Supplementary Information

General Information:

Chemicals used were of ACS grade and purchased from Sigma-Aldrich, Fisher, Acros, Oakwood, and Chem-Impex. Pyridine, DMF, acetonitrile, and THF were HPLC grade and further purified in a solvent system containing drying columns. 1,4-dioxane was purchased in a sure-seal bottle and the dry MeOH was distilled over magnesium and iodine.

Experimental:

Compound **3**: Uridine (10.0 g, 40.5 mmol) and DMAP (100 mg, 0.819 mmol) were dissolved in 250 mL of pyridine and acetic anhydride (13.2 mL, 139.2 mmol) was added. The reaction was stirred for 4 hrs at 25° C before being quenched with water. The solvent was removed be rotary evaporation and coevaporated twice with toluene. The crude compound was purified by flash chromatography (ethyl acetate) to yield **3** as a white solid (14.1 g, 38.07 mmol, 94%). ^{1}H NMR (500 MHz, (CD$_3$)$_2$CO) δ 2.054 (s, 3H), 2.087 (s, 3H), 2.091 (s, 3H), 4.352 (m, 3H), 5.427 (dd, *J*=6.0, 4.5 Hz, 1H), 5.507 (t, *J*=5.5 Hz, 1H), 5.709 (d, *J*=8.0 Hz, 1H), 6.021 (d, *J*=5.0 Hz, 1H), 7.700 (d, *J*=8.5 Hz, 1H), 10.390 (s, 1H). ^{13}C NMR (125 MHz, (CD$_3$)$_2$CO), δ 20.87, 20.97, 20.18, 64.46, 71.61, 73.93, 81.23, 89.53, 103.96, 141.95, 151.77, 163.87, 170.60, 170.62, 171.17. HRMS (DART) Calcd for $C_{15}H_{18}N_2O_9$ 371.10905; Found, 371.10835

Compound **4**: **3** (920 mg, 2.10 mmol), ceric ammonium nitrate (2.30 g, 4.20 mmol) and LiCl (110 mg, 2.52 mmol) were dissolved in 40 mL of acetic acid and 40 mL of acetonitrile. The reaction was heated to 80° C for 8 hrs before being cooled to ambient temperature and quenched with water. The solvents were removed under vacuum and coevaporated several times with ethanol. The crude product was dissolved in ethyl acetate and washed with water, saturated $NaHCO_3$ and brine. The solvent was removed under vacuum and the compound was purified by column chromatography (3:1 ethyl acetate to hexanes) to yield **4,** as a white foam (815 mg, 1,73 mmol, 82%). ^1H NMR (500 MHz, $(CD_3)_2CO$) δ 2.06 (s, 3H), 2.09 (2, 3H), 2.13 (s, 3H), 4.40 (m, 3H), 5.44, (dd, *J*=6.0, 5.0 Hz, 1H), 5.53 (dd, *J*=6.5, 5.5 Hz, 1H), 6.05 (d, *J*=5.0 Hz, 1H), 8.02 (s, 1H), 10.64 (s, 1H). ^{13}C NMR (125 MHz, $(CD_3)_2CO$), δ 20.81, 20.91, 21.26, 64.18, 71.22, 74.22, 81.45, 89.54, 110.06, 138.71, 150.83, 159.73, 170.50, 170.51, 171.05. HRMS (DART) Calcd for $C_{15}H_{18}ClN_2O_9$ 405.07008; Found, 405.07108.

Compound **5**: Compound **4** (3.38 g, 8.34 mmol) was dissolved in 150 mL of 7N NH_3 in MeOH and stirred for 5 hrs. The solvent was removed by rotary evaporation and the crude compound was dried on vacuum. The material was dissolved in 200 mL of dry acetone and 200 μL of H_2SO_4 was added dropwise. The reaction was stirred for 7 hrs before being slowly quenched with saturated $NaHCO_3$. The acetone was removed by rotary evaporation and the compound was extracted from the aqueous layer with ethyl acetate. The organic layer was washed with brine and the solvent was removed by rotary evaporation. The crude material was purified by flash chromatography (4:1 ethyl acetate to hexanes) to yield 5 as a white solid (2.10 g, 6.59 mmol, 79%). ^1H NMR (400 MHz, $(CD_3)_2CO$) δ 1.33 (s, 3H), 1.52 (s, 3H), 3.83 (m, 2H), 4.25 (q, *J*=3.2 Hz, 1H), 4.94 (dq, *J*=6.4, 4.0 Hz, 1H) 5.97 (d, *J*=2.8 Hz, 1H), 8.26 (s, 1H), 10.51 (s, 1H). ^{13}C NMR (100 MHz, $(CD_3)_2CO$), δ 26.05, 28.07, 63.21, 81.98, 86.10, 88.44, 93.44, 109.44, 114.80, 140.02. HRMS (DART) Calcd for $C_{12}H_{16}ClN_2O_6$ 319.06969; Found, 319.06913.

