Design and synthesis of Coenzyme A analogues as Aurora kinase A inhibitors: an exploration of the roles of the pyrophosphate and pantetheine moieties

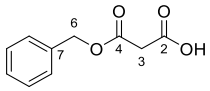
Fiona Bellany, Yugo Tsuchiya, Trang M. Tran, A. W. Edith Chan, Helen Allan, Ivan Gout and Alethea B. Tabor

Supporting Information

Contents

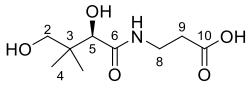
Procedures and data for literature compounds

*3-(Benzyloxy)-3-oxopropanoic acid (**12**)*[S1]



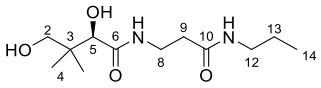
A solution of 2,2-dimethyl-1,3-dioxane-4,6-dione (5.00 g, 34.7 mmol) and benzyl alcohol (3.95 mL, 38.2 mmol) in toluene (24 mL) was heated to reflux for 4 h. The reaction mixture was cooled to RT and concentrated *in vacuo*. Purification by flash column chromatography (Gradient: 0 – 5% MeOH/CH_2Cl_2) gave **137** (4.76 g, 71%) as a colourless oil; R_f 0.24 (1% MeOH/CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.57 (1H, br, OH), 7.41 – 7.33 (5H, m, Ar), 5.21 (2H, s, H6) and 3.49 (2H, s, H3);^{13}C NMR (150 MHz, $CDCl_3$) δ 171.8 (C2), 166.7 (C4), 140.5 (C7), 128.6 (Ar, overlapping signals), 67.8 (C6) and 41.1 (C3); HRMS calc'd for $C_{10}H_{10}O_4$ expected 194.0579, found 194.0576. The data is in good agreement with the literature values.[S1]

(R)-3-(2,4-Dihydroxy-3,3-dimethylbutanamido)propanoic acid[S2]



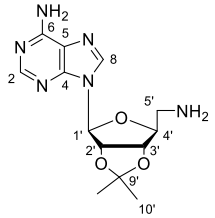
Sodium pantothenate (3.00 g, 12.4 mmol) in MeOH (20 mL) was washed through Amberlite® IR120 resin (2.5 g per mmol). The free acid was eluted with methanol (~1L). The elutions were concentrated *in vacuo* to give the title compound (3.05 g, quantitative) as a colourless oil; R_f 0.36 (10% MeOH/CH_2Cl_2); $[\alpha]_D^{20}$ +24.3 (c 1.6, MeOH) (lit.[S2] +82.4 (c 1.3, MeOH)); ^{1}H NMR (600 MHz, d_6-DMSO) δ 12.03 (1H, br, OH), 7.71 (1H, t, *J* = 5.9 Hz, NH), 5.41 (1H, br, OH), 4.49 (1H, br, OH), 3.69 (1H, s, H5), 3.36 – 3.19 (3H, m, H2 and H8), 3.18 – 3.14 (1H, m, H2), 2.38 (2H, td, *J* = 6.9 and 1.8 Hz, H9), 0.79 (3H, s, H4) and 0.77 (3H, s, H4); ^{13}C NMR (150 MHz, d_6-DMSO) δ 173.1 (C6), 173.0 (C10), 74.9 (C5), 68.0 (C2), 51.4 (C3), 34.3 (C8), 33.9 (C9), 20.9 (C4) and 20.3 (C4); HRMS calc'd for $C_9H_{18}O_5N$ expected 220.1185, found 220.1189. The data is in good agreement with the literature values.[S2]

*(R)-2,4-Dihydroxy-3,3-dimethyl-N-(3-oxo-3-(propylamino)propyl)butanamide (**17**)*[S3]



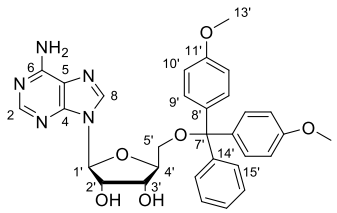
To pantothenic acid (2.80 g, 12.8 mmol) in anhydrous DMF (13 mL) at 0 °C was added DPPA (4.14 mL, 19.2 mmol), then NEt_3 (3.75 mL, 26.9 mmol). The solution was stirred at 0 °C for 20 min before propylamine (1.68 mL, 20.5 mmol) was added dropwise. The reaction was stirred at RT for 18 h. The reaction was concentrated *in vacuo*. DMF was azeotroped using toluene. Purification using flash column chromatography (Gradient: 0 - 8% MeOH/CH_2Cl_2) gave **17** (2.65 g, 79%) as a colourless oil; R_f 0.49 (10% MeOH/CH_2Cl_2); $[\alpha]_D^{20}$ +68.5 (c 0.5, MeOH); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.47 (1H, t, *J* = 6.0 Hz, NH), 6.17 (1H, br, NH), 4.00 (1H, s, H5), 3.62 – 3.50 (2H, m, H8), 3.49 (2H, s, H2), 3.22 – 3.16 (2H, m, H12), 2.44 (2H, t, *J* = 6.0 Hz, H9), 1.55 – 1.46 (2H, m, H13), 1.00 (3H, s, H4) and 0.94 – 0.89 (6H, m, H4 and H14); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.8 (C6), 171.6 (C10), 77.6 (C5), 71.1 (C2), 41.5 (C12), 39.6 (C3), 35.9 (C9), 35.4 (C8), 23.6 (C13), 21.6 (C4), 20.6 (C4) and 11.5 (C14); HRMS calc'd for $C_{12}H_{25}O_4N_4$ expected 261.1814, found 261.1811. The data is in good agreement with the literature values.[S3]

*9-((3aS,4S,6S,6aS)-6-(Aminomethyl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)-9H-purin-6-amine (**19**)*[S4]



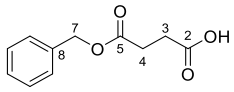
To a solution of protected adenosine **11** (8.00 g, 26.1 mmol) and phthalimide (4.22 g, 28.7 mmol) in THF (45 mL) was added triphenylphosphine (7.53 g, 28.7 mmol), followed by DIAD (5.65 mL, 28.7 mmol) and the reaction was stirred at RT for 5 h. The resulting white solid was filtered, washed with cold Et_2O and dried. The crude product and hydrazine hydrate (4.06 mL, 130 mmol) were refluxed in EtOH (50 mL) for 16 h. The resulting white solid was filtered, washed with EtOH and the filtrate concentrated *in vacuo* to give **19** (3.51 g, 44%, 80% purity) as an off-white solid; R_f 0.24 (5% MeOH/CH_2Cl_2); mp 190 – 193 °C (lit.[S5] 206 – 208 °C); $[\alpha]_D^{20}$ -23.5 (c 0.7, MeOH) (lit.[S5] -35.8 (c 1, MeOH)); ^{1}H NMR (600 MHz, CD_3OD) δ 8.27 (1H, s, H8), 8.20 (1H, s, H2), 6.15 (1H, d, *J* = 2.6 Hz, H1'), 5.46 (1H, dd, *J* = 6.2 and 2.8 Hz, H2'), 5.02 (1H, dd, *J* = 6.2 and 3.2 Hz, H3'), 4.28 – 4.22 (1H, m, H4'), 2.94 (2H, d, *J* = 6.0 Hz, H5'), 1.59 (3H, s, H10') and 1.37 (3H, s, H10'); ^{13}C NMR (150 MHz, CD_3OD) δ 157.4 (C6), 154.0 (C2), 150.2 (C4), 142.0 (C8), 120.7 (C5), 115.7 (C9'), 91.7 (C1'), 88.0 (C4'), 84.9 (C2'), 83.2 (C3'), 44.4 (C5'), 27.5 (C10') and 25.6 (C10'); HRMS calc'd for $C_{13}H_{19}N_6O_3$ expected 307.1519, found 307.1517. The data is in good agreement with the literature values.[S5]

*(2S,3S,4R,5S)-2-(6-Amino-9H-purin-9-yl)-5-((bis(4-methoxyphenyl)(phenyl)methoxy)methyl)tetrahydrofuran-3,4-diol (**28**)*[S6]



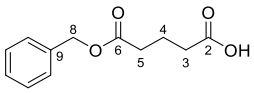
To a solution of adenosine **27** (12.0 g, 44.9 mmol) in pyridine (90 mL) at RT was added NEt_3 (12.5 mL, 89.8 mmol) and DMAP (1.35 g, 11.2 mmol). Then 4,4'-dimethoxytrityl chloride (16.7 g, 49.4 mmol) in pyridine (65 mL) was added dropwise. The reaction was stirred at RT for 20 h. The reaction mixture was concentrated *in vacuo*. The crude residue was dissolved in CH_2Cl_2 (500 mL) and then washed with H_2O (500 mL) and brine (500 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification using flash column chromatography (Gradient: 2%, 4% then 7% MeOH/CH_2Cl_2) gave **28** (8.75 g, 34%) as an off-white solid; R_f 0.16 (5% MeOH/CH_2Cl_2); mp 132 - 134 °C (lit.[S6] 142 – 144 °C); $[\alpha]_D^{20}$ -11.6 (c 0.4, MeOH); ^{1}H NMR (600 MHz, *d*$_6$-DMSO) δ 8.26 (1H, s, H8), 8.10 (1H, s, H2), 7.38 – 7.33 (2H, m, H15'), 7.30 (2H, br, NH_2), 7.27 – 7.18 (7H, m, H9' and H15'), 6.85 – 6.79 (4H, m, H10'), 5.92 (1H, d, *J* = 4.6 Hz, H1'), 5.55 (1H, br, OH), 5.21 (1H, br, OH), 4.73 – 4.68 (1H, m, H2'), 4.34 – 4.29 (1H, m, H3'), 4.08 – 4.04 (1H, m, H4'), 3.72 (6H, s, H13') and 3.24 – 3.16 (2H, m, H5'); ^{13}C NMR (150 MHz, *d*$_6$-DMSO) δ 158.1 (C11'), 156.1 (C6), 152.6 (C2), 149.3 (C4), 144.9 (C8), 139.7 (C14'), 135.6 (C8'), 129.7 (C9'), 127.8 (C15'), 127.7 (C15'), 126.7 (C15'), 119.2 (C5), 113.1 (C10'), 87.9 (C1'), 85.5 (C7'), 82.9 (C4'), 73.0 (C2'), 70.6 (C3'), 63.7 (C5') and 55.0 (C13'); HRMS calc'd for $C_{31}H_{32}O_6N_5$ expected 570.2353, found 570.2338. The data is in good agreement with the literature values.[S6]

*4-(Benzyloxy)-4-oxobutanoic acid (**30**)*[S7]



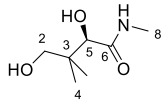
To a solution of succinic anhydride (5.00 g, 49.9 mmol) in CH_2Cl_2 (25 mL) was added benzyl alcohol (5.68 mL, 59.3 mmol) and cooled to 0 °C. Then, NEt_3 (8.27 mL, 59.3 mmol) and DMAP (91 mg, 0.75 mmol) were added at 0 °C and the reaction stirred at RT for 16 h. The solution was concentrated *in vacuo*. The residue was dissolved in Et_2O (100 mL) and washed with sat. $NaHCO_3$ solution (3 x 50 mL). The combined aqueous layers were acidified with 1M HCl solution to pH 2 before extracting with Et_2O (200 mL). The organic layer was washed with brine (200 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo* to give **30** (6.50 g, 63%) as a colourless oil; R_f 0.68 (10% MeOH/CH_2Cl_2; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.99 (1H, br, OH), 7.44 – 7.26 (5H, m, Ar), 5.17 (2H, s, H7) and 2.76 – 2.65 (4H, m, H3 and H4); ^{13}C NMR (150 MHz, $CDCl_3$) δ 178.4 (C2), 172.3 (C5), 135.6 (C8), 128.8 (Ar), 128.7 (Ar), 128.5 (Ar), 66.6 (C7) and 29.1 (C3 and C4); HRMS calc'd for $C_{11}H_{13}O_4$ expected 209.0814, found 209.0816. The data is in good agreement with the literature values.[S7]

*5-(Benzyloxy)-5-oxopentanoic acid (**34**)*[S8]



To a solution of glutaric anhydride (5.00 g, 43.8 mmol) in CH_2Cl_2 (65 mL) was added benzyl alcohol (4.98 mL, 48.2 mmol) and cooled to 0 °C. Then, NEt_3 (6.70 mL, 48.2 mmol) and DMAP (80 mg, 0.65 mmol) were added at 0 °C and the reaction stirred at RT for 16 h. The solution was concentrated *in vacuo*. The residue was dissolved in Et_2O (100 mL) and washed with sat. $NaHCO_3$ solution (3 x 50 mL). The combined aqueous layers were acidified with 1M HCl solution to pH 2 before extracting with Et_2O (200 mL). The organic layer was washed with brine (200 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo* to give **34** (5.98 g, 61%) as a colourless oil; R_f 0.74 (10% MeOH/CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.59 (1H, br, OH), 7.41 – 7.31 (5H, m, Ar), 5.13 (2H, s, H8), 2.50 – 2.40 (4H, m, H3 and H5) and 2.02 – 1.94 (2H, m, H4); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.2 (C2), 173.2 (C6), 136.2 (C9), 128.7 (Ar), 128.6 (Ar), 128.5 (Ar), 66.5 (C8), 33.4 (C5), 33.3 (C3) and 20.0 (C4); HRMS calc'd for $C_{12}H_{15}O_4$ expected 223.0970, found 223.0975. The data is in good agreement with the literature values.[S8]

*(R)-2,4-Dihydroxy-N-3,3-trimethylbutanamide (**40**)*[S9]



To a solution of D-pantolactone (2.00 g, 15.3 mmol) in MeOH (6 mL) was added *N*-methylamine (40% aqueous solution, 1.6 mL, 20.6 mmol). The reaction was stirred at RT for 3 h. The reaction was concentrated *in vacuo* to give **40** (2.40, 97%) as a colourless oil; R_f 0.45 (5% MeOH/CH_2Cl_2); $[\alpha]_D^{20}$ +49.6 (c 1.0, MeOH); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.04 (1H, d, *J* = 4.5 Hz, NH), 4.73 (1H, br, OH), 4.00 (1H, s, H5), 3.50 – 3.43 (2H, m, H2), 2.81 (3H, d, *J* = 4.5 Hz, H8), 0.96 (3H, s, H4) and 0.89 (3H, s, H4); ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.8 (C6), 75.8 (C5), 71.1 (C2), 39.4 (C3), 25.4 (C8), 21.2 (C4) and 20.5 (C4); HRMS calc'd for $C_7H_{16}NO_3$ expected 162.1130, found 162.1133. The data is in good agreement with the literature values.[S9]

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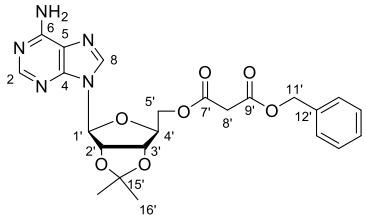
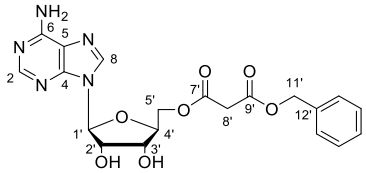
^{1}H and ^{13}C spectral assignments of novel compounds

*((3aS,4S,6S,6aS)-6-(6-Amino-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl benzyl malonate (**13**)*



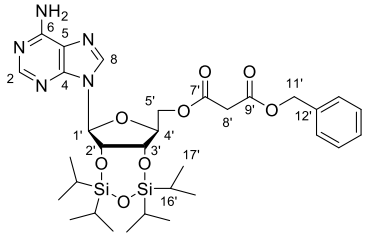
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.32 (1H, s, H2), 7.89 (1H, s, H8), 7.37 – 7.28 (5H, m, Ar), 6.27 (2H, br, NH_2), 6.10 (1H, s, H1'), 5.42 (1H, d, *J* = 6.4 Hz, H2'), 5.15 (1H, d, *J* = 12.0 Hz, H11'), 5.13 (1H, d, *J* = 12.0 Hz, H11'), 5.04 (1H, dd, *J* = 6.4 and 3.4 Hz, H3'), 4.50 – 4.29 (3H, m, H4'and H5'), 3.41 (1H, d, *J* = 10.0 Hz, H8'), 3.38 (1H, d, *J* = 10.0 Hz, H8'), 1.60 (3H, s, H16') and 1.38 (3H, s, H16'); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.3 (C7' or C9'), 166.0 (C7' or C9'), 155.9 (C6), 153.3 (C2), 149.3 (C4), 139.8 (C8), 135.2 (C12'), 128.5 (Ar, overlapping signals), 120.3 (C5), 102.7 (C15'), 90.9 (C1'), 84.8 (C4'), 84.3 (C2'), 81.6 (C3'), 67.5 (C11'), 64.9 (C5'), 41.3 (C8'), 27.3 (C16') and 25.5 (C16').

*((2S,3R,4S,5S)-5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methylbenzyl malonate (**14**)*



^{1}H NMR (600 MHz, CD_3OD) δ 8.34 (1H, s, H8), 8.27 (1H, s, H2), 7.38 – 7.24 (5H, m, Ar), 6.03 (1H, d, *J* = 4.9 Hz, H1'), 5.14 (2H, apparent s, H11'), 4.66 (1H, t, *J* = 4.9 Hz, H2'), 4.44 (2H, dd, *J* = 4.0 Hz, 2.5 Hz, H5'), 4.33 (1H, t, *J* = 4.9 Hz, H3') and 4.27 (1H, q, *J* = 4.5 Hz, H4'); ^{13}C NMR (150 MHz, CD_3OD) δ 168.0 (C7' or C9'), 167.9 (C7' or C9'), 155.1 (C6), 150.4 (C2), 142.3 (C8), 136.9 (C4), 129.5 (Ar, overlapping signals), 120.5 (C5), 90.3 (C1'), 83.6 (C4'), 75.3 (C2'), 71.6 (C3'), 68.2 (C11'), 65.5 (C5') and 41.66 (C8'). Note: C8' signal is not seen in ^{1}H NMR as it is exchangeable with NMR solvent.

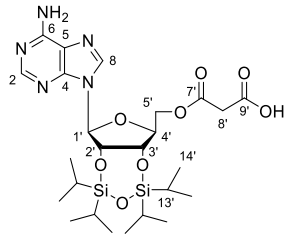
*((5aS,6S,8S,8aS)-8-(6-Amino-9H-purin-9-yl)-2,2,4,4-tetraisopropyltetrahydrofuro[3,4-f][1,3,5,2,4]trioxadisilepin-6-yl)methyl benzyl malonate (**15**)*



^{1}H NMR (600 MHz, $CDCl_3$) δ 8.32 (1H, s, H2), 7.98 (1H, s, H8), 7.36 – 7.29 (5H, m, Ar), 5.99 (1H, d, *J* = 3.4 Hz, H1'), 5.91 (2H, br, NH_2), 5.17 (2H, apparent s, H11'), 5.09 (1H, dd, *J* = 4.9 and 3.4 Hz, H2'), 4.72 (1H, dd, *J* = 6.4 and 4.9 Hz, H3'), 4.53 (1H, dd, *J* = 12.0 and 3.2 Hz, H5'), 4.41 (1H, dd, *J* = 12.0 and 5.2 Hz, H5'), 4.33 (1H, ddd, *J* = 6.4, 5.2 and 3.2 Hz, H4'), 3.46 (2H, apparent s, H8') and 1.10 – 0.99 (28H, m, H16' and H17'); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.2 (C7' and C9'), 155.7 (C6), 153.2 (C2), 149.6 (C4), 140.2 (C8), 135.2 (C12'), 128.6 (Ar,

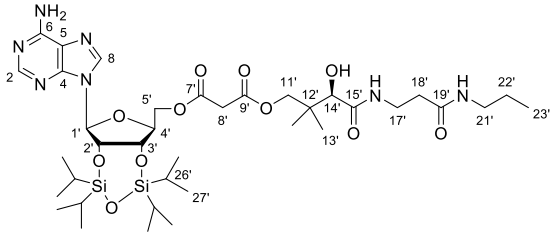
overlapping signals), 120.5 (C5), 90.6 (C1'), 81.7 (C4'), 75.7 (C2'), 72.6 (C3'), 67.5 (C11'), 64.6 (C5'), 41.4 (C8'), 17.4 (C17') and 13.5 (C16').

*3-(((5aS,6S,8S,8aS)-8-(6-Amino-9H-purin-9-yl)-2,2,4,4-tetraisopropyltetrahydrofuro[3,4-f][1,3,5,2,4]trioxadisilepin-6-yl)methoxy)-3-oxopropanoic acid (**16**)*



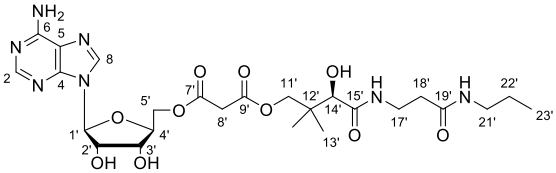
^{1}H NMR (600 MHz, d_6-DMSO) δ 12.91 (1H, br, OH), 8.38 (1H, s, H8), 8.14 (1H, s, H2), 7.36 (1H, br, NH_2), 6.00 (1H, d, *J* = 5.2 Hz, H1'), 5.17 (1H, t, *J* = 5.2 Hz, H2'), 4.74 (1H, t, *J* = 4.7 Hz, H3'), 4.39 (1H, dd, *J* = 11.9 and 4.8 Hz, H5'), 4.28 (1H, dd, *J* = 11.9 and 5.6 Hz, H5'), 4.19 (1H, q, *J* = 4.8 Hz, H4'), 3.40 (2H, apparent s, H8') and 1.09 – 0.92 (28 H, m, H13' and H14'); ^{13}C NMR (150 MHz, d_6-DMSO) δ 167.9 (C9'), 166.8 (C7'), 156.2 (C6), 152.8 (C2), 149.3 (C4), 139.7 (C8), 119.1 (C5), 81.7 (C1'), 81.7 (C4'), 74.8 (C2'), 72.3 (C3'), 63.9 (C5'), 41.4 (C8'), 17.2 (C17') and 12.5 (C16').

*((5aS,6S,8S,8aS)-8-(6-Amino-9H-purin-9-yl)-2,2,4,4-tetraisopropyltetrahydrofuro[3,4-f][1,3,5,2,4]trioxadisilepin-6-yl)methyl ((R)-3-hydroxy-2,2-dimethyl-4-oxo-4-((3-oxo-3-(propylamino)propyl)amino)butyl) malonate (**18**)*



^{1}H NMR (600 MHz, $CDCl_3$) δ 8.30 (1H, s, H2), 8.09 (1H, s, H8), 7.52 (1H, t, *J* = 6.0 Hz, NH), 6.75 (1H, d, *J* = 4.5 Hz, OH), 6.07 (2H, br, NH_2), 6.04 (1H, s, H1'). 5.73 (1H, t, *J* = 5.6 Hz, NH), 4.97 (1H, d, *J* = 3.7 Hz, H2'), 4.64 (1H, dd, *J* = 12.4 and 2.3 Hz, H5'), 4.49 – 4.42 (2H, H3' and H5'), 4.40 – 4.35 (2H, m, H4' and H11'), 4.15 (1H, d, *J* = 4.9 Hz, H14'), 3.84 (1H, d, *J* = 10.9 Hz, H11'), 3.67 – 3.59 (1H, m, H17'), 3.56 – 3.49 (1H, m, H17'), 3.48 (2H, apparent s, H8'), 3.29 – 3.16 (2H, m H21'), 2.51 – 2.37 (2H, m, H18'), 1.74 – 1.56 (2H, m, H22') and 1.17 – 0.89 (37H, m, H13', H23', H26' and H27'); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.5 (C15'), 171.4 (C19'), 166.7 (C9'), 166.0 (C7'), 155.3 (C6), 153.5 (C2), 149.0 (C4), 138.4 (C8), 119.6 (C5), 91.0 (C1'), 81.1 (C4'), 76.3 (C2'), 73.8 (C14'), 71.8 (C11'), 71.5 (C3'), 63.0 (C5'), 41.4 (C8'), 41.3 (C21'), 38.5 (C12'), 35.6 (C17'), 35.2 (C18'), 22.9 (C22'), 21.9 (C13'), 18.9 (C13'), 14.5 (C27'), 13.7 (C26') and 13.0 (C23').

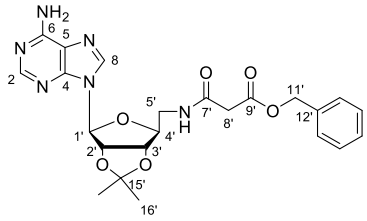
*((2S,3R,4S,5S)-5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl ((R)-3-hydroxy-2,2-dimethyl-4-oxo-4-((3-oxo-3-(propylamino)propyl)amino)butyl) malonate (**1**)*



^{1}H NMR (600 MHz, CD_3OD) δ 8.28 (1H, s, H8), 8.21 (1H, s, H2), 6.02 (1H, d, *J* = 4.5 Hz, H1'), 4.72 (1H, t, *J* = 4.5 Hz, H2'), 4.45 (2H, dd, *J* = 14.5 and 4.0 Hz, H5'), 4.39 (1H, t, *J* = 5.0 Hz, H3'), 4.29 – 4.26 (1H, m, H4'), 4.11 (1H,

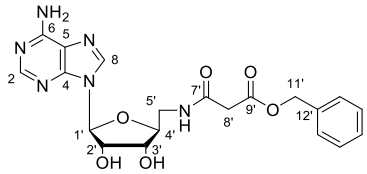
d, *J* = 10.5 Hz, H11'), 3.95 (1H, d, *J* = 10.5 Hz, H11'), 3.86 (1H, s, H14'), 3.50 – 3.39 (2H, m, H17'), 3.10 (2H, t, *J* = 6.5 Hz, H21'), 2.40 (2H, t, *J* = 6.8 Hz, H18'), 1.54 – 1.45 (2H, m, H22'), 0.95 (3H, s, H13') and 0.92 – 0.88 (6H, m, H13' and H23'); ^{13}C NMR (150 MHz, CD_3OD) δ 175.3 (C15'), 173.6 (C19'), 168.2 (C9'), 168.0 (C7'), 157.6 (C6), 153.4 (C2), 150.6 (C4), 142.0 (C8), 121.0 (5), 90.1 (C1'), 83.4 (C4'), 79.3 (C14'), 75.7 (C2'), 72.7 (C11'), 71.7 (C3'), 65.9 (C5'), 42.4 (C21'), 41.6 (C8'), 39.6 (C12'), 36.4 (C17' and C18'), 23.6 (C22'), 20.7 (C13'), 20.6 (C13') and 11.7 (C23'). Note: C8' signal is not seen in ^{1}H NMR as it is exchangeable with NMR solvent.

*Benzyl 3-((((3aS,4S,6S,6aS)-6-(6-amino-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl)amino)-3-oxopropanoate (**20**)*



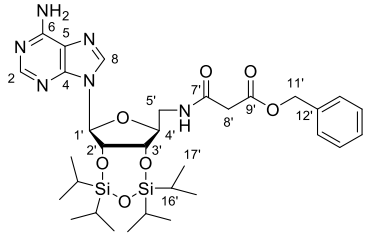
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.70 (1H, d, *J* = 7.9 Hz, NH), 8.26 (1H, s, H2), 7.85 (1H, s, H8), 7.28 – 7.20 (5H, m, H13'), 6.12 (2H, br, NH_2), 5.8 (1H, d, *J* = 4.9 Hz, H1'), 5.19 (1H, dd, *J* = 6.0 and 4.9 Hz, H2'), 5.13 (1H, d, *J* = 12.5 Hz, H11'), 5.10 (1H, d, *J* = 12.5 Hz, H11'), 4.89 (1H, dd, *J* = 6.0 and 2.0 Hz, H3'), 4.49 (1H, q, *J* = 2.0 Hz, H4'), 4.17 (1H, ddd, *J* = 14.4, 8.8 and 2.5 Hz, H5'), 3.48 (2H, apparent s, H8'), 3.29 (1H, dt, *J* = 14.4 and 2.5 Hz, H5'), 1.62 (3H, s, H16') and 1.36 (3H, d, H16'); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.4 (C9'), 166.0 (C7'), 156.1 (C6), 152.6 (C8), 148.8 (C4), 140.6 (C2), 135.2 (C12'), 128.6 (Ar, overlapping signals), 121.2 (C5), 114.8 (C15'), 92.8 (C1'), 83.7 (C4'), 82.4 (C2'), 81.7 (C3'), 67.4 (C11'), 42.9 (C8'), 41.4 (C5'), 27.6 (C16') and 25.3 (C16').

*Benzyl 3-((((2S,3R,4S,5S)-5-(6-amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl)amino)-3-oxopropanoate (**21**)*



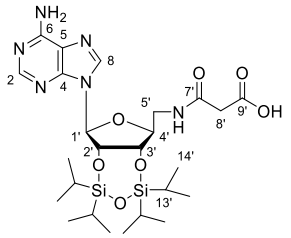
^{1}H NMR (600 MHz, *d*$_6$-DMSO) δ 8.51 (1H, s, H8), 8.45 (1H, t, *J* = 5.8 Hz, NH), 8.33 (1H, s, H2), 8.20 (2H, br, NH_2), 7.37 – 7.29 (5H, m, Ar), 5.90 (1H, d, *J* = 6.0 Hz, H1'), 5.51 (2H, br, OH), 5.11 (2H, apparent s, H11'), 4.64 (1H, t, *J* = 6.0 Hz, H2'), 4.09 (1H, t, *J* = 4.7 Hz, H3'), 3.97 (1H, dt, *J* = 5.8 and 4.7 Hz, H4'), 3.50 – 3.38 (2H, m, H5') and 3.35 (2H, apparent s, H8'); ^{13}C NMR (150 MHz, *d*$_6$-DMSO) δ 167.8 (C9'), 165.4 (C7'), 153.9 (C6), 149.7 (C4), 148.9 (C2), 141.3 (C8), 135.9 (C12'), 128.4 (Ar), 128.0 (Ar), 127.8 (Ar), 119.2 (C5), 87.7 (C1'), 83.5 (C4'), 73.0 (C2'), 71.2 (C3'), 65.9 (C11'), 42.4 (C8') and 41.2 (C5').

