# AN INVESTIGATION OF THE STRUCTURE OF THE NITRATION PRODUCTS OF 1-PHENYL-5-STYRYLTETRAZOLE USING THE MASS-SPECTROMETRIC METHOD

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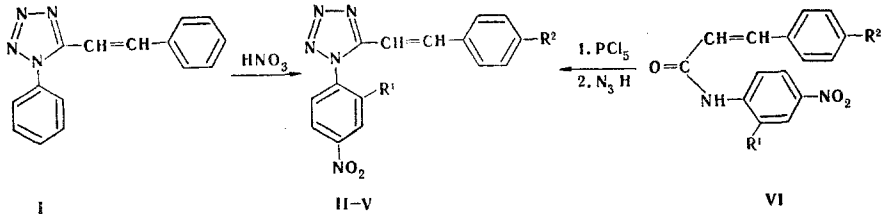
Depending on the reaction conditions, the nitration of 1-phenyl-5-styryltetrazole (I) with nitric acid and nitrating mixture give 1-(4-nitrophenyl)-5-styryltetrazole, 1-(4-nitrophenyl)-5-(4-nitrostyryltetrazole), and 1-(2,4-dinitrophenyl)-5-(4-nitrostyryl)tetrazole. The structures of the compounds obtained have been established by an analysis of their mass spectra and of the mass spectra of model compounds. The positions and sequences of entry of the nitro groups have been determined.

We have recently shown [1] that 1-aryl-5-methyltetrazoles, containing an unreactive methyl group, take part in condensation with aryl aldehydes only in the presence of DMSO with the formation of 1-aryl-5-styryltetrazoles. It appeared of interest to investigate the nature of the mutual influence of the tetrazole ring and phenyl residues in the electrophilic substitution reactions of such compounds. With this aim, in the present work we have studied the nitration of the simplest representative of this series of compounds, 1-phenyl-5-styryltetrazole (I).

The nitration of 1,5-substituted tetrazoles has been studied inadequately. It is known only that the nitration of 1-phenyltetrazole with nitric acid at 40°C leads to 1-(4-nitrophenyl)tetrazole [2], and the nitration of 1,5-diphenyltetrazole with nitrating mixture at 100°C gives 1-(4-nitrophenyl)-5-)4-nitrophenyl)tetrazole but the sequence of entry of the nitro groups was not considered [3].

When 1-phenyl-5-styryltetrazole (I) was nitrated with nitric acid (d 1.5) at 15°C, after crystallization from amyl alcohol we isolated two substances, with yields of ~60 and 35%, the elementary analyses of which were close to those for mono- and dinitro derivatives, respectively. Raising the temperature to 45-50°C enabled the yield of the dinitro product to be increased to 80%. By the action of nitrating mixture at 50°C we obtained a compound containing, according to elementary analysis, three nitro groups.

To establish the structures of the compounds obtained and to determine the sequence of entry of the nitro groups into the molecule of the tetrazole (I), we synthesized model compounds. Taking literature information into account, for this purpose we obtained the most probable mono- and dinitro derivatives namely: 1-(4-nitrophenyl)-5-styryltetrazole (II), 1-(4-nitrophenyl)-5-(4-nitrostyryl)tetrazole (III), and 1-(2,4-dinitrophenyl)-5-styryltetrazole (IV).




I II–V VI

II $R^1=R^2=H$; III $R^1=H$, $R^2=NO_2$; IV $R^1=NO_2$, $R^2=H$; V $R^1=R^2=NO_2$

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TABLE 1. m/e Values and Relative Intensities (in Percentages of the Maximum) of the Peaks of the Ions in the Mass Spectra of Model Compounds and the Products of the Nitration of the Tetrazole (I)*

