

Supporting Information

Asymmetric Synthesis of Novel Thioiso Dideoxynucleosides with Exocyclic Methylene as Potential Antiviral Agents

Prashantha Gunaga,¹ Masanori Baba,² and Lak Shin Jeong^{1,*}

¹Laboratory of Medicinal Chemistry, College of Pharmacy, Ewha Womans University, Seoul 120-750, Korea and ² Center for Chronic Viral Diseases, Division of Human Retrovirology, Faculty of Medicine, Kagoshima University, 8-35-1 Sakuragaoka, Kagoshima 890-8520, Japan

Table of Contents

Experimental procedures for the syntheses of 6-10	S2 – S4
Experimental procedures for the syntheses of thiosugars (13-17)	S4 – S7
Experimental procedures for the syntheses of cis-nucleosides (19-25)	S7 – S12
Experimental procedures for the syntheses of trans-nucleosides (26-33)	S12 – S17

General Methods. Melting points are uncorrected. ^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were measured in CDCl_3 or CD_3OD and chemical shifts are reported in parts per million (δ) downfield from tetramethylsilane as internal standard. Flash column chromatography was performed using silica gel 60 (230-400 mesh).

(3*R*,5*S*)-Methyl 3-deoxy-3-methylene-D-erythro-pentofuranoside (6). Acetyl chloride (0.2 mL) was added dropwise to anhydrous methanol (15 mL) (equivalent to 1% HCl), at ambient temperature under nitrogen. This solution was added to **5** (1.85 g, 0.01 mol) and the mixture was stirred under nitrogen at room temperature for 6 h. The reaction mixture was neutralized with triethylamine and evaporated. The residue was purified by flash silica gel column chromatography (hexane/EtOAc = 1:2) to give **6** (1.4 g, 88%) as an oil.

α -anomer: ^1H NMR (CDCl_3) δ 3.41 (s, 3 H), 3.58 (dd, $J = 5.6, 12.0$ Hz, 1 H), 3.73 (dd, $J = 3.6, 12.0$ Hz, 1 H), 4.34 (m, 1 H), 4.81 (d, $J = 1.2$ Hz, 1 H), 4.84 (s, 1 H), 5.19 (s, 1 H), 5.46 (s, 1 H). Anal. Calcd. for $\text{C}_7\text{H}_{12}\text{O}_4$: C, 52.49; H, 7.55; O, 39.96. Found: C, 52.88; H, 7.53.

β -anomer: ^1H NMR (CDCl_3) δ 3.44 (s, 3 H), 3.62 (dd, $J = 4.8, 11.6$ Hz, 1 H), 3.76 (dd, $J = 3.6, 11.6$ Hz, 1 H), 4.48 (m, 1 H), 4.57 (m, 1 H), 4.92 (d, $J = 4.8$ Hz, 1 H), 5.13 (t, $J = 4.0$ Hz, 1 H), 5.36 (t, $J = 4.0$ Hz, 1 H). Anal. Calcd for $\text{C}_7\text{H}_{12}\text{O}_4$: C, 52.49; H, 7.55; O, 39.96. Found: C, 52.27; H, 7.86.

(3*R*,5*S*)-Methyl 3,5-di-*O*-benzyl-3-deoxy-3-methylene-D-erythro-pentofuranoside (7). A solution of **6** (1.166 g, 7.28 mmol) in anhydrous THF (20 mL) was cooled in ice under nitrogen atmosphere. To this mixture were added NaH (0.874 g, 60% in oil, 21.86 mmol) and BnBr (2.98 g, 17.48 mmol) followed by *n*- Bu_4NI (0.538 g, 1.45

mmol). The reaction mixture was stirred for 6 h at ambient temperature. The reaction mixture was neutralized with acetic acid, extracted with EtOAc, washed with water, dried and evaporated. The residue was purified by flash silica gel column chromatography (hexane/EtOAc = 4:1) to give **7** (2.12 g, 88%) as an oil.

α -anomer: $^1\text{H NMR}$ (CDCl_3) δ 3.39 (s, 3 H), 3.50 (dd, $J = 6.4, 10.8$ Hz, 1 H), 3.59 (dd, $J = 3.6, 10.8$ Hz, 1 H), 4.36 (m, 1 H), 4.57 (d, $J = 1.6$ Hz, 1 H), 4.68 (m, 4 H), 4.87 (d, $J = 4.0$ Hz, 1 H), 5.19 (t, $J = 2.0$ Hz, 1 H), 5.46 (t, $J = 2.0$ Hz, 1 H), 7.33 (m, 10 H). Anal. Calcd for $\text{C}_{21}\text{H}_{24}\text{O}_4$: C, 74.09; H, 7.11; O, 18.80. Found: C, 74.08; H, 7.51.

β -anomer: $^1\text{H NMR}$ (CDCl_3) δ 3.34 (s, 3 H), 3.57 (dd, $J = 2.4, 6.4$ Hz, 2 H), 4.14 (s, 1 H), 4.62 (m, 4 H), 4.62 (m, 1 H), 4.97 (s, 1 H), 5.35 (s, 1 H), 5.37 (s, 1 H), 7.32 (m, 10 H). Anal. Calcd for $\text{C}_{21}\text{H}_{24}\text{O}_4$: C, 74.09; H, 7.11; O, 18.80. Found: C, 74.03; H, 7.02.

(3*R*,5*S*)-3,5-Di-*O*-benzyl-3-deoxy-3-methylene-D-erythro-pentofuranose (8). A mixture of **7** (1.92 g, 5.6 mmol) in dioxan (25 mL) and aqueous HCl (8 M, 25 mL) was stirred for 24 h at ambient temperature. Reaction was quenched with NaHCO_3 . The mixture was evaporated to half its volume and extracted with EtOAc, dried and evaporated. The residue was purified by flash silica gel column chromatography (hexane/EtOAc = 4:1) to give **8** (1.37 g, 74%) as an oil.

α, β -anomeric mixture: $^1\text{H NMR}$ (CDCl_3) δ 3.51 (dd, $J = 5.2, 10.4$ Hz, 1 H), 3.59 (m, 2 H), 3.72 (dd, $J = 2.8, 10.4$ Hz, 1 H), 4.07 (s, 1 H), 4.34 (m, 1 H), 4.50 (d, $J = 3.2$ Hz, 1 H), 4.68 (m, 4 H), 4.74 (m, 1 H), 4.85 (s, 2 H), 5.21 (t, $J = 2.4$ Hz, 1 H), 5.24 (s, 1 H), 5.29 (s, 1 H), 5.36 (t, $J = 2.4$ Hz, 1 H). 7.31 (m, 20 H). Anal. Calcd for $\text{C}_{20}\text{H}_{22}\text{O}_4$: C, 73.60; H, 6.79; O, 19.61. Found: C, 73.87; H, 6.98.

