2- and 3-Acetylpyrroles: A Combined Calorimetric and Computational Study

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A combined experimental and computational study on the thermochemistry of 2- and 3-acetylpyrroles was performed. The enthalpies of combustion and sublimation were measured by static bomb combustion calorimetry and Knudsen effusion mass-loss technique, respectively, and the standard ($p° = 0.1$ MPa) molar enthalpies of formation, in the gaseous phase, at $T = 298.15$ K, were determined. Additionally, the gas-phase enthalpies of formation were estimated by G3(MP2)//B3LYP calculations, using several gas-phase working reactions, and were compared with the experimental ones. N−H bond dissociation enthalpies, gas-phase acidities and basicities, proton and electron affinities and ionization enthalpies were also calculated. Experimental and theoretical results are in good agreement and show that 2-acetylpyrrole is thermodynamically more stable than the 3-isomer. The substituent effects of the acetyl group in pyrrole, thiophene and pyridine rings were also analyzed.

1. Introduction

Pyrrole and its derivatives have been receiving great attention due to the growing abundance of pyrrolic components in natural products, pharmaceuticals, and new materials. They are important structural fragments used in the synthesis of drugs with high therapeutic potential, as Atorvastatine (Lipitor),[1] a pentasubstituted pyrrole, which is used for the treatment of high cholesterol and triglyceride levels, and Pyrrolnitrin,[2] a drug with high antifungal activity. Pyrrole is a very important biochemical material, being the major constituent of naturally occurring tetrapyrroles, including the porphyrins of heme, vitamin B_{12}, and chlorophyll, and so, they are usually called the pigments of life.[3] Pyrroles and derivatives show occurrence in food systems, and because of their organoleptic properties, some pyrroles are used as flavor additives.[4] Polymerization of pyrrole and its derivatives yields the polypyrroles, which are conducting polymers and, for that reason, also called pyrrole blacks; they found application in the area of new materials because of their chemical, thermal, and electrical stabilities, as well as easiness of preparation. They are used as battery materials, as pacifying layers for semiconductors, especially in photoelectrochemical solar cells, inhibiting photocorrosion, and as catalysts.[5]

With respect to applications of acetylpyrroles, 2-acetylpyrrole possesses hepatoprotective properties, showing liver-function-facilitating activity.[6] Moreover, it is a volatile compound naturally occurring in foods, like vegetables, bread, meat, and alcoholic and roasted products. It has a sweet, nutty, and tea-like odor and flavor, being applied in baked, fried, and roasted flavorings,[7] and its aroma is included in tobacco smoke[8] and in Japanese green tea.[9] Some pyrrole derivatives, including 2-acetylpyrrole, have been identified in sweet whey powder,[10] popcorn,[11] and coffee, showing a great antioxidant activity.[12,13] In Japan, several compounds, including 2- and 3-acetylpyrroles, are used as flavoring substances.[14]

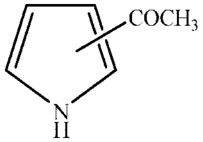

Figure 1. Structural formula of (2- or 3-) acetylpyrrole.

The intrinsic properties of the acetylpyrroles are directly connected with the structure and stability of these compounds. Therefore, it is not surprising to see that some attention of the scientific community has been given recently to these compounds. Camarillo et al. had presented a single-crystal X-ray study of 2-acetylpyrrole that established its molecular structure.[15] This molecule has a unit cell with a monoclinic crystal system and a space group $P2_1/c$. It forms centrosymmetric dimers in the solid state, through intermolecular N−H···O hydrogen bonds between amine and carbonyl groups.

The aim of the present work is to contribute to the better knowledge of the thermodynamic and thermochemical properties of the two title compounds, as well as to establish some relationships between structure, energetics, and reactivity. Thus, we present a detailed experimental and computational study on the energetics of the 2- and 3-acetylpyrroles, whose structural formulas are depicted in Figure 1. The standard ($p° = 0.1$ MPa) molar enthalpies of formation, in the crystalline state, of the two isomers, at $T = 298.15$ K, were derived from the standard massic energies of combustion, measured by static bomb calorimetry. The Knudsen mass-loss effusion technique was used to measure the vapor pressures as a function of temperature of the two crystalline compounds. From the temperature dependence of the vapor pressure, the molar enthalpies and entropies of sublimation, at the mean temperature of the experimental temperature range, were derived. Standard molar enthalpies, entropies, and Gibbs energies of sublimation, at the temperature of 298.15 K, were calculated using estimated values for the heat

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capacity differences between the gas and the crystal phases of each compound.

The standard ($p° = 0.1$ MPa) molar enthalpies of formation, in the gaseous phase, were derived from the experimental results and they were also estimated by G3(MP2)//B3LYP calculations, using several working reactions. This composite method has been also used to obtain values for other thermodynamic properties, namely N−H bond dissociation enthalpies, gas-phase acidities and basicities, proton and electron affinities, and ionization enthalpies, properties that are important for the description of several reaction mechanisms.

2. Experimental Section

2.1. Materials and Purity Control. Commercial samples of 2-acetylpyrrole [CAS 1072-83-9] and 3-acetylpyrrole [CAS 1072-82-8] were obtained from Alfa−Aesar, with massic fraction purities of 0.98 and 0.97, respectively. The two solids were purified by successive vacuum sublimations, and the purities were checked by gas−liquid chromatography and from the consistent results obtained after the combustion experiments, as well as by the closeness to unity of the carbon dioxide recovery ratios. The average ratios of the mass of the samples, together with the standard deviations of the mean were (1.000023 ± 0.000112) for 2-acetylpyrrole and (1.00029 ± 0.00017) for 3-acetylpyrrole. In the case of 2-acetylpyrrole, the specific density used to calculate the true mass from apparent mass in air was, $\rho = 1.224\ \mathrm{g \cdot cm^{-3}}$,[15] whereas for 3-acetylpyrrole the value used, $\rho = 1.106\ \mathrm{g \cdot cm^{-3}}$, was determined from the ratio mass/volume of a pellet of the compound (made in vacuum, with an applied pressure of $10^5\ \mathrm{kg \cdot cm^{-2}}$).

2.2. Combustion Calorimetry. The standard molar energies of combustion were measured in a static bomb calorimeter, equipped with a twin valve bomb (type 1108, Parr Instrument Company), made of stainless steel and with an internal volume of 0.342 $\mathrm{dm^3}$. The apparatus and technique have been previously described.[16,17]

The bomb used in the combustion experiments was calibrated with benzoic acid (NIST Thermochemical Standard 39j with a certified massic energy of combustion, under bomb conditions, of $-26434 \pm 3\ \mathrm{J \cdot g^{-1}}$),[18] following the procedure described by Coops et al.[19] From one set of six calibration experiments that were performed in oxygen atmosphere, at a pressure of 3.04 MPa and in the presence of 1.00 $\mathrm{cm^3}$ of deionized water placed in the bomb, the value of the energy equivalent of the calorimeter was found to be $\varepsilon(\mathrm{calor}) = 16\,012.8 \pm 1.1\ \mathrm{J \cdot K^{-1}}$, for an average mass of water added to the calorimeter of 3119.6 g; the quoted uncertainty is the standard deviation of the mean.

Solid samples of compounds were burned in pellet form, in oxygen, at a pressure $p = 3.04$ MPa, with 1.00 $\mathrm{cm^3}$ of deionized water added to the bomb. The calorimeter temperatures were measured to $\pm 1 \times 10^{-4}$ K, at time intervals of 10 s, with a quartz crystal thermometer (Hewlett Pachard HP 2804 A), interfaced to a PC. 100 Readings were taken for the fore, the mean, and the after periods and the program LABTERMO[20] was used for data acquisition, for control of the calorimeter temperature, and to compute the adiabatic temperature change. The electrical energy for the ignition was determined from the change in potential difference across a capacitor when discharged through the platinum ignition wire of diameter 0.05 mm. For the cotton thread fuse of empirical formula $\mathrm{CH_{1.686}O_{0.843}}$, $-\Delta_c u° = 16\,240\ \mathrm{J \cdot g^{-1}}$,[21] a value which has been previously confirmed in our laboratory. *n*-Hexadecane (Aldrich, mass fraction >0.999) stored under nitrogen was used as combustion auxiliary of the two compounds, with the purpose of avoiding carbon soot residue formation. Two different samples of *n*-hexadecane were used. For 2-acetylpyrrole, $\Delta_c u°(n\text{-hex}) = -47\,193.3 \pm 3.3\ \mathrm{J \cdot g^{-1}}$, and for the combustion of 3-acetylpyrrole, $\Delta_c u°(n\text{-hex}) = -47\,150.4 \pm 1.3\ \mathrm{J \cdot g^{-1}}$.

