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Identifying ylide ions and methyl migrations in the gas phase: the decarbonylation reactions of simple ionized N-heterocycles

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Abstract

The decarbonylation reactions of ionized 2-acetylpyridine, 2-acetylpyrazine, and 2-acetylthiazole have been investigated using the multiple collision technique of neutralization–reionization/collision-induced dissociation mass spectrometry and related techniques. The resultant heterocyclic $C_6H_7N^{\cdot+}$, $C_5H_6N_2^{\cdot+}$, and $C_4H_5NS^{\cdot+}$ ions were identified as 2-methylene-1,2-dihydropyridine, $\mathbf{6}^{\cdot+}$, 2-methylene-1,2-dihydropyrazine, $\mathbf{9}^{\cdot+}$, and 2-methylene-2,3-dihydrothiazole, $\mathbf{12}^{\cdot+}$, respectively. This result refutes proposals in the older literature that the decarbonylation would involve a methyl transfer yielding the 2-methyl species 2-methylpyridine ($\mathbf{2}^{\cdot+}$), 2-methylpyrazine ($\mathbf{8}^{\cdot+}$), and 2-methylthiazole ($\mathbf{11}^{\cdot+}$). Literature proposals for a methyl transfer in the dissociation of ionized dimethyl-2,3-pyridinedicarboxylate and methyl-4-pyridinecarboxylate were also examined, but could not be substantiated either. However, the proposed gas phase synthesis of the N-methylpyridinium ylide, $\mathbf{1}^{\cdot+}$, from ionized methyl-2-pyridinethiocarboxylate did provide evidence for a genuine methyl migration. To reinforce these conclusions, the dissociation characteristics of isomers structurally related to $\mathbf{6}^{\cdot+}$ ($\mathbf{3}^{\cdot+}$– $\mathbf{5}^{\cdot+}$ and $\mathbf{7}^{\cdot+}$), to $\mathbf{9}^{\cdot+}$ ($\mathbf{10}^{\cdot+}$) and to $\mathbf{12}^{\cdot+}$ ($\mathbf{13}^{\cdot+}$– $\mathbf{15}^{\cdot+}$) were also considered. Exploratory quantum chemical calculations (at the B3LYP/6-31G* level of theory) indicate that $\mathbf{6}^{\cdot+}$ and $\mathbf{12}^{\cdot+}$ are among the most stable isomers in the $C_6H_7N^{\cdot+}$ and $C_4H_5NS^{\cdot+}$ systems, lying 24 and 19 kcal/mol lower in energy than $\mathbf{2}^{\cdot+}$ and $\mathbf{11}^{\cdot+}$, respectively. Their neutral counterparts, however, are considerably less stable: **6** is calculated to be 27 kcal/mol higher in energy than **2**. Nevertheless, from neutralization–reionization experiments it follows that the neutral counterparts of the ionized decarbonylation products **6**, **9**, and **12** are stable molecules on the microsecond time scale. Significant 1,3-hydrogen shift barriers hinder the interconversion of both the ions and the neutrals into their 2-methyl substituted counterparts, thus accounting for their stability in the dilute gas phase. (Int J Mass Spectrom 195/196 (2000) 71–83) © 2000 Elsevier Science B.V.

Keywords: Neutralization–reionization mass spectrometry; Density functional calculations; Decarbonylation

1. Introduction

A profusion of mass spectrometric methods is available for the determination of structures and elucidation of reaction pathways for gaseous ions and molecules [1]. Several of these, including tandem sector and Fourier transform ion cyclotron resonance (FTICR) mass spectrometries, have been aimed at characterizing six-membered ring containing N-heterocyclic $C_6H_7N^{\cdot+}$ isomers including the methyl picolines $\mathbf{2}^{\cdot+}$– $\mathbf{4}^{\cdot+}$ [2] and the N- and 2-methylene pyridinium ylides $\mathbf{5}^{\cdot+}$ and $\mathbf{6}^{\cdot+}$ [3–6]. The recognition

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Dedicated to the memory of Professor R.R. Squires.

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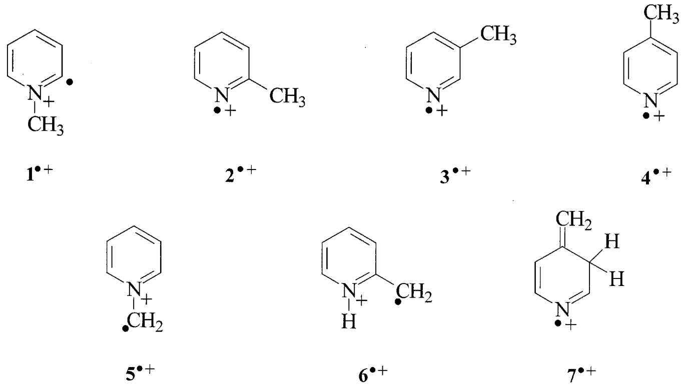

$\mathbf{1}^{\bullet+}$ $\mathbf{2}^{\bullet+}$ $\mathbf{3}^{\bullet+}$ $\mathbf{4}^{\bullet+}$ $\mathbf{5}^{\bullet+}$ $\mathbf{6}^{\bullet+}$ $\mathbf{7}^{\bullet+}$

Diagram 1.

of six structural isomers was not precluded by the limited number of distinguishing features in collision-induced dissociation (CID) [7], charge-stripping (CS), and neutralization–reionization (NR) [8] mass spectrometry experiments [4–6]. However, despite the application of this battery of techniques and even chemometric methods of analysis [4,5], further innovation is still required to demonstrate to what extent the various isomeric ions may be capable of interconversion and to confirm that they have indeed stable (nonisomerizing) neutral counterparts for the less common C_6H_7N molecules. In this context, it should be noted that the radical cation, $C_5H_4NCH_3^{\cdot+}$, $\mathbf{1}^{\cdot+}$, has appeared among several proposals accounting for the dissociation of 2-substituted pyridines by methyl group transfer [9,10]. Furthermore, loss of CO from ionized 2-acetylpyridine has been reported [11,12] but without any structural characterization of the product ion. In light of the attention devoted to the chemistry of other 2-keto pyridines [12] and related 2-carboxylic acid [13] and ester derivatives [14], it seems prudent to probe the $C_6H_7N^{\cdot+}$ (*m/z* 93) ions from 2-acetylpyridine.

There are additional systems immediately pertinent to the study of methyl migrations and structures of N-heterocycles. For example, closely related to the picoline radical cations are ionized methylpyrazine, $\mathbf{8}^{\cdot+}$, and two of its distonic isomers, the 2-methylene pyrazinium ion $\mathbf{9}^{\cdot+}$, and the 5-methylpyrazinium ion $\mathbf{10}^{\cdot+}$. Another consists of the set of isomeric $C_4H_5NS^{\cdot+}$ species including ionized 2-methylthiazole, $\mathbf{11}^{\cdot+}$, the methylene dihydrothiazoles, $\mathbf{12}^{\cdot+}$ and $\mathbf{13}^{\cdot+}$, and the N-methyl and S-methyl ylide ions, $\mathbf{14}^{\cdot+}$ and $\mathbf{15}^{\cdot+}$.

