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THERMOPHYSICAL PROPERTIES OF CYTIDINE AND DEOXYCYTIDINE MONO- AND HEMIPHOSPHATES

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Abstract

The calorimetric (DSC) and derivative thermogravimetric (DTG) measurements for crystalline mono- and hemiphosphates of cytidine and deoxycytidine have been performed. The results for four examined salts confirm the influence of presence (or absence) of 2'OH group in ribose ring on stability (or lability) of the crystal structure of examined salts.

Keywords: cytidine, deoxycytidine mono- and hemiphosphates, thermophysical properties

Introduction

Cytidine (Cyd) and deoxycytidine (dCyd) belong to the fundamental fragments of nucleic acids RNA and DNA. The monophosphates of Cyd and dCyd: $CydH^+ \cdot H_2PO_4^-$ and $dCydH^+ \cdot H_2PO_4^-$ are interesting for us mainly because of their crystal structures [1]. In the crystals, the $H_2PO_4^-$ anions join the neighbouring ribose and deoxyribose rings, 'mimicking' the native 3'–5' internucleotide phosphodiester bonds (scheme 1 [2–4]). The X-ray analysis of the two monophosphates has shown that they are isostructural to a very high degree [2, 3]. In spite of the isomorphism, important differences in physico-chemical properties are observed, for example differences in solubility, in ability of forming hemiphosphates [1]. It has to be stressed out that Cyd hemiphosphate has been obtained very recently [5].

The aim of this work is to obtain information on thermophysical properties of Cyd and dCyd mono- and hemiphosphates, comparatively. A better understanding interactions inside the crystals of examined salts is the purpose of our study.

Experimental

The objects of this study were: crystalline monophosphates of cytidine ($CydH^+ \cdot H_2PO_4^-$) and deoxycytidine ($dCydH^+ \cdot H_2PO_4^-$), crystalline hemiphos-

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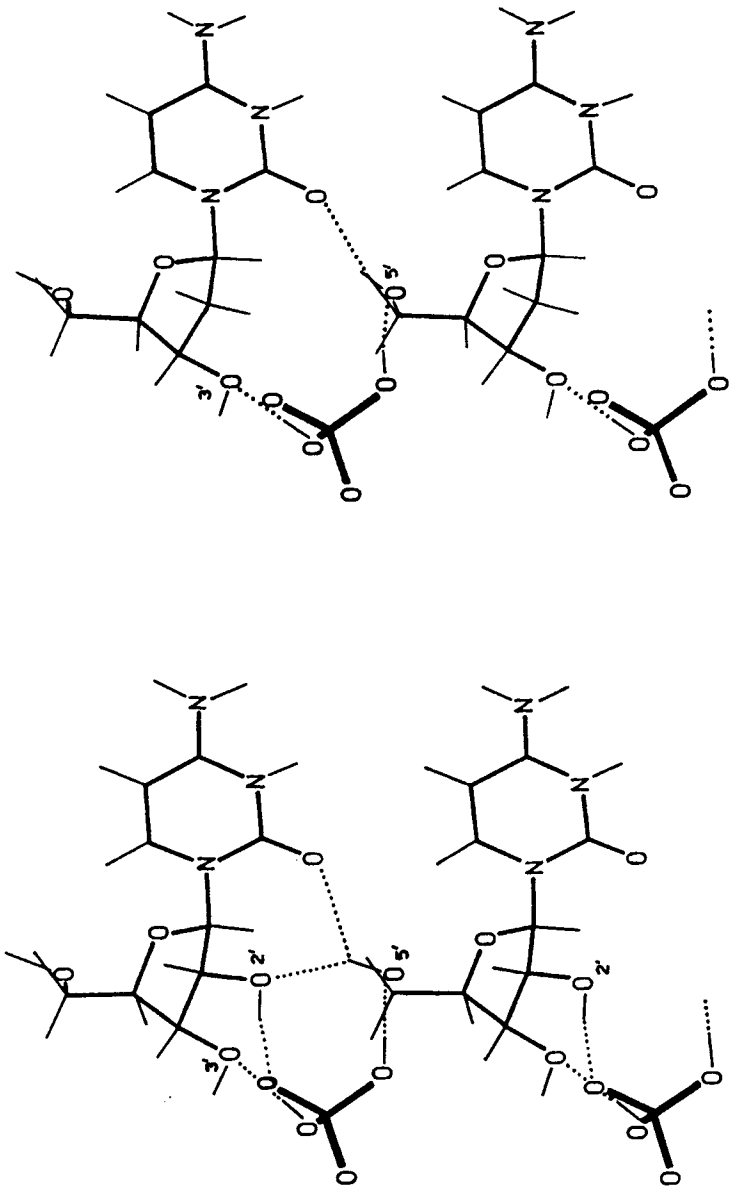