*Benzyl 3-((((5aS,6S,8S,8aS)-8-(6-amino-9H-purin-9-yl)-2,2,4,4-tetraisopropyltetrahydrofuro[3,4-f][1,3,5,2,4]trioxadisilepin-6-yl)methyl)amino)-3-oxopropanoate (**22**)*



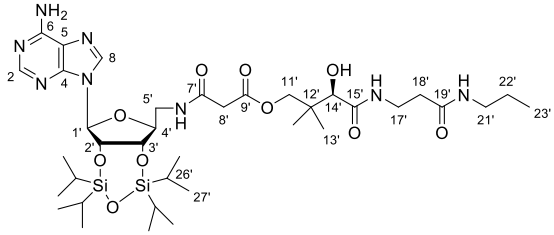
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.72 (1H, d, *J* = 6.8 Hz, NH), 8.33 (1H, s, H2), 7.89 (1H, s, H8), 7.38 – 7.29 (5H, m, Ar), 5.96 (2H, br, NH_2), 5.79 (1H, d, *J* = 7.0 Hz, H1'), 5.16 (2H, apparent s, H11'), 5.03 (1H, dd, *J* = 7.0 and 5.0 Hz, H2'), 4.53 (1H, dd, *J* = 5.0 and 2.3 Hz, H3'), 4.37 (1H, q, *J* = 3.0 Hz, H4'), 4.14 (1H, ddd, *J* = 14.5, 8.8 and 3.0 Hz, H5'), 3.47 (1H, d, *J* = 15.0 Hz, H8'), 3.40 (1H, d, *J* = 15.0 Hz, H8'), 3.31 (1H, dt, *J* = 14.3 and 3.0 Hz, H5') and 1.13 – 0.87 (28H, m, H16' and H17'); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.0 (C9'), 165.6 (C7'), 155.8 (C6), 152.5 (C2), 149.2 (C4), 141.1 (C8), 135.3 (C12'), 128.6 (Ar, overlapping signals), 121.3 (C5), 90.9 (C1'), 85.8 (C4'), 75.4 (C2'), 73.6 (C3'), 67.4 (C11'), 47.8 (C8'), 41.3 (C5'), 17.5 (C17') and 13.2 (C16').

*3-((((5aS,6S,8S,8aS)-8-(6-Amino-9H-purin-9-yl)-2,2,4,4-tetraisopropyltetrahydrofuro[3,4-f][1,3,5,2,4]trioxadisilepin-6-yl)methyl)amino)-3-oxopropanoic acid (**23**)*



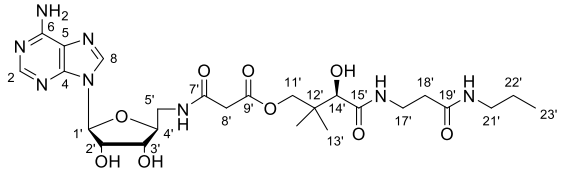
^{1}H NMR (600 MHz, *d*$_6$-DMSO) δ 8.66 (1H, br, NH), 8.46 (1H, s, H8), 8.16 (1H, s, H2), 7.37 (2H, br, NH_2), 5.94 (1H, d, *J* = 6.4 Hz, H1'), 5.15 (1H, dd, *J* = 6.4 and 4.9 Hz, H2'), 4.59 (1H, dd, *J* = 5.0 and 3.2 Hz, H3'), 4.05 (1H, dt, *J* = 5.0 and 3.0 Hz, H4') 3.50 – 3.40 (2H, m, H5'), 3.34 (1H, br, OH), 3.11 (2H, apparent s, H8') and 1.13 – 0.83 (28H, m, H13' and H14'); ^{13}C NMR (150 MHz, *d*$_6$-DMSO) δ 169.5 (C9'), 166.8 (C7'), 156.2 (C6), 152.7 (C2), 149.4 (C4), 140.1 (C8), 119.3 (C5), 87.2 (C1'), 83.9 (C4'), 74.7 (C2'), 73.1 (C3'), 42.9 (C8'), 41.0 (C5'), 17.3 (C14') and 13.2 (C13').

*(R)-3-Hydroxy-2,2-dimethyl-4-oxo-4-((3-oxo-3-(propylamino)propyl)amino)butyl 3-((((5aS,6S,8S,8aS)-8-(6-amino-9H-purin-9-yl)-2,2,4,4-tetraisopropyltetrahydrofuro[3,4-f][1,3,5,2,4]trioxadisilepin-6-yl)methyl)amino)-3-oxopropanoate (**24**)*



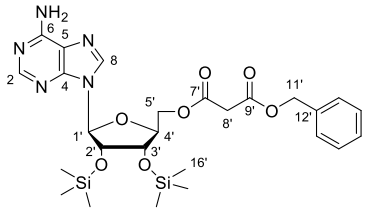
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.97 (1H, d, *J* = 8.2 Hz, NH), 8.31 (1H, s, H2), 7.90 (1H, d, H8), 7.59 (1H, t, *J* = 5.8 Hz, NH), 6.40 (2H, br, NH_2), 6.09 (1H, br, NH), 5.80 (1H, d, *J* = 6.6 Hz, H1'), 4.98 (1H, dd, *J* = 6.6 and 5.1 Hz, H2'), 4.48 (1H, dd, *J* = 5.1 and 2.5 Hz, H3'), 4.37 (1H, q, *J* = 2.5 Hz, H4'), 4.26 (1H, d, *J* = 10.6 Hz, H11'), 4.14 (1H, ddd, *J* = 14.4, 9.1 and 2.5 Hz, H5'), 4.02 (1H, s, H14'), 3.77 (1H, d, *J* = 10.6 Hz, H11'), 3.68 – 3.60 (1H, m, H17'), 3.54 – 3.37 (3H, m, H8' and H17'), 3.29 (1H, dt, *J* = 14.4 and 2.5 Hz, H5'), 3.21 – 3.13 (2H, m, H21'), 2.51 – 2.39 (2H, m, H18'), 1.53 – 1.45 (2H, m, H22') and 1.12 – 0.86 (37H, m, H13', H23', H26' and H27'); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.1 (C15'), 171.4 (C19'), 168.0 (C9'), 166.1 (C7'), 156.7 (C6), 152.4 (C2), 148.9 (C4), 140.8 (C8), 121.1 (C5), 91.0 (C1'), 85.6 (C4'), 75.6 (C2'), 74.3 (C14'), 73.5 (C3'), 71.8 (C11'), 42.6 (C8'), 41.5 (C21'), 41.1 (C5'), 38.3 (C12'), 36.1 (C18'), 35.5 (C17'), 22.8 (C22'), 21.8 (C13'), 19.7 (C13'), 17.5 (C27'), 12.9 (C26') and 11.5 (C23').

*(R)-3-Hydroxy-2,2-dimethyl-4-oxo-4-((3-oxo-3-(propylamino)propyl)amino)butyl 3-((((2S,3R,4S,5S)-5-(6-amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl)amino)-3-oxopropanoate (**3**)*



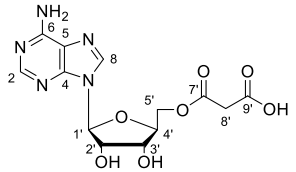
^{1}H NMR (600 MHz, CD_3OD) δ 8.26 (1H, s, H8), 8.25 (1H, s, H2), 5.92 (1H, d, *J* = 6.2 Hz, H1'), 4.80 (1H, t, *J* = 6.2 Hz, H2'), 4.25 – 4.18 (2H, m, H3' and H4'), 4.08 (1H, d, *J* = 10.6 Hz, H11'), 3.94 (1H, d, *J* = 10.6 Hz, H11'), 3.86 – 3.81 (2H, m, H5' and H14'), 3.49 – 3.39 (3H, m, H5' and H17'), 3.35 (2H, apparent s, H8'), 3.12 – 3.08 (2H, m, H21'), 2.42 (2H, t, *J* = 6.7 Hz, H18'), 1.53 – 1.45 (2H, m, H22'), 0.96 (3H, s, H13'), 0.93 (3H, s, H13') and 0.90 (3H, t, *J* = 7.4 Hz, H23'); ^{13}C NMR (150 MHz, CD_3OD) δ 176.1 (C15'), 175.3 (C19'), 169.4 (C9'), 168.8 (C7'), 157.5 (C6), 153.8 (C2), 150.4 (C4), 142.2 (C8), 121.1 (C5), 90.8 (C1'), 85.5 (C4'), 77.2 (C14'), 75.7 (C2'), 74.5 (C3'), 72.8 (C11'), 49.5 (C8'), 42.5 (C5'), 42.4 (C21'), 39.5 (C12'), 36.9 (C17' and C18'), 23.6 (C22'), 21.6 (C13'), 21.4 (C13') and 11.7 (C23').

((2S,3S,4S,5S)-5-(6-Amino-9H-purin-9-yl)-3,4-bis((trimethylsilyl)oxy)tetrahydrofuran-2-yl)methyl benzyl malonate (***25***)



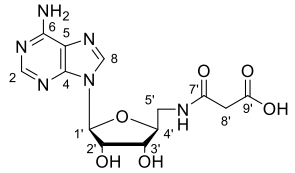
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.34 (1H, s, H2), 7.96 (1H, s, H8), 7.36 – 7.30 (5H, m, Ar), 6.02 (2H, br, NH_2), 5.90 (1H, d, *J* = 4.1 Hz, H1'), 5.18 (2H, apparent s, H11'), 4.96 (1H, t, *J* = 4.5 Hz, H2'), 4.54 (1H, d, *J* = 3.8 Hz, H5'), 4.42 – 4.35 (2H, m, H3' and H5'), 4.29 (1H, q, *J* = 4.0 Hz, H4'), 3.48 (2H, apparent s, H8'), 0.16 (9H, s, H16') and 0.01 (9H, s, H16'); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.2 (C7' and C9'), 155.7 (C6), 153.0 (C2), 149.7 (C4), 140.2 (C8), 135.2 (C12'), 128.6 (Ar, overlapping signals), 120.6 (C5), 89.8 (C1'), 81.9 (C4'), 74.2 (C2'), 71.7 (C3'), 67.5 (C11'), 64.3 (C5'), 41.4 (C8') and 0.26 (C16').

*3-(((2S,3R,4S,5S)-5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methoxy)-3-oxopropanoic acid (**2**)*



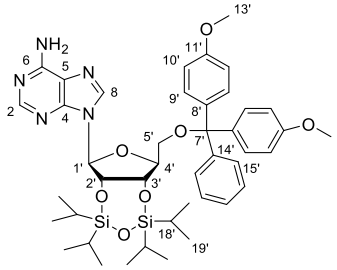
^{1}H NMR (600 MHz, *d*$_6$-DMSO) δ 8.34 (1H, s, H8), 8.15 (1H, s, H2), 7.32 (2H, br, NH_2), 5.91 (1H, d, *J* = 5.3 Hz, H1'), 4.64 (1H, t, *J* = 5.3 Hz, H2'), 4.36 (1H, dd, *J* = 12.0 and 3.8 Hz, H5'), 4.25 – 4.20 (2H, m, H3' and H5'), 4.11 – 4.07 (1H, m, H4') and 3.35 (2H, apparent s, H8'); ^{13}C NMR (150 MHz, *d*$_6$-DMSO) δ 168.2 (C9'), 167.3 (C7'), 156.1 (C6), 152.7 (C2), 149.4 (C4), 139.8 (C8), 119.2 (C5), 87.7 (C1'), 81.6 (C4'), 72.9 (C2'), 70.7 (C3'), 64.0 (C5') and 42.1 (C8').

*3-((((2S,3R,4S,5S)-5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl)amino)-3-oxopropanoic acid (**4**)*



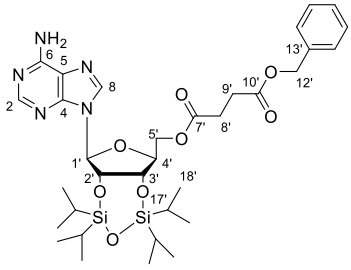
^{1}H NMR (600 MHz, CD_3OD) δ 8.49 (1H, s, H2), 8.40 (1H, s, H8), 6.02 (1H, d, *J* = 5.7 Hz, H1'), 4.74 (1H, t, *J* = 5.7 Hz, H2'), 4.27 (1H, dd, *J* = 5.1 and 4.1 Hz, H3'), 4.19 – 4.14 (1H, m, H4'), 3.72 (1H, dd, *J* = 14.2 and 5.6 Hz, H5') and 3.56 (1H, dd, *J* = 14.2 and 4.3 Hz, H5'); ^{13}C NMR (150 MHz, CD_3OD) δ 171.5 (C9'), 169.4 (C7'), 152.3 (C6), 150.1 (C4), 146.8 (C8), 144.2 (C2), 120.8 (C5), 90.5 (C1'), 85.4 (C4'), 75.2 (C2'), 72.6 (C3'), 49.5 (C8') and 42.5 (C5'). Note: C8' signal is not seen in ^{1}H NMR as it is exchangeable with NMR solvent.

*9-((5aS,6S,8S,8aS)-8-((Bis(4-methoxyphenyl)(phenyl)methoxy)methyl)-2,2,4,4-tetraisopropyltetrahydrofuro[3,4-f][1,3,5,2,4]trioxadisilepin-6-yl)-9H-purin-6-amine (**29**)*



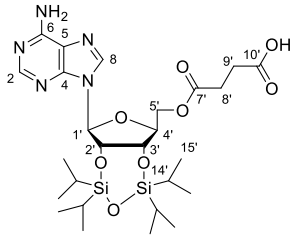
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.31 (1H, s, H2), 8.11 (1H, s, H8), 7.47 – 7.41 (2H, m, H15'), 7.36 – 7.31 (4H, m, H9'), 7.29 – 7.16 (3H, m, H15'), 6.83 – 6.78 (4H, m H10'). 6.10 (2H, br, NH_2), 6.06 (1H, d, *J* = 4.7 Hz, H1'), 5.11 (1H, d, *J* = 4.7 Hz, H2'), 4.78 (1H, t, *J* = 4.7 Hz, H3'), 4.29 – 4.25 (1H, m, H4'), 3.78 (6H, s, H13'), 3.50 (1H, dd, *J* = 10.7 and 3.4 Hz, H5'), 3.33 (1H, dd, *J* = 10.7 and 3.4 Hz, H5') and 1.13 – 0.92 (28H, m, H18' and H19'); ^{13}C NMR (150 MHz, $CDCl_3$) δ 158.7 (C11'), 155.7 (C6), 153.2 (C2), 150.0 (C4), 144.8 (C14'), 139.3 (C8), 135.9 (C8'), 130.1 (C9'), 128.3 (C15'), 128.2 (C15'), 127.0 (C15'), 120.3 (C5), 113.5 (C10'), 89.0 (C1'), 86.6 (C7'), 84.3 (C4'), 76.2 (C2'), 73.2 (C3'), 63.3 (C5'), 55.3 (C13'), 17.2 (C19') and 13.7 (C18').

*((5aS,6S,8S,8aS)-8-(6-Amino-9H-purin-9-yl)-2,2,4,4-tetraisopropyltetrahydrofuro[3,4-f][1,3,5,2,4]trioxadisilepin-6-yl)methyl benzyl succinate (**31**)*



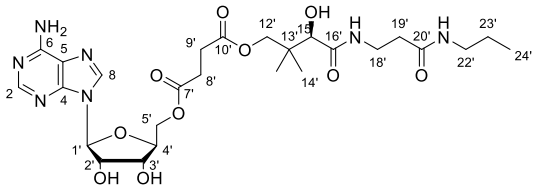
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.32 (1H, s, H2), 8.00 (1H, s, H8), 7.38 – 7.29 (5H, m, Ar), 5.99 (1H, d, *J* = 3.2, H1'), 5.88 (2H, br, NH_2), 5.13 (2H, s, H12'), 5.09 (1H, dd, *J* = 4.8 and 3.2 Hz, H2'), 4.70 (1H, dd, *J* = 6.1 and 4.8 Hz, H3'), 4.51 – 4.46 (1H, m, H5'), 4.36 – 4.31 (2H, m, H4' and H5'), 2.72 – 2.64 (4H, m, H8' and H9') and 1.11 – 0.97 (28H, m, H17' and H18'); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.1 (C7' and C10'), 155.5 (C6), 152.9 (C2), 149.6 (C4), 139.7 (C8), 135.8 (C13'), 128.5 (Ar, overlapping signals), 120.5 (C5), 90.5 (C1'), 81.8 (C4'), 75.8 (C2'), 72.7 (C3'), 66.8 (C12'), 63.9 (C5'), 29.1 (C8'), 29.0 (C9'), 17.3 (C18') and 13.6 (C17').

*4-(((5aS,6S,8S,8aS)-8-(6-Amino-9H-purin-9-yl)-2,2,4,4-tetraisopropyltetrahydrofuro[3,4-f][1,3,5,2,4]trioxadisilepin-6-yl)methoxy)-4-oxobutanoic acid (**32**)*



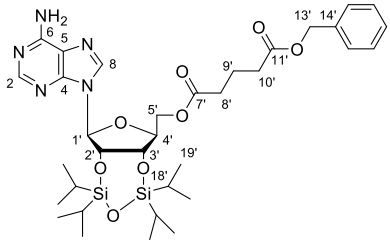
^{1}H NMR (600 MHz, CD_3OD) δ 8.32 (1H, s, H8), 8.19 (1H, s, H2), 6.05 (1H, d, *J* = 4.5 Hz, H1'), 5.20 (1H, t, *J* = 4.5 Hz, H2'), 4.76 (1H, t, *J* = 5.2 Hz, H3'), 4.47 – 4.35 (2H, m, H5'), 4.32 – 4.27 (1H, m, H4'), 3.32 – 3.29 (4H, m, H8' and H9') and 2.63 – 2.56 (28H, m, H14' and H15'); ^{13}C NMR (150 MHz, CD_3OD) δ 176.0 (C10'), 173.9 (C7'), 157.3 (C6), 153.9 (C2), 150.6 (C4), 141.9 (C8), 120.6 (C5), 90.6 (C1'), 83.9 (C4'), 77.7 (C2'), 73.8 (C3'), 64.3 (C5'), 30.1 (C8'), 30.0 (C9'), 17.9 (C15') and 14.6 (C14').

*((2S,3R,4S,5S)-5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl ((R)-3-hydroxy-2,2-dimethyl-4-oxo-4-((3-oxo-3-(propylamino)propyl)amino)butyl) succinate (**5**)*



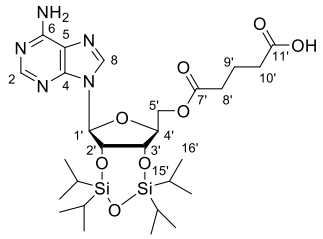
^{1}H NMR (600 MHz, CD_3OD) δ 8.29 (1H, s, H8), 8.21 (1H, s, H2), 6.01 (1H, d, *J* = 4.6 Hz, H1'), 4.74 (1H, t, *J* = 4.6 Hz, H2'), 4.44 – 4.35 (3H, m, H3' and H5'), 4.27 – 4.24 (1H, m, H4'), 4.03 (1H, d, *J* = 10.5, H12'), 3.89 (1H, d, *J* = 10.5 Hz, H12'), 3.86 (1H, s, H15'), 3.51 – 3.39 (2H, m, H18'), 3.13 - 3.08 (2H, m, H22'), 2.66 - 2.64 (4H, m, H8' and H9'), 2.43 – 2.38 (2H, m, H19'), 1.53 – 1.45 (2H, m, H23'), 0.96 (3H, s, H14') and 0.93 – 0.89 (6H, m, H14' and H24'); ^{13}C NMR (150 MHz, CD_3OD) δ 175.4 (C16'), 173.9 (C7'), 173.8 (C10'), 173.6 (C20'), 157.3 (C6), 153.9 (C2), 150.6 (C4), 141.3 (C8), 120.5 (C5), 90.3 (C1'), 83.5 (C4'), 75.8 (C2'), 75.2 (C3'), 71.7 (C12'), 71.5 (C15'), 65.1 (C5'), 42.3 (C22'), 39.3 (C13'), 36.4 (C18' and C19'), 30.3 (C8' and C9'), 23.5 (C23'), 21.6 (C14'), 20.9 (C14') and 11.7 (C24').

*((5aS,6S,8S,8aS)-8-(6-Amino-9H-purin-9-yl)-2,2,4,4-tetraisopropyltetrahydrofuro[3,4-f][1,3,5,2,4]trioxadisilepin-6-yl)methyl benzyl glutarate (**35**)*



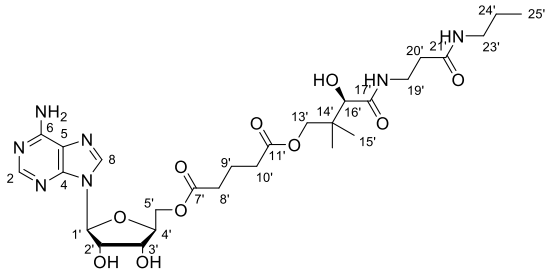
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.30 (1H, s, H2), 7.97 (1H, s, H8), 7.39 -7.29 (5H, m, Ar), 6.01 – 5.97 (3H, m, NH_2 and H1'), 5.11 (2H, s, H13'), 5.09 (1H, dd, *J* = 4.7 and 3.3 Hz, H2'), 4.69 (1H, dd, *J* = 6.4 and 4.7 Hz, H3'), 4.48 – 4.44 (1H, m, H5'), 4.34 – 4.29 (2H, m, H4' and H5'), 2.44 – 2.38 (4H, m, H8' and H10'), 1.96 (2H, qn, *J* = 7.4 Hz, H9') and 1.10 – 1.00 (28H, m, H18' and H19'); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.7 (C7' and C11'), 155.6 (C6), 152.9 (C2), 149.6 (C4), 139.8 (C8), 136.0 (C14'), 128.7 (Ar), 128.6 (Ar), 128.5 (Ar), 120.4 (C5), 90.5 (C1'), 81.8 (C4'), 75.7 (C2'), 72.7 (C3'), 66.4 (C13'), 63.7 (C5'), 33.6 (C8'), 33.5 (C10'), 20.2 (C9'), 17.3 (C19') and 13.4 (C18').

*5-(((5aS,6S,8S,8aS)-8-(6-Amino-9H-purin-9-yl)-2,2,4,4-tetraisopropyltetrahydrofuro[3,4-f][1,3,5,2,4]trioxadisilepin-6-yl)methoxy)-5-oxopentanoic acid (**36**)*



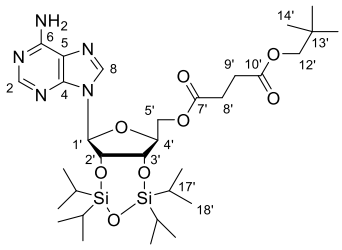
^{1}H NMR (600 MHz, CD_3OD) δ 8.29 (1H, s, H8), 8.19 (1H, s, H2), 6.04 (1H, d, *J* = 4.4 Hz, H1'), 5.26 (1H, t, *J* = 4.7 Hz, H2'), 4.78 (1H, t, *J* = 5.1 Hz, H3'), 4.45 – 4.32 (2H, m, H5'), 4.29 (1H, q, *J* = 4.4 Hz, H4'), 2.40 – 2.28 (4H, m, H8' and H10'), 1.89 – 1.81 (2H, m, H9') and 1.17 – 0.89 (28H, m, H15' and H16'); ^{13}C NMR (150 MHz, CD_3OD) δ 177.0 (C11'), 174.2 (C7'), 157.4 (C6), 153.9 (C2), 150.6 (C4), 141.6 (C8), 120.6 (C5), 90.7 (C1'), 83.7 (C4'), 76.8 (C2'), 74.0 (C3'), 64.1 (C5'), 34.1 (C8'), 34.0 (C10'), 21.4 (C9'), 17.6 (C16') and 14.7 (C15').

*((2S,3R,4S,5S)-5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl ((R)-3-hydroxy-2,2-dimethyl-4-oxo-4-((3-oxo-3-(propylamino)propyl)amino)butyl) glutarate (**6**)*



^{1}H NMR (600 MHz, CD_3OD) δ 8.27 (1H, s, H8), 8.20 (1H, s, H2), 6.01 (1H, d, *J* = 4.4 Hz, H1'), 4.75 (1H, t, *J* = 4.8 Hz, H2'), 4.43 – 4.35 (3H, m, H3' and H5'), 4.27 – 4.23 (1H, m, H4'), 4.02 (1H, d, *J* = 9.5 Hz, H13'), 3.90 (1H, d, *J* = 9.5 Hz, H13'), 3.86 (1H, s, H16'), 3.51 – 3.39 (2H, m, H19'), 3.12 – 3.08 (2H, m, H23'), 2.50 – 2.35 (6H, m, H8', H10' and H20'), 1.92 – 1.85 (2H, m, H9'), 1.53 – 1.45 (2H, m, H24'), 0.96 (3H, s, H15') and 0.94 – 0.88 (6H, m, H15' and H25'); ^{13}C NMR (150 MHz, CD_3OD) δ 175.4 (C17'), 174.6 (C11'), 173.9 (C7'), 173.5 (C21'), 157.3 (C6), 153.9 (C2), 150.6 (C4), 141.2 (C8), 120.6 (C5), 90.4 (C1'), 83.4 (C4'), 75.8 (C16'), 75.1 (C2'), 71.8 (C3'), 71.3 (C13'), 64.8 (C5'), 42.3 (C23'), 39.4 (C14'), 36.8 (C19' and C20'), 33.8 (C8' and C10'), 23.6 (C24'), 21.6 (C9'), 21.1 (C15'), 20.8 (C15') and 11.8 (C25').

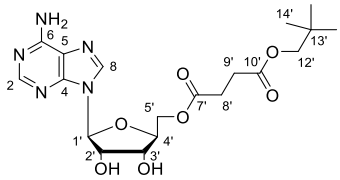
((5aS,6S,8S,8aS)-8-(6-Amino-9H-purin-9-yl)-2,2,4,4-tetraisopropyltetrahydrofuro[3,4-f][1,3,5,2,4]trioxadisilepin-6-yl)methyl neopentyl succinate (**39**)



^{1}H NMR (600 MHz, $CDCl_3$) δ 8.31 (1H, s, H2), 8.00 (1H, s, H8), 5.99 (1H, d, *J* = 3.3 Hz, H1'), 5.90 (2H, br, NH_2), 5.08 (1H, dd, *J* = 4.7 and 3.3 Hz, H2'), 4.69 (1H, t, *J* = 4.7 Hz, H3'), 4.50 – 4.46 (1H, m, H5'), 4.35 – 4.31 (2H, m, H4' and H5'), 3.77 (2H, apparent s, H12'), 2.67 – 2.65 (4H, m, H8' and H9'), 1.09 – 1.01 (28H, m, H17' and H18') and 0.91 (9H, s, H14'); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.3 (C7' and C10'), 155.4 (C6), 152.7 (C2), 149.6 (C4),

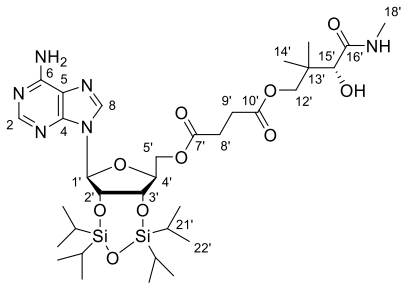
139.7 (C8), 120.5 (C5), 90.4 (C1'), 81.8 (C4'), 75.8 (C12'), 74.3 (C2'). 72.7 (C3'), 63.9 (C5'), 31.4 (C8' and C9'), 29.1 (C13'), 26.5 (C14'), 17.3 (C18') and 13.2 (C17').

((2S,3R,4S,5S)-5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl neopentyl succinate (**7**)



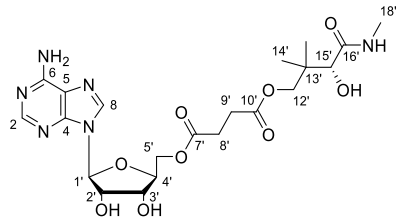
^{1}H NMR (600 MHz, CD_3OD) δ 8.28 (1H, s, H8), 8.20 (1H, s, H2), 6.01 (1H, d, *J* = 4.5 Hz, H1'), 4.74 (1H, t, *J* = 4.9 Hz, H2'), 4.44 – 4.33 (3H, m, H3' and H5'), 4.27 – 4.23 (1H, m, H4'), 3.76 (1H, d, *J* = 10.5 Hz, H12'), 3.73 (1H, d, *J* = 10.5 Hz, H12'), 3.32 – 3.29 (4H, m, H8' and H9') and 2.65 (9H, s, H14'); ^{13}C NMR (150 MHz, CD_3OD) δ 174.0 (C10'), 173.8 (C7'), 157.3 (C6), 153.9 (C2), 150.6 (C4), 141.3 (C8), 120.5 (C5), 90.3 (C1'), 83.5 (C4'), 75.1 (C12'), 75.0 (C2'), 71.8 (C3'), 65.1 (C5'), 32.1 (C13'), 29.9 (C8' and C9') and 26.7 (C14').

((5aS,6S,8S,8aS)-8-(6-Amino-9H-purin-9-yl)-2,2,4,4-tetraisopropyltetrahydrofuro[3,4-f][1,3,5,2,4]trioxadisilepin-6-yl)methyl ((R)-3-hydroxy-2,2-dimethyl-4-(methylamino)-4-oxobutyl) succinate (**41**)



^{1}H NMR (600 MHz, $CDCl_3$) δ 8.29 (1H, s, H2), 8.09 (1H, s, H8), 6.81 (1H, d, *J* = 5.0 Hz, NH), 6.13 (2H, br, NH_2), 6.02 (1H, d, *J* = 2.6 Hz, H1'), 5.06 (1H, dd, *J* = 4.7 and 2.6 Hz, H2'), 4.70 (1H, dd, *J* = 6.8 and 4.7 Hz, H3'), 4.56 – 4.50 (1H, m, H5'), 4.36 – 4.28 (2H, m, H4' and H5'), 4.23 (1H, d, *J* = 10.8 Hz, H12'), 4.05 (1H, s, H15'), 3.84 (1H, d, *J* = 10.8 Hz, H12'), 2.83 (3H, d, *J* = 5.0 Hz, H18'), 2.63 – 2.58 (4H, m, H8' and H9'), 1.10 – 1.04 (31H, m, H14', H21' and H22') and 0.93 (3H, s, H14'); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.2 (C16'), 172.7 (C10'), 172.2 (C7'), 155.2 (C6), 152.6 (C2), 149.4 (C4), 139.8 (C8), 120.0 (C5), 90.6 (C1'), 81.7 (C4'), 76.2 (C2'), 74.4 (C15'), 72.2 (C3'), 71.0 (C12'), 63.0 (C5'), 38.7 (C13'), 29.5 (C8' and C9'), 25.8 (C18'), 21.5 (C14'), 19.9 (C14'), 17.5 (C22') and 13.6 (C21').

