Synthesis of terpenoid bis-α-sulfanyl oximes and macrocycles on their basis

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A reaction of simple α,ω-dithiolates with (+)-3-carene and (−)-α-pinene β-nitroso chlorides goes through the substitution for the chlorine atoms at the quaternary carbon atoms with retention of configuration leading to the corresponding bis-α-sulfanyl oximes. Their reaction with dichloromethane under conditions of phase-transfer catalysis takes place at the oxime hydroxyl and gives sulfur-containing macrocyclic compounds.

Key words: 3-carene, α-pinene, nitrosochlorination, ethanedithiol, sulfides, oximes, propane-1,3-dithiol, macrocyclic compounds.

Nitroso chlorides of natural monoterpenes are convenient starting compounds for the synthesis of various optically active intermediate products for organic synthesis. By now, reactions of nitroso chlorides with amines to form α-amino oximes have been studied in details,[1] which gave rise to a number of coordination compounds[2] and nitrogen-containing macrocycles.[3—6] At the same time, a reaction of monoterpene nitroso chlorides with α,ω-dithiols has not been studied. Macrocyclic compounds, especially optically active derivatives, are of extreme interest as chiral ligands in the reactions of asymmetric metal complex catalysis,[7] molecular sensors,[8,9] enzyme models, precursors of complexes of the "guest—host" type.[10,11] Prospective for practical purposes sulfur-containing macrocycles are of special interest among them, though methods for their preparation are developed less in details as compared to those for oxa- and aza-analogs. In the present work, we describe simple and efficient method for the synthesis of bis-α-sulfanyl oximes from unsaturated monoterpene hydrocarbons such as (+)-3-carene and (−)-α-pinene, converted to the corresponding nitroso chlorides as key intermediates.

A reaction of dimeric nitroso chlorides **1** or **2** with a solution of the corresponding dithiolate in anhydrous methanol under an inert gas leads to bis-α-sulfanyl oximes **3—6** (Schemes 1 and 2). The process was carried out with vigorous stirring for 10 h at room temperature, in the case of reaction of pinene nitroso chloride (**2**) with potassium propane-1,3-dithiolate, at 0 °C. The highest yields of ethane-1,2-dithiol derivatives **3** and **4** were achieved when Na^+ has been used as a counter ion, whereas for propane-1,3-dithiol derivatives **5** and **6**, with K^+ ion. Such a behavior can be explained by a template effect of an alkali metal cation,[12] analogous to that observed upon formation of crown ethers.

The structures of compounds obtained were established by spectroscopic methods. The high resolution mass spectra exhibit peaks corresponding to the molecular ions of the form $C_{22}H_{36}N_2O_2S_2$ for **3** and **4** and ion of the form $C_{23}H_{38}N_2O_2S_2$ for compound **5**. No peak of molecular ion was found for compound **6**, however, the elemental analysis data agree with the molecular formula of bis-α-sulfanyl oxime ($C_{23}H_{38}N_2O_2S_2$). A molecular mass of 430±22 was obtained for compound **6** by vapor-phase osmometry in chloroform, with a theoretical value being 438, that confirms the formation of bis-α-sulfanyl oxime. The IR spectra of compounds **3—6** show the absence of the absorption band of the S—H-groups and the presence of the vibration band of the O—H group. The ^{1}H NMR spectra of these compounds exhibit signals for the terpene moiety of the molecule and signals (as a rule, of complex splitting) belonging to the protons of the dimethylene or trimethylene bridge. The ^{13}C NMR spectra of compounds **3** and **4** show the presence of 11 signals for the carbon atoms, the spectra of compounds **5** and **6**, 12 signals, whereas, according to the mass spectrometric and vapor-phase osmometric data, compounds **3** and **4** contain 22 carbon atoms and compounds **5** and **6**, 23 atoms, that indicates formation of a C_2-symmetric derivative.