Compound **6**: **5** (994 mg, 3.12 mmol) was dissolved in 20 mL of DMF and a solution of Methyltriphenoxyphosphonium iodide (2.12 g, 4.68 mmol) in 30 mL of DMF was added. The reaction was stirred for 30 mins before being quenched with saturated $Na_2S_2O_3$. The solvent was removed by rotary evaporation and the crude material was dissolved in ethyl acetate and washed with saturated $Na_2S_2O_3$ and water. The ethyl acetate was evaporated and the product recrystallized from chloroform and hexanes to yield **6** as a white solid (1.16 g, 2.71 mmol, 87%). ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 1.33 (s, 3H), 1.51 (s, 3H), 4.45 (dd, *J*=10.0, 6.0 Hz, 1H), 3.58 (dd, *J*=10.0, 7.2 Hz, 1H), 4.23 (dq, *J*=6.0, 4.0 Hz, 1H), 4.83 (dd, *J*=6.4, 3.6 Hz, 1H), 5.20 (dd, *J*=6.4, 2.0 Hz, 1H), 5.84 (d, *J*=2.0 Hz, 1H), 8.05 (s, 1H), 10.61 (s, 1H). ^{13}C NMR (100 MHz, $(CD_3)_2CO$), δ 6.55, 25.96, 27.84, 85.40, 85.91, 88.56, 95.75, 109.78, 115.34, 141.45. HRMS (DART) Calcd for $C_{12}H_{15}ClIN_2O_5$ 428.97142; Found, 428.97090.

Compound **7**: **6** (1.01 g, 2.36 mmol) was dissolved in 50 mL of THF and brought to a reflux. A solution of Bu_3SnH (0.720 mL, 2.71 mmol) and AIBN (12.0 mg, 73.1 μmol) in 10 mL of THF was added via syringe pump over two hours. The reaction was continued for another two hours at reflux before being cooled to ambient temperature and the solvent removed by rotary evaporation. The crude material was dissolved in MeOH and washed three times with hexanes. The MeOH was evaporated and the material was dried under vacuum. The intermediate was then dissolved in 40 mL of dry MeOH and NaOMe (0.92mL of 25 wt% in MeOH, 11.8 mmol) was added. The mixture was heated to reflux for three hours. The reaction was cooled to ambient temperature and the excess NaOMe was neutralized with 0.1 M HCl. The solvent was removed and the crude material was dry packed onto silica gel (4.00 g) and purified by column chromatography (95:5 DCM to MeOH) to yield **7** as a white solid (452 mg, 1.70 mmol, 72%). ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 1.30 (s, 3H), 1.43 (s, 3H), 2.76 (d, *J*=15.2 Hz, 1H), 3.19 (ddd, *J*=18.8, 6.8, 2.0 Hz, 1H), 4.59 (d, *J*=6.8 Hz, 1H), 4.81 (d, *J*=2.4 Hz, 2H), 5.41 (t, *J*=1.6 Hz, 1H), 6.01 (s, 1H), 9.98 (s, 1H). ^{13}C NMR (100 MHz, $(CD_3)_2CO$), δ 25.55, 26.83, 80.82, 81.60, 84.04, 86.03, 86.87, 102.05, 114.19, 150.12. HRMS (DART) Calcd for $C_{12}H_{15}N_2O_5$ 267.09810; Found, 267.09842.

