Synthesis and thermochemical study of quinoxaline-\(N\)-oxides: enthalpies of dissociation of the N–O bond

Miguel L. F. Viveiros\(^a\), Vera L. S. Freitas\(^a\), Nuno Vale\(^a\), José R. B. Gomes\(^{a,b}\), Paula Gomes\(^a\) and Maria D. M. C. Ribeiro da Silva\(^{a*}\)

The synthesis of three new quinoxaline mono-\(N\)-oxides derivatives, namely, 2-tert-butoxycarbonyl-3-methylquinoxaline-\(N\)-oxide, 2-phenylicarbamoyl-3-ethylquinoxaline-\(N\)-oxide, and 2-carbamoyl-3-methylquinoxaline-\(N\)-oxide, from their corresponding 1,4-di-\(N\)-oxides is reported. Samples of these compounds were used for a thermochemical study, which allowed derivation of their gaseous standard molar enthalpies of formation, \(\Delta_f^\text{m} H_m^\circ\) (g), from their enthalpies of formation in the condensed phase, \(\Delta_f^\text{cr} H_m^\circ\) (cr), determined by static bomb combustion calorimetry, and from their enthalpies of sublimation, \(\Delta^\text{D} H_m^\circ\), determined by Calvet microcalorimetry. Finally, combining the \(\Delta_f^\text{m} H_m^\circ\) (g) for the quinoxaline-\(N\)-oxides derived in this work with literature values for the corresponding 1,4-di-\(N\)-oxides and atomic oxygen, the bond dissociation enthalpies for cleavage of the first N–O bond in the di-\(N\)-oxides, \(D^\text{H}_1\text{(N–O)}\), were obtained and compared with existing data. Copyright © 2011 John Wiley & Sons, Ltd.

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**Keywords:** dissociation enthalpy N–O bond; quinoxaline mono-\(N\)-oxides derivatives; synthesis; thermochemistry

**INTRODUCTION**

The interest in a large range of compounds with the \(N\)-oxide functional group has been expanded significantly over the past two decades because of their remarkable success in a broad variety of applications as oxidizing agents. Some of these compounds, particularly the quinoxaline derivatives, assumed relevant importance because of their selective biological activities\(^{5–6}\) related with inherent pharmacological and toxicological properties\(^{7,8}\). Energetic studies on compounds containing terminal N–O bonds in different molecular environments have been developed in our research group\(^{9–18}\) with the main goal of evaluating the influence of the chemical vicinity on that bond. In this context, computational and experimental studies have been extensively developed for quinoxaline 1,4-di-\(N\)-oxides\(^{19–20}\). More recently, with the possibility of synthesizing very pure samples of two quinoxaline derivatives containing only a single dative N–O bond, the first experimental thermochemical study for quinoxaline-\(N\)-oxide derivatives has been reported\(^{13}\). The present work reports the experimental study of the energetics of three new quinoxaline mono-\(N\)-oxide derivatives whose structures are represented in Scheme 1, that is, 2-tert-butoxycarbonyl-3-methylquinoxaline-\(N\)-oxide (4.1), 2-phenylicarbamoyl-3-methylquinoxaline-\(N\)-oxide (4.2), and 2-carbamoyl-3-methylquinoxaline-\(N\)-oxide (4.3). Their syntheses have been performed from the corresponding 1,4-di-\(N\)-oxides (compounds 3.1–3.3, Scheme 1) by selective reduction.

The standard \((p^\circ = 0.1\text{MPa})\) massic energies of combustion in oxygen of the three compounds were measured with a high precision static bomb calorimeter, from which the values of the standard molar enthalpies of formation in the crystalline phase at \(T = 298.15\text{K}\) were derived. The enthalpies of sublimation of the three compounds were determined from high temperature Calvet microcalorimetry measurements. Combining the standard molar enthalpies of formation in the crystalline phase with the enthalpies of sublimation of each compound, the corresponding standard \((p^\circ = 0.1\text{MPa})\) molar enthalpies of formation in the gas phase at \(T = 298.15\text{K}\) were obtained. The latter results were used to obtain the experimental values for the first N–O bond dissociation enthalpy in the parent di-\(N\)-oxide quinoxalines based on their standard molar enthalpies of formation in the gas phase that were previously reported in the literature\(^{11,12}\).

