

## Calorimetric and Computational Study of 2- and 3-Acetyl-1-methylpyrrole Isomers

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This work reports the enthalpies of formation in the condensed and gas phases of 2-acetyl-1-methylpyrrole and 3-acetyl-1-methylpyrrole, derived from the standard ( $p^\circ = 0.1$  MPa) molar enthalpies of combustion, in oxygen,  $\Delta_c H_m^\circ$ , measured by static bomb combustion calorimetry and the standard molar enthalpies of vaporization,  $\Delta_f^\circ H_m^\circ$ , at  $T = 298.15$  K, obtained by high-temperature Calvet microcalorimetry. The theoretically estimated gas-phase enthalpies of formation were calculated from high-level ab initio molecular orbital calculations at the G3(MP2)//B3LYP level; the computed values compare very well with the experimental results obtained in this work and show that the 2-acetyl-1-methylpyrrole is thermodynamically more stable than the 3-isomer. Furthermore, this composite method was also applied in the calculation of bond dissociation enthalpies, gas-phase basicities, proton and electron affinities, and adiabatic ionization enthalpies.

## 1. Introduction

Pyrrole-containing compounds are extensively used in synthetic organic chemistry<sup>1–5</sup> and material science.<sup>6</sup> They are widely found in natural biomolecules like hemoglobin, cytochromes, and chlorophyll (naturally occurring tetrapyrroles), playing an important role in respiration and photosynthesis. Pyrroles and derivatives are used as building blocks in a variety of pharmacologically active compounds. These nitrogen five-membered heterocyclic compounds have been employed as antioxidant,<sup>7</sup> antibacterial,<sup>8,9</sup> ionotropic,<sup>10,11</sup> antitumor,<sup>12</sup> anti-inflammatory,<sup>13</sup> and antifungal agents.<sup>14,15</sup> Several pyrrole derivatives have also been reported in various processed foods and beverages,<sup>16–18</sup> and because of their organoleptic properties, some of them are used as flavor additives.<sup>19</sup> For example, 2-acetyl-1-methylpyrrole was identified in roasted coffee,<sup>20,21</sup> and 3-acetyl-1-methylpyrrole is present in potato chips<sup>22</sup> and in boiled scallop aroma.<sup>23</sup>

As part of our broad research program on the experimental and computational thermochemical studies of nitrogen heterocyclic compounds, we have recently focused our attention on substituted pyrroles, for which we reported a calorimetric and computational study of 2- and 3-acetylpyrroles,<sup>24</sup> 2-pyrrolecarboxylic acid, and 1-methyl-2-pyrrolecarboxylic acid.<sup>25</sup> Thus, this paper reports a detailed thermochemical experimental and computational study of 2-acetyl-1-methylpyrrole and 3-acetyl-1-methylpyrrole, whose structural formulas are depicted in Figure 1. The standard ( $p^\circ = 0.1$  MPa) molar enthalpies of formation, in the liquid phase, at  $T = 298.15$  K, of the two studied compounds, were determined by means of static bomb combustion calorimetry. High-temperature Calvet microcalorimetry allowed the determination of the respective standard molar enthalpies of vaporization, at  $T = 298.15$  K. These experimental values enable the derivation of the standard molar enthalpies of formation, in the gaseous phase. Additionally, the gas-phase standard molar enthalpies of formation of these two compounds were estimated computationally as well as the

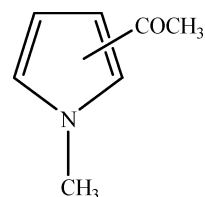


Figure 1. Structural formula of (2- or 3-) acetyl-1-methylpyrrole.

$\text{NCH}_2\text{—H}$  bond dissociation enthalpies, gas-phase basicities, proton and electron affinities, and adiabatic ionization enthalpies.

## 2. Experimental Section

**2.1. Materials and Purity Control.** The 2-acetyl-1-methylpyrrole [CAS 932-16-1] and 3-acetyl-1-methylpyrrole [CAS 932-62-7] were supplied by Alfa Aesar and Sigma-Aldrich Chemical Co., with mass fraction purities of 0.98 and 0.99, respectively.

The samples, both liquid at room temperature, were purified by repeated distillations under reduced pressure, and the purities were checked by gas–liquid chromatography and from the closeness to unity of the combustion carbon dioxide recovery ratios.

The average ratio of the mass of carbon dioxide recovered after combustion to that calculated from the mass of samples used in each experiment were  $(0.99995 \pm 0.00039)$  for 2-acetyl-1-methylpyrrole and  $(1.00017 \pm 0.00025)$  for 3-acetyl-1-methylpyrrole, where the uncertainties are twice the standard deviation of the mean.

