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Pyrimidine-ylidenes produced using neutralization–reionization mass spectrometry and probed by density functional methods

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Abstract

The potential energy surface comprising ionized pyrimidine, $\mathbf{1}^{\cdot+}$, and eight of its hydrogen-shift isomers, as well as that of the corresponding neutrals was explored at a level of theory (B3LYP/TZVP) that has proven adequate for related species. The computations predicted that among the isomers there are four $C_4H_4N_2^{+}$ distonic radical cations, $\mathbf{2}^{\cdot+}$– $\mathbf{5}^{\cdot+}$, of comparable stability to $\mathbf{1}^{\cdot+}$, and transition state calculations indicated that high barriers separate these stable ions. Thus, the ions $\mathbf{2}^{\cdot+}$–$\mathbf{5}^{\cdot+}$ should also be viable chemical species, and indeed mass spectrometry based experiments lead to the generation and characterization of three of the four, that is $\mathbf{2}^{\cdot+}$, $\mathbf{3}^{\cdot+}$, and $\mathbf{4}^{\cdot+}$, as stable ions in the gas phase. Ions $\mathbf{2}^{\cdot+}$– $\mathbf{4}^{\cdot+}$ were identified on the basis of their collision-induced dissociation characteristics in the mass spectrometer. The ions $\mathbf{2}^{\cdot+}$ and $\mathbf{3}^{\cdot+}$ obtained by dissociative electron impact ionization were subjected to neutralization–reionization mass spectrometry (NRMS). From collision-induced dissociation spectra of the intense NRMS survivor ions, it follows that the neutral ylide/carbene counterparts, i.e. pyrimidine-4-ylidene, **2**, and pyrimidine-2-ylidene, **3**, have lifetimes of at least microseconds in the rarefied gas phase. The interpretation of the experimental observations that **2** and **3** are viable chemical species in gaseous environs was supported computationally. According to the calculations the neutral isomers **2** – **5** each represent a minimum separated by high hydrogen-shift barriers, although situated some 50 kcal/mol higher in energy than **1**, pyrimidine itself. However, molecules **4** and **5** remained elusive since ions $\mathbf{4}^{\cdot+}$, only obtainable by a collision-induced dissociation process, were not amenable to NR experiments and a viable strategy to produce a beam of pure ions $\mathbf{5}^{\cdot+}$ could not be realized. (Int J Mass Spectrom 210/211 (2001) 43–57) © 2001 Elsevier Science B.V.

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1. Introduction

There exists certain classes of molecules which attract a great deal of attention and appear to be constantly under study. A prime example are molecules which possess a pyrimidine moiety, a structural motif which appears in a number of biologically important species including the nitrogenous bases guanine, thymine, adenine, cytosine, and the vitamin

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Dedicated to Professor Nico Nibbering on the occasion of his imminent retirement, in appreciation of his seminal contributions to the field of gas-phase ion chemistry.

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thiamin. As a consequence, numerous experimental and theoretical studies have been reported dealing with various intrinsic properties of pyrimidine **1** and its derivatives [1–9]. However, the so-called hydrogen-shift isomers of pyrimidine have not been explicitly studied, although they have been invoked as reactive intermediates in solution chemistry. For instance, pyrimidine-2-ylidene, **3**, was proposed as a short-lived intermediate en route to **1** in a study of the decarboxylation kinetics of 2-pyrimidinecarboxylic acid in solution [10]. The reaction sequence is analogous to that postulated earlier by Hammick and co-workers for 2-pyridinecarboxylic acid [11].

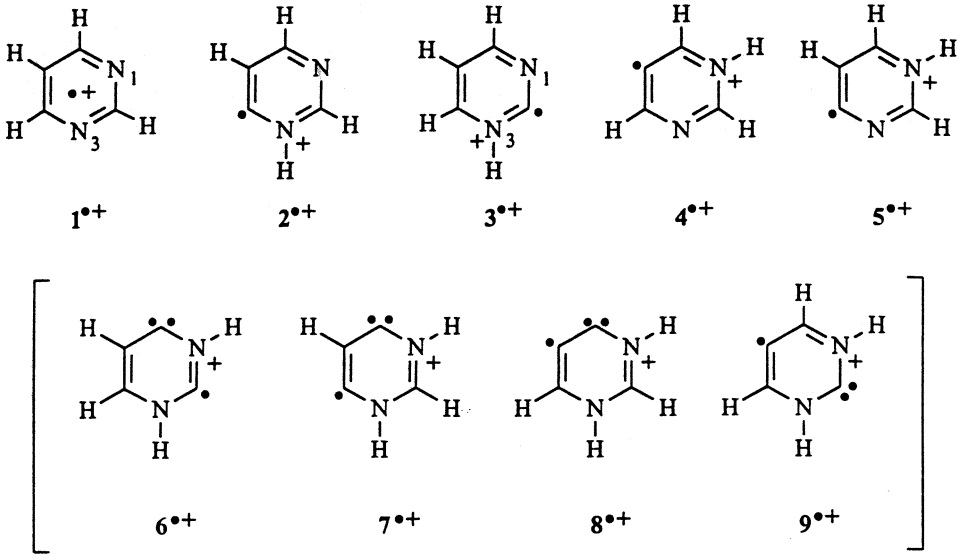
As Maier and Reisenauer found during a characterization of the (vitamin B_1-like) 2,3-dihydrothiazol-2-ylidene even the use of modern matrix isolation methods does not entirely remove all obstacles presented by the reactive nature of most ylides/carbenes in condensed phases [12]. Consequently, to study such fundamental reactive intermediates one may take advantage of the gas phase where intermolecular reactions are essentially absent [13]. The confines of a mass spectrometer offer such an environment, and since the inception of neutralization–reionization (NR) mass spectrometry over 20 years ago [14] numerous elusive species have been identified using this technique, which involves the one-electron reduction (or oxidation) of their corresponding radical ions. Several laboratories have used neutralization–reionization mass spectrometry (NRMS) to generate archetypal carbenes e.g. CH_3–C–OH [15], H_2N–C–OH [16], H_2N–C–NH_2 [16(c)] from their radical cations [17]. As both NR methodology and computational chemistry continue to develop, larger systems may now come under scrutiny. In 1996 our laboratories produced the Hammick intermediate [18], then the Wanzlick's and Arduengo's carbenes, i.e. imidazol-2-ylidene [19]. In this context, it is important to note that these neutral carbenes and ylides are much higher in energy than their molecular isomers, whereas appealingly this is not true for the ionic counterparts. By way of example, theory and experiment have established the comparable stability of ionized pyridine and its α-ylide isomer [18], which are separated by high isomerization barriers. The accessibility of C_5H_5N pyridine-related and other $C_4H_4N_2$ pyrazine-type ions led to the successful production of pyridine-3-ylidene [20] and the two isomers pyrazine-2-ylidene and pyrazine-3-ylidene [21]. The combination of NRMS and computational chemistry also proved advantageous in a recent study of protonated pyrimidine's neutral counterpart, a proposed model compound in studies of DNA radiation damage [22]. More, recently Flammang et al. demonstrated that the 1,2-hydrogen-shift isomers of ionized pyridine, thiazole and imidazole undergo characteristic ion-molecule association reactions with dimethyldisulfide, an approach that will certainly prove fruitful in revealing other such species [23].

