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Thermochemistry of some methoxypyridines

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ABSTRACT

The standard ($p^o = 0.1$ MPa) molar enthalpies of formation, at $T = 298.15$ K, for the liquids 2-methoxypyridine, 4-methoxypyridine and 2,6-dimethoxypyridine were determined by static bomb combustion calorimetry. The standard molar enthalpies of vaporization, at $T = 298.15$ K, were measured by Calvet microcalorimetry. The standard ($p^o = 0.1$ MPa) molar enthalpies of formation of the three compounds studied, in the gaseous phase, at $T = 298.15$ K have been derived from the corresponding standard molar enthalpies of formation in the liquid phase and the standard molar enthalpies of vaporization, yielding $((-42.7 \pm 1.9), (-18.2 \pm 1.8)$ and $(-233.5 \pm 1.8))$ $\text{kJ} \cdot \text{mol}^{-1}$, for 2-methoxypyridine, 4-methoxypyridine and 2,6-dimethoxypyridine, respectively.

1. Introduction

The methoxy substituents are donor groups that in the absence of steric hindrance of other attached groups to aromatic rings prefer planar conformation, since there is a stabilizing effect of the methoxy group on the aromatic ring, due to conjugation between the π lone-pair orbital and the aromatic system. Some studies made on methoxybenzene derivatives showed that when two methoxy groups are attached in adjacent positions of the ring, as in the case of 1,2- 1,2,3- and 1,2,4-methoxybenzenes, there is a large destabilization relative to methoxybenzene. Steric repulsions between nearby methoxy groups favor non-planar conformations with the methoxy groups taking opposite orientations relative to the aromatic ring [1–4].

Methoxypyridines have been used in the synthesis of several alkaloids of the *Lycopodium* family whose pharmacological interest has increased due to their use as potential treatment of Alzheimer's disease [5–8]. The methoxypyridine group is uniquely effective as a masked pyridine because the methoxy group significantly mitigates the basicity of the pyridine nitrogen via an inductive electronic withdrawing effect [9].

The present work aims to study the influence of methoxy-substitution in the pyridine ring. The standard molar enthalpies of formation of 2-methoxypyridine, 4-methoxypyridine and 2,6-dimethoxypyridine, in the gaseous state, were obtained by the experimental determination of the standard molar energies of combustion, measured by static bomb calorimetry, and of the enthalpies of vaporization, measured by Calvet microcalorimetry.

The results are interpreted in terms of the energetic increments for the introduction of the methoxy group in the pyridine ring and are compared with the same substitution in some benzene derivatives.

2. Experimental

2.1. Compounds and purity control

The three studied compounds, obtained from Aldrich Chemical Co with minimum mole fractions purities: 2-methoxypyridine [CAS 1628-89-3], 0.98, 4-methoxypyridine [CAS 620-08-6], 0.97 and 2,6-dimethoxypyridine [CAS 6231-18-1], 0.98, were purified by successive fractional distillations under reduced pressure and their purity controls were assessed to be a minimum 0.999 molar fraction from gas–liquid chromatography. The purity of the compounds was also checked from the average ratios of the mass of carbon dioxide recovered from the combustion to that calculated from the mass of sample as: 0.99415 for 2-methoxypyridine, 0.99980 for 4-methoxypyridine and 0.99908 for 2,6-dimethoxypyridine. The low value of mass carbon dioxide recovered for the 2-methoxypyridine is due to the presence of moisture. The mass of water was determined by Carl–Fischer having been obtained the value of 0.00538, consistent with the determined percentage of CO_2 recovered. Table 1 presents the origin and purification details of the samples used in the experiments.

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TABLE 1
Purification details of the methoxypyridines.

