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Ring-opening and recyclization of 3,4-diacylfuroxans by nitrogen nucleophiles

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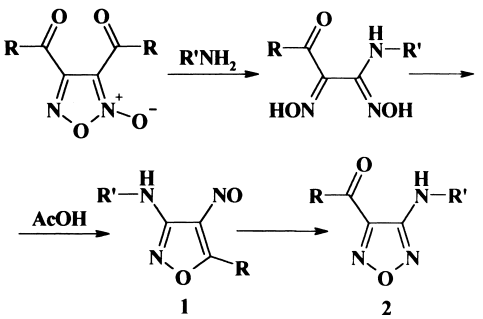
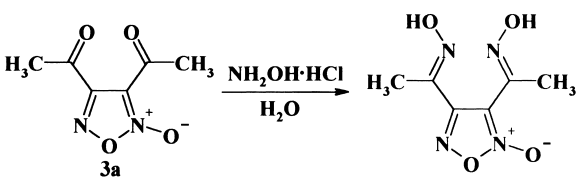
Abstract—Interaction of 3,4-diacylfuroxans with hydroxylamine hydrochloride results in the formation of substituted 4,5-bis (hydroximino)-4,5-dihydroisoxazoles, whereas the reaction of 3,4-bis(4-methylfurazanoyl-3)furoxan with hydrazine hydrate in acetic acid affords 3-[4,5-bis(hydroximino)-4,5-dihydro-1*H*-pyrazol-3-yl]-4-methylfurazan. *N*-Acyl-, *N*-nitro-, *N*-alkyl- and *N*-adamantyl derivatives of the latter compound have been synthesized. X-Ray structure determinations together with density functional theoretical calculations are reported.

Derivatives of furoxans owing to their easy preparation and a remarkable susceptibility to ring opening and recyclization under the action of nucleophiles are very promising for the synthesis of various heterocyclic systems. The structure of products depends on the character of the bond in the furoxan ring being broken. The most thoroughly studied are those reactions in which the C–C bond of the furoxan ring remains intact, among them should be mentioned the so-called Beirut reaction, in the course of which the furoxan ring in benzofuroxans transforms under the action of sufficiently strong bases into five- and six-membered heterocycles (imidazoline or pyrazine), the Boulton–Katritzky rearrangement,[1] recyclization of the furoxan ring into 1,2,3-triazole-1-oxide on the interaction of 4-amino-(4-alkylamino)-3-nitrofuroxans with primary amines, etc.[2] Special attention in the series of these reactions has focused on the recyclization of 3,4-diacylfuroxans under the action of nitrogen nucleophiles because of the contradictory literature data on the subject. Indeed, the true structure of the products of interaction of diacylfuroxans with amines, which eventually proved to be 4-nitrosoisoxazoles **1**, had not been established for a long time (Scheme 1). The latter are capable to isomerize into another heterocyclic system, the furazan derivatives **2**, either spontaneously or under heating in acetyl chloride, acetic anhydride and acetic acid solutions.[3a,b] The behavior of 3,4-diacylfuroxans **3** in reactions with hydroxylamine and hydrazine deserves special attention. Only the carbonyl



Scheme 1.

groups of 3,4-diacetylfuroxan are affected in the reaction with hydroxylamine hydrochloride in aqueous solution, the furoxan ring remaining intact (Scheme 2).[4] However, when 3,4-diaroylfuroxans **3b–d** and 3,4-bis (4-methylfurazanoyl-3)furoxan **3e** reacted with hydroxylamine hydrochloride in pyridine solution, 3-aryl- and 3-(4-methylfurazanyl-3)-4,5-bis(hydroximino)-4,5-dihydroisoxazoles **4b–e** were formed, i.e. the furoxan ring under these conditions undergoes recyclization into isoxazole (Scheme 3).[5]



Scheme 2.

Keywords: furoxans; isoxazoles; pyridazines; rearrangement.
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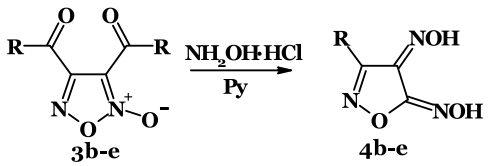
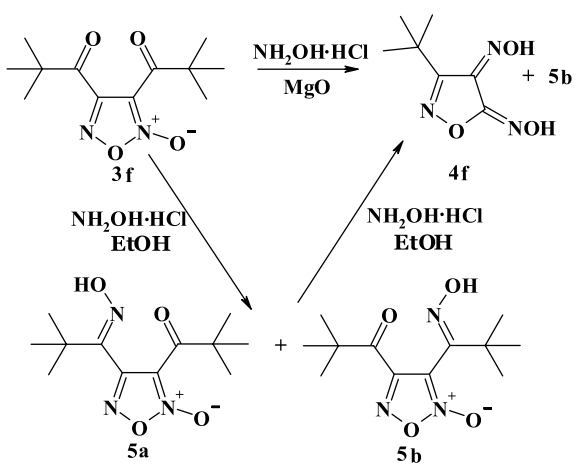
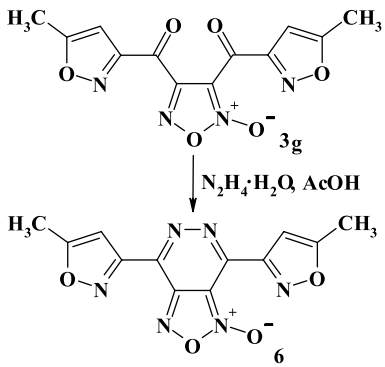


Scheme 3.