Scheme 1 The two analogous fragments from the crystal structures of Cyd and dCyd monophosphates

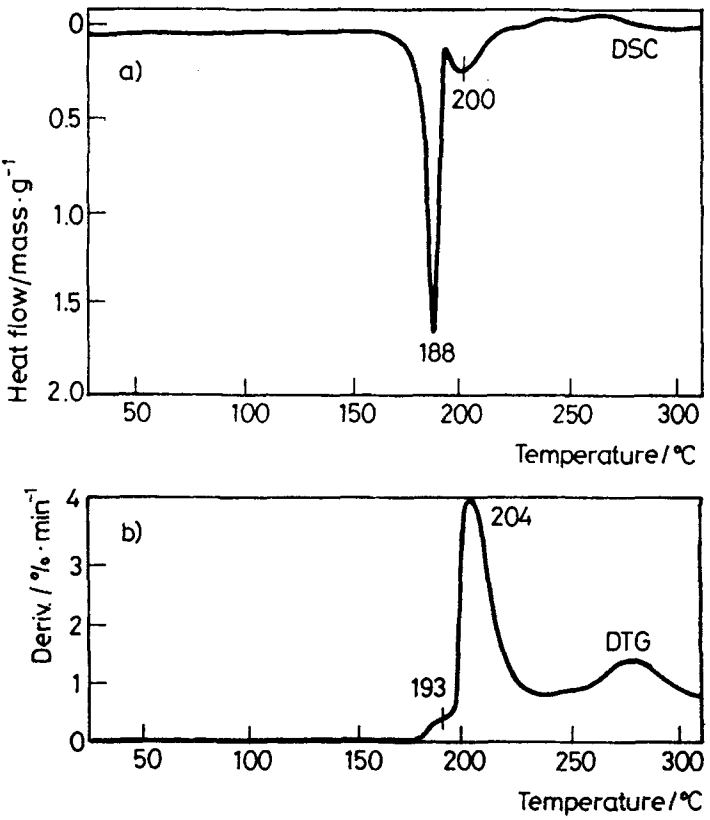

Fig. 1 DSC and DTG curves for Cyd monophosphate

phates of cytidine ($(Cyd)_2H^+ \cdot H_2PO_4^-$) and deoxycytidine ($(dCyd)_2H^+ \cdot H_2PO_4^-$). These salts were obtained, in the framework of multi-years cooperation, from Institute of Bioorganic Chemistry in Poznań.

The calorimetric (DSC) and derivative thermogravimetric (DTG) measurements were performed by means the differential scanning calorimeter DSC 910 and thermogravimetric analyzer TGA 951, produced by DuPont. The samples of phosphates were heated in the range 30–320°C using rates of heating 5 deg·min^{-1}. Numerical analysis of experimental data was realized by means of the standard software of DuPont 2100 Thermal Analyst: 'Interactive DSC Data Analysis Program – Heats and Temperatures of Transition' and 'TGA Data Analysis Program – Compositional Analysis'.