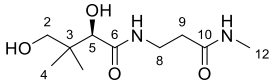
((2S,3R,4S,5S)-5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl ((R)-3-hydroxy-2,2-dimethyl-4-(methylamino)-4-oxobutyl) succinate (**8**)



^{1}H NMR (600 MHz, CD_3OD) δ 8.29 (1H, s, H8), 8.20 (1H, s, H2), 6.02 (1H, d, *J* = 4.5 Hz, H1'), 4.74 (1H, t, *J* = 4.9 Hz, H2'), 4.55 – 4.35 (3H, m, H3' and H5'), 4.27 – 4.23 (1H, m, H4'), 4.03 (1H, d, *J* = 10.6 Hz, H12'), 3.90 (1H, d, *J* = 10.6 Hz, H12'), 3.86 (1H, s, H15'), 2.74 (3H, s, H18'), 2.66 – 2.63 (4H, m, H8' and H9'), 0.96 (3H, s, H14') and 0.92 (3H, s, H14'); ^{13}C NMR (150 MHz, CD_3OD) δ 176.1 (C10'), 173.9 (C16'), 173.8 (C7'), 157.3 (C6), 153.9 (C2),

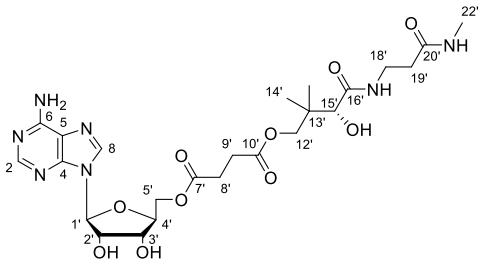
150.6 (C4), 141.2 (C8), 120.5 (C5), 90.3 (C1'), 83.5 (C4'), 76.0 (C15'), 75.2 (C2'), 71.8 (C3'), 71.4 (C12'), 65.1 (C5'), 39.3 (C13'), 29.9 (C8' and C9'), 25.8 (C18'), 21.5 (C14') and 20.8 (C14').

(R)-2,4-Dihydroxy-3,3-dimethyl-N-(3-(methylamino)-3-oxopropyl)butanamide (**42**)



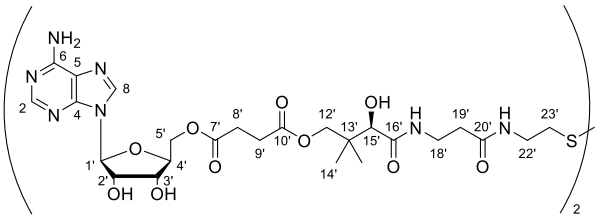
^{1}H NMR (600 MHz, CD_3OD) δ 3.89 (1H, s, H5), 3.54 – 3.41 (3H, m, H2 and H8), 3.38 (1H, d, *J* = 11.0 Hz, H2), 2.71 (3H, s, H12), 2.41 (2H, t, *J* = 6.7 Hz, H9), 0.91 (3H, s, H4) and 0.90 (3H, s, H4); ^{13}C NMR (150 MHz, CD_3OD) δ 176.1 (C6), 174.3 (C10), 77.3 (C5), 70.3 (C2), 40.3 (C3), 36.4 (C8 and C9), 26.5 (C12), 21.3 (C4) and 20.9 (C4).

((2S,3R,4S,5S)-5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl ((R)-3-hydroxy-2,2-dimethyl-4-((3-(methylamino)-3-oxopropyl)amino)-4-oxobutyl) succinate (**9**)



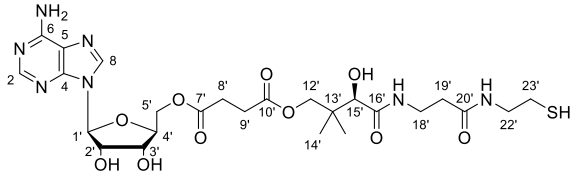
^{1}H NMR (600 MHz, CD_3OD) δ 8.50 (1H, s, H8), 8.41 (1H, s, H2), 6.08 (1H, d, *J* = 4.5 Hz, H1'), 4.74 (1H, t, *J* = 4.8 Hz, H2'), 4.42 – 4.34 (3H, m, H3' and H5'), 4.30 – 4.27 (1H, m, H4'), 4.02 (1H, d, *J* = 10.6 Hz, H12'), 3.88 (1H, d, *J* = 10.6 Hz, H12'), 3.84 (1H, s, H15'), 3.52 – 3.39 (2H, m, H18'), 2.70 – 2.68 (4H, m, H8' and H9'), 2.65 (3H, s, H22'), 2.41 (2H, t, *J* = 6.6 Hz, H19'), 0.95 (3H, s, H14') and 0.92 (3H, s, H14'); ^{13}C NMR (150 MHz, CD_3OD) δ 175.4 (C10'), 174.0 (C7'), 173.9 (C16'), 173.8 (C20'), 152.3 (C6), 150.0 (C4), 145.9 (C2), 143.9 (C8), 120.7 (C5), 90.7 (C1'), 83.9 (C4'), 75.9 (C15'), 75.5 (C2'), 71.7 (C3'), 71.5 (C12'), 64.9 (C5'), 39.5 (C13'), 36.4 (C18' and C19'), 29.9 (C8' and C9'), 26.4 (C22'), 21.5 (C14') and 20.8 (C14').

(10R,29R)-1-((2R,3S,4R,5R)-5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)-10,29-dihydroxy-9,9,30,30-tetramethyl-3,6,11,15,24,28-hexaoxo-2,7-dioxa-19,20-dithia-12,16,23,27-tetraazahentriacontan-31-yl (((2S,3R,4S,5S)-5-(6-amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl) succinate (**46**)



^{1}H NMR (600 MHz, CD_3OD) δ 8.29 (1H, s, H8), 8.20 (1H, s, H2), 6.02 (1H, d, *J* = 4.5 Hz, H1'), 4.74 (1H, t, *J* = 5.0 Hz, H2'), 4.44 – 4.35 (3H, m, H3' and H5'), 4.28 - 4.24 (1H, m, H4'), 4.03 (1H, d, *J* = 10.5 Hz, H12'), 3.88 (1H, d, *J* = 10.5 Hz, H12'), 3.86 (1H, s, H15'), 3.50 – 3.44 (4H, m, H18' and H22'), 2.81 – 2.75 (2H, m, H23'), 2.66 – 2.63 (4H, m, H8' and H9'), 2.46 – 2.40 (2H, m, H19'), 0.95 (3H, s, H14') and 0.92 (3H, s, H14'); ^{13}C NMR (150 MHz, CD_3OD) δ 175.5 (C10'), 174.0 (C7'), 173.9 (C16'), 173.8 (C20'), 157.6 (C6), 153.9 (C2), 150.6 (C4), 141.3 (C8), 120.5 (C5), 90.3 (C1'), 83.4 (C4'), 75.9 (C15'), 75.2 (C2'), 71.8 (C3'), 71.5 (C12'), 65.2 (C5'), 39.6 (C22'), 39.3 (C13'), 38.4 (C23'), 36.8 (C18' and C19'), 30.7 (C8' and C9'), 21.7 (C14') and 20.8 (C14').

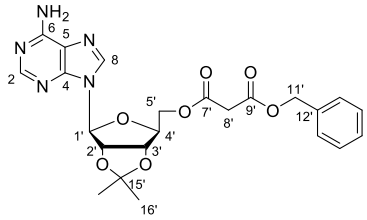
((2S,3R,4S,5S)-5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl ((R)-3-hydroxy-4-((3-((2-mercaptoethyl)amino)-3-oxopropyl)amino)-2,2-dimethyl-4-oxobutyl) succinate (**10**)

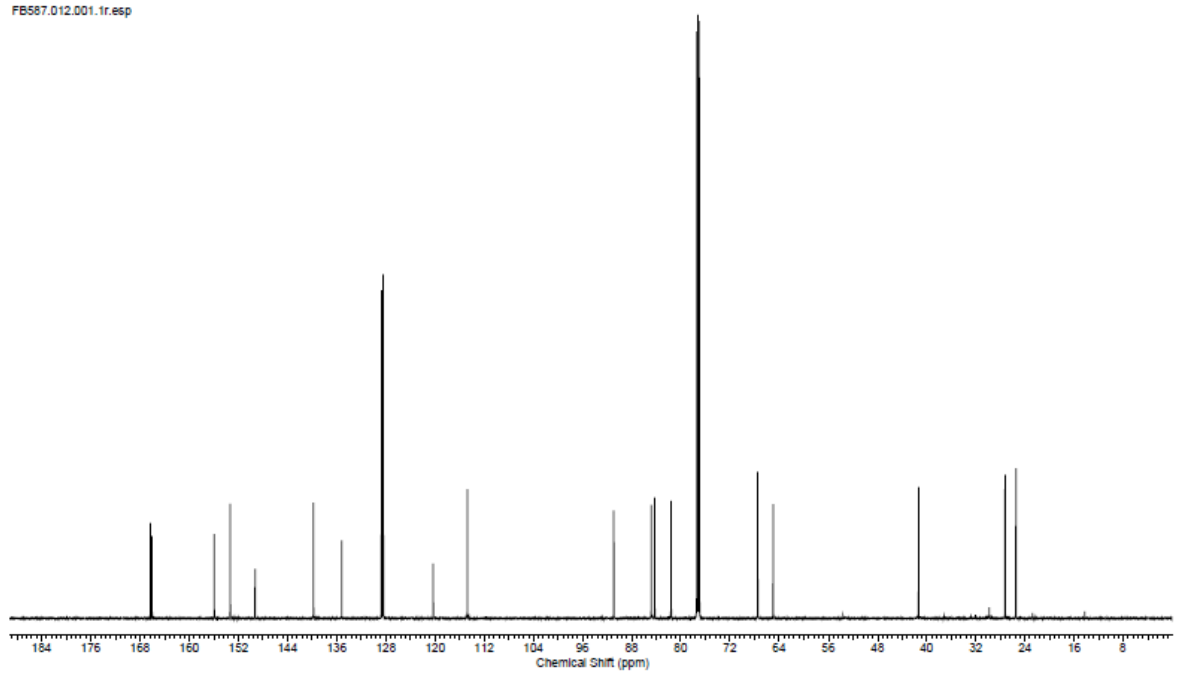


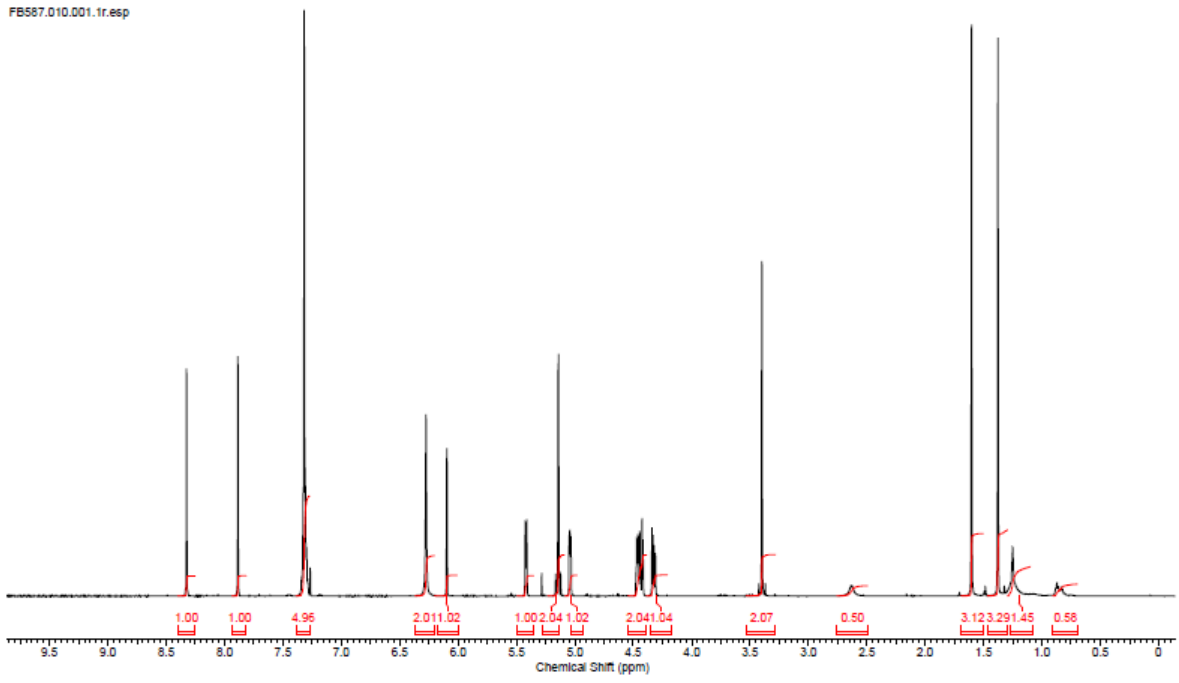
^{1}H NMR (600 MHz, CD_3OD) δ 8.49 (1H, s, H8), 8.40 (1H, s, H2), 6.08 (1H, d, *J* = 4.6 Hz, H1'), 4.74 (1H, t, *J* = 4.9 Hz, H2'), 4.42 – 4.35 (3H, m, H3' and H5'), 4.30 – 4.27 (1H, m, H4'), 4.01 (1H, d, *J* = 10.5 Hz, H12'), 3.89 (1H, d, *J* = 10.5 Hz, H12'), 3.85 (1H, s, H15'), 3.52 – 3.39 (2H, m, H18'), 3.33 – 3.28 (2H, m, H22'), 2.66 – 2.63 (2H, m, H8' and H9'), 2.60 – 2.55 (2H, m, H23'), 2.45 – 2.41 (2H, m, H19'), 0.96 (3H, s, H14') and 0.93 (3H, s, H14'); ^{13}C NMR (150 MHz, CD_3OD) δ 175.4 (C7'), 174.0 (C10'), 173.9 (C16'), 173.8 (C20'), 152.4 (C6), 150.0 (C5), 146.1 (C2), 143.9 (C8), 120.7 (C4), 90.7 (C1'), 83.9 (C4'), 76.0 (C13'), 75.5 (C2'), 71.7 (C3'), 71.5 (C12'), 65.9 (C5'), 43.9 (C22'), 39.3 (C13'), 36.4 (C18' and C19'), 29.9 (C8' and C9'), 24.5 (C23'), 21.6 (C14') and 20.8 (C14').

^{1}H and ^{13}C spectra of novel compounds

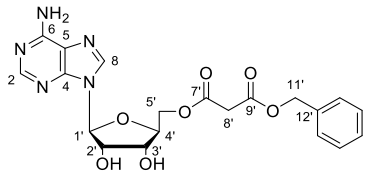
*((3aS,4S,6S,6aS)-6-(6-Amino-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl benzyl malonate (**13**)*

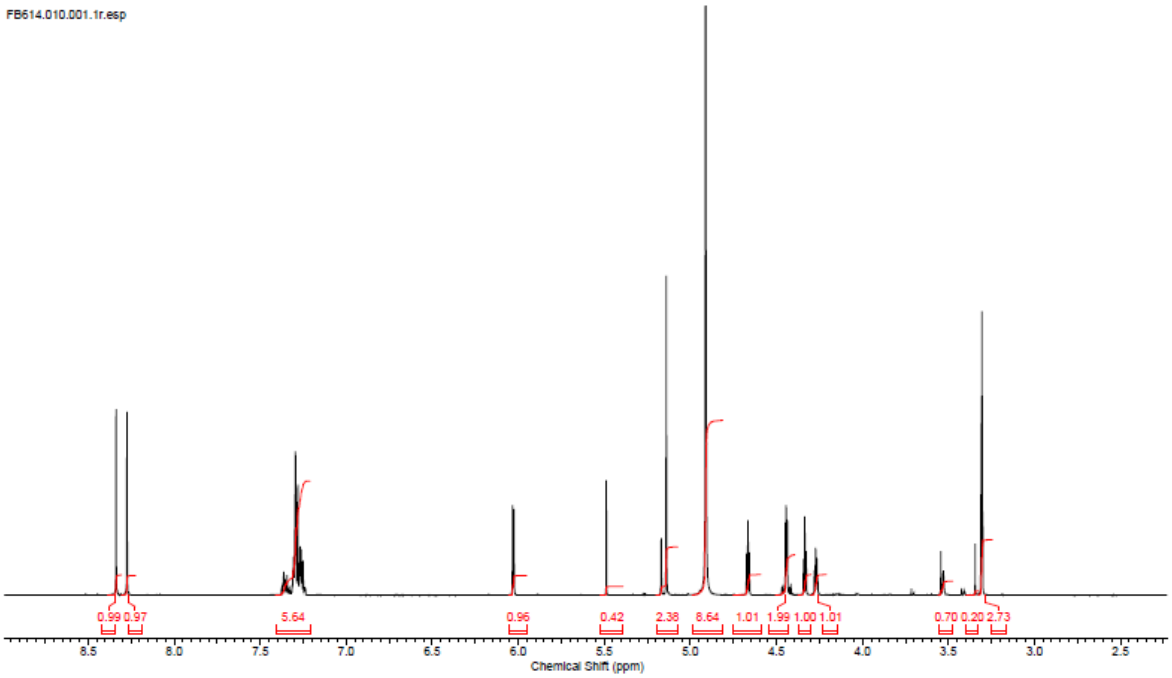


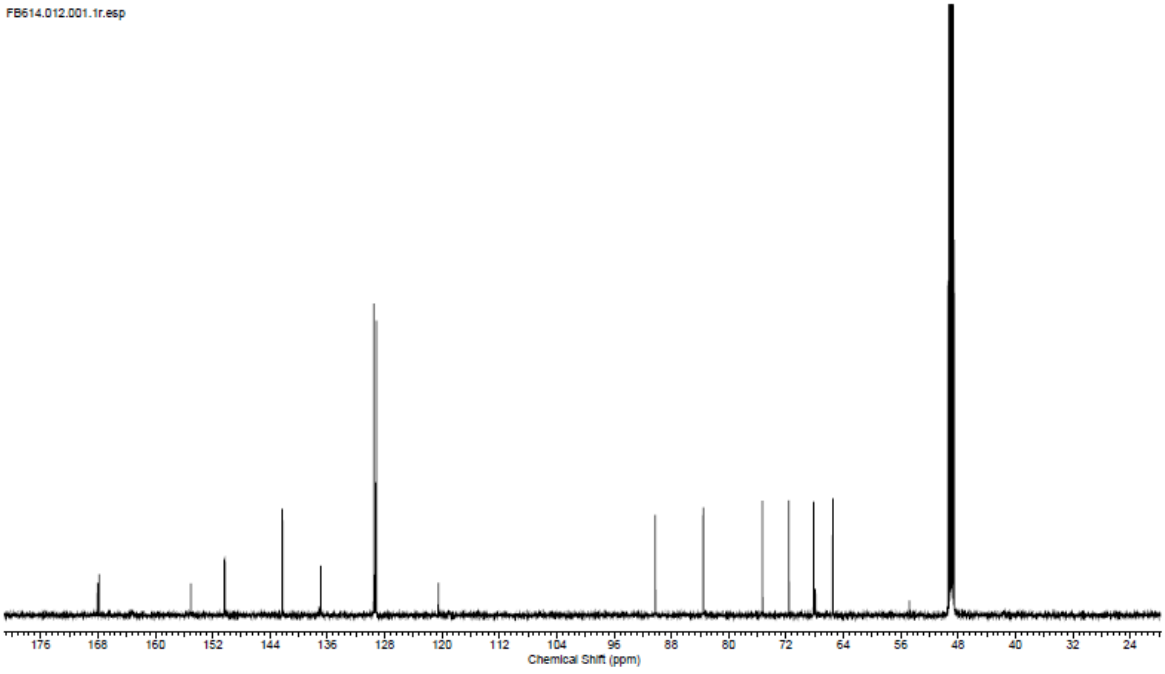




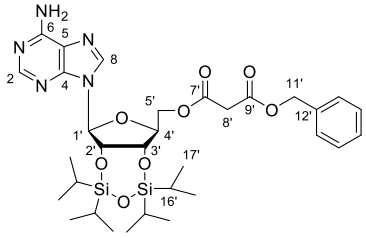
*((2S,3R,4S,5S)-5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methylbenzyl malonate (**14**)*

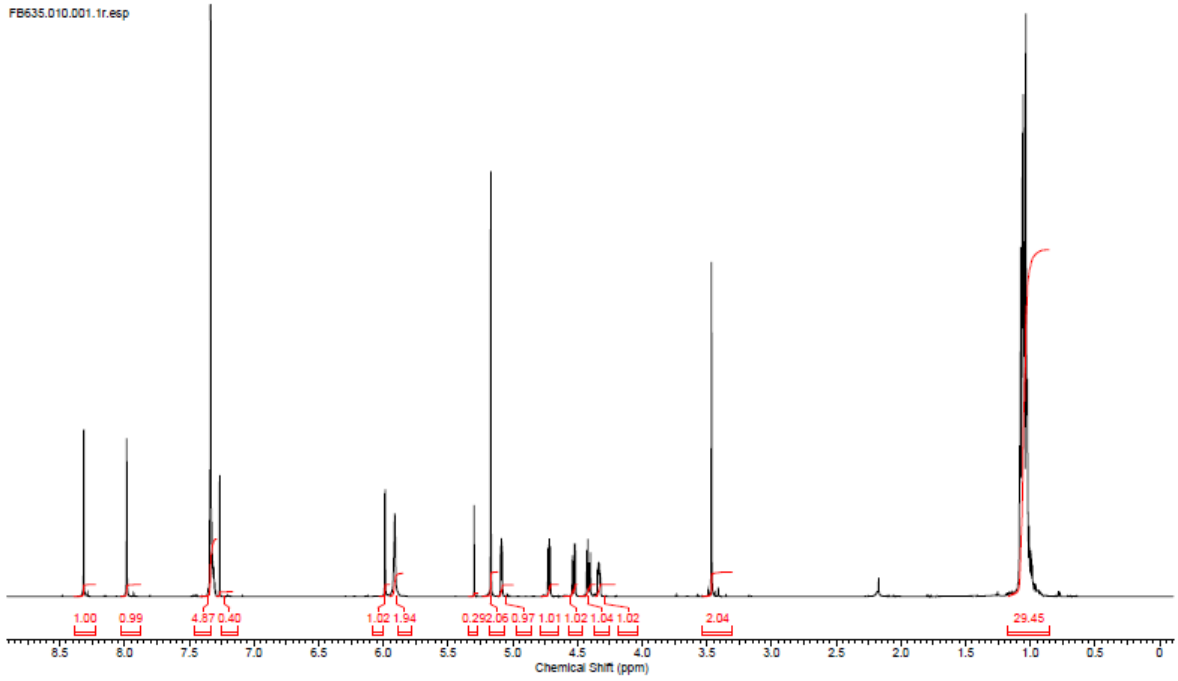


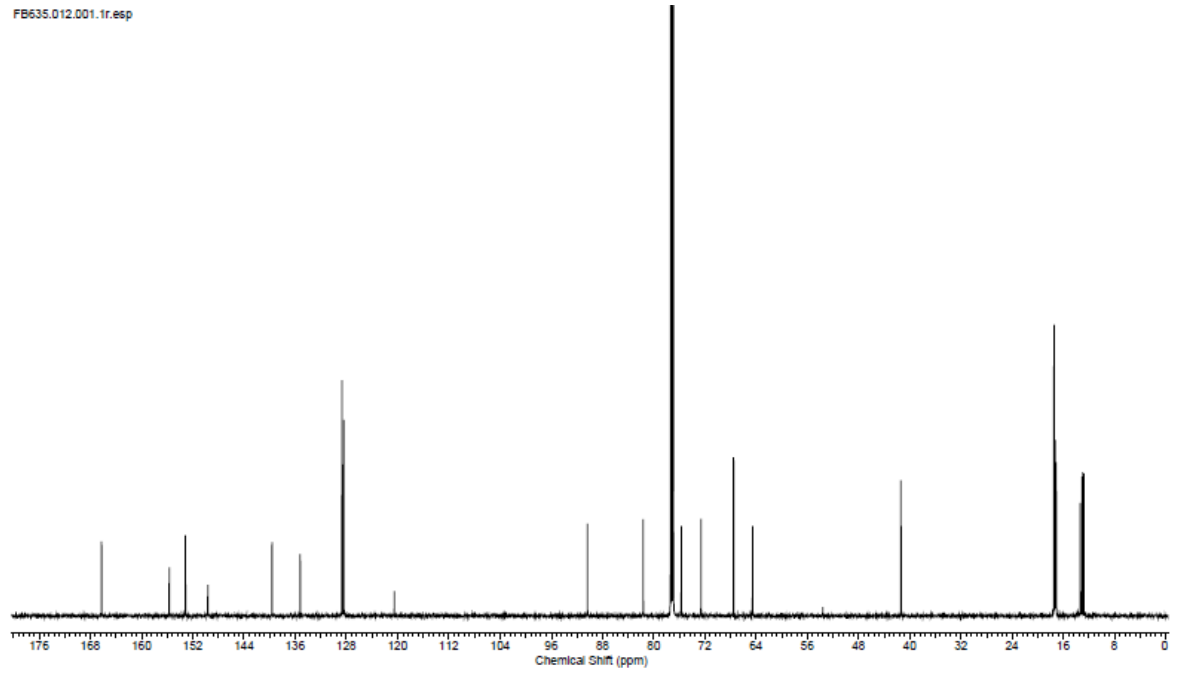




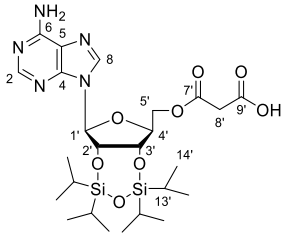
*((5aS,6S,8S,8aS)-8-(6-Amino-9H-purin-9-yl)-2,2,4,4-tetraisopropyltetrahydrofuro[3,4-f][1,3,5,2,4]trioxadisilepin-6-yl)methyl benzyl malonate (**15**)*

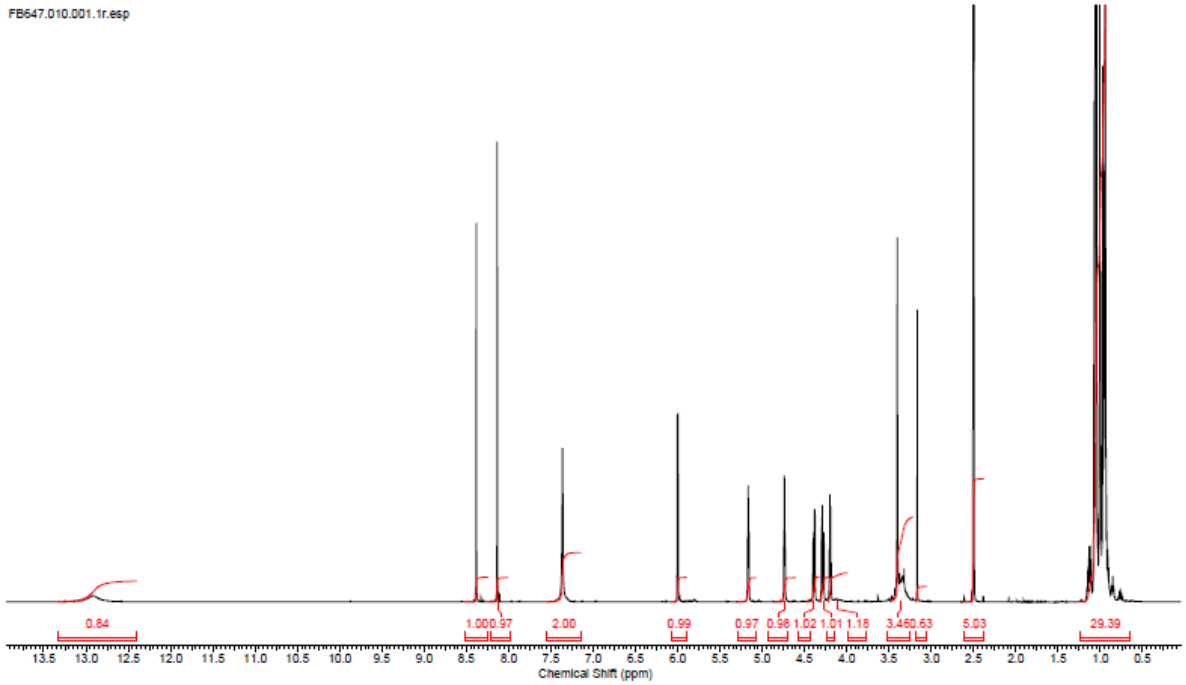


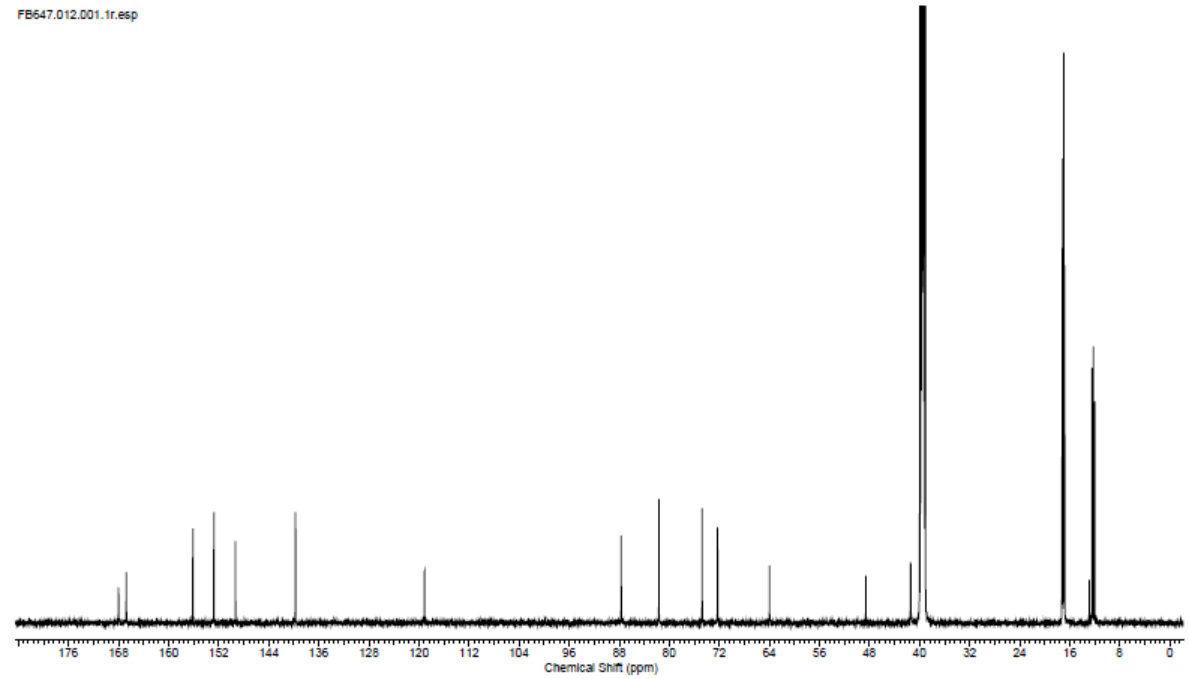




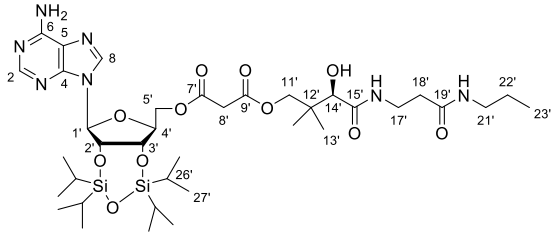
*3-(((5aS,6S,8S,8aS)-8-(6-Amino-9H-purin-9-yl)-2,2,4,4-tetraisopropyltetrahydrofuro[3,4-f][1,3,5,2,4]trioxadisilepin-6-yl)methoxy)-3-oxopropanoic acid (**16**)*