**EXPERIMENTAL**

**Synthesis and purification**

The quinoxaline di-\(N\)-dioxides (3.1–3.3, Scheme 1) were prepared from benzofuroxan (1) and the appropriate \(\beta\)-ketoester/amide (2) following the method described by Robertson and Kasubick\(^{21}\). Briefly,
THERMOCHEMICAL STUDY OF QUINOXALINE-N-OXIDES

Scheme 1. Synthetic route (in black) to quinoxaline mono-N-oxides 4.1–4.3 via regioselective monooxygenation of 3.1–3.3 with trimethyl phosphate (A): smaller structures in grey (including nonregioselective reduction of 3 with phosphorus trichloride, B), are included to provide pictorial support to the Discussion section.

benzofuroxan (1, 1 mmol) was suspended in propan-2-ol and the appropriate β-ketoester/amide (2, 0.7 mmol) was added. The reaction was allowed to proceed at 60°C for about 30 (3.2, 3.3) to 150 (3.1) min on a thermostated water bath, then a catalytic amount of calcium hydroxide (0.05 mmol) was added portion-wise periodically. Di-N-oxides 3.2 and 3.3 readily precipitated from the reaction mixture and were simply isolated by suction filtration followed by thorough washing of the solid with ice-cold propan-2-ol. In turn, di-N-oxide 3.1 was significantly soluble in the reaction medium and had to be isolated by adsorption liquid chromatography on silica, using dichloromethane/methanol 40 : 1 (v/v) as eluant. All the di-N-oxides 3.1–3.3 were obtained as tan solids in 10% (3.1) to quantitative (3.2, 3.3) yields.

The 3 compounds were then selectively monooxygenated with trimethyl phosphate, as described by Dirlam and McFarland. In brief, the di-N-oxides (0.05 mmol) were suspended in either propan-2-ol (3.1) or methanol (3.2, 3.3), then trimethyl phosphate (0.03 mmol) was added and the mixture refluxed for 2 h. The N-oxides, 4.1–4.3, were precipitated from the reaction mixture upon cooling to room temperature and were isolated by suction filtration followed by thorough washing with ice-cold methanol. N-oxides 4.1 and 4.3 were additionally submitted to purification by column chromatography on silica, using dichloromethane/methanol mixtures as eluents. After a final step of recrystallization from methanol for all 4 compounds, they were obtained as pale tan solids in 10% (4.3) to 50% (4.1, 4.2) yields.

The structures and composition of 4.1–4.3 were confirmed by electrospray ionization-ion trap mass spectrometry (ESI-IT MS), proton (1H) and carbon-13 (13C) nuclear magnetic resonance (NMR) and elemental analysis. All analytical and spectral data, and spectral traces and compound melting temperatures, are provided in the Supplementary Material.

Prior to the calorimetric measurements, the compounds were dried under high-vacuum conditions. The composition of both compounds were confirmed by the ratio of the mass of carbon dioxide recovered in the combustion experiments to that calculated from the mass of the sample; the average ratios and the respective uncertainties (twice the standard deviation of the means) were 0.9997 ± 0.0005 for 4.1, 1.0006 ± 0.0002 for 4.2, and 1.0012 ± 0.0007 for 4.3.

The specific densities of the different samples were assumed to be 1.0 g cm⁻³, estimated from the mass and volume of pellets of each compound.

The relative atomic masses used for the elements were those recommended by the IUPAC Commission in 2007.

Static bomb combustion calorimetry

The energies of combustion of compounds 4.1–4.3 were measured using a static bomb calorirometer, whose bomb with an internal volume 0.290 dm³ has a twin valve system as previously reported.

