First Asymmetric Synthesis of (+)-Sordidin and (–)-7-*epi*-Sordidin, Aggregation Pheromones of the Banana Weevil *Cosmopolites sordidus*

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Keywords: Pheromones / Asymmetric synthesis / SAMP/RAMP-Hydrazones / Quaternary stereocenters / Epoxide opening

The asymmetric synthesis of (1*S*,3*R*,5*R*,7*S*)-(+)-sordidin and 7-*epi*-(1*S*,3*R*,5*R*,7*R*)-(–)-sordidin, both components of the natural male-produced aggregation pheromone of the banana weevil *Cosmopolites sordidus* (Germar), starting from 2,2-dimethyl-1,3-dioxan-5-one is described. Two of the stereogenic centers were generated by three α-alkylations of the corresponding RAMP-hydrazone. Diastereoselective epoxide opening as another key step of the synthesis employing the aza-enolate of 3-pentanone SAEP-hydrazone as nucleophile and subsequent acidic intramolecular acetalisation furnished the sordidin C-7 epimers in good overall yield (39 %) as a 1.5:1 diastereomeric mixture. The epimers could be separated by preparative GC and thus, each of them could be obtained in high diastereomeric and enantiomeric purity (*de* ≥ 97 %, *ee* ≥ 98 %).

Introduction

The banana weevil *Cosmopolites sordidus* (Germar) is the most important world-wide insect pest of banana plants.[1] These longlived weevils lay their eggs in the rhizome of the plant. The larvae hatch and then feed and tunnel in the rhizome of the plant, weakening it and leading to snapping of the rhizome at ground level before the bunch is ripe. The first evidence for a volatile male-produced pheromone was given by Budenberg et al. in 1993.[2] In 1995 Ducrot et al. reported the isolation and identification of the major pheromone compound,[3] for which they proposed the trivial name sordidin. They also carried out the first synthesis, including a Baeyer–Villiger oxidation as the key step.[4] Further syntheses were published by Ducrot,[5] Oehlschlager,[6] Mori,[7] and Kitching.[8] Recently, Wardrop et al. reported on the synthesis of *rac*-7-*epi*-sordidin employing a regioselective rhodium(II)-catalysed intramolecular diazocarbonyl C–H insertion as key step.[9] Since the conversion of *rac*-7-*epi*-sordidin to *rac*-sordidin has been discribed by Mori et al., the latter synthesis also constitutes a formal synthesis of *rac*-sordidin (**1**).[7]

To the best of our knowledge, all of these former approaches are based on the concept of ex-chiral-pool synthesis or led to a racemic mixture of the title pheromones. To date no asymmetric synthesis leading directly to the enantiomerically pure major pheromone (+)-sordidin (**1**) has been published.

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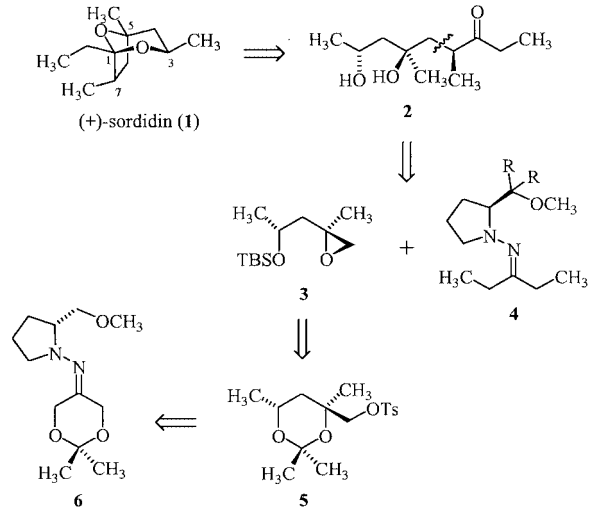
We now wish to report on the first asymmetric synthesis of (1*S*,3*R*,5*R*,7*S*)-(+)-sordidin (**1**), the main component of the pheromone and its epimer, 7-*epi*-(1*S*,3*R*,5*R*,7*R*)-(–)-sordidin (7-*epi*-**1**), starting from the dioxanone RAMP-hydrazone **6** as a chiral 1,3-dihydroxyacetone equivalent.

As is depicted in Scheme 1, our retrosynthetic analysis led us to the dihydroxy ketone **2**, which after intramolecular acetalisation would lead to the target pheromone. The dihydroxy ketone **2** was planned to be prepared by diastereoselective ring opening of the epoxide **3** with either enantiomerically pure 3-pentanone SAMP- (R = H) or SAEP- (R = Et) -hydrazone **4** in one of the key steps of the synthesis. To create the desired configuration in oxirane **3**, it would be necessary to start from the tosyl dioxane **5**, which in turn



Scheme 1. Retrosynthetic analysis of sordidin (**1**).

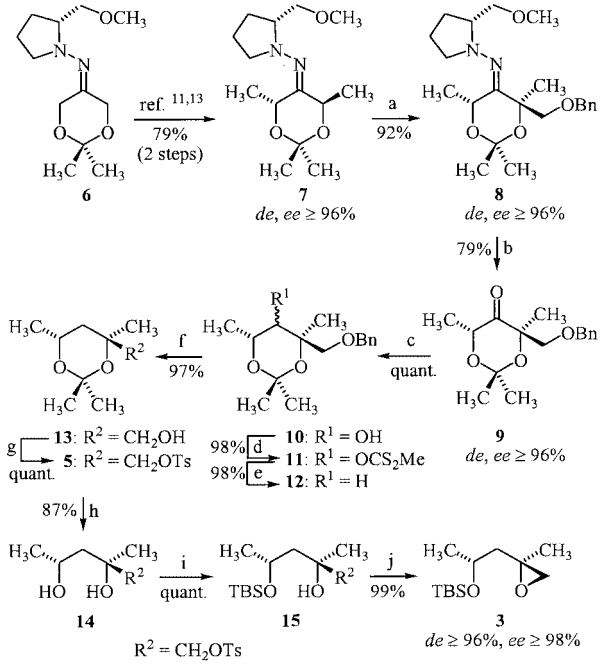
 DOI: 10.1002/ejoc.200500112

leads back to the RAMP-hydrazone **6**, the starting material for asymmetric alkylations using the SAMP/RAMP-hydrazone methodology.[10]

Initial attempts to employ a related iodide instead of epoxide **3** as electrophile in the final alkylation step, unfortunately failed.