3,4-Dipivaloylfuroxan[6] **3f** also forms isoxazole **4f** on reaction with hydroxylamine hydrochloride in aqueous alcoholic solution. These observations[6] contradict the formerly reported preparation of the dioxime when 3,4-dibenzoylfuroxan **3b** was treated with $NH_2OH{\cdot}HCl$ in aqueous alcohol.[7] Earlier it was suggested that formation of the isoxazole ring during the interaction of 3,4-dibenzoylfuroxan with hydroxylamine proceeds via oximation of the carbonyl group at the 'furazan' side of the diacylfuroxan molecule. The subsequent nucleophilic attack on the carbonyl group at position 4 of the so formed monooxime by the second hydroxylamine molecule via ring opening to produce α-oximinonitrile oxide and its intramolecular cyclization leads to the isoxazole.[5a] This suggestion was experimentally proved with 3,4-dipivaloylfuroxan **3f** as an example. Using a two-fold excess of hydroxylamine hydrochloride in the absence of base afforded a 10:4.3 mixture of isomeric monooximes **5a** and **5b** (according to ^1H NMR spectroscopy) (Scheme 4). A repeated treatment of the mixture of isomers **5a** and **5b** with hydroxylamine hydrochloride furnished isoxazole **4f**, monooxime **5b** remaining intact. When the reaction of 3,4-dipivaloylfuroxan **3f** with hydroxylamine hydrochloride was conducted in the presence of magnesium oxide or potassium hydrocarbonate, it resulted in the formation of isoxazole **4f** and monooxime **5b** in approximately equal amounts. The structures of monooxime **5b** and isoxazole **4f** have been proved by means of X-ray diffraction studies (vide infra). The results obtained support the above suggestion on the mechanism of rearrangement of diacylfuroxans into isoxazole derivatives under the action of hydroxylamine. Unfortunately, all attempts to trap the intermediate α-oximinonitrile oxide with added dipolarophiles (styrene, butene-1,4-diol etc.) failed (Scheme 5).

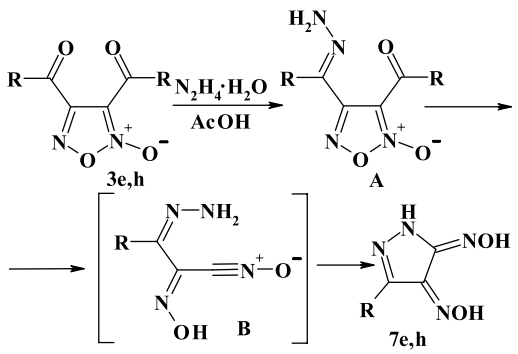


Scheme 4.

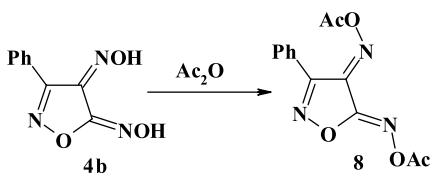


Scheme 5.

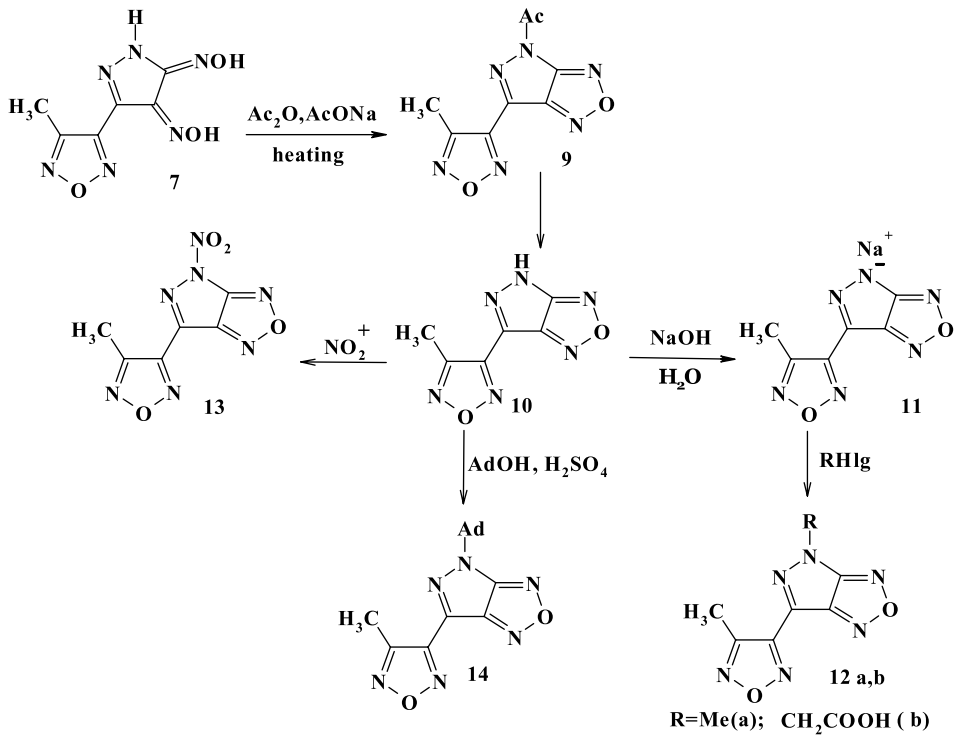
These results are somewhat at variance with the behavior of 3,4-diacylfuroxans in the reaction with another nitrogen nucleophile, hydrazine. Unsubstituted hydrazine, when used as a weakly basic hydrazinium cation, reacts with the carbonyl groups of diaroylfuroxans to afford corresponding azines.[8–10] Similar to 3,4-dipivaloyl- (**3f**) and 3,4-diaroylfuroxans, 3,4-bis (5-methylisoxazoloyl-3)furoxan **3g** with hydrazine in acetic acid also forms 4,7-bis(5-methylisoxazoloyl-3)pyridazino[4,5-*c*]furoxan **6g**. Quite surprisingly, when 3,4-bis(4-methyl-3-furazanoyl)- and 3,4-bis(3-methyl-4-furoxanoyl)furoxans **3e**,**h** reacted with hydrazine hydrate, 3-[4,5-bis-(hydroximino)-4,5-dihydro-1*H*-pyrazol-3-yl)-4-methylfurazan **7e**[11,12] and 4-[4,5-bis(hydroximino)-4,5-dihydro-1*H*-pyrazol-3-yl)-3-methylfuroxan **7h**, respectively, were isolated instead of the expected azines. Formation of the 4,5-dihydroximinopyrazole system was earlier observed only upon the interaction of diacylfuroxans with phenylhydrazine.[2] Apparently, recyclization of diacylfuroxans **3e**,**h**, similar to the reactions reported earlier,[2] begins with the attack of hydrazine on one of the carbonyl groups of the diacylfuroxan **3**. The intermediate hydrazone **A** upon interaction with the second hydrazine molecule



Scheme 6.



