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C,C-Coupling with Sulfur-Stabilized Carbanions – 6.[1]

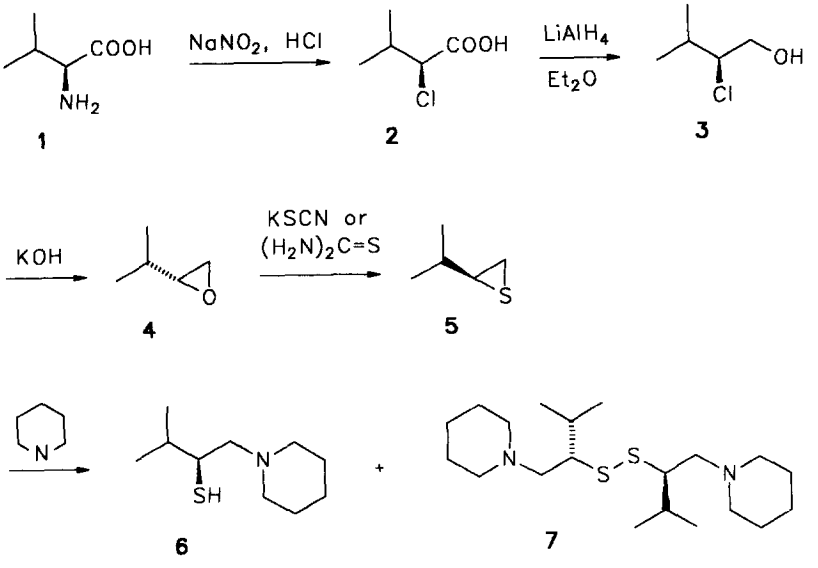
Preparation and Electrophilic Substitution of 1-[3-Methyl-2-(2-thiolanylthio)-butyl]piperidine and Dethioacetalization of Semicyclic Dithioacetals[2]

Claudia Birk,[3] Jürgen Voss*

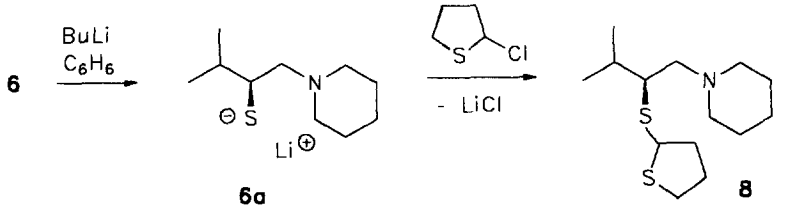
Institut für Organische Chemie der Universität Hamburg, Martin-Luther-King-Platz 6,
D-20146 Hamburg, Germany

Abstract: 1-[3-Methyl-2-(2-thiolanylthio)butyl]piperidine (**8**) is obtained from L-valine *via* enantiomerically pure 1-(2-mercapto-3-methylbutyl)piperidine (**6**). The diastereoisomers are separated by column chromatography and the reactions of the carbanion **8a** with electrophiles are studied. - Semicyclic dithioacetals **12** - **15** are converted into the corresponding carbonyl compounds with [bis(trifluoroacetoxy)iodo]benzene (PIFA). Phenyl dichlorophosphate (PDCP) in the presence of sodium iodide and DMF is found to be a reagent for selective cleavage of the exocyclic C-S bond. By using DOWEX 50W and paraformaldehyde in acetone/water a cleavage of both acetalic C-S bonds is achieved in certain cases. Copyright © 1996 Elsevier Science Ltd

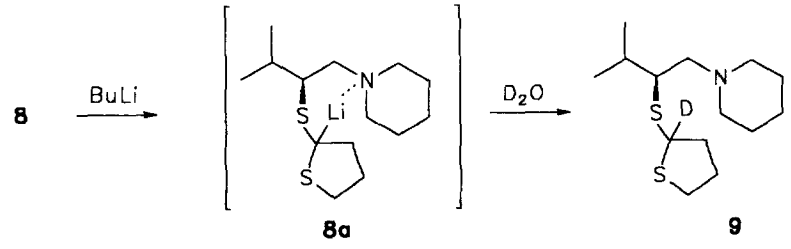
1-[3-Methyl-2-(2-thiolanylthio)butyl]piperidine (**8**) was prepared in order to obtain a precursor of a 2-lithio-2-(alkylthio)thiolane **8a**, which was expected to exhibit a stable configuration at its carbanion center due to the formation of a lithium chelate complex. L-Valine and D,L-valine were used as starting material for this synthesis. In the first step L-valine (**1**) was converted into (*S*)-2-chloro-3-methylbutanoic acid (**2**) with retention of the configuration at its chiral center. After reduction of **2** with lithium aluminium hydride the resulting chlorohydrine **3** was transformed into the epoxide **4** by an intramolecular S_N2 reaction. Reaction of **4** with potassium thiocyanate or thiourea yielded the corresponding thiirane **5** under inversion at the asymmetric center. (*S*)-2-Isopropylthiirane (**5**) could be ring opened regioselectively with piperidine at the less hindered carbon atom to yield the piperidinothiol **6**. The corresponding disulfide **7** was obtained as a side product. The enantiomeric purity of compound **2**, **3**, **4**, and **5** was proved by gas chromatography using a chiral stationary phase.



Reaction of lithium (*R*)-3-methyl-1-(1-piperidyl)butane-2-thiolate (**6a**) with 2-chlorothiolane in THF gave **1**-[3-methyl-2-(2-thiolanylthio)butyl]piperidine (**8**) in 82 % yield. The two diastereoisomers (2*S*, 2'*S*)-**8** and (2*S*, 2'*R*)-**8** obtained in a 1:1 ratio were separated by column chromatography.

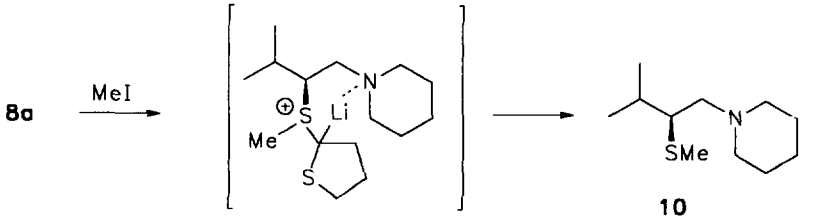


The semicyclic dithioacetal **8** was readily deprotonated with butyllithium in THF at -40°C. The carbanion **8a** was quenched with deuterium oxide to form **9** with a deuterium content of 74 % as determined from its ^{1}H NMR spectrum, i.e. the integrals of the 2'-H signal of unchanged **8** and the isopropyl signal. At lower temperature no reaction was observed even when deuterated methanol was used



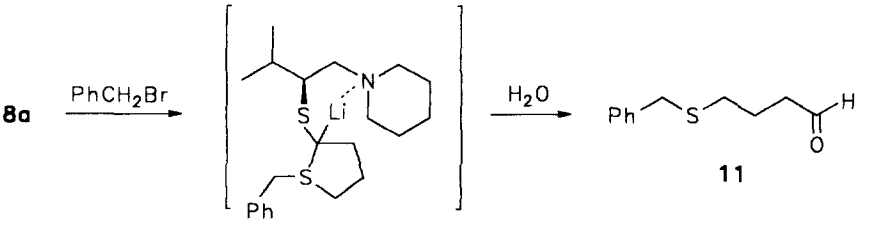
instead of deuterium oxide, which tends to crystallize out of the solution. Higher temperatures lead to decomposition of the lithium complex **8a**. Compound **9** consisted of two diastereoisomers in a ratio of about 1:1, though a single pure diastereoisomer of **8** was used as starting material. Its ^{1}H NMR spectrum showed four methyl doublets of isopropyl groups instead of only two which one would observe for one diastereoisomer. Obviously the lithium chelate **8a** does not exhibit the expected stable configuration at -40°C and, as a consequence of rapid inversion at C-2', both stereoisomers of **9** are formed.

Other electrophiles such as alkyl halides or aldehydes did not attack the carbanionic center. When alkyl halides were used as electrophiles an alkylation at one of the sulfur atoms was favoured. E.g. reaction of methyl iodide with the lithium chelate **8a** gave 1-[3-methyl-2-(methylthio)butyl]piperidine (**10**) in 43 % yield. This result can be explained by assuming methylation at the exocyclic sulfur atom to form **10a** followed by a cleavage of the sulfonium ion.



10a **10**

Experiments with benzyl bromide as electrophile lead to dethioacetalization yielding 4-(benzylthio)butanal (**11**). In this case obviously benzylation at the endocyclic sulfur atom with subsequent hydrolysis of **11a** occurs.



11a **11**

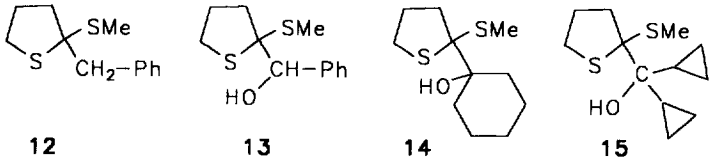
Acetaldehyde or benzaldehyde do not react with the lithium chelate **8a** to form the expected carbinols. Only unchanged starting material **8** was recovered besides some decomposition and polymerization products.

The observed unexpectedly low overall reactivity of **8a** as a carbanion seems to be due to steric hindrance and pronounced stabilization of the carbanion by the lithium counterion, which is fixed by complexation.

