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Molecular energetics of alkyl substituted pyridine *N*-oxides

An experimental study

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Abstract The standard ($p° = 0.1$ MPa) energies of combustion in oxygen, at $T = 298.15$ K, for the solid compounds 2-methylpyridine-*N*-oxide (2-MePyNO), 3-methylpyridine-*N*-oxide (3-MePyNO) and 3,5-dimethylpyridine-*N*-oxide (3,5-DMePyNO) were measured by static-bomb calorimetry, from which the respective standard molar enthalpies of formation in the condensed phase were derived. The standard molar enthalpies of sublimation, at the same temperature, were measured by Calvet microcalorimetry. From the standard molar enthalpy of formation in gaseous phase, the molar dissociation enthalpies of the N–O bonds were derived, and compared with values of the dissociation enthalpies of other N–O bonds available for other pyridine-*N*-oxide derivatives.

Keywords *N*-oxide organic compounds · Energy of combustion · Standard molar enthalpies · Static bomb · Calorimetry · Calvet microcalorimetry

Introduction

Several of *N*-oxide organic compounds have shown to undergo selective reduction under anaerobic conditions, and are believed to be likely bioreducing agents able to act selectively on hypoxic cells of solid tumors. In this context, formation of *N*-oxide derivatives has been attracting the research interest from many viewpoints that include very important pharmacological applications for which the basic knowledge of chemical bonding has to be expanded [1–4].

The breaking and making of chemical bonds involved in chemical processes justifies the need for thermochemical data for key compounds, to provide credible correlations between structure and energetics, from which it will be possible to estimate data for unstudied related compounds. In our Research Group, the molecular energetics of nitrogen heterocyclic compounds, with terminal N–O bonds, has been one of our main interests during the last decade [5], in order to derive the dissociation enthalpy of the N–O bond, $DH^{\mathrm{o}}_{\mathrm{m}}(\mathrm{N{-}O})$. Indeed several classes of compounds with N–O terminal bonds have been studied, with particular attention devoted to quinoxaline *N,N*-dioxides [5–10], pyrazine *N,N*-dioxides [5, 11, 12], phenazine *N,N*-dioxides [5–13], benzofurazan *N*-oxides [5]. The state of art concerning the energetics on pyridine *N*-oxide derivatives is summarized below. Shaofeng and Pilcher [14] determined the standard molar enthalpy of formation of crystalline pyridine *N*-oxide as $\Delta_{\mathrm{f}}H^{\mathrm{o}}_{\mathrm{m}}(\mathrm{cr}) = (8.6 \pm 2.3)\ \mathrm{kJ\,mol^{-1}}$, using solution-reaction calorimetry, and the standard molar enthalpy of sublimation, $\Delta^{\mathrm{g}}_{\mathrm{cr}}H^{\mathrm{o}}_{\mathrm{m}} = (79.3 \pm 1.0)\ \mathrm{kJ\,mol^{-1}}$, by Calvet microcalorimetry. From the value of $\Delta_{\mathrm{f}}H^{\mathrm{o}}_{\mathrm{m}}(\mathrm{g}) = (87.9 \pm 2.5)\ \mathrm{kJ\,mol^{-1}}$, it has been possible to derive the $DH^{\mathrm{o}}_{\mathrm{m}}(\mathrm{N{-}O})$ as $(301.7 \pm 2.8)\ \mathrm{kJ\,mol^{-1}}$. Independent measurements by da Silva et al. [15], applying the same method to determine the enthalpy of formation of the crystalline compound and a Knudsen method to measure the enthalpy of sublimation, led to a value of $DH^{\mathrm{o}}_{\mathrm{m}}(\mathrm{N{-}O}) = (300.0 \pm 1.8)\ \mathrm{kJ\,mol^{-1}}$, in good agreement with the one obtained by Pilcher, although a very high value

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for the a $DH^{o}_{m}(N{-}O)$ on the class of pyridine *N*-oxides. The use of combustion techniques with this compound is very difficult, since crystalline pyridine *N*-oxide is highly hygroscopic. Steele et al. [16] were able to overcome this problem and used the combustion calorimetry to determine the standard molar enthalpy of formation of pyridine *N*-oxide, in the condensed phase, as (44.1 ± 0.5) kJ mol^{-1}. Using this value, the derived value of the bond enthalpy of dissociation is $DH^{o}_{m}(N{-}O) = (266.2 \pm 2.0)$ kJ mol^{-1}, an acceptable value [5], showing that the reaction-solution calorimetric result was in error by ≈ 36 kJ mol^{-1}.

