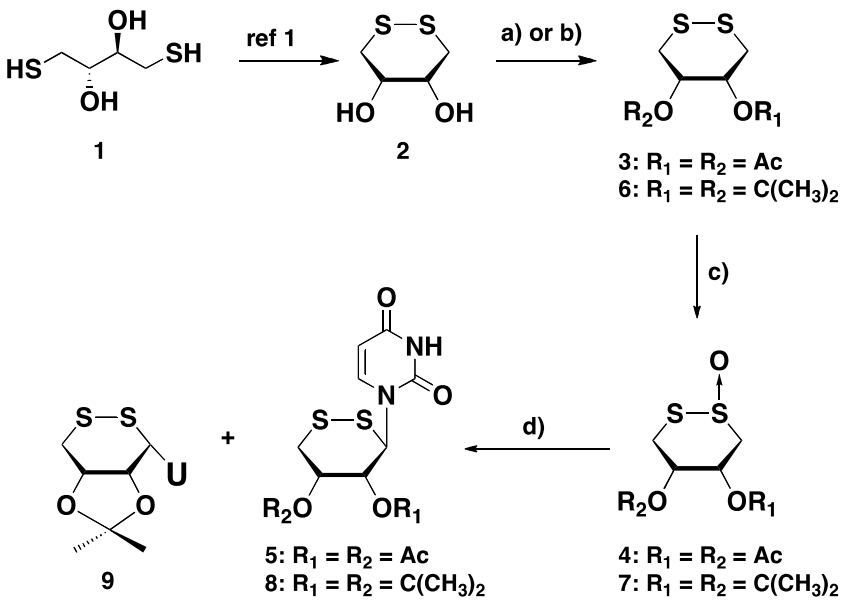
Electronic Supplementary Material (ESI) for Chemical Communications
This journal is © The Royal Society of Chemistry 2013

Supplementary Information

Synthesis of a novel 1,2-dithianenucleoside via Pummerer-like reaction, followed by Vorbruggen glycosylation between 1,2-dithiane derivative and uracil

Tadashi Miyazawa, Kouhei Umezaki, Noriko Tarashima, Kazuhiro Furukawa, Takashi Ooi, Noriaki Minakawa

General Methods. Physical data were measured as follows: Melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded at 400 or 500 MHz and 100 or 125 MHz instruments (Bruker AV500 or AV400) in $CDCl_3$ or DMSO-d_6 as the solvent with tetramethylsilane as an internal standard. Chemical shifts are reported in parts per million (□), and signals are expressed as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), or br (broad). All exchangeable protons were detected by addition of D_2O. Mass spectra were measured by Waters Micromass LTC PREMIER. X-ray crystallographic analysis was performed with a Rigaku RAXIS-RAPID instrument (Rigaku Corporation). A software, "CrystalStructure 3.6.0 (Rigaku Corporation)" was used for solving the data. TLC was done on Merck Kieselgel F254 precoated plates. Silica gel used for column chromatography was Merck silica gel 60 (70–230 mesh).



Scheme S1

***cis*-4,5-Diacetoxy-1,2-dithiane (3)**.[15] A solution of **1** (1.5 g, 9.7 mmol) in 10% aq. KOH–MeOH (36 mL, 1:5) was stirred for 48 h under O_2 atmosphere. After being cooled to 0 °C, the reaction mixture was neutralized with saturated aq. NH_4Cl, and the reaction mixture was concentrated *in vacuo*. The residue was coevaporated with toluene, and then MeOH was added to the residue. The resulting insoluble materials were filtered off, and the filtrate was concentrated *in vacuo* to give crude **2**. To a solution of the resulting **2** in dry CH_3CN (97 mL) were added Et_3N

(6.7 mL, 48.6 mmol), acetic anhydride (4.6 mL, 48.6 mmol), and DMAP (200 mg, 1.9 mmol), and the whole was stirred for 2 h at room temperature. The reaction was quenched by addition of MeOH and the solvent was removed *in vacuo*. The residue was partitioned between AcOEt and H_2O, and the separated organic layer was further washed with saturated aqueous $NaHCO_3$, followed by brine. The organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by a silica gel column, eluted with hexane/AcOEt (4:1–2:1), to give **3** (1.75 g, 76% as a yellow solid): ^{1}H NMR ($CDCl_3$); δ 5.17(m, 2 H), 3.23–2.66 (m, 4 H), 2.09 (s, 6 H).

(4*S*, 5*R*)-4,5-Diacetoxy-1-oxo-1,2-dithiane(4).[15] To a solution of **3** (1.74 g, 7.4 mmol) in CH_2Cl_2 (20 mL) was added a solution of mCPBA (2.0 g, 8.1 mmol) in CH_2Cl_2 (5 mL) dropwisely at –78 °C. After being stirred at the same temperature, the reaction was quenched by addition of saturated aqueous $NaHCO_3$. The reaction mixture was partitioned between AcOEt and H_2O, and the separated organic layer was further washed with H_2O, followed by brine. The organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by a silica gel column, eluted with hexane/AcOEt (2:1–1:2), to give **4** as a 7:1mixture of diastereomers (1.64 g, 88% as a white solid). As analytical samples, each diastereomer was purified by a silica gel column.

