

Mass Spectrometry of Onium Compounds. XXVIII.* Pyrolysis of Methonium Salts

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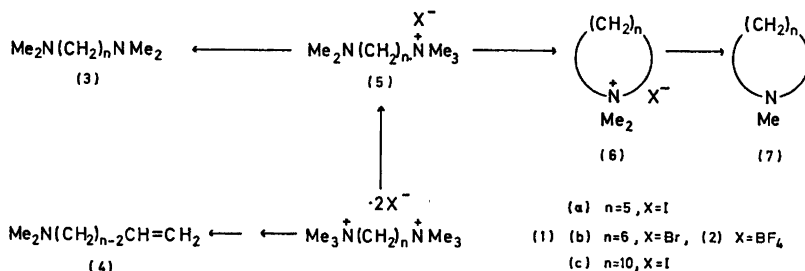
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Pyrolytic reactions of methonium salts in the mass spectrometer have been analysed. Formation of the corresponding *bis*-dimethylamines and dimethylamino-olefins are characteristic in the higher mass range of the spectra. Their formation is aided by moderately nucleophilic anions. Electron impact fragmentations are discussed.

The mass spectra from involatile *N*-quaternary salts are formed through superimposition of the fragmentation spectra from the volatile pyrolysis products. A complication in spectral analysis may be variations in relative peak intensities with recording conditions and with time in accordance with the relative volatilities of the components. The major pyrolytic fragmentation paths, however, can be rationalised in terms of the nature of the substituents attached to the quaternary nitrogen atoms.²⁻⁶ This report extends earlier studies of onium compounds in the mass spectrometer to *bis-N*-quaternary compounds; such knowledge is of interest for analytical studies of "methonium" type drugs⁷ and related compounds by mass spectrometry.

The penta-, hexa-, and decamethonium salts (1) in which the nitrogen atoms are bridged by five, six, and ten methylene groups, respectively, were available for studies. The pyrolytic behaviour of the bromide (1*b*) and the iodides (1*a*, 1*c*) were compared with the corresponding fluoroborates (2). The fluoroborate anion is partially pyrolysed to the strongly basic fluoride anion; Hofmann elimination reactions will thus be promoted. The more nucleophilic bromide and iodide ions are likely to favour substitution reactions.⁸ The expected differences are apparent by comparison of the spectra for each pair. One or two major pyrolytic pathways are desirable to ease interpretation of the spectra and increase sensitivity. An important factor is here the nature of the anion.

Several possibilities exist for product formation from the *N*-quaternary salts. In the present series major volatile products were the *bis*-dimethylamines (3) and the dimethylamino-olefins (4); methyl halides and trimethylamine are concurrently formed. Especially formation of trimethylamine may at first sight complicate interpretation of the spectra; its fragmentation,



Scheme 1.

Table 1. Relative intensities of the major ions in the mass spectra of tertiary amines.

| (3a) <i>m/e</i> | % | (3b) <i>m/e</i> | % | (3c) <i>m/e</i> | % | (4a) <i>m/e</i> | % | (4b) <i>m/e</i> | % |
|--------------------|-----|--------------------|-----|--------------------|-----|--------------------|-----|--------------------|-----|
| 158 | 0.5 | 172 | 1 | 228 | 2 | 113 | 3 | 127 | 4 |
| 114 | 2 | 128 | 3 | 213 | 1 | 98 | 8 | 99 | 0.5 |
| 98 | 5 | 127 | 4 | 184 | 1 | 84 | 12 | 98 | 0.5 |
| 84 | 4 | 114 | 2 | 142 | 0.5 | 71 | 3 | 84 | 4 |
| 70 | 2 | 84 | 7 | 128 | 1 | 58 | 100 | 71 | 1 |
| 58 | 100 | 58 | 100 | 114 | 0.5 | 42 | 8 | 58 | 100 |
| 42 | 3 | 42 | 5 | 84 | 3 | 30 | 4 | 42 | 5 |
| 30 | 3 | 30 | 3 | 58 | 100 | | | 30 | 3 |
| | | | | 42 | 3 | | | | |
| | | | | 30 | 3 | | | | |

