Synthesis of 4,6-dinitro-3-R-benzo[*d*]isoxazoles and their transformations under the action of nucleophiles

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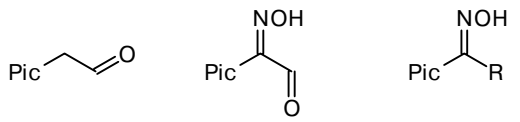
A new procedure was developed for the preparation of 4,6-dinitro-3-R-benzo[*d*]isoxazoles (R are derivatives of the aldehyde group) based on 2,4,6-trinitrophenylacetaldehyde. The resulting compounds are characterized by the regiospecific substitution of the nitro group at position 4 under the action of anionic nucleophiles RS^-, RO^-, F^-, or N_3^-, which allowed the development of a new method for the preparation of previously unknown 4-Nu-6-nitro-3-R-benzo[*d*]isoxazoles (Nu is the residue of a nucleophile). At the same time, oxidative nucleophilic substitution under the action of anions of some β-dicarbonyl compounds leads to the replacement of the hydrogen atom at position 7 with the corresponding C-nucleophiles.

Key words: benzoisoxazoles, nitro compounds, nucleophilic substitution.

Previously[1] within the framework of the program for the chemical utilization of explosive 2,4,6-trinitrotoluene (TNT), we have developed a procedure for the preparation of 2,4,6-trinitrophenylacetaldehyde (**1**) and synthesized a series of its derivatives (**2** and **3a—e**).[2]

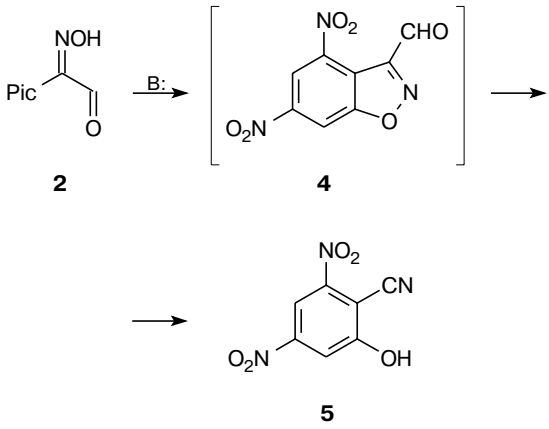


1 **2** **3a—e**

Pic is 2,4,6-trinitrophenyl

R =  (**3a**), —CH=NOMe (**3b**), —CH=NNHPh (**3c**), —CH=NNHCOPh (**3d**), —CH=NPh (**3e**)

Scheme 1



Further studies of products of TNT processing (**1—3**) were aimed at constructing compounds containing the minimum number of nitro groups and a heterocyclic core. The latter are of most interest as potential biologically active substances, which can find use, for example, in pharmacology and agricultural chemistry.

We found that the reactions of bases (B:) with 2-oximino-2-picrylacetaldehyde (**2**) afforded nitrile of 4,6-dinitrosalicylic acid (**5**)[2] (Scheme 1).

Analogous transformations are known for the series of benzo[*d*]isoxazoles containing the carbonyl or carboxyl group at position 3.[3,4] According to the published data, the reactions proceed through the stage of formation of 4,6-dinitrobenzo[*d*]isoxazole **4** followed by simultaneous decarbonylation and the isozaxole-ring opening.

We assumed that conversion of the aldehyde group in oxime **2** into the dioxolane or azomethine group (compounds **3a—e**) can enable us to perform intramolecular nucleophilic substitution of the nitro group to form stable benzoisoxazoles. Actually, treatment of oximes **3a—e** with K_2CO_3 in EtOH gave rise to stable 4,6-dinitro-3-R-benzo[*d*]isoxazoles (**6a—e**) (Scheme 2).

Isoxazoles **6b—e** can be synthesized directly from oxime **2** without isolation of intermediate products **3b—e**. In this case, the products are prepared in higher yields (with respect to the initial oxime **2**) and the procedure for the synthesis is simplified. It should be noted that only one example of 4,6-dinitrobenzo[*d*]isoxazoles, *viz.*, 5-hydroxy-4,6-dinitrobenzo[*d*]isoxazole,[5] has been known previously.

The structures of benzoisoxazoles **6** were confirmed by ^1H and ^{13}C NMR spectroscopy. The assignment of the signals for the hydrogen and carbon atoms in compound **6a** was made based on analysis of the two-

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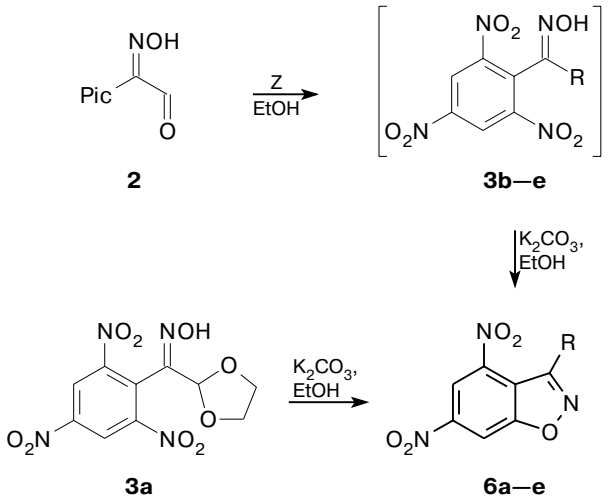
Scheme 2



Compound	R	Z	Yield (%)
6a		—	87
6b	—CH=NOMe	H_2NOMe	68
6c	—CH=NNHPh	$PhNHNH_2 \cdot HCl$	85
6d	—CHNNHCOPh	$PhCONHNH_2$	53
6e	—CH=NPh	$PhNH_2 \cdot HCl$	82

dimensional (HMBC) ^1H-^{13}C NMR spectrum (the 1 : 1 DMSO-d_6—CCl_4 mixture as the solvent; Fig. 1). The position of the signal for the H(7) proton was determined from the coupling with the C(7a) atom possessing the highest chemical shift (δ_C 163.8). The assignment of all other signals was easily made using the data on the arrangement of the H(7)/C(7a) pair (see Fig. 1).

