MASS SPECTROMETRY OF INDOLE COMPOUNDS

(REVIEW)

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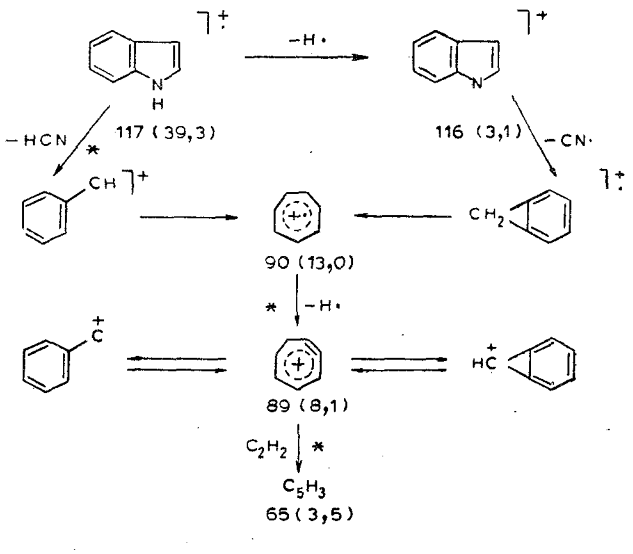
The behavior of the simplest indole systems upon electron impact is examined. The rearrangements occurring during the first stages of the disintegration are discussed, and the effect of these processes on dissociative ionization is demonstrated. The possible disintegration mechanisms were confirmed in a number of cases by investigation of labeled compounds and by the application of high-resolution mass spectrometry, kinetic methods, and low-voltage mass spectrometry.

The present review is devoted to an examination of the behavior of the simplest indole systems during electron impact. Research on the mass spectrometry of positively charged ions is discussed. Special attention is directed to the rearrangement processes occurring in the first stages of the disintegration of the molecular ion, since it is precisely these processes that usually lead to the development of the most intense characteristic peaks. Studies devoted to the quantitative characteristics of dissociative ionization are not considered in this review.

The cited literature encompasses publications that have appeared up to October 1972.

Indole and Methylindoles

The disintegration of indole under the influence of electron impact proceeds extremely selectively: there are only three intense peaks with masses of 116, 90, and 89 in its mass spectrum, in addition to the molecular ion (mass 117) and the corresponding doubly charged ion [1-3]. Metastable peaks corresponding to the following processes were observed in the mass spectrum of indole [3]: $117^+ \rightarrow 90^+ + 27$, apparent mass 69.2; $90^+ \rightarrow 89^+ + 1$, apparent mass 88.0; $89^+ \rightarrow 63^+ + 26$, apparent mass 44.5.

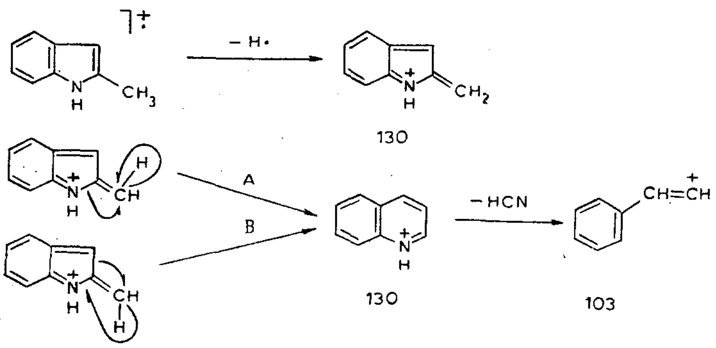


K. A. Timiryazev Agricultural Academy, Moscow. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 291-309, March, 1974. Original article submitted July 24, 1973.

The metastable ions make it possible to represent the disintegration of indole by means of the scheme presented above.*

The ions with masses 90 and 89 are probably dehydrotropylium ions. The metastable ion, which indicates detachment of C_2H_2, indirectly confirms the presence of a seven-membered hydrocarbon structure, for which this sort of disintegration is extremely characteristic. However, the possibility of the existence of other structures is not excluded [4].

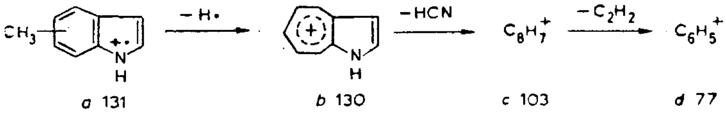
The presence of an alkyl substituent leads to cleavage of the β-bond with respect to the aromatic system and to the formation of an intense peak of $(M-1)^+$ ions for the methylindoles. As for methylpyrroles, as well as the O and S analogs, it is assumed that this sort of cleavage leads to expansion of the five-membered ring of the indole system to a six-membered ring and to the formation of a quinolinium cation [1, 5-7].



Ring expansion may be realized either with migration of the C–C bond (path A) or migration of the C–N bond (path B). Marx and Djerassi [8], in a study of the isotopic distribution in the $(M-H-HCN)^+$ ion with mass 103 in the mass spectrum of 2-methylindole labeled with C^{13} at the methyl group and in the 2 position, concluded that path A is preferred, but ~ 14% of the ions with mass 103 are formed via a path other than paths A and B; from all appearances, cleavage of the phenyl ring occurs here.

The disintegration of seven isomeric methylindoles was correlated by Powers [9]. During dissociative ionization, C-methylindoles initially lose hydrogen with subsequent expansion of one of the rings and formation of ions b or *f*, which in turn lose HCN and give the $C_8H_7^+$ ion with mass 103. The latter lose C_2H_2 and form the $C_6H_5^+$ ion. N-Methylindoles undergo disintegration in a similar manner, but another route is also possible [equation (3)].

The use of a kinetic method of analysis [11, 12] for methylindoles [10] with application of the metastable ions showed that the $(M-1)^+$ ions in the mass spectra of 4-, 5-, 6-, and 7-methylindoles have very close energy distributions and structures. This is evidence for randomization (intermixing) of the substituent in the $(M-1)^+$ ion. The results do not enable one to draw any concrete conclusions whatsoever regard-



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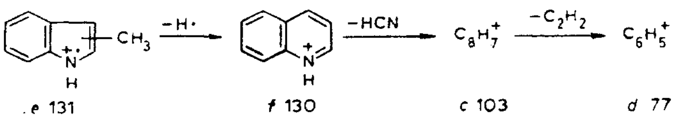

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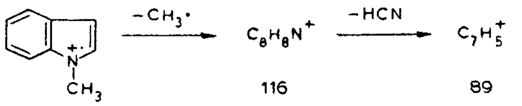

(3)

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*Here and elsewhere, the numbers under the formulas represent the ratio of the mass to the charge (m/e), the numbers in parentheses represent the intensity of the peak of the corresponding ion in percent of the total ion current, the numbers in brackets represents the intensity of the ion peak in percent of the maximum peak in the spectrum, and an asterisk indicates the presence of the corresponding metastable ion.

ing the structure of the ions; they may be either azaazulenium ions (ion b) or some other type of ion (for example, linear and polyunsaturated ions).

