Collisional activation of protonated halogeno-pyridines: different behaviour of target gases

Hung Thanh Le [a,c], Pascal Gerbaux [b], Robert Flammang [b,1], Minh Tho Nguyen [a,*]

[a] *Department of Chemistry, University of Leuven, Celestijnenlaan 200F, B-3001 Leuven, Belgium*
[b] *Laboratory of Organic Chemistry, University of Mons-Hainaut, Avenue Maistriau 19, B-7000 Mons, Belgium*
[c] *Faculty of Chemical Engineering, Ho Chi Minh City University of Technology, Ho Chi Minh City, Viet Nam*

Received 21 December 1999; in final form 13 April 2000

Abstract

Protonated 2-Cl and 2-Br-pyridines undergo facile dehalogenation upon high energy (8 keV range) collisional activation provided the target is NO, or even better O_2, instead of He or Ar. In the low energy regime (20–30 eV range), debromination occurs more readily than dechlorination, but the peculiar behaviour of O_2 in favouring an X-loss over a HX-elimination, is no longer detected (using a MS^3 instrument). B3LYP/6-31G(d) calculations on X-pyridines with X = F, Cl and Br on positions 2, 3 and 4, suggest that, if a protonated pyridine is formed in the lower-lying triplet state following strong interaction with O_2 or NO having higher spin, the loss of Cl or Br becomes almost spontaneous (F-loss is more difficult). Proton affinity PA(pyridine) = 940 ± 15 kJ/mol, is decreased by 5–15 kJ/mol upon halogenation. © 2000 Elsevier Science B.V. All rights reserved.

1. Introduction

The use of molecular oxygen (O_2) as a target gas has became a common technique in collisional activation (CA) mass spectrometry as it increases significantly the yield of the charge stripping process (CS being a production of doubly charged species) [1,2] and the yield of the reionization of fast neutral beams generated in neutralization–reionization (NR) mass spectrometry experiments [3].

As a target, molecular oxygen behaves in most cases just like helium or nitrogen generating the same fragment ions in similar abundances. In some instances, O_2 accentuates, however, certain reactions or even induces new fragmentation reactions that were not observed at all when using helium or argon as a target [4–9]. We report in this Letter another case of such unexpected behaviour detected for protonated halogenated pyridines that readily undergo dehalogenation upon oxygen collisional activation. As for an interpretation, the production of a lower-lying triplet state of these ions is proposed on the basis of quantum chemical computations.

2. Mass spectrometric experiments

All the spectra were recorded on a large-scale (Micromass AutoSpec 6F) tandem mass spectrometer of EBE©EBE geometry (E stands for electric

* Corresponding author. Fax: +32-16-32-79-92; e-mail: minh.nguyen@chem.kuleuven.ac.be
[1] E-mail: robert.flammang@umh.ac.be

sector, B for magnetic sector and © for the collision cell used in the present work) [10]. Typical conditions were 8 kV accelerating voltage, 1 mA emission current and 70 eV ionizing electron energy. The pyridines were protonated in the chemical ionization source by using methanol as the reagent gas at an estimated pressure of 0.5–1.0 Torr.

The high energy CA spectra were obtained by a linked scanning of the fields of the three last sectors (MS2) after mass selection of the protonated pyridines by the three first sectors (MS1). The pressure of the collision gas was adjusted in order to reduce the ion beam by 30–50%.

The low energy CA spectra were obtained with the same instrument operating in the hybrid mode in which a radiofrequency-only quadrupole collision cell fitted with deceleration and acceleration lenses is inserted between MS1 and MS2 [11,12]. In these experiments, a beam of mass-selected (MS1) ions is decelerated to ca. 20–30 eV and undergoes collision with a target gas in the quadrupole cell. All the ions generated in the quadrupole were thereafter reaccelerated at 8 keV and mass-analyzed by a scanning of the field of the magnet of MS2.

All the samples were commercially available (Aldrich) and used without further purification. The collision gases were supplied by Praxair: oxygen 2.6, nitric oxide 2.0 and helium 5.0.

