REARRANGEMENTS OF 1-OXA-2-AZOLES

9.* REARRANGEMENTS OF HYDRAZIDOXIMES OF 1,2,4-OXADIAZOLE-3-CARBOXYLIC ACID

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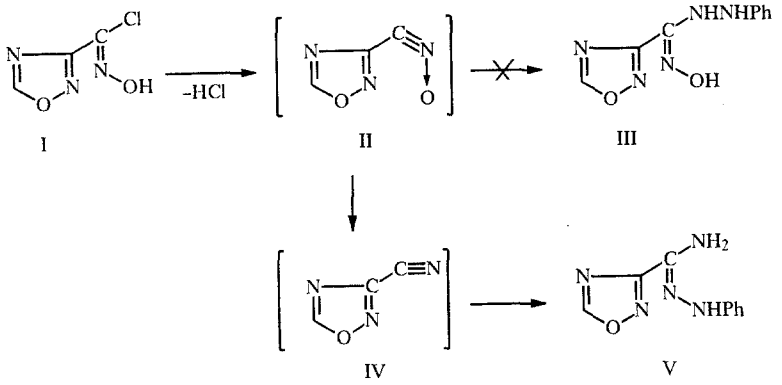
Reactions of acid chlorides of 1,2,4-oxadiazole-3-carbohydroximic acids with hydrazines lead to the formation of unstable hydrazidoximes, which readily undergo rearrangement to hydrazinofurazans. In the reaction with 4-nitrophenylhydrazine, the parallel reaction, leading to the formation of the amidrazone which undergoes rearrangement to the diaminotriazole, also proceeds simultaneously.

Rearrangements of the amidoximes of 1,2,4-oxadiazole-3-carboxylic acids are a convenient method for the isolation of derivatives of diaminofurazan [2, 3]. The present communication is dedicated to the investigation of the possible synthesis of 3-amino-4-hydrazinofurazan derivatives by this method. Until the present, only individual examples of the synthesis of hydrazinofurazans are known [4, 5]; due to the difficulty of the access to them, their properties have not been studied.

The amidoximes of 1,2,4-oxadiazole-3-carboxylic acids are readily formed in the reaction of acid halides of 1,2,4-oxadiazole-3-carbohydroximic acids with amines [3]. However, in the attempt to synthesize the hydrazidoxime (III) by this method using the reaction of the chloroxime (I) with phenylhydrazine, the amidrazone (V) was obtained [1]:



I II III IV V

This is associated with the fact that the intermediate nitrile oxide (II) does not add phenylhydrazine, but is reduced to the nitrile (IV). The last then binds phenylhydrazine with the formation of the amidrazone (V).

Continuing the investigations, we studied the reactions of acid halides of 1,2,4-oxadiazole-3-carbohydroximic acids with other hydrazine derivatives. It could be expected that the hydrazines, which have weaker reductive properties, will react differently with the nitrile oxides. In fact, the reaction proceeds by two routes with 4-nitrophenylhydrazine, leading to the mixture of two products, one of which was identified as the hydrazinofurazan (XIII), and the second as the amidrazone (IX).

*For Communication 8, see [1].

