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Synthesis of Isomeric Hydroxysulphides (Sulphones) Based on 3,5,8-Trioxaspiro[bicyclo[5.1.0]octane-4,1′-cyclohexane]

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Abstract

Five- and seven-membered cyclic ketals of 3-phenylsulphanylbutane-1,2,4-triol were obtained *via* thiolysis of 3,5,8-trioxaspiro[bicyclo[5.1.0]octane-4,1′-cyclohexane] thiophenol, followed by isomerisation. The syntheses were carried out using the methods of green chemistry (reactions in water without the use of organic solvents). The thiolysis in basic medium proceeds in a selective manner resulting in the formation of ketal from 1,3-dioxepane series only. In hot water, by the contrast, a mixture of isomeric spiroacetals is formed. The obtained β-hydroxysulphides and their acetates were oxidized to yield corresponding sulphones. The structure of the isomeric products was confirmed by the method of 1D and 2D NMR spectroscopy and X-ray diffraction analysis.

Key words: thiolysis, acylation, oxidation, isomerisation, epoxy acetals, green chemistry

INTRODUCTION

It is known that the condensation of butane-1,2,4-triol with acetone [1, 2], cyclohexanone [2], dimethyl benzophenone [3, 4] under the conditions of thermodynamic control of the reaction results in forming a mixture of isomeric ketals such as dioxolane and dioxane, with a significant predominance of a five-membered derivative. It is important to note that the nitrogen-containing derivatives of 2,2-disubstituted 1,3-dioxolanes (dexoxadrol, etoxadrol) represent pharmaceuticals [3, 4].

Sulphur-containing alcohols serve as convenient synthones for obtaining a variety of objects [5-7]. So, β-hydroxysulphides are used in the synthesis of allyl alcohols [8], cyclic sulphides [9], thioketones [10], natural compounds [11], as well as compounds with pharmacological and (or) biological activity [12]. Dianiones of β-hydroxy sulphones [13] provide the basis for the preparation of lactones [14], as well as of 2,5-disubstituted tetrahydrofurans [15]. Anions of these species are used for obtaining vinyl sulphones [16], as well as the products of reductive elimination [17]. Finally, the phenylsulphonyl fragment is also in high demand in organic synthesis [18].

This work represents the first phase that includes thiolysis of 3,5,8-trioxaspiro[bicyclo-[5.1.0]-octane-4,1′-cyclohexane] **I** by thiophenol, resulting in the formation of a hidden sulphanyl-derivative of 3-phenylbutane-1,2.4-triol [19]. Reactions were performed those include the reduction of seven-membered acetal series (compounds **III** and **IV**) and the functionalization of hydroxyl and sulphide groups. The structure of the compounds was proved using the methods of one- and two-dimensional NMR spectroscopy (^{1}H–^{1}H COSY, ^{1}H–^{13}C HETCOR, APT, DEPT), gas chromatography/mass spectrometry, elemental analysis and XRD structural analysis.

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were registered on a Bruker Avance 400 spectrometer (the operating frequency being 400.13 MHz and 100.61 for the ^1H and ^{13}C nuclei, respectively) at 25 °C, using $CDCl_3$ as a solvent, and HMDS as internal standard.

The chromatography-mass spectrometric investigation was carried out using a DFS mass spectrometer, Thermo Electron Corp. (USA). The method of ionization was electron impact. The energy of ionizing electrons was equal to 70 eV; the ion source temperature amounted to 280 °C. We used a DB-5MS capillary column (Agilent), 30 m long, 0.254 mm in diameter. Helium was used as a carrier gas. The carrier gas flow rate through the column was equal to 1 mL/min. The processing of mass spectral data was performed using Xcalibur program. Before entering into the device injector, the sample under investigation was dissolved in chromatographically pure benzene to obtain the concentration of about 10^{-6}/μL. The sampling volume was equal to 1 μL.

The analysis of the crystals was performed at the Laboratory of Diffraction Research Methods of the Arbuzov Institute of Organic and Physical Chemistry, Kazan Scientific Centre of the RAS, by means of a Smart Apex II CCD diffractometer (λMoK_α).

The crystals of compound **IIc** are colourless, prismoid, and monoclinic. $C_{18}H_{24}O_6S$. M 368.44. a 12.378(5), b 21.210(8), c 6.987(3) Å, β 91.745(5)°, V 1833.5(13) Å^3, d_c 1.335, Z 4, space group $P2_1/c$; φ- and ω-scanning; 19 758 independent reflections were measured, for 2429 of those $I > 2\sigma(I)$.

The crystals of compound **IIIa** are colourless, prismoid, and tetragonal. $C_{16}H_{22}O_5S$. M 326.41. a 23.566(10), b 23.566(10), c 5.908(3) Å, V 3281(3) Å^3, d_c 1.322, Z 8, space group $P4_2/n$; φ- and ω-scanning; 52 602 independent reflections were measured, for 645 of those $I > 2\sigma(I)$.

