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MASS SPECTROMETRY OF BISBENZYLISOQUINOLINE ALKALOIDS.

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The potential importance of mass spectrometry as a technique for structure determination in the 1-benzyl-1,2,3,4-tetrahydroisoquinoline alkaloid field has recently been revealed [1),2)].

In this paper, the authors wish to communicate some interesting results of a systematic investigation of mass spectral measurements*1 of bisbenzylisoquinoline alkaloids [3), 4), 5)].

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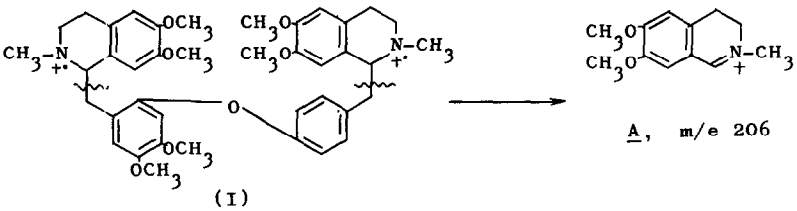
*1 The mass spectra were taken with a Hitachi Mass Spectrometer Model RMU-6D equipped with direct inlet system (Model MG-150). Chamber voltage, 80 eV ; Total emission, 80 μA ; Ion accel. voltage, 900 V.

[1] Tetramethylmagnolamine (I)



(I)

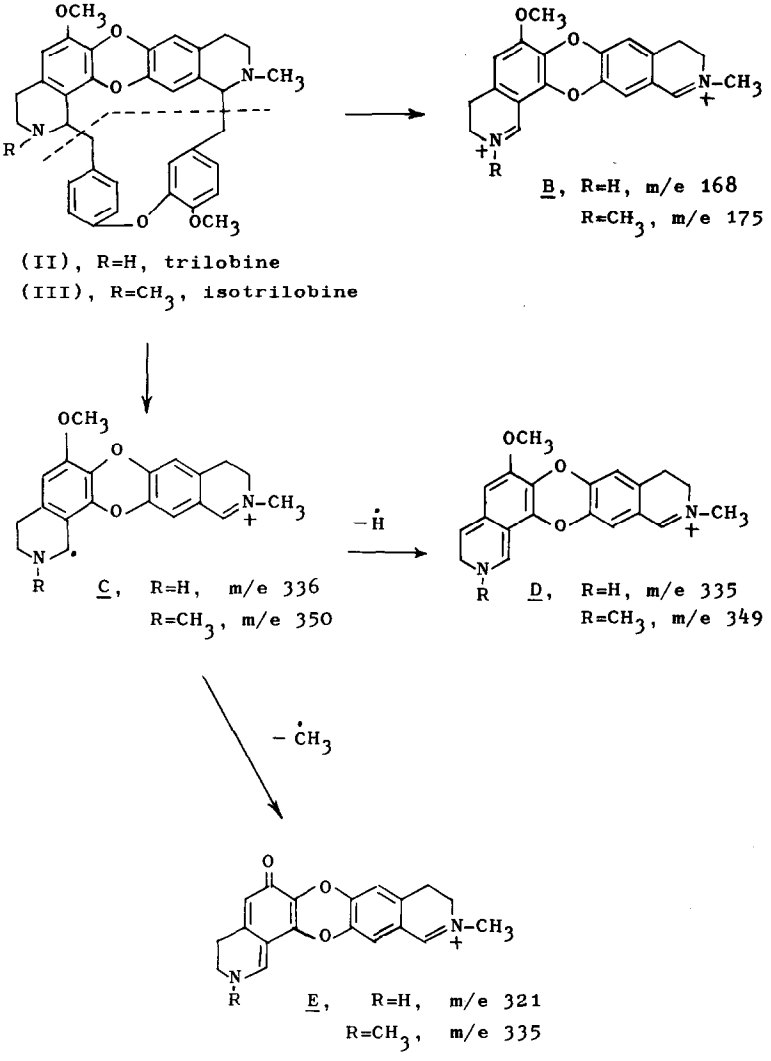
The mass spectrum of tetramethylmagnolamine (I) shows the base peak ion at m/e 206 (A), which should be the same fragment ion as that of 1-substituted-2-methyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline derivatives [1), 2)]. Loss of a methyl radical from A gives an ion at m/e 191, and successive loss of a hydrogen gives a fragment ion at m/e 190.

[2] Trilobine Type Alkaloids.

Alkaloids, such as trilobine (II) and isotrilobine (III), with a dibenzo-p-dioxin moiety undergo characteristic fragmentation paths, which were defined on the basis of mass shifts.

