Structural and Stereochemical Diversity from (±)-2,2-Dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-one − Application to the Synthesis of Polyketide Segments of Natural Products

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The racemic title compound has been transformed into both cyclic and acyclic segments of bioactive natural products, including the C10–C17 segment of pederin, the C12–C19 (C12′–C19′) segment of disorazole and the C1–C9 segment of auriside. A methodology for the opening of six-membered ring acetals, containing *gem*-dimethyl groups, to δ-hydroxy-1,3-dithianes has been developed.

We have developed an efficient strategy for synthesizing polyketides from a few selected 8-oxabicyclo[3.2.1]oct-6-en-3-ones.[1] These oxabicyclics can be regarded as multiple aldol addition equivalents and can be elaborated to polyketides with high or complete stereocontrol. Much further work on [4+3] cycloadducts, obtained from a variety of allyl cations and allyl cation equivalents, has appeared during 2001.[2] Very recently, two oxabicyclics have been shown to serve as simple and effective precursors for the synthesis of *C*-glycosides of all three stereochemical categories (D-L, D-D and also L-L) and of hybrid and nonnatural carbohydrates.[3] Our present target molecules are shown in Scheme 1, and all contain aldol functionality.

The title compound may be regarded as a mixture of two key single-isomers **1** and ***ent*-1** and can be prepared in 40 g batches.[4] Reduction with L-selectride provided the enantiomeric mixture of axial alcohols, which were protected to give **2** and ***ent*-2** (Scheme 2).[5] Asymmetric hydroboration[6] of the olefinic double bond with either (−)-Ipc_2BH or (+)-Ipc_2BH required careful temperature control (−15 °C). Oxidation of the resulting alcohols to the ketones **3** and **4**, and also the ketones ***ent*-3** and ***ent*-4**, proceeded smoothly by use of PCC. Subsequent Baeyer−Villiger ring-expansion gave the series of four lactone acetals **5** and **6**, and also ***ent*-5** and ***ent*-6**.[7] At this stage, separation by flash chromatography was feasible and individual constitutional and stereoisomers were obtained.[8] Each [3.3.1]lactone acetal can be elaborated separately and serves as a valuable building block in the synthesis of prominent polyoxygenated natural products.[9]

Previously, the synthesis of the "northern half" of bryostatin has been described (cf. Scheme 3).[10]

Whereas the opening of the acetal **7** to afford the five-membered ring dithioketal **8a** was comparatively simple, the related opening with 1,3-propanedithiol to provide the *six*-membered ring dithioketal was far more difficult (Scheme 4). Eventually, methoxy acetal **9** was opened in nitromethane to give diol **10**,[10] leaving the benzyl group intact at low temperature. Opening and deprotection[11] proceeded best in acetonitrile at higher temperature, giving triol **11**.[12,13] Presumably, nucleophilic sulfur facilitates deprotection through 6-*endo*-*tet* interaction (cf. ***i***).[14] Thus, tuning of deprotection by choice of solvent and temperature is feasible.

For the synthesis of the polyketide segment of the disorazoles we selected the methoxy acetal **9a**, which is available from lactone **6** (Scheme 4−5) and is anomerically pure, simplifying spectroscopy. One-carbon homologation of primary alcohol **9a** was carried out by oxidation to the aldehyde **12** and subsequent Grignard reaction (Scheme 5). The diastereomeric alcohols **13a** and **13b** were converted into the *trans* olefin **14** under Saytzeff-like conditions. Lewis acid-mediated opening and simultaneous sulfur-assisted deprotection furnished **15**, the C12−C19 segment (C12′−C19′ segment) of the disorazoles.

Alternatively, aldehyde **12** was subjected to a two-carbon homologation to give the α,β-unsaturated ester **16**

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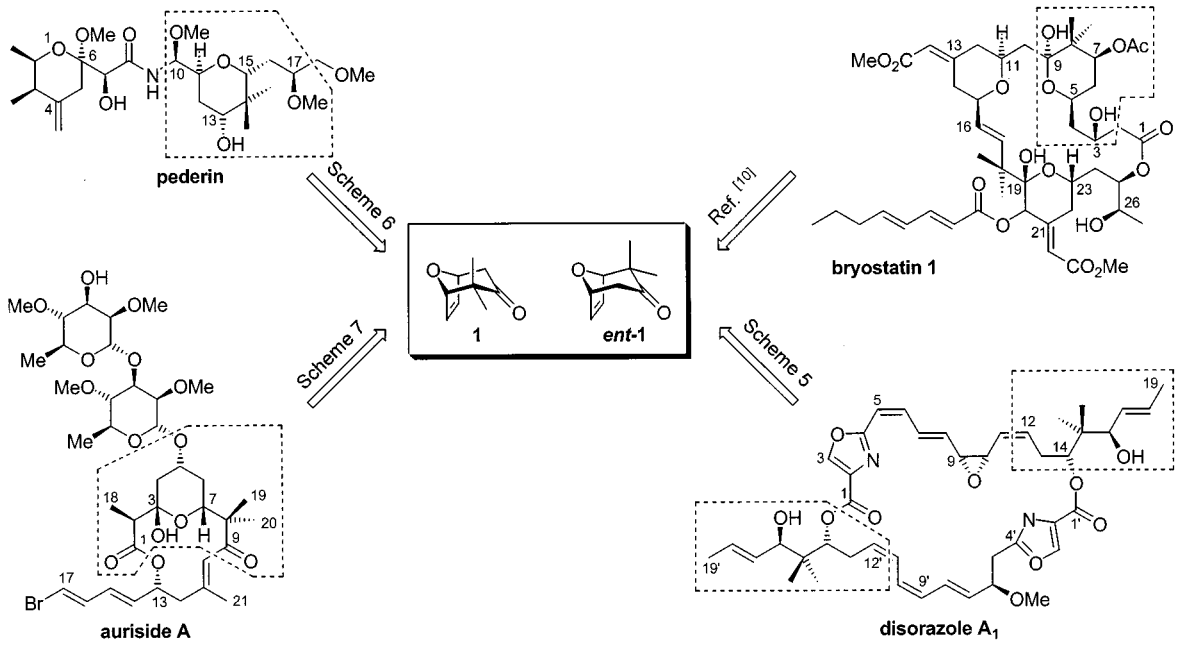
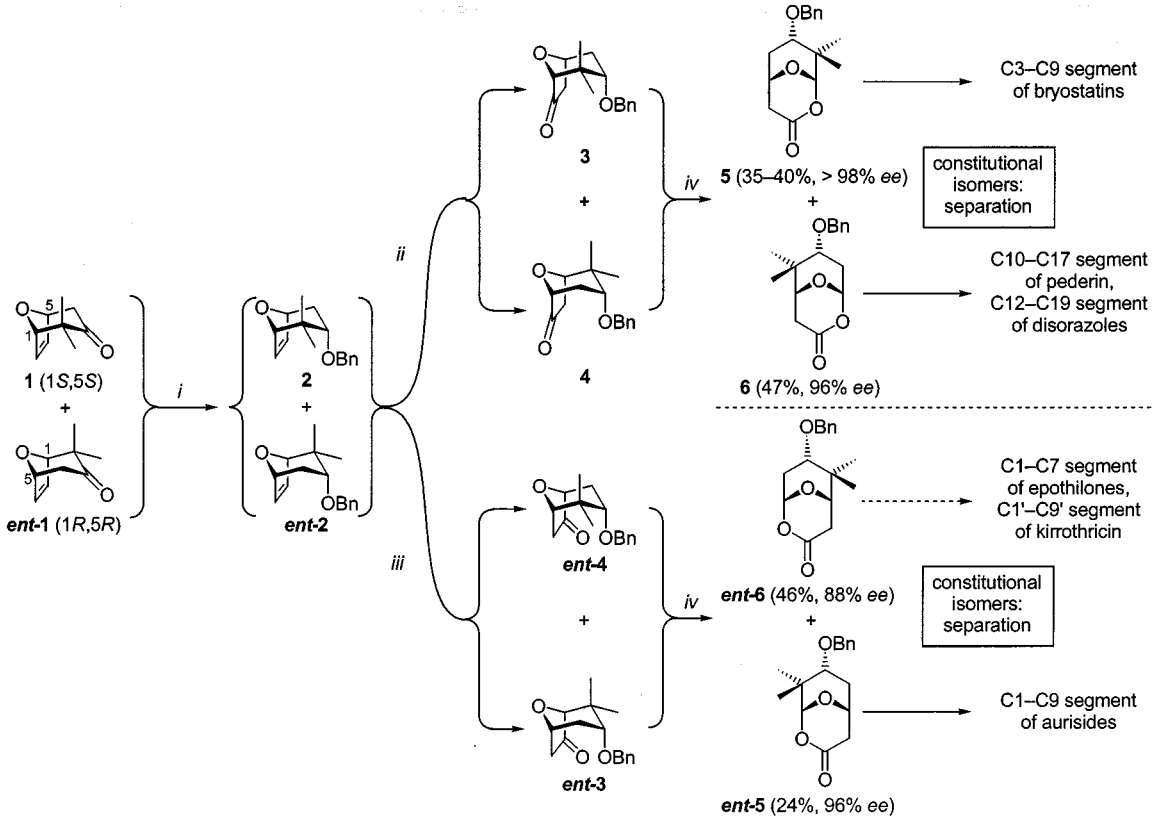
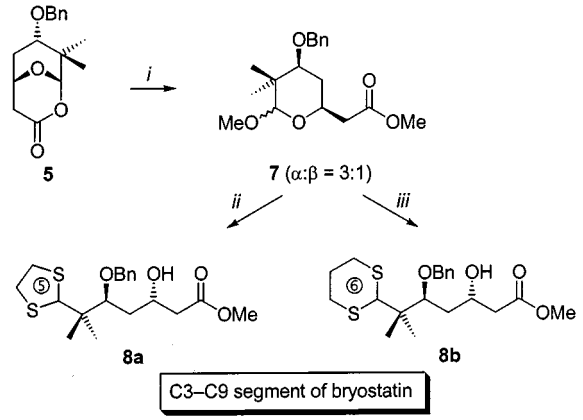