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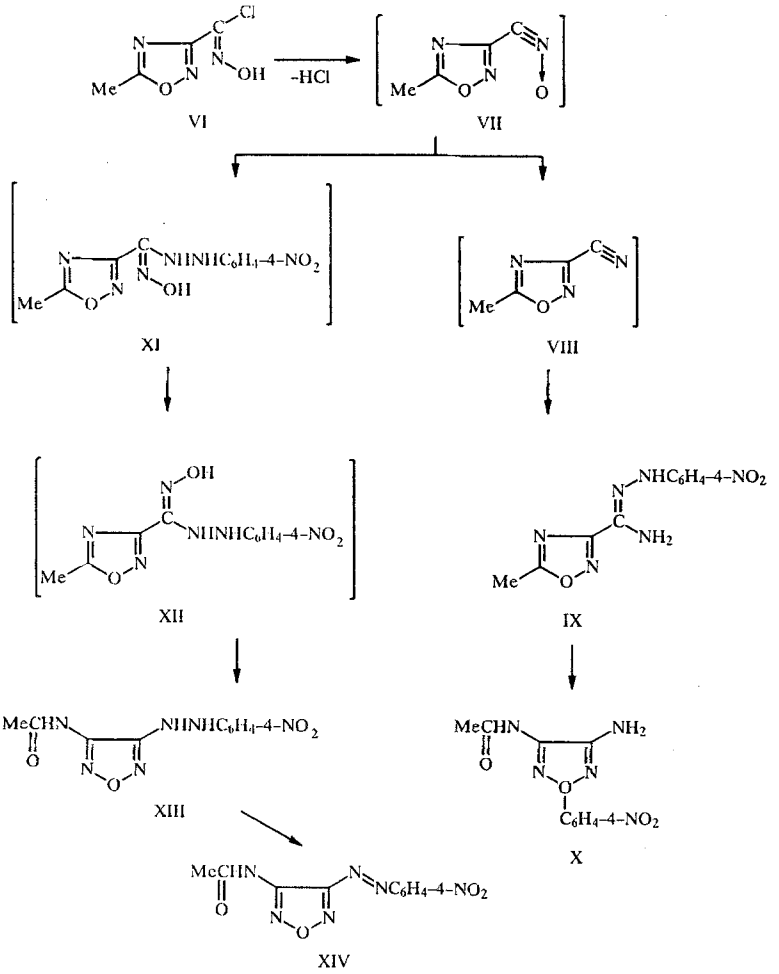
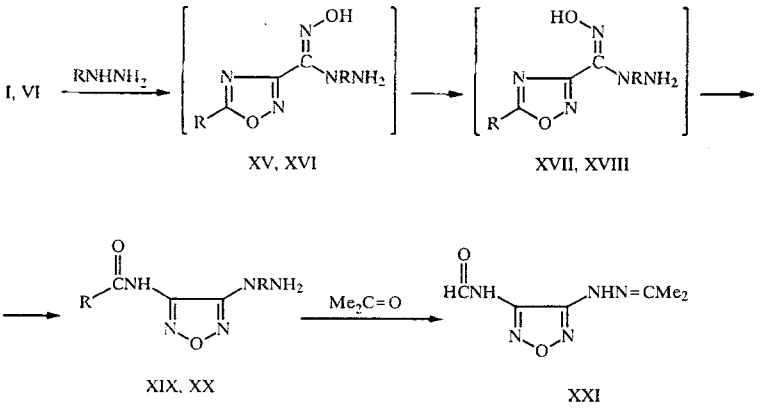


The product of the addition of 4-nitrophenylhydrazine to the nitrile oxide (VIII) — the hydrazidoxime (XI) — is unstable, and undergoes rearrangement to the hydrazinofurazan (XIII). Since the addition of nucleophiles to nitrile oxides proceeds regiospecifically and leads to the Z-isomers, it is evident that the stage of the isomerization of the Z-hydrazidoxime (XI) to the E-hydrazidoxime (XII) proceeds the rearrangement stage. The 4-nitrophenylamidrazone (IX) is stable and, in contrast to the phenylamidrazone (V), does not spontaneously undergo rearrangement to the diaminotriazole. This rearrangement proceeds when the amidrazone (IX) is melted in the presence of copper powder. It is interesting that the hydrazinofurazan (XIII) is oxidized under these conditions to the azo derivative (XIV).

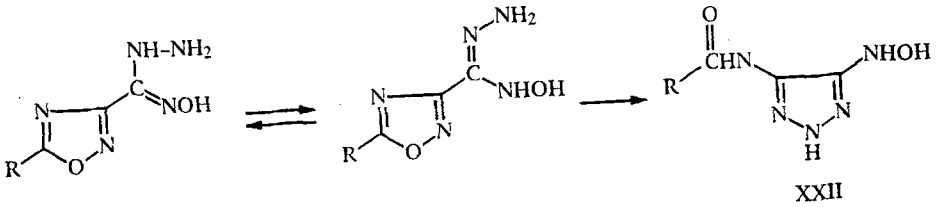
The reaction of the chloroximes (I) and (VI) with hydrazine and methylhydrazine only proceeds by the route associated with the intermediate formation of the hydrazidoximes (XV) and (XVI), leading finally to the hydrazinofurazans (XIX) and (XX).