The close intensity ratios of the metastable and corresponding daughter ions for 2- and 3-methylindoles and their considerable difference from the remaining isomers make it possible to assume another structure for the $(M-1)^+$ ions, for example, a quinolinium ion (structure *f*), which is in agreement with the conclusions drawn by Marx and Djerassi [8]. According to the kinetic investigations, the structure of the $(M-1)^+$ ion in the mass spectrum of 1-methylindole differs considerably from the structure of the $(M-1)^+$ ions formed in the disintegration of 2- and 3-methylindoles.

The intensity ratios of the metastable peak and the peak of the daughter ion obtained for the process ion c (mass 103) → ion d (mass 77) are close for the mass spectra of all of the isomers except for N-methylindole. This fact provides evidence that detachment of HCN from two energically different $C_9H_7N^+$ ions is accompanied by intensive skeletal rearrangement and leads to the formation of $C_8H_7^+$ ions, which are structurally and energically similar for all of the C-methylindoles.

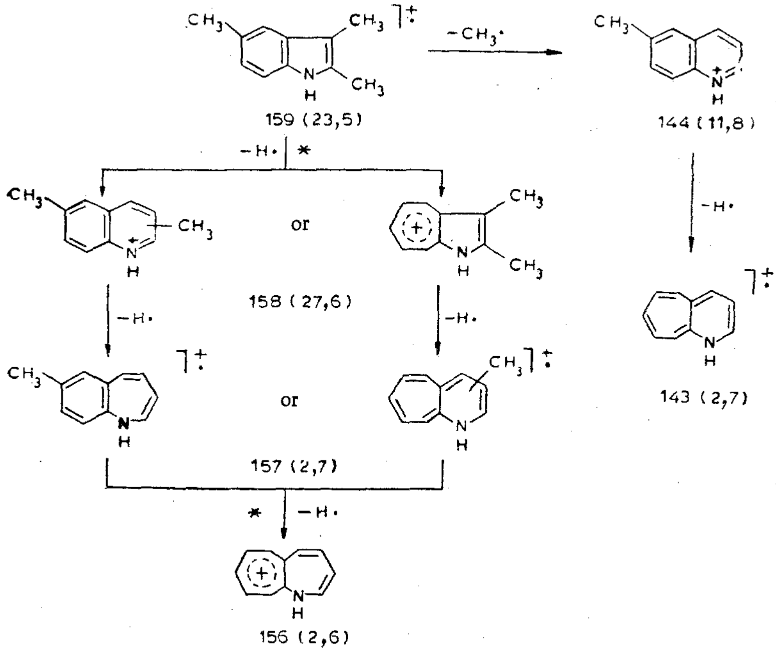
The data are confirmed [10] by an analysis of the spectra of the kinetic energies of the ions [13, 14].

Three types of rearrangement processes leading to expansion of the rings are fundamentally possible for di-, tri-, and polymethylindoles [15-18].

1. Loss of a hydrogen atom of the methyl group in the 1, 2, and 3 positions of indole with subsequent expansion of the pyrrole ring and formation of a quinoline structure. This same process is possible when at least two adjacent methyl groups are present with loss of one of them and hydrogen migration.

2. Loss of two hydrogen atoms by two methyl groups in the pyrrole ring of indole or loss of a hydrogen atom of the methyl group of the methylquinolinium ion (which is formed earlier) with subsequent expansion of it to an azepinium ion. The latter on losing a hydrogen atom can be converted to an azatropylium ion. The loss of CH_3 and H is also possible when three methyl groups are present in the pyrrole ring of indole.

3. Loss of a hydrogen atom (one of the two vicinal methyl groups) of the methyl group in the benzene ring of the indole with its subsequent expansion to the corresponding tropylium structure:



The intensity of the peaks of the $(M-15)^+$ ion in dimethyl-, trimethyl-, tetramethyl-, and pentamethylindoles [17] increases linearly as the number of methyl substituents increases. However, the ratio of the intensities of the peaks of the $(M-15)^+$ ions to the number of methyl groups in the indole system remains constant and is independent of this number and of the orientation of the methyl groups. In other words, the methyl groups in the extremely unsymmetrical indole system behave as if they were under absolutely identical conditions, and the probability of their detachment is independent of the position. This fact provides indirect evidence of randomization of the methyl substitutent over the entire indole system in the case of di-, tri-, and polysubstituted systems.

The dissociative ionization of alkylindoles [5, 7, 18] with substituents larger than methyl is realized with predominant cleavage of the C–C bond of the alkyl chain in the β-position relative to the indole system; this process is often accompanied by migration of a hydrogen atom and formation of a pseudomolecular rearranged ion.

1,7-Dimethylene- and 1,7-Trimethyleneindoles

Ions formed via three principal directions can be isolated in the disintegration of 1,7-dimethylene-2,3-dimethylindole in the first stages under the influence of electron impact. First, rearranged ions that are formed with the expansion of the pyrrole ring during detachment from the starting molecule of one or two hydrogen atoms or a methyl group are similar to the ions observed in the disintegration of 2,3-dimethylindole. Second, since there is a saturated five-membered ring condensed with the aromatic system of indole in the molecule, it undergoes extremely intensive dehydrogenation, both in the stage involving disintegration of the molecular ion and in the stage involving formation (without disintegration of the saturated ring) of fragment ions. Finally, rather intensive disintegration of the saturated ring with splitting out of C_2H_2, C_2H_3, and C_2H_4 particles occurs in the molecule under the influence of electron impact.