The energy equivalent of the caloriometer ϵ(calor) was determined using benzoic acid ([CAS 65-85-0], Standard Reference Material (SRM 391) supplied by the National Institute of Standards and Technology), having a maccic energy of combustion, under bomb conditions, of (26434 ± 3) J g⁻¹. The energy equivalent of the caloriometer ϵ(calor) = (15546.3 ± 1.3) KJ⁻¹ (the uncertainty quoted is the standard deviation of the mean), corresponding to an average mass of 2900.0 g of water added to the caloriometer, was determined from eight calibration experiments made under oxygen at p = 3.04 MPa and using 1.00 cm³ of water added to the bomb.

For the combustion experiments, the crystalline samples were burnt in pellet form. Because the yields on the synthesis of the compounds were low, we decided to decrease the amount of compound used in each experiment and used n-hexadecane (CAS 544-76-3, ≥ 99%, Aldrich Chemical Co. (Milwaukee, Wisconsin, USA)) as an auxiliary of the combustion measurements to achieve the adequate rise in temperature during the combustion. The measured standard massic energy of combustion of the sample of n-hexadecane used for the studies of compounds 4.1 and 4.2 was −Δu(calor) = (47,150.4 ± 2.4) J g⁻¹, while that for 4.3 was −Δu(calor) = (47,193.3 ± 3.3) J g⁻¹.

All the samples were ignited at T = 298.15 ± 0.001 K in oxygen at p = 3.04 MPa with 1.00 cm³ of deionized water previously added to the bomb. The electrical energy for ignition ΔU(ign.) was determined from the change in potential difference across a 1400 μF capacitor when discharged through the platinum ignition wire. For the cotton thread fuse, with empirical formula CH₁.₆₈₆O₀.₈₄₃, the massic energy of combustion is Δu(calor) = −16,240 J g⁻¹.[27] The corrections for nitric acid formation, ΔU(HNO₃), were based on the value −59.7 kJ mol⁻¹[28] for the molar energy of formation of 0.1 mol dm⁻³ HNO₃(aq) from N₂(g), O₂(g), and H₂O(l). An estimated pressure coefficient of specific energy: (Δu(calor)/Tp) = −0.2 J g⁻¹ K⁻¹ at T = 298.15 K, a typical value for most organic compounds,[29] was assumed. The mass of compound, m(cpd), used in each experiment was determined from the total mass of carbon dioxide, m (CO₂, total), produced after an allowance for that formed from the combustion of the cotton thread fuse and the n-hexadecane. For each compound, the standard massic energy of combustion, Δu(calor), was calculated using the procedure given by Hubbard et al.[20]

Calvet microcalorimetry

The standard molar enthalpies of sublimation of compounds 4.1–4.3 were measured by Calvet High Temperature Microcalorimetry, using the ‘vacuum-sublimation drop microcalorimetric method’. Samples of about 3–5 mg contained in a thin glass capillary tube were dropped at room temperature into a hot reaction vessel in a high temperature Calvet microcalorimeter (SETARAM HT 1000D (Lyon, France)) held at T = 390 K, T = 443 K, and T = 458 K for compounds 4.1, 4.2, and 4.3, respectively, and then removed from the hot zone by vacuum sublimation. The observed enthalpies of sublimation were corrected to T = 298.15 K, using Δu[subl] = (47,193.3 ± 3.3) J g⁻¹.

For each compound, the standard massic energy of combustion, Δu(calor), was calculated using the procedure given by Hubbard et al.[20]
where $R_1 = \text{OC(CH}_2}_2$, $R_2 = \text{OCH}_2\text{CH}_2$, $R_3 = \text{CH}_3\text{CH}_2\text{CH}_2$, $R_4 = \text{C(H}_2)_6$, and $x = 1$ in the case of 4.1; $R_1 = \text{NHPh}$, $R_2 = \text{CH}_3$, $R_3 = \text{NH}_2\text{Ph}$, and $x = 2$ in the case of 4.2; and $R_1 = \text{NH}_2$, $R_2 = \text{CH}_3$, $R_3 = \text{CH}_3\text{CH}_2$, $R_4 = \text{CH}_3\text{NH}_2$, and $x = 1$ in the case of 4.3. The microcalorimeter was calibrated in situ for the working temperatures with naphthalene, $\Delta H_{\text{m}}^0$ (naphthalene, cr) = (72.60 ± 0.60) kJ mol$^{-1}$[33] using the same procedure for the calibration experiments.

