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Fragmentation at Electron Impact of Nitro Derivatives of 1,2,4-Oxadiazole and 1,2,3-Triazole

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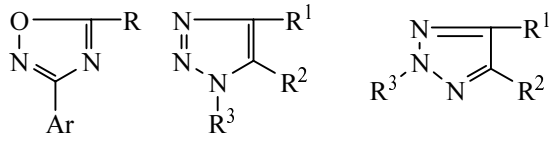
Abstract—Mass spectra were investigated of a series of 3-aryl-5-(nitromethyl)-1,2,4-oxadiazole derivatives and of *N*-methylated (benzylated) isomeric 4-(dinitromethyl)-1,2,3-triazoles. The principal fragmentation processes of these compounds involve the heterocycle opening and/or liberation of nitrogen-containing fragments followed by formation of the most stable fragment ions.

Heterocyclic compounds originating from 1,2,4-oxadiazole and 1,2,3-triazole found recently extensive application as biologically active compounds. Phenoxymethyl derivatives of 1,2,4-oxadiazole possess antiischemic and antiarrhythmic activity [1], oxadiazole sulfamide and hydrazine derivatives are characterized by antimycobacterial activity [2]. Nitrofuryl and imidazole derivatives of oxadiazole are effiectrive against *Staphylococcus aureus* [3] and their application is also suggested as antihistosomatic drugs [4]. Among derivatives of 4-nitromethyl 1,2,3-triazole derivatives were found compounds with fungicidal, herbicidal [5], and growth-regulating activity [6]. The wide range of application calls attention also to the mass spectra of this class compounds. Quite a number of publications describes the dissociative ionization of 1,2,4-oxadiazoles and 1,2,3-triazoles under electron impact [7–13]. Mass spectra were investigated of amino- [7, 8] and alkyl-substituted oxadiazoles [9], 1,2,4-oxa-diazole indolyl derivatives [10], oxadiazolylpyrazines [11], diphenyl and triphenyl derivatives of 1,2,3-triazoles [12, 13]. Yet the information on the mass spectra of polynitromethyl derivatives of 1,2,4-oxadiazoles and 1,2,3-triazoles is virtually lacking in the literature.

In this study we investigated the pathways of dissociative fragmentation at electron impact of series of 3-aryl-5-(nitromethyl)-1,2,4-oxadiazole derivatives **I–V** and 4-(dinitromethyl)-1,2,3-triazole derivatives **VI–XI** shown on Schemes 1 and 2.

The objects for the study were selected in order to get comparative data on fragmentation of oxadiazoles and triazoles and to discover diagnostic peaks for identification of polynitromethyltriazole isomers.



I–V **VI–VIII** **IX–XI**

Ar = 3-$O_2NC_6H_4$ (**I, V**), 4-BrC_6H_4 (**II**), 2-MeO-3,5-$Cl_2C_6H_2$ (**III**), 4-$MeOC_6H_4$ (**IV**); R = $C(NO_2)_2Cl$ (**I**), $C(NO_2)_2CO_2Et$ (**II**), $C(NO_2)ClCO_2Et$ (**III, IV**), $C(NO_2)_3$ (**V**); R^1 = $C(NO_2)_3$ (**VI, VIII, IX, XI**), $C(NO_2)_2CO_2Et$ (**VII, X**); R^2 = H (**VI, VII, IX, X**), Ph (**VIII, XI**); R^3 = Me (**VI, VII, IX, X**), CH_2Ph (**VIII, XI**).