The specific densities used to calculate the true mass from apparent mass in air and the boiling temperatures of 2-acetyl-1-methylpyrrole and 3-acetyl-1-methylpyrrole were, respectively,  $\rho = 1.051 \text{ g}\cdot\text{cm}^{-3}$ <sup>26</sup> and  $T = 473\text{–}474$  K at  $p = 101.3$  kPa and  $\rho = 1.038 \text{ g}\cdot\text{cm}^{-3}$ <sup>27</sup> and  $T = 421\text{–}423$  K at  $p = 2000$  Pa.

**2.2. Combustion Calorimetry.** The standard massic energies of combustion of 2- and 3-acetyl-1-methylpyrroles were measured by static bomb combustion calorimetry, using an isoperibol system equipped with a twin valve bomb, model 1108 (Parr Instrument, Illinois, USA), made of stainless steel and with an

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internal volume of 0.342 dm<sup>3</sup>. The bomb calorimeter, subsidiary apparatus, and technique have been previously described in the literature.<sup>28,29</sup>

The energy equivalent of the calorimeter was determined from the combustion of benzoic acid (NIST Thermochemical Standard 39j), with a massic energy of combustion, under bomb conditions, of  $-26434 \pm 3 \text{ J} \cdot \text{g}^{-1}$ .<sup>30</sup> The value of the energy equivalent of the calorimeter was found to be  $\varepsilon(\text{calor}) = 15995.3 \pm 2.0 \text{ J} \cdot \text{K}^{-1}$ , as a mean of six calibration experiments, for an average mass of water added to the calorimeter of 3119.6 g; the quoted uncertainty refers to the standard deviation of the mean. The calibration procedure was the one suggested by Coops et al.<sup>31</sup>

The liquid samples of the two studied compounds were burnt and contained in sealed polyethylene bags, for which we have determined the massic energy of combustion as  $\Delta_c u^\circ = -46282.4 \pm 4.8 \text{ J} \cdot \text{g}^{-1}$ , with 1.00 cm<sup>3</sup> of deionized water introduced into the bomb, which was purged twice to remove air, before being charged with 3.04 MPa of oxygen.

For all combustion experiments, the calorimeter temperatures were measured with a precision of  $\pm 1 \times 10^{-4} \text{ K}$ , at time intervals of 10 s, with a quartz crystal thermometer (Hewlett Packard HP 2804 A), interfaced to a PC programmed to collect data and to compute the adiabatic temperature change, by means of the program LABTERMO.<sup>32</sup>

For the cotton thread fuse of empirical formula  $\text{CH}_{1.686}\text{O}_{0.843}$ ,  $\Delta_c u^\circ = -16240 \text{ J} \cdot \text{g}^{-1}$ .<sup>33</sup> This value has been previously confirmed in our laboratory. The electrical energy for ignition was measured from the change in potential difference on the discharge of a 1400  $\mu\text{F}$  capacitor through a platinum ignition wire of diameter 0.05 mm. The amount of  $\text{HNO}_3$  produced in the combustion experiments was quantified by acid–base volumetric titrations of the bomb aqueous solutions; the corrections were based on  $-59.7 \text{ kJ} \cdot \text{mol}^{-1}$  for the molar energy of formation of 0.1 mol·dm<sup>-3</sup>  $\text{HNO}_3(\text{aq})$  from  $\text{N}_2(\text{g})$ ,  $\text{O}_2(\text{g})$ , and  $\text{H}_2\text{O}(\text{l})$ .<sup>34</sup> The amount of substance used in each experiment and on which the energy of combustion was based was determined from the total mass of carbon dioxide produced, taking into account that formed from the combustion of the cotton thread fuse and of the polyethylene.

An estimated value of pressure coefficient of massic energy, at  $T = 298.15 \text{ K}$ ,  $(\partial u/\partial p)_T = -0.2 \text{ J} \cdot \text{g}^{-1} \cdot \text{MPa}^{-1}$ , typical for most organic compounds,<sup>35</sup> was used for both studied compounds. The standard state corrections were calculated by the procedure given by Hubbard et al.<sup>36</sup>

The molar mass used for the two studied isomers was  $123.1525 \text{ g} \cdot \text{mol}^{-1}$ , according to the relative atomic weights recommended by the IUPAC Commission in 2005.<sup>37</sup>

**2.3. High-Temperature Calvet Microcalorimetry.** The standard molar enthalpies of vaporization of the two isomers were measured using the drop-microcalorimetric technique for vacuum sublimation, described by Skinner et al.,<sup>38</sup> for the sublimation of solid compounds and adapted in our laboratory for liquid vaporizations.<sup>39</sup> Both the apparatus and the technique have been previously described.<sup>40</sup>

The microcalorimeter was calibrated making use of the reported standard molar enthalpy of vaporization of *n*-undecane (Aldrich, mass fraction purity greater than 0.99),  $\Delta_f^\circ H_m^\circ(298.15 \text{ K}) = 56.580 \pm 0.566 \text{ kJ} \cdot \text{mol}^{-1}$ .<sup>41</sup> The calibration constant, *k*, of the calorimeter was obtained as the average of six independent experiments for the predefined temperature,  $k(T = 335 \text{ K}) = 1.0014 \pm 0.0025$ , where the uncertainty presented is the standard deviation of the mean.