NMR spectrum of diastereomer A; ^{1}H NMR ($CDCl_3$); δ 5.75 (m, 1 H), 5.43 (m, 1 H), 3.97 (m, 1 H), 3.43–3.30 (m, 3 H), 2.17 (s, 3 H), 2.05 (s, 3 H).

NMR spectrum of diastereomer B; ^{1}H NMR ($CDCl_3$); δ 5.46 (m, 1 H), 5.26 (ddd, 1 H, J= 2.7, 3.3 and 11.3 Hz), 4.02 (dd, 1 H, J= 11.3 and 13.6 Hz), 4.00 (dd, 1 H, J= 5.0 and 13.6 Hz), 3.23 (dd, 1 H, J= 2.7 and 12.5 Hz), 2.84 (dd, 1 H, J= 3.3 and 12.5 Hz), 2.16 (s, 3 H), 2.10 (s, 3 H).

4,5-*O*-(1-Methylethylidene)-1,2-dithiane (6). In the same manner as described above, compound **1** (5.0 g, 32.8 mmol) was converted into the 1,2-dithiane derivarive **2**. Then, the resulting crude **2** was dissolved in acetone (110 mL), and 2,2-dimethoxypropane (29 mL, 200 mmol) and *p*-TsOH (1.25 g, 6.6 mmol) were added to the solution. After being stirred for 10 min at room temperature, the reaction was quenched by addition of saturated aqueous $NaHCO_3$ at 0 °C, and the solvent was removed *in vacuo*. The residue was partitioned between AcOEt and H_2O, and

the separated organic layer was further washed with H_2O, followed by brine. The organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by a silica gel column, eluted with hexane/AcOEt (3:1–2:1), to give **3** (1.75 g, 97% as a white solid). Analytical sample was crystalized from Hexane to give **3** as white crystals: mp 48.5–49 °C; ESIMS-LR *m*/*z* = 215 (MNa^+); ^{1}H NMR ($CDCl_3$) δ 4.20 (m, 2 H), 3.16 (m, 4 H), 1.55 and 1.38 (each s, each 3 H).^{13}C NMR ($CDCl_3$);δ 108.33, 70.73, 35.71, 28.30, 26.64. *Anal*. Calcd for $C_7H_{12}O_2S_2$: C, 43.72; H, 6.29. Found: C, 43.42; H, 6.11.

(4*S*, 5*R*)- 4,5-*O*-(1-Methylethylidene)-1-oxo-1,2-dithiane(7). In the same manner as described for **4**, **6** (880 mg, 4.6 mmol) in CH_2Cl_2 (12 mL) was treated with mCPBA (1.24 g, 5.0 mmol) at –78 °C afforded **7** (789 mg, 83% as a white solid). As analytical samples, each diastereomer was purified by a silica gel column. ESIMS-LR *m*/*z* = 231 (MNa^+).

Physical data of diastereomer A: mp 100–101 °C (crystallized from hexane/AcOEt); ESIMS-LR *m*/*z* = 231 (MNa^+); ^{1}H NMR ($CDCl_3$); δ 4.47 (m, 1 H), 4.19 (ddd, 1 H, *J* = 4.0, 6.0, and 10.5 Hz), 3.78 (dd, 1 H, *J* = 3.8 and 13.3 Hz), 3.58 (dd, 1 H, *J* = 6.0 and 14.3 Hz), 3.23 (dd, 1 H, *J* = 10.5 and 14.3 Hz), 3.13 (dd, 1 H, *J* = 9.8 and 13.3 Hz), 1.51 and 1.36 (each s, each 3 H); ^{13}C NMR ($CDCl_3$);δ 24.84, 25.59, 28.12, 55.17, 70.93, 72.41, 110.06. *Anal*. Calcd for $C_7H_{12}O_3S_2$: C, 40.36 ; H, 5.81. Found: C, 40.18 ; H,5.74 .

