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Thermochemistry of Some Derivatives of 2- and 4-Piperidone

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Standard ($p° = 0.1$ MPa) massic energies of combustion for 2-piperidone, 1-methyl-2-piperidone, 1-benzyl-2-piperidone, 1-methyl-4-piperidone, 1-ethyl-4-piperidone, and 1-benzyl-4-piperidone were measured at $T = 298.15$ K by static bomb calorimetry. The standard molar enthalpies of formation in the condensed phase were derived. The standard molar enthalpies of vaporization at $T = 298.15$ K of the piperidone and derivatives studied were determined by high-temperature Calvet microcalorimetry. The respective standard molar enthalpies of formation in the gaseous phase, at $T = 298.15$ K, were derived. These results are discussed in terms of molecular structure contributions.

Introduction

Among the piperidine derivatives, piperidones are important intermediates in several synthetic reactions[1]. Due to the known therapeutic properties of piperidones and due to the presence of a keto function that facilitates the introduction of other substituents on the piperidine ring, piperidones are widely used in the synthesis of new drugs. For example, 2-piperidones were found to be good selective EP4 receptor agonists[2] while the 4-piperidone derivatives were found to be good row materials for preparation of analgesics[3] and other compounds that have an effect on the central nervous system.[4]

The literature data on experimental thermochemical work of piperidones are scarce: the standard molar enthalpy of formation of the 2-piperidone in solid phase was determined by Strepikeev et al.[5] as $\Delta_f H_m^\circ$ (2-piperidone, cr) = (−306.59 ± 0.80) kJ·mol^{-1}, and the standard molar enthalpy of formation in liquid phase of 1-methyl-2-piperidone was derived by Kozina et al.[6] as $\Delta_f H_m^\circ$ (1-methyl-2-piperidone, l) = (−293.13 ± 0.91) kJ·mol^{-1}. These properties for these two compounds were re-determined in the present work. Lebedev et al.[7] measured the standard molar enthalpy of formation in the condensed and in the gaseous phases for the 2,2,4,4-tetramethylpiperidone as $\Delta_f H_m°(\text{cr}) = (-206.9 \pm 2.0)$ kJ·mol^{-1} and $\Delta_f H_m^\circ(\text{g}) = (-273.5 \pm 6.2)$ kJ·mol^{-1}, respectively. Yan and Pilcher[8] by combustion calorimetry of 2,6-piperidione derived $\Delta_f H_m^\circ(\text{cr}) = (-487.7 \pm 0.8)$ kJ·mol^{-1} and $\Delta_f H_m^\circ(\text{g}) = (-393.6 \pm 1.8)$ kJ·mol^{-1}.

As part of our systematic study of the thermochemical properties of piperidine derivatives, in the present work we report the standard molar enthalpies of formation in the condensed and gaseous phases, at $T = 298.15$ K, and the standard molar enthalpies of transition from the condensed to the gaseous phase of the solid 2-piperidone and of the liquids 1-methyl-2-piperidone, 1-methyl-4-piperidone, 1-benzyl-2-piperidone, 1-benzyl-4-piperidone, and 1-ethyl-4-piperidone.

Experimental Section

Materials. The 2-piperidone derivatives [namely, 2-piperidone (CAS Registry No. (or CASRN) 675-20-7), 1-methyl-2-piperidone (CASRN 931-20-4), 1-benzyl-2-piperidone (CASRN 4783-65-7)] and the 4-piperidone derivatives [1-methyl-4-piperidone (CASRN 1445-73-4), 1-ethyl-4-piperidone (CASRN 3612-18-8), and 1-benzyl-4-piperidone (CASRN 3612−20−2)], whose structural forms are shown in Figure 1, were all obtained commercially from the Sigma-Aldrich Chemical Co. The compound 2-piperidone in the solid phase was purified by vacuum sublimation, while all the others, which are liquids, were purified by fractional distillation under reduced pressure, stored, and handled under nitrogen atmosphere. As the amount of the compound used in each experiment was based on the amount of CO_2 produced in the combustion reaction, the purification process of each compound was repeated until the carbon dioxide recovery ratios were satisfactory as carbon dioxide determination is a good indication of the purity and dryness of the materials. The densities of the compounds, at $T = 298.15$ K, as well the CO_2 recovery ratios obtained experimentally are presented in Table 1. In the case of 1-methyl-2-piperidone, 1-benzyl-2-piperidone, and 1-methyl-4-piperidone, these compounds absorbed a small amount of water when they were handled during the experiments as indicated by the lower values for the CO_2 recoveries, which is expected to have no influence in the value of the massic energy of combustion since the amount of compound used was based on the mass of CO_2 produced in the combustion experiments. The presence of water in these compounds was confirmed by Karl Fischer titration. GLC and DSC experiments were carried out for liquids and solids, respectively, to confirm the absence of other impurities than water in all compounds studied.

