

Experimental and Computational Thermochemical Study and Solid-Phase Structure of 5,5-Dimethylbarbituric Acid

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This paper reports an experimental and computational thermochemical study on 5,5-dimethylbarbituric acid and the solid-phase structure of the compound. The value of the standard ($p^\circ = 0.1$ MPa) molar enthalpy of formation in the gas phase at $T = 298.15$ K has been determined. The energy of combustion was measured by static bomb combustion calorimetry, and from the result obtained, the standard molar enthalpy of formation in the crystalline state at $T = 298.15$ K was calculated as $-(706.4 \pm 2.2)$ kJ·mol⁻¹. The enthalpy of sublimation was determined using a transference (transpiration) method in a saturated NB₂ stream, and a value of the enthalpy of sublimation at $T = 298.15$ K was derived as (115.8 ± 0.5) kJ·mol⁻¹. From these results a value of $-(590.6 \pm 2.3)$ kJ·mol⁻¹ for the gas-phase enthalpy of formation at $T = 298.15$ K was determined. Theoretical calculations at the G3 level were performed, and a study on molecular and electronic structure of the compound has been carried out. Calculated enthalpies of formation are in reasonable agreement with the experimental value. 5,5-Dimethylbarbituric acid was characterized by single crystal X-ray diffraction analysis. In the crystal structure, N–H···O=C hydrogen bonds lead to the formation of ribbons connected further by weak C–H···O=C hydrogen bonds into a three-dimensional network. The molecular and supramolecular structures observed in the solid state were also investigated in the gas phase by DFT calculations.

1. Introduction

Two basic properties of chemical compounds are their structure and energy. These are intimately related because the energy associated with a particular structure depends on the atoms, types of bonds, bonds angles, and torsional angles that form the molecular framework.¹ Enthalpies of formation are often helpful in the understanding of the structural, conformational, and reactivity trends exhibited by molecules. The data are needed to estimate the amount of energy released or absorbed in a chemical reaction, in calculating other thermodynamics functions, and, more importantly, in assessing the relative stability of molecules. One of the purposes of thermochemistry is to derive the enthalpies of formation of compounds from their elements, and to relate the energy to structure and chemical binding.^{2,3}

Over the past years, we have been involved in the thermochemical study of the energetics of nitrogen-containing compounds such as amides,⁴ β -lactams,⁵ azoles,⁶ and cyclic ureas.⁷ We are presently involved in the study of the thermochemistry of barbituric acid derivatives (2,4,6(1*H*,3*H*,5*H*)-pyrimidinetrione derivatives) with the aim of developing an 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 gas-phase enthalpies of formation of barbiturates can be useful for the estimation of the thermochemical properties of related compounds that are not easy to study experimentally. These enthalpies will also contribute to an understanding of the influence of steric, electrostatic, and stereoelectronic interactions produced by substituents on the thermochemical stability of these molecules.

Barbituric acid derivatives were introduced for medical use a century ago,⁸ several years after the synthesis in 1864 by von Baeyer of the parent compound, barbituric acid.⁹ Barbiturates act as central nervous system depressants, and by virtue of this, they produce a wide spectrum of physiological effects. They are used as sedatives, hypnotics, soporifics, anticonvulsants, or as adjuncts in anesthesia.¹⁰ Other applications of barbituric acid derivatives include their use as antivirals,¹¹ in photochemical nanoscience,¹² as dyes,¹³ polymers,¹⁴ dental materials,¹⁵ water-thinned or oil-based inks,¹⁶ and as polymerization catalysts.¹⁷ In the context of a systematic study of the thermodynamic properties of this family of compounds and despite the important uses and applications of barbituric acids derivatives, reliable experimental thermochemical studies are scarce. We have recently published the thermochemical study of the parent compound barbituric acid¹⁸ and its 5,5-diethyl derivative (barbital).¹⁹

The purpose of the present work is to study the energy–structure relationship of 5,5-dimethylbarbituric acid whose formula is presented in Figure 1. The approach selected is a combination of experimental determinations of the enthalpy of formation,

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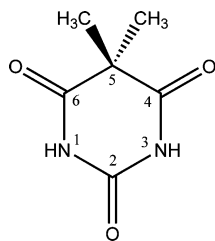


Figure 1. Schematic formula of 5,5-dimethylbarbituric acid.

and molecular structure coupled with high-level *ab initio* calculations. The crystal structure of 5,5-dimethylbarbituric acid has been determined since only molecular complexes with *N,N'*-diphenylmelamine and *N,N'*-di(*tert*-butyl)melamine have been reported (Cambridge Crystallographic Database,²⁰ CSD hereinafter, version 5.30, update of September 2009).

2. Experimental Procedures

2.1. Material and Purity Control. 5,5-Dimethylbarbituric acid [CAS 24448-94-0] was commercially available from Fluka. The sample was carefully dried under vacuum and no further purification was needed. Determination of purity, assessed by HPLC and differential scanning calorimetry (DSC), using the fractional fusion technique,²¹ indicated that the mole fraction of impurities in the compound was less than 0.0001.

2.2. X-ray Crystallography. Crystals of commercial 5,5-dimethylbarbituric acid were used in this study. The X-ray data were collected on a Nonius Kappa CCD diffractometer²² at room temperature. The structure was solved by direct methods²³ and refined using the SHELX97 program²⁴ operating under the WinGx program package,²⁵ and the illustrations have been drawn with PLATON²⁶ under WinGx.