Airoldi and Gonçalves [17], using solution-reaction calorimetry, determined the standard molar enthalpies of formation of crystalline 2-, 3-, and 4-methylpyridine-*N*-oxides as, respectively (10.3 ± 0.8) kJ mol^{-1}, (8.8 ± 0.7) kJ mol^{-1} and (12.9 ± 0.9) kJ mol^{-1}. This last compound, 4-methylpyridine-*N*-oxide, was also studied by Lebedev [18] applying combustion calorimetry techniques, obtaining the value $\Delta_f H^{o}_{m}(\mathrm{cr}) = -(0.5 \pm 2)$ kJ mol^{-1}. Independent measurements by combustion calorimetry carried out in our Research Group, yielded a value for the standard molar enthalpies of formation of crystalline 4-methylpyridine-*N*-oxide, $\Delta_f H^{o}_{m}(\mathrm{cr}) = (5.6 \pm 2.1)$ kJ mol^{-1} [19], which is not in agreement neither with the values measured by Lebedev et al. [18] or by Airoldi and Gonçalves [17].

The systematic study of pyridine *N*-oxide derivatives by our Research Group was extended to numerous other compounds such as nitro [19, 20], carboxy [19, 20], hydroxyl [19], cyano[19], and carboxamide pyridine N–O derivates [21].

Besides our interest on the values of the gaseous enthalpies of formation of the pyridine *N*-oxides, we have been investigating the effect of the chemical environment of the nitrogen heterocycle *N*-oxides, on the dissociation enthalpy of the terminal (N–O) bond.

In the present paper, the standard ($p^{\circ} = 0.1$ MPa) molar enthalpies of formation, at $T = 298.15$ K, for three pyridine *N*-oxide derivatives (2-methylpyridine-*N*-oxide, 2-MePyNO; 3-methylpyridine-*N*-oxide, 3-MePyNO, and 3,5-dimethylpyridine-*N*-oxide, 3,5-DMePyNO) (Fig. 1), were derived from static-bomb calorimetry. The enthalpies of sublimation of 2-methylpyridine-*N*-oxide and 3,5-dimethylpyridine-*N*-oxide were measured by Calvet microcalorimetry; the enthalpy of sublimation of 3-methylpyridine-*N*-oxide has been estimated, due to the difficulties to perform the respective experimental measurements. These values were used to derive the standard molar enthalpies of formation, in the gaseous phase, of the corresponding compounds.

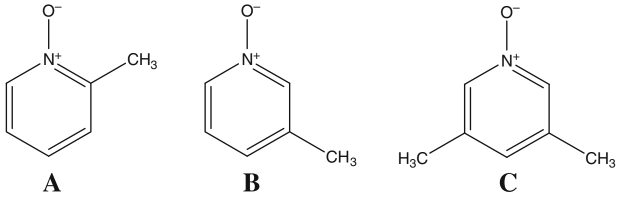


Fig. 1 Structural formula for 2-MepyNO (**a**), 3-MePyNO (**b**), and 3,5-DMPyNO (**c**)

The compound 2-methylpyridine-*N*-oxide has a very low melting point ($T = 322.95$ K, [22]), and it can continue in a metastable liquid phase, without crystallizing for a long period, when it is cooled under the melting temperature. For that we decided to measure vapor pressure of this compound, using a static apparatus based on a capacitance diaphragm gauge.

From the standard molar enthalpies of formation in the gaseous phase of the three alkylpyridine *N*-oxide derivatives studied and from the standard molar enthalpies of formation in gaseous phase of the three the corresponding alkylpyridine derivatives, the molar dissociation enthalpies of the N–O bonds were derived. Comparisons were made with values in other pyridine-*N*-oxide derivatives.

Experimental

Synthesis of materials and purity control

The 2-MePyNO (Acros Organics, 98%) and 3-MePyNO (Aldrich, 98%) were purchased from commercial sources and submitted to purification by fractional distillation under reduced pressure. 3,5-DMePyNO was prepared by the peroxyacetic acid oxidation of 3,5-dimethylpyridine according to the published synthetic procedure of Essery and Schofield [23]. 3,5-Dimethylpyridine and 30% hydrogen peroxide were dissolved in acetic acid, and the resulting mixture was heated at 343–353 K for 12 h, with additional 30% of hydrogen peroxide being added at the 3-h mark. The reaction mixture was then cooled and basified with sodium hydroxide solution. The product was extracted into chloroform, dried over anhydrous sodium carbonate, and then distilled under reduced pressure. The experimentally determined mass fractions for 3,5-DMePyNO were in agreement with the expected values for C_7H_9NO: found: C, 0.6821; H, 0.0744; N, 0.1131; calculated: C, 0.6827; H, 0.0737; N, 0.1137.

As the compounds have shown to be hygroscopic, before the combustion experiments they were dried and handled under dry nitrogen atmosphere. However, a small amount of water was absorbed when they were handled during the experiments, as shown by the CO_2 recoveries from the combustions. The absence of other impurities than water was confirmed by GLC. The average ratios of the mass of carbon dioxide recovered after the combustion to those calculated from the mass of sample were: for 2-MePyNO (0.99672 ± 0.00053), for 3-MepyNO (0.99910 ± 0.00005 and for 3,5-DMeNO (0.99200 ± 0.00005) with the uncertainties being the standard deviations of the mean.