XV, XVII, XIX R=H; VI, XVI, XVIII, XX R=Me

In contrast to 4-nitrophenylhydrazine, methylhydrazine adds to the nitrile oxide at the substituted nitrogen atom. This is explained by the fact that the electron-donor methyl group increases the nucleophilicity of the amino group connected to it, and, on the other hand, the electron-acceptor 4-nitrophenyl group lowers it.

It should be noted that the rearrangement of hydrazidoximes may, in principle, also proceed by another rout with the participation of the hydrazine fragment, and not the oxime fragment.

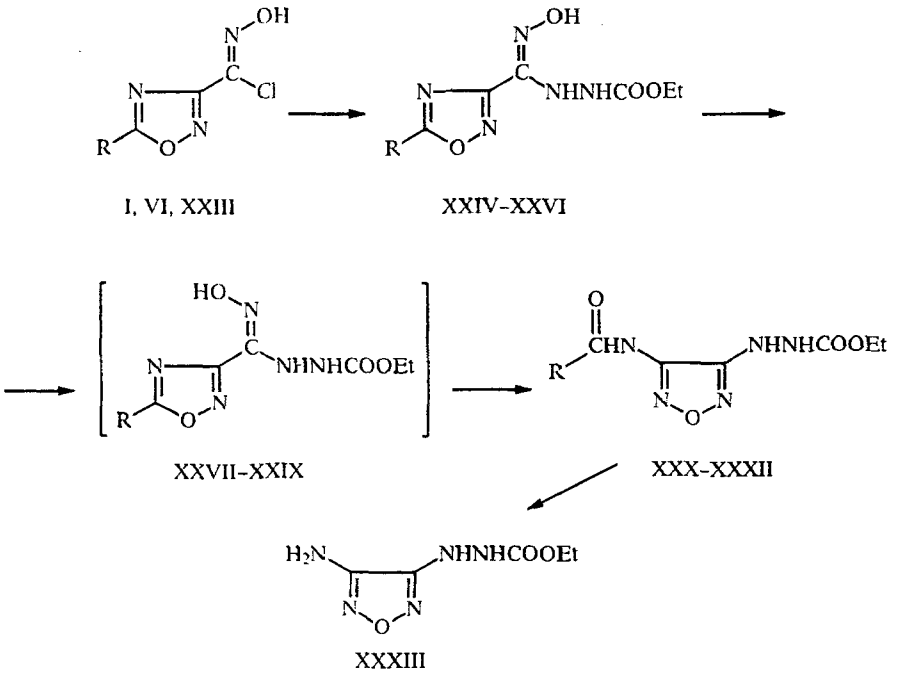


XXII

Such a rearrangement should lead not to furazans, but to the triazole derivative (XXII). However, the signals of the protons of the primary amino group in the PMR spectra of the rearranged products confirm the structure of the compounds (XIX) and (XX). Moreover, the hydrazinofurazan (XIX) forms the hydrazone (XXI) in the reaction with acetone.

The hydrazidoximes (XV) and (XVI), as well as (XI), are unstable and undergo immediate rearrangement to hydrazinofurazans in the course of the reaction. The more stable hydrazidoximes are obtained from ethyl hydrazinecarboxylate. As in the case of 4-nitrophenylhydrazine, the reaction with the nitrile oxide occurs at the unsubstituted amino group.