Scheme 1. Selected structural and stereochemical diversity from (±)-**1**

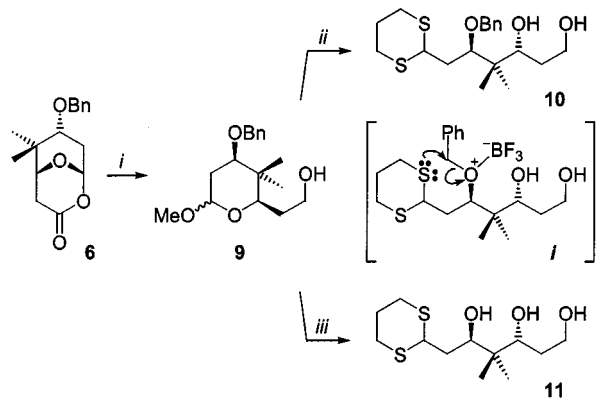


Scheme 2. The synthetic tree from (±)-**1**; *Reaction conditions: i*) 1. L-selectride, THF, 2 h, −78 °C; NaOH, H_2O_2, 2 h, room temp. (98%); 2. BnBr, NaH, THF, 1 h, reflux (98%); *ii*) 1. (−)-Ipc_2BH, THF, 3 days, −15 °C; NaOH, H_2O_2, 1 h, room temp. (92%); 2. PCC, CH_2Cl_2, 16 h, room temp. (96%); *iii*) 1. (+)-Ipc_2BH, Et_2O, 9 days, −15 °C; NaOH, H_2O_2, 2 h, room temp. (87%); 2. PCC, CH_2Cl_2, 17 h, room temp. (84%); *iv*) *m*-CPBA, $NaHCO_3$, CH_2Cl_2, 17 h, room temp.

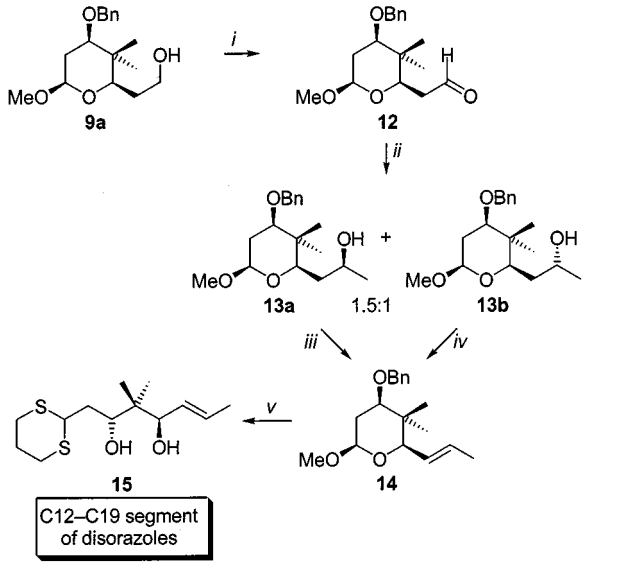
(Scheme 6). The ring-opening procedure with 1,3-propanedithiol/BF_3·Et_2O in acetonitrile[12] gave diol **17**, which on base-induced intramolecular Michael addition[15] stereoselectively afforded the desired *trans C*-glycoside **18**, corresponding to the C10−C17 segment of pederin [11 steps from **1**/***ent*-1**, 17% yield (50% maximum yield)].



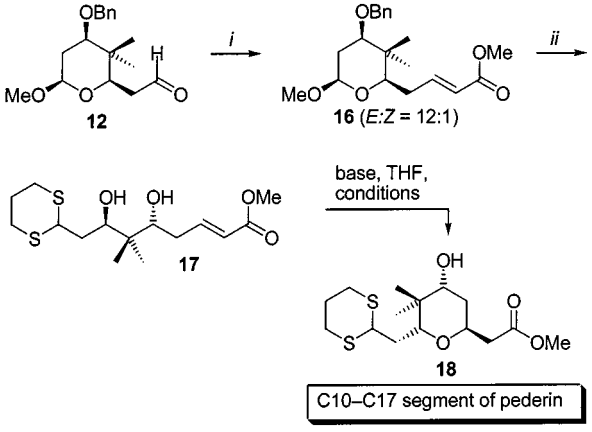
Scheme 3. Ring-opening of **5** and of the anomeric methoxy acetal **7α,β**; *Reaction conditions: i)* H^+ (catal.), MeOH, $MgSO_4$, reflux, 16 h (99%); *ii*) $HS(CH_2)_2SH$ (3.0 equiv.), $BF_3{\cdot}Et_2O$, CH_2Cl_2, room temp., 0.5 h (93%); *iii*) $HS(CH_2)_3SH$ (3.0 equiv.), $BF_3{\cdot}Et_2O$, $MeNO_2$, $-20 \rightarrow -15$ °C, 0.5 h (91%)



Scheme 4. Route to acyclic building blocks **10** and **11**; *Reaction conditions: i*) 1. H^+ (catal.), MeOH, $MgSO_4$, reflux, 16 h (99%); 2. DIBAH, toluene, $-78 \rightarrow 0$ °C, 1 h (88%); *ii*) $HS(CH_2)_3SH$ (1.5 equiv.), $BF_3{\cdot}Et_2O$ (4.5 equiv.), $MeNO_2$, $-20 \rightarrow -10$ °C, 3 h (81%); *iii*) $HS(CH_2)_3SH$ (1.5 equiv.), $BF_3{\cdot}Et_2O$, (5.5 equiv.), MeCN, 0 °C → room temp., 2.5 h (73%)



Scheme 5. One-carbon homologation of **9a** to **15**; *Reaction conditions: i*) Dess–Martin periodinane, CH_2Cl_2, 1 h, 0 °C (93%); *ii*) MeMgBr (2.0 equiv.), THF, $-50 \rightarrow 0$ °C, 0.5 h (88%); *iii*) 1. MsCl, Et_3N, CH_2Cl_2, 0 °C, 45 min (85%); 2. DBU (4 equiv.), toluene, 85 °C, 26 h (35%); *iv*) 1. MsCl, Et_3N, CH_2Cl_2, $-50 \rightarrow 0$ °C, 2 h (90%); 2. DBU (10 equiv.), toluene, 110 °C, 18 h (10%); *v*) $HS(CH_2)_3SH$ (1.5 equiv.), $BF_3{\cdot}Et_2O$ (3.0 equiv.), $MeNO_2$, $-20 \rightarrow 0$ °C, 45 min (40%)



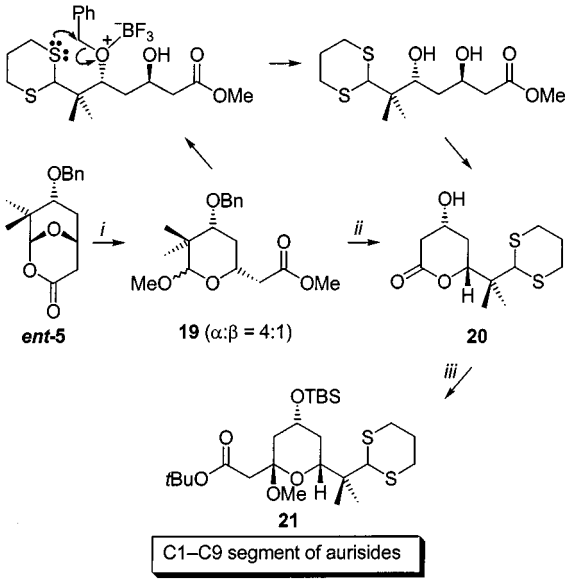
Scheme 6. Synthesis of the 2,6-*trans*-configured C-glycoside **18**; *Reaction conditions: i*) Ph_3PCHCO_2Me, CH_2Cl_2, room temp., 24 h (94%); *ii*) $HS(CH_2)_3SH$ (1.5 equiv.), $BF_3{\cdot}Et_2O$ (3.5 equiv.), MeCN, 0 °C → room temp., 1.5 h (90%)

