ACTA CHEMICA SCANDINAVICA 27 (1973) 589–594

Mass Spectrometry of Onium Compounds

Part XVI.[1] Pyrolytic Fragmentation of Amino Acid Betaines

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The pyrolytic behaviour in the mass spectrometer of a series of *N*-quaternary amino acid homologues has been investigated. The pyrolysis process is dependent on the number of methylene carbons separating the functional groups.

Electron induced fragmentations are discussed in relevant cases.

The salt like characteristics of *N*-quaternary amino acids and the frequent lack of a readily accessible chromophore for absorption spectroscopy complicates identification and estimation in low concentration in natural sources. The pyrolytic behaviour of such compounds in the mass spectrometer should therefore be of both theoretical and analytical interest. Recently we reported the mass spectrometry behaviour of the liver component carnitine and fatty acid esters thereof.[2] This work concerns simple aliphatic *N*-quaternary amino acids where the functional groups are separated by series of methylene groups. High resolution has been used in the determination of the composition of major fragments discussed.

$$(CH_3)_3N^+-(CH_2)_n-CO_2^-$$

I $n=1$, II $n=2$, III $n=3$, IV $n=4$, V $n=5$

The spectra recorded are formed through superimposition of the fragmentation spectra from the pyrolysis products present in the gas phase. The relative peak intensities will vary with conditions and with time in accordance with relative volatilities of the components.

The base peak in the spectrum of trimethylamine is at *m/e* 58 [M−H], the molecular ion intensity being 45 %.[3] Some *m/e* 58 species are also formed by α-cleavage from dimethylaminomethylene derivatives after electron impact and when present with trimethylamine will increase the relative intensity of the *m/e* 58 signal.

For the glycine betaine (I), which is an α-amino acid derivative, esterification is the most important pyrolytic process. With two or three methylene carbons between the functional groups (II, III) no ester formation is seen. Esterification reappears again with four methylene groups (IV), however, and is the only important process for $n = 5$ and probably also for higher homologues. The near absence of the corresponding acid in the spectra is ascribed to low volatility with high probability for esterification.

A decision between intra- or the more likely inter-alkylation process was made in each case where ester is formed by allowing homogeneous mixtures of the amino acid, quaternized with trideuteriomethyl iodide and with methyl iodide, to evaporate in the mass spectrometer. Invariably, when the spectra were recorded after a short time, four equally intense peaks were found which correspond to the molecular ion. For the glycyl betaine these were at *m/e* 117 ($(CH_3)_2NCH_2CO_2CH_3$), *m/e* 120 ($(CH_3)_2NCH_2CO_2CD_3$), *m/e* 123 ($(CD_3)_2NCH_2CO_2CH_3$), and *m/e* 126 ($(CD_3)_2NCH_2CO_2CD_3$). Therefore the transalkylation is an intermolecular process. When the spectra were recorded after the sample had been kept for some time in the instrument, the intermediate molecular ion peaks showed increased intensities. This is due to transfer of a methyl group from the quaternary nitrogen to a tertiary nitrogen which thereby is requaternized and can take part in the esterification reactions.

The spectrum of the β-alanine (II) shows that liberation of trimethylamine is the only important process with concomitant formation of acrylic acid or its isomeric β-lactone (*m/e* 72). In deuterium oxide atmosphere two peaks were found at *m/e* 72 and *m/e* 73. The intensity of the latter was about half that of the former. Deuterium exchange is in accordance with acrylic acid formation, the exchange being incomplete under these experimental conditions.* The reason for complete dominance of the Hofmann elimination lies in carboxyl group activation of the hydrogens on the β-carbon relative to the quaternary nitrogen. Trimethylamine and acrylic acid are also the products from preparative pyrolysis.[4]

With three methylenes (III) the carboxylate group is in position for γ-lactone formation and Hofmann elimination is competitively excluded, partly because the β-carbon is no longer activated. Coformation of the isomeric β,γ-unsaturated acid could be excluded since no deuterium was incorporated in the molecular ion at *m/e* 86 when the spectrum was recorded in deuterium oxide atmosphere. Preparative pyrolysis takes the same course.[4]

For $n = 4$, δ-lactone (*m/e* 100) and its fragments account for part of the ion current, but the more important pyrolytic pathway seems to go through the ester (*m/e* 159) (Fig. 2). These results agree with pyrolytic observations.[5] With five methylene groups, as discussed above, ester formation is the only important pyrolytic process (Fig. 3).