Here we set out to examine the structure and stability of the hydrogen shift isomers of pyrimidine, arguably the most important of the $C_4H_4N_2$ diazines by the NR methodology. Ab initio calculations predicted that ionized pyrimidine, $\mathbf{1}^{\cdot+}$, has four hydrogen shift isomers of comparable stability residing in deep potential wells, viz. the ions $\mathbf{2}^{\cdot+}$–$\mathbf{5}^{\cdot+}$ shown in Scheme 1. Their neutral counterparts are also calculated to be stable and, although they lie 40–65 kcal/mol higher in energy than pyrimidine, **1**, isomerization is prevented by barriers in the range 85–130 kcal/mol. Thus, these pyrimidine-ylidenes should all be observable chemical species in the mass spectrometer, provided their ionic counterparts can be generated in an isomerically pure form.

2. Experimental and computational details

2.1. Computational aspects

Determinations of the structures, energies and frequencies were performed computationally on IBM/RS6000 workstations and on CRAY computers at the Konrad-Zuse Zentrum für Informationstechnik, Berlin, using the GAUSSIAN 94 program package [24]. It is necessary to consider low-lying electronic states in diazine chemistry [2] and it is also well known that care must be taken to employ methods that adequately describe the electronic structure of ylide and diradical species. Having demonstrated less susceptibility to



Scheme 1. Ionized pyrimidine and its hydrogen shift isomers.

spin contamination than second-order Møller-Plesset [25] and reasonable accuracy compared with complete active space self-consistent field and highly correlated coupled cluster type calculations for pyridine and pyrazine isomers [18,20,21], our preference was to use a hybrid density functional approach. We performed calculations on the neutral and ionic $C_4H_4N_2$ species using the Becke-style 3 parameter using the Lee-Yang-Parr correlation functional (B3LYP) hybrid density functional theory (DFT) [26,27] options employing Becke's [28] empirical three-parameter fit for mixing HF and DFT exchange-energy terms as implemented in Gaussian 94 [29]. Unrestricted calculations following the Kohn-Sham model were carried out for the open-shell species [27]. All the neutral species and their respective radical cations are identified as genuine minima characterized by a positive definite Hessian matrix at B3LYP level of theory. Geometry optimizations were performed in two stages, first with the standard 6-31G** basis set [30] and then to improve the quality of the results with Ahlrichs' polarized TZVP basis set [31]. All relative energies were corrected for zero-point vibrational energy (ZPVE) contributions. No scaling of the ZPVE was performed for the B3LYP fundamentals.

2.2. Experimental procedures

The mass spectrometric experiments were performed at McMaster University on the VG Analytical ZAB-R. The details of this BE_1E_2 geometry instrument and also for the acquisition of NR mass spectra have been previously described [32]. Ionized precursors were generated in the mass spectrometer ion source by 70 eV electron ionization or by chemical ionization with CH_3OH as a reagent gas and accelerated by a 10 kV potential. In NR experiments the magnet (B) allows a beam of mass-selected ions into the region preceding E_1, the first electric sector. As the fast moving ions traverse the region they pass through the first of two small gas cells where interactions with N,N-dimethylaniline vapour neutralize a small fraction by electron transfer. On exit a positively charged deflector ensures that only neutrals enter the second cell where encounters with oxygen molecules cause some of the high-speed neutrals to be reionized. A PC-based data acquisition system (Mommers Technologies Inc., Ottawa, Canada) controls the E_1 scans and the recording of mass spectra. Similarly, but with the first cell empty and the deflector switched off collision-induced dissociation mass spectra were obtained in the same region. The NR/CID and CID

mass spectra were obtained by scanning E_2, with E_1 set at a fixed potential, the appropriate gases in the first two cells and oxygen collision gas in third small cell located between E_1 and E_2. For the analysis of the *m/z* 80 ions $\mathbf{4}^{\cdot+}$, generated from 10 keV *m/z* 159 precursor ions the first collision chamber was held at +3000 V. This way the *m/z* 80 possessed ~7 keV translational energy, which facilitates a comparison with the other spectra.

Pyrimidine, 2-chloropyrimidine, and 5-bromopyrimidine were used as purchased (Aldrich Chemical Co., St. Louis). Methyl-4-pyrimidinecarboxylate was made by $KMnO_4$ oxidation of 4-methylpyrimidine followed by esterification with MeOH [33]. Methyl-2-pyrimidinecarboxylate was prepared in a four-step procedure. 2-chloropyrimidine was converted to 2-cyanopyrimidine [34] in a two-step process. The nitrile was hydrolyzed to the carboxylic acid, which was then esterified [35]. Samples were introduced to the mass spectrometer via either an all-glass heated inlet system equipped with a leak valve or a direct insertion-type probe having a glass bore and reservoir.

Table 1
Calculated energies (B3LYP/TZVP) for the $C_4H_4N_2^{*+}$ radical cations $\mathbf{1}^{\cdot+}$–$\mathbf{9}^{\cdot+}$ and isomerization barriers for 1,2-hydrogen migrations

Species	Doublet (Hartree)	ZPVE (kcal/mol)	E_{rel}^{a} (kcal/mol)
$\mathbf{1}^{\cdot+}$	−264.072 22	47.2	**0.0**
$\mathbf{2}^{\cdot+}$	−264.061 20	48.0	**7.7**
$\mathbf{3}^{\cdot+}$	−264.068 71	48.5	**3.5**
$\mathbf{4}^{\cdot+}$	−264.060 04	48.3	**8.8**
$\mathbf{5}^{*}$	−264.071 59	48.5	**1.7**
TS $\mathbf{1}^{\cdot+}/\mathbf{2}^{\cdot+}$	−263.965 21	42.8	**62.8**
TS $\mathbf{1}^{\cdot+}/\mathbf{3}^{\cdot+}$	−263.958 46	43.3	**67.5**
TS $\mathbf{2}^{\cdot+}/\mathbf{4}^{\cdot+}$	−263.946 80	43.9	**75.4**
TS $\mathbf{4}^{\cdot+}/\mathbf{5}^{\cdot+}$	−263.942 63	43.8	**77.9**
$\mathbf{6}^{\cdot+}$	−264.018 35	48.2	34.8
$\mathbf{7}^{\cdot+}$	−263.999 39	47.8	46.3
$\mathbf{8}^{\cdot+}$	−263.999 92	48.2	46.4
$\mathbf{9}^{\cdot+}$	−264.009 69	48.2	26.3
TS $\mathbf{3}^{\cdot+}/\mathbf{6}^{\cdot+}$	−263.914 82	43.1	94.6
TS $\mathbf{2}^{\cdot+}/\mathbf{6}^{\cdot+}$	−263.933 14	43.3	83.4
TS $\mathbf{2}^{\cdot+}/\mathbf{7}^{\cdot+}$	−263.922 72	43.5	90.1
TS $\mathbf{7}^{\cdot+}/\mathbf{8}^{\cdot+}$	−263.875 51	43.3	119.5
TS $\mathbf{4}^{\cdot+}/\mathbf{8}^{\cdot+}$	−263.917 80	43.6	93.4
TS $\mathbf{5}^{\cdot+}/\mathbf{6}^{\cdot+}$	−263.931 53	43.4	84.5
TS $\mathbf{4}^{\cdot+}/\mathbf{9}^{\cdot+}$	−263.929 61	43.6	85.9
TS $\mathbf{6}^{\cdot+}/\mathbf{9}^{\cdot+}$	−263.900 66	43.6	104.1

[a]Relative energies are corrected for ZPVE contributions.

