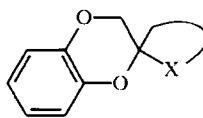


## NEW BIHETEROCYCLIC SPIRO SYSTEM – SPIRO- [1,4-BENZODIOXIN-2(3H),2'(3'H)-BENZOTHIAZOLE]

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*A convenient preparative method has been developed for obtaining 3'-methylspiro[1,4-benzodioxin-2(3H),2'(3'H)-benzothiazole], the first representative of biheterocyclic spiro compounds of a new type.*

Biheterocyclic spiro compounds of general formula A containing 1,4-benzodioxin fragment are little known. Representatives of them described up to the present time contain nodal carbon atom included in partially or completely hydrogenated furan [1], 1,4-oxazine [2], pyran [3-6], dioxolane [7-10], or pyrrole [11] rings. These spiro compounds were synthesized by the cyclocondensation of 2-functionalized derivatives of 1,4-benzodioxin-2(3H)-ols [2,8] or cycloaddition of *o*-quinones to functionalized unsaturated compounds and their hetero analogs [6,11]. Some spiro compounds are found in natural materials [9,10]. Among the spiro compounds being considered there are compounds possessing antitumor and antiviral activity, fungicides, and inhibitors of neoplasms [4,5,7-10]. From what has been said further modifications of compounds of structure A seemed expedient.



X = heteroatom

We have developed an accessible method of obtaining a new 1,4-benzodioxin-containing biheterocyclic spiro system, containing benzothiazoline ring as the second hetero component.

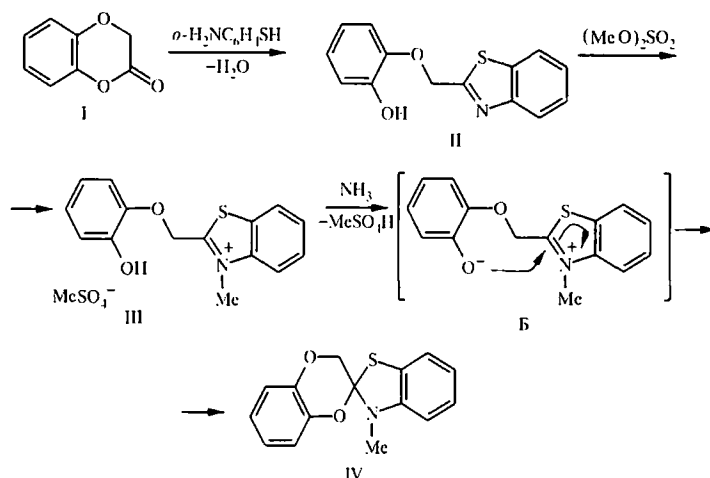
The synthesis was carried out in three stages. Benzothiazole II functionalized at position 2 was obtained by the reaction of 1,4-benzodioxin-2(3H)-one I with *o*-aminothiophenol. Subsequent quaternization with dimethyl sulfate occurred selectively with the formation of quaternary salt III. Finally the target spiro compound IV was obtained by treating salt III with aqueous ammonia solution. The transformation occurred probably as deprotonation with the intermediate formation of the unstable zwitterionic form B, the intramolecular selfcondensation of which with simultaneous selfneutralization of the polar centers gave the final product.

Compound IV was a crystalline pale yellow substance, which darkened on storage in light at 20-25°C and was converted into a resinous substance of unestablished composition. On storage without access to air or light at 0°C its properties were unchanged for over six months. Spiro compound IV was readily soluble in chloroform, benzene, and acetone, moderately in alcohol, and poorly in hexane and water, which is in agreement with its low polarity.

The structure of the synthesized compounds was confirmed by data of IR and <sup>1</sup>H NMR spectroscopy (see Experimental). Comparison of the <sup>1</sup>H NMR spectra of the starting materials, compounds II, III, and the target compound IV confirmed the spiro structure of the latter. We note the main differences of the <sup>1</sup>H NMR spectrum of the spiro compound. The chemical nonequivalence of protons of the methylene group located on the asymmetric carbon atom was confirmed by the corresponding signal as a doublet of doublets. The relatively high field appearance

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of the  $\text{CH}_2$  group signal indicates its proximity to the  $sp^3$ -hybridized carbon atom. The relatively high field appearance of the N-methyl group signal indicates the absence of a positive charge on the nitrogen atom. Additional confirmation of the formation of a spiro system, without possible molecular rearrangement, is the identity of the spectra of the spiro compound IV and of the initial compound III (ignoring the signal of the methyl sulfate anion) in the acid solvent  $\text{CF}_3\text{COOD}$ . The latter data indicate the breaking of the spiro system in acid medium, i.e. the reversibility of the process of formation of the compound IV.