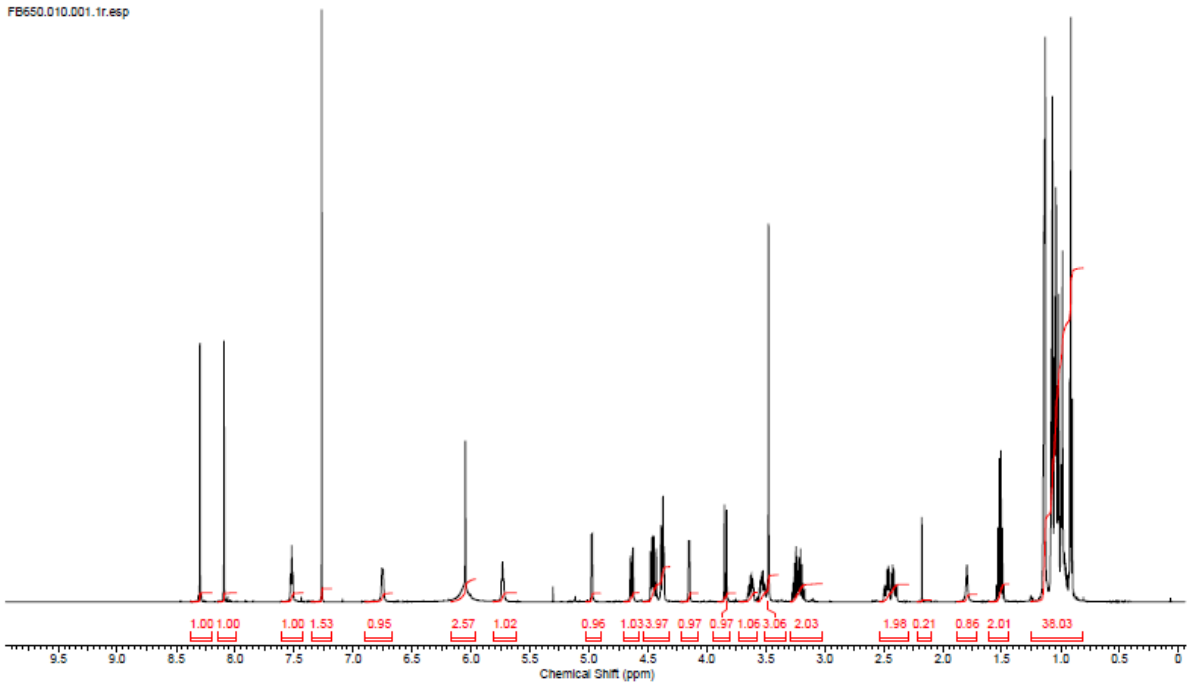


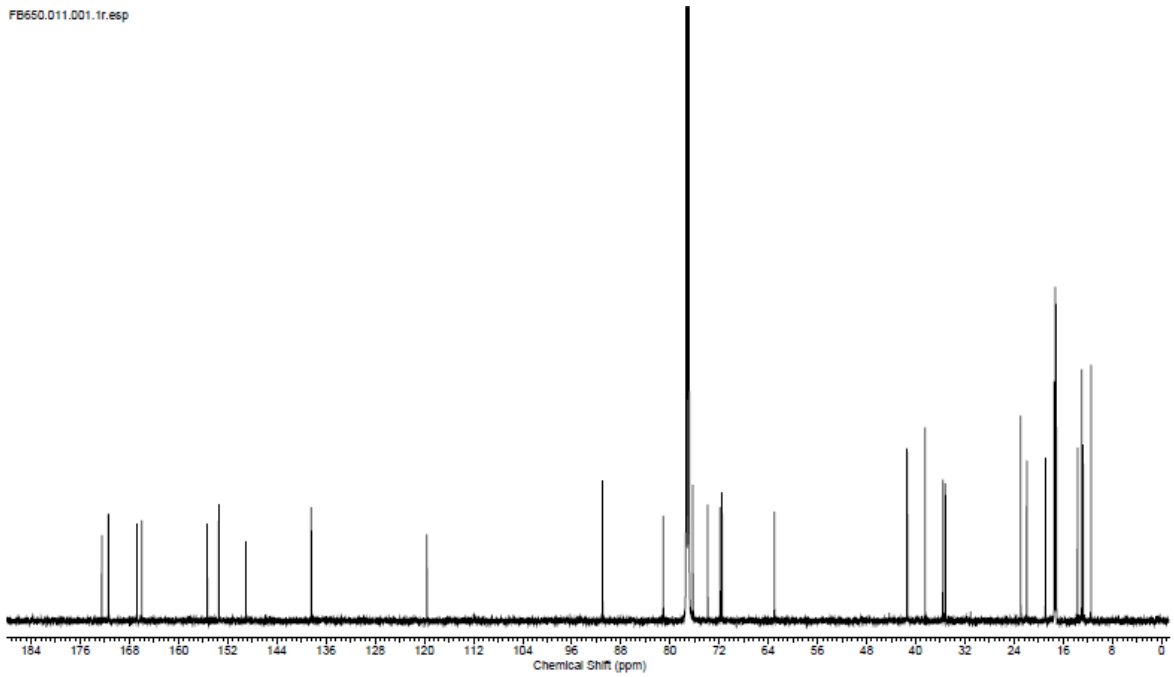




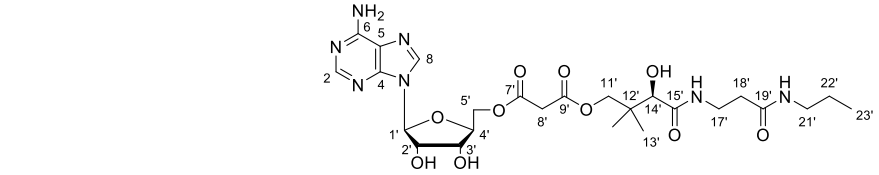
*((5aS,6S,8S,8aS)-8-(6-Amino-9H-purin-9-yl)-2,2,4,4-tetraisopropyltetrahydrofuro[3,4-f][1,3,5,2,4]trioxadisilepin-6-yl)methyl ((R)-3-hydroxy-2,2-dimethyl-4-oxo-4-((3-oxo-3-(propylamino)propyl)amino)butyl) malonate (**18**)*

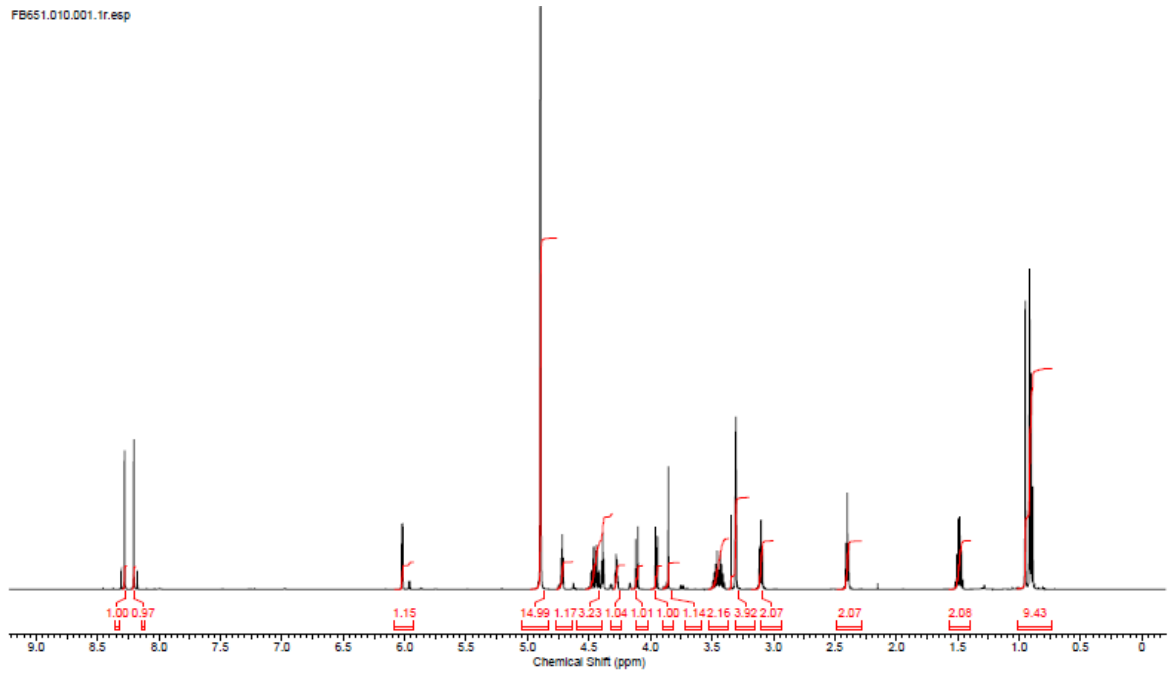


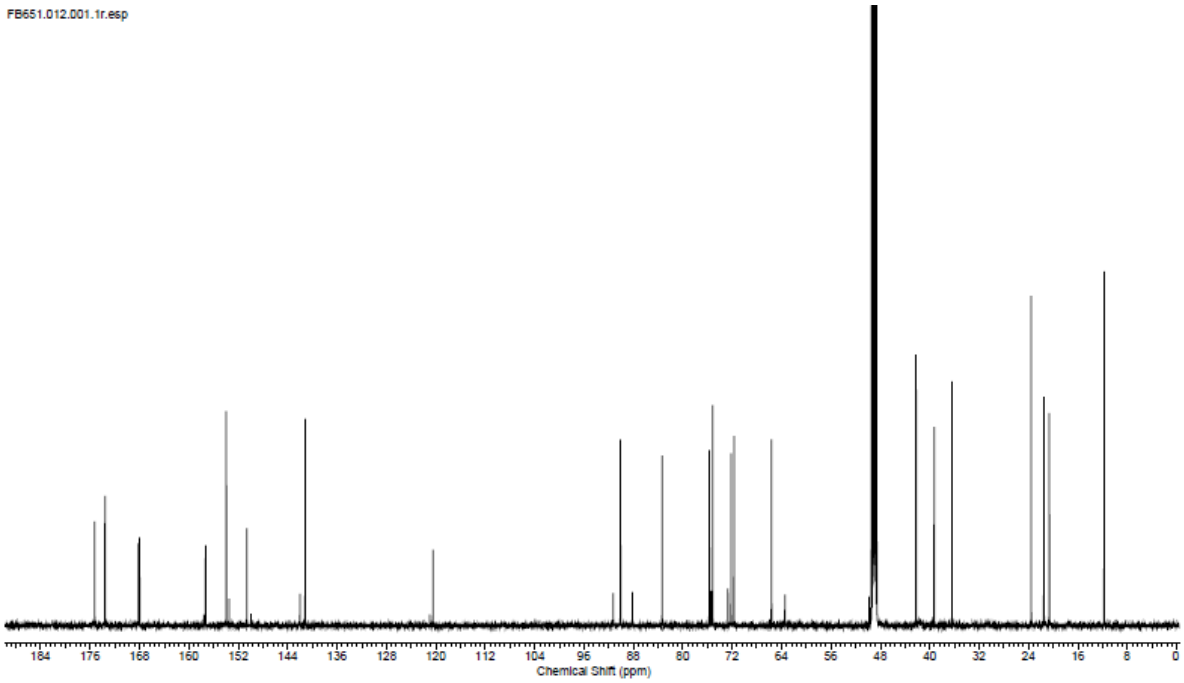




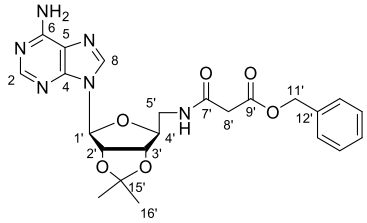
*((2S,3R,4S,5S)-5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl ((R)-3-hydroxy-2,2-dimethyl-4-oxo-4-((3-oxo-3-(propylamino)propyl)amino)butyl) malonate (**1**)*

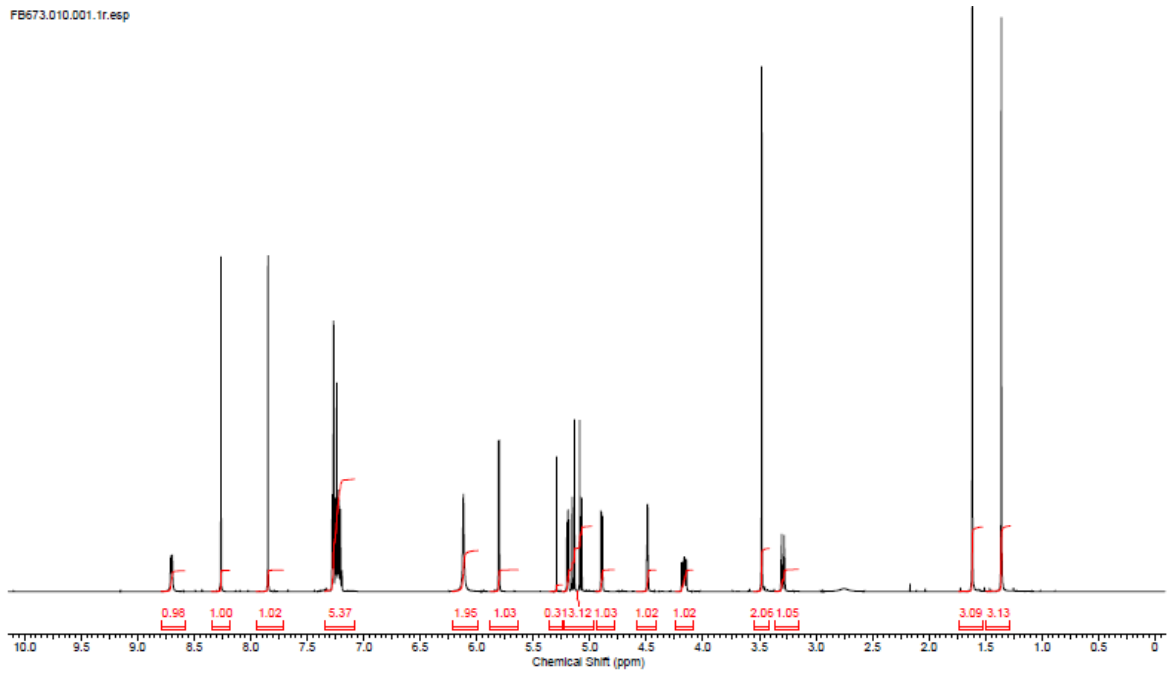


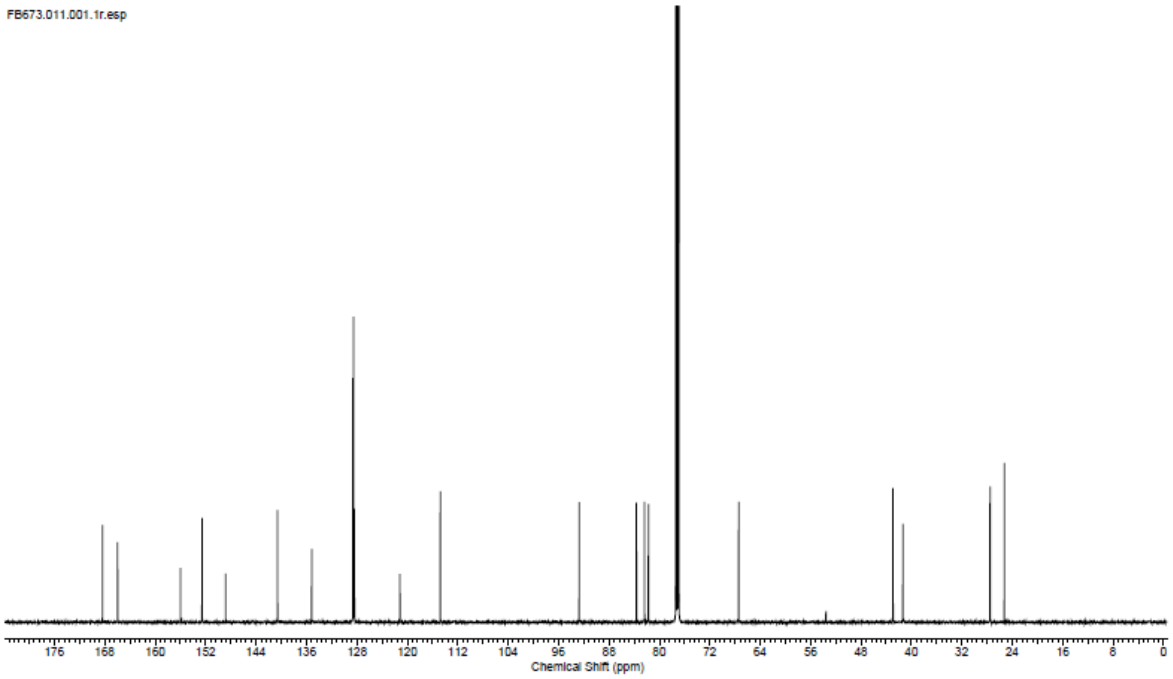




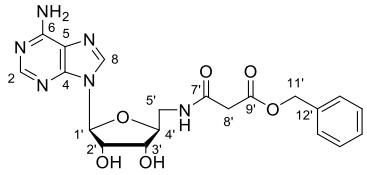
*Benzyl 3-((((3aS,4S,6S,6aS)-6-(6-amino-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl)amino)-3-oxopropanoate (**20**)*

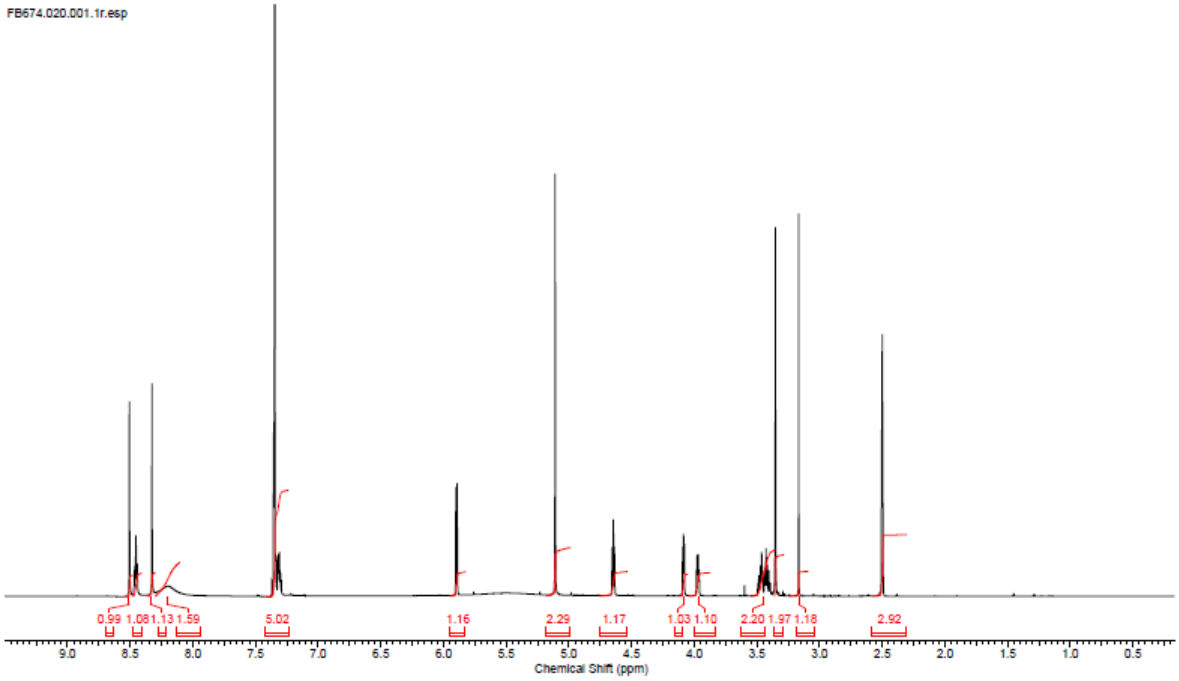


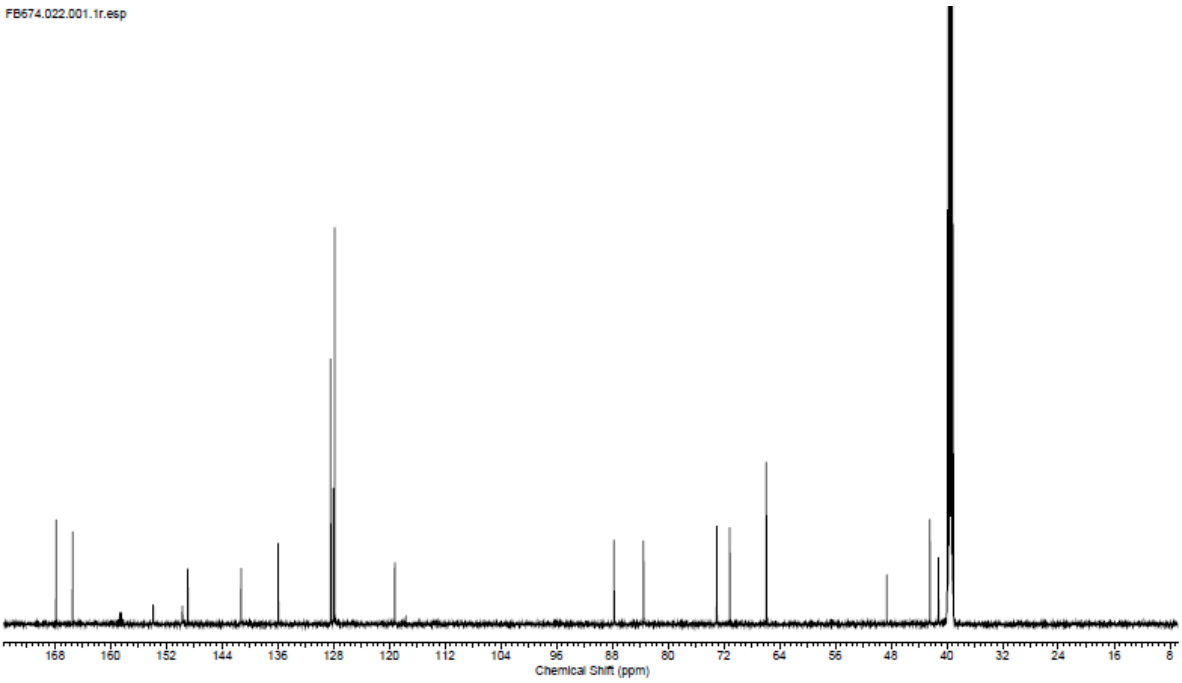




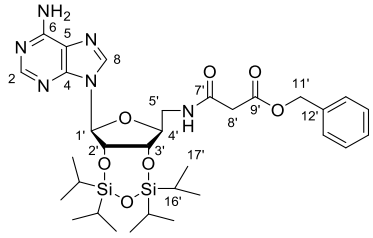
*Benzyl 3-((((2S,3R,4S,5S)-5-(6-amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl)amino)-3-oxopropanoate (**21**)*

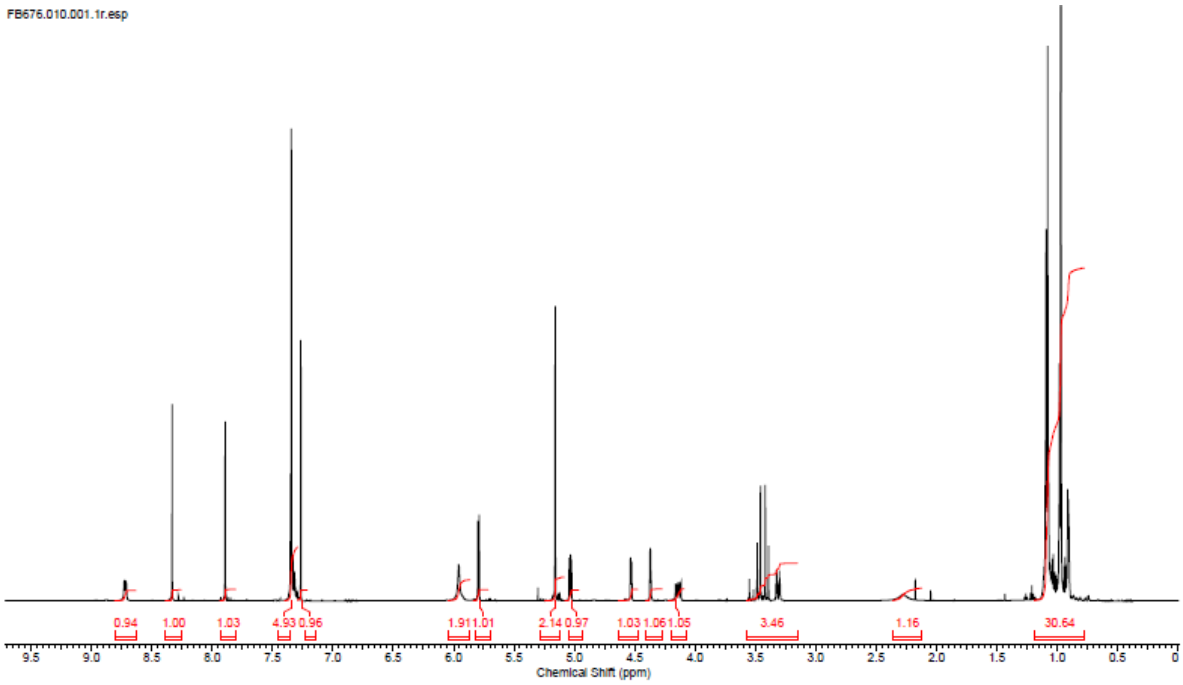


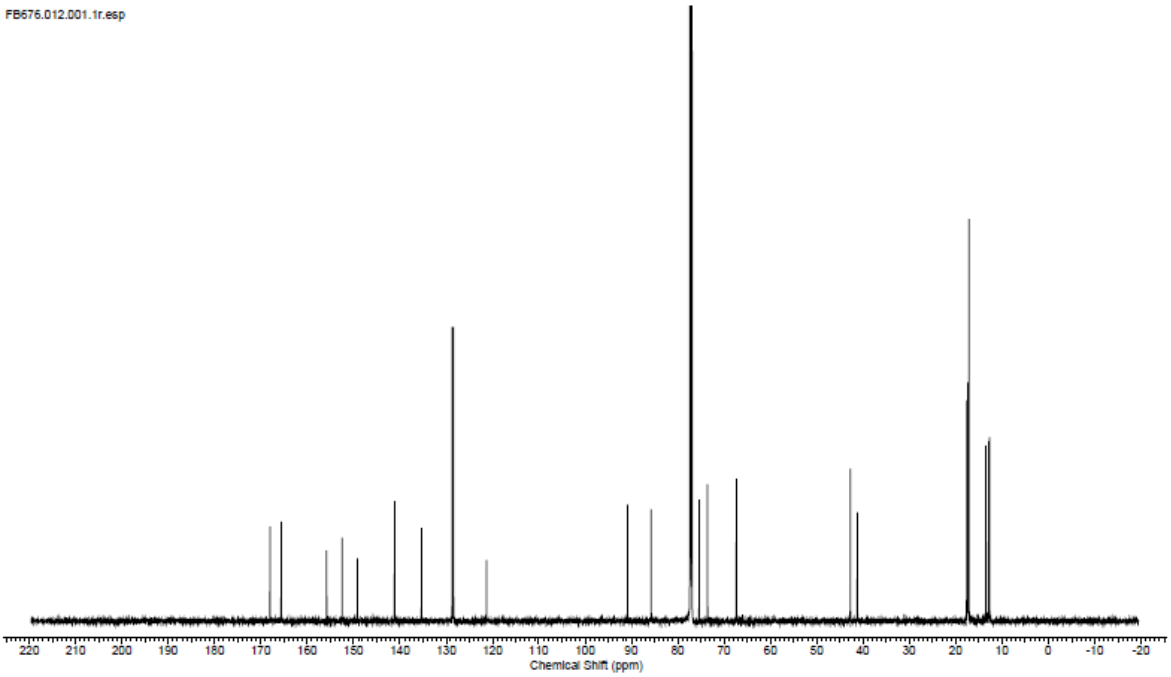




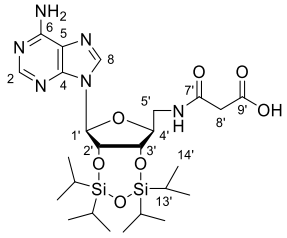
*Benzyl 3-((((5aS,6S,8S,8aS)-8-(6-amino-9H-purin-9-yl)-2,2,4,4-tetraisopropyltetrahydrofuro[3,4-f][1,3,5,2,4]trioxadisilepin-6-yl)methyl)amino)-3-oxopropanoate (**22**)*

