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SHORT COMMUNICATIONS

(2,3-Dibromopropyl)sulfonylarenes in S,N-Tandem Heterocyclizations. A New Synthesis of Thiazolopyrimidines

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Pyrimidine derivatives occupy an important place in the chemistry of heterocyclic compounds, for they exhibit a broad spectrum of biological activity [1]. Molecules of many biologically active natural compounds include five-membered saturated rings fused to a pyrimidine base; examples are batzelladines [2], ptilomycalins [3], and saxitoxins [4].

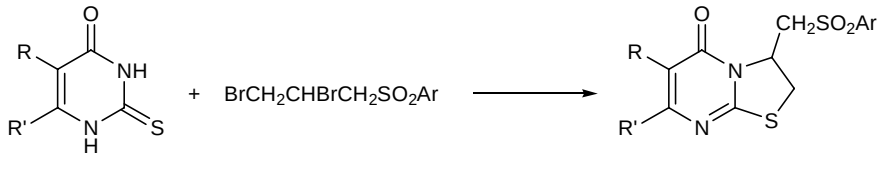
While continuing our studies in the field of tandem heterocyclizations [5, 6], we have synthesized dihydrothiazolo[3,2-*a*]pyrimidines via S,N-tandem alkylation of 2-thiouracils with aryl 2,3-dibromopropyl sulfones. All reactions were carried out in ethanol, the molar ratio of aryl 2,3-dibromopropyl sulfone **II**, nucleophile **I**, and potassium hydroxide was 1:2:4, and the reaction mixture was stirred for 8 h at room temperature. The yields of products **IIIa**–**IIIh** were 80–90%. The structure of compounds **IIIa**–**IIIh** was proved by the ^{1}H NMR and mass spectra. In addition, the structure of **IIIa** in crystal was studied by X-ray analysis. The structure of molecule **IIIa** is shown in figure.

The ^{1}H NMR spectra of **IIIa**–**IIIh** contained signals from the CH_2CHCH_2 group, which gave rise to an *AA'XMM'* system with two chiral centers typical of a thiazolidine ring. Compounds **IIIa**–**IIId** showed in the mass spectra the following most characteristic fragment ions: $[M - CO]^+$, $[M - SO_2 - OH]^+$, $[M - SO_2 - SH]^+$. The mass spectra of **IIIe**–**IIIh** contained peaks from the $[M - Me]^+$, $[M - Me - CO]^+$, and $[M - Me - CH_3CN]^+$ ions. The fragmentation patterns were proposed in accordance with the data of [7, 8]. The absence of isomeric products in the reaction mixtures indicates high chemo- and regioselectivity of the process and suggests concerted mechanism typical of tandem reactions [9].

7-Amino-3-phenylsulfonylmethyl-2,3-dihydro-5*H*-[1,3]thiazolo[3,2-*a*]pyrimidin-5-one (IIIa). Yield 95%, mp 263–264°C (from EtOH–DMF). ^{1}H NMR spectrum, δ, ppm: 3.75 d (1H, CH), 3.66 m (2H, CH_2), 3.79 m (1H, CH), 4.73 s (1H, H_{arom}), 5.11 m (1H, CH), 6.35 br.s (2H, NH_2), 6.67 m (2H, H_{arom}), 7.75 m (1H, H_{arom}), 7.94 d (2H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 323 (31.8) $[M]^+$, 259 (1.8), 226 (31.6), 154 (100).

7-Amino-3-(4-methylphenylsulfonylmethyl)-2,3-dihydro-5*H*-[1,3]thiazolo[3,2-*a*]pyrimidin-5-one (IIIb). Yield 89%, mp 134–135°C (from EtOH–DMF). ^{1}H NMR spectrum, δ, ppm: 2.47 s (3H, CH_3), 3.69 m (1H, CH), 3.78 m (2H, CH_2), 3.91 m (1H, CH), 4.75 s (1H, H_{arom}), 4.94 m (1H, CH), 6.37 br.s (2H, NH_2), 7.42 d (2H, H_{arom}), 7.82 d (2H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 337 (27.7) $[M]^+$, 273 (1.2), 258 (0.6), 240 (29.8), 168 (100).

7-Amino-3-(4-nitrophenylsulfonylmethyl)-2,3-dihydro-5*H*-[1,3]thiazolo[3,2-*a*]pyrimidin-5-one (IIIc). Yield 86%, mp 242–243°C (from EtOH–DMF).



