Synthesis of (2-bromo-2-hydroxyiminoacetyl)furazans(or furoxans) and 3,4-bis[furazanoyl(or furoxanoyl)]furoxans

A. S. Kulikov, N. N. Makhova, and L. I. Khmel'nitskii*

N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences,
47 Leninsky prosp., 117913 Moscow, Russian Federation.
Fax: +7 (095) 135 5328

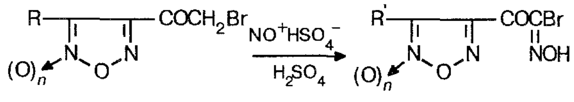
(2-Bromo-2-hydroxyiminoacetyl)furazans and -furoxans were synthesized by nitrosation of bromoacetylfurazans and -furoxans with nitrosylsulfuric acid in conc. H_2SO_4. An efficient method for preparing the previously unknown 3,4-bis[furazanoyl(or furoxanoyl)]furoxans has been proposed; it consists of the reaction of acetylfurazans and acetylfuroxans with a mixture of a nitrating reagent and a catalytic amount of a nitrosating reagent in conc. H_2SO_4.

Key words: nitrosation; nitration; methyl ketones; bromomethyl ketones; diketones; furazans; furoxans; hydroximoyl bromides.

It was shown previously[1] that 1,3-dihalo-2-propanone and 1,3-dihalo-1-hydroxyimino-2-propanone can be successfully nitrosated with nitrosylsulfuric acid in conc. H_2SO_4 to give 1,3-dihalo-1,3-dihydroxyimino-2-propanones. In the present work we studied the behavior in this reaction of bromoacetyl derivatives of furazan (**1**) and furoxan (**2**) synthesized by us[2] with the aim of preparing the previously unknown (2-bromo-2-hydroxyiminoacetyl)furazans (**3**) and -furoxans (**4**), which may be regarded as potential reagents for the synthesis of 3,4-bis[furazanoyl(or furoxanoyl)]furoxans.

Reaction conditions, which we used previously[1] for 1,3-dihalo-2-propanones, turned out to be suitable for nitrosation of compounds **1** and **2**. For example, the reaction of **1** or **2** with nitrosylsulfuric acid (conc. H_2SO_4, ≤ 20 °C, 3 h) afforded the corresponding hydroxyimino derivatives of furazans **3** and furoxans **4** in high yields (Scheme 1). The resulting compounds **3** and **4** (except for nitro derivative **3c**) are stable and are not hydrolyzed in air.

Scheme 1

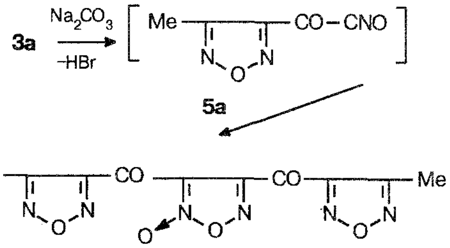


1, 2 **3, 4** (55—72 %)

1a, **3a**: R = R' = CH_3, n = 0
1b, **3b**: R = $BrCH_2CO$, R' = BrC(NOH)CO, n = 0
1c, **3c**: R = R' = NO_2, n = 0
2a, **4a**: R = R' = CH_3, n = 1
2b, **4b**: R = $BrCH_2CO$, R' = BrC(NOH)CO, n = 1

The possibility of synthesizing 3,4-bis(furazanoyl)furoxans (**6**) from compounds **3** has been proved using dehydrobromination of furazan **3a** as an example. Treatment of an ethereal solution of **3a** with an aqueous solution of Na_2CO_3 at 0 °C (typical conditions for preparing nitrile oxides from halides of hydroximic acids)[3] yielded 3,4-bis(4-methyl-3-furazanoyl)furoxan (**6a**), the first representative of bis(furazanoyl)furoxans, which is apparently formed as a result of cyclodimerization of the intermediate nitrile oxide **5a** (Scheme 2). However, the yield of **6a** proved to be low (9 %), and, according to TLC, the reaction mixture contained by-products.

