SIMILARITIES BETWEEN THERMOLYSIS AND MASS SPECTROMETRIC FRAGMENTATION OF TETRAZOLES (REVIEW)

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Both thermolysis and dissociative ionization of tetrazole and its derivatives form products of the same elemental composition. This similarity permits mass spectrometry to be used to predict thermal conversions and the compositions of thermolysis products.

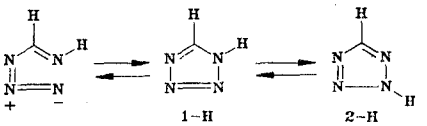
According to the general assumptions of quantum chemistry, which considers a molecule to be the aggregate of all electrons in the field of all nuclei, the radical cation that forms in the bombardment of a molecule by fast electrons is a different quantum chemical system. In this case the analogies* observed between mass spectrometric fragmentation (MSF) and high energy chemistry, primarily of thermolysis, remain controversial [1-7]. Thus, e.g., the widespread position concerning the random nature of some coincidences does not deny the similarity but limits it to a narrow class of compounds [1, 2]. The theme of the present review is the verification of this position by comparison of the thermolysis and the dissociative ionization of tetrazole and its derivatives.

The problem is solved by taking into account the prototropic and ring–chain tautomerism that is typical of this class of compounds. Such an approach enables us to relate the features of the processes to tautomeric conversions and the reactivities of the various tautomers. The results of the comparisons are discussed in relation to the growing tendencies to use these similarities to predict new thermal reactions and to determine ion structures and MSF mechanisms.

This review covers publications on tetrazole thermolysis and MSF through 1983. The separate aspects of the chemistry and practical application of tetrazoles in various fields of medicine, engineering, and agriculture were previously discussed in [9-12].

UNSUBSTITUTED TETRAZOLE

According to the general theoretical assumptions, tetrazole, I, can exist in three isomeric forms that are determined by prototropic and ring–chain tautomerism:



I

In the ground state at room temperature tetrazole has a cyclic structure [9]. The ratio of 1-H and 2-H tautomers depends on the state of aggregation, or, in solution, on solvent polarity. In the crystal and in a polar solvent the polar 1-H structure is preferred [13-15] (μ = 5.46 D [16]), while in the gas phase (T_{subl} 40° [9]) and in a nonpolar solvent the less polar 2-H tautomer is more stable [17] (μ = 2.65 D [16]).

The data for the high temperature thermolysis and MSF are so far unknown, but the specificity of these processes permits the assumption that in both cases all three tautomers take part in the decomposition.

*According to the definition of an analogy as a partial resemblance or a resemblance in a particular feature [8], here and subsequently in the text the formation of products of the same elemental composition will be meant.

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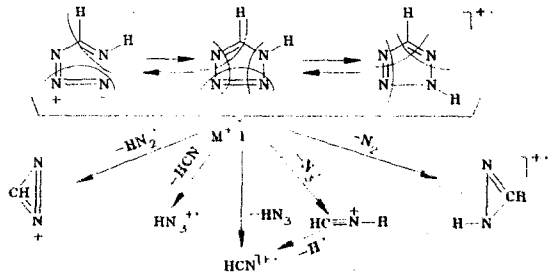
Noting the coincidence of the main directions of fragmentation of tetrazole (I) and its 1- and 2-methyl derivatives [18], those authors show that the prototropic structures of the molecular ion (M^+) are represented by both 1-H and 2-H tautomers.

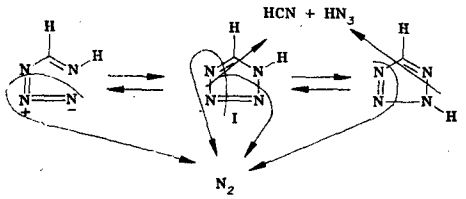
Scheme 1



In the general case, considering that the amount of energy transmitted to the molecule by electron impact is sufficient to form the azide structure, M^+ of compound I must be considered as a set of three tautomers, which also determine the experimentally observed elimination of N_2, HCN, and HN_3 molecules and N_3 and HN_2 radicals [18].

The gas phase thermolysis of I (180-225°C) forms N_2, HCN, and HN_3 [19]; the data are incomplete, because in spite of the principle of conservation of mass, the compounds corresponding to nitrogen elimination are not shown. The appearance of all the listed products can be explained by the decomposition of both 1-H and 2-H tautomers; the formation of N_2, by that of azidic molecules:

Scheme 2

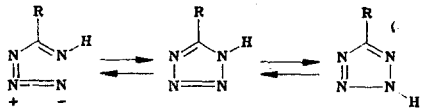


The possibility cannot be excluded that product composition is due to the decomposition of all three tautomers. The position of the tautomeric equilibrium depends on temperature, and heating stabilizes the state with the higher entropy, i.e., it shifts the equilibrium from 2-H toward the azide.

Although the proportions of the reactive forms of I at high temperature and under electron impact are not known, the observed features of thermolysis and MSF do not contradict the assumptions of structural chemistry. Here at least, three types of reaction that are observed in mass spectrometry also occur in thermolysis (Schemes 1 and 2).

5-SUBSTITUTED TETRAZOLES

Like tetrazole itself, the 5-substituted tetrazoles can exist in three tautomeric forms, and like it they have a cyclic structure in the ground state:

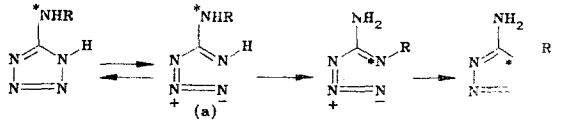


The dependence of the prototropic equilibrium on the nature of the substituent, the state of aggregation, and the polarity of the solvent have long been disputed [10]. Only very recently have data appeared on the predominant stability of the 1-H tautomer in polar solvents and in the crystalline state [12].

In agreement with this conclusion is a study of the thermolysis of 5-amino substituted tetrazoles [9]. When these compounds are heated in a melt, a solution, or a suspension (160-220°), the substituent undergoes a reversible 1,3-migration (scheme 3). The reaction shown proceeds via intermediate formation of the azide a, which is possible only for the 1-H structure of 5-amino-substituted tetrazoles. (See Scheme 3.)

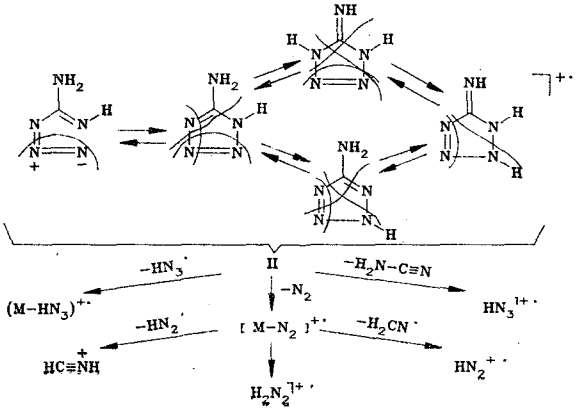
This process is an intramolecular rearrangement and is not directly related to the decomposition. The behavior of these compounds under more severe temperature conditions or

Scheme 3



under photolysis has not been discussed in the literature. Data on the MSF of this series of compounds are extremely limited. Only 5-amintotetrazole (II) [20] is an exception.

