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To the 100th Anniversary of A.N. Pudovik

Synthesis of New Bicyclic Compounds Containing Fused Sulfolane and Pyrazolidine Rings

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Abstract—3-Aryl-6a-methyl-6-nitro-1-carbamoylhexahydrothieno[2,3-*d*]pyrazole-4,4-dioxides, novel original bicyclic species consisting of fused pyrazolidine and sulfolane rings, and 1,4-adducts were obtained by reacting 2-benzylidene-3-methyl-4-nitro-3-thiolene-1,1-dioxide and its derivatives with semicarbazide.

Keywords: sulfolane, pyrazolidine, bicyclic compounds, nitrosulfodienes, semicarbazide, nucleophilic addition, heterocyclization

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Thiolene- and thiolane-1,1-dioxides (sulfolenes and sulfolanes) are widely used as synthons for practically important substances [1–5]. Of particular interest are polycyclic sulfolane derived species, among which are found analogues of anthracycline-type antibiotics [6], neuroleptic, sedative, analgesic and anticonvulsant drugs [7, 8], as well as substances exhibiting activity against influenza neuraminidase [1, 9] and histamine receptors blockers [10].

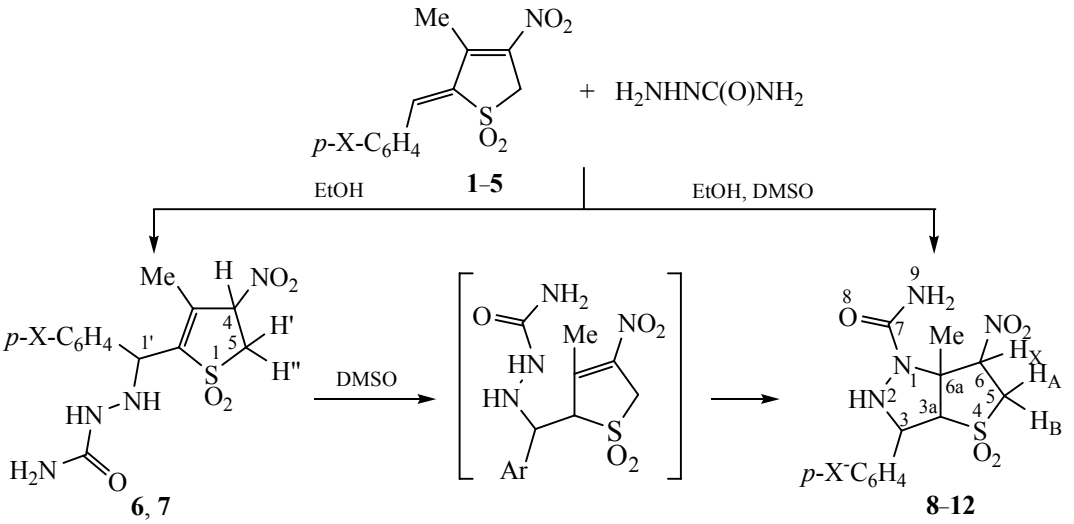
The original condensed bicyclic compounds containing sulfolane fragment have been previously obtained by us through interaction of *s-trans*-nitrosulfodienes of thiolene-1,1-dioxide series, 2-benzylidene-3-methyl-4-nitro-3-thiolene-1,1-dioxides **1**–**5**, with binucleophiles [11–13]. In particular, the reactions with the cyclic β-diketones (dimedone, dihydroresorcinol) led to the formation of compounds consisting of nitrosulfolane ring fused to the chroman system [12]. Bicyclic nitrosulfolane derivatives with pyrazolidine system have been prepared by reacting with phenylhydrazine [13].

Given the wide practical significance of pyrazolidine and its derivatives [9, 14, 15], it seemed logical to continue research to develop methods for producing bicyclic pirazolidine species through interaction of nitrosulfodienes **1**–**5** with semicarbazide. It was found that the synthetic result of these reactions is largely dependent on the duration of the experiments and the nature of the solvent (ethanol, DMSO).

