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An unexpected transformation of 3,4-bis(isocyanato)furoxan into 3,3′-bi(1,2,4-oxadiazol-5-one)

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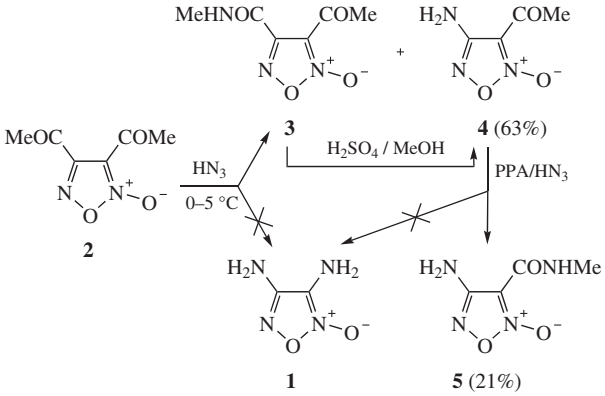
A transformation of 3,4-bis(isocyanato)furoxan into 3,3′-bi(1,2,4-oxadiazol-5-one) by the action of water was unexpectedly found. The structure of the product was established by spectroscopic and X-ray methods; a mechanism of the transformation is suggested.

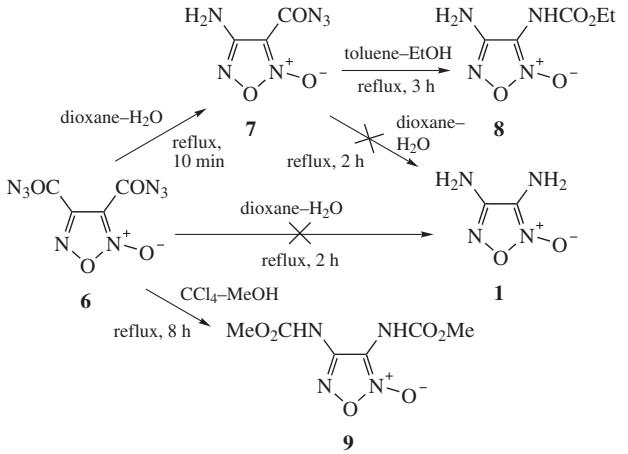
3,4-Diamino-1,2,5-oxadiazole 2-oxide (3,4-diaminofuroxan) **1** is so far unknown contrary to well-known and stable diaminofurazan,[1] although a large number of both 3- and 4-monoaminofuroxans with different substituents at the second carbon atom of the furoxan ring have been described.[2–4] The most general method for the preparation of 3-amino-4-arylfuroxans is oxidation of the *amphi*-form of 1-amino-2-arylglyoximes, whereas 4-amino-3-arylfuroxans are obtained by thermal isomerization of 3-amino isomers.[5] However, amino glyoximes with non-aromatic substituents (Me, NH_2, NHAlk and H), exist only in the *trans*-form and are not capable of generating the corresponding furoxans by oxidation of the glyoxime fragment.[6,7] The *trans*-position of oxime groups in these amino glyoximes is most likely to be preferable due to the appearance of strong H bonds.

Previously, we developed two new methods for the preparation of aminofuroxans based on sextet rearrangements at nitrogen atoms: the Schmidt rearrangement of methylfuroxanyl ketones[8] and the Curtius rearrangement of azidocarbonyl furoxans.[9] We showed that only one of the two MeCO groups in 3,4-diacetylfuroxan **2** underwent the Schmidt rearrangement even in an excess of HN_3 in $CHCl_3$ (or CH_2Cl_2) in the presence of concentrated H_2SO_4, to result in a mixture of expected 3-acetyl-4-(acetylamino)furoxan **3** and its hydrolysis product, 3-acetyl-4-aminofuroxan **4**. Then, a method to synthesize amine **4** by the hydrolysis of amide **3** directly in the obtained mixture was developed. The 3-acetyl group in compound **4** underwent the Schmidt rearrangement in the presence of polyphosphoric acid (PPA) as a catalyst; however, only the second possible product of the rearrangement, the *N*-methylamide of 4-aminofuroxan-3-carboxylic acid **5**, was isolated in a low yield instead of expected diaminofuroxan **1**, although initial amine **4** was completely consumed in the reaction (Scheme 1).