Scheme 2



6a

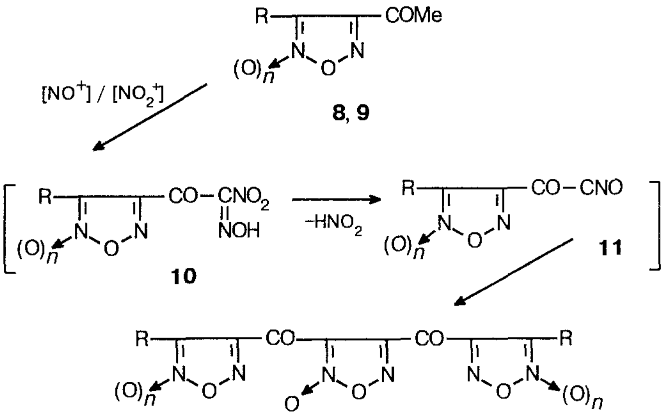
Therefore, to prepare type **6** and **7** compounds we used another approach, which is based on the known[4,5] method for the synthesis of diaroylfuroxans by the reaction of aryl methyl ketones with nitrating reagents in the presence of catalytic amounts of nitrosating reagents. Acetyl derivatives of furazan (**8**) and furoxan (**9**) were used as the starting compounds. We have found that this reaction should be carried out with a great excess of

---

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 3, pp. 485—488, March, 1994.

H_2SO_4 (at an HNO_3 : AcOH : H_2SO_4 molar ratio of 1 : 6 : 30, in the presence of catalytic amounts of $NaNO_2$), rather than under the normally used conditions.[4,5] When compounds **8** or **9** are treated with this mixture at room temperature, 3,4-bis(furazanoyl)furoxans **6a**, **6c** or 3,4-bis(3-methyl-4-furoxanoyl)furoxan (**7a**) are obtained in high yields. One may assume[4,5] that the reaction begins with nitrosation at the methyl group of the acetyl fragment of the molecule followed by nitration of the resulting aldoximes to give nitrolic acids (**10**). The latter spontaneously eliminate nitrous acid (the nitrosating reagent necessary for the reaction is thus recovered) to afford nitrile oxides (**11**) which dimerize into the corresponding cyclobis[furazanoyl(or furoxanoyl)]furoxans **6** and **7** (Scheme 3).

Scheme 3



6, **7** (68–75 %)

8a, **6a**: R = Me, n = 0
8c, **6c**: R = NO_2, n = 0
9a, **7a**: R = Me, n = 1

It is evident from this scheme that high acidity of the medium is necessary for the first reaction stage, nitrosation of the acetyl groups deactivated by the electron-withdrawing furazane or furoxane ring, to be successfully accomplished.

Methyl derivatives of bis-substituted furoxans **6a** and **7a** obtained in the crystalline state are stable compounds, whereas dinitro derivative **6c** isolated from the reaction mixture as an oil gradually decomposes even at room temperature. The structures of **3**, **4**, **6**, and **7** were confirmed by spectroscopic methods. The compounds synthesized may be of interest as synthons for preparing furazan and furoxan derivatives using transformations involving bromo(hydroxyimino)acetyl and carbonyl groups.

Experimental

IR spectra were recorded on a UR-20 spectrometer for pellets with KBr. ^1H, ^{13}C, and ^{14}N NMR spectra were measured in acetone-d_6 on a Bruker AM-300 spectrometer operating at 300, 75.5, and 21.5 MHz, respectively. Chemical shifts are referred to TMS as the internal standard (^1H and ^{13}C* NMR) or $MeNO_2$ as the external standard (^{14}N NMR). Mass spectra were obtained on a Varian MAT CH-6 mass spectrometer. TLC was carried out on Silufol UV-254 plates, which were vizualized by spraying with a 1 % solution of diphenylamine in C_2H_5OH followed by heating.