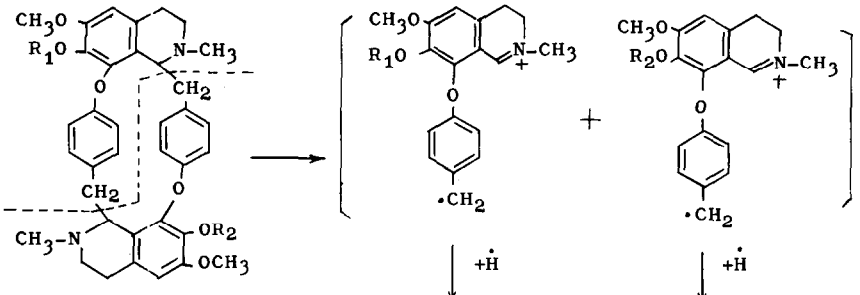
The most strong and diagnostic peak of trilobine (II) appears at m/e 168 (B , R=H), which shifts to m/e 175 in the mass spectrum of isotrilobine (III). Another significant peak of trilobine and isotrilobine appears at m/e 336, and at m/e 350, respectively, which corresponds to structure C . This would be a key intermediate of successive fragmentation ions. Loss of a hydrogen from C affords an ion D (R=H, m/e 335; R=CH_3, m/e 349). On the other hand, loss of methyl radical of the

methoxyl group from C generates an ion E (R=H, m/e 321; R=CH_3, m/e 335).



[3] Isochondodendrine Type Alkaloids.

As a typical example, the most intense ion peak of cycleanine (IV) occurs at m/e 312 (F = G). The fragment should be formed by the fission at dotted line with a hydrogen transfer. The source of the transferred hydrogen is not apparent and any suggestion must therefore be speculative.



(IV) $R_1=R_2=CH_3$

(V) $R_1=R_2=CD_3$

(VI) $R_1=CH_3$, $R_2=C_2H_5$

(VII) $R_1=R_2=C_2H_5$

As shown in TABLE 1, the strong peak at m/e 312 of cycleanine shifted to m/e 315 (O,O-bis-trideuteromethylisochondodendrine (V)), and to m/e 326 (O,O-diethylisochondodendrine(VII)). Further support for the correctness of the initial fission of the molecule is provided by the spectrum of (VI) which shows strong peaks at m/e 312 and 326. The notable feature in the isochondodendrine type alkaloids are appearance of the fragment ions at $(M-91)^{++}/2$ (though their intensities were weak. c.f. TABLE 1).

TABLE I

Characteristic Fragments of Isochondodendrine Type Alkaloids.

m/e	M^+	$(M-91)^{++}/2$	F	G
(IV)	622	265.5	312	F = G
(V)	628	268.5	315	F = G
(VI)	636	272.5	312	326
(VII)	650	279.5	326	F = G

[4] Oxyacanthine-Berbamine Type Alkaloids.

A typical member of berbamine group is isotetrandrine (VIII). Isotetrandrine (M^+ 622) reveals a characteristic doubly charged ion at m/e 198 (H), which then eliminates a methoxyl and a methyl radical to give an ion at m/e 175 (I). The doubly charged ion at m/e 175 would be the same fragment ion as isotrilobine (III).

A peak at m/e 396, represented by J , is probably a key intermediate ion for further fragmentation. Loss of a hydrogen from J gives an ion at m/e 395 (L) , and in turn fragment L affords a fragment ion at m/e 364 (M) and at m/e 349 (N) by loss of methoxyl and successive loss of methyl radicals, respectively. Loss of a methyl radical from J gives an ion at m/e 381 (K). Alkaloids of oxyacanthine group suffer the same fragmentation processes. As shown in TABLE 2, spectra of deuterium labelled compounds demonstrate the correctness of above arguments. Cepharanthine having a methylenedioxy grouping instead of vicinal dimethoxyl groupings of O-methyloxyacanthine gives a doubly charged ion at m/e 190, which corresponds to H, and no fragment corresponding to I. This presents a support for the fragmentation H ⟶ I.