Combustion calorimetry

The standard massic energies of combustion of the compounds studied experimentally, i.e., 2-MePyNO, 3-MePYNO, and 3,5-DMePyNO, all in the solid phase, were measured by static-bomb combustion calorimetry, using two different isoperibol static-bomb calorimeters: Calorimeter 1 for 2-MePyNO and Calorimeter 2 for the other two compounds. In the experiments performed with Calorimeter 1, a twin valve bomb, model 1105 (Parr Instrument, IL, USA) of internal volume 0.340 cm^3 was used. A detailed description of the apparatus and the technique can be found in the literature [24, 25]. The bomb used with Calorimeter 2 has an internal volume of 0.290 cm^3 and the description of this combustion calorimeter can also be found in literature [26–28]. Both calorimeters were calibrated by combustion of thermochemical standard benzoic acid, sample NBS 39j, with $\Delta_c u = -(26434 \pm 3)\ \mathrm{J\,g^{-1}}$ [29], under experimental conditions, and found to be $\varepsilon_{cal} = (15917.4 \pm 1.4)\ \mathrm{J\,K^{-1}}$, for Calorimeter 1, and $\varepsilon_{cal} = (15553.3 \pm 0.9)\ \mathrm{J\,K^{-1}}$, for Calorimeter 2**.** The calibrations followed the procedure previously described [30], and the results were corrected to give the energy equivalents, ε_{cal}, corresponding to the average mass of water added to the calorimeters of 3119.6 and 2900 g, respectively, for Calorimeter 1 and Calorimeter 2. The uncertainties quoted are the standard deviations of the mean, of at least 6 experiments for Calorimeter 1 and 11 for Calorimeter 2.

The solid compounds were pressed into pellet form. As they have shown to be hygroscopic, the pellets were burnt enclosed in sealed Melinex bags, with 0.025 mm of thickness and a massic energy of combustion of $\Delta_c u^o = -(22902 \pm 5)\ \mathrm{J\,g^{-1}}$ [31], corrected for the mass fraction of water $w = 0.0032$ [31].

All substances were burnt in an oxygen atmosphere, with 1.00 cm^3 of water added to the bomb, at an initial pressure of 3.04 MPa, after purging the bomb twice with oxygen to remove the air. The calorimetric temperatures were measured at time intervals of 10 s, and at least 100 readings were taken for each the fore, the main and the after periods. The ignition was made at $T = (298.150 \pm 0.001)$ K, by the discharge of a 1400 µF capacitor through the platinum ignition wire. A cotton-thread fuse with empirical formula of $CH_{1.686}O_{0.843}$ was used, with a massic energy of combustion of $-\Delta_c u^o = 16240\ \mathrm{J\,g^{-1}}$ [30]. At the end of each combustion experiment, the amount of compound burnt in that experiment was determined from the total mass of CO_2 produced, taking into account that formed from cotton-thread fuse and from Melinex. The amount of HNO_3 formed was determined by titration of the aqueous solution resulting from washing the inside of the bomb. If a small amount of carbon was formed inside the crucible, its amount was determined by weight and taken into account for the calculation of the massic energy of combustion.

Calvet Microcalorimetry

The standard molar enthalpies of sublimation of 2-MePyNO and 3,5-DMePyNO were measured by Calvet High Temperature Microcalorimetry using a similar technique to that described by Skinner and Snelson [32]. Samples about 3–5 mg contained in a thin glass capillary tube were dropped at the room temperature, into the hot reaction vessel, in a high temperature Calvet microcalorimeter (SETARAM HT 1000D) held at $T = 355$ K for 2-MePyNO and at $T = 371$ K for 3,5-DMePyNO, and then removed from the hot zone by vacuum sublimation. The observed enthalpies of sublimation were corrected to $T = 298.15$ K, using $\Delta_{298.15\mathrm{K}}^{T} H_m^o$ (g) estimated by a group method based on the values from Stull et al. [33]. The microcalorimeters were calibrated in situ for the working temperatures with naphthalene $(\Delta_{cr}^{g} H_m^o(\text{naphthalene, cr}) = (72.60 \pm 0.60)\ \mathrm{kJ\,mol^{-1}}$ [34]) using the same procedure for the calibration experiments.

Vapor pressure measurements

As the compound 2-methylpyridine-*N*-oxide has low melting point and it remains in the liquid state for a long period, without crystallizing, it was decided to measure the vapor pressures of this compound, at different temperatures, using a static apparatus based on a capacitance diaphragm gauge. The apparatus, the measuring procedure and the results obtained from the vapor pressure measurements of recommended reference materials (naphthalene, benzoic acid, benzophenone and ferrocene) have been described in the literature [35].

The pressure is measured by a capacitance diaphragm absolute gauge MKS Baratron 631A11TBFP. This sensor is capable of measuring in the pressure range of [5–1333] Pa and in the temperature range of [253–473] K, with an accuracy better than 0.5% of the reading pressure, as stated by the manufacturer. To avoid condensation of the sample, the temperature of the vacuum line was maintained 10–20 K above the sample temperature and the pressure sensor diaphragm is self controlled at $T = 473$ K.