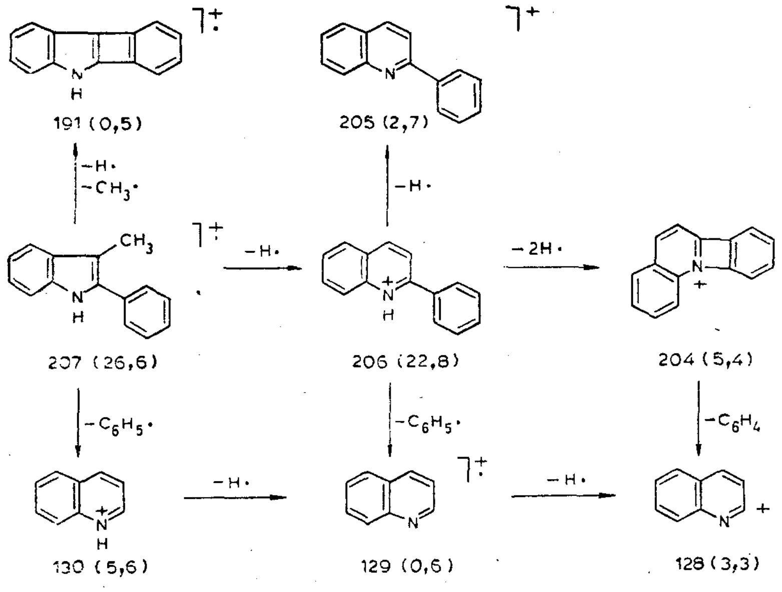
The disintegration of 1,7-trimethylene-2,3-dimethyl- and -1,3,5-trimethylindole is basically similar, but there are substantial differences associated with replacement of the five-membered saturated ring by a six-membered ring.

Phenyl- and Benzylindoles

The mass spectra of phenylindoles were examined in [9, 19]. The principal act of the dissociative ionization of isomeric 2- and 3-phenylindoles [19] is the formation of an ion with mass 165, which corresponds to the fluorenyl cation structure, which may be formed both during splitting out of CH_2N from the molecular ion and during detachment of a hydrogen cyanide molecule from the $(M-1)^+$ ion; the detachment of the above-indicated groupings from 2-phenylindole without rearrangement is unlikely.

The metastable peak with mass 141.5, which corresponds to the process $192^+ \rightarrow 165^+ + 27$ in the mass spectra of phenylindoles, attests to probable rearrangement of the $(M-1)^+$ ion with subsequent splitting out of HCN, although one cannot exclude the possibility of rearrangement of the molecular ion.

The introduction of a methyl group into the phenylindole molecule (3-methyl-2-phenylindole, 2-methyl-3-phenylindole, and 2-methyl-7-phenylindole) leads to great differences in the mass spectra of the isomeric compounds [19]. The rearranged $(M-H)^+$ ion, which apparently has the quinoline structure, and the other two rearranged ions basically determine the paths of the subsequent disintegration.



Cleavage of the bond between the phenyl and indole rings, which corresponds to the formation of the $(M-77)^+$ ion, while being absolutely uncharacteristic for phenylindoles, is realized to a considerable degree in the case of 3-methyl-2-phenyl- and 2-methyl-3-phenylindole. It might be assumed that the driving force of these processes is ring expansion and the formation of quinolinium ions. If this process is unlikely, the intensity of the $(M-77)^+$ peak decreases sharply [19].

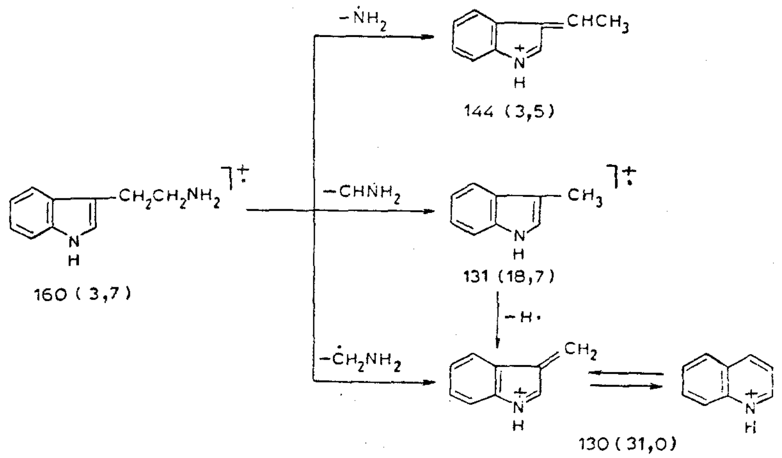
Detachment of a methyl group, accompanied by splitting out of a hydrogen atom to form a new bond between the phenyl substituent and the indole system competes with detachment of a phenyl group. In the case of 2-methyl-7-phenylindole, cyclization with the participation of the nitrogen atom and the formation of a stable five-membered ring is energically more favorable.

Methylphenylindoles are characterized by an extremely significant dehydrogenation process [19]. In addition to the peaks of the examined $(M-1)^+$, $(M-2)^+$ and $(M-3)^+$ ions, there are also $(M-4)^+$ peaks [and sometimes even up to $(M-8)^+$ peaks] in the mass spectra.

The disintegration of 1-benzylindole [20] and 2,3-dimethyl-1-benzylindole [18] proceeds with ring expansion and predominant localization of the positive charge on the phenyl ring; this leads to the most probable formation of the $C_7H_7^+$ ion. The $(M-77)^+$ ions which correspond to detachment of a phenyl group, are absent. The formation of $(M-H)^+$, $(M-15)^+$, and $C_7H_7^+$ ions from the molecular ion and of the $C_5H_5^+$ ion from the tropylium ion is confirmed by the corresponding metastable peaks. The introduction of four fluorine atoms into the benzene ring of 1-benzylindole changes the direction of disintegration only slightly [21].

Tryptamine and Methyltryptamines

The disintegration of tryptamine [6] under the influence of electron impact proceeds primarily at the β-bond with the splitting out of a CH_2NH_2 group and formation of an immonium ion with mass 130, which can rearrange to a stable quinolinium ion, as described for 2- and 3-methylindoles. The formation of this ion is also possible from the ion with mass 131, which is obtained in the splitting out of a $CHNH_2$ group from the starting molecule [6].



The disintegration of methyltryptamines [22-24] is basically analogous to the disintegration of tryptamine. Disintegration at the β-bond with migration of a hydrogen atom and formation of an $(M-29)^+$ ion, similar to the ion with mass 131 in the spectrum of tryptamine, is confirmed by the presence of the corresponding metastable processes. Competition in the formation of these ions and the $(M-30)^+$ ions, which have the quinolinium ion structure and are obtained during cleavage of this same β-bond without hydrogen migration, is observed in the mass spectra of tryptamine and methyltryptamines. The probability of the occurrence of these processes depends markedly on the energy of the ionizing electrons [2].

Phenyltryptamines

The introduction of a phenyl substituent into the 1 position of the 2-methyltryptamine, tryptamine, and methyltryptamine molecules [6, 25] has practically no effect on the intensity of the disintegration processes of the aminoethyl side chain at the β-bond with splitting out of CH_2NH_2 and $CHNH_2$ groups. As before, the most intense peaks in the mass spectra correspond to these processes, which are confirmed by the corresponding metastable ions.

