

The enthalpies of dissociation of the N—O bonds in two quinoxaline derivatives

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The present work reports the first experimental thermochemical study of mono-*N*-oxides derived from quinoxaline, namely, 3-methoxycarbonyl-2-methyl-quinoxaline *N*-oxide and 3-ethoxycarbonyl-2-methyl-quinoxaline *N*-oxide. The values of the enthalpies of formation, in the condensed state, and of the enthalpies of sublimation, derived from static bomb calorimetry and Calvet microcalorimetry measurements, respectively, are combined to derive the standard molar enthalpies of formation in the gaseous phase for these two compounds. From the latter values, the first and second N—O bond dissociation enthalpies for the corresponding di-*N*-oxides have been obtained. The gas-phase experimental results are also compared with calculated data obtained with a density functional theory approach. Copyright © 2008 John Wiley & Sons, Ltd.

Supporting information may be found in the online version of this article.

Keywords: enthalpy of formation; enthalpy of dissociation; density functional theory; calorimetry; synthesis

INTRODUCTION

Quinoxaline derivatives play an important role in the development of new therapeutic agents, due to their relevant antibacterial, antiviral or antifungal activities. The oxidation of one or both nitrogen atoms of the heterocyclic ring increases the diversity of their biological properties, since their potential to act as oxidizing agents leads to a large variety of therapeutic applications. These compounds are used as medicinal feed additives^[1,2] and they are also used as bioreductive cytotoxic agents/species,^[3,4] as a consequence of the hypoxia-selective activity evidenced by some quinoxaline di-*N*-oxides.^[5–8]

Over the last decade, experimental and theoretical energetic studies have been expanded to several quinoxaline 1,4-di-*N*-oxides, in order to evaluate the influence of the chemical vicinity on the dissociation enthalpies of the N—O bonds.^[9–16] However, experimental studies for quinoxaline 1-*N*-oxide derivatives have not been described so far, mainly due to the difficulty in obtaining convenient amounts of highly pure samples of those compounds.

Recently, we have been able to synthesize very pure samples of two quinoxaline derivatives containing only a single dative N—O bond, by selective reduction of the corresponding 1,4-di-*N*-oxides previously prepared from benzofuroxan and the appropriate β -ketoester, allowing the experimental study of its molecular energetics by standard thermochemical approaches. Thus, the present work reports the first experimental thermochemical study of mono-*N*-oxide quinoxalines, namely, 3-methoxycarbonyl-2-methyl-quinoxaline *N*-oxide, **1**, and 3-ethoxycarbonyl-2-methyl-quinoxaline *N*-oxide, **2**, with structures shown in Scheme 1.

A static bomb calorimeter was used to determine the standard molar energies of combustion, in oxygen and at $T = 298.15$ K, of the two title compounds from which the values of the standard molar enthalpies of formation, in the condensed phase, were derived. Furthermore, the standard molar enthalpies of sublima-

tion, at $T = 298.15$ K, were obtained by high temperature Calvet microcalorimetry using the vacuum sublimation drop method. Finally, combining the standard molar enthalpies of formation in the condensed phase and the corresponding enthalpies of sublimation allowed us to derive the standard ($p^\circ = 0.1$ MPa) molar enthalpies of formation in the gas phase, at $T = 298.15$ K, for both compounds. The latter values were used to obtain the experimental values for the first N—O bond dissociation enthalpy in the parent di-*N*-oxide quinoxalines since their corresponding standard molar enthalpies of formation in the gas phase were previously reported in the literature.^[9,10]

