Synthesis of isomeric 1,3- and 1,4-bis[3(4)-nitrofuroxan-4(3)-yl]nitrobenzenes by nitration of the corresponding isomeric 1,3- and 1,4-bis[3(4)-nitrofuroxan-4(3)-yl]benzenes

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Isomeric 1,3- and 1,4-bis[3(4)-nitrofuroxan-4(3)-yl]nitro(dinitro)benzenes were synthesized in high yields by nitration of the corresponding 1,3- and 1,4-bis[3(4)-nitrofuroxan-4(3)-yl]benzenes with a mixture of 100% nitric acid and concentrated sulfuric acid. The influence of 3- and 4-nitrofuroxanyl fragments on the regioselectivity of the nitration was revealed. The structure of 1,3-bis(4-nitrofuroxan-3-yl)-4-nitrobenzene was confirmed by X-ray diffraction analysis. 1,3- and 1,4-Bis(3-nitrofuroxan-4-yl)nitrobenzenes underwent thermal isomerization to more thermodynamically favorable 1,3- and 1,4-bis(4-nitrofuroxan-3-yl)nitrobenzenes.

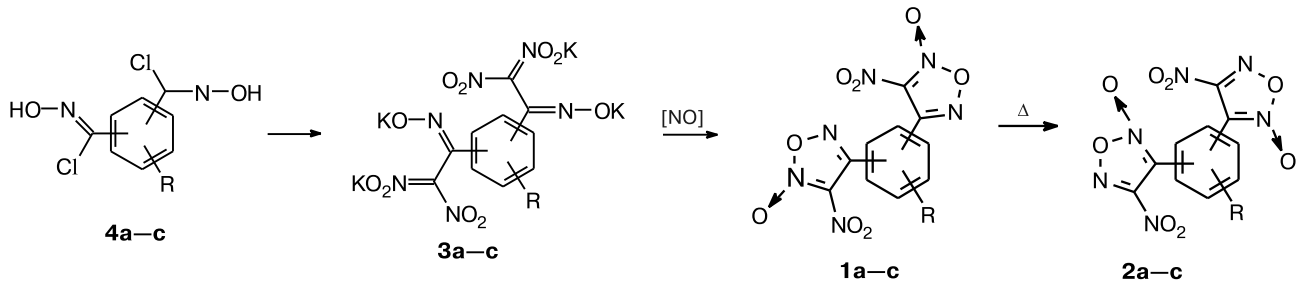
Key words: isomeric 1,3- and 1,4-bis[3(4)-nitrofuroxan-4(3)-yl]benzenes, 1,3- and 1,4-bis[3(4)-nitrofuroxan-4(3)-yl]nitro(dinitro)benzenes, nitration, regioselectivity, thermal isomerization, X-ray diffraction analysis.

Recently,[1,2] we have developed a convenient approach to the structures bearing two nitrofuroxanyl fragments in one aromatic ring, *viz.*, 1,3- (**1a**,**c**) and 1,4-bis(3-nitrofuroxan-4-yl)benzenes (**1b**) and their isomers 1,3- (**2a**,**c**) and 1,4-bis(4-nitrofuroxan-3-yl)benzenes (**2b**). Compounds **1a**—**c** were synthesized by nitrosation of tetrapotassium salts **3a**—**c**, which have been prepared from the known[2] 1,3- and 1,4-di(hydroximoyl chlorides) **4a**—**c**. Thermal isomerization of 3-nitroisomers **1a**—**c** resulted in thermodynamically more stable compounds **2a**—**c** (Scheme 1).

In the present work, we studied the possibility of aromatic ring nitration of compounds **1a**—**c** and **2a**—**c**. In the investigation, we planned to estimate the influence of isomeric nitrofuroxanyl fragments as well as the Me groups (compounds **1c** and **2c**) on the regioselectivity of the nitration reactions. The compounds bearing the nitrofuroxanyl substituents along with the nitro groups in one benzene ring are of interest as prospective energetic compounds.