Chemical name	CAS	Provenance	Initial mole fraction purity	Purification method	Final mass fraction purity	Analysis method
2-Methoxypyridine(l)	1628-89-3	Aldrich Chemical Co	0.98	distillation	0.9942	CO_2 recovery; Carl-Fischer
4-Methoxypyridine(l)	620-08-6	Aldrich Chemical Co	0.97	distillation	0.9998	CO_2 recovery
2,6-Dimethoxypyridine(l)	6231-18-1	Aldrich Chemical Co	0.98	distillation	0.9991	CO_2 recovery

The densities, at $T = 298.15$ K, were taken for 2-methoxypyridine as $1.038\ g \cdot cm^{-3}$ [10], for 4-methoxypyridine as $1.075\ g \cdot cm^{-3}$ [10] and for 2,6-dimethoxypyridine as $1.053\ g \cdot cm^{-3}$ [10].

The relative atomic masses used are those recommended by the IUPAC Commission in 2011 [11].

2.2. Combustion calorimetry

The combustion experiments were performed with an isoperibol calorimetric system. The bomb calorimeter, subsidiary apparatus and technique have been described beforehand in the literature [12,13].

In all combustion experiments, $1.00\ cm^3$ of deionised water was introduced into the bomb, which is a twin-valve static combustion bomb Type 1105, Parr Instrument Company, made of stainless steel, with an internal volume of $0.340\ cm^3$. The bomb was purged twice to remove air, before being charged with oxygen, at $p = 3.04$ MPa.

Combustion of certificated benzoic acid (NIST Standard Reference Material 39j) was used for calibration of the bomb. Its massic energy of combustion is $-(26434 \pm 3)\ J \cdot g^{-1}$ under certificate conditions [14]. The calibration results were corrected to give the energy equivalent ε_{calor} corresponding to the average mass of water added to the calorimeter: 3119.6 g. From six calibration experiments, $\varepsilon_{calor} = (15905.7 \pm 1.0)\ J \cdot K^{-1}$, where the uncertainty quoted is the standard deviation of the mean.

For all experiments, the calorimeter temperatures were measured to $\pm(1 \cdot 10^{-4})$ K, at time intervals of 10 s, with a quartz crystal thermometer (Hewlett Packard HP 2804A), interfaced to a PC. At least 100 readings of the temperature were taken before the ignition of the samples which were made at $T = (298.150 \pm 0.001)$ K by the discharge of a 1400 μF capacitor through the platinum ignition wire. After ignition, 100 readings were taken for each the main and the after periods. Data acquisition and control of the calorimeter were performed using the program LABTERMO [15].

The liquids, 2-methoxypyridine, 4-methoxypyridine and 2,6-dimethoxypyridine, were burned in sealed polyester bags made of Melinex (0.025 mm of thickness) with massic energy of combustion $\Delta_c u^o = -(22902 \pm 5)\ J \cdot g^{-1}$ [16], a value which was confirmed in our Laboratory. The mass of Melinex used in each experiment was corrected for the mass fraction of water ($w = 0.0032$). For the cotton thread fuse of empirical formula $CH_{1.686}O_{0.843}$, the massic energy of combustion was assigned to $\Delta_c u^o = -16240\ J \cdot g^{-1}$ [17], a value previously confirmed in our Laboratory.

The electrical energy for ignition was determined from the change in potential difference across the capacitor when discharged through the platinum ignition wire. The corrections for nitric acid formation were based on $59.7\ kJ \cdot mol^{-1}$ [18], for the molar energy of formation of $0.1\ mol \cdot dm^{-3}$ $HNO_3(aq)$ from N_2, O_2, and $H_2O(l)$. All the necessary weighings were made on a Mettler Toledo AT201 microbalance, sensitivity $\pm(1 \cdot 10^{-6})$ g, and corrections from apparent mass to true mass were made. An estimated pressure coefficient of specific energy, $(\partial u/\partial p)T = -0.2\ J \cdot g^{1} \cdot MPa^{1}$ at $T = 298.15$ K, a typical value for most organic compounds [19], was assumed. For each compound, the massic energy of combustion, $\Delta_c u^o$, was calculated by the procedure given by Hubbard *et al.* [20]. The amount of compound used in each experiment was determined from the total mass of carbon dioxide (Mettler Toledo AT 201 balance, sensitivity $\pm(1 \cdot 10^{-5})$ g), produced during the experiments taking into account that formed from the combustion of the cotton-thread fuse and from Melinex.

