Stereoselective Total Synthesis of Goniothalesdiol A *via* Chiron Approach

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The stereocontrolled synthesis of goniothalesdiol A, a dihydroxylated tetrahydropyran compound, has been accomplished using D-ribose as chiral precursor. The key steps involved are aryl *Grignard* reaction, stereoselective alkoxy-directed keto reduction, and intramolecular oxy-*Michael* addition.

Introduction. – Goniothalesdiol A (**1**) and goniothalesacetate, a new class of styryl lactones [1], were isolated from the stems of a southern Taiwan tree Goniothalamus *amuyon*. The styryl lactones and acetogenins are two major types of bioactive compounds isolated from the *Goniothalamus* (Annonaceae) species. The structure and relative configuration of **1** were determined on the basis of NMR spectroscopy, and the absolute configuration was predicted by biosynthesis [2] (*Fig.*).

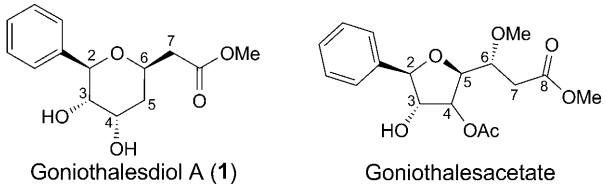
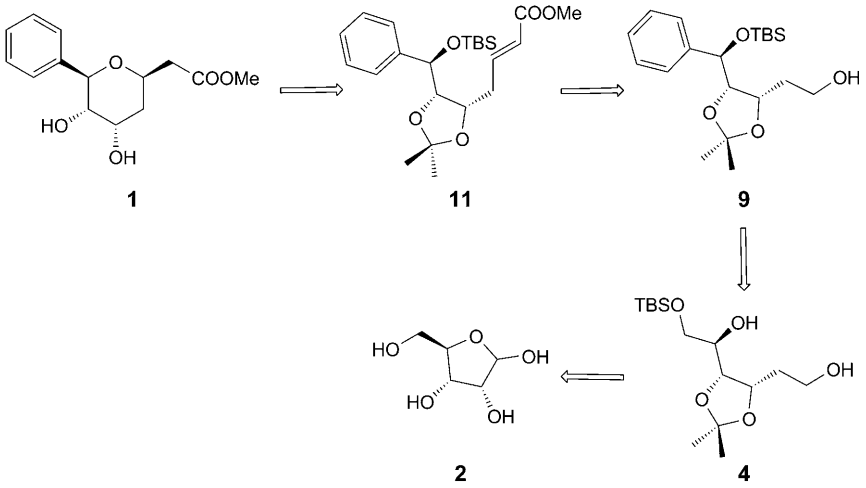


Figure. *Chemical structures of goniothalesdiol A and goniothalesacetate*

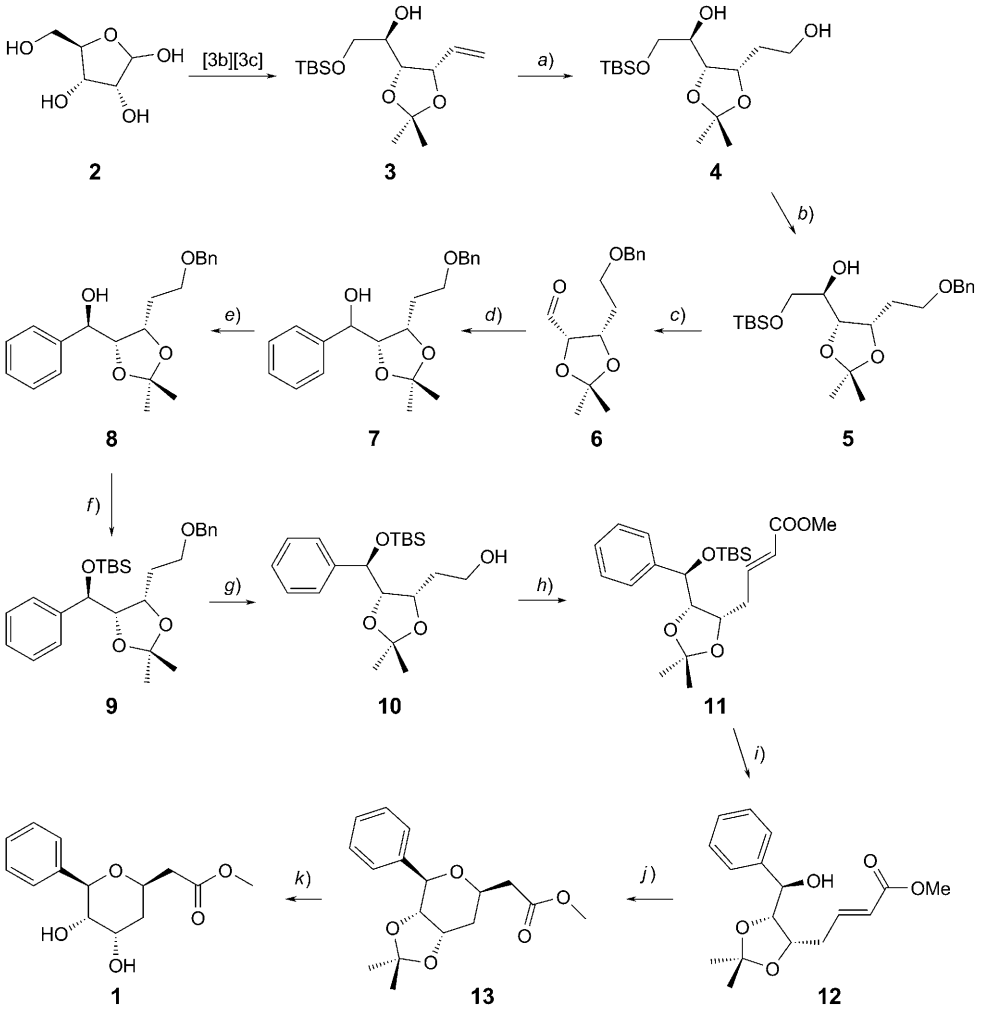
Recently, we have reported the first stereoselective total synthesis of goniothalesdiol A [3] employing the *Sharpless* kinetic resolution to construct the stereogenic center C(2) and the C(3)/C(4) *syn*-diol arrangement. In the present study, we wish to report the stereocontrolled total synthesis of natural goniothalesdiol A utilizing inexpensive and readily available D-ribose (**2**) *via* the chiron approach. The retrosynthetic analysis is presented in *Scheme 1*. Our synthetic approach began with enantiomerically pure D-ribose (**2**) which was converted into the pyran moiety through a series of stereocontrolled chemical transformations, which include *Grignard* addition and C_1 *Wittig* reaction for extending a C-chain by incorporating the C=C bond in the final precursor, which in turn permits the intramolecular oxy-*Michael* reaction.

