ISSN 1070-4280, Russian Journal of Organic Chemistry, 2019, Vol. 55, No. 10, pp. 1469–1475. © Pleiades Publishing, Ltd., 2019.
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Synthesis and Oxidation of Myrtanethiol and Its Functional Derivatives with Chlorine Dioxide

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Received March 28, 2019; revised August 10, 2019; accepted August 13, 2019

Abstract—*cis*-Myrtanethiol and a mixture of diastereoisomeric myrtanethiols were synthesized starting from (–)-β-pinene. Their oxidation with chlorine dioxide afforded a number of derivatives such as disulfides, S-thiol-sulfonates, sulfonyl chlorides, and sulfonic acids. The effects of reaction conditions (solvent nature, reactant molar ratio, reaction time, catalyst) on the yield and ratio of the products were studied. The corresponding sulfonyl chloride was obtained in quantitative yield by oxidation of thiol in the presence of vanadyl acetyl-acetonate, and optimal conditions were found for quantitative formation of myrtanesulfonic acid.

Keywords: monoterpenoids, selective oxidation, chlorine dioxide, thiol, sulfonate, sulfonyl chloride, sulfonic acid, catalysis, vanadyl acetylacetonate.

DOI: 10.1134/S107042801910004X

Terpenes are natural biologically active compounds possessing bactericidal, analgesic, and mucolytic properties and are used as fungicides and antiviral agents [1]. A promising strategy in the synthesis of new biologically active compounds is based on the combination of terpene fragments and various sulfur-containing pharmacophoric groups [2]. We previously showed that pinane sulfonothioates exhibit antimicrobial activity against *Candida albicans*, *Staphylococcus aureus*, and *Cryptococcus neoformans* [3]. Organic sulfonic acids and sulfonyl chlorides are known to be widely used as intermediate products in the synthesis of medicines [4].

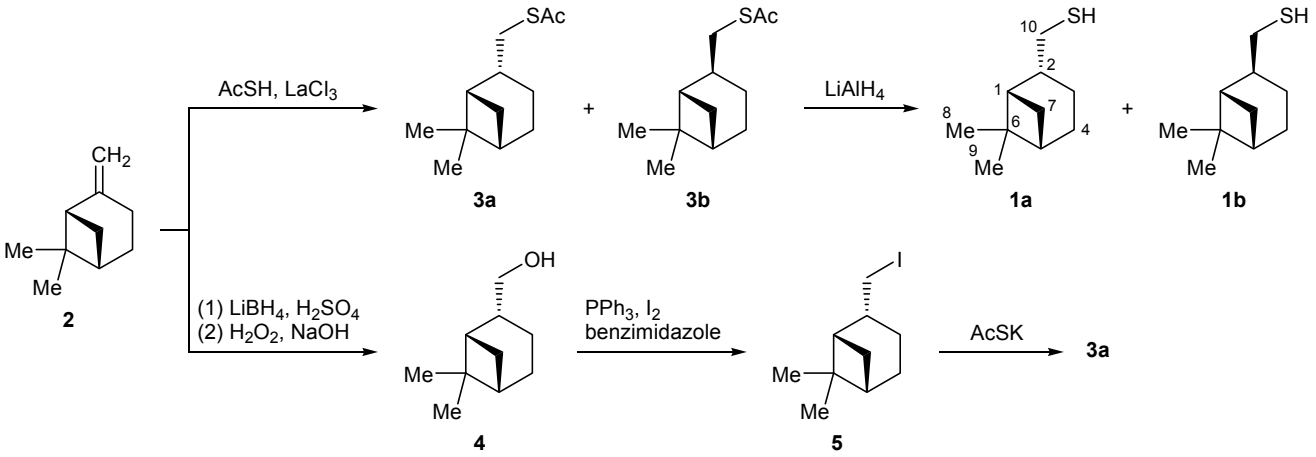
In this article we report the oxidation of myrtanethiol with chlorine dioxide, which produced chiral sulfur- and oxygen-containing terpenoids of the pinane series. The effect of the reaction conditions and substrate functionalization on the reactivity of the latter was also studied.

Initially, we tried to synthesize thiol **1a** by addition of thioacetic acid to the double bond of (–)-β-pinene (**2**) in the presence of a Lewis acid and subsequent reduction of thioacetate **3a** (Scheme 1). However, the addition products were diastereoisomeric thioacetates (*R*)-**3a** and (*S*)-**3b** which we failed to separate by column chromatography. In order to increase the stereoselectivity toward predominant formation of **3a**, such reaction conditions as temperature (–10 to 20°C), solvent (methylene chloride, pyridine), and Lewis acid ($ZnCl_2$, $AlCl_3$, $LaCl_3$) were varied. The best result (75% *de* of **3a**) was obtained by carrying out the reaction in methylene chloride at room temperature in the presence of $LaCl_3$ (Scheme 1).