Earlier,[3] the nitration of 3-aryl-4-nitrofuroxans (aryl is phenyl (**5a**), 2-nitrophenyl (**5b**), 4-nitrophenyl (**5c**), and 3-nitrophenyl (**5d**)) has been studied. A mixture of equal volumes of 100% nitric acid and concentrated sulphuric acid (the molar ratio substrate : HNO_3 = 1 : 10) was used in all cases. It was shown that the nitration of 4-nitro-3-phenylfuroxan (**5a**) proceeded in high yields even at 0 °C and afforded a mixture of approximately equal amounts of 4-nitro- and 3-nitrophenyl derivatives **5c**

Scheme 1



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and **5d**. Thus, the 4-nitrofuroxanyl fragment is a mixed *ortho(para)*- and *meta*-directing group in the nitration of the phenyl fragment. In the nitration of 2-, 3-, and 4-nitrophenyl derivatives, it is the nitro group already present in the benzene ring that determined which position the second nitro group will occupy and the reaction resulted in *meta*-dinitrocompounds **5e,f** only. The existing nitro group in compounds **5b—d** was deactivating, thus, the introduction of the second nitro group required that the temperature was increased to 35—45 °C (for 3-nitrophenyl derivative **5d**) and to 25—30 °C (for 2- and 4-nitrophenyl compounds **5b,c**) (Scheme 2).

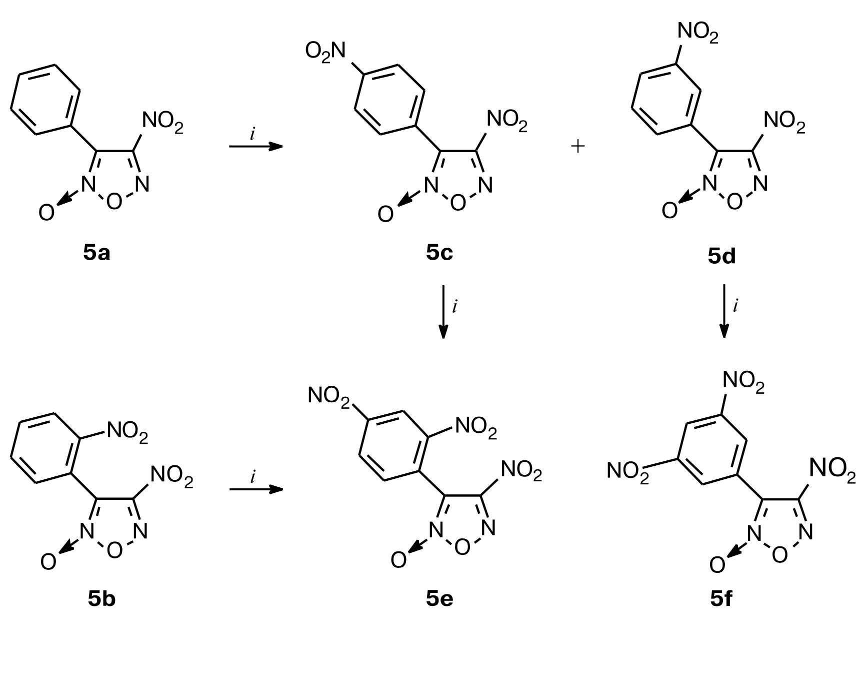
In the present work, we used a mixture of equal volumes of 100% nitric acid and 97% sulphuric acid for the nitration of compounds **1a—c** and **2a—c** bearing two nitrofuroxanyl fragments at one aromatic ring. However, the deactivating effect of two nitrofuroxanyl groups of compounds **1a—c** and **2a—c** required performing the benzene ring nitration at higher temperatures (50—55 °C) as compared with 3-aryl-4-nitrofuroxanyl derivatives **5a—d** (0—45 °C). In all cases, the mononitrocompounds **6a—c** and **7a—c** were obtained in high yields (80—90%) (Scheme 3).

The regioselectivity of the aromatic ring nitration depended on the structures of the starting compounds. It was found that the nitration of 1,3-bis(3-nitrofuroxan-4-yl)benzene (**1a**) bearing the furoxan-4-yl moieties resulted in 5-nitro isomer **6a**, while the nitration of 1,3-bis-(4-nitrofuroxan-3-yl)benzene (**2a**) where the aromatic ring bears the furoxan-3-yl fragment afforded 4-nitro derivative **7a**. It is evident that two 4-nitrofuroxan-3-yl fragments in positions 1 and 3 of the benzene ring exhibit a concerted *ortho(para)*-directing effect in the aromatic ring nitration in contrast to the 3-nitrofuroxan-4-yl fragments, which are *meta*-directing (see Scheme 3). This different directing ability of the isomers of the nitrofuroxans is cased by the features of distribution of the electron density in the furoxan ring. As a whole, the furoxan ring (similarly to the furazan ring) has a strong electron-withdrawing effect. However, it is the higher electron density[4] on the C(3) atom of the furoxan ring due to the resonance influence of the *N*-oxide fragment that activates the *ortho*- and *para*-positions of the aromatic ring of compound **2a** for electrophilic attack.