3. Results and discussion

3.1. Computation of energies for pyrimidine isomers and their radical cations

Structurally the pyrimidine hydrogen shift isomers can be divided into two groups by virtue of their N–H bond count. The members of the group possessing a single N–H bond are more stable than those from the group with two N–H bonds, as radical cations ($\mathbf{2}^{\cdot+}$–$\mathbf{5}^{\cdot+}$ in Table 1) and as neutrals (singlet or triplet state **2** – **5** in Table 2), so they appear most amenable to experimental identification. Although the neutrals **2**–**5** are elevated in energy with respect to **1** (by 42–67 and 77–86 kcal/mol in the singlet and triplet states, respectively) the ions $\mathbf{2}^{\cdot+}$– $\mathbf{5}^{\cdot+}$ are comparable in stability to ionized pyrimidine, with the least stable ion $\mathbf{4}^{\cdot+}$ only 8.8 kcal/mol above $\mathbf{1}^{\cdot+}$. The adiabatic ionization energies will be discussed more specifically in the context of the NR experiments but the values for the isomers should be smaller than for pyrimidine, the smallest being 6.88 and 5.59 eV for singlet and triplet **9**. There are large energy barriers separating all the species. Transition structures that connect the stable structures are situated at least 35 kcal/mol above for the neutrals and even further, by 43.8 kcal/mol or more, above for the ions. We were unable to locate transition structures connecting neutral **3** to **1** and **6** in their triplet forms but from prior work on pyridine, pyrazine and imidazole [18–21] we assume these will be similarly endothermic. The B3LYP/TZVP structural parameters computed for **1** were in good agreement with previous theoretical and experimental findings [2]. A canonical type singlet carbene structure is predicted for ground state **2**, see Table 3. In both the triplet state **2** and the radical cation $\mathbf{2}^{\cdot+}$, the carbon–carbon bond lengths are swapped and the characteristic angle is wider (123° versus 108.4°), which with their overall structural similarity suggests localization of the charge in-plane at the unsaturated carbon atom. From the data in Table 4, analogous

Table 2
Calculated energies (B3LYP/TZVP) for the $C_4H_4N_2$ neutral molecules **1**–**9** and isomerization barriers for 1,2-hydrogen migrations

Species	Singlet (Hartree)	ZPVE (kcal/mol)	E_{rel}^{a} (kcal/mol)	Triplet (Hartree)	ZPVE (kcal/mol)	E_{rel}^{a} (kcal/mol)
1	−264.409 54	48.2	**0.0**	−264.281 91	44.2	84.1
2	−264.342 03	48.1	**42.3**	−264.280 57	45.5	86.2
3	−264.329 58	47.5	**49.5**	−264.293 95	45.6	77.8
4	−264.315 69	47.3	**58.1**	−264.280 65	45.3	86.0
5	−264.301 07	46.8	**66.7**	−264.286 05	45.6	82.9
TS **1/2**	−264.268 21	43.7	**84.2**	−264.188 94	41.75	140.0
TS **1/3**	−264.261 21	43.1	**88.0**			
TS **2/4**	−264.214 74	43.6	**117.7**	−264.195 32	42.2	136.4
TS **4/5**	−264.194 88	43.0	**129.6**	−264.181 25	42.3	145.3
6	−264.291 33	48.3	74.3	−264.244 28	46.2	109.7
7	−264.256 36	47.7	95.7	−264.218 43	45.6	125.4
8	−264.226 33	46.5	113.3	−264.211 60	45.3	129.3
9	−264.280 12	47.6	80.7	−264.242 37	45.8	110.4
TS **3/6**	−264.204 55	43.6	124.1			
TS **2/6**	−264.210 31	43.7	120.6	−264.168 79	41.7	152.6
TS **2/7**	−264.191 29	43.4	132.2	−264.151 46	41.0	162.7
TS **7/8**	−264.132 80	42.8	168.3	−264.108 24	41.5	190.4
TS **4/8**	−264.164 48	42.6	148.2	−264.138 36	41.3	171.2
TS **5/6**	−264.189 37	43.2	133.2	−264.167 98	42.0	153.4
TS **4/9**	−264.201 44	43.4	125.8	−264.168 12	41.7	153.0
TS **6/9**	−264.170 86	43.7	145.3	−264.155 38	42.6	161.9

[a]Relative energies are corrected for ZPVE contributions.

predictions arise for **3** and $\mathbf{3}^{\cdot+}$ wherein the NCN angle changes from 111.8° (singlet) to 121.4° (triplet) or 120.3° (doublet radical cation) and the adjacent imino nitrogen–carbon bonds are altered. Their lengths change from 1.385 and 1.324 (singlet) to 1.249 and 1.406 (triplet) or 1.269 and 1.347 A° (doublet radical cation).

3.2. Generation and characterization of $C_4H_4N_2$ radical cations

To probe the stability of the above mentioned hydrogen shift isomers of pyrimidine with the NR methodology, it first becomes necessary to characterize the radical cations, $\mathbf{1}^{\cdot+}$– $\mathbf{5}^{\cdot+}$. The search for appropriate precursor molecules to the putative ions $\mathbf{2}^{\cdot+}$– $\mathbf{4}^{\cdot+}$ was straightforward but unfortunately a strategy to generate isomerically pure ions $\mathbf{5}^{\cdot+}$ could not be realized. Electron impact ionization of pyrimidine yields a simple mass spectrum dominated by molecular ions $\mathbf{1}^{\cdot+}$ and principal fragment ions at *m/z* 53 (loss of HCN) and *m/z* 26 ($C_2H_2^{+}$) [4]. By analogy

Table 3
Selected calculated geometric parameters for **2** (singlet), **2** (triplet), and $\mathbf{2}^{\cdot+}$ (doublet) at the B3LYP/TZVP level of theory[a]

Parameter	**2** (singlet)	**2** (triplet)	$\mathbf{2}^{*}$ (doublet)
$H–C_2$	1.089	1.086	1.087
$H–N_3$	1.016	1.013	1.022
$H–C_6$	1.089	1.083	1.088
$H–C_5$	1.088	1.085	1.084
$C_2–N_3$	1.362	1.428	1.376
$N_3–C_4$	1.379	1.384	1.328
$C_4–C_5$	1.432	1.348	1.368
$C_2–N_1$	1.306	1.287	1.305
$N_1–C_6$	1.362	1.368	1.342
$C_6–C_5$	1.379	1.436	1.410
$H–C_2–N_3$	117.3	114.8	117.0
$C_2–N_3–H$	116.0	117.1	119.8
$C_2–N_3–C_4$	127.4	115.2	119.4
$N_3–C_4–C_5$	108.4	123.3	122.9
$H–C_6–C_5$	121.7	121.6	120.0
$C_6–C_5–H$	118.7	120.9	122.4
$C_4–C_5–C_6$	123.1	116.8	114.1
$C_2–N_1–C_6$	115.0	119.9	118.9
$N_1–C_6–C_5$	123.3	120.6	123.6
$H–N_3–C_4–C_5$	—	−24.8	0.0

[a]Bond lengths are in angstroms and angles in degrees. Atom numbering as shown in scheme 5

Table 4
Selected calculated geometric parameters[a] for **3** (singlet), **3** (triplet), and $\mathbf{3}^{\cdot+}$ (doublet) at the B3LYP/TZVP level of theory[b]

Parameter	**3** (singlet)	**3** (triplet)	$\mathbf{3}^{\cdot+}$ (doublet)
C_2–N_3	1.399	1.366	1.344
C_2–N_1	1.385	1.249	1.269
N_3–C_4	1.357	1.423	1.362
C_4–C_5	1.370	1.376	1.384
N_1–C_6	1.324	1.406	1.347
C_6–C_5	1.411	1.403	1.402
N_3–H	1.013	1.007	1.019
C_4–H	1.086	1.081	1.085
C_6–H	1.092	1.081	1.086
C_5–H	1.083	1.086	1.084
C_2–N_3–C_4	128.2	117.2	119.1
C_2–N_3–H	114.4	121.4	120.3
N_3–C_4–C_5	117.7	117.7	118.7
N_3–C_4–H	118.1	116.8	117.1
C_4–C_5–C_6	115.7	121.1	118.2
C_4–C_5–H	121.9	118.9	120.5
N_3–C_2–N_1	111.8	126.2	124.3
C_2–N_1–C_6	122.0	120.1	120.0
N_1–C_6–C_5	124.7	117.7	119.8
N_1–C_6–H	116.5	117.9	117.7