Mass spectra of oxadiazoles **I–V** contained peaks of molecular ions $M^{+\cdot}$ of low intensity (7–12 rel%) and in some cases also peaks of ions $[M - H]^+$. Further fragmentation of $M^{+\cdot}$ involved a cleavage of the oxadiazole ring, ejection of the nitromethyl substituent, and elimination of nitrogen-containing fragments (Scheme 1). In the series of compounds **I–V** under investigation among the most favorable processes of the primary dissociative ionization of $M^{+\cdot}$ the reactions of retro-1,3-dipolar cyclization are worth mentioning, and also the cleavage of the nitromethyl substituent from the azole ring. The retro-1,3-dipolar cyclization took three main routes: with the rupture of $O–C^5$ and $C^3–N^4$ bonds (path *a*), $O–N^1$ and $C^3–N^4$ bonds (path *b*), or $O–N^1$ and $N^4–C^5$ bonds (path *c*). This conclusion is supported by the presence of sufficiently intense peaks from arising

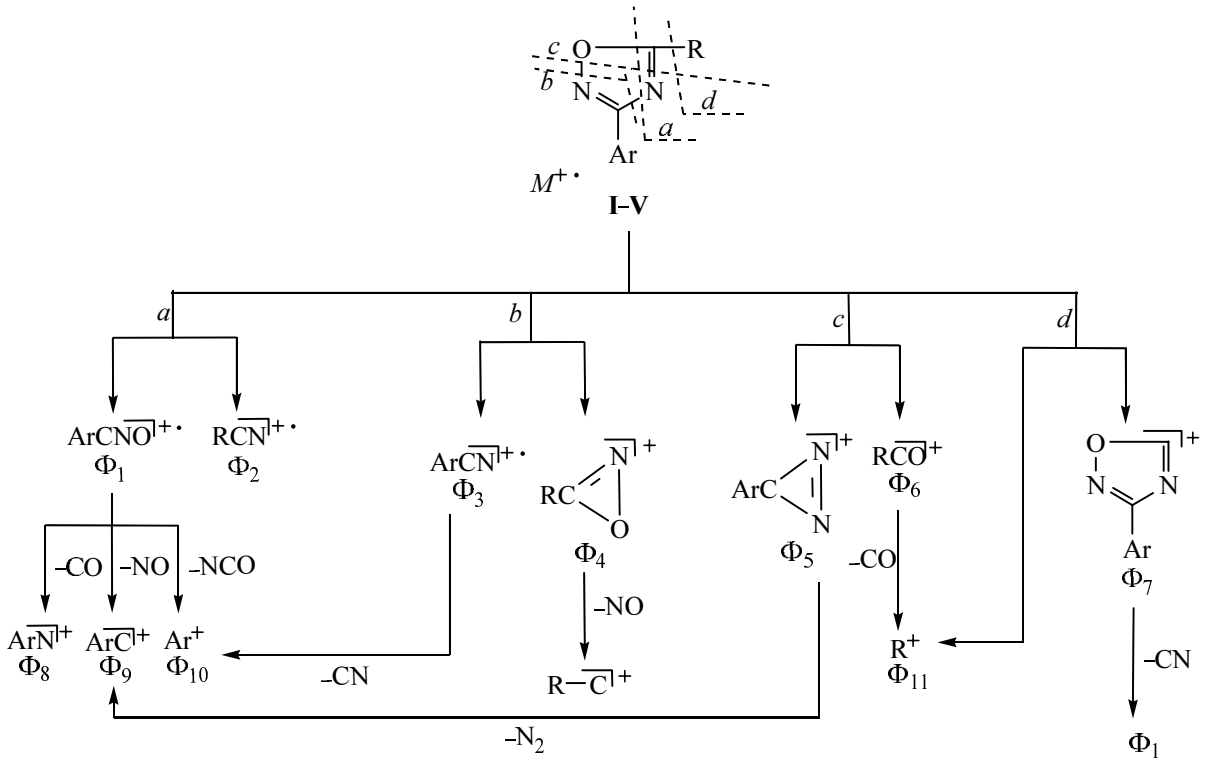
Mass spectra of 3-aryl-5-(nitromethyl)-1,2,4-oxadiazoles **I–V** and 4-(dinitromethyl)-1,2,3-triazoles **VI–XI**