Generation of carbonyl compounds from the corresponding open-chain or cyclic thioacetals is not a trivial task since simple acid-catalyzed hydrolysis is not possible.[4,5] Dethioacetalization of semicyclic dithioacetals is even more complicated.[2,3,6] Reagents containing Hg^{2+} ions are not suitable for semicyclic dithioacetals since the carbonyl compounds, which are generated, contain SH groups and therefore form insoluble mercaptides. Furthermore, acid catalyzed or alkylative dethioacetalization methods often yield polymers. In continuation of our research on semicyclic dithioacetals we attempted to find a reagent that is

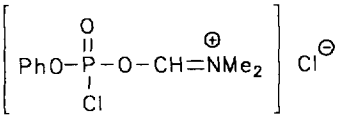
able to cleave both acetalic C-S bonds and yield the corresponding carbonyl compound. To reach this aim we selected reagents which work under mild conditions and have proved to be effective in the dethioacetalization of cyclic or open chain dithioacetals.

We chose the semicyclic dithioacetals **12** - **15** as model compounds which we prepared by deprotonation of 2-(methylthio)thiolane with n-butyllithium and subsequent reaction with a suitable electrophile (benzyl bromide, aldehyde or ketone).[7]



12 **13** **14** **15**

According to the literature dethioacetalization of cyclic or open chained thioacetals can be achieved with phenyl dichlorophosphate (PDCP) in the presence of sodium iodide and DMF.[8,9] Lack of sodium iodide leads to longer reaction times, and if DMF is absent no reaction is observed at all. Till now two different reaction mechanisms are discussed. Their application to the reaction of semicyclic thioacetals is shown in the scheme below:



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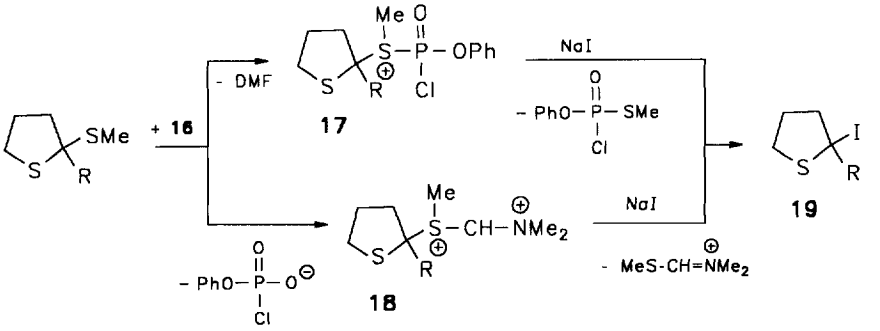
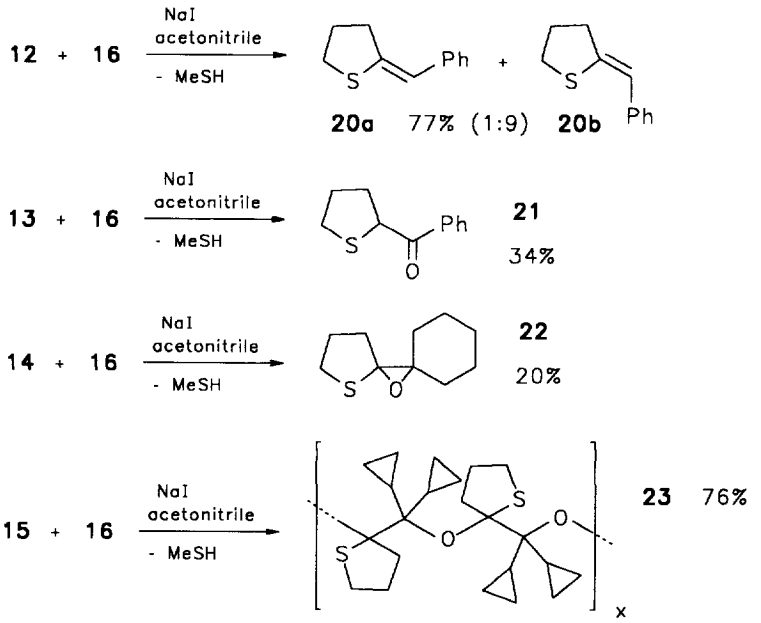


Liu and Yu[8] assume an exchange of the chloride for iodide at the PDCP which should increase the reactivity of the phosphorus atom. Garcia, Arrieta and Palomo[9] suggest an activation of PDCP by reaction with DMF to give the corresponding iminium compound **16**. This iminium compound possesses two positive polarized centers suitable for an attack at the sulfur atom. Electrophilic attack of the phosphorus atom leads to **17** as intermediate, whereas reaction at the iminium carbon gives **18**. According to Liu and Yu[8] the phosphate group is substituted by iodide to form **19** in the next step.

We could not detect intermediates like **17**, **18**, or **19** during the reaction of **12** - **15** with PDCP but found elimination or substitution products. In our experiments PDCP turned out to be a reagent for

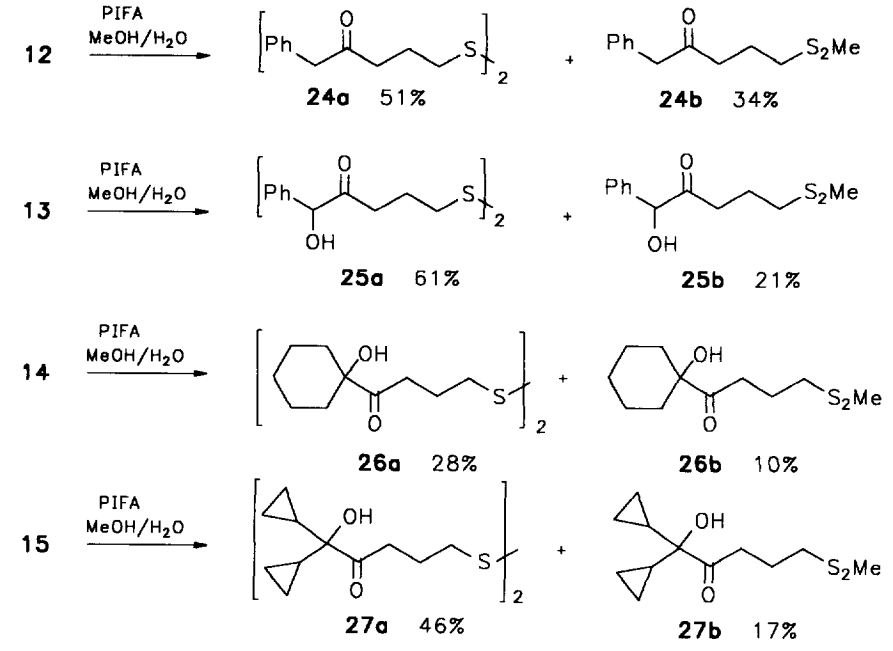
selective cleavage of the exocyclic C-S-bond. Generation of a carbonyl group at the acetalic carbon atom was, however, not achieved.

Cleavage reactions of **12** and **13** gave the β-elimination products **20** and **21**. When the teriary carbinol **14** was used 1,3-elimination under formation of the dispirooxirane **22** took place. - These results can be explained with the formation of a carbenium ion after the cleavage of the exocyclic C-S bond. The carbenium ion is stabilized by proton elimination (→ **20, 21**) or intramolecular nucleophilic attack of the hydroxyl group (→ **22**). - Only an oligomer was formed from the carbinol **15**. According to its ^{13}C NMR spectrum it contains intact thiolane and cyclopropane rings and might therefore exhibit structure **23**.



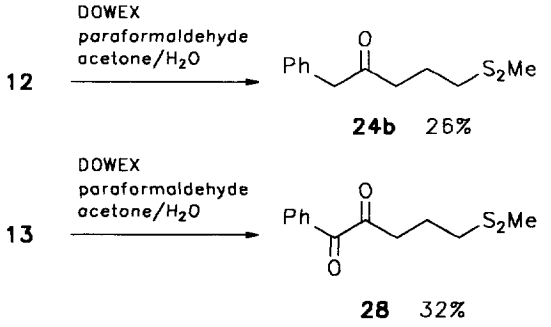
[Bis(trifluoroacetoxy)iodo]benzene is known to be a mild dethioacetalization reagent.[10] Very short reaction times are needed and it is suitable for educts containing other sensitive functional groups. Each of our model compounds **12, 13, 14,** and **15** was converted into the corresponding carbonyl compounds in good yield. Since the reagent exhibits oxidizing properties disulfides are formed instead of thiols, which should be the primary intermediates. The mixtures of symmetric (**24a, 25a, 26a, 27a**) and asymmetric disulfides (**24b, 25b, 26b, 27b**) which we obtained were, however, difficult to separate by column chromatography. We therefore tried to optimize the reaction conditions with respect to the yield and selectivity by variation of the applied equivalents of reagent and the composition of the solvent (*cf.* **Exp.**). As we found out, educts containing a hydroxyl group require longer reaction times which can be shortened by using a larger excess of reagent. If the solvent contains too much water the solubility of the educt decreases and longer reaction times are necessary. When we used methanol/acetone instead of water/acetone as solvent, we did not obtain the corresponding O,O-acetals in contrast to the literature,[10] but instead the carbonyl compounds in low yield. This might be due to lack of water for the hydrolysis.

We also expected acidic ion exchangers in the presence of paraformaldehyde[11,12] to give good results. DOWEX 50W was preferred to Amberlyst 15 because shorter reaction times should be required.