The energetic correction for the nitric acid formation, $\Delta U(\mathrm{HNO_3})$ was based on $-59.7\ \mathrm{kJ \cdot mol^{-1}}$ for the molar energy of formation of 0.1 $\mathrm{mol \cdot dm^{-3}}$ $\mathrm{HNO_3(aq)}$ from $\mathrm{N_2(g)}$, $\mathrm{O_2(g)}$, and $\mathrm{H_2O(l)}$.[22] The amount of compound, *m*(cpd), used in each experiment was determined from the total mass of carbon dioxide produced after allowance for that formed from the cotton thread fuse and *n*-hexadecane.

At $T = 298.15$ K, a pressure coefficient of specific energy, $(\partial u/\partial p)_T$, for these solids was assumed to be $-0.2\ \mathrm{J \cdot g^{-1} \cdot MPa^{-1}}$, a typical value for organic solids.[23] For each compound, $-\Delta_c u°$ was calculated by the procedure given by Hubbard et al.[24] The atomic weights used were those recommended by the IUPAC Commission in 2005.[25]

2.3. Knudsen Effusion Technique. The vapor pressures of the crystals, at several temperatures, were measured by the mass-loss Knudsen effusion technique.

Due to their low melting point, 2-acetylpyrrole was studied in an apparatus that enables work at temperatures under room temperature and the simultaneous operation of three Knudsen cells, each of them with three different effusion holes. This apparatus, which from now on will be referred as Knudsen-1, was already described in the literature.[26]

For the 3-acetylpyrrole compound, the vapor pressures were also measured at several temperatures using a Knudsen effusion apparatus which enables the simultaneous operation of nine aluminum effusion cells (Knudsen-2). A full description of the main features of the apparatus, as well as the measuring procedure and the technique have been reported before.[27] The nine effusion cells are placed in cylindrical holes inside three aluminum blocks, each one with three cells. Each block is maintained at a constant temperature, different from the other two blocks.

The measurements were extended through a selected temperature interval of ca. 20 K, chosen to correspond to measured vapor pressures in the range 0.1−1.0 Pa. The effusion cells were weighed before and after each experiment to determine the mass of sublimed compound, Δm, during a convenient effusion time period, *t*, in a system evacuated to a pressure near 1×10^{-4} Pa. The vapor pressure, *p*, at each temperature, *T*, of the experiment, was calculated by means of the equation

$$p = (\Delta m / A_o w_o t)(2\pi RT/M)^{1/2} \tag{1}$$

where A_o is the area of the effusion orifice, w_o is the respective Clausing factor, *R* is the gas constant, and *M* is the molar mass of the effusing vapor.

For 2-acetylpyrrole, studied with the Knudsen-1 apparatus, the thickness of the effusion holes was 0.0125 mm and their areas and Clausing factors were as follows: hole 1, $A_o/\mathrm{mm^2} = 0.5053$, $w_o = 0.989$; hole 2, $A_o/\mathrm{mm^2} = 0.7765$, $w_o = 0.991$; hole 3, $A_o/\mathrm{mm^2} = 1.1370$, $w_o = 0.992$. For the Knudsen-2 apparatus, the areas and Clausing factors of the effusion orifices, made in platinum foil of 0.0125 mm thickness, are presented in the Supporting Information, Table S1.

3. Computational Details

The composite G3(MP2)//B3LYP method was used to estimate the enthalpy of formation of the two title acetylpyrroles.[28] This method is composed by a series of separately performed standard ab initio calculations with the aim of introducing successive corrections to the energy, initially calculated at a less expensive computational approach. First, the B3LYP/6-31G(d) approach is used for the full-optimization and the calculation of the frequencies of the molecule. Then, for the previously optimized geometries, two additional calculations are performed at higher levels of theory (QCISD(T)/6-31G(d) and MP2/GTMP2Large) with the aim of diminishing errors of the initial B3LYP/6-31G(d) energy, correcting correlation and basis set deficiencies. The energies (with added zero-point vibrational energies scaled by 0.96 as usual with the G3(MP2)//B3LYP method) computed by this composite method, at $T = 0$ K, are corrected for $T = 298.15$ K by introducing the vibrational, translational, rotational and the pV terms computed at the B3LYP/6-31G(d) level. Finally, the enthalpies of formation, in the gaseous phase, for the 2- and 3-acetylpyrroles, were estimated through their atomization reactions as used with standard Gaussian-N theories, as well as by using a set of working reactions involving auxiliary molecules, whose thermochemical properties are well established experimentally.

This approach was also used to compute the cationic, anionic and radical species obtained from the two neutral 2- and 3-acetylpyrroles in order to estimate their N−H bond dissociation enthalpies, gas-phase acidities and basicities, proton and electron affinities, and ionization enthalpies. It is worth pointing out here that following conventions, gas-phase proton affinity (PA) and electron affinity (EA), were calculated as

$$A + H^+ \rightarrow AH^+ \qquad PA = -\Delta H_r \tag{2}$$

$$A + e^- \rightarrow A^- \qquad EA = -\Delta H_r \tag{3}$$

where A can be pyrrole, 2-acetylpyrrole, or 3-acetylpyrrole. Additionally, for comparison purposes, calculations were also performed with the B3LYP and MP2 methods together with the 6-311+G(2d,2p) basis set (the ZPVE were not scaled in these two cases).

All calculations have been performed by means of the Gaussian 03 computer code.[29]

4. Results and Discussion

4.1. Experimental Thermochemistry. Results for one combustion experiment of each compound are given in Table 1: $\Delta m(H_2O)$ is the deviation of the mass of water added to the calorimeter from 3119.6 g, ΔU_Σ is the correction to the standard state (Washburn corrections), and the other symbols have been previously defined.[24,30]

The internal energy for the isothermal bomb process, ΔU(IBP), was calculated through eq 4:

$$\Delta U(\mathrm{IBP}) = -\{\varepsilon(\mathrm{calor}) + c_p(H_2O, l)\,\Delta m(H_2O) + \varepsilon_f\}\Delta T_{ad} + \Delta U(\mathrm{ign}) \tag{4}$$

where ΔT_{ad} is the calorimeter temperature change corrected for the heat exchange and the work of stirring. Detailed results of each combustion experiment, for the studied compounds, are given in the Supporting Information, Tables S2 and S3.

TABLE 1: Typical Combustion Results, at $T = 298.15$ K, ($p° = 0.1$ MPa), for the Studied Compounds[a]

	2-acetylpyrrole	3-acetylpyrrole
$m(CO_2$, total)/g	1.89927	1.61618
m(cpd)/g	0.44344	0.33601
m'(fuse)/g	0.00240	0.00299
m''(n-hex)/g	0.26447	0.25672
ΔT_{ad}/K	1.59439	1.37527
ε_f/J·K^{-1}	16.64	16.59
$\Delta m(H_2O)$/g	−0.1	0
$-\Delta U$(IBP) [b]/J	25555.74	22043.96
ΔU(fuse)/J	38.98	48.56
ΔU(n-hex)/J	12481.10	12104.35
$\Delta U(HNO_3)$/J	34.01	27.40
ΔU(ign)/J	0.77	0.78
ΔU_Σ/J	11.80	9.43
$-\Delta_c u°$/J·g^{-1}	29293.37	29327.16

[a] $m(CO_2$, total) is the mass of CO_2 recovered in each combustion; m(cpd) is the mass of compound burnt in each experiment; m'(fuse) is the mass of the fuse (cotton) used in each experiment; m''(n-hex) is the mass of n-hexadecane used as auxiliary of combustion; ΔT_{ad} is the corrected temperature rise; ε_f is the energy equivalent of the contents in the final state; $\Delta m(H_2O)$ is the deviation of mass of water added to the calorimeter from 3119.6 g; ΔU(IBP) is the energy change for the isothermal combustion reaction under actual bomb conditions and includes ΔU(ignition); ΔU(fuse) is the energy of combustion of the fuse (cotton); ΔU(n-hex) is the energy of combustion of n-hexadecane used as auxiliary of combustion; $\Delta U(HNO_3)$ is the energy correction for the nitric acid formation; ΔU(ign) is the electric energy for the ignition; ΔU_Σ is the standard state correction; $\Delta_c u°$ is the standard massic energy of combustion. [b] ΔU(IBP) includes ΔU(ignition).

