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Supporting Information

# Amino Acid Modified RNA Bases as Building Blocks of an Early Earth RNA-Peptide World

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## 1. General Experimental Methods

Chemicals were purchased from Sigma-Aldrich, TCI, Fluka, ABCR, Carbosynth or Acros Organics and used without further purification. Some of the strands were purchased from Metabion or Ella Biotech. Reagent-grade dry solvents (Sigma-Aldrich, Acros Organics) were stored over molecular sieves and handled under inert gas atmosphere. Reactions and chromatography fractions were monitored by qualitative thin-layer chromatography (TLC) on silica gel F254 TLC plates from Merck KGaA. Flash column chromatography was performed on Geduran® Si60 (40-63 μm) silica gel from Merck KGaA. NMR spectra were recorded on Bruker AVIIIHD 400 spectrometers (400 MHz). $^{1}$H NMR shifts were calibrated to the residual solvent resonances: DMSO-$d_6$ (2.50 ppm), $CDCl_3$ (7.26 ppm), Acetone-$d_6$ (2.05 ppm), $CD_2Cl_2$ (5.32 ppm). $^{13}$C NMR shifts were calibrated to the residual solvent: DMSO-$d_6$ (39.52 ppm), $CDCl_3$ (77.16 ppm), Acetone-$d_6$ (29.84 ppm), $CD_2Cl_2$ (53.84 ppm). All NMR spectra were analysed using the program MestreNova 10.0.1 from Mestrelab Research S. L. High resolution mass spectra were measured by the analytical section of the Department of Chemistry of the Ludwigs-Maximilians-Universität München on the spectrometer MAT 90 (ESI) from Thermo Finnigan GmbH. IR spectra were recorded on a PerkinElmer Spectrum BX II FT-IR system. All substances were directly applied as solids or on the ATR unit. Analytical RP-HPLC was performed on an analytical HPLC Waters Alliance (2695 Separation Module, 2996 Photodiode Array Detector) equipped with the column Nucleosil 120-2 C18 from Macherey Nagel using a flow of 0.5 ml/min, a gradient of 0-30% of buffer B in 45 min was applied. Preparative RP-HPLC was performed on a HPLC Waters Breeze (2487 Dual λ Array Detector, 1525 Binary HPLC Pump) equipped with the column VP 250/32 C18 from Macherey Nagel using a flow of 5 ml/min, a gradient of 0-25% of buffer B in 45 min was applied for the purifications. Oligonucleotides were purified using the following buffer system: buffer A: 100 mM $NEt_3$/HOAc (pH 7.0) in $H_2O$ and buffer B: 100 mM $NEt_3$/HOAc in 80% (v/v) acetonitrile. The pH values of buffers were adjusted using a MP 220 pH-meter (Metter Toledo). Oligonucleotides were detected at wavelength: 260 nm. Melting profiles were measured on a JASCO V-650 spectrometer. Calculation of concentrations was assisted using the software OligoAnalyzer 3.0 (Integrated DNA Technologies: https://eu.idtdna.com/calc/analyzer). For strands containing artificial bases, the extinction coefficient of their corresponding canonical-only strand was employed without corrections. Matrix-assisted laser desorption/ionization-time-of-flight (MALDI-TOF) mass spectra were recorded on a Bruker Autoflex II. For MALDI-TOF

measurements, the samples were desalted on a 0.025 µm VSWP filter (Millipore) against $ddH_2O$ and co-crystallized in a 3-hydroxypicolinic acid matrix (HPA).

## 2. Synthesis of the Phosphoramidite Building-Blocks

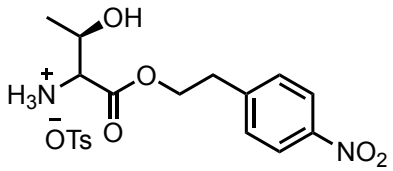
### 2.1. Synthesis of RNA building blocks

**Npe-protection of carboxy group of amino acid**

The reaction was performed according to the procedure published before. [1]

L-amino acid (1 eq.), 2-(4-nitrophenyl)ethanol (npe-OH, 3 eq.) and TsOH (3 eq.) were refluxed in toluene overnight in a *Dean-Stark* apparatus. The solution was cooled to room temperature and $Et_2O$ was added. The oily residue was decanted, and the upper layer was removed to collect the oil. Precipitation of was induced by adding to the oil MeOH and $Et_2O$.

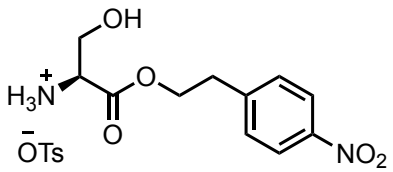
**Compound 4**




**Yield**: 70%; **IR**: $\tilde{\nu}$ = 3401 (w), 2930 (s), 2892 (s), 2858 (s), 1730 (s), 1510 (vs), 1465 (s), 1300 (vs), 1258 (s), 1167 (s), 1010 (s), 895 (w), 832 (s) $cm^{-1}$; **$^1$H NMR (400 MHz, DMSO-*d*$_6$) δ**: 8.2 – 8.1 (m, 5H), 7.58 (d, *J* = 8.8 Hz, 2H), 7.48 (d, *J* = 8.2 Hz, 2H), 7.11 (d, *J* = 8.2 Hz, 2H), 5.6 (br. s., 1H), 4.45 (t, *J* = 6.2 Hz, 2H), 4.1 – 4.0 (m, 1H), 3.89 (d, *J* = 4.0 Hz, 1H), 3.10 (t, *J* = 6.2 Hz, 2H), 2.29 (s, 3H), 1.14 (d, *J* = 6.6 Hz, 3H); **$^{13}$C NMR (101 MHz, DMSO-*d*$_6$) δ**: 168.2, 146.5, 146.3, 137.7, 130.4, 128.1, 125.6, 123.5, 65.4, 64.9, 57.9, 33.8, 20.7, 20.0; **HRMS (ESI)**: calculated for $C_{12}H_{17}N_2O_5^+$: m/z = 269.1137 $[M+H]^+$; found: m/z = 269.1140 $[M+H]^+$.

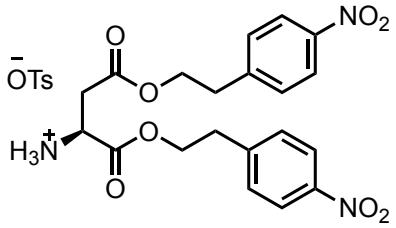
The analytical data is in agreement with the literature.[1]

**Compound 5**



**Yield**: 75%; **IR**: $\tilde{\nu}$ = 3400 (w), 2931 (s), 2894 (s), 2858 (s), 1730 (s), 1510 (vs), 1465 (s), 1300 (vs), 1258 (s), 1167 (s), 1010 (s), 895 (w), 832 (s) $cm^{-1}$; **$^1$H NMR (400 MHz, DMSO-$d_6$) δ**: 8.34 (br. s, 3H), 8.16 (d, *J* = 8.9 Hz, 2H), 7.58 (d, *J* = 8.9 Hz, 2H), 7.50 (d, *J* = 8.0 Hz, 2H), 7.12 (d, *J* = 8.0 Hz, 2H), 4.49 – 4.36 (m, 2H), 4.11 (br. s, 1H), 3.74 – 3.73 (m, 2H), 3.08 (t, *J* = 6.4 Hz, 2H), 2.28 (s, 3H); **$^{13}$C NMR (101 MHz, DMSO-$d_6$) δ**: 168.0, 146.3, 138.0, 130.4, 128.2, 125.6, 123.5, 65.4, 59.5, 54.2, 33.9, 20.9; **HRMS (ESI)**: calculated for $C_{11}H_{15}N_2O_5^+$: m/z = 255.0981 $[M+H]^+$; found: m/z = 255.0977 $[M+H]^+$.

**Compound 6**



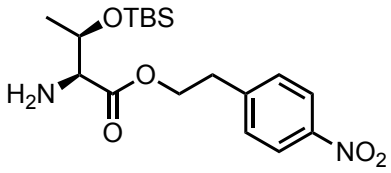

**Yield**: 82 %; **IR**: $\tilde{\nu}$ = 3402 (w), 2933 (s), 2894 (s), 2858 (s), 1730 (s), 1689 (s), 1514 (vs), 1469 (s), 1310 (vs), 1258 (s), 1167 (s), 1010 (s), 895 (w), 834 (s) $cm^{-1}$; **$^1$H NMR (400 MHz, DMSO-$d_6$) δ**: 8.42 (s, 3H), 8.16 – 8.11 (m, 4H), 7.55 – 7.48 (m, 6H), 7.12 (d, *J* = 7.9 Hz, 2H), 4.37 (t, *J* = 6.3 Hz, 2H), 4.34 – 4.30 (m, 1H), 4.26 (q, *J* = 6.3 Hz, 2H), 3.01 (q, *J* = 6.5 Hz, 4H), 2.85 (qd, *J* = 17.5, 5.1 Hz, 2H), 2.28 (s, 3H); **$^{13}$C NMR (101 MHz, DMSO-$d_6$) δ**: 169.0, 168.1, 146.4, 146.3, 145.3, 138.0, 130.3, 130.2, 128.2, 125.6, 123.5, 123.5, 65.7, 64.7, 48.4, 34.1, 33.8, 33.7, 20.8; **HRMS (ESI)**: calculated for $C_{20}H_{22}N_3O_8^+$: m/z = 432.1401 $[M+H]^+$; found: m/z = 432.1405 $[M+H]^+$.

**General procedure of hydroxy group protection with TBSCl**

The reaction was performed according to the procedure published before. [1]

Npe-protected ester (1 eq.) was dissolved in pyridine and treated with one half of TBSCl (3 eq.) and 1*H*-imidazole (3 eq.). After 10 min, the second half was added, and the reaction mixture was left to stir at room temperature overnight. The mixture was diluted with $CH_2Cl_2$ and washed successively with sat. $NaHCO_3$ solution and $H_2O$. The organic layer was dried, evaporated and purified by flash chromatography eluting with $CH_2Cl_2$/MeOH (10/1, v/v) to afford the target compound as an oil.

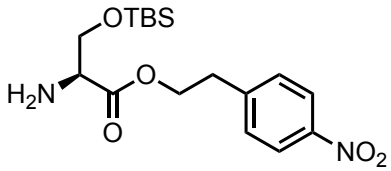
**Compound 7**




**Yield**: 94%; **IR**: $\tilde{\nu}$ = 3854 (w), 3745 (w), 2930 (w), 2856 (w), 1735 (vs), 1601 (s), 1518 (vs), 1472 (w), 1463 (w), 1374 (w), 1344 (vs), 1251 (s), 1155 (s), 1076 (s), 967 (s), 835 (s), 775 (s), 747 (s) $cm^{-1}$; **$^1$H NMR (400 MHz, $CDCl_3$) δ**: 8.16 (d, *J* = 8.6 Hz, 2H), 7.38 (d, *J* = 8.6 Hz, 2H), 4.41 (dt, *J* = 11.0, 6.8 Hz, 1H), 4.29 – 4.16 (m, 2H), 3.24 (d, *J* = 2.8 Hz, 1H), 3.06 (t, *J* = 6.8 Hz, 2H), 1.20 (d, *J* = 6.3 Hz, 3H), 0.80 (s, 9H), -0.01 (s, 3H), -0.10 (s, 3H); **$^{13}$C NMR (101 MHz, $CDCl_3$) δ**: 174.3, 147.0, 145.6, 129.9, 123.9, 69.6, 64.5, 60.9, 35.0, 25.7, 21.0, 17.9, -4.2, -5.2; **HRMS (ESI)**: calculated for $C_{18}H_{31}N_2O_5Si^+$: m/z = 383.2002 $[M+H]^+$; found: m/z = 383.1997 $[M+H]^+$.

The analytical data is in agreement with the literature.[1]

**Compound 8**

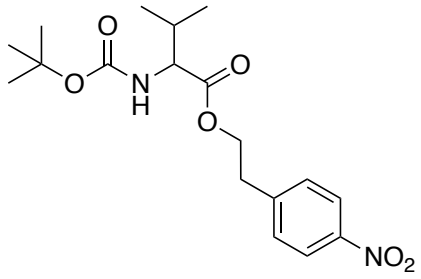



**Yield**: 96%; **IR**: $\tilde{\nu}$ = 3854 (w), 3745 (w), 2955 (w), 2930 (w), 2856 (w), 1735 (vs), 1601 (s), 1518 (vs), 1472 (w), 1374 (w), 1344 (vs), 1251 (s), 1155 (s), 1075 (s), 967 (s), 855 (w), 835 (s), 775 (s), 747 (s) $cm^{-1}$; **$^1$H NMR (400 MHz, $CDCl_3$) δ**: 8.13 (d, *J* = 8.6 Hz, 2H), 7.36 (d, *J* = 8.6 Hz, 2H), 4.34 (q, *J* = 6.7 Hz, 2H), 3.82 (dd, *J* = 9.8, 3.7 Hz, 1H), 3.73 (dd, *J* = 9.8, 3.0 Hz, 1H), 3.47 (s, 1H), 3.04 (t, *J* = 6.7 Hz, 2H), 0.81 (s, 9H); **$^{13}$C NMR (101 MHz, $CDCl_3$) δ**: 173.9, 146.9, 145.6, 129.8, 123.8, 65.4, 64.4, 56.5, 34.9, 25.7, 18.2, -5.5, -5.6; **HRMS (ESI)**: calculated for $C_{17}H_{29}N_2O_5Si^+$: m/z = 369.1846 $[M+H]^+$; found: m/z = 369.1842 $[M+H]^+$.

**General procedure for npe-ester formation of Boc-protected amino acid**

Boc-amino acid (1 eq.) was dissolved in $CH_2Cl_2$ under inert atmosphere and cooled to 0 °C. Then npeOH (1.3 eq.) and $PPh_3$ (1.3 eq.) were added followed by slow addition of DIAD (1.3 eq.). The reaction mixture was left to stir for 2 h at room temperature. Then the solution was washed with water, organic phase was dried over $Na_2SO_4$ and evaporated. The crude product was purified by flash chromatography to afford the target product.

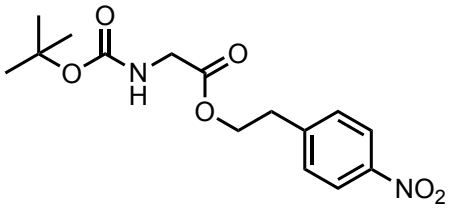
**Compound 12**



Eluent: Hex/EtOAc (4/1, v/v).

**Yield**: 96%; **IR**: $\tilde{\nu}$ = 3397 (w), 2975 (w), 1751 (s), 1709 (vs), 1519 (vs), 1391 (w), 1366 (w), 1345 (vs), 1159 (vs), 1056 (w), 905 (vs), 723 (vs) $cm^{-1}$; **$^1$H NMR (400 MHz, $CDCl_3$) δ**: 8.15 (d, *J* = 8.6 Hz, 2H), 7.38 (d, *J* = 8.6 Hz, 2H), 4.95 (d, *J* = 8.7 Hz, 1H), 4.38 (t, *J* = 6.6 Hz, 2H), 4.15 (dd, *J* = 9.0, 4.8 Hz, 1H), 3.06 (t, *J* = 6.6 Hz, 2H), 2.05 – 1.97 (m, 1H), 1.41 (s, 9H), 0.88 (d, *J* = 6.8 Hz, 3H), 0.78 (d, *J* = 6.8 Hz, 3H); **$^{13}$C NMR (101 MHz, $CDCl_3$) δ**: 172.4, 155.7, 146.9, 145.5, 129.8, 123.8, 79.9, 64.5, 58.6, 34.9, 31.2, 28.4, 19.0, 17.6; **HRMS (ESI)**: calculated for $C_{18}H_{27}N_2O_6^+$: m/z = 367.1869 $[M+H]^+$; found: m/z = 367.1874 $[M+H]^+$.

**Compound 13**

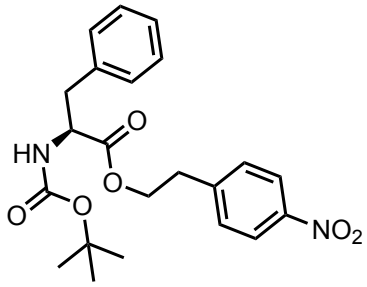


Eluent: Hex/EtOAc (3/1, v/v).

**Yield**: 85%; **IR**: $\tilde{\nu}$ = 3396 (w), 2978 (w), 2254 (w), 1750 (s), 1707 (vs), 1601 (w), 1518 (vs), 1391 (w), 1366 (w), 1345 (vs), 1250 (w), 1159 (vs), 1056 (w), 905 (vs), 727 (vs) $cm^{-1}$; **$^1$H NMR (400 MHz, $CDCl_3$) δ**: 8.10 (d, *J* = 8.6 Hz, 2H), 7.38 (d, *J* = 8.6 Hz, 2H), 4.97 (d, *J* = 9.2 Hz, 1H), 4.39 (t, *J* = 6.6 Hz, 2H), 3.87 (d, *J* = 5.8 Hz, 2H), 3.06 (t, *J* = 6.6 Hz, 2H), 1.43 (s, 9H); **$^{13}$C NMR (101 MHz, $CDCl_3$) δ**: 170.3, 155.8, 147.0, 145.4, 129.9, 123.9, 80.3, 64.7, 42.4, 34.9, 28.4; **HRMS (ESI)**: calculated for $C_{15}H_{21}N_2O_6^+$: m/z = 325.1400 $[M+H]^+$; found: m/z = 325.1398 $[M+H]^+$.

The analytical data is in agreement with the literature.[2]

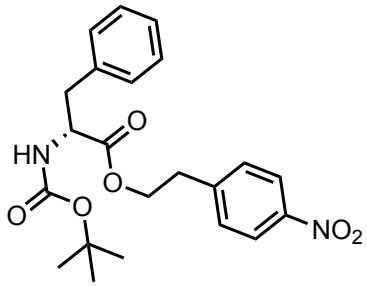
**Compound 14a**




Eluent: Hex/EtOAc (4/1, v/v).

**Yield**: 81%; **IR**: $\tilde{\nu}$ = 3426 (w), 3356 (w), 1740 (w), 1709 (vs), 1602 (w), 1518 (vs), 1495 (s), 1344 (vs), 1249 (w), 1159 (vs), 1056 (w), 855 (s), 733 (s), 698 (vs) $cm^{-1}$; **$^1$H NMR (400 MHz, $CDCl_3$) δ**: 8.15 (d, *J* = 8.7 Hz, 2H), 7.31 (d, *J* = 8.7 Hz, 2H), 7.25 – 7.20 (m, 3H), 7.04 (d, *J* = 5.6 Hz, 2H), 4.90 (d, *J* = 8.4 Hz, 1H), 4.54 (q, *J* = 6.4 Hz, 1H), 4.39 – 4.25 (m, 2H), 3.07 – 2.93 (m, 4H), 1.41 (s, 9H); **$^{13}$C NMR (101 MHz, $CD_2Cl_2$) δ**: 171.8, 155.0, 146.9, 145.3, 135.8, 129.8, 129.2, 128.6, 127.1, 123.8, 80.1, 64.7, 54.5, 38.4, 34.7, 28.3; **HRMS (ESI)**: calculated for $C_{22}H_{26}N_2O_6Na^+$: m/z = 437.1683 $[M+Na]^+$; found: m/z = 437.1684 $[M+Na]^+$.

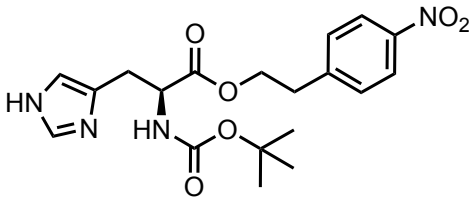
**Compound 14b**




Eluent: Hex/EtOAc (4/1, v/v).

**Yield**: 85%; **IR**: $\tilde{\nu}$ = 3443 (w), 3375 (w), 2977 (w), 2929 (w), 1740 (w), 1709 (vs), 1602 (w), 1517 (vs), 1495 (s), 1343 (vs), 1248 (w), 1157 (vs), 1055 (w), 855 (s), 747 (s), 698 (vs) $cm^{-1}$; **$^1$H NMR (400 MHz, $CDCl_3$) δ**: 8.16 (d, *J* = 8.7 Hz, 2H), 7.33 (d, *J* = 8.7 Hz, 2H), 7.30 – 7.20 (m, 3H), 7.07 (d, *J* = 6.2 Hz, 2H), 4.97 (d, *J* = 8.4 Hz, 1H), 4.56 (q, *J* = 6.2 Hz, 1H), 4.40 – 4.27 (m, 2H), 3.08 – 2.93 (m, 4H), 1.43 (s, 9H); **$^{13}$C NMR (101 MHz, $CDCl_3$) δ**: 171.8, 155.1, 146.9, 145.4, 135.9, 129.8, 129.2, 128.6, 127.1, 123.8, 80.0, 64.7, 54.5, 38.4, 34.7, 28.3; **HRMS (ESI)**: calculated for $C_{22}H_{30}N_3O_6^+$: m/z = 432.2129 $[M+NH_4]^+$; found: m/z = 432.2131 $[M+NH_4]^+$.

**Compound 19**



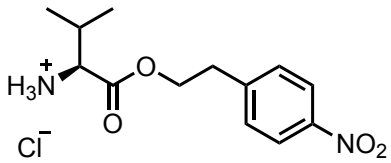
Boc-histidine (0.5 g, 1.96 mmol, 1 eq.), 2-(4-nitrophenyl)ethanol (0.655 g, 3.92 mmol, 2 eq.), DMAP (0.048 g, 0.39 mmol, 0.20 eq.) and HBTU (0.967 g, 2.55 mmol, 1.3 eq.) were dissolved in DMF (4 ml) under inert atmosphere. Diisopropylamine (686 µl, 4.90 mmol, 2.5 eq.) was added dropwise and the reaction mixture was stirred overnight at room temperature. The resulting solution was diluted with EtOAc (30 ml) and quenched with saturated $NH_4Cl$ solution (15 ml). The organic layer was washed with water, dried and the solvents were removed *in vacuo*. The crude product was purified by flash chromatography on silica gel (2% to 5% MeOH in DCM) to obtain the target product as a pale-yellow foam.

**Yield**: 93%; **IR**: $\tilde{\nu}$ =2977 (w), 1699 (vs), 1600 (s), 1516 (vs), 1391 (w), 1365 (w), 1344 (vs), 1250 (w), 1160 (vs), 1108 (w), 1054 (w), 1016 (w), 855 (vs), 748 (w), 697 (w) $cm^{-1}$; **$^1$H NMR (400 MHz, $CDCl_3$) δ**: 8.18 – 8.07 (m, 2H), 7.58 (s, 1H), 7.41 – 7.30 (m, 2H), 6.72 (s, 1H), 5.77 (d, $J$ = 8.2 Hz, 1H), 4.51 (q, $J$ = 6.2 Hz, 1H), 4.34 (t, $J$ = 6.6 Hz, 2H), 3.06 – 3.00 (m, 4H), 1.41 (s, 9H); **$^{13}$C NMR (101 MHz, $CDCl_3$) δ**: 172.1, 155.7, 147.1, 145.7, 135.2, 134.2, 130.0, 123.9, 115.9, 80.2, 64.9, 53.6, 34.9, 29.7, 28.5; **HRMS (ESI)**: calculated for $C_{19}H_{25}N_4O_6^+$: m/z = 405.1769 $[M+H]^+$; found: m/z = 405.1765 $[M+H]^+$.

**General procedure for deprotection of Boc-protecting group**

Npe-protected amino acid was dissolved in 4M HCl/Dioxane mixture at 0 °C. The reaction mixture was left to stir for 2 h and afterwards was evaporated to dryness. The resulting product was used for further steps without additional purification.

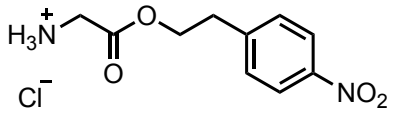
**Compound 15**



**Yield**: 99%; **IR**: $\tilde{\nu}$ = 3335 (w), 2964 (w), 2850 (w), 1741 (s), 1604 (w), 1516 (vs), 1464 (w), 1379 (vs), 1232 (vs), 1215 (s), 1170 (w), 1043 (w), 969 (w), 857 (s), 751 (s), 700 (s) $cm^{-1}$; **$^1$H**

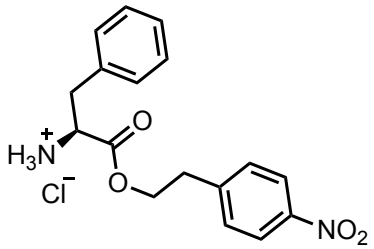
**NMR (400 MHz, DMSO-$d_6$) δ**: 8.66 (br. s, 3H), 8.17 (d, *J* = 8.6 Hz, 2H), 7.62 (d, *J* = 8.6 Hz, 2H), 4.46 (dtd, *J* = 23.3, 11.1, 6.3 Hz, 2H), 3.76 (d, *J* = 4.5 Hz, 1H), 3.11 (t, *J* = 6.3 Hz, 2H), 2.10 (tt, *J* = 11.6, 5.8 Hz, 1H), 0.84 (d, *J* = 3.0 Hz, 3H), 0.82 (d, *J* = 3.0 Hz, 3H). **$^{13}$C NMR (101 MHz, DMSO-$d_6$) δ**: 168.8, 146.3, 130.4, 123.4, 65.3, 57.2, 33.8, 29.2, 18.3, 17.4 **HRMS (ESI)**: calculated for $C_{13}H_{19}N_2O_4^+$: m/z = 267.1339 $[M+H]^+$; found: m/z = 267.1139 $[M+H]^+$.

**Compound 16**



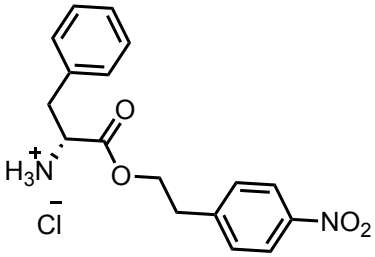
**Yield**: 99%; **IR**: $\tilde{\nu}$ = 2949 (w), 1746 (s), 1515 (vs), 1310 (vs), 1238 (vs), 1053 (w), 955 (s), 905 (s) 856 (s), 698 (s) $cm^{-1}$; **$^1$H NMR (400 MHz, DMSO-$d_6$) δ**: 8.30 (br. s, 3H), 8.18 (d, *J* = 8.7 Hz, 2H), 7.59 (d, *J* = 8.7 Hz, 2H), 4.44 (t, *J* = 6.4 Hz, 2H), 3.77 (s, 2H), 3.09 (t, *J* = 6.4 Hz, 2H); **$^{13}$C NMR (101 MHz, DMSO-$d_6$) δ**: 167.6, 156.2, 146.3, 130.4, 123.5, 67.9, 33.9, 28.2, 22.0; **HRMS (ESI)**: calculated for $C_{10}H_{13}N_2O_4^+$: m/z = 225.0870 $[M+H]^+$; found: m/z = 225.0868 $[M+H]^+$.
The analytical data is in agreement with the literature.[2]

**Compound 17a**



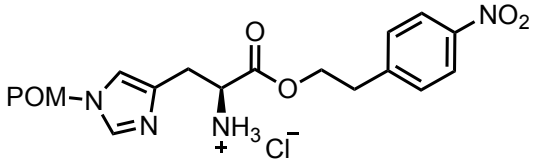
**Yield**: 99%; **IR**: $\tilde{\nu}$ = 3142 (w), 2988 (w), 2802 (w), 1740 (vs), 1601 (s), 1518 (vs), 1490 (vs), 1351 (vs), 1232 (vs), 1191 (s), 1102 (s), 981 (s), 856 (vs), 755 (vs), 736 (vs), 706 (vs) $cm^{-1}$; **$^1$H NMR (400 MHz, DMSO-$d_6$) δ**: 8.74 (br. s, 3H), 8.16 (d, *J* = 8.7 Hz, 2H), 7.49 (d, *J* = 8.7 Hz, 2H), 7.33 – 7.21 (m, 3H), 7.12 (dd, *J* = 7.8, 1.8 Hz, 2H), 4.33 (t, *J* = 6.3 Hz, 2H), 4.20 (dd, *J* = 7.8, 5.5 Hz, 1H), 3.16 (dd, *J* = 14.0, 5.5 Hz, 1H), 3.06 – 2.89 (m, 3H); **$^{13}$C NMR (101 MHz, DMSO-$d_6$) δ**: 168.9, 146.3, 134.9, 130.4, 129.4, 128.5, 127.2, 123.4, 65.4, 53.3, 35.8, 33.7; **HRMS (ESI)**: calculated for $C_{17}H_{19}N_2O_4^+$: m/z = 315.1339 $[M+H]^+$; found: m/z = 315.1332 $[M+H]^+$.

**Compound 17b**



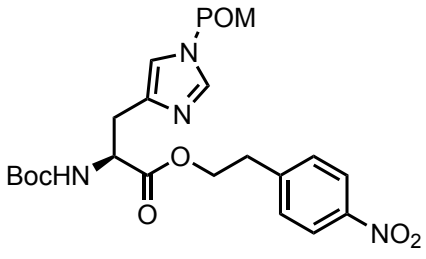
**Yield**: 99%; **IR**: $\tilde{\nu}$ = 3146 (w), 2988 (w), 2802 (w), 1740 (vs), 1602 (s), 1518 (vs), 1490 (vs), 1351 (vs), 1232 (vs), 1192 (s), 1102 (s), 856 (vs), 755 (vs), 736 (vs), 705 (vs) $cm^{-1}$; **$^1$H NMR (400 MHz, DMSO-$d_6$) δ**: 8.91 (br. s., 3H), 8.12 (d, *J* = 8.7 Hz, 2H), 7.46 (d, *J* = 8.7 Hz, 2H), 7.27 – 7.20 (m, 3H), 7.12 (d, *J* = 6.4 Hz, 2H), 4.29 (t, *J* = 6.4 Hz, 2H), 4.19 – 4.08 (m, 1H), 3.21 (dd, *J* = 14.1, 5.0, 1H), 3.10 – 2.88 (m, 3H); **$^{13}$C NMR (101 MHz, DMSO-$d_6$) δ**: 168.9, 146.3, 134.8, 130.4, 129.4, 128.5, 127.2, 123.4, 65.4, 53.3, 35.8, 33.7; **HRMS (ESI)**: calculated for $C_{17}H_{19}N_2O_4^+$: m/z = 315.1339 $[M+H]^+$; found: m/z = 315.1332 $[M+H]^+$.

**Compound 21**



**Yield**: 98%; **IR**: $\tilde{\nu}$ = 2960 (w), 1737 (vs), 1624 (w), 1598 (w), 1516 (vs), 1454 (w), 1415 (w), 1351 (vs), 1282 (w), 1188 (w), 1124 (vs), 1045 (w), 1008 (w), 854 (s), 774 (w), 749 (w), 701 (w) $cm^{-1}$; **$^1$H NMR (400 MHz, DMSO-$d_6$) δ**: 8.69 (s, 3H), 8.21 – 8.15 (m, 2H), 7.59 – 7.55 (m, 2H), 7.51 (s, 1H), 6.04 (s, 2H), 4.39 (m, 3H), 3.56 (s, 1H), 3.17 (d, *J* = 6.9 Hz, 2H), 3.04 (td, *J* = 6.4, 3.9 Hz, 2H), 1.13 (s, 9H); **$^{13}$C NMR (101 MHz, DMSO-$d_6$) δ**: 176.7, 168.2, 146.4, 146.1, 137.4, 130.4, 123.5, 120.0, 69.2, 66.4, 65.6, 51.1, 38.2, 33.7, 26.5; **HRMS (ESI)**: calculated for $C_{20}H_{27}N_4O_6^+$: m/z = 419.1925 $[M+H]^+$; found: 419.1919 $[M+H]^+$.

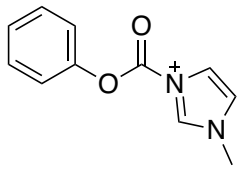
**Compound 20**



The histidine derivative **19** (0.745 g, 1.84 mmol, 1 eq.) was dissolved in DMF (12 mL) under $N_2$ atmosphere at 0 °C. Subsequently, $K_2CO_3$ (0.509 g, 3.68 mmol, 2 eq.) was added and the mixture was stirred for 40 min. Chloromethylpivalate (319 µl, 2.21 mmol, 1.2 eq.) was added dropwise at 0°C and the reaction mixture was left to warm to room temperature while stirring for 5 h. Catalytic amounts of KI were added and the mixture was stirred for another 1 h. The resulting suspension was diluted with EtOAc (75 ml) and quenched with saturated $NH_4Cl$ solution (35 ml). The organic phase was washed with water, dried over $Na_2SO_4$ and concentrated *in vacuo*. The crude mixture was purified by flash chromatography on silica gel (40% isohexane in EtOAc to pure EtOAc). The pivalate protected histidine derivative was obtained as a yellow oil.