The results obtained from the various MS experiments are recorded in Tables 1 and 2, as well as in

Table 1
High energy (8 keV) CA spectra of protonated 2-halogenopyridines $2H^+X$ (X = F, Cl, Br) using helium, nitric oxide or oxygen as the collision gas (normalized values in %)

X	Target gas	HX-elimination	X-elimination	Charge stripping
$2H^+F$	Helium	96	4	–[a]
	Nitric oxide	93	7	–
	Oxygen	93	7	–
$2H^+Cl$	Helium	85	13	2
	Nitric oxide	58	38	4
	Oxygen	41	43	16
$2H^+Br$[b]	Helium	81	18	1
	Nitric oxide	50	42	8
	Oxygen	38	37	25

[a] These peaks are not taken into account as severe interference with singly charged ions cannot be excluded.
[b] Experiments performed on the [81]Br containing ions in order to eliminate interferences.

Table 2
Low energy (ca. 30 eV) CA spectra of protonated 2-halogenopyridines $2H^+$ using argon and molecular oxygen as a collision gas

X	Collision gas	HX-elimination (%)	X-elimination (%)
$2H^+F$	Argon	100	–
	Oxygen	100	–
$2H^+Cl$	Argon	87	13
	Oxygen	93	7
$2H^+Br$	Argon	69	31
	Oxygen	71	29

Figs. 1 and 2. First we found that the protonation occurs exclusively on the nitrogen atom. There is also no evidence for the formation of other forms such an 'ipso' structure. In the N-protonated form, the transfer of a H-atom from one to another position of the ring implies a unimolecular rearrangement that is not favored in the high energy CA regime. The most prominent fragmentation observed when fast (8 keV) protonated 2-halogeno-(X)-pyridines $2H^+F$ (X = F), $2H^+Cl$ (X = Cl) and $2H^+Br$ (X = Br), collide with helium in a field-free region of the mass spectrometer is the loss of hydrogen halogenide (HX) producing 2-pyridyl cations [13–16] (see for instance Fig. 1a for protonated 2-chloropyridine). The loss of the halogen atom (X˙) is also detected, but to a much lesser extent. Previous results in the literature have shown that carbenic radical cations are actually produced in this reaction rather than the more conventional pyridine molecular ions [15,17].

We have also repeated the CA experiment using argon as the target and found that the X-loss is very similar to that observed with helium. Thus it is apparent that the mass of the target is not an important factor in this case.

Surprisingly, replacement of helium by oxygen tends to increase very significantly the yield of dechlorination (cf. Table 1). As a matter of fact, the loss of Cl˙, relative to the loss of HCl, is amplified by a factor of ca. 7 when replacing helium by oxygen as the target gas. Nitric oxide behaves similarly to oxygen. The charge stripping reaction is also strongly enhanced (mainly with oxygen), but this effect has already been described in the literature and attributed to near resonant electron capture [18].

The relative abundances of the losses of HX and X$^{\cdot}$ upon collisional activation in the radiofrequency-only quadrupole collision cell are given in Table 2. In these low kinetic energy conditions, protonated 2-fluoropyridine eliminates only hydrogen fluoride (HF) irrespective of the nature of the collision gas. For protonated 2-chloropyridine and 2-bromopyridine (Figs. 1 and 2), a loss of atomic halogen becomes significant, but it is clear that the use of oxygen, under low energy conditions, does not favour this reaction as it is detected in the high energy CA spectra. Note, however, that the HX elimination is not the subject of this study. A question of interest is whether there is any relationship between the relative abundance of the X-loss and the polarisability of the target gases. Our observations for the Cl-derivatives are as follows (in parentheses are the polarisabilities taken from Ref. [19]): He: 13% (0.2), O$_2$: 43% (1.6), Ar: 6% (1.7), N$_2$: 20%
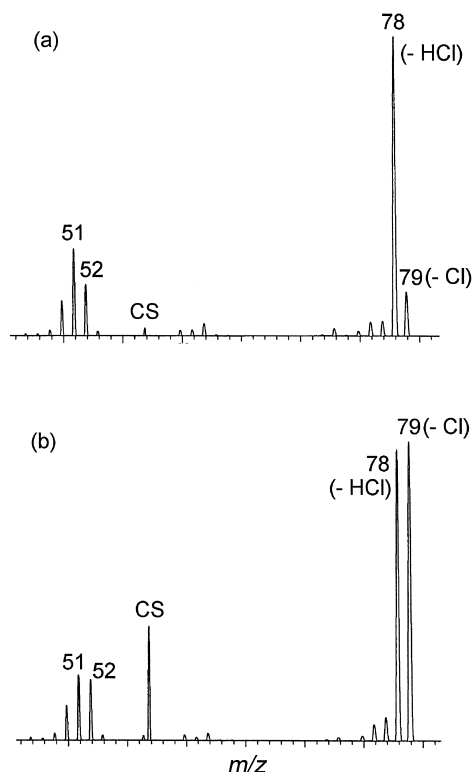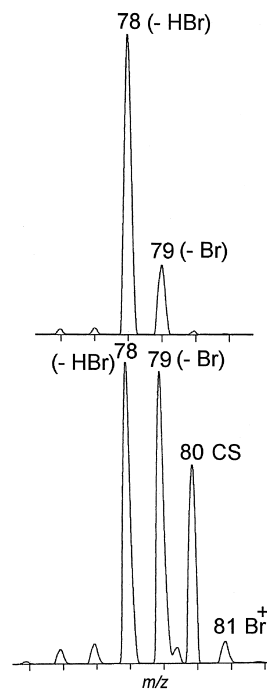

