

Characterization of Ionized Heterocyclic Carbenes by Ion-Molecule Reactions

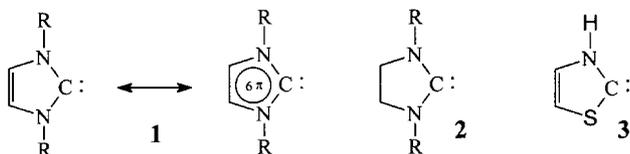
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1,2-Hydrogen shift isomers of ionized pyridine, thiazole and imidazole are readily characterized by the study of their associative ion-molecule reactions with dimethyl disulfide in the quadrupole collision cell of a new hybrid sector-quadrupole-sector mass spectrometer. Efficient trapping reactions of $\text{CH}_3\text{S}^\cdot$ radicals are indeed observed and the actual structure of the adduct $[\text{M} + \text{CH}_3\text{S}]^+$ ions is clearly indicated by their high-energy collisional activation mass spectra. These trapping reactions are not observed for the 'conventional' pyridine, thiazole and imidazole molecular ions, which only react by charge exchange producing m/z 94, $[\text{CH}_3\text{SSCH}_3]^{+\cdot}$, ions. Copyright © 1999 John Wiley & Sons, Ltd.

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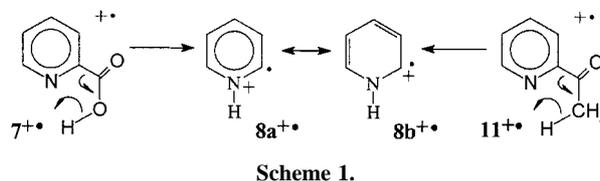
The chemistry of heterocyclic carbenes witnessed a revival in 1991 with the isolation and structural characterization of crystalline compound **1** ($\text{R} = 1$ -adamantyl).¹ Such carbenes are now readily accessible and show rich reaction chemistry, as ligands in organometallic catalysts for example.² Theoretical calculations have confirmed that such carbenes possess aromatic stabilization.³ However, these molecules have stable nonaromatic counterparts such as compound **2** ($\text{R} = t$ -butyl).⁴ The successful isolation of carbene **2** has been ascribed to kinetic reasons (in contrast to **1**) and is thus critically dependent on the bulk of the R substituent.⁴



As far as the unsubstituted parent compounds are concerned, the absence of steric hindrance rules out kinetic stabilization and so prevents such species being isolable under normal conditions. Matrix-isolation techniques have proved to be very efficient for detecting such molecules.⁵ Thiazol-2-ylidene (**3**) was isolated in a matrix following photochemical-induced extrusion of CO_2 from thiazol-2-carboxylic acid (**4**).⁶ Neutralization-reionization mass spectrometry (NRMS) is an alternative powerful technique for studying molecules that are sensitive to intermolecular isomerization, but relatively stable toward unimolecular rearrangement as the experiments are performed on solitary gaseous species.⁷ Imidazol-2-ylidene (**1**, $\text{R} = \text{H}$) and thiazol-2-ylidene (**3**⁺) radical cations were generated by dissociative ionization of imidazole-2-carboxaldehyde (**5**) and acetyl-2-thiazole (**6**), respectively. Both ions were reduced in the NRMS experiments and the gas-phase stability of the corresponding neutral counterparts was established.^{8,9}

The dissociative ionization of 2-picolinic acid (**7**) leads to

the generation of pyridine-2-ylid radical cations (**8**⁺), the so-called Hammick intermediate.¹⁰ These ions were characterized by collisional activation (CA) and were differentiated from the molecular ions of pyridine (**9**) on the basis of the m/z 28: m/z 26 peak branching ratio. Actually, isomer **8**⁺ is characterized by a ratio of 0.86, whereas fewer HCNH^+ ions (m/z 28) are generated from ionized pyridine (**9**⁺, ratio = 0.41).¹⁰ The neutral carbene was generated by one-electron reduction of the radical cations in an NRMS experiment.