Combustion Measurements. The static bomb combustion calorimeter used in this work to measure the standard ($p° = 0.1$ MPa) massic energies of combustion has already been described in the literature.[9,10] The calorimeter and the bomb (a twin-valve combustion bomb, type 1105, Parr Instruments Company) made of stainless steel with an internal volume of 0.340 dm^3 were calibrated by combustion of the NIST Thermochemical Standard for benzoic acid. For the compound 1-methyl-2-piperidone, the energy equivalent of the calorimeter (ϵ_{cal}) was determined as $\epsilon_{cal} = (15908.78 \pm 0.77)$ J·K^{-1} from six independent combustion experiments with benzoic acid, BAS 693976/01, [$\Delta_c u = (-26435.1 \pm 3.5)$ J·g^{-1} under bomb conditions[11]]. For the other compounds, the calibration was made

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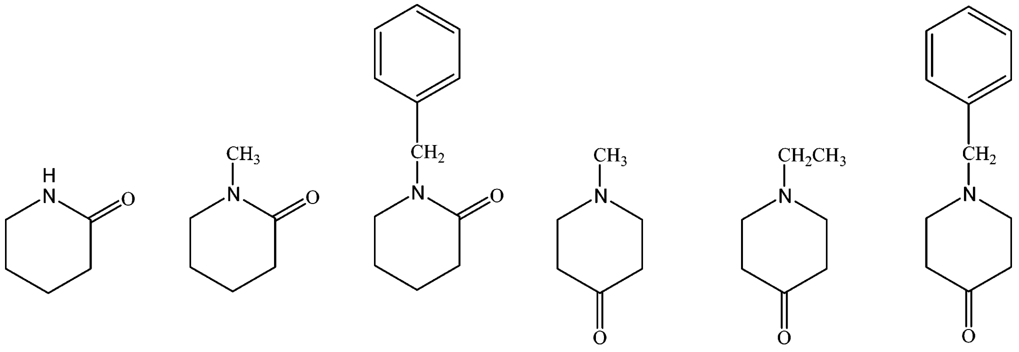


Figure 1. Structural formulas of 2-piperidone (**1**), 1-methyl-2-piperidone (**2**), 1-benzyl-2-piperidone (**3**), 1-methyl-4-piperidone (**4**), 1-ethyl-4-piperidone (**5**), and 1-benzyl-4-piperidone (**6**).

Table 1. Physical Properties of the Compounds

compound	formula	M / g·mol^{-1}	% CO_2 recovery[a]	ρ / kg·m^{-3}
2-piperidone(cr)	C_5H_9NO	99.131	99.973 ± 0.030	1.02[b]
1-methyl-2-piperidone(l)	$C_6H_{11}NO$	113.158	99.861 ± 0.141	0.997[c]
1-benzyl-2-piperidone(l)	$C_{12}H_{15}NO$	189.254	99.863 ± 0.047	1.07[c]
1-methyl-4-piperidone(l)	$C_6H_{11}NO$	113.158	99.330 ± 0.134	0.973[c]
1-ethyl-4-piperidone(l)	$C_7H_{13}NO$	127.184	100.011 ± 0.003	0.944[c]
1-benzyl-4-piperidone(l)	$C_{12}H_{15}NO$	189.254	99.945 ± 0.015	1.021[c]

[a] Mean and standard deviation of the mean. [b] Determined experimentally. [c] www.sigmaaldrich.com.

with NIST Thermochemical Standard for benzoic acid. The certified value of the National Institute of Standards and Technology for the benzoic acid used, sample 39j, was $\Delta_c u = (-26434 \pm 3)$ J·g^{-1}.[12] Under experimental conditions and from six independent experiments, the energy equivalent was determined as $\epsilon_{cal} = (15905.72 \pm 0.96)$ J·K^{-1}, using the same procedure as described previously.[13] The energy equivalent was corrected to the average mass of water added to the calorimeter, 3119.6 g, weighed with an accuracy of ± 10^{-1} g in a Mettler PC 8000 balance with the uncertainty associated to ϵ_{cal} being the standard deviation of the mean.