According to published data [1], polarized lanthanum chloride–acid complex is oriented at the sterically more accessible side of the double bond. Due to steric hindrances created by geminal methyl groups, the approach of a bulky thioacetate anion to the C^2 carbon atom is hampered; therefore, small hydrogen atom coordinates to C^2. The addition of the complex is synchronous without formation of a carbocation, as follows from the conservation of the pinane structure; reactions involving species with a localized charge usually lead to the formation of isomerization products.

The reduction of mixture **3a**/**3b** with an equimolar amount of $LiAlH_4$ [5] also afforded a chromatographically inseparable mixture of diastereoisomeric thiols (*R*)-**1a** and (*S*)-**1b** at a ratio of 7:1 (75% *de*) which was determined from the intensity of the 10-H signals in the ^1H NMR spectrum. The configuration of **1a** and **1b** was proved by two-dimensional NOESY

Scheme 1.



data which revealed coupling between protons on C^{10} and C^{8} for **1a** and between 2-H and 8-H for **1b** (Fig. 1). Steric interaction between 2-H and 8-H in molecule **1b** induces a significant upfield shift of signals of these protons and the corresponding carbon nuclei in the NMR spectra relative to those of isomer **1a**. In the ^{13}C NMR spectrum of **1b**, the C^{2} and C^{8} nuclei resonated at δ_C 38.8 and 20.1 ppm, whereas the C^{2} and C^{8} signals of **1a** were located at δ_C 45.3 and 23.2 ppm, respectively; the differences in the chemical shifts of the other carbons did not exceed 1.0–1.5 ppm.

Since our attempts to obtain diastereomerically pure thiol **1a** according to the above described scheme were unsuccessful, the target compound was synthesized in a different way. For this purpose, (–)-β-pinene **2** was subjected to hydroboration–oxidation to *cis*-myrtanol **4** [6], which was converted to iodide **5** according to a modified procedure [7], the latter was treated with potassium thioacetate [8], and thioacetate **3a** thus formed was reduced [5] to thiol **1a** (Scheme 1).

Thiols **1** were oxidized with chlorine dioxide according to the procedures described by us previously [3, 9, 10] for functional derivatives **1c** and **1d**. Chlorine dioxide was used a commercially available aqueous solution or was transferred to organic solvents. The oxidation was carried out with both pure isomer **1a** and diastereoisomer mixture **1a**/**1b** with the goal of separating the obtained derivatives by column chromatography. Depending on the conditions, the main products in the oxidation of **1a** and **1b** were disulfides **6**, thiolsulfonates **7**, sulfonyl chlorides **8**, and sulfonic acids **9** (Scheme 2). However, the (*R*)- and (*S*)-diastereoisomers of **6**–**9** were characterized by similar chromatographic mobilities, and we failed to separate them by column chromatography. The diastereoisomer ratio of **6**–**9** was the same as that of initial thiols **1** (7:1).

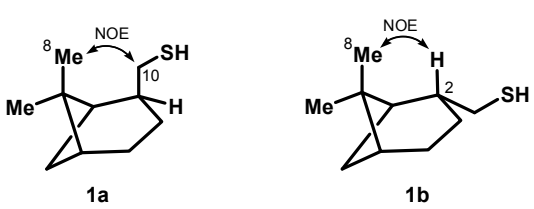
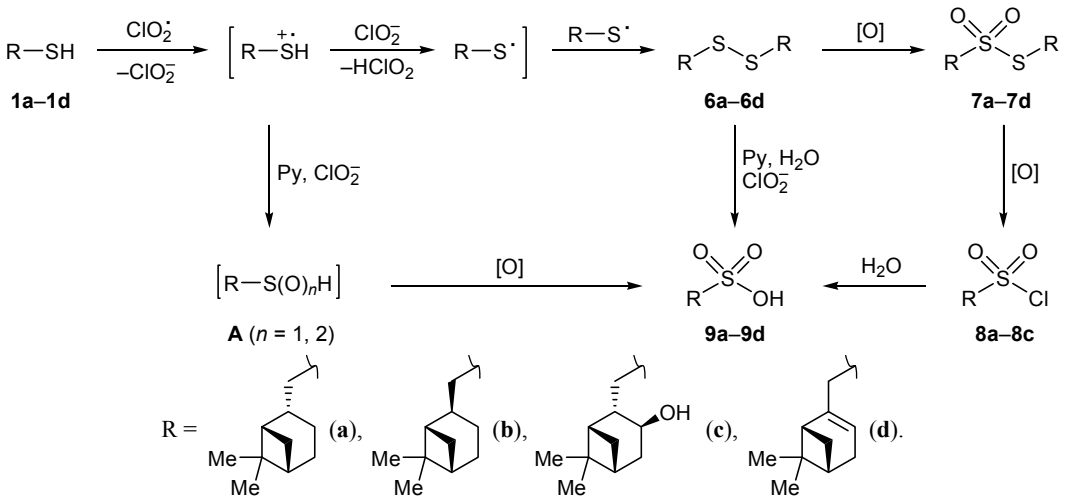


Fig. 1. Correlations in the NOESY spectra of thiols **1a** and **1b**.