Since the regioselectivity of the nitration of 1,4-isomers **1b** and **2b** is invariant, the new nitro groups occupy only position 2 of the aromatic rings in compounds **6b** and **7b** regardless of the position of the nitro group in the nitrofuroxanyl fragment of the starting compounds. In the nitration of the Me-substituted derivatives **1c** and **2c**, the direction of the introduction of the nitro groups was entirely defined by the electron donating effect of the Me group so that 4-nitroderivatives **6c** and **7c** formed. The nitration of compound **1c** results in dinitro compound **6d** in a moderate yield along with mononitro compound **6c**. However, our attempts to completely transform compound **6c** into dinitro derivative **6d** by the nitration failed, the first nitro group is deactivating and the subsequent nitration required increasing the temperature, which in turn cased the isomerisation of the furoxan rings (see Scheme 3).

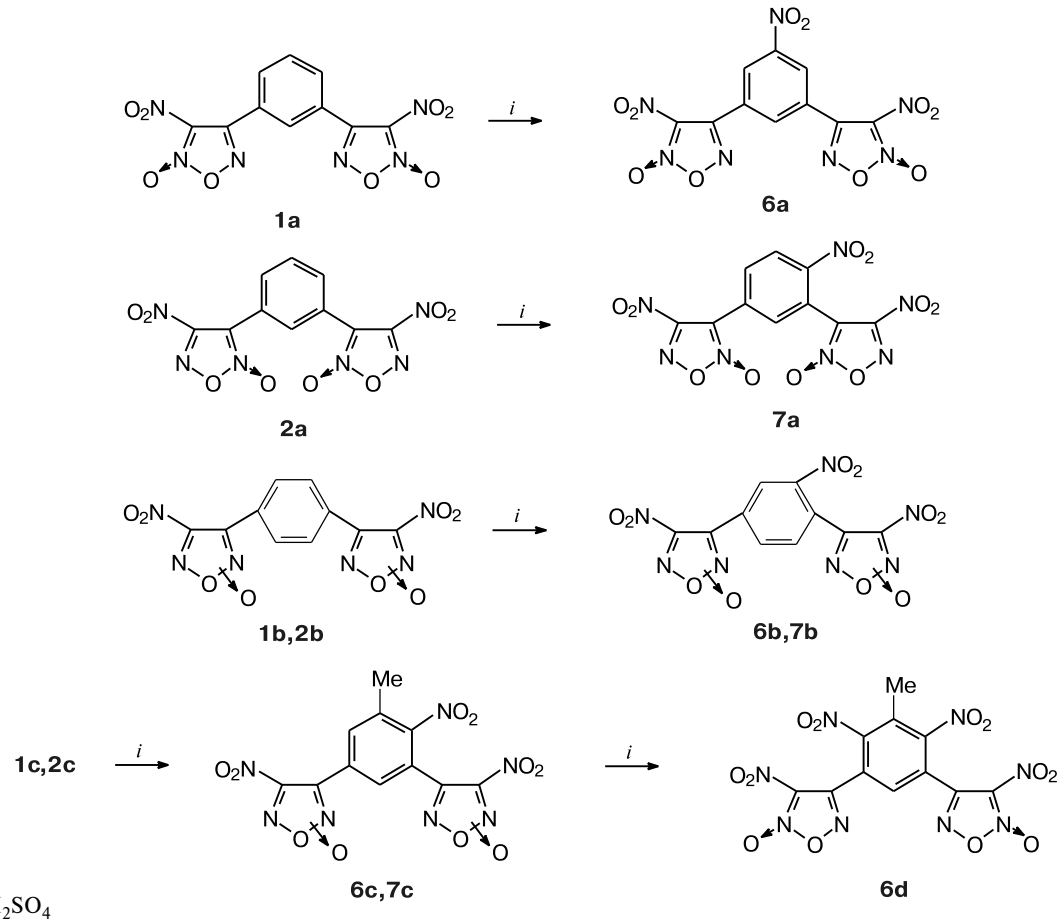
Another convenient approach to the 4-nitrofuroxan derivatives is the thermal isomerization of their 3-nitro-

