

Experimental and Computational Thermochemical Study of 2-Thiobarbituric Acid: Structure–Energy Relationship

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ABSTRACT: This paper reports an experimental and computational thermochemical study on 2-thiobarbituric acid (2-thioxodihydropyrimidine-4,6(1*H*,5*H*)-dione), [CAS 504-17-6]. The value of the standard ($p^0 = 0.1$ MPa) molar enthalpy of formation in the gas phase at $T = 298.15$ K has been determined. The energy of combustion was measured by bomb combustion calorimetry, using a rotatory bomb, and from the result obtained, the standard molar enthalpy of formation in the crystalline state at $T = 298.15$ K was calculated as $-(396.8 \pm 0.9)$ kJ·mol⁻¹. The enthalpy of sublimation was determined using a transference (transpiration) method in a saturated N₂ stream and a value of the enthalpy of sublimation at $T = 298.15$ K was derived as (118.3 ± 2.2) kJ·mol⁻¹. From these results a value of $-(278.5 \pm 2.4)$ kJ·mol⁻¹ for the gas-phase enthalpy of formation at $T = 298.15$ K was determined. Theoretical calculations at the G3 and G4 levels were performed, and a study of the molecular and electronic structure of the compound has been carried out. Calculated enthalpies of formation are in very good agreement with the experimental value.



1. INTRODUCTION

Thermodynamic data such as the enthalpy of formation, symbolized $\Delta_f H^\circ_m$, offer a powerful tool for the understanding of the relative importance of steric, electrostatic, and stereoelectronic interactions that are responsible for the contrasting structural, conformational, and reactivity trends exhibited by oxygen- and sulfur-containing six-membered heterocycles.¹ In this regard, comparison of the enthalpies of formation of related compounds is particularly useful because it reveals their relative stability, as a consequence of the stabilizing and repulsive interactions of interest. On the other hand, quantum chemistry is valuable in the *ab initio* prediction of both molecular structure and energetics.² Comparison between enthalpies of formation in the gas state determined from calorimetric experiments and computational methods, from an optimized structure, represents a powerful tool for the study of the correlation between structure and the energetics of molecules.

Over the past few years, we have been involved in the systematic thermochemical study of selected oxygen and sulfur five- and six-membered heterocycles. The fundamental interest of our work is to develop an understanding of structural effects on thermodynamic stabilities that are reflected in the gas-phase enthalpies of formation of the compounds studied and on the influence of steric, electrostatic, and stereoelectronic interactions produced by substituents on the thermochemical properties on these molecules.

We are presently involved in the study of the thermochemistry of barbituric acid (2,4,6(1*H*,3*H*,5*H*)-pyrimidinetrione) and its derivatives. 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 acid

derivatives,^{3–6} reliable experimental thermochemical studies in literature are scarce.⁷ We have recently published thermochemical studies of the parent compound barbituric acid⁷ and its 5,5-dimethyl,⁸ 1,3-dimethyl,⁹ and 5,5-diethyl (barbital) derivatives.^{10,11} We have also reported thermophysical studies of 2-thiobarbituric acid¹² and some methyl and ethyl derivatives of barbituric acid.¹³

The aim of the present work is to study the energy–structure relationship of 2-thiobarbituric acid (2-thioxodihydropyrimidine-4,6(1*H*,5*H*)-dione) **1**, whose schematic formula is presented in Figure 1. As for barbituric acid, several substituted

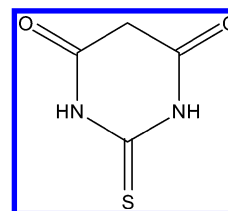


Figure 1. Schematic formula of 2-thiobarbituric acid, **1**.

2-thiobarbituric acids have long been used for their pharmaceutical properties.¹⁴ This compound also has corrosion inhibition properties,¹⁵ and it is an important compound in biological chemistry and medicine.