Scheme 1. *Retrosynthetic Analysis of Goniothalesdiol A*



Results and Discussion. – Our synthesis started with compound **3**, which was prepared from D-ribose (**2**) according to reported procedures [4][5]. The olefin derivative **3** was converted to the corresponding primary alcohol **4** by hydroboration with a dicyclohexyl borane – dimethyl sulfide (DMS) complex in dry THF, followed by oxidation with H_2O_2 to give product **4** in 81% yield [6] (*Scheme 2*). The chemoselective protection of **4** with benzyl bromide (BnBr) in the presence of NaH afforded benzyl ether **5** in 97% yield. Deprotection of the (*t*-Bu)Me_2Si (TBS) ether **5** using Bu_4NF (TBAF) gave the diol in 95% yield [4]. Oxidative cleavage of the diol with silica gel-supported $NaIO_4$ furnished the aldehyde **6** in 95% [7]. Addition of PhMgBr to the aldehyde in Et_2O gave the secondary alcohol **7** in 63% yield as inseparable mixture of diastereoisomers [8]. To obtain the required diastereoisomer as the major product, **7** was oxidized with IBX (= 1-hydroxy-1λ^3,2-benziodoxol-3(1*H*)-one 1-oxide) in DMSO/CH_2Cl_2 1:3 to give a keto product, which was subsequently subjected to stereoselective alkoxy-directed keto reduction with $Zn(BH_4)_2$ in THF at $-20°$ to afford compound **8** as the major isomer in 57% yield in two steps [9]. The chiral precursor **8** was protected as TBS ether **9** in 95% yield using (*t*-Bu)Me_2SiCl (TBSCl) and 1*H*-imidazole. Oxidative cleavage of **9** with DDQ gave the primary alcohol **10** in 95% yield. The *Swern* oxidation of **10** gave the corresponding aldehyde in quantitative yield, which was further subjected to *Horner–Wadsworth–Emmons* olefination with methyl (diethoxyphosphoryl)acetate ($(EtO)_2P(O)CH_2COOMe$) to furnish the α,β-unsaturated ester **11** in 93% yield [10]. Deprotection of the TBS ether with TBAF in dry THF at room temperature afforded the hydroxy ester **12** in 95% yield. Compound **12** was treated with TsOH in benzene at room temperature to form the pyran skeleton in **13** by means of intramolecular oxy-*Michael* addition of OH at C(2) onto the (*E*)-configured C(6)=C(7) bond. Eventual deprotection of acetonide using TsOH in MeOH at room temperature afforded the target molecule goniothalesdiol A (**1**) in 78% yield (*Scheme 2*) [11].

