

SYNTHESIS OF NEW

3,4-DISUBSTITUTED FURAZANS

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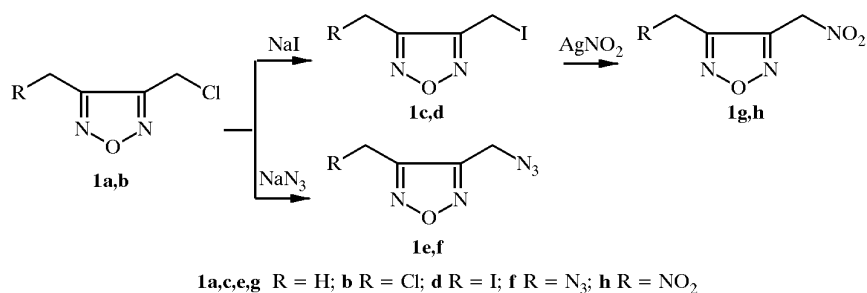
A series of new 3,4-substituted furazans was synthesized on the basis of the mutual transformations of the functional groups in halogenomethyl and bisacyl derivatives of furazan.

Keywords: 3-acetyl-4-(1,1-dinitroethyl)furazan, 3-halogenomethyl-4-methylfurazan, 3,4-diazidomethyl-furazan, 3,4-diacetylfurazan, 3,5-dihalogenomethylfurazans, 3,4-disubstituted furazans, 3,6-dimethyl- and 3,4-dicyclopropylpyridazino[4,5-*c*]furazan 4,5-dioxides, 3,4-dinitromethylfurazan, 3,4-di(cyclopropyl-carbonyl)furazan.

Furazans represent a unique type of heterocyclic compounds and have been studied vigorously in the last decade [1-9]. The introduction of substituents containing azido, nitro, nitroxy, nitramino, and other so-called energy-containing groups in the positions 3,4 of the furazan molecule leads to the production of highly dense and fairly stable compounds that are promising for the creation of high-energy materials and compositions [10].

In the present work we propose methods for the production of a series of new 3,4-disubstituted furazans based on the mutual transformations of the functional groups in furazan reference compounds with retention of the main heterocycle. As such compounds we studied the comparatively accessible halogenomethyl and acyl derivatives of furazan. We synthesized 4-(chloromethyl)-3-methyl- and 3,4-di(chloromethyl)furazans (**1a, b**) according to the previously described procedure [11] by the direct chlorination of dimethylfurazan on heating. The synthesis of the bromomethyl derivatives of furazan by bromination of dimethylfurazan with bromosuccinimide in the presence of benzoyl peroxide was described earlier [12]. However, this method gives poorly reproducible results. At the same time, in a number of cases it is necessary to have the iodomethyl-substituted furazans **1c,d**, which we synthesized from the corresponding chlorides **1a,b** by the action of sodium iodide in acetone (Scheme 1) [13].

Scheme 1



Using the halogenomethyl derivatives of furazan **1a-d** as the initial reference substrates, we realized a series of nucleophilic substitution reactions (Scheme 1). This made it possible to extend the number of available functional derivatives of furazan.

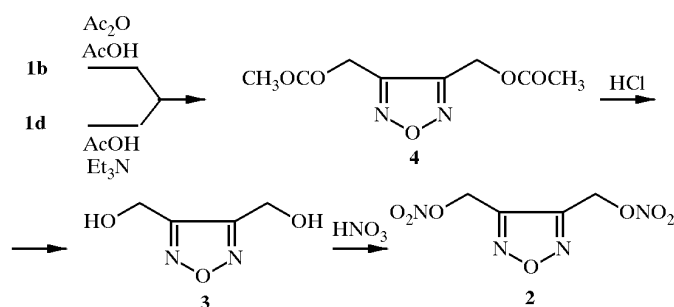
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Thus, when chlorides **1a,b** were heated with sodium azide in DMSO, high yields of 3-azidomethyl-4-methylfuran (**1e**) and 3,4-di(azidomethyl)furan (**1f**) in the form of stable liquid substances were obtained. According to the data from thermogravimetric analysis and differential scanning calorimetry bisazide (**1f**) evaporates without decomposition ($E_A = 50 \pm 12$ kJ/mole). The sample was thermally stable up to 180°C, and the range of decomposition was 180-255°C.

