Experimental and computational thermochemical study of 1,3,5-trimethyl-, 1,5,5-trimethyl-, and 1,3,5,5-tetramethyl-barbituric acids

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ABSTRACT

This paper reports an experimental and computational thermochemical study on three barbituric acid derivatives: 1,3,5-trimethylbarbituric acid or (1,3,5-trimethyl-2,4,6(1H,3H,5H)pyrimidinetrione, CAS 7358-61-4), 1,5,5-trimethylbarbituric acid or (1,5,5-trimethyl-2,4,6(1H,3H,5H)pyrimidinetrione, CAS 702-47-6), and 1,3,5,5-tetramethylbarbituric acid or (1,3,5,5-tetramethyl-2,4,6(1H,3H,5H)pyrimidinetrione, CAS 13566-66-0). Values of standard (p^0 = 0.1 MPa) molar enthalpies of formation in the gas phase at T = 298.15 K have been derived from experiment. Energies of combustion were measured by static bomb combustion calorimetry and standard molar enthalpies of formation in the crystalline state at T = 298.15 K were calculated. Enthalpies of sublimation were derived from temperature dependence of vapour pressures measured by transpiration method. From these results, values of $-(570.6 \pm 2.3)$, $-(599.4 \pm 1.4)$, and $-(605.1 \pm 2.9)$ kJ · mol^{-1} for the gas-phase enthalpies of formation at T = 298.15 K of 1,3,5-trimethylbarbituric acid, 1,5,5-trimethylbarbituric acid, and 1,3,5,5-tetramethylbarbituric acid, respectively, were determined. Theoretical calculations at the G3 and G4 levels were performed, and a study of the molecular and electronic structure of the compounds has been carried out. Calculated enthalpies of formation were in good agreement with the experimental values.

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1. Introduction

Over the past years, we have been involved in the study of the thermochemistry of barbituric acid or (2,4,6(1H,3H,5H)-pyrimidine-trione) and its derivatives, with the aim to develop the understanding of the structural effects on their thermodynamic stabilities that are reflected in the gas-phase enthalpies of formation. On the other hand, reliable values of the enthalpies of formation in the gas phase for the family of barbiturates can be used for the estimation of the thermochemical properties that are not easy to study experimentally for related compounds having similar groups, and also to contribute to the study of the influence of steric, electrostatic, and stereoelectronic interactions produced by substituents on the thermochemical stability of these molecules. We have recently published thermochemical studies of the parent compound barbituric acid [1] and its 5,5-dimethyl [2], 1,3-dimethyl [3] and 5,5-diethyl (barbital) [4,5] derivatives, and of a sulfur-containing barbituric

acid, 2-thiobarbituric acid [6]. We have also reported thermophysical studies of some methyl and ethyl derivatives of the barbituric acid [7], and the 2-thiobarbituric acid [8]. The aim of the present work is to study the energy-structure relationship of three new methyl derivatives: 1,3,5-trimethylbarbituric acid or (1,3,5-trimethyl-2,4,6(1H,3H,5H)pyrimidinetrione), 1,5,5-trimethylbarbituric acid or (1,5,5-trimethyl-2,4,6(1H,3H,5H)pyrimidinetrione), and 1,3,5,5-tetramethylbarbituric acidor (1,3,5,5-tetramethyl-2,4,6(1H,3H,5H)pyrimidinetrione), whose structures are presented in figure 1.

2. Experimental

2.1. Materials and purity control

The preparation and purification of the three barbituric acid derivatives were described in details in our previous publication [7]. For the present work, 1,3,5-trimethylbarbituric acid was in addition sublimated at 80 °C/0.1 Torr giving a fusion temperature of (90.0 to 90.9) °C.

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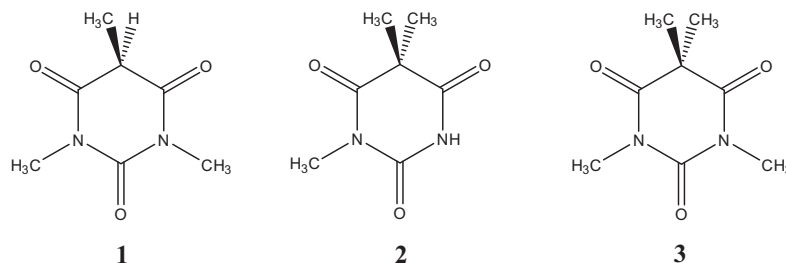E-mail address: rnotario@iqfr.csic.es (R. Notario).

FIGURE 1. Structures of 1,3,5-trimethylbarbituric acid **1**, 1,5,5-trimethylbarbituric acid **2**, and 1,3,5,5-tetramethylbarbituric acid **3**.

2.2. Combustion calorimetry

An isoperibol bomb calorimeter was used for the measurement of energy of combustion of the barbituric acid derivates. The detailed procedure has been described previously [11]. We used small polyethylene pieces as the auxiliary material (table 1) in order to reach 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 ε_{calor} was determined with a standard reference sample of benzoic acid (sample SRM *39j*, N.I.S.T.). Correction for nitric acid formation was based on the titration with $0.1 \, mol \cdot dm^{-3}$ NaOH (aq.). The sample masses were reduced to vacuum, taking into consideration their densities (table 2).

