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Synthesis of 4*H*-[1,2,3]Triazolo[4,5-*c*][1,2,5]oxadiazole 5-Oxide and its *N*- and *O*-Alkyl Derivatives

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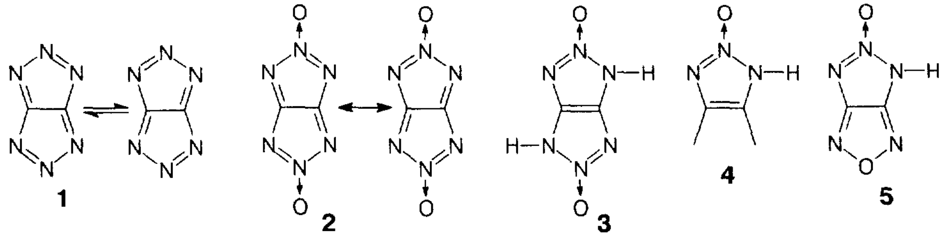
Abstract: The synthetic route to the fused 1,2,3-triazole 2-oxide systems *via* intramolecular cyclization of *N*-nitroso and azido groups is described. The title compounds are characterized by ^{1}H, ^{13}C, ^{14}N, ^{15}N and ^{17}O NMR spectroscopy. Copyright © 1996 Elsevier Science Ltd

The MNDO calculations predicted that 1,2,3,4,5,6-hexaazapentalene (**1**), as well as pentalene itself, should be antiaromatic in character and possess a structure with localized double bonds[1]. In contrast, preference was given to the structure with delocalized double bonds for its 2,5-dioxide **2**[1]. Formally, compound **2** can be regarded as aromatic, although it has an 8 π-electron cyclic system. In this connection, it would be of interest to synthesize this compound. Triazolotriazole **3** could be used as a precursor of **2** but its preparation seems to be problematic as it consists of two 1,2,3-triazole 2-oxide moieties (**4**), the synthesis of which has not been adequately investigated[2].

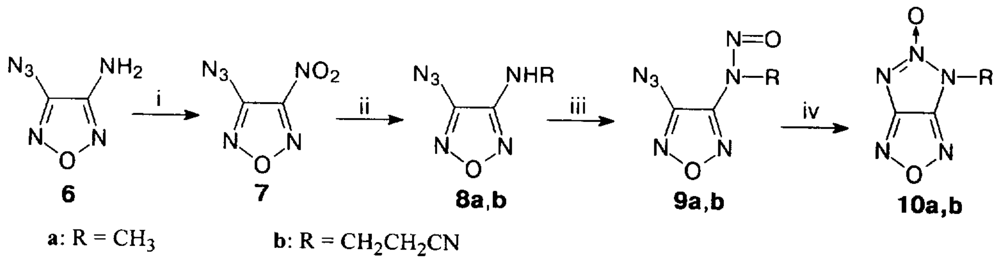


So, our first step was to synthesize a model compound **5**, where the 1,2,3-triazole 2-oxide moiety is fused with a furazan ring. Herein we describe this synthesis starting from azidoaminofurazan[3] **6**, easily obtained from diaminofurazan.

The amino group of **6** was oxidized with N_2O_5 to give the nitro derivative[4] **7** in accord with our previous procedure[5]. The nitro group was easily replaced by methylamine to yield **8a** and by cyanoethylamine to yield **8b**. The nitrosation of **8** gave rise to *N*-nitroso compounds **9a,b**.