Allowing for the various tautomeric conversions, M^+ of II can be represented by the following set of structures:



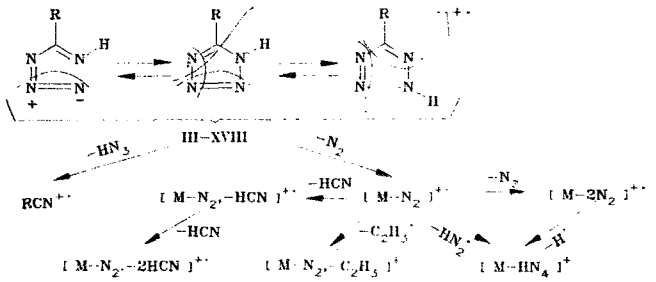
These reactions are proposed for any of the alternative structures of M^+. Account is taken of not only tetrazole ring but also amine–imine tautomerism [10].

In contrast to the 5-amino substituted tetrazoles the thermal reactions and dissociative ionization of other compounds of this series have been studied in more detail.

MSF of the 5-substituted tetrazoles III-XVIII, goes by two general paths (Scheme 4). One involves the ejection of a N_2 molecule and the formation of a $[M-N_2]^+$ molecule; in the case of III, subsequent decomposition of the latter is accompanied by release of HN_2 or C_2H_3 radicals [18]; in the case of the 5-aryl(heteroaryl)tetrazoles VI-XVIII, by successive elimination of two molecules of HCN or N_2 [21-24], The $R-C\equiv N^{+\cdot}$ ion is formed in all cases [18, 21-23].

In addition to these reactions, in the fragmentation of 5-methyltetrazole, III, a N_3 or HN_2 particle is ejected from M^+ with elimination of both a ring hydrogen and a methyl hydrogen (due to the high mobility of the methyl hydrogens) [18]. The latter is confirmed by the mass spectrum of the deuterated derivative, IV.

Scheme 4



III R=CH_3; IV R=CD_3; V R=CF_3 [18]; VI R=C_6H_5 [21—23]; VII R=2-$CH_3C_6H_4$; VIII R=3-$CH_3C_6H_4$; IX R=4-$CH_3C_6H_4$ [22]; X R=4-HOC_6H_4; XI R=4-$CH_3OC_6H_4$; XII R=4-ClC_6H_4; XIII R=BrC_6H_4 [23]; XIV R=$NO_2C_6H_4$ [21, 23]; XV R=naphthyl; XVI R=2-thienyl XVII R=2-pyrrolyl ; XVIII R=2-furyl [23]

The formation of $[M-HN_4]^+$ in [23] has been attributed to M^+ decomposition. Such an interpretation is contradicted by the concepts of inter-ring bond strength in systems like biphenyl [25], and is not confirmed by studies of the dissociative ionization of other tetrazoles [26-28].

Returning to the general decomposition reactions of III-XVIII (Scheme 4), it should be noted that analysis of MSF does not permit us to determine from which tautomer the fragment

ions form. Elimination of a nitrogen molecule can be explained by decomposition of M^+ of any structure; ejection of HN_3, by fragmentation of both 1-H and 2-H tautomers. This question might be clarified by a study of tetrazoles tagged with ^{15}N at various positions of the tetrazole ring. A similar approach would be valuable in estimating tautomeric conversions during the ionization of tetrazole itself.

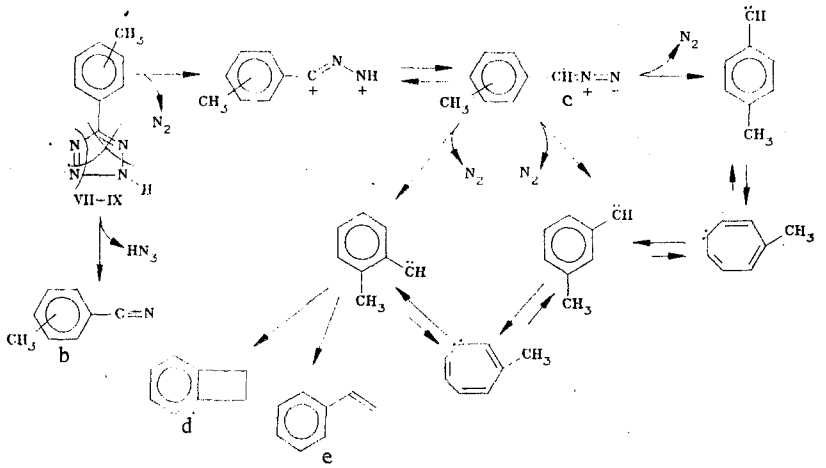
In the case under consideration, however, comparison of MSF and thermolysis leads to definite conclusions.

Thermal decomposition of 5-substituted tetrazoles proceeds in full agreement with the main directions of MSF. Formation of HN_3, R—C≡N, and N_2 molecules and a nitrile-imine bipolar ion was observed in the thermolysis of 5-(benzyl)mercaptotetrazoles [29], diazatatrazole [9], phenyltetrazole [22, 30, 31], tetrazolylazadimethylaniline [32], and isomeric 5-tolyltetrazoles [22].

The subsequent conversions of nitrilimine give products of various structures, depending on whether the thermolysis occurs in melt, solution, or gas phase. Product composition is also affected by the reaction temperature and by the rate at which it is reached.

Pulsed gas-phase thermolysis of the isomeric 5-tolyltetrazoles VII-IX (400-800°, 10^{-5} Pa), forms a mixture of products; from it there were separated N_2, HN_3, tolylnitriles b, tolyldiazomethane c, benzocyclobutene d, and its isomer styrene e, [22]. The occurrence of these compounds was attributed by the authors to the decomposition of the 2-H tautomer of 5-tolyltetrazoles by two independent paths:

Scheme 5



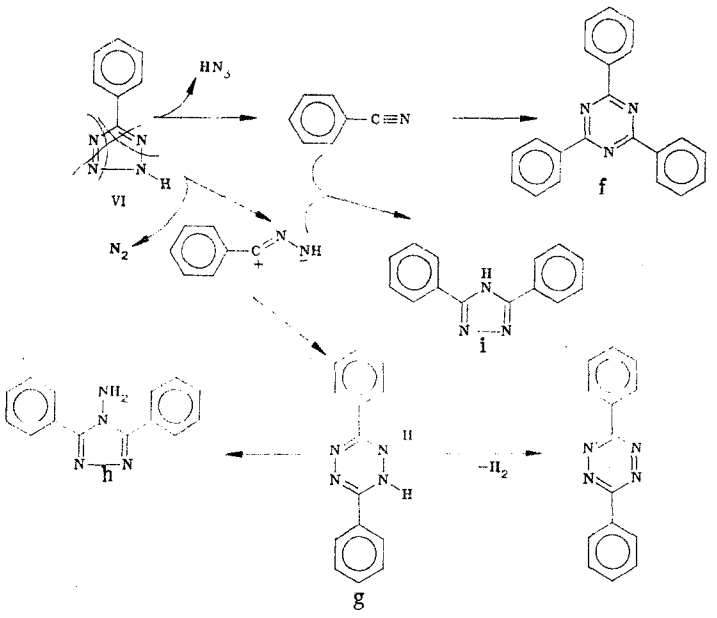
Under the same conditions, 5-phenyltetrazole decomposes to form HN_3 and benzonitrile, as well as N_2, fulvalene, and ethynylcyclopentadiene [22]. Different product composition was obtained in the thermolysis of 5-phenyltetrazole (160-220°) in mesitylene or 1,3-dimethoxybenzene solution [30, 31]: (See Scheme 6).

