

Electrospray ionization and liquid secondary ion mass spectrometric study of N-heterocyclic carbenes and their 1,2,4-triazolium salt precursors

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Abstract

N-Heterocyclic carbenes and their 1,2,4-triazolium salt precursors were analyzed by electrospray ionization (ESI) and liquid secondary ion mass spectrometry (LSIMS). It was found that under applied conditions the C5 carbene center is formed from $[M + ClO_4]^+$ ion, where M corresponds to the 1,2,4-triazolium dicationic system, by loss of $HClO_4$ molecule. Further decomposition of formed carbene ions, namely $[M - H]^+$ ion, consist in the breaking of triazolium ring and loss bulky substituents from N1 and N4 atoms through the hydrogen transfer to the carbene center. This is in contrast to the $[M]^{2+}$ carbene precursor ions for which only the loss of N1 substituent occurred as a simple heterolytic bond cleavage.

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1. Introduction

The azolium-derived salts are used in many branches of chemistry. From among this class of conjugates the 1,2,4-triazolium derivatives have attracted considerable attention. They are used in the form of ionic liquids which found applications in catalytic and organic reactions [1,2], as an efficient chiral catalyst in the asymmetric benzoin condensation [3], as reagents for synthesis of carbene metal complexes

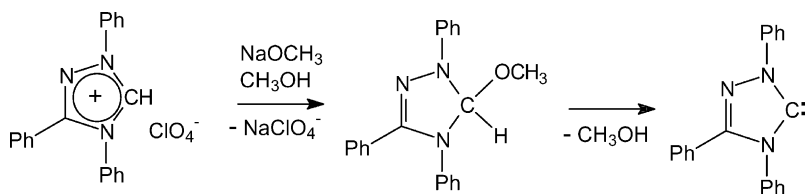
[4,5] and as precursors of N-heterocyclic carbenes [6,7]. In contrast to the other azolium cations, from which the carbenes were formed by deprotonation in basic environment, the 1,2,4-triazolium cation yielded carbene by elimination of methanol from intermediate 5-methoxytriazole as shown in Scheme 1 [6,7].

Mass spectrometric study of carbenes, including N-heterocyclic carbenes, has been extensively carried out by the electron ionization method [8]. The carbenic radical cation (odd-electron ion) has been obtained by dissociation of respective ionized parent compounds. For example, dihydroxycarbene was formed from molecular ion of oxalic acid or dihydroxyfumaric acid [9], diaminocarbene was obtained from

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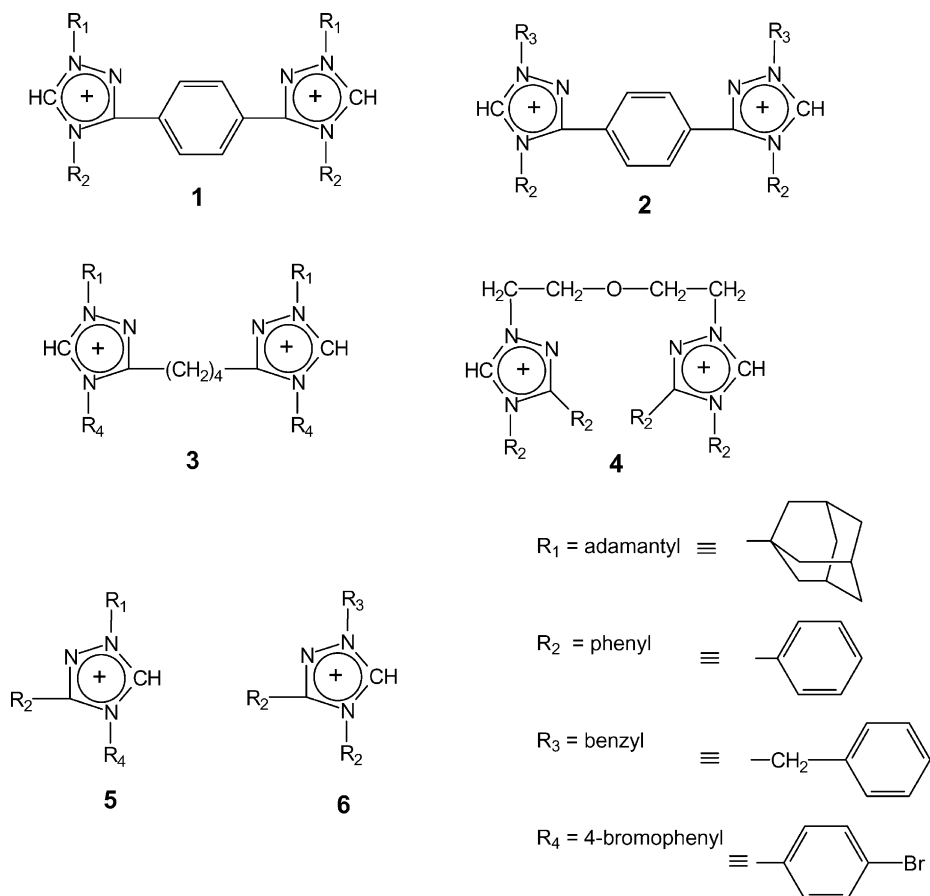
E-mail address: franski@main.amu.edu.pl (R. Frański).