Due to the presence of two nitro groups in the electron-deficient benzoisoxazole molecule and the presence of the masked aldehyde group at position 3, compounds **6** show considerable promise for further conversions. In our opinion, nucleophilic substitution of the nitro group is the most interesting reaction. This process allows one to introduce various functional substituents into benzoisoxazole and makes it possible to safely deprotect the aldehyde group (and to use it further) by decreasing the number of electron-withdrawing groups without the subsequent opening of the isoxazole ring. In deciding on particular nucleophiles and a procedure for the synthesis, we leaned upon our experience on similar processes in the series of derivatives of 2,4,6-trinitrobenzoic acid.[6,7]

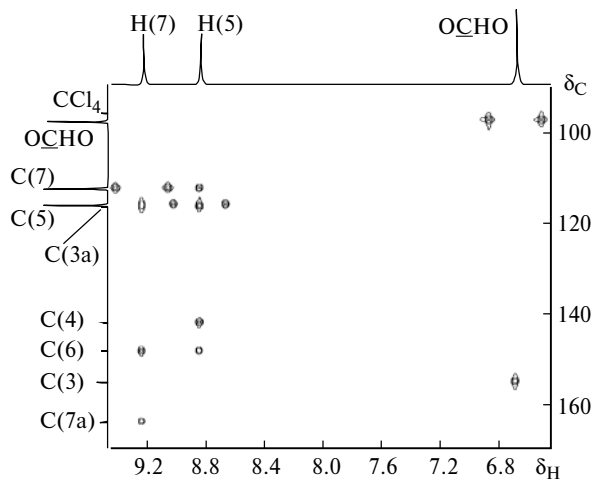
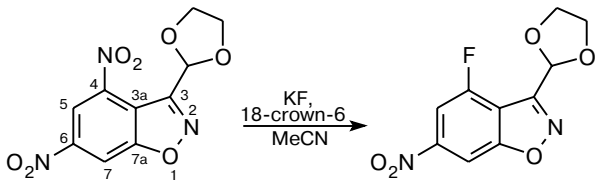


Fig. 1. Two-dimensional (HMBC) ^1H-^{13}C NMR spectrum of compound **6a**.

We studied the reactions of benzoisoxazoles **6** with inorganic nucleophiles, *viz.*, with fluoride and azide ions. Under the phase transfer catalysis conditions, the reaction of benzoisoxazole **6a** with KF upon refluxing in anhydrous MeCN gave rise to a product (**7**) of substitution of one nitro group (Scheme 3).

Scheme 3



6a **7** (20% yield)

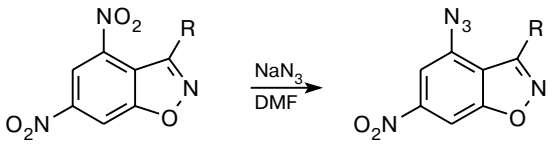
Based on the results of spectral studies (^1H, ^{13}C, and ^{19}F NMR spectroscopy) of compound **7**, it was unambiguously proved that the fluorine atom is located at position 4. Thus, the ^1H NMR spectrum has signals for two aromatic protons (δ 8.0 and 8.6) the first of which occurs as a doublet of doublets with the large spin-spin coupling constant $^3J_{H-F}$ = 9.2 Hz, whereas the second signal exists as a doublet with $^4J_{H-H}$ = 1.45 Hz. If the substitution of the nitro group occurred at position 6, both aromatic protons would have similar spin-spin coupling constants J_{H-F}, which was not observed in the spectra.

The reactions of dinitrobenzoisoxazoles **6a—c** with sodium azide proceeded much more readily (at 20 °C) (Scheme 4).

The replacement of the nitro group with the azido group proceeded in high yield only at position 4. The position at which the displacement occurred was revealed by analogy with the replacement of the nitro group with the fluoride ion (hereinafter, the regioselectivity of the reaction was determined from the data of ^1H NMR spectroscopy of the reaction mixture).

A wide variety of organic nucleophiles can displace the nitro group in 4,6-dinitrobenzo[*d*]isoxazoles. The *in situ* generation of organic nucleophiles, unlike inorganic nucleophiles (which are anions of alkali-metal salts), requires the addition of a base (most often of K_2CO_3) to the reaction mixture.