In this case, the formation of the thermolysis products is controlled by the secondary reactions of benzonitrile and C-phenylnitrilimine. Thus the formation of cyaphenine f is related to benzonitrile trimerization; nitrilimine dimerization accounts for diphenyldihydrotetrazine g and its isomer 4-amino-3,5-diphenyl-1,2,4-triazole h. Finally, the reaction of benzonitrile with nitrilimine (by 1,3-addition) gives 3,5-diphenyl-1,2,4-triazole i (Scheme 6). Of similar nature are the reactions of the C,N-nitrilimines generated in the thermolysis of 2,5-disubstituted tetrazoles. The structure of the latter excludes the possibility of tautomeric conversions. It follows that in the case of the 5-substituted tetrazoles nitrilimine formation is due to decomposition of the 2-H tautomer. The alternative thermolysis path, related to the formation of HN_3 and nitriles, does not exclude the participation of both the 1-H and 2-H forms of the starting compounds.

The probability of bimolecular reactions of nitrilimine is determined by its stability. Since the stability of the bipolar ion depends on solvent polarity and the chemical nature of the substituent at the 5-position of the tetrazole ring, these factors can be expected to appreciably affect product composition and decomposition rate.

This conclusion is confirmed by kinetic studies of the thermolysis of some 5-(p-substituted)phenyltetrazoles (where X is H, CF_3, NO_2, OCH_3, CH_3, Cl) [31]. As solvent polarity

Scheme 6



decreases in the sequence benzonitrile > nitrobenzene > N,N'-dimethylaniline > diphenylmethane > phenyl ether, the rate constant of nitrogen accumulation increases. This feature is usually interpreted as a reduction in the extent of charge distribution in the transition complex, which in turn corresponds to the formation of nitrilimine simultaneously with release of nitrogen.

From what has been discussed, a number of conclusions can be drawn.

In ionization and in thermolysis of 5-substituted tetrazoles the reaction paths are the same, regardless of whether the thermal reaction takes place in the gas phase or in solution (cf. Schemes 5 and 6). In the first case, by virtue of the similarity of experimental conditions, the similarity is more complete, and persists in the subsequent decomposition of $[M-N_2]^+$ and tolyldiazomethane with ejection of a nitrogen molecule (cf. Schemes 4 and 5). Thus it is most unlikely that the same reactions of the same compounds but under different experimental conditions (viz., dissociative ionization and thermolysis) are due to different structures of M^+ and neutral molecule. Hence, since N_2 elimination in thermolysis of 5-substituted tetrazoles is determined by decomposition of the 2-H tautomer, dissociative ionization by the same path should also be via reaction of the 2-H tautomer. In these processes the reactive form of molecules and radical cations is different from the structure of 5-substituted tetrazoles (1-H tautomer) in the crystal or in solution at room temperature. But the other decomposition path in ionization and thermolysis, the products of which are respectively the $RCN^{+\cdot}$ and HN_3 particles and the substances R-C≡N and HN_3, can be explained (as noted above) by starting from the 1-H and 2-H structures of the test compounds.

These conclusions are confirmed by the features of MSF and thermolysis of the 2- and 2,5-substituted tetrazoles.

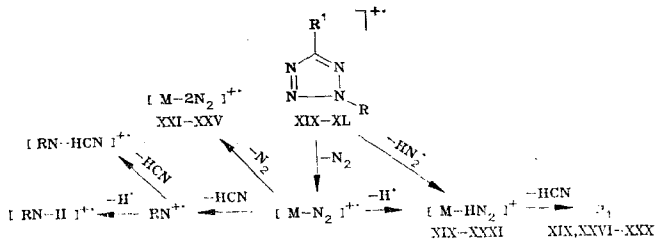
2 AND 2,5-SUBSTITUTED TETRAZOLES

The structure of 2- and 2,5-substituted tetrazoles excludes the possibility of the prototropic tautomeric conversions that are typical of the compounds previously discussed. Therefore MSF is more selective. (See Scheme 7.)

Here, as with the 5-substituted tetrazoles, the main decomposition path involves ejection of a nitrogen molecule [18, 21, 24, 33, 34].

Study of the fragmentation of 2-methyl-5-phenyl tetrazole tagged with ^{15}N showed that this reaction goes with elimination of $N_{(3)}N_{(4)}$ as a nitrogen molecule [21]. Similar studies were not carried out with 2- and 5-substituted tetrazoles; very probably with these compounds the formation of $[M-N_2]^+$ follows the same mechanism. In the opposite case it is difficult to explain the similar values for stability to electron impact and for relative peak intensities of molecular and fragment ions in the mass spectra, or the general features of $[M-N_2]^+$ fragmentation (Scheme 7).

Scheme 7



XIX R=CH_3, R^1=H; XX R=CD_3, R^1=H [18]; XXI R=C_6H_5, R^1=H; XXII R=C_6D_5, R^1=H; XXIII R=4-BrC_6H_4, R^1=H; XXIV R=4-$NO_2C_6H_4$, R^1=H; XXV R=4-$NH_2C_6H_4$, R^1=H [27]; XXVI R=R^1=CH_3; XXVII R=CH_3, R^1=CD_3; XXVIII R=CF_3, R^1=CH_3 [18]; XXIX R=CH_3, R^1=C_6H_5; XXX R=C_6H_5, R^1=4-$NO_2C_6H_4$ [21]; XXXI R=C_6H_5, R^1=CH_2OH; XXXII R=C_6H_5, R^1=COOH; XXXIII R=C_6H_5, R^1=CO_2CH_3 [33]; XXXIV R=C_6H_5, R^1=CH_2Cl; XXXV R=C_6H_5, R^1=CH_2SH; XXXVI R=C_6H_5, R^1=CHO; XXXVII R=C_6H_5, R^1=$CH_2NHC_6H_5$; XXXVIII R=C_6H_5, R^1=methylpiperidine; XXXIX R=4-NO_2CH_5, R^1=CH_2Cl; XL R=4-$NO_2C_6H_4$, R^1=COOH [34]

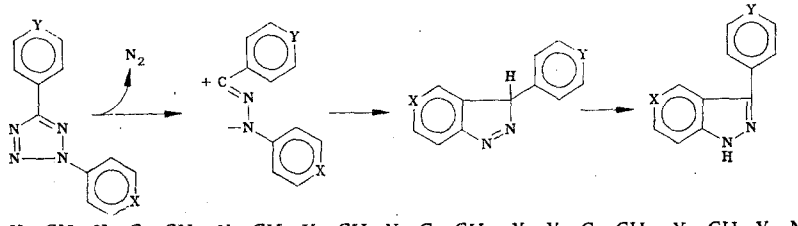
The elimination of HCN or N_2 molecules noted above (Scheme 4) by $[M-N_2]^+$ ions that form in 5-aryltetrazole decomposition here has its analog in the ejection of R^1CN or N_2 molecules.

These general features are also typical of the decomposition of isomeric 5- and 2-methyltetrazoles. Along with N_2 elimination there is also the removal of a HN_2 particle [18]. As shown by the mass spectra of deuterated XX and XXII, a methyl hydrogen takes part in this reaction. Such a reaction is also typical of 2,5-disubstituted tetrazoles with a methyl group at the 2- or 5-position.