For the purification of the reaction products we used the method of adsorption chromatography on silica gel L (100/160 m). As the eluent, we used a mixture of petroleum ether (40–70) – ethyl acetate with a varied ratio between the components. Monitoring the course of the reactions and the quality of the separation of reaction mixtures was performed using TLC on Silufol plates (the developer represented a mixture of ethanol, sulphuric acid and anisic aldehyde with the component ratio 90 : 5 : 5, respectively). Thiophenol and oxone (Acros Organics) were used for the syntheses. The purification and drying of the solvents was carried out according to the methods described in [20]. The calculation of the ^1H NMR spectra was carried out using SpinWorks 2.5.5 software.

3,5,8-Trioxaspiro[bicyclo[5.1.0]octane-4,1'-cyclohexane] (I). To 1.7 g (10 mmol) of 7,12-dioxaspiro[5,6]dodecyl-9-ene in 30 mL of acetone and 4 g (47.6 mmol) of $NaHCO_3$ at a room temperature was added a solution of 8 g (13 mmol) of oxone in 30 mL of water, dropwise under stirring. The reaction mixture was further stirred for 1.5 h. The reaction was monitored by means of TLC. The product obtained was extracted with methylene chloride (2 × 40 mL). The water was saturated with sodium chloride to perform re-extraction. The organic phases were joined together and dried then over magnesium sulphate. After the vacuum distillation a liquid was obtained with boiling point 147–149 °C (90 mm Hg), ref. [21] – 133 °C (15 mm Hg), the yield 83.5 %.

10-(Phenylsulphanyl)-7.12-dioxaspiro-[5.6]dodecane-9-ol (II). i) To a solution of 0.13 g (1.2 mmol) of thiophenol and 0.05 g (1.33 mmol) of sodium hydroxide in methanol (3 mL) was added 0.3 g (1.63 mmol) of epoxide **I**. The mixture was boiled with a backflow condenser during 1.5 h; the progress of the reaction was monitored by means of TLC. After removing the methanol in vacuum, a gold-coloured residue was dissolved in diethyl ether, an alkali precipitate was filtered off. The organic phase was washed with 2 M NaOH solution (3 × 2 mL) and dried over magnesium sulphate. The product was purified using a column chromatography (using a mixture of petroleum ether and ethyl acetate at a ratio of 4 : 1 as the eluent). We obtained 0.26 g of colourless crystals, m. p. 61–62 °C, the yield 74.3 %.

^1H NMR spectrum, δ, ppm: 1.34–1.64 m (10 H, C_5H_{10}); 3.04 d (1H, OH, $^3J(H^9OH) = 4.5$ Hz); 3.16 m (1H, H^{10}, $^3J(H^{10}H^9) = 7.0$ Hz, $^3J(H^{10}H^{11}{}_A) = 6.4$ Hz, $^3J(H^{10}H^{11}{}_B) = 2.5$ Hz); 3.63 м (1H, H^9, $^3J(H^9H^8{}_A) = 6.5$ Hz, $^3J(H^9H^8{}_B) = 0$ Hz); 3.65 m (1H, $H^8{}_A$, $^2J(H^8{}_AH^8{}_B) = -10.8$ Hz); 3.77 m (1H, $H^{11}{}_A$, $^2J(H^{11}{}_AH^{11}{}_B) = -12.7$ Hz); 4.01 m (1H, $H^{11}{}_B$); 4.07 m (1H, $H^8{}_B$); 7.18–7.45 m (5H, C_6H_5).

^{13}C NMR, δ, ppm: 22.95, 22.97, 25.45, 33.51 (C^2–C^6), 54.95 (C^{10}), 60.07 (C^{11}), 61.56 (C^8), 71.12 (C^9), 101.75 (C^1), 127.24, 129.10, 131.67, 133.74 (C_6H_5). Found, %: C 65.38, H 7.69. $C_{16}H_{22}O_3S$. Calculated, %: C 65.28, H 7.53.

ii) A mixture of 0.19 g (1.73 mmol) of thiophenol, 0.01 g (0.09 mmol) of K_2CO_3, and 0.3 g (1.63 mmol) of epoxide **I** was heated until the first bubbles appeared, and then the heating was stopped. There was a short-time (<1 min), boiling-up the mixture observed with an abrupt rising the temperature. The reaction mass was cooled, the product was purified by means of a column chromatography (using a mixture of petroleum ether and ethyl acetate at a ratio of 4 : 1 as the eluent). We obtained 0.43 g of colourless crystals, m. p. 61–62 °C, the yield 90 %.

iii) A mixture of 0.52 g (2.82 mmol) of epoxide **I**, 0.35 g (3.11 mmol) of thiophenol, 0.005 g of DABCO (0.03 mmol) and 6 mL of H_2O was heated during 90 min using a water bath (80–90 °C), under stirring, with a backflow condenser. The reaction was monitored by means of TLC. The product was extracted by methylene chloride (3 × 15 mL), dried over magnesium sulphate, and then it was purified by means of a column chromatography (using a mixture of petroleum ether and ethyl acetate at a ratio of 4 : 1 as the eluent). We obtained 0.79 g of colourless crystals, m. p. 61–62 °C, the yield 95.2 %.

