Translated from *Uspekhi Khimii*, **45**, 1870-1894 (1976) U.D.C. 543.51 : 547.94; 547.7

Mass Spectrometry of Quinolizidine Alkaloids

N.S.Vul'fson and V.G.Zaikin

General and specific modes of breakdown on electron bombardment are surveyed for certain simple quinolizidine derivatives, including substances of natural origin, and many quinolizidine alkaloids of the cytisine, sparteine, and matrine series. Mass spectrometry can be used to establish the structure of this class of naturally occurring compounds. A list of 36 references is included.

CONTENTS

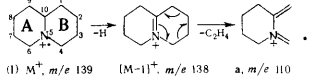
I. Introduction 959
II. Quinolizidine and its simple derivatives 959
III. Quinolizidine alkaloids 961

I. INTRODUCTION

Alkaloids derived from quinolizidine occur widely in the vegetable kingdom. The structures of several dozen natural quinolizidine alkaloids have now been established, and several stereoisomeric compounds, not yet found in Nature, as well as derivatives possessing valuable pharmacological properties, have been prepared from them. Some steroidal alkaloids containing the quinolizidine system, as well as lycopodium alkaloids, can formally be included. However, we have considered it advisable to restrict the present Review to those quinolizidine alkaloids whose degradation on electron bombardment conforms most closely to the rules characteristic of the quinolizidine system. Lycopodium alkaloids and the corresponding steroidal alkaloids are less interesting from this point of view, since the quinolizidine part of the molecule is insufficiently specifically developed in their mass spectra (the modes of decomposition of lycopodium alkaloids on electron bombardment have been summarised in a monograph[1]). The present Review covers mass-spectrometric investigations of quinolizidine and its simple derivatives, including those of natural origin, as well as the more complicated quinolizidine alkaloids belonging to the cytisine, sparteine, and matrine groups.

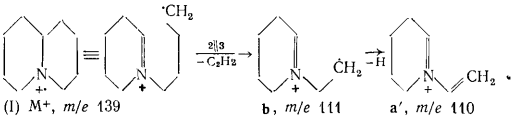
II. QUINOLIZIDINE AND ITS SIMPLE DERIVATIVES

Detailed reviews have appeared on the behaviour under electron bombardment of quinolizidine itself (I) and its deutero-analogues[2-5]. The maximum peak in the mass spectrum of (I) corresponds to the $[M - 1]^+$ ion, the peak due to the molecular ion being only about half as intense[4]. Analysis of the mass spectra of the analogues labelled with deuterium at the 1,4 and 2,10 positions showed that the above ion is formed by preferential elimination of the hydrogen atom from the $C_{(10)}$ carbon atom, whereas at most 11% of the hydrogen is lost from $C_{(4)}$ and $C_{(6)}$ adjacent to the nitrogen atom[5]. Further breakdown of the $[M - 1]^+$ ion, on the pattern of a retrodiene reaction (RDR), yields an ion (a) having m/e = 110:



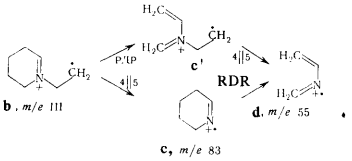
(I) M^+, m/e 139 $[M-1]^+$, m/e 138 a, m/e 110

It is supposed furthermore that this 110 ion may be formed from the molecular ion by successive rupture of the $C_{(10)}-C_{(1)}$ and $C_{(2)}-C_{(3)}$ bonds with elimination of an ethylene molecule and formation of an m/e 111 ion (b), which then loses a hydrogen atom. The 110 ion will then have the structure a'[4]:



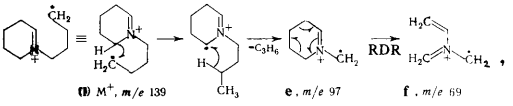
(I) M^+, m/e 139 b, m/e 111 a', m/e 110

Nor can it be excluded that (a') may be formed from the $[M - 1]^+$ ion as a result of elimination of an ethylene molecule with rupture of the above two bonds accompanied by migration of a hydrogen atom from $C_{(4)}$ to $C_{(10)}$. Elimination of an ethylene molecule from ion b by rupture of $C_{(4)}-C_{(5)}$ or a retrodiene type of breakdown in ring *A* yields ions having m/e 83 (c or c'), which then lose another ethylene molecule to give the ion d with m/e 55:



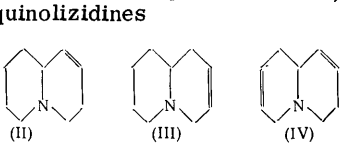
b, m/e 111 c', c, m/e 83 d, m/e 55

The characteristic ion e with m/e 97 is formed directly from the molecular ion (I). It was shown by means of deuterated analogues[3] that formation of this ion (e) is due to elimination of the $C_{(1)}-_{(3)}$ atoms accompanied by countermigration of hydrogen atoms:



(I) M^+, m/e 139 e, m/e 97 f, m/e 69

The introduction of double bonds into the quinolizidine molecule results in appreciable simplification of the mass spectrum[6]. The peaks due to molecular and $[M - 1]^+$ ions are very intense in the spectra of Δ^1-, Δ^2-, and $\Delta^{1,7}$-dehydroquinolizidines



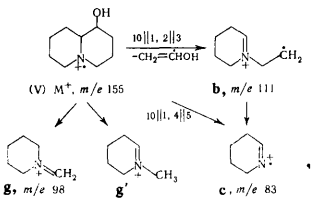
(II) (III) (IV)

[with (II) and (IV) the latter ions are the most intense in the spectrum]. The c ion, formed by a retrodiene type of breakdown in the B ring and then decomposing to the ion d, has the maximum intensity in the spectrum of (III).

The spectra of (II) and (IV) are characterised by unsaturated analogues of c ions with *m/e* 80 and 81. That of (II) also contains a peak due to an unsaturated analogue of the ion a′ with *m/e* 108.

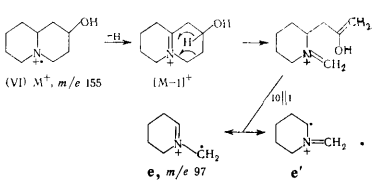
The introduction of a hydroxy-group into the quinolizidine molecule in principle leaves unchanged the modes of breakdown of the main skeleton under electron bombardment. However, the intensities with which certain processes occur depend both on the presence of such a group and on its position.

The peaks of molecular and $[M - 1]^+$ ions in the mass spectra[5] of 1-, 2-, and 3-hydroxyquinolizidines (V)–(VII) are quite intense; they are more intense with (VI) and (VII) than with (V), and in these two cases the $[M - 1]^+$ ions are more intense than the molecular ions. The main peaks in the spectra of (V) and (VII) are due to the ions c with *m/e* 83. This ion may be formed from (V) either directly from the molecular ion by rupture of $C_{(10)}$–$C_{(1)}$ and $C_{(4)}$–$C_{(5)}$ bonds or from the b ion with *m/e* 111 by loss of an ethylene molecule in the rupture of the $C_{(4)}$–$C_{(5)}$ bond:



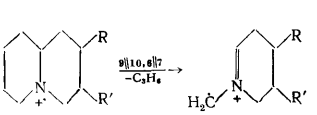
In the case of (VII) the ion c is formed only bh the first route[5].

Analysis of the mass spectra of deuterated analogues showed that the next most intense peak in the spectrum of (V) with *m/e* 98 is due to the isomeric ions g and g′, formed directly from the molecular ion by rupture of the $C_{(10)}$–$C_{(1)}$ and $C_{(3)}$–$C_{(4)}$ bonds with migration of a hydrogen atom to the charged particle. The most intense peak in the spectrum of (VI) is an ion having *m/e* 97 (e or e′):



The peaks due to ions a–c are moderately intense in the spectrum of (VI). Whereas the peaks due to $[M - OH]^+$ ions are relatively weak in the spectra of (V) and (VII), the corresponding peak in the spectrum of (VI) is similar in intensity to that due to the molecular ion.

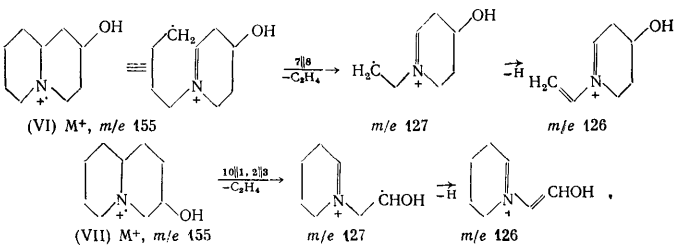
A peculiarity of the breakdown of the hydroxy-derivatives (VI) and (VII) under electron bombardment is the formation of several oxygen-containing fragments almost completely absent from the spectrum of (V). Both the former compounds are characterised by fairly intense peaks due to ions having *m/e* 113 (h and h′ respectively), resulting from rupture of $C_{(6)}$–$C_{(7)}$ and $C_{(9)}$–$C_{(10)}$ bonds with localisation of the charge on the oxygen-containing fragment:



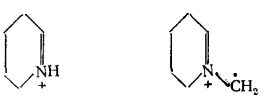
M+, (VI) R=OH, R′=H, *m/e* 155
(VII) R=H, R′=OH

m/e 113, h, R=OH, R′=H;
h′, R=H, R′=OH.