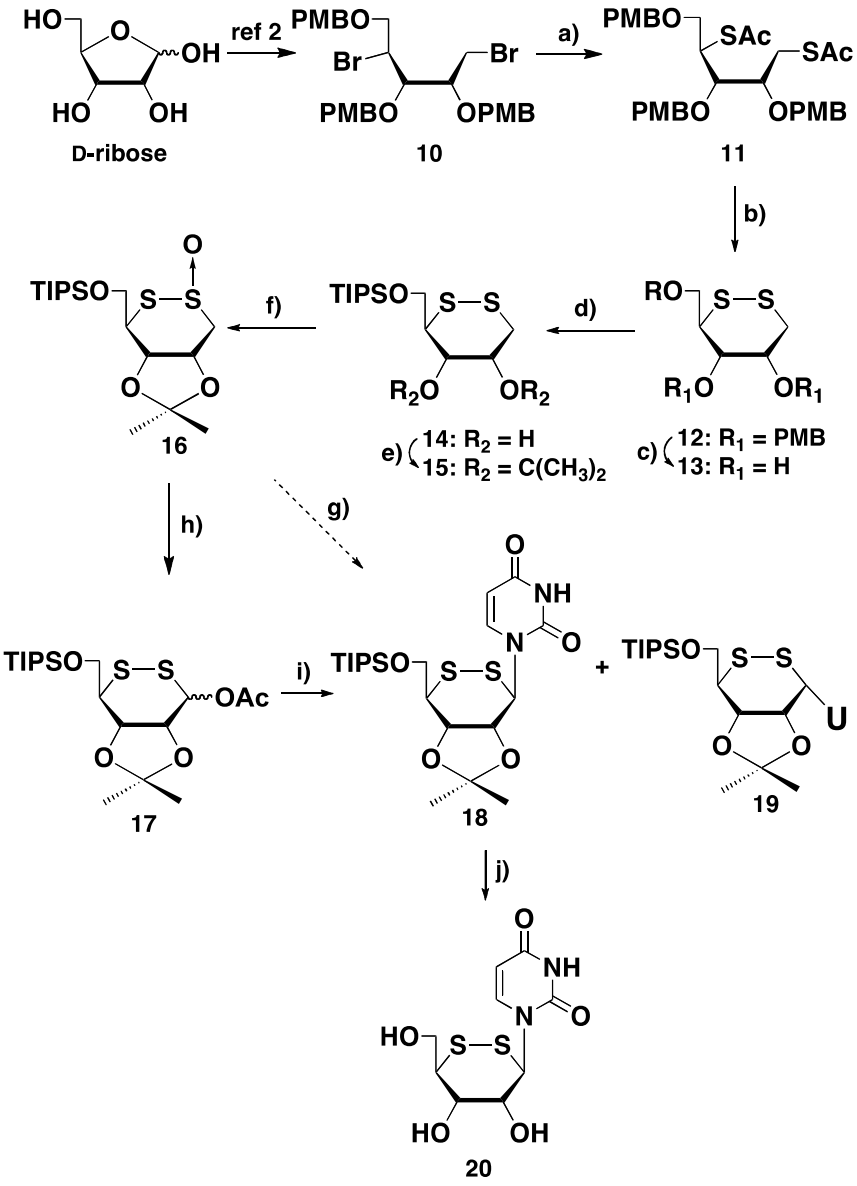
Physical data of diastereomer B: mp 73–74 °C (crystallized from hexane/AcOEt); ESIMS-LR *m*/*z* = 231 (MNa^+); ^{1}H NMR ($CDCl_3$); δ 4.76 (ddd, 1 H, *J* = 5.3, 6.3, and 9.3 Hz), 4.60 (ddd, 1H, *J* = 3.3, 6.3, and 7.3 Hz), 3.71 (dd, 1 H, *J* = 5.3 and 13.3 Hz), 3.58 (dd, 1 H, *J* = 3.3 and 3.8 Hz), 3.12 (dd, 1 H, *J* = 7.3 and 13.8 Hz), 3.10 (dd, 1 H, *J* = 9.3 and 13.3 Hz), 1.50 and 1.39 (each s, each 3 H); ^{13}C NMR ($CDCl_3$);δ 25.88, 27.71, 28.79, 51.95, 68.05, 70.70, 109.23. *Anal*. Calcd for $C_7H_{12}O_3S_2$: C, 40.36; H, 5.81. Found: C, 40.21 ; H, 5.64.

1-[(3*R*,4*R*,5*S*)-4,5-O-(1-Methylethylidene)-1,2-dithianyl]uracil (8) and 1-[(3*S*,4*R*,5*S*)-4,5-O-(1-methylethylidene)-1,2-dithianyl]uracil (9). To a suspension of uracil (112 mg, 1.0 mmol) in dry toluene (2 mL) were added triethylamine (280 μL, 2.0 mmol) and

TMSOTf (723 μL, 4.0 mmol), and the mixture was stirred at room temperature until giving two-phase clear solution. Dry CH_3CN (3.0 mL) was added to the above solution, which gave an one-phase clear solution, and the whole was added to a solution of **7** (104 mg, 0.5 mmol) in dry CH_3CN (3.0 mL) dropwise over 10 min via a cannula. An additional triethylamine (280 μL, 2.0 mmol) in dry toluene (1.5 mL) was added dropwise to the reaction mixture at 0 °C. After being stirred for 10 min at the same temperature, the reaction was quenched by addition of saturated aqueous $NaHCO_3$ at 0 °C, and the reaction mixture was partitioned between AcOEt and H_2O. The separated organic layer was washed with saturated aqueous $NaHCO_3$, followed by brine. The organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by a silica gel column, eluted with MeOH in $CHCl_3$ (0%–5%), to give **8** (49 mg, 32% as a white solid) and **9** (26 mg, 17% as a coloreless glass).

Physical data of **8**: mp 212–214 °C (dec.) (crystallized from MeOH); ESIMS-LR *m*/*z* = 325 (MNa^+); ^{1}H NMR ($CDCl_3$); δ 8.24 (brs, 1 H), 7.17 (d, 1 H, *J* = 8.0 Hz), 5.76 (dd, 1 H, *J* = 1.8 and 8.0 Hz), 5.60 (d, 1 H, *J* = 9.8 Hz), 4.65 (m, 1 H), 4.40 (dd, 1 H, *J* = 4.5 and 9.8 Hz), 3.49 (dd, 1 H, *J* = 3.3 and 15.1 Hz), 3.27 (dd, 1 H, *J* = 3.0 and 15.1 Hz), 1.62 and 1.40 (each s, each 3 H); ^{13}C NMR ($CDCl_3$); δ 162.13, 149.94, 140.92, 109.81, 103.56, 74.51, 74.39, 36.93, 28.17, 26.63; Anal. Calcd for $C_{11}H_{14}N_2O_4S_2$•1/2 H_2O: C, 42.43 ; H, 4.86 ; N, 9.00. Found: C, 42.50 ; H, 4.52 ; N, 8.93.