Experimental results

Results for a typical combustion experiment of each compound are given in Table 1, where $\Delta m(H_2O)$ is the deviation of the mass of water added to the calorimeter

Table 1 Results of a typical combustion experiment, at $T = 298.15$ K

Experiment	2-MePyNO	3-MePyNO	3,5-DMePyNO
m (CO_2, total)/g	1.08916	2.37025	2.01950
m (cpd)/g	0.41168	0.88856	0.80575
m (melinex)/g	0.03817	0.09753	–
m (fuse)/g	0.00345	0.00256	0.00242
ΔT_{ad}/ K	0.85702	1.90908	1.69000
ε_{f}/ J K^{-1}	15.46	15.14	15.00
Δm (H_2O)/g	0.0	−2.6	−3.1
$-\Delta U$ (IBP)^{a}/J	13654.04	29699.44	26287.36
ΔU (melinex)/J	874.27	2233.53	–
ΔU (fuse)/J	56.03	41.57	39.30
ΔU (HNO_3)/J	29.79	61.29	55.15
ΔU (ign)/J	0.74	1.19	1.15
ΔU (Carbon)/J	–	66.0	–
ΔU_{Σ}/J	8.32	19.66	15.22
$-\Delta_{\mathrm{c}}u^{\mathrm{o}}$/J g^{-1}	30814.30	30846.98	32488.60

$m(CO_2$, total) is the total mass of carbon dioxide recovered in the combustion; m(cpd) is the mass of compound burnt in each experiment; m(melinex) is the mass of Melinex used to enclose the compounds; m(fuse) is the mass of the cotton-thread fuse; ΔT_{ad} is de adiabatic temperature rise; $\varepsilon_{\mathrm{f}}$is the energy equivalent of the calorimeter including the contents of the bomb in the final state; $\Delta m(H_2O)$ is the deviation of the mass of water added to the calorimeter from 3119.6 g (calorimeter 1) or 2900.0 g (calorimeter 2); ΔU(IBP) is the energy change for 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 supplied for ignition, ΔU(carbon) is the energy correction for the carbon residue soot formation; $\Delta U_{\Sigma}$is the standard state correction; $\Delta_{\mathrm{c}}u^{\mathrm{o}}$ is the massic energy of combustion of the compound

[a] ΔU(IBP) already includes ΔU(ign)

Table 2 Individual values of the massic energy of combustion,$\Delta_{\mathrm{c}}u^{\mathrm{o}}$, for the compounds, at $T = 298.15$ K

2-MePyNO	3-MePyNO	3,5-DMePyNO
$-\Delta_{\mathrm{c}}u^{\mathrm{o}}$/ J g^{-1}		
30814.30	30846.98	32488.60
30778.57	30794.12	32541.44
30787.61	30856.17	32551.53
30784.90	30858.57	32553.29
30797.12	30803.28	32538.94
30780.26	30841.94	32522.37
	30820.33	32539.42
$-\langle\Delta_{\mathrm{c}}u^{\mathrm{o}}\rangle$/(J g^{-1})		
30790.5 ± 5.5	30831.6 ± 9.8	32533.7 ± 8.5

from 3119.6 g (calorimeter 1) or from 2900.0 g (calorimeter 2), with the internal energy for the isothermal bomb process, ΔU_{IBP}, calculated according to the Eq. 1.

$$\Delta U_{\mathrm{IBP}} = -\{\varepsilon_{\mathrm{cal}} + \Delta m_{\mathrm{H_2O}} c_p(\mathrm{H_2O,l}) + \varepsilon_{\mathrm{f}}\}\Delta T_{\mathrm{ad}} + \Delta U_{\mathrm{ignition}}. \qquad (1)$$

ΔU(fuse) is the energy of combustion of the cotton-thread fuse and ΔU(melinex) the energy of combustion of the melinex used in the experiments. The corrections for nitric acid formation, $\Delta U(HNO_3)$, were based on −59.7 kJ mol^{-1}, for the molar energy of formation of 0.1 mol dm^{-3} HNO_3(aq), from N_2 (g), O_2 (g) and H_2O (l) [36] and ΔU(ign) is the electrical energy supplied for ignition. For each compound, the 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 [37]. The correction to the standard state, ΔU_{Σ}, and the massic energy of combustion, $\Delta_{\mathrm{c}}u^{\mathrm{o}}$, were calculated by the procedure of Hubbard et al. [38]. The relative atomic masses used were those recommended by the IUPAC Commission in 2005 [39]. For all compounds studied, the individual values of $\Delta_{\mathrm{c}}u^{\mathrm{o}}$, together with the means and their standard deviations, are given in Table 2.

Table 3 lists, for each compound, the derived values for the standard molar energy ($\Delta_{\mathrm{c}}U^{\mathrm{o}}_{\mathrm{m}}$) and enthalpy ($\Delta_{\mathrm{c}}H^{\mathrm{o}}_{\mathrm{m}}$) of combustion and the standard molar enthalpy of formation, $\Delta_{\mathrm{f}}H^{\mathrm{o}}_{\mathrm{m}}$, in the condensed phase. The uncertainties of the standard molar energies and enthalpies of combustion are twice the final overall standard deviation of the mean, and include the uncertainties in calibration [40, 41] as well as the respective uncertainties of the auxiliary compounds used.