RESULTS

Target compounds were successfully obtained following the synthetic route A to target structures 4 depicted in Scheme 1. Compounds 4.1 and 4.2 were obtained in acceptable global yields (~50%), whereas compound 4.3 was synthesized in a very low yield (~10%) mainly because of the very low solubility of its dioxygenated precursor 3.3 in low molecular weight alcohols. In any case, the compounds were isolated with the mean values, $\Delta m$ (H2O) is the difference between the mass of water added to the calorimeter and the microcalorimeter was calibrated in the case of $4.1$ in the case of $\frac{\Delta U}{\text{mol}}$ and $\Delta U$ is the energy correction for the nitric acid formation; $\Delta U$ (fuse) is the energy of combustion of the fuse (cotton) used in the experiment; $\Delta U$ is the corrected temperature rise; $\Delta U$ (ign) is the electrical energy for the ignition; $\Delta U$ (ign) is the energy correction for the in situ determination, $\Delta U$ is the standard maccsic energy of combustion.

For the combustion reaction of each compound yielding N$_2$ (g), CO$_2$ (g) and H$_2$O (l), the individual values of $\Delta U$ and their standard deviations are given in Table 2. Because the quantity available for experimental work involving compound 4.3 was very small, only five experiments were possible. In the case of 4.2, the quantity of the compound synthesized was also small and, more importantly, it was seen to degrade during storage. In fact, because of the low yields from the syntheses, the quantities for each compound were small thus preventing a large number of experiments, and hence, preventing the reduction of the uncertainties associated with each of the experimental results.

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

<table>
<thead>
<tr>
<th></th>
<th>4.1</th>
<th>4.2</th>
<th>4.3</th>
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<tbody>
<tr>
<td>$m$(CO$_2$, total)/ g</td>
<td>1.47614</td>
<td>1.31360</td>
<td>1.21882</td>
</tr>
<tr>
<td>$m$(cpd)/ g</td>
<td>0.34504</td>
<td>0.31149</td>
<td>0.38088</td>
</tr>
<tr>
<td>$m$(fuse)/ g</td>
<td>0.00292</td>
<td>0.00311</td>
<td>0.00258</td>
</tr>
<tr>
<td>$m$(n-hexadecane) / g</td>
<td>0.21053</td>
<td>0.16827</td>
<td>0.12556</td>
</tr>
<tr>
<td>$\Delta U_{\text{ad}}$/ K</td>
<td>1.27472</td>
<td>1.09678</td>
<td>1.00229</td>
</tr>
<tr>
<td>$\Delta U_{\text{ign}}$ (J K$^{-1}$)</td>
<td>14.81</td>
<td>14.37</td>
<td>14.14</td>
</tr>
<tr>
<td>$\Delta m$(H2O)/ g</td>
<td>0.7</td>
<td>1.7</td>
<td>-3.4</td>
</tr>
<tr>
<td>$\Delta U$ (IBP)/ J</td>
<td>19,839.76</td>
<td>17,074.49</td>
<td>15,581.86</td>
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<tr>
<td>$\Delta U$ (fuse)/ J</td>
<td>47.42</td>
<td>50.51</td>
<td>41.90</td>
</tr>
<tr>
<td>$\Delta U$ (HNO$_3$)/ J</td>
<td>25.34</td>
<td>23.70</td>
<td>38.21</td>
</tr>
<tr>
<td>$\Delta U$ (n-hexadecane)/ J</td>
<td>9926.61</td>
<td>7933.92</td>
<td>5925.38</td>
</tr>
<tr>
<td>$\Delta U$ (ign)/ J</td>
<td>0.54</td>
<td>0.54</td>
<td>0.61</td>
</tr>
<tr>
<td>$\Delta U_{\text{u}}$/ J</td>
<td>8.93</td>
<td>8.56</td>
<td>9.19</td>
</tr>
<tr>
<td>$-\Delta U_{\text{u}}$/ (J g$^{-1}$)</td>
<td>28,491.98</td>
<td>29,077.27</td>
<td>25,133.60</td>
</tr>
</tbody>
</table>

