MASS SPECTROMETRY AND STEREOCHEMISTRY OF HETEROCYCLIC COMPOUNDS

(REVIEW)

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The possibilities of the application of mass spectrometry for the determination of the orientation of substituents, the stereochemistry of ring fusion, and the configuration of an asymmetric heteroatom are examined. The possibility of the use of the differences in the ionization and appearance potentials of epimers for the solution of stereochemical problems in series of heterocyclic compounds is discussed.

The use of mass spectrometry for the solution of stereochemical problems has recently become of increasing interest to researchers. As a rule, the mass spectra of stereoisomers are qualitatively similar but differ quantitatively to a greater or lesser extent. These quantitative differences are associated with the rates, under the influence of electron impact, of both rearrangement processes and reactions due to simple bond cleavage. It may be assumed that the differences in the ease of simple bond cleavage are due to differences in the internal energies (enthalpies) of the epimers, whereas the differences in the distances between the migrating molecular fragments and the molecular fragments undergoing elimination most often affect the probability of the occurrence of rearrangement processes. Despite the fact that we usually do not know the structure and conformations of the fragmented molecular ions, the principles of conformational analysis can be successfully used to explain the differences in the fragmentation of the stereoisomers. The latter fact confirms the assumption that the structures of many molecular ions are close to the structures of the starting neutral molecules, i.e., substantial skeletal rearrangements do not occur in the molecular ions after ionization prior to fragmentation.

For the mass-spectrometric comparison of stereoisomers it is important to know the absolute rate constants of fragmentation of the molecular ions; however, these constants cannot be obtained from ordinary mass spectra. The application of mass spectrometry for the solution of stereochemical problems therefore includes an analysis of the quantitative differences between the spectra of the stereoisomers. These differences may be expressed in terms of a) the ratio of the intensity of the molecular (or fragment) ion to the total ion current $([F]^+/\Sigma I)\cdot 10^{-2}$ (in percent of the total ion current); b) the ratio of the intensities of the peaks of two ions arising from the same precursor $[F_1]^+/[F_2]^+$; c) the ratio of the intensities of the fragment and molecular ions $[F]^+/[M]^+$. As applied to molecular ions of stereoisomers, ratios of the $([M]^+/\Sigma I)\cdot 10^{-2}$ type make it possible to estimate the differences in their stabilities.

In a review [1] devoted to stereoisomeric effects in mass spectra it was emphasized that it is important to lower the temperature of the ion source and to use low ionizing-electron energies to simplify the spectra of stereoisomers and to obtain large quantitative differences between them.

It follows from statistical theory that the ratios of the rate constants of fragmentation of the molecular ions (k_A/k_B) in a specific process are proportional to $(E + \Delta\varepsilon - E_0/E - E_0)^{m-1}$ (where E and $E + \Delta\varepsilon$ are the internal energies of the ions for two sterioisomers A and B, E_0 is the activation energy, and the term $m - 1$ pertains to the effective number of oscillators, among which the energy is distributed). From this equation it might have been expected that the differences between the mass spectra of stereoisomers A and B would increase as E decreases, i.e., as the energy of the electrons decreases [1, 2]. In other

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words, inequalities of the following type should be satisfied for the intensity ratios noted above (for example, for ratio c):

$$\frac{([F]^+/[M]^+)_A}{([F]^+/[M]^+)_B} \text{ low strain} > \frac{([F]^+/[M]^+)_A}{([F]^+/[M]^+)_B} 70\ B > 1$$

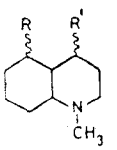
However, in the case of a study of the $C_{(2)}$ and $C_{(4)}$ stereosiomers of 1,2-dimethyl-4-alkyldecahydro-4-quinolols and other isomers it was shown [3] that a decrease in the energies of the ionizing electrons does not always lead to an increase in the quantitative differences between the mass spectra of the stereoisomers and that the above-indicated inequalities are not satisfied. Curves of the ionization efficiency, which expressed the dependence of the $[M - CH_3]^+/[M]^+ = Z$ intensity ratios on the energies of the ionizing electrons, were obtained to prove this. A comparison of the Z_A/Z_B ratios for any pairs of epimers showed that they do not depend on the ionizing electron energy. It was also noted that a decrease in the latter does not give rise to an appreciable increase in the quantitative differences in the intensities of the ions due to both simple cleavage and rearrangement processes. Thus decreasing the ionizing-electron energy to distinguish stereoisomers is ineffective in some cases. In addition, the reproducibility of the spectra obtained at low energies is often unsatisfactory, as a result of which high-voltage spectra are more convenient for the identification of stereoisomers.

A decrease in the temperature of the ion source is evidently an important condition in the mass spectrometric analysis of stereoisomers. This is particularly true for labile compounds, which are capable of thermal tranformations. At the same time, in the case of relatively stable compounds even prolonged contact with heated surfaces does not lead to substantial leveling of the mass spectra. In this respect it is interesting to ascertain the possibilities of the application of gas-chromatographic mass spectrometry for the analysis of mixtures of stereoisomers, since when chromatographic introduction is used, the substance on passing along the column and through the molecular separator is in contact for a long time with heated surfaces, the temperature of which is usually quite high. It has been shown [4] for mixtures of stereoisomers in the 1,2-dimethyl- and 1-ethyl-2-methyl-4-alkyldecahydro-4-quinolol series, the mass spectrometric comparison of which will be examined below, that the quantitative differences between the mass spectra of these stereoisomers are basically retained on passing from direct introduction into the ion source to gas-chromatographic introduction.

If one compares the mass spectrometric behavior of carbocyclic and heterocyclic compounds, one may note that the most energically favorable rearrangement processes, for which regioselectivity and stereoselectivity of the migrating groups are not always characteristic, are characteristic for the former. However, in the case of heterocyclic compounds, particularly N-heterocyclic compounds, reactions associated with simple bond cleavage are frequently expressed more distinctly, and rearrangement processes take place more selectively. This peculiarity of heterocyclic compounds makes it possible to hope that one will be able to obtain values that correlate with the difference in the internal energies in the mass-spectrometric investigation of pairs of stereoisomers in this series.

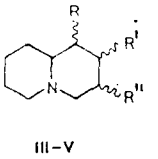
Orientation of the Substituents

Of the heterocyclic compounds, the greatest amount of mass-spectrometric study has been devoted to various stereoisomeric nitrogen heterocycles, particularly their hydroxy derivatives. In contrast to carbocyclic alcohols, the molecular ions of heterocyclic alcohols eliminate, as a rule, a hydroxy group rather than the elements of water. In most of the known cases one cannot determine the configuration of the hydroxy-containing center only from the intensity of the $[M - OH]^+$ ion peak. In fact, no differences whatsoever were detected in the mass spectra of epimeric 4- (I) and 5-hydroxy-1-methyl-trans-decahydroquinolines (II) [5] or in the mass spectra of 1- (III), 2- (IV), and 3-hydroxyquinolizidines (V) [6].