(2*R*,4*S*)-2,5-Bis-benzyloxy-3-methylene-pentane-1,4-diol (9). To a solution of **8** (1.36 g, 4.2 mmol) in anhydrous THF (15 mL) was added lithium borohydride at 0 °C

under nitrogen atmosphere and the solution was stirred at ambient temperature for 24 h. The reaction was quenched with water and extracted with EtOAc. The organic layer was dried and concentrated. The residue was purified by flash silica gel column chromatography (hexane/EtOAc = 2:1) to give **9** (1.23 g, 91%) as an oil: $[\alpha]_D^{25} -24.66^\circ$ (c 1.70, CHCl_3); $^1\text{H NMR}$ (CDCl_3) δ 3.51 (dd, $J = 8.4, 10.0$ Hz, 1 H), 3.61 (dd, $J = 3.6, 10.0$ Hz, 1 H), 3.67 (m, 2 H), 4.06 (m, 1 H), 4.31 (m, 1 H), 4.55 (m, 4 H), 5.36 (s, 1 H), 5.40 (s, 1 H), 7.33 (m, 10 H). Anal. Calcd for $\text{C}_{20}\text{H}_{24}\text{O}_4$: C, 73.15; H, 7.37; O, 19.49. Found: C, 72.82; H, 7.61.

(4S)-Methanesulfonic acid 2-[(1R)-benzyloxy-2-methanesulfonyloxy-ethyl]-1-benzyloxymethyl-allyl ester (10). To a solution of **9** (1.24 g, 3.77 mmol) in anhydrous CH_2Cl_2 (20 mL) were added pyridine (3.1 mL, 37.7 mmol) and methanesulfonyl chloride (1.75 mL, 22.63 mmol) and the mixture stirred at ambient temperature for 3 h. The reaction was quenched with NaHCO_3 . The organic layer was washed with water, 0.01M HCl and finally with brine and dried. Solvent was evaporated and the residue was purified by flash silica gel column chromatography (hexane/EtOAc = 2:1) to give **10** (1.27 g, 70%): $^1\text{H NMR}$ (CDCl_3) δ 2.94 (s, 3 H), 2.99 (s, 3 H), 3.65 (m, 2 H), 4.27 (m, 2 H), 4.41 (m, 1 H), 4.52 (m, 4 H), 5.23 (dd, $J = 4.4, 7.6$ Hz, 1 H), 5.57 (d, $J = 9.6$ Hz, 2 H), 7.30 (m, 10 H). Anal. Calcd for $\text{C}_{22}\text{H}_{28}\text{O}_8\text{S}_2$: C, 54.53; H, 5.82; O, 26.41; S, 13.23. Found: C, 54.40; H, 5.80.

(3R, 5R)-5-Hydroxymethyl-4-methylene-tetrahydrothiophen-3-ol (13). To a stirred solution of **12** (370 mg, 1.03 mmol) in dry CH_2Cl_2 (8 mL) was added borontrichloride (4.11 mL of 1M solution in CH_2Cl_2 , 4.12 mmol) at -78°C under nitrogen atmosphere and the mixture was stirred for 3 h at -78°C . The mixture was quenched with MeOH and neutralized with triethylamine, and evaporated to dryness. The residue was

purified by flash silica gel column chromatography (hexane/EtOAc = 1:2) to give **13** (139 mg, 85%): $[\alpha]_{\text{D}}^{25} -27.37^{\circ}$ (*c* 1.10, CHCl₃); ¹H NMR (CDCl₃) δ 2.82 (dd, *J* = 3.6, 11.2 Hz, 1 H), 3.04 (dd, *J* = 4.4, 11.2 Hz, 1 H), 3.44 (s, 1 H), 3.57 (s, 2 H), 4.00 (m, 1 H), 4.09 (m, 1 H), 4.63 (m, 1 H), 5.15 (s, 1 H), 5.36 (s, 1 H); ¹³C NMR (CDCl₃) δ 38.8, 51.3, 66.0, 76.4, 112.2, 151.5. Anal. Calcd for C₆H₁₀O₂S: C, 49.29; H, 6.89; O, 21.89; S, 21.93. Found: C, 49.59; H, 6.98.

(3*R*,5*R*)-5-(*tert*-Butyldiphenylsilyloxy)methyl-4-methylene-tetrahydrothiophen-3-ol (14). TBDPSCl (3.1 mL, 11.9 mmol) was added to the mixture of **13** (1.74 g, 11.9 mmol) and imidazole (0.852 g, 12.5 mmol) in DMF (20 mL) at 0 °C. The mixture was stirred at room temperature for 24 h. Water was added and the mixture stirred for 10 minutes. The solvent was removed under reduced pressure. The residue was partitioned between EtOAc and water. The organic phase was washed with water and brine, dried and evaporated. The residue was purified by flash silica gel column chromatography (hexane/EtOAc = 4:1) to give **14** (4.061 g, 91%): $[\alpha]_{\text{D}}^{25} -28.75^{\circ}$ (*c* 0.8, CHCl₃); ¹H NMR (CDCl₃) δ 1.12 (s, 9 H), 2.81 (dd, *J* = 3.6, 11.6 Hz, 1 H), 3.02 (dd, *J* = 4.8, 11.6 Hz, 1 H), 3.26 (d, *J* = 8.8 Hz, 1 H), 3.77 (d, *J* = 4.8 Hz, 2 H), 3.96 (t, *J* = 4.6 Hz, 1 H), 4.61 (m, 1 H), 5.09 (s, 1 H), 5.33 (s, 1 H), 7.41 (m, 6 H), 7.69 (m, 4 H); ¹³C NMR (CDCl₃) δ 19.5, 26.9, 39.1, 50.6, 68.3 (4-CH), 76.8, 111.8, 127.9, 130.0, 130.1, 132.9, 133.0, 135.9, 136.0, 151.7. Anal. Calcd for C₂₂H₂₈O₂SSi: C, 68.70; H, 7.34; O, 8.32; S, 8.34; Si, 7.30 Found: C, 68.67; H, 7.73.

