

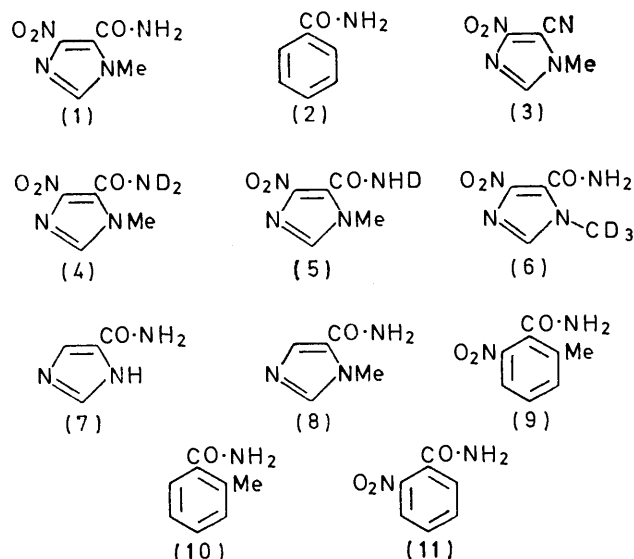
# High Resolution Mass Spectrometry. Part X.<sup>1</sup> Loss of Water from the Molecular Ions of Aromatic Amides

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Thermal loss of water by aromatic amides in the mass spectrometer is well known; it is now shown that when the amide group is flanked by both a methyl and a nitro-group elimination of water occurs by an electron-impact process. In view of the results of deuterium-labelling studies a mechanism is proposed for this loss in the case of 1-methyl-4-nitroimidazole-5-carboxamide. It is further shown that the resulting ion does not have the nitrile structure.

DURING an investigation of the mass spectral behaviour of imidazoles, it was noticed that 1-methyl-4-nitroimidazole-5-carboxamide (1) loses water very readily in an electron-impact-induced process. This is unusual behaviour for an amide, although thermal loss of water at usual source temperatures is well known. Thus in the mass spectrum of benzamide, for instance, at 200 °C the ion at  $m/e$  103 ( $M - H_2O$ ) is the base peak.<sup>2</sup> Lowering of the inlet reservoir temperature to 140 °C reduces the intensity of the  $m/e$  103 ion to 3.8% of the new base peak at  $m/e$  105.



We have determined the mass spectra of compounds (1)–(11) using a direct inlet system. The compositions of all ions discussed have been confirmed by accurate mass measurements at high resolving power. Observed values were within 5 p.p.m. of calculated values.

As expected, the mass spectrum of benzamide (2) showed an intense ion at  $m/e$  103 due to loss of water, at a source temperature of 250 °C. Reduction of the source temperature to 110 °C resulted in an 80% reduction in the intensity of this ion, thus confirming Cotter's conclusion<sup>3</sup> that the high ion intensity at  $m/e$  103 obtained at high temperatures is due to pyrolysis. However a corresponding reduction of the source

temperature caused no significant decrease in the intensity of the  $M - H_2O$  ion obtained from the amide (1), indicating that the loss of water in this case is not a thermal process but an electron-impact one. This was supported by the presence of a metastable ion at  $m/e$  135.9 (170  $\rightarrow$  152).

If the electron-impact-induced loss of water from the molecular ion of the amide (1) is analogous to the thermal loss of water, *i.e.* it occurs *via* a 1,2-elimination, the resulting ion would be expected to have the same structure, but not necessarily the same internal energy as the molecular ion formed from the nitrile (3). The ion at  $m/e$  152 obtained from the amide (1) could have an internal energy equal to or higher than that obtained from (3), but not less.<sup>4</sup> If the  $M - H_2O$  ion at  $m/e$  152, obtained from (1), had the same structure and same internal energy as the molecular ion of (3), the two ions (being identical) would be expected to show identical metastable peaks for the further loss of NO. If the  $M - H_2O$  ion from (1) had the same structure as, but higher energy than, the molecular ion of (3), the metastable peak for the further loss of NO from  $m/e$  152 generated from (1) should be at least as wide as the corresponding metastable peak for (3), perhaps even wider if the excess energy is released as kinetic energy. However the observed metastable peak for the loss of NO from the  $M - H_2O$  ion (at  $m/e$  152) in the case of the amide (1) was a sharp one at  $m/e$  97.9, whereas that for the loss of NO from the molecular ion of (3) (at  $m/e$  152) was flat-topped and extended from  $m/e$  96.8 to 99.2. The two ions of  $m/e$  152 have, therefore, different structures, and the loss of water from the molecular ion of the amide cannot be occurring *via* a simple 1,2-elimination.