2-(1,4-dioxaspiro[4.5]dec-2-yl)-2(phenylsulphanyl) ethanol (III). A solution of 1 g (3.4 mmol) of dioxepan **II** in chloroform was boiled with a backflow condenser during 20 min in the presence of a catalytic amount of *p*-toluenesulphonic acid. The product was purified by means of a column chromatography (using a mixture of petroleum ether and ethyl acetate at a ratio of 7 : 1 as the eluent). We obtained 0.85 g of colourless oil **III**, the yield 85 %.

^{1}H NMR spectrum, δ, ppm: 1.32–1.73 m (10H, C_5H_{10}); 2.60–2.86 s (1H, OH); 3.37 m (1H, C$\underline{H}$S, $^3J(H^2C\underline{H}S)$ = 4.57 Hz, $^3J(H^1{}_AC\underline{H}S)$ = 5.45 Hz, $^3J(H^1{}_BC\underline{H}S)$ = 6.61 Hz); 3.77 m (1H, $H^1{}_A$, $^2J(H^1{}_AH^1{}_B)$ = −11.6 Hz); 3.87 m (1H, $H^1{}_B$); 3.98 m (1H, $H^3{}_A$, $^2J(H^3{}_A\ H^3{}_B)$ = −8.4 Hz), ^3J ($H^3{}_AH^2$) = 7.0 Hz); 4.07 m (1H, $H^3{}_B$, $^3J(H^3{}_BH^2)$ = 6.45 Hz); 4.45 m (1H, H^2); 7.24–7.49 m (5H, C_6H_5). ^{13}C NMR, δ, ppm: 23.66, 23.88, 25.01, 34.49, 35.73 (C^6-C^{10}), 53.21 (C$\underline{H}$S), 62.32 ($\underline{C}H_2OH$), 66.20 (C^3), 75.40 (CHO), 110.23 (C^5), 127.29, 129.05, 131.88, 134.07 (C_6H_5). Chromatography-mass spectrum (EI): *m/z* (%) = 294 (M^+, 46), 265 (9), 251 (51), 207 (6), 179 (55), 161 (14), 151 (18), 141 (100), 123 (32), 110 (77), 98 (12), 83 (26), 81 (35), 69 (46), 55 (31).

Technique for obtaining ketals III and IV in an aqueous medium in the presence of DABCO. A mixture of 0.49 g (2.66 mmol) of epoxide **I**, 0.33 g (3.03 mmol) of thiophenol, 0.005 g of DABCO (0.03 mmol) and 6 mL of H_2O was heated during 3 h using a water bath (80–90 °C) under stirring, with a backflow condenser. The reaction was monitored by means of TLC. The product was extracted by methylene chloride (3 × 15 mL), dried over magnesium sulphate, being then isolated by means of column chromatography (using a mixture of petroleum ether and ethyl acetate at a ratio of 6 : 1 as the eluent). We obtained 0.59 g of ketal **III** (75 % yield) and 0.15 g of a pale yellow oily substance **IV** (19 % yield).

3-(Phenylsulphanyl)-1,5-dioxaspiro[5.5]undec-2-yl] methanol (IV). ^{1}H NMR spectrum, δ, ppm: 1.29–1.82 m (10H, C_5H_{10}); 3.25 m (1H, H^3, $^3J(H^3H^2)$ = 3.83 Hz, $^3J(H^3H^4{}_A)$ = 8.71 Hz, $^3J(H^3H^4{}_B)$ = 5.26 Hz); 3.95 m (1H, $H^4{}_A$, $^2J(H^4{}_AH^4{}_B)$ = −9.39 Hz); 3.99 m (1H, $H^4{}_B$); 4.03 m (1H, C$\underline{H}_A$OH, $^2J(C\underline{H}_A\underline{H}_BOH)$ = −7.86 Hz, $^3J(H^2C\underline{H}_AOH)$ = 7.05 Hz); 4.06 m (1H, C$\underline{H}_B$OH, $^3J(H^2C\underline{H}_BOH)$ = 6.42 Hz); 4.49 m (1H, H^2); 7.16–7.54 m (5H, C_6H_5). ^{13}C NMR, δ, ppm: 51.48 (C^3), 61.93 (C^4), 66.95 ($\underline{C}H_2OH$), 74.79 (C^2), 109.87 (C^6). The signals of six-membered carbocycles are omitted.