The structure of the isolated compounds was confirmed by NMR, IR, and mass spectra and elemental analyses. In the ^{13}C NMR spectra of **6**–**9**, the C^{10} signal appeared downfield from the corresponding signal of **1** (δ_C 31.4, 46.2, 70.4, 73.4, and 59.1 ppm for **1a** and **4a**–**9a**, respectively). The IR spectra of **7a**–**9a** contained bands due to symmetric and antisymmetric vibrations of the sulfonyl group at 1128, 1321 (**7a**), 1168, 1377 (**8a**), 1002, 1028, 1051, 1167, 1215 cm^{-1} (**9a**).

We studied the effects of solvent nature, reactant ratio, reaction time, and catalyst on the reactivity of thiol **1a** in the oxidation with ClO_2. The presence of functional groups in the substrate molecule was also considered by comparing the results with those obtained previously for thiols **1c** and **1d** [3, 9]. The reactions were carried out in anhydrous hexane, methylene chloride, acetonitrile, and pyridine, as well as with water as co-solvent when aqueous ClO_2 was used. It was found that the solvent nature and polarity affect the reaction rate. In the oxidation of **1a** with 2 equiv of ClO_2 in hexane–water and methylene chloride–water, 6–10% of the initial thiol remained unchanged after 0.5 h (Table 1, entry nos. 3, 10), and the major product was disulfide **6a** (57–59%). The reaction of **1a** with ClO_2 in polar aqueous acetonitrile

Scheme 2.



gave deep oxidation products **8a** and **9a** in 38 and 62% yield, respectively (entry no. 6). Increase of the reaction rate with solvent polarity indicated the formation of polar intermediates.

The reaction in aqueous pyridine as solvent, other conditions being equal, gave disulfide **6a** (18%) and sulfonic acid **9a** (82%), whereas 38% of **6a** and 62% of **9a** were formed in anhydrous pyridine (entry nos. 16, 19). When the reaction time was prolonged to 2 h, sulfonic acid **9a** was obtained in quantitative yield (entry nos. 17, 20). No sulfonyl chloride **8a** was detected in pyridine, since chlorine-containing ions arising from the reduction of ClO_2 are bound by the solvent; therefore, chlorine dioxide acts only as oxidant.

Presumably, the oxidation in pyridine involves intermediate formation of sulfenic and sulfinic acids (**A**) that are stable in basic pyridine medium. In addition, nucleophilic character of the solvent hampers solvation of ClO_2^- ion formed in the first oxidation step (Scheme 2), which makes it more active and thus increases the reaction rate.

The product composition also depended on the reactant molar ratio and reaction time. Increase in the **1a**–ClO_2 ratio from 1:1 to 1:2 and of the reaction time from 0.5 to 1 h in aqueous acetonitrile favored hydrolysis of sulfonyl chloride **8a** to sulfonic acid **9a**, so that the fraction of the latter increased from 25 to 67%, while the fraction of **8a** decreased from 54 to 33% (entry nos. 5–8).

Comparison of the results of oxidation of thiol **1a** and its functional derivatives **1c** [3] and **1d** [9] with ClO_2 showed that the substrate reactivity decreases in the series **1c** > **1a** > **1d**. In the oxidation of these thiols in hexane–water (**1**/ClO_2 ratio 1:0.5, reaction time 0.5 h), the conversion of hydroxy thiol **1c** was complete, and the conversions of **1a** and **1d** were 71 and 39%, respectively (entry no. 2). The presence of a C=C double bond in molecule **1d** reduces the rate of oxidation of intermediate compounds **6d** and **7d** and hence increases the selectivity for their formation. In the oxidation of **1d** with 2 equiv of ClO_2 in aqueous acetonitrile, the yield of thiolsulfonate **7d** was 85% after 1 h [9], whereas thiol **1a** was oxidized mainly to compounds **8a** and **9a**, and no **7a** was detected (entry no. 8). The oxidation of **1d** in hexane–water quantitatively produced the corresponding disulfide **6d**, while the yields of disulfides **6a** (entry no. 4) and **6c** [3] were about 50%.

