Novel synthesis of 3,4-dicyanofuroxan

Tat'yana M. Mel'nikova, Tat'yana S. Novikova, Lenor I. Khmel'nitskii and Aleksei B. Sheremetev*

N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 119992 Moscow, Russian Federation.
Fax: +7 095 135 5328; e-mail: sab@cacr.ioc.ac.ru

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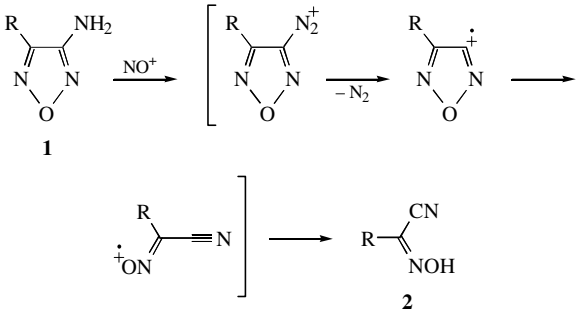
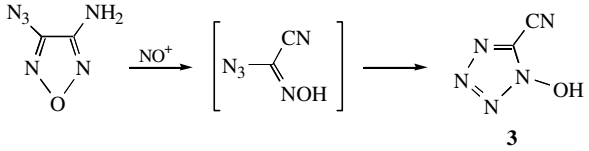
3,4-Dicyanofuroxan was synthesised by diazotization of aminofurazans bearing the second substituent that can be eliminated as a cationic species.

Reactions of aminofurazans **1**, where R = alkyl or (hetero)aryl, with nitrosating agents is known to produce α-hydroxyiminoacetonitrile derivatives **2**.[1] The formation of acyclic products **2** has been attributed to the initial elimination of dinitrogen from the diazonium cation, the migration of a cationic centre with ring cleavage and the trapping of a proton from the medium.



Despite the relative ease of this cleavage reaction, its synthetic potential appears to be unexplored. To the best of our knowledge, only a single example of its effective utilization for preparation of 1-cyano-2-hydroxytetrazole **3** was reported.[2]



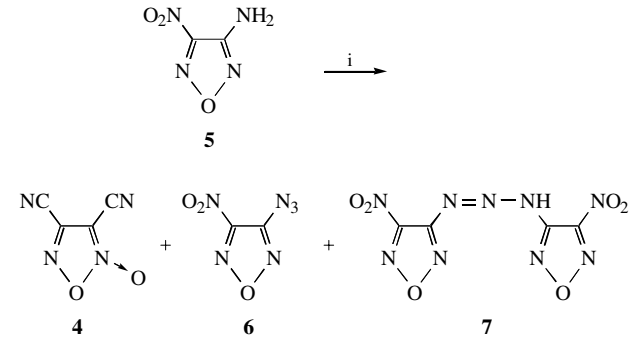
We believed that the diazotization reaction can be a versatile route to heterocyclic compounds *via* a ring opening/reclosure strategy.

Here, we demonstrate that 3,4-dicyanofuroxan **4** can be prepared *via* diazotization of aminofurazans bearing the second substituent that can be eliminated as a cationic particle.

The treatment of 3-amino-4-nitrofurazan **5**[3] with 3–6 equivalents of $NaNO_2$ in H_2SO_4/AcOH at 30–35 °C afforded furoxan **4**† in 4–8% yield and an additional water-insoluble product, 3-azido-4-nitrofurazan **6**,† in 2–5% yield. Pure compound **4** was obtained by preparative chromatography on silica gel. However, the diazotization of **5** resulted in water-soluble triazene **7**† (59–77%) as a principal product (Scheme 1).

The reaction of 3-aminofurazancarboxylic acid **8**[7] under similar conditions‡ afforded furoxan **4** as a single water-insoluble product in 22% yield (Scheme 2).

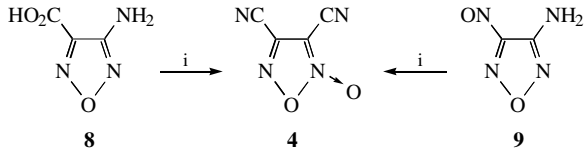
The most successful diazotization approach to compound **4** appears to be a similar reaction‡ of readily available 3-amino-4-nitrosofurazan **9**,§ in which **4** was obtained in 72% yield after



Scheme 1 *Reagents and conditions*: i, $NaNO_2/H_2SO_4$, **5** in AcOH, 30–35 °C, 1–2 h.