Scheme 2



a) BH_3–DMS (dimethyl sulfide), cyclohexene, then H_2O_2, 0° to r.t, 12 h; 81%. *b*) NaH, BnBr, Bu_4NI (TBAI), dry THF, reflux, 3 h; 97%. *c*) 1. Bu_4NF (TBAF), dry THF; 95%; 2. $NaIO_4$–silica gel, CH_2Cl_2, 30 min, 95%. *d*) PhMgBr, THF, −78° to r.t., overnight; 63% (inseparable mixture of diastereoisomers). *e*) 1. 1-Hydroxy-1λ^3,2-benzodioxol-3(1*H*)-one 1-oxide (IBX), CH_2Cl_2/DMSO 3:1, 180–200°, 12 h; 67%; 2. $Zn(BH_4)_2$, THF, −20°, 12 h; 85% (de 90%). *f*) (*t*-Bu)Me_2SiCl (TBSCl), 1*H*-imidazole, CH_2Cl_2, 0–25°, 4 h; 95%. *g*) 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), CH_2Cl_2, 25°, 2 h; 95%. *h*) 1. Oxalyl chloride, dry DMSO, dry CH_2Cl_2, −78°, Et_3N; quant.; 2. $(EtO)_2P(O)CH_2COOMe$, ^{t}BuOK, THF, −78 to 0°; 93% ((*E*)/(*Z*) 8:1). *i*) TBAF, dry THF, 25°, 2 h; 95%. *j*) TsOH, benzene, 4 h. *k*) TsOH, MeOH, 25°, 2 h; 78% (for 2 steps).

In conclusion, we have described a concise synthesis of goniothalesdiol A (**1**) from D-ribose (**2**) in a highly stereoselective manner. Goniothalesdiol A has been synthesized in nine steps using an oxy-*Michael* reaction for the construction of the

cis-tetrahydropyran-2,6-diyl moiety. The two key reactions, *i.e.*, a *Grignard* addition to aldehyde **6**, followed by a stereoselective alkoxy-directed keto reduction, are involved in the formation of the precursor **8** as the major product, which is a key intermediate for the total synthesis of goniothalesdiol A (**1**).

Experimental Part

General. Solvents were dried over standard drying agents and freshly distilled prior to use. The reagents were purchased from *Aldrich* and *Acros*, and were used without further purification unless otherwise stated. All moisture-sensitive reactions were carried out under N_2. Org. solns. were dried over anh. Na_2SO_4 and concentrated *in vacuo* below 40°. Column chromatography (CC): silica gel (SiO_2; *Acme*'s 60–120 mesh). Optical rotations: *Horiba* high sensitive polarimeter *SEPA-300* at 25°. IR Spectra: *Perkin-Elmer IR-683* spectrophotometer with NaCl optics. ^{1}H- (200 and 300 MHz) and ^{13}C-NMR (50 and 75 MHz) spectra: *Varian Gemini FT-200* and *Bruker Avance 300* instruments with TMS as internal standard in $CDCl_3$; *J* values in Hz. MS: *Agilent Technologies 1100* Series (Agilent Chemistation Software).

6-O-*[(*tert-*Butyl)(dimethyl)silyl]-1,2-dideoxy-3,4*-O-*(1-methylethylidene)*-D-ribo-*hex-1-enitol* (**3**). To a stirred suspension of D-ribose (**2**; 8 g, 53.29 mmol) in acetone (100 ml) was added dropwise conc. H_2SO_4 (0.24 ml) at r.t., and the mixture was stirred at r.t. for 3 h. The mixture was neutralized with solid $NaHCO_3$ (5 g), filtered, and evaporated under reduced pressure to give a colorless syrup. The resulting syrup was purified by CC (SiO_2; hexane/AcOEt 1:2) to give acetonide-protected ribose (9.42 g, 93%) as a colourless syrup.

To a stirred soln. of acetonide-protected ribose (7.0 g , 36.8 mmol) in dry CH_2Cl_2 (50 ml) were added 1*H*-imidazole (6.26 g, 88.0 mmol) and TBSCl (6.44 g, 42.8 mmol) at r.t., and the mixture was stirred for 3 h at r.t. The reaction was quenched with ice-cold H_2O, and the mixture was diluted with AcOEt. The org. layer was extracted with AcOEt, and the org. layers were washed with brine, dried (Na_2SO_4), and evaporated under reduced pressure. The resulting syrup was purified by CC (SiO_2; hexane/AcOEt 7:3) to give TBS protected ribose acetonide (10.0 g, 89%) as a colorless oil (9:1 anomeric mixture).