(3*S*,5*R*)-5-(*tert*-Butyldiphenylsilyloxy)methyl-4-methylene-tetrahydrothiophen-3-ol (15). A stirred mixture of **14** (325 mg, 0.8 mmol), benzoic acid (258 mg, 2.12 mmol) and triphenylphosphine (666 mg, 2.54 mmol) in dry THF (10 mL) was cooled in ice. DEAD (0.4 mL, 2.54 mmol) was added to the mixture at 0 °C and the stirring was

continued for one more hour at 0 °C. Reaction mixture was evaporated and the residue was subjected to flash silica gel column chromatography (hexane/EtOAc = 8:1) to give corresponding benzoylated derivative. The syrupy mass was dissolved in CH₂Cl₂ (2 mL) and to this solution was added the ammonia in methanol (20 mL). The mixture was stirred under pressure at ambient temperature for 24 h. Solvent was evaporated and the residue was purified by flash silica gel column chromatography (hexane/EtOAc = 4:1) to give **15** (245 mg, 75%): [α]_D²⁵ -93.0° (*c* 1.09, CHCl₃); ¹H NMR (CD₃OD) δ 1.06 (s, 9 H), 2.65 (dd, *J* = 6.8, 10.8 Hz, 1 H), 3.03 (dd, *J* = 6.0, 10.8 Hz, 1 H), 3.66 (dd, *J* = 6.8, 10.0 Hz, 1 H), 3.74 (dd, *J* = 6.6, 10.0 Hz, 1 H), 3.98 (t, *J* = 6.6 Hz, 1 H), 4.62 (t, *J* = 10.8 Hz, 1 H), 5.13 (s, 1 H), 5.26 (s, 1 H), 7.40 (m, 6 H), 7.67 (m, 4 H); ¹³C NMR (CDCl₃) δ 19.5, 27.0, 36.9, 49.6, 68.4, 75.8, 110.4, 127.9, 129.9, 133.5, 133.6, 135.9, 151.2. Anal. Calcd for C₂₂H₂₈O₂SSi: C, 68.70; H, 7.34; O, 8.32; S, 8.34; Si, 7.30. Found: C, 68.99; H, 7.02.

(R)-4-(2-Hydroxyethylidene)-tetrahydrothiophen-3-ol (16). The mixture of *E* and *Z* -**11** (1.1 g, 3.37 mmol) were converted to **16** (340 mg, 69%) according to the procedure used in the synthesis of **13**: ¹H NMR (CDCl₃) δ 2.71 (dd, *J* = 5.6, 10.8 Hz, 1 H), 3.00 (dd, *J* = 5.6, 10.8 Hz, 1 H), 3.42 (d, *J* = 14.8 Hz, 1 H), 3.56 (d, *J* = 15.0 Hz, 1 H), 4.16 (d, *J* = 6.2 Hz, 1 H), 4.63 (t, *J* = 5.6 Hz, 1 H), 5.79 (t, *J* = 5.6 Hz, 1 H); ¹³C NMR (CDCl₃) δ 28.7, 37.2, 59.7, 76.4, 123.9, 143.1. Anal. Calcd for C₆H₁₀O₂S: C, 49.29; H, 6.89; O, 21.89; S, 21.93. Found: C, 49.69; H, 6.54.

(R)-4-[2-(tert-Butyldiphenylsilyloxy)ethylidene]-tetrahydrothiophen-3-ol (Z-17, E-17). The mixture of *E*- and *Z*-**16** (303 mg, 2.1 mmol) was converted to silyl derivatives using the procedure reported for **14**. Flash silica gel column chromatography (hexane/EtOAc = 4:1) gave **Z-17** (518 mg, 65%) and **E-17** (165 mg,

21%).

E-17: ^1H NMR (CDCl_3) δ 1.01 (s, 9 H), 2.79 (dd, $J = 2.8, 12.0$ Hz, 1 H), 2.91 (dd, $J = 4.8, 12.0$ Hz, 1 H), 3.34 (d, $J = 14.0$ Hz, 1 H), 3.53 (d, $J = 14.0$ Hz, 1 H), 4.32 (m, 2 H), 4.73 (s, 1 H), 5.65 (m, 1 H), 7.41 (m, 6 H), 7.65 (m, 4 H); ^{13}C NMR (CDCl_3) δ 19.3, 26.9, 35.2, 40.2, 61.9, 71.7, 125.3, 127.9, 128, 130.0, 130.1, 133.3, 135.8, 136.0, 144.4. Anal. Calcd for $\text{C}_{22}\text{H}_{28}\text{O}_2\text{SSi}$: C, 68.70; H, 7.34; O, 8.32; S, 8.34; Si, 7.30. Found: C, 68.71; H, 7.33.

Z-17: ^1H NMR (CDCl_3) δ 1.01 (s, 9 H), 2.66 (dd, $J = 4.8, 11.6$ Hz, 1 H), 2.93 (dd, $J = 4.6, 11.6$ Hz, 1 H), 3.16 (d, $J = 14.8$ Hz, 1 H), 3.25 (d, $J = 15.2$ Hz, 1 H), 4.23 (dd, $J = 0.8, 6.0$ Hz, 2 H), 4.58 (m, 1 H), 5.80 (m, 1 H), 7.43 (m, 6 H), 7.67 (m, 4 H); ^{13}C NMR (CDCl_3) δ 19.3, 26.9, 28.9, 38.0, 61.8, 76.9, 125.2, 127.9, 129.9, 133.6, 133.7, 135.7, 135.8, 141.7. Anal. Calcd for $\text{C}_{22}\text{H}_{28}\text{O}_2\text{SSi}$: C, 68.70; H, 7.34; O, 8.32; S, 8.34; Si, 7.30. Found: C, 68.66; H, 7.71.