The generation and the structural characterization of the whole set of the hydrogen shift isomers of ionized pyridine has very recently been achieved by collisional activation.^{11,12} It was shown that, based on labelling experiments, kinetic energy release analyses and collisional activation studies, four isomers are clearly distinguishable. Of particular importance were the minor but structure-indicative differences in the CA mass spectra, the most critical of these being again the m/z 28: m/z 26 ratio and the doubly charged ion intensities.¹²

We report here successful attempts for the characterization of ionized heterocyclic carbenes by performing associative ion-molecule reactions in a radio frequency (rf)-only quadrupolar collision cell inserted within electric and magnetic sectors. The radical cations of azacyclohexadien-2-ylidene (**8**⁺) and pyridine were first selected as the target ions. Some experiments on ionized *N*-methyl azacyclohexadien-2-ylidene (**10**⁺), the carbenic isomer of picolines, have also been performed. The associative bimolecular chemistry of the molecular ions of two 5-membered heterocyclic carbenes, imidazol-2-ylidene (**1**, $\text{R} = \text{H}$) and thiazol-2-ylidene (**3**) radical cations, was also investigated.

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EXPERIMENTAL

The spectra were recorded on a large scale tandem mass spectrometer (Micromass AutoSpec 6F, Manchester, UK) of $E_1B_1^{\text{C}}E_2q^{\text{C}}E_3B_2E_4$ geometry (E stands for electric sector, B for magnetic sector, C for the collision cells used in the present work and q for a rf-only quadrupole collision cell). General conditions of experiments are the same as presented in previous papers.^{13–15} In this hybrid sector-quadrupole-sector configuration, the spectrometer allows the study of associative ion-molecule reactions at near thermal translational energies and the consecutive collisional activation of the reaccelerated (8 keV) product ions.¹⁶ Briefly, beams of mass-selected ions (with the first three sectors $E_1B_1E_2$) were decelerated to ca. 5 eV and focused into the quadrupole collision cell pressurized with the reagent gas (10^{-3} Torr estimated pressure). The reaction products were then reaccelerated to 8 keV and separated by scanning the field of the second magnet (B_2). The CA spectrum of a specific ion-molecule product can also be recorded by a linked scanning of $E_3B_2E_4$ after collisional activation in the cell located in front of E_3 .

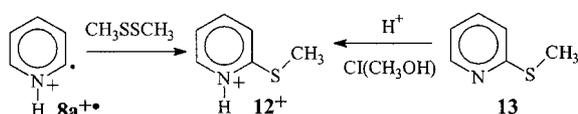
All the samples used in this work were commercially available (Resco Trade-Aldrich) except for 2-methylthiopyridine 17a (**13**) and 2-acetylthiopyridine 17b (**21**) which were synthesized following literature indications.

RESULTS AND DISCUSSION

Pyridine (9^+) and pyridin-2-ylid (8^+) radical cations

As reported earlier, 8^+ radical cations are readily generated following dissociative ionization (loss of CO_2) of 2-picolinic acid¹⁰ (**7**) or dissociative ionization (loss of ketene) of 2-acetylpyridine (**11**) (Scheme 1). The mesomeric structure $8a^{+\bullet}$ of these ions is clearly distonic.¹⁸ Dimethyl disulfide (CH_3SSCH_3 , DMDS) is a very useful neutral reagent to probe the distonic character of radical ions.¹⁹ In contrast to conventional radical cations, which usually undergo fast charge exchange with DMDS, distonic radical cations abstract $\text{CH}_3\text{S}^\bullet$ from DMDS.¹⁹

The 8^+ radical cations react with DMDS in the quadrupole collision cell by abstraction of $\text{CH}_3\text{S}^\bullet$ (m/z 126, 75%) and by charge exchange (m/z 94, 25%) (Scheme 2, Fig. 1(a)). The signal at m/z 52 arises from unimolecular dissociation (loss of CHN) of the mass-selected metastable ions. As expected, the reaction between the molecular ions of pyridine 9^+ and DMDS is different, the charge exchange reaction being the dominant process (99.5%). In order to obtain more information about the actual structure of the m/z 126 ions, their CA mass spectrum at high kinetic energy (8 keV) was recorded (Fig. 1(b)). This spectrum was found to be very similar to the CA spectrum of an authentic sample of protonated 2-methylthiopyridine (12^+) generated by chemical ionization of 2-methylthiopyridine (**13**) using methanol as the reagent gas. The main collisionally induced fragmentations lead to the losses of $\text{CH}_3\text{S}^\bullet$ (m/z 79) and CH_3^\bullet (m/z 111).