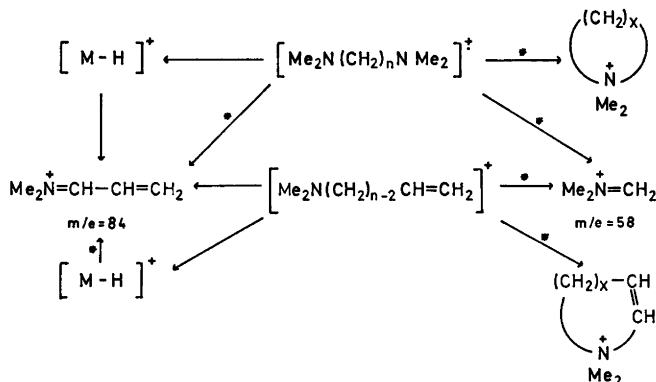
however, has been studied in some detail.⁸ The mass spectral behaviour of the bisdimethylamines and the dimethylamino-olefins on the other hand, had to be ascertained; these compounds with the exception of (4c) were therefore synthesised separately and their spectra recorded.

Bridged diamines on electron induced fragmentation are often characterised by low intensity molecular ion,⁹ a short bridge between the amino functions and *N*-substitution such as in 1,4-tetramethylaminobutane may increase the molecular ion intensity considerably.¹⁰ In the present series the base peak for both the diamines (3) and the olefins (4) was at *m/e* 58 [CH₂NMe₂]⁺; this fragment is formed primarily by α-cleavage of a bridge carbon-carbon bond. The molecular ion intensities were of the order 0.5–2 %.

The elemental compositions of the fragments discussed have been determined by high resolu-

tion. Expulsion of the dimethylamine radical is seen in the spectra of the bis-dimethylamines but not in the spectra of the dimethylamino-olefins. The process is therefore thought to be caused by the second amino group leading to a cyclic ammonium structure; accordingly this path is important for (3a) which can form a six-membered ring and was absent for (3c). The functional groups may also interact in other ways. Thus the diamines show loss of the dimethylaminomethylene radical [Me₂NCH₂][•] presumably with formation of cyclic ammonium structures. In general dimethylamino-alkyl radical expulsions are less important if the other amino function can be formulated as part of a medium size ring but signals corresponding to six-, five-, and three-membered rings are present. The dimethylamino-olefins show similar fragmentation patterns.

Hydrogen rearrangements are common phenomena in unsaturated aliphatic hydrocarbons.



Scheme 2.

In the dimethylamino-olefins the observed radical expulsions can be rationalised in terms of the various rearranged molecular ions; formation of unsaturated cyclic ammonium structures are postulated for the cations.

By far the most dominating peak in the spectra is due to the *N,N*-dimethylimmonium ion at *m/e* 58. The base peak in the spectrum of trimethylamine is also at *m/e* 58 $[M-H]^+$; the relative intensity of the trimethylamine molecular ion is 45 %. Accordingly the base peak in the spectra of the methonium salts is also found at *m/e* 58 (Fig. 1 and 2). The relative intensities of the trimethylamine peak in the spectra of the halides were 25 (1*a*), 16 (1*b*), and 8 % (1*c*), the figures for the fluoroborates were 35 (2*a*), 24 (2*b*), and 20 (2*c*). The fluoroborates had to be heated at 310–330 °C in the probe to give a sufficient ion current while the other salts were kept at 220 °C. The figures show that fragmentation of the bisdimethylamine and the dimethylamino-olefin is a major contributor to the mass number 58. More trimethylamine is formed from the compound with the shortest methylene bridge. More trimethylamine is also formed in the fluoroborate series. The relatively nucleophilic bromide and iodide ions cause extensive dealkylations at the lower temperature while the more electronegative fluoride ion possibly together with the fluoroborate ion, requires higher activation and then acts more as a base in Hofmann elimination. The relative intensities of the molecular ions of the diamines support this conclusion; the figures for the bromide and iodides were 0.5 (1*a*), 1 (1*b*), and 2 % (1*c*); and 0 (2*a*), 0 (2*b*), and 1 % (2*c*) for the fluoroborates. Corresponding figures for the molecular ions of the dimethylamino-olefins

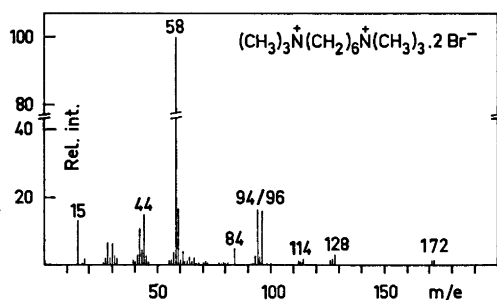


Fig. 1.