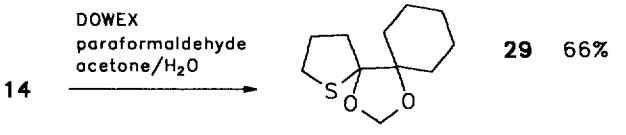


PIFA = $PhI(OCOCF_3)_2$

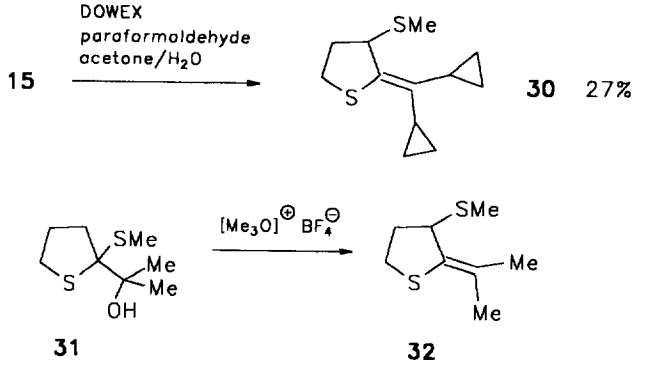
Dethioacetalization of **12** gave the asymmetric disulfide **24b** as the only product, which was also obtained when **12** was cleaved with [bis(trifluoroacetoxy)iodo]benzene. The symmetric product **24a** could not be detected. Unexpectedly oxidation of the secondary hydroxyl group occurred during the dethioacetalization of **13** to yield the α-diketone **28**.[13]



An interesting dispiro compound **29** was obtained from **14**. Possibly acid-catalyzed reaction between formaldehyde and the hydroxyl group of **14** yields a hemiacetal, which then cyclizes under elimination of methanethiol to form the 1,3-dioxolane ring of **29**.



Reaction of **15** with DOWEX 50W and paraformaldehyde yielded a product which surprisingly exhibits the structure **30**. According to its ^1H and expecially its ^{13}C NMR spectrum four cyclopropane-CH_2 and two thiolane-CH_2 groups as well as two cyclopropane-CH, each one thiolane-CH and SCH_3 group and two quaternary olefinic carbon centers are present in the molecule (*cf.* **Exp.**). The migration of the methylthio substituent obviously takes place via an acid-catalyzed elimination/addition process and is accompanied by dehydration to form **30**. A similar rearrangement is observed if the related 2-(1-hydroxy-1-methylethyl)-2-(methylthio)thiolane (**31**), the adduct of acetone to the anion of 2-(methylthio)thiolane, is treated with trimethyloxonium tetrafluoroborate to form 2-isopropylidene-3-(methylthio)thiolane (**32**).[6]



EXPERIMENTAL

General. **IR** (film): Perkin Elmer FT-IR 1720 X. - ^1H and ^{13}C NMR: Bruker AC250 P (250 MHz) and AMX 400 (400 MHz); assignment by DEPT measurements. - **MS**: Varian MAT CH 7; **HRMS**: VG-Analytical 70-205S. - Column chromatography: Merck silica gel 60 (mesh 70 - 230). THF was dried by 5 d refluxing over potassium under a nitrogen atmosphere, ether by refluxing over lithium aluminium hydride and piperidine by refluxing over sodium hydroxide. Deprotonations were carried out using 1.6n butyllithium solutions in hexane. The enantiomeric purity of compound **2** - **5** was analysed by gas chromatography with chiral stationary phases. For comparison the compounds **2** - **5** were therefore also prepared as racemates starting from D,L-valine.

(S)-2-Chloro-3-methylbutanoic acid (**2**).[14] After dissolving 46.8 g (0.4 mol) of L-valine (**1**) in 500 ml 6n hydrochloric acid, 44.0 g (0.64 mol) of finely powdered sodium nitrite were added in small portions at 0°C. The solution was stirred at 0°C for 6 h. Then the solution was warmed up to room temperature and extracted 4 times with each 80 ml of trichloromethane. The organic layer was dried over sodium sulfate and the solvent was removed. Distillation of the residue yielded 38.0 g (70 %) of **2**. - B.p. 109°C/16 Torr (Lit.[15]: b.p. 98°C/16 Torr). - Enantiomeric excess: 95 % [25 m silica capillary with octakis(3-O-butyryl-2,6-di-O-pentyl)-γ-CD]. **IR** (film): ν = 2976, 1723 (C=O), 1390, 1207, 1116, 463. - **^1H NMR** (250 MHz, $CDCl_3$): δ = 1.09 (d, 3H, $CH(CH_3)_2$, J = 6.8 Hz), 1.11 (d, 3H, $CH(CH_3)_2$, J = 6.8 Hz), 2.38 (m, 1H, $CH(CH_3)_2$, 4.21 (d, 1H, CHCl, J = 6.0 Hz). - **^{13}C NMR** (63 MHz, $CDCl_3$): δ = 17.81 (prim., $CH(CH_3)_2$), 19.63 (prim., $CH(CH_3)_2$, 32.51 (tert., $CH(CH_3)_2$), 63.95 (tert., CHCl), 175.13 (quart., COOH).

(S)-2-Chloro-3-methylbutanol (**3**).[15] - A solution of 13.6 g (100 mmol) **2** in 50 ml dry ether was quickly added to a suspension of 3.8 g (100 mmol) lithium aluminium hydride in 100 ml ether at 0°C. After 15 min refluxing 10 ml water and 2n sulfuric acid were added dropwise at 0°C until the precipitate was dissolved. The aqueous layer was extracted 3 times with each 50 ml trichloromethane and the organic phase was dried over sodium sulfate. After removing the solvent distillation of the residue gave 8.0 g (65 %) of **3** as a colourless liquid. - B.p. 72°C/18 Torr (Lit.[15]: b.p. 80°C/60 Torr). - Enantiomeric excess: 98 % [25 m silica capillary with octakis(3-O-butyryl-2,6-di-O-pentyl)-γ-CD]. - **IR** (film): ν = 3368 (O-H), 2968, 2878, 1465, 1389, 1370, 1075, 1029, 797 (C-Cl), 440, 406. - **^{1}H NMR** (250 MHz, $CDCl_3$): δ = 1.02 (d, 3H, $CH(CH_3)_2$, J = 6.8 Hz), 1.04 (d, 3H, $CH(CH_3)_2$, J = 6.8 Hz), 1.80 (s, 1H, CH_2OH), 2.05 (m, 1H, $CH(CH_3)_2$, J = 6.0 Hz), 3.73 (dd, 1H, CH_2OH, J = 11.6 Hz, 7.6 Hz), 3.82 (dd, 1H, CH_2OH, J = 11.6, 4.0 Hz), 3.92 (m, 1H, CHCl). - **^{13}C NMR** (63 MHz, $CDCl_3$): δ = 18.14 (prim., $CH(CH_3)_2$), 19.96 (prim., $CH(CH_3)_2$), 31.46 (tert., $CH(CH_3)_2$), 65.43 (sec. CH_2OH), 71.89 (tert., CHCl).

(R)-1,2-Epoxy-3-methylbutane (**4**).[15] - 7.84 g (140 mmol) of finely powdered potassium hydroxide were added to 8.66 g (70 mmol) **3**. Distillation yielded 5.2 g (87 %) of **4** as a colourless liquid. - B.p. 71°C/760 Torr (Lit.[15]: b.p. 81.5°C/760 Torr). - Enantiomeric excess: 97 % [25 m silica capillary with octakis(3-O-butyryl-2,6-di-O-pentyl)-γ-CD]. - **IR** (gas): ν = 3048 (C-H), 2975, 1479, 1379, 1263, 1135, 933, 875, 834, 484. - **^{1}H NMR** (250 MHz, $CDCl_3$): δ = 0.96 (d, 3H, $CH(CH_3)_2$, J = 6.8 Hz), 1.04 (d, 3H, $CH(CH_3)_2$, J = 6.8 Hz), 1.49 (m, 1H, $CH(CH_3)_2$), 2.35 (m, 1H, CHO), 2.69 (dd, 1H, CH_2O, J = 3.6, 4.4 Hz), 2.73 (dd, 1H, CH_2O, J = 3.6, 3.2 Hz). - **^{13}C NMR** (63 MHz, $CDCl_3$): δ = 18.14 (prim., $CH(CH_3)_2$), 19.03 (prim., $CH(CH_3)_2$), 30.79 (tert., $CH(CH_3)_2$), 46.10 (sec., CH_2O), 57.64 (tert., CHO).

(S)-1,2-Epithio-3-methylbutane (**5**). - *Method 1*[16]: To a mixture of 6.22 g (72 mmol) **4**, 10 ml water and 10 g ice 7.0 g (92 mmol) thiourea were added at 0°C. After 3 h stirring at 20°C the aqueous layer was extracted 4 times with dichloromethane, the organic layer was dried over sodium sulfate and the solvent was carefully removed. Distillation of the residue yielded 3.0 g (41 %) of **5**. - B.p. 107°C/760 Torr (Lit.[17]: b.p. 116°C/760 Torr). - Enantiomeric excess: 94 % [25 m silica capillary with 6-Methyl-2,3-pentyl-β-CD]. - **IR** (Film): ν = 2961, 2871, 1461, 1366, 1048, 964. - **^{1}H NMR** (250 MHz, $CDCl_3$): δ = 1.07 (d, 3H, $CH(CH_3)_2$, J = 6.6 Hz), 1.09 (d, 3H, $CH(CH_3$, J = 6.6 Hz), 1.34 (m, 1H, $CH(CH_3)_2$), .17 (dd, 1H, CH_2S, J = 1.2, 5.6 Hz), 2.46 (dd, 1H, CH_2S, J = 6.4, 1.2 Hz), 2.71 (m, 1H, CHS). - **^{13}C NMR**, (63 MHz, $CDCl_3$): δ = 21.62 (prim., $CH(CH_3)$), 21.79 (prim. $CH(CH_3)$), 24.84 (sec., CH_2S), 35.15 (tert., $CH(CH_3)_2$), 43.17 (tert., CHS). - *Method 2*[18]: A solution of 760 mg (8.8 mmol) **4** in 1 ml water and 1.06 g (11 mmol) potassium thiocyanate was stirred for 36 h at room temperature. Work-up as above yielded 420 mg (47 %) of **5**. - Enantiomeric excess: 95 %.