Compd. no.	*m/z* (I_{rel},%)
I	328 (8.2) $[M]^{+\cdot}$, 327 $[M-H]^+$, 313 (1.1), 273 (1.9), 264 (1.8), 250 (1.9), 223 (3), 221 (14.9), 207 (7), 205 (16.2), 190 (31.6) $[M-R]^+$ Φ_7, 182 (27.4) Φ_4, 179 (6), 168 (26.7) (RCO^+) Φ_6, 167 (28) Φ_2, 165 (42.3) ($ArCNO^{+\cdot}$) Φ_1, 162 (44) ($ArCN_2^{+\cdot}$) Φ_5, 155 (21.4), 153 (29), 149 (100) ($ArCN^{+\cdot}$) Φ_3, 140 (2.8), 136 (12.7) (ArN^+), 134 (96) (ArC^+), 125 (12.7), 122 (6.8) (Ar^+), 111 (15), 102 (33.8), 90 (9.4), 76 (12), 75 (27.4), 63 (5), 52 (7.5), 50 (15), 46 (73) ($NO_2^{+\cdot}$), 30 (31.5) ($NO^{+\cdot}$)
II	399 (11.5) $[M]^{+\cdot}$, 398 (3.8) $[M-H]^+$, 328 (15), 331 (8.5), 282 (18), 252 (21), 222 (35) $[M-R]^+$ Φ_7, 220 (33) Φ_4, 205 (41) (RCO^+) Φ_6, 204 (32) ($R-CN^{+\cdot}$) Φ_2, 199 (28.7) ($ArCNO^{+\cdot}$) Φ_1, 196 (62) ($ArCN_2^{+\cdot}$) Φ_5, 190 (4), 183 (100) ($ArCN^{+\cdot}$) Φ_3, 171 (8), 168 (6.3) (ArC^+), 156 (13) (Ar^+), 155 (9), 143 (5), 127 (25), 116 (7.5), 102 (48.7), 90 (4), 76 (2.6), 63 (22.5), 50 (40), 46 (75.5) ($NO_2^{+\cdot}$), 30 (37) ($NO^{+\cdot}$)
III	409 (12.5) $[M]^{+\cdot}$, 374 (11.8), 326 (21), 261 (18.2), 243 (33) $[M-R]^+$ Φ_7, 235 (17), 219 (26.4) ($ArCNO^{+\cdot}$) Φ_1, 213(34) ($ArCN_2^{+\cdot}$) Φ_5, 210 (29.3) Φ_4, 203 (100) ($ArCN^{+\cdot}$) Φ_3, 195 (31) (RCO^+) Φ_6, 194 (27) ($RCN^{+\cdot}$) Φ_2, 190 (14.2) (ArN^+), 188 (13) (ArC^+), 176 (19.5) (Ar^+), 174 (10), 157 (23.3), 146 (14), 123 (15.5), 96 (37), 82 (42), 72 (8.4), 61 (21), 56 (8.7), 46(8.5) ($NO_2^{+\cdot}$) , 35 (11.3) (Cl^+), 30 (6.2) ($NO^{+\cdot}$)
IV	340 (21.5) $[M]^{+\cdot}$, 339 (6.1) $[M-H]^+$, 271 (2.6), 261 (9.2), 259 (31.4), 257 (36.6), 233 (11.7), 231 (14.2), 217 (18.7), 210 (21) Φ_4, 195 (23.4) (RCO^+) Φ_6, 194 (38) ($RCN^{+\cdot}$) Φ_2, 177 (9.1), 173 (35) $[M-R]^+$ Φ_7, 150 (34) ($ArCNO^{+\cdot}$) Φ_1, 147 (60.5) ($ArCN_2^{+\cdot}$) Φ_5, 134 (100) ($ArCN^{+\cdot}$) Φ_3, 121 (6.1) (ArN^+), 119 (7.9) (ArC^+), 107 (13.2) (Ar^+), 103 (29.2), 90 (37.6), 77 (45), 64 (39), 57 (11.5), 50 (41.7), 46 (14) ($NO_2^{+\cdot}$), 35 (4.5) (Cl^+), 30 (1.3) ($NO^{+\cdot}$)