In order to investigate the mechanism of the elimination of water from compound (1), deuterium-labelled analogues of (1) were prepared and examined. The mass spectrum of the product obtained from (1) by repeated treatment with  $CH_3OD$ , showed it to be largely 1-methyl-4-nitroimidazole-5-dideuteriocarboxamide (4), but the monodeuteriated compound (5) and some non-deuteriated (1) were also present. The resulting spectrum was thus considerably more complex than that of pure (1), but the useful feature was the presence of

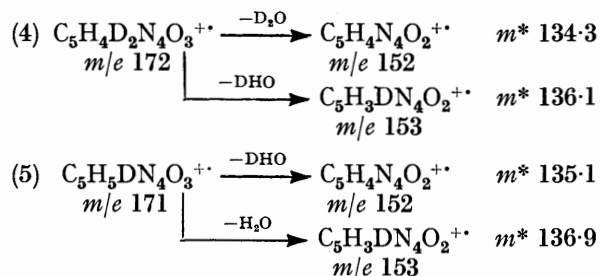
<sup>1</sup> Part IX, J. M. Midgley, B. J. Millard, W. B. Whalley, and C. J. Smith, *J. Chem. Soc. (C)*, 1971, 19.

<sup>2</sup> J. L. Cotter, *J. Chem. Soc.*, 1964, 5477.

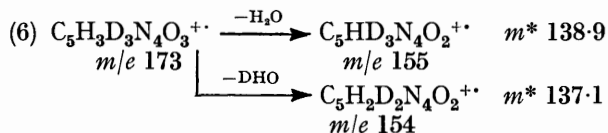
<sup>3</sup> J. L. Cotter, *J. Chem. Soc.*, 1965, 5742.

<sup>4</sup> D. H. Williams, R. G. Cooks, and I. Howe, *J. Amer. Chem. Soc.*, 1968, 90, 6759.

metastable ions at  $m/e$  134.3, 135.1, 136.1, and 136.9. These arose from the following fragmentations:



The mass spectrum of 4-nitro-1-trideuteriomethylimidazole-5-carboxamide (6) exhibited metastable ions at  $m/e$  138.9 and 137.1, indicating the following fragmentation processes:



At first sight these observations could be interpreted in either of two ways:

(a) The operation of two different mechanisms for the elimination of water from the amide. Thus since compound (4) lost both HDO and  $D_2O$ , it could be inferred that one mechanism involved loss of both the amide hydrogen atoms, whereas the second mechanism involved one amide hydrogen atom and one hydrogen atom from another part of the molecule. The loss of HDO from (6) showed this other hydrogen atom to originate from the methyl group.

(b) Hydrogen-deuterium scrambling prior to the elimination of water with the operation of a single mechanism.

If two different mechanisms were involved, it would be unlikely that both would have the same energy requirement, and the ions formed by the two mechanisms would be expected to have different appearance potentials. However the appearance potentials of the ions at  $m/e$  154 and 155 in the spectrum of compound (6) were the same within the limits of experimental error (see Table). Although this fact does not completely

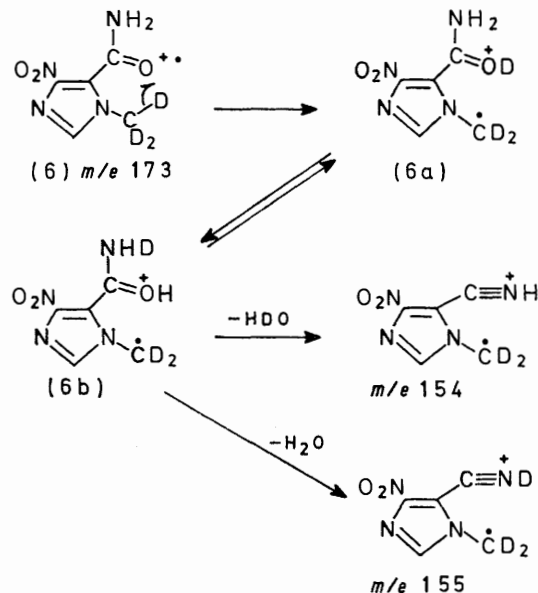
Appearance potentials for ions from the amide (6)

Ion	$m/e$	Appearance potential (eV)	Mean (eV)
$C_5H_2D_2N_4O_2$	154	$9.96 \pm 0.1$	9.915
$C_5HD_3N_4O_2$	155	$9.87 \pm 0.1$	9.91
		$9.96 \pm 0.1$	

exclude the operation of two different mechanisms, it makes this explanation unlikely, especially as one of the mechanisms would involve the loss of  $H_2O$  by a 1,2-elimination with formation of the nitrile ion. This, as the metastable peak shape for the further loss of NO shows, is not formed. The alternative explanation, involving hydrogen scrambling prior to the elimination of water has, therefore, to be preferred. However, if the

deuterium atoms in compound (6) were equilibrated throughout the molecule prior to water elimination, the ratio of loss of  $H_2O$ , HDO, and  $D_2O$  would be 20 : 60 : 20, respectively (excluding isotope effects). However the ions at  $m/e$  153 due to loss of  $D_2O$  was insignificant, neither was a metastable ion observed for loss of  $D_2O$ . This fact therefore rules out scrambling of the hydrogen and deuterium atoms.