The effects of solvent nature and thiol structure on the stability of the oxidation products were revealed. When thiol **1d** was oxidized with 2 equiv of ClO_2 in methylene chloride, the reaction mixture contained unidentified desulfurization and ring-opening products, whereas the oxidation of **1a** and **1c** in methylene chloride gave compounds **7a**–**9a** and **7c**–**9c**, and no desulfurization was observed (entry no. 9).

As we showed previously, the use of $VO(acac)_2$ as catalyst in the oxidation of hydroxycaranethiols [3] and diphenyl disulfide [11] increases the selectivity with respect to sulfonyl chlorides. Therefore, thiols **1a** and **1d** were subjected to catalytic oxidation. In the reaction of **1a** with 2 equiv of ClO_2 in methylene chloride in the presence of $VO(acac)_2$, the yield of **8a** increased from 33 to 82% in 0.5 h, and it reached 98% after 2 h (Table 1; entry nos. 9, 12, 13). No catalytic effect was observed when the reaction was carried out in methylene chloride–water (yield of **8a** 45%; entry no. 14). The absence of catalytic effect in the oxidation

Table 1. Oxidation of thiol **1a** with chlorine dioxide under different conditions

No.	Solvent	Molar ratio **1a**:ClO_2	Reaction time, h	Product composition,[a] %				
				1a	**6a**	**7a**	**8a**	**9a**
1	C_6H_{14}	1:0.5	0.5	–	70	11	14	5
2	C_6H_{14}–H_2O	1:0.5	0.5	29	48	10	4	9
3	C_6H_{14}–H_2O	1:2	0.5	10	57	15	8	10
4	C_6H_{14}–H_2O	1:2	1	–	53	21	4	22
5	CH_3CN–H_2O	1:1	0.5	–	–	21	54	25
6	CH_3CN–H_2O	1:2	0.5	–	–	–	38	62
7	CH_3CN–H_2O	1:1	1	–	–	14	48	38
8	CH_3CN–H_2O	1:2	1	–	–	–	33	67
9	CH_2Cl_2	1:2	0.5	–	–	26	33	41
10	CH_2Cl_2–H_2O	1:2	0.5	6	59	16	10	9
11	CH_2Cl_2–H_2O	1:2	2	–	–	49	29	22
12	CH_2Cl_2[b]	1:2	0.5	–	–	18	82	–
13	CH_2Cl_2[b]	1:2	2	–	–	–	98	2
14	CH_2Cl_2–H_2O[b]	1:2	2	–	–	41	45	14
15	C_5H_5N	1:0.5	0.5	–	47	6	–	47
16	C_5H_5N	1:2	0.5	–	38	–	–	62
17	C_5H_5N	1:2	2	–	–	–	–	98
18	C_5H_5N–H_2O	1:0.5	0.5	–	33	–	–	67
19	C_5H_5N–H_2O	1:2	0.5	–	18	–	–	82
20	C_5H_5N–H_2O	1:2	2	–	–	–	–	98

[a] According to the ^1H NMR data.
[b] In the presence of $VO(acac)_2$.

of thiol **1d** in methylene chloride is likely to be related to the instability of intermediates in that solvent.

The reactions of thiols **1a**–**1c** with chlorine dioxide in pyridine quantitatively afforded sulfonic acids **9a**–**9c**. The yield of **9d** was lower (74%) [9] due to formation of the corresponding pyridinium salt.

In summary, we have synthesized pure *cis*-myrtanethiol and a mixture of diastereoisomeric myrtanethiols, and their oxidation with chlorine dioxide afforded the corresponding disulfides, thiolsulfonates, sulfonyl chlorides, and sulfonic acids. The effect of the reaction medium on the product composition has been revealed, and optimal conditions for the preparation of particular products have been found. Disulfide **6a** was synthesized in 68% yield in weakly polar hexane. The maximum concentration of thiolsulfonate **7a** (49%) was observed in methylene chloride–water. The oxidation in pyridine quantitatively afforded sulfonic acid **9a**, and sulfonyl chloride **8a** was formed in almost quantitative yield in methylene chloride in the presence of $VO(acac)_2$ as a catalyst. The presence of water in methylene chloride eliminates the catalytic effect of $VO(acac)_2$. By contrast, the presence of water in pyridine accelerates the reaction and favors formation of sulfonic acid.

Functional groups in the substrate molecules influence their reactivity which decreases in the series hydroxymyrtanethiol > myrtanethiol > myrtenethiol. The reduced reactivity of the latter favors selective formation of intermediate products, disulfide (98% in hexane–water), and thiolsulfonate (85% in acetonitrile). The oxidation of myrtenethiol in methylene chloride is accompanied by desulfurization and ring opening, whereas the other thiols are readily oxidized to sulfo derivatives with retention of the pinane structure.