V	398 (8.8) $[M]^{+\cdot}$, 193 (26) Φ_4, 190 (32) $[M-R]^+$ Φ_7, 178 (27.2) (RCO^+) Φ_6, 177 (31) Φ_2, 165 (48) ($ArCNO^{+\cdot}$) Φ_1, 163 (6), 162 (32) ($ArCN_2^{+\cdot}$) Φ_5, 150 (3.5), 149 (100) ($ArCN^{+\cdot}$) Φ_3, 137 (9.4) (ArN^+), 135 (5.2) (ArC^+), 123 (6.0) (Ar^+), 114 (24.4), 102 (12.2), 88 (19.5), 76 (43.9), 70 (24), 62 (19), 50 (34), 46 (86) ($NO_2^{+\cdot}$), 39 (17), 30 (44) ($NO^{+\cdot}$)
VI	186 (0.9) $[M-NO_2]^{+\cdot}$ Φ_1, 110 (2.5) $[M-2NO_2-NO]^{+\cdot}$ Φ_2, 108 (1.8), 83 (1.4), 54 (1.5), 53 (2.1), 46 (3) ($NO_2^{+\cdot}$), 44 (5.8), 43 (1.4) (MeN_2^+) Φ_3, 42 (1.4), 39 (1.5), 38 (1.5), 30 (100) ($NO^{+\cdot}$), 29 (3.5)
VII	213 (14.4) $[M-NO_2]^{+\cdot}$ Φ_1, 198 (1.4), 185 (1.4), 156 (3.6), 155 $[M-NO_2-NO-CO]^{+\cdot}$ (66), 138 (8), 110 (18) $[M-NO_2-NO-CO_2Et]^{+\cdot}$ Φ_2, 94 (33), 93 (6.5), 83 (5), 82 (6.5), 68 (5), 67 (40.5), 66 (47), 55 (16), 53 (44), 51 (1.4), 46 ($NO_2^{+\cdot}$) (2.5), 43 (6.7) (MeN_2^+) Φ_3, 42 (100) ($MeNCH^+$), 39 (18.6), 30 (7.2) ($NO^{+\cdot}$), 29 (58), 27 (33)
VIII	383 (3.2) $[M]^{+\cdot}$, 340 (2), 339 (22), 337 (100) $[M-NO_2]^{+\cdot}$ Φ_5, 292 (2.6) $[M-C_7H_7]^+$, 247 (2.1) $[M-NO_2-C_7H_7]^{+\cdot}$, 233 (3.2) $[M-C(NO_2)_3]^+$, 218 (3.5), 217 (5.1), 204 (3.2), 195 (2), 194 (16) ($PhCNCH_2Ph^+$), 191 (2.6), 189 (2.2), 180 (4.1), 178 (1.6), 165 (1.6), 157 (1.9), 129 (4.9), 115 (3.2), 106 (3.2), 105 (3), 92 (19), 91 (62) ($C_7H_7^+$) Φ_4, 89 (2.6), 77 (2.2), 65 (11), 51 (1.4), 30 (1.4) ($NO^{+\cdot}$)
IX	186 (1.8) $[M-NO_2]^{+\cdot}$ Φ_1, 141 (1.1), 124 (1.6), 110 (3.3) $[M-2NO_2-NO]^{+\cdot}$ Φ_2, 108 (4.9), 83 (4.3), 81 (2.6), 69 (1.4), 56 (1.4), 53 (3.2), 52 (2.6), 45 (5.5), 43 (21) (MeN_2^+) Φ_3, 42 (3.3), 41 (1.6), 40 (1.8), 39 (3.4), 38 (4.4), 30 (100) ($NO^{+\cdot}$), 29 (5.6)
X	213 (6.5) $[M-NO_2]^{+\cdot}$ Φ_1, 168 (1.4), 124 (2.8), 123 (1.7), 111 (3.9), 110 (97) $[M-NO_2-NO-CO_2Et]^+$ Φ_2, 96 (1.4), 83 (6.4), 68 (2.5), 57 (1.4), 55 (2), 53 (2), 51 (1.4), 46 (21) ($NO_2^{+\cdot}$), 44 (3), 43 (27) (MeN_2^+) Φ_3, 42 (1.5) ($MeNCH^+$), 41 (2), 39 (2.8), 31 (2), 30 (100) ($NO^{+\cdot}$), 29 (40)
XI	383 (0.2) $[M]^{+\cdot}$, 337 (2) $[M-NO_2]^{+\cdot}$ Φ_5, 292 (1) $[M-C_7H_7]^+$, 157 (1.6), 105 (2), 104 (1.9) ($PhCN^{+\cdot}$), 91 (59) ($C_7H_7^+$) Φ_4, 89 (1.6), 77 (4.4), 76 (1.6), 65 (11), 63 (2), 51 (4.4), 50 (1.9), 46 (21) ($NO_2^{+\cdot}$), 41 (1.6), 39 (3.7), 30 (100) ($NO^{+\cdot}$)

