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Supporting Information

Synthesis of disaccharide nucleoside analogues as potential poly(ADP-ribose) polymerase-1 inhibitors

Meng Zheng, Martin Mex, Kathrin H. Götz and Andreas Marx*

Department of Chemistry and Konstanz Research School Chemical Biology, University of Konstanz, Universitätstraße 10, 78457 Konstanz, Germany

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Synthetic Procedures

General Information

All reagents and solvents were purchased from commercial vendors and used without further purification. Column chromatography was carried out using silica gel 60M (particle size 0.040 – 0.063 mm) as the stationary phase and TLC was performed on precoated silica gel plates (0.025 mm thick, 60 GF 254, Merck), observed under UV light and stained with cerium molybdate solution in water/ethanol. The disaccharide nucleoside analogues **1a-j** and **2a-j** were purified via medium pressure liquid chromatography (MPLC), which was performed on a *Büchi* Sepacore flash system X10, using RP-18 pre-packed columns (25-40 μm, 10 g, from *Götec*), and gradients of MQ/MeCN were used with flow rates of 10 mL/min. NMR spectra were recorded on Bruker Avance III 400 MHz and 600 MHz spectrometers, calibrated using residual non deuterated solvent as internal reference. HRMS spectra were measured on a Bruker Daltonics microTOF II mass spectrometer with electrospray ionization (ESI) as the ionization source. Glycosylation donor 1,2-di-*O*-acetyl-3,5-di-*O*-benzoyl-arabino-furanose (**3**) and acceptor 6-chloro-9-[3',5'-*O*-(1,1,3,3-tetra*iso*propyldisiloxane-1,3-diyl)-β-D-ribo-furanoside]-purine (**4**) were prepared based on previously published protocols[1, 2].

6-Chloropurine-9-β-D-[3',5'-*O*-(1,1,3,3-tetra*iso*propyl-disiloxane-1,3-diyl)-2'-*O*-α-D-(2''-*O*-acetyl-3'',5''-di-*O*-benzoyl-arabinofuranosyl)]ribofuranoside (5). Glycosylation donor **3** (4.11 g) was stirred with 1.5 mL of $SnCl_4$ in 50 mL of dry DCE at 0 °C under N_2 for 30 minutes. Then 3.11 g of acceptor **4** in 25 mL of dry DCE were added dropwise into the stirred solution over 15 minutes. The reaction solution was stirred at 4 °C for 20 hours. Saturated aqueous solution of $NaHCO_3$ (45 mL) was added to the reaction mixture and the suspension was stirred at 0 °C for 30 minutes. The mixture was diluted with 150 mL of DCM and 50 mL of water. Parts of the organic phase were separated. The rest of the mixture was filtered through Celite. Combined organic phases were washed with 100 mL of water, dried over Na_2SO_4 and evaporated to dryness. The crude product was applied to silica gel column chromatography using PE/EA (8:1→5:1→3:1), to give 3.93 g of white foam **5** as product; yield 76%. ^{1}H NMR (400 MHz, acetone-d_6) δ 8.69 (s, 1H, H-2), 8.61 (s, 1H, H-8), 8.11 – 8.06 (m, 4H, Bz), 7.70 – 7.63 (m, 2H, Bz), 7.55 – 7.51 (m, 4H, Bz), 6.33 (s, 1H, H-1'), 5.71 (s, 1H, H-1''), 5.50 (d, J = 5.4 Hz, 2H, H-2'', H-3''), 5.03 (d, J = 4.8 Hz, 1H, H-2'), 4.90

(dd, *J* = 9.3, 4.8 Hz, 1H, H-3'), 4.84 (q, *J* = 4.3 Hz, 1H, H-4''), 4.77 (dd, *J* = 11.9, 3.5 Hz, 1H, H-5''a), 4.66 (dd, *J* = 12.0, 4.7 Hz, 1H, H-5''b), 4.32 (d, *J* = 1.6 Hz, 1H, H-4'), 4.29 (d, *J* = 3.9 Hz, 1H, H-5'a), 4.11 – 4.07 (m, 1H, H-5'b), 2.13 (s, 3H, -CH_3), 1.11 – 0.87 (m, 28H, ^{i}Pr) ppm. ^{13}C NMR (101 MHz, acetone-d_6) δ 170.2 (Me**C**OO-), 166.4, 166.3 (Ph**C**O-), 152.5 (C-2), 151.9 (C-4), 150.9 (C-6), 145.1 (C-8), 134.5, 134.1 (Ph), 133.4 (C-5), 130.9, 130.6, 130.5, 130.4, 129.5, 129.4 (Ph), 105.6 (C-1''), 89.9 (C-1'), 82.7 (C-4'), 82.4 (C-4''), 82.1 (C-2''), 79.2 (C-3''), 79.0 (C-2'), 69.1 (C-3'), 64.3 (C-5''), 60.8 (C-5'), 20.8 (**C**H_3COO-), 17.9, 17.8, 17.7, 17.7, 17.6, 17.5, 17.4, 17.3 (($\mathbf{C}H_3$)$_2$CH-), 14.1, 13.7, 13.7, 13.3 ((CH_3)$_2$**C**H-) ppm. HRMS (ESI-TOF) m/z: $[M+H]^+$ Cal. for $C_{43}H_{56}ClN_4O_{12}Si_2^+$ 911.3116; found 911.3067.

6-Chloropurine-9-β-D-[3',5'-*O*-(1,1,3,3-tetra*iso*propyl-disiloxane-1,3-diyl)-2'-*O*-α-D-(3'',5''-di-*O*-benzoylarabino-furanosyl)]ribofuranoside (6). Disaccharide nucleoside **5** (1.81 g) was stirred with 1 mL of DIPEA in 100 mL of MeOH at 0 °C for 3 hours. The solvent was removed under reduced pressure. The crude product was applied to silica gel flash column chromatography using PE/EA (5:1→3:1), to give 1.29 g of **8** as a colourless foam; yield 74%. ^{1}H NMR (400 MHz, acetone-d_6) δ 8.72 (s, 1H, H-2), 8.61 (s, 1H, H8), 8.12 – 8.05 (m, 4H, Bz), 7.68 – 7.60 (m, 2H, Bz), 7.53 – 7.44 (m, 4H, Bz), 6.32 (s, 1H, H-1'), 5.64 (s, 1H, H-1''), 5.32 (d, *J* = 4.1 Hz, 1H, H-3''), 5.01 (d, *J* = 4.2 Hz, 1H, OH), 4.94 (d, *J* = 4.8 Hz, 1H, H-2'), 4.85 (dd, *J* = 9.5, 4.8 Hz, 1H, H-3'), 4.80 (dt, *J* = 5.7, 4.1 Hz, 1H, H-4''), 4.71 (dd, *J* = 11.7, 4.1 Hz, 1H, H-5''a), 4.63 – 4.58 (m, 2H, H-5''b, H-2''), 4.33 – 4.26 (m, 2H, H-4', H-5'a), 4.10 (dd, *J* = 13.6, 2.6 Hz, 1H, H-5'b), 1.13 – 0.89 (m, 28H, ^{i}Pr) ppm. ^{13}C NMR (101 MHz, acetone-d_6) δ 166.5 (Ph**C**O-), 152.5 (C-2), 151.9 (C-4), 150.9 (C-6), 144.8 (C-8), 134.3, 134.0 (Ph), 133.4 (C-5), 131.0, 130.8, 130.6, 130.4, 129.4, 129.3 (Ph), 108.3 (C-1''), 90.2 (C-1'), 82.7 (C-4'), 82.3 (C-4''), 81.8 (C-3''), 80.6 (C-2''), 79.4 (C-2'), 69.0 (C-3'), 65.1 (C-5''), 60.8 (C-5'), 17.9, 17.8, 17.7, 17.6, 17.5, 17.4, 17.3 (($\mathbf{C}H_3$)$_2$CH-), 14.1, 13.7, 13.4 ((CH_3)$_2$**C**H-) ppm. HRMS (ESI-TOF) m/z: $[M+H]^+$ Cal. for $C_{41}H_{54}ClN_4O_{11}Si_2^+$ 869.3011; found 869.2980.

6-Chloropurine-9-β-D-[3',5'-*O*-(1,1,3,3-tetra*iso*propyl-disiloxane-1,3-diyl)-2'-*O*-α-D-(3'',5''-di-*O*-benzoylribo-furanosyl)]ribofuranoside (7). To a stirred solution of protected disaccharide nucleoside **6** (1.56 g) in 15 mL of dry DMSO, 0.87 mL of acetic anhydride were added and the resulting solution was stirred under N_2 at r.t. for 20 hours. The reaction solution was diluted by addition of 30 mL EtOH. Subsequently, 340 mg of sodium borohydride were added and the reaction was stirred for another

1.5 hours at 0 °C. The reaction was quenched by addition of 3 mL acetone, diluted with 75 mL of brine and extracted with 120 mL of EA. The organic phase was washed twice with 60 mL of brine, dried over Na_2SO_4 and evaporated to dryness. The crude product was applied to silica gel column chromatography using PE/EA (5:1→3:1) to give 938 mg of **7** as a white foam; yield 60%. ^{1}H NMR (400 MHz, acetone-d_6) δ 8.72 (s, 1H, H-2), 8.59 (s, 1H, H-8), 8.29 – 8.23 (m, 2H, Bz), 8.07 – 8.02 (m, 2H, Bz), 7.67 – 7.62 (m, 2H, Bz), 7.51 (t, *J* = 7.7 Hz, 4H, Bz), 6.30 (s, 1H, H-1'), 5.63 (d, *J* = 3.6 Hz, 1H, H-1''), 5.56 – 5.46 (m, 1H, H-3''), 4.97 (d, *J* = 4.8 Hz, 1H, H-2'), 4.87 (dd, *J* = 9.6, 4.8 Hz, 1H, H-3'), 4.80 – 4.75 (m, 1H, H-4''), 4.64 – 4.47 (m, 4H, H-5'', H-4', H-2''), 4.33 (dd, *J* = 13.3, 1.5 Hz, 1H, H-5'a), 4.09 (dd, *J* = 13.4, 2.6 Hz, 1H, H-5'b), 1.14 – 0.83 (m, 28H, ^{i}Pr) ppm. ^{13}C NMR (101 MHz, acetone-d_6) δ 166.5, 166.5 (Ph**C**O-), 152.5 (C-2), 152.0 (C-4), 150.9 (C-6), 144.9 (C-8), 134.1, 134.1 (Ph), 133.4 (C-5), 131.1, 131.0, 130.9, 130.3, 129.5, 129.2 (Ph), 102.9 (C-1''), 90.5 (C-1'), 82.6 (C-4'), 82.2 (C-4''), 80.5 (C-2'), 73.0 (C-2''), 72.6 (C-3'), 69.0 (C-3''), 65.1 (C-5''), 60.7 (C-5'), 17.9, 17.8, 17.7, 17.7, 17.5, 17.5, 17.4, 17.3 ((**C**H$_3$)$_2$CH-), 14.1, 13.8, 13.7, 13.3 ((CH$_3$)$_2$**C**H-) ppm. HRMS [EXI-MS] m/z: $[M+H]^+$ Cal. for $C_{41}H_{54}ClN_4O_{11}Si_2^+$ 869.3011; found 869.2961.

General procedure for the synthesis of 1a-e and 2a-e. Precursor (0.1 mmol) **6** (for **1a-e**) or **7** (for **2a-e**) was stirred with 80 equivalents of respective amine in 6 mL of dry MeOH at 160 °C under microwave irradiation for 30 minutes. The solution was concentrated under reduced pressure and dried *in vacuo*. The residue was stirred with 57 μL of TEA·3HF in 8 mL of dry THF at 0 °C for 4 hours. The solvent was removed under reduced pressure. The residue was dissolved in 25 mL of water and washed with 25 mL of DCM. The aqueous phase was concentrated and applied to RP-MPLC purification. The purified product was lyophilized to remove residual solvent.

2'-*O*-α-D-Arabinofuranosyladenosine (1a). Precursor **6** was treated with ammonia in methanol, to give 21 mg of **1a** as white foam; yield 53%. ^{1}H NMR (400 MHz, D_2O) δ 8.43 (d, *J* = 2.9 Hz, 1H, H-8), 8.39 (d, *J* = 3.3 Hz, 1H, H-2), 6.25 (dd, *J* = 6.1, 2.9 Hz, 1H, H-1'), 5.03 (s, 1H, H-1''), 4.93 (d, *J* = 6.3 Hz, 1H, H-2'), 4.60 (s, 1H, H-3'), 4.36 (s, 1H, H-4'), 4.16 (s, 2H, H-2'', H-4''), 3.94 (q, *J* = 13.1, 11.3 Hz, 3H, H-3'', H-5'), 3.76 (dd, *J* = 33.0, 8.3 Hz, 2H, H-5'') ppm. ^{13}C NMR (101 MHz, D_2O) δ 150.2 (C-2), 145.3 (Ar), 141.2 (C-8), 107.5 (C-1'), 87.0 (C-1''), 86.3 (C-4'), 84.5 (C-4''), 80.8 (C-2''), 78.5 (C-2'), 76.3 (C-3''), 70.7 (C-3'), 61.6 (C-5'), 61.1 (C-5'') ppm. HRMS [ESI-MS] m/z: [M+H]+ Cal. for $C_{15}H_{22}N_5O_8^+$ 400.1463; found 400.1445.

***N*^{6}-Methyl-2'-*O*-α-D-arabinofuranosyladenosine (1b).** Precursor **6** was treated with methylamine in methanol, to give 16 mg of **1b** as white foam; yield 39%. ^{1}H NMR (400 MHz, methanol-d_4) δ 8.25 (s, 1H, H-8), 8.21 (s, 1H, H-2), 6.07 (d, J = 6.4 Hz, 1H, H-1'), 4.89 (d, J = 1.0 Hz, 1H, H-1''), 4.85 (dd, J = 6.5, 4.9 Hz, 1H, H-2'), 4.45 (dd, J = 5.0, 2.5 Hz, 1H, H-3'), 4.15 (q, J = 2.6 Hz, 1H, H-4'), 4.10 (dt, J = 5.3, 4.1 Hz, 1H, H-4''), 4.01 (dd, J = 2.5, 1.1 Hz, 1H, H-2''), 3.89 – 3.85 (m, 2H, H-3'', H-5'a), 3.74 (dd, J = 12.6, 2.8 Hz, 1H, H-5'b), 3.66 (dd, J = 11.8, 4.0 Hz, 1H, H-5''a), 3.59 (dd, J = 11.8, 5.3 Hz, 1H, H-5''b), 3.09 (s, 3H, Me) ppm. ^{13}C NMR (101 MHz, methanol-d_4) δ 156.9 (C-6), 153.6 (C-2), 141.3 (C-8), 121.5 (C-5), 109.5 (C-1''), 89.3 (C-1'), 88.3 (C-4'), 87.9 (C-4''), 82.3 (C-2''), 80.0 (C-2'), 78.5 (C-3''), 72.8 (C-3'), 63.4 (C-5'), 63.1 (C-5'') ppm. HRMS [ESI-MS] m/z: $[M+H]^+$ Cal. for $C_{16}H_{24}N_5O_8^+$ 414.1619; found 414.1596

***N*^{6}-Ethyl-2'-*O*-α-D-arabinofuranosyladenosine (1c).** Precursor **6** was treated with ethylamine in methanol, to give 32 mg of **1c** as white foam; yield 75%. ^{1}H NMR (400 MHz, D_2O) δ 8.27 (s, 1H, H-8), 8.14 (s, 1H, H-2), 6.16 (d, J = 6.3 Hz, 1H, H-1'), 5.01 (d, J = 1.7 Hz, 1H, H-1''), 4.83 (dd, J = 6.3, 5.2 Hz, 1H, H-2'), 4.56 (dd, J = 5.2, 3.0 Hz, 1H, H-3'), 4.34 (q, J = 3.1 Hz, 1H, H-4'), 4.17 – 4.12 (m, 2H, H-2'', H-4''), 4.00 – 3.94 (m, 2H, H-3'', H-5'a), 3.89 (dd, J = 12.9, 3.5 Hz, 1H, H-5'b), 3.78 (dd, J = 12.3, 3.4 Hz, 1H, H-5''a), 3.68 (dd, J = 12.3, 5.8 Hz, 1H, H-5''b), 3.53 (d, J = 8.2 Hz, 2H, -C**H**$_2$Me), 1.29 (t, J = 7.3 Hz, 3H, -C**H**$_3$) ppm. ^{13}C NMR (101 MHz, D_2O) δ 153.9 (C-6), 152.0 (C-2), 139.9 (C-8), 119.2 (C-5), 107.4 (C-1''), 86.9 (C-1'), 86.2 (C-4'), 84.5 (C-4''), 80.7 (C-2''), 78.7 (C-2'), 76.2 (C-3''), 70.7 (C-3'), 61.5 (C-5'), 61.1 (C-5''), 36.0 (-**C**H$_2$Me), 13.7 (-**C**H$_3$). HRMS [ESI-MS] m/z: $[M+H]^+$ Cal. for $C_{17}H_{26}N_5O_8^+$ 428.1776; found 428.1755.

***N*^{6}-*Iso*propyl-2'-*O*-α-D-arabinofuranosyladenosine (1d).** Precursor **6** was treated with *iso*propylamine in methanol, to give 34 mg of **1d** as white foam; yield 77%. ^{1}H NMR (400 MHz, methanol-d_4) δ 8.34 (s, 1H, H-8), 8.28 (s, 1H, H-2), 6.15 (d, J = 6.4 Hz, 1H, H-1'), 4.97 (d, J = 1.0 Hz, 1H, H-1''), 4.93 (dd, J = 6.5, 4.9 Hz, 1H, H-2'), 4.54 (m, 2H, H-3', -C**H**Me$_2$), 4.23 (q, J = 2.5 Hz, 1H, H-4'), 4.18 (dt, J = 5.3, 4.1 Hz, 1H, H-4''), 4.10 (dd, J = 2.5, 1.1 Hz, 1H, H-2''), 3.98 – 3.92 (m, 2H, H-3'', H-5''a), 3.82 (dd, J = 12.5, 2.7 Hz, 1H, H-5''b), 3.74 (dd, J = 11.8, 3.9 Hz, 1H, H-5'a), 3.67 (dd, J = 11.8, 5.3 Hz, 1H, H-5'b), 1.37 (s, 3H, Me), 1.36 (s, 3H, Me) ppm. ^{13}C NMR (101 MHz, methanol-d_4) δ 155.5 (C-6), 153.7 (C-2), 141.2 (C-8), 121.1 (C-5), 109.5 (C-1''), 89.3 (C-1'), 88.3 (C-4''), 87.9 (C-4'), 82.3 (C-2''), 80.0 (C-2'), 78.5 (C-3''),

72.8 (C-3'), 63.4 (C-5'), 63.1 (C-5''), 43.6 (-**C**HMe$_2$), 22.9 (-**C**H$_3$) ppm. HRMS [ESI-MS] m/z: [M+H]$^+$ Cal. for $C_{18}H_{28}N_5O_8^+$ 442.1932; found 442.1915.

***N*^{6}-Ethyl-*N*^{6}-methyl-2'-*O*-α-D-arabinofuranosyladenosine (1e).** Precursor **6** was treated with ethylmethylamine in methanol, to give 43 mg of **1e** as white foam; yield 97%. ^{1}H NMR (400 MHz, methanol-*d*$_4$) δ 8.21 (s, 1H, H-8), 8.17 (s, 1H, H-2), 6.09 (d, *J* = 6.4 Hz, 1H, H-1'), 4.92 (d, *J* = 1.0 Hz, 1H, H-1''), 4.87 (dd, *J* = 6.5, 4.9 Hz, 1H, H-2'), 4.47 (dd, *J* = 5.0, 2.5 Hz, 1H, H-3'), 4.17 (q, *J* = 2.5 Hz, 1H, H-4'), 4.12 (dt, *J* = 5.3, 4.1 Hz, 1H, H-4''), 4.09 – 4.00 (m, 3H, H-2'', -C**H**$_2$Me), 3.89 (ddd, *J* = 8.8, 4.1, 2.5 Hz, 2H, H-3'', H-5'a), 3.75 (dd, *J* = 12.5, 2.7 Hz, 1H, H-5'b), 3.68 (dd, *J* = 11.8, 4.0 Hz, 1H, H-5''a), 3.61 (dd, *J* = 11.8, 5.3 Hz, 1H, H-5''b), 3.49 – 3.34 (m, 3H,-NC**H**$_3$), 1.24 (t, *J* = 7.0 Hz, 3H, -CH$_2$C**H**$_3$) ppm. ^{13}C NMR (101 MHz, methanol-*d*$_4$) δ 155.5 (C-6), 152.9 (C-2), 150.6 (C-4), 140.1 (C-8), 121.6 (C-5), 109.5 (C-1''), 89.2 (C-1'), 88.2 (C-4''), 87.9 (C-4'), 82.3 (C-2''), 79.8 (C-2'), 78.5 (C-3''), 72.8 (C-3'), 63.4 (C-5'), 63.1 (C-5''), 46.5 (-**C**H$_2$Me), 36.5 (-N**C**H3), 12.9 (-CH$_2$**C**H$_3$) ppm. HRMS [ESI-MS] m/z: [M+H]$^+$ Cal. for $C_{18}H_{28}N_5O_8^+$ 442.1932; found 442.1921.

2'-*O*-α-D-Ribofuranosyladenosine (2a). Precursor **7** was treated with ammonia in methanol, to give 26 mg of **2a** as white foam; yield 65%. ^{1}H NMR (400 MHz, D$_2$O) δ 8.40 (s, 1H, H-8), 8.28 (s, 1H, H-2), 6.27 (d, *J* = 6.2 Hz, 1H, H-1'), 5.13 (d, *J* = 4.0 Hz, 1H, H-1''), 4.95 (dd, *J* = 6.3, 5.1 Hz, 1H, H-2'), 4.61 (dd, *J* = 5.2, 3.1 Hz, 1H, H-3'), 4.40 – 4.37 (m, 1H, H-4'), 4.26 (ddd, *J* = 4.7, 3.5, 2.6 Hz, 1H, H-4''), 4.15 – 4.09 (m, 2H, H-2'', H-3''), 3.99 (dd, *J* = 12.9, 2.8 Hz, 1H, H-5''a), 3.91 (dd, *J* = 12.9, 3.5 Hz, 1H, H-5''b), 3.75 (dd, *J* = 12.4, 3.6 Hz, 1H, H-5'a), 3.68 (dd, *J* = 12.4, 4.7 Hz, 1H, H-5'b) ppm. ^{13}C NMR (101 MHz, D$_2$O) δ 155.8(C-6), 152.7 (C-2), 148.5 (C-4), 140.8 (C-8), 119.2 (C-5), 102.0 (C-1''), 87.0 (C-1'), 86.2 (C-4'), 85.5 (C-4''), 79.1 (C-2'), 71.5 (C-2''), 70.9 (C-3'), 69.8 (C-3''), 61.6 (C-5', C-5'') ppm. HRMS [ESI-MS] m/z: [M+H]$^+$ Cal. for $C_{15}H_{22}N_5O_8^+$ 400.1463; found 400.1447.

***N*^{6}-Methyl-2'-*O*-α-D-ribofuranosyladenosine (2b).** Precursor **7** was treated with methylamine in methanol, to give 22 mg of **2b** as white foam; yield 53%. ^{1}H NMR (400 MHz, D$_2$O) δ 8.25 (s, 1H, H-8), 8.14 (s, 1H, H-2), 6.16 (d, *J* = 6.2 Hz, 1H, H-1'), 5.11 (d, *J* = 4.1 Hz, 1H, H-1''), 4.86 (dd, *J* = 6.2, 5.1 Hz, 1H, H-2'), 4.56 (dd, *J* = 5.2, 3.0 Hz, 1H, H-3'), 4.35 (q, *J* = 3.0 Hz, 1H, H-4'), 4.26 – 4.21 (m, 1H, H-4''), 4.09 (m, 2H, H-2'', H-3''), 3.96 (dd, *J* = 12.9, 2.7 Hz, 1H, H-5''a), 3.87 (dd, *J* = 12.9, 3.5 Hz, 1H, H-5''b), 3.71 (dd, *J* = 12.4, 3.6 Hz, 1H, H-5'a), 3.64 (dd, *J* = 12.4, 4.7 Hz, 1H, H-5'b), 3.05 (s, 3H, -CH$_3$) ppm. ^{13}C NMR (101 MHz, D$_2$O) δ 154.9 (C-6), 152.4 (C-2),

139.8 (C-8), 101.9 (C-1''), 86.9 (C-1'), 86.1(C-4'), 85.4 (C-4''), 79.1 (C-2'), 71.5 (C-2''), 70.9 (C-3'), 69.7 (C-3''), 61.5, 61.5 (C-5', C-5'') ppm. HRMS [ESI-MS] m/z: $[M+H]^+$ Cal. for $C_{16}H_{24}N_5O_8^+$ 414.1619; found 414.1603.

***N*^{6}-Ethyl-2'-*O*-α-D-ribofuranosyladenosine (2c).** Precursor **7** was treated with ethylamine in methanol, to give 28 mg of **2c** as white foam; yield 66%. ^{1}H NMR (400 MHz, D_2O) δ 8.28 (s, 1H, H-8), 8.16 (s, 1H, H-2), 6.19 (d, *J* = 6.2 Hz, 1H, H-1'), 5.13 (d, *J* = 4.1 Hz, 1H, H-1''), 4.87 (dd, *J* = 6.2, 5.1 Hz, 1H, H-2'), 4.57 (dd, *J* = 5.1, 3.1 Hz, 1H, H-3'), 4.36 (q, *J* = 3.1 Hz, 1H, H-4'), 4.25 (dt, *J* = 4.7, 3.2 Hz, 1H, H-4''), 4.11 (qd, *J* = 6.2, 3.4 Hz, 2H, H-2'', H-3''), 3.97 (dd, *J* = 12.9, 2.8 Hz, 1H, H-5'a), 3.89 (dd, *J* = 12.9, 3.5 Hz, 1H, H-5'b), 3.73 (dd, *J* = 12.4, 3.6 Hz, 1H, H-5''a), 3.66 (dd, *J* = 12.4, 4.7 Hz, 1H, H-5''b), 3.55 (br, 2H, -C**H**$_2$Me), 1.30 (t, *J* = 7.3 Hz, 3H, -C**H**$_3$) ppm. ^{13}C NMR (101 MHz, D_2O) δ 153.9 (C-6), 152.0 (C-2), 140.0 (C-8), 119.2 (C-5), 101.9 (C-1''), 86.9 (C-1'), 86.1 (C-4'), 85.5 (C-4''), 79.2 (C-2'), 71.6 (C-3'), 70.9 (C-2''), 69.8 (C-3''), 61.5, 61.5 (C-5', C-5''), 35.9 (-**C**H$_2$Me), 13.7 (-**C**H$_3$) ppm. HRMS [ESI-MS] m/z: $[M+H]^+$ Cal. for $C_{17}H_{26}N_5O_8^+$ 428.1776; found 428.1761.