Scheme 4

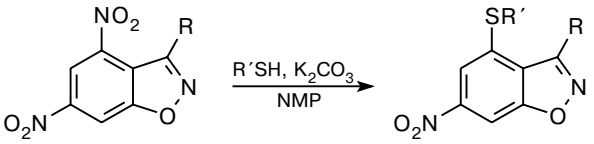


6a—c **8a—c**

Compound	R	Yield (%)
8a		75
8b	—CH=NOMe	94
8c	—CH=NNHPh	89

The reactions of benzoisoxazoles **6a—c** with S-nucleophiles were exemplified by the reactions with thiols in *N*-methylpyrrolidone (NMP) in the presence of K_2CO_3. It was found that thiophenol, α-toluenethiol, and thioglycolic esters displace the nitro group even at room temperature to give previously unknown sulfides **9** in high yields (Scheme 5).

Scheme 5



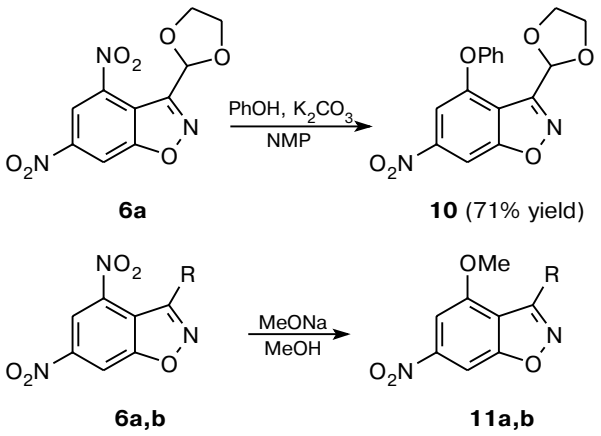
6a—c **9a—h**

Compound	R	R′	Yield (%)
9a		Ph	71
9b	»	—CH_2Ph	55
9c	»	—CH_2CO_2Me	95
9d	»	—CH_2CO_2Et	80
9e	—CH=NOMe	Ph	89
9f	»	—CH_2CO_2Me	74
9g	—CH=NNHPh	Ph	67
9h	»	—CH_2CO_2Me	90

These reactions, like the reactions with inorganic nucleophiles, are regiospecific and proceed exclusively at position 4. In our opinion, the conclusion about the direction of the substitution can be made by comparing the ^{13}C NMR spectra of the initial and final benzoisoxazoles (for example, **6a** and **9a**). After the displacement of the nitro group, the chemical shifts of the signals for the C(4), C(7), and C(3a) atoms were changed most substantially, whereas the chemical shifts of all other signals of the benzoisoxazole fragment remained virtually unchanged, which confirmed our assumption.

O-Nucleophiles are less active than their S-analogs. However, in spite of this fact, the replacement of the nitro group by the phenol fragment or the methoxy group proceeded rather smoothly (Scheme 6).

Scheme 6



6a **10** (71% yield)

6a,b **11a,b**

11a: R =  , 56% yield

11b: R = —CH=NOMe, 58% yield

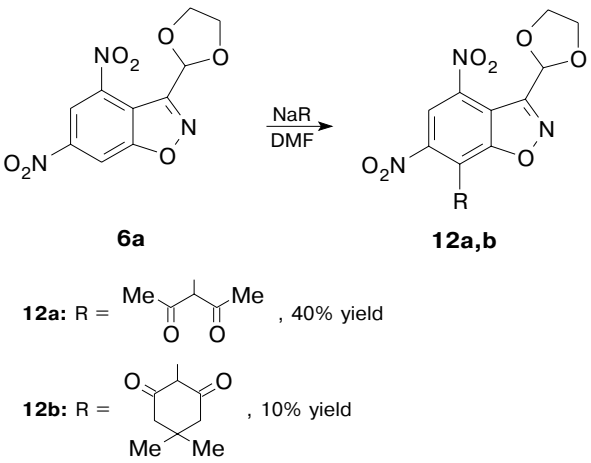
The performance of the reaction under more drastic conditions (higher temperature, the use of strong bases) did not reduce the selectivity of the process. As before, only one nitro group at position 4 was displaced (the direction of the reaction was determined by analogy with the replacement by S-nucleophiles).

Therefore, we developed a convenient procedure for the synthesis of previously unknown 4-Nu-6-nitro-3-R-benzo[*d*]isoxazoles **7—11** (Nu is the nucleophilic fragment) based on dinitrobenzoisoxazoles **6**.

The reactions of 4,6-dinitrobenzoisoxazoles with C-nucleophiles were studied using the reactions of compound **6a** with Na derivatives of 1,3-dicarbonyl compounds as an example. Instead of the expected replacement of the nitro group at position 4, we observed oxidative nucleophilic replacement of hydrogen at position 7 with the corresponding C-nucleophile giving rise to compounds **12** (Scheme 7).

Although these reactions have been described for other nitroaromatic compounds,[8,9] they were performed for the first time in the case of benzo[*d*]isoxazoles. We determined the direction of oxidative substitution based on analysis of the spectral data for the starting benzoisoxazole **6a** and products **12a,b**. For example, the disappearance of the signal for the H(7) atom in the ^1H NMR spectra of compounds **12a,b** (compared to the spectrum of the starting acetal **6a**) and the presence of the signals for all other aromatic and aliphatic protons

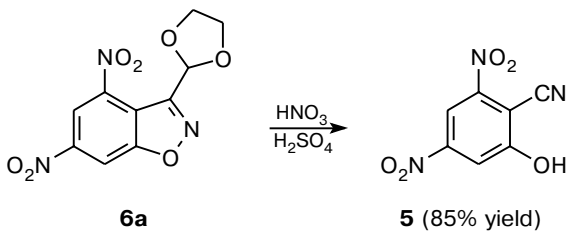
Scheme 7



allows one to unambiguously determine the direction of the nucleophilic attack. Another possible 5-regioisomer was not formed.