Scheme 2.

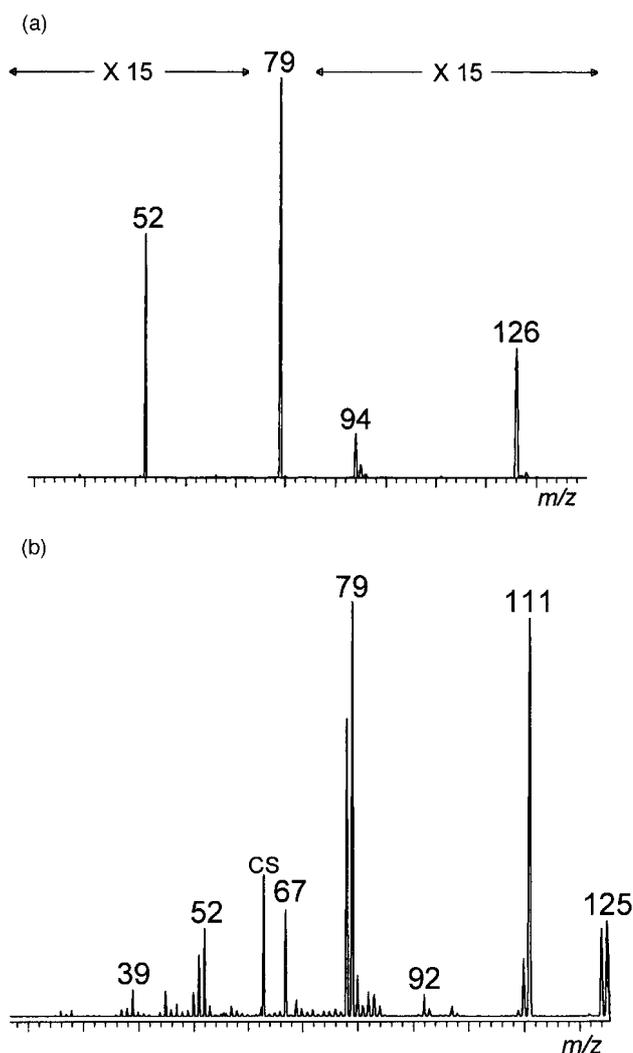


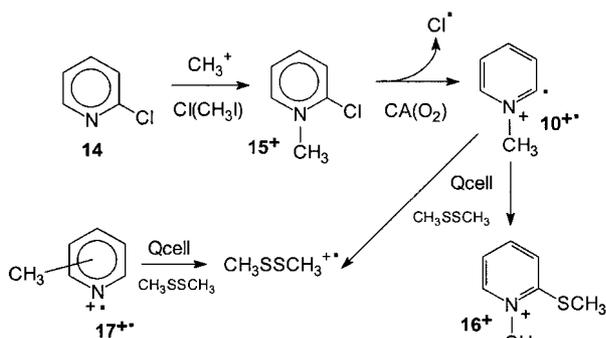
Figure 1. Reaction between 8^+ (m/z 79) and DMDS in the Qcell: (a) mass spectrum of the ion-molecule reaction products and (b) CA(O_2) mass spectrum of the generated m/z 126 cations.

The identification of the 12^+ ions by these CA experiments unambiguously confirms that the m/z 79 ions generated by dissociative ionization of 2-picolinic acid or 2-acetylpyridine have the carbenic structure $8a^{+\bullet}$.