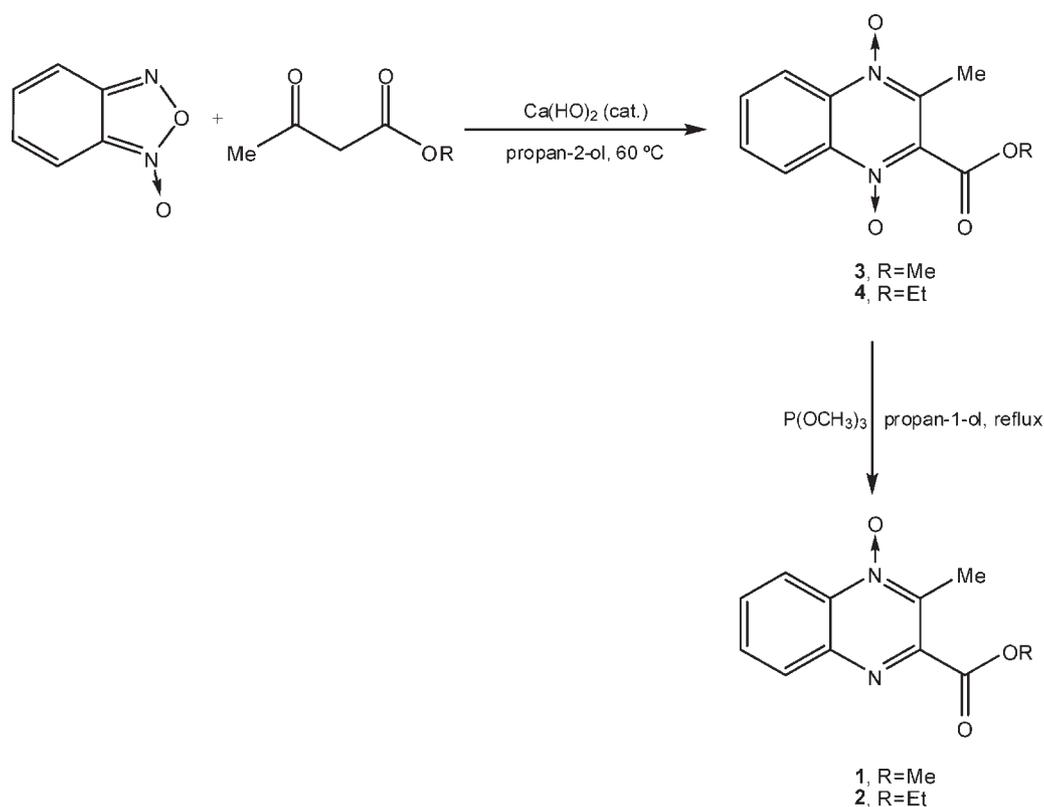
The experimental results for first N—O bond dissociation enthalpies were used to calibrate a computational approach that was used to calculate either the enthalpies of formation of the quinoxaline derivatives or of dissociation of the second N—O bond.

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Scheme 1. Synthetic route to quinoxaline mono-*N*-oxides

EXPERIMENTAL DETAILS

Synthesis and purification

The quinoxaline di-*N*-dioxides (**3** and **4**, Scheme 1) were prepared from benzofuroxan and the appropriate β -ketoester, following the method described by Robertson and Kasubick.^[17] The di-*N*-oxides were then selectively monodeoxygenated with trimethyl phosphite, as described by Dirlam and McFarland,^[18] to yield the corresponding mono-*N*-oxides (**1** and **2**, Scheme 1). The products precipitated from the reaction mixture were isolated by suction filtration and recrystallized from methanol. The structure and purity of both **1** and **2** were confirmed by ¹H-NMR, ¹³C-NMR and elemental analysis, as detailed in the Supplementary Material. Prior to calorimetric measurements, the compounds were further purified by vacuum sublimation.

The fusion temperatures for compounds **1** and **2**, as determined by differential scanning calorimetry (DSC), are 382 K and 360–361 K, respectively. A redetermination of the temperatures of fusion on the cooled samples, already melted in the DSC, leads to the same values, showing that there was no decomposition during fusion.

The average ratios of the mass of carbon dioxide recovered to that calculated from the mass of sample, together with the standard deviation of the mean, were: (0.9991 \pm 0.0005) and (1.0005 \pm 0.0007) for compounds **1** and **2**, respectively. The densities of both samples were assumed to be $\rho = 1.0 \text{ g} \cdot \text{cm}^{-3}$ (estimated from the weight and volume of a pellet for each compound).

Combustion calorimetry

The combustion experiments were performed with a static-bomb calorimeter originally assembled in the National Physical

Laboratory, Teddington, U.K.^[19] and in the University of Manchester,^[20] and now installed in the Thermochemistry Laboratory in the University of Porto, Portugal.^[21] The twin valve bomb, with an internal volume of 0.290 dm³ and wall thickness of 1 cm, is made of stainless steel. Both the apparatus and the operating technique have been described already in the literature.^[19–21]

The energy equivalent of the calorimeter was determined from the combustion of benzoic acid (NIST Standard Reference Material 39j) with a massic energy of combustion, under standard bomb conditions, of $-(26434 \pm 3) \text{ J} \cdot \text{g}^{-1}$. From 11 calibration experiments, $\epsilon(\text{cal}) = (15553.3 \pm 0.9) \text{ J} \cdot \text{K}^{-1}$, for an average mass of water added to the calorimeter of 2900.0 g.