**Yield**: 55%; **IR**: 2850 (w), 2600 (w), 1738 (vs), 1624 (w), 1598 (w), 1573 (w), 1516 (vs), 1454 (w), 1414 (w), 1350 (vs), 1282 (w), 1191 (w), 1124 (vs), 1044 (w), 1008 (w), 854 (vs), 773 (w), 749 (w), 701 (w) $cm^{-1}$; **$^1$H NMR (400 MHz, $CDCl_3$) δ**: 8.19 – 8.14 (m, 2H), 7.54 (d, *J* = 1.4 Hz, 1H), 7.42 – 7.36 (m, 2H), 6.71 (s, 1H), 5.81 (d, *J* = 8.2 Hz, 1H), 5.73 (s, 2H), 4.51 (dt, *J* = 8.2, 5.3 Hz, 1H), 4.34 (t, *J* = 6.7 Hz, 2H), 3.04 (t, *J* = 6.7 Hz, 2H), 2.97 (t, *J* = 5.2 Hz, 2H), 1.42 (s, 9H), 1.14 (s, 9H); **$^{13}$C NMR (101 MHz, $CDCl_3$) δ**: 177.9, 172.0, 155.7, 147.0, 145.8, 138.3, 130.0, 123.9, 117.3, 79.9, 77.4, 67.7, 64.7, 53.5, 38.9, 35.0, 30.1, 28.5, 27.0; **HRMS (ESI)**: calculated for $C_{25}H_{35}N_4O_8^+$: m/z = 519.2449 $[M+H]^+$; found: m/z = 519.2441 $[M+H]^+$.

**Compound 22**



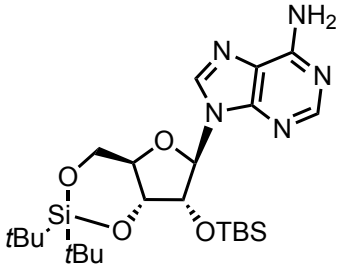
The reaction was conducted according to a published procedure.[3]

Phenyl chloroformate (4 ml, 31.9 mmol, 1 eq.) was dissolved in dry $CH_2Cl_2$ under nitrogen and cooled to 0 °C. Then *N*-methylimidazole (2.54 ml, 31.9 mmol, 1 eq.) was added dropwise. The mixture was allowed to stir at room temperature for 2 hours. Afterwards the reaction mixture was filtered, the precipitate was washed with $CH_2Cl_2$ and dried.

**Yield**: 95%; **IR**: $\tilde{\nu}$ = 2926 (w), 1783 (vs), 1588 (w), 1536 (w), 1372 (s), 1330 (s), 1232 (vs), 749 (vs), 689 (s) $cm^{-1}$; **$^1$H NMR (400 MHz, DMSO-*$d_6$*) δ**: 10.29 (s, 1H), 8.37 (s, 1H), 8.02 (s, 1H), 7.43 – 7.58 (m, 5H), 4.01 (s, 3H); **$^{13}$C NMR (101 MHz, DMSO-*$d_6$*) δ**: 157.5, 135.6, 129.3, 123.1, 121.3, 119.5, 118.6, 115.3, 35.4.

The analytical data is in agreement with the literature.[3]

**Compound 24**



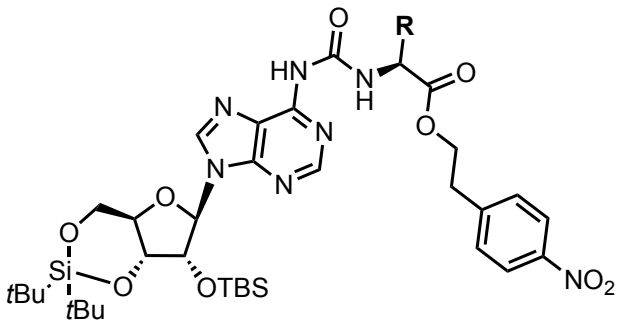
Compound was synthesized following the procedure published earlier.[4]

Adenosine **23** (1 g, 3.74 mmol, 1 eq.) was suspended in DMF and di-*tert*-butylsilyl ditriflate (1.46 ml, 4.49 mmol, 1.2 eq.) was added dropwise under stirring at 0 °C. The resulting solution was stirred at 0°C for 45 min. Then imidazole (1.27 g, 18.7 mmol, 5 eq.) was added and the reaction was warmed to room temperature over a period of 30 min. Then TBSCl (0.68 g, 4.49 mmol, 1.2 eq.) was added and the reaction was heated to 60 °C overnight. Subsequently, the reaction mixture was diluted with EtOAc and washed with water and brine. The organic layer was dried and evaporated. The residue was purified by flash chromatography (Hex/EtOAc, 1/1, v/v).

**Yield**: 76%; **IR**: $\tilde{\nu}$ = 3148 (w), 2933 (w), 2859 (w), 2361 (w), 1677 (s), 1604 (s), 1598 (w), 1576 (w), 1473 (w), 1426 (w), 1363 (w), 1329 (w), 1302 (w), 1258 (w), 1200 (w), 1166 (w), 1136 (w), 1105 (w), 1064 (vs), 1009 (s), 890 (w), 828 (vs), 786 (w), 754 (w), 729 (w) $cm^{-1}$; **$^1$H NMR (400 MHz, $CDCl_3$) δ**: 8.31 (s, 1H), 7.83 (s, 1H), 6.12 (br. s, 2H), 5.91 (s, 1H), 4.61 (d, *J* = 4.7 Hz, 1H), 4.50 (ddd, *J* = 16.5, 9.3, 4.7 Hz, 2H), 4.25 – 4.17 (m, 1H), 4.03 (dd, *J* = 10.5, 9.3 Hz, 1H), 1.07 (s, 9H), 1.04 (s, 9H), 0.92 (s, 9H), 0.16 (s, 3H), 0.14 (s, 3H); **$^{13}$C NMR (101 MHz, $CDCl_3$) δ**: 155.5, 152.8, 149.3, 138.9, 120.4, 92.6, 75.9, 75.6, 74.8, 67.9, 27.6, 27.1, 26.0, 22.9, 20.5, 18.4, -4.2, -4.8; **HRMS (ESI)**: calculated for $C_{24}H_{44}N_5O_4Si_2^+$: m/z = 522.2932 $[M+H]^+$; found: m/z = 522.2926 $[M+H]^+$.

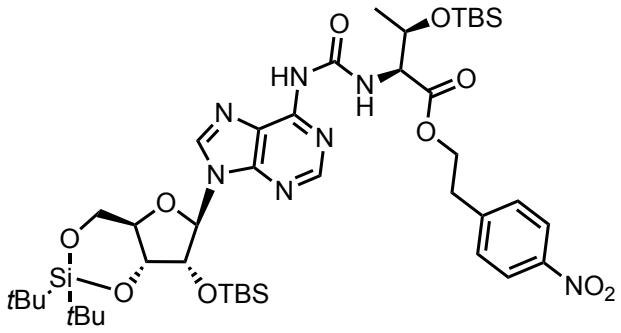
The analytical data is in agreement with the literature.[4]

**General procedure for amino acid attachment to the adenosine derivative**



The silyl-protected adenosine derivative **24** (1 eq.) was dissolved in dry $CH_2Cl_2$ under nitrogen atmosphere. 1-*N*-methyl-3-phenoxycarbonyl-imidazolium chloride (**22**, 2 eq.) was added to the reaction mixture and the resulting suspension was stirred at room temperature for 2 hours (the solution in time becomes clear). Afterwards the protected amino acid (2 eq.) was added together with TEA (2 eq.) as a solution in $CH_2Cl_2$ and the resulting solution was stirred overnight at room temperature. The reaction was quenched by addition of saturated aqueous $NaHCO_3$ solution. The solution was extracted three times with $CH_2Cl_2$, and the organic phase was dried, filtered and concentrated *in vacuo*. The residue was purified by flash chromatography eluting with Hex/EtOAc to give product as white foam.

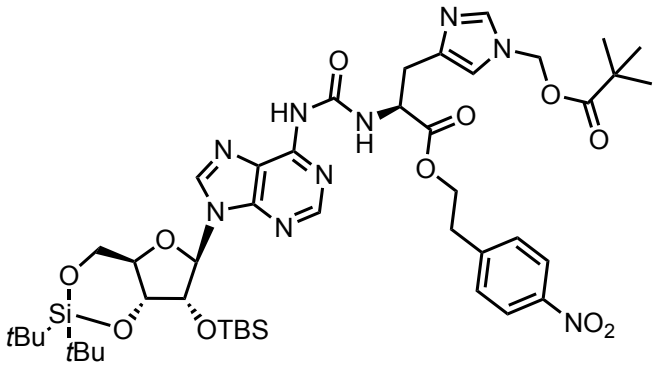
**Compound 25**




Eluent: Hex/EtOAc (4/3, v/v).

**Yield**: 91%; **IR**: $\tilde{\nu}$ = 3237 (w), 2931 (s), 2857 (s), 1737 (s), 1701 (vs), 1610 (s), 1520 (vs), 1465 (s), 1345 (s), 1250 (s), 1136 (w), 1057 (s), 998 (w), 894 (w), 840 (s), 777 (s) $cm^{-1}$; **$^1$H NMR (400 MHz, $CDCl_3$) δ**: 10.05 (d, *J* = 9.0 Hz, 1H), 8.56 (s, 1H), 8.41 (s, 1H), 8.16 (s, 1H), 7.94 (d, *J* = 8.6 Hz, 2H), 7.32 (d, *J* = 8.6 Hz, 2H), 5.99 (s, 1H), 4.64 (d, *J* = 4.6 Hz, 1H), 4.60-4.46 (m, 3H), 4.33-4.24 (m, 2H), 4.20-4.29 (m, 1H), 4.05 (dd, *J* = 10.5, 9.1 Hz, 1H), 3.03 (t, *J* = 6.5 Hz, 2H), 1.25 (d, *J* = 6.5 Hz, 3H), 1.08 (s, 9H), 1.05 (s, 9H), 0.95 (s, 9H), 0.90 (s, 9H), 0.19 (s, 3H), 0.16 (s, 3H), 0.07 (s, 3H), -0.04 (s, 3H); **$^{13}$C NMR (101 MHz, $CDCl_3$) δ**: 171.1, 154.6, 151.3, 150.3, 149.8, 146.8, 145.7, 141.6, 129.9, 123.7, 121.1, 92.6, 76.0, 75.7, 75.0, 68.8, 68.0, 64.8, 59.8, 35.0, 27.7, 27.2, 26.1, 25.7, 22.9, 21.3, 20.6, 18.5, 18.0, -4.1, -4.8, -5.2; **HRMS (ESI)**: calculated for $C_{43}H_{72}N_7O_{10}Si_3^+$: m/z = 930.4643 $[M+H]^+$; found: m/z = 930.4640 $[M+H]^+$.

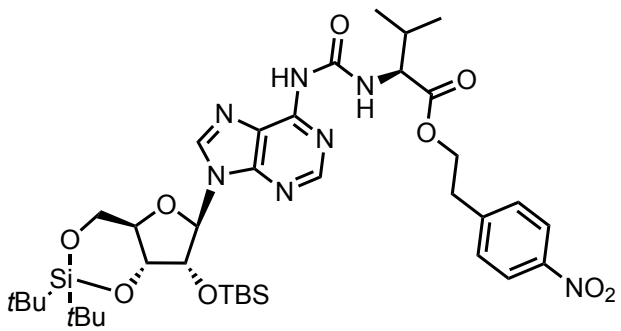
**Compound 26**



Eluent: 10% $CH_2Cl_2$ in EtOAc to pure EtOAc.

**Yield**: 86%; **IR**: $\tilde{\nu}$ = 3854 (w), 3745 (w), 3650 (w), 2932 (w), 2858 (w), 2361 (w), 2341 (w), 1735 (s), 1670 (s), 1654 (w), 1610 (w), 1587 (w), 1521 (vs), 1472 (s), 1395 (w), 1345 (vs), 1252 (w), 1166 (w), 1118 (vs), 1055 (vs), 999 (w), 894 (w), 826 (vs), 781 (s), 750 (w) $cm^{-1}$; **$^1$H NMR (400 MHz, $CDCl_3$) δ**: 10.05 (dd, *J* = 7.6, 3.7 Hz, 1H), 8.45 (s, 1H), 8.08 (s, 1H), 8.06 – 8.02 (m, 3H), 7.59 (d, *J* = 1.3 Hz, 1H), 7.41 – 7.35 (m, 2H), 6.86 (dd, *J* = 5.3, 1.3 Hz, 1H), 5.96 (d, *J* = 7.0 Hz, 1H), 5.74 (d, *J* = 2.6 Hz, 2H), 4.94 – 4.85 (m, 1H), 4.60 (dd, *J* = 6.0, 4.6 Hz, 1H), 4.53 – 4.46 (m, 2H), 4.42 (tq, *J* = 6.5, 1.7 Hz, 2H), 4.24 (tdd, *J* = 9.8, 5.0, 2.8 Hz, 1H), 4.08 – 4.00 (m, 1H), 3.23 – 3.12 (m, 2H), 3.07 (t, *J* = 6.5 Hz, 2H), 1.09 (s, 9H), 1.08 (s, 9H), 1.05 (s, 9H), 0.94 (s, 9H), 0.17 (s, 3H), 0.15 (s, 3H); **$^{13}$C NMR (101 MHz, $CDCl_3$) δ**: 177.8, 171.7, 153.6, 151.3, 150.2, 149.8, 146.9, 145.8, 141.2, 138.4, 138.1, 123.0, 123.8, 121.1, 117.3, 92.6, 76.0, 75.7, 74.9, 67.9, 67.7, 64.7, 55.5, 38.8, 35.0, 30.7, 27.7, 27.2, 26.9, 26.1, 22.9, 20.5, 18.5, 1.3, -4.2; **HRMS (ESI)**: calculated for $C_{45}H_{68}N_9O_{11}Si_2^+$: m/z = 966.4571 $[M+H]^+$; found: m/z = 966.4576 $[M+H]^+$.

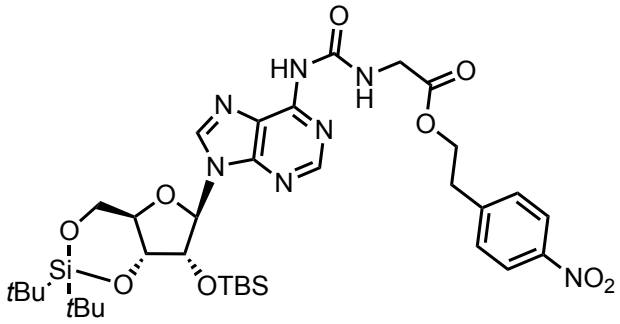
**Compound 27**



Eluent: Hex/EtOAc (4/3, v/v).

**Yield**: 78%; **IR**: $\tilde{\nu}$ = 3230 (w), 2960 (w), 2960 (w), 2858 (w), 1741 (s), 1702 (vs), 1611 (s), 1520 (vs), 1466 (s), 1345 (vs), 1250 (s), 1139 (vs), 1057 (vs), 999 (s), 894 (s), 810 (vs), 781 (s) $cm^{-1}$; **$^1$H NMR (400 MHz, $CDCl_3$) δ**: 10.01 (d, *J* = 8.4 Hz, 1H), 8.50 (s, 1H), 8.17 (s, 1H), 8.07 (d, *J* = 8.3 Hz, 2H), 7.28 (d, *J* = 8.3 Hz, 2H), 5.98 (s, 1H), 4.61 (d, *J* = 4.6 Hz, 1H), 4.56 – 4.38 (m, 5H), 4.20-4.29 (m, 1H), 4.07 (dd, *J* = 10.5, 9.1 Hz, 1H), 3.09 (t, *J* = 6.5 Hz, 2H), 2.28 – 2.21 (m, 1H), 1.08 (s, 9H), 1.05 (s, 9H), 1.00 (d, *J* = 6.5 Hz, 3H), 0.95 (s, 12H), 0.18 (s, 3H), 0.16 (s, 3H); **$^{13}$C NMR (101 MHz, $CDCl_3$) δ**: 171.1, 154.1, 152.2, 151.1, 149.8, 146.9, 145.6, 141.5, 129.9, 126.4, 123.7, 121.1, 92.6, 75.9, 75.7, 74.9, 67.9, 64.8, 58.8, 35.0, 30.9, 27.7, 27.2, 26.1, 22.9, 20.4, 19.5, 18.4, 18.0, -4.2, -4.9; **HRMS (ESI)**: calculated for $C_{38}H_{60}N_7O_9Si_2^+$: m/z = 814.3991 $[M+H]^+$; found: m/z = 814.3976.

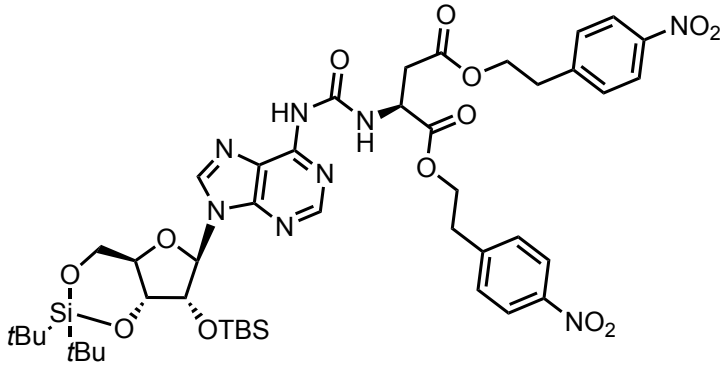
**Compound 28**




Eluent: Hex/EtOAc (4/3, v/v).

**Yield**: 72%; **IR**: $\tilde{\nu}$ = 3239 (w), 2932 (s), 2858 (s), 1749 (s), 1703 (vs), 1611 (s), 1520 (vs), 1468 (s), 1345 (s), 1252 (s), 1141 (w), 1055 (s), 990 (w), 894 (w), 826 (s), 750 (s) $cm^{-1}$; **$^1$H NMR (400 MHz, $CDCl_3$) δ**: 9.95 (br. s, 1H), 8.50 (s, 1H), 8.21 – 8.03 (m, 3H), 7.38 (d, *J* = 8.6 Hz, 2H), 5.98 (s, 1H), 4.60 (d, *J* = 4.7 Hz, 1H), 4.57 – 4.40 (m, 4H), 4.30 – 4.17 (m, 3H), 4.10 – 4.03 (m, 1H), 3.09 (t, *J* = 6.6 Hz, 2H), 1.08 (s, 9H), 1.05 (s, 9H) 0.94 (s, 9H), 0.17 (s, 3H), 0.16 (s, 3H); **$^{13}$C NMR (101 MHz, $CDCl_3$) δ**: 170.0, 154.2, 151.2, 150.2, 149.9, 147.0, 145.5, 141.4, 129.9, 123.8, 121.1, 92.5, 76.0, 75.7, 74.9, 67.9, 42.2, 35.0, 27.6, 27.2, 26.0, 22.9, 20.5, 18.5, -4.1, -4.9; **HRMS (ESI)**: calculated for $C_{35}H_{54}N_7O_9Si_2^+$: m/z = 772.3522 $[M+H]^+$; found: m/z = 772.3504 $[M+H]^+$.

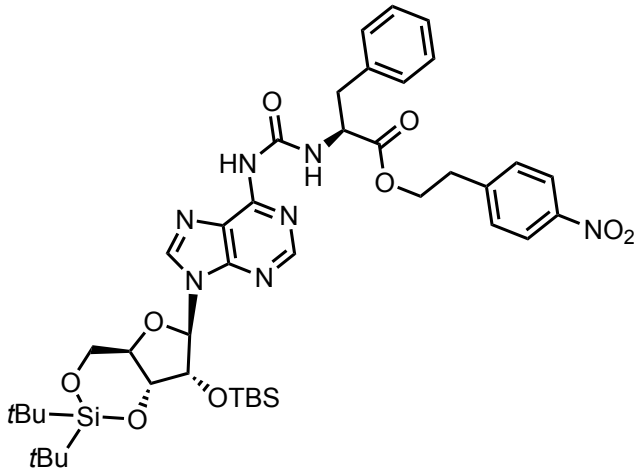
**Compound 29**



Eluent: Hex/EtOAc (2/1, v/v).

**Yield**: 87%; **IR**: $\tilde{\nu}$ = 3229 (w), 2953 (w), 2929 (w), 2857 (w), 1735 (s), 1693 (s), 1607 (s), 1589 (s), 1517 (vs), 1469 (s), 1391 (w), 1310 (vs), 1292 (w), 1251 (w), 1210 (w), 835 (s) $cm^{-1}$; **$^1$H NMR (400 MHz, $CDCl_3$) δ**: 10.28 (s, 1H), 8.42 (s, 1H), 8.22 – 8.12 (m, 1H), 8.07 (d, *J* = 8.6 Hz, 2H), 7.96 (d, *J* = 8.6 Hz, 2H), 7.37 – 7.30 (m, 4H), 6.00 (s, 1H), 4.93 – 4.89 (m, 1H), 4.64 (d, *J* = 4.6 Hz, 1H), 4.51 (ddd, *J* = 9.2, 4.9, 2.7 Hz, 2H), 4.46 – 4.40 (m, 2H), 4.39 – 4.22 (m, 3H), 4.09 – 4.05 (m, 1H), 3.08 – 2.94 (m, 6H), 1.07 (s, 9H), 1.05 (s, 9H), 0.95 (s, 9H), 0.19 (s, 3H), 0.17 (s, 3H); **$^{13}$C NMR (101 MHz, $CDCl_3$) δ**: 179.8, 170.7, 153.7, 149.8, 146.9, 146.8, 145.5, 145.4, 129.8, 123.8, 123.6, 120.9, 92.6, 75.9, 75.7, 74.9, 67.9, 65.0, 64.5, 49.7, 36.5, 34.9, 34.8, 27.6, 27.1, 26.0, 22.8, 20.5, 18.4, -4.2, -4.9; **HRMS (ESI)**: calculated for $C_{45}H_{63}N_8O_{13}Si_2^+$: m/z = 979.4053 $[M+H]^+$; found: m/z = 979.4056.

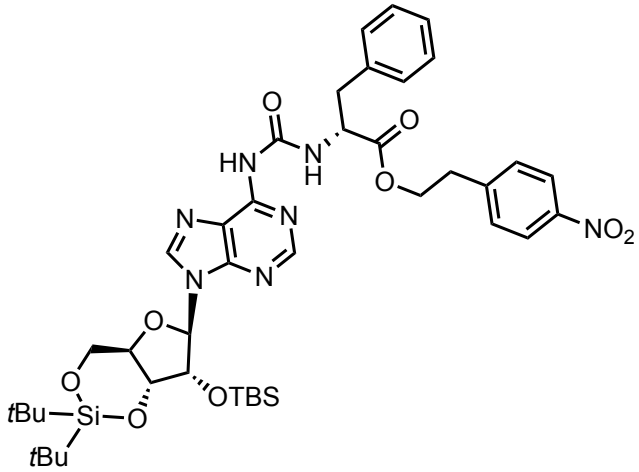
**Compound 30a**



**Yield**: 68%; **IR**: $\tilde{\nu}$ = 3190 (w), 2933 (w), 2858 (w), 1742 (w), 1702 (vs), 1612 (s), 1587 (w), 1521 (vs), 1469 (vs), 1345 (vs), 1253 (s), 1057 (s), 1000 (w), 828 (vs) $cm^{-1}$; **$^1$H NMR (400 MHz, $CD_2Cl_2$) δ**: 10.00 (d, *J* = 7.5 Hz, 1H), 8.94 (s, 1H), 8.37 (d, *J* = 1.2 Hz, 2H), 8.00 (d, *J* =

8.7 Hz, 2H), 7.39 – 7.26 (m, 5H), 7.21 – 7.17 (m, 2H), 6.02 (s, 1H), 4.89 – 4.76 (m, 1H), 4.60 (d, *J* = 4.6 Hz, 1H), 4.54 – 4.46 (m, 2H), 4.40 (td, *J* = 6.5 Hz, 1.7 Hz, 2H), 4.31 – 4.22 (m, 1H), 4.16 – 4.06 (m, 1H), 3.18 (d, *J* = 6.8 Hz, 2H), 3.03 (t, *J* = 6.5 Hz, 2H), 1.10 (s, 9H), 1.06 (s, 9H), 0.96 (s, 9H), 0.20 (s, 3H), 0.18 (s, 3H); **$^{13}$C NMR (101 MHz, $CD_2Cl_2$) δ**: 171.5, 153.8, 150.7, 150.2, 149.8, 146.7, 145.9, 142.2, 136.4, 129.8, 129.5, 128.5, 127.1, 123.4, 120.8, 92.2, 75.8, 75.7, 74.8, 67.7, 64.6, 54.9, 37.8, 34.7, 27.3, 26.9, 25.7, 22.6, 20.2, 18.2, -4.6, -5.2; **HRMS (ESI)**: calculated for $C_{42}H_{60}N_7O_9Si_2^+$: m/z = 862.3986 $[M+H]^+$; found: m/z = 862.3995 $[M+H]^+$.

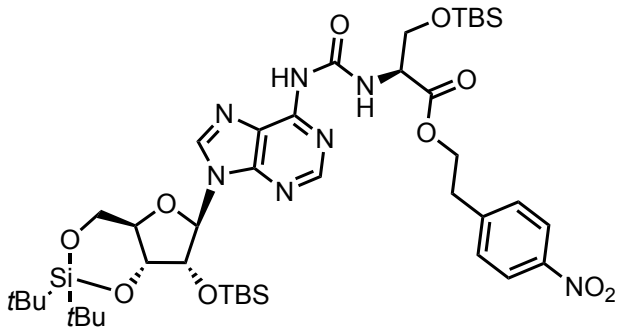
**Compound 30b**




Eluent: Hex/EtOAc (4/1, v/v).

**Yield**: 71%; **IR**: $\tilde{\nu}$ = 3192 (w), 2933 (w), 2858 (w), 1740 (w), 1700 (vs), 1611 (s), 1520 (vs), 1466 (vs), 1345 (vs), 1252 (s), 1166 (w), 1139 (w), 1054 (vs), 998 (s), 893 (s), 826 (vs), 736 (vs) $cm^{-1}$; **$^1$H NMR (400 MHz, $CD_2Cl_2$) δ**: 10.01 (d, *J* = 7.6 Hz, 1H), 8.96 (s, 1H), 8.37 (s, 2H), 8.00 (d, *J* = 8.7 Hz, 1H), 7.37 – 7.22 (m, 5H), 7.22 – 7.14 (m, 2H), 6.03 (s, 1H), 4.90 – 4.81 (m, 1H), 4.61 (d, *J* = 4.5 Hz, 1H), 4.54 – 4.45 (m, 2H), 4.39 (t, *J* = 6.4 Hz, 2H), 4.32 – 4.21 (m, 1H), 4.16 – 4.05 (m, 1H), 3.19 (d, *J* = 6.2 Hz, 2H), 3.02 (t, *J* = 6.4 Hz, 2H), 1.09 (s, 9H), 1.06 (s, 9H), 0.96 (s, 9H), 0.20 (s, 3H), 0.18 (s, 3H); **$^{13}$C NMR (101 MHz, $CD_2Cl_2$) δ**: 171.4, 153.6, 150.8, 150.2, 149.8, 146.7, 145.9, 141.8, 136.4, 129.8, 129.5, 128.5, 127.1, 123.4, 120.8, 92.2, 75.9, 75.7, 74.8, 67.7, 64.6, 54.9, 37.9, 34.7, 27.3, 26.8, 25.7, 22.6, 20.2, 18.2, -4.6, -5.3.; **HRMS (ESI)**: calculated for $C_{42}H_{60}N_7O_9Si_2^+$: m/z = 862.3986 $[M+H]^+$; found: m/z = 862.3996 $[M+H]^+$.

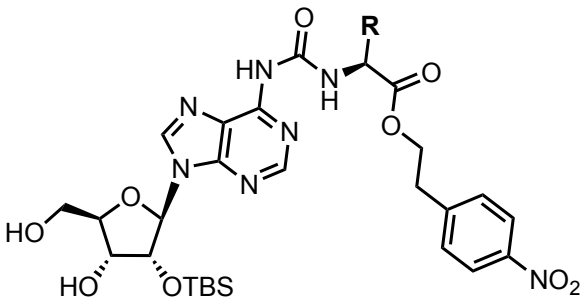
**Compound 31**




Eluent: Hex/EtOAc (1/1, v/v).

**Yield**: 85%; **IR**: $\tilde{\nu}$ = 3238 (w), 2931 (s), 2859 (s), 1737 (s), 1701 (vs), 1610 (s), 1520 (vs), 1470 (s), 1345 (s), 1251 (s), 1136 (w), 1057 (s), 998 (w), 899 (w), 840 (s), 778 (s) $cm^{-1}$; **$^1$H NMR (400 MHz, $CDCl_3$) δ**: 10.18 (d, *J* = 8.3 Hz, 1H), 8.61 (s, 1H), 8.44 (s, 1H), 8.19 (s, 1H), 8.02 (d, *J* = 8.6 Hz, 2H), 7.35 (d, *J* = 8.7 Hz, 2H), 5.99 (s, 1H), 4.72 (dt, *J* = 8.4, 2.8 Hz, 1H), 4.61 (d, *J* = 4.6 Hz, 1H), 4.50 (td, *J* = 9.8, 4.9 Hz, 2H), 4.43 (t, *J* = 6.5 Hz, 2H), 4.24 (td, *J* = 10.0, 5.0 Hz, 1H), 4.14 (dd, *J* = 10.1, 2.7 Hz, 1H), 4.07 (dd, *J* = 10.5, 9.1 Hz, 1H), 3.91 (dd, *J* = 10.1, 3.1 Hz, 1H), 3.06 (t, *J* = 6.5 Hz, 2H), 1.08 (s, 9H), 1.05 (s, 9H), 0.94 (s, 9H), 0.88 (s, 10H), 0.18 (s, 3H), 0.16 (s, 3H); **$^{13}$C NMR (101 MHz, $CDCl_3$) δ**: 170.6, 153.9, 151.2, 150.3, 149.8, 146.9, 145.6, 141.6, 129.8, 123.7, 121.1, 92.5, 75.9, 75.7, 74.9, 67.9, 64.8, 64.6, 55.7, 34.9, 27.6, 27.1, 26.0, 25.7, 22.8, 20.5, 18.4, 18.2, -4.2, -4.8, -5.3, -5.6; **HRMS (ESI)**: calculated for $C_{42}H_{70}N_7O_{10}Si_3^+$: m/z = 916.4492 $[M+H]^+$; found: m/z = 916.4501 $[M+H]^+$.

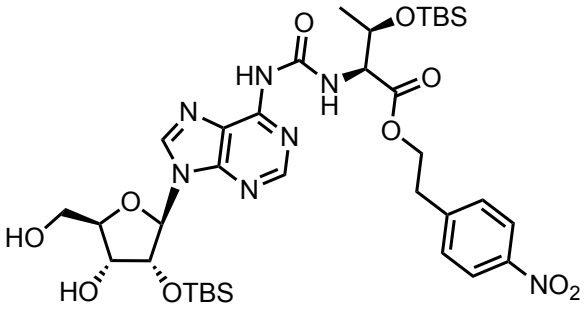
**General procedure for deprotection 3'-5'-silyl protecting group:**




The modified adenosine (0.86 mmol) was dissolved in $CH_2Cl_2$ under $N_2$ atmosphere and transferred into a plastic flask. Pyridine (1 ml) was added and the solution was cooled in an ice-bath. Then Py*$(HF)_n$ (140 µl) was added and the mixture was stirred at 0 °C for 2 h. The reaction was quenched with sat. $NaHCO_3$ and extracted with $CH_2Cl_2$. Organic phase was washed with

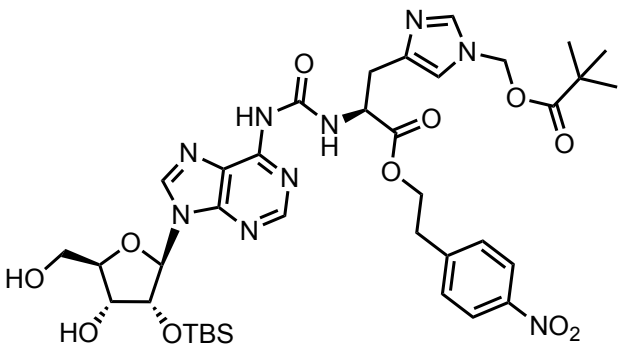
water and dried over $Na_2SO_4$. The solvents were removed in vacuo. The crude product was purified by flash chromatography eluting with $CH_2Cl_2$/MeOH (9/1, v/v) to afford the product as a colourless foam.

**Compound 32**



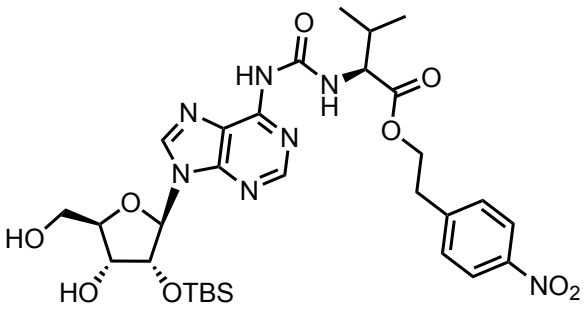

**Yield**: 95%; **IR**: $\tilde{\nu}$ = 3244 (w), 2952 (w), 2929 (w), 2856 (w), 1736 (w), 1695 (s), 1610 (s), 1588 (s), 1520 (vs), 1469 (s), 1345 (vs), 1313 (w), 1250 (vs), 1129 (w), 1093 (s), 835 (vs), 760 (vs) $cm^{-1}$; **$^1$H NMR (400 MHz, $CDCl_3$) δ**: 9.90 (d, *J* = 9.1 Hz, 1H), 8.50 (s, 1H), 8.46 (s, 1H), 8.10 – 8.08 (m, 3H), 7.37 (d, *J* = 8.6 Hz, 2H), 5.85 (d, *J* = 7.0 Hz, 1H), 5.10 (dd, *J* = 7.0, 4.7 Hz, 1H), 4.59 (dd, *J* = 9.1, 1.5 Hz, 1H), 4.53 – 4.41 (m, 2H), 4.41 – 4.34 (m, 2H), 4.34 – 4.26 (m, 1H), 3.98 (dd, *J* = 13.0, 1.5 Hz, 1H), 3.78 (dd, *J* = 13.0, 1.5 Hz, 1H), 3.07 (t, *J* = 6.7 Hz, 2H), 1.24 (d, *J* = 6.7 Hz, 3H), 0.89 (s, 9H), 0.81 (s, 9H), 0.05 (s, 3H), -0.06 (s, 3H), -0.14 (s, 3H), -0.34 (s, 3H); **$^{13}$C NMR (101 MHz, $CDCl_3$) δ**: 170.9, 154.0, 151.3, 150.9, 149.3, 147.1, 145.6, 143.0, 130.0, 123.9, 91.5, 87.7, 74.9, 72.7, 68.8, 65.13, 63.3, 59.8, 35.0, 25.7, 21.3, 18.1, 18.0, -4.0, -5.0, -5.1, -5.2; **HRMS (ESI)**: calculated for $C_{35}H_{56}N_7O_{10}Si_2^+$: m/z = 790.3622 $[M+H]^+$; found: m/z = 790.3612 $[M+H]^+$.