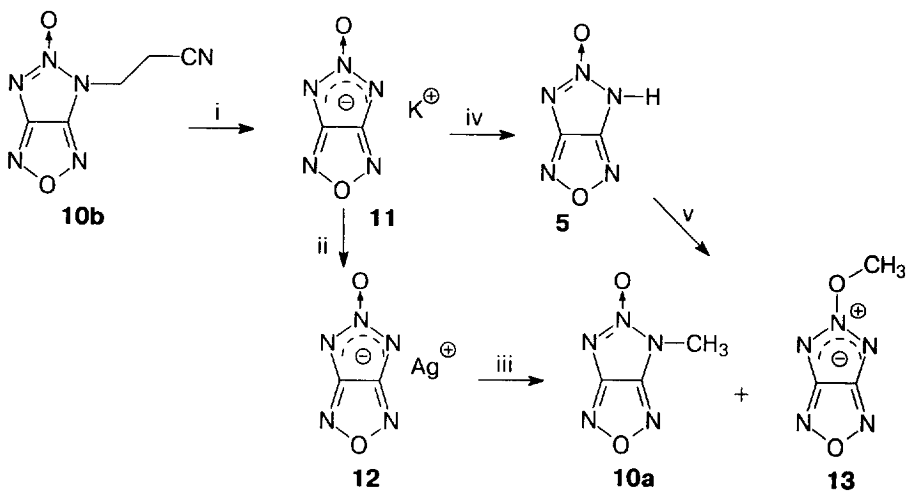
The intramolecular cyclization involving *N*-nitroso group and azido group is the key stage in this synthetic route to 1,2,3-triazole 2-oxide fragment. This kind of cyclization was not described previously[6].

When **9a** was heated in toluene, the cyclization took place to give **10a,b**. The structure of **10** was proved with the help of ^{13}C, ^{14}N, ^{15}N and ^{17}O NMR studies (see Table 1). The use of INEPT and SPT pulse sequences in ^{15}N NMR investigations made it possible to determine the mutual arrangement of nitrogen atoms in 1,2,3,-triazole 2-oxide moiety.



Scheme 1. i: N_2O_5 (6 equv.), CH_3CN, -25° → 0°C, then 16 h at 0°C, oil, 63%; ii: **8a**, CH_3NH_2 aq., CH_3CN, 30 min, 20°C, 89%; **8b**, $NCCH_2CH_2NH_2$ excess, CH_3CN, reflux, 1 h, 70%; iii: **9a**, $NaNO_2$, HCl, H_2O/dioxane, 0°C, 30 min, 90%, **9b**, $NaNO_2$, AcOH/H_2O, 5°C, 1 h, 91%; iv, toluene, reflux, **10a**, 2 h, 92%; **10b**, 3 h, 70%.

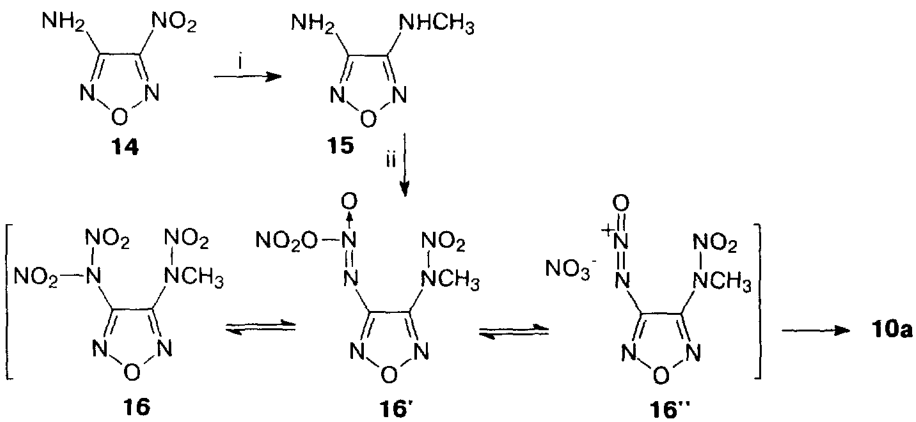
When **10b** was treated with potassium methoxide in methanol, the cyanoethyl group was readily eliminated yielding the potassium salt **11**. Methylation of the silver salt **12**, obtained from K-salt gave rise to the *N*-methylated product **10a** and the *O*-methylated product **13** in 9:1 ratio. When **5**, obtained by acidification of K-salt **11**, was treated with diazomethane, the *O*-methylated product became predominant. Isomer ratio **10a**:**13** was 3:4.



Scheme 2. i: $KOCH_3$, CH_3OH, 10°C, 97%; ii: $AgNO_3$, H_2O, 98%; iii: CH_3I, CH_3CN, 20°C, 8 h, chromatographed (silica gel, $CHCl_3$) (**10a**, 86%, **13**, 10%); iv: dry HCl, acetone; v: CH_2N_2, ether (**10a**, 52%; **13**, 39%).