Results and Discussion

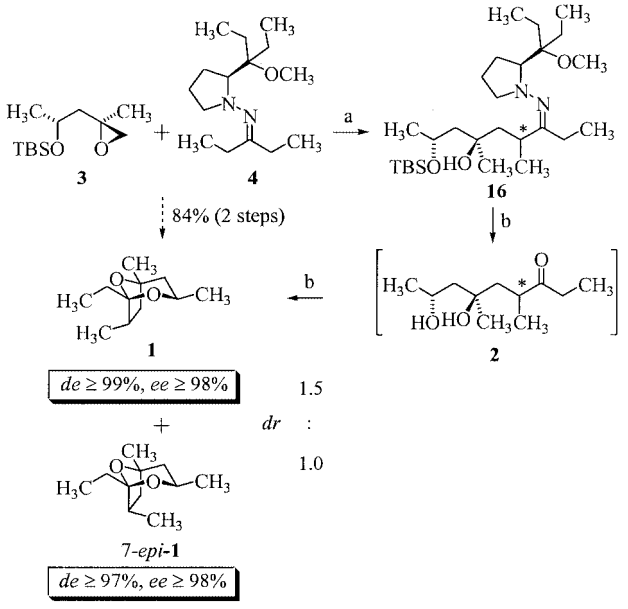
As outlined in Scheme 2, our asymmetric synthesis of the key intermediate epoxide **3** started from 2,2-dimethyl-1,3-dioxan-5-one RAMP-hydrazone **6**, available by condensation of (*R*)-1-amino-2-methoxymethylpyrrolidine (RAMP) with the corresponding dioxanone.[11,12] Double alkylation of hydrazone **6** with methyl iodide at the α- and α′-positions was carried out under standard conditions for this system (*t*BuLi, THF, –78 °C, 2 h, then MeI, –100 °C to room temperature, 15 h) and led to the *trans*-dimethylated hydrazone **7** in 79% yield for two steps and excellent stereoselectivity (*de*, *ee* ≥ 96%).[11,13] In the next step, the quaternary stereocenter bearing the desired tertiary alcohol function was generated using benzyloxymethyl chloride (BOMCl) as the electrophile to trap the lithiated hydrazone **7** according to our dioxanone procedure.[14] The α-quaternary hydrazone **8** was thus obtained in very good yield (92%) and excellent diastereomeric and enantiomeric excesses (*de*, *ee* ≥ 96%, ^{13}C NMR, GC) with the required *cis* relationship of the methyl substituents at the α- and α′-positions as a consequence of the typical relative topicity in RAMP-hydrazone alkylations in the third step. Subsequent ozonolysis at –78 °C occurred without epimerisation and provided the trisubstituted dioxanone **9** in 79% yield. As it has been previously demonstrated in related substrate cases, the most efficient reaction sequence for the removal of the oxo group is a radical deoxygenation according to the Barton–McCombie protocol.[15] Thus, ketone **9** was reduced with sodium borohydride to a diastereomeric mixture of the alcohols **10** (*dr* = 1:4), which were converted into the corresponding xanthates **11** in excellent yield (98%, 2 steps). Reduction of the xanthates **11** was easily accomplished with tributyltin hydride and a catalytic amount of AIBN in refluxing toluene and furnished the dioxane **12** in 98% yield. In the next step the benzyl protecting group of the primary alcohol had to be transformed into a leaving group in order to generate, after cleavage of the acetonide, an epoxide moiety at the quaternary carbon atom. This protection and leaving group had to be stable against acidic conditions and therefore the tosylate group was chosen. To achieve deprotection of the benzyl group first the benzyl ether **12** was cleaved with calcium in liquid ammonia to the primary alcohol **13** in excellent yield (97%). The standard hydrogenation protocol (Pd/C) for removal of benzyl protecting groups did not work in this case. Furthermore, initial attempts to convert the alcohol **13** directly into the corresponding iodide using triphenylphosphane, imidazole and iodine, failed. Next the alcohol **13** was transformed to the corresponding tosylate **5** in practically quantitative yield. Cleavage of the acetonide occurred either by treatment of **5** with trifluoroacetic acid in a biphasic system (THF/H_2O) or with 3 N HCl in aqueous methanol at room temperature. The latter conditions revealed the diol **14** bearing a secondary and a tertiary alcohol function in 87% yield, slightly better than the TFA conditions (84%). According to the retrosynthetic analysis given in Scheme 1, the secondary alcohol function had to be protected previous to the tertiary one. This was achieved by using 1 equiv. each of TBSOTf and 2,6-lutidine and afforded chemoselectively and quantitatively the alcohol **15** leaving the less reactive tertiary alcohol unprotected. Deprotonation of the tertiary alcohol with paraffin-free sodium hydride (4.0 equiv.) in dry THF afforded the oxirane **3** in 99% yield and in virtually diastereomerically pure form according to ^{13}C NMR spectroscopy (*de* ≥ 96%) without the need of further purification. The enantiomeric excess (*ee* ≥ 98%) of this key intermediate **3** was determined by chiral stationary phase GC based on the available enantiomeric oxirane *ent*-**3**, which was synthesized starting from 2,2-dimethyl-1,3-dioxan-5-one SAMP-hydrazone *ent*-**6**.



Scheme 2. Synthesis of the key intermediate **3**. a) 1. *t*BuLi, THF, –78 °C, 2. BOMCl, –100 °C to room temperature; b) O_3, CH_2Cl_2, –78 °C; c) $NaBH_4$, MeOH, 0 °C; d) 1. NaH, THF, 0 °C, 2. CS_2, MeI; e) nBu$_3$SnH, AIBN, toluene, reflux; f) Ca/NH_3; g) Et_3N, DMAP, CH_2Cl_2, TsCl, room temperature; h) 3N HCl, H_2O/MeOH, room temperature; i) 2,6-lutidine, CH_2Cl_2, TBSOTf, 0 °C; j) NaH, THF, 0 °C.

Finally, the oxirane **3** was opened by the aza-enolate of 3-pentanone SAEP-hydrazone **4** in the presence of anhydrous LiCl (6.0 equiv.) as additive according to a modified literature procedure for enolate oxirane ring openings.[16] In our case, a large excess of aza-enolate (9.2 equiv.), generated from 3-pentanone SAEP-hydrazone **4** and LDA (11.0 equiv.), was required to reach a complete conversion in this reaction. Related aza-enolates derived from 3-penta-

none SAMP-hydrazone and 3-pentanone *N*,*N*-dimethylhydrazone instead of **4** did not improve the results. Thus, the mixture of the crude product hydrazone **16** and the excess of hydrazone **4** was directly used in an acidic acetalisation reaction utilizing aqueous 3 N HCl in a biphasic system (H_2O/*n*-pentane) and gave after column chromatography a diastereomeric mixture of sordidin (**1**) and 7-*epi*-sordidin (7-*epi*-**1**) in 84% yield over two steps in a 1.5:1 ratio (Scheme 3).



Scheme 3. Final steps of the asymmetric synthesis of sordidin and 7-*epi*-sordidin. a) 1. LiCl, LDA, THF, –78 °C, **4**, 1 h, then 0 °C, 10 min, 2. **3**, –78 °C to room temperature, 15 h; b) 3 N HCl, H_2O/*n*-pentane, room temperature, 6 d.

Obviously, under the acidic conditions applied, both the TBS protecting group and the hydrazone moiety were hydrolysed, followed by an intramolecular acetalisation to the target pheromone in one single step. However, the diastereoselectivity, which has apparently been obtained by prior asymmetric epoxide opening of **3** with the aza-enolate of 3-pentanone SAEP-hydrazone **4** has been affected under the acidic conditions causing substantial C-7 epimerisation as it has been previously observed by Mori et al.[7]

Gratifyingly, we succeeded in separating the desired sordidin epimers by preparative gas chromatography. As a result, both could be obtained in diasteromerically pure form according to GC analysis (in the case of sordidin: *de* ≥ 99%; in the case of 7-epi-sordidin: *de* ≥ 97%) and with high enantiomeric excess for each epimer (*ee* ≥ 98%).

Conclusions

In summary, we have described the first asymmetric synthesis of the banana weevil aggregation pheromones sordidin and 7-*epi*-sordidin in 14 steps with excellent diastereo- and enantiomeric excesses (*de* ≥ 97%, *ee* ≥ 98) and in 39% overall yield, starting from 2,2-dimethyl-1,3-dioxan-5-one RAMP-hydrazone. Both diastereomers were separated by preparative GC and their NMR spectroscopic data[6] and optical rotation values[17] are consistent with those given in the literature.

