Oxidative transformations of diisobornyl disulfide*

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Oxidation of diisobornyl disulfide with *m*-chloroperoxybenzoic acid, lead tetracetate, and chlorine dioxide was studied. Depending on the reaction conditions, the following products with the increasing oxidation number of the sulfur atom were obtained: diisobornyl trisulfide, isobornyl isobornanethiosulfinate, isobornanesulfinyl chloride, isobornanesulfinic, isobornanesulfonic acid and their esters.

Key words: diisobornyl disulfide, oxidation, chlorine dioxide, sulfinic esters, sulfonic esters, sulfinyl chlorides, disulfides, trisulfides, tetrasulfides, terpenoids.

Studies on oxidation of terpene thiols and terpene disulfides are of great interest since they provide an open access to the oxygen-containing terpene derivatives widely used for asymmetric synthesis of novel compounds.[1] Among thiol derivatives applied for asymmetric synthesis, sulfinyl chlorides are most known;[2—4] however, terpene sulfinyl chlorides have not been synthesized to date due to high lability of the terpene moiety and instability of these compounds. Sulfonic acids and their esters are other important class of compounds having numerous applications in organic synthesis and pharmaceutical industry, *e.g.*, for the synthesis of sulfocamphocaine, semi-synthetic penicillins, and cephalosporins.[5] Up to the present time, synthesis of oxygen-containing derivatives of terpene thiols are scarcely studied despite very promising synthetic potential of these compounds.

In the present work, we first performed comparative studies of the oxidation of diisobornyl disulfide **1** with *m*-chloroperoxybenzoic acid (MCPBA), lead tetraacetate ($Pb(OAc)_4$), and chlorine dioxide (ClO_2) with the aim to find a new synthetic potential of these oxidants, establish the features of the reactions and the possibility of the selective oxidation of terpene disulfide.

Results and Discussion

It is known that MCPBA oxidation of disulfides in low polar aprotic solvents leads to products with increasing oxidation states, namely, thiosulfinates, thiosulfonates, and sulfonic acids.[6—8] Oxidation of aromatic disulfides with $Pb(OAc)_4$ in alcohols resulting in sulfinic esters is most extensively studied.[9] Chlorine dioxide was successfully used in the synthesis of dialkyl and diaryl thiosulfonates, sulfonic acids, and sulfonyl chlorides.[10—12] In the present work, we first performed oxidation of terpene disulfide with $Pb(OAc)_4$ and ClO_2; earlier we used MCPBA for oxidation of terpene disulfides bearing menthane and neomenthane moieties.[13]

Oxidation of disulfide **1** with 1 equiv. of MCPBA in $CHCl_3$ or CH_2Cl_2 gives diastereomeric thiosulfinate **2** in quantitative yield (Scheme 1). Compound **2** is stable only in solution and readily decomposes upon solvent removal. The attempts to isolate thiosulfinate **2** by silica gel column chromatography failed owing to complete decomposition of **2**. The main decomposition products are the starting disulfide **1**, formed *via* disproportionation (see Scheme 1, route *i*) characteristic for all thiosulfinates, and thiocamphor **3**, arising from elimination (see Scheme 1, route *ii*) characteristic of cyclic thiosulfinates. Apparently, these reactions are also give rise to thiosulfonate **4** and isobornanesulfenic acid **5**.[14,15]

Thiosulfinate **2** was isolated as a diastereomeric mixture (*de* 35%) by neutral Al_2O_3 column chromatography and the structures of diastereomers were studied by NMR and IR spectroscopy. IR spectrum diastereomers **2** exhibit intensive bands of the S=O stretching vibrations at 1076 cm^{-1}. In ^1H spectrum, the protons of the isobornyl moieties bonded to the sulfanyl and sulfinyl groups resonate, respectively, at δ 3.23 and 3.48 for the major isomer and at δ 3.13 and 3.39 for the minor isomer. In ^{13}C NMR spectrum, two diastereomeric thiosulfinates **2** appear also as two sets of the signals ascribed to non-equivalent isobornyl fragments.

It is known that due to low stability, thiosufinates can react with alcohols following nucleophilic substitution mechanism to give more stable sulfinic esters.[16] Adding

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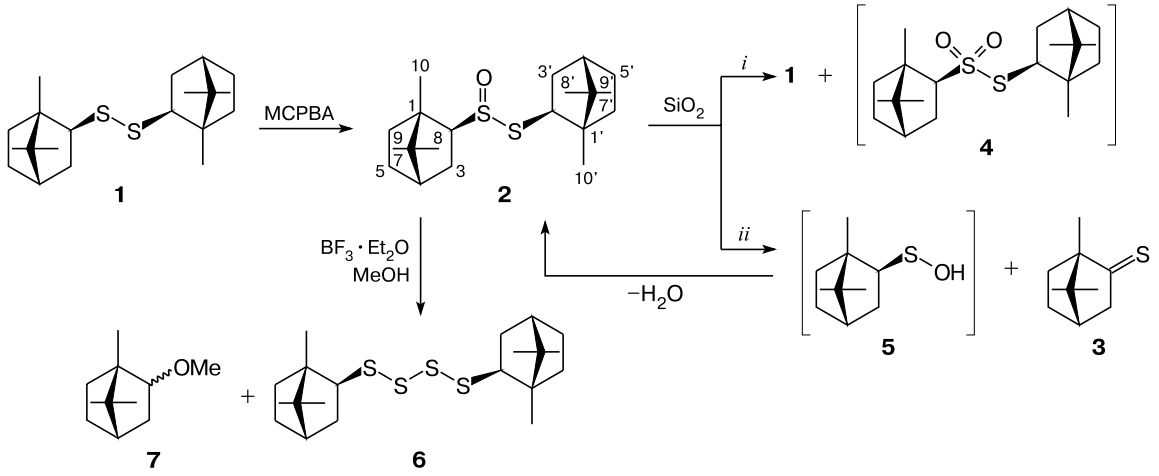
Scheme 1



i. Disproportionation, *ii.* Elimination.