***N*^{6}-*Iso*propyl-2'-*O*-α-D-ribofuranosyladenosine (2d).** Precursor **7** was treated with *iso*propylamine in methanol, to give 32 mg of **2d** as white foam; yield 72%. ^{1}H NMR (400 MHz, D_2O) δ 8.29 (s, 1H, H-8), 8.20 (s, 1H, H-2), 6.19 (d, *J* = 6.3 Hz, 1H, H-1'), 5.08 (d, *J* = 4.0 Hz, 1H, H-1''), 4.89 (dd, *J* = 6.3, 5.1 Hz, 1H, H-2'), 4.56 (dd, *J* = 5.2, 2.9 Hz, 1H, H-3'), 4.35 (m, 2H, H-4', -C**H**Me$_2$), 4.22 (dd, *J* = 5.0, 2.6 Hz, 1H, H-4''), 4.11 – 4.04 (m, 2H, H-2'', H-3''), 3.95 (dd, *J* = 12.9, 2.8 Hz, 1H, H-5'a), 3.87 (dd, *J* = 12.9, 3.5 Hz, 1H, H-5'b), 3.71 (dd, *J* = 12.4, 3.6 Hz, 1H, H-5''a), 3.64 (dd, *J* = 12.4, 4.7 Hz, 1H, H-5''b), 1.33 (d, *J* = 1.3 Hz, 3H, -C**H**$_3$), 1.31 (d, *J* = 1.3 Hz, 3H, -C**H**$_3$) ppm. ^{13}C NMR (101 MHz, D_2O) δ 153.6 (C-6), 152.3 (C-2), 140.0 (C-8), 101.9 (C-1''), 86.9 (C-1'), 86.2 (C-4'), 85.4 (C-4''), 79.1 (C-2'), 71.5 (C-3'), 70.9 (C-2''), 69.7 (C-3''), 61.6, 61.5 (C-5', C-5''), 21.7 (-CH$_3$) ppm. HRMS [ESI-MS] m/z: $[M+H]^+$ Cal. for $C_{18}H_{28}N_5O_8^+$ 442.1932; found 442.1933.

***N*^{6}-Ethyl-*N*^{6}-methyl-2'-*O*-α-D-ribofuranosyladenosine (2e).** Precursor **7** was treated with ethylmethylamine in methanol, to give 44 mg of **2e** as white foam with quantitative yield. ^{1}H NMR (400 MHz, D_2O) δ 8.23 (s, 1H, H-8), 8.06 (s, 1H, H-2), 6.16 (d, *J* = 6.0 Hz, 1H, H-1'), 5.14 (d, *J* = 4.2 Hz, 1H, H-1''), 4.83 (d, *J* = 5.5 Hz, 1H, H-2'), 4.55 (dd, *J* = 5.2, 3.2 Hz, 1H, H-3'), 4.35 (q, *J* = 3.1 Hz, 1H, H-4'), 4.24 (dt, *J* = 6.3, 3.3 Hz, 1H, H-4''), 4.10 (qd, *J* = 6.2, 3.4 Hz, 2H, H-2'', H-3''), 3.97 (dd, *J* = 12.9, 2.7 Hz, 1H, H-5'a), 3.89 (dd, *J* = 12.9, 3.4 Hz, 1H, H-5'b), 3.85 – 3.75 (m, 2H, -

C**H**$_2$Me), 3.72 (dd, *J* = 12.4, 3.6 Hz, 1H, H-5''a), 3.65 (dd, *J* = 12.4, 4.7 Hz, 1H, H-5''b), 3.24 (s, 3H, -NC**H**$_3$), 1.17 (t, *J* = 7.1 Hz, 3H, -CH$_2$C**H**$_3$) ppm. ^{13}C NMR (101 MHz, D$_2$O) δ 152.9 (C-6), 151.1 (C-2), 148.3 (C-4), 138.7 (C-8), 119.1 (C-5), 101.8 (C-1''), 87.0 (C-1'), 86.0 (C-4'), 85.4 (C-4''), 79.1 (C-2'), 71.6 (C-3'), 70.9 (C-2''), 69.8 (C-3''), 61.5 (C-5', C-5''), 46.1 (-**C**H$_2$Me), 36.4 (-N**C**H$_3$), 11.8 (-CH$_2$**C**H$_3$) ppm. HRMS [ESI-MS] m/z: [M+H]$^+$ Cal. for $C_{18}H_{28}N_5O_8^+$ 442.1932; found 442.1919.

General procedure to achieve 1f and 2f. Precursor **6** or **7** (0.1 mmol) was stirred with 0.52 mL of morpholine in 6 mL of dry MeOH at 160 °C under microwave irradiation for 1 hour. The solution was concentrated under reduced pressure. The residue was stirred with 0.2 mL of 40% methylamine/methanol solution in 4 mL of MeOH at r.t. for 12 hours. Afterwards solvent was removed and the residue dried under reduced pressure. 57 μL of TEA·3HF in 8 mL of dry THF were added to the dry residue and stirred at 0 °C for 4 hours. The solvent was removed under reduced pressure. The residue was dissolved in 25 mL of water and washed with 25 mL of DCM. The aqueous phase was concentrated and applied to RP-MPLC for purification. The purified product was lyophilized to remove residual solvent.

***N*^{6}-Morphlinyl-2'-*O*-α-D-arabinofuranosyladenosine (1f).** Precursor **6** was treated with morpholine in methanol, to give 39 mg of **1f** as white foam; yield 83%. ^{1}H NMR (400 MHz, D$_2$O) δ 8.30 (s, 1H, H-8), 8.15 (s, 1H, H-2), 6.16 (d, *J* = 6.1 Hz, 1H, H-1'), 5.04 (d, *J* = 1.7 Hz, 1H, H-1''), 4.82 (dd, *J* = 6.2, 5.2 Hz, 2H, H-2'), 4.56 (dd, *J* = 5.2, 3.1 Hz, 1H, H-3'), 4.34 (q, *J* = 3.1 Hz, 1H, H-4'), 4.19 – 4.14 (m, 2H, H-2'', H-4''), 4.08 (t, *J* = 4.8 Hz, 4H, N(C**H**$_2$)$_2$), 4.00 – 3.95 (m, 2H, H-3'', H-5'a), 3.91 – 3.84 (m, 5H, H-5'b, O(C**H**$_2$)$_2$), 3.80 (dd, *J* = 12.3, 3.4 Hz, 1H, H-5''a), 3.70 (dd, *J* = 12.3, 5.8 Hz, 1H, H-5''b) ppm. ^{13}C NMR (101 MHz, D$_2$O) δ 153.5 (C-6), 151.8 (C-2), 149.2 (C-4), 139.0 (C-8), 119.6 (C-5), 107.4 (C-1''), 87.0 (C-1'), 86.2 (C-4'), 84.6 (C-4''), 80.8 (C-2''), 78.6 (C-2'), 76.3 (C-3''), 70.7 (C-3'), 66.4 (O(**C**H$_2$)$_2$-), 61.6 (C-5'), 61.2 (C-5''), 45.6 (-N(**C**H$_2$)$_2$-) ppm. HRMS [ESI-MS] m/z: [M+H]+ Cal. for $C_{19}H_{28}N_5O_9^+$ 470.1882; found 470.1861.

***N*^{6}-Morphlinyl-2'-*O*-α-D-ribofuranosyladenosine (2f).** Precursor **7** was treated with morpholine in methanol, to give 15 mg of **2f** as white foam; yield 32%. ^{1}H NMR (400 MHz, D$_2$O) δ 8.34 (s, 1H, H-8), 8.24 (s, 1H, H-2), 6.22 (d, *J* = 6.1 Hz, 1H, H-1'), 5.11 (d, *J* = 4.1 Hz, 1H, H-1''), 4.89 (t, *J* = 5.6 Hz, 1H, H-2'), 4.56 (dd, *J* = 5.2, 3.1 Hz, 1H, H-3'), 4.35 (q, *J* = 3.2 Hz, 1H, H-4'), 4.23 (q, *J* = 3.9 Hz, 1H, H-4''), 4.17 (t, *J* = 4.8 Hz, 4H, -N(C**H**$_2$)$_2$), 4.09 (qd, *J* = 6.3, 3.4 Hz, 2H, H-2'', H-3''), 3.96 (dd, *J* = 13.0, 2.7

Hz, 1H, H-5'a), 3.92 – 3.85 (m, 5H, H-5'b, O(C**H**$_2$)$_2$), 3.71 (dd, *J* = 12.4, 3.6 Hz, 1H, H-5''a), 3.64 (dd, *J* = 12.4, 4.7 Hz, 1H, H-5''b) ppm. ^{13}C NMR (101 MHz, D_2O) δ 153.6 (C-6), 151.7 (C-2), 149.3 (C-4), 139.3 (C-8), 119.8 (C-5), 101.9 (C-1''), 87.0 (C-1'), 86.1 (C-4'), 85.4 (C-4''), 79.0 (C-2'), 71.5 (C-3'), 70.9 (C-2''), 69.7 (C-3''), 66.4 (O(**C**H$_2$)$_2$), 61.5 (C-5', C-5''), 45.8 (-N(**C**H$_2$)$_2$) ppm. HRMS [ESI-MS] m/z: [M+H]+ Cal. for $C_{19}H_{28}N_5O_9^+$ 470.1882; found 470.1862.

General procedure for the synthesis of 1g-h, and 2g-h. Precursor (0.1 mmol) **6** (for **1g**, **1h**) or **7** (for **2g**, **2h**) was stirred with 6 equivalents of sodium alkoxide in 6 mL of dry alcohol at 0 °C for 4 hours. The reaction was quenched by addition of 28.8 μL of acetic acid. The reaction mixture was concentrated under reduced pressure and dried. 66 μL of TEA·3HF in 8 mL of dry THF were added to the residue and the mixture was stirred at 0 °C for 5 hours. The solvent was removed under reduced pressure and the residue was dissolved in 25 mL of water. After washing with 25 mL of DCM the aqueous phase was concentrated and applied to RP-MPLC purification. The purified product was concentrated and subsequently lyophilized to remove the residual solvent.

***O*^{6}-Methyl-2'-*O*-α-D-arabinofuranosylinosine (1g).** Precursor **6** was treated with sodium methoxide in methanol, to give 40 mg of **1g**; yield 96%. ^{1}H NMR (400 MHz, D_2O) δ 8.53 (m, 2H, H-8, H-2), 6.29 (d, *J* = 6.0 Hz, 1H, H-1'), 5.02 (d, *J* = 1.7 Hz, 1H, H-1''), 4.91 (t, *J* = 5.6 Hz, 1H, H-2'), 4.58 (dd, *J* = 5.2, 3.3 Hz, 1H, H-3'), 4.35 (q, *J* = 3.4 Hz, 1H, H-4'), 4.21 (s, 3H, -OCH$_3$), 4.17 – 4.12 (m, 2H, H-2'', H-4''), 4.00 – 3.92 (m, 2H, H-3'', H-5''a), 3.89 (dd, *J* = 12.8, 3.8 Hz, 1H, H-5''b), 3.78 (dd, *J* = 12.3, 3.4 Hz, 1H, H-5'a), 3.68 (dd, *J* = 12.3, 5.8 Hz, 1H, H-5'b) ppm. ^{13}C NMR (101 MHz, D_2O) δ 161.1 (C-6), 152.1 (C-2), 150.7 (C-4), 142.5 (C-8), 121.3 (C-5), 107.4 (C-1''), 87.1 (C-1'), 86.2 (C-4'), 84.5 (C-4''), 80.7 (C-2''), 78.6 (C-2'), 76.3 (C-3''), 70.6 (C-3'), 61.4, 61.1 (C-5', C-5''), 55.0 (-O**C**H$_3$) ppm. HRMS [ESI-MS] m/z: [M+H]+ Cal. for $C_{16}H_{23}N_4O_9$ 415.1460; found 415.1446.

***O*^{6}-Ethyl-2'-*O*-α-D-arabinofuranosylinosine (1h).** Precursor **6** was treated with sodium ethoxide in ethanol, to give 29 mg of **1h**; yield 68%. ^{1}H NMR (400 MHz, D_2O) δ 8.50 (s, 1H, H-8), 8.47 (s, 1H, H-2), 6.27 (d, *J* = 6.0 Hz, 1H, H-1'), 5.02 (d, *J* = 1.6 Hz, 1H, H-1''), 4.90 (t, *J* = 5.6 Hz, 1H, H-2'), 4.62 (q, *J* = 7.1 Hz, 2H, -OC**H**$_2$Me), 4.58 (dd, *J* = 5.2, 3.3 Hz, 1H, H-3'), 4.35 (q, *J* = 3.3 Hz, 1H, H-4'), 4.14 (tt, *J* = 5.9, 2.7 Hz, 2H, H-4'', H-2''), 4.00 – 3.92 (m, 2H, H-3'', H-5'a), 3.89 (dd, *J* = 12.9, 3.8 Hz, 1H, H-5'b), 3.78 (dd, *J* = 12.3, 3.4 Hz, 1H, H-5''a), 3.67 (dd, *J* = 12.3, 5.8 Hz, 1H, H-5''b), 1.51 (t, *J* = 7.1 Hz, 3H, -CH$_3$) ppm. ^{13}C NMR (101 MHz, D_2O) δ 160.7 (C-6),

152.0 (C-2), 150.7 (C-4), 142.4 (C-8), 121.3 (C-5), 107.4 (C-1''), 87.1 (C-1'), 86.2 (C-4'), 84.5 (C-4''), 80.7 (C-2''), 78.7 (C-2'), 76.2 (C-3''), 70.6 (C-3'), 64.5 (-O**C**H_2Me), 61.4, 61.1 (C-5', C-5''), 13.6 (-**C**H_3) ppm. HRMS [ESI-MS] m/z: [M+H]+ Cal. for $C_{17}H_{25}N_4O_9^+$ 429.1616; found 429.1603.

***O*^{6}-Methyl-2'-*O*-α-D-ribofuranosylinosine (2g).** Precursor **7** was treated with sodium methoxide in methanol, to give 42 mg of **2g** in quantitative yield. ^{1}H NMR (400 MHz, D_2O) δ 8.55 (s, 2H, H-2, H-8), 6.33 (d, *J* = 5.8 Hz, 1H, H-1'), 5.16 (d, *J* = 4.1 Hz, 1H, H-1''), 4.97 (t, *J* = 5.5 Hz, 1H, H-2'), 4.62 (dd, *J* = 5.2, 3.5 Hz, 1H, H-3'), 4.38 (q, *J* = 3.4 Hz, 1H, H-4'), 4.19 – 4.11 (m, 4H, H-4'', -C**H**$_3$), 4.15 – 4.09 (m, 2H, H-2'', H-3''), 3.99 (dd, *J* = 12.8, 2.9 Hz, 1H, H-5'a), 3.91 (m, 1H, H-5'b), 3.74 (dd, *J* = 12.4, 3.5 Hz, 1H, H-5''a), 3.67 (m, 1H, H-5''b) ppm. ^{13}C NMR (101 MHz, D_2O) δ 161.1 (C-6), 152.1 (C-2), 150.7 (C-4), 142.6 (C-8), 121.3 (C-5), 101.9 (C-1''), 87.2 (C-1'), 86.1 (C-4'), 85.5 (C-4''), 79.1 (C-2'), 71.5 (C-3'), 70.7 (C-2''), 69.8 (C-3''), 61.5, 61.4 (C-5', C-5''), 55.0 (-O**C**H_3) ppm. HRMS [ESI-MS] m/z: [M+H]+ Cal. for $C_{16}H_{23}N_4O_9^+$ 415.1460; found 415.1448.

***O*^{6}-Ethyl-2'-*O*-α-D-ribofuranosylinosine (2h).** Precursor **7** was treated with sodium ethoxide in ethanol, to give 20 mg of **2h** as white foam; yield 43%. ^{1}H NMR (400 MHz, D_2O) δ 8.50 (s, 1H, H-8), 8.45 (s, 1H, H-2), 6.28 (d, *J* = 5.8 Hz, 1H, H-1'), 5.15 (d, *J* = 4.2 Hz, 1H, H-1''), 4.93 (t, *J* = 5.5 Hz, 1H, H-2'), 4.64 – 4.57 (m, 3H, H-3', -OC**H**$_2$Me), 4.36 (q, *J* = 3.4 Hz, 1H, H-4'), 4.24 (dt, *J* = 4.7, 3.3 Hz, 1H, H-4''), 4.10 (qd, *J* = 6.2, 3.4 Hz, 2H, H-2'', H-3''), 3.97 (dd, *J* = 12.9, 2.9 Hz, 1H, H-5'a), 3.89 (dd, *J* = 12.9, 3.7 Hz, 1H, H-5'b), 3.72 (dd, *J* = 12.4, 3.6 Hz, 1H, H-5''a), 3.65 (dd, *J* = 12.4, 4.7 Hz, 1H, H-5''b), 1.51 (t, *J* = 7.1 Hz, 3H, -OCH_2C**H**$_3$).ppm. ^{13}C NMR (101 MHz, D_2O) δ 160.7 (C-6), 152.1 (C-2), 150.7 (C-4), 142.5 (C-8), 121.3 (C-5), 101.9 (C-1''), 87.2 (C-1'), 86.1 (C-4'), 85.5 (C-4''), 79.2 (C-2'), 71.6 (C-3'), 70.8 (C-2''), 69.8 (C-3''), 64.6 (-O**C**H_2Me), 61.5, 61.5 (C-5', C-5''), 13.7 (-CH_2**C**H_3) ppm. HRMS [ESI-MS] m/z: [M+H]+ Cal. for $C_{17}H_{25}N_4O_9^+$ 429.1616; found 429.1603.

General procedure for the synthesis of 1i and 2i. Precursor (0.1 mmol) **6** (for **1**) or **7** (for **2**) was stirred with 20 mg of sodium thiomethoxide in 2 mL of dry DMSO at 55 °C for 48 hours. The solution was diluted with 15 mL of EA and washed with water. The organic phase was dried over Na_2SO_4 and concentrated to dryness. The residue was stirred with 0.5 mL of 40% methylamine/methanol solution in 5 mL of MeOH at r.t. for 12 hours. The solvent was removed under reduced pressure and dried *in vacuo*. 57 µL of TEA·3HF in 8 mL of dry THF were added to the residue and the mixture was

stirred at 0 °C for 4 hours. The solvent was removed under reduced pressure. The residue was dissolved in 25 mL of water and washed with 25 mL of DCM. The aqueous phase was concentrated and applied to RP-MPLC for purification. The purified product was concentrated and subsequently lyophilized to remove the residual solvent.

***S*^{6}-Methyl-2'-*O*-α-D-arabinofuranosyl-6-thioionsine (1i).** Precursor **6** was treated with sodium methanethiol, to give 18 mg of **1i**; yield 42%. ^{1}H NMR (400 MHz, D_2O) δ 8.66 (s, 1H, H-2), 8.60 (s, 1H, H-8), 6.31 (d, *J* = 5.8 Hz, 1H, H-1'), 5.08 (d, *J* = 1.7 Hz, 1H, H-1''), 4.93 (t, *J* = 5.6 Hz, 1H, H-2'), 4.61 (dd, *J* = 5.2, 3.5 Hz, 1H, H-3'), 4.38 (q, *J* = 3.4 Hz, 1H, H-4'), 4.21 – 4.14 (m, 2H, H-2'', H-4''), 4.03 – 3.96 (m, 2H, H-3'', H-5'a), 3.93 (dd, *J* = 12.8, 3.9 Hz, 1H, H-5'b), 3.81 (dd, *J* = 12.3, 3.4 Hz, 1H, H-5''a), 3.70 (dd, *J* = 12.3, 5.8 Hz, 1H, H-5''b), 2.73 (s, 3H, -C**H**$_3$) ppm. ^{13}C NMR (101 MHz, D_2O) δ 162.5 (C-6), 151.8 (C-2), 146.8 (C-4), 143.1 (C-8), 130.9 (C-5), 107.4 (C-1''), 87.1 (C-1'), 86.2 (C-4'), 84.5 (C-4''), 80.8 (C-2''), 78.7 (C-2'), 76.3 (C-3''), 70.5 (C-3'), 61.4 (C-5'), 61.1 (C-5''), 11.5 (-**C**H$_3$) ppm. HRMS [ESI-MS] m/z: [M+H]+ Cal. for $C_{16}H_{23}N_4O_8S^+$ 431.1231; found 431.1210.

***S*^{6}-Methyl-2'-*O*-α-D-ribofuranosyl-6-thioionsine (2i).** Precursor **7** was treated with sodium thiomethoxide, to give 34 mg of **2i**; yield 79%. ^{1}H NMR (400 MHz, D_2O) δ 8.68 (s, 1H, H-2), 8.61 (s, 1H, H-8), 6.33 (d, *J* = 5.7 Hz, 1H, H-1'), 5.19 (d, *J* = 4.2 Hz, 1H, H-1''), 4.97 (t, *J* = 5.5 Hz, 1H, H-2'), 4.62 (dd, *J* = 5.2, 3.7 Hz, 1H, H-3'), 4.39 (q, *J* = 3.5 Hz, 1H, H-4'), 4.26 (dt, *J* = 4.8, 3.3 Hz, 1H, H-4''), 4.17 – 4.09 (m, 2H, H-2'', H-3''), 4.00 (dd, *J* = 12.8, 2.9 Hz, 1H, H-5'a), 3.92 (dd, *J* = 12.9, 3.9 Hz, 1H, H-5'b), 3.74 (dd, *J* = 12.4, 3.6 Hz, 1H, H-5''a), 3.67 (dd, *J* = 12.4, 4.7 Hz, 1H, H-5''b), 2.74 (s, 3H, -SC**H**$_3$) ppm. ^{13}C NMR (101 MHz, D_2O) δ 162.5 (C-6), 151.8 (C-2), 146.8 (C-4), 143.2 (C-8), 131.0 (C-5), 101.9 (C-1''), 87.2 (C-1'), 86.0 (C-4'), 85.5 (C-4''), 79.1 (C-2'), 71.5 (C-3'), 70.7 (C-2''), 69.8 (C-3''), 61.5, 61.4 (C-5', C-5''), 11.5 (-**C**H$_3$) ppm. HRMS [ESI-MS] m/z: [M+H]+ Cal. for $C_{16}H_{23}N_4O_8S^+$ 431.1231; found 431.1229.

General procedure for the synthesis of 1j and 2j. Precursor (0.1 mmol) **6** (for **1**) or **7** (for **2**) was stirred with 15 mg of thiourea in 6 mL of EtOH at r.t. for 20 hours. The solution was concentrated under reduced pressure. The residue was dissolved in 25 mL of DCM and washed with water. The organic phase was dried over Na_2SO_4 and concentrated to dryness. The residue was stirred with 0.5 mL of 40% methylamine/methanol solution in 5 mL of MeOH at r.t. for 12 hours. The solvent was removed under reduced pressure and the residue was dried *in vacuo*. 57 μL of

TEA·3HF in 8 mL of dry THF were added to the residue and the mixture was stirred at 0 °C for 4 hours The solvent was removed under reduced pressure. The residue was dissolved in 25 mL of water and washed with 25 mL of DCM. The aqueous phase was concentrated and applied to RP-MPLC purification. The purified product was concentrated and subsequently lyophilized to remove the residual solvent.

6-Mercaptopurine-9-(2'-*O*-α-D-arabinofuranosyl)ribofuranoside (1j). Precursor **6** was treated with thiourea, to give 24 mg of **1j** as product; yield 58%. ^{1}H NMR (400 MHz, D_2O) δ 8.32 (s, 1H, H-8), 8.17 (s, 1H, H-2), 6.17 (d, *J* = 6.3 Hz, 1H, H-1'), 4.99 (d, *J* = 1.7 Hz, 1H, H-1''), 4.84 (dd, *J* = 6.3, 5.2 Hz, 1H, H-2'), 4.55 (dd, *J* = 5.2, 3.0 Hz, 1H, H-3'), 4.33 (q, *J* = 3.1 Hz, 1H, H-4'), 4.13 (m, 2H, H-2'', H-4''), 3.98 – 3.92 (m, 2H, H-3'', H-5'a), 3.87 (dd, *J* = 12.9, 3.6 Hz, 1H, H-5'b), 3.78 (dd, *J* = 12.4, 3.4 Hz, 1H, H-5''a), 3.67 (dd, *J* = 12.3, 5.8 Hz, 1H, H-5''b) ppm. ^{13}C NMR (101 MHz, D_2O) δ 155.6 (C-6), 152.6 (C-2), 148.4 (C-4), 140.7 (C-8), 119.1 (C-5), 107.4 (C-1''), 87.0 (C-1'), 86.3 (C-4'), 84.6 (C-4''), 80.8 (C-2''), 78.7 (C-2'), 76.3 (C-3''), 70.7 (C-3'), 61.6 (C-5'), 61.1 (C-5'') ppm. HRMS [ESI-MS] m/z: [M+H]+ Cal. for $C_{15}H_{21}N_4O_8S^+$ 417.1075; found 417.1053.