I, II

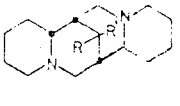
I R=H, R'=OH; II R=OH, R'=H



III–V

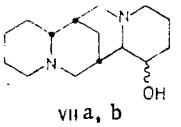
III R=OH, R'=R''=H; IV R=R''=H, R'=OH; V R=R'=H, R''=OH

Differences between the mass spectra of 8-hydroxysparteine (VIa) and its $C_{(8)}$ epimer (VIb) and the mass spectra of retamine (VIIa) and epiretamine (VIIb) were found only in [7]. In the case of the first pair the $[M - OH]^+$ ion peaks with m/e 193 and 114 were more intense in the spectrum of VIb. In the fragmentation of the molecular ions of VIIa and VIIb the OH group is unexpectedly eliminated in the form of water, and the intensity of this process is considerably higher for alcohol VIIb, which contains an equatorial OH group. Neuner-Jehle and co-workers [7] explain this difference in terms of the possibility of dehydration via a 1,4-elimination mechanism (after conversion of the ring to the boat form), which should proceed more readily in the case of an equatorial OH group (the cis-1,4-H/OH configuration). This is perhaps the only example of an analogy in the character of the fragmentation between carbocyclic and N-heterocyclic alcohols.



VI a, b

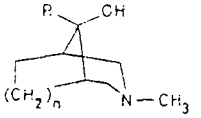
VI a R=H, R'=OH; b R=OH, R'=H



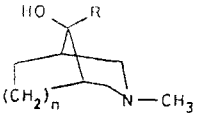
VII a, b

VII a β-OH; b α-OH

In the nitrogen heterocycle series the stereochemical peculiarities are displayed more acutely in the rates of elimination of alkyl substituents or hydrogen atoms. The orientation of the OH group can even be sometimes determined on the basis of such data. Research [8] in which the mass spectra of epimeric 3-azabicyclo[3.2.1]octanols, 3-azabicyclo[3.3.1]nonanols, and 3-azabicyclo[4.3.1]decanols (VIIIa, b) were studied is very domonstrative in this respect.



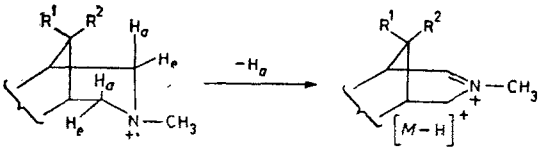
VIIIa



VIIIb

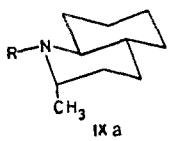
VIIIa,b R=H, CH_3 or C_6H_5; n=1-3

The intensity of the $[M - OH]^+$ ion peaks in the spectra of these compounds is also virtually independent of the stereochemistry. At the same time, the magnitude of the $[M - H]^+$ ion peaks is related to the stereochemical peculiarities of the investigated compounds. For any pairs of epimers the $[M - H]^+$ ion peak was more intense in the spectrum of the stereoisomers in which a large substituent attached to the bridge carbon atom was oriented on the nitrogen atom side.

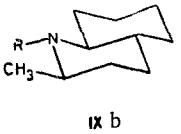


This result can be explained by the fact that a 1,3-diaxial interaction of the R^2 substituent with the axial hydrogen atom (H_α) exists in the M^+ ions. As a result, the bulkier R^2 substituent ($H < CH_3 < OH < C_6H_5$) stimulates detachment of an α-hydrogen atom. A similar regularity is also observed in the case of methoxy derivatives of azabicyclononane (R^1 and R^2 = H and OCH_3): the $[M - H]^+$ ion peak is larger in the case of compounds with an axial CH_3O group (R^1 = H, R^2 = OCH_3) than in the spectrum of its epimer. It should be noted that the differences between the spectra of the epimers decrease in the case of azabicyclodecane derivatives, possibly because of the fact that this system is conformationally more labile.

The effect of the orientation of the alkyl group on the ease of its detachment under the influence of electron impact has been demonstrated in a number of cases. In a study of the mass spectra of stereoisomeric 2-methyl- and 1,2-dimethyl-trans-perhydroquinolines (IXa, b) it was noted [9] that the development of the $[M - CH_3]^+$ ion is more likely for epimers with an axial 2-CH_3 group (IXa) than in the case of their equatorial epimers (IXb).



IX a



IX b

IX a,b R=H, CH_3

It has similarly been observed [10] that in the case of stereoisomeric 1-methyl-trans-quinolizidinines the axial CH_3 group is detached more easily under the influence of electron impact than the equatorial CH_3 group. In this connection, it should be noted that the $[M - CH_3]^+/[M]^+$ ratios for epimeric 1- and 2-methyl-trans-decalines are several times larger in the case of compounds with an equatorial CH_3 group than in the case of compounds with an axial CH_3 group [11]. The hypothesis as to the reasons for such anomalous behavior of methyldecalines advanced in [11] seems doubtful to us. The same fact that an axial alkyl group is eliminated more easily in the case of heterocyclic compounds has been confirmed in a large number of examples and has been used successfully for the determination of the configuration of the corresponding asymmetric center.

The mass-spectrometric method has been successfully applied in a number of studies [12-17] for the determination of the configurations at $C_{(2)}$ and $C_{(4)}$ in trans-fused 2-methyl-4-alkyldecahydro-4-quinolols (A, B, and C). The mass spectra of the investigated epimers are distinguished by the $[M - CH_3]^+/[M]^+$ intensity ratios (Table 1). It has been shown [17] that the $[M - CH_3]^+$ ion is due to detachment of only a 2-CH_3 group. A greater value of the indicated ratio is always observed in the spectra of epimers of the A type regardless of the size of the R and R' groups. This fact made it possible to conclude that the 2-CH_3 group in their molecules is axial, since in this case a 1,3-cis-diaxial interaction of the 2-CH_3 group and one of the substituents attached to $C_{(4)}$ is realized. Moreover, the lower value of the $[M - CH_3]^+/[M]^+$ ratio in the spectra of epimers of the B and C type constitutes evidence for an equatorial orientation of the 2-CH_3 group. It should be emphasized that in the case of these compounds a 1,3-interaction of the axial 2-CH_3 group with the axial substituent attached to $C_{(4)}$, which, as noted in [18], may stimulate elimination of an alkyl group, evidently has a particularly strong effect on the ease of splitting out of the axial 2-CH_3 group.

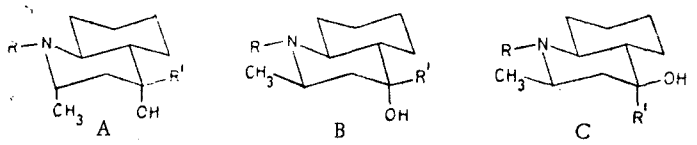
Since unsaturated substituents (C≡CH, CH=CH_2, or C≡C–CH=CH_2) attached to $C_{(4)}$ are not split out under the influence of electron impact, the configuration of this center in compounds of the B and C type was determined on the basis of the ease of ejection of 4-C_2H_5 or 4-C_4H_9 groups from the molecular ions of the corresponding saturated tertiary alcohols, which are readily obtained without a change in the stereochemistry by hydrogenation of the unsaturated alcohols. Higher $[M - R']^+/[M]^+$ ratios were found in the spectra of epimers C, and this made it possible to assign a 4*a*-alkyl-4e-OH configuration to them and, consequently, a 4e-alkyl-4*a*-OH configuration to compounds of the B type. One cannot determine the stereochemistry at the $C_{(4)}$ center in decahydroquinolols A on the basis of mass-spectrometric data when their epimers are not available.