The in details analysis of the ^{1}H and ^{13}C NMR spectra of compounds obtained and comparison of the spectral data (chemical shifts, $^{2,3}J_{H-H}$ and $^3J_{C-H}$ spin-spin coupling constants) with the corresponding parameters of nitrogen analogs studied earlier[1,13] allows us to draw the following conclusion: the formation of products **3—6** from the corresponding nitroso chlorides is characterized, first,

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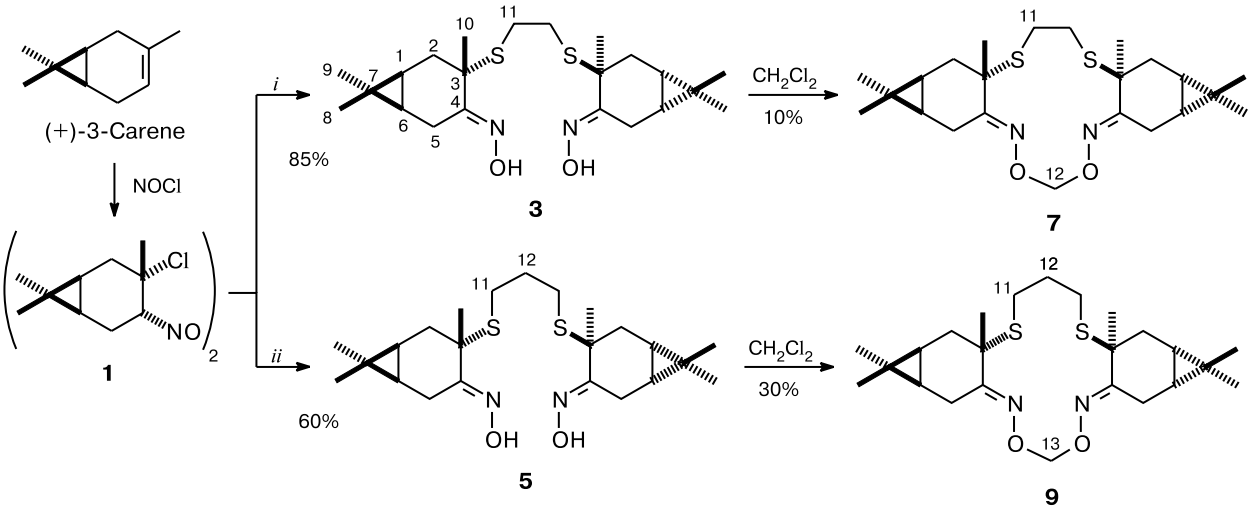
Scheme 1

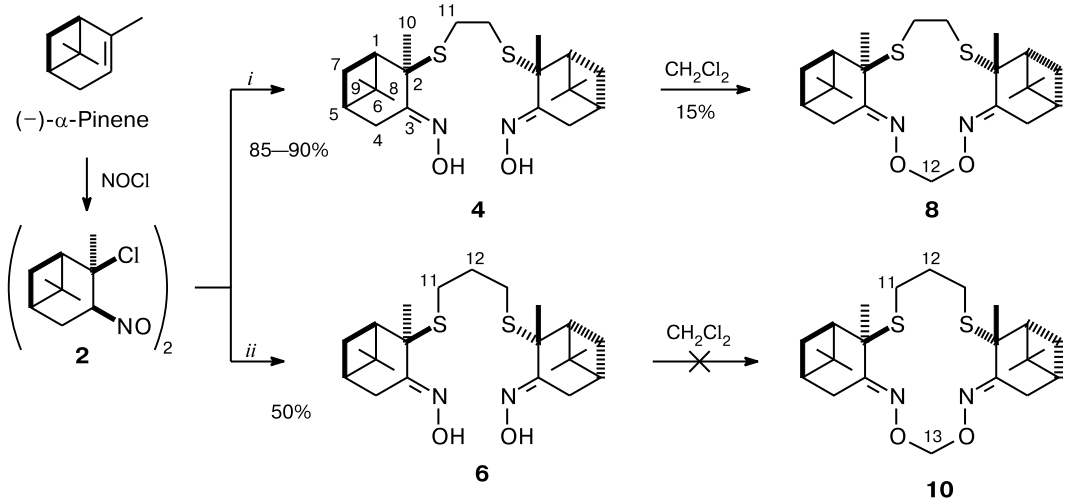


Reagents: *i*. $NaSCH_2CH_2SNa$; *ii*. $KSCH_2CH_2CH_2SK$.

by retention of configuration at the quaternary carbon atom on substitution of the chlorine atom at this carbon for the sulfur-containing group and, second, the *E*-configuration of the oxime groups formed. The retention of configuration of the reacting quaternary carbon atom can be explained by the mechanism of the chlorine atom substitution in nitroso chlorides.[13] Thus, the reaction of nitroso chlorides with a base (alkali metal thiolate) leads to dehydrochlorination and formation of nitrosoolefins. The latter react with a thiolate molecule, the attack of which occurs from the sterically less hindered side of the double bond. Earlier,[14,15] the stereochemistry of compound **3** was additionally confirmed by the X-ray diffraction data for its complexes with copper and nickel chlorides.

