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REACTION MECHANISM OF GASEOUS ORGANIC CATIONS–21†

SKELETAL REARRANGEMENT OF IONIZED N-ARYL-3,4-DIPHENYLISOXAZOL-5(2H)-ONE

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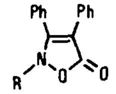
Abstract—Ionized N-aryl-3,4-diphenylisoxazol-5(2H)-one isomers react unimolecularly in the gas-phase mainly via carbon dioxide elimination. The observed ring contraction closely resembles the reported behaviour of the corresponding neutral compounds in solution. The reacting species were produced by electron impact (EI) and field ionization (FI) and analyzed by MS/MS through the determination of specific metastable ions (MI) decompositions.

The chemistry of ionized isoxazolones and related systems in a non-interacting environment has attracted particular attention because of the analogies often encountered with the condensed phase behaviour of the corresponding neutral molecules.[1-8] Thermally allowed processes characterize the breakdown pathways of 3-phenylisoxazol-5(4H)-one radical cations,[1,4] while the -CH tautomer, i.e. that having the double bond in position 2, is the most stable isomer among those which can be populated by prototropic shift within unsubstituted ionized isoxazol-5-ones,[8] thus resembling the solution phase observations.[9] Some N-methylisoxazol-5(2H)-one isomers have been investigated in the gas-phase in the form of ionized radical cations in order to reveal reaction channels which eventually could characterize the chemistry of this "blocked" isomer.[8] However, the presence of a methyl group linked to the charged nitrogen site of the heterocyclic moiety provides weakly bound protons, as verified both in solution[10] and in the gas-phase,[11] which can be involved in many complex rearrangement processes,[8] masking to some extent the expected behaviour of the nucleus itself. N-Aryl isomers are now readily accessible by adding the corresponding nitroso compound to diphenylcyclopropenone,[12,13] and some of them have shown a peculiar behaviour when treated with nucleophiles.[12]

RESULTS AND DISCUSSION

The effect of functional group interaction in determining the population of competing and consecutive unimolecular decays of isoxazol-5(2H)-one nucleus can be estimated by examining the reactivity of the N-aryl-3,4-diphenyl isomers **1-3** (Scheme 1). Even without X-ray data, an out-of-plane configuration can be assigned to the phenyl rings in the position 3 and 4 of the nucleus. The stereochemistry of (Z)-stilbene moieties is, in fact, well defined. Furthermore, X-ray analysis of the isomeric 2-methyl-3-phenylisoxazol-5-(2H)-one, whose conformational equilibria are affected by similar steric constraints, shows that the rotamer exhibiting a torsion angle of 50° between the phenyl group and the plane of the five-membered ring is preferentially populated in the condensed phase.[9] The unpaired spin density of the odd-electron molecular ion should be stabilized by conjugation, strongly affecting the population of specific electronic states and thus the reactivity of the radical cation. Experimental evidence recently reported has also shown that the neutral rotational quanta are preserved to great extent in the low excited molecular ions.[14] In the model compounds under examination the substituents in position 3 and 4 of the nucleus play the unique role that they cannot provide enolizable protons, moreover, they are less involved in thestabilization of the electronic state populated by the removal of one electron from the five-membered heterocyclic counterpart of the reacting systems. When those ions are produced by means of a 70 eV electron beam, different excited vibro-rotational species can be obtained. The population of competing decompositions pathways is, therefore, a function of the ion's internal energy. Highly activated precursors, decomposing within 10^{-6} s from their formation, give reaction products which are displayed by the stable ion spectrum, obtained by scanning the magnet at V/E constant ratio in a double focussing reversed geometry mass spectrometer. The unimolecular decompositions of those ions possessing a lower internal energy content and having the required half-life (10^{-5} sec) to decompose within the time scale of the instrument can be



1. R = C_6H_5-
2. R = p-Br-C_6H_4-
3. R = o-Me-p-NO_2-C_6H_3-

Scheme 1.

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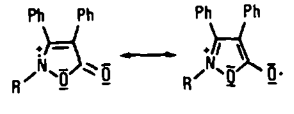
†For Part 20 see Ref. 4.

selectively detected from the metastable ion (MI) spectrum and recorded by scanning the electrostatic sector at V/B constant ratio in a MS/MS experiment.[15] Isoxazolone **1**, activated by hydride addition, displayed, in solution, reaction pathways strongly dependent on the adopted experimental conditions,[12] therefore, information on the chemistry of the gaseous ionized isoxazolones **1–3** will be gathered by comparing the results obtained from the decomposition pathways of fast and slow reacting species.