The quantitative differences are considerably smaller in the spectra of stereoisomeric 1,4-dialkyl-trans-decahydro-4-quinolols D and E, which do not contain an asymmetric center at $C_{(2)}$ [19]; the mass spectra became particularly similar when the size of substituent R attached to the nitrogen atom increases (Table 2). A particularly good correlation of the stabilities of the molecular ions with the internal energy of the epimer is observed for N-methyl derivatives. In fact, the stabilities of the molecular ions ($[M]^+/\Sigma_n \cdot 10^{-2}$) in a series of ethynyl alcohols are higher for the epimers with an axial 4-C≡CH group (D), whereas for ethyl alcohols a high stability is characteristic for compounds of the E type with an equatorial 4-C_2H_5 group (Table 2). It is known that the conformational energies of the substituents increase in the order C≡CH < OH < C_2H_5, and the more stable isomer (which has a lower enthalpy) for ethynyl alcohols should have the bulkier OH group in the equatorial position, whereas compounds with an equatorial 4-C_2H_5 group are more stable for ethyl alcohols. Thus the differences in the enthalpies of the nonionized molecules are retained in their molecular ions also in the case of the compounds under consideration.

The configuration at $C_{(4)}$ in compounds D and E can be determined on the basis of an analysis of the spectra of the 4-ethyl-substituted compounds from the ease of elimination of the C_2H_5 radical. As in the above case, the axial 4-C_2H_5 group is split out more readily than the equatorial group (Table 2).

A very interesting phenomenon is observed in the case of these compounds. Whereas the rate of elimination of a 4-C_2H_5 radical is higher for less stable (ethyl-substituted) alcohols with an axial 4-C_2H_5 group than for their more stable equatorial epimers, the probability of other fragmentation pathways increases in the latter case. Thus, for example, the $[M - CH_3]^+/[M]^+$ intensity ratios (the $[M - CH_3]^+$ ionscorresponds to fragmentation of N – C_2H_5

TABLE 1. $[M - CH_3]^+/[M]^+$ and $[M - R']^+/[M]^+$ Intensity Ratios in the Mass Spectra of Decahydroquinolols



A B C

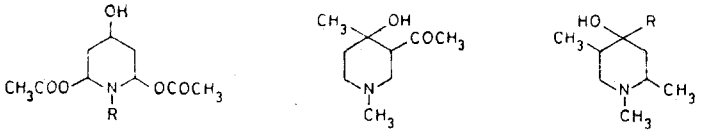
R	R'	$[M-CH_3]^+/[M]^+$			$[M-R']^+/[M]^+$		
		A	B	C	A	B	C
CH_3	$C\equiv CH$	6.0	3.3	3.3	—	—	—
CH_3	$CH=CH_2$	5.9	3.6	3.7	—	—	—
CH_3	C_2H_5	7.4	3.8	4.4	5.0	3.4	8.0
C_2H_5	$C\equiv CH$	5.0	3.8	3.4	—	—	—
C_2H_5	$CH=CH_2$	5.6	3.1	3.0	—	—	—
C_2H_5	C_2H_5	6.1	3.9	3.1	5.3	3.6	8.5
CH_3	$C\equiv C-CH=CH_2$	4.2	2.1	3.1	—	—	—
CH_3	n-C_4H_9	7.2	4.4	4.2	5.1	4.3	8.5
H	$C\equiv C-CH=CH_2$	7.6	2.3	3.0	—	—	—
H	n-C_4H_9	10.8	3.9	5.5	7.5	4.2	8.2

or N—iso-C_3H_7 groups) are higher in the mass spectra of epimers E with an equatorial 4-C_2H_5 substituent than in the spectra of the less stable epimers (Table 2). This fact can evidently be explained as follows. Detachment of a C_2H_5 radical, the activation energy (E_α) of which is lower than for epimers with an equatorial 4-C_2H_5 group, is more favorable for compounds with an axial 4-C_2H_5 group. In the case of the equatorial epimers "side" reactions whose activation energies in this case are closer to the E_α of formation of the $[M - C_2H_5]^+$ ion naturally begin to proceed more actively.

In [20, 21], which are devoted to mass-spectrometric studies of $C_{(2)}$ and $C_{(4)}$ epimeric secondary alcohols of the 2-methyl-, 1,2-dimethyl-, and N-alkyl-2-methylperhydro-4-quinolol series, it was also confirmed that the axial 2-CH_3 group is eliminated more easily than the equatorial group under the influence of electron impact. It was also noted that the intensity of the $[M - OH]^+$ ion peak at low ionizing-electron energies (20 eV) depends on the orientation of the 4-OH group: the $[M - OH]^+$ ion peak is more intense in the case of an axial orientation.

On the basis of the absolute intensities of the peaks for $C_{(2)}$ and $C_{(4)}$ stereoisomeric 2-methyl-4-benzoyloxydecahydroquinolines it was concluded [22] that the molecular ions of the stereoisomers that contain an axial C_6H_5COO group attached to $C_{(4)}$ readily split out a C_6H_5COOH molecule (to give an $[M - 122]^+$ ion) and a $C_6H_5COO^\bullet$ radical (to give an $[M - 121]^+$ ion) than their equatorial epimers.

Some of the regularities observed in the fragmentation of stereoisomeric perhydroquinolols have also been noted during a study of the conformationally more labile piperidine derivatives [23]. The mass spectra of stereoisomeric 2,6-diacetoxy-4-hydroxypiperidines (X) were found to be sensitive to the orientation of the 4-OH group but virtually independent of the orientation of the 2-$OCOCH_3$ substituent. In the case of both N—H and N—CH_3 derivatives the $[M - CH_3COO - H_2O]^+$ ion peaks in the spectra of compounds with an equatorial OH group were almost twice as intense as in the spectra of their axial epimers. In the case of stereoisomers of 1,4-dimethyl-3-acetyl-4-hydroxypiperidine (XI) it has been shown that the quantitative difference between the spectra of the stereoisomers vanishes in the absence of a substituent in the α position relative to the nitrogen atom, the detachment of which stabilizes the cyclic structure of the resulting ion. This may be associated with primary opening of the ring after ionization of the molecule and thereby with a decrease in the nonbonded interactions.

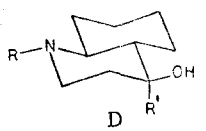


X XI XII

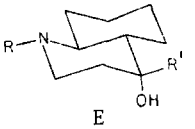
X R=H or CH_3 (2e,4e,6e; 2e,4a,6e; 2a,4a,6e)

XII R=C_6H_5 (2e,4e-OH,5e; 2e,4a-OH,5e); R=m-$C_6H_4CH_3$ (2e,4e-OH,5e; 2a,4a-OH,5e; 2a,4a-OH,5e; 2e,4a-OH,5e); R=C_2H_5 (4a-OH; 4e-OH)

TABLE 2. Ratios of the Intensities of the Peaks of Some Ions in The Mass Spectra of Decahydroquinolols



D

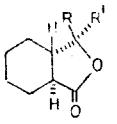


E

R	R′	$[M]^+/\Sigma_n \times 10^{-2}$		$[M-C_2H_5]^+/[M]^+$		$[M-CH_3]^+/[M]^+$	
		D	E	D	E	D	E
CH_3	C≡CH	8,2	6,2	—	—	—	—
CH_3	C_2H_5	6,4	7,4	6,2	5,0	—	—
C_2H_5	C≡CH	7,6	7,3	—	—	—	—
C_2H_5	C_2H_5	5,7	6,4	6,2	5,1	0,5	1,0
n-C_3H_7	C≡CH	4,3	4,1	—	—	—	—
n-C_3H_7	C_2H_5	4,0	4,4	11,0	11,6	—	—
i-C_3H_7	C≡CH	6,5	6,4	—	—	—	—
i-C_3H_7	C_2H_5	5,4	5,6	5,6	4,1	1,6	2,7

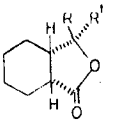
Substantial differences are observed in spectra of stereoisomeric trimethyl-4-hydroxypiperidines XII containing a substituent in the 2 position. For these alcohols the $[M - C_2H_5]^+$ ion peaks are more intense in the case of an axial orientation of the 4-C_2H_5 group, and this may be a criterion for the determination of the configuration at $C_{(4)}$. Assuming an analogy in the probabilities of splitting out of axial and equatorial 2-CH_3 groups with perhydroquinoline derivatives, the authors proposed the configuration at $C_{(2)}$ for some compounds.