EXPERIMENTAL

The IR spectra were recorded on a Shimadzu IR Prestige 21 spectrometer (Japan) with Fourier transform from samples prepared as thin films. The ^1H and

^{13}C NMR spectra were recorded on a Bruker Avance-300 instrument (Germany) at 300.17 and 75.48 MHz, respectively, using $CDCl_3$ and DMSO-d_6 as solvents. Complete assignment of the ^{1}H and ^{13}C signals was made with the aid of two-dimensional homo- (^{1}H–^{1}H COSY, ^{1}H–^{1}H NOESY) and heteronuclear experiments (^{1}H–^{13}C HSQC, HMBC). The mass spectra were obtained on a high-performance liquid chromatograph coupled with a Thermo Finnigan LCQ Fleet mass-selective detector (USA) (negative ion detection; water, methanol, and acetonitrile were used as solvents). Analytical thin-layer chromatography was performed on Sorbfil plates using petroleum ether–diethyl ether (9:1) as eluent (**1a**, **1b**, **6a**, **6b**, **7a**, **7b**, **8a**, **8b**); spots were visualized by treatment with a solution of phosphomolybdic acid in ethanol, aqueous potassium permanganate, or a 0.2% solution of Bromocresol Green in ethanol (**8a**, **8b**, **9a**, **9b**). The elemental compositions were determined with an EA 1110 CHNS-O automated analyzer. All reactions were carried out in freshly distilled solvents. Silica gel (0.06–0.2 mm, Alfa Aesar) was used for column chromatography with the same solvents as in TLC; sulfonic acids **9a** and **9b** were eluted with methanol. The product ratios were determined by ^{1}H NMR from the intensity of the 10-H signals.

(–)-β-Pinene (**2**) was commercial product with a purity of 99%, $[\alpha]_D^{25} = -22°$ (from Sigma–Aldrich). Commercial aqueous solution of chlorine dioxide manufactured by *Mondi SLPK* corporation (Russia) was used. Organic solutions of chlorine dioxide were prepared by extraction from aqueous solution, followed by drying the extract over anhydrous Na_2SO_4; the concentration of ClO_2 was determined by titration according to [12].

(1*S*,2*R*,5*S*)-2-(Iodomethyl)-6,6-dimethylbicyclo-[3.1.1]heptane (5). *cis*-Myrtanol **4**, 0.154 g (1 mmol), was dissolved in 7 mL of toluene, and 0.314 g (1.2 mmol) of triphenylphosphine, 0.236 g (2 mmol) of benzimidazole, and 0.305 g (1.2 mmol) of iodine were added with stirring. The mixture was refluxed for 1 h, and a saturated aqueous solution of $Na_2S_2O_3$ was added in portions until the iodine color disappeared. The mixture was extracted with chloroform, the extract was dried over Na_2SO_4, filtered, and evaporated, and the residue was purified by silica gel chromatography using petroleum ether as eluent. Yield 90%, $[\alpha]_D^{22} = -42.8°$ (c = 0.2, $CHCl_3$). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.92 d (1H, 7α-H, J = 9.3 Hz), 1.01 s (3H, 8-H), 1.24 s (3H, 9-H), 1.43–1.60 m (1H, 3α-H), 1.85–2.00 m (3H, 4-H, 5-H), 2.01–2.17 m (2H, 1-H, 3β-H), 2.33–2.54 m (2H, 2-H, 7β-H), 2.29 d.d (2H, 10-H, J = 7.9, 4.0 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 15.33 (C^{10}), 23.09 (C^8), 23.38 (C^3), 25.87 (C^4), 27.84 (C^9), 33.17 (C^7), 38.59 (C^6), 41.20 (C^5), 44.30 (C^2), 46.81 (C^1).

Reaction of β-pinene with thioacetic acid. Thioacetic acid, 0.076 g (1 mmol), was added with stirring to a solution of 0.136 g (1 mmol) of β-pinene in 5 mL of methylene chloride, and 0.021 g (0.1 mmol) of $LaCl_3$ was then added. The mixture was stirred for 2 h, 20 mL of water was added, and the mixture was extracted with chloroform (3×15 mL). The combined extracts were dried over Na_2SO_4, the solvent was removed under reduced pressure, and the residue was subjected to chromatography on silica gel using petroleum ether as eluent. The product was a mixture of C^2-diastereoisomeric thioacetates (*R*)-**3a** and (*S*)-**3b** at a ratio of 7:1.

***S*-[(1*S*,2*R*,5*S*)-6,6-Dimethylbicyclo[3.1.1]heptan-2-yl]methyl ethanethioate (3a).** Yield 78%, $[\alpha]_D^{24} = -22.3°$ (c = 0.4, $CHCl_3$). The spectral characteristics of **3a** were identical to those reported in [5].