Fig. 2. CA spectra (partim) of protonated 2-bromopyridine **2H$^+$Br** using: (upper) helium, or (lower) oxygen, as the collision gas. CS refers to the charge stripping reaction. The experiments were performed on the [81]Br containing ions (*m/z* 160).

(1.9) and NO: 38% (3.0). It is thus clear that no relationship between these quantities could be derived.

3. Quantum chemical calculations

We now attempt to search for a possible interpretation of the peculiar difference in the behaviour of the collision gases used in CA experiments, namely oxygen and nitric oxide on the one hand, and helium and argon on the other hand. It can first be noted that both O$_2$ and NO molecules possess an open-shell electronic ground state. Therefore it appears reasonable to propose that when collided with oxygen gas, which has a triplet ground state, the selected ions could be somehow formed in a lower-lying excited state prior to dissociation, with preponderant populations of excited states. Such an electronic transition differs presumably from those reached when inert helium or argon gas was used; in the latter cases, the

Fig. 1. CA spectra of protonated 2-chloropyridine **2H$^+$Cl** using helium (a) or oxygen (b) as the collision gas. CS refers to the charge stripping reaction.

ions therefore undergo collisional dissociation essentially in their electronic ground state. In other words, the observed difference in collision gases behaviour may be interpreted as a consequence of a more abundant formation during the CA process, of the target ions in an excited state when O_2 and NO (having a doublet ground state) were used.

In search for some quantitative information which could lend a certain support for this proposition, we have carried out ab initio quantum chemical calculations on a series of mono-halogeno(X)-pyridines, in which the halogens X occupy the positions 2, 3 and 4 of the ring, and include fluorine, chlorine and bromine. For each pyridine considered, the neutral, ionized, and protonated forms have been examined. In the latter, both singlet and triplet states, the doubly charged cation, as well as the carbenic (or similar) product have been found to be formed from a loss of the halogen radical X˙. For this purpose, we have made use of the density functional theory (DFT) with the popular hybrid B3LYP functional [20,21], in conjunction with the d-polarized 6-31G(d) basis set. Recent studies [22–25] on similar systems have shown that as far as the relative energies are concerned, this method provides results comparable to a higher level quadratic configuration interaction and coupled-cluster theories of molecular orbital methods. The absolute differences between B3LYP and CCSD(T) values thus amount to, at most, 10–15 kJ/mol, and are thus quite acceptable for our present purpose. On the other hand, use of the DFT method allows us to avoid the problem of spin contamination in UHF-wave functions, which could be severe in some doublet and triplet states. An obvious shortcoming of UHF-based methods is that the open-shell singlet states cannot be calculated. All calculations were performed with the aid of the Gaussian 94 set of programs [26].

Geometries of the structures considered were optimized and subsequently characterized by harmonic vibrational analyses that also provide zero-point energy corrections (ZPE) to relative energies. Throughout this section, bond distances are given in ångstrom and relative energies in kJ/mol. Unless otherwise noted, the latter were derived from B3LYP/6-31G(d) + ZPE calculations.