Scheme 1. Formation of carbene from 1,2,4-triazolium salt precursor.

aminoguanidine [10], *N*-hydropyridinium carbene (N-heterocyclic carbene) was formed from 2-picolinic acid [11,12]. The gas-phase isomerization of the obtained carbene radical cation usually requires passing a high energy barrier [8]. Neutralization–reionization mass spectrometry has been intensively used for the differentiation of carbene ions from respective

isomeric ions [13–20], however, isomerization can proceed in this experiment [21]. Interesting results were obtained by performing ion–molecule reactions between small ionized carbene and different molecules [22], or between N-heterocyclic carbenic ions and dimethyl disulfide [23]. The protonated C-halogeno-1,2,4-triazoles also yielded carbenic ion



Scheme 2. Triazolium cations studied.

by collision-activated dehalogenation, provided that oxygen was used as collision gas [24].

In this work the so-called soft ionization techniques, namely liquid secondary ion mass spectrometry (LSIMS) and electrospray ionization (ESI), have been applied for mass spectrometric study of 1,2,4-triazolium salts and N-heterocyclic carbenes derived

from them. The even-electron carbene ions are formed from triazolium salts used under the ionization conditions applied. The chemistry of N-heterocyclic carbenes has been widely studied [6,7], therefore, it is worth learning how these compounds can be analyzed by using mass spectrometric techniques, namely ESI and LSIMS, and how even-electron carbene ions