In ethanol solution (18°C) the reactions of chloro-, bromo- and nitro-substituted dienes **3**–**5** with semicarbazide proceeded for 24 h, and the case of methyl analog **2** the reaction required 72 h. In all the cases the target bicyclic compounds, 3-aryl-6a-methyl-6-nitro-1-carbamoylhexahydrothieno[2,3-*d*]pyrazole-4,4-dioxides **9**–**12**, were produced in yields 37–70%. Compounds **9**–**11** were isolated as mixtures of two diastereomers in a ratio of from 4.7 : 1 to 1 : 1. Only compound **12** was found as stereohomogeneous product.

When reacting benzylidenenitrothiolene-1,1-dioxide **1** (ethanol, 18°C, 24 h), a mixture of the aza-Michael adduct **6** and bicycle **8** was obtained in a ratio of 10 : 1; compound **6** was isolated in pure. A similar 1,4-adduct **7** was obtained starting from diene **5** (ethanol, 18°C, 18 h). Similar 1,4-adducts have been previously synthesized when reacting dienes **1**–**5** with aroylhydrazines [16].

Scheme 1.



X = H (**1**, **6**, **8**), Me (**2**, **9**), Cl (**3**, **10**), Br (**4**, **11**), NO_2 (**5**, **7**, **12**).

In DMSO solution (18°C, 24 h) the reactions of dienes **1**–**5** with semicarbazide afforded bicyclic compounds **8**–**12** in a higher yield (up to 84%) compared to the reaction carried out in ethanol; wherein the diastereomers ratio of the adducts **9**–**11** obtained in different conditions was close.

Bicyclic compounds **8** and **12** were also obtained from the adducts **6** and **7** (yield ~40%) when exposed in DMSO solution (18°C).

It should be noted that in all cases nitro-substituted diene **5** was the most active: its high electron deficiency contributed to the formation of the bicycle **12** with a maximum (84%) yield. In contrast, an effect of electron-donating substituent decreased activity of diene **2**, resulting in the need to use two-fold excess of semicarbazide, an increase in the reaction time to 72 h and reducing the yield of compound **9** (37%).

In general, the experimental data confirmed that the formation of target bicyclic compounds **8**–**12** is the result of a domino reaction discussed earlier in [12, 13]. The process comprises nucleophilic 1,4-addition of semicarbazide to dienes **1**–**5**, allyl-vinyl isomerization of intermediate aza-adduct and final Ad_N process with the participation of the second nucleophilic site of the hydrazine moiety. Allyl-vinyl isomerization is due to the high lability of the double bond in nitrothiolenedioxide system under the action of polar solvents [11, 17] and is consistent with the requirements of Baldwin's rule, according to which 5-*exo-trig* cyclization is energetically more favorable process [18]. It should be noted that the addition of phenylhydrazine to Δ^2-sulfolenes has been known to occur in more rigid conditions under the action of a base [19].

Compounds **6**–**12** are colorless crystalline substances, stable in storage. Their structure was confirmed by IR, ^1H and ^{13}C NMR spectroscopy, as well as X-ray diffraction data.

The IR spectra of the adducts **6**, **7**, and bicyclic compounds **8**–**12** contained absorption bands of non-conjugated nitro (1566–1564, 1370–1367 cm^{-1}) and sulfonyl (1318–1312, 1123–1121 cm^{-1}) groups, as well as NH-groups (3460–3421 and 3264–3228 cm^{-1}). The absorbance at 1680–1665 and 1566–1554 cm^{-1} was due the stretching of the amide group; the absorption band in the range of 1600–1592 cm^{-1} corresponded to the stretching of aromatic ring.

The ^1H NMR spectra aza-adducts **6** and **7** contained double set of the signals, indicating that they exist as a mixture of diastereomers in a ratio of 1 : 1. Isomers with more upfield manifestation of the methyl protons and downfield signal of the methine C^4H proton are marked with the letter "**a**;" and conversely more downfield signal of CH_3 moiety and upfield signal of C^4H proton correspond to isomer **b**. Diastereomers **a** and **b** were characterized by close chemical shift values and the same spectral pattern. For example, the protons of methyl groups of the both diastereomers of **6** appeared as the singlets at 1.91 and 1.93 ppm, respectively. Nitromethyne (C^4H) and methylene