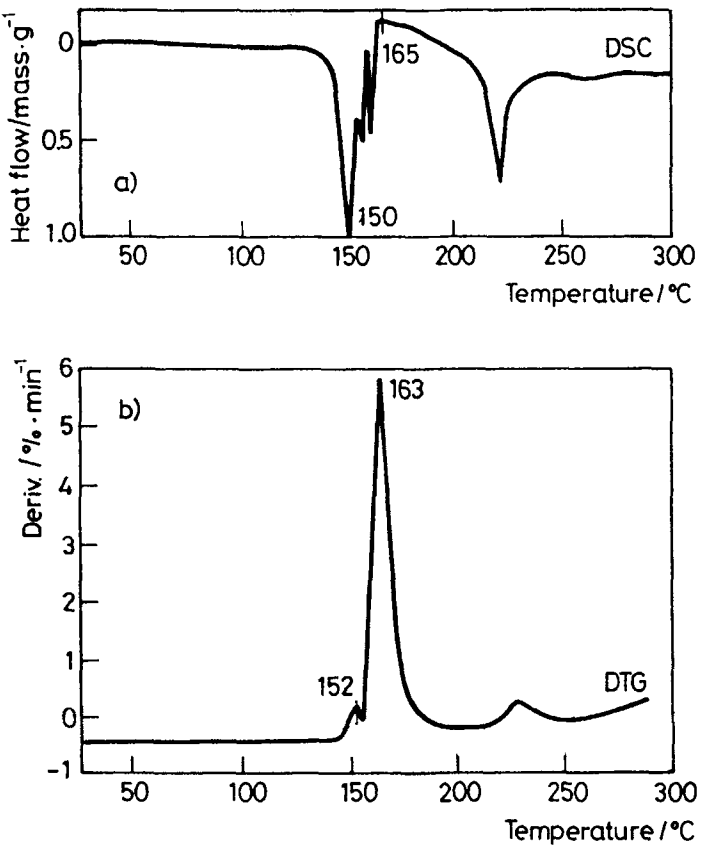

Fig. 2 DSC and DTG curves for dCyd monophosphate

Results and discussion

The results of DSC and DTG analysis for the four examined salts are presented in Figs 1–4. In every figure the curve (a) presents the heat flow (DSC) and the curve (b) – the rate of relative mass loss (DTG) of the same object. The values given at DTG diagrams inform of the temperatures of the peaks of rate of mass loss. The results show that the processes of melting and decomposition (destruction of glycoside bonds and then dehydration and carbonization of ribose rings) take place in different ways in the four phosphates. Comparison of DSC and DTG profiles for Cyd and dCyd monophosphates (Figs 1, 2) indicates significant differences of thermophysical properties is spite of isostructurality of these salts. The first endothermic effect (Fig. 1), with minimum at 188°C, is connected with melting of Cyd monophosphate. The second small effect (min.

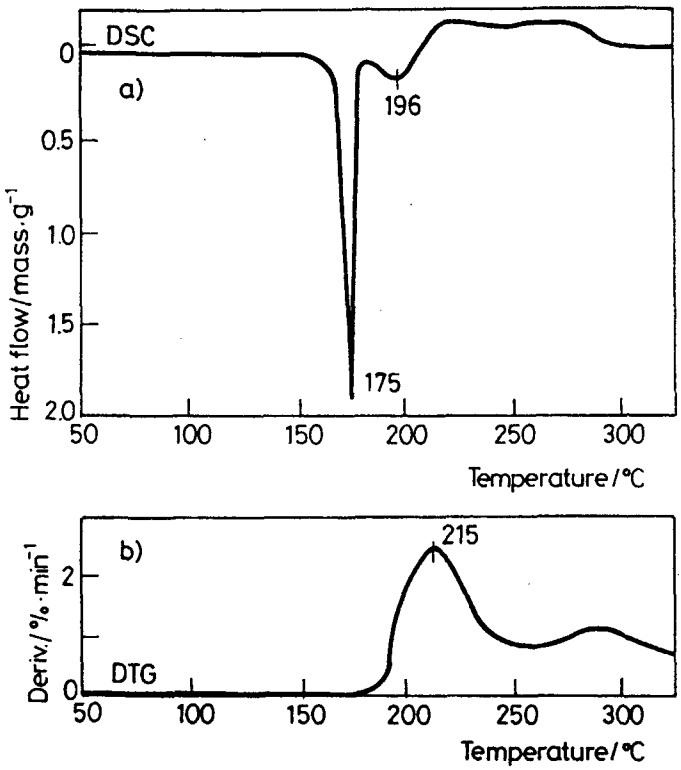

Fig. 3 DSC and DTG curves for Cyd hemiphosphate

at 200°C) is related to several processes of decomposition taking place in the already melted salt. The large peak of mass loss characterizes these decomposition processes. Differences of about 40 K in the melting and then the decomposition temperatures of both salts (Figs 1, 2) suggest lower stability of dCyd monophosphate structure. This result coincides with the observed better solubility of dCyd monophosphate in different solvents [1]. Also the tendency of this salt for easy transformation into dimeric dCyd hemiphosphate is confirmed by DSC and DTG measurements (Fig. 4). The endothermic effect, with minimum at 184°C, is accompanied by intensive mass loss (max. at 190°C) connected with decomposition. The fact that the dCyd hemiphosphate decomposes without melting, at temperature 34 K higher than dCyd mono-salt melts, proves higher stability of dCyd hemiphosphate structure.