When we compare MSF of 2- and 5- or 2,5-substituted tetrazoles, it is impossible not to notice the definite resemblance in their behavior under electron impact, which extends also to the thermal and photochemical reactions. In both cases the main decomposition process is the ejection of a nitrogen molecule and the formation of nitrilimine. The composition of the final products is determined by subsequent nitrilimine reactions and depends on the experimental conditions.

In pulsed gas-phase thermolysis (400-500°, 10^{-3} gPa), 2,5-diaryltetrazoles decompose to the respective indazoles in quantitative yield [35]:

Scheme 8



X=Y=CH; X=C—CH_3, Y=CH; X=CH, Y=C—CH_3; X=Y=C—CH_3; X=CH, Y=N

In the case under consideration, the nitrilimine produced by heating cyclizes to indazole, whereas the 5-substituted tetrazoles isomerize to aryldiazomethane, apparently due to the high mobility of the hydrogen atom (cf. Schemes 5 and 8).

In solution, just as in gas-phase thermolysis, the initial decomposition state is the formation of nitrogen and C,N-nitrilimine [36-42]. For 2,5-diphenyltetrazole this reaction is characterized by the activation parameters E_{act} = 135.6 kJ/mole (32.4 kcal/mole) and ΔS_{298} = 2.6 eu [37]. The activation entropy shows that thermal decomposition proceeds from an activated complex, the geometry of which is close to that of the initial state. The approved thermolysis mechanism, according to these data, also confirms the analysis of the correlation diagrams [38].

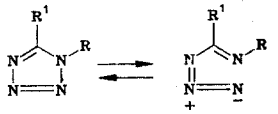
Due to the stabilizing effect of the solvent molecules the subsequent chemical conversions of nitrilimines in solution are represented mainly by bimolecular reactions. The nitrilimines themselves dimerize to dihydrotetrazines [36], and with dipolarophiles they react via 1,3-cycloaddition to form five-membered heterocycles (the Huisgen reaction). The features of the latter have been discussed in detail in reviews [39-42]. A group of recent publications is devoted to the latest advances in this field [43-45].

When we compare the data on thermolysis and MSF of the discussed compounds and the 5-substituted tetrazoles, we must note the coincidence of the thermal decompositions with elimination of N_2 and formation of nitrilimine. For reactions in solution this involves formation of tetrasubstituted tetrazines; and under conditions of gas-phase thermolysis, formation of indazole (Scheme 8) and its isomer aryldiazomethane (Scheme 5).

Similar features also distinguish the dissociative ionization of these compounds, as expressed by the nature and path of the subsequent decomposition of $[M-N_2]^{+\cdot}$. Hence when we take account of the similar stability to electron impact and the identity of the relative intensity peaks of the molecular and fragment ions, it follows that decomposition of 5-substituted tetrazoles is determined by the 2-H tautomer of M^+. Thus our conclusion concerning the agreement in structure of M^+ and the neutral molecule of these compounds, based on the comparison of dissociative ionization with thermolysis, has received additional confirmation in the identity of the respective reactions of 2- and 2,5-substituted tetrazoles.

1- AND 1,5-DISUBSTITUTED TETRAZOLES

In the 1- and 1,5-substituted tetrazoles, the isomerism of the tetrazole ring is limited by ring–chain tautomers.



The position of the tautomeric equilibrium depends on the temperature and the chemical nature of the substituents on nitrogen and carbon.

Most of this series of compounds are stable in the cyclic (tetrazole) form up to the decomposition temperature. Exceptions are the previously described isomerization of 5-amino-substituted tetrazoles [9] and the rearrangement of 5-mercaptotetrazoles to thiatriazoles [46].

Thermolysis of 1-monosubstituted tetrazoles is practically unstudied (an exception is the thermolysis of 1-trimethylsilyltetrazole [47]. Information on dissociative ionization is more substantial, but it too is limited by the small number of compounds.

MSF of 1-methyltetrazole and its trideuteromethyl analog [18] forms ions of the same elemental composition as in the corresponding reaction of 5- and 2-methyltetrazoles, but differing in the relative peak intensities of the molecular and fragment ions. The mass spectra of the isomeric aryl- and disubstituted tetrazoles are also noticeably different [18, 21, 24]. In the cited publications the nature of these differences is not discussed. But undoubtedly they are determined by the structures of the molecular and fragment ions, and are intimately involved in the fragmentation mechanism. These questions have been considered more fully for the 1,5-disubstituted tetrazoles.

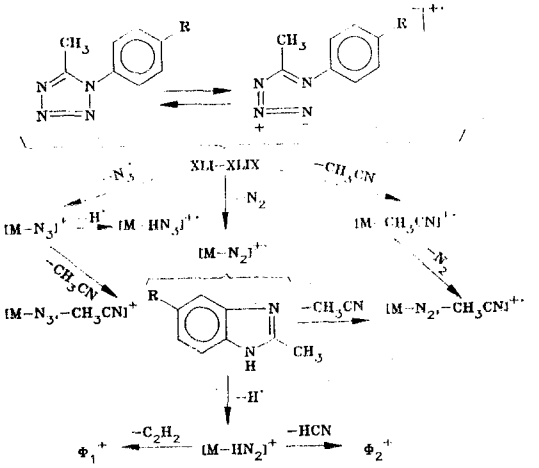
Dissociative ionization of the 1-(p-substituted)phenyl-5-methyltetrazoles XLI–XLIX proceeds predominantly with expulsion of a nitrogen molecule. The removal of a N_3 particle is less probable, and only compounds in which R = Cl or NO_2 eliminate a CH_3CN molecule [27]. In the formation of the mass spectrum these reactions are not significant, and when the energy of the ionizing electrons is reduced (20 eV) they do not appear. (See Scheme 9).

In the mass spectrum of 1-methyl-5-phenyltetrazole-$^{15}N_{1(4)}$ [21] N_2 elimination is accompanied by the equally probable ejections of $N_{(3)}N_{(4)}$ and $N_{(2)}N_{(3)}$ molecules. The subsequent fragmentation of $[M-N_2]^+$ shows that it corresponds in structure to 2-methylbenzimidazole [27], as demonstrated by the identical spectra of the metastable ions.

The dissociative ionization of these tetrazoles does not involve the inter-ring bond. This feature is distinctive for the conjugation of the aryl and heteroaryl parts of M^+; it is confirmed by the correlation of $\log I_{[M-N_2]^+}/I_{M^+}$ with the σ-constants of the substituents [28].

Conjugated structures with a shortened inter-ring bond are usually characterized by high stability to electron impact. But in this case the M^+ peak intensity is no more than several percent. In our view, this contradiction is eliminated if we take into account that in the 1,5-substituted tetrazoles XLI–XLIX removal of a nitrogen molecule proceeds with participation of the open (azomethine) form of M^+. In agreement with this conclusion are the elimination of $N_{(2)}N_{(3)}$ and the correlation mentioned above.