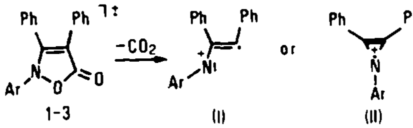
The stable ion spectra of radical cations **1–3** are characterized by the presence of abundant molecular ions, as evidenced by the peaks at *m/z* 313(1), 391 + 393(2) and 372(3), whose relative intensity, with respect to the base peak, was 100, 81 and 100% respectively. The observed stability can be ascribed to the "aromatization effect" upon electron bombardment[16] which results from the removal of one electron from the HOMO of the molecule. The ionized radical cation, thus obtained, in fact, can be described by an aromatic isoxazole type structure (Scheme 2). The spectra of the compounds under investigation show a remarkable uniformity despite the different degree of substitution of the aromatic ring linked to the nuclear nitrogen. Three major reactions characterize the breakdown pathways of the fast decomposing precursors **1–3**: carbon dioxide loss and the formation of fluorenil and N-arylbenzonitrile cations. The former process corresponds to the formation of the fragment ions at *m/z* 269, 347 + 349, and 328 in the 70 eV spectra of the fast decomposing ionized precursors, carrying 80, 70 and 61% of the ionic current of the base peak, respectively. CO_2 elimination is also the dominant reaction populated by the slow reacting molecular ions, occurring in the range of 81–92% yield in the MI spectra of the parent radical cations **2** (*m/z* 313), **2** (*m/z* 391) and **3** (*m/z* 372) (Table 1).



Scheme 2.

The primary formed nitrogen containing fragment thus obtained might have linear or cyclic structures. A nitrene-type radical cation (I) (Scheme 3) should correspond to the open form, while a fully aryl-substituted ionized azirine (II) might be the possible three-membered ring obtained by the examined reaction. Azirines have been isolated[17] or proposed as intermediates in the thermally[18] and photochemically[19] allowed ring-opening reactions which occur, in condensed phase, from substituted isoxazoles, via N,O-bond fission.

Furthermore, linear structure of type (I) resemble the reacting configuration which corresponds to the transition state for the thermally allowed C, N bond breakage undergone by ionized azirine, in the condensed[20] and in the gas-phase.[21] Since those $(M–CO_2)^{+\cdot}$ ions are among the most abundant fragments displayed by the stable ion spectra, an azirinium structure (II) fits better the requirements of a species which should be in a potential well. The formation of abundant fragments at *m/z* 165 represent another major and populated reaction pathway, at short times, by the sampled molecules, at the extent of 58–100%, with respect to the base peak. The latter is not observed in the low internal energy decompositions of the molecular ions **1–3**, as shown by the unimolecular reactions displayed by the correspondent MI spectra, reported in Table 1. The



Scheme 3.

Table 1. MI spectra of $M^{+\cdot}$ and $(M–CO_2)^{+\cdot}$ ions obtained from compounds 1–3

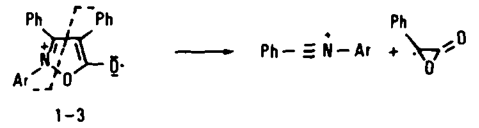
SAMPLE	PARENT (m/z)	DAUGHTER IONS m/z (neutral loss, %)
1	$M^{+\cdot}$ (313)	$\underline{296}$ ($OH^{\cdot}$, 1,5%), $\underline{269}$ (CO_2, 92%), $\underline{221}$ ($PhNH^{\cdot}$, 4,5%), $\underline{180}$($C_8H_5O_2^{\cdot}$,2%)
	$(M-CO_2)^{+\cdot}$(269)	$\underline{254}$(19.5%), $\underline{242}$(HCN,3.5%), $\underline{192}$ ($C_6H_5^{\cdot}$, 8%), $\underline{166}$ (PhCN,69%)
2	$M^{+\cdot}$ (391)	$\underline{347}$(CO_2,88%), $\underline{267}$(CO_2+HBr,8%),$\underline{258}$($C_8H_5O_2^{\cdot}$,2%) $\underline{221}$($C_6H_4BrNH^{\cdot}$,3%)
	$(M-CO_2)^{+\cdot}$(347)	$\underline{334}$(22%), $\underline{267}$(HBr,635%), $\underline{258}$($C_7H_5^{\cdot}$,7,5%) $\underline{244}$(PhCN,3%), $\underline{166}$ (O-Br-C_6H_4CN,4%)
3	$M^{+\cdot}$(372)	$\underline{355}$($OH^{\cdot}$,4,5%), $\underline{328}$(CO_2,81%), $\underline{282}$($CO_2+NO_2^{\cdot}$,6%), $\underline{239}$ ($C_8H_5O_2^{\cdot}$,3%), $\underline{221}$ (O-CH_3-pNO_2-$C_6H_3NH^{\cdot}$,5,5%)
	$(M-CO_2)^{\cdot}$(328)	$^{\cdot}\underline{298}$($-NO^{\cdot}$,17%),$\underline{282}$ ($-NO_2^{\cdot}$,77%), $\underline{269}$(6%)

