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SHORT COMMUNICATIONS

(2,3-Dibromopropylsulfonyl)arenes in S,N-Tandem Heterocyclizations. New Synthesis of Triazolothiazolidines

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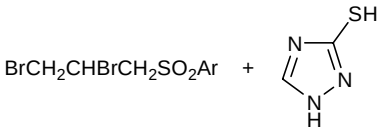
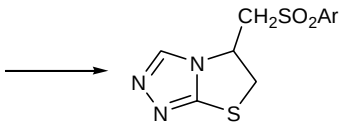
Development of new methods for the preparation of fused thiazolidine derivatives is important, for these compounds exhibit high pharmacological activity [1–3]. Thiazolidine ring is a structural fragment of many biologically active compounds, especially of penicillin derivatives. However, the known methods for the synthesis of such heterocycles are few in number and fairly laborious, and the yields of the target products are poor [4–6].

We have developed a new and convenient procedure for the synthesis of triazolothiazolidines on the basis of S,N-tandem alkylation of 1,2,4-triazole-3-thiol with vicinal dibromopropyl sulfones.



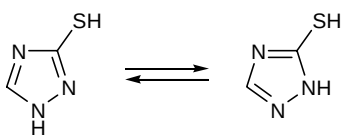
Ia–Id **II**



IIIa–IIId

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

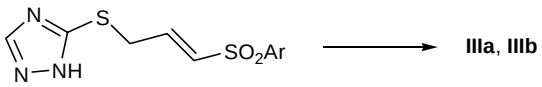
Triazole **II** can exist as two tautomers: 1,2,4-triazole-3-thiol (**IIa**) and 1,2,4-triazole-5-thiol (**IIb**). Interconversion of tautomers **IIa** and **IIb** is very fast, and their separation is difficult; however, tautomer **IIa** seems to be preferable [7]. The reaction under study involves exclusively tautomer **IIb**, i.e., 2,3-dibromopropyl sulfones may be regarded as a specific trap of 1,2,4-triazole-5-thiol.



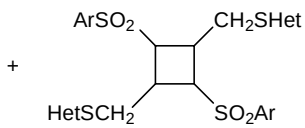
IIa **IIb**

All reactions were performed by stirring the reactants in ethanol at room temperature (reaction time 8 h). The molar ratio **I**:**II**:KOH was 1:2:4. The yields of products **IIIa**–**IIId** were 80–90%. Their structure was proved by the ^{1}H NMR and mass spectra and by the GC–MS data. The purity of the products was 98–100%. The ^{1}H NMR spectra of **IIIa**–**IIId** contained signals from the CH_2CHCH_2 fragment as an *AA'XMM'* system. Nonequivalence of the CH_2S protons indicates formation of a thiazolidine ring possessing two chiral centers. In the mass spectra of **IIIa**–**IIId**, the most characteristic are the following fragment ion peaks: $[M - SO_2]^{+\cdot}$, $[M - SO_2 - Me]^+$, $[M - SO_2 - SH]^+$, $[M - SO_2 - N_2 - HCN]^{+\cdot}$, $[M - ArSO_2]^+$ (*m*/*z* 140). The fragmentation scheme is consistent with the data of [8, 9].

It should be noted that the reactions with compounds **Ia** and **Ib** were accompanied by formation of minor products (2%) with molecular weights of 562 and 590, respectively. Presumably, intermediate arylsulfonylallylsulfanyl-1,2,4-triazoles **IV**, apart from



IVa, **IVb** 98%



Va, **Vb** (2%)

Het = 1,2,4-triazol-5-yl.

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intramolecular cyclization, undergo [2+2]-cyclodimerization with formation of the corresponding cyclobutane derivatives. In the other cases, the reaction was chemo- and regioselective, indicating its concerted character intrinsic to tandem reactions [10].

6-(Phenylsulfonylmethyl)-5,6-dihydro[1,3]thiazolo[3,2-*c*][1,2,4]triazole (IIIa). Yield 80%, mp 111–112°C (from ethanol). ^{1}H NMR spectrum, δ, ppm: 3.47 d.d (1H, CH), 3.77 d (1H, CH), 4.18 d.d (1H, CH), 4.28 d.d (1H, CH), 5.01 m (1H, CH), 7.78 s (1H, H_{arom}), 7.60–7.96 m (5H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 281 (3.8) $[M]^+$, 217 (49.2), 202 (17.4), 184 (5.2), 162 (4.6), 140 (100), 77 (74.7).

6-(4-Methylphenylsulfonylmethyl)-5,6-dihydro-[1,3]thiazolo[3,2-*c*][1,2,4]triazole (IIIb). Yield 80%, mp 114–116°C (from ethanol). ^{1}H NMR spectrum, δ, ppm: 2.48 s (3H, CH_3), 3.46 d.d (1H, CH), 3.75 d (1H, CH), 4.20 d.d (1H, CH), 4.31 d.d (1H, CH), 5.03 m (1H, CH), 7.66 s (1H, H_{arom}), 7.44 d (2H, H_{arom}), 7.68 d (2H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 295 (4.6) $[M]^+$, 241 (48.3), 216 (18.5), 198 (5.4), 176 (4.7), 140 (100).

6-(4-Nitrophenylsulfonylmethyl)-5,6-dihydro-[1,3]thiazolo[3,2-*c*][1,2,4]triazole (IIIc). Yield 90%, mp 140–141°C (from ethanol). ^{1}H NMR spectrum, δ, ppm: 3.98 d.d (1H, CH), 4.22 d (1H, CH), 4.39 d.d (1H, CH), 4.55 d.d (1H, CH), 7.84 s (1H, H_{arom}), 8.24 d (2H, H_{arom}), 8.36 d (2H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 326 (4.3) $[M]^+$, 262 (52.2), 247 (15.8), 229 (4.5), 207 (4.2), 140 (100).

6-(2-Naphthylsulfonylmethyl)-5,6-dihydro[1,3]-thiazolo[3,2-*c*][1,2,4]triazole (IIId). Yield 85%, mp 89–90°C (from ethanol). ^{1}H NMR spectrum, δ, ppm: 3.36 t (1H, CH), 3.86 (1H, CH), 4.22 d.d (1H, CH), 4.30 d.d (1H, CH), 5.05 m (1H, CH), 7.70 (1H, H_{arom}), 7.68 m (2H, H_{arom}), 7.78 m (4H, H_{arom}), 8.53 s (1H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 331 (2.8) $[M]^+$, 267 (51.2), 252 (16.4), 234 (4.9), 212 (4.3), 140 (100), 127 (76.5).

The mass spectra were obtained on a Micromass ZDM-2000 GC–MS system (electrospray ionization, positive ions) and on an MKh-1321 instrument (electron impact, 70 eV, direct sample admission into the ion source). The ^{1}H NMR spectra were measured from solutions in $CDCl_3$ on Bruker AM-500 and Mercury 400BB spectrometers at 500.13 and 399.98 MHz, respectively, using the solvent as reference.

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