(R)-1-(2-Mercapto-3-methylbutyl)piperidine (**6**).[19,20] - A solution of 2.17 (21 mmol) **5** and 8.0 ml (6.9 g, 80 mmol) piperidine in 40 ml THF was stirred at room temperature for 5 d. Then the solvent was removed and the residue was distilled at 0.6 Torr to yield 2.4 g (13 mmol, 62 %) **6** as colourless liquid, b.p. 57°C/0.6 Torr and 1.1 g (3.0 mmol, 28 %) of the disulfide **7**, b.p. 101 - 109°C/0.6 Torr. - **IR** (Film): ν = 2937, 2798, 2520 (SH), 1466, 1383, 1304, 1156, 1110, 1040, 994, 861, 777. - **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.84 (d, 3H, $CH(CH_3)_2$, J = 7.0 Hz), 0.95 (d, 3H, $CH(CH_3)_2$, J = 7.0 Hz), 1.31 - 1.37 (m, 2H, piperidyl-4-CH_2), 1.43 - 1.50 (m, 4H, piperidyl-3- and -5-CH_2), 2.11 - 2.18 (m, 1H, $CH(CH_3)_2$), 2.19 - 2.39 (m, 6H, CH_2N, piperidyl-2- and -6-CH_2), 2.41 (d, 1H, SH, J = 7.5 Hz), 2.73 - 2.80 (m, 1H, CHSH). - **^{13}C NMR**, (63 MHz, $CDCl_3$): δ = 18.10 (prim., $CH(CH_3)$), 19.92 (prim., $CH(CH_3)_2$), 24.45 (sec., piperidyl-4-C), 26.02 (sec., 2C, piperidyl-3-C and -5-C), 29.28 (tert., $CH(CH_3)_2$), 45.33 (tert., CHSH), 54.97 (sec., 2C, piperidyl-2-C and -6-C), 61.02 (sec., CHSH-CH_2-N). - MS (70 eV): *m/z* (%) = 187 (2) [M^+], 154 (2) [M^+- SH], 144 (1) [M^+- C_3H_7], 138 (1), 110 (1)

[$C_7H_{12}^+$], 99 (9), 98 (100) [$C_6H_{12}N^+$], 96 (3). - $C_{10}H_{21}NS$ (187.2); calcd. C 64.16, H 11.22, N 7.48, S 17.13; found C 63.84, H 11.25, N 8.28, S 17.02. - **HRMS**: calcd. 187.1395; found 187.1355 [M^+]. *Bis[(R)-3-methyl-1-(1-piperidyl)-2-butyl)] disulfide* (7): **IR** (film): ν = 2942, 2802, 1469, 1380, 1300, 1108, 1043, 996, 860. - ^{1}**H NMR** (400 MHz, $CDCl_3$): δ = 0.95 (d, 6H, $CH(CH_3)_2$, J = 6.7 Hz), 0.99 (d, 6H, $CH(CH_3)_2$, J = 6.7 Hz), 1.87 (m, 2H, $CH\text{-}CH(CH_3)_2$), 1.40 (m, 4H, piperidyl-4-CH_2), 1.52 - 1.61 (m, 8H, piperidyl-3-CH_2 and -5CH_2), 2.21 - 2.50 (m, 12H, $CHCH_2N$, piperidyl-2-CH_2 and -6-CH_2), 3.02 (m, 2H, CHS-). - ^{13}**C NMR** (63 MHz, $CDCl_3$): δ = 18.08 (prim., 2C, $CH(CH_3)_2$), 20.77 (prim., 2C, $CH(CH_3)_2$), 24.49 (sec., 2C, piperidyl-4-*C*), 26.10 (sec. 4C, piperidyl-3-*C* and -5-*C*), 31.24 (tert., 2C, $CH(CH_3)_2$), 45.32 (tert., 2C, CHS), 54.58 (sec., 4C, piperidyl-2-*C* and -6-*C*), 64.29 (sec., 2C, $CH\text{-}CH_2$-N).

1-[3-Methyl-2-(2-thiolanylthio)butyl]piperidine (8). - The reaction was carried out under nitrogen atmosphere. Preparation of the *2-chlorothiolane* solution: At room temperature 2.0 g (15 mmol) of N-chlorosuccinimide were slowly added to a solution of 1.24 g (14 mmol) thiolane in 100 ml benzene. After 3 h stirring at room temperature the precipitate was removed by filtration. - Preparation of *lithium (R)-3-methyl-1-(1-piperidyl)butane-2-thiolate* (6a): To a solution of 1.87 g (10 mmol) **6** in 10 ml benzene 6.9 mol 1.6 n-butyllithium solution was added at room temperature and the mixture was stirred for 1 h. - Then the 2-chlorothiolane solution was slowly dropped into the solution of **6a** at room temperature. The mixture was stirred over night. The organic layer was washed with aqueous sodium carbonate solution, dried over sodium sulfate and the solvent was removed. The brown residue was worked up by column chromatography (200 g silica gel, trichloromethane) to yield 550 mg (20 %) of (2*S*,2'*S*)-**8**, 0.9 g (33 %) of a mixture of the diastereoisomers and 800 mg (29 %) of (2*S*,2'*R*)-**8**. - **IR** (film, diastereomeric mixture): ν = 2932, 2796, 1441, 1383, 1349, 1302, 1270, 1229, 1156, 1140, 990, 963, 885, 861, 781, 758, 680, 446. - ^{1}**H NMR** (400 MHz, $CDCl_3$); (2*S*,2'*S*)-**8**: δ = 0.81 (d, 3H, $CH(CH_3)_2$, J = 7.0 Hz), 0.89 (d, 3H, $CH(CH_3)_2$, J = 6.7 Hz), 1.30 - 1.41 (m, 2H, piperidyl-4-CH_2), 1.46 - 1.57 (m, 4H, piperidyl-3- and -5-CH_2), 1.94 - 2.25 (m, 5H, $CH(CH_3)_2$, thiolanyl-3- and -4-CH_2), 2.24 - 2.27 (m, 4H, piperidyl-2- and -6-CH_2), 2.47 (d, 2H, $CH\text{-}CH_2$-N, J = 7.0 Hz), 2.70 - 2.87 (m, 2H, thiolanyl-5-*CH* and -SCH), 2.95 - 3.03 (m, 1H, thiolanyl-5-CH_2), 4.72 (bt, 1H, thiolanyl-2-*CH*, J = 4.1 Hz). (2*S*,2'*R*)-**8**: δ = 0.86 (d, 3H, $CH(CH_3)_2$, J = 6.6 Hz), 1.02 (d, 3H, $CH(CH_3)_2$, J = 6.6 Hz), 1.38 - 1.42 (m, 2H, piperidyl-4-CH_2), 1.50 - 1.60 (m, 4H, piperidyl-3- and -5-CH_2), 1.99 - 2.13 (m, 3H, $CH(CH_3)_2$, 2H of thiolanyl-3- or -4-CH_2), 2.16 - 2.25 (m, 2H, 2H of thiolanyl-3- or -4-CH_2), 2.36 (bs, 4H, piperidyl-2- and -6-CH_2), 2.41 - 2.51 (m, 2H, $CH\text{-}CH_2$-N), 2.65 - 2.88 (m, 2H, 1H of thiolanyl-5-CH_2 and SCH), 2.99 - 3.04 (m, 1H, 1H of thiolanyl-5-CH_2), 4.79 (dd, 1H, thiolanyl-2-*CH*, J = 5.6, 4.1 Hz). - ^{13}**C NMR** (100 MHz, $CDCl_3$); (2*S*,2'*S*)-**8**: δ = 17.24 (prim., $CH(CH_3)_2$), 20.11 (prim., $CH(CH_3)_2$), 24.01 (sec., piperidyl-4-CH_2), 25.62 (sec., 2C, piperidyl-3- and -5-CH_2), 28.38 (sec., thiolanyl-3- or -4-CH_2), 29.07 (tert., $CH(CH_3)_2$), 32.33 (sec., thiolanyl-5-CH_2), 38.52 (sec., thiolanyl-3- or -4-CH_2), 51.20 (tert., SCH), 52.62 (tert., thiolanyl-2-CH), 54.65 (sec., 2C, piperidyl-2- and -6-CH_2), 63.16 (sec., $CH\text{-}CH_2N$). (2*S*,2'*R*)-**8**: δ = 17.57 (prim., $CH(CH_3)_2$), 20.06 (prim., $CH(CH_3)_2$), 24.02 (sec., piperidyl-4-CH_2), 25.65 (sec., piperidyl-3- and -5-CH_2), 28.95 (sec., thiolanyl-3- or -4-CH_2), 29.61 (tert., $CH(CH_3)_2$), 32.51 (sec., thiolanyl-5-CH_2), 38.43 (sec., thiolanyl-3- or -4-CH_2), 51.12 (tert., SCH<), 53.68 (tert., thiolanyl-2-CH), 54.69 (sec., 2C, piperidyl-2- and 6-CH_2), 63.50 (sec., $CH\text{-}CH_2$-piperidyl). - MS (70 eV): *m/z* (%) = 273 (0.04) [M^+], 155 (25), 98 (100) [$C_6H_{12}N^+$], 87 (46) [$C_4H_7S^+$], 86 (40) [$C_4H_6S^+$], 85 (39) [$C_5H_{11}N^+$], 84 (46) [$C_5H_{10}N^+$], 69 (20), 59 (14), 56 (22) [$C_4H_8^+$ or $C_3H_6N^+$], 55 (54), 53 (16), 46 (11) [CH_3S^+].