same reaction is not populated either by the slow reacting $(M-CO_2)^+$ fragments which, on the contrary, gave in the metastable region daughter ions at m/z 166 with 69 and 4% yield in the case of **1** and **2** respectively. The latter does not compete with other rearrangement processes occurring from the low excited isomeric $(M-CO_2)^+$ species at m/z 328, produced by **3**, while it was accompanied by the formation of 3% p-bromo-substituted analog, at m/z 244, in the MI spectrum of the same type of ions originating from **2**.

Fluorenil and hydrofluorenil cations are the most stable structures corresponding to m/z 165 and 166 fragments.[22] Formation of the ion m/z 165 represents also a reaction profile which is common to the decompositions of nitrogen containing ionized molecules where, a diphenylmethane type moiety is present or can be produced by fast phenyl group migrations.[23] The occurrence of the latter in the fragmentation of isoxazolones **1–3** corresponds to an extensive ring degradation originating either from reaction pathway allowed to high internal energy molecular ions or from a stepwise decompositions of the same species involving activated intermediates as the triphenylazirinium radical cations. The situation can be somewhat different in the metastable region where low activation energy processes are preferentially populated. In those experimental conditions, in fact, m/z 165 ions can be formed by consecutive H radical loss from the hydrofluorenic species produced from the low excited $(M-CO_2)^+$ fragments, according to Scheme 4. The ring enlargement to ionized indole structures has been proposed on the ground of the data, available for similar systems both in the condensed[24] and in the gas-phase.[21] Moreover, it accounts also for the observed equivalence in the formal loss of aryl cyanide from the precursor m/z 347 species obtained from **2**, which gave rise to daughter ions at m/z 166 and 244 with approximatively the same yields (Table 1).

Finally, the chemistry of the fast reacting ionized isoxazolones is also characterized by the production of N-arylbenzonitrile cations, present at m/z 180, 258 + 260 and 239, in the stable ion spectra of 1, 2 and 3 respectively. The same process occurs only in the range of 2–3%, when long-living molecular ions **1–3** are sampled in the second drift region of the instrument (Table 1).

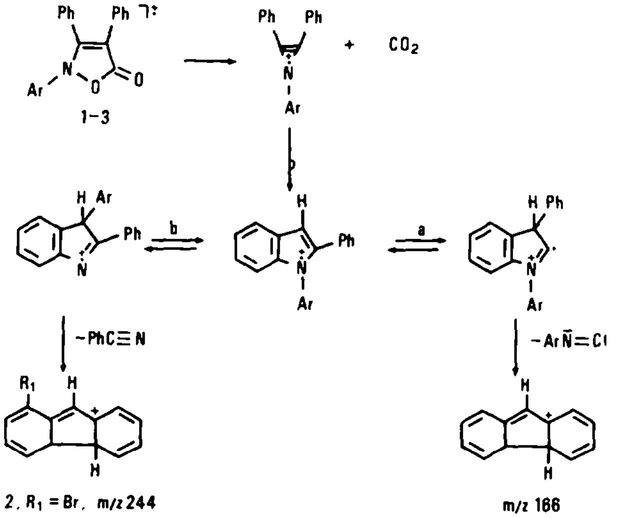
The observed behaviour can be explained by assuming that only bond breakages are required to release, directly from the ionized isoxazolones, the "preformed" immonium moiety, *via* an highly activated transition state and that this reaction compete more effectively in the fast decompositions processes. (Scheme 5).



