Differentiation of the pyridine radical cation from its distonic isomers by ion–molecule reactions with dioxygen

Karl J. Jobst, Julien De Winter, Robert Flammang, Johan K. Terlouw, Pascal Gerbaux

1. Introduction

Dissociation of a gaseous organic ion from its isomers is commonly based upon high-energy collision-induced dissociation (CID) mass spectra of mass selected ions. However, this approach may be difficult or even impossible to realize if a set of isomeric ions only displays common dissociation pathways [1]. As an alternative, the reactivity of the ion under investigation may be probed by interactions with selected neutral molecules. Apart from charge exchange and protonation reactions, highly structure-specific associative ion–molecule reactions may occur, which readily distinguish the ion from its structural isomers [1]. This is especially true for distonic ions, because of their unique tendency to exhibit radical-type reactivity [2,3].

A case in point concerns our previous work [4a–c] on the pyridine ion and its distonic (1,2-H shift) isomers shown in Scheme 1. The distonic isomers are remarkably stable relative to ionized pyridine but are separated by high interconversion barriers. Consequently, these isomers can be differentiated on the basis of the m/z 28 (HCNH+)::26 (C2H2+·) peak intensity ratio in their high-energy CID mass spectra [4a,b].

However, an easier differentiation was achieved in our more recent study of this system [4c,5] by associative ion–molecule reactions involving a variety of neutral reagents, including H2O. Neutral water does not react with the pyridine ion, but its α-distonic isomer was found to readily generate the 2-pyridone ion, by an O-atom transfer [4c].

The mechanism for this intriguing reaction, however, was not established. This prompted us to use model chemistry calculations (CBS-QB3) to probe various mechanistic scenarios and to perform complementary experiments with the new, more versatile, ion–molecule reaction chamber of the Mons Autospec 6F mass spectrometer. It appears that H2O is not reacting neutral that produces the 2-pyridone ion of the above reaction, but rather O2 from air co-introduced with the water vapour. Theory and experiment agree that the exothermic reaction of O2 with the pyridine-2-ylid ion leads to loss of 1O from a stable peroxide-type adduct ion at m/z 111. Similarly, pyridine-3-ylid ions (3) generate 3-pyridone ions, but the reaction in this case is thermoneutral. The m/z 111:95 peak intensity ratios in the spectra of the ion–molecule products from ions 2 and 3 may serve to differentiate the isomers.

2. Experimental methods

2.1. Tandem mass spectrometry

The experiments were performed on the Mons AutoSpec 6F (Waters, Manchester), a six-sector magnetic deflection instrument of EBBEEB geometry (E = Electric sector, B = Magnetic sector) [6a]. The instrument is equipped with four conventional collision chambers (C1–4) to realize high-energy collision-induced dissociations; an early modification [6b] involved the installation of

**ARTICLE INFO**

Article history:
Received 25 May 2009
Received in revised form 19 June 2009
Accepted 22 June 2009
Available online 30 June 2009

Keywords:
Ion–molecule reactions
Isomer differentiation
Pyridine ylid
Model chemistry
Astrochemistry

**ABSTRACT**

In a previous study on the pyridine ion (1) and the pyridine-2-ylid isomer (2), we reported that ions 2 readily react with H2O to produce 2-pyridone ions at m/z 95, by O-atom abstraction. The mechanism for this intriguing reaction, however, was not established. This prompted us to use model chemistry calculations (CBS-QB3) to probe various mechanistic scenarios and to perform complementary experiments with the new, more versatile, ion–molecule reaction chamber of the Mons Autospec 6F mass spectrometer. It appears that H2O is not reacting neutral that produces the 2-pyridone ion of the above reaction, but rather O2 from air co-introduced with the water vapour. Theory and experiment agree that the exothermic reaction of O2 with the pyridine-2-ylid ion leads to loss of 1O from a stable peroxide-type adduct ion at m/z 111. Similarly, pyridine-3-ylid ions (3) generate 3-pyridone ions, but the reaction in this case is thermoneutral. The m/z 111:95 peak intensity ratios in the spectra of the ion–molecule products from ions 2 and 3 may serve to differentiate the isomers.