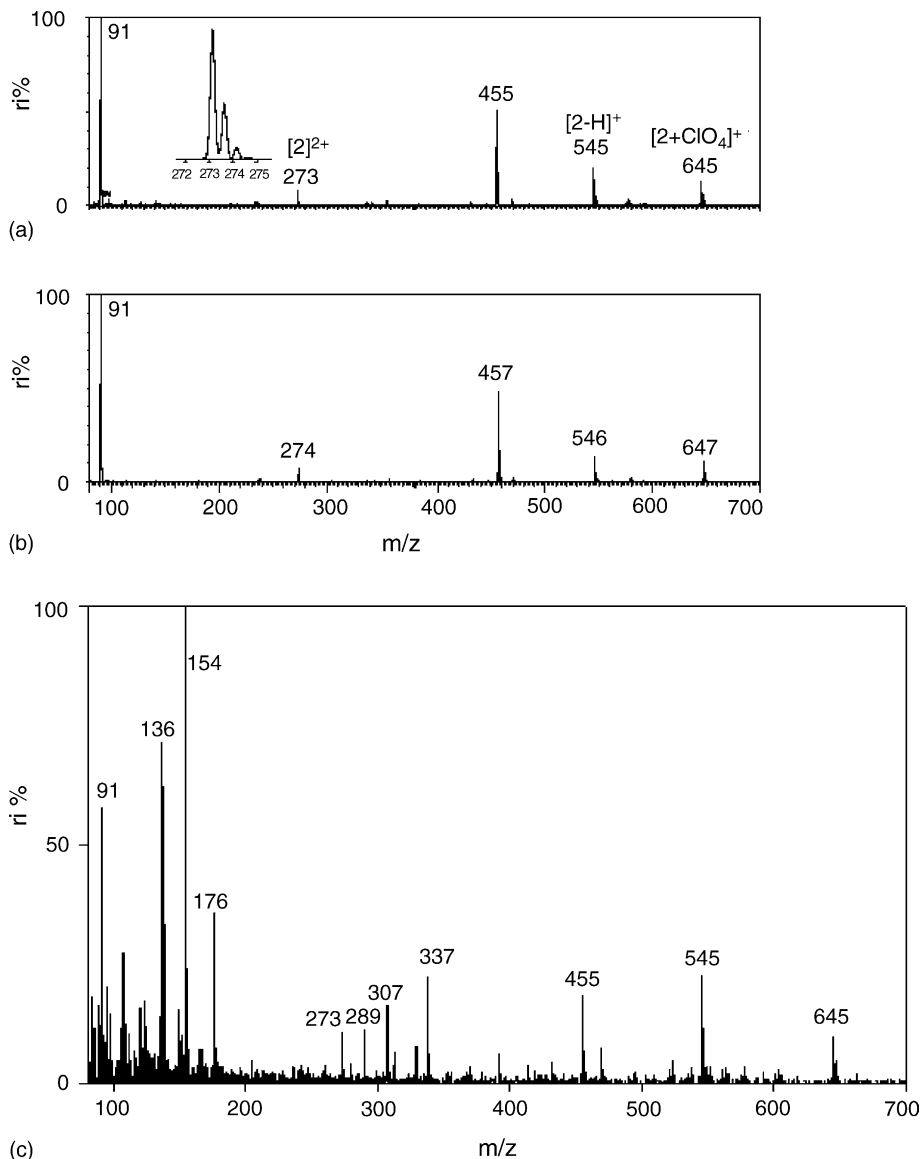


Fig. 1. The ESI mass spectrum of perchlorate (2) recorded by using CH₃OH (a); by using CH₃OD (b); LSI mass spectrum of perchlorate (2) (c).

behave in the gas phase. The compounds studied are perchlorates of triazolium cations shown in Scheme 2.

2. Experimental

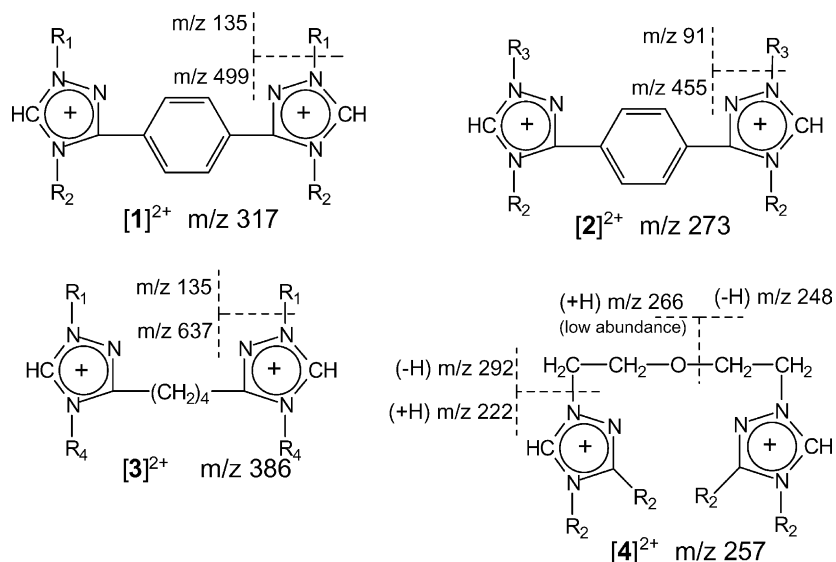
The synthesis of the compounds studied was performed as described elsewhere [25–27]. The two-stage procedure consisting in the ring transformation of the appropriate 1,2,4-oxadiazole with amines and the subsequent quaternization of triazole formed with adamantyl bromide and/or benzyl chloride as alkylating reagents, was applied. Compound **4** was obtained from 3,4-diphenyl-1,2,4-triazole and dichloroethyl ether upon heating in dimethylformamide.