A different pattern obtains in the formation of ions with *m/e* 126 and 127, for analysis of the mass spectra of deuterated analogues of (VI) and (VII) indicates different mechanisms of formation and hence different structures:

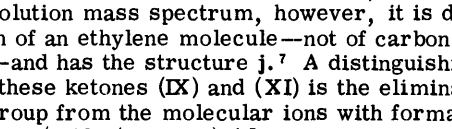


A distinguishing feature of the mass spectrum of (VII) is the quite considerable intensity of peaks due to $[c + 1]^+$ and g ions with *m/e* 84 and 98 respectively. The spectra of all the above compounds contain not very intense peaks due to $[e - 1]^+$ ions with *m/e* 96.



Introduction of a keto-group into the quinolizidine molecule has a still more marked effect on the character of the mass spectrum. Spectra have been described for the derivatives (VIII)–(XI) with this group in positions 1–4 [4,7] and their deuterated analogues. They all differ significantly in the intensity of the peak due to the molecular ion: with (IX) and (XI) these peaks are the most intense, with (X) the intensity is ~60%, and with (VIII) only ~30%. Although a hydrogen atom is eliminated from the molecular ion in all cases, this process is less characteristic of the ketones (VIII)–(XI) than of the previous examples. The position of the keto-group has a very significant influence on the breakdown of the molecular ion, although in many cases the resulting ions have the same structure as previously. Successive elimination of a carbon monoxide molecule and a hydrogen atom with formation of ions having *m/e* 125 and 124 is most characteristic of the molecular ions of (VIII) and (X), and is confirmed by the spectra of the deuterated analogues and by the presence of the corresponding metastable peaks in the spectra[4]. In both cases different structures were ascribed to these ions, which the Reviewers regard as unsound.

Peaks due to ions with *m/e* 125 and 124 are completely absent from the mass spectrum of (IX) [4], whereas the 125 peak is present in the spectrum of (XI); according to a high-resolution mass spectrum, however, it is due to elimination of an ethylene molecule—not of carbon monoxide—and has the structure j.[7] A distinguishing feature of these ketones (IX) and (XI) is the elimination of a methyl group from the molecular ions with formation of ions having *m/e* 138 (k and k′).[4,7]



The spectra of all the ketones examined contain peaks due to ions of the previous types a and c–g; the b ion is apparent only in the spectrum of (IX). The high-resolution

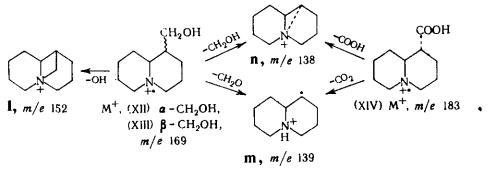
mass spectrum indicates that the 97 peak in the case of (X) is composite, representing not only ions e and e′ but also ions of composition C_7H_{13} and C_6H_9O.

It must be emphasised that the above ions of types a–g are in general present in the mass spectra of all quinolizidine alkaloids, their intensity varying with the type of fusion of the rings and with the nature and position of substituents.

III. QUINOLIZIDINE ALKALOIDS

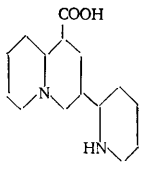
1. Simple Alkaloids

The mass spectra of the simplest quinolizidine alkaloids—lupinine (XII), isolupinine (XIII), and lupininic acid (XIV)—were described by Spiteller et al.[8] as long ago as 1964. The spectra of the epimeric alcohols (XII) and (XIII) differ little. The peaks of molecular and $[M - 1]^+$ ions are fairly intense. These compounds undergo not only the above modes of decomposition giving the ions a–g but also fragmentation of the hydroxymethyl group, with elimination of a hydroxyl radical or a formaldehyde molecule (giving the ions *l* and m with *m/e* 152 and 139 respectively), and loss of a hydroxymethyl radical yields the ion n with *m/e* 138:

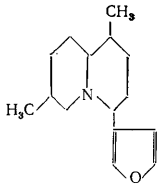


The peaks of *l* and n ions are among the most intense in the spectrum. The maximum peaks in the spectra of (XII) and (XIII) are produced by c and *l* ions respectively. The c peak predominates also in the spectrum of the acid (XIV), about threefold the intensity of the molecular ion. Loss of carboxyl and of carbon dioxide yields respectively n and m ions.

The mass spectra of α-epilupininic acid, its ethyl ester, amide, piperidide, and morpholide, and also aphyllinic acid (XV), its amide, methyl ester, and several other derivatives have been described[9]. Whereas the molecular ion of α-epilupininic acid breaks down on electron bombardment mainly similarly to (XIV), aphyllinic acid (XV) exhibits special trends resulting from the presence of a piperidine residue in its molecule. The principal feature of the spectrum of (XV) is the peak of the *m/e* 84 ion, which, though corresponding in structure to the $[c + 1]^+$ ion, is nevertheless due entirely to localisation of charge on the piperidyl residue. The remaining peaks in the spectrum of (XV) are far less intense than the 84 peak. Among fragments formed at the expense of the quinolizidine ring the most clearly evident are the a, e, and g ions. The $[M - 84]^+$ and $[M - 83]^+$ ion peaks owe their appearance to detachment of the piperidyl residue with localisation of the charge on the quinolizidine moiety. Several other peaks in the spectrum of (XV) may be explained by preliminary cyclisation of the molecular ion by elimination of a water molecule from the carboxyl and the secondary amino-group with formation of the polyheterocyclic structure of aphylline (see below).

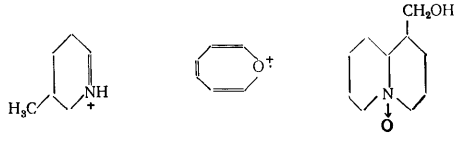


(XV)



(XVI)

In the mass spectrum of deoxynupharidine (XVI)[10] the moderately intense peak due to the molecular ion is accompanied by the strongest peak at *m/e* 98, due to a homologue of the $[c + 1]^+$ ion formed by rupture of the $C_{(10)}-C_{(1)}$ and $C_{(4)}-C_{(5)}$ bonds. When the same bonds are broken but with localisation of the charge on the other moiety and migration of a hydrogen atom from the charged particle, an ion having *m/e* 136 is formed. A third, fairly intense peak at 94 is due to the oxatropylium radical-ion resulting from localisation of charge on the furan substituent.



m/e 98 *m/e* 94 (XVII)

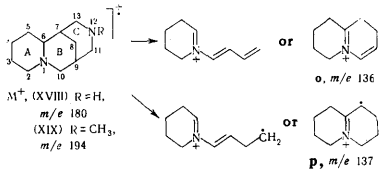
In concluding this subsection we must mention that mass spectra have been described also for two lupinine *N*-oxides (XVII) epimeric at the nitrogen atom[11]. Unfortunately, one of the spectra clearly corresponds to an impure compound, so that it is impossible to assess the effect of the stereochemistry on the decomposition of the molecular ions of these epimers on electric bombardment. From the spectrum of the pure epimer, however, it appears that the main path involves the successive elimination of a hydroxy-group and an oxygen atom from the molecular ion. The presence of an ion peak at 138 is probably due to elimination of a formaldehyde molecule from the $[M - OH]^+$ ion.

2. Cytisine Series

Ring *A* of the parent compound of this group of quinolizidine alkaloids (cytisine) has an α-pyridone structure, which has a significant influence on the general pattern of decomposition of this compound under electron bombardment. The successive hydrogenation and reduction of cytisine yields tetrahydrocytisine and deoxytetrahydrocytisine. The latter contains the quinolizidine structure in "pure form", so we considered it advisable to begin our survey of this group of alkaloids at this compound, and then pass to tetrahydrocytisine and cytisine, in order to trace the influence of functional groups introduced into ring *A* on the type of breakdown under conditions of mass spectrometry.

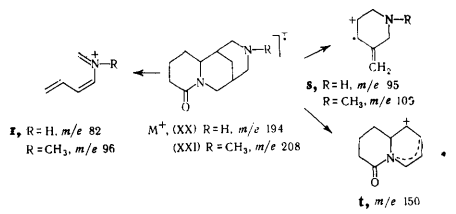
The mass spectra of deoxytetrahydrocytisine (XVIII) and its *N*-methyl derivative (XIX)[8] contain fairly intense peaks of molecular ions. The maximum peaks in the two spectra are due to g and g′ ions respectively, while the e peaks are considerably less intense. Both these ions result almost entirely from rupture of $C_{(6)}-C_{(7)}$ and $C_{(9)}-C_{(10)}$ bonds with localisation of charge on the *A* ring. This is confirmed by the constancy of the peaks on passing

from (XVIII) to (XIX) and the displacement of both peaks by 2 amu in the spectrum of 2,2-dideuterated (XVIII). Among fragments noted earlier as characterising the quinolizidine system, peaks of [e – 1] ions (also formed from ring *A*) and a ions are present in the spectra of (XVIII) and (XIX). Breakdown of the molecular ion of (XVIII) involves ejection of the nitrogen atom at position 12 as amino or methylamino. With (XIX) the peak of the $[M - CH_3NH]^+$ ion with *m/e* 164 is accompanied by the $[M - (CH_3)_2N]^+$ peak at 150 and the peak of the $[M - 15]^+$ ion. The spectra of (XVIII) and (XIX) are characterised by pairs of peaks due to ions having *m/e* 136 (o) and 137 (p)



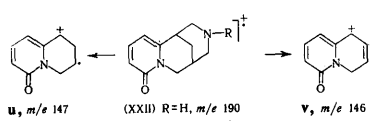
for whose formation several complicated rearrangement mechanisms have been suggested[8]. As will be seen later, o and p ions are characteristic also of quinolizidine alkaloids.