Interestingly, an attempt to prepare aldehyde **4** by hydrolysis of cyclic acetal **6a** with a mixture of sulfuric and nitric acids led to the formation of nitrile of 4,6-dinitrosalicylic acid (Scheme 8) due, apparently, to the opening of the isoxazole ring of intermediate aldehyde **4** (see also Scheme 1).

Scheme 8



Therefore, we developed a general procedure for the synthesis of 4,6-dinitro-3-R-benzo[*d*]isoxazoles and used the resulting compounds for the synthesis of various 4-substituted 6-nitro-3-R-benzo[*d*]isoxazoles by nucleophilic displacement of the nitro group.

Experimental

The ^{1}H and ^{19}F NMR spectra were measured on a Bruker AC-200 spectrometer. The ^{13}C NMR spectra were recorded on a Bruker AM-300 spectrometer. The chemical shifts (δ) are given relative to Me_4Si (^{13}C and ^{1}H) or $CFCl_3$ (^{19}F). All samples studied by NMR spectroscopy were prepared in DMSO-d_6. The IR spectra were recorded on a Specord-M-80 instrument in KBr pellets. The mass spectra were measured on a Kratos MS-30 instrument (EI, 70 eV). The course of the reactions and the purities of the compounds were monitored by TLC on Silufol UV-254 plates. Methanol, acetonitrile, and dimethylformamide were dried.[10] Other solvents were used without additional purification.

To determine the regioselectivity of the reaction in *N*-methylpyrrolidone, an aliquot of the reaction mixture was dissolved in DMSO-d_6 and the spectra were recorded in the region of 5—11 ppm. In the case of the reaction in DMF, an aliquot of the reaction mixture was preliminarily diluted with water, and all possible products were extracted with AcOH. To remove DMF, the extracts were washed with dilute aqueous HCl. After evaporation of AcOH, the ^{1}H NMR spectrum of the residue was recorded.

3-(1,3-Dioxolan-2-yl)-4,6-dinitrobenzo[*d*]isoxazole (6a). Potassium carbonate (1.15 g, 8.32 mmol) was added to a solution of compound **3a** [2] (2.6 g, 7.93 mmol) in 95% EtOH (15 mL). The reaction mixture was stirred at 20 °C for 24 h. The precipitate that formed was filtered off, washed with water, dried in air, and recrystallized from EtOH. Product **6a** was obtained in a yield of 2 g, m.p. 102—104 °C (EtOH). ^{1}H NMR: 3.92—4.11 (m, 4 H, $(CH_2)_2$); 6.70 (s, 1 H, OCHO); 8.79 (s, 1 H, H(5)); 9.27 (s, 1 H, H(7)). ^{13}C NMR: 64.7 (OCH_2CH_2O); 97.4 (OCHO); 112.4 (C(7)); 116.1 (C(5)); 116.2 (C(3a)); 141.9 (C(4)); 148.3 (C(6)); 155.2 (C(3)); 163.8 (C(7a)). Found (%): C, 42.69; H, 2.62. $C_{10}H_7N_3O_7$. Calculated (%): C, 42.72; H, 2.51.

Synthesis of benzoisoxazoles 6b—e (general procedure). A mixture of equimolar amounts of compound **2** [2] and the corresponding amine, hydrazine, or hydroxylamine (as hydrochlorides or free bases) was refluxed in 95% EtOH for 3 h. Then the mixture was cooled to 20 °C and an equimolar amount of K_2CO_3 was added (in the case of hydrochlorides, a larger amount of K_2CO_3 should be used to neutralize the acid). The mixture was stirred at 20 °C for 24 h. The precipitate that formed was filtered off, washed with water, dried, and recrystallized from EtOH. The yields of the products are given in Scheme 2.

4,6-Dinitrobenzo[*d*]isoxazole-3-carbaldehyde *O*-methyloxime (6b), m.p. 106—107 °C. ^{1}H NMR: 4.07 (s, 3 H, Me); 8.53 (s, 1 H, CH=N); 8.81 (s, 1 H, H(5)); 9.15 (s, 1 H, H(7)). ^{13}C NMR: 62.6, 111.9, 115.7, 116.3, 138.7, 142.5, 148.3, 150.5, 163.6. Found (%): C, 40.74; H, 2.32. $C_9H_6N_4O_6$. Calculated (%): C, 40.61; H, 2.27.

4,6-Dinitrobenzo[*d*]isoxazole-3-carbaldehyde *N*-phenylhydrazone (6c), m.p. 214—215 °C. ^{1}H NMR: 6.85 (m, 1 H, Ph); 7.12 (m, 2 H, Ph); 7.25 (m, 2 H, Ph); 8.19 (s, 1 H, CH=N); 8.68 (s, 1 H, H(5)); 9.03 (s, 1 H, H(7)). ^{13}C NMR: 110.7, 112.9, 114.8, 118.5, 120.4, 123.0, 128.8, 136.8, 143.7, 148.2, 153.4. Found (%): C, 51.24; H, 2.62. $C_{14}H_9N_5O_5$. Calculated (%): C, 51.38; H, 2.77.