2-Thiobarbituric acid has been previously investigated¹⁶ by single crystal X-ray diffraction, 1D and 2D (¹H, ¹³C, and ¹⁵N)

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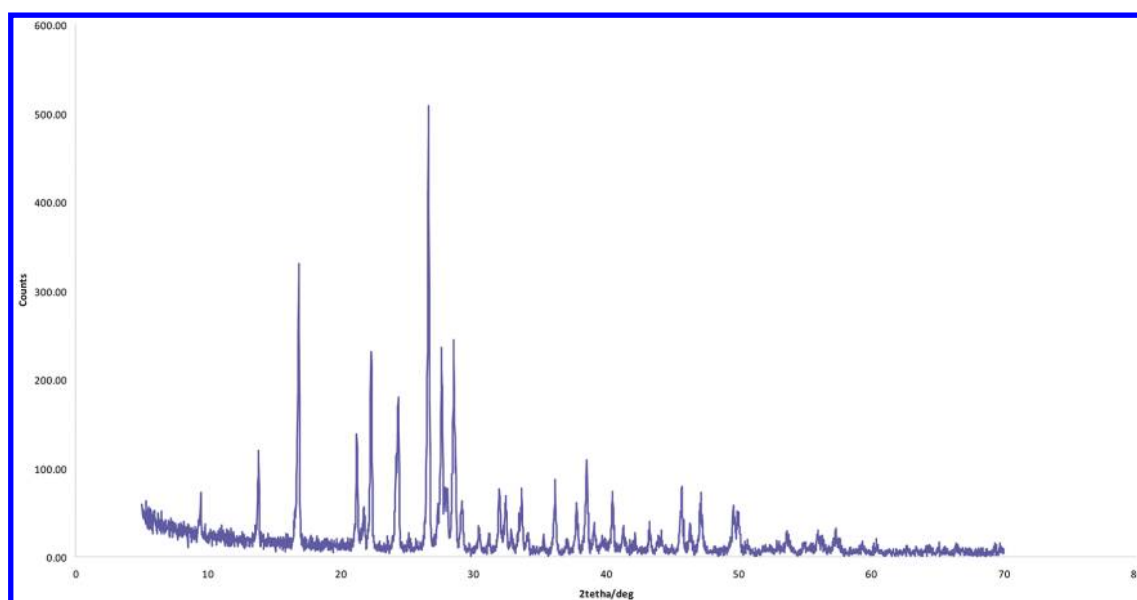


Figure 2. Powder X-ray diffraction analysis of 2-thiobarbituric acid (x -axis = $2\theta/\text{deg}$).

solid-state NMR spectroscopy, Raman spectroscopy, and X-ray powder diffraction at various temperatures and by differential scanning calorimetry (DSC). The compound is known to exist in various tautomeric and polymorphic forms, all of which are converted to the structure shown in Figure 1 upon heating.¹⁶

2. EXPERIMENTAL PROCEDURES

2.1. Material and Purity Control. 2-Thiobarbituric acid [CAS 504-17-6] was commercially available from Fluka. The sample was carefully dried under vacuum and no further purification was needed to be performed. Determination of purity, assessed by HPLC and differential scanning calorimetry (DSC) using the fractional fusion technique,¹⁷ indicated that the mole fraction of impurities in the compound was less than 0.0002.

2.2. X-ray Diffraction Studies. Powder X-ray diffraction analysis (PXRD hereinafter) was used to identify the polymorphic forms of the commercial sample. The powder patterns for the compound was collected on a PANalytical XPert PRO MPD powder diffractometer (Cu K α). The powder pattern of the commercial sample of 2-thiobarbituric acid is provided in Figure 2.

Based on the comparison with a previous work of Chierotti et al.,¹⁶ the tautomeric form of the commercial sample of 2-thiobarbituric acid used in this work is given as the 4-keto-2-thione-6-hydroxy tautomer (**2**, Figure 3). This converts to **1** at about $T = 463\text{ K}$.¹²

2.3. Procedure for Thermochemical Measurements.

2.3.1. Differential Scanning Calorimetry. The behavior of the

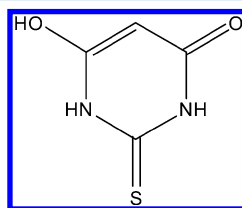


Figure 3. Tautomeric form of commercial 2-thiobarbituric acid, at $T = 298.15\text{ K}$, **2**.

sample of 2-thiobarbituric acid as a function of temperature was studied by differential scanning calorimetry. A DSC Pyris 1 instrument from Perkin-Elmer equipped with an intracooler unit was used to study the possible existence of phase transitions in the temperature interval (from $T = 253$ to 443 K), where the thermochemical measurements were done and no transitions in the solid state were observed.

