Comprehensive thermodynamic study of methylprednisolone

A.V. Knyazev [a],[*],[1], V.N. Emel'yanenko [b],[c],[*],[2], N.N. Smirnova [a], D.H. Zaitsau [b], O.V. Stepanova [a], A.S. Shipilova [a], A.V. Markin [a], E.V. Gusarova [a], S.S. Knyazeva [a], S.P. Verevkin [b]

[a] Lobachevsky University, Gagarin Prospekt 23/2, 603950 Nizhni Novgorod, Russia
[b] Department of Physical Chemistry and Department "Science and Technology of Life, Light and Matter", University of Rostock, Dr.-Lorenz-Weg 1, D-18059 Rostock, Germany
[c] Department of Physical Chemistry, Kazan Federal University, Kremlevskaya str. 18, 420008 Kazan, Russia

ABSTRACT

In the present work the temperature dependence of heat capacity for methylprednisolone has been measured for the first time over the temperature range from 6 to 350 K using by precision adiabatic vacuum calorimetry. Based on the experimental data, the thermodynamic functions of the methylprednisolone, namely, the heat capacity, enthalpy $H°(T) − H°(0)$, entropy $S°(T) − S°(0)$ and Gibbs function $G°(T) − H°(0)$ have been evaluated from the experimental values for the range from $T \to 0$ to 350 K. Standard molar enthalpy of combustion ($−11898.9 ± 6.7$) kJ·mol^{-1} of the methylprednisolone was measured for the first time using high-precision combustion calorimeter. The standard molar enthalpy of formation in the crystalline state ($−1045.8 ± 7.3$) kJ·mol^{-1} of compound at 298.15 K was derived from the combustion experiments. The standard molar enthalpy of sublimation at 298.15 K ($194.5 ± 2.2$) kJ·mol^{-1} was measured by using the quartz-crystal microbalance (QCM). Using combination of the adiabatic and combustion calorimetry with the result from QCM, the thermodynamic functions of the methylprednisolone at $T = 298.15$ K and $p = 0.1$ MPa have been calculated.

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1. Introduction

Methylprednisolone (CAS 83-43-2) is a glucocorticoid. Methylprednisolone is used to treat many different inflammatory conditions like arthritis, lupus, psoriasis, ulcerative colitis, allergic disorders, gland (endocrine) disorders, and conditions that affect the skin, eyes, lungs, stomach, nervous system, or blood cells. The locally injected methylprednisolone delivered by chitosan-β-glycerophosphate hydrogel might be a promising treatment for facial nerve damage [1]. This work is a continuation of systematic studies of bioactive compounds. Recently [2–7], we have investigated the thermodynamic properties of vitamins and steroid hormones. Among the goals of this work is the calorimetric determination of the standard thermodynamic functions of the methylprednisolone with the further purpose of describing biochemical and industrial processes with its participation.

2. Experimental

2.1. Sample

Methylprednisolone was purchased from company Hongsu Fan. The absence of water in Methylprednisolone was determined by Karl Fischer titration. The certificate (purity control performed by mass spectrometry (Fig. 1S) with a preliminary chromatographic separation) and Karl Fischer titration led us to conclude that the methylprednisolone sample studied (the content of impurities 0.1 wt.%) was an individual crystalline compound (Table 1S).

2.2. Apparatus and measurement procedure

To measure the heat capacity C_p^o of the tested substance in the range from 6 to 350 K a BKT-3.0 automatic precision adiabatic vacuum calorimeter with discrete heating was used. The calorimeter design and the operation procedure were described earlier [8]. The calorimeter was tested by measuring the heat capacity of high-purity copper and reference samples of synthetic corundum and K-2 benzoic acid. The analysis of the results showed that standard uncertainty of the heat capacity of the substance at helium temperatures was within ±2%, then it decreased to ±0.5% as the temperature was rising to 40 K, and was equal to ±0.2% at $T > 40$ K.