Lavorato *et al.* have performed theoretical calculations on this system¹² and, from their results, the enthalpy of formation of 8^+ can be estimated to be 995 kJ/mol, while the ionization energy (IE) of **8** amounts to ca. 6.8 eV.²⁰ Based on the reported heat of formation of protonated 2-methylthiopyridine,²⁰ it is therefore possible to estimate the enthalpy of the reaction $8^+ + \text{DMDS} \rightarrow 12^+ + \text{CH}_3\text{S}^\bullet$ which reveals an exothermicity of 110 kJ/mol. Moreover, the charge exchange reaction, $8^+ + \text{DMDS} \rightarrow 8 + \text{DMDS}^{\bullet+}$, is found to be endothermic by 115 kJ/mol [IE (DMDS)^{20b} - IE (**8**)]. This figure contrasts with the exothermicity of the charge exchange reaction in the case of the pyridine molecular ions, 9^+ , 120 kJ/mol.²⁰ All these theoretical figures are thus in good accord with the experimental results.

Picoline (17^+) and N-methylpyridin-2-ylid (10^+) radical cations

The chemical ionization-collisional activation (CI-CA)



Scheme 3.

sequence applied to generate the radical cations of azacyclohexadien-3(4)-ylidene^{11,12} was adapted to produce $10^{+\bullet}$ (Scheme 3). Chemical ionization of 2-chloropyridine (**14**) using methyl iodide as the Cl gas leads to nitrogen methylation.²¹ The structure of the cations produced (15^+) was probed by collisional activation. These ions are then mass-selected and subjected to collision with O_2 . The yield of the dechlorination reaction is highly dependent on the nature of the collision gas. Oxygen and nitric oxide are the best targets to perform this reaction; the yield decreases dramatically if helium is used as the target. The peculiar role of oxygen in high-energy collisional activation has been stressed on several occasions.²² Under these conditions, the collisionally excited ions intensely expel a chlorine atom and the resulting radical cations ($10^{+\bullet}$) are focused into the quadrupolar collision cell pressurized with DMDS. The interaction of the $10^{+\bullet}$ ions with dimethyl disulfide leads (Fig. 2), as expected, to the production of *N*-methyl-2-thiomethylpyridinium ions (16^+ , m/z 140) by CH_3S^{\bullet} abstraction, besides charge exchange (m/z 94). Again, signals observed at m/z 65, 66 and 67 arise from fragmentations of the selected m/z 93 ions.

Although direct identification of the actual structure of the 16^+ cations by collisional activation was not feasible for sensitivity reasons, the fact that ionized 2-, 3- and 4-picolines ($17^{+\bullet}$) only react with DMDS by charge exchange strongly supports the formation of the ionized carbene $10^{+\bullet}$.

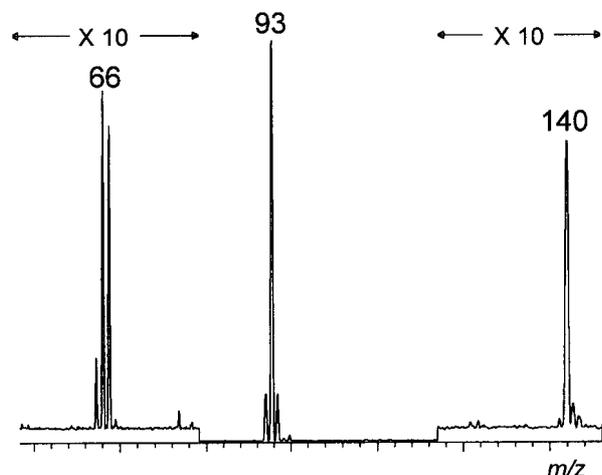


Figure 2. Reaction between $10^{+\bullet}$ (m/z 93) and DMDS in the Qcell: mass spectrum of the ion-molecule reaction products.