(2R,4R)-[4-(6-Chloropurin-9-yl)-3-methylene-tetrahydrothiophen-2-yl]methanol

(19). To a solution of **18** (450 mg, 0.8 mmol) in dry THF (20 mL) was added dropwise *n*-tetrabutyl ammonium fluoride (0.95 mL of 1 M solution in THF, 0.95 mmol) under nitrogen atmosphere and the mixture stirred for 15 minutes. The solvent was evaporated and the residue was subjected to flash column chromatography (hexane:EtOAc = 1:1) to obtain **19** (185 mg, 76%): MS (FAB) m/z 283 (MH^+); UV (MeOH) λ_{max} 265 nm (pH 7); $[\alpha]_{\text{D}}^{25} +32.43^\circ$ (c 0.37, MeOH); ^1H NMR (CD_3OD) δ 3.26 (dd, $J = 6.8, 11.6$ Hz, 1 H), 3.54 (dd, $J = 8.8, 11.6$ Hz, 1 H), 3.86 (dd, $J = 1.6, 5.6$ Hz, 2 H), 4.05 (t, $J = 5.6$ Hz, 1 H), 4.87 (t, $J = 2.0$ Hz, 1 H), 5.32 (t, $J = 2.0$ Hz, 1 H), 5.87 (t, $J = 6.8$ Hz, 1 H), 8.69 (s, 1 H), 8.71 (s, 1 H); ^{13}C NMR (CD_3OD) δ 34.6, 52.2, 63.1, 67.3, 113.3, 132.2, 147.7, 149.2, 151.6, 153.1, 153.2. Anal. Calcd for $\text{C}_{11}\text{H}_{11}\text{ClN}_4\text{OS}$: C, 46.73; H, 3.92; Cl, 12.54; N,

19.82; O, 5.66; S, 11.34. Found: C, 46.85; H, 3.69; N, 19.81.

(2R,4R)-[4-(6-Aminopurin-9-yl)-3-methylene-tetrahydrothiophen-2-yl]methanol

(20). A solution of **19** (37 mg, 0.13 mmol) in methanolic ammonia (10 mL) was stirred at 80 °C for 12 h in a pressure tube. The solvent was evaporated and the residue was subjected to flash silica gel column chromatography (dichloromethane:methanol = 8:1) to yield **20** (26 mg, 75%): MS (FAB) m/z 264 (MH^+); UV (MeOH) λ_{max} 260 nm (pH 7); $[\alpha]_D^{25}$ +28.57 (c 0.14, MeOH); 1H NMR (CD_3OD) δ 3.23 (dd, $J = 7.2, 11.6$ Hz, 1 H), 3.48 (dd, $J = 9.6, 11.6$ Hz, 1 H), 3.91 (dd, $J = 5.6, 4.4$ Hz, 2 H), 4.06 (t, $J = 5.6$ Hz, 1 H), 4.79 (t, $J = 2.0$ Hz, 1 H), 5.32 (t, $J = 2.0$ Hz, 1 H), 5.75 (t, $J = 7.2$ Hz, 1 H), 8.19 (s, 1 H), 8.25 (s, 1 H); ^{13}C NMR (CD_3OD) δ 34.9, 51.99, 62.6, 67.9, 112.6, 120.1, 142.0, 149.7, 150.6, 153.8, 157.6. Anal. Calcd for $C_{11}H_{13}N_5OS$: C, 50.17; H, 4.98; N, 26.60; O, 6.08; S, 12.18. Found: C, 49.95; H, 4.75; N, 26.62.

(2R,4R)-[4-(6-Methylaminopurin-9-yl)-3-methylene-tetrahydrothiophen-2-yl]-

methanol (21). A solution of **19** (46 mg, 0.16 mmol) in methanol (5 mL) and methyl amine in water (6 mL) was stirred at 80 °C for 12 h added in a pressure tube. The solvent was evaporated and the residue was subjected to flash silica gel column chromatography (dichloromethane:methanol = 10:1) to yield **21** (36 mg, 79%): MS (FAB) m/z 278 (MH^+); UV (MeOH) λ_{max} 266 nm (pH 7); $[\alpha]_D^{25}$ +33.33 (c 0.24, MeOH); 1H NMR (CD_3OD) δ 3.12 (br s, 3 H), 3.24 (dd, $J = 7.6, 11.2$ Hz, 1 H), 3.49 (dd, $J = 10.0, 11.2$ Hz, 1 H), 3.91 (m, 2 H), 4.06 (t, $J = 5.4$ Hz, 1 H), 4.78 (t, $J = 2.0$ Hz, 1 H), 5.31 (t, $J = 2.2$ Hz, 1 H), 5.74 (t, $J = 7.6$ Hz, 1 H), 8.19 (s, 1 H), 8.24 (s, 1 H); ^{13}C NMR (CD_3OD) δ 34.9, 49.3, 51.9, 62.6, 68.0, 112.5, 120.4, 141.4, 148.2, 149.8, 153.7, 156.8. Anal. Calcd for $C_{12}H_{15}N_5OS$: C, 51.97; H, 5.45; N, 25.25; O, 5.77; S, 11.56. Found: C, 51.95; H, 5.83; N, 24.81.

(3R,5R)-9-(5-Hydroxymethyl-4-methylene-tetrahydrothiophen-3-yl)-9H-purin-6-ol

(22). To a stirred solution of **19** (29 mg, 0.10 mmol) in methanol (10 mL) were added NaOMe (22 mg, 0.4 mmol) and mercaptoethanol (32 mg, 0.4 mmol) and the mixture was refluxed for 24 h. The solution was cooled and acidified with acetic acid. The solvent evaporated and the resulting residue was subjected to flash silica gel column chromatography (dichloromethane:methanol = 5:1) to yield **22** (22 mg, 82%): MS (FAB) m/z 265 (MH^+); UV (MeOH) λ_{max} 250 nm (pH 7); $[\alpha]_D^{25}$ +27.27° (c 0.22, MeOH); 1H NMR (CD_3OD) δ 3.21 (dd, J = 7.6, 11.6 Hz, 1 H), 3.46 (dd, J = 9.6, 11.6 Hz, 1 H), 3.84 (m, 2 H), 4.01 (t, J = 5.6 Hz, 1 H), 4.78 (t, J = 2.2 Hz, 1 H), 5.29 (t, J = 1.8 Hz, 1 H), 5.73 (t, J = 7.6 Hz, 1 H), 8.02 (s, 1 H), 8.06 (s, 1 H); ^{13}C NMR (CD_3OD) δ 34.7, 52.0, 62.8, 67.6, 112.6, 125.6, 141.4, 146.8, 149.6, 150.2, 159.2. Anal. Calcd for $C_{11}H_{12}N_4O_2S$: C, 49.99; H, 4.58; N, 21.20; O, 12.11; S, 12.13. Found: C, 49.68; H, 4.36; N, 21.08.

(3R,5R)-1-(5-Hydroxymethyl-4-methylene-tetrahydrothiophen-3-yl)-5-methyl-1H-pyrimidine-2,4-dione (23).