The presence of the lactam carbonyl in the *A* ring of tetrahydrocytisine (XX) and its *N*-methyl derivative (XXI) has a significant influence on the type of breakdown under electron bombardment[12]. The principal peaks in their mass spectra correspond to $[M - 112]^+$ and $[M - 99]^+$ ions. They are formed by complicated rearrangements involving destruction of the polyheterocyclic system, and have been ascribed the structures **r** and **s**; elimination of the elements of ring *C* from (XX) and (XXI) yields an *m/e* 150 ion (t):



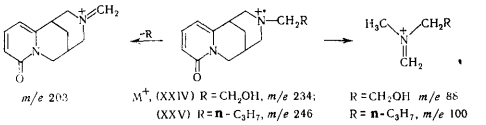
However, elimination of $CH_3NH\cdot$ and $(CH_3)_2NH\cdot$ radicals from the molecular ions of these alkaloids is not observed.

The molecular ions of cytisine (XXII) and *N*-methylcytisine (XXIII)—alkaloids containing an aromatised *A* ring—are very stable. The spectrum of (XXII) contains not only the peak due to the $[M - CH_3NH]^+$ ion but also a pair of peaks (equal in intensity to the molecular ion) having *m/e* 147 and 146, corresponding to the ions u and v formed by elimination of the elements of ring *C*:

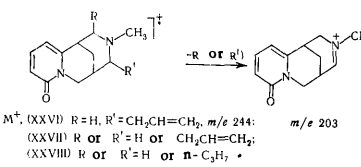


Unexpectedly, the spectrum of (XXIII) differs markedly from that of (XXII). Thus the u peak is almost completely absent, and the $(CH_3)_2N^+ : CH_2$ ion with *m/e* 58 produces the maximum peak in the spectrum. The corresponding ion with *m/e* 44 from (XXII) is very weak. This effect is attributed to the different abilities of the $N_{(12)}$ atoms in (XXII) and (XXIII) to localise the positive charge. The spectra of (XXII) and (XXIII) also contain peaks at *m/e* 160 due to $[M - CH_3NH]^+$ and $[M - (CH_3)_2N]^+$ ions respectively.

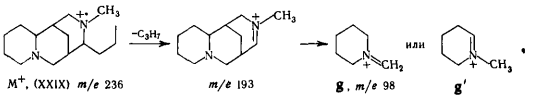
In several cases the cytisine group of alkaloids can be distinguished from the sparteine and matridine groups simply on the basis of molecular weight, since the first group do not contain the *D* ring. Although several dimeric cytisine alkaloids and those containing substituents in the *C* ring are now known, with consequently considerably higher molecular weights, the problem can still be solved quite simply, since the substituent is easily detached on electron bombardment, yielding one of the maximum ion peaks in the spectrum, and dimeric molecules are broken "in half", so that the low-molecular regions resemble the spectra of the corresponding monomeric derivatives. For example, the main peaks in the spectra of *N*-hydroxyethylcytisine (XXIV) [13] and *N*-n-butylcytisine (XXV) [14] represent ions with *m/e* 203, corresponding to detachment of part of the $N_{(12)}$-substituent; they are accompanied by peaks peculiar to cytisine, and the 58 peak characteristic of *N*-methylcytisine is replaced by peaks displaced to *m/e* 88 and 100:



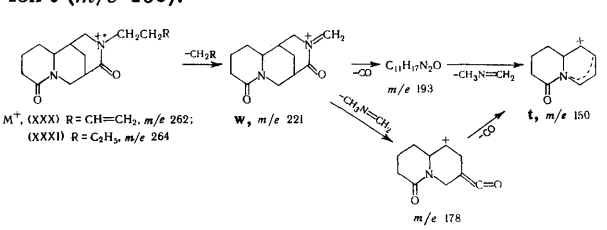
Alkyl groups located in the α-position relative to the nitrogen atom in the *C* ring of cytisine alkaloids are readily split off, so that the mass spectra of tinctorine (XXVI) [15], the perhaps identical alteramine (XXVII) [14], and also dihydroalteramine (XXVIII) [14] contain peaks of ions having *m/e* 203 together with those of ions characteristic of breakdown of the cytisine ring system:



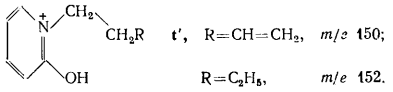
Similarly, the most intense peak in the spectrum of hexahydroalteramine (XXIX) [14] corresponds to the $[M - n\text{-}C_3H_7]^+$ ion, which then breaks down into a g or g′ ion:



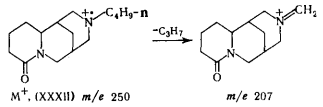
In tetrahydro-11-oxorhombifoline (XXX) and its dihydro-derivative (XXXI) the *C* ring contains a lactam carbonyl as well as an alkyl group[16]. Nevertheless, the maximum peak in the spectrum of (XXX) is due to an ion formed by detachment of part of the alkyl substituent. This ion with *m/e* 221 (w) then loses carbon monoxide and $CH_3N : CH_2$, being converted into ions 193 and 178, which in turn eliminate $CH_3N : CH_2$ and CO respectively to form the ion t (*m/e* 150):



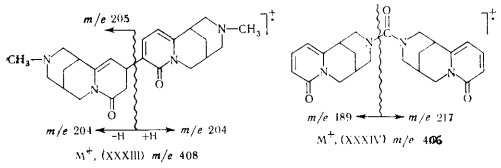
However, analysis of the mass spectrum of the 3,3-dideutero-analogue of (XXX) showed that the 150 peak is only partly displaced to 152, and is therefore composite, being due both to the t ion and to an ion t′ formed by rupture of bonds in the *B* ring with preservation of the *C* ring:



Breakdown of the molecular ion (XXXI) is essentially analogous to that of (XXX), differing only in containing a peak at 152 due to the t′ ion. The main peak in the mass spectrum of hexahydrorhombifoline (XXXII), briefly described in Ref. 17, is also due to the deoxy-analogue of the w ion with *m/e* 207, whose breakdown leads to ions at 138, 112, and 58:

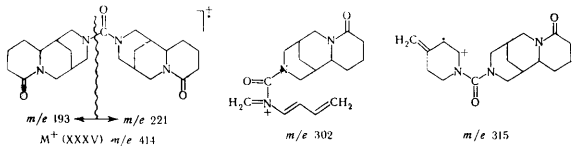


The spectrum of the dimeric cytisine alkaloid—dimethamine (XXXIII) [18]—contains a very small peak of the molecular ion and intense ion peaks at 205 and 204, due to breakage of the molecule "in half" (accompanied by migration of a hydrogen atom to or from the charged particle):



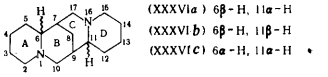
The spectrum of (XXXIII) also contains ion peaks typical of *N*-methylcytisine—at 160 [M^{+}_{Cyt} – $(CH_3)_2N$], 146 (v), and the maximum at 58 $(CH_3)_2N^{+}$: CH_2—see above.

Argentine (XXXIV) belongs to a different type of dimeric cytisine alkaloids. Its mass spectrum [19,20] contains a fairly intense peak of the molecular ion and most intense peaks at 189 and 217 due to ions formed by rupture of carbon–nitrogen bonds around the central carbonyl group. Analogous breakages lead to ions with *m/e* 193 and 221, which give intense peaks in the spectrum of octahydroargentine (XXXV). [19,20] Ions at 302 and 315 are diagnostically important in the latter spectrum, for they are characteristic of the tetrahydrocytisine skeleton and are more complicated analogues of ions r and k respectively:



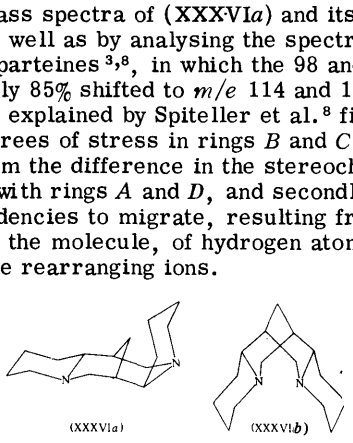
3. Sparteine Series

The simplest naturally occurring member of this series of alkaloids, which contains no functional group, is sparteine itself (XXXVI*a*), whose molecule is formed by two quinolizidine residues with a bridge between them



Two other stereoisomers are known—α-isosparteine (XXXVI*b*) and β-isosparteine (XXXVI*c*)—as well as its *d*-enantiomer, pachycarpine (XXXVII). In principle molecular ions of these compounds break down in the same ways, although certain quantitative differences exist between the mass spectra of (XXXVI*a*) and (XXXVI*b*)[8], in particular in the ratio of the peaks of ions having *m/e* 98 and 137. The mass spectra of (XXXVI*a*) and (XXXVII) should be absolutely identical, since as optical enantiomers they have the same internal energy. Nevertheless, a difference in intensity between individual peaks (measured as percentages of the total ion current) was reported [17] between the spectra of (XXXVI*a*) and (XXXVII) obtained under the same conditions. To the Reviewers this appears strange; the attempt [17] to explain the difference by the possibility of interaction between the electric field and the molecule and by the spatial orientation of the molecule before ionisation does not stand up to criticism.