The values of the standard molar enthalpies of formation in the condensed phase, at $T = 298.15$ K, $\Delta_{\mathrm{f}}H^{\mathrm{o}}_{\mathrm{m}}(\mathrm{cr})$, were derived from $\Delta_{\mathrm{c}}H^{\mathrm{o}}_{\mathrm{m}}$, using the values of the standard molar enthalpies of formation of liquid water and gaseous carbon dioxide, respectively, $\Delta_{\mathrm{f}}H^{\mathrm{o}}_{\mathrm{m}}(\mathrm{H_2O,l}) = -(285.830 \pm 0.042)$ kJ mol^{-1} [42] and $\Delta_{\mathrm{f}}H^{\mathrm{o}}_{\mathrm{m}}(\mathrm{CO_2,g}) = -(393.51 \pm 0.13)$ kJ mol^{-1} [42].

Results of the microcalorimetric determinations of the enthalpy of sublimation of 2-MePyNO and 3,5-DMePyNO, are given in the Table 4. The values of the enthalpies of sublimation, at the experimental temperature T, correspond to the mean values of six independent experiments with the uncertainties given by their standard deviations. The observed molar enthalpies of sublimation,$\Delta^{\mathrm{g},T}_{\mathrm{cr},298.15\mathrm{K}}H_{\mathrm{m}}$, were corrected to $T = 298.15$ K using $\Delta^{T}_{298.15\mathrm{K}}H^{\mathrm{o}}_{\mathrm{m}}$ (g) estimated by a group scheme based on the values of Stull et al. [33]. The schemes applied for these corrections are: 2-MePyNO = 2-MePy + NO and 3,5-DMePyNO = 2 × 3-MePy − Py + NO, which gives, at $T = 355.4$ K, $\Delta^{355.4\mathrm{K}}_{298.15\mathrm{K}}H^{\mathrm{o}}_{\mathrm{m}}(2\text{ - MePyNO}) = 7.20$ kJ mol^{-1} and at $T = 371.0$ K, $\Delta^{371.0\mathrm{K}}_{298.15\mathrm{K}}H^{\mathrm{o}}_{\mathrm{m}}(3,5\text{ - DMePyNO}) = 11.32$ kJ mol^{-1}. The uncertainties associated to the standard molar enthalpies or sublimation, at $T = 298.15$ K, are twice the standard deviation of the mean and include the uncertainty associated with the calibration procedure.

Table 3 Derived standard ($p° = 0.1$ MPa) molar energies of combustion, $\Delta_c U^o_m$, standard molar enthalpies of combustion, $\Delta_c H^o_m$, and standard molar enthalpies of formation for the compounds in the condensed phase, $\Delta_f H^o_m$(cr), at $T = 298.15$ K

Compound	$-\Delta_c U^o_m/\mathrm{kJ\,mol^{-1}}$	$-\Delta_c H^o_m/\mathrm{kJ\,mol^{-1}}$	$\Delta_f H^o_m(\mathrm{cr})/\mathrm{kJ\,mol^{-1}}$
2-MePyNO (cr)	3360.0 ± 1.6	3361.9 ± 1.6	0.4 ± 1.8
3-MePyNO (cr)	3364.5 ± 2.2	3366.4 ± 2.3	4.9 ± 2.4
3,5-DMePyNO (cr)	4006.6 ± 2.2	4009.7 ± 2.2	−31.1 ± 2.4

Table 4 Microcalorimetric standard ($p°= 0.1$ MPa) molar enthalpies of sublimation, at $T = 298.15$ K

Compound	Number of experiments	T/K	$\Delta^{g,T}_{cr,298.15K}H_m/\mathrm{kJ\,mol^{-1}}$	$\Delta^{T}_{298.15K}H^o_m(g)/\ \mathrm{kJ\,mol^{-1}}$	$\Delta^g_{cr}H^o_m(T = 298.15\mathrm{K})/\mathrm{kJ\,mol^{-1}}$
2-MePyNO (cr)	6	355.4	100.07 ± 0.50	7.20	92.9 ± 1.9
3,5-DMePyNO (cr)	6	371.0	112.2 ± 1.2	11.32	100.9 ± 2.3

Table 5 Derived standard ($p° = 0.1$ MPa) molar enthalpies of formation, $\Delta_f H^o_m$, and of sublimation, $\Delta^g_{cr}H^o_m$, at $T = 298.15$ K

Compound	$\Delta_f H^o_m$(cr)/ kJ mol^{-1}	$\Delta^g_{cr}H^o_m$/ kJ mol^{-1}	$\Delta_f H^o_m$(g)/ kJ mol^{-1}
2-MePyNO	0.4 ± 1.8	92.9 ± 1.9	93.3 ± 2.6
3-MePyNO	4.9 ± 2.3	[91 ± 6][a]	95.9 ± 6.4
3,5-DMePyNO	−31.1 ± 2.4	100.9 ± 2.3	69.8 ± 3.3

[a] Estimated from literature values for the pyridine isomers [44]

The values of the standard molar enthalpies of formation in the condensed state, together with the ones of the enthalpies of sublimation, yield the standard molar enthalpies of formation of the studied compounds in the gaseous state, which are registered in Table 5.