(C^5H_2) protons of each isomer gave rise to three-spin system. In particular, in the spectrum of diastereomer **a** these signals have the following chemical shift values (ppm): 3.82 (d.d, 1H, C^5H', $^2J_{H'H''}$ = 15.0, $^3J_{H'C^4H}$ = 8.5 Hz), 4.00 (d.d, 1H, C^5H'', $^2J_{H'H''}$ = 15.0, $^3J_{H''C^4H}$ = 6.7 Hz), 5.98 (d.d, 1H, C^4H, $^3J_{H'C^4H}$ = 8.5, $^3J_{H''C^4H}$ = 6.7 Hz). Exocyclic methine protons ($C^{1'}H$) of the both diastereomers appeared as broad singlet at 5.11 ppm; the hydrazine protons resonated as multiplets at 5.86–5.97 and 7.05–7.12 ppm. Downfield multiplets (7.25–7.37, 7.45–7.53 ppm) corresponded to the aromatic protons.

The ^1H NMR spectra of bicyclic compounds **8**–**11** contain the signals of all protons of two diastereomers at ratios from 4.7 : 1 to 1 : 1 (see the table). In all cases the signals of the methyl and nitromethyne protons of the major isomer **a** are shifted to more strong and more weak fields, respectively, in comparison with those of the minor diastereomer **b**. For example, the singlet of the methyl protons at 1.20 ppm belonged to the stereoisomer **10a**, and the signal at 1.56 ppm corresponded to the isomer **10b**. The protons C^5H_2 and C^6H coupled to form a three-spin ABX system. In the spectuf of compound **10a** and **10b** they appeared as doublets of doublets at 3.84, 3.91, 5.95 ($^2J_{AB}$ = 15.5, $^3J_{AX}$ = 6.7, $^3J_{BX}$ = 1.8 Hz) and 3.81, 4.07, 5.26 ppm ($^2J_{AB}$ = 13.1, $^3J_{AX}$ = 6.1, $^3J_{BX}$ = 12.2 Hz), respectively. The methyne proton $C^{3a}H$ of isomer **10a** resonated as a singlet at 4.12 ppm. The doublets at 5.08 and 5.42 ppm (^3J = 5.8 Hz) corresponded to the C^3H and NH protons, respectively. The aromatic ring protons manifested as doublets at 7.38 and 7.50 ppm. Reliable assignments of the signals in the ^{13}C NMR spectra of compounds **10** and **12** were performed taking advantage of HMQC and HMBC methods. Thus, according to the HMQC data, in the spectrum of **12** the signal at 71.73 ppm was assigned to C^{6a} atom. Assignment of the signals at 76.69 and 85.54 ppm to $C^{3a}H$ and C^6 atoms was made on the basis of their correlation with the $C^{3a}H$ and C^6H protons, respectively. The signal of C^5 atom (53.98 ppm) was revealed due to a correlation with the C^5H_2 protons. Atom C^3 correlated with the aromatic protons (HMBC) was observed at 60.62 ppm. The chemical shifts of the aromatic carbon atoms (128.58, 132.26, 145.97, 147.50 ppm) and the carbonyl group (156.21 ppm) correspond to the literature data [20].

Structure of bicyclic products was also confirmed by X-ray diffraction analysis by the example of compound **10**. Due to the presence of an inversion center in the molecule of **10**, there were two crystallographically equivalent molecules of 3-*para*-chlorophenyl-6a-methyl-6-nitro-1-carbamoylhexahydrothieno[2,3-*d*]pyrazole-4,4-dioxide enantiomers **10a** and **10a'**. For enantiomer **10a** the nitro moiety was found to be disordered due to a reversal at the chiral C^6 center (Fig. 1). Two partial occupancy orientations were identified of 65% and 35% occupancy. This fact is explained by the presence in the crystal of two diastereomers **10a** and **10b**. Since in the second molecule **10a'** disordering was not observed, then the resulting diastereomeric ratio was fund to be 4.7 : 1, which is quite comparable with the ^1H NMR data.

In the unit cell of compound **10**, a partially occupied (0.35) water molecule was also localized, the presence of which is realized in the case of diastereomer **10b**. Moreover, the molecule of **10** contained sparsely occupied and quite disordered isopropanol position, which is considered as a diffuse contribution to the total scattering without localization of the atomic positions by means of SQUEEZE/PLATON software [21]. The total approximate number of the solvent molecules (one molecule per unit cell, i. e., 0.25 per the chemical formula) in the model **10** was calculated taking into account 39 specific electrons and the overall capacity of the voids volume available to the solvent (184 e/Å^3).