Physical data of **9**: ESIMS-LR *m*/*z* = 325 (MNa^+); ESIMS-HR (MNa^+) calcd for $C_{11}H_{14}N_2O_4NaS_2$ 325.0293, found 325.0280; ^{1}H NMR ($CDCl_3$); δ 9.25 (brs, 1 H), 7.66 (d, 1 H, *J* = 8.0 Hz), 6.29 (d, 1 H, *J* = 2.5 Hz), 5.73 (d, 1 H, *J* = 8.0 Hz), 4.40 (dd, 1 H, *J* = 2.5 and 4.3 Hz), 4.36 (ddd, 1 H, *J* = 4.3, 5.8, and 10.3 Hz), 2.95 (dd, 1 H, *J* = 10.3 and 14.0 Hz), 2.83 (dd, 1 H, *J* = 5.8 and 14.0 Hz), 1.59 and 1.36 (each s, each 3 H); ^{13}CNMR ($CDCl_3$); δ 162.42, 150.02, 142.58, 110.74, 102.73, 75.50, 73.86, 58.40, 34.09, 28.61, 27.12.



Scheme S2

(2*S*,3*S*,4*R*)-2,5-Dibromo-1,3,4-tris-*p*-methoxybenzyloxypentane (10).[18] To a solution of 2,3,5-Tri-*O*-*p*-methoxybenzyl-D-ribitol[18] (27.9 g, 54.5 mmol) in dry pyridine (145 mL) was added MsCl (14.8 mL, 0.19 mol) and the whole mixture was stirred for 30 min at 0 °C. The reaction was quenched by addition of ice, and the reaction mixture concentrated *in vacuo*. The residue was partitioned between AcOEt and H_2O, and the separated organic layer was further washed with saturated aqueous $NaHCO_3$, followed by brine. The organic layer was dried (Na_2SO_4) and concentrated *in vacuo*, and the residue was coevaporated with toluene to give the crude dimesylate as a yellow oil. The resulting dimesylate in methyl ethyl ketone (130 mL) containing lithium

bromide (45.5 g, 0.52 mol) was heated for 5 h under reflux. The residue was partitioned between AcOEt and H_2O, and the separated organic layer was further washed with saturated aqueous $NaHCO_3$, followed by brine. The reaction mixture was allowed to cool to room temperature and concentrated *in vacuo*. The residue was partitioned between AcOEt and H_2O, and the separated organic layer was further washed with H_2O, followed by brine. The organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by a silica gel column, eluted with hexane/AcOEt (7:1–3:1), to give **10** (20.9 g, 62% as a yellow oil): ^{1}H NMR ($CDCl_3$); δ□7.32–7.21(m, 6 H), 6.86(m, 6 H), 4.68–4.46 (m, 6 H), 4.40(m, 1 H), 3.79 (s, 9 H), 3.89(m, 1 H), 3.76–3.69(m, 4 H), 3.64(m, 1 H).

(2*R*,3*S*,4*R*)-2,5-Dithioacetyl-1,3,4-tris-*p*-methoxybenzyloxypentane (11). To a solution of **10** (20.8 g, 32.7 mmol) in dry DMF (32 mL) was added potassium thioacetate (26.0 g, 0.2 mol) and the whole mixture was stirred for 7 h at 100 °C. The reaction mixture was allowed to cool to room temperature and concentrated *in vacuo*. The residue was partitioned between AcOEt and H_2O, and the separated organic layer was further washed with H_2O, followed by brine. The organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by a silica gel column, eluted with hexane/AcOEt (6:1–3:1), to give **11** (7.6 g, 37% as a brown oil): ESIMS-LR *m*/*z* = 651 (MNa^+); ESIMS-HR (MNa^+) calcd for $C_{33}H_{40}O_8NaS_2$ 651.2062, found 651.2078; ^{1}H NMR ($CDCl_3$);□δ□7.22 (m, 6 H), 6.84 (m, 6 H), 4.53–4.39 (m, 6 H), 3.90 (m, 1 H), 3.84 (dd, 1 H, *J* = 4.8 and 5.5 Hz), 3.79 (s, 9 H), 3.63 (m, 2 H), 3.43 (dd, 1 H, *J* = 5.5 and 6.5 Hz), 3.33 (dd, 1 H, *J* = 4.3 and 14.1 Hz), 3.18 (dd, 1 H, *J* = 5.3 and 14.1 Hz), 2.35 (s, 3 H), 2.30 (s, 3 H); ^{13}C NMR ($CDCl_3$);□δ□196.07, 195.01, 159.64, 159.58, 130.39, 130.20, 129.99, 129.68, 114.09, 114.04, 78.66, 78.44, 73.43, 72.96, 71.83, 70.07, 55.63, 45.02, 31.07, 30.99, 30.01.