6-Mercaptopurine-9-(2'-*O*-α-D-ribofuranosyl)ribofuranoside (2j). Precursor **7** was treated with thiourea, to give 28 mg of **2j**; yield 67%. ^{1}H NMR (400 MHz, D_2O) δ 8.30 (s, 1H, H, H-8), 8.21 (s, 1H, H-2), 6.21 (d, *J* = 6.3 Hz, 1H, H-1'), 5.13 (d, *J* = 4.1 Hz, 1H, H-1''), 4.90 (t, *J* = 5.7 Hz, 1H, H-2'), 4.58 (dd, *J* = 5.2, 3.1 Hz, 1H, H-3'), 4.37 (q, *J* = 3.2 Hz, 1H, H-4'), 4.25 (d, *J* = 3.8 Hz, 1H, H-4''), 4.14 – 4.09 (m, 2H, H-2'', H-3''), 3.98 (dd, *J* = 12.9, 2.8 Hz, 1H, H-5'a), 3.95 – 3.88 (m, 1H, H-5'b), 3.74 (dd, *J* = 12.4, 3.6 Hz, 1H, H-5''a), 3.67 (dd, *J* = 12.4, 4.7 Hz, 1H, H-5''b) ppm. ^{13}C NMR (101 MHz, D_2O) δ 154.9 (C-6), 152.3 (C-2), 140.0 (C-8), 101.9 (C-1''), 86.9 (C-1'), 86.2 (C-4'), 85.5 (C-4''), 79.1 (C-2'), 71.5 (C-3'), 70.9 (C-2''), 69.8 (C-3''), 61.5, 61.5 (C-5', C-5'') ppm. HRMS [ESI-MS] m/z: [M+H]+ Cal. for $C_{15}H_{21}N_4O_8S^+$ 417.1075; found 417.1052.

PARP-1 (ARTD1) inhibition assay

PARP-1 Chemiluminescent Assay Kit (catalogue #: 80551) was purchased from BPS Bioscience, San Diego, USA. In this assay, PARylation reaction was performed with biotinylated NAD^+ in the presence of activated DNA to simulate the DNA damage-dependent PARyaltion *in vitro*. PAR formation was then visualized using streptavidin coupled horseradish peroxidase. In case PAR was formed the streptavidin binds to the biotinylated PAR attached to the modified protein and the horseradish peroxidase can oxidize luminol to 3-aminophthalate. The thereby emitted light (chemiluminescence) can be quantified and used as a direct readout of PARP-1 (ARTD1) activity.

The assay was performed following the provided protocol unless stated otherwise. After coating the reaction wells (96-well module plate, VWR 62409-300, provided in the Kit) with histone, compounds **1a-j** or **2a-j** were incubated separately with PARP-1 (ARTD1) at 25 °C for 20 minutes in the histone coated reaction wells in assay buffer. Then PARylation reaction was initiated by addition of "assay mixture" containing biotinylated NAD^+ and activated DNA. Incubation was continued at 25 °C for 1 hour. Following the recommended protocol, the reaction mixture was removed from the plates and the wells were washed with PBST. Afterwards, the immobilised samples were treated with streptavidin-HRP followed by washing and addition of HRP substrate to produce a chemiluminescent signal that was read out with a TECAN infinite M200 plate reader (Lumniescence mode; label 1; attenuation none; integration time 1000 ms; settle time 100 ms; temperature 26 °C). The effect of the molecules were evaluated with the relative enzymatic activity in the presence of different molecules normalized to a reaction without any inhibitor after subtracted the blank data (without PARP-1). All the tests are biological duplicated each with three technical replicates. The dose response curve and regression equation was fitted using Origin 8.0 software.

Table S1 The measurement of chemiluminescence emission, two biological replicates. (* The emission was the average of three technical replicates.)

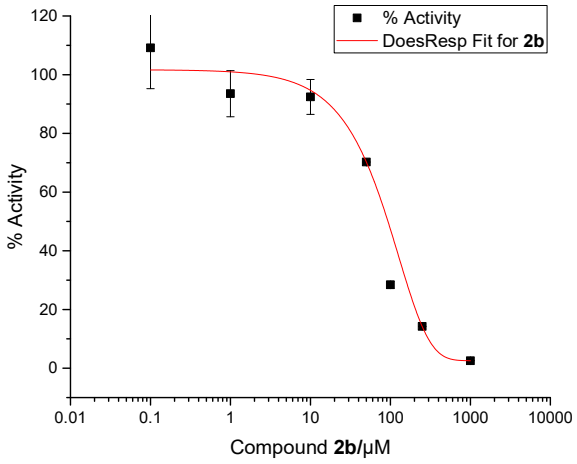
	Compound (250 μM)	*Emission of replicate A**	*Emission of replicate B**
with PARP-	-	4733632 ± 18751	2939358 ± 20736
Blank (w/o PARP-1)	-	80710 ± 17158	34921 ± 7431
Derivatives	**1a**	2540585 ± 20703	1837832 ± 18363
	1b	3546733 ± 22984	2672206 ± 30758
	1c	3840493 ± 3210	2653774 ± 60730
	1d	4449284 ± 28174	3009104 ± 39251
	1e	4718800 ± 12827	2747919 ± 38201
	1f	4713814 ± 9903	2771135 ± 89255
	1g	3117714 ± 26648	2313066 ± 25739
	1h	3933499 ± 24615	2637330 ± 22103
	1i	3990501 ± 12567	2461109 ± 66785
	1j	2997507 ± 24204	2128686 ± 25001
	2a	3313572 ± 12278	2471969 ± 67977
	2b	108594 ± 17980	257687 ± 3591
	2c	2887449 ± 10517	2271341 ± 37596
	2d	1749491 ± 2603	952009 ± 21887
	2e	3350914 ± 5658	2043270 ± 29749
	2f	2843974 ± 5974	2026821 ± 15381
	2g	2032444 ± 7328	1925357 ± 26922
	2h	3142735 ± 8194	1750857 ± 7128
	2i	2813400 ± 13956	1692345 ± 11685
	2j	1521562 ± 4518	1600863 ± 15997

Figure S1 Dose dependent inhibition of PARP-1 (ARTD1) by **2b**.

a) Measured chemiluminescence emission of two biological replicates. (* The emission was the average of three technical replicates.)

	*[**2b**] / µM*	*Emission of replicate A**	*Emission of replicate B**
with PARP-1	-	6543832 ± 14994	5367149 ± 36162
Blank (w/o PARP-1)	-	120252 ± 20660	117486 ± 21007
Derivatives	0.1	6238631 ± 11566	6577140 ±16212
	1	5623950 ± 62055	5439142 ± 21043
	10	5676369 ± 29400	5281306 ± 33163
	50	4632432 ± 8130	3806036 ± 24938
	100	1869493 ± 25462	1672964 ± 1588
	250	912295 ± 19815	751048.3 ± 6694
	1000	285441 ± 10903	251007 ± 8032

b) The normalized enzymatic activity of PARP-1 (ARTD1)



c) The regression equation of the nonlinear fit curve and the calculated IC_{50} value

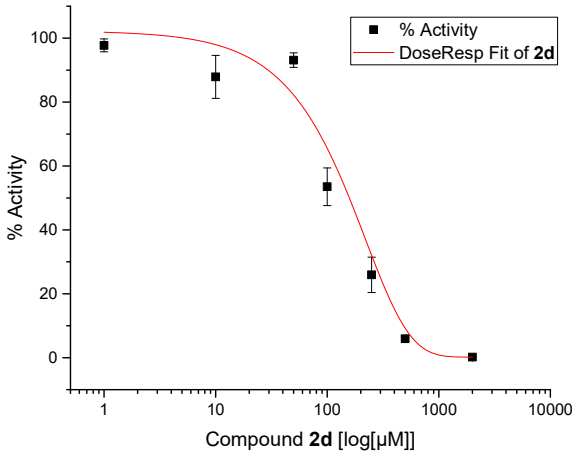
Model	DoseResp	
Equation	y = A1 + (A2-A1)/(1 + 10^((LOGx_0-x)*p))	
Reduced Chi-Sqr	83.59137	
Adj. R-Square	0.99997	
	Value	Standard Error
A1	2.54926	0.13373
A2	414.50863	2443.99752
LOGx_0	-120.40528	832.93894
p	-0.00414	0.00217
span	411.95936	2444.03163
IC_{50}	93.4 (µM)	3,7 (µM)

Figure S2 Dose dependent inhibition of PARP-1 (ARTD1) of compound **2d**.

a) Measured chemoluminescence emission of two biological replicates. (* The emission was average of three technical replicates.)

	[2d] / µM	*Emission of replicate A**	*Emission of replicate B**
with PARP-1	0	7033063 ± 13004	7516343 ± 22994
Blank (w/o PARP-1)	0	56866 ± 6803	44043 ± 7314
Derivatives	1	6734105 ± 24119	7500026 ± 72042
	10	6656073 ± 31578	6108476 ± 25745
	50	6709630 ± 38531	6833905 ± 35710
	100	4200954 ± 29453	3600917 ± 23438
	250	2252838 ± 21794	1569427 ± 3343
	500	531476 ± 8013	424634 ± 634
	2000	69943 ± 3688	57519 ± 5047

b) The normalized enzymatic activity of PARP-1 (ARTD1)

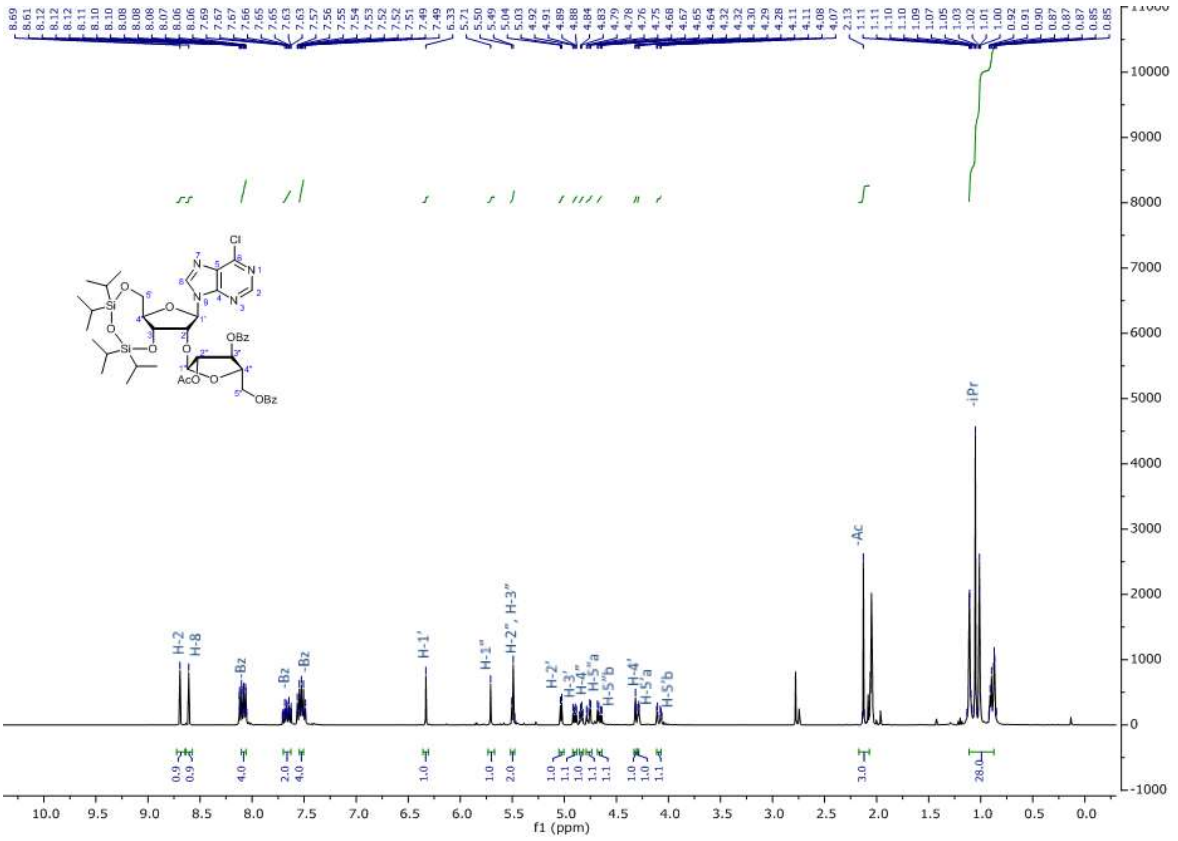


c) The regression equation of the nonlinear fit curve and the calculated IC_{50} value

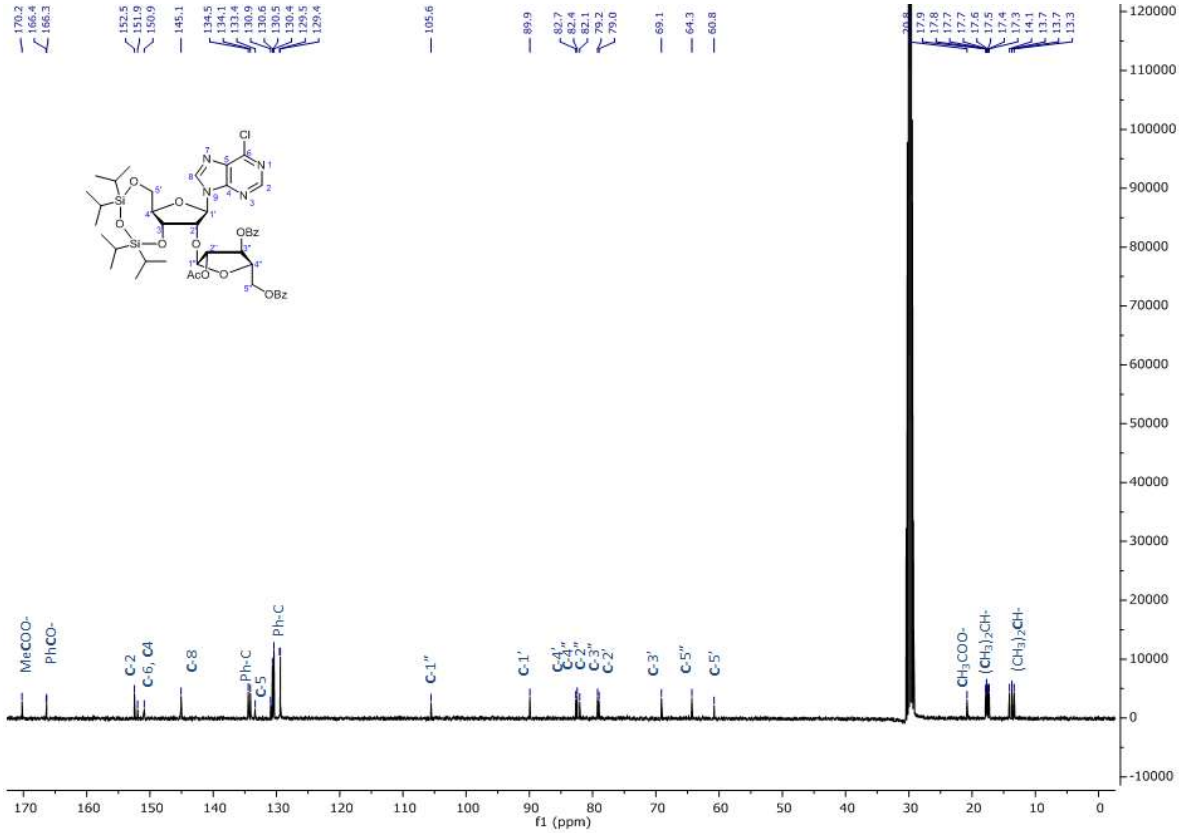
Model	DoseResp	
Equation	y = A1 + (A2-A1)/(1 + 10^((LOGx_0-x)*p))	
Reduced Chi-Sqr	12.51473	
Adj. R-Square	0.98386	
	Value	Standard Error
A1	0.18178	0.0.01805
A2	577.10001	1398.04985
LOGx_0	-295.15632	585.28031
p	-0.00226	0.00022
span	576.91823	1398.05225
IC_{50}	158.2 (µM)	17,7 (µM)

Compound **5**

^{1}H NMR

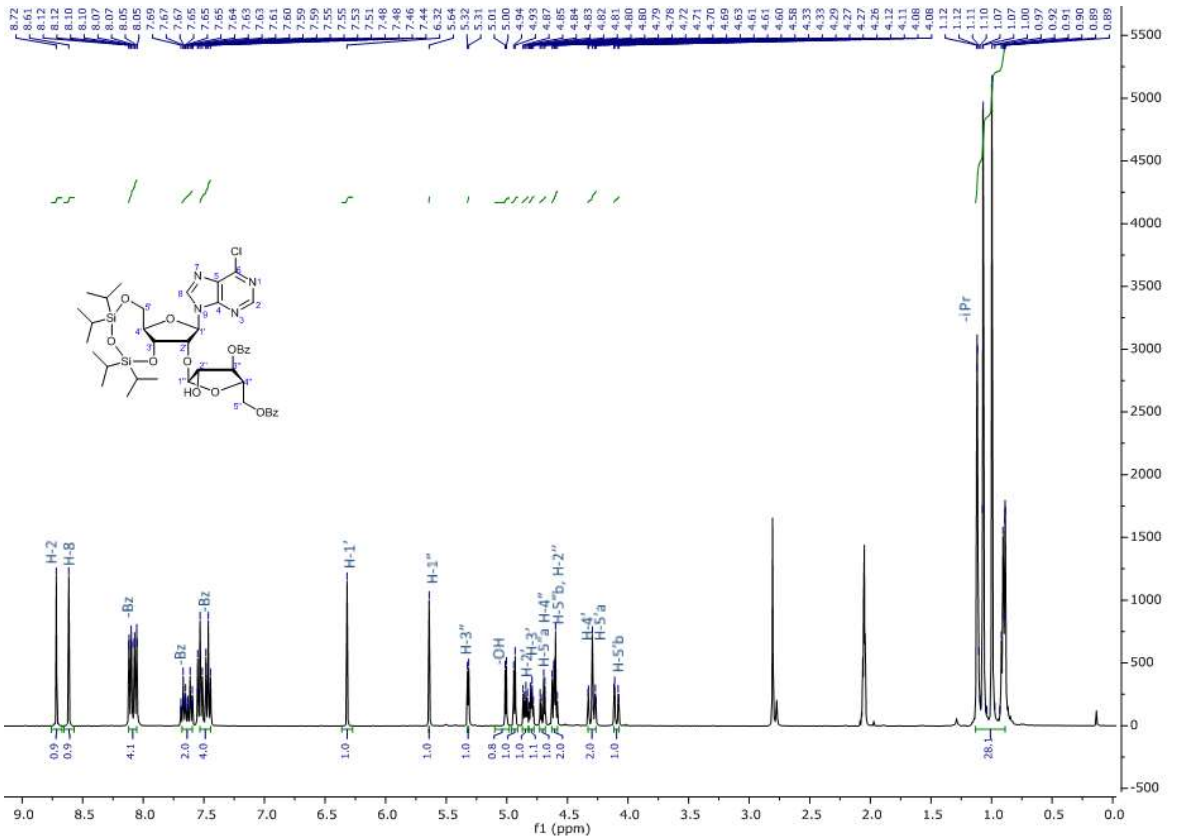


^{13}C NMR



Compound **6**

^{1}H NMR



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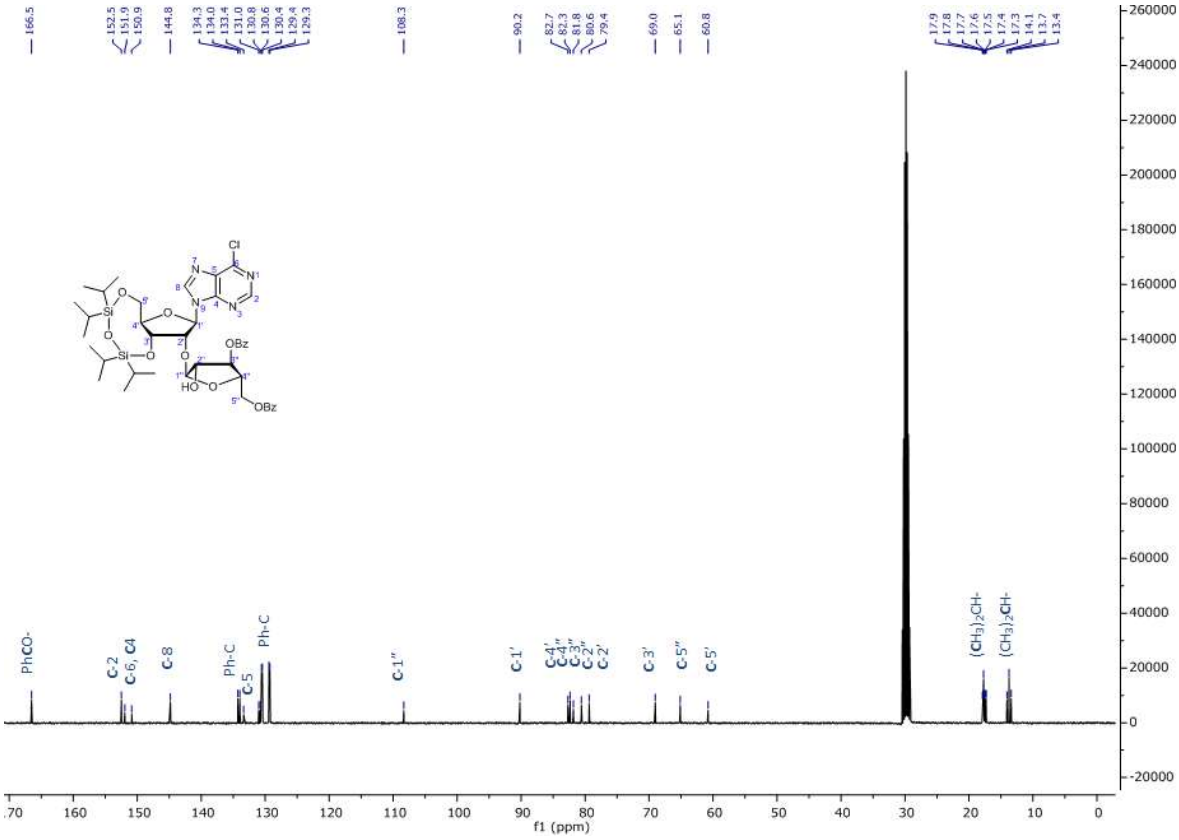

Compound **7**

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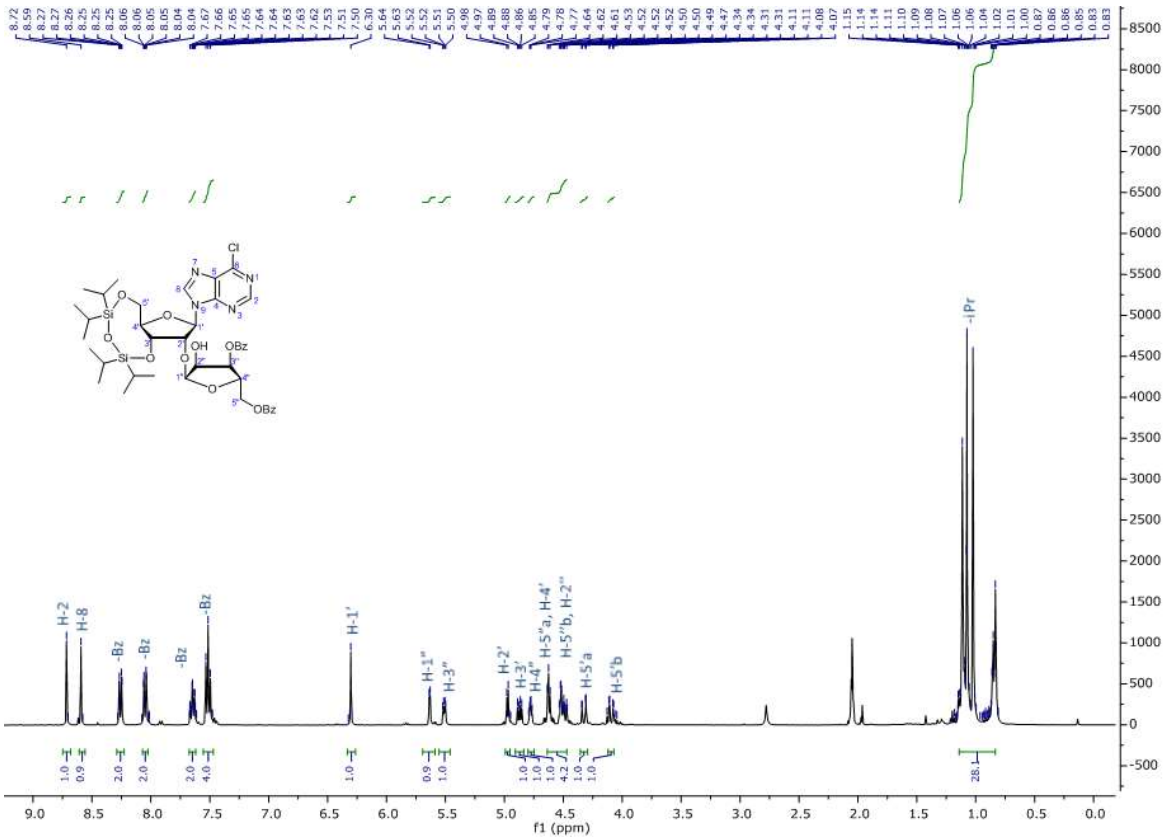