TABLE 2: Individual Values of Standard ($p° = 0.1$ MPa) Massic Energies of Combustion, $\Delta_c u°$, of the Compounds, at $T = 298.15$ K

2-acetylpyrrole	3-acetylpyrrole
$-\Delta_c u°$/J·g^{-1}	
29 301.12	29 325.75
29 301.02	29 335.95
29 299.18	29 312.63
29 289.46	29 327.16
29 292.18	29 310.22
29 293.37	29 328.96
29 302.05	
$-\langle\Delta_c u°\rangle$/J·g^{-1}	
29 296.9 ± 1.9[a]	29 323.4 ± 4.1[a]

[a] Mean value and standard deviation of the mean.

TABLE 3: Derived Standard ($p° = 0.1$ MPa) Molar Energies of Combustion, $\Delta_c U°_m$, Standard Molar Enthalpies of Combustion, $\Delta_c H°_m$, and Standard Molar Enthalpies of Formation, $\Delta_f H°_m$, for the Crystalline Compounds, at $T = 298.15$ K

compound	$-\Delta_c U°_m$(cr)/ kJ·mol^{-1}	$-\Delta_c H°_m$(cr)/ kJ·mol^{-1}	$-\Delta_f H°_m$(cr)/ kJ·mol^{-1}
2-acetylpyrrole	3197.0 ± 1.0	3198.9 ± 1.0	162.6 ± 1.3
3-acetylpyrrole	3199.9 ± 1.2	3201.8 ± 1.2	159.7 ± 1.5

Table 2 lists the individual values of $-\Delta_c u°$, together with the mean value, $\langle\Delta_c u^o\rangle$, and its standard deviations; the values of $\Delta_c u°$ are referred to the combustion reaction, represented by eq 5

$$C_6H_7NO(cr) + \frac{29}{4}O_2(g) \rightarrow 6CO_2(g) + \frac{7}{2}H_2O(l) + \frac{1}{2}N_2(g) \tag{5}$$

The derived standard molar energies and enthalpies of combustion and the standard molar enthalpies of formation of

TABLE 4: Knudsen Effusion Results for 2-Acetylpyrrole

		p/Pa			10^2 $\Delta\ln(p/\mathrm{Pa})$		
T/K	t/s	hole 1	hole 2	hole 3	hole 1	hole 2	hole 3
277.15	23111	0.162	0.146	0.151	7.5	− 2.8	0.4
279.15	22341	0.200	0.187	0.185	2.9	−3.5	− 5.0
281.16	21031	0.254	0.243	0.241	1.8	− 2.6	− 3.6
283.17	15857	0.345	0.319	0.313	7.6	− 0.4	− 2.5
285.12	14480	0.394	0.415	0.402	− 2.9	2.2	− 0.9
287.14	14871	0.547	0.520	0.497	5.6	0.6	− 4.1
289.15	11363	0.694	0.667	0.645	5.6	1.6	− 1.7
291.12	10663	0.811	0.806	0.780	− 1.8	− 2.5	− 5.7
293.15	10228	1.103	1.053	1.021	5.5	0.9	− 2.2

TABLE 5: Knudsen Effusion Results for 3-Acetylpyrrole[a]

			p/Pa			10^2 $\Delta\ln(p/\mathrm{Pa})$		
T/K	t/s	orifices	small	medium	large	small	medium	large
316.09	26 168	A1-B4-C7	0.116	0.114	0.113	2.7	0.8	−0.7
318.13	26 168	A2-B5-C8	0.145	0.143	0.143	2.0	0.7	0.2
320.20	26 168	A3-B6-C9		0.175	0.175		−2.0	−2.1
322.10	19 258	A1-B4-C7	0.225	0.215	0.217	2.4	−2.4	−1.3
324.15	19 258	A2-B5-C8	0.280	0.278	0.272	2.2	1.4	−0.6
326.21	19 258	A3-B6-C9		0.336	0.330		−1.4	−3.1
328.10	18 151	A1-B4-C7	0.425	0.411	0.411	2.2	−1.2	−1.1
330.14	18 151	A2-B5-C8	0.520	0.518	0.501	1.3	1.0	−2.4
332.20	18 151	A3-B6-C9		0.603	0.616		−4.8	−2.8
334.08	10 908	A1-B4-C7	0.789	0.785	0.768	3.1	2.5	0.4
336.09	10 908	A2-B5-C8	0.950	0.949	0.934	1.5	1.4	−0.3
338.20	10 908	A3-B6-C9		1.165	1.146		1.1	−0.6

[a] Detailed data of the effusion orifices (diameter and Clausing factors) of the Knudsen-2 effusion apparatus are presented in the supporting information.

TABLE 6: Experimental Results for 2- and 3-Acetylpyrroles, where a and b Are from the Clausius−Clapeyron Equation, $\ln(p/\mathrm{Pa}) = a - b(T/\mathrm{K})$ and $b = \Delta_{\mathrm{cr}}^{\mathrm{g}}H_{\mathrm{m}}^{\mathrm{o}}(\langle T\rangle)/R$; $R = 8.314472\ \mathrm{J\cdot K^{-1}\cdot mol^{-1}}$

orifices	a	b	$\langle T\rangle$/K	$p(\langle T\rangle)$/Pa	$\Delta_{\mathrm{cr}}^{\mathrm{g}}H_{\mathrm{m}}^{\mathrm{o}}(\langle T\rangle)/\mathrm{kJ\cdot mol^{-1}}$	$\Delta_{\mathrm{cr}}^{\mathrm{g}}S_{\mathrm{m}}(\langle T\rangle,p(\langle T\rangle))/\mathrm{J\cdot K^{-1}\cdot mol^{-1}}$
2-Acetylpyrrole						
hole 1	33.24 ± 0.74	9724 ± 212			80.8 ± 1.8	
hole 2	34.25 ± 0.35	10024 ± 99			83.3 ± 0.8	
hole 3	33.31 ± 0.38	9763 ± 108			81.2 ± 0.9	
global results	33.60 ± 0.41	9837 ± 117	285.15	0.408	81.8 ± 1.0	286.9 ± 3.5
3-Acetylpyrrole						
A1-A2-A3	33.25 ± 0.10	11192 ± 33			93.1 ± 0.3	
B4-B5-B6	33.44 ± 0.30	11262 ± 98			93.6 ± 0.8	
C7-C8-C9	33.30 ± 0.17	11217 ± 55			93.3 ± 0.5	
global results	33.30 ± 0.17	11215 ± 55	327.15	0.375	93.2 ± 0.5	284.9 ± 1.5

the compounds, in the crystalline state, at $T = 298.15$ K are given in Table 3. For each compound and in accordance with normal thermochemical practice, the uncertainties assigned to the molar enthalpies of combustion and formation are twice the overall standard deviations of the mean and include the uncertainties in calibration and in the auxiliary quantities used.[31,32] The values of the standard molar enthalpies of formation, in the crystalline phase, $\Delta_{\mathrm{f}}H_{\mathrm{m}}^{\mathrm{o}}(\mathrm{cr})$, were derived from $\Delta_{\mathrm{c}}H_{\mathrm{m}}^{\mathrm{o}}(\mathrm{cr})$ using the values of the standard molar enthalpies of formation of $H_2O(\mathrm{l})$, $-285.830 \pm 0.042\ \mathrm{kJ\cdot mol^{-1}}$, and $CO_2(\mathrm{g})$, $-393.51 \pm 0.13\ \mathrm{kJ\cdot mol^{-1}}$.[33]

The experimental results obtained from the Knudsen effusion experiments are summarized in Tables 4 and 5 for 2- and 3-acetylpyrroles, respectively. The standard molar enthalpies of sublimation, at the mean temperature of the experimental range, were derived by fitting data to the integrated form of the Clausius−Clapeyron equation, $\ln(p/\mathrm{Pa}) = a - b(T/\mathrm{K})^{-1}$, where a is a constant and $b = \Delta_{\mathrm{cr}}^{\mathrm{g}}H_{\mathrm{m}}^{\mathrm{o}}(\langle T\rangle)/R$. In these tables, $10^2\ \Delta\ln(p/\mathrm{Pa})$ are the residuals of the Clausius−Clapeyron equation, derived from least-squares adjustments.

