

MASS SPECTROMETRIC STUDIES OF ELUSIVE MOLECULES THAT CONTAIN AN N^+-X^- BOND

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This review will be concerned with the gas phase chemistry of 1,2- and 1,3-dipolar systems that contain a carbon–nitrogen bond. Although most of these compounds are stable molecules under normal conditions, certain congeners are reactive species that cannot be prepared using conventional procedures. The isolation and observation of these elusive compounds therefore require appropriate experimental conditions such as those provided by the gas phase of a mass spectrometer. In these experiments, the radical cations, corresponding to the molecule under study, must be prepared via indirect procedures, including dissociative electron ionization, on-line flash-vacuum pyrolysis-mass spectrometry, or ion-molecule reactions. Their characterization is mainly based on collisional activation and ion-molecule reactions. The formation of the corresponding highly reactive neutrals is attempted by neutralization-reionization mass spectrometry. This review presents more than one hundred different molecules together with their methods of

preparation and the experiment used to identify them. © 2000 John Wiley & Sons, Inc., Mass Spec Rev 19, 367–389, 2000
Keywords: mass spectrometry; dipoles; collisional activation; neutralization–reionization; ion/molecule reactions; theoretical studies

I. INTRODUCTION

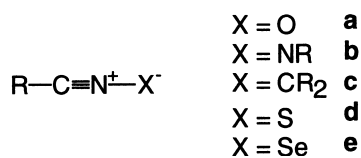
1,2-Dipolar systems that contain a carbon–nitrogen bond are well-known compounds that can formally be classified in three different families. The first important class incorporates the carbon–nitrogen triple bond as a structural feature (at least in a formal sense). These compounds are the nitrile oxides (Grundmann et al., 1971), represented by the general structure **a** and their nitrogen, carbon, sulfur, and selenium counterparts, the nitrile imines **b** (Bertrand et al., 1994), ylides **c** (Huisgen et al., 1962; Janulis et al., 1984), sulfides **d** (Paton, 1989; Wentrup et al., 1991), and selenides **e** (Pedersen, Harrit et al., 1977; Pedersen & Hacker, 1977), respectively (Scheme 1).

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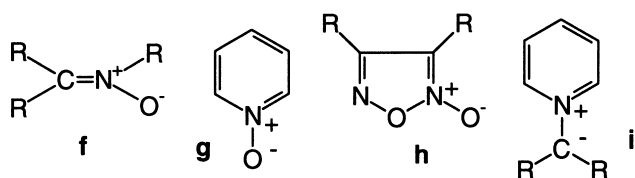
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Abbreviations are listed in the Appendix.

SCHEME 1



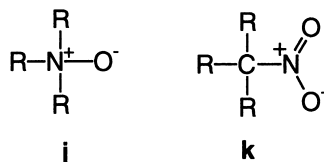
Nitrones **f** (Barton et al., 1979), heterocyclic *N*-oxides (Katritzky et al., 1971), such as azines *N*-oxides **g** or furoxans **h**, and heterocyclic *N*-ylides **i** (Linn et al., 1965; Catteau et al., 1975; Abramovitch et al., 1976) constitute the dipolar compounds that contain a carbon-nitrogen double bond (Scheme 2).

SCHEME 2



Finally, the third class incorporates species with a carbon-nitrogen single bond, such as amine oxides **j** (Barton et al., 1979) or nitro compounds **k** (Barton et al., 1979) (Scheme 3).

SCHEME 3



Most of the title compounds are stable molecules that can be prepared and stored under normal conditions. However, certain congeners are reactive species that cannot be prepared following conventional procedures. The corresponding radical cations must, therefore, be prepared *via* indirect procedures, including dissociative electron ionization, on-line flash-vacuum pyrolysis-mass spectrometry (Brown et al., 1992), or ion-molecule reactions (Stirk, Kiminkinen et al., 1992; Kenttämäa, 1994; Eberlin, 1997). Their characterization is mainly based on collisional activation (Levsen et al., 1976) and ion-molecule reactions (Stirk, Kiminkinen et al., 1992; Kenttämäa, 1994; Eberlin, 1997). High level theoretical calculations are often used in order to confirm the experimental results. The formation of the corresponding highly reactive neutrals is attempted by neutralization-reionization mass spectrometry (NRMS) (Wesdemiotis et al., 1987; Holmes, 1989; McLafferty, 1990; Plisnier et al., 1990; Goldberg et al., 1994; Schalley et al., 1998). During the past few years, NRMS has moreover been developed as an efficient method for the generation and

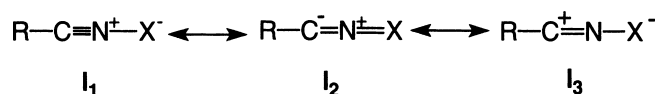
structural characterization of elusive neutral molecules and as a useful tool for probing their chemical reactivity (Schalley et al., 1998).

The aim of the present review is to make a survey of the mass spectrometric studies related to the elusive and highly reactive dipolar molecules that contain an N^+-X^- bond.

II. DIPOLAR COMPOUNDS THAT CONTAIN A CARBON-NITROGEN TRIPLE BOND

The 1,2-dipoles that contain a carbon-nitrogen triple bond can be represented as a resonance hybrid of the canonical forms shown in Scheme 4. Of these, the all-octet structures **I₁** and **I₂** contribute largely to the actual ground states of nitrile ylides, imines, oxides, sulfides, and selenides, whereas structure **I₃** accounts for the propensity of such compounds to undergo 1,3-dipolar cycloaddition (Huisgen, 1963; Huisgen, 1968). This reaction is a particularly evident and well-studied feature of the reactivity of nitrile oxides (Grundmann et al., 1971), nitrilimines (Bertrand et al., 1994), nitrile ylides (Huisgen et al., 1962; Janulis et al., 1984), and nitrile sulfides (Paton, 1989). However, nitrile selenides fail to react with dipolarophiles (Pedersen & Hacker, 1977; Pedersen, Harrit et al., 1977). That inactivity can be attributed to the fact that nitrile selenides are less stable and are more prone to fragmentation than other congeners (Pedersen & Hacker, 1977; Pedersen, Harrit et al., 1977).

SCHEME 4



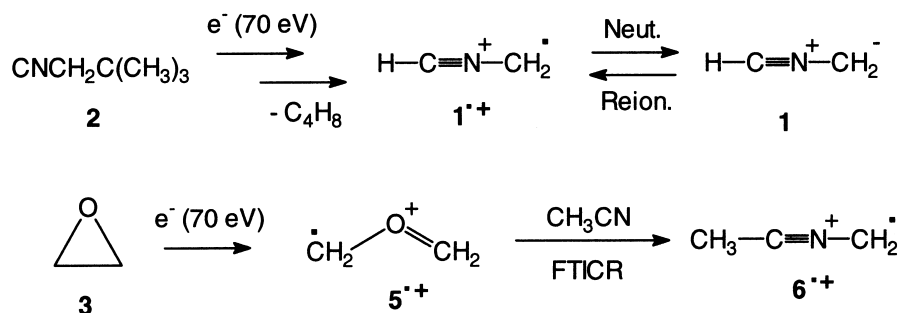
Although most of the nitrilimines (Bertrand et al., 1994) and nitrile ylides (Huisgen et al., 1962; Janulis et al., 1984) are highly reactive and, therefore, not isolable molecules. Some of them with large substituents (for instance, an adamantyl group) are isolable at room temperature, and their structures have been established by X-Ray crystallography (Janulis et al., 1984; Bertrand et al., 1994).

As far as the chalcogeno derivatives are concerned, several nitrile oxides can be isolated as solids by a judicious choice of substituents (Grundmann et al., 1969). On the other hand, nitrile sulfides are known only as reactive intermediates in solution (trapping experiments with dipolarophiles) or in matrix at low temperature (Wentrup et al., 1998). Moreover, there is good evidence for the existence of the selenide compounds at low temperatures (<100 K); however, attempts to trap them as 1,3-dipolar cycloadducts have failed so far (Pedersen & Hacker, 1977; Pedersen, Harrit et al., 1977).

A. Nitrile *N*-ylides, $R-C\equiv N^+-CR_2^-$

The unsubstituted formonitrile ylide radical cation, $H-C\equiv N^+-CH_2^-$ (**1⁺**), has been prepared in the gas phase by fragmentation of the molecular ions of 2,2-dimethylpropylisocyanide, $CN-CH_2-C(CH_3)_3$ (**2**) (Goldberg et al., 1993). These ions have been characterized by collisional activation, whereas the NRMS methodology has been used in order to obtain direct evidence for the existence of neutral $HCNCH_2$ in the gas phase (Scheme 5) (Goldberg et al., 1993). It is worth noting that the preparation of this molecule in an argon matrix (10 K), its spectroscopic identification and its theoretical relationship with other C_2H_3N isomers have been simultaneously described (Maier et al., 1993).

SCHEME 5



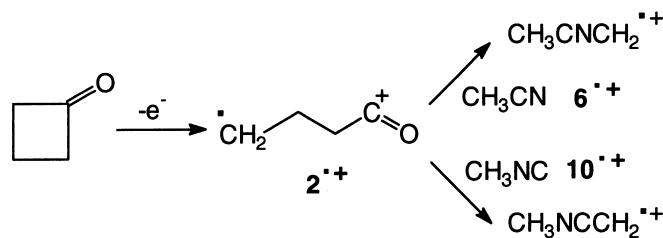
The ionization of oxirane (**3**) or 1,3-dioxolane (**4**) leads to the generation of the acyclic distonic ion $\text{CH}_2^+-\text{O}^+=\text{CH}_2$ (**5⁺**) (Bouma et al., 1978; Bouma et al., 1979; Wesdemiotis et al., 1990). The gas phase chemistry of this distonic radical cation has been extensively investigated (Corderman et al., 1976; Bouma et al., 1980; Lange 1993), and the most interesting ion-molecule reaction of **5⁺** is the net CH_2^+ transfer that leads to the formation of new distonic ions in several cases. The reaction of acetonitrile with **5⁺** has been studied in the gas phase, using FT-ICR mass spectrometry (Rusli et al., 1990). Consonant with previous studies (Corderman et al., 1976; Bouma et al., 1980; Lange, 1993), CH_2^+ is transferred to the electron lone-pair of the nitrogen atom of CH_3CN to generate $\text{CH}_3-\text{C}\equiv\text{N}^+-\text{CH}_2^-$ (**6⁺**) (Scheme 5).

These radical cations can also be prepared during the interaction between $\text{CH}_3-\text{Cl}^+-\text{CH}_2^-$ radical cations (**7⁺**) and acetonitrile (Weiske et al., 1984). The distonic ion $\text{CH}_2\text{CH}_2\text{CH}_2^+$ (**8⁺**) is now believed to be formed by the ring opening of internally excited ionized cyclopropane (Sack et al., 1985; Skancke et al., 1995; Bouchoux et al., 2000). Reactions that involve proton or CH_2^+ transfer dominate the reactions of ionized cyclopropane with many neutral molecules, including acetonitrile (Rusli et al., 1990). Rusli and Schwarz (Rusli et al., 1990) have reported a branching ratio of 10% for the transfer of CH_2^+ and 90% for the transfer of H^+ to acetonitrile.