(3*R*,4*S*,5*R*)-4,5-Bis-*p*-methoxybenzyloxy-3-*p*-methoxybenzyloxymethyl-1,2-dithiane (12). A solution of **11** (7.6 g, 12.1 mmol) in 10% aq. KOH–MeOH (84 mL, 1:5) was stirred for 8 h under O_2 atmosphere. After being cooled to 0 °C, the reaction mixture was neutralized with saturated aq. NH_4Cl, and the reaction mixture was concentrated *in vacuo*. The residue was partitioned between AcOEt and H_2O, and the separated organic layer was further washed with H_2O,

followed by brine. The organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by a silica gel column, eluted with hexane/AcOEt (6:1–3:1), to give **12** (4.79 g, 73% as a brown oil): ESIMS-LR *m*/*z* = 565 (MNa^+); ESIMS-HR (MNa^+) calcd for $C_{29}H_{34}O_6NaS_2$ 565.1694, found 565.1650; ^{1}H NMR ($CDCl_3$); δ 7.23 (m, 6 H), 6.86 (m, 6 H), 4.56–4.41 (m, 6 H), 3.89–3.75 (m, 4 H), 3.80 (s, 9 H), 3.50 (m, 1 H), 3.22 (m, 1 H), 2.78 (m, 1 H); ^{13}C NMR ($CDCl_3$); δ 159.05, 129.48, 129.43, 129.18, 113.65, 113.62, 80.18, 78.94, 72.55, 71.27, 71.16, 68.19, 55.13, 46.99, 30.59.

(3*R*,4*S*,5*R*)-4,5-Dihydroxy-3-hydroxymethyl-1,2-dithiane (13). A solution of **12** (4.79 g, 8.83 mmol) in TFA–CH_2Cl_2 (20 mL, 1:4) was stirred for 5 h at room temperature. The reaction mixture was concentrated *in vacuo*, and the residue was coevaporated with MeOH several times. Then, the resulting precipitates were filtered off, washed with MeOH. The solvent was removed *in vacuo*, and the residue was purified by a silica gel column, eluted with $CHCl_3$/MeOH (19:1–17:3), to give **13** (1.35 g, 84% as a colorless oil): ESIMS-LR *m*/*z* = 205 (MNa^+); ESIMS-HR (MNa^+) calcd for $C_5H_{10}O_3NaS_2$ 204.9969, found 205.0009; ^{1}H NMR (DMSO-d_6); δ 4.85 (br s, 3 H, exchangable with D_2O), 3.86 (m, 1 H), 3.75–3.55 (m, 3 H), 3.16 (m, 1 H), 2.97 (m, 1 H), 2.75 (m, 1 H); ^{13}C NMR (DMSO-d_6); δ 75.56, 73.89, 64.34, 52.18, 32.36.

(3*R*,4*S*,5*R*)-4,5-Dihydroxy-3-triisopropylsiloxymethyl-1,2-dithiane (14). To a solution of **13** (1.2 g, 6.58 mmol) in dry DMF (32 mL) were added triisopropylsilyl chloride (1.5 mL, 7.24 mmol) and imidazole (0.99 g, 14.5 mmol), and the whole mixture was stirred for 5 h at room temperature. The reaction was quenched by addition of ice, and the solvent was removed *in vacuo*. The residue was partitioned between AcOEt and H_2O, and the separated organic layer was further washed with H_2O, followed by brine. The organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by a silica gel column, eluted with hexane/AcOEt (5:1–1:1), to give **14** (2.0 g, 91% as a brown oil): ESIMS-LR *m*/*z* = 361 (MNa^+); ESIMS-HR (MNa^+) calcd for $C_{14}H_{30}O_3NaS_2Si$ 361.1303, found 361.1303; ^{1}H NMR (DMSO-d_6); δ 4.85 (br s, 2 H, exchangable with D_2O), 4.12 (m, 1 H), 3.92 (m, 1 H), 3.80 (m, 1 H), 3.61 (m, 1 H), 3.31 (m, 1 H), 2.98 (m, 1 H), 2.79 (m, 1 H) ; ^{13}C NMR ($CDCl_3$); δ□74.74, 67.07, 60.30, 48.19, 33.52, 17.78, 11.63.

This journal is © The Royal Society of Chemistry 2013

(3*R*,4*S*,5*R*)-4,5-*O*-(1-Methylethylidene)-3-triisopropylsiloxymethyl-1,2-dithiane (15). To a solution of **14** (2.0 g, 5.9 mmol) in acetone (20 mL) were added 2,2-dimethoxypropane (5.3 mL, 41 mmol) and *p*TsCl (0.22 g, 1.2 mmol), and the whole mixture was stirred for 10 min at room temperature. The reaction was quenched by addition of saturated aqueous $NaHCO_3$ at 0 °C, and the solvent was removed *in vacuo*. The residue was partitioned between AcOEt and H_2O, and the separated organic layer was further washed with H_2O, followed by brine. The organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by a silica gel column, eluted with hexane/AcOEt (49:1–24:1), to give **15** (1.98 g, 98% as a brown oil): ESIMS-LR *m*/*z* = 401 (MNa^+); ESIMS-HR (MNa^+) calcd for $C_{17}H_{34}O_3NaS_2Si$ 401.1616, found 401.1655; ^{1}H NMR ($CDCl_3$); δ 4.33 (m, 1 H), 4.22 (dd, 1 H, *J* = 4.6 and 8.7 Hz), 4.11 (dd, 1 H, *J* = 4.5 and 10.4 Hz), 3.98 (dd, 1 H, *J* = 5.0 and 10.4 Hz), 3.31 (dd, 1 H, *J* = 3.7 and 14.6 Hz), 3.26 (m, 1 H), 3.18 (dd, 1 H, *J* = 4.5 and 14.6 Hz), 1.52 and 1.38 (each s, each 3 H), 1.07 (m, 21 H); ^{13}C NMR ($CDCl_3$); δ 108.14, 72.73, 71.14, 62.96, 51.89, 36.58, 28.60, 26.86, 18.12, 12.04.