Scheme 1

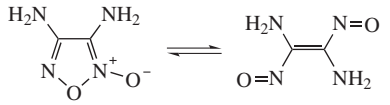
A possible use of the Curtius rearrangement for obtaining diaminofuroxan **1** was shown for model 3,4-bis(azidocarbonyl)-furoxan **6** by heating in a dioxane–water mixture at 80 °C.[9] The reaction was completed in 30 min; however, 4-amino-3-azidocarbonylfuroxan **7**, the product of the rearrangement of only one azidocarbonyl group, was obtained. The second azidocarbonyl group underwent the Curtius rearrangement under more forcing conditions by refluxing in a toluene–EtOH mixture for 3 h to generate 4-amino-3-(ethoxycarbonylamino)furoxan **8**. The Curtius rearrangement of 3,4-bis(azidocarbonyl)furoxan **6** in a CCl_4–MeOH mixture for 8 h resulted in 3,4-bis(methoxycarbonylamino)furoxan **9**. However, the heating of compounds **6** or **7** in dioxane–water mixture at 100 °C accomplished the overall decomposition of both initial compounds, but once more diaminofuroxan **1** was not obtained (Scheme 2).



Scheme 2

To estimate the stability of diaminofuroxan **1** in the gas phase, comparative quantum-chemical calculations were performed for this compound and for its open form **1′** by MP2/6-311G.†[10] The calculations showed that, taking into account zero-point vibration, compound **1** was 14.69 kcal mol^{-1} more stable than its open form **1′**. An analysis of the geometry in the gas phase

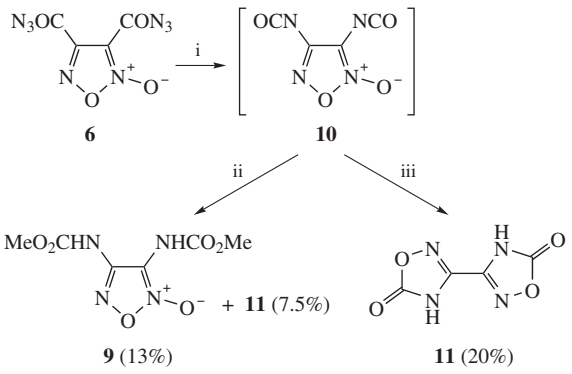
indicated that both amino groups in compound **1** were pyramidal. In spite of considerable lengthening of the O(1)–N(2) bond (1.444 Å), its value matches the range of values typical of the known furoxan derivatives with primary and secondary amino groups.[11] The low stability of diaminofuroxan **1** in solution found experimentally is probably related to the solvation effects that stabilize open form **1′**.



1 **1′**

Although it appears from the experimental data that 3,4-diaminofuroxan **1** is unstable both in the presence of acids (Schmidt rearrangement) and at increased temperature (Curtius rearrangement), but yet it could be stable at ambient temperature and in the absence of acids. Therefore, in this research, we attempted to synthesize a precursor of compound **1**, 3,4-bis(isocyanato)furoxan **10**, by the Curtius rearrangement of 3,4-bis(azidocarbonyl)furoxan **6** at an elevated temperature followed by cooling the reaction mixture and treating with water at room temperature.

For the synthesis of compound **10**, 3,4-bis(azidocarbonyl)furoxan **6** was refluxed in dry CCl_4 for 2 h in an argon flow and then the reaction mixture was cooled to room temperature.



Scheme 3 *Reagents and conditions*: i, CCl_4, reflux, 2 h; ii, MeOH, 20 °C; iii, H_2O, 20 °C.

† IR spectra were measured on a UR-20 spectrometer; ^1H and ^{13}C NMR spectra were recorded on a Bruker AM300 (300 MHz for ^1H and 75.5 MHz for ^{13}C) spectrometer ($CDCl_3$ was used as the internal standard). ^{13}C NMR spectra were recorded under proton decoupling conditions. Mass spectra were measured on a Finnigan MAT INCOS-50 instrument. Compound **12** exhibited satisfactory elemental analyses. TLC was carried out on Silufol UV-254 plates. Melting points were measured on a Gallenkamp instrument (Sanyo). 3,4-Bis(azidocarbonyl)furoxan **10** was synthesized according to ref. 9.

