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SHORT COMMUNICATIONS

## Synthesis of Thiosulfonates with Functional Groups in the Aliphatic Chain

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Thiosulfonates of the general formula  $RSO_2SR^1$  having functional substituents in the *S*-alkyl chain exhibit high biological activity; the presence of a hydroxy group increases their solubility in water [1, 2]. Esters containing hydroxy groups are usually obtained in poor yields (15–40%) by alkylation of metal thiosulfonates with ethylene halohydrins in aqueous acetone on heating [2].

With the goal of searching for new methods of synthesis of thiosulfonates we have performed for the first time reactions of alkali metal thiosulfonates with oxiranes. By reaction of 2-chloromethyloxirane with alkali metal thiosulfonates in aqueous alcohol in the presence of Lewis acid at  $20^{\circ}$ C we have synthesized *S*-(2-hydroxy-3-chloropropyl) thiosulfonates in 56–84% yield. We have thus demonstrated the possibility for opening of the oxirane ring by the action of thiosulfonic acid salts. Thio esters were derived from alkali metal salts of 3-acetylamino-4-methoxybenzenethiosulfonic acid (**Ia**), 1,1-dioxotetra-hydrothiophene-3-thiosulfonic acid (**Ib**), 4-acetyl-aminobenzenethiosulfonic acid (**Ic**).

$$RSO_{2}SM + H_{2}C - CHCH_{2}Cl$$

$$Ia - Ie$$

$$ZnCl_{2} - RSO_{2}SCH_{2}CH(OH)CH_{2}Cl$$

$$IIa - IIe$$

$$I, II, R = 4-MeO-3-AcNHC_{6}H_{3} (a), \int_{O} O (b),$$

$$4-AcNHC_{6}H_{4} (c), 4-MeC_{6}H_{4} (d), Ph (e); M = K, Na.$$

The procedure is also applicable to other oxiranes, such as bis[4-(2,3-epoxy-1-propoxy)phenyl] sulfone

and 2,2-bis[4-(2,3-epoxy-1-propoxy)phenyl]propane. This makes it possible to synthesize thiosulfonates with various functional groups in the *S*-alkyl chain. The proposed method ensures preparation of thiosulfonates with high yields from accessible reagents.

The structure and purity of products **IIa–IIe** were proved by the IR (Specord 75IR, KBr) and <sup>1</sup>H NMR spectra (Varian VXR, DMSO- $d_6$ , HMDS), elemental analyses, and TLC data (Silufol UV-254, acetone– chloroform, 10:1).

S-(3-Chloro-2-hydroxypropyl) thiosulfonates IIa–IIe (general procedure). A solution of 16.7 mmol of anhydrous zinc(II) chloride in 10 ml of 80% ethanol was added to a solution of 33.4 mmol of salt Ia–Ie in 50 ml of 80% ethanol. 2-Chloromethyloxirane, 2.1 ml (26.8 mmol), was added at 20°C, the mixture was kept for 12 h at 20°C, the precipitate was filtered off, and the filtrate was diluted with a threefold volume of water and was extracted with diethyl ether ( $3 \times 60$  ml). The extract was washed with water ( $2 \times 60$  ml), dried over anhydrous magnesium sulfate, and evaporated under reduced pressure.

*S*-(3-Chloro-2-hydroxypropyl) 3-acetylamino-4-methoxybenzenethiosulfonate (IIa). Yield 65%. mp 88–90°C. IR spectrum, v, cm<sup>-1</sup>: 1124, 1320 (SO<sub>2</sub>); 1562, 1592, 1600 (Ar); 1636 (NH); 1666 (C=O); 3200–3600 (OH). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 1.93 s (3H, COCH<sub>3</sub>), 2.8 (2H, CH<sub>2</sub>Cl, *AB* system, <sup>2</sup>J = 21, <sup>3</sup>J = 5.7 Hz), 3.43 (2H, SCH<sub>2</sub>, *AB* system, <sup>2</sup>J = 21, <sup>3</sup>J = 5.7 Hz), 3.67 s (3H, CH<sub>3</sub>O), 4.4–4.6 br.s (1H, OH), 4.7 quint (1H, HOCH, <sup>3</sup>J = 5.7 Hz), 7.9 d (1H, 5-H<sub>arom</sub>, <sup>3</sup>J = 9.7 Hz), 8.24 d (1H, 6-H<sub>arom</sub>, <sup>3</sup>J = 9.7 Hz), 8.9 s (1H, 2-H<sub>arom</sub>), 10.4 s (1H, NH). Found, %: Cl 9.99; N 3.51; S 16.92. C<sub>12</sub>H<sub>17</sub>ClNO<sub>5</sub>S<sub>2</sub>. Calculated, %: Cl 10.07; N 3.96; S 18.12.