Scheme 7.



Scheme 8.

splits off an acyl hydrazide with the simultaneous opening of the furoxan ring (intermediate **B**). The electronegative 1,2,5-oxadiazole ring present in compound **A** obviously facilitates the rearrangement of the latter via nitrile oxide **B** into pyrazole **7** (Scheme 6).

The behavior of 4,5-bis (hydroximino) isoxazole derivative **4b** and 3-[4,5-bis(hydroximino)-4,5-dihydro-1*H*-pyrazol-3-yl)-4-methylfurazan **7** during their attempted dehydration to the corresponding furazans was not unambiguous. Unsuccessful attempts to prepare isoxazolo [4,5-*c*]furazans by dehydration of 4,5-bis(hydroximino)-4,5-dihydroisoxazoles are well known; in particular, heating in aqueous KOH afforded only 3-hydroxyfurazancarboxylic acid,[2] whereas treatment with $SOCl_2$ furnished 3-hydroxy-4-cyanohydroximinomethylfurazan.[2] Our attempt to prepare isoxazolo[4,5-*c*]furazan by treatment of 4,5-bis (hydroximino)derivative **4b** with acetic anhydride also failed: at 20°C only diacetate **8** was obtained, the latter upon heating above its melting point or during recrystallization decomposes with the loss of acetyl moieties and formation of unidentified products (Scheme 7). As distinct from **4b**, 3-[4,5-bis(hydroximino)-4,5-dihydro-1*H*-pyrazol-3-yl)-4-methylfurazan **7** upon heating with acetic anhydride in the presence of sodium acetate dehydrates producing 6-(4-methylfurazanyl-3)-4-acetylpyrazolo[3,4-*c*]furazan.[11,12] In basic media, the *N*-acetyl group of **9** is readily saponified leading to 6-(4-methylfurazan-3-yl)-4*H*-pyrazolo[3,4-*c*]furazan **10**. Compound **10**, being a NH-acid, under the action of aqueous NaOH forms salt **11**, alkylation of which with alkyl halides affords *N*-alkyl derivatives **12a**,**b**. Nitration of compound **10** with mixed acid furnishes *N*-nitro derivative **13**; adamantylation of **10** in concentrated H_2SO_4 results in the formation of *N*-adamantyl derivative **14**.The results obtained demonstrated that the facility of rearrangement of diacylfuroxans under the action of such nucleophiles as hydroxylamine and hydrazine depends both on the structure of the acyl moiety and on reaction conditions; in particular, the electron-accepting properties of the furazanoyl substituent promote the recyclization of the furoxanyl moiety into the isoxazolyl one in the reaction with hydroxylamine and into the pyrazolyl one in the reaction with hydrazine (Scheme 8).

1. Computational results

Recent investigations have shown that density functional theoretical (DFT) methods can provide reliable tools for the prediction of geometries and energies of a wide variety of organic (and inorganic) compounds, especially in those cases where classical Hartree–Fock (HF) methods (or even Møller–Plesset calculations of second order) fail[14] (e.g. for furoxans and benzofuroxans).[15] A variety of functionals have been used in these calculations and it has been

Table 1. Computational results for compounds **4f** (**4f-a** to **4f-g**) and **5b** (**5b-a**, **5b-b**)

Compound	*E* (in a.u.)[a,b]	*E* (in a.u.)[b,c]
	−663.11035 (6.4)	−663.32739 (6.0)
4f-b	−663.10951 (7.0)	−663.32574 (7.1)
4f-c	−663.10898 (7.3)	−663.32368 (8.4)
4f-d	−663.10710 (8.5)	−663.32237 (9.2)
4f-e	−663.10773 (8.1)	−663.32116 (9.9)
4f-f	−663.12061 (0.0)	−663.33699 (0.0)
4f-g	−663.10473 (10.0)	−663.32044 (10.4)
5b-a	−933.66618 (0.0)	–
5b-b	−933.66345 (1.7)	–

[a] B3LYP/6-31G(d).
[b] Relative energies (in kcal/mol).
[c] B3LYP/6-311+G(2d,p)// B3LYP/6-31G(d).

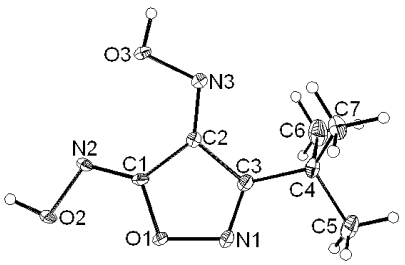


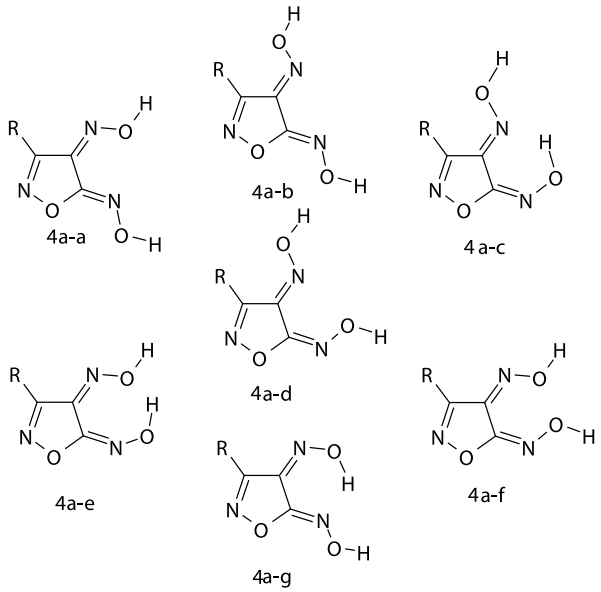
Figure 1. Crystal structure of **4f** (co-crystal with C_6H_{12}) with labeling and displacement ellipsoids drawn at 50% probability level.

