Unimolecular Reaction Sequence in the Electron Impact Induced Fragmentation of some Methylenoxazolidinones (1)

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The unimolecular processes of some methylenoxazolidinones bombarded in the gas phase by electrons have been investigated by MIKE analysis, precise mass measurements and isotopic labelling studies. The overall delocalisation effect of the substitution on the nitrogen contained has been ascertained through the study of the reaction mechanism and of the possible reacting ionic structures.

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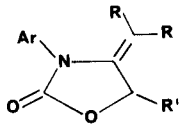
The potential usefulness of mass spectrometry in providing unique information for the investigation of organic chemistry is well established (2). However, the point of particular interest in stimulating application still remains the structural elucidation of complex organic molecules, although a remarkable increase in the number of novel aspects of unimolecular reactions of charged species has been found (3). The interpretative procedure employed to deduce structural formulae is dependent on the amount of data which is derived from a mass spectrum. The reliability of these data depends to a large extent upon circumstantial evidence available on the chemical behaviour of the ionized compound in question; the understanding of electron impact mass spectra thus requires appropriate emphasis on recent developements in methodology (4). In fact, the explanation of fragmentation modes of precursor ions can be obtained by a correct knowledge of the relationships among reactive ions in the mass spectrometer.

Unimolecular decompositions of organic ions in the gas phase can be thoroughly investigated by means of systematic (MIKE) mass spectrometry (5-7), especially in the case of heterocyclic compounds (8). Application of the above mentioned method, used in conjunction with computer assisted exact mass measurements and with deuterium labelling experiments, is illustrated by the determination of reaction sequence occurring from substituted 4-methylenoxazolidin-2-ones (I-IV) (9,10) exposed to electron impact. The most important decomposition pattern has also been examined in detail with respect to fragmentation mechanism, to possible reacting ionic structures of fragment ions and to intramolecular hydrogen transfer processes.



	Ar	R	R'
I	Ph	H	H
II	Tol	H	H
III	Ph	H	Me
IV	Ph	D	H

Formula I

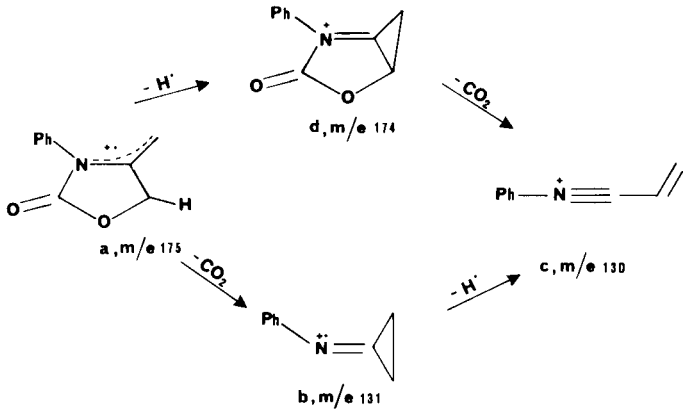
Classical mass spectrometry of some systems analogous to the compounds concerned has previously been performed (11) and marked differences have now been revealed which depend on the substitution pattern and on the substituent group on the nitrogen atom of the molecules being studied in accordance with the general trend of nitrogen containing cations (8b,12,13). In fact, the mass spectra of aryl substitued oxazolidinones which had received attention in the past were found to show very reactive molecular ions, thus low intense molecular peaks were observed in the range of 5 to 30% of the respective base peak (11). Furthermore, elimination of CO_2 was a process of minor importance (less than 1%) in some of those *N,O*-heterocyclic compounds and did not even occur in others (11). In contrast to this chemical reactivity, compounds I and II show mass spectra where the base peaks are due to the molecular ions $C_{10}H_9NO_2$ at mass 175 and $C_{11}H_{11}NO_2$ at mass 189, while in the mass spectrum of III the molecular ion $C_{11}H_{11}NO_2$ (m/e 189) is 47% of the base peak, *i.e.* m/e 130 (C_9H_8N). This clearly indicates an inherent thermodynamic stability of the ions examined towards fragmentation which can be explained in terms of the greater delocalisation effect induced by the enamine moiety and by the aryl group directly bonded to the nitrogen atom, thus permitting a longer life-time for the molecular ions.

The above conclusion is also supported by the experimental evidence that mass spectra of compounds I, II, and III are dominated by the peaks due to nitrogen containing ions, *i.e.*, m/e 131 (C_9H_9N, 26%), m/e 130 (C_9H_8N, 72%), m/e 118 (C_8H_8N, 10%) and m/e 103 (41%; C_7H_5N, 61% + C_8H_7, 39%) for I, and a similar situation is also found for homologous ions from II (m/e 145, 25%; m/e 144, 50%; m/e 130, 15%; m/e 117, 45%) and from III (m/e 145, 18%, m/e 144, 31%; m/e 130, 100%).