10-(Phenylsulphanyl)-7,12-dioxaspiro-[5.6]dodecane-9-ol (IIa). To a solution of 1.2 g (4.08 mmol) of dioxepan **II** in 20 mL of aqueous acetone (1 : 1) and 1.63 g (19.4 mmol) of $NaHCO_3$ at a room temperature, was added 3.26 g (5.3 mmol) of oxone, in portions. The reaction mixture was further stirred during 1 h, chloroform was added. The aqueous phase was separated, saturated with sodium chloride, and extracted then with chloroform. The organic phases were joined together and dried over magnesium sulphate. The product was purified by means of a column chromatography (using a mixture petroleum ether and ethyl acetate at a ratio of 2 : 1 as the eluent). We obtained 1.13 g of colourless crystals, m. p. 103–104 °C, the yield 85 %.

^{1}H NMR spectrum, δ, ppm: 1.3–1.6 m (10H, C_5H_{10}); 3.19 m (1H, H^{10}, $^3J(H^{10}H^9)$ = 7.63 Hz, $^3J(H^{10}H^{11}{}_A)$ = 3.15 Hz, $^3J(H^{10}H^{11}{}_B)$ = 8.7 Hz);

3.68 m (1H, $H^8{}_A$, $^2J(H^8{}_AH^8{}_B)$ = −12.25 Hz, $^3J(H^8{}_A H^9)$ = 8.35 Hz); 3.73 m (1H, $H^{11}{}_A$, $^2J(H^{11}{}_AH^{11}{}_B)$ = −12.95 Hz); 3.82 m (1H, $H^8{}_B$, $^3J(H^8{}_BH^9)$ = 3.65 Hz); 3.84 m (1H, $H^{11}{}_B$); 4.21 m (1H, H^9); 7.56−7.92 m (5H, C_6H_5). ^{13}C NMR, δ, ppm: 22.79, 22.81, 25.27, 32.89, 33.10 (C^2−C^6), 55.51 ($C^{11(8)}$), 62.56 ($C^{8(11)}$), 67.49 (C^9), 69.48 (C^{10}), 102.00 (C^1) 128.67, 129.41, 134.33, 137.61 (C_6H_5). Chromatography-mass spectrum (EI): *m/z* (%) = 326 (M^+, 6), 284 (3), 283 (18), 265 (3), 211 (5), 168 (7), 143 (9), 141 (13), 125 (91), 99 (50), 98 (33), 94 (20), 78 (25), 77 (72), 69 (34), 55 (100).

10-(Phenylsulphanyl)-7.12-dioxaspiro-[5.6]dodecane-9-yl acetate (IIb). To a solution of 0.51 g (1.73 mmol) dioxepan **II** in 20 mL of CH_2Cl_2, under stirring, was added successively 0.26 g (2.59 mmol) Ac_2O, 0.26 g (2.59 mmol) Et_3N and 0.005 g (0.017 mmol) DMAP. In 3 h, the reaction mixture was washed with the saturated aqueous solutions of $NaHCO_3$ (10 mL) and NaCl (2 × 10 mL). The organic phase was dried over magnesium sulphate. The product was purified by means of a column chromatography (using a mixture petroleum ether and ethyl acetate at a ratio of 7 : 1 as the eluent). We obtained 0.51 g of colourless oil, the yield 87.5 %.

^{1}H NMR spectrum, δ, ppm: 1.36−1.71 m (10H, C_5H_{10}); 2.08 s (3H, CH_3); 3.29 m (1H, H^{10}, $^3J(H^{10}H^9)$ = 6.5 Hz, $^3J(H^{10}H^{11}{}_A)$ = 7.1 Hz, $^3J(H^{10}H^{11}{}_B)$ = 2.65); 3.74 m (1H, $H^8{}_A$, $^2J(H^8{}_A\ H^8{}_B)$ = −12.6 Hz, $^3J(H^8{}_AH^9)$ = 6.55 Hz); 3.78 m (1H, $H^{11}{}_A$, $^2J(H^{11}{}_A\ H^{11}{}_B)$ = −12.45 Hz); 4.01 m (1H, $1H^8{}_B$, $^3J(H^8{}_B\ H^9)$ = 2.55 Hz); 4.04 m (1H, $H^{11}{}_B$); 4.87 (1H, H^9); 7.22−7.54 m (5H, C_6H_5). ^{13}C NMR, δ, ppm: 20.90 (CH_3), 22.82, 22.87, 26.37, 33.08, 33.61 (C^2−C^6), 51.88 (C^{10}), 59.77 (C^{11}), 60.44 (C^8), 73.42 (C^9), 101.01 (C^1), 127.11, 128.01, 131.01, 133.80 (C_6H_5), 169.98 (CO). Chromatography-mass spectrum (EI): *m/z* (%) = 336 (M^+, 4), 307 (6), 293 (87), 276 (52), 208 (9), 178 (97), 165 (77), 149 (27), 137 (96), 110 (100), 99 (74), 81 (16), 69 (44).