To a mixture of methyl(triphenyl)phosphonium iodide (52 g, 130 mmol) and ^{t}BuOK (7.4 g, 64 mmol) was added dry THF (240 ml), and the mixture was stirred at r.t. under N_2 for 4 h. Then, the stirring was stopped, and the solid was allowed to settle down. The clear supernatant orange-yellow liquid was transferred into the soln. of TBS-protected ribose acetonide (10 g, 32 mmol) in dry THF (40 ml) at −78°. The mixture was then slowly allowed to attain r.t. After 3 h, the reaction was quenched with crushed ice, and the mixture was diluted with AcOEt. The org. layer was separated and dried (Na_2SO_4), filtered, and evaporated under reduced pressure. The resulting syrup was purified by CC (SiO_2; hexane/AcOEt 3:2) to give **3** (9.2 g, 82%). Pale-yellow syrup. $[\alpha]_D^{28} = -3.5$ ($c = 1.0$, $CHCl_3$). IR (neat): 3557, 2931, 2858, 1746, 1641, 1466, 1376, 1254, 1217, 1117, 1060, 838, 779, 671. ^{1}H-NMR (300 MHz, $CDCl_3$): 5.99 (*ddd*, $J = 6.0$, 10.5, 17.0, 1 H); 5.38 (*td*, $J = 1.5$, 17.0, 1 H); 5.23 (*td*, $J = 1.5$, 10.5, 1 H); 4.64 (*t*, $J = 6.0$, 1 H); 3.98 (*dd*, $J =$ 6.7, 9.8, 1 H); 3.77 (*dd*, $J = 3.0$, 9.8, 1 H); 3.71–3.52 (*m*, 2 H); 2.34 (*d*, $J = 6.0$, 1 H); 1.44 (*s*, 3 H); 1.33 (*s*, 3 H); 0.91 (*s*, 9 H); 0.08 (*s*, 6 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 134.2; 117.5; 108.7; 78.81; 77.4; 69.4; 64.4; 27.8; 25.4; 18.3. HR-ESI-MS: 325.1812 ($[M + Na]^+$, $C_{15}H_{30}NaO_4Si^+$; calc. 325.1811).

6-O-*[(*tert-*Butyl)(dimethyl)silyl]-2-deoxy-3,4*-O-*(1-methylethylidene)*-D-ribo-*hexitol* (**4**). To the stirred soln. of cyclohexene (12.03 ml, 11.9 mmol) in dry THF (15 ml) was added $BH_3 \cdot DMS$ (5.65 ml, 59.6 mmol) dropwise at 0°, and stirring was continued for 1 h at 0°. At the same temp., a soln. of **3** in dry THF (100 ml) was added to the mixture, and, after 1 h, the mixture was allowed to warm to r.t. and stirred for further 12 h. The mixture was cooled to 0°, then H_2O_2 (20 ml, 30%) and NaOH (20%, 63 ml) were added, and the mixture was stirred for 4 h. Then, the mixture was extracted with AcOEt (2 × 500 ml). The org. extracts were washed with H_2O and brine, and dried (Na_2SO_4). Evaporation of the solvent, followed by purification of the crude product by CC (SiO_2; hexane/AcOEt 95:5), afforded **4** (7.2 g, 81%). Pale liquid. $[\alpha]_D^{33} = -18.1$ ($c = 1.0$, $CHCl_3$). IR (neat): 3447, 2932, 2853, 1641, 1473, 1376, 1254, 1110, 1055, 835. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.92–4.87 (*m*, 1 H); 4.40–4.29 (*m*, 2 H); 3.92–3.77 (*m*, 4 H); 2.28 (br. *s*, 1 H); 1.83–1.60 (*m*, 2 H); 1.45 (*s*, 3 H); 1.35 (*s*, 3 H); 0.90 (*s*, 9 H); 0.05 (*s*, 3 H); 0.04 (*s*,

3 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 108.4; 75.7; 74.5; 72.1; 62.2; 60.5; 31.7; 27.7; 25.7; 25.5; 21.2; 18.5. HR-ESI-MS: 343.4888 ($[M+Na]^+$, $C_{15}H_{32}NaO_5Si^+$; calc. 343.1917).

1-O-*Benzyl-6*-O-*[(*tert-*butyl)(dimethyl)silyl]-2-deoxy-3,4*-O-*(1-methylethylidene)*-D-ribo-*hexitol* (**5**). To a mixture of NaH (0.55 g, 60 wt.-% in mineral oil, 13.7 mmol) in dry THF (80 ml) was added a soln. of **4** (4 g, 12.5 mmol) in dry THF (20 ml) at 0°. After 20 min, BnBr (1.65 ml, 13.7 mmol) was added, and the stirring was continued for 2 h at r.t. The reaction was quenched by the addition of a sat. soln. of NH_4Cl (20 ml), and the mixture was extracted with AcOEt. The org. extracts were washed with H_2O and brine, and dried (Na_2SO_4). Evaporation of the solvent, followed by purification of the crude product by CC (SiO_2; hexane/AcOEt 95:5) afforded **5** (4.97 g, 92%). Pale-yellow liquid. $[\alpha]_D^{33} = -10$ ($c = 0.5$, $CHCl_3$). IR (neat): 3547, 2932, 2853, 1746, 1641, 1464, 1376, 1254, 1210, 1110, 1060, 838, 756. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.39–7.17 (*m*, 5 H); 4.83 (*d*, $J = 11.3$, 1 H); 4.42 (*d*, $J = 11.3$, 1 H); 4.31–4.23 (*m*, 1 H); 4.06 (*dd*, $J = 5.7$, 9.0, 1 H); 3.99 (*dd*, $J = 1.9$, 11.3, 1 H); 3.77–3.63 (*m*, 2 H); 3.49 (*ddd*, $J = 2.1$, 5.1, 9.0, 1 H); 2.0 (br. *s*, 1 H); 1.79–1.64 (*m*, 2 H); 1.36 (*s*, 3 H); 1.24 (*s*, 2 H); 0.84 (*s*, 9 H); 0.01 (*s*, 6 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 138.5; 128.3; 127.6; 108.0; 76.9; 72.7; 67.5; 64.5; 29.9; 28.2; 25.8; 25.7;18.3; −5.5; −5.4. HR-ESI-MS: 433.6126 ($[M+Na]^+$, $C_{22}H_{38}NaO_5Si^+$; calc. 433.2386).