The quantitative aspects so far mentioned are of great value in estimating the directing power of functional groups contained in the pentacyclic nuclei I-III in determining preferential cleavages. On closer inspection of primary and secondary reactions associated with compounds I to III, it is possible to extract information on the relative abilities of the lactone-lactame functional group and the delocalized *N*-aryl enamine one in controlling the unimolecular decomposition. MIKE measurements demonstrate that molecular ions *a* undergo elimination of H, CO, CHO, CO_2,

and C_2HO_2 in the second drift region of a "reversed" geometry instrument (5) with relative abundance ratios of 0.7% and 0.6% for CO and CHO loss, 96.0% for CO_2 loss and 2.7% for C_2HO_2 loss; the elimination of hydrogen radical can not be accurately measured since the corresponding peak appears too close to the precursor ion.

The major pathway involves either initial loss of CO_2 leading to production of m/e 131 (*b*, C_9H_8N) with successive hydrogen loss to m/e 130 (*c*, C_9H_8N) or rupture of a C-H bond with the formation of a very unstable even-electron ion *d*, m/e 174 which expels carbon dioxide so that it will probably give the same ion *c*, m/e 130. These consecutive processes are clarified by considering Scheme 1. Support for the formulation of ions *b* (C_9H_9N, m/e 131), *c* (C_9H_8N, m/e 130) and *d* ($C_{10}H_8NO_2$, m/e 174) as formal structures reported in Scheme 1 is derived by deuterium labelling results from compound IV and by their subsequent fragmentation behaviour, even if possible acyclic diradical structures and/or mixture of structures might be assumed.

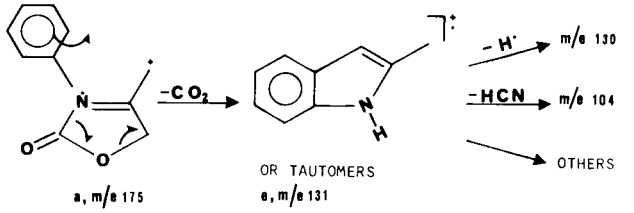


Scheme 1

The specifically deuterated compound IV has been employed to investigate the probable origin of the hydrogen radical lost and the possible hydrogen transfer processes which may or may not take place within the ions under study. Ions a' ($C_{10}H_7D_2NO_2$, m/e 177) from IV undergo elimination of H (~ 0.15 of the height of the most abundant peak), CO (2.0%), CHO (1.8%), CO_2 (84.7%) and C_2HO_2 (11.4%) as shown by the MIKE spectrum. Therefore, the results from compound IV verify that neutral species containing hydrogen atoms are lost without previous H-D scrambling in competition with slow reactions which occur within 10^{-5}s. in the mass spectrometer. Furthermore, assuming that the aryl group is not involved in the decomposition processes in question, as is also confirmed by additional data reported below, it is on the basis of the evidence available most reasonable to suggest the reaction sequences of Scheme 1. Both fragmentation pathways occur from ionized I *via* H elimination from position 5 which precedes or follows CO_2 loss. Since intramolecular hydrogen transfer reactions can not be observed, it is clear that the activation energy for H, CHO and C_2HO_2 loss is below that for H/D scrambling. The preference for loss of H at 5 may be controlled by the delocalized system, shown in Scheme 1, and the high reactivity of m/e 174 ions (relative intensity ≅ 1% of the base peak of the mass spectrum of I) can be explained by its ring strained structure.

MIKE analysis of fragment ions *b*, m/e 131 and *c*, m/e 130 illustrates that the ion structures suggested will most probably be the reacting ones, but some contribution from the rearrangement process might be envisaged. In fact, metastable decompositions of ions *b* obtained from I as shown in Scheme 1 yields products ions m/e 130 (by far the most intense peak of the spectrum, a factor of 10ca. compared to the second most intense one), m/e 104 (13% of the total ion current of all the fragments with the exception of m/e 130), m/e 103 (34%), m/e 91 (5%), m/e 78 (28%), m/e 77 (18%) and m/e 51 (2%). Therefore, results for product ions *b* demand that, apart from loss of H·, the fragmentation process should involve an initial ion structure which can easily eliminate C_2H_4 and competitively yields $C_6H_6^{+\bullet}$ (m/e 78) and $C_6H_5^+$ (m/e 77), *i.e.* *b*, as well as a different decomposition channel leading to loss of HCN; this is an abudant peak of the MIKE spectrum.