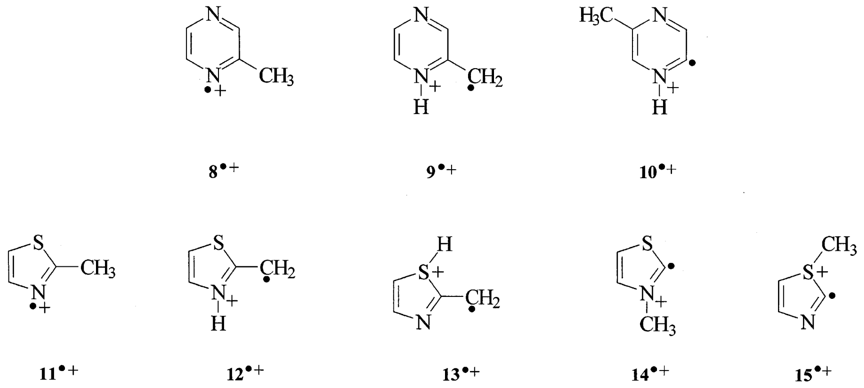

$\mathbf{8}^{\bullet+}$ $\mathbf{9}^{\bullet+}$ $\mathbf{10}^{\bullet+}$ $\mathbf{11}^{\bullet+}$ $\mathbf{12}^{\bullet+}$ $\mathbf{13}^{\bullet+}$ $\mathbf{14}^{\bullet+}$ $\mathbf{15}^{\bullet+}$

Diagram 2.

As a means to obtain additional structural and mechanistic insight on these N-heterocycles, we have employed the multiple collision technique of reionization/collision-induced dissociation (NR/CID) mass spectrometry [15]. The application of NR/CID as a structural assignment tool offers advantages in systems where isomeric ions (and neutrals) are not easily distinguished by the separate application of either CID and/or NR mass spectrometry. This may occur for several reasons: (1) mixtures of ions may be generated from ionized precursor molecules, (2) the isomeric ions (or neutrals) may interconvert either spontaneously or as a result of the collision process prior to fragmenting, (3) the ions may access only a limited number of dissociation channels, which do not result in fragment ions bearing unique mass-to-charge values, or (4) in NR experiments reionized neutral fragments may interfere. The third scenario may often be interrogated by performing tandem mass spectrometry (MS/MS) experiments, and through isotopic labeling experiments, whereas the occurrence of the first two is usually more difficult to identify.

With this in mind, we report here an analysis of CID and NR/CID experiments on the above mentioned systems aided by selected ab initio calculations. Literature proposals involving methyl migration in substituted pyridine, pyrazine [16], and thiazole [17] radical cations have also been re-examined. On one hand, we were not able to find support for an earlier postulate for methyl transfer in the dissociation of dimethyl-2,3-pyridinedicarboxylate but on the other hand found evidence of the missing N-methylpyridinium ylide ion $\mathbf{1}^{\cdot+}$ [10]. The decarbonylation of ionized 2-acetylpyrazine and 2-acetylthiazole appears to proceed analogously to that of the 2-acetylpyridine ion, yielding the 2-methylene radical cation derivatives rather than the 1-methyl or 2-methyl species.

2. Experimental procedure

The tandem mass spectrometric experiments used to generate and characterize the C_6H_7N, $C_5H_6N_2$, and C_4H_5NS ions and neutrals were performed at McMaster University on the VG Analytical ZAB-R. This BE_1E_2 (B = magnet, E = electric sector) instrument and the details of the NR mass spectrum acquisition have been previously described [18], hence only a brief overview is provided here. The ions of interest, e.g. *m/z* 93 in the case of $C_6H_7N^{\cdot+}$, are mass-selected by B and subsequently (in a small gas cell located between B and E_1) subjected to collision with N,N-dimethylaniline. This results in neutralization by fast electron transfer of a fraction of the 10 keV source generated ions. After exiting the cell, the remaining ions are deflected by a positively charged electrode so that only a beam of fast moving neutral species enters a second gas cell. Here reionization takes place by collisions with oxygen molecules. The resulting ions are analyzed by scanning E_1 to produce the conventional NR mass spectrum. If instead the reionized species are selectively transmitted at a fixed E_1 setting, and oxygen gas is introduced in a third cell located between E_1 and E_2, a NR/CID mass spectrum characteristic of the reionized neutrals can be obtained by scanning E_2. Comparative CID experiments are performed analogously but with the deflector electrode switched off. Spectra were recorded with a PC-based data system (Mommers Technologies Inc., Ottawa, Canada).

The precursor molecules methyl-2-pyridinethiocarboxylate [10], bis(ethoxycarbonyl)-pyridinium methylide [19], 2-propylpyrazine [20], and methyl-5-methylpyrazine-2-carboxylate [21] were synthesized according to literature procedures. All other compounds were purchased from commercial sources and used without further purification.

Samples were introduced into the mass spectrometer via an all-glass heated inlet system equipped with a leak valve or a direct insertion-type probe having a glass bore and reservoir. At indicated pressures (monitored by a remote ionization gauge) of typically 10^{-6} Torr, ions were formed by electron ionization (70 eV) at a source temperature of 120 °C. The proton-bound dimer of 2-methylpyridine was produced in a chemical ionization source at a measured pressure of $\sim 6 \times 10^{-5}$ Torr.

The computations were performed with the GAUSSIAN 94 series of programs [22] on workstations at the TU-Berlin and McMaster University. Geometries were optimized using the standard basis set 6-31G* and vibrational frequencies estimated with the popular hybrid density functional method B3LYP [23], employing Becke's empirical three-parameter fit for mixing the Hartree-Fock and density functional exchange terms. All structures had no negative eigenvalues, and the data presented are corrected for zero-point vibrational energy (ZPVE) contributions. The ZPVE were scaled by a factor of 0.9806 [24] for the B3LYP fundamentals. The $\langle S^2 \rangle$ expectation value of the noninteracting Kohn-Sham determinant was in all cases very close to the exact values.

3. Results and discussion

3.1. Generation and characterization of C_6H_7N isomers

As first reported by Ferretti and Flanagan [11a], dissociative electron ionization (EI) of 2-acetylpyridine produces in its normal EI mass spectrum ions at *m/z* 93 by loss of CO. To investigate the structure of the resulting $C_6H_7N^{\cdot+}$ ions, i.e. to differentiate these ions from their isomers, the technique of collision-induced dissociation was employed. Seven cyclic $C_6H_7N^{\cdot+}$ isomers were generated via EI of the appropriate substituted pyridine precursors. The cations $\mathbf{2}^{\cdot+}$– $\mathbf{4}^{\cdot+}$ were realized by simple electron ionization of their neutral counterparts while $\mathbf{1}^{\cdot+}$, $\mathbf{5}^{\cdot+}$, $\mathbf{6}^{\cdot+}$ and $\mathbf{7}^{\cdot+}$ were obtained by dissociative EI of methyl-2-pyridinethiocarboxylate [10], bis(ethoxy-carbonyl) pyridinium methylide [5,25], 2-propylpyridine [5], and 4-pyridylacetic acid, respectively.