**Compound 33**



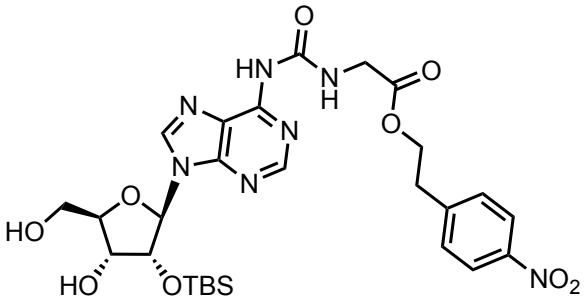
**Yield**: 75%; **IR**: $\tilde{\nu}$ = 3854 (w), 3745 (w), 3650 (w), 3230 (w), 2930 (w), 2857 (w), 2361 (w), 2341 (w), 1740 (s), 1699 (vs), 1611 (w), 1587 (w), 1520 (vs), 1472 (s), 1395 (w), 1345 (vs), 1253 (w), 1119 (vs), 1091 (w), 1058 (w), 1030 (w), 983 (w), 914 (w), 856 (vs), 779 (vs), 747(w), 670 (w) $cm^{-1}$; **$^1$H NMR (400 MHz, $CDCl_3$) δ**: 10.05 – 9.98 (m, 1H), 8.50 (d, *J* = 3.1 Hz, 1H), 8.18 – 8.10 (m, 3H), 8.01 (d, *J* = 9.1 Hz, 1H), 7.60 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.44 – 7.37 (m, 2H), 6.84 (d, *J* = 1.4 Hz, 1H), 5.99 – 5.93 (m, 1H), 5.81 (dd, *J* = 7.3, 5.4 Hz, 1H), 5.77 – 5.71 (m, 2H), 5.08 (dt, *J* = 7.3, 5.1 Hz, 1H), 4.90 (dt, *J* = 7.2, 5.4 Hz, 1H), 4.42 (q, *J* = 6.3 Hz, 2H), 4.39 – 4.34 (m, 2H), 3.98 – 3.92 (m, 1H), 3.82 – 3.72 (m, 1H), 3.23 – 3.13 (m, 2H), 3.08 (dt, *J* = 13.8, 6.6 Hz, 2H), 2.83 (s, 1H), 1.09 (s, 9H), 0.80 (s, 9H), -0.18 (s, 3H), -0.40 (s, 3H); **$^{13}$C NMR (101 MHz, $CDCl_3$) δ**: 177.8, 171.8, 153.2, 151.1, 150.9, 149.3, 147.0, 145.8, 143.0, 138.2, 138.1, 130.0, 123.9, 123.1, 117.4, 91.4, 87.8, 74.7, 73.0, 67.7, 65.0, 63.5, 53.5, 38.8, 35.0, 30.6, 26.9, 25.7, 18.0, -5.1, -5.2; **HRMS (ESI)**: calculated for $C_{37}H_{52}N_9O_{11}Si^+$: m/z = 826.3550 $[M+H]^+$; found: m/z = 826.3559 $[M+H]^+$.

**Compound 34**



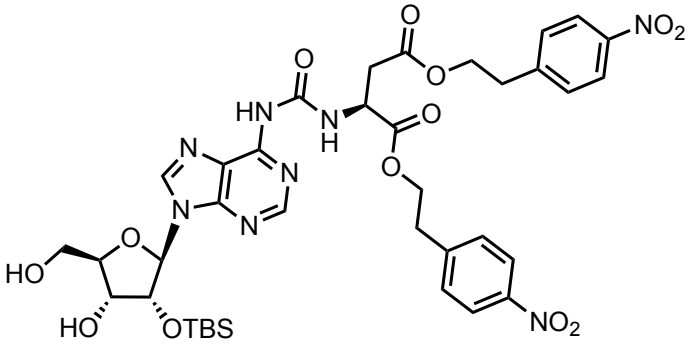

**Yield**: 95%; **IR**: $\tilde{\nu}$ = 3245 (w), 2930 (w), 2857 (w), 1743 (s), 1695 (vs), 1590 (s), 1518 (vs), 1471 (s), 1344 (vs), 1252 (s), 1212 (w), 1188 (s), 1130 (w), 1085 (s), 836 (vs) $cm^{-1}$; **$^1$H NMR (400 MHz, Acetone-$d_6$) δ**: 10.01 (d, *J* = 8.4 Hz, 1H), 8.50 (s, 1H), 8.17 (s, 1H), 8.07 (d, *J* = 8.3 Hz, 2H), 7.28 (d, *J* = 8.3 Hz, 2H), 5.98 (s, 1H), 4.61 (d, *J* = 4.6 Hz, 1H), 4.56 – 4.38 (m, 6H), 4.20-4.29 (m, 1H), 4.07 (dd, *J* = 10.5, 9.1 Hz, 1H), 3.09 (t, *J* = 6.5 Hz, 2H), 1.00 (d, *J* = 6.5 Hz, 3H), 0.96 (d, *J* = 6.5 Hz, 3H), 0.95 (s, 9H), 0.18 (s, 3H), 0.16 (s, 3H); **$^{13}$C NMR (101 MHz, $CDCl_3$) δ**: 172.2, 154.4, 151.6, 149.5, 147.0, 145.5, 143.3, 136.5, 129.9, 123.7, 122.0, 91.2, 87.6, 74.7, 72.8, 64.7, 63.4, 58.7, 35.0, 30.9, 25.6, 19.4, 17.9, -5.2, -5.3; **HRMS (ESI)**: calculated for $C_{30}H_{44}N_7O_9Si^+$: m/z = 674.2970 $[M+H]^+$; found: m/z = 674.2974 $[M+H]^+$.

**Compound 35**




**Yield**: 97%; **IR**: $\tilde{\nu}$ = 3250 (w), 2932 (w), 2859 (w), 1740 (s), 1680 (vs), 1595 (s), 1520 (vs), 1470 (s), 1340 (vs), 1254 (s), 1213 (w), 1168 (s), 1130 (w), 1085 (s), 836 (vs) $cm^{-1}$; **$^1$H NMR (400 MHz, $CDCl_3$) δ**: 9.92 (t, *J* = 5.7 Hz, 1H), 8.92 (br. s, 1H), 8.54 (s, 1H), 8.25 (s, 1H), 8.13 (d, *J* = 8.7 Hz, 2H), 7.39 (d, *J* = 8.7 Hz, 2H), 5.87 (d, *J* = 7.2 Hz, 1H), 5.07 (dd, *J* = 7.2, *J* = 4.7 Hz, 1H), 4.44 (t, *J* = 6.7 Hz, 2H), 4.37 (m, 2H), 4.20 (t, *J* = 5.2 Hz, 2H), 3.97 (d, *J* = 13.0 Hz, 1H), 3.77 (d, *J* = 13.0 Hz, 1H), 3.09 (t, *J* = 6.7 Hz, 2H), 2.94 (br. s, 1H), 0.78 (s, 9H), -0.19 (s, 3H), -0.38 (s, 3H); **$^{13}$C NMR (101 MHz, $CDCl_3$) δ**: 169.9, 154.0, 150.8, 149.5, 147.0, 145.4, 143.6, 129.9, 123.9, 122.0, 91.2, 87.6, 74.8, 72.8, 64.9, 63.3, 42.2, 34.9, 25.6, 17.9, -5.2; **HRMS (ESI)**: calculated for $C_{27}H_{37}N_7O_9Si^+$: m/z = 632.2495 $[M + H]^+$; found m/z = 632.2492.

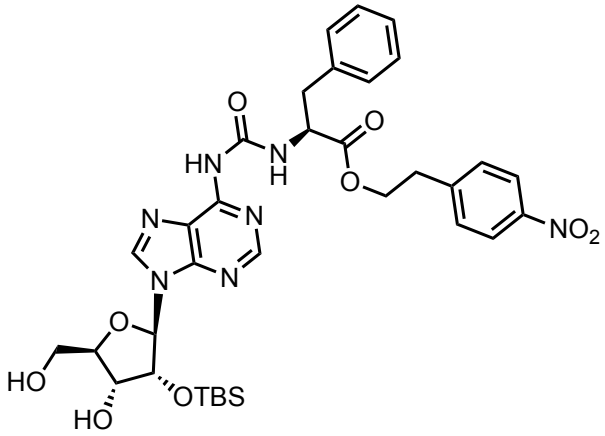
**Compound 36**




**Yield**: 98%; **IR**: $\tilde{\nu}$ = 3229 (w), 2953 (w), 2929 (w), 2857 (w), 1735 (s), 1693 (s), 1607 (s), 1589 (s), 1517 (vs), 1469 (s), 1391 (w), 1310 (vs), 1292 (w), 1251 (w), 1210 (w), 835 (s) $cm^{-1}$; **$^1$H NMR (400 MHz, Acetone-$d_6$) δ**: 10.30 (d, *J* = 7.9 Hz, 1H), 9.41 (s, 1H), 8.77 (s, 1H), 8.50 (s, 1H), 8.10 (d, *J* = 8.8 Hz, 2H), 8.06 (d, *J* = 8.8 Hz, 2H), 7.54 (dd, *J* = 8.7, 7.4 Hz, 4H), 6.12 (d, *J* = 5.8 Hz, 1H), 5.07 (s, 1H), 5.00 – 4.95 (m, 1H), 4.90 (dt, *J* = 7.9, 5.3 Hz, 1H), 4.49 – 4.31 (m, 5H), 4.23 (q, *J* = 2.4 Hz, 1H), 4.06 (s, 1H), 3.92 (dd, *J* = 12.4, 2.1 Hz, 1H), 3.79 (d, *J* = 12.2 Hz, 1H), 3.10 (dt, *J* = 12.6, 6.4 Hz, 4H), 3.02 (d, *J* = 5.5 Hz, 2H), 0.79 (s, 9H), -0.08 (s, 3H), -0.21 (s,

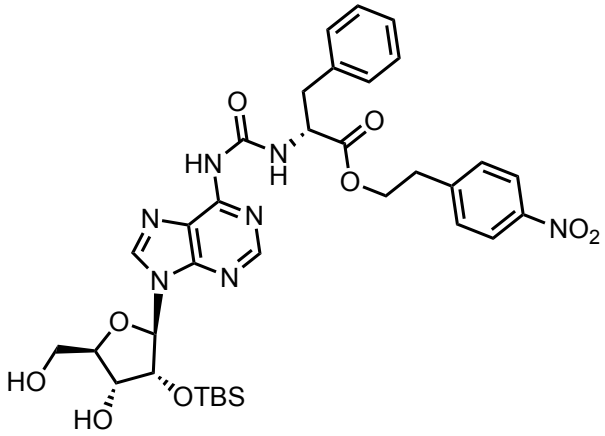
3H); **$^{13}$C NMR (101 MHz, Acetone-$d_6$) δ**: 171.3, 171.2, 154.2, 151.4, 150.9, 150.6, 147.6, 147.4, 147.2, 144.3, 136.6, 131.0, 124.1, 121.9, 90.6, 87.6, 76.8, 72.4, 65.8, 65.1, 62.9, 50.6, 37.1, 35.2, 27.2, 26.0, 18.6, -4.9, -5.1; **HRMS (ESI)**: calculated for $C_{37}H_{47}N_8O_{13}Si^+$: m/z = 839.3032 $[M+H]^+$; found: m/z = 839.3041 $[M+H]^+$.

**Compound 37a**



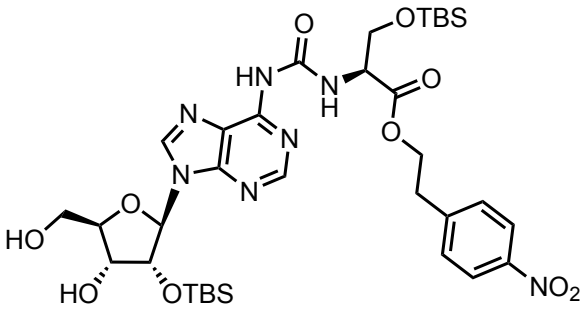

**Yield**: 80%; **IR**: $\tilde{\nu}$ = 3240 (w), 2929 (w), 2857 (w), 1742 (w), 1699 (vs), 1613 (s), 1520 (vs), 1471 (s), 1345 (vs), 1255 (w), 839 (s) $cm^{-1}$; **$^1$H NMR (400 MHz, $CD_2Cl_2$) δ**: 9.83 (d, *J* = 7.4 Hz, 1H), 8.63 (s, 1H), 8.40 (s, 1H), 8.18 (s, 1H), 8.10 (d, *J* = 8.7 Hz, 2H), 7.38 (d, *J* = 8.7 Hz, 2H), 7.33 – 7.21 (m, 2H), 7.19 – 7.14 (m, 2H), 5.87 (d, *J* = 7.2 Hz, 1H), 5.64 (dd, *J* = 11.6 Hz, *J* = 2.3 Hz, 1H), 5.07 (dd, *J* = 7.2 Hz, *J* = 4.7 Hz, 1H), 4.87 – 4.80 (m, 1H), 4.45 – 4.32 (m, 4H), 3.93 (d, *J* = 12.9 Hz, 1H), 3.79 – 3.69 (m, 1H), 3.17 (d, *J* = 6.2 Hz, 2H), 3.05 (t, *J* = 6.6 Hz, 2H), 2.93 (s, 1H), 0.79 (s, 9H), -0.19 (s, 3H), -0.38 (s, 3H); **$^{13}$C NMR (101 MHz, $CD_2Cl_2$) δ**: 171.4, 153.1, 150.7, 150.5, 149.8, 149.3, 146.8, 145.8, 143.3, 136.3, 129.8, 129.4, 128.3, 127.2, 123.5, 91.0, 87.6, 74.8, 72.7, 64.7, 63.1, 54.9, 37.8, 34.7, 25.3, 17.7, -5.6, -5.7; **HRMS (ESI)**: calculated for $C_{34}H_{44}N_7O_9Si^+$: m/z = 722.2965 $[M+H]^+$; found: m/z = 722.2971 $[M+H]^+$.

**Compound 37b**



**Yield**: 78%; **IR**: $\tilde{\nu}$ = 3229 (w), 2930 (w), 2858 (w), 1740 w), 1697 (vs), 1612 (s), 1519 (vs), 1470 (s), 1345 (vs), 1254 (s), 1216 (w), 838 (vs), 781 (s), 736 (vs), 700 (s) $cm^{-1}$; **$^1$H NMR (400 MHz, $CD_2Cl_2$) δ**: 9.79 (br. s, 1H), 8.58 (br. s, 1H), 8.39 (s, 1H), 8.17 (t, *J* = 4.0 Hz, 1H), 8.05 (d, *J* = 8.7 Hz, 2H), 7.35 (d, *J* = 8.7 Hz, 2H), 7.32 – 7.23 (m, 2H), 7.21-7.15 (m, 2H), 5.87 (d, *J* = 7.1 Hz, 1H), 5.61 (dd, *J* = 11.6 Hz, 2.4 Hz, 1H), 5.05 (dd, *J* = 7.2 Hz, 4.7 Hz, 1H), 4.82 (q, *J* = 6.2 Hz, 1H), 4.46 – 4.30 (m, 4H), 3.93 (d, *J* = 12.9 Hz, 1H), 3.79 – 3.68 (m, 1H), 3.17 (d, *J* = 6.2 Hz, 2H), 3.03 (t, *J* = 6.5 Hz, 3H), 2.88 (s, 1H), 0.80 (s, 9H), -0.17 (s, 3H), -0.36 (s, 3H); **$^{13}$C NMR (101 MHz, $CD_2Cl_2$) δ**: 171.4, 153.1, 150.7, 150.5, 149.8, 149.3, 146.8, 145.8, 143.3, 136.3, 129.8, 129.4, 128.5, 128.3, 127.2, 123.5, 91.0, 87.6, 74.8, 72.7, 64.7, 63.1, 54.9, 37.8, 34.7, 25.3, 17.7, -5.6, -5.7; **HRMS (ESI)**: calculated for $C_{34}H_{43}N_7O_9SiNa^+$: m/z = 744.2784 $[M+Na]^+$; found: m/z = 744.2776 $[M+Na]^+$.

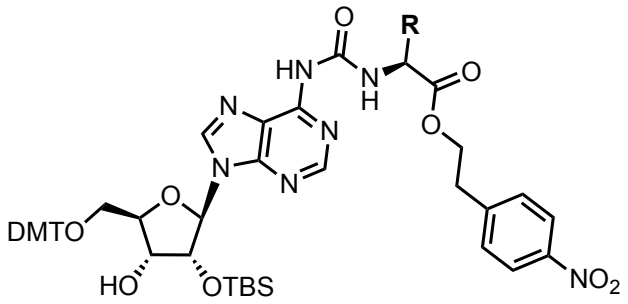
**Compound 38**



**Yield**: 96%; **IR**: $\tilde{\nu}$ = 3240 (w), 2950 (w), 2927 (w), 2856 (w), 1737 (w), 1695 (s), 1611 (s), 1589 (s), 1520 (vs), 1469 (s), 1346 (vs), 1313 (w), 1250 (vs), 1130 (w), 1093 (s), 835 (vs), 780 (vs) $cm^{-1}$; **$^1$H NMR (400 MHz, Acetone-$d_6$) δ**: 10.11 (d, *J* = 8.2 Hz, 1H), 9.13 (s, 1H), 8.72 (s, 1H), 8.52 (s, 1H), 8.11 (d, *J* = 8.7 Hz, 2H), 7.59 (d, *J* = 8.7 Hz, 2H), 6.13 (d, *J* = 6.1 Hz, 1H), 5.07 (dd, *J* = 8.7, 3.8 Hz, 1H), 4.99 (dd, *J* = 6.1, 4.7 Hz, 1H), 4.66 (dt, *J* = 8.3, 3.0 Hz, 1H), 4.45 (td, *J*

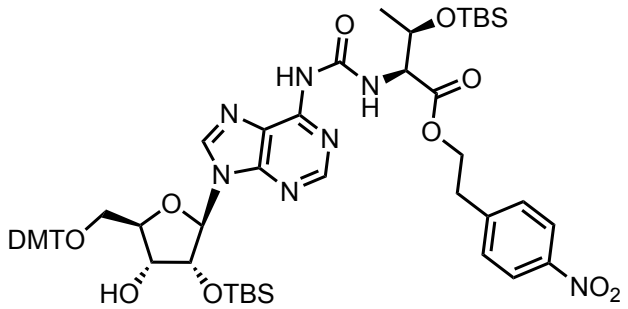
= 6.5, 1.2 Hz, 2H), 4.39 (td, *J* = 4.3, 2.5 Hz, 1H), 4.22 (p, *J* = 2.8 Hz, 1H), 4.15 (dd, *J* = 10.3, 2.9 Hz, 1H), 4.04 (d, *J* = 3.8 Hz, 1H), 3.98 (dd, *J* = 10.2, 3.2 Hz, 1H), 3.94 – 3.87 (m, 1H), 3.78 (ddd, *J* = 12.4, 8.5, 2.5 Hz, 1H), 3.16 (t, *J* = 6.3 Hz, 2H), 0.88 (s, 9H), 0.79 (s, 9H), 0.07 (s, 3H), 0.02 (s, 3H), -0.08 (s, 3H), -0.23 (s, 3H); **$^{13}$C NMR (101 MHz, Acetone-*d*$_6$) δ**: 171.0, 154.1, 151.4, 151.0, 147.4, 144.1, 131.1, 124.2, 122.1, 90.5, 87.8, 76.8, 72.6, 65.7, 64.3, 63.0, 56.4, 35.3, 27.2, 26.1, 26.0, 18.7, 18.6, -4.9, -5.2, -5.3, -5.6; **HRMS (ESI)**: calculated for $C_{34}H_{54}N_7O_{10}Si_2Na^+$: m/z = 798.3290 $[M+Na]^+$; found: m/z = 798.3288 $[M+Na]^+$.

**General procedure for DMT protection:**




The 3'-5'-deprotected adenosine derivative (1 eq.) was dissolved in pyridine under $N_2$ atmosphere. DMT chloride (1.5 eq.) was added in two portions and the mixture was stirred at room temperature overnight. Then the volatiles were evaporated, and crude product was purified by flash chromatography eluting with $CH_2Cl_2$/MeOH (10/1/, v/v) with an addition of 0.1% of pyridine, unless otherwise specified, to afford the DMT protected derivative as white foam.

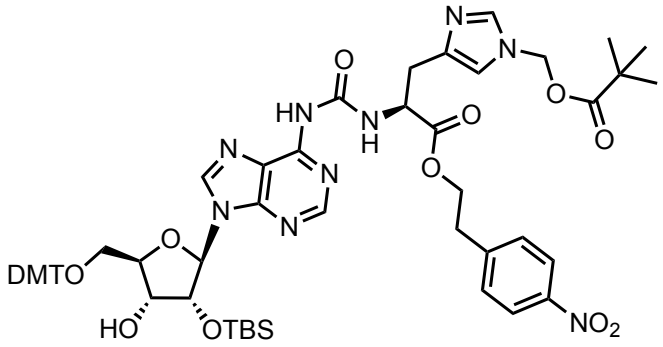
**Compound 39**




**Yield**: 90%; **IR**: $\tilde{\nu}$ = 3350 (w), 2930 (w), 2856 (w), 1729 (w), 1684 (s), 1608 (s), 1521 (vs), 1464 (s), 1345 (vs), 1248 (vs), 1174 (w), 1094 (w), 10033 (s), 827 (vs), 777 (vs) cm$^{-1}$; **$^1$H NMR (400 MHz, Acetone-*d*$_6$) δ**: 10.00 (d, *J* = 9.0 Hz, 1H), 8.95 (s, 1H), 8.55 (s, 1H), 8.40 (s, 1H), 7.98 (d, *J* = 8.7 Hz, 2H), 7.59 – 7.46 (m, 4H), 7.35 (dd, *J* = 9.0, 3.0 Hz, 4H), 7.28 – 7.13 (m, 4H), 6.83

(dd, *J* = 9.0, 3.0 Hz, 4H), 6.16 (d, *J* = 4.6 Hz, 1H), 5.16 (t, *J* = 4.6 Hz, 1H), 4.61 – 4.48 (m, 3H), 4.45 – 4.35 (m, 2H), 4.33 – 4.26 (m, 1H), 3.99 (d, *J* = 5.8 Hz, 1H), 3.75 (s, 6H), 3.51 – 3.44 (m, 2H), 3.12 (t, *J* = 6.2 Hz, 2H), 1.27 (d, *J* = 6.2 Hz, 3H), 0.91 (s, 9H), 0.85 (s, 9H), 0.09 (s, 3H), 0.06 (s, 3H), -0.05 (s, 6H); **$^{13}$C NMR (101 MHz, Acetone-*d*$_6$) δ**: 171.6, 159.6, 154.8, 151.5, 151.3, 147.5, 146.1, 136.7, 131.1, 130.9, 129.7, 129.0, 128.5, 127.5, 126.1, 124.1, 121.9, 113.8, 90.2, 87.1, 84.8, 76.3, 71.9, 69.6, 65.6, 64.4, 60.3, 55.5, 35.3, 26.1, 25.9, 21.5, 18.7, 18.5, -4.1, -4.6, -4.8, -5.2; **HRMS (ESI)**: calculated for $C_{56}H_{74}N_7O_{12}Si_2^+$: m/z = 1092.4929 $[M+H]^+$; found: m/z = 1092.4937 $[M+H]^+$.

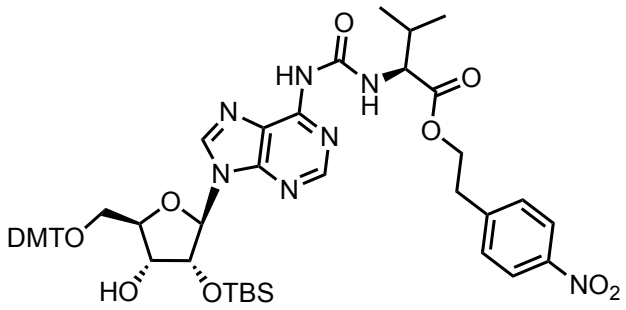
**Compound 40**




Eluent: 10% $CH_2Cl_2$ in EtOAc to pure EtOAc containing 0.1% of pyridine.

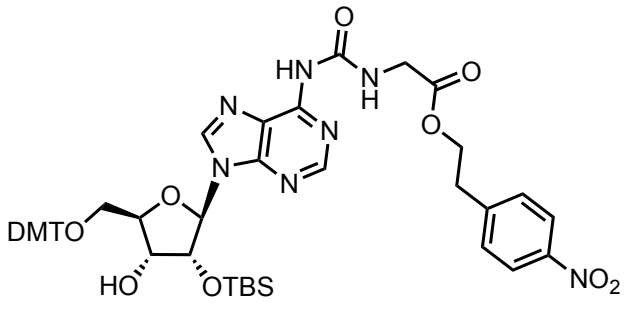
**Yield**: 85%; **IR**: $\tilde{\nu}$ = 3854 (w), 3746 (w), 3650 (w), 3630 (w), 2931 (w), 2361 (w), 2341 (w), 1740 (s), 1700 (vs), 1654 (w), 1609 (s), 1587 (w), 1559 (w), 1508 (vs), 1472 (s), 1396 (w), 1345 (s), 1300 (w), 1250 (vs), 1176 (s), 1118 (vs), 1032 (vs), 986 (w), 912 (w), 835 (vs), 781 (s), 751 (w), 700 (w) $cm^{-1}$; **$^1$H NMR (400 MHz, Acetone-*d*$_6$) δ**: 10.11 – 10.06 (m, 1H), 8.61 – 8.55 (m, 1H), 8.47 (s, 1H), 8.45 (s, 1H), 8.13 – 8.05 (m, 2H), 7.71 (d, *J* = 1.4 Hz, 1H), 7.63 – 7.55 (m, 2H), 7.53 – 7.46 (m, 2H), 7.40 – 7.32 (m, 4H), 7.28 (td, *J* = 8.2, 7.7, 2.0 Hz, 2H), 7.25 – 7.18 (m, 1H), 7.06 (s, 1H), 6.88 – 6.81 (m, 4H), 6.13 (d, *J* = 4.4 Hz, 1H), 5.88 (s, 2H), 5.10 (t, *J* = 4.6 Hz, 1H), 4.75 (dq, *J* = 8.0, 4.2, 3.3 Hz, 1H), 4.56 – 4.51 (m, 1H), 4.47 – 4.36 (m, 2H), 4.30 – 4.25 (m, 1H), 4.03 – 3.93 (m, 1H), 3.77 (s, 3H), 3.76 (s, 3H), 3.50 – 3.40 (m, 2H), 3.16 – 3.11 (m, 2H), 3.12 – 3.04 (m, 2H), 1.05 (s, 9H), 0.86 (s, 9H), 0.06 (s, 3H), -0.04 (s, 3H); **$^{13}$C NMR (101 MHz, Acetone-*d*$_6$) δ**: 177.9, 172.1, 159.6, 153.9, 151.7, 151.3, 147.7, 147.6, 146.1, 143.3, 139.2, 138.8, 136.7, 131.1, 131.0, 130.0, 129.0, 128.6, 127.6, 124.6, 124.1, 118.2, 113.9, 90.1, 87.1, 84.7, 76.4, 71.9, 71.8, 68.8, 66.2, 64.4, 55.5, 39.2, 35.3, 31.0, 27.0, 26.1, 18.7, -4.6, -4.8; **HRMS (ESI)**: calculated for $C_{58}H_{70}N_9O_{13}Si^+$: m/z = 1128.4857 $[M+H]^+$; found: m/z = 1128.4885 $[M+H]^+$.

**Compound 41**




**Yield**: 70%; **IR**: $\tilde{\nu}$ = 2929 (w), 1735 (w), 1684 (w), 1569 (s), 1508 (vs), 1464 (s), 1344 (s), 1249 (vs), 1176 (w), 1015 (s), 800 (vs) 749 (s) $cm^{-1}$; **$^1$H NMR (400 MHz, Acetone-$d_6$) δ**: 10.02 (d, *J* = 9.0 Hz, 1H), 8.55 (s, 1H), 8.51 (s, 1H), 8.11 (d, *J* = 8.7 Hz, 2H), 7.59 (d, *J* = 8.7 Hz, 2H), 7.52 – 7.47 (m, 2H), 7.37 (dd, *J* = 9.0, 2.2 Hz, 4H), 7.30 – 7.13 (m, 4H), 6.86 – 6.82 (m, 4H), 6.16 (d, *J* = 4.6 Hz, 1H), 5.16 (t, *J* = 4.6 Hz, 1H), 4.57 – 4.39 (m, 5H), 4.30 (q, *J* = 4.6 Hz, 1H), 4.00 (d, *J* = 5.8 Hz, 1H), 3.76 (s, 6H), 3.47 (d, *J* = 4.2 Hz, 2H), 3.16 (t, *J* = 6.5 Hz, 2H), 2.31 – 2.30 (m, 1H), 0.99 (d, *J* = 6.5 Hz, 3H), 0.95 (d, *J* = 6.5 Hz, 3H), 0.85 (s, 9H), 0.06 (s, 3H), -0.04 (s, 3H); **$^{13}$C NMR (101 MHz, Acetone-$d_6$) δ**: 172.2, 159.5, 154.3, 151.6, 151.3, 147.4, 146.1, 143.5, 136.6, 131.0, 130.0, 128.9, 128.9, 127.5, 126.1, 124.2, 121.7, 113.8, 90.3, 87.0, 84.7, 76.4, 71.9, 65.2, 64.3, 59.5, 55.4, 35.3, 31.5, 26.1, 19.6, 18.7, 18.2, -4.6, -4.8; **HRMS (ESI)**: calculated for $C_{51}H_{62}N_7O_{11}Si^+$: m/z = 976.4277 $[M+H]^+$; found: m/z = 976.4287 $[M+H]^+$.

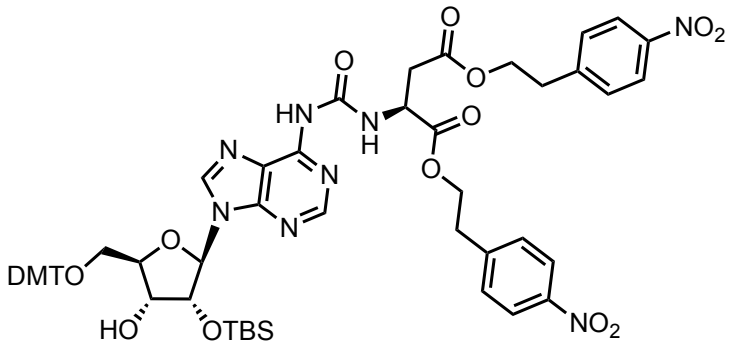
**Compound 42**




**Yield**: 85%; **IR**: $\tilde{\nu}$ = 2931 (w), 1748 (w), 1703 (s), 1609 (s), 1588 (w), 1509 (s), 1469 (s), 1345 (vs), 1250 (vs), 1177 (vs), 1035 (w), 835 (s) $cm^{-1}$; **$^1$H NMR (400 MHz, Acetone-$d_6$) δ**: 9.93 (t, *J* = 5.5 Hz, 1H), 9.05 (br. s, 1H), 8.58 (s, 1H), 8.46 (s, 1H), 8.11 (d, *J* = 8.7 Hz, 2H), 7.58 (d, *J* = 8.7 Hz, 2H), 7.54 – 7.47 (m, 2H), 7.41 – 7.33 (m, 4H), 7.31 – 7.23 (m, 2H), 7.23 – 7.16 (m, 1H), 6.88 – 6.78 (m, 4H), 6.16 (d, *J* = 4.4 Hz, 1H), 5.10 (dd, *J* = 4.7 Hz, 1H), 4.53 (t, *J* = 5.1 Hz, 1H), 4.44 (t, *J* = 6.4 Hz, 2H), 4.30 (dt, *J* = 4.4 Hz, 1H), 4.13 (d, *J* = 5.5 Hz, 2H), 4.00 (d, *J* = 5.7 Hz,

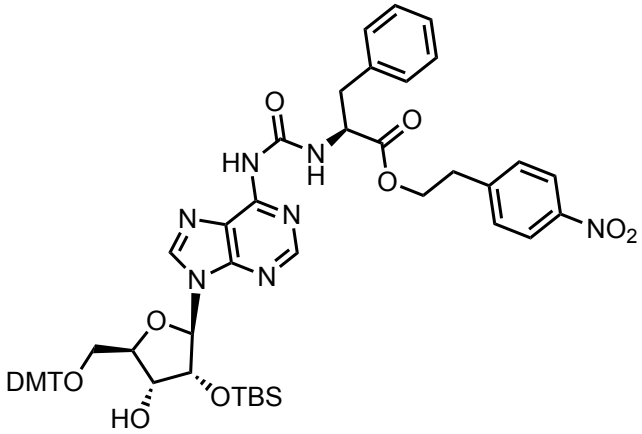
1H), 3.75 (s, 6H), 3.53 – 3.42 (m, 2H), 3.13 (t, *J* = 6.4 Hz, 2H), 0.85 (s, 9H), 0.05 (s, 3H), -0.05 (s, 3H); **$^{13}$C NMR (101 MHz, Acetone-*d*$_6$) δ**: 170.6, 159.6, 154.6, 151.7, 151.3, 151.2, 147.6, 147.4, 146.1, 143.6, 136.7, 131.1, 130.9, 129.1, 129.0, 128.6, 127.5, 124.2, 121.7, 113.8, 90.0, 87.1, 84.8, 76.4, 72.0, 65.2, 64.4, 55.5, 42.6, 35.3, 26.1, 18.7, -4.7, -4.8; **HRMS (ESI)**: calculated for $C_{48}H_{55}N_7O_{11}Si^+$: m/z = 934.3802 $[M + H]^+$; found: m/z = 934.3812 $[M + H]^+$.

