STANDARD MOLAR ENTHALPY OF FORMATION OF 1-CYANO-ACETYLPIPERIDINE

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The standard (p^0=0.1 MPa) molar enthalpy of formation of 1-cyanoacetylpiperidine, in the crystalline state, at T=298.15 K, has been derived from measurements of its standard massic energy of combustion, by static bomb combustion calorimetry, as $\Delta_\text{f}H_\text{m}^0$= –217.1±1.4 kJ mol^{-1}. The standard molar enthalpy of sublimation was measured, at T=298.15 K, by the microcalorimetric sublimation technique as $\Delta_\text{cr}^\text{g}H_\text{m}^0$=103.5±1.9 kJ mol^{-1}.

Keywords: *Calvet microcalorimetry, combustion calorimetry, 1-cyanoacetylpiperidine, enthalpy of combustion, enthalpy of formation, enthalpy of sublimation*

Introduction

Nitrogen heterocycle compounds are a class of molecules present in many products with a wide range of applications. Among them, the piperidine ring is a structural element present in many natural and industrial products, with special relevance in medicine, where the piperidine motif can be found in drugs or drug candidates with promising therapeutic use, as it can be seen by the large number of publications present in literature about this subject. However, the large importance of the piperidines contrasts with the few published studies concerning the energetics of this class of molecules. Studies concerning thermochemical properties of molecules pay an important role in understanding the relationship between structure, energetics and reactivity, which are fundamental parameters in chemical reactions and process optimization.

Due to the importance of this family of compounds and to fill in the lack of thermodynamic values for them, we carried out a detailed thermochemical study of several piperidine derivatives [1–8]. As part of this project, the present work reports the experimental determination of the standard (p^0=0.1 MPa) molar enthalpies of formation, in the condensed and in the gaseous phases, at T= 298.15 K, of 1-cyanoacetylpiperidine (Fig. 1). These values in the condensed phase were derived from the measurements of standard massic energies of combustion, using a static bomb calorimeter while the standard molar enthalpy of sublimation was measured by Calvet microcalorimetry.
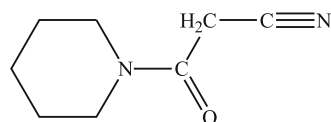

Fig. 1 Structural formula for 1-cyanoacetylpiperidine

From these two sets of results, the standard molar enthalpy of formation in the gaseous state, at the temperature 298.15 K, was derived.

Experimental

Materials

Compounds and purity control

1-Cyanoacetylpiperidine [CAS 15029-30-8], was obtained commercially from Aldrich Chemical Co. with initial purity of 0.98 mass fraction and purified twice by sublimation under reduced pressure. The final purity was determined recovering the carbon dioxide produced in the combustion experiments and also checked by g. l. c.. The average ratios of the mass of carbon dioxide recovered after combustion, to that calculated from the mass of sample, was 0.99974±0.00021, where the uncertainties are the standard deviations of the means.

Methods

Combustion calorimetry

The standard molar energy of combustion of 1-cyanoacetylpiperidine was determined in an isoperibol calori-

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meter equipped with a static combustion bomb, type 1105, Parr Instruments Company, made of stainless steel and with an internal volume of 0.340 cm^3. The apparatus used and the experimental procedure have been described in [9, 10].

The calibration of the calorimeter was performed by combustion of benzoic acid Thermochemical Standard, sample BAS 693976/01, with massic energy of combustion, under bomb conditions, of $\Delta_c u$= –26435.1±3.5 J g^{-1} [11], and corrected to give the energy equivalent, ε_{cal}, corresponding to the average mass of water added to the calorimeter, 3119.6 g. From six calibration experiments, ε_{cal}=15915.8±0.8 J K^{-1} using the calibration procedure as described in [12]. The uncertainty quoted is the standard deviation of the mean.