Structural parameters of the stereoisomers of 3-*p*-chlorophenyl-6a-methyl-6-nitro-1-carbamoylhexahydrothieno[2,3-*d*]pyrazole-4,4-dioxide **10a**, **10a'**, and **10b** close. Their molecules contained *cis*-fused pyrazolidine and sulfolane rings, each of which had an *envelope* conformation. In the case of isomer **10a** C^3 atom of pyrazolidine ring (torsion angle $N^2N^1C^{6a}C^{3a}$ = 9.9°) and C^6 atom of sulfolane ring (torsion angle $C^5S^4C^{3a}C^{6a}$ 4.11°) were out of plane to give rise torsion angles $C^3C^{3a}C^{6a}N^1$ = –27.2° and $S^4C^{3a}C^{6a}C^6$ = –20.1°, respectively.

The nitro group in the molecules of **10a** and **10a'** was *trans*-position relative pyrazolidine ring (torsion angles $N^1C^{6a}C^6N^{21}$ = 161.8° and 157.5°, respectively). In contrast, in the molecule of **10b** it was *cis*-oriented (torsion angle $N^1C^{6a}C^6N^{212}$ = 66.8°). In all cases S=O bonds were located substantially perpendicular to the sulfolane ring plane (for isomer **10a** torsion angles equaled $O^{19}S^4C^{3a}C^{6a}$ = –119.52°, $O^{20}S^4C^{3a}C^{6a}$ = –109.14°); the amide group was located nearly in the pyrazolidine ring plane (torsion angle $N^2N^1C^7O^9$ = 177.14°). Chiral centers in the molecules of **10a** and **10b** have the

^{1}H NMR spectral (CD_3CN) data for 3-aryl-6a-methyl-6-nitro-1-carbamoylhexahydrothieno[2,3-*d*]pyrazole-4,4-dioxides **8–12**[a]

Comp. no.	δ, ppm (*J*, Hz)						
	CH_3	$C^5H_AH_B$	C^6H_X	$C^{3a}H$	C^3H	NH	NH_2
8a	1.25 s	4.10–4.15 m, 4.20–4.22 m	5.83–5.85 m	4.20–4.22 m	4.90–4.95 m	5.83–5.85 m	6.46 s
8b	1.60 s	4.10 d.d, 4.38 d.d $^2J_{AB}$ = 14.0, $^3J_{AX}$ = 6.6, $^3J_{BX}$ = 10.6	5.32 d.d	4.20–4.22 m	4.90–4.95 m	5.83–5.85 m	6.30 s
9a	1.21 s	3.85 d.d, 3.90 d.d $^2J_{AB}$ = 15.7, $^3J_{AX}$ = 7.6, $^3J_{BX}$ = 1.8	5.26 d.d	4.09 s	5.04 d ^3J = 5.8	5.37 d	5.40–5.94 br.s
9b	1.57 s	3.80 d.d, 4.05 d.d $^2J_{AB}$ = 15.5, $^3J_{AX}$ = 6.4, $^3J_{BX}$ = 11.6	5.26 d.d	4.06 s	5.01 d ^3J = 5.8	5.60 d	5.40–5.94 br.s
10a	1.20 s	3.84 d.d, 3.91 d.d $^2J_{AB}$ = 15.5, $^3J_{AX}$ = 6.7, $^3J_{BX}$ = 1.8	5.95 d.d	4.12 s	5.08 d ^3J = 5.8	5.42 d	5.20–5.94 br.s
10b	1.56 s	3.81 d.d, 4.07 d.d $^2J_{AB}$ = 13.1, $^3J_{AX}$ = 6.1, $^3J_{BX}$ = 12.2	5.26 d.d	4.06 s	5.04 d ^3J = 5.8	5.66 d	5.20–5.94 br.s
11a	1.20 s	3.84 d.d, 3.90 d.d $^2J_{AB}$ = 15.7, $^3J_{AX}$ = 6.7, $^3J_{BX}$ = 1.8	5.95 d.d	4.11 s	5.06 d ^3J = 5.5	5.41 d	5.42–5.80 br.s
11b	1.56 s	3.80 d.d, 4.06 d.d $^2J_{AB}$ = 13.3, $^3J_{AX}$ = 5.5, $^3J_{BX}$ = 12.2	5.26 d.d	4.05 s	5.02 d ^3J = 5.8	5.66 d	5.42–5.80 br.s
12	1.19 s	4.16–4.28 m	5.87 m	4.33 s	5.09 d ^3J = 5.8	5.96 d	6.50 s