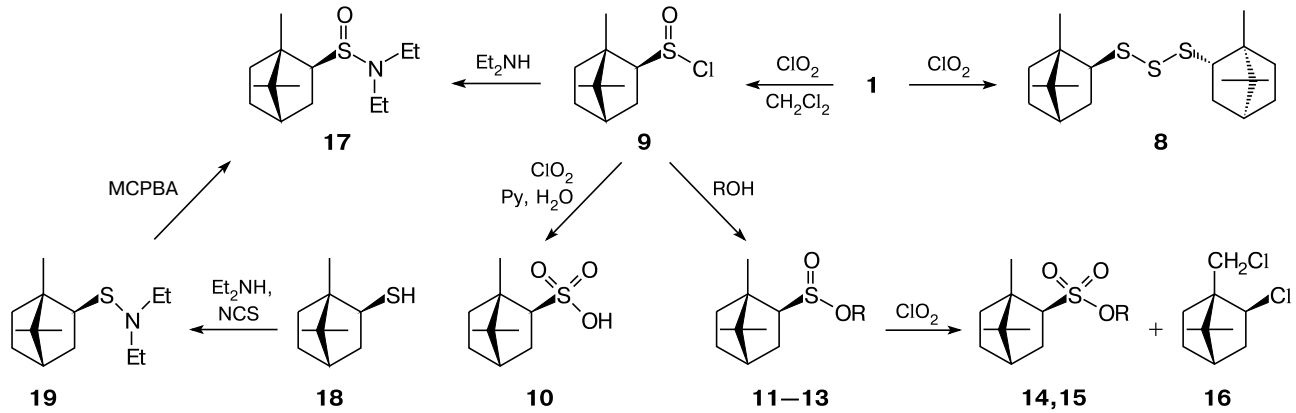
MeOH to a solution of thiosulfinate **2** does not produce the corresponding ester; however, refluxing the reaction mixture for 3—4 h in the presence of $BF_3 \cdot Et_2O$ surprisingly gives tetrasulfide **6** in 70% yield and ether **7** (see Scheme 1). Formation of tetrasulfides by thermal decomposition of thiosulfinates was previously described,[14] though up to present there are no unambiguous data on mechanism of this reaction.

Structure of tetrasulfide **6** was determined by IR and NMR spectroscopy and mass spectrometry and confirmed by elemental analysis data. IR spectra of tetrasulfide **6** and disulfide **1** are identical due to the absence of the functional groups with strong absorptions. In ^{1}H NMR spectrum, the H(2) signal of tetrasulfide **6** is shifted to the lower field as compared to disulfide **1** (from δ 2.95 to 3.35). No noticeable differences in the ^{13}C NMR spectral patterns for compounds **1** and **6** are observed; only insignificant up field shift of the C(2) signal of tetrasulfide **6** (δ 64.0) relative to the analogous signal of disulfide **1** (δ 64.8) can be mentioned.

Attempt to perform oxidation of disulfide **1** with increased amount of MCPBA (up to 4 equiv.) results in desulfurization of **1** to produce camphor.

Oxidation of disulfide **1** with ClO_2 gives the following main products: diisobornyl trisulfide (**8**), isobornanesulfinyl chloride (**9**), isobornanesulfonic acid (**10**), sulfinic and sulfonic esters **11**—**15**, and 2,10-dichloride **16** (Scheme 2). Solvent, reactant molar ratio, and the order of the reactant mixing affect the structure of the products and their yields. Heptane, CH_2Cl_2, alcohols, and pyridine (waterfree and with addition of water) were used as the solvents. Earlier,[17] we found that the order of the reactant mixing affected the structure of the products formed upon ClO_2 oxidation of 1-methyl-2-sulfanylimidazole. In the present

Scheme 2

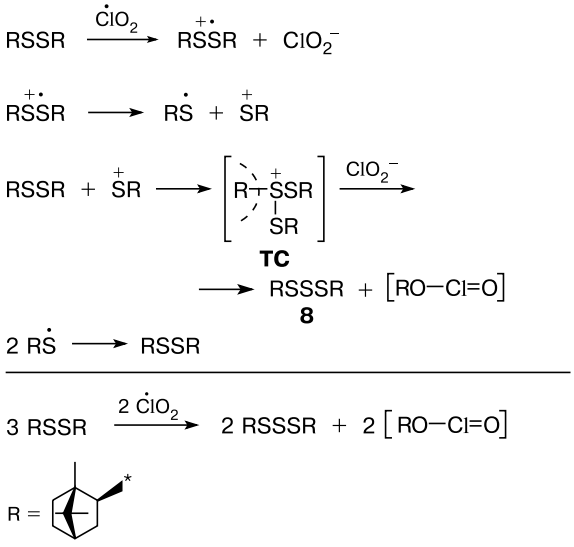


R = Me (**11**); Et (**12**, **14**); Bu^t (**13**, **15**)

work, we also used two orders of the reactant mixing. In the first case, the gaseous ClO_2 was fed by doses into a solution of disulfide **1** (oxidation with a lack of the oxidizer, method ***A***); in the second case, a solution of disulfide **1** was added by doses to a solution of ClO_2 (oxidation with an excess of oxidizer, method ***B***).

It was found that oxidation of disulfide **1** in the solvents mentioned above with 0.7 equiv. of ClO_2 following method ***A*** yields trisulfide **8** (see Scheme 2). This reaction direction is not typical for the oxidation of dialkyl and diaryl sulfides and is favored in non-polar solvent. In heptane, the yield of compound **8** is 78%. It is known[18,19] that the formation of a radical cation is the first step of ClO_2 oxidation of disulfides (Scheme 3). Further fragmentation of the radical cation gives a sulfenium cation, RS^+, and an RS· radical. The sulfenium cation reacts with another disulfide molecule to form an intermediate trisulfide cation **TC**. Through the action of nucleophile, *e.g.*, ClO_2^-, the R—S bond of intermediate **TC** breaks to provide trisulfide **8** and unstable compound of the chlorite type, ROClO. The RS· radicals dimerize to give a new disulfide molecule.