Table 6 presents, for each hole used and for the global treatment, all of the (p,T) points obtained for each studied compound, the detailed parameters of the Clausius−Clapeyron equation, together with the calculated standard deviations and the standard molar enthalpies of sublimation at the mean temperature of the experiments $T = \langle T\rangle$. The equilibrium pressure at this temperature, $p(\langle T\rangle)$, and the entropies of sublimation, at equilibrium conditions, are also presented. The plots of $\ln p = f(1/T)$ for the global results of the two compounds studied experimentally are presented in Figure 2. The (p,T) values, calculated from the (p,T) equations for the crystalline compounds, within the experimental range of pressures used, 0.1−1.0 Pa, are presented in Table 7. Sublimation enthalpies, at $T = 298.15$ K, were derived from the sublimation enthalpies calculated at the mean temperature $\langle T\rangle$ of the experiments, by the equation

$$\Delta_{\mathrm{cr}}^{\mathrm{g}}H_{\mathrm{m}}^{\mathrm{o}}(T = 298.15\ \mathrm{K}) = \Delta_{\mathrm{cr}}^{\mathrm{g}}H_{\mathrm{m}}^{\mathrm{o}}(\langle T\rangle) + \Delta_{\mathrm{cr}}^{\mathrm{g}}C_{p,\mathrm{m}}^{\mathrm{o}}(298.15 - \langle T\rangle) \quad (6)$$

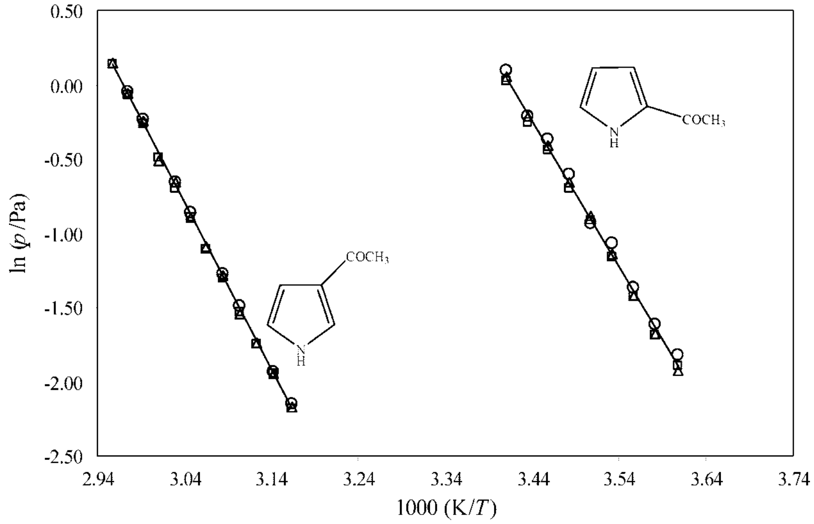


Figure 2. Plots of ln(*p*/Pa) against 1/*T* for 2- and 3-acetylpyrroles: ○, small holes; △, medium holes; □, large holes.

TABLE 7: Calculated (*p, T*) Values from the Vapour Pressure Equations for the Studied Compounds

	T/K									
p/Pa	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0
2-acetylpyrrole	274.0	279.4	282.6	285.0	286.9	288.4	289.7	290.8	291.9	292.8
3-acetylpyrrole	315.0	321.3	325.0	327.8	329.9	331.7	333.2	334.5	335.7	336.8

TABLE 8: Values of the Standard ($p° = 0.1$ MPa) Molar Enthalpies, $\Delta_{\mathrm{cr}}^{\mathrm{g}}H_{\mathrm{m}}^{\mathrm{o}}$, Entropies, $\Delta_{\mathrm{cr}}^{\mathrm{g}}S_{\mathrm{m}}^{\mathrm{o}}$, and Gibbs Energies $\Delta_{\mathrm{cr}}^{\mathrm{g}}G_{\mathrm{m}}^{\mathrm{o}}$, of Sublimation, at $T = 298.15$ K, for the Studied Compounds

compound	$\Delta_{\mathrm{cr}}^{\mathrm{g}}H_{\mathrm{m}}^{\mathrm{o}}$/ kJ·mol^{-1}	$\Delta_{\mathrm{cr}}^{\mathrm{g}}S_{\mathrm{m}}^{\mathrm{o}}$/ J·K^{-1}·mol^{-1}	$\Delta_{\mathrm{cr}}^{\mathrm{g}}G_{\mathrm{m}}^{\mathrm{o}}$/ kJ·mol^{-1}
2-acetylpyrrole	81.2 ± 1.0	181.5 ± 3.5	27.1 ± 1.4
3-acetylpyrrole	94.7 ± 0.5	185.7 ± 1.5	39.3 ± 0.7

TABLE 9: Standard ($p° = 0.1$ MPa) Molar Enthalpies of Formation, in Both Crystalline and Gaseous Phases, and Standard Molar Enthalpies of Sublimation, at $T = 298.15$ K

compound	$-\Delta_{\mathrm{f}}H_{\mathrm{m}}^{\mathrm{o}}$(cr)/ kJ·mol^{-1}	$\Delta_{\mathrm{cr}}^{\mathrm{g}}H_{\mathrm{m}}^{\mathrm{o}}$/ kJ·mol^{-1}	$-\Delta_{\mathrm{f}}H_{\mathrm{m}}^{\mathrm{o}}$(g)/ kJ·mol^{-1}
2-acetylpyrrole	162.6 ± 1.3	81.2 ± 1.0	81.4 ± 1.6
3-acetylpyrrole	159.7 ± 1.5	94.7 ± 0.5	65.0 ± 1.6

According to estimations made by other authors,[34] the value of $\Delta_{\mathrm{cr}}^{\mathrm{g}}C_{\mathrm{p,m}}^{\mathrm{o}}$ was assumed to be −50 J·K^{-1}·mol^{-1}, a value that has already been used in previous works devoted to other organic compounds.[35−39]

The standard molar enthalpies, entropies and Gibbs energies of sublimation of each compound, at $T = 298.15$ K, are given in Table 8.

Combining the derived standard molar enthalpies of formation, in the crystalline phase, with the standard molar enthalpies of sublimation, yield the standard molar enthalpies of formation, in the gaseous phase, at $T = 298.15$ K, of 2- and 3-acetylpyrrole, presented in Table 9.