### Table 2. Individual values of the maccsic energy of combustion, $\Delta U_{\text{u}}$, at $T$ = 298.15 K. All values in J g$^{-1}$

<table>
<thead>
<tr>
<th></th>
<th>4.1</th>
<th>4.2</th>
<th>4.3</th>
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<tbody>
<tr>
<td>28,466.35</td>
<td>29,114.81</td>
<td>25,100.51</td>
<td></td>
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<tr>
<td>28,480.01</td>
<td>29,077.27</td>
<td>25,171.11</td>
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<tr>
<td>28,491.98</td>
<td>29,068.70</td>
<td>25,133.60</td>
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</tr>
<tr>
<td>28,492.19</td>
<td>29,061.74</td>
<td>25,106.57</td>
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<tr>
<td>28,418.07</td>
<td>29,127.09</td>
<td>25,147.72</td>
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</tr>
<tr>
<td>28,420.99</td>
<td>29,140.90</td>
<td>25,131.9</td>
<td></td>
</tr>
<tr>
<td>28,461.6 ± 6.9</td>
<td>29,098.4 ± 13.6</td>
<td>25,131.9 ± 13.0</td>
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</table>
Table 3. Derived standard (p° = 0.1 MPa) molar values in the condensed phases at T = 298.15 K. All values in kJ mol−1

<table>
<thead>
<tr>
<th>Compound</th>
<th>−ΔfU°m(cr)</th>
<th>−ΔfH°m(cr)</th>
<th>ΔfH°m(cr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.1</td>
<td>7408.3 ± 6.1</td>
<td>7412.0 ± 6.1</td>
<td>−383.7 ± 6.1</td>
</tr>
<tr>
<td>4.2</td>
<td>8127.1 ± 10.3</td>
<td>8129.0 ± 10.3</td>
<td>−25.0 ± 10.4</td>
</tr>
<tr>
<td>4.3</td>
<td>5106.8 ± 7.4</td>
<td>5106.2 ± 7.4</td>
<td>−111.9 ± 7.5</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Compound</th>
<th>No. of experiments</th>
<th>T / K</th>
<th>ΔfH°m(T=298.15 K)</th>
<th>ΔfH°m(g)</th>
<th>ΔfH°m(T=298.15 K)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.1</td>
<td>6</td>
<td>390</td>
<td>160.5 ± 3.1</td>
<td>19.7</td>
<td>140.8 ± 3.1</td>
</tr>
<tr>
<td>4.2</td>
<td>6</td>
<td>443</td>
<td>195.0 ± 2.3</td>
<td>49.9</td>
<td>145.1 ± 2.3</td>
</tr>
<tr>
<td>4.3</td>
<td>6</td>
<td>458</td>
<td>177.6 ± 0.6</td>
<td>39.6</td>
<td>138.0 ± 0.6</td>
</tr>
</tbody>
</table>

Table 5. Derived standard (p° = 0.1 MPa) standard molar enthalpies in the condensed and gaseous phases, at T = 298.15 K, and enthalpies of sublimation. All values in kJ mol−1

<table>
<thead>
<tr>
<th>Compound</th>
<th>ΔfH°m (cr)</th>
<th>ΔfH°m(g)</th>
<th>ΔfH°m(T=298.15 K)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.1</td>
<td>−383.7 ± 6.1</td>
<td>140.8 ± 3.1</td>
<td>140.8 ± 3.1</td>
</tr>
<tr>
<td>4.2</td>
<td>−25.0 ± 10.4</td>
<td>145.1 ± 2.3</td>
<td>145.1 ± 2.3</td>
</tr>
<tr>
<td>4.3</td>
<td>−111.9 ± 7.5</td>
<td>138.0 ± 0.6</td>
<td>138.0 ± 0.6</td>
</tr>
</tbody>
</table>