Table 6 Experimental data of vapor pressure for 2-MePyNO in liquid state

T/K	p/Pa	Δp^a/Pa
2-MePyNO (l)		
328.64	134.5	2.2
331.63	157.5	0.9
334.60	184.7	0.2
337.59	211.3	−5.4
340.56	251.7	−1.5
343.55	295.6	0.3
346.52	338.6	−4.2
349.51	394.6	−2.2
352.49	465.2	7.5
355.46	530.2	4.3

[a] $\Delta p = p - p_{\mathrm{calc}}$, where p_{calc} is calculated from the Clarke and Glew equation

The vapor pressure of 2-MePyNO was measured in the liquid state. The experimental data of the vapor pressure for the studied compound are listed in Table 6. The experimental data were fitted by the Clarke and Glew equation [43].

$$R \cdot \ln\left(\frac{p}{p^o}\right) = -\frac{\Delta^g_l G^o_m}{\theta} + \Delta^g_l H^o_m(\theta) \times \left(\frac{1}{\theta} - \frac{1}{T}\right) + \Delta^g_l C^o_{p,m}(\theta)\left[\left(\frac{\theta}{T}\right) - 1 + \ln\left(\frac{T}{\theta}\right)\right] \qquad (2)$$

where p is the vapor pressure, p^o is a selected reference pressure, θ is a selected reference temperature, and R is the molar gas constant ($R = 8.314472$ J K^{-1} mol^{-1}), $\Delta^g_l G^o_m$ is the standard molar Gibbs energy of vaporization at the selected reference pressure (the gaseous phase is supposed to have characteristics of an ideal gas at the pressure p^o),

Table 7 Parameters of Clarke and Glew equation for 2-MePyNO (l) at the reference temperature $T = 298.15$ K and pressure $p° = 10^5$ Pa

Compound	$\Delta^g_l G^o_m$/J mol^{-1}	$\Delta^g_l H^o_m$/J mol^{-1}
2-MePyNO (l)	21334 ± 63	54333 ± 488

$\Delta^g_l C^o_{p,m} = -100\,\mathrm{J\,K^{-1}\,mol^{-1}}$

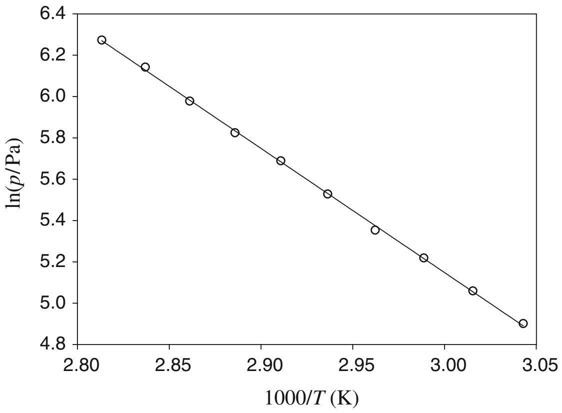


Fig. 2 Plot of ln(p/Pa) versus 1/T (K) for the experimental data of vapor pressure for 2-methylpyridine-*N*-oxide in liquid state. [a]From [44], [b]from [5], and this work

Table 8 Comparison of the mean bond dissociation enthalpies derived in this work with others reported in the literature