1-O-*Benzyl-2-deoxy-3,4*-O-*(1-methylethylidene)-5*-C-*phenyl*-D-erythro-*pentitol* (**7**). To a well-stirred soln. of **5** (4.5 g, 10.9 mmol) in anh. THF (50 ml) was added 1M Bu_4NF (13.2 ml, 13.2 mmol) at 0°. Then, the reaction was quenched with ice flakes, and the mixture was concentrated under reduced pressure. The mixture was extracted with AcOEt (3 × 50 ml). The combined org. layers were washed with H_2O and brine, and dried (Na_2SO_4). After removing the volatiles under reduced pressure, the crude product was purified by CC (SiO_2; hexane/AcOEt 85:15) to afford the pure vicinal diol (3.06 g, 95%). Colorless liquid. $[\alpha]_D^{33} = +4.8$ ($c = 0.15$, $CHCl_3$). IR (neat): 3650, 3554, 2952, 1744, 1464, 1377, 1254, 1210, 1060, 840, 757. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.41–7.26 (*m*, 5 H); 4.67 (*d*, $J = 11.7$, 1 H); 4.48 (*d*, $J = 10.7$, 1 H); 4.41–4.35 (*m*, 1 H); 4.21 (*dd*, $J = 5.8$, 8.8, 1 H); 3.93 (*dd*, $J = 3.9$, 11.7, 1 H); 3.84 (*dd*, $J = 1.9$, 11.7, 1 H); 3.82–3.71 (*m*, 2 H); 3.57–3.52 (*m*, 1 H); 2.05 (br. *d*, $J = 14.6$, 1 H); 1.84–1.76 (*m*, 2 H); 1.44 (*s*, 3 H); 1.35 (*s*, 2 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 138.6; 128.5; 128.4; 127.7; 108.1; 76.8; 72.7; 71.1; 67.4; 64.3; 29.8; 28.0; 25.8; 25.7. HR-ESI-MS: 297.5447 ($[M+H]^+$, $C_{16}H_{24}O_5^+$; calc. 297.5449).

$NaIO_4$ (25.7 g, 120.0 mmol) was dissolved in 50 ml of hot H_2O (70°) in a 250-ml round-bottomed flask. To the hot soln. was added SiO_2 (230–400 mesh, 100 g) with vigorous swirling and shaking. The resulting SiO_2 coated with $NaIO_4$ was in a powder form and was free-flowing. The reagent can be kept in a bottle for 1 month with negligible loss of activity. To a vigorously stirred suspension of SiO_2-supported $NaIO_4$ reagent (23.6 g) in CH_2Cl_2 (75 ml) in a 25-ml round-bottomed flask was added a soln. of the vicinal diol (3.5 g, 11.8 mmol) in CH_2Cl_2 (75 ml). The reaction was monitored by TLC until disappearance of the starting material (generally 10–30 min). The mixture was filtered through a sintered glass funnel, and the filter cake was thoroughly washed with $CHCl_3$ (45–150 ml). Removal of solvents from the filtrate afforded the aldehyde **6**, which was directly used for the next reaction.