(3*R*,4*S*,5*R*)-4,5-*O*-(1-Methylethylidene)-1-oxo-3-triisopropylsiloxymethyl-1,2-dithiane (16). To a solution of **15** (1.9 g, 5.2 mmol) in dry CH_2Cl_2 (26 mL) was added a solution of mCPBA (1.42 g, 5.75 mmol) in CH_2Cl_2 (5 mL) dropwisely at –78 °C, and the whole mixture was stirred for 10 min at the same temperature. The reaction was quenched by addition of saturated aqueous $NaHCO_3$ at –78 °C. The reaction mixture was partitioned between AcOEt and H_2O, and the separated organic layer was further washed with H_2O, followed by brine. The organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by a silica gel column, eluted with hexane/AcOEt (7:1–4:1), to give **16** as a 4 :1 mixture of diastereomers (1.78 g, 86% as a colorless oil). Analytical samples were purified by a silica gel column: ESIMS-LR *m*/*z* = 395 (MH^+); ESIMS-HR (MH^+) calcd for $C_{17}H_{34}O_4NaS_2Si$ 417.1565, found 417.1602.

NMR spectrum of diastereomer A: ^{1}H NMR ($CDCl_3$); δ 4.58 (ddd, 1 H, *J* = 3.5, 5.5 and 7.8 Hz), 4.30 (dd, 1 H, *J* = 4.3 and 10.5 Hz), 4.26 (dd, 1 H, *J* = 5.5 and 9.5 Hz), 4.13 (t, 1 H, *J* = 10.5 Hz), 3.55 (dd, 1 H, *J* = 3.5 and 13.6 Hz), 3.16 (dd, 1 H, *J* = 7.8 and 13.6 Hz), 3.06 (ddd, 1 H, *J* = 4.3, 9.5 and 10.5 Hz), 1.50 and 1.37 (each s, each 3 H), 1.07 (m, 21H, TIPS); ^{13}C NMR ($CDCl_3$) δ

109.25, 71.24, 70.18, 61.64, 55.77, 43.80, 28.30, 26.20, 18.30, 12.23.

NMR spectra of diastereomer B: ^{1}H NMR ($CDCl_3$); δ 4.71 (dd, 1 H, *J* = 6.0 and 10.3 Hz), 4.38 (dd, 1 H, *J* = 2.3 and 10.5 Hz), 4.20 (ddd, 1 H, *J* = 4.0, 6.0 and 10.3 Hz), 4.09 (dd, 1 H, *J* = 2.8 and 10.5 Hz), 3.84 (dd, 1 H, *J* = 4.0 and 13.3 Hz), 3.80 (m, 1 H), 2.98 (dd, 1 H, *J* = 10.3 and 13.3 Hz), 1.49 and 1.36 (each s, each 3 H), 1.07 (m, 21 H); ^{13}C NMR ($CDCl_3$) δ 109.76, 72.85, 71.66, 62.25, 55.31, 43.29, 27.87, 25.32, 17.79, 11.73.

(4*R*,5*S*,6*R*)-3-Acetoxy-4,5-*O*-(1-methylethylidene)-6-triisopropylsiloxymethyl-1,2-dithiane (17). A solution of **16** (1.75 g, 4.4 mmol) in acetic anhydride (22 mL) was heated for 33 h under reflux. After being cooled to room temperature, the reaction mixture was poured into saturated aqueous $NaHCO_3$ at 0 °C. Then, the whole was partitioned between AcOEt and H_2O, and the separated organic layer was further washed with saturated aqueous $NaHCO_3$, followed by brine. The organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by a silica gel column, eluted with hexane/AcOEt (30:1–20:1), to give **17** as a 1:1 mixture of diastereomers (0.37 g, 19% as a orange oil). Analytical samples were purified by a silica gel column: ESIMS-LR *m*/*z* = 459 (MNa^+); ESIMS-HR calcd for $C_{19}H_{36}O_5NaS_2Si$ 459.1671, found 459.1633.

NMR spectra of diastereomer A: ^{1}H NMR ($CDCl_3$); δ 6.01 (d, 1 H, *J* = 4.8 Hz), 4.48 (dd, 1 H, *J* = 4.8 and 7.5 Hz), 4.16 (t, 1 H, *J* = 4.8 Hz), 4.14 (dd, 1 H, *J* = 5.5 and 10.5 Hz), 4.00 (dd, 1 H, *J* = 5.5 and 10.5 Hz), 3.26 (dt, 1 H, *J* = 5.5 and 7.5 Hz), 2.16 (s, 3 H), 1.52 and1.36 (each s, each 3 H), 1.07 (m, 21 H); ^{13}C NMR ($CDCl_3$); δ□169.15, 108.50, 74.60, 74.45, 73.56, 62.88, 50.27, 28.38, 26.73, 21.15, 18.08, 12.01.