Besides $\text{CH}_2\text{XCH}_2^+$ ions ($\text{X}=\text{O}$, **5⁺** and $\text{X}=\text{CH}_2$, **8⁺**), ionized ketene (Drewello et al., 1987) and ionized cyclobutanone (**9⁺**) (Stirk et al., 1993) have also been reported as efficient methylene transfer reagents. In fact, upon ionization, cyclobutanone spontaneously undergoes ring opening to generate the distonic ion $\text{CH}_2\text{CH}_2\text{CH}_2\text{C}^+=\text{O}$ (**9⁺**) (Boon et al., 1984; Heinrich et al., 1988; Dass et al., 1990). Acetonitrile *N*-methylide, $\text{CH}_3-\text{C}\equiv\text{N}^+-\text{CH}_2^-$ (**6⁺**), and *N*-methylketenimine, $\text{CH}_3-\text{N}^+\equiv\text{C}-\text{CH}_2^-$ (**10⁺**), radical cations have been prepared by ion-molecule reactions between **9⁺** and acetonitrile or methyl isocyanide (Scheme 6) (Gerbaux et al., 1998). The ion structures have been identified with the use of different experimental conditions that include FT-ICR experiments,

high- and low-energy collisional processes and ion-molecule reactions (dimethyl disulfide and pyridine as the neutral reagents) within a quadrupolar cell (rf-only) installed in a large-scale tandem mass spectrometer (Gerbaux et al., 1998). All experiments demonstrate that **6⁺** and **10⁺** ions are stable distonic species that do not easily interconvert (Gerbaux et al., 1998). The observation of an intense recovery signal (RS) that corresponds to survivor ions in the NR spectra of **6⁺** and **10⁺** ions indicated that neutral **6** and **10** are both stable species in the gas phase. A theoretical study has also been realized (Salpin et al., 1999).

SCHEME 6



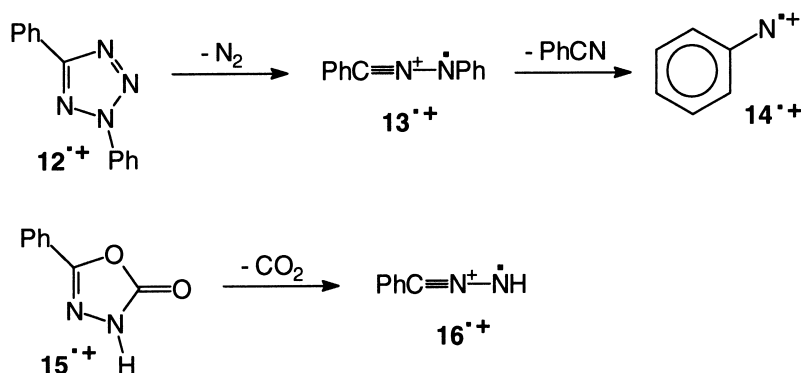
Finally, under chemical ionization conditions, the C-C ring-opened oxirane radical cations (**5⁺**) transfer a methylene group to benzonitrile (de Koster et al., 1993), yielding the *N*-methylenebenzonitrile radical cations (**11⁺**) with a high selectivity. The structures of these ions

have been established by collisionally induced dissociations of these ions compared with isomeric reference ions (de Koster et al., 1993).

B. Nitrilimines, $R-C\equiv N^+-NR^-$

The combination of collisional activation (CA) and mass-analyzed ion kinetic energy (MIKE) techniques was used to demonstrate the decay sequence (2,5-diphenyltetrazole) $^{+}$ (12^{+}) \rightarrow (diphenylnitrilimine) $^{+}$ (13^{+}) \rightarrow (phenylnitrene) $^{+}$ (14^{+}) (Scheme 7) (Wentrup et al., 1981).

SCHEME 7



Collisional activation experiments also showed that the $(M-\text{CO}_2)^+$ ions produced from the molecular ions of 2-phenyl-1,3,4-oxadiazole-5-one (**15**) have the phenylnitrilimine (**16**) structure (Scheme 7) (Maquestiau et al., 1982).

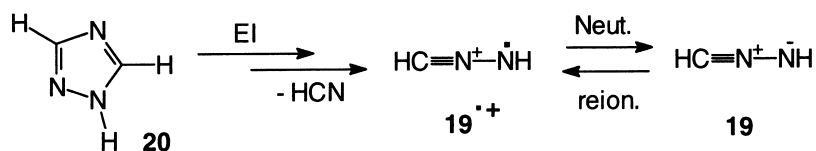
As far as the ions are concerned, the possibility to observe stable ionized nitrilimines in the gas phase seemed, therefore, confirmed. However, no direct observation of a thermally generated nitrilimine was at that time reported, and there was no evidence for the existence of discrete neutral nitrilimines in the gas phase. In order to observe a nitrilimine in thermal reactions, gas-phase

reactions proved to be the best in this respect. Flash-vacuum pyrolysis of *C*-phenyl-2-trimethylsilyltetrazole (**17**) at 710 K gave gaseous *C*-phenyl-2-trimethylsilylnitrilimine, $\text{Ph-C}\equiv\text{N}^+-\text{N}^--\text{SiMe}_3$ (**18**), which was introduced directly into the ion source of a mass spectrometer. The molecular ion from **17** disappeared as a result of the pyrolysis, leaving an intense signal that corresponded to the radical cations $18^{+\cdot}$. The collisional activation mass spectrum of $18^{+\cdot}$ was significantly different from those of the isomeric species 1-phenyl-3-trimethylsilylcarbodiimide ($\text{Ph-N}=\text{C}=\text{N-SiMe}_3$) and phenyl(trimethylsilyl)-

diazomethane ($\text{Ph-C}(\text{N}_2)\text{SiMe}_3$) (Wentrup et al., 1985).

It is obvious that NRMS represents a very useful tool when the preparation of elusive neutral molecules in the gas phase is considered. Recently, neutral HCNNH (**19**), a new isomer of diazomethane, has been generated in the gas phase by neutralization of the corresponding α -distonic ions, HCNNH^+ ($19^{+\cdot}$) (Goldberg et al., 1994). The dissociative ionization of 1,2,4-triazole (**20**) gives rise to the $19^{+\cdot}$ distonic ions (Scheme 8). The structure of these ions has been established by collisional activation experiments and comparison with the behavior of ionized diazomethane (Goldberg et al., 1994).

SCHEME 8



generation with short contact times and subsequent electron ionization was attempted. However, nitrilimines with *N*-aryl groups were observed to undergo rapid cyclization to indazoles in the gas phase (Wentrup et al., 1978). Furthermore, *N*-methyl and related nitrilimines were shown to isomerize in the gas phase to azines and carbodiimides (Fischer et al., 1980). A non-isomerizing *N*-substituent was therefore required and *N*-silyl substi-

C. Nitrile *N*-oxides, $R-C\equiv N^+-O^-$

The family of compounds with the empirical formula CHNO and their salts have played an important role in the development of chemistry. Although these compounds have been the subject of chemical research since the sixteenth century, our knowledge about them is still incomplete.

The earliest known representatives of this family are the salts of fulminic acid. The preparation of the gold salt (gold fulminate) was described by alchemists such as S. Schwartzer (active from 1585 in the court of the Saxon elector) and his contemporary, the Benedictine monk Basilius Valentinus. The mercury salt (mercury fulminate) was already known to Cornelius Drebbel (1572–1634) and to Johann Kunckel von Löwenstern (1630–1703). The interest in these salts of fulminic acid resided in their simple preparation and their usefulness as explosives (Grundmann et al., 1971).

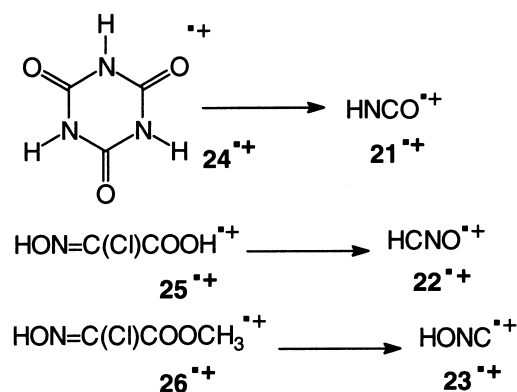
Almost two centuries later, between 1823 and 1825, the silver salts of fulminic acid and isocyanic acid were at the center of one of the most important discoveries of modern chemistry. On determining the empirical formula of silver fulminate, Liebig and Gay-Lussac observed that a year earlier Wöhler had found exactly the same composition for silver cyanate. After some less than pleasant arguments and a careful reexamination of the work of both group, Liebig and Wöhler had to recognize that, in spite of different properties, the two substances actually had the same empirical formula. One year later, the term “isomerism” was coined for this concept (Grundmann et al., 1971).

According to the IUPAC rules (IUPAC, 1969), compounds RONC are “fulminates” and hence HONC should be termed “fulminic acid”. However, HCNO is frequently called fulminic acid, following its historical trivial name. In fact, HNCO, HOCN, HCNO, and HONC are, respectively, known as isocyanic acid, cyanic acid, fulminic acid, and isofulminic acid. Because of their historic importance and their possible participation in interstellar chemistry, these four CHNO isomers have received considerable attention from theoreticians (Popinger et al., 1977; Teles et al., 1989; Pinnavaia et al., 1993; Mebel et al., 1996).

As far as the corresponding ionized species are concerned, the isomeric ions [HNCO]⁺ (**21**⁺), [HCNO]⁺ (**22**⁺) and [HONC]⁺ (**23**⁺) have been generated by dissociative ionization of cyanuric acid (**24**), chlorooximinooacetic acid (**25**) and methyl chlorooximinooacetate (**26**), respectively (Scheme 9) (Hop et al., 1989). The differentiation between these isomers has been realized by comparison of their collision-induced fragmentations. The neutralization–reionization technique was then used to identify their neutral counterparts as stable species in the gas phase (Hop et al., 1989). The ions and the corresponding neutrals were not observed to isomerize or tautomerize.

Ions of CHNO composition can also be prepared by dissociative ionization of 1,2,5-oxadiazole (Pedersen et al., 1975). However, the actual structure of the so-produced radical cations was not discussed at the time and only the mass spectrum of the heterocyclic precursor was reported.

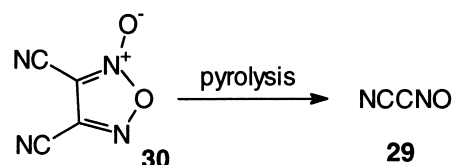
SCHEME 9



Pedersen et al. have also studied the dissociative ionization of 3,4-disubstituted-1,2,5-oxadiazoles, such as the dimethyl (**27**) and the diphenyl (**28**) species (Pedersen et al., 1975). In order to establish the structures of the ions produced from **27** to **28**, we have recently recorded their CA spectra and the observed fragmentations have been interpreted on the basis of the RCNO connectivities (R: H, CH₃ and Ph) (Gerbaux, 1999).

The cyanogen *N*-oxide NCCNO molecule (**29**) was recently identified in the gas phase (Pasinszki et al., 1995; 1996). Neutral NCCNO, generated from its stable ring dimer dicyanofuroxan (**30**) by low-pressure thermolysis, was characterized by HeI photoelectron, photoionization mass, ultraviolet, and infrared spectroscopies (Scheme 10). As far as the mass spectrometric studies were concerned, the pyrolysis tube was connected directly to the inlet of a combined HeI/HL_{α,β,γ} photoionization mass spectrometer (PIMS). Formation of **29** started at 400°C, and the conversion of **30** to **29** was complete at 550°C (Pasinszki et al., 1995; 1996).

