J. Chem. Thermodynamics 64 (2013) 187–192

Contents lists available at SciVerse ScienceDirect

J. Chem. Thermodynamics

journal homepage: www.elsevier.com/locate/jct

Enthalpies of formation of 5,6-dihydro-5-methyluracil and 5,6-dihydro-6-methyluracil

Luísa M.P.F. Amaral *, Piotr Szterner, Manuel A.V. Ribeiro da Silva

Centro de Investigação em Química, Department of Chemistry and Biochemistry, Faculty of Science, University of Porto, Rua do Campo Alegre, 687, P-4169-007 Porto, Portugal

ARTICLE INFO

Article history:
Received 20 February 2013
Received in revised form 18 March 2013
Accepted 1 May 2013
Available online 17 May 2013

Keywords:
Thermochemistry
Combustion calorimetry
Energy of combustion
Enthalpy of formation
Enthalpy of sublimation
Knudsen effusion
5,6-Dihydro-5-methyluracil
5,6-Dihydrothymine
5,6-Dihydro-6-methyluracil

ABSTRACT

The standard ($p^\circ = 0.1$ MPa) molar enthalpy of combustion, $\Delta_c H_m^\circ$, of two crystalline compounds, 5,6-dihydro-5-methyluracil and 5,6-dihydro-6-methyluracil, were determined, at $T = 298.15$ K, using a static bomb combustion calorimeter. The vapor pressures as a function of the temperature were measured for those compounds, by the Knudsen effusion technique, and the standard molar enthalpies of sublimation at the mean temperature of the vapor pressure measurements were derived from the Clausius–Clapeyron equation, and corrected to $T = 298.15$ K using an estimated value for $\Delta_{cr}^{g} C_{p,m}^\circ$. These values were used to derive the standard molar enthalpies of formation of the two compounds studied, in the condensed and gaseous phases. Some considerations about the relative stability of the two isomers were made and compared with similar compounds.

1. Introduction

Uracil and other structural analogue compounds have been extensively studied, mainly because many of them exhibit interesting biological and pharmacological activities [1]. The uracil derivatives deserve particular attention among all series of nucleic pyrimidine bases, playing an important role in the field of biology, as fundamental constituents of nucleic acid.

The structure and properties of uracil are expected to be substantially influenced by the presence of substituents acting on the electron density of this compound, modifying the intermolecular interactions. The effects of substituents on the pattern of hydrogen bonding of uracil derivatives may contribute to elucidate the connection between the structure of the compound and its biological functions [2,3]. In this context, the compounds containing an uracil core and a substituent in 5-position have stimulated an exceptional interest in biochemistry and pharmacology.

The 5,6-dihydrouracil (DHU) is a rare pyrimidine base occurring naturally in transfer-RNAs [4], produced in large amounts by exposure of DNA to ionizing radiation under anoxic conditions [5,6]. Repair enzymes, such as *Escherichia coli* endonuclease III or *Saccharomyces cerevisiae* redoxendonuclease, recognize and excise DHU in DNA [5,7]. It has also been suggested that 5,6-dihydrouracil/uracil ratio in plasma of patients with cancer is a prognostic indicator for the toxicity of 5-fluorouracil-based chemotherapy [8]. The 5,6-dihydro-5-methyluracil (5,6-dihydrothymine, DHT) is the major product formed under oxygen-free gamma irradiation of thymine [9,10]. 5,6-Dihydrouracil itself is an intermediate in the catabolism of uracil [11], whereas 5,6-dihydro-5-methyluracil is an intermediate in the catabolism of thymine [12].

We are involved in an extensive research project on the thermodynamic properties of uracil derivatives, having already been reported several studies involving uracil with amino, nitro, methyl and halogen substituentes [13–15] as well as thiouracil and two methyl-2-thiouracil isomers [16].