For converting the energy of the actual bomb process to that of the isothermal process, and reducing to standard state, the conventional procedure was applied. To derive $\Delta_f H_m^{\circ}$ (cr) from the molar enthalpy of combustion $\Delta_c H_m^{\circ}$, molar enthalpies of formation of H_2O (l): $-(285.830 \pm 0.042) \, kJ \cdot mol^{-1}$ and CO_2 (g): $-(393.51 \pm 0.13) \, kJ \cdot mol^{-1}$ have been used as assigned by *CODATA* [12]. The total uncertainty was calculated according to the guidelines presented by Olofsson [13]. The uncertainty assigned to $\Delta_f H_m^{\circ}$ (cr) is twice the overall standard deviation and includes the uncertainties from calibration, from the combustion energies of the auxiliary materials, and the uncertainties of the enthalpies of formation of the reaction products H_2O and CO_2.

2.3. Vapour pressure measurements

Vapour pressures and enthalpies of sublimation, $\Delta_{cr}^g H_m$, of barbituric acid derivates were determined using the transpiration method [14,15]. A sample of approximately 0.5 g was mixed with glass beads and placed in a thermostatted U-tube of length 10 cm and diameter 0.5 cm. Preheated nitrogen stream was passed through the U-tube at constant temperature (± 0.1 K). The flow rate of the nitrogen stream was measured using a soap film bubble flow meter (± 0.2 to 0.3)% and optimised in order to reach the saturation equilibrium of the transporting gas at each temperature under study. The material transported was collected in a cold trap. The amount of condensed product was determined by weighing (± 0.0001 g).

The saturated vapour pressure p_i at each temperature T_i was calculated from the amount of product collected within a definite period of time. Assuming that Dalton's law of partial pressures when applied to the nitrogen stream saturated with the substance i of interest is valid, values of p_i were calculated:

$$p_i = m_i \cdot R \cdot T_a / V \cdot M_i; \quad V = V_{N2} + V_i; \quad (V_{N2} \gg V_i), \tag{1}$$

where $R = 8.31447 \, J \cdot K^{-1} \cdot mol^{-1}$; m_i is the mass of the transported compound, M_i is the molar mass of the compound, and V_i; is its volume contribution to the gaseous phase. V_{N2} is the volume of transporting gas and T_a is the temperature of the soap film bubble flow meter. The volume of transporting gas V_{N2} was determined from the flow rate and time measurements.

The following equation:

$$R \cdot \ln p_i = a + \frac{b}{T} + \Delta_{cr}^g C_p \cdot \ln\left(\frac{T}{T_0}\right), \tag{2}$$

was fitted to the experimental p, T data using a and b as adjustable parameters. T_0 appearing in equation (2) is an arbitrarily chosen reference temperature (which has been chosen to be 298.15 K). Consequently, from equation (2) the expression for the sublimation enthalpy at temperature T is derived:

$$\Delta_{cr}^g H_m(T) = -b + \Delta_{cr}^g C_p \cdot T. \tag{3}$$

Values of $\Delta_{cr}^g C_p$ have been derived using experimental values of the isobaric molar heat capacities C_p^{cr} of barbituric acid derivatives [7] (table S1 in electronic supplementary materials, Online Resource) according to a procedure developed by Chickos and Acree [16].

2.4. Computational details

Standard *ab initio* molecular orbital calculations were performed with the Gaussian 09 [17] series of programs. The energy of the compounds studied was calculated using Gaussian-n theory, at the G3 [18] and G4 [19] levels. The G3- and G4-calculated energies, at $T = 0$ K, and enthalpies, at $T = 298$ K, for 1,3,5-trimethylbarbituric acid, 1,5,5-trimethylbarbituric acid, and 1,3,5,5-tetramethylbarbituric acid, are presented in electronic supplementary materials (Online Resource, table S2).

TABLE 1
Provenance, purification and analysis details of the compounds studied.

Chemical name	CAS	Provenance	Purification method	Final mass fraction purity[d]
1,3,5-Trimethylbarbituric acid	7358-61-4	This work[a]	Sublimation	0.9999
1,5,5-Trimethylbarbituric acid	702-47-6	This work[b]	Crystallisation	0.9999
1,3,5,5-Tetramethylbarbituric acid	13566-66-0	This work[c]	Crystallisation	0.9999

[a] Prepared from diethyl methylmalonate and *N,N′*-dimethylurea according to a literature procedure [7,9].
[b] Prepared from diethyl dimethylmalonate and *N*-methylurea according to a literature procedure [7,10].
[c] Prepared by methylation of the sodium salt of 1,5,5-trimethylbarbituric acid with methyl iodide according to a literature procedure [7].
[d] Determined by HPLC and DSC.