<u>Compound **8**</u>: The acetonide protected cyclized product **7** (165 mg, 0.619 mmol) and selenium dioxide (206 mg, 1.86 mmol) were dissolved in 1,4-dioxane (15 mL). The reaction mixture was heated to 85^o C for 24 hours. The solvent was removed by rotary evaporation and the crude material was dry packed on silica gel before being purified by column chromatography (95:5 DCM to MeOH) to yield **8** as a white solid (122 mg, 0.436 mmol, 70%). ^{1}H NMR (500 MHz, $(CD_3)_2CO$) δ 1.34 (s, 3H), 1.49 (s, 3H), 4.86 (s, 1H), 5.08 (m, 2H), 6.17 (s, 1H), 6.18 (s, 1H), 10.47 (s, 1H). ^{13}C NMR (125 MHz, $(CD_3)_2CO$), δ 25.61, 26.77, 81.85, 85.02, 88.76, 88.84, 104.29, 115.82, 142.93,

150.20, 163.32, 186.59. HRMS (DART) Calcd for $C_{12}H_{13}N_2O_6$ 281.07736; Found, 281.07694.

Compound **9**: Compound **8** (400 mg, 1.429 mmol) was dissolved THF (12 mL) and $NaBH_4$ (65.0 mg, 1.714 mmol) was slowly added. The reaction was stirred for 2 hrs and the solvent was removed by rotary evaporation. The crude material was dry packed on silica gel (1.2 g) and purified by column chromatography (95:5 DCM to isopropanol) to yield **9** as a white solid (306 mg, 1.09 mmol, 76%) ^{1}H NMR (500 MHz, Pyridine-D5), δ 1.38 (s, 3H), 1.58 (s, 3H), 4.91 (d, *J*=6.5 Hz, 1H), 4.94 (d, *J*=6.0 Hz), 5.18 (d, *J*=6.0 Hz, 1H), 5.45 (d, *J*=5.5 Hz, 1H), 6.37 (s, 1H), 6.60 (s, 1H), 13.44 (s, 1H). ^{13}C NMR (125 MHz, Pyridine-D5), δ 25.31, 26.58, 63.31, 78.91, 84.58, 85.17, 87.17, 101.90, 113.79, 151.09, 154.91, 164.42. HRMS (DART) Calcd for $C_{12}H_{15}N_2O_6$ 283.09301; Found, 283.09301.

Compound **10:** The acetonide protected **7** (250 mg, 0.938 mmol) was dissolved in a 50/50 mixture of water and trifluoroacetic acid (7 mL each) and stirred at ambient temperature for 10 hours. The solvent was removed by rotary evaporation and coevaporated three times with ethanol. The crude deprotected product was coevaporated with pyridine twice before being dissolved in pyridine with DMAP (12.0 mg, 93.8 μmol). Acetic anhydride (354 μL, 3.75 mmol) was added dropwise and the mixture was stirred for 6 hours. The reaction was quenched with water and the solvent was removed by rotary evaporation and coevaporated twice with toluene. The crude product was dry packed onto silica gel (1.25 g) and purified by flash chromatography (95:5 DCM to isopropanol) to yield **10** as a white solid (239 mg, 0.796 mmol, 82%) ^{1}H NMR (500 MHz, Pyridine-D5) δ 2.03 (s, 3H), 2.06 (s, 3H), 2.92 (d, *J*=18.5 Hz, 1H), 3.28 (ddd, *J*=18.5, 6.5, 2.0 Hz, 1H), 4.88 (d, *J*=7.0 Hz, 1H), 5.65 (d, *J*=6.0 Hz, 1H), 5.67 (s, 1H), 5.98 (d, *J*=6.0 Hz, 1H), 6.72 (s, 1H), 13.42 (s, 1H). ^{13}C NMR (125 MHz, Pyridine-D5), δ 20.60, 20.68, 30.84, 75.75, 77.21, 80.40, 86.78, 102.60, 148.31, 151.30, 163.89, 169.87, 170.47. HRMS (DART) Calcd for $C_{13}H_{15}N_2O_7$ 311.08793; Found, 311.08679.