© 2009 Elsevier B.V. All rights reserved.
The decarbonylation involves two transition states (ring-opening and loss of CO from the resulting intermediate) the quoted TS refers to the second step.

\[
\text{Protonated pyridine} + D_1 \rightarrow 3\text{-Pyridone ion} \rightarrow \text{TS 3-pyridone ion} \rightarrow \text{Pyrrole ion} + CO + 3\text{O} – 249 \quad [c]
\]

\[
\text{TS 2-pyridone ion} \rightarrow \text{D} – 2\text{-Pyridone ion} – \text{Pyrrole ion} \text{D} – \quad \text{TS HBRC}
\]

Collision-induced dissociation with \( \text{N}_2 \) in chamber C4, and its CID configuration is: C1E1B1C2E2–HEX–C3E3B2C4E4.

Energetic data from CBS-QB3 calculations for the ion–molecule reactions of pyridine-2-ylid and pyridine-3-ylid ions described in Schemes 3 and 4 [a].

Table 1

<table>
<thead>
<tr>
<th>Structure</th>
<th>CBS-QB3 ( \Delta H^{0\text{cal}} ) [0 K]</th>
<th>QB3 ( \Delta H^{0\text{cal}} )_ {298}</th>
<th>EXPT [b] ( \Delta H^{0\text{cal}} )_ {298}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ion 1 (pyridine ion)</td>
<td>–247.49201</td>
<td>248</td>
<td>–</td>
</tr>
<tr>
<td>Ion 2 (pyridine-2-ylid ion)</td>
<td>–247.4903</td>
<td>247</td>
<td>–</td>
</tr>
<tr>
<td>Ion 3 (pyridine-3-ylid ion)</td>
<td>–247.49293</td>
<td>246</td>
<td>–</td>
</tr>
<tr>
<td>Ion 2+H(_2)O</td>
<td>–189 [c]</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>HBRC1</td>
<td>–323.85403</td>
<td>173</td>
<td>–</td>
</tr>
<tr>
<td>TS HBRC1 ( \rightarrow ) 2</td>
<td>–323.846581</td>
<td>178</td>
<td>–</td>
</tr>
<tr>
<td>Ion D1a</td>
<td>–323.86587</td>
<td>165</td>
<td>–</td>
</tr>
<tr>
<td>Protonated pyridine ( *)OH</td>
<td>–187 [c]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protonated pyridine</td>
<td>–248.1815</td>
<td>178</td>
<td></td>
</tr>
<tr>
<td>2-Pyridone ion + H(_2)</td>
<td>–178</td>
<td>176</td>
<td>176</td>
</tr>
<tr>
<td>2-Pyridone ion</td>
<td>–322.68334</td>
<td>178</td>
<td>176</td>
</tr>
<tr>
<td>Ion D2</td>
<td>–397.72966</td>
<td>190</td>
<td>–</td>
</tr>
<tr>
<td>2-Pyridone ion + ( ^1)O</td>
<td>–237 [c]</td>
<td>236</td>
<td></td>
</tr>
<tr>
<td>TS 2-pyridone ion → pyrrole ion</td>
<td>–322.60929</td>
<td>283 [d]</td>
<td></td>
</tr>
<tr>
<td>Pyrrole ion + CO + ( ^1)O</td>
<td>–249 [c]</td>
<td>248</td>
<td></td>
</tr>
<tr>
<td>Pyrrole ion</td>
<td>–209.4311</td>
<td>217</td>
<td>215</td>
</tr>
<tr>
<td>Ion D3</td>
<td>–397.72656</td>
<td>202</td>
<td>–</td>
</tr>
<tr>
<td>3-Pyridone ion + ( ^1)O</td>
<td>–246</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>TS 3-pyridone ion → pyrrole ion</td>
<td>–322.56735</td>
<td>310 [d]</td>
<td></td>
</tr>
<tr>
<td>3-Pyridone ion</td>
<td>–322.66798</td>
<td>187</td>
<td>–</td>
</tr>
</tbody>
</table>