DISCUSSION

The identification of final compounds as pure isomers 4 was made on the basis of previous research by Dirlam and McFarland,[22] and of NMR data obtained as follows. Reduction of compounds 3 was carried out using trimethyl phosphite (Scheme 1, A), which according to Dirlam and McFarland, allows for selective monodeoxygenation of the nitrogen farthest from the 3-methyl group in quinoxaline di-N-oxides like 3 (R ≠ H), having electron withdrawing substituents in carbon 2 (e.g., 3 where R = CH2 or OCH3; 3-methyl-2-trifluoromethylquinoxaline-1,4-dioxide).[22] These authors demonstrated, by 1H-NMR, that while monodeoxygenation of structures such as 3 with trimethyl phosphite is regioselective, other reducing agents such as phosphorus trichloride or sodium dithionite lead to a mixture of the two possible monodeoxygenation products plus the fully deoxygenated quinoxaline (Scheme 1, B). For instance, reduction of methyl 3-methyl-2-quinoxalinecarboxylate 1,4-dioxide (structure 3 where R = OCH3) with phosphorous trichloride yields a mixture that, according to 1H-NMR analysis, is composed of 57% methyl 3-methyl-2-quinoxalinecarboxylate 1-oxide, 16% methyl 2-methyl-3-quinoxalinecarboxylate 1-oxide and 27% methyl 3-methyl-2-quinoxalinecarboxylate. Detection of such mixtures by 1H-NMR is straightforward because the presence/absence of an N–O bond significantly affects the chemical shifts of neighboring protons, namely, those of the aromatic proton H-8 and of vicinal protons in the C-2 substituent (see Scheme 1 for atom numbering). Thus, the 6 value for the methyl substituent differs between each of the two possible monodeoxygenation products and also between these and the fully deoxygenated quinoxaline.[22] Also, the latter usually presents all aromatic protons (H-5 to H-8) clustered in an unresolved multiplet at ~7.7–8.0 ppm, whereas peaks from protons H-5 and H-8 shift to higher values in monodeoxygenated derivatives, appearing at ~8.5 and ~8.2 ppm, respectively.[22] The same authors have also unequivocally shown that the selective monodeoxygenation of compounds like 3 with trimethyl phosphite occurred on the nitrogen farthest apart from the methyl group, as the subsequent reaction of the sole monodeoxygenation product obtained with acetic anhydride/acetic acid gives the corresponding 3-acetoxymethylquinoxaline 5 (Scheme 1). The formation of 5 can only take place if the remaining N–O bond is on the nitrogen closest to the methyl group.[22]

A simple inspection of the 1H-NMR spectra of our monodeoxygenation products (Supporting Material) clearly shows that the compounds are pure isomers. This is further reinforced by the very sharp melting point intervals observed, which are strong indicators of high purity, and by the fact that no peak duplication was observed in the corresponding 13C-NMR spectra, as would be expected if mixtures had been obtained. Furthermore, the multiplicity pattern obtained for the aromatic protons H-5 to H-8 in 4.1–4.3 corresponds to three multiplets at 1:2:1 relative intensities, as previously observed by Abadaleh et al. for analogous amino acid and ester quinoxaline-4-oxides, whereas their 1-oxide isomers exhibited two multiplets with 1:3 relative intensities.[37] Chemical shifts observed both in the proton and carbon-13 NMR spectra of 4.1–4.3 were also in agreement with previously reported data on similar quinoxaline-4-oxides.[38–39]
Therefore, in view of all the above, we can unequivocally identify our final products as 4.1–4.3.

The experimental standard molar enthalpies of formation reported in this work were used to derive the values for the first N–O bond dissociation enthalpies, $DH_1$(N–O), in the parent di-N-oxide quinoxalines (compounds 3), that is, the energy associated with the following gaseous reaction:

$$\text{R} = \text{OC((CH$_3$)$_3$ or NHPh or NH$_2$}$$

using the standard molar enthalpies of formation in the gas phase previously reported in the literature for compounds 3.1, 3.2, and 3.3\textsuperscript{11,12} and for atomic oxygen, $\alpha_{\text{O}}$\textsubscript{298.15 K} = 298.15 K. The uncertainties are twice the overall standard deviation of the mean. All values in kJ mol\textsuperscript{-1}. The mean values reported for the cleavage of both dative N–O bonds, $DH_1$(N–O), in the 1,4-di-N-oxides listed above are 255.8 ± 2.0 kJ mol\textsuperscript{-1}\textsuperscript{19} 254.0 ± 2.3 kJ mol\textsuperscript{-1}\textsuperscript{19} and 260.9 ± 2.7 kJ mol\textsuperscript{-1}\textsuperscript{40} respectively, for quinoxaline-N,N'-dioxide, pyrazine-N,N'-dioxide and 2,3-dimethylquinoxaline-N,N'-dioxide.