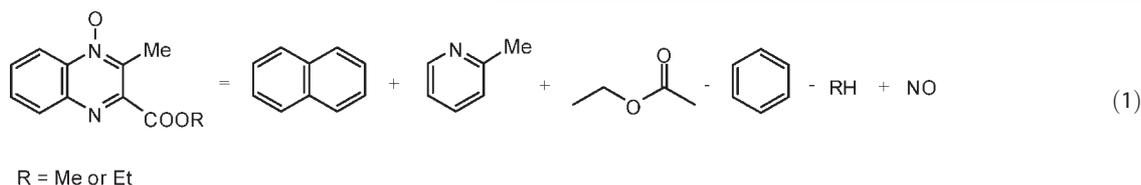
In all combustion experiments, samples in pellet form were ignited at $T = (298.150 \pm 0.001) \text{ K}$, in oxygen at a pressure $p = 3.04 \text{ MPa}$, with a volume of 1.00 cm³ of water added to the bomb. In the experiments made for **2**, *n*-hexadecane (99+%, Aldrich, $\rho = 0.773 \text{ g} \cdot \text{cm}^{-3}$ ^[22]) was used as an auxiliary combustion material (standard massic energy of combustion, $\Delta_c u^\circ = -(47141.4 \pm 3.6) \text{ J} \cdot \text{g}^{-1}$) in order to produce an appropriate increase of temperature. The massic energy of combustion for the cotton thread fuse ($\rho = 1.50 \text{ g} \cdot \text{cm}^{-3}$, $c_p = 1.48 \text{ J} \cdot \text{K}^{-1} \cdot \text{g}^{-1}$, $M = 27.700 \text{ g} \cdot \text{mol}^{-1}$ ^[23]) of empirical formula CH_{1.686}O_{0.843} is $\Delta_c u^\circ = -16250 \text{ J} \cdot \text{g}^{-1}$.^[24] Corrections for nitric acid formation were based on $-59.7 \text{ kJ} \cdot \text{g}^{-1}$ for the molar energy of formation of 0.1 mol $\cdot \text{dm}^3$ HNO₃(aq) from N₂(g), O₂(g), and H₂O(l).^[25] At $T = 298.15 \text{ K}$, $(\partial u / \partial p)_T$ for the solid was assumed to be $-0.2 \text{ J} \cdot \text{g}^{-1} \cdot \text{MPa}^{-1}$, a typical value for organic solids. The amount of substance used in each combustion experiment was determined from the total mass of carbon dioxide produced after allowance for that formed from the cotton thread fuse and hexadecane. For each experiment, the value of $\Delta_c u^\circ$ was

calculated by using the procedure given by Hubbard *et al.*^[26] The relative atomic masses used were those recommended by the IUPAC Commission in 2005.^[27]

Calvet microcalorimetry

The standard molar enthalpies of sublimation of the two *N*-oxide quinoxalines were measured using the vacuum sublimation drop-microcalorimetric technique.^[28] Samples of about 3 mg of the crystalline compounds contained in a small thin glass capillary tube sealed at one end, and a blank capillary with similar mass, were simultaneously dropped at room temperature into the hot reaction vessel in the Calvet high-temperature microcalorimeter (Setaram HT 1000), held at $T = 385$ K in the case of **1** and at $T = 378$ K in the case of **2**, and then removed from the hot zone by sublimation under reduced pressure. 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 sublimation $\{H_m^{\circ}(\text{g}, T) - H_m^{\circ}(\text{cr}, 298.15 \text{ K})\}$ were corrected to $T = 298.15$ K using $\Delta_{298.15}^T H_m^{\circ}(\text{g})$ estimated by a group method of energy contributions based on data of Stull *et al.*^[29] and Equ. 1. Finally, the microcalorimeter was calibrated *in situ* for these measurements by using naphthalene, $\Delta_{\text{cr}}^{\circ} H_m^{\circ} = (72.5 \pm 0.1) \text{ kJ} \cdot \text{mol}^{-1}$.^[30]



Computational details

The molecular structures of all compounds considered in this work have been initially optimized with the B3LYP method together with the 6-31G(d) basis set.^[31,32] The geometries obtained have been characterized as true minima after the computation of the vibrational frequencies at the same level of theory. This set of calculations also yield the thermal corrections for $T = 298.15$ K that was added to the energy obtained with the same DFT approach but using a larger basis set. Thus, starting from the previously optimized structures, the B3LYP/6-311+G(2d,2p) approach was used to further optimize the geometry and to obtain the energies of all compounds that were used throughout this work. The absolute enthalpies of all compounds which were used to estimate the standard molar enthalpies of formation and enthalpies of N–O bond dissociation are B3LYP/6-311+G(2d,2p)//B3LYP/6-31G(d) values. All the calculations have been performed by means of the Gaussian 98 computer code.^[33]