1-[2-(2-Deutero-2-thiolanylthio)-3-methylbutyl]piperidine (**9**): 1.2 mmol n-Butyllithium were added to a solution of 300 mg (1.0 mmol) **8** in 15 ml THF at -40°C. After 2 h stirring at -40°C 0.5 ml deuterium oxide were dropped into the solution and stirring was continued for 16 h. Then aqueous sodium hydrogen carbonate solution was added and the aqueous phase was extracted 3 times with each 15 ml trichloromethane. The organic layer was dried over magnesium sulfate, the solvent was removed and the residue was worked up by column chromatography (50 g silica gel/trichloromethane). The degree of deuteration (74 %, diastereomeric ratio 1:1) was determined from the **^{1}H NMR** spectrum: The integrals of the 1-thiolanyl-H and the isopropyl-CH_3 signals were compared. The degree of deuteration could not be increased by using an excess of deuterated methanol instead of deuterium oxide.

1-[3-Methyl-2-(methylthio)butyl]piperidine (**10**): 1.5 mmol n-Butyllithium were added to a solution of 380 mg (1.4 mmol) **8** in 15 ml THF at -40°C. After 2 h stirring at -40°C 213 mg (1.5 mmol) iodomethane were added dropwise and the solution was stirred for 4 h. Then aqueous sodium hydrogen carbonate solution was added and the aqueous phase was extracted 3 times with each 15 ml trichloromethane. The organic layer was dried over magnesium sulfate, the solvent was removed and the residue was worked up by column chromatography (50 g silica gel/trichloromethane) to yield 120 mg (0.6 mmol, 43 %) **10** and 110 mg (29 %) of the racemized educt **8**. - **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.98 (d, 3H, CH(CH_3)$_2$, J = 6.6 Hz), 1.01 (d, 3H, CH(CH_3)$_2$, J = 6.6 Hz), 1.37 - 1.43 (m, 2H, piperidyl-4-CH_2), 1.52 - 1.58 (m, 4H, piperidyl-3- and 5-CH_2), 2.05 - 2.12 (m, 1H, C*H*(CH$_3$)$_2$), 2.12 (s, 3H, SCH_3), 2.35 - 2.52 (m, 6H, piperidyl-2- and 6-CH_2, CH-CH_2N), 2.60 (dt, 1H, C*H*(SMe)-CH$_2$, J = 7, 4.1 Hz). - **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 15.35 (prim., S*C*H$_3$), 17.47 (prim., CH(*C*H$_3$)$_2$), 19.47 (prim., CH(*C*H$_3$)$_2$), 24.01 (sec., piperidyl-4-*C*H$_2$), 25.53 (sec., 2C, piperidyl-3- and -5-*C*H$_2$), 30.11 (tert., CH(CH$_3$)$_2$), 51.83 (tert., *C*H(SMe)), 54.61 (sec., 2C, piperidyl-2- and -6-*C*H$_2$), 63.17 (sec., CH-CH$_2$N). - **MS** (70 ev): *m/z* (%) = 201 (1.6) [M$^+$], 185 (1.3), 155 (29), 138 (32), 110 (7), 99 (51), 98 (100) [$C_6H_{12}N^+$], 96 (21), 87 (24), 86 (16), 85 (61), 84 (32), 82 (8), 71 (6), 70 (23), 69 (30), 67 (9), 61 (17), 59 (9), 58 (6), 57 (11), 56 (22), 55 (67), 47 (10).

4-(Benzylthio)butanal (**11**): 1.7 mmol n-Butyllithium were added to a solution of 400 mg (1.5 mmol) **8** in 15 ml THF at -40°C. After 2 h stirring at -35°C 291 mg (1.7 mmol) benzyl bromide were added dropwise and the solution was stirred for 16 h. Then aqueous sodium hydrogen carbonate solution was added and the aqueous phase was extracted 3 times with each 15 ml trichloromethane. The organic layer was dried over magnesium sulfate, the solvent was removed and the residue was worked up by column chromatography (60 g silica gel/trichloromethane) to yield 110 mg (38 %) **11**. - **^{1}H NMR** (250 MHz, $CDCl_3$): δ = 1.72 - 1.84 (m, 2H, CH$_2$CH_2CH$_2$), 2.47 (t, 2H, CH$_2$CH_2S, J = 7.1 Hz), 2.55 (dt, 2H, CH_2CHO, J < 0.5 Hz, J = 7.1 Hz), 3.60 (s, 2H, CH_2Ph), 7.12 - 7.30 (m, 5H, Ar-*H*), 9.69 (t, 1H, C*H*O, J < 0.5 Hz). - **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 21.06 (sec.), 30.17 (sec.), 35.62 (sec.), 42.15 (sec.), 126.59 (tert.), 128.07 (tert., 2C), 128.39 (tert., 2C), 137.65 (quart.), 209.07 (quart., *C*HO). - MS (70 eV): *m/z* (%) = 194 (5) [M$^+$], 103 (7) [$C_4H_7OS^+$], 92 (15), 91 (100), 57 (6).

2-Benzyl-2-(methylthio)thiolane (**12**), *2-(1-hydroxy-1-phenylmethyl)-2-(methylthio)thiolane* (**13**), and *2-(1-hydroxycyclohexyl)-2-(methylthio)thiolane* (**14**) were obtained as previously described.[7]

2-(1,1-Dicyclopropyl-1-hydroxymethyl)-2-(methylthio)thiolane (**15**) was prepared analogously[7] from 0.75 g (5.6 mmol) 2-(methylthio)thiolane, 6.2 mmol n-butyllithium (15 % in hexane) and 0.74 g (6.7 mmol) dicyclopropylketone (Aldrich) and purified by column chromatography (eluent $CHCl_3$). - Yield: 0.60 g (44 %) colourless liquid. - **IR**: ν = 3446 (OH), 3086, 3003, 2961, 2927, 2859, 1613, 1443, 1384, 1298, 1265, 1235, 1210, 1197, 1170, 1116, 1072, 1061, 998, 925, 899, 878, 859, 838, 817, 783, 765, 729, 682, 656. - **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.21-0.34 (m, 2H, cyclopropyl-H), 0.36-0.47 (m, 3H,

cyclopropyl-H), 0.47-0.62 (m, 3H, cyclopropyl-H), 1.32-1.47 (m, 2H, cyclopropyl-H), 2.10-2.20 (m, 2H, 4-H), 2.21-2.30 (m, 1H, 3-H), 2.25 (s, 1H, OH), 2.31 (s, 3H, SCH_3), 2.43-2.50 (m, 1H, 3-H), 2.83-2.90 (m, 1H, 5-H), 2.92-2.98 (m, 1H, 5-H). - **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 0.98 (sec., cyclopropyl-C), 1.11 (sec., cyclopropyl-C), 1.13 (sec., cyclopropyl-C), 1.46 (sec., cyclopropyl-C), 16.81 (tert., cyclopropyl-C), 17.06 (tert., cyclopropyl-C), 19.42 (prim., SCH_3), 29.57 (sec.), 33.47 (sec.), 39.91 (sec.), 74.11 (quart. COH), 84.16 (quart. 2-C). - **MS** (70 eV): *m/z* = 196 (13) [M^+ - CH_3SH], 155 (34), 135 (10), 134 (60), 133 (53), 113 (21), 111 (92), [$C_5H_3OS^+$], 87 (35) [$C_5H_{11}O^+$], 85 (17), 69 (100) [$C_4H_5O^+$], 55 (12) [$C_3H_3O^+$], 48 (12) [CH_3S^+], 47 (17) [CH_2S^+]. - **HRMS**: cald. 197.1000; found 197.0973 [M^+ - SCH_3].

Dethioacetalization with Phenyl Dichlorophosphate (PDCP) in the Presence of Sodium Iodide and DMF in Acetonitrile.

General: The reaction was carried out under nitrogen in dry acetonitrile; protection from daylight was necessary. 1.1 Equivalents of PDCP were added to a solution of 1.0 equivalent of the semicyclic dithioacetal and 4 equivalents of sodium iodide in acetonitrile at room remperature. After 10 min. 1.1 equivalents of DMF were added. When the starting material could no more be detected by TLC, the solution was poured into 7 % aqueous potassium hydroxide solution. The aqueous layer was extracted 2 times with tetrachloromethane, the organic layer was dried over magnesium sulfate and the solvent was removed. The residue was worked up by column chromatography. The amounts of chemicals used for these reactions are given in the text below.