[a] \( E_{\text{total}} \) in Hartrees, all other components are in kcal mol\(^{-1}\); [b] Ref. [16]; [c] The CBS-QB3 derived enthalpies for H\(_2\)O, \( ^1\)O and CO are \( \approx 58.2, 8.8, 59.4 \text{ and } –26.9 \text{ kcal mol}^{-1} \); [d] The decarbonylation involves two transition states (ring-opening and loss of CO from the resulting intermediate) the quoted TS refers to the second step.

3. Results and discussion

3.1. The associative ion–molecule reaction of the pyridine-2-ylid ion with H\(_2\)O

Pyridine-2-ylid ions (2) are readily generated in the dissociative ionization of 2-acetylpyridine [5] by the route depicted in Scheme 2. In good agreement with the results of our previous study [4c], the reaction of mass selected ions 2 with H\(_2\)O vapour in the hexapole reaction chamber of our mass spectrometer leads to the formation of \( m/z \) 95 product ions, as witnessed by the spectrum of Fig. 1a. Under the same conditions, pyridine ions (1) are unreactive.

The (high-energy) CID mass spectrum of these \( m/z \) 95 product ions, see Fig. 1d, is closely similar to that of the molecular ions produced in the EI mass spectrum of the 2-hydropyridine/pyridine-2-one system of tautomers [9]. This result, and the fact that the reaction with D\(_2\)O as the reagent exclusively generates \( m/z \) 95 ions, led to the proposal [4c] that the 2-pyridone ion chemistry [8]. The identity of local minima and connecting transition states (TS) was confirmed by frequency analysis. Enthalpies derived from this and other model chemistries are expected to be of chemical accuracy \( \pm 2 \text{ kcal mol}^{-1} \). However, as pointed out by a reviewer, for the peroxy-type ions D\(_2\) and D\(_3\), the performance of the method may be compromised by an inadequate reference wave function.

The complete set of computational results including the optimized geometries is available from the authors upon request.
is the major reaction product from the $m/z$ 97 adduct ion comprised of $\text{H}_2\text{O}$ and ion 2.

The model chemistry calculations of Scheme 3 show that the interaction of a single water molecule with ion 2 may yield hydrogen-bridged radical cation $\text{HBRC}_1$ [10]. This ion could be envisaged to isomerize into $\text{D1a}$ or $\text{D1b}$ but neither pathway appears to be energetically feasible:

(i) The isomerization of $\text{HBRC}_1$ into $\text{D1a}$ involves a prohibitively high TS at 197 kcal mol$^{-1}$ for the formation of the intermediate ion $\text{HBRC}_2$. This ion, see Table 1, is predicted to dissociate by loss of OH$^\bullet$ (which is not experimentally observed!) rather than rearrange into ion $\text{D1a}$.

(ii) Adduct ion $\text{D1b}$, generated by C–O bond formation, is not even a minimum. Finally, the subsequent 1,2- and 1,1-H$_2$ elimination reactions from $\text{D1a}$ and $\text{D1b}$ are expected to have considerable energy barriers.

Thus, despite the exothermicity of the reaction, the scenario of Scheme 3 predicts that the bulk of the $m/z$ 97 adduct ions dissociate by loss of water. In line with this prediction, the $m/z$ 97 adduct ions do not lose $\text{H}_2$ to any significant extent in their CID mass spectrum (not shown). Instead, these ions primarily back-dissociate into ions 2 and $\text{H}_2\text{O}$. It is therefore highly unlikely that the 2-pyridone ion is generated in the reaction of a water molecule with ion 2.

