

One-pot synthesis of 4,4'-diamino-3,3'-bifurazan

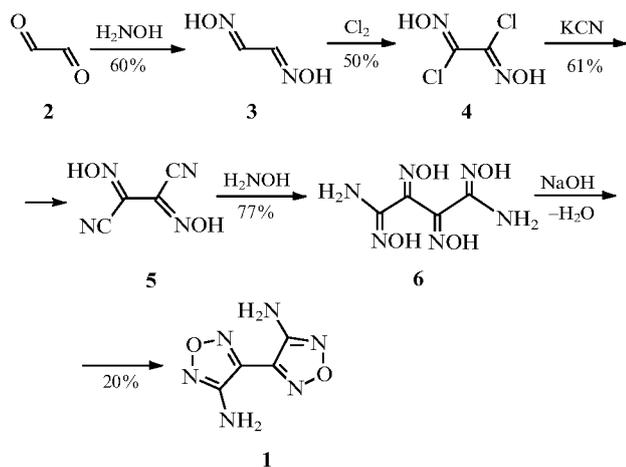
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The title compound **1** has been synthesized by a one-pot procedure starting from 3,4-di(hydroximinomethyl)furoxan **7** and hydroxylamine, with pH increasing over the course of the reaction from 1 to 10.

Aminofurazans are well known for their usage as precursors to biologically active compounds and energetic materials. Some methods of synthesis and properties of these useful compounds have been reviewed by Andrianov and Ereemeev.¹ The most common syntheses of aminofurazans involve the initial preparation of aminoglyoximes and their subsequent intramolecular base-catalysed condensation. A limited set of aminofurazans is available, largely because no satisfactory general route for the synthesis of aminoglyoximes appears to have been developed, as well as the extreme conditions required for their dehydration to aminofurazans.

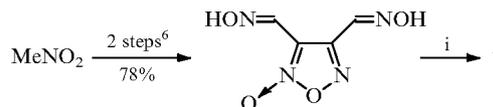
In the course of our recent work² on the design, synthesis and investigation of functionalized furazans, we were interested in the synthesis of 4,4'-diamino-3,3'-bifurazan **1** which was a precursor for some of our target molecules. Earlier, Coburn reported a multistep, low-yield procedure for the synthesis of **1**[†] starting with dichloroglyoxime synthesized from glyoxal (Scheme 1). It should be noted that the overall yield starting from commercially available glyoxal **2** was only about 3%, and some intermediate products and reagents were extremely toxic. There are considerable difficulties that must be overcome for this method to be practical.



Scheme 1

We therefore sought a straightforward and simple method for the synthesis of **1**. One intriguing possibility is use of the Boulton-Katritzky rearrangement.⁴

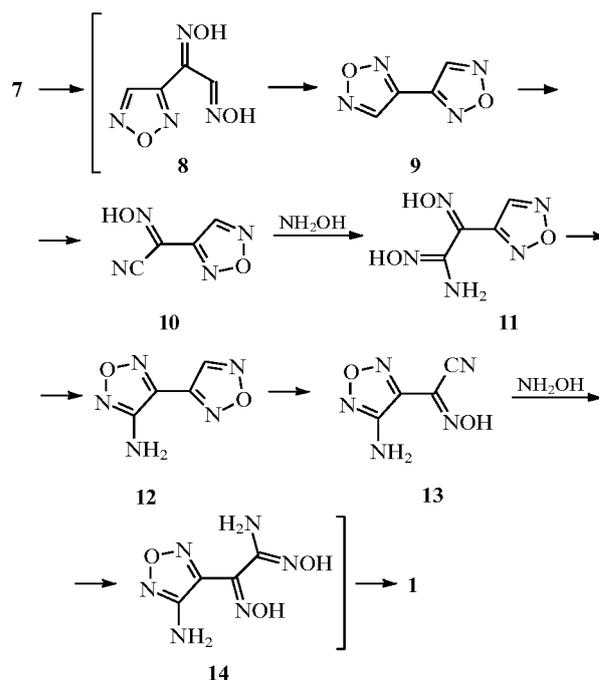
In this communication we elaborate a new, one-pot method for the preparation of **1**. The strategy is based on the known ability of 1,2,5-oxadiazoles possessing an oxime group in the side chain to undergo this rearrangement⁴ as well as the transformation of monosubstituted furazan into aminoglyoximes with hydroxylamine.⁵ We utilized readily available 3,4-di(hydroximinomethyl)furoxan **7** as the key precursor in the investigation.^{6,7} A proposed pathway to **1** is outlined in Scheme 2.



Scheme 2 Reagents and conditions: i, NH₂OH·HCl (15 mol), pH 1→10, 45 °C→reflux, 4 h.