SCHEME 10

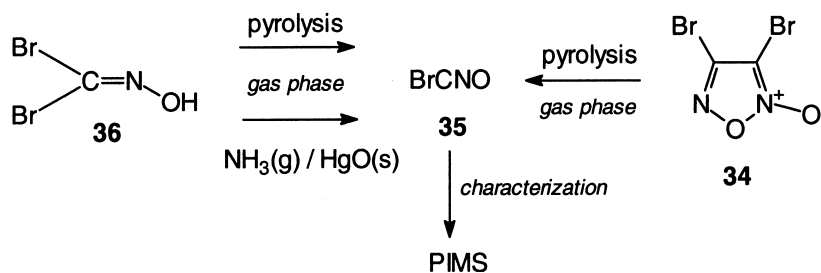


In the previous experiments, the identification of NCCNO⁺ radical cations (**29**⁺) in PIMS was based on the observation of two signals at *m/z* 68 (NCCNO⁺) and *m/z* 30 (NO⁺) (Pasinszki et al., 1995; 1996). In order to confirm unambiguously the structure of the ions produced (and thus the structure of the pyrolysis product) and that no isomerization to the more stable NCNCO isomer (Feher et al., 1995) occurs, pyrolysis of **30** was followed by tandem mass spectrometry (Flash–vacuum pyrolysis/MS/MS (Brown et al., 1992)). In such experiments, the structure of the pyrolysis product was deduced from a

collisional activation experiment performed on-line on the corresponding radical cations (29^+). The fragments observed in the CA spectrum of $C_2N_2O^+$ ions were consistent with the proposed NCCNO connectivity. However, a peak of low intensity at m/z 40 (loss of CO) suggested a partial contribution of isomeric NCNCO $^+$ ions (Flammang et al., 1997). Pure NCCNO $^+$ ions (29^+) can be produced by dissociative ionization of 3,4-dicyano-1,2,5-oxadiazole (**31**). Neutralization–reionization has, moreover, confirmed the stability of neutral NCCNO in the gas phase (Flammang et al., 1997).

Pasinszki et al. (1995) also reported the gas phase generation of a quite similar species—the cyanogen di-*N*-oxide molecule, ONCCNO (**32**). This unstable compound was produced in high yield from *in situ* flow pyrolysis reactions of gaseous dichloroglyoxime (**33**) or dibromofuroxan (**34**) precursors (Pasinszki et al., 1995). This structurally novel transient species was characterized *inter alia* by HeI/HL $_{\alpha}$ PIMS. Actually, these spectra were found very simple and confirmed the identification of ONCCNO $^+$ (32^+) radical cations. Indeed, the molecular ions (m/z 84) and only two fragments (NO $^+$ and ONCC $^+$) were detected with HeI radiation. Fragmentation is usually reduced with HL $_{\alpha}$ radiation, and this phenomenon was reflected by a strong increase of the precursor ions and the disappearance of the ONCC $^+$ fragments (Pasinszki et al., 1995).

SCHEME 11



Finally, the haloformonitrile oxide, BrCNO (**35**), was also generated in the gas phase by (i) thermolysis or base treatment (gaseous ammonia or solid HgO) of gaseous dibromoformaldoxime (**36**) or (ii) by thermolysis of dibromofuroxan (**34**) (Pasinszki et al., 1995). HeI/HL $_{\alpha}$ PIMS was also used in this case to elucidate the structure of **35** (Pasinszki et al., 1995) (Scheme 11).

D. Nitrile *N*-sulfides, R-C≡N $^+$ -S $^-$

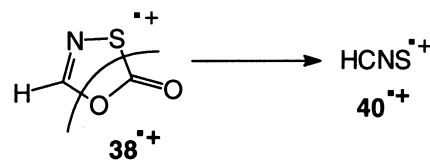
In contrast to the well-known nitrile *N*-oxides, the *N*-sulfides are short-lived intermediates that cannot usually be identified under ordinary reaction conditions (Paton 1989; Wentrup et al., 1991). This relative unstability is caused by the bonding arrangement in *N*-sulfides that

involves an S-atom, at the negative end of the dipole of the coordinate C≡N→S, with an electronegativity smaller than that of the N atom. Another molecule that shows this unusual type of bonding is dinitrogen *N*-sulfide, N≡N→S. N $_2$ O is a particularly stable and unreactive molecule. In contrast, N $_2$ S is a reactive species that has only recently been spectroscopically detected (Wentrup et al., 1986; Bender et al., 1988). This molecule was produced by flash–vacuum pyrolysis of 5-phenyl-1,2,3,4-thiaziazole (**37**) and identified, *inter alia*, by on-line mass spectrometry (Wentrup et al., 1986; Bender et al., 1988).

As a general rule, nitrile *N*-sulfide radical cations can be directly prepared by dissociative ionization of heterocyclic precursors that contain the CNS linkage. For instance, after electron ionization, 1,3,4-oxadiazole-2-one (**38**) eliminates CO $_2$, yielding CHNS $^+$ radical cations (Kambouris et al., 1991). In order to determine the structure of the so-produced ions, their collisional activation spectrum was compared to the CA spectrum of reference HNCNS $^+$ (39^+) radical cations. Both spectra were found to be remarkably different—the signal at m/z 44 (CS $^+$) observed in the CA spectrum of HNCNS $^+$ (39^+) ions was replaced by a strong peak at m/z 46 that corresponded to NS $^+$ cations for the *N*-sulfide ions. Given the structure of the starting material (**38**). This clear difference demonstrated that the m/z 59 ions, formed by fragmentation of **38**, have the HCNS $^+$ structure (40^+)

(Scheme 12) (Kambouris et al., 1991). Finally, the neutral counterpart was generated in the diluted gas phase by collision-induced neutralization of a beam of fast 40^+ ions (NRMS experiment) (Kambouris et al., 1991).

SCHEME 12



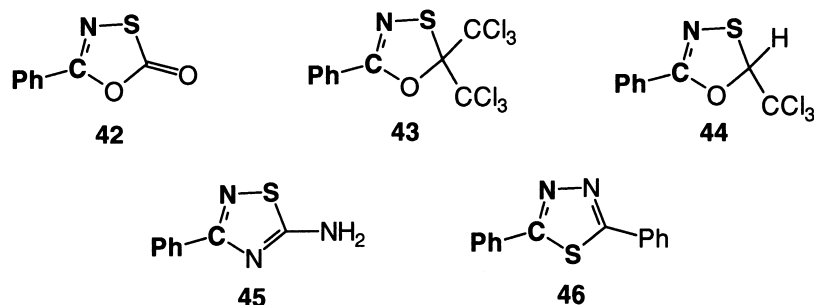
Benzonitrile *N*-sulfide radical cations, PhCNS $^+$ (**41 $^+$**), were generated, in a similar way, by electron ionization of several heterocyclic precursors such as those

(42–46) presented in Scheme 13 (Maquestiau et al., 1990). Again, the connectivity of the so-produced ions was established by collisional activation and comparison with the fragmentation observed in the case of the isomeric ions—ionized phenylthiocyanate (47) and phenylisothiocyanate (48).

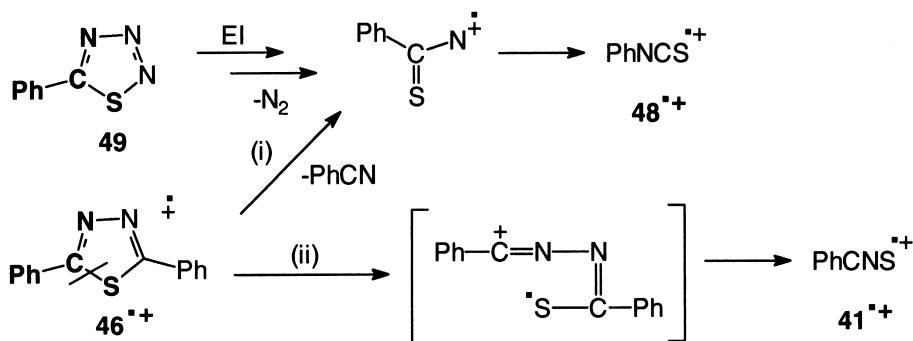
reionization mass spectrometries have allowed the identification of nitrile *N*-sulfides (NCCNS, CH₃SCNS and ClCNS) as ions and neutrals (Scheme 15) (Flammang et al., 1996).

As far as 4-carboxamido-5-cyano-1,2,5-thiadiazole (54) was concerned, the behavior was found to be more

SCHEME 13



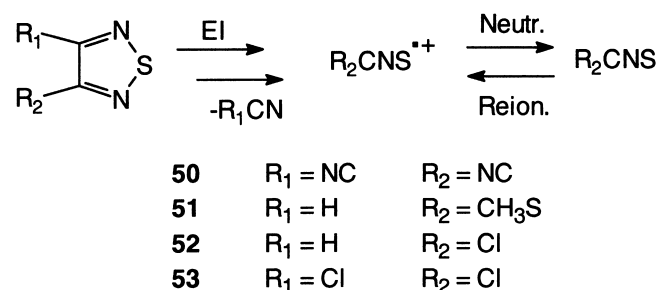
SCHEME 14



Considering the structure of the precursor molecule 46, it was expected that the structure of the C₅H₅NS⁺ ions derived therefrom would be identical to that of the [M-N₂]⁺ ions generated from the thiaziazole 49 (Scheme 14). The so-produced ions were identified as the molecular ions of phenylisothiocyanate (48) by collisional activation (Maquestiau et al., 1990). The production of these ions implies that the thiobenzoyl nitrene radical cation undergoes a Curtius-type rearrangement into 48⁺. However, the ionization of 46 and the subsequent loss of benzonitrile produces a mixture of 41⁺ and 48⁺, which have been proposed to be formed via pathways (i) and (ii) depicted in Scheme 14 (Maquestiau et al., 1990). Anyway, the NRMS methodology was also used to probe the gas-phase stability of the neutral molecule, 41.

Recently, we used 3,4-disubstituted-1,2,5-thiadiazoles (50–53) to produce in the gas-phase a series of new ionized nitrile *N*-sulfides (Flammang et al., 1996). 1,2,5-thiadiazoles (50–53) that bear CN, SCH₃, and Cl substituents were investigated under electron ionization conditions. Collisional activation and neutralization–

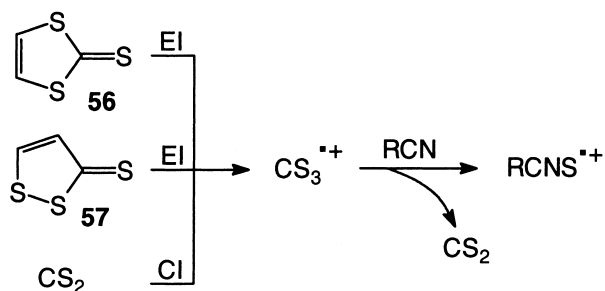
SCHEME 15



complex. Metastable molecular ions of 54 eliminate carbon monoxide, and formation of 4-amino-5-cyano-1,2,5-thiadiazole radical cations (55⁺) was proposed. A very small peak (*m/z* 74, about 1%), corresponding to a consecutive fragmentation (loss of cyanogen) of these ions, was also observed in the mass spectrum of 54. The collisionally induced dissociations of these radical cations were ascribed to the cyanamide *N*-sulfide structure, NH₂CNS (Flammang et al., 1996).

These results were supported by chemical ionization of nitriles, using carbon disulfide as the reagent gas (Flammang et al., 1996). Several ions are produced in the source during the self-chemical ionization of carbon disulfide (Praet et al., 1990). The most important ion-molecule reaction yields m/z 108 radical cations, CS_3^+ (Praet et al., 1974). Their CA spectrum suggested the carbon *S*-sulfide connectivity, SCSS, but a similar pattern can also be expected for the isomeric carbon trisulfide, SC(S)S (Gerbaux et al., 1997). In fact, very similar CA spectra of the CS_3^+ ions were obtained upon dissociative ionization of the isomeric dithiolethiones **56** and **57** (Scheme 16) (Sülzle et al., 1990). Whatever the actual structure of these CS_3^+ radical cations is, the main important feature, as far as the present review is concerned, is that these CS_3^+ ions (or part of these) readily react with nitriles by sulfur transfer (Scheme 16) (Flammang et al., 1996; Gerbaux et al., 1997).