3-Methyl-4-nitromethylfuran (**1g**) and 3,4-di(nitromethyl)furan (**1h**) were obtained by the reaction of iodides **1c,d** with silver nitrite in ether. Side products of the reactions were the corresponding nitrites and their hydrolysis products, which were isolated with an overall yield of 5-10% by column chromatography.

The synthesis of 3,4-di(nitroxymethyl)furan (**2**) has not been described in the literature, but some of its properties were known [14]. In order to obtain the dinitroxymethyl derivative **2** we first studied the problem of the synthesis of 3,4-di(hydroxymethyl)furan (**3**). The synthesis of this diol is familiar from patent data [15], according to which it can be obtained from dichloride **1b** through the formation of the corresponding diacetate **4** followed by hydrolysis. We found that this method often leads to the production of mixed 3,4-disubstituted furazans and a more effective method for the production of diacetate **4** under laboratory conditions is acetalization of diiodide **1d** by acetic acid in the presence of triethylamine. Under these conditions the overall yield of diol **3** amounted to 63%.

Scheme 2



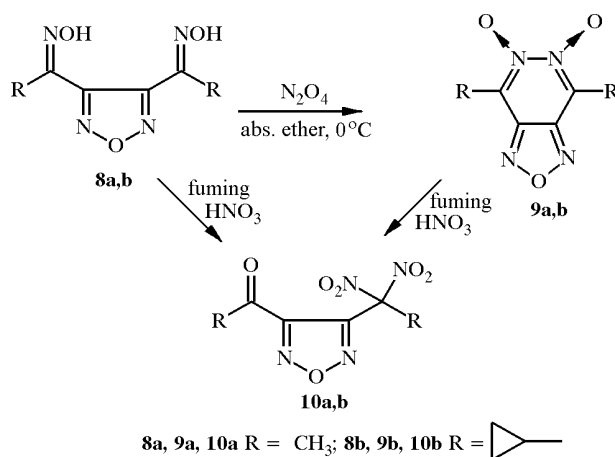
Diol **3** is nitrated smoothly by a mixture of nitric and sulfuric acids with the formation of the corresponding nitroxymethyl derivative **2** with a yield of 54%. A pure sample of this dinitrate **2** was first obtained for comparison by an alternative synthesis from diiodide **1d** and silver nitrate.

Diketones of the furazan series are of particular interest for the synthesis of various 3,4-disubstituted furazans. 3,4-Diacetylfuran (**5**) was obtained by the known method by reduction of 3,4-diacetylfuroxan with tin chloride [16]. The other diketone – 3,4-di(cyclopropylcarbonyl)furan (**6**) was first synthesized by us by reduction of the corresponding furoxan diketone **7**. It was found that reduction of 3,4-di(cyclopropylcarbonyl)furoxan (**7**) [17] by the action of tin chloride made it possible to synthesize diketone **6** with a yield of $\leq 20\%$, but variation of the conditions of this reaction did not lead to an improvement in the yield. We were able to increase the yield of diketone **6** substantially using triethyl phosphite in benzene as reducing agent.

Using the synthesized diketones **5** and **6** as reference compounds, we studied the possibility of using them for the synthesis of nitro-substituted furazans. For this purpose diketones **5** and **6** were transformed into the corresponding dioximes **8a,b** and were studied in nitration under various conditions.

We found that during treatment of oximes **8a,b** with nitrogen tetroxide in ether at 0°C the N,N' -dioxides of annelated furazanopyridazines **9a,b** were formed instead of the expected geminal dinitro derivatives of furazans. Only individual examples of the furoxan analogs of this little-investigated group of compounds had been described previously [18].