A suspension of PhMgBr was generated *in situ* with Mg turnings (0.95 g, 39 mmol) and PhBr (2.78 ml, 26 mmol) in dry THF at r.t. under N_2. Then, a soln. of **6** (3.5 g, 13 mmol) in THF (15 ml) was added slowly at −78° under inert atmosphere. After 2 h, the mixture was warmed to r.t. and left overnight until completion of the reaction, and then the reaction was quenched by addition of sat. aq. NH_4Cl (25 ml), and the mixture extracted with AcOEt (3 × 100 ml). The combined org. layers were washed with H_2O and brine, and dried (Na_2SO_4). Removal of solvent, followed by CC (SiO_2; hexane/AcOEt 95:5) gave **7** (3.0 g, 63%). Colorless oil. IR (neat): 3434, 2924, 2855, 1718, 1603, 1492, 1455, 1377, 1205, 1074, 889, 755. ^{1}H-NMR (300, $CDCl_3$): 7.42–7.22 (*m*, 10 H); 4.58–4.53 (*m*, 1 H); 4.53 (*s*, 2 H); 3.93–3.7 (*m*, 1 H); 3.68–3.55 (*m*, 2 H); 3.30–3.20 (*m*, 1 H); 2.85 (*d*, $J = 9.0$, 1 H); 2.20–1.92 (*m*, 1 H); 1.90–1.76 (*m*, 1 H); 1.56 (*s*, 3 H); 1.39 (*s*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 139.3; 137.5; 128.3; 127.7; 127.4; 127.1; 98.8; 73.0; 72.5; 66.6; 34.1; 29.6. HR-ESI-MS: 365.1731 ($[M+Na]^+$, $C_{21}H_{26}NaO_4^+$; calc. 365.1728).

*(5*R*)-1*-O-*Benzyl-2-deoxy-3,4*-O-*(1-methylethylidene)-5*-C-*phenyl*-D-erythro-*pentitol* (**8**). To a stirred soln. of IBX (4.6 g, 16.4 mmol) in DMSO (2.33 ml, 32.8 mmol) was added **7** (3.0 g, 8.21 mmol) in anh. CH_2Cl_2 (50 ml) dropwise at r.t. The mixture was kept under reflux at 180–200° for 12 h; then it was cooled to r.t., extracted with Et_2O (3 × 100 ml), and filtered through a *Celite* pad. The filtrate was washed with sat. $NaHCO_3$ and brine. The org. layer was dried (Na_2SO_4). The evaporation of solvent, followed by

purification of the crude product by flash-CC (SiO_2; hexane/AcOEt 6:4) yielded the pure ketone (2 g, 67%), which was directly used for the next reaction.

A soln. of ketone (2.0 g, 7.25 mmol), obtained from the oxidation of alcohol **7** (2 g, 7.25 mmol) in THF (20 ml) under N_2, was cooled to $-20°$, and $Zn(BH_4)_2$ (2.8 ml of a 2M soln. in THF, 5.45 mmol) was added slowly during 10 min. After stirring for 12 h at the same temp., the reaction was quenched by addition of sat. aq. NH_4Cl. The resulting mixture was extracted with AcOEt. The combined org. layers were washed with brine, dried (Na_2SO_4), and evaporated *in vacuo*. The residue was subjected to CC (SiO_2; hexane/AcOEt 9:1) to give **8** (1.68 g, 85%). Colorless oil. $[\alpha]_D^{25} = -51.4$ ($c = 0.7$, $CHCl_3$). IR (neat): 3434, 2924, 2855, 1718, 1603, 1492, 1455, 1377, 1205, 1074, 889, 755. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.42–7.23 (*m*, 10 H); 4.56 (*d*, $J = 3.0$, 1 H); 4.53 (*s*, 2 H); 3.92–3.80 (*m*, 1 H); 3.69–3.56 (*m*, 2 H); 3.30–3.20 (*t*, $J = 9.1$, 1 H); 2.93 (*d*, $J = 2.3$, 1 H); 2.0–1.90 (*m*, 1 H); 1.90–1.77 (*m*, 1 H); 1.60 (*s*, 3 H); 1.40 (*s*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 139.3; 137.5; 128.3; 127.7; 127.4; 127.1; 98.8; 73.0; 72.5; 66.6; 34.1; 29.6. HR-ESI-MS: 365.1729 ($[M+Na]^+$, $C_{21}H_{26}NaO_4^+$; calc. 365.1728).

*(5*R*)-1-*O*-Benzyl-5-*O*-[(*tert*-butyl)(dimethyl)silyl]-2-deoxy-3,4-*O*-(1-methylethylidene)-5-*C*-phenyl-*D*-erythro-pentitol* (**9**). To a stirred soln. of **8** (1.50 g, 4.37 mmol) and 1*H*-imidazole (0.357 g, 5.25 mmol) in anh. CH_2Cl_2 (800 ml) was added TBSCl (0.65 g, 4.8 mmol) dropwise at 0°, and stirring was continued for 4 h at r.t. The reaction was quenched with ice flakes, and the mixture was extracted with CH_2Cl_2 (3 × 500 ml). The combined org. layers were washed with H_2O and brine, and dried (Na_2SO_4). Removal of solvent, followed by CC (SiO_2; hexane/AcOEt 95:5), furnished **9** (1.89 g, 95%). Colorless liquid. $[\alpha]_D^{31} = -4.1$ ($c = 1$, $CHCl_3$). IR (neat): 3031, 2925, 2854, 1719, 1603, 1452, 1377, 1205, 1075, 899, 755. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.26–7.19 (*m*, 10 H); 4.53 (*s*, $J = 8.7$, 1 H); 4.47 (*s*, 2 H); 4.28 (*qd*, $J = 2.3, 5.5$, 1 H); 4.32–4.24 (*m*, 1 H); 4.11 (*dd*, $J = 5.5, 8.5$, 1 H); 3.66–3.52 (*m*, 2 H); 2.12–2.02 (*m*, 1 H); 1.86–1.74 (*m*, 1 H); 1.28 (*s*, 3 H); 1.15 (*s*, 3 H); 0.78 (*s*, 9 H); −0.5 (*s*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 141.6; 140.5; 128.4; 127.7; 126.7; 108.5; 85.4; 77.4; 74.0; 72.5; 69.0; 34.3; 29.7; 27.2; 26.3; 18.5; −4.4. HR-ESI-MS: 479.2592 ($[M+Na]^+$, $C_{27}H_{40}NaO_4^+$; calc. 479.2596).