A convenient preparative method has therefore been developed for synthesizing 3'-methylspiro-[2,3-dihydro-1,4-benzodioxine-2(3H),2'(3'H)-benzothiazole] and the possibility of the existence of this type of spiro system has been established in principle.

## EXPERIMENTAL

The IR spectra were obtained on an UR 20 instrument in KBr disks. The  $^1\text{H}$  NMR spectra were recorded on a Varian VXR 300 spectrometer with an operating frequency of 300 MHz, solvents were  $\text{CDCl}_3$ ,  $\text{CF}_3\text{COOD}$ , and  $\text{DMSO}-d_6$ , internal standard was HMDS. A check on the progress of reactions and the homogeneity of the compounds synthesized was effected by TLC on Silufol UV 254 plates in the solvent system benzene-ethanol, 9 : 1 (visualization in UV light). Compound I was obtained by the method proposed in [12].

**2-(o-Hydroxyphenoxy)methylbenzothiazole (II).** Mixture of compound I (49.5 g; 0.33 mol) and *o*-aminothiophenol (41.25 g; 0.33 mol) in *o*-xylene (60 ml) was warmed until the beginning of an exothermic reaction. After its extinguishment, water which had separated was removed by boiling the reaction mixture with a reflux condenser fitted with a Dean – Stark head. After cooling the solution, the crystalline residue which separated was filtered off, and washed with hexane. Yield was 79.72 g (94%), mp 99–101°C (nitromethane). IR spectrum: 3360 (OH)  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR spectrum ( $\text{CDCl}_3$ ),  $\delta$ , ppm: 5.42 (2H, s,  $\text{CH}_2$ ); 6.74–7.00 (4H, m,  $\text{C}_6\text{H}_4$ ); 7.16–8.07 (4H, m,  $\text{SC}_6\text{H}_4$ ); (in  $\text{CF}_3\text{COOD}$ ): 5.48 (2H, s,  $\text{CH}_2$ ); 6.62 (4H, m,  $\text{OC}_6\text{H}_4$ ); 7.13–7.87 (4H, m,  $\text{SC}_6\text{H}_4$ ). Found, %: C 65.0; H 4.4; N 5.3.  $\text{C}_{14}\text{H}_{11}\text{NO}_2\text{S}$ . Calculated, %: C 65.4; H 4.3; N 5.4.

**2-(o-Hydroxyphenoxy)methyl-3-methylbenzothiazolium Methyl Sulfate (III).** Mixture of compound II. (10.28 g; 0.04 mol), freshly distilled dimethyl sulfate (5.67 g; 0.045 mol), and 2-propanol (20 ml) was boiled under reflux for 1 h. After cooling, the crystalline solid which separated was filtered off, and washed with 2-propanol. Yield was 13.94 g (91%), mp 136–139°C (decomp.) (1-propanol). IR spectrum: 3400–3525  $\text{cm}^{-1}$  (OH).  $^1\text{H}$  NMR spectrum ( $\text{CF}_3\text{COOD}$ ),  $\delta$ , ppm: 2.97 (3H, s,  $\text{OCH}_3$ ); 3.44 (3H, s,  $\text{NCH}_3$ ); 5.55 (2H, s,  $\text{CH}_2$ ); 6.62 (4H, m,  $\text{OC}_6\text{H}_4$ ); 7.15–7.88 (4H, m,  $\text{SC}_6\text{H}_4$ ). Found, %: C 50.4; H 4.9; N 3.8.  $\text{C}_{16}\text{H}_{17}\text{NO}_6\text{S}_2$ . Calculated, %: C 50.1; H 4.5; N 3.6.

**3'-Methylspiro[1,4-benzodioxine-2(3H),2'(3'H)-benzothiazole] (IV).** 25% aqueous ammonia solution (10 ml) was added dropwise during 3–5 min to stirred solution of compound III (15.32 g; 0.04 mol) in water (40 ml) in atmosphere of argon. The product which separated was filtered off, washed with water, and dried in air

at 20-25°C. Yield 10.30 g (95%); mp 119-120.5°C (2-propanol). <sup>1</sup>H NMR spectrum (DMSO-d<sub>6</sub>), δ, ppm: 3.02 (3H, s, NCH<sub>3</sub>); 4.67-4.76 (2H, dd, *J* = 10 Hz, CH<sub>2</sub>); 6.63-7.24 (8H, m, 2C<sub>6</sub>H<sub>4</sub>); (CF<sub>3</sub>COOD): 3.96 (3H, s, NCH<sub>3</sub>); 5.54 (2H, s, CH<sub>2</sub>); 6.60 (4H, m, OC<sub>6</sub>H<sub>4</sub>); 7.14-7.90 (4H, m, SC<sub>6</sub>H<sub>4</sub>). Found, %: C 66.6; H 4.7; N 5.2. C<sub>15</sub>H<sub>13</sub>NO<sub>2</sub>S. Calculated, %: C 66.4; H 4.8; N 5.2.

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