Scheme 3



Mass spectrum of trisulfide **8** reveals the molecular ion peak with *m/z* 370. IR spectra of compound **8** and disulfide **1** are similar. In ^{13}C NMR spectrum of trisulfide **8**, the C(2) signal is shifted to the higher fields (δ 63.2) as compared to the C(2) signal of disulfide **1** (δ 64.8). ^1H NMR spectrum of trisulfide **8** exhibits a low field shift of the H(1) proton (δ 3.19) in respect of the same signal of disulfide **1** (δ 2.95). Retention of the isobornyl skeleton is shown by the 2D NMR techniques (HSQC, COSY, NOESY, and HMBC). Elemental analysis data confirm the trisulfide composition.

In contrast to MCPBA-mediated oxidation, no thiosulfinates were found upon oxidation of **1** with ClO_2 in CH_2Cl_2. The main product of oxidation of disulfide **1** with 2-fold excess of aqueous ClO_2 in CH_2Cl_2 is a mixture of diastereomeric isobornanesulfinyl chlorides **9** (*de* 47%) with the content in the reaction mixture up to 75% (see Scheme 2). In ^{13}C NMR spectrum of compound **9**, the C(2) signals lie in the lower field (δ 82.7, 82.4) relative to the C(2) signal of disulfide **1** (δ 64.7). Since attempts to isolate sulfinyl chlorides **9** by SiO_2 and Al_2O_3 column chromatography lead to their decomposition, we synthesized more stable diastereomeric sulfinamides **17** in 53% total yield (*de* 10%) by the reaction of **9** with Et_2NH. The structure of sulfinamides **17** was confirmed by the counter synthesis (see Scheme 2). Isobornane thiol **18** reacts with Et_2NH in the presence of NCS to give sulfenamide **19**, which further is oxidized with MCPBA (1 mol) to yield compound **17** (*de* 26%). As compared to compound **9**, ^{13}C NMR spectrum of sulfonamide **17** exhibits a strong field shift of the C(2) signals (*cf.* δ 73.1, 68.7 for **17** and δ 82.7, 82.3 for **9**) and also signals for the ethyl groups of the diethylamine moiety at δ 14.6 (Me) and δ 41.5 (CH_2). The NOESY NMR experiments revealed the retention of the isobornyl moiety in the structure of compounds **9** and **17**.

As mentioned above, the MCPBA-mediated oxidation of disulfide **1** in MeOH does not produce isobornanesulfinic esters. In contrast to this result, oxidation of **1** with the ClO_2 excess in MeOH proceeds with full conversion of the substrate to afford a mixture of two diastereomeric methyl 2-isobornylsulfinates **11** (in equimolar amounts) and sulfonic acid **10**.

For ClO_2 oxidation of disulfide **1**, EtOH and Bu^iOH were also tested as the solvents. Depending on the molar reactant ratio, the corresponding sulfinic (**12**, **13**) or sulfonic (**14**, **15**) esters were obtained. NMR spectra of sulfinic esters **12** and **13** contain two sets of the signals for the isobornyl and alkoxy groups indicating the presence of two diastereomers. The C(2) atoms of diastereomers **12** and **13** resonate in lower field (δ 75.2, 74.2 for **12** and δ 75.5, 75.6 for **13**) as compared with the C(2) signal of the disulfide **1** (δ 64.7). Apparently, esters **11**—**13** are the products of the replacement of the Cl atom in compound **9** by the RO group (R = Me, Et, Bu^i) (see Scheme 2).

Further oxidation of sulfinates **12**, **13** with the ClO_2 excess affords sulfonates **14** and **15** in high yields (65—85%). Esters **14** and **15** are the $C_{10}H_{17}SO_2OR \cdot ROH$ solvates with the apparent strong H-bonding between the molecules. NMR spectra of these compounds exhibit the isobornyl group signals and two sets of the alkoxy group signals, which differ in the chemical shifts with the integral intensity ratio of 1 : 1 (^1H NMR data). Thus, in ^{13}C NMR spectrum of ester **14**, the carbon atom signal of the $O\underline{C}H_2CH_3$ fragment covalently bonded to the oxygen atom is shifted downfield (δ 65.8) in respect to the signal of the analogous atom of the alcohol (δ 59.0) bound to the

ester molecule by other bond type, perhaps, by the H-bond. In ^{1}H spectra, the proton of the alcohol hydroxy group resonates in the low field (δ 8.5—11.0) suggesting its strong deshielding by the electron-withdrawing SO_2O group. Adding alcohol to the solution of the adduct results in the additional signals in the NMR spectrum. Attempts to remove the alcohol traces by aqueous extraction failed due to good water solubility of the esters. Upon isolation of esters **14** and **15** by column chromatography on SiO_2 or neutral Al_2O_3 using diethylamine as an eluent, esters transform into the corresponding diethylammonium hydrosulfonates.

Dichloro-substituted derivative **16** with content up to 45% (^{1}H NMR data) is the predominant by-product of the ClO_2 oxidation of disulfide **1** in organic solvents. Chlorination can be explained by the participation in the reaction of the chloride ions and chlorine radicals, which are the forms of the exhaustive reduction of the oxidizer.[19,20] This reaction direction is favored by both the lack of ClO_2 in the reaction mixture (the mixing of the reagents by method ***A***) and the long reaction time. Adding pyridine to the reaction mixture leads to a noticeable decrease in the content of the by-product **16** in the reaction mixture and to an increase in the target product yields, since pyridine binds free H^+ and Cl^-. Thus, the yields of esters **14** and **15** in the reactions carried out in the presence of pyridine increases from 45—50 to 85% (^{1}H NMR data). Oxidation of compound **1** in aqueous pyridine or aqueous alcohols results quantitatively in sulfonic acid **10**.

The attempts to synthesize ester of isobornanesulfinic acid by oxidation of **1** with 5-fold excess of $Pb(OAc)_4$ in MeOH following the published procedure[9] failed due apparently to the steric effects of the isobornyl groups and poor coordination of the bulky oxidizing agent to sulfur atoms.