RESULTS

The results of a typical static bomb combustion experiment for each compound studied are given in Table 1. In this Table, ΔU_{Σ} is

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

	Compound	
	1	2
$m(\text{CO}_2, \text{total})/\text{g}$	1.16332	1.36218
$m(\text{compound})/\text{g}$	0.52583	0.39024
$m(\text{fuse})/\text{g}$	0.00275	0.00229
$m(\text{hexadecane})/\text{g}$	—	0.15130
$\Delta T_{\text{ad}}/\text{K}$	0.85617	1.12572
$\varepsilon_f/(\text{J} \cdot \text{K}^{-1})$	13.87	14.48
$\Delta m(\text{H}_2\text{O})/\text{g}$	−0.7	0.0
$-\Delta U(\text{IBP})/\text{J}$	13325.93	17524.93
$\Delta U(\text{hexadecane})/\text{J}$	—	7141.34
$\Delta U(\text{fuse})/\text{J}$	44.66	37.19
$\Delta U(\text{HNO}_3)/\text{J}$	32.57	30.81
$U(\text{ign})/\text{J}$	0.73	1.19
U_{Σ}/J	10.21	9.21
$-(\Delta_c u^{\circ}/\Delta \text{J} \cdot \text{g}^{-1})$	25174.98	26407.31

the energy correction to the standard state and the rest of the terms have the same meaning as those described in reference [26]. The energy associated with the isothermal bomb process, $\Delta U(\text{IBP})$, after ignition of the samples at the reference

temperature was obtained from Equ. 2. In this equation $\Delta m(\text{H}_2\text{O})$ is the deviation of the mass of water added to the calorimeter from 2900.0 g, i.e., mass assigned to $\varepsilon(\text{cal})$, ε_f is the energy of the bomb contents after ignition, ΔT_{ad} is the adiabatic temperature rise, and $\Delta U(\text{ign})$ is the ignition energy:

$$\Delta U(\text{IBP}) = -\{\varepsilon(\text{cal}) + \Delta m(\text{H}_2\text{O})c_p(\text{H}_2\text{O}, \text{l}) + \varepsilon_f\}\Delta T_{\text{ad}} + \Delta U(\text{ign}) \quad (2)$$

The individual values of $-\Delta_c u^{\circ}$ together with the mean value, $\langle \Delta_c u^{\circ} \rangle$ and its standard deviations are given, for each compound, in Table 2, where $\Delta_c u^{\circ}$ refers to the idealized combustion reaction yielding $\text{N}_2(\text{g})$, $\text{CO}_2(\text{g})$, and $\text{H}_2\text{O}(\text{l})$. Unfortunately, only a small amount of **2** was available for the combustion experiments and, therefore, only four experiments were possible.

The standard molar energies, $\Delta_c U_m^{\circ}(\text{cr})$, and enthalpies, $\Delta_c H_m^{\circ}(\text{cr})$, of combustion at $T = 298.15$ K and in the condensed phase are given in Table 3. The standard molar enthalpies of formation in crystalline state, $\Delta_f H_m^{\circ}(\text{cr})$, were derived from $\Delta_c H_m^{\circ}(\text{cr})$ by using the standard molar enthalpies of formation of $\text{CO}_2(\text{g})$ and $\text{H}_2\text{O}(\text{l})$, at $T = 298.15$ K, $-(393.51 \pm 0.13) \text{ kJ} \cdot \text{mol}^{-1}$,^[34] and $-(285.830 \pm 0.040) \text{ kJ} \cdot \text{mol}^{-1}$,^[34] respectively. The $\Delta_f H_m^{\circ}(\text{cr})$ values are $-(262.4 \pm 4.2) \text{ kJ} \cdot \text{mol}^{-1}$ and $-(302.7 \pm 7.3) \text{ kJ} \cdot \text{mol}^{-1}$ for compounds **1** and **2**, respectively. In accordance with normal thermochemical practice,^[35,36] the uncertainties assigned to the standard molar enthalpies of combustion are, in each case, twice

Table 2. Individual values of the massic energy of combustion, $\Delta_c u^\circ$, at $T = 298.15$ K