2.3. Procedure for Thermochemical Measurements.

2.3.1. Differential Scanning Calorimetry. The behavior of the sample as a function of temperature was studied by differential scanning calorimetry. A Pyris 1 instrument from Perkin-Elmer equipped with an intracooler unit was used to monitor purity and to study the fusion process and the possible existence of phase transitions in the solid sample at temperatures above 260 K. For experiments made in the temperature interval 150 to 298 K, a Mettler DSC30 was used. Both apparatuses were previously calibrated in temperature and energy with reference materials. Temperature and power scales were calibrated²⁷ at heating rates of 0.04 and 0.17 K·s⁻¹. The temperature scales were calibrated by the melting temperature of the high-purity reference materials: hexafluorobenzene, tin, and indium.²⁸ The power scales were calibrated with high-purity indium.²⁸

Thermograms of samples hermetically sealed in aluminum pans were recorded in a nitrogen atmosphere. All the pans with the samples were weighed on a Mettler AT21 microbalance with a detection limit of 1×10^{-6} g, before and after the experiments to confirm that no product had volatilized.

After calibration, several runs with high-purity benzoic acid and indium as reference materials²⁸ were performed under the same conditions as the experimental determinations. The accuracies associated with measurements of temperature and enthalpy of fusion were calculated as the percentage deviation of the experimental data with respect to the values given in the literature,²⁸ in all cases the deviations were lower than 0.2 and 2.0% for temperature and enthalpy determinations, respectively.²⁹

For the determination of the purity and the temperature and enthalpy of fusion, a heating rate of 0.04 K·s⁻¹ was used, and five samples weighing 1–2 mg were recorded. A fresh sample was used for each run.

Different scans at heating rates of 0.04 and 0.17 K·s⁻¹ were performed to determine the possible existence of phase transitions in the sample over the temperature range from $T = 150$ K to its melting temperature.

2.3.2. Combustion Calorimetry. An isoperibol calorimeter equipped with a static bomb was used for the measurements of the energy of combustion. The apparatus, technique, and procedure have been described.³⁰ Calorimetric temperatures of the calorimeter were measured within $\pm 1 \times 10^{-4}$ K by means of a 100 Ω platinum resistance thermometer, using a calibrated resistance bridge (Model F300, Automatic System Laboratories Ltd.) interfaced to a microcomputer programmed to calculate the adiabatic temperature change. The energy equivalent of the calorimeter, ε (calor), was determined from the combustion of benzoic acid, NIST standard reference sample 39j, having a specific energy of combustion, $\Delta_c u = -(26434 \pm 3)$ J·g⁻¹, under certificate conditions. From eight calibration experiments ε (calor) = (14262.6 ± 2.5) J·K⁻¹, where the uncertainty quoted is the standard deviation of the mean. Frequent calibration experiments were made throughout the series of combustion experiments. The energy of combustion of 5,5-dimethylbarbituric acid was determined by burning the solid samples in pellet form in oxygen. In order to obtain complete reactions of combustion vaseline and polyethylene were used as auxiliary substances. The combustion bomb was flushed and filled with oxygen, previously freed from combustible impurities and an initial pressure of oxygen of 3.04 MPa was used. Details of the characterization and physical properties of 5,5-dimethylbarbituric acid and auxiliary substances used in this work are collected in Table 1.

After disassembly of the calorimeter, the bomb gases were slowly released and the absence of CO was confirmed with Dräger tubes (sensitivity level $\approx 1 \times 10^{-6}$ mass fraction). No traces of carbon residue (soot) were observed in any of the runs. The absence of NO₂⁻ was checked by calibrated ionic chromatography using a Dionex DX-120-chromatographic apparatus with a sensitivity level of 0.1 ppm for the measurements of NO₂⁻. The nitric acid content in the bomb liquid was determined by titration with 0.1 mol dm⁻³ NaOH (aq). The corrections for

TABLE 1: Properties at $T = 298.15$ K^a

compound	M g·mol ⁻¹	ρ g·cm ⁻³	$(\delta V/\delta T)_P \cdot 10^{-7}$ dm ³ ·g ⁻¹ ·K ⁻¹	c_p J·K ⁻¹ ·g ⁻¹	$\Delta_c u_m^{\circ}(\text{cr})$ J·g ⁻¹
polyethylene	13.5582 ^{b,c}	0.918	7.650	1.99	-(46371 ± 4) ^c
vaseline	14.0266	0.870 ^d	8.374 ^e	2.22 ^f	-(46086 ± 5) ^d
cotton	27.700 ^{g,c}	1.5	9.69 ^h	1.48	-(17410 ± 37) ^c
5,5-dimethylbarbituric acid	156.1393	1.444 ⁱ	(3.354)	1.4	

^a The value in parentheses was estimated. ^b Corresponding to an empirical formula of C_{0.960}H_{2.000}. ^c Determined in our laboratory. ^d Value taken from ref 31. ^e Value taken from ref 32. ^f Value taken from ref 33. ^g Corresponding to an empirical formula of C_{1.000}H_{1.740}O_{0.871}. ^h Value taken from ref 34. ⁱ This work, calculated from X-ray data.

nitric acid formation³⁵ were based on the value of $-59.7 \text{ kJ mol}^{-1}$ for the standard molar energy of formation of $0.1 \text{ mol} \cdot \text{dm}^{-3} \text{ HNO}_3(\text{aq})$ from $\text{N}_2(\text{g})$, $\text{O}_2(\text{g})$, and $\text{H}_2\text{O}(\text{l})$. All samples were weighed with a Mettler AT-21 microbalance, sensitivity was $\pm 1 \times 10^{-6} \text{ g}$, and corrections of apparent mass to mass were made. For these corrections, conversion of the energy of the actual bomb process to that of the isothermal process, and for the correction to standard states, the values given in Table 1 were used. Corrections to the standard states were made according to Hubbard et al.³⁶ The atomic weights of the elements were those recommended by IUPAC in 2006.³⁷ The energy of solution of carbon dioxide in water at 298.15 K , $\Delta_{\text{sol}}U(\text{CO}_2)$, was taken as $-17.09 \text{ kJ} \cdot \text{mol}^{-1}$, and the solubility constant, $K(\text{CO}_2)$, as $0.03440 \text{ mol} \cdot \text{dm}^{-3} \cdot \text{atm}^{-1}$ at $T = 298.15 \text{ K}$.³⁸

From the combustion energy, $\Delta_c u^\circ$, the enthalpy of formation in the condensed state, $\Delta_f H_m^\circ(\text{cr})$, at $T = 298.15 \text{ K}$ was calculated.