The combustion experiments were made in oxygen at p = 3.04 MPa, with 1.00 cm^3 of water added to the bomb. As 2-piperidone is hygroscopic, it was necessary to seal the pellets of this compound in polyester bags made of Melinex film with 0.025 mm thickness to prevent the absorption of water during the combustion experiments. The liquid samples were also burnt-sealed in Melinex bags. The mass of Melinex used in each experiment was corrected for the mass fraction of water (0.0032), and the mass of CO_2 produced was calculated using the factor reported in the literature.[14] The weighings necessary within the combustion experiments (namely, of the Melinex bag, the compound under study, the cotton-thread fuse, and the platinum crucible containing the sample) were done with an accuracy of ±10−^{5} g with a Mettler AT240 balance. The ignitions were made at $T = (298.150 \pm 0.001)$ K by discharge of a 1400 μF capacitor through the platinum ignition wire. A cotton-thread of empirical formula $CH_{1.686}O_{0.843}$ [13] was used as the fuse. All temperature readings were made with a quartz crystal thermometer (Hewlett-Packard HP 2804 A) interfaced to a PC. At least 100 readings, at time intervals of 10 s, were taken for the initial, main, and final periods of the combustion experiments.

At the end of the experiments, the CO_2 produced was determined. The gases produced in combustion were driven through CO_2 recovering tubes, filled with Carbosorb AS self-indicating and previously weighed with a Mettler AT201 balance. Subsquently, the amount of HNO_3 formed was determined by titration of the solution resulting from washing the inside of the bomb, and the eventual presence of carbon soot was verified. If only a small quantity of carbon was formed inside the crucible, this amount was taken into account for the massic energy of combustion. If carbon residue was formed on the bomb walls, the experiment was rejected.

Calvet Microcalorimetric Measurements. The standard molar enthalpy of sublimation of 2-piperidone was measured using the same method described by Skinner and co-workers,[15] the "vacuum sublimation drop microcalorimetric method". For the vaporization of the other liquid compounds, the same procedure, previously tested for liquid vaporization in our laboratory,[16] was used. The apparatus and technique have been already described in the literature.[17] Samples of about 4−5 mg of each compound, contained in thin glass capillary tubes sealed at one end, were dropped from room temperature into the hot reaction vessel in the Calvet high-temperature microcalorimeter (Setaram HT 1000D) held at a predefined temperature, T, and then removed from the hot zone by vacuum vaporization. The temperatures of the calorimeter at which the experiments were carried out were the following ones: for 2-piperidone and 1-methyl-4-piperidone, T = 334 K; for 1-methyl-2-piperidone, T = 355 K; for 1-benzyl-2-piperidone, T = 427 K; and for 1-ethyl-4-piperidone and 1-benzyl-4-piperidone, the temperature was T = 358 K. The thermal correction for the glass capillary was made by dropping tubes of nearly equal masses into each of the twin cells.

The calibration constants of the calorimeter, k_{cal}, were obtained as the average of at least six independent calibration experiments, following the same procedure as the one previously described for the compounds. For the liquid compounds, n-undecane was used to calibrate, in situ, the calorimeter using its reported standard molar enthalpy of vaporization at T = 298.15 K, $\Delta_{\mathrm{l}}^{\mathrm{g}}H_{\mathrm{m}}^{\circ} = (56.580 \pm 0.566)$ kJ·mol^{-1},[18] and yielding the following values: at T = 334 K, $k_{cal} = (1.0134 \pm 0.0075)$; at T = 355 K, $k_{cal} = (1.0177 \pm 0.0075)$; at T = 358 K, $k_{cal} = (1.0167 \pm 0.0021)$; at T = 427 K, $k_{cal} = (1.0200 \pm 0.0044)$. At the experimental temperature of the sublimation of the 2-piperidone, T = 334 K, the calorimeter was calibrated with naphthalene with standard molar enthalpy of sublimation, at T = 298.15 K, of $\Delta_{\mathrm{cr}}^{\mathrm{g}}H_{\mathrm{m}}^{\circ} = (72.60 \pm 0.60)$ kJ·mol^{-1},[18] yielding $k_{cal} = (0.9913 \pm 0.0063)$.