Experimental Section

General Remarks: All reagents were of commercial quality used from freshly opened containers. Solvents were dried and purified by conventional methods prior to use. Tetrahydrofuran was freshly distilled under argon from sodium/lead alloy. *t*BuLi (15% in *n*-pentane) and *n*BuLi (1.6 N in hexane) were purchased from Merck, Darmstadt. Diisopropylamine was distilled from CaH_2 and stored over molecular sieves. Reactions were conducted using standard Schlenk techniques under argon. Preparative column chromatography: Merck silica gel 60, particle size 0.040–0.063 mm (230–240 mesh). Analytical TLC: silica gel 60 F_{254} plates from Merck, Darmstadt. Optical rotation values were measured with a Perkin–Elmer P241 polarimeter, solvents used were of Merck UVASOL quality. Microanalyses were obtained with an Elementar Vario EL. Mass spectra were recorded with Varian MAT 212 (EI, 70 eV, 1 mA) and with Finnigan MAT SSQ 7000 (CI, 100 eV) spectrometers. High-resolution MS: Finningan MAT, MAT 95. IR spectra were obtained with a Perkin–Elmer FT/IR 1760 instrument. ^1H and ^{13}C NMR spectra were recorded with Varian VXR 300, Varian Gemini 300 or Varian Inova 400 spectrometers. All measurements were performed with tetramethylsilane as internal standard. The chiral auxiliaries RAMP [(*R*)-1-amino-2-(methoxymethyl)pyrrolidine] and SAMP [(*S*)-1-amino-2-(methoxymethyl)pyrrolidine] were prepared from (*R*)-proline or (*S*)-proline according to literature procedures.[18] 2,2-Dimethyl-1,3-dioxan-5-one was prepared according to the procedure described by Hoppe et al.[19] Benzyloxymethyl chloride was prepared according to a literature procedure.[20]

[(4*S*,5*E*,6*R*)-4-(Benzyloxymethyl)-2,2,4,6-tetramethyl-1,3-dioxan-5-ylidene][(*R*)-2-(methoxymethyl)pyrrolidin-1-yl]amine [(*S*,*R*,*R*)-8]: To a solution of α,α′-dimethylated 2,2-dimethyl-1,3-dioxan-5-one RAMP-hydrazone (*R*,*R*,*R*)-**7** (3.20 g, 11.8 mmol) in dry THF (24 mL) *t*BuLi (12 mL, 17.8 mmol) was slowly added at –78 °C. After stirring for 1.5 h, the reaction mixture was cooled to –100 °C, BOMCl (2.8 g, 19.3 mmol) was added dropwise and the solution was stirred for 1 h. Then the mixture was allowed to warm to room temperature over a period of 15 h and quenched with a pH 7 buffer (36 mL). The aqueous phase was extracted with Et_2O (400 mL) and the organic phase was washed with brine (20 mL). The combined aqueous phases were extracted with Et_2O (70 mL) and the combined organic layers were dried ($MgSO_4$). Removal of the solvent under reduced pressure and purification of the residue by flash chromatography (SiO_2, Et_2O/*n*-pentane, 1:7) afforded (*S*,*R*,*R*)-**8** as a colourless solid. Yield: 4.28 g (92%). *de* ≥ 96% (^{13}C NMR). $[\alpha]_D^{26}$ = +40.2 (*c* = 1.31, $CHCl_3$). (*R*,*S*,*S*)-**8**: $[\alpha]_D^{26}$ = –43.7 (*c* = 1.73, $CHCl_3$). Further analytical data are consistent with those reported in the literature.[14]

(4*R*,6*R*)-4-(Benzyloxymethyl)-2,2,4,6-tetramethyl-1,3-dioxan-5-one [(*R*,*R*)-9]: A solution of (*S*,*R*,*R*)-**8** (4.14 g, 10.6 mmol) in CH_2Cl_2 (40 mL) was ozonolyzed at –78 °C. Removal of the solvent under reduced pressure and purification of the residue by flash chromatography (Et_2O/*n*-pentane, 1:4) afforded (*R*,*R*)-**9** as a colourless oil. Yield: 2.33 g (79%). *de* ≥ 96% (^{13}C NMR). $[\alpha]_D^{26}$ = +140.5 (*c* = 1.01, $CHCl_3$). (*S*,*S*)-**9**: $[\alpha]_D^{26}$ = –131.5 (*c* = 1.08, $CHCl_3$). Further analytical data are consistent with those reported in the literature.[14]

(4*R*,6*R*)-4-(Benzyloxymethyl)-2,2,4,6-tetramethyl-1,3-dioxan-5-ol [(*R*,*R*/*S*,*R*)-10]: To a solution of (*R*,*R*)-**9** (1.71 g, 6.1 mmol) in

MeOH (30 mL) was added $NaBH_4$ (0.46 g, 12.3 mmol) at 0 °C. The solution was stirred for 4 h. After removal of the solvent under reduced pressure, the residue was diluted with Et_2O. The organic phase was washed with water and brine and dried ($MgSO_4$). Removal of the solvent under reduced pressure afforded (*R*,*R*/*S*,*R*)-**10** as a colorless oil. Yield: 1.72 g (100%). *dr* = 4:1. $[\alpha]_D^{26}$ = +15.1 (*c* = 1.00, $CHCl_3$). *ent*-**10**: $[\alpha]_D^{26}$ = –15.4 (*c* = 1.17, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3564 cm^{-1} (m), 3485 (m), 3089 (w), 3064 (w), 3029 (m), 2989 (s), 2936 (s), 2868 (m), 1497 (m), 1454 (s), 1380 (s), 1333 (w), 1308 (m), 1248 (s), 1202 (s), 1169 (s), 1152 (s), 1090 (s), 1055 (s), 1005 (s), 977 (s), 903 (w), 888 (w), 841 (m), 812 (m), 739 (m), 699 (m), 597 (w), 540 (w). *Major isomer*: ^1H NMR (400 MHz, C_6D_6): δ = 1.21 (d, *J* = 6.4 Hz, 3 H, CHC*H*$_3$), 1.39 (s, 3 H, CC*H*$_3$), 1.55 [s, 3 H, CH(OH)CC*H*$_3$], 2.04 (d, *J* = 11.0 Hz, 1 H, O*H*), 3.27 [d, *J* = 9.2 Hz, 1 H, C(CH$_3$)C*H*HO], 3.33 (dd, *J* = 11.0, 1.5 Hz, 1 H, C*H*OH), 3.47 [d, *J* = 9.2 Hz, 1 H, C(CH$_3$)CH*H*O], 3.98 (dq, *J* = 6.4, 1.5 Hz, 1 H, CH$_3$C*H*CHOH), 4.19 (d, *J* = 12.2 Hz, 1 H, OC*H*H), 4.27 (d, *J* = 12.2 Hz, 1H OCH*H*), 7.07–7.20 (m, 5 H, C_6H_5) ppm. ^{13}C NMR (100 MHz, C_6D_6): δ = 17.5 (CH*C*H$_3$), 23.7 (C*C*H$_3$), 25.5 [C(*C*H$_3$)CH$_3$], 31.7 [C(CH$_3$)*C*H$_3$], 65.1 (*C*HCH$_3$), 68.6 (O*C*H$_2$Ph), 73.5 [C(CH$_3$)*C*H$_2$O], 75.2 (*C*CH$_3$), 77.6 (*C*HOH), 98.9 [*C*(CH$_3$)CH$_3$], 127.7 (*mC*Ph), 128.5 (*oC*Ph), 128.5 (*pC*Ph), 138.4 (*C*Ph) ppm. *Minor isomer*: ^1H NMR (400 MHz, C_6D_6): δ = 1.39 (d, *J* = 6.1 Hz, 3 H, CHC*H*$_3$), 1.40 (s, 3 H, CC*H*$_3$), 1.45 [s, 3 H, CH(OH)CC*H*$_3$], 1.47 (s, 3 H, CC*H*$_3$), 2.90 (d, *J* = 6.1 Hz, 1 H, O*H*), 3.36 [d, *J* = 9.2 Hz, 1 H, C(CH$_3$)C*H*HO], 3.38 (dd, *J* = 6.1, 8.2 Hz, 1 H, C*H*OH), 3.76 [d, *J* = 9.2 Hz, 1 H, C(CH$_3$)CH*H*O], 3.93 (dq, *J* = 8.2, 6.1 Hz, 1 H, C*H*CH$_3$), 4.12 (d, *J* = 12.0 Hz, 1 H, OC*H*H), 4.17 (d, *J* = 12.0 Hz, 1 H, OCH*H*), 7.07–7.20 (m, 5 H, *H*Ph) ppm. ^{13}C NMR (100 MHz, C_6D_6): δ = 19.8 (CH*C*H$_3$), 25.5 (C*C*H$_3$), 26.4 [C(*C*H$_3$)CH$_3$], 31.2 [C(CH$_3$)*C*H$_3$], 68.4 (*C*HCH$_3$), 73.7 (O*C*H$_2$Ph), 75.4 [C(CH$_3$)*C*H$_2$O], 77.6 (*C*CH$_3$), 77.7 (*C*HOH), 98.9 [*C*(CH$_3$)CH$_3$], 127.7 (*mC*Ph), 128.5 (*oC*Ph), 128.5 (*pC*Ph), 138.4 (*C*Ph) ppm. MS (EI, 70 eV): *m*/*z* (%) = 279 (3) [M^+ – 1], 265 (14), 165 (11), 158 (56), 101 (37), 92 (13), 91 (100), 59 (41), 58 (12). $C_{16}H_{24}O_4$ (280.36): calcd. C 68.55, H 8.63; found C 68.38, H 8.60.

