REACTION OF FUROXANENITROLIC ACIDS WITH NITROGEN TETROXIDE

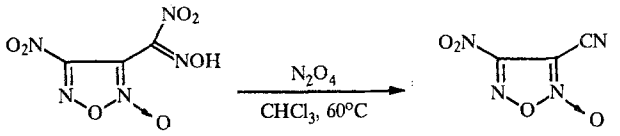
O. A. Rakitin, V. A. Ogurtsov, E. A. Khaibullina, T. I. Godovikova, and L. I. Khmel'nitskii

It has been found that the main direction of the reaction of furoxanenitrolic acids with N_2O_4 is the formation of the corresponding nitrile oxides and their subsequent conversions.

In a previous communication [1] we described the synthesis of the following furoxanenitrolic acids: 4-nitrofuroxane-3-nitrolic acid (I), furoxane-3,4-dinitrolic acid (II), and furoxane-4-nitrolic acid (III). Continuing this work, we investigated the reactivity of these compounds. It is known that the formation of new heterocyclic structures, starting with nitrolic acids, includes a stage of splitting out HNO_2 and the formation of a nitrile oxide, which subsequently interacts with compounds containing multiple bonds: C≡C [2], C≡N [3], N=N [4]. Therefore, the first step in our study was the determination of whether HNO_2 could be split out from the acids I-III.

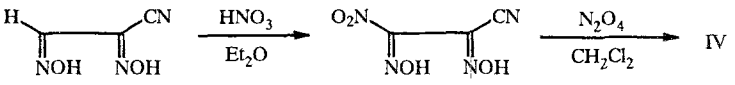
We had found previously that the elimination of HNO_2 from nitrolic acids and their conversions to nitrile oxides can usually be accomplished by rather mild heating [5]. However, the acids I and II proved to be rather rather stable substances, which are only partly decomposed when they are boiled in $CHCl_3$ or CH_3CN. A more thorough investigation of this reaction showed that nitriding and oxidizing agents (in particular nitrogen oxides) accelerate the decomposition of furoxanenitrolic acids. Therefore, we carried out a more detailed investigation of the reaction of compounds I-III with N_2O_4 (see Table 1). It had been shown previously [6] that in the case of arylnitrolic acids, this reaction leads to aryltrinitromethanes.

We established that the interaction of the nitrolic acid I with N_2O_4 in $CHCl_3$ at 60°C leads unexpectedly to 4-nitro-3-cyanofuroxane (IV):



I IV

Such a conversion of the nitrolo grouping to a nitrile grouping had not been reported previously. Therefore, in order to prove the structure of compound IV, we carried out its countersynthesis, starting with cyanoglyoxime (V) through the nitro derivative (VI), by means of scheme analogous to that used for obtaining 4-nitro-3-chlorofuroxane [7]:



V VI

The structure of the synthesized product was proven by means of elemental analyses and IR, mass, and NMR spectra, all of which were identical to those of compound IV obtained from the acid I.

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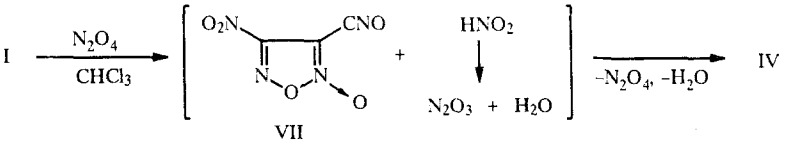
TABLE 1. Interaction of Furoxanenitrolic Acids I-III with N_2O_4

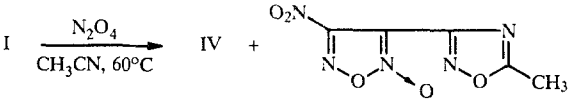
Original compound	Reaction conditions			Results of reaction		
	solvent	T, °C	time, h	product	R_f	yield, %
I	$CHCl_3$	60	6	IV	0,20	28
	CH_3CN	60...70	4	IV	0,20	14
				VIII	0,11	35
II	Dioxane	45	2	IX	0,20	35
	Dioxane	70	6	IV	0,20	27
III	$CHCl_3$	60	6	IV	0,20	26
	CH_3CN	60	7	IV	0,20	7
				VIII	0,11	19

The conversion of the nitrolo grouping to the cyano grouping proceeds through an intermediate nitrile oxide (VII), which is the usual product from HNO_2 elimination. The HNO_2 supplies N_2O_3, which removes an oxygen atom from compound VII to give a nitrile, as we had described previously for other nitrile oxides [8]:



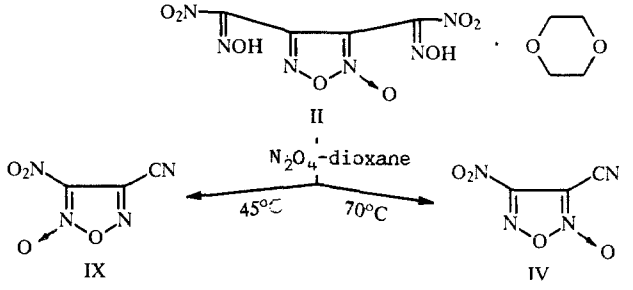
VII

For proof of the existence of the nitrile oxide VII in the reaction medium, we carried out the reaction of the acid I with N_2O_4 in CH_3CN. And in fact, from the reaction mixture, along with the nitrile IV, we isolated 4-nitro-3-(5-methyl-1,2,4-oxadiazolyl-3)furoxane (VIII), which is the product of interaction of the nitrile oxide VII with CH_3CN:



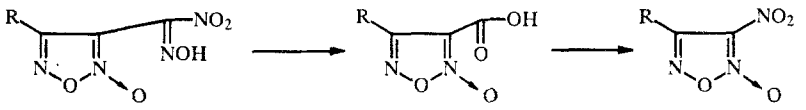
VIII

An investigation of the reaction of the furoxanedinitrolic acid II with N_2O_4 showed that the result of the reaction depends on the temperature. At 45°C, 3-nitro-4-cyanofuroxane (IX) is formed; but at 70°C, its more stable isomer IV is obtained, apparently as a result of conversion of the initially formed furoxane IX:



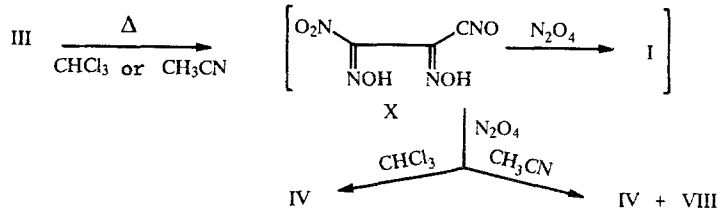
The replacement of the nitrolic acid grouping in position 4 by a cyano group proceeds in a manner similar to what was described above in the example of compound I. The conversion of this substituent in position 3 of the furoxane ring to a nitro

group apparently takes place through a reaction of destructive (or substitutive) nitration of furoxanecarboxylic acids. These acids may be obtained as a result of oxidative deoximation, as was described in [9] in the example of alkanenitrolic acids:



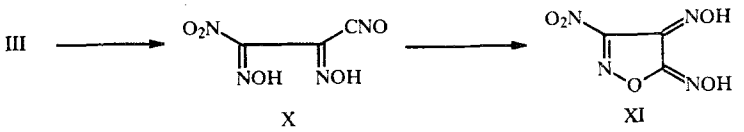
In the interaction of furoxane-4-nitrolic acid III with N_2O_4, we recovered the same products as in the case of the acid I: the nitrile IV (when the reaction was carried out in $CHCl_3$) or a mixture of compounds IV and VIII (in CH_3CN).

The conversions apparently proceed in the following manner: First, the acid III is opened, forming the nitrile oxide X, which, interacting with N_2O_4, is converted to nitrofuroxanenitrolic acid I, as was described previously for other α-hydroxyiminonitrile oxides [10], after which the acid I reacts with N_2O_4 in the same manner as described above:

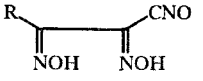


In order to establish the presence of the nitrile oxide X in the reaction medium, we studied the isomerization of the acid III in solution in CH_2Cl_2. The IR spectrum of this solution exhibited a band at 2295 cm^{-1} ($\nu_{C=N-O}$) providing evidence of the presence of the nitrile oxide X; the intensity of this band increased during the course of one hour. We also observed the gradual disappearance of the band at 1635 cm^{-1} corresponding to the stretching vibration of the C=N bond of the furoxane ring. Gradual disappearance of the nitrile oxide X from the solution was accelerated considerably by adding a small quantity of H_2O. Thus, in solutions in an organic solvent, the acid III is isomerized to the nitrile oxide X. In the presence of N_2O_4, the nitrile oxide X is further converted to the oxide I.

If the isomerization of compound III is performed in the absence of N_2O_4, the oxide X that is formed undergoes intramolecular cyclization to a new isoxazole ring (compound XI); the highest yield of XI is obtained when the reaction is performed in water:



Two oximes of the isoxazole series have been described in the literature: 4,5-bis(hydroxyimino)isoxazole [11] and 3-hydroxyiminomethyl-4,5-bis(hydroxyimino)isoxazole [12]. In both cases, the mechanism postulated for the formation of these compounds includes a stage of formation and intramolecular cyclization of α,β-bis(hydroxyimino)propionitrile oxides:



R = H [11], R = CH=NOH [12]

In our case, formation of the analogous nitrile oxide X has been confirmed for the first time, and it has been proven that this compound is an intermediate in the synthesis of bis(hydroxyimino)isoxazoles.