Calorimetric Calculations and Results

Typical combustion experiments for each of the six compounds are summarized in Table 2. The detailed results for all the combustion experiments of each compound, together with

Table 2. Typical Combustion Experiments, at $T = 298.15$ K, for Each Compound[a]

experiment	2-piperidone	1-methyl-2-piperidone	1-benzyl-2-piperidone	1-methyl-4-piperidone	1-ethyl-4-piperidone	1-benzyl-4-piperidine
$m(CO_2$, total)/g	1.39837	1.52769	1.96535	1.60130	2.04489	2.16416
m(cpd)/g	0.59536	0.60157	0.66430	0.63434	0.80315	0.73610
m(Melinex)/g	0.03170	0.05121	0.04691	0.05024	0.04207	0.04650
m(fuse)/g	0.00260	0.00410	0.00259	0.00370	0.00240	0.00276
ΔT_{ad}/K	1.16208	1.29360	1.53881	1.38672	1.79860	1.71631
$\epsilon_f/(J\cdot K^{-1})$	16.08	16.55	16.44	16.62	17.23	16.58
$\Delta m(H_2O)$/g	−0.1	0	0	0	+ 0.1	0
$-\Delta U(IBP)^b$/J	18501.90	20601.03	24501.15	22084.10	28639.75	27327.58
ΔU(Melinex)/J	726.01	1172.85	1074.39	60.09	963.59	1065.02
ΔU(fuse)/J	42.22	66.58	42.06	1150.69	38.98	44.82
$\Delta U(HNO_3)$/J	40.54	37.49	35.46	42.33	54.51	44.00
ΔU(ign)/J	0.90	1.19	1.14	1.19	0.78	0.75
$-\Delta U$(carbon)/J	0	0	0	0	6.60	7.92
ΔU_Σ/J	9.72	10.26	13.47	10.69	13.18	14.92
$-\Delta_c u°/J\cdot g^{-1}$	29700.53	32103.76	35126.64	32820.11	34333.95	35546.79

[a] $m(CO_2)$ is the mass of CO_2 recovered in the combustion. m(cpd) is the mass of compound burned in each experiment. m(Melinex) is the mass of Melinex used to enclose the samples. m(fuse) is the mass of fuse (cotton) used in each experiment. ΔT_{ad} is the corrected temperature rise. ϵ_f is the energy equivalent of 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. ΔU(Melinex) is the energy of combustion of the Melinex used in each experiment. ΔU(fuse) is the energy of combustion of the fuse (cotton). $\Delta U(HNO_3)$ is the energy correction for the nitric acid formation. ΔU(ign) is the electrical energy for ignition. ΔU(carbon) is the massic energy correction for the carbon residue soot. ΔU_Σ is the standard state correction. $\Delta_c u°$ is the standard massic energy of combustion. [b] ΔU(IBP) already includes the ΔU(ign).

Table 3. Individual Values of the Massic Energy of Combustion, $\Delta_c u°$, for All Compounds, at $T = 298.15$ K

2-piperidone(cr)	1-methyl-2-piperidone(l)	1-benzyl-2-piperidone(l)	1-methyl-4-piperidone(l)	1-ethyl-4-piperidone(l)	1-benzyl-4-piperidine(l)
		$-\Delta_c u°/(J\cdot g^{-1})$			
29695.38	32103.76	35126.64	32820.11	34344.09	35548.81
29700.53	32118.17	35132.98	32821.86	34338.56	35546.79
29694.43	32123.86	35147.24	32825.19	34333.95	35576.81
29680.53	32132.07	35126.44	32820.70	34336.09	35556.00
29709.13	32147.54	35133.62	32826.91	34336.67	35569.06
29710.38	32146.29	35129.10	32807.14	34332.42	35555.82
		$-<\Delta_c u°>/(J\cdot g^{-1})$			
29698.4 ± 4.5	32128.6 ± 6.9	35132.7 ± 3.2	32820.3 ± 2.8	34337.0 ± 1.7	35558.9 ± 4.8

Table 4. Condensed Phase Standard ($p° = 0.1$ MPa) Molar Thermochemical Functions at $T = 298.15$ K