SCHEME 16



This reaction (Gerbaux et al., 1997) was studied with a new kind of hybrid mass spectrometer of EBEqEBE geometry (E stands for electric sector, B for magnetic sector, and q for an rf-only quadrupolar collision cell) (Figure 1) (Bateman et al., 1992; Flammang et al., 1995). Briefly, the experiments on the quadrupole consist of the selection of a beam of fast ions (8 keV) with the three first sectors ($E_1B_1E_2$), the retardation of these ions to *ca.* 5 eV, and the reaction with a reagent gas in the cell (pressure of the reagent gas is estimated to be *ca.* 10^{-3} Torr). After reacceleration to 8 keV, all the ions present in the quadrupole are separated and mass measured by scanning the field of the second magnet. More interestingly, the high energy CA spectra of these ions can be recorded by a linked scanning of the three last sectors ($E_3B_2E_4$) or by a conventional scanning of the field of the last electric sector after mass selection with the second magnet (Figure 1) (Bateman et al., 1992; Flammang et al., 1995). The sulfur-transfer reaction was performed in the chemical ionization source of this spectrometer and also in the quadrupolar cell in very high yield (Flammang et al., 1996; Gerbaux et al., 1997). The CS_3^+ ions were found to be very efficient agents for this S^+ transfer to the nitrogen of nitriles; thus giving nitrile *N*-sulfide radical cations, $RCNS^+$ ions

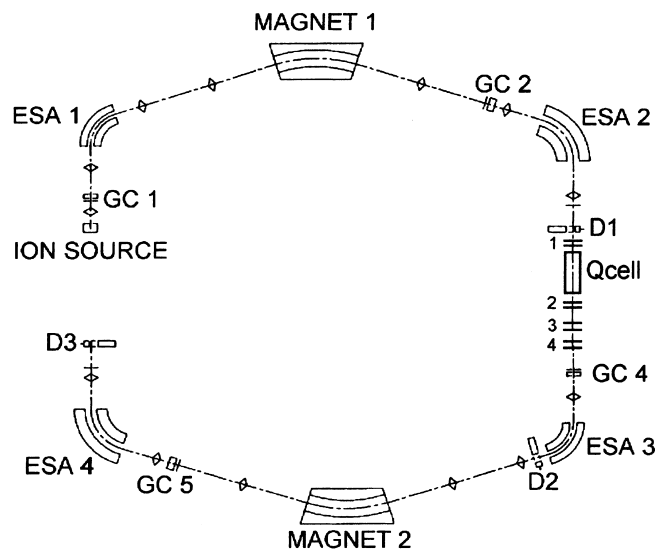


FIGURE 1. Schematic representation of the Mons' AutoSpec 6F mass spectrometer in the hybrid configuration with added Qcell. ESA = electrostatic sector, Magnet = magnetic sector, 1 = deceleration lenses, 2 = acceleration lenses, 3 = Y/Z lenses, 4 = demagnification lenses, D = off-axis detector and Qcell = quadrupolar cell.

($R=H, CH_3, C_2H_5, C_3H_7, C_6H_5, Cl, Br,$ and I). The connectivity of the so-produced ions was probed by collisional activation and comparison with the CA spectra of isomeric isothiocyanate radical cations, $RCNS^+$. The corresponding neutral molecules were found by NRMS to be viable species in the gas phase (Flammang et al., 1996; Gerbaux et al., 1997). More recently, methyl cyanate *N*-sulfide radical cations, CH_3OCNS^+ , were prepared by dissociative ionization of 3,4-dimethoxy-1,2,5-thiadiazole (**58**) (Flammang et al., 1999). It is important to note that, during this work, neutral and ionic methoxy isothiocyanate, CH_3ONCS , were generated for the first time (Flammang et al., 1999).

The characterization of nitrile *N*-sulfide molecular ions can also be achieved by the study of associative ion-molecule reaction between these ions and nitric oxide as the reagent gas (Flammang et al., 1999; Gerbaux, 1999). For instance, when a beam of CH_3OCNS^+ radical cations is allowed to interact with nitric oxide, in an rf-only quadrupole cell or in an FT-ICR cell, the major ion-molecule reaction observed is a S^+ transfer to nitric oxide to generate ON^+S cations (m/z 62). In contrast, isomeric CH_3ONCS^+ ions only react with nitric oxide by charge exchange (Flammang et al., 1999). This contrasting behavior is easily explained on the basis of ionization energies: the IE of methoxyisothiocyanate and methyl cyanate *N*-sulfide have been estimated to 9.0 eV and 8.1 eV by *ab initio* calculations (Flammang et al., 1999), whereas the IE of nitric oxide amounts to 9.25 eV (Lias

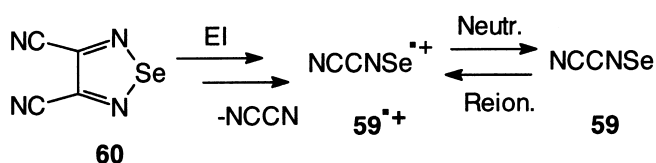
et al., 1999). It is important to note that the IEs of the nitrile *N*-sulfides are usually lower than the IEs of the corresponding isothiocyanates by *ca.* 0.8 eV (Flammang et al., 1996; Gerbaux, 1999).

E. Nitrile *N*-selenides, R-C≡N⁺-Se⁻

As already mentioned, nitrile *N*-selenides were elusive compounds that were never isolated nor directly observed (Pedersen & Hacker, 1977; Pedersen, Harrit et al., 1977).

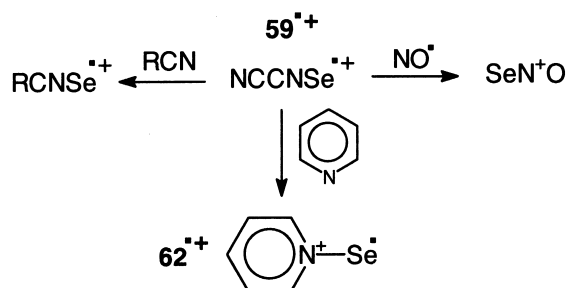
Recently, cyanogen *N*-selenide radical cations, NCCNSe^{•+} (**59**⁺), was directly prepared in an EI source by dissociative ionization (loss of cyanogen) of 3,4-dicyano-1,2,5-selenadiazole (**60**) (Scheme 17) (Gerbaux et al., 1998). The collisional activation spectrum of the so-produced *m/z* 132 ions indicated the NCCNSe connectivity as evidenced by the observed collision-induced fragmentations: loss of NC[•], loss of [•]CCN, and production of cyanogen ions (Gerbaux et al., 1998). This spectrum was *inter alia* compared to that of NCSeCN⁺ (**61**⁺) isomeric ions. The latter ions can be easily prepared by direct ionization of the neutral molecule, NCSeCN, obtained by reacting cyanogen bromide with potassium selenocyanate in ether (Hauge, 1979). The main difference between both spectra is that the prominent fragmentation in the case of NCCNSe^{•+} (**59**⁺) is the loss of neutral cyanogen, whereas the base peak in the spectra of NCSeCN⁺ (**61**⁺) corresponds to the loss of NC[•] (Gerbaux, 1999).

SCHEME 17



The NR spectrum of these **59**⁺ radical cations, obtained by consecutive collisions with xenon and oxygen, features a weak but significant recovery signal. The decreasing intensity of the recovery signal in the NCCNX series X=O (Flammang et al., 1997), S (Flammang et al., 1996), and Se (Gerbaux et al., 1998)) is consistent with theoretical calculations that show that the energy requirement for the dissociation into NCCN+X decreases with the electronegativity of X; however, the process remains endothermic in the three cases. It was indeed found, at the G2(MP2,SVP) level of theory, that the endothermicities of the reaction NCCNX→NCCN+X follow the sequence O > S > Se, being respectively 415, 244, and 187 kJ/mol (Flammang et al., 1997). This result is, moreover, in connection with the relative stabilities of RCNX species in the condensed phase (*vide supra*).

SCHEME 18



The associative ion-molecule reactions of NCCNSe^{•+} (**59**⁺) with several neutral reagents were investigated (Gerbaux et al., 1998). **59**⁺ Radical cations react with nitriles by Se^{•+} transfer, generating the corresponding nitrile *N*-selenides. This peculiar behavior was also observed when the interaction between these **59**⁺ ions and nitric oxide or pyridine was performed in a quadrupolar collision cell (Scheme 18) (Gerbaux et al., 1998). The interaction between NCCNSe^{•+} (**59**⁺) and pyridine leads to new distonic ions—the molecular ions of pyridine *N*-selenide (**62**^{•+}) (*vide infra*).

As far as the Se^{•+} transfer to nitriles is concerned, this reaction was used in order to prepare in the gas phase (CI source or quadrupolar cell) several nitrile *N*-selenide radical cations, RCNSe^{•+} (R=H, CH₃, NH₂, Cl, Br, I, Ph, and CH₃S) (Gerbaux et al., 1998). The connectivities of all these ions were established by collisional activation.

Some reference ions were prepared by dissociative ionization or selenation of isonitriles. Indeed, the molecular ions of the selenadiazole **63** give HNCSe^{•+} (**64**^{•+}) through a complex sequence of reactions that involved probably an [1,4] hydrogen transfer on the ring nitrogen and the losses of HNCS and cyanogen (Scheme 19). The CA spectrum of these ions was compared to that of the HCNCSe^{•+} (**65**^{•+}) obtained by Se^{•+} transfer to HCN. The signal that corresponded to the loss of HC (NSe^{•+}) is replaced in the case of **64**^{•+} ions by a loss of HN (CSe^{•+}) indicative of the isoselenocyanate structure (**64**). Methyl isoselenocyanate, CH₃NCSe^{•+} (**66**^{•+}), and phenyl isoselenocyanate, PhNCSe^{•+} (**67**^{•+}) were prepared in very good yield by direct selenation of the corresponding isonitriles (Gerbaux et al., 1998). The differentiation between CH₃CNCSe^{•+} (**68**^{•+}) or PhCNCSe^{•+} (**69**^{•+}), obtained by Se^{•+} transfer to acetonitrile or benzonitrile, and CH₃NCSe^{•+} (**66**^{•+}), or PhNCSe^{•+} (**67**^{•+}) was readily confirmed after recording the CA spectra of both isomers (Gerbaux et al., 1998).

The interaction between RCNSe^{•+} radical cations and nitric oxide can also be used when the structural characterization of the *N*-selenide connectivity is attempted. Indeed, competitively with charge exchange, SeNO⁺ cations are generated during the interaction between RCNSe^{•+} radical cations and nitric oxide in the quadru-

pole cell. However, no SeNO^+ cations are detected when the isomeric RNCSe^+ ions interact with this neutral reagent (Gerbaux, 1999).