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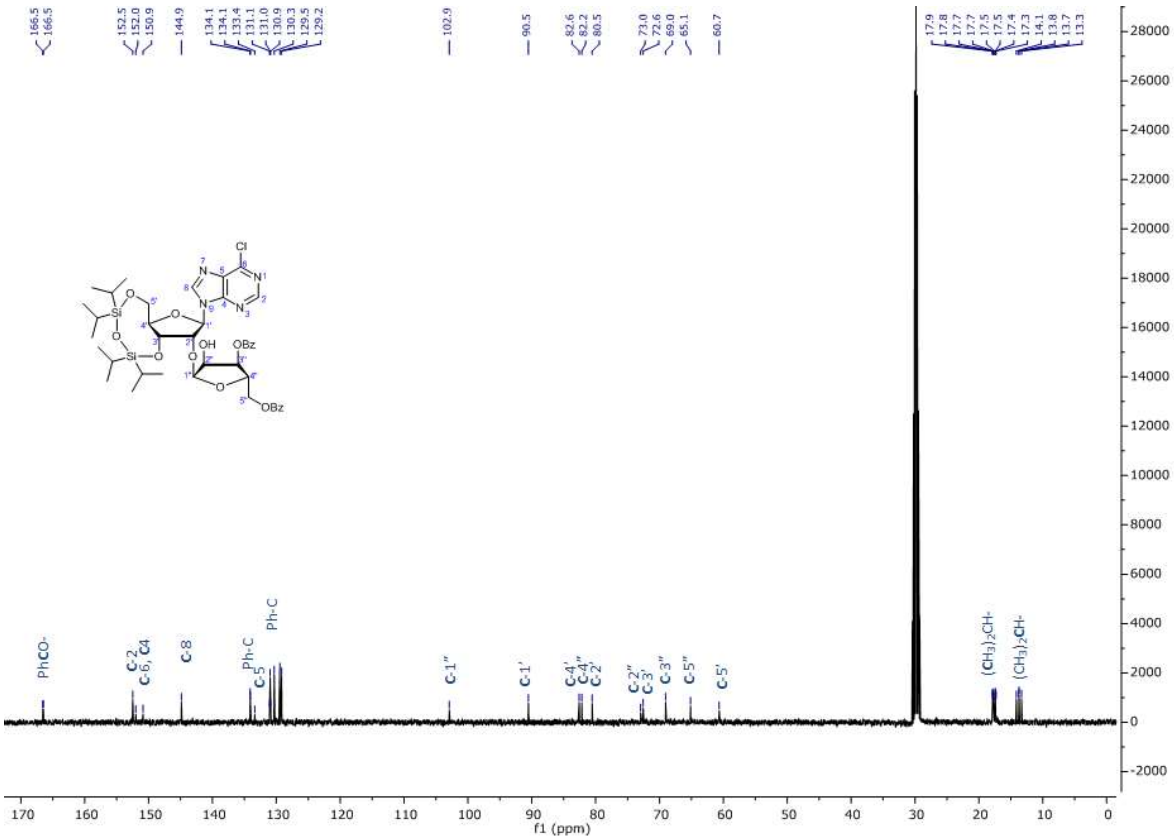
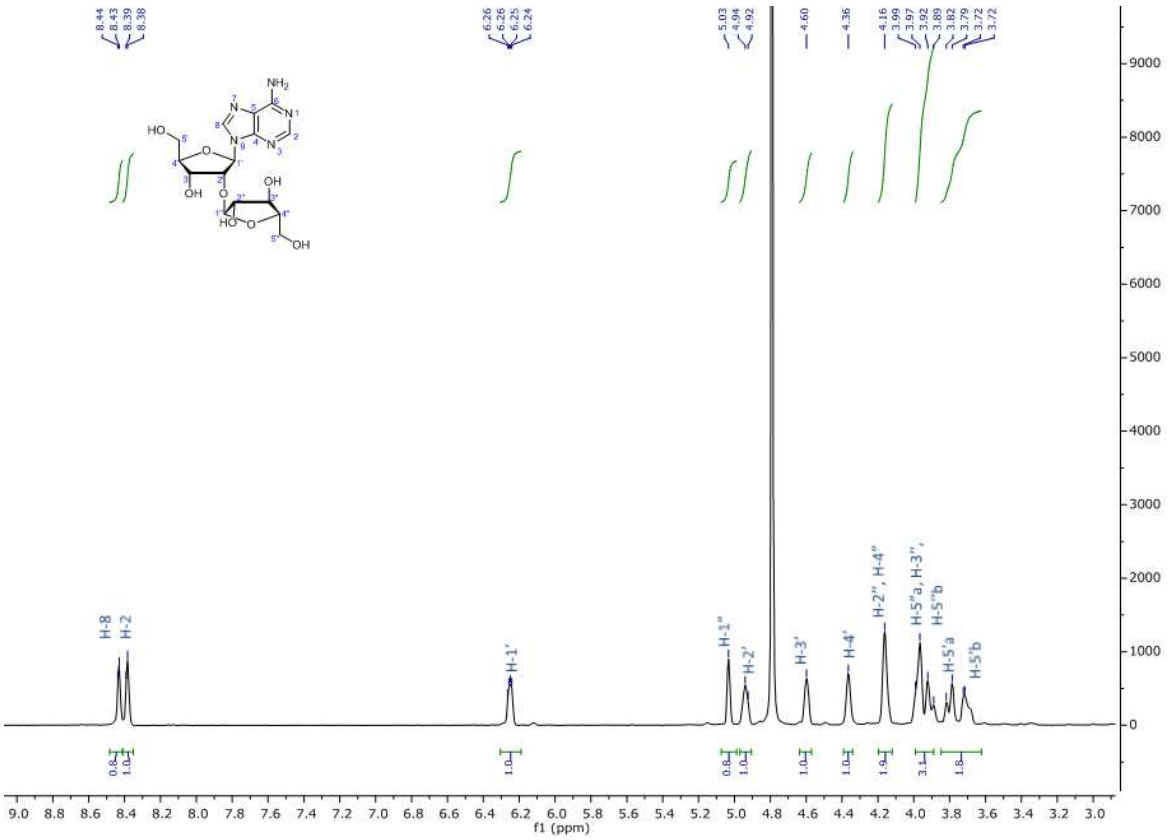


Compound **1a**

^{1}H NMR



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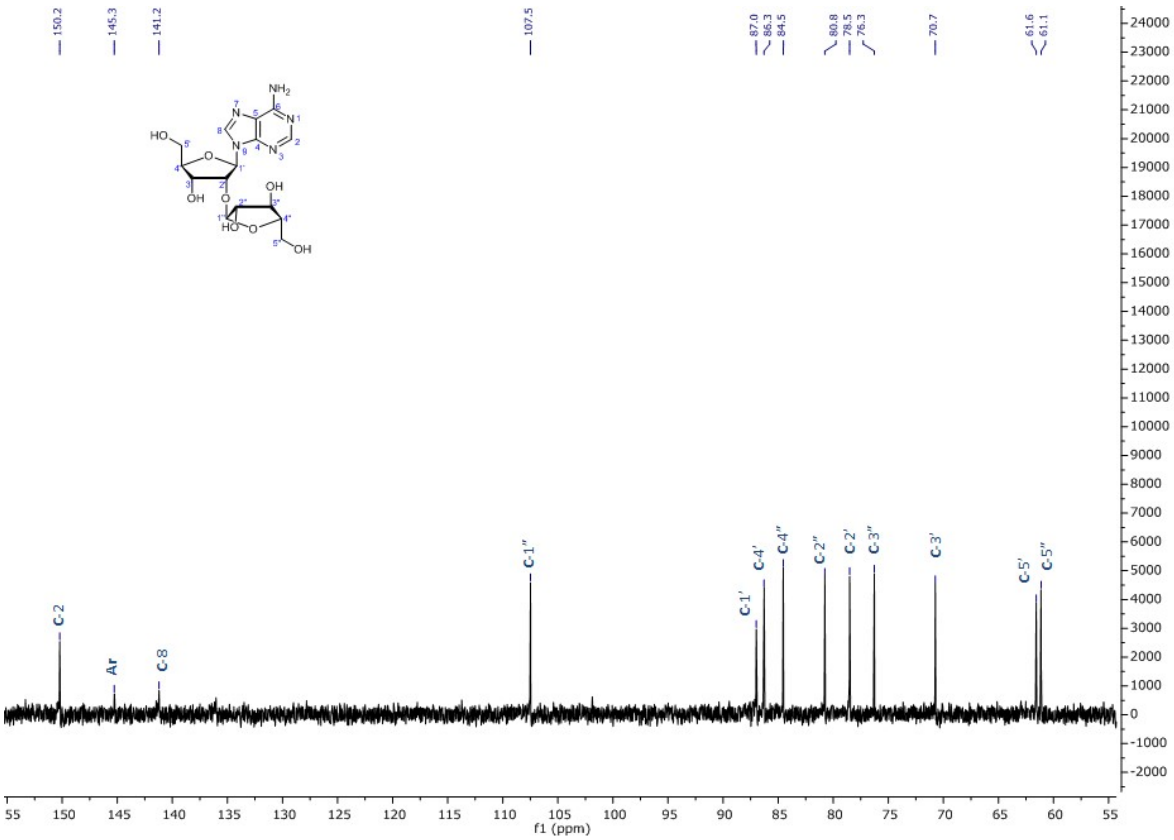
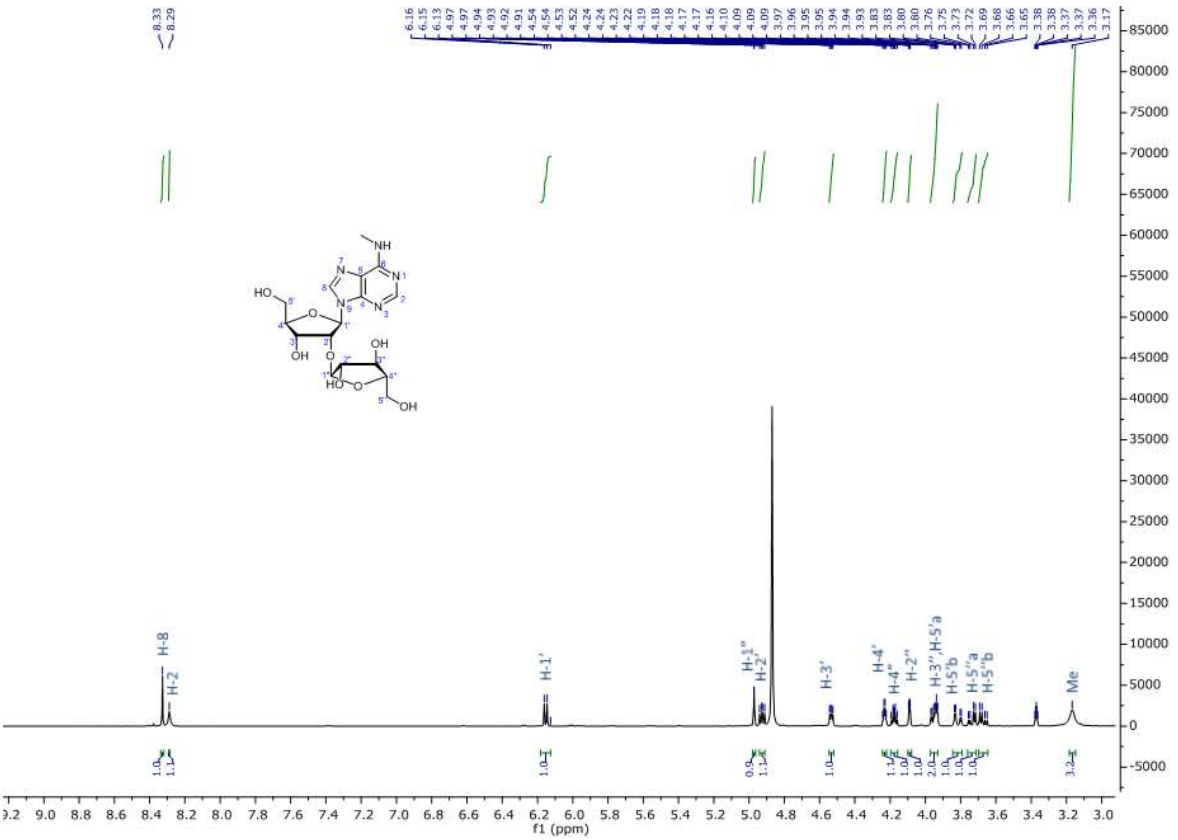


Compound **1b**

^{1}H NMR



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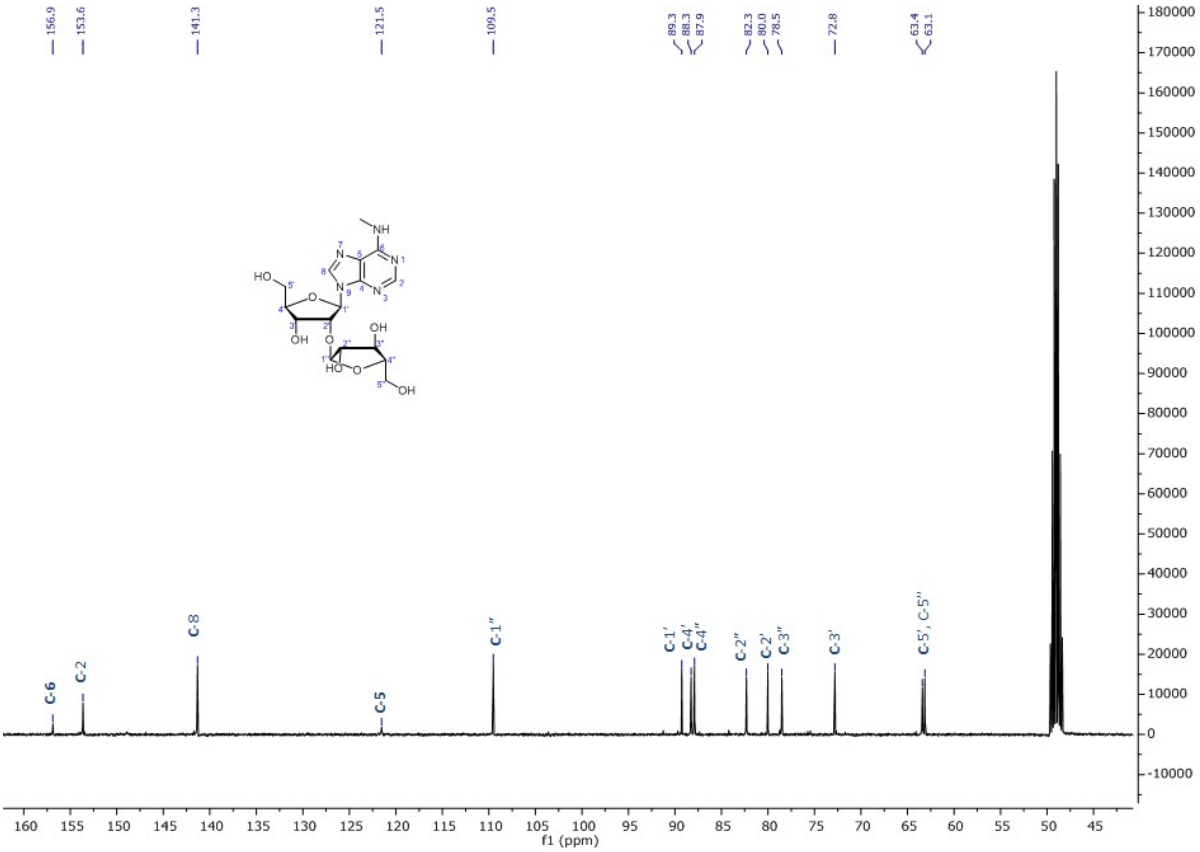

Compound **1c**

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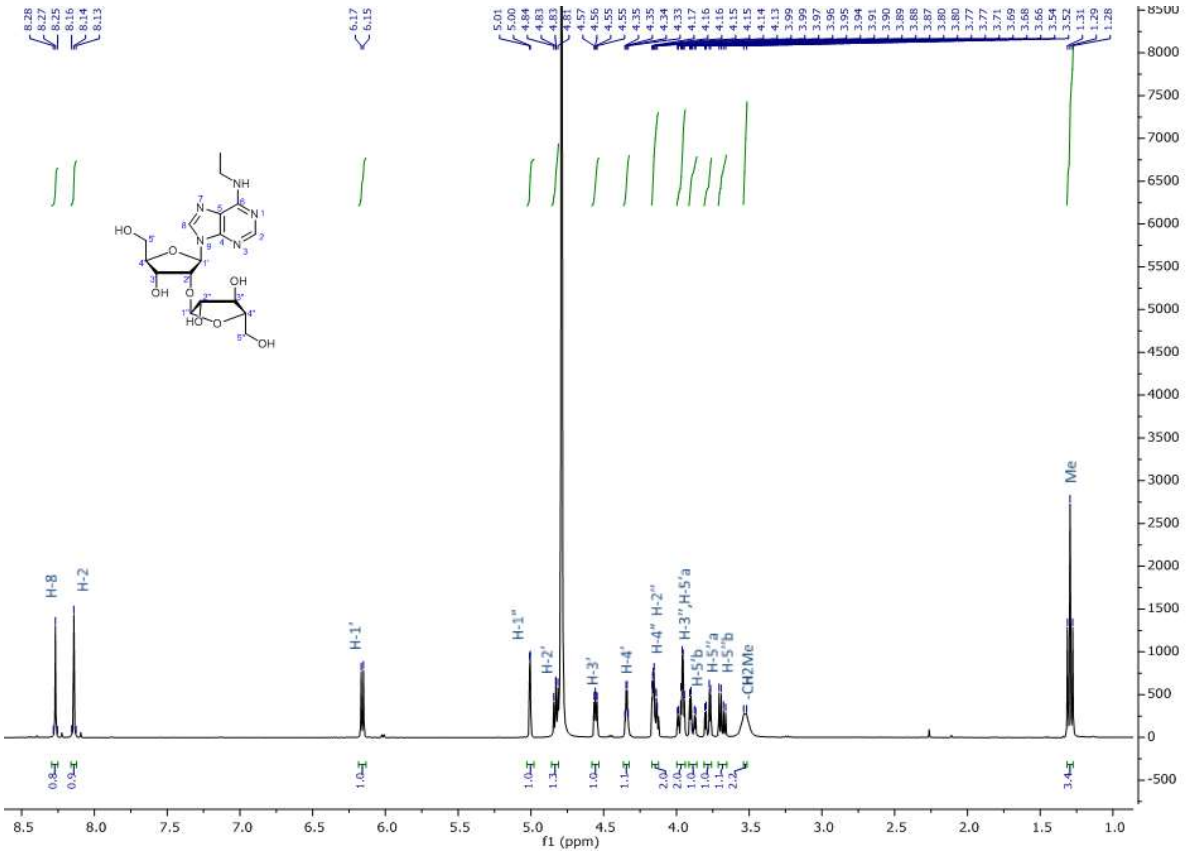

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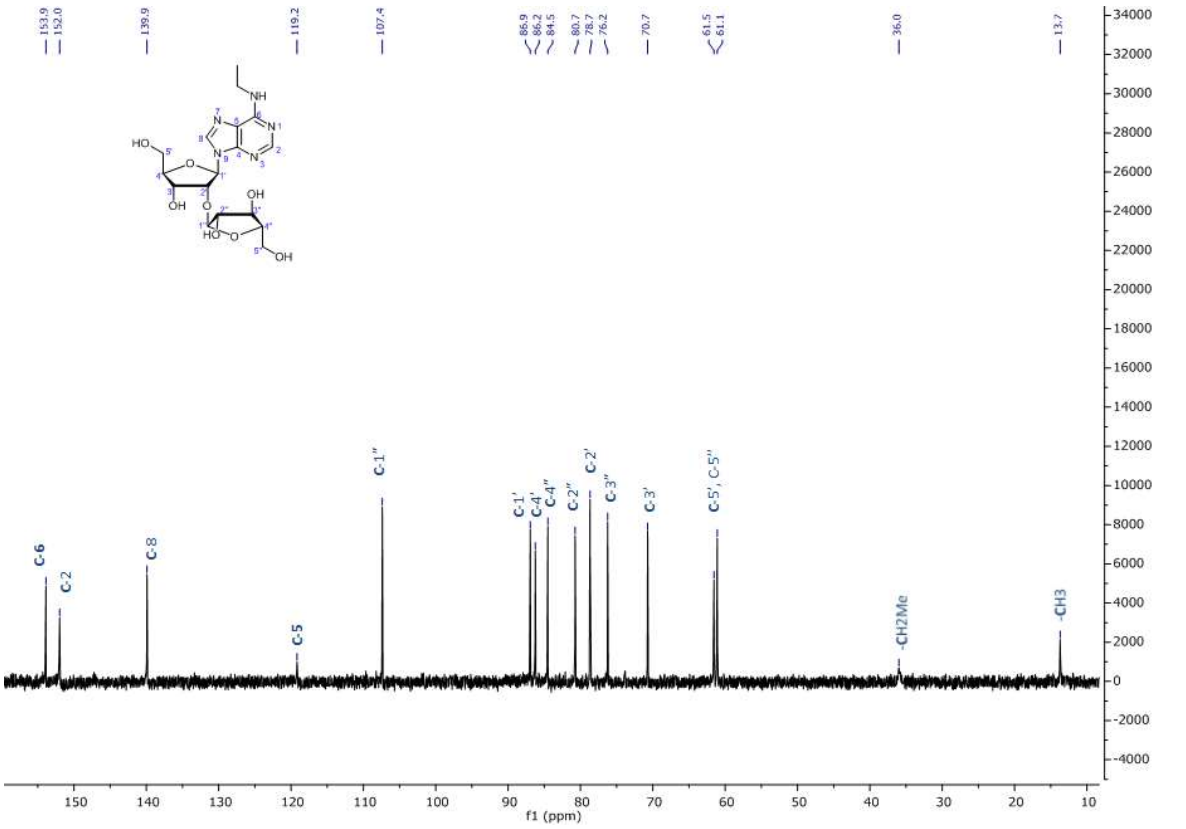

Compound **1d**

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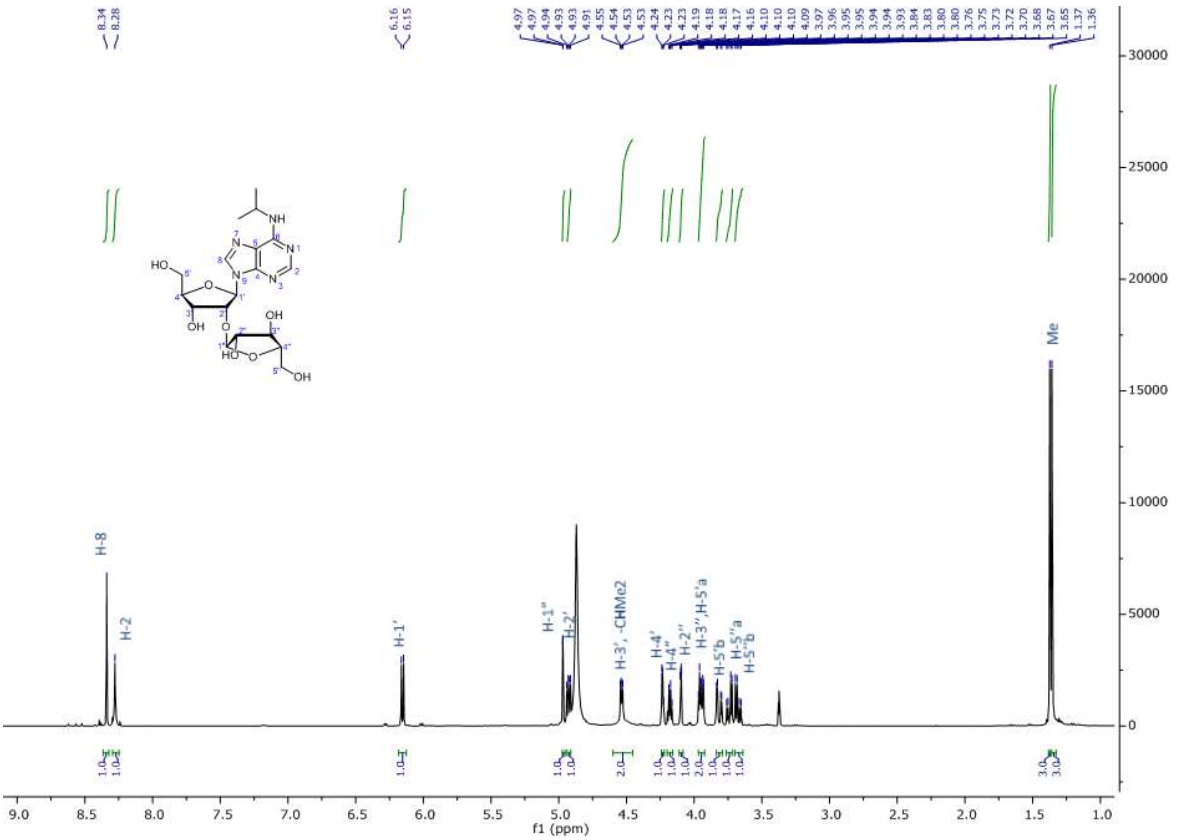