The LSI mass spectra were recorded on an AMD 604 double sector mass spectrometer of reversed B/E geometry (AMD Inteca, Germany). The primary ion beam was supplied by a CsI gun (12 keV, Cs⁺). The secondary ion beam was accelerated to 8 kV. The 3-nitrobenzyl alcohol was used as matrix. The B/E-linked scan mass spectra of metastable ions were recorded on the same instrument.

The ESI mass spectra were recorded on a Waters/Micromass (Manchester, UK) ZQ mass spectrometer

equipped with a Harvard Apparatus syringe pump. The sample solution were prepared in methanol (Aldrich). The samples were infused into the ESI source using a Harvard pump at a flow rate of 40 $\mu\text{L min}^{-1}$. The ESI source potentials were 3 kV on capillary, 0.5 kV on lens, 4 V on extractor, and 30 V on cone. The source and desolvation temperatures were 120 and 300 °C, respectively. Nitrogen was used as nebulizing and desolvation gas at flow rates of 100 and 300 L h^{-1} , respectively.

The ESI CID mass selected experiments for double charged triazolium cation were performed on API 365 PE SCIEX triple quadrupole mass spectrometer (Applied Biosystems, Canada). The sample solution (methanol) were infused into the ESI source using a Harvard pump at a flow rate of 10 $\mu\text{L min}^{-1}$. Source parameters were: capillary voltage 4 kV, nebulizer gas 12, curtain gas 8 (arbitrary units, N₂ in both cases). The entrance ion optics voltages were optimized for maximum production and transmission of the ions of interest. The pressure of the collision gas (nitrogen) has been set at 3 (arbitrary units, approximately 3×10^{-3} mbar). Collision cell parameters were: entrance potential 10 V, exit potential 15 V. Collision energy (CE) has been adjusted manually in the range



Scheme 3. The fragmentation pathway of doubly charged **1–4** cations.

between 10 and 40 eV to achieve the best results. The increase in CE did not affect the fragmentation pattern observed, only the relative ion abundances have been changed.

3. Results and discussion

The ESI and LSI mass spectra of perchlorate (**2**) are shown in Fig. 1 as representative examples. Separation of isotope peaks by half units for double charged ions is observed as shown in Fig. 1a. The ESI mass spectrum recorded by using CH₃OD is shown in Fig. 1b. Its comparison with the spectrum recorded by using CH₃OH (and with LSI mass spectrum (Fig. 1c) clearly indicates that two hydrogens, namely those at C5 positions of triazole rings, have acid properties and thus they can be exchanged into deuterium. Analogous results proving the H/D exchange were obtained for imidazolium carbene precursor salts [28]. In the LSI mass spectrum the matrix ions (m/z 136, 154, 289, 307) are also observed. In both ESI and LSI mass spectrum the fragment ions formed due to the so-called in source fragmentation are observed. The mass spectrometric decomposition of these ions are discussed further in the text on the basis of mass selected experiments.

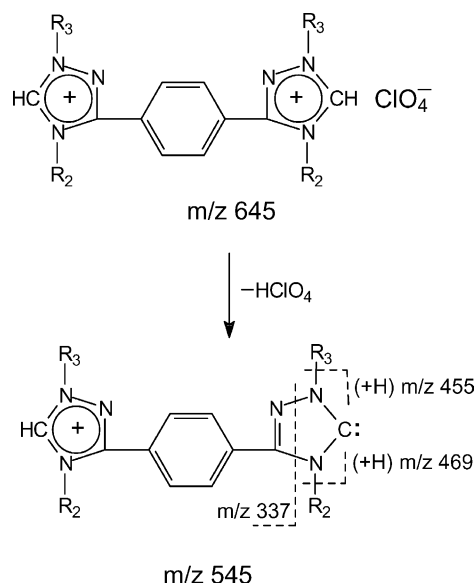
Deprotonation of [2]²⁺ (m/z 273) leads to the singly charged [2-H]⁺ ion (m/z 545). For deuterium derivatives the respective mass shift are observed (Fig. 1). However, on the ESI CID mass spectra of mass selected double charged triazolium cations (**1–4**), instead of the proton loss, the elimination of N1 substituent by a simple heterolytic bond cleavage for **1–3** and cleavage of oxyethylene bridge accompanied by hydrogen transfer for **4** proceeds. The observed fragmentation patterns are shown in Scheme 3. In general, the CID decomposition of these cations can be regarded as a charge separation reaction [29,30].