This led us to consider the possibility that the 2-pyridone ion is generated by another reagent. A plausible candidate would be triplet (biradical) O$_2$ molecules from air co-introduced with the water vapour. Such a reaction would not be unprecedented: reactions of distonic ions and O$_2$ have been observed previously [11,12]. Indeed, a drawback of the present inlet system is that, despite multiple freeze/pump cycles, air may be co-introduced into the hexapole cell when dealing with reagents of low volatility. This prompted us to examine the interaction of pyridine-2-ylid ions with pure oxygen.

### 3.2. The associative ion–molecule reaction of the pyridine-2-ylid ion (2) with dioxygen

Fig. 1b shows the mass spectrum of the products of the ion–molecule reaction of pyridine-2-ylid ions ($m/z$ 79) and pure oxygen. That 2-pyridone ions are readily generated in the reaction is revealed by the intense peak at $m/z$ 95 and its corresponding CID mass spectrum, which is identical with that shown in Fig. 1d.

These observations are rationalized by the model chemistry calculations of Scheme 4a, which show that the initial interaction between ion 2 and O$_2$ leads to the remarkably stable covalently...
Scheme 3. The ion–molecule reaction of the pyridine-2-ylid ion 2 with H_2O. The numbers refer to 298 K enthalpies in kcal mol\(^{-1}\) derived from CBS-QB3 calculations.

bound species D_2. This peroxide-type ion enjoys considerable stabilization, c. 50 kcal mol\(^{-1}\), relative to the combined enthalpies of ion 2 and O_2. Our calculations further show that loss of ^1O from ion D_2 yields the 2-pyridone ion in a process that is continuously exothermic by 11 kcal mol\(^{-1}\) relative to the combined enthalpies of ion 2 and O_2.

The spectrum of Fig. 1b also shows peaks at m/z 52, 66 and 67, whose formation deserves comment. The signal at m/z 52 (C_4H_4^+) is readily attributed to the spontaneous and collision-induced loss of HCN from the mass selected 2-ylid ions [4a], but the other two ions must result from associative ion–molecule reactions between the 2-ylid ion and O_2.

The m/z 67 ion, readily identified as the pyrrole ion on the basis of its CID mass spectrum (not shown), likely originates from decarbonylating 2-pyridone ions: see the CID mass spectrum of Fig. 1d, where m/z 67 is the base peak. The calculated TS for the decarbonylation is quite high (283 kcal mol\(^{-1}\)), in line with the results of a previous study on isomeric C_5H_5NO^+ ions [9].

This raises the question as to why this energy demanding reaction is observed. First, we note that the EI generated 2-ylid reactant ions may have up to ~70 kcal mol\(^{-1}\) of internal energy, the estimated energy requirement for the spontaneous loss of HCN [4a,d]. Thermalization of these ions by (unreactive) collisions with the neutral reagent takes place in the hexapole cell but this process may be rather inefficient in our experimental set-up. Perhaps more likely, ions entering the hexapole cell have a minimum translational energy of ~5 eV, so that collision-induced dissociation may still compete with collisional cooling. In line with this, Fig. 1c shows that the relative intensity of the m/z 67 (and m/z 52) peak decreases considerably when the O_2 pressure is raised.

The spectrum of Fig. 1c indicates that the m/z 66 ion also results from a high-energy process. Its CID mass spectrum (not shown)

Scheme 4. Potential energy diagrams describing the associative ion–molecule reactions of (a) the pyridine-2-ylid ion 2 and (b) the pyridine-3-ylid ion 3 with dioxygen. Numbers in square bracket refer to CBS-QB3 derived 298 K enthalpies in kcal mol\(^{-1}\).
may be that of a C₄H₄N⁺ isomer for which, unfortunately, reference spectra are not available. Several pathways for its formation can be envisaged, but in the absence of further information, these remain highly speculative. The CID mass spectrum of Fig. 1e, indicates that one route may involve decarbonylation of the weakly detected m/z 94 ions in the spectrum of Fig. 1b.

The most important feature of Fig. 1c is that at the elevated O₂ pressure, the m/z 111 adduct ion (D2) becomes observable. The fact that its CID mass spectrum shows a significant peak at m/z 95, see Fig. 1f, underlines our proposal that dioxygen, rather than water, reacts with the pyridine-2-ylid ion.