Compound	
1	2
25165.40	26399.52
25174.98	26407.31
25199.58	26450.17
25155.43	26378.19
25204.76	
25202.32	
$(-\langle \Delta_c u^\circ \rangle^a / (\text{J} \cdot \text{g}^{-1}))$	
-25183.8 ± 8.7	-26409 ± 15

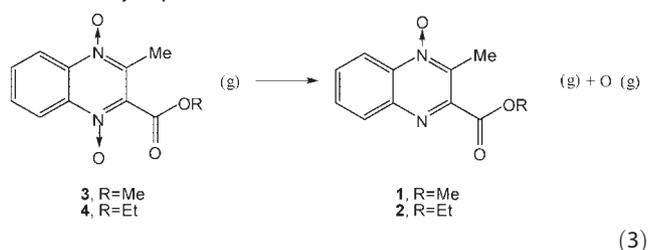
^a Mean values and standard deviation of the mean.

the overall standard deviation of the mean and include the uncertainties in calibration and in the values of auxiliary quantities used.

The results from the Calvet microcalorimetry experiments for compounds **1** and **2** are reported in Table 4. The standard molar enthalpies of sublimation are, respectively, $(118.1 \pm 3.3) \text{ kJ} \cdot \text{mol}^{-1}$ and $(129.2 \pm 4.1) \text{ kJ} \cdot \text{mol}^{-1}$.

The standard molar enthalpies of formation in the gas phase and at $T = 298.15$ K for the two compounds under study are obtained by summing the data given in the last columns of Tables 3 and 4. Thus, the $\Delta_f H_m^\circ(\text{g})$ values are $-(144.3 \pm 5.3) \text{ kJ} \cdot \text{mol}^{-1}$ and $-(174 \pm 8) \text{ kJ} \cdot \text{mol}^{-1}$ for compounds **1** and **2**, respectively, and appear in Table 5. Note that the last value is anchored on a standard enthalpy of formation in the crystalline state obtained from only four experiments.

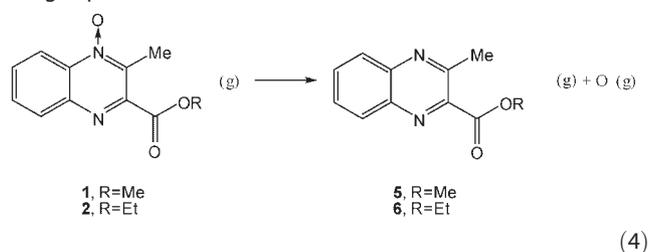
The first standard molar N—O bond dissociation enthalpy in the gas phase, $DH_1(\text{N—O})$, for the quinoxaline di-*N*-oxides **3** and **4** are obtained from the standard molar enthalpies of formation of the species appearing in the gaseous reaction described by Equ. 3.

**Table 3.** Derived standard ($p^\circ = 0.1$ MPa) molar values ($\text{kJ} \cdot \text{mol}^{-1}$) in the crystalline phases, at $T = 298.15$ K^a

Compound	$-\Delta_c U_m^\circ(\text{cr})$	$-\Delta_c H_m^\circ(\text{cr})$	$\Delta_f H_m^\circ(\text{cr})$
1	5495.4 ± 3.9	5495.4 ± 3.9	-262.4 ± 4.2
2	6133.1 ± 7.1	6134.4 ± 7.1	-302.7 ± 7.3

^a The uncertainties are twice the overall standard deviation of the mean.

The results for compounds **3** and **4** were determined in previous works and their $\Delta_f H_m^\circ(\text{g})$ values are $-(148.7 \pm 3.2) \text{ kJ} \cdot \text{mol}^{-1}$,^[9] and $-(178.0 \pm 4.3) \text{ kJ} \cdot \text{mol}^{-1}$,^[10] respectively. Those for compounds **1** and **2** are given in Table 5. The enthalpy of formation for atomic oxygen was taken from the literature, $\Delta_f H_m^\circ(\text{g}) = 249.18 \pm 0.10 \text{ kJ} \cdot \text{mol}^{-1}$.^[34] From the values given above it comes that $DH_1(\text{N—O}) = 253.6 \pm 6.2 \text{ kJ} \cdot \text{mol}^{-1}$ for compound **3** and $DH_1(\text{N—O}) = 253 \pm 9 \text{ kJ} \cdot \text{mol}^{-1}$ for compound **4**. These results are $\sim 10 \text{ kJ} \cdot \text{mol}^{-1}$ higher than the value of $DH_1(\text{N—O})$ calculated previously for compound **4** with the B3LYP/6-311 + G(2d,2p)//B3LYP/6-31G(d) calculations approach, i.e., $DH_1(\text{N—O}) = 242.9 \text{ kJ} \cdot \text{mol}^{-1}$.^[10] Coincidentally, the experimental results reported above are identical to the calculated $DH_1(\text{N—O})$ value when the N—O bond cleaved is that closer to the methyl group in **4**.^[10] The second (N—O) bond dissociation enthalpies, $DH_2(\text{N—O})$, computed in that work, Equ 4, for compound **4** were $257.9 \text{ kJ} \cdot \text{mol}^{-1}$ and $267.0 \text{ kJ} \cdot \text{mol}^{-1}$ when the second N—O bond broken was near the methyl or the ethoxycarbonyl groups, respectively. Experimental results for the $DH_2(\text{N—O})$ could not be obtained since it was not possible for us to prepare pure samples of compounds **5** and **6**, hence preventing the determination of their standard molar enthalpies of formation in the gas phase.