2.3.3. Vapor Pressure Measurements. Vapor pressures and enthalpies of sublimation, $\Delta_{\text{tr}} H_m^\circ$, of 5,5-dimethylbarbituric acid were determined by using the method of transference in a saturated stream of nitrogen. The method has been described previously³⁹ and has proved to give results in agreement with other established techniques for determining vapor pressures of pure substances and enthalpies of vaporization from the temperature dependence of the vapor pressure. About 0.5 g of the sample was mixed with glass beads and placed in a thermostatted U-tube of length 10 cm and diameter 0.5 cm . A preheated nitrogen stream was passed through the U-tube at constant temperature ($\pm 0.1 \text{ K}$). The flow rate of the nitrogen stream was measured using a soap bubble flow meter (± 0.2 – 0.3%) and optimized in order to reach the saturation equilibrium of the transporting gas at each temperature under study. On the one hand, the flow rate of the nitrogen stream in the saturation tube should not be too slow in order to avoid the transport of material from the U-tube due to diffusion. On the other hand, the flow rate should be not too fast in order to reach saturation of the nitrogen stream with a compound. We tested our apparatus at different flow rates of carrier gas in order to check the lower boundary of the flow below which the contribution of the vapor condensed in the trap by diffusion becomes comparable to the transpired one. In our apparatus the contribution due to diffusion was negligible at a flow rate up to $0.5 \text{ dm}^3 \cdot \text{h}^{-1}$. The upper limit for our apparatus where the speed of nitrogen could already disturb the equilibration was at a flow rate of $12.5 \text{ dm}^3 \cdot \text{h}^{-1}$. Thus, we carried out the experiments in the flow rate interval of $9 \text{ dm}^3 \cdot \text{h}^{-1}$ which ensured that the transporting gas was in saturated equilibrium with the coexisting solid phase in the saturation tube. The transported amount of material was condensed in a cooled trap. The amount of condensed product was determined by weighing ($\pm 0.0001 \text{ g}$).

The saturated vapor pressure p_i^{sat} 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 is valid as applied to the nitrogen stream saturated with the substance i of interest, values of p_i^{sat} were calculated:

$$P_1^{\text{sat}} = m_i R T_a / V M_i; \quad V = V_{\text{N}_2} + V_i; \quad (V_{\text{N}_2} \gg V_i) \quad (1)$$

where $R = 8.31451 \text{ J} \cdot \text{K}^{-1} \cdot \text{mol}^{-1}$, m_i is the mass of transported compound, M_i is the molar mass of the compound, and V_i is its volume contribution to the gaseous phase. V_{N_2} is the volume of transporting gas and T_a is the temperature of the soap bubble

TABLE 2: Results of a Typical Combustion Experiment on 5,5-Dimethylbarbituric Acid^a

m' (compound)/g ^b	0.530587
m'' (polyethene)/g ^b	0.094902
m''' (vaseline)/g ^b	0.072408
m'''' (fuse)/g ^b	0.002475
$\Delta T_c / \text{K} = (T_f - T_i + \Delta T_{\text{corr}}) / \text{K}$	1.2144
ε (calor) $(-\Delta T_c) / \text{kJ}^c$	-17.3208
ε (cont) $(-\Delta T_c) / \text{kJ}^d$	-0.0201
$\Delta U_{\text{ign}} / \text{kJ}^e$	0.0008
$\Delta U_{\text{dec}} (\text{HNO}_3) / \text{kJ}^f$	0.0445
ΔU (corr to std states) / kJ^g	0.0096
$-m'' \Delta_c u^\circ$ (polyethene) / kJ	4.4008
$-m''' \Delta_c u^\circ$ (vaseline) / kJ	3.3371
$-m'''' \Delta_c u^\circ$ (fuse) / kJ	0.0431
$\Delta_c u^\circ$ (compound) / $\text{kJ} \cdot \text{g}^{-1}$	-17.9139

^a For a definition of the symbols see refs 36 and 46. $T_{\text{th}} = 298.15 \text{ K}$; $V_{\text{bomb}} = 0.380 \text{ dm}^3$; $p_{\text{gas}}^i = 3.04 \text{ MPa}$; $m_{\text{water}}^i = 1.00 \text{ g}$. ^b Masses obtained from apparent mass. ^c ε (calor), energy equivalent of the whole system less the content of the bomb. ^d ε (cont), energy equivalent of the contents of the bomb. $\varepsilon(\text{cont})(-\Delta T_c) = \varepsilon^i(\text{cont})(T - 298.15 \text{ K}) + \varepsilon^i(\text{cont})(298.15 \text{ K} - T^f + \Delta T_{\text{corr}})$. ^e Experimental energy of ignition. ^f Experimental energy of formation of nitric acid. ^g Energy of correction to standard states.

