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SHORT COMMUNICATIONS

3,4-Dibromosulfolane in S,N-Tandem Heterocyclizations. Synthesis and Crystalline Structure of Tetrahydrothienothiazinopurines

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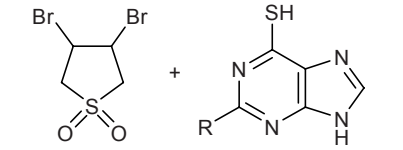
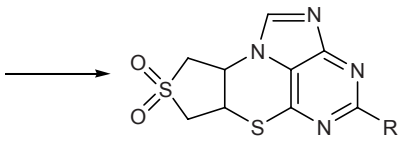
Known [1] cyclizations of 3,4-dibromsulfolane originate from its ability to generate under basic conditions 3-bromo-2,3-dihydrothiophene 1,1-dioxide [2] which acts as dienophile and undergoes regio- and stereoselective [4+2]-cycloaddition reactions. Participation of the C^3 and C^4 atoms in heterocyclizations was reported only for the reaction of 3,4-dibromosulfolane with *o*-phenylenediamine [3].

In the preceding communication [4] we proposed a convenient procedure for the synthesis of difficultly accessible heterocyclic systems via S,N-tandem heterocyclization of 3,4-dibromosulfolane with thiouracils. In continuation of our studies on one-pot syntheses of polyfunctional heterocyclic compounds possessing useful properties, in the present paper we report on the *peri*-condensation of 3,4-dibromosulfolane with 6-sulfanylpurine (**Ia**) and 6-thioguanine (**Ib**).

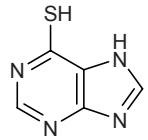


Ia, **Ib**

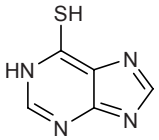


IIa, **IIb**

Among eight possible tautomeric forms of 6-sulfanylpurine [5], only two may be involved in S,N-tandem reactions. Although heterocyclizations of the N^1H tautomer have been reported [6], we detected no compounds with *ortho*-fused rings among the reaction products.



N^7H tautomer



N^1H tautomer

The reactions were carried out in ethanol at a dibromosulfolane–**Ia** (**Ib**)–KOH molar ratio of 1:2:4 under stirring for 8 h at room temperature. The yields of compounds **IIa** and **IIb** thus formed were 75–80%. Their structure was confirmed by the ^1H NMR and mass spectra. In the ^1H NMR spectra of **IIa** and **IIb** we observed signals from the $CH_2CHCHCH_2$ fragment

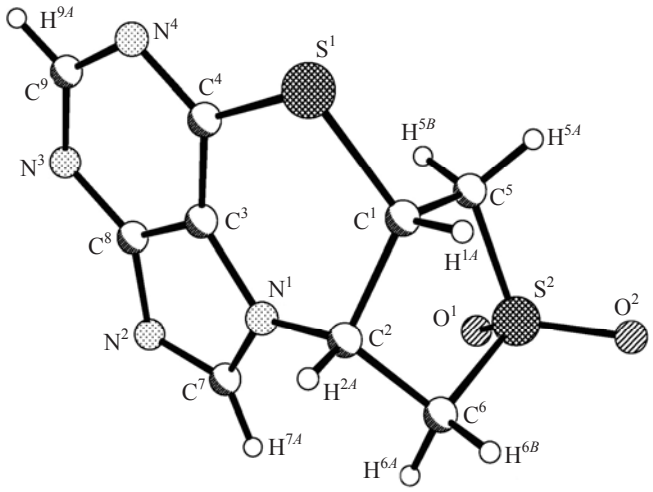


Fig. 1. Structure of the molecule of 6a,7,9,9a-tetrahydrothieno[3′,4′:5,6][1,4]thiazino[4,3,2-*gh*]purine 8,8-dioxide (**IIa**) according to the X-ray diffraction data.