Samples of about 6–9 mg of liquid compounds were introduced in thin glass capillary tubes sealed at one end. The

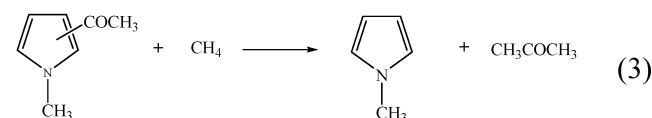
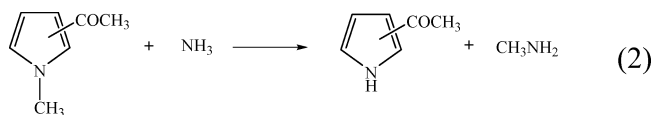
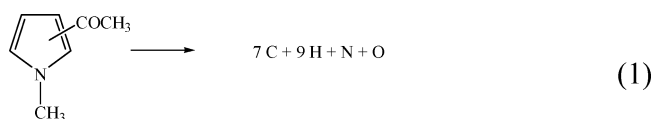
sample and the blank reference capillary tubes were simultaneously dropped into the hot reaction vessel, held at a suitable predefined temperature *T*, and then removed from the hot zone by vacuum vaporization.

The thermal corrections for the differences in the mass of both capillary tubes and different sensibilities of the two measuring cells were obtained by making separate blank correction experiments, dropping empty tubes of nearly equal mass into each of the twin cells.<sup>40</sup>

### 3. Computational Details

The standard ab initio molecular orbital calculations for the 2- and 3-acetyl-1-methylpyrroles were performed with Gaussian 03 computer code,<sup>42</sup> and the composite G3(MP2)//B3LYP approach was the methodology employed.<sup>43</sup> In this method, the geometry full-optimization and calculation of the frequencies of the molecule is done through the B3LYP/6-31G(d) approach. Then, single-point calculations are carried out at higher levels of theory: QCISD(T)/6-31G(d) and MP2/GTMP2Large. The energies computed at  $T = 0 \text{ K}$  were thermally corrected for  $T = 298.15 \text{ K}$  by introducing the vibrational, translational, rotational, and *pV* terms.

The enthalpies of formation of 2- and 3-acetyl-1-methylpyrroles were estimated by considering the following gas-phase atomization and working reactions



These reactions have been chosen taking into consideration the availability of accurate experimental thermochemical data of the species there involved.

The same composite approach was also used to calculate the  $\text{NCH}_2\text{--H}$  bond dissociation enthalpies, gas-phase basicities, proton and electron affinities, and adiabatic ionization enthalpies.

By convention, gas-phase basicity ( $\Delta G_{\text{basicity}}$ ), proton affinity (PA), and electron affinity (EA) were calculated as



where A = 2-acetyl-1-methylpyrrole or 3-acetyl-1-methylpyrrole.

**TABLE 1: Typical Combustion Results, at  $T = 298.15$  K ( $p^\circ = 0.1$  MPa), for the Studied Compounds<sup>a</sup>**

	2-acetyl-1-methylpyrrole	3-acetyl-1-methylpyrrole
$m(\text{CO}_2, \text{total})/\text{g}$	1.94828	1.55414
$m(\text{cpd})/\text{g}$	0.48166	0.32738
$m'(\text{fuse})/\text{g}$	0.00296	0.00305
$m''(\text{pol})/\text{g}$	0.23541	0.23275
$\Delta T_{\text{ad}}/\text{K}$	1.63765	1.32473
$\varepsilon_f/\text{J} \cdot \text{K}^{-1}$	16.63	16.26
$\Delta m(\text{H}_2\text{O})/\text{g}$	0	0
$-\Delta U(\text{IBP})^b/\text{J}$	26221.09	21209.96
$\Delta U(\text{fuse})/\text{J}$	48.07	49.53
$\Delta U(\text{pol})/\text{J}$	10895.35	10772.24
$\Delta U(\text{HNO}_3)/\text{J}$	38.27	29.62
$\Delta U(\text{ign})/\text{J}$	0.85	1.03
$\Delta U_\Sigma/\text{J}$	12.07	8.89
$-\Delta_c u^\circ/\text{J} \cdot \text{g}^{-1}$	31614.27	31613.66

<sup>a</sup>  $m(\text{CO}_2, \text{total})$  is the mass of  $\text{CO}_2$  recovered in each combustion;  $m(\text{cpd})$  is the mass of compound burnt in each experiment;  $m'(\text{fuse})$  is the mass of the fuse (cotton) used in each experiment;  $m''(\text{pol})$  is the mass of polyethylene used in each experiment;  $\Delta T_{\text{ad}}$  is the corrected temperature rise;  $\varepsilon_f$  is the energy equivalent of the contents in the final state;  $\Delta m(\text{H}_2\text{O})$  is the deviation of mass of water added to the calorimeter from 3119.6 g;  $\Delta U(\text{IBP})$  is the energy change for the isothermal combustion reaction under actual bomb conditions and includes  $\Delta U(\text{ignition})$ ;  $\Delta U(\text{fuse})$  is the energy of combustion of the fuse (cotton);  $\Delta U(\text{pol})$  is the energy of combustion of the polyethylene;  $\Delta U(\text{HNO}_3)$  is the energy correction for the nitric acid formation;  $\Delta U(\text{ign})$  is the electric energy for the ignition;  $\Delta U_\Sigma$  is the standard state correction;  $\Delta_c u^\circ$  is the standard massic energy of combustion. <sup>b</sup>  $\Delta U(\text{IBP})$  includes  $\Delta U(\text{ign})$ .

