Available online at www.sciencedirect.com
ScienceDirect
Mendeleev Commun., 2014, **24**, 203–205

Mendeleev Communications

5-Nitro-7,8-furoxanoquinoline: a new type of fused nitroarenes possessing Diels–Alder reactivity

Maxim A. Bastrakov,*[a] Aleksei M. Starosotnikov,[a] Ivan V. Fedyanin,[b] Vadim V. Kachala[a] and Svyatoslav A. Shevelev[a]

[a] *N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 119991 Moscow, Russian Federation. Fax: +7 499 135 5328; e-mail: b_max82@mail.ru*
[b] *A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, 119991 Moscow, Russian Federation*

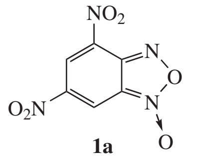
DOI: 10.1016/j.mencom.2014.06.004

Reaction of 8-chloro-5,7-dinitroquinoline with sodium azide afforded isomeric 5-nitro-7,8-furoxanoquinolines, whose nitroethene fragment can act as dienophile and heterodiene in the Diels–Alder cycloaddition.

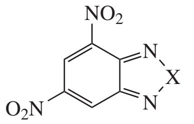
Within the framework of our search for new syntheses of condensed heterocyclic systems from aromatic nitro compounds we study the ability of nitroarenes fused with electron-deficient heterocycles to undergo cycloaddition reactions. In these transformations, annelation of five- or six-membered cycle to the aromatic fragment C=C–NO_2 is accomplished by dearomatization of a nitroarene nucleus.

Pericyclic [4+2]-cycloaddition reactions are uncommon for aromatic compounds, including nitroarenes.[1] However, Terrier and coworkers[2–4] revealed a number of fused nitroarenes, the so called ‘superelectrophiles’. These compounds undergo Diels–Alder reactions (pericyclic [4+2]-cycloaddition reactions) in accordance with normal and inverse electron demands, *i.e.* act as dienophiles or heterodienes, respectively.

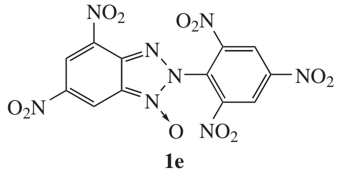
Currently, only a few superelectrophiles are known, especially 4,6-dinitrobenzofuroxan **1a** and 4,6-dinitrobenzofurazan **1b** and some their analogues **1c–g**.[2–5]



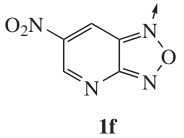
1a



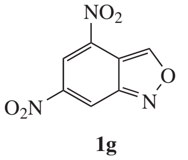
1b X = O
1c X = Se
1d X = S



1e

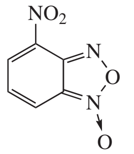


1f

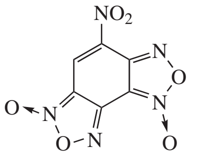


1g

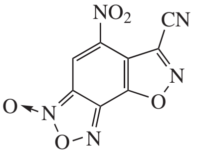
The extension of the range of superelectrophiles seems actual. One direction of our research is the study of the annelation effect of different electron-withdrawing aromatic rings to 4-nitrobenzofuroxan **2a** at C^6–C^7 bond (compounds **1a**, **2b–e**) on the ability of these compounds to undergo Diels–Alder and 1,3-dipolar cycloaddition reactions.