In all the experiments, 1.00 cm^3 of water was added to the bomb and the crystalline compound was burnt in pellet form, into a platinum crucible. The combustion bomb was flushed twice and filled with oxygen to p=3.04 MPa; the ignition was made at T=298.150±0.001 K, by the discharge of a 1400 µF capacitor through the platinum ignition wire (ϕ=0.05 mm, Goodfellow, mass fraction 0.9999), and using a cotton thread fuse with empirical formula CH$_{1.686}$O$_{0.843}$, with $\Delta_c u^0$(fuse)= –16250 J g^{-1} [12]. The calorimeter temperatures were measured to ±1·10^{-4} K, at time intervals of 10 s, with a quartz crystal thermometer (Hewlett Packard HP 2804A), interfaced to a PC. 100 readings were taken for the main period and both the fore and after periods. At the end of each experiment, the amount of compound used in that experiment was determined from the total mass of CO$_2$ produced during the combustion experiment, taking into account that formed from the combustion of the cotton-thread fuse. For that, the gases in the bomb at the end of the experiment were driven through CO$_2$ recovering tubes, filled with Carbosorb AS self-indicating, and previously weighed. The amount of HNO$_3$ formed was determined by titration of the aqueous solution resulting from washing the inside of the bomb.

High temperature microcalorimetry

The standard molar enthalpy of sublimation of 1-cyanoacetylpiperidine was determined with a Calvet High Temperature Microcalorimeter (Setaram, HT 1000D), using the 'vacuum sublimation' drop microalorimetric method, previously described by Skinner *et al.* [13]. Each sample of compound, contained in a thin glass capillary tube sealed at one end, was dropped from room temperature into the reaction cell in the hot zone of the calorimeter, held at T=370 K, and then removed from the hot zone by vacuum

sublimation. Simultaneously, a similar empty capillary tube was dropped in the reference cell. The thermal corrections for the glass capillaries were made by dropping tubes of nearly equal mass into each of the twin cells. A detailed description of the apparatus and technique can be found in [14].

The observed molar enthalpy of sublimation, $\Delta_{\mathrm{cr,\,298.15\,K}}^{\mathrm{g,\,370.1\,K}} H_m$, is corrected to T=298.15 K, using $\Delta_{298.15\,K}^{370.1\,K} H_m^0$ (g) estimated by a group scheme based on the values of Messerly *et al.* [15] and Stull *et al.* [16]. The scheme used was as follows:

1-Cyanoacetyl-piperidine   Piperidine   ACN   Acetaldehyde   Ethane
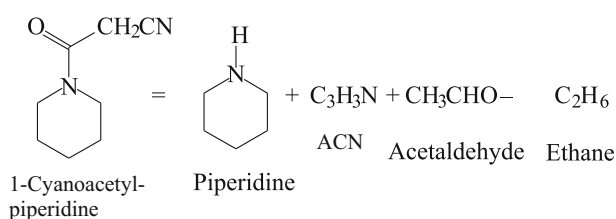
which yielded $\Delta_{298.15\,K}^{370.1\,K} H_m^0$ (g, 1-cyanoacetylpiperidine)=12.58 kJ mol^{-1}.

The microcalorimeter was calibrated with naphthalene, using the same experimental procedure for the calibration experiments as the one used for the experiments with the compound and considering the value of $\Delta_{cr}^g H_m^0$ (naphthalene, cr)=72.60±0.60 kJ mol^{-1}, at T=298.15 K [17]. From 6 independent experiments, the value of the calibration constant for this temperature was k_{cal} (T=370 K)=0.9997±0.0025, with the uncertainty as the standard deviation of the mean. The values of the enthalpies of sublimation of naphthalene, at the temperature of the calibration experiments, was calculated from its value at T=298.15 K using the literature value of $\Delta_{298.15\,K}^T H_m^0$ (g), from Stull *et al.* [16].