***S*-[(1*S*,2*S*,5*S*)-6,6-Dimethylbicyclo[3.1.1]heptan-2-yl]methyl ethanethioate (3b).** The spectral data were obtained from the spectra of mixture **3a**/**3b**. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.80 s (3H, 8-H), 0.84–0.93 m (1H, 7α-H), 1.20 s (3H, 9-H), 1.33–1.40 m (1H, 3α-H), 1.74–1.79 m (2H, 4-H), 1.78–1.85 m (1H, 1-H), 1.87–1.94 m (1H, 5-H), 2.05–2.16 m (2H, 2-H, 3β-H), 2.31–2.42 m (1H, 7β-H), 2.33 s (3H, $COCH_3$), 2.80 d.d (2H, 10-H, J = 17.6, 7.4 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 20.04 (C^8), 23.22 (C^3), 24.19 (C^4), 26.64 (C^9), 30.61 ($CO\mathbf{C}H_3$), 33.30 (C^7), 34.95 (C^{10}), 35.14 (C^2), 38.65 (C^6), 40.74 (C^5), 45.00 (C^1), 196.00 ($\mathbf{C}OCH_3$). Found, %: C 67.91; H 9.41; S 15.16. $C_{12}H_{20}OS$. Calculated, %: C 67.87; H 9.49; S 15.10.

Thiols **1a** and **1b** were synthesized according to the procedure described in [5]. Yield 72%, $[\alpha]_D^{22} = -38.5°$ (c = 0.2, $CHCl_3$). The spectral characteristics of **1a** were identical to those reported in [5].

[(1*S*,2*S*,5*S*)-6,6-Dimethylbicyclo[3.1.1]heptan-2-yl]methanethiol (1b). The spectral data were obtained from the spectra of mixture **1a**/**1b**. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.83 s (3H, 8-H), 0.87–0.95 m (1H, 7α-H), 1.22 s (3H, 9-H), 1.26–1.36 m (2H, SH, 3α-H), 1.72–1.84 m (2H, 4-H), 1.86–1.99 m (2H, 1-H, 5-H), 2.01–2.14 m (2H, 2-H, 3β-H), 2.33–2.43 m (1H, 7β-H), 2.39–2.46 m (2H, 10-H). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 20.09 (C^8), 23.27 (C^3), 24.20 (C^4),

26.65 (C^9), 30.56 (C^{10}), 33.27 (C^7), 38.63 (C^6), 38.82 (C^2), 40.89 (C^5), 44.65 (C^1).

Oxidation of thiols with chlorine dioxide (*general procedure*). The overall volume of the reaction mixture was calculated for a thiol concentration of 0.02 M. The progress of reactions was monitored by TLC.

a. A solution of 0.17 g (1 mmol) of thiol **1a** or mixture **1a**/**1b** in an organic solvent was added with stirring to an aqueous–organic solution of 0.135 g (2 mmol) of chlorine dioxide, and the mixture was kept for 0.5–2 h. The organic phase was separated, the solvent was distilled off under reduced pressure, and the residue was subjected to silica gel chromatography to isolate compounds **6**–**8**; sulfonic acids **9** were isolated by evaporation of the aqueous phase.

b. Thiol **1a** or mixture **1a**/**1b**, 0.17 g (1 mmol), was dissolved in methylene chloride, 0.027 g (0.1 mmol) of $VO(acac)_2$ was added with stirring, and a solution of 0.135 g (2 mmol) of ClO_2 in methylene chloride was then added. After 2 h, the solvent was distilled off, and the dry residue was subjected to chromatography on silica gel.

Bis[(1*S*,2*R*,5*S*)-(6,6-dimethylbicyclo[3.1.1]heptan-2-yl)methyl] disulfide (6a). *a*. Ratio **1a**:ClO_2 = 1:0.5, solvent hexane, reaction time 0.5 h. Yield 68%. The spectral characteristics of **6a** were identical to those reported in [13].