The CID mass spectra of the putative ions $\mathbf{1}^{\cdot+}$– $\mathbf{7}^{\cdot+}$ obtained in the third field free region of the three sector magnetic deflection instrument, are presented in Fig. 1. In basic agreement with the study of Flammang and co-workers [5], the spectra of the 2-methylpyridine ion $\mathbf{2}^{\cdot+}$ [Fig. 1(a)] and its methylene isomer $\mathbf{6}^{\cdot+}$ [Fig. 1(b)] are similar but they do exhibit characteristic differences [26]. Perhaps the most structure diagnostic of these is the CH_2 loss peak at *m/z* 79 in the spectrum of the 2-methylene isomer $\mathbf{6}^{\cdot+}$. Furthermore, several fragment ion clusters show differences in their relative abundance: for example the *m/z* 26 ($C_2H_2^{\cdot+}$) : 28 (CH_2N^+) peak intensity ratio is 1.5 for $\mathbf{2}^{\cdot+}$ and 0.8 for $\mathbf{6}^{\cdot+}$. The enhanced *m/z* 28 ($H{-}C{\equiv}N{-}H^+$) intensity is characteristic of a pyridine ring bearing a N–H moiety [15,27]. The more intense charge stripping peak (++) at *m/z* 46.5 in Fig. 1(b) is further revealing of the ylide structure of $\mathbf{6}^{\cdot+}$. The N-methylene ylide ion $\mathbf{5}^{\cdot+}$ [Fig. 1(e)] is characterized by an even lower *m/z* 78 (– CH_3) : 79 (– CH_2) peak intensity ratio, a result of the N–C bond proffered for cleavage. The arguments presented above also account for its fairly high *m/z* 26 : 28 peak intensity ratio, 1.75, and the intense charge stripping peak at *m/z* 46.5.

The remaining isomers of conventional structure, 3- and 4-methylpyridine ($\mathbf{3}^{\cdot+}$ and $\mathbf{4}^{\cdot+}$) exhibit, see Figs. 1(g) and 1(h), only weak doubly charged ion peaks and they are easily distinguished from $\mathbf{2}^{\cdot+}$ on the basis of the reduced *m/z* 78 intensity [2], as is also observed in their normal mass spectra. However, differentiation of $\mathbf{3}^{\cdot+}$ and $\mathbf{4}^{\cdot+}$ on the basis of their CID mass spectra is clearly not possible.

The decarbonylation reaction of the 2-acetylpyridine ion has been proposed to yield ion $\mathbf{1}^{\cdot+}$, via a 1,3 methyl shift to the ring nitrogen [12]. However, the source generated product ions yield a CID mass spectrum which is superimposable upon that of Fig. 1(b), indicating that the ion generated is $\mathbf{6}^{\cdot+}$. Next, the structure of the *m/z* 93 ions generated from metastable 2-acetylpyridine ions was probed. The metastable ion/collision-induced dissociation sequence provides a MI/CID mass spectrum, Fig. 1(c), identical to the CID mass spectrum of the source generated ions, Fig. 1(b), thus indicating that the decarbonylation yields isomerically pure ions $\mathbf{6}^{\cdot+}$. A possible mechanism for the generation of $\mathbf{6}^{\cdot+}$ from ionized 2-acetylpyridine ($\mathbf{I}^{\cdot+}$) is presented in Scheme 1 along with that proposed earlier for its generation from ionized 2-propylpyridine ($\mathbf{II}^{\cdot+}$) [5,12]. In both cases the initial step involves the transfer of a hydrogen radical to the ring nitrogen. For 2-propylpyridine this is followed by C_2H_4 loss via a McLafferty rearrangement whereas 2-acetylpyridine decarbonylates by an ipso [28] type rearrangement.

We further note that the decarbonylation reaction is associated with a large reverse activation energy. Metastable 2-acetylpyridine ions lose CO with a

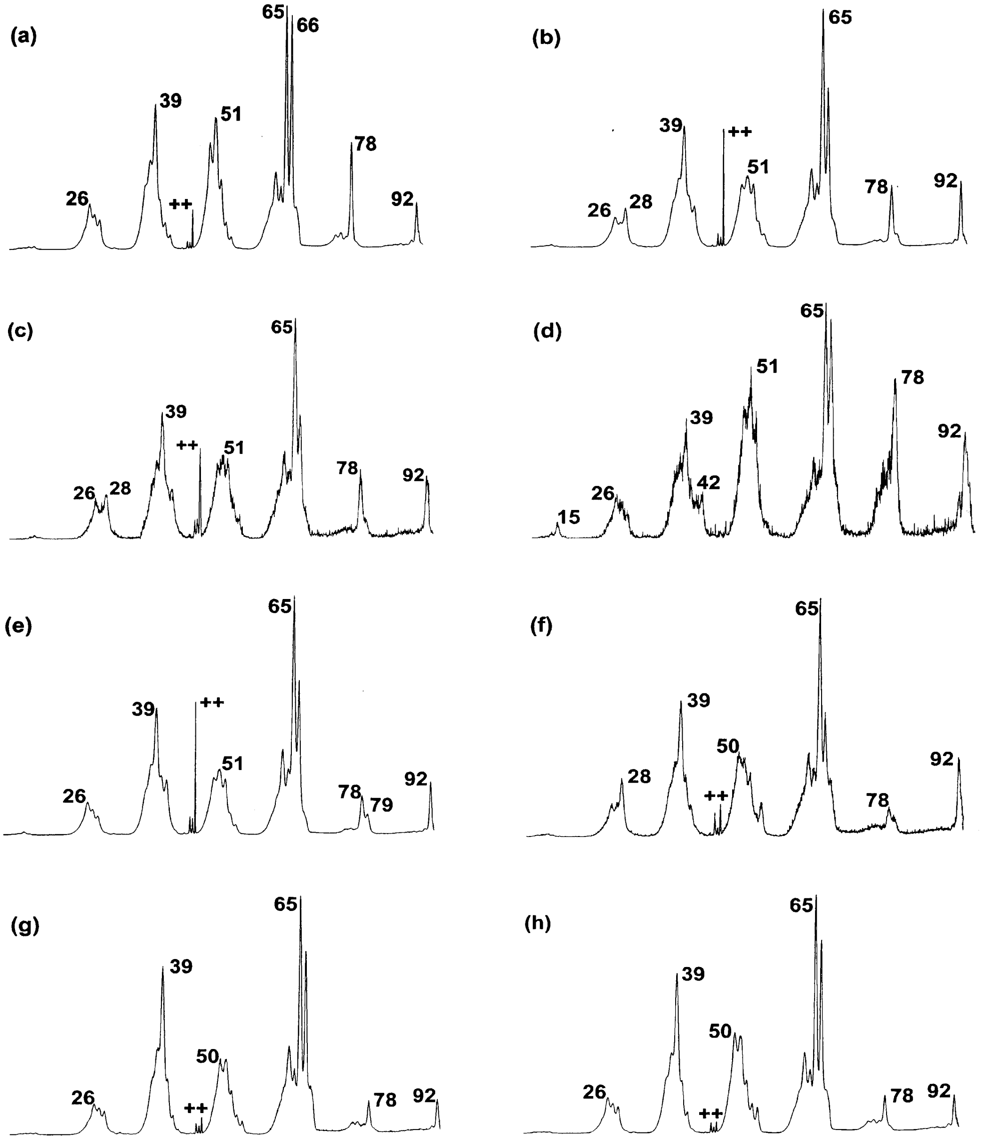
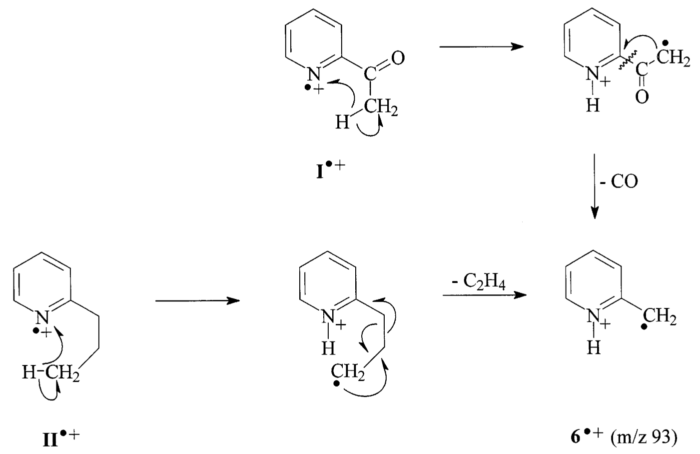