Scheme 9



XLI R=H; XLII R=CH_3; XLIII R=OCH_3; XLIV R=OC_2H_5; XLV R=NH_2; XLVI R=$N(CH_3)_2$; XLVII R=Cl; XLVIII R=NO_2; XLIX R=COOH [27]

As a rule, an electron acceptor group at a nitrogen in 1,5-substituted tetrazoles shifts the tetrazole ⇄ azide equilibrium toward the azide [9]. In this connection it might be expected that the weak inductive effect of the phenyl radical, which increases appreciably with the introduction of substituents such as Cl and NO_2, should favor stabilization of the azide structure. On the other hand, compounds with an aryl substituent in the 5-position and a methyl group on nitrogen are more stable in the cyclic (tetrazole) form. Evidently this is also typical of dissociative ionization, and determines the high M^+ peak intensity of 1-methyl-5-phenyltetrazole (isomeric with tetrazole XLI) and the predominant ejection of N_3 or CH_2N_2 (cf. [21] and [27]).

One of the features of the decomposition of isomeric methylphenyltetrazoles is the formation of $[M-HN_2]^+$. Its relative peak intensity in the mass spectrum depends on the location of the methyl group in the tetrazole ring, and also on the mobility of hydrogen atoms in going from methyl to methylene and methine groups. In the case of α-(1-phenyl-5-tetrazolyl)-β-(4-phenyl)ethylene and its derivatives, ejection of a HN_2 radical becomes the main path of MSF. The relative probability of this reaction is determined by the number and location of nitro groups. While elimination of a hydrogen predominates for LIII and LIV, ejection of a HN_2 radical predominates for the other compounds of this series [48] (Scheme 10). Formation of $[M-HN_2]^+$ is probably related to the rearrangement of M^+ to a tetrazoline structure, and does not exclude the possible removal of H and N_2 in a different sequence. (See Scheme 10).

The subsequent fragmentation of the fragment ion $[M-HN_2]^+$ coincides with the decomposition of 1,3-disubstituted pyrazole and/or 2-arylquinoline (Φ_3 ion). The removal of a hydroxy group and the direct elimination of an NO_2 radical represent the "ortho effect," [49] and are more typical of an ion with a quinoline structure.

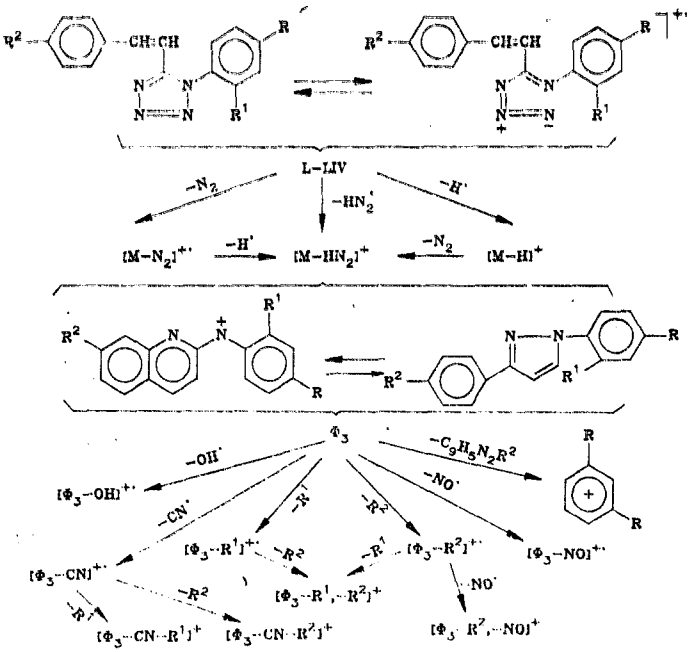
The dissociative ionization of 1-phenyl-5-mercaptotetrazoles LV-LXXII [50, 51] is distinctly different from the fragmentation of the compounds just discussed. Nevertheless it is fully compatible with the assumption of azide–tetrazole (j, k) and thione–thiol (j, n) tautomerism. (See Scheme 11.)

First of all we must distinguish the elimination of a thiatetrazolyl radical to form $(R^1)^{+\cdot}$ ion, which is typical only of mercaptotetrazoles. Possibly this fragmentation path is due to an alternate M^+ structure (1–q), which confirms the formation of $(R^1)^+$ ion from compounds of well-known thione structure (LXXI and LXXII).

Mercaptotetrazoles are distinguished by low peak intensity of the $[M-N_2]^+$ ion. Elimination of a nitrogen molecule is shown weakly and competes with removal of an R^1N_3 radical. Compounds whose structure permits thione–thiol tautomerism [52] show removal of an HN_3 particle. In the case of LXXI and LXXII such decomposition corresponds to ejection of a R^1N_3 particle. Apparently hydrazoic acid splits out also in the case of LXX, but the absence of high-resolution data does not exclude the ejection of a CH_3N_2 particle.

The ejection of a nitrogen molecule and a sulfur atom to form $[M-N_2S]^+$ (Scheme 11) is noted by the authors of [50, 51, 53] as a unique feature of the decomposition of these com-

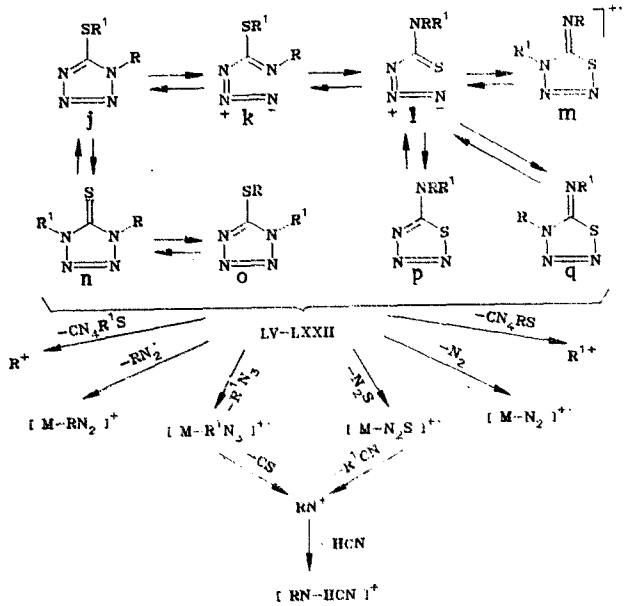
Scheme 10



L R=R¹=R²=H; LI R=R¹=H, R²=Cl; LII R=R²=NO₂, R¹=H; LIII R=NO₂, R¹=R²= =H; LIV R=R¹=NO₂, R²=H [48]

pounds. We note, however, that this reaction can be explained by isomerization of M^+ of mercaptotetrazole to aminothiatriazole. A similar rearrangement with intermediate formation of an azide tautomer was observed when the respective tetrazoles were heated to 160° [46] (Scheme 12). We note that dissociative ionization and thermal decomposition of thiatriazoles proceeds with elimination of a nitrogen molecule and a sulfur atom [54].