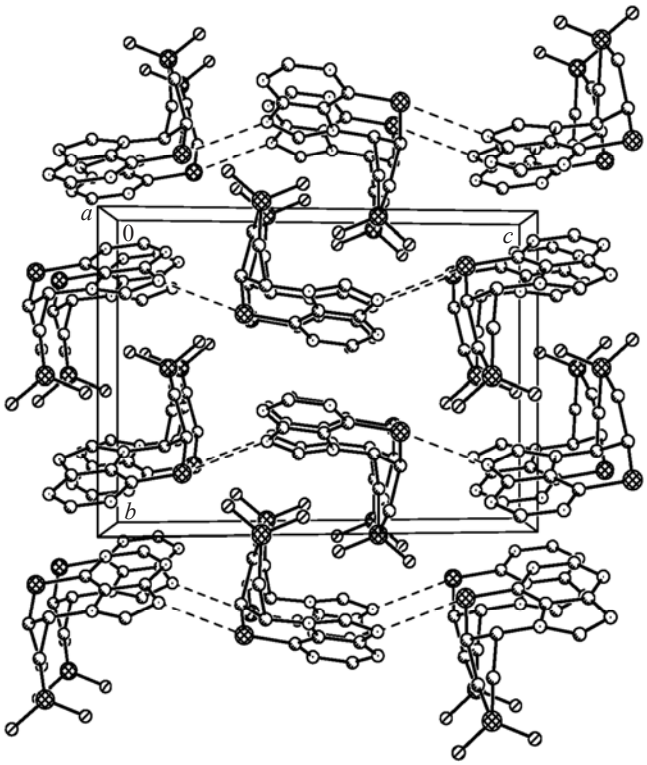


Fig. 2. A fragment of crystal packing of 6a,7,9,9a-tetrahydrothieno[3′,4′:5,6][1,4]thiazino[4,3,2-*gh*]purine 8,8-dioxide (**IIa**) (projection along the *a* axis; hydrogen atoms are not shown).

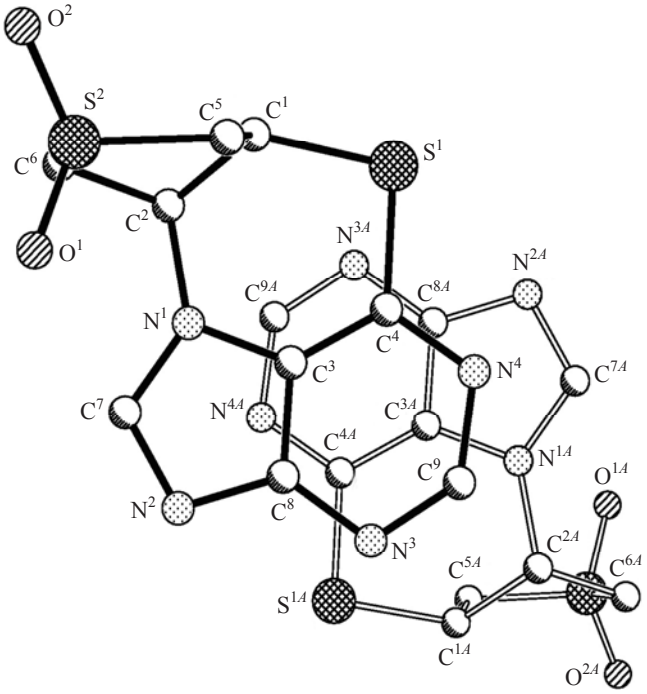


Fig. 3. Stacking interactions between two molecules of 6a,7,9,9a-tetrahydrothieno[3′,4′:5,6][1,4]thiazino[4,3,2-*gh*]-purine 8,8-dioxide (**IIa**) in crystal.

(*ABCMM′X*) possessing four chiral centers, which is typical of 3,4-fused thiophene 1,1-dioxides. Compounds **IIa** and **IIb** characteristically showed peaks from the following fragment ions in the mass spectra: $[M - SO_2]^{+\cdot}$, $[M - SO_2 - H]^{+\cdot}$, $[M - SO_2 - CH_3]^{+\cdot}$, $[M - SO_2 - C_2H_4]^{+\cdot}$, $[M - SO_2 - SH]^{+\cdot}$. The fragmentation patterns were assumed in accordance with the data of [7, 8]. The absence of isomeric products indicates high chemo- and regioselectivity of the process, which suggests concerted mechanism inherent to tandem reactions [9].