4,6-Dinitrobenzo[*d*]isoxazole-3-carbaldehyde *N*-benzoylhydrazone (6d), m.p. 221—222 °C. ^{1}H NMR: 7.50—7.72 (m, 3 H, Ph); 7.95 (m, 2 H, Ph); 8.85 (s, 1 H, H(5)); 8.94 (s, 1 H, CH=N); 9.31 (s, 1 H, H(7)); 12.45 (br.s, 1 H, NH). ^{13}C NMR: 112.2, 115.8, 117.2, 128.0, 128.2, 131.9, 132.9, 136.2, 142.5, 148.1, 152.9, 159.4, 163.7. Found (%): C, 50.69; H, 2.62. $C_{15}H_9N_5O_6$. Calculated (%): C, 50.71; H, 2.55.

4,6-Dinitrobenzo[*d*]isoxazole-3-carbaldehyde *N*-phenylimine (6e), m.p. 197—198 °C. ^{1}H NMR: 7.33—7.55 (m, 5 H, Ph); 8.85 (s, 1 H, H(5)); 9.05 (s, 1 H, CH); 9.20 (s, 1 H, H(7)). ^{13}C NMR: 111.5, 115.5, 116.0, 121.4, 127.9, 129.2, 142.9, 148.5, 148.8, 149.2, 154.5, 163.7. Found (%): C, 53.61; H, 2.70. $C_{14}H_8N_4O_5$. Calculated (%): C, 53.85; H, 2.58.

3-(1,3-Dioxolan-2-yl)-4-fluoro-6-nitrobenzo[*d*]isoxazole (7). Anhydrous KF (0.42 g, 7.2 mmol) and 18-crown-6 (0.12 g, 0.4 mmol) were added to a solution of compound **6a** (1.0 g, 3.6 mmol) in anhydrous MeCN (10 mL). The reaction mixture was refluxed for 48 h and concentrated to dryness. The residue was

washed with water, dissolved in chloroform, and dried over $MgSO_4$. The solvent was evaporated and the residue was chromatographed on a column with silica gel (Silpearl, $CHCl_3$). Product **7** was obtained in a yield of 0.17 g (20%), m.p. 88—90 °C. ^{1}H NMR: 4.08—4.30 (m, 4 H, 2 CH_2); 6.25 (d, 1 H, OCHO, $^5J_{H-F}$ = 1.5 Hz); 8.05 (d.d, 1 H, H(5), $^3J_{H-F}$ = 9.2 Hz, $^4J_{H-H}$ = 1.5 Hz); 8.58 (d, 1 H, H(7), $^4J_{H-H}$ = 1.5 Hz). ^{13}C NMR: 65.4 (s, OCH_2CH_2O); 96.1 (s, OCHO); 102.9 (d, C(7), $^4J_{C-F}$ = 5.0 Hz); 105.7 (d, C(5), $^2J_{C-F}$ = 25.1 Hz); 112.9 (d, C(3a), $^2J_{C-F}$ = 22.5 Hz); 149.7 (d, C(6), $^3J_{C-F}$ = 8.2 Hz); 154.0 (d, C(4), $^1J_{C-F}$ = 251.4 Hz); 155.1 (d, C(3), $^3J_{C-F}$ = 5.5 Hz); 163.7 (d, C(7a), $^4J_{C-F}$ = 8.1 Hz). ^{19}F NMR: −104.31. Found (%): C, 47.02; H, 2.80. $C_{10}H_7FN_2O_5$. Calculated (%): C, 47.25; H, 2.78.

Synthesis of compounds 8a—c (general procedure). Sodium azide (0.1 g, 1.53 mmol) was added to a solution of 4,6-dinitrobenzo[*d*]isoxazole **6a—c** (1.5 mmol) in DMF (5 mL). The reaction mixture was stirred at 20 °C for 24 h, poured into water, and acidified to pH 2. The precipitate that formed was filtered off, washed with water, and recrystallized from EtOH. The yields of the products are given in Scheme 4.

4-Azido-3-(1,3-dioxolan-2-yl)-6-nitrobenzo[*d*]isoxazole (8a), m.p. 72—74 °C. ^{1}H NMR: 4.10—4.40 (m, 4 H, $(CH_2)_2$); 6.55 (s, 1 H, OCHO); 7.95 (s, 1 H, H(5)); 8.25 (s, 1 H, H(7)). ^{13}C NMR: 65.1, 96.5, 102.0, 108.4, 115.6, 136.3, 149.6, 155.8, 163.4. IR, ν/cm^{-1}: 2140 (N_3); 1550, 1360 (NO_2). Found (%): C, 43.51; H, 2.39. $C_{10}H_7N_4O_5$. Calculated (%): C, 43.33; H, 2.55.

4-Azido-6-nitrobenzo[*d*]isoxazole-3-carbaldehyde *O*-methyloxime (8b), m.p. 164—166 °C. ^{1}H NMR: 4.08 (s, 3 H, Me); 8.05 (s, 1 H, H(5)); 8.42 (s, 1 H, CH=N); 8.47 (s, 1 H, H(7)). ^{13}C NMR: 62.7, 102.3, 108.9, 116.1, 136.4, 137.3, 149.8, 150.4, 163.3. IR, ν/cm^{-1}: 2135 (N_3); 1540, 1360 (NO_2). Found (%): C, 41.38; H, 2.25. $C_9H_6N_6O_4$. Calculated (%): C, 41.23; H, 2.31.