The thiosugar **15** (42 mg, 0.11 mmol) was converted to a mixture of *N*- and *O*-glycosylated products (hexane/EtOAc = 4:1) using Mitsunobu conditions. The mixture (65 mg, 0.11 mmol) was dissolved in THF (5 mL) and cooled in ice under nitrogen atmosphere. To the above stirring solution, acetic acid (0.003 mL, 0.05 mmol) and TBAF (0.119 mL, 1 M solution in THF, 0.119 mmol) were added dropwise and the mixture stirred at room temperature for 12 h. The mixture was evaporated and the residue was purified by flash chromatography (hexane/EtOAc = 1:2) to give the corresponding desilylated *N*-isomer (25 mg, 65%) and the *O*-isomer (6 mg, 16%).

***N*-isomer:** UV (MeOH) λ_{max} 253.5 nm (pH 7); 1H NMR ($CDCl_3$) δ 1.93 (s, 3 H), 3.08

(dd, $J = 7.6, 11.2$ Hz, 1 H), 3.19 (dd, $J = 10.6, 11.2$ Hz, 1 H), 3.86 (d, $J = 4.8$ Hz, 2 H), 3.94 (m, 1 H), 5.10 (s, 1 H), 5.39 (s, 1 H), 5.61 (t, $J = 7.6$ Hz, 1 H), 7.57 (t, $J = 7.6$ Hz, 2 H), 7.63 (s, 1 H), 7.73 (t, $J = 7.4$ Hz, 1 H), 7.96 (d, $J = 8.0$ Hz, 1 H).

O-isomer: UV (MeOH) λ_{\max} 269.5 nm (pH 7); ^1H NMR (CDCl_3) δ 1.94 (s, 3 H), 2.93 (dd, $J = 4.8, 12.0$ Hz, 1 H), 3.26 (dd, $J = 5.6, 12.0$ Hz, 1 H), 3.63 (dd, $J = 8.0, 11.2$ Hz, 1 H), 3.77 (dd, $J = 6.0, 11.2$ Hz, 1 H), 3.89 (t, $J = 7.6$ Hz, 1 H), 5.32 (s, 1 H), 5.47 (s, 1 H), 5.95 (t, $J = 4.8$ Hz, 1 H), 7.60 (s, 1 H).

Desilylated *N*-isomer (41 mg, 0.11 mmol) was dissolved in methanolic ammonia (10 mL) in a sealed tube and the mixture was stirred at ambient temperature for 12 h. The solvent was evaporated and the residue was subjected to flash column chromatography (dichloromethane:methanol = 10:1) to yield **23** (26 mg, 97%): MS (FAB) m/z 255 (MH^+); UV (MeOH) λ_{\max} 270 nm (pH 7); $[\alpha]_{\text{D}}^{25} +57.89^\circ$ (c 0.19, MeOH); ^1H NMR (CD_3OD) δ 1.86 (s, 3 H), 3.01 (dd, $J = 7.2, 10.4$ Hz, 1 H), 3.11 (t, $J = 10.4$ Hz, 1 H), 3.85 (d, $J = 5.6$ Hz, 2 H), 3.93 (t, $J = 5.4$ Hz, 1 H), 4.99 (s, 1 H), 5.34 (s, 1 H), 5.63 (t, $J = 7.2$ Hz, 1 H), 7.44 (s, 1 H); ^{13}C NMR (CD_3OD) δ 12.4, 33.4, 51.5, 63.1, 67.9, 111.8, 112.1, 140.3, 149.2, 153.2, 166.5. Anal. Calcd for $\text{C}_{11}\text{H}_{14}\text{N}_2\text{O}_3\text{S}$: C, 51.95; H, 5.55; N, 11.02; O, 18.87; S, 12.61. Found: C, 51.91; H, 5.56; N, 11.05.

(3*R*,5*R*)-1-(5-hydroxymethyl-4-methylene-tetrahydrothiophen-3-yl)-1*H*-

pyrimidine-2,4-dione (24). The thiosugar **15** (65 mg, 0.17 mmol) was converted to compound **24** using the similar procedure used in the preparation of **23**.

Desilylated N-isomer: 22.1 mg; 29%; UV (CDCl_3) λ_{\max} 255 nm (pH 7); ^1H NMR (CDCl_3) δ 3.09 (m, 2 H), 3.87 (m, 2 H), 3.95 (m, 1 H), 5.11 (s, 1 H), 5.37 (s, 1 H), 5.65 (m, 1 H), 5.82 (d, $J = 8.8$ Hz, 1 H), 7.52 (m, 2 H), 7.65 (m, 1 H), 7.93 (m, 2 H).

Desilylated O-isomer (debenzoylated form): 8.8 mg; 12%; UV (CDCl_3) λ_{\max} 265 nm

(pH 7); ^1H NMR (CDCl_3) δ 3.01 (dd, $J = 4.4, 11.6$ Hz, 1 H), 3.30 (dd, $J = 5.6, 11.6$ Hz, 1 H), 3.74 (dd, $J = 7.2, 11.2$ Hz, 1 H), 3.82 (dd, $J = 6.0, 11.2$ Hz, 1 H), 3.98 (t, $J = 7.2$ Hz, 1 H), 5.32 (s, 1 H), 5.46 (s, 1 H), 5.95 (t, $J = 5.6$ Hz, 1 H), 6.14 (d, $J = 6.8$ Hz, 1 H), 7.74 (d, $J = 6.8$ Hz, 1 H).

Compound 24: 86%; MS (FAB) m/z 241 (MH^+); UV (MeOH) λ_{max} 264.5 (pH 7); $[\alpha]_{\text{D}}^{25} +42.11^\circ$ (c 0.19, MeOH); ^1H NMR (CD_3OD) δ 3.07 (dd, $J = 7.6, 9.6$ Hz, 2 H), 3.82 (dd, $J = 1.2, 6.0$ Hz, 2 H), 3.93 (m, 1 H), 4.99 (t, $J = 1.8$ Hz, 1 H), 5.35 (t, $J = 2.0$ Hz, 1 H), 5.64 (t, $J = 7.6$ Hz, 1 H), 5.69 (d, $J = 8.4$ Hz, 1 H), 7.61 (d, $J = 8.4$ Hz, 1 H); ^{13}C NMR (CD_3OD) δ 33.6, 51.6, 63.3, 67.9, 103.2, 112.1, 144.8, 149.2, 159.5, 166.0. Anal. Calcd. for $\text{C}_{10}\text{H}_{12}\text{N}_2\text{O}_3\text{S}$: C, 49.99; H, 5.03; N, 11.66; O, 19.98; S, 13.35. Found: C, 49.95; H, 5.05; N, 11.63.