In summary, in the present work the direction of oxidation of diisobornyl disulfide with MCPBA, $Pb(OAc)_4$, and ClO_2 were studied. Oxidation of disulfide **1** with equivalent amount of MCPBA yields unstable thiosulfinates and the increase in the amount of the oxidizer leads to desulfurization. Lead tetraacetate does not react with disulfide **1** even at prolonged reflux, while ClO_2 oxidation gives wide range of the products with the selectivity depending on the solvent nature, molar reagent ratio, and the order of the reagent mixing. For instance, an important condition for obtaining the oxygen-containing derivatives (sulfinyl chloride, sulfonic acids and their esters) is the oxidant excess in the reaction mixture (method ***B***). Sequential addition of ClO_2 (oxidation with the lack of the oxidizer, method ***A***) in low polar heptane leads to diisobornyl trisulfide in high yield (78%) and, in some cases, to desulfurization and chlorination.

Experimental

IR spectra were recorded on a Shimadzu IR Prestige 21 Fourier transform spectrometer as neat samples or using KBr pellets. Melting points were determined with a Gallencamp-Sanyo apparatus. ^{1}H and ^{13}C NMR spectra were run on a Bruker Avance-300 instrument (working frequencies of 300.17 and 75.48 MHz, respectively) in $CDCl_3$, the chemical shifts are given in the δ scale relative to the residual solvent signals as internal standard. The signals in the ^{1}H and ^{13}C NMR spectra were ascribed using 2D homonuclear (^{1}H—^{1}H COSY, ^{1}H—^{1}H NOESY) and heteronuclear (^{1}H—^{13}C HSQC, HMBC) NMR experiments. Enantiomeric excesses were calculated from ^{1}H NMR data based on the integral intensity ratio of the signals of the protons at the second carbon atom of the sulfinyl group. Mass spectra were recorded using the LC/MS system comprising a high performance liquid chromatograph and a Thermo Finnigan LCQ Fleet ion trap mass spectrometer operating on the positive ion mode. Optical rotations were measured on an automatic digital polarimeter Krüss P3002RS. Thin layer chromatography was performed on a precoated Sorbfil plates using mixtures of the following solvents CH_2Cl_2, $CHCl_3$, and Et_2O, the spots were visualized using solutions of $KMnO_4$ and phosphomolybdic acid in EtOH. Elemental analyses were performed on an EA 1110 CHNS-O elemental analyzer. For column chromatography, silica gel (0.06—0.2 mm, Alfa Aesar) and neutral Al_2O_3 (0.05—0.15 mm, pH 7.0±0.5, Sigma-Aldrich) were used, the same solvent mixtures as for TLC were used as eluents.

Bis((1*S*,2*S*,4*S*)-1,7,7-trimethylbicyclo[2.2.1]hept-2-yl) disulfide (1). Synthesis of this compound and its physicochemical characteristics are described in Refs 21 and 22.

MCPBA-mediated oxidation of isobornyl disulfide (1). To a solution of disulfide **1** (0.5 g) in CH_2Cl_2 (10 mL), 70—75% MCPBA (0.370 g, 1.5 mmol, technical grade) was slowly added portionwise. The mixture was stirred for 10 min until complete consumption of disulfide (TLC monitoring). Then solvent was removed *in vacuo* until the volume of the residue was ~3 mL. The residue was chromatographed on either silica gel or neutral Al_2O_3, in both cases CH_2Cl_2 was used as an eluent. Silica gel column chromatography gave only products of thiosulfinate decomposition, *i.e.*, disulfide **1** and thiocamphor **3**. Thiosulfinates **2** were isolated by Al_2O_3 column chromatography. Thiosulfinates **2** are poorly stable compounds, therefore the spectral studies of these compounds were carried out immediately after isolation.

(1*S*,2*S*,4*S*)-1,7,7-Trimethylbicyclo[2.2.1]hept-2-yl (1*S*,2*S*,4*S*)-1,7,7-trimethylbicyclo[2.2.1]heptane-2-thiosulfinate (2). Mixture of diastereomers, *de* 35%. Yield 93%. MS (ESI, 5 kV), *m/z* (I_{rel} (%)): 355 $[M + H]^+$ (34). IR, ν/cm^{-1}: 1076 (S=O). ^{1}H NMR ($CDCl_3$), δ: 0.82—1.09 (m, 36 H, Me(8), Me(8´), Me(9), Me(9´), Me(10), Me(10´)); 1.09—2.64 (several overlapped signals, 28 H, H(3), H(3´), H(4), H(4´), H(5), H(5´), H(6), H(6´)); 3.13 (dd, 1 H, H(2´)^1, J = 9.1 Hz, J = 5.6 Hz); 3.23 (dd, 1 H, H(2´)^2, J = 9.8 Hz, J = 5.8 Hz); 3.39 (dd, 1 H, H(2)^1, J = 9.1 Hz, J = 5.7 Hz); 3.48 (dd, 1 H, H(2)^2, J = 9.3 Hz, J = 6.0 Hz).

Decomposition of thiosulfinate 2 in the presence of $BF_3 \cdot Et_2O$. Mixture of thiosulfinates were synthesized as described above, the solvents were removed, and MeOH (5 mL) $BF_3 \cdot Et_2O$ (2 drops) were added. The mixture was refluxed for 3—4 h until complete decomposition of thiosulfinates. The products were purified by column chromatography.