4-Azido-6-nitrobenzo[*d*]isoxazole-3-carbaldehyde *N*-phenylhydrazone (8c), m.p. 214—215 °C. ^{1}H NMR: 6.99 (m, 1 H, Ph); 7.15 (m, 2 H, Ph); 7.32 (m, 2 H, Ph); 8.00 (s, 1 H, H(5)); 8.25 (s, 1 H, CH=N); 8.45 (s, 1 H, H(7)); 11.22 (s, 1 H, NH). ^{13}C NMR: 102.3, 109.1, 112.9, 118.6, 120.7, 122.7, 129.3, 136.4, 144.1, 149.6, 153.6, 163.3. Found (%): C, 52.18; H, 2.73. $C_{14}H_9N_7O_3$. Calculated (%): C, 52.02; H, 2.81.

Synthesis of compounds 9a—h and 10 (general procedure). The corresponding thiol or PhOH (1.5 mmol) and K_2CO_3 (0.21 g, 1.5 mmol) were added to a solution of 4,6-dinitrobenzo[*d*]isoxazole **6a—c** (1.5 mmol) in NMP (5 mL). The reaction mixture was stirred at 20 °C for 24 h (in the case of PhOH, at 80 °C), poured into water, and acidified to pH 2. The precipitate that formed was filtered off, washed with water, and recrystallized from EtOH. The yields of the products are given in Schemes 5 and 6.

3-(1,3-Dioxolan-2-yl)-6-nitro-4-phenylthiobenzo[*d*]isoxazole (9a), m.p. 133—134 °C (EtOH). ^{1}H NMR: 4.05—4.30 (m, 4 H, 2 CH_2); 6.51 (s, 1 H, OCHO); 7.27 (s, 1 H, H(5)); 7.50—7.74 (m, 5 H, Ph); 8.40 (s, 1 H, H(7)). ^{13}C NMR: 65.1 (2 CH_2); 96.7 (CHO); 103.0 (C(7)); 116.0 (C(5)); 120.6 (C(3a)); 129.2 (Ph); 130.4 (Ph); 130.6 (Ph); 134.9 (Ph); 137.0 (C(4)); 149.2 (C(6)); 156.3 (C(3)); 163.1 (C(7a)). Found (%): C, 56.03; H, 3.24. $C_{16}H_{12}N_2O_5S$. Calculated (%): C, 55.81; H, 3.51.

4-Benzylthio-3-(1,3-dioxolan-2-yl)-6-nitrobenzo[*d*]isoxazole (9b), m.p. 106—107 °C (EtOH). ^{1}H NMR: 4.02—4.23 (m, 4 H, 2 CH_2); 4.50 (s, 2 H, SCH_2); 6.51 (s, 1 H, OCHO); 7.18—7.42 (m, 3 H, Ph); 7.49 (m, 2 H, Ph); 8.05 (s, 1 H, H(5)); 8.50 (s, 1 H, H(7)). ^{13}C NMR: 36.8, 65.0, 96.9, 102.4, 115.7, 121.4, 127.5, 128.5, 129.0, 135.2, 136.4, 149.0, 156.3, 162.7. Found (%): C, 56.69; H, 3.81. $C_{17}H_{14}N_2O_5S$. Calculated (%): C, 56.98; H, 3.94.

Methyl 2-[3-(1,3-dioxolan-2-yl)-6-nitrobenzo[*d*]isoxazol-4-yl]thioacetate (9c), m.p. 100—102 °C (EtOH). ^{1}H NMR: 3.73 (s, 3 H, OMe); 4.10—4.21 (m, 4 H, 2 CH_2); 4.29 (s, 2 H, CH_2); 6.50 (s, 1 H, OCHO); 8.07 (s, 1 H, H(5)); 8.51 (s, 1 H, H(7)). Found (%): C, 45.76; H, 3.61. $C_{13}H_{12}N_2O_7S$. Calculated (%): C, 45.88; H, 3.55.

Ethyl 2-[3-(1,3-dioxolan-2-yl)-6-nitrobenzo[*d*]isoxazol-4-yl]thioacetate (9d), m.p. 89—90 °C (EtOH). ^{1}H NMR: 1.25 (t, 3 H, Me, ^3J = 7.0 Hz); 4.10—4.32 (m, 8 H, 4 CH_2 (Et, dioxolane, CH_2C=O)); 6.51 (s, 1 H, OCHO); 8.10 (s, 1 H, H(5)); 8.43 (s, 1 H, H(7)). ^{13}C NMR: 13.9, 34.7, 61.3, 64.9, 96.7, 102.7, 116.0, 121.4, 135.2, 149.0, 156.0, 162.6, 168.0. Found (%): C, 47.49; H, 4.17; S, 8.88. $C_{14}H_{14}N_2O_7S$. Calculated (%): C, 47.45; H, 3.98; S, 9.05.

6-Nitro-4-phenylthiobenzo[*d*]isoxazole-3-carbaldehyde *O*-methyloxime (9e), m.p. 117—118 °C (EtOH). ^{1}H NMR: 4.05 (s, 3 H, OMe); 7.50—7.60 (s, 6 H, Ph, H(5)); 8.57 (s, 1 H, CH=N); 8.74 (s, 1 H, H(7)). ^{13}C NMR: 62.7, 104.0, 117.9, 121.8, 129.9, 130.5, 133.6, 135.6, 138.2, 149.2, 151.9, 162.8. Found (%): C, 54.54; H, 3.43; S, 9.62. $C_{15}H_{11}N_3O_4S$. Calculated (%): C, 54.70; H, 3.37; S, 9.74.