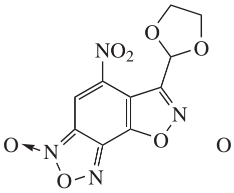
2a



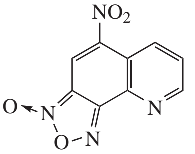
2b



2c



2d



2e

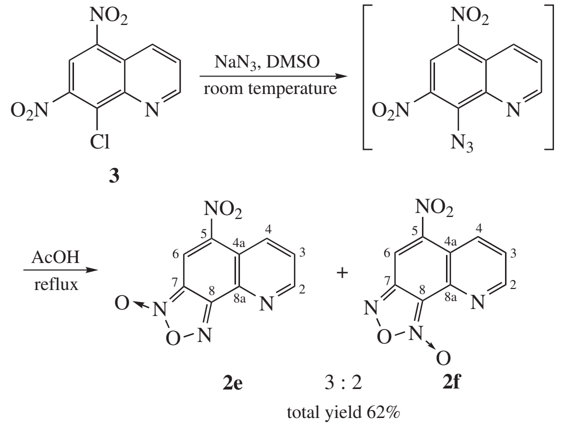
Nitrobenzofuroxan **2a** is a reasonable starting-point in this search. It does not undergo Diels–Alder reaction.[6] However, introduction of a nitro group at 6-position gives one of the best-studied Diels–Alder reactants of the fused nitroarene series – 4,6-dinitrobenzofuroxan **1a**.[1–4] Annulation of another furoxan ring to **2a** affords 4-nitrobenzodifuroxan **2b** which is very active in Diels–Alder reactions. Recently it was shown[1,8] that annulation to **2a** at C^6–C^7 bond of isoxazole yields compounds **2c**,**d** which are also susceptible to Diels–Alder addition.

These results indicate that the Diels–Alder reactivity is a property of 4-nitrobenzofuroxan derivatives having strong electron-withdrawing substituents (*e.g.*, nitro group) at 6-position or π-deficient azole annulated at C^6–C^7 bond. In this connection it was of interest to reveal more factors responsible for such a transformation.[9]

Herein, we studied whether a compound constructed by annelation of a simplest azine (pyridine) to a molecule of **2a** at C^6–C^7 bond to give 5-nitro-7,8-furoxanoquinoline **2e**[1,10] can undergo Diels–Alder reaction. Compound **2e** was prepared from available 8-chloro-5,7-dinitroquinoline **3** (Scheme 1, see ref. 11 and references cited therein) by nucleophilic substitution of its chlorine atom and further thermolysis of the intermediate *o*-nitroazide in boiling acetic acid.†

---

† *5-Nitro[1,2,5]oxadiazolo[3,4-*h*]quinoline 3-oxide* **2e** and *5-nitro[1,2,5]-oxadiazolo[3,4-*h*]quinoline 1-oxide* **2f**. Sodium azide (0.14 g, 2.2 mmol) was added to a solution of chloroarene **3** (0.5 g, 2 mmol) in DMSO (20 ml). The mixture was stirred for 0.5 h at room temperature and poured into water. The precipitate was filtered off, dissolved in AcOH (100 ml) and



Scheme 1

According to NMR data, the product represents an inseparable 3:2 mixture of two regioisomers with different positions of exocyclic N–O bond of the furoxan ring (**2e** and **2f**). Such an isomerism is common for benzofuroxans, usually the isomers easily interconvert into each other in solutions, while the more thermodynamically stable one can be isolated in crystal form.[12] However, in our case the ratio of regioisomers in crystal cell was 87:13 (Figure 1).[‡] X-ray diffraction study of crystals **2e**/**2f** revealed that the both stereoisomers form a solid solution. The isomers occupy the same crystallographic position with the atoms of the quinoline moiety being common, and furoxan part is disordered by two positions. The relative occupancy of the two disordered positions was refined to be of *ca.* 87:13, which differs from the NMR data. However, it seems reasonable that in the case of solid solution the ratio of components may vary and hence the two isomers cannot be separated by crystallization.

The ring system in crystals of **2e**/**2f** is virtually planar with the maximal out-of-plane distance for the atom C(10) equal to 0.102(3) Å. Bond lengths and angles of the molecular fragments are typical of the similar compounds (Figure 1). The distinct feature of **2e**/**2f** in crystal is significant angle between the average planes of nitro group and the quinoline ring equal to 57.5(4)°, that may be caused by relatively strong intermolecular O···O interaction [2.867(4) Å] between oxygen atoms of the nitro groups. Note that according to X-ray data the length of C(5)–C(6) bond bearing NO_2 group is 1.326(4) Å which is nearly the same as in nitroethene (1.322 Å).[13] Therefore, the high pericyclic reactivity of compounds **2e**,**f** could be expected.