Differences in the ease of splitting out of CH_3 groups with different orientations were noted [24] in the spectra of stereoisomeric 3-methylhexahydrophthalides XIII and XIV, which contain a methyl group in the five-membered ring. The $[M - CH_3]^+/[M]^+$ ratio in the spectrum of trans-fused lactone XIIIa, which contains a pseudoaxial CH_3 group, is almost three times as high as in the spectrum of lactone XIIIb, which has a pseudoequatorial CH_3 group. At the same time, this ratio is higher by a factor of six in the spectrum of cis-fused lactone XIVa, which has a pseudoaxial CH_3 group, than in the case of lactone XIVb.



XIII a,b

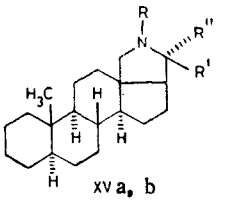
XIII a R=H, R′=CH_3; b R=CH_3, R′=H



XIV a,b

XIV a R=CH_3, R′=H; b R=H, R′=CH_3

High stereospecificity of the ejection of a methyl radical in the fragmentation of 20-methylconanines (XVa, b) was observed by means of the introduction of a deuterium label [25]. As in the preceding case, substituents in the gem-dimethyl grouping here do not have pure axial or equatorial character. It is apparent from a comparison of the $[M - CH_3]^+/[M - CD_3]^+$ ratios that the α-CH_3 group is eliminated much more easily from the M^+ ion (Table 3). To explain this behavior of the differently oriented CH_3 group it was assumed that its α orientation facilitates elimination because of the absence of steric hindrance in this direction.



XV a, b

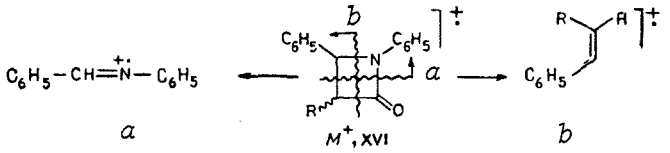
XV a R′=CH_3, R″=CD_3; b R′=CD_3, R″=CH_3

In the case of four-membered rings there are no axial or equatorial substituents, and we are dealing only with cis or trans isomerism. The mass spectra of isomeric β-lactams XVI were very sensitive to the mutual orientation of the vicinal phenyl and alkyl groups [26]. Two principal fragmentation pathways associated with cleavage of the four-membered ring into

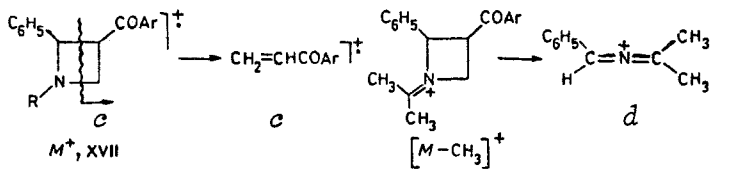
TABLE 3. $[M - CH_3]^+/[M - CD_3]^+$ Ratios in the Mass Spectra of Conanines XV

R	XVa	XVb
CH_3	1/14	15/1
OH	1/8	10/1
H	1/6	6/1

"halves" and the formation of ions *a* and *b* are characteristic for them. The intensity of the *a* ion peak is considerably higher in the spectra of the cis isomers. At the same time, the formation of ion *b* is more likely in the case of trans isomers. With respect to both of these features, the differences in the spectra of the isomers increase as the size of R increases (Table 4). The driving force of the more facile formation of ion *a* for the cis isomers is evidently liquidation of the pronounced strain of the lactam ring, which is due to the cis-oriented substituents. With regard to ion *b*, the nonbonded interactions of the alkyl and phenyl groups that are present in the cis isomers remain in it, and the formation of the trans isomer (with respect to the double bond) of ion *b* is therefore more favorable. It is completely obvious that the processes involving the formation of ions *a* and *b* are competitive.

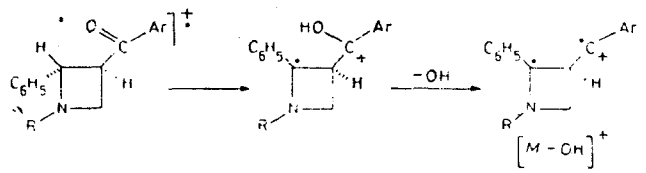


A similar dependence of the probability of cleavage of the four-membered ring on the mutual orientation of the C_6H_5 and COAr groups was also observed for 1-alkyl-2-phenyl-3-aroylazetidines (XVII) [27]. Thus the peaks of the *c* and *d* ions, during the formation of which the steric hindrance due to interaction of the C_6H_5 and COAr groups is eliminated, were considerably more intense in the spectra of the cis isomers than in the spectra of their trans isomers.



XVII R = *t*-C_4H_9, Ar = C_6H_5; R = *t*-C_4H_9, Ar = *p*-$C_6H_5C_6H_4$; R = C_6H_5, Ar = *p*-$C_6H_5C_6H_4$

In addition it was found that the $[M - OH]^+$ ion peak, which is absent in the spectra of the cis isomers, is always observed in the spectra of the trans isomers. It has been assumed that the 2-H atom is favorably oriented for the realization of the subsequent rearrangement only in the trans isomers:

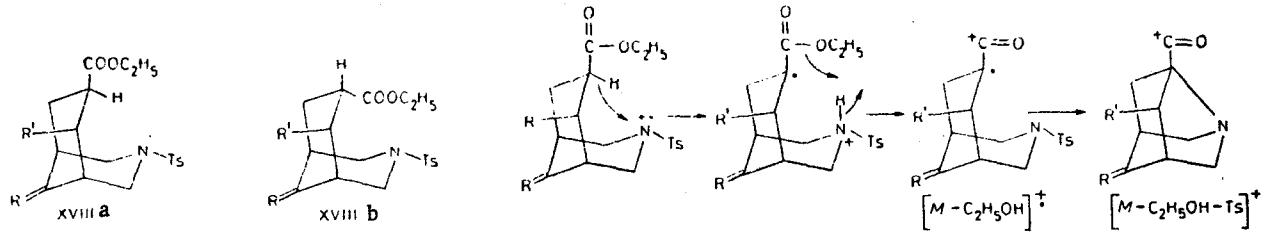


Pronounced differences were observed [28] in the mass spectra of $C_{(7)}$ epimeric N-tosyl-3-aza-7-carbethoxybicyclo[3.3.1]nonanes (XVIIa, b). Whereas ethanol is eliminated from the M^+ ions of exo isomers XVIIIa, this process is not observed at all for endo isomers XVIIIb. The authors feel that migration of a hydrogen atom from $C_{(7)}$ to the nitrogen atom with subsequent splitting out of C_2H_5OH with the participation of this hydrogen atom may occur in the molecular ion of XVIIIa. It was shown by means of the 7-deutero analog that 77% of the deuterium atom actually enters into the composition of the ethanol. The subsequent ejection