As can be seen, the $DH_1$(N–O) values derived from the experimental enthalpies of formation span a range of 40 ± 17 kJ mol\textsuperscript{-1}; the less positive value, corresponding to a more labile bond, is found for 3.1, 242.4 ± 9.0 kJ mol\textsuperscript{-1}, while the most positive value is found for compound 3.2, 282 ± 14 kJ mol\textsuperscript{-1}. The latter may be considered only as qualitative because of the larger uncertainties associated with the experimental result providing further support for the quality of the values reported before for compounds 3.2 and 4.2. The value derived for compound 3.3, 255.6 ± 7.4 kJ mol\textsuperscript{-1}, is within the associated uncertainty identical to those reported before for compounds 3.4 and 3.5 (Table 6).\textsuperscript{13} First, it is possible to conclude that the tert-butoxycarbonyl, the phenylcarbamoyl, and the carbamoyl groups have a larger destabilization effect than the methyl group and hence the dative N–O bonds adjacent to the former groups are cleaved first (Scheme 1). Then, from the numerical data reported above for $DH_1$(N–O), it can be concluded that the tert-butoxycarbonyl group causes a larger destabilization which allowed the determination of their $\Delta H_m^\circ(g)$ by isoperibol static bomb calorimetry and Calvet microcalorimetry.\textsuperscript{19,40} The mean values reported for the cleavage of both dative N–O bonds, $DH_{m}(N-O)$, in the 1,4-di-N-oxides listed above are 255.8 ± 2.0 kJ mol\textsuperscript{-1}\textsuperscript{19} 254.0 ± 2.3 kJ mol\textsuperscript{-1}\textsuperscript{19} and 260.9 ± 2.7 kJ mol\textsuperscript{-1}\textsuperscript{40} respectively, for quinoxaline-N,N'-dioxide, pyrazine-N,N'-dioxide and 2,3-dimethylquinoxaline-N,N'-dioxide.

$\text{X1, 4} – \text{di} – \text{N} – \text{oxide(g)} \rightarrow \text{X(g)} + 2\text{O(g)}$  \textsuperscript{(4)}

where X is quinoxaline or pyrazine or derivatives of these compounds obtained by replacing H with other chemical groups, whose gaseous enthalpies of formation are also reported in literature.\textsuperscript{9} In the case of the dimethyl derivative of quinoxaline, the Becke, three-parameter, Lee–Yang–Parr (B3LYP)/6-311 + G(2d,2p), $DH_{m}(N-O) = 260.8$ kJ mol\textsuperscript{-1}, and B3LYP/6-311 + G(2d,2p)/B3LYP/6-31 G(d), $DH_{m}(N-O) = 260.6$ kJ mol\textsuperscript{-1}, calculated values were found to be in excellent agreement with the experimental result providing further support for the quality of the $DH_{m}(N-O)$ derived for these 1,4-di-N-oxides.\textsuperscript{40} The $DH_{m}(N-O)$ obtained for 2,3-dimethylquinoxaline 1,4-di-N-oxide clearly suggests that the $DH_{m}(N-O)$ for cleavage of a N–O bond in an adjacent position to the methyl groups in 2,3-dimethylquinoxaline 1,4-di-N-oxide, that is, methyl groups attached to positions 2 or 3 of the ring, is ≤ 260.9 ± 2.7 kJ mol\textsuperscript{-1}. In principle, this limiting