Compounds **11*S*** and **11*R***: The diacetate protected **10** (965 mg, 3.11 mmol), selenium dioxide (345 mg, 3.11 mmol), and tertbuoxide (4.31 mL of a 70 wt% solution in H_2O, 31.10 mmol) was dissolved in 60 mL of 1,4-dioxane and heated to 90° C for 10 hours. The reaction mixture was cooled and 3.00 g of activated charcoal was added to absorb the stench. The mixture was filtered through Celite and the solvent was removed by rotary evaporation. The crude material dry packed onto silica gel (4.00 g) and was purified by flash chromatography (95:5 DCM to isopropanol) to yield each diastereomer as a white solid (**11*S***: 209 mg, 0.64 mmol, 21%; **11*R***: 629 mg, 1.93 mmol, 62%). Compound **11*S***: ^{1}H NMR (500 MHz, Pyridine-D5) δ 2.00 (s, 3H), 2.04 (s, 3H), 5.09 (d, *J*=6.5 Hz, 1H), 5.29 (dd, *J*=6.0, 1.5 Hz, 1H), 6.10 (d, *J*=6.0 Hz, 1H), 6.34 (d, *J*=6.3 Hz, 1H), 6.385 (s, 1H), 6.72 (s, 1H), 13.49 (s, 1H). ^{13}C NMR (125 MHz, Pyridine-D5), δ 20.66, 20.68, 64.32, 71.09, 76.55, 83.85, 87.78, 102.54, 151.04, 154.41, 164.43, 169.72, 169.99. HRMS (DART) Calcd for $C_{13}H_{15}N_2O_8$ 327.08284; Found, 327.08230. Compound **11*R***: ^{1}H NMR (500 MHz, Pyridine-D5) δ 2.05 (s, 3H), 2.09 (s, 3H), 5.01 (s, 1H), 5.16 (s, 1H), 5.71 (d, *J*=6.0 Hz, 1H), 6.01 (d, *J*=6.0 Hz, 1H), 6.28 (s, 1H), 6.77 (s, 1H), 13.52 (s, 1H). ^{13}C NMR (125 MHz, Pyridine-D5), δ 20.66, 20.69, 66.47, 72.82, 75.83, 87.01, 87.33, 105.08, 151.14, 152.18, 164.46, 169.96, 170.65. HRMS (DART) Calcd for $C_{13}H_{15}N_2O_8$ 327.08284; Found 327.08248.