Following our work on [3.3.1]lactone acetals **5** and **6**, we opened the lactone acetal ***ent*-5** and obtained the anomeric ester **19** (Scheme 7). In a one-pot procedure, the rearrangement cascade[12] with sulfur-assisted deprotection of the benzyl group and subsequent lactonization provided dithioacetal **20**, the termini of which are again fully differentiated. Lactonization was completed by addition of trifluoroacetic acid. Two-carbon homologation and protecting group manipulations gave the C1–C9 segment **21** of auri-

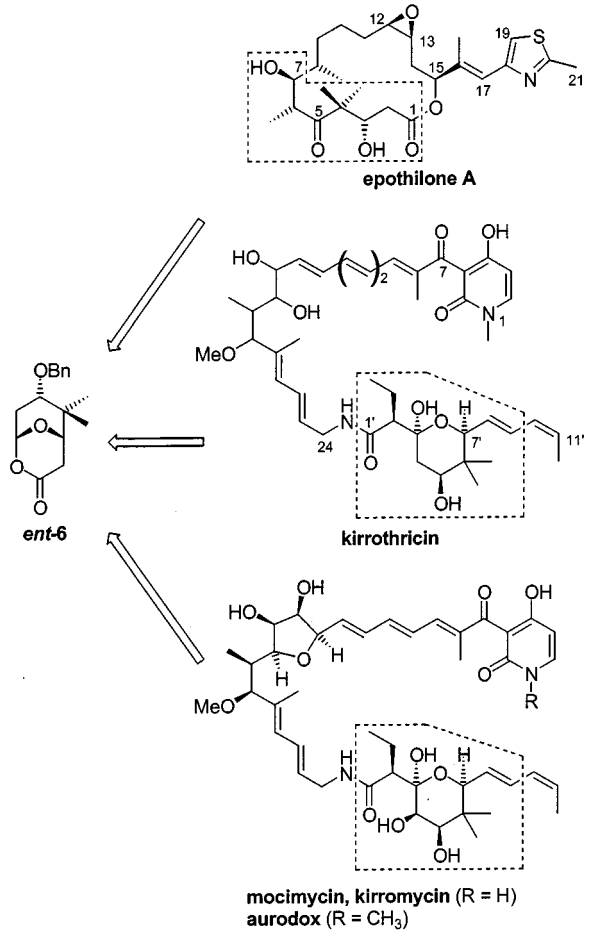
Table 1. Optimization of the Michael addition

Entry	Base	Conditions	Yield [%]	*trans*:*cis*[a]
1	4.0 equiv. NaH	0 °C → room temp., 4 h	decomposition	–
2	2.5 equiv. KO*t*Bu	−50 °C, 7 h	30	71:29
3	2.5 equiv. KO*t*Bu	−78 °C → room temp., 3 h; room temp., 1 h	65	69:31
4	3.0 equiv. NaH	−78 °C, 6 h; −20 °C, 18 h	75	67:33
5	2.2 equiv. NaH	−78 °C → 0 °C (2.5 h)	63	80:20

[a] The relative configuration of the new stereocentre was confirmed by NOE and NOESY experiments.



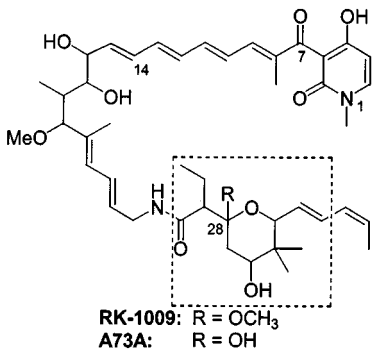
Scheme 7. Rearrangement cascade from ***ent*-5** to lactone **20** and synthesis of protected hemiacetal **21**; *Reaction conditions: i*) H^+ (catal.), MeOH, $MgSO_4$, reflux, 17 h (92%); *ii*) 1. $HS(CH_2)_3SH$ (1.5 equiv.), $BF_3{\cdot}Et_2O$ (5 equiv.), MeCN, room temp., 16 h; 2. TFA (1 equiv.), CH_2Cl_2, room temp., 4 h (75%); *iii*) 1. TBSCl, imidazole, DMF, room temp., 2 h; 2. CH_3CO_2tBu (5 equiv.), LDA, THF, −78 → 0 °C, 2 h; 3. citric acid (2 equiv.), MeOH, reflux, 6 h (60%)



Scheme 8. Further applications of [3.3.1]lactone acetals in natural product synthesis and in polyketide pattern recognition

side A [10 steps from **1**/***ent*-1**, 8% yield (maximum yield 50%)].

Our fourth lactone acetal ***ent*-6** is an epothilone C1−C7 building block[16] and should also be useful as a kirrothricin[17] and aurodox[18] component (Scheme 8). Recently, the antibiotics RK-1009 and A73A have been reported (Scheme 9). Although their relative and absolute stereochemistry have not yet been assigned[19] they are structurally very similar to kirrothricin, studied by Zeeck and his co-workers.



Scheme 9. Antibiotics from *Streptomyces spiroverticillatus*

In conclusion we have prepared a range of fully differentiated polyketide precursors and polyketide segments by a robust methodology. All highly functionalized, small molecules and their derivatives are of interest in parallel chemistry as part of a high-quality collection of polyketide segments and in target-oriented total asymmetric synthesis.

Experimental Section

General Remarks: Infrared spectra were recorded on a Perkin−Elmer 1710 infrared spectrometer. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker AM 400 spectrometer in deuterated chloroform unless otherwise stated, with tetramethylsilane as internal standard. Mass spectra were recorded on a Finnigan MAT 312 (70 eV) or a VG Autospec spectrometer at room temp. unless otherwise stated. All substances recorded were pure by spectroscopic (^1H and ^{13}C NMR) and chromatographic standards; 1° (primary), 2° (secondary), 3° (tertiary), 4° (quaternary) are used in the ^{13}C NMR data. Preparative column chromatography was performed on J. T. Baker silica gel (particle size 30−60 μm). Analytical TLC was carried out on aluminium-backed 0.2 mm 60 F_{254} silica gel plates (E. Merck). THF was distilled over sodium and benzophenone before use. CH_2Cl_2 (DCM) was distilled over CaH_2 before use. DMF was dried over BaO and distilled over CaH_2 before use. Methyl *tert*-butyl ether (MTBE), diethyl ether (E), light petroleum ether (PE, bp 40−60 °C), MeCN and $MeNO_2$ were distilled before use.

General Procedure for the Opening of Methoxy Acetals with 1,3-Propanedithiol/$BF_3{\cdot}Et_2O$: 1,3-Propanedithiol (1.5−2 equiv.) was added to a solution of methoxy acetal (1 equiv.) in $MeNO_2$ or MeCN (10 mL/mmol). The mixture was cooled down (−20 °C for solvent $MeNO_2$, 0 °C for solvent MeCN), and $BF_3{\cdot}Et_2O$ (3−5.5

equiv.) was added slowly. After 0.5−2 h at −20 → 0 °C (for solvent $MeNO_2$) or at 0 °C → room temp. (for solvent MeCN) the reaction was terminated by addition of MTBE, solid $NaHCO_3$ and sat. aq. $NaHCO_3$ solution at 0 °C. The layers were separated quickly and the aqueous phase was neutralized carefully with concd. HCl and extracted with MTBE (2−5×). The combined organic phase was washed with brine and dried (Na_2SO_4/Na_2CO_3, 2:1). The solvent was removed and the crude product was purified by column chromatography.