***O*-(4*R*,6*R*)-4-(Benzyloxymethyl)-2,2,4,6-tetramethyl-1,3-dioxan-5-yl *S*-Methyl Dithiocarbonate [(*R*,*R*/*S*,*R*)-11]:** To a solution of (*R*,*R*/*S*,*R*)-**10** (1.76 g, 6.3 mmol) in dry THF (60 mL) under argon a 60% suspension of NaH in mineral oil (0.50 g, 12.5 mmol) was added at 0 °C. After 30 min, CS_2 (1.3 mL, 21.9 mmol) was added dropwise. Stirring was continued for additional 30 min and iodomethane (1.2 mL, 18.8 mmol) was added. The mixture was stirred at room temperature overnight. The suspension was hydrolysed with water and extracted with Et_2O (2 × 250 mL). The combined organic layers were washed with satd. aqueous NH_4Cl solution (40 mL) and brine (40 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Purification of the residue by column chromatography (silica gel, Et_2O/*n*-pentane, 1:2) afforded (*R*,*R*/*S*,*R*)-**11** as a yellow oil. Yield: 2.31 g (98%). *dr* = 4:1. e*nt*-**11**: $[\alpha]_D^{26}$ = –44.8 (*c* = 1.18, $CHCl_3$). IR (film): $\tilde{\nu}$ = 2988 cm^{-1} (m), 2937, 2864 (m), 1721 (w), 1497 (w), 1454 (m), 1425 (w), 1412 (w), 1379 (s), 1316 (m), 1272 (m), 1218 (s), 1154 (s), 1064 (s), 1029 (m). *Major isomer*: $[\alpha]_D^{26}$ = +64.5 (*c* = 1.02, $CHCl_3$). ^1H NMR (400 MHz, C_6D_6): δ = 1.20 (d, *J* = 6.3 Hz, 3 H, CHC*H*$_3$), 1.29 [d, *J* = 0.6 Hz, 3 H, C(CH$_3$)C*H*$_3$], 1.46 (s, 3 H, CC*H*$_3$), 1.50 [d, *J* = 0.6 Hz, 3 H, CC*H*$_3$(CH$_3$)], 2.13 (s, 3 H, SC*H*$_3$), 3.33 [d, *J* = 9.6 Hz, 1 H, C(CH$_3$)C*H*HO], 3.49 [d, *J* = 9.6 Hz, 1 H, C(CH$_3$)CH*H*O], 4.15 [dq, *J* = 6.3, 2.5 Hz, 1 H, (CH$_3$)C*H*CHO], 4.29 (d, *J* = 12.4 Hz, 1 H, OC*H*HC$_6$H$_5$), 4.33 (d, *J* = 12.1 Hz, 1 H, OCH*H*C$_6$H$_5$), 6.26 (d, *J* = 2.5 Hz, 1 H, C*H*OC=S), 7.08–7.30 (m, 5 H, C_6H_5) ppm. ^{13}C NMR (100 MHz, C_6D_6): δ = 17.1 (CH*C*H$_3$), 18.7 (C*C*H$_3$), 22.7 (S*C*H$_3$), 25.9, 31.1 [C(*C*H$_3$)*C*H$_3$], 64.9 (*C*HCH$_3$), 73.5, 75.7 [C(CH$_3$)*C*H$_2$O, O*C*H$_2$Ph], 76.3 (*C*CH$_3$), 79.6 (*C*HOC=S), 99.5 [*C*(CH$_3$)CH$_3$], 127.8 (*oC*Ph), 127.9 (*pC*Ph), 128.6 (*mC*Ph), 138.6 (*C*Ph), 217.3 (*C*=S) ppm. *Minor isomer*: $[\alpha]_D^{26}$ = –12.2 (*c* = 1.10, $CHCl_3$). ^1H NMR (400 MHz, C_6D_6): δ = 1.39 [d, *J* = 0.6 Hz, 3 H, C(*CH*$_3$)*C*H$_3$], 1.43 (d, *J* = 6.6 Hz, 3 H, CHC*H*$_3$), 1.44 [d, *J* = 0.6 Hz, 3 H, C(*C*H$_3$)C*H*$_3$], 1.59 (s, 3 H, CC*H*$_3$), 2.10 (s, 3 H, SC*H*$_3$), 3.35 [d, *J* = 8.8 Hz, 1 H, C(CH$_3$)C*H*HO], 3.67 [d, *J* = 8.8 Hz, 1 H, C(CH$_3$)CH*H*O], 4.04 (dq, *J* = 6.6, 4.4 Hz, 1 H, C*H*CH$_3$), 4.29 (d, *J* = 12.1 Hz, 1 H, OC*H*HC$_6$H$_5$), 4.33 (d, *J* = 12.1 Hz, 1 H, OCH*H*C$_6$H$_5$), 5.80 (d, *J* = 4.7 Hz, 1 H, C*H*OC=S), 7.08–7.30 (m, 5 H, C_6H_5) ppm. ^{13}C NMR (100 MHz, C_6D_6): δ = 18.9 (CH*C*H$_3$), 21.0 (C*C*H$_3$), 24.9 (S*C*H$_3$), 24.5, 31.14 [C(*C*H$_3$)*C*H$_3$], 68.8 (*C*HCH$_3$), 73.7 [C(CH$_3$)*C*H$_2$O], 74.6 (O*C*H$_2$Ph), 75.4 (*C*CH$_3$), 84.5 (*C*HOC=S), 99.5 [*C*(CH$_3$)CH$_3$], 127.9 (*oC*Ph, *pC*Ph), 128.5 (*mC*Ph), 138.7 (*C*Ph), 215.8 (*C*=S) ppm. MS (EI, 70 eV): *m*/*z* (%) = 370 (0.5) [M^+], 249 (10), 191 (15), 141 (27), 97 (5), 91 (100). $C_{18}H_{26}O_4S_2$ (370.53): calcd. C 58.35, H 7.07; found C 57.91, H 6.76.