**Table 4.** Calorimetric values for the standard ($p^\circ = 0.1$ MPa) molar enthalpies of sublimation, at $T = 298.15$ K^a

Compound	No. of expts	T.	$\Delta_{\text{cr}, 298.15\text{K}}^{g, T} H_m^\circ$	$\Delta_{298.15\text{K}}^T H_m^\circ(\text{g})$	$\Delta_{\text{cr}}^g H_m^\circ(T = 298.15\text{K})$
		K	$\text{kJ} \cdot \text{mol}^{-1}$	$\text{kJ} \cdot \text{mol}^{-1}$	$\text{kJ} \cdot \text{mol}^{-1}$
1	7	385	140.4 ± 3.3	22.3	118.1 ± 3.3
2	6	378	151.4 ± 4.1	22.2	129.2 ± 4.1

^a The uncertainties are twice the overall standard deviation of the mean.

Table 5. Derived standard ($p^\circ = 0.1$ MPa) molar enthalpies of formation, enthalpies of sublimation and enthalpies of N-O bond dissociation ($\text{kJ} \cdot \text{mol}^{-1}$) at $T = 298.15$ K^a

Compound	$\Delta_f H_m^\circ(\text{cr})$	$\Delta_{\text{cr}}^\circ H_m^\circ$	$\Delta_f H_m^\circ(\text{g})$	DH_1	DH_2
1	-262.4 ± 4.2^b	118.1 ± 3.3^b	-144.3 ± 5.3^b	$259.3 \pm [7.3]^f$	
2	-302.7 ± 7.3^b	129.2 ± 4.1^b	-174 ± 8^b	$254 \pm [9]^f$	
3			-148.7 ± 3.2^c	253.6 ± 6.2^b	$259.3 \pm [7.3]^f$
4			-178.0 ± 4.3^d	253 ± 9^b	$254 \pm [9]^f$
5			$-134.2 \pm [5.0]^e$		
6			$-168.8 \pm [5.0]^e$		

^a The uncertainties are twice the overall standard deviation of the mean.

^b Experimental result from this work.

^c Experimental result from reference.^[9]

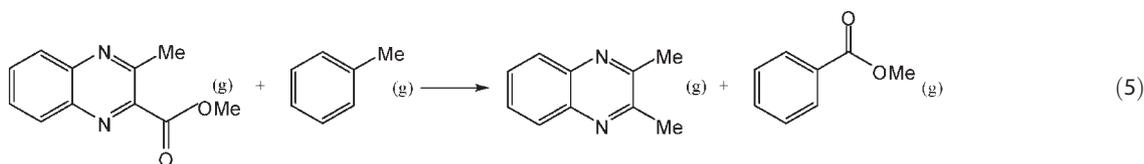
^d Experimental result from reference.^[10]

^e Calculated value from this work. Deviation was estimated.

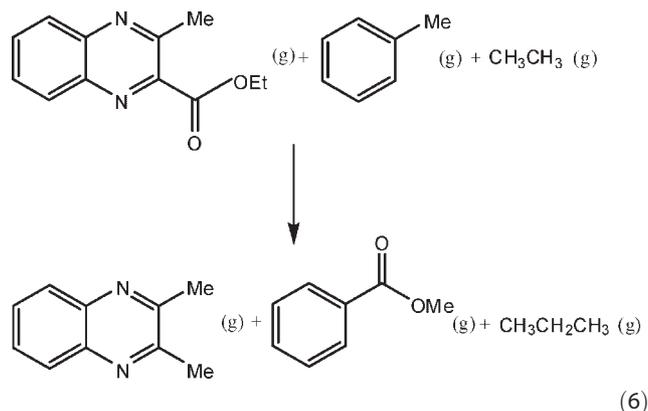
^f Suggested value from this work.