TABLE 3: Experimental Energies of Combustion of 5,5-Dimethylbarbituric Acid (all values in $\text{kJ} \cdot \text{g}^{-1}$)

run	$-\Delta_c u^\circ$
1	17.9094
2	17.9372
3	17.9040
4	17.9277
5	17.9095
6	17.9194
7	17.9464
8	17.9479
9	17.9416
10	17.9139
mean and standard deviation of the mean	(17.9257 ± 0.0053)

TABLE 4: Experimentally Determined Standard ($p^\circ = 0.1 \text{ MPa}$) Molar Energy of Combustion and Standard Molar Enthalpies of Combustion and Formation in the Crystalline State at $T = 298.15 \text{ K}$ for 5,5-Dimethylbarbituric Acid (values in $\text{kJ} \cdot \text{mol}^{-1}$)

$\Delta_c U_m^\circ(\text{cr})$	$\Delta_c H_m^\circ(\text{cr})$	$\Delta_f H_m^\circ(\text{cr})$
-2798.9 ± 2.2	-2797.7 ± 2.2	-706.4 ± 2.2

meter. The volume of transporting gas V_{N_2} was determined from the flow rate and time measurements.

2.4. Computational Details. Standard ab initio molecular orbital calculations⁴⁰ were performed with the Gaussian 03 series of programs.⁴¹ The energy of the compound studied was calculated using Gaussian-n theory, at the G3 level.^{42,43}

G3 corresponds effectively to calculations at the QCISD(T)/G3large level, G3large being a modification of the 6-311+G(3df,2p) basis set, including more polarization functions for the second row (3d2f), less on the first row (2df), and other changes to improve uniformity. In addition, some core polarization functions are added.⁴² Single-point energy calculations are carried out on MP2(Full)/6-31G(d)-optimized geometries, incorporating scaled HF/6-31G(d) zero-point vibrational energies, a so-called higher-level correction to accommodate remaining deficiencies, and spin-orbit correction for atomic species only.⁴²

We have also reoptimized the geometry at the MP2(Full)/6-31G(3df,2p) level to obtain a more reliable molecular structure for the compound studied.

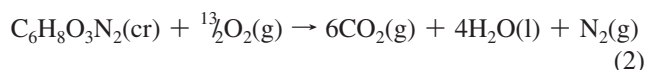
According to the Cambridge Crystallographic Database,²⁰ molecules of the anhydrous 5,5'-alkylbarbituric acid derivatives including the parent compound self-assemble into six hydrogen bonding networks.¹⁸ Of them, the two single chain models formed by six molecules (the minimum needed for the representation of the six motifs) idealized for the 5,5-dimethylbarbituric acid monomer have been optimized at three different DFT levels of calculation, B3LYP/6-31G(*d*), B3LYP/6-31+G(*d,p*), and B3LYP/6-31++G(*d*).

The charge distribution has been analyzed using a population partition technique, the natural bond orbital (NBO) analysis of Reed and Weinhold.⁴⁴ The NBO analysis has been performed using the NBO program⁴⁵ implemented in the Gaussian 03 package.⁴¹

3. Results and Discussion

3.1. Experimental Results. 3.1.1. Phase Transitions. Differential scanning calorimeters were used to study the possible existence of phase transitions in the solid sample and to study the fusion process. No phase transitions were observed in the temperature interval between $T = 150$ K to the melting temperature. The determined temperature and enthalpy of fusion were $T_{\text{fus}} = (548.7 \pm 0.6)$ K, and $\Delta_{\text{fus}}H = (34.8 \pm 0.2)$ kJ·mol⁻¹. All temperatures were taken as onset temperatures. The uncertainties were taken as standard deviations.

3.1.2. Experimental Enthalpy of Formation. Results for a typical combustion experiment on 5,5-dimethylbarbituric acid are given in Table 2 and correspond to the reaction:



The individual values of $-\Delta_{\text{c}}H^\circ$, the mean value and its standard deviation, are given in Table 3.

Table 4 lists the derived standard molar enthalpies of combustion and formation in the crystalline state at $T = 298.15$ K. In accordance with the normal thermochemical practice, the uncertainty assigned is twice the overall standard deviation of the mean and includes the uncertainties in calibration and in the auxiliary quantities used.⁴⁷ To derive $\Delta_{\text{f}}H^\circ_{\text{m}}(\text{cr})$ from $\Delta_{\text{c}}H^\circ_{\text{m}}(\text{cr})$, the ATcT values of the standard molar enthalpies of formation at $T = 298.15$ K of $\text{H}_2\text{O}(\text{l})$ and $\text{CO}_2(\text{g})$, $-(285.823 \pm 0.0033)$ and $-(393.473 \pm 0.014)$ kJ·mol⁻¹, respectively, were used.⁴⁸

3.1.3. Enthalpy of Sublimation. Our experimental vapor pressures of 5,5-dimethylbarbituric acid have been measured over a 60 K temperature range. The following equation:

$$R \ln p_i^{\text{sat}} = a + \frac{b}{T} + \Delta_{\text{cr}}^{\text{g}}C_p \ln\left(\frac{T}{T_0}\right) \quad (3)$$

was fit to the experimental p , T data using a and b as adjustable parameters. T_0 appearing in eq 3 is an arbitrarily chosen reference temperature (which has been chosen to be 298.15 K). Consequently, from eq 3 the expression for the vaporization enthalpy at temperature T is derived (eq 4).

$$\Delta_{\text{cr}}^{\text{g}}H_{\text{m}}(T) = -b + \Delta_{\text{cr}}^{\text{g}}C_p T \quad (4)$$

