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Short Communication

THERMAL BEHAVIOUR OF 1,3-DIMETHYL-4-ALKYLAMINO-5-NITROSOURACILS

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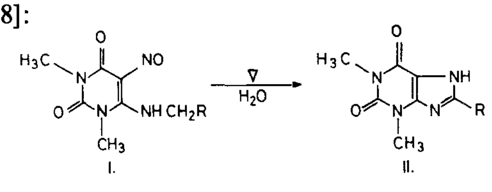
The thermally initiated cyclocondensation of 1,3-dimethyl-4-alkylamino-5-nitrosouracils (I), giving rise to the 8-substituted theophyllines (II), was studied by DSC. The corresponding reaction enthalpies were determined for six derivatives of I.

The methods of thermal analysis are becoming an important tool for the study of organic substances, e.g. investigation of their phase transitions, structures, thermal stabilities, molecular rearrangements and chemical reactions [1–5]. A very interesting field for the use of these methods is the investigation of the decomposition of these substances in the solid phase, and determination of the corresponding thermodynamic and kinetic parameters and the mechanism of the investigated process. Attention has recently also been paid to the thermal investigation of purines [6] and metal complexes of the derivatives of 6-amino-5-nitrosouracils [7].

One valuable method of preparation of the 8-substituted theophyllines (II) is the thermally-initiated cyclocondensation of 1,3-dimethyl-4-alkylamino-5-nitrosouracils (I) [8]:



In this study, we used DSC under non-isothermal conditions for the thermochemical study of this reaction, which has not previously been reported.

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Experimental

The derivatives of I (R = H, CH_3, *iso*-C_3H_7, $CH_2C_6H_5$, CH_2OH, CH_2CH_2OH) were prepared by the nitrosation of 1,3-dimethyl-4-alkylaminouracils with propyl nitrite in methanol. The structures of the prepared compounds were confirmed by spectral methods (UV, IR, and ^1H NMR spectrometry).

The DSC measurements were carried out with a DSC–2 calorimeter (Perkin–Elmer) in a dynamic nitrogen atmosphere with a flow rate of 20 ml min^{-1}. The heating rate was 10 deg min^{-1}. The samples (0.5–1.6 mg) were placed in aluminium sample pans, which were either covered with a lid or closed by means of a perforated cover. Indium was used as standard for calibrating the temperature scale and determining the enthalpic changes.

Results and discussion

There are two conspicuous peaks in the DSC curve obtained by thermal investigation of the derivatives of I in the temperature interval between 320 and 700 K. The first exothermic peak corresponds to the cyclocondensation (1), and the second one is to be attributed to melting or sublimation of the product, which depends on the type of closure of the samples.

A relatively distinct exothermic reaction was observed in the region 360–440 K. In contrast to other derivatives, we can observe a complex peak with two tips, at 420 K and 424 K, in the DSC record of the reaction exotherm of the benzyl derivative of I. The first tip is poorly expressed. Its origin is not clear for the present. The values of the total molar reaction enthalpy (ΔH_R) calculated from the area under the exotherm are given in Table 1. The different kinds of closure of the

Table 1 Thermometric and enthalpic data characterizing the course of cyclocondensation (1)

Compound	R	Temperature, K$^+$			$-\Delta H$, kJ mol^{-1}
		T_i	T_p	T_f	
1	H	404	423	439	212 ± 7
2	CH_3	369	403	416	219 ± 5
3	iso-C_3H_7	368	391	407	224 ± 9
4	$CH_2C_6H_5$	390	425	432	235 ± 14
5	CH_2OH	399	423	431	190 ± 5
6	CH_2CH_2OH	365	391	406	178 ± 6

$^+$ T_i, T_p and T_f denote the initial, maximum and final temperatures of the DSC peak of the reaction samples had no observable influence on the determination of ΔH_R. Certain differences in the originally published data [9] may be due to different heating rates.

The results reveal the influence of the structure of the substituent, which may also be observed in the increasing values of ΔH_R found for derivatives 1–4. This may be connected with steric relations and with the structure in the solid phase. On the other hand, the considerable decrease in the values of ΔH_R for the OH-substituted compounds must be caused by the polar character of this group.

The investigated solid-state reaction (1) of the type $A_s \rightarrow B_s + C_g$ was also observed visually with a heating microscope (Kofler). The information thus obtained about the occurrence or non-occurrence of melting before reaction is important not only from the aspect of the estimation of the reaction enthalpy itself, but also from the aspect of kinetic analysis, which will be subject matter of the subsequent communication [10]. As concerns the first derivative, melting affecting the determination of ΔH_R was observed before the reaction. No melting was observed for other compounds, though the occurrence of local melting cannot be excluded [11].

From preliminary calculations of the kinetics of this reaction by means of the integral method of Coats–Redfern [12], it may be assumed that the reaction of derivative 2 (in the non-isothermal regime) is governed by a kinetic equation of the first order, the activation energy being ≈ 206 kJ mol^{-1} [10].

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