TABLE 4. Intensities of the *a* and *b* Ion Peaks in the Mass Spectra of Lactams XVI

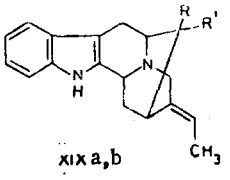
Substituent	Stereochemistry	Intensities of the ions, $\%\Sigma_n$	
		a	*b*
CH_3	cis	9,2	25,1
	trans	6,1	32.4
C_2H_5	cis	14,3	17,5
	trans	9,2	29,2
i-C_3H_7	cis	21,4	9,8
	trans	9,0	19,0
t-C_4H_9	cis	29,0	2,9
	trans	9,7	13,4

of a tosyl radical from the $[M - C_2H_5OH]^+$ ion is also observed only for the XVIIIa isomers (Table 5).



A characteristic feature of the mass spectra of endo isomers XVIIIb is the maximum intensity of $[M - Ts]^+$ peaks, which are less intense in the spectra of their epimers. It is possible that upon formation of the $[M - Ts]^+$ ion from the endo isomers there occurs a preliminary migration of OC_2H_5 groups to the nitrogen atom, after which the Ts radical splits off and a cyclic lactan is formed (Table 5).

One should also note the study by Djerassi and co-workers [29], who determined the configuration at $C_{(16)}$ in polyneuredine (XIXa) and accuamidine (XIXb) on the basis of mass-spectrometric data. The mass spectra of the latter, which were recorded with the use of a heatable inlet system, are distinguished by the intensities of the $[M - OH]^+$ and $[M - H_2O]^+$ ion peaks. Whereas the spectrum of XIXb contains a considerable $[M - OH]^+$ ion peak, the $[M - H_2O]^+$ ion peak is very intense in the case of XIXa. Similarly, the most intense peak in the spectrum of the acetate of XIXb corresponds to ejection of the CH_3COO group from the M^+ ion, whereas the most intense peak in the spectrum of the acetate of XIXa corresponds to ejection of CH_3COOH.



XIXa R = CH_2OH, R' = $COOCH_3$,
b R = $COOCH_3$, R' = CH_2OH

It follows from the mass spectrum of the N—D analog of the acetate of XIXa that the hydrogen atom departs from the nitrogen atom of the indole ring in the elimination of CH_3CO-OH. The larger peaks of the $[M - H_2O]^+$ and $[M - CH_3COOH]^+$ ions in the spectra of XIXa and its acetate, respectively, consequently are explained by the closeness of the CH_2OR and NH groups. However, it should be noted that the indicated differences vanished completely in the mass spectra of XIXa, b and their acetates recorded by means of direct introduction of the samples into the ion source. Thus the difference observed when a heatable inlet system was used due to thermal decomposition of the substance prior to electron impact. This example shows that high-temperature introduction of samples, such as with a heatable inlet system, maybe useful in the identification of stereoisomers.

No differences in the ease of splitting out of a CH_2OH group from the molecular ions of lupinine and isolupinine [$C_{(1)}$ epimeric 1-hydroxymethylquinolizidines] or other differences were observed in the mass spectra [30].

TABLE 5. Relative Intensities of the Peaks of Some Ions in the Mass Spectra of Bicyclo[3.3.1]nonanes XVIII

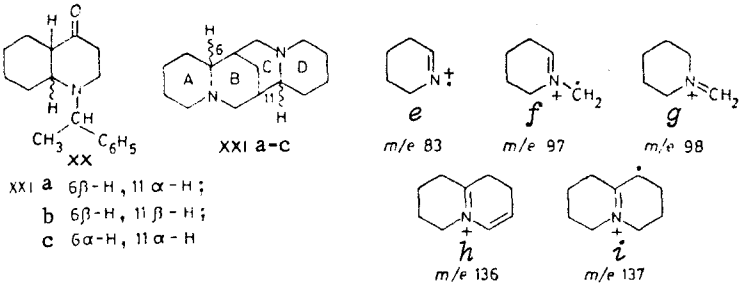
R	R′	Intensity, % of the principal ion					
		$[M-C_2H_5OH]^+$		$[M-C_2H_5OH-Ts]^+$		$[M-Ts]^+$	
		XVIIIa	XVIIIb	XVIIIa	XVIIIb	XVIIIa	XVIIIb
O	$COOC_2H_5$	70	—	100	11	49	100
$(-CH_2S)_2$	$COOC_2H_5$	20	—	73	4	75	100
H_2	$COOC_2H_5$	48	—	100	5	40	100
H_2	H	69	1	2	3	69	100

Stereochemistry of Ring Fusion

Differences in the stereochemistry of ring fusion are also quite frequently reflected in the mass spectra. However, in this case the behavior of the stereoisomers under the influence of electron impact cannot always be predicted, since this type of cis, trans isomerism may affect the rates of both rearrangement reactions and reactions due to simple bond cleavage. The stabilities of the molecular ions may also depend on the character of the ring fusion. In the general case differences in the stereochemistry of ring fusion are manifested in the rates of those reactions that lead to elimination of the strain caused by one or another type of fusion. A favorable orientation of the migrating groups quite often affects the rate of fragmentation.

cis- and trans-Decahydroquinolines and their N-methyl and N-benzoyl derivatives that do not contain substituents attached to the carbon atoms have virtually identical mass spectra [31]. At the same time, the mass spectra of cis- and trans-fused 2-methyldecahydroquinolines [9] and 2-methyl- and 1,2-dimethyl-4-hydroxydecahydroquinolines [20] and their benzoates [22] differ quite substantially with respect to the intensities of the M^+, $[M - CH_3]^+$ and $[M - C_3H_7]^+$ ion peaks (the latter rearranged ion is due to cleavage of the alicyclic ring): whereas higher intensity of the $[M - CH_3]^+$ ions and a lower intensity of the $[M - C_3H_7]^+$ ions are characteristic for the trans isomers, the opposite situation is observed for the cis isomers. The transition from trans- to cis-fusion is also accompanied by an increase in the intensity of the M^+ peak.

The mass spectra of cis- and trans-fused N-(α-phenylethyl)decahydro-4-quinolones (XX) differ quite substantially in a quantitative respect: the stability of the molecular ion is somewhat lower, and the fragmentation processes (such as ejection of CH_3, C_3H_7, and other radicals from M^+) are more active for the cis isomers than for the trans isomers [32].

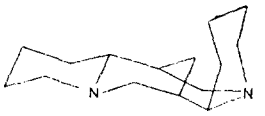


XXI a 6β-H, 11α-H;
b 6β-H, 11β-H;
c 6α-H, 11α-H

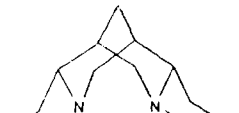
A number of interesting dependences of the character of the fragmentation on the stereochemistry of the ring fusion were observed during a study of quinolizidine alkaloids. In this case the phenomenon of the so-called "latent" stereochemistry, in which the stereospecificity of the formation of identical fragments from different portions of the molecule can be detected only by means of deuterium labeling (an example of "latent" stereochemistry was presented above for XVa and XVb), was demonstrated. A quinolizidine alkaloid — sparteine (its d antipode is pachycarpine) — is widespread in nature; two of its stereoisomers — α- (XIIb) and β-isosparteine (XXIc) — which differ with respect to the stereochemistry of the fusion of the A/B and C/D rings, are also known. The mass spectra of all three isomers are quite similar in a quantitative respect.