A value of $\Delta_{\text{cr}}^{\text{g}}C_p = 21.9$ J·mol⁻¹·K⁻¹ has been derived from the experimental isobaric molar heat capacities of solid 5,5-dimethylbarbituric acid $C_p^{\text{cr}} = 141.1$ J·mol⁻¹·K⁻¹, according

TABLE 5: Results from Measurements of the Vapor Pressure p of 5,5-Dimethylbarbituric Acid Using the Transpiration Method

T , ^a K	m , ^b mg	V_{N_2} , ^c dm ³	p , ^d Pa	$p_{\text{exp}} - p_{\text{calc}}$, Pa	$\Delta_{\text{cr}}^{\text{g}}H_{\text{m}}$, kJ·mol ⁻¹
$\Delta_{\text{cr}}^{\text{g}}H_{\text{m}}(298.15 \text{ K}) = (115.76 \pm 0.51) \text{ kJ·mol}^{-1}$					
$\ln(p/\text{Pa}) = 315.79/R - 122292.46/R(T, \text{K}) - 21.9/R \ln(T, \text{K})/298.15$					
400.0	12.3	124.24	1.55	0.00	113.53
405.1	17.4	116.68	2.34	-0.03	113.42
408.4	16.2	78.09	3.24	0.13	113.35
414.8	19.0	56.98	5.26	0.06	113.21
419.9	14.7	30.12	7.67	-0.07	113.10
420.7	16.4	32.31	7.98	-0.26	113.08
423.7	90.0	136.20	10.37	0.02	113.01
429.5	18.8	19.30	15.31	-0.65	112.89
433.4	18.9	13.92	21.34	0.12	112.80
438.4	15.4	8.02	30.13	-0.19	112.69
443.3	21.9	7.87	43.96	1.30	112.59
448.3	21.4	5.60	60.37	0.40	112.48
453.1	26.7	5.07	83.20	0.64	112.37
457.9	24.7	3.48	112.10	-0.75	112.27

^a Temperature of saturation. ^b Mass of transferred sample, condensed at $T = 299$ K. ^c Volume of nitrogen, used to transfer mass m of sample; gas-flow 9.08 dm³/h was constant throughout the measurements. ^d Vapor pressure at temperature T , calculated from m and the residual vapor pressure at the cooling temperature $T = 299$ K.

TABLE 6: Experimentally Determined Thermodynamic Quantities at $T = 298.15$ K for 5,5-Dimethylbarbituric Acid (all values in kJ·mol⁻¹)

$\Delta_{\text{c}}H_{\text{m}}^\circ$	$\Delta_{\text{f}}H_{\text{m}}^\circ(\text{cr})$	$\Delta_{\text{cr}}^{\text{g}}H_{\text{m}}$	$\Delta_{\text{f}}H_{\text{m}}^\circ(\text{g})$
-2797.7 ± 2.2	-706.4 ± 2.2	115.8 ± 0.5	-590.6 ± 2.3

to the procedure developed by Chickos.⁴⁹ In order to assess the uncertainty of the sublimation enthalpy, the experimental data were approximated with the linear equation $\ln(p_i^{\text{sat}}) = f(T^{-1})$ using the method of least-squares. The uncertainty in the enthalpy of sublimation was assumed to be identical to the average deviation of experimental $\ln(p_i^{\text{sat}})$ values from this linear correlation, and uncertainties in values of $\Delta_{\text{cr}}^{\text{g}}C_p$ were not taken into account. Experimental results and parameters a and b are listed in Table 5.

Table 6 summarizes the values of the standard molar enthalpy of combustion, $\Delta_{\text{c}}H_{\text{m}}^\circ$, sublimation, $\Delta_{\text{cr}}^{\text{g}}H_{\text{m}}$, and

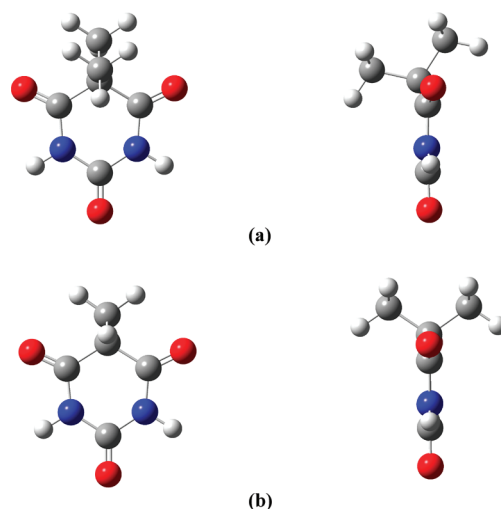


Figure 2. Front and side view of the molecular structure of 5,5-dimethylbarbituric acid optimized (a) at the MP2(Full)/6-31G(*d*) level; (b) at the MP2(Full)/6-31G(3*df*,2*p*) level.