It was found that deprotonated **1–4** cations are formed from ions containing perchlorate by loss of HClO₄ molecule as evidenced by LSI B/E mass spectrum of [2 + ClO₄]⁺ ion (m/z 645) shown in Fig. 2a. It is clear that the [2-H]⁺ ion formed (m/z 545) is

carbene. Its further decomposition consists in the loss of mass 90 (fragment ion of m/z 455), 208 (fragment ion of m/z 337), and 76 (fragment ion of m/z 469, although this is a minor process) as result from its B/E mass spectrum (Fig. 2b).

The formation and decomposition of carbene occur through the pathway shown in Scheme 4. Formation of fragment ion of m/z 337 confirms that we really deal with carbene since this process requires the cleavage of N1–N2 bond. It was already found that the cleavage of N–N bond, situated at α position to the carbene center, occurs spontaneously [31]. Note that the breaking of triazole ring does not occur in the absence of carbene center (Scheme 3).

The loss of N1 and N4 substituents (m/z 455) occurs with hydrogen transfer from the eliminated neutral fragment to the fragment ion formed. This is also in contrast to the triazolium cations **1–3**, for which hydrogen transfer is not observed in the case of N1 substituent elimination, and loss of N4 substituent is not observed at all (Scheme 3). It seems to be reasonable that hydrogens are transferred to the reactive carbene center. Analogous results were obtained for **1** and **3**,



Scheme 4. Formation and decomposition of 1,2,4-triazolium carbene.

