MASS SPECTRA OF PROAPORPHINE ALKALOIDS

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Received August 1st, 1973

The mass spectral behaviour of the proaporphine alkaloids is discussed. The fragmentation processes strongly depend on the character of the spirane ring and also on the substitution of the aromatic ring.

The proaporphine alkaloids belong according to the reductive stage of their spirane ring to several types whose mass spectral behaviour considerably differs. The mass spectra of the alkaloids with a spirocyclohexadienone moiety have been discussed[1–5], but no systematical attention has been paid to the other types[6–8]. Recently we have successfully used the mass spectrometry in a structural study on roemeronine, roemeramine[7] and especially on roehybrine[8]. The variability of the fragmentation processes along with the finding that the mass spectral behaviour is surprisingly influenced by the substitution of the aromatic ring prompted us to a more detailed study of the problem.

High resolution measurements were used troughout the study to establish the composition of the fragment ions discussed. The presentation of results is hoped to give a general view on the mass spectral fragmentation of the proaporphine alkaloids.

Alkaloids with the Spirocyclohexadienone Moiety

The main fragmentation paths of alkaloids with the spirocyclohexadienone grouping are known[1–5] and may be illustrated by Scheme 1 for mecambrine (*Ia*, Fig. 1*a*).

The molecular ion forms usually the base peak of the spectrum, the M − 1 peak (*a*) reaching approximately 40% of its intensity. The M − 1 fragment eliminates readily a molecule of carbon monoxide affording the ion *b* characteristically abundant for this group of alkaloids. The ionized molecule loses methylenimine by the retro-Diels–Alder fission of the tetrahydroisoquinoline system and gives the fragment *c*, abundant in all types of proaporphine alkaloids. The alkaloids with the N-methyl group show the ion *c* at mass M − 43, the secondary bases at M − 29. In the latter case, the ions *c* coalesce with fragments *b*. In the mass spectra of mecambrine and pronuciferine

(*Ib*, Fig. 1*b*), the ions *c* were accompanied by isobaric species M − (CH_3 + CO) (10% in *Ia* and 20% in *Ib*, resp.).

The main fission products are subjected to secondary fragmentations depending on the character of the substituents present. In the spectrum of mecambrine, the peaks at *m/e* 236, 224 and 194 may be interpreted as *b* − CH_2O, *c* − CO and *c* − CO—CH_2O, resp. The peaks of masses 165, 152, 139 and 115 belong to the hydrocarbon fragments with the composition $C_{13}H_9$ (d^2), $C_{12}H_8$, $C_{11}H_7$ and C_9H_9, resp.

The spectra of proaporphine alkaloids show in the higher mass range a series of small peaks belonging to the ions formed by elimination of parts of the spirane system. The recognition of these fragments supplies an additional structural evidence. High resolution measurements on mecambrine (*Ia*) and pronuciferine (*Ib*) and inspection of published low resolution spectra of crotonosine (*Ic*), N-methylcrotonosine (*Id*) and stepharine[2] (*Ie*) revealed the presence of fragments M − 54 (M − C_3H_2.O), M − 55 (M − C_3H_3O) and M − 81 (M − C_5H_5O), ion *e*. The relatively abundant ion *f* (M − 106) in the mass spectrum of mecambrine arises from the ionized molecule by elimination of the C_7H_6O species. The formation of the ion *f* is bound surprisingly to the presence of the methylenedioxide group in the molecule, the other compounds *Ib*—*Ie* form the ion *g*, lacking one hydrogen atom. The fragments M − 55, M − 81, M − 106 and M − 107 are easily discernible at following masses:

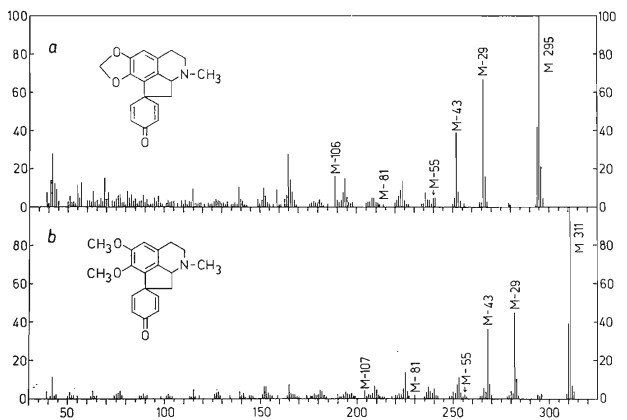
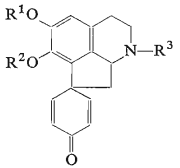


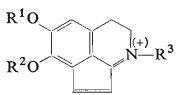
FIG. 1

Mass Spectrum *a* of Mecambrine (*Ia*); *b* of Pronuciferine (*Ib*)

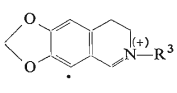


Ia; $R^1 + R^2 = CH_2$, $R^3 = CH_3$
Ib; $R^1 = R^2 = R^3 = CH_3$
Ic; $R^1 = R^3 = H$, $R^2 = CH_3$

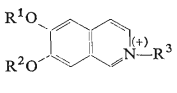
Id; $R^1 = H$, $R^2 = R^3 = CH_3$
Ie; $R^1 = R^2 = CH_3$, $R^3 = H$



e



f



g

240, 214, 189, —, at *Ia*; 256, 230, - -, 204 at *Ib*; 228, 202, ····, 176 at *Ic*; 242, 216, – –, 190 at *Id* and *Ie*.

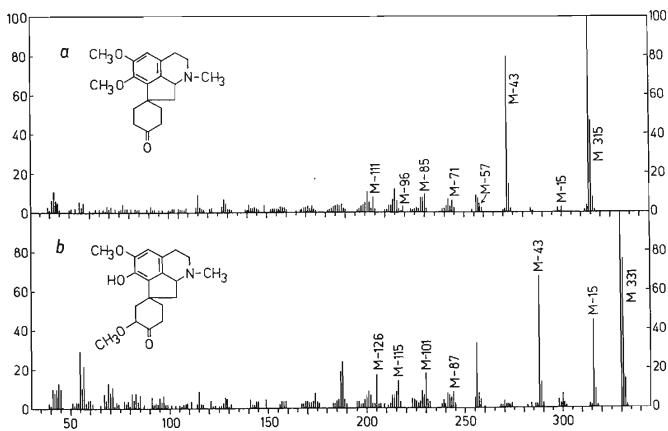


FIG. 2

Mass Spectrum *a* of Roemeronine (*IIa*); *b* of Amuronine (*IIb*)

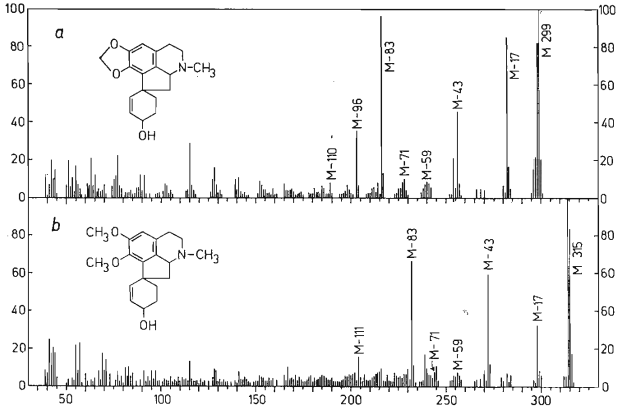


FIG. 3

Mass Spectrum *a* of Dihydroamuronine (*IIIa*); *b* of Roehybrine (*IIIb*)