Fig. 1. CID mass spectra (3ffr, 7 keV ions, collision gas O_2) of $C_6H_7N^{\cdot+}$ (*m/z* 93) ions generated from (a) ionized 2-methylpyridine, (b) ionized 2-acetylpyridine or 2-propylpyridine, (c) metastable 2-acetylpyridine ions, (d) metastable methyl-2-pyridinethiocarboxylate ions, (e) ionized bis(ethoxycarbonyl)pyridinium methylide, (f) metastable 4-pyridylacetic acid ions, (g) ionized 3-methylpyridine, and (h) ionized 4-methylpyridine.

kinetic energy release of 890 meV but this process is in competition with the loss of CH_2=C=O (metastable peak intensity ratio 10:1). The loss of ketene yields the α-ylide ion of pyridine and the activation energy for this process is ~26 kcal/mol [15]. A similar value must obtain for the decarbonylation but its calculated minimum energy requirement is 44 kcal/mol lower [29,30] and thus this process is indeed characterized by a high reverse activation energy.

Evidence for a true methyl migration was eventually obtained, thereby validating the (unverified) proposal by Budzikiewicz and co-workers [10] for the

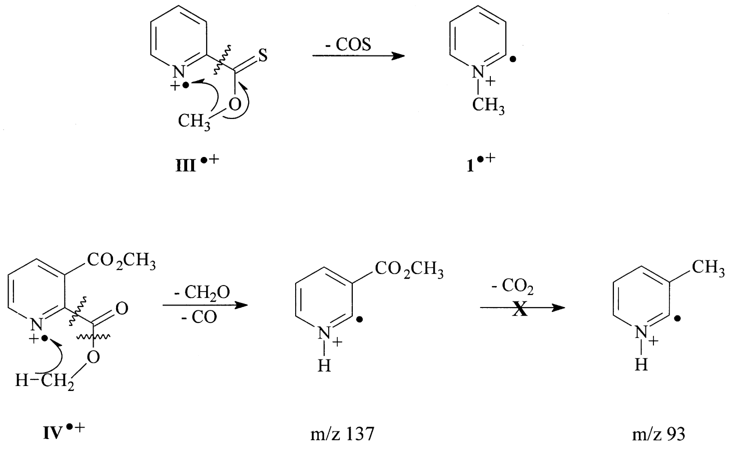


Scheme 1.

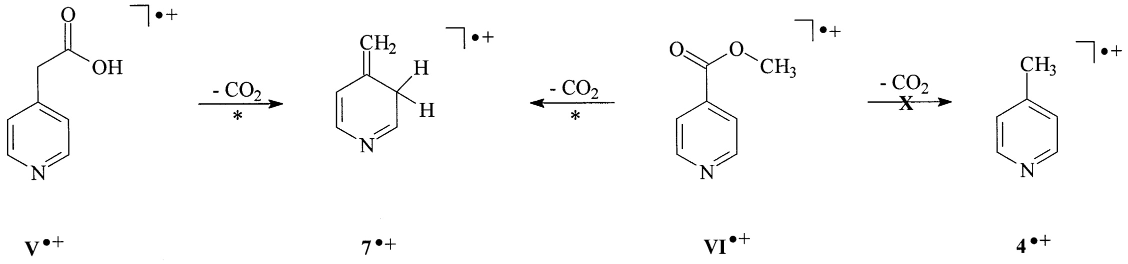
formation of the N-methyl ylide ion $\mathbf{1}^{\cdot+}$ from ionized methyl-2-pyridinethiocarboxylate, $\mathbf{III}^{\cdot+}$, as depicted in Scheme 2. Ions $\mathbf{1}^{\cdot+}$ are abundantly generated from the low energy (metastable) ions $\mathbf{III}^{\cdot+}$ by loss of COS. The CID mass spectrum [Fig. 1(d)] of these ions is characterized by an intense $CH_3^{\cdot}$ loss (*m/z* 78) and tell-tale peaks at *m/z* 42 (CH_3NCH^+) and *m/z* 15 (CH_3^+). In the methyl-d$_3$ isotopomer *m/z* 42 is shifted to *m/z* 45 and *m/z* 15 to *m/z* 18, confirming the transfer of the intact methyl group.