## 4. Results and Discussion

**4.1. Condensed Phase and Phase Transition.** Detailed results for one experiment of each studied compound are given in Table 1, where  $\Delta m(\text{H}_2\text{O})$  is the deviation of the mass of water added to the calorimeter from 3119.6 g, the mass assigned for  $\varepsilon(\text{calor})$ ;  $\Delta U_\Sigma$  is the correction to the standard state; and the remaining quantities are as previously described.<sup>36,44</sup> The internal energy for the isothermal bomb process,  $\Delta U(\text{IBP})$ , was calculated through eq 7, once the samples were ignited at  $T = 298.150 \pm 0.001$  K

$$\Delta U(\text{IBP}) = -\{\varepsilon(\text{calor}) + c_p(\text{H}_2\text{O}, \text{l}) \cdot \Delta m(\text{H}_2\text{O}) + \varepsilon_f\} \Delta T_{\text{ad}} + \Delta U(\text{ign}) \quad (7)$$

where  $\Delta T_{\text{ad}}$  is the calorimeter temperature change corrected for the heat exchange and the work of stirring. Detailed results of each combustion experiment, for the compounds studied, are given in the Supporting Information, Tables S1 and S2.

The individual values of  $\Delta_c u^\circ$ , together with the respective mean value,  $\langle \Delta_c u^\circ \rangle$ , and their standard deviations are presented in Table 2. The values of  $\Delta_c u^\circ$  refer to the idealized combustion reaction, described by eq 8

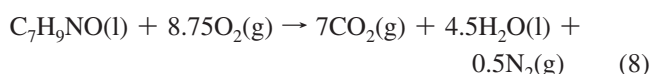


Table 3 presents the derived standard molar values for the energy,  $\Delta_c U_m^\circ(\text{l})$ , and enthalpy,  $\Delta_c H_m^\circ(\text{l})$ , of combustion reaction 8, as well as the standard molar enthalpies of formation,  $\Delta_f H_m^\circ(\text{l})$ , in the liquid phase, at  $T = 298.15$  K.

The uncertainties of the standard molar energies and enthalpies of combustion are twice the overall standard deviation of

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

2-acetyl-1-methylpyrrole	3-acetyl-1-methylpyrrole
$-\Delta_c u^\circ/\text{J} \cdot \text{g}^{-1}$	
31604.38	31623.17
31631.62	31626.18
31603.43	31611.78
31623.94	31628.63
31614.27	31600.62
31623.20	31613.66
$-\langle \Delta_c u^\circ \rangle/(\text{J} \cdot \text{g}^{-1})$	
$(31616.8 \pm 4.7)^a$	$(31615.4 \pm 4.2)^a$

<sup>a</sup> Mean value and standard deviation of the mean.

**TABLE 3: Derived Standard ( $p^\circ = 0.1$  MPa) Molar Energies of Combustion,  $\Delta_c U_m^\circ$ , Standard Molar Enthalpies of Combustion,  $\Delta_c H_m^\circ$ , and Standard Molar Enthalpies of Formation,  $\Delta_f H_m^\circ$ , for the Liquid Compounds, at  $T = 298.15$  K**

compound	$-\Delta_c U_m^\circ(\text{l})/\text{kJ} \cdot \text{mol}^{-1}$	$-\Delta_c H_m^\circ(\text{l})/\text{kJ} \cdot \text{mol}^{-1}$	$-\Delta_f H_m^\circ(\text{l})/\text{kJ} \cdot \text{mol}^{-1}$
2-acetyl-1-methylpyrrole	$3893.7 \pm 1.9$	$3896.8 \pm 1.9$	$144.0 \pm 2.1$
3-acetyl-1-methylpyrrole	$3893.5 \pm 1.9$	$3896.6 \pm 1.9$	$144.2 \pm 2.1$

the mean and include the uncertainties in calibration and in the values of the auxiliary quantities used.<sup>45,46</sup>

The values of the  $\Delta_f H_m^\circ(\text{l})$ , at  $T = 298.15$  K, were derived from the values of  $\Delta_c H_m^\circ(\text{l})$ , using the values of  $\Delta_f H_m^\circ$  of  $\text{H}_2\text{O}(\text{l})$ ,  $-285.830 \pm 0.042$  kJ  $\cdot$  mol<sup>-1</sup>, and of  $\text{CO}_2(\text{g})$ ,  $-393.51 \pm 0.13$  kJ  $\cdot$  mol<sup>-1</sup>.<sup>47</sup>