3,3′-Bi(1,2,4-oxadiazol-5-one) **11**: a solution of 25.1 g (112 mmol) of 3,4-bis(azidocarbonyl)furoxan **10** in 500 ml of CCl_4 dried over P_2O_5 was refluxed for 2 h in light current of argon. A formation of different gases was fixed during refluxing. Then, the reaction mixture was cooled to room temperature and 6 ml of water and 100 ml of acetone were added. The formed precipitate was filtered, dissolved in 200 ml of MeOH and after scavenging filtration the solvent was evaporated to formation of thick mass. The precipitate was filtered, washed with small amount of MeOH and dried in a vacuum desiccator. A small amount of product was isolated from mother solutions. The total yield of compound **11** was 19.6%; mp > 320 °C, R_f 0.36 [eluent $CHCl_3$–EtOAc, 1:1 (v/v)]. ^1H NMR ([$^2H_6$]DMSO) δ: 7.2 (br. s, 2H, NH). ^{13}C NMR ([$^2H_6$]DMSO) δ: 147.4 [C(3)], 159 (C=O). IR (ν/cm^{-1}): 732, 756, 788, 893, 939, 989, 1045, 1069, 1097, 1177, 1259, 1278, 1353, 1442, 1490, 1546, 1590, 1748, 1773, 1804, 2760, 3000, 3070, 3150, 3250, 3340, 3433, 3468. MS, *m*/*z* (%): 170 (100), 140 (11), 129 (31), 128 (22), 112 (51), 84 (20), 53 (24), 46 (74.5), 45, 44, 43 (> 100). UV (MeOH, ν_{max}/nm): 215.

Various gases were released in the course of the reaction. To identify the released gases at the thermolysis of compound **6**, we carried out this reaction in an IR-20 spectrometer (a CaF_2 cell; thickness of 0.6 mm) in the same solvent at 65 °C during 2 h. The brown NO_2 release was observed during the ongoing reaction and in the IR spectrum the emergence of absorption bands of different gaseous products and a gradual increase in their intensity [1740 (N_2O_4),[12] 1810, 1840 (NO),[12] 2220 (N_2O),[12] 2345 (CO_2)[13] cm^{-1}] were detected. Simultaneously, the absorption bands of the azide groups (2135–2155 cm^{-1}) disappeared and absorption bands of the NCO groups (1398, 2258, 2280 cm^{-1}) appeared. These were evidently formed by the thermal decomposition of the 3,4-bis(isocyanato)furoxan **10** generated.

To support the existence of 3,4-bis(isocyanato)furoxan **10** upon completing the rearrangement of compound **6**, the reaction mixture was treated with MeOH after cooling. In this case, the expected 3,4-bis(methoxycarbonylamino)furoxan **9** in 13% yield, and a new compound 3,3′-bi(1,2,4-oxadiazol-5-one) **11** in 7% yield, were isolated by preparative TLC.‡ When the reaction mixture was treated with water instead of MeOH, compound **11** was isolated in 20% yield (Scheme 3).

The structure of compound **11** was established from the elemental analysis and spectral characteristics (IR, ^1H and ^{13}C NMR spectroscopy and mass spectrometry), and additionally by X-ray data. The physicochemical characteristics of compound **9** were in agreement with those of the compound described in the literature.[9]

In crystal **11**, the molecule occupies a special position, the center of symmetry, which leads to a coplanar disposition of the 1,2,4-oxadiazole rings. The bond lengths and angles in **11** are similar to those of 3,4-diphenyl-1,2,4-oxadiazol-5-one.[14] Molecules of **11** in the crystal are assembled into corrugated layers by strong N–H···O bonds (N···O 2.750 Å). These associates are interconnected into a 3D framework by strong O···π interactions between the C=O group and O(2) and N(4) atoms of the ring [O(6)···O(2) and O(6)···N(4) are 2.963(1) and 3.040(1) Å] (Figure 1).

The formation of compound **11** was unexpected. In view of its low yield and the formation of a considerable amount of gases concurrent with the Curtius rearrangement of 3,4-bis(azidocarbonyl)furoxan **6**, we assume that 3,4-bis(isocyanato)furoxan **10** also has low thermal stability. This fact is in conformity with literature data on the low thermal stability of furoxans with electron-withdrawing substituents.[15] Nevertheless, compound **10** did not fully decompose to gases. The formation of bisurethane **9** testifies the presence of 3,4-bis(isocyanato)furoxan **10** in the reaction mixture. Evidently, this amount of compound **10** served as a precursor of compound **11** after treatment of the reaction residue with water.