2.3. High temperature microcalorimetry

The standard molar enthalpies of vaporization of the three compounds studied were measured with a Calvet High Temperature Microcalorimeter (Setaram, HT 1000D) [21], using for the liquid compounds a similar technique [22] to that described for the sublimation of solids [23]. Samples of about (4 to 8) mg of liquid compound, contained in a small thin glass capillary tube sealed at one end, and a blank capillary, were simultaneously dropped at room temperature into the hot reaction vessels in the Calvet high-temperature microcalorimeter held at a predefined convenient temperature, T, and were removed from the hot zone by vacuum evaporation. The thermal corrections for the glass capillary tubes were determined in separate experiments, and were minimized, as far as possible, by dropping tubes of nearly equal mass, to within ±10 μg, into each of the twin calorimeter cells.

The observed enthalpies of vaporization, $\Delta^{g,T}_{l,298.15K}H^o_m$, were corrected to $T = 298.15$ K using values of $\Delta^{T}_{298.15K}H^o_m(g)$ estimated by a group method that is: 2- or 4-methoxypyridine = pyridine + dimethylether−methane; 2,6-dimethoxypyridine = pyridine + 2 dimethyl ether−2 methane, based on data of Stull *et al.* [24], where T is the temperature of the hot reaction vessel. The microcalorimeter was calibrated *in situ* for these measurements using the reported standard molar enthalpy of vaporization of undecane [25].

3. Results

Results for a typical combustion experiment of each compound are given in table 2, were $\Delta m(H_2O)$ is the deviation of the mass of water added to the calorimeter from 3116.9 g, the mass assigned to ε_{calor}, and ΔU_{Σ} is the correction to the standard state. The remaining terms have been previously described [20]. The samples were ignited at $T = (298.150 \pm 0.001)$ K, with

$$\Delta U(\mathrm{IPB}) = -\{\varepsilon_{\mathrm{calor}} + \Delta m(\mathrm{H_2O})c_p(\mathrm{H_2O},l) + \varepsilon_{\mathrm{f}}\}\Delta T_{\mathrm{ad}} + \Delta U(\mathrm{ign}), \quad (1)$$

where $\Delta U(\mathrm{IBP})$ is the energy associated to the isotherm bomb process, ε_f is the energy of the bomb contents after ignition, $\Delta U(\mathrm{ign})$ is the ignition energy and ΔT_{ad} is the adiabatic temperature rise .

Detailed values of each combustion experiment performed for each compound studied are given in tables S1, S2 and S3 of the Supporting Information.

The individual values of $\Delta_c u^o$ together with the mean value, $\langle \Delta_c u^o \rangle$, and its standard deviation, are given, for each compound, in table 3 and refer to the combustion reactions represented by equation (2) for 2 and 4 - methoxypyridine and equation (3) for 2,6 - dimethoxypyridine.

$$\mathrm{C_6H_7NO}(l) + 7.25\mathrm{O_2}(g) \ \rightarrow\ 6\mathrm{CO_2}(g) + 0.5\mathrm{N_2}(g) + 3.5\mathrm{H_2O}(l) \quad (2)$$

$$\mathrm{C_7H_9NO_2}(l) + 8.25\mathrm{O_2}(g) \ \rightarrow\ 7\mathrm{CO_2}(g) + 0.5\mathrm{N_2}(g) + 4.5\mathrm{H_2O}(l) \quad (3)$$

Table 4 contains the derived standard molar energies and enthalpies of combustion and the standard molar enthalpies of formation for 2-methoxypyridine, 4-methoxypridine and