Methyl 2-[3-(methoxyiminomethyl)-6-nitrobenzo[*d*]isoxazol-4-yl]thioacetate (9f), m.p. 111—112 °C (EtOH). ^{1}H NMR: 3.70 (s, 3 H, Me); 4.08 (s, 3 H, NOMe); 4.33 (s, 2 H, CH_2); 8.10 (s, 1 H, H(5)); 8.62 (s, 1 H, CH=N); 8.75 (s, 1 H, H(7)). ^{13}C NMR: 34.8, 52.7, 62.8, 103.9, 117.4, 122.2, 134.6, 138.6, 149.4, 152.0, 162.4, 169.1. Found (%): C, 44.14; H, 3.63; S, 9.72. $C_{12}H_{11}N_3O_6S$. Calculated (%): C, 44.31; H, 3.41; S, 9.86.

6-Nitro-4-phenylthiobenzo[*d*]isoxazole-3-carbaldehyde *N*-phenylhydrazone (9g), m.p. 206—207 °C (EtOH). ^{1}H NMR: 6.92 (t, 1 H, Ph, ^3J = 7.4 Hz); 7.15—7.35 (m, 4 H, Ph); 7.52 (s, 1 H, H(5)); 7.60—7.70 (m, 5 H, Ph); 8.40 (s, 1 H, CH=N); 8.55 (s, 1 H, H(7)); 11.23 (s, 1 H, NH). ^{13}C NMR: 102.0, 111.7, 115.1, 119.3, 121.9, 128.1, 129.0, 129.4, 130.5, 131.6, 133.1, 135.7, 144.0, 149.0, 154.7, 162.9. Found (%): C, 61.24; H, 3.42. $C_{20}H_{14}N_4O_3S$. Calculated (%): C, 61.53; H, 3.61.

Methyl 2-[6-nitro-3-(phenylhydrazonomethyl)benzo[*d*]isoxazol-4-yl]thioacetate (9h), m.p. 210—211 °C (EtOH). ^{1}H NMR: 3.67 (s, 3 H, Me); 4.30 (s, 2 H, CH_2); 6.94 (t, 1 H, Ph, ^3J = 7.4 Hz); 7.15—7.35 (m, 4 H, Ph); 8.05 (s, 1 H, H(5)); 8.32 (s, 1 H, CH=N); 8.50 (s, 1 H, H(7)); 11.21 (br.s, 1 H, NH). ^{13}C NMR: 34.4, 52.7, 103.2, 112.9, 115.7, 120.5, 121.8, 123.3, 129.3, 134.9, 144.0, 149.1, 154.7, 162.6, 169.0. Found (%): C, 52.89; H, 3.51. $C_{17}H_{14}N_4O_5S$. Calculated (%): C, 52.84; H, 3.65.

3-(1,3-Dioxolan-2-yl)-6-nitro-4-phenoxybenzo[*d*]isoxazole (10), m.p. 134—135 °C (EtOH). ^{1}H NMR: 4.00—4.12 (m, 4 H, $(CH_2)_2$); 6.44 (s, 1 H, CH); 7.25—7.40 (m, 4 H, H(5), Ph); 7.63 (m, 2 H, Ph); 8.45 (s, 1 H, H(7)). ^{13}C NMR: 65.4, 96.8, 100.2, 103.9, 115.1, 120.4, 126.0, 130.6, 150.1, 152.7, 153.8, 156.3, 164.0. Found (%): C, 58.78; H, 3.76. $C_{16}H_{12}N_2O_6$. Calculated (%): C, 58.54; H, 3.68.

Synthesis of compounds 11a,b (general procedure). A 3 *M* solution of MeONa in MeOH (0.5 mL) was added to a suspension of 4,6-dinitrobenzo[*d*]isoxazole **6a,b** (1.5 mmol) in MeOH (10 mL). The reaction mixture was stirred at 20 °C for 24 h and poured into water. The precipitate that formed was filtered off, washed with water, and recrystallized from EtOH. The yields of the products are given in Scheme 6.

3-(1,3-Dioxolan-2-yl)-4-methoxy-6-nitrobenzo[*d*]isoxazole (11a), m.p. 150—152 °C (EtOH). ^{1}H NMR: 4.03—4.19 (m, 4 H, 2 CH_2); 4.08 (s, 3 H, Me); 6.45 (s, 1 H, OCHO); 7.65 (s, 1 H, H(5)); 8.20 (s, 1 H, H(7)). ^{13}C NMR: 57.0, 65.2, 96.8, 98.6, 99.9, 114.0, 150.6, 154.4, 156.4, 163.5. Found (%): C, 49.42; H, 3.71. $C_{11}H_{10}N_2O_6$. Calculated (%): C, 49.63; H, 3.79.

4-Methoxy-6-nitrobenzo[*d*]isoxazole-3-carbaldehyde *O*-methyloxime (11b), m.p. 202—203 °C (EtOH). ^{1}H NMR: 4.03 (s, 3 H, OMe); 4.09 (s, 3 H, NOMe); 7.70 (s, 1 H, H(5)); 8.33 (s, 1 H, CH=N); 8.48 (s, 1 H, H(7)). ^{13}C NMR: 57.3, 62.7, 99.0, 100.6, 114.5, 137.4, 138.2, 151.0, 154.6, 163.4. Found (%): C, 47.94; H, 3.80. $C_{10}H_9N_3O_5$. Calculated (%): C, 47.81; H, 3.61.