2.3.2. Rotating-Bomb Combustion Calorimetry. For the measurement of the energies of combustion, a calorimetric system with a constant-temperature jacket and a rotating bomb was used. This system was originally developed by S. Sunner at the University of Lund, Sweden.¹⁸ The device was manufactured in Lund in the seventies of the last century and after successful work at the University of Freiburg, Germany (Prof. C. Rüchardt and Dr. H.-D. Beckhaus), it was modified at the University of Rostock in our working group. We have improved the temperature maintaining control unit, the ignition circuit and updated the data acquisition system.¹⁹ The isothermal jacket consists of a thermostatted bath with a cavity of exactly the same shape as the calorimeter. Water in the jacket is stirred and a pump circulates water through the thermostatted lid. The water jacket is maintained at a constant temperature of $T = (298.150 \pm 0.003)\text{ K}$. The calorimeter can is suspended in the jacket well and consists of a stainless-steel vessel containing a weighted amount of water and a closely fitting cover, a stirrer of the water, an electric heater, and the mechanism for bomb rotation. The bomb can be rotated simultaneously axially and end-overend. The stainless-steel combustion bomb has an internal volume of 0.2511 dm^3 and a wall thickness of about 1 cm . The bomb is completely lined with platinum. All the internal fittings, electrodes, and crucible are fabricated from platinum. Calorimetric temperatures were measured to within $\pm 1 \times 10^{-5}\text{ K}$ by means of Hart Scientific 1006 Micro-Therm with the measuring time interval of 100 s . The bomb, which initially contains air at atmospheric pressure and 10 cm^3 of water, is assembled and charged with oxygen to a total pressure of $p = 3.0\text{ MPa}$ at $T = 293.15\text{ K}$ without previous flushing. This is the usual technique for the combustion experiments with compounds containing sulfur.¹⁹

Solid samples were pelleted before combustion. For mass determinations a Mettler AT-21 microbalance with the certified reproducibility 2×10^{-6} g was used. The initial temperature of the combustion experiment was chosen to reach a final temperature close to $T = 298.15$ K. The energy of reaction was always referred to the final temperature, $T = 298.15$ K. Combustion is initiated by an electrical device connected to the computer which automatically fires the ignition circuit at the programmed time. The initial, main, and final periods were about 22 min. Rotation of the bomb was started 2 min after ignition and was ended after 12 min of rotation. The energy equivalent of the calorimeter $\varepsilon_{\text{calor}} = (25045.6 \pm 1.6) \text{ J} \cdot \text{K}^{-1}$ was determined using benzoic acid (NIST standard reference sample 39j with the certified massic energy of combustion $\Delta_c u = -(26434 \pm 3) \text{ J} \cdot \text{g}^{-1}$) under the same conditions in which the experiments were done with rotation and 10 cm^3 water added to the bomb.

After completion of the combustion experiments, the bomb was discharged and the liquid content of the bomb quantitatively transferred into a volumetric flask together with the rinsing water and diluted to a volume of 250 cm^3 . An aliquot of 25 cm^3 of the bomb solution was boiled for 5 min to remove the dissolved carbon dioxide, and the solution titrated with the $0.1 \text{ mol} \cdot \text{dm}^{-3}$ NaOH (aq) to determine the total amount of acid. The quantity of nitric acid was taken as the difference between the total acid and the theoretical quantity of sulfuric acid calculated from the mass of sample. The correction for energy of formation of the nitric acid from $\text{N}_2(\text{g})$, $\text{O}_2(\text{g})$, and $\text{H}_2\text{O}(\text{l})$ was based on the value of $-59.7 \text{ kJ} \cdot \text{mol}^{-1}$ for the molar internal energy of formation of $0.1 \text{ mol} \cdot \text{dm}^{-3}$ HNO_3 (aq).²⁰ The combustion products were examined for carbon monoxide and SO_2 (Dräger tube, mass fraction sensitivity of $\approx 1 \times 10^{-6}$) and unburned carbon, but none was detected. Such experiments, where even small traces of soot were observed, were rejected. The sample masses were reduced to vacuum, using the densities of the sample and auxiliary compounds (Table 1).