The above results support the fact of the crucial importance of presence (or absence) of 2'OH group for stability (or lability) of crystal structures of examined monophosphates.

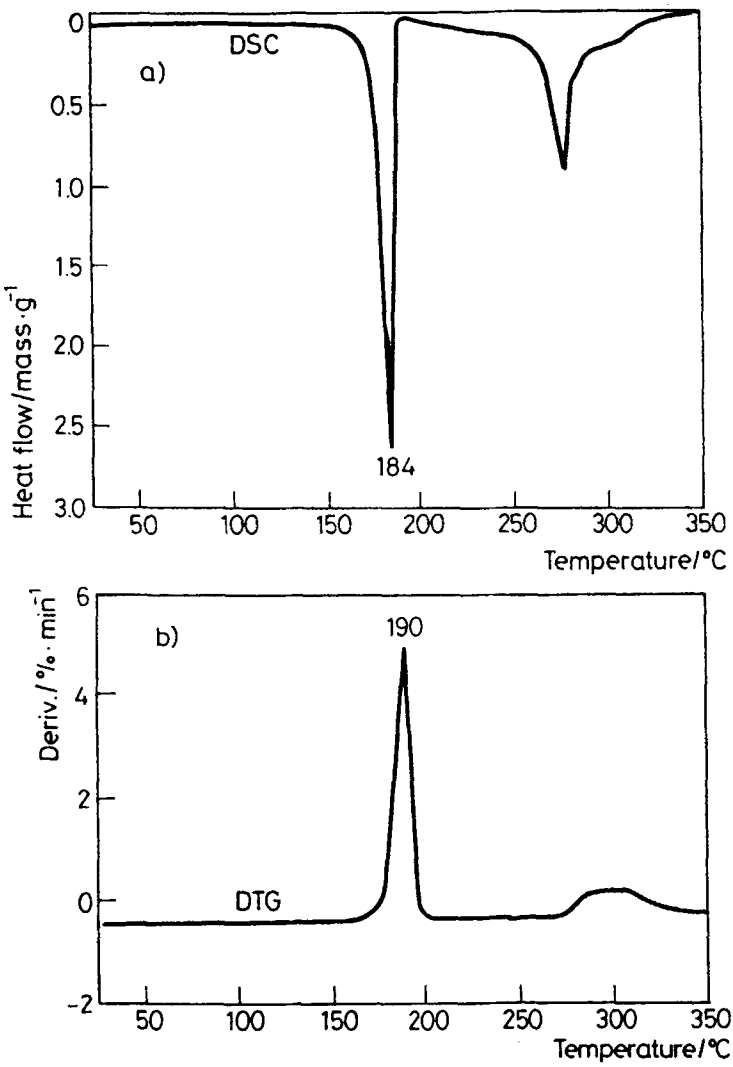

Fig. 4 DSC and DTG curves for dCyd hemiphosphate

The preparation of Cyd hemiphosphate is a difficult task. The only method known till now is synthesis in solid-state (unpublished). It is comprehensible when comparing the DSC profiles of mono- and hemiphosphates of Cyd (Figs 1, 3). The Cyd hemi-salt melts at temperature 13 K lower then Cyd mono-salt. This indicates that the crystal structure of Cyd hemi-salt is less stable and explains, to some extend, why Cyd forms with H_3PO_4 in solution only crystalline mono-phosphate even in different stoichiometric ratio Cyd/H_3PO_4 [1]. The similarity of DSC profiles for mono- and hemiphosphates of Cyd sug-

gests that some features of Cyd monophosphate crystal structure have been preserved in the structure of Cyd hemi-salt. The crystal structure of Cyd hemiphosphate has not still been solved. Taking into account the properties of dCyd hemiphosphate crystal structure [5], the presented results of thermophysical analysis and IR spectra (unpublished) one can predict some properties of this unknown structure.

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Zusammenfassung — Es wurden DSC- und DTG-Messungen an kristallinen Mono- und Hemiphosphaten von Cytidin und Desoxycytidin durchgeführt. Die erhaltenen Ergebnisse für vier untersuchte Salze bestätigen den Einfluß der Gegenwart (oder Abwesenheit) der 2'OH-Gruppen im Ribosering auf die Stabilität (oder Labilität) der Kristallstruktur der untersuchten Salze.