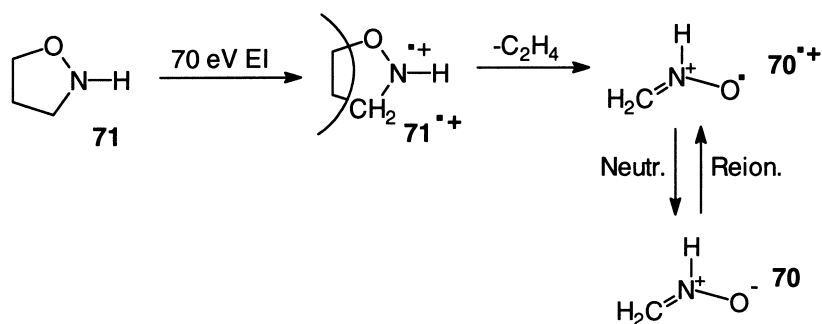
SNO^+ formation is also a prominent process when RCNS^+ radical cations are allowed to react with nitric oxide (*vide supra*), whereas NO^+ is the major product in the case of nitrile oxide molecular ions (Flammang et al., 1997; Gerbaux, 1999). These different reactivities were tentatively explained on the basis of the N–X (X=O, S, and Se) bond lengths in the case of the NCCNX^+ radical cations. Indeed, these N–X bond lengths are 1.237 Å, 1.685 Å, and 1.857 Å for, respectively, NCCNO^+ , NCCNS^+ , and NCCNSe^+ radical cations (Flammang, et al., 1997; Gerbaux, 1999). When compared to the lengths of the double N=X bonds in H–N=X —1.237 Å, 1.59 Å, and 1.754 Å for, respectively, HNO, HNS, and HNSe—the N–O bond in NCCNO^+ is clearly a double bond, whereas this N–X bond is best described as a single bond in the case of the sulfur and selenium compounds. The double character of the N–O bond in NCCNO^+ could explain the observed different chemical behaviors (Flammang et al., 1997; Gerbaux, 1999).

III. DIPOLAR COMPOUNDS CONTAINING A CARBON-NITROGEN DOUBLE BOND

A. Non-cyclic Compounds

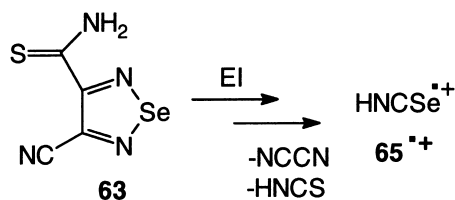
Formaldonitrone, $\text{CH}_2=\text{N}(\text{H})\text{–O}$ (**70**), the hitherto elusive simplest organic nitron, was prepared transiently in the gas phase by femtosecond collisional neutralization of its radical cation (Polasek et al., 2000). NRMS studies rely on an unambiguous generation of a precursor ion. Formaldonitrone ions were produced by ring cycloreversion in 1,2-oxazolidine radical cation (**71**^{•+}) (Scheme 20) and were characterized by collisionally activated dissociation mass spectra and *ab initio* calculations. Nitron **70** was found to be remarkably stable in an isolated state in sharp contrast with the high reactivity of nitron in the condensed phase. This stability was confirmed by the presence in the NR spectrum of a very intense recovery signal. On the other hand, the unimolecular decomposition of neutral **70** and reionized **70**^{•+} were distinguished by variable time measurements. The obtained data clearly showed that dissociation of neutral **70** was negligible and, therefore, that most of the NR products were formed

SCHEME 20



Finally, the stability of neutral nitrile *N*-selenides was probed by NRMS and *ab initio* calculations. The neutral nitrile *N*-selenides were found by experiment and theory to be observable species in the gas phase (Gerbaux et al., 1998). These experiments have constituted the first direct observation of these elusive intermediates (Pedersen and Hacker, 1977; Pedersen, Harrit et al., 1977).

SCHEME 19



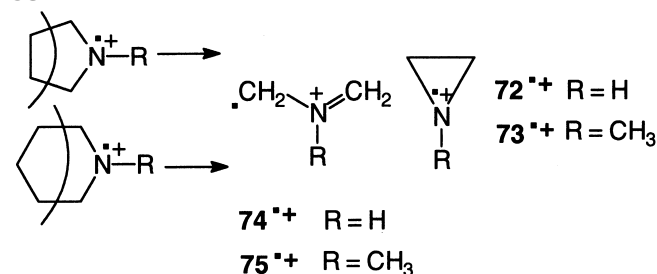
after collisional reionization (Polasek et al., 2000). It was demonstrated that vertical electron capture in **70**^{•+} was accompanied by unusually small Franck–Condon effects, as documented by very similar adiabatic ionization ($\text{IE}_a(\mathbf{70}) = 9.40 \text{ eV}$) and vertical recombination ($\text{RE}(\mathbf{70}) = 9.35 \text{ eV}$) energies (Polasek et al., 2000). Hence, **70** formed in the ground electronic state should be stable (Polasek et al., 2000).

The ring-opened isomers of aziridine (**72**) and *N*-methylaziridine (**73**) radical cations, respectively **74**^{•+} and **75**^{•+}, have been tentatively suggested to be formed when ionized pyrrolidines and piperidines dissociate in the mass spectrometer ion source (Scheme 21) (Duffield et al., 1965). Electron paramagnetic resonance studies indicated that aziridine radical cations (**72**^{•+}) formed in frozen freon

matrix undergo spontaneous ring opening (to give **74**⁺) (Qui et al., 1986). On the basis of kinetic energy release measurements, Holmes and Terlouw came to the conclusion that the aziridine radical cation (**72**⁺) and **74**⁺ are indistinguishable (Holmes, et al., 1976). However, collisional activation and charge-stripping experiments indicated that gas-phase aziridine radical cations (**72**⁺) and the isomeric distonic ions **74**⁺ (prepared from pyrrolidine or piperidine) are different species and, therefore, that stable **72**⁺ ions do not ring open (Maquestiau et al., 1979). This conclusion was, moreover, supported by calculations (Lien et al., 1984) and by NRMS experiments (Shaffer et al., 1993). Indeed, it was demonstrated that the behaviors upon NRMS of the molecular ions of aziridine (**72**⁺) and of the open-ring form (**74**⁺) are quite different. Differences are particularly observed in the relative abundances of the survivor ions; the order of the survivor ion relative intensities being **74**⁺ > **72**⁺. These differences were explained on the basis of Franck-Condon effects. Actually, calculations showed very significant Franck-Condon effects in the neutralization and reionization of aziridine, but not in the case of singlet $\text{CH}_2\text{NHCH}_2^{\cdot}$ (**74**) (Shaffer et al., 1993).

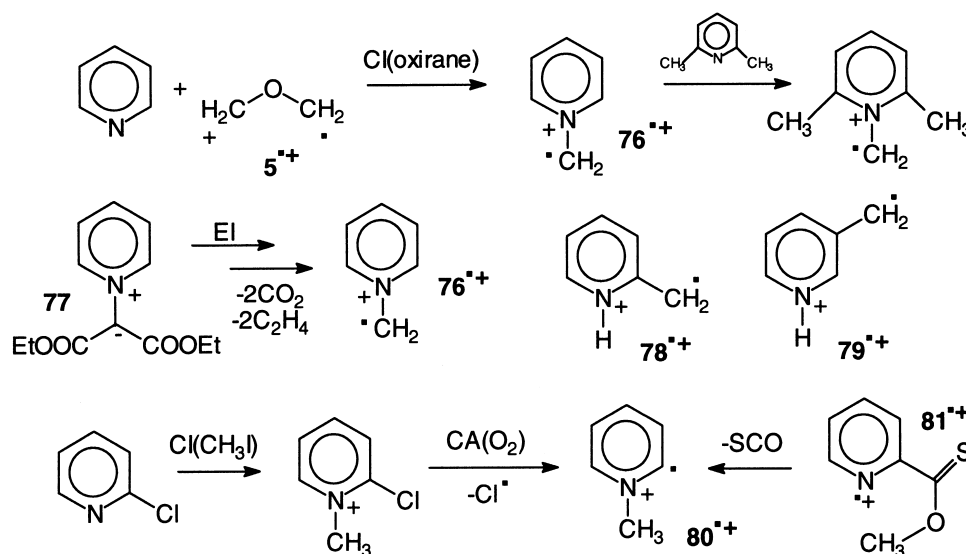
More recently, Hammerum et al. examined the methylated species, **73**⁺ and **75**⁺ generated from ionized *N*-methylpiperidine or *N*-methylpyrrolidine (Scheme 21) (Hammerum et al., 2000). They showed that both radical cations are not distinguishable on the basis of their collision-induced behavior. The authors concluded that *N*-methylaziridine (**73**) undergoes spontaneous ring opening upon ionization. However, the energy barrier for the ring opening of **73**⁺ ions into the more stable **75**⁺ ions was estimated to amount to 63 kJ/mol (Hammerum et al., 2000). Therefore, it is better to suggest that the

N-methylaziridine molecular ions (**73**⁺) can undergo spontaneous ring opening to **75**⁺ below the threshold for fragmentation.

SCHEME 21


B. 6-Membered Heterocyclic Compounds

Upon chemical ionization conditions, the C-C ring-opened oxirane radical cation **5**⁺ transfers an ionized methylene group to pyridine (Scheme 22). This reaction leads to the regioselective formation of the 1-methylene-pyridinium radical cation **76**⁺. Experimental evidence for this ion arose from collisional activation of the reaction product ions compared with the 2-, 3-, and 4-picoline (de Koster et al., 1990). The so-produced distonic ions can be distinguished from isomeric picoline molecular ions because the former gave characteristic $[\text{M}-\text{CH}_2]^+$ and a doubly charged ion, after collisional activation. Moreover, Yu et al. found out that the **76**⁺ ions could also be prepared during the reaction between the radical cations of cyclopropane, ketene, or the C_3H_6^+ ions generated by fragmentation of ionized tetrahydrofuran, with neutral pyridine (Yu et al., 1993). Furthermore, the distonic species quantitatively transfers CH_2^+ to more nucleophilic, substituted pyridines, such as 2,6-dimethylpyridine (Scheme 22).

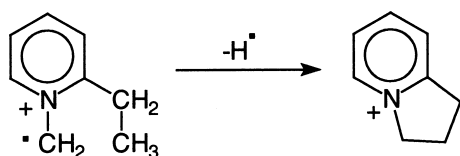
SCHEME 22


The 1-methylenepyridinium radical cation $76^{+\bullet}$ can also be obtained in electron ionization conditions: the molecular ions of bis(ethoxy-carbonyl)pyridinium methylene ($77^{+\bullet}$) expel carbon dioxide and ethene, generating $76^{+\bullet}$ radical cations (Scheme 22) (Flammang et al., 1992). In this study, collisional activation and charge-stripping mass spectra have allowed the identification of six $[C_6H_7N]^+$ isomers; namely, the molecular ions of the three picolines, ionized 2- ($78^{+\bullet}$) and 3-methylene dehydropyridines ($79^{+\bullet}$), and ionized pyridinium methylene ($76^{+\bullet}$). More recently, the missing *N*-methylpyridinium ylid ($80^{+\bullet}$) ion was prepared by (i) dissociative ionization of methyl-2-pyridinethiocarboxylate (**81**) (Lavorato et al., 2000); or (ii) by collision-induced dechlorination (oxygen is required as the target gas) of *N*-methylated 2-chloropyridine (Gerbaux et al., 1999) (Scheme 22).

The NRMS results suggested that neutral pyridinium methylene (**76**) is a stable molecule when isolated in the rarefied gas phase of the mass spectrometer (de Koster et al., 1990). The existence of this intermediate was previously proposed to explain some condensed-phase reactions (Daniels et al., 1960). For instance, diazomethane, CH_2N_2 , was found to react with pyridine to yield 2-picoline. The high yield and specificity of attack at the 2-position seem to be in variance with the carbonium ion properties associated with carbenes and with the preferential electrophilic substitution of pyridine at the 3-position. In fact, the results described were explained by an initial attack of carbene at the nitrogen atom of pyridine, giving **76** as intermediate, followed by an intramolecular rearrangement (Daniels et al., 1960).

CH_2^+ transfer from 5^+ radical cations to several substituted pyridines was investigated by multistage mass spectrometric experiments performed in a pentaquadrupole mass spectrometer (Gozzo et al., 1995). Reactions with pyridine, 2-, 3- and 4-ethyl-, 2-methoxy-, and 2-*n*-propyl pyridines occur mainly by transfer of CH_2^+ to the nitrogen, which yields distonic *N*-methylene pyridinium ions. The MS/MS/MS spectra of these products displayed very characteristic collision-induced dissociation chemistry, which is greatly affected by the position of the substituent on the pyridine ring. *Ortho* isomers undergo a δ -cleavage-cyclization process induced by the free-radical character of the methylene group (for instance, see Scheme 23). Bicyclic pyridinium cations are obtained (Gozzo et al., 1995).