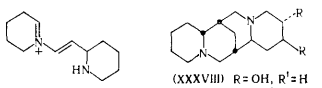
The main peaks in the mass spectra of (XXXVI*a*, *b*) and (XXXVII) [8,21] are due to the molecular, g, and p ions (the latter two with *m/e* 98 and 137 respectively); the peaks due to the ions c + 1, e, and o (84, 97, and 136) are of moderate intensity. Because of the apparent symmetry of the molecules (XXXVI*a–c*) it might be assumed that the ions c, c + 1, e, e – 1, g, o, and p are equally likely to be formed by rupture of bonds in ring *B* or in ring *C*, i.e. that the first five ions may contain ring *A* or *D* to equal extents, and that the last two ions may equally contain rings *A* + *B* or *C* + *D*. With sparteine (XXXVI*a*), however, in which the fusion of rings *A* and *B* is *trans*, whereas that of *C* and *D* is *cis*, only e and o ions are equally likely to contain an *A* or a *D* ring, and hence *A* + *B* or *C* + *D*, as Spiteller et al. showed [8] in experiments using a deuterium label. The ions c + 1 and g are 85–90% formed from the *A* ring, whereas p ions result from the *A* + *B* rings. The Reviewers have obtained similar results [21] from a comparison of the mass spectra of (XXXVI*a*) and its 3,3-dideutero-analogue, as well as by analysing the spectra of 13- and 14-hydroxysparteines [3,8], in which the 98 and 137 peaks have been only 85% shifted to *m/e* 114 and 153 respectively. The effect is explained by Spiteller et al. [8] firstly by the different degrees of stress in rings *B* and *C* in (XXXVI*a*) resulting from the difference in the stereochemistry of their fusion with rings *A* and *D*, and secondly by the different tendencies to migrate, resulting from the stereochemistry of the molecule, of hydrogen atoms involved in forming these rearranging ions.



The α-isosparteine molecule (XXXVI*b*), in which both *A–B* and *C–D* ring fusions are *trans*, is symmetrical, in contrast to the sparteine molecule. Therefore equally probable formation of g and p ions (*m/e* 98 and 137) may

be expected from ring *A* or *D* and from *A* + *B* or *C* + *D* respectively, since in this case rings *B* and *C* are energetically equivalent. This suggestion was tested by preparing[20] the 3,4,5,6-tetradeutero-analogue of α-isosparteine, whose mass spectrum showed that the peak of the g ions was at least half displaced by 4 amu (to *m/e* 102). The p ion peak is accompanied by equally strong peaks at *m/e* 138, 139, and 140. Since the 137 ion undergoes rearrangement, and the displacement of the peak suggests that hydrogen atoms from the *A* ring are involved in its formation, it may be concluded that with α-isosparteine, in contrast to sparteine itself, the g and p ions are equally formed by charge localisation on fragments containing both *A* and *A* + *B* and *D* and *C* + *D* rings.

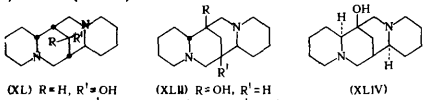
Analysis of the mass spectrum of the 3,3-dideutero-analogue of sparteine has shown[20,21] that formation of the ion t with *m/e* 150 is independent of the stereochemistry of *A* – *B* and *C* – *D* ring fusion and is due to the equally probable localisation of charge on fragments containing the rings *A* + *B* and *C* + *D*. The diagnostically most significant feature of the mass spectra of sparteine and its stereoisomers, enabling them to be distinguished from the isomeric matridine derivatives (see below), is the presence of fairly intense $[M - 41]^+$ ion peaks having *m/e* 193. This ion is probably formed from the molecular ion of sparteine by elimination of a cyclopropyl or an allyl radical on the rupture of bonds in rings *B* and *C*, which is supported by the mass spectra of the corresponding deutero-analogues[8,20,21]. In the view of Spiteller et al.[3] this ion has the structure x.



x, *m/e* 193 (XXXVIII) R = OH, R' = H (XXXIX) R = H, R' = OH

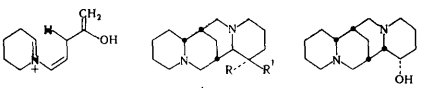
The paper by these workers[3] was devoted mainly to a mass-spectrometric study of hydroxy-derivatives of sparteine. The paths along which the molecular ions of 13-hydroxysparteine (XXXVIII)[8] and its 14*e*-isomer (XXXIX)[3] decompose are analogous to those described for sparteine itself with, as already noted above, the peaks of g and p ions displaced by 16 amu owing to charge localisation on the oxygen-containing moiety. In both cases the $[M - 41]^+$ ion peaks exhibit appreciable intensity. The presence of the hydroxy-group in (XXXVIII) and (XXXIX) is shown in the spectrum of the former by the appearance of an $[M - 17]^+$ ion peak, and in that of the latter by a pair of peaks due to $[M - 17]^+$ and $[M - 18]^+$ ions.

The mass spectra of 8-hydroxy- and 8-epihydroxy-sparteine (XL) and (XLI) differ fairly strongly from those of the preceding compounds. Thus peaks of p ions (*m/e* 137) are regularly absent, but are replaced by some of the most intense peaks of the hydroxylated analogues of p ions (*m/e* 153). The spectra also contain fairly intense peaks of o ions (136), obviously formed from these analogues by ejection of the hydroxyl radical. Among ions typical of the quinolizidine system and containing no hydroxy-group, a, e, and g are present in the spectra of (XL) and (XLI). The peaks of $[M - 41]^+$ ions have been replaced by $[M - 57]$ ion peaks: i.e. formation of these ions involves loss of a hydroxy-group in neutral species, which provides additional conformation of the origin of the x ion (*m/e* 193) in the case of sparteine. The hydroxyl is eliminated from the molecular ions of (XL) and (XLI).



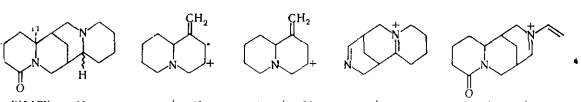
(XL) R = H, R' = OH (XLI) R = OH, R' = H (XLII) R = OH, R' = H (XLIII) R = H, R' = OH (XLIV)

The decomposition paths of 7- and 9-hydroxysparteines (XLII) and (XLIII) and also of 7-hydroxy-β-isosparteine (XLIV) are fairly similar and somewhat recall those for (XL) and (XLI). In all cases the g ion peaks are dominant. In contrast to the preceding compounds, peaks due to o ions (*m/e* 136) are absent from (XLII)–(XLIV), but peaks appear at 166, due to ions formed by elimination of the elements of the *D* ring[3]. A peculiarity of these mass spectra is the presence of $[M - 57]^+$ together with $[M - 41]^+$ ion peaks.



m/e 166 (XLV) R' = OH, R = H (XLVa) R' = H, R = OH (XLVI)

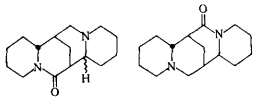
In contrast to all the above hydroxysparteines, the molecular ions of retamine (XLV), epiretamine (XLV*a*), and 12*e*-hydroxy-α-isosparteine (XLVI) are fairly easily dehydrated, with the $[M - H_2O]^+$ ion providing one of the main peaks in the spectrum of (XLV*a*). Explaining the increased intensity of the peak of the dehydration ion in the spectrum of epiretamine in comparison with that of retamine (containing respectively an equatorial and an axial hydroxyl), Spiteller et al.[3] suggest that the *D* ring in the former compound can pass into the boat form and thus ensure easier detachment of a water molecule by 1,4-diaxial elimination. The main peak in the spectra of all three compounds corresponds to the g ion, and the spectra also contain several peaks due to the decompositon of $[M - H_2O]^+$. A peculiarity of the spectra of these compounds is that the $[M - 41]^+$ have been replaced by the $[M - 43]^+$ ion peaks



(XLVII) α-H (XLVIIa) β-H y, *m/e* 149 y + 1, *m/e* 150 *m/e* 177 [M – 29]

In the spectra of all the oxosparteines the peaks of the molecular ions are of moderate intensity. The spectra of lupanine (XLVII)[12] and α-isolupanine (XLVII*a*)[21] are almost identical. The peaks of c + 1, e, and g ions, which retain the *D* ring, are weak; the dominating peaks are due to o ions (*m/e* 136), formed directly from the molecular ions, as indicated by the presence of the corresponding metastable peaks. The charge is localised on the fragment containing the *C* + *D* ring system. Cleavage of the *B* ring yields in both cases ions having *m/e* 149 and 150 (y and y + 1). The composition of the latter ion is supported only by a slight shift of the corresponding peak to 152 in the spectrum of the 3,3-dideutero-analogue of α-isolupanine[21]. In the range of mass numbers from *m/e* 150 to the molecular ion the spectra of both compounds contain low-intensity peaks, among which the most interesting are at 177, due to $C_{11}H_{17}N_2$ ions according to the high-resolution mass spectrum of (XLVII*a*), and also $[M - 29]^+$ ion peaks due to elimination of an ethyl radical from the *D* ring. Thus here, as with tetrahydrocytisine, the presence of a lactam carbonyl in the *A* ring does not favour charge localisation on ions containing this ring.