The hydrazidoximes (XXIV) and (XXVI) were obtained in the form of unstable oil-forming products. Attempts to purify them by crystallization or chromatography are accompanied by rearrangement and the formation of hydrazinofurazans. In the case of the derivative (XXXII), the hydrolysis of the trifluoroacetamide group takes place simultaneously with the formation of the furazan (XXXIII). In contrast to that, the hydrazidoxime (XXV) is obtained in the crystalline form. This compound is stable, and its rearrangement was successfully carried out when it was heated in the presence of copper powder.



I, VI, XXIII

XXIV-XXVI

XXVII-XXIX

XXX-XXXII

XXXIII

XXIV, XXVII, XXX R=H; XXV, XXIII, XXXI R=Me; XXIII, XXVI, XXIX, XXXII R=CF_3

The high stability of the hydrazidoximes (XXIV)-(XXVI) by comparisonwith (XI), (XV), and (XVI) is explained by the presence of the electron-acceptor ester group. On the one hand, this leads to an increase in the barrier to the Z-E-isomerization, and, on the other hand, it lowers the nucleophilicity of the oxygen atom of the oxime group, which leads to an increase in the barrier to the rearrangement.

EXPERIMENTAL

The PMR spectra were taken on the Bruker WH-90 spectrometer using DMSO-D_6 and the internal standard of TMS. The IR spectra were taken on the Perkin–Elmer 580B instrument using Nujol. The data of the elemental analysis for C, H, and N correspond with the calculated data.

4-Nitrophenylamidrazone of 5-Methyl-1,2,4-oxadiazole-3-carboxylic Acid (VI) ($C_{10}H_{10}N_6O_3$) and 4-Acetamido-3-(4-nitrophenylhydrazino)furazan (XIII) ($C_{10}H_{10}N_6O_4$). To the solution of 1.53 g (10 mmole) of 4-nitrophenylhydrazine and 0.6 g (6 mmole) of triethylamine in 50 ml of ethanol is added, dropwise at room temperature, the solution of 0.8 g (5 mmole) of the chloroxime (VI) in 20 ml of ethanol. After 1 h, the reaction mixture is concentrated in vacuo. Ethyl acetate is added to the residue, and the triethylamine salt is filtered off. The filtrate is washed with water and dried over Na_2SO_4. The ethyl acetate is distilled off in vacuo, and the residue is suspended in 20 ml of ether. The residue is filtered off. The yield of 0.2 g (15%) of the amidrazone (IX) is obtained; it has the mp 235-237°C. The PMR spectrum is as follows: 2.60 ppm (3H, s, CH_3), 6.49 ppm (2H, s, NH_2), 7.01 ppm (2H, d, 2,6-C_6H_2), 8.02 ppm (2H, d, 3,5-C_6H_2), and 9.72 ppm (1H, s, NH). The IR spectrum is as follows: 3470 and 3360 cm^{-1} (NH_2) and 1610 cm^{-1} (C=N).

The ether filtrate is chromatographed on silica gel using the eluent ether prior to the isolation of 0.4 g (28%) of the furazan (XIII) with the mp 182-184°C. The PMR spectrum is as follows: 2.04 ppm (3H, s, CH_3), 6.77 ppm (2H, d, 2,6-C_6H_2), 7.99 ppm (2H, d, 3,5-C_6H_2), 8.38 ppm (1H, s, NH), 9.15 ppm (1H, s, NH), and 10.65 ppm (1H, s, NH). The IR spectrum is as follows: 3480 cm^{-1} (NH), 3280 cm^{-1} (NH), 3190 cm^{-1} (NH), 1670 cm^{-1} (C=O), and 1615 cm^{-1} (C=N).

4-Amino-5-acetamido-2-(4-nitrophenyl)-1,2,3-triazole (X) ($C_{10}H_{10}N_6O_3$). The mixture of 0.3 g (1.1 mmole) of the amidrazone (IX) and 0.3 g of copper powder is heated to the melting temperature. After cooling the mixture, 10 ml of ethanol are added; the mixture is filtered, and the filtrate is concentrated. The yield of 0.15 g (50%) of the triazole (X), with the mp 228-230°C, is obtained. The PMR spectrum is as follows: 2.06 ppm (3H, s, CH_3), 5.90 ppm (2H, s, NH_2), 7.83 ppm (2H, d, 2,6-C_6H_2), 8.30 ppm (2H, d, 3,5-C_6H_2), and 10.55 ppm (1H, s, NH).