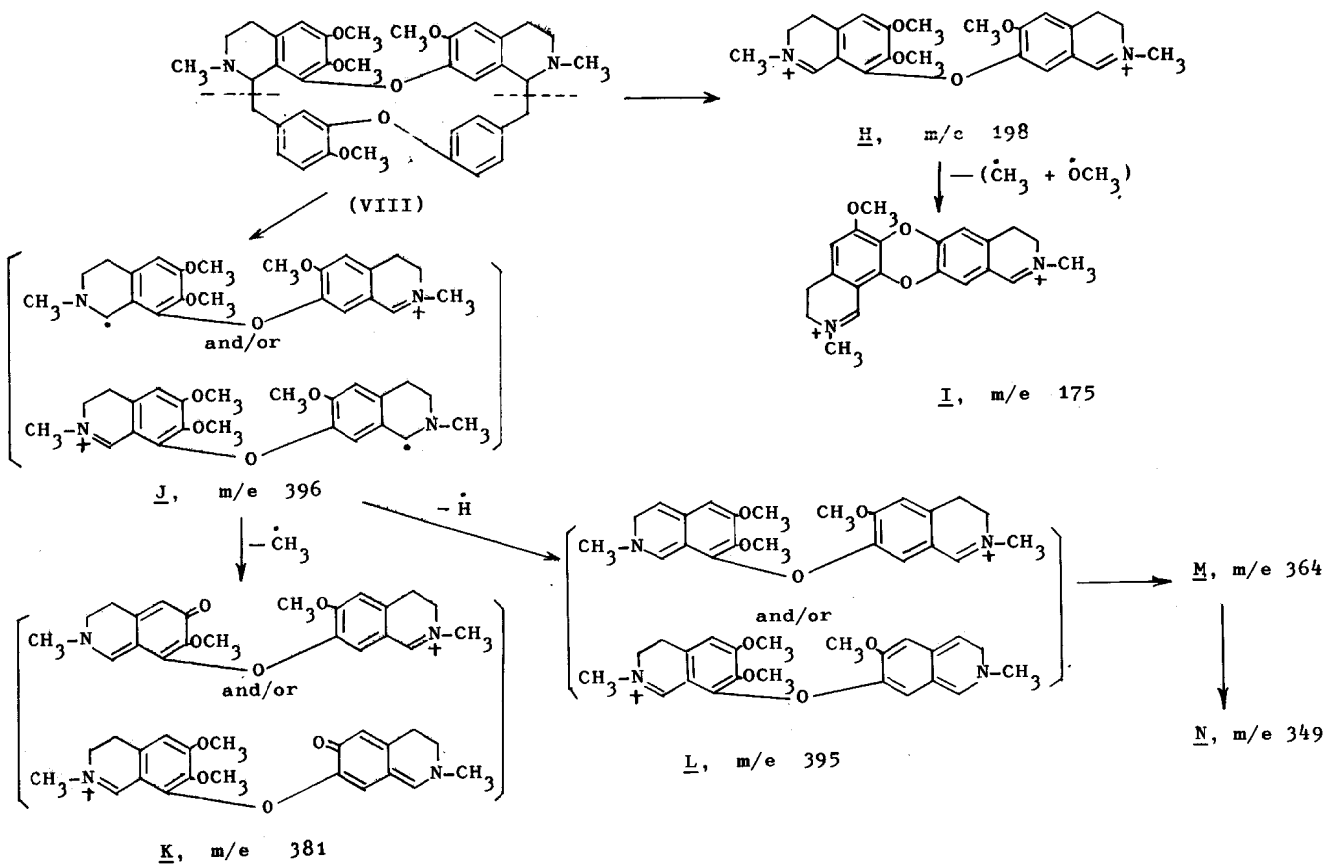

(VIII)
H, m/e 198
— (·CH3 + ·OCH3)
I, m/e 175
J, m/e 396
and/or
— ·CH3
— ·H
K, m/e 381
and/or
L, m/e 395
and/or
M, m/e 364
N, m/e 349

TABLE 2 *2

Characteristic Fragments of Oxyacanthine-Berbamine Type Alkaloids.

	m/e	M^+	j	l	k	m	n	h	i	
isotetrandrine (VIII)		622	396	395	381	364	349	198	175	174
tetrandrine (IX)		622	396	395	381	364	349	198	175	174
phaeanthine (X)		622	396	395	381	364	349	198	175	174
O-methylrepandine (XI)		622	396	395	381	364	349	198	175	174
O-trideuteromethyl-berbamine (XII)		625	396	395	381	364	349	198	175	174
O-trideuteromethyl-oxyacanthine (XIII)		625	396	395	381	364	349	198	175	174
O,O-bis-trideuteromethyl-obamegine (XIV)		628	399	398	384	367	352	199.5	175	174
cepharanthine (XV)		606	380	379	365	348	333	190		174
N-ethyldihydroepistephanine (XVI) [6]		636	410	409	395	378	363	205	182	174

*2 The structure of fragments j, l, k, m, n, h, and i correspond to those of ions J, L, K, M, N, H, and I of isotetrandrine (VIII).

A peak common to all of the oxyacanthine-berbamine type alkaloids, so far as investigated, appear at m/e 174, but the genesis and composition are not apparent.

From the data stated above, it can be concluded that structural classifications of bisbenzylisoquinoline alkaloids according to the number and the mode of diphenyl ether linkages are well correlated with their mass spectrometric fragmentations, and the utility of mass spectrometry in structural studies in the field of bisbenzylisoquinoline alkaloids is also demonstrated.

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