Compound **13** is a new mesoionic structure[7]. Its NMR characteristics as well as MS data differs strongly from N-methyl isomer (see Table 1).

Furthermore, we attempted to synthesize **10a** using our previous method based on intramolecular reaction of $N{=}N{=}O^+$ cation with nucleophiles[8]. The starting compound in this synthetic route was aminomethylaminofurazan **15**, obtained by replacing the nitro group of aminonitrofurazan **14** with methylamine. The treatment of **15** with the excess of nitronium tetrafluoroborate indeed afforded **10a**. This reaction could be rationalized by polar mechanism involving dissociation of intermediate **16'** to give the ion pair **16''** followed by cyclization and loss of NO_2^+ cation.

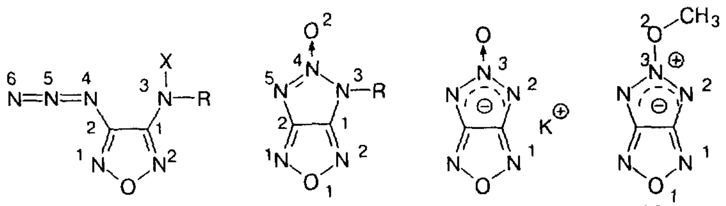


Scheme 3. i: CH_3NH_2, DMSO, 20°C, 4 h, 84%; ii: NO_2BF_4, CH_3CN, -10 → 24°C, then 5 h at 20°C, chromatograped (silica gel, $CHCl_3$), 12%.

Unfortunately, the yield of cyclic product **10a** did not exceed 12%. For the major part, the intermolecular reaction took place providing an azoxy compound[9].

All new compounds gave the expected mass spectra and satisfactory elemental analyses.

Table 1. Spectroscopic data[a] and physical constants for **8—11, 13** and **15**.



8a,b; 9a,b **10a,b** **11** **13**

8a: mp 34—36°C; NMR ($CDCl_3$), δ (**^{1}H**) 2.97 (d, 3 H, J=5.2 Hz, CH_3), 4.22 (br., 1 H, NH); δ (**^{13}C**) 30.8 (CH_3), 145.1 (C-2, d, ^3J=1.5 Hz), 151.6 (dq C-1, ^2J=2.5 Hz, ^3J=3.5 Hz); δ (**^{14}N**) -357 (N-3, $\Delta\nu_{1/2}$=1000 Hz), -145 (N-5, $\Delta\nu_{1/2}$=35 Hz); δ (**^{15}N**), (INEPT) -21.1 (N-2, ^3J=3.0 Hz, ^4J=0.3 Hz), -343.0 (N-3, ^1J=92.4 Hz, ^2J=0.9 Hz).

8b: mp 42—44°C; NMR ($CDCl_3$), δ (**^{1}H**) 2.79 (t, 2 H, J=6.3 Hz, CH_2CN), 3.61 (q, 2 H, J=6.3 Hz, CH_2N), 4.71 (br. t, 1 H, NH); δ (**^{13}C**) 17.4 ($\underline{C}H_2CN$), 40.2 (CH_2N), 118.1 (CN), 145.2 (C-2, d, ^3J=1.4 Hz), 149.8 (C-1, dt, ^3J=4.2 Hz, ^2J=2.6 Hz); δ (**^{14}N**) -145 (N-5, $\Delta\nu_{1/2}$=60 Hz); δ (**^{15}N**), (INEPT) -333.8 (NH, ^1J=93.3 Hz, ^3J=3.3 Hz).

9a: mp 22—24°C; NMR ($CDCl_3$), δ (**^{1}H**) 3.50 (s); δ (**^{13}C**) 31.0 (CH_3), 147.8 (C-2), 149.3 (C-1); δ (**^{14}N**) -145.8 (N-5, $\Delta\nu_{1/2}$=80 Hz); δ (**^{15}N**), (INEPT) -142.2 (N-3, ^2J=1.4 Hz), 8.3 (N-2, ^4J=1.0 Hz), 175.8 (N=O, ^3J=1.0 Hz).