The structure of dioxide **IIa** was unambiguously proved by X-ray analysis (Fig. 1). The bond lengths and bond and torsion angles in molecule **IIa** approach the corresponding standard values [10]. The crystalline structure of compound **IIa** is characterized by shortened $S^1 \cdots N^{2'}$ contacts [$-0.5 + x$, $0.5 - y$, $-0.5 + z$; d = 3.071(5) Å; Fig. 2]. The other C–H···O, C–H···N, and C–H···S contacts should be regarded as common van der Waals interactions. The sulfur-containing heterorings in molecule **IIa** are nonplanar. The S^1 atom lies in the plane of the aromatic bicyclic system (its deviation from the $N^1C^3C^4$ plane is 0.025 Å), while the C^1 and C^2 atoms deviate from the $N^1C^3C^4S^1$ plane in opposite directions by 0.482 and 0.211 Å, respectively. The conformation of the 1,4-thiazine ring is close to *twist*. The five-membered sulfur-containing heteroring adopts an *envelope*-like conformation, where the C^2 atom deviates from the $C^1C^5S^2C^6$ plane by 0.636 Å (the average deviation of the other atoms from that plane does not exceed ±0.05 Å).

The aromatic fragments of the neighboring molecules of **IIa** in crystal give rise to stacking interactions [11]: the distance between their planes is 3.40 Å. The shortest distances in the centrosymmetric dimer (Fig. 3) are $C^3 \cdots C^{9A}$ 3.44 ($-x$, $1 - y$, $1 - z$) and $C^8 \cdots C^{4A}$ 3.49 Å ($-x$, $1 - y$, $1 - z$).

6a,7,9,9a-Tetrahydrothieno[3′,4′:5,6][1,4]thiazino[4,3,2-*gh*]purine 8,8-dioxide (IIa). Yield 80%, mp 301–302°C (from EtOH–DMF). ^{1}H NMR spectrum, δ, ppm: 3.08 d.d (1H, CH), 3.87 d.d (1H, CH), 3.93 d.d (1H, CH), 4.45 d.d (1H, CH), 4.87 br.s (1H, CH), 5.40 br.s (1H, CH), 8.77 s (1H, H_{arom}), 8.91 s (1H, H_{arom}). Mass spectrum, m/z (I_{rel}, %): 268 (100) $[M]^+$, 204 (78.2), 203 (10.4), 189 (5.6), 176 (9.7), 171 (26.8).

6a,7,9,9a-Tetrahydrothieno[3′,4′:5,6][1,4]thiazino[4,3,2-*gh*]purin-4-amine 8,8-dioxide (IIb). Yield 75%, mp 288–289°C (from EtOH–DMF). ^{1}H NMR spectrum, δ, ppm: 3.16 d.d (1H, CH), 3.88 m (2H, 2CH), 4.49 d.d (1H, CH), 4.92 m (1H, CH), 5.53 m

(1H, CH), 7.24 s (2H, NH_2), 8.86 m (1H, H_{arom}). Mass spectrum, m/z (I_{rel}, %): 283 (100) $[M]^+$, 219 (66.9), 218 (9.2), 204 (5.7), 191 (8.7), 186 (27.1).

X-Ray diffraction data for compound **IIa**. Monoclinic crystals, $C_9H_8N_4O_2S_2$, M 268.31, space group $P2_1/n$, with the following unit cell parameters (100 K): a = 6.552(1), b = 10.430(2), c = 14.775(3) Å; β = 98.612(5)°; V = 998.3(4) Å^3; Z = 4; d_{calc} = 1.785 g/cm^3, μ(MoK_α) = 5.27 cm^{-1}. Intensities of 9353 reflections (1935 of which were idependent, R_{int} = 0.094) were measured on a Bruker SMART APEX II automatic diffractometer with a coordinate detector [graphite monochromator, λ(MoK_α) = 0.71073 Å, $2\theta_{max}$ = 52°, 100 K]. The structure was solved by the direct method and was refined by the full-matrix least-squares procedure with respect to F^2_{hkl} with anisotropic thermal parameters for all non-hydrogen atoms. The positions of hydrogen atoms were calculated from geometry considerations and were refined using the riding model. The final divergence factors were R_1 = 0.0592 [with respect to F_{hkl} for 1100 reflections with $I > 2\sigma(I)$] and wR_2 = 0.1210, S = 0.977 (with respect to F^2_{hkl} for all independent reflections). All calculations were performed using SHELXTL software package [12].

The mass spectra were recorded on a Micromass ZDM-2000 LC–MS instrument (electrospray ionization, positive ion detection) and on an MKh-1321 mass spectrometer (electron impact, 70 eV; direct sample admission into the ion source). The ^{1}H NMR spectra were measured from solutions in DMSO-d_6 on a Bruker AM-500 spectrometer (500.13 MHz) using the residual proton signal of the solvent as reference.

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