Scheme 2



i. HNO_3, H_2SO_4

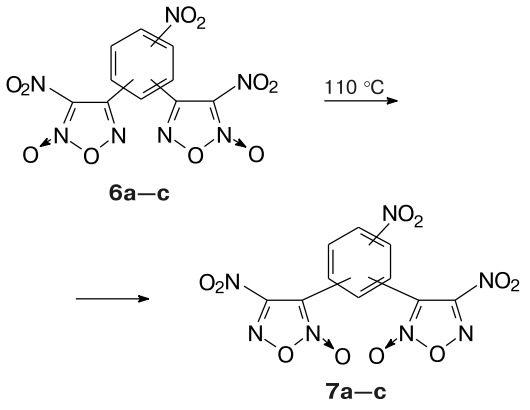
Scheme 3



i. HNO_3, H_2SO_4

furoxanyl analogs. Nitrofuroxanyl derivatives **6a—c** were easily transformed into the more thermodynamically stable 4-nitro isomers **7a—c** in almost quantitative yields after heating under reflux for 5 h in toluene (Scheme 4).

Scheme 4



R = H (**a,b**), Me (**c**)

The structures of the prepared compounds were confirmed by elemental analysis and spectral data (Tables 1 and 2); the structure of compound **7a** was also confirmed by X-ray diffraction analysis. Though the mass spectra of all synthesized compounds have no peaks of molecular ions, all of them contain the peaks of fragment ions formed upon the loss of one or several NO and NO_2 fragments from the molecular species (see Table 2). This is one of the most characteristic properties of the nitrofuroxan derivatives.[4]

The X-ray diffraction analysis data indicate that the structure of compound **7a** is 2,4-bis(4-nitrofuroxan-3-yl)-1-nitrobenzene (Fig. 1). The furoxan rings and the nitro groups of these fragments are coplanar. The benzene ring substituents have different orientation relative to the plane of the aromatic ring, the torsion angles are 21.1(2)° for the nitro group and 70.6(3) and 48.7(3)° for the nitrofuroxan fragments. Evidently, this difference is caused by steric repulsion between the furoxan substituent at the C(7) atom and the nitro group at the C(6) atom and also the presence of numerous short intermolecular interactions O...O in the crystal lattice. Notably, the furoxan ring which forms the larger angle with the benzene ring is disordered over

Table 1. Yields and selected physicochemical characteristics of 1,3- and 1,4-bic[3(4)-nitrofuroxan-4(3)-yl]nitro(dinitro)benzenes **6a—d** and **7a—c**

Compound	Yield (%)	M.p. /°C	R_f	Found / Calculated (%)			Molecular formula
				C	H	N	
6a	87	154—155	0.16[a]	31.37 / 31.51	0.76 / 0.79	25.74 / 25.72	$C_{10}H_3N_7O_{10}$
6b	85	164—166	0.40[a]	31.52 / 31.51	0.81 / 0.79	25.71 / 25.72	$C_{10}H_3N_7O_{10}$
6c	83	107—108	0.31[b]	30.12 / 30.01	0.87 / 0.92	25.52 / 25.46	$C_{11}H_5N_7O_{10}$
6d	14	171—172	0.11[b]	33.47 / 33.43	1.35 / 1.28	24.68 / 24.81	$C_{11}H_4N_8O_{12}$
7a	81	166—167	0.17[b]	31.64 / 31.51	0.83 / 0.79	25.70 / 25.72	$C_{10}H_3N_7O_{10}$
7b	90	186—188	0.17[b]	31.42 / 31.51	0.74 / 0.79	25.78 / 25.72	$C_{10}H_3N_7O_{10}$
7c	80	125—127	0.18[b]	33.38 / 33.43	1.24 / 1.28	24.83 / 24.81	$C_{11}H_5N_7O_{10}$

[a] Eluent — CCl_4—EtOAc, 5 : 1. [b] Eluent — CCl_4—EtOAc, 10 : 1.

