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Thermochemical study of the ethylpyridine and ethylpyrazine isomers

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Received 17th July 2003, Accepted 8th October 2003
First published as an Advance Article on the web 27th October 2003

The standard ($p° = 0.1$ MPa) molar energies of combustion in oxygen, at $T = 298.15$ K, of four liquids: 2-ethylpyridine, 4-ethylpyridine, ethylpyrazine and 2,3-diethylpyrazine were measured by static bomb calorimetry in an oxygen atmosphere. The values of the standard molar enthalpies of vaporization, at $T = 298.15$ K, were obtained by Calvet microcalorimetry, allowing the calculation of the standard molar enthalpies of formation of the compounds, in the gas phase, at $T = 298.15$ K: 2-ethylpyridine (79.4 ± 2.6) kJ mol^{-1}; 4-ethylpyridine (81.0 ± 3.4) kJ mol^{-1}; ethylpyrazine (146.9 ± 2.8) kJ mol^{-1}; and 2,3-diethylpyrazine (80.2 ± 2.9) kJ mol^{-1}.

The most stable geometries of all ethylpyridine and ethylpyrazine isomers were obtained using the density functional theory with the B3LYP functional and two basis sets: 6-31G* and 6-311G**. These calculations were then used to obtain estimates of the enthalpies of formation of all isomers, including those not experimentally studied, through the use of isodesmic reactions. A discussion of the relationship between structure and energetics of the isomers is also presented.

Introduction

Pyridines and pyrazines form the basic structures of innumerable compounds of both theoretical and practical interest.[1] Our laboratory has been interested in the study of the thermochemistry of aromatic heterocyclic compounds. So, following previous work on the thermochemistry of phenylpyridines[2] and methyldiazines[3] we decided to study the ethylpyridine and ethylpyrazine isomers. The selected approach is a combination of experimental determinations and high-level theoretical calculations of enthalpies of formation in the gas phase.

In the present work we report the standard molar enthalpies of formation of 2-ethylpyridine (2-EtPy), 4-ethylpyridine (4-EtPy), ethylpyrazine (EtPyz) and 2,3-diethylpyrazine (2,3-DEtPyz) in the gas phase, obtained from measurements of combustion energies using a static bomb calorimeter and of the values for the enthalpies of vaporization of the compounds measured by Calvet microcalorimetry. Density functional theory calculations with the B3LYP functional were also performed in order to obtain the most stable geometries and the standard enthalpies of formation for all possible isomers, including those which were not studied in the laboratory, through the use of isodesmic reactions.

Results and discussion

Experimental results

Results for a typical combustion experiment on each compound are given in Table 1, where $\Delta m(\mathrm{H_2O})$ is the deviation of the mass of water added to the calorimeter from the average mass assigned to $\varepsilon_{\mathrm{cal}}$, and ΔU_Σ is the correction to the standard state, as combustion experiments were carried out in oxygen at $p = 3.04$ MPa. The remaining quantities are as previously described.[4] For the cotton-thread fuse, empirical formula $\mathrm{CH_{1.686}O_{0.843}}$, $\Delta_c u° = -16250$ J g^{-1}.[5] The corrections for nitric acid formation $\Delta U(\mathrm{HNO_3})$ were based on -59.7 kJ mol^{-1},[6] for the molar energy of formation of 0.1 mol dm^{-3} $\mathrm{HNO_3(aq)}$ from $\mathrm{N_2}$, $\mathrm{O_2}$, and $\mathrm{H_2O(l)}$. As samples were ignited at $T = 298.15$ K,

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

where $\Delta U(\mathrm{IBP})$ is the energy associated with the isothermal bomb process, ε_{f} is the energy of the bomb contents after ignition and ΔT_{ad} is the adiabatic temperature rise. The individual results of all combustion experiments, together with the mean value and its standard deviation, are given for each compound in Table 2. Table 3 lists the derived standard molar energies and enthalpies of combustion, $\Delta_c U^\circ_m$ (l) and $\Delta_c H^\circ_m$ (l), and the standard molar enthalpies of formation for the compounds in liquid phase $\Delta_f H^\circ_m$ (l) at 298.15 K. 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[7] and in the values of auxiliary quantities. To derive $\Delta_f H^\circ_m$ (l) from $\Delta_c H^\circ_m$ (l) the standard molar enthalpies of formation of $\mathrm{H_2O(l)}$ and $\mathrm{CO_2(g)}$, at $T = 298.15$ K, -285.830 ± 0.042 kJ mol^{-1} [8] and -393.51 ± 0.13 kJ mol^{-1},[8] respectively, were used.