Budzikiewicz et al. [10] also proposed a methyl migration in the formation of the *m/z* 93 $C_6H_7N^{\cdot+}$ ions from dimethyl-2,3-pyridinedicarboxylate ions $\mathbf{IV}^{\cdot+}$, as depicted in Scheme 2. However, loss of CO_2 from *m/z* 137 does not figure in either the MI or the CID mass spectrum of the *m/z* 137 ions in Scheme 2. Moreover, high resolution measurements showed that the *source* generated *m/z* 93 ions largely consist of $C_5H_3NO^{\cdot+}$ ions with only a small contribution of $C_6H_7N^{\cdot+}$. Corroborating this, the mass spectrum of the dimethyl-d$_6$ isotopomer displays peaks at *m/z* 93 ($C_5H_3NO^{\cdot+}$) and *m/z* 97 ($C_6H_3D_4N^{\cdot+}$), with a ratio of 4:1. The CID mass spectrum of the labeled *m/z* 97 ions was obtained and despite the lack of reference spectra, it does indicate that a clean generation of the product ion shown in Scheme 2 is highly improbable.

The remaining isomer studied, $\mathbf{7}^{\cdot+}$, was generated from ionized 4-pyridylacetic acid, $\mathbf{V}^{\cdot+}$, as depicted in



Scheme 2.



Scheme 3.

Scheme 3. Careful analysis of spectra obtained at various ion source temperatures indicated that the source generated ions of putative structure $\mathbf{7}^{\cdot+}$ were contaminated with 4-methylpyridine ions $\mathbf{4}^{\cdot+}$ originating from thermal decarboxylation of the parent acid. An unadulterated ensemble of ions $\mathbf{7}^{\cdot+}$ could be obtained from the unimolecular dissociation of metastable 4-pyridylacetic acid molecular ions. Their CID mass spectrum, see Fig. 1(f), is characterized by the lowest *m/z* 26 : 28 peak intensity ratio of the set, 0.63, and a relatively intense peak at *m/z* 79 ($-\mathrm{CH_2}$) adjacent to a weak *m/z* 78 ($-\mathrm{CH_3}$) signal. The presence of charge stripping peaks at *m/z* 46.5 and 45.5 of comparable abundance completes its structure characterization.*

To document another proposed methyl migration, the $C_6H_7N^{\cdot+}$ ions produced from methyl-4-pyridinecarboxylate ($\mathbf{VI}^{\cdot+}$) were examined. In 1972, Neeter and Nibbering [32] postulated that the decarboxylation of $\mathbf{VI}^{\cdot+}$ in the metastable time frame yields the 4-methylpyridine ion, see Scheme 3. However, we surmise that this is not the case since the resulting MI/CID mass spectrum of the product ion (not shown) is virtually identical with that presented in Fig. 1(f), indicating that $\mathbf{7}^{\cdot+}$ is the isomer produced. High resolution experiments showed that the *source* generated *m/z* 93 ions consist of a 1:1 mixture of $C_6H_7N^{\cdot+}$ and $C_5H_3NO^{\cdot+}$ ions. Thus, the CID mass spectrum (not shown) of these ions is that of a mixture and the structure of the weak *source* generated $C_6H_7N^{\cdot+}$ ions remains unresolved.

To further characterize the ions and to probe the stability of the elusive neutrals **5** and **6**, Flammang and co-workers have also reported the NR spectra of $\mathbf{2}^{\cdot+}$– $\mathbf{7}^{\cdot+}$. One proposal from their study is that the intense “survivor ion” peaks in the spectra of $\mathbf{5}^{\cdot+}$ and $\mathbf{6}^{\cdot+}$ reflect the stability of their neutral counterparts. Evidence for this proposal comes from the presence of structure diagnostic signals in the NR spectra. However, consistent with our own observations (not shown), the intensity distribution of the various clusters of fragment ions in the NR spectra is considerably different from those in the CID spectra. One reason for this discrepancy (see Sec. 1) could be interference from reionized neutral fragments. To verify that these differences are not due to an isomerically impure initial beam of source generated ions and/or a partial isomerization upon neutralization, we have obtained the NR/CID spectrum of $\mathbf{5}^{\cdot+}$ and $\mathbf{6}^{\cdot+}$ along with that of the conventional isomer $\mathbf{2}^{\cdot+}$. These spectra are presented in Fig. 2 along with the CID mass spectra (3ffr) of the corresponding source generated ions.

For ions $\mathbf{5}^{\cdot+}$ and $\mathbf{6}^{\cdot+}$, the NR/CID and CID mass spectra [Fig. 2(a)–(d)] are closely similar, indicating (1) that the ions and their neutral counterparts are stable noninterconverting species in the gas phase, (2) that the initial ion beams consisted of isomerically

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* Ions $\mathbf{7}^{\cdot+}$ depicted in Diagram 1 do not contain a pyridine ring bearing a N–H moiety. Nevertheless, the *m/z* 28 ($\mathrm{H{-}C{\equiv}N{-}H^+}$) ion intenstiy is enhanced in the CID spectrum and this has led a reviewer to propose that ions $\mathbf{7}^{\cdot+}$ are ionized 4-methylene-1,4-dihydropyridine. This possibility cannot be excluded, but we note that our proposal is based upon the structure diagnostic peak at *m/z* 54, rationalized by Flammang *et al.* [5] to originate from the direct bond cleavage $\mathbf{7}^{\cdot+} \rightarrow \mathrm{H{-}C{\equiv}N{-}CH{=}CH_2^+} + \mathrm{H{-}C{\equiv}C{-}CH_2^{\cdot}}$. From a MS/MS spectrum and comparison with reference spectra [31] we conclude the *m/z* 54 ions likely have the proposed structure. Moreover, their major CID dissociation involves loss of C_2H_2 and formation of *m/z* 28 ($\mathrm{H{-}C{\equiv}N{-}H^+}$) and this may explain the enhanced *m/z* 28 intensity in the spectrum of $\mathbf{7}^{\cdot+}$.