10-(phenylsulphanyl)-7,12-dioxaspiro[5.6]-dodecane-9-yl acetate (IIc). The substance was obtained using the procedure analogous to the synthesis of sulphone **IIa** from 0.14 g (0.42 mmol) dioxepan **IIb**. We obtained 0.13 g of colourless crystals, m. p. 133−134 °C, the yield 87 %.

^{1}H NMR spectrum, δ, ppm: 1.32−1.61 m (10H, C_5H_{10}); 1.86 s (3H, CH_3); 3.33 m (1H, H^{10}, $^3J(H^{10}\ H^9)$ = 5.9 Hz, $^3J(H^{10}\ H^{11}{}_A)$ = 6.55 Hz, $^3J(H^{10}\ H^{11}{}_B)$ = 3.05 Hz); 3.65 m (1H, $H^8{}_A$, $^2J(H^8{}_A\ H^8{}_B)$ = −12.75 Hz, $^3J(H^8{}_A\ H^9)$ = 6.4 Hz); 3.79 m (1H, $H^8{}_B$, $^3J(H^8{}_B\ H^9)$ = 2.9 Hz); 4.09 m (1H, $H^{11}{}_A$, $^2J(H^{11}{}_A\ H^{11}{}_B)$ = −12.9 Hz); 4.16 m (1H, $H^{11}{}_B$); 5.25 m (1H, H^9); 7.53−7.96 m (5H, C_6H_5). ^{13}C NMR spectrum, δ, ppm: 20.79 (CH_3), 22.81, 22.85, 25.33, 32.78, 32.97 (C^2−C^6), 55.58 (C^{11}), 60.33 (C^8), 67.27 (C^{10}), 68.95 (C^9), 102.36 (C^1), 128.95, 129.18, 134.02, 138.79 (C_6H_5), 169.61 (CO). Chromatography-mass spectrum (EI): *m/z* (%) = 326 (M^+, 6), 284 (3), 283 (18), 265 (3), 211 (5), 168 (7), 143 (9), 141 (13), 125 (91), 99 (50), 98 (33), 94 (20), 78 (25), 77 (72), 69 (34), 55 (100).

2-(1,4-dioxaspiro[4.5]dec-2-yl)-2-(phenylsulphanyl) ethanol (IIIa). The substance was obtained by means of a procedure analogous to the synthesis of sulphone **IIa**, from 0.62 g (2.1 mmol) of dioxolane **III**. We obtained 0.6 g of white crystals, m. p. 66−67 °C, the yield 87.2 %.

^{1}H NMR spectrum, δ, ppm: 1.13−1.54 m (10H, C_5H_{10}); 2.95 m (1H, OH, ^3J ($H^1{}_AOH$) = 7.4 Hz, ^3J ($OHH^1{}_B$) = 6.8 Hz); 3.47 m (1H, C<u>H</u>S, $^3J(H^2C\underline{H}S)$ = 6.85 Hz, $^3J(H^1{}_AC\underline{H}S)$ = 3.3 Hz, $^3J(H^1{}_BC\underline{H}S)$ = 6.45 Hz); 3.84 m (1H, $H^3{}_A$, $^2J(H^3{}_AH^3{}_B)$ = −8.9 Hz, $^3J(H^3{}_AH^2)$ = 7.05 Hz); 4.08 m (1H, $H^1{}_A$, $^2J(H^1{}_AH^1{}_B)$ = −13.00 Hz); 4.12 m (1H, $H^3{}_B$, $^3J(H^3{}_BH^2)$ = 6.3 Hz); 4.13 m (1H, $H^1{}_A$); 4.43 m (1H, H^2); 7.55−7.96 m (5H, C_6H_5). ^{13}C NMR, δ, ppm: 23.52, 24.80, 34.32, 35.68 (C^6−C^{10}), 57.75 ($\underline{C}H_2OH$), 65.94 (C^3), 68.90 (<u>C</u>HS), 71.72 (C^2), 110.21 (C^5), 128.71, 129.10, 134.01, 139.13 (C_6H_5). Chromatography-mass spectrum (EI): *m/z* (%): 326 (M^+, 5), 297 (9), 283 (38), 265 (15), 211 (7), 143 (59), 141 (22), 125 (35), 110 (14), 98 (25), 81 (14), 78 (19), 77 (58), 69 (78), 55 (100).

2-(1,4-Dioxaspiro[4.5]dec-2-yl)-2-(phenylsulphanyl) acetate (IIIb). The substance was obtained by means of a procedure analogous to the synthesis of acetate **IIb**, from 0.62 g (2.11 mmol) of dioxolane **III**. We obtained 0.64 g of colourless oil, the yield 90.7 %.