| Nominal designation of the ion | Model compound | | | | Nitration products of the tetrazole (I) | | |
|---|---|---|---|---|---|---|---|
| | I | II | III | IV | mononitro derivative | dinitro derivative | trinitro derivative |
| $[M+1]^+$ | | 294 (6,7) | 339 (3,2) | 339 (10,2) | 294 (5,3) | 339 (3,0) | |
| $M^+$ | 248 (12,8) | 293 (41,6) | 338 (25,4) | 338 (57,8) | 293 (38,6) | 338 (22,6) | 383 (11,5) |
| $[M-H]^+$ | 247 (8,7) | 292 (90,1) | 337 (9,4) | 337 (100,0) | 292 (88,4) | 337 (6,3) | |
| $[M-R^1]^+$ | | | | 292 (4,1) | | | 337 (4,6) |
| $\Phi^+$ | 220 (10,6) | 265 (3,6) | 310 (11,9) | | | 310 (9,1) | |
| | 219 (100,0) | 264 (23,2) | 309 (69,1) | 309 (3,0) | 264 (21,8) | 309 (63,1) | 309 (10,2) |
| $[\Phi-OH]^+$ | | | | 292 (4,1) | | | 292 (13,2) |
| $[\Phi-R^2]^+$ | 218 (10,2) | | 263 (82,2) | 263 (38,0) | | 263 (79,4) | 263 (46,2) |
| $[\Phi-NO]^+$ | | 234 (9,6) | | | 234 (8,3) | | |
| $[\Phi-NO_2]^+$ | | 218 (100,0) | | | 218 (100,0) | | |
| $K_2$ | | | 217 (100,0) | 217 (12,0) | | 217 (100,0) | 217 (27,0) |
| $K_3$ | | | 233 (17,7) | 233 (7,0) | | 233 (16,1) | 233 (6,1) |
| $K_1$ | 193 (15,8) | 238 (14,0) | 283 (63,7) | | 238 (14,2) | 283 (58,6) | 283 (9,7) |
| $\Phi_1$ $[K_1-R^2]^+$ | | | | | | | |
| $[K_1-NO_2]^+$ | 192 (6,1) | 192 (27,5) | 237 (21,7) | | 192 (26,5) | 237 (18,6) | 237 (5,2) |
| $[\Phi_1-NO]^+$ | | | 207 (22,3) | 206 (3,4) | | 207 (18,8) | 207 (4,0) |
| $[\Phi_1-NO_2]^+$ | | | 191 (54,8) | 191 (6,7) | | 191 (45,6) | 191 (8,0) |
| K | | 122 (13,0) | 122 (35,9) | 167 (4,0) | 122 (12,6) | 122 (28,2) | 167 (7,8) |
| 165† | (7,7) | (11,5) | (10,8) | (5,0) | (13,2) | (9,9) | (18,1) |
| 128 | (4,0) | (30,6) | (22,1) | (21,2) | (28,6) | (18,3) | (8,8) |
| 116 | (9,8) | (18,2) | (28,3) | (20,0) | (17,4) | (26,3) | (9,5) |
| 115 | (8,1) | (21,7) | (15,4) | (22,2) | (22,4) | (11,4) | (11,8) |
| 103 | (6,4) | (52,6) | (12,3) | (57,6) | (51,8) | (12,5) | (11,0) |
| 102 | (4,6) | (34,5) | (70,4) | (49,4) | (36,2) | (68,1) | (23,6) |
| 91 | (35,5) | (15,1) | (13,1) | (30,6) | (16,9) | (17,3) | (18,9) |
| 90 | (14,1) | (56,1) | (96,0) | (95,8) | (60,3) | (86,4) | (100,0) |

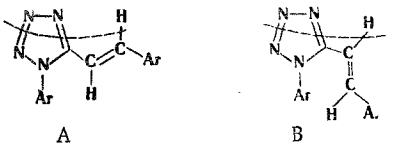
*The peaks of ions with intensities >3% are given. In the region of high values as far as m/e 90.
†m/e Values.

We used Braun's method [3] for the synthesis of these compounds. From $R^2$-cinnamoyl chlorides and $2R^1$-4-nitro-substituted anilines we obtained a series of amines (VI) which, on reaction with $PCl_5$ were converted into imidochlorides and then by the action of hydrazoic acid into the tetrazoles (II-IV).

To compare the mono-, di-, and trinitro derivatives obtained in the nitration of the tetrazole (I) and the compounds of authentic structure that we had synthesized, we used the mass-spectrometric method.*

Analysis of the mass spectra of the initial product (I) and of the model tetrazoles (II-IV) showed that the molecular ions ($M^+$) eliminate an $N_2H$ radical exclusively (Tables 1 and 2). This is obviously due primarily to steric factors.† When a free electron pair is present in the heterocycle and a mobile hydrogen atom in the ethylenic fragment of the molecule (β-cleavage relative to the aryl or heterocyclic part of the molecule [10]), the synchronous ejection of a hydrogen atom together with the $N_2$ molecule is possible. The mobility of the hydrogen atom in the molecular ion is additionally confirmed by the presence in the mass spectra of the peaks of the ions $[M-H]^+$ (Table 1).