4-Acetamido-3-(4-nitrophenylazo)furazan (XIV) ($C_{10}H_{10}N_6O_4$). This compound is obtained analogously to the triazole (X) from the hydrazinofurazan (XIII). The mp is 192-194°C. The PMR spectrum is as follows: 2.14 ppm (3H, s, CH_3), 8.18 ppm (2H, d, 2,6-C_6H_2), 8.45 ppm (2H, d, 3,5-C_6H_2), and 10.73 ppm (1H, s, NH). The mass spectrum has the m/z 276 M^+. The yield is 48%.

3-Hydrazino-4-formamidofurazan (XIX) ($C_3H_5N_5O_2$). To the solution of 1.0 g (20 mmole) of hydrazine hydrate in 15 ml of ethanol is added, dropwise at 0-5°C, the solution of 1.18 g (8 mmole) of the chloroxime (I) in 40 ml of ethanol. After 10 min, the reaction mixture is concentrated in vacuo. Water is added to the residue. The residue is filtered off, and the yield of 0.78 g (68%) of the hydrazinofurazan (XIX) with the mp 124-126°C is obtained. The PMR spectrum is as follows: 4.49 ppm (2H, s, NH_2), 7.18 ppm (H, s, NH), 8.33 ppm (1H, s, CH), and 8.56 ppm (1H, s, NH).

3-Isopropylidenehydrazino-4-formamidofurazan (XXI) ($C_6H_9N_5O_2$). The hydrazinofurazan (XIX) (0.5 g, 3.5 mmole) is dissolved in 10 ml of acetone. After 20 min, the acetone is evaporated in vacuo. Water is added to the residue. The product is filtered off, and the yield of 0.5 g (78%) of the hydrazone (XXI) with the mp 178-179°C is obtained. The PMR spectrum is as follows: 1.83 ppm (3H, s, CH_3), 1.90 ppm (3H, s, CH_3), 8.51 ppm (1H, s, CH), 8.93 ppm (1H, s, NH), and 10.7 ppm (1H, s, NH).

4-Acetamido-3-(1-methylhydrazino)furazan (XX) ($C_5H_9N_5O_2$). To the solution of 0.5 g (11 mmole) of methylhydrazine in 25 ml of ethanol is added, in portions at 0-5°C, 0.8 g (5 mmole) of the chloroxime (VI). The residue is filtered off after 30 min, and the yield of 0.4 g (47%) of the hydrazinofurazan (XX) is obtained. The mp is 169-171°C (from ethanol). The PMR spectrum is as follows: 2.07 ppm (3H, s, CH_3), 2.98 ppm (3H, s, CH_3N), 4.93 ppm (2H, s, NH_2), and 10.24 ppm (1H, s, NH). The IR spectrum is as follows: 3340 and 3215 cm^{-1} (NH_2), 3185 cm^{-1} (NH), 1710 cm^{-1} (C=O), and 1608 cm^{-1} (C=N).

2-(Ethoxycarbonyl)hydrazidoxime of 5-Methyl-1,2,4-oxadiazole-3-carboxylic Acid (XXV) ($C_7H_{11}N_5O_4$). To the solution of 1.04 g (10 mmole) of ethyl hydrazinecarboxylate and 1.21 g (12 mmole) of triethylamine in 20 ml of ethanol is added, dropwise at 0-5°C, the solution of 1.61 g (10 mmole) of the chloroxime (VI) in 30 ml of ethanol. After 1 h, the reaction

mixture is concentrated in vacuo, and water is added to the residue. The product is filtered off. The yield of 0.82 g (35%) of the hydrazidoxime (XXV), with the mp 186-187°C (from ethanol), is obtained. The PMR spectrum is as follows: 1.07 ppm (3H, t, CH_3), 2.54 ppm (3H, s, CH_3), 3.90 ppm (2H, q, CH_2), 8.03 ppm (1H, s, NH), 8.87 ppm (1H, s, NH), and 10.56 ppm (1H, s, OH). The IR spectrum is as follows: 3322 cm^{-1} (NH), 3290 cm^{-1} (NH), 3230 cm^{-1} (OH), 1705 cm^{-1} (C=O), and 1630 cm^{-1} (C=N).