**Compound 43**




**Yield**: 95%; **IR**: $\tilde{\nu}$ = 2930 (w), 1734 (s), 1698 (s), 1607 (s), 1509 (vs), 1466 (s), 1370 (vs), 1248 (s), 1174 (s), 1032 (s), 829 (vs), 699 (s) $cm^{-1}$; **$^1$H NMR (400 MHz, Acetone-*d*$_6$) δ**: 10.29 (d, *J* = 7.9 Hz, 1H), 9.18 (s, 1H), 8.60 (s, 1H), 8.42 (s, 1H), 8.10 – 8.04 (m, 4H), 7.58 – 7.51 (m, 4H), 7.39 – 7.36 (m, 4H), 7.30 – 7.25 (m, 2H), 7.21 – 7.18 (m, 2H), 6.86 – 6.82 (m, 5H), 6.17 (d, *J* = 4.2 Hz, 1H), 5.10 (t, *J* = 4.5 Hz, 1H), 4.85 (dt, *J* = 7.9, 5.2 Hz, 1H), 4.56 (q, *J* = 5.2 Hz, 1H), 4.46 – 4.28 (m, 5H), 4.02 (d, *J* = 5.9 Hz, 1H), 3.75 (d, *J* = 2.1 Hz, 6H), 3.53 – 3.44 (m, 2H), 3.13 – 3.06 (m, 4H), 3.00 – 2.96 (m, 2H), 0.86 (s, 9H), 0.07 (s, 3H), 0.03 (s, 3H); **$^{13}$C NMR (101 MHz, Acetone-*d*$_6$) δ**: 171.3, 171.2, 159.5, 154.2, 151.5, 150.6, 147.4, 147.2, 146.1, 143.6, 136.7, 131.0, 130.0, 129.0, 128.6, 127.5, 124.2, 113.8, 90.1, 87.0, 84.6, 76.4, 71.8, 65.7, 65.1, 64.3, 55.4, 50.6, 37.1, 35.2, 26.1, 18.6, -4.6, -4.8; **HRMS (ESI)**: calculated for $C_{58}H_{64}N_8O_{15}SiNa^+$: m/z = 1163.4158 $[M+Na]^+$; found: m/z = 1163.4159 $[M+Na]^+$.

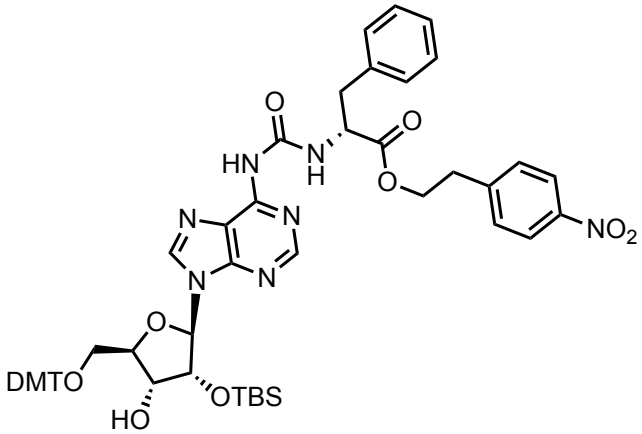
**Compound 44a**




Eluent: $CH_2Cl_2$/MeOH (20/1, v/v).

**Yield**: 82%; **IR**: $\tilde{\nu}$ = 3245 (w), 2952 (w), 2931 (w), 1741 (w), 1699 (s), 1608 (s), 1587 (w), 1519 (s), 1509 (s), 1469 (w), 1345 (s), 1249 (s), 1176 (s), 1034 (w), 834 (s), 783 (w), 735 (vs), 701 (vs) $cm^{-1}$; **$^1$H NMR (400 MHz, $CD_2Cl_2$) δ**: 9.83 (d, *J* = 7.5 Hz, 1H), 8.29 (s, 1H), 8.17 (s, 1H), 8.06 (d, *J* = 8.7 Hz, 2H), 8.00 (s, 1H), 7.46 (d, *J* = 6.8 Hz, 2H), 7.38 – 7.32 (m, 7H), 7.31 – 7.20 (m, 7H), 7.18 – 7.14 (m, 2H), 6.82 (d, *J* = 8.9 Hz, 4H), 6.02 (d, *J* = 5.0 Hz, 1H), 5.02 (t, *J* = 5.0 Hz, 1H), 4.80 (q, *J* = 6.3 Hz, 1H), 4.44 – 4.32 (m, 3H), 4.24 (q, *J* = 3.8 Hz, 1H), 3.77 (s, 6H), 3.48 (dd, *J* = 10.7 Hz, *J* = 3.2 Hz, 1H), 3.39 (dd, *J* = 10.7 Hz, *J* = 4.3 Hz, 1H), 3.16 (d, *J* = 6.3 Hz, 2H), 3.03 (t, *J* = 6.5 Hz, 2H), 2.67 (d, *J* = 4.7 Hz, 1H), 0.85 (s, 9H), 0.01 (s, 3H), -0.12 (s, 3H); **$^{13}$C NMR (101 MHz, $CD_2Cl_2$) δ**: 171.5, 153.3, 150.8, 150.6, 149.8, 149.4, 146.8, 145.8, 143.6, 136.2, 135.9, 129.9, 129.4, 128.5, 128.3, 127.2, 123.7, 123.6, 121.8, 91.0, 87.5, 74.8, 72.7, 64.8, 63.1, 54.8, 37.8, 34.7, 25.3, 17.7, -5.7; **HRMS (ESI)**: calculated for $C_{55}H_{62}N_7O_{11}Si^+$: m/z = 1024.4271 $[M+H]^+$; found: m/z = 1024.429 $[M+H]^+$.

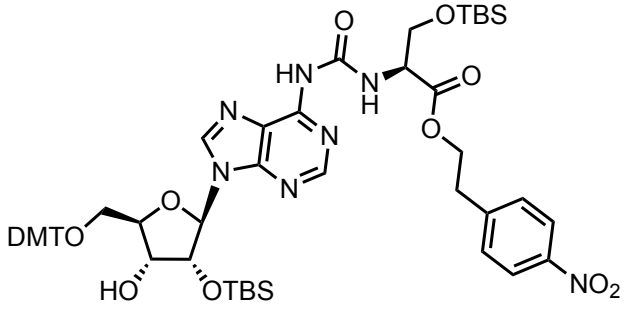
**Compound 44b**




Eluent: $CH_2Cl_2$/MeOH (20/1, v/v).

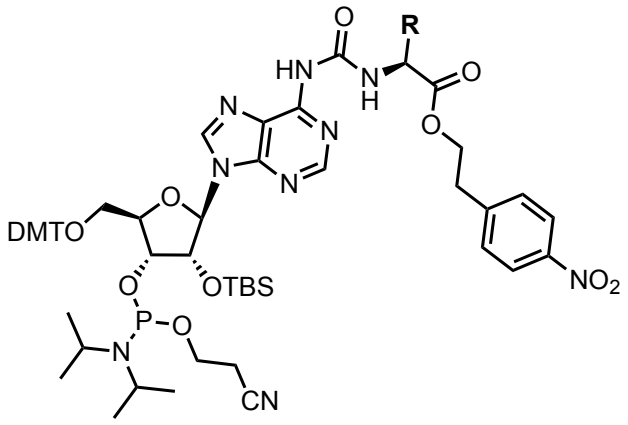
**Yield**: 85%; **IR**: $\tilde{\nu}$ = 3231 (w), 2930 (w), 2858 (w), 1741 (w), 1697 (s), 1612 (s), 1587 (w), 1518 (vs), 1470 (s), 1344 (vs), 1253 (w), 1180 (w), 1134 (w), 1085 (w), 836 (s), 780 (s), 734 (vs), 698 (vs) $cm^{-1}$; **$^1$H NMR (400 MHz, $CD_2Cl_2$) δ**: 9.83 (d, *J* = 7.5 Hz, 1H), 8.58 (br. s, 1H), 8.32 (s, 1H), 8.19 (s, 1H), 8.06 (d, *J* = 8.7 Hz, 2H), 7.99 (s, 1H), 7.46 (d, *J* = 6.9 Hz, 2H), 7.38 – 7.31 (m, 7H), 7.31 – 7.21 (m, 7H), 7.20 – 7.16 (m, 2H), 6.82 (d, *J* = 8.9 Hz, 4H), 6.05 (d, *J* = 4.7 Hz, 1H), 4.94 (t, *J* = 5.0 Hz, 1H), 4.81 (q, *J* = 6.3 Hz, 1H), 4.44 – 4.33 (m, 3H), 4.24 (q, *J* = 3.8 Hz, 1H), 3.77 (s, 6H), 3.48 (dd, *J* = 10.7 Hz, 3.1 Hz, 1H), 3.41 (dd, *J* = 10.7 Hz, 4.2 Hz, 1H), 3.16 (d, *J* = 6.9 Hz, 2H), 3.03 (t, *J* = 6.5 Hz, 2H), 2.66 (d, *J* = 5.0 Hz, 1H), 0.86 (s, 9H), 0.02 (s, 3H), -0.09 (s, 3H); **$^{13}$C NMR (101 MHz, $CD_2Cl_2$) δ**: 171.4, 153.4, 150.7, 150.5, 149.8, 149.4, 146.8, 145.9, 143.7, 136.3, 129.9, 129.5, 128.5, 128.3, 127.2, 123.5, 123.5, 121.8, 91.0, 87.5, 74.9, 72.7, 64.8, 63.1, 54.9, 37.8, 34.7, 25.3, 17.8, -5.6; **HRMS (ESI)**: calculated for $C_{55}H_{62}N_7O_{11}Si^+$: m/z = 1024.4271 $[M+H]^+$; found: m/z = 1024.4291 $[M+H]^+$.

**Compound 45**



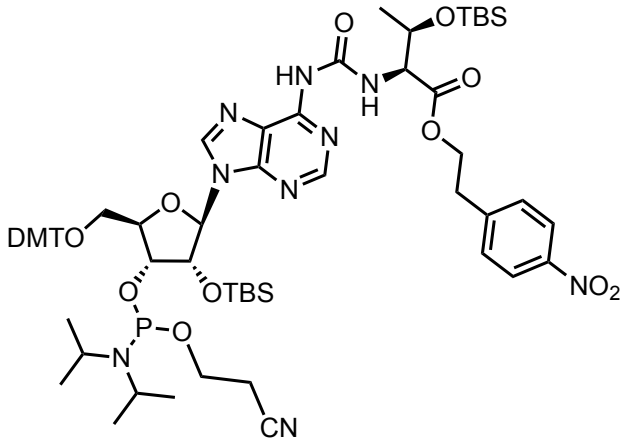

**Yield**: 90%; **IR**: $\tilde{\nu}$ = 2930 (w), 1740 (s), 1694 (s), 1607 (w), 1582 (w), 1519 (vs), 1465 (w), 1345 (s), 1249 (s), 1176 (w), 1110 (w), 1034 (w), 820 (vs), 778 (s), 699 (w) $cm^{-1}$; **$^1$H NMR (400 MHz, Acetone-*d*$_6$) δ**: 10.13 (d, *J* = 8.2 Hz, 1H), 8.99 (s, 1H), 8.58 (s, 1H), 8.44 (s, 1H), 8.09 (d, *J* = 8.7 Hz, 2H), 7.58 (d, *J* = 8.7 Hz, 2H), 7.51 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.39 (d, *J* = 2.5 Hz, 2H), 7.37 (d, *J* = 2.4 Hz, 2H), 7.32 – 7.18 (m, 4H), 6.87 – 6.83 (m, 4H), 6.18 (d, *J* = 4.7 Hz, 1H), 5.13 (t, *J* = 5.0 Hz, 1H), 4.62 (dt, *J* = 8.2, 2.8 Hz, 1H), 4.53 (q, *J* = 5.0 Hz, 1H), 4.45 (t, *J* = 6.3 Hz, 2H), 4.30 (td, *J* = 4.6, 3.4 Hz, 1H), 4.14 (dd, *J* = 10.2, 2.8 Hz, 1H), 3.96 (dd, *J* = 10.2, 2.8 Hz, 1H), 3.77 (s, 6H), 3.48 (qd, *J* = 10.5, 4.1 Hz, 2H), 3.16 (t, *J* = 6.3 Hz, 2H), 0.89 (s, 9H), 0.85 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H), 0.03 (s, 3H), -0.06 (s, 3H); **$^{13}$C NMR (101 MHz, Acetone-*d*$_6$) δ**: 170.0, 159.5, 154.1, 151.6, 150.6, 147.4, 146.1, 143.6, 136.7, 131.1, 130.9, 129.0, 128.6, 127.6, 124.6, 124.2, 121.8, 113.8, 89.9, 87.1, 84.9, 76.5, 72.0, 65.8, 64.3, 56.4, 55.4, 35.3, 27.2, 26.1, 18.7, 18.4, -4.6, -4.9, -5.3, -5.5; **HRMS (ESI)**: calculated for $C_{55}H_{71}N_7O_{12}Si_2Na^+$: m/z = 1100.4597 $[M+Na]^+$; found: m/z = 1100.4620 $[M+Na]^+$.

**General synthesis of RNA phosphoramidites**



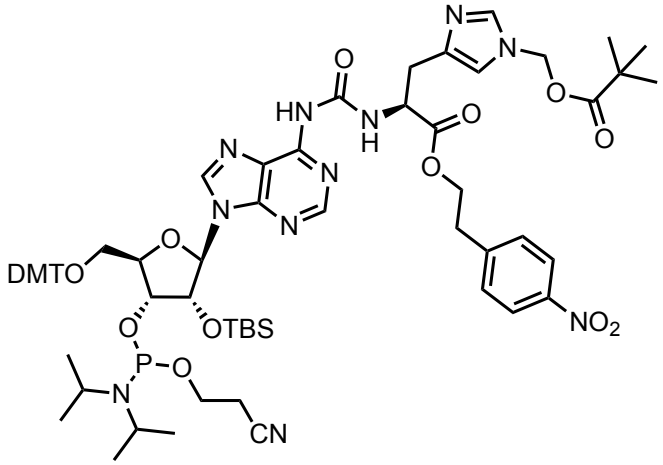

In an oven-dried flask under argon atmosphere, 5'-DMT protected compound (1 eq.) was dissolved in $CH_2Cl_2$ and cooled to 0 °C. Hünig's base (4 eq.) was added dropwise followed by the addition of 2-cyanoethyl *N,N*-diisopropylchlorophosphoramidite (2.5 eq.). The solution was stirred at room temperature for 2 h. The reaction was quenched by addition of sat. $NaHCO_3$ solution, and then extracted three times with $CH_2Cl_2$. The organic phase was dried over $Na_2SO_4$, filtered and concentrated in vacuo. The residue was purified by flash chromatography, eluting with Hex/EtOAc (1/1, v/v) containing 0.1% of pyridine, unless otherwise specified. The phosphoramidite was obtained as a mixture of diastereomers as white foam.

**Compound 46**




**Yield**: 85%; **$^{31}$P NMR (162 MHz, Acetone-$d_6$) δ**: 150.16, 148.45; **HRMS (ESI)**: calculated for $C_{65}H_{91}N_9O_{13}PSi_2^+$: m/z = 1292.6007 $[M+H]^+$; found: m/z = 1292.6033 $[M+H]^+$.

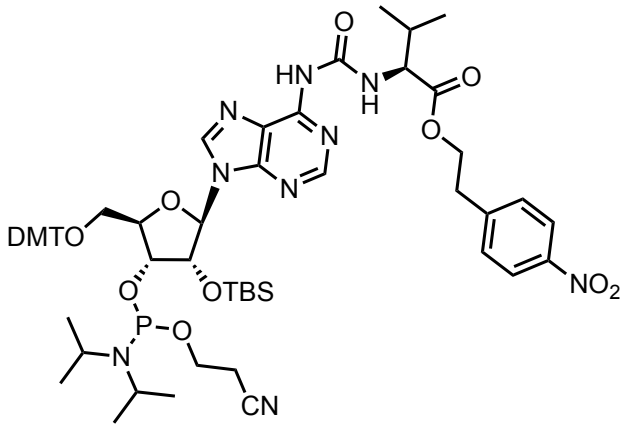
**Compound 47**



Eluent: 30% $CH_2Cl_2$ in EtOAc containing 0.1% of pyridine.

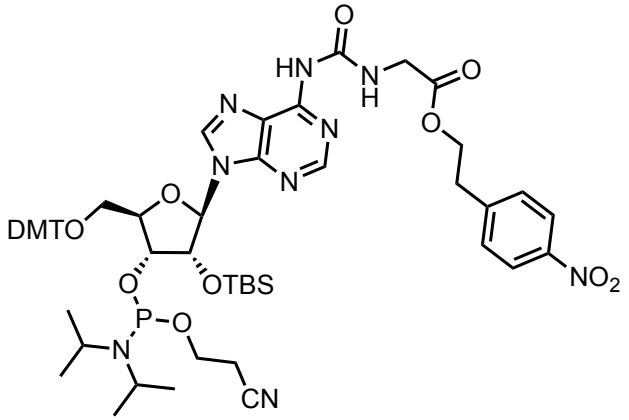
**Yield**: 66%; **$^{31}$P NMR (162 MHz, Acetone-*d*$_6$) δ**: 150.26, 148.61; **HRMS (ESI)**: calculated for $C_{67}H_{87}N_{11}O_{14}PSi^+$: m/z = 1328.5935 $[M+H]^+$; found: m/z = 1328.5944 $[M+H]^+$.

**Compound 48**



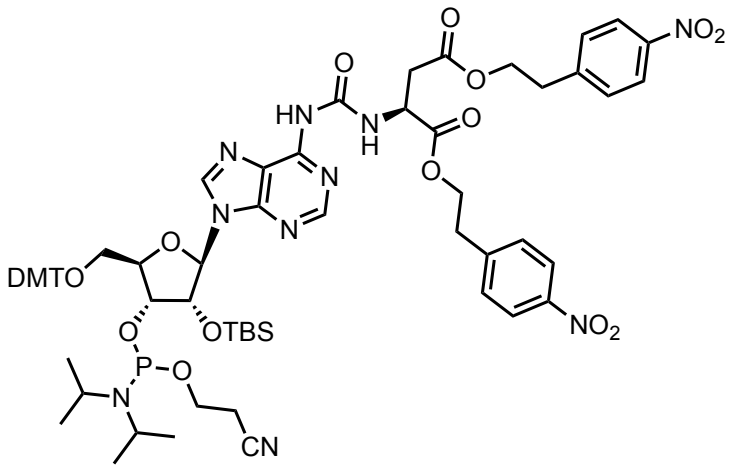
**Yield**: 87%; **$^{31}$P NMR (162 MHz, Acetone-*d*$_6$) δ**: 150.22, 148.65; **HRMS (ESI)**: calculated for $C_{60}H_{79}N_9O_{12}PSi^+$: m/z = 1176.5355 $[M+H]^+$; found: m/z = 1176.5359 $[M+H]^+$.

**Compound 49**



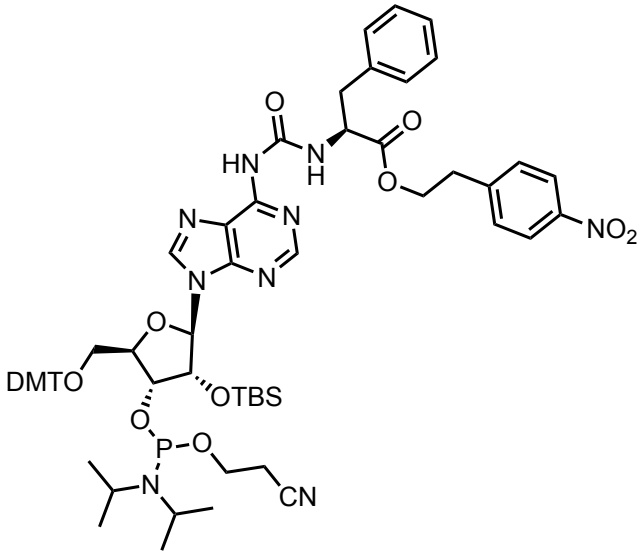

**Yield**: 86%; **$^{31}$P NMR (162 MHz, Acetone-*d*$_6$) δ**: 150.32, 148.60; **HRMS (ESI)**: calculated for $C_{57}H_{72}N_9O_{12}SiPSi^+$: m/z = 1134.4880 $[M+H]^+$; found: m/z = 1134.4894 $[M + H]^+$.

**Compound 50**



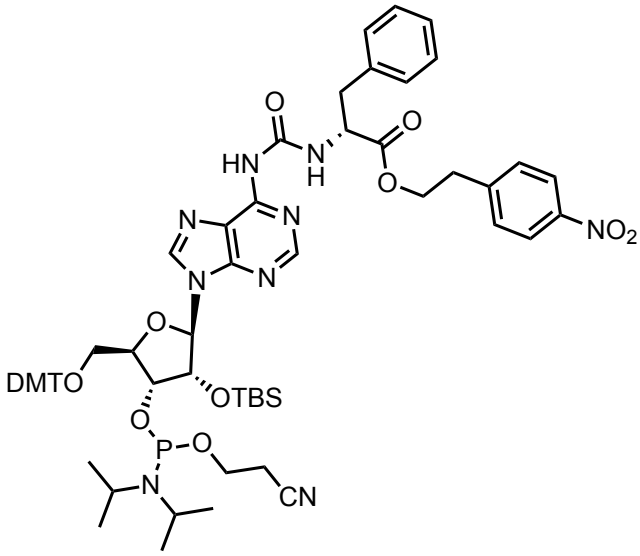

**Yield**: 65%; **$^{31}$P NMR (162 MHz, Acetone-*d*$_6$) δ**: 150.15, 148.67; **HRMS (ESI)**: calculated for $C_{67}H_{82}N_{10}O_{16}PSi^+$: m/z = 1341.5417 $[M+H]^+$; found: m/z = 1341.5437 $[M+H]^+$.

**Compound 51a**



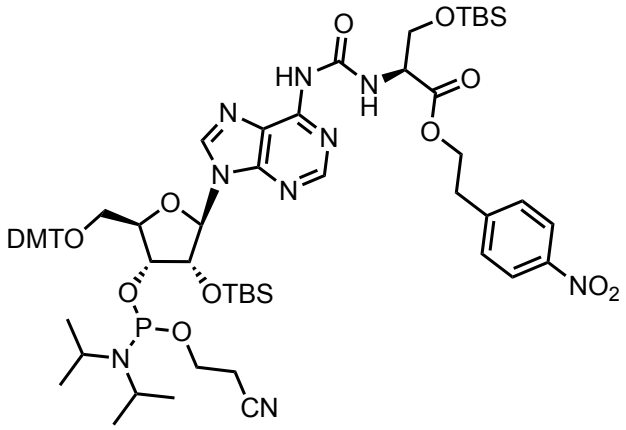

**Yield**: 67%; **$^{31}$P NMR (162 MHz, $CD_2Cl_2$) δ**: 150.7, 149.1; **HRMS (ESI)**: calculated for $C_{64}H_{79}N_9O_{12}PSi^+$: m/z = 1224.5350 $[M+H]^+$; found: m/z = 1224.5374 $[M+H]^+$.

**Compound 51b**




**Yield**: 67%; **$^{31}$P NMR (162 MHz, $CD_2Cl_2$) δ**: 150.6, 148.9; **HRMS (ESI)**: calculated for $C_{64}H_{79}N_9O_{12}PSi^+$: m/z = 1224.5350 $[M+H]^+$; found: m/z = 1224.5383 $[M+H]^+$.

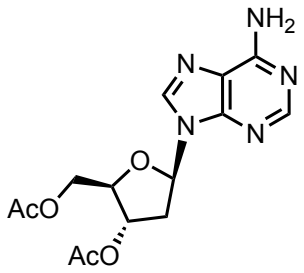
**Compound 52**




**Yield**: 70%; **$^{31}$P NMR (162 MHz, Acetone-$d_6$) δ**: 150.34, 148.45; **HRMS (ESI)**: calculated for $C_{64}H_{89}N_9O_{13}PSi_2^+$: m/z = 1278.5856 $[M+H]^+$; found: m/z = 1278.5877 $[M+H]^+$.

## 2.2. Synthesis of DNA building block

**Compound 54**



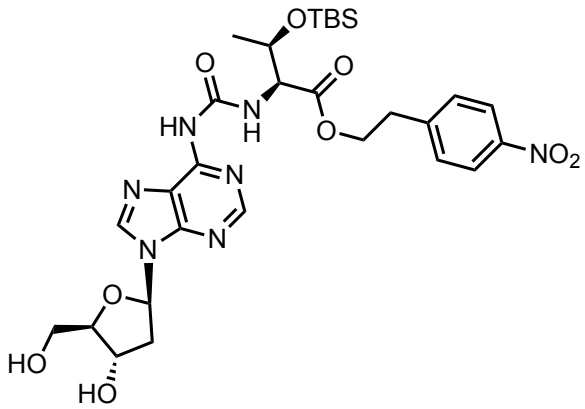

The compound was synthesized according to the published procedure.[5]

Acetic anhydride (1.1 ml, 11.5 mmol, 6.2 eq.) was added to a mixture of deoxyadenosine monohydrate **53** (0.5 g, 1.85 mmol, 1 eq.), pyridine (7 ml) and 4-(dimethylamino)pyridine (25 mg, 0.4 mmol, 0.1 eq.). The reaction mixture was stirred at room temperature for 4 hours. Subsequently, iced water was added, and the mixture was concentrated and co-evaporated with toluene. The compound was used for further steps without additional purification.

**Yield**: 99%; **$^1$H NMR (400 MHz, $CDCl_3$) δ**: 8.23 (s, 1H), 7.92 (s, 1H), 7.26 (s, 2H), 6.34 (dd, *J* = 7.9, 6.0 Hz, 1H), 5.34 – 5.32 (m, 1H), 4.32 – 4.24 (m, 3H), 2.87 – 2.80 (m, 1H), 2.57 – 2.52 (m, 1H), 2.04 (s, 3H), 2.00 (s, 3H). **HRMS (ESI)**: calculated for $C_{14}H_{18}N_5O_5^+$: m/z = 336.1302 $[M+H]^+$; found: m/z = 336.1305 $[M+H]^+$.

The analytical data is in agreement with the literature.[5]

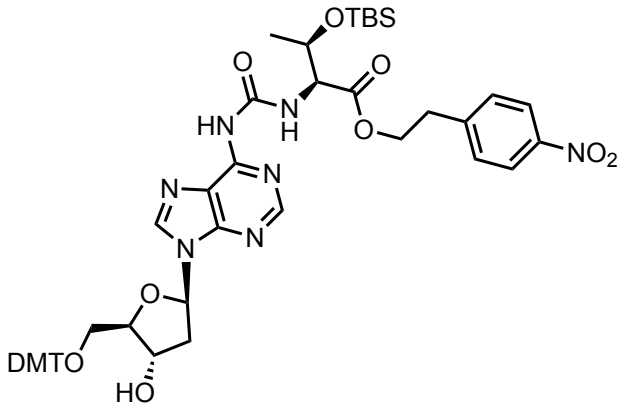
**Compound 55**




The acetyl-protected deoxyadenosine derivative **54** (0.5 g, 1.5 mmol, 1 eq.) was dissolved in dry $CH_2Cl_2$ under nitrogen atmosphere. 1-*N*-methyl-3-phenoxycarbonyl-imidazolium chloride (**22**; 0.71 g, 3 mmol, 2 eq.) was added to the reaction mixture and the resulting suspension was stirred at room temperature for 2 hours (the solution in time becomes clear). Afterwards the protected threonine derivative **7** (1.1 g, 3 mmol, 2 eq.) was added together with TEA (415 µl, 3 mmol, 2 eq.) as a solution in $CH_2Cl_2$ and the resulting solution was stirred overnight at room temperature. The reaction was quenched by addition of saturated aqueous $NaHCO_3$ solution. The solution was extracted three times with $CH_2Cl_2$, and the organic phase was dried, filtered and concentrated *in vacuo*. The acetyl groups were immediately deprotected with 7N $NH_3$/MeOH (2 ml). After stirring 2 hours at room temperature, the reaction mixture was evaporated. The residue was purified via flash chromatography eluting with $CH_2Cl_2$/MeOH (10/1, v/v).

**Yield**: 65%; **IR**: $\tilde{\nu}$ = 3227 (w), 2929 (w), 2855 (w), 1734 (w), 1686 (vs), 1610 (s), 1587 (s), 1518 (vs), 1465 (vs), 1344 (vs), 1312 (w), 1248 (s), 1213 (w), 1094 (vs), 939 (s), 827 (vs) $cm^{-1}$; **$^1$H NMR (400 MHz, Acetone-$d_6$) δ**: 10.02 (d, *J* = 8.6 Hz, 1H), 9.40 (s, 1H), 8.70 (s, 1H), 8.39 (s, 1H), 7.91 (d, *J* = 8.2 Hz, 2H), 7.47 (d, *J* = 8.2 Hz, 2H), 6.54 (t, *J* = 6.7 Hz, 1H), 4.67 (s, 1H), 4.51 (d, *J* = 9.3 Hz, 2H), 4.38 (t, *J* = 5.6 Hz, 2H), 4.09 (s, 1H), 3.86 – 3.67 (m, 2H), 3.08 (t, *J* = 5.6 Hz, 2H), 2.90 (dt, *J* = 13.0, 6.7 Hz, 1H), 2.52 – 2.41 (m, 1H), 2.01 (s, 1H), 1.93 (s, 1H), 1.23 (d, *J* = 5.9 Hz, 3H), 0.88 (s, 9H), 0.05 (s, 3H), -0.06 (s, 3H); **$^{13}$C NMR (101 MHz, Acetone-$d_6$) δ**: 171.5, 155.1, 151.1, 150.9, 147.4, 144.2, 130.9, 124.0, 122.0, 89.8, 86.8, 72.6, 69.5, 65.5, 63.3, 41.4, 35.2, 30.6, 26.0, 21.5, 20.5, 18.4, -4.2, -5.2; **HRMS (ESI)**: calculated for $C_{29}H_{42}N_7O_9Si^+$: m/z = 660.2813 $[M+H]^+$; found: m/z = 660.2812 $[M+H]^+$.

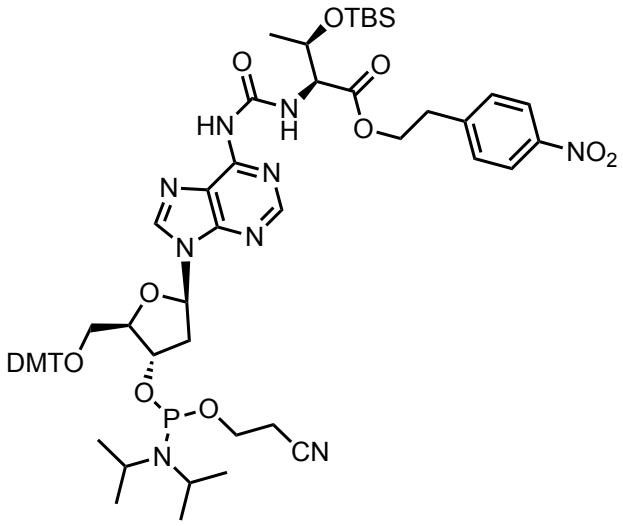
**Compound 56**




The 3'-5'-deprotected adenosine derivative **55** (0.34 g, 0.52 mmol, 1 eq.) was dissolved in pyridine under $N_2$ atmosphere. DMT chloride (0.26 g, 0.77 mmol, 1.5 eq.) was added in two portions and the mixture was stirred at room temperature overnight. Then the volatiles were evaporated, and crude product was purified by flash chromatography eluting with $CH_2Cl_2$/MeOH (10/1/, v/v) with an addition of 0.1% of pyridine to afford the DMT protected derivative.