Table 1. Formula, Density ρ ($T = 293 \text{ K}$), Massic Heat Capacity C_p ($T = 298.15 \text{ K}$), and Expansion Coefficients $(\delta V/\delta T)_p$ of the Materials Used in the Present Study

compounds	formula	ρ ($\text{g} \cdot \text{cm}^{-3}$)	C_p^a ($\text{J} \cdot \text{K}^{-1} \text{ g}^{-1}$)	$10^{-6} \cdot (\delta V/\delta T)_p^b$ ($\text{dm}^3 \cdot \text{K}^{-1}$)
2-thiobarbituric acid	$\text{C}_4\text{H}_4\text{SO}_2\text{N}_2$	1.61 ^c	0.952 ^d	0.1
cotton ^e	$\text{CH}_{1.774}\text{O}_{0.887}$	1.500	1.67	0.1

^aFrom dsc measurements. ^bEstimated. ^cFrom ref 21. ^dFrom dsc measurements, ref 17. ^eFrom 10 combustion experiments, $\Delta_c u^\circ = -(16945.2 \pm 4.2) \text{ J} \cdot \text{g}^{-1}$.

The atomic weights used were those recommended by the IUPAC Commission in 2009.²² For converting the energy of the actual combustion process to that of the isothermal process and reducing to standard states, the conventional procedure was applied.²³

A second standard material is generally used in combustion calorimetry to verify the chemistry of the combustion process and to control accuracy of the energy corrections involved into the data treatment. Thianthrene is commonly proposed as the reference material for combustion calorimetry of sulfur-containing compounds.²⁴ We used a sample of thianthrene (NIST standard reference sample SRM 1656) to check our

experimental and calculation procedures.¹⁹ The experimental value for thianthrene $\Delta_c u^\circ = -(33470.3 \pm 2.3) \text{ J} \cdot \text{g}^{-1}$ perfectly agrees with the recommended value, $\Delta_c u^\circ = -(33468 \pm 4) \text{ J} \cdot \text{g}^{-1}$.²⁴ Such a good agreement was an evidence that the calibration procedure as well as the system of corrections applied for calculation of combustion energy were comprised properly.

2.3.3. Vapor Pressure Measurements. Vapor pressures and enthalpy of sublimation, $\Delta_{\text{cr}}^\circ H_m$, of 2-thiobarbituric acid were determined using the method of transference in a saturated stream of nitrogen. The method has been described in detail before^{25,26} and has proven to give results in agreement with other established techniques. The temperature dependence of the vapor pressures was used to determine the enthalpies of sublimation of the pure substances. A sample of approximately 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 film bubble flow meter (± 0.2 – 0.3%) and optimized to reach the saturation equilibrium of the transporting gas at each temperature under study. We tested our apparatus at different flow rates of the 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 flow rates down to $0.5 \text{ dm}^3 \cdot \text{h}^{-1}$. The upper limit for our apparatus was a flow rate of $10.5 \text{ dm}^3 \cdot \text{h}^{-1}$. Thus, we carried out the experiments in the using flow rates ranging about $5 \text{ dm}^3 \cdot \text{h}^{-1}$, which ensured that transporting gas was in saturated equilibrium with the coexisting solid phase in the saturation tube. The material transported was condensed in a cold 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 when applied to the nitrogen stream saturated with the substance i of interest is valid, values of p_i^{sat} were calculated:

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

where $R = 8.31447 \text{ J} \cdot \text{K}^{-1} \cdot \text{mol}^{-1}$, 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_{N_2} 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_{N_2} , was determined from the flow rate and time measurements.

2.4. Computational Details. Standard ab initio molecular orbital calculations were performed with the Gaussian 09²⁷ series of programs. The energy of the compound studied was calculated²⁸ using Gaussian-n theory at the G3²⁹ and G4³⁰ levels.

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. 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

Table 2. Results for Combustion Experiments at $T = 298.15$ K ($p^\circ = 0.1$ MPa) of the 2-Thiobarbituric Acid^a