* Corresponding authors at: Department of Physical Chemistry and Department "Science and Technology of Life, Light and Matter", University of Rostock, Dr.-Lorenz-Weg 1, D-18059 Rostock, Germany (V.N. Emel'yanenko).

E-mail addresses: knyazevav@gmail.com (A.V. Knyazev), vladzimir.yemelyanen-ko@uni-rostock.de (V.N. Emel'yanenko).

[1] To whom correspondence concerning the heat capacity measurements and data evaluation should be addressed.
[2] To whom correspondence concerning the combustion calorimetry and QCM measurements should be addressed.

An isoperibol static bomb calorimeter described previously [9] was used for measurements of energies of combustion of the methylprednisolone. The solid sample of compound was weighed with a microbalance of 10^{-6} g resolution. We used small polyethylene pieces prepared from commercial 1 ml ampoules (Fa. NeoLab, Heidelberg, Germany) as an auxiliary material in order to achieve completeness of combustion. The combustion products were examined for carbon monoxide (Dräger tube) and unburned carbon, but none was detected. The energy equivalent of the calorimeter $\varepsilon_{calor} = (14800.9 \pm 0.9)$ J·K^{-1} (standard deviation of the mean from 10 experiments) was determined with a standard reference sample of benzoic acid (SRM 39j, N.I.S.T.). Correction for nitric acid formation was based on the titration with 0.1 mol·dm^{-3} NaOH (aq.). The relative atomic masses used for the elements were calculated as the mean of the bounds of the interval of the standard atomic weights recommended by the IUPAC commission in 2011 [10] for each of these elements.

2.3. Quartz-crystal microbalance technique

Molar enthalpy of sublimation for methylprednisolone was measured using the QCM method. In short, a sample of a compound is placed in an open cavity inside of the thermostat block and it is exposed to vacuum (10^{-5} Pa) with the whole open surface of the loaded compound (Langmuir evaporation). The QCM is placed directly over the measuring cavity containing the sample. During the sublimation into vacuum, a certain amount of sample is deposited on the quartz crystal. The sublimation enthalpies were derived from the temperature dependences of the experimentally measured change in the vibrational frequency of the quartz crystal. The change of the vibrational frequency Δf was directly related to the mass deposition Δm on the crystal according to Sauerbrey equation [11]:

$$\Delta f = -C \cdot f^2 \cdot \Delta m \cdot S_C^{-1} \tag{1}$$

where f is the fundamental frequency of the crystal (6 MHz in this case) with $\Delta f \ll f$, S_C is the surface of the crystal, and C is a constant. Thus, the rate of frequency shift proportional to the sublimation rate and vapor pressure of the sample [12]:

$$p_{sat} = \frac{K^{\cdot}}{\alpha \gamma} \frac{df}{dt} \sqrt{\frac{T}{M}} \tag{2}$$

All constants corresponding to Knudsen and Sauerbrey [11] equations, as well as, the geometrical parameters of the experimental setup are introduced into K' value. The absolute value of K' was evaluated with the help of available in the literature data on QCM-Knudsen vapor pressure determination for [C$_n$mim][NTf$_2$] [13,14], [C$_n$Py][NTf$_2$] [15] and [C$_n$C$_n$im][NTf$_2$] [16] and own results on sublimation rate of these specimen with QCM-Langmuir technique [17–20]. The α and γ values seen in Eq. (4) are the condensation and surface roughness coefficients. As a matter of fact for liquid samples used for K' evaluation the $\alpha\gamma$ product was equal unity. While studying the crystal samples this values should be taken into account. But determination of these coefficients is not possible, from the other side their absolute values doesn't affect the temperature dependence p_{sat}. Therefore we introduce the product of $\alpha\gamma p_{sat}$ as the measured value (see Table 5).