Bis[(1*S*,2*S*,5*S*)-(6,6-dimethylbicyclo[3.1.1]-heptan-2-yl)methyl] disulfide (6b). *a*. Ratio (**1a**/**1b**):ClO_2 = 1:0.5, solvent hexane, reaction time 0.5 h. Yield 68% (isomer mixture **6a**/**6b** at a ratio of 7:1). The spectral data were obtained from the spectra of mixture **6a**/**6b**. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.87 s (6H, 8-H), 1.02–1.09 m (2H, 7α-H), 1.24 s (6H, 9-H), 1.28–1.36 m (2H, 3α-H), 1.76–1.87 m (4H, 4-H), 1.87–2.06 m (6H, 1-H, 2-H, 5-H), 2.04–2.13 m (2H, 3β-H), 2.37–2.45 m (2H, 7β-H), 2.63 d.d (4H, 10-H, J = 6.9, 3.0 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 20.12 (C^8), 23.41 (C^3), 24.26 (C^4), 26.66 (C^9), 32.58 (C^7), 38.66 (C^6), 40.29 (C^2), 40.86 (C^5), 44.61 (C^1), 45.83 (C^{10}). Found, %: C 71.03; H 10.04; S 18.90. $C_{20}H_{34}S_2$. Calculated, %: C 70.94; H 10.12; S 18.94.

***S*-[(1*S*,2*R*,5*S*)-6,6-Dimethylbicyclo[3.1.1]heptan-2-yl]methyl (1*S*,2*R*,5*S*)-6,6-dimethylbicyclo[3.1.1]-heptan-2-yl)methanesulfonothioate (7a).** *a*. Ratio **1a**:ClO_2 = 1:2, solvent methylene chloride–water, reaction time 2 h. Yield 45%. IR spectrum (KBr), ν, cm^{-1}: 1321 (SO_2, asym.), 1128 (SO_2, sym.). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.87–0.96 m (1H, 7α′-H), 1.00–1.09 m (1H, 7α-H), 1.03 s (3H, 8-H), 1.06 s (3H, 8′-H), 1.23 s (3H, 9-H), 1.25 s (3H, 9′-H), 1.47–1.59 m (1H, 3α-H), 1.62–1.74 m (1H, 3α′-H), 1.81–2.14 m (9H, 1-H, 1′-H, 3β-H, 4-H, 4′-H, 5-H, 5′-H), 2.15–2.30 m (1H, 3β′-H), 2.33–2.50 m (2H, 7β-H, 7β′-H), 2.75–2.98 m (2H, 2-H, 2′-H), 3.22 d (2H, 10′-H, J = 7.9 Hz), 3.40–3.51 m (2H, 10-H). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 21.70 ($C^{3'}$), 21.87 (C^3), 23.13 (C^8, $C^{8'}$), 25.80 ($C^{4'}$), 25.89 (C^4), 27.53 ($C^{9'}$), 27.79 (C^9), 32.47 ($C^{7'}$), 33.18 (C^7), 35.29 ($C^{2'}$), 36.00 (C^2), 37.07 ($C^{6'}$), 37.36 (C^6), 40.64 ($C^{5'}$), 41.05 (C^5), 42.68 ($C^{10'}$), 45.14 ($C^{1'}$), 46.50 (C^1), 70.28 (C^{10}). Found, %: C 64.91; H 9.19; S 17.34. $C_{20}H_{34}O_2S_2$. Calculated, %: C 64.82; H 9.25; S 17.30.

[(1*S*,2*R*,5*S*)-6,6-Dimethylbicyclo[3.1.1]heptan-2-yl]methanesulfonyl chloride (8a). *b*. Ratio **1a**:ClO_2 = 1:2. solvent methylene chloride, reaction time 2 h. Yield 96%, transparent viscous liquid, $[\alpha]_D^{23}$ = –28.3° (c = 0.5, $CHCl_3$). IR spectrum (KBr), ν, cm^{-1}: 1377 (SO_2, asym.), 1168 (SO_2, sym.). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.01–1.12 m (1H, 7α-H), 1.05 s (3H, 8-H), 1.26 s (3H, 9-H), 1.64–1.81 m (1H, 3α-H), 1.90–2.08 m (3H, 4-H, 5-H), 2.06–2.17 m (1H, 1-H), 2.18–2.35 m (1H, 3β-H), 2.39–2.51 m (1H, 7β-H), 2.89–3.03 m (1H, 2-H), 3.85 d (2H, 10-H, J = 6.5 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 21.37 (C^3), 23.09 (C^8), 25.61 (C^4), 27.42 (C^9), 32.31 (C^7), 36.60 (C^2), 38.36 (C^6), 40.52 (C^5), 46.09 (C^1), 73.38 (C^{10}). Found, %: C 50.79; H 7.19; S 13.61. $C_{10}H_{17}ClO_2S$. Calculated, %: C 50.73; H 7.24; S 13.54.