Results from microcalorimetric measurements of the enthalpies of vaporization are presented in Table 4. The observed enthalpies of vaporization, at  $T$ ,  $\Delta_f^T H_m^\circ$ , were corrected to  $T = 298.15$  K,  $\Delta_f^{\circ} H_m^\circ(298.15 \text{ K})$ , considering eq 9.

$$\Delta_{298.15 \text{ K}}^T H_m^\circ(\text{g}) = \int_{298.15 \text{ K}}^T C_{p,m}^\circ(\text{g}) dT \quad (9)$$

The gas-phase molar heat capacities of 2-acetyl-1-methylpyrrole (eq 10) and of 3-acetyl-1-methylpyrrole (eq 11) were derived from statistical thermodynamics using the vibrational frequencies from DFT calculations, B3LYP/6-31G(d) approach (scaled by 0.9614).<sup>48</sup> The gas-phase molar heat capacities for 2-acetyl-1-methylpyrrole and 3-acetyl-1-methylpyrrole between 150 and 600 K are listed in the Supporting Information, Table S3. The uncertainties associated with the values of  $\Delta_f^{\circ} H_m^\circ(298.15 \text{ K})$  are twice the overall standard deviation of the mean and include the uncertainties in calibration and in the gas-phase molar heat capacity.

$$C_{p,m}^\circ(\text{g})/(\text{J} \cdot \text{K}^{-1} \cdot \text{mol}^{-1}) = -5.69256 \times 10^{-7}(T/\text{K})^3 + 4.79416 \times 10^{-4}(T/\text{K})^2 + 2.71598 \times 10^{-1}(T/\text{K}) + 38.9776 \quad (R^2 = 0.99996) \quad (10)$$

$$C_{p,m}^\circ(\text{g})/(\text{J} \cdot \text{K}^{-1} \cdot \text{mol}^{-1}) = -5.75608 \times 10^{-7}(T/\text{K})^3 + 4.94017 \times 10^{-4}(T/\text{K})^2 + 2.59354 \times 10^{-1}(T/\text{K}) + 42.8551 \quad (R^2 = 0.99996) \quad (11)$$

By combining the standard molar enthalpies of formation in the liquid phase,  $\Delta_f H_m^\circ(\text{l})$ , with the standard molar enthalpies

**TABLE 4: Standard ( $p^\circ = 0.1$  MPa) Molar Enthalpies of Vaporization,  $\Delta_f H_m^\circ$ , for the Two Liquid Compounds, at  $T = 298.15$  K, Determined by Calvet Microcalorimetry**

compound	number of experiments	$T$ K	$\Delta_f^T H_m^\circ$ kJ·mol <sup>-1</sup>	$\Delta_{298.15\text{ K}}^T H_m^\circ(\text{g})$ kJ·mol <sup>-1</sup>	$\Delta_f H_m^\circ(298.15\text{ K})$ kJ·mol <sup>-1</sup>
2-acetyl-1-methylpyrrole	5	334.7	64.2 ± 0.2	5.6608 ± 0.0007	58.5 ± 1.3
3-acetyl-1-methylpyrrole	5	334.8	73.1 ± 0.4	5.7233 ± 0.0007	67.4 ± 1.6

**TABLE 5: Comparison between the Experimental and Computed G3(MP2)//B3LYP Gas-Phase Enthalpies of Formation of 2- and 3-Acetyl-1-Methylpyrroles, at  $T = 298.15$  K<sup>a</sup>**

compound	$-\Delta_f H_m^\circ(\text{g})/\text{kJ}\cdot\text{mol}^{-1}$				experimental
	atomization reaction (eq 1)	eq 2	eq 3	G3(MP2)//B3LYP	
2-acetyl-1-methylpyrrole	82.9 (−2.6)	85.1 (−0.4)	85.0 (−0.5)		85.5 ± 2.5
3-acetyl-1-methylpyrrole	74.9 (−1.9)	75.5 (−1.3)	77.0 (0.2)		76.8 ± 2.6

<sup>a</sup> Enthalpic differences between the experimental and computed values are given in parentheses.

of vaporization,  $\Delta_f H_m^\circ(298.15\text{ K})$ , the standard molar enthalpies of formation in the gaseous phase,  $\Delta_f H_m^\circ(\text{g})$ , were calculated and are registered in Table 5.

**4.2. Gas-Phase: Molecular Structures.** The molecular structures of 2-acetyl-1-methylpyrrole and 3-acetyl-1-methylpyrrole were fully optimized with the G3(MP2)//B3LYP composite approach, at the B3LYP/6-31G(d) level of theory, and are presented in Figure 2. Bond distances and bond angles obtained at this level of theory are also shown in Figure 2.