The cyclization of bis-α-sulfanyl oximes **3—6** was carried out by coupling the hydroxy groups with dichloromethane under conditions of phase-transfer catalysis. It turned out that in the case of bis-α-sulfanyl oximes **3** and **4**, it is reasonable to use the dicyclohexyl-18-crown-6—50% aqueous KOH system, whereas a combination of tetrabutylammonium hydroxide—50% aq. NaOH proved less efficient. In the case of bis-α-sulfanyl oxime **5**, a combination of tetrabutylammonium hydroxide as a phase-transfer catalyst and 50% aq. NaOH at 40—50 °C proved the

Scheme 2



Reagents: *i*. $NaSCH_2CH_2SNa$; *ii*. $KSCH_2CH_2CH_2SK$.

most efficient. It is likely that the macrocyclization follows the generally accepted mechanism for the formation of ethers under conditions of phase-transfer catalysis.[16] Unfortunately, in the case of compound **6** a desired macrocycle **10** was not obtained, the reaction resulted in the formation of a very complex mixture of products, apparently oligomers, due to intermolecular coupling.

All the macrocyclic compounds **7—9** synthesized are colorless crystalline substances, whose IR spectra display the absence of absorption bands of the hydroxy group of the oxime fragment. The high resolution mass spectra of these substances exhibit peaks of molecular ions corresponding to the molecular formulas $C_{23}H_{36}N_2O_2S_2$ for compounds **7** and **8** and $C_{24}H_{38}N_2O_2S_2$ for compound **9**. The ^1H and ^{13}C NMR spectra indicates the C_2-symmetry of the structure with the second order axis of rotation going through the carbon atom of the linker methylene group and the middle of the C—C bond of the ethylene bridge for compounds **7** and **8** and through the central carbon atom of the propylene bridge for compound **9**.

Experimental

The following reactants were used in the work: (−)-α-pinene (96% *ee*, Fluka), (+)-3-carene (≥99.5% *ee*) with $[\alpha]_{578}^{20}$ +16.0 (d_4^{20} 0.863) obtained by distillation of turpentine from an ordinary pine-tree, ethane-1,2-dithiol and propane-1,3-dithiol (Fluka). (+)-3-Carene and (−)-α-pinene nitroso chlorides were obtained by passing gaseous nitrosyl chloride over the solution of terpene in dichloromethane.[13] All the solvents were used freshly distilled. TLC was performed on Sorbfil plates with bound layer of silica gel on aluminum foil. Visualization of components was performed by sprinkling the plates with visualization solutions and subsequent heating to 100—150 °C. A solution of vanillin (1 g of vanillin + 5 mL of conc. H_2SO_4 + 100 mL of 95% aq. EtOH) and iron chloride (10 g of $FeCl_3 \cdot 6\ H_2O$ + 100 mL of 95% aq. EtOH) were used as reagents for the visualization. Silica gel with the particle size 0.100—0.140 mm was used for column chromatography (grinding and fractionation were made in the Experimental Chemical Production of NIOKh SB RAS). The NMR spectra were recorded on a Bruker AC-200 (200.13 MHz for ^1H, 50.32 MHz for ^{13}C), Bruker AV-300 (300 MHz for ^1H, 75.45 MHz for ^{13}C), and Bruker DRX-500 (500.13 MHz for ^1H, 125.75 MHz for ^{13}C) spectrometers for solutions with concentration 20—40 mg mL^{-1} at 25—30 °C using residual signals of the solvent ($CDCl_3$) as a reference: δ_H 7.24, δ_C 76.90. Assignment of signals was performed using the ^{13}C NMR spectra recorded in the *J*-modulation regime (noise proton coupling, the opposite phase for the signals of atoms with even number of bonded protons with tuning on the constant J = 135 Hz) and the two-dimensional spectra of $^1H—^1H$ homonuclear correlation, $^{13}C—^1H$ heteronuclear correlation on the direct spin-spin coupling constants (J = 135 Hz), and $^{13}C—^1H$ heteronuclear correlation on the remote spin-spin coupling constants (J = 10 Hz). The atom numerations for interpreting the NMR spectra are given in Schemes 1 and 2. IR spectra were recorded on a Bruker Vector-22 spectrophotometer for solutions in CCl_4 (*c* 1%) or KBr (*c* 0.25%). Optical rotation was measured on a Polamat A polarimeter. Melting points were measured on a Kofler heating stage. Mass spectra were obtained on a Finnigan MAT-8200 (EI, 70 eV) mass spectrometer. Elemental analysis was performed on a Hewlett Packard 185 and Carlo Erba 1106 microanalysers.

