INDOLES

XXVII.* MASS SPECTROMETRY OF COMPOUNDS WITH ESERINE AND HOMOESERINE SKELETONS

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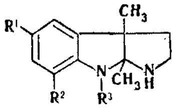
The mass spectra of 12 derivatives of dinordeoxy-9-methyleseroline and dinordeoxy-10-methylhomoeseroline were obtained. The effect of the nature and position of substituents on the stability and character of disintegration of the molecular ion was examined. A mechanism for the formation of rearranged $\overset{+}{RC_6H_4NH_2}$ pseudomolecular ions is proposed.

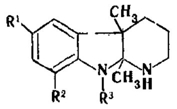
The literature contains only fragmentary information regarding the mass-spectrometric investigation of eserine and its derivatives [2-3]. The aim of the present study was a detailed investigation of systems of this type, a search for the regularities in the dissociative ionization, and a determination of the relationships between the paths of disintegration of the molecular ion and the structural peculiarities of the molecule. In this research, the mass spectra of derivatives of dinordeoxy-9-methyleseroline (I-VII) and dinordeoxy-10-methylhomoeseroline (VIII-XII), which are structural analogs of the alkaloid eserine (physostigmine), were investigated for the first time.

The mass spectra were obtained with an MKh-1303 spectrometer at ionizing electron energies of 50, 30, 20, and 15 eV; the temperature of the ionization chamber and the inlet system was 250°C. The intensities of the peaks of the most characteristic ions in the mass spectra of the compounds and the $S_{1/2}$ (disintegration selectivity [4]) values are presented in Tables 1 and 2.

The resistance to electron impact of dinordeoxy-9-methyleseroline derivatives is somewhat higher than that of the corresponding homoeserolines and is close to the W_M values for tryptamines.



I-VII



VIII-XII

Compound	R^1	R^2	R^3	Compound	R^1	R^2	R^3
I	H	CH_3	H	VIII	H	H	H
II	CH_3	H	H	IX	CH_3	H	H
III	CH_3O	H	H	X	H	CH_3O	H
IV	H	CH_3O	H	XI	H	H	CH_3
V	H	H	CH_3	XII	H	$CH_2—CH_2$	
VI	H	H	$PhCH_2$				
VII	H	$CH_2—CH_2$					

As in the case of tryptamines [5], the introduction of a methyl or methoxy group into the benzene ring or the $N_{(a)}$ position leads to an increase in the stability of the molecular ions.

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*See [1] for communication XXVI.

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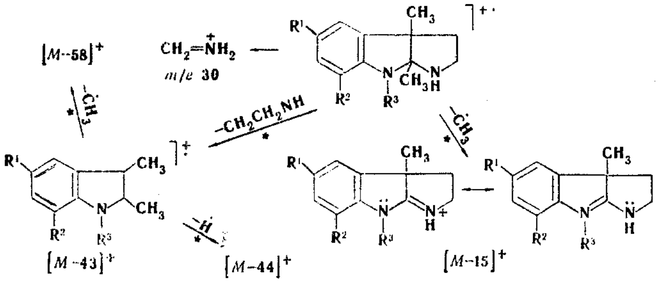
TABLE 1. Intensities of the Peaks of the Most Characteristic Ions in the Mass Spectra of Dinordeoxy-9-methyleserolines

Compound	W_M	$S_{1/2}$	$M-15$	$M-30$	$M-31$	$M-43$	$M-44$	$M-58$	$M-96$	$CH_2=\overset{+}{N}H_2$
I	4,3	7	1,8	8,1	1,2	13,8	15,0	3,9	0,2	2,0
II	4,0	12	1,1	4,8	1,1	12,2	11,5	3,8	0,2	2,1
III	5,0	18	1,3	2,6	2,5	9,7	7,4	3,0	0,4	1,7
IV	4,4	19	1,2	2,6	2,1	10,3	7,4	2,9	0,3	1,3
V	5,6	11	2,4	7,0	0,7	10,4	15,6	5,3	0,3	0,3
VI	4,0	15	0,7	1,0	0,1	6,2	3,2	0,6	1,2	0,3
VII	4,5	15	1,1	1,0	0,3	3,3	7,9	0,4	1.7	0,3

It follows from an analysis of the mass spectra of I-XII that the pyrrolidine or piperidine ring undergoes cleavage most readily during electron impact. The stability of the molecular ions of these compounds is therefore in many ways bound up with the probability of the localization of the charge on the $N_{(b)}$ atom. The introduction of a substituent into the eseroline or homoeseroline molecule leads to charge redistribution in the molecular ion in such a way that a definite portion of it now becomes tied up with the substituent. In this case, the relative fraction of charge localized on $N_{(b)}$ and, consequently, the probability of disintegration of the pyrrolidine or piperidine rings decrease, which will lead to an increase in the W_M value. The fact that W_M is smaller for homoeserolines than for eserolines is evidence for more intensive disintegration of the piperidine ring as compared with the pyrrolidine ring during electron impact.