^{1}H NMR spectrum, δ, ppm: 1.34−1.75 m (10H, C_5H_{10}); 2.02 s (3H, CH_3); 3.39 m (1H, C<u>H</u>S, $^3J(H^2C\underline{H}S)$ = 4.0 Hz, $^3J(H^1{}_AC\underline{H}S)$ = 7.75 Hz, $^3J(H^1{}_BC\underline{H}S)$ = 6.0 Hz); 3.99 m (1H, $H^3{}_A$, $^2J(H^3{}_AH^3{}_B)$ = −8.25 Hz, $^3J(H^3{}_AH^2)$ = 6.85 Hz); 4.08 m (1H, $H^3{}_B$, $^3J(H^3{}_BH^2)$ = 6.47 Hz); 4.27 m (1H, $H^1{}_A$, $^2J(H^1{}_AH^1{}_B)$ = −11.45 Hz), 4.36 m (1H, $H^1{}_B$); 4.38 m (1H, H^2); 7.22−7.50 m (5H, C_6H_5). ^{13}C NMR, δ, ppm: 20.64 (CH_3), 23.64, 23.79, 25.00, 34.50, 35.58 (C^6−C^{10}), 49.82 ($\underline{C}HS$), 64.17 (C^1), 66.41 (C^3), 74.28 (C^2), 110.11 (C^5), 127.12, 128.92, 131.70, 134.22 (C_6H_5), 170.46 (CO). Chro-

matography-mass spectrum (EI): m/z (%) = 336 (M^+, 42), 307 (19), 294 (32), 293 (100), 276 (10), 233 (4), 196 (3), 179 (40), 161 (23), 141 (94), 123 (35), 110 (52), 97 (8), 83 (29), 81 (35), 69 (37), 55 (40).

2-(1,4-dioxaspiro[4.5]dec-2-yl)-2-(phenylsulphanyl) acetate (IIIc). The substance was obtained by means of a procedure analogous to the synthesis of sulphone **IIc**, from 0.5 g (1.49 mmol) of dioxolane **IIIb**. We obtained 0.41 g of colourless crystals, m. p. 68–69 °C, the yield 75.5 %.

^{1}H NMR spectrum, δ, ppm: 1.28–1.57 m (10H, C_5H_{10}); 1.85 s (3H, CH_3); 3.64 m (1H, C<u>H</u>S, $^3J(H^2C\underline{H}S)$ = 6.0 Hz, $^3J(H^1{}_AC\underline{H}S)$ = 3.5 Hz, $^3J(H^1{}_BC\underline{H}S)$ = 6.4 Hz); 3.88 m (1H, $H^3{}_A$, $^2J(H^3{}_AH^3{}_B)$ = −9.1 Hz, $^3J(H^3{}_AH^2)$ = 6.6 Hz); 4.12 m (1H, $H^3{}_B$, $^3J(H^3{}_BH^2)$ = 6.4 Hz); 4.51 m (1H, $H^1{}_A$, $^2J(H^1{}_AH^1{}_B)$ = −12.54 Hz); 4.55 m (1H, $H^1{}_B$); 4.66 m (1H, H^2); 7.38–8.12 m (5H, C_6H_5). ^{13}C NMR, δ, ppm: 20.44 (CH_3), 23.60, 23.64, 24.90, 34.20, 35.66 (C^6–C^{10}), 58.64 (C^1), 65.62 (<u>C</u>HS), 65.69 (C^3), 71.35 (C^2), 110.15 (C^5), 128.79, 129.02, 133.89, 139.62 (C_6H_5), 170.06 (CO). Mass spectrum (MALDI TOF): m/z = 391 $(M + Na)^+$, 407 $(M + K)^+$. Chromatography-mass spectrum (EI): m/z (%): 308 (8), 279 (16), 265 (83), 194 (3), 137 (6), 125 (37), 97 (7), 81 (9), 78 (14), 77 (42), 69 (17), 55 (100).

RESULTS AND DISCUSSION

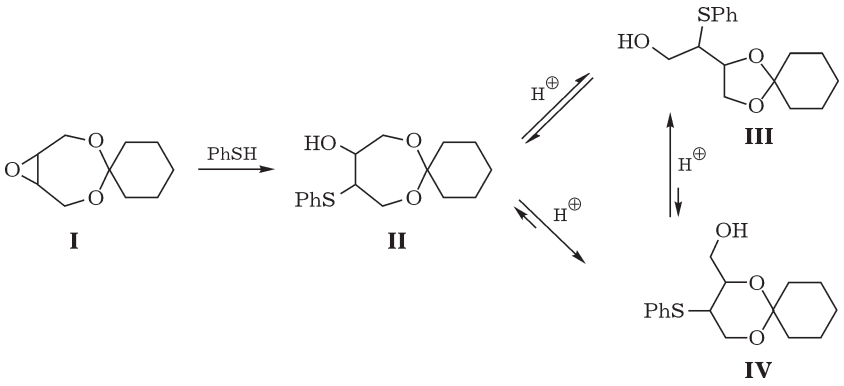
The thiolysis of epoxide **I** by thiolate anion derived from thiophenol and NaOH in methanol results in the formation of 1,3-dioxepan **II** with 74 % yield, which is in a good agreement with the data from [22].