	expt 1	expt 2	expt 3	expt 4	expt 5	expt 6
$m(\text{substance})/\text{g}^b$	0.813017	1.007702	0.850196	0.714645	0.707561	0.749168
$m(\text{cotton})/\text{g}^b$	0.001063	0.001111	0.000829	0.000885	0.000984	0.000862
$\Delta T_c/\text{K}^c$	0.530647	0.657796	0.553521	0.466759	0.462208	0.488592
$(\epsilon_{\text{calor}}) \cdot (-\Delta T_c)/\text{J}^d$	-13290.2	-16474.7	-13863.1	-11690.1	-11576.1	-12236.9
$(\epsilon_{\text{cont}}) \cdot (-\Delta T_c)/\text{J}^d$	-28.11	-34.42	-29.10	-24.29	-23.69	-24.96
$\Delta U_{\text{decomp}} \text{HNO}_3/\text{J}$	37.0	48.3	9.8	38.5	35.4	26.3
$\Delta U_{\text{dil}} \text{H}_2\text{SO}_4/\text{J}$	-0.69	-2.83	-1.06	-0.10	-0.05	-0.31
$\Delta U_{\text{corr}}/\text{J}^e$	12.59	13.35	13.09	11.62	11.59	12.09
$-m' \cdot \Delta_c u'/\text{J}$	18.01	18.82	14.04	14.99	16.67	14.60
$\Delta_c u^\circ(\text{cr})/(\text{J} \cdot \text{g}^{-1})$	-16298.2	-16303.1	-16296.6	-16300.8	-16304.1	-16296.6

^aFor the definition of the symbols see ref 23, macrocalorimeter: $T_h = 298.15$ K; $V(\text{bomb}) = 0.2511$ dm³; $p^i(\text{gas}) = 3.00$ MPa; $m^i(\text{H}_2\text{O}) = 10.00$ g. ^bMasses obtained from apparent masses. ^c $\Delta T_c = T^f - T^i + \Delta T_{\text{corr}}$; $(\epsilon_{\text{cont}}) \cdot (-\Delta T_c) = (\epsilon_{\text{cont}}^f) \cdot (T^f - 298.15 \text{ K}) + (\epsilon_{\text{cont}}^i) \cdot (298.15 \text{ K} - T^i + \Delta T_{\text{corr}})$. ^d $\epsilon = 25045.07 \pm 3.0$ J/K. ^e ΔU_{corr} , the correction to standard states, is the sum of items 81–85, 87–90, 93, and 94 in ref 23.

accommodate remaining deficiencies, and spin–orbit correction for atomic species only.²⁹

G4 is the more recent⁴¹ theory developed in the Gaussian-n theories. The G4 theory modifies the G3 theory in five ways, including (a) an extrapolation procedure to obtain the Hartree–Fock limit for inclusion in the total energy calculation, (b) an increase in the d -polarization sets to $3d$ on the first-row atoms and to $4d$ on the second-row atoms, with reoptimization of the exponents for the $4d$ set, (c) the replacement of the QCISD(T) method by CCSD(T), (d) geometries and zero-point energies obtained at the B3LYP/6-31G(2df,p) level, and (e) two new higher level correction parameters to account for deficiencies in radicals and in species having only one electron pair in the valence space.³⁰

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. The charge distribution has been analyzed using a population partition technique, the natural bond orbital (NBO) analysis of Reed and Weinhold.^{31–33} The NBO analysis has been performed using the NBO program³⁴ implemented in the Gaussian 09 package.²⁷

3. RESULTS AND DISCUSSION

3.1. Experimental Results. Results of the combustion experiments with 2-thiobarbituric acids are given in Table 2. The values of $\Delta_c u^\circ$ refer to the general idealized reaction

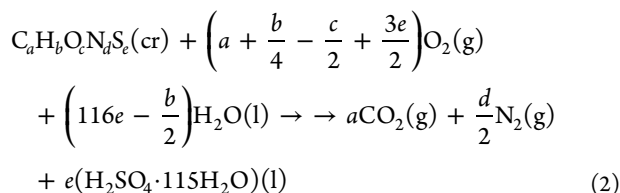


Table 3 lists the specific energy of combustion, $\Delta_c u^\circ(\text{cr})$, and the derived standard molar enthalpies of combustion, $\Delta_c H_m^\circ$, and formation, $\Delta_f H_m^\circ$, in the crystalline state at $T = 298.15$ K.