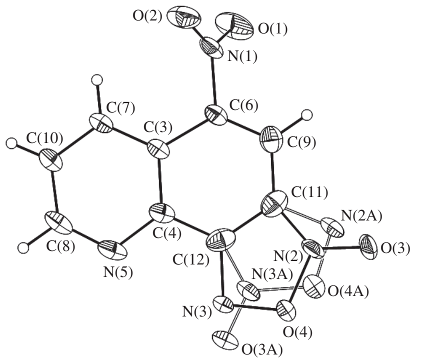
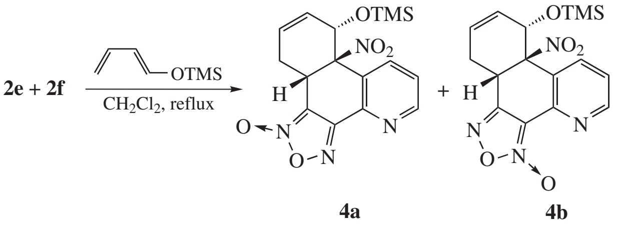


Figure 1 General view of **2e**/**2f** in crystal in thermal ellipsoid representation (p = 30%). Selected bond lengths (Å): O(1)–N(1) 1.210(3), O(2)–N(1) 1.204(3), N(1)–C(6) 1.474(4), N(5)–C(8) 1.323(4), N(5)–C(4) 1.357(4), C(3)–C(7) 1.382(4), C(3)–C(4) 1.405(4), C(3)–C(6) 1.470(4), C(4)–C(12) 1.423(4), C(6)–C(9) 1.326(4), C(7)–C(10) 1.382(4), C(8)–C(10) 1.393(4), C(9)–C(11) 1.416(5), C(11)–N(2) 1.315(12), C(11)–N(2A) 1.405(13), C(11)–C(12) 1.421(5), C(12)–N(3A) 1.299(13), C(12)–N(3) 1.412(12), O(3)–N(2) 1.237(11), O(4)–N(3) 1.394(11), O(4)–N(2) 1.485(12), O(3A)–N(3A) 1.222(10), O(4A)–N(2A) 1.370(10), O(4A)–N(3A) 1.464(12).

Furoxans **2e**,**f** really undergo Diels–Alder reaction both as dienophile and as heterodiene. Their reactivity towards dienes was studied taking 1-trimethylsilyloxy-1,3-butadiene as an example. The reaction was carried out in boiling dichloromethane on using excess diene to give an inseparable mixture of regioisomers **4a** + **4b** (3:1), total yield 25% (Scheme 2).[§] Nitrovinyl fragment of compounds **2e**,**f** acts as dienophile, which denotes that the reaction proceeds in accordance with normal electron demands (see ref. 1).



Scheme 2

---

heated under reflux for 4 h. The solvent was partially evaporated *in vacuo* and the residue was poured into water. The product was filtered, washed with water and dried in air. Total yield 62%, mp 187–189 °C. Found (%): C, 46.66; H, 1.51; N, 23.84. Calc. for $C_9H_4N_4O_4$ (%): C, 46.56; H, 1.74; N, 24.13.

For **2e**: ^{1}H NMR (600 MHz, DMSO-d_6) δ: 9.11 (d, 1H, H^2, J 3.9 Hz), 8.58 (d, 1H, H^4, J 8.4 Hz), 8.54 (s, 1H, H^6), 7.96 (dd, 1H, H^3, J 8.4 and 4.4 Hz). ^{13}C NMR (150 MHz, DMSO-d_6) δ: 152.21 (C^2), 150.47 (C^8), 147.22 (C^5), 139.71 (C^{8a}), 133.76 (C^4), 126.39 (C^3), 122.38 (C^{4a}), 112.21 (C^6), 112.12 (C^7).

For **2f**: ^{1}H NMR (600 MHz, DMSO-d_6) δ: 9.03 (d, 1H, H^2, J 4.1 Hz), 8.77 (s, 1H, H^6), 8.45 (d, 1H, H^4, J 8.3 Hz), 7.85 (dd, 1H, H^3, J 8.4 and 4.5 Hz). ^{13}C NMR (150 MHz, DMSO-d_6) δ: 152.09 (C^2), 150.55 (C^5), 150.13 (C^8), 137.88 (C^{8a}), 133.09 (C^4), 124.85 (C^3), 120.51 (C^{4a}), 115.48 (C^6), 108.22 (C^7).