Bis((1*S*,2*S*,4*S*)-1,7,7-trimethylbicyclo[2.2.1]hept-2-yl) tetrasulfide (6). Colorless liquid. Yield 70%. Found (%): C, 59.58; H, 8.58; S, 31.84. $C_{20}H_{34}S_4$. Calculated (%): C, 59.65; H, 8.51; S, 31.84. MS (ESI, 5 kV), *m/z* (I_{rel} (%)): 402 $[M]^+$ (8), 233

$[C_{10}H_{17}SSS]^+$ (8), 201 $[C_{10}H_{17}SS]^+$ (13), 169 $[C_{10}H_{17}S]^+$ (9), 137 $[C_{10}H_{17}]^+$ (58). IR, ν/cm^{-1}: 578 (C—S), 617 (C—S), 797, 930, 1454, 2953. ^{1}H NMR ($CDCl_3$), δ: 0.87 (s, 3 H, Me(8)); 0.94 (s, 3 H, Me(9)); 1.09 (s, 3 H, Me(10)); 1.10—1.37 (m, 2 H, H_{endo}(5), H_{endo}(6)); 1.65—1.87 (m, 3 H, H(4), H_{exo}(5), H_{exo}(6)); 1.87—2.15 (m, 2 H, H_{endo}(3), H_{exo}(3)); 3.35 (dd, 1 H, H(2), J = 9.1 Hz, J = 6.2 Hz). ^{13}C NMR, δ: 14.2 (C(10)), 20.0 (C(8)), 20.5 (C(9)), 27.4 (C(5)), 38.4 (C(6)), 40.3 (C(3)), 46.0 (C(4)), 47.3 (C(7)), 50.1 (C(1)), 64.0 (C(2)).

2-Methoxy-1,7,7-trimethylbicyclo[2.2.1]heptane (7), a mixture of diastereomers. Yield 30%. Spectral characteristics are identical to those published earlier.[23]

Oxidation of diisobornyl disulfide 1 with ClO_2. ***A.*** A mixture of air and ClO_2 (0.40 g, 6.0 mmol) was bubbled during 2—3 h through a solution of disulfide **1** (0.2 g, 0.6 mmil) in an appropriate solvent (10 mL). Prior to use, ClO_2 was dried by passing through the tubes with concentrated H_2SO_4 and $CaCl_2$. The course of the reaction was monitored by TLC. The products were isolated by column chromatography.

B. To a solution of ClO_2 (0.12 g, 1.8 mmol) in an appropriate solvent (10 mL), disulfide **1** (0.2 g, 0.6 mmol) was added and the mixture was stirred for 0.5—3 h, then the solvent was removed *in vacuo*. The course of the reaction was monitored by TLC. The products were isolated by column chromatography.

Bis((1*S*,2*S*,4*S*)-1,7,7-trimethylbicyclo[2.2.1]hept-2-yl) trisulfide (8) was obtained by method ***A*** using heptane as a solvent. White powder. Yield 78%. MS (ESI, 5 kV), *m/z* (I_{rel} (%)): 371 $[M + H]^+$ (100), 137 $[C_{10}H_{17}]^+$ (51). Found (%): C, 64.62; H, 9.21; S, 25.90. $C_{20}H_{34}S_3$. Calculated (%): C, 64.86; H, 9.19; S, 25.95. IR, ν/cm^{-1}: 736, 781, 1375, 1454, 2922. ^{1}H NMR ($CDCl_3$), δ: 0.86 (s, 3 H, Me(8)); 0.93 (s, 3 H, Me(9)); 1.06 (s, 3 H, Me(10)); 1.19—1.29 (m, 2 H, H_{endo}(5), H_{endo}(6)); 1.65—1.79 (m, 3 H, H(4), H_{exo}(5), H_{exo}(6)); 1.78—2.04 (m, 2 H, H_{endo}(3), H_{exo}(3)); 3.35 (dd, 1 H, H(2), J = 8.83 Hz, J = 6.27 Hz). ^{13}C NMR, δ: 14.1 (C(10)), 20.0 (C(8)), 20.5 (C(9)), 27.4 (C(5)), 38.4 (C(6)), 40.3 (C(3)), 46.0 (C(4)), 47.3 (C(7)), 50.0 (C(1)), 63.2 (C(2)).

(1*S*,2*S*,4*S*)-1,7,7-Trimethylbicyclo[2.2.1]heptane-2-sulfinyl chloride (9) was obtained by method ***B***. Reaction time was 0.5 h; CH_2Cl_2 and H_2O were used as the solvents. According to NMR data, the content of **9** in the reaction mixture was 70—75%. A mixture of diastereomers in a ratio of **A** : **B** = 75 : 25. IR, ν/cm^{-1}: 1145 (S=O). ^{1}H NMR ($CDCl_3$), δ, diastereomer **A**: 0.92 (s, 3 H, Me(8)); 0.96 (s, 3 H, Me(9)); 1.11 (s, 3 H, Me(10)); 1.15—1.37 (m, 2 H, H_{endo}(5), H_{endo}(6)); 1.60—2.40 (m, 5 H, H_{endo}(3), H_{exo}(3), H(4), H_{exo}(5), H_{exo}(6)); 3.53 dd, 1 H, H(2), J = 9.10 Hz, J = 6.75 Hz). ^{13}C NMR, δ: 13.9 (C(10)), 19.8 (C(8)), 20.1 (C(9)), 27.1 (C(5)), 33.0 (C(6)), 39.4 (C(3)), 43.1 (C(1)), 44.6 (C(4)), 47.3 (C(7)), 82.8 (C(2)).

(1*S*,2*S*,4*S*)-1,7,7-Trimethylbicyclo[2.2.1]heptane-2-sulfonic acid (10) was obtained by method ***B***; EtOH, H_2O were used as the solvents. Impurities were removed from the reaction mixture by extraction with CH_2Cl_2. Colorless liquid. Yield 91%. Found (%): C, 44.22; H, 9.01; S, 11.86. $C_{10}H_{18}SO_3 \cdot 3H_2O$. Calculated (%): C, 44.12; H, 8.82; S, 11.76. MS (ESI, 5 kV), *m/z* (I_{rel} (%)): 220 $[M + 2H]^+$ (50), 202 $[M - H_2O]^+$ (33), 137 $[C_{10}H_{17}]^+$ (92). IR, ν/cm^{-1}: 883 (S—O), 1067 (SO_2), 1179 (SO_2), 3441 (OH). ^{1}H NMR ($CDCl_3$), δ: 0.92 (s, 3 H, Me(8)); 1.10 (s, 3 H, Me(9)); 1.23 (s, 3 H, Me(10)); 1.16—1.38 (m, 2 H, H_{endo}(5), H_{endo}(6)); 1.58—1.92 (m, 3 H, H(4), H_{exo}(5), H_{exo}(6)); 2.17—2.39 (m, 2 H, H_{endo}(3), H_{exo}(3)); 3.32 (t, 1 H, H(2), J = 8.82 Hz); 9.42 (s, 1 H, OH). ^{13}C NMR, δ: 12.8 (C(10)), 20.4 (C(8)), 20.6 (C(9)), 26.7 (C(5)), 33.5 (C(6)), 40.0 (C(3)), 44.7 (C(4)), 48.1 (C(7)), 50.6 (C(1)), 70.2 (C(2)).