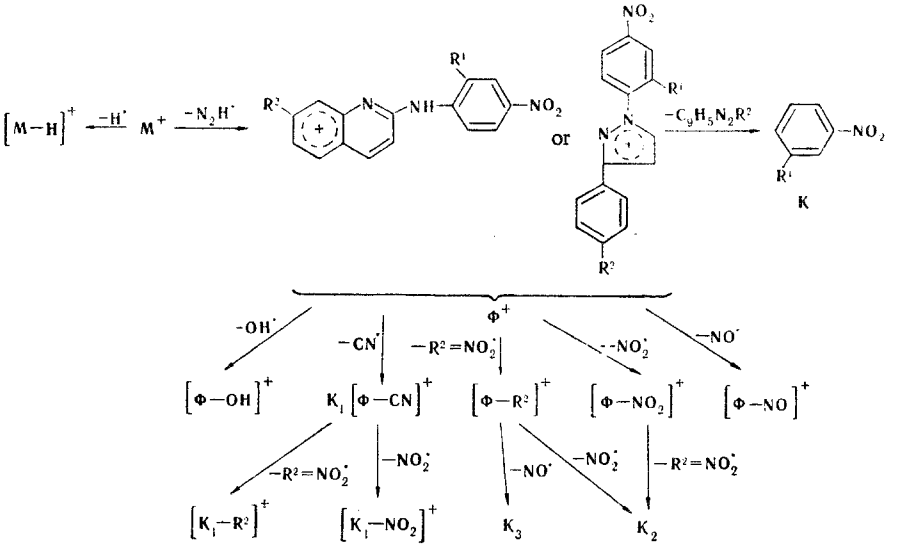
*The PMR method was not used because of difficulties in interpreting the poorly resolved signals
†It has been shown previously that the first stage of the fragmentation of $M^+$ for 1-arylte-trazoles is the ejection of a $N_2$ molecule [4-8]. No migration of hydrogen from the aryl part of the molecule was observed. The ejection of 29 amu from $M^+$ is known only for 1-methylte-trazole [9].



A B

It may be assumed that the synchronous ejection of a $N_2H$ radical takes place under the conditions of coplanarity of the tetrazole nucleus and the ethylenic part of the molecule (regardless of a cis or trans configuration of type A or B).

As a result of this fragmentation, a rearrangement ion is formed (with a lowering of the energy of the ionizing electrons, the intensity of the peak of this ion rises by a factor of 1.5-5), which can be assigned the structure of the cation of a 1,3-disubstituted pyrazole or a substituted 2-arylaminoquinoline ($\Phi^+$ ion). According to the mass spectra of the metastable ions (DADI technique [7, 11]) and high resolution mass spectra (Table 2), the $\Phi^+$ ion then decomposes by various channels (Scheme), giving the peaks of the ions $[\Phi-OH]^+$, $[\Phi-CN]^+$, $[\Phi-NO_2]^+$, $[\Phi-NO]^+$, $[\Phi-NO_2, -NO_2]^+$, which is characteristic for nitro-substituted aryls The number of nitro groups in the compounds determines the sequence of elimination of 46 amu from the $\Phi^+$ ion or the presence of peaks of ions with the structures $C_6H_4NO_2$ (m/e 122) and $C_6H_3(NO_2)_2$ (m/e 167).




As follows from Table 1, the positions of the nitro groups in the phenyl nuclei are shown by several mass-spectrometric processes. For example, an increase in the intensity of the peak of the $[M-H]^+$ ion relative to the $M^+$ peak takes place where the electron-accepting nitro group is present in the phenyl nucleus attached to the $N_1$ atom [compounds (II) and (IV)], while the presence of a nitro group in the benzene nucleus of the styryl fragment causes a decrease in the relative intensity of the peak [compound (III)]. Another specific indication permitting the positions of the nitro groups in the aromatic nuclei to be determined is the splitting out of a $N_2H$ radical. It can be seen from Table 1 that with a rise in the number of nitro groups in the N-phenyl nucleus of the molecule the intensity of the peak of the $\Phi^+$ ion appreciably diminishes. When a nitro group is present in the ortho position of the N-phenyl nucleus [compound (IV)], the splitting out of a OH· particle from the $\Phi^+$ ion is observed, and also the direct ejection of a nitro group (probably $R^1$) from $M^+$. Both processes can be explained on the basis of the idea of the "ortho effect" [12] and they are more characteristic for the $\Phi^+$ ion, which has a quinoline structure. These fragmentation acts are confirmed by the spectra of the metastable ions and by the results of high-resolution mass spectrometry (Table 2). The peak with the ion with m/e 292 is present in the MS in the form of a symmetrical doublet with the empirical formula $C_{15}H_8N_4O_3$ (determined 292.0588; calculated 292.0596) and $C_{15}H_{10}N_5O_2$ (determined 292.0738; calculated 292.0734).