[a] ^{1}H NMR spectra of compound **8** and **12** recorded in DMSO-d_6 solution. Aromatic protons appeared in the range of 7.36–8.17 ppm.

following configuration: C^3 – *R*, C^{3a} – *R*, C^{6a} – *R*, C^6 – *S* (**10a**); C^3 – *R*, C^{3a} – *R*, C^{6a} – *R*, C^6 – *R* (**10b**).

Packing in the crystal was due two type of intermolecular hydrogen bonding (Fig. 2): between the oxygen atom of sulfonyl group and N^2H hydrogen atom (S–O^{20}···H–N^2 = 2.092 Å), as well as between the atoms of amide moieties (N^9–H^{9A}···$O^{8'}$ = 1.999 Å). As a result, two centrosymmetric dimers formed. Atomic coordinates, bond lengths and angles were deposited in the Cambridge Crystallographic Data Centre (CCDC 1444528).

Thus, the products of 1,4-addition of semicarbazide to 2-benzylidene-3-methyl-4-nitro-3-thiolene-1,1-dioxide and to its *p*-nitro-substituted analog have been synthesized. The method of the synthesis of original bicyclic compounds containing sulfolane and pyrazolidine fused rings has been developed. In addition, the effect of the solvent nature, ethanol or DMSO, on the reaction route has been revealed and a possible mechanism has been proposed.

EXPERIMENTAL

Physico-chemical studies were performed at the Center for Collective Use, Herzen State Pedagogical University of Russia. X-Ray diffraction studies were performed at the X-Ray Diffraction Centre, St. Petersburg State University.

NMR spectra were recorded with a Jeol ECX400A spectrometer (399.78 MHz) relative to the residual undeuterated solvent signals. IR spectra were registered with a Shimadzu IRPrestige-21 Fourier spectrometer form KBr pellets. Elemental analysis was performed with an Eurovector EA 3000 (CHN Dualmode) analyzer.

X-Ray diffraction studies were performed at 210 K with a Bruker Kappa Apex II Duo diffractometer equipped with a CCD-detector (MoK_α, graphite monochromator). The unit cell parameters [*a* = 7.6014(4), *b* = 13.8670(7), *c* = 16.7861(8) Å, α = 106.7740(10)°,