Much higher yields (>90 %) were obtained in the course of the reaction in water and with no solvent in the presence of potash. In the latter case, in order to improve product yield and reduce the reaction time we modified the well-known technique described in [23], by means of heating the reaction mixture. The latter two methods meet the requirements of the modern strategy of so-called Green Chemistry, whose principal objective is to develop environmentally safe approaches to synthetic processes. One of these techniques consists in the replacing an organic solvent by water [23–27], liquid CO_2 or performing reactions without solvent.

It appeared that spiroketal **II** at a room temperature in the chloroform solution containing a catalytic amount of p-toluenesulphonic acid undergoes isomerisation, and after 3 h the prevailing component (~9 : 1) is presented by a five-membered ketal **III** (Fig. 1). The fact obtained is in a good agreement with the data from [28] concerning the relative thermodynamic efficiency of the five-membered ketals of polyols.

The hydroxyl and sulphide functional groups of obtained isomers **II** and **III** were transformed into acetate and sulphone ones (Figs. 2, 3). This fact allowed us to obtain crystalline samples suitable for investigation by the X-ray diffraction method. So, the structure of the seven-membered ketal was confirmed through its derivative **IIc**, whereas the structure of isomeric five-membered ketal was confirmed through hydroxy sulphone **IIIa**.

Performing the thiolysis of epoxy ketal **I** under the conditions of synthesizing ketal **II** in hot water for a much longer time (3 h) crucially alters the composition of the reaction products. Instead of the obtained earlier dioxepan **II** with an almost quantitative yield, using a



I II III IV

Fig. 1. Formation of isomeric spiroketals **II–IV**.

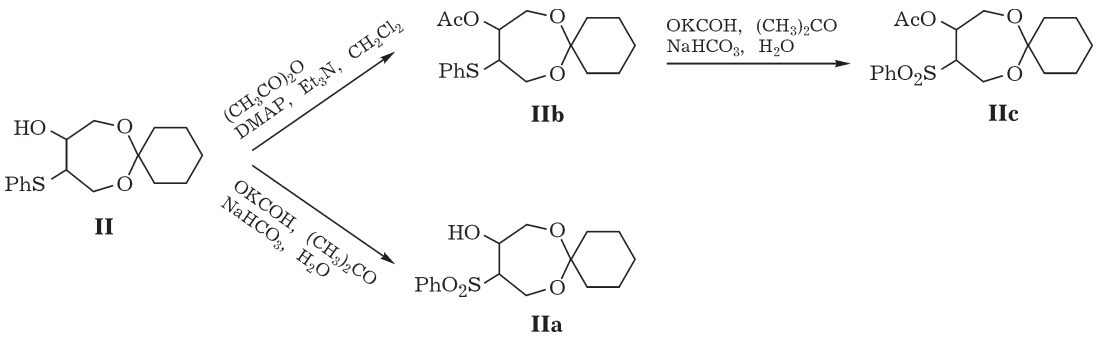


Fig. 2. Synthesis of acetoxy and sulphonyl derivatives of ketal **II**.

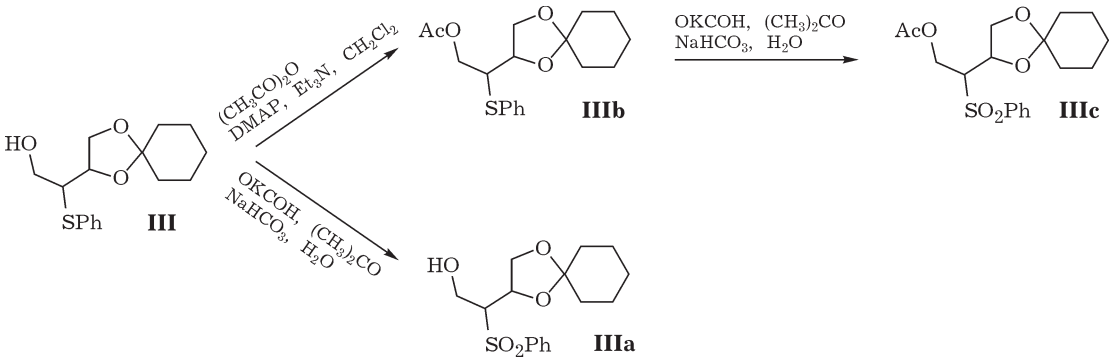


Fig. 3. Synthesis of acetoxy and sulphonyl derivatives of ketal **III**.