(3*R*,5*R*)-5-Benzyloxy-6-(1,3-dithian-2-yl)-4,4-dimethylhexane-1,3-diol (10): Methoxy acetal **9** (80 mg, 0.27 mmol), $HS(CH_2)_3SH$ (50 μL, 0.49 mmol) and $BF_3{\cdot}Et_2O$ (154 μL, 1.25 mmol) in $MeNO_2$ were allowed to react for 3 h at −10 °C according to the general procedure. Chromatography (MTBE) afforded **10** (80 mg, 81%), highly viscous oil, $[\alpha]_D^{20}$ = +30.1 (*c* = 1, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3628, 3460, 2976, 2900, 1424, 1344, 1296, 1236, 1068, 1024, 908 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.82/1.11 [s, 3 H, C(CH_3)$_2$], 1.50−1.58 (m, 1 H, CH_2CHOH), 1.64−1.75 (m, 1 H, CH_2CHOH), 1.77−1.92 (m, 2 H, SCHSCH_2, O*H*), 1.97 (ddd, ^2J = 14.0, ^3J = 10.8, ^3J = 2.4 Hz, 1 H, SCHSCH_2), 2.03−2.13 (m, 2 H, SCH$_2$CH_2CH$_2$S), 2.68 (ddd, ^2J = 14.1, ^3J = 11.7, ^3J = 2.4 Hz, 1 H, SCH_2CH$_2$CH_2S), 2.75−2.86 (m, 4 H, SCH_2CH$_2$CH_2S), 3.73 (dd, ^3J = 9.5, ^3J = 2.4 Hz, 1 H, C*H*OBn), 3.83 (t, ^3J = 4.5 Hz, 1 H, CH_2OH), 3.91 (dd, ^3J = 10.8, ^3J = 2.1 Hz, 1 H, C*H*OH), 3.99 (dd, ^3J = 10.9, ^3J = 3.9 Hz, 1 H, SC*H*S), 4.0.3−4.11 (br. s, 1 H, O*H*), 4.71/4.78 (d, ^2J = 11.3 Hz, 2 H, CH_2Ph), 7.27−7.39 (m, 5 H, Ar-*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.2/22.5 [1°, C(*C*H$_3$)$_2$], 25.9 (2°, SCH$_2$*C*H$_2$CH$_2$S), 30.0/30.7 (2°, SCH$_2$CH$_2$*C*H$_2$S), 32.8 (2°, *C*H$_2$COH), 37.0 (2°, SCHS*C*H$_2$), 41.3 [4°, *C*(CH$_3$)$_2$], 44.8 (3°, S*C*HS), 62.4 (2°, *C*H$_2$OH), 75.8 (2°, *C*H$_2$Ph), 76.4 (3°, *C*HOH), 86.1 (3°, *C*HOBn), 127.8 (3°, *o*-Ar-*C*), 128.0 (3°, *p*-Ar-*C*), 128.6 (3°, *m*-Ar-*C*), 138.0 (4°, Ar-*C*). MS (140 °C): *m*/*z* (%) = 370 (2) [M^+], 279 (3), 262 (16), 253 (4), 197 (2), 187 (7), 163 (3), 155 (8), 145 (31), 133 (25), 129 (9), 119 (38), 111 (4), 107 (7), 105 (4), 91 (100), 83 (8), 81 (5), 77 (3), 75 (9). HRMS calcd. for $C_{19}H_{30}O_3S_2$: 370.1636, found 370.1633.

(3*R*,5*R*)-6-(1,3-Dithian-2-yl)-4,4-dimethylhexane-1,3,5-triol (11): Methoxy acetal **9** (95 mg, 0.32 mmol), $HS(CH_2)_3SH$ (63 μL, 0.58 mmol) and $BF_3{\cdot}Et_2O$ (218 μL, 1.77 mmol) in MeCN were allowed to react for 2.5 h at room temp. according to the general procedure. Chromatography (MTBE → MTBE/MeOH, 4:1) afforded **11** (66 mg, 73%), highly viscous oil. IR ($CHCl_3$): $\tilde{\nu}$ = 3624, 3448, 2968, 2936, 2804, 1468, 1424, 1336, 1276, 1240, 1064, 908 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.84/0.98 [m, 7 H, C(CH_3)$_2$, O*H*], 1.60−1.98 [m, 6 H, SCH$_2$CH_2CH$_2$S, CH(OH)CH_2-CH$_2$OH, SCHSCH_2CHO*H*], 2.08−2.18 (m, 1 H, SCH$_2$CH_2CH$_2$S), 2.79−3.00 (m, 4 H, SCH_2CH$_2$CH_2S), 3.70−3.97 (m, 4 H, SCHSCH$_2$C*H*OH, C*H*OHCH$_2$CH_2OH), 4.05 (br. s, 1 H, O*H*), 4.32 (dd, ^3J = 10.0, ^3J = 4.0 Hz, 1 H, SC*H*S). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.9/21.1 [1°, C(*C*H$_3$)$_2$], 26.0 (2°, SCH$_2$*C*H$_2$CH$_2$S), 30.0/30.5 (2°, SCH_2CH$_2$*C*H$_2$S), 32.5 (2°, *C*H$_2$COH), 37.7 (2°, SCHS*C*H$_2$CHOH), 39.9 [4°, *C*(CH$_3$)$_2$], 44.7 (3°, S*C*HS), 62.6 (2°, *C*H$_2$OH), 75.2 (3°, *C*HOHCH$_2$CH$_2$OH), 79.8 (3°, SCHSCH$_2$*C*HOH). MS (130 °C): *m*/*z* (%) = 281 (9) [M^+ + 1], 280 (13) [M^+], 263 (5), 235 (2), 187 (4), 167 (27), 155 (6), 149 (69), 145 (25), 132 (11), 119 (37), 113 (8), 111 (3), 106 (30), 104 (4), 98 (9), 86 (62), 84 (100), 72 (59). HRMS calcd. for $C_{12}H_{24}O_3S_2$: 280.1167, found 280.1166.

(2*S*,4*R*,6*R*)-1-(4-Benzyloxy-6-methoxy-3,3-dimethyltetrahydropyran-2-yl)propan-2-ol (13a) and (2*R*,4*R*,6*R*)-1-(4-Benzyloxy-6-methoxy-3,3-dimethyltetrahydropyran-2-yl)propan-2-ol (13b): Dess−Martin periodinane (551 mg, 1.3 mmol) in DCM (3 mL) was added slowly at 0 °C to a solution of alcohol **9a** (295 mg, 1 mmol) in DCM (5 mL). The mixture was stirred for 1 h at 0 °C and then added to a mixture of 1 N NaOH and MTBE (1:1, 40 mL). The aqueous layer was extracted with MTBE (2×). The combined organic layer was washed with brine, dried (Na_2SO_4) and concentrated. Purification of the residue by chromatography (MTBE/PE, 1:1) gave aldehyde **12** (273 mg, 93%), colourless liquid. The aldehyde **12** was dissolved in THF (9 mL) and the solution was cooled to −50 °C. MeMgBr (0.62 mL, 1.86 mmol, 3 M solution in E) was added dropwise, and the reaction mixture was allowed to reach 0 °C within 30 min. Sat. aq. NH_4Cl solution (15 mL) was added, and the aqueous phase was extracted with MTBE (3×). The combined organic phase was washed with brine, dried (Na_2SO_4) and concentrated. Column chromatography (MTBE/PE, 1:1) afforded minor epimer **13b** (65 mg), major epimer **13a** (92 mg) and a mixture of both epimers (95 mg) (252 mg altogether, 82%). Data for **13a**, highly viscous oil, $[\alpha]_D^{20}$ = −22.2 (*c* = 1; $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3501, 2966, 2931, 2867, 1716, 1602, 1453, 1387, 1273, 1230, 1165, 1065, 991 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.91/0.92 [s, 3 H, C(CH_3)$_2$], 1.23 [d, ^3J = 6.2 Hz, 3 H, C(OH)CH_3], 1.48−1.73 (m, 3 H, CH$_3$OCHCH_2-ax, CHCH_2CHOH), 1.95−2.09 (br. s, 1 H, O*H*), 2.13 (ddd, ^2J = 12.3, ^3J = 4.5, ^3J = 2.4 Hz, 1 H, CH$_3$OCHCH_2-eq), 3.10 (dd, ^3J = 11.8, ^3J = 4.5 Hz, 1 H, C*H*OBn), 3.28 (dd, ^3J = 10.7, ^3J = 1.9 Hz, 1 H, C*H*CH$_2$CHOH), 3.49 (s, 3 H, OCH_3), 4.01−4.11 (m, 1 H, C*H*OH), 4.30 (dd, ^3J = 10.0, ^3J = 2.3 Hz, 1 H, CH$_3$OC*H*), 4.42/4.64 (d, ^2J = 11.8 Hz, 1 H, CH_2Ph), 7.24−7.36 (m, 5 H, Ar-*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.4 [1°, C(OH)*C*H$_3$], 22.4/24.0 [1°, C(*C*H$_3$)$_2$], 33.1 (2°, CH$_3$OCH*C*H$_2$), 37.2 (2°, *C*H$_2$CHOH), 38.2 [4°, *C*(CH$_3$)$_2$], 56.5 (1°, O*C*H$_3$), 65.2 (3°, *C*HOH), 71.1 (2°, *C*H$_2$Ph), 76.9 (3°, *C*HCH$_2$CHOH), 81.3 (3°, *C*HOBn), 101.7 (3°, CH$_3$O*C*H), 127.5 (3°, *o*-Ar-*C*), 127.5 (3°, *p*-Ar-*C*), 128.3 (3°, *m*-Ar-*C*), 138.6 (4°, Ar-*C*). MS (60 °C): *m*/*z* (%) = 308 (1) [M^+], 200 (1), 179 (2), 162 (43), 151 (3), 135 (2), 113 (3), 105 (13), 91 (100), 81 (3), 70 (7). HRMS calcd. for $C_{18}H_{28}O_4S$: 308.1988, found 308.1989. Data for **13b**, highly viscous oil, $[\alpha]_D^{20}$ = −10.6 (*c* = 0.5, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3506, 2999, 2970, 2935, 2869, 1716, 1602, 1452, 1388, 1275, 1230, 1166, 1061, 991 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.91/0.94 [s, 3 H, C(CH_3)$_2$], 1.19 [d, ^3J = 6.2 Hz, 3 H, C(OH)CH_3], 1.51−1.70 (m, 3 H, CH$_3$OCHCH_2-ax, CHCH_2CHOH), 2.14 (ddd, ^2J = 12.3, ^3J = 4.5, ^3J = 2.4 Hz, 1 H, CH$_3$OCHCH_2-eq), 3.10 (dd, ^3J = 11.8, ^3J = 4.5 Hz, 1 H, C*H*OBn), 3.18 −3.24 (m, 1 H, C*H*CH$_2$CHOH), 2.52−3.62 (br. s, 1 H, O*H*), 4.42/4.64 (d, ^2J = 11.8 Hz, 1 H, CH_2Ph), 4.34 (dd, ^3J = 10.0, ^3J = 2.3 Hz, 1 H, CH$_3$OC*H*), 3.93−4.02 (m, 1 H, C*H*OH), 3.47 (s, 3 H, OCH_3), 7.25−7.37 (m, 5 H, Ar-*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.5 [1°, C(OH)*C*H$_3$], 22.5/23.4 [1°, C(*C*H$_3$)$_2$], 33.0 (2°, CH$_3$OCH*C*H$_2$), 36.5 (2°, *C*H$_2$CHOH), 38.5 [4°, *C*(CH$_3$)$_2$], 56.6 (1°, O*C*H$_3$), 68.4 (3°, *C*HOH), 71.1 (2°, *C*H$_2$Ph), 80.9/81.8 (3°, *C*HOBn, *C*HCH$_2$CHOH), 102.0 (3°, CH$_3$O*C*H), 127.5 (3°, *o*-Ar-*C*), 127.6 (3°, *p*-Ar-*C*), 128.3 (3°, *m*-Ar-*C*), 148.5 (4°, Ar-*C*). MS (70 °C): *m*/*z* (%) = 308 (0.5) [M^+], 277 (0.6), 250 (0.7), 217 (0.8), 200 (3), 179 (2), 162 (53), 136 (53), 112 (9), 105 (7), 91 (100), 81 (8), 70 (17).