Scheme 3



4,7-Dimethyl- and 4,7-di(cyclopropyl)furazano[3,4-*d*]pyridazine 5,6-dioxides **9a,b** were obtained with yields of 61 and 22% respectively in the form of stable high-melting compounds. Their structure and molecular formula were established by spectral data and elemental analysis.

In order to obtain the geminal dinitro derivatives of furazan we studied nitration of dioximes **8a,b** with nitric acid. It was found that the reaction of dioxime **8a** with concentrated nitric acid gave a 43% yield of furazanopyridazine **9a**. When fuming nitric acid was used in this reaction a different compound – 3-acetyl-4-(1,1-dinitroethyl)furazan (**10a**) was isolated. The same compound is formed during the action of fuming nitric acid on dioxide **9a**. The reaction probably takes place through cleavage of the N–N bond of the pyridazine ring with intermediate formation of 3,4-di(1,1-dinitroethyl)furazan, which releases nitrogen oxides under the reaction conditions and is converted into compound **10a**. Analogous transformations were observed earlier for the furoxan analogs in this reaction [19]. The spectral data of the nitration product **10a** obtained by the two different methods (Scheme 3) coincide.

The reaction of dioxime **8b** with fuming nitric acid probably leads to the formation of the tetranitro derivative with the participation of two cyclopropylcarbonyl groups. This derivative decomposes vigorously on removal of the solvent to 3-(1-cyclopropylmethyl-1,1-dinitro)-4-cyclopropylcarbonylfurazan (**10b**). Its structure was confirmed by the data from the ^1H NMR and IR spectra. In the proton spectrum there are two groups of signals corresponding to the nonequivalent cyclopropane fragments. In the IR spectrum there is a strong absorption band in the region of 1710 cm^{-1} (carbonyl group), and there are absorption bands at 1560 and 1310 cm^{-1} corresponding to the vibrations of the geminal dinitro group.

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were recorded on Varian VXR-400 and Varian FT-80A instruments (400 and 80 MHz respectively) with TMS or HMDS as internal standard. The IR spectra were recorded in thin layers on an UR-20 instrument. The chromat-mass spectra were obtained on a Finnigan Mat Incos-50 instrument at 70 eV. The reactions and purity of the compounds were monitored by TLC on Silufol UV-254 plates. Silpearl UV-254 (L 40/100) was used for column chromatography. Differential scanning analysis was conducted on a Perkin-Elmer DSK-1b calorimeter with heating at 16 deg/min . Chlorides **1a,b** were obtained by the method [11]. 3,4-Diacetylfurazan (**5**) was obtained by the method [16]. 3,4-Di(cyclopropylcarbonyl)furoxan (**7**) was obtained by the method [17]. The spectral characteristics and the yields of the synthesized compounds are given in Table 1.