(E,Z)-2-Benzylidenethiolane (**20a, 20b**): 156 mg (0.7 mmol) 2-Benzyl-2-(methylthio)thiolane (**12**), 0.42 g (2.8 mmol) sodium iodide, 0.16 g (0.77 mmol) PDCP, 0.06 g (0.77 mmol) DMF. Reaction time: 40 min; Column chromatography: 35 g silica gel, solvent: tetrachloromethane. Yield: 95 mg (77 %), *E/Z*-ratio = 1:9. - **^{1}H NMR** (250 MHz, $CDCl_3$): *E-Isomer* **20b**: δ = 2.04 (quint., 2H, J = 6.8 Hz, 4-CH_2), 2.83 (dt, 2H, J = 6.8, J = 0.8 Hz, CH_2-C=CH), 3.14 (t, 2H, J = 6.8 Hz, 5-CH_2), 6.48 (t, 1H, J = 0.8 Hz, C=CHPh), 7.07-7.19 (m, 2H, Ar-H), 7.27-7.34 (m, 2H, Ar-H), 7.37-7.44 (m, 1H, Ar-H). *Z-Isomer* **20b**: differs from the E-isomer with respect to the following signals: δ = 2.14 (quint., 2H, J = 6.8 Hz, 4-CH_2), 3.08 (t, 2H, J = 6.8 Hz, 5-CH_2), 6.42 (t, 1H, J = 0.9 Hz, CHPh). - **^{13}C NMR** (63 MHz; $CDCl_3$): *E-Isomer* **20a**: δ = 28.4 (sec.), 35.6 (sec.), 40.21 (sec.), 117.0 (tert., C=*C*HPh), 125.7 (tert., Ar-C), 127.7 (tert., Ar-C), 128.3 (tert., Ar-C), 137.7 (quart., Ar-C), 143.1 (quart., *C*=CHPh). *Z-Isomer* **20b**: δ = 31.0 (sec.), 32.9 (sec.), 34.3 (sec.), 117.2 (tert., CHPh), 125.7 (tert., Ar-C), 128.3 (tert., Ar-C), 137.8 (quart., Ar-C), 143.1 (quart., *C*=CHPh).

2-Benzoylthiolane (**21**): 70 mg (0.31 mmol) 2-(1-Hydroxy-1-phenylmethyl)-2-(methylthio)thiolane (**13**), 1.16 mmol sodium iodide, 0.32 mmol PDCP, 0.32 mmol DMF. Reaction time: 70 min; Column chromatography over 3 g silica gel, solvent: $CHCl_3/CCl_4$ = 1:2). Yield: 20 mg (34 %). - **^{1}H NMR** (250 MHz, $CDCl_3$): δ = 2.01 (m, 1H, 1H of 3-CH_2), 2.17 (m, 1H, 1H of 4-CH_2), 2.21 (m, 1H, 1H of 4-CH_2), 2.62 (m, 1H), 2.94 (m, 2H, 5-CH_2), 4.74 (m, 1H, 2-CH), 7.27-7.59 (m, 3H, Ar-H), 7.91-8.01 (m, 2H, Ar-H). - **^{13}C NMR** (63 MHz): δ = 31.2 (sec.), 31.4 (sec.), 34.0 (sec.), 49.4 (tert., *C*H-C=O), 127.2 (tert., Ar-C), 128.6 (tert., Ar-C), 133.1 (tert., Ar-C), 136.0 (quart., Ar-C), 196.3 (quart., C=O). - *1-Thia-6-oxadispiro[4.1.5.0]dodecane* (**22**): 188 mg (0.81 mmol) 2-(1-Hydroxycyclohexyl)-2-(methylthio)thiolane (**14**), 0.72 mmol sodium iodide, 0.20 mmol PDCP, 0.20 mmol DMF. Reaction time: 1 h; Column chromatography over 20 g silica gel, solvent: tetrachloromethane. Yield: 30 mg (20 %). - **IR**: ν = 2932, 2872, 1645, 1449, 1245, 1000, 780. - **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 1.48-1.54 (m, 6H, 9-, 10-, 11-CH_2), 2.05 (quint., 2H, 3-CH_2), 2.12-2.17 (m, 4H, 8-CH_2 and 12-CH_2), 2.51 (t, 2H, 4-CH_2), 2.99 (t, 2H, 2-CH_2). - **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 25.88 (sec.), 26.42 (sec.), 26.85 (sec.),

29.79 (sec.), 31.69 (sec.), 31.69 (sec.), 32.54 (sec.), 33.87 (sec.), 126.08 (quart.), 129.81 (quart.). - **MS** (70 eV): *m/z* = 184 (6) [M^+], 153 (11), 114 (19), 107 (13), 105 (34), 107 (13), 105 (34), 103 (23), 99 (15), 91 (16), 84 (12), 81 (42), 79 (27), 77 (18), 71 (22), 69 (32), 67 (20), 65 (15), 59 (10), 55 (100) [$C_3H_3O^+$], 54 (11), 53 (19), 51 (18), 47 (15) [CH_3S^+], 46 (16) [CH_2S^+]. - **HRMS**: calcd. 184.0922 [M^+], 168.0973 [M^+ - O], found: 184.0931, 168.0945.

Dethioacetalization of 468 mg (2.02 mmol) *2-(1,1-dicyclopropyl-1-hydroxymethyl)-2-(methylthio)thiolane* (**15**) with 8.08 mmol sodium iodide, 2.22 mmol PDCP, and 2.22 mmol DMF (reaction time: 45 min) and subsequent column chromatography over 30 g silica gel/solvent: trichloromethane lead to 300 mg (76 %) of an oligomer of the possible structure **23**. - ^{13}C **NMR** (100 MHz, $CDCl_3$): δ = 0.05-0.85 (m, cyclopropyl-H), 1.05-1.91 (m), 1.95-2.10 (m), 2.15-2.68 (m), 2.89-3.15 (m).

Dethioacetalization with [Bis(trifluoroacetoxy)iodo]benzene (PIFA).

General: 1.5 to 2.5 equivalents of PIFA were added to a solution of the semicyclic dithioacetal in methanol/water at room temperature. When no more starting material could be detected by TLC the solution was poured into saturated aqueous sodium bicarbonate solution. The aqueous layer was extracted 3 times with ether, the organic layer was dried over magnesium sulfate and the solvent was removed. The residue was worked up by column chromatography. The solvent used for the elution of the products and other details are given in the table below.

Table. Reaction Conditions for the Dethioacetalization with PIFA

Educt	eq. of PIFA	Reaction time	Solvent ($MeOH/H_2O$ -ratio)	Yield[a] total [%]	Yield[a] asym. [%]	Yield[a] sym. [%]	Eluent used for chromatography
12	1.5	10 min	MeOH	21	21	0	PE/Et_2O 25:1
12	1.5	10 min	(9 : 1)	49	28	21	PE/Et_2O 5:1
12	2.5	5 min	(9 : 1)	85	51	34	b)
13	2.5	10 min	MeOH	15	3	13	
13	2.4	1 d	MeOH	25	5	20	CH_2Cl_2/MeOH 10:1
13	2.5	10 min	(9 : 1)	41	1	40	
13	2.5	90 min	(9 : 1)	58	19	39	CH_2Cl_2 b)
13	2.5	10 min	(1 : 1)	63	6	57	b)
13	1.5	10 min	(1 : 1)	44	6	38	
13	2.5	15 min	H_2O	14	2	12	
14	2.5	20 min	(1 : 1)	38	10	28	$CHCl_3$
15	2.5	30 min	(1 : 1)	60	16	44	$CHCl_3$

a) The yields were determined by ^1H NMR spectroscopy with 1,2-diphenylethane as reference substance.

b) Conditions of the preparative experiment.

5-(Methyldithio)-1-phenylpentan-2-one (**24b**). - Yield 106 mg (34 %) from 291 mg (1.30 mmol) **12**. - **IR**: ν = 3029, 2916, 1713 (C=O), 1609, 1496, 1454, 1413, 1365, 1308, 1125, 1075, 952, 700. - ^1H **NMR** (250 MHz, $CDCl_3$): δ = 1.96 (quint., 2H, $CH_2CH_2CH_2$, J = 7.0 Hz), 2.36 (s, 3H, SCH_3), 2.60 (t, 2H, $CH_2CH_2CH_2$), 2.65 (t, 2H, $CH_2CH_2CH_2$, J = 7.0 Hz), 3.70 (s, 2H, $PhCH_2$), 7.18-7.24 (m, 2H, Ar-H),

7.27-7.38 (m, 3H, Ar-H). - **^{13}C NMR** (63 MHz, $CDCl_3$): δ = 22.79 (sec., SCH_2), 23.17 (prim., SCH_3), 37.05 (sec., $CH_2CH_2CH_2$), 39.94 (sec., CH_2-CO-), 50.30 (sec., CH_2Ph), 127.09 (tert., Ar-C, C-4'), 128.78 (tert., Ar-C, C-3' and C-5'), 129.40 (tert., Ar-C, C-2' and C-6'), 134.35 (quart. Ar-C, C-1'), 207.58 (quart., C=O). - **MS** (70 eV): *m/z* = 240 (1) [M^+], 162 (9), 161 (89) [$M^+ - S_2CH_3$], 149 (7), 101 (5), 93 (9), 92 (9), 91 (100) [$C_7H_7^+$], 79 (15), [$S_2CH_3^+$], 73 (23), 65 (18), 45 (8). - **HRMS**: calcd.: 240.0643 [M^+], found: 240.0647.