ions Φ_1–Φ_6 (26–100 rel%) with charge localization on both parts of the molecule (see table).

Fragmentation of oxadiazoles **I–V** involving elimination of the nitromethyl substituent (path *d*) afforded the peak of ion Φ_7 of medium intensity (21–35 rel%). This process occurred apparently due to good stabilization of the cation center of ion $[M-R]^+$ ensured by the conjugation with the p-electron system of the benzene ring. Ions of the primary dissociation Φ_1–Φ_7 suffer further fragmentation along the pathways characteristic of nitriles, diazo compounds, and nitro compounds [14]. However despite the common frag-

Scheme 1.



mentation character of oxadiazoles **I–V** the accumulation of nitro groups in the nitromethyl substituent results in appearance of additional concurrent fragmentation paths of molecular ions. Thus the mass spectra of compounds **I, II**, and **V** are distinguished by appearance of ion $NO^{+\cdot}$ peak with *m/z* 30 (31–44 rel%), and of ion $NO_2^{+\cdot}$ peak with *m/z* 46 (73–86 rel%) apparently originating from more intense fragmentation process involving nitro groups characteristic of polynitromethanes [15]. At the same time peaks of these ions in the spectra of compounds **III** and **IV** are of low intensity (1–14 rel%).

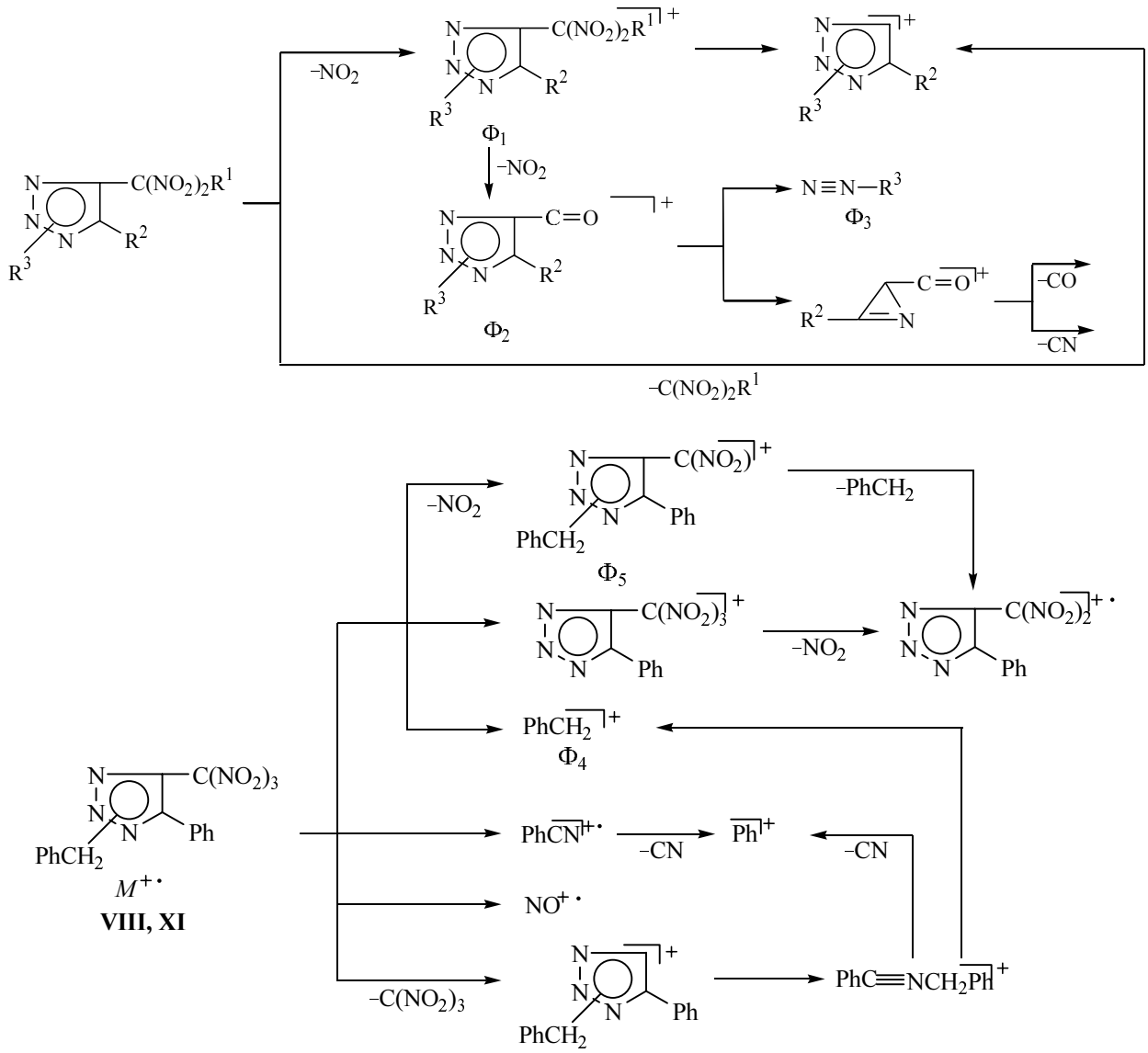