(4*S*,6*R*)-4-(Benzyloxymethyl)-2,2,4,6-tetramethyl-1,3-dioxane [(*S*,*R*)-12]: Tri-*n*-butyltin hydride (3.4 mL, 12.9 mmol) was dissolved in toluene (80 mL) in a Schlenk flask. The solution was post-purged with argon for 10 min and was then heated to reflux. The xanthate (*R*,*R*/*S*,*R*)-**11** (1.58 g, 4.3 mmol) dissolved in toluene (10 mL) was added dropwise by cannula over a period of 3 h. During the addition a satd. solution of AIBN in toluene (1.1 mL, 0.2 mL/mmol xanthate) was added dropwise by cannula and the solution was stirred under reflux for 3 h. After complete conversion of the starting material had been indicated by TLC, the solvent was removed under reduced pressure. Column chromatography (silica gel, first: Et_2O/pentane, 1:20 to remove the tin by-products, second: Et_2O/*n*-pentane, 1:5) yielded (*S*,*R*)-**12** as a colourless oil. Yield: 1.11 g (98%). *de* ≥ 96% (^{13}C NMR). $[\alpha]_D^{26}$ = +2.5 (*c* = 1.11, $CHCl_3$). *ent*-**12**: $[\alpha]_D^{26}$ = –2.1 (*c* = 1.32, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3088 cm^{-1} (w), 3064 (w), 3030 (m), 2975 (s), 2934 (s), 2915 (s), 2868 (s), 1497 (m), 1454 (s), 1405 (m), 1377 (s), 1315 (m), 1246 (s), 1200 (s), 1165 (s), 1146 (s), 1102 (s), 1050 (s), 1029 (m), 1009 (s), 985 (s), 970 (m), 908 (m), 876 (m), 844 (m), 737 (s), 699 (s). ^1H NMR (400 MHz, C_6D_6): δ = 1.10 (d, *J* = 6.0, 3 H, CHC*H*$_3$), 1.25 [ddd, *J* = 13.2, 11.0, 0.6 Hz, 1 H, CH(CH$_3$)C*H*H], 1.37 [d, *J* = 0.6 Hz, 3 H, CC*H*$_3$(CH$_3$)], 1.40 (s, 3 H, CC*H*$_3$), 1.53 [d, *J* = 0.6 Hz, 3 H, C(CH$_3$)C*H*$_3$], 1.72 [dd, *J* = 13.5, 3.0 Hz, 1 H, CH(CH$_3$)CH*H*], 3.27 [dd, *J* = 8.8, 0.6 Hz, 1 H, C(CH$_3$)C*H*HO], 3.48 [d, *J* = 8.8 Hz, 1 H, C(CH$_3$)CH*H*O], 3.9 (ddq, *J* = 3.0, 6.1, 11.0 Hz, 1 H, C*H*CH$_3$), 4.30 (d, *J* = 12.4 Hz, 2 H, OC*H*HC$_6$H$_5$), 4.34 (d, *J* = 12.4 Hz, 2 H, OCH*H*C$_6$H$_5$), 7.10 (m, 1 H, C*H*$_{p\text{-arom.}}$), 7.18 (m, 2 H, C*H*$_{m\text{-arom.}}$), 7.25 (m, 2 H,C*H*$_{o\text{-arom.}}$) ppm. ^{13}C NMR (100 MHz, C_6D_6): δ = 22.5 (CH*C*H$_3$), 26.2 [C(*C*H$_3$)CH$_3$], 29.0 (C*C*H$_3$), 32.1 [C(CH$_3$)*C*H$_3$], 39.3 [CH(CH$_3$)*C*H$_2$], 62.0 (*C*HCH$_3$), 72.8 (*C*CH$_3$), 73.4 (O*C*H$_2$Ph), 76.1 (C*C*H$_2$O), 98.52 [*C*(CH$_3$)CH$_3$], 127.6 (*oC*Ph), 128.1 (*pC*Ph), 128.4 (*mC*Ph), 128.8 (*C*Ph) ppm. MS (EI, 70 eV): *m*/*z* (%) = 249 (23) [M^+ – CH_3], 143 (69), 101 (22), 99 (15), 91 (100), 85 (38), 59 (23). $C_{16}H_{24}O_3$ (264.36): calcd. C 72.60, H 9.15; found C 72.15, H 9.50.

[(4*S*,6*R*)-2,2,4,6-Tetramethyl-1,3-dioxan-4-yl]methanol [(*S*,*R*)-13]: Pieces of calcium (0.52 g, 20.8 mmol) were added to liquid NH_3 (75 mL) in a three-necked flask fitted with a dry ice condenser. The benzyl ether (*S*,*R*)-**12** (1.10 g, 4.15 mmol) dissolved in dry THF (5 mL) was added at –78 °C to the stirred dark blue solution. After 30 min, the cooling bath was removed and the solution was kept under reflux (–33 °C) for 2 h. The reaction was quenched with solid NH_4Cl and the NH_3 was evaporated at room temperature. The residue was diluted with Et_2O. The organic phase was washed with water and brine and dried ($MgSO_4$). Removal of the solvent under reduced pressure afforded (*S*,*R*)-**13** as a colorless oil without fur-

ther purification. Yield: 0.70 g (97%). *de* ≥ 96% (^{13}C NMR). $[\alpha]_D^{26}$ = –8.9 (*c* = 1.05, $CHCl_3$). *ent*-**13**: $[\alpha]_D^{25}$ = +14.3 (*c* = 1.40, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3453 cm^{-1} (s), 2976 (s), 2936 (s), 2882 (m), 1451 (m), 1378 (s), 1316 (m), 1243 (s), 1231 (s), 1199 (s), 1150 (s), 1123 (m), 1058 (s), 1039 (s), 1006 (s), 982 (s), 964 (m), 934 (w), 909 (m), 872 (w), 841 (m). ^{1}H NMR (400 MHz, C_6D_6): δ = 1.06 (d, *J* = 6.0 Hz, 3 H, CHCH_3), 1.15 (dd, *J* = 10.7, 13.5 Hz, 1 H, C$H_{ax}H_{eq}$CHCH$_3$), 1.23 (s, 3 H, CCH_3), 1.31 [s, 3 H, C(CH_3)CH$_3$], 1.42 (dd, *J* = 3.9, 13.5 Hz, 1 H, CH$_{ax}H_{eq}$CHCH$_3$), 1.46 [s, 3 H, C(CH$_3$)CH_3], 2.28 (s, 1 H, CH$_2$O*H*), 3.26 (dd, *J* = 7.4, 11.0 Hz, 1 H, C*H*HOH), 3.44 (dd, *J* = 4.4, 10.7 Hz, 1 H, CH*H*OH), 3.75 (ddq, *J* = 3.8, 6.1, 14.3 Hz, 1 H, C*H*CH$_3$) ppm. ^{13}C NMR (100 MHz, C_6D_6): δ = 22.5 (CH*C*H$_3$), 25.6 [C(*C*H$_3$)CH$_3$], 28.0 (C*C*H$_3$), 31.6 [C(CH$_3$)*C*H$_3$], 38.9 [CH(CH$_3$)*C*H$_2$], 62.1 (*C*HCH$_3$), 68.5 [C(CH$_3$)*C*H$_2$OH], 73.2 (*C*CH$_3$), 98.8 [*C*(CH$_3$)CH$_3$] ppm. MS (EI, 70 eV): *m*/*z* (%) = 159 (33) [M^+ – CH_3], 143 (59), 101 (32), 99 (35), 85 (56), 81 (13), 59 (100), 57 (15), 55 (12). $C_9H_{18}O_3$ (174.24): calcd. C 62.04, H 10.41; found C 61.65, H 10.21.