A NIST WebBook[9] and Pedley's book[10] give values for the enthalpy of formation of liquid 2-ethylpyridine, 1.5 kJ mol^{-1} and 1.1 ± 4.1 kJ mol^{-1}, respectively, which are quite different from the value we obtained in this work, (34.7 ± 2.5) kJ mol^{-1}.

Measurements of the enthalpies of vaporization $\Delta^g_l H^\circ_m$ are given in Table 4 with uncertainties of twice the standard deviation of the mean. The derived enthalpies of formation, in both the liquid and gaseous phases, for the two compounds are summarized in Table 5.

A recent compilation by Chickos and Acree[11] lists values of the vaporization enthalpies for both 2-ethylpyridine ($\Delta^g_l H^\circ_m = 43.9$ kJ mol^{-1}, at $T_m = 338$ K; range $T = 323$ to 373 K) and 4-ethylpyridine ($\Delta^g_l H^\circ_m = 45.3$ kJ mol^{-1}, at $T_m = 348$ K, range $T = 333$ to 372 K). These values can be corrected to 298.15 K, using the equation[11]

$$\Delta^g_l H^\circ_m\,(298.15\ \mathrm{K}) = \Delta^g_l H^\circ_m\,(T_m) + [10.58 + 0.26\,C_{pl}\,(298.15\ \mathrm{K})] \times (T_m - 298.15) \quad (2)$$

DOI: 10.1039/b308097h

Table 1 Typical combustion experiments, at $T = 298.15$ K

	2-EtPy	4-EtPy	EtPyz	2,3-DEtPyz
$m(\mathrm{CO_2}, \text{total})/\mathrm{g}$	1.95037	1.85610	1.71735	1.35603
$m(\text{cpd})/\mathrm{g}$	0.64169	0.60801	0.65613	0.47451
$m'(\text{fuse})/\mathrm{g}$	0.00238	0.00231	0.00261	0.00298
$m''(\text{melinex})/\mathrm{g}$	0.04439	0.04557	0.04848	0.05439
$\Delta T_{\mathrm{ad}}/\mathrm{K}$	1.60078	1.52191	1.44127	1.14590
$\varepsilon_{\mathrm{cal}}/\mathrm{J\ K^{-1}}$	15908.3 ± 1.0	15908.3 ± 1.0	15908.3 ± 1.0	16013.8 ± 1.2
$\varepsilon_{\mathrm{f}}/\mathrm{J\ K^{-1}}$	16.41	16.31	16.15	15.84
$\Delta m(\mathrm{H_2O})/\mathrm{g}$	0.1	−0.2	0.0	0.1
$-\Delta U(\mathrm{IBP})/\mathrm{J}$	25492.63	24234.55	23094.12	18368.84
$-\Delta U(\text{melinex})/\mathrm{J}$	1016.59	1043.55	1110.25	1245.72
$-\Delta U(\text{fuse})/\mathrm{J}$	38.65	37.51	42.39	48.40
$-\Delta U(\mathrm{HNO_3})/\mathrm{J}$	43.28	40.95	66.27	41.67
$-\Delta U(\text{carbon})/\mathrm{J}$	0.00	0.00	0.00	0.00
$\Delta U(\text{ign.})/\mathrm{J}$	1.18	1.19	0.92	1.19
$-\Delta U_{\Sigma}/\mathrm{J}$	13.43	12.72	13.95	9.64
$-\Delta_{\mathrm{c}}u^{\circ}/\mathrm{J\ g^{-1}}$	37992.64	37990.54	33317.09	35873.26