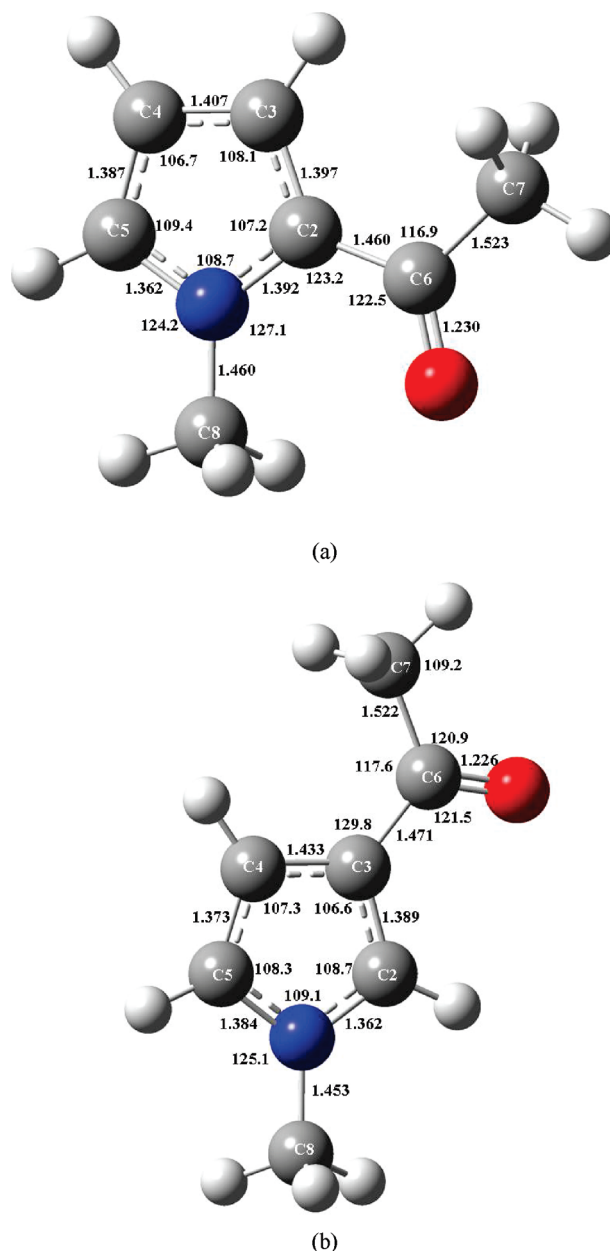
For both studied compounds, the calculated molecular structures are almost planar, pertaining to the symmetry point group  $C_1$ .

At the G3(MP2)//B3LYP level, the N-CH<sub>3</sub>O=syn is the preferred conformation for 2-acetyl-1-methylpyrrole (Figure 2); the N-CH<sub>3</sub>O=anti conformation is ca. 24 kJ·mol<sup>-1</sup> less stable than the N-CH<sub>3</sub>O=syn. This was already reported by us for 1-methyl-2-pyrrolecarboxylic acid,<sup>25</sup> in which the N-CH<sub>3</sub>O=anti conformation is ca. 8.9 kJ·mol<sup>-1</sup> less stable than the N-CH<sub>3</sub>O=syn. However, for 2-acetyl-1-methylpyrrole, the enthalpic difference between the two conformations is higher than in 1-methyl-2-pyrrolecarboxylic acid, showing that there is a higher destabilizing interaction between the -CH<sub>3</sub> from the acetyl group and the N-CH<sub>3</sub> group (2-acetyl-1-methylpyrrole, anti conformation) than between the -OH group from the carboxylic group and the N-CH<sub>3</sub> group (1-methyl-2-pyrrolecarboxylic acid, anti conformation).

For 3-acetyl-1-methylpyrrole, the N-CH<sub>3</sub>O=syn is also the most stable conformation (Figure 2). However, the difference between both types of structures is only 1.2 kJ·mol<sup>-1</sup>.

There is a very good agreement between the calculated geometric parameters for 2-acetyl-1-methylpyrrole and for 1-methyl-2-pyrrolecarboxylic acid.<sup>25</sup> For both title compounds, the geometrical parameters agree well with the corresponding ones found for 2- and 3-acetylpyrroles, previously reported by us.<sup>24</sup>

**4.3. Gas-Phase Theoretical Enthalpies of Formation.** The gas-phase enthalpies of formation of both studied compounds were estimated considering the computed enthalpies of reactions described by eqs 1–3 and the experimental enthalpies of formation in the gaseous phase of the other atoms and molecules there involved. The values of  $\Delta_f H_m^\circ(\text{g})$  used were: carbon, 716.67 kJ·mol<sup>-1</sup>;<sup>49</sup> hydrogen, 218.00 kJ·mol<sup>-1</sup>;<sup>49</sup> oxygen, 249.17 kJ·mol<sup>-1</sup>;<sup>49</sup> nitrogen, 472.68 kJ·mol<sup>-1</sup>;<sup>49</sup> ammonia, -45.90 kJ·mol<sup>-1</sup>;<sup>49</sup> 2-acetylpyrrole, -81.4 ± 1.6 kJ·mol<sup>-1</sup>;<sup>24</sup> 3-acetylpyrrole, -65.0 ± 1.6 kJ·mol<sup>-1</sup>;<sup>24</sup> methylamine, -23.4



**Figure 2.** Optimized most stable configurations for the 2-acetyl-1-methylpyrrole (syn) (a) and 3-acetyl-1-methylpyrrole (syn) (b). Distances are in Å and angles in degrees.