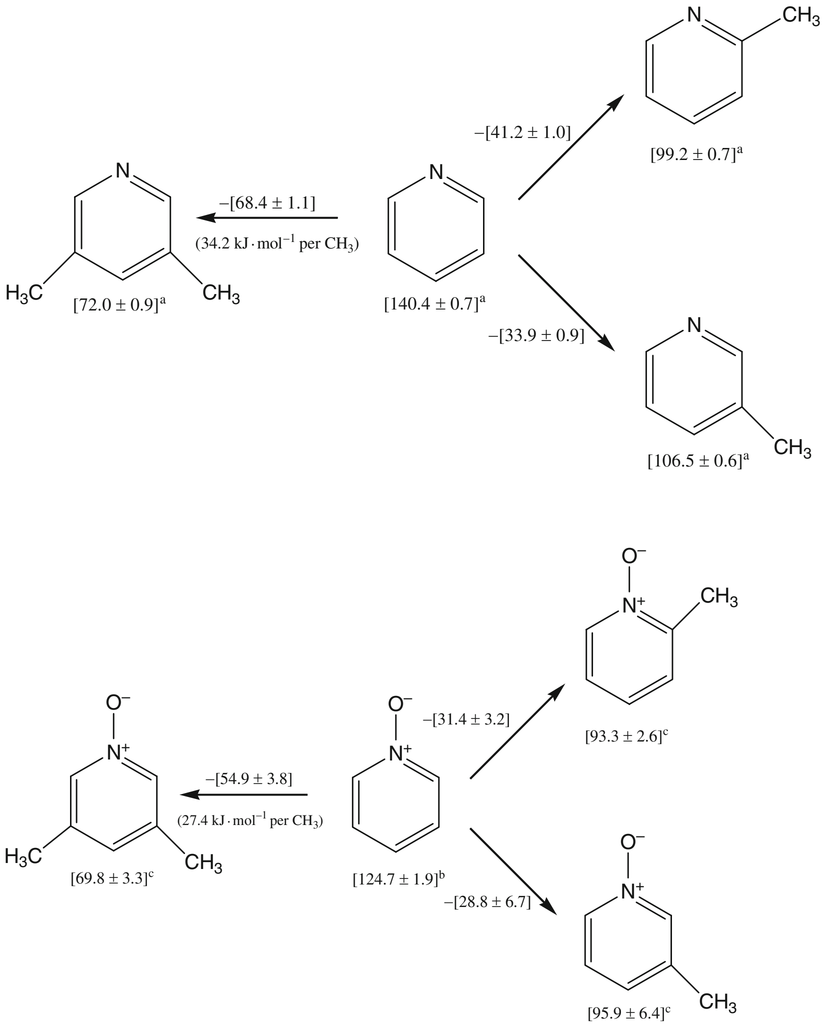
	$\Delta_f H_m^o(g)/\text{kJ mol}^{-1}$		$\Delta_f H_m^o(g)/\text{kJ mol}^{-1}$	$DH_m^o(\text{N–O})/\text{kJ mol}^{-1}$
Py	140.4 ± 0.7[a]	PyNO	124.7 ± 1.9[b]	264.9 ± 2.0
2-MePy	99.2 ± 0.7[a]	2-MePyNO	93.3 ± 2.6[c]	255.1 ± 2.7
3-MePy	106.5 ± 0.6[a]	3-MePyNO	95.9 ± 6.4[c]	259.8 ± 6.5
3,5-DMePy	72.0 ± 0.9[a]	3,5-DMePyNO	69.8 ± 3.3[c]	251.4 ± 3.4

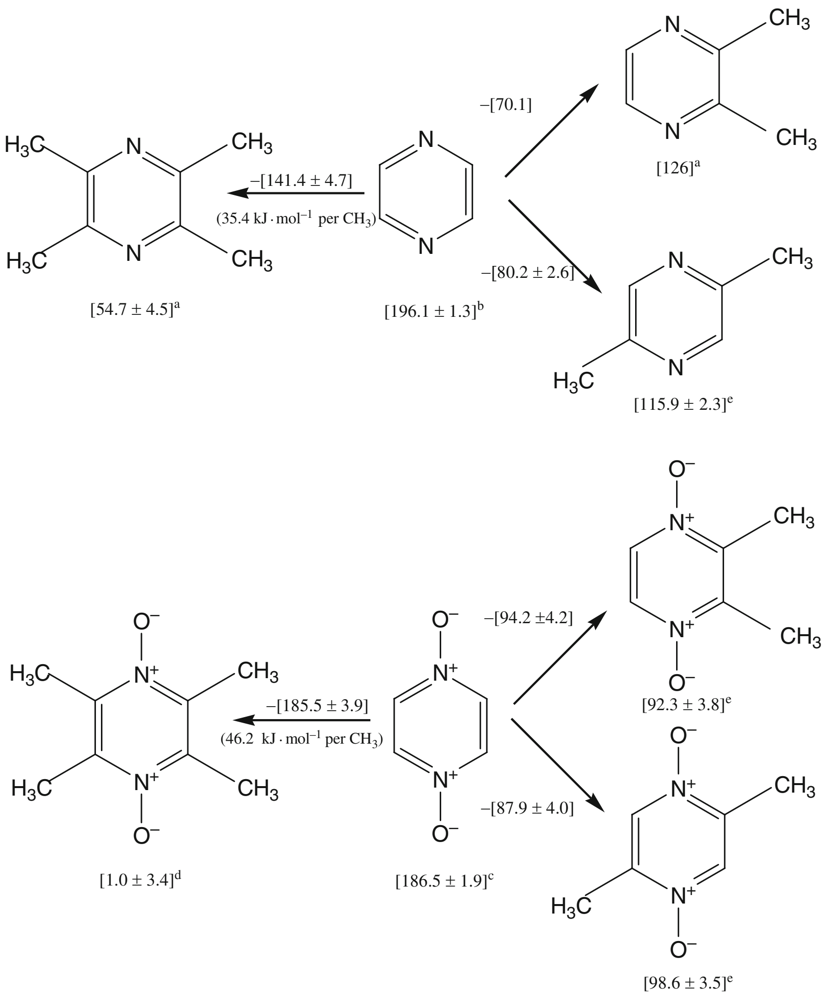
[a]From [44], [b]from [5], and [c]this work

$\Delta_l^g H_m^o$ is the standard molar enthalpy of vaporization and $\Delta_l^g C_{p,m}^o$ is the difference between the heat capacities of the ideal gas and the liquid phase. In this work was considered for reference temperature $\theta = 298.15$ K and standard pressure $p^o = 10^5$ Pa.