Table 2 Individual values of the massic energy of combustion, at $T = 298.15$ K

$-\Delta_{\mathrm{c}}u^{\circ}/\mathrm{J\ g^{-1}}$			
2-EtPy	4-EtPy	EtPyz	2,3-DEtPyz
37973.92	38007.65	33248.82	35863.13
37963.24	38011.30	33270.14	35847.50
37972.01	37935.59	33317.09	35876.28
37979.85	37990.54	33308.99	35901.80
38028.28	38027.37	33296.87	35854.47
37992.64	38060.61	33290.35	35873.26
38030.22	38040.85	33265.77	35885.60
38012.24	37929.32	33278.01	35878.22
	37945.99	33312.82	
	37990.03	33252.50	
		33291.87	
		33326.27	
		33307.19	
$-\langle\Delta_{\mathrm{c}}u^{\circ}\rangle/\mathrm{J\ g^{-1}}$			
37994.0 ± 9.3	37993.9 ± 14.2	33289.7 ± 6.9	35872.5 ± 6.1

Table 3 Derived standard (p° = 0.1 MPa) molar values (kJ mol^{-1}), at $T = 298.15$ K

	$-\Delta_{\mathrm{c}}U^{\circ}_{\mathrm{m}}$ (l)	$-\Delta_{\mathrm{c}}H^{\circ}_{\mathrm{m}}$ (l)	$\Delta_{\mathrm{f}}H^{\circ}_{\mathrm{m}}$ (l)
2-EtPy	4071.2 ± 2.3	4075.5 ± 2.3	34.7 ± 2.5
4-EtPy	4071.2 ± 3.2	4075.5 ± 3.2	34.7 ± 3.3
EtPyz	3600.0 ± 1.9	3602.5 ± 1.9	98.1 ± 2.1
2,3-DEtPyz	4885.7 ± 2.2	4890.7 ± 2.2	27.6 ± 2.4

Table 6 Calculated energies (hartree) and zero-point vibrational energies (kJ mol^{-1}) of the ethylpyridine isomers

Compound	$E_{\mathrm{B3LYP/6\text{-}31G*}}$	$E_{\mathrm{B3LYP/6\text{-}311G**}}$	$E_{\mathrm{ZP/B3LYP/6\text{-}31G*}}$
Py	−248.284942	−248.349880	233.75
2-EtPy	−326.919601	−327.006462	382.39
3-EtPy	−326.917083	−327.003134	382.58
4-EtPy	−326.917785	−327.003954	382.62

Table 7 Calculated energies (hartree) and zero-point vibrational energies (kJ mol^{-1}) of the ethylpyrazine isomers

Compound	$E_{\mathrm{B3LYP/6\text{-}31G*}}$	$E_{\mathrm{B3LYP/6\text{-}311G**}}$	$E_{\mathrm{ZP/B3LYP/6\text{-}31G*}}$
Pyz	−264.317226	−264.384453	202.27
EtPyz	−342.952779	−343.041912	350.88
2,3-DEtPyz	−421.584963	−421.695916	499.99
2,5-DEtPyz	−421.588043	−421.699014	499.18
2,6-DEtPyz	−421.588212	−421.699166	499.37
TriEtPyz	−500.220166	−500.352901	648.30
TetraEtPyz	−578.852194	−579.006661	797.06

where C_{pl} (298.15 K) = 190 J K^{-1} mol^{-1} was estimated using a group additivity method. The calculated values for the enthalpies of vaporization, at $T = 298.15$ K, of 2-ethylpyridine and of 4-ethylpyridine are respectively, 46.1 kJ mol^{-1} and 48.2 kJ mol^{-1}. Our experimental values (Table 4) are lower but not in bad agreement.

Theoretical results

Total energies E identified by the subscripts B3LYP/6-31G* and B3LYP/6-311G** as well as zero-point vibrational energies E_{ZP} of all the possible ethylpyridine and ethylpyrazine isomers are presented, respectively, in Tables 6 and 7.