*(5*R*)-5-*O*-[(*tert*-Butyl)(dimethyl)silyl]-2-deoxy-3,4-*O*-(1-methylethylidene)-5-*C*-phenyl-*D*-erythro-pentitol*. (**10**). To a stirred soln. of **9** (1.75 g, 3.85 mmol) in 9:1 CH_2Cl_2 (18 ml) and H_2O (2 ml) was added DDQ (6.75 g, 15.35 mmol) at 0°. The mixture was stirred at r.t. for 4 h. The reaction was quenched with $NaHCO_3$, and the aq. layer was extracted with AcOEt (3 × 100 ml). The combined org. layer were washed with brine and dried (Na_2SO_4). Removal of solvent followed by CC (SiO_2; hexane/AcOEt 85:15) afforded **10** (1.33 g, 95% yield). Colorless liquid. $[\alpha]_D^{31} = +28$ ($c = 0.25$, $CHCl_3$). IR (neat): 3448, 2925, 2854, 1604, 1455, 1375, 1072, 895, 763. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.38–7.25 (*m*, 5 H); 4.48 (*d*, $J = 8.56$, 1 H); 3.95 (*td*, $J = 2.4, 8.6$, 1 H); 3.83–3.71 (*m*, 2 H); 3.38 (*t*, $J = 8.6$, 1 H); 2.35 (br. *d*, 1 H); 2.11–1.94 (*m*, 1 H); 1.76–1.56 (*m*, 1 H); 1.62 (*s*, 3 H); 1.46 (*s*, 3 H); 0.75 (*s*, 9 H); 013 (*s*, 3 H); −0.97 (*s*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 137.8; 128.3; 127.5; 126.7; 109.2; 85.4; 78.4; 61.2; 34.3; 27.6; 27.4; 26.2; 18.5; −4.5. HR-ESI-MS: 389.2125 ($[M+Na]^+$, $C_{20}H_{34}NaO_4Si^+$; calc 389.2124).

*Methyl (2*E*)-4-{(4*S*,5*S*)-5-[(*R*)-{[(*tert*-Butyl)(dimethyl)silyl]oxy}(phenyl)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl}but-2-enoate* (**11**). To a stirred soln. of oxalyl chloride (0.3 ml, 3.56 mmol) in dry CH_2Cl_2 (15 ml) was added DMSO (0.33 ml, 4.64 mmol) in dry CH_2Cl_2 (10 ml) dropwise at −78°. The mixture was stirred for 15 min at the same temp. To this mixture was added dropwise a soln. of **10** (1.0 g, 2.73 mmol) in dry CH_2Cl_2 (10 ml), and stirring was continued for another 1 h at −78°. Then, Et_3N (2.28 ml, 16.4 mmol) was added to the mixture, and the mixture was warmed to r.t. After addition of H_2O (50 ml), the layers were separated, and the aq. layer was extracted with CH_2Cl_2 (3 × 50 ml). The combined org. layers were washed with H_2O and brine, dried (Na_2SO_4), and concentrated *in vacuo*. The resulting residue (quant. yield) was used directly for the next step.

$(EtO)_2P(O)CH_2COOMe$ (0.8 g, 8.3 mmol) was added to a suspension of ^{t}BuOK (0.47 g, 4 mmol) in THF (10 ml) at 0° under N_2. After stirring at r.t. for 30 min, the soln. was cooled to −78°, and a soln. of aldehyde (0.8 g, 2 mmol) in THF (5 ml), obtained from **10**, was added. After 30 min, the mixture was allowed to warm to 0° and stirred for another 30 min. Then, the reaction was quenched with sat. aq. NH_4Cl (8 ml) and extracted with AcOEt (3 × 30 ml), washed with brine, and dried (Na_2SO_4). Filtration and evaporation of the solvent *in vacuo* furnished the crude **11** (0.79 g, 93%), which was subjected to CC (SiO_2; hexane/AcOEt 9:1). $[\alpha]_D^{25} = -53$ ($c = 0.3$, $CHCl_3$). IR (neat): 2925, 2854, 1727, 1657, 1463, 1437, 1381, 1261, 1165, 1095, 864, 836, 778. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.37–7.20 (*m*, 5 H); 7.00–6.87 (*m*,