S-(3-Chloro-2-hydroxypropyl) 1,1-dioxotetrahydrothiophene-3-thiosulfonate (IIb). Yield 56%. Oily substance. IR spectrum, v, cm<sup>-1</sup>: 1156, 1344 (SO<sub>2</sub>, ring); 1136, 1308 (SO<sub>2</sub>); 3300–3600 (OH). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 2.3 (2H, CH<sub>2</sub>Cl, *AB* system, <sup>2</sup>J = 23.2, <sup>3</sup>J = 5.15 Hz), 3.4–3.8 m (8H, CH<sub>2</sub>, ring), 4.4–4.6 br.s (1H, OH), 4.7 q (1H, CHOH, <sup>3</sup>J = 5.15 Hz), 5.2 m (8H, CH<sub>2</sub>, ring). Found, %: Cl 11.02; S 29.66. C<sub>7</sub>H<sub>13</sub>ClNO<sub>5</sub>S<sub>3</sub>. Calculated, %: Cl 11.48; S 31.15.

*S*-(3-Chloro-2-hydroxypropyl) 4-acetylaminobenzenethiosulfonate (IIc). Yield 84%, mp 210°C. IR spectrum, v, cm<sup>-1</sup>: 1112, 1306 (SO<sub>2</sub>); 1562, 1584, 1598 (Ar); 1628 (NH); 1678 (C=O); 3300–3600 (OH). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 2.0 s (3H, COCH<sub>3</sub>), 2.8 (2H, CH<sub>2</sub>Cl, *AB* system, <sup>2</sup>*J* = 21.3, <sup>3</sup>*J* = 5.5 Hz), 3.6 (2H, SCH<sub>2</sub>, *AB* system, <sup>2</sup>*J* = 21, <sup>3</sup>*J* = 5.5 Hz), 4.4 br.s (1H, OH), 4.7 q (1H, CH, <sup>3</sup>*J* = 5.5 Hz), 7.4 d (2H, H<sub>arom</sub>, <sup>3</sup>*J* = 9.3 Hz), 8.1 d (2H, H<sub>arom</sub>, <sup>3</sup>*J* = 9.3 Hz), 10.1 s (1H, NH). Found, %: Cl 10.52; N 4.28; S 20.04. C<sub>11</sub>H<sub>14</sub>ClNO<sub>4</sub>S<sub>2</sub>. Calculated, %: Cl 10.95; N 4.32; S 19.80.

*S*-(3-Chloro-2-hydroxypropyl) 4-toluenethiosulfonate (IId). Yield 72%, mp 49–50°C. IR spectrum, ν, cm<sup>-1</sup>: 1142, 1324 (SO<sub>2</sub>); 1580, 1590, 1594 (Ar); 3200–3600 (OH). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 1.7 s

(3H, CH<sub>3</sub>), 2.8 (2H, CH<sub>2</sub>Cl, *AB* system,  ${}^{2}J = 23.2$ ,  ${}^{3}J = 5.3$  Hz), 3.6 (2H, CH<sub>2</sub>S, *AB* system,  ${}^{2}J = 23$ ,  ${}^{3}J = 5.3$  Hz), 4.1–4.3 br.s (1H, OH), 4.5 q (1H, CHOH,  ${}^{3}J = 5.3$  Hz), 7.3 d (2H, H<sub>arom</sub>,  ${}^{3}J = 8.3$  Hz), 8.0 d (2H, H<sub>arom</sub>,  ${}^{3}J = 8.3$  Hz). Found, %: Cl 12.18; S 22.58. C<sub>10</sub>H<sub>13</sub>ClO<sub>3</sub>S<sub>2</sub>. Calculated, %: Cl 12.58; S 22.84.

*S*-(3-Chloro-2-hydroxypropyl) benzenethiosulfonate (IIe). Yield 75%, oily substance. IR spectrum, v, cm<sup>-1</sup>: 1146, 1306 (SO<sub>2</sub>); 1586, 1594, 1606 (Ar); 3200–3600 (OH). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 2.7 (2H, CH<sub>2</sub>Cl, *AB* system, <sup>2</sup>*J* = 25, <sup>3</sup>*J* = 5.5 Hz), 3.6 (2H, SCH<sub>2</sub>, *AB* system, <sup>2</sup>*J* = 25, <sup>3</sup>*J* = 5.5 Hz), 4.1–4.3 br.s (1H, OH), 4.7 q (1H, CH, <sup>3</sup>*J* = 5.5 Hz), 7.4–7.8 m (5H, H<sub>arom</sub>). Found, %: Cl 13.18; S 23.86. C<sub>9</sub>H<sub>11</sub>ClO<sub>3</sub>S<sub>2</sub>. Calculated, %: Cl 13.29; S 24.04.

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