The characteristic (for phenylindoles) processes of formation of ions corresponding to subsequent splitting out of hydrogen atoms in the mass spectra of phenyltryptamine appear only after disintegration of the side chain.

The behavior of 1,2-diphenyltryptamine is similar to the behavior of the corresponding phenylindoles. Just as in phenylindole, disruption of conjugation, which is associated with the noncoplanarity of the molecular ion, leads to a decrease in the stability of the primary ion, and, as a consequence, to the occurrence of disintegration via a large number of paths. The most intense peaks correspond to ions associated with disintegration at the β-bond of the side chain and the formation of rearranged ions with subsequent dehydrogenation, which leads to ions with aromatic structures.

The disintegration of benzyltryptamines reflects the competition in the possibility of localization of the charge on various portions of the molecule.

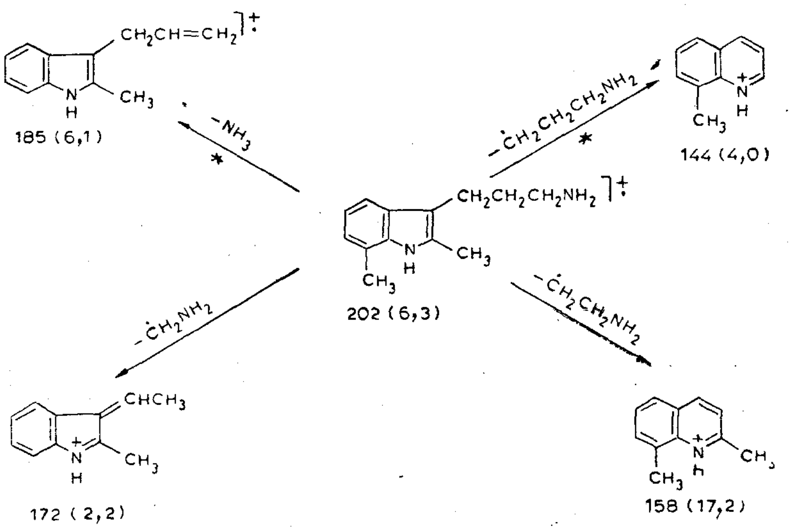
Thus the disintegration of aryltryptamines to a considerable degree is in agreement with the dissociative ionization of the corresponding indoles. However, the processes characteristic for the analogous indole derivatives proceed only after disintegration of the side aminoethyl chain of tryptamine. As in phenylindoles, the ions formed by successive dehydrogenation correspond to aromatic structures.

Homotryptamines

An increase in the length of the aminoalkyl side chain as compared with tryptamines (dimethylhomotryptamine) changes the behavior of these systems only relatively little under the influence of electron impact [6]. Just as in tryptamines, the primary act of disintegration is cleavage of the side chain with splitting out of CH_2NH_2 and $CHNH_2$ groups, although the second process becomes less intense. However, disintegration paths absent or uncharacteristic for tryptamines begin to manifest themselves in these compounds. As seen from the scheme for the disintegration of 2,7-dimethylhomotryptamine, the disintegration of the C−N bond with splitting out of ammonia, which is not too intense in the spectrum of tryptamine and is almost completely absent in the spectra of methyltryptamines, leads to a third (with respect to intensity) ion in the mass spectrum. Processes involving cleavage at the γ-bond relative to the indole system, which are activated by the effect of an amino group [the characteristic (for amines) disintegration at the α-bond with respect to the amine nitrogen], also are quite intensive. However, the possibility of complete splitting out of an aminoalkyl group with migration of hydrogen from the adjacent methyl substituent and expansion of the pyrrole ring of the indole system is most characteristic for homotryptamines. This process was not realized in tryptamines, inasmuch as the coordinated effect of the aromatic system and of the amino group leads only to cleavage of the β-bond. The subsequent disintegration of the resulting ions is similar to that described for methylindole and methyltryptamines.

Stability of Alkyl- and Aryl-Substituted Indoles and Tryptamines

Compounds of the indole series are extremely resistant to electron impact. In the dissociative ionization of indole, $\sim 40\%$ of the total ion current (W_M) goes into the production of the molecular ion fraction, and the peak corresponding to it is a maximum in the mass spectrum. The introduction of the first methyl substituent reduces the resistance of the molecule to electron impact by a factor of almost two. The introduction of the second and third methyl groups also lowers W_M, but to a considerably lesser extent; the addition of a fourth and fifth substituent leads to an increase in the stability [26]. A similar picture is also observed in the disintegration of tryptamine [26].



The observed increase in W_M as the volume of the molecule increases can take place only in the case of some rearrangements of the molecular ion itself. This may be reflected in a change in the structure of the fragment ions of identical mass that are formed in the first stages of the disintegration of the molecular ion [27].

Monophenylindoles [9] differ considerably with respect to their stability as a function of the position of the phenyl group. The increased electron density in the 3 position of the indole system, due to the optimum conditions for its conjugation with the phenyl substituent, leads to an increase in W_M of 60 relative % for 3-phenylindole as compared with 2-phenylindole and even to a slight increase as compared with indole. The introduction of yet another phenyl group (2,7-diphenylindole) leads to an increase in W_M as a result of stabilization of the molecular ion due to the electron-donor phenyl substituents. One might have expected a certain further increase in W_M in triphenylindoles. However, a greater than twofold decrease in the stability, caused by two adjacent phenyl groups which disrupt the coplanarity of the molecular ion and the conjugation of the phenyl groups with the indole system, is observed in 2,3,7-triphenylindole. The possibility of the occurrence of profound disintegration via a large number of paths is a consequence of this.

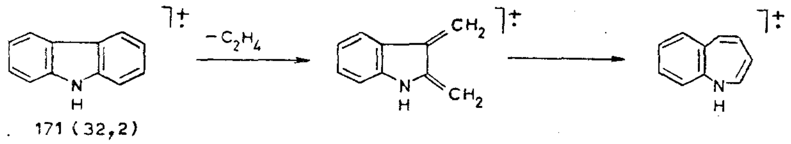
Carbazoles and Tetrahydrocarbazoles

In comparison with the corresponding aromatic hydrocarbons, carbazoles have extremely high resistances to electron impact [28, 29]. The mass spectra of these compounds are simple: the maximum peak corresponds to the molecular peak in the spectrum, and disintegration of the compound takes place extremely selectively. Apart from the molecular ion peak with mass 167 $(C_{12}H_9N)^+$ in the mass spectrum of carbazole itself, only ion peaks with masses 139 $(C_{11}H_7)^+$ and 140 $(C_{10}H_6N)^+$ have adequate intensities. The elementary compositions of these ions were established on the basis of a precise measurement of the masses [29].

