

Hormones and their properties

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INTRODUCTION

Hydrocortisone acetate is a corticosteroid with anti-inflammatory properties. Hydrocortisone acetate may stimulate superoxide dismutase production as well as release antioxidants [1]. Hydrocortisone acetate can be used for biochemical research. As a sugar cortical hormone drug, it can anti-allergic, antitoxin, resistance to shock action [2]. Hydrocortisone acetate is used in combination with antimicrobial agents in veterinary ophthalmic ointments, such as TriOptic-S[®] which consists of three antibiotics (bacitracin zinc, neomycin sulfate, and polymyxin B sulfate) and hydrocortisone acetate [3].

MATERIALS AND METHODS

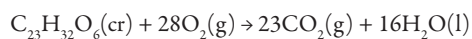
Hydrocortisone acetate was purchased from Fluka. According to the certificate of Fluka the content of impurities (0.1 wt %) led us to conclude that the hydrocortisone acetate sample studied was an individual crystalline compound.

The energy of combustion, $\Delta_c U$, of hydrocortisone acetate was measured in a calorimeter (V-08) with a static bomb and an isothermal shield. It should be noted that while checking the calorimeter by burning succinic acid, prepared at D.I. Mendeleev Research Institute of Metrology (the value of the standard enthalpy of combustion of the acid coincided with the certificate value within $\pm 0.017\%$). For complete combustion of hydrocortisone acetate we used benzoic acid as an auxiliary substance.

The low-temperature X-ray diffraction was carried out on a Shimadzu X-ray diffractometer XRD-6000 (Cu K α radiation, geometry θ - 2θ) in the 2θ range from 5° to 60° with scan increment of 0.02° using Attachment TTK-450 (Anton Paar) in the temperature interval from 150K to 425K.

RESULTS AND DISCUSSION

The experimental data on burning of hydrocortisone acetate are presented in Table 1. As a result, the energies and enthalpies of combustion of hydrocortisone acetate at $T = 298.15\text{K}$ and standard pressure were determined. The values are for the reaction:



In brackets are given the physical states of reagents: (cr), crystalline; (g), gaseous; (l), liquid. The pressure in the oxygen bomb for the combustion of samples was 3.0 MPa. Transfer the high pressure to the standard state ($p = 0.1\text{MPa}$) was performed similarly the work [4].

The data on the enthalpy of combustion of the crystalline hydrocortisone acetate was used to estimate enthalpy of combustion and formation at $T = 298.15\text{K}$ and $p = 0.1\text{MPa}$.

$\Delta_f H^\circ_m(\text{C}_{23}\text{H}_{32}\text{O}_6, \text{cr}) = -1307.0 \pm 11.6 \text{ kJ mol}^{-1}$. The values conform to the following process: $23\text{C}(\text{gr}) + 16\text{H}_2(\text{g}) + 3\text{O}_2(\text{g}) \rightarrow \text{C}_{23}\text{H}_{32}\text{O}_6(\text{cr})$

where in the brackets are indicated the physical states of reagents: (gr), graphite; (g), gaseous; (cr), crystalline. Correlation analysis showed that the dependence of the enthalpy of formation of steroids on the molecular weight is described by a linear equation (Figure 1). Our results are in good agreement with the available statistics.

Table 1. Experimental data on combustion energy for hydrocortisone acetate at $T = 298.15\text{K}$

Value	Experiment					
	1	2	3	4	5	6
msam (g) a	0.18276	0.16896	0.19852	0.15442	0.17874	0.13300
mC6H5COOH (g) a	0.94808	1.20330	1.08466	1.08966	0.76961	1.17895
mthread (g) a	0.00165	0.00173	0.00170	0.00171	0.00215	0.00177
W (J K ⁻¹) b	14805	14805	14805	14805	14805	14805
Δt (K) c	2.07134	2.49998	2.34836	2.23645	1.74485	2.38130
$-\Delta_c U_\Sigma$ (J) d	30666.2	37012.2	34767.5	33110.6	25832.5	35255.2
$-\Delta_c U_{\text{C}_6\text{H}_5\text{COOH}}$ (J) e	25085.8	31838.9	28699.7	28831.9	20363.6	31194.6

Value	Experiment					
$-\Delta cU_{\text{thread}}$ (J) e	27.6	29.0	28.5	28.6	36.0	29.6
$-\Delta cU_{\text{HNO}_3}$ (J) f	3.1	2.9	5.4	1.9	1.9	1.7
$-\Delta cU_{\text{C}}$ (J) g	6.6	6.6	8.2	6.9	6.6	11.5
$-\Delta cU$ (J g ⁻¹) h	30402.2	30468.7	30435.7	30469.5	30421.8	30382.0

$-\Delta cU = 30430.0 \pm 28.8 \text{ J g}^{-1} = 12309.0 \pm 11.6 \text{ kJ mol}^{-1}$, the mean energy of combustion of hydrocortisone acetate, $-\Delta c m = 12304.7 \pm 11.6 \text{ kJ mol}^{-1}$, the energy of combustion of hydrocortisone acetate at standard pressure.