TABLE 1. The Spectral Characteristics and Yields of the Synthesized Compounds

Compound	Solvent	¹ H NMR spectrum, δ , ppm	¹³ C NMR spectrum, δ , ppm	IR spectrum, ν , cm ⁻¹	Mass spectrum (m/z)	Yield, %
1b	CDCl ₃	2.42 (3H, s, CH ₃); 4.36 (2H, s, CH ₂)	152.55 (C _{cyclic}); 150.40 (C _{cyclic}); 8.40 (CH ₃); -5.10 (CH ₂)	—	224 [M ⁺]; 97 [-I]	77
1d	CDCl ₃	4.49 (4H, s, CH ₂)	—	—	350 [M ⁺]; 223 [-I]	74
1e	CDCl ₃	2.49 (3H, s, CH ₃); 4.61 (2H, s, CH ₂)	—	2120	—	98
1f	CDCl ₃	4.68 (4H, s, 2CH ₂)	149.47 (C _{cyclic}); 40.11 (CH ₂)	2120	—	98
1g	CDCl ₃	2.45 (3H, s, CH ₃); 5.69 (2H, s, CH ₂)	151.44 (C _{cyclic}); 145.64 (C _{cyclic}); 66.75 (CH ₂); 8.18 (CH ₃)	—	97 [M-NO ₂]	70
1h	CDCl ₃	5.85 (4H, s, 2CH ₂)	—	—	198 [M]	36
2	CDCl ₃	5.72 (4H, s, 2CH ₂)	—	—	52 (5); 43 (100); 30 (8); 28 (10)	45
3	DMSO-d ₆	5.0 (4H, s, 2CH ₂)	151.40 (C _{cyclic}); 54.13 (CH ₂)	—	130 [M ⁺]; 113 [-OH]	63
6	CDCl ₃	2.6 (2H, m, 2CH); 1.3 (4H, m); 1.1 (4H, m)	191.82 (C=O); 151.72 (C _{cyclic}); 21.57 (CH); 13.66 (CH ₂)	—	—	60
7	CDCl ₃	2.82 (1H, m, CH); 2.62 (1H, m, CH); 1.35 (4H, m); 1.25 (4H, m)	191.41 (C=O); 188.46 (C=O); 153.57 (C _{cyclic}); 111.42 (C _{cyclic}); 67.65 (CH); 31.60 (CH); 20.82; 19.87; 14.25; 13.74 (CH ₂)	—	—	—
8a	CD ₃ OD	2.2 (6H, s, 2CH ₃)	—	—	—	71
8b	CD ₃ OD	2.46 (2H, m, 2CH); 0.9 (4H, m); 0.8 (4H, m)	—	—	—	51
9a	DMSO-d ₆	2.6 (6H, s, 2CH ₃)	146.29 (C _{fur}); 119.10 (C _{cyclic}); 18.19 (CH ₃)	—	—	61
9b	DMSO-d ₆	2.29 (2H, m, 2CH); 1.37 (4H, m); 1.18 (4H, m)	—	—	—	22
10a	CDCl ₃	2.74 (3H, s, CH ₃); 2.67 (3H, s, CH ₃)	—	1600, 1320	—	54
10b	CDCl ₃	2.95 (1H, m, CH _{cyclic}); 2.68 (1H, m, CH _{cyclic}); 1.34 (m, 4H _{cyclic}); 1.22 (m, 4H _{cyclic})	—	1710, 1560, 1310	—	18

3-Iodomethyl-4-methylfuran (1c) and 3,4-Di(iodomethyl)furan (1d). To solution of sodium iodide (30 g, 0.2 mol) in dry acetone we added with stirring a mixture of mono- and dichlorides **1a,b** (4.6 g). The reaction mass was stirred for 1.5 h and evaporated on a rotary evaporator. The residue was extracted with ether (3 × 100 ml) on the filter. The ether extract was evaporated. After vacuum distillation we obtained 5.3 g of iodide **1c** (bp 56°C/0.05 mm Hg) and 0.8 g of diiodide **1d**.

3-Azidomethyl-4-methylfurazan (1e). Solution of chloro derivative **1a** (0.2 g, 1.5 mmol) and sodium azide (0.1 g, 1.5 mmol) in absolute DMSO (5 ml) was stirred at 60°C. The reaction mixture was then decomposed with water (8 ml), extracted with methylene chloride (3 × 5 ml), washed with water (3 × 5 ml), and dried with magnesium sulfate. After evaporation of the solvent we obtained 0.2 g of azide **1e** in the form of an oil.

3,4-Di(azidomethyl)furazan (1f). From dichloride **1b** (2.43 g, 0.15 mol) and sodium azide (1.95 g, 0.03 mol) in absolute DMSO (20 ml) under analogous conditions we obtained 2.56 g of diazide **1f**; d_4^{20} 1.386 g/cm³. Found, %: C 26.37; H 2.29. C₄H₄N₈O. Calculated, %: C 26.67; H 2.22.