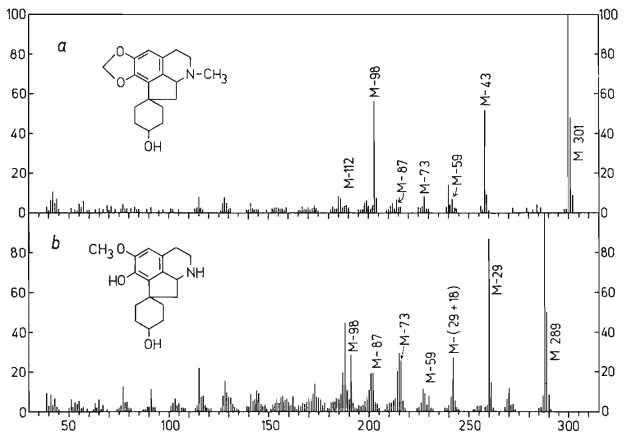
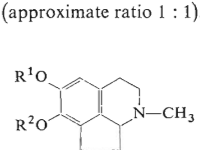


FIG. 4

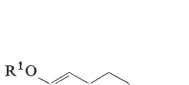
Mass Spectrum *a* of Roemeramine (*IV*); *b* of Amuroline (*IVb*)

Alkaloids with the Cyclohexenone Grouping

High resolution data were colected in this group of alkaloids for roemeronine (*IIa*, Fig. 2*a*)[7] and amuronine (*IIb*, Fig. 2*b*). Increasing saturation of the spirane ring destabilizes the molecular ion, the fragment M − 1 reaches 70–95% of its abundance. The molecular ion forms the base peak in the spectra of roemeramine (*IIa*) and linearisine[2] (*IIc*), in the spectrum of amuronine the highest peak belongs to the isobaric ions M − 43. Fragment *b*, abundant in the preceding group of alkaloids, becomes unimportant. A characteristic fission product arises by elimination of ketene from the M − 1 ion. In spectra of N-methylated alkaloids, this ion is isobaric with the fragment *c* (approximate ratio 1 : 1).

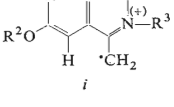


IIa; $R^1 + R^2 = CH_2$
IIb; $R^1 = R^2 = CH_3$
IIc; $R^1 = H$, $R^2 = CH_3$

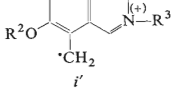


h

Ions M − 57 (M − C_3H_5O), M − 69 (M − C_4H_5O, *h*) and M − 83 (M − C_5H_7. .O, *e*) often form the highest peaks in the satellite groups. They are usually accompanied by fragments 1–2 hydrogen atoms lighter. Roemeronine (*IIa*) shows a relatively intense peak M − 94 (M − C_6H_6O) which is practically absent in spectra of *IIb* or *IIc*. Plausible formulations of this ion may be *i* or *i'*. The mass spectrum



i

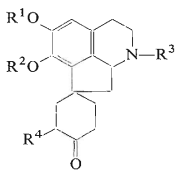


i'

of roemeronine contains a relatively abundant ion *f* (M − C_7H_8O) of mass 189 which affords fragment of *m/e* 159 by splitting off a molecule of formaldehyde. In the mass spectra of amuronine (*IIb*) and linearisine[2] (*IIc*) the ions *g* (*m/e* 204 and 190, resp.) contain again one hydrogen less than the ion *f* of roemeronine.

Alkaloids with the Spirocyclohexanone Grouping

From this group, dihydroamuronine (*IIIa*, Fig. 3*a*) and roehybrine (*IIIb*, Fig. 3*b*) were studied. Low resolution spectra of tetrahydrostepharine (*IIIc*) and N-methyllitsericinone (*IIId*) were described by Japanese authors[6].