Table 2. Experimental and calculated bond distances (in Å) for compounds **4f** and **5**

Bond	4f		5	
	Exp.	Calcd[a]	Exp.	Calcd[a]
A	1.452	1.423	1.361	1.355
B	1.287	1.293	1.308	1.310
C	1.467	1.471	1.421	1.429
D	1.455	1.465	1.319	1.330
E	1.365	1.370	1.478	1.477
F	1.274	1.285	1.220	1.220

[a] B3LYP/6-31G(d).

demonstrated that the hybrid functional B3LYP gives accurate optimized geometries for a wide range of molecules.[14,16] Therefore, it seemed of interest whether this functional together with suitable basis sets can also be used successfully to describe molecules like **4f** and **5b**, where computational results can be judged against X-ray structure determinations. Compound **4f** may exist as several isomers (conformers), some of which are given in the scheme (**4a-a** to **4a-g**). B3LYP/6-31G(d) optimizations[17] reveal that **4a-f** is the most stable (see Table 1) in contrast to experimental results, where **4a-a** is found to be present in the crystalline state. The same holds for B3LYP/6-311+G(2d,p)//B3LYP/6-31G(d)[18,19] calculations. Obviously, a strong intramolecular hydrogen bond in a six-membered ring together with a favorable steric arrangement of the oxime moiety (compared with **4a-c**) is the reason for this preference, which is the result of a gas-phase calculation. In the crystalline environment **4a-a** can form intermolecular hydrogen bonds (Fig. 1), which obviously



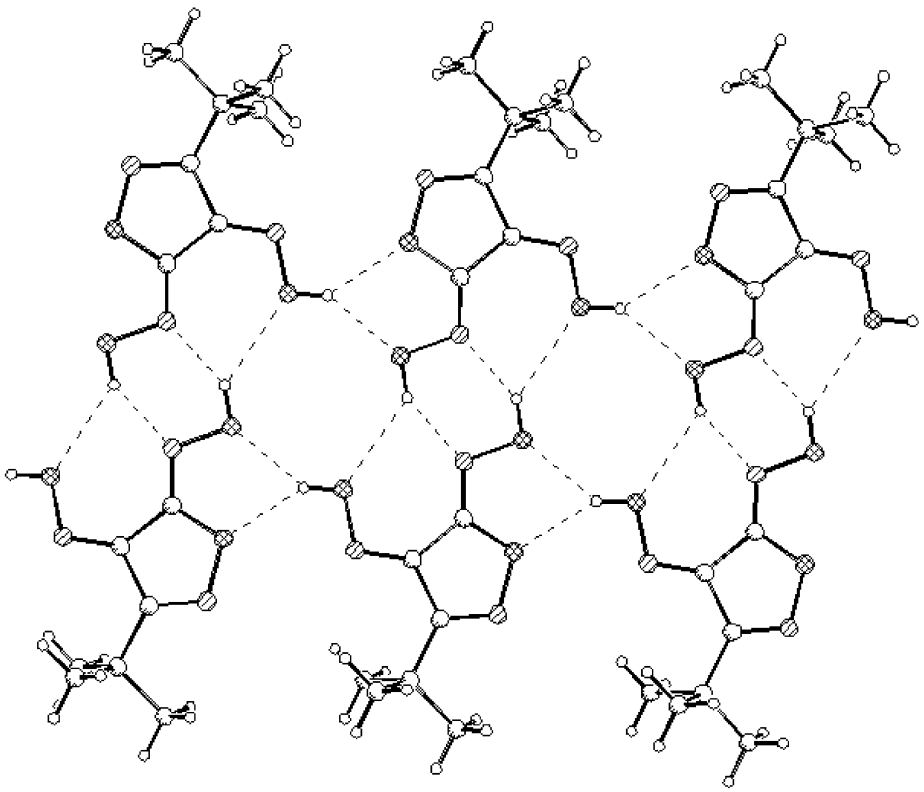


Figure 2. Crystal structure of **4f** (co-crystal with C_6H_{12}) with view on (010) (hydrogen bonding is shown as dotted lines).

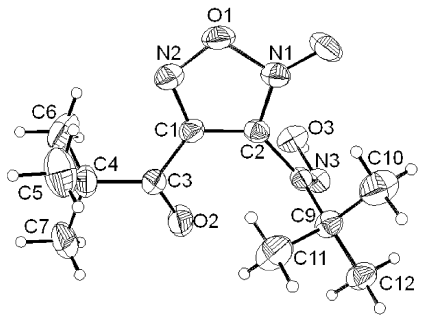
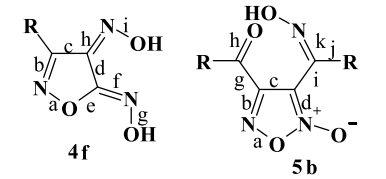
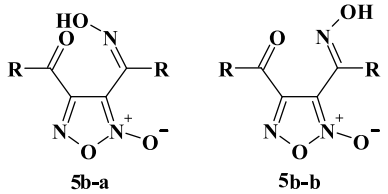


Figure 3. Crystal structure of **5b** with labeling and displacement ellipsoids drawn at 50% probability level.

favor this isomer. Interestingly, **4a**-**a** is computed as the second stable isomer, although the energy differences to other isomers (conformers) are small (Table 1). Calculated bond lengths for **4a**-**a** agree quite well with experimental results (Table 2).