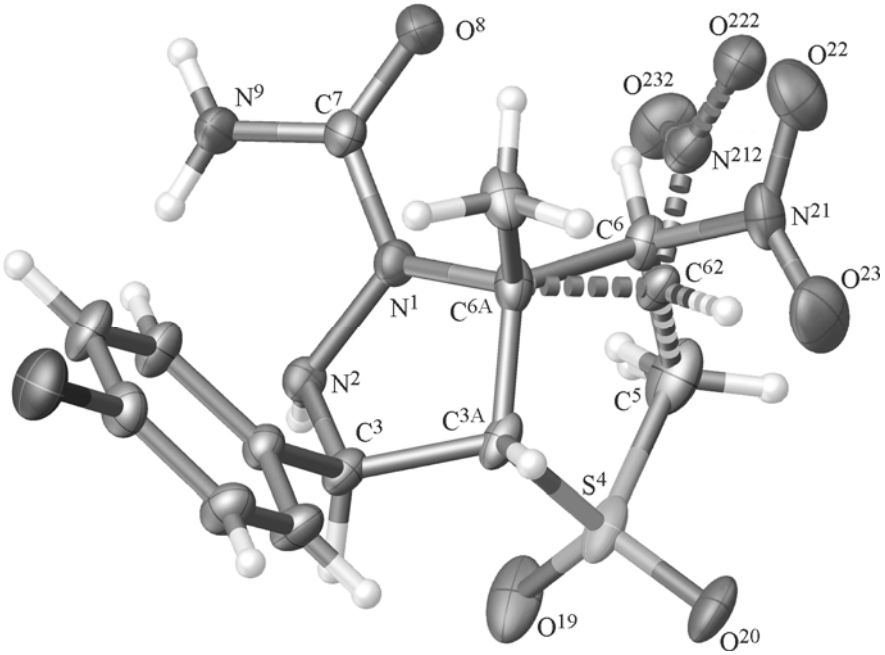


Fig. 1. Crystal structure of the molecule of compound **10**. Disordered nitro group of **10b** is shown by dotted line.

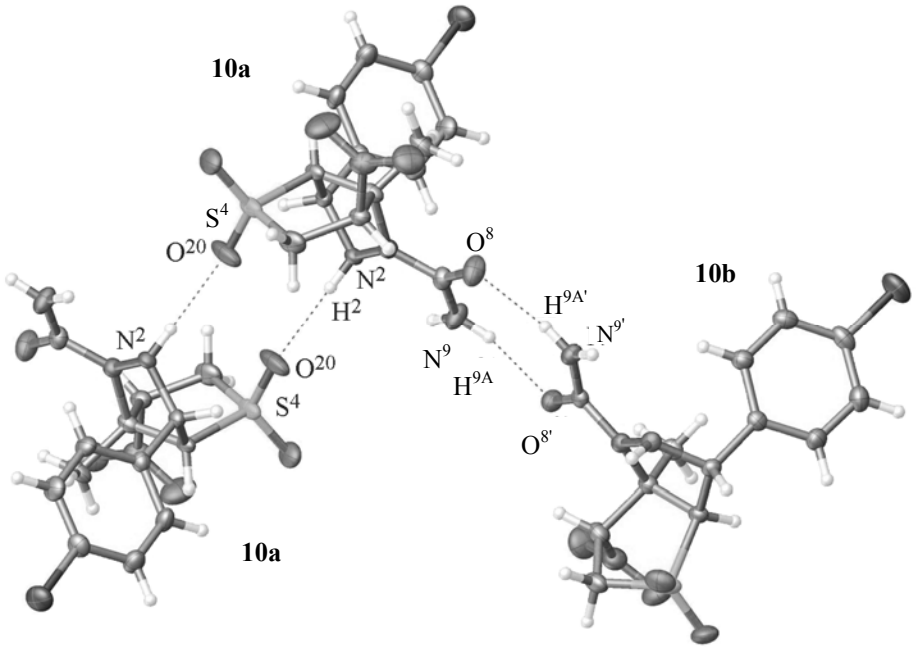


Fig. 2. Hydrogen bonding in the crystal of compound **10**. Disordered nitro group of **10b** was omitted.

β = 90.2660(10)°, γ = 93.4250(10)°, V = 1690.64(15) Å^3, Z = 4] were refined by means of least squares method on the basis of 16912 reflections with 2θ within 2.53°–55.00°. Absorption correction was made using SADABS software [22]. The structure was solved in the space group P-1 by direct methods and refined to R_1 = 0.045 (wR_2 = 0.126) for 6223 independent reflections with $|F_0| \geq 4s_F$ using SHELXL-97 [23] and OLEX2 [24] programs. Positions of the hydrogen atoms of organic molecules were calculated by means of SHELX software, where U_{iso}(H) = 1.5U_{eq}(C) and C–H 0.96 Å for CH_3, U_{iso}(H) = 1.2U_{eq}(C) and C–H 0.97 Å for CH_2, U_{iso}(H) = 1.2U_{eq}(C) and C–H 0.93 Å for CH moieties of the cyclic fragments, U_{iso}(H) = 1.2U_{eq}(C) and C–H 0.98 Å for tertiary CH species, U_{iso}(H) = 1.2U_{eq}(N) and N–H 0.86 Å for NH and NH_2 groups.

Starting nitrosulfodienes **1**–**5** were prepared by the known methods [16, 25].