TABLE 7: Experimental and Calculated Geometric Parameters for 5,5-Dimethylbarbituric Acid (bond distances in angstroms, and bond angles in degrees)

	this study	CSD HIBKAE/PIYDUW	MP2(FULL)/6-31G(d)	MP2(Full)/6-31G(3df,2p)
N1–C2	1.373(3)	1.361(5)/1.373(4)	1.388	1.379
C2–N3	1.377(2)	1.381(5)/1.363(4)	1.388	1.379
N3–C4	1.382(3)	1.369(5)/1.367(4)	1.389	1.376
C4–C5	1.525(3)	1.509(6)/1.514(5)	1.517	1.508
C5–C6	1.524(2)	1.514(5)/1.508(5)	1.517	1.508
C6–N1	1.396(3)	1.369(5)/1.368(4)	1.389	1.376
C2–O1	1.230(3)	1.219(5)/1.219(4)	1.219	1.207
C4–O2	1.223(2)	1.220(5)/1.207(5)	1.223	1.212
C6–O3	1.211(2)	1.211(5)/1.202(5)	1.223	1.212
C5–C7	1.562(3)	1.542(5)/1.539(8)	1.544	1.526
C5–C8	1.532(3)	1.511(5)/1.514(6)	1.526	1.526
C6–N1–C2	126.3(1)	125.2(3)/124.7(2)	127.6	128.0
N1–C2–N3	116.2(1)	117.6(3)/118.1(3)	113.8	114.1
C2–N3–C4	126.0(1)	124.2(3)/125.1(3)	127.6	128.0
N3–C4–C5	117.8(1)	119.7(3)/118.3(3)	116.2	117.2
C4–C5–C6	112.7(1)	112.6(3)/114.0(3)	114.2	115.6
C5–C6–N1	116.8(1)	118.8(3)/118.7(3)	116.2	117.2
O1–C2–N1	123.0(1)	122.5(4)/120.5(3)	123.1	123.0
O1–C2–N3	120.8(1)	119.9(3)/121.5(3)	123.1	123.0
O2–C4–N3	119.9(1)	119.2(3)/120.5(3)	120.6	120.8
O2–C4–C5	122.3(1)	121.1(3)/121.1(3)	123.0	122.0
O3–C6–C5	122.9(1)	121.4(3)/121.5(3)	123.0	122.0
O3–C6–N1	120.2(2)	119.8(3)/119.7(3)	120.6	120.8
C4–C5–C7	106.6(1)	106.3(3)/106.1(3)	106.4	107.7
C4–C5–C8	110.5(1)	110.6(3)/10.1(3)	109.8	107.7
C6–C5–C7	106.1(1)	106.0(3)/106.4(3)	106.4	107.7
C6–C5–C8	110.4(1)	110.6(3)/109.8(3)	109.8	107.7
N3–C4–C5–C6	21.8(2)	13.2(5)/12.6(4)	22.4	0.1
C4–C5–C6–N1	–22.7(2)	–16.3(5)/–8.8(4)	–22.4	–0.1
C5–C6–N1–C2	12.8(2)	10.6(6)/0.9(4)	14.3	0.1
C6–N1–C2–N3	0.3(2)	–0.1(5)/3.9(4)	–4.2	0.0
N1–C2–N3–C4	–1.7(2)	–3.5(5)/0.5(5)	4.2	0.0
C2–N3–C4–C5	–10.4(2)	–3.9(5)/–9.0(5)	–14.3	–0.1

formation in the crystalline, $\Delta_f H_m^\circ(\text{cr})$, and gaseous state, $\Delta_f H_m^\circ(\text{g})$ at $T = 298.15$ K.

No experimental results for the energies and enthalpies of combustion, sublimation, and formation have been found in the literature for comparison with our results.

3.2. Molecular and Electronic Structure. 5,5-Dimethylbarbituric acid contains two mobile hydrogen atoms, and so it may exist in five tautomeric forms differing from each other by the position of the hydrogens, which may be bound to either nitrogen or oxygen atoms. Calculations at the B3LYP/6-31G(*d*) level show the triketo tautomer to be the most stable one in the gas phase, followed by the two monohydroxy tautomers, 2,4-diketo-6-hydroxy and 4,6-diketo-2-hydroxy, but they are much

less stable, 69.4 and 89.9 kJ mol^{–1}, respectively. The higher stability of the triketo form is associated with the much stronger double bond of C=O compared with the strength of C=N bonds. The high energy differences from the other tautomers suggest that the gas phase of 5,5-dimethylbarbituric acid consists of a single molecular species.

The MP2(Full)/6-31G(*d*)-optimized structure is not planar, but an envelope conformation with the C₅ atom out of the planarity, in agreement with the crystal structure obtained in this work (see below). However, the MP2(Full)/6-31G(3df,2p)-optimized structure presents a planar six-membered ring. DFT calculations using B3LYP with different basis sets show the same planar structure. MP2(Full)/6-31G(*d*)- and MP2(Full)/6-

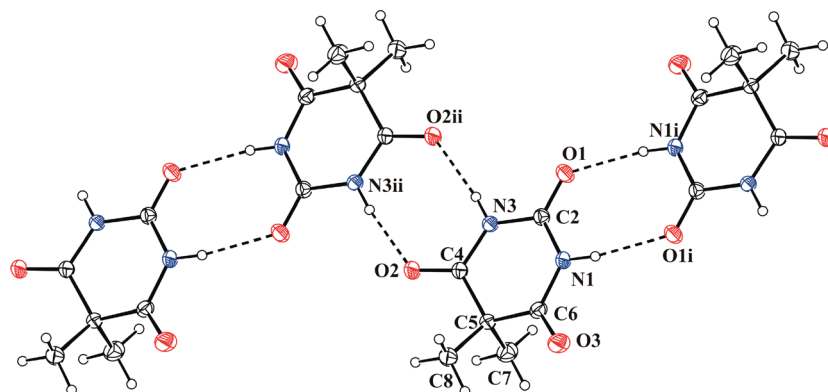


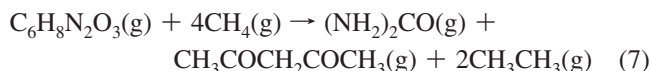
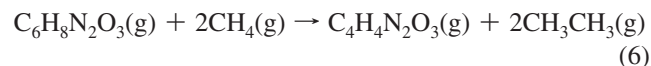
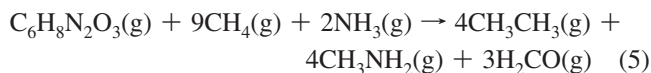
Figure 3. 1-D supramolecular structure of **1** showing the numbering system and the double dimeric association: N1–H···O1(*i* = –1 – *x*, 1 – *y*, 1 – *z*), N3–H···O2(*ii* = 1 – *x*, –*y*, 1 – *z*), N1···O1 = 2.907(4), H···O1 = 2.06 Å, N1–H···O1 = 168°, N3···O2 = 2.877(5), H···O2 = 2.02 Å, and N3–H···O2 = 173°.