Preparation of (2-bromo-2-hydroxyaminoethyl)furazans (3) and furoxans (4) (general procedure). At ≤ 20 °C $NaNO_2$ (1 g) was poured into a stirred mixture of 6 mL of conc. H_2SO_4 and 1.5 mL of 60 % oleum. 10 mmol (or 5 mmol in the case of **1b** and **2b**) of bromoacetylfurazan **1** or -furoxan **2** was added to the resulting suspension. After 3 h the reaction mixture was poured into 25 g of crushed ice and extracted with CH_2Cl_2 (4×10 mL), and the extracts were washed with water (3×8 mL) and dried with $MgSO_4$. The solvent was evaporated *in vacuo*, and the residue (except **3c**) was triturated in the cold with a small amount of CCl_4. The resulting crystals of **3** or **4** were filtered off, washed on the filter with a small amount of cold CCl_4, and dried in air.

3-(2-Bromo-2-hydroxyiminoacetyl)-4-methylfurazan (3a). Yield 1.65 g (72 %), m.p. 115–116 °C, R_f 0.18 ($CHCl_3$). Found (%): C, 25.49; H, 1.75; Br, 34.02; N, 18.05. $C_5H_4BrN_3O_3$. Calculated (%): C, 25.66; H, 1.72; Br, 34.15; N, 17.96. IR, ν/cm^{-1}: 750, 800, 820, 920, 985, 1040, 1060, 1120, 1360, 1450, 1480, 1570, 1590, 1695, 3320. ^1H NMR, δ: 2.52 (s, Me); 13.77 (s, OH). MS, m/z (I_{rel} (%)): 235 (42); 234 (85); 233 (46); 232 (81); 155 (100); 152 (68); 150 (66); 111 (75).

3,4-Bis(2-bromo-2-hydroxyiminoacetyl)furazan (3b). Yield 1.01 g (56 %), m.p. 178–179 °C, R_f 0.65 ($CHCl_3$—MeCOMe, 3 : 1). Found (%): C, 19.68; H, 0.70; Br, 43.01; N, 15.27. $C_6H_2Br_2N_4O_5$. Calculated (%): C, 19.48; H, 0.54; Br, 43.20; N, 15.15. IR, ν/cm^{-1}: 780, 850, 1050, 1280, 1420, 1590, 1695, 3350. ^1H NMR, δ: 13.80 (br.s, OH). MS, m/z (I_{rel} (%)): 372 (2); 370 (4); 368 (2); 292 (10); 291 (90); 290 (10); 289 (100); 248 (85); 247 (45); 246 (82); 245 (35).

3-(2-Bromo-2-hydroxyiminoacetyl)-4-nitrofurazan (3c). Yield 1.46 g (55 %) (yellow oil), R_f 0.42 ($CHCl_3$). IR, ν/cm^{-1}: 825, 1000, 1020, 1040, 1130, 1180, 1350, 1570, 1720, 3450. ^1H NMR, δ: 13.88 (br.s, OH).

4-(2-Bromo-2-hydroxyiminoacetyl)-3-methylfuroxan (4a). Yield 1.80 g (72 %), m.p. 132 °C, R_f 0.23 ($CHCl_3$). Found (%): C, 23.90; H, 1.66; Br, 32.11; N, 16.78. $C_5H_4BrN_3O_4$. Calculated (%): C, 24.02; H, 1.61; Br, 31.96; N, 16.81. IR, ν/cm^{-1}: 750, 820, 1060, 1110, 1240, 1310, 1370, 1475, 1620, 1710, 3300. ^1H NMR, δ: 2.30 (s, Me); 13.22 (s, OH).