Ia, **Ib** **IIa–IId** **IIIa–IIIh**

I, R = H, R' = NH_2 (**a**); R = Et, R' = Me (**b**); **II**, Ar = Ph (**a**), 4-MeC_6H_4 (**b**), 4-$O_2NC_6H_4$ (**c**), 2-naphthyl (**d**); **III**, R = H, R' = NH_2, Ar = Ph (**a**), 4-MeC_6H_4 (**b**), 4-$O_2NC_6H_4$ (**c**), 2-naphthyl (**d**); R = Et, R' = Me, Ar = Ph (**e**), 4-MeC_6H_4 (**f**), 4-$O_2NC_6H_4$ (**g**), 2-naphthyl (**h**).

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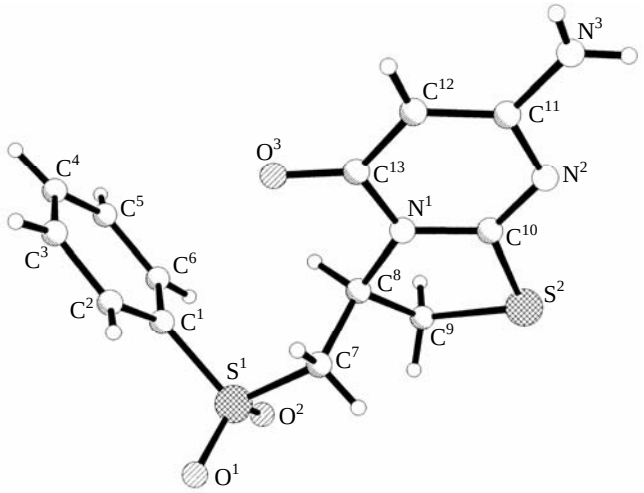

Structure of the molecule of 7-amino-3-phenylsulfonylmethyl-2,3-dihydro-5*H*-[1,3]thiazolo[3,2-*a*]pyrimidin-5-one (**IIIa**) according to the X-ray diffraction data (hydrogen atoms are not shown).

^{1}H NMR spectrum, δ, ppm: 3.61 d (1H, CH), 3.74 m (2H, CH_2), 3.89 m (1H, CH), 4.69 s (1H, H_{arom}), 5.06 m (1H, CH), 6.33 br.s (2H, NH_2), 8.23 d (2H, H_{arom}), 8.44 d (2H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 368 (28.8) $[M]^+$, 304 (2.1), 289 (0.9), 271 (33.1), 199 (100).

7-Amino-3-(2-naphthylsulfonylmethyl)-2,3-dihydro-5*H*-[1,3]thiazolo[3,2-*a*]pyrimidin-5-one (IIId). Yield 82%, mp 177–178°C (from EtOH–DMF). ^{1}H NMR spectrum, δ, ppm: 3.61 m (1H, CH), 3.72 m (2H, CH_2), 3.78 m (1H, CH), 4.75 s (1H, H_{arom}), 5.31 m (1H, CH), 6.36 br.s (2H, NH_2), 7.68 m (2H, H_{arom}), 7.89 d (1H, H_{arom}), 8.02 d (1H, H_{arom}), 8.13 m (2H, H_{arom}), 8.58 s (1H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 373 (29.2) $[M]^+$, 309 (2.1), 294 (1.1), 276 (30.8), 204 (100).

6-Ethyl-7-methyl-3-phenylsulfonylmethyl-2,3-dihydro-5*H*-[1,3]thiazolo[3,2-*a*]pyrimidin-5-one (IIIe). Yield 85%, mp 168–169°C (from EtOH). ^{1}H NMR spectrum, δ, ppm: 0.92 t (3H, CH_3), 2.05 s (3H, CH_3), 2.21 m (2H, CH_2), 3.64 m (1H, CH), 3.82 m (2H, CH_2), 3.96 m (1H, CH), 4.97 m (1H, CH), 7.63 m (2H, H_{arom}), 7.72 m (1H, H_{arom}), 7.96 d (2H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 350 (62.2) $[M]^+$, 335 (49.6), 307 (0.8), 294 (2.2), 181 (100).

