaction realized in the solid-state.

The values of reaction enthalpies (H_r), as well as the thermometric data characterizing the cyclization reaction of the derivatives of N-aryl-N'-(2-benzyl-pyridinium) thioureates are presented in Table 1.

Table 1 Reaction enthalpies of the N-aryl-N'-(2-benzylpyridinium)thioureates (heating rate 5 and [a]2.5 K min^{-1})

Compound		H_r/ J g^{-1}	H_r/ kJ mol^{-1}	T_m/°C	T/°C
No.	R				
I	4-$CH_3C_6H_4$[a]	118.4 5.9	39.5 2.0	113, 127	83–148
II	4-$CH_3OC_6H_4$	92.9 4.6	32.5 1.6	132	101–157
III	4-$CH_3COC_6H_4$	56.2 4.6	20.3 1.6	137	99–168
IV	4-ClC_6H_4	29.0 3.4	10.3 1.2	129	113–145
V	4-BrC_6H_4	211.3 8.8	84.1 3.5	137, 139	118–169
VI	2-CH_3, 4-ClC_6H_4	314.8 8.7	115.8 3.2	136, 142	116–192

The complex shape of the reaction exotherm allows to suppose the multistep course of the process, as in the case of compounds **I**, **V** and **VI**.

The molar reaction enthalpies were in the range of 10–116 kJ mol^{-1} according to the type of substituent. The values of specific reaction enthalpies were in the range of 29–315 J g^{-1}. On the basis of different structure of the reactant it may be assumed that the value of reaction enthalpy depends on the electronic and especially steric effects of the substituent in the NH group of starting compound. Significantly lower values of reaction enthalpy were observed for compounds **III** and **IV**. This fact may be explained by partial melting of reactant during the reaction even at low heating rate.

*Thermal behaviour of 2-arylamino-4H-benzo[d][1,3]thiazines (**1**–**6**)*

The melting process of forming reaction products – benzothiazines was also studied. Melting temperatures and enthalpies, together with the calculated associated entropies for 2-arylamino-4H-benzo[*d*][1,3]thiazines are given in Table 2. The melting entropy (S_f) was calculated from the relation $S_f = H_f/T_f$, where H_f is the melting enthalpy and T_f the temperature of melting.

The values of melting enthalpy are in the range 16–29 kJ mol^{-1}. Enthalpy of melting for compound 6 was also determined after cooling by repeated heating. The difference between two obtained H_f values was within 5%.

The values of melting temperatures (T_f) of benzothiazines determined by DSC were in good agreement with those obtained by hot-stage microscope for the same compounds prepared by organic synthesis in solution and published in [9]. The value of T_f 175.2°C was determined by DSC for compound **1** in accordance with the literature data 170°C as well as for compound **2** 163°C (DSC) *vs*. literature data 168°C [9].

Table 2 Melting enthalpies and entropies of 2-arylamino-4H-benzo[*d*][1,3]thiazines determined by DSC (heating rate 5 and [a]2.5 K min^{-1})

Compound		H_f/ kJ mol^{-1}	T_f/°C	S_f/ J $(mol\ K)^{-1}$
No.	*R*			
1	4-$CH_3C_6H_4$[a]	19.9 0.7	175.2 0.2	44.38
2	4-$CH_3OC_6H_4$	16.1 1.2	163.0 0.4	36.92
3	4-$CH_3COC_6H_4$[a]	28.6 1.8	185.6 0.2	62.35
4	4-ClC_6H_4	27.5 1.1	203.2 0.5	57.74
5	4-BrC_6H_4	24.5 0.7	205.1 0.2	51.23
6	2-CH_3, 4-ClC_6H_4	17.5 1.3	222.6 0.7	35.30

Quench cooling a melt often leads to the amorphous product which on heating undergoes glass transition followed by crystallization [10, 11]. Similar phenomenon was possible to observe in the case of benzothiazine derivative **3** (Fig. 3). After first melting and quench cooling the melt was in the second DSC run of heating occurred an exothermic process preceding the melting at 190°C and showing the reversibility.

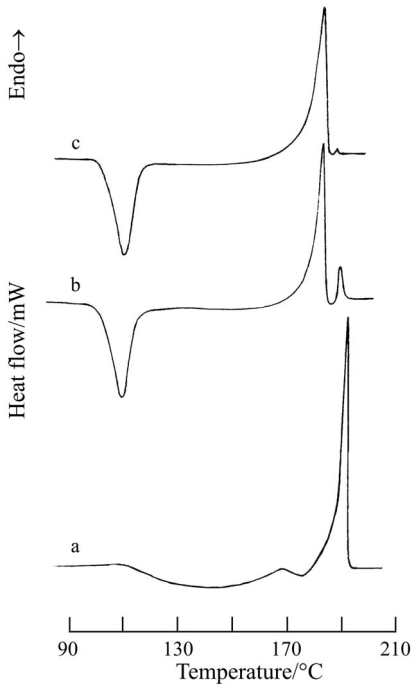

Fig. 3 The DSC scans of the benzothiazine derivative 3 (*R*=4-$CH_3COC_6H_4$); a – the first heating, b – the second heating after quench cooling the melt, and c – the third heating, heating rate 20 K min^{-1}

The exothermic peak at about 110°C in the DSC curve probably corresponds to the cold crystallization of amorphous form of benzothiazine followed by melting at lower temperature. No glass transition was observed.

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