Results and discussion

The results of the combustion experiments of 1-cyanoacetylpiperidine are given in Table 1 where Δm(H$_2$O) is the deviation of the mass of water added to the calorimeter from 3119.6 g, ΔU(IBP), is the internal energy for the isothermal bomb process, calculated according to the Eq. (1):

$$\Delta U \text{(IBP)}=$$
$$=\{\varepsilon_{cal} +\Delta m_{H_2O} c_p (H_2O, l)+\varepsilon_f\}\Delta T_{ad} +\Delta U \text{(ign)} \quad (1)$$

ΔU(fuse) is the correction for the cotton thread fuse combustion and ΔU(ign) is the electrical energy supplied for ignition, determined from change of the potential difference across the capacitor when discharged, ΔU(HNO$_3$) is the correction for nitric acid formation, based on –59.7 kJ mol^{-1}, for the molar energy of formation of 0.1 mol dm^{-3} HNO$_3$(aq), from

Table 1 Combustion experiments at T=298.15 K

Experiment	1	2	3	4	5	6
m(CO$_2$, total)/g	1.87282	1.94289	–	2.26685	–	1.76778
m(cpd)/g	0.80679	0.83739	0.90630	0.97724	0.69903	0.76153
m(fuse)/g	0.00399	0.00355	0.00363	0.00382	0.00447	0.00378
ΔT_{ad}/K	1.55350	1.61189	1.74406	1.88409	1.34689	1.46580
ε_f/J K^{-1}	16.58	16.64	16.84	17.05	16.30	16.23
Δm(H$_2$O)/g	0.0	0.0	0.0	–0.1	0.0	+0.1
$-\Delta U$(IBP)[a]/J	24749.77	25680.23	27786.70	29959.70	21457.60	23352.60
ΔU(fuse)/J	64.80	57.65	58.95	62.04	72.59	61.39
ΔU(HNO$_3$)/J	59.24	62.86	66.03	69.43	51.11	55.82
ΔU(ign)/J	1.18	1.11	0.78	1.08	1.18	1.18
ΔU_Σ/J	14.53	15.12	16.52	18.02	12.43	13.63
$-\Delta_c u^0$/J g^{-1}	30505.09	30505.02	30503.37	30504.49	30501.51	30493.56
%$_{CO_2}$	99.970	99.956	(99.974)	99.936	(99.974)	100.033
			$<\Delta_c u^0>$= –30502.2±1.8 J g^{-1}			

m(CO$_2$, total) – total mass of carbon dioxide recovered in the combustion; m(cpd) – mass of compound burnt in each experiment; m(fuse) – mass of the cotton thread fuse; ΔT_{ad} – adiabatic temperature rise; ε_f – energy equivalent of the calorimeter including the contents of the bomb in the final state; Δm(H$_2$O) – deviation of the mass of water added to the calorimeter from 3119.6 g; ΔU(IBP) – energy change for the isothermal combustion reaction under actual bomb conditions; ΔU(fuse) – energy of combustion of the fuse (cotton); ΔU(HNO$_3$) – energy correction for the nitric acid formation; ΔU(ign) – electrical energy supplied for ignition, ΔU_Σ – standard state correction; $\Delta_c u^0$ – massic energy of combustion of the compound. [a]ΔU(IBP) already includes ΔU(ign)

Table 2 Derived standard (p^0=0.1 MPa) molar energy of combustion, $\Delta_c U_m^0$, standard molar enthalpy of combustion, $\Delta_c H_m^0$, and the standard molar enthalpy of formation for the compound in the condensed phase, $\Delta_f H_m^0$(cr), at T=298.15 K

| Compound	$-\Delta_c U_m^0$(cr)/	$-\Delta_c H_m^0$(cr)/	$-\Delta_f H_m^0$(cr)/
	kJ mol^{-1}		
1-Cyanoacetylpiperidine (cr)	4642.24±0.92	4645.96±0.92	217.1±1.4

N$_2$ (g), O$_2$ (g) and H$_2$O (l) [18]. ΔU_Σ is the correction to the standard state calculated by the procedure of Hubbard *et al.* [19] and $\Delta_c u^0$ is the massic energy of combustion of the compound. For each experiment, $\Delta_c u^0$ was calculated as previously described [19].

