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A REARRANGEMENT PROCESS IN SUBSTITUTED ISOXAZOLIDINE MOLECULAR IONS

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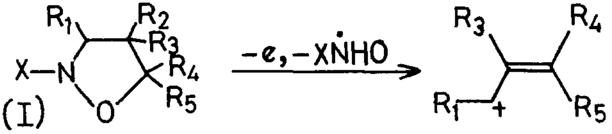
In the course of our studies on the synthesis and properties of substituted isoxazolidines,[1] we have recently become interested in their mass spectral behaviour. There have been few previous reports on the mass spectra of such compounds[2] and we wish to describe an interesting fragmentation process, occurring with rearrangement in the molecular ion prior to fragmentation, in N-alkyl and N-aryl isoxazolidines. This fragmentation can be of some assistance in structural assignment.

Various substituted isoxazolidines (I) show, as their main fragmentation process from the molecular ions, loss of X-$\dot{N}$HO.



(I)

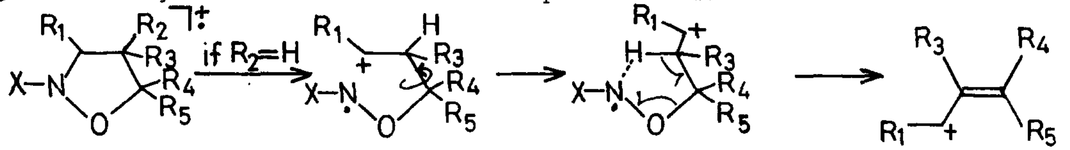
(X=Me, Ph;R_1=Ar, PhCO;R_2=H;R_3=H, Ar, alkyl, condensed urethane;R_4=H, Ar, condensed urethane; R_5=Ar, alkyl, condensed urethane)

The identity of the neutral fragment has been established by accurate mass measurement of parent and daughter ions. In each case there are appropriate metastable peaks in the first[3] and second drift region of a double focussing mass spectrometer. This fragmentation reaction remains important even in the presence of such functionalities as benzoyl or condensed urethane. Lablache-Combier et al.[2b] have reported the mass spectra of substituted isoxazolidines containing acetyl and ethylene ketal groups, which show similar intense loss of X$\dot{N}$HO. Competition between single bond cleavage and rearrangement process has been observed for both R_1=PhCO(II) and Ph(III), but in the case of the better leaving group (II) the former reaction is more effective. Comparison of the intensities of the second drift region metastable peaks for the rearrangement (m^*_R) and direct cleavage (m^*_C) reactions in compounds II and III at high (70 eV) and low (16 eV, II; 14 eV, III) energy, shows that in each case the rearrangement process has the lower activation energy. The better leaving group (PhCO;

II) competes more effectively with the rearrangement, as is shown by the ratios of the metastable peaks at low energy:- II m^*_C/m^*_R = 0.55; III m^*_C/m^*_R = 0.

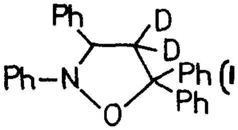
When C-4 is fully substituted ($R_2,R_3 \neq H$) the rearrangement is not observed, thus demonstrating that the process can be of use in determining the substitution pattern of the isoxazolidine ring.

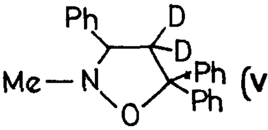
The mechanism proposed for this rearrangement involves fission of the C-N bond, and formation of an intermediate which allows loss of $X\dot{N}HO$ from a 5-membered cyclic transition state as depicted below.



Fission of the C-O bond followed by elimination of $XN\dot{O}H$ *via* a similar 5-membered cyclic transition state is also possible, but we think that the proposed intermediate will be the more stable because of the difference in bond energy and electronegativity between the two heteroatoms.

The mechanism requires a specific hydrogen transfer from C-4; to confirm this, deuterium labelling studies were undertaken.


(IV)


(V)

The mass spectra of IV and V show specific loss of fragmentmm/e 109 ($Ph\dot{N}DO$) and m/e 47 ($Me\dot{N}DO$) respectively, thus confirming the origin of the hydrogen lost as C-4 and the validity of the postulated fragmentation mechanism.

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