	$-\Delta_c U^\circ_m$	$-\Delta_c H^\circ_m$	$-\Delta_f H^\circ_m$(cr or l)
compound	$kJ\cdot mol^{-1}$	$kJ\cdot mol^{-1}$	$kJ\cdot mol^{-1}$
2-piperidone(cr)	2944.0 ± 1.2	2947.1 ± 1.2	306.7 ± 1.4
1-methyl-2-piperidone(l)	3635.6 ± 1.9	3639.9 ± 1.9	293.2 ± 2.0
1-benzyl-2-piperidone(l)	6649.0 ± 2.2	6655.8 ± 2.2	210.0 ± 2.7
1-methyl-4-piperidone(l)	3713.9 ± 1.2	3718.2 ± 1.2	214.9 ± 1.4
1-ethyl-4-piperidone(l)	4367.1 ± 1.3	4372.7 ± 1.3	239.8 ± 1.6
1-benzyl-4-piperidone(l)	6729.7 ± 2.6	6736.5 ± 2.6	129.3 ± 3.0

the mean value of the standard massic energies of combustion, $\Delta_c u°$, are presented in the Supporting Information (Tables S1 to S6). The mass of compound, m(cpd), used in each experiment was determined from the total mass of CO_2 produced in each combustion, $m(CO_2$, total), taking into account the amount of CO_2 produced by the combustion of the fuse and of the Melinex film and that lost due to eventual carbon formation in incomplete combustions. The small amounts of water present in 1-methyl-2-piperidone, 1-benzyl-2-piperidone, and 1-methyl-4-piperidone is expected to have negligible effects on the values of the energy of combustion since the amount of compound used in each combustion experiment is calculated from the mass of CO_2 produced in that combustion experiment.

The internal energy for the isothermal bomb process, ΔU(IPB), was calculated according to $\Delta U(IPB) = -\{\epsilon_{cal} + \Delta m(H_2O)c_p(H_2O, l) + \epsilon_f\}\Delta T_{ad} + \Delta U(ign)$, where $\Delta m(H_2O)$ is the deviation of the mass of water added to the calorimeter from the average mass (3119.6 g) assigned to ϵ_{cal}, $c_p(H_2O, l)$ is the heat capacity of liquid water, ϵ_f is the energy equivalent of the bomb contents in the final state, ΔT_{ad} is the adiabatic temperature change corrected for the heat exchange and the work of stirring, and ΔU(ign) is the electrical energy of ignition. The energies of combustion of the Melinex and of the cotton-thread fuse were calculated from the respective massic energies of combustion: $\Delta_c u°(\text{Melinex}) = (-22902 \pm 5)\ J\cdot g^{-1}$ [14] and $\Delta_c u°(\text{fuse}) = -16250\ J\cdot g^{-1}$.[13] The correction for nitric acid formation, $\Delta U(HNO_3)$, was based on $-59.7\ kJ\cdot mol^{-1}$,[19] for the molar energy of formation of 0.1 $mol\cdot dm^{-3}$ HNO_3(aq) from N_2(g), O_2(g), and H_2O(l). In the experiments with carbon residue soot formation during the combustion, the necessary energetic correction for its formation was based on $\Delta_c u°(\text{carbon}) = -33\ J\cdot g^{-1}$.[20]

The electrical energy for ignition, ΔU(ign), was determined from the change in potential difference across a capacitor when discharged through the platinum wire. For all compounds, the corrections to standard state, ΔU_Σ, and the calculation of $\Delta_c u°$ were made as described by Hubbard et al.[21] For each compound it was assumed that $(\partial u/\partial T)_T$ was $-0.2\ J\cdot g^{-1}MPa^{-1}$ at $T = 298.15$ K, a typical value for organic compounds.[22]

The molar masses used for the elements were those recommended in 2001 by the IUPAC Commission.[23] The molar masses of each compound are registered in Table 1. The individual values of the standard massic energy of combustion, $\Delta_c u°$, for all the combustion experiments of each compound, together with the mean values and their standard deviation, are presented in Table 3.

Table 4 lists for each compound the derived values for the standard molar energies ($\Delta_c U^\circ_m$) and enthalpies ($\Delta_c H^\circ_m$) of the combustion reactions according to eq 1 for 2-piperidone, eq 2 for 1-methyl-2-piperidone and 1-methyl-4-piperidone, eq 3 for

Table 5. Individual Values of the Standard Molar Enthalpy of Vaporization or Sublimation for the Compounds, at the Experimental Temperatures[a]