### 3.3. The associative ion–molecule reaction of the pyridine-3-ylid ion (3) with dioxygen

We have also studied the reaction of pyridine-3-ylid ions 3 with dioxygen to see if the distonic isomers 2 and 3 can be differentiated. Ions 3 can conveniently be generated by the dissociative ionization of 2,3-diacetylpyridine, as depicted in Scheme 5.

In line with the calculations of Scheme 4b, which predict that the O-atom abstraction of dioxygen by the radical site of ion 3 is a thermoneutral reaction, Fig. 2a displays a sizeable peak at m/z 95 for the reaction of ion 3 with dioxygen.

The CID mass spectrum of these m/z 95 ions is shown in Fig. 2c. The spectrum is virtually the same as that of the 3-pyridone ions generated by demethylation of protonated 3-methoxy-pyridine [9]. However, the CID mass spectra of 2- and 3-pyridone reported in Ref. [9] are closely similar and the same obtained for the CID spectra of Figs 1d and 2c.

Thus, ions 2 and 3 cannot be differentiated on the basis of the CID mass spectra of the m/z 95 ions. However, there is a striking difference in the relative abundance of the m/z 111 and 95 ions generated in the two reactions. Comparison of Figs 1b and 2a shows that at a relatively low O₂ pressure, the m/z 111 adduct ion is observed with ion 3 but not with ion 2. This is in agreement with our calculations, namely that the O-atom abstraction is exothermic for ion 2 and thermoneutral for ion 3. Thus, incipient ions D2 are more prone to dissociate prior to collisional stabilization than ions D3. This trend is paralleled in the mass spectra of Figs 1c and 2b where a higher oxygen pressure was used in the hexapole cell. The m/z 111:95 peak intensity ratio may therefore serve to differentiate ions 2 and 3.

Finally, we note that adduct ions D2 or D3 are unlikely to further react with O₂ under our experimental conditions. Exploratory calculations indicate that the reaction of D2 with O₂ is exothermic (by c. 15 kcal mol⁻¹), and that dissociation of the resulting [D2−O−O]⁺ adduct ion into 2-pyridone + O₂ is more energy demanding (by c. 25 kcal mol⁻¹) than back-dissociation into D2 + O₂.

### 4. Conclusions

The previously reported [4c] formation of the 2-pyridone ion from the pyridine-2-ylid ion and H₂O appears to refer to the reaction of O₂ from air co-introduced with the water vapour. Theory and experiment agree that this exothermic reaction leads to loss of ^3O from a stable peroxide-type adduct ion at m/z 111. Similarly, pyridine-3-ylid ions (3) generate 3-pyridone ions, but the reaction in this case is thermoneutral. The m/z 111:95 peak intensity ratios in the spectra of the ion–molecule products from ions 2 and 3 reflect the different energy requirements and may serve as a diagnostic tool to differentiate the isomers.

The reported O-atom abstraction may well represent a general reaction of distonic heterocyclic ions: work in progress shows that the distonic ions of pyrimidine [13], imidazole [14] and thiazole [14] show the same behaviour. The reaction of O₂ with the distonic ions of the prebiotic pyrimidine molecule may be of interest to astrochemistry [15].

---

**Scheme 5.** The generation of pyridine-3-ylid ions by dissociative ionization of 2,3-diacetylpyridine.
Acknowledgements

PG (Research Associate), RF and JDW (Research Fellow) are grateful to the “Fonds pour la Recherche Scientifique” (FRS-FNRS) for financial support in the acquisition of the Waters AutoSpec 6F and for continuing support. JKT and KJJ thank the Natural Sciences and Engineering Research Council of Canada (NSERC) for financial support, SHARCNET for the computational resources and Dr. P.C. Burgers for valuable discussions.

References

   (b) S. Gronert, Chem. Rev. 101 (2001) 329;