Compound **5b** may also exist as several isomers (conformers), two of which (**5b**-**a**, **5b**-**b**) have been considered in more detail. B3LYP/6-31G(d) calculations reveal that **5b**-**a** should be slightly more stable than **5b**-**b** in agreement with X-ray structure results. As has already been pointed out, geometries of furoxans and benzofuroxans cannot be described adequately by HF (or even MP2) methods,[15] but DFT calculations (e.g. B3LYP/6-31G(d)) yield results, which are in good to excellent agreement with experimental structure determinations. The same holds for **5b**-**a** (Table 2). In conclusion it can be stated that for both **4f** and **5b** the agreement between theory and experiment is good to excellent (Figs. 2 and 3).





2. Experimental

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC-300 spectrometer with DMSO as internal standard. IR spectra were determined on a Perkin–Elmer Spectrum 1000 spectrometer on KBr bed. Mass spectra were recorded on a Varian CH-6 instrument (70 eV electron impact ionization). Details of the crystal structure, crystal data and results of the structure refinement for **4f** and **5b** are given in Table 3. All non-hydrogen atoms were refined using anisotropic displacement parameters. The C–H hydrogen atoms were positioned with idealized geometry and were refined with isotropic displacement parameters using a riding model. The O–H hydrogen atoms were located in the difference map and refined with varying coordinates and isotropic displacement parameters. One carbon atom of the cyclohexane molecule in **4f** co-crystal is disordered over two positions and was refined using a split model. This ring is located on the center of inversion.[20] The initial 3,4-bis(4-methylfurazanoyl-3)furoxan **3e** and 3,4-dipivaloylfuroxan **3f** were synthesized according to Refs. 13,7, respectively. 3,4-Bis (5-methylisoxazoloyl-3) furoxan **3g** was prepared as reported in Ref. 21.

2.1. Oximation of 3,4-dipivaloylfuroxan 3f with hydroxylamine hydrochloride

In ethanol. A mixture of a solution of $NH_2OH{\cdot}HCl$ (2.78 g, 40 mmol) in a minimal volume of water and a solution of furoxan **3f** (2.54 g, 10 mmol) in 30 mL of ethanol was stirred at room temperature for 24 h. The reaction mixture was diluted with water; the precipitated solid was filtered off and recrystallized from *n*-hexane. The mixture of isomeric monooximes of **5a** and **5b** (2.2 g, 82%) (in ratio 10:4.3) was obtained as a white solid, mp 100–113°C. [Found: C, 53.50; H, 7.24; N, 15.62. $C_{12}H_{19}N_3O_4$ requires C, 53.52; H, 7.11; N, 15.60%]; ν_{max} (KBr) 3247, 2969, 234, 1696, 1608, 1484, 1458, 1432, 1395, 1368, 1322, 1078, 1057, 1002, 987, 961, 927, 828, 794, 769, 754 cm^{-1}.

In the presence of magnesium oxide. A solution of NH_2-OH·HCl (5.56 g, 80 mmol) in a minimal volume of water and a solution of furoxan **3f** (2.54 g, 10 mmol) in 30 mL of

Table 3. Crystal data and results of the structure refinement for **4f** and **5b**

Compound	4f	5b
Formula	$C_6H_{11}N_3O_3{\cdot}0.5C_6H_{12}$	$C_{12}H_{19}N_3O_4$
MW (g/mol)	227.27	269.30
Crystal colour	Red	Colourless
Crystal system	Triclinic	Monoclinic
Space group	*P*-1	$P2_1c$
A (Å)	6.5113 (7)	6.268 (1)
B (Å)	7.7399 (8)	12.180 (2)
C (Å)	12.887 (1)	19.137 (4)
α (°)	106.53 (1)	–
β (°)	94.98 (1)	95.23 (3)
γ (°)	103.64 (1)	–
V (Å^3)	596.7 (1)	1454.9 (5)
Temperature (K)	130	170
Z	2	4
D_{calcd} (g/cm^3)	1.265	1.229
F(000)	244	576
2θ-range	3–54°	3–54°
h/*k*/*l* ranges	−8/8, −9/9, −16/16	−0/8, −15/1, −24/24
Diffractometer	STOE IPDS	Nonius CAD4
μ (Mo Kα) (mm^{-1})	0.09	0.09
Measured refl.	3608	3962
$R_{int.}$	0.0435	0.0152
Independent refl.	2314	3183
Refl. with $I>2\sigma(I)$	2024	2283
Structure solution	SHELXS-94	SHELXS-86
Structure refinement	SHELXL-97	SHELXL-97
Refined parameters	165	182
R_1 [$I>2\sigma(I)$]	0.0448	0.0387
wR_2 (all data)	0.1245	0.1156
GoF	1.084	1.023
Min./max. res. (e/Å^3)	0.32/−0.30	0.23/−0.14