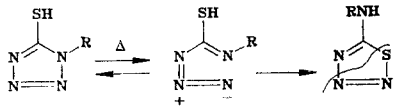
Scheme 11



R¹=H; LV R=C₆H₅; LVI R=CH₂C₆H₅; LVII R=CH₂CH=CH₂; LVIII R=*n*-C₁₂H₂₅ [50]; LIX R=2-CH₃C₆H₄; LX R=3-CH₃C₆H₄; LXI R=4-CH₃C₆H₄; LXII R=2-ClC₆H₄; LXIII R=3-ClC₆H₄; LXIV R=4-ClC₆H₄; LXV R=4-BrC₆H₄; LXVI R=2-CH₃OC₆H₄; LXVII R=3-CH₃OC₆H₄; LXVIII R=4-CH₃OC₆H₄ [51]; LXIX R=C₆H₅, R¹=S-5-(1-C₆H₅); tetrazoline; LXX R=C₆H₅, R¹=CH₃ [50]; LXXI R=C₆H₅, R¹(n)=methylpiperidine; LXXII R=C₆H₅, R¹(n) = methylmorpholine [50]

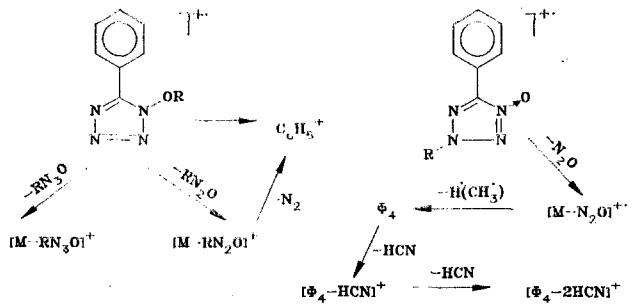
Of the oxygen analogs of 5-mercaptotetrazoles, the mass spectrum of 5-phenoxyl-1-phenyltetrazole has been considered in the literature; its fragmentation under electron impact follows the general regularities of the decomposition of 1,5-disubstituted tetrazoles [55].

Scheme 12



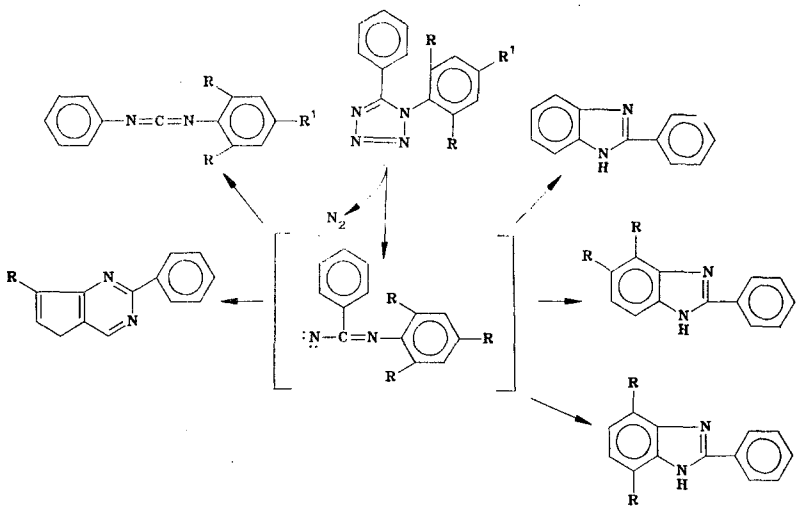
In 1,5-disubstituted tetrazoles with a hydroxy group at the 1-position the nature of dissociative ionization changes fundamentally. The mass spectrum of 1-alkoxy-5-phenyltetrazoles [56] is an example of the effect of structural isomerism in the hydroxy derivatives.

Scheme 13



Heating these compounds (200°, 10 min) initiates a rearrangement to form 3-alkyltetrazolyl 1-oxides, which are distinguished from their precursors by the mechanism of their decomposition (Scheme 13, R = CH_3, C_2H_5). This is the only case of a lack of correspondence between reactions initiated by electron impact and thermolysis, in the 1,5-disubstituted tetrazoles.

Scheme 14



R=R'=H; R=CH_3; R'=H; R=R'=CH_3

Like MSF, the thermal decomposition of 1,5-disubstituted tetrazoles is distinguished by high selectivity. The main thermolysis path is elimination of a nitrogen molecule $N_{(2)}N_{(3)}$ to form a nitrene, the subsequent conversions of which are determined by experimental conditions and the structure of the substituents in the tetrazole ring.

In the pulsed gas-phase thermolysis (600°; 10^{-3} hPa) of 1,5-diphenyltetrazoles these reactions are either cyclization or rearrangement, to form 2-phenylbenzimidazole and N,N'-diphenylcarbodiimide, respectively. For 1,5-diaryltetrazoles with a substituent in the o-position of the phenyl ring, the subsequent nitrene conversions are more complicated rearrangements [57, 58] (Scheme 14).

Like gas-phase thermolysis, heating 1,5-diaryltetrazoles in melt or solution (200-230°) forms N,N'-diarylcarbodiimides and 2-arylbenzimidazoles as main products [59, 60]. In contrast to the publications previously discussed, these authors relate the appearance of these compounds to the decomposition of the azide tautomer, and assume that the tetrazole ring opens in the first stage of the reaction. In the case of 1-aryl-5-methyltetrazoles [61, 62] this assumption agrees with derivatographic analysis, pyrolysate composition, and the dynamics of its formation with increase of temperature (Scheme 15, Fig. 1).

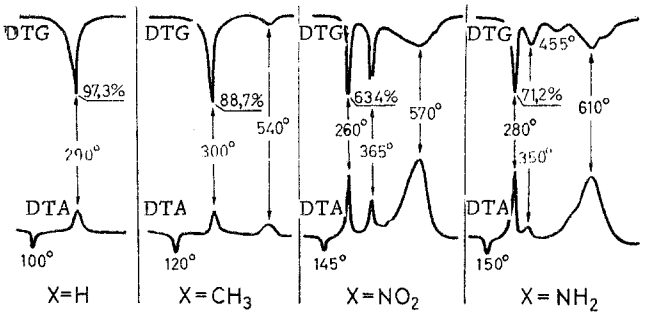
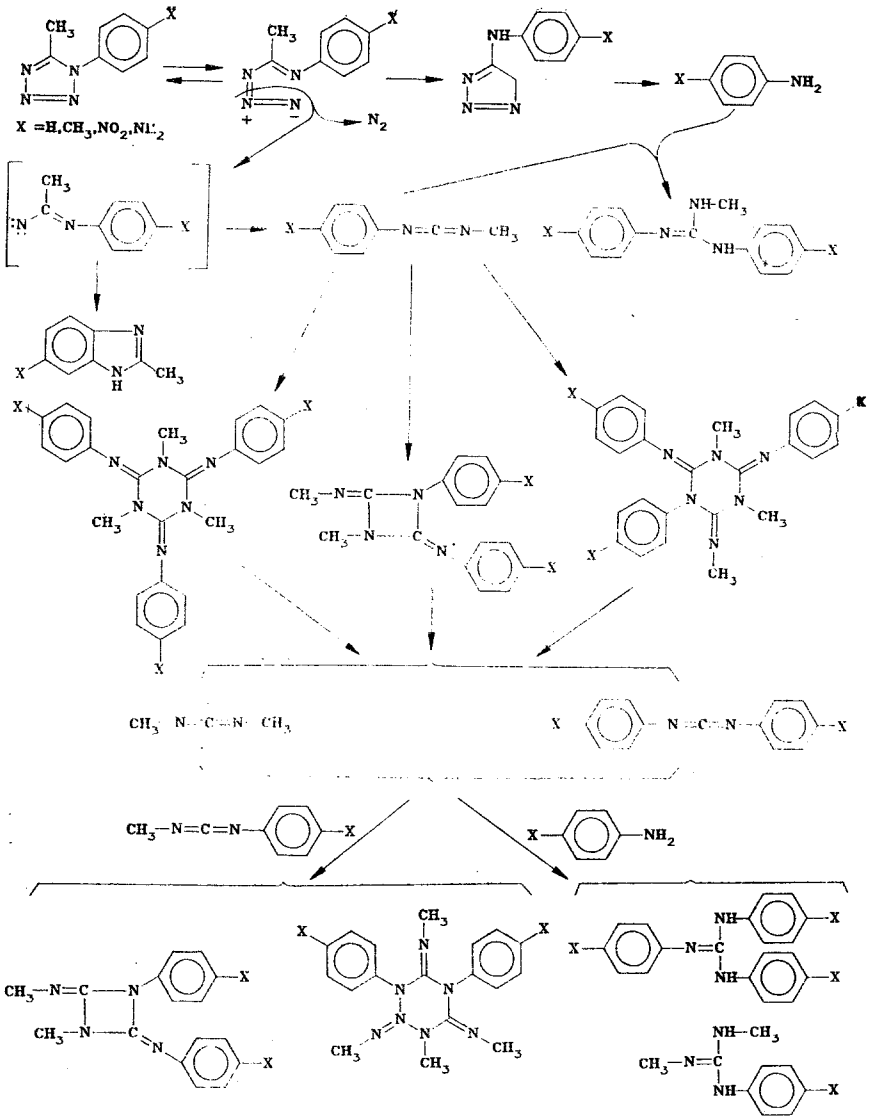