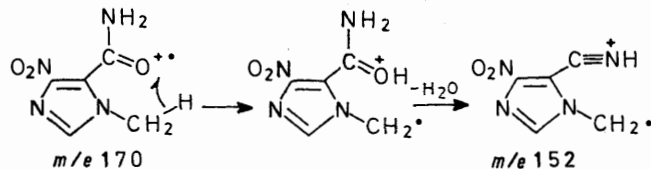
A mechanism which would account for all these observations, namely that only  $H_2O$  and HDO are lost from (6) and that the resulting ion does not have the nitrile structure, is shown in Scheme 1. Initial transfer



SCHEME 1

of deuterium is followed by localised scrambling between this deuterium and the amide hydrogen atoms. If complete equilibration of these three atoms occurred, the ratio of loss of  $H_2O$  and HDO would be 33.3 : 66.6 respectively if isotope effects are neglected. In the normal ions the observed ratio is 38 : 62, whereas for the metastable ions it is 45 : 55. This ratio implies a slight preference for (6a) over (6b).

The mechanism for the loss of water from the unlabelled molecule (1) can then be simply written as in Scheme 2. The presence of the *N*-methyl group is seen



SCHEME 2

to be essential since this is the source of one of the eliminated hydrogens. The nitro-group probably repels the carbonyl group into a position suitable for this hydrogen to be transferred. Investigation of the mass spectra of imidazole-4(5)-carboxamide<sup>5</sup> (7) and 1-methylimidazole-5-carboxamide (8) showed that they do not

<sup>5</sup> I. E. Balaban, *J. Chem. Soc.*, 1932, 2425.

readily eliminate water. The presence of both a methyl group and a nitro-group flanking the carboxamide group is therefore essential for the elimination of water.

The question now arises whether this water loss is unique to the imidazole ring system or whether it is more general in nature. To test this point 2-methyl-6-nitrobenzamide was examined. This compound (9) also lost water under electron impact. The  $M - H_2O$  ion at  $m/e$  162 observed at a source temperature of 200 °C was only insignificantly reduced in intensity by lowering the source temperature to 100 °C, indicating that the loss of water was not pyrolytic. The presence of a metastable ion at  $m/e$  145.8 confirms the loss of water by the fragmentation  $m/e$  180  $\rightarrow$  162. Water was also lost from *o*-toluamide (10), but this was shown to be a pyrolytic process, since reduction of the source temperature from 250 to 100 °C reduced the loss of water by 93%. No metastable ion was observed for this loss of water. *o*-Nitrobenzamide (11) did not lose water by either pyrolysis or electron-impact at a source temperature of 230 °C. These results confirm that the presence of both the nitro- and methyl groups is necessary for the electron-impact-induced elimination of water to occur, and that such an elimination is not confined to the imidazole ring system.

#### EXPERIMENTAL

Spectra were determined with an A.E.I. MS 902 mass spectrometer using a direct inlet system. The beam energy was 70 eV. The source temperatures used varied from 100

† For details of Supplementary Publications, see Notice to Authors No. 7 in *J. Chem. Soc. (A)*, 1970, Issue No. 20 (items of less than 10 pp. are supplied as full size copies).

to 250 °C. Data are given in Supplementary Publication No. SUP 20641 (3 pp.).† Accurate mass measurements were carried out at a resolving power of 20,000 (10% valley). The appearance potentials (Table) were determined by the linear extrapolation method.

Benzamide (2), *o*-toluamide (10), *o*-nitrobenzamide (11), and 2-methyl-6-nitrobenzamide (9) were prepared from the commercially available acids *via* the acid chlorides, by standard methods.

1-Methyl-4-nitroimidazole-5-carboxamide (1) was prepared<sup>6</sup> from 5-bromo-1-methylimidazole. The latter was prepared according to ref. 7 but with methyl iodide instead of dimethyl sulphate, and had the same properties as reported.

4-Nitro-1-trideuteriomethylimidazole-5-carboxamide (6).—This was prepared as for compound (1) by using trideuterio-methyl iodide in place of methyl iodide; m.p. 264–265 °C.

1-Methylimidazole-5-carboxamide (8).—4-Amino-1-methylimidazole-5-carbonitrile<sup>8</sup> (1 g) was diazotised with sodium nitrite and hydrochloric acid. The solution was warmed with excess of ethanol on a steam-bath for 15 min, then treated with concentrated sulphuric acid (8 ml), and heating was continued for 2 h. The solution was cooled, diluted with twice its volume of water, neutralised with sodium carbonate, and extracted with chloroform (3  $\times$  50 ml). The combined extracts were dried (MgSO<sub>4</sub>) and evaporated. The brown solid was recrystallised twice from acetone to yield the *carboxamide* as needles, m.p. 184° (Found: C, 47.9; H, 5.6; N, 33.6. C<sub>5</sub>H<sub>7</sub>N<sub>3</sub>O requires C, 48.0; H, 5.6; N, 33.6%).

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<sup>6</sup> J. Sarasin and E. Wegmann, *Helv. Chim. Acta*, 1924, **7**, 713.

<sup>7</sup> I. E. Balaban and F. L. Pyman, *J. Chem. Soc.*, 1924, 1564.

<sup>8</sup> F. Montequi, *Anales real Soc. españ. Fís. Quím.*, 1927, 182.