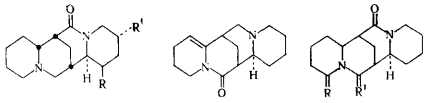
If the lactam carbonyl is located in the *B* ring, as in aphylline (XLVIII) and epiaphylline (XLVIII*a*)[12], the peaks of t and y ions are much less intense, while the peaks of o ions remain the most intense. The $[M - CO]^+$ ion peaks exhibit considerable intensity, and peaks appear at 191 and 192 owing to elimination of CH_3CH_2CO and CH_2CH_2CO particles from rings *B* and *C* of the molecular ions.



(XLVIII) α-H (XLIX)
(XLVIIIa) β-H

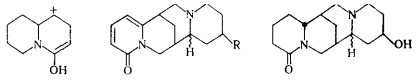
In the case of 17-oxosparteine (XLIX) [12] the main peak corresponds to the e ion (*m/e* 97), and is accompanied by strongly intensified a and g peaks. The presence of a fairly intense $[M - CO]^+$ ion peak and an appreciable pair of peaks at 191 and 192 is characteristic of the spectrum of (XLIX). In contrast to lupanine, the spectra of (XLVIII), (XLVIII*a*), and (XLIX) contain y + 1 ion peaks that are considerably more intense than the y ion peaks (at 150 and 149).

Introduction of a 14*e*-hydroxy-group into the 17-oxosparteine molecule (L) [12] hardly affects the pattern of decomposition under electron bombardment. The main peaks are still those of e and g ions, and an $[M - CO]^+$ ion peak is also observed, but ejection of the hydroxyl as a radical or a water molecule is completely absent. In the case of "17-oxoretamine" (12*a*--hydroxy-17-oxosparteine) (LI) [12] the $[M - 17]^+$, e, and g ion peaks are dominant, while peaks due to other ions are weak.



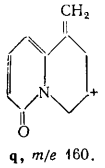
(L) R = H, R' = OH (LII) (LIII) R = O, R' = H_2
(LI) R = OH, R' = H (LIV) R = H_2, R' = O

The presence of a double bond in the *A* ring of aphyllidine (LII) [12] prevents cleavage of bonds in the *B* ring, but the *C* ring opens fairly easily. The main peaks in the spectrum of (LII) are therefore due to e and g ions. In the spectrum of the dilactam—17-oxolupanine (LIII) [12]—on the other hand, the main peak is due to the t ion (*m/e* 150), which was regarded as containing *A* and *B* rings. The same peak predominates also in the spectrum of 10,17-dioxosparteine (LIV) [12], but is accompanied by an intense peak at 152, possibly due to an ion having the structure z.



z, *m/e* 152 (LV) α-H, R = H (LVII)
(LV*a*) β-H, R = H
(LVI) R = OH

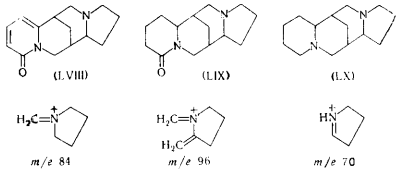
Two naturally occurring stereoisomers—anagyrine (LV) and *d*-thermopsine (LV*a*)—are sparteine alkaloids containing an aromatic ring *A*. Their mass spectra differ little [8,20,21], although peaks of individual ions may vary slightly in relative intensity. The strongest peaks in both spectra are due to g ions (*m/e* 98); they also contain peaks of o ions containing the *C* + *D* ring system, v ions, and q ions (*m/e* 136, 146, and 160 respectively).



q, *m/e* 160.

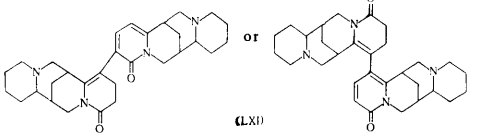
Analysis of mass-spectrometric results proved that the alkaloid argentamine (LVI) [22] was a hydroxy-derivative of thermopsine. Its spectrum contained an intense peak of the molecular ion with *m/e* 260 which exceeds the molecular weight of anagyrine (LV) and *d*-thermopsine (LV*a*) by 16 amu, although the breakdown of molecular ions of all three compounds follows closely similar routes. Only the peaks of ions that in the cases of (LV) and (LV*a*) definitely contain the *D* ring move up by 16 amu on passing to the compound (LVI). Thus the peaks of g and o are displaced to *m/e* 114 and 152 respectively, whereas the peaks of v and q ions, which do not contain the *D* ring, remain fixed.

A similar situation is found on comparing the mass spectra of tetrahydroargentamine (LVII) and lupanine (XLVII) or α-isolupanine (XLVII*a*). The most intense peaks in the spectra of the latter two compounds—of o and y ions, containing *C* and *D* rings—are completely displaced by 16 amu to *m/e* 152 and 165 respectively on passing to (LVII). These results prove that the alkaloids (LVI) contains a hydroxy-group in the *D* ring, whose position at $C_{(13)}$ follows from the complete identity of the mass spectra of deoxytetrahydroargentamine and 13-hydroxysparteine (XXXVIII). [8]



(LVIII) (LIX) (LX)
m/e 84 *m/e* 96 *m/e* 70

Interesting work was undertaken by Yunusov et al. [23] on the mass spectra of leontidine (LVIII) and its tetrahydro- and deoxytetrahydro-derivatives (LIX) and (LX), which contain a five-membered instead of a six-membered *D* ring. In the spectrum of (LVIII) the ions containing *A* and *B* rings (v and q) have the same mass numbers as in the spectrum of anagyrine (LV), whereas ions of types a and g, containing a five-membered ring, have *m/e* 96 and 84 respectively, with the latter the maximum peak in the spectrum (as with anagyrine, when it has *m/e* 98). A similar situation obtained in the spectrum of (LIX), in which the peak of the t ion (*m/e* 150) was accompanied by a peak at 136 corresponding to an analogue of the y + 1 ion with a five-membered ring. In the spectrum of deoxytetrahydroleontidine (LX) the ions with *m/e* 84, 98, and 137, containing *A* and *B* rings, correspond to c + 1, g, and p ions, whereas the ions at 96 and 70 are analogues of a and c + 1 ions resulting from a five-membered *D* ring.



or

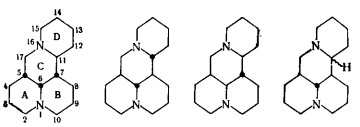
(LXI)

In concluding this subsection we must mention results [24] for the mass spectrum of the dimeric sparteine alkaloid diteramine (LXI), which contains a small peak of the molecular ion, a peak of an ion corresponding to the molecular ion of thermopsine with *m/e* 244, and also peaks of v and q ions. The g ion peak is the maximum, which is typical of the spectra of thermopsine and anagyrine.

4. Matrine Series.

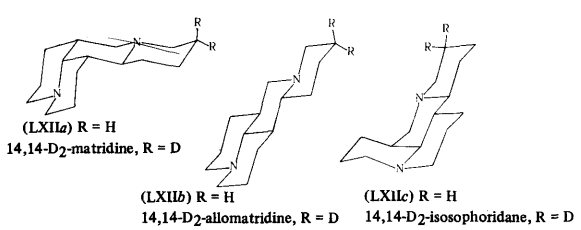
Alkaloids of this type differ from the sparteine series in the mode of fusion of the two quinolizidine systems. Unsubstituted matrine alkaloids have not yet been discovered in Nature, in contrast to the situation in the

sparteine series. Isomers of sparteine in the matrine series have been obtained only artificially, by reducing carbonyl-containing compounds. Because of the special mode of fusion of the quinolizidine residues, a larger number of stereoisomers can be expected in the matrine than in the sparteine series. Four stereoisomers—matridine (LXII*a*), allomatridine (LXII*b*), isosophoridane (LXII*c*), and sophoridane (LXII*d*)—have been obtained from the corresponding naturally occurring or synthetic compounds of the matrine series containing a carbonyl group in the *D* ring.