On comparing the MSs of the model compounds and of the nitration products, it was found that the MS of the mononitro derivative was identical with that of model compound (II) and the MS of the dinitro derivative was identical with that of (III) and differed from the MS

TABLE 2. High-Resolution Mass Spectra of the Model Compounds and the Products of the Nitration of the Tetrazole (I) (M/ΔM = 15,000; PPA as standard)

| Arbitrary designation of the ion | Compound | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | I | | | (II) and the mononitro derivative | | | (III) and the dinitro derivative | | | trinitro derivative | | |
| | obs. | calc. | composition of the ion | obs. | calc. | composition of the ion | obs. | calc. | composition of the ion | obs. | calc. | composition of the ion |
| M+ | 248,1044 | ,1062 | $C_{15}H_{12}N_4$ | 293,0878<br>293,0900 | ,0912 | $C_{15}H_{11}N_5O_2$ | 338,0753<br>338,0760 | 338,0764 | $C_{15}H_{10}N_6O_4$ | 383,0610 | ,0614 | $C_{15}H_9N_7O_6$ |
| [M—H]+ | | | | 292,0804<br>292,0844 | ,0834 | $C_{15}H_{10}N_5O_2$ | | | | | | |
| [M—$R^1$]+ | | | | | | | | | | 337,0670 | ,0685 | $C_{15}H_9N_6O_4$ |
| Φ+ | 219,0913 | ,0922 | $C_{15}H_{11}N_2$ | 264,0776<br>264,0804 | ,0773 | $C_{15}H_{10}N_3O_2$ | 309,0620<br>309,0611 | ,0623 | $C_{15}H_9N_4O_4$ | 309,0606 | ,0623 | $C_{15}H_9N_4O_4$ |
| [Φ—NO]+ | | | | 234,0763<br>234,0753 | ,0793 | $C_{15}H_{10}N_2O$ | | | | | | |
| [Φ—$NO_2$]+ | | | | 218,0837<br>218,0813 | ,0843 | $C_{15}H_{10}N_2$ | | | | | | |
| [Φ—OH]+ | | | | | | | | | | 292,0581 | ,0596 | $C_{15}H_8N_4O_3$ |
| $K_1$, [Φ—CN]+ | 193,0882 | ,0892 | $C_{15}H_{11}N$ | 238,0766<br>238,0740 | ,0742 | $C_{14}H_{10}N_2O_2$ | 283,0580<br>283,0583 | ,0593 | $C_{14}H_9N_3O_4$ | 283,0572 | ,0593 | $C_{14}H_9N_3O_4$ |
| $\Phi_1$ [$K_1$—$NO_2$]+ | | | | 192,0790 | ,0813 | $C_{14}H_{10}N$ | 237,0638 | ,0664 | $C_{14}H_9N_2O_2$ | | | |
| [$K_1$—$R^2$]+ | | | | 192,0805 | | | 237,0635 | | | | | |
| [Φ—$R^2$]+ | | | | | | | 263,0703<br>263,0719 | ,0694 | $C_{15}H_9N_3O_2$ | 263,0678 | ,0694 | $C_{15}H_9N_3O_2$ |
| $K_2$ | | | | | | | 217,0793<br>217,0811 | ,0765 | $C_{15}H_9N_2$ | | | |
| *m/e* 128 | | | | 128,0470<br>128,0486 | ,0500 | $C_9H_6N$ | | | | | | |

of compound (IV) (Tables 1 and 2). These facts permit the unambiguous assignment to the mononitro derivative of the structure of 1-(4-nitrophenyl)-5-styryltetrazole and to the dinitro derivative of the structure of 1-(4-nitrophenyl)-5-(4-nitrostyryl)tetrazole.

The nature of the fragmentation of $M^+$ of the nitration product containing, according to the results of elementary analysis, three nitro groups differed considerably from the MSs of the model compounds (II) and (III). In the first stage of fragmentation a nitro group was split out. A similar process was observed in the MS of the nitro compound (IV). The appearance in the MS of the peak of an ion with m/e 167 (Table 1) also indicates that the two nitro groups have been introduced into the phenyl ring attached to the tetrazole. Furthermore, the MS shows the splitting out of a hydroxy group (Table 2). All this permits the trinitro derivative obtained to be assigned the structure of 1-(2,4-dinitrophenyl)-5-(4-nitrostyryl)-tetrazole (V). It must be mentioned that after the splitting out of the nitro group a $N_2$ molecule is ejected, and not a $N_2H^{\cdot}$ particle, as was reported previously, and the ion $\Phi^+$ formed is similar in structure to the $[M - N_2H]^+$ ion for compound (III). The subsequent fragmentation of the $\Phi^+$ ion takes place by the scheme described above.