Scheme 5.

Fluorenil and N-arylbenzonitrile cations formation represent unimolecular decompositions of high diagnostic value in the structure determination of the examined molecules by mass spectrometry. However, the corresponding reaction coordinates are allowed only to those molecular ions, which possess enough internal energy to decompose within 10^{-6} s from their formation. Previously discussed data actually seem to indicate that when mild experimental conditions are chosen, the high energy resonance stabilized radical cations **1–3** react mainly via carbon dioxide extrusion.

An alternative way of producing low energy excited radical cations, which can then react in energetic conditions closely resembling those in condensed phase, is the employment of softer ionization procedure than previously examined electron bombardment. Since the isoxazolones **1–3** can be volatilized without appreciable thermal decomposition by properly setting the temperature parameters of the ion source region, the field ionization method (FI)[25]

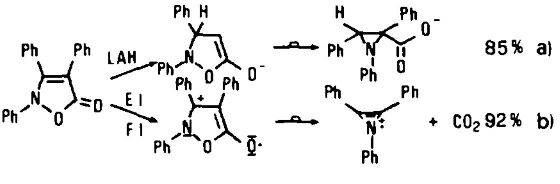


Scheme 4.

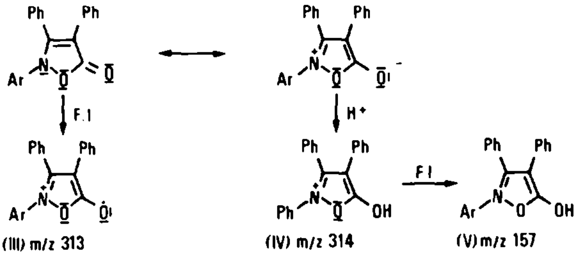
can be a suitable technique to give further insights into the chemistry of the examined heterocyclic nucleus, complementing the information already examined. The computer-assisted averaged spectrum obtained by field ionization of the triphenylisoxazolone (1) showed peaks at 315, 314, 313 and 157 corresponding to mono and doubly charged molecular and quasi-molecular ions, which carry more than 95% of the total ion current, as expected for a soft ionization method. $(M + H)^+$ formation at *m/z* 314 can be interpreted in terms of some acid-base reactions involving the chemisorbed species on the emitter surface:[25] their intensity, in fact, has been shown to be a function of the sample pressure and cathode temperature. When an activated unheated emitter was used, the relative intensity of those ions (12% of the base peak, after correction for the isotopic contribution of the molecular radical cation at *m/z* 313) accounted for the formation of a stable ionized species, which can likely correspond to the 5-hydroxy-2,3,4-triphenylisoxazolium ion IV (Scheme 6). The occurrence, in the same experimental conditions, of 5.3% of $(M+H)^{2+}$(V) at *m/z* 157 can be the result of a field ionization process experienced by the protonated species (IV), in agreement with the accepted mechanism of multiply charged ions formation by FIMS.[26,27] In the FI spectrum under examination only two fragment peaks were detected at *m/z* 269 and 270 of relative intensity 2.5 and 2.4% respectively, with respect to the base peak. Those ions correspond to CO_2 eliminations from the precursor odd and even-electron molecular ions. FI experiments, therefore, support the previous observation, that when low internal energy ionized 5-(2H)-isoxazolones **1–3** are studied they dissociate mainly *via* carbon dioxide elimination.

The most important aspect of the chemistry of the sampled molecules seems to be therefore, the liability of the N–O sigma bond in that particular ring environment. Similar reaction channels can be activated, in the condensed phase, when a trigonal carbon is available in the 5 position of a N–O five-membered heterocyclic molecule.[12,28] The same system (1), in particular, rearranges to aziridine derivatives when treated with hydride donors. This process has been explained in terms of a dominant interaction occurring between the HOMO of the N–O bond and the LUMO of the double bond in position 3 giving rise to a (1,3)-sigmatropic migration of the nitrogen atom. A quantum-mechanical treatment of a model system allowed the generalization of this reaction profile, ascribing the source of the observed behaviour at the N–O bond in the molecular framework which is weaker because of its low bond-electron density.[12] The same property seems to provide the driving force for the unimolecular dissociation of the corresponding low-excited ionized species thus showing that the population of that particular reaction profile is not confined to closed-shell systems only.