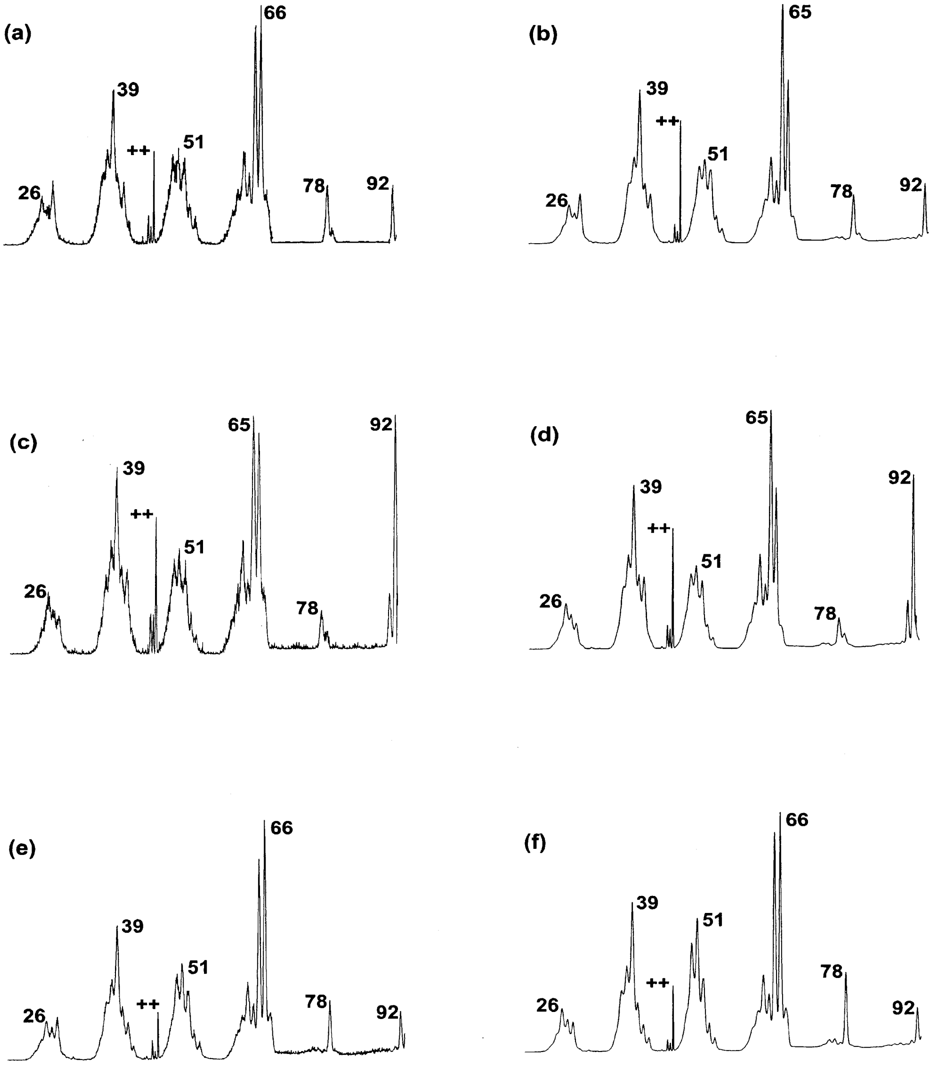


Fig. 2. NR/CID and comparative CID mass spectra (3ffr, 10 keV ions, collision gas O_2) of $C_6H_7N^{\cdot+}$ (*m/z* 93) ions. (a), (b) NR/CID and CID spectra of $C_6H_7N^{\cdot+}$ from ionized 2-acetylpyridine; (c), (d) NR/CID and CID spectra of $C_6H_7N^{\cdot+}$ from ionized bis(ethoxycarbonyl)pyridinium methylide; (e), (f) NR/CID and CID spectra of ionized 2-methylpyridine.

pure ions, and (3) that the structure diagnostic portions of the NR spectra are obscured by contributions from reionized neutral fragments. Note that when comparisons are made between the NR/CID and CID mass spectra, the signal at *m/z* 66 (– H,C,N), which is largely of metastable origin and thus sensitive to the method of ion preparation, is not considered.

Interestingly enough, it is the NR/CID [Fig. 2(e)] and the CID [Fig. 2(f)] mass spectra of ionized 2-methylpyridine that exhibit a difference in the *m/z* 26:28 peak intensity ratio, such that the NR/CID spectrum of $\mathbf{2}^{\cdot+}$ could be argued to be that of a mixture of ions $\mathbf{2}^{\cdot+}$ and $\mathbf{6}^{\cdot+}$. Considering that the neutral counterpart of $\mathbf{2}^{\cdot+}$ is much more stable than that of $\mathbf{6}^{\cdot+}$ (see the following), the possibility can be excluded that part of the neutralized ions **2** isomerize into **6**. Similarly, the possibility can be discarded that a significant fraction of the ions $\mathbf{2}^{\cdot+}$ generated by electron impact isomerizes into the more stable species $\mathbf{6}^{\cdot+}$, via a 1,3-H transfer. This is because the neutralization–reionization efficiency of $\mathbf{2}^{\cdot+}$ is four times greater than that of $\mathbf{6}^{\cdot+}$. It is therefore more likely that we are dealing with a significant degree of postcollisional isomerization upon *collisional* ionization of the neutral species **2**.

To test this hypothesis, a fast moving beam of *neutral* species **2** was produced in the second field free region from the 10 keV mass selected proton-bound dimer of **2** via the collision-induced dissociation into $[\mathbf{2} + \mathrm{H}]^+$ (5 keV) + **2** (5 keV). By using the deflector electrode, all ionic species were removed from the beam, thus allowing only the fast moving *neutrals* **2** to collide with O_2 in a second collision chamber, held at +2 kV. The resulting 7 keV *m/z* 93 ions were selectively transmitted into the third field free region and subjected to CID. The resulting partial CID mass spectrum, Fig. 3(a), resembles the NR/CID spectrum presented in Fig. 3(b), indicating that the common *collisional* ionization event is largely responsible for the significant degree of postcollisional isomerization of $\mathbf{2}^{\cdot+}$ into $\mathbf{6}^{\cdot+}$. For comparison, the 7 keV CID mass spectrum of the source generated $\mathbf{2}^{\cdot+}$ ions is presented in Fig. 3(c). The 1,3-H transfer involved in the isomerization $\mathbf{2}^{\cdot+} \rightarrow \mathbf{6}^{\cdot+}$ undoubtedly imposes a high barrier (~50 kcal/mol) upon the reaction. However, one should also consider that ions $\mathbf{2}^{\cdot+}$ may contain up to 75 kcal/mol internal energy before any dissociation process becomes possible [33,34]. An increase in the average internal energy resulting from a *collisional* ionization event [35] could promote significantly isomerization of $\mathbf{2}^{\cdot+}$, thus accounting for the observed differences in the NR/CID and CID mass spectra.

Finally, since ion $\mathbf{1}^{\cdot+}$ could only be obtained through the dissociation of metastable precursor ions, NR experiments were not feasible and thus its neutral counterpart remains unobserved.

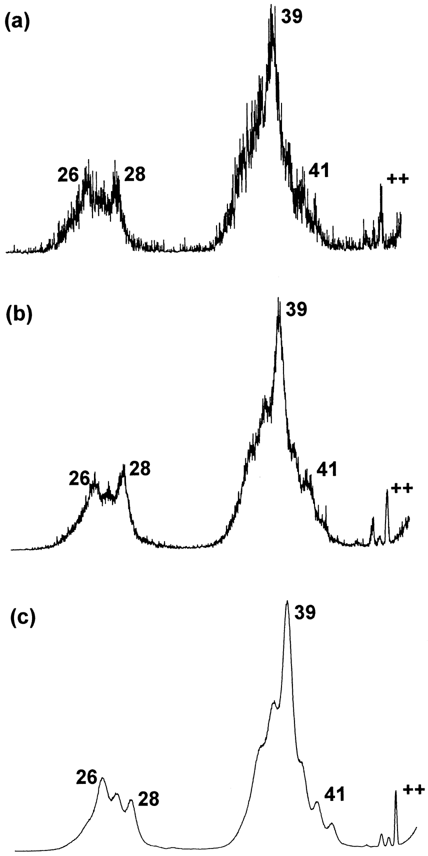


Fig. 3. Partial CID mass spectra (3ffr, 7 keV ions, collision gas O_2) of the *m/z* 93 ions derived from (a) collisional ionization of 2-methylpyridine produced by the decomposition of its proton-bound dimer (see text for details), (b) neutralization-reionization of 2-methylpyridine ions, and (c) 2-methylpyridine subjected to electron ionization.