Table 2. ^1H, ^{13}C, ^{14}N NMR (DMSO-d_6), IR, and MS data of compounds **6a—d** and **7a—c**

Compound	IR, ν/ cm^{-1}	^1H NMR, δ, J/Hz [MS, m/z (I_{rel} (%))]	^{13}C NMR, δ [^{14}N NMR, δ, $\Delta\nu_{1/2}$ /Hz]
6a	3420, 1644, 1628, 1544, 1420, 1352, 1264, 1172, 1040, 1016, 908, 856, 820, 752, 728, 692, 668	8.62 (s, 1 H, C(2), Ar); 8.98 (s, 2 H, C(4), C(6), Ar) [351 $[M - NO]^+$ (2), 305 $[M - NO - NO_2]^+$ (12) 245 $[M - 3\,NO - NO_2]^+$ (19), 229 $[M - 2\,NO - 2\,NO_2]^+$ (9) 173 (100), 144 (17), 127 (72), 100 (39)]	126.89 (C(3) of the furoxan ring); 127.60, 136.01, 136.62 (C(1), C(2), C(3), C(4), C(6), Ar); 147.63 (CNO_2, Ar); 150.47 (C(4) of the furoxan ring) [−36.75, $\Delta\nu_{1/2} = 22.4$]
6b	3440, 1636, 1624, 1536, 1424, 1348, 1272, 1204, 1016, 988, 848, 804, 788, 732, 668	8.16, 8.47 (both d, 2 H, C(2), C(3), Ar, $^3J = 7.8$); 8.92 (s, 1 H, C(6), Ar) [305 $[M - NO - NO_2]^+$ (63), 263 $[M - NO - NO_2 - CNO]^+$ (61), 245 $[M - 3\,NO - NO_2]^+$ (25), 229 $[M - 2\,NO - 2\,NO_2]^+$ (12), 201 (22), 187 (43), 173 (79), 169 (90), 144 (90), 127 (61), 100 (100)]	126.12 (C(3) of the furoxan ring); 126.56 (C(3) of the furoxan ring); 121.99, 129.52, 133.82, 135.08, 135.71 (C(1), C(2), C(3), C(4), C(6), Ar); 146.72 (CNO_2, Ar); 149.96 (C(4) of the furoxan ring); 150.28 (C(4) of the furoxan ring) [−38.59, $\Delta\nu_{1/2} = 20.6$]
6c	3430, 3076, 1636, 1544, 1516, 1428, 1348, 1264, 1192, 1012, 904, 852, 820, 736, 668	2.61 (s, 3 H, CH_3); 8.22 (s, 1 H, C(6), Ar); 8.29 (s, 1 H, C(2), Ar) [318 $[M - NO - NO_2 - 1]^+$ (14), 272 $[M - NO - 2\,NO_2 - 1]^+$ (35), 242 $[M - 2\,NO - 2\,NO_2 - 1]^+$ (38), 169 (100), 157 (37), 142 (37), 129 (42), 114 (86)]	23.42 (CH_3); 124.10 (C(3) of the furoxan ring); 126.46 (C(3) of the furoxan ring); 127.77, 133.19, 136.22, 138.54, 142.10 (C(1), C(2), C(3), C(5), C(6), Ar); 153.53 (CNO_2, Ar); 155.27 (C(4) of the furoxan ring); 155.63 (C(4) of the furoxan ring) [−36.73, $\Delta\nu_{1/2} = 15.0$]

(*to be continued*)

Table 2 (*continued*)