(2*R*,4*R*,6*R*)-4-Benzyloxy-6-methoxy-3,3-dimethyl-2-propenyltetrahydropyran (14): Et_3N (91 μL, 0.65 mmol) was added at 0 °C to a solution of alcohol **13a** (80 mg, 0.25 mmol) in DCM (2 mL), followed by MsCl (24 μL, 0.31 mmol). The mixture was stirred for 45 min at 0 °C and then diluted with MTBE and H_2O. The organic layer was washed with 2 N HCl. The aqueous phase was extracted with MTBE (2×), and the combined organic layer was washed with brine and dried ($MgSO_4$). After removal of the solvent and chromatography, the mesylate alcohol (82 mg, 85%) was obtained. DBU (66 μL, 0.44 mmol) was added to a solution of the mesylate (42 mg,

0.11 mmol) in toluene (0.4 mL), and the mixture was heated to 85 °C for 26 h. The mixture was cooled to room temp., diluted with MTBE and washed with 0.5 N HCl. The aqueous layer was extracted with MTBE (2×) and the combined organic phase was washed with brine and dried (Na_2SO_4). After removal of the solvent and chromatography, the *Z* olefin (2.5 mg, 8%), the terminal olefin (3.2 mg, 10%) and the desired *E* olefin **14** (11 mg, 35%), colourless liquid, were obtained. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89−0.92 [s, 3 H, C(CH_3)$_2$], 1.53−1.62 (m, 1 H, CH_3OCHCH_2-ax), 1.70−1.75 (m, 3 H, CHCHCHCH_3), 2.12 (ddd, ^2J = 12.4, ^3J = 4.5, ^3J = 2.4 Hz, 1 H, CH_3OCHCH_2-eq), 3.13 (dd, ^3J = 11.8, ^3J = 4.5 Hz, 1 H, C*H*OBn), 3.40 (d, ^3J = 6.9 Hz, 1 H, C*H*CHCHCH$_3$), 3.50 (s, 3 H, OCH_3), 4.31 (dd, ^3J = 9.9, ^3J = 2.3 Hz, 1 H, CH_3OCH), 4.43/4.64 (d, ^2J = 11.8 Hz, 1 H, CH_2Ph), 5.46−5.54 (ddd, ^3J = 15.4, ^3J = 6.9, ^4J = 1.5 Hz, 1 H, CHC*H*CHCH$_3$), 5.63−5.73 (m, 1 H, CHCHC*H*CH$_3$), 7.36−7.25 (m, 5 H, Ar-*H*).

(2*R*,4*R*)-1-(1,3-Dithian-2-yl)-3,3-dimethylhept-5-ene-2,4-diol (15): Methoxy acetal **14** (10 mg, 0.036 mmol), HS(CH$_2$)$_3$SH (10 μL, 0.11 mmol) and BF_3·Et_2O (13 μL, 0.11 mmol) in $MeNO_2$ were allowed to react for 45 min at 0 °C according to the general procedure. Chromatography (MTBE/PE, 1:3 → 1:1) afforded **15** (4 mg, 40%), colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.02/1.04 [s, 3 H, C(CH_3)$_2$], 1.31 [d, ^2J = 6.4 Hz, CH(OH)CHCHCH_3], 1.68−1.93 (m, 4 H, SCH$_2$CH_2CH$_2$S, SCHSCH_2CHOH, O*H*), 2.10−2.18 (m, 1 H, SCH$_2$CH_2CH$_2$S), 2.72−2.98 (m, 5 H, SCH_2CH$_2$CH_2S, O*H*), 3.27−3.36 [m, 1 H, C*H*(OH)CHCHCH$_3$], 3.63 (dd, ^3J = 12.5, ^3J = 1.8 Hz, 1 H, SCHSCH$_2$C*H*OH), 4.05 (br. s, 1 H, O*H*), 4.26 (dd, ^3J = 10.3, ^3J = 4.0 Hz, 1 H, SC*H*S), 5.27−5.34 [m, 1 H, C(OH)CHC*H*CH$_3$], 5.45 [dd, ^3J = 15.7, ^4J = 0.8 Hz, 1 H, CH(OH)C*H*CHCH$_3$]. MS (140 °C): *m*/*z* (%) = 277 (1) [M$^+$ + 1], 259 (100) [M$^+$ − OH], 205 (4), 185 (2), 163 (9), 161 (10), 137 (1), 135 (7), 133 (15), 119 (66), 107 (24), 106 (12), 97 (37), 96 (61), 81 (11), 75 (14), 73 (12). HRMS calcd. for $C_{13}H_{23}O_1S_2$: 259.1190, found 259.1188.

Methyl (2*R*,4*R*,6*R*)-4-(4-Benzyloxy-6-methoxy-3,3-dimethyltetrahydropyran-2-yl)but-2-enoate (16): A solution of Ph_3PCHCO_2Me (1.04 g, 3.11 mmol) in DCM (6 mL) was added dropwise at room temp to a solution of aldehyde **12** (260 mg, 0.89 mmol) in DCM (3 mL). The mixture was stirred for 24 h and then reduced to half its original volume. The crude product was purified by column filtration (MTBE/PE, 1:8) to give **16** (290 mg, 94%), colourless liquid. IR ($CHCl_3$): ṽ = 3008, 2964, 2936, 2844, 1716, 1660, 1436, 1328, 1276, 1232, 1168, 1092, 1072 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.94 [s, 6 H, C(CH_3)$_2$], 1.55 (ddd, ^2J = 12.4, ^3J = 11.8, ^3J = 9.9 Hz, 1 H, CH_3OCHCH_2-ax), 2.13 (ddd, ^2J = 12.4, ^3J = 4.5, ^3J = 2.3 Hz, 1 H, CH_3OCHCH_2-eq), 2.37−2.42 (m, 2 H, CHCH_2CHCH), 3.04 (dd, ^3J = 7.3, ^3J = 5.4 Hz, 1 H, C*H*CH$_2$CHCH), 3.10 (dd, ^3J = 11.8, ^3J = 4.5 Hz, 1 H, C*H*OBn), 3.48 (s, 3 H, CH_3OCH), 3.72 (s, 3 H, CO_2CH_3), 4.25 (dd, ^3J = 9.9, ^3J = 2.3 Hz, 1 H, CH_3OCH), 4.42/4.64 (d, ^2J = 11.8 Hz, 1 H, CH_2Ph), 5.90 (dt, ^3J = 15.7, ^4J = 1.4 Hz, 1 H, CHC*H*CO$_2$CH$_3$), 7.03 (dt, ^3J = 15.7, ^3J = 7.0 Hz, 1 H, C*H*CHCO$_2$CH$_3$), 7.26−7.36 (m, 5 H, Ar-*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.4/22.6 [1°, C(*C*H$_3$)$_2$], 31.8 (2°, CHC*H*$_2$CHCH), 33.1 (2°, CH_3OCHCH_2), 38.6 [4°, *C*(CH$_3$)$_2$], 51.4 (1°, CO_2CH_3), 56.5 (1°, *C*H$_3$OCH), 71.2 (2°, *C*H$_2$Ph), 79.3 (3°, *C*HCH$_2$CHCH), 81.1 (3°, *C*HOBn), 101.5 (3°, CH_3OCH), 122.4 (3°, CH*C*HCO$_2$CH$_3$), 127.5 (3°, *o*-Ar-*C*), 127.6 (3°, *p*-Ar-*C*), 147.0 (3°, *C*HCHCO$_2$CH$_3$), 138.6 (4°, Ar-*C*), 128.5 (3°, *m*-Ar-*C*), 167.0 (4°, *C*O$_2$CH$_3$). MS (60 °C): *m*/*z* (%) = 348 (2) [M$^+$], 316 (2), 279 (2), 249 (6), 219 (2), 169 (3), 162 (36), 154 (11), 149 (5), 141 (3), 125 (2), 122 (2), 111 (6), 105 (8), 95 (4), 91 (100), 87 (9), 86 (31), 81 (5), 77 (3), 71 (7). HRMS calcd. for $C_{20}H_{28}O_5$: 348.1937, found 348.1935.