9b: mp 51—52°C; NMR ($CDCl_3$), δ (**^{1}H**) 2.72 (t, 2 H, J=6.4 Hz, CH_2CN), 4.33 (t, 2 H, CH_2N); δ (**^{13}C**) 15.3 ($\underline{C}H_2CN$), 38.9 (CH_2N), 116.1 (CN), 147.9 (C-2), 148.1 (C-1, br. t, ^3J=2.4 Hz); δ (**^{14}N**) -149 (N-5, $\Delta\nu_{1/2}$=100 Hz);
δ (**^{15}N**) 177.3 (N=O), 10.9, 5.8 (N-1 and N-2), -130.3, -132.1 (N-6 and CN), -140.2 (N-3), -148.1 (N-5).

10a: mp 95—96°C (CCl_4); NMR (acetone-d_6), δ (**^{1}H**) 4.06 (s); δ (**^{13}C**) 33.9 (CH_3), 147.5 (C-1, q, ^3J=2.0 Hz), 157.4 (C-2); δ (**^{14}N**) -199 (N-3, $\Delta\nu_{1/2}$=1000 Hz), -124 (N-5, $\Delta\nu_{1/2}$=700 Hz), -41 (N-4, $\Delta\nu_{1/2}$=70 Hz), -7 (N-1 and N-2, $\Delta\nu_{1/2}$=1000 Hz); δ (**^{15}N**) -192.5 (N-3, br.), -120.9 (N-5, br.), -40.3 (N-4), -12.9 (N-2), 1.6 (N-1); δ (**^{15}N**), (INEPT) -192.5 (N-3, q, ^2J=1.4 Hz), -40.3 (N-4, q, ^3J=2.2 Hz), -12.9 (N-2, q, ^4J=0.1 Hz); δ (**^{17}O**) 400 (O-2, $\Delta\nu_{1/2}$=400 Hz), 458 (O-1, $\Delta\nu_{1/2}$=400 Hz);

IR (KBr) 700, 780, 790, 825, 910, 1015, 1112, 1138, 1350, 1362, 1418 (w), 1522, 1540, 1590, 1672 cm^{-1}; **MS** (E.I.) *m/z* (%) 141 (M^+, 20), 71 (17), 67 (100), 53 (16), 45 (33).

10b: mp 71—72°C ($CHCl_3$); NMR (acetone-d_6), δ (**^{1}H**) 3.22 (t, 2 H, *J*=6.4 Hz, CH_2CN), 4.88 (t, 2 H, CH_2N); δ (**^{13}C**) 16.9 ($\underline{C}H_2CN$), 44.0 (CH_2N), 117.5 (CN), 147.1 (C-1, ^3J=2.6 Hz), 157.9 (C-2); δ (**^{14}N**) –11 (N-1 and N-2, $\Delta\nu_{1/2}$=1000 Hz), –43 (N-4, $\Delta\nu_{1/2}$=150 Hz); –128 (CN and N-5, $\Delta\nu_{1/2}$=800 Hz); δ (**^{15}N**), (SPT from H δ 4.88) –188.4 (N-3, ^2J=1.3 Hz), –42.4 (N-4, ^3J=2.6 Hz), –12.0 (N-2); δ (**^{15}N**), (SPT from H δ 3.22) –188.7 (N-3, ^3J=3.6 Hz), –126.7 (CN, ^3J=2.6 Hz).

11: mp 204—205°C (EtOH) (decomp.); NMR (D_2O), δ (**^{13}C**) 158.20; δ (**^{14}N**) –11.5 (N-3, $\Delta\nu_{1/2}$=100 Hz); δ (**^{15}N**) –125.2 (N-2,) –19.3 (N-1), –11.7 (N-3).