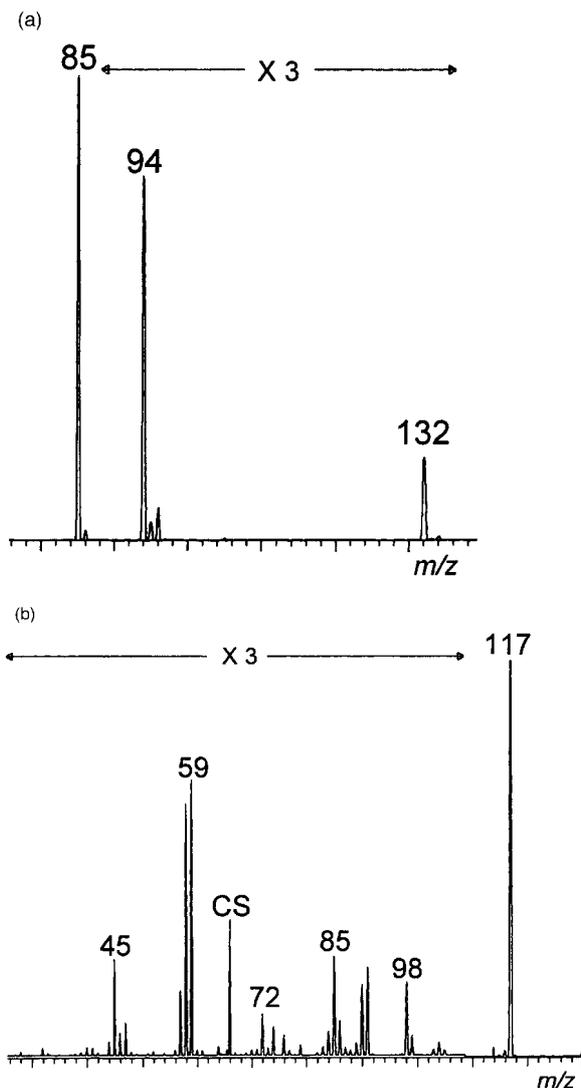
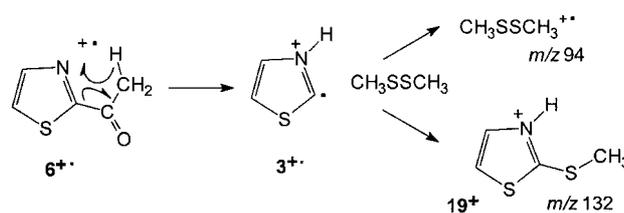


Figure 3. Reaction between $3^{+\bullet}$ (m/z 85) and DMDS in the Qcell: (a) mass spectrum of the ion-molecule reaction products and (b) CA(O_2) mass spectrum of the generated m/z 132 cations.

Thiazole ($18^{+\bullet}$) and thiazol-2-ylidene ($3^{+\bullet}$) radical cations

The loss of ketene ($CH_2=C=O$) from the molecular ions of 2-acetylthiazole (**6**) leads to the production of thiazol-2-ylidene ($3^{+\bullet}$) radical cations. The carbenic structure of the ions formed was established by McGibbon *et al.* by collisional activation experiments.⁹ Actually, collisionally excited $3^{+\bullet}$ radical cations decompose *inter alia* by producing $HNCS^{+\bullet}$ ions (ethyne elimination). The corresponding signal is *not* observed in the CA spectrum of the thiazole radical cations ($18^{+\bullet}$).



Scheme 4.