‡ *Crystallographic data*. Crystals of **11** ($C_4H_2N_4O_4$, M = 170.10) are monoclinic, space group $P2_1/n$, at 100 K: a = 4.7465(4), b = 5.4001(4) and c = 11.6671(9) Å, β = 95.912(6)°, V = 297.46(4) Å^3, Z = 2 (Z' = 0.5), d_{calc} = 1.899 g cm^{-3}, μ(MoKα) = 1.72 cm^{-1}, F(000) = 172. Intensities of 3698 reflections were measured with a Smart APEX II CCD diffractometer [λ(MoKα) = 0.71072 Å, ω-scans, $2\theta < 60°$] and 873 independent reflections [R_{int} = 0.0253] were used in further refinement. The structure was solved by a direct method and refined by the full-matrix least-squares technique against F^2 in the anisotropic–isotropic approximation. Hydrogen atoms were located from the Fourier synthesis and refined in the isotropic approximation. For **11** the refinement converged to wR_2 = 0.0770 and GOF = 1.021 for all independent reflections [R_1 = 0.0336 was calculated against F for 748 observed reflections with $I > 2\sigma(I)$]. All calculations were performed using SHELXTL PLUS 5.0.

CCDC 729414 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2009.

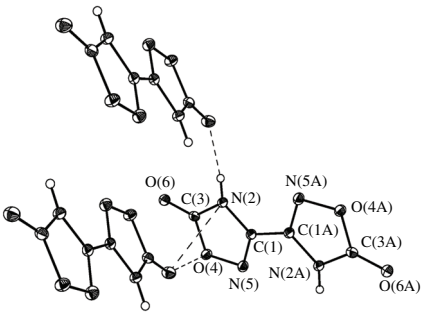
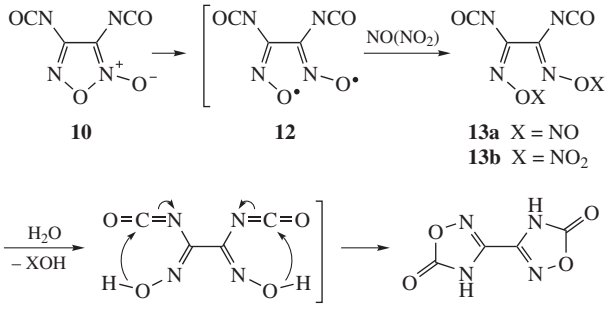


Figure 1 General view of **11** and a fragment of crystal packing illustrating the intermolecular contacts in crystal. The principal bond lengths (Å): C(1)–N(5) 1.297(1), C(1)–N(2) 1.362(1), C(1)–C(1A) 1.451(2), N(2)–C(3) 1.361(1), C(3)–O(6) 1.210(1), C(3)–O(4) 1.370(1), O(4)–N(5) 1.425(1).

A hypothetic pathway of the transformation is presented in Scheme 4. It is known[16,17] that the weakest bond in the furoxan ring is O(1)–N(2). This bond was probably broken on heating to result in biradical **12**, which could enter a reaction with NO or NO_2 identified at the thermal decomposition of compound **10** to generate compound **13a** or **13b**. They were apparently hydrolysed by treatment with water to 1,2-diisocyanatoglyoxime **14**, which was cyclized to the bicyclic compound **11**. The emergence of compound **11** in 7% yield at reaction mixture treatment with MeOH may be explained by the presence of a small water amount in MeOH. As a whole, the results allowed us to conclude that 3,4-diaminofuroxan **1** is unstable not only at high temperature or in the presence of acids but also under neutral conditions at room temperature.



10 **12** **13a** X = NO **13b** X = NO_2 **14** **11**

Scheme 4

In an attempt to understand extremely low stability of diaminofuroxan **1**, we looked at the known data regarding the furoxan ring structure. The furoxan ring is capable of tautomerism with transfer of the *N*-oxide oxygen atom from one nitrogen atom to another where the rate of isomerization of one or other isomer depends on the nature of the substituents at the 3- or 4-position of the furoxan ring.[16,17] The tautomerism passes through the open form – a dinitrosoethylene intermediate (*e.g.*, **1′**). A tendency to occupy the 4-position (the furazan side of the molecule) is expressed especially clearly in amino and alkoxy groups. In particular, 3-aminofuroxans with Ph or Me substituents at the 4-position transform easily and completely to the corresponding 4-amino isomers; UV irradiation is necessary for the reverse reaction. This phenomenon could be caused by the presence of the *N*-oxide oxygen atom in the furoxan molecule and a combination of inductive and mesomeric effects of the substituents. The *N*-oxide oxygen atom creates a notable negative charge on the C(3)-carbon atom of the furoxan ring.[18,5] Since electron-withdrawing *–I* effect of the amino group is weaker than its electron-donating *+M* effect, one may suppose that the latter should be opposed by the higher electronic density at the C(3) atom and, therefore, the amino group should occupy the furazan side of the molecule. Where both substituents are amino groups (3,4-diaminofuroxan **1**), the open form **1′** (or any another form), evidently proved to be more stable than the cyclic one in solution due to the solvation effects.

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