IIIa; $R^1 = R^2 = R^3 = CH_3$, $R^4 = H$
IIIb; $R^1 + R^2 = CH_3 + OH$, $R^3 = CH_3$, $R^4 = CH_3O$
IIIc; $R^1 = R^2 = CH_3$, $R^3 = R^4 = H$
IIId; $R^1 + R^2 = CH_2$, $R^3 = CH_3$, $R^4 = H$

Fragment M − 1 forms the base peak in spectra of all these compounds. The molecular ion of alkaloids where $R^4 = H$ is approximately 50% b.p. All compounds exhibit an intense peak of retro-Diels–Alder product *c*. Dihydroamuronine (*IIIa*) affords by fragmentation in the spirane moiety the ions M − 57, M − 71 (*h*), M − 85 (*e*), M − 96 (*i*) and M − 111. Ions M − 111 (M − $C_7H_{11}O$) correspond again to *g*. Peaks at masses 215 and 201 belong to fragments *c* − C_3H_3O and *c* − C_4H_7O, resp. The alternative structures of roehybrine (*IIIb*) were deduced mostly on the basis of mass spectral measurements[8]. The mass spectrum exhibits a relatively intense peak M − 15, low in the spectra of *IIIa* and *IIIc*. Elimination of the methyl group occurs, therefore, mainly from the methoxyl group of the spirane moiety and the ion so formed possesses likely the structure of an aldehydoacylium ion. The presence of the methoxyl group in the molecule of the alkaloid manifests itself by splitting off methanol from fragment *c*. During fragmentations of the spirane moiety, the methoxyl group forms part of the leaving species, the resulting ions M − 87 (M − $C_4H_7O_2$), M − 101 (M − $C_5H_9O_2$ *h*), M − 115 (M − C_6H_{11}. $.O_2$, *e*) and M − 126 (M − $C_7H_{10}O_2$, *i*) are of medium abundance (to 17% b.p.)

In the spectrum of N-methyllitsericinone (*IIId*), the ion *i* exhibits an extremely high intensity (50% b.p.) due to substitution by the methylenedioxide grouping. In the mass spectrum of the phenolic alkaloid roehybrine, the intensity of ion *i* is much lower (17% b.p.) and becomes unimportant in the spectrum of dihydroamuronine (3·5% b.p.). The presence of an intense peak M − 98 in the spectrum of oridine (*Vb*) and absence of the analogous ion M − 94 in the spectrum of linearisine (*IIc*) indicates that the fragmentation path leading to the fragments *i* takes place easier

with phenolic alkaloids bearing the hydroxyl group in position 1. The occurrence of the fragment *i* in the spectrum of roehybrine allows, therefore, to prefer tentatively the 1-hydroxy-2-methoxy structure to the alternative 1-methoxy-2-hydroxy formulation.

Alkaloids with the Spirocyclohexenol Grouping

Mass spectra of alkaloids of this group represented by roemeramine (*IVa*, Fig. 4*a*) and amuroline (*IVb*, Fig. 4*b*) are quite characteristic. The peaks of the molecular group belong to the highest peaks of spectra, the base peak being M with roemeramine and M − 1 with amuroline. Ion *c*, the product of the retro-Diels–Alder fission of the tetrahydroisoquinoline system, retains its high intensity common to all proaporphine alkaloids. Diagnostic of the subgroup of alkaloids are abundant ions M − 17 (*l*) formed by elimination of the allylic hydroxyl and abundant M − 83 ions. The fragments M − 83 (*m*) arise from the ionized molecule by loss of the C_5H_7O species, the process being accompanied by transfer of a hydrogen atom towards the charged particle. The fragments M − 59 and M − 71 possess only a low abundance and are accompanied by satellite ions 1 – 2 hydrogen atoms lighter. In the spectrum of roemeramine (*IVa*), the intensity of the peak *i* (M − 96) is rather enhanced (35% b.p.)