In analogy with similar system in gas and condensed phase (13), the unimolecular decomposition of isomeric reference ions *c*, m/e 131 from methylindole (V) has been examined. The metastable decompositions of *c* ($C_9H_9N^{+\bullet}$; m/e 131) generated from V have been investigated by MIKE mass spectrometry and are the following: formation of product ions m/e 130 (≅ 20 times the next most abundant peak), m/e 104 (70% of the total ion current of the MIKE spectrum excluding m/e 130), m/e 103 (16%), m/e 89 (3.4%), m/e 77 (4.3%), m/e 63 (3.3%) and m/e 51 (3%). Employing the criterion of metastable abundance ratios as a method for determining the structures of the reactive ions examined (4,13), it is possible to differentiate *b* and *c* radical ions according to their precursors. However, it should be noted that similarities are found where the loss of H radical, C_2H_4, $C_3H_4N^{\bullet}$, $C_5H_6N^{\bullet}$ and particularly HCN are concerned. In order to interpret the behaviour pattern of ions *b*, which in the case of HCN loss, would require a deep seated skeletal reorganization, it seems plausible to suggest that a reaction channel, alternative to the one of Scheme 1, may be in operation during the formation of these ions or that a successive rearrangement takes place before their subsequent decompositions. In fact, the enamine moiety of ion-



Scheme 2

ised I can give rise to an electrophilic cyclisation onto the orthoposition of the aryl group bonded to the nitrogen, thus producing the expulsion of CO_2 and the formation of an ion structure responsible for some of the unimolecular decomposition processes, as shown in Scheme 2. The alternative reaction path and/or the further isomerisation process, characteristic of immonium ions *c* and other similar ones (13, 14) subsequent to the ion formation, introduce appreciable internal energy differences thus justifying the differences observed in the abundance ratios and in some appearance of metastable transitions (8b,15,16).

Information on competitive rearrangements in ions *b* has been obtained by studying the behaviour of the corresponding deuterium-labelled species generated from the specifically marked precursor IV. The deuterium-labelling experiment on *b'*, m/e 133 ($C_9H_7D_2N$ from IV) show that H and D are eliminated to ions m/e 132 and 131 in the ratio of 81% and 19% respectively. Therefore, loss of hydrogen radical appears to be preceded by a completely reversible intramolecular hydrogen transfer reaction which leads to the almost equivalent participation of H and D atoms in the process occurring from ions of sufficient lifetime of the order of 10^{-5} s. For the $C_9H_7D_2N^{+\bullet}$ ion from compound IV, the statistical ratio is H, 78; D, 22; which is very close to the observed ratios with an isotope effect operating in favour of H loss.

A possible complication arises from the examination of hydrogen cyanide and ethylene loss, since probable overlapping of DCN and C_2H_4 expulsion might both be in the process of occurring. A portion of the MIKE spectrum related to values of electrostatic sector potential among 413V and 381V is reproduced in Fig. 1 and corresponds to the region for metastable peaks due to the loss of 27 to 30 mass units from the precursor ion m/e 133, *b'*. The observed ratio among peaks m/e 106, 105 and 103 is 16.7:13.1:70.2. On the basis of the foregoing experimental results, it is possible to conclude that ethylene does not involve any previous hydrogen equilibration reaction, but incorporates only two hydrogen and two deuterium atoms when lost in a specific manner in agreement with a reacting ion structure *b*, as shown in Scheme 1. On the other hand, the figures for hydrogen cyanide loss from *b'* are HCN, 56:DCN, 44; the calculated abundances being: 78:22. These data confirm that the latter elimination is associated with a rearrangement but that either partial H-D scrambling takes place during this process or H is heavily retained for some reason which is not altogether clear. However, it is important to emphasize the fact that metastable transitions m/e 133 to m/e 78 and m/e 77 occur without H-D scrambling and, therefore, as mentioned above, hydrogen atoms on the aromatic nucleus retain their initial identity in the majority of the reactions and even after two decomposition processes. The intensities of the remaining metastable decompositions are too low to give measurements which are sufficiently reliable to draw a quantitative conclusion.

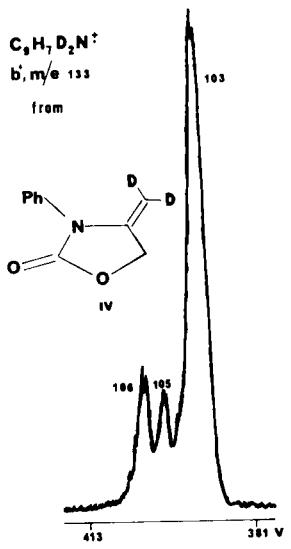


Figure 1. Part of the MIKE spectrum of m/e 133 precursor ions from [4-$^2H_2$]methylene-3-phenyl-1,3-oxazolidin-2-one (IV).

The apparent contrasting evidence on intramolecular hydrogen transfer reactions, *i.e.*, loss of H and HCN elimination behaves differently from the other decompositions, can be reconciled by the above proposed alternative formation path for ions m/e 131 from *a* which also provides an explanation for these decompositions (see Scheme 2); thus these $C_9H_9N^{+\bullet}$ ions are sampled in a mixture of structures responsible for the observed differences of chemical reactivity towards isomerisation.