The detachment of C_2H_3 from the molecular ion is observed only in the mass spectrum of carbazole; substituted carbazoles eliminate only H_2CN from the molecular ion, while N-methyl-substituted carbazoles also eliminate a methyl group. Detachment of a substituent is not observed in the case of N-aryl-substituted carbazoles; detachment of H_2CN is also blocked in this case.

The mass spectra of tetrahydrocarbazole and methyl-, phenyl-, and benzyl-substituted tetrahydrocarbazoles [30] are characterized by intense, successive dehydrogenation of the system, both in the stage involving the molecular ion and in the stage involving the ions formed after splitting out of the substituent. A considerable portion of the ions formed as a result of dehydrogenation arise from the $(M-1)^+$ ion. The intensity of the peaks of the $(M-1)^+$ ions depends to a considerable degree on the nature of the substituent in the indole ring.

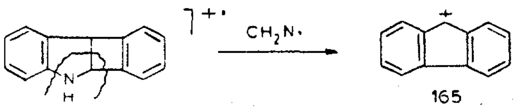
In addition to dehydrogenation, disintegration at the β bonds with respect to the indole system with splitting out of an ethylene molecule, possibly with the following rearrangement, is common for all of the tetrahydrocarbazoles:



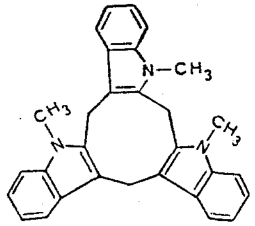
Indole-Containing Condensed Systems

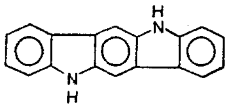
The overwhelming majority of compounds of this type, particularly compounds with an indole ring condensed with nitrogen-containing rings, are indole alkaloids and therefore are beyond the scope of the present review. However, an examination of relatively simple systems that do not enter into the indicated classes of natural compounds is of undoubted interest.

The mass spectra of benzindole and dihydrobenzindole were described by Pandit and co-workers [31, 32] and Leeh [33]. An investigation of 2,3-phenylenedihydroindoles showed [34] that the most probable process involves elimination of CH_2N and formation of an ion with mass 165, which corresponds to the fluorenyl cation structure. It is interesting to note that simple disintegration of the four-membered ring does not occur during electron impact of this compound.



A mass-spectrometric method was used by Bergman and co-workers [35, 36] for the identification of the products of macrocyclic condensation of indoles and simple aldehydes. Thus the reaction of 1-methylindole with formaldehyde gave a trimer, the mass spectrum of which has a molecular ion peak of secondary intensity. Indolo[3,2-b]carbazole was identified in the case of the condensation of indole and formaldehyde.

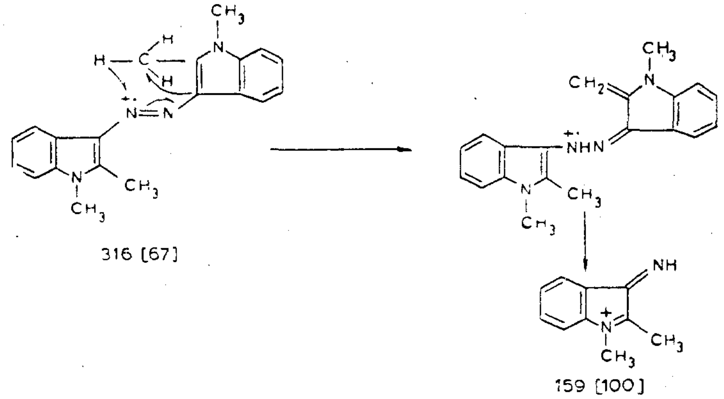




The mass spectra of methylindolylcarbazoles formed during thermal and catalytic dimerization of vinylindole were examined in [37]. The mass spectra of indolylmethylpiperidines were also described [38].

An investigation of the mass spectra of N-skatylbenzimidazole, N-skatyl-2-methyl- and N-skatyl-2-benzylbenzimidazole, and N-skatyl-1,2,3-benzotriazoles showed that the disintegration of these compounds during electron impact is realized via the expected paths and leads to readily identified fragments that are formed from the methylindole or imidazole (triazole) portions of the molecule. The molecular peaks are intense, and an ion with mass 130 with the probable structure of the quinolinium cation corresponds to the maximum peak in all of the mass spectra [39].

In the dissociative ionization of methyl-substituted 3,3'-azoindoles [40], disintegration at the β-bond with the formation of $(M-1)^+$ ions is suppressed by other processes. The maximum peak corresponds to an ion with mass 159; this ion is formed as a result of migration of a hydrogen of the methyl group to the nitrogen atom of the azo group with subsequent cleavage of the N–N bond. Charge localization on the nitrogen atom of the azo group probably precedes the indicated process.



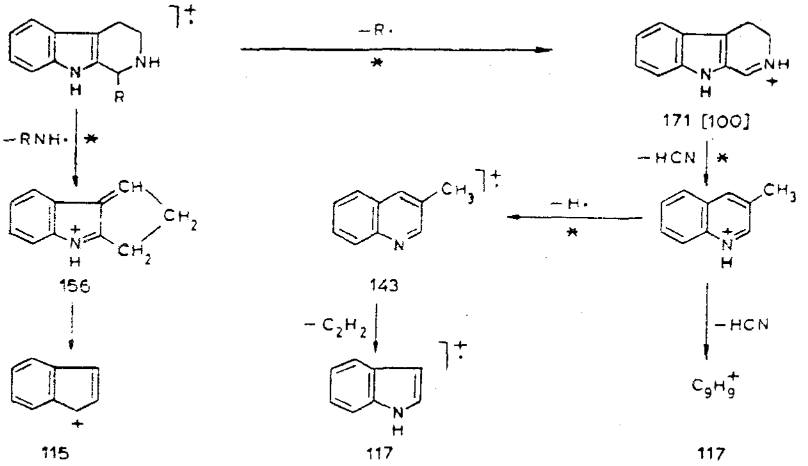
The mass spectra of hexahydroazepine[2,3-b]indoles were investigated by Hester [41], and the simplest derivatives of pyridoindoles were studied in [42-47].

Biemann [42] found that the disintegration of 1-alkyl-β-carbolines with an alkyl chain containing more than two carbon atoms proceeds with McLafferty rearrangement.