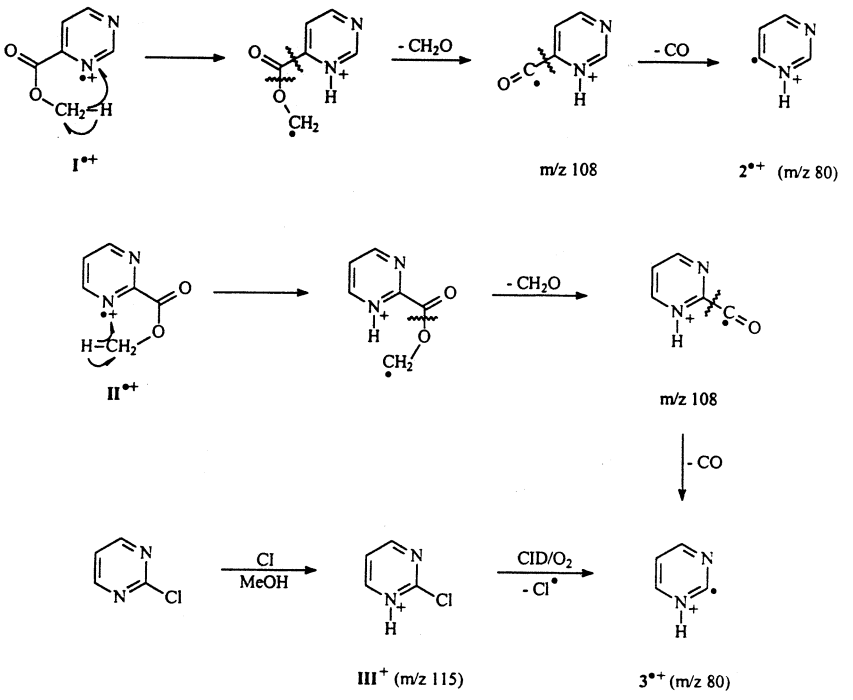
[a]Geometries of the other species including the saddle points are available upon request from the authors.
[b] Bond lengths are in angstroms and angles in degrees. Atom numbering as shown in Scheme 6

with earlier work on the pyridine [18] and pyrazine [21] systems, ions $\mathbf{2}^{\cdot+}$ and $\mathbf{3}^{\cdot+}$ should be obtainable by dissociative electron ionization of the appropriate methyl esters, *viz.* methyl-4-pyrimidinecarboxylate (**I**) and methyl-2-pyrimidinecarboxylate (**II**). These two esters do indeed show a prominent *m/z* 80 peak in their conventional electron impact mass spectrum, which is cleanly shifted to *m/z* 81 in the spectra of the CD_3-labeled isotopomers, **I**-d_3 and **II**-d_3. As shown in Scheme 2, the proposed formation of $\mathbf{2}^{\cdot+}$ and $\mathbf{3}^{\cdot+}$ involves a 1,5-H transfer to a ring N atom followed by consecutive losses of CH_2O and CO. Ions $\mathbf{4}^{\cdot+}$ could not be generated by dissociative electron impact but collision-induced dissociation of protonated 5-bromopyrimidine, see Scheme 3, provided a viable alternative. Unfortunately, however, this method of ion preparation does not lend itself to NR experiments with the available instrumentation and thus the neutral counterpart of $\mathbf{4}^{\cdot+}$ could not be studied.

The isomeric cations $\mathbf{1}^{\cdot+}$– $\mathbf{4}^{\cdot+}$ were characterized using the technique of collision-induced dissociation (CID) mass spectrometry. Upon inspection of the CID mass spectra shown in Fig. 1, it becomes immediately apparent that a number of common dissociation pathways exists of which loss of HCN, yielding the peak at *m/z* 53, is the most prominent. Nevertheless, there are characteristic differences between the spectra, which enable isomer differentiation. The most significant are the *m/z* 26 ($C_2H_2^{\cdot+}$) : 28 ($HC{\equiv}NH^+$) peak intensity ratio and the intensity of the charge stripping peak, denoted as "++". For the pyrimidine radical cations $\mathbf{1}^{\cdot+}$ a high *m/z* 26:28 ratio, 3.33 ± 0.03, is observed and a charge stripping peak at *m/z* 40 is absent, see Fig. 1(a). In contrast, see Fig. 1(b), the CID spectrum of the putative ion $\mathbf{2}^{\cdot+}$ displays a *m/z* 26:28 ratio of 1.14 ± 0.03 and a sizable charge stripping peak indicative of an ylide structure. As documented in previous work on the pyridine [18] and pyrazine [21] systems, the ionic ylide isomers are more prone to produce *m/z* 28 ions $H{-}C{\equiv}N^+{-}H$, via a high energy direct bond cleavage reaction, than their ionized parent heterocycles which have no –CH–NH– moiety. In agreement with this proposal, the CID spectrum of the *m/z* 81 ions from **I**-d_3 shows a clean shift of *m/z* 28 to *m/z* 29, whereas *m/z* 26 remains unchanged.

The CID mass spectrum of $\mathbf{3}^{\cdot+}$, Fig. 1(c), again exhibits a structure diagnostic *m/z* 26:28 ratio, 0.83 ± 0.03, but compared to that of $\mathbf{2}^{\cdot+}$ the charge stripping peak is less intense. Of even greater structure diagnostic value is the weak peak at *m/z* 54. From a CID experiment in the third field free region (ffr) it follows that these *m/z* 54 ions have the elemental composition C_3H_4N [36] and thus they represent a highly structure specific loss of · CN. This process would presumably be similarly diagnostic for ion $\mathbf{5}^{\cdot+}$.

Ions $\mathbf{3}^{\cdot+}$ also show a prominent loss of $H^{\cdot}$, see Fig. 1(c). Surprisingly, the product generated is not the stable 2-pyrimidyl cation [37], since the CID mass spectrum of the isotopomer $\mathbf{3}^{\cdot+}$(N–D) shows a specific loss of $H^{\cdot}$, not $D^{\cdot}$, see Fig. 1(d). Further, because the CID spectrum of the $[\mathbf{3}{-}H]^+$ ions is dominated by the loss of HCN whereas the pyrimidyl cation, generated by loss of $Cl^{\cdot}$ from 2-chloropyrimidine [37], loses both C_2H_2 and HCN to about the same extent.

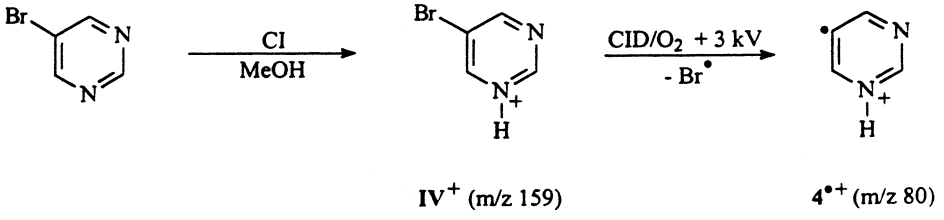


Scheme 2. Generation of radical cations $\mathbf{2}^{\cdot+}$ and $\mathbf{3}^{\cdot+}$.