Table 4 Standard molar enthalpies of vaporization, at $T = 298.15$ K

	No. of expts	T/K	$\Delta_{\mathrm{l},\,298.15\,\mathrm{K}}^{\mathrm{g},\,T}H^{\circ}_{\mathrm{m}}/\mathrm{kJ\ mol^{-1}}$	$\Delta_{298.15\,\mathrm{K}}^{T}H^{\circ}_{\mathrm{m}}(\mathrm{g})/\mathrm{kJ\ mol^{-1}}$	$\Delta_{\mathrm{l}}^{\mathrm{g}}H^{\circ}_{\mathrm{m}}$ (298.15 K)/kJ mol^{-1}
2-EtPy	6	363	54.1 ± 1.0	9.4	44.7 ± 0.8
4-EtPy	6	363	55.7 ± 2.2	9.4	46.3 ± 0.7
EtPyz	6	363	57.9 ± 1.9	9.1	48.8 ± 1.9
2,3-DEtPyz	6	384	69.8 ± 1.7	17.2	52.6 ± 1.7

Table 5 Derived standard (p° = 0.1 MPa) molar values, at $T = 298.15$ K, for the enthalpies of formation in the gas phase

	$\Delta_{\mathrm{f}}H^{\circ}_{\mathrm{m}}$ (l)/kJ mol^{-1}	$\Delta_{\mathrm{l}}^{\mathrm{g}}H^{\circ}_{\mathrm{m}}$/kJ mol^{-1}	$\Delta_{\mathrm{f}}H^{\circ}_{\mathrm{m}}$ (g)/kJ mol^{-1}
2-EtPy	34.7 ± 2.5	44.7 ± 0.8	79.4 ± 2.6
4-EtPy	34.7 ± 3.3	46.3 ± 0.7	81.0 ± 3.4
EtPyz	98.1 ± 2.1	48.8 ± 1.9	146.9 ± 2.8
2,3-DEtPyz	27.6 ± 2.4	52.6 ± 1.7	80.2 ± 2.9

Table 8 Calculated B3LYP/6-311G** bond lengths (Å) and bond angles (°) of the ethylpyridine isomers

	Py	2-EtPy	3-EtPy	4-EtPy
1–2	1.337	1.342	1.335	1.336
2–3	1.393	1.399	1.399	1.392
3–4	1.392	1.391	1.396	1.397
4–5	1.391	1.391	1.391	1.397
5–6	1.394	1.393	1.393	1.392
6–1	1.336	1.334	1.336	1.336
C_b–7	—	1.511	1.511	1.510
7–8	—	1.537	1.539	1.539
1–2–3	123.7	121.9	124.7	123.8
2–3–4	118.5	119.3	116.7	119.5
3–4–5	118.5	118.8	119.5	116.7
4–5–6	118.5	118.0	118.5	119.5
5–6–1	123.7	123.7	123.2	123.9
6–1–2	117.2	118.3	117.3	116.6
α[a]	—	116.2	121.2	121.6
C_b–7–8	—	112.4	113.0	112.6
θ[b]	—	69.8	−93.8	89.1

C_b carbon atom of the pyridinic ring; [a] α represents the angle 1–2–7, 2–3–7 and 3–4–7, respectively, for 2-, 3- and 4-ethylpyridine. [b] θ represents the dihedral angle 1–2–7–8, 2–3–7–8 and 3–4–7–8 for 2-, 3- and 4-ethylpyridine, respectively.

Geometries

The optimum geometries obtained with the two basis sets, 6-31G* and 6-311G**, are very similar. So, for the sake of conciseness we just report the B3LYP/6-311G** results. For the pyridines these are shown in Table 8 (the geometric parameters referring to the C–H bonds have been omitted). Fig. 1 displays the atom numbering scheme used. Table 8 also presents the dihedral angles θ which define the orientation of the ethyl group relative to the pyridinic ring in the three ethylpyridine isomers. We may conclude from the analysis of the values of the θ angles that in the 3- and 4-isomers the ethyl group lies out of the plane of the ring, assuming an almost perpendicular conformation (dihedral angles of −93.8° and 89.1°, respectively). A similar conformational behavior has also been found for ethylbenzene, for which experimental studies in the gaseous-phase (*supersonic molecular jet spectroscopy*)[12] and theoretical studies (empirical molecular mechanics[12] and *ab initio* STO-3G[13]) suggest that the C_α–C_β bond of the ethyl group is perpendicular to the plane of the aromatic ring. The authors suggest that this preference for a perpendicular conformation in ethylbenzene results from unfavourable steric interactions between the methyl group and the *ortho* hydrogen atom of the aromatic ring, in the planar conformation. We may conclude that the same occurs in the isomers 3- and 4-ethylpyridine. However, in the case of the 2-ethylpyridine isomer the ethyl group is not truly found perpendicular to the plane of the ring, as evidenced from the dihedral angle N_1–C_2–C_7–C_8 of 69.8° (conformation *syn-gauche*). This fact seems to be the result of a favourable interaction between one of the hydrogen atoms of the methyl group and the non-bonded electron pair of the nitrogen atom in the pyridinic ring. This interaction can also be observed in the phenylpyridine isomers,[2] where the dihedral angle which defines the orientation of the phenyl group relative to the pyridinic ring, is only 27.9° in the 2-phenylpyridine isomer, being much lower than the torsion angles of 45.6° and 43.5° observed in the 3- and 4-isomers, respectively.