13: mp 53-54°C; NMR ($CDCl_3$): δ (**^{1}H**) 4.74 (s); δ (**^{13}C**) 65.4 (CH_3), 160.5; δ (**^{14}N**) –110 (N-2, $\Delta\nu_{1/2}$=700 Hz), –50 (N-3, $\Delta\nu_{1/2}$=150 Hz), –26 (N-1, $\Delta\nu_{1/2}$=900 Hz); δ (**^{17}O**) 192 (O-2, $\Delta\nu_{1/2}$=750 Hz), 501 (O-1, $\Delta\nu_{1/2}$=400 Hz); **IR** (KBr) 775 (w), 795 (w), 805, 825, 955, 995, 1055 (w), 1165, 1220, 1295, 1345, 1430, 1440, 1455, 1530 (w) cm^{-1}; **MS** (E.I.) *m/z* (%) 141 (M^+,78), 54 (100), 52 (26).

15: mp 111—113°C (CCl_4); NMR (DMSO-d_6) δ (**^{1}H**) 2.82 (d, 3 H, *J*=5 Hz), 5.80 (br. s, 2 H, NH_2), 5.94 (br. q, 1 H, NH); δ (**^{13}C**) 30.3 (CH_3), 149.0 (C-NH_2, d, ^3J=0.7 Hz), 151.4 (C-NH, dq, ^3J=3.3 Hz, ^2J=2.4 Hz); δ (**^{15}N**), (INEPT) –341.6 (NH, d, *J*=92.4 Hz), –342.5 (NH_2, t, *J*=85.9 Hz).

[a]NMR spectra were recorded on AM 300 Bruker instrument. The chemical shifts were measured relative to internal TMS (^{1}H, ^{13}C) or external CH_3NO_2 (^{14}N, ^{15}N) and H_2O (^{17}O) reference (δ=0.0 ppm). The INEPT and SPT pulse sequences were used for ^{15}N signal observation.

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2. For 2-hydroxytriazole, see ref. (a); N-alkyltriazole 2-oxides fused with benzene (ref. b) or pyridine ring (ref. c) were obtained by UV irradiation of appropriate N-alkyltriazole 3-oxides; (a) Kishida, H.; Shudo, A.; Sakamoto, N.; Fujimoto, H.; Umeda, K. Japan patent 05,222,006, 1993; Chem. Abstr. **1994**, *120*, 25611j; (b) Serve, M. P.; Feld, W. A.; Seybold, P. G.; Steppel, R. N. *J. Heterocycl. Chem.* **1975**, *12*, 811—812; (c) Hubert, A. J.; Anthoine, G. *Bull. Soc. Chim. Belges.* **1969**, *78*, 553—560.
3. Tselinskii, I. V.; Mel'nikova, S. F.; Vergizov, S. N. *Zh. Org. Khim.* **1981**, *17*, 1123—1124.
   Caution! Compound **6** as well as **8**—**14** and especially **7** should be handled as potentially explosive materials.
4. The analytical and spectroscopic data of **7** completely agree with the structure suggested.
5. Churakov, A. M.; Semenov, S. E.; Ioffe, S. L.; Strelenko, Yu. A.; Tartakovsky, V. A. *Mendeleev Commun.* **1995**, 102—103.
6. After we had begun this study, the thermal reaction of 2-(*N*-nitroso-*N*-alkylamino)-3-azido-1,4-naphtoquinones yielding 1-alkyl-1,2,3-triazole 2-oxide derivatives was published: Gornostaev, L. M.; Timoshkova, N. A.; Sakilidi, V. T. *The Fifteenth International Congress of Heterocyclic Chemistry*, Taipei, 1995, PO2-169.
7. For closely related 5-phenyl-5*H*[1,2,3]-triazolo[4,5-c][1,2,5]oxadiazole see: Matsumoto, A.; Yoshida, M.; Simamura, O. *Bull. Chem. Soc. Jap.* **1974**, *47*, 1493—1495; Benson, F. R. *The High Nitrogen Compounds*; Wiley: New York, 1984; pp. 93-95; for review on furazanes fused to five-membered rings see: A. B. Sheremetev A. B. J. *Heterocyclic Chem.* 1995, **32**, 371—385.
8. For the intramolecular reaction of diazonio oxide cation with *tert*-butylazoxy group resulting in benzo-1,2,3,4-tetrazine 1,3-dioxide see: Churakov, A. M.; Ioffe, S. L.; Tartakovsky, V. A. *Mendeleev Commun.* **1991**, 101.
9. For intermolecular reactions of this type see ref. 5.

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