The total uncertainty of $\Delta_f H_m^\circ(\text{cr})$ was calculated according to the guidelines presented by Olofsson.³⁵ The uncertainty assigned to $\Delta_f H_m^\circ(\text{cr})$ is twice the overall standard deviation

Table 3. Thermochemical data at $T = 298.15$ K ($p^\circ = 0.1$ MPa) for 2-thiobarbituric acid

$\Delta_c u^\circ(\text{cr})/\text{J} \cdot \text{g}^{-1}$	$\Delta_c H_m^\circ(\text{cr})/\text{kJ} \cdot \text{mol}^{-1}$	$\Delta_f H_m^\circ(\text{cr})/\text{kJ} \cdot \text{mol}^{-1}$
-16299.9 ± 1.3	-2350.9 ± 0.8	-396.8 ± 0.9

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 , CO_2 , and H_2SO_4 in 115 $\text{H}_2\text{O}(\text{l})$. To derive $\Delta_f H_m^\circ(\text{cr})$ from $\Delta_c H_m^\circ$, at $T = 298.15$ K, the standard molar enthalpies of formation of $\text{H}_2\text{O}(\text{l})$, $-(285.830 \pm 0.042)$ kJ·mol⁻¹,³⁶ $\text{CO}_2(\text{g})$, $-(393.51 \pm 0.13)$ kJ·mol⁻¹,³⁶ and H_2SO_4 in 115 $\text{H}_2\text{O}(\text{l})$, $-(887.81 \pm 0.42)$ kJ·mol⁻¹,²⁰ were used.

Enthalpy of Sublimation. The temperature dependency of the vapor pressures of barbituric acid derivatives have not been reported in the literature previously. Our experimental vapor pressures have been measured between 411.6 and 442.2 K (see Table 4).

Table 4. Results from Measurements of the Vapor Pressure p of 2-Thiobarbituric Acid Using the Transpiration Method

T^a (K)	m^b (mg)	$V_{(\text{N}_2)}^c$ (dm ³)	gas flow (dm ³ /h)	p^d (Pa)	$(p_{\text{exp}} - p_{\text{calc}})$ (Pa)	$\Delta_c H_m^\circ$ (kJ·mol ⁻¹)
2-thiobarbituric acid $\Delta_c H_m^\circ(298.15 \text{ K}) = (118.3 \pm 2.2)$ kJ·mol ⁻¹						
$\ln(p/\text{Pa}) = \frac{312.62}{R} - \frac{125512.97}{R \cdot (T, \text{K})} - \frac{21.4}{R} \ln\left(\frac{T, \text{K}}{298.15}\right)$						
411.6	15.3	244.2	5.3	1.07	-0.03	115.84
416.8	12.4	127.4	5.3	1.66	-0.02	115.73
421.9	36.6	238.0	5.3	2.62	0.11	115.62
427.0	20.2	94.4	5.3	3.65	-0.07	115.51
432.0	40.4	121.2	5.3	5.69	0.26	115.40
437.0	10.4	22.4	5.3	7.92	0.08	115.29
442.2	10.2	16.0	5.3	10.87	-0.51	115.18

^aTemperature of saturation. ^bMass of transferred sample. condensed at $T = 293$ K. ^cVolume of nitrogen. used to transfer mass m of sample. ^dVapor pressure at temperature T calculated from m and the residual vapor pressure at the cooling temperature $T = 293$ K.

The following equation:

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

was fitted 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 in this case is 298.15 K). Consequently, from eq 3 the expression for the vaporization enthalpy at temperature T is

$$\Delta_{\text{cr}}^\circ H_m(T) = -b + \Delta_{\text{cr}}^\circ C_p \cdot T \quad (4)$$

A value of $\Delta_{\text{cr}}^{\text{g}}C_p = 21.4 \text{ J}\cdot\text{mol}^{-1}\cdot\text{K}^{-1}$ has been derived from the experimental isobaric molar heat capacity of solid 2-thiobarbituric acid $C_p^{\text{cr}} = 137.6 \text{ J}\cdot\text{mol}^{-1}\cdot\text{K}^{-1}$, according to the procedure developed by Chickos.³⁷ Experimental results, and parameters a and b are listed in Table 4.

Table 5 summarizes the values of the standard molar enthalpy of combustion, $\Delta_{\text{c}}H_{\text{m}}^{\circ}(\text{cr})$, sublimation, $\Delta_{\text{cr}}^{\text{g}}H_{\text{m}}^{\circ}$, and

Table 5. Experimentally Determined Thermodynamic Quantities at $T = 298.15 \text{ K}$ for 2-Thiobarbituric Acid^a

$\Delta_{\text{c}}H_{\text{m}}^{\circ}(\text{cr})$	$\Delta_{\text{f}}H_{\text{m}}^{\circ}(\text{cr})$	$\Delta_{\text{cr}}^{\text{g}}H_{\text{m}}^{\circ}$	$\Delta_{\text{f}}H_{\text{m}}^{\circ}(\text{g})$
-2350.9 ± 0.8	-396.8 ± 0.9	118.3 ± 2.2	-278.5 ± 2.4

^aAll values in $\text{kJ}\cdot\text{mol}^{-1}$.