1 h. No other products were detected. Moreover, when this reaction was carried out in the presence of a solvent able to extract product **4** but not dissolving starting compound **9** (for example, CH_2Cl_2–pentane, 1:1), pure **4** was isolated in 91% yield.

The mechanism for the formation of **4** is proposed in Scheme 3. The reaction proceeds *via* dinitrogen elimination from diazonium cation **10** to give labile furazan cation **11**. Calculations¶ suggest that in **11** cleavage of N–O bond nearer to the carbocation centre, would be preferred. This results in acyclic cation **12**. The intermediate is stabilised by elimination of a cationic species (NO_2^+ from **5**, H^+ and CO_2 from **8** or NO^+ from **9**) to form cyanogen mono-*N*-oxide **13**. The dimerization of nitrile oxide **13** produced target furoxan **4**.††



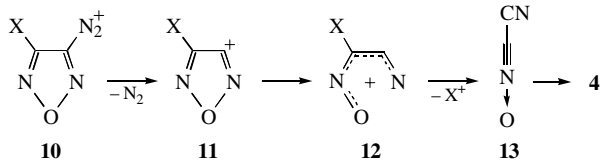
Scheme 2 *Reagents and conditions*: i, $NaNO_2/H_2SO_4$, **8** or **9** in AcOH, 30–35 °C, 1–2 h.

† Compounds **4**,[4] **6**,[5] and **7**[5,6] corresponded to materials described previously.

‡ *General procedure*. Sodium nitrite (15 mmol) was added to conc. H_2SO_4 (90 mmol) at 0–5 °C; then, a solution of an aminofurazan (3–10 mmol) in AcOH (~10 ml) was added dropwise at room temperature. After stirring at 30–35 °C for 1–2 h and cooling to room temperature, the reaction mixture was poured into CH_2Cl_2–H_2O. The organic layer was washed and dried over Na_2SO_4. After the removal of the solvent, the residue was purified by sublimation. Furoxan **4** was obtained as off-white flakes, mp 42–42.5 °C (lit.,[4] 42 °C).

§ *The synthesis of 3-amino-4-nitrosofurazan* **9** was carried out by a modification of the procedure reported for the synthesis of other nitrosofurazans.[8] To a mixture of benzene (200 ml) and 27.5% H_2O_2 (145 ml, 1290 mmol) at 5–10 °C, $Na_2WO_4 \cdot 2H_2O$ (16.5 g, 50 mmol) (in small portions) and then H_2SO_4 (10 ml, 180 mmol) were added. 3,4-Diaminofurazan (5 g, 50 mmol) was added slowly, and the resulting mixture was stirred at 10–15 °C for 1.5 h. The green organic layer was separated. An additional portion of benzene (100 ml) was introduced. The emulsion was stirred at room temperature for 1 h, and the organic layer was separated. The green extracts were combined, washed and dried over Na_2SO_4. The solvent was removed on a rotary evaporator, and the residue was purified by sublimation to provide 4.92 g (86.4%) of dimeric nitroso compound **9** as a khaki solid: mp 79–80 °C; UV-VIS (CCl_4, λ_{max}/nm): 750. IR (KBr, ν/cm^{-1}): 3439, 3335, 1639, 1490, 1420, 1310–1290, 1120, 1020, 890, 780. Found (%): C, 20.97; H, 1.91; N, 49.01. Calc. for $C_4H_4N_8O_4$ (%): C, 21.06; H, 1.76; N, 49.12.

¶ To estimate the strength of chemical bonds, we calculated the enthalpies of dissociation by semi-empirical quantum-chemical methods (MOPAC code).



10 **11** **12** **13**

Scheme 3

3,4-Dicyanofuroxan **4** is an important building block in organic synthesis,[4,9–15] and exhibits interesting biological and pharmacological properties, for instance, as a vasodilator.[16] It can be used as an ingredient of explosives[17] and rocket propellants.[11,18] Previously, compound **4** was prepared by oxidation of dicyanoglyoxime,[12] by treatment of cyanoacetic acid with nitrating mixtures,[9,17] and by dehydration of 3,4-bis-(hydroxyiminomethyl)furoxan.[19] Although these reactions are effective, alternative processes with other precursors may be very useful.

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†† The synthesis of **4** by dimerization of **13** was discussed previously.[9,10]

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