To complement the experimental observations ab initio calculations were performed on four selected isomers viz. $\mathbf{1}^{\cdot+}$, $\mathbf{2}^{\cdot+}$, $\mathbf{5}^{\cdot+}$, and $\mathbf{6}^{\cdot+}$ as well as their neutral counterparts. The results are summarized in Table 1. Not surprisingly, the most stable species among the ionic isomers is not ionized 2-methylpyridine $\mathbf{2}^{\cdot+}$, but rather $\mathbf{6}^{\cdot+}$, which lies 24 kcal/mol lower in energy. The N-methylene isomer $\mathbf{5}^{\cdot+}$ is also more stable than $\mathbf{2}^{\cdot+}$, by 11 kcal/mol, but $\mathbf{1}^{\cdot+}$ is higher in energy, by 9 kcal/mol. These results are in fair agreement with a previous AM1 study [5] where $\mathbf{6}^{\cdot+}$ and $\mathbf{5}^{\cdot+}$ were found to be more stable than $\mathbf{2}^{\cdot+}$, by 33 and 10 kcal/mol, respectively. For the neutral counterparts, the relative stability of **6** and **2** is reversed, with **6** predicted to be 27 kcal/mol higher in energy than **2**, the most stable neutral of the set. Neutrals **1** and **5** are even higher in energy but, as could be experimentally verified for **5**, they do represent stable species on the potential energy

Table 1
Calculated energies for selected C_6H_7N and C_4H_5NS ions and neutrals at the B3LYP/6-31G* level of theory[a]

Species	B3LYP	$\langle S^2 \rangle$	ZPVE[c]	E_{rel}[b]
$C_6H_7N^{\cdot+}$ isomers				
1$^{\cdot+}$	−287.278 36	0.778	75.1	9
2$^{\cdot+}$	−287.289 11	0.756	73.3	0
5$^{\cdot+}$	−287.309 82	0.775	74.6	−11
6$^{\cdot+}$	−287.330 99	0.770	75.3	−24
C_6H_7N isomers				
1	−287.519 85		74.4	54
2	−287.605 79		74.6	0
5	−287.531 37		73.9	46
6	−287.562 54		74.5	27
$C_4H_5NS^{\cdot+}$ isomers				
11$^{\cdot+}$	−608.054 34	0.759	50.0	19
12$^{\cdot+}$	−608.086 32	0.769	51.5	0
13$^{\cdot+d}$	−608.029 55	0.776	50.6	35
14$^{\cdot+}$	−608.011 00	0.761	51.5	42
15$^{\cdot+}$	−607.961 66	0.759	49.7	77

[a] Total energies in Hartree, relative and zero-point vibrational energies are in kcal/mol.
[b] Relative energies include the ZPVE.
[c] ZPVE determined at B3LYP and scaled by 0.9806.
[d] Note that the optimized geometry of this ion represents an open chain structure, see text.

surface. Although the isomeric ions and neutrals have considerably different stabilities, they must be separated by sizable barriers which hinder a facile intramolecular isomerization.

3.2. Generation and characterization of $C_5H_6N_2$ and C_4H_5NS isomers

The decarbonylation of 2-acetylpyrazine and 2-acetylthiazole ions may be expected to occur analogously to that established for ionized 2-acetylpyridine. If so, the prominent *m/z* 94 and *m/z* 99 ions in their mass spectra should have the structures **9**$^{\cdot+}$ and **12**$^{\cdot+}$ rather than **8**$^{\cdot+}$ (2-methylpyrazine) and **11**$^{\cdot+}$ (2-methylthiazole), as proposed in the literature [16,17]. For the pyrazine system, this is confirmed by an analysis of the CID and NR/CID spectra presented in Fig. 4. As with the $C_6H_7N^{\cdot+}$ system, the CID spectra of the ions generated by the loss of CO from the 2-acetyl precursor and the loss of C_2H_4 from the 2-propyl precursor are virtually identical. A representative spectrum is shown in Fig. 4(a). It is clearly characteristic of the 2-methylene structure **9**$^{\cdot+}$ and, see Fig. 4(c), considerably different from that of the 2-methyl-pyrazine isomer **8**$^{\cdot+}$. For **9**$^{\cdot+}$ the structure diagnostic signals at *m/z* 80 and 47 (charge stripping peak) as well as the characteristic *m/z* 26:28 peak intensity ratio are reproduced in the CID spectrum, Fig. 4(b), of the intense survivor ion in the NR spectrum. Not only does this attest to the isomeric purity of the decarbonylation product, it also shows that 2-methylene-1,2-dihydropyrazine, **9**, is a stable, noninterconverting species in the dilute gas phase. For ion **8**$^{\cdot+}$ the NR/CID and CID spectra are also closely similar and thus the postcollisional isomerization effect observed for 2-methylpyridine is clearly absent in the pyrazine analogue. Since the *m/z* 67 peak in the CID spectra contains a large metastable ion (MI) contribution, it is not considered in the comparisons.

Another pyrazine ylide ion, **10**$^{\cdot+}$, was also probed for the stability of its neutral counterpart. The ion was generated from the dissociative ionization of methyl-5-methylpyrazine-2-carboxylate, **VII**$^{\cdot+}$, as depicted in Scheme 4 [36]. A distinct CID mass spectrum was obtained, see Fig. 4(e), which is closely similar, see Fig. 4(f), to the CID spectrum of the intense survivor