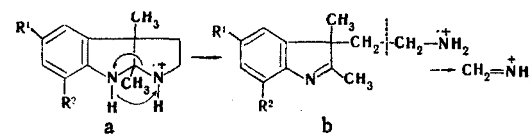
The most probable primary directions of dissociative ionization of eserolines are disintegration of the pyrrolidine ring, detachment of a methyl group, and formation of ions with mass 30 ($CH_2=NH_2^+$). The disintegration of the pyrrolidine ring with splitting out of a CH_2CH_2NH particle from the molecular ion will lead to the formation of one of the most intense ion peaks in the mass spectra of eserolines $(M-43)^+$. The structure of the $(M-43)^+$ ions probably corresponds to the structure of the pseudomolecular ions of 2,3-dimethylindole derivatives. The splitting out of a methyl group from the molecular ions leads to a structure with possible delocalization of charge between two nitrogen atoms.



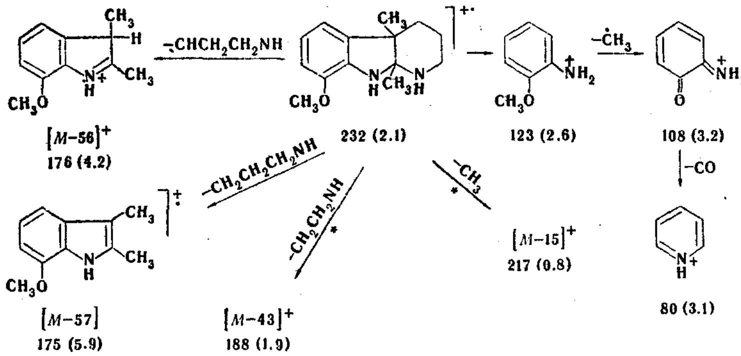
It is interesting to note that the W_M and I_{M-R} values, where R = CH_3 and CH_3O, change symbatically. We also observed a similar correlation between the stability of the molecular ions and the probability of splitting out of a substituent for other compounds [6]. In fact, the introduction of a donor substituent, which stabilizes the molecular ion, leads to an increase in the probability of charge localization on the benzene ring and the $N_{(a)}$ atom. This in turn is responsible for the observed more intense splitting out of a methyl or methoxy group from the molecular ion as a consequence of the disintegrating effect of the proximity of the charge on the bond between the substituent and the molecular framework.

The intensity of the $(M-15)^+$ ion peaks (and W_M also) is higher in the mass spectra of both eserolines and homoeserolines if the methyl group is bonded to the $N_{(a)}$ atom, promoting localization of charge on it.

The $CH_2=NH_2^+$ ions can be formed only from those molecular ions in which the charge is localized on the $N_{(b)}$ atom. The introduction of a methyl or methoxy group into the benzene ring leads to an appreciable decrease in their intensity. The sharpest decrease in the intensity of the $CH_2=NH_2^+$ ion peaks (by a factor of six to seven) is always observed when the methyl group is bonded to $N_{(a)}$. It should be noted that, in this case, the absence of the hydrogen atom of the $N_{(a)}-H$ bond, which could previously participate in migration to form rearranged ion (b), also apparently plays a role in addition to the higher probability of localization of the charge on the nitrogen atom bonded to the methyl group. The pronounced difference in the intensity of the $CH_2=NH_2^+$ ion peaks when the substituent is bonded to the benzene ring or to the $N_{(a)}$ atom makes it possible to rapidly and reliably identify these isomers.



Just as for eserolines themselves, the most intense peaks in the mass spectra in the case of dissociative ionization of homoeserolines correspond to the formation of pseudomolecular ions [$(M-57)^+$] of 2,3-dimethylindole derivatives.



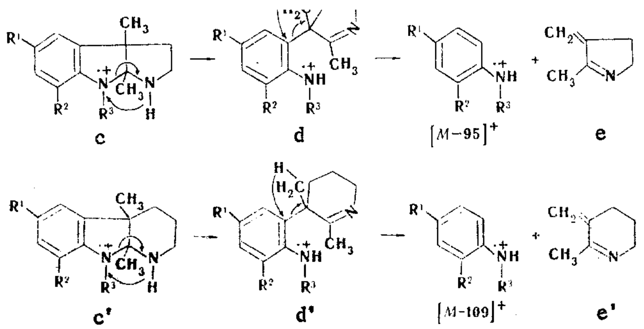
An interesting feature of the mass spectra of homoeserolines is the presence in them of intense peaks of ions that correspond to the protonated form of indole. The formation of these $(M-56)^+$ ions is associated with migration of one of the hydrogen atoms of the piperidine ring during its disintegration with the removal of a $CHCH_2CH_2NH$ particle. One does not observe a similar process for eserolines, which would involve the loss of a $CHCH_2NH$ particle to give $(M-42)^+$ ions. A possible reason for the appearance of ions that correspond to the protonated form of indole in the mass spectra of homoeserolines and their absence in the mass spectra of eserolines is the lower capacity for stabilization of the $CHCH_2NH$ particle through cyclization as compared with $CHCH_2CH_2NH$.