31G(3*df*,2*p*)-optimized structures of 5,5-dimethylbarbituric acid are shown in Figure 2, and the calculated bond distances and angles are collected in Table 7 for their comparison with the X-ray results.

Atomic charges have been calculated by the natural bond orbital (NBO) population analysis scheme, at the MP2(Full)/6-31G(3*df*,2*p*) level of theory. Positive charge is located at C atoms of the carbonyl groups (1.015 at C₂, and 0.862 at C₄ and C₆ atoms), whereas negative charge is located at N atoms (−0.777), O atoms (−0.701 at O atom bonded at C₂, and −0.682 at O atoms bonded at C₄ and C₆ atoms), and also the C₅ atom bonded to the two methyl groups (−0.268). It is observed that the charge separation between the C₂ and O carbonyl group is higher than those on the other two carbonyl groups (1.716 versus 1.544).

3.3. Theoretical Determination of the Enthalpy of Formation. The standard procedure to obtain enthalpies of formation in Gaussian-n theories is through atomization reactions.⁵⁰ Several authors⁵¹ have shown that more accurate heats of formation can be derived using isodesmic or homodesmotic⁵² reactions rather than atomization energies. As Raghavachari et al.⁵³ have pointed out, one of the deficiencies of the isodesmic reaction approach is that many different isodesmic reactions can be set up for the same molecule yielding different results. These authors have proposed, using a standard set of isodesmic reactions, the “bond separation reactions”,⁴⁰ where all formal bonds between non-hydrogen atoms are separated into the simplest parent molecules containing these same kinds of linkages, to derive the theoretical enthalpies of formation.

In this work we have calculated the enthalpy of formation of 5,5-dimethylbarbituric acid, C₆H₈N₂O₃, using the atomization reaction, the bond separation isodesmic reaction 5, and another two isodesmic reactions taking barbituric acid, C₄H₄N₂O₃ (reaction 6) and urea and acetylacetone (reaction 7) as references:



The G3-calculated enthalpies of formation obtained⁵⁴ from the atomization reaction, −598.9 kJ·mol^{−1}, from the isodesmic reaction 6, −601.1 kJ·mol^{−1}, and from isodesmic reaction 7, −597.9 kJ·mol^{−1}, give an average value of −599.3 kJ·mol^{−1}, in a reasonable agreement with the experimental value determined in this work, −590.6 ± 2.3 kJ·mol^{−1}. The value calculated using the isodesmic bond separation reaction 5, −609.6 kJ·mol^{−1}, is higher than the other calculated values, and it has not been used in the determination of the mean value.

3.4. X-ray Crystallography. As far as the Cambridge Crystallographic Database²⁰ is concerned, the crystal structure of the 5,5-dimethylbarbituric acid has not been reported probably because of the small size and quality of the crystals. However, two molecular complexes with *N,N'*-diphenylmelamine⁵⁵ and *N,N'*-di(*tert*-butyl)melamine⁵⁶ (CSD codes: HIBKAE and PIYDUW) have been previously described.

The molecular structure of 5,5-dimethylbarbituric acid is very similar, in terms of bond distances and angles, to that in the

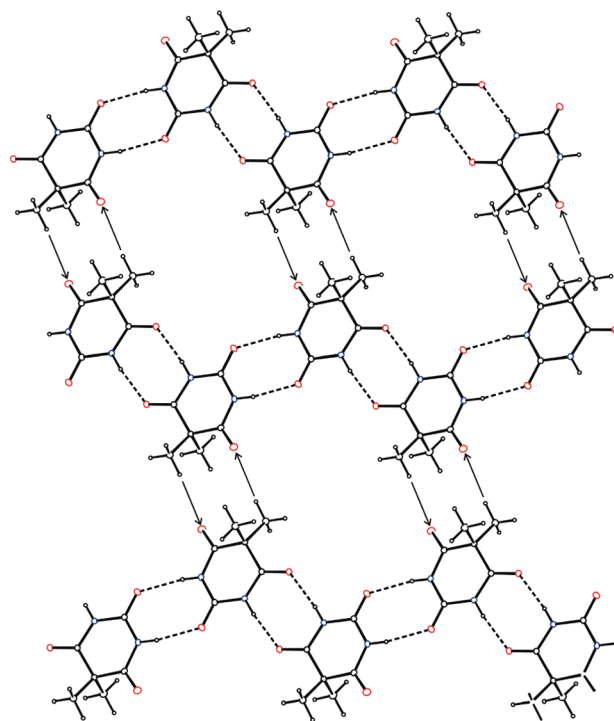


Figure 4. 2-D structure showing the linkage of the tapes through C–H···O=C contacts (arrows represent the hydrogen contacts: C8–H8a···O3(−*x*, 1 − *y*, −*z*): 3.533(8), 2.62 Å for the C8···O3 and H8a distances and 160° for the C8–H8a···O3 angle).