SCHEME 23



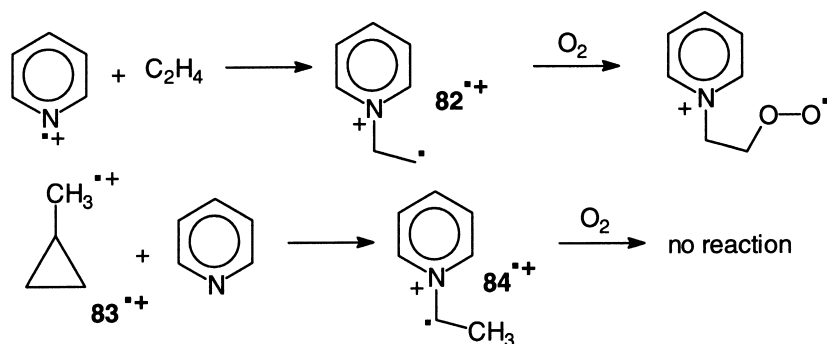
The reaction of the pyridine radical cation with neutral ethene yields an aromatic β -distonic ion, $C_5H_5N^+-CH_2CH_2$ ($82^{+\bullet}$) (Scheme 24). The CA spectrum of these latter ions is distinctively different from the CA spectra of the conventional isomers—the ethylpyridine radical cations. The so-produced β -distonic ion was also compared to another distonic structural isomer, that is directly related to the subject of this review: the reaction between ionized methylcyclopropane ($83^{+\bullet}$) and neutral pyridine affords an α -distonic ion, $C_5H_5N^+-CH-CH_3$ ($84^{+\bullet}$) (Yu et al., 1993) (Scheme 24). $82^{+\bullet}$ and $84^{+\bullet}$ radical cations were, moreover, clearly differentiated by studying their associative bimolecular chemistry with oxygen. To probe the structure and reactivity of both distonic ions, dioxygen was chosen because it is a diradical, and distonic ions are expected to be reactive at their radical site (Stirk, Kiminkinen et al., 1992; Kenttämäa, 1994). Whereas $82^{+\bullet}$ reacts with dioxygen to yield an adduct $[M+O_2]^+$, the isomeric ions ($84^{+\bullet}$) were totally unreactive toward the neutral reagent (Yu et al., 1993). A possible explanation is that the radical site is delocalized in this system, whereas the radical site is isolated from the ring in the β -isomer.

It is known that a significant portion of the m/z 58 ionic population generated from 4-methyl-1,3-dioxolane (**85**) has the C–C ring-opened form (i.e., the distonic ion $^+CH_2-O-CH-CH_3$ ($86^{+\bullet}$)) (van de Guchte et al., 1990). These ions, by analogy with the behavior of $CH_2^+-O-CH_2$ (5^+) (Corderman et al., 1976; Bouma et al., 1980; Lange 1993), react with neutral pyridine—both by CH_2^+ and $CH-CH_3^+$ transfers. As expected, $84^{+\bullet}$ radical cations are generated during the interaction between $86^{+\bullet}$ ions and pyridine (Sorrilha et al., 1996).

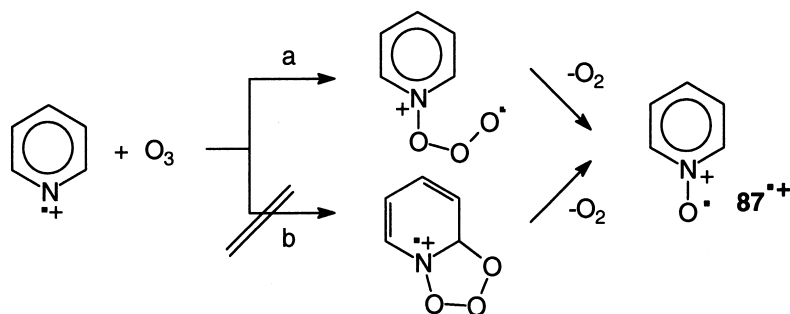
In the gas phase, neutral ozone (O_3) transfers an oxygen atom to several positive ions, such as the molecular ions of (substituted) pyridines or pyrimidine (Mendes et al., 1998) to form pyridine *N*-oxide ($87^{+\bullet}$) and pyrimidine *N*-oxide ($88^{+\bullet}$) ions, respectively as demonstrated by pentaquadrupole double- and triple-stage mass spectrometry. On the other hand, the transfer of oxygen does not occur in the inverse reactions; i.e., those reactions of ionized ozone with the corresponding neutral heterocyclic compounds. The very high ionization energy of ozone (12.43 eV) compared with, for instance, pyridine (9.25 eV), makes dominant the charge exchange reaction. *Ab initio* calculations suggest that O-transfer from ozone to ionized pyridine yields ionized pyridine *N*-oxide ($87^{+\bullet}$) via simple nucleophilic addition of ozone (route a) as opposed to a 1,3-dipolar cycloaddition (route b) (Scheme 25) (Mendes et al., 1998).

The peculiar behavior of molecular oxygen in collisional activation mass spectrometry has been stressed on several occasions (McGibbon et al., 1994; Flammang et al., 1996; 1999; Gerbaux et al., 1999). Briefly, collision of gaseous ions at high kinetic energy with oxygen

SCHEME 24



SCHEME 25

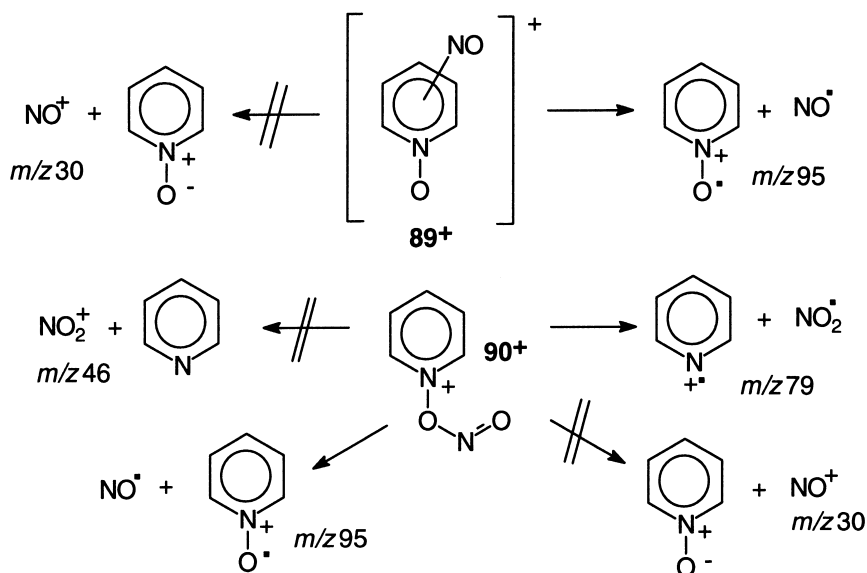


induces specific fragmentations that are not observed, or of very low intensity, with helium or argon. As for an interpretation, the influence of the high multiplicity of molecular oxygen was proposed (McGibbon et al., 1994; Flammang et al., 1996; 1999; Gerbaux et al., 1999). As far as pyridine *N*-oxide molecular ions (87⁺) are concerned (Flammang et al., 2000), collisional activation at high kinetic energy (8 keV) induces an unexpected loss of 16 mass units (oxygen), provided that molecular oxygen or nitric oxide is used as the target gas and not helium or argon. Molecular ions of pyridine are produced in these experiments. This peculiar fragmentation seems to be correlated with the high multiplicity of the target molecules (triplet ground state for oxygen and doublet for nitric oxide). *Ab initio* calculations show that the lowest-lying quartet electronic state of the pyridine *N*-oxide radical cation (87⁺) lies about 3.9 eV above the doublet ground state. The most interesting feature is that the energy of pyridine radical cation plus oxygen atom lies about 70 kJ/mol *below* the quartet state of pyridine *N*-oxide radical cation (87⁺), thus making the fragmentation somewhat exothermic. In view of this result, it is tempting to suggest that this oxygen elimination does occur in its excited quartet state rather than in its ground doublet state. The formation of the quartet is likely due to a spin-forbidden transition induced by the interaction between oxygen (triplet) and the molecular ions of pyridine *N*-oxide (87⁺).

In the low translational energy regime (*ca.* 20–30 eV), a loss of oxygen is also detected, whatever may be the nature of the collision gas (argon, oxygen, or nitric oxide), and the relative intensity of this reaction increases with the kinetic energy of the ions (Flammang et al., 2000).

At near-thermal energies (*ca.* 5 eV), the molecular ions of pyridine oxide (87⁺) react with nitric oxide to apparently generate two different ion–molecule complexes or intermediates responsible for the production of the [M+NO]⁺ (*m/z* 125) and [M–O]⁺ (*m/z* 79) ions. These proposals are summarized in Scheme 26. The complex 89⁺ could be stable enough to be detected at *m/z* 125, whereas the complex 90⁺ should dissociate by loss of NO₂. The less energy-demanding fragmentation of a complex such as 89⁺ should be the loss of nitric oxide (*m/z* 95) or the loss of pyridine oxide with the formation of NO⁺ cations (*m/z* 30). The nature of the predominant dissociation can be readily predicted to be the loss of neutral nitric oxide on the basis of the relative ionization energies: IE (pyridine oxide) = 8.38 eV and IE (nitric oxide) = 9.25 eV. For the looser complex 90⁺, four products are expected for simple cleavage reactions of N–O bonds: the loss of NO[•] or NO⁺, or the loss of NO₂ or NO₂⁺. Again, on the basis of ionization energies, a significant formation of NO⁺ or NO₂⁺ is not expected. A confirmation of the proposed mechanism was found in the study of the reaction between 4-cyanopyridine *N*-

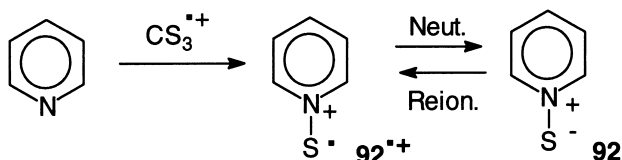
SCHEME 26



oxide (91^+) and nitric oxide. Indeed, in keeping with the fact that the ionization energy of 4-cyanopyridine (IE = 9.9 eV) is higher than the IE of NO_2 (IE = 9.75 eV), NO_2^+ cations are produced during the fragmentation of the complex (Flammang et al., 2000). The deoxygenation mechanism of pyridine oxide molecular ions (87^+) appears, therefore, highly dependent upon the experimental conditions including target gas and kinetic energy (Flammang et al., 2000).

As described previously in the present review, CS_3^+ radical cations transfer very efficiently S^+ to nitriles, yielding nitrile *N*-sulfide radical cations (Scheme 16) (Flammang et al., 1996; Gerbaux et al., 1997). The reaction between neutral pyridine and CS_3^+ ions (Gerbaux et al., 1997) was recently attempted in order to generate the unknown pyridine *N*-thioxide radical cations (92^+) (Scheme 27).