2-piperidone(cr)	1-methyl-2-piperidone(l)	1-benzyl-2-piperidone(l)	1-methyl-4-piperidone(l)	1-ethyl-4-piperidone(l)	1-benzyl-4-piperidine(l)
		$\Delta_{\mathrm{cr\ or\ l,\ 298.15\ K}}^{g,T}H_{\mathrm{m}}^{\circ}$			
82.77	67.95	120.12	58.28	65.77	91.18
83.57	67.97	121.19	57.75	65.64	91.72
81.39	68.38	120.80	59.64	66.34	91.20
84.39	68.11	122.48	59.74	66.38	90.41
81.71	67.91	121.86	58.97	67.60	89.42
83.40	68.15		59.69		
		$<\Delta_{\mathrm{cr\ or\ l,\ 298.15\ K}}^{g,T}H_{\mathrm{m}}^{\circ}>/(\mathrm{kJ\cdot mol^{-1}})$			
82.87 ± 0.47	68.08 ± 0.07	121.29 ± 0.41	59.01 ± 0.34	66.35 ± 0.35	90.79 ± 0.40

[a] For 2-piperidone and 1-methyl-4-piperidone, T = 334 K. For 1-methyl-2-piperidone, T = 355 K. For 1-benzyl-2-piperidone, T = 427K. For 1-ethyl-4-piperidone and 1-benzyl-4-piperidone, T = 358 K.

1-benzyl-2-piperidone and for 1-benzyl-4-piperidone, and eq 4 for 1-ethyl-4-piperidone:

$$C_5H_9NO(cr) + \frac{27}{4}O_2(g) \rightarrow 5CO_2(g) + \frac{9}{2}H_2O(l) + \frac{1}{2}N_2(g) \quad (1)$$

$$C_6H_{11}NO(l) + \frac{33}{4}O_2(g) \rightarrow 6CO_2(g) + \frac{11}{2}H_2O(l) + \frac{1}{2}N_2(g) \quad (2)$$

$$C_{12}H_{15}NO(l) + \frac{61}{4}O_2(g) \rightarrow 12CO_2(g) + \frac{15}{2}H_2O(l) + \frac{1}{2}N_2(g) \quad (3)$$

$$C_7H_{13}NO(l) + \frac{39}{4}O_2(g) \rightarrow 7CO_2(g) + \frac{13}{2}H_2O(l) + \frac{1}{2}N_2(g) \quad (4)$$

In accordance with normal thermochemical practice, the uncertainties assigned to the standard molar enthalpies of combustion are, in each case, twice the overall standard deviation of the mean and include the uncertainties in calibration[24,25] and in the values of the auxiliary quantities. The values of the standard molar enthalpies of formation in the condensed phase, $\Delta_f H_m^\circ$ (cr or l), registered in Table 4, were derived from $\Delta_c H_m^\circ$ using the values at T = 298.15 K of the standard molar enthalpies of formation of liquid water and gaseous carbon dioxide, respectively: $\Delta_f H_m^\circ(H_2O,\ l) = (-285.830 \pm 0.042)$ kJ·mol^{-1} [26] and $\Delta_f H_m^\circ(CO_2,\ g) = (-393.51 \pm 0.13)$ kJ·mol^{-1}.[26]

The individual values for the standard molar enthalpies of sublimation, together with the mean and the corresponding standard deviation, of 2-piperidone and for the vaporization of 1-methyl-2-piperidone, 1-benzyl-2-piperidone, 1-methyl-4-piperidone, 1-ethyl-4-piperidone, and 1-benzyl-4-piperidone, all at the experimental working temperature, are given in Table 5. These values were corrected to T = 298.15 K, using $\Delta_{298\ K}^{T}H_m^\circ(g)$ estimated by a group scheme based on the values of Messerly et al.[27] and Stull et al.[28] The schemes applied for the different compounds were as follows:

2-piperidone = piperidine + cyclohexanone − cyclohexane

1-methyl-2- or 4-piperidone = piperidine + cyclohexanone −
cyclohexane + methylamine − ammonia

1-benzyl-2- or 4-piperidone = piperidine +
cyclohexanone − cyclohexane + methylamine −
ammonia + methylbenzene − methane

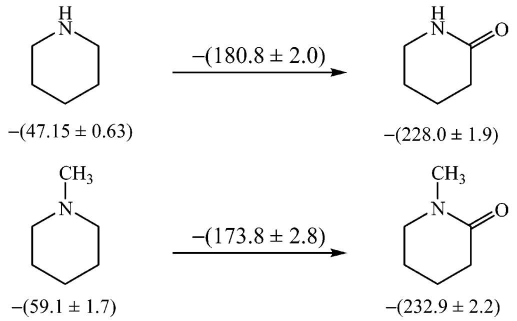
and

1-ethyl-4-piperidone = piperidine + cyclohexanone −
cyclohexane + ethylamine −ammonia