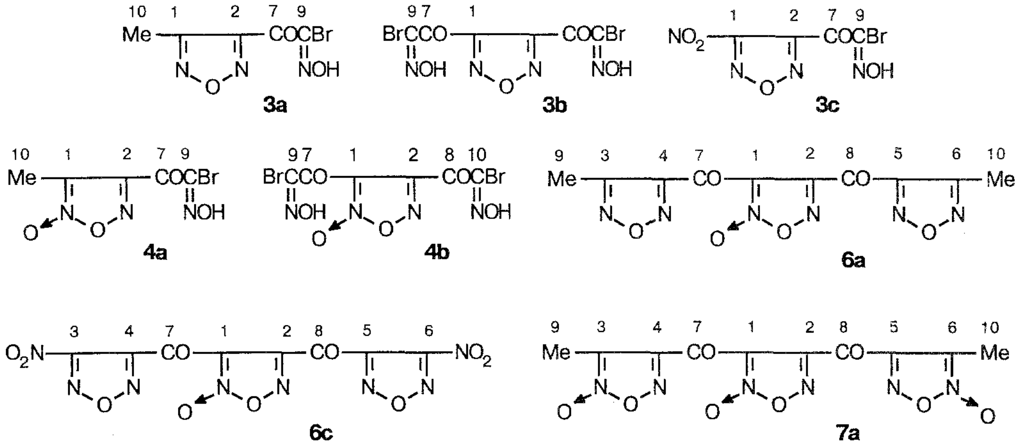
3,4-Bis(2-bromo-2-hydroxyiminoacetyl)furoxan (4b). Yield 1.18 g (61 %), m.p. 176 °C, R_f 0.61 ($CHCl_3$—MeCOMe, 3 : 1). Found (%): C, 18.81; H, 0.61; Br, 41.35; N, 14.39. $C_6H_2Br_2N_4O_6$. Calculated (%): C, 18.67; H, 0.52; Br, 41.41; N, 14.52. IR, ν/cm^{-1}: 740, 760, 790, 840, 860, 1050, 1080, 1190, 1240, 1335, 1430, 1600, 1700, 3380. ^1H NMR, δ: 13.57 (s, OH); 13.65 (s, OH). MS, m/z (I_{rel} (%)): 208 (90); 123 (100); 121 (95); 95 (84); 93 (87).

3,4-Bis(4-methyl-3-furazanoyl)furoxan (6a). ***a.*** A solution of Na_2CO_3 (0.8 g, 7.5 mmol) in 10 mL of water was added dropwise at 0 °C to a stirred solution of **3a** (3.51 g, 15 mmol) in 20 mL of ether. The reaction mixture was stirred for 15 min at ~20 °C, and the ethereal layer was separated,

---

* The data of the ^{13}C NMR spectra of the resulting compounds are presented in Table 1.

Table 1. ^{13}C NMR spectra (δ, J/Hz) of compounds **3a—c**, **4a,b**, **6a**, **6c**, and **7a**



Compound	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	C(7)	C(8)	C(9)	C(10)
3a	152.88 ^2J = 7.3	151.21 ^3J = 2.5					176.70		131.93	9.16
3b	151.69						174.35		132.82	
3c	155.91	153.17					177.27		130.64	
4a	113.23	154.56					175.65		137.71	9.07
4b	110.98	152.54					171.45	173.93	132.44	132.59
6a	109.82	151.55	151.55 ^2J = 7.5	149.77 ^3J = 2.5	150.11 ^3J = 2.5	151.81 ^2J = 7.5	170.39	174.04	8.79	8.91
6c	103.71	142.24	146.06	143.71	144.21	146.41	174.16	174.59		
7a	110.85	152.39	111.81	154.26	154.28	112.13	171.66	174.82	8.70	8.82

washed with 10 mL of water, and dried with $MgSO_4$; the solvent was evaporated *in vacuo*. According to TLC ($CHCl_3$), the residue was a mixture of four compounds. Recrystallization from a CCl_4—$CHCl_3$ mixture (2:1) gave 0.20 g of furoxan **6a**, m.p. 96 °C, R_f 0.64 ($CHCl_3$). Found (%): C, 39.33; H, 2.06; N, 27.30. $C_{10}H_6N_6O_6$. Calculated (%): C, 39.23; H, 1.98; N, 27.45. IR (ν/cm^{-1}): 770, 780, 880, 910, 940, 1450, 1490, 1620, 1720, 2940. ^1H NMR, δ: 2.61 (s, Me); 2.66 (s, Me). MS, m/z (I_{rel} (%)): 306 (12) [M$^+$]; 276 (14); 223 (37); 207 (44); 195 (35); 163 (90); 112 (83); 111 (100).