[‡] *Crystallographic data for* **2e**/**2f**: at 120 K crystals of $C_9H_4N_4O_4$ are monoclinic, space group $P2_1/c$, a = 8.479(2), b = 14.384(3) and c = 7.848(2) Å, and β = 111.261(7)°, V = 892.0(4) Å^3, Z = 4, M = 232.16, d_{calc} = 1.729 g cm^{-3}, μ(MoKα) = 1.41 cm^{-1}, F(000) = 472. Intensities of 3942 reflections were measured with a Smart 1000 CCD diffractometer at 120 K [λ(MoKα) = 0.71072 Å, ω-scans with a 0.3° step and 15 s per frame exposure, $2\theta < 54°$], and 1917 independent reflections (R_{int} = 0.0408) were used in further refinement. The structure was solved by direct method and refined by the full-matrix least-squares technique against F^2_{hkl} in the anisotropic approximation. Hydrogen atoms bonded to carbon were placed into calculated positions and refined in riding model with U_{iso}(H) = 1.2U_{eq}(C). The refinement converged to R_1 = 0.0574 [calculated against F_{hkl} for 995 observed reflections with $I > 2\sigma(I)$], wR_2 = 0.1567 and GOF = 0.991. All calculations were performed using SHELX software package.[13]

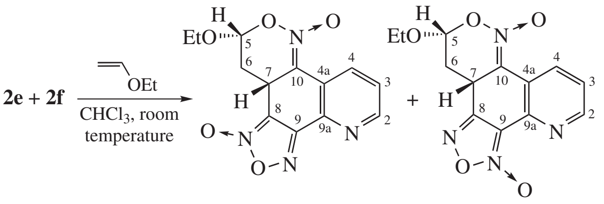
CCDC 993621 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* http://www.ccdc.cam.ac.uk. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2014.

[§] *7b-Nitro-8-(trimethylsilyloxy)-7b,8,11,11a-tetrahydrobenzo[*f*][1,2,5]oxadiazolo[3,4-*h*]quinoline 1-oxide* **4a** and *7b-nitro-8-(trimethylsilyloxy)-7b,8,11,11a-tetrahydrobenzo[*f*][1,2,5]oxadiazolo[3,4-*h*]quinoline 3-oxide* **4b**. 1-(Trimethylsilyloxy)-1,3-butadiene (0.5 ml) was added to a solution of furoxans **2e**+**2f** (0.1 g, 0.43 mmol) in 10 ml of CH_2Cl_2 and the mixture was refluxed for 24 h until the complete conversion of the starting compound (TLC). Then hexane (50 ml) was added and the precipitate formed was filtered off and purified by flash chromatography (SiO_2, $CHCl_3$). Yield 25%, mp 162–164 °C. Found (%): C, 51.56; H, 4.68; N, 14.92. Calc. for $C_{16}H_{18}N_4O_5Si$ (%): C, 51.32; H, 4.85; N, 14.96.

For **4a**: ^{1}H NMR (600 MHz, $CDCl_3$) δ: 0.16 (s, 9H), 1.73 (dd, 1H, J 19.1 and 10.3 Hz), 2.92–2.98 (m, 1H), 4.51 (dd, 1H, J 10.2 and 7.2 Hz), 5.31–5.33 (m, 1H), 5.84–5.86 (m, 1H), 5.90–6.05 (m, 1H) 7.57 (dd, 1H, J 8.2 and 4.7 Hz), 8.00 (d, 1H, J 6.9 Hz), 8.85–8.86 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 152.29, 150.34, 143.55, 136.54, 130.24, 127.41, 126.04, 125.47, 107.13, 92.12, 65.71, 29.53, 27.91, 0.06.