**TABLE 6: G3(MP2)//B3LYP Computed NCH<sub>2</sub>–H Bond Dissociation Enthalpies (BDE), Gas-Phase Basicities,  $\Delta G_{\text{basicity}}$ , Proton, PA, and Electron Affinities, EA, and Ionization Enthalpies, IE, at  $T = 298.15$  K, for 2-Acetyl-1-methylpyrrole and 3-Acetyl-1-methylpyrrole<sup>a</sup>**

compound	NCH <sub>2</sub> –H BDE	$\Delta G_{\text{basicity}}$	PA	EA	IE
2-acetyl-1-methylpyrrole	395.3	874.6	907.5 (O)	–20.5	800.1
3-acetyl-1-methylpyrrole	390.2	888.9	922.1 (O)	–48.3	797.1

<sup>a</sup> All values are in kJ·mol<sup>–1</sup>.

$\pm 1.0$  kJ·mol<sup>–1</sup>,<sup>50</sup> methane,  $-74.4 \pm 0.4$  kJ·mol<sup>–1</sup>,<sup>50</sup> 1-methylpyrrole,  $103.1 \pm 0.5$  kJ·mol<sup>–1</sup>,<sup>50</sup> and propanone,  $-217.1 \pm 0.7$  kJ·mol<sup>–1</sup>.<sup>50</sup>

The calculated enthalpies of formation are listed and compared with the experimental data in Table 5. As can be seen in the referred table, the agreement between the experimental and the G3(MP2)//B3LYP values is excellent. The maximum deviations from the experimental results are 2.6 and 1.9 kJ·mol<sup>–1</sup> for 2-acetyl-1-methylpyrrole and 3-acetyl-1-methylpyrrole, respectively, obtained using the respective atomization reaction. These deviations are within the interval defined by the uncertainty associated to the experimental values. For both compounds, the results estimated with the reaction described by eq 3 are almost equal to experimental results (deviations of 0.5 and 0.2 kJ·mol<sup>–1</sup> for 2-acetyl-1-methylpyrrole and 3-acetyl-1-methylpyrrole, respectively). It is also important to emphasize that three different reactions (atomization and working reactions) lead to estimated results that are in excellent agreement with the experimental data obtained in this work.

The computed G3(MP2)//B3LYP enthalpies for the compounds studied, auxiliary molecules, and atoms used in the atomization and working reactions are listed in Table S4 in the Supporting Information.

**4.4. Other Gas-Phase Thermodynamic Properties.** The G3(MP2)//B3LYP approach was used to compute some other thermodynamic properties for 2- and 3-acetyl-1-methylpyrroles. The calculated values of NCH<sub>2</sub>–H bond dissociation enthalpies (BDE), gas-phase basicities ( $\Delta G_{\text{basicity}}$ ), proton (PA) and electron affinities (EA), and adiabatic ionization enthalpies (IE) are reported in Table 6. This composite approach was applied in a previous work for the estimation of the referred thermodynamic properties of pyrrole, and the calculated values are in great agreement with the experimental or computational data found in the literature.<sup>24</sup>

No experimental or computational data for the two title compounds have been found in the literature for comparison with our results.

The calculated NCH<sub>2</sub>–H bond dissociation enthalpy for 2-acetyl-1-methylpyrrole (395.3 kJ·mol<sup>–1</sup>) is similar to that found for 1-methyl-2-pyrrolicarboxylic acid (396.7 kJ·mol<sup>–1</sup>), reported by us in a previous work.<sup>25</sup> For 3-acetyl-1-methylpyrrole, the enthalpy required for NCH<sub>2</sub>–H bond scission is ca. 5 kJ·mol<sup>–1</sup> lower than that corresponding in the 2-isomer. The NCH<sub>2</sub>–H bond dissociation enthalpies of both title compounds were compared with the C–H BDE of methylamine. Burkey et al.<sup>51</sup> reported an experimental value of 393.3 kJ·mol<sup>–1</sup>. Computationally, Wayner et al.,<sup>52</sup> using the G2(MP2) method, found C–H BDEs for methylamine of 388 kJ·mol<sup>–1</sup>, and Leroy et al.<sup>53</sup> using ab initio MP4/6-31+G(2df,p)/MP2/6-31G(d,p) obtained 391.6 kJ·mol<sup>–1</sup>. The calculated NCH<sub>2</sub>–H BDEs for 2-acetyl-1-methylpyrrole and 3-acetyl-1-methylpyrrole were

395.3 and 390.2 kJ·mol<sup>–1</sup>, which agree well with the reported results for methylamine.