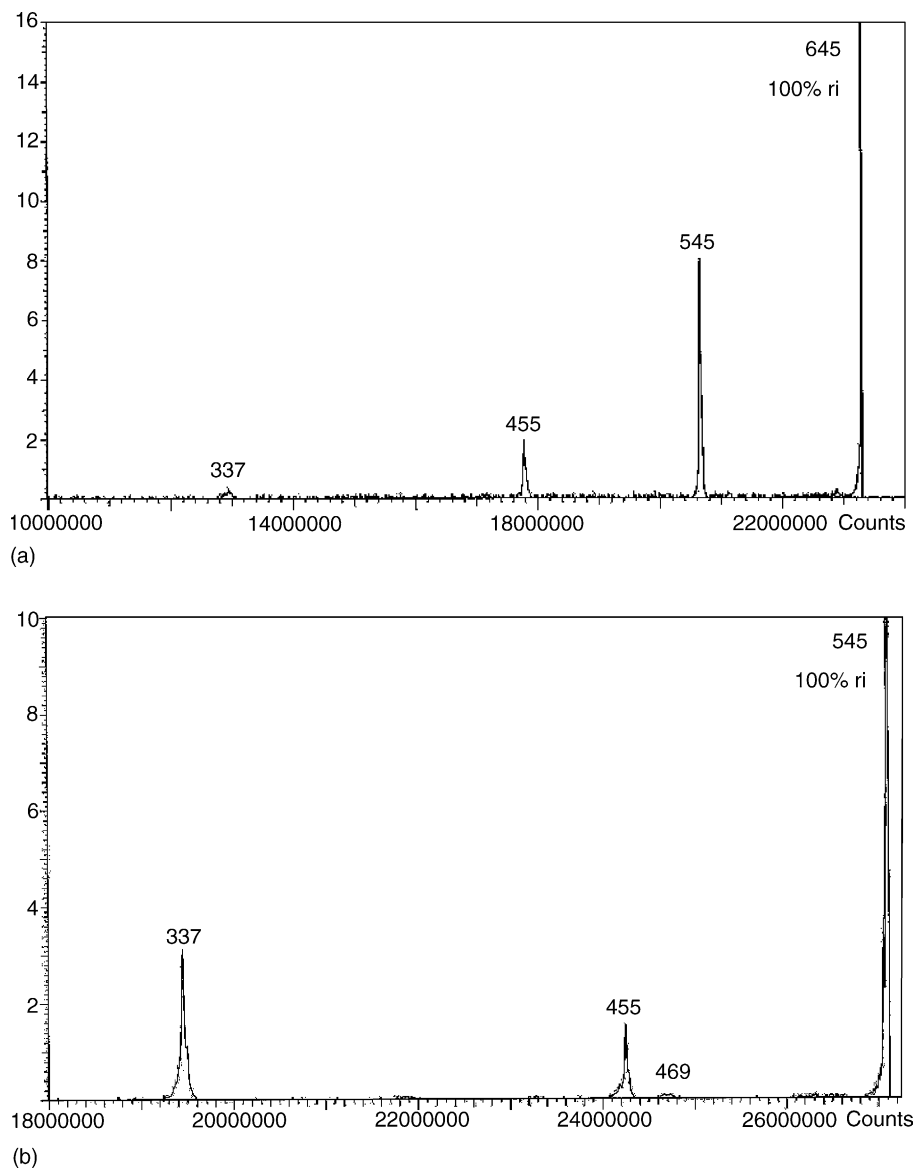


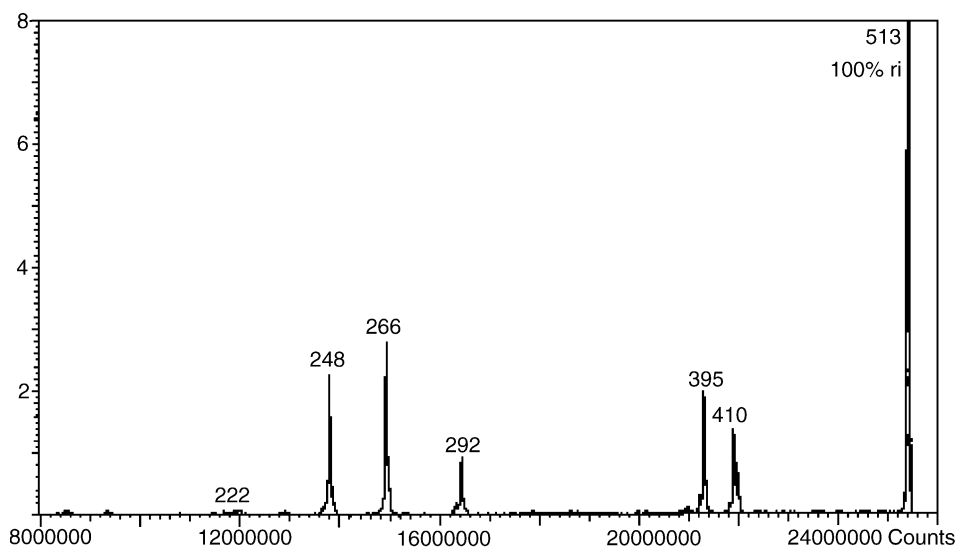
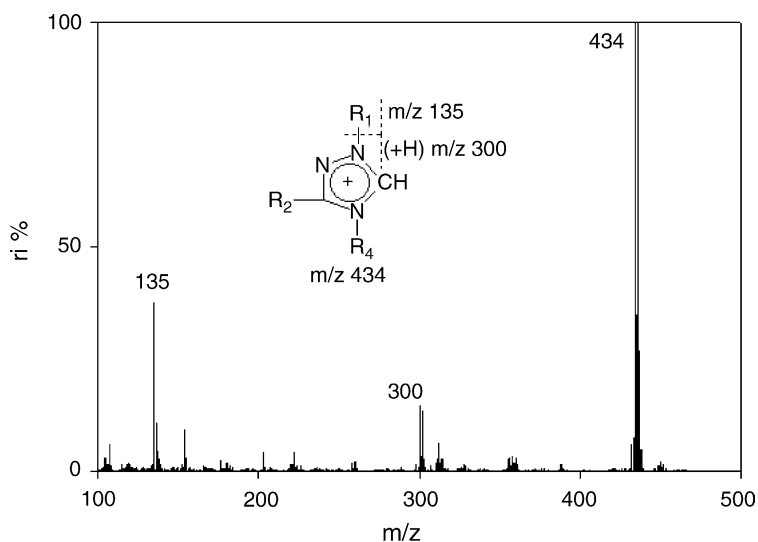
Fig. 2. The B/E mass spectrum of $[2 + \text{ClO}_4]^+$ ion (a) and $[2 - \text{H}]^+$ ion (b).

