Novel synthesis of 3,4-dicyanofuroxan

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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 -hydroxyimino-acetonitrile 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 NaNO₂ in H₂SO₄/AcOH at 30–35 °C afforded furoxan 4^{\dagger} in 4–8% yield and an additional water-insoluble product, 3-azido-4-nitrofurazan 6^{\dagger} 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^{\dagger} (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^{\ddagger} 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 CO₂ 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, NaNO₂/H₂SO₄, 8 or 9 in AcOH, 30–35 °C, 1–2 h.

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

 $^{^{\}dagger}$ Compounds 4,4 6,5 and 75.6 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 CH₂Cl₂–H₂O. The organic layer was washed and dried over Na₂SO₄. 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% H₂O₂ (145 ml, 1290 mmol) at 5-10 °C, Na2WO4·2H2O (16.5 g, 50 mmol) (in small portions) and then H₂SO₄ (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 Na₂SO₄. 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 (CCl₄, 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.



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 explosives¹⁷ 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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