Synthesis of bis-α-sulfanyl oximes from ethane-1,2-dithiol (general procedure). Ethane-1,2-dithiol (0.24 g, 2.5 mmol) was added to a solution of NaOH (0.20 g, 5.0 mmol) in MeOH (30 mL) under Ar at 20 °C and the reaction mixture was stirred for 30 min. The solution obtained was added to a suspension of a dimeric terpenoid nitroso chloride (2.00 g, 2.5 mmol) in THF (10 mL) with vigorous stirring and kept stirred for 10 h. After the reaction reached completion (TLC monitoring, until spots of the starting dithiols disappeared), the solvent was evaporated *in vacuo*, the residue was stirred in a mixture of EtOAc (30 mL) and H_2O (30 mL), the organic layer was separated, the aqueous layer was extracted with EtOAc (2×30 mL), a combined organic extract was dried with anhydrous Na_2SO_4 and concentrated *in vacuo*. An oily product obtained was subjected to chromatography on SiO_2 in the hexane—EtOAc solvent system.

1,2-Bis{[(1*S*,3*S*,4*E*,6*R*)-4-hydroxyimino-3,7,7-trimethylbicyclo[4.1.0]hept-3-yl]sulfanyl}ethane (3)[17]. The yield was 85%, colorless crystals with m.p. 145—148 °C (from EtOAc); $[\alpha]_{578}^{14}$ +138 (*c* 0.61, $CHCl_3$). HRMS: found *m/z* 424.22220 [M^+]; $C_{22}H_{36}N_2O_2S_2$. Calculated M = 424.22181. MS, *m/z* (I_{rel}(%)): 424 (4), 258 (32), 166 (100), 150 (18), 107 (38), 106 (26), 105 (21), 79 (21), 69 (19), 55 (25), 43 (62), 41 (42). IR (KBr), ν/cm^{-1}: 3345 (O—H), 1638 (C=N). ^1H NMR ($CDCl_3$), δ: 0.76 (s, 6 H, C(8)H_3); 0.81 (ddd, 2 H, C(1)H, J = 9.5 Hz, J = 9.3 Hz, J = 5.3 Hz); 0.96 (ddd, 2 H, C(6)H, J = 9.3 Hz, J = 8.5 Hz, J = 1.7 Hz); 1.03 (s, 6 H, C(9)H_3); 1.34 (s, 6 H, C(10)H_3); 1.49 (dd, 2 H, *pro-R*-C(2)H, J = 15.4 Hz, J = 5.3 Hz); 2.15 (dd, 2 H, *pro-S*-C(2)H, J = 15.4 Hz, J = 9.5 Hz); 2.45—2.60 (m, 4 H, C(11)H_2); 2.60 (dd, 2 H, *pro-R*-C(5)H, J = 19.2 Hz, J = 8.5 Hz); 2.68 (dd, 2 H, *pro-S*-C(5)H, J = 19.2 Hz, J = 1.7 Hz); 9.85 (br.s, 2 H, OH). ^{13}C NMR ($CDCl_3$), δ: 15.01 (C(8)); 17.26 (C(1)); 18.34 (C(5)); 18.82 (C(7)); 19.12 (C(6)); 25.24 (C(10)); 27.92 (C(9)); 29.27 (C(2)); 34.37 (C(11)); 47.99 (C(3)); 161.14 (C(4)).b