**Yield**: 72%; **IR**: $\tilde{\nu}$ = 2960 (w), 2930 (w), 1734 (w), 1696 (s), 1609 (s), 1586 (w), 1520 (vs), 1509 (vs), 1467 (s), 1345 (vs), 1304 (w), 1250 (vs), 1175 (s), 1095 (w), 1034 (s), 940 (w), 828 (vs), 777 (s), 699 (w) $cm^{-1}$; **$^1$H NMR (400 MHz, Acetone-$d_6$) δ**: 10.02 (d, *J* = 9.1 Hz, 1H), 8.98 (s, 1H), 8.52 (s, 1H), 8.34 (s, 1H), 7.96 (d, *J* = 8.7 Hz, 2H), 7.51 (d, *J* = 8.7 Hz, 2H), 7.42 (d, *J* = 7.1 Hz, 2H), 7.31 – 7.28 (m, 4H), 7.24 – 7.12 (m, 3H), 6.79 – 6.74 (m, 4H), 6.55 (t, *J* = 6.4 Hz, 1H), 4.76 (q, *J* = 4.2 Hz, 1H), 4.64 – 4.58 (m, 1H), 4.55 (ddd, *J* = 10.6, 7.7, 1.5 Hz, 2H), 4.41 (t, *J* = 6.2 Hz, 2H), 4.25 – 4.18 (m, 1H), 3.74 (d, *J* = 3.3 Hz, 6H), 3.43 (dd, *J* = 10.2, 5.9 Hz, 1H), 3.35 (dd, *J* = 10.2, 4.0 Hz, 1H), 3.17 – 3.10 (m, 3H), 2.58 – 2.52 (m, 1H), 1.29 (d, *J* = 6.3 Hz, 3H), 0.93 (s, 9H), 0.11 (s, 3H), -0.01 (s, 3H); **$^{13}$C NMR (101 MHz, Acetone-$d_6$) δ**: 171.6, 159.4, 154.9, 151.2, 151.0, 147.4, 146.1, 143.9, 136.8, 131.0, 130.9, 130.8, 128.9, 128.4, 127.4, 124.0, 122.0, 113.7, 87.7, 86.8, 86.1, 72.6, 69.6, 65.4, 65.1, 60.3, 55.4, 40.0, 35.3, 26.0, 21.5, 18.4, -4.1, -5.2; **HRMS (ESI)**: calculated for $C_{50}H_{60}N_7O_{11}Si^+$: m/z = 962.4120 $[M+H]^+$; found: m/z = 962.4136 $[M+H]^+$.

**Compound 57**




In an oven-dried flask under argon atmosphere, 5'-DMT protected compound **56** (0.1 g, 0.1 mmol, 1 eq.) was dissolved in $CH_2Cl_2$ and cooled to 0 °C. Hünig's base (72 µl, 0.4 mmol, 4 eq.) was added dropwise followed by the addition of 2-cyanoethyl *N,N*-diisopropylchlorophosphoramidite (60 µl, 0.25 mmol, 2.5 eq.). The solution was stirred at room temperature for 2 h. The reaction was quenched by addition of sat. $NaHCO_3$ solution, and then extracted three times with $CH_2Cl_2$. The organic phase was dried over $Na_2SO_4$, filtered and concentrated in vacuo. The residue was purified by flash chromatography, eluting with Hex/EtOAc (1/2, v/v) containing 0.1% of pyridine. The phosphoramidite was obtained as a mixture of diastereomers as white foam.

**Yield**: 62%; **$^{31}$P NMR (162 MHz, Acetone-$d_6$) δ**: 148.00, 146.59; **HRMS (ESI)**: calculated for $C_{59}H_{76}N_9NaO_{12}PSi^+$: m/z = 1184.5018 $[M+Na]^+$; found: m/z = 1184.5021 $[M+Na]^+$.

## 3. Synthesis and Purification of Oligonucleotides

All of the oligonucleotides used in this study were synthesized on a 1 μmol scale using a DNA automated synthesizer (Applied Biosystems 394 DNA/RNA Synthesizer) with standard phosphoramidite chemistry. The phosphoramidites of canonical ribonucleosides were purchased from Glen Research and Sigma-Aldrich. Oligonucleotides containing non-canonical nucleosides were synthesized in DMT-OFF mode using phosphoramidites (Bz-A, Dmf-G, Ac-C, U) with BTT in $CH_3CN$ as an activator, DCA in $CH_2Cl_2$ as a deblocking solution and $Ac_2O$ in pyridine/THF as a capping reagent. For deprotection of npe-group the solid support was treated with DBU solution (10% in THF, 1 ml) for 2 h at room temperature. Subsequently, the supernatant was removed, and the beads were washed with THF and dried under vacuum. The solid support was suspended in a mixture of aqueous ammonia and methylamine (1:1, 1 ml) at room temperature for 1 h. The supernatant was removed, and the beads were washed with water. The supernatant and washings were combined, and the solvents were evaporated under reduced pressure. The residue was subsequently heated with a solution of triethylamine trihydrofluoride (125 μl) in DMSO (50 μl) at 65 °C for 1.5 h. The RNA was precipitated by addition of aqueous NaOAc solution (3M, 25 μl) and *n*-butanol (1 ml). To ensure complete precipitation, the sample was incubated at -80 °C for 1 h. After centrifugation (4 °C, 4000 rpm, 15 min), the supernatant was removed, and the precipitated RNA was lyophilized. The oligonucleotides were further purified by reverse-phase HPLC using a Waters Breeze (2487 Dual λ Array Detector, 1525 Binary HPLC Pump) equipped with the column VP 250/32 C18 from Macherey Nagel. Oligonucleotides were purified using the following buffer system: buffer A: 100 mM $NEt_3$/HOAc, pH 7.0 in $H_2O$ and buffer B: 100 mM $NEt_3$/HOAc in 80 % (v/v) acetonitrile. A flow rate of 5 ml/min with a gradient of 0-25 % of buffer B in 30 min was applied for the purifications. Analytical RP-HPLC was performed on an analytical HPLC Waters Alliance (2695 Separation Module, 2996 Photodiode Array Detector) equipped with the column Nucleosil 120-2 C18 from Macherey Nagel using a flow of 0.5 mL/min, a gradient of 0-30% of buffer B in 45 min was applied. Calculation of concentrations was assisted using the software OligoAnalyzer 3.0 (Integrated DNA Technologies: https://eu.idtdna.com/calc/analyzer). For strands containing non-canonical base, the extinction coefficient of their corresponding canonical-only strand was employed without corrections. The structural integrity of the synthesized oligonucleotides was analyzed by MALDI-TOF mass measurements.

Sequences of synthesized strands:

**ON1**: 5' GUCt$^{6}$ACCUGA 3'

**ON2**: 5' GUCg$^{6}$ACCUGA 3'

**ON3**: 5' GUCval$^{6}$ACCUGA 3'

**ON4**: 5' GUChis$^{6}$ACCUGA 3'

**ON5**: 5' GUCasp$^{6}$ACCUGA 3'

**ON6**: 5' GUC-L-phe$^{6}$ACCUGA 3'

**ON7**: 5' GUC-D-phe$^{6}$ACCUGA 3'

**ON8**: 5' AUCGt$^{6}$ACUACGt$^{6}$AAUCGCt$^{6}$AACCG 3'

**ON9**: 5' AGAUGUG-ser$^{6}$A-asp$^{6}$A-his$^{6}$A-GAGAUGA 3'

**ODN1**: 5' d(GTCt$^{6}$dACCTGA) 3'

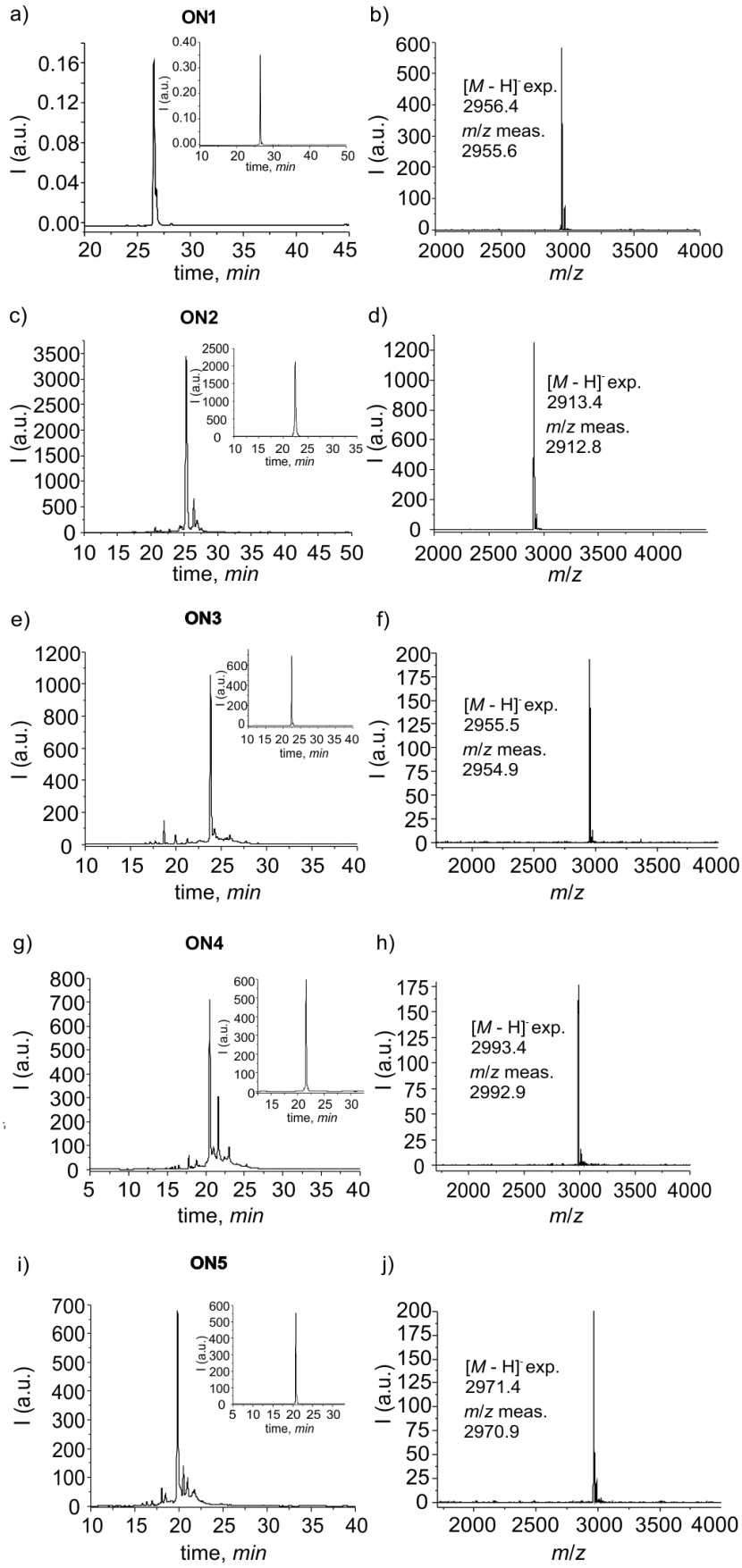



**Figure S1**. HPLC and MALDI data of oligonucleotides **ON1**-**ON5**.

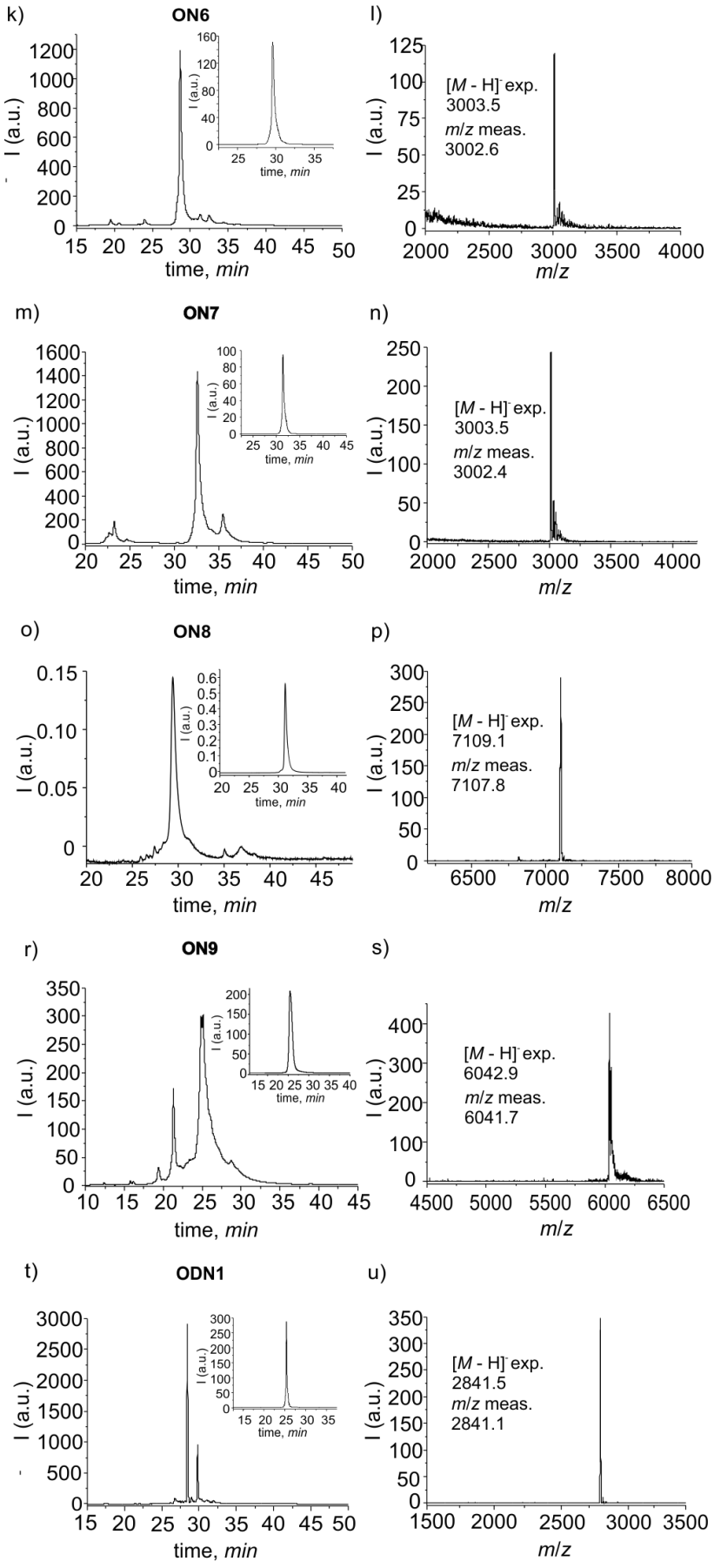


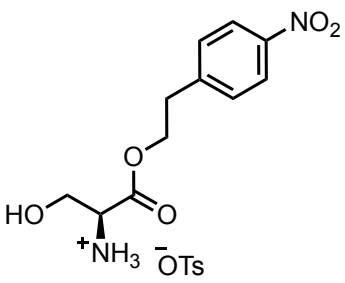

**Figure S2**. HPLC and MALDI data of oligonucleotides **ON6-ODN1**.

## 4. UV Melting Curve Measurements

The UV melting curves were measured on JASCO V-650 spectrometer using 10 mm QS cuvettes, purchased from Hellma Analytics. A solution (80 μL) of equimolar amounts of oligonucleotides (4 μM each) in the buffer solution containing 10 mM sodium phosphate buffer (pH 7.0) and 150 mM NaCl was heated at 90 °C for 2 min and gradually cooled to 4 °C prior to the measurement. Melting profiles were recorded at temperatures between 5 and 75 °C with a ramping and scanning rate of 1 °C/min at 260 nm. All samples were measured at least three times. $T_m$ values from each measurement were calculated using the "fitting curve" method and presented as an average of three independent measurements.

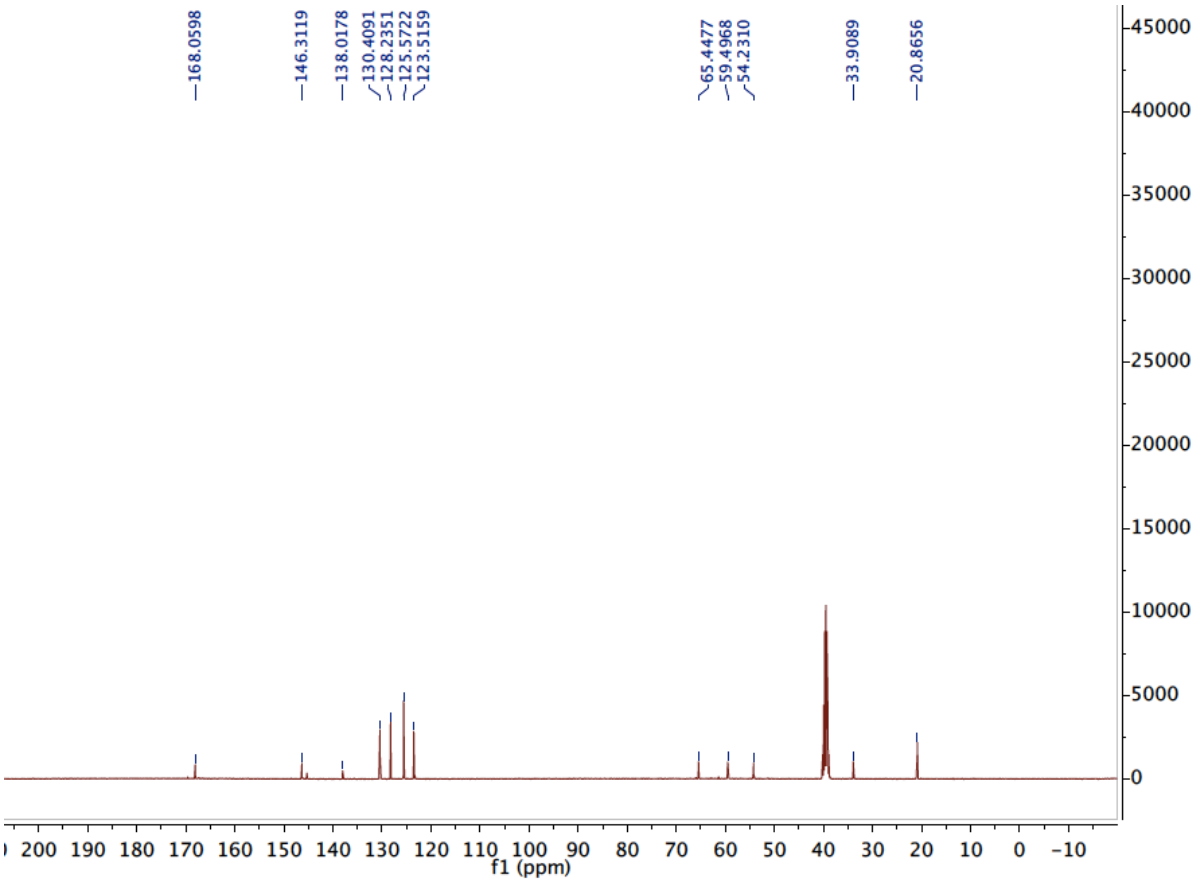
## 5. NMR spectra

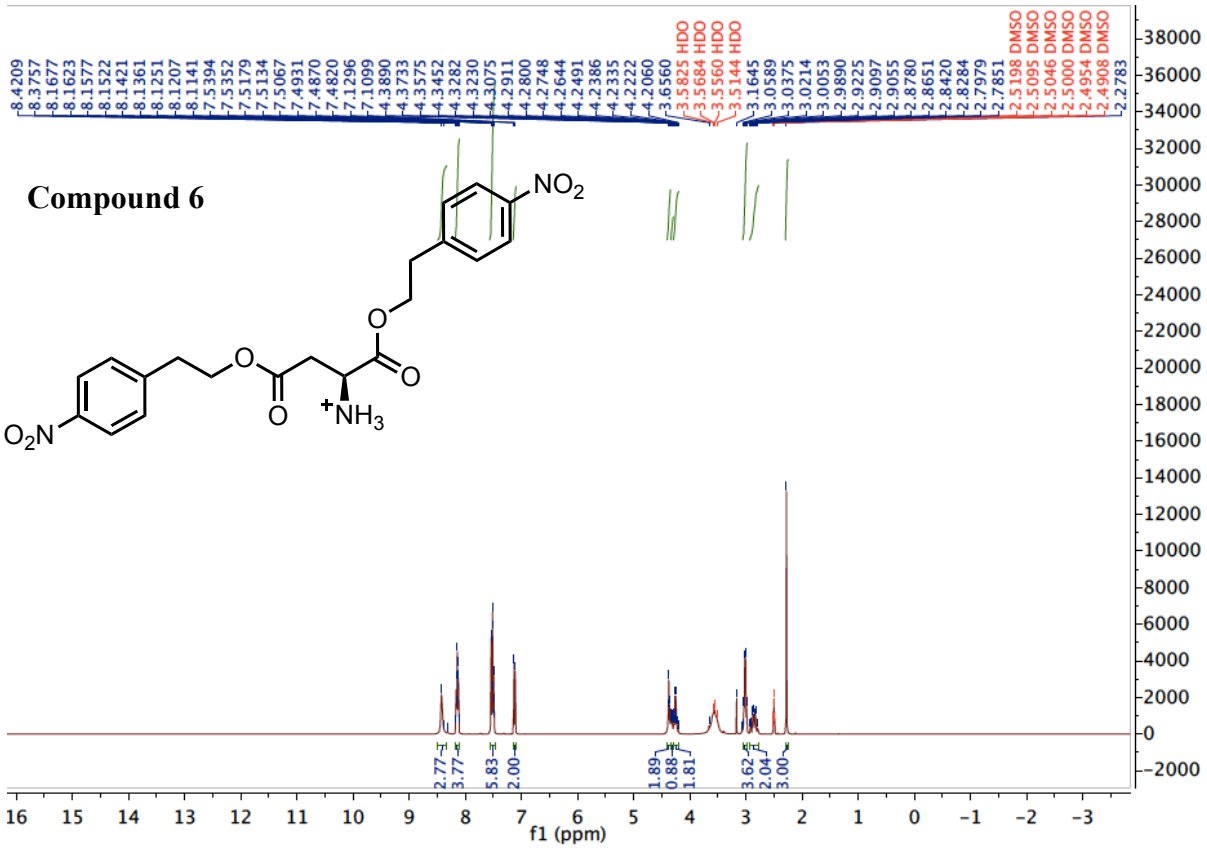
**Compound 5**










Compound 6
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O
O
O
O
+NH3
O2N
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8.3757
8.1677
8.1623
8.1577
8.1522
8.1421
8.1361
8.1251
8.1207
8.1141
7.5394
7.5352
7.5179
7.5134
7.5067
7.4931
7.4870
7.4820
7.1296
7.1099
4.3890
4.3733
4.3575
4.3452
4.3282
4.3230
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4.2911
4.2800
4.2748
4.2644
4.2491
4.2386
4.2335
4.2222
4.2060
3.6560
3.5825 HDO
3.5684 HDO
3.5560 HDO
3.5144 HDO
3.1645
3.0589
3.0375
3.0214
3.0053
2.9890
2.9225
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2.00
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1.81
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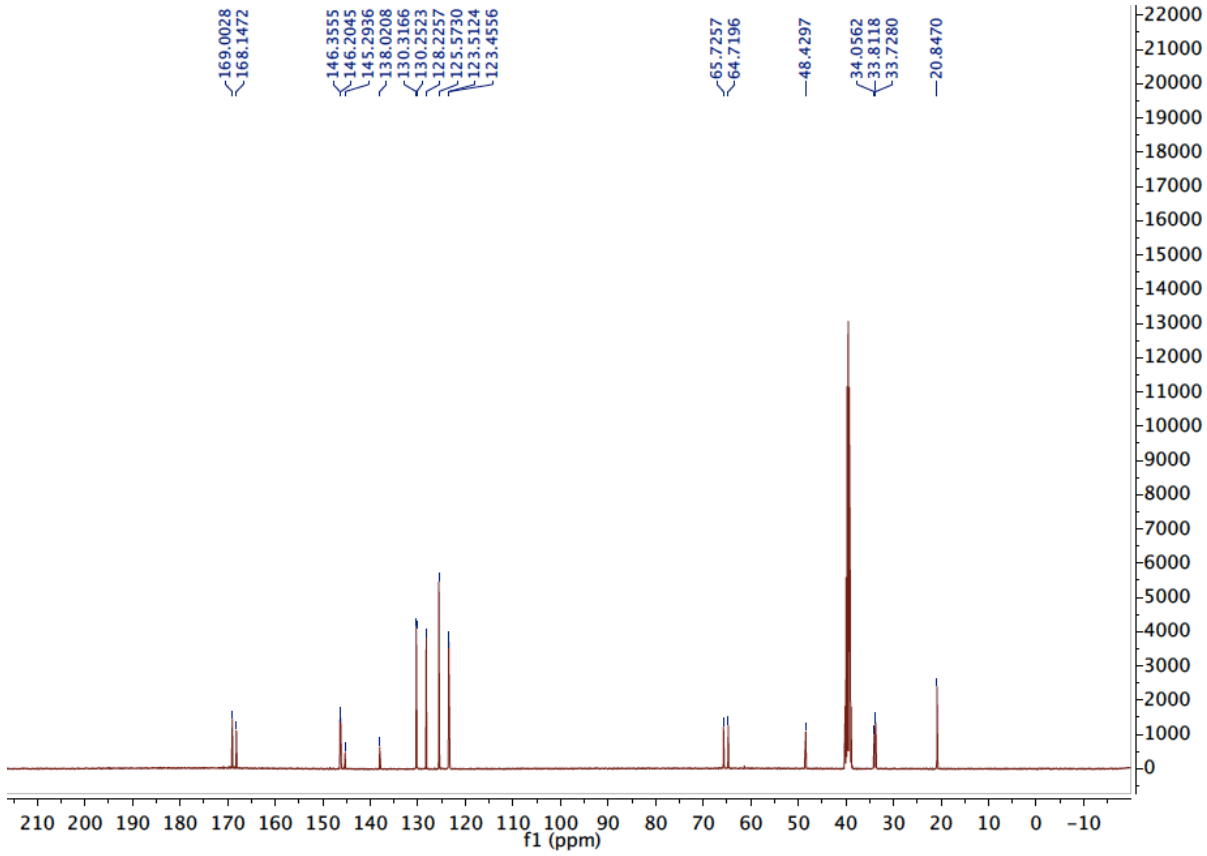
2.04
3.00
f1 (ppm)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146.3555
146.2045
145.2936
138.0208
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130.2523
128.2257
125.5730
123.5124
123.4556
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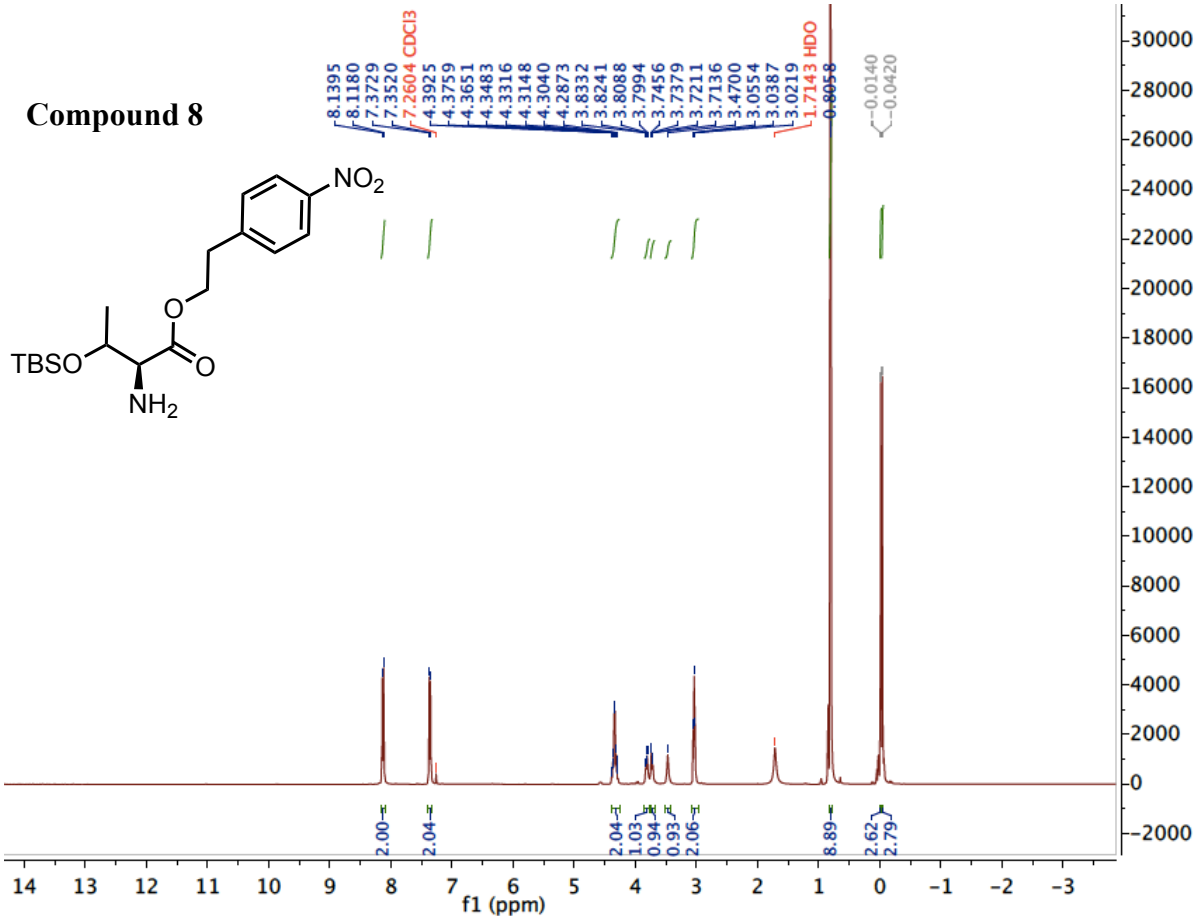
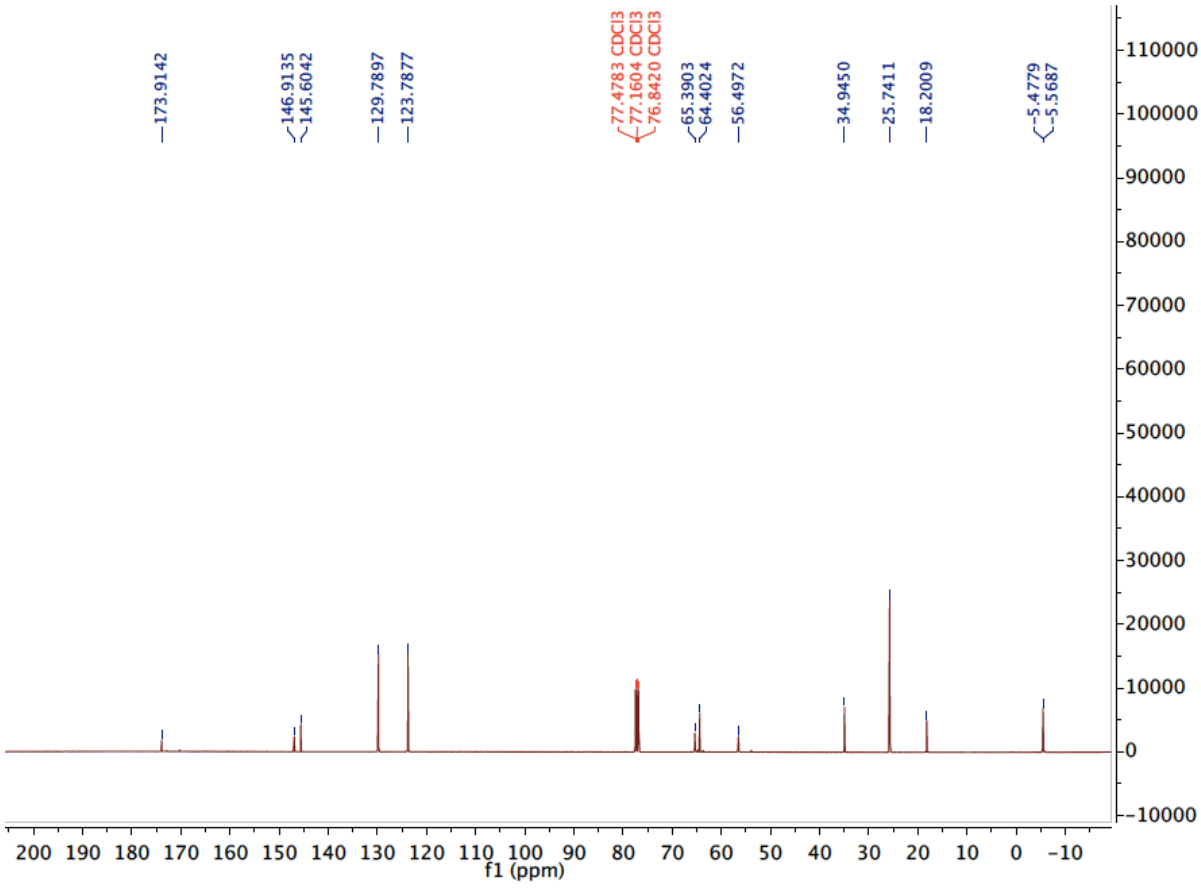
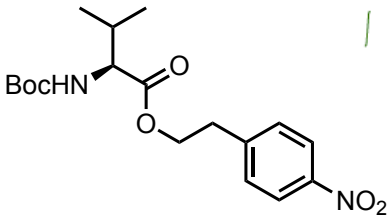
33.8118
33.7280
20.8470
f1 (ppm)

