reaction mixture was stirred at room temperature for 0.5 h. The methanol was evaporated. The residue was dried and crystallized from ethylacetate. Recrystallization from 2-propanol yielded 0.3 g (55%) of colorless crystals with mp 93-95 °C. IR spectrum: 1730, 1745 (C=O), 3420 cm^{-1} (NH).

***N*-Methyl-*N*-(methoxycarbonylacetyl)-2-hydroxyethylamine (X).** A $CHCl_3$ solution (3 ml) of IX (0.2 g, 0.95 mmole) was treated with stirring with Et_3N (0.096 g, 0.09 mmole). The reaction mixture was kept at room temperature for 48 h. The $CHCl_3$ was evaporated. The residue was washed with ethylacetate. The solvent was evaporated. The residue was chromatographed in CH_3CN on an alumina column. Yield 0.09 g (54%) of light-yellow oil. TLC: R_f 0.51 (CH_3CN). IR spectrum: 1650, 1745 (C=O), 3450 cm^{-1} (OH).

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4-AMINOFURAZAN-3-HYDROXIMIC HALIDES

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The nitrile-N-oxide formed by dehydrohalogenation of 4-aminofurazan-3-hydroximic halides cyclizes to form 1,4,2,5-dioxadiazines, isoxazoles, isoxazolines, 1,2,4-oxadiazolines, tetrazoles, and 1,3,4-thiaoxazoles.

Nitrile-*N*-oxides, being very reactive compounds, are used to synthesize functionalized oximes and various heterocycles containing the C=N—O group (isoxazoles, 1,2,4- and 1,2,5-oxadiazoles, 1,2,4,5-oxatriazoles, 1,4,2-dioxazoles, 1,2,4-oxadiazines, 1,4,2,5-dioxadiazines, et al.) [1]. The possibility of preparing such a wide range of compounds from the nitrile oxides stimulates research in this area. Recently we prepared the first halides of a series of furazanhydroximic acids [2]. Hydroximic halides are direct precursors of nitrile oxides, into which they are converted by dehydrohalogenation. As a rule, dehydrohalogenation is effected by basic reagents (bases, amines) under very mild conditions, usually at temperatures near 0 °C. The high reactivity of acyl halides and nitrile oxides limits the number of functional groups that can be present in their molecules. Therefore, in particular, it was doubted that nitrile oxides containing a primary amine could exist [1].

Thus, the properties of 4-aminofurazan-3-hydroximic halides, which contain a primary amine on the furazan ring, are especially interesting. Obviously, the ability of two groups that are very reactive toward each other to exist simultaneously in the molecule is due to that fact that the reactivity of one of them is sharply decreased. It can be assumed that in this instance this is the amine group. The furazan ring is a strong electron acceptor and is known significantly to reduce the nucleophilicity of the amine in aminofurazans [3]. As a result, they difficultly react as ordinary amines. They do not form salts with dilute mineral acids. Obviously, they cannot cause oxime halides to lose hydrogen halide. However, the oximic halide in furazans I and II is still highly reactive. We have previously demonstrated that they readily react with amines to form *N*-substituted amidoximes [4].

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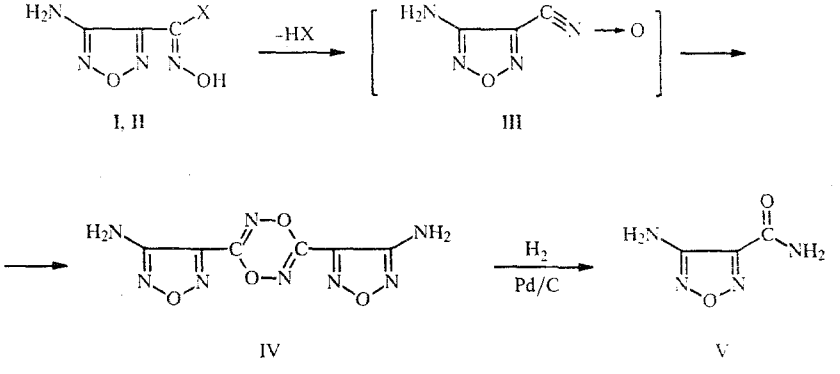
TABLE 1. Characteristics of IV-XVIII