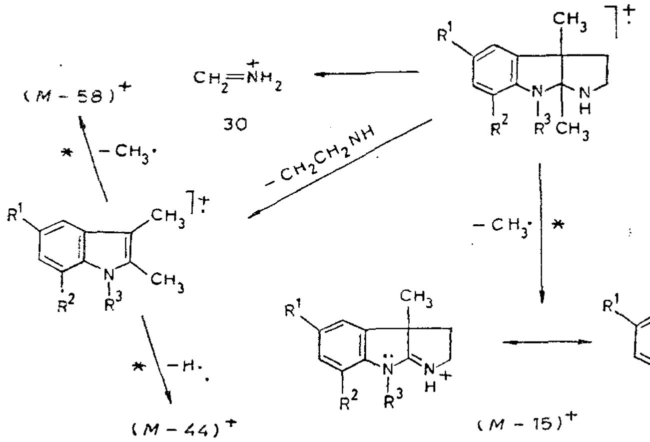
Coutts and co-workers [46] investigated 12 substituted β-carbolines using deuterium-labeled compounds and high-resolution mass spectrometry.

The disintegration of 1-alkyl-1,2,3,4-tetrahydro-β-carbolines is realized in the first stage with detachment of an alkyl radical (R) or with elimination of RNH. The resulting $(M-R)^+$ion with mass 171 corresponds to the maximum peak in the spectrum. This ion on disintegration gives a number of intense peaks. The use of high-resolution mass spectrometry showed that in the disintegration of 1-methyl-1,2,3,4-tetrahydrocarboline, 67% of the ions with nominal mass 117 are $C_8H_7N^+$ ions, while 33% are $C_9H_9^+$ ions. The second path of disintegration leads to ions with mass 156, which subsequently eliminate CH_3CN and form ions with mass 115.

Rather little study has been devoted to the mass spectra of compounds with the eserine and homoeserine skeletons [48-51]. The most probable primary paths of dissociative ionization of the eserolines are disintegration of the pyrrolidine ring, detachment of a methyl group, and formation of ions with mass 30 ($CH_2=\overset{+}{N}H_2$).



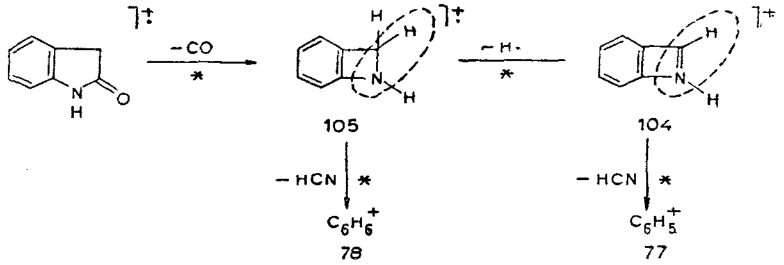
The disintegration of the pyrrolidine ring with detachment of a CH_2CH_2NH particle from the molecular ion leads to the formation of one of the most intense ion peaks in the mass spectra of eserolines – $(M-43)^+$. The structure of the $(M-43)^+$ ions probably corresponds to the structure of the pseudomolecular ions of 2,3-dimethylindole derivatives. Detachment of a methyl group from the molecular ions leads to a structure with possible charge delocalization between two nitrogen atoms [51].



Just as in the case of the eserolines themselves, in the case of dissociative ionization of homoeserolines [51] the most intense peaks in the mass spectra correspond to the formation of pseudomolecular ions of 2,3-dimethylindole derivatives – $(M-57)^+$. An interesting peculiarity of the mass spectra of homoeseroline is the presence in them of intense ion peaks corresponding to the protonated form of indole.

Oxygen-Containing Indole Compounds

The mass spectra of 2-ketoindolines have been investigated by a number of authors [9, 52-58]; the general scheme of the first stages of the disintegration can be illustrated in the following manner:



It has been assumed that the carbon in the HCN eliminated from ions with mass 105 and 104 is removed from the methylene group of the 2-keto-indoline. In conformity with this, a mechanism for the removal of HCN with hydrogen migration to the aromatic ring has been proposed. This mechanism contradicts the data of Brown and Butcher [59], who investigated the mechanism of the pyrolysis of carbon-labeled 2-ketoindolines at 850° and 0.7 mm. Proceeding from this, Brown and Butcher [59] investigated the high-resolution mass spectra of (3-C^{13})-2-ketoindoline. It was observed that in the case of the M−CO−HCN process, detachment of $HC^{13}N$ corresponds only to a small portion of the ions (~30%), while a large portion of the ions (~70%) correspond to elimination of $HC^{12}N$. The fractions of the corresponding ions for the M−CO−H−HCN process are 25 and 75%. Thus it can be supposed that the prevailing process is elimination of unlabeled HCN, probably with removal of carbon from the 7a position.

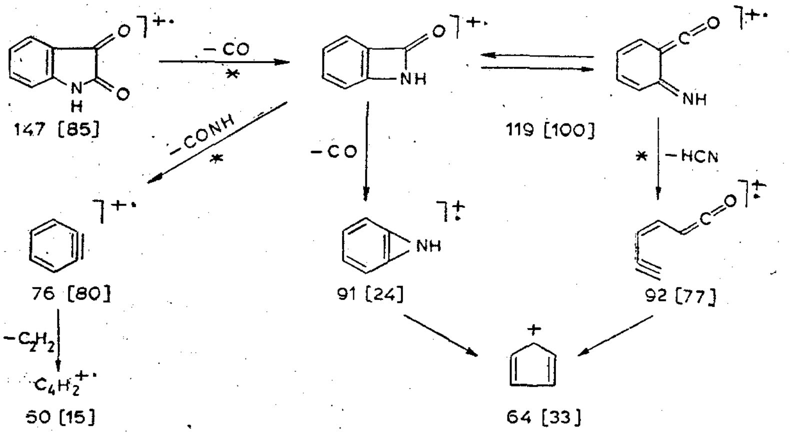
The mass spectra of 4-, 5-, 6-, and 7-hydroxyskatoles are extremely similar [60]. An investigation of the disintegration processes by means of high-resolution mass spectrometry led to the conclusion that all four isomers form an ion with mass 118 principally due to elimination of CO from the $(M-H)^+$ ion; a total of 5-20% of ions with the same nominal mass is formed during the detachment of H_2CN from the molecular ion. According to a kinetic method for the investigation of metastable ions, the $(M-H)^+$ ions have identical structures; this indicates randomization of the substituent in the investigated isomers.