(LXII*a*) (LXII*b*) (LXII*c*) (LXII*d*)

The main peaks in the mass spectra of these compounds[25] are due to c + 1, e, e − 1, g, o, and p ions. From their structures it could be supposed that these ions would be formed most efficiently by the rupture of bonds in the *C* ring. The ions p and o (*m/e* 137 and 136) would then contain the *A* + *B* ring system, the c + 1 ion (84) the *D* ring, and the e, e − 1, and g ions (97, 96, and 98) the *D* ring and the $C_{(17)}$ atom. However, incomplete data for the mass spectrum of the 15,15-dideutero-analogue of matridine[26] indicate that the *D* ring is almost completely absent from g ions, which are therefore formed by the rupture of at least three bonds in rings *A* (or *B*) and *C*. This result seemed to the Reviewers unexpected and requiring further refinement. A mass-spectrometric investigation was therefore undertaken on the 14,14-dideutero-analogues both of matridine itself (LXII*a*) and of its stereoisomers (LXII*b*, *c*).[25] This revealed the clear influence of the stereochemistry of these compounds on their mode of breakdown under electron bombardment.



(LXII*a*) R = H
14,14-D_2-matridine, R = D

(LXII*b*) R = H
14,14-D_2-allomatridine, R = D

(LXII*c*) R = H
14,14-D_2-isosophoridane, R = D

The mass spectra of the unlabelled compounds (LXII*a*–*d*) are qualitatively similar, but quantitatively allomatridine (LXII*b*) resembles sophoridane (LXII*d*), while matridine (LXII*a*) resembles isosophoridane (LXII*c*). The most noticeable feature of the spectra of the first two stereoisomers is predominance of peaks due to the molecular ions, whereas the peaks of the p ion (*m/e* 137) are dominant in the spectra of the second pair. The great stability of molecular ions of (LXII*b*) and (LXII*d*) may obviously be due to the predominantly *trans*-fusion of rings in their tetracyclic system: in the former all the rings are *trans*-fused, and in the latter *A*–*B*, *A*–*C*, and *B*–*C* *trans*-fusion can be regarded as proved, while the type of fusion of rings *C* and *D* has not been finally proved[27,28]. Matridine (LXII*a*) and isosophoridane (XLII*c*), however, each contain two energetically less favourable *cis*-fused systems.

There are also other quantitative differences in the mass spectra of these stereoisomers, which cannot yet be explained owing to the absence of additional data on the elementary composition of the ions, the mechanisms of their formation, and the energetics of the molecules.

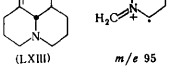
Comparison of the mass spectra of the 14,14-dideutero-analogues of matridine, allomatridine, and isosophoridane with those of the unlabelled alkaloids showed[25] that such characteristic peaks as those due to ions having *m/e* 151, 150 (y + 1), 137 (p), 136 (o), and 96 (e − 1) are not displaced by the introduction of the deuterium label at position 14: i.e. with these compounds the ions result from localisation of charge on the 1-nitrogen atom and do not contain the *D* ring. Yet the peaks of ions with *m/e* 98 and 84 (g and c + 1) differ in structure depending on the stereochemistry of the compound.

The peaks of g ions from matridine and isosophoridane are only ~24% and ~27% respectively due to ions containing the *D* ring, the majority of these ions resulting from localisation of charge on the 1-nitrogen atom and containing an *A* or *B* ring. Consequently, different mechanisms of formation of g ions can be assumed for these compounds, each involving the rupture of at least three carbon–carbon bonds. In the absence of the spectra of deuterated analogues labelled in either ring *A*, *B*, or *C*, however, it is difficult to make any definite statement. In the decomposition of allomatridine, in contrast to the above two compounds, the g ion is formed predominantly (~80%) by charge localisation on the 16-nitrogen atom and contains the *D* ring. In this case the mechanism of formation evidently involves cleavage of the $C_{(7)}$–$C_{(11)}$ and $C_{(5)}$–$C_{(17)}$ bonds with migration of a hydrogen atom to the charged particle.

The above differences in the breakdown paths of the stereoisomers of matridine can obviously be attributed to the fact that in (LXII*b*) all ring fusions are *trans*, whereas in (LXII*a*) the *A*–*C* and *B*–*C* fusions are *cis*, as are the *A*–*B* and *A*–*C* fusions in (LXII*c*). A primary consequence may be the facilitation of bond fission in the *A*, *B*, and *C* rings of molecular ions of the latter two compounds, whereas in the first compound the bonds are equally strong in all rings, so that here the most advantageous process occurs, involving the rupture of two bonds in the *C* ring. It must also be borne in mind that the g ion can undergo rearrangement, so that its ease of formation may be influenced not only by the energy factor but also by the distance between the centres of migration.

The stereochemistry of the tetracyclic skeleton of compounds (LXII*a*–*d*) influences also the decomposition routes leading to formation of the rearranging c + 1 ions. The mass spectra of the 14,14-dideuterated analogues of allomatridine and isosophoridane contain corresponding peaks displaced by 2 amu and to some extent by 1 amu: i.e. with these compounds the c + 1 ion contains predominantly the *D* ring. In the spectrum of 14,14-dideutero-matridine, however, the 1-amu displacement of the peak of this ion is only slight.

It is noteworthy that the c + 1, e, e − 1, and g ions are almost completely absent from the spectrum of 5,17-dehydroallomatridine (LXIII),[20] but an intense peak of an ion having *m/e* 95 appears.

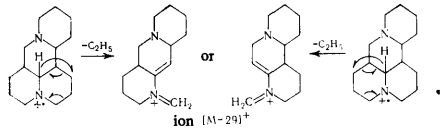


(LXIII) *m/e* 95

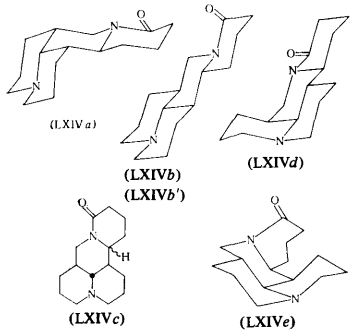
The mass spectra of (LXII*a*) and (LXII*c*) contain fairly intense ion peaks at 162, which are only small in the case of stereoisomers of sparteine. However, an ion with *m/e* 162 can hardly be diagnostically significant, since the

intensity of its peak is also small in the spectrum of (LXII*b*). It is difficult to judge the origin of this ion; we know only that it contains neither the $C_{(14)}$ [26] nor the $C_{(15)}$ [25] atom, and has the composition $C_{11}H_{16}N$ according to the high-resolution mass spectrum of (LXII*c*).[21]

The spectra of (LXII*a–d*) contain also weak peaks of $[M - 43]^+$ and $[M - 29]^+$ ions but, in contrast to those of sparteine stereoisomers, no $[M - 41]$ peaks. It is supposed[21,29] that the $[M - 43]^+$ ion is formed by elimination of a propyl radical or an aziridine molecule. Formation of the $[M - 29]^+$ ion, however, is regarded as involving elimination of an ethyl radical from the *A* or *B* ring, but not from *D*, which is supported by the mass spectra of the 14,14-dideutero-analogues of the stereoisomers (LXII*a–c*) [25]:



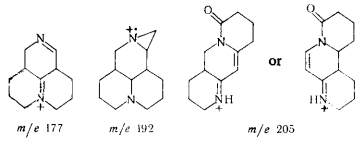
Derivatives of (LXII*a–d*) containing a lactam carbonyl in the *D* ring are often encountered in Nature. Most thorough studies have been made of the mass spectra of matrine (LXIV*a*) [20,21,30], leontine (LXIV*b*) [31], sophoridine (LXIV*c*), the synthetic enantiomer of leontine—allomatrine (LXIV*b′*) and isosophoridine (LXIV*d*).[20,21,30]. Data have appeared[32] on the mass spectrum of darvasamine (LXIV*e*), which was regarded as the first naturally occurring *cis-A–B* stereoisomer of matrine.



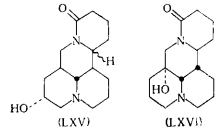
The most characteristic feature of the mass spectra of these compounds in comparison with those of their isomers in the sparteine series (lupanine and α-isolupanine) comprises the exceptionally intense peaks of molecular and $[M - 1]^+$ ions, the former being rather higher in the case of matrine (LXIV*a*), with the opposite relation in the spectra of the other stereoisomers. Formation of the $[M - 1]^+$ ion is assumed to involve elimination of the 6-hydrogen atom. This may well be so, since the majority of $[M - 1]^+$ ions from quinolizidine itself (I) are formed by ejection of the hydrogen atom from the angular position 10 (Section II).[5] An attempt to relate the stability of the polycyclic system solely with the intensity of the molecular ion peaks was unsuccessful, since all these compounds (LXIV*a–d*) exhibited similar intensities of these ions measured as percentages of the total ion current[31]. Nevertheless, the sum of the intensities of molecular and $[M - 1]^+$ ion peaks was greatest with leontine (LXIV*b*), in agreement with the least stress in the completely *trans*-fused tetracyclic system. Matrine exhibits the lowest sum of the peak intensities of these ions.

Among ions representing the quinolizidine system formed by rings *A* and *B* in the molecules (LXIV*a–d*) the peaks due to **c**, **c** + 1, **e**, and **g** are lower in their spectra than in those of oxygen-free derivatives in the cytisine, sparteine, and matridine series. In the case of compounds (LXIV*a–d*) these ions in fact result exclusively from rings *A* and *B*, which is confirmed by the unchanged position of their peaks when a deuterium label is introduced into the *D* ring.[20,21] The peaks of o and p ions are moderately intense. The presence of the corresponding metastable peak in the spectrum of matrine indicates that in this case the o ion may be formed directly from the molecular ion[20,21].