The temperature dependences of vapor pressures were fitted with the Clarke-Glew equation [21]:

$$R/\ln(\alpha\gamma p_{sat}/p^\circ) = -\frac{\Delta_{cr}^g G_m^\circ(T_0)}{T_0} - \Delta_{cr}^g H_m^\circ(T_0)\left(\frac{1}{T} - \frac{1}{T_0}\right)$$
$$+ \Delta_{cr}^g C_{pm}^\circ\left(\frac{T_0}{T} - 1 - \ln\left(\frac{T}{T_0}\right)\right), \tag{3}$$

T_0 appearing in Eq. (3) is an arbitrarily chosen reference temperature, which we have set to 298 K. The temperature dependent sublimation enthalpy $\Delta_{cr}^g H_m^\circ(T)$ obtained from the QCM study is given by:

$$\Delta_{cr}^g H_m^\circ(T) = \Delta_{cr}^g H_m^\circ(T_0) + \Delta_{cr}^g C_{pm}^\circ(T - T_0) \tag{4}$$

The extended uncertainty with confidential level of 0.95 ($k \approx 2$) was used in QCM study.

3. Results and discussion

3.1. Heat capacity

The C_p° measurements were carried out between 6 and 350 K (Table 2S). The mass of the sample loaded in the calorimetric ampoules of the BKT-3.0 device was 0.3598 g. 126 experimental C_p° values were obtained in four series of experiments. The heat capacity of the sample varied from 30% to 50% of the total heat capacity of calorimetric ampoule + substance over the range between 6 and 350 K. The experimental points of C_p° were fitted by means of the least-squares method and polynomial equations (Eqs. (1) and (2)) of the C_p° versus temperature have been obtained. The corresponding coefficients (A, B, C, etc.) are given in Table 1

$$C_p^\circ = A + B \cdot (T/30) + C \cdot (T/30)^2 + D \cdot (T/30)^3 + E \cdot (T/30)^4$$
$$+ F \cdot (T/30)^5 + G \cdot (T/30)^6 + H \cdot (T/30)^7 + I \cdot (T/30)^8$$
$$+ J \cdot (T/30)^9 \tag{1}$$

$$lnC_p^\circ = A + B \cdot ln(T/30) + C \cdot ln^2(T/30) + D \cdot ln^3(T/30)$$
$$+ E \cdot ln^4(T/30) + F \cdot ln^5(T/30) + G \cdot ln^6(T/30)$$
$$+ H \cdot ln^7(T/30) + I \cdot ln^8(T/30) + J \cdot ln^9(T/30) + K \cdot ln^{10}(T/30) \tag{2}$$

Partitioning into 3 intervals of the temperature dependence of the heat capacity contributes to the best smoothing of the experimental curve. Their root mean square deviation from the averaging $C_p^\circ = f(T)$ curve was ±0.15% in the range $T = (7–40)$ K, ±0.075% from $T = (40$ to $80)$ K and ±0.050% between $T = (80$ and $346)$ K. The experimental values of the molar heat capacity of methylprednisolone over the range from 6 to 350 K and the averaging $C_p^\circ = f(T)$ plot are presented in Fig. 1. The heat capacity C_p° of this substance gradually increases with rising temperature and does not show any peculiarities.

3.2. Thermodynamic functions

To calculate the standard thermodynamic functions (Table 2) of methylprednisolone, C_p° values were extrapolated from the starting temperature of the measurement (approximately 7 K) to 0 K by the Debye function of heat capacity [22]:

$$C_p^\circ = nD\left(\frac{\theta_D}{T}\right), \tag{3}$$

where D is the symbol of Debye's function, n = 3 and $\theta_D(C_{22}H_{30}O_5) = 62.7$ K are specially selected parameters [22]. Eq. (3) with the above parameters describes the experimental C_p° values of the compound between 7 K and 10 K with the relative standard uncertainty of ±1.15%. In calculating the functions, it was assumed that Eq. (3) reproduces the C_p° values of methylprednisolone at $T < 7$ K with the same relative standard uncertainty.

The calculations of $H^\circ(T) - H^\circ(0)$ and $S^\circ(T) - S^\circ(0)$ were made by the numerical integration of $C_p^\circ = f(T)$ and $C_p^\circ = f(\ln T)$ curves,