As seen from the scheme of the disintegration of X and the data in Table 2, intense $(M-109)^+$ ion peaks are observed in the mass spectra of homoeserolines; they are formed as a result of cleavage of the indoline ring and migration to the charged fragment of two hydrogen atoms. Despite the cleavage of four bonds and loss of a particle of high mass during the disintegration of the molecular ions, this is the lowest energy process of the primary paths of dissociative ionization of homoeserolines. Thus, for example, the intensity of the peaks of these ions for IX increases from 2.1 to 7.0% (relative to the total ion current) on passing from 50 to 15 eV. The formation of $(M-109)^+$ probably proceeds in one step from the rearranged molecular ions and is accompanied by splitting out of a stable valence-saturated particle. This process corresponds to the formation of $(M-95)^+$ ions for eserolines. It follows from the data in Tables 1 and 2 that $(M-109)^+$ ions are formed in all cases with a much higher probability than that of the formation of $(M-95)^+$ ions.

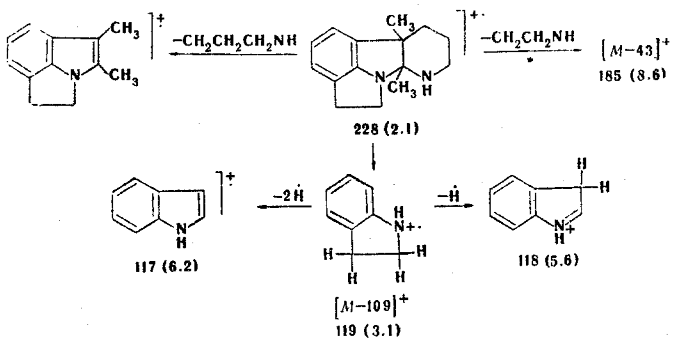
These reactions can be represented by the following schemes for eserolines and homoeserolines:

TABLE 2. Intensities of the Peaks of the Most Characteristic Ions in the Mass Spectra of Dinordeoxy-10-methylhomoeserolines

Comp.	W_M	$S_{1/2}$	$M-15$	$M-30$	$M-31$	$M-43$	$M-44$	$M-56$	$M-57$	$M-58$	$M-109$	$\overset{+}{CH_2=NH_2}$
VIII	0,8	7	0,7	0,8	0,5	3,4	3,2	11,9	10,7	11,1	0,6	5,0
IX	2,9	14	1,3	0,6	0,3	2,5	4,1	6,6	8,4	10,3	2,1	1,5
X	2,1	24	0,8	0,9	1,3	1,9	1,8	4,2	5,9	4,8	2,6	1,1
XI	3,1	24	3,0	1,0	0,4	1,5	2,0	3,2	6,1	5,4	2,5	0,2
XII	2,1	15	1,2	0,3	0,3	8,6	2,2	2,8	1,2	3,5	3,1	0,2



A rearranged molecular ion (d) is formed from molecular ion (c). The β-(o-aminoaryl)pyrroline structure (d) that develops during the rearrangement is an intermediate structure in the synthesis of eseroline in the step preceding its formation. Since the ions formed in both reactions are identical, the difference in the intensities of their peaks in the mass spectra of eserolines and homoeserolines should be associated with the stability of the neutral particles. The angular strain in structure (e) should be higher than the strain in structure (e'); the formation of an (e') particle is preferred from an energy point of view, and one may consequently expect a higher probability for the occurrence of this reaction for homoeserolines. Within each group of eseroline or homoeseroline compounds the probability of the occurrence of the reaction is higher, the higher the capacity of the substituent for localization of the charge on $N_{(a)}$.



The dissociative ionization of III and IX, which contain a dimethylene bridge, is similar to the disintegration of the remaining derivatives (Tables 1 and 2). The formation of $(M-95)^+$ and $(M-109)^+$ ions proceeds with a higher probability at an ionizing electron energy of 50 eV, and the difference in the character of the particle split out shows up to a lesser degree. As a result of this sort of disintegration, an ion with mass 119, which probably has the indoline structure, is formed. This ion undergoes subsequent dehydrogenation with splitting out of one or two hydrogen atoms and the formation of a protonated form of indolenine or indole.

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