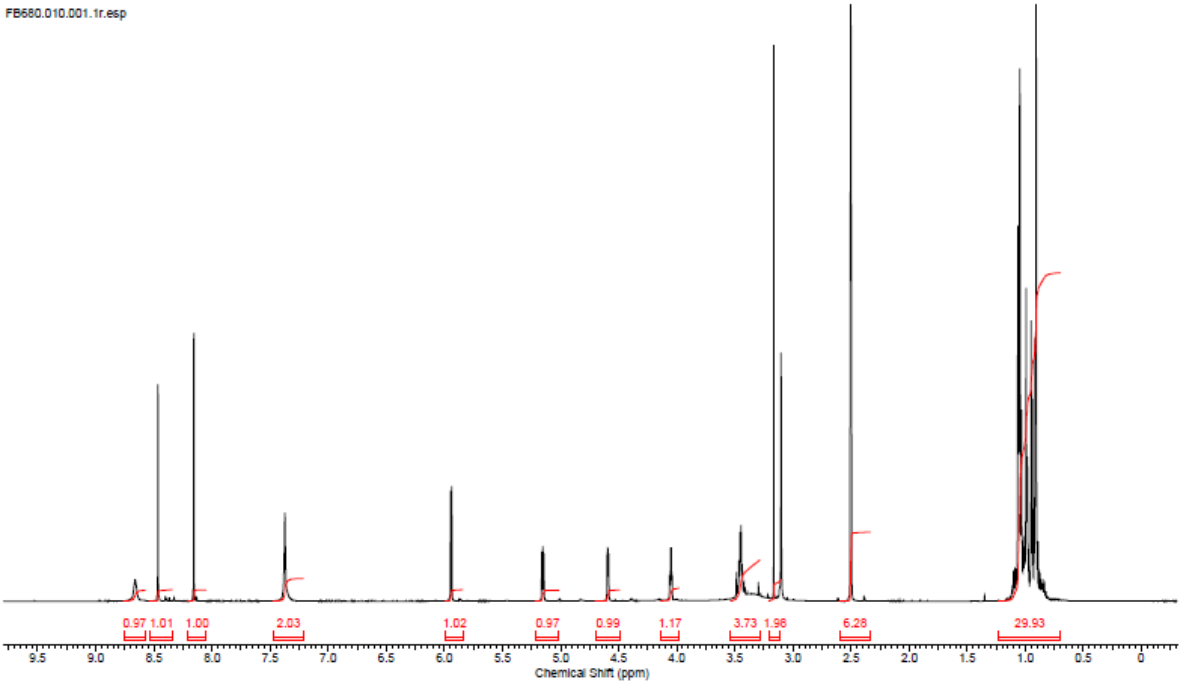


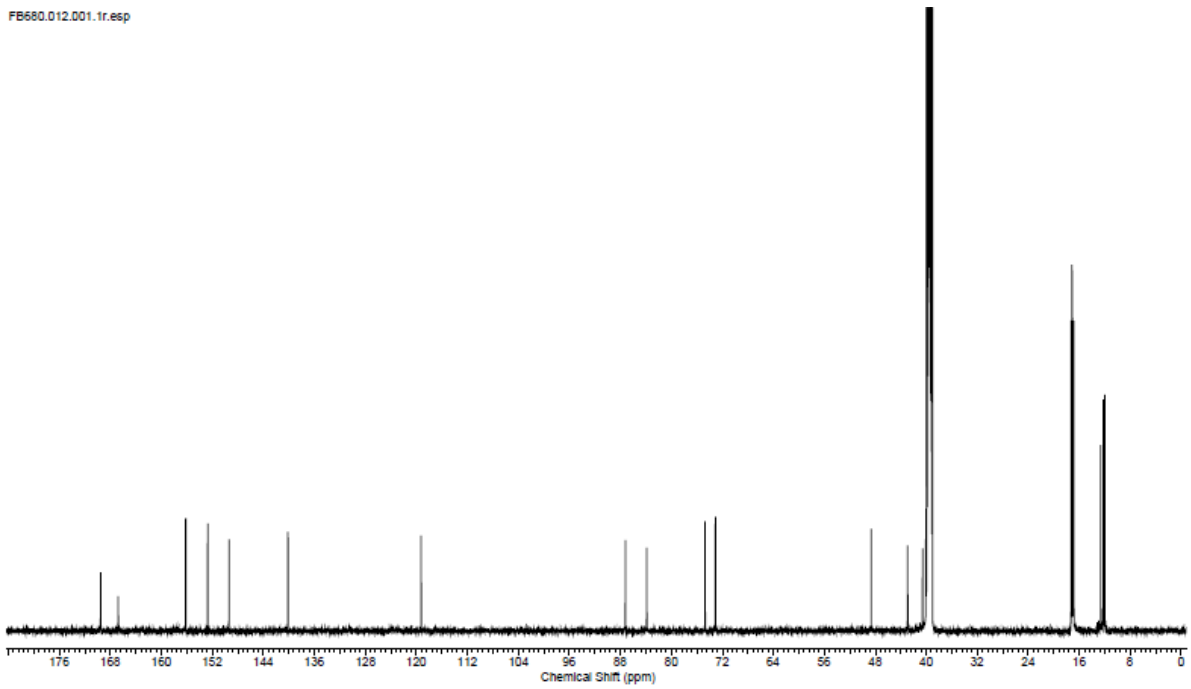




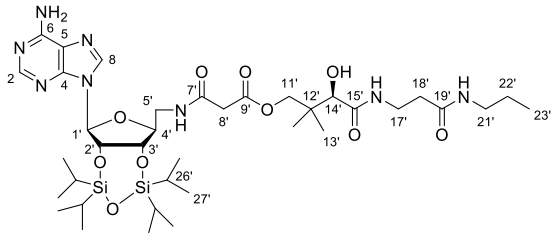
*3-((((5aS,6S,8S,8aS)-8-(6-Amino-9H-purin-9-yl)-2,2,4,4-tetraisopropyltetrahydrofuro[3,4-f][1,3,5,2,4]trioxadisilepin-6-yl)methyl)amino)-3-oxopropanoic acid (**23**)*

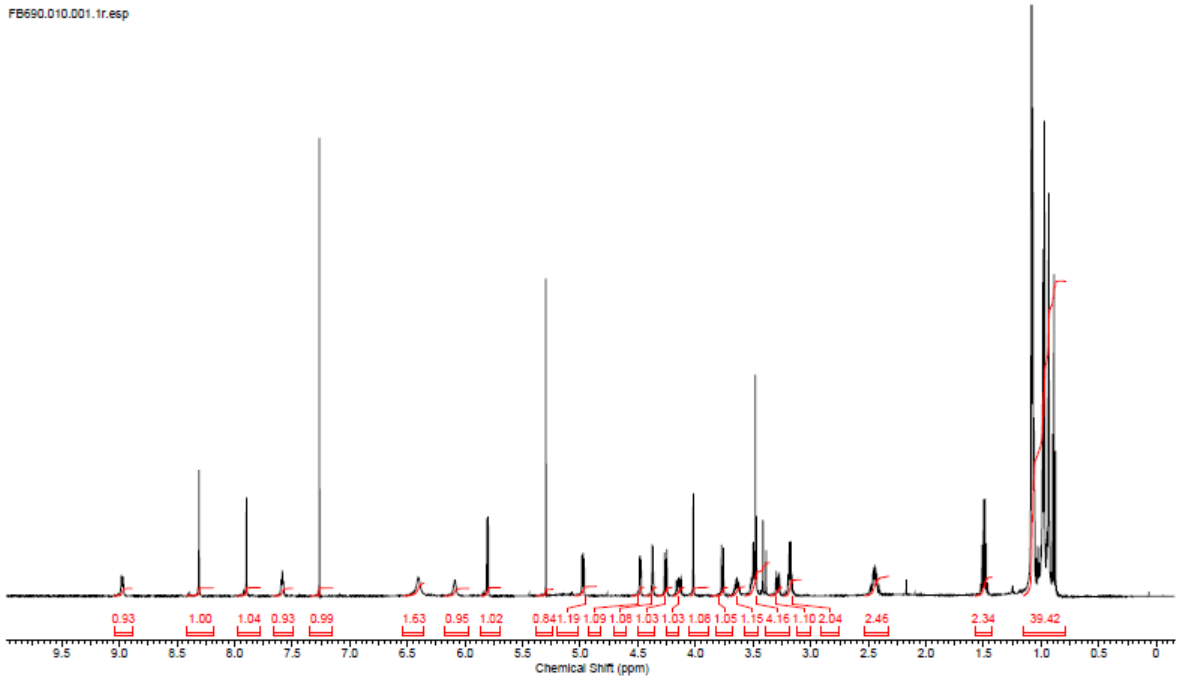


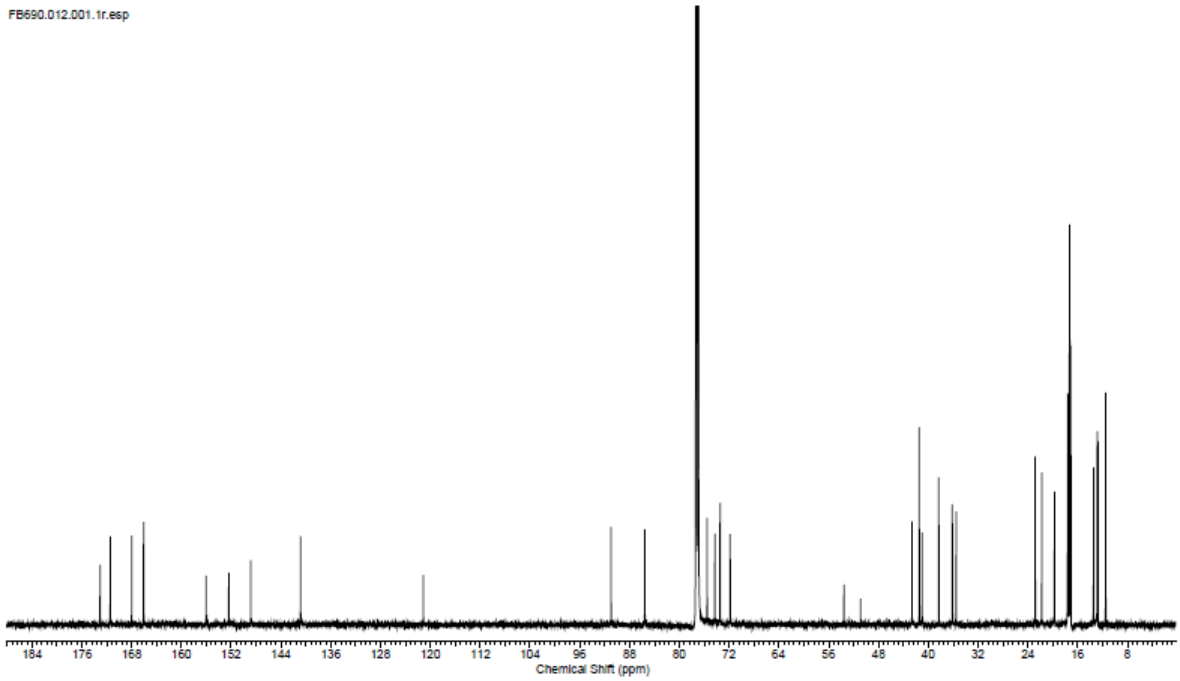




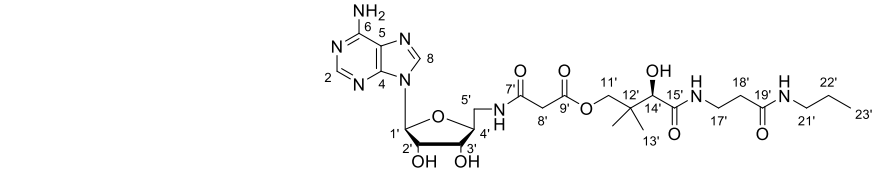
*(R)-3-Hydroxy-2,2-dimethyl-4-oxo-4-((3-oxo-3-(propylamino)propyl)amino)butyl 3-((((5aS,6S,8S,8aS)-8-(6-amino-9H-purin-9-yl)-2,2,4,4-tetraisopropyltetrahydrofuro[3,4-f][1,3,5,2,4]trioxadisilepin-6-yl)methyl)amino)-3-oxopropanoate (**24**)*

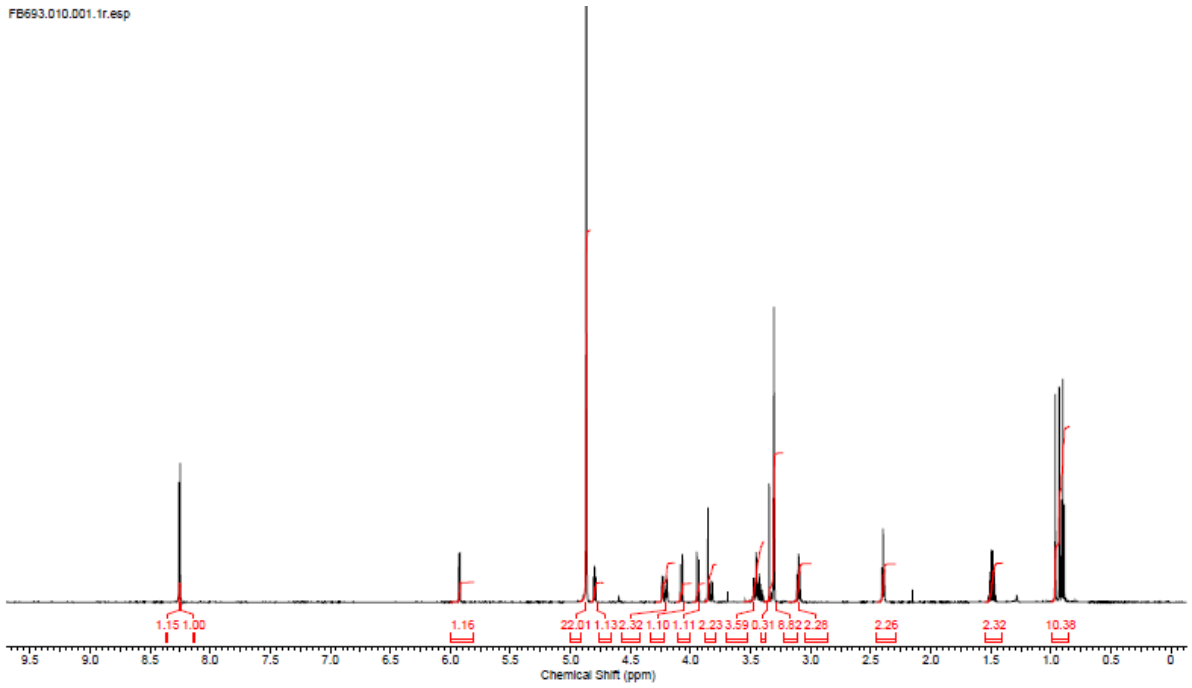


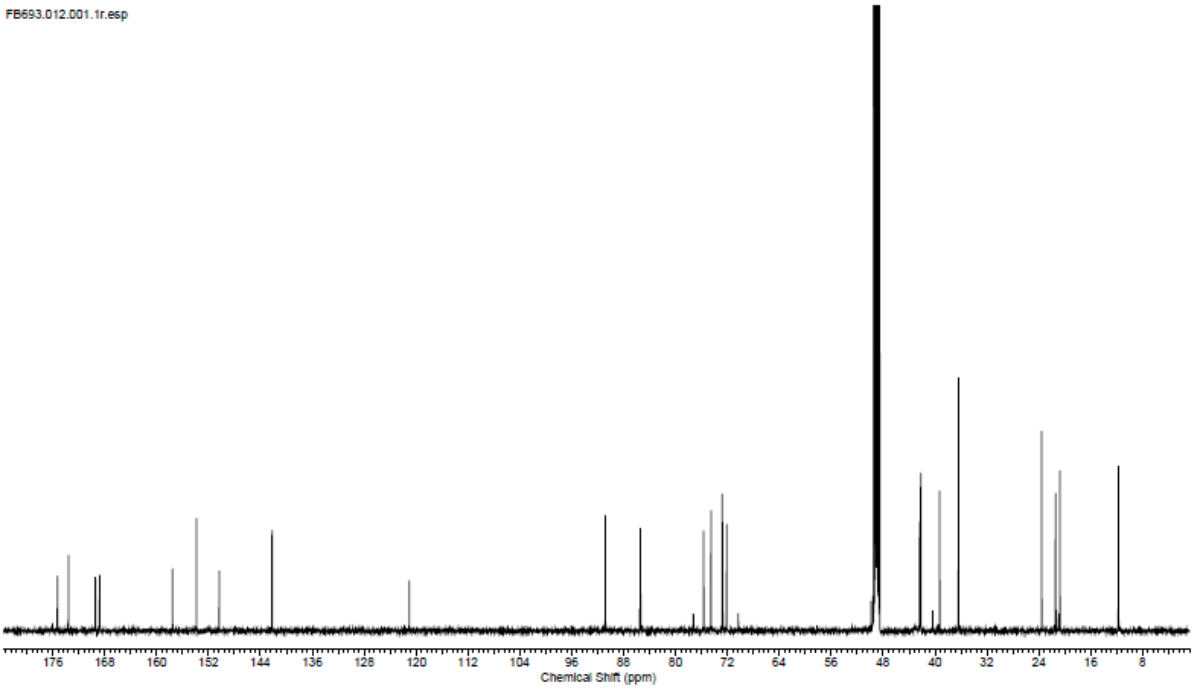




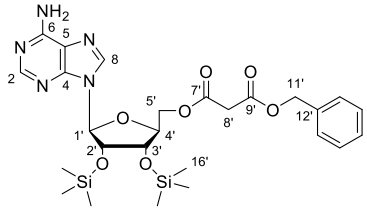
*(R)-3-Hydroxy-2,2-dimethyl-4-oxo-4-((3-oxo-3-(propylamino)propyl)amino)butyl 3-((((2S,3R,4S,5S)-5-(6-amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl)amino)-3-oxopropanoate (**3**)*

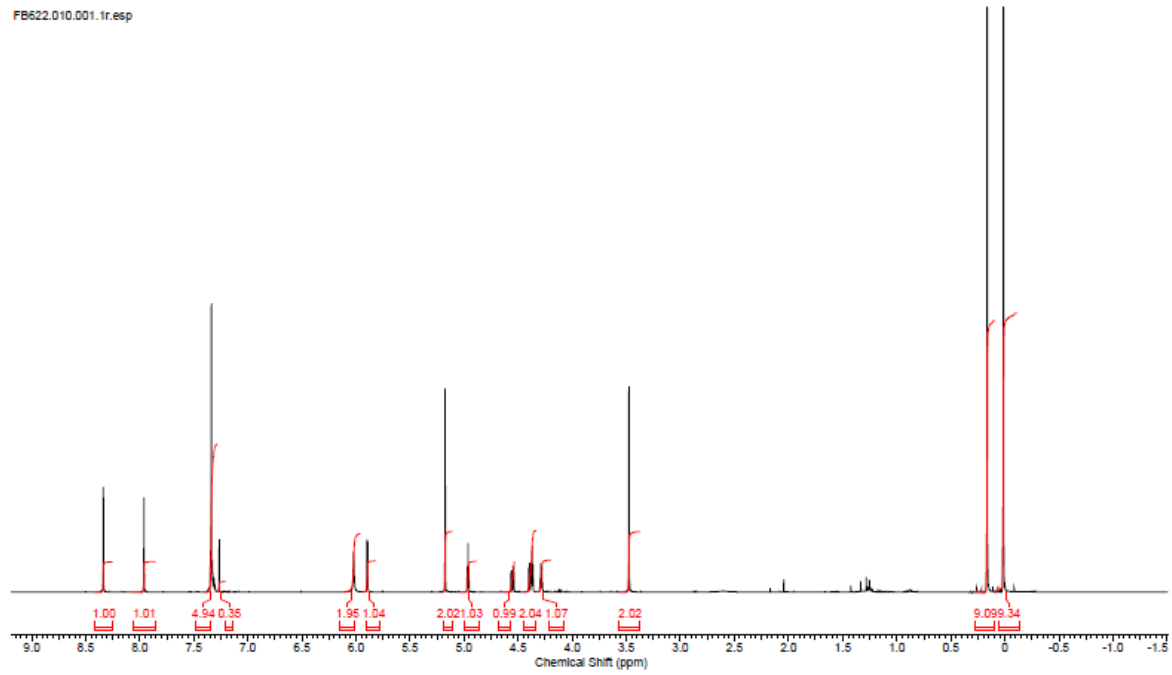


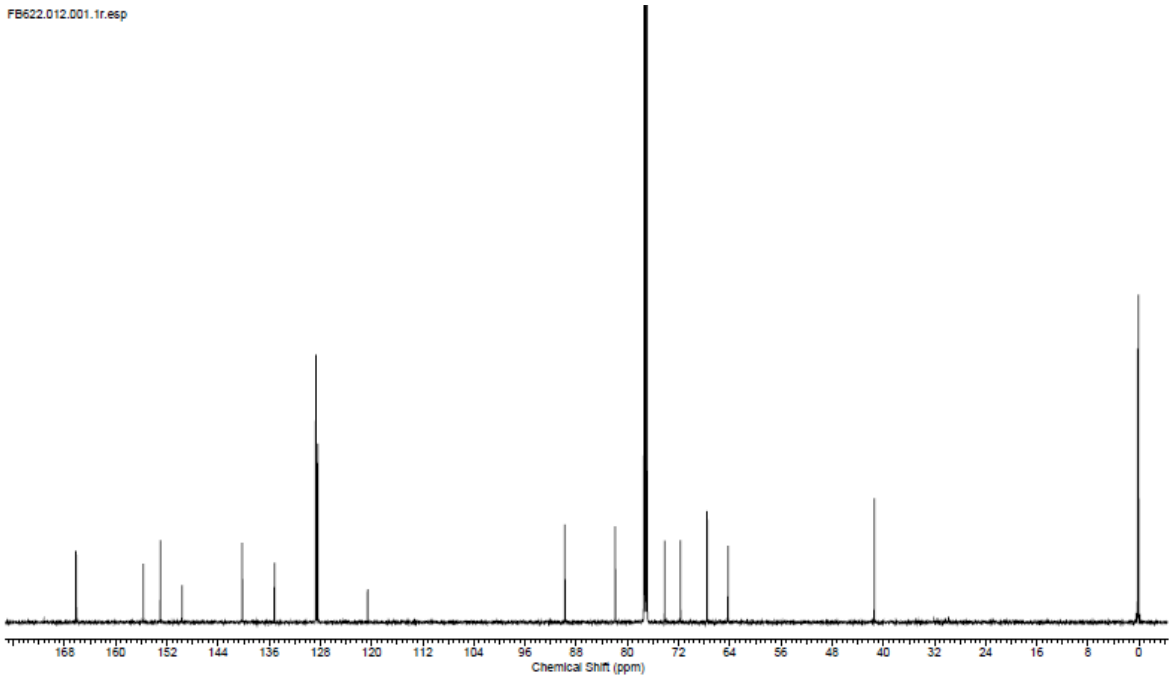




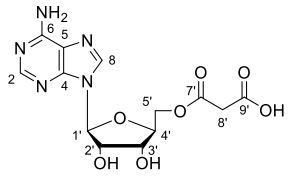
((2S,3S,4S,5S)-5-(6-Amino-9H-purin-9-yl)-3,4-bis((trimethylsilyl)oxy)tetrahydrofuran-2-yl)methyl benzyl malonate (***25***)

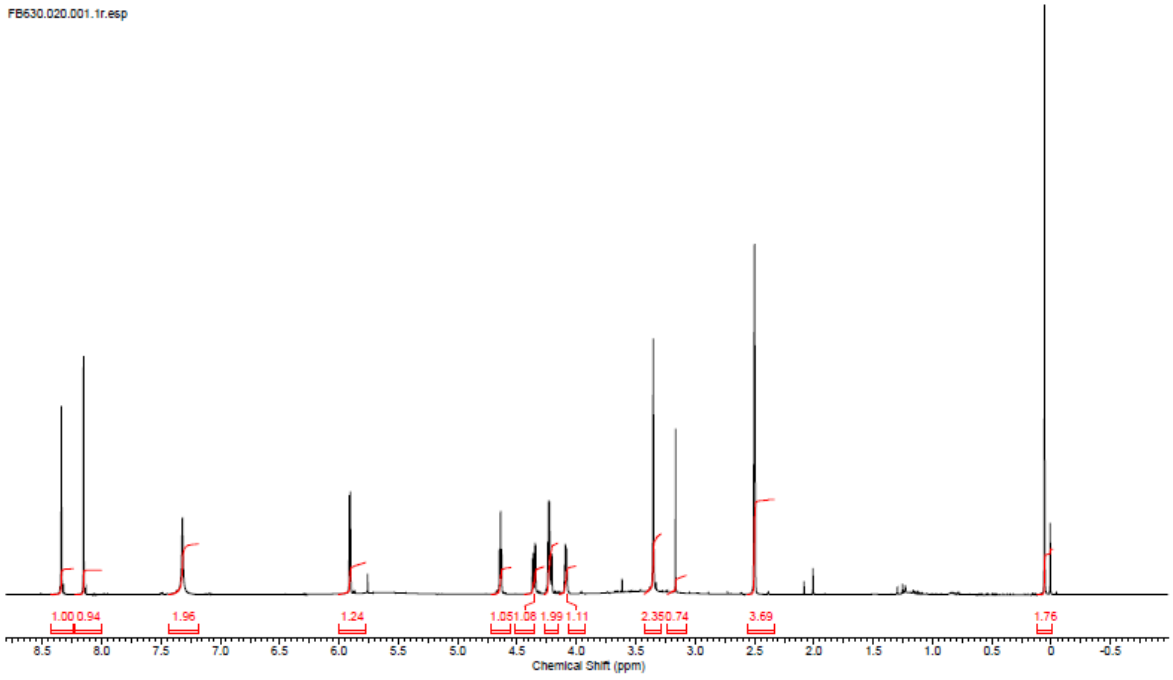


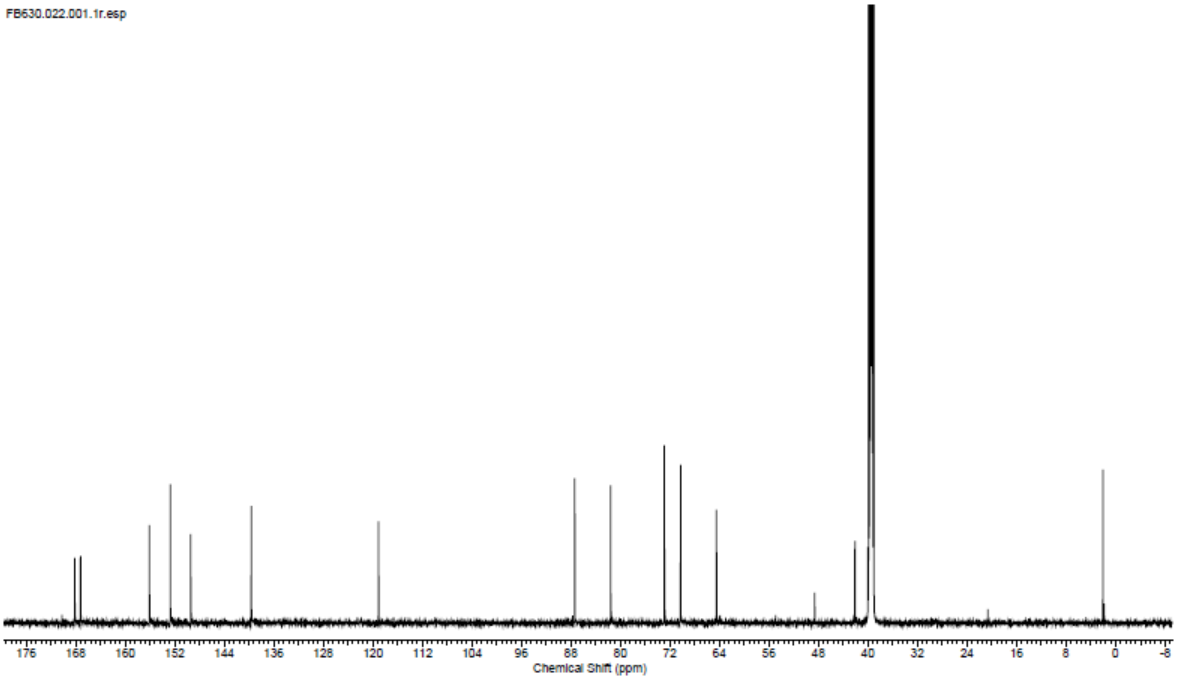




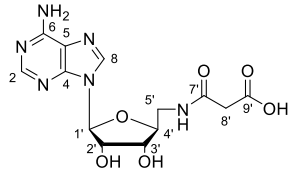
*3-(((2S,3R,4S,5S)-5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methoxy)-3-oxopropanoic acid (**2**)*

