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SHORT COMMUNICATIONS

Aryl 2,3-Dibromopropyl Sulfones in S,N-Tandem Heterocyclizations. New Synthesis of Thiazinopurines

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Undoubtedly, pyrimidine and purine derivatives occupy an important place in the chemistry of heterocyclic compounds, for these heterocycles constitute a part of numerous biologically active natural compounds, including nucleosides and nucleotides. Various purine and pyrimidine analogs and derivatives have been synthesized and studied as pharmacologically active substances or drugs [1]. Pharmacologically active tricyclic analogs of purine, such as imidazopurinones [2], pyrimidoindoles [3], and imidazopurines [4, 5], are used as substances which compete with adenosine for binding with receptors and as antiviral agents.

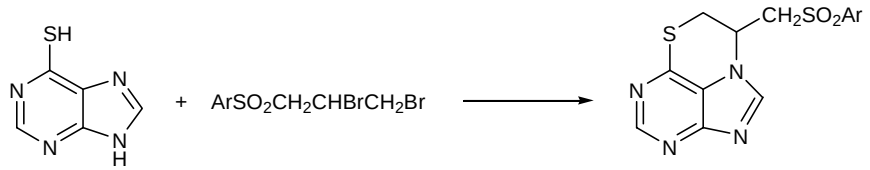
Generally, cyclization of a molecule leads to loss of its conformational flexibility. Such rigidly fixed conformations could possess a sharply increased phylogenetic affinity for a target structure provided that the parent scaffold is biologically active. This is clearly demonstrated by the structure of etorphine which is a morphine derivative containing an additional six-membered carbon ring: it is more active than morphine by three orders of magnitude [6, 7].

We propose a convenient procedure for the synthesis of thiazinopurines via S,N-tandem alkylation of 6-sulfanylpurine with aryl 2,3-dibromopropyl sulfones. The reactions were carried out by stirring a mixture of the reactants (aryl 2,3-dibromopropyl sulfone **Ia**–**Id**, 6-sulfanylpurine, and potassium hydroxide at a ratio of 1:2:4) for 8 h at room temperature. The yields of compounds **IIa**–**IId** were 85–95%. Their structure was confirmed by the ^{1}H NMR and mass spectra. In addition, the structure of thiazinopurine **IId** was unambiguously proved by X-ray analysis. The general view of molecule **IId** is shown in figure.

The ^{1}H NMR spectra of **IIa**–**IId** contained signals from the CH_2CHCH_2 moiety (*AA'XMM'*) possessing two chiral centers. In the mass spectra of **IIa**–**IId**, the following ion peaks were the most characteristic (*m*/*z*): $[M - ArSO_2]^+$ (191), $[M - 1 - ArSO_2]^+$ (190), $[M - ArSO_2CH_2]^+$ (177), $[M - ArSO_2CH_2CH_2]^+$ (163), $[M - ArSO_2CH{=}CH{-}CH_3]^+$ (150). The fragmentation pattern was proposed on the basis of the data in [8, 9]. The absence of isomeric products in the reaction mixtures indicates that the process is chemo- and regioselective and that it follows a concerted mechanism typical of tandem reactions [10].

7-(Phenylsulfonylmethyl)-7,8-dihydro[1,4]thiazino[4,3,2-*gh*]purine (IIa). Yield 85%, mp 206–207°C (from EtOH). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.38 m (1H, CH), 3.56 m (1H, CH), 3.72 m (2H, CH_2), 5.52 m (1H, CH), 7.63 m (5H, H_{arom}), 8.32 m (1H, H_{arom}), 8.92 s (1H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 332 (79.2) $[M]^+$, 191 (100), 190 (60.1), 177 (38.6), 163 (26.4), 150 (6.4), 139 (9.8), 119 (10.2).