**Compound 8**

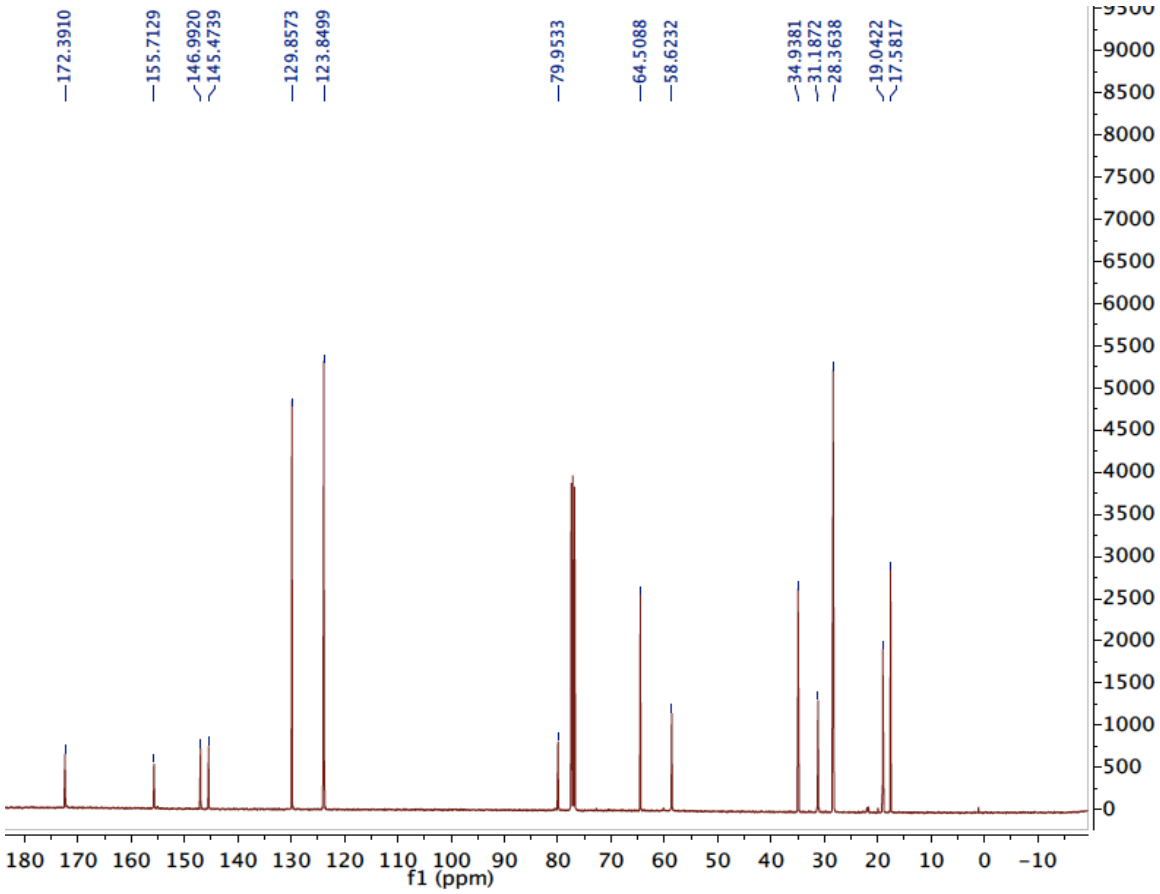

8.1395
8.1180
7.3729
7.3520
7.2604 CDCl3
4.3925
4.3759
4.3651
4.3483
4.3316
4.3148
4.3040
4.2873
3.8332
3.8241
3.8088
3.7994
3.7456
3.7379
3.7211
3.7136
3.4700
3.0554
3.0387
3.0219
1.7143 HDO
0.8058
0.0140
-0.0420
2.00
2.04
2.04
1.03
0.94
0.93
2.06
8.89
2.62
2.79
f1 (ppm)


173.9142
146.9135
145.6042
129.7897
123.7877
77.4783 CDCl3
77.1604 CDCl3
76.8420 CDCl3
65.3903
64.4024
56.4972
34.9450
25.7411
18.2009
5.4779
-5.5687
f1 (ppm)

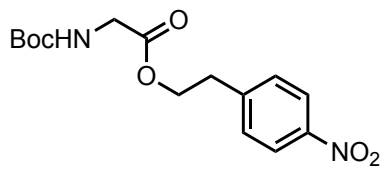
**Compound 12**


BocHN
O
O
NO2

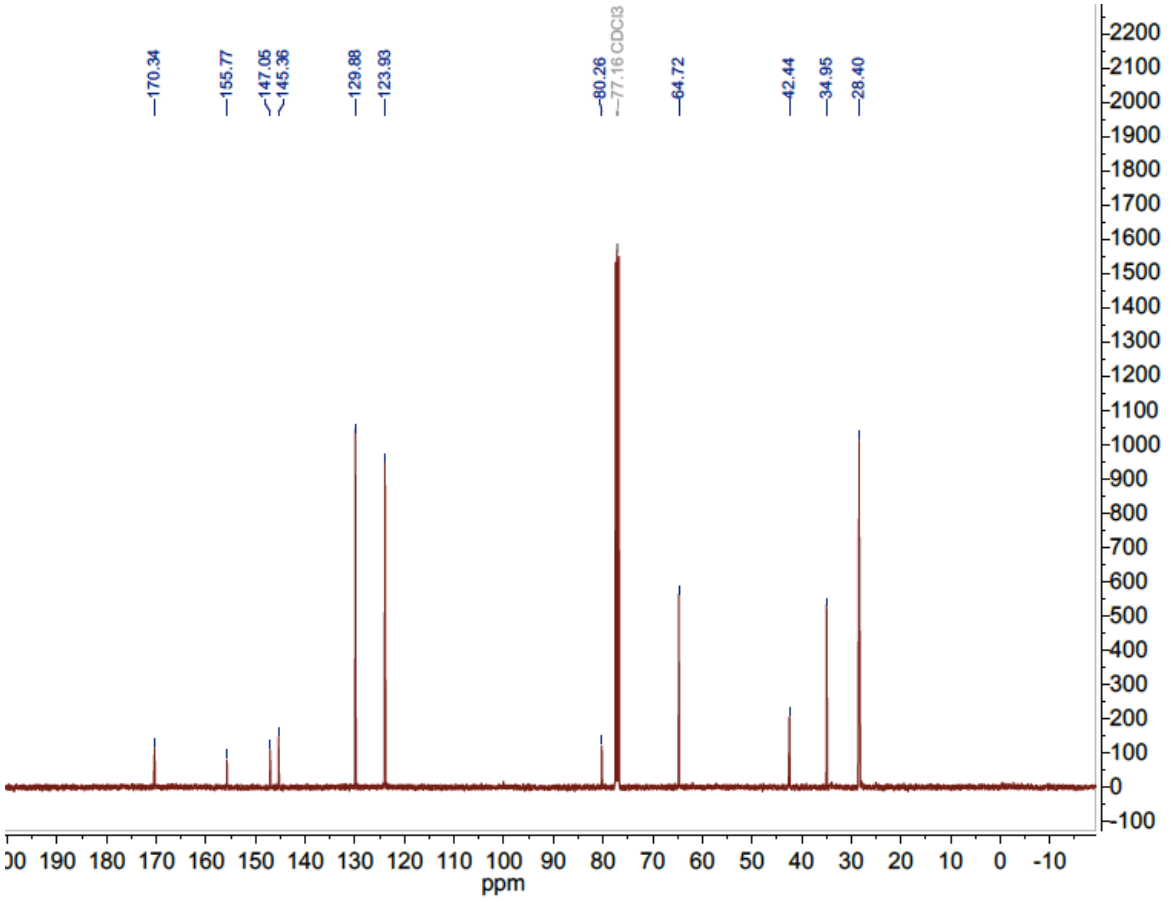

8.1602
8.1387
7.3903
7.3689
4.9567
4.9350
4.3967
4.3801
4.3635
4.1655
4.1535
4.1432
4.1311
3.0765
3.0599
3.0433
1.4120
0.8838
0.8668
0.7845
0.7674
2.00
2.01
0.90
2.03
0.85
2.04
1.03
9.71
3.06
3.16
f1 (ppm)


172.3910
155.7129
146.9920
145.4739
129.8573
123.8499
79.9533
64.5088
58.6232
34.9381
31.1872
28.3638
19.0422
17.5817
f1 (ppm)

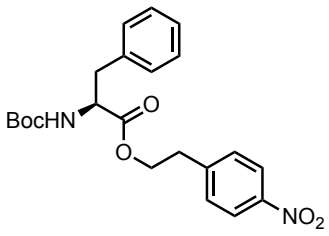
**Compound 13**


BocHN
O
O
NO2


8.17
8.15
7.39
7.37
7.26 CDCl3
4.97
4.41
4.39
4.38
3.88
3.86
3.08
3.06
3.05
1.43
2.00
2.04
0.85
2.08
2.05
2.02
9.41
ppm

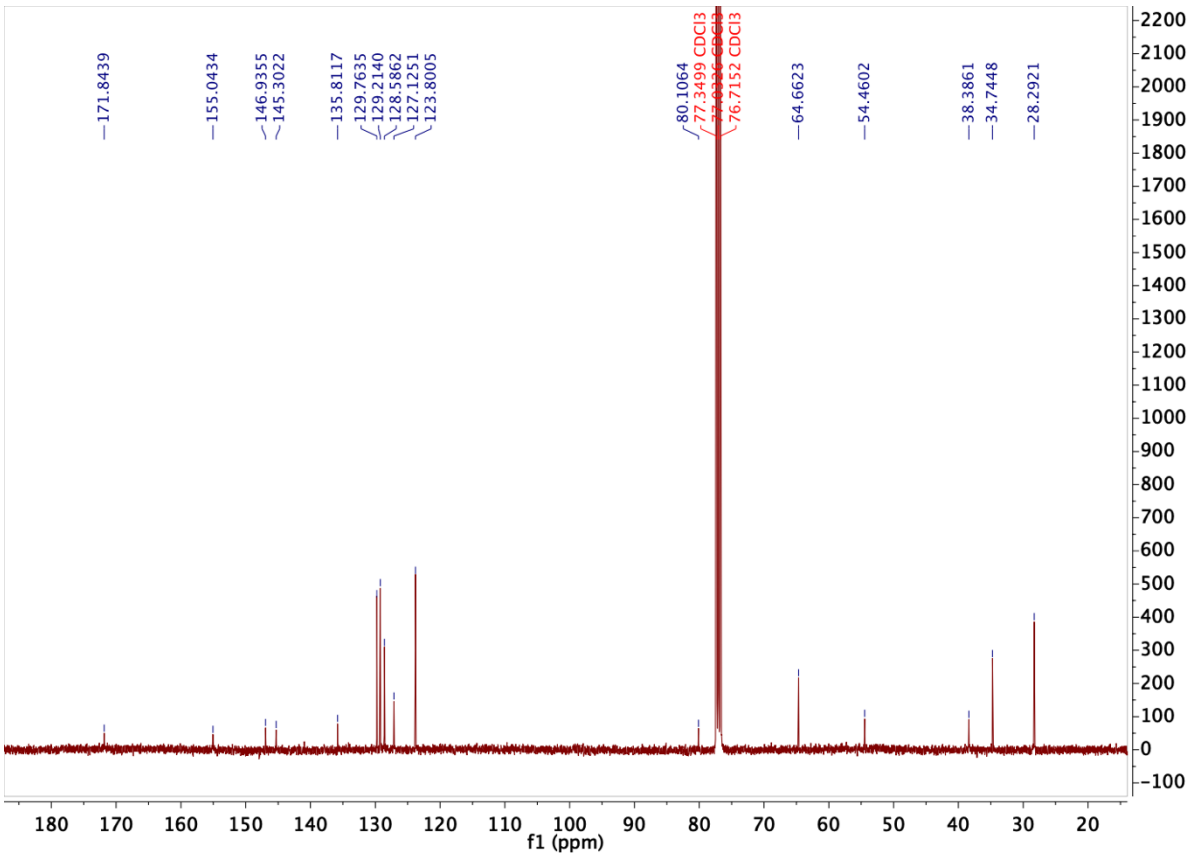

170.34
155.77
147.05
145.36
129.88
123.93
80.26
77.16 CDCl3
64.72
42.44
34.95
28.40
ppm

**Compound 14a**

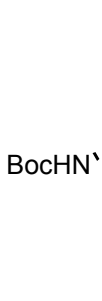






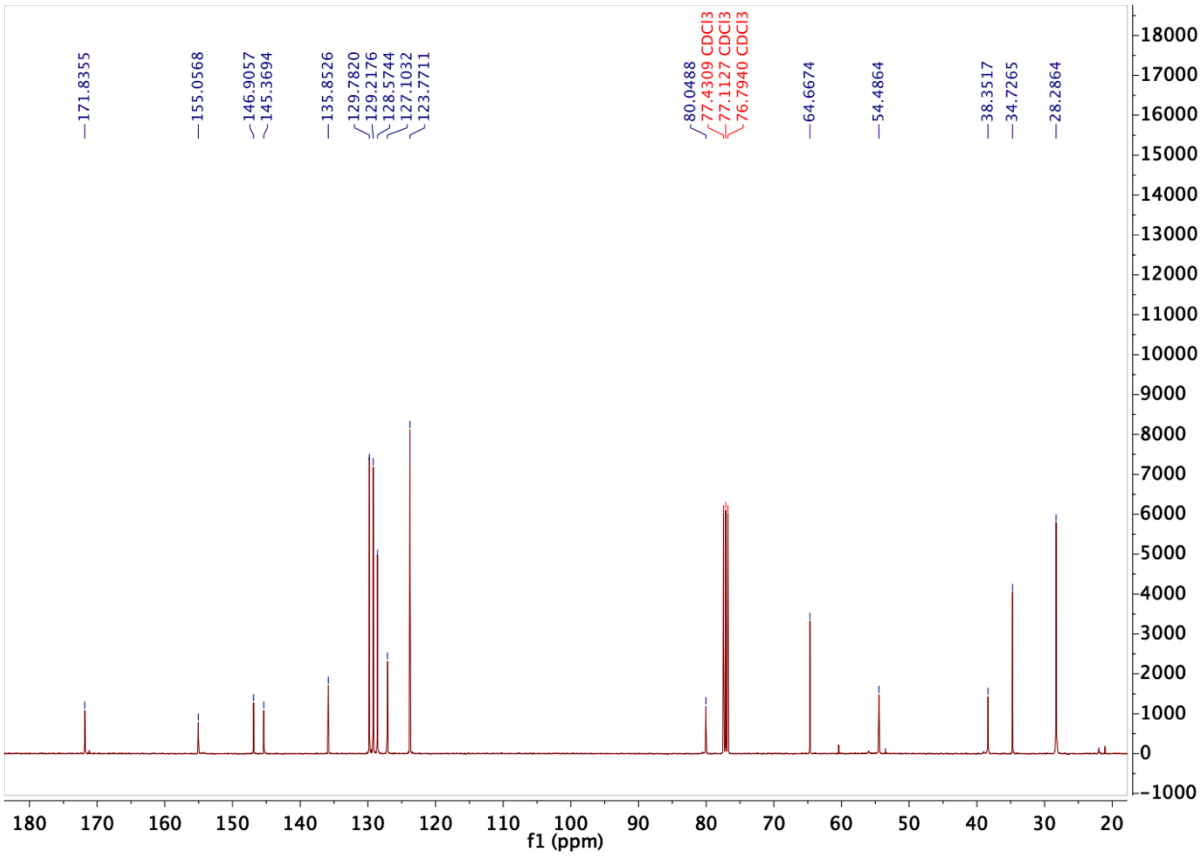


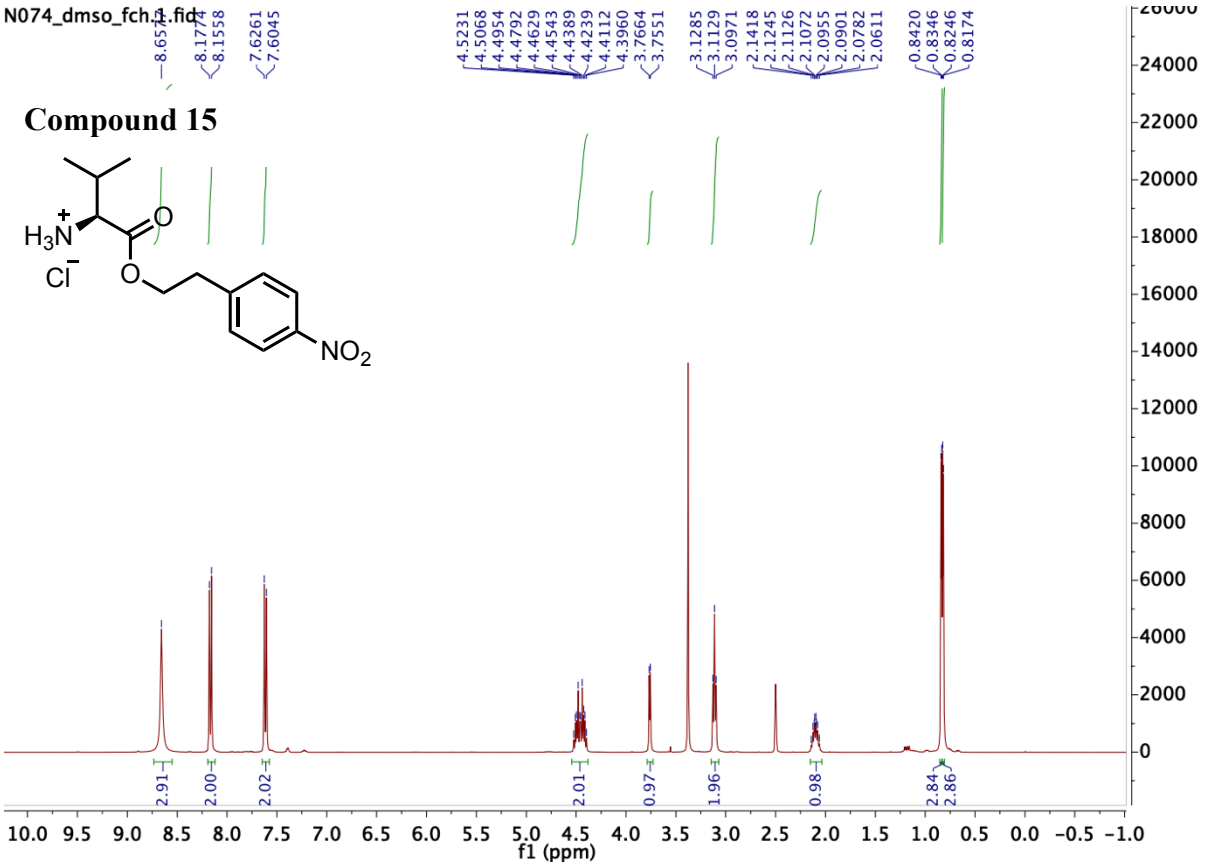
**Compound 14b**





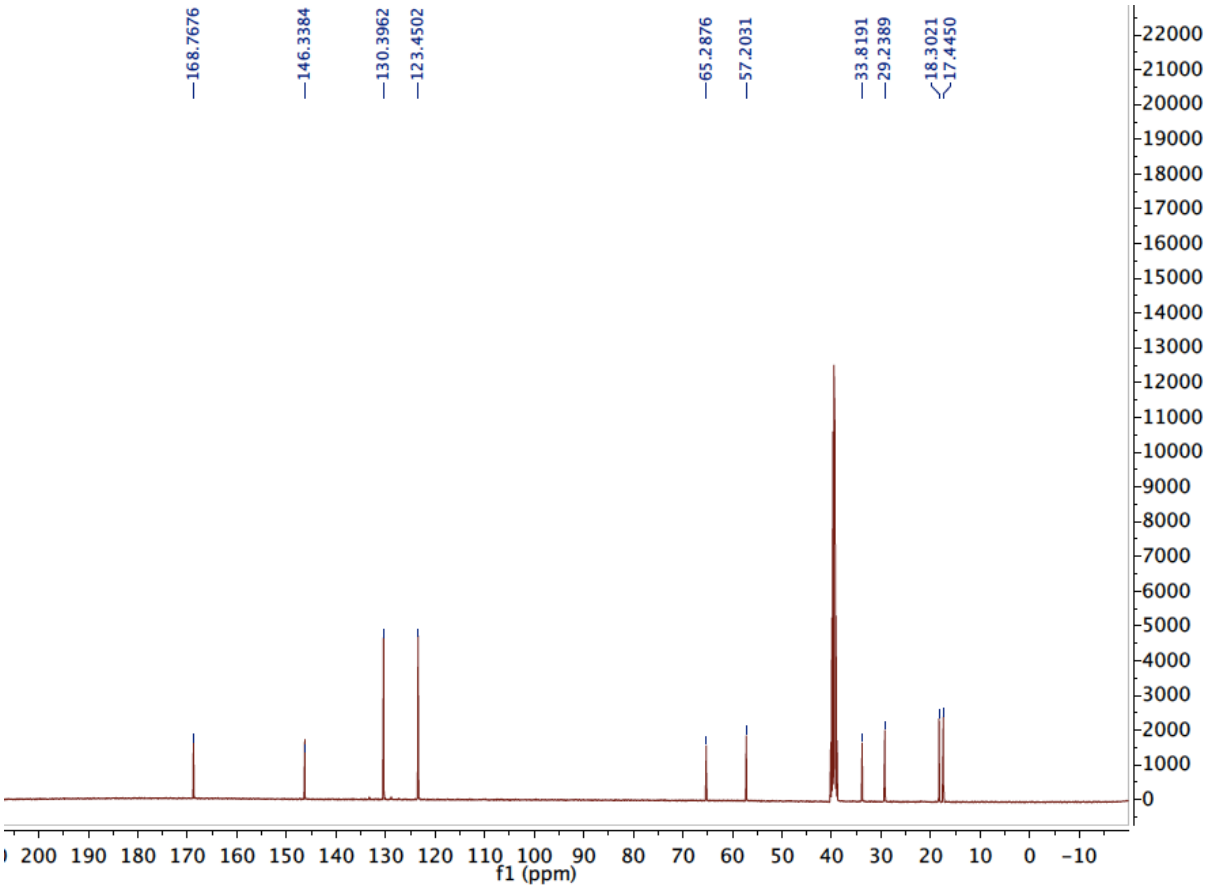




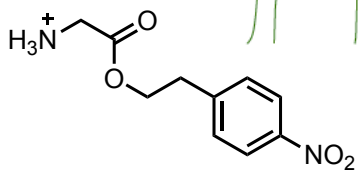

N074_dmso_fch.1.fid
8.6574
8.1774
8.1558
7.6261
7.6045
4.5231
4.5068
4.4954
4.4792
4.4629
4.4543
4.4389
4.4239
4.4112
4.3960
3.7664
3.7551
3.1285
3.1129
3.0971
2.1418
2.1245
2.1126
2.1072
2.0955
2.0901
2.0782
2.0611
0.8420
0.8346
0.8246
0.8174
2.91
2.00
2.02
2.01
0.97
1.96
0.98
2.84
2.86
f1 (ppm)

**Compound 15**

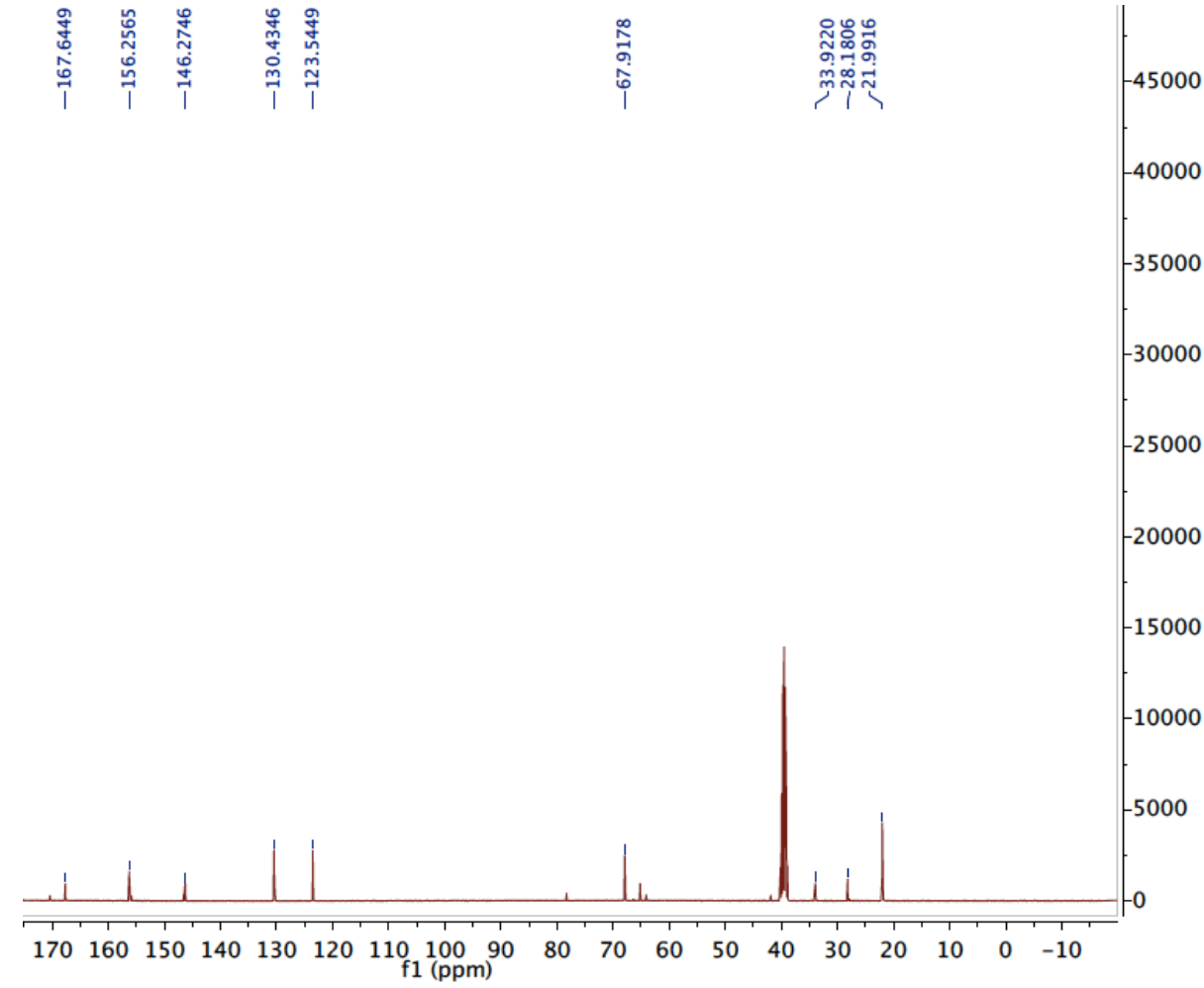

H3N
Cl
O
O
NO2

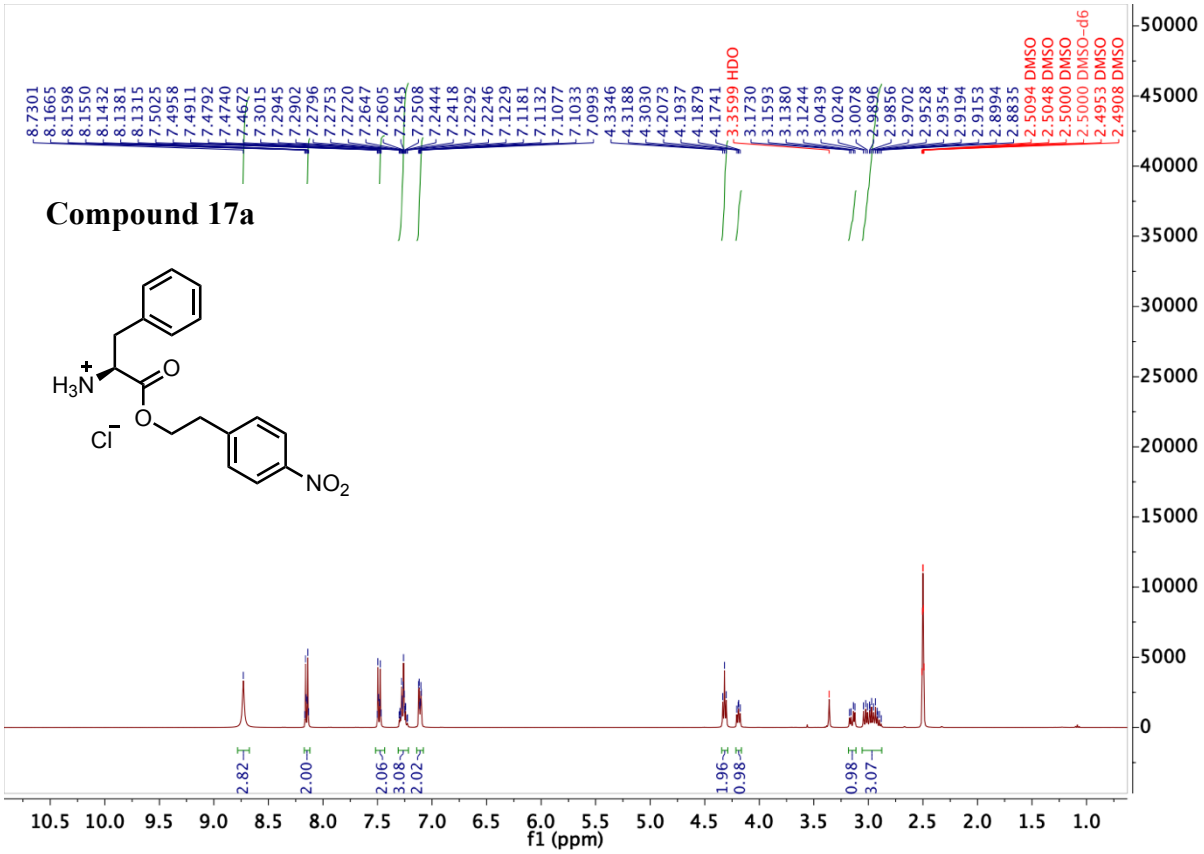

168.7676
146.3384
130.3962
123.4502
65.2876
57.2031
33.8191
29.2389
18.3021
17.4450
f1 (ppm)