The wide applicability of the intramolecular rearrangement of five-membered N,O-heterocyclic substrates, where an electron pair at position 5 of the nucleus is conjugated with the adjacent N-O bond is well illustrated by the reactivity of 2,3,4-triphenylisoxazol-5-(2H)-one **1** both in solution and in the gas-phase, as summarized in Scheme 7. Both 1,4 hydride addition (path a) and one electron removal (path b) cause the population of reacting intermediates possessing an electronic configuration which lowers the activation energy for the unimolecular N,O σ-bond cleavage to give the observed ring contraction. On the other hand, when more energy is deposited into the reacting species other reaction channels become competitive. When isoxazolone **1**, in fact, is treated in solution with $LiAlH_4$, the nature and relative yields of the reaction products strongly depend on the adopted experimental conditions;[12] similarly the activated ionized species **1–3**, i.e. those decomposing at short times, gave product ions, corresponding to extensive degradations of the nucleus, in competition with the discussed carbon dioxide elimination. In conclusion, the lowest activation energy reaction pathways of ionized isoxazol-5-(2H)-one ring system correspond to carbon dioxide elimination. This process is a function of the ring framework itself and does not depend either on the experimental conditions or on the electron configuration of the reacting molecule. The observed behaviour could be affected, at least for radical cation substrates, by the effect of the substituents which can drive the population of competing processes lowering the activation energy of alternative reaction pathways.[8,29]



Scheme 7.



Scheme 6.

Table 2. Spectral data for 5-(2H)-Isoxazolones 1–3

Compd	IR spectra cm^{-1}	Mass spectra m/z (rel. intensity)
1 m.p. 201–202	1720 (CO), 1580, 1555 1490, 1430, 1360, 950, 920, 770, 700.	e.i.: 314(20), 313($M^{+\cdot}$ 100), 269(80), 221(5), 180(24), 166(23), 165(90) f.i.: 315(4,8), 314($M+H^{+}$,35), 313($M^{+\cdot}$, 200), 157($M+H^{2+\cdot}$,5,3), 270(2,5), 269(2,4)
2 m.p. 168–9	1725 (CO), 1600, 1555, 1480, 1430, 1362, 1075, 950, 845, 782, 768, 700, 715, 700, 690, 510.	e.i.: 394(22), 393(81),392(20), 391($M^{+\cdot}$,80). 349(72), 347(70), 267(37), 260(62), 258(64), 166(38), 165(100).
3 m.p. 194–196°	1745(CO), 1590, 1530, 1490, 1360, 1320, 970, 810, 800, 780, 770, 760, 730, 710.	e;i.: 373(23), 372($M^{+\cdot}$, 100), 328(61), 282(20), 239(78), 193(23), 166(15), 165(58).

EXPERIMENTAL

Mass spectra were recorded on a Varian MAT CH-5. DF mass spectrometer equipped with a combined EI/FI source and a Spectro-System SS 100 computer. EI experiments were carried out at 1.000 of resolution power with an electron beam energy of 70 eV and at a constant acceleration potential of 3 kV. FI measurements were performed at 1.000 of resolution power and at +3 anode and −7 kV cathode potentials, using activated commercial emitters. The reported FI spectrum corresponds to the computer assisted average of the best eight acquisitions at constant emitter temperature and sample pressure. Samples were introduced through the direct inlet system at a source temperature of 200° and probe temperature of 120°.

MI spectra were obtained by scanning the electric sector voltage at constant V/B ratio according to the MIKE technique.[30]

The synthesis of compound **1** has already been described.[12] Compounds **2** and **3** were obtained by a similar procedure, starting from p-bromo-nitrosobenzene[31] and o-methyl-p-nitro-nitrosobenzene.[32] Analytical samples have been crystallized twice from methanol to get (**2**) and (**3**) as pale yellow needles m.p. 168–69° and 194–196° respectively.

M.ps were obtained with a Kofler hot-stage apparatus and are uncorrected. IR spectra were recorded on a Perkin–Elmer 377 instrument from 1% KBr pellets.

Physico-chemical data for compounds **1–3** are reported in Table 2.

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