Compound	IR, ν/ cm^{-1}	^{1}H NMR, δ, *J*/Hz [MS, *m*/*z* (I_{rel} (%))]	^{13}C NMR, δ [^{14}N NMR, δ, $\Delta\nu_{1/2}$ /Hz]
6d	3400, 3240, 3088, 2920, 1636, 1544, 1444, 1352, 1268, 1172, 1104, 1012, 916, 888, 792	2.72 (s, 3 H, CH_3); 8.09 (s, 1 H, C(2), Ar) [343 [M – 2 NO – NO_2 – 1]$^+$ (1), 318 [M – NO – 2 NO_2]$^+$ (5), 181 (7), 157 (50), 129 (11), 114 (100)]	20.99 (CH_3); 127.26 (C(3) of the furoxan ring); 122.25, 137.15, 145.53 (C(1), C(2), C(3), C(5), Ar); 147.48 (CNO_2, Ar); 150.51 (C(4) of the furoxan ring) [–38.62, $\Delta\nu_{1/2}$ = 15.5]
7a	3420, 3100, 2928, 2872, 1644, 1572, 1616, 1484, 1360, 1280, 1128, 1024, 984, 824, 740	8.39, 8.69 (both d, 2 H, C(5), C(6), Ar, ^3J = 9.1); 8.41 (s, 1 H, C(2), Ar) [351 [M–NO]$^+$ (2), 305 [M – NO – NO_2]$^+$ (6), 259 [M – NO – 2 NO_2]$^+$ (13), 245 [M – 3 NO – NO_2]$^+$ (4), 229 [M – 2 NO – 2 NO_2]$^+$ (15), 185 (19), 173 (31), 144 (58), 127 (80), 100 (100)]	108.37 (C(3) of the furoxan ring); 109.63 (C(3) of the furoxan ring); 115.77, 126.45, 127.83, 134.54, 135.58 (C(1), C(2), C(3), C(5), C(6), Ar); 148.10 (CNO_2, Ar); 158.15 (C(4) of the furoxan ring); 158.58 (C(4) of the furoxan ring) [–35.54, $\Delta\nu_{1/2}$ = 32.3]
7b	3440, 3116, 1636, 1616, 1576, 1548, 1520, 1492, 1352, 1308, 1280, 1128, 1076, 1012, 984, 888, 840, 792, 728, 660	8.27, 8.44 (both d, 2 H, C(5), C(6), Ar) 8.94 (s, 1 H, C(3), Ar) [305 [M – NO – NO_2]$^+$ (5.5), 275 [M – 2 NO – NO_2]$^+$ (5.5), 259 [M – NO – 2 NO_2]$^+$ (9), 229 [M – 2 NO – 2 NO_2]$^+$ (9), 187 (30), 173 (82), 144 (46), 127 (100), 100 (93)]	108.58 (C(3) of the furoxan ring); 109.56 (C(3) of the furoxan ring); 117.83, 126.00, 127.62, 133.99, 136.24 (C(1), C(2), C(3), C(4), C(6) Ar); 146.77 (CNO_2, Ar); 154.87 (C(4) of the furoxan ring); 155.40 (C(4) of the furoxan ring) [–35.65, $\Delta\nu_{1/2}$ = 31.0]
7c	3430, 2924, 2876, 1636, 1624, 1576, 1532, 1512, 1352, 1304, 1192, 1080, 1052, 1024, 912, 896, 828, 776, 752, 716, 684, 664	2.58 (s, 3 H, Me); 8.21, 8.28 (both s, 2 H, C(2), C(6), Ar) [364 [M – NO – 1]$^+$ (1), 349 [M – NO_2]$^+$ (1), 319 [M – NO – NO_2]$^+$ (34), 273 [M – NO – 2 NO_2]$^+$ (19), 243 [M – 2 NO – 2 NO_2]$^+$ (27), 217 (17), 201 (20), 183 (31), 170 (85), 158 (41), 142 (67), 129 (44), 114 (94), 91 (100)]	18.62 (CH_3); 116.45 (C(3) of the furoxan ring); 120.39 (C(3) of the furoxan ring); 128.14, 129.04, 131.39, 134.67, 137.48, (C(1), C(2), C(3), C(5), C(6), Ar); 149.16 (CNO_2, Ar); 150.85 (C(4) of the furoxan ring); 151.30 (C(4) of the furoxan ring) [–35.33, $\Delta\nu_{1/2}$ = 39.5]

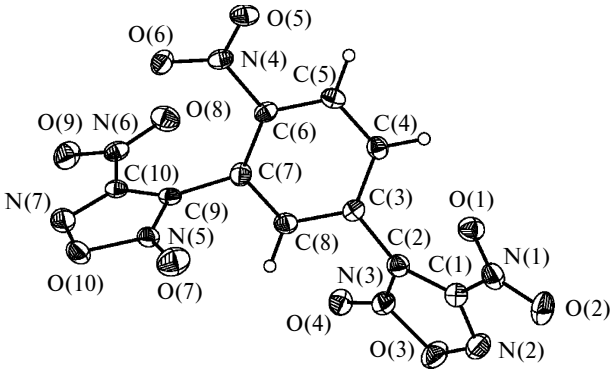


Fig. 1. General view of compound **7a**. Non-hydrogen atoms are given with 50% probability thermal ellipsoids. The disorder of the nitrofuroxan fragments is not shown.

two positions (see Experimental), which makes impossible detailed analysis of intra- and intermolecular interactions.