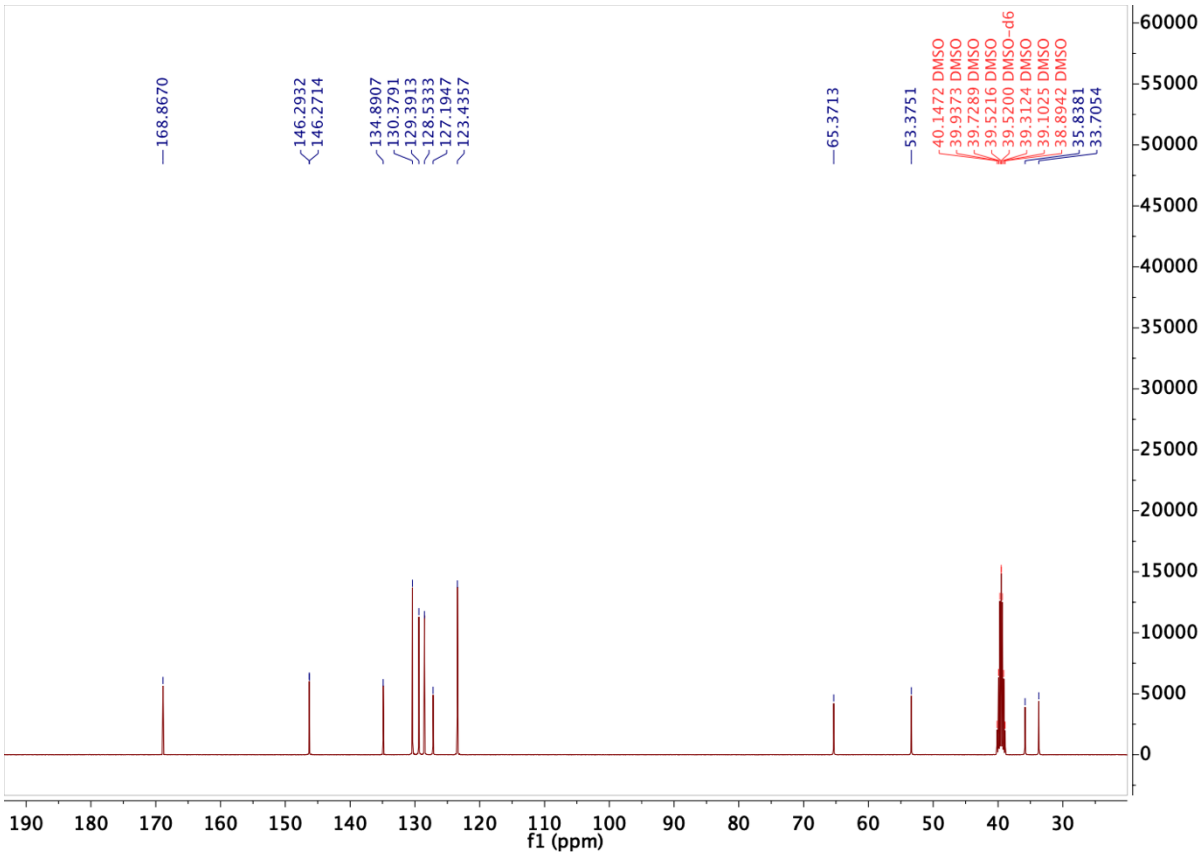
**Compound 16**

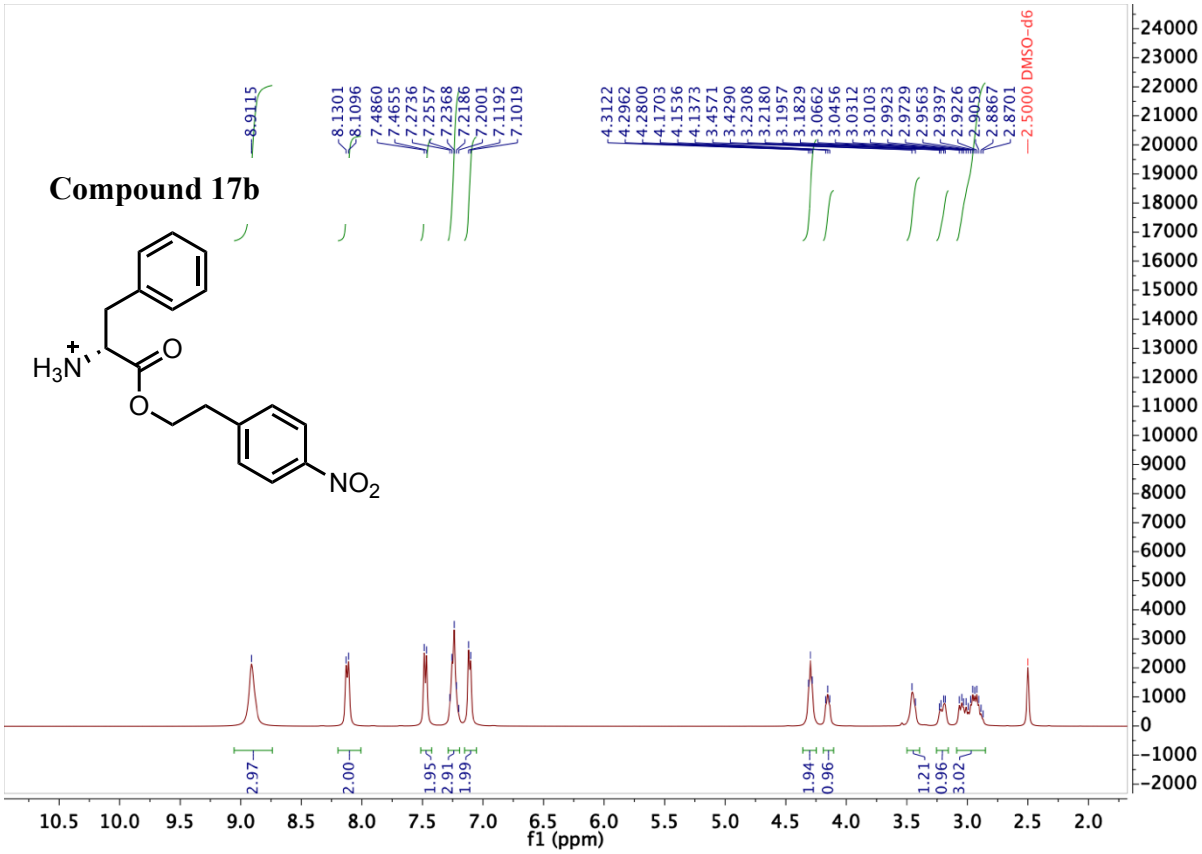

H3N
O
O
NO2

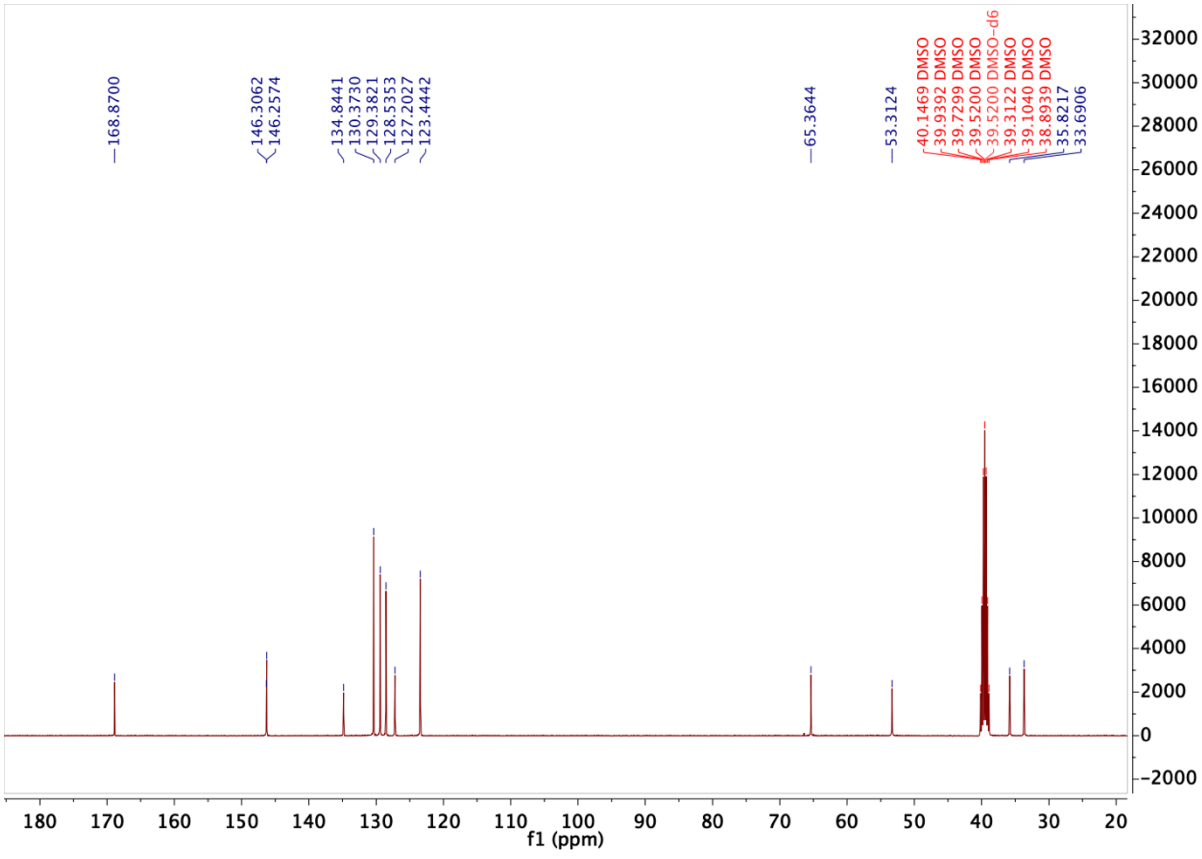

8.3031
8.1929
8.1712
7.6006
7.5788
4.4551
4.4391
4.4232
3.7735
3.1060
3.0901
3.0742
2.74
1.98
2.00
1.90
1.89
1.94
f1 (ppm)


167.6449
156.2565
146.2746
130.4346
123.5449
67.9178
33.9220
28.1806
21.9916
f1 (ppm)

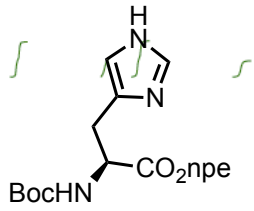

Compound 17a
8.7301
8.1665
8.1598
8.1550
8.1432
8.1381
8.1315
7.5025
7.4958
7.4911
7.4792
7.4740
7.4672
7.3015
7.2945
7.2902
7.2796
7.2753
7.2720
7.2647
7.2605
7.2545
7.2508
7.2444
7.2418
7.2292
7.2246
7.1229
7.1181
7.1132
7.1077
7.1033
7.0993
4.3346
4.3188
4.3030
4.2073
4.1937
4.1879
4.1741
3.3599 HDO
3.1730
3.1593
3.1380
3.1244
3.0439
3.0240
3.0078
2.9856
2.9702
2.9528
2.9354
2.9194
2.9153
2.8994
2.8835
2.5094 DMSO
2.5048 DMSO
2.5000 DMSO
2.5000 DMSO-d6
2.4953 DMSO
2.4908 DMSO
2.82
2.00
2.06
3.08
2.02
1.96
0.98
0.98
3.07
f1 (ppm)


168.8670
146.2932
146.2714
134.8907
130.3791
129.3913
128.5333
127.1947
123.4357
65.3713
53.3751
40.1472 DMSO
39.9373 DMSO
39.7289 DMSO
39.5216 DMSO
39.5200 DMSO-d6
39.3124 DMSO
39.1025 DMSO
38.8942 DMSO
35.8381
33.7054
f1 (ppm)

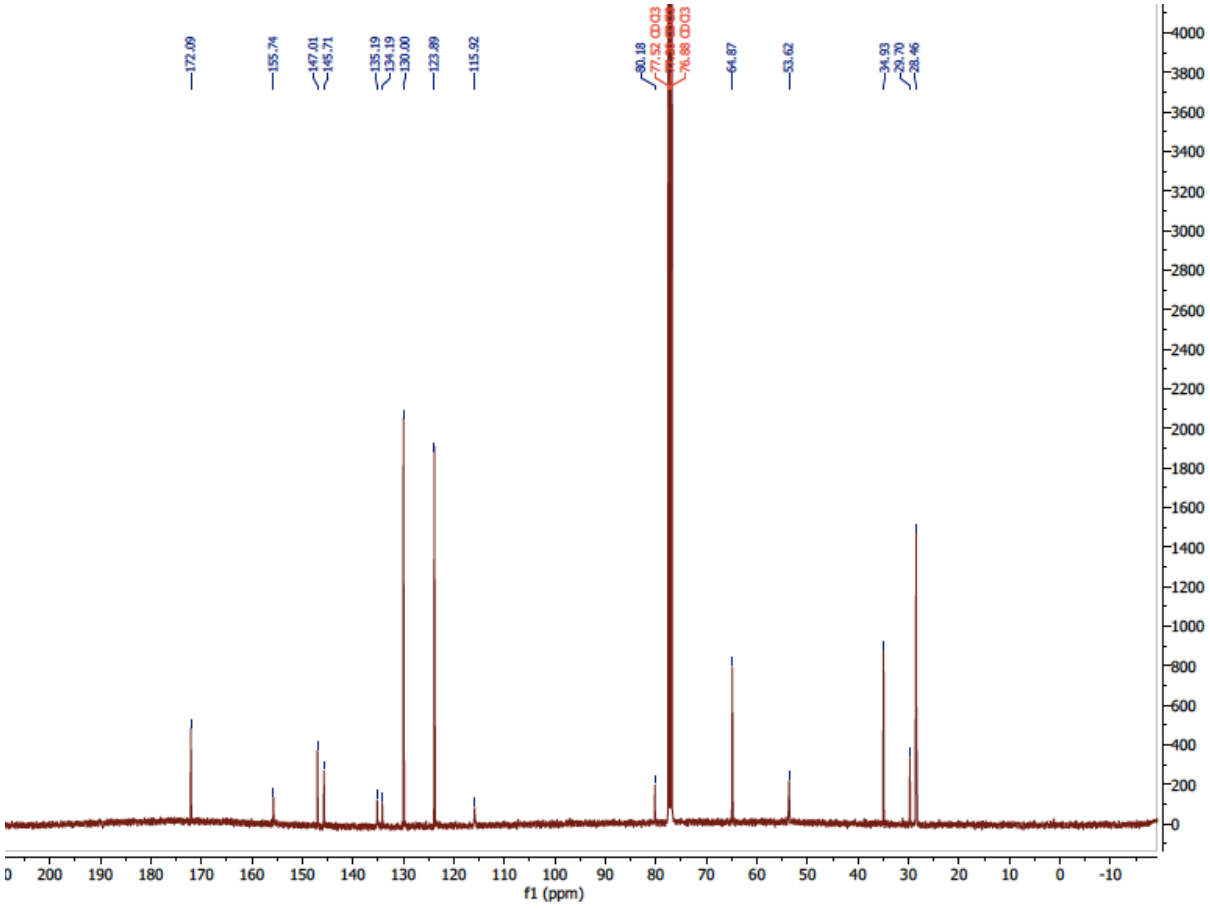

Compound 17b
8.9115
8.1301
8.1096
7.4860
7.4655
7.2736
7.2557
7.2368
7.2186
7.2001
7.1192
7.1019
4.3122
4.2962
4.2800
4.1703
4.1536
4.1373
3.4571
3.4290
3.2308
3.2180
3.1957
3.1829
3.0662
3.0456
3.0312
3.0103
2.9923
2.9729
2.9563
2.9397
2.9226
2.9059
2.8867
2.8701
2.5000 DMSO-d6
2.97
2.00
1.95
2.91
1.99
1.94
0.96
1.21
0.96
3.02
f1 (ppm)


168.8700
146.3062
146.2574
134.8441
130.3730
129.3821
128.5353
127.2027
123.4442
65.3644
53.3124
40.1469 DMSO
39.9392 DMSO
39.7299 DMSO
39.5200 DMSO
39.5200 DMSO-d6
39.3122 DMSO
39.1040 DMSO
38.8939 DMSO
35.8217
33.6906
f1 (ppm)

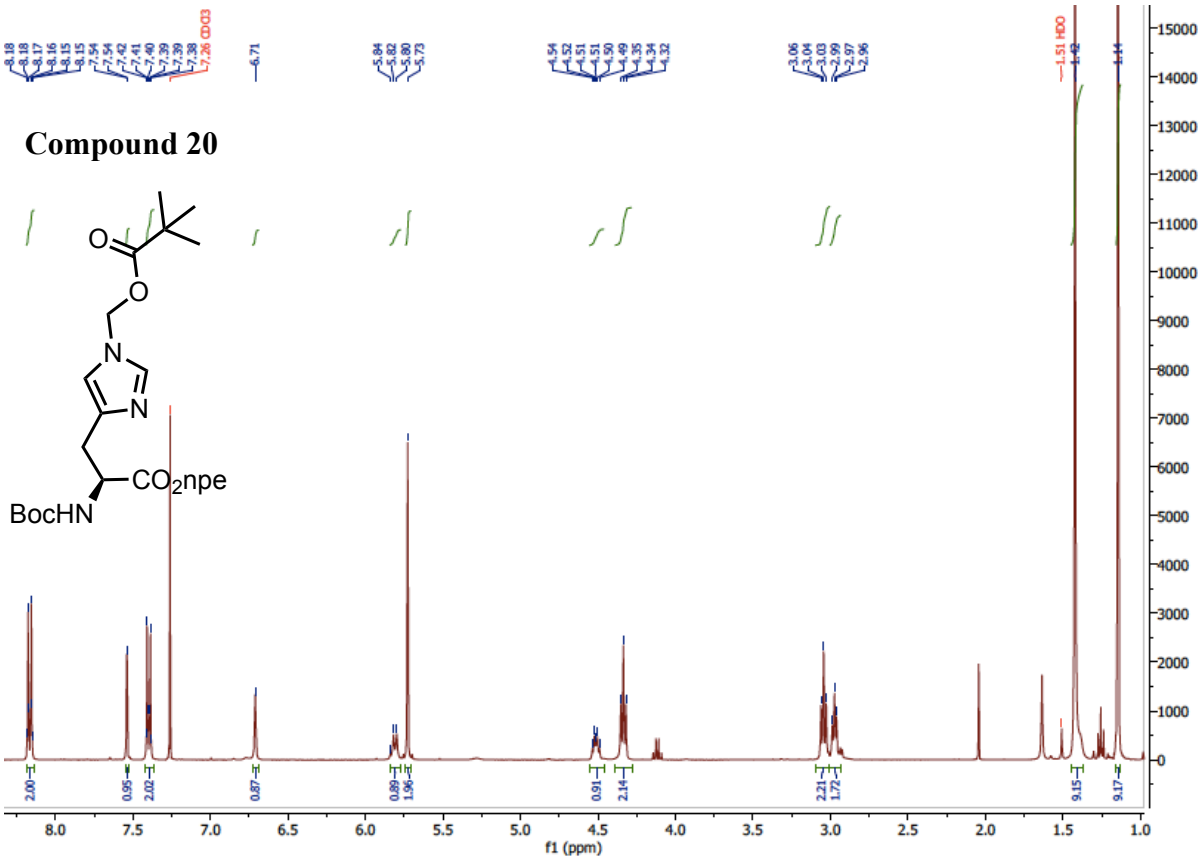
**Compound 19**

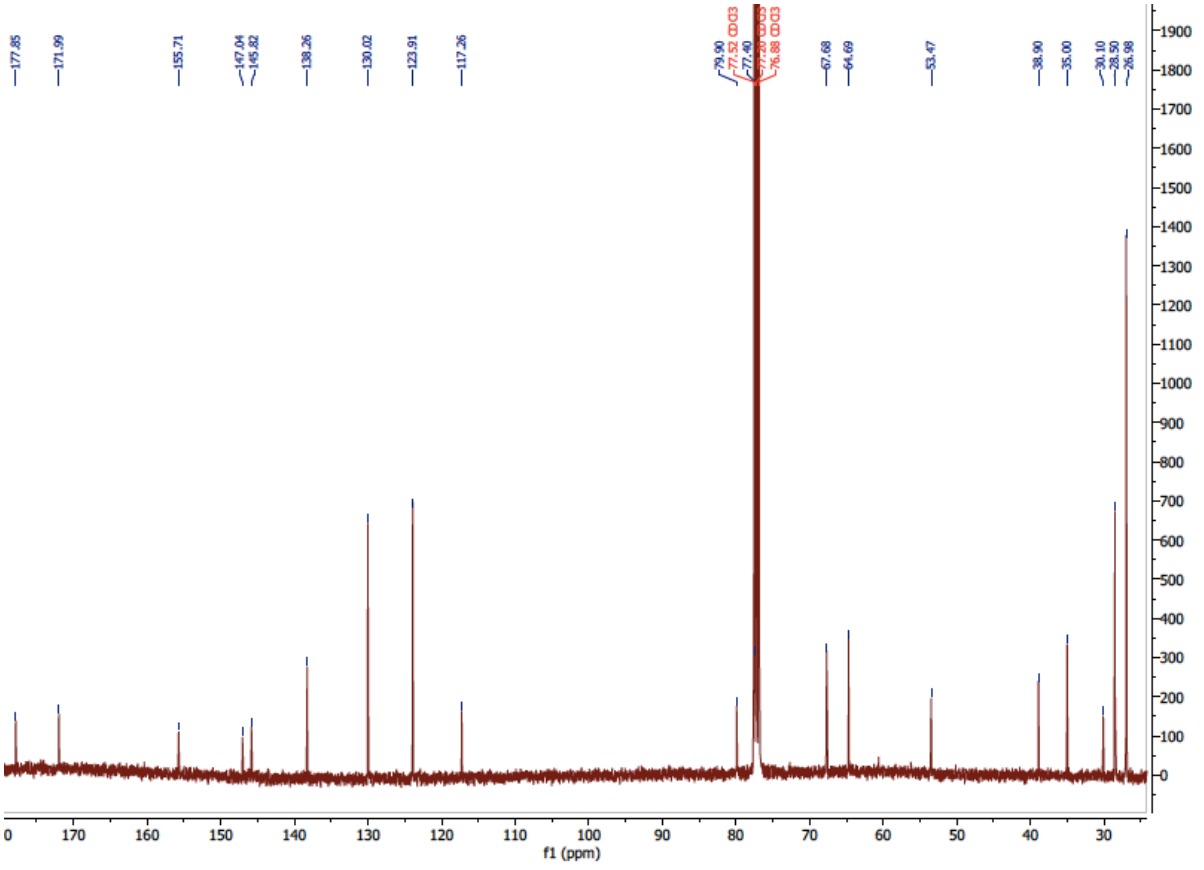

H
N
N
CO2npe
BocHN


8.14
8.14
8.13
8.12
8.12
7.58
7.37
7.37
7.36
7.35
7.26 CDCl3
6.72
5.78
5.76
4.53
4.52
4.50
4.48
4.36
4.34
4.32
3.04
3.03
3.02
3.01
1.41
1.99
1.07
2.05
0.92
0.79
0.88
2.06
3.92
9.11
f1 (ppm)

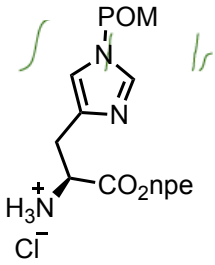

172.09
155.74
147.01
145.71
135.19
134.19
130.00
123.89
115.92
80.18
77.52 CDCl3
76.88 CDCl3
64.87
53.62
34.93
29.70
28.46
f1 (ppm)

**Compound 20**



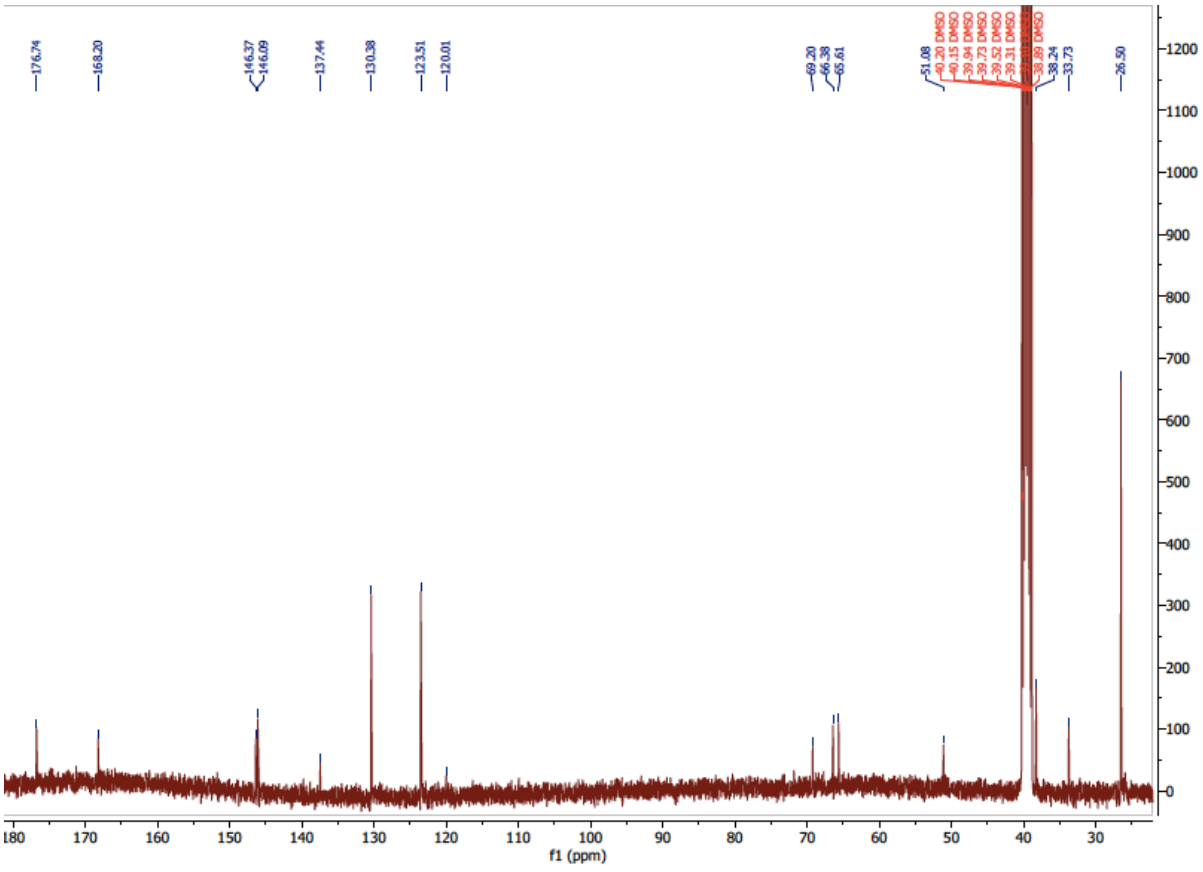



**Compound 21**

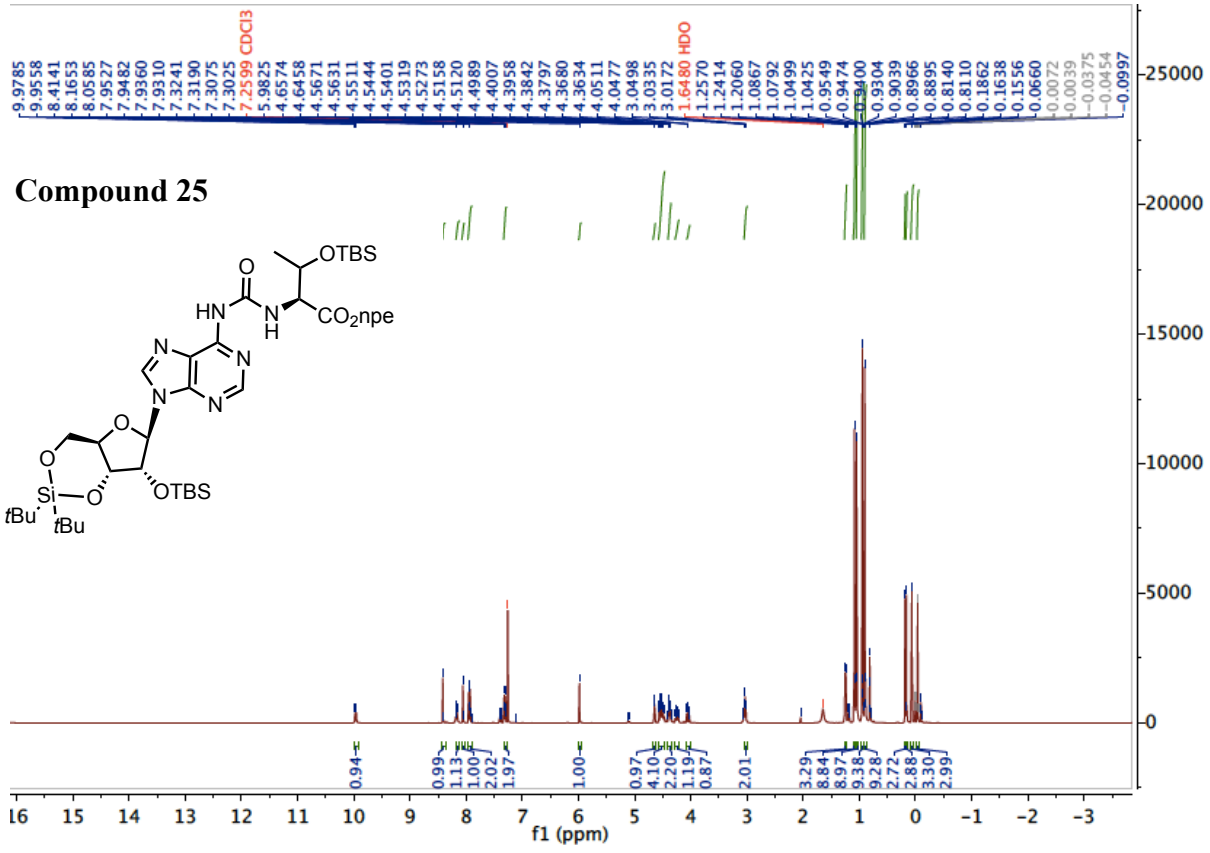


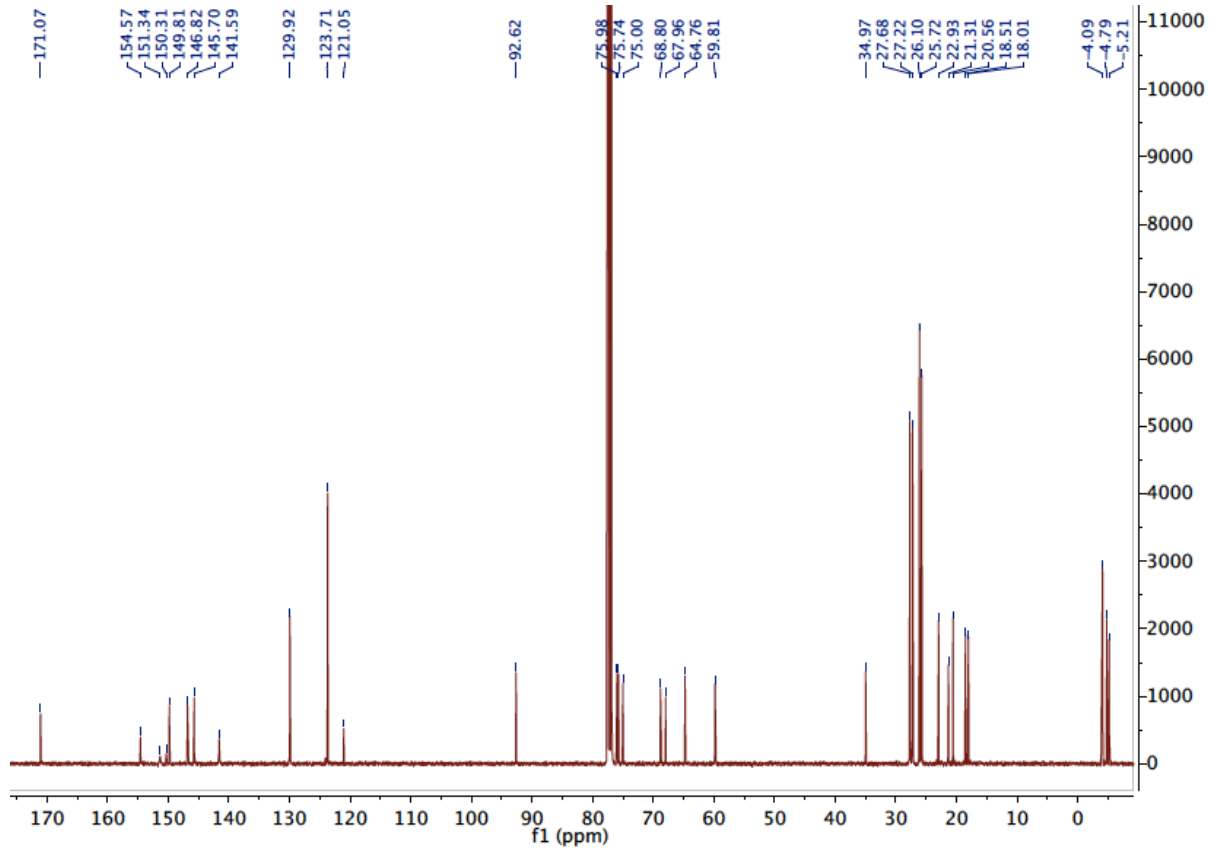




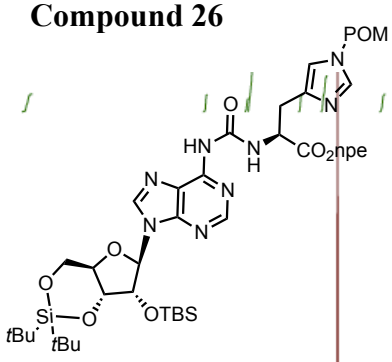


**Compound 25**


9.9785
9.9558
8.4141
8.1653
8.0585
7.9527
7.9482
7.9360
7.9310
7.3241
7.3190
7.3075
7.3025
7.2599 CDCl3
5.9825
4.6574
4.6458
4.5671
4.5631
4.5511
4.5444
4.5401
4.5319
4.5273
4.5158
4.5120
4.4989
4.4007
4.3958
4.3842
4.3797
4.3680
4.3634
4.0511
4.0477
3.0498
3.0335
3.0172
1.6480 HDO
1.2570
1.2414
1.2060
1.0867
1.0792
1.0499
1.0425
0.9549
0.9474
0.9400
0.9304
0.9039
0.8966
0.8895
0.8140
0.8110
0.1862
0.1638
0.1556
0.0660
0.0072
0.0039
-0.0375
-0.0454
-0.0997
OTBS
O
HN
N
H
CO2npe
N
N
N
N
O
O
Si
O
OTBS
tBu
tBu
0.94
0.99
1.13
1.00
2.02
1.97
1.00
0.97
4.10
2.20
1.19
0.87
2.01
3.29
8.84
8.97
9.38
9.28
2.72
2.88
3.30
2.99
f1 (ppm)