These observations make it highly unlikely that the six-membered ring structure of $\mathbf{3}^{\cdot+}$ remains intact upon H$^{\cdot}$ loss. Guided by the results of exploratory calculations on the relative stability of the $[\mathbf{3} - \mathrm{H}]^{+}$ product ions, we tentatively propose that the reaction occurs as indicated in Scheme 4.

Another possibility involves ring opening by cleavage of the N3–C4 bond followed by loss of H$^{\cdot}$ from C5. Our calculations indicated that the resulting product ion, H–C≡C–$^{+}$CH–N=C=N–H, is 11 kcal/mol higher in energy than the 2-pyrimidyl cation, whereas the ion depicted in Scheme 4 is of comparable stability. We further note that loss of H$^{\cdot}$ from the heteroatom in $\mathbf{3}^{\cdot+}$ may involve a sizable reverse barrier.

Ions $\mathbf{3}^{\cdot+}$ were also generated by a second independent method. Under chemical ionization conditions, using methanol as the reagent gas, 2-chloropyrimidine molecules were protonated, accelerated and subsequently transmitted into the 2ffr of the instrument. The fast moving ions $\mathbf{III}^{+}$, see Scheme 2, were then collided with oxygen and the resulting 7 keV *m/z* 80 ions generated upon loss of Cl$^{\cdot}$ were selectively transmitted into the 3ffr of the instrument and collided with oxygen. The resulting CID mass spectrum was indistinguishable from that obtained for the *m/z* 80 source



Scheme 3. Generation of radical cation $\mathbf{4}^{\cdot+}$.

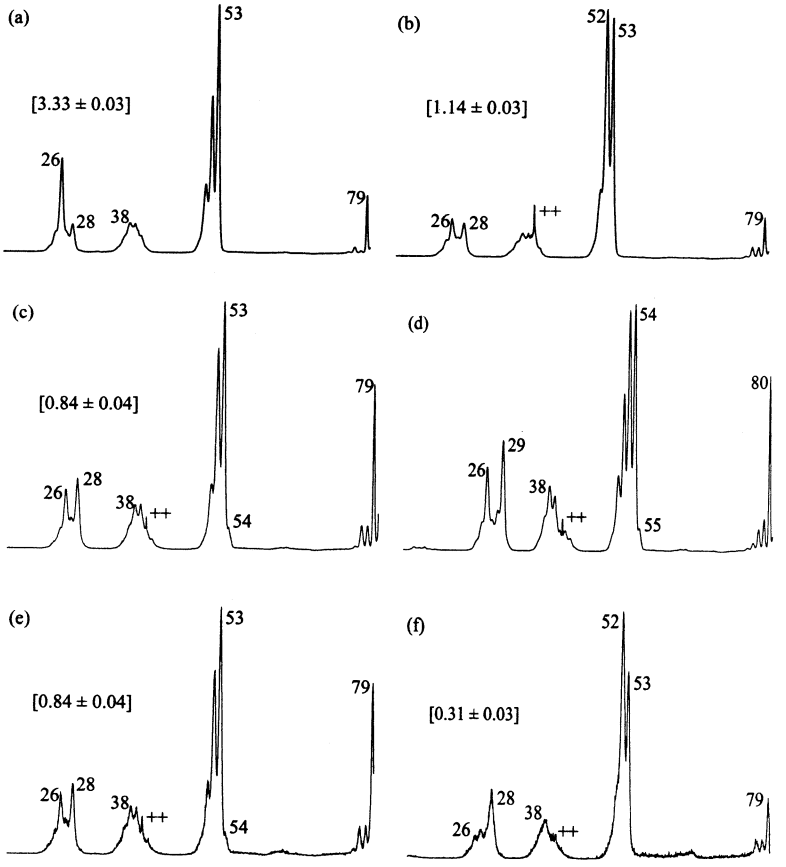
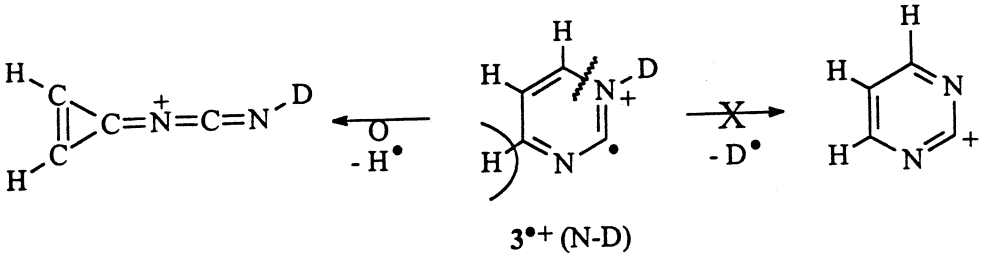
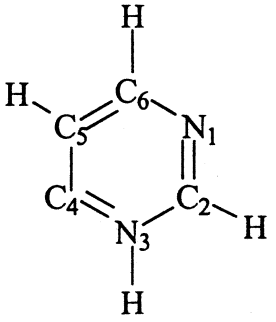


Fig. 1. CID [O_2] mass spectra (7 keV, 3ffr) of the *m/z* 80 ions from (a) ionized pyrimidine ($\mathbf{1}^{\cdot+}$); (b) ionized methyl-4-pyrimidinecarboxylate, yielding $\mathbf{2}^{\cdot+}$; (c) ionized methyl-2-pyrimidinecarboxylate, yielding $\mathbf{3}^{\cdot+}$; (d) methyl-d_3-2-pyrimidinecarboxylate, yielding $\mathbf{3}^{\cdot+}$(N–D); (e) metastable *m/z* 108 ions from ionized methyl-2-pyrimidinecarboxylate, yielding $\mathbf{3}^{\cdot+}$; (f) collision-induced dissociation of protonated 5-bromopyrimidine, yielding $\mathbf{4}^{\cdot+}$. Note that the *m/z* 26:28 ratios quoted in the spectra depend on the translational energy of the ions and also on the differences in energy resolution for dissociations in the 2ffr vs. 3ffr, see Figs. 3 and 4.

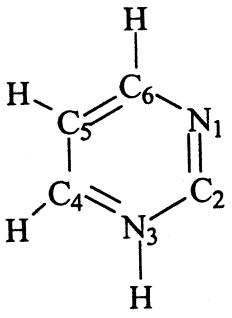
generated ions from the ester $\mathbf{II}^{\cdot+}$, Fig. 1(c), confirming that a common ion, $\mathbf{3}^{\cdot+}$, is produced in the two processes. Further attesting to our proposal that these ions also have a high isomeric purity is the observation that the CID spectrum of the *metastably* generated *m/z* 80 ions from the ester precursor, see Fig.



Scheme 4. Fragmentation of deuterium isotope labeled ions $\mathbf{3}^{\cdot+}$(N–D).



Scheme 5.



Scheme 6.

1(e), is virtually identical with the spectrum presented in Fig. 1(c).

The third hydrogen shift isomer, $\mathbf{4}^{\cdot+}$, was generated by the chemical ionization, CID sequence described above for ion $\mathbf{3}^{\cdot+}$, but using 5-bromopyrimidine (**IV**) as the precursor. See Scheme 3 and Sec. 2.2 for further details. The resulting CID spectrum, see Fig. 1(f), displays the lowest *m/z* 26:28 ratio of the set, 0.31 ± 0.04, in keeping with the fact that ions $\mathbf{4}^{\cdot+}$ cannot generate *m/z* 26 ($HC{\equiv}CH^{\cdot+}$) ions by direct bond cleavage, whereas *m/z* 28, $HC{\equiv}NH^{+}$, can readily be generated.