As for a convention, each of the structures examined is denoted by a combination of letters and numbers, for example, **2NF** or **4H⁺Br-t**, that are defined as follows: (i) the first number $n = 2$, 3 or 4 indicates the substitution position of the halogen on the six-membered ring; (ii) **N** stands for a neutral, **H⁺** a N-protonated pyridine, **d⁺** a doublet dication resulting from a charge-stripping of the protonated form H⁺, and **c⁺** the carbene radical cation generated upon a halogen-loss of H⁺; (iii) **F**, **Cl** or **Br** corresponds to the halogen; (iv) for a protonated form, **s** (singlet) and **t** (triplet) specifies its electronic state. Due to the rather large number of the species considered, and to the fact that the geometric properties are not directly relevant to the purpose of the
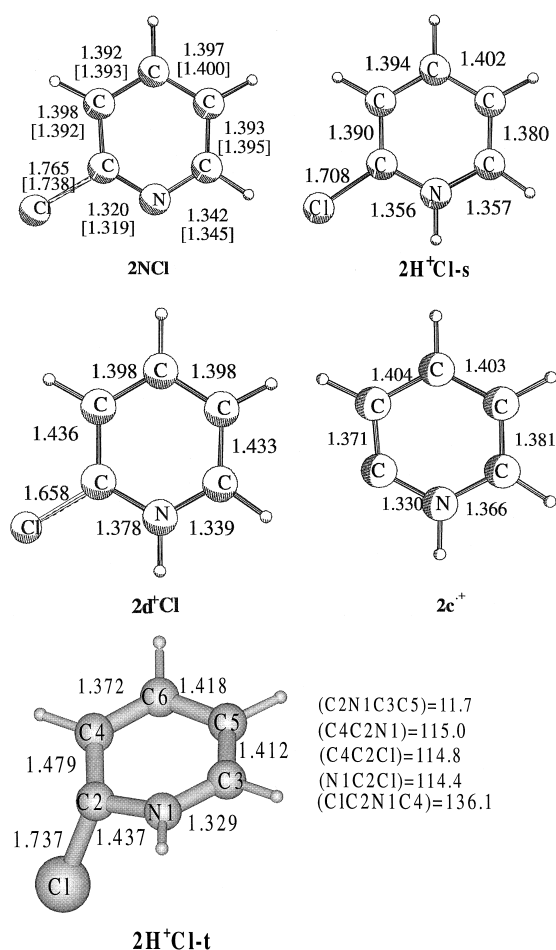

Fig. 3. Selected B3LYP/6-31G(d) distances of the structures related to *2-chloro-pyridine*. **N** stands for neutral, **H⁺** protonated, **s** singlet, **t** triplet, **d⁺** dication, and **c⁺** carbene ion. For **2NCl**, experimental values taken from Ref. [25] are given in parentheses.

present work, only a representative selection of structures concerning *2-chloro-pyridine* are recorded in Fig. 3. The latter includes the calculated distances of the neutral **2NCl**, protonated singlet **2H⁺Cl-s** and triplet **2H⁺Cl-t**, dicationic **2d⁺Cl** and carbene ion **2c⁺**. A perspective representation of the triplet structure **2H⁺Cl-t** is given showing the ring distortion; the other structures are planar or nearly planar. For the sake of simplicity in the presentation of data, the calculated total and zero-point energies are also omitted. The calculated relative energies are schematically given in both Figs. 4 and 5.

The molecular structures of 2-, 3- and 4-chloropyridines have been analysed in detail in a recent experimental and theoretical study [27]. We note that for 2-Cl-pyridine, except for the C − Cl distance (cf. Fig. 3), the B3LYP values for the ring agree remark-