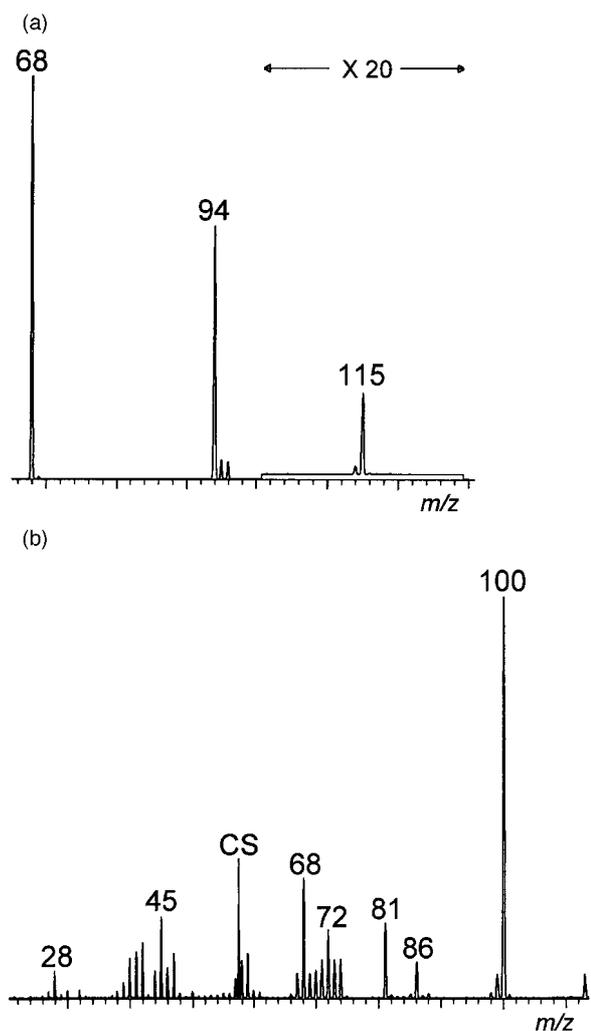


Figure 4. Reaction between 1^{+} (m/z 68) and DMS in the Qcell: (a) mass spectrum of the ion-molecule reaction products and (b) CA(O_2) mass spectrum of the generated m/z 115 cations.

Two ion species are produced in good yields when the 3^{+} ions interact with DMS in the quadrupolar collision cell (Fig. 3(a)). The signal at m/z 132 corresponds to cations generated by CH_3S^{\cdot} abstraction from neutral DMS, while molecular ions of DMS (m/z 94, 84%) are produced by charge exchange (Scheme 4). As expected, 18^{+} radical cations react exclusively with DMS by charge exchange. From the calculations of McGibbon *et al.*, the adiabatic ionization energy of the neutral species 3 was estimated to be about 8.1 eV.⁹ The ionization energy of thiazole is available from the literature (9.08 eV).²⁰ It is not surprising, therefore, that charge exchange is a very efficient process in both cases, given the lower ionization energy of DMS (8.0 eV).^{20b}

The CA mass spectrum of the m/z 132 cations is shown in Fig. 3(b). The loss of CH_3^{\cdot} (m/z 117) constitutes the most intense fragmentation of the collisionally excited ions. The corresponding signal is also very intense in the case of protonated 2-methylthiopyridine (12^{+}). However, while the loss of CH_3S^{\cdot} is the base peak of the CA spectrum of the 12^{+} ions (Fig. 1(b)), the intensity of the corresponding signal in the CA spectrum of 19^{+} (m/z 85) is significantly less intense. This different behavior is not unexpected if calculated formation enthalpies of 8^{+} , 3^{+} are compared (995¹² against 1115⁹ kJ/mol).

Imidazole (20^{+}) and imidazol-2-ylidene (1^{+}) radical cations

Imidazol-2-ylidene radical cations (1^{+}) have been prepared by dissociative ionization of imidazole-2-carboxaldehyde (**5**).⁸ In the present work, the 1^{+} radical ions have however been produced starting from 2-acetyl-imidazole (**21**) which, after ionization, readily expels ketene to generate m/z 68 ions. For the sake of comparison, the CA spectrum of these ions has been compared with the CA spectrum of imidazole molecular ions (20^{+}). In accord with the literature,⁸ both spectra are readily differentiated by the signal corresponding to the extrusion of ethyne (formation of carbodiimide, $H-N=C=N-H$, radical cations), this signal being completely absent in the CA spectrum of 20^{+} .

The 1^{+} radical ions react with neutral DMS by charge exchange (m/z 94) and by CH_3S^{\cdot} abstraction (m/z 115), as shown in Fig. 4(a). The reaction leading to m/z 115 ions is not observed during the interaction between 20^{+} and DMS, products of the charge exchange process being the sole ions detected (EI (**20**) = 8.81 eV²⁰).

The main collisionally induced fragmentation (Fig. 4(b)) of the m/z 115 cations is the loss of the methyl radical (m/z 100) and, besides this decomposition, the most characteristic reaction is the loss of CH_3S^{\cdot} leading back to the precursor carbenic ions.

CONCLUSIONS

Trapping reactions of CH_3S^{\cdot} radicals by ionized heterocyclic carbenes from neutral dimethyl disulfide are of high structural diagnostic value as their 'conventional' heterocyclic isomers only react by charge exchange with the same reagent. Similar studies are in progress in our laboratory to extend this type of experiment to carbene ions or ylid ions derived from 1,2,4-triazoles.^{22c} It is also worthy of note that all the experiments described in this work were performed on a *single* mass spectrometer of sector-quadrupole-sector configuration.

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