Compound	Empirical formula	T_{mp}, °C	PMR spectrum; δ, ppm		Yield, %
			NH_2	other protons	
IV	$C_6H_4N_8O_4$	221...223	6,52	—	62
VI	$C_7H_{10}N_4O_3$	120...122	6,36	1,15 (3H, t, *J*=6,8 Hz, CH_3), 3,18 (1H, d.d, *J*=1,8 and 18,0 Hz, 4-CH), 3,65 (1H, d.q., *J*=9,5 and 6,8 Hz, CHO), 3,68 (1H, d.d, *J*=6,8 and 18,0 Hz, 4-CH), 3,78 (1H, d.q, *J*=9,5 and 6,8 Hz, CHO), 5,88 (1H, d.d *J*=1,8 and 6,8 Hz, 5-CH)	73
VII	$C_7H_8N_4O_4$	108...109	6,34	3,68 (1H, d.d, *J*=6,5 and 17,6 Hz, 4-CH), and 3,73 (3H, s, CH_3), 3,85 (1H, d.d, *J*=12,0 and 17,6 Hz, 4-CH), 5,41 (1H, d.d *J*=6,5 and 12,0 Hz, 5-CH)	69
VIII	$C_6H_5N_5O_2$	185...187	6,38	3,93 (1H, d.d, *J*=6,8 and 17,3 Hz, 4-CH), 3,99 (1H, d.d, *J*=10,6 and 17,3 Hz, 4-CH), 5,91 (1H, d.d, *J*=6,8 and 10,6 Hz, 5-CH)	78
IX	$C_{11}H_8N_4O_2$	213...215	6,38	7,49...8,02 (5H, m, C_6H_5), 7,62 (1H, s, CH)	73
X	$C_6H_6N_4O_3$	166...168	6,37	4,67 (2H, d, CH_2), 5,79 (1H, t, OH), 6,91 (1H, s, CH)	72
XI	$C_8H_{14}N_6O_2$	133...134	6,28	1,40 (6H, s, CH_3C), 2,60 (6H, s, CH_3N)	68
XII	$C_3H_3N_7O_2$	177...178	6,16	12,51 (1H, s, OH)	69
XIV	$C_3H_3N_7O_2$	182...183	6,58		71
XVI	$C_4H_3N_5O_2S$	> 300	6,50		59
XVII	$C_5H_5ClN_4O_3$	120...121	6,46	2,34 (3H, s, CH_3)	84
XVIII	$C_7H_7BrN_4O_4$	106...108	—	2,09 (3H, s, CH_3), 2,31 (3H, s, CH_3), 11,01 (1H, s, NH)	77

Note: Compound IV was recrystallized from dioxane; IX, from CH_3CN; XII, from H_2O; others, from 2-propanol.

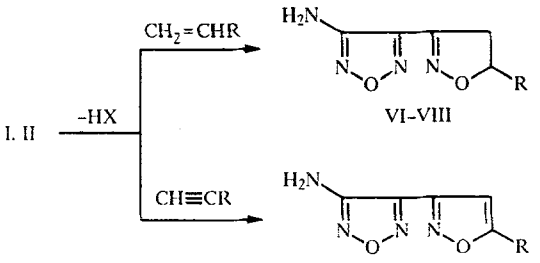
In continuation of our investigations, we have studied the reactions of I and II that give the cyclic derivatives. One of these reactions is the dimerization of the nitrile oxides. The nitrile oxide III, which is formed through dehydrohalogenation of I and II by Et_3N, is unstable and cannot be isolated pure since it immediately dimerizes.

The dimerization of nitrile oxides usually gives furoxans and much more rarely 1,4,2,5-dioxadiazines and 1,2,4-oxadiazoles. The ^{13}C NMR spectrum of the prepared dimer exhibits only three signals (135.9, 153.5, and 155.0 ppm). This indicates that the molecule is symmetric. Thus, the asymmetric furoxan and 1,2,4-oxadiazole structures in which all six C atoms are nonequivalent are excluded. The structure of 1,4,2,5-dioxadiazine IV is confirmed by the fact that reduction with H_2 on Pd produces 4-aminofurazan-3-carboxamide (V). Derivatives of 1,4,2,5-dioxadiazine are characteristically reduced with ring opening and formation of amides [5].



I X=Cl, II X=Br

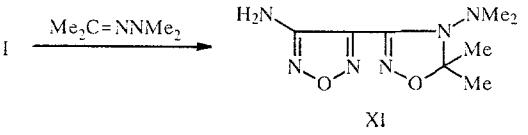
In the presence of compounds with double and triple C—C bonds, the nitrile oxide III reacts by cycloaddition to form the isoxazolines VI—VIII and the isoxazoles IX and X:



VI R=OEt, VII R=COOMe, VIII R=C≡N, IX R=Ph, X R=CH_2OH

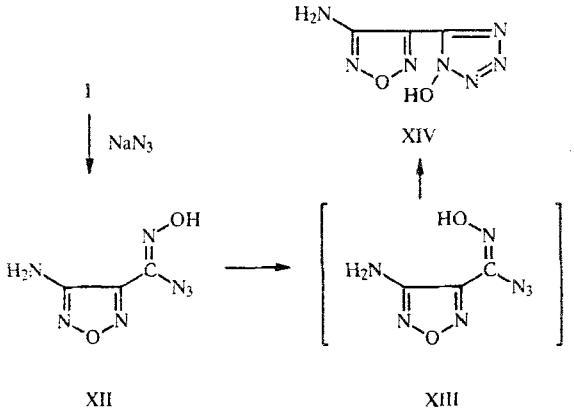
The cycloaddition reaction is regiospecific. In all instances, derivatives containing the R substituent at the 5-position of the isoxazole or isoxazoline ring are formed. This is consistent with the size of the chemical shifts for the heterocycle protons (Table 1). The protons of the isoxazoline ring in the PMR spectrum give an ABX system whereas the protons of the ethoxy group in VI give an ABX_3 system.