1 H); 5.83 (*d*, *J* = 15.8, 1 H); 4.43 (*d*, *J* = 9.0, 1 H); 3.80–3.65 (*m*, 1 H); 3.70 (*s*, 3 H); 3.31 (*t*, *J* = 9.0, 1 H); 2.70–2.60 (*m*, 1 H); 2.28–2.15 (*m*, 1 H); 1.54 (*s*, 3 H); 1.34 (*s*, 3 H); 0.73 (*s*, 9 H); 0.14 (*s*, 3 H); 0.04 (*s*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 145.7; 128.7; 128.3; 122.7; 78.1; 73.8; 73.1; 34.8; 29.4; 25.8; 19.4; −4.1; −5.7. HR-ESI-MS: 443.2228 ($[M+Na]^+$, $C_{23}H_{36}NaO_5Si^+$; calc 443.2229).

*Methyl (2*E*)-4-{(4*S*,5*R*)-5-[(*R*)-Hydroxy(phenyl)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl}but-2-enoate* (**12**). To a well-stirred soln. of **11** (0.7 g, 1.58 mmol) in anh. THF (15 ml) was added 1M Bu_4NF (1.9 ml, 1.9 mmol) at 0°. Then, the reaction was quenched with ice flakes, and the mixture was concentrated under reduced pressure. The mixture was extracted with AcOEt (3 × 50 ml). The combined org. layers were washed with H_2O and brine, and dried (Na_2SO_4). After removing the volatiles under reduced pressure, the crude product was purified by CC (SiO_2; hexane/AcOEt 85:15) to afford **12** (0.49 g, 95%). Colorless liquid. $[\alpha]_D^{31} = +8.4$ ($c = 0.4$, $CHCl_3$). IR (neat): 3434, 2924, 1728, 1657, 1464, 1437, 1380, 1260, 1166, 1096, 865, 836, 778. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.36–7.20 (*m*, 5 H); 6.98–6.88 (*m*, 1 H); 5.83 (*d*, *J* = 15.8, 1 H); 4.20 (*d*, *J* = 4.5, 1 H); 4.15–4.08 (*m*, 1 H); 3.90–3.86 (*m*, 1 H); 3.70 (*s*, 3 H); 2.70–2.62 (*m*, 1 H); 2.28–2.16 (*m*, 1 H); 1.54 (*s*, 3 H); 1.36 (*s*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 168.0; 145.8; 141.1; 128.3; 122.9; 78.1; 73.8; 73.1; 52.0; 34.8; 29.4. HR-ESI-MS: 329.1359 ($[M+Na]^+$, $C_{17}H_{22}NaO_5Si^+$; calc 329.1360).

Goniothalesdiol A (= *Methyl (7*R*)-3,7-Anhydro-2,4-dideoxy-7-phenyl*-D-ribo-*heptonate*; **1**). To a stirred soln. of **12** (0.3 g, 0.51 mmol) in benzene (4 ml) was added TsOH (0.03g, 0.1 mmol). The mixture was stirred at r.t. for 3 h, and the solvent was removed under reduced pressure. The crude residue **13** was dissolved in 2 ml MeOH, and TsOH was added; the resulting mixture was stirred overnight at r.t. The solvent was removed under reduced pressure. The crude residue was subjected to CC (SiO_2; hexane/AcOEt 6:4) to afford **1** (0.15 g, 78%). White solid. M.p. 92°. $[\alpha]_D^{27} = -27$ ($c = 0.3$, $CHCl_3$). IR (neat): 3405, 2918, 2848, 2373, 1730, 1435, 1200, 1170, 1068. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.40–7.28 (*m*, 5 H); 4.54 (*d*, *J* = 9.8, 1 H); 4.45–4.35 (*m*, 1 H); 4.24–4.19 (*m*, 1 H); 3.68 (*s*, 3 H); 3.49 (*dd*, *J* = 9.8, 3.0, 1 H); 2.61 (*dd*, *J* = 15.1, 7.5, 1 H); 2.45 (*dd*, *J* = 15.1, 6.0, 1 H); 2.11 (*ddd*, *J* = 13.5, 3.0, 2.2, 3 H); 1.76 (*ddd*, *J* = 12.0, 3.0, 2.2, 1 H); 1.40 (*s*, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 171.3; 139.2; 128.4; 128.2; 127.3; 77.7; 72.6; 68.4; 67.0; 51.6; 40.3; 37.1. HR-ESI-MS: 267.1228 ($[M+H]^+$, $C_{14}H_{19}O_5^+$; calc. 267.1232).

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Received September 24, 2009