(3*R*,5*R*)-4-Amino-1-(5-hydroxymethyl-4-methylene-tetrahydrothiophen-3-yl)-1*H*-pyrimidin-2-one (25). A solution of **24** (36 mg, 0.15 mmol) in anhydrous pyridine (6 mL) was treated with acetic anhydride (0.15 mL, 1.59 mmol) and the mixture was stirred at ambient temperature for 5 h. The residue was evaporated and diluted with ethyl acetate. The organic layer was washed with dilute HCl, saturated NaHCO_3 solution and brine dried with MgSO_4 , filtered and evaporated. The residue was used in the next step without further purification. A solution of residue (50 mg), 1,2,4-triazole (0.237 g, 3.42 mmol) and phosphorus oxychloride (0.27 mL, 2.91 mmol) in acetonitrile (9 mL) was treated with triethylamine (0.39 mL, 2.79 mmol). The mixture was stirred at ambient temperature for 15 h. Additional triethylamine (0.3 mL) and water were added, and the reaction mixture was stirred at ambient temperature for 10 min. After the addition of methylene chloride (50 mL), the mixture was washed with saturated NaHCO_3 solution and brine, dried, filtered and evaporated. The residue was used in the

next step without further purification. The above residue was dissolved in 1,4-dioxane (5 mL) and ammonium hydroxide (28%, 1.5 mL) was added and the mixture was stirred at ambient temperature for 15 h. After removal of all the volatiles, the residue was dissolved in methanolic ammonia (3 mL) and stirred overnight at ambient temperature. The reaction mixture was evaporated and the residue was purified by flash chromatography (methylene chloride/methanol = 5:1) to obtain **25** (15 mg, 42%) and the unconverted uracil analogue **24** (12 mg, 34%) was recovered.

MS (FAB) m/z 240 (MH^+); UV (MeOH) λ_{max} 275 nm (pH 7); $[\alpha]_D^{25} +40^\circ$ (c 0.1, MeOH); 1H NMR (CD_3OD) δ 2.98 (dd, $J = 4.4, 9.6$ Hz, 2 H), 3.73 (d, $J = 5.2$ Hz, 2 H), 3.84 (t, $J = 5.2$ Hz, 1 H), 4.79 (t, $J = 2.2$ Hz, 1 H), 5.21 (t, $J = 2.4$ Hz, 1 H), 5.61 (t, $J = 9.6$ Hz, 1 H), 5.79 (d, $J = 7.6$ Hz, 1 H), 7.51 (d, $J = 7.6$ Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 34.1, 51.9, 64.4, 67.9, 96.6, 111.6, 145.2, 149.9, 159.1, 167.6. Anal. Calcd. for $C_{10}H_{13}N_3O_2S$: C, 50.19; H, 5.48; N, 17.56; O, 13.37; S, 13.40. Found: C, 50.18; H, 5.44; N, 17.54.

(3S,5R)-9-[5-(tert-Butyldiphenylsilyloxy)methyl-4-methylene-tetrahydrothiophen-3-yl]-6-chloro-9H-purine (26). The glycosyl donor **14** (132 mg, 0.13 mmol) was converted to **26** (98 mg, 55%, EtOAc/hexane = 1:3) as a colourless viscous liquid, employing the same conditions used in the synthesis of compound **18**: UV ($CDCl_3$) λ_{max} 266 nm (pH 7); 1H NMR ($CDCl_3$) δ 1.09 (s, 9 H), 3.21 (dd, $J = 6.4, 12.0$ Hz, 1 H), 3.38 (dd, $J = 6.8, 12.0$ Hz, 1 H), 3.85 (m, 2 H), 4.17 (m, 1 H), 4.93 (s, 1 H), 5.34 (s, 1 H), 5.85 (td, $J = 1.2, 6.4$ Hz, 1 H), 7.41 (m, 6 H), 7.69 (m, 4 H), 8.25 (s, 1 H), 8.76 (s, 1 H); ^{13}C NMR (CD_3OD) δ 19.5, 27.0, 35.5, 51.2, 60.6, 68.2, 113.9, 127.9, 127.9, 129.9, 130.1, 133.1, 133.2, 133.3, 135.7, 135.8, 144.2, 147.4, 151.4, 151.8, 152.2. Anal. Calcd for $C_{27}H_{29}ClN_4OSSi$: C, 62.23; H, 5.61; Cl, 6.80; N, 10.75; O, 3.07; S, 6.15; Si,

5.39. Found: C, 62.03; H, 5.58; N, 10.99.

(2R,4S)-[4-(6-Chloropurin-9-yl)-3-methylene-tetrahydrothiophen-2-yl]methanol

(27). Compound **26** (450 mg, 0.85 mmol) was converted to **27** (141 mg, 50%, hexane/EtOAc = 1:1), using the procedure utilized in the preparation of **19**.

MS (FAB) m/z 283 (MH^+); UV (MeOH) λ_{max} 265 nm (pH 7); $[\alpha]_D^{25}$ -160.87 (c 0.23, MeOH); 1H NMR (CD_3OD) δ 3.41 (dd, $J = 2.8, 6.8$ Hz, 2 H), 3.73 (dd, $J = 6.8, 10.8$ Hz, 1 H), 3.82 (dd, $J = 6.0, 10.8$ Hz, 1 H), 4.21 (td, $J = 6.8, 1.2$ Hz, 1 H), 4.91 (t, $J = 1.6$ Hz, 1 H), 5.37 (t, $J = 1.6$ Hz, 1 H), 5.94 (td, $J = 6.8, 1.6$ Hz, 1 H), 8.66 (s, 1 H), 8.75 (s, 1 H); ^{13}C NMR (CD_3OD) δ 35.1, 52.5, 62.5, 67.6, 113.8, 132.4, 147.4, 149.2, 151.6, 153.1, 153.2. Anal. Calcd for $C_{11}H_{11}ClN_4OS$: C, 46.73; H, 3.92; Cl, 12.54; N, 19.82; O, 5.66; S, 11.34 Found: C, 46.50; H, 3.89; N, 19.42.

(2R,4S)-[4-(6-Aminopurin-9-yl)-3-methylene-tetrahydrothiophen-2-yl]methanol

(28). Compound **27** (39 mg, 0.14 mmol) was converted to **28** (28 mg, 78%, dichloromethane/methanol = 6:1), following the procedure utilized in the preparation of **20**.