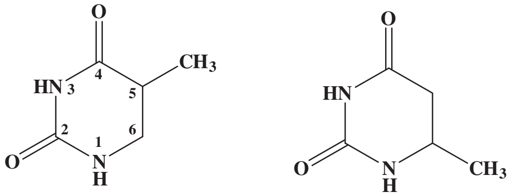
The present work reports the standard molar enthalpies of formation for 5,6-dihydro-5-methyluracil and 5,6-dihydro-6-methyluracil, in the crystalline phase, (structural formulae are shown in figure 1), at $T = 298.15$ K, derived from the standard massic energies of combustion, in oxygen, at $T = 298.15$ K, measured by static bomb combustion calorimetry.

The standard molar enthalpies of sublimation of the compounds, at the mean temperature of the experiments temperature range, were obtained by the application of the Clausius–Clapeyron equation to the values of the vapor pressure determined by the Knudsen mass-loss effusion technique at different temperatures. The value obtained for each compound was corrected for

---

* Corresponding author. Tel.: +351 220402515.
E-mail address: luisaamaral@fc.up.pt (L.M.P.F. Amaral).

0021-9614/$ - see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.jct.2013.05.002



5,6-dihydro-5-methyluracil 5,6-dihydro-6-methyluracil

FIGURE 1. Structural formula of 5,6-dihydro-5-methyluracil (with atomic numbering) and 5,6-dihydro-6-methyluracil.

$T = 298.15$ K, using an estimated value for the heat capacity differences between the corresponding gas and crystal phases.

The combination of the values of the standard molar enthalpy of formation, in the crystalline phase, and the standard molar enthalpy of sublimation, allowed the calculation of the standard molar enthalpy of formation, in the gaseous phase, at $T = 298.15$ K.

2. Experimental

2.1. Materials and purity control

The origin and purification details of the samples of 5,6-dihydro-5-methyluracil and 5,6-dihydro-6-methyluracil used in this work are summarized in table 1. The purity of the compounds was checked by gas–liquid chromatography, performed on an Agilent 4890D Gas Chromatography equipped with an HP-5 column, cross-linked, 5% diphenyl and 95% dimethylpolysiloxane (15 · 0.530 mm · i.d · 1.5 μm film thickness), and using nitrogen as carrier gas, as being ⩾0.9998 mass fraction. The purities were also confirmed by the recoveries of the carbon dioxide resulting from the combustion experiments. The average ratios of the mass of carbon dioxide recovered from the combustion to that calculated from the mass of sample were: (0.9998 ± 0.0001) for 5,6-dihydro-5-methyluracil and (0.9995 ± 0.0002) for 5,6-dihydro-6-methyluracil. The specific densities for 5,6-dihydro-5-methyluracil and 5,6-dihydro-6-methyluracil were taken as $\rho = 1.149\ \text{g} \cdot \text{cm}^{-3}$ for both compounds [17].

The relative atomic masses used were those recommended by the IUPAC Commission in 2009 [18].

2.2. Combustion calorimetry

The calorimetric system used to measure the standard molar energies of combustion is an isoperibol static bomb calorimeter, whose detailed description, subsidiary apparatus, and technique have been described previously in the literature [19,20].

The bomb used was a twin-valve combustion bomb (Parr oxygen bomb 1105) made of stainless steel and with an internal volume of 0.340 cm^3.

The calorimeter calibration was done by combustion of certificated benzoic acid NBS Standard Reference Material, Sample 39j, with massic energy of combustion of $-(26434 \pm 3)\ \text{J} \cdot \text{g}^{-1}$ under certificate conditions [21]. The calibration results were corrected to give the energy equivalent of the calorimeter, $\varepsilon_{\text{calor}}$, corresponding to the average mass of 3119.6 g of water added to the calorimeter. From six independent calibration experiments performed, $\varepsilon_{\text{calor}} = (15905.0 \pm 0.8)\ \text{J} \cdot \text{K}^{-1}$, where the uncertainty quoted is the standard deviation of the mean.