ethanol was stirred at ambient temperature for 24 h, after which MgO (0.8 g, 20 mmol) was added to it and stirred until the MgO had dissolved (2 days). After dilution with water (100 mL), the precipitated solid was filtered off, the filtrate was treated with ether (3×50 mL), the organic layer was separated, dried ($MgSO_4$) and the solvent evaporated in vacuo. The combined solids were treated with boiling *n*-hexane (25 mL) and filtered. The precipitate was washed with boiling chloroform (10 mL) and dried in air. Compound **4f** (0.78 g, 42%) was obtained as a white solid, mp 152–153°C. [Found: C, 45.51; H, 6.09; N, 22.61. $C_7H_{11}N_3O_3$ requires C, 45.40; H, 5.99; N, 22.69%]; ν_{max} (KBr) 3434, 3234, 2968, 1659, 1608, 1481, 1462, 1396, 1370, 1340, 1240, 1179, 1054, 998, 954, 889, 787, 755, 741, 719 cm^{-1}; δ_H (300 MHz, DMSO) 13.69 (1H, s, NOH), 11.49 (1H, s, NOH), 1.35 (18H, s, ^tBu); δ_C (75 MHz, DMSO) 165.79, 149.18, 142.23, 34.52, 28.29. After cooling of the extract (*n*-hexane) the precipitate was filtered off and dried in air giving 2.6 g (87%) of compound **5b** (1.05 g, 39%) as a white solid, mp 101–102°C. [Found: C, 53.50; H, 7.23; N, 15.62. $C_{12}H_{19}N_3O_4$ requires C, 53.52; H, 7.11; N, 15.60%]; δ_H (300 MHz, DMSO) 11.90 (1H, s, NOH), 1.33 (9H, s, ^tBu), 1.17 (9H, s, ^tBu); δ_C (75 MHz, DMSO) 197.1, 154.1, 148.8, 109.2, 45.23, 38.54, 29.14, 26.85.

2.1.1. 4,7-Bis(5-methylisoxazol-3-yl)pyridazino[4,5-*c*]furoxan (6). A mixture of 3,4-diacylfuroxan **3g** (3.0 g, 10 mmol), glacial acetic acid (25 mL) and a solution of 98% hydrazine hydrate (1 g, 20 mmol) in acetic acid (5 mL) was stirred at room temperature for 24 h, the precipitated solid was filtered off, washed with water, dried in air giving compound **6** (2.6 g, 87%)as yellow plates, mp 179–180°C (dec.). [Found: C, 48.10; H, 2.62; N, 27.89. $C_{12}H_8N_6O_4$ requires C, 48.01; H, 2.69; N, 27.99%]; δ_H (300 MHz, DMSO) 7.15 (1H, s, CH), 6.92 (1H, s, CH), 2.62 (3H, s, CH_3), 2.59 (3H, s, CH_3); δ_C (75 MHz, DMSO) 172.7, 172.2, 158.68, 157.6, 146.1, 144.7, 142.7, 108.8, 103.1, 101.9, 12.7, 12.7.

2.1.2. 3-[4,5-Bis(hydroximino)-4,5-dihydro-1*H*-pyrazol-3-yl)-4-methylfurazan (7e) and 4-[4,5-bis(hydroximino)-4,5-dihydro-1*H*-pyrazol-3-yl)-3-methylfuroxan (7h). These compounds were prepared analogously to compound **6** from 33 mmol of 3,4-diacylfuroxan **3e** or **3h** and 65 mmol of 98% hydrazine hydrate in glacial acetic acid (100 mL). Compound **7e** is a yellow powder, mp 225°C (dec.). [Found: C, 34.10; H, 2.90; N, 39.90. $C_6H_6N_6O_3$ requires C, 34.29; H, 2.88; N, 39.99%]; ν_{max} (KBr) 3327, 3264, 1640, 1406, 1369, 1236, 1104, 1036, 989, 938, 730 cm^{-1}; δ_H (300 MHz, DMSO) 13.50 (1H, s, NOH), 12.21 (1H, s, NH), 11.61 (1H, s, NOH), 2.57 (3H, s, CH_3); δ_C (75 MHz, DMSO) 151.7, 147.1, 143.9, 143.5, 134.4, 10.7. Compound **7h** is a yellow powder, mp 196–198°C (dec.). [Found: C, 31.85; H, 2.69; N, 37.21. $C_6H_6N_6O_4$ requires C, 31.87; H, 2.67; N, 37.16%]; ν_{max} (KBr) 3319, 1640, 1607, 1567, 1499, 1451, 1406, 1275, 1099, 1051, 983, 921, 844 cm^{-1}; δ_H (300 MHz, DMSO) 13.41 (1H, s, NOH), 12.19 (1H, s, NH), 11.67 (1H, s, NOH), 2.37 (3H, s, CH_3); δ_C (75 MHz, DMSO) 149.5, 142.9, 142.3, 133.7, 111.6, 9.3.

2.1.3. 3-Phenyl-4,5-bis (acetoximino)-4,5-dihydroisoxazole (8). A mixture of 3-phenyl-4,5-bis(hydroximino)-4,5-dihydroisoxazole **4b** (3.0 g, 14.6 mmol) and acetic anhydride (50 mL) was kept at room temperature with stirring for 3 days. The precipitate was filtered off, washed with water (3×50 mL) and dried in air giving compound **8** (2.33 g, 64%) as colorless needles, mp 152–153°C (dec.). [Found: C, 53.91; H, 3.89; N, 14.59. $C_{13}H_{11}N_3O_5$ requires C, 53.98; H, 3.83; N, 14.53%]; δ_H (300 MHz, DMSO) 8.13 (2H, d, Ph), 7.61 (3H, m, Ph), 2.40 (3H, s, CH_3), 2.34 (3H, s, CH_3).

2.1.4. 6-(4-Methylfurazanyl-3)-4-acetylpyrazolo[3,4-*c*]furazan (9). A solution of 1.8 g (8.6 mmol) of dioxime **7e** and anhydrous AcONa (2.2 g, 27 mmol) in 20 mL of acetic anhydride was refluxed with stirring for 15 min. After cooling the mixture was poured into 100 mL of cooled water, the precipitated solid was filtered off, washed with water and dried in air. Compound **9** (1.4 g, 70%) was obtained as a white solid, mp 119–120°C (CCl_4). [Found: C, 41.16; H, 2.72; N, 36.07. $C_8H_6N_6O_3$ requires C, 41.03; H, 2.58; N, 35.89%]; ν_{max} (KBr) 3457, 1743 (C═O), 1627, 1495, 1442, 1371, 1319, 1297, 1146, 1019, 969, 868, 613 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 2.80 (3H, s, CH_3), 2.81 (3H, s, CH_3); δ_C (75 MHz, $CDCl_3$)166.4, 157.6, 152.8, 150.5, 145.4, 130.9, 21.60, 10.1.