which yielded for 2-piperidone, at T =334.1 K, $\Delta_{298.15\ K}^{334.1K}H_m^\circ(g)$ = 4.22 kJ·mol^{-1}; for 1-methyl-2-piperidone, at T = 354.9 K, $\Delta_{298.15\ K}^{354.9K}H_m^\circ(g)$ = 7.78 kJ·mol^{-1}; for 1-benzyl-2-piperidone, at T = 426.9 K, $\Delta_{298.15\ K}^{426.9K}H_m^\circ(g)$ = 30.03 kJ·mol^{-1}; for 1-methyl-4-piperidone, at T = 334.5 K, $\Delta_{298.15\ K}^{334.5K}H_m^\circ(g)$ = 4.83 kJ·mol^{-1}; for 1-ethyl-2-piperidone, at T = 357.8 K, $\Delta_{298.15\ K}^{357.8K}H_m^\circ(g)$ = 9.68 kJ·mol^{-1}; and for 1-benzyl-4-piperidone, at T = 357.8 K, $\Delta_{298.15\ K}^{357.8K}H_m^\circ(g)$ = 12.84 kJ·mol^{-1}. The standard molar enthalpies of sublimation or vaporization, at T = 298.15 K, for each compound are given in Table 6, where the uncertainties are twice the overall standard deviation of the mean and include the uncertainties in calibration. The derived standard molar enthalpies of formation in the solid or liquid states and in the gaseous phase, at T = 298.15 K, are also summarized in Table 6.

Discussion and Conclusions

The experimental thermochemical results presented in this work enable one to establish the enthalpic effect due to the presence of the keto group in the piperidine ring. Considering the standard molar enthalpy of formation in gaseous phase of piperidine, $\Delta_f H_m^\circ$(piperidine, g) = (−47.15 ± 0.63) kJ·mol^{-1},[29] and 1-methylpiperidine, $\Delta_f H_m^\circ$(1-methylpiperidine, g) = (−59.1 ± 1.7) kJ·mol^{-1},[30] previously published, and the values reported in this work for 2-piperidone and 1-methyl-2-piperidone, $\Delta_f H_m^\circ$(2-piperidone, g) = (−280.0 ± 1.9) kJ·mol^{-1} and $\Delta_f H_m^\circ$(1-methyl-2-piperidone, g) = (−232.9 ± 2.2) kJ·mol^{-1}, the enthalpic increment due to oxidation of the piperidine to 2-piperidone is (−180.8 ± 2.0) kJ·mol^{-1}, a value slightly higher than that verified for the oxidation of 1-methylpiperidine to 1-methyl-2-piperidone, (−173.8 ± 2.8) kJ·mol^{-1}, as can be seen in the following scheme (all the values in kJ·mol^{-1}):

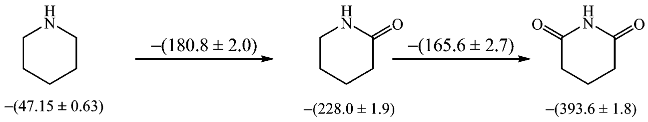


These results suggest that the stabilization of 2-piperidone due to electronic delocalization between the oxygen and nitrogen lone pair of electrons is not so evident in the case of 1-methyl-2-piperidone and may be caused by stereochemical effects on the methyl group. The introduction of a second carbonyl group

Table 6. Derived Standard ($p^\circ = 0.1$ MPa) Molar Enthalpies of Formation, $\Delta_f H_m^\circ$, and of Phase Transition, $\Delta_{cr\ or\ l}^{g} H_m^\circ$, at T = 298.15 K

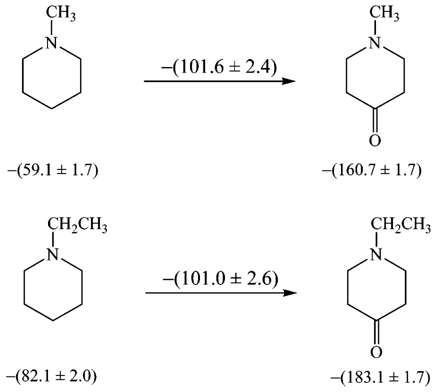
compound	$-\Delta_f H_m^\circ$(cr or l) kJ·mol^{-1}	$\Delta_{cr\ or\ l}^{g} H_m^\circ$ kJ·mol^{-1}	$-\Delta_f H_m^\circ$(g) kJ·mol^{-1}
2-piperidone(cr)	306.7 ± 1.4	78.7 ± 1.3	228.0 ± 1.9
1-methyl-2-piperidone (l)	293.2 ± 2.0	60.30 ± 0.90	232.9 ± 2.2
1-benzyl-2-piperidone (l)	210.0 ± 2.7	91.3 ± 1.0	118.7 ± 2.9
1-methyl-4-piperidone (l)	214.9 ± 1.4	54.2 ± 1.0	160.7 ± 1.7
1-ethyl-4-piperidone (l)	239.8 ± 1.6	56.67 ± 0.63	183.1 ± 1.7
1-benzyl-4-piperidone (l)	129.3 ± 3.0	77.95 ± 0.76	51.4 ± 3.1