^a m_{sam} , $m_{\text{C}_6\text{H}_5\text{COOH}}$, m_{thread} , masses of the tested sample, benzoic acid and a cotton thread, respectively.

^b W , the energy equivalent of the calorimeter.

^c Δt , the temperature rise in the experiment, adjusted for heat transfer.

^d $\Delta_c U_{\Sigma}$, the total energy released during the experiment.

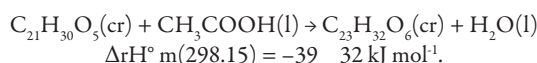
^e $\Delta_c U_{\text{C}_6\text{H}_5\text{COOH}}$, $\Delta_c U_{\text{thread}}$, amounts of energy released on burning benzoic acid and cotton thread, respectively.

^f $\Delta_c U_{\text{HNO}_3}$, the energy of formation of nitric acid.

^g $\Delta_c U_{\text{C}}$, the energy incomplete combustion of carbon.

^h $\Delta_c U$, the energy released on burning of hydrocortisone acetate.

Hydrocortisone and acetic acid under the condition of azabenzene can be used to manufacture hydrocortisone acetate. The standard enthalpy of the acylation reaction of hydrocortisone into hydrocortisone acetate was calculated.



The standard enthalpy of formation of hydrocortisone acetate (see 3.1) and the corresponding substances hydrocortisone ($\Delta_f H^\circ \text{m}(\text{C}_{21}\text{H}_{30}\text{O}_5, \text{cr}) = -1070.0 \pm 30.0 \text{ kJ mol}^{-1}$), acetic acid ($\Delta_f H^\circ \text{m}(\text{CH}_3\text{COOH}, \text{l}) = -483.52 \pm 0.36 \text{ kJ mol}^{-1}$) and water ($\Delta_f H^\circ \text{m}(\text{H}_2\text{O}, \text{l}) = -285.830 \pm 0.040 \text{ kJ mol}^{-1}$) were used. The reaction is exothermic and deeper thermodynamic analysis will be possible if the entropy of the reaction will be determined. The large error in the enthalpy of the reaction is due to a large error in the enthalpy of formation of hydrocortisone.

Next task of the work was the X-ray diffraction investigation of compound with the purpose of definition of the thermal expansion coefficients. The temperature dependence of the unit cell parameters is described by the following polynomial:

$$a = 7.353 \cdot 10^{-8} \cdot T^2 + 3.00899 \cdot 10^{-4} \cdot T + 8.81107 \quad (150 \leq T \leq 450 \text{ K})$$

$$b = 1.14685 \cdot 10^{-6} \cdot T^2 + 5.07692 \cdot 10^{-5} \cdot T + 13.58276 \quad (150 \leq T \leq 450 \text{ K})$$

$$c = 1.6703 \cdot 10^{-7} \cdot T^2 - 2.6633 \cdot 10^{-5} \cdot T + 8.8156 \quad (150 \leq T \leq 450 \text{ K})$$

$$\beta = 4.4076 \cdot 10^{-6} \cdot T^2 - 2.468 \cdot 10^{-3} \cdot T + 102.317 \quad (150 \leq T \leq 450 \text{ K})$$

$$V = 8.465 \cdot 10^{-5} \cdot T^2 + 5.3876 \cdot 10^{-2} \cdot T + 1029.66 \quad (150 \leq T \leq 450 \text{ K}).$$

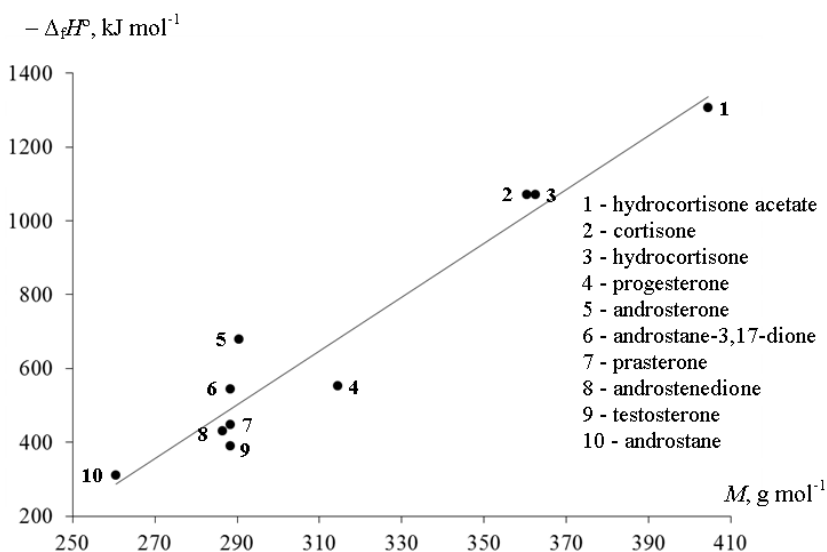


Figure 1. Dependence of the enthalpy of formation of steroids on the molecular weight

The unit cell parameters not change dramatically with temperature. Typically, organic crystals are characterized the large changes in unit cell parameters. In addition, the change in the monoclinic angle is virtually absent, which is also not typical for the monoclinic system. This indicates a significant interaction between the molecules in the crystal, particularly in the form of an extensive network of hydrogen bonds.