3-Methyl-4-nitromethylfurazan (1g). To suspension of silver nitrite (0.7 g, 4.5 mmol) in absolute ether (5 ml) in atmosphere of argon with cooling to 0°C under stirring, we added dropwise over 2 h ether solution of iodide **1c** (0.78 g, 3.5 mmol). The reaction mixture was stirred at 0°C for 24 h and then at room temperature until the initial iodide had disappeared (TLC control). The silver salts were filtered off and washed with ether. The ether fractions were combined, and the solvent was evaporated on a rotary evaporator. We obtained 0.35 g of nitrofurazan **1g** and 0.035 g (7% yield) of 3-methyl-4-nitritomethylfurazan. The mixture was separated by preparative column chromatography (R_f 0.21, 4:1 hexane–ethyl acetate).

3,4-Di(nitromethyl)furazan (1h). This compound was synthesized by the method described above from diiodide **1d** (0.5 g, 1.4 mmol) and silver nitrite (1.81 g, 11.8 mmol) in absolute ether (5 ml). We obtained 0.10 g of dinitrofurazan **1h**, 0.03 g (10%) of 3,4-di(nitritomethyl)furazan, and 0.02 g (7%) of 3-nitritomethyl-4-nitromethylfurazan. The mixture was separated by preparative column chromatography (R_f 0.21, 4:1 hexane–ethyl acetate).

3,4-Di(hydroxymethyl)furazan (3). To solution of glacial acetic acid (17.8 g, 18 ml, 0.3 mol) and triethylamine (18.8 g 25.8 ml, 0.186 mol) in acetone (50 ml) we added iodide **1d** (2.24 g, 0.0064 mol). The transparent solution was boiled for 45 min and extracted with ether (2 × 50 ml). The organic layer was washed with water (30 ml), with saturated sodium bicarbonate solution (30 ml), and again with water (2 × 30 ml) and dried with magnesium sulfate. The solvent was evaporated on a rotary evaporator, and 1.19 g (87%) of diacetate **4** were isolated. Isolated product was mixed with hydrochloric acid (d_4^{20} 1.16, 7 ml) and glacial acetic acid (1.5 ml) and kept for 20 h at 90–95°C. The reaction mixture was cooled, water and acetic acid were evaporated on a rotary evaporator, and 0.53 g of diol **3** (bp 155–156°C) were obtained by distillation of the residue.

3,4-Di(nitroxymethyl)furazan (2). A. To mixture of fuming nitric acid (0.8 ml) and concentrated sulfuric acid (0.8 ml) at ≤ 0°C we added diol **3** (0.2 g, 1.54 mol). The reaction mass was stirred at ≤ 5°C for 15 min, and water (4 ml) was then cautiously added drop by drop. The reaction mixture was extracted with chloroform (3 × 5 ml), and the extracts were washed with water (3 × 10 ml) and dried with magnesium sulfate. We obtained 0.15 g of dinitrate **2**.

B. To solution of silver nitrate (0.6 g, 3.5 mmol) in absolute acetonitrile (3.4 ml) we added solution of diiodo derivative **1d** (0.3 g, 0.86 mmol) in acetonitrile (1 ml). After 3 days at room temperature the precipitate was filtered off, and the filtrate was poured into ice water (30 ml). The oil was separated, the mother solution was extracted with methylene chloride (2 × 15 ml), and the extract was dried with magnesium sulfate. The solvent was evaporated on a rotary evaporator, and 0.16 g (84%) of dinitrate **2** were obtained.