SCHEME 27



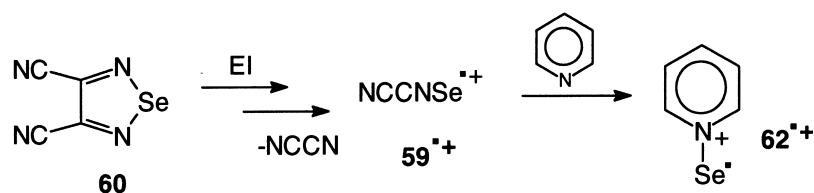
Chemical ionization of pyridine (carbon disulfide as the CI gas) or direct interaction between CS_3^+ and neutral pyridine in a quadrupole collision cell leads to the formation of $[\text{C}_5\text{H}_5\text{NS}]^+$ radical cations. Collisional activation of appropriate reference ions (the molecular ions of isomeric mercaptopyridines (93 – 95^+)) was used to demonstrate the actual structure of the produced ions.

The main difference between the CA spectrum of pyridine *N*-thioxide radical cations (92^+) and those of the reference ions is that the loss of sulfur is the base peak in the case of the ions generated by sulfur transfer to pyridine. This single bond cleavage is therefore characteristic of the proposed pyridine *N*-thioxide structure (92). The stability of neutral 92 in the gas phase was also established by NRMS (Gerbaux et al., 1997) (Scheme 27). Finally, several reactions were performed in a quadrupole collision cell with reagent molecules recognized as excellent trapping agents for distonic ions: dimethyl disulfide, dimethyl diselenide, pyridine-*d*₅, and nitric oxide. 92^+ Radical cations react with nitric oxide or pyridine-*d*₅ by sulfur transfer to generate SNO^+ cations or pyridine-*d*₅ *N*-thioxide ions, respectively. Both reactions were not observed in the case of the reference ions. Although the abstraction of thiomethyl or selenomethyl radicals was observed for all the radical cations considered, the resulting $[\mathbf{92}(\mathbf{93}\text{--}\mathbf{95})+\text{S}(\text{Se})\text{CH}_3]^+$ cations were clearly differentiated by consecutive collisional activation (Gerbaux et al., 1997).

The molecular ions of pyridine *N*-thioxide (92^+) can also be prepared during the reaction between nitrile *N*-sulfide radical cations, such as NCCNS^+ or ClCNS^+ , and neutral pyridine (Gerbaux, 1999).

As far as the selenide compound is concerned, it is possible to transfer Se^+ from cyanogen *N*-selenide radical cations, NCCNSe^+ (59^+), to neutral pyridine. As already mentioned, NCCNSe^+ ions are readily obtained by dissociative ionization (loss of cyanogen) of 3,4-dicyano-1,2,5-selenadiazole (60^+) (*vide supra*). The reaction between 59^+ and pyridine (Scheme 28) can be performed in a chemical ionization source or in a quadrupole

SCHEME 28



collision cell (Gerbaux et al., 1999). Because the most nucleophilic center of the pyridine ring is the nitrogen atom, the expected structure for the [C₅H₅NSe]⁺ adduct is the pyridine *N*-selenide structure (**62**).

The structure of this new dicationic ion has been established by high energy collisional activation (comparison with the collision-induced behavior of 2-selenopyridine molecular ions (**96**⁺) as reference ions) and associative ion-molecule reactions with methyl isocyanide, pyridine-*d*₅, dimethyl disulfide, and dimethyl diselenide.

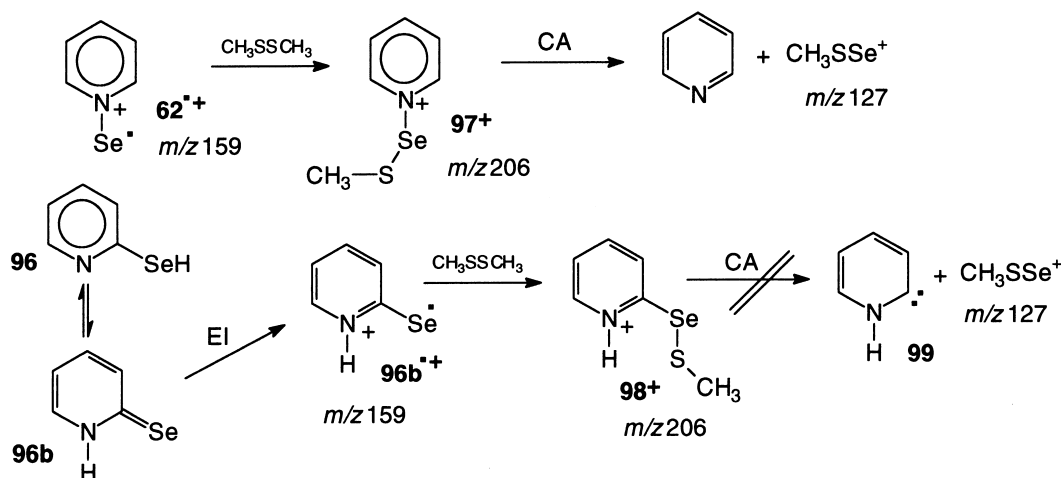
For instance, the interaction between **62**⁺⁺ ions and isocyanide leads to the formation of methyl isoselenocyanate ions, CH₃NCSe⁺; however, this reaction was not observed when 2-selenopyridine molecular ions (**96**⁺) are the mass-selected ions.

The interpretation of the reaction between isomeric **62/96**⁺ and dimethyl disulfide was less straightforward. Indeed, both ions react with dimethyl disulfide by thiomethyl radical abstraction (Figure 2) (Scheme 29). This process was demonstrated to be indicative of the presence of a dicationic structure (Stirk et al., 1992). Therefore, the observation of this reaction in the peculiar case of **96**⁺ ions was not expected. However, 2-selenopyridine (**96**) can exist in the gas phase as the tautomeric 2-pyridine-selenone structure (**96b**) (Scheme 29). The vertical ionization (EI) of **96b** is likely to lead to the formation

of a dicationic ion, in which the positive charge is localized on the nitrogen atom, whereas the radical site is the selenium atom (Scheme 29). The formation of such a dicationic structure (**96b**⁺⁺) could consequently rationalize the thiomethyl radical abstraction.

In order to gain more information on the structures (**97**–**98**⁺) of the ions produced in these ion-molecule reactions, their high kinetic energy (8 keV) CA spectra were recorded (Figure 2). It is worth noting here that such an experiment can only be performed with the new kind of hybrid mass spectrometer of EBEqEBE geometry developed in our laboratory (Bateman et al., 1992; Flammang et al., 1995). The main difference between both spectra is that the CA spectrum of **98**⁺ cations shows a very strong decrease in the intensity of the *m/z* 127 peak (CH₃SSe⁺ cations). The interpretation of the contrasting behavior of **97**⁺ and **98**⁺ is straightforward. Lavorato and co-workers have indeed very recently calculated that neutral azacyclohexadiene-2-ylidene, **99**, is 50 kcal/mol less stable than neutral pyridine (Lavorato et al., 1996; 1998; 2000). In contrast, the relative stability of the corresponding radical cations has been found inverse—the cyclic carbene ions, **99**⁺, are more stable than the conventional pyridine molecular ions. It is thus not surprising that the process leading to the generation of CH₃SSe⁺ cations plus the neutral carbene **99** in the fragmentation of **98**⁺ is thermodynamically disfavored (Scheme 29) (Figure 2).

SCHEME 29



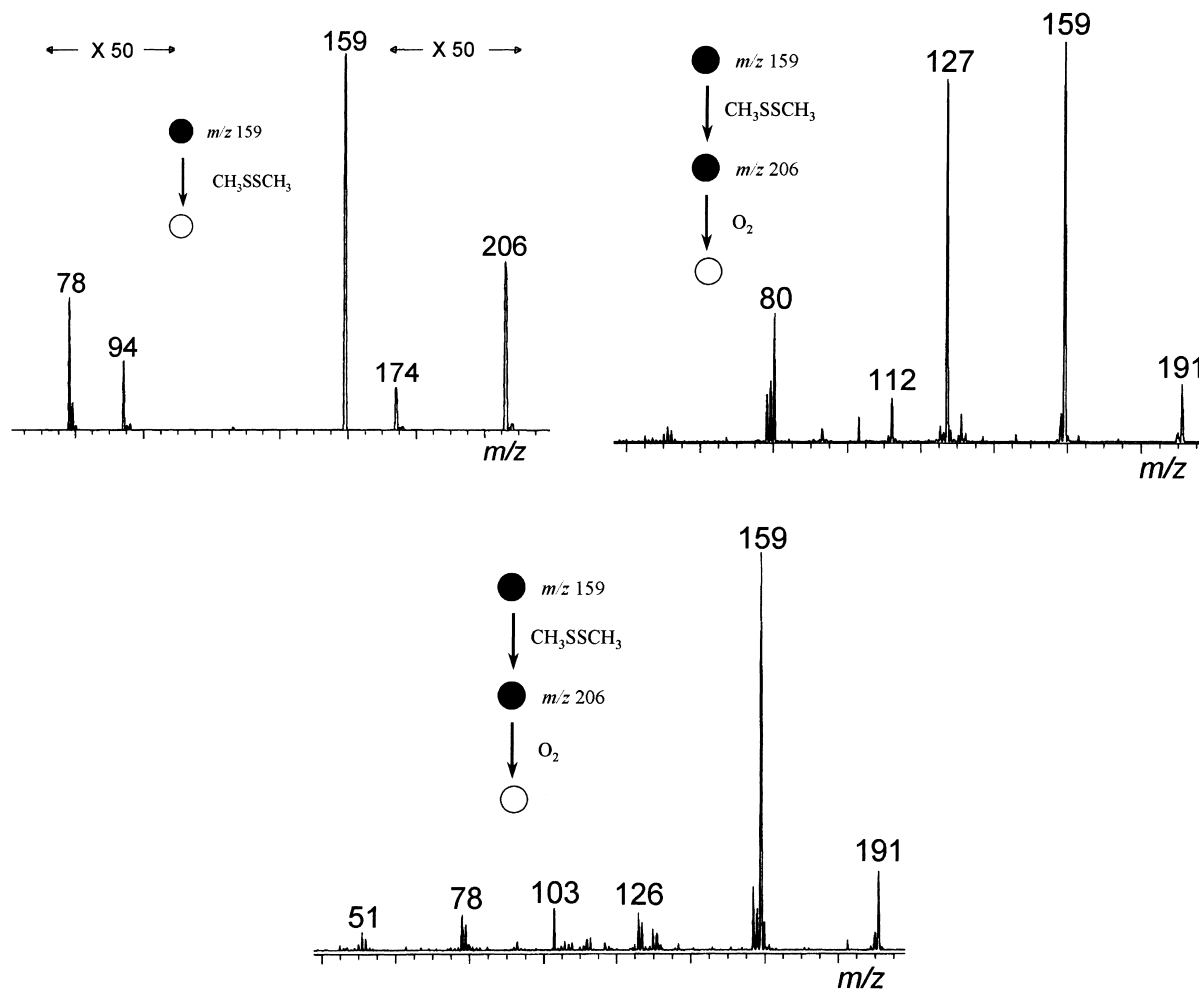


FIGURE 2. Reaction between pyridine *N*-selenoxide radical cations (62^+) and dimethyl disulfide in the Qcell: (a) mass spectrum of the ion-molecule products and (b) CA (oxygen) spectrum of the $(62+\text{CH}_3\text{S})^+$ (m/z 206) cations. Reaction between 2-selenopyridine radical cations (96^+) and dimethyl disulfide in the Qcell: (c) CA (oxygen) spectrum of the $(96+\text{CH}_3\text{S})^+$ (m/z 206) cations. The terminology introduced by Schwartz *et al.* (*Anal.Chem.*, 1990, 62, 1809) is used to schematise the sequence of reactions: a filled circle represents a fixed (or selected) mass; an open circle, variable (or scanned) mass, whereas the neutral reagent or collision gas that causes the mass transitions is shown between the circles.