Methyl (1*S*,2*S*,4*S*)-1,7,7-trimethylbicyclo[2.2.1]heptane-2-sulfinate (11), a mixture of diastereomers, was obtained by method ***A*** using MeOH as the solvent. Colorless liquid. Total yield 42%. A mixture of diastereomers in a ratio of **A** : **B** = 1 : 1. Found (%): C, 61.62; H, 9.21; S, 15.01. $C_{11}H_{20}SO_2$. Calculated (%): C, 61.11; H, 9.26; S, 14.81. MS (ESI, 5 kV), *m/z* (I_{rel} (%)): 217 $[M + H]^+$ (75), 201 $[M + H - OH]^+$ (15), 149 $[CH_2{=}CHCH(CH_3)CH(S(O)OH_2)CH_3]^+$ (91), 137 $[M - CH_3OSO]^+$ (100). IR, ν/cm^{-1}: 682, 711 (S—O); 970, 999 (C—O); 1122 (S=O). ^{1}H NMR ($CDCl_3$), δ, diastereomers **A**, **B**: 1.18—1.40 (m, 4 H, H_{endo}(5), H_{endo}(6)); 1.59—1.84 (m, 6 H, H(4), H_{endo}(5), H_{exo}(6)); diastereomer **A**: 0.91 (s, 3 H, Me(8)); 0.95 (s, 3 H, Me(9)); 1.13 (s, 3 H, Me(10)); 1.82—1.93 (m, 2 H, H_{endo}(3), H_{exo}(3)); 2.65 (dd, 1 H, H(2), J = 9.31 Hz, J = 5.98 Hz); 3.74 (s, 3 H, OC$\underline{H}_3$)); diastereomer **B**: 0.90 (s, 3 H, Me(8)); 0.93 (s, 3 H, Me(9)); 1.02 (s, 3 H, Me(10)); 2.08—2.20 (m, 2 H, H_{endo}(3), H_{exo}(3)); 2.79 (dd, 1 H, H(2), J = 9.86 Hz, J = 5.86 Hz); 3.82 (s, 3 H, OC$\underline{H}_3$). ^{13}C NMR, δ, diastereomers **A**, **B**: 13.7, 13.2 (C(10)); 19.6, 19.8 (C(8)); 20.0 (C(9)); 27.3, 27.4 (C(5)); 31.3, 30.7 (C(3)); 39.2, 38.6 (C(6)); 44.7, 44.9 (C(4)); 47.6, 47.7 (C(7)); 49.3, 49.0 (C(1)); 53.1, 54.7 (O$\underline{C}H_3$); 75.2, 74.3 (C(2)).

Ethyl (1*S*,2*S*,4*S*)-1,7,7-trimethylbicyclo[2.2.1]heptane-2-sulfinate (12), a mixture of diastereomers, was obtained by method ***A*** using EtOH as a solvent. Colorless liquid. According to NMR data, total content of the ester **12** in the reaction mixture was 48%. A mixture of diastereomers in a ratio of **A** : **B** = 36 : 64. Found (%): C, 62.81; H, 9.62; S, 13.81. $C_{12}H_{22}SO_2$. Calculated (%): C, 62.61; H, 9.57; S, 13.91. MS (ESI, 5 kV), *m/z* (I_{rel} (%)): 231 $[M + H]^+$ (100), 149 $[CH_2{=}CHCH(CH_3)CH(S(O)OH_2)CH_3]^+$ (10), 137 $[C_{10}H_{17}]^+$ (47). IR, ν/cm^{-1}: 921 (S—O), 1111 (S=O). ^{1}H ($CDCl_3$), δ, diastereomers **A**, **B**: 1.55—2.10 (m, 14 H, H_{endo}(3), H_{exo}(3), H(4), H_{endo}(5), H_{exo}(5), H_{endo}(6), H_{exo}(6)); 0.84—1.17 (m, 18 H, Me(8, 9, 10)); 1.16—1.54 (m, 6 H, $OCH_2C\underline{H}_3$); 4.01—4.34 (m, 4 H, $OC\underline{H}_2CH_3$); diastereomer **A**: 2.70 (dd, 1 H, H(2), J = 9.39 Hz, J = 5.87 Hz); diastereomer **B**: 2.82 (dd, 1 H, H(2), J = 9.98 Hz, J = 5.87 Hz). ^{13}C NMR, δ, diastereomers **A**, **B**: 13.7, 13.3 (C(10)); 15.8 ($CH_2\underline{C}H_3$); 19.8, 19.6 (C(8)); 20.5, 20.0 (C(9)); 27.2, 27.3 (C(5)); 31.5, 30.8 (C(3)); 39.2, 38.6 (C(6)); 44.7, 44.9 (C(4)); 47.5, 48.0 (C(7)); 50.2, 50.1 (C(1)); 64.0, 64.2 ($O\underline{C}H_2CH_3$); 75.2, 74.2 (C(2)).