[(4*S*,6*R*)-2,2,4,6-Tetramethyl-1,3-dioxan-4-yl]methyl Toluene-4-sulfonate [(*S*,*R*)-5]: To a solution of (*S*,*R*)-**13** (0.89 g, 3.9 mmol) in dry CH_2Cl_2 (50 mL) were added NEt_3 (1.1 mL, 8.0 mmol) and a catalytical amount of DMAP. The mixture was stirred at room temperature for 1 h and TsCl (1.14 g, 6.0 mmol) was added. The resulting mixture was stirred at room temperature for 20 h. After TLC monitoring had indicated that conversion was incomplete, additional NEt_3 (0.5 mL) and TsCl (0.30 g) were added. The mixture was stirred again for 48 h until completion of the reaction. CH_2Cl_2 (20 mL) and satd. aqueous NH_4Cl solution (5 mL) were added. The organic layers were washed with a satd. aqueous NH_4Cl solution, water and brine and were dried with $MgSO_4$. Column chromatography (silica gel, Et_2O/*n*-pentane, 1:1) gave (*S*,*R*)-**5** as a bright yellow sirup. Yield: 1.30 g (100%). *de* ≥ 96% (^{13}C NMR). $[\alpha]_D^{26}$ = +18.0 (*c* = 1.05, $CHCl_3$). *ent*-**5**: $[\alpha]_D^{26}$ = –19.2 (*c* = 1.42, $CHCl_3$). IR (film): $\tilde{\nu}$ = 2991 cm^{-1} (m), 2937 (m), 1656 (w), 1599 (m), 1561 (w), 1543 (w), 1497 (m), 1459 (m), 1359 (s), 1309 (m), 1291 (m), 1252 (m), 1191 (s), 1179 (s), 1158 (s), 1122 (m), 1098 (m), 1082 (m), 1050 (m), 1009 (s), 981 (s), 964 (s), 938 (m), 909 (m), 860 (s), 842 (s), 819 (s), 792 (m), 766 (m), 671 (s), 632 (w), 590 (w), 558 (s), 529 (m), 516 (m). ^{1}H NMR (400 MHz, C_6D_6): δ = 0.97 (d, *J* = 6.0 Hz, 3 H, CHCH_3), 1.06 (dd, *J* = 11.0, 13.7 Hz, 1H C*H*HCHCH$_3$), 1.14 (s, 3 H, CCH_3), 1.21 [s, 3 H, C(CH_3)CH$_3$], 1.36 [s, 3 H, C(CH$_3$)CH_3], 1.38 (dd, *J* = 3.0, 13.7 Hz, 1 H, CH*H*CHCH$_3$), 1.91 (s, 3 H, C_6H_4CH_3), 3.61 (ddq, *J* = 3.3, 6.0, 12.1 Hz, 1 H, C*H*CH$_3$), 3.88 (d, *J* = 9.6 Hz, 1 H, C*H*HOSO$_2$), 4.07 (d, *J* = 9.6 Hz, 1 H, CH*H*OSO$_2$), 6.80 (m, 2 H, C$H_{arom.}$), 7.76 (m, 2 H, C$H_{arom.}$) ppm. ^{13}C NMR (100 MHz, C_6D_6): δ = 21.1 (*C*H$_3$Ph), 22.2 (CH*C*H$_3$), 25.6 [C(*C*H$_3$)CH$_3$], 28.1 (C*C*H$_3$), 31.7 [C(CH$_3$)*C*H$_3$], 38.3 [CH(CH$_3$)*C*H$_2$], 61.6 (*C*HCH$_3$), 71.3 (*C*CH$_3$), 73.6 [C(CH$_3$)*C*H$_2$O], 98.8 [*C*(CH$_3$)CH$_3$], 128.1 (*oC*Ph), 129.7 (*mC*Ph), 133.6 (*C*PhCH$_3$), 144.4 (SO_2*C*Ph) ppm. MS (EI, 70 eV): *m*/*z* (%) = 314 (13), 313 (92) [M^+ – CH_3], 157 (22), 156 (10), 155 (95), 143 (100), 141 (11), 101 (34), 99 (54), 97 (26), 92 (11), 91 (55), 85 (61), 81 (33), 65 (12), 59 (25). $C_{16}H_{24}O_5S$ (328.43): calcd. C 58.51, H 7.37; found C 58.86, H 7.22.

(2*S*,4*R*)-2,4-Dihydroxy-2-methylpentyl Toluene-1-sulfonate [(*S*,*R*)-14]: Tosylate (*S*,*R*)-**5** (1.00 g, 3.0 mmol) was dissolved in methanol (6.1 mL) at room temperature and aqueous 3 N HCl (6.07 mL) was added. After stirring for 30 min, the conversion was complete (TLC monitoring). Then solid $NaHCO_3$ was added until the aqueous phase showed neutral conditions. The mixture was extracted with Et_2O (2 × 150 mL) and the combined organic layers were dried with $MgSO_4$. Removal of the solvent under reduced pressure and purification of the crude product by column chromatography (silica gel, Et_2O) afforded (*S*,*R*)-**14** as a colorless wax. Yield: 0.76 g (87%). *de* ≥ 96% (^{13}C NMR). $[\alpha]_D^{26}$ = +12.1 (*c* = 1.19, $CHCl_3$). *ent*-**14**: $[\alpha]_D^{26}$ = –13.4 (*c* = 1.23, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3378 cm^{-1} (m), 2972 (m), 2931 (m), 1598 (m), 1495 (w), 1455 (m), 1428 (m), 1401 (m), 1358 (vs), 1308 (w), 1292 (w), 1212 (m), 1190 (vs), 1176 (vs), 1140 (s), 1098 (s), 1039 (w), 1020 (w), 980 (vs), 909 (w), 848 (s), 833 (s), 816 (s), 787 (m), 686 (w), 668 (vs), 575 (m), 555 (s), 531 (w), 505 (w). ^{1}H NMR (400 MHz, C_6D_6): δ = 0.90 (d, *J* = 6.0 Hz, 3 H, CH*C*H$_3$), 1.13 [s, 3 H, C(OH)CH_3], 1.44 [m, 2 H, CH_2CH(OH)CH$_3$], 1.89 (s, 3 H, CCH_3), 3.93 (d, *J* = 9.3 Hz, 1 H, C*H*HOTs), 3.89 [m, 1 H, C*H*(OH)], 4.18 (d, *J* = 9.3 Hz, 1 H, CH*H*OTs), 6.80 (m, 2 H, *mH*Ph), 7.78 (m, 2 H, *oH*Ph) ppm. ^{13}C NMR (100 MHz, C_6D_6): δ = 21.2 (Ph*C*H$_3$), 24.6 (CH*C*H$_3$), 26.6 (C*C*H$_3$), 44.8 [CH(CH$_3$)*C*H$_2$], 65.4 (*C*HCH$_3$), 71.4 (*C*CH$_3$), 74.4 [C(CH$_3$)*C*H$_2$O], 128.1 (*oC*Ph), 128.8 (*mC*Ph), 133.4 (*C*PhCH$_3$), 144.5 (SO_2*C*Ph) ppm. MS (EI, 70 eV): *m*/*z* (%) = 289 (0.9) [M^+], 229 (12), 155 (35), 103 (100), 92 (12), 91 (30), 85 (28), 61 (33), 59 (11), 45 (9). $C_{13}H_{20}O_5S$ (288.36): calcd. C 54.15, H 6.99; found C 54.00, H 7.04.

(2*S*,4*R*)-4-[(*tert*-Butyldimethylsilyl)oxy]-2-hydroxy-2-methylpentyl Toluene-1-sulfonate [(*S*,*R*)-15]: A solution of (*S*,*R*)-**14** (0.65 g, 2.3 mmol) in dry CH_2Cl_2 (20 mL) was cooled to 0 °C and 2,6-lutidine (0.26 mL, 2.3 mmol) was added. After stirring for 15 min, TBSOTf (0.53 mL, 2.3 mmol) was added. The mixture was allowed to warm to room temperature and was stirred for another 3 h until completion of conversion was indicated by TLC monitoring. The resulting reaction mixture was washed with water and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried with $MgSO_4$ and the solvent was removed under reduced pressure. Column chromatography (silica gel, Et_2O/*n*-pentane, 1:2) gave (*S*,*R*)-**15** as a colorless oil. Yield: 1.30 g (100%). *de* ≥ 96% (^{13}C NMR). $[\alpha]_D^{26}$ = –3.8 (*c* = 1.09, $CHCl_3$). *ent*-**15**: $[\alpha]_D^{26}$ = +4.2 (*c* = 1.24, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3457 cm^{-1} (m), 2956 (s), 2931 (s), 2886 (m), 2858 (s), 1599 (w), 1495 (w), 1472 (m), 1411 (m), 1368 (vs), 1292 (w), 1257 (s), 1190 (vs), 1178 (vs), 1138 (vs), 1098 (s), 1080 (m), 1045 (s), 1020 (w), 977 (vs), 926 (s), 890 (m), 838 (vs), 814 (s), 779 (vs), 713 (w), 686 (m), 667 (vs), 575 (m), 555 (vs), 531 (m). ^{1}H NMR (400 MHz, C_6D_6): δ = 0.02 [s, 3 H, Si(CH_3)CH$_3$C(CH$_3$)$_3$], 0.05 [s, 3 H, Si(CH$_3$)CH_3C(CH$_3$)$_3$], 0.88 [s, 9 H, Si(CH$_3$)$_2$C(CH_3)$_3$], 0.92 (d, *J* = 6.0 Hz, 3 H, CHCH_3), 1.18 [s, 3 H, C(OH)CH_3], 1.56 [m, 2 H, CH_2CH(OH)CH$_3$], 1.88 (s, 3 H, CCH_3), 3.90 (d, *J* = 9.3 Hz, 1 H, C*H*HOSO$_2$), 4.12 (m, 1 H, C*H*CH$_3$), 4.22 (d, *J* = 9.3 Hz, 1 H, CH*H*OSO$_2$), 4.35 (s, 1 H, O*H*), 6.75 (m, 2 H, *mH*Ph), 7.78 (m, 2 H, *oH*Ph) ppm. ^{13}C NMR (100 MHz, C_6D_6): δ = –4.9, –3.4 [Si(*C*H$_3$)$_2$], 17.8 [*C*(CH$_3$)$_3$], 21.1 (Ph*C*H$_3$), 25.0 (CH*C*H$_3$), 25.9 [SiC(*C*H$_3$)$_3$], 26.6 (C*C*H$_3$), 45.5 [CH(CH$_3$)*C*H$_2$], 67.6 (*C*HCH$_3$), 70.8 [*C*(CH$_3$)OH], 74.4 [C(CH$_3$)*C*H$_2$O], 127.9 (*oC*Ph), 129.7 (*mC*Ph), 133.5 (*C*PhCH$_3$), 144.3 (SO_2*C*Ph) ppm. MS (EI, 70 eV): *m*/*z* (%) = 345 (3) [M^+ – C(CH$_3$)$_3$], 301 (12), 231 (11), 230 (16), 229 (100), 217 (57), 174 (10), 173 (85), 159 (56), 155 (22), 129 (11), 119 (29), 115 (12), 99 (15), 91 (24), 81 (14), 75 (50), 73 (21). $C_{19}H_{34}O_5SSi$ (402.62): calcd. C 56.68, H 8.51; found C 56.33, H 8.45.