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

Brunetti and Piacente³⁸ measured vapor pressures and the sublimation enthalpy for 2-thiobarbituric acid, using the torsion method. Available vapor pressures are compared on the Figure 4. Surprisingly, a large spread of experimental data was

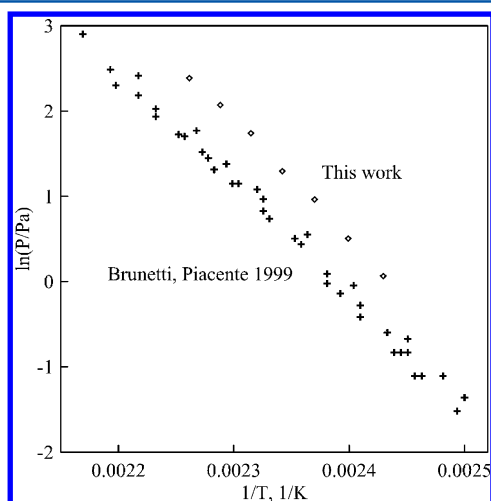


Figure 4. Comparison of vapor pressures of 2-thiobarbituric acid from the torsion method (Brunetti and Piacente³⁸) and the transpiration method (this work).

observed for data from torsion method in contrast to the clear linear dependence obtained from transpiration. The absolute vapor pressure values from torsion method were also systematically lower in comparison to the transpiration. Such a difference could appear due to possible error in calibration of the torsion apparatus. In contrast, the transpiration method does not need any calibration. In spite of the systematic shift of absolute vapor pressures the slopes of the both pressure temperature dependences (see Figure 4) were very similar. The slopes are responsible for sublimation enthalpy. Brunetti and Piacente³⁸ calculated a value of $\Delta_{\text{cr}}^{\text{g}}H_{\text{m}} = (110 \pm 4) \text{ kJ}\cdot\text{mol}^{-1}$ at 430 K . We adjusted their value to the reference temperature in the same way as our own result (see Table 5) and derived $\Delta_{\text{cr}}^{\text{g}}H_{\text{m}} = (113.3 \pm 4) \text{ kJ}\cdot\text{mol}^{-1}$ at 298 K , which is about $5 \text{ kJ}\cdot\text{mol}^{-1}$ lower than our own result (see Table 5), but due to the large uncertainties, the sublimation enthalpies from both methods are in acceptable agreement within the boundaries of experimental uncertainties.

3.2. Molecular and Electronic Structure. 2-Thiobarbituric acid contains three functional groups with mobile hydrogen

atoms, one CH_2 and two NH groups, and three potentially enolizable groups, two $\text{C}=\text{O}$ and one $\text{C}=\text{S}$, that allows the existence of a large number of tautomers. There are 10 possible tautomeric forms for 2-thiobarbituric acid whose stabilities have been studied computationally.^{39–41}

All the studies suggest that in the gas phase (and in nonpolar solutions) the 4,6-diketo-2-thione tautomer, **1**, is the most stable one, and the high energy differences from the other tautomers ($32\text{--}38 \text{ kJ}\cdot\text{mol}^{-1}$ lower than the second-most stable isomer, depending of the method of calculation used)⁴¹ suggest that the gas phase of 2-thiobarbituric acid consists of a single molecular species, in agreement with thermodynamic experimental data.³⁸

The first reported²¹ crystal structure of 2-thiobarbituric acid (monoclinic system, space group $P2_1/c$), characterized by the presence of 4,6-diketo-2-thione tautomer (**1**, Figure 1) conflicts with solid-state IR spectroscopic studies⁴¹ that indicate the presence of the 4-keto-2-thione-6-hydroxy tautomer (**2**, Figure 3). Very recently, Chierotti et al.¹⁶ have identified new polymorphs where the 2-thiobarbituric molecules are present in the enol form and another one where a 50:50 ordered mixture of enol/keto tautomers are present. In methanol solution (and in other polar solvents), there is an equilibrium⁴¹ between both tautomers, confirmed by NMR spectroscopy.⁴² This behavior in the solid state and in polar solutions is different to that observed in barbituric acid where the triketo form is the most stable one in the solid, gas, and solution phases.⁷