In contrast to the corresponding isomers in the sparteine series, spectra of the stereoisomers (LXIV*a–d*) contain, in the range from *m/e* 150 to the molecular ion, fairly intense peaks due mainly to cleavage of bonds in the *D* ring. The high-resolution mass spectrum of (LXIV*a*) indicated[20,21] that the ion with *m/e* 161 had the composition $C_{10}H_{11}NO$, whereas the 162 ion was due to $C_{10}H_{12}NO$ and $C_{11}H_{16}N$ ions in the proportion 55 : 45. An appreciable peak at 177, most characteristic in the spectrum of allomatrine, was due to the $C_{11}H_{17}N_2$ ion formed by elimination of the *D* ring. Elimination of part of the latter from (LXIV*a–d*) as C_3H_4O gave a comparatively stable $C_{12}H_{20}N_2$ radical-ion with *m/e* 192.[20,21,26]



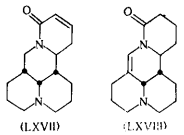
It was shown by deuterium labelling[20,21] that a propyl radical could be eliminated from ring *A* or *B*, to give an ion with *m/e* 205. It is interesting that, in contrast to oxygen-free derivatives of the sparteine and matridine series, the $[M - 29]^+$ ion peak of (LXIV*a–d*) is due to $C_{13}H_{19}N_2O$ and $C_{14}H_{23}N_3$ ions[20,21], which have therefore been formed by elimination of an ethyl radical and of (CO + H) respectively.



The structure of the alkaloid 3α-hydroxysophoridine (LXV) was established from the rules of the breakdown of molecular ions of matrine and sophoridine[13]. The presence of the hydroxy-group in (LXV) and also in sophoranol (5α-hydroxymatrine) (LXVI) [20,21] is the reason for the appearance of $[M - 17]^+$ ion peaks in their mass spectra, these being the highest in that of (LXVI). The majority of peaks in this spectrum arise directly from the molecular ion, so that peaks typical of matrine (LXIV*a*) are displaced by 16 amu to larger masses, since most of these ions include *A* and *B* rings. For example, the **e** – 1 peak (*m/e* 96) is accompanied in the spectrum of (LXVI) by an ion peak at 112. The origin of these peaks was confirmed by analysing the mass spectrum of 6,7-dideuterosophoranol.[20,21]

Breakdown of the molecular ion of sophocarpine—13,14-dehydromatrine (LXVII) [26,30]—follows the same routes as that of matrine. Ions containing the *A–C* ring system have the same mass numbers in the two cases, whereas ions resulting from cleavage of ring *A* or *B* are 2 amu lighter from the former compound. This applies

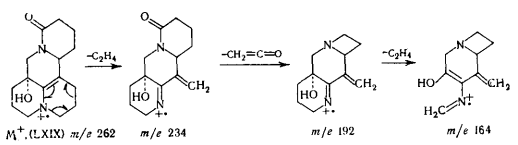
e.g. to the $[M - 29]^+$ and $[M - 43]^+$ ions, produced by elimination of an ethyl or a propyl radical from ring *A* or *B*.



(LXVII) (LXVIII)

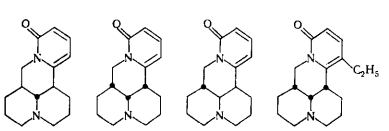
The presence of a double bond in ring *C*, as in leontalbine—5,17-dehydromatrine (LXVIII)—inhibits processes involving cleavage of this ring[26]. At the same time ring *D* may be eliminated either entirely with formation of an ion having *m/e* 175 (a dehydro-analogue of the 177 ion in the case of matrine) or partly to give the $[M - C_3H_4O]^+$ ion. The $[M - 29]^+$ and $[M - 43]^+$ ion peaks in the spectrum of matrine have been replaced in that of leontalbine (LXVIII) by peaks due to $[M - 28]^+$ and $[M - 42]^+$ ions.

In contrast to sophoranol (LXVI), the intensity of the $[M - 17]^+$ peak drops sharply in the spectrum of 6,7-dehydro-5-hydroxymatrine (LXIX) [20,21], and the molecular-ion peak is accompanied by an equal peak of the $[M - 1]^+$ ion. The [M - 28] peak (*m/e* 234) is much more intense in the spectrum of (LXIX), but weak in all the above spectra of matrine alkaloids. Its considerable intensity is most likely due to the possibility of a retrodiene type of decomposition in ring *B*:



M^+.(LXIX) *m/e* 262 *m/e* 234 *m/e* 192 *m/e* 164

Further decomposition of the 234 ion involves either elimination of a hydroxyl radical to form a 217 ion, whose peak is among the most intense in the spectrum, or elimination of a keten molecule to give a 192 ion, which then undergoes a retrodiene breakdown with elimination of an ethylene molecule and formation of an ion with *m/e* 164. A keten molecule is eliminated also from the 217 ion, to give a 175 ion.

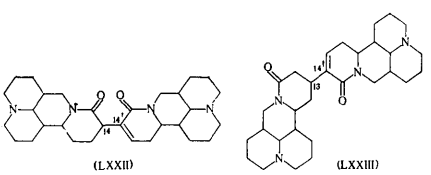


(LXX*a*) (LXX*b*) (LXX*c*) (LXXI)

Aromatisation of the *D* ring in matrine alkaloids increases still further the difference between their mass spectra and those of the corresponding derivatives in the sparteine series (see above). As with the stereoisomers of matrine, peaks due to molecular and $[M - 1]^+$ ions exhibit great (sometimes maximum) intensity in the spectra of isosophoramine (LXX*a*) [20,21,30], sophoramine (LXX*b*) [20,30], neosophoramine (LXX*c*) [33], and 12-ethylsophoramine (LXXI) [20], whereas peaks due to g ions (*m/e* 98) containing the *D* ring dominate the spectra of the corresponding sparteine derivatives (above). It is interesting that the change in the relative intensities of molecular and $[M - 1]^+$ ion peaks on passing from isosophoramine (LXX*a*) to sophoramine (LXX*b*) is analogous to the change on passing from allomatrine to matrine (above). This is obviously connected with the analogy in the stereochemistry of the fusion of rings *A*, *B*, and *C* in these two pairs of compounds. The intensities of peaks due to g ions are very weak in the spectra of (LXX*a–c*) and (LXXI), since their formation from ring *A* or *B* requires the rupture of more than two bonds, which is obviously disadvantageous. One of the most intense peaks in the spectra of (LXX*b*), (LXX*c*)†, and (LXXI) is that of the o ion (*m/e* 136), while the peaks at 146 and 160 (v and q) typical of the spectra of anagyrine and *d*-thermopsine (above), are small and shift by 28 amu to *m/e* 174 and 188 on passing to (LXXI).

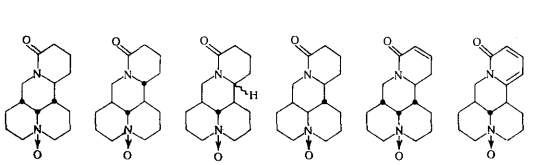
The stereochemistry of the molecules (LXX*a–c*) has a fairly significant quantitative influence on their spectra. Thus (LXX*a*) is characterised by high intensity of the y ion peak (*m/e* 149), while that of the o peak drops sharply. The opposite pattern is found for the spectra of (LXX*b*) and (LXX*c*), however, and with the latter compound all peaks are weak other than those of molecular, $[M - 1]^+$, and o ions. According to the high-resolution mass spectrum of (LXX*a*) the not very intense peaks (around 15–25% of the maximum) of $[M - 29]^+$ ions with *m/e* 215, present in the spectra of all three isomers, represent the compositions $C_{13}H_{15}N_2O$ and $C_{14}H_{19}N_2$. Hence they are formed by elimination either of an ethyl radical or of a carbonyl group together with a hydrogen atom[20,21].

The mass spectra of goebeline—the naturally occurring dimeric matrine alkaloid—and its dihydro-derivative have been given[34] to establish their structure, but with no unambiguous evidence for the suggested site (14,14′) of linking of the two moieties (LXXII). We can accept that the goebeline molecule comprises residues of matrine and sophocarpine or their stereoisomers. The mass spectrum of goebeline contains a peak due to the molecular ion together with a pair of peaks corresponding to the molecular and $[M - 1]^+$ ions of sophocarpine, though the remainder of the spectrum below this pair differs quite strongly from the spectrum of sophocarpine with respect to the intensities of the peaks.



(LXXII) (LXXIII)

The mass spectrum of deuterated goebeline, obtained by exchange with deuteroethanol in the presence of sodium deuteroxide in oxolan, indicates the predominant incorporation of four deuterium atoms[20]. This excludes the possibility of 14,14′-linking of matrine and sophocarpine residues, since the same method of deuteration introduces two and three deuterium atoms into the former and into the latter respectively, whereas only three deuterium atoms should enter with 14,14′-linking. The Reviewers regard 13,14′-linking of matrine and sophocarpine residues (LXXIII) as most probable, although this question is by no means finally settled.