6-Ethyl-7-methyl-3-(4-methylphenylsulfonylmethyl)-2,3-dihydro-5*H*-[1,3]thiazolo[3,2-*a*]pyrimidin-5-one (IIIf). Yield 91%, mp 159–160°C (from EtOH). ^{1}H NMR spectrum, δ, ppm: 0.95 t (3H, CH_3), 2.04 s (3H, CH_3), 2.18 m (2H, CH_2), 2.45 s (3H, CH_3), 3.69 m (3H, CH_3), 3.91 m (1H, CH), 4.91 m (1H, CH), 7.42 d (2H, H_{arom}), 7.82 d (2H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 364 (60.1) $[M]^+$, 349 (50.8), 321 (0.9), 308 (1.7), 195 (100).

6-Ethyl-7-methyl-3-(4-nitrophenylsulfonylmethyl)-2,3-dihydro-5*H*-[1,3]thiazolo[3,2-*a*]pyrimidin-5-one (IIIg). Yield 80%, mp 193–194°C (from EtOH). ^{1}H NMR spectrum, δ, ppm: 0.93 t (3H, CH_3), 2.03 s (3H, CH_3), 2.18 s (2H, CH_2), 3.65 m (1H, CH), 3.82 m (1H, CH), 3.99 m (1H, CH), 4.13 m (1H, CH), 5.05 m (1H, CH), 8.28 d (2H, H_{arom}), 8.45 d (2H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 395 (61.8) $[M]^+$, 380 (48.6), 352 (1.1), 339 (2.6), 226 (100).

6-Ethyl-7-methyl-3-(2-naphthylsulfonylmethyl)-2,3-dihydro-5*H*-[1,3]thiazolo[3,2-*a*]pyrimidin-5-one (IIIh). Yield 88%, mp 160–161°C (from EtOH). ^{1}H NMR spectrum, δ, ppm: 0.90 t (3H, CH_3), 2.04 s (3H, CH_3), 2.21 m (2H, CH_2), 3.65 d (1H, CH), 3.82 m (3H, CH_3), 5.23 m (1H, CH), 7.68 m (2H, H_{arom}), 7.89 d (1H, H_{arom}), 8.02 d (1H, H_{arom}), 8.14 m (2H, H_{arom}), 8.54 s (1H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 400 (63.5) $[M]^+$, 385 (48.8), 357 (1.1), 344 (2.5), 231 (100).

The mass spectra were obtained on a Micromass ZDM-2000 GC–MS system (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 recorded from solutions in DMSO-d_6 on a Bruker AM-500 spectrometer (500.13 MHz) using residual proton signal of the solvent as reference. X-Ray analysis of a single crystal (0.32×0.30×0.26 mm) of compound **IIIa** was performed at 293 K using an Enraf–Nonius CAD-4 diffractometer. The structure was solved by the direct method using SHELX-97 software package [10].

REFERENCES

1. Roth, H.J. and Fenner, H., *Stuttgart: Deutscher Apotheker*, 2000, p. 441.
2. Patil, A.D., Kumar, N.V., Kokke, W.C., Bean, M.F., Freyer, A.J., De Brosse, C., Mai, S., Truneh, A., Faulkner, D.J., Carte, B., Breen, A.L., Hertzberg, R.P., Johnson, R.K., Westley, J.W., and Potts, B.C.M., *J. Org. Chem*., 1995, vol. 60, p. 1182.
3. Heys, L., Moore, C.G., and Murphy, P.J., *Chem. Soc. Rev*., 2000, vol. 29, p. 57.
4. Kishi, Y., *Heterocycles*, 1980, vol. 14, p. 1477.

5. Shklyarenko, A.A., Yakovlev, V.V., and Chistokletov, V.N., *Russ. J. Org. Chem*., 2004, vol. 40, p. 591.
6. Shklyarenko, A.A., Yakovlev, V.V., and Chistokletov, V.N., *Russ. J. Org. Chem*., 2004, vol. 40, p. 1067.
7. Ponomarev, D.A. and Takhistov, V.V., *Recent Advances in Analytical Techniques*, Attaur-Rahman, M., Ed., Reading: Hardwood Academic, 2002, p. 369.
8. Ponomarev, D.A., Golovin, A.V., and Takhistov, V.V., *Eur. J. Mass Spectrom*., 2002, vol. 8, p. 409.
9. Nicolaou, K.C., Montagnon, T., and Snyder, S.A., *Chem. Commun*., 2003, p. 551.
10. Sheldrik, G.M., *SHELX-97*, Göttingen: Univ. of Göttingen, 1997.