The conclusions regarding the structural integrity of the ions $\mathbf{1}^{\cdot+}$– $\mathbf{4}^{\cdot+}$ derived from the CID experiments are supported by the quantum chemical calculations. Ionized pyrimidine, $\mathbf{1}^{\cdot+}$, is predicted to be the most stable isomer but the four hydrogen shift isomers $\mathbf{2}^{\cdot+}$– $\mathbf{5}^{\cdot+}$ are only slightly higher in energy. Moreover, the five ions are separated by considerable 1,2-H shift barriers, in the 60–80 kcal/mol energy range, which prevents their facile isomerization.

Buff and Dannacher [6], in a photoelectron–photoion coincidence study of diazine cations, have determined the critical energy for the loss of HCN from ionized pyrimidine. This process represents the dissociation reaction of lowest energy requirement for $\mathbf{1}^{\cdot+}$. It dominates the MI spectrum, see Table 5, and also the CID mass spectrum, see Fig. 1(a). The measured critical energy, ~63 kcal/mol, dictates that the heat of formation of the resulting $C_3H_3N^{\cdot+}$ product ion is ≤293 kcal/mol. We also note that this critical energy is close to the calculated barriers for isomerization into the H-shift isomers $\mathbf{2}^{\cdot+}$ and $\mathbf{3}^{\cdot+}$. Therefore, it is conceivable that the *m/z* 53 ion dominating the MI spectra of all three species, see Table 5, represents loss of HCN from a common reacting configuration. This, indeed, seems to be likely since the CID mass spectra of the metastably generated *m/z* 53 $C_3H_3N^{\cdot+}$ ions from $\mathbf{1}^{\cdot+}$, $\mathbf{2}^{\cdot+}$, and $\mathbf{3}^{\cdot+}$ are indistinguishable, see Fig. 2(a) for a representative spectrum. The resulting *m/z* 53 product ion is clearly not ionized acrylonitrile (ΔH_f = 296 kcal/mol [38]) as proposed by Buff and Dannacher [6]: its CID mass spectrum is shown in Fig. 2(b) and is entirely different. Instead, we propose that the ion is $H_2C{=}C{=}C{=}N{-}H^{\cdot+}$, which is calculated at the B3LYP/cc-pvdz level of theory to be 13 kcal/mol more stable than $CH_2{=}CH{-}C{\equiv}N^{\cdot+}$. The a priori plausible isomers $H{-}C{\equiv}C{-}C(H){=}N{-}H^{\cdot+}$ and $H{-}C{=}CH{-}C{=}N{-}H^{\cdot+}$ are higher in energy, by 17 and 6 kcal/mol, respectively. The CID spectrum of this cumulene type isomer is expected to be dominated by loss of H˙to produce the N-protonated cyanoacetylene product ion

Table 5
Metastable ion mass spectra of the *m/z* 80 ions $\mathbf{1}^{\cdot+}$–$\mathbf{3}^{\cdot+}$

	Isomer		
(*m/z*)	$\mathbf{1}^{\cdot+}$	$\mathbf{2}^{\cdot+}$	$\mathbf{3}^{\cdot+}$
54[b]	...	...	3
53	100 (32)[a]	100 (13)	100 (32)
52[b]	3	5	4
28[b]	...	...	1
26[b]	2	...	1

[a]Values in parentheses refer to $T_{0.5}$ values in meV.
[b]Peak may contain a CID contribution from residual collision gas.

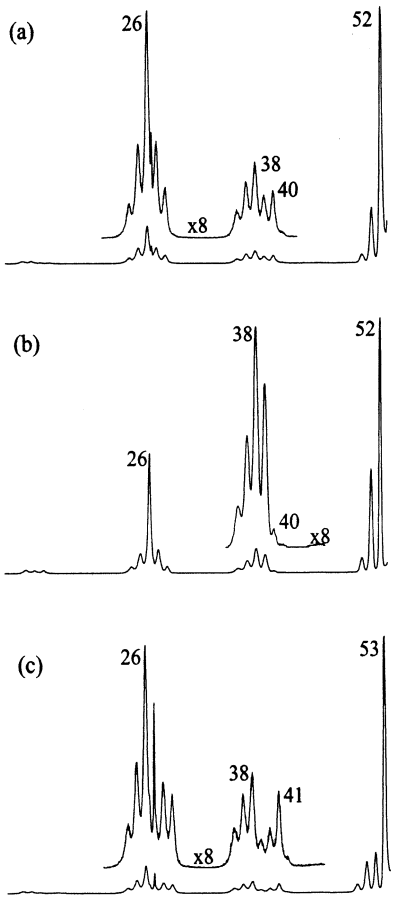


Fig. 2. CID [O_2] mass spectra (7 keV, 3ffr) of the *m/z* 53 $C_3H_3N^{\cdot+}$ ions generated from: (a) loss of HCN from 10 keV metastable ions $\mathbf{3}^{\cdot+}$; (b) electron ionization of acrylonitrile. (c) represents the CID spectrum of *m/z* 54 $C_3H_2DN^{\cdot+}$ ions generated by the specific loss of HCN from 10 keV metastable ions $\mathbf{3}^{\cdot+}$(N–D).

H–C≡C–C≡N–H^+, the direct bond cleavage of lowest energy requirement. $\Delta\Delta H_f$ [H–C≡C–C≡N–H^+ + H$^{\cdot}$] is 321 kcal/mol [38], whereas $\Delta\Delta H_f$ [HC≡$CH^{\cdot+}$ + HCN] is 349 kcal/mol; the latter process dominates the CID and MI spectra of ionized acrylonitrile. CID mass spectra of the *m/z* 54 ions generated by the specific collision-induced loss of HCN from the metastable *m/z* 81 ions of the N-D labelled isotopomers of $\mathbf{2}^{\cdot+}$ and $\mathbf{3}^{\cdot+}$ (generated from **I**-d_3 and **II**-d_3, respectively) were also obtained. These spectra, which appear to be indistinguishable, are represented by Fig. 2(c). Although they attest to the structure assignment of the product ion, mechanistic proposals for the intriguing mechanism(s) for the loss of HCN from metastable ions $\mathbf{1}^{\cdot+}$–$\mathbf{3}^{\cdot+}$ must await analysis of selected D [7] and ^{13}C labeled isotopomers of $\mathbf{1}^{\cdot+}$.

In any case, the picture that emerges from the experimental and computational results is that the H-shift isomers $\mathbf{2}^{\cdot+}$, $\mathbf{3}^{\cdot+}$ and $\mathbf{4}^{\cdot+}$ represent stable species on the $C_4H_4N_2^{\cdot+}$ potential energy surface, unambiguously characterized by their high energy collision-induced dissociation reactions into $C_2H_2^{\cdot+}$, H–C≡N–H^+ and $C_3H_4N^+$ (loss of CN$^{\cdot}$).

3.3. Generation and characterization of $C_4H_4N_2$ neutral entities

Following the successful characterization of the ionic isomers$\mathbf{1}^{\cdot+}$– $\mathbf{4}^{\cdot+}$ by CID, the NR spectra of $\mathbf{1}^{\cdot+}$– $\mathbf{3}^{\cdot+}$ were obtained to probe the structure and stability of the elusive species **2** and **3**. The NR spectra are presented in Fig. 3, together with their CID spectra obtained at the same accelerating voltage. Clearly, the NR spectra of $\mathbf{1}^{\cdot+}$ and $\mathbf{2}^{\cdot+}$, which are both dominated by an intense survivor signal, show a fragment ion distribution similar to that of their corresponding CID spectra. Thus, it may be tentatively concluded that the neutral counterpart of $\mathbf{2}^{\cdot+}$ is a stable species in the gas phase. However, the structure characteristic *m/z* 26:28 ratios in the CID spectra of $\mathbf{1}^{\cdot+}$ and $\mathbf{2}^{\cdot+}$ are not exactly reproduced in the NR spectra and this raises the question whether a partial isomerization upon neutralization takes place. This point will be addressed in the next section where the CID spectra of the survivor ions in the NR spectra are examined.