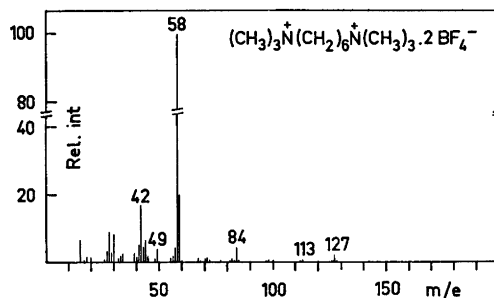


Fig. 2.

were 2 (1*a*), 2 (1*b*), and 0.5 (1*c*) which are to be compared with 0.5 (2*a*), 2 (2*b*), and 3 (2*c*).

After demethylation of the one amino group another demethylation or Hofmann elimination must occur. Alternatively the Hofmann elimination occurs initially. The products from two Hofmann eliminations, however, were not seen.

Ions with mass number corresponding to the dihalides of the methylene bridge or the corresponding halo-olefins were absent. Long-chain aliphatic halides, however, may display very weak molecular ions but contain significant signal for ions after halogen expulsion;¹¹ the absence of corresponding signals in the present series excludes such structures as major pyrolytic components. Nor are signals due to amino-halides present. In this case expulsion of the halogen and formation of a cyclic ammonium structure would be expected to show up in the spectra. The mass number for these ions is the same as after dimethylamine radical expulsions from the diamines (3). A comparison of the relative intensities for this mass number in the spectra of the diamines (3) and the spectra from the methonium salts suggest that amino halides are not important pyrolytic products. These observations show that the nucleophilic attack by the halide ion is mainly on the methyl carbon rather than on the α -carbon of the methylene bridge.

Another pyrolytic reaction to be considered is internal cyclisation with trimethylamine displacement after initial demethylation in the other amino function. The involatile, cyclic ammonium product may then undergo a Hofmann elimination to the dimethylamino-olefin or undergo demethylation; cyclisation was found important for the pentamethonium iodide lead-

ing to a six-membered ring; thus the intensity of the mass number corresponding to *N*-methylpiperidine was 13.5 % with $[M-H]^+$ 40 %. Support for the former being a molecular ion was forthcoming by the substantial increase in the relative intensity of this species in low-energy spectra. The relative intensities of the corresponding peaks in the spectra of the hexamethonium bromide were 1 (*m/e* 113) and 1.5 % (*m/e* 112); and the relative intensity of the higher mass number was increased to 8 % in the low energy spectra. Corresponding signals in the spectra of the decamethonium iodide were absent. These results reflect the relative tendencies for ring formation. This reaction path will also depend on the availability of a tertiary amino function and is therefore favoured in the presence of nucleophilic anions. Thus in the spectra of the fluoroborates the signal intensity for the cyclic product from the methonium salts was reduced to 1 % and were absent in the spectra of the other isomers.

EXPERIMENTAL

The mass spectra were recorded on an AEI MS902 mass spectrometer attached to an AEI DS 30 data system. The electron energy was 70 eV and the ionising current 100 μ A. The compounds were introduced by the heated direct insertion probe; the iodide and bromide methonium salts at 220 °C and the fluoroborates at 310–330 °C. The source temperature was 220 °C.

Commercial methonium bromide or iodides were used. The fluoroborates were available from concentrated aqueous solutions of these salts by addition of 40 % fluoroboric acid; the fluoroborates crystallised directly or after concentration of the solution.

The bisdimethylamines (3) were synthesised from the corresponding dibromides.¹² The dimethylamino-olefins (4) were synthesised from piperidine and hexamethylenimine by quaternisation with methyl iodide and the products ground together with solid sodium hydroxide and pyrolysed.¹³

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