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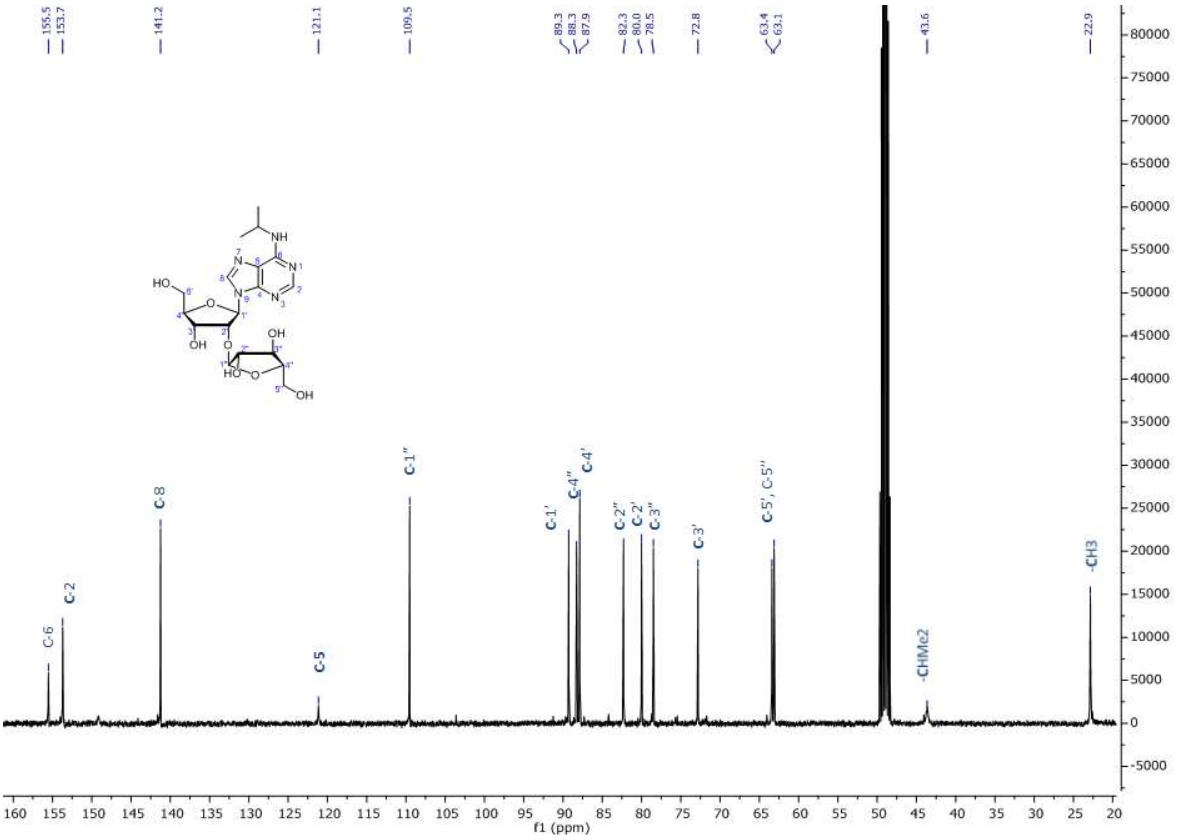
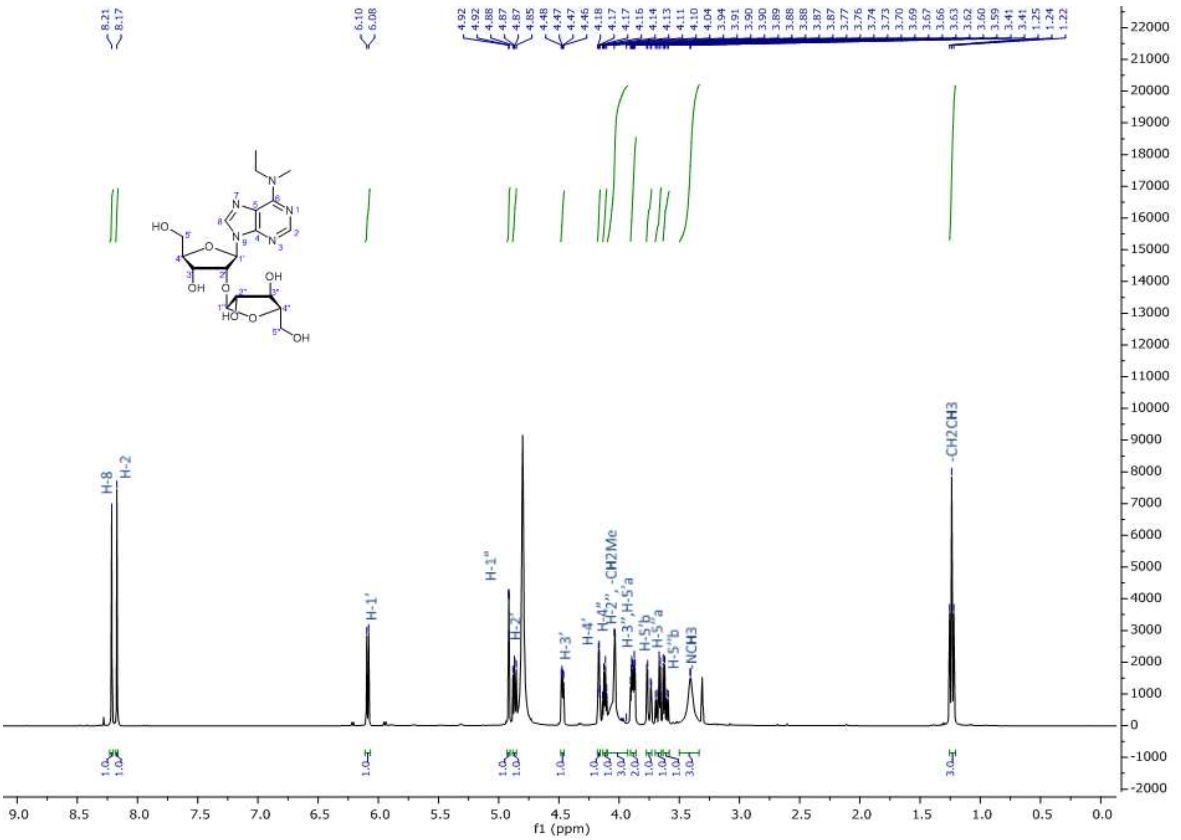


Compound **1e**

^{1}H NMR



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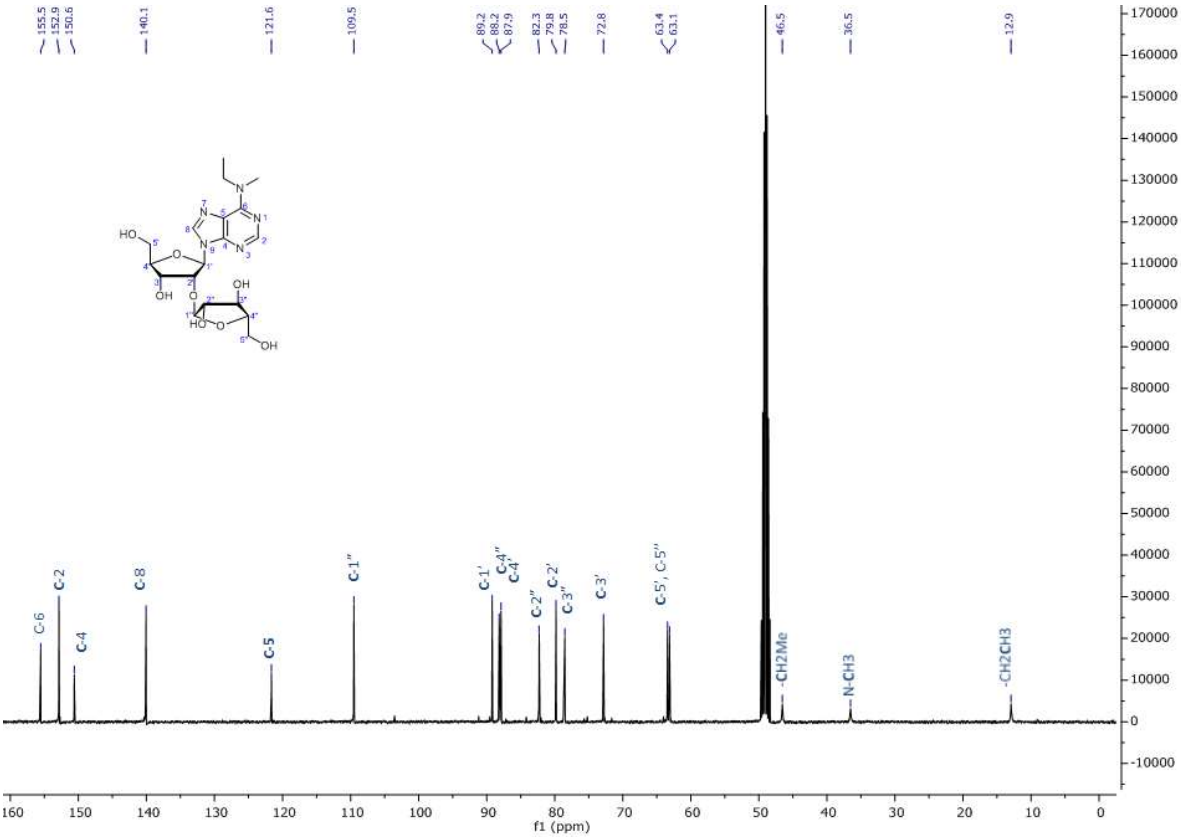

Compound **1f**

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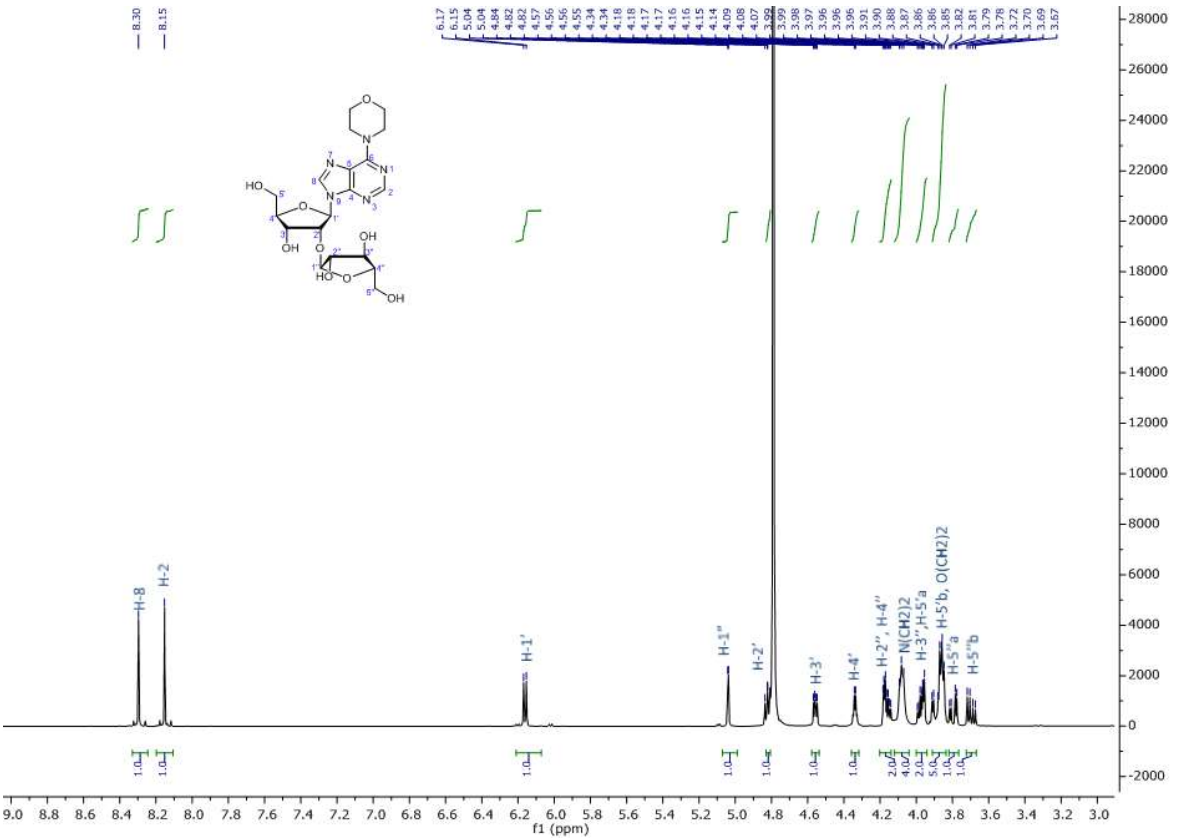
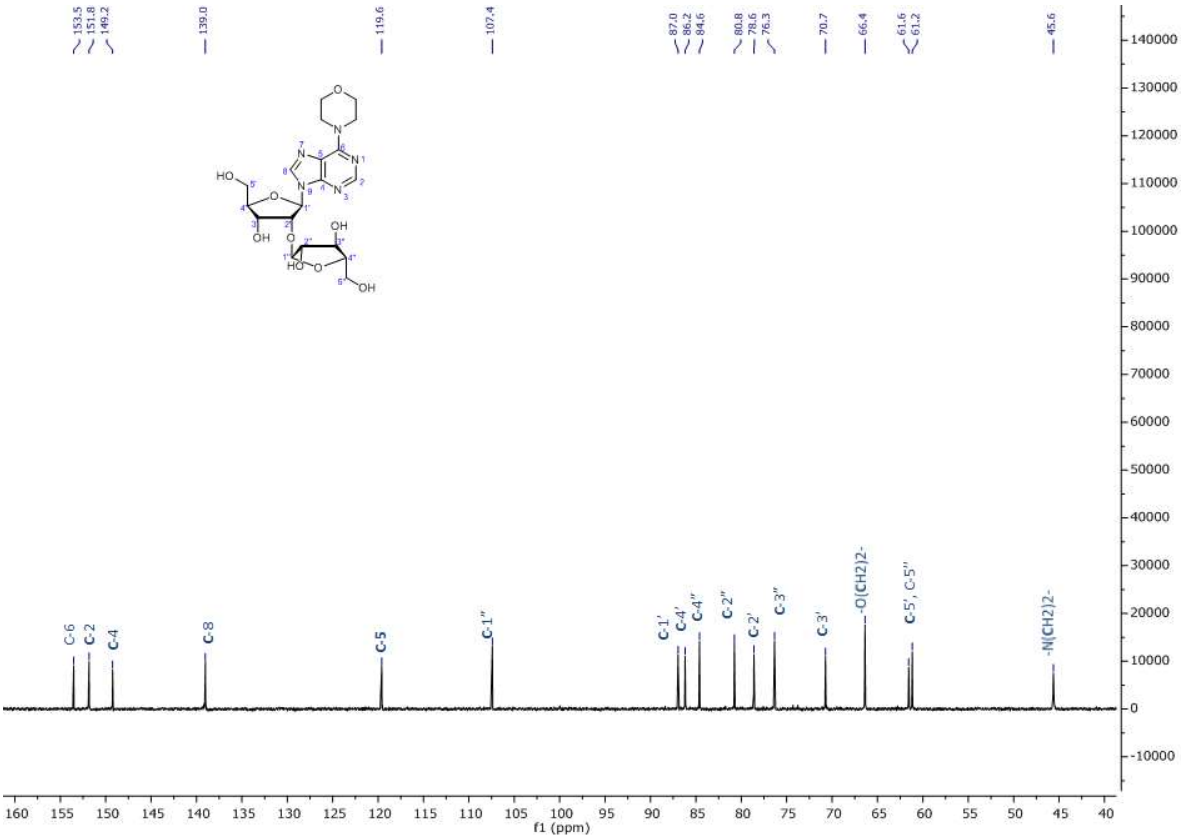
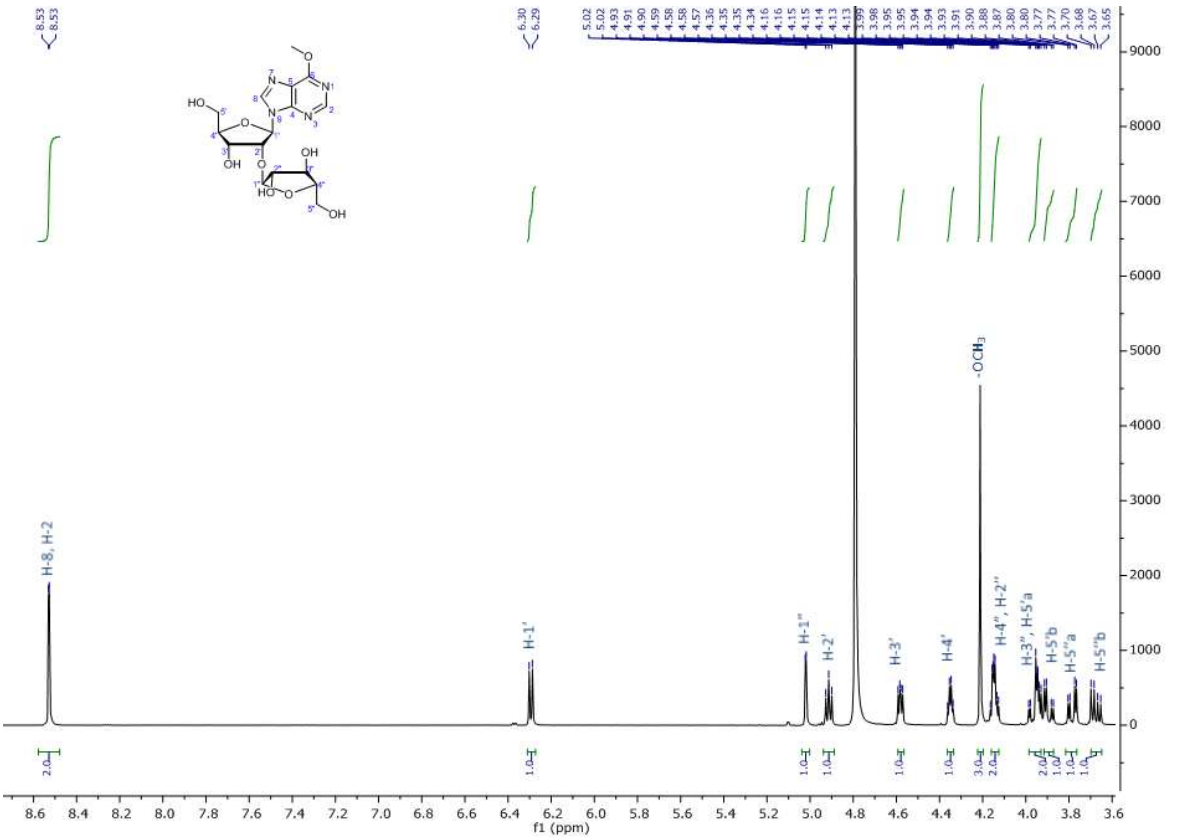


^{13}C NMR



Compound **1g**

^{1}H NMR



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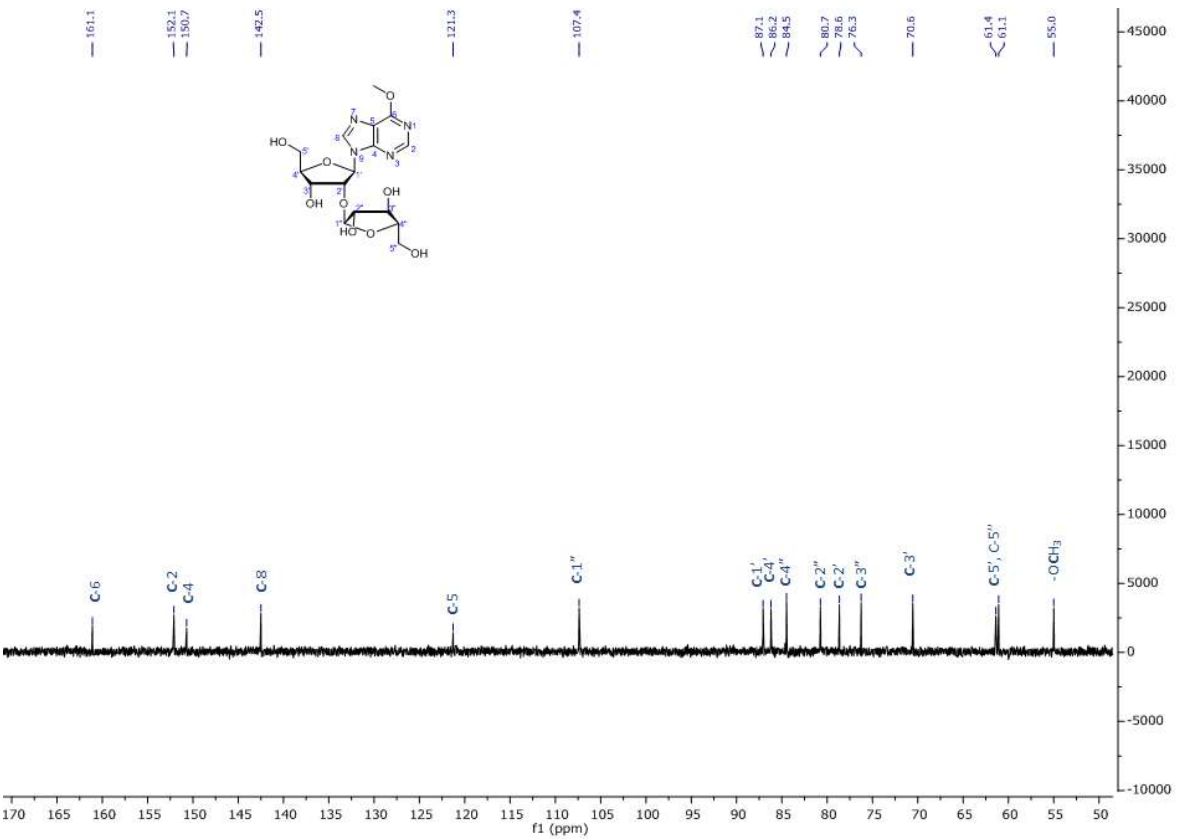
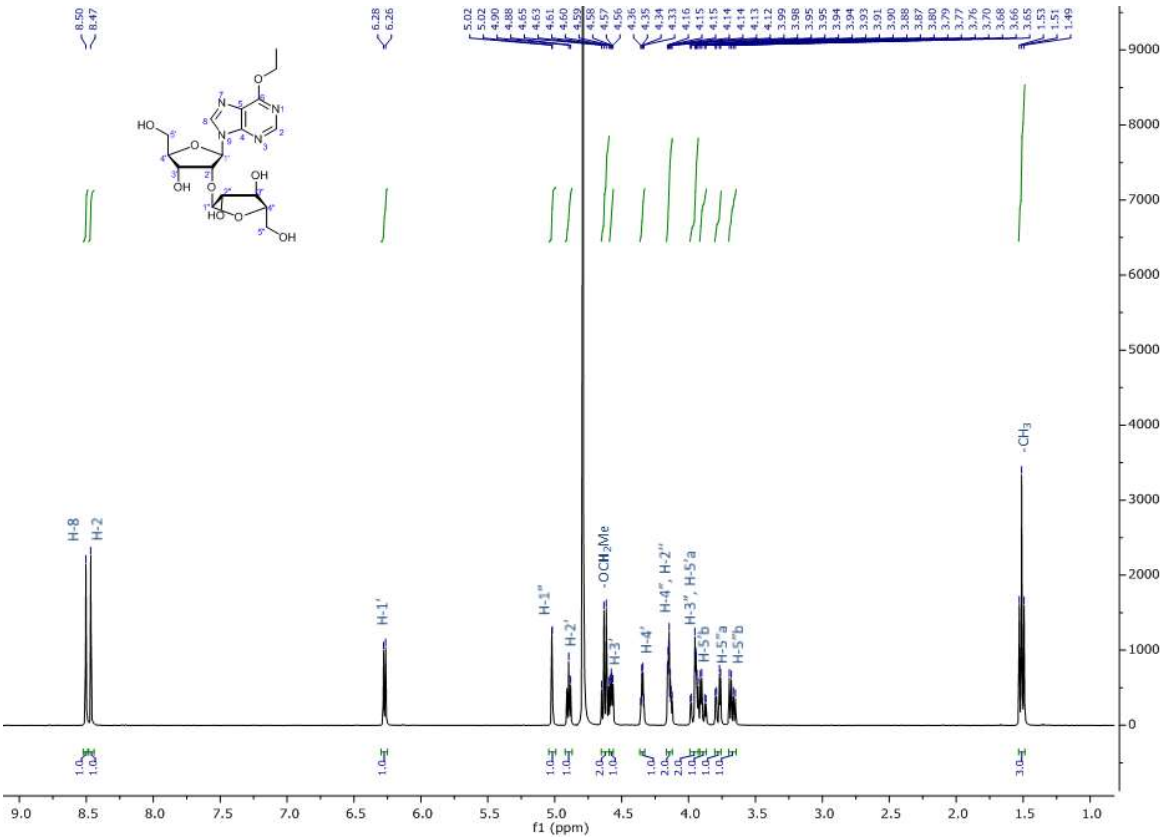