NMR spectra of diastereomer B: ^{1}H NMR ($CDCl_3$); δ 6.16 (d, 1 H, *J* = 3.0 Hz), 4.46 (dd, 1 H, *J* = 5.0 and 9.0 Hz), 4.41 (dd, 1 H, *J* = 3.0 and 5.0 Hz), 4.12 (dd, 1 H, *J* = 4.3 and 10.5 Hz), 4.01 (dd, 1 H, *J* = 4.3 and 10.5 Hz), 3.25 (dt, 1 H, *J* = 4.3 and 9.0 Hz), 2.16 (s, 3 H), 1.54 and 1.39(each s, each 3 H), 1.07 (m, 21 H); ^{13}C NMR ($CDCl_3$); δ□169.34, 109.86, 74.60, 74.45, 73.56, 62.41, 51.78, 27.93, 26.56, 21.19, 18.08, 12.01.

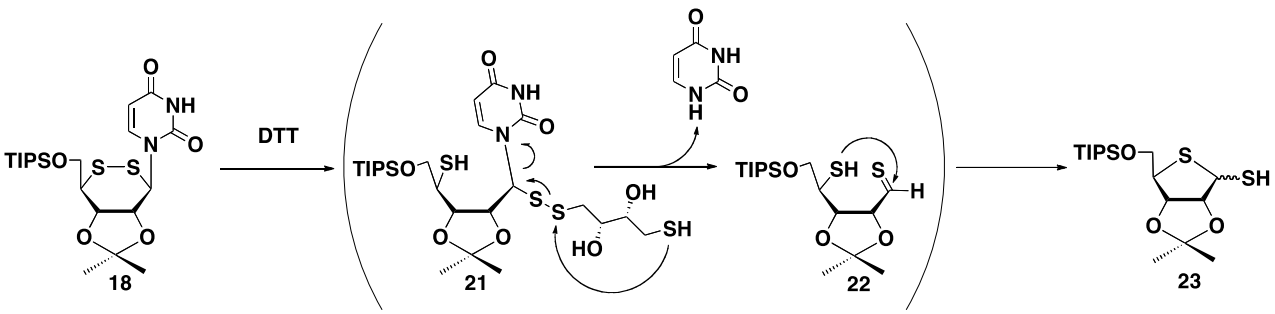
1-[(3*R*,4*R*,5*S*,6*R)*-4,5-*O*-(1-Methylethylidene)-6-triisopropylsiloxymethyl-1,2-Dithianyl]uracil (18) and 1-[(3*S*,4*R*,5*S*,6*R)*-4,5-*O*-(1-methylethylidene)-6-triisopropylsiloxymethyl-1,2-Dithianyl]uracil (19). To a suspension of **17** (233 mg, 0.53 mmol) and uracil (120 mg, 1.07 mmol) in dry CH_3CN (3 mL) was added *N*,*O*-bis(trimethylsilyl)acetamide (0.52 mL, 2.14 mmol), and TMSOTf (0.24 mL, 1.3 mmol) was added to the resulting clear solution at 0 °C. Then, the whole mixture was heated for 5 h under reflux. After being cooled to room temperature, the reaction mixture was quenched by addition of saturated aqueous $NaHCO_3$ at 0 °C. Then, the whole was partitioned between AcOEt and H_2O, and the separated organic layer was further washed with saturated aqueous $NaHCO_3$, followed by brine. The organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by a silica gel column, eluted with hexane/AcOEt (9:1–3:2), to give **18** (95 mg, 37% as a brown oil) and **19** (40 mg, 15% as a brown form).

Physical data of **18**: ESIMS-LR *m*/*z* = 511 (MNa^+); ESIMS-HR (MNa^+) calcd for $C_{21}H_{36}N_2O_5NaS_2Si$ 511.1733, found 511.1706; ^{1}H NMR ($CDCl_3$); δ 8.18 (br s, 1 H, exchangable with D_2O), 7.39 (d, 1 H, *J* = 8.2 Hz), 5.78 (d, 1 H, , *J* = 7.6 Hz), 5.75 (d, 1 H, *J* = 8.2 Hz), 4.80 (t, 1 H, *J* = 4.7 Hz), 4.38 (dd, 1 H, *J* = 4.7 and 7.6 Hz), 4.17 (dd, 1 H, *J* = 6.9 and 10.4 Hz), 4.14 (dd, 1 H, *J* = 5.4 and 10.4 Hz), 3.33 (ddd, 1 H, $J_{6',5'}$ = 4.7, 5.4, and 6.9 Hz), 1.57 and 1.37 (each s, each 3 H), 1.07 (m, 21 H); ^{13}C NMR ($CDCl_3$); δ 163.01, 150.15, 140.77, 108.92, 103.15, 74.20, 73.87, 63.09, 60.05, 49.55, 28.15, 26.53, 18.08, 11.98.