The experimental enthalpic increments for the introduction of a $-$COCH$_3$ group in positions 2- and 3- of the pyrrole ring ($\Delta_{\mathrm{f}}H_{\mathrm{m}}^{\mathrm{o}}$ for pyrrole is 108.3 ± 0.5 kJ·mol^{-1}, ref 40) are, respectively, −189.7 ± 1.7 and −173.3 ± 1.7 kJ·mol^{-1}. These increments are compared in Figure 3 with those calculated for the insertion of the acetyl group in two other cyclic species, namely, thiophene and pyridine. The enthalpic increments for the introduction of an acetyl group in the 2 and 3 positions of the thiophene and pyridine were calculated through the following $\Delta_{\mathrm{f}}H_{\mathrm{m}}$ literature values: $\Delta_{\mathrm{f}}H_{\mathrm{m}}^{\mathrm{o}}$(thiophene, g) = 115.0 ± 1.0 kJ·mol^{-1},[41] $\Delta_{\mathrm{f}}H_{\mathrm{m}}^{\mathrm{o}}$(2-acetylthiophene, g) = −59.2 ± 2.1 kJ·mol^{-1},[42] $\Delta_{\mathrm{f}}H_{\mathrm{m}}^{\mathrm{o}}$(3-acetylthiophene, g) = −54.5 ± 1.8 kJ·mol^{-1},[42] $\Delta_{\mathrm{f}}H_{\mathrm{m}}^{\mathrm{o}}$(pyridine, g) = 140.4 ± 0.7 kJ·mol^{-1},[43] $\Delta_{\mathrm{f}}H_{\mathrm{m}}^{\mathrm{o}}$(2-acetylpyridine, g) = −41.3 ± 2.9 kJ·mol^{-1},[44] and $\Delta_{\mathrm{f}}H_{\mathrm{m}}^{\mathrm{o}}$(3-acetylpyridine, g) = −35.2 ± 2.8 kJ·mol^{-1}.[44] The introduction of an acetyl group into the 2 positions of pyrrole, thiophene, or pyridine compounds is always more favorable than insertion at the 3 positions. The enthalpic differences caused by the introduction of a $-$COCH$_3$ group in thiophene, pyridine, and pyrrole are −174.2 ± 2.3, −181.7 ± 3.0, and −189.7 ± 1.7 kJ·mol^{-1}, respectively. These differences show that the interaction between the O atom from the $-$COCH$_3$ group and the H atom from the N$-$H bond in the latter is much more efficient than the interaction between the same O atom and the ring's heteroatom (S in the case of thiophene and N for pyridine ring). Furthermore, due to the size of the heteroatom (S or N) in the ring, the destabilizing interaction between the O atom from the $-$COCH$_3$ group and the N atom in pyridine is smaller than the identical interaction between the O and S atoms in the thiophene ring. In the case of substitution at the 3 position, it can be noticed through the schemes presented in Figure 3 that addition of an acetyl group causes, within the associated experimental uncertainties, almost the same effects in the three aromatic rings, showing the inexistence of the (de)stabilizing effects produced by the interaction between the O atom from the $-$COCH$_3$ group and the heteroatom in the ring. The discussion above directs us to the conclusion that, in the case of acetylpyrrole, the large enthalpic stabilization upon the introduction of a $-$COCH$_3$ group, and consequent larger 2 → 3 isomerization enthalpy, may be due to internal hydrogen bonding. In fact, as shown in the subsequent section, the experimental and computational structures of 2-acetylpyrrole have the hydrogen atom of the N$-$H group slightly moved to the carbonyl oxygen atom suggesting the formation of an intramolecular N$-$H···O bond. A topological analysis with the Topmod program,[45] aiming at the location of critical points in the electronic charge density distribution in the region between

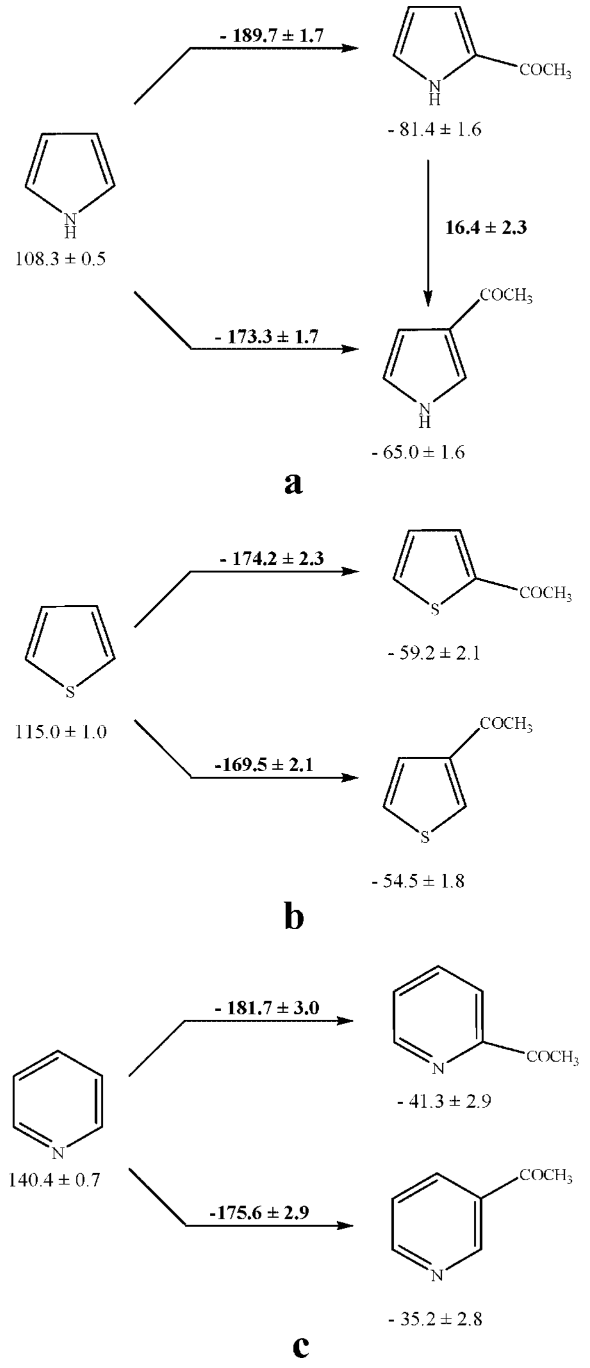


Figure 3. Enthalpic increments (kJ·mol^{-1}) of the introduction of a $-COCH_3$ group in the 2 and 3 positions of (a) pyrrole, (b) thiophene, and (c) pyridine and enthalpies of isomerization 2 → 3.

the H and O atoms, revealed a bond critical point with electron localization function, $\eta = 0.116$, electron density $\rho = 0.019$ and Laplacian of the electron density, $\nabla^2\rho = 0.055$, calculated at the B3LYP/6-311+G(2d,2p) level of theory.

4.2. Molecular Structures and Computational Thermochemistry. As it was referred to in the Introduction, structural crystal data determined by single-crystal X-ray for 2-acetylpyrrole have been described by Camarillo et al.[15] The experimental X-ray results are compared with those computed with the B3LYP/6-31G(d), B3LYP/6-311+G(2d,2p), and MP2/6-311+G(2d,2p) approaches in the Supporting Information.

The most stable molecular structures of 2- and 3-acetylpyrroles, optimized at the B3LYP/6-31G (d) level of theory (G3(MP2)//B3LYP calculations), with selected distances and angles, are shown

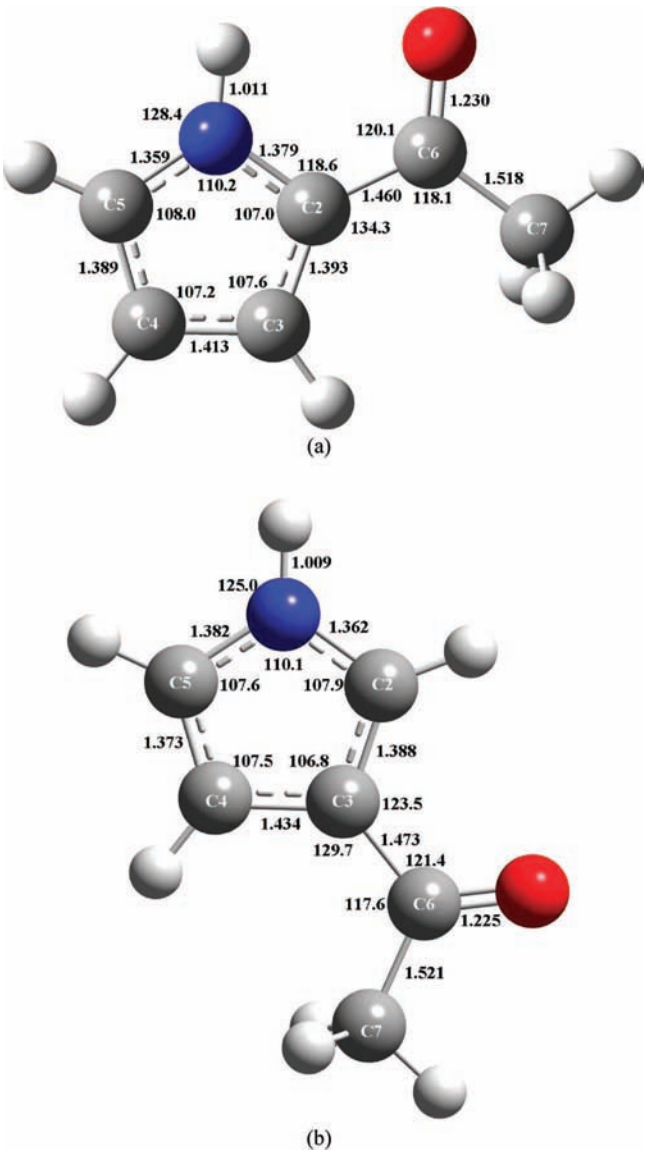


Figure 4. Optimized most stable configurations for the (a) 2-acetylpyrrole (syn) and (b) 3-acetylpyrrole (syn). Distances are in Å and angles in degrees.