[(1*S*,2*S*,5*S*)-6,6-Dimethylbicyclo[3.1.1]heptan-2-yl]methanesulfonyl chloride (8b). *b*. Ratio (**1a**/**1b**):ClO_2 = 1:2, solvent methylene chloride, reaction time 2 h. Yield of **8a**/**8b** 95% (7:1). IR spectrum (KBr), ν, cm^{-1}: 1377 (SO_2, asym.), 1168 (SO_2, sym.). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.92 s (3H, 8-H), 0.98–1.10 m (1H, 7α-H), 1.11 s (3H, 9-H), 1.60–1.78 m (1H, 3α-H), 1.80–1.91 m (2H, 4-H), 1.94–2.03 m (3H, 1-H, 3β-H, 5-H), 2.36–2.48 m (1H, 7β-H), 2.83–2.91 m (1H, 2-H), 3.70 d (2H, 10-H, J = 6.6 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 20.01 (C^8), 23.20 (C^3), 25.61 (C^4), 26.50 (C^9), 32.30 (C^7), 32.62 (C^2), 39.74 (C^6), 40.20 (C^5), 45.08 (C^1), 72.53 (C^{10}). Found, %: C 50.79; H 7.19; S 13.61. $C_{10}H_{17}ClO_2S$. Calculated, %: C 50.73; H 7.24; S 13.54.

[(1*S*,2*R*,5*S*)-6,6-Dimethylbicyclo[3.1.1]heptan-2-yl]methanesulfonic acid (9a). *a*. Ratio **1a**:ClO_2 = 1:2, solvent pyridine–water, reaction time 2 h. Yield 98%, transparent viscous liquid, $[\alpha]_D^{23}$ = –9.6° (c = 0.3, $CHCl_3$). IR spectrum (KBr), ν, cm^{-1}: 1215, 1167 (SO_2,

asym.), 1051, 1028, 1002 (SO_2, sym.). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 0.85–0.94 m (1H, 7α-H), 0.94 s (3H, 8-H), 1.14 s (3H, 9-H), 1.48–1.67 m (1H, 3α-H), 1.75–1.95 m (3H, 4-H, 5-H), 1.91–2.01 m (2H, 3β-H, 1-H), 2.20–2.38 m (1H, 7β-H), 2.41–2.53 m (1H, 2-H), 2.75 d (2H, 10-H, J = 6.6 Hz), 7.18 br.s (1H, OH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 22.12 (C^3), 23.34 (C^8), 26.22 (C^4), 28.13 (C^9), 32.66 (C^7), 36.83 (C^2), 38.46 (C^6), 40.88 (C^5), 46.27 (C^1), 59.51 (C^{10}). Mass spectrum (ESI, 5 kV), m/z (I_{rel}, %): 217.29 (100) $[M - H]^-$, 97.00 (48) $[C_7H_{13}]$. Found, %: C 55.47; H 8.36; S 14.55. $C_{10}H_{18}O_3S$. Calculated, %: C 55.05; H 8.26; S 14.68.

[(1*S*,2*S*,5*S*)-6,6-Dimethylbicyclo[3.1.1]heptan-2-yl]methanesulfonic acid (9b). *a*. Ratio (**1a**/**1b**):ClO_2 = 1:2, solvent pyridine–water. Yield of **9a**/**9b** 98% (7:1). IR spectrum (KBr), ν, cm^{-1}: 1215, 1167 (SO_2, asym.), 1051, 1028, 1002 (SO_2, sym.). ^{1}H NMR spectrum (DMSO-d_6,), δ, ppm: 0.81 s (3H, 8-H), 0.93–1.02 m (1H, 7α-H), 1.16 s (3H, 9-H), 1.55–1.65 m (1H, 3α-H), 1.65–1.73 m (2H, 4-H), 1.76–1.85 m (1H, 3β-H), 1.92–1.99 m (1H, 1-H), 2.20–2.38 m (2H, 5-H, 7β-H), 2.35–2.41 m (1H, 2-H), 2.59 d (2H, 10-H, J = 6.6 Hz), 7.18 br.s (1H, OH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 20.45 (C^8), 23.30 (C^3), 24.49 (C^4), 27.03 (C^9), 31.94 (C^2), 32.66 (C^7), 38.69 (C^6), 40.66 (C^5), 45.15 (C^1), 58.00 (C^{10}). Mass spectrum (ESI, 5 kV), m/z (I_{rel}, %): 217.29 (100) $[M - H]^-$, 97.00 (48) $[C_7H_{13}]$. Found, %: C 55.55; H 8.41; S 14.61. $C_{10}H_{18}O_3S$. Calculated, %: C 55.05; H 8.26; S 14.68.

FUNDING

This study was financially supported by the Ural Branch of the Russian Academy of Sciences (project no. 18-3-3-17).

ACKNOWLEDGMENTS

The spectral and analytical data were obtained using the facilities of the “Chemistry” joint center at the Institute of Chemistry, Komi Scientific Center (Ural Branch, Russian Academy of Sciences).

CONFLICT OF INTERESTS

The authors declare the absence of conflict of interests.

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