ably well with the results obtained in a recent gas phase electron diffraction study [27]. The geometric changes induced by halogen substitution are rather small, amounting to a few thousandths of an ångstrom for the bond distances, irrespective of the substitution position. As expected, the ring structure is modified substantially upon N-protonation. In the singlet protonated forms, the ring remains planar, even though some distances are compressed whereas those around the nitrogen atom are stretched (up to 0.035 Å); especially the C − X distance shows a compression of about 0.06 Å. It seems that a strong electron delocalization of the X-lone pair which stabilizes the positive charge and in the same time shortens the C − X distance. Except for the C − X distances, geometric parameters of the planar singlet protonated species are quite similar to each other.
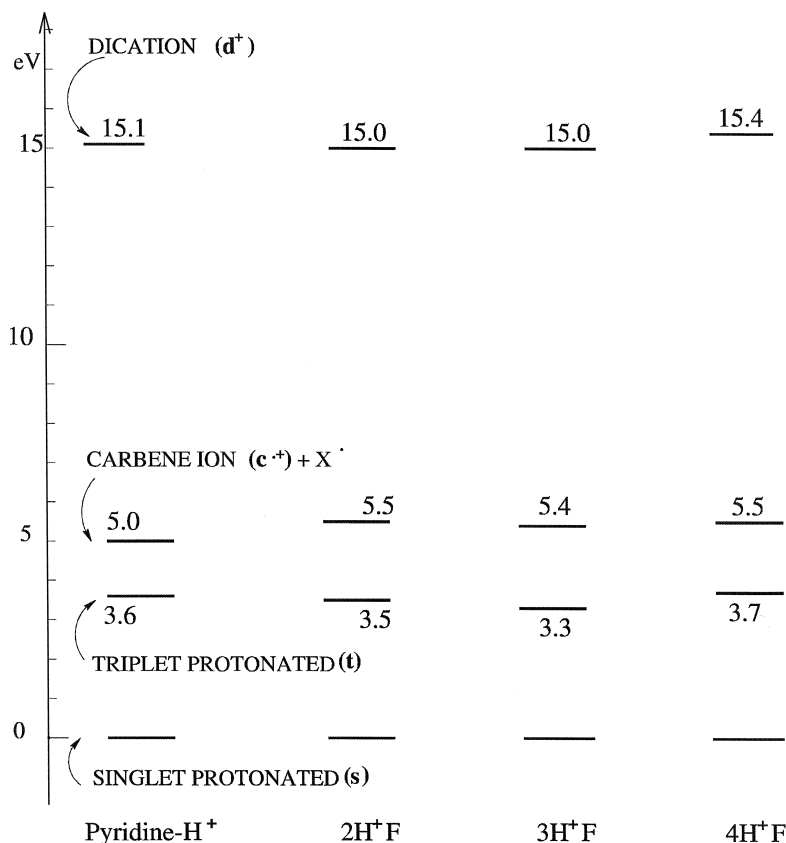

Fig. 4. Schematic comparison of the energy levels, relative to the corresponding singlet protonated form, of the parent pyridine, and 2-, 3-, 4-fluoro pyridines. Energies given in eV are obtained from B3LYP/6-31G(d) + ZPE computations. For 3-pyridine, the fragment is not formally a carbene, but an isomer.
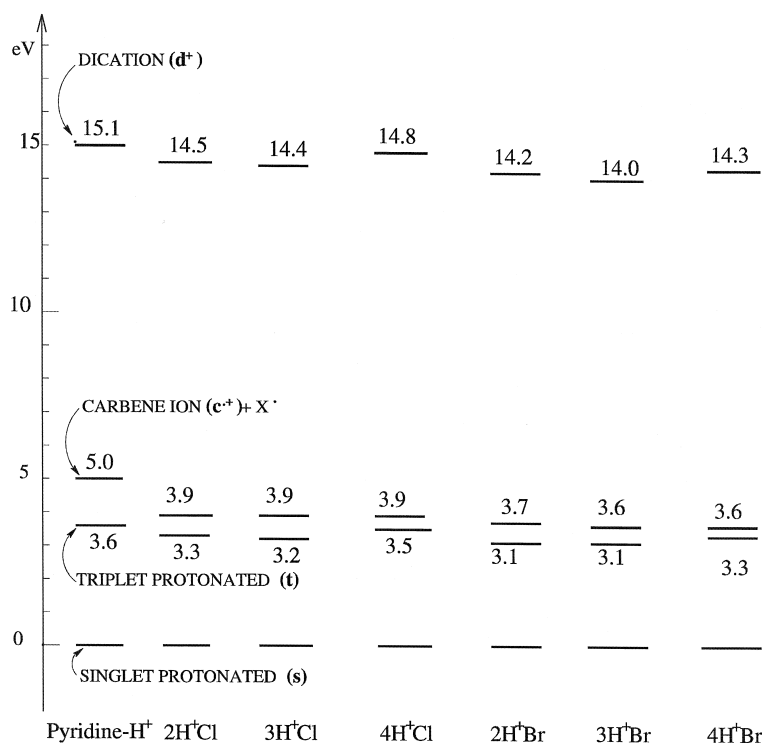
Fig. 5. Schematic comparison of the energy levels (eV) relative to the corresponding singlet protonated form, of 2-, 3-, 4-chloro- and bromo-pyridines. Energies are obtained from B3LYP/6-31G(d) + ZPE computations. For 3-pyridine, the fragment is not formally a carbene, but an isomer.