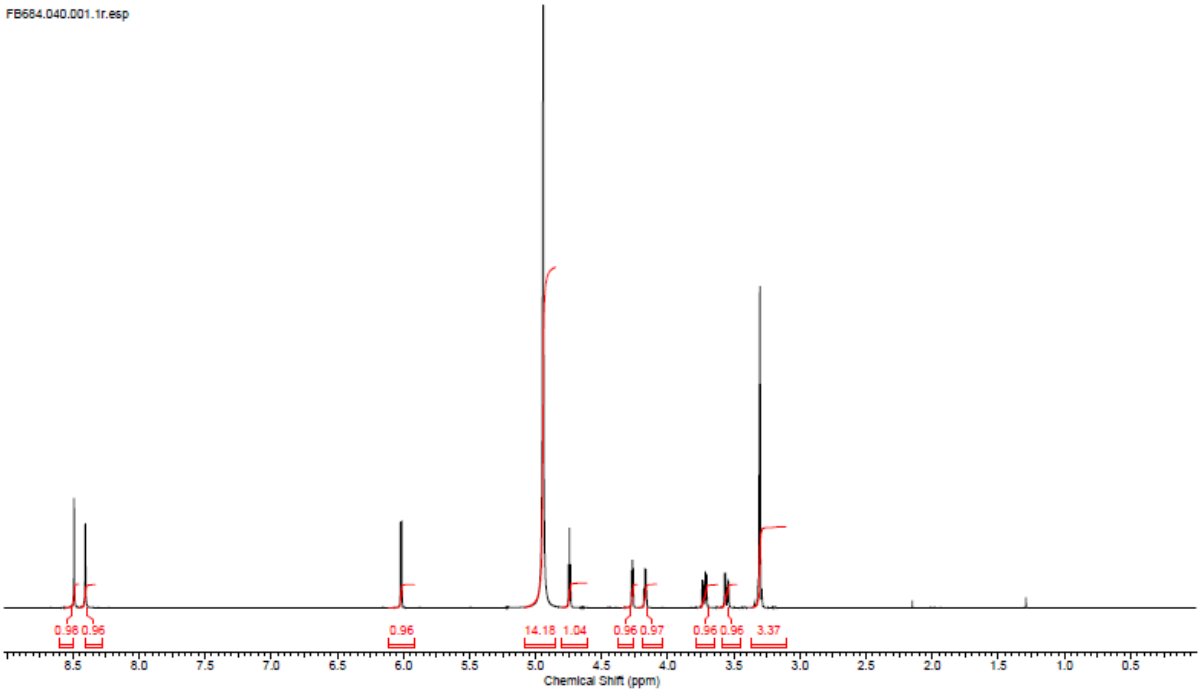


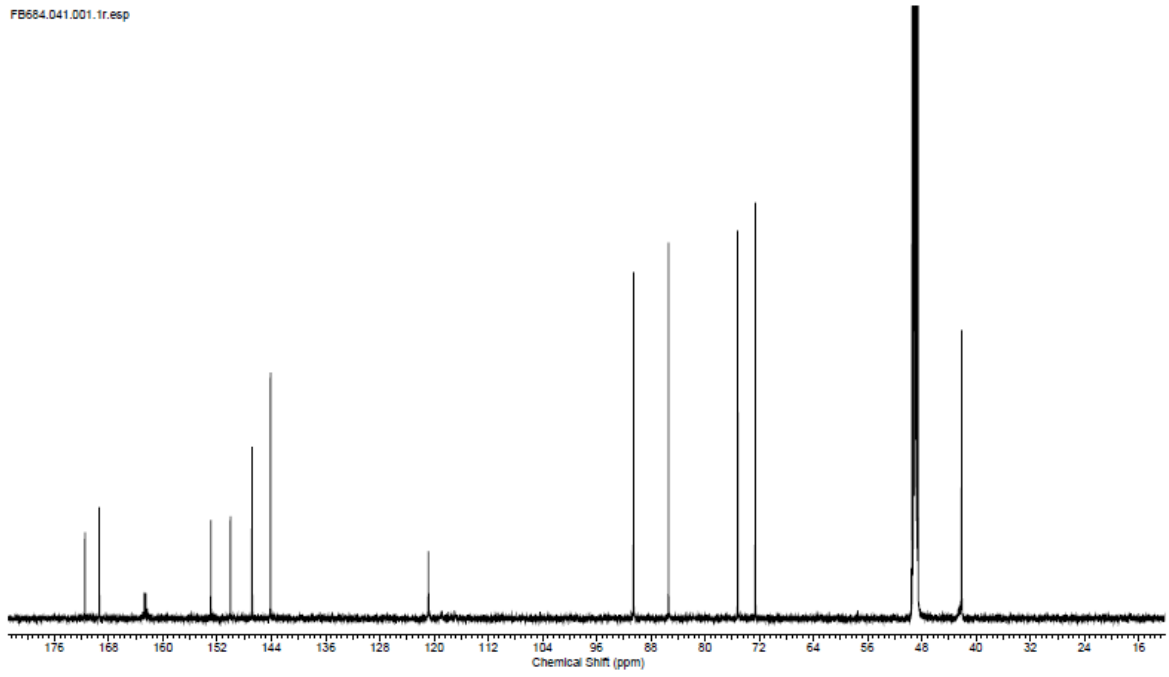




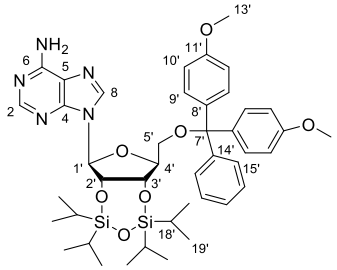
*3-((((2S,3R,4S,5S)-5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl)amino)-3-oxopropanoic acid (**4**)*

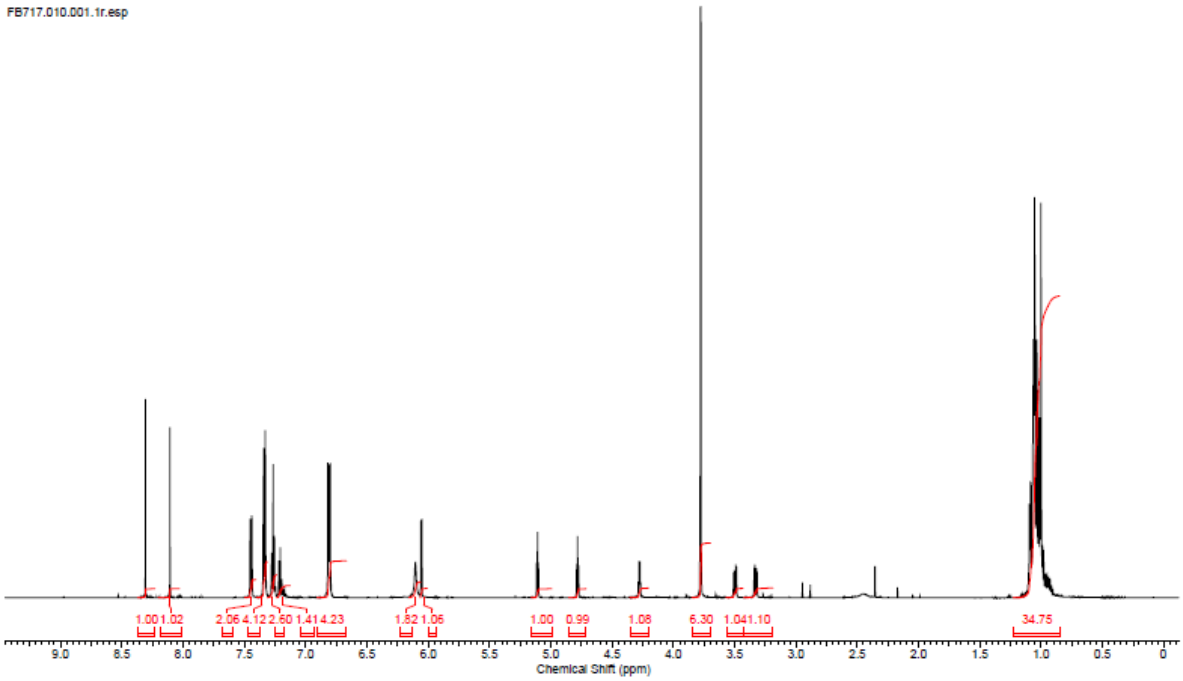


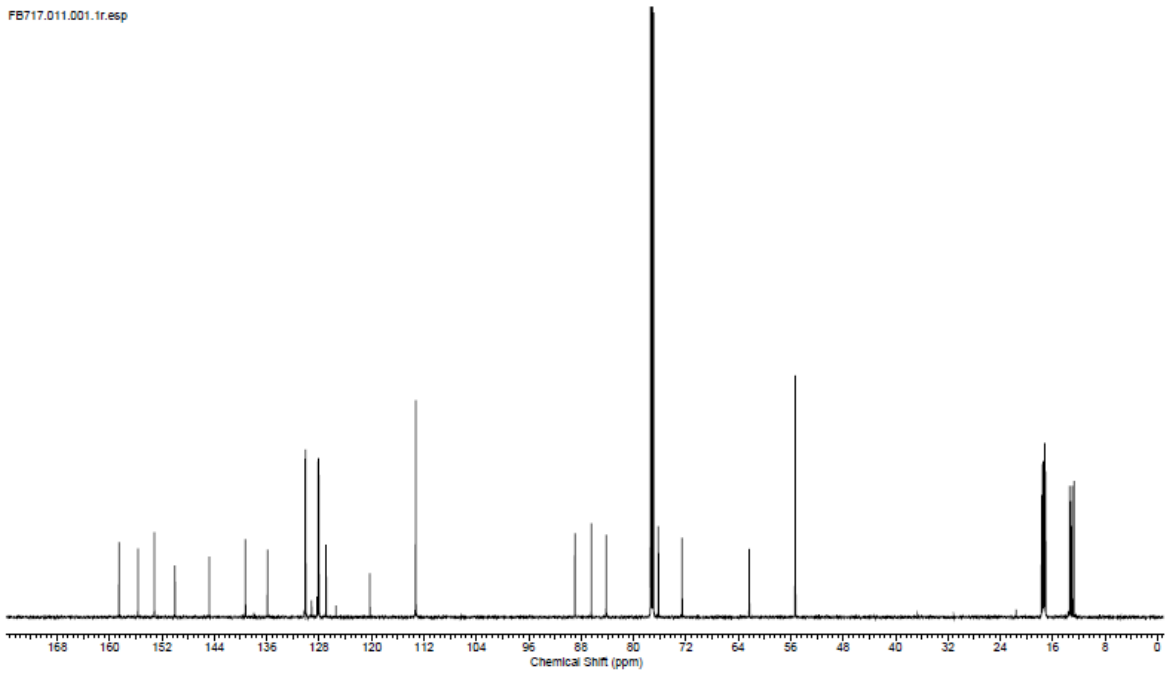




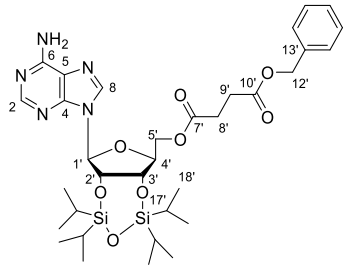
*9-((5aS,6S,8S,8aS)-8-((Bis(4-methoxyphenyl)(phenyl)methoxy)methyl)-2,2,4,4-tetraisopropyltetrahydrofuro[3,4-f][1,3,5,2,4]trioxadisilepin-6-yl)-9H-purin-6-amine (**29**)*

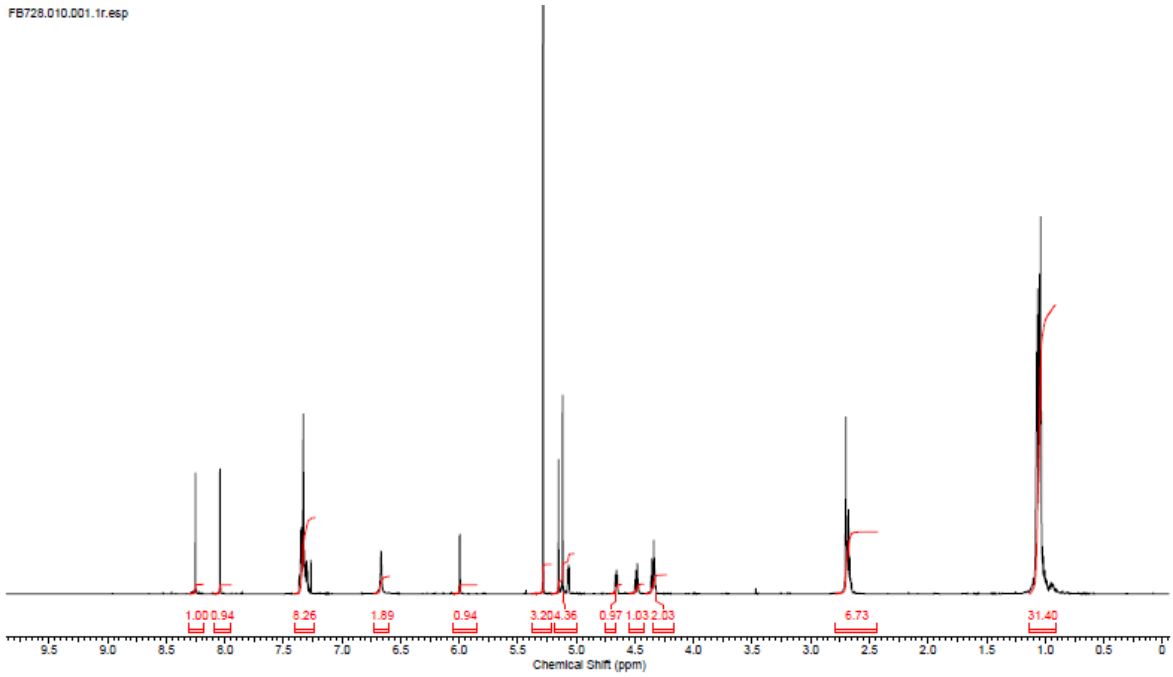


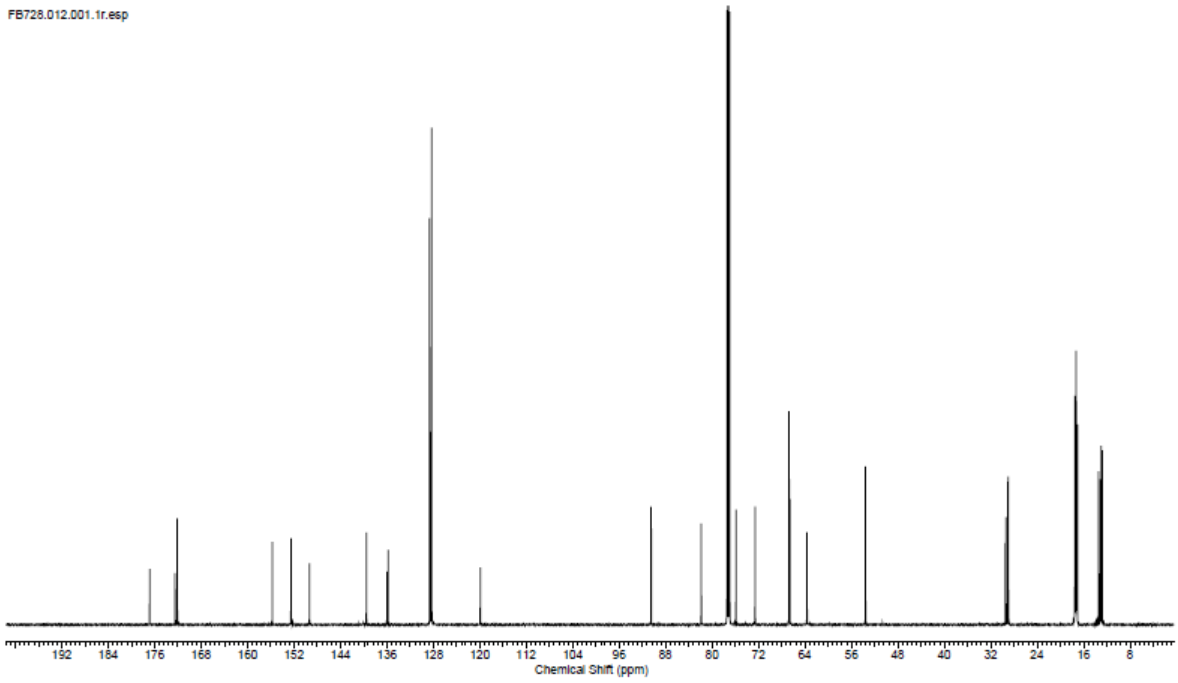




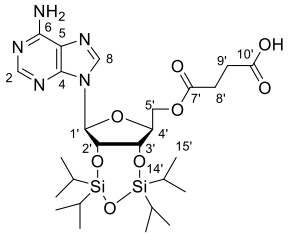
*((5aS,6S,8S,8aS)-8-(6-Amino-9H-purin-9-yl)-2,2,4,4-tetraisopropyltetrahydrofuro[3,4-f][1,3,5,2,4]trioxadisilepin-6-yl)methyl benzyl succinate (**31**)*

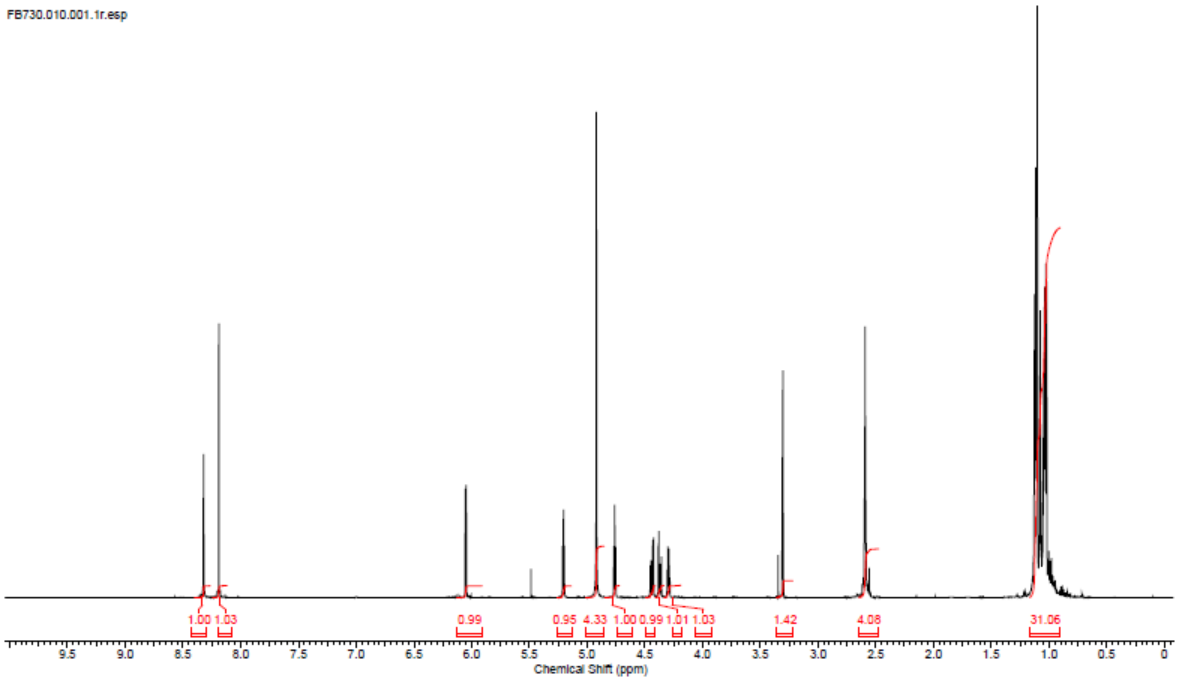


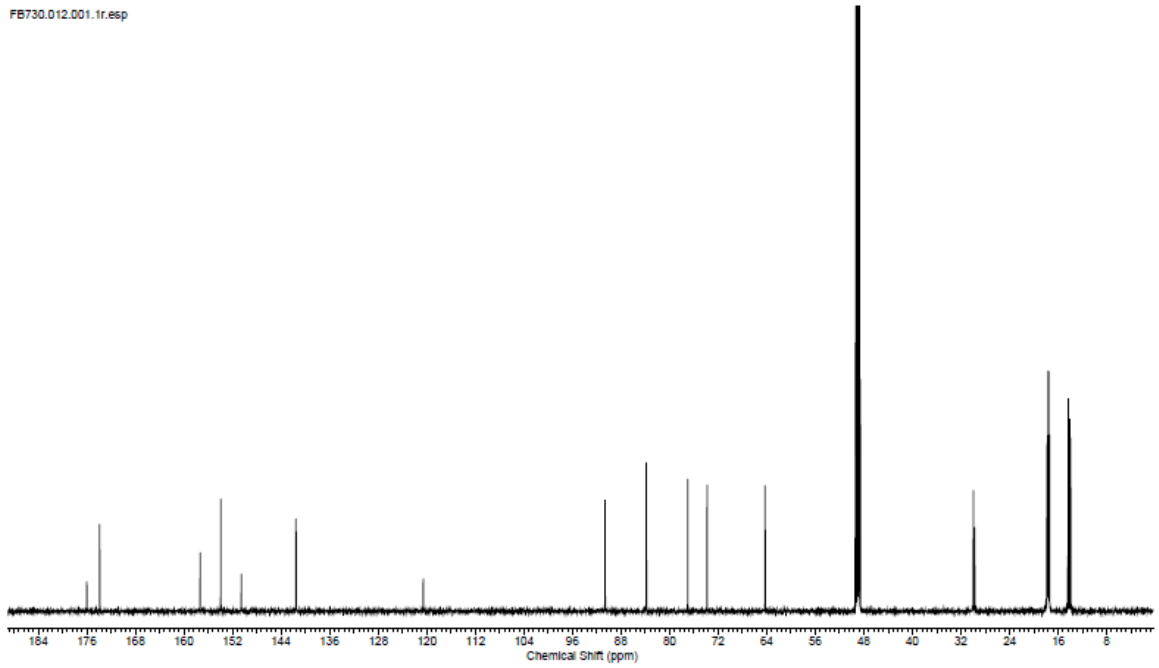




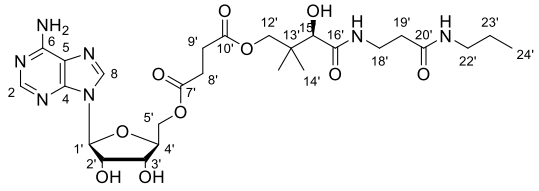
*4-(((5aS,6S,8S,8aS)-8-(6-Amino-9H-purin-9-yl)-2,2,4,4-tetraisopropyltetrahydrofuro[3,4-f][1,3,5,2,4]trioxadisilepin-6-yl)methoxy)-4-oxobutanoic acid (**32**)*

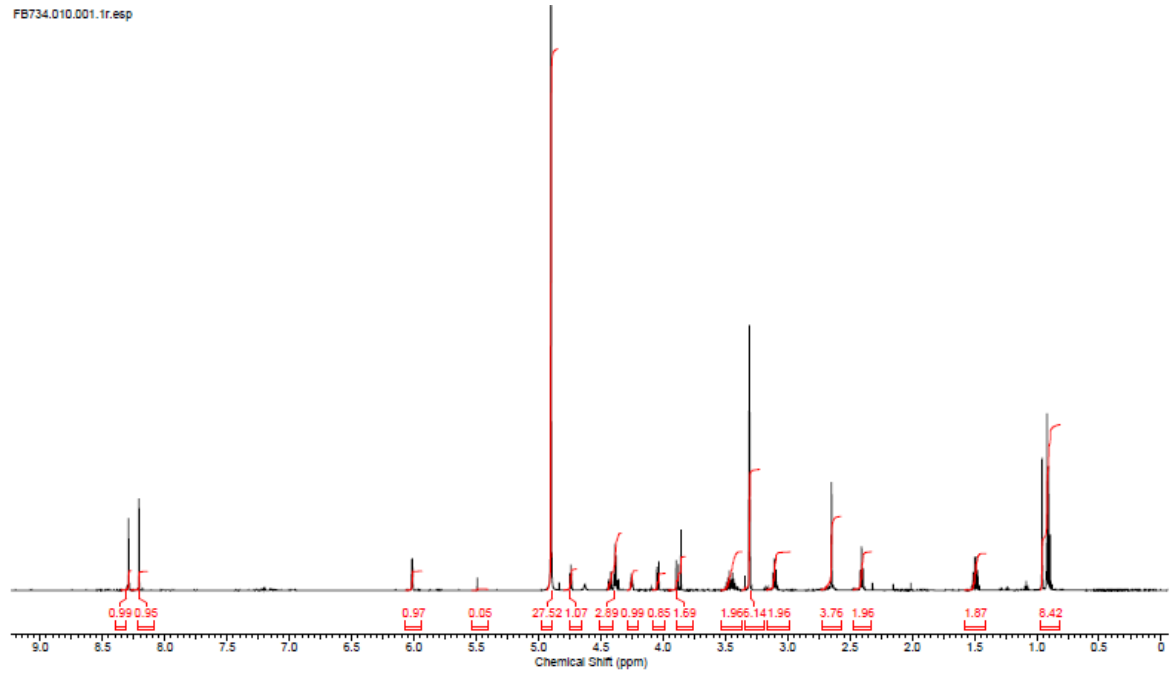


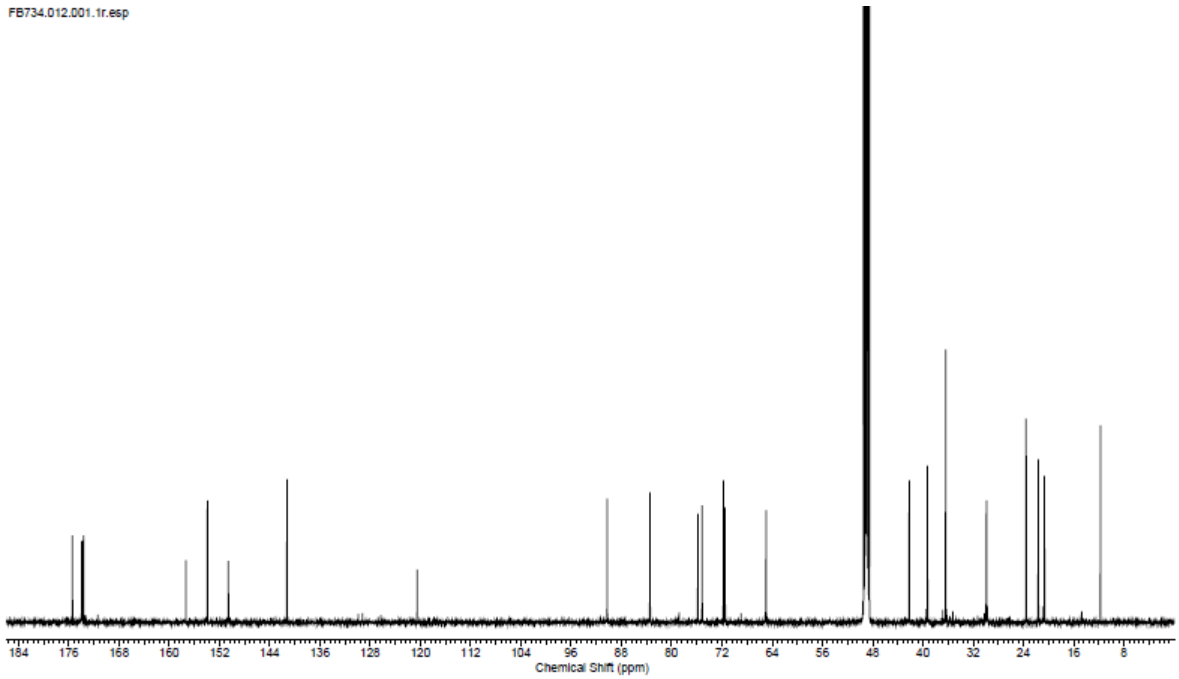




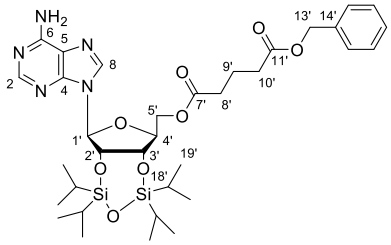
*((2S,3R,4S,5S)-5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl ((R)-3-hydroxy-2,2-dimethyl-4-oxo-4-((3-oxo-3-(propylamino)propyl)amino)butyl) succinate (**5**)*

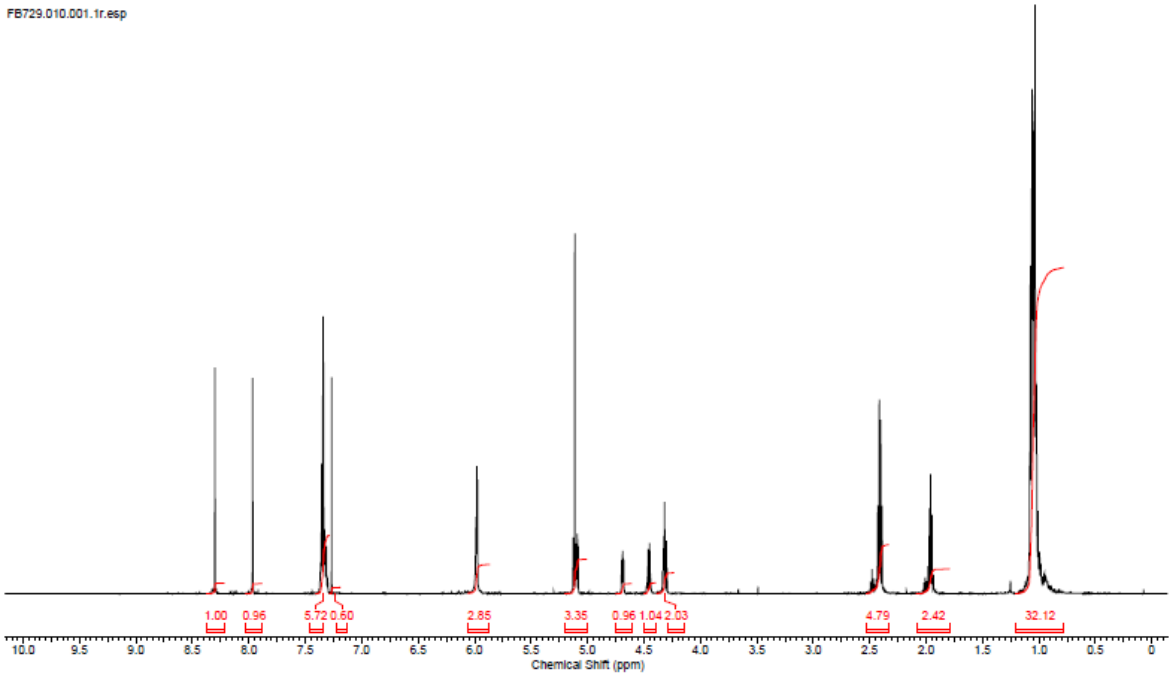


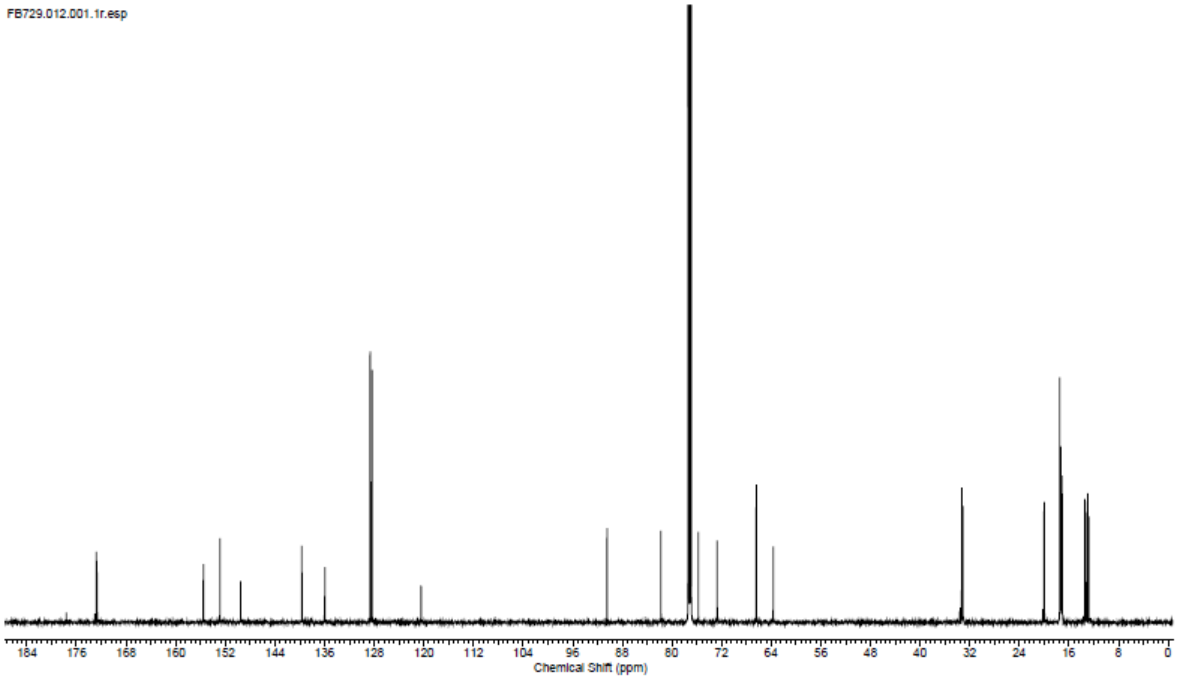




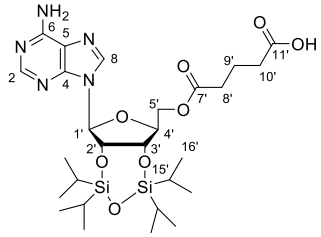
*((5aS,6S,8S,8aS)-8-(6-Amino-9H-purin-9-yl)-2,2,4,4-tetraisopropyltetrahydrofuro[3,4-f][1,3,5,2,4]trioxadisilepin-6-yl)methyl benzyl glutarate (**35**)*