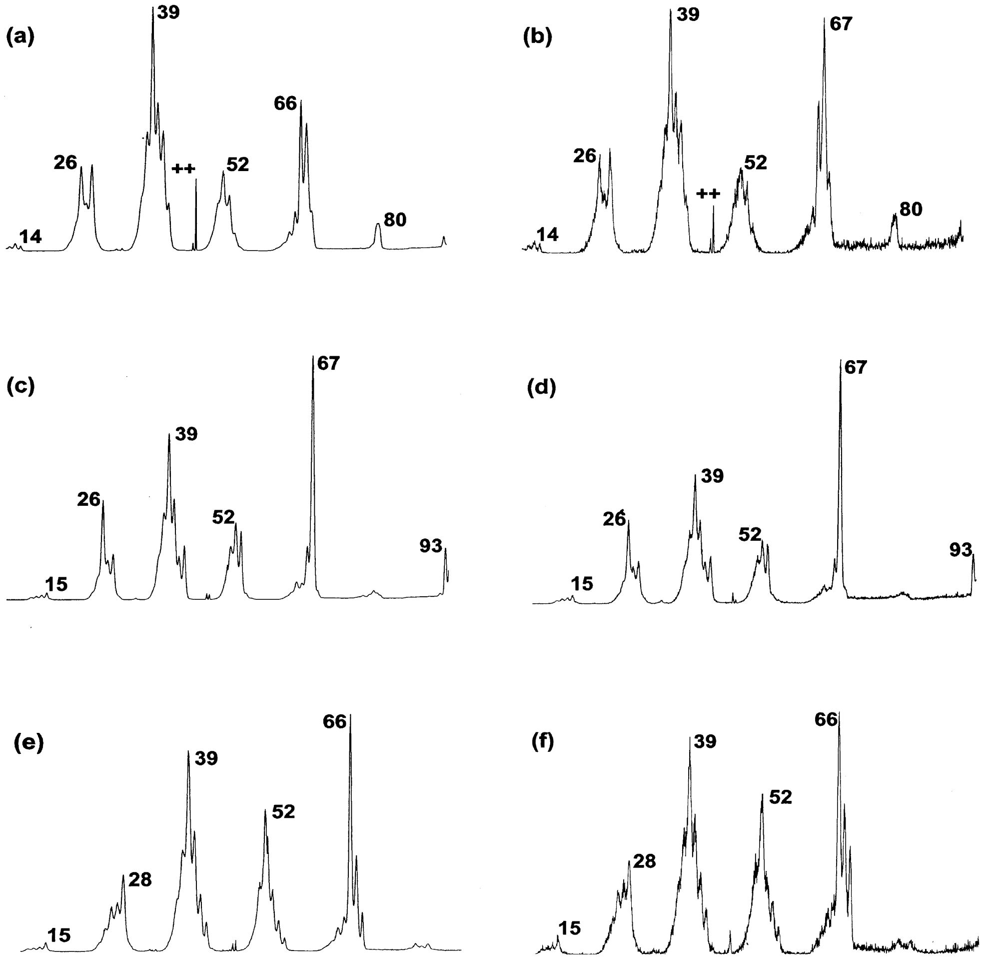
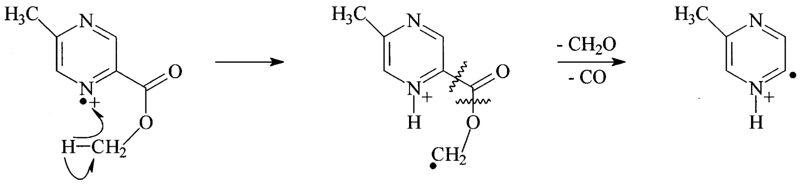


Fig. 4. NR/CID and comparative CID mass spectra (3ffr, 10 keV ions, collision gas O_2) of $C_5H_6N_2^{\cdot+}$ (*m/z* 94) ions. (a), (b) CID and NR/CID spectra of $C_5H_6N_2^{\cdot+}$ from ionized 2-acetylpyrazine or 2-propylpyrazine; (c), (d) CID and NR/CID spectra of ionized methylpyrazine; (e), (f): CID and NR/CID spectra of $C_5H_6N_2^{\cdot+}$ from ionized methyl-5-methylpyrazine-2-carboxylate. Spectra (e) and (f) are dominated by a peak at *m/z* 93, which is not shown because it is largely of metastable origin.

peak in the NR spectrum. This leaves little doubt that 5-methyl-1,2-dihydropyrazine, **10**, is a stable species in the gas phase.

For the thiazole system, the decarbonylation of the 2-acetyl precursor and the C_2H_4 elimination from the 2-propyl precursor again yielded product ions of the



$\mathbf{VII}^{\bullet+}$

$\mathbf{10}^{\bullet+}$

Scheme 4.

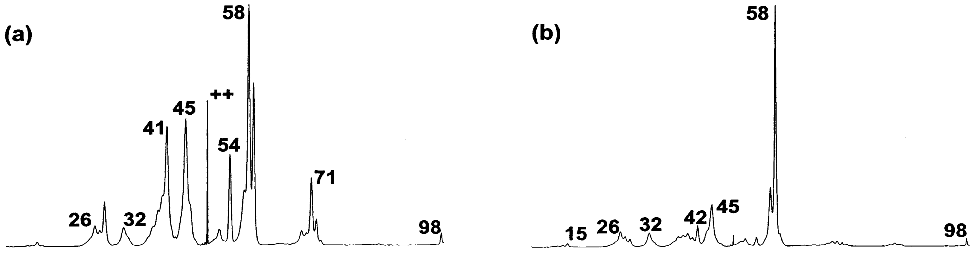


Fig. 5. CID mass spectra (10 keV ions, collision gas O_2) of $C_4H_5NS^{\cdot+}$ (*m/z* 99) ions generated from ionized (a) 2-acetylthiazole or 2-propylthiazole and (b) 2-methylthiazole.

same structure, as witnessed by their superimposable CID mass spectra. A representative spectrum is shown in Fig. 5(a). Unlike the situation with the pyridine and pyrazine analogues, this spectrum is markedly different from that of the 2-methyl substituted isomer $\mathbf{11}^{\cdot+}$, see Fig. 5(b). The CID mass spectrum of the decarbonylation product ion is characterized by unique peaks at *m/z* 71 (loss of $CH_2N^{\cdot}$), *m/z* 59 (loss of C_2HN), *m/z* 54 (loss of $CHS^{\cdot}$), and an intense charge stripping peak at *m/z* 49.5. These CID features are compatible with the expected 2-methylene-1,2-dihydrothiazole structure $\mathbf{12}^{\cdot+}$ but they do not necessarily rule out that the structurally related 2-methylene isomer $\mathbf{13}^{\cdot+}$ is (co)-generated in the decarbonylation.

However, the computational results indicate that this is unlikely. Not only is $\mathbf{13}^{\cdot+}$ found to undergo ring opening upon geometry optimization, but the resulting minimum energy structure, $CH_2{=}C{=}N{-}C(H){=}C(H)SH^{\cdot+}$ lies 35 kcal/mol higher in energy than $\mathbf{12}^{\cdot+}$. The N-methyl and S-methyl ylide isomers $\mathbf{14}^{\cdot+}$ and $\mathbf{15}^{\cdot+}$ retain their cyclic structure upon geometry optimization, but these species are even higher in energy, see Table 1. Thus, we conclude that the decarbonylation of 2-acetylthiazole occurs as established for the pyridine and pyrazine analogues and yields $\mathbf{12}^{\cdot+}$ as the product ion. A NR experiment yielded intense "survivor" ions. Their CID spectrum appeared to be indistinguishable from that of the source generated ions (spectra not shown), confirming that 2-methylene-2,3-dihydrothiazole, **12**, is also a stable species in the rarefied gas phase.

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