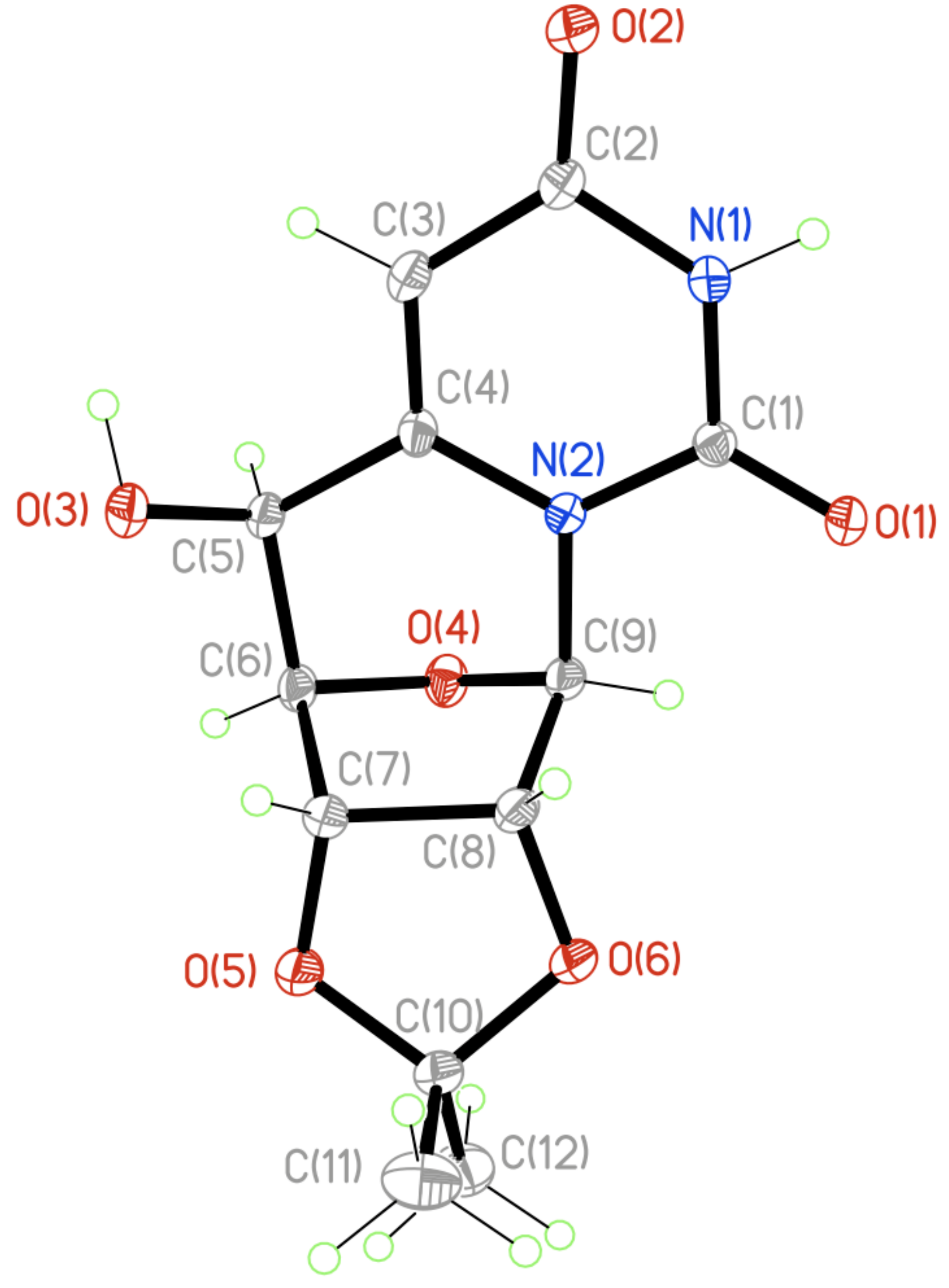
<u>Compounds **1*S*** and **1*R***</u>: Compound **1*S*** can be prepared from either **11*S*** or from compound **9.** If compound **9** is used as the starting material, it (142 mg, 0.504 mmol) is dissolved in a mixture of water and trifluoroacetic acid (8 mL each). The reaction is stirred at room temperature for 4 hrs before the solvent is removed by rotary evaporation. The material is coevaporated twice with water before being dry packed on silica gel (500 mg) and purified by column chromatography (94:6 ethyl acetate to ethanol) to yield **1*S*** as a white solid (107 mg, 0.442 mmol, 88%). If starting with **11*S***, it (32 mg, 0.098 mmol) is dissolved in 7N NH_3 in MeOH (10 mL) and stirred for 5 hrs. The solvent was removed by rotary evaporation and the crude material was dry packed on silica gel (100 mg) before being purified using column chromatography (94:6 ethyl acetate to ethanol) to yield **1*S*** as a white solid (21 mg, 0.085 mmol, 87%). ^{1}H NMR (500 MHz, Pyridine-D5) δ 4.74 (d, *J*=6.0 Hz, 1H), 4.99 (d, *J*=5.5 Hz, 1H), 5.23 (m, 2H), 6.42 (d, *J*=1.5 Hz, 1H), 6.69 (s, 1H). ^{13}C NMR (125 MHz, Pyridine-D5) δ 65.03, 69.76, 76.48, 87.18, 90.66, 101.58, 151.45, 155.89, 164.67. HRMS (DART) Calcd for $C_9H_{11}N_2O_6$ 243.06171; Found 243.06314.

1*R* was prepared from **11*R***. **11*R*** (62 mg, 0.19 mmol) was dissolved in 7N NH_3 in MeOH (13 mL) and stirred for 5 hrs. The solvent was removed by rotary evaporation and the crude material was dry packed on silica gel (250 mg) before being purified by column chromatography (94:6 ethyl acetate to ethanol) to yield **1*R***

as a white solid (40 mg, 0.16 mmol, 87%). ^{1}H NMR (500 MHz, Pyridine-D5) δ 4.66 (s, 2H), 4.79 (t, *J*=1.0 Hz, 1H), 5.11 (s, 1H), 6.24 (s, 1H), 6.71 (s, 1H). ^{13}C NMR (125 MHz, Pyridine-D5) δ 67.21, 71.80, 75.76, 90.16, 90.50, 104.65, 151.65, 153.43, 164.91. HRMS (DART) Calcd for $C_9H_{11}N_2O_6$ 243.06171; Found 243.06228.