The maximum peak in the mass spectrum of isatin [52, 61] is formed in the elimination of CO from the molecular ion. Subsequent disintegration is realized via three alternative paths: one of them is associated with removal of HCN with subsequent detachment of CO, while the second is associated with removal of CO and subsequent detachment of HCN; detachment of CONH leading to an ion with mass 76 is also possible. Thus all three heteroatoms of isatin are eliminated in the formation of these primary ions [52].

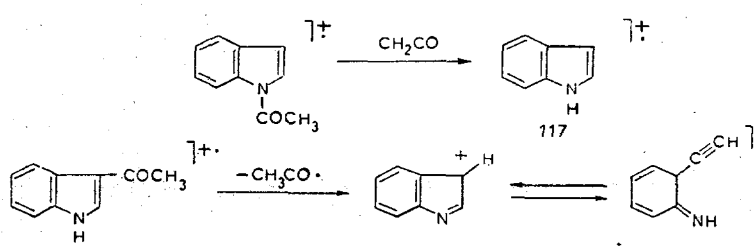
The disintegration of the isomeric formylindole [9, 62] is realized via a common scheme with the formation of qualitatively similar mass spectra.

$$M^+ \xrightarrow{-H} 144^+ \xrightarrow{-CO} 116^+ \xrightarrow{-HCN} 89^+ \xrightarrow{-C_2H_2} 63^+$$

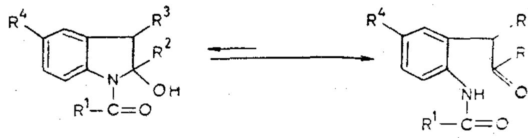
The incomplete mass spectra of 1- and 3-acetylindoles have been published; the formation of a maximum peak (mass 117), which corresponds to detachment of ketene, is characteristic for 1-acetylindole [7, 63].



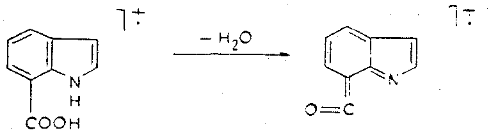
The maximum peak in the mass spectrum of 3-acetylindole corresponds to the $(M-CH_3CO)^+$ ion with mass 116.



An investigation of 10-substituted 1-acyl-2-indolinols showed that the predominant form for all of the investigated compounds in the gas phase is the open form [64].

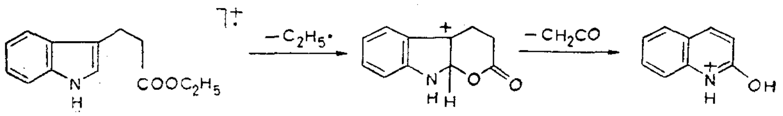


The disintegration of isomeric indolecarboxylic acids [9] proceeds with successive elimination of OH, CO, and HCN, but an ortho effect is manifested in the case of the 7-substituted isomer, and water is removed in the first step.



The disintegration of nitriles, amides, esters, and other derivatives of indolecarboxylic acid [9, 32, 62, 65-67] proceeds in accordance with the general principles of the behavior of aromatic acid derivatives during electron impact and therefore does not require additional consideration.

Chizhov and co-workers [68-70] have described the so-called oxygen rearrangement in esters of aliphatic-aromatic and unsaturated acids, which is induced by electron impact and consists in the migration of one of the oxygen atoms of the carboxyl group to the unsaturated portion of the molecule. It has been shown [70] that this rearrangement also occurs in the case of dissociative ionization of the indole analog of β-phenyl-propionic acid esters.



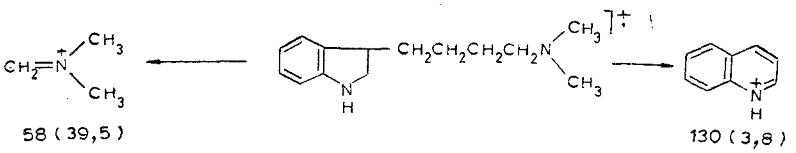
The introduction of a methyl group into the α-position of the pyrrole ring hinders rearrangement. Shortening of the chain length also leads to complete suppression of the rearrangement. Consequently, rearrangement in the 4-position of the indole ring does not occur.

A large number of representatives of other types of oxygen-containing derivatives of indoles have also been investigated by mass spectrometry: methoxyindoles [9], methoxytryptamines [22], methyl, benzyl, and methoxy derivatives of tryptophols and homotryptophols [1], carbonyl derivatives of isatin [72], 2-substituted derivatives of 3-benzoylindoles [73], methoxybenzylindoles [74], indolylpyruvic acid [75], hydroxyindoloindolizines [76], and 2-phenylisatogen [77].

Indole Compounds with Other Functional Substituents. Systems with Several Substituents

The presence of two different substituents in the indole ring may lead to a sharp change in the mass spectrum as compared with the spectra of monosubstituted derivatives primarily because of the possibility of charge localization on different groups of the molecule. The interaction of these groups in the excited molecule or in the molecular ion has a lesser but sometimes substantial effect (especially when the two groups are adjacent). In a number of cases, one of the substitutents determines the pattern of disintegration during electron impact of the disubstituted systems [9, 78].

An increase in the length of the aminoalkyl group, branching of it, or replacement of nitrogen atoms of the amino group by alkyl groups or acyl groups leads to the development of new processes that are not typical for the disintegration of tryptamines and homotryptamines. Thus the mass spectrum of 3-(δ-dimethyaminobutyl)indole illustrates the possibility of charge localization in both the indole systems and on the nitrogen of the dimethylamino group, with predominance of the second process [18, 78].

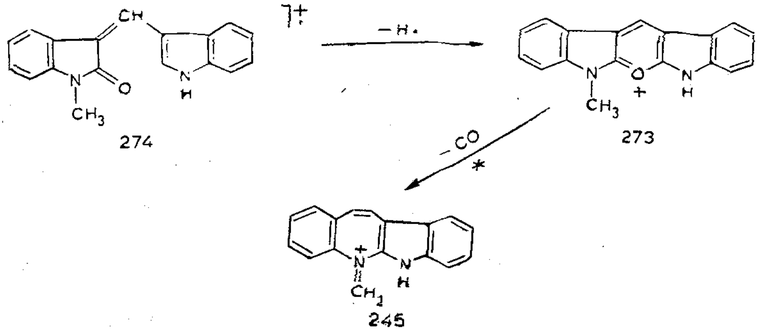


The mass spectrum of 1-(4-chlorobenzoxy)-2-methylindole attests to cleavage of the alkyl-oxygen bond in the molecular ion [58]. The charge is localized with greater probability on the acyl portion of the molecule (mass 139), which subsequently disintegrates with elimination of CO (mass 111) and Cl (mass 75). Disintegration of the indole-containing fragment (mass 146) is realized with elimination of O (mass 130); the subsequent path is analogous to the disintegration of 2-methylindole.