The MP2(Full)/6-31G(3df,2p)-optimized structure of 2-thiobarbituric acid is shown in Figure 5. The heavy atom

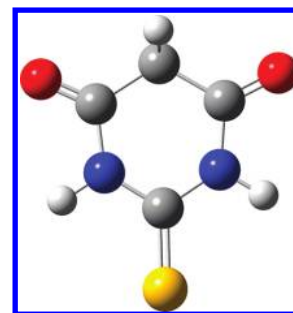


Figure 5. MP2(Full)/6-31G(3df,2p)-optimized structure of 2-thiobarbituric acid.

skeleton is fully planar at this level of calculation and the molecule possess C_{2v} symmetry. The calculated bond lengths and angles are in good agreement with those of 2-thiobarbituric acid (polymorph II), as determined¹⁶ by X-ray diffraction (CSD refcode THBARB01).⁴³ The experimental crystal structure is not fully planar but has an envelope conformation (the angle between CCC and NCN planes is 8°).

Atomic charges have been calculated by the natural bond orbital (NBO) population analysis scheme. Positive charge is located at C atoms of the carbonyl groups (0.850) and in C_2 atom (0.340), whereas a negative charge is located at N atoms (-0.749), O atoms (-0.664), S atom (-0.129), and in the C_5 atom (-0.641). By comparing the net charges in barbituric⁷ and 2-thiobarbituric acids, one sees that $\text{C}=\text{S}$ bond in 2-thiobarbituric acid is much less polar (0.469) than $\text{C}=\text{O}$ bond (1.710) in barbituric acid, and the N atoms in 2-thiobarbituric acid show a negative charge slightly smaller than in barbituric acid (-0.749 vs -0.785). Given that the charges of the

remaining atoms are practically the same in the two acids, one is induced to think⁴⁰ that crystalline forces push the molecules to approach each other so much that enolization occurs in order to gain energy through formation of intermolecular hydrogen bonding.

3.3. Theoretical Determination of the Enthalpy of Formation. The standard procedure in obtaining enthalpies of formation in Gaussian-n theories is through atomization reactions.^{44,45} The enthalpy of formation of 2-thiobarbituric acid, calculated at the G3 and G4 levels of theory, has the same value, $-280.2 \text{ kJ}\cdot\text{mol}^{-1}$. This value is in very good agreement with the experimental value measured in this work, $-(278.5 \pm 2.4) \text{ kJ}\cdot\text{mol}^{-1}$.

We have already discussed above that the experimental enthalpy of sublimation of thiobarbituric acid measured by torsion method³⁸ and adjusted to 298.15 K was about $5 \text{ kJ}\cdot\text{mol}^{-1}$ lower than those determined in this work. Nevertheless, the results from quantum chemistry matched better to the experimental $\Delta_f H_m^\circ(\text{g})$ if the enthalpy of sublimation from the transpiration was used. Indeed, the enthalpies of formation of 2-thiobarbituric acid, calculated at the G3 and G4 levels of theory, have the identical value of $-280.2 \text{ kJ}\cdot\text{mol}^{-1}$. This value is in very good agreement with the experimental value derived in this work, $-(278.5 \pm 2.4) \text{ kJ}\cdot\text{mol}^{-1}$, provided that we use the own $\Delta_{\text{cr}} H_m^\circ = (118.3 \pm 2.2) \text{ kJ}\cdot\text{mol}^{-1}$ (see Table S).

The difference between the experimental enthalpies of formation of barbituric⁷ and thiobarbituric acids, $255.8 \text{ kJ}\cdot\text{mol}^{-1}$, is similar to that observed⁴⁶ in other pairs of carbonyl/thiocarbonyl compounds: acetamide/thioacetamide ($251.0 \text{ kJ}\cdot\text{mol}^{-1}$), urea/thiourea ($258.4 \text{ kJ}\cdot\text{mol}^{-1}$), and tetramethylurea/tetramethylthiourea ($250.3 \text{ kJ}\cdot\text{mol}^{-1}$).

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Notes

The authors declare no competing financial interest.

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