Isobutyl (1*S*,2*S*,4*S*)-1,7,7-trimethylbicyclo[2.2.1]heptane-2-sulfinate (13), a mixture of diastereomers, was obtained by method ***A*** using Bu^{i}OH as a solvent. Colorless liquid. According to NMR data, total content of ester **13** in the reaction mixture is 42%. A mixture of diastereomers in a ratio of **A** : **B** = 60 : 40. Found (%): C, 65.19; H, 10.01; S, 12.69. $C_{14}H_{26}SO_2$. Calculated (%): C, 65.12; H, 10.08; S, 12.40. MS (ESI, 5 kV), *m/z* (I_{rel} (%)): 259 $[M + H]^+$ (100), 137 $[C_{10}H_{17}]^+$ (38). IR, ν/cm^{-1}: 974, 1000 (C—O); 1115 (S=O). ^{1}H NMR ($CDCl_3$), δ, diastereomers **A**, **B**: 1.54—2.34 (m, 16 H, C$\underline{H}(CH_3)_2$, H_{endo}(3), H_{exo}(3), H(4), H_{endo}(5), H_{exo}(5), H_{endo}(6), H_{exo}(6)); 3.96 (d, 4 H, $C\underline{H}_2CH(CH_3)_2$, J = 6.46 Hz); diastereomer **A**: 0.91 (s, 3 H, Me(8)); 0.96 (s, 3 H, Me(9)); 1.10 (s, 3 H, Me(10)); 2.87 (dd, 1 H, H(2), J = 9.39 Hz, J = 5.87 Hz); diastereomer **B**: 0.90 (s, 3 H, Me(8)); 0.94 (s, 3 H, Me(9)); 0.99 (s, 3 H, Me(10)); 2.95 (dd, 1 H, H(2), J = 9.98 Hz, J = 5.87 Hz). ^{13}C NMR, δ, diastereomers **A**, **B**: 13.7, 13.5 (C(10)); 18.6 ($C(CH(\underline{C}H_3)_2)$; 19.5 (C(8)); 19.7

(C(9)); 27.1, 27.2 (C(5)); 28.0, 29.0 ($\underline{C}H(CH_3)_2$)); 32.5, 31.0 (C(3)); 38.9, 38.5 (C(6)); 44.8, 44.6 (C(4)); 47.7, 47.8 (C(7)); 49.5, 49.3 (C(1)); 74.6, 74.0 (C(2)); 75.6, 76.5 ($\underline{C}H_2CH(CH_3)_2$).

Ethyl (1*S*,2*S*,4*S*)-1,7,7-trimethylbicyclo[2.2.1]heptane-2-sulfonate (14) was obtained by method ***A*** using ClO_2 (0.48 g, 7.2 mmol) as an oxidant and pyridine and EtOH as the solvents. Colorless liquid. Yield 85%. Found (%): C, 57.19; H, 9.69; S, 10.69. $C_{12}H_{22}SO_3 \cdot C_2H_5OH$. Calculated (%): C, 57.53; H, 9.59; S, 10.96. MS (ESI, 5 kV), *m/z* (I_{rel} (%)): 248 $[M + 2H]^+$ (37), 217 $[C_{10}H_{17}SO_3]^+$ (71), 149 $[CH_2{=}CHCH(CH_3)CH(S(O)OH_2)CH_3]^+$ (61), 137 $[C_{10}H_{17}]^+$ (60). IR, ν/cm^{-1}: 925 (S—O); 1010 ($\nu_{sym}(SO_2)$); 1055, 1172 ($\nu_{asym}(SO_2)$); 1228. ^{1}H NMR ($CDCl_3$), δ: 0.90 (s 3 H, Me(8)); 1.08 (s, 3 H, Me(9)); 1.20 (s, 3 H, Me(10)); 1.13—1.35 (m, 2 H, H_{endo}(5), H_{endo}(6)); 1.35 (t, 6 H, $CH_2C\underline{H}_3$, *J* = 7.04 Hz); 1.54—2.00 (m, 4 H, H_{endo}(3), H(4), H_{exo}(5), H_{exo}(6)); 2.16—2.34 (m, 1 H, H_{exo}(3)); 3.26 (t, 1 H, H(2), *J* = 8.80 Hz); 4.14—4.32 (m, 2 H, $C\underline{H}_2CH_3$). ^{13}C NMR, δ: 12.7 (C(10)), 14.7 ($CH_2\underline{C}H_3$), 20.4 (C(8)), 20.6 (C(9)), 26.7 (C(5)), 33.5 (C(6)), 40.0 (C(3)), 44.7 (C(4)), 48.0 (C(7)), 50.4 (C(1)), 67.1 ($\underline{C}H_2CH_3$), 69.9 (C(2)).

Isobutyl (1*S*,2*S*,4*S*)-1,7,7-trimethylbicyclo[2.2.1]heptane-2-sulfonate (15) was obtained by method ***A*** using ClO_2 (0.48 g, 7.2 mmol) as an oxidant and Bu^iOH as a solvent. Colorless liquid. Yield 78%. Found (%): C, 61.59; H, 10.39; S, 9.49. $C_{14}H_{26}SO_3 \cdot C_4H_9OH$. Calculated (%): C, 62.07; H, 10.34; S, 9.20. MS (ESI, 5 kV), *m/z* (I_{rel} (%)): 276 $[M + 2H]^+$ (43), 217 $[C_{10}H_{17}SO_3]^+$ (59), 149 $[CH_2{=}CHCH(CH_3)CH(S(O)OH_2)CH_3]^+$ (68), 137 $[C_{10}H_{17}]^+$ (65). IR, ν/cm^{-1}: 927 (S—O); 1013 ($\nu_{sym}(SO_2)$); 1056, 1178 ($\nu_{asym}(SO_2)$); 1225. ^{1}H NMR ($CDCl_3$), δ: 0.90 (s, 3 H, Me(8)); 0.98 (t, 6 H, $CH_2CH(C\underline{H}_3)_2$, *J* = 6.75 Hz); 1.09 (s, 3 H, Me(9)); 1.22 (s, 3 H, Me(10)); 1.16—1.32 (m, 2 H, H_{endo}(5), H_{endo}(6)); 1.59—1.87 (m, 4 H, H_{endo}(3), H(4), H_{exo}(5), H_{exo}(6)); 1.84—1.95 (m, 1 H, $C\underline{H}(CH_3)_2$); 2.27 (td, 1 H, H_{exo}(3), *J* = 8.51 Hz, *J* = 4.11 Hz); 3.28 (t, 1 H, H(2), *J* = 8.80 Hz); 3.96 (d, 2 H, $C\underline{H}_2CH(CH_3)_2$, *J* = 6.46 Hz). ^{13}C NMR, δ: 12.8 (C(10)), 18.7 ($CH(\underline{C}H_3)_2$), 20.4 (C(8)), 20.6 (C(9)), 26.7 (C(5)), 29.0 ($\underline{C}H(CH_3)_2$), 35.5 (C(3)), 40.0 (C(6)), 44.7 (C(4)), 48.0 (C(7)), 50.4 (C(1)), 69.9 (C(2)), 76.7 ($\underline{C}H_2CH(CH_3)_2$).