Bis-(4-oxo-5-phenylpentyl) disulfide (**24a**). - Yield: 127 mg (51 %) from 291 mg (1.30 mmol) **12**. - **IR**: ν = 3062, 3029, 2931, 1708 (C=O), 1603, 1496, 1454, 1411, 1365, 1309, 1190, 1125, 1076, 921, 733, 700. - **^{1}H NMR** (250 MHz, $CDCl_3$): δ = 1.91 (quint., 4H, $CH_2CH_2CH_2$, J = 7.2 Hz), 2.57 (t, 4H, $CH_2CH_2CH_2$, J = 7.2 Hz), 2.59 (t, 4H, $CH_2CH_2CH_2$, J = 7.2 Hz), 3.68 (s, 4H, CH_2Ph), 7.17-7.23 (m, 4H, Ar-H), 7.25-7.38 (m, 6H, Ar-H). - **^{13}C NMR** (63 MHz, $CDCl_3$): δ = 22.78 (sec., 2C, SCH_2), 37.74 (sec., 2C, $CH_2CH_2CH_2$), 39.92 (sec., 2C, CH_2-CO), 50.26 (sec., 2C, CH_2Ph), 127.08 (tert., 2C, Ar-C, C-4'), 128.77 (tert., 4C, Ar-C, C-3' and C-5'), 129.40 (tert., 4C, Ar-C, C-2' and C-6'), 134.13 (quart., 2C, Ar-C, C-1'), 207.51 (quart., 2C, C=O). - **MS** (70 eV): *m/z* = 386 (1) [M^+], 193 (8) [$M^+/2$], 163 (13), 161 (100) [$C_{11}H_{13}O^+$], 92 (7), 91 (95) [$C_7H_7^+$], 65 (9), 55 (5). - **HRMS**: calcd.: 193.0658, 161.0966, found: 193.0658 [$C_{11}H_{13}OS$, ($M^+/2$)], 161.0964 ($C_{11}H_{13}O^+$),

1-Hydroxy-5-(methyldithio)-1-phenylpentan-2-one (**25b**). - Yield: 158 mg (21 %) from 723 mg (3.01 mmol) **13**. - **IR**: ν = 3652 (OH), 3031, 2917, 2856, 1714 (C=O). 1677, 1454, 1253, 1192, 1063, 701. - **^{1}H NMR** (250 MHz, $CDCl_3$): δ = 1.95 (m, 2H, $CH_2CH_2CH_2$, J = 7.3, 6.8 Hz), 2.33 (s, 3H, SCH_3), 2.47-2.65 (m, 4H, $CH_2CH_2CH_2$, J = 7.3, 6.8 Hz), 4.30 (bs, 1H, OH), 5.10 (s, 1H, CHOH), 7.35 (d, 2H, J = 7.6 Hz, Ar-H), 7.38 (dd, 2H, J = 4.4, 7.6 Hz, Ar-H), 7.38 (t, 1H, Ar-H, J = 7.6 Hz). - **^{13}C NMR** ($CDCl_3$, 63 MHz): δ = 22.75 (sec., $CH_2CH_2CH_2$), 23.12 (prim., SCH_3), 35.99 (sec., $CH_2CH_2CH_2$), 36.80 (sec., $CH_2CH_2CH_2$), 79.80 (tert., CHOH), 127.39 (tert., 2C, Ar-C), 128.82 (tert., Ar-C), 129.08 (tert., 2C, Ar-C), 137.95 (quart., Ar-C), 208.87 (quart., C=O). - **MS** (70 eV): *m/z* = 256 (4) [M^+], 209 (4) [$M^+ - SCH_3$], 177 (24) [$M^+ - S_2CH_3$], 151 (6), 149 (55) [$C_9H_9O_2^+$], 107 (100) [$C_7H_7O^+$], 105 (61) [$C_7H_5O^+$], 103 (40) [$C_8H_7^+$], 79 (53) [$S_2CH_3^+$], 77 (32) [$C_6H_5^+$], 73 (32), 72 (66), 71 (13), 51 (21) [$C_3H_4^+$], 47 (14) [SCH_3^+], 45 (17) [CHS^+]. -
$C_{12}H_{16}O_2S_2$ (256.39): calcd.: C 56.22, H 6.29, S 25.01, found: C 56.12, H 6.24, S 24.60.

Bis(5-hydroxy-4-oxo-5-phenylpentyl) disulfide (**25a**). - Yield: 97 mg (61 %) from 297 mg (1.24 mmol) **13**. - **IR**: ν = 3430 (OH), 2939, 1713 (C=O), 1600, 1494, 1455, 1407, 1192, 1120, 702, 616. - **^{1}H NMR** (250 MHz, $CDCl_3$, mixture of diastereoisomers): δ = 1.77-2.05 (m, 4H, $CH_2CH_2CH_2$, J = 7.0 Hz), 2.40-2.65 (m, 8H, $CH_2CH_2CH_2$, J = 7.0 Hz), 3.70 (bs, 2H, CHOH), 5.10 (s, 2H, CHOH), 7.28-7.40 (m, 10H, Ar-H). - **^{13}C NMR** (63 MHz, $CDCl_3$, mixture of diastereoisomers): δ = 22.71 (sec., 2C, $CH_2CH_2CH_2$), 35.94 (sec., 2C, $CH_2CH_2CH_2$), 37.44 (sec., 2C, $CH_2CH_2CH_2$), 79.79 (tert., 2C, CHOH), 127.31 and 127.37 (tert., each 2C, Ar-C), 128.82 and 128.91 (tert., each 2C, Ar-C), 129.07 and 129.14 (tert., each 2C, Ar-C), 137.83 and 137.97 (quart., each 2C, Ar-C), 207.25 and 208.29 (quart., C=O). - **MS** (70 eV): *m/z* = 418 (1) [M^+], 311 (3) [$M^+ - C_7H_7$], 209 (27) [$M/2^+ - S$], 205 (5), 149 (7) [$C_9H_9O_2^+$], 131 (13) [$C_9H_7O^+$], 117 (13), 108 (25), 107 (98) [$C_7H_7O^+$], 106 (11), 105 (100) [$C_7H_5O^+$], 103 (48) [$C_8H_7^+$], 102 (7), 91 (14) [$C_7H_7^+$], 80 (78), 78 (13), 77 (96), [$C_6H_5^+$], 72 (11), 55 (10), 51 (29) [$C_3H_4^+$], 45 (14) [CHS^+].

1-(1-Hydroxycyclohexyl)-4-(methyldithio)butan-1-one (**26b**). - Yield: 22 mg (10 %) from 200 mg (0.86 mmol) **14**. - **IR**: ν = 3477 (OH), 2937, 2879, 1708, 1445, 1361, 1275, 1154, 991. - **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 1.45-1.51 (m, 2H, cyclohexyl-H), 1.61-1.79 (m, 8H, cyclohexyl-H), 2.04 (quint., 2H, $CH_2CH_2CH_2$), 2.40 (s, 3H, SCH_3), 2.72 (dt, 4H, $CH_2CH_2CH_2$), 3.36 (s, 1H, COH). - **^{13}C NMR** (100

MHz, $CDCl_3$): δ = 21.02 (sec., cyclohexyl-C), 22.67 (sec., $CH_2CH_2CH_2$), 23.10 (prim., SCH_3), 25.23 (sec., 2C, cyclohexyl-C), 33.82 (sec., SCH_2), 33.90 (sec., 2C, cyclohexyl-C), 37.00 (sec., CO-CH_2), 77.97 (quart., COH), 214.06 (quart., C=O). - **MS** (70 eV): *m/z* = 248 (1) $[M]^+$, 170 (23), $[M^+ - 79]$, 103 (13), $[C_4H_7OS^+]$, 102 (2), $[M^+ - 47]$, 99 (100), $[C_6H_{11}O^+]$, 79 (29), 71 (10), 55 (22), 47 (6), $[CH_3S^+]$. - **HRMS**: calcd: 248.0947 (M^+), 169.1229 ($M^+ - S_2CH_3$), found: 248.0903, 169.1239.

Bis[4-(1-hydroxycyclohexyl)-4-oxobutyl] disulfide (**26a**). -Yield: 48 mg (28 %). - **IR**: ν = 3477 (OH), 2937, 1711 (C=O), 1445, 1363, 1275, 1154, 991. - **^{1}H NMR** (400 MHz, $CDCl_3$, mixture of diastereoisomers). δ = 1.44-1.48 (m, 4H, cyclohexyl-H), 1.59-1.74 (m, 16H, cyclohexyl-H), 2.00 (m, 4H, $CH_2CH_2CH_2$, J = 7.0 Hz), 2.66-2.73 (m, 8H, $CH_2CH_2CH_2$), 3.42 (bs, 2H, COH). - **^{13}C NMR** (100 MHz, $CDCl_3$, mixture of diastereoisomers): *Diastereoisomer 1*: δ = 20.47 (sec., 2C), 22.16 (sec., 2C), 24.58 (sec., 2C), 24.67 (sec., 2C), 33.28 (sec., 2C), 33.33 (sec., 2C), 33.39 (sec., 2C), 37.18 (sec., 2C), 77.43 (quart., 2C, COH), 214.16 (quart., 2C, C=O). *Diastereoisomer 2* differs from Diastereoisomer *1* with respect to the following signals: δ = 20.40 (sec., instead of 20.47), 22.12 (sec., instead of 22.16). - **MS** (70 eV): *m/z* = 201 (6), $[M/2^+]$, 169 (17), 103 (21), 99 (100), 86 (13), 81 (54), 79 (13), 69 (12), $[C_4H_5O^+]$, 67 (14), 55 (22), $[C_3H_3O^+]$. - **HRMS**: found: 201.0935 ($C_{10}H_{17}O_2S$, $[M/2^+]$), calcd: 201.0949.