Thus, by the aid of the mass-spectrometric method we have established the positions of the nitro groups in the products of the nitration of 1-phenyl-5-styryltetrazole and have shown that the tetrazole ring, like other azoles [13], orients an electrophilic substituent into the para and ortho positions. Furthermore, we have established the sequence of substitution: the first nitro group enters the phenyl ring attached to the nitrogen atom of the heterocycle, and the next one enters the benzene ring of the styryl fragment. The third nitro group is directed into the ortho position of the phenyl ring attached to the heterocycle.

## EXPERIMENTAL

The mass spectra were obtained on a Varian MAT-311-A instrument with direct introduction of the substance into the ion source. Recording conditions: accelerating voltage 3 kV, ionizing voltage 70 V, cathode emission current 300 μA. Thin-layer chromatography was performed on Silufol UV-254 plates in the chloroform–ethanol (25:1) system. : 1) system.

1-Phenyl-5-styryltetrazole (I) was obtained as described previously [1].

1-(4-Nitrophenyl)-5-styryltetrazole (II). With vigorous stirring, 10.4 g (0.05 mole) of $PCl_5$ was added to a mixture of 13.4 g (0.05 mole) of β-phenylacrylic acid 4-nitroanilide and 100 ml of dry benzene. The mixture was stirred at 60-80°C until the evolution of HCl ceased, the last traces of HCl were driven out with air, the mixture was cooled to 10°C, and a benzene solution of 0.07 mole of $HN_3$ was added. The resulting mixture was left at 20°C for 12 h and was boiled for 6 h, and was then cooled and 10 g of the nitro derivative (II) was filtered off. The filtrate yielded another 2 g of compound (II). The total yield was 75%. Light yellow crystals with mp 217-218°C (from acetic acid). Found: C 61.5; H 3.8; N 24.3%. $C_{15}H_{11}N_5O_2$. Calculated: C 61.4; H 3.8; N 23.9%.

The following were obtained similarly: 1-(4-nitrophenyl)-5-(4-nitrostyryl)tetrazole (III) from β-(4-nitrophenyl)acrylic acid 4-nitroanilide. Yield 87%, mp 275-276°C (from DMFA). Found: C 53.2; H 3.0; N 24.8%. $C_{15}H_{10}N_6O_4$. Calculated: C 53.1; H 3.0; N 24.8%; and 1-(2,4-dinitrophenyl)-5-styryltetrazole (IV) from β-phenylcinnamic acid 2,4-dinitroanilide. Yield 71%, mp 167°C (according to the literature [3], mp 167°C).

Nitration of 1-Phenyl-5-styryltetrazole (I). With stirring and cooling, 2.48 g (0.01 mole) of compound (I) was added to 12 ml of $HNO_3$ (d 1.5) and the reaction mixture was kept for 2.5-3 h and was poured onto 100 g of ice. The resulting precipitate was filtered off, washed with water, and dried. It was boiled in 100 ml of n-amyl alcohol and the mixture was filtered hot to give 1.2 g (35%) of the dinitro derivative. mp 276-278°C (decomp. from aqueous DMFA). Found: C 53.2; H 3.1; N 24.5%. $C_{15}H_{10}N_6O_4$. Calculated: C 53.1; H 3.0; N 24.8%. After cooling, the filtrate deposited 1.75 g (60%) of the mononitro derivative. This was crystallized from amyl alcohol and aqueous DMFA. Found: C 60.6; H 3.8; N 24.5%. $C_{15}H_{11}N_5O_2$. Calculated: C 61.4; H 3.8; N 23.9%. The mononitro derivative was contaminated with the dinitro derivative (according to TLC and elementary analysis).

1-(2,4-Dinitrophenyl)-5-(4-nitrostyryl)tetrazole (V). With stirring, 2.5 g (0.01 mole) of 1-phenyl-5-styryltetrazole was added at 0°C to a mixture of 25 ml of nitric acid (d 1.5) and 2 ml of sulfuric acid. The mixture was heated at 50°C for 5 h, and was then cooled to 20°C and poured onto 100 g of ice, and the precipitate was filtered off, washed with ethanol, and dried. Yield 3.25 g (96%). mp 230-232°C (decomp., from acetic acid). Found: N 25.8%. $C_{15}H_9N_7O_6$. Calculated: N 25.6%.

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