Thermal expansion coefficient is the quantitative characteristic of thermal expansion. We used the formula $\alpha L = 1/L \cdot (\Delta L / \Delta T)$, where αL - coefficient of thermal expansion, L - unit cell parameter. Value of the thermal expansion coefficient in given direction corresponds to length of radius-vector, which is traced from origin of coordinates to edge of figure of expansion. The thermal expansion of the hydrocortisone acetate is very anisotropic, and its thermal expansion coefficient depends significantly on temperature (Table 2). We found that the anisotropy of thermal expansion increases with increasing temperature, and the most intensive expansion of the structure observed along the crystallographic axis b . For the construction of 3D version of the thermal expansion diagram algorithm for Maplesoft© can be used [5] (Figure 2). These figures allow presenting the anisotropy of the thermal expansion of the crystal at a certain temperature.

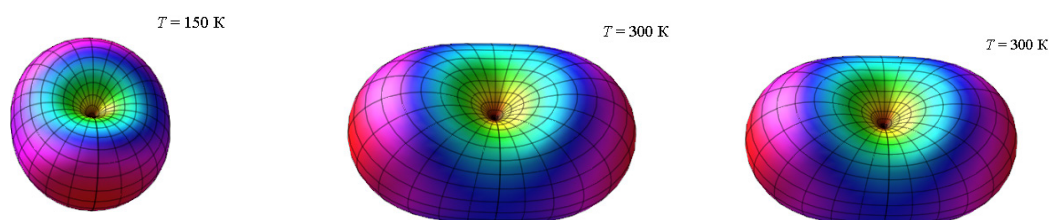


Figure 2. 3D thermal expansion diagrams for hydrocortisone acetate

In addition, we calculated the temperature dependence of the density of the crystal on the basis of the temperature dependence of the unit cell volume. The density of hydrocortisone acetate ($\rho = 1.288 \text{ g cm}^{-3}$) evaluated in work [6], which are also calculated from X-ray data at temperature 298 K. Our results are in good agreement with this work and presented as the temperature dependence.

Table 2. Parameters of unit cells and thermal expansion coefficients vs. temperature for hydrocortisone acetate

T, K	a, Å	b, Å	c, Å	β , °	V, Å ³
150	8.855 (14)	13.608 (30)	8.812 (9)	101.99 (14)	1039.6 (20)
175	8.868 (12)	13.623 (26)	8.817 (8)	101.97 (12)	1042.0 (17)
200	8.874 (12)	13.633 (27)	8.817 (8)	102.02 (12)	1043.3 (18)
225	8.877 (12)	13.657 (27)	8.816 (8)	102.00 (12)	1045.5 (18)
250	8.892 (11)	13.679 (23)	8.820 (7)	101.99 (10)	1049.5 (15)
275	8.904 (11)	13.681 (24)	8.821 (7)	101.95 (11)	1051.3 (16)
300	8.904 (12)	13.704 (27)	8.821 (8)	102.05 (12)	1052.6 (18)
325	8.917 (12)	13.722 (25)	8.827 (8)	102.03 (11)	1056.3 (17)
350	8.930 (12)	13.740 (26)	8.827 (8)	102.00 (11)	1059.5 (17)
375	8.934 (10)	13.753 (22)	8.829 (7)	101.95 (10)	1061.3 (15)
400	8.940 (11)	13.781 (25)	8.832 (8)	101.91 (11)	1064.5 (17)
425	8.951 (12)	13.811 (27)	8.833 (8)	102.02 (12)	1067.9 (18)
450	8.963 (11)	13.846 (24)	8.838 (7)	102.22 (11)	1071.2 (16)
T, K	$\alpha_a \cdot 105, \text{K}^{-1}$	$\alpha_b \cdot 105, \text{K}^{-1}$	$\alpha_c \cdot 105, \text{K}^{-1}$	$\alpha_\beta \cdot 105, \text{K}^{-1}$	$\alpha_V \cdot 105, \text{K}^{-1}$
150	3.7	2.9	0.27	-1.1	7.2
200	3.7	3.7	0.46	-0.7	8.2
250	3.8	4.6	0.65	-0.3	9.1
300	3.9	5.4	0.83	0.2	10.0
350	4.0	6.2	1.0	0.6	11.0
400	4.0	7.0	1.2	1.0	11.9
450	4.1	7.8	1.4	1.5	12.8

CONCLUSIONS

The general aim of these investigations was to report the results of the thermodynamic study of the hydrocortisone acetate. The standard enthalpy of formation is determined by using combustion calorimetry. The thermochemical analysis of the acylation reaction of hydrocortisone into hydrocortisone acetate showed that the reaction is exothermic. Thermal expansion of the crystal in a wide temperature range was studied and was identified priority direction for expansion (crystallographic axis b).

ACKNOWLEDGEMENTS

The work was performed with the financial support of the Russian Foundation of Basic Research (Project Number 13-03-00152).

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