although the peaks of fragment ions formed by loss of N1 and N4 substituents were characterized by different relative abundances. For **3** the loss of bromine atom was also observed.

In the case of carbene derived from **4**, the cleavage of N1–N2 bond occurs (fragment ion of m/z 410) and cleavage of oxyethylene bridge proceed analogously

as for $[\mathbf{4}]^{2+}$ ion (Scheme 3) as evidenced by B/E mass spectrum of $[\mathbf{4} - \text{H}]^+$ ion shown in Fig. 3. There is also the fragment ion of m/z 395 whose formation is difficult to rationalize.

For single charged triazolium cations **5** and **6** the observation of carbene was not possible since this compound could not be charged. Their decomposition

Fig. 3. The B/E mass spectrum of $[4-H]^+$ ion.Fig. 4. The LSI mass spectrum of **5** and fragmentation pattern observed (the matrix ions are characterized by very low abundances).

consist in the formation of the ion corresponding to the N1 substituent (R_1^+ for **5** and R_3^+ for **6**) as was confirmed by ESI and LSI mass spectra (fragmentation “in source”) and B/E mass spectra (metastable decays). In the case of **5** the loss of N1 substituent also occurs with hydrogen transfer as shown in Fig. 4.

4. Conclusions

Under ESI and LSI mass spectrometric conditions the N-heterocyclic carbenes are formed from $[M + ClO_4]^+$ ions, where M corresponds to the 1,2,4-triazolium dicationic system, by loss of $HClO_4$ molecule. The loss of proton from $[M]^{2+}$ ions was

not observed. Mass spectrometric decomposition of the carbene ions occurs through the breaking of triazolium ring and loss bulky substituents from N1 and N4 atoms via hydrogen transfer to the C5 carbene center. This is an evident influence of the reactive carbene atom since for $[M]^{2+}$ carbene precursor ions (**1–3**) only the loss of N1 substituent occurred as a simple heterolytic bond cleavage.