A similar pattern of the primary fragmentation is also observed for 4-(dinitromethyl)-1,2,3-triazoles **VI**, **IX** and **VII, X** isomeric with respect to location of the N-methyl group (Scheme 2). Peaks of molecular ions are lacking, and maximal remains the peak of $NO^{+\cdot}$ ion with *m/z* 30 (72–100 rel%).

Peaks of ions containing fragments of triazole ring are also observed: Φ_1 with *m/z* 186 (1 and 2 rel%) for compounds **VI** and **IX**, and with *m/z* 213 (0.2 and 3 rel%) for compounds **VII** and **X**, and also a peak Φ_2 of ion $[M - 2NO_2–NO]^{+\cdot}$ with *m/z* 110 (0.1–3 rel%). Although the intensity of these peaks in the mass spectra of pairs of compounds **VI, IX** and **VII, X** is different, they are hardly suitable for isomers identification because of low overall intensity. The solution of this problem may be attained by comparison in the mass spectra of isomers **VI** and **IX** of peak Φ_3 from ion $[N_2CH_3]^+$ with *m/z* 43. Its intensity in the mass spectrum of compound **IX** amounts to 21 rel% and in that of compound **VI** to 1.4 rel%. Large difference in the intensity of the peak in the spectra of isomers **VI** and **IX** is due to the difference in their initial structures and consequently in the structure of their molecular and fragment ions. This fragmentation path is almost improbable for compound **VI**.