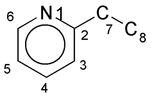

Fig. 1 Atom numbering scheme of the ethylpyridine isomers.

The equilibrium geometries, obtained using the 6-311G** basis set, of all ethylpyrazine isomers are reported in Table 9 as well as the dihedral angles θ which define the orientation of the ethyl group relative to the pyrazinic ring. In Fig. 2 is shown the numbering of the atoms. In all isomers the C_α–C_β bond of the ethyl group is not in the plane of the aromatic ring, as observed for the ethylpyridine isomers. The dihedral angle N–C_b–C_α–C_β reveals a deviation from the truly perpendicular conformation from about 20 to 25°, unless there exists another substituent at the *ortho* position relative to the former. In such cases, which occur in 2,3-DEtPyz, in TriEtPyz and in TetraEtPyz, the ethyl groups assume a perpendicular conformation and orient themselves to opposite sides of the plane of the aromatic ring, minimizing in this way the steric repulsions between them. This behaviour is in agreement with that observed in an experimental study (*supersonic molecular jet spectroscopy*)[12] in the gas-phase of the conformation of the three diethylbenzene isomers. The authors concluded that, in the most stable conformation of these isomers, the C_α–C_β bond is perpendicular to the plane of the ring and the ethyl groups are on opposite sides of the plane of the ring.

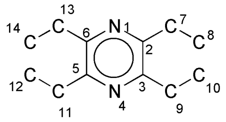

Fig. 2 Atom numbering scheme of the ethylpyrazine isomers.

From the observed geometries, we may conclude that the most stable conformation of the ethylpyridine and ethylpyrazine isomers is obviously determined by the relative importance of two interactions: the stabilizing interaction hydrogen–nitrogen and the destabilizing interaction hydrogen–hydrogen.

Calculated enthalpies of formation. To access the relative stability of the ethylpyridine and ethylpyrazine isomers and to estimate their enthalpies of formation we have considered the following isodesmic reactions:

For the ethylpyridines

$$C_7H_9N + C_6H_6 \longrightarrow C_5H_5N + C_8H_{10}$$

and for the ethylpyrazines

$$\begin{gathered} C_6H_8N_2 + C_6H_6 \longrightarrow C_4H_4N_2 + C_8H_{10} \\ C_8H_{12}N_2 + 2\,C_6H_6 \longrightarrow C_4H_4N_2 + 2\,C_8H_{10} \\ C_{10}H_{16}N_2 + 3\,C_6H_6 \longrightarrow C_4H_4N_2 + 3\,C_8H_{10} \\ C_{12}H_{20}N_2 + 4\,C_6H_6 \longrightarrow C_4H_4N_2 + 4\,C_8H_{10} \end{gathered}$$

whose energies represent, respectively, the effect of the ethyl group on the stability of the pyridinic and pyrazinic ring measured relative to its effect on the stability of benzene. These reactions being of the isodesmic type (the number of bonds of any formal type is conserved in each side of the equations) are likely to largely cancel the correlation errors, thus leading to reliable estimates of the enthalpies of formation for the isomers. The energies of benzene, ethylbenzene, pyridine and pyrazine have been obtained using the same calculation procedures described for the pyridine and pyrazine isomers.