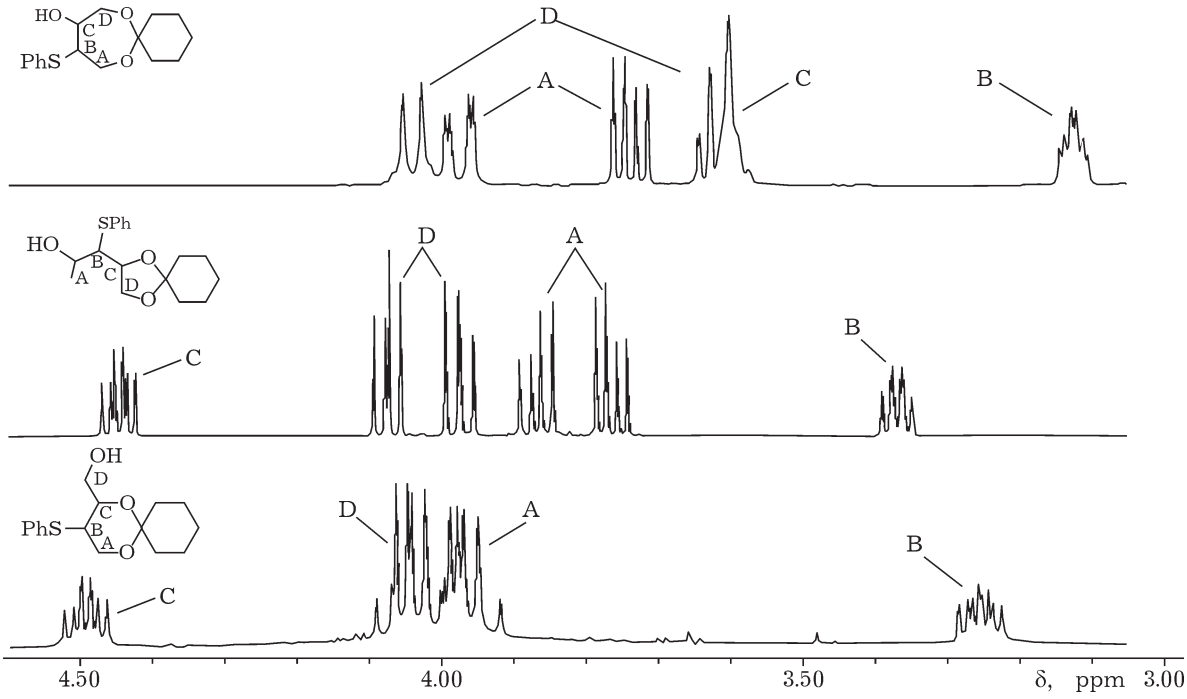


Fig. 4. ^{1}H NMR spectra of isomeric ketals **II**–**IV**.

chromatographing procedure on a column with silica gel we isolated dioxolane **III** and an oily substance **IV** (after the elution the yields were equal to 75 and 19 %, respectively).

Figure 4 demonstrates the ^{1}H NMR spectra of isomers **II–IV** (the signals of the phenyl and cyclohexane rings are not presented), whose characteristic feature consists in the multiplet signals within the range of 3–4.5 ppm, corresponding to the butane fragment of molecules. The presence of signals corresponding to acetal and butane carbon atoms at ~100 and 50–77 ppm, respectively, allows one to attribute compound **IV** to the class of cyclic acetals. In addition, at a room temperature, ketal **IV** was entirely transformed into ketal **III** within two weeks when stored in a vial with deuterochloroform.

The latter fact also serves as an evidence for the cyclic acetal-like, namely, 1,3-dioxane-like structure of compound **IV**, wherein the presence of an axial substituent at the atom results in straining the cycle to a considerable extent. For example, the value of ΔG^o for 2-methyl substituent in 1,3-dioxane amounts to 3.98 kcal/mol [29], so the chair-like 2,2-disubstituted 1,3-dioxane **IV** is transformed into 1,3-dioxolane **III**, thereby avoiding unfavourable syn-axial 1,3-$CH_2 \cdots H$ interaction.

The content of hydrogen cations H^+ in the hot water is much higher compared to that at room temperature therein [30–32], which promotes the catalytic process of disclosing the acetal cycles.

It should be noted that the preparative method we proposed in order to obtain the five-membered ketals opens up possibilities for the directed synthesis of compounds promising from the standpoint of biological activity, basing on the challenging functionalization of the hydroxyl group.

CONCLUSION

Using the methods of green chemistry, we obtained three possible cyclic spiroketals derived from 3-phenylsulphanylbutane-1,2,4-triol in the reaction between 3,5,8-trioxaspiro[bicyclo[5.1.0]-octane-4,1′-cyclohexane] with thiophenol.

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