The behaviour of the hydroiodide salts of I – V was also investigated. The Hofmann elimination in II, or γ-lactone formation in III, were not affected. For the other acids (I, IV, V) the intensity of the ester molecular ion was more than halved. The relative intensity (*m/e* 58) of the methyl iodide signal (*m/e* 142) was 40 – 50 %.

* Unpublished observations.

The spectrum of II is due to superimposition of the fragmentation spectra from acrylic acid [6] and trimethylamine [3] and that of III is due to γ-lactone [7] and trimethylamine.

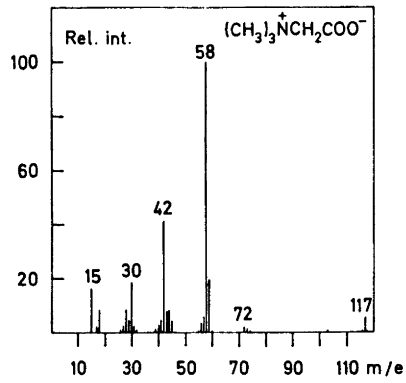
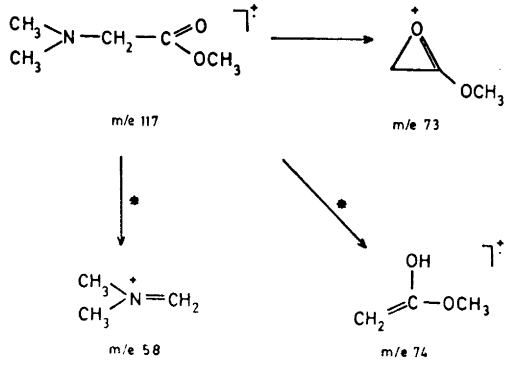


Fig. 1.

The glycine spectrum (Fig. 1) shows the gas phase molecules to be the transalkylated ester (*m/e* 117) and trimethylamine. The major peaks in the spectrum of trimethylamine [3] are at *m/e* 59 (45 %), *m/e* 58 (100 %), *m/e* 42 (42 %), *m/e* 30 (35 %), *m/e* 28 (18 %), and *m/e* 15 (20 %). The relative intensity of the base peak (*m/e* 58) in the spectrum of I is more than twice that in trimethylamine and its main origin is therefore the ester at *m/e* 117 (Scheme 1). α-Cleavage to nitrogen so strongly directs the fragmentation that other pathways are of little importance. The intensities of the *m/e* 42, 30, and 15 species are much reduced compared to the same fragments from trimethylamine. The increase in relative stability of the *m/e* 58 species is even more evident from the spectrum of V (Fig. 3) where the relative intensities of the

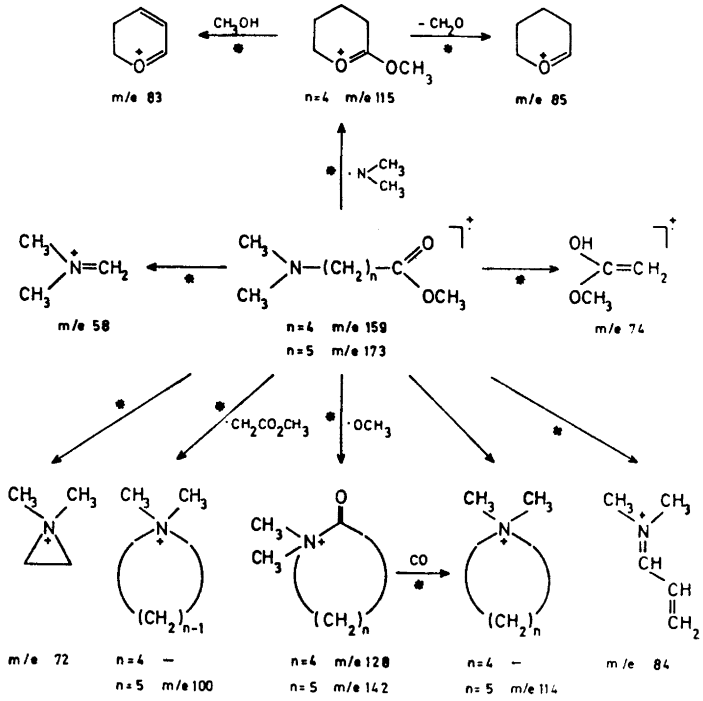


Scheme 1.

m/e 42, 30, and 15 species are below 10 %. Two energetically different structures of the *m/e* 58 species therefore exist. The weak signal at *m/e* 74 is due to

McLafferty rearrangement with transfer of a hydrogen from one of the *N*-methyl groups. Methoxyl expulsion (*m/e* 86), which is important for the esters discussed below, is hardly seen.