The calculated reaction energies, at $T = 0$ K, $\Delta_r E_{T=0\,\mathrm{K}}$, for the ethylpyridines are presented in Table 10. The 2-ethylpyridine is predicted to be the most stable of the three isomers and 3-ethylpyridine the least stable one. This results most probably, as mentioned above, from the stabilizing interaction between one of the hydrogen atoms of the methyl group and the non-bonded electron pair of the nitrogen atom in the pyridinic ring. However, the experimental results for the *ortho*, (79.4 ± 2.6) kJ mol^{-1}, and *para*, (81.0 ± 3.4) kJ mol^{-1}, isomers are not very different; considering the experimental uncertainties, they are equal.

From the results of the calculated reaction energies, at $T =$ 0 K, $\Delta_r E_{T=0\,\mathrm{K}}$, for the ethylpyrazines presented in Table 11 we

Table 9 Calculated B3LYP/6-311G** bond lengths (Å) and bond angles (°) of the ethylpyrazine isomers

	Pyz	EtPyz	2,3-DEtPyz	2,5-DEtPyz	2,6-DEtPyz	TriEtPyz	TetraEtPyz
1–2	1.335	1.340	1.340	1.339	1.338	1.338	1.337
2–3	1.395	1.401	1.412	1.399	1.400	1.411	1.406
3–4	1.335	1.333	1.339	1.332	1.333	1.337	1.337
4–5	1.335	1.334	1.333	1.340	1.333	1.338	1.336
5–6	1.394	1.393	1.390	1.399	1.400	1.397	1.407
6–1	1.335	1.333	1.333	1.332	1.338	1.332	1.336
2–7	—	1.508	1.511	1.508	1.510	1.512	1.512
7–8	—	1.537	1.538	1.537	1.538	1.538	1.538
3–9	—	—	1.511	—	—	1.512	1.512
9–10	—	—	1.538	—	—	1.538	1.538
5–11	—	—	—	1.508	—	1.508	1.512
11–12	—	—	—	1.537	—	1.537	1.538
6–13	—	—	—	—	1.511	—	1.512
13–14	—	—	—	—	1.539	—	1.538
1–2–3	122.0	120.3	120.8	119.9	120.3	120.4	120.2
2–3–4	122.0	122.9	120.7	122.9	122.4	120.8	120.2
3–4–5	115.9	116.2	117.8	117.2	116.5	118.9	119.5
4–5–6	122.1	121.6	121.5	119.9	122.4	119.8	120.2
5–6–1	122.0	122.1	121.5	122.9	120.3	122.3	120.2
6–1–2	115.9	117.0	117.7	117.2	118.2	118.0	119.5
1–2–7	—	117.4	115.7	117.6	117.5	115.9	115.9
2–7–8	—	112.3	112.3	112.4	112.5	112.4	112.4
4–3–9	—	—	115.7	—	—	115.7	115.8
3–9–10	—	—	112.3	—	—	112.3	112.4
4–5–11	—	—	—	117.6	—	117.6	115.9
5–11–12	—	—	—	112.4	—	112.5	112.4
1–6–13	—	—	—	—	117.5	—	115.9
6–13–14	—	—	—	—	112.4	—	112.4
1–2–7–8		72.0	−85.6	−69.8	68.7	−85.8	−84.8
4–3–9–10	—	—	−85.3	—	—	−85.3	−84.6
4–5–11–12	—	—	—	69.4	—	−67.8	−84.9
1–6–13–14	—	—	—	—	70.0	—	−84.9

Table 10 Calculated reaction energies, at $T = 0$ K, enthalpies, at $T = 298.15$ K and standard enthalpies of formation in the gas phase, at $T = 298.15$ K, of the ethylpyridines (all values in kJ mol^{-1})

	$\Delta_r E_{T=0\ K}$		$\Delta_r H^\circ_{T=298.15\ K}$			$\Delta_f H^\circ_m$ (calc.)		
	B3LYP		B3LYP			B3LYP		
	6-31G*	6-311G**	6-31G*	6-311G**	exp.	6-31G*	6-311G**	$\Delta_f H^\circ_m$ (exp.)
2-EtPy	8.3	10.7	8.5	10.9	8.1 ± 2.9	79.1	76.7	79.4 ± 2.6
3-EtPy	1.7	2.0	1.7	2.0	—	85.9	85.6	—
4-EtPy	3.5	4.1	3.5	4.1	6.6 ± 3.6	84.1	83.5	81.0 ± 3.4