An estimated pressure coefficient of massic energy, $(\partial u/\partial p)_T$, at T=298.15 K, was assumed to be –0.2 J g^{-1} MPa^{-1}, a typical value for most organic compounds [20]. The atomic masses of the elements were those recommended by the IUPAC Commission in 2005 [21].

The mean value of $\Delta_c u^0$ and its standard deviation, is also given in Table 1.

Table 2 lists the derived standard molar values for the energy, $\Delta_c U_m^0$, and enthalpy, $\Delta_c H_m^0$, of combustion, referred to the combustion reaction of 1-cyanoacetylpiperidine, according to Eq. (2) as well as the standard molar enthalpy of formation, $\Delta_f H_m^0$, in the condensed phase.

$$C_8H_{12}N_2O(cr)+10.5O_2(g)\rightarrow$$
$$\rightarrow 8CO_2(g)+6H_2O(l)+N_2(g) \qquad (2)$$
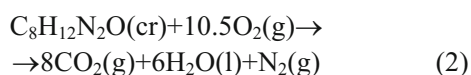
The uncertainties of the standard molar energies and enthalpies of combustion are twice the overall standard deviation of the mean, and include the uncertainties in calibration [22, 23].

The value of the standard molar enthalpy of formation in the condensed phase, $\Delta_f H_m^0$(cr), was derived from $\Delta_c H_m^0$, using the values, at T=298.15 K, of the standard molar enthalpies of formation of liquid water and gaseous carbon dioxide, respectively, $\Delta_f H_m^0$ (H$_2$O, l)= –285.830±0.042 kJ mol^{-1} [24] and $\Delta_f H_m^0$ (CO$_2$, g)= –393.51±0.13 kJ mol^{-1} [24].

Results for the enthalpy of sublimation are given in Table 3.

Combining the standard molar enthalpy of formation in the condensed phase with its standard molar enthalpy of sublimation, the standard molar enthalpy of formation in the gas-phase, at T=298.15 K, has been derived as $\Delta_f H_m^0$ (g)= –113.6±2.4 kJ mol^{-1}. The results are presented in Table 4.

A detailed analysis of our result is not possible to be done at the present state of knowledge since there are no results available concerning the energetics of other

Table 3 Microcalorimetric standard (p^0=0.1 MPa) molar enthalpies of sublimation, at T=298.15 K

Compound	N^o of experim.	T/K	$\Delta_{\text{cr, 298 K}}^{\text{g, T}} H_{\text{m}}^0$/	$\Delta_{\text{298.15 K}}^{\text{T}} H_{\text{m}}^0 (\text{g})$/	$\Delta_{\text{cr}}^{\text{g}} H_{\text{m}}^0$ T=298.15 K/
			kJ mol^{-1}		
1-Cyanoacetylpiperidine (cr)	5	370.1	116.10±0.39	12.58	103.5±1.9

Table 4 Derived standard (p^0=0.1 MPa) molar enthalpies of formation, $\Delta_{\text{f}} H_{\text{m}}^0$, and of sublimation, $\Delta_{\text{cr}}^{\text{g}} H_{\text{m}}^0$, at T=298.15 K

Compound	$-\Delta_{\text{f}} H_{\text{m}}^0$ (cr)/	$\Delta_{\text{cr}}^{\text{g}} H_{\text{m}}^0$/	$-\Delta_{\text{f}} H_{\text{m}}^0$ (g)/
	kJ mol^{-1}		
1-Cyanoacetylpiperidine (cr)	217.1±1.4	103.5±1.9	113.6±2.4

cyanoacetylpiperidines. Nevertheless this is a useful contribution for the study of the energetics of cyano compounds and also of the piperidine derivatives.

Acknowledgements

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