(LXXIV*a*) (LXXIV*b*) (LXXIV*c*) (LXXIV*d*) (LXXV) (LXXVI)

†According to Monakhova et al.[33] these peaks are maxima in the spectra of (LXX*b*) and (LXX*c*), which for the former compound is inconsistent with other results[20].

In conclusion we must consider briefly a mass-spectrometric study of *N*-oxides of matrine (LXXIV*a*), allomatrine (LXXIV*b*), sophoridine (LXXIV*c*), isosophoridine (LXXIV*d*), sophocarpine (LXXV), and isosophoramine (LXXVI).[35] Their mass spectra usually contain weak peaks of the molecular ions. The $[M - 16]^+$ and $[M - 17]^+$ peaks are considerably more intense, and sometimes the main peaks in the spectra. The first peak in this pair is due to elimination of an oxygen atom, whereas the second peak may be due to various processes—further loss of a hydrogen atom from the [M −16] ion, single-stage ejection of the *N*-oxide oxygen and a hydroxyl hydrogen atom, or elimination of an oxygen atom from the $[M - 1]^+$ ion. Comparison of the ratios $I_{[M - 17]^+}/I_{[M - 16]^+}$ in the spectra of the *N*-oxides and $I_{[M - 1]^+}/I_{[M]^+}$ in those of the corresponding unoxidised alkaloids indicates that the first of these paths is insignificant. Yet the presence of the corresponding metastable peaks in the spectra of the *N*-oxides is evidence that $[M - 17]^+$ ions are formed at least partly by elimination of a hydroxyl radical from the molecular ions in a single stage. The hydrogen atom present in this radical has been eliminated from a different position from that from which the hydrogen atom is eliminated from the unoxidised alkaloids to form the $[M - 1]^+$ ions.

The majority of ions produced by electron bombardment of the *N*-oxides are formed directly from $[M - 17]^+$ ion. The mass spectra of the stereoisomeric *N*-oxides [LXXIV*a*–*d*) differ quantitatively among themselves mainly in the relative intensities of the $[M - 16]^+$, $[M - 17]^+$, $[M - 18]^+$, and $[M - 19]^+$ ion peaks, as well as of the peaks having *m/e* 148 and 150. In general the spectra of the *N*-oxides in the range of mass numbers below the [M − 17] peaks resemble those of the corresponding unoxidised alkaloids, but the peaks of ions characteristic of the latter are often accompanied by peaks 1 amu lower, which proves that they are due to ions containing rings *A* and *B*.

Thus all the results surveyed above provide convincing evidence that mass spectrometry can be used to assign quinolizidine alkaloids to a particular series, to determine the nature and the position of functional groups, to establish the structure of new alkaloids of this class, and in some cases also to elucidate the stereochemistry of ring fusion.

While the manuscript was being prepared for the press a more detailed study appeared[36] of the fragmentation of deoxynupharidine (XVI) and related alkaloids involving the use of high-resolution mass spectra and deuterated analogues.

REFERENCES

1. H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Structure Elucidation of Natural Products by Mass Spectrometry", Vol. 1, "Alkaloids", Holden-day Inc., San Francisco, 1964, p. 203.
2. G. Spiteller and H. Spiteller-Friedmann, Angew. Chem., **77**, 393 (1963).
3. N. Neuner-Jehle, D. Schumann, and G. Spiteller, Monatsh., **98**, 836 (1967).
4. M. Hussain, J. S. Robertson, and T. R. Watson, Austral. J. Chem., **23**, 773 (1970).
5. M. Hussain, J. S. Robertson, and T. R. Watson, Org. Mass Spectrom., **4**, 109 (1970).
6. T. Miyadera and Y. Kishida, Tetrahedron, **25**, 209 (1969).
7. M. Hussain, J. S. Robertson, and T. R. Watson, Austral. J. Chem., **23**, 1057 (1970).
8. N. Neuner-Jehle, H. Nesvadba, and G. Spiteller, Monatsh., **95**, 687 (1964).
9. E. Kh. Timbekov, F. Sh. Eshbaev, Kh. A. Aslanov, A. S. Sadykov, A. I. Ishbaev, and T. K. Kasymov, Khim. Prirod. Soed., 194 (1972).
10. O. Achmatowicz, H. Banaszek, and G. Spiteller, Tetrahedron Letters, 927 (1964).
11. T. K. Yunusov, V. B. Leont'ev, F. G. Kamaev, Kh. A. Aslanov, and A. S. Sadykov, Khim. Prirod. Soed., 477 (1972).
12. D. Schumann, N. Neuner-Jehle, and G. Spiteller, Monatsh., **99**, 390 (1968).
13. T. E. Monakhova, N. F. Proskurnina, O. N. Tolkachev, V. S. Kabanov, and M. E. Perel'son, Khim. Prirod. Soed., 59 (1973).
14. R. V. Shaimardanov, S. Iskandarov, and S. Yu. Yunusov, Khim. Prirod. Soed., 169 (1971).
15. D. Knofel and H. R. Schutte, J. prakt. Chem., **312**, 887 (1970).
16. S. McLean, A. G. Harrison, and D. G. Murray, Canad. J. Chem., **45**, 751 (1967).
17. E. Kh. Timbekov and Kh. A. Aslanov, in "Khimiya Rastitel'nykh Veshchestv" (Chemistry of Plant Substances), USSR Academy of Sciences, Tashkent Branch, 1972, p. 54.
18. S. Iskandarov, V. I. Vinogradova, R. A. Shaimardanov, and S. Yu. Yunusov, Khim. Prirod. Soed., 218 (1972).
19. Fam Khoang Ngok, Yu. K. Kushmuradov, Kh. A. Aslanov, and A. S. Sadykov, Khim. Rastitel'nykh Veshchestv, 3, 99 (1968).
20. Z. S. Siyavidinova, Candidate's Thesis, Institute of the Chemistry of Natural Compounds, USSR Academy of Sciences, Moscow, 1974.
21. N. S. Vul'fson, Z. S. Siyavidinova, and V. G. Zaikin, Khim. Geterotsikl. Soed., 251 (1974).
22. Fam Khoang Ngok, Yu. K. Kushmuradov, Kh. A. Aslanov, A. S. Sadykov, Z. S. Ziyavidinova, V. G. Zaikin, and N. S. Vul'fson, Khim. Prirod. Soed., 111 (1970).
23. S. Iskandarov, R. A. Shaimardanov, and S. Yu. Yunusov, Khim. Prirod. Soed., 631 (1971).
24. V. I. Vinogradova, S. Iskandarov, and S. Yu. Yunusov, Khim. Prirod. Soed., 87 (1972).
25. N. S. Wulfson, Z. S. Zijavidinova, and V. G. Zaikin, Org. Mass Spectrom., **7**, 1313 (1973).
26. S. Iskandarov and S. Yu. Yunusov, Khim. Prirod. Soed., 137 (1968).
27. D. Dzh. Kamalitdinov, S. Iskandarov, and S. Yu. Yunusov, Khim. Prirod. Soed., 409 (1969).
28. A. I. Begisheva, Kh. A. Aslanov, Z. U. Petrochenko, and A. S. Sadykov, Khim. Prirod. Soed., 55 (1971).
29. N. S. Vul'fson, V. G. Zaikin, Z. S. Ziyavidinova, Yu. K. Kushmuradov, Kh. A. Aslanov, and A. S. Sadykov, Abstracts of an International Symposium on the Chemistry of Natural Compounds, Riga, 1970, p. 537.
30. V. G. Zaikin, Z. S. Ziyavidinova, N. S. Vul'fson, Yu. K. Kushmuradov, Kh. A. Aslanov, and A. S. Sadykov, "Tezisy Dokladov I Vsesoyuznoi Konferentsii po Mass-spektrometrii" (Abstracts of Papers at the First All-Union Conference on Mass Spectrometry), Leningrad, 1969, p. 178.
31. S. Iskandarov, Ya. V. Rashkes, D. Dzh. Kamalitdinov, and S. Yu. Yunusov, Khim. Prirod. Soed., 331 (1969).

32. A. Zunnunzhanov, S. Iskandarov, and S. Yu. Yunusov, Khim. Prirod. Soed., 851 (1971).
33. T. E. Monakhova, O. N. Tolkachev, V. S. Kabanov, M. E. Perel'son, and N. F. Proskurnina, Khim. Prirod. Soed., 472 (1974).
34. S. Iskandarov, B. Sadykov, Ya. V. Rashkes, and S. Yu. Yunusov, Khim. Prirod. Soed., 347 (1972).
35. V. G. Zaikin, Z. S. Ziyavidinova, and N. S. Vul'fson, Izv. Akad. Nauk SSSR, Ser. Khim., 1734 (1974).
36. R. T. LaLonde C. F. Wong, J. T. Woolever, E. Auer, K. C. Das, and A. I.-M. Tsui, Org. Mass Spectrom., 9, 714 (1974).

Shemyakin Institute of Bio-organic Chemistry, USSR Academy of Sciences, Moscow