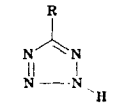
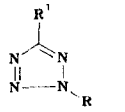
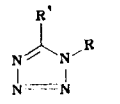
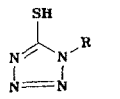
Fig. 1. Differential thermal analysis (DTA) and thermogravimetry (DTG) of 1-(p-substituted)-phenyl-5-methyltetrazoles.

Scheme 15

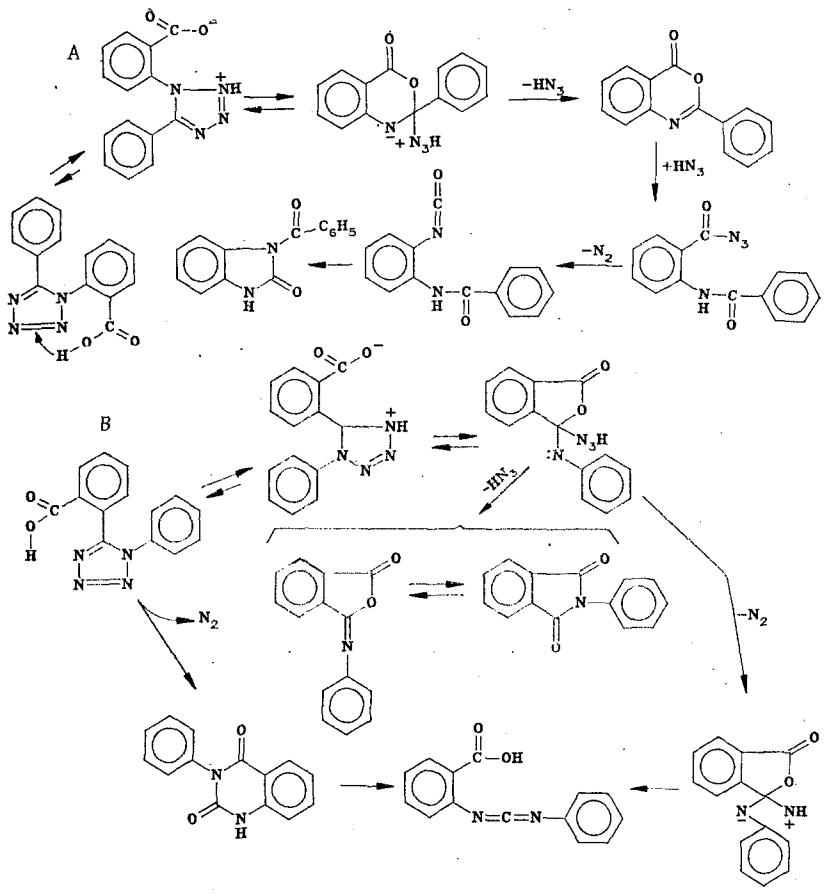


The tetrazoles with X = CH_3 are distinguished by an endo effect on the DTA curve (Fig. 1) that precedes a reaction in which weight is lost (the tautomeric tetrazole ⇄ azide conversions require expenditure of heat [9]). Isomerization of the starting compounds is also confirmed by: the minimal decomposition temperature of the nitro derivative, due to stabilization of the azide structure by the electronegative substituent [9]; the first-order elimination of N_2 [61]; and finally the product composition that is typical of thermal reactions of organic azides [63-66].

TABLE 1. Analogy between Dissociative Ionization and Thermolysis of Tetrazole Derivatives

Compound	Dissociative ionization	Thermolysis
	$[R-C\equiv N]^{+\cdot}$ and HN_3, $[M-N_2]^{+\cdot}$ and N_2 (Scheme 4)	Gas phase: $R-C\equiv N$ and HN_3; $R-CH=\overset{+}{N}=\overset{-}{N}$ and N_2 (Scheme 5) Reaction in solution: $R-C\equiv N$ and HN_3; $R-\overset{+}{C}=N-\overset{-}{N}H$ and N_2 (Scheme 6)
	$[M-N_2]^{+\cdot}$ and N_2 (Scheme 7)	Gas phase: indazoles and N_2 (Scheme 8). Reaction in solution: $R^1-\overset{+}{C}=N-\overset{-}{N}R$ and N_2
	$[M-N_2]^{+\cdot}$ and N_2 (Scheme 9)	Gas phase and solution: carbodiimides or 2-substituted benzimidazoles and N_2 (Schemes 14 and 15)
	Formation of $[M-N_2S]^{+\cdot}$ as a rearrangement	Elimination of N_2 and S as decomposition of product of isomerization to thiatriazole (Scheme 12)

Scheme 16



The formation of unsymmetrical carbodimides and 2-methylbenzimidazoles is determined by the structure and reactivity of the nitrene that is expected from decomposition of the azide tautomer; the appearance of anilines (indicated in Scheme 15) has an analogy with the known rearrangements of 5-mercapto- and 5-aminotetrazoles (cf. Schemes 3 and 12). Other compounds in the pyrolysate are related to the polymerization of N-methyl-N'-arylcarbodiimides (Scheme 15). For a gas-phase reaction, the conditions of which exclude the possibility of bimolecular processes, these processes are not typical.

In the 1,5-disubstituted tetrazole series, the nature of the substituent has an appreciable effect on the course of the thermal conversion. In confirmation we bring a number of examples (we note only that they involve compounds whose mass spectra have not been discussed in the literature).

Decomposition of 1-(o-carboxyl)phenyl-5-phenyltetrazole (160-220°) is accompanied by release of HN_3 and formation of 2-phenyl-4H-3,1-benzoxazinone-4 as main product [67] (Scheme 16, A). Thermolysis of the isomeric 5-(o-carboxy)phenyl-1-phenyltetrazole under the same conditions gives HN_3, N-phenylphthalanine, and 8-phenyltetrahydroquinazolinedione-2,4 [68] (Scheme 16, B).

The mechanism of these reactions assumes the intermediate formation of a bipolar ion, the subsequent decomposition of which, by ejection of HN_3 or N_2, gives the observed products.