TABLE 10: Comparison between the Experimental and Computed G3(MP2)//B3LYP Gas-Phase Enthalpies of Formation of 2- and 3-Acetylpyrroles, at T = 298.15 K[a]

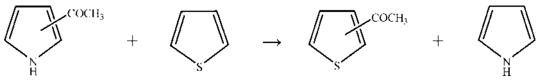
	2-acetylpyrrole		3-acetylpyrrole	
	$-\Delta_f H^o_m(g)$/ kJ·mol^{-1}		$-\Delta_f H^o_m(g)$/ kJ·mol^{-1}	
reaction	experimental	G3(MP2)// B3LYP	experimental	G3(MP2)// B3LYP
(7)	81.4 ± 1.6	84.2 (2.8)	65.0 ± 1.6	67.4 (2.4)
(8)		84.8 (3.4)		70.0 (5.0)
(9)		85.5 (4.1)		70.7 (5.7)
(10)		84.1 (2.7)		69.3 (4.3)
(11)		82.7 (1.3)		67.9 (2.9)
(12)		80.3 (−1.1)		68.2 (3.2)
atom.				
(13)		81.6 (0.2)		66.8 (1.8)
mean value		83.3 ± 0.7		68.6 ± 0.5

[a] Enthalpic differences between the experimental and computed values are given in parentheses. All values are in kJ·mol^{-1}.

in Figure 4. In a general way, there are not significant differences between the geometrical parameters of pyrrole, also determined in this work (N−H = 1.008 Å; N−C_2 = N−C_5 = 1.375 Å; C_2−C_3 = C_2−C_3 =1.378 Å; C_3−C_4 =1.425 Å; C_2NC_5 = 109.8°; NC_2C_3 = C_4C_5N = 107.7°; $C_2C_3C_4$ = $C_3C_4C_5$ = 107.4°) and its acetyl derivatives (Figure 4).

2-Acetylpyrrole is almost planar, pertaining to the symmetry point group C_1, whereas the 3 isomer is planar, symmetry point group C_s, as the analogues derived from thiophene.[42] N−H,O-syn is the preferred conformation for both isomers, being the N−H,O-anti conformation 17.3 and 0.8 kJ·mol^{-1} less stable than the N−H,O-syn, for 2- and 3-acetylpyrroles, respectively. The H atom from the N−H group of the pyrrole ring in the 2-acetylpyrrole appears to be slightly tilted in the direction of the −$COCH_3$ group, being the C_5NH angle larger than the C_2NH (128.4° vs 121.4°, respectively). Furthermore, in 2-acetylpyrrole, the distance between the H atom from the N−H group of the pyrrole ring and the oxygen atom from the acetyl group is 2.456 Å, which is approximately the H···ONO distance found in 2-nitropyrrole (2.400 Å), i.e., between the H atom from the N−H group of the pyrrole ring and the oxygen atom from the nitro group.[46]

The enthalpies of formation, in the gaseous phase, at T = 298.15 K, of the two acetylpyrroles isomers have been estimated from the G3(MP2)//B3LYP enthalpies together with the working reactions 7−12 or with the reaction of atomization (13)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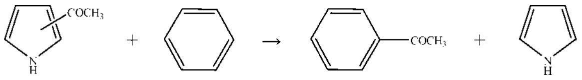
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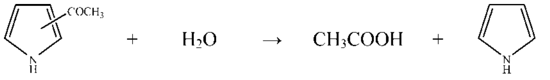

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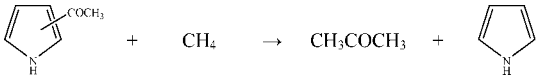

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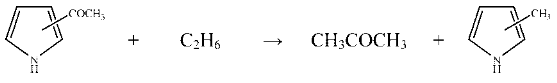

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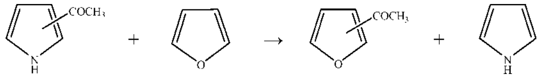
(12)

$$C_6H_7NO(g) \rightarrow 6\,C(g) + 7\,H(g) + N(g) + O(g) \quad (13)$$

The results obtained are presented in Table 10 and were calculated combining the enthalpy of each reaction with the experimental standard molar enthalpies of formation in the gas phase of each molecule (or atom) in the reaction, except the one we want to determine. The obtained theoretical results are in very good agreement with the experimentally derived gas-phase enthalpies of formation; the maximum deviations from the experimental results are 4.1 and 5.7 kJ·mol^{-1} for 2- and 3-acetylpyrroles, respectively. It is important to emphasize that, for both compounds, the use of the atomization reaction provides the best estimates with maximum deviations of only 0.2 and 1.8 kJ·mol^{-1} for 2- and 3-acetylpyrroles, respectively. A mean value of theoretical $\Delta_f H_m^o(g)$, for each isomer, is also presented in Table 10. The computed G3(MP2)//B3LYP enthalpies for the compounds studied, auxiliary molecules, and atoms used in the working reactions are listed in Table S5 and the standard molar enthalpies of formation, in the gaseous phase, for the auxiliary species are presented in Table S6, both in the Supporting Information.

Additionally, for comparison purposes the gas-phase enthalpies of formation of the two isomers were also computed with the B3LYP density functional and with MP2 method. In both cases, the atomic electron density was described by the 6-311+G(2d,2p) basis set. B3LYP and MP2 results are presented in the Supporting Information.

The composite G3(MP2)//B3LYP method was also used to compute some other thermodynamic properties, such as N−H bond dissociation enthalpies, gas-phase acidities and basicities, proton and electron affinities and ionization enthalpies. The calculated values for the two acetylpyrroles isomers, as well as for the pyrrole molecule are presented in Table 11.

As it can be seen in Table 11, the computed results obtained in this work for pyrrole almost match previous experimental or calculated data found in literature. Starting with the gas phase acidity and basicity for pyrrole, the deviation from the literature values is only ±2.0 and +1.0; −2.7 kJ·mol^{-1}, respectively. In what concerns to the proton affinities, the preferred protonation

TABLE 11: G3(MP2)//B3LYP Computed N−H Bond Dissociation Enthalpies, N−H BDE, Gas-Phase Acidities, $\Delta G_{acidity}$ and Basicities, $\Delta G_{basicity}$, Proton, PA, and Electron Affinities, EA, and Ionization Enthalpies, IE, at T = 298.15 K, for Pyrrole and 2- and 3-Acetylpyrroles[a]

compound	N−H BDE	$\Delta G_{acidity}$	$\Delta G_{basicity}$	PA	EA	IE
pyrrole	398.1	1470.0	841.1	872.9 (C2)	−184.3	798.5
	385[48]	1468.0 ± 8.4[57]	843.8[58]	874 (C2)[59]	−230.1 ± 12.6[54]	791.8 ± 0.5[47]
	396.6[49]	1472.0 ± 8.4[60]	843.1[46]	875.4[58]		
	401.6[50]	1468.2 ± 8.4[52]	840.1[46]	876.5 (C2)[46]		
	387.6 ± 4.8[51]			873.2 (C2)[46]		
	393.0 ± 0.5[52]					
	404.2[53]					
	414.2 ± 25.1[54]					
2-acetylpyrrole	408.3	1419.7	858.5	892.9 (O)	−16.6	818.7
						841.3 ± 4.8[55]
3-acetylpyrrole	400.8	1406.3	869.6	900.6 (O)	−55.7	818.3

[a] All values are in kJ·mol^{-1}.

site in pyrrole is the carbon atom directly bound to the heteroatom. The results are in good agreement with the ones given in literature, being the maximum deviation −3.6 kJ·mol^{-1}. The computed ionization enthalpy (IE), a property that measures the capacity of the compound to act as electron-donor species, is also in agreement with the literature value presented in Table 11. The IE value taken from the literature results from an evaluation done by Lias,[47] based on a series of experimental IE values determined by several different methods, ranging from 773.8 to 810.5 kJ·mol^{-1}. Our computed IE value is within this range.