b. Furazan **8a** (1.01 g, 8 mmol) was added at 20 °C to a mixture of 1 mL of HNO_3 (d = 1.4 g cm^{-3}), 20 mL of conc. H_2SO_4, 6 mL of glacial MeCOOH, and several crystals of $NaNO_2$. The reaction mixture was stirred for 2 h and poured onto 80 g of crushed ice; the precipitate was filtered off and washed with water. The mother liquor was extracted with CH_2Cl_2 (2×20 mL), the extracts were washed with water (3×10 mL) and dried with $MgSO_4$, and the solvent was evaporated *in vacuo*. Recrystallization from a CCl_4—$CHCl_3$ (2:1) mixture gave 0.83 g (68 %) of compound **6a** identical to the product prepared by procedure ***a***.

3,4-Bis(4-nitro-3-furazanoyl)furoxan (6c). Furazan **8c** (1.26 g, 8 mmol) was added to a mixture of 1 mL of HNO_3 (d = 1.4 g cm^{-3}), 20 mL of conc. H_2SO_4, 6 mL of glacial MeCOOH, and several crystals of $NaNO_2$. The reaction mixture was stirred for 2 h and poured onto 80 g of crushed ice. The product was extracted with CH_2Cl_2 (4×20 mL), and the extract was washed with water (3×10 mL), dried with $MgSO_4$, concentrated *in vacuo* to a volume of 10 mL, quickly filtered through a thin layer of silica gel, and concentrated until its weight no longer changed to give 1.18 g (75 %) of furoxan **6c** (yellow oil). R_f 0.60 ($CHCl_3$—$MeCOOC_2H_5$, 3 : 1). IR (ν/cm^{-1}): 790, 810, 1020, 1070, 1150, 1250, 1280, 1320, 1555, 1600, 1685. ^{14}N NMR, δ: −38.63 (NO_2); −38.31 (NO_2).

3,4-Bis(3-methyl-4-furoxanoyl)furoxan (7a). Furoxan **9a** (1.14 g, 8 mmol) was added to a mixture of 1 mL of HNO_3 (d = 1.4 g cm^{-3}), 20 mL of conc. H_2SO_4, 6 mL of glacial MeCOOH, and several crystals of $NaNO_2$. The reaction mixture was stirred for 2 h and poured onto 80 g of crushed ice. The precipitate was washed with water to give 1.05 g (75 %) of furoxan **7a**, m.p. 112 °C, R_f 0.57 ($CHCl_3$—MeCOMe, 3 : 1). Found (%): C, 34.52; H, 1.80; N, 24.07. $C_{10}H_6N_6O_8$. Calculated (%): C, 34.43; H, 1.73; N, 24.14. IR (ν/cm^{-1}): 770, 800, 850, 910, 1060, 1095, 1215, 1310, 1330, 1380, 1430, 1470, 1615, 1630, 1710, 2940. ^1H MNR, δ: 2.39 (s, Me); 2.40 (s, Me). MS, m/z (I_{rel} (%)): 338 (28) [M$^+$]; 308 (24); 292 (31); 278 (26); 239 (100); 203 (41); 195 (63); 179 (96).

References

1. A. S. Kulikov, N. N. Makhova, and L. I. Khmel'nitskii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1991, 506 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1991, **40**, 438 (Engl. Transl.)].

2. A. B. Sheremetev, A. S. Kulikov, and L. I. Khmel'nitskii, *Izv. Akad. Nauk, Ser. Khim.*, 1993, 774 [*Russ. Chem. Bull.*, 1993, **42**, 708 (Engl. Transl.)].
3. L. I. Khmel'nitskii, S. S. Novikov, and T. I. Godovikova, in *Khimiya furoksanov. Stroenie i sintez* [*Chemistry of Furoxans. Structure and Synthesis*], Nauka, Moscow, 1981, 140 (in Russian).
4. H. Snyder and N. E. Boyer, *J. Am. Chem. Soc.*, 1955, **77**, 4233.
5. T. Nakagone and R. N. Castle, *J. Heterocycl. Chem.*, 1968, **5**, 379.

Received June 21, 1993