Physical data of **19**: ESIMS-LR *m*/*z* = 511 (MNa^+); ESIMS-HR (MNa^+) calcd for $C_{21}H_{36}N_2O_5NaS_2Si$ 511.1733, found 511.1738; ^{1}H NMR ($CDCl_3$); δ 8.35 (brs, 1 H, exchangable with D_2O), 7.65 (d, 1 H, *J* = 8.2 Hz), 6.25 (d, 1 H, , *J* = 2.7 Hz), 5.70 (d, 1 H, *J* = 2.2 and 8.2 Hz), 4.44 (dd, 1 H, *J* = 2.7 and 4.4 Hz), 4.36 (dd, 1 H, *J* = 4.4 and 10.4 Hz), 4.11 (dd, 1 H, *J* = 3.2 and 10.4 Hz), 3.98 (dd, 1 H, *J* = 4.4 and 10.4 Hz), 3.18 (ddd, 1 H, *J* = 3.2, 4.4, and 10.4 Hz), 1.54 and 1.35 (each s, each 3 H), 1.00 (m, 21 H); ^{13}C NMR ($CDCl_3$); δ 163.03, 150.29, 142.84, 110.26,

102.61, 75.87, 74.24, 61.83, 58.79, 52.31, 28.65, 27.07, 18.08, 11.97.

1-[(3*R*,4*R*,5*S*,6*R*)-4,5-Dihydroxy-6-hydroxymethyl-1,2-dithianyl]uracil (20). A solution of **18** (73 mg, 0.15 mmol) in trifluoroacetic acid-CH_2Cl_2 (2 mL, 1:1) was stirred for 25 h at room temperature. The solvent was removed *in vacuo*, and the residue was coevaporated with MeOH, and then toluene. The residue was purified by a silica gel column, eluted with MeOH in $CHCl_3$ (15%–25%), to give **20** (40 mg, 91% as a brown solid). Analytical sample was crystalized from MeOH to give **20** as white crystals: mp 204–206 °C (dec.) (crystallized from MeOH); ESIMS-LR *m*/*z* = 315 (MNa^+); ^{1}H NMR (DMSO-d_6, 70 ℃) δ 7.63 (dd, 1 H, *J* = 4.0 and 8.2 Hz), 5.72 (d, 1 H, *J* = 9.8 Hz), 5.62 (dd, 1 H, *J* = 1.6 and 8.2 Hz), 5.34 (br s, 2 H, exchangable with D_2O), 5.06 (br s, 1 H, exchangable with D_2O), 4.28 (dd, 1 H, *J* = 2.2 and 3.5 Hz), 4.09 (dd, 1 H, *J* = 2.2 and 9.8 Hz), 3.92 (dd, 1 H, *J* = 3.8 and 11.3 Hz), 3.91 (dd, 1 H, *J* = 6.9 and 11.3 Hz), 3.10 (ddd, 1 H, *J* = 3.5, 3.8 and 6.9 Hz); ^{13}C NMR ($CDCl_3$); δ 164.02, 151.13, 142.10, 102.56, 71.78, 67.70, 59.59, 55.55, 49.16; *Anal*. Calcd for $C_9H_{12}N_2O_5S_2$: C, 36.98; H, 4.14; N, 9.58. Found: C, 36.88; H, 4.28; N, 9.53.



Scheme S3

2, 3-*O*-(1-Methylethylidene)-5-*O*-triisopropylsilyl-1, 4-dithio-D-ribofuranoside (23). To a solution of **18** (24 mg, 0.05 mmol) in dry CH_2Cl_2 (2.0 mL) was added dithiothreitol (30 mg, 0.2 mmol) and Et_3N (14μL, 0.1 mmol), and the whole mixture was stirred for 4 h at room temperature. The solvent was removed *in vacuo*, and the residue was purified by a silica gel column, eluted with AcOEt in hexane (5%) and then MeOH in $CHCl_3$ (15–20%), to give **23** as a 1:1 mixture of

This journal is © The Royal Society of Chemistry 2013

diastereomers (12 mg, 63% as a colorless oil) and uracil (2.7 mg, 49% as a white solid): ESIMS-LR *m*/*z* = 401 (MNa^+); ESIMS-HR calcd for $C_{17}H_{34}O_3NaS_2Si$ 401.1616, found 401.1646.

NMR spectra of diastereomer A: ^{1}H NMR ($CDCl_3$); δ 4.88 (m, 1 H), 4.65 (m, 2 H), 3.98 (dd, 1 H, *J* = 3.8 and 10.3 Hz), 3.77 (dd, 1 H, *J* = 5.3 and 10.3 Hz), 3.31 (m, 1 H), 2.28 (d, 1 H, *J* = 10.8 Hz), 1.56 and 1.37 (each s, each 3 H), 1.07 (m, 21 H); ^{13}C NMR ($CDCl_3$); δ□□□

NMR spectra of diastereomer B: ^{1}H NMR ($CDCl_3$); δ 4.96 (dd, 1 H, *J* = 2.0 and 5.5 Hz), 4.72 (dd, 1 H, *J* = 2.7 and 6.0 Hz), 4.48 (dd, 1 H, *J* = 2.7 and 5.5 Hz), 4.01 (dd, 1 H, *J*= 8.8 and 10.3 Hz), 3.84 (dd, 1 H, *J*= 6.0 and 10.3 Hz), 3.54 (ddd, 1 H, *J* = 2.0 , 6.0 and 8.8 Hz), 2.44 (d, 1 H, *J* = 6.0 Hz), 1.52 and 1.32(each s, each 3 H), 1.07 (m, 21 H); ^{13}C NMR ($CDCl_3$); δ□□□