3,4-Di(cyclopropylcarbonyl)furazan (6). To solution of furoxan **7** (1 g, 4.5 mmol) in benzene (4 ml) while stirring in an inert atmosphere we added dropwise triethyl phosphite (1.12 g, 6.7 mmol) (slight heating was observed). After addition of the calculated amount of the reducing agent the reaction mixture was heated for a further 5 h at 80–85°C, then cooled to room temperature and washed with 2 N sulfuric acid (4 ml) and with water (3 × 5 ml) to remove the excess of phosphite and triethyl phosphate. The benzene solution was dried with magnesium sulfate and evaporated. The residue with a mass of 1 g was purified by preparative column chromatography (R_f 0.55, 4:1 hexane–ethyl acetate). We obtained 0.55 g of diketone **6**. Found, %: C 58.35; H 5.13. C₁₀H₁₀N₂O₃. Calculated, %: C 58.25; H 4.85.

3,4-Diacetylfurazan Dioxime (8a). To mixture of barium carbonate (1.8 g, 9.1 mmol) and NH₂OH·HCl (1 g, 14.4 mmol) in water (5 ml) we added solution of diketone **5** (1 g, 6.5 mmol) in 96% alcohol (15 ml). The reaction mixture was boiled for 7.5 h and was then evaporated to dryness. Benzene was added, and the mixture was heated to boiling. The hot benzene solution was filtered, the filtrate was evaporated, and the residue was dried under vacuum. We obtained 0.85 g of oxime **8a**; mp 108°C.

3,4-Di(cyclopropylcarbonyl)furazan Dioxime (8b). This compound was synthesized by the method described above from barium carbonate (0.62 g, 3.1 mmol), NH₂OH·HCl (0.42 g, 6.0 mmol) in water (2.5 ml), and diketone **6** (0.25 g, 1.2 mmol) in alcohol (5.5 ml). We obtained 0.14 g of dioxime **8b**.

4,7-Dimethylfurazano[3,4-*d*]pyridazine 5,6-Dioxide (9a). To absolute ether (2 ml) while cooling to 0°C we added liquid N₂O₄ (0.5 g, 5.4 mmol). We then added quickly in three portions dioxime **8a** (0.1 g, 0.54 mmol). The mixture was stirred with cooling for 30 min and then at room temperature for a further 1 h. The obtained light-yellow precipitate was filtered off and dried under vacuum at 2 mm Hg. We obtained 0.06 g of compound **9a**; mp 193°C. Found, %: C 39.38; H 3.31; N 30.48. C₆H₆N₄O₃. Calculated, %: C 39.57; H 3.31; N 30.76.

4,7-Dicyclopropylfurazano[3,4-*d*]pyridazine 5,6-Dioxide (9b). To solution of dioxime **8b** (0.2 g, 0.85 mmol) in absolute ether (2 ml) at 0°C we added liquid N₂O₄ (0.78 g, 8.5 mmol). The reaction mass was stirred at 0-5°C for 1.5 h. The formed precipitate was filtered off and dried in air. We obtained 0.04 g of compound **9b**; mp 141°C (decomp.).

3-Acetyl-4-(1,1-dinitroethyl)furazan (10a). A. To 100% nitric acid (0.5 ml) we added dioxime **8a** (0.08 g, 0.43 mmol), while keeping the temperature at 5-10°C. The mixture was kept at this temperature for 1 h, after which it was poured onto ice, then extracted with methylene chloride and dried with magnesium sulfate. We obtained 0.05 g of compound **10a**.

B. To 100% nitric acid (0.92 ml) we added dioxide **9a** (0.08 g, 0.44 mmol) at 5-10°C. The mixture was kept at this temperature for 2 h, then poured onto ice and extracted with chloroform (2 × 3 ml). The extract was dried with magnesium sulfate, and 0.07 g (66%) of dinitro compound **10a** were obtained.

3-(1-Cyclopropylmethyl-1,1-dinitro)-4-cyclopropylcarbonylfurazan (10b). This compound was synthesized by the method A described above. From dioxime **8b** (0.1 g, 0.42 mmol) and 100% nitric acid (0.5 ml) we obtained 0.02 g of furazan **10b**.

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