***tert*-Butyldimethyl[(*R*)-1-{[(*S*)-2-methyloxiran-2-yl]prop-2-yl}-oxy]silane [(*S*,*R*)-3]:** In a Schlenk flask under argon a 60% suspension of NaH in mineral oil (0.16 g, 4.1 mmol) was washed paraffin-free with several portions of dry *n*-pentane. The residue was carefully dried in vacuo and the resulting colourless powder was purged with argon. Then dry THF (40 mL) were added and the suspension was cooled to 0 °C. The tertiary alcohol (*S*,*R*)-**15** (0.41 g, 1.0 mmol) was added dropwise and the suspension was stirred at this temperature for 2 h and then at room temperature overnight. After complete conversion had been indicated by TLC monitoring, the suspension was quenched with a pH 7 buffer. The aqueous layer was

extracted with Et_2O and the combined organic layers were dried with $MgSO_4$. Removal of the solvent under reduced pressure afforded pure (*S*,*R*)-**3** as a colourless oil. Yield: 0.23 g (99%). *de* ≥ 96% (^{13}C NMR). *ee* ≥ 98% (chiral GC, Chirasil-dex 25m, 1 bar H_2). $[\alpha]_D^{24}$ = +0.3 (*c* = 1.21, $CHCl_3$). *ent*-**3**: $[\alpha]_D^{26}$ = –0.3 (*c* = 1.89, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3038 cm^{-1} (w), 2932 (vs), 2858 (vs), 1467 (s), 1379 (s), 1255 (vs), 1208 (w), 1139 (vs), 1108 (s), 1080 (s), 1056 (vs), 1003 (vs), 932 (s), 835 (vs), 808 (vs), 776 (vs), 720 (w), 658 (w), 516 (w). ^1H NMR (400 MHz, C_6D_6): δ = 0.00, 0.02 [s, 6 H, $Si(CH_3)_2$], 0.92 [s, 9 H, $Si(CH_3)_2C(CH_3)_3$], 1.04 (d, *J* = 6.0 Hz, 3 H, $CHCH_3$), 1.17 (s, 3 H, CCH_3), 1.45–1.51 [dd, *J* = 8.2, 14.0, 1 H, $CH(CH_3)CHH$], 1.59 [ddd, *J* = 1.1, 4.4, 13.7 Hz, 1 H, $CH(CH_3)CHH$], 2.31 (dd, *J* = 1.1, 5.2 Hz, 1 H, $CHHO$), 2.45 (d, *J* = 5.2 Hz, 1 H, $CHHO$), 3.79–3.87 (m, 1 H, $CHCH_3$) ppm. ^{13}C NMR (100 MHz, C_6D_6): δ = –4.9, –4.3 [$Si(CH_3)_2$], 17.9 [$Si(CH_3)_2C(CH_3)_3$], 21.1 (CCH_3), 24.4 ($CHCH_3$), 25.8 [$Si(CH_3)_2C(CH_3)_3$], 47.1 [$CH(CH_3)CH_2$], 54.0 [$C(CH_3)CH_2O$], 54.2 (CCH_3), 66.3 ($CHCH_3$) ppm. MS (EI, 70 eV): *m*/*z* (%) = 215 (3) [$M^+ - CH_3$], 174 (12), 173 (90), 167 (10), 159 (26), 155 (23), 149 (24), 129 (73), 115 (16), 103 (28), 99 (15), 97 (12), 85 (16), 83 (11), 81 (13), 75 (100), 73 (42), 71 (22), 69 (11), 57 (29), 55 (14). $C_{12}H_{26}O_2Si$ (230.42): calcd. C 62.55, H 11.37; found C 62.90, H 11.17.

[(*S*)-2-(1-Ethyl-1-methoxypropyl)pyrrolidin-1-yl](1-ethylpropylidene)-amine [(*S*)-4]: A solution of pentan-3-one (2.80 g, 32.5 mmol) and (2*S*)-(1-ethyl-1-methoxypropyl)pyrrolidine (4.66 g, 25.00 mmol) in cyclohexane (70 mL) was refluxed for 3 h using a Dean–Stark trap. Then the solvent was removed under reduced pressure and the crude hydrazone was obtained as a brown oil. High-vacuum distillation afforded (*S*)-**4** as an orange oil. Yield: 5.76 g (91%); b.p. 125 °C/0.015 Torr. $[\alpha]_D^{27}$ = +366.9 (*c* = 1.46, $CHCl_3$). IR (CH_3Cl): $\tilde{\nu}$ = 2968 cm^{-1} (vs), 2881 (vs), 2826 (s), 1629 (w), 1460 (s), 1376 (w), 1120 (m), 1086 (s), 943 (w), 922 (w). ^1H NMR (300 MHz, C_6D_6): δ = 0.86–1.12 (m, 12 H, CH_3CH_2), 1.44–2.42 [m, 13 H, $(CH_3CH_2)_2C{=}N$, $NCHC(CH_2CH_3)_2$, NCH_2CH_2, $NCH_2CH_2CH_2$, $NCH_{cis}H_{trans}$], 2.96–3.06 (m, 1 H, $NCH_{cis}H_{trans}$), 3.34 (s, 3 H, OCH_3), 3.75 (dd, *J* = 9.4, 7.2 Hz, 1 H, NC*H*) ppm. ^{13}C NMR (75 MHz, C_6D_6): δ = 7.9, 8.4, 10.4, 11.0 (CH_3CH_2), 23.8, 24.0, 24.3, 25.3, 27.3, 27.8 [$(CH_3CH_2)_2C{=}N$, $NCHC(CH_2CH_3)_2$, NCH_2CH_2, $NCH_2CH_2CH_2$], 49.9 (OCH_3), 57.3 (NCH_2), 72.0 (NCH), 79.6 [$C(CH_2CH_3)_2$], 166.9 (*C*=N) ppm. MS (EI, 70 eV): *m*/*z* (%) = 255 (31) [$M^+ - 1$], 254 (29), 253 (27), 225 (13), 224 (16), 223 (100), 153 (86). HRMS: calcd. 254.2358; found 254.2359.