2-(1'-Semicarbazido-1'-phenyl)methyl-3-methyl-4-nitro-2-thiolene-1,1-dioxide (6). A mixture of 0.17 g (1.5 mmol) of semicarbazide hydrochloride and 1.5 mL of 1 M. sodium hydroxide solution was added with stirring to a suspension of 0.26 g (1 mmol) of nitrosulfodiene **1** in 7 mL of ethanol. The reaction mixture was stirred for 24 h at room temperature. Then precipitate was filtered off and dried in air. According to ^{1}H NMR, it was a mixture of adduct **6** and bicyclic product **8** in a ratio of 10 : 1. After washing the mixture with 5 mL of hot ethanol on a sintered glass filter, compound **6** was isolated as a mixture of two diastereomers in a 1 : 1 ratio. Yield 0.26 g (70%), mp 140–145°C. Found, %: C 45.83; H, 4.71; N 16.49. $C_{13}H_{16}N_4O_5S$. Calculated, %: C 45.88; H 4.74; N 16.46.

2-(1'-Semicarbazido-1'-*p*-nitrophenyl)methyl-3-methyl-4-nitro-2-thiolene-1,1-dioxide (7) was prepared similarly; reaction time – 18 h. The product was isolated as a mixture of two diastereomers in a ratio of 1 : 1. Yield 0.16 g (84%), mp 123–126°C. **Diastereomer 7a.** ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.90 s (3H, Me), 3.75 d.d (1H, C^5H', $^2J_{H'H''}$ = 15.0, $^3J_{H'C^4H}$ = 8.5 Hz), 3.85 d.d (1H, C^5H'', $^2J_{H'H''}$ = 15.0, $^3J_{H''C^4H}$ = 6.7 Hz), 4.91 br.s (1H, $C^{1'}H$), 6.59–6.62 m (2H, NH, N'H), 5.68 d.d (1H, C^4H, $^3J_{H'C^4H}$ = 8.5, $^3J_{H''C^4H}$ = 6.7 Hz), 7.95 m (2H, NH_2), 7.75 d (2H, C_6H_4), 8.18 d (2H, C_6H_4). **Diastereomer 7b.** ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.92 s (3H, Me), 3.71 d.d (1H, C^5H', $^2J_{H'H''}$ = 15.0, $^3J_{H'C^4H}$ = 8.5 Hz), 3.91 d.d (1H, C^5H'', $^2J_{H'H''}$ = 15.0, $^3J_{H''C^4H}$ = 6.4 Hz), 4.91 br.s (1H, $C^{1'}H$), 6.59–6.62 m (2H, NH, N'H), 5.62 d.d (1H, C^4H, $^3J_{H'C^4H}$ = 8.5, $^3J_{H''C^4H}$ = 6.4 Hz), 7.95 m (2H, NH_2), 7.75 d (2H, C_6H_4), 8.18 d (2H, C_6H_4). Found N, %: 17.80. $C_{13}H_{15}N_5O_7S$. Calculated N, %: 18.17.

3-Phenyl-6a-methyl-6-nitro-1-carbamoylhexahydrothieno[2,3-*d*]pyrazole-4,4-dioxide (8). *a*. A mixture of 0.17 g (1.5 mmol) of semicarbazide hydrochloride and 1.5 mL of 1 M sodium hydroxide solution was added with stirring to a solution of 1 mmol of nitrosulfodiene **1** in 7 mL of DMSO. The reaction mixture was stirred for 24 h at room temperature, then poured into 20 mL of crushed ice. The resulting precipitate was collected on a sintered glass filter, washed with distilled water (~ 50 mL) and dried. Compound **8** was obtained as a mixture of two diastereomers in a ratio of 4 : 1. Yield 0.11 g (32%), mp 155–158°C (isopropanol). Found N,%: 16.03. $C_{13}H_{16}N_4O_5S$. Calculated N, %: 16.46.

b. Compound **8** was synthesized as a mixture of two diastereomers in a ratio of 4 : 1 by exposure of 0.34 g (1 mmol) of adduct **6** in DMSO for 10 h at 18°C. The reaction mixture was poured into 20 mL of crushed ice. The resulting precipitate was collected on a sintered glass filter, washed with distilled water (~50 mL) and dried. Yield 0.13 g (37%), mp 155–158°C (isopropanol).