(1*S*,2*S*,4*S*)-2-Chloro-1-chloromethyl-7,7-dimethylbicyclo[2.2.1]heptane (16) was obtained by method ***A***. Reaction time was 2.5 h. Yield up to 45%. Spectral data of the sample are in agreement with those published earlier.[24]

(1*S*,2*S*,4*S*)-*N*,*N*-Diethyl-1,7,7-trimethylbicyclo[2.2.1]heptane-2-sulfinamide (17). The reaction mixture containing compound **9** was mixed with Et_2NH following the known procedure.[25] Colorless heavy liquid. Total yield 53%. A mixture of diastereomers in a ratio of **A** : **B** = 63 : 37. Found (%): C, 65.37; H, 10.53; S, 12.40; N, 5.48. $C_{14}H_{27}NOS$. Calculated (%): C, 65.32; H, 10.57; S, 12.45; N, 5.44. MS (ESI, 5 kV), *m/z* (I_{rel} (%)): 258 $[M + H]^+$ (100), 240 $[M + H - OH]^+$ (22), 137 $[C_{10}H_{17}]^+$ (40). IR, ν/cm^{-1}: 1061 (S=O), 893 (S–N). ^{1}H NMR ($CDCl_3$), δ, diastereomers **A**, **B**: 1.08—1.46 (m, 16 H, $CH_2C\underline{H}_3$, H_{endo}(5), H_{endo}(6)); 1.45—1.84 (m, 8 H, H_{endo}(3), H(4), H_{exo}(5), H_{exo}(6)); 2.93—3.35 (m, 8 H, $C\underline{H}_2CH_3$); diastereomer **A**: 0.86 (s, 3 H, Me(8)); 0.98 (s, 3 H, Me(9)); 1.21 (s, 3 H, Me(10)); 2.12—2.24 (m, 1 H, H_{exo}(3)); 2.82 (dd, 1 H, H(2), *J* = 9.98 Hz, *J* = 5.87 Hz); diastereomer **B**: 0.88 (s, 3 H, Me(8)); 0.94 (s, 3 H, Me(9)); 1.19 (s, 3 H, Me(10)); 1.75—1.84 (m, 1 H, H_{exo}(3)); 2.63 (dd, 1 H, H(2), *J* = 9.83 Hz, *J* = 5.72 Hz). ^{13}C NMR, δ, diastereomer **A**, **B**: 13.4, 14.1 (C(10)); 14.6 ($CH_2\underline{C}H_3$); 19.9, 20.0 (C(8)); 20.0 (C(9)); 27.5, 27.3 (C(5)); 31.7, 33.7 (C(3)); 39.2, 39.1 (C(6)); 41.5 ($\underline{C}H_2CH_3$)); 45.1, 44.9 (C(4)); 47.8, 47.6 (C(7)); 49.3, 48.7 (C(1)); 68.7, 73.1 (C(2)).

(1*S*,2*S*,4*S*)-2-Diethylaminosulfanyl-1,7,7-trimethylbicyclo[2.2.1]heptane (19). A round-bottom flask cooled to –25 °C was charged with Et_2NH (15—20 mL) followed by addition of NCS (0.133 g, 1.0 mmol). The mixture was stirred for 5 min, then isobornyl thiol **18** (0.170 g, 1 mmol) in anhydrous THF (3 mL) was added and stirring was continued for 15 min. After warming up to 20 °C, the solvent and amine excess were removed *in vacuo* and the residue was purified by column chromatography (elution with ethyl acetate). Colorless liquid. Yield 90%. $[\alpha]^{22}_D$ + 40.5 (*c* 0.31, Me_2CO). Found (%): C, 69.62; H, 11.30; N, 5.75; S, 13.24. $C_{14}H_{27}NS$. Calculated (%): C, 69.65; H, 11.27; N, 5.80; S, 13.28. IR, ν/cm^{-1}: 642 (C—S), 898 (S—N). ^{1}H NMR ($CDCl_3$), δ: 0.78 (s, 3 H, Me(8)); 0.83 (s, 3 H, Me(9)); 1.05 (s, 3 H, Me(10)); 1.10—1.18 (m, 1 H, H_{endo}(5)); 1.18 (t, 6 H, $CH_2C\underline{H}_3$, *J* = 7.0 Hz); 1.20—1.31 (m, 1 H, H_{endo}(6)); 1.61—1.79 (m, 3 H, H(4), H_{exo}(5), H_{exo}(6)); 1.86—1.99 (m, 2 H, H_{endo}(3), H_{exo}(3)); 2.69 (dd, 1 H, H(2), *J* = 8.4 Hz, *J* = 7.2 Hz); 2.95 (q, 4 H, $C\underline{H}_2CH_3$, *J* = 7.0 Hz). ^{13}C NMR, δ: 13.8 ($CH_2\underline{C}H_3$)), 14.6 (C(10)), 19.7 (C(9)), 20.6 (C(8)), 27.6 (C(5)), 38.3 (C(6)), 41.6 (C(3)), 46.0 (C(4)), 46.8 (C(7)), 49.6 (C(1)), 52.1 ($\underline{C}H_2CH_3$), 56.6 (C(2)).

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