in position 6 to form the 2,6-piperidinone compound, $\Delta_f H_m^\circ$(2,6-piperidinone, g) = (−393.6 ± 1.8) kJ·mol^{-1} [8], decreases the enthalpy by (−165.6 ± 2.7) kJ·mol^{-1}, an increment that is lower than the one verified for the oxidation of the piperidine to 2-piperidone:



The diminution of the enthalpic increment with the successive introduction of carbonyl groups is a possible result of stereochemical repulsion effects of the lone pair of electrons.

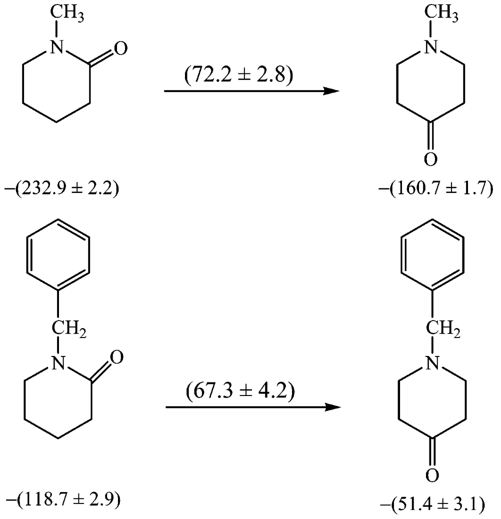
In the same way, the enthalpic increment concerning the oxidation of the piperidine ring in position 4 can be analyzed in the scheme presented below:



The enthalpic increment verified to the oxidation of 1-methylpiperidine and 1-ethylpiperidine [$\Delta_f H_m^\circ$(1-ethylpiperidine, g) = (−82.1 ± 2.0) kJ·mol^{-1} [31]] to respectively 1-methyl-4-piperidone and 1-ethyl-4-piperidone is, in both cases, ≈ −101 kJ·mol^{-1}, which is smaller from those found for the oxidation in position 2 of the piperidine ring alone. Since the ketone group is in a position far from the nitrogen atom, the electronic delocalization between the oxygen on the lone pair of the nitrogen is reduced. So, the influence of this factor for the molecule stabilization could be less expressive.

Considering now the isomerization of the 1-methyl-2-piperidinone and 1-benzyl-2-piperidinone to respectively 1-methyl-4-piperidinone and 1-benzyl-4-piperidinone, the enthalpic increments are (−72.2 ± 2.8) kJ·mol^{-1} for methyl derivatives and (−67.3± 4.2) kJ·mol^{-1} for benzyl derivatives, values that are identical, within the associated uncertainties.

Finally, the experimental results for the enthalpies of formation, in the condensed phase, for 2-piperidone, $\Delta_f H_m^\circ$(2-piperidone, cr) = (−306.7 ± 1.4) kJ·mol^{-1}. and 1-methyl-2-piperidone, $\Delta_f H_m^\circ$(1-methyl-2-piperidone, l) = (−293.2± 2.0) kJ·mol^{-1}, are in agreement with those published by Strepikeev et al. [5] and Kozina and Skuratov,[6] respectively, $\Delta_f H_m^\circ$(2-piperidone, cr) = (−306.59 ± 0.80) kJ·mol^{-1} and $\Delta_f H_m^\circ$(1-methyl-2-piperidone, l) = (−293.13 ± 0.91) kJ·mol^{-1}.



Supporting Information Available:

Tables S1 to S6 list details of the results of the experimental determination of the massic energies of combustion of 2-piperidone, 1-methyl-2-piperidone, 1-benzyl-2-piperidone, 1-methyl-4-piperidone, 1-ethyl-4-piperidone, and 1-benzyl-4-piperidone. This material is available free of charge via the Internet at http://pubs.acs.org.

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