2.1.5. 6-(4-Methylfurazanyl-3)-4*H*-pyrazolo[3,4-*c*]furazan (10). The mixture of acetylpyrazole **9** (2.5 g, 11 mmol) and a solution of NaOH (1 g, 25 mmol) in water (80 mL) was kept with stirring until the complete dissolution of the initial compound (10 min), acidified with concentrated HCl to pH 1–2. The precipitated solid was filtered off and dried in air. Compound **10** (1.9 g, 90%) was obtained as a pale yellow solid, mp 137–138°C ($CHCl_3$). [Found: C, 37.45; H, 2.19; N, 43.78. $C_6H_4N_6O_2$ requires C, 37.51; H, 2.10; N, 43.74%]; ν_{max} (KBr) 3360, 3261, 1635, 1595, 1583, 1500, 1423, 1389, 1288, 1073, 999, 978, 895, 846, 781, 676 cm^{-1}; δ_H (300 MHz, DMSO) 14.48 (1H, s, NH), 2.69 (3H, s, CH_3); δ_C (75 MHz, DMSO) 161.2, 152.6, 151.2, 147.1, 125.2, 10.2.

2.1.6. Sodium salt of 6-(4-methylfurazanyl-3)-4*H*-pyrazolo[3,4-*c*]furazan (11). The mixture of pyrazole **10** (1.0 g, 5.2 mmol) and concentrated aqueous solution of NaOH (0.4 g, 10 mmol) was stirred for 5 min at 40–50°C, cooled to room temperature. The precipitate was filtered off, dried, washed with ether and dried again. Compound **11** (0.9 g, 82%) was obtained as a yellow solid. [Found: C, 33.60; H, 1.48; N, 39.21. $C_6H_3N_6O_2Na$ requires C, 33.66; H, 1.41; N, 39.25%]; δ_H (300 MHz, DMSO) 2.73 (3H, s, CH_3); δ_C (75 MHz, DMSO) 174.9, 153.1, 150.6, 149.5, 118.6, 11.0.

2.1.7. 4-Methyl-6-(4-methylfurazanyl-3)-pyrazolo[3,4-*c*]furazan (12a). A mixture of pyrazole **10** (1.0 g, 5.2 mmol), methyl iodide (0.9 g, 6.3 mmol) and a solution of KOH (0.29 g, 5.2 mmol) in ethanol (20 mL) was refluxed for 1 h, diluted by water (50 mL), the precipitate was filtered off, washed successively with 5% aqueous NaOH, with water, and dried in air. Compound **12a** (0.9 g, 87%) was obtained as a yellow solid. mp 107–108°C. [Found: C, 40.88; H, 3.00; N, 40.66. $C_7H_6N_6O_2$ requires C, 40.78; H, 2.93; N, 40.76%]; δ_H (300 MHz, DMSO) 4.09 (3H, s, CH_3), 2.69 (3H, s, CH_3); δ_C (75 MHz, DMSO) 161.23, 152.87, 151.33, 147.06, 124.22, 10.26.

2.1.8. 4-Carboxymethyl-6-(4-methylfurazanyl-3)-pyrazolo[3,4-*c*]furazan (12b). A mixture of pyrazole **10** (1.0 g, 5.2 mmol), chloroacetic acid (0.5 g, 5.3 mmol) and a solution of KOH (0.58 g, 10.4 mmol) in water (20 mL) was boiled for 5 h. After cooling and acidifying with concentrated HCl to pH 1–2 the precipitate was filtered off and dried in air. Compound **12b** (1 g, 77%) was obtained as a yellow solid, mp 187–188°C. [Found: C, 38.31; H, 2.40; N, 33.62. $C_8H_6N_6O_4$ requires C, 38.41; H, 2.42; N, 33.59%]; ν_{max} (KBr) 2958, 1735 (C=O), 1633, 1498, 1447, 1402, 1281, 1261, 1134, 1025, 924, 889, 837, 750 cm^{-1}; δ_H (300 MHz, DMSO) 8.95 (1H, s, OH), 5.39 (2H, s, CH_2), 2.69 (3H, s, CH_3); δ_C (75 MHz, DMSO) 169.27, 161.02, 153.07, 151.49, 146.96, 125.59, 52.61, 10.21.

2.1.9. 6-(4-Methylfurazanyl-3)-4-nitropyrazolo[3,4-*c*]furazan (13). Pyrazole **10** (1.0 g, 5.2 mmol) was added to a mixture of 3 mL HNO_3 (d 1.5 g/cm^3) and 3 mL of concentrated H_2SO_4. The reaction mass was kept at room temperature for 20 min and poured on ice, the precipitate was filtered off and dried in air. Compound **13** (0.9 g, 74%) was obtained as a yellow solid, mp 85–86°C (dec.). [Found: C, 30.41; H, 1.32; N, 41.39. $C_6H_3N_7O_4$ requires C, 30.39; H, 1.28; N, 41.35%]; ν_{max} (KBr) 3422, 1646 (NO_2), 1429, 1276 (NO_2), 1129, 1092, 1040, 1020, 991, 913, 842, 802, 730, 712 cm^{-1}; δ_H (300 MHz, DMSO) 2.76 (3H, s, CH_3); δ_C (75 MHz, DMSO) 156.23, 153.29, 151.96, 146.14, 130.90, 10.10.