In the triplet state, the molecular structure undergoes, as expected, a significant distortion. While the six-membered pyridine ring is only marginally puckered, the C–(Cl)–carbon atom becomes strongly pyramidal with a significant lengthening of the C − Cl distance as compared with that in the singlet counterpart (1.708 Å in **2H⁺Cl-s** and 1.737 Å in **2H⁺Cl-t**). In principle, five (5) distinct triplet structures could be formed depending on the location of the triplet centre. Fig. 3 displays the energetically lowest-lying triplet in which the substituted carbon (C–X) is pyramidalized **2H⁺Cl-t**. The dication species **2d⁺Cl** remains also essentially planar. For their part, the carbene radical cation **2c⁺** and its neutral counterpart as well as the isomerisation process have been studied in detail in a recent paper [22]. We note that these distonic radical cations also exhibit nearly planar conformations.

Regarding the energetic results, a few relevant points can be mentioned.

(a) The singlet state is confirmed to be the ground state of all nitrogen-protonated pyridines considered. At the B3LYP/6-31G(d) + ZPE level, the proton affinity is calculated to be PA(N) = 940 kJ/mol for the parent pyridine, with an expected error of ± 15 kJ/mol. Following mono-substitution either by X = F, Cl or Br, the PA is reduced to about 905 kJ/mol for 2-X-, 915 kJ/mol for 3-X- and 925 kJ/mol for 4-X-pyridines. It turns out that for each substitution position, there is a difference of, at most, 5 kJ/mol between the PA's of halogenated pyridines.

(b) The triplet is an excited state of the protonated pyridine lying about 3.0–3.5 eV above the corresponding singlet ground state. Upon halogenation, the triplet–singlet energy gap is slightly reduced. The most marked effect is found for the 2- and 3-bromine derivatives (reduction up to 0.5 eV), followed by the 2- and 3-chlorine ones (0.4 eV). The 4-substitution induces a consistently smaller reduction. Compared with its higher homologues, fluorine

induces a smaller effect on this quantity. As mentioned above, the method employed in this work does not allow the singlet open-shell state to be characterized. Therefore, we could not establish yet as to whether the triplet is the lowest-lying excited state of protonated pyridines.

(c) In the parent pyridine, the fragments arising from a H-loss (carbene ion + H) are calculated to lie about 5.0 and 1.4 eV above the singlet and triplet protonated forms, respectively. Upon fluorine substitution, these gaps tend to enlarge to 5.5 and 2.0 eV. On the contrary, they are significantly reduced following chlorine and bromine substitution. As a matter of fact, the separation between the fragments and the triplet state amounts to only 0.3 eV in the 4-bromo-derivative (cf. Fig. 5). In other words, this result apparently lends a quantitative support for the proposition stated above that if a protonated pyridine could be formed, with a higher population, in its lower-lying triplet state following interaction with the oxygen collision gas, then the loss of a halogen atom becomes, in some cases, an almost spontaneous process. Of course, this implies an inherent assumption that the deactivation of the excited triplet to the singlet ground state is going slower than the C–X bond cleavage.

A lengthening of 0.03 Å of the C–Cl bond distance in going from the singlet to the triplet state of the protonated species, as mentioned above, could also facilitate the C–Cl bond cleavage in the higher spin state. Using the same argument, the charge stripping (CS) process is equally accelerated due to the smaller gap between the triplet ion (t) and the corresponding dication (d^+).

The energy levels shown in Figs. 4 and 5 are also consistent with the mass spectrometric results described in the previous section in that chloro- and bromo-derivatives tend to undergo easy elimination of the X atom, whereas it is not the case for fluoro-counterparts. It should be stressed that a detailed mechanism of an eventual triplet formation during the collisional activation is not clear to us yet.

4. Concluding remarks

Using a combination of tandem mass spectrometric methodologies, it is shown that dehalogenation of protonated 2-halogenopyridines produces carbenic (ylid) radical cations, isomers of the more conventional pyridine molecular ions. The dehalogenation reaction is a very efficient process in the high energy (8 keV) collisional activation regime, provided the target is molecular oxygen or nitric oxide. The helium or argon gas shows a different behaviour. In the low energy regime (20–30 eV), debromination occurs more readily than dechlorination, but the peculiar behaviour of molecular oxygen is no longer detected. Quantum chemical results at the B3LYP/6-31G(d) + ZPE level suggest that preponderant formation and subsequent dissociation of the lowest-lying triplet protonated species provide a reasonable rationalization for the difference in behaviour of collision gases. The proton affinity of pyridine is also calculated, PA(pyridine) = 940 ± 15 kJ/mol; this quantity tends to be decreased by 5 to 15 kJ/mol upon halogenation.