The disintegration of tryptophan ethyl ester at the β-bond leads to a quinolinium ion with mass 130 (the maximum peak in the spectrum); only an insignificant portion of the ions (2%) is formed in the case of alternative charge localization on the substituent (ions with mass 102) [7, 79]; 4,7-dihydrotryptophan disintegrates similarly [80].

The identical character of the mass spectra of 5-, 6-, and 7-hydroxyindole-3-carboxylic acids is a consequence of the randomization of one of the substituents [60]. The sharp contrast between these spectra and the mass spectrum of the 4-isomer is due to 3,4-trans-interaction, which leads in this case to suppression of the elimination of OH and an increase in the probability of the removal of H_2O.

The mass spectra of 2-ketoindolinyl-3-methines [55] differ markedly from the mass spectrum of 1-methyl-2-ketoindoline with respect to the low intensity of the molecular ion peak; in some cases, the doubly charged molecular ion corresponds to the peak of secondary intensity in the mass spectrum. The disintegration of 2-ketoindolinyl-3-methines, in addition to the usual transformations of indole compounds during electron impact, proceeds with condensation and the formation of a rearranged 1-methylbenz[b]azepinium ion.

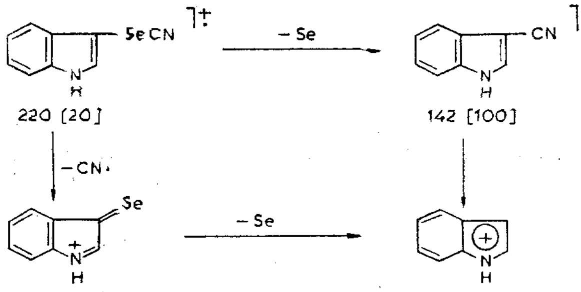


The mass spectra of 1-ethyl-5-hydroxy-6-methoxy- and 5-hydroxy-6-methoxyindole, 1-(3-acetoxybenzyl)-5,6-diacetoxyindole [81], 1,5-dimethoxy-3-(dimethylaminomethyl)indole [82], 6-hydroxy-, 5,6-dihydroxy-, and 6-methoxy-2-carbethoxyindoles, 6-hydroxy-5,7-dibromo-2-acetamidomethylindole [83], 6-hydroxy-5-methoxy-3-(acetamidoethyl)indole [84], indolimicinic acid [85], peracetyltryptamine [47], acetyltryptophan derivatives [86-88], N-mesidino-2-methyl-Δ^2-pyrroline [18], 3-indolylacetic acid derivatives [89], 5- and 7-nitro-2-ketoindolines, 2-hydroxy-5,7-dinitroindole [90], 1,3-dimethyl-2-picryliminoindole [91], N-[2-(3-indolyl)ethyl]pyrrolidinomaleinimide [92], products of the autooxidative dimerization of various alkylindoles [93, 94], indodidthiones [57, 95], benzodithiinindoles [96], 2-ethylthioindole derivatives [15, 97], indolyl toluene sulfonates [98], and 3-indolyl thiocyanates [99] have also been studied.

Selenium-Containing Indole Compounds

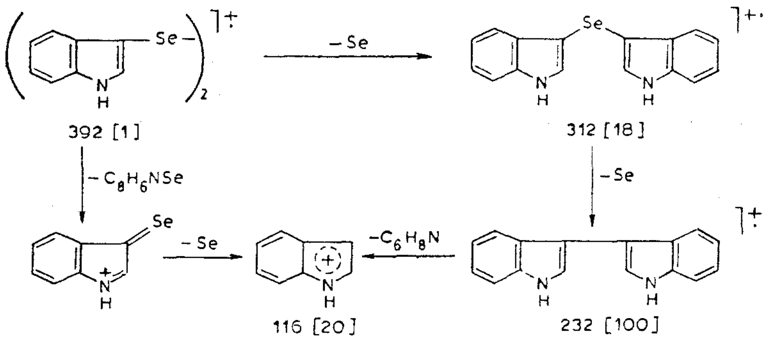
An extremely specific group of selenium-containing indoles was the subject of the steadfast attention of Agenaas [100-103] and, in part, Bergman [104].

An investigation of the mass spectra of 3-selenocyanatoindole and its 1- and 3-methyl-substituted derivatives and of 3,3'-diindolyl diselenide and its methyl-substituted derivatives showed that selenocyanate compounds, like aromatic selenocyanates, disintegrate in the first step with removal of Se and CN.

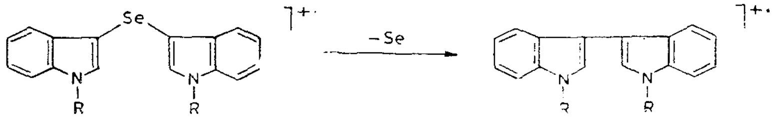


The selenium-containing indole fragment subsequently disintegrates to form either selenium-containing fragments or indole fragments [100].

The disintegration of diindolyl diselenides is also similar to that of the corresponding aromatic analogs, and the principal peaks in the mass spectrum are formed during the elimination of Se.



3,3-Diindolyl selenides also undergo simultaneous disintegration of both Se–C bonds and "recombination" of the fragments [104].



This type of disintegration is probably a general one for aryl selenides [100]. A similar process apparently also occurs during electronic impact of diphenyl sulfide, diphenyl disulfide, benzophenone, and azobenzene, although the intensity of the $C_{12}H_{10}^+$ ion peak is lower. It is interesting to note that this peak is not present in the mass spectrum of diphenyl ether.

A comparison of the mass spectra of 3-indolylmethyl benzyl selenide, di(3-indolyl)methyl selenide, and di(3-indolyl)methyl diselenide with the spectra of the corresponding sulfur analogs provides evidence [103] that the primary paths of disintegration and the intensity of the overwhelming number of peaks of analogous ions are similar for the S and Se indole compounds. However, in each pair of mass spectra there are differences that make it possible to readily distinguish between the indicated compounds. These differences show up particularly distinctly in rearrangement processes, for example, those associated with migration of a hydrogen atom during cleavage of the S–Se or C–S bonds.

The mass spectra of 5-selenocyanatoindoles, 5,5'-diindolyl diselenides, and the corresponding indoline analogs have been studied [101]. The disintegration of these compounds, which have intense molecular ion peaks, is realized with elimination of Se, HSe, and CN from the selenocyanate group. The presence of a saturated five-membered ring in the case of indoline derivatives leads to the appearance of additional channels for disintegration.

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