1,2-Bis{[(1*R*,2*R*,3*E*,5*R*)-3-hydroxyimino-2,6,6-trimethylbicyclo[3.1.1]hept-2-yl]sulfanyl}ethane (4). The yield was 85—90%. Colorless crystals with m.p. 164—168 °C (from EtOAc); $[\alpha]_{578}^{14}$ −153 (*c* 0.63, $CHCl_3$). HRMS: found *m/z* 424.22181 [M^+]; $C_{22}H_{36}N_2O_2S_2$. Calculated M = 424.22134. MS, *m/z* (I_{rel}(%)): 424 (1), 258 (68), 167 (74), 166 (100), 150 (42), 124 (61), 110 (93), 107 (38), 106 (56), 79 (42), 69 (32), 43 (56), 41 (59). IR (KBr), ν/cm^{-1}: 3287 (O—H), 936 (N—O). ^1H NMR ($CDCl_3$), δ: 0.83 (s, 6 H, C(8)H_3); 1.22 (s, 6 H, C(9)H_3); 1.60 (s, 6 H, C(10)H_3); 1.76 (d, 2 H, *pro-R*-C(7)H, J = 10.6 Hz); 1.87—1.91 (m, 2 H, C(5)H, C(1)H); 2.22 (dddd, 2 H, *pro-S*-C(7)H, J = 10.6 Hz, J = 6.0 Hz, J = 6.0 Hz, J = 2.6 Hz); 2.48 (dd, 2 H, *pro-S*-C(4)H, J = 18.5 Hz, J = 1.9 Hz); 2.55—2.64 (m, 2 H, C(11)H_a); 2.71—2.80 (m, 2 H, C(11)H_b); 2.84 (ddd, 2 H, *pro-R*-C(4)H, J = 18.5 Hz, J = 1.9 Hz, J = 1.9 Hz); 9.3 (br.s, 2 H, OH). ^{13}C NMR ($CDCl_3$), δ: 22.32 (C(8)); 27.36 (C(10) or C(9)); 27.46 (C(9) or C(10)); 28.54 (C(7)); 29.37 (C(4)); 30.14 (C(11)); 37.97 (C(5)); 40.41 (C(6)); 51.10 (C(1)); 54.25 (C(2)); 160.10 (C(3)).

Synthesis of bis-α-sulfanyl oximes from propane-1,3-dithiol (general procedure). Propane-1,3-dithiol (0.36 g, 2.5 mmol) was added to a solution of KOH (0.28 g, 5.0 mmol) in MeOH (50 mL) under Ar, the reaction mixture was stirred for 30 min, followed by addition of a dimeric terpenoid nitroso chloride (2.0 g, 2.5 mmol) and keeping for 10 h under stirring. After the reaction

reached completion (TLC monitoring, until spots of the starting dithiols disappeared), the solvent was evaporated *in vacuo*, the residue was stirred in a mixture of EtOAc (30 mL) and H_2O (30 mL), the organic layer was separated, the aqueous layer was extracted with EtOAc (2×30 mL), a combined organic extract was dried with anhydrous Na_2SO_4 and concentrated *in vacuo*. An oily product obtained was subjected to chromatography on SiO_2 in the hexane—EtOAc solvent system.

1,3-Bis{[(1*S*,3*S*,4*E*,6*R*)-4-hydroxyimino-3,7,7-trimethylbicyclo[4.1.0]hept-3-yl]sulfanyl}propane (5). The synthesis was carried out at 20 °C. The yield was 60%. Yellowish oil with $[\alpha]_{578}^{14}$ +121 (*c* 0.56, EtOAc). HRMS: found *m/z* 438.23638 [M^+], $C_{23}H_{38}N_2O_2S_2$. Calculated M = 424.23746. MS, *m/z* (I_{rel}(%)): 272 (16), 166 (100), 121 (11), 107 (25), 106 (24), 43 (18), 41 (14). IR (KBr), ν/cm^{-1}: 3482 (O—H), 1618 (C=N). ^{1}H NMR ($CDCl_3$), δ: 0.76 (s, 6 H, C(8)H_3); 0.81 (ddd, 2 H, C(1)H, *J* = 9.5 Hz, *J* = 9.3 Hz, *J* = 5.3 Hz); 0.95 (dd, 2 H, C(6)H_3, *J* = 9.3 Hz, *J* = 8.5 Hz); 1.01 (s, 6 H, C(9)H_3); 1.38 (s, 6 H, C(10)H_3); 1.50 (dd, 2 H, *pro-R*-C(2)H, *J* = 15.5 Hz, *J* = 5.3 Hz); 1.67 (tt, 2 H, C(12)H, *J* = 7.5 Hz, *J* = 7.5 Hz); 2.14 (dd, 2 H, *pro-S*-C(2)H, *J* = 15.5 Hz, *J* = 9.5 Hz); 2.25 (ddd, 2 H, C(11)H_a, *J* = 12.3 Hz, *J* = 7.5 Hz, *J* = 7.5 Hz); 2.47 (ddd, 2 H, C(11)H_b, *J* = 12.3 Hz, *J* = 7.5 Hz, *J* = 7.5 Hz); 2.55 (dd, 2 H, *pro-R*-C(5), *J* = 19.0 Hz, *J* = 8.5 Hz); 2.82 (d, 2 H, *pro-S*-C(5)H, *J* = 19.0 Hz); 10.0 (br.s, 2 H, OH). ^{13}C NMR ($CDCl_3$), δ: 14.87 (C(8)); 17.27 (C(1)); 18.29 (C(5)); 18.97 (C(7)); 19.28 (C(6)); 25.13 (C(10)); 27.65 (C(2)); 27.78 (C(9)); 29.36 (C(12)); 34.60 (C(11)); 47.81 (C(3)); 161.71 (C(4)).