For both title compounds, the introduction of a proton into each one occurs in the same position of the ring, i.e., in the oxygen of the acetyl group, which was already observed for 2- and 3-acetylpyrroles<sup>24</sup> (the preferred protonation site is the oxygen of the acetyl group), for 2- and 3-nitropyrroles<sup>54</sup> (the protonation occurs preferentially on the oxygen of the nitro group), and for 2-pyrrolicarboxylic acid and 1-methyl-2-pyrrolicarboxylic acid (both acids protonate on the carbonyl oxygen atom).<sup>25</sup> The N atom was found to be the least favorable protonation site for 2- and 3-acetyl-1-methylpyrroles, 2- and 3-acetyl-, 2- and 3-nitropyrroles, 2-pyrrolicarboxylic acid, and 1-methyl-2-pyrrolicarboxylic acid. The introduction of a methyl group into the N-position of 2- and 3-acetylpyrroles, to yield the respective 2- and 3-acetyl-1-methylpyrroles, increases the proton affinity by 14.6 and 21.5 kJ·mol<sup>–1</sup>. This was also verified, in a previous work, for the 2-pyrrolicarboxylic acid and its *N*-methyl derivative.<sup>25</sup> The computed proton affinities presented in Table 6 also show that O protonation occurs with more difficulty in 2-acetyl-1-methylpyrrole than in the respective 3-isomer.

The full set of computed proton affinities is reported in Table S5, in the Supporting Information.

The computed electron affinities reported in Table 6, show that the addition of an electron to the 3-acetyl-1-methylpyrrole is more unfavorable than when an electron is added to the 2-derivative. This behavior was already observed in 2- and 3-acetylpyrroles.<sup>24</sup> The entrance of an acetyl group in the 2-position of 1-methylpyrrole favors the electron affinity toward the entrance of a carboxylic group (EA =  $-20.5$  kJ·mol<sup>–1</sup> vs  $-38.2$  kJ·mol<sup>–1</sup>, respectively).<sup>25</sup> Regarding to the ionization enthalpies, it is possible to conclude that both studied isomers have almost the same electron donor capacity, as was found for 2- and 3-acetylpyrroles. However, the energy required to remove an electron from 1-methyl-2-pyrrolicarboxylic acid is 11.7 kJ·mol<sup>–1</sup> higher than that needed for 2-acetyl-1-methylpyrrole.<sup>25</sup>

## 5. Conclusions

A combined experimental and computational study was performed, and the standard molar enthalpies of formation, in the gaseous phase,  $\Delta_f H_m^\circ(\text{g})$ , at  $T = 298.15$  K, for 2- and 3-acetyl-1-methylpyrroles were obtained. Experimentally, these values were derived from the standard molar enthalpies of combustion and of vaporization, at  $T = 298.15$  K, retrieved from static bomb combustion calorimetry and Calvet microcalorimetry experiments. The experimental  $\Delta_f H_m^\circ(\text{g})$  values are  $-85.5 \pm 2.5$  kJ·mol<sup>–1</sup> and  $-76.8 \pm 2.6$  kJ·mol<sup>–1</sup>, for 2- and 3-acetyl-1-methylpyrroles, respectively.

The G3(MP2)//B3LYP approach was used to estimate the gas-phase enthalpies of formation of the title compounds, at  $T = 298.15$  K, and by considering several appropriate working reactions. All computed values are in excellent agreement with the experimental data here reported, all in the range of the experimental uncertainty. Other thermodynamic properties of the 2- and 3-acetyl-1-methylpyrroles were also calculated by means of this composite method.

**Acknowledgment.** Thanks are due to Fundação para a Ciência e a Tecnologia, F.C.T., Lisbon, Portugal, and to FEDER for financial support to Centro de Investigação em Química, University of Porto. A.F.L.O.M.S. thanks FCT and the European Social Fund (ESF) under the Community Support Framework

(CSF) for the award of the postdoctoral fellowship (SFRH/BPD/41601/2007).

**Supporting Information Available:** Data and the details of all the combustion calorimetry experiments for the 2-acetyl-1-methylpyrrole and 3-acetyl-1-methylpyrrole, the computational gas-phase molar heat capacities for 2-acetyl-1-methylpyrrole and 3-acetyl-1-methylpyrrole, G3(MP2)//B3LYP enthalpies (energies plus thermal corrections for  $T = 298.15$  K) for the 2-acetyl-1-methylpyrrole and 3-acetyl-1-methylpyrrole, for the auxiliary molecules, and for the atoms used in the several working reactions, and G3(MP2)//B3LYP computed proton affinities, PA, at  $T = 298.15$  K, for 2-acetyl-1-methylpyrrole and 3-acetyl-1-methylpyrrole. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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JP911323C