There are in the literature several values for the gas-phase N−H bond dissociation enthalpy (BDE) of pyrrole. Computationally, Rimarčík et al.[48] using PBE0/TZVP, Bacskay et al.[49] using a modified G2(MP2) approach considering CASSCF/cc-pVDZ geometries and frequencies and Gomes et al.[50] using (RO)B3LYP/6-311+G(2d,2p)//(U) B3LYP/6-31G(d) obtained N−H BDEs of 385, 396.6, and 401.6 kJ·mol^{-1}, respectively. Experimentally, Wei et al. determined a value of 387.6 ± 4.8 kJ·mol^{-1} from photofragment velocity map imaging,[51] Gianola et al. cited a value of 393.0 ± 0.5 kJ·mol^{-1},[52] Bordwell et al. reported a BDE of 404.2 kJ·mol^{-1} from experiments in DMSO using a electrochemical method,[53] and Richardson et al., using ion cyclotron resonance mass spectrometry, obtained a N−H BDE of 414.2 ± 25.1 kJ·mol^{-1}.[54] Our theoretical result, 398.1 kJ·mol^{-1}, lies in the range of available computed and experimental data. Richardson et al. also obtained, through ion cyclotron resonance mass spectrometry, the electron affinity of pyrrole as being −230.1 ± 12.6 kJ·mol^{-1} (minus sign added by convention), this value being somewhat higher than that obtained in this work.[54] Through the above exposed, due to the remarkable agreement between the experimental and theoretical data obtained from the literature and the G3(MP2)//B3LYP computed values for pyrrole, one expects that this theoretical method would be also a good choice for the calculation of the thermodynamic properties for other substituted pyrroles, which are presented below. Both the 2- and 3-acetylpyrroles protonate preferentially at the oxygen of the acetyl group, which was also confirmed for the 2- and 3-nitropyrroles (the preferred protonation site is in the oxygen of the nitro group).[45] The N atom is the least favorable protonation site for pyrrole and for its 2- and 3-acetyl and nitro derivatives. For acetyl and nitropyrroles, the protonation in the oxygen atom of the substituent group is more favored in the 3-isomer than in the 2-isomer. The introduction of acetyl groups into the pyrrole ring increases the proton affinity by 20 and 27.7 kJ·mol^{-1}, respectively. The entire set of computed proton affinities is given in Table S8, in the Supporting Information.

Thermodynamic data for these two isomers is scarce in the literature; only the IE of 2-acetylpyrrole, which was measured by Linda et al. in the early 1970s through the electron impact technique, was found. The experimental value obtained by Linda et al. differs by 22.6 kJ·mol^{-1} from the result (818.7 kJ·mol^{-1}) computed in this work.[55] Similar enthalpic differences were found when some of the experimental results available for the three fluoroanilines were compared with calculated data obtained with the same G3(MP2)//B3LYP approach,[56] whereas in a single case, the agreement was excellent (<5 kJ·mol^{-1}). The computed IE for the 2-acetylpyrrole is identical to that calculated for the 3 isomer and ~20 kJ·mol^{-1} more positive than the IE calculated for pyrrole. Looking to the computed values for the electron affinity, it is found that the addition of an electron to pyrrole is drastically disadvantageous than when an electron is added to the acetyl derivatives.

The computed N−H BDEs for the two acetylpyrroles isomers are close to that computed for pyrrole. The 2-acetylpyrrole BDE is slightly larger than the 3 isomer, supporting a constructive interaction between the oxygen atom from the $-COCH_3$ group and the H−N group from the pyrrole ring. The calculated acidities for these two compounds show that the removal of a proton in 3-acetylpyrrole is slightly easier than in 2-acetylpyrrole ($\Delta G_{\text{acidity}} = 1406$ vs 1420 kJ·mol^{-1}, respectively).

5. Conclusions

A combined experimental and computational study has been performed aiming the determination of the standard molar enthalpies of formation, in the gaseous phase, at $T = 298.15$ K, for 2- and 3-acetylpyrroles. Static bomb combustion calorimetry and the Knudsen effusion mass-loss technique were used to obtain the standard molar enthalpies of formation, in the condensed phase and the standard molar enthalpies of sublimation, at $T = 298.15$ K, from which the experimental standard molar enthalpies of formation, in the gaseous phase, were derived. The G3(MP2)//B3LYP approach was used to estimate the gas-phase enthalpies of formation of the title compounds using either the atomization or several working reactions. It was found that this computational method yields results that are in good agreement with the experimental ones, giving further support to the derived experimental results. The best agreement between experimental and computational standard molar gas-phase enthalpies of formation was obtained using atomization reactions. Both experimental and theoretical methods show that 2-acetylpyrrole is thermodynamically more stable than the 3 isomer.

N−H bond dissociation enthalpies, gas-phase acidities and basicities, proton and electron affinities and ionization enthalpies of pyrrole, 2- and 3-acetyl derivatives were also calculated through the G3(MP2)//B3LYP approach. For pyrrole, the computed values were found to be in good agreement with the available experimental data in the literature. As for the acetyl derivatives there are no experimental data available in the literature for these properties (except for IE of 2-acetylpyrrole) and due to the remarkable agreement found for pyrrole, we do believe that the computed values for the acetylated pyrroles are reliable.

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Supporting Information Available: Detailed data of the effusion orifices (diameter and Clausing factors) of the Knudsen effusion apparatus (Knudsen-2); data and details of all the combustion calorimetry experiments for the 2- and 3-acetylpyrroles; comparison of selected structural parameters for 2- and 3-acetylpyrroles calculated with different computational approaches; G3(MP2)//B3LYP enthalpies (energies plus thermal corrections for $T = 298.15$ K) for the 2- and 3-acetylpyrroles, for the auxiliary molecules and for the atoms included in the several working reactions considered; standard molar enthalpies of formation, at $T = 298.15$ K, taken from the literature; comparison between the experimental and computed B3LYP/6-311+G(2d,2p) and MP2/6-311+G(2d,2p) gas-phase enthalpies of formation for 2- and 3-acetylpyrroles, at $T = 298.15$ K;

G3(MP2)//B3LYP computed proton affinities, PA, at $T = 298.15$ K for pyrrole and for the 2- and 3-acetylpyrroles. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) http://www.lipitor.com (29/07/2008).

(2) Kirner, S.; Hammer, P. E.; Hill, D. S.; Altmann, A.; Fischer, I.; Weislo, L J; Lanahan, M.; Pée, K.-H.; Lingon, J. M *J. Bacteriol.* **1998**, *180*, 1939–1943.

(3) Battersby, A. R. *Nat. Prod. Rep.* **2000**, *17*, 507–526.

(4) Maga, J. A. *J. Agric. Food Chem.* **1981**, *29*, 691–694.

(5) Street, G. B. Polypyrrole - From Powders to Plastic. In *Handbook of Conducting Polymers*; Skotheim, T. A., Ed.; Marcel Dekker: New York, 1986; Vol. 1, Chapter 8.

(6) Ito, M.; Shimura, H.; Watanabe, N.; Tamai, M.; Takahashi, A.; Tanaka, Y.; Arai, I.; Hanada, K. *Agric. Biol. Chem.* **1991**, *55*, 2117–2121.

(7) Rowe, D. J., Chemistry and Technology of Flavors and Fragrances; Blackwell Publishing Ltd., 2005 (available online at books.google.com).

(8) Sakaki, T.; Fukuhara, K.; Niino, K.; Sakuma, H.; Sugawara, S. *Agric. Biol. Chem.* **1985**, *49*, 1785–1791.

(9) Hattori, S.; Takagaki, H.; Fujimori, T. *Food Sci. Technol. Res.* **2005**, *11*, 171–174.

(10) Mahajan, S. S.; Goddik, L.; Qian, M. C. *J. Dairy Sci.* **2004**, *87*, 4057–4063.

(11) Buttery, R. G.; Ling, L. C.; Stern, D. J. *J. Agric. Food Chem.* **1997**, *45*, 837–843.

(12) Fuster, M. D.; Mitchell, A. E.; Ochi, H.; Shibamoto, T. *J. Agric. Food Chem.* **2000**, *48*, 5600–5603.

(13) Yanagimoto, K.; Lee, K.-G.; Ocho, H.; Shibamoto, T. *J. Agric. Food Chem.* **2002**, *50*, 5480–5484.