1,3-Bis{[(1*R*,2*R*,3*E*,5*R*)-3-hydroxyimino-2,6,6-trimethylbicyclo[3.1.1]hept-2-yl]sulfanyl}propane (6). The synthesis was carried out at 0 °C. The yield was 50%, colorless crystals with m.p. 159—160 °C (hexane—$CHCl_3$), $[\alpha]_{589}^{23}$ −188 (*c* 0.79, $CHCl_3$). Found (%): C, 63.13; H, 8.76; N, 6.44; S, 14.37. $C_{23}H_{38}N_2O_2S_2$. Calculated (%): C, 62.97; H, 8.73; N, 6.39; S, 14.62. Obtained (vapor-phase osmometry in $CHCl_3$): M = 430±22; calculated: M = 438. IR (KBr), ν/cm^{-1}: 3311 (O—H), 937 (N—O). ^{1}H NMR ($CDCl_3$), δ: 0.91 (s, 6 H, C(8)H_3); 1.28 (s, 6 H, C(9)H_3); 1.66 (s, 6 H, C(10)H_3); 1.75 (tt, 2 H, C(12)H, *J* = 7.2 Hz, *J* = 7.2 Hz); 1.88 (d, 2 H, *pro-R*-C(7)H, *J* = 10.6 Hz); 1.94—1.98 (m, 4 H, C(5)H, C(1)H); 2.29 (dddd, 2 H, *pro-S*-C(7)H, *J* = 10.6 Hz, *J* = 6.3 Hz, *J* = 6.3 Hz, *J* = 2.7 Hz); 2.60 (dd, 2 H, *pro-S*-C(4)H, *J* = 18.4 Hz, *J* = 1.5 Hz); 2.60—2.69 (m, 4 H, C(11)H_2); 2.9 (ddd, 2 H, *pro-R*-C(4)H, *J* = 18.4 Hz, *J* = 2.9 Hz, *J* = 2.9 Hz); 8.99 (s, 2 H, OH). ^{13}C NMR ($CDCl_3$), δ: 22.50 (C(8)); 27.29 (C(10) or C(9)); 27.57 (C(9) or C(10)); 27.97 (C(7)); 29.00 (C(12)); 29.50 (C(4)); 30.17 (C(11)); 38.09 (C(5)); 40.55 (C(6)); 51.27 (C(1)); 53.71 (C(2)); 161.15 (C(3)).

Preparation of macrocycles from bis-α-sulfanyl oximes (general procedure). A mixture of CH_2Cl_2 (40 mL), PhMe (30 mL), bis-α-sulfanyl oxime (0.43 g, 1 mmol), dicyclohexyl-18-crown-6 (5—7 mg), and 50% aq. KOH (5—10 mL) was vigorously stirred at room temperature (15—25 °C) for 1—4 days (TLC monitoring, until spots of the starting dithiols disappeared). After the reaction reached completion, the aqueous and organic phases were separated, the aqueous phase was extracted with CH_2Cl_2 (2×30 mL). Organic extracts were combined, washed with H_2O (2×50 mL), dried with anhydrous $MgSO_4$, and concentrated *in vacuo* to obtain oily product, which was spontaneously crystallized after 1 week. The product was purified by chromatography on SiO_2.