In the present work, we have computed the $DH_1(\text{N—O})$ and $DH_2(\text{N—O})$ values for compound **3** at the B3LYP/6-311+G(2d,2p)//B3LYP/6-31G(d) level of theory. The optimized structures, energies, and thermal corrections for $T = 298.15$ K are given as Supplementary Material. The calculated results are $242.9 \text{ kJ} \cdot \text{mol}^{-1}$ and $266.8 \text{ kJ} \cdot \text{mol}^{-1}$, respectively, i.e., identical to those calculated for compound **4**. Again, the calculated enthalpies for the dissociation of the first N—O bond in compounds **3** and **4** are in satisfactory agreement with the experimental results. In fact, suggesting that computed values have an uncertainty of $\sim 5.0 \text{ kJ} \cdot \text{mol}^{-1}$, the experimental and theoretical values do overlap.

It is possible to estimate the $\Delta_f H_m^\circ(\text{g})$ value for compound **5** by computing the enthalpy of the working reaction described by Equ. 5:



and by using the experimental $\Delta_f H_m^\circ(\text{g})$ values for toluene, $\Delta_f H_m^\circ(\text{g}) = 50.0 \pm 0.6 \text{ kJ} \cdot \text{mol}^{-1}$,^[37] for 2,3-dimethylquinoxaline, $\Delta_f H_m^\circ(\text{g}) = 172.9 \pm 3.0 \text{ kJ} \cdot \text{mol}^{-1}$,^[9] and for methylbenzoate, $\Delta_f H_m^\circ(\text{g}) = -(287.9 \pm 2.4) \text{ kJ} \cdot \text{mol}^{-1}$.^[37] Combining all these values with the computed enthalpy of the reaction described by Equ. 5, which is $-30.8 \text{ kJ} \cdot \text{mol}^{-1}$, it comes that the $\Delta_f H_m^\circ(\text{g})$ for compound **5** is $-134.2 \text{ kJ} \cdot \text{mol}^{-1}$. The accuracy of this value can be tested if we use a similar strategy to compute the enthalpy of formation of **3** based on the experimental enthalpy of 2,3-dimethylquinoxaline di-N-oxide, $\Delta_f H_m^\circ(\text{g}) = 149.4 \pm 4.5 \text{ kJ} \cdot \text{mol}^{-1}$.^[10] The computed enthalpy of formation for **3** is $\Delta_f H_m^\circ(\text{g}) = -145.7 \text{ kJ} \cdot \text{mol}^{-1}$, in excellent agreement with the experimental value, $\Delta_f H_m^\circ(\text{g}) = -(148.7 \pm 3.2) \text{ kJ} \cdot \text{mol}^{-1}$,^[9] giving further support to the result estimated for **5**. Using the experimental enthalpy of formation for compound **1** and the calculated value for compound **5**, both obtained in this work, the standard molar N—O bond dissociation enthalpy for compound **3** is $DH_2(\text{N—O}) = 259.3 \pm [7.3] \text{ kJ} \cdot \text{mol}^{-1}$ (Table 5).



Using a similar strategy to that employed above, one can also estimate the $\Delta_f H_m^\circ(\text{g})$ for compounds **4** and **6**. The working reaction used to obtain the enthalpy of formation of compound **6** is that described by Equ. 6 while a similar reaction but with quinoxaline di-N-oxides was used to calculate that for compound **4**. The enthalpies of reaction calculated with the B3LYP/6-311+G(2d,2p)//B3LYP/6-31G(d) approach were $-28.5 \text{ kJ} \cdot \text{mol}^{-1}$ and $-17.1 \text{ kJ} \cdot \text{mol}^{-1}$ for the reaction described by Equ. 5 containing or not quinoxaline di-N-oxide derivatives, respectively. Using the experimental results introduced above for toluene, methylbenzoate, 2,3-dimethylquinoxaline and 2,3-dimethylquinoxaline di-N-oxide and those for ethane, $\Delta_f H_m^\circ(\text{g}) = -(83.8 \pm 0.3) \text{ kJ} \cdot \text{mol}^{-1}$, and propane, $\Delta_f H_m^\circ(\text{g}) = -(104.7 \pm 0.5) \text{ kJ} \cdot \text{mol}^{-1}$, also taken from the compilation of thermochemical data due to Pedley,^[37] the estimated enthalpies of formation for compounds **4** and **6** are, respectively, $-180.9 \text{ kJ} \cdot \text{mol}^{-1}$ and $-168.8 \text{ kJ} \cdot \text{mol}^{-1}$. The result estimated for compound **4** is in excellent agreement with the