In view of the apparent symmetry of the XXIa-c molecules one might have assumed that the *e*, *e* + 1, *f*, *f* − 1, and *g*-*i* ions are formed with equal probabilities as a result of cleavage of the bonds in the B and C rings, i.e., that the first five ions can, to an equal extent, contain fragments of A or D rings, whereas the last two ions can contain A + B or

C + D fragments. However, it was shown by means of deutero analogs [30, 33] that in the case of sparteine (XXIa) only the *f* and *h* ions equally probably contain, respectively, A and D and A + B and C + D fragments. However, 85-90% of ions *e* + 1 and *g* are formed through the A ring, and ion *i* is formed through the A + B rings. This effect is associated with the fact that the stereochemistry of fusion of the A/B and C/D rings in XXIa differs. Because of this, the B and C rings have different strains, and the hydrogen atoms that participate in the formation of the indicated ions have different tendencies to undergo migration.



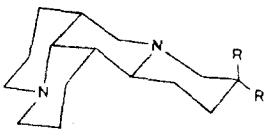
XXIa



XXIb

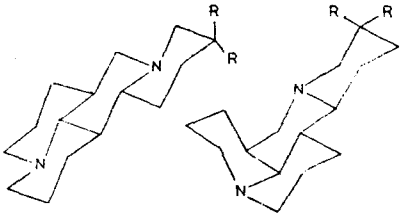
In contrast to sparteine (XXIa), the α-isosparteine (XXIb) molecule, which has trans-fused A/B and C/D rings, is symmetrical. One may therefore expect equally probable formation of ions *g* and *i* through the A or D and A + B or C + D rings, respectively, since the B and C rings in this case are equivalent with respect to energy. This assumption was confirmed by an analysis of the mass spectrum of 3,4,5,6-tetradeutero-α-isosparteine [34], in which no less than half of the *g* ion peak is shifted 4 amu (to m/e 102). With regard to the *i* ion peak, peaks with intensities equal to its intensity at m/e 138, 139, and 140 appear along with it. Considering the fact that the ion with m/e 137 is a rearranged ion and that a hydrogen atom from the A ring participates in its formation, judging from the character of the shift, one may conclude that, in contrast to sparteine, in the case of α-isosparteine (XXIb) *g* and *i* ions are formed to an equal extent as a result of charge localization on the fragment containing both A and A + B and D and C + D rings.

Elements of "latent" stereochemistry are also observed in the mass spectra of stereoisomers of another quinolizidine system — namely, matridine (XXIIa), allomatridine (XXIIb), and isosophoridan (XXIIc). A characteristic feature of the spectrum of allomatridine (XXIIb) is the predominance in it of an M^+ peak, whereas *i* ion peaks (m/e 137) dominate in the spectrum of XXIIa and XXIIc. The high stability of the M^+ ion of allomatridine may be due to the fact that all of the rings in the four-ring system are trans-fused, whereas matridine (XXIIa) and isosophoridan (XXIIc) each contain two energically less favorable cis-fused systems.



XXIIa

XXII a-c R = H, D



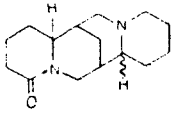
XXIIb XXIIc

As in the case of sparteines, the mass spectra of these compounds contain the principal peaks of *e* + 1, *f*, *f* − 1, and *g*-*i* ions. On the basis of an examination of the structures of the compounds one might have assumed that the most favorable mode of formation of the enumerated ions should include cleavage of the bonds in the C ring. In this case the *i* and *h* ions should contain A + B rings, the *e* + 1 ions should include the D ring, and the *f*, *f* − 1, and the *g* ions should include the D ring and the $C_{(17)}$ atom. A comparison of the mass spectra of 14,14-dideutero analogs of XXIIa-c with the spectra of unlabeled compounds showed [35] that the *i*, *h*, and *f* − 1 ion peaks are not shifted when the label is introduced, i.e., the corresponding ions in the case of the compounds under consideration are due to charge localization on the $N_{(1)}$ atom and do not contain D rings. At the same time, the ions with m/e 98 (*g*) and 84 (*e* + 1) have different origins, depending on the stereochemistry of the compound. It was found that in the case of matridine (XXIIa) and isosophoridan (XXIIc) only ~24 and 27%, respectively, of the *g* ions contain a D ring, while the remainder contain A and B rings. However, in the fragmentation of allomatridine (XXIIb) the *g* ion is primarily (~80%) formed as a result of cleavage of the 7—11 and 5—17 bonds and contains a D ring. Since the A/C and B/C rings in matridine (XXIIa) and A/B and A/C rings in isosophoridan (XXIIc) are cis-fused, bond cleavage in the A, B, and C rings may be facilitated, and the *g* ion may be formed as a result of different processes. At the same time, since the bonds in allomatridine (XXIIb), which

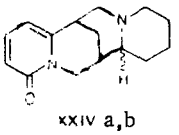
has a completely trans-fused system, are strong in all of the rings, the most favorable process, which involves cleavage of two bonds in the C ring, evidently takes place here. One should still bear in mind that the *g* ion is a rearranged ion, and not only the energy factor but also the distance between the migration centers therefore affect the ease of its formation.

It should be noted that the stereochemistry of XXIIa-c also affects the fragmentation pathways that lead to the *e* + 1 ion. The corresponding peak in the mass spectra of 14,14-dideutero analogs of allomatridine and isosophoridan is shifted 2 amu (and, partially, 1 amu), i.e., the charge is primarily localized on the D ring. However, only a slight shift (1 amu) of this peak is observed in the spectrum of 14,14-dideuteromatridine.

The mass spectra of carbonyl derivatives of sparteine and α-isosparteine — lupanine (XXIIIa) [36] and α-isolupanine (XXIIIb) [33] — are virtually identical. There is also little difference in the spectra of their unsaturated analogs — anagyrine (XXIVa) and d-thermopsine (XXIVb) [30, 33].



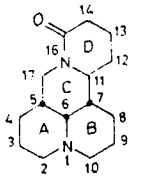
XXIII a,b



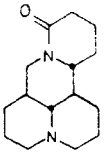
XXIV a,b

XXIII a,b, XXIV a α-H ; b β-H

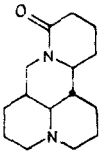
In a quantitative respect the mass spectra of the stereoisomeric matrine (XXVa), allomatrine (XXVb), and isosophoridine (XXVc) differ appreciably [33]; however, in view of the absence of data on the energetics and mechanisms of the formation of the characteristic ions, no correlation between the spectra and the stereochemistry can be made. An attempt to link the stability of the polycyclic system of the compounds under consideration only with the intensity of the M^+ ion peaks was unsuccessful, since the intensities in percent of the total ion current were close [37]. At the same time, the sum of the intensities of the M^+ and $[M-1]^+$ ion peaks is a maximum in the case of allomatrine (XXVb), and this is in agreement with the minimum strain of the completely trans-fused four-ring system. This sum is a minimum for matrine (XXVa).