(1*R*,3*E*,8*E*,11*R*,13*S*,15*R*,20*R*,22*S*)-12,12,15,20,23,23-Hexamethyl-4,8-diaza-5,7-dioxa-16,19-dithiapentacyclo-[20.1.0.0^{3,20}.0^{9,15}.0^{11,13}]tricosa-3,8-diene (7). The yield was 10%. Colorless crystals with m.p. 202—206 °C (hexane—EtOAc), $[\alpha]_{589}^{25}$ +173 (*c* 1.00, $CHCl_3$). HRMS: found *m/z* 436.22229 [$M]^+$, $C_{23}H_{36}N_2O_2S_2$. Calculated M = 436.22181. MS, *m/z* (I_{rel}(%)): 436 (62), 180 (31), 166 (81), 150 (79), 149 (52), 148 (100), 119 (69), 108 (72), 107 (79), 93 (54), 91 (39), 81 (44), 79 (43), 67 (40), 59 (33), 55 (29), 43 (59), 41 (65). IR (CCl_4), ν/cm^{-1}: 1620 (C=N), 1013 (C—O). ^{1}H NMR ($CDCl_3$), δ: 0.73 (s, 6 H, C(8)H_3); 0.77 (ddd, 2 H, C(1)H, *J* = 10 Hz, *J* = 9 Hz, *J* = 5 Hz); 0.91 (t, 2 H, C(6)H, *J* = 9 Hz, *J* = 2 Hz); 1.00 (s, 6 H, C(9)H_3); 1.35 (s, 6 H, C(10)H_3); 1.53 (dd, 2 H, *pro-R*-C(2)H, *J* = 16 Hz, *J* = 5 Hz); 2.1 (dd, 2 H, *pro-S*-C(2)H, *J* = 16 Hz, *J* = 10 Hz); 2.40 (m, 2 H, C(11)H_a); 2.44 (m, 2 H, C(11)H_b); 2.61 (dd, 2 H, *pro-R*-C(5), *J* = 20 Hz, *J* = 9 Hz); 2.74 (dd, 2 H, *pro-S*-C(5)H, *J* = 20 Hz, *J* = 2 Hz); 5.54 (s, 2 H, OCH_2O). ^{13}C NMR ($CDCl_3$), δ: 14.76 (C(8)); 16.95 (C(1)); 18.52 (C(5)); 18.95 (C(7)); 19.08 (C(6)); 25.29 (C(10)); 27.58 (C(9)); 29.28 (C(2)); 33.77 (C(11)); 48.94 (C(3)); 94.83 (C(12)); 161.61 (C(4)).

(1*R*,3*E*,8*E*,11*R*,13*R*,14*R*,19*R*,20*R*)-12,12,14,19,21,21-Hexamethyl-4,8-diaza-5,7-dioxa-15,18-dithiapentacyclo-[18.1.1.1^{11,13}.0^{3,19}.0^{9,14}]tricosa-3,8-diene (8). The yield was 15%. Colorless crystals with m.p. 147—150 °C (hexane—EtOAc), $[\alpha]_{589}^{25}$ −192 (*c* 1.22, $CHCl_3$). HRMS: found *m/z* 436.22093; $C_{23}H_{36}N_2O_2S_2$. Calculated: M = 436.22181. MS, *m/z* (I_{rel}(%)): 436 (16), 240 (33), 182 (80), 166 (73), 165 (55), 150 (64), 148 (93), 134 (47), 124 (45), 107 (100), 94 (36), 93 (36), 91 (28), 87 (41), 79 (45), 69 (67), 43 (62), 41 (73). IR (CCl_4), ν/cm^{-1}: 1624 (C=N), 1051 (C—O). ^{1}H NMR ($CDCl_3$), δ: 0.92 (s, 6 H, C(8)H_3); 1.28 (s, 6 H, C(9)H_3); 1.64 (s, 6 H, C(10)H_3); 1.89—1.99 (m, 4 H, C(5)H, C(1)H); 1.91 (d, 2 H, *pro-R*-C(7)H, *J* = 10.7 Hz); 2.29 (dddd, 2 H, *pro-S*-C(7)H, *J* = 10.7 Hz, *J* = 6.2 Hz, *J* = 6.2 Hz, *J* = 2.8 Hz); 2.54 (m, 2 H, C(11)H_a); 2.64 (dd, 2 H, *pro-S*-C(4)H, *J* = 18.2 Hz, *J* = 2.0 Hz); 2.98 (ddd, 2 H, *pro-R*-C(4)H, *J* = 18.2 Hz, *J* = 2.0 Hz, *J* = 2.0 Hz); 3.11 (m, 2 H, C(11)H_b); 5.48 (s, 2 H, OCH_2O). ^{13}C NMR ($CDCl_3$), δ: 22.31 (C(8)); 27.54 (C(10) or C(9)); 27.93 (C(9) or C(10)); 30.23 (C(7) or C(4)); 30.27 (C(4) or C(7)); 30.54 (C(11)); 38.67 (C(5)); 41.02 (C(6)); 51.77 (C(1)); 54.64 (C(2)); 96.88 (C(12)); 162.85 (C(3)).

