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SHORT COMMUNICATIONS

3,4-Dibromotetrahydro-λ⁶-thiophene 1,1-Dioxide in S,N-Tandem Heterocyclizations. Synthesis of Tetrahydrothieno-thiazolopyrimidines

A. A. Shklyarenko and V. V. Yakovlev

"Applied Chemistry" Russian Research Center, pr. Dobrolyubova 14, St. Petersburg, 197198 Russia
e-mail: synthon@inbox.ru

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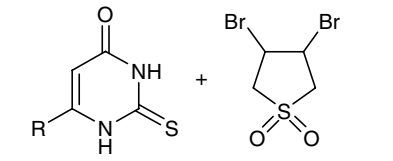
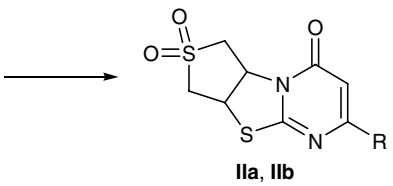
Pyrimidine derivatives possess important pharmacological properties [1]. Among these, the most prominent are such naturally occurring alkaloids as batzelladines [2], ptilomycalins [3], saxitoxins [4], and luotonins [5]; their molecules include five-membered saturated rings fused to a pyrimidine base. We previously showed [6] that 2,3-dibromopropyl sulfones readily undergo heterocyclization with 2-thiouracils. While continuing studies on tandem heterocyclizations, we have synthesized tetrahydrothienothiazolopyrimidine derivatives via S,N-tandem alkylation of 2-thiouracils **Ia** and **Ib** with 3,4-dibromotetrahydro-λ⁶-thiophene 1,1-dioxide. The reactions were carried out in ethanol at room temperature, the reactant ratio dibromosulfolane–2-thiouracil **I**–potassium hydroxide being 1:2:4; the reactions were complete in 8 h, and the yields of products **IIa** and **IIb** were 78–80%.



Ia, **Ib**



IIa, **IIb**

R = NH_2 (**a**), MeO (**b**).

Products **IIa** and **IIb** were isolated as individual substances, and their structure was confirmed by the ^{1}H NMR and mass spectra. The ^{1}H NMR spectra of **IIa** and **IIb** contained signals from the $CH_2CHCHCH_2$ fragment as an *ABMM'NN'* spin system having four chiral centers. In the mass spectra of **IIa** and **IIb**, the most characteristic were peaks from the following fragment ions: $[M - SO_2H]^+$, $[M - SO_2]^+$, $[M - SO_2 - SH]^+$, $[M - SO_2 - SH - C_2H_2]^+$. The fragmentation pattern was proposed on the basis of published data [7, 8]. The absence of isomeric compounds among the products indicates that the reaction is chemo- and regioselective and that the process follows a concerted mechanism typical of tandem reactions [9].

2-Amino-5a,6,8,8a-tetrahydro-4*H*-7λ⁶-thieno-[3',4':4,5][1,3]thiazolo[3,2-*a*]pyrimidin-4-one 7,7-dioxide (IIa). Yield 78%, mp 276–277°C (from EtOH–DMF). ^{1}H NMR spectrum, δ, ppm: 3.38 m (2H, CH), 3.65 m (2H, CH), 4.56 m (1H, CH), 4.85 s (1H, H_{arom}), 5.33 m (1H, CH), 6.38 br.s (2H, NH_2). Mass spectrum, *m*/*z* (I_{rel}, %): 259 (100) $[M]^+$, 194 (30.5), 195 (51.1), 162 (62.2), 136 (58.8).

2-Methoxy-5a,6,8,8a-tetrahydro-4*H*-7λ⁶-thieno-[3',4':4,5][1,3]thiazolo[3,2-*a*]pyrimidin-4-one 7,7-dioxide (IIb). Yield 80%, mp 263–264°C (from EtOH–DMF). ^{1}H NMR spectrum, δ, ppm: 3.56 m (2H, CH), 3.68 m (2H, CH), 3.77 s (3H, CH_3), 4.79 m (1H, CH), 5.33 s (1H, H_{arom}), 5.43 m (1H, CH). Mass spectrum, *m*/*z* (I_{rel}, %): 274 (100) $[M]^+$, 209 (36.6), 210 (52.4), 177 (64.9), 151 (48.6).

The ^{1}H NMR spectra were recorded 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. The mass spectra (electron

impact, 70 eV) were obtained on an MKh-1321 mass spectrometer with direct sample admission into the ion source. LC–MS analysis was performed on a Micromass ZDM-2000 instrument (electrospray ionization, positive ion registration).

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