In the higher esters the fragmentation is also dominated by the amino function in such a way that the amino nitrogen is present in most of the important fragments. This is not unexpected since the fragmentation process will be determined by charge distribution and relative rates. The charge will largely reside on the amino group since this has much the lower ionization potential but its direction of fragmentation will be modified by interaction with the ester group.[9–11] Thus McLafferty rearrangement gives a weak signal at *m/e* 74 while methoxyl group expulsion is relatively strong. The latter mode of fragmentation is probably favoured by stabilization through the amino group (Scheme 2, Figs. 2 and 3).



Scheme 2.

An important fragment in both spectra is found at *m/e* 84. In Scheme 2 its genesis is indicated directly from the molecular ion. Metastable defocusing shows that these species also originate from primary fragments. The base peak at *m/e* 58 is formed directly from the molecular ion but metastable defocusing shows that it is also formed from several precursor ions. IV gives

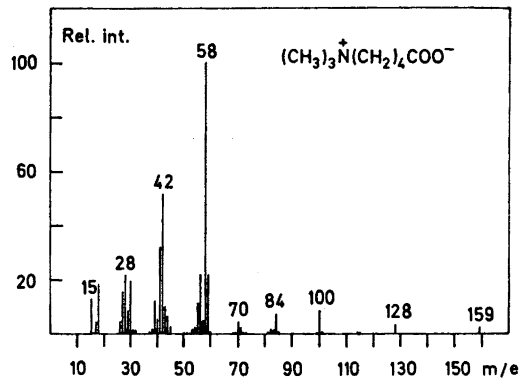


Fig. 2.

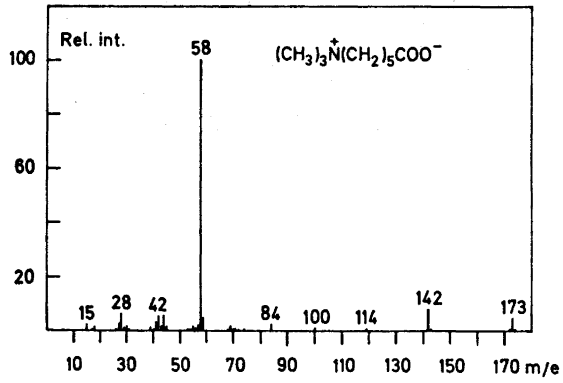


Fig. 3.

a relatively strong ion at *m/e* 115. The corresponding fragment in V is not important. On the other hand, V gives an ion at *m/e* 100 by δ-cleavage which can be formulated as a pyrrolidinium ion.

The low energy spectrum (16 eV) of V increases the molecular ion and the *m/e* 100 intensity by a few per cent. The low and high energy spectra are very similar since in both cases the major ion current is carried by the *m/e* 58 species. The low energy spectrum of IV also shows a slight increase in the molecular ion intensity but the major increase, from about 20 to 40 %, is in the *m/e* 59 species, showing the presence of trimethylamine.

The spectrum of IV also contains the fragmentation of δ-lactone. The major fragments from the latter are at *m/e* 42 (base peak in the spectrum of pure δ-lactone) and at *m/e* 56 ($M-CO_2$, 45 %). The other peaks of 10 – 20 % relative intensity are at *m/e* 100 (M), *m/e* 71 ($M-CHO$), *m/e* 55 ($M-HCO_2$), and *m/e* 41 ($M-CH_2CO_2H$).[8]

The spectra of the hydroiodides show the additional weak molecular ions (*m/e* 143 and *m/e* 159) of the respective acids. These will fragment very much in the same way as the esters.

EXPERIMENTAL

The spectra were recorded on an AEI MS-902 mass spectrometer by direct insertion. The source temperature was kept at 210 – 220°, the electron energy and trap current at 70 eV and 100 μA respectively.

The hydroiodides were prepared by quaternization of the corresponding primary amines with methyl iodide.[12] The trideuteriomethyl derivatives were similarly prepared. The zwitterions were generated by passage of an aqueous solution of the hydroiodides through DEAE – Sephadex. The evaporation temperature of the eluates should be low to avoid decomposition.

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Received June 28, 1972.