On the other hand, the reaction of furoxans **2e**,**f** with ethyl vinyl ether (as reagent and solvent) at room temperature afforded cyclic nitronates **5a** and **5b** (3:1), total yield 76% (Scheme 3).¶ In this case, the cycloaddition also occurs at nitrovinyl fragment which acts as heterodiene C=C–N(O)=O. This reaction meets inverse electron demands (see ref. 1).

In conclusion, the annelation of a pyridine ring in molecule **2a** leads to compounds **2e**,**f** possessing Diels–Alder reactivity. One can expect that annelation of more electron-deficient aromatic azines such as pyridines with –I and –M substituents, polyazines, *N*-pyridinium compounds would result in formation of novel aromatic nitro compounds capable of readily undergoing [4+2]-cycloaddition. It can be anticipated that it will be possible to replace the furoxan ring of **2a** with less electron-withdrawing fragments or substituents (NO_2, SO_2R, CN, *etc.*) with retaining the Diels–Alder reactivity, which seems promising for the expanding of synthetic potential of fused quinolines.



5a **5b**

Scheme 3

New compounds were characterized by elemental analysis, ^{1}H and ^{13}C NMR spectra.

This work was supported by the Russian Foundation for Basic Research (project no. 14-03-31508 mol_a) and Grant of the President of the Russian Federation for State Support to Young Russian scientists (grant no. MK-3599.2013.3).

References

1 S. A. Shevelev and A. M. Starosotnikov, *Chem. Heterocycl. Compd.*, 2013, **49**, 92 (*Khim. Geterotsikl. Soedin.*, 2013, 102).
2 F. Terrier, *Modern Nucleophilic Aromatic Substitution*, Wiley, 2013.
3 E. Buncel and F. Terrier, *Org. Biomol. Chem.*, 2010, **8**, 2285.
4 F. Terrier, J. M. Dust and E. Buncel, *Tetrahedron*, 2012, **68**, 1829.
5 A. M. Starosotnikov, M. A. Leontieva, M. A. Bastrakov, A. V. Puchnin, V. V. Kachala and S. A. Shevelev, *Mendeleev Commun.*, 2010, **20**, 165.
6 S. Lakhdar, R. Goumont, T. Boubaker, M. Mokhtari and F. Terrier, *Org. Biomol. Chem.*, 2006, **4**, 1910.
7 S. Kurbatov, R. Goumont, J. Marrot and F. Terrier, *Tetrahedron Lett.*, 2004, **45**, 1037.
8 A. M. Starosotnikov, M. A. Bastrakov, S. A. Shevelev, R. Goumont and F. Terrier, *Abstracts of the International Conference on New Directions in Heterocyclic Chemistry*, Kislovodsk, 2009, p. S-441.
9 A. F. Pozharskii, *Teoreticheskie osnovy khimii geterotsiklov (Theoretical Basis of Heterocyclic Chemistry)*, Khimiya, Moscow, 1985 (in Russian).
10 (*a*) M. A. Bastrakov, A. M. Starosotnikov and S. A. Shevelev, *Abstracts of the 17th European Symposium on Organic Chemistry*, Crete, 2011, p. 1.290; (*b*) M. A. Bastrakov, A. M. Starosotnikov and S. A. Shevelev, *Abstracts of XXV European Colloquium on Heterocyclic Chemistry*, Reading, UK, 2012, PP-2.
11 M. A. Bastrakov, A. I. Leonov, A. M. Starosotnikov, I. V. Fedyanin and S. A. Shevelev, *Russ. Chem. Bull., Int. Ed.*, 2013, **62**, 1052 (*Izv. Akad. Nauk, Ser. Khim.*, 2013, 1051).
12 L. I. Khmel'nitskii, S. S. Novikov and T. I. Godovikova, *Khimiya furoksanov: reaktsii i primenenie (Chemistry of Furoxans: Reactions and Applications)*, Nauka, Moscow, 1996, p. 13 (in Russian).
13 P. Noesberger, A. Bauder and H. H. Guenthard., *Chem. Phys.*, 1973, **1**, 426.
14 G. M. Sheldrick, *Acta Crystallogr., Sect. A*, 2008, **64**, 112.