The nitrile oxide also readily adds to a C—N double bond. The reaction with acetone dimethylhydrazone under these conditions produces the 4,5-dihydro-1,2,4-oxadiazole with the dimethylamino group in the 4-position:



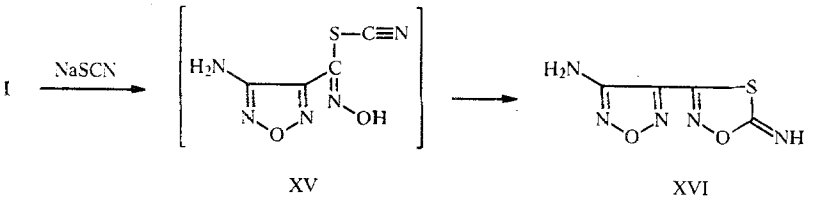
XI

Reactions of nitrile oxides with nucleophiles usually give acyclic compounds, the corresponding oximes. However, in certain instances these oximes can further cyclize. The reaction of I with sodium azide produced the oximic azide XII. Nucleophiles are known regiospecifically to add to nitrile oxides to form only the Z-oximes [6]. The Z-isomer of XII is stable over long periods. However, treatment with HCl in ether readily isomerizes it to the unstable E-oxime XIII, which cyclizes to the hydroxytetrazole XIV:



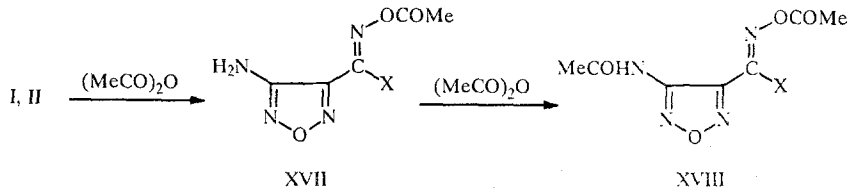
XII XIII

Apparently, the oxime XV is also an intermediate during the reaction of III with KSCN, which gives the 1,3,4-thiaoxazole derivative XVI as a final product:



XV XVI

All of the examined conversions demonstrate the high reactivity of the nitrile oxide toward addition and cycloaddition. However, the amino group in all instances is unaffected. The amino group does react during acetylation with acetic anhydride. The oxime is acylated first:



XVII

XVIII

XVII X=Cl, XVIII X=Br

EXPERIMENTAL

The ^1H (90 MHz) and ^{13}C (22.63 MHz) NMR spectra were taken on a Bruker WH-90 spectrometer and ^1H (360 MHz) spectra on a Bruker WH-360 spectrometer in DMSO-D_6 solution with TMS internal standard. IR spectra were recorded on a Perkin—Elmer 580B instrument in nujol.

Elemental analyses for C, H, and N agreed with those calculated. Yields and characteristics of the products are given in Table 1.

3,6-Di-(4-aminofurazan-3-yl)-1,4,2,5-dioxadiazine (IV). A CH_3CN solution (30 ml) of oximic halide I or II (0.01 g) was treated dropwise with stirring at 0-5 °C with a CH_3CN solution (10 ml) of Et_3N (2.02 g, 0.02 mole). The precipitate was filtered off after 20 min and washed with water. IR spectrum: 3460 and 3320 (NH_2), 1010 cm^{-1} (furazan).

Reduction of 3,6-Di-(4-aminofurazan-3-yl)-1,4,2,5-dioxadiazine (IV). A DMF solution (100 ml) of IV (2.0 g, 8 mmole) was reduced by H_2 at 30 °C and 3 atm using Pd/C as catalyst. The DMF was vacuum distilled after 6 h. Water was added to the residue. The product was filtered off and recrystallized from water. Yield 1.27 g (62%) with mp 174-175 °C (lit. 174-176 °C [7]). PMR spectrum: 6.31 (2H, br. s, NH_2), 8.02 and 8.38 ppm (1H each, s, s, NH_2). IR spectrum: 3445, 3330, and 3232 (NH_2), 1683 (C=O), 1008 cm^{-1} (furazan). ^{13}C NMR spectrum: 141.5 and 157.6 (furazan), 161.5 ppm (C=O).