Compound **1h**

^{1}H NMR



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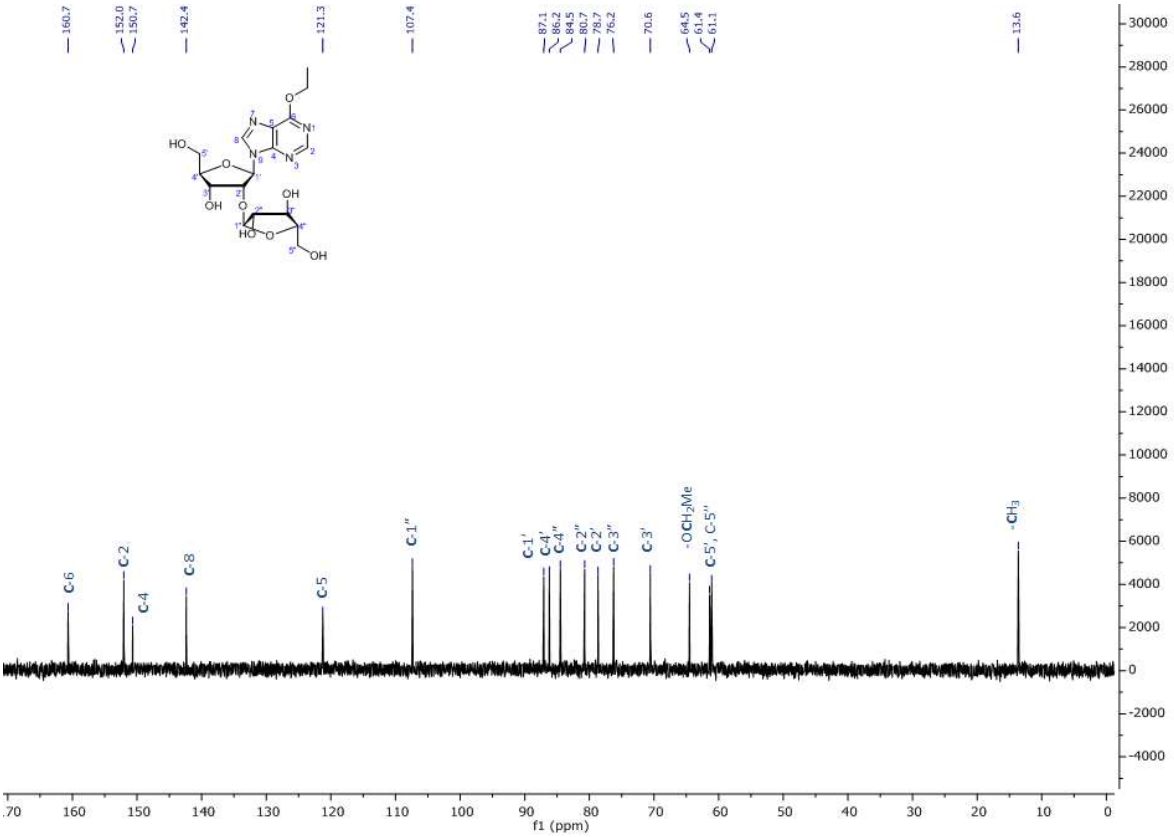
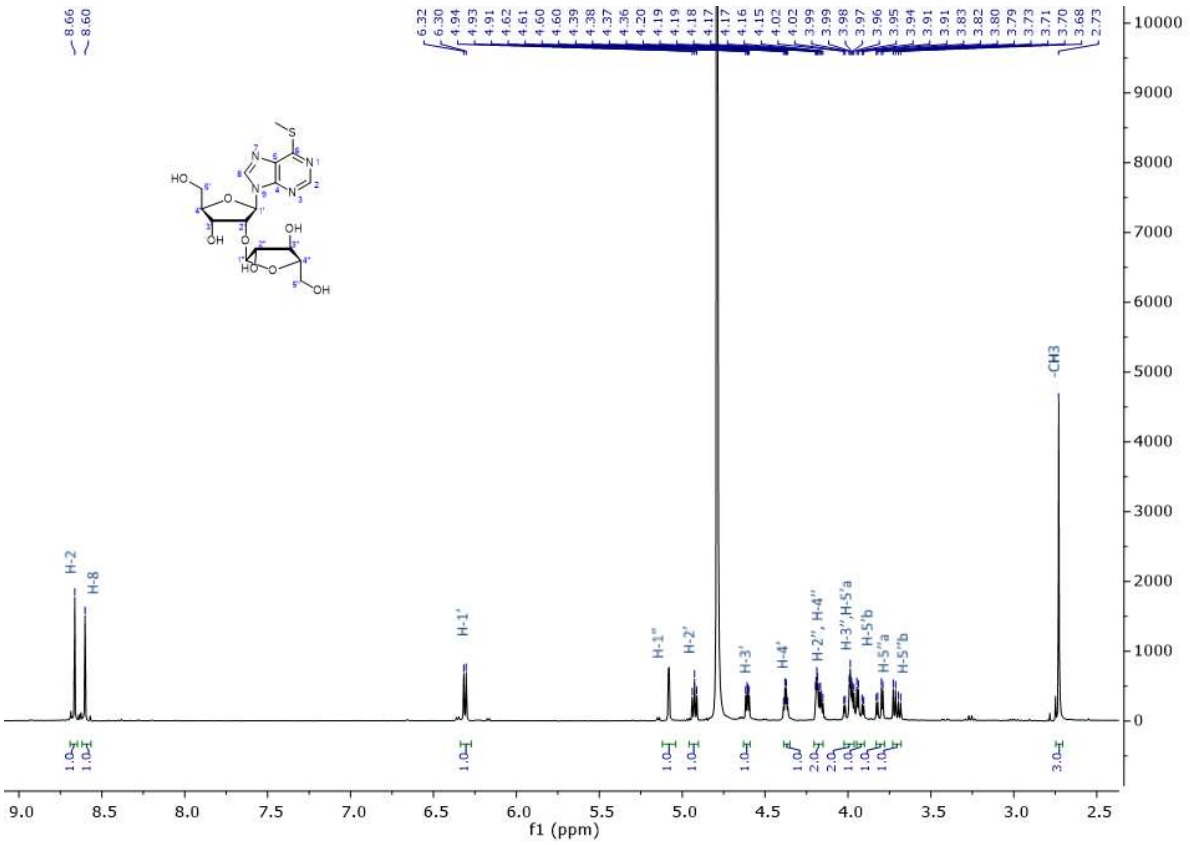


Compound **1i**

^{1}H NMR



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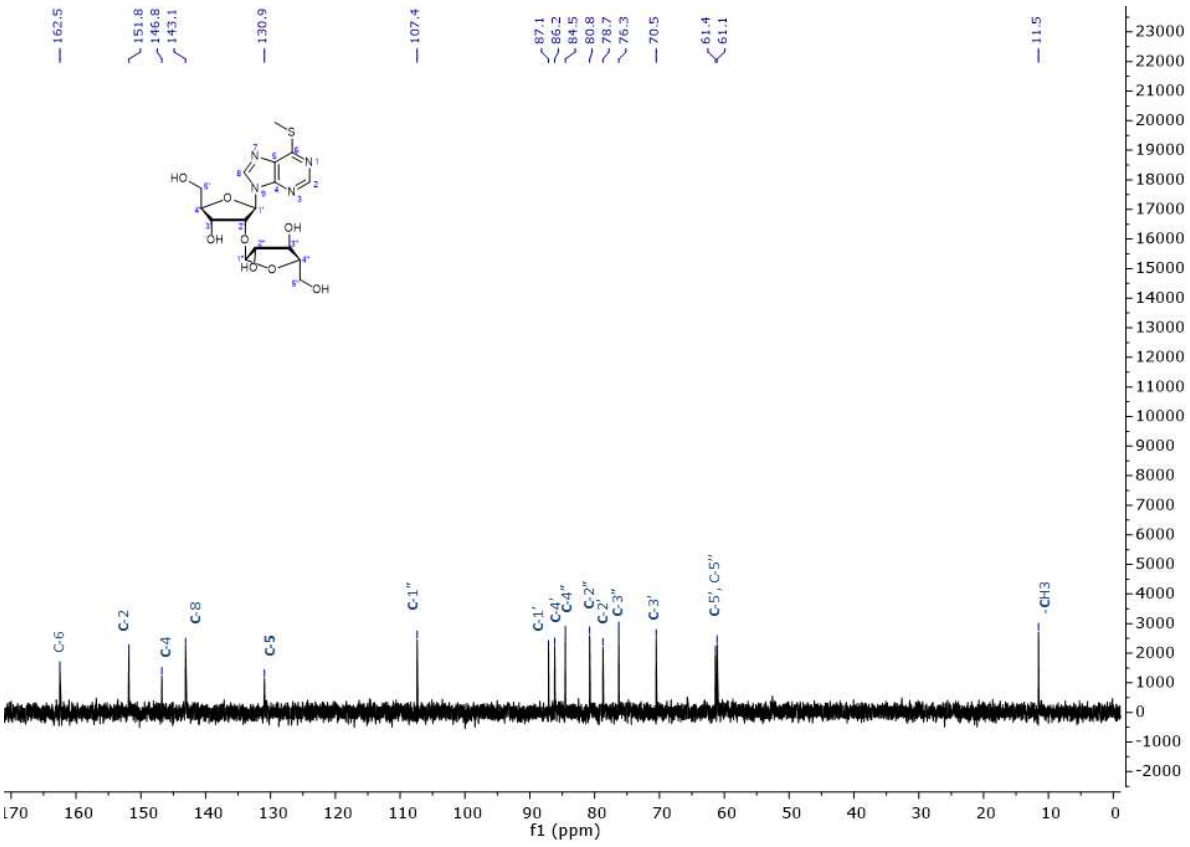
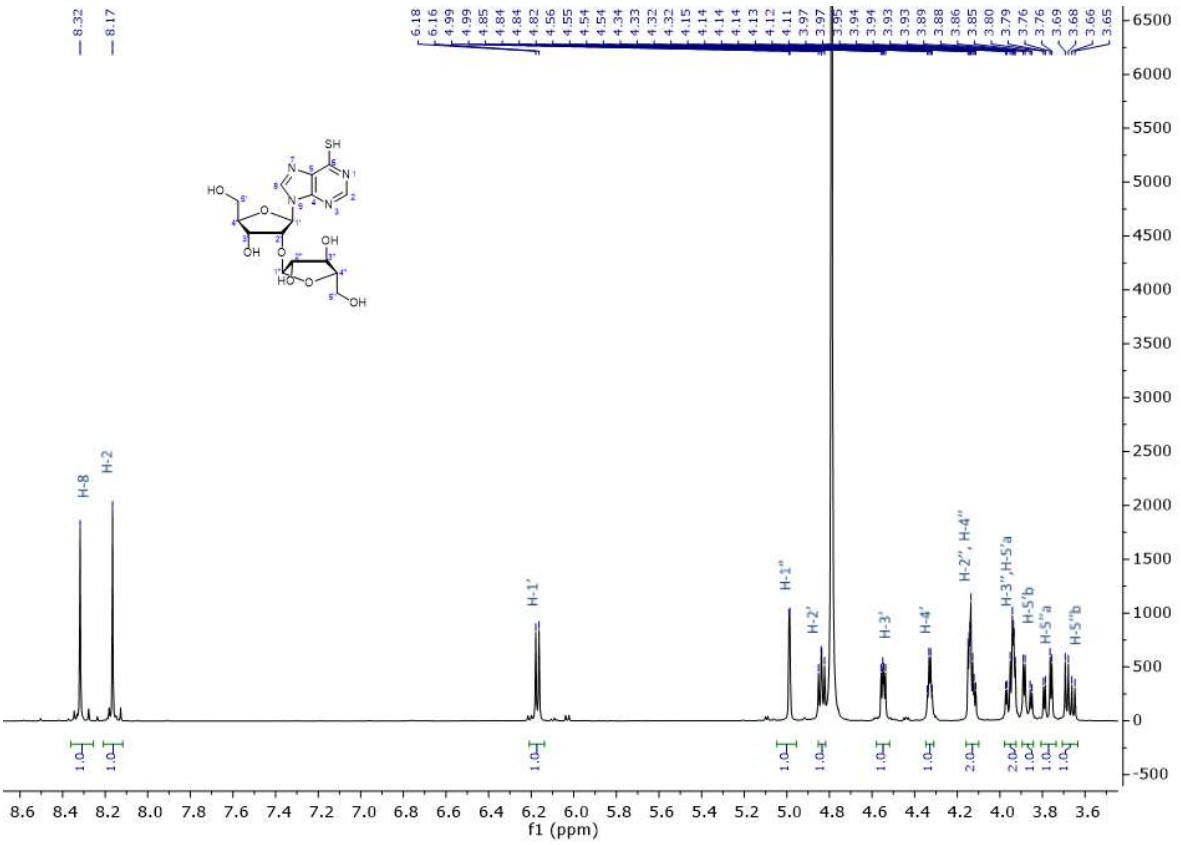


Compound **1j**

^{1}H NMR



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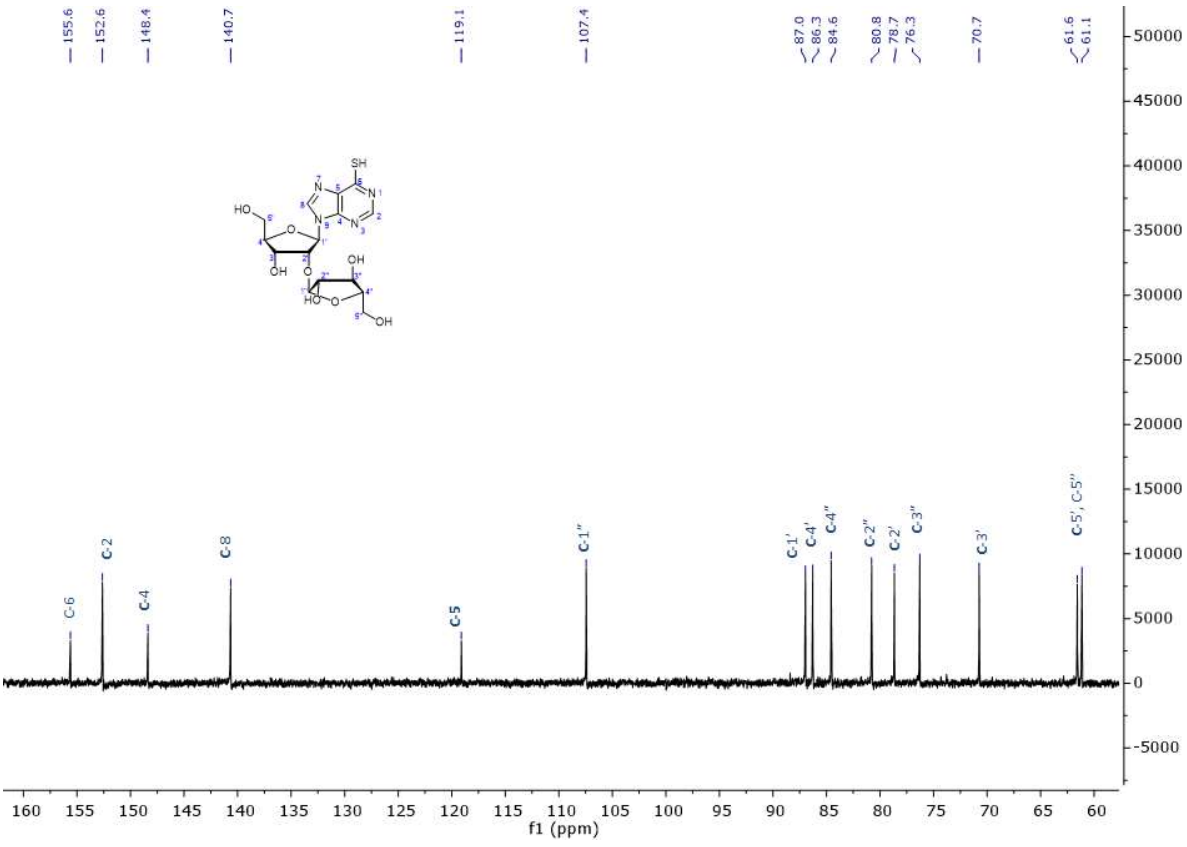
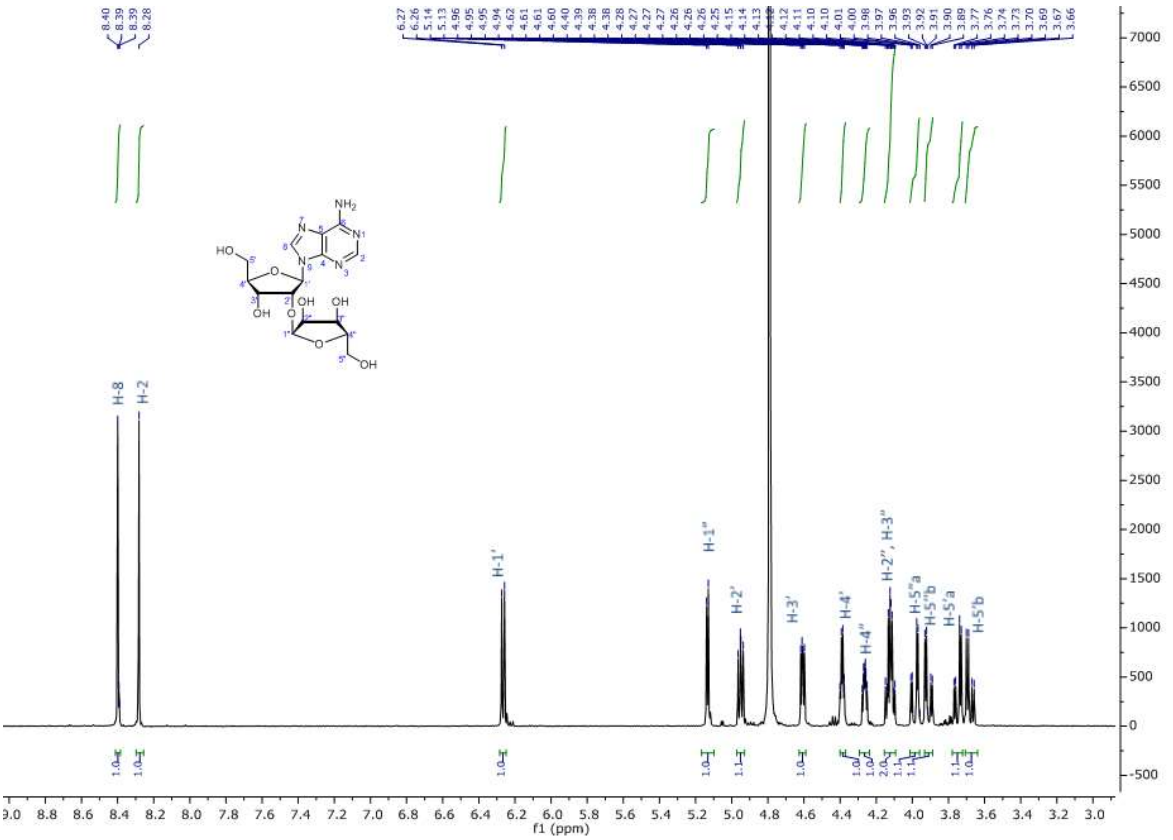
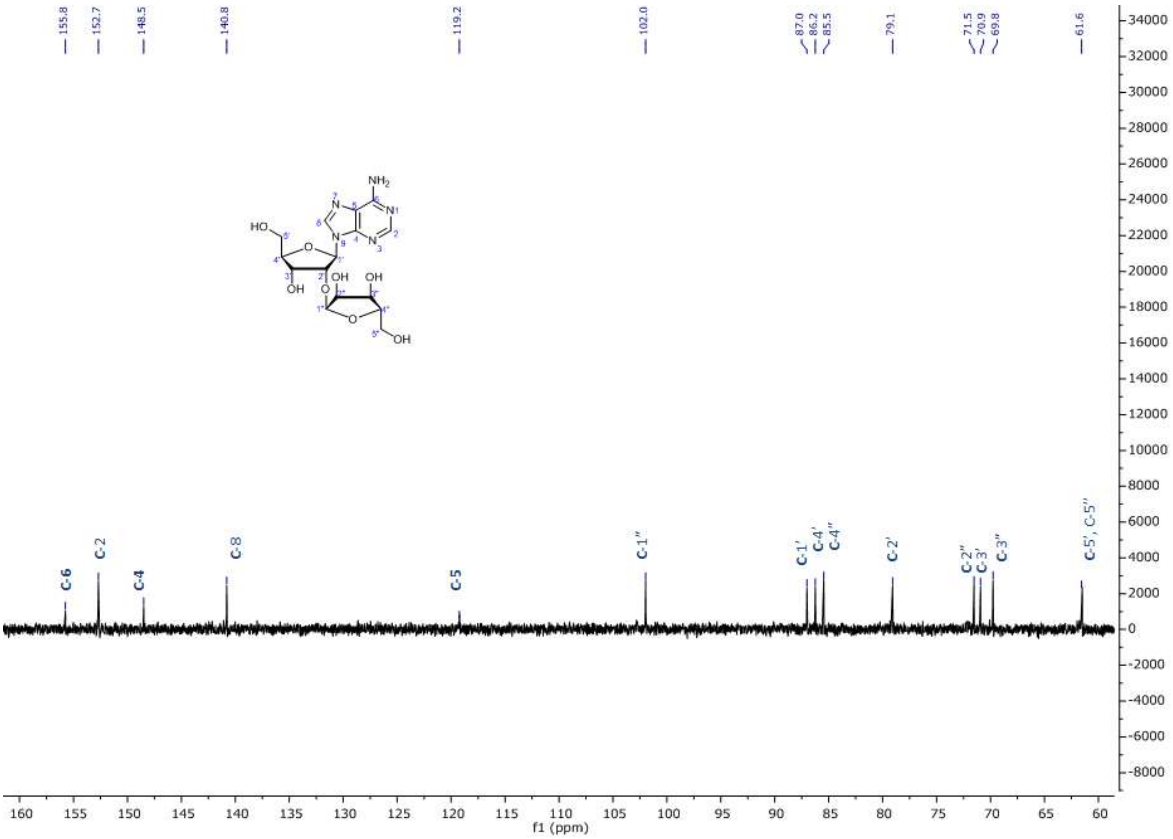