\begin{table}
\centering
\begin{tabular}{|l|l|l|l|l|}
\hline
\textbf{R} & \textbf{1,4-di-N-oxides} & \textbf{$\Delta H_m^\circ(g)$} & \textbf{mono-N-oxide} & \textbf{$\Delta H_m^\circ(g)$} & \textbf{$DH_1$(N–O)} \\
\hline
\text{OC(\text{CH$_3$)$_3$}} & \textbf{3.1} & \text{-236.1 ± 5.9}\textsuperscript{[12]} & \textbf{4.1} & \text{-242.9 ± 6.8}\textsuperscript{\textsuperscript{1}} & \text{242.4 ± 9.0} \\
\text{NHPh} & \textbf{3.2} & \text{87.5 ± 9.5}\textsuperscript{[11]} & \textbf{4.2} & \text{120 ± 11}\textsuperscript{\textsuperscript{1}} & \text{282 ± 14} \\
\text{NH$_3$} & \textbf{3.3} & \text{19.7 ± 5.5}\textsuperscript{[11]} & \textbf{4.3} & \text{26.1 ± 7.5}\textsuperscript{\textsuperscript{1}} & \text{255.6 ± 7.4} \\
\text{OCH$_3$} & \textbf{3.4} & \text{-148.7 ± 3.2}\textsuperscript{[19]} & \textbf{4.4} & \text{-144.3 ± 5.3}\textsuperscript{[13]} & \text{253.6 ± 6.2}\textsuperscript{[13]} \\
\text{OCH$_2$CH$_3$} & \textbf{3.5} & \text{-178.0 ± 4.3}\textsuperscript{[40]} & \textbf{4.5} & \text{-174 ± 8}\textsuperscript{[13]} & \text{253 ± 9}\textsuperscript{[13]} \\
\hline
\end{tabular}
\caption{Derived standard ($p^\circ=0.1 \text{ MPa}$) molar enthalpies of formation, $\Delta H_m^\circ(g)$, and enthalpies of N–O bond dissociation, $DH_1$(N–O), at $T = 298.15 \text{ K}$. The uncertainties are twice the overall standard deviation of the mean. All values in kJ mol\textsuperscript{-1}. \textsuperscript{7}This work.}
\end{table}
value can be used with enhanced confidence because the $DH_1$ (N–O) calculated for 2,3-dimethylquinoxaline-N,N'-dioxide using the same density functional theory approach and basis sets was $-252$ kJ·mol$^{-1}$.[40] The 260.9 ± 2.7 kJ·mol$^{-1}$ value was also found to be valid for the $DH_1$ (N–O) values calculated for 3.5 and also for 3-benzyl-2-methyl-quinoxaline 1,4-di-N-oxide.[40] Therefore, the $DH_1$ (N–O) for compound 3.2 is probably not accurate and must be used with caution. In the cases of compounds 3.1 and 3.3, the $DH_1$ (N–O) values seem to be accurate even though they are associated with large uncertainties. Why is that so? On one hand, the $DH_1$ (N–O) values derived above and, on the other hand, these values are in quite good agreement with the experimental values reported (crystalline and gaseous states) were derived at $T = 298.15$ K.

The gas phase standard molar enthalpies of formation for the mono-N-oxides were combined with existing literature values for the corresponding di-N-oxides and for atomic oxygen allowing the determination of the standard molar enthalpies of dissociation of the N–O bond from which their standard molar enthalpies of combustion and of formation (crystalline and gaseous states) were derived at $T = 298.15$ K.

CONCLUSIONS

Experimental thermochemical work involving static bomb calorimetry and Calvet microcalorimetry has been performed for three quinoxaline derivatives containing a single dative N→O bond, namely 2-tert-butoxy carbonyl-3-methylquinoxaline-N-oxide, 2-phenyl carbamoyl-3-methyl quinoxaline-N-oxide, and 2-carbomoyl-3-methyl quinoxaline-N-oxide. The two calorimetric techniques were used to measure their energies of combustion and the enthalpies of sublimation from which their standard molar enthalpies of combustion and of formation (crystalline and gaseous states) were derived at $T = 298.15$ K.

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SUPPLEMENTARY MATERIAL

Analytical and structural data on compounds 4.1, 4.2 and 4.3 (melting points, elemental analyses, MS/NMR data and spectra).

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