References

- [1] H. Olivier-Bourbigou, L. Magna, *J. Mol. Catal. A: Chemical* 182/183 (2002) 419.
- [2] B.B. Vestergaard, N.J. Bjerrum, I. Petrushina, H.A. Hjuler, R.W. Berg, M. Begtrup, *J. Electrochem. Soc.* 140 (1993) 3108.
- [3] D. Enders, U. Kallfass, *Angew. Chem. Int. Ed. Engl.* 41 (2002) 1743.
- [4] D. Enders, H. Gielen, J. Runsink, K. Breuer, S. Brode, K. Bochn, *Eur. J. Inorg. Chem.* (1998) 913.
- [5] G. Bertrand, E. Díez-Barra, J. Fernández-Baeza, H. Gornitzka, A. Moreno, A. Otero, R.I. Rodríguez-Curiel, J. Tejada, *Eur. J. Inorg. Chem.* (1999) 1965.
- [6] W.A. Herrmann, C. Köcher, *Angew. Chem. Int. Ed. Engl.* 36 (1997) 2162.
- [7] D. Enders, K. Brauer, G. Raabe, J. Runsink, J.H. Teles, J.P. Melder, K. Ebel, S. Brode, *Angew. Chem. Int. Ed. Engl.* 34 (1995) 1021.
- [8] R. Flammang, M.T. Nguyen, G. Bouchoux, P. Gerbaux, *Int. J. Mass Spectrom.* 202 (2000) A8.
- [9] P.C. Burgers, G.A. McGibbon, J.K. Terlouw, *Chem. Phys. Lett.* 224 (1994) 539.
- [10] G.A. McGibbon, C.A. Kingsmill, J.K. Terlouw, *Chem. Phys. Lett.* 222 (1994) 129.
- [11] D. Lavorato, J.K. Terlouw, T.K. Dargel, W. Koch, G.A. McGibbon, H. Schwarz, *J. Am. Chem. Soc.* 118 (1996) 11898.
- [12] D. Lavorato, J.K. Terlouw, G.A. McGibbon, T.K. Dargel, W. Koch, H. Schwarz, *Int. J. Mass Spectrom. Ion Processes* 179/180 (1998) 7.
- [13] R. Feng, C. Wesdemiotis, F.W. McLafferty, *J. Am. Chem. Soc.* 109 (1987) 6521.
- [14] C. Wesdemiotis, F.W. McLafferty, *J. Am. Chem. Soc.* 109 (1987) 4760.
- [15] C. Wesdemiotis, B. Leyh, A. Fura, F.W. McLafferty, *J. Am. Chem. Soc.* 112 (1990) 8655.
- [16] J. Polce, C. Wesdemiotis, *J. Am. Chem. Soc.* 112 (1990) 8655.
- [17] M.T. Nguyen, T.L. Nguyen, H.Y. Le, *J. Phys. Chem. A* 103 (1999) 5758.
- [18] G.A. McGibbon, P.C. Burgers, J.K. Terlouw, *Int. J. Mass Spectrom. Ion Processes* 136 (1994) 191.
- [19] T.K. Dargel, W. Koch, D.J. Lavorato, G.A. McGibbon, J.K. Terlouw, H. Schwarz, *Int. J. Mass Spectrom. Ion Processes* 175/186/187 (1999) 925.
- [20] G.A. McGibbon, J. Hrusak, D.J. Lavorato, H. Schwarz, J.K. Terlouw, *Chem. Eur. J.* 3 (1997) 232.
- [21] C. Aubry, M.J. Polce, J.L. Holmes, P.M. Mayer, L. Radom, *J. Am. Chem. Soc.* 119 (1997) 9039.
- [22] J. Chamote-Rooke, P. Morgues, G. van der Rest, H.E. Audier, *Int. J. Mass Spectrom.* 226 (2003) 249.
- [23] P. Gerbaux P, M. Barbieux-Flamman, Y. Van Haverbeke, R. Flamman, *Rapid Commun. Mass Spectrom.* 13 (1999) 1707.
- [24] R. Flammang, M. Barbieux-Flammang, H.T. Le, M.T. Nguyen, J. Barthelot, J. Tortajada, *Int. J. Mass Spectrom.* 199 (2000) 221.
- [25] N.I. Korotkikh, G.F. Rayenko, O.P. Shvaika, *Rep. Ukr. Acad. Sci.* 2 (2000) 135.
- [26] N.I. Korotkikh, G.F. Rayenko, A.V. Kiselyov, A.V. Knishevitsky, O.P. Shvaika, A.H. Cowley, J.N. Jones, C.L.B. Macdonald, *Synthesis and Modification of Heterocycles*, Iridium-Press, Moscow, 2002 (English).
- [27] N.I. Korotkikh, A.V. Kiselyov, G.F. Rayenko, N.M. Oliynik, O.P. Shvaika, *Rep. Ukr. Acad. Sci.* 6 (2003).
- [28] E. Alcalde, N. Mesquida, M. Vilaseca, *Rapid Commun. Mass Spectrom.* 14 (2000) 1443.
- [29] S. Hsieh, J.H.D. Eland, *J. Mass Spectrom.* 31 (1996) 1054.
- [30] Z. Szilágyi, L. Drahos, K. Vékey, *J. Mass Spectrom.* 32 (1997) 689.
- [31] D.J. Pasto, J.P. Freeman, *J. Am. Chem. Soc.* 107 (1985) 4090.