XXV a



XXV b

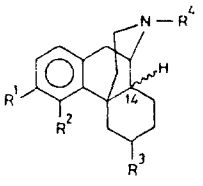


XXV c

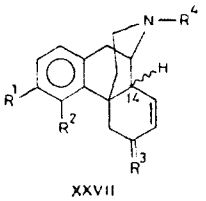
(The three-dimensional structures are given above for the oxygen-free analogs).

It should be noted that the M^+ ion peak is more intense than the $[M-1]^+$ ion peak in the mass spectra of both matrine (XXVa) and its 11,12,13,14-tetradehydro analog (sophoramine), whereas the reverse situation is observed in the spectra of allomatrine and the analogous unsaturated product (isosophoramine) [38].

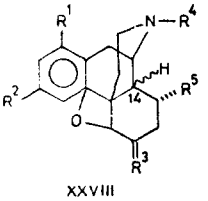
Interesting fragmentation stereoselectivity that is not associated with the strain of the system was observed in the case of morphine derivatives XXVI-XXVIII [39]. The ion peak with mass 44 + R^4 was more intense for all of the isomers with cis-fused B and C rings than for the trans isomers (Table 6).



XXVI



XXVII



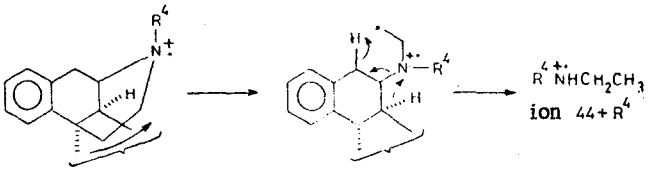
XXVIII

A mechanism for the formation of the 44 + R^4 ion that includes migration of a hydrogen atom from the 14 position was proposed to explain this difference. In the trans isomers this atom is too far from the $C_{(15)}$ and N atoms to participate in the four-membered transition state leading to the ion under consideration. The conditions for this rearrangement

TABLE 6. Intensity of the Ion Peak with m/e 44 + R^4 in the Mass Spectra of Compounds of the XXVI-XXVIII Type

Compound	R^1	R^2	R^3	R^4	R^5	Intensity of the $44+R^4$ Ion ($\%\Sigma_{40}$)	
						cis	trans
XXVI	OH	H	H	CH_2—◁	—	2,3	0,2
	OCH_3	OH	H	CH_3	—	5,8	0,2
	OCH_3	OH	OH	CH_3	—	3,6	0,2
XXVII	OCH_3	OH	O	CH_3	—	0,5	0,01
XXVIII	Br	OCH_3	O	CH_3	H	4,5	0,9
	H	OCH_3	H_2	CH_3	OH	4,2	1,3

are favorable in the cis isomers, and this may be the reason for the greater ease of formation of this ion:



Large differences in the ease of elimination of carbon monoxide, which were determined from the $[M - CO]^+/[M]^+$ ratio, were observed in the mass spectra of cis- and trans-1,2,3,6-tetrahydrophthalic anhydrides (XXIXa, b) [40]. Of interest in this case is the fact that the molecular ions of the more stable cis isomers lose CO most readily (the $[M - CO]^+/[M]^+$ intensity ratios are presented in parentheses).

XXIXa

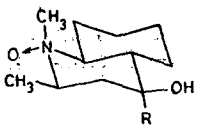
XXIX b

XXIXa R=H (26), R=CH_3 (5,1);
b R=H (0,06), R=CH_3 (0,03)

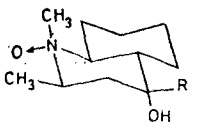
The mass spectra of the above-examined cis- and trans-hexahydrophthalides (XIIIa, b and XIVa, b) differ quite markedly with respect to the ratio of the intensity of the ion peaks with m/e 81 (the cyclohexenyl ion) and 61 (the cyclopentenyl ion) [24]. The J_{81}/J_{67} intensity ratio is greater than unity for the cis isomers, whereas it is less than unity for the trans iosmers. No explanation for this difference has yet been given.

Asymmetric Heteroatom

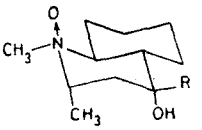
Very little research has been devoted to the mass-spectrometric study of compounds that are epimeric with respect to a heteroatom, and there are absolutely no data pertaining to the stereoisomeric cyclic sulfoxides. The mass spectra of stereoisomeric N-oxides of 1,2-dimethyl-4-alkyl-trans-perhydro-4-quinolols (XXX-XXXII) have been studied in greatest detail [41, 42].



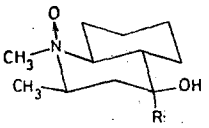
XXX a



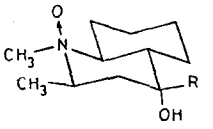
XXXI a



XXXII



XXXb



XXXI b

The mass spectra of epimeric N-oxides differ very greatly in a quantitative respect. Regardless of the nature of substituent R, the spectra of the stereoisomers can be divided into two groups — A and B. Significant M^+ peaks, which are more intense than the peaks of

TABLE 7. Relationship between the Type of Mass Spectrum and the Chromatographic Mobilities of N-Oxides XXX and XXXI

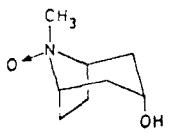
Compound	R=C≡CH		R=CH=CH$_2$		R=C$_2$H$_5$		R=C≡CH		R=CH=CH$_2$		R=C$_2$H$_5$	
	XXXa	XXXb	XXXa	XXXb	XXXa	XXXb	XXXIa	XXXIb	XXXIa	XXXIb	XXXIa	XXXIb
Type of spectrum	A	B	A	B	A	B	A	B	A	B	A	B
R_f	0,56	0,35	0,66	0,41	0,66	0,47	0,46	0,68	0,51	0,63	0,44	0,60

$[M - CH_3]^+$, $[M - O]^+$, $[M - OH]^+$, $[M - H_2O]^+$, $[M - CH_3 - O]^+$ and some other ions, are characteristic for the first group, whereas the reverse situation is observed for group B. Intense peaks of dehydrated $[M - H_2O]^+$ ions, due to the elimination of the 4-OH group, are particularly characteristic for the group B spectra.

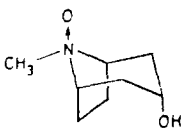
A dependence of the type of mass spectrum on the chromatographic mobilities of epimers has been found (Table 7) [41]. Epimers with an equatorial 4-OH group have greater R_f values and give mass spectra of the A type, whereas epimers XXXb have smaller R_f values and mass spectra of the B type. In the case epimers XXXIa, b, higher R_f values and mass spectra of the B type are characteristic for XXXIb, whereas lower R_f values and spectra of the A type are characteristic for XXXIa. This correlation, which was proposed for the determination of the configuration at $C_{(4)}$ in molecules of the starting bases or their analogs, reflect a certain spatial orientation of the polar groups (N → O and OH) in the investigated N-oxides. It should be noted that N-oxides XXXII also have spectra of the B type.

It is apparent that the type of mass spectrum (A or B) does not depend on the mutual spatial orientation of the N → O and 4-OH groups but only on the orientation of the N → O group: spectra of the A type are characteristic for N-oxides with an equatorial N → O group, and spectra of the B type are characteristic for N-oxides with an axial N → O group. On the basis of the form of the mass spectrum it has been proposed that, with respect to the character of the fragmentation and the greater tendency to lose water, the N-oxides with an axial N → O group are similar to carbocyclic alcohols.