References

[1] K. Lammertsma, P.v.R. Schleyer, H. Schwarz, Angew. Chem. Int. Ed. Engl. 28 (1989) 1321.
[2] K. Vekey, Mass Spectrom. Rev. 14 (1995) 195.
[3] C.A. Schalley, G. Hornung, D. Schroder, H. Schwarz, Chem. Soc. Rev. 27 (1998) 91.
[4] R. Flammang, K. Gallez, Y. Van Haverbeke, M.W. Wong, C. Wentrup, Rapid Commun. Mass Spectrom. 10 (1996) 232.
[5] G.A. McGibbon, P.C. Burgers, J.K. Terlouw, Int. J. Mass Spectrom. Ion Processes 136 (1994) 191.
[6] C. Aubry, J.L. Holmes, J. Phys. Chem. A 102 (1998) 6441.
[7] R. Flammang, P. Gerbaux, M.M. Wong, Chem. Phys. Lett. 300 (1999) 183.
[8] P. Gerbaux, M. Barbieux-Flammang, Y. Van Haverbeke, R. Flammang, Rapid Commun. Mass Spectrom. 13 (1999) 1707.
[9] R. Flammang, V. Henrotte, M. Barbieux-Flammang, M.T. Nguyen, Eur. Mass Spectrom. 6 (2000) 3.

[10] R.H. Bateman, J. Brown, M. Lefevere, R. Flammang, Y. Van Haverbeke, Int. J. Mass Spectrom. Ion Processes 115 (1992) 205.

[11] R. Flammang, Y. Van Haverbeke, C. Braybrook, J. Brown, Rapid Commun. Mass Spectrom. 9 (1995) 795.

[12] P. Gerbaux, Y. Van Haverbeke, R. Flammang, J. Mass Spectrom. 32 (1997) 1170.

[13] F.C. Gozzo, M.N. Eberlin, J. Org. Chem. 64 (1999) 2188.

[14] M. Carvalho, F.C. Gozzo, M.A. Mendes, R. Sparrapan, C. Kascheres, M.N. Eberlin, Chem. Eur. J. 4 (1998) 1161.

[15] D. Lavorato, J.K. Terlouw, T.K. Dargel, W. Koch, G.A. McGibbon, H. Schwarz, J. Am. Chem. Soc. 118 (1996) 11898.

[16] F.T. Turecek, J.K. Wolken, M. Sadilek, Eur. Mass Spectrom. 4 (1998) 321.

[17] P. Gerbaux, Y. Van Haverbeke, R. Flammang, J. Mass Spectrom. 32 (1997) 1170.

[18] M.P. Barbalas, F. Turecek, F.W. McLafferty, Org. Mass Spectrom. 17 (1982) 155.

[19] J.E. Bartmess, R.H. Georgiadis, Vacum 33 (1983) 149.

[20] A.D. Becke, J. Chem. Phys. 98 (1993) 1372.

[21] C. Lee, W. Yang, R.G. Parr, Phys. Rev. B 37 (1988) 785.

[22] D.J. Lavorato, J.K. Terlouw, G.A. McGibbon, T.K. Dargel, W. Koch, H. Schwarz, Int. J. Mass Spectrom. 179 (1998) 7.

[23] M.T. Nguyen, T.L. Nguyen, H.T. Le, J. Phys. Chem. A 103 (1999) 5758.

[24] H.T. Le, T.L. Nguyen, D. Lahem, R. Flammang, M.T. Nguyen, Phys. Chem. Chem. Phys. 1 (1999) 755.

[25] P.C. Gomez, L.F. Pacios, J. Phys. Chem. A 103 (1999) 739.

[26] M.J. Frisch et al., Gaussian 94, Rev. C3, Gaussian, Pittsburgh, PA, 1995.

[27] B.C. Smart, C.A. Morrision, P.M. Papathomas, C.A. Brookman, H.E. Robertson, D.W.H. Rankin, J. Chem. Soc. Perkin Trans. 2 (1999) 745.