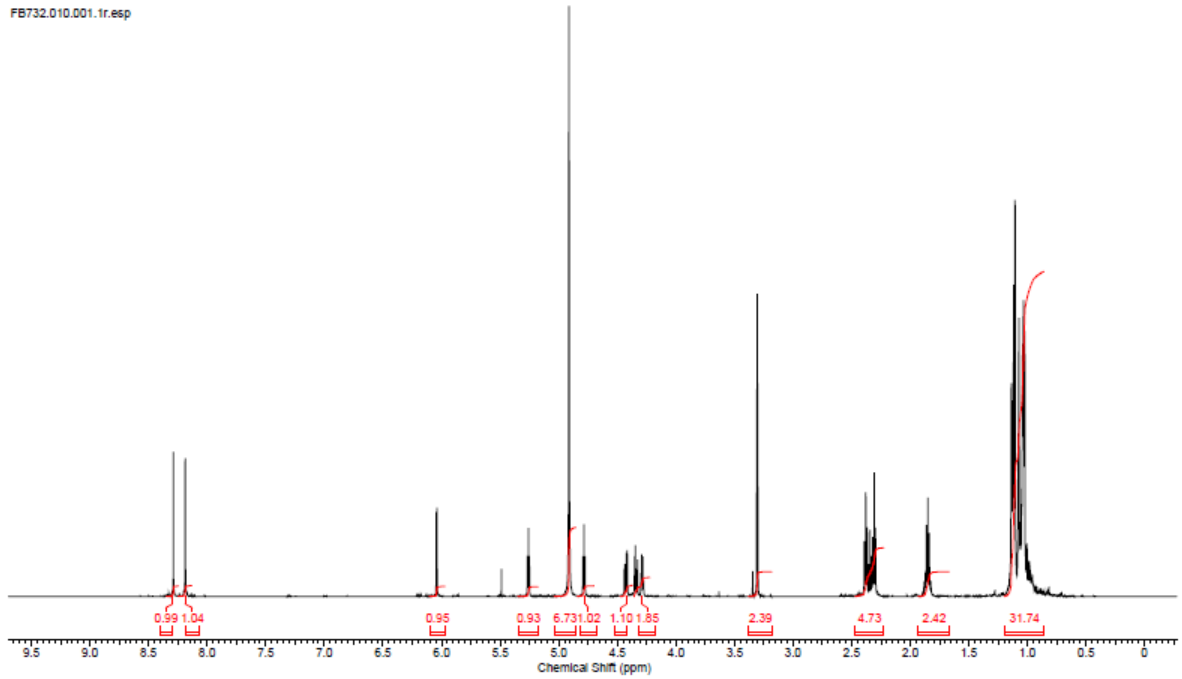


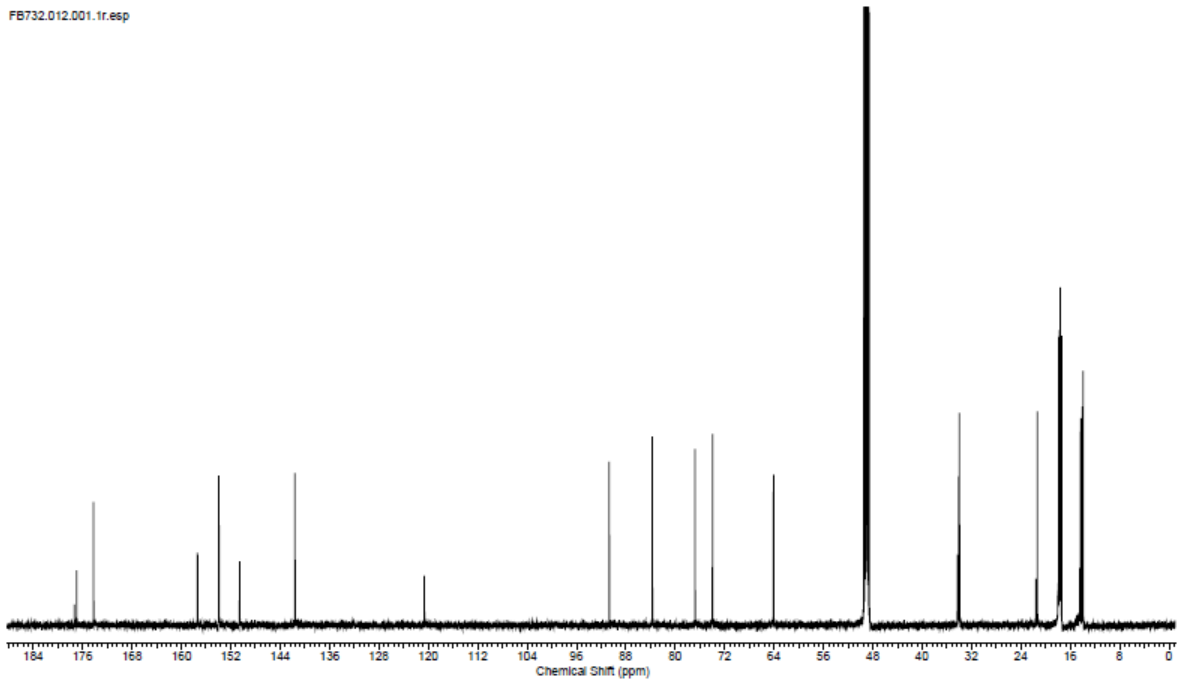




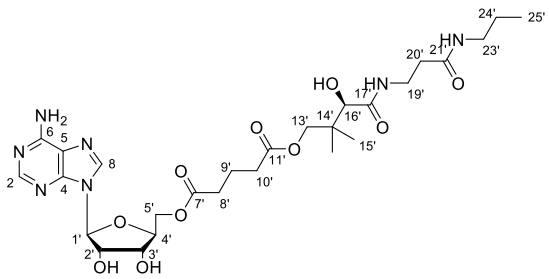
*5-(((5aS,6S,8S,8aS)-8-(6-Amino-9H-purin-9-yl)-2,2,4,4-tetraisopropyltetrahydrofuro[3,4-f][1,3,5,2,4]trioxadisilepin-6-yl)methoxy)-5-oxopentanoic acid (**36**)*

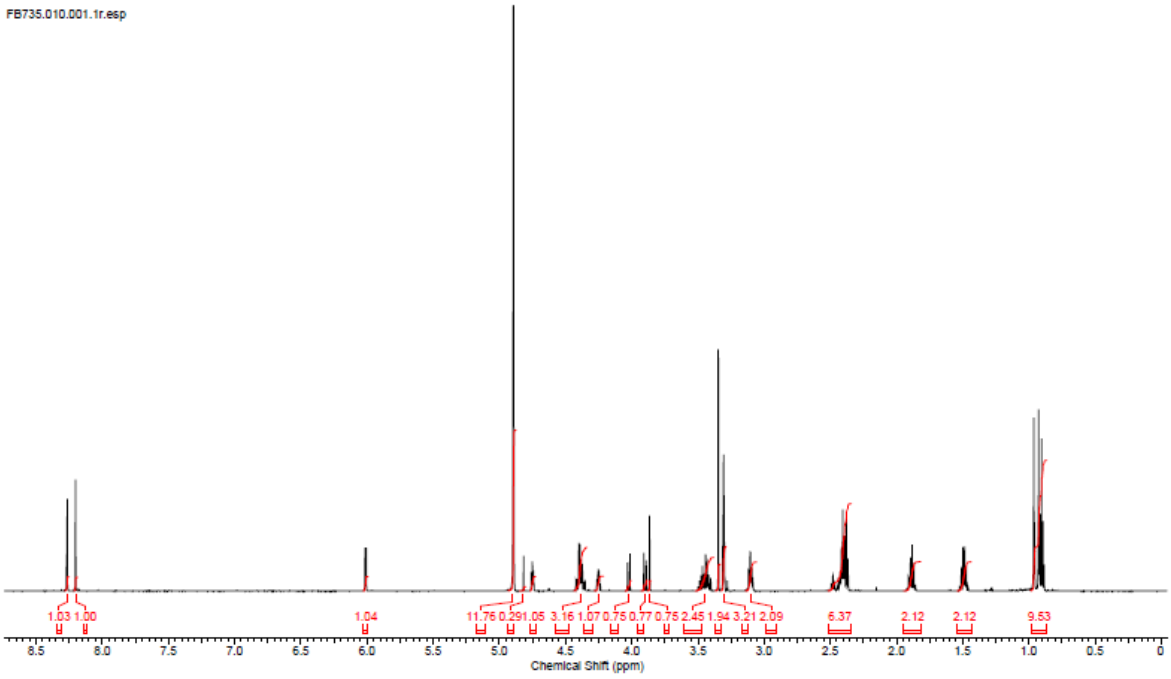


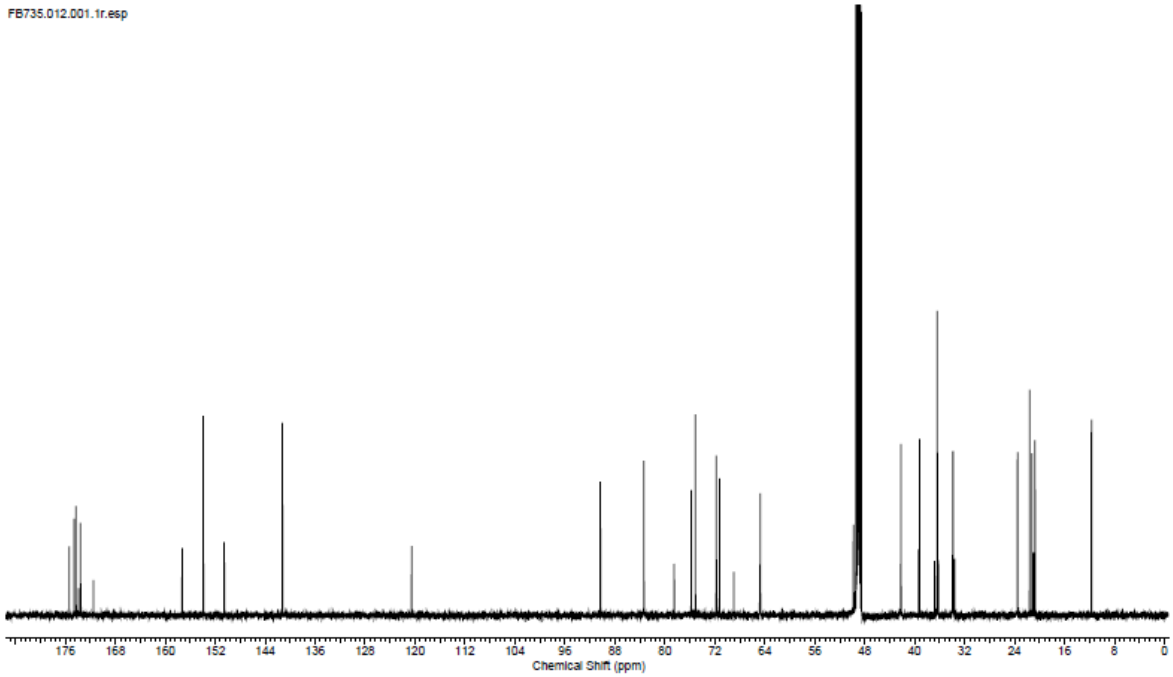




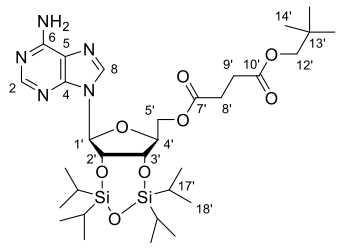
*((2S,3R,4S,5S)-5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl ((R)-3-hydroxy-2,2-dimethyl-4-oxo-4-((3-oxo-3-(propylamino)propyl)amino)butyl) glutarate (**6**)*

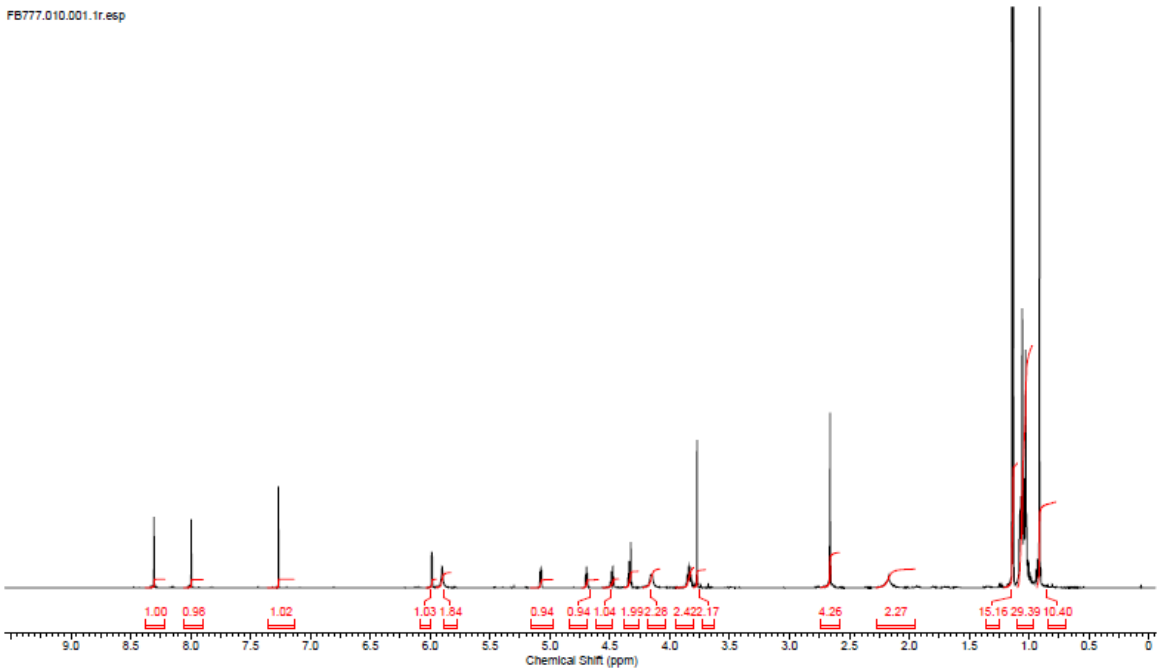


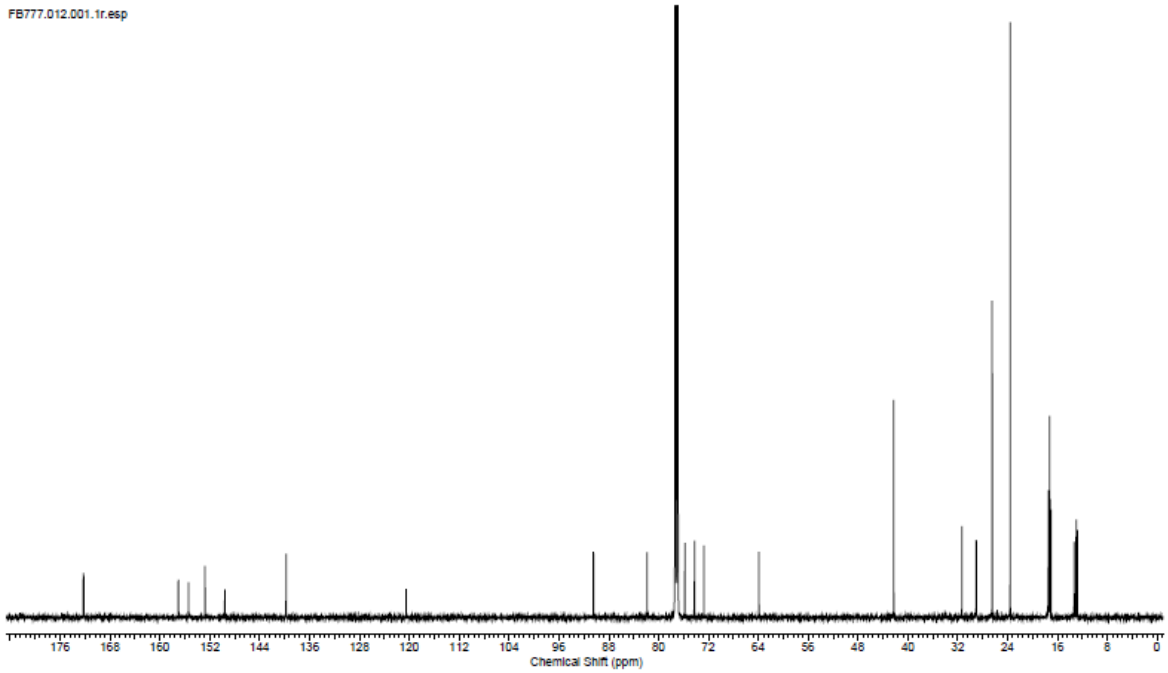




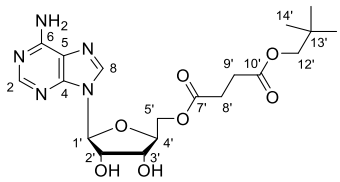
((5aS,6S,8S,8aS)-8-(6-Amino-9H-purin-9-yl)-2,2,4,4-tetraisopropyltetrahydrofuro[3,4-f][1,3,5,2,4]trioxadisilepin-6-yl)methyl neopentyl succinate (**39**)

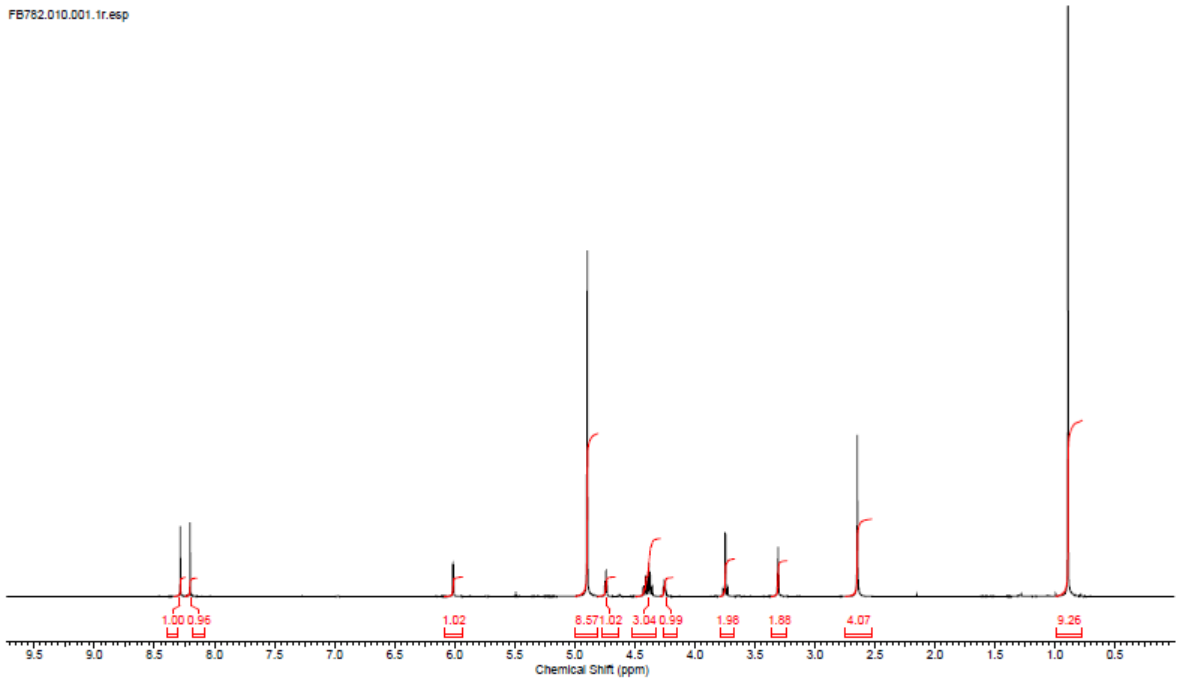


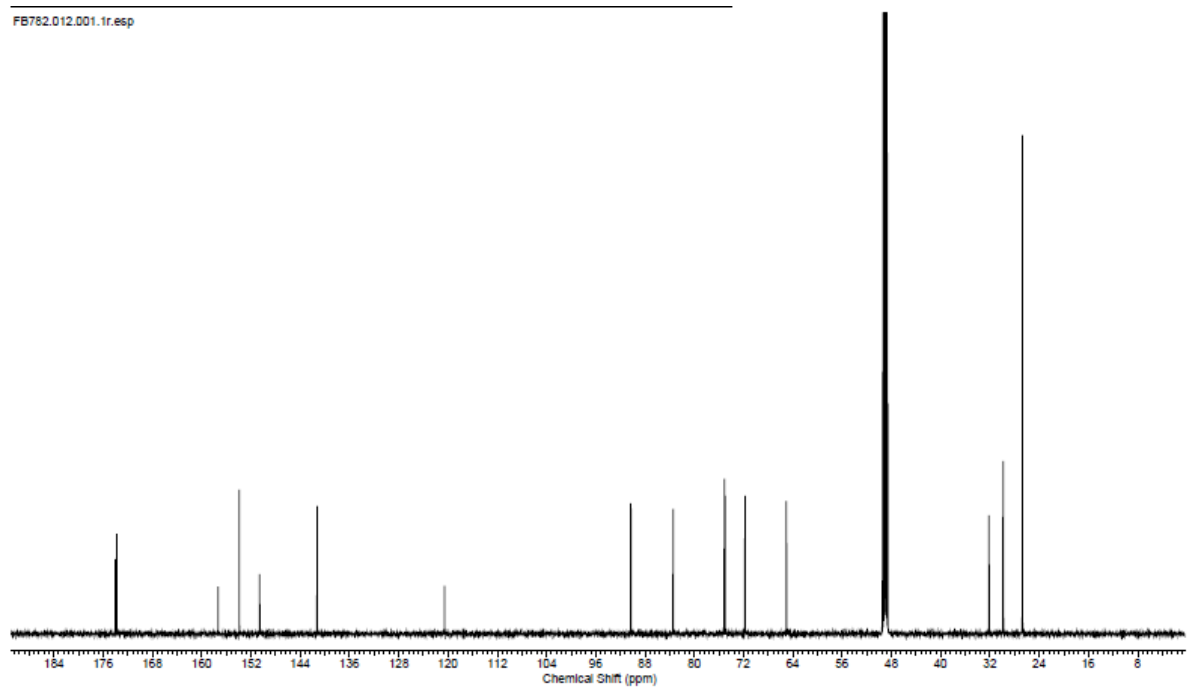




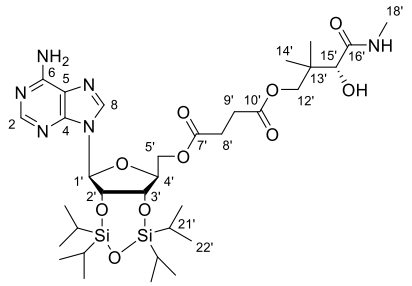
((2S,3R,4S,5S)-5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl neopentyl succinate (**7**)

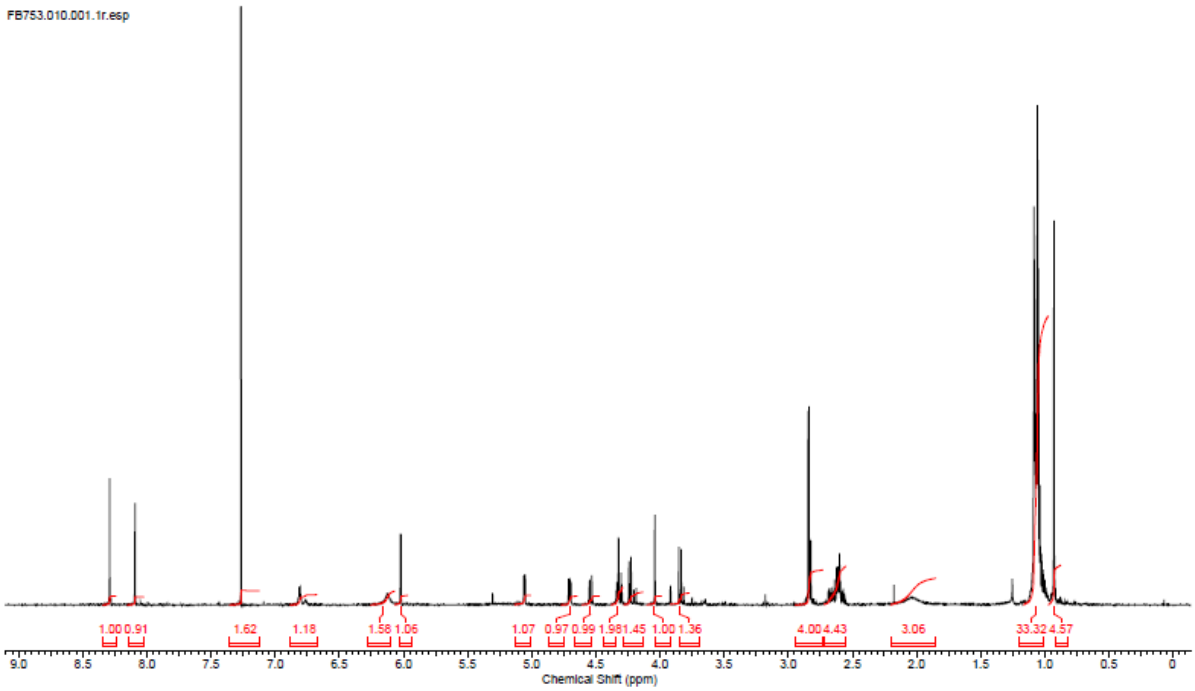


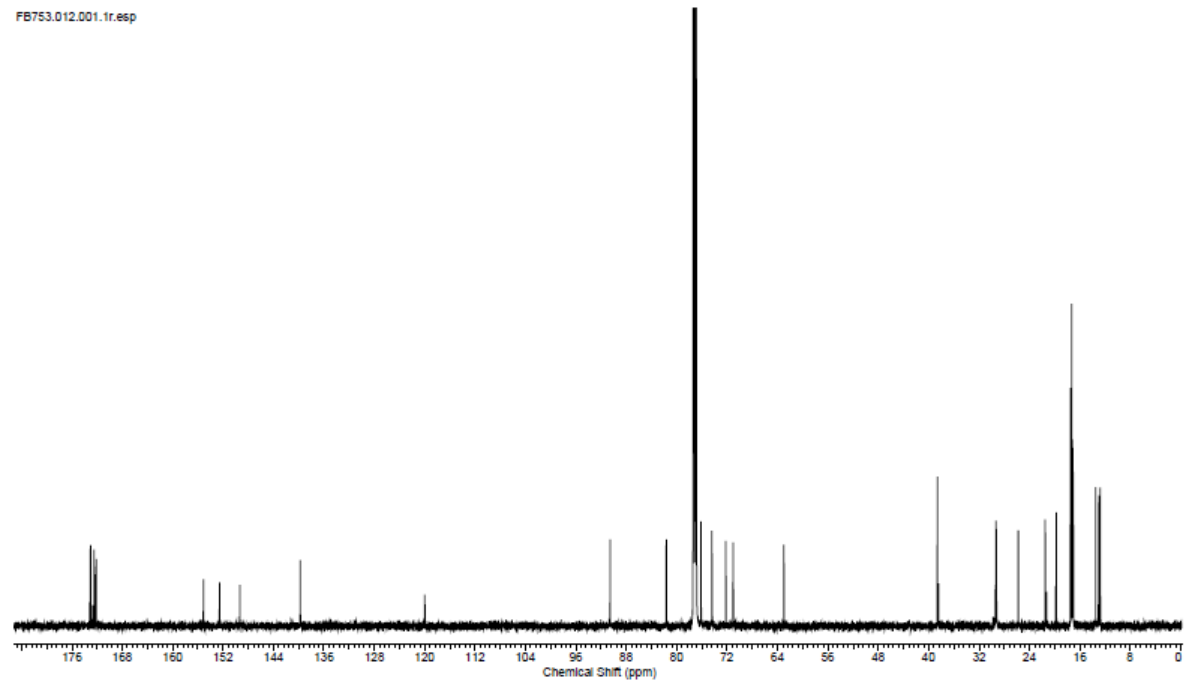




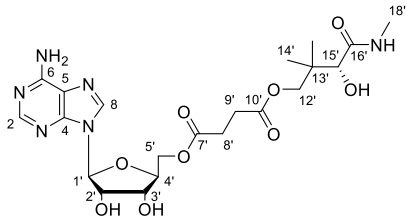
((5aS,6S,8S,8aS)-8-(6-Amino-9H-purin-9-yl)-2,2,4,4-tetraisopropyltetrahydrofuro[3,4-f][1,3,5,2,4]trioxadisilepin-6-yl)methyl ((R)-3-hydroxy-2,2-dimethyl-4-(methylamino)-4-oxobutyl) succinate (**41**)