To a certain extent similar differences in the character of the fragmentation are also observed in the case of epimeric tropine N-oxides (XXXIIIa, b). From incomplete mass-spectral data [43] it followed that the $[M - H_2O]^+$ ion is present only in the spectrum of the compound to which the XXXIIIa stereochemistry was assigned. However, the stereochemistry of these compounds was later [44] re-examined, and it was found that N-oxide XXXIIIa should have an axial orientation of the N → O group. Thus with respect to the tendency to eliminate water, the N-oxide with an axial N → O group is more similar to carbocyclic alcohols here also.



XXXIII a



XXXIII b

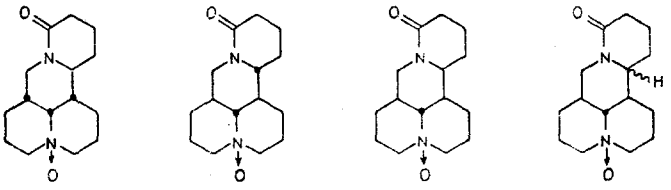
The mass spectra of stereoisomeric N-oxides of matrine (XXXIVa), allomatrine (XXXIVb), isosophoridine (XXXIVc), and sophoridine (XXXIVd), which differ with respect to both the sterochemistry of the ring fusion and the configuration of the asymmetric nitrogen atom, have been examined [45]. In a quantitative respect the mass spectra differ rather markedly, but the lack of data on the nature of the hydrogen atom eliminated in the composition of the OH radical has made it impossible to make a correlation between the character of the spectrum and the stereochemistry, since most of the ions in the spectra are genetically related to the $[M - OH]^+$ ion. Only differences in the relative intensities of the M − 16, M − 17, M − 18, and M − 19 peaks have been noted. (See scheme at top of next page).

Ionization and Appearance Potentials

As we have already noted above, the difference in the enthalpies (ΔH) of the stereoisomers most likely affects the difference in the rates of the reactions due to simple bond cleavage, whereas the rates of the rearrangement processes are primarily associated with a favorable orientation of the migrating groups. It may be assumed that the magnitudes of the

TABLE 8. Correlation of the Differences in the Enthalpies of the Ground States of Stereoisomers with the Difference in the AP and IP

Compound	Source of nonbonded interactions	ΔH_f, kJ/mole	
		measured from the difference in the AP or IP	independent determination
XXXV	Axial 4- or 6-CH_3 group	14,2±1,3 (AP)	14,0±2,9
	Axial 2-CH_3 group	15,9±1,3 (AP)	16,3±5,0
	Chair form ⇌ twist form	35,6±2,1 (AP)	34,7±5,0
XXXVI	Axial 4-CH_3 group	6,5±1,4 (IP) 9,6±1,1 (AP)	7,5
	Axial 6-CH_3 group	10,9±1,4 (IP) 13,0±1,1 (AP)	12,3
	Chair form ⇌ twist form	22,5±4,0 (AP)	24—27



XXXIVa XXXIVb XXXIVc XXXIVd

ionization potentials (IP) and appearance potentials (AP) of the fragments formed as a result of simple bond cleavage reflect the difference in the internal energies of the stereoisomers. However, for quite some time it was not possible to measure the IP and AP of stereoisomers with sufficient accuracy to be able to correlate them with the energy differences of stereoisomers due to nonbonded interactions. Pihlaja and co-workers [46-48] were able to determine the IP and AP of some conformationally labile stereoisomers by the method of electron impact with surprisingly high reproducibility (~0.01 eV) only relatively recently. The authors, to their credit, acknowledged that their measured values are not absolute, but they were able to correlate the difference in the IP and AP of the stereoisomers with the difference in the internal energies. It was proposed that the thermochemical stability of a gaseous ion affects its subsequent decomposition and that the surplus energy due to steric interactions is realized during the fragmentation process; the conformational energy realized in a number of cases reflects the difference in the enthalpies between the configurational isomers.

Stereoisomeric 2-substituted and unsubstituted 4,6-dimethyl-1,3-dioxanes (XXXV) and 1,3-oxathianes (XXXVI), for each pair of stereoisomers of which primary fragmentation reactions with the formation of an identical ion are characteristic, were used for the investigation. The primary fragmentation reaction for dioxanes XXXV that do not contain substituents attached to $C_{(2)}$ is the formation of $[M - H]^+$ ions, whereas the primary reaction for the other compounds is the formation of $[M - CH_3]^+$ ions.

XXXV XXXVI

XXXV, XXXVI R=R'=H; R=H, R'=CH_3; R=R'=CH_3

It was shown that the difference in the AP of the $[M - R]^+$ ions and even in the IP of the molecules in pairs of stereoisomers is very close to the difference between the enthalpies of the ground states of the molecules (Table 8).

Thus the following equations are satisfied for this class of compounds and perhaps for others also:

$$\text{AP}\,[A^+] - \text{AP}\,[A_1^+] = \Delta H_f[M_1] - \Delta H_f[M];$$
$$\text{IP}\,[M^+] - \text{IP}\,[M_1^+] = \Delta H_f[M_1] - \Delta H_f[M]$$

Although no one has confirmed them, these results predict the possibility of using the IP and AP for the solution of problems of conformational analysis and stereochemistry. One cannot exclude the possibility that this approach to the solution of the stereochemical problem is limited primarily to heterocyclic compounds for which high regioselectivity and

stereoselectivity of the fragmentation are characteristic. However, at present we do not have a sufficient number of correlations at our disposal, and, as Pihlaja and co-workers have pointed out [48], one must use ionization and appearance potentials with caution for the solution of stereochemical problems.

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STRUCTURE OF "FURFURAMIDE" AND "FURFURINE"

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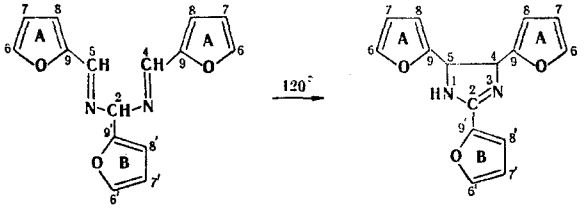
UDC 547.727'781

The structures of α,α-bis(furfurylideneimino)silvan ("furfuramide" or N,N'-difurfurylidene-2-furanmethanediamine) and the product of its thermal cyclization 2,4,5-tris(α-furyl)-2-imidazoline ("furfurine") were confirmed by comparison of the IR, UV, ^{1}H and ^{13}C NMR, and mass spectra. It is shown that acetylation of the latter with acetic anhydride in the case of heating of the reagents without a solvent or in pyridine takes place with opening of the imidazoline ring and leads to the formation of 1,2-bis(α-furyl)-1-acetamido-2-(α-furoylamido)ethane.

The extensive application of α,α-bis(furfurylideneimino)silvan ("furfuramide" or N,N-difurfurylidene-2-furanmethanediamine) (I) and 2,4,5-tris(α-furyl)-2-imidazoline ("furfurine") (II) in the production of furan and furan–epoxide resins [1, 2] has recently made it necessary to ascertain and refine their structures. The process for the production of furan and furan–epoxide resins with the use of I presupposes its thermal treatment at temperatures above its melting point (117°C). The aim of the present research was therefore to refine the structures of starting I and its isomer obtained under thermal cyclization conditions:



I II

Structural formula I for "furfuramide" was proposed by Schiff [3]. In 1885 Klaus and Scherbel [4] proposed that the thermal cyclization of I leads to the formation of a compound

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