The parameters of the Clarke and Glew equation (Eq. 2) are presented in Table 7, and the experimental vapor pressure measurements and the predicted data from the fitted equation are shown in Fig. 2. The upper limit of the vapor pressure measurements was defined by indication of traces of decomposition of the sample at temperatures above 360 K. Due to the short temperature interval, $\Delta_l^g C_{p,m}^o$ was not derived directly from the fitting, being taken as -100 J K^{-1} mol^{-1} and used in the fitting. With the enthalpy of sublimation measured by high Calvet microcalorimetry and the enthalpy of vaporization measured by the capacitance diaphragm, it is calculated a value of (38.6 ± 2.0) kJ·mol^{-1} for the fusion enthalpy of 2-MePyNO.

Scheme 1 Enthalpic effect due to substitution of methyl groups in Pyridine and Pyridine-*N*-oxide (all values in kJ mol^{-1}). [a] From [44], [b] from [5], [c] this work





Scheme 2 Enthalpic effect due to substitution of methyl groups in Pyrazine and Pyrazine *N*,*N*-dioxide (all values in kJ mol^{-1}). [a][46], [b][47], [c][48], [d][11], and [e][12]

Discussion

The standard molar enthalpy of formation, in condensed phase, for 2-MePyNO and 3-MePyNO have already been published by Airoldi and Gonçalves [17], measured by reaction-solution calorimetry, as $\Delta_f H^o_m$(2-MePyNO, cr) = (10.5 ± 0.8) kJ mol^{-1} and $\Delta_f H^o_m$(3-MePyNO, cr) = (8.8 ± 0.7) kJ mol^{-1}. These values are somewhat different from those obtained in this work: $\Delta_f H^o_m(\text{2-MePyNO, cr}) = (0.4 \pm 1.7)\ \text{kJ mol}^{-1}$ and $\Delta_f H^o_m(\text{3-MePyNO, cr}) = (5.0 \pm 2.3)\ \text{kJ mol}^{-1}$.

Since the compounds under study are extremely hygroscopic, its handling is very difficult, so it was impossible to determine experimentally the standard molar enthalpy of sublimation for 3-MePyNO. This was estimated based on literature [44] values of the pyridine isomers.

The standard molar enthalpies of dissociation of the N–O bond, $DH^o_m(\text{N}-\text{O})$, on 2-MePyNO, 3-MePyNO, and 3,5-DMePyNO were derived from the values of the standard molar enthalpies of formation, in gaseous phase, of those *N*-oxide alkylderivatives and of 2-MePy, 3-MePy, and 3,5-DMePy, respectively, and $\Delta_f H^o_m(\text{O, g}) = (249.18 \pm 0.10)\ \text{kJ mol}^{-1}$ [42], according to the gaseous reaction, X-PyNO → X-Py + O, where X = 2-Me, 3-Me, or 3,5-DMe. These values are summarized in Table 8. The analysis of the values of $DH^o_m(\text{N}-\text{O})$ calculated for the studied compounds, allows us to conclude that the presence of the substituting groups in pyridine molecule does not induce significant effects in the N–O bond, since the values remain fairly constant and within the expected interval of (260 ± 10) kJ mol^{-1} [5]. None of the three methylpyridine-*N*-oxide derivatives studied here have a functional group in the 2- and/or 6-ring position capable of hydrogen bond formation with the oxygen atom of the *N*-oxide group. Except for three pyridinecarboxiamide *N*-oxides [21], the pyridine *N*-oxides having $DH^o_m(\text{N}-\text{O})$ values outside of the (260 ± 10) kJ mol^{-1} interval have had either a –COOH [19] or –OH [45] functional group in the 2-position.

Scheme 1 presents the comparison of the enthalpic increments due to the introduction of methyl groups in positions 2-, 3- and 3,5- in Py and PyNO. The effect of stabilization due to the introduction of methyl groups observed in Py is slightly superior than in PyNO. This tendency in stabilization is even more evident for the substitution in position 2- of Py, probably due to stereochemical interactions between the methyl group and the oxygen in PyNO.

It is interesting also to analyse Scheme 2, where the enthalpic increments due to the introduction of methyl groups in positions 2- and 3-, 2- and 5-, or 2-, 3-, 5-, and 6- in pyrazine (Pz) are compared with those in pyrazine *N,N-dioxide* (PzDNO). For 2,3-DMePz may be considered that each CH_3 group is in an *ortho* position relatively to a nitrogen atom, resulting in a lower stabilization than in pyridine. On the other hand, for 2,5-DMePz may be considered that each CH_3 group is in an *ortho* position or in a *meta* position relatively to a nitrogen atom, resulting a stabilization similar to that in 2-methylpyridine. Identical comments may be done for the compound 2,3,5,6-TMePz, where the stabilization for each CH_3 group is identical to that in 2,3-DMePz. In what concerns the stabilization energy for methyl substitutions in the ring PzDNO, that is higher than in PyNO ring, resulting in a tendency to a decrease of the dissociation enthalpy of the N–O bond in pyridine oxides, comparatively with the average of the dissociation enthalpy of that bond in pyrazine *N,N*-dioxide derivatives.

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