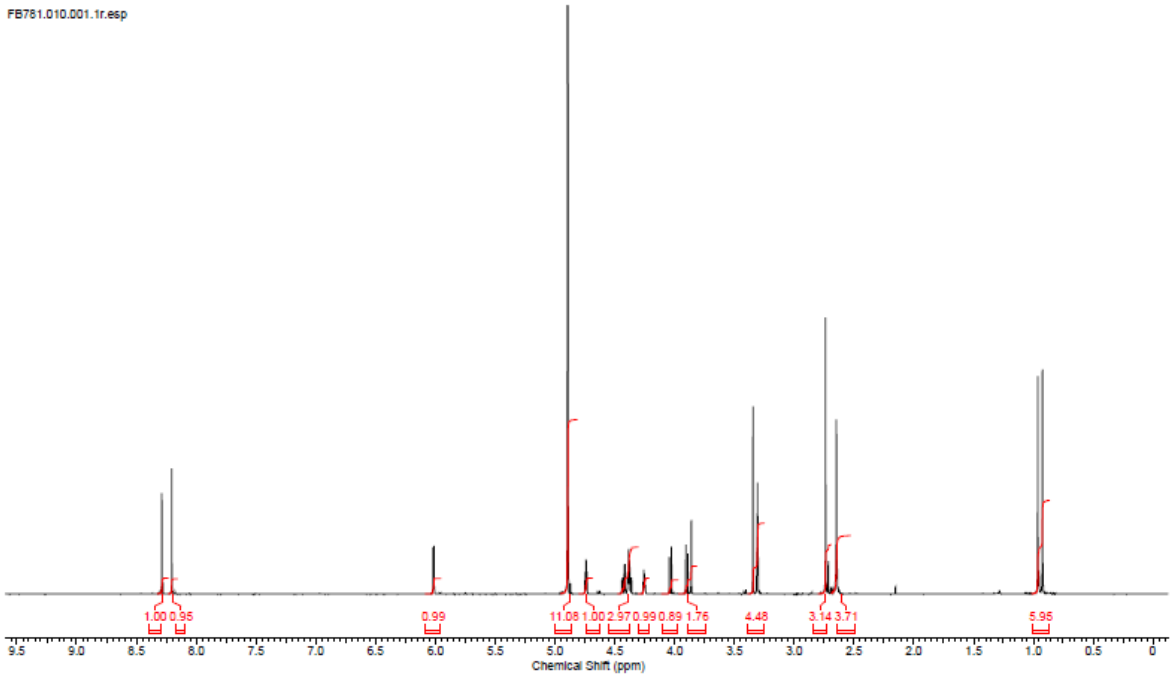


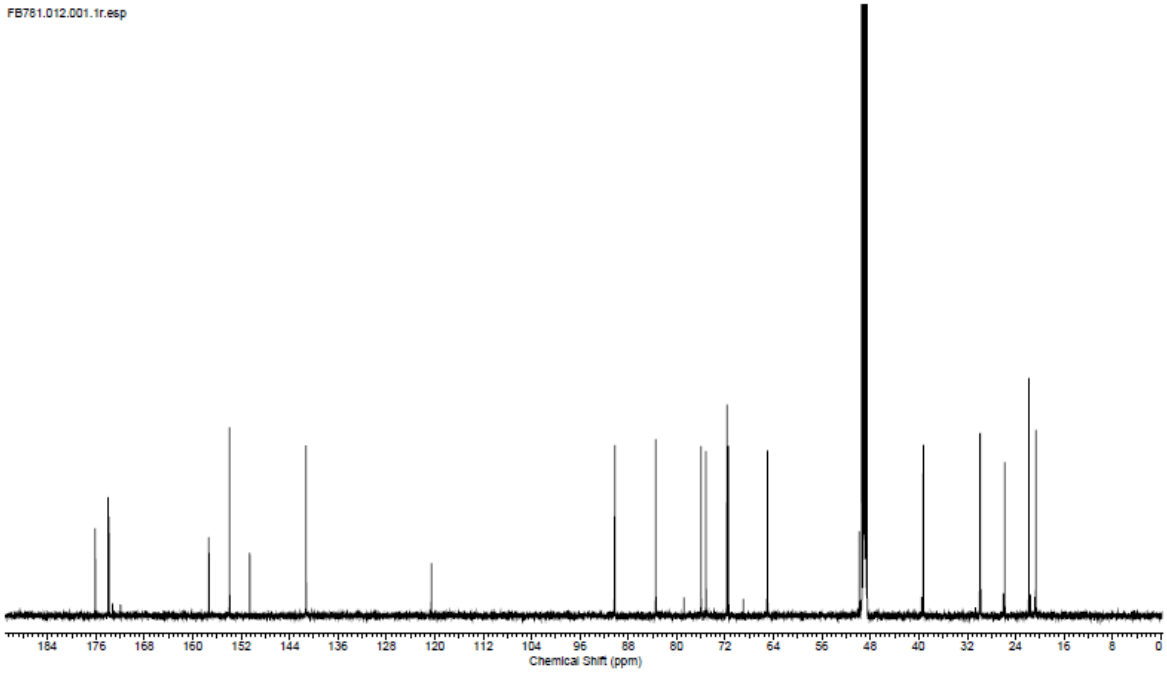




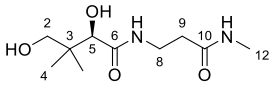
((2S,3R,4S,5S)-5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl ((R)-3-hydroxy-2,2-dimethyl-4-(methylamino)-4-oxobutyl) succinate (**8**)

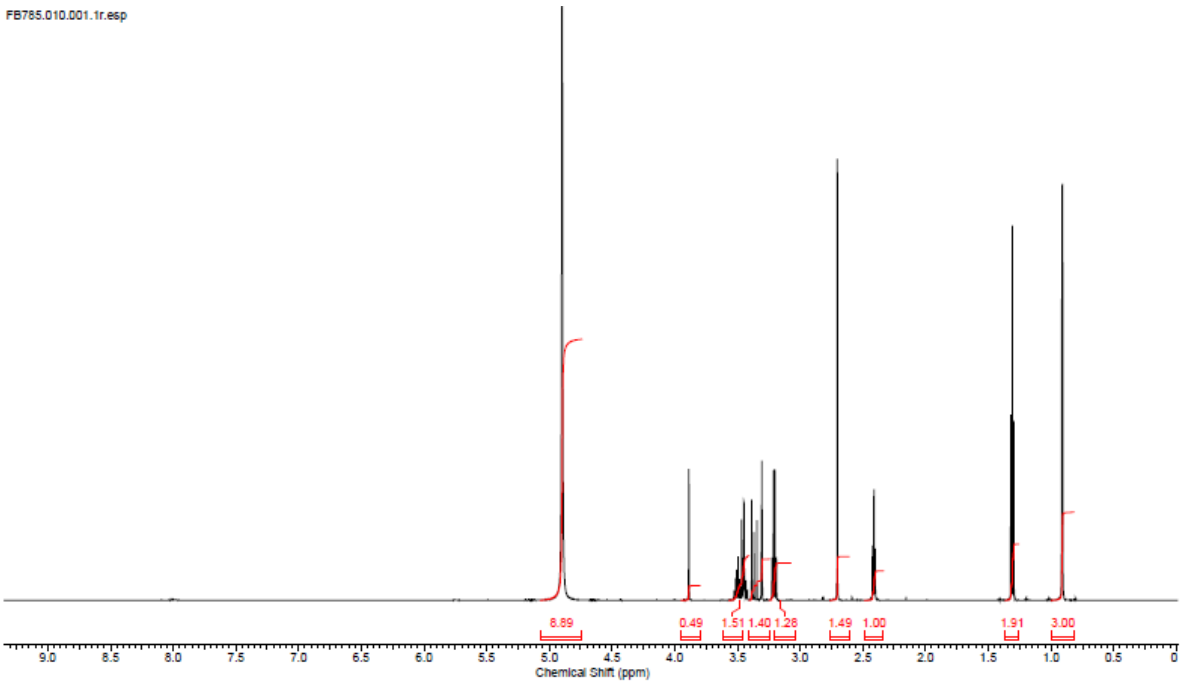


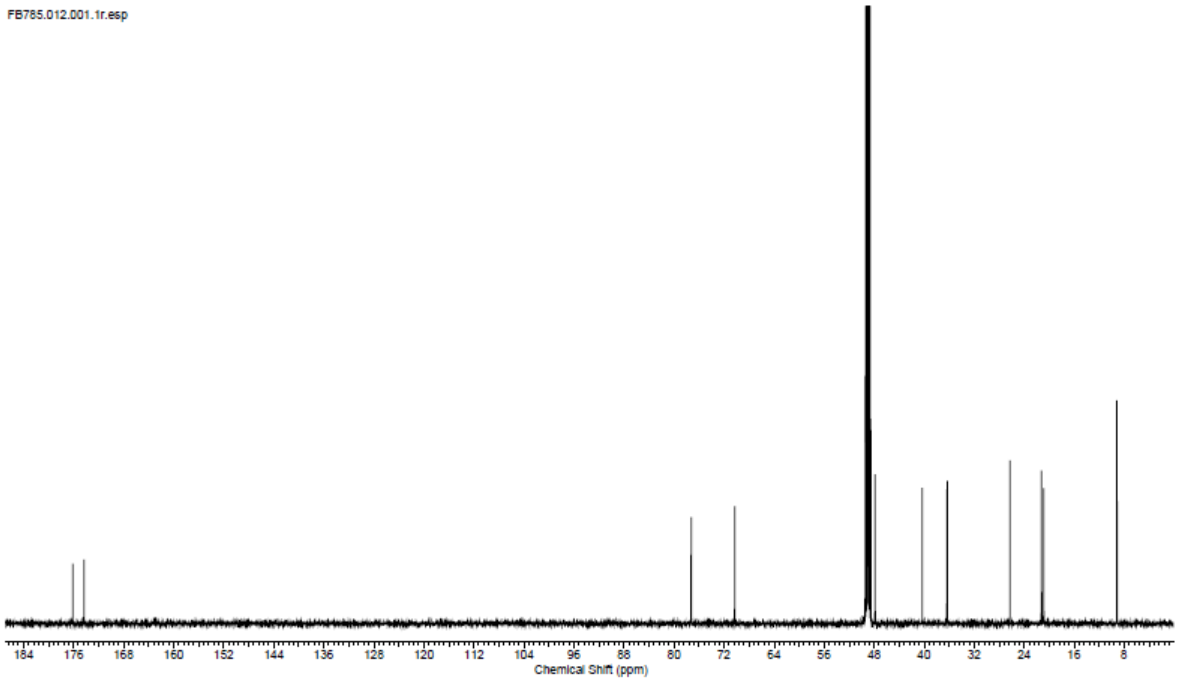




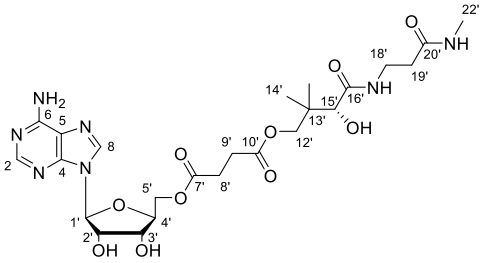
(R)-2,4-Dihydroxy-3,3-dimethyl-N-(3-(methylamino)-3-oxopropyl)butanamide (**42**)

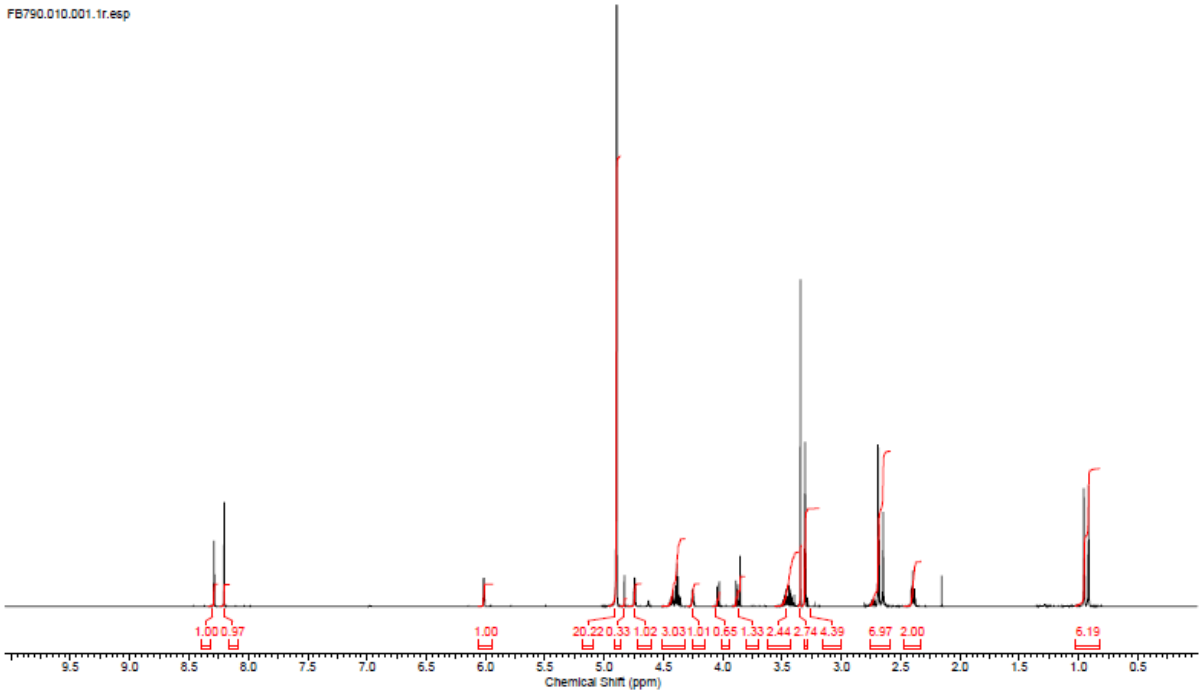


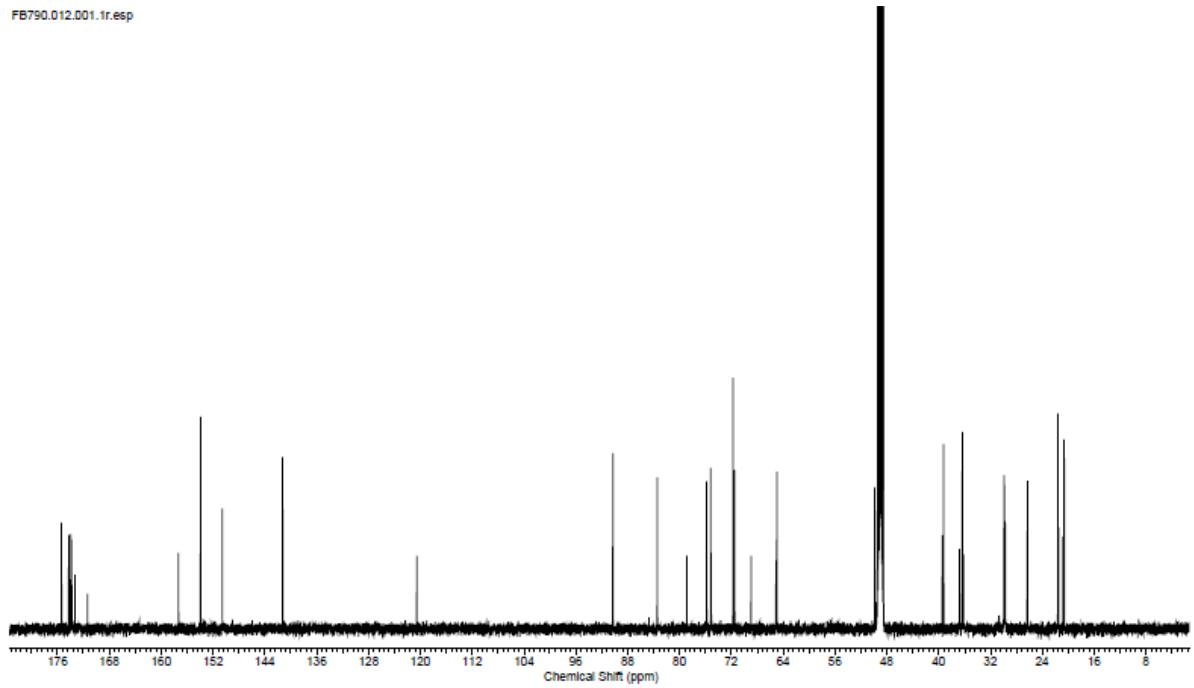




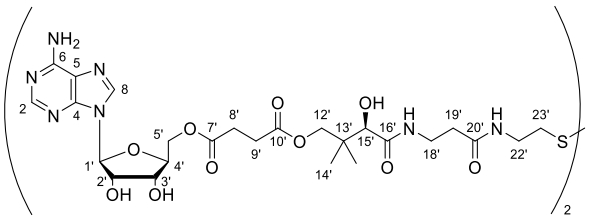
((2S,3R,4S,5S)-5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl ((R)-3-hydroxy-2,2-dimethyl-4-((3-(methylamino)-3-oxopropyl)amino)-4-oxobutyl) succinate (**9**)

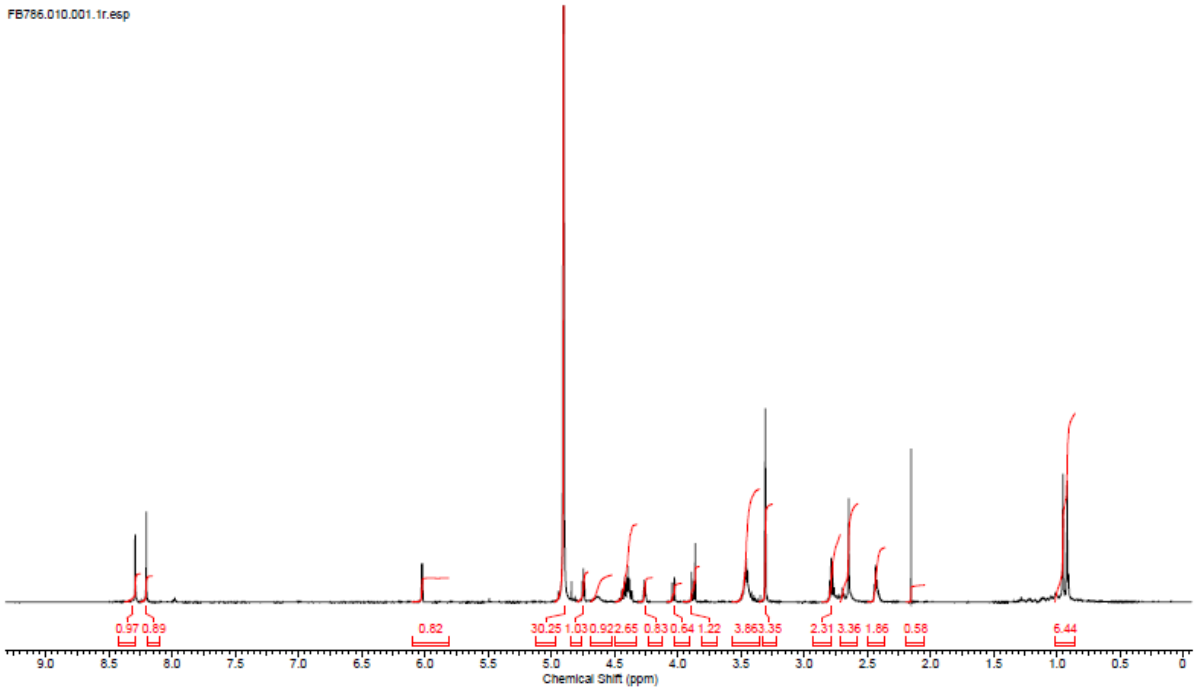


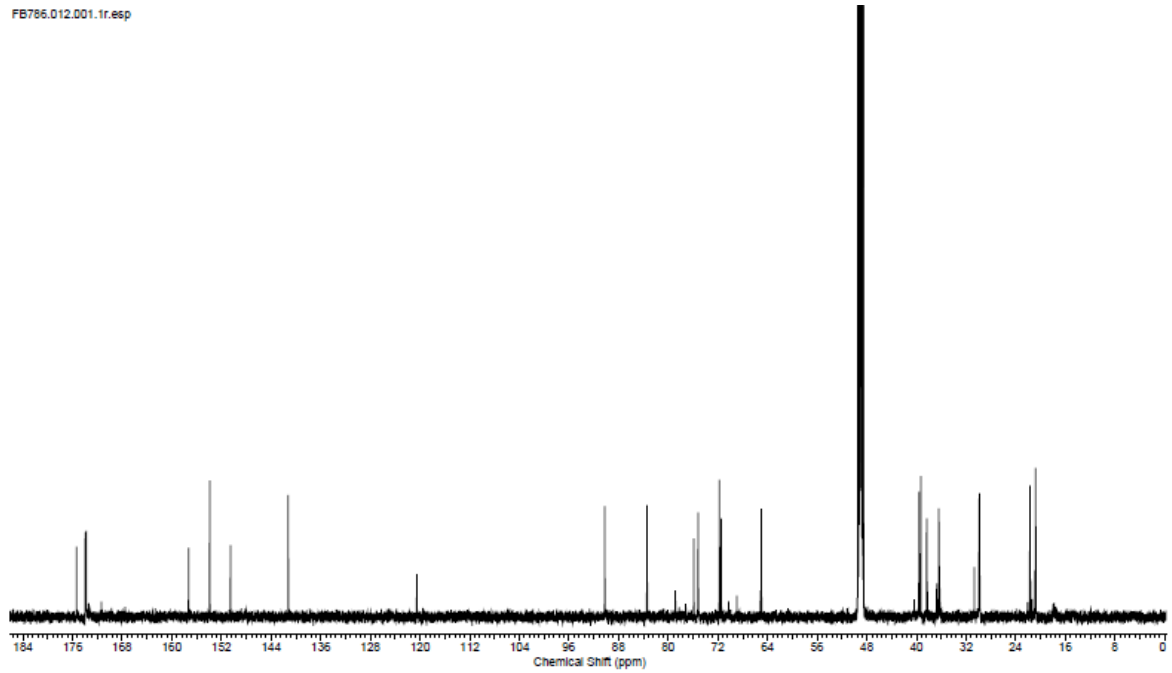




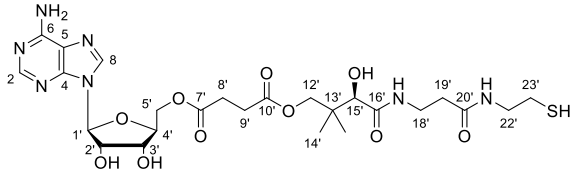
(10R,29R)-1-((2R,3S,4R,5R)-5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)-10,29-dihydroxy-9,9,30,30-tetramethyl-3,6,11,15,24,28-hexaoxo-2,7-dioxa-19,20-dithia-12,16,23,27-tetraazahentriacontan-31-yl (((2S,3R,4S,5S)-5-(6-amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl) succinate (**46**)

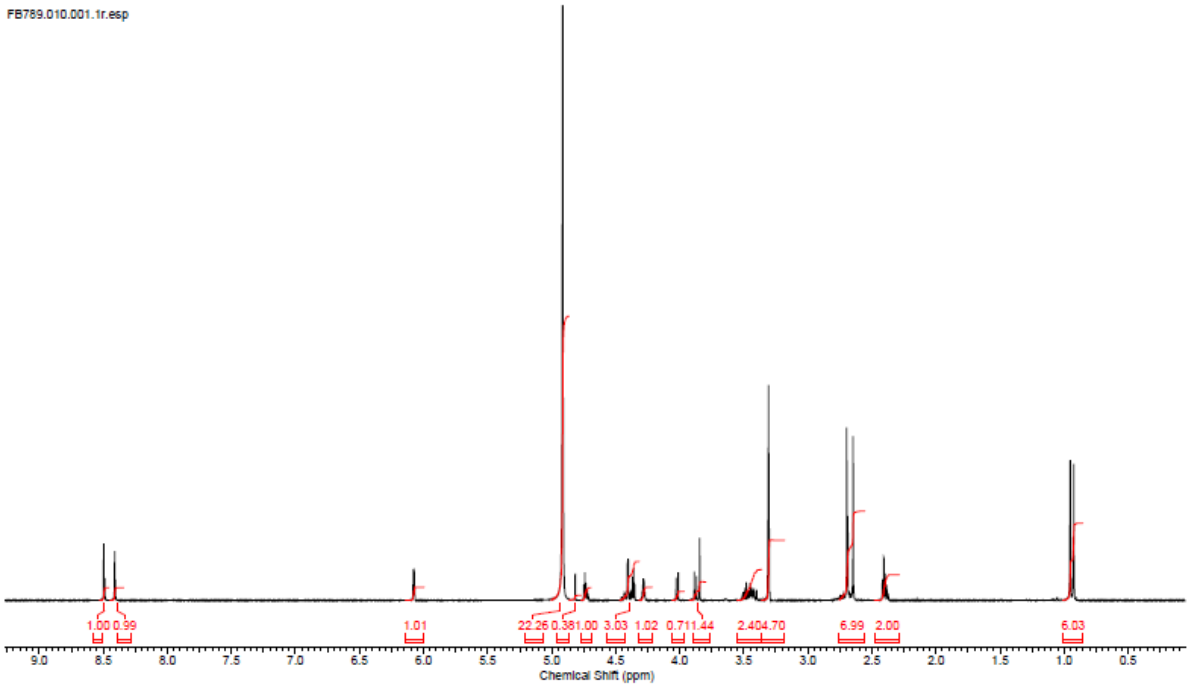


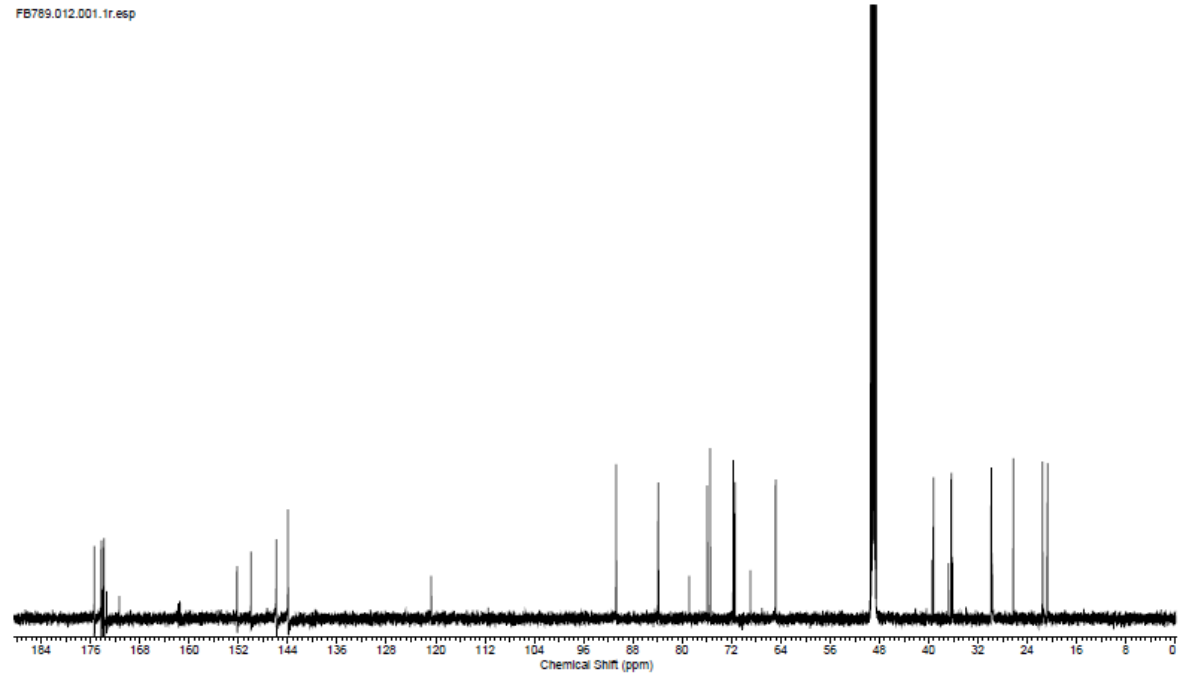




((2S,3R,4S,5S)-5-(6-Amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl ((R)-3-hydroxy-4-((3-((2-mercaptoethyl)amino)-3-oxopropyl)amino)-2,2-dimethyl-4-oxobutyl) succinate (**10**)







Concentration µM	AKA activity remaining %	
	Compound 1	Compound 2
4	109.0	115.0
20	110.8	107.8
100	90.4	81.7
500	63.9	39.9
2500	42.8	21.6

Concentration µM	AKA activity remaining %	
	Compound 3	Compound 4
4.8	94.8	88.3
24	102.0	93.1
120	88.2	89.0
600	69.9	64.8
3000	20.9	18.6

Concentration µM	AKA activity remaining %	
	Compound 5	Compound 6
24	95.7	97.0
120	88.8	88.6
600	46.0	49.1
3000	2.5	4.2

Concentration µM	AKA activity remaining %			
	Compound 7	Compound 8	Compound 9	Compound 10
62.5	82.0	96.0	97.8	49.8
125	73.0	92.7	93.5	46.7
250	63.1	87.3	85.5	41.5
500	47.7	74.7	74.6	35.1
1000	31.5	56.0	59.4	26.3
2000	22.1	36.7	39.9	19.6

Concentration µM	AKA activity remaining %	
	Compound 10 + DTT	Compound 10 -DTT
3.2	100.7	86.9
16	97.9	66.2
80	93.8	55.2
400	65.5	39.3
2000	25.5	20.7

* Results are the mean of two independent measurements