Received: 14th April 2014; Com. 14/4349

For **4b**: ^{1}H NMR (600 MHz, $CDCl_3$) δ: 0.16 (s, 9H), 1.61–1.78 (m, 1H), 2.92–2.98 (m, 1H), 4.61 (dd, 1H, *J* 10.6 and 7.2 Hz), 5.31–5.33 (m, 1H), 5.84–5.86 (m, 1H), 5.90–6.05 (m, 1H), 7.46 (dd, 1H, *J* 8.1 and 4.8 Hz), 7.96 (d, 1H, *J* 6.8 Hz), 8.84–8.85 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 156.52, 152.11, 137.03, 136.36, 130.24, 126.12, 125.83, 124.64, 113.23, 92.61, 65.75, 31.08, 30.21, 0.06.

¶ *(10*R**,11a*R**)-10-Ethoxy-11,11a-dihydro-10*H*-[1,2,5]oxadiazolo-[3,4-*h*][1,2]oxazino[3,4-*f*]quinoline 1,8-dioxide* **5a** and *(10*R**,11a*S**)-10-ethoxy-11,11a-dihydro-10*H*-[1,2,5]oxadiazolo[3,4-*h*][1,2]oxazino-[3,4-*f*]quinoline 3,8-dioxide* **5b**. Ethyl vinyl ether (5 ml) was added to a solution of furoxans **2e**+**2f** (0.1 g, 0.43 mmol) in 5 ml of $CHCl_3$. The mixture was stirred for 0.5 h at room temperature and hexane (50 ml) was added. The resulting precipitate was filtered off and dried in air. Yield 76%, mp 190–192 °C (decomp.). Found (5): C, 51.64; H, 4.00; N, 18.81. Calc. for $C_{13}H_{12}N_4O_5$ (%): C, 51.32; H, 3.98; N, 18.41.

For **5a**: ^{1}H NMR (600 MHz, CD_3CN) δ: 1.10 (t, 3H, Me, *J* 7.2 Hz), 2.24–2.26 (m, 1H, H^6), 3.42–3.44 (m, 1H, H^6), 3.75–3.78 (m, 1H, CH_2), 4.01–4.05 (m, 1H, CH_2), 4.23 (dd, 1H, H^7, *J* 12.5 and 5.8 Hz), 5.72–5.75 (m, 1H, H^5), 7.68 (dd, 1H, H^3, *J* 8.4 and 4.7 Hz), 8.78 (d, 1H, H^4, *J* 4.5 Hz), 9.43 (d, 1H, H^2, *J* 8.4 Hz). ^{13}C NMR (150 MHz, CD_3CN) δ: 14.08 ($MeCH_2$), 28.94 (C^7), 31.57 (C^6), 65.11 ($MeCH_2$), 103.16 (C^5), 110.76 (C^{10}), 123.98 (C^{4a}), 126.44 (C^3), 134.76 (C^2), 140.93 (C^{9a}), 150.58 (C^4), 151.56 (C^8).

For **5b**: ^{1}H NMR (600 MHz, CD_3CN) δ: 1.10 (t, 1H, Me, *J* 7.2 Hz), 2.27–2.32 (m, 1H, H^6), 3.40–3.44 (m, 1H, H^6), 3.75–3.78 (m, 1H, CH_2), 4.01–4.05 (m, 1H, CH_2), 4.44 (dd, 1H, H^7, *J* 10.8 and 6.4 Hz), 5.72–5.75 (m, 1H, H^5), 7.58 (dd, 1H, H^3, *J* 8.4 and 4.7 Hz), 8.73 (d, 1H, H^4, *J* 4.7 Hz), 9.38 (d, 1H, H^2, *J* 8.4 Hz). ^{13}C NMR (150 MHz, CD_3CN) δ: 14.11 ($MeCH_2$), 30.68 (C^7), 35.51 (C^6), 65.18 ($MeCH_2$), 102.94 (C^5), 113.25 (C^{10}), 121.96 (C^{4a}), 124.83 (C^3), 134.48 (C^2), 139.71 (C^{9a}), 150.17 (C^4), 153.88 (C^8).