Methyl (5*R*,7*R*)-8-(1,3-Dithian-2-yl)-5,7-dihydroxy-6,6-dimethyloct-2-enoate (17): Methoxy acetal **16** (70 mg 0.20 mmol), HS(CH$_2$)$_3$SH (24 μL, 0.24 mmol) and BF_3·Et_2O (86 μL, 0.70 mmol) in MeCN were allowed to react for 1.5 h at room temp. according to the general procedure. Chromatography (MTBE/PE, 1:1) afforded **17** (60 mg, 90%), viscous oil. IR ($CHCl_3$): ṽ = 3680, 3604, 3488, 2952, 2928, 2856, 1716, 1656, 1436, 1328, 1276, 1228, 1196, 1044, 980 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93/0.95 [m, 3 H, C(CH_3)$_2$], 1.18−1.39 (br. s, 1 H, O*H*), 1.83−1.98 (m, 3 H, SCH$_2$CH_2CH$_2$S, SCHSCH_2CHOH), 2.09−2.18 (m, 1 H, SCH$_2$CH_2CH$_2$S), 2.29−2.47 (m, 2 H, CH_2CHCH), 2.82−2.99 (m, 4 H, SCH_2CH$_2$CH_2S), 3.10−3.39 (br. s, 1 H, O*H*), 3.68 (dd, ^3J = 10.0, ^3J = 2.5 Hz, 1 H, C*H*(OH)CH$_2$CHCH), 3.73 (s, 3 H, OCH_3), 3.88 (dd, ^3J = 9.7, ^3J = 2.4 Hz, 1 H, SCHSCH$_2$C*H*OH), 4.29 (dd, ^3J = 9.3, ^3J = 4.9 Hz, 1 H, SC*H*S), 5.94 (dt, ^3J = 15.4, ^4J = 1.4 Hz, 1 H, CHC*H*CO$_2$CH$_3$), 6.99−7.09 (m, 1 H, C*H*CHCO$_2$CH$_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.1 [1°, C(*C*H$_3$)$_2$], 26.1 (2°, SCH$_2$*C*H$_2$CH$_2$S), 29.9/30.6 (2°, SCH_2CH$_2$*C*H$_2$S), 34.5 (2°, *C*H$_2$CHCH), 36.7 [4°, *C*(CH$_3$)$_2$], 37.5 (2°, SCHS*C*H$_2$CHOH), 43.6 (3°, S*C*HS), 51.5 (1°, O*C*H$_3$), 74.3 (3°, SCHSCH$_2$*C*HOH), 78.0 (3°, *C*H(OH)CH$_2$CHCH), 123.1 (3°, CH*C*HCO$_2$CH$_3$), 145.8 (3°, *C*HCHCO$_2$CH$_3$), 167.0 (4°, *C*O$_2$CH$_3$). MS (150 °C): *m*/*z* (%) = 334 (7) [M$^+$], 316 (9), 302 (2), 279 (7), 242 (3), 235 (15), 217 (5), 200 (9), 199 (5), 187 (9), 167 (15), 149 (40), 132 (24), 129 (15), 119 (100), 111 (13), 107 (13), 100 (15), 97 (19), 95 (21), 85 (14), 72 (47). HRMS calcd. for $C_{15}H_{26}O_4S_2$: 334.1272, found 334.1273.

Methyl (2*S*,4*R*,6*R*)-6-{[(1,3-Dithian-2-yl)methyl]-4-hydroxy-5,5-dimethyltetrahydropyran-2-yl}acetate (18): Diol **17** (72 mg, 0.21 mmol) in THF (1.5 mL) was added slowly at −78 °C to a suspension of NaH (19 mg, 0.47 mmol, 60% suspension in mineral oil) in THF (1 mL). The mixture was allowed to reach 0 °C within 2.5 h, after which the reaction was terminated by addition of 2 N HCl/MeOH (1:2, 2 mL). MTBE and H_2O were added and the aqueous layer was extracted with MTBE (2×). The combined organic phase was washed with brine and dried ($MgSO_4$). Chromatography (MTBE/PE, 1:3) afforded an inseparable mixture of *trans* and *cis* *C*-glycoside (4:1) (44 mg, 63%), highly viscous oil. **Data for Major Epimer *trans*-18:** $[\alpha]_D^{20}$ = +7.3 (*c* = 0.2, $CHCl_3$). IR ($CHCl_3$): ṽ = 3617, 2977, 2953, 2904, 1735, 1437, 1367, 1236, 1172, 1087, 1028, 908 cm^{-1}. NMR signals were assigned by 2D techniques: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88/0.98 [s, 3 H, C(CH_3)$_2$], 1.37−1.48 (m, 1 H, CH_2CHOH), 1.50−1.65 (br. s, 1 H, O*H*), 1.67−1.74 (m, 1 H, SCHSCH_2CH), 1.76−1.93 (m, 2 H, SCH$_2$CH_2CH$_2$S, CH_2CHOH), 2.00−2.11 (m, 2 H, SCH$_2$CH_2CH$_2$S, SCHSCH_2CH), 2.41−2.64 (m, 1 H, CH_2CO$_2$CH$_3$), 2.77−2.97 (m, 5 H, SCH_2CH$_2$CH_2S, CH_2CO$_2$CH$_3$), 3.57 (dd, ^3J = 10.9, ^3J = 1.8 Hz, 1 H, SCHSCH$_2$C*H*), 3.59 (dd, ^3J = 11.5, ^3J = 4.0 Hz, 1 H, C*H*OH), 3.71 (s, 3 H, OCH_3), 4.16 (dd, ^3J = 11.3, ^3J = 2.9 Hz, 1 H, SC*H*S), 4.53−4.45 (m, 1 H, C*H*CH$_2$CO$_2$CH$_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.3/23.5 [1°, C(*C*H$_3$)$_2$], 26.3 (2°, SCH$_2$*C*H$_2$CH$_2$S), 29.8/30.5 (2°, SCH_2CH$_2$*C*H$_2$S), 34.7 (2°, SCHS*C*H$_2$CH), 35.1 (2°, *C*H$_2$CHOH), 38.5 [4°, *C*(CH$_3$)$_2$], 40.9 (2°, *C*H$_2$CO$_2$CH$_3$), 44.2 (3°, S*C*HS), 51.6 (1°, O*C*H$_3$), 67.5 (3°, *C*HCH$_2$CO$_2$CH$_3$), 72.1 (3°, *C*HOH), 73.9 (3°, SCHSCH$_2$*C*H), 171.6 (4°, *C*O$_2$CH$_3$). MS (70 °C): *m*/*z* (%) = 334 (100) [M$^+$], 316 (44), 286 (5), 218 (4), 201 (25), 192 (9), 188 (8), 164 (6), 161 (3), 145 (37), 133 (28), 132 (59), 119 (75), 99 (7), 73 (15), 71 (63). HRMS calcd. for $C_{15}H_{26}O_4S_2$: 334.1272, found 334.1274. **Data for Minor Epimer *cis*-18:** NMR signals were assigned by 2D techniques: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.82/0.93 [s, 3 H, C(CH_3)$_2$],