We have found that slow addition of an aqueous solution of KOH to a suspension of **7** and a hydroxylamine salt in aqueous DMSO, with stirring and heating, results in the formation of **1**. The product was separated by a simple filtration after cooling. The yield of **1**[†] was 18% (from **7**), and 14% reckoning up commercially available nitromethane. Two by-products, 3-aminofurazancarboxylic acid⁸ (10%) and furazandicarboxylic acid⁹ (7%), can be isolated if required from the filtrate by acidification.

This transformation is closely related to Wieland's finding¹⁰ that **7** readily undergoes cleavage of the furoxan ring to produce, depending on the reaction conditions, a wide variety of rearrangement products.¹¹ A suggested sequence involves a series of reactions connected with the opening and closure of heterocycles. Our view of how **1** is formed is outlined in Scheme 3. Here it is proposed that the Boulton-Katritzky rearrangement produces glyoxime **8** in the normal manner which dehydrates to **9**. The bifurazan **9** can then undergo a proton shift^{5,11,12} to produce **10**, which subsequently reacts with NH₂OH to give **11**. Dehydration of **11** generates a monoamine **12**. A repeat of the previous reaction three times to form the second aminofurazan moiety leads to the final



Scheme 3

[†] The identity of product **1** was confirmed by NMR spectroscopy, mp, MS, IR, and comparison with the literature data.³

product 1.[†] It should be noted that an analogous treatment of an authentic sample of the bifurazan **9** with hydroxylamine affords 1[†] in 39% yield, whereas at pH 10 only tetraoxime **6** (64%) was produced.

In conclusion, we have demonstrated that treatment of **7** with hydroxylamine provides a new and versatile approach to the one-pot synthesis of **1**. The starting compounds and reagents for this reaction are readily available and inexpensive. We believe that this is by far the simplest route to **1** currently available, and are now exploring the use of the products in various reactions.

References

- 1 V. G. Andrianov and A. V. Ereemeev, *Khim. Geterotsikl. Soedin.*, 1984, 1155 [*Chem. Heterocycl. Compd. (Engl. Transl.)*, 1984, 937].
- 2 (a) V. A. Dorokhov, E. A. Shagova, T. S. Novikova, A. B. Sheremetev and L. I. Khmel'nitskii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1988, 2363 (*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1988, 37, 2128); (b) T. S. Novikova, T. M. Mel'nikova, O. V. Kharitonova, V. O. Kulagina, N. S. Aleksandrova, A. B. Sheremetev, T. S. Pivina, L. I. Khmel'nitskii and S. S. Novikov, *Mendeleev Commun.*, 1994, 138 and references therein.
- 3 M. D. Coburn, *J. Heterocycl. Chem.*, 1968, 5, 83; *J. Labelled Compds. Radiopharm.*, 1985, 22, 183.
- 4 For the review on the synthesis of furazans by rearrangement of 3-acyl-1-oxa-2-azole oximes, see: V. G. Andrianov and A. V. Ereemeev, *Khim. Geterotsikl. Soedin.*, 1990, 1443 [*Chem. Heterocycl. Compd. (Engl. Transl.)*, 1990, 1199].
- 5 A. B. Sheremetev and I. V. Ovchinnikov, *Heteroatom. Chem.*, in press.
- 6 (a) H. Wieland, A. Baumann, C. Reizenegger, W. Scherer, J. Thiele, J. Will, H. Hausmann and W. Frank, *Ann.*, 1925, 444, 7; (b) T. Hoshino and T. Mukaiyama, *Japan Patent* 599855, 1959 (*Chem. Abstr.*, 1960, 54, 7738).
- 7 (a) F. De Sarlo, A. Guarna, A. Brandi and A. Goti, *Tetrahedron*, 1985, 41, 5181; (b) T. I. Godovikova, S. P. Golova, Yu. A. Strelenko, M. Yu. Antipin, Yu. T. Struchkov and L. I. Khmel'nitskii, *Mendeleev Commun.*, 1994, 7 and references therein.
- 8 G. Longo, *Gazz. Chim. Ital.*, 1931, 61, 575.
- 9 L. Wolff, *Ber.*, 1895, 28, 69.
- 10 (a) H. Wieland, W. Frank and Z. Kitasato, *Ann.*, 1925, 444, 42; (b) H. Wieland, Z. Kitasato and F. Fromm, *Ann.*, 1929, 475, 54.
- 11 C. Grundmann, G. W. Nickel and R. K. Bansal, *Liebigs Ann. Chem.*, 1975, 1029.
- 12 A. Munno, V. Bertini, P. Rasero, N. Picci and L. Bonfanti, *Atti Accad. Naz. Linc.*, 1978, 64(4), 385 and references therein.

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