(1*R*,3*E*,8*E*,11*R*,13*S*,15*R*,21*R*,23*S*)-12,12,15,21,24,24-Hexamethyl-4,8-diaza-5,7-dioxa-16,20-dithiapentacyclo-[21.1.0.0^{3,21}.0^{9,15}.0^{11,13}]tetracosa-3,8-diene (9). A mixture of CH_2Cl_2 (20 mL), PhH (30 mL), bis-α-sulfanyl oxime **5** (0.87 g, 2 mmol), 10% aq. $Bu_4N^+OH^-$ (0.5 mL), and 50% aq. NaOH (5—10 mL) was refluxed for 10 h with vigorous stirring. After the reaction reached completion, aqueous and organic phases were separated. The aqueous phase was extracted with CH_2Cl_2 (2×30 mL). The organic extracts were combined, washed with H_2O (2×50 mL), dried with anhydrous $MgSO_4$, and concentrated *in vacuo* to obtain an oily product, which was spontaneously crystallized after 1 week. The product was purified by chromatography on SiO_2. The yield was 30%. Colorless crystals with $[\alpha]_{589}^{29}$ +262 (*c* 0.76, $CHCl_3$). HRMS: found *m/z* 450.23720 [M]+; $C_{24}H_{38}N_2O_2S_2$. Calculated: M = 450.23746. MS, *m/z* (I_{rel}(%)): 344 (74), 166 (70), 150 (75), 149 (71), 134 (42), 133 (43), 123 (20), 107 (100), 106 (81), 94 (23), 93 (56), 91 (37), 92 (37), 81 (42), 79 (42), 77 (24), 69 (24), 67 (42), 59 (21), 55 (26), 43 (47), 41 (69). IR (KBr), ν/cm^{-1}: 1609 (C=N), 1022 (C—O). ^{1}H NMR ($CDCl_3$), δ: 0.73 (s, 6 H, C(8)H_3); 0.77 (ddd, 2 H, C(1)H, *J* = 9.6 Hz, *J* = 9.6 Hz, *J* = 5.1 Hz); 0.88 (ddd, 2 H,

C(6)H, J = 9.6 Hz, J = 8.1 Hz, J = 1.9 Hz); 0.99 (s, 6 H, C(9)H_3); 1.35 (s, 6 H, C(10)H_3); 1.48 (dd, 2 H, *pro-R*-C(2)H, J = 15.5 Hz, J = 5.1 Hz); 1.72 (tt, 2 H, C(12)H, J = 7.4 Hz, J = 6.8 Hz); 2.1 (dd, 2 H, *pro-S*-C(2)H, J = 15.5 Hz, J = 9.6 Hz); 2.13 (ddd, 2 H, C(11)H_a, J = 13.9 Hz, J = 7.4 Hz, J = 7.4 Hz); 2.55 (ddd, 2 H, C(11)H_b, J = 13.9 Hz, J = 6.8 Hz, J = 6.8 Hz); 2.59 (dd, 2 H, *pro-R*-C(5)H, J = 19.6 Hz, J = 8.1 Hz); 2.67 (dd, 2 H, *pro-S*-C(5)H, J = 19.6 Hz, J = 1.9 Hz); 5.41 (s, 2 H, OCH_2O). ^{13}C NMR ($CDCl_3$), δ: 14.70 (C(8)); 17.22 (C(1)); 18.60 (C(5)); 18.75 (C(6)); 19.30 (C(7)); 25.57 (C(10)); 27.57 (C(9)); 28.98 (C(2)); 31.73 (C(12)); 34.00 (C(11)); 48.43 (C(3)); 95.43 (C(13)); 161.89 (C(4)).

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