In all combustion experiments, a total of 1.00 cm^3 of water was introduced into the bomb, which was then closed and purged twice with oxygen, to remove air, before being charged with 3.04 MPa of oxygen. The ignition of the samples, in the pellet form, were made at $T = (298.150 \pm 0.001)$ K, by discharge of a 1400 μF capacitor through a platinum ignition wire, using a cotton thread fuse, with empirical formula $CH_{1.686}O_{0.843}$, having a massic energy of combustion of $\Delta_c u = -16240\ \text{J} \cdot \text{g}^{-1}$ [22]. This value has been previously confirmed in our laboratory.

The n-hexadecane (Aldrich, mass fraction >0.999), stored under nitrogen, was used as auxiliary combustion for the two compounds studied. The standard massic energy of combustion values of the two different samples of n-hexadecane used are as follows: for all the experiments of 5,6-dihydro-5-methyluracil and for the experiments 1 to 4 of 5,6-dihydro-6-methyluracil, $\Delta_c u^\circ$ (n-hexadecane) = $-(47126 \pm 4.1)\ \text{J} \cdot \text{g}^{-1}$, and for the experiments 5 and 6 of 5,6-dihydro-6-methyluracil, $\Delta_c u^\circ$ (n-hexadecane) = $-(47150.4 \pm 3.6)\ \text{J} \cdot \text{g}^{-1}$.

The corrections for nitric acid formation were based on $-59.7\ \text{kJ} \cdot \text{mol}^{-1}$ [23], for the molar energy of formation of $0.1\ \text{mol} \cdot \text{dm}^{-3}$ HNO_3(aq) from N_2, O_2, and H_2O(l). The quantity of HNO_3 formed was determined by titration of the aqueous solution resulting from washing the inside of the bomb. In the experiments with carbon residue soot formation during the combustion, the necessary energetic correction for its formation was based on $\Delta_c u^\circ = -33\ \text{J} \cdot \text{g}^{-1}$ [22]. An estimated pressure coefficient of specific energy, $(\partial u/\partial p)_T = -0.2\ \text{J} \cdot \text{g}^{-1} \cdot \text{MPa}^{-1}$, at $T = 298.15$ K, a typical value for most organic compounds [24] was assumed.

The amount of substance used in each experiment was determined from the total mass of carbon dioxide produced after allowance for that formed from the cotton threat fuse, n-hexadecane and that lost due to eventual carbon formation. Corrections from apparent mass to true mass were made.

For each compound, the massic energy of combustion, $\Delta_c u^\circ$, was calculated by the procedure given by Hubbard *et al.* [25].

2.3. Vapor pressures measurements

For the two compounds, the vapor pressures were measured at several temperatures using a Knudsen effusion apparatus which enable the simultaneous operation of nine aluminium effusion cells [26]. This apparatus has been tested by measuring vapor pressures between (0.1 and 1.0) Pa, over temperature ranges of *ca.* 20 K of benzoic acid, phenanthrene, anthracene, benzanthrone, and 1,3,5-triphenylbenzene. The measured vapor pressures and the derived enthalpies of sublimation of the test substances are in excellent agreement with literature results for those compounds. The nine effusion cells are contained in cylindrical holes inside three aluminium blocks, three cells per block. Each block is kept at constant temperature, different from the other two blocks.

TABLE 1
Purification details of 5,6-dihydro-5-methyluracil and 5,6-dihydro-6-methyluracil.

Chemical name	CAS	Provenance	Initial mass fraction purity	Purification method	Final mass fraction purity	Analysis method
5,6-Dihydro-5-methyluracil (cr)	696-04-8	Alfa Aesar®	0.98	Sublimation	0.9998	CO_2 recovery
5,6-Dihydro-6-methyluracil (cr)	2434-49-3	Alfa Aesar®	0.99	Sublimation, recrystallization from water	0.9995	CO_2 recovery