2.1.10. 4-Adamantyl-6-(4-methylfurazanyl-3)-pyrazolo[3,4-*c*]furazan (14). A solution of pyrazole **10** (0.5 g, 2.6 mmol) and adamantanol-**1** (0.44 g, 2.9 mmol) in 94% H_2SO_4 (10 mL) was stirred at room temperature for 24 h, poured into 50 mL of icy water, the precipitated solid was filtered off, washed with water and dried in air. Compound **14** (0.7 g, 82%) was obtained as a yellow solid, mp 226–227°C. [Found: C, 58.95; H, 5.61; N, 25.69. $C_{16}H_{18}N_6O_2$ requires C, 58.89; H, 5.56; N, 25.75%]; δ_H (300 MHz, DMSO) 2.76 (3H, s, CH_3), 2.34 (9H, m, Ad), 1.84 (6H, m, Ad); δ_C (75 MHz, DMSO) 159.2, 152.4, 150.3, 146.5, 123.9, 61.5, 42.0, 10.1.

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References

1. For a recent theoretical study see: Eckert, J. F.; Rauhut, G.; Katritzky, A. R.; Steel, P. J. *J. Am. Chem. Soc.* **1999**, 121.
2. Khmel'nitskii, L. I.; Novikov, S. S.; Godovikova, T. I. *Khimija furoxanov: Reaktsii i primenenie (Chemistry of Furoxans: Reactions and Applications)*. 2nd ed. Nauka: Moscow, 1996; p 430, in Russian.
3. (a) Holleman, A. F. *Ber. Dtsch. Chem. Ges.* **1888**, *21*, 2835–2840. (b) Wieland, H.; Gmelin, T. *Liebigs Ann. Chem.* **1910**, *375*, 297–307. (c) Bertelson, R. C.; Glanz, K. D.; McQuain, D. B. *J. Heterocycl. Chem.* **1969**, *6*, 317–324.
4. Behrend, R.; Tryller, H. *Liebigs Ann. Chem.* **1894**, *283*, 209.
5. (a) Tselinsky, I. V.; Melnikova, S. F.; Pirogov, S. V.; Shaposhnikov, S. D.; Näther, C.; Traulsen, T.; Friedrichsen, W. *Heterocycl. Commun.* **2000**, *6*, 35–40. (b) Shaposhnikov, S. D.; Pirogov, S. V.; Mel'nikova, S. F.; Tselinsky, I. V. *Zh. Org. Khim. (Russ. J. Org. Chem.)* **2000**, *36*, 1745–1746.
6. Tselinsky, I. V.; Mel'nikova, S. F.; Pirogov, S. V.; Shaposhnikov, S. D. *Khim.Geterotsykl. Soed.* **1999**, 1259–1261, in Russian.
7. Scarpati, R.; Rippa, M. *Gazz. Chim. Ital.* **1958**, *88*, 804–811.
8. Snyder, H.; Boyer, N. E. *J. Am. Chem. Soc.* **1955**, *77*, 4233–4238.
9. Ponzio, G.; Ruggeri, G. *Gazz. Chim. Ital.* **1926**, *56*, 733–745.
10. Durio, E. *Gazz. Chim. Ital.* **1931**, *61*, 589–596.
11. Kulikov, A. S.; Machova, N. N.; Khmel'nitskii, L. I.; Izv, A. N. *Ser. Khim. (Russ. Chem. Bull., Ser. Chem.)* **1994**, 485–487.
12. Shaposhnikov, S. D.; Pirogov, S. V.; Mel'nikova, S. F.; Tselinsky, I. V. *Trudy 1-oj Vserossijskoy Konferentsii po khimii geterotsiklov*. Proceedings of the First All-Russion Conference on the Chemistry of Heterocycles, Suzdal, Sept 19–23, 2000; p 417 (in Russian).
13. Tselinsky, I. V.; Mel'nikova, S. F.; Pirogov, S. V.; Shaposhnikov, S. D. *Zh. Org. Khim. (Russ. J. Org. Chem.)* **2000**, *36*, 786–787.
14. (a) Hehre, W. J.; Lou, L. *A Guide to Density Functional Calculations*. *SPARTAN*, Wavefunction, Inc: Irvine, CA, 1997. (b) Koch, W.; Holthusen, M. C. *A Chemist's Guide to Density Functional Theory*. 2nd ed. Wiley-VCH: Weinheim, 2001.
15. (a) Seminario, J. M.; Concha, M. C.; Politzer, P. *J. Comput. Chem.* **1992**, *13*, 177. (b) Ponder, M.; Fowler, J. F.; Schaefer, III., H. F. *J. Org. Chem.* **1994**, *59*, 6431. (c) Friedrichsen, W. *J. Phys. Chem.* **1994**, *98*, 12933. (d) Friedrichsen, W. *J. Chem. Res. (S)* **1995**, 120. *J. Chem. Res.* (*M*) **1995**, 878. (e) Friedrichsen, W. *J. Mol. Struct. (Theochem)* **1995**, *342*, 23. (f) Klenke, B.; Friedrichsen, W. *Tetrahedron* **1966**, *52*, 743. (g) Rauhut, G. *J. Comput. Chem.* **1996**, *17*, 1848. (h) Klenke, B.; Friedrichsen, W. *J. Mol. Struct. (Theochem)* **1998**, *451*, 263. (i) Eckert, F.; Rauhut, G. *J. Am. Chem. Soc.* **1998**, *120*, 13478.
16. Bauschlicher, Jr. C. W. *Chem. Phys. Lett.* **1995**, *246*, 40.
17. All calculations reported in this paper have been performed with the program system GAUSSIAN 98.[18]
18. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J.V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C.Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98, Revision A.9*; Gaussian, Inc.: Pittsburgh, PA, 1998.
19. Terminology: Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*. Wiley: New York, 1986.
20. Crystallographic data have been deposited with the Cambridge

Crystallographic Data Centre (**4f** CCDC 192013, **5a** CCDC 192012). Copies may be obtained free of charge on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1E2, UK (fax: int. Code +44-1223/3-36-033, e-mail: deposit@chemcrys.cam.ac.uk).

21. Cramer, C. *Ber.* **1892**, *25*, 713–721.