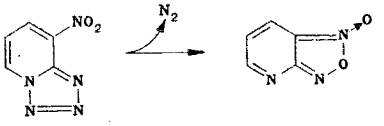
Another example of participation of the o-group in thermolysis is the conversion of 8-nitrotetrazolopyridine to 1,2,5-oxidiazolo-[3,4]pyridine [65] (Scheme 17).

5-Tetrazolylacetic acids decarboxylate when heated. The corresponding conversions of 1-tetrazolylacetic acid form resins of undetermined structure [70]. The esters of these compounds decompose to oxadiazoles [71].

Thermolysis of 1-trimethylsilyl-5-trimethylsilylaminotetrazole along with the corresponding carbodiimide forms cyanamide polymer and trimethylsilyl azide, which are not observed in the thermal reactions of diaryltetrazoles [47].

In spite of the different experimental conditions, the thermolysis and the dissociative ionization of the 1,5-disubstituted tetrazoles discussed above show much in common.

Scheme 17



The mass spectrometric data give much reason to speak of the fragmentation of 1,5-disubstituted tetrazoles with an azidic ion. The supporting evidence is: the low peak intensity of M^+ that is typical of organic azides; the elimination of the $N_{(2)}N_{(3)}$ molecule; and the general nature of 5-mercaptotetrazole rearrangement upon ionization or thermolysis (Schemes 11 and 12). Finally, isomerization to azide corresponds to thermodynamic circumstances under which an increase in the energy of the system shifts the equilibrium to the state with the higher entropy.

This assumption, which is valid also under the conditions of the thermal experiment, determines the direction of the tautomeric conversions when the temperature is raised.

CONCLUSION

Independent studies of thermolysis and MSF presented in this review show convincingly that formation of products of identical elemental composition is typical of most groups of compounds of this class. Some examples of similar agreement are given in Table 1.

In the case of 5-aryltetrazoles the similarity in the behavior of ion and neutral molecule follows two successive stages: the $[M-N_2]^{+\cdot}$ ion and aryldiazomethane, indicated in Table 1, undergo decomposition with elimination of a nitrogen molecule.

The ejection of N_2 with the formation of $[M-N_2]^{+\cdot}$ and C,N-nitrilimines or nitrenes (Schemes 8, 14, and 15) is a common path for fragmentation and thermal decomposition of 2,5- and 1,5-disubstituted tetrazoles. This is reason to assume that in the latter case this reaction is preceded by a general rearrangement to the azide structure (Table 1). Specifically this demonstrates the common features of dissociative ionization and thermolysis of 5-mercaptotetrazoles.

The similarities appear most fully when the experimental conditions of thermolysis and mass spectrometry are as much alike as possible. It is not an accident, therefore, that pulsed gas-phase thermolysis, where chemcial conversions proceed exclusively by an intramolecular mechanism, shows a aimilarity to dissociative ionization that follows several successive steps (see Schemes 4 and 5). For thermolysis in condensed phase, e.g., in solution, the similarity to fragmentation is limited to the initial decomposition steps (see Schemes 4 and 6).

Thus under various experimental conditions for the same compounds, the same reactions and even reaction sequence, including skeletal rearrangement, are observed.

If this is not an accident, but a regularity common to the thermolysis and the dissociative ionization of any organic compound, then when we consider the typical ion decompositions as analogs of thermal processes (Table 1), we can predict the nature and direction of chemical conversions during heating and (on the basis of structural information) mass spectrometry, as well as product composition.

Our conclusions are:

I. The following monomolecular reactions can be forecast: molecular isomerization (cyclization, recyclization, tautomeric conversion, substituent migration); molecular elimination (thermal decomposition to form biradical or bipolar compounds); radical dissociation (radical formation followed by disproportionation or isomerization of the primary products).

II. Thermal reactions are not limited by the initial stage. But since the mass spectra of the primary products are known, then by applying conclusion I to them, we can estimate the sequence of monomolecular thermolysis processes.

III. In thermolysis in melt or solution the primary decomposition products can react with one another to form compounds composed of structural fragments corresponding to the initial decomposition stage. The structures of these compounds can be forecast on the basis of data on the nature of the monomolecular reactions.

IV. Finally, since the energy of the ion at least at its ionization potential exceeds that of the molecule taking part in the thermal reaction, it is most unlikely that radical dissociation processes unobserved in mass spectrometry can take place under the less severe conditions of thermolysis.

Guided by the work on methyl aryl ketazines, the mass spectra of which show rearrangement with ejection of nitriles, thermal cyclizations were found for pyrroles, pyrazolines, benzodiazepines, pyridazines, and phthalazines [62]. Similar considerations led to the discovery of thermal rearrangements of allyl hydrazones to azo compounds [72]. Similar generalizations were formulated for the Diels–Alder reaction [73] and the Wolff rearrangement of diazoketones [74].

These similarities can be used to solve structural problems. For instance, from the fact that only anti-isomers undergo the Beckmann rearrangement it may be expected that in ionization only the same isomers should undergo the reactions typical of acid amides. The results of [75] agree with this conclusion.

Finally, the advances that have been reported in forecasting thermolyses mean that it may be possible to forecast the mass spectra of any compound by using information concerning its thermolysis.

No other approaches to solving this problem are known in mass spectrometry.

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STABILITY AND SPECTRAL CHARACTERISTICS OF 3-METHYL-3-PHENYL-1-ARYLPHTHALYL IONS

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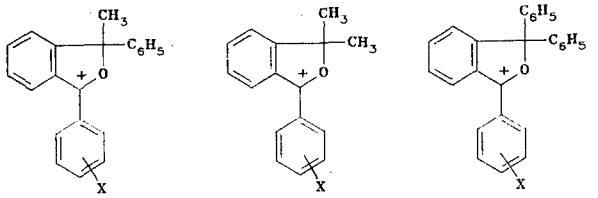
3-Methyl-3-phenyl-1-aryphthalyl ions are more stable than 3,3-diphenyl ions, but less stable than 3,3-dimethyl-1-arylphthalyl ions. The effect of substituents at $C_{(3)}$ and $C_{(1)}$ on stability and spectral characteristics of the ions is discussed.

In the preceding work [1] on the acid–base conversions of 3,3-disubstituted 1-arylphthalyl ions we established that substituents at the 3-position, structurally distant from the reactive center, affect the stability of the ions substantially because of an inductive effect. Although the ions previously studied differed from one another in the electronic and steric structures of the substituents at $C_{(3)}$, nevertheless in each compound the two substituents were the same. To obtain more detailed information about the effect of the substituents at the 3-position, it was of interest to us to study the stability and spectral characteristics of a series of phthalyl ions containing two different substituents, e.g., methyl and phenyl, at $C_{(3)}$, and to compare the results with those described for the model series IIa-g and IIIa-g.



I a-g II a-g III a-g

I—III a X=H; b X=*p*-CH_3; c X=*m*-CH_3; d X=*p*-CH_3O; e X=*p*-Cl, f X=*p*-$(CH_3)_2N$; g X=*p*-$(C_2H_5)_2N$

For this purpose, by the reaction of 3-methyl-3-phenylphthalide with arylmagnesium halide followed by treatment with perchloric acid we obtained the respective perchlorates I'a-g, which contain the 3-methyl-3-phenyl-1-arylphthalyl cations Ia-g.

The cyclic structure of Ia-g and the presence of a carbenium-oxonium group were confirmed by electron spectroscopy; the absorption curves resemble those of the cations IIa-g

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