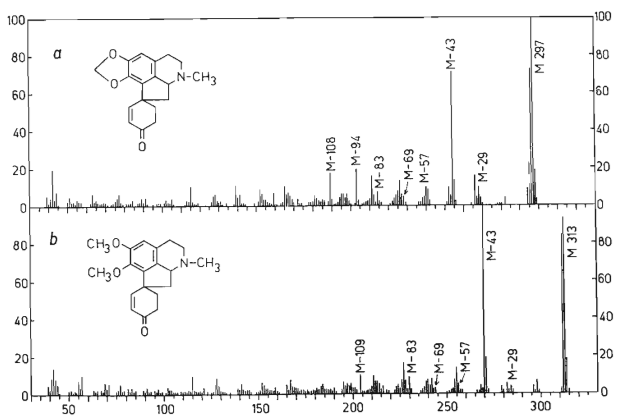
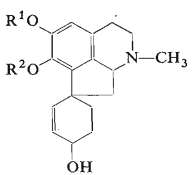
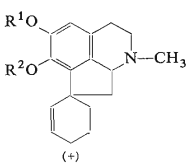


FIG. 5

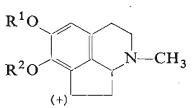
Mass Spectrum *a* of Hexahydromecambrine (*Va*); *b* of Oridine (*Vb*)



IVa; $R^1 + R^2 = CH_2$
IVb; $R^1 = R^2 = CH_3$



l

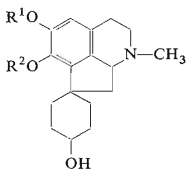


m

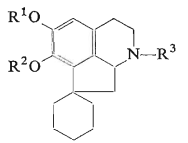
due to the methylenedioxide substituent. Amuroline (*IVb*) does not show this peak to a significant extent. Both alkaloids differ in the elimination of the C_7-unit: roemeramine gives the ion *f*, amuroline fragment *g*.

Alkaloids with the Spirocyclohexanol Grouping

In the mass spectra of the hexahydromecambrine (*Va*, Fig. 5*a*) and oridine (*Vb*, Fig. 5*b*), M − 1 fragments form the base peaks, the molecular ions possess only half of their abundance. Ions *c* in this group of alkaloids split off a molecule of water.



Va; $R^1 + R^2 = CH_2$
Vb; $R^1 = CH_3$, $R^2 = H$



VIa; $R^1 + R^2 = CH_2$, $R^3 = CH_3$
VIb; $R^1 = R^2 = CH_3$, $R^3 = H$

Fragments M − 59 (M − C_3H_7O), M − 73 (M − C_4H_9O, *h*), M − 87 (M − $C_5H_{11}O$, *e*) and M − 98 M − $C_6H_{10}O$, *i*), are present in both spectra. The substitution sensitive ion *i* forms the second most intense peak in the spectrum of the methylenedioxide derivative *Vb*. The spectrum of hexahydromecambrine contains a small peak of the fragment *f* (M − $C_7H_{12}O$). The peak of the medium intensity at mass 188 shown by oridine is a dublet of isobaric ions (9 : 1) M − ($CH_3 + C_5H_{10}O$) and *c* − C_4H_8O.

Derivatives with the Spirocyclohexane Grouping

Mass spectra of synthetic compounds, deoxo-N-methyllitsericinone (*VIa*) and deoxotetrahydrostepharine (*VIb*) have been described[6]. Abundant ions are M (40% b.p.),

M − 1 (b.p.) and *c*. The compound substituted by methylenedioxide group (*VIa*) exhibits the fragment *i* with a striking abundance (60% b.p.), the peak being practically absent in the spectrum of the dimethoxy derivative *VIb*.

EXPERIMENTAL

The mass spectra were recorded on an AEI-MS 902 mass spectrometer (electron energy 70 eV, trap current 350 μA, source temperature 120–140°C, using direct inlet system). All mass measurements were within 5 p.p.m.

The author wishes to thank to Dr W. Döpke, Humboldt University, Berlin, Dr J. Slavík, Purkyně-University, Brno and Dr K. Bernauer, F. Hoffmann-La Roche, Basel, for the generous gift of the samples and Mrs M. Vokáčová for technical assistance.

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Translated by J. Plíml.