EXPERIMENTAL

The IR spectra were taken in a Specord instrument in KBr tablets, the mass spectra in a Varian CH-6 instrument. The ^1H and ^{13}C NMR spectra were obtained in a Bruker AM-300 instrument (300 and 75.5 MHz, respectively), in $(CD_3)_2CO$, internal standard TMS. The melting points were determined in Boetius apparatus with a heating rate of 4°C/min close to the melting point.

For compounds IV, VIII, IX, and XI, the elemental analyses for C, H, and N matched the calculated values.

Reaction of Furoxanenitrolic Acids with N_2O_4 (General Procedure). To a solution of 4 mmoles of the nitrolic acid (or the complex of furoxane-3,4-dinitrolic acid with dioxane) II in 10 ml of the solvent indicated in Table 1, a solution of 1.4 ml (24 mmoles) of N_2O_4 in 10 ml of the same solvent was added dropwise. The mixture was held (temperature and time indicated in Table 1), after which the solvent was driven off; then 50 ml of CH_2Cl_2 was added to the residue, and the solution was washed with water and dried over $MgSO_4$. After driving off the solvent, the residue was chromatographed in a column with L 40/100 silica gel (eluent 2:1 CCl_4—$CHCl_3$).

4-Nitro-3-cyanofuroxane (IV, $C_3N_4O_4$), mp 48-49°C. IR spectrum, cm^{-1}: 2265 (C≡N), 1675 (C=N), 1590 and 1363 (NO_2). M^+ 156. ^{13}C NMR spectrum, δ, ppm: 95.0 (C—CN), 104.7 (C=N), 157.6 (C—NO_2).

4-Nitro-3-(5-methyl-1,2,4-oxadiazolyl-3)furoxane (VIII, $C_5H_3N_5O_5$), bp 112°C/10 mm Hg, n_D^{20} 1.5341. IR spectrum, cm^{-1}: 1650 (C=N), 1575 and 1335 (NO_2). M^+ 213. ^1H NMR spectrum, δ, ppm: 2.72 (CH_3).

3-Nitro-4-cyanofuroxane (IX, $C_3N_4O_4$), mp 50-52°C. IR spectrum, cm^{-1}: 1675 (C=N), 1560 and 1350 (NO_2). M^+ 156. ^{13}C NMR spectrum, δ, ppm: 106.7 (C=N), 126.5 (C—NO_2), 130.3 (C—CN).

Nitrocyanoglyoxime (VI) $C_3H_2N_4O_4$). To a suspension of 2.34 g (20 mmoles) of cyanoglyoxime [13] in 50 ml of Et_2O, 11 ml (50 mmoles) of 25% HNO_3 was added dropwise with stirring. After 3 h, the organic layer was separated, washed with water, and dried over $MgSO_4$. Then the solvent was driven off, and 5 ml of CF_3COOH was added to the residue. The precipitated product was filtered off, washed with cold CF_3COOH, and dried. Obtained 0.95 g (30%) of VI, mp 55-56°C. IR spectrum, cm^{-1}: 3450 (OH), 2260 (C≡N), 1665 (C=N), 1590 and 1360 (NO_2).

Oxidation of Oxime VI. To a suspension of 0.3 g (1.9 mmoles) of the oxime VI in 7 ml of CH_2Cl_2, a solution of 0.25 ml (4 mmoles) of N_2O_4 in 4 ml of CH_2Cl_2 was added dropwise with stirring. After 2 h, the solvent was driven off, 15 ml of H_2O was added to the residue, and the product was extracted with CH_2Cl_2. The extract was dried over $MgSO_4$ and the solvent was driven off, obtaining 0.28 g (94%) of the furoxane IV, mp 48-49°C.

Dioxime of 3-Nitroisoxazole-4,5-dione (XI, $C_3H_2N_4O_5$). To a solution of 0.7 g (4 mmoles) of the acid III in 10 ml of CH_2Cl_2, 2 ml of water was added while stirring. After 3 h, the aqueous layer was taken off and extracted with ether. The extract was washed with water and dried over $MgSO_4$. After evaporating the solvent, obtained 0.67 g (96%) of the dioxime XI, mp 126°C. IR spectrum, cm^{-1}: 3270 (OH), 1545 and 1388 (NO_2). M^+ 174. ^1H NMR spectrum, δ, ppm: 6.43 (OH). ^{13}C NMR spectrum, δ, ppm: 161.76 (C—NO_2), 149.17 (O—C=NOH), 134.73 (C=NOH).

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