1,1-Dicyclopropyl-1-hydroxy-5-(methyldithio)pentan-2-one (**27b**). Yield: 54 mg (17 %) from 300 mg (1.23 mmol) **15**. - **IR**: ν = 3464 (OH), 3091, 3011, 2952, 1710 (C=O), 1356, 1122, 1013, 829. - **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.18-0.30 (m, 4H, cyclopropyl-H), 0.41-0.49 (m, 2H, cyclopropyl-H), 0.60-0.67 (m, 2H, cyclopropyl-H), 1.00-1.08 (m, 2H, cyclopropyl-H), 2.11 (quint., 2H, $CH_2CH_2CH_2$, J = 7.0 Hz), 2.41 (s, 3H, SCH_3), 2.74 (t, 2H, $CH_2CH_2CH_2$, J = 7.0 Hz), 2.90 (t, 2H, $CH_2CH_2CH_2$, J = 7.0 Hz), 3.36 (s, 1H, COH). - **^{13}C NMR** (100 MHz, $CDCl_3$): δ = -1.26 (sec., 2C, cyclopropyl-C), 0.78 (sec., 2C, cyclopropyl-C), 16.08 (tert., 2C, cyclopropyl-C), 22.78 (sec., $CH_2CH_2CH_2$), 23.12 (prim., SCH_3), 33.73 (sec., $CH_2CH_2CH_2$), 37.02 (sec., $CH_2CH_2CH_2$), 75.99 (quart., COH), 212.67 (quart., C=O). - **MS** (70 eV): *m/z* = 166 (6), $[M^+ - CH_3SSCH_3]$, 153 (5), $[C_{10}H_{16}O^+]$, 112 (7), 111 (100) $[C_7H_{11}O^+]$, 79 (10), 73 (5), 69 (61), $[C_4H_5O^+]$, 55 (9).

Bis(5,5-dicyclopropyl-5-hydroxy-4-oxopentyl) disulfide (**27a**). - Yield: 121 mg (46 %) from 300 mg (1.23 mmol) **15**. - **IR**: ν = 3464 (OH), 3091, 3011, 1710 (C=O), 1356, 1122, 1013, 829, 707. - **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.15-0.27 (m, 8H, cyclopropyl-H), 0.39-0.46 (m, 4H, cyclopropyl-H), 0.58-0.64 (m, 4H, cyclopropyl-H), 0.98-1.05 (m, 4H, cyclopropyl-H), 2.07 (quint., 4H, $CH_2CH_2CH_2$, J = 7.0 Hz), 2.70 (t, 4H, $CH_2CH_2CH_2$, J = 6.9 Hz), 2.88 (t, 4H, $CH_2CH_2CH_2$, J = 7.0 Hz), 3.32 (s, 2H, COH). - **^{13}C NMR** (100 MHz, $CDCl_3$): δ = -1.22 (sec., 2C, cyclopropyl-C), 0.84 (sec., 2C, cyclopropyl-C), 16.12 (tert., 2C, cyclopropyl-C), 22.87 (sec., $CH_2CH_2CH_2$), 33.76 (sec., $CH_2CH_2CH_2$), 37.76 (sec., $CH_2CH_2CH_2$), 76.03 (quart., COH), 212.67 (quart., C=O). - **MS** (70 eV): *m/e* = 426 (0.2), $[M^+]$, 221 (5), 213 (10), 125 (5), 112 (11), 111 (100) $[C_7H_{11}O^+]$, 69 (44) $[C_4H_5O^+]$, 55 (7). - **HRMS**: calcd: 426.1929, found: 426.1899 (M^+).

Dethioacetalization with Dowex W50® and Paraformaldehyde in Acetone:

General: 125 mg DOWEX W50® and 450 mg (5 mmol) paraformaldehyde were added to a solution of 0.5 mmol of the semicyclic dithioacetal in 10 ml dry acetone containing one drop of water and the solution was refluxed until no educt could be detected by TLC. The mixture was filtered and the solvent removed. The residue was worked up by column chromatography.

Dethioacetalization of 112 mg (0.5 mmol) **12** gave 30 mg (26 %) **24b**.

5-(Methyldithio)-1-phenylpentane-1,2-dione (**28**): from 120 mg (0.5 mmol) **13**. Yield: 40 mg (32 %). - **IR**: ν = 3077, 2920, 1713 (C=O), 1673 (C=O), 1597, 1450, 1266, 1101, 905, 788, 691. - **^{1}H NMR** (400

MHz, $CDCl_3$): δ = 2.11-2.18 (m, 2H, $CH_2CH_2CH_2$, J = 7.12, 7.14 Hz), 4.21 (s, 3H, SCH_3), 2.79 (t, 2H, SCH_2, J = 7.14 Hz), 3.04 (t, 2H, CH_2-CO, J = 7.12 Hz), 7.43-7.56 (m, 2H, m-Ar-H), 7.61-7.66 (m, 1H, p-Ar-H), 7.78-8.00 (m, 2H, o-Ar-H), - **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 21.81 (prim.), 22.72 (sec.), 36.52 (sec.), 36.58 (sec.), 128.15 (quart.), 128.43 (tert, 2C, m-Ar-C), 129.81 (tert, 2C, o-Ar-C), 134.21 (tert, p-Ar-C), 191.43 (quart., C=O), 201.82 (quart., C=O). - **MS** (70 eV): *m/z* = 254 (1.2) [M^+], 148 (22), 106 (8), 105 (100) [$PhCO^+$), 87 (12), 79 (8), 77 (44), 73 (14), 51 (15). - **HRMS** calcd: 254.0452, 207.0480, 149.0095, 105.0374, found: 254.0436 [M^+], 207.0480 ($C_{11}H_{11}O_2S$), 149.0094 ($C_5H_9OS_2$), 105.0328 (C_4H_9OS).

1-Thia-6,8-dioxadispiro[4.3.5.0]tetradecane (**29**): from 116 mg (0.5 mmol) **14**, 50 mg (5 mmol) paraformaldehyde; reaction time: 3 h; Column chromatography over 50 g silica gel, solvent: trichloromethane. Yield: 70 mg (66 %) **29**. - **IR:** ν = 2932, 2861, 2755, 1713, 1449, 1317, 1088, 1041, 990, 932, 904, 836, 782, 731. - **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 1.09-1.20 (m, 1H), 1.30 (dt, 1H, J = 4.58, J = 13.2 Hz), 1.39 (dt, 1H, J = 5.08, J = 12.7 Hz), 1.51-1.79 (m, 7H), 1.88-1.95 (m, 1H), 2.07-2.26 (m, 3H), 2.28-2.82 (m, 1H, 1H of thiolanyl-5-CH_2), 2.98-3.03 (m, 1H, 1H of thiolanyl-5-CH_2), 5.01 (s, 2H, OCH_2O). - **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 21.45 (sec.), 22.56 (sec.), 25.10 (sec.), 28.10 (sec.), 30.88 (sec.), 31.52 (sec.), 32.80 (sec.), 37.33 (sec.), 81.88 (quart.), 91.08 (sec.), 107.10 (quart.). - **MS** (70 eV): *m/z* = 214 (11) [M^+], 116 (26), 113 (23), 112 (100), 111 (27), 97 (37), 87 (14), 86 (14), 85 (10), 84 (41), 81 (36), 79 (16), 67 (38), 58 (22), 55 (47), 54 (25), 53 (14). - **HRMS** calcd: 214.1028, 116.0296, 113.0966, 112.0888, 111.0810, 103.0218, found: 214.1008, [M^+], 116.0280 ($C_5H_8OS^+$), 113.0889 ($C_7H_{13}O^+$), 112.0836 ($C_7H_{12}O^+$), 111.0737 ($C_7H_{11}O^+$), 103.0165 ($C_4H_7OS^+$).

Dethioacetalization of 2-(1,1-dicyclopropyl-1-hydroxymethyl)-2-(methylthio)thiolane (**15**): 116 mg (0.5 mmol) **15**, 50 mg (5 mmol) paraformaldehyde. Reaction time 160 min; column chromatography over 50 g silica gel, solvent: trichloromethane. Yield: 30 mg (27 %) of *2-(dicyclopropylmethylene)-3-(methylthio)thiolane* (**30**). - **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.49-0.55, (m, 1H, cyclopropyl-H), 0.57-0.74 (m, 6H, cyclopropyl-H), 0.81-0.89 (m, 1H, cyclopropyl-H), 1.18-1.25 (m, 1H, cyclopropyl-H), 1.49-1.55 (m, 1H, cyclopropyl-H), 2.07-2.16 (m, 1H, 4-H), 2.16 (s, 3H, SCH_3), 2.27-2.32 (m, 1H, 4-H), 2.95-2.99 (m, 1H, 5-H), 3.31-3.38 (m, 1H, 5-H), 4.45 (d, J = 5.1 Hz, 1H, 3-H). - **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 2.37 (sec., cyclopropyl-CH_2), 2.91 (sec., cyclopropyl-CH_2), 3.30 (sec., cyclopropyl-CH_2), 3.64 (sec., cyclopropyl-CH_2), 11.97 (tert., cyclopropyl-CH), 12.04 (prim., SCH_3), 12.45 (tert., cyclopropyl-CH), 27.51 (sec., C-4), 32.78 (sec., C-5), 47.16 (tert., C-3), 126.09 (quart., C-2'), 136.16 (quart., C-2).

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