1.76−1.93 (m, 5 H, $SCH_2CH_2CH_2S$, CH_2CHOH, $SCHSCH_2CH$), 2.00−2.11 (m, 1 H, $SCH_2CH_2CH_2S$), 2.41−2.64 (m, 1 H, $CH_2CO_2CH_3$), 2.77−2.97 (m, 5 H, $SCH_2CH_2CH_2S$, $CH_2CO_2CH_3$), 3.30 (dd, ^3J = 10.9, ^3J = 1.8 Hz, 1 H, $SCHSCH_2CH$), 3.46 (dd, ^3J = 11.7, ^3J = 4.7 Hz, 1 H, $CHOH$), 3.70 (s, 3 H, OCH_3), 3.78−3.87 (m, 1 H, $CHCH_2CO_2CH_3$), 4.13 (dd, ^3J = 11.3, ^3J = 4.8 Hz, 1 H, $SCHS$); NOE $CHCH_2CO_2CH_3$ irradiated $SCHSCH_2CH$ (9.1%), $CHOH$ (3.2%), $CHOH$ irradiated $CHCH_2CO_2CH_3$ (4.5%), $SCHSCH_2CH$ (7.0%). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.4/22.1 [1°, $C(CH_3)_2$], 26.2 (2°, $SCH_2CH_2CH_2S$), 29.7/30.5 (2°, $SCH_2CH_2CH_2S$), 33.6 (2°, $SCHSCH_2CH$), 36.5 (2°, CH_2CHOH), 37.6 (2°, $CH_2CO_2CH_3$), 38.4 [4°, $C(CH_3)_2$], 44.4 (3°, SCHS), 51.7 (1°, OCH_3), 72.6 (3°, $CHCH_2CO_2CH_3$), 75.4 (3°, CHOH), 79.7 (3°, $SCHSCH_2CH$), 171.4 (4°, CO_2CH_3).

(4*R*,6*R*)-6-{1-[(1,3-Dithian-2-yl)-1-methylethyl]}-4-hydroxytetrahydropyran-2-one (20): Methoxy acetal **19** (α:β, 4:1) (1.0 g 3.1 mmol), $HS(CH_2)_3SH$ (470 μL, 4.65 mmol) and $BF_3{\cdot}Et_2O$ (1.91 mL, 15.5 mmol) in MeCN were allowed to react for 16 h at room temp. according to the general procedure. After workup and removal of the solvents, the reaction was driven to completion by addition of TFA (119 μL, 1.55 mmol) to a solution in DCM (20 mL). Chromatography (PE/MTBE, 2:3) afforded **20** (646 mg, 75%), white solid, m.p. 99−103 °C, $[\alpha]_D^{20}$ = −11.2 (*c* = 1, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3400, 2971, 2934, 2901, 1725, 1464, 1421, 1371, 1245, 1216, 1160, 1066, 987, 934, 902, 834, 778, 658 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.08/1.19 [s, 3 H, $C(CH_3)_2$], 1.56−1.67 [m, 1 H, $CH_2CHC(CH_3)_2$], 1.76−1.89 (m, 1 H, $SCH_2CH_2CH_2S$), 2.06−2.15 (m, 1 H, $SCH_2CH_2CH_2S$), 2.23−2.31 (m, 1 H, $CH_2CHC(CH_3)_2$], 2.35−2.43 (br. s, 1 H, OH), 2.47 (dd, ^3J = 17.0, ^3J = 8.0 Hz, 1 H, $CH_2C{=}O$), 2.84−3.00 (m, 5 H, $SCH_2CH_2CH_2S$, $O{=}CCH_2$), 4.24−4.33 (m, 1 H, CHOH), 4.36 (s, 1 H, SCHS), 4.52 [dd, ^3J = 12.0, ^3J = 3.0 Hz, 1 H, $OCHC(CH_3)_2$]. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.9 (1°, CH_3), 20.1 (1°, CH_3), 26.2 (2°, $SCH_2CH_2CH_2S$), 31.3 (2°, $SCH_2CH_2CH_2S$), 32.3 [2°, $CH_2CHC(CH_3)_2$], 39.5 (2°, $CH_2C{=}O$), 41.9 [4°, $C(CH_3)_2$], 57.7 (3°, SCHS), 63.8 (3°, CHOH), 79.8 (3°, $CHC(CH_3)_2$], 171.0 (4°, C=O). MS (110 °C): *m*/*z* (%) = 276 (14) [M^+], 197 (4), 161 (5), 149 (16), 121 (10), 119 (100), 115 (8), 107 (10), 106 (21), 91 (23), 88 (5), 84 (5), 73 (11), 69 (11). HRMS calcd. for $C_{12}H_{20}O_3S_2$: 276.0854, found 276.0855.

***tert*-Butyl (2*S*,4*R*,6*R*)-{4-(*tert*-Butyldimethylsilanyloxy)-6-[1-(1,3-dithian-2-yl)-1-methylethyl]-2-methoxytetrahydropyran-2-yl}acetate (21):** Imidazole (108 mg, 1.59 mmol) and TBSCl (224 mg, 1.48 mmol) were added at 0 °C to a solution of dithiane **20** (293 mg, 1.06 mmol) in DMF (6 mL). The mixture was stirred for 2 h at room temp., and then H_2O (≈2 mL) was added. MTBE was added and the layers were separated. The aqueous phase was extracted with MTBE (3×) and the combined organic phase was washed with brine and dried ($MgSO_4$). The solvent was removed and the crude product was purified by column chromatography (PE/MTBE, 5:1) to give (4*R*,6*R*)-4-(*tert*-butyldimethylsilanyloxy)-6-[1-(1,3-dithian-2-yl)-1-methylethyl]tetrahydropyran-2-one (341 mg, 82%), colourless oil, $[\alpha]_D^{20}$ = +4.1 (*c* = 1, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 2952, 2928, 2855, 1737, 1463, 1422, 1371, 1350, 1249, 1215, 1156, 1109, 1079, 1058, 1109, 1079, 990, 888, 835, 775, 669 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.08/0.09 [s, 3 H, $Si(CH_3)_2$], 0.89 [s, 9 H, $SiC(CH_3)_3$], 1.07/1.17 [s, 3 H, $C(CH_3)_2$], 1.54−1.66 [m, 1 H, $CH_2CHC(CH_3)_2$], 1.76−1.89 (m, 1 H, $SCH_2CH_2CH_2S$), 2.07−2.15 [m, 2 H, $SCH_2CH_2CH_2S$, $CH_2CHC(CH_3)_2$], 2.43 (dd, ^3J = 17.0, ^3J = 8.0 Hz, 1 H, $CH_2C{=}O$), 2.78−3.00 (m, 5 H, $SCH_2CH_2CH_2S$, $O{=}CCH_2$), 4.13−4.21 (m, 1 H, CHOTBS), 4.39 (s, 1 H, SCHS), 4.51 [dd, ^3J = 12.0, ^3J = 3.0 Hz, 1 H, $OCHC(CH_3)_2$]. ^{13}C NMR (100 MHz, $CDCl_3$): δ = −4.8 [1°, $Si(CH_3)_2$], 17.9 [4°, $SiC(CH_3)_3$], 19.8 [1°, $C(CH_3)_2$], 19.9 [1°, $C(CH_3)_2$], 25.6 [1°, $SiC(CH_3)_3$], 26.3 (2°, $SCH_2CH_2CH_2S$), 31.3 (2°, $SCH_2CH_2CH_2S$), 33.0 [2°, $CH_2CHC(CH_3)_2$], 40.2 (2°, $CH_2C{=}O$), 41.9 [4°, $C(CH_3)_2$], 57.8 (3°, SCHS), 64.7 (3°, CHOTBS), 79.4 [3°, $CHC(CH_3)_2$], 170.6 (4°, C=O). MS: *m*/*z* (%) = 390 (7) [M^+], 333 (5), 225 (4), 132 (6), 121 (5), 119 (50), 101 (5), 84 (16), 77 (6), 75 (100), 73 (5), 69 (5). HRMS calcd. for $C_{18}H_{34}O_3S_2Si$: 390.1719, found 390.1721.