4-Acetamido-3-(2-ethoxycarbonylhydrazino)furazan (XXXI) ($C_7H_{11}N_5O_4$). The mixture of 0.07 g (0.3 mmole) of the hydrazidoxime (XXV) and 0.07 g of copper powder in 5 ml of acetonitrile is boiled for 15 min. The reaction mixture is filtered, and the filtrate is concentrated in vacuo. Water is added to the residue, and the product is filtered off. The yield of 0.05 g (71%) of the hydrazinofurazan (XXXI), with the mp 188-189°C, is obtained. The PMR spectrum is as follows: 1.12 ppm (3H, t, CH_3), 2.03 ppm (3H, s, CH_3), 3.99 ppm (2H, q, CH_2), 8.07 ppm (1H, s, NH), 9.33 ppm (1H, s, NH), and 10.58 ppm (1H, s, NH). The IR spectrum is as follows: 3320 cm^{-1} (NH), 3240 cm^{-1} (NH), 1730 cm^{-1} (C=O), 1675 cm^{-1} (C=O), and 1615 cm^{-1} (C=N).

4-Formamido-3-(2-ethoxycarbonylhydrazino)furazan (XXX) ($C_6H_9N_5O_4$). To the solution of 1.04 g (10 mmole) of ethyl hydrazinecarboxylate and 1.21 g (12 mmole) of triethylamine in 20 ml of ethanol is added, dropwise at 10°C, the solution of 1.48 g (10 mmole) of the chloroxime (I) in 50 ml of ethanol. After 30 min, the reaction mixture is concentrated in vacuo. Ethyl acetate is added to the residue, and the triethylamine salt is filtered off. The filtrate is partially concentrated prior to the chromatography on silica gel using the eluent of the 2:1 mixture of ethyl acetate–hexane. The yield of 0.64 g (30%) of the hydrazinofurazan (XXX), with the mp 134-136°C, is obtained. The PMR spectrum is as follows: 1.11 ppm (3H, t, CH_3), 3.98 ppm (2H, q, CH_2), 8.16 ppm (1H, s, NH), 8.40 ppm (1H), br. s, CH), 9.35 ppm (1H, s, NH), and 10.57 ppm (1H, s, NH). The IR spectrum is as follows: 3180-3280 cm^{-1} (NH), 1728 cm^{-1} (C=O), 1705 cm^{-1} (C=O), and 1620 cm^{-1} (C=N).

4-Amino-3-(2-ethoxycarbonylhydrazino)furazan (XXXIII) ($C_5H_9N_5O_3$). To the solution of 1.04 g (10 mmole) of ethyl hydrazinecarboxylate and 1.5 g (15 mmole) of triethylamine in 20 ml of ethanol is added, dropwise at 10°C, the solution of 2.16 g (10 mmole) of the chloroxime (XXIII) in 20 ml of ethanol. After 30 min, the mixture is concentrated in vacuo. The product is extracted from the residue with ethyl acetate. After the distillation of the ethyl acetate, an oil which crystallizes on standing for 3-4 days is obtained. Ether is added, and the product is filtered off. The yield of 0.6 g (32%) of the hydrazinofurazan (XXXIII), with the mp 167-168°C, is obtained. The PMR spectrum is as follows: 1.16 ppm (3H, t, CH_3), 4.02 ppm (2H, q, CH_2), 5.82 ppm (2H, s, NH_2), 8.09 ppm (1H, s, NH), and 9.27 ppm (1H, s, NH).

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