In conclusion, we studied the aromatic ring nitration of isomeric 1,3- and 1,4-bis[3(4)-nitrofuroxan-4(3)-yl]-benzenes, which revealed the influence of the 3- and 4-nitrofuroxanyl fragments on the direction of the nitration, and prepared the corresponding 1,3- and 1,4-bis[3(4)-nitrofuroxan-4(3)-yl]nitrobenzenes in high to excellent yields.

Experimental

IR spectra were recorded on a UR-20 spectrometer (KBr pellets). NMR spectra were recorded on Bruker WM-250 (^{1}H,

250 MHz) and Bruker AM-300 (^{13}C, 75.5 MHz; ^{14}N, 21.5 MHz) spectrometers in DMSO-d_6 using Me_4Si (^{1}H and ^{13}C) as the internal standard or $MeNO_2$ (^{14}N) as the external standard. Mass spectra were obtained on a Varian MAT CH 6 instrument (EI, 70 eV). Thin layer chromatography was performed on Silufol UV-254 plates with the visualization by UV light.

X-ray diffraction study. The crystals of compound **7a** at 100 K are orthorhombic, space group *Pbca*, a = 13.4057(16), b = 10.6094(13), c = 19.251(2) Å, V = 2738.0(6) Å^3, Z = 8 (Z' = 1), d_{calc} = 1.849 g cm^{-3}, μ(MoKα) = 1.70 cm^{-1}, F(000) = = 1536. The intensities of 28515 reflections were measured at 100 K on a SMART APEX II CCD diffractometer (λ(MoKα) = = 0.71072 Å, ω-scanning mode, 2θ < 60°) and 3291 independent reflections (R_{int} = 0.0551) were used for the further refinement. The structure was solved by the direct methods and refined by the full-matrix least-squares method with anisotropic displacement parameters based on F_{hkl}^2. The furoxan fragment in the position 2 of the benzene ring is disordered over two directions with occupancy factors of 0.8, 0.2 that could be described as superposition of two nitrofuroxan rings bearing different location of nitro- and nitroxyl groups relative to the plane of the benzene ring. All hydrogen atoms were positioned geometrically and refined using fixed thermal parameters $B_{iso} = 1.2C_{iso}$ anisotropically. The final uncertainty factors for compound **7a** were R_1 = 0.0454 (calculations based on F_{hkl} for 2742 reflections with $I > 2\sigma(I)$), wR_2 = 0.1130 (calculations based on F_{hkl}^2 for all 3291 reflections), GOF = 1.015. All calculation were carried out using the SHELXTL 5.10 program package.[5] The coordinates of the atoms and details of X-ray diffraction experiment have been deposited with the Cambridge Crystallographic Data Centre (CCDC 776986).

Synthesis of 1,3(1,4)-[bis(3(4)nitrofuroxan-4(3)yl]nitrobenzenes 6a—d and 7a—c (general procedure). 100% HNO_3 (10 mL) was gradually (3—4 min) added to a solution of furoxan **1a—c** or **2a—c** (2 mmol) in 97% H_2SO_4 (10 mL) at room temperature. Temperature was increased to 50—55 °C and the reaction mixture was stirred for 1 h. After cooling to room temperature, the reaction mixture was poured onto ice (10 mL). The solid was filtered off and washed with large amount of water and dried on air.

According to TLC, the nitration of compound **1c** resulted in a mixture of **6c** and **6d**. These compounds were separated by preparative TLC (CCl_4—EtOAc, 10 : 1).

Isomerisation of 1,3(1,4)-[bis(3-nitrofuroxan-4-yl]nitrobenzenes 6a—c into 1,3(1,4)[bis(4-nitrofuroxan-3-yl]nitrobenzenes 7a—c (general procedure). A suspension of furoxans **6a—c** (1 mmol) in toluene (10 mL) was refluxed for 5 h. The reaction mixture was cooled, furoxans **7a—c** were filtered off and dried on air. Furoxans **7a—c** were obtained in 94—96% yields and were identical to those prepared by the nitration judging by the spectral data.

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