*n*BuLi (1.6 mL, 2.6 mmol, 1.6 M solution in hexane) was added dropwise at 0 °C to a solution of diisopropylamine (0.41 mL, 2.9 mmol) in THF (2 mL). After 15 min the mixture was cooled to −78 °C and *tert*-butyl acetate (0.39 mL, 2.9 mmol) was added dropwise. The resulting mixture was stirred for 45 min at −78 °C, and then (4*R*,6*R*)-4-(*tert*-butyldimethylsilanyloxy)-6-[1-(1,3-dithian-2-yl)-1-methylethyl]tetrahydropyran-2-one (228 mg, 0.584 mmol) in THF (0.8 mL) was added. The mixture was allowed to reach 0 °C within 2 h, and sat. aq. NH_4Cl solution (1 mL) was added. The aqueous phase was extracted with MTBE (3×) and the combined organic phase was dried (Na_2SO_4). Removal of the solvent and column chromatography (PE/MTBE, 20:1) provided *tert*-butyl (2*S*,4*R*,6*R*)-{4-(*tert*-butyldimethylsilanyloxy)-6-[1-(1,3-dithian-2-yl)-1-methylethyl]-2-hydroxytetrahydropyran-2-yl}acetate (267 mg, 90%), colourless oil, $[\alpha]_D^{20}$ = −35.4 (*c* = 0.5, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3461, 2955, 2930, 2856, 1713, 1462, 1421, 1391, 1367, 1294, 1249, 1217, 1148, 1111, 1071, 1010, 947, 879, 835, 775, 668 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.07/0.08 [s, 3 H, $Si(CH_3)_2$], 0.88 [s, 9 H, $SiC(CH_3)_3$], 1.00/1.05 [s, 3 H, $C(CH_3)_2$], 1.16−1.27 (m, 1 H, $HOCCH_2$), 1.42−1.52 [m, 1 H, $CH_2CHC(CH_3)_2$], 1.50 [s, 9 H, $OC(CH_3)_3$], 1.74−1.87 (m, 2 H, $HOCCH_2$, $SCH_2CH_2CH_2S$), 2.02 (ddd, ^2J = 12.0, ^3J = 5.0, ^3J = 1.0 Hz, $SCH_2CH_2CH_2S$), 2.07 [d, ^2J = 14.0 Hz, 1 H, $CH_2CHC(CH_3)_2$], 2.51 (d, ^2J = 12.0 Hz, 2 H, CH_2CO_2tBu), 2.76−3.01 (m, 4 H, $SCH_2CH_2CH_2S$), 4.12 [dd, ^3J = 12.0, ^3J = 2.0 Hz, 1 H, $CHC(CH_3)_2$], 4.12−4.19 (m, 1 H, CHOTBS), 4.26 (s, 1 H, SCHS), 4.96 (br. s, 1 H, OH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = −4.7/−4.6 [1°, $Si(CH_3)_2$], 18.1 [4°, $SiC(CH_3)_3$], 20.1/20.2 [1°, $C(CH_3)_2$], 25.9 [4°, $SiC(CH_3)_3$], 26.5 (2°, $SCH_2CH_2CH_2S$), 28.2 [1°, $OC(CH_3)_3$], 31.1/31.3 (2°, $SCH_2CH_2CH_2S$), 34.8 [2°, $CH_2CHC(CH_3)_2$], 41.2 [4°, $C(CH_3)_2$], 44.3 [2°, $CH_2C(OH)CH_2$], 45.5 (2°, CH_2CO_2tBu), 58.7 (3°, SCHS), 65.9 (3°, CHOTBS), 71.1 [3°, $CHC(CH_3)_2$], 81.4 [4°, $OC(CH_3)_3$], 96.5 [3°, $CHC(CH_3)_2$], 171.5 (4°, CO_2tBu). MS (80 °C): *m*/*z* (%) = 506 (3) [M^+], 488 (7), 245 (8), 161 (5), 143 (9), 120 (15), 107 (7), 85 (7), 75 (7), 73 (100), 71 (7), 69 (5). HRMS calcd. for $C_{24}H_{46}O_5S_2Si$: 506.2556, found 506.2556.

A mixture of *tert*-butyl (2*S*,4*R*,6*R*)-{4-(*tert*-butyldimethylsilanyloxy)-6-[1-(1,3-dithian-2-yl)-1-methylethyl]-2-hydroxytetrahydropyran-2-yl}acetate (53.0 mg, 0.105 mmol), citric acid monohydrate (50 mg, 0.24 mmol) and MeOH (2.5 mL) was heated to reflux for 6 h and then diluted with MTBE. The organic layer was washed with sat. aq. $NaHCO_3$ solution. The combined aqueous layer was reextracted with MTBE (3×) and the combined organic phase was washed with brine and dried ($MgSO_4$). The solvent was evaporated and the residue was purified by chromatography (PE/MTBE, 20:1) to afford **21** (44 mg, 81%), colourless oil. IR ($CHCl_3$): $\tilde{\nu}$ = 2931, 2899, 2856, 1725, 1460, 1422, 1367, 1311, 1277, 1247, 1168, 1148, 1101, 1069, 1036, 1002, 964, 903, 836, 776, 675 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.06/0.07 [s, 3 H, $Si(CH_3)_2$], 0.88 [s, 9 H, $SiC(CH_3)_3$], 1.07/1.12 [s, 3 H, $C(CH_3)_2$], 1.16−1.27 (m, 1 H, $MeOCCH_2$), 1.46 [s, 9 H, $OC(CH_3)_3$], 1.44−1.57 [m, 1 H,

$CH_2CHC(CH_3)_2$], 1.75−1.90 (m, 2 H, $MeOCCH_2$, $SCH_2CH_2CH_2S$), 2.05−2.18 (m, 2 H, $CH_2CHC(CH_3)_2$, $SCH_2CH_2CH_2S$), 2.48 (d, ^2J = 14.0 Hz, 1 H, CH_2CO_2tBu), 2.66 (d, ^2J = 14.0 Hz, 1 H, CH_2CO_2tBu), 2.96−2.79 (m, 4 H, $SCH_2CH_2CH_2S$), 3.27 (s, 3 H, OCH_3), 3.84 [dd, ^3J = 12.0, ^3J = 2.0 Hz, 1 H, $CHC(CH_3)_2$], 4.06 (m, 1 H, CHOTBS), 4.26 (s, 1 H, SCHS). FAB-MS: *m/z* (%) = 520 (8) [M^+], 490 (20), 488 (90), 375 (44), 357 (100), 301 (18), 285 (6), 259 (21), 245 (70), 187 (82), 173 (20), 143 (6).

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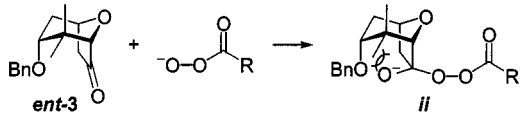
[7] It was noticeable that Baeyer−Villiger rearrangement to [3.3.1]lactone acetals **5** and ***ent*-5** was less efficient (maximum yield 50%), presumably because formation of the tetrahedral intermediate ***ii*** is sterically inhibited:



[8] Silica gel, cyclohexane/EtOAc (8:1).

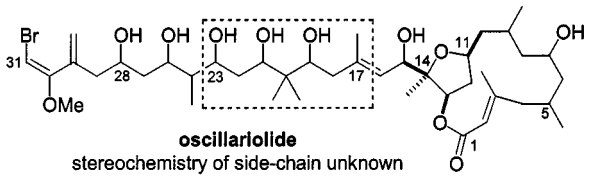
[9] In the presence of trimethylsilyl triflate, [3.3.1]lactone acetals are also excellent glycosyl donors: [9a] O. Gaertzen, A. M. Misske, P. Wolbers, H. M. R. Hoffmann, *Synlett* **1999**, 1041. [9b] O. Gaertzen, A. M. Misske, P. Wolbers, H. M. R. Hoffmann, *Tetrahedron Lett.* **1999**, *40*, 6359; see also ref.[3]

[10] A. Vakalopoulos, T. F. J. Lampe, H. M. R. Hoffmann, *Org. Lett.* **2001**, *3*, 929.

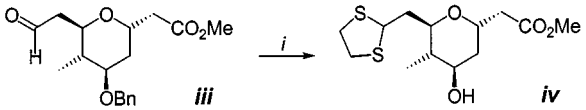
[11] Deprotection of the benzyl group with $BF_3{\cdot}Et_2O$/EtSH: K. Fuji, K. Ichikawa, M. Node, E. Fujita, *J. Org. Chem.* **1979**, *44*, 1661.

[12] A. Vakalopoulos, H. M. R. Hoffmann, *Org. Lett.* **2001**, *3*, 177.

[13] *O*-Benzylated diol **10** and triol **11** are also useful polyketide building blocks: e.g., C17−C23 segment of oscillariolide:



[14] Attempted simultaneous protection/deprotection of ***iii*** to ***iv*** was unsatisfactory: P. M. Schäfer, unpublished work.



i: 1.5 equiv. $HS(CH_2)_2SH$, 10 equiv. $BF_3{\cdot}Et_2O$, MeCN, 18 h, r.t., 10%

[15] Basic cyclization conditions afford *C*-glycosides: [15a] A. J. F. Edmunds, W. Trueb, *Tetrahedron Lett.* **1997**, *38*, 1009. [15b] J. M. Betancort, V. S. Martín, J. M. Padrón, J. M. Palazón, M. A. Ramírez, M. A. Soler, *J. Org. Chem.* **1997**, *62*, 4570. [15c] E. Alvarez, M.-L. Candenas, R. Pérez, J. L. Ravelo, J. D. Martín, *Chem. Rev.* **1995**, *95*, 1953. [15d] J. M. Palazón, M. A. Soler, M. A. Ramírez, V. S. Martín, *Tetrahedron Lett.* **1993**, *34*, 5467. [15e] D. A. Evans, E. M. Carreira, *Tetrahedron Lett.* **1990**, *31*, 4073; B. Maurer, A. Grieder, W. Thommen, *Helv. Chim. Acta* **1979**, *62*, 44; C. Schneider, A. Schuffenhauer, *Eur. J. Org. Chem.* **2000**, 73−82.

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