Compound **2a**

^{1}H NMR

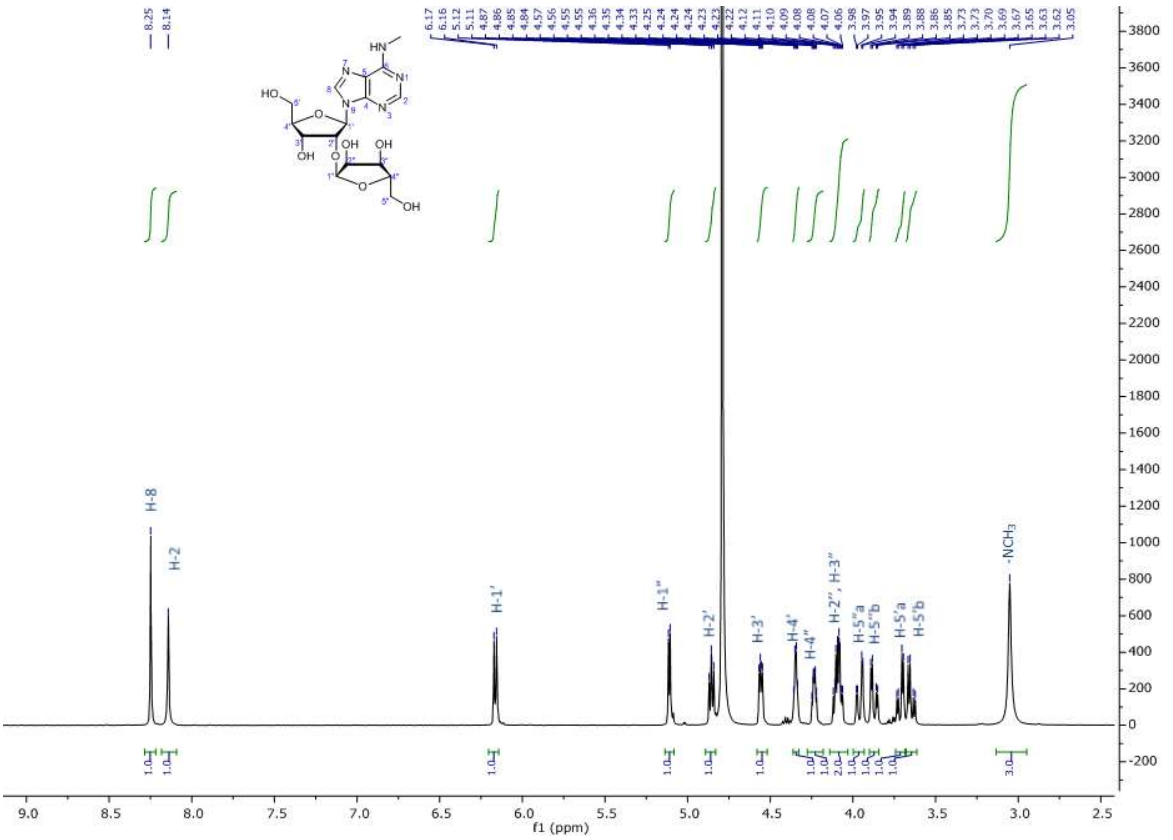


^{13}C NMR

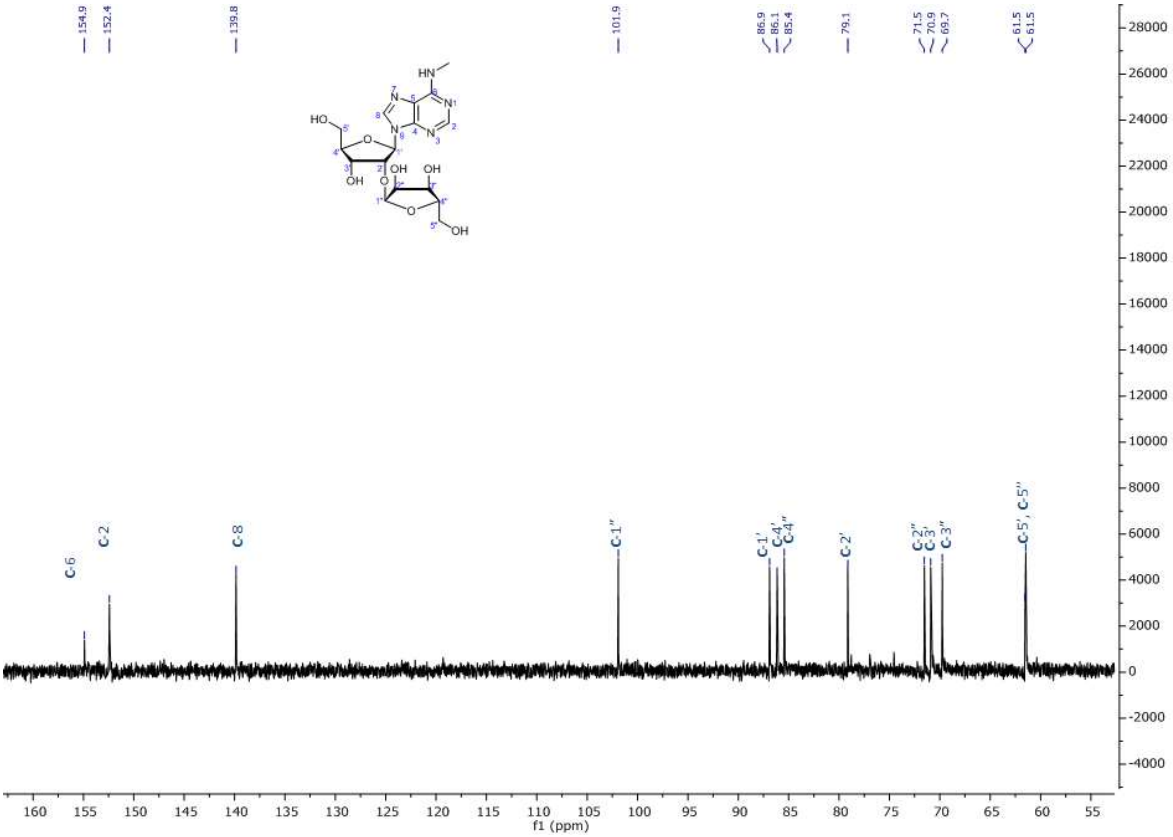


Compound **2b**

^{1}H NMR

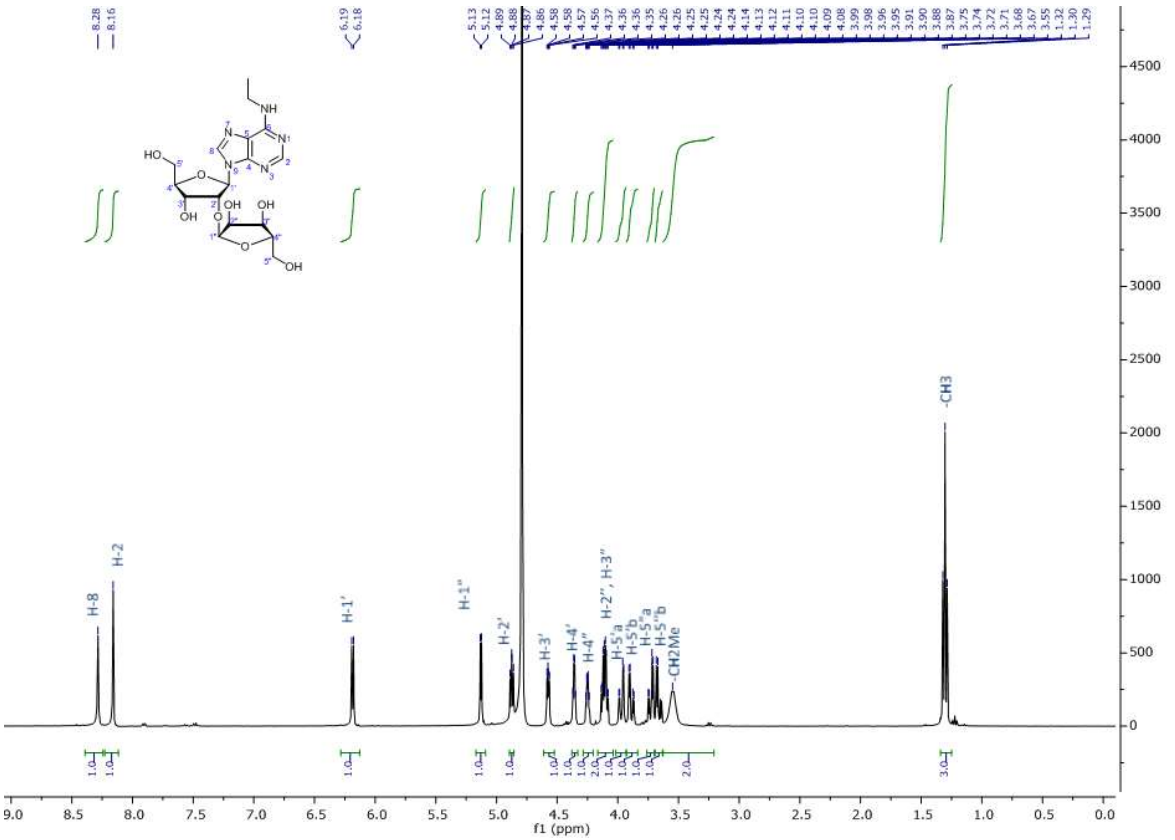


^{13}C NMR

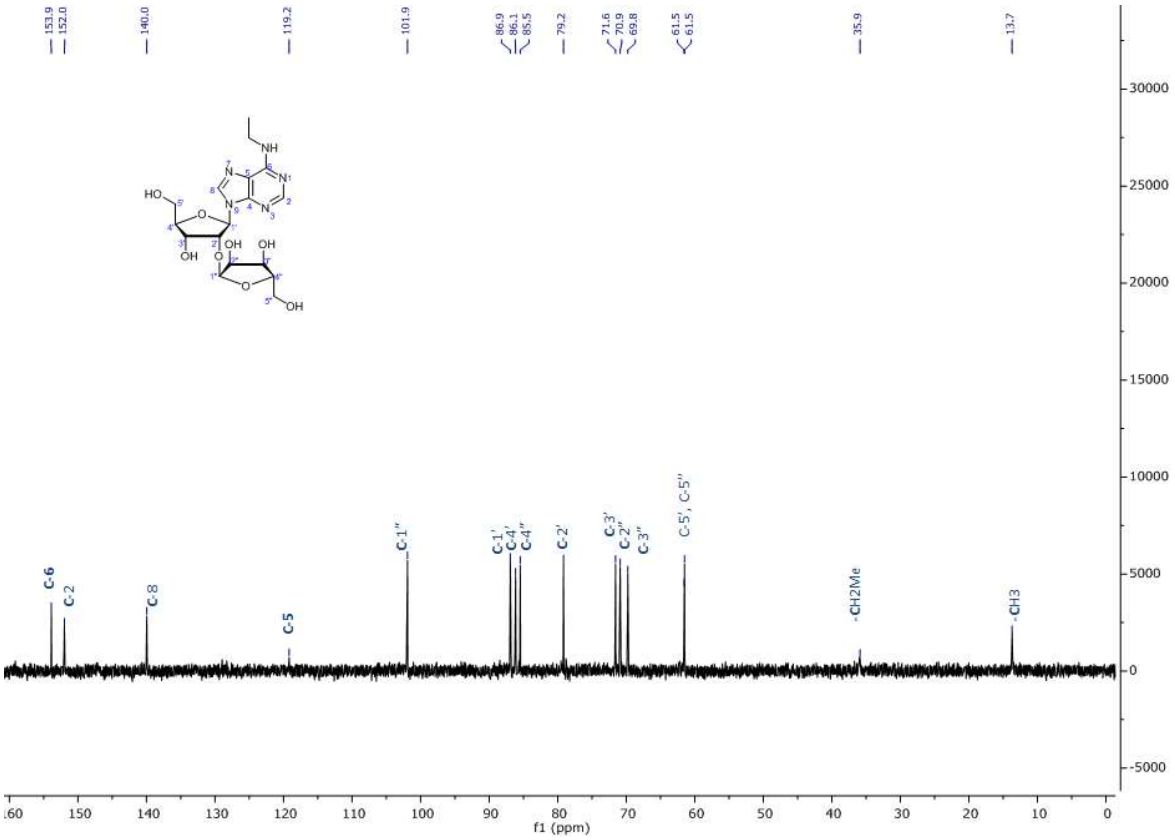


Compound **2c**

^{1}H NMR

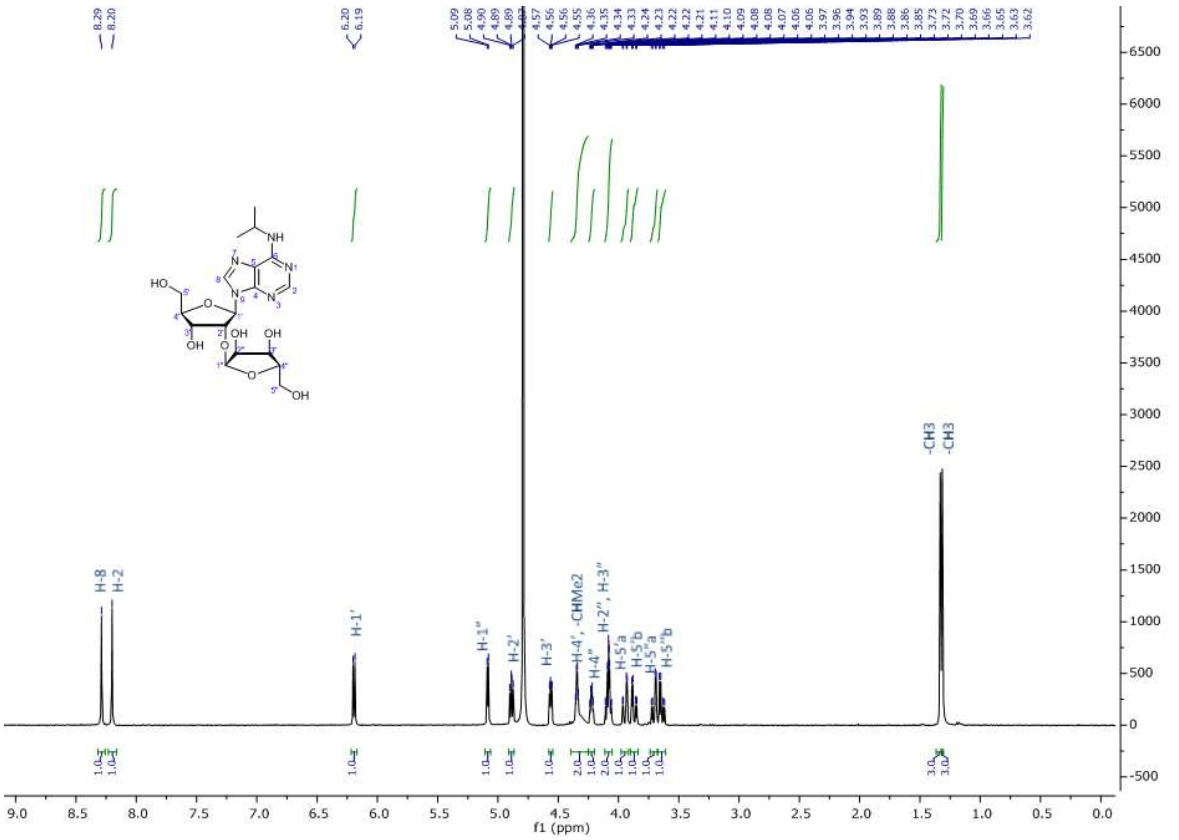


^{13}C NMR

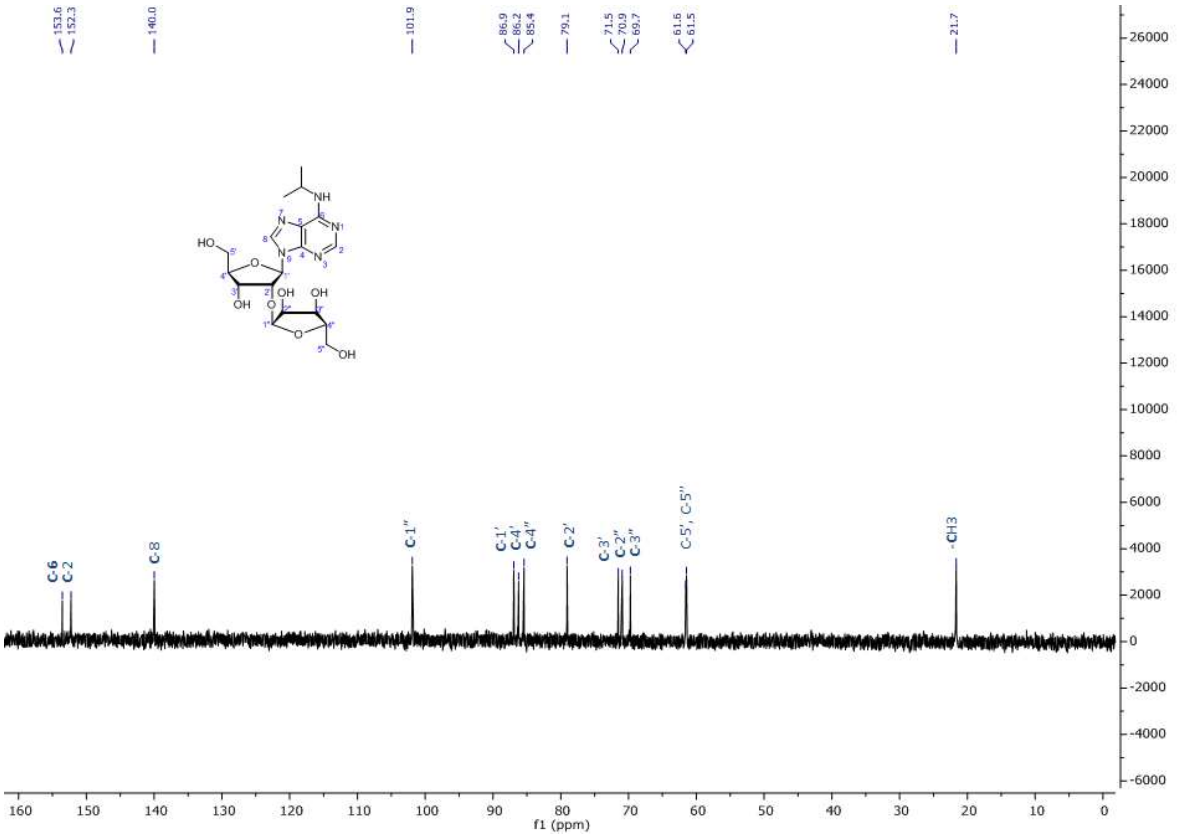


Compound **2d**

^{1}H NMR

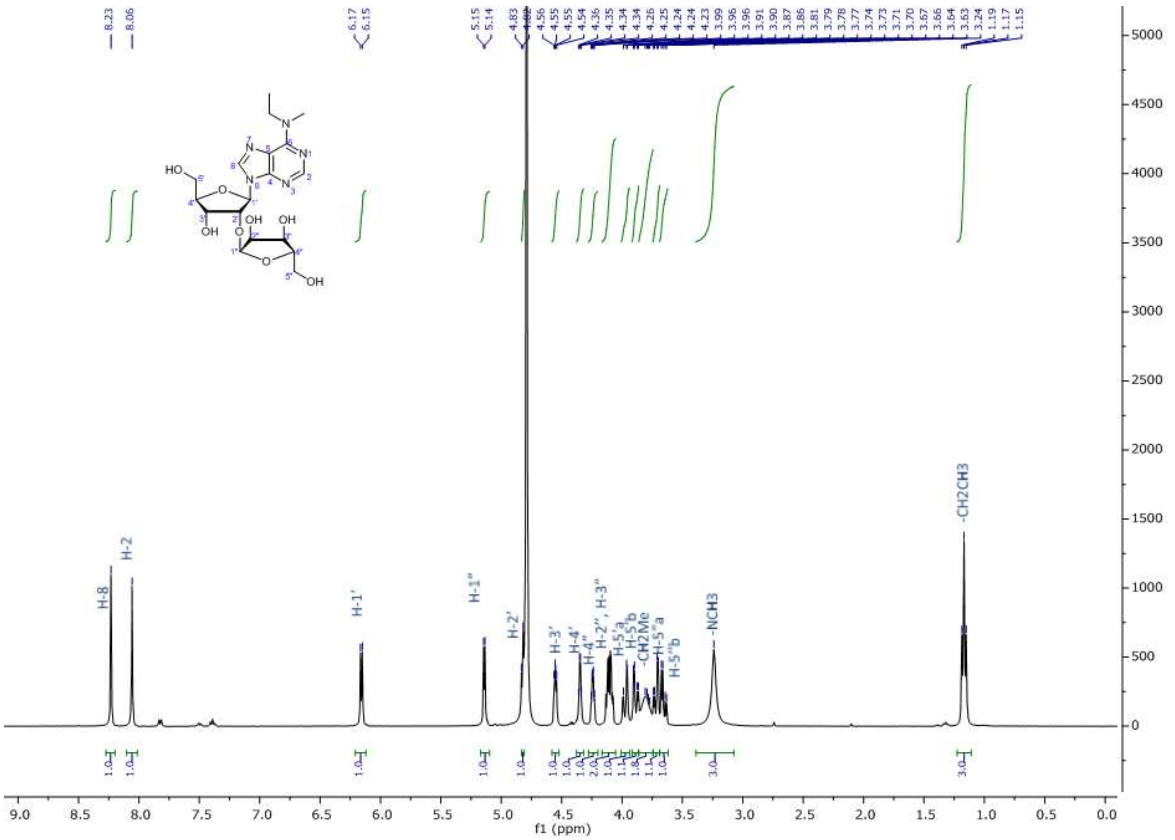


^{13}C NMR



Compound **2e**

^{1}H NMR



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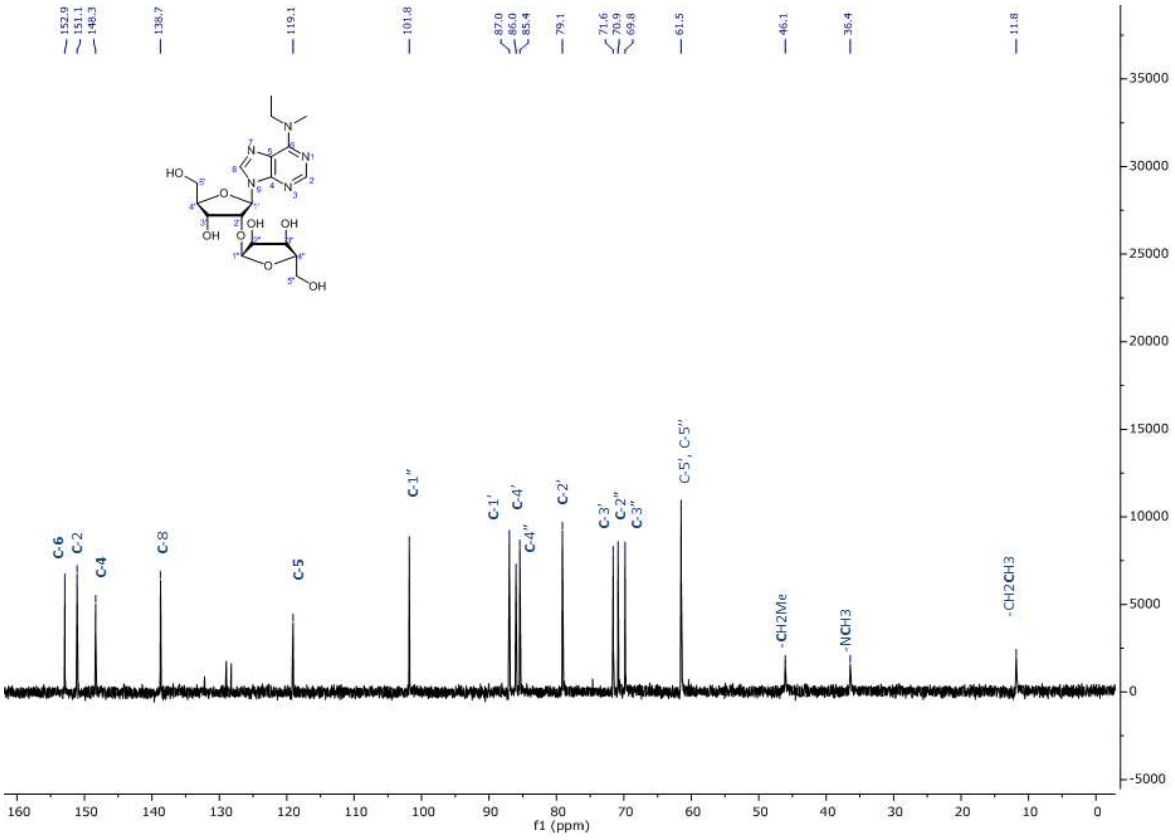
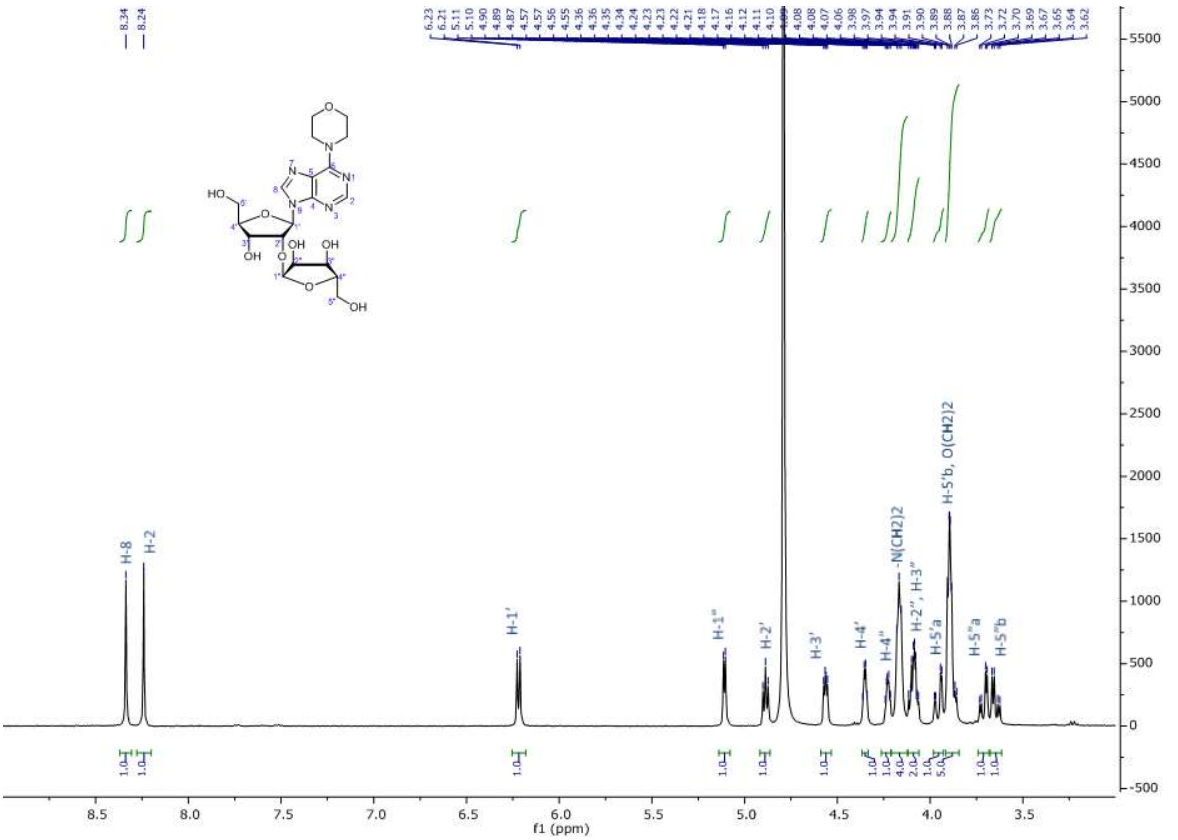
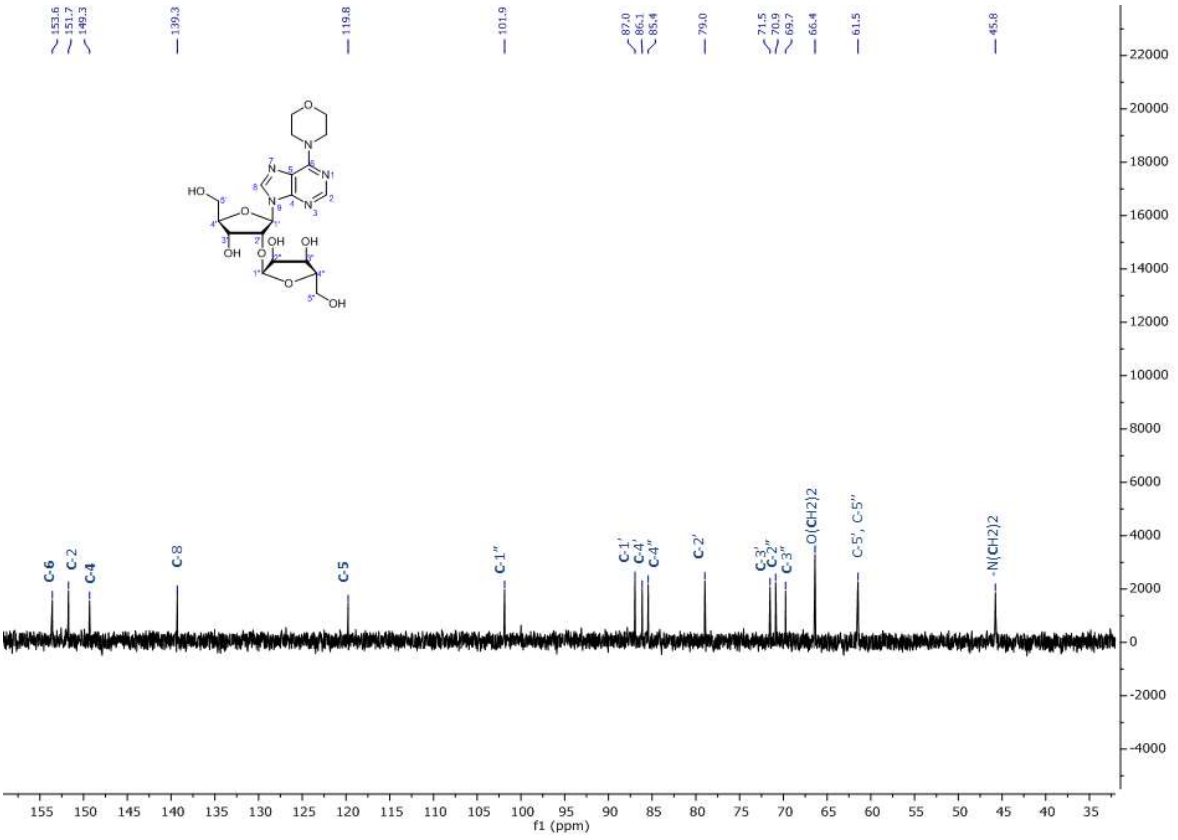