3-*p*-Chlorophenyl-6a-methyl-6-nitro-1-carbamoylhexahydrothieno[2,3-*d*]pyrazole-4,4-dioxide (10). *a*. A mixture of 0.17 g (1.5 mmol) of semicarbazide hydrochloride and 1.5 mL of 1 M. sodium hydroxide solution was added with stirring to a suspension of 1 mmol of nitrosulfodiene **3** in 7 mL of ethanol. The reaction mixture was stirred for 24 h at room temperature. The resulting precipitate was collected on a sintered glass filter, washed with ethanol and air dried. Compound **10** was obtained as a mixture of two diastereomers in a ratio of 4.7 : 1. Yield 0.15 g (40%), mp 167–171°C (isopropanol). **Diastereomer 10a.** ^{13}C NMR spectrum (CD_3CN), δ_C, ppm: 19.46 (Me), 54.25 (C^5), 60.55 (C^3), 71.62 (C^{6a}), 76.31 (C^{3a}), 85.25 (C^6), 129.02, 129.06, 132.81, 132.85, 137.01 (Ar), 156.21 (C=O). **Diastereomer 10b.** ^{13}C NMR spectrum (CD_3CN), δ, ppm: 21.70 (Me), 51.92 (C^5), 57.01 (C^3), 72.80 (C^{6a}), 82.24 (C^{3a}), 84.82 (C^6), 129.02, 129.06, 132.81, 132.85, 137.01 (Ar), 156.21 (C=O). Found, %: C 41.53; H 4.07; N 14.68. $C_{13}H_{15}N_4O_5SCl$. Calculated, %: C 41.66; H 4.03; N 14.95.

b. A mixture of 0.17 g (1.5 mmol) of semicarbazide hydrochloride and 1.5 mL of 1 M. sodium hydroxide solution was added with stirring to a solution of 1 mmol of nitrosulfodiene **3** in 7 mL of DMSO. The reaction mixture was stirred for 24 h at room temperature, then poured into 20 mL of crushed ice. The resulting precipitate was collected on a sintered glass filter, washed with distilled water (~50 mL) and dried. Compound **10** was obtained as a mixture of two diastereomers in a ratio of 4.7 : 1. Yield 0.24 g (64%), mp 167–171°C (isopropanol).

3-*p*-Tolyl-6a-methyl-6-nitro-1-carbamoylhexahydrothieno[2,3-*d*]pyrazole-4,4-dioxide (9) was obtained similarly as a mixture of two diastereomers in a ratio of 2.5 : 1 using a double excess of semicarbazide and reaction time of 72 h. Yield 0.12 g (37%), mp 168–170°C (isopropanol). Found N, %: 15.42. $C_{14}H_{18}N_4O_5S$. Calculated N, %: 15.81. When using

DMSO solution, the target product yield was 0.14 g (40%).

3-*p*-Bromophenyl-6a-methyl-6-nitro-1-carbamoylhexahydrothieno[2,3-*d*]pyrazole-4,4-dioxide (11) was obtained as a mixture of two diastereomers in a ratio of 1 : 1. Yield 0.17 g (40%), mp 189–191°C (isopropanol). Found, %: C 37.02; H 3.51; N 13.18. $C_{13}H_{15}N_4O_5SBr$. Calculated, %: C 37.24; H 3.61; N 13.36. When using DMSO solution, the title product yield was 0.33 g (82%).

3-*p*-Nitrophenyl-6a-methyl-6-nitro-1-carbamoylhexahydrothieno[2,3-*d*]pyrazole-4,4-dioxide (12) was obtained as a single stereoisomer. Yield 0.27 g (70%), mp 165–168°C (isopropanol). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 20.55 (Me), 53.98 (C^5), 60.62 (C^3), 71.73 (C^{6a}), 76.69 (C^{3a}), 85.54 (C^6), 128.58, 132.26, 145.97, 147.50 (Ar), 156.21 (C=O). Found N, %: 17.84. $C_{13}H_{15}N_5O_7S$. Calculated N, %: 18.17. When using DMSO solution, the title product yield was 0.32 g (84%).

Compound **12** was prepared as a single stereoisomer when exposing adduct **7** (0.19 g, 0.5 mmol) in DMSO solution for 6 h at 18°C. Yield 0.08 g (40%).

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