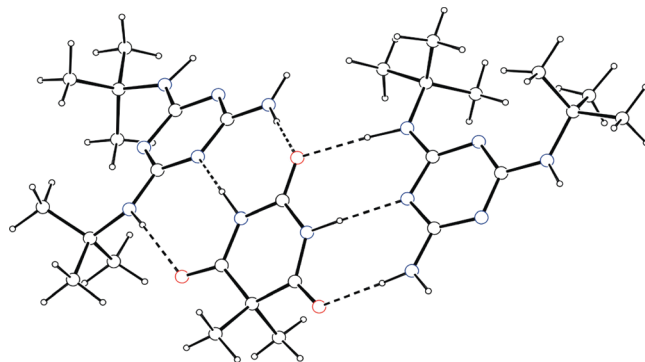


Figure 5. 1-D supramolecular structure of *N,N'*-di(*tert*-butyl)melamine (CSD refcode PIYDUW) showing the triad of hydrogen bonds between the two components of the molecular complex.

molecular complexes but differs in the puckering of the ring although all of them present a slightly distorted envelope conformation flapping at C5 (Table 7).

The geometry of 5,5-dimethylbarbituric acid monomer optimized at MP2(FULL)/6-31G(*d*) level agrees with the experimental results as shown in Table 7, while the optimization at MP2(Full)/6-31G(3*df*,2*p*) (see Table 7), B3LYP/6-31G(*d*), B3LYP/6-31+G(*d,p*), and B3LYP/6-31++G(*d*) levels results in planar molecules.

The crystal structure is mainly dominated by N–H···O=C intermolecular hydrogen bonds. Each molecule is connected by pairs of centrosymmetric hydrogen bonds to two neighboring molecules, forming a wavy tape with C₂²(10)[R₂²(8)] graph set notation⁵⁷ and leaving one keto group (O3) free of this type of interaction (Figure 3). However, this group is involved in weak C8–H8a···O3(−*x*, 1 − *y*, −*z*) and C7–H7c···O3(*x* + 1, *y* − 1, *z*) interactions, the first responsible for formation of sheets (Figure 4) and the second for the cohesion of them (3.533(8)/3.630(4), 2.62/2.71 Å for the C8/C7···O3 and H8a/

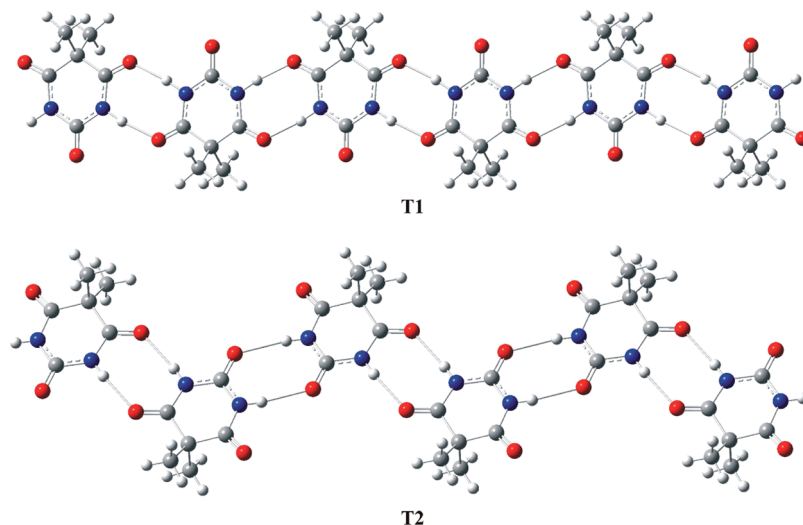


Figure 6. Optimized 1D hydrogen-bonding motifs.

7c...O3 distances and 160/162° for the angle at the H8a/H7c atoms, respectively). This 1-D supramolecular motif has been revealed as the most common association displayed by alkyl-barbituric acid derivatives (see T2 mode in Figure 6).¹⁸

In the molecular complexes,^{55,56} with a balanced donor/acceptor ratio of hydrogen bonds, a triad of hydrogen bonds (two N–H...O and one N–H...N bonds) involving all C=O groups in the 5,5-dimethylbarbituric acid molecule link alternatively the two components of the complex into tapes (Figure 5).

As the donor/acceptor ratio < 1, two types of 1D H-bonded assemblies enabling double H-bonding interactions can be expected depending on the carbonyl group not involved in the hydrogen bonding pattern (labeled T1 and T2 in Figure 6) analogous to those for previously reported motifs¹⁸ for alkyl-barbituric acid derivatives.

The two computational models (T1 and T2), six molecules each, have been optimized at B3LYP/6-31G(*d*), B3LYP/6-31+G(*d,p*), and B3LYP/6-31++G(*d*) levels of calculation. The T1 motif was obtained to have lower energy than T2 by 2.1 kcal mol^{−1} in the first case with reverse results by 0.6 and 0.4 kcal mol^{−1} for the second and third levels of calculation as found previously for barbituric acid itself.¹⁸ Two general trends can be observed among the different levels of calculation: (1) the optimization of monomer and supramolecular motifs predict planar and almost planar six-membered rings instead of an envelope conformation as at the MP2(Full)/6-31G(*d*) level and as observed by X-ray analysis (Table 7); (2) hydrogen bonding causes N–H and C=O bond lengthening whereas the C–N bonds directly involved in the intermolecular interactions (N1–C6, N3–C4 in T1 and N1–C2, N3–C4 in T2) increases its partial double-bond character as illustrated in the Supporting Information.

Supporting Information Available: Additional information and crystallographic data (CIF file) has been deposited with the Cambridge Crystallographic Data CCDC 753388. This material is available free of charge via the Internet at <http://pubs.acs.org>

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