Crystal Structures:

Crystal structures of compounds **9** and **11*R*** were obtained by the slow evaporation of a solution of the compounds in methanol. Ellipsoid plots are shown below. Cif files are also available in the supplementary information.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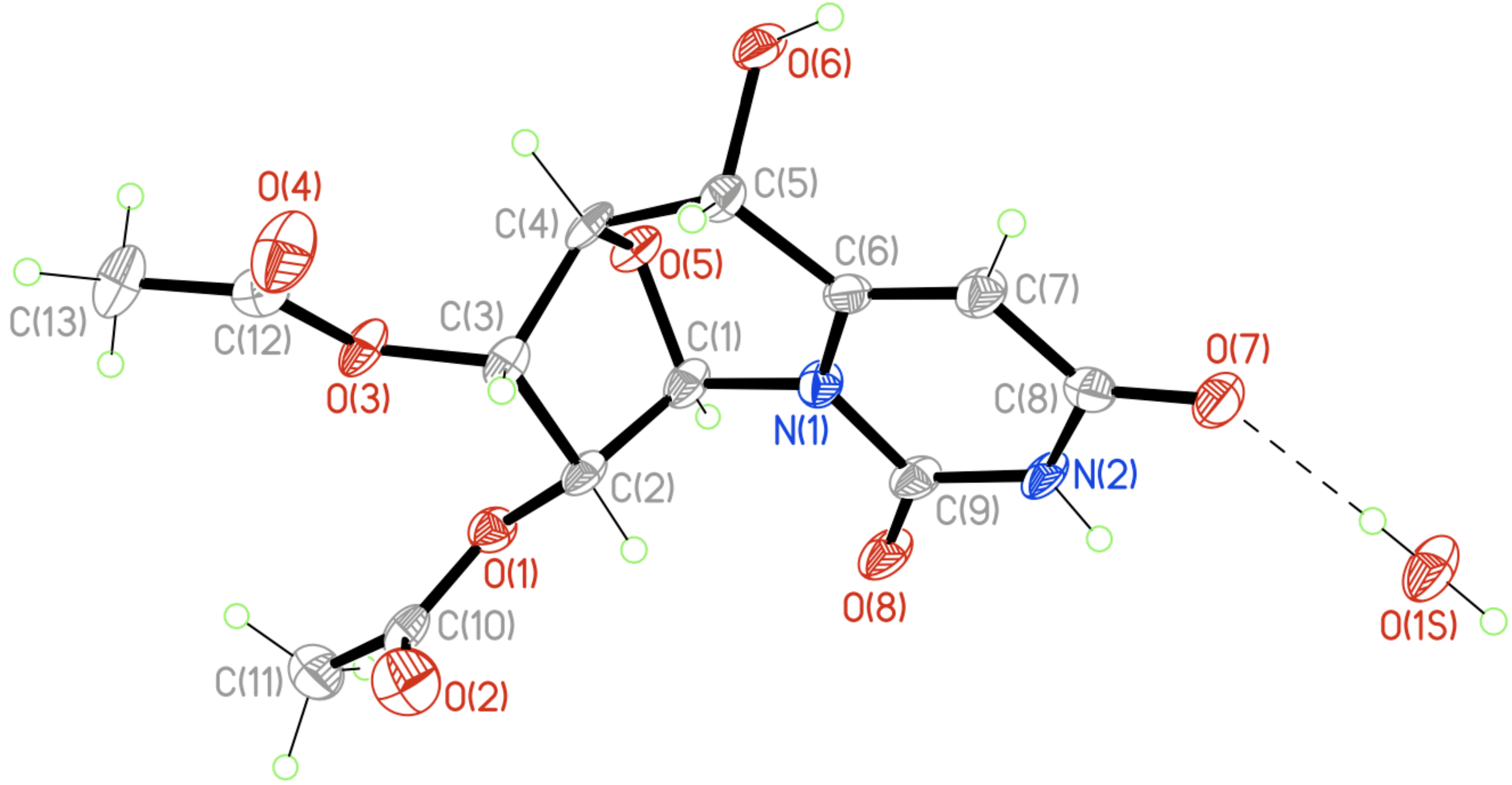
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