Table 11 Calculated reaction energies, at $T = 0$ K, enthalpies, at $T = 298.15$ K and standard enthalpies of formation in the gas phase, at $T = 298.15$ K, of the ethylpyrazines (kJ mol^{-1})

	$\Delta_r E_{T=0\ K}$		$\Delta_r H^\circ_{T=298.15\ K}$			$\Delta_f H^\circ_m$ (calc.)		
	6-31G*	6-311G**	6-31G*	6-311G**	exp.	6-31G*	6-311G**	$\Delta_f H^\circ_m$ (exp.)
EtPyz	10.7	13.0	10.9	13.2	−3.7 ± 3.3	132.3	130.0	146.9 ± 2.8
2,3-DEtPyz	12.6	16.9	12.8	17.1	10.2 ± 3.9	77.6	73.3	80.2 ± 2.9
2,5-DEtPyz	20.7	25.1	21.3	25.6	—	69.1	64.8	—
2,6-DEtPyz	21.2	25.5	21.6	25.9	—	68.8	64.5	—
TriEtPyz	22.5	28.7	22.8	29.1	—	14.8	8.5	—
TetraEtPyz	23.9	32.0	24.3	32.4	—	−39.5	−47.6	—

can observe that the calculation method predicts an essentially linear stabilization of the pyrazine ring upon ethyl substitution. The energetic increment observed on the introduction of two ethyl groups in *meta* (2,5-diethylpyrazine) and *para* (2,6-diethylpyrazine) positions equals twice the energetic increment observed on the introduction of only one ethyl group in the pyrazinic ring. However, steric repulsion between the two ethyl groups in 2,3-diethylpyrazine seems to be the reason for the lower stability of this isomer when compared with the other two (the additive rule is not observed). The introduction of three ethyl groups corresponds to the sum of the energetic increment for the introduction of two ethyl groups in the *ortho* position and the energetic increment for the introduction of only one ethyl group. The energetic stabilization observed on the introduction of four ethyl groups in the pyrazinic ring equals twice that obtained for the introduction of two ethyl groups *ortho*. In a previous study[3] the same energetic effect for methyl substitutions in pyrazine was observed.

To compare the theoretical with experimental results the reaction enthalpies were calculated from the reaction energies, by adding the zero-point vibrational energies and the thermal corrections from $T = 0$ K to $T = 298.15$ K. The resulting reaction enthalpies, at $T = 298.15$ K, and the estimates of the standard enthalpies of formation (including those not studied experimentally) are also presented in Tables 10 and 11, together with the derived experimental enthalpy values (the standard enthalpies of formation of the auxiliary molecules are known with high precision and accuracy and were taken from Pedley[10]).

Besides the correct description of the relative stability of the ethylpyridine isomers we can observe that the theoretical results reproduce very closely the experimental values. The errors are within the experimental deviation.

The error for the ethylpyrazine isomer is about 15 kJ mol^{-1} with both methods of calculation. For 2,3-diethylpyrazine the B3LYP/6-31G* result is in good agreement with the experimental value but the B3LYP/6-311G** result is different from the experimental one by about 7 kJ mol^{-1}.

Experimental

Materials

The ethylpyridines and ethylpyrazines studied are commercial products (Aldrich Chemical Co.) and were purified by vacuum distillation until the combustion results were consistent and the carbon dioxide recovery ratios were satisfactory. The average ratios, together with the standard deviation of the mean, of the mass of carbon dioxide recovered to that calculated from the mass of sample were: 2-ethylpyridine [100-71-0], (0.9982 ± 0.0003); 4-ethylpyridine [536-75-4], (0.9978 ± 0.0004); ethylpyrazine [13925-00-3], (0.9972 ± 0.0003) and 2,3-diethylpyrazine [15707-24-1], (0.9998 ± 0.0003). The densities of the samples were: 2-EtPy, $\rho = 0.937$ g cm^{-3};[14] 4-EtPy, $\rho = 0.942$ g cm^{-3};[14] EtPyz, $\rho = 0.984$ g cm^{-3} [14] and 2,3-DEtPyz, $\rho = 0.963$ g cm^{-3}.[14] The purity of all compounds was also assessed by gas chromatography and the IR spectra were also taken as additional criteria of purity.