Synthesis of compounds 12a,b (general procedure). A 3 *M* solution of MeONa in MeOH (0.6 mL) was added to a solution of the corresponding diketone (1.8 mmol) in MeOH (5 mL). The solvent was evaporated and the residue was dissolved in DMF (5 mL). The resulting solution was added to a solution of dinitrobenzo[*d*]isoxazole **6a** (0.5 g, 1.8 mmol) in DMF (5 mL). The reaction mixture was stirred at 20 °C for 24 h, poured into water, and acidified to pH 2. The precipitate that formed was filtered off, washed with water, dried, and recrystallized from $CHCl_3$. The yields of the products are given in Scheme 7.

3-[3-(1,3-Dioxolan-2-yl)-4,6-dinitrobenzo[*d*]isoxazol-7-yl]pentane-2,4-dione (12a), m.p. 214—216 °C ($CHCl_3$). ^{1}H NMR: 1.87 (s, 6 H, 2 CH_3); 3.96—4.20 (m, 4 H, 2 CH_2); 6.73 (s, 1 H, OCHO); 8.78 (s, 1 H, H(5)); 16.61 (br.s, 1 H, OH enol). ^{13}C NMR: 23.8, 64.8, 97.5, 101.9, 115.2, 117.6, 119.7, 142.0, 148.8, 155.6, 163.3, 190.0. Found (%): C, 47.41; H, 3.53. $C_{15}H_{13}N_3O_9$. Calculated (%): C, 47.50; H, 3.45.

2-[3-(1,3-Dioxolan-2-yl)-4,6-dinitrobenzo[*d*]isoxazol-7-yl]-5,5-dimethylcyclohexane-1,3-dione (12b), m.p. 166—167 °C ($CHCl_3$). ^{1}H NMR: 1.23 (s, 6 H, 2 CH_3); 2.51 (s, 4 H, 2 $CH_2C{=}O$); 3.93—4.20 (m, 4 H, OCH_2CH_2O); 6.70 (s, 1 H, OCHO); 8.65 (s, 1 H, H(5)). ^{13}C NMR: 27.7, 28.3, 32.0, 64.7, 97.6, 112.2, 117.2, 119.9, 140.1, 148.3, 155.1, 163.1. Found (%): C, 51.61; H, 4.16. $C_{18}H_{17}N_3O_9$. Calculated (%): C, 51.56; H, 4.09.

Hydrolysis of 3-(1,3-dioxolan-2-yl)-4,6-dinitrobenzo[*d*]isoxazole (6a). A mixture of concentrated H_2SO_4 (2 mL), 70% HNO_3 (2 mL), and compound **6a** (0.56 g, 2 mmol) was stirred at 80—90 °C for 8 h, poured into ice water (20 mL), and extracted with AcOEt (3 × 30 mL). The extract was washed with water and dried over $MgSO_4$. The solvent was evaporated *in vacuo* and the residue was recrystallized from $CHCl_3$. Nitrile of 4,6-dinitrosalicylic acid (**5**) was obtained in a yield of 0.36 g (85%), m.p. 187—188 °C (*cf.* lit. data:[2] 187—188 °C).

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References

1. V. A. Tartakovsky, S. A. Shevelev, M. D. Dutov, A. Kh. Shakhnes, A. L. Rusanov, L. G. Komarova, and A. M. Andrievsky, *Problems of Trotyl (TNT) Processing into Condensation Monomers, Polymers and Dyes* in *Conversion Concepts for Commercial Applications and Disposal Technologies of Energetic Systems*, Ed. H. Krause, Kluwer Academic Publishers, Dordrecht, 1997, 137—149.
2. V. M. Vinogradov, I. L. Dalinger, A. M. Starosotnikov, and S. A. Shevelev, *Mendeleev Commun.*, 2000, 140.
3. N. E. Burlinson, M. E. Sitzman, L. A. Kaplan, and E. Kayser, *J. Org. Chem.*, 1979, **44**, 3695.
4. K.-H. Wunsch and A. J. Boulton, *Adv. Heterocyclic Chem.*, 1967, **8**, 277.
5. H. Lindemann, H. Konitzer, and S. Romanoff, *Justus Liebigs Ann. Chem.*, 1927, **456**, 284.
6. I. L. Dalinger, T. I. Cherkasova, V. M. Khutoretskii, and S. A. Shevelev, *Mendeleev Commun.*, 2000, 72.
7. T. K. Shkineva, I. L. Dalinger, S. I. Molotov, and S. A. Shevelev, *Tetrahedron Lett.*, 2000, **41**, 4973.
8. F. Terrier, *Nucleophilic Aromatic Displacement. The Influence of the Nitro Group, Chapter 5*, VCH Publishers Inc., New York, 1991, 259—284.
9. M. P. Roze, E. L. Berzin´sh, and O. Ya. Neiland, *Zh. Org. Khim.*, 1987, **23**, 2629 [*J. Org. Chem. USSR*, 1987, **23** (Engl. Transl.)].
10. A. J. Gordon and R. A. Ford, *The Chemist's Companion. A Handbook of Practical Data, Techniques, and References*, Wiley, New York, 1972.

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