The NR mass spectrum of $\mathbf{3}^{\cdot+}$, see Fig. 3(e), is considerably different from that of $\mathbf{1}^{\cdot+}$ and $\mathbf{2}^{\cdot+}$: its survivor ion signal is of only moderate intensity relative to the fragment ions. Nevertheless, the structure diagnostic *m/z* 26:28 CID ratio has remained virtually unchanged, 0.70 ± 0.03 versus 0.75 ± 0.03 in the NR mass spectrum. The telltale peak at *m/z* 54 is also present in the NR spectrum and thus it may be tentatively concluded that pyrimidine-2-ylidene is also a stable species in the gas phase. However, further analysis of the survivor ion structure is warranted here too, since the intensity distributions of the clusters at *m/z* 36–40 and *m/z* 51–54 in the NR

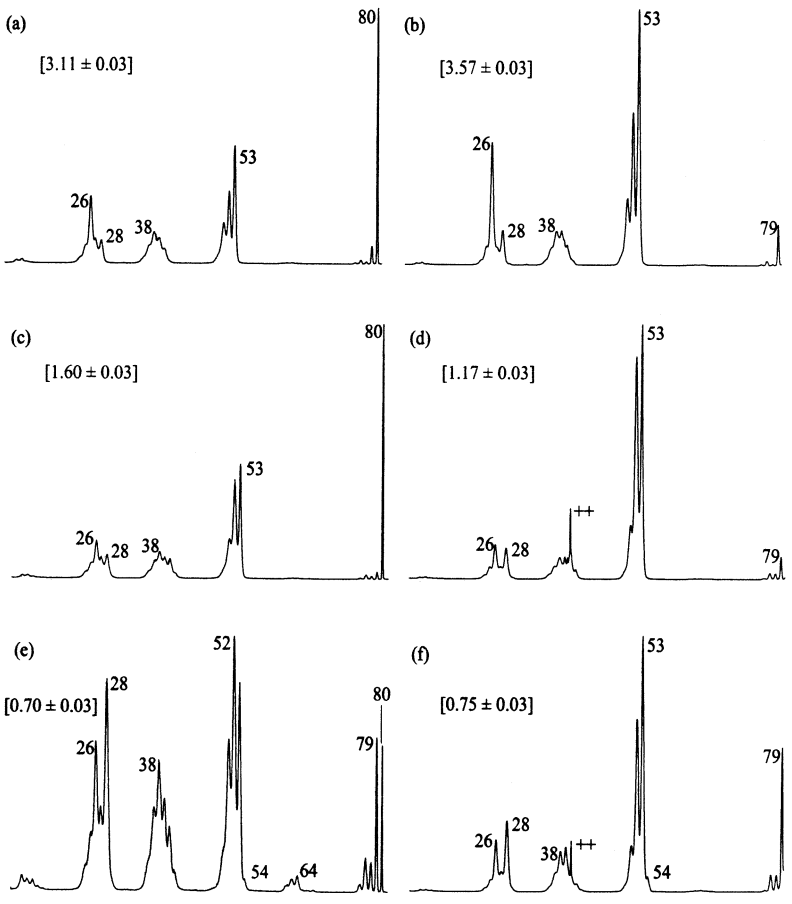


Fig. 3. NR [NDMA/O_2] and comparative CID [O_2] mass spectra (8 keV, 2ffr) of ionized pyrimidine $\mathbf{1}^{\cdot+}$, (a) and (b); ions $\mathbf{2}^{\cdot+}$ from ionized methyl-4-pyrimidinecarboxylate, (c) and (d); and ions $\mathbf{3}^{\cdot+}$ from methyl-2-pyrimidinecarboxylate, (e) and (f).

spectrum are clearly different from those in the CID spectrum.

As argued before, [18–21], a CID experiment on the mass selected "survivor" ions in a NR spectrum may facilitate the interpretation of NR spectra contaminated with reionized neutral fragments from decomposition of the incipient neutral and/or neutrals generated by collision-induced dissociation. In addition, the technique provides a useful tool to probe the isomeric purity of the source-generated ions subjected to the neutralization process and the structure integrity of the neutrals thereby produced from.

For ions $\mathbf{1}^{\cdot+}$ and $\mathbf{2}^{\cdot+}$, the (partial) NR/CID and corresponding CID mass spectra are shown in Fig. 4. The pyrimidine radicals cations, $\mathbf{1}^{\cdot+}$, display NR/CID and CID mass spectra which are essentially superimposable. Thus, in agreement with the theoretical observations discussed previously, the stable source generated ions $\mathbf{1}^{\cdot+}$ do not isomerize to any of their H-shift isomers $\mathbf{2}^{\cdot+}$– $\mathbf{5}^{\cdot+}$. The partial NR/CID mass spectrum of $\mathbf{2}^{\cdot+}$ shows a *m/z* 26:28 ratio, 1.32 ± 0.05, which is slightly but significantly higher than the structure diagnostic ratio derived from the CID spectrum, 1.16 ± 0.03. The similarity of the two spectra confirms that the ions generated in the neutralization–reionization processes are largely $\mathbf{2}^{\cdot+}$. The enhanced *m/z* 26 intensity in the NR/CID spectrum points out the presence of a small fraction of pyrimidine radical cations. One possibility is that the initial ion beam is not isomerically pure, possibly because a minor frac-