Combustion calorimetry

The combustion experiments were performed with a static bomb calorimeter. The apparatus and technique have been described.[15,16] Benzoic acid (Bureau of Analysed Samples, Thermochemical Standard, BCS-CRM-190 p) was used for calibration of the calorimeter. Its massic energy of combustion is $\Delta_c u = -(26432.3 \pm 3.8)$ J g^{-1}, under certificate conditions. The calibration results were 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 performed $\varepsilon_{\text{cal}} = (15908.3 \pm 1.0)$ J K^{-1}, where the uncertainty quoted is the standard deviation of the mean. For combustion experiments on 2,3-diethylpyrazine we changed from the bomb Parr model 1105, to a bomb Parr model 1108. With this bomb the determined value of ε_{cal} was (16013.8 ± 1.2) J K^{-1}. Sealed melinex bags were used in combustion of the liquid compounds using the technique described by Skinner and Snelson,[17] who determined the specific energy of combustion of dry melinex as $\Delta_c u^\circ = -(22902 \pm 5)$ J g^{-1}. This value was confirmed in our laboratory. The amount of substance m(cpd) used in each experiment was determined from the total mass of carbon dioxide $m(\text{CO}_2$, total) produced after allowance for that formed from the cotton thread fuse and melinex.

Calvet microcalorimetry

The enthalpies of vaporization were measured using the "vacuum sublimation" drop microcalorimetric method,[18] which, in the case of vaporization, was previously tested in the Porto laboratory.[19] Samples, about 7–11 mg of the liquid, contained in thin glass capillary tubes sealed at one end, were dropped, at room temperature, into the hot reaction vessel, in a high temperature Calvet microcalorimeter held at a convenient temperature T, and then removed from the hot zone by vacuum vaporization. The observed enthalpies of vaporization were corrected to $T = 298.15$ K using the value of $\Delta_{298.15\,\text{K}}^{T} H_{\text{m}}^{\circ}$ (g) estimated by a group method with values from Stull *et al.*[20] The microcalorimeter was calibrated *in situ* for these measurements using the reported enthalpy of vaporization of undecane.[10]

Computational details

The most stable conformations of all possible ethylpyridine and ethylpyrazine isomers were obtained using the density functional theory (DFT) with the Becke 3-parameter hybrid exchange[21] and Lee–Yang–Parr[22] correlation density functional (B3LYP). Two different basis sets were used: the double-ξ valence plus polarization 6-31G* [23] and the 6-311G** triple-ξ valence plus polarization.[24]

The harmonic vibrational frequencies were calculated through construction and diagonalization of the Hessian matrices at the B3LYP/6-31G* level of theory in order to characterize these equilibrium geometries as true minima of the potential energy surface and to evaluate the corrections needed to estimate energies at any temperature different from 0 K. The harmonic vibrational frequencies were scaled by the factor 0.96[25] in order to correct for anharmonicity. All calculations were performed using the UK version of GAMESS.[26,27]

Acknowledgements

Thanks are due to Fundação para a Ciência e Tecnologia for financial support given to the Faculty of Science of the University of Porto (project PBIC/C/QUI/2193). M. S. Miranda thanks F. C. T. for the award of a research grant under PRAXIS XXI (research grant n° BD/9287/96).

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26 GAMESS-UK is a package of *ab initio* programs written by M. F. Guest, J. H. van Lenthe, J. Kendrick, K. Schoffel, and P. Sherwood, with contributions from R. D. Amos, R. J. Buenker, H. J. J. van Dam, M. Dupuis, N. C. Handy, I. H. Hillier, P. J. Knowles, V. Bonacic-Koutecky, W. von Niessen, R. J. Harrison, A. P. Rendell, V. R. Saunders, A. J. Stone and A. H. de Vries. The package is derived from the original GAMESS code due to M. Dupuis, D. Spangler and J. Wendoloski, NRCC Software Catalog, Vol. 1, Program No. QG01 (GAMESS), 1980.

27 The DFT module within GAMESS-UK was developed by Dr P. Young under the auspices of EPSRC's Collaborative Computational Project No. 1 (CCP1) (1995–1997).