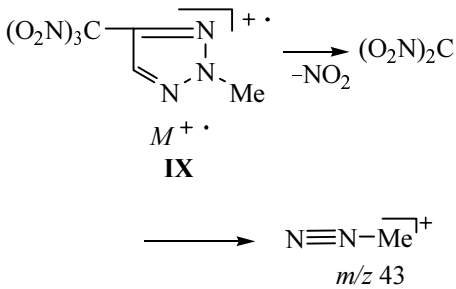
The identification of isomers **VII** and **X** can be performed using as analytical peaks those of ions $[HCN–Me]^+$ with *m/z* 42 and $[N_2–Me]^+$ with *m/z* 43. In the mass spectrum of isomer **VII** peak of ion with *m/z* 43 is of intensity 6 rel% whereas the peak of ion with *m/z* 42 is the most abundant (100 rel%). It is presumable that the ion of *m/z* 42 forms at fragmentaion of the triazole ring, and its most probable precursor is the ion $[M - NO_2]^{+\cdot}$ although the formation of this ion from other precursors, e.g., from ion $[M - NO_2–NO–CO]^{+\cdot}$ with *m/z* 155, cannot be excluded.

In the mass spectrum of compound **X** the peak of ion with *m/z* 42 (2 rel%) is hardly observable, and the intensity of the ion peak of *m/z* 43 is 27 rel%.

Scheme 2.

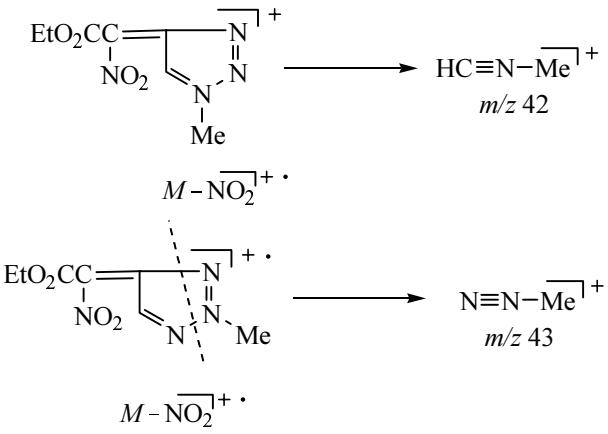


Incorporation of phenyl and benzyl substituents into the triazole ring significantly affected the pattern of mass spectra of isomers **VIII** and **XI** (Scheme 2). These substituents are capable of efficient delocalization of a positive charge thus stabilizing the ions containing them in the structure. Spectra of compounds **VIII** and **XI** contain molecular ion peaks $M^{+\cdot}$ with *m/z* 383 of low intensity (0.2–3 rel%). At the same time these compounds are able to undergo a favorable "benzyl" rupture resulting in appearance of a strong peak of ion $[C_7H_7]^+$ Φ_4 with *m/z* 91 (62, 59 rel% respectively). It should be noted that the principal path of molecular ion decomposition for isomer **VIII** is elimination of NO_2 molecules furnishing ion $[M-NO_2]^{+\cdot}$ Φ_5 with *m/z* 337 (100 rel%), whereas the peak of ion $[NO]^{+\cdot}$ is weak (2 rel%), and the peak of ion $[NO_2]^+$ is lacking. The pattern in the mass spectrum of compound **XI** is the opposite: the peak of ion $[M-NO_2]^{+\cdot}$ is weak, (2 rel%), and the intensity of peak from ion $[NO]^{+\cdot}$ is maximal. This fact may be ascribed to



different stability of ions $[M - NO_2]^{+\cdot}$ arising from isomers **VIII** and **XI**.

In the case of isomer **VIII** the carbocation site of the ion $[M-NO_2]^+$ is conjugated with the π-electron system of benzene ring, but this conjugation is absent in the ion originating from isomer **XI** resulting in sharp difference in the pattern of mass spectra belonging to these compounds.



Mass spectra of azoles studied contain additionally a large number of ion peaks which may correspond to several empirical formulas. As a result a more detailed interpretation of the mass spectra is complicated.

EXPERIMENTAL

Compounds under study were prepared by the following published procedures: compounds **I** and **II** [16]; compounds **III** and **IV** [17], compound **V** [18], compounds **VI, VII, IX**, and **X** [19], compounds **VIII** and **XI** [20].

Mass spectra were measured on GC-MS spectrometer Finnigan SSQ- 7000 with direct input of sample, ionizing electrons energy 70 eV, vaporizer temperature 90–150°C.

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