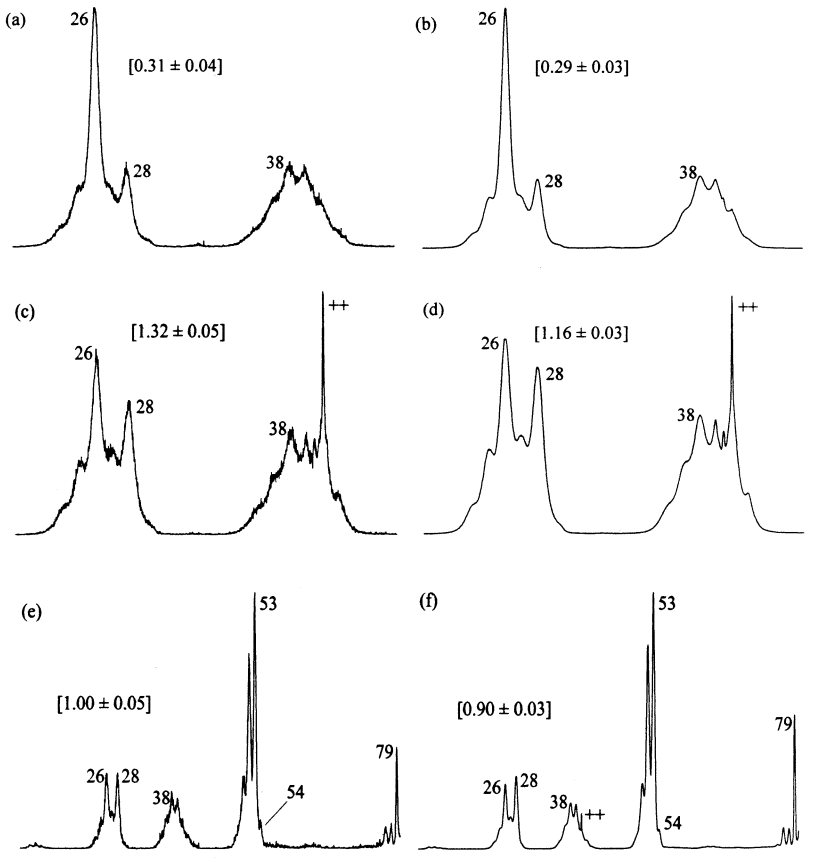


Fig. 4. NR/CID [O_2] and comparative CID [O_2] mass spectra (8 keV, 3ffr) of *m/z* 80 ions $\mathbf{1}^{\cdot+}$–$\mathbf{3}^{\cdot+}$. (a) and (b) Partial NR/CID and CID spectra of ionized pyrimidine $\mathbf{1}^{\cdot+}$; (c) and (d) Partial NR/CID and CID spectra of pyrimidine-4-ylidene ions $\mathbf{2}^{\cdot+}$; (e) and (f) NR/CID and CID spectra of pyrimidine-2-ylidene ions, $\mathbf{3}^{\cdot+}$.

tion of the methyl-4-pyrimidinecarboxylate thermally decomposes into pyrimidine prior to ionization. To test this hypothesis, the structure of the *m/z* 80 ions generated by loss of CO from metastable *m/z* 108 ions, see Scheme 2, was examined by collision-induced dissociation. The *m/z* 80 ions thereby generated from have a much lower internal energy content so that any spontaneous isomerization of the ions will be greatly suppressed. The resulting CID mass spectrum (result not shown) showed a *m/z* 26:28 ratio which is slightly, but significantly, lower than that of the source generated ions, 1.03 ± 0.04 versus 1.14 ± 0.03. This supports our proposal that the source generated *m/z* 80 ions from the ester do contain a small contribution from ionized pyrimidine. We estimate it to be ~5% based upon a linear combination of the *m/z* 26:28 CID peak intensity ratios for $\mathbf{1}^{\cdot+}$ and $\mathbf{2}^{\cdot+}$ and considering that their relative neutralization–reionization efficiency is 1.8. Thus, we conclude that pyrimidine-4-ylidene, **2**, is indeed a stable, noninterconverting, species in the rarefied gas phase.

The prior experiments further indicate that it is the singlet state of the ylide/carbene **2** which has been accessed, rather than the triplet state. From the theoretical results and the experimental ΔH_f (**1**), 47 kcal/mol [38], the heat of formation of singlet **2** is assessed as 89 kcal/mol, whereas ΔH_f = 133 kcal/mol for the triplet state. Combined with ΔH_f ($\mathbf{2}^{\cdot+}$) = 268 kcal/mol (from the calculated energy difference between $\mathbf{1}^{\cdot+}$ and $\mathbf{2}^{\cdot+}$ in Table 2 and ΔH_f ($\mathbf{1}^{\cdot+}$)=260

kcal/mol [38]), ionization energies (IEs) of ~7.7 and 5.8 eV obtain for the singlet and triplet states of **2**. The first three vertical IEs of the neutralization agent, N,N-dimethylaniline (NDMA), are 7.5, 9.0, and 9.8 eV, respectively [39]. Therefore, a close-to-resonant vertical electron transfer from NDMA to **2** is available for the formation of **2** (singlet), but not **2** (triplet). In its optimized geometry the triplet is non-planar but otherwise not greatly different from the ion structure and except for its closed carbene angle (108.4°) neither is the singlet, so unfavourable Franck-Condon factors should not militate against formation of the singlet either.

The near resemblance of the NR/CID and CID spectra of $\mathbf{3}^{\cdot+}$, compare Fig. 4(e) and (f), leaves little doubt that pyrimidine-2-ylidene, **3**, is a stable species in the gas phase too. A NR/CID spectrum of the isotopomer $\mathbf{3}^{\cdot+}$(N–D) was also obtained (spectrum not shown) and it, too, is closely similar to the CID spectrum of the source generated ions, see Fig. 1(d). There is a slight bias toward *m/z* 26 in the two NR/CID spectra, again indicative of the presence of a minor fraction of pyrimidine ions. However, unlike the situation with the ions $\mathbf{2}^{\cdot+}$, there is no evidence that the primary beam of ions $\mathbf{3}^{\cdot+}$ is contaminated with ions $\mathbf{1}^{\cdot+}$. Although the possibility cannot be ruled out that a small fraction of the incipient neutral species **3** isomerizes into the more stable pyrimidine structure, it is more likely that the collisional *ionization* event promotes the isomerization [40]. Oxidation/reduction via the triplet state is unlikely for **3** on energetic grounds. As for **2**, the singlet and triplet states of **3** have ΔH_f values of 97 and 125 kcal/mol and IEs of 7.2 and 6.0 eV, respectively. Although, the isomerization barriers for a 1,2-H transfer are also like those of **2**, a more significant difference in geometry around the site of carbene spin density may impact upon neutralization to (reionization from) singlet **3**. Based on enthalpy data (ΔH_f **2**(s) = 89 kcal/mol and $\Delta\Delta H_f$ [4-pyrimidyl]$^{\cdot}$ + H$^{\cdot}$ = 149 kcal/mol [38,41]; ΔH_f **3**(s) = 97 kcal/mol and $\Delta\Delta H_f$ [2-pyrimidyl]$^{\cdot}$ + H$^{\cdot}$ = 144 kcal/mol [38,41]) dissociation from the singlet state is comparably endothermic for both **2** and **3** since loss of H$^{\cdot}$ requires 60 and 47 kcal/mol, respectively. Thus, there is little reason to assume that the neutralization of $\mathbf{2}^{\cdot+}$ and $\mathbf{3}^{\cdot+}$ yields neutrals with a greatly different internal energy distribution and isomerization/dissociation behaviour. Nevertheless, the NR spectrum of $\mathbf{3}^{\cdot+}$ shows a much weaker survivor ion, see Fig. 3(e). This we attribute largely to the collisional *ionization* event: the degree of dissociation in the NR spectra of $\mathbf{3}^{\cdot+}$ appears to be strongly dependent on the translational energy of the neutralized ion beam. For example, the relative survivor ion intensity in the NR spectra of $\mathbf{1}^{\cdot+}$ and $\mathbf{2}^{\cdot+}$ decreases by a factor of 3 when the translational energy of the primary ion beam for neutralization is raised from 8 to 10 keV, whereas the survivor ion in the NR spectrum of $\mathbf{3}^{\cdot+}$ decreases by a factor of 8. Our interpretation is that considerably more internal energy is deposited in the collisional ionization of **3** than in that of **2** or **1** and that this causes a minor fraction of the incipient *reionized* neutrals **3** to isomerize into $\mathbf{1}^{\cdot+}$.

4. Summary

Evidence has been provided that pyrimidine-4-ylidene (**2**) and pyrimidine-2-ylidene (**3**) in their singlet states are stable, noninterconverting species in the rarefied gas phase. Access to the neutral carbene/ylides was afforded by the capability to generate essentially homogenous beams containing the stable radical cation precursors by dissociative ionization of selected molecules. Despite their elevated energies with respect to ions and neutrals **1**–**5**, isomers **6**–**9** are predicted to lie in substantial energy wells and so may also be detectable if their stable ionic counterparts can be generated in sufficient abundance, which appears an interesting challenge. Since aminocarbenes are utilitarian as ligands in transition metal catalysis complexes there may be impetus for further characterization of the pyrimidine-ylidene structures, their ionized counterparts, and their reactive behaviour.

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