Although the NR spectrum of pyridine *N*-selenide molecular ions (62^+) features a significant recovery signal, the interpretation of the NR results was not straightforward and did not unambiguously confirm the stability of the neutral dipole in the gas phase (Gerbaux *et al.*, 1999).

C. 5-Membered Heterocyclic Compounds

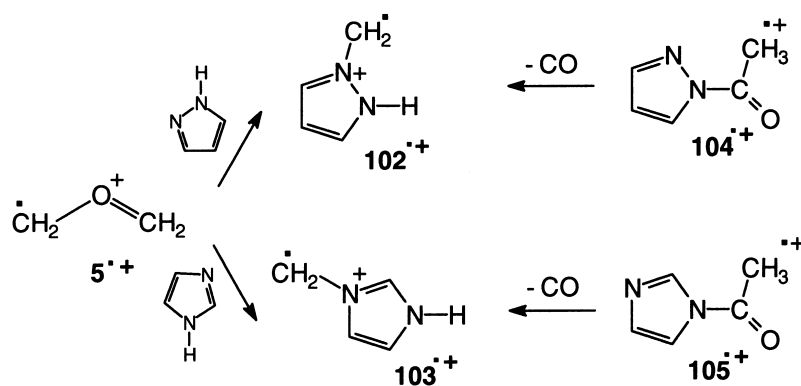
In a chemical ionization source, the C–C ring-opened oxirane radical cation ($\text{CH}_2^+-\text{O}-\text{CH}_2$ (5^+)) transfers a methylene group to imidazole (**100**) and pyrazole (**101**) (de Koster *et al.*, 1994). The structures of the $[\text{M}+14]^+$ reaction product ions have been established by collisionally induced dissociation spectrometry. The results

demonstrated that the produced ions were different from the molecular ions of methylimidazole and methylpyrazole. The methylene transfer reaction from ionized oxirane to pyrazole and imidazole yields, respectively, 1-methylene-2*H*-pyrazolium (102^+) and 1-methylene-3*H*-imidazolium (103^+) α -distonic radical cations (Scheme 30).

Ab initio molecular orbital calculations were also used to estimate the relative stabilities of $102/103^+$ ions and some of their isomers. The calculations predicted lower heats of formation for $102/103^+$ ions compared to those of *N*-methyl substituted pyrazole and imidazole.

Moreover, the CA spectra of $102/103^+$ ions were found to be very similar with those of the radical cations prepared by decarbonylation of the molecular ions of

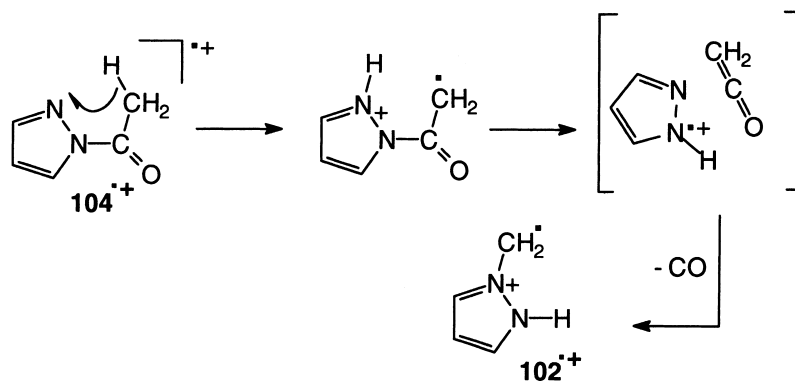
SCHEME 30



1-acetylpyrazole (**104**) or 1-acetylimidazole (**105**), respectively (Maquestiau et al., 1984; 1985) (Scheme 30). The proposed mechanism that leads to the decarbonylation of ionized 1-acetylpyrazole (**104**⁺) was presented in Scheme 31, and could involve the intermediacy of an ion/neutral complex constituted by the molecular ions of pyrazole and neutral ketene (Maquestiau et al., 1984; 1985; Flammang et al., 2000).

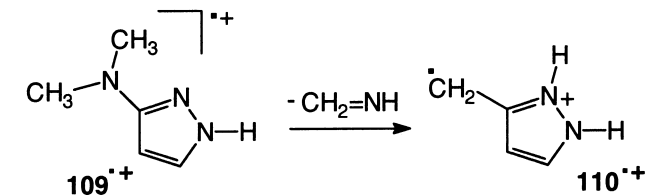
(dimethyl disulfide(selenide) as reagent gas). Finally, the distinction between **102**⁺ and **110**⁺ radical cations was carried out on the basis of the absence of the CH₂⁺ transfer reaction in the specific case of **110**⁺ ions, and on the basis of the CA experiments performed on the [**102**(**110**)⁺+CH₃S]⁺ cations. Actually, the base peak of the CA spectrum of the [**102**⁺+CH₃S]⁺ cations was observed at *m/z* 61 for CH₃SCH₂⁺ cations (loss of neutral

SCHEME 31



Recently, the [**104**-CO]⁺ radical cations (**102**⁺) were reinvestigated with ion–molecule reactions (Flammang et al., 2000). The reactivity of these **102**⁺ ions with some neutral species (nitric oxide, dimethyl disulfide, dimethyl diselenide, perdeuterated acetonitrile, and pyridine) was compared with that of reference ions; namely, the molecular ions of 1-methyl-, 3(5)-methyl-, and 4-methylpyrazoles (**106**–**108**⁺). A distonic reference structure (**110**⁺) was also considered, and was prepared by loss of formimine (CH₂=NH) from ionized 3-dimethylaminopyrazole (**109**) (Scheme 32).

First, the differentiation between the classical radical cations **106**–**108**⁺ and both distonic structures (**102**⁺ and **110**⁺) was readily achieved because only the distonic ions react by thiomethyl(selenomethyl) radical abstraction



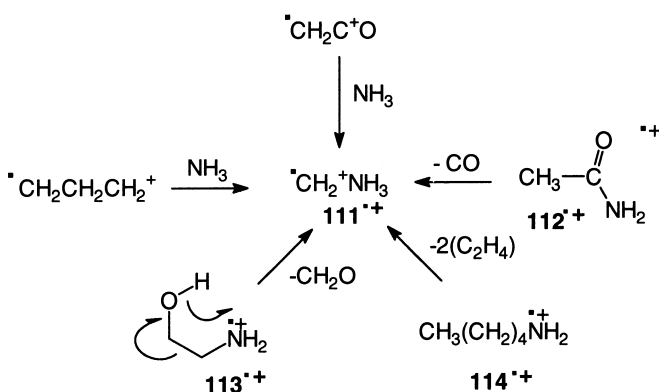
SCHEME 32

pyrazole), whereas these fragment ions were not present in the case of [**110**⁺+CH₃S]⁺ cations. The occurrence of a peak at *m/z* 61 was not expected in the latter case because it should result in the elimination of a less stable ylide isomer of pyrazole (Flammang et al., 2000).

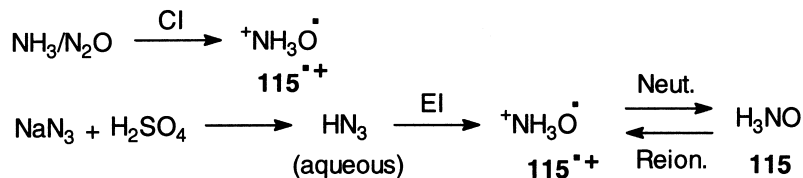
IV. DIPOLAR COMPOUNDS DERIVED FROM AMMONIA

The simplest distonic amine ion is $\cdot\text{CH}_2\text{NH}_3^+$ (**111**⁺) (Scheme 33). This radical cation is the product of reaction between ionized cyclopropane and ammonia (Gross et al., 1971; 1972). As previously mentioned, the ring opening of internally excited ionized cyclopropane leads to the distonic ion $\cdot\text{CH}_2\text{CH}_2\text{CH}_2^+$ (**8**⁺) (Sack et al., 1985; Skancke 1995; Bouchoux et al., 2000). These latter ions are responsible for the transfer of CH_2^+ to ammonia (Scheme 33). $\cdot\text{CH}_2\text{NH}_3^+$ radical cations (**111**⁺) can also be formed by reaction of ionized ketene with ammonia (Iraqi et al., 1991). Further, ionized acetamide (**112**⁺) dissociates to give $\cdot\text{CH}_2\text{NH}_3^+$ ions (Drewello et al., 1987). Other routes to this distonic ion include the loss of

SCHEME 33



SCHEME 34



formaldehyde from ionized 2-aminoethanol (**113**⁺) (Sack et al., 1985) and the loss of two ethylene molecules from ionized *n*-pentylamine (**114**⁺) (Hammerum, 1988). The structure of the $\cdot\text{CH}_2\text{NH}_3^+$ radical cations (**111**⁺) has been identified by collisional activation and by ion-molecule reactions (Drewello et al., 1987). Wesdemiotis et al. used NRMS (Hg as the neutralization gas and oxygen as the reionization gas) and observed recovered $\cdot\text{CH}_2\text{NH}_3^+$ radical cations (**111**⁺) in good yield (Wesdemiotis et al., 1986). Holmes reported that the NR spectrum (Xe as the neutralization gas) also features an intense recovery signal (Holmes, 1989).

The generation of ammonia oxide (**115**) represented a major challenge to experimentalists who work in the field

of elusive molecules. Actually, the fact that homologs like trialkylamine oxides are well-known storable compounds indicates that the atom connectivity $\text{R}_3\text{N}-\text{O}$ is not inherently unstable. Therefore, for $\text{R}=\text{H}$ the main problem is to prevent the isomerization of **115** to the more stable hydroxylamine (**116**). This isomerization can be avoided by preparing the elusive molecule from the identified corresponding ions in the gas phase of a mass spectrometer. A mixture of NH_3 and N_2O was subjected to chemical ionization; indeed one may consider N_2O as a donor of oxygen atom to afford ammonia oxide ions (**115**⁺) (Brönstrup et al., 1998). Surprisingly, electron ionization of an aqueous HN_3 solution also yields reasonable amounts of $[\text{H}_3,\text{N},\text{O}]^+$ radical cations (Brönstrup et al., 1998) (Scheme 34). The mechanism of $[\text{H}_3,\text{N},\text{O}]^+$ formation has not been established. Although ion-molecule reactions cannot be ruled out, the fact that the highest yields of $[\text{H}_3,\text{N},\text{O}]^+$ ions were obtained under electron ionization conditions suggests that a volatile, hitherto uncharacterized, $\text{N}_2\text{H}_2\text{O}$ compound is liberated from an aqueous mixture of NaN_3 and H_2SO_4 .

In any event, $[\text{H}_3,\text{N},\text{O}]^+$ radical cations obtained upon chemical ionization or electron ionization conditions featured very similar CA spectra confirming the production of similar ions. Moreover, these spectra were found to be very different from the CA spectrum of ionized hydroxylamine (**116**⁺). The observed differences were interpreted on the basis of the production of ammonia oxide molecular ions (**115**⁺). Finally, NRMS experiments supported the gas-phase existence of the long-sought neutral ammonia oxide (**115**) (Brönstrup et al., 1998).

V. APPENDIX

- B: Magnetic sector
- CA: Collisional Activation
- CI: Chemical ionization
- CID: Collision-Induced Dissociation
- CS: Charge Stripping
- E: Electric sector
- eV: electron volt
- FT-ICR: Fourier Transform Ion Cyclotron Resonance
- IE: Ionization Energy
- MIKE: Mass-analyzed Ion Kinetic Energy spectroscopy
- MS: Mass Spectrometry
- NRMS: Neutralization Reionization Mass Spectrometry

PIMS: PhotoIonization Mass Spectrometry
 q: quadrupole collision cell
 RE: Recombination Energy
 rf-only: radiofrequency—only
 RS: Recovery Signal

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