7-(4-Methylphenylsulfonylmethyl)-7,8-dihydro-[1,4]thiazino[4,3,2-*gh*]purine (IIb). Yield 92%,



Ia–Id **IIa–IId**

Ar = Ph (**a**), 4-MeC_6H_4 (**b**), 4-$O_2NC_6H_4$ (**c**), 2-naphthyl (**d**).

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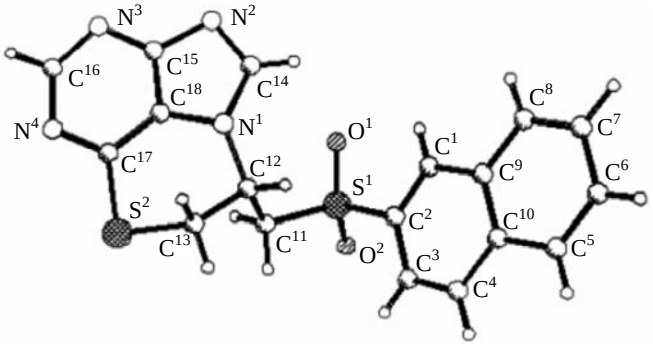

Molecular structure of 7-(2-naphthylsulfonylmethyl)-7,8-dihydro[1,4]thiazino[4,3,2-*gh*]purine (**IId**) according to the X-ray diffraction data.

mp 232°C (from EtOH). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.45 s (3H, CH_3), 3.39 d.d (1H, CH), 3.62 d.d (2H, CH_2), 3.71 d.d (1H, CH), 5.57 (1H, CH), 7.38 d (2H, H_{arom}), 7.77 d (2H, H_{arom}), 8.31 s (1H, H_{arom}), 8.92 s (1H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 346 (82.3) $[M]^+$, 191 (100), 190 (62.2), 177 (40.8), 163 (27.3), 150 (6.7), 139 (9.9), 119 (10.4).

7-(4-Nitrophenylsulfonylmethyl)-7,8-dihydro-[1,4]thiazino[4,3,2-*gh*]purine (IIc). Yield 87%, mp 275°C (decomp., from EtOH–DMF). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.71 m (2H, CH), 4.08 d (2H, CH_2), 5.55 m (1H, CH), 8.29 d (2H, H_{arom}), 8.44 d (2H, H_{arom}), 8.49 s (1H, H_{arom}), 8.68 s (1H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 377 (76.4) $[M]^+$, 191 (100), 190 (62.2), 177 (40.2), 163 (26.6), 150 (6.5), 139 (10.3), 119 (10.6).

7-(2-Naphthylsulfonylmethyl)-7,8-dihydro[1,4]-thiazino[4,3,2-*gh*]purine (IId). Yield 95%, mp 251–252°C (from EtOH–DMF). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.68 d.d (1H, CH), 3.78 d.d (1H, CH), 4.11 m (2H, CH_2), 5.52 m (1H, CH), 7.73 m (2H, H_{arom}), 7.96 d (1H, H_{arom}), 8.09 d (1H, H_{arom}), 8.21 t (2H, H_{arom}), 8.55 s (1H, H_{arom}), 8.68 s (1H, H_{arom}), 8.75 s (1H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 382 (72.5) $[M]^+$, 191 (100), 190 (60.8), 177 (38.4), 163 (22.3), 150 (6.0), 139 (10.2), 119 (10.4).

The ^{1}H NMR spectra were recorded from solutions in DMSO-d_6 or $CDCl_3$ on a Bruker AM-500 spectrometer operating at 500.13 MHz. Signals from residual protons in the deuterated solvents were used as reference. The mass spectra (electron impact, 70 eV) were obtained on an MKh-1321 instrument with direct sample admission into the ion source. The X-ray diffraction data for a single crystal of compound **IId** ($0.42\times0.38\times0.32$ mm) were acquired on an Enraf–Nonius CAD-4 diffractometer at 293 K. The structure was solved by the direct method using SHELX-97 software package [11].

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