MS (FAB) m/z 264 (MH^+); UV (MeOH) λ_{max} 260 nm (pH 7); $[\alpha]_D^{25}$ -147.1° (c 0.17, MeOH); 1H NMR (CD_3OD) δ 3.32 (dd, $J = 3.6, 7.2$ Hz, 2 H), 3.66 (dd, $J = 6.8, 11.2$ Hz, 1 H), 3.78 (dd, $J = 6.4, 11.2$ Hz, 1 H), 4.15 (td, $J = 1.6, 6.8$ Hz, 1 H), 4.77 (t, $J = 1.6$ Hz, 1 H), 5.30 (t, $J = 2.0$ Hz, 1 H), 5.74 (td, $J = 1.6, 7.2$ Hz, 1 H), 8.18 (s, 1 H), 8.19 (s, 1 H); ^{13}C NMR (CD_3OD) δ 35.1, 52.4, 61.5, 67.8, 113.0, 120.1, 141.7, 149.5, 150.5, 153.9, 157.9. Anal. Calcd for $C_{11}H_{13}N_5OS$: C, 50.17; H, 4.98; N, 26.60; O, 6.08; S, 12.18 Found: C, 50.23; H, 4.85; N, 26.57.

(2R,4S)-[4-(6-Methylaminopurin-9-yl)-3-methylene-tetrahydrothiophen-2-

yl]methanol (29). Compound **27** (44 mg, 0.156 mmol) was converted to **29** (32 mg,

74%, dichloromethane/methanol = 10:1), following the procedure utilized in the preparation of **21**.

MS (FAB) m/z 278 (MH^+); UV (MeOH) λ_{max} 266.5 nm (pH 7); $[\alpha]_D^{25}$ -147.6° (c 0.21, MeOH); 1H NMR (CD_3OD) δ 3.12 (br s, 3 H), 3.34 (dd, $J = 4.8, 7.6$ Hz, 2 H), 3.69 (dd, $J = 6.8, 11.2$ Hz, 1 H), 3.79 (dd, $J = 5.6, 11.2$ Hz, 1 H), 4.16 (td, $J = 1.6, 6.8$ Hz, 1 H), 4.77 (t, $J = 1.8$ Hz, 1 H), 5.32 (t, $J = 1.8$ Hz, 1 H), 5.75 (td, $J = 1.6, 7.6$ Hz, 1 H), 8.15 (s, 1 H), 8.26 (s, 1 H); ^{13}C NMR (CD_3OD) δ 35.1, 48.7, 52.4, 61.4, 67.8, 112.9, 120.2, 141.0, 149.5, 150.5, 153.9, 157.1. Anal. Calcd for $C_{12}H_{15}N_5OS$: C, 51.97; H, 5.45; N, 25.25; O, 5.77; S, 11.56 Found: C, 51.85; H, 5.85; N, 25.64.

(3S,5R)-9-(5-Hydroxymethyl-4-methylene-tetrahydrothiophen-3-yl)-9H-purin-6-ol

(30). Compound **27** (34 mg, 0.12 mmol) was converted to **30** (25.5 mg, 82%, dichloromethane/methanol = 5:1), following the procedure utilized in the preparation of **22**.

MS (FAB) m/z 265 (MH^+); UV (MeOH) λ_{max} 249.5 nm (pH 7); $[\alpha]_D^{25}$ -120.3° (c 0.133, MeOH); 1H NMR (CD_3OD) δ 3.33 (dd, $J = 2.0, 7.2$ Hz, 2 H), 3.65 (dd, $J = 7.2, 11.2$ Hz, 1 H), 3.75 (dd, $J = 5.6, 11.2$ Hz, 1 H), 4.13 (td, $J = 2.0, 7.2$ Hz, 1 H), 4.79 (s, 1 H), 5.29 (s, 1 H), 5.74 (td, $J = 1.6, 7.2$ Hz, 1 H), 8.00 (s, 1 H), 8.12 (s, 1 H); ^{13}C NMR (CD_3OD) δ 35.2, 52.5, 61.9, 67.7, 113.1, 125.4, 141.0, 146.8, 149.6, 150.3, 159.2. Anal. Calcd for $C_{11}H_{12}N_4O_2S$: C, 49.99; H, 4.58; N, 21.20; O, 12.11; S, 12.13. Found: C, 49.93; H, 4.56; N, 21.22.

(3S,5R)-1-(5-Hydroxymethyl-4-methylene-tetrahydrothiophen-3-yl)-5-methyl-1H-

pyrimidine-2,4-dione (31). The thiosugar **14** (211 mg, 0.55 mmol) was converted to compound **31** using the same procedure used in the synthesis of **23**. The mixture of *N,O*-isomers (330 mg, 0.55 mmol) was converted to the desilylated *N*-isomer

(hexane/EtOAc = 1:2, 63 mg, 42%) and to the corresponding *O*-isomer (debenzoyleated form, 28 mg, 14%), following the procedure utilized in the preparation of **25**.

Desilylated *N*-isomer: 63 mg; 42%; UV (MeOH) λ_{\max} 253 nm (pH 7); ^1H NMR (CDCl_3) δ 1.97 (s, 3 H), 2.92 (dd, $J = 6.4, 12.0$ Hz, 1 H), 3.33 (dd, $J = 7.2, 12.0$ Hz, 1 H), 3.69 (m, 2 H), 4.09 (td, $J = 1.2, 7.2$ Hz, 1 H), 5.15 (s, 1 H), 5.45 (s, 1 H), 5.76 (m, 1 H), 7.21 (s, 1 H), 7.50 (s, 2 H), 7.66 (m, 1 H), 7.92 (m, 2 H); ^{13}C NMR (CD_3OD) δ 12.9, 34.4, 52.6, 59.9, 66.3, 111.7, 113.9, 129.4, 130.6, 131.7, 135.3, 137.5, 147.0, 150.2, 162.3, 162.7, 168.9.

Desilylated *O*-isomer (debenzoyleated form): 28 mg; 14%; UV (MeOH) λ_{\max} 269.5 nm (pH 7); ^1H NMR (CDCl_3) δ 1.99 (s, 3 H), 2.88 (dd, $J = 5.8, 11.6$ Hz, 1 H), 3.32 (dd, $J = 6.0, 11.6$ Hz, 1 H), 3.72 (m, 1 H), 4.07 (td, $J = 1.2, 5.6$ Hz, 1 H), 5.26 (s, 1 H), 5.41 (s, 1 H), 5.91 (t, $J = 5.8$ Hz, 1 H), 7.55 (s, 1 H).