Compound **2f**

^{1}H NMR

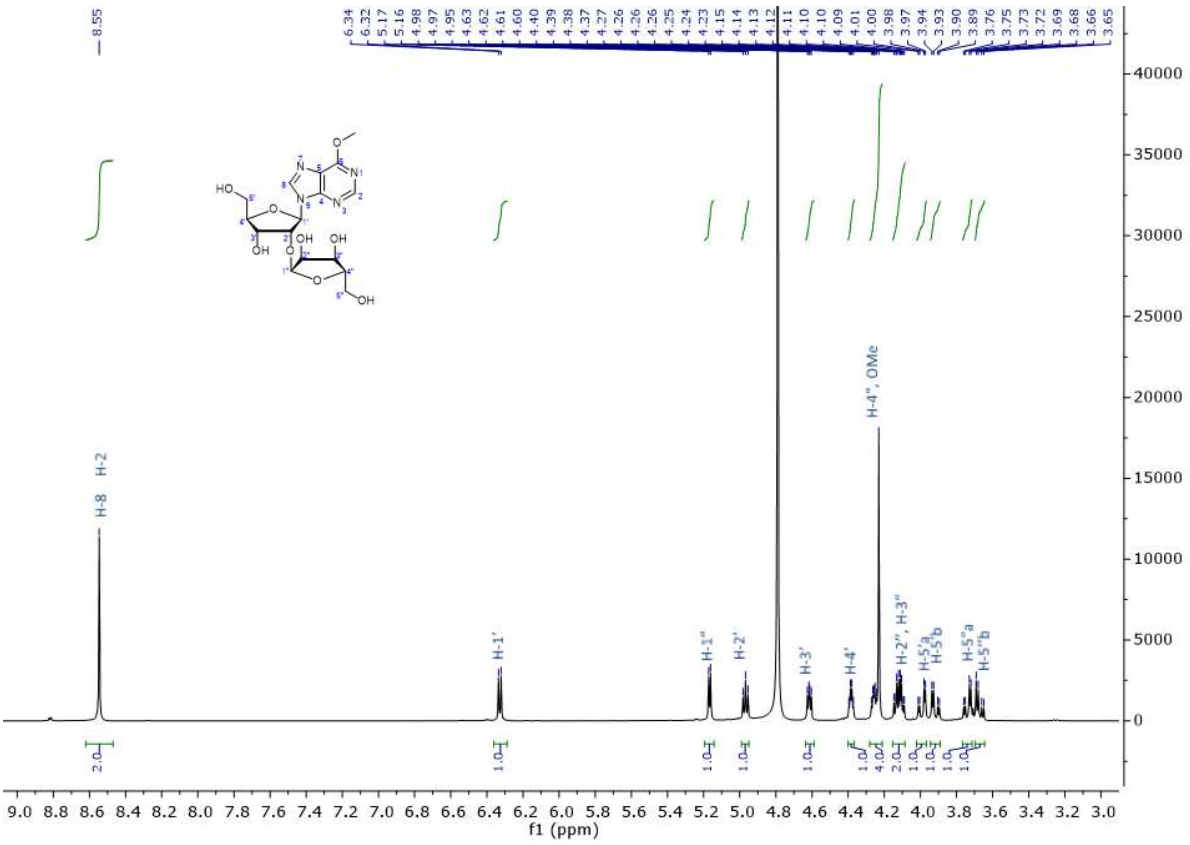


^{13}C NMR

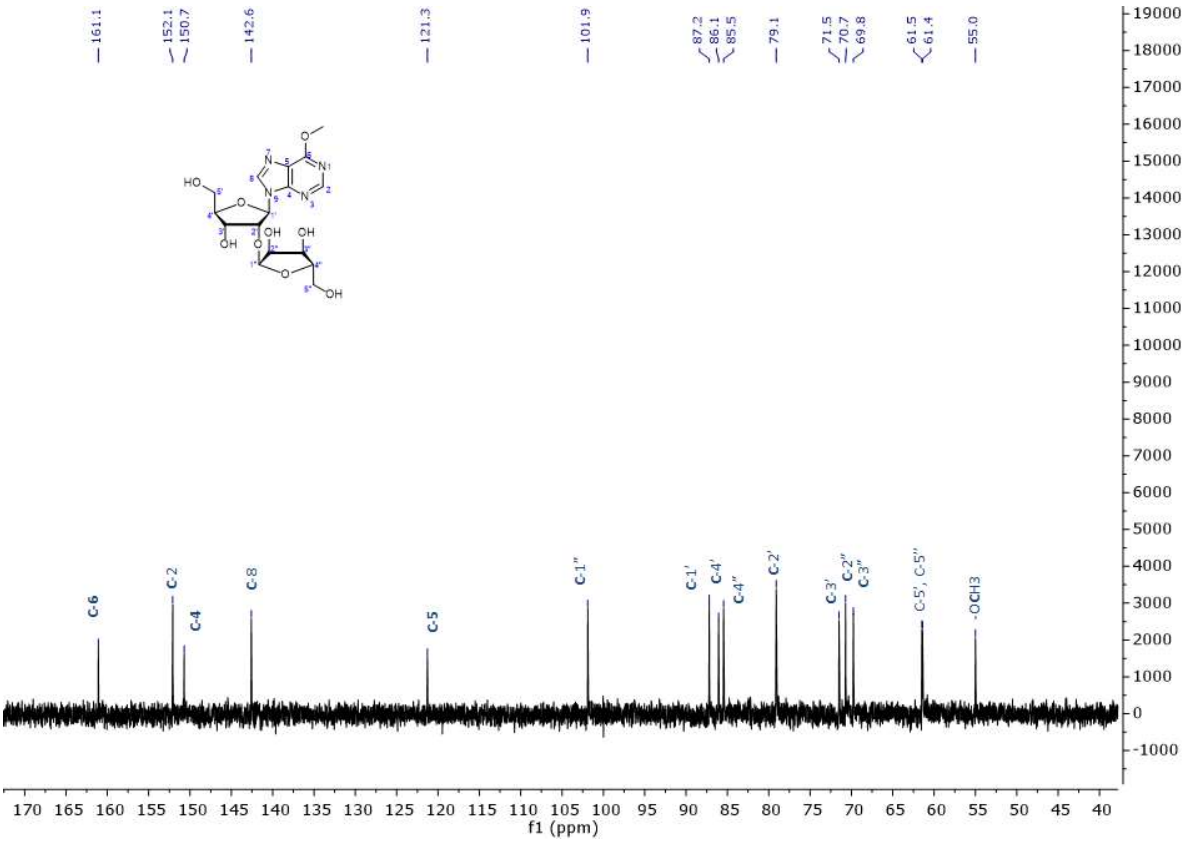


Compound **2g**

^{1}H NMR

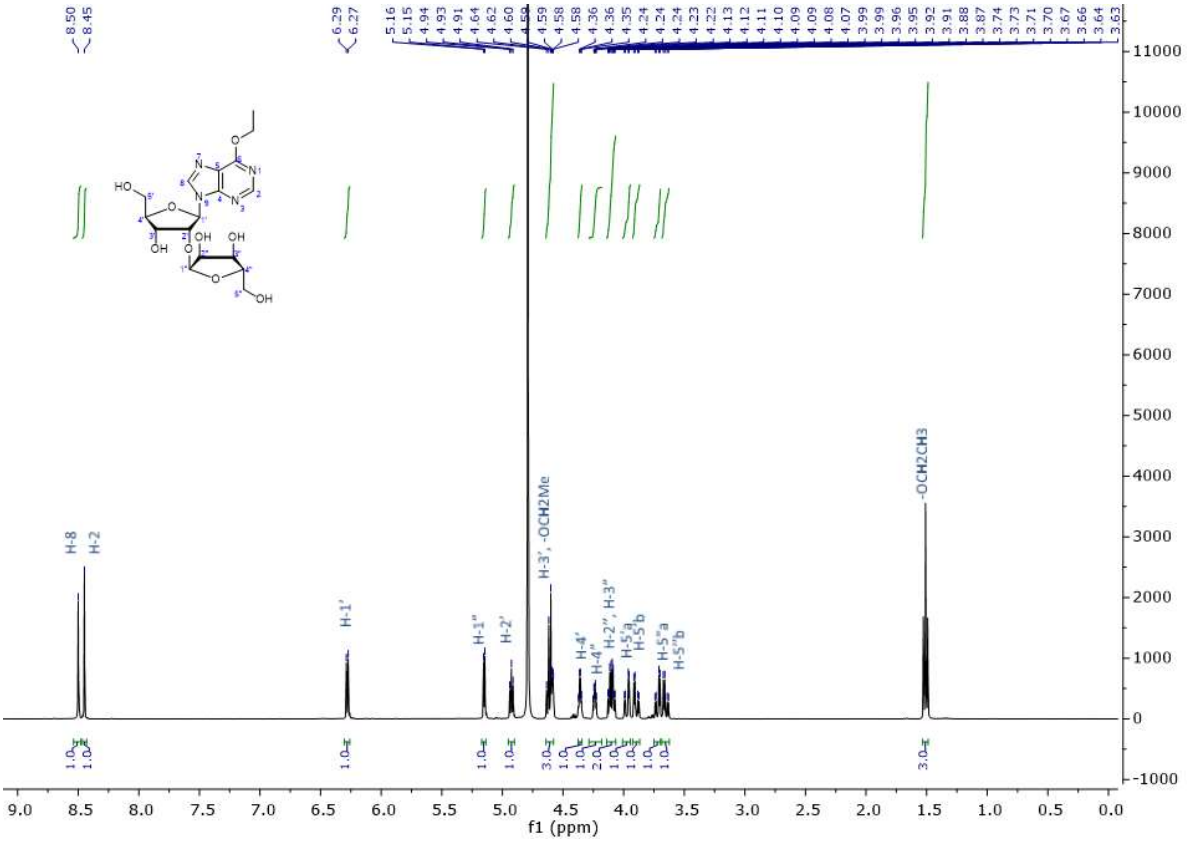


^{13}C NMR

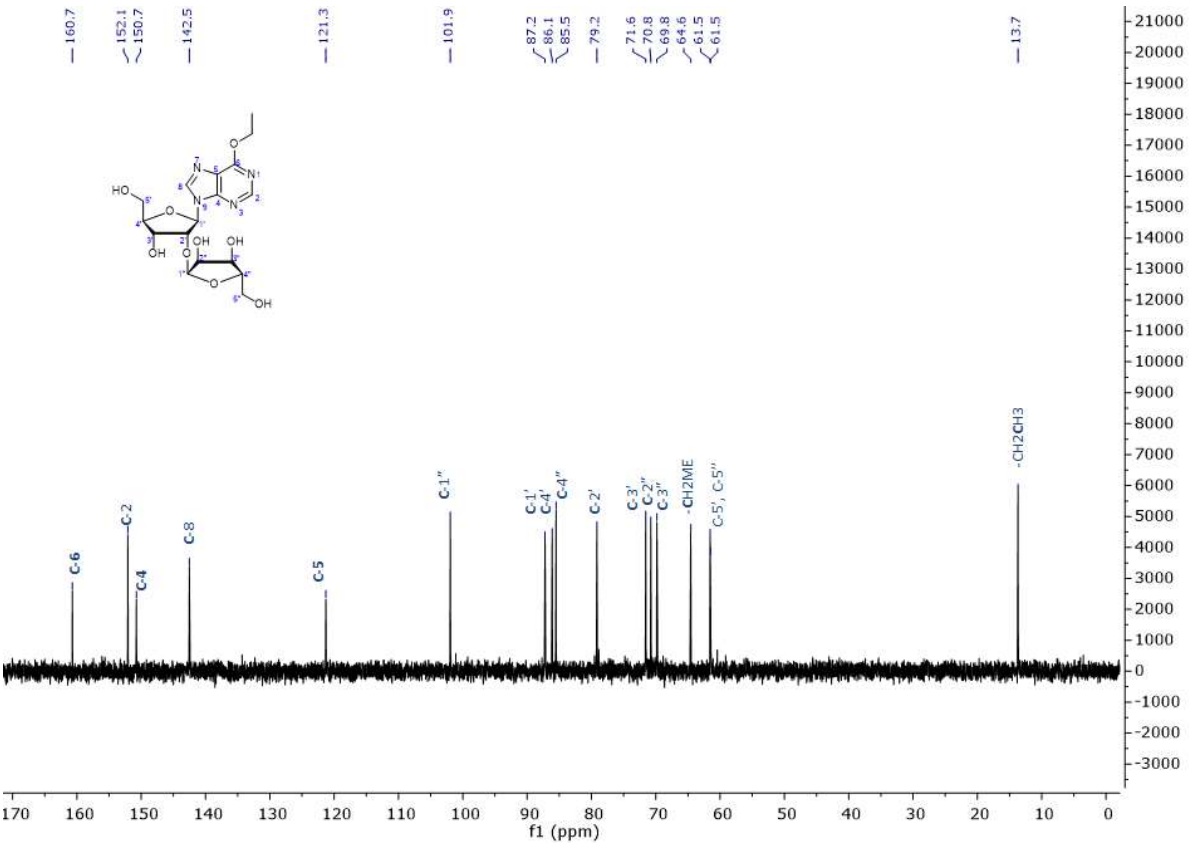


Compound **2h**

^{1}H NMR

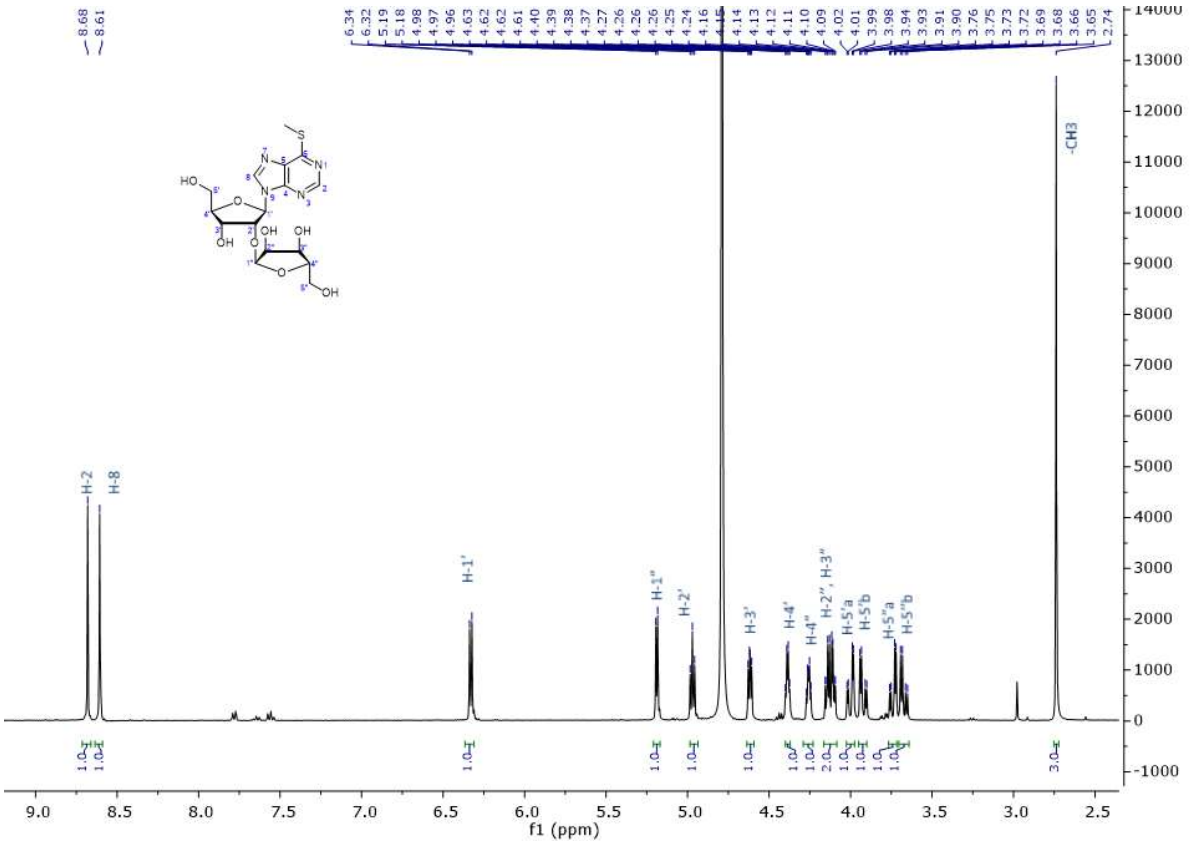


^{13}C NMR

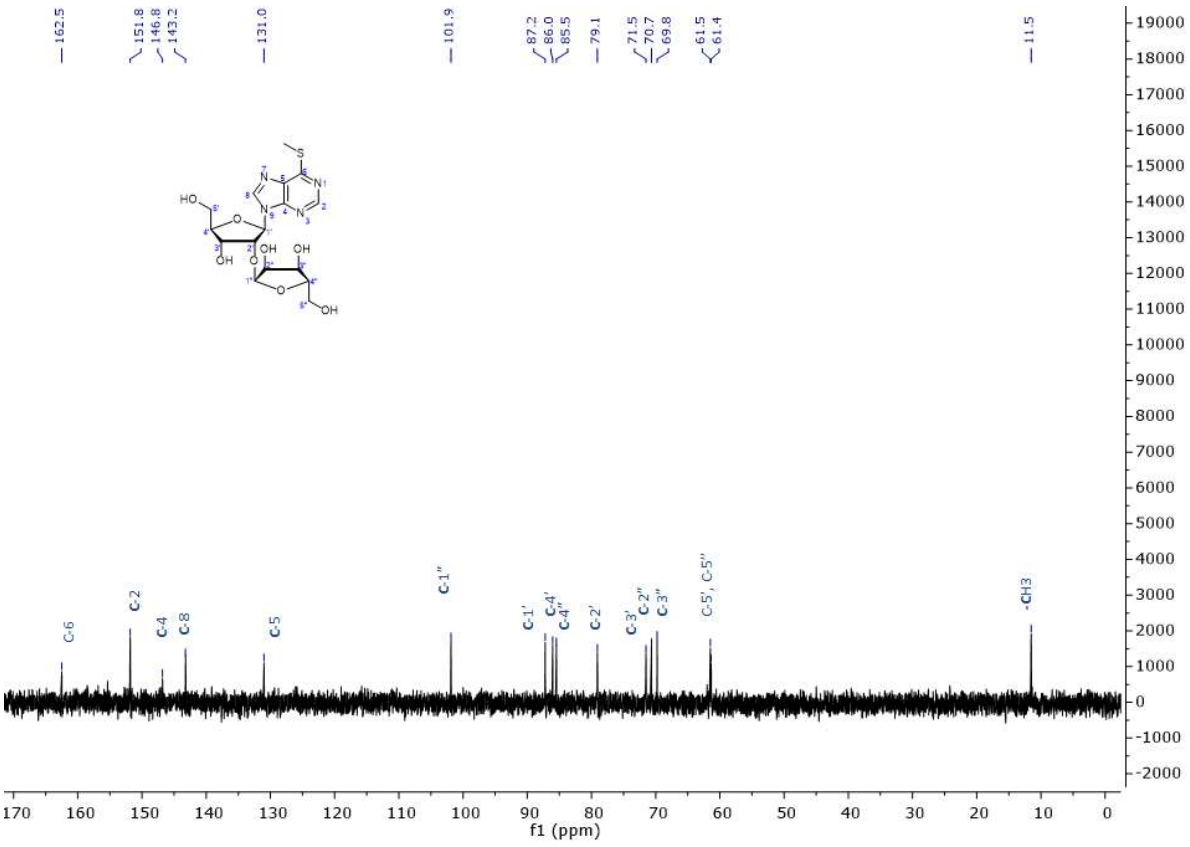


Compound **2i**

^{1}H NMR

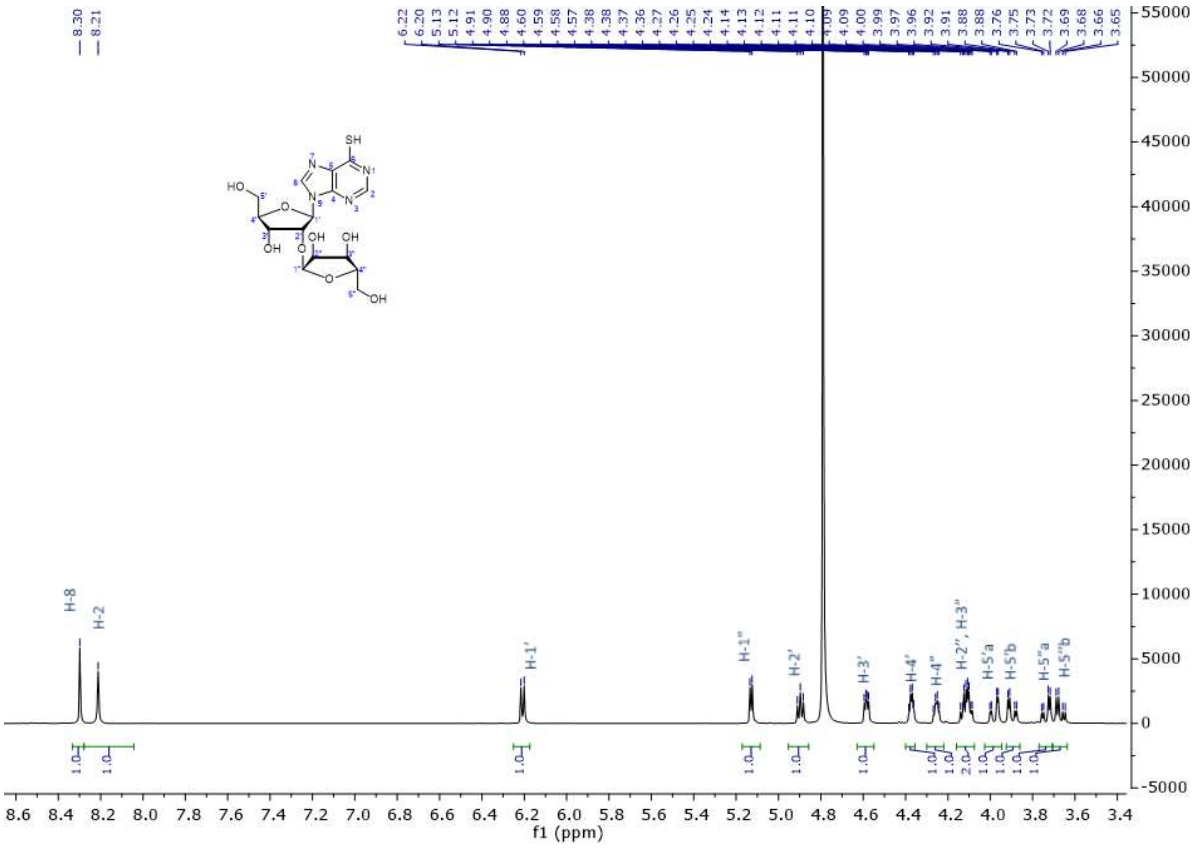


^{13}C NMR



Compound **2j**

^{1}H NMR



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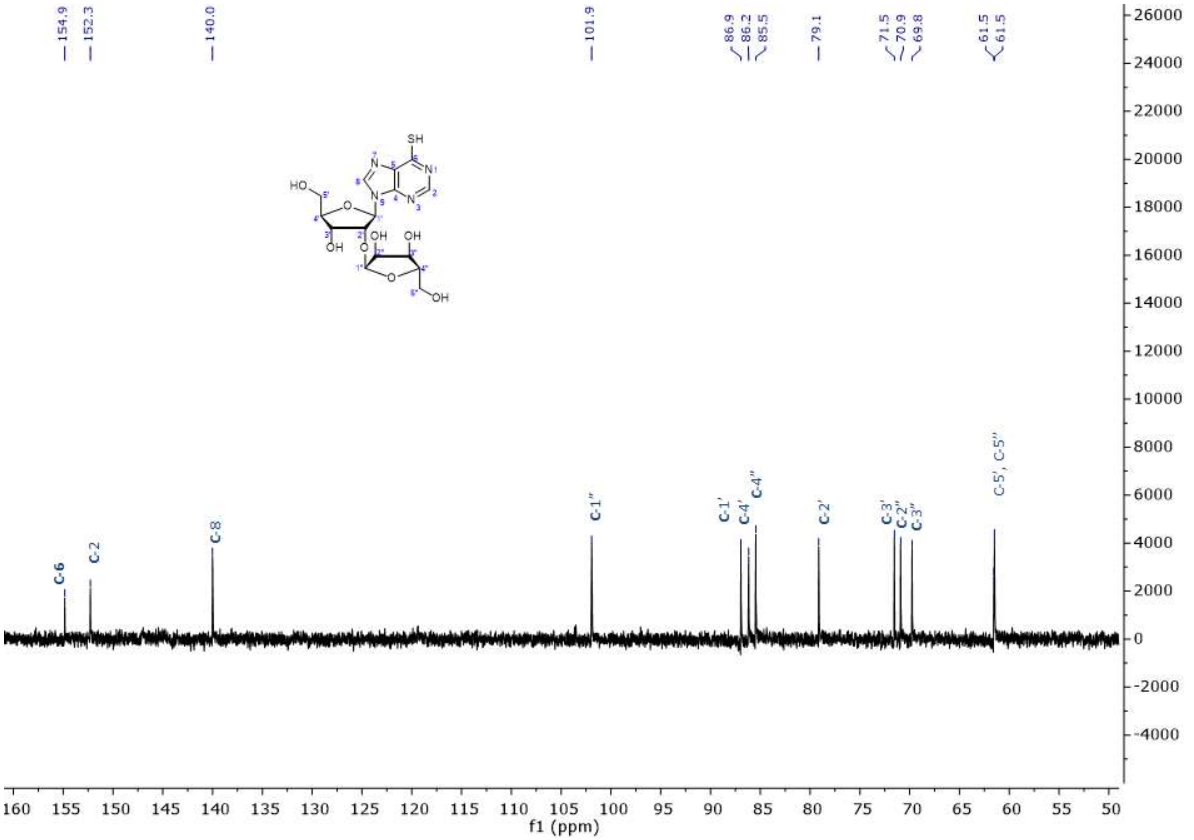

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2. P. I. Abronina, N. M. Podvalnyy, S. L. Sedinkin, K. G. Fedina, A. I. Zinin, A. O. Chizhov, V. I. Torgov and L. O. Kononov, *Synthesis*, 2012, **44**, 1219-1225.