(1*S*,3*R*,5*R*,7*S*)-(+)-Sordidin and 7-*epi*-(1*S*,3*R*,5*R*,7*R*)-(–)-Sordidin (1 and 7-*epi*-1): LiCl (0.40 g, 8.8 mmol) was dehydrated in a Schlenk flask at 120 °C in vacuo (0.1 Torr) for 20 min and suspended in dry THF (14 mL). To the stirred suspension diisopropylamine (2.3 mL, 16.0 mmol) was added. The suspension was cooled to –78 °C and *n*BuLi (6.4 mL, 16.0 mmol) was added by syringe using a pump. The suspension was allowed to warm to 0 °C for 10 min, then it was cooled again to –78 °C and 3-pentanone SAEP-hydrazone **4** (0.34 g, 13.4 mmol) diluted in dry THF (10 mL) was added dropwise. The metalation reaction mixture was stirred at this temperature for 1 h, then it was allowed to warm to 0 °C for 10 min to be again cooled to –78 °C for adding the oxirane (*S*,*R*)-**3** (0.34 g, 1.46 mmol) diluted in dry THF (3 mL) through a double-ended needle. The suspension was allowed to warm to room temperature overnight and was quenched with a pH 7 buffer (26 mL). The aqueous layer was extracted with Et_2O, washed with desalted water, satd. aqueous NaCl solution and the combined organic layers were dried with $MgSO_4$. Removal of the solvent under reduced pressure furnished the crude product **16** (plus excess of **4**) as a yellow oil, which was used in the next step without further purification. The crude product of the former step was dissolved in *n*-pentane (14.0 mL) at room temperature and aqueous 3 N HCl (3.0 mL) was added. The two-phase system was stirred until complete conversion to the product had been indicated by TLC monitoring (6 d). The aqueous phase was neutralized with satd. aqueous $NaHCO_3$ solution, extracted with Et_2O and the combined organic layers were finally washed with a pH 7 buffer und dried with $MgSO_4$. The solvent was removed under reduced pressure and further purification by column chromatography (silica gel, Et_2O/*n*-pentane, 1:10) gave sordidin (**1**) and 7-*epi*-sordidin (7-*epi*-**1**) as a mixture with a ratio 1.5:1 as colourless oil. Yield: 0.23 g (84% over two steps). The two epimers could be separated by preparative GC (Varian 1200, 2 m × 2.06 mm i.d. pre-column, coverage: 20% CW-20M, mesh 100/120, 3 m × 2.06 mm i.d. main column, coverage: 20% CW-20M, mesh 60/80, steel columns, isotherm at 120 °C). IR (CH_3Cl): $\tilde{\nu}$ = 2970 cm^{-1} (vs), 2934 (vs), 2878 (vs), 1458 (s), 1378 (s), 1252 (w), 1196 (s), 1162 (m), 1136 (s), 1091 (w), 1036 (m), 1001 (m), 941 (s), 914 (w), 883 (w), 831 (w), 462 (w). (1*S*,3*R*,5*R*,7*S*)-(+)-sordidin (**1**): *de* ≥ 99% (after preparative GC, according to GC analysis). *ee* ≥ 98% (based on determined *ee* of epoxide **3**). $[\alpha]_D^{24}$ = +25.1 (*c* = 0.94, Et_2O); ref.[17]: $[\alpha]_D^{21}$ = +26.0 (*c* = 0.48, Et_2O). ^1H NMR (400 MHz, C_6D_6): δ = 0.87 [d, *J* = 7.1 Hz, 3 H, $CCH(CH_3)$], 0.93 [dd, *J* = 3.6, 12.6 Hz, 1 H, $OCH(CH_3)CHH$], 0.97 [ddd, *J* = 1.6, 4.7, 12.4 Hz, 1 H, $CCH(CH_3)CHH$], 1.14 [d, *J* = 6.1 Hz, 3 H, $OCH(CH_3)CH_2$], 1.20 [s, 3 H, $C(CH_3)$], 1.21 (t, *J* = 7.4 Hz, 3 H, CH_3CH_2), 1.27 [dd, *J* = 12.6, 11.0 Hz, 1 H, $OCH(CH_3)CHH$], 1.68 (dq, *J* = 7.4, 14.8 Hz, 1 H, CH_3CHH), 1.79 [dd, *J* = 8.8, 12.4 Hz, 1 H, $CCH(CH_3)CHH$], 1.88 (dq, *J* = 7.4, 13.7 Hz, 1 H, CH_3CHH), 2.15 [m, 1 H, $CCH(CH_3)CH_2$], 3.72 [m, 1 H, $OCH(CH_3)CH_2$] ppm. ^{13}C NMR (100 MHz, C_6D_6): δ = 8.4 (CH_3CH_2), 20.0 (CH_3CHC), 22.3 ($OCHCH_3$), 26.8 (CH_3C), 27.9 (CH_3CH_2), 40.5 (CH_3CHC), 44.2 [$OCH(CH_3)CH_2$], 45.0 [$CCH(CH_3)CH_2C$], 64.5 [$OCH(CH_3)CH_2$], 78.3 [$OC(CH_3)$], 108.4 (OCO) ppm. 7-*epi*-(1*S*,3*R*,5*R*,7*R*)-(–)-Sordidin (7-*epi*-**1**): *de* ≥ 97% (after preparative GC, according to GC analysis). *ee* ≥ 98% (based on determined *ee* of epoxide **3**). $[\alpha]_D^{24}$ = –6.9 (*c* = 1.11, Et_2O). ref.[17]: $[\alpha]_D^{21}$ = –7.6 (*c* = 0.48, Et_2O). ^1H NMR (400 MHz, C_6D_6): δ = 0.98 [dd, *J* = 3.8, 12.6 Hz, 1 H, $OCH(CH_3)CHH$], 0.99 [d, *J* = 7.1, 3 H, $CCH(CH_3)CH_2$], 1.13 [d, *J* = 6.0 Hz, 3 H, $OCH(CH_3)CH_2$], 1.15 (t, *J* = 7.5 Hz, 3 H, CH_3CH_2), 1.17 [m, 1 H, $CCH(CH_3)CHH$], 1.22 [s, 3 H, $C(CH_3)$], 1.34 [dd, *J* = 12.1, 12.1 Hz, 1 H, $OCH(CH_3)CHH$], 1.63 (dq, *J* = 7.4, 15.1 Hz, 1 H, CH_3CHH), 1.75 [dd, *J* = 12.4, 13.5 Hz, 1 H, $CCH(CH_3)CHH$], 1.87 (dq, *J* = 7.4, 14.0 Hz, 1 H, CH_3CHH), 2.08 [m, 1 H, $CCH(CH_3)CH_2$], 3.85 [m, 1 H, $OCH(CH_3)CH_2$] ppm. ^{13}C NMR (100 MHz, C_6D_6): δ = 8.3 (CH_3CH_2), 12.9 (CH_3CHC), 22.5 ($OCHCH_3$), 26.7 (CH_3C), 29.8 (CH_3CH_2), 41.6 (CH_3CHC), 42.6 [$OCH(CH_3)CH_2$], 44.6 [$CCH(CH_3)CH_2C$], 65.5 [$OCH(CH_3)CH_2$], 78.3 [$OC(CH_3)$], 107.4 (OCO) ppm. MS (EI, 70 eV): *m*/*z* (%) = 185 (0.2) [$M^+ + 1$], 184 (4) [M^+], 142 (20), 113 (27), 110 (12), 95 (100), 85 (11), 83 (29), 57 (66). HRMS: calcd. 184.1463; found 184.1463.

Acknowledgments

This work was supported by the Deutsche Forschungsgemeinschaft (Graduiertenkolleg 440, Sonderforschungsbereich 380) and the Fonds der Chemischen Industrie. We would like to thank Degussa AG, BASF AG, Bayer AG and Wacker Chemie for donations of chemicals. Further we would like to thank Dr. D. Belder, Max-Planck-Institut für Kohlenforschung, Mülheim an der Ruhr, for the preparative GC separations.

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Received February 10, 2005
Published Online: May 3, 2005