Compound 31: 71%; MS (FAB) m/z 255 (MH^+); UV (MeOH) λ_{\max} 269.5 nm (pH 7); $[\alpha]_{\text{D}}^{25} -152.63$ (c 0.19, MeOH); ^1H NMR (CD_3OD) δ 1.87 (s, 3 H), 3.01 (dd, $J = 8.4, 11.6$ Hz, 1 H), 3.18 (dd, $J = 7.4, 11.6$ Hz, 1 H), 3.62 (dd, $J = 6.8, 11.2$ Hz, 1 H), 3.73 (dd, $J = 6.0, 11.2$ Hz, 1 H), 4.07 (t, $J = 6.8$ Hz, 1 H), 4.93 (s, 1 H), 5.34 (s, 1 H), 5.67 (t, $J = 8.4$ Hz, 1 H), 7.38 (s, 1 H); ^{13}C NMR (CD_3OD) δ 12.5, 33.9, 52.8, 61.5, 67.8, 112.0, 112.5, 140.0, 149.0, 153.0, 163.0. Anal. Calcd for $\text{C}_{11}\text{H}_{14}\text{N}_2\text{O}_3\text{S}$: C, 51.95; H, 5.55; N, 11.02; O, 18.87; S, 12.61. Found: C, 51.81; H, 5.52; N, 11.41.

(3*S*,5*R*)-1-(5-Hydroxymethyl-4-methylene-tetrahydrothiophen-3-yl)-1*H*-

pyrimidine-2,4-dione (32). The thiosugar **14** (395 mg, 1.03 mmol) was converted to compound **32** using the same procedure used in the synthesis of **24**.

Desilylated *N*-isomer: 162 mg; 46%; UV (MeOH) λ_{\max} 254 nm (pH 7); ^1H NMR (CDCl_3) δ 2.91 (dd, $J = 5.6, 12.0$ Hz, 1 H), 3.33 (dd, $J = 7.2, 12.0$ Hz, 1 H), 3.69 (m, 2

H), 4.08 (t, $J = 6.4$ Hz, 1 H), 5.21 (s, 1 H), 5.48 (s, 1 H), 5.74 (t, $J = 7.2$ Hz, 1 H), 5.86 (d, $J = 8.4$ Hz, 1 H), 7.42 (d, $J = 8.4$ Hz, 1 H), 7.52 (t, $J = 7.6$ Hz, 2 H), 7.67 (t, $J = 7.6$ Hz, 1 H), 7.93 (m, 2 H).

Desilylated *O*-isomer: 22 mg; 6%; UV (MeOH) λ_{\max} 262.5 nm (pH 7); ^1H NMR (CDCl_3) δ 2.92 (dd, $J = 6.4, 11.2$ Hz, 1 H), 3.33 (dd, $J = 5.6, 11.2$ Hz, 1 H), 3.74 (m, 2 H), 4.09 (td, $J = 1.6, 5.2$ Hz, 1 H), 5.29 (s, 1 H), 5.42 (s, 1 H), 5.97 (td, $J = 1.2, 6.4$ Hz, 1 H), 6.15 (d, 1 H, 5-CH, $J = 6.4$ Hz), 7.44 (m, 2 H, Ph), 7.58 (m, 1 H, Ph), 7.55 (d, $J = 6.4$ Hz, 1 H), 8.09 (d, $J = 7.6$ Hz, 2 H).

Compound 32: 90%; MS (FAB) m/z 241 (MH^+); UV (MeOH) λ_{\max} 265.5 nm (pH 7); $[\alpha]_{\text{D}}^{25} -196.15^\circ$ (c 0.26, MeOH); ^1H NMR (CD_3OD) δ 2.96 (dd, $J = 7.6, 11.6$ Hz, 1 H), 3.02 (dd, $J = 7.2, 11.6$ Hz, 1 H), 3.61 (dd, $J = 6.0, 11.2$ Hz, 1 H), 3.71 (dd, $J = 6.0, 11.2$ Hz, 1 H), 4.03 (td, $J = 1.6, 6.0$ Hz, 1 H), 4.98 (t, $J = 1.8$ Hz, 1 H), 5.35 (t, $J = 2.0$ Hz, 1 H), 5.63 (m, 1 H), 5.67 (d, $J = 8.4$ Hz, 1 H), 7.54 (d, $J = 8.4$ Hz, 1 H); ^{13}C NMR (CD_3OD) δ 34.4, 52.9, 61.9, 67.7, 103.1, 113.0, 144.5, 149.2, 152.9, 166.3. Anal. Calcd for $\text{C}_{10}\text{H}_{12}\text{N}_2\text{O}_3\text{S}$: C, 49.99; H, 5.03; N, 11.66; O, 19.98; S, 13.35. Found: C, 49.95; H, 5.06; N, 11.63.

(3*S*,5*R*)-4-Amino-1-(5-hydroxymethyl-4-methylene-tetrahydrothiophen-3-yl)-1*H*-pyrimidin-2-one (33). Compound **32** (60 mg, 0.5 mmol) was converted to **33** (dichloromethane/methanol = 5:1, 15.5 mg, 26%) with recovered **32** (26 mg, 43%), following the procedure reported for the preparation of compound **25**.

MS (FAB) m/z 240 (MH^+); UV (MeOH) λ_{\max} 275.5 nm (pH 7); $[\alpha]_{\text{D}}^{25} -180.55^\circ$ (c 0.36, MeOH); ^1H NMR (CD_3OD) δ 2.95 (dd, $J = 7.6, 11.6$ Hz, 1 H), 3.22 (dd, $J = 7.2, 11.6$ Hz, 1 H), 3.62 (dd, $J = 6.8, 10.8$ Hz, 1 H), 3.73 (dd, $J = 6.4, 10.8$ Hz, 1 H), 4.06 (td, $J = 1.2, 6.8$ Hz, 1 H), 4.92 (t, $J = 1.8$ Hz, 1 H), 5.35 (t, $J = 1.8$ Hz, 1 H), 5.76 (td, $J = 2.0,$

7.2 Hz, 1 H), 5.89 (d, $J = 7.6$ Hz, 1 H), 7.56 (d, $J = 7.6$ Hz, 1 H); ^{13}C NMR (CD_3OD) δ 34.9, 53.1, 62.9, 67.7, 96.5, 111.6, 144.0, 149.8, 159.0, 167.6. Anal. Calcd for $\text{C}_{10}\text{H}_{13}\text{N}_3\text{O}_2\text{S}$: C, 50.19; H, 5.48; N, 17.56; O, 13.37; S, 13.40 Found: C, 50.58; H, 5.15; N, 17.04.