Furthermore, ions of composition $C_9H_8N^+$ (m/e 130) of possible structure *c*, shown in Scheme 1, are mainly generated from m/e 131, but also directly from the molecular ions *a*, m/e 175, as evidenced by the appearance of the appropriate peak by the refocusing method (4). The latter transition may be due to the rapid consecutive occurrence of both porcesses described in Scheme 1, since precursor metastable ions m/e 175 reside 4 X 10^{-6} s ca. in the second drift region of the double focusing mass spectrometer used, which is sufficiently long to allow fragmentations. Ions m/e 130 undergo metastable decompositions with loss of H_2, HCN and C_3H_3N whose relative abundances are 11%, 30% and 59% respectively. The major fragmentation route from $C_9H_8N^+$ ions involves the formation of $C_6H_5^+$ fragmentations which can be explained in terms of the C-N bond rupture between the aromatic ring and the nitrogen containing group, thus confirming the hypothesis outlined in Scheme 1. Further information from deuterated analogous ions are meaningless since m/e 133 precursors from IV have been shown to give H and D loss in an equivalent manner (see above).

As expected, the homologous compound II shows identical behaviour under electron impact and this is clearly

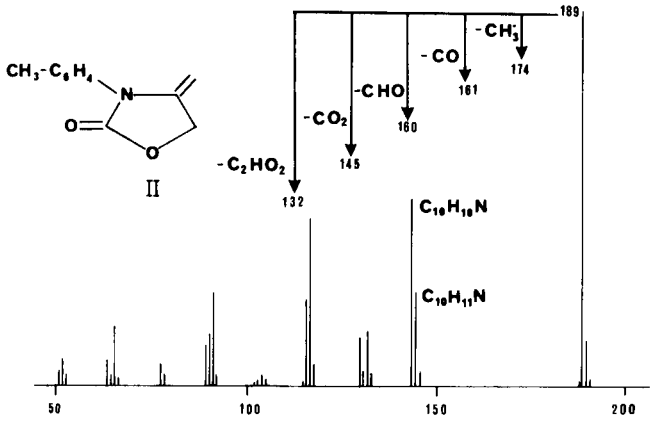


Figure 2. Mass spectrum of 4-methylene-3-p-tolyl-1,3-oxazolidin-2-one (II) with MIKE transitions.

seen from its mass spectrum reported in Fig. 2, where MIKE transitions are also indicated. A similar situation is also found in the case of compound III, which is an isomer of II and a different homologous of I. The experimental data related to the classical mass spectrum are reported in Fig. 3.

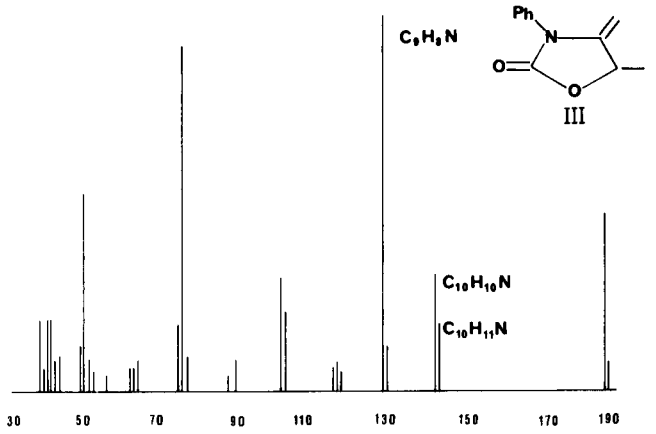


Figure 3. Classical mass spectrum of 5-methyl-4-methylene-3-phenyl-1,3-oxazolidin-2-one (III).

The most significant conclusions arising from the mass spectrometric analysis of compounds I to IV are that (a) the enamine group of the system controls those unimolecular fragmentations which lead to the more intense peaks of the mass spectra and which bear the greatest significance in indicating the structure of the original molecule; (b) the same functional group provides the possibility for rearrangement processes yielding competing reactions channels for the decomposition of molecular ions; (c) the different degrees of intramolecular hydrogen transfer reactions in fragment ions demonstrated by deuterium labelling experiments is consonant with the formation of a mixture of ionic structures (7) for some secondary reaction products.

EXPERIMENTAL

The mass spectra were recorded on a Varian MAT CH5-DF mass spectrometer with an electron-beam energy of 70eV and at a constant acceleration potential of 3KV and exact mass measurements at a minimum resolution of 10000 were obtained from a Spectro System SS-100 computer. Samples were introduced *via* the direct inlet system at a source temperature of 120-150°. Metastable transitions were determined using the MIKE technique (5) and the refocussing mode (4). Compounds I to IV were prepared as previously described (10) and were tlc pure.

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