(14) http://www.jetro.go.jp/en/market/regulations/pdf/flavor2003aug-e.pdf (03/07/2008).

(15) Camarillo, E. A.; Flores, H.; Amador, P.; Bernès, S. *Acta Crystallogr.* **2007**, *E63*, o2593–o2594.

(16) Ribeiro da Silva, M. A. V.; Ribeiro da Silva, M. D. M. C.; Pilcher, G. *Rev. Port. Quím.* **1984**, *26*, 163–172.

(17) Ribeiro da Silva, M. A. V.; Ribeiro da Silva, M. D. M. C.; Pilcher, G. *J. Chem. Thermodyn.* **1984**, *16*, 1149–1155.

(18) *Certificate of Analysis, Standard Reference Material 39j Benzoic Acid Calorimetric Standard*; NBS: Washington, 1995.

(19) Coops, J.; Jessup, R. S.; van Nes, K. G. In *Experimental Thermochemistry*; Rossini, F. D., Ed.; Interscience: New York, 1956; Vol. 1, Chapter 3.

(20) Santos, L. M. N. B. F. Ph.D. Thesis, University of Porto, 1995.

(21) Good, W. D.; Scott, D. W.; Waddington, G. *J. Phys. Chem.* **1956**, *60*, 1080–1089.

(22) The NBS Tables of Chemical Thermodynamic Properties. *J. Phys. Chem. Ref. Data* **1982**, *11* (Suppl. 2).

(23) Washburn, E. N. *J. Res. Natl. Bur. Stand. (U.S.)* **1933**, *10*, 525–558.

(24) Hubbard, W. N.; Scott, D. W.; Waddington, G. In *Experimental Thermochemistry*; Rossini, F. D., Ed.; Interscience: New York, 1956; Vol. 1, Chapter 5.

(25) Wieser, M. E. *Pure Appl. Chem.* **2006**, *78*, 2051–2066.

(26) Ribeiro da Silva, M. A. V.; Monte, M. J. S. *Thermochim. Acta* **1990**, *171*, 169–183.

(27) Ribeiro da Silva, M. A. V.; Monte, M. J. S.; Santos, L. M. N. B. *J. Chem. Thermodyn.* **2006**, *38*, 778–787.

(28) Baboul, A. G.; Curtiss, L. A.; Redfern, P. C.; Raghavachari, K. *J. Chem. Phys.* **1999**, *110*, 7650–7657.

(29) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A.Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03*, revision C.02; Gaussian, Inc.:Wallingford, CT, 2004.

(30) Westrum, E. F. In *Combustion Calorimety*; Sunner, S.; Månsson, M., Eds.; Pergamon: Oxford, 1979; Vol. 1, Chapter 7.

(31) Rossini, F. D. In *Experimental Thermochemistry*; Rossini, F. D., Ed.; Interscience: New York, 1956; Vol. 1, Chapter 14.

(32) Olofsson, G. In *Combustion Calorimety*; Sunner, S.; Månsson, M., Eds.; Pergamon: Oxford, 1979; Vol. 1, Chapter 6.

(33) Cox, J. D., Wagman, D. D., Medvedev, V. A., Eds. *CODATA Key Values for Thermodynamics*; Hemisphere: New York, 1989.

(34) Burkinshaw, P. M.; Mortimer, C. T. *J. Chem. Soc., Dalton Trans.* **1984**, 75–77.

(35) Ribeiro da Silva, M. A. V.; Amaral, L. M. P. F.; Santos, A. F. L. O. M.; Gomes, J. R. B. *J. Chem. Thermodyn.* **2006**, *38*, 367–375.

(36) Ribeiro da Silva, M. A. V.; Amaral, L. M. P. F.; Santos, A. F. L. O. M.; Gomes, J. R. B. *J. Chem. Thermodyn.* **2006**, *38*, 748–755.

(37) Ribeiro da Silva, M. A. V.; Santos, A. F. L. O. M. *J. Chem. Thermodyn.* **2008**, *40*, 166–173.

(38) Ribeiro da Silva, M. A. V.; Santos, A. F. L. O. M *J. Chem. Thermodyn.* **2008**, *40*, 1451–1457.

(39) Ribeiro da Silva, M. A. V.; Amaral, L. M. P. F.; Santos, A. F. L. O. M. *J. Chem. Thermodyn.* **2008**, *40*, 1588–1593.

(40) Scott, D. W.; Berg, W. T.; Hossenlopp, I. A.; Hubbard, W. N.; Messerly, J. F.; Todd, S. S.; Douslin, D. R.; McCullough, J. P.; Waddington, G. *J. Phys. Chem.* **1967**, *71*, 2263–2270.

(41) Hubbard, W. N.; Scott, D. W.; Frow, F. R.; Waddington, G. *J. Am. Chem. Soc.* **1955**, *77*, 5855–5858.

(42) Roux, M. V.; Temprado, M.; Jiménez, P.; Notário, R.; Chickos, J. S.; Santos, A. F. L. O. M.; Ribeiro da Silva, M. A. V. *J. Phys. Chem. A* **2007**, *111*, 11084–11092.

(43) Pedley, J. B. *Thermochemical Data and Structures of Organic Compounds*; Thermodynamics Research Centre: College Station, TX, 1994.

(44) Freitas, V. L. S.; Oliveira, L. I. P.; Ribeiro da Silva, M. D. M. C. *J. Chem. Thermodyn.* **2007**, *39*, 39–43.

(45) Noury, S.; Krokidis, X.; Fuster, F.; Silvi, B. *Comput. Chem.* **1999**, *23*, 597–604.

(46) Esseffar, M.; Quintanilla, E.; Dávalos, J. Z.; Abboud, J. L. M.; Mó, O.; Yáñez, M.; New, J. *Chem.* **2002**, *26*, 1567–1574.

(47) Lias, S. G. Ionization Energy Evaluation. In NIST Chemistry WebBook, NIST Standard Reference Database Number 69; Linstrom, P. J., Mallard, W. G., Eds.; National Institute of Standards and Technology: Gaithersburg MD, 2005; http://webbook.nist.gov.

(48) Rimarčik, J.; Lukeš, V.; Klein, E.; Griesser, M.; Kelterer, A.-M. *Chem. Phys.* **2008**, *353*, 177–184.

(49) Bacskay, G. B.; Martoprawiro, M.; Mackie, J. C. *Chem. Phys. Lett.* **1998**, *290*, 391–398.

(50) Gomes, J. R. B.; Ribeiro da Silva, M. D. M. C.; Ribeiro da Silva, M. A. V. *J. Phys. Chem. A* **2004**, *108*, 2119–2130.

(51) Wei, J.; Kuczmann, A.; Riedel, J.; Renth, F.; Temps, F. *Phys. Chem. Chem. Phys.* **2003**, *5*, 315–320.

(52) Cited in Gianola, A. J.; Ichino, T.; Hoenigman, R. L; Kato, S.; Bierbaum, V. M.; Lineberger, W. C. *J. Phys. Chem. A* **2004**, *108*, 10326–10335.

(53) Bordwell, F. G.; Zhang, X.; Cheng, J.-P. *J. Org. Chem.* **1991**, *56*, 3216–3219.

(54) Richardson, J. H.; Stephenson, L. M.; Brauman, J. I. *J. Am. Chem. Soc.* **1975**, *97*, 1160–1162.

(55) Linda, P.; Marino, G.; Pignataro, S. *J. Chem. Soc. B* **1971**, 1585–1587.

(56) Ribeiro da Silva, M. A. V.; Ferreira, A. I. M. C. L.; Gomes, J. R. B. *J. Phys. Chem. B* **2007**, *111*, 2052–2061.

(57) Bartmess, J. E.; Scott, J. A.; McIver, R. T., Jr. *J. Am. Chem. Soc.* **1979**, *101*, 6046–6056.

(58) Hunter, E. P.; Lias, S. G. *J. Phys. Chem. Ref. Data* **1998**, *27*, 413–656.

(59) Kabli, S.; van Beelen, E. S. E.; Ingemann, S.; Henriksen, L.; Hammerum, S *Int. J. Mass Spectrom.* **2006**, *249−150*, 370–378.

(60) Cumming, J. B.; Kebarle, P. *Can. J. Chem.* **1978**, *56*, 1–9.

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