experimental result published previously, i.e., $\Delta_f H_m^0(g) = -(178.0 \pm 4.3) \text{ kJ} \cdot \text{mol}^{-1}$.^[10] That for compound **6** differs by $\sim 9 \text{ kJ} \cdot \text{mol}^{-1}$ from that previously estimated with another working reaction, c.f. $-(159.2 \pm [5.0]) \text{ kJ} \cdot \text{mol}^{-1}$.^[10] Nevertheless, it is possible to suggest a value for the standard molar enthalpy of dissociation of the second (N—O) in compound **4** using the experimental $\Delta_f H_m^0(g)$ result for compound **2** and the estimated result for compound **6** obtained in this work. The suggested value is also reported in Table 5 and it is $DH_2(\text{N—O}) = 254 \pm [9] \text{ kJ} \cdot \text{mol}^{-1}$. Importantly, the present work clearly shows that the energy required to cleave the N—O bonds is almost unchanged with $R = \text{CH}_3$ or CH_2CH_3 confirming previous assumptions.^[13]

Finally, it must be stressed out here that the differences between calculated and experimental $DH_1(\text{N—O})$ and $DH_2(\text{N—O})$ are of about $10 \text{ kJ} \cdot \text{mol}^{-1}$, almost included in the uncertainties associated with the experimental results (Table 5). Nevertheless, these discrepancies have obvious influences on the experimental or calculated $DH_{2-1} = DH_2(\text{N—O}) - DH_1(\text{N—O})$ differences for compounds **3** and **4**. The experimental DH_{2-1} values are $5.7 \pm [9.6] \text{ kJ} \cdot \text{mol}^{-1}$ and $1.0 \pm [12.7] \text{ kJ} \cdot \text{mol}^{-1}$ for compounds **3** and **4**, respectively. The calculated DH_{2-1} values are much higher, i.e., $23.9 \text{ kJ} \cdot \text{mol}^{-1}$ and $24.1 \text{ kJ} \cdot \text{mol}^{-1}$ for **3** and **4**, respectively. Nevertheless, one is able to retrieve a clear conclusion from the values above, i.e., the DH_{2-1} values for compounds **3** and **4** are similar.

CONCLUSIONS

Experimental thermochemical work involving static bomb calorimetry and Calvet microcalorimetry has been performed for the first time on quinoxaline derivatives containing a single dative N—O bond. These quinoxaline *N*-oxide derivatives have a methyl and methoxycarbonyl or ethoxycarbonyl groups attached to positions 2 and 3. The standard molar enthalpies of formation in the gas phase at $T = 298.15 \text{ K}$ were used to obtain novel standard molar enthalpies of dissociation of the N—O bond in the parent quinoxaline di-*N*-oxides based solely on experimental results. In fact, previous experimental enthalpies of dissociation for this class of compounds were a mean of the first and second dissociation enthalpic data.

The enthalpies of dissociation of the first N—O bond in 3-methoxycarbonyl-2-methyl-quinoxaline di-*N*-oxide and 3-ethoxycarbonyl-2-methyl-quinoxaline di-*N*-oxide are $253.6 \text{ kJ} \cdot \text{mol}^{-1}$ and $253 \text{ kJ} \cdot \text{mol}^{-1}$, respectively. These identical values confirm previous assumptions stating that different substituents in the carbonyl group attached to the quinoxaline ring had identical effects on the strength of the N—O bonds since the carbonyl group acts like a firewall that blocks the effects of the different substituents on the quinoxaline moiety.

Complementary computational study supported all the experimental results obtained in the present work and permitted also to estimate enthalpies of formation for 3-methoxycarbonyl-2-methyl-quinoxaline and 3-ethoxycarbonyl-2-methyl-quinoxaline compounds as well as of the enthalpies of dissociation of the second N—O bond in the parent di-*N*-oxides.

SUPPLEMENTARY MATERIAL

Spectroscopic (NMR) and analytical (elemental analysis) data of the title compounds, **1** and **2**. Table SM1 with B3LYP/

6-311 + G(2d,2p) selected optimized parameters for compounds **1**, **3**, and **5**. Table SM2 with the energies and thermal corrections ($T = 298.15 \text{ K}$) for all species considered in the present work. This material is available free of charge in Wiley Interscience.

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