Dihydroisoxazolylfurazans VI-VIII and Isoxazolylfurazans XI and X. An ethanol solution (20 ml) of oximic halides I or II (10 mmole) and the corresponding unsaturated compound (13 mmole) was treated dropwise with stirring at 10-15 °C with an aqueous (15 ml) solution of $NaHCO_3$ (1.09 g, 13 mmole). The precipitate was filtered off. The filtrate was evaporated under vacuum. The residue was combined with the precipitate and washed with water. The product was recrystallized.

4-Amino-3-(5-ethoxy-4,5-dihydroisoxazol-3-yl)furazan (VI). IR spectrum: 3459 and 3340 (NH_2), 1640 (C=N), 1010 cm^{-1} (furazan).

4-Amino-3-(5-ethoxycarbonyl-4,5-dihydroisoxazol-3-yl)furazan (VII). IR spectrum: 3471 and 3328 (NH_2), 1755 (C=O), 1012 cm^{-1} (furazan).

4-Amino-3-(5-cyano-4,5-dihydroisoxazol-3-yl)furazan (VIII). IR spectrum: 3461 and 3340 (NH_2), 1641 (C=N), 998 cm^{-1} (furazan).

4-Amino-3-(5-phenylisoxazol-3-yl)furazan (IX). IR spectrum: 3462 and 3320 (NH_2), 3130 (CH of the ring), 1011 cm^{-1} (furazan).

4-Amino-3-(5-hydroxymethylisoxazol-3-yl)furazan (X). IR spectrum: 3475 and 3360 (NH_2), 3240 (OH), 3130 (CH of the ring), 998 cm^{-1} (furazan).

3-(4-Aminofurazan-3-yl)-5,5-dimethyl-4-dimethylamino-4,5-dihydro-1,2,4-oxadiazole (XI). An acetone (20 ml) solution of acetone dimethylhydrazone (1.50 g, 15 mmole) and Et_3N (1.52 g, 15 mmole) was treated dropwise with stirring at 0-5 °C with an acetone (20 ml) solution of I (1.63 g, 10 mmole). The acetone was vacuum distilled after 20 min. Water was added to the residue. The product was filtered off. IR spectrum: 3460 and 3358 (NH_2), 1012 cm^{-1} (furazan).

4-Aminofurazan-3-hydroximic Azide (XII). An aqueous solution (10 ml) of NaN_3 (2.28 g, 35 mmole) was treated dropwise with stirring at 15-20 °C with an acetone (30 ml) solution of I (4.88 g, 30 mmole). The solvents were vacuum

distilled after 30 min. Water was added to the residue. The precipitate of the azide XII was filtered off and washed with water. IR spectrum: 3461 and 3322 (NH_2), 3248 (OH), 2169 (N_3), 986 cm^{-1} (furazan).

5-(4-Aminofurazan-3-yl)-1-hydroxytetrazole (XIV). An absolute ether solution (30 ml) of XII (3.1 g, 18 mmole) was saturated with HCl and kept for 24 h. The ether was vacuum distilled. The residue was treated with CH_2Cl_2. The tetrazole XIV was filtered off. IR spectrum: 3450 and 3330 (NH_2), 3200 (OH), 987 cm^{-1} (furazan).

3-(4-Aminofurazan-3-yl)-2-imino-1,3,4-thiaoxazole (XVI). An aqueous solution (10 ml) of KSCN (3.88 g, 40 mmole) was treated dropwise with stirring at 5-10 °C with an ethanol solution (20 ml) of I (1.63 g, 10 mmole). The precipitate was filtered off after 30 min. The solvents were vacuum distilled. Water was added to the residue. The precipitate of XVI was filtered off. IR spectrum: 3463 and 3325 (NH_2), 3250 (NH), 1670 (C=N), 999 cm^{-1} (furazan).

4-Aminofurazan-3-acetoximoyl Chloride (XVII). An acetic anhydride suspension (6 ml) of I (1.63 g, 10 mmole) was stirred at 40 °C until the solid completely dissolved. The reaction mixture was cooled. Water (40 ml) was added. The mixture was stirred for 20 min. The precipitate was filtered off. IR spectrum: 3475 and 3380 (NH_2), 1793 (C=O), 1118 cm^{-1} (furazan).

4-Acetamidofurazan-3-acetoximoyl bromide (XVIII). An acetic anhydride suspension (4 ml) of II (0.5 g, 2.4 mmole) was heated at 80 °C for 10 min. The reaction mixture was cooled. Water (20 ml) was added. The mixture was stirred for 20 min. The precipitate was filtered off. IR spectrum: 3229 (NH), 1808 (C=O), 1718 (C=O), 1020 cm^{-1} (furazan).

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