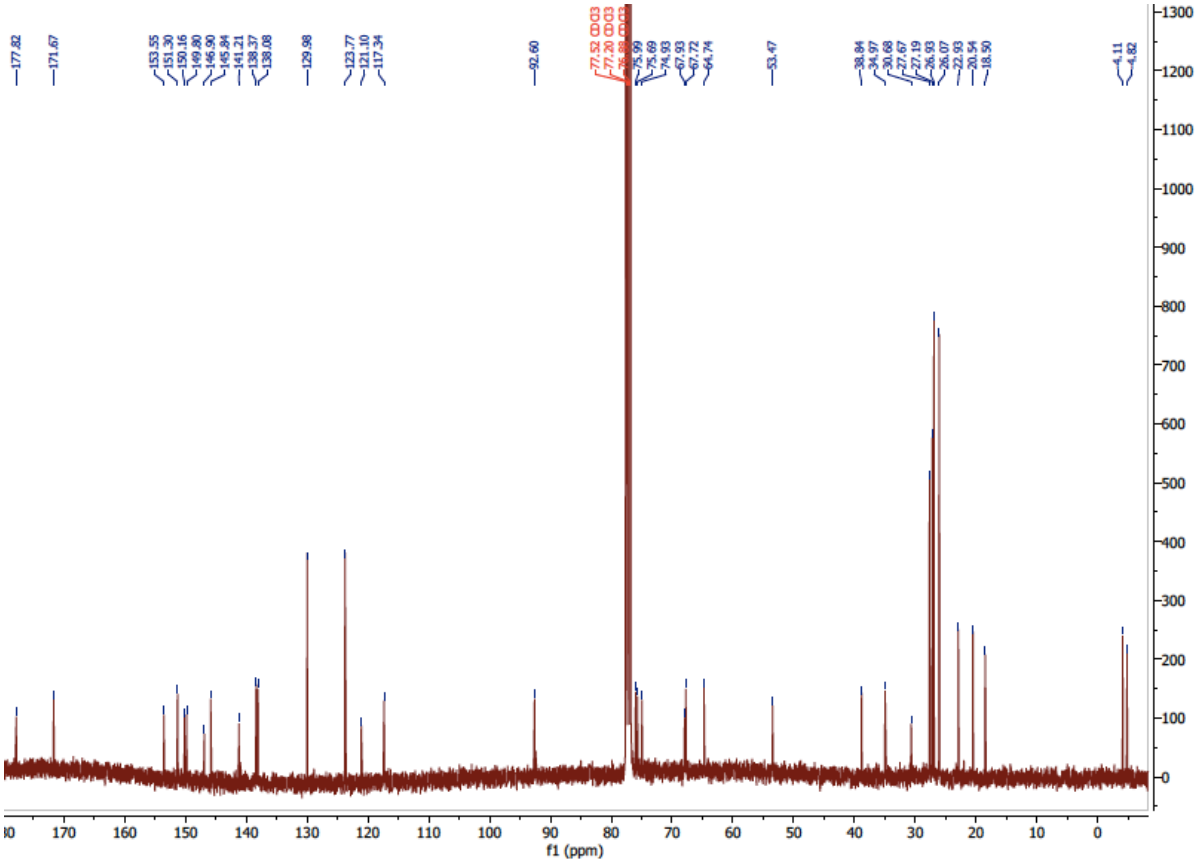

171.07
154.57
151.34
150.31
149.81
146.82
145.70
141.59
129.92
123.71
121.05
92.62
75.98
75.74
75.00
68.80
67.96
64.76
59.81
34.97
27.68
27.22
26.10
25.72
22.93
21.31
20.56
18.51
18.01
-4.09
-4.79
-5.21
f1 (ppm)

**Compound 26**

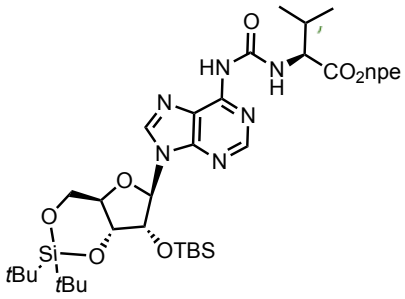






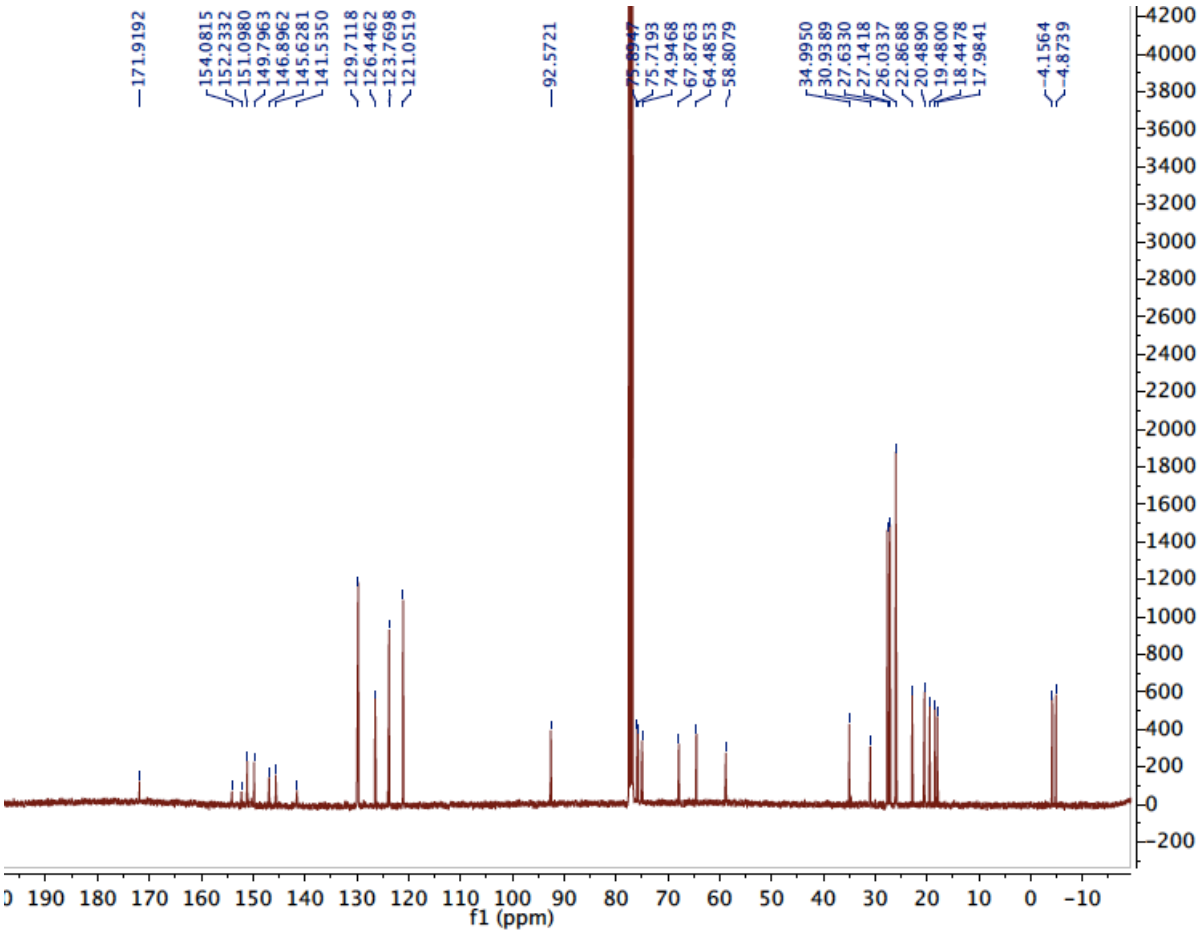


**Compound 27**

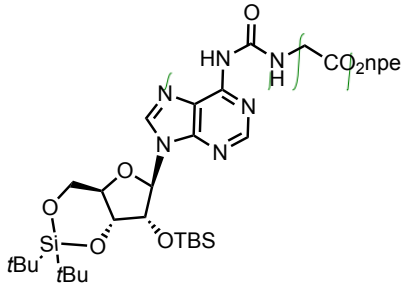




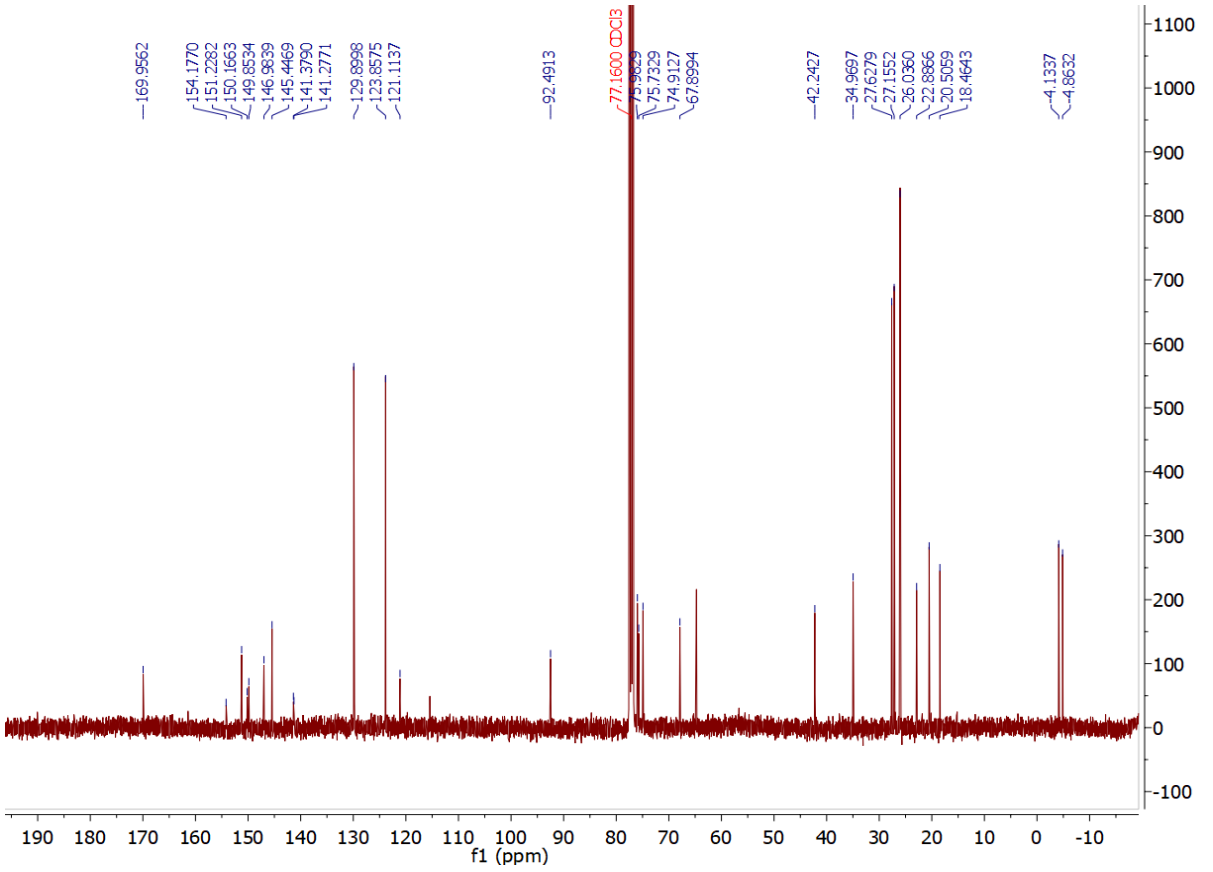




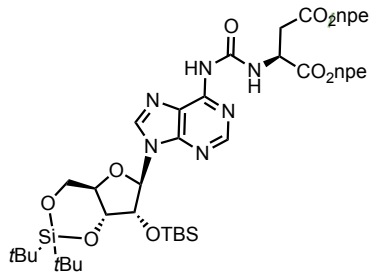
**Compound 28**


O
HN
N
H
CO2npe
N
N
N
N
O
O
Si
O
OTBS
tBu
tBu

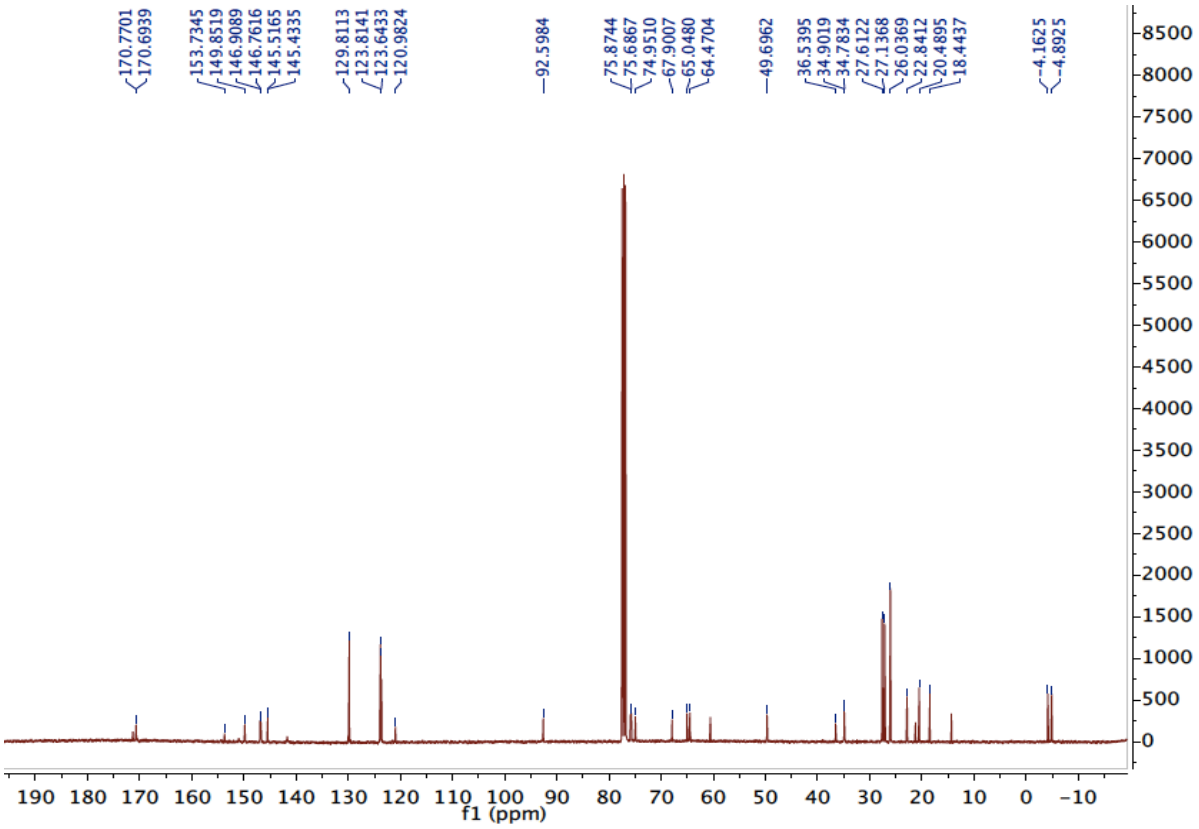

9.9445
8.5048
8.1342
8.1058
8.0848
7.3924
7.3710
7.2600 CDCl3
5.9834
4.6065
4.5953
4.5188
4.5060
4.4953
4.4833
4.4712
4.4640
4.4595
4.4475
4.4310
4.2774
4.2649
4.2520
4.2395
4.2274
4.2148
4.1992
4.1852
4.0864
4.0631
4.0373
3.1062
3.0897
3.0731
1.0794
1.0472
0.9403
0.1730
0.1551
0.95
1.01
3.13
2.07
1.10
1.00
4.15
3.15
1.15
2.05
9.16
10.16
9.56
6.16
f1 (ppm)

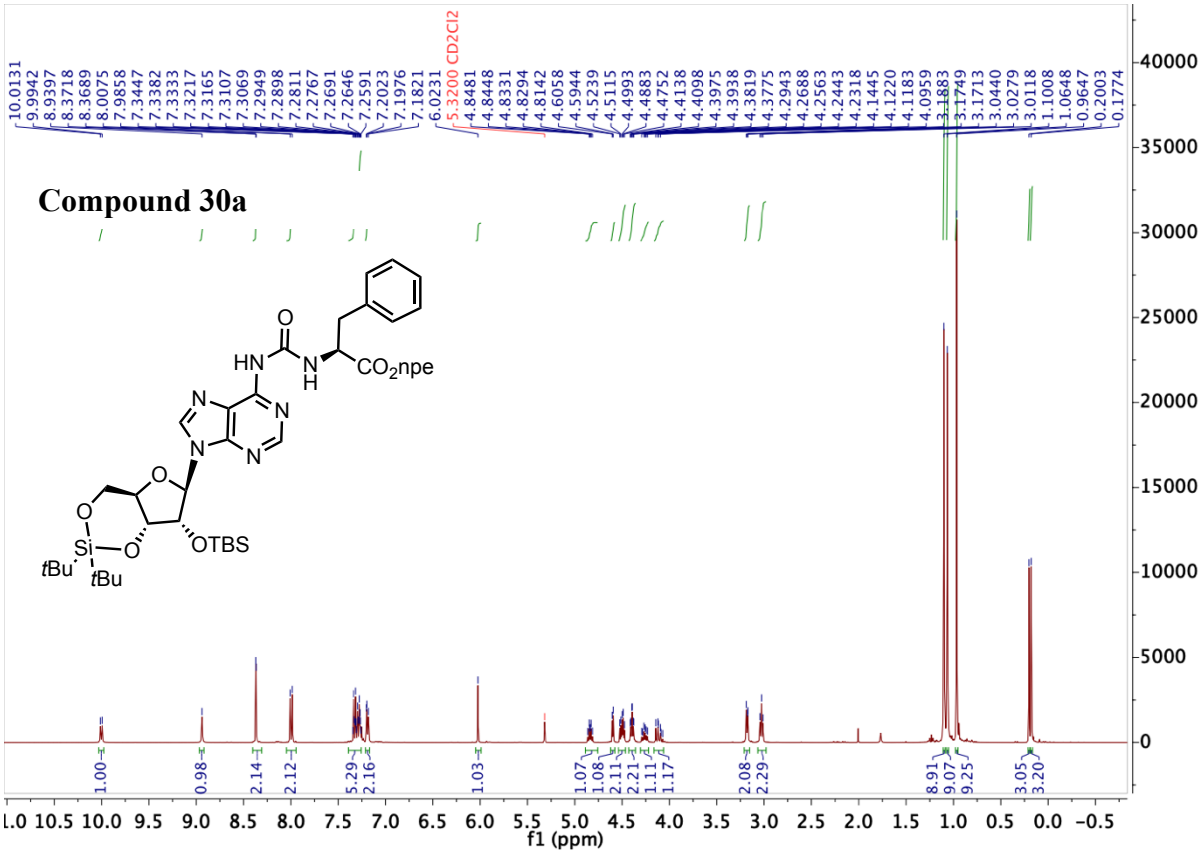

169.9562
154.1770
151.2282
150.1663
149.8534
146.9839
145.4469
141.3790
141.2771
129.8998
123.8575
121.1137
92.4913
77.1600 CDCl3
75.9629
75.7329
74.9127
67.8994
42.2427
34.9697
27.6279
27.1552
26.0360
22.8866
20.5059
18.4643
-4.1337
-4.8632
f1 (ppm)

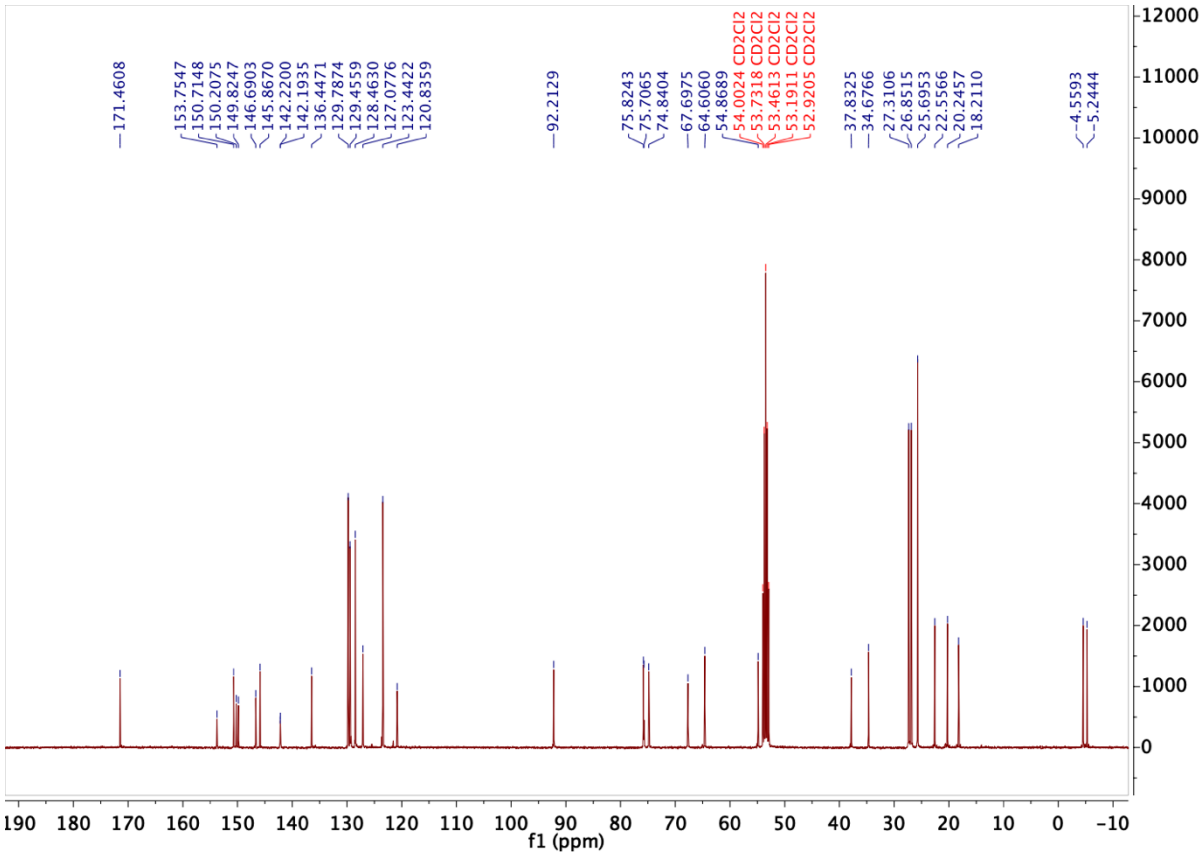
**Compound 29**

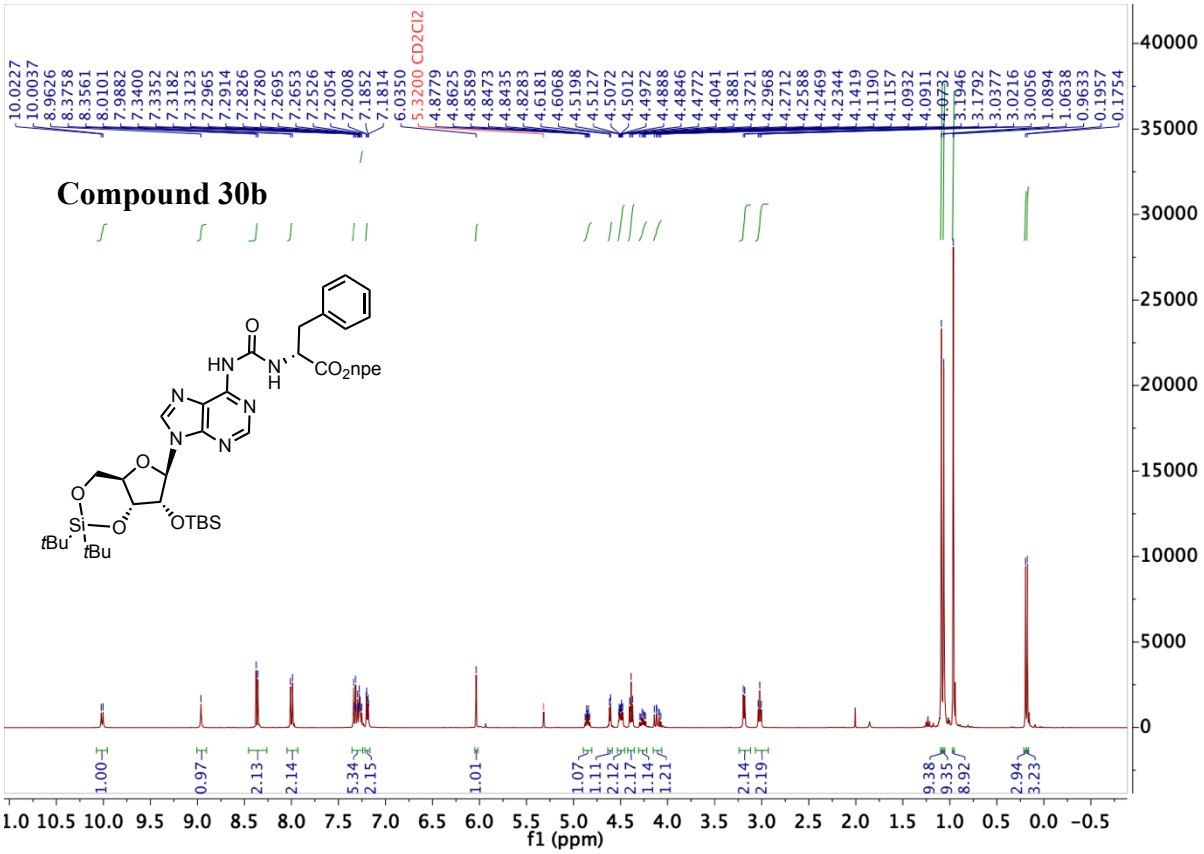

CO2npe
CO2npe
HN
O
N
H
N
N
N
N
O
O
Si
O
OTBS
tBu
tBu

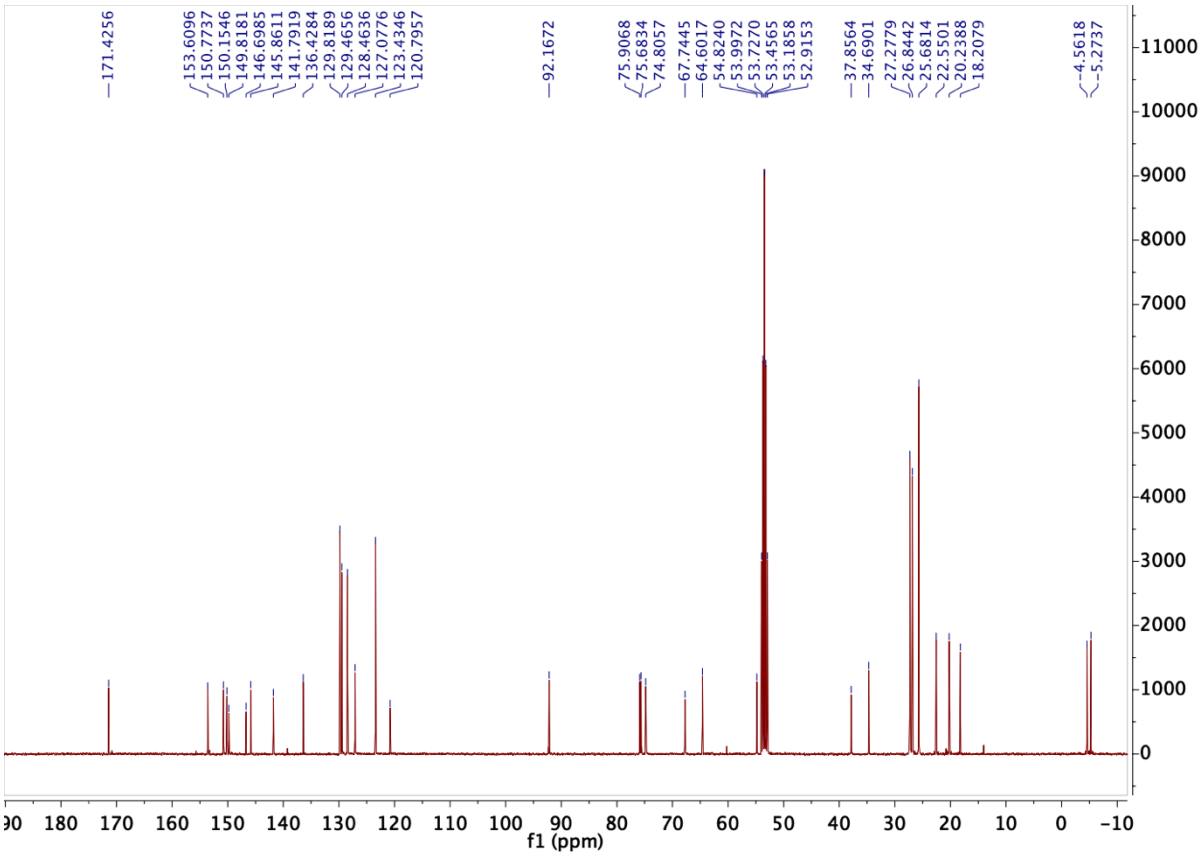

CDCl3
f1 (ppm)


f1 (ppm)

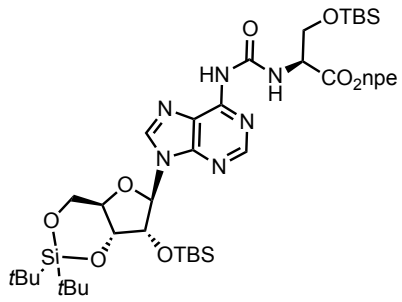

Compound 30a
HN
O
N
H
N
CO2npe
N
N
N
O
O
Si
O
OTBS
tBu
tBu
f1 (ppm)


f1 (ppm)

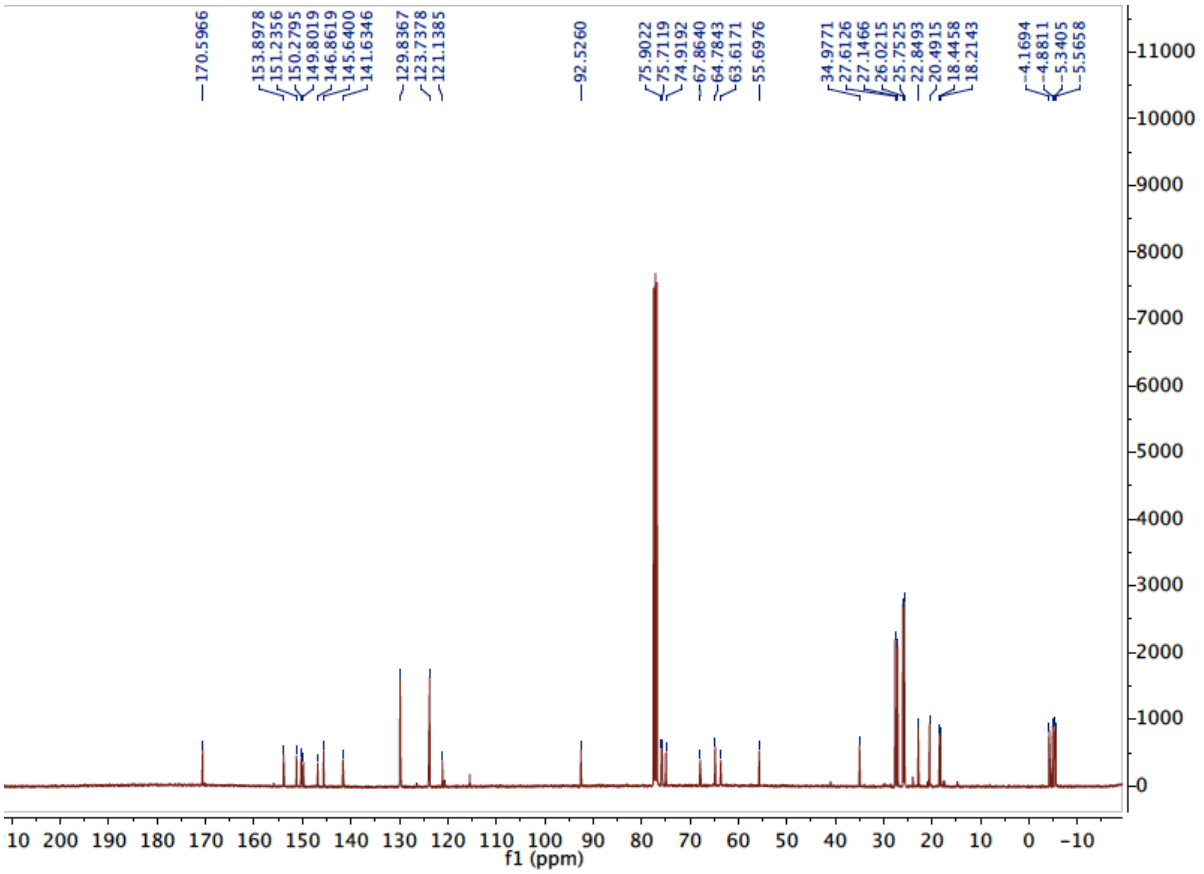

Compound 30b
CD2Cl2
f1 (ppm)


f1 (ppm)

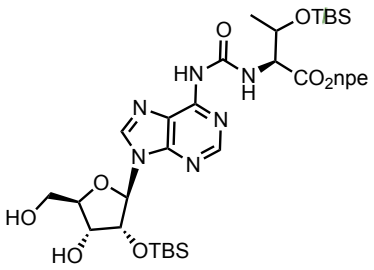
**Compound 31**


OTBS
O
HN
N
H
CO2npe
N
N
N
N
O
O
Si
O
OTBS
tBu
tBu


10.1944
10.1736
8.6125
8.4449
8.1930
8.0311
8.0096
7.3647
7.3429
7.2604 CDCl3
5.9892
4.7371
4.7301
4.7231
4.7163
4.7094
4.7022
4.6148
4.6033
4.5345
4.5228
4.5102
4.4980
4.4862
4.4734
4.4416
4.4254
4.4090
4.2759
4.2633
4.2506
4.2380
4.2259
4.2134
4.1522
4.1454
4.1268
4.1202
4.0980
4.0749
4.0715
4.0489
3.9304
3.9226
3.9051
3.8974
3.0785
3.0622
3.0459
1.0826
1.0474
0.9400
0.8826
0.1844
0.1761
0.1555
0.1454
0.0440
0.0077
0.97
0.91
0.96
1.08
1.98
2.08
1.00
0.99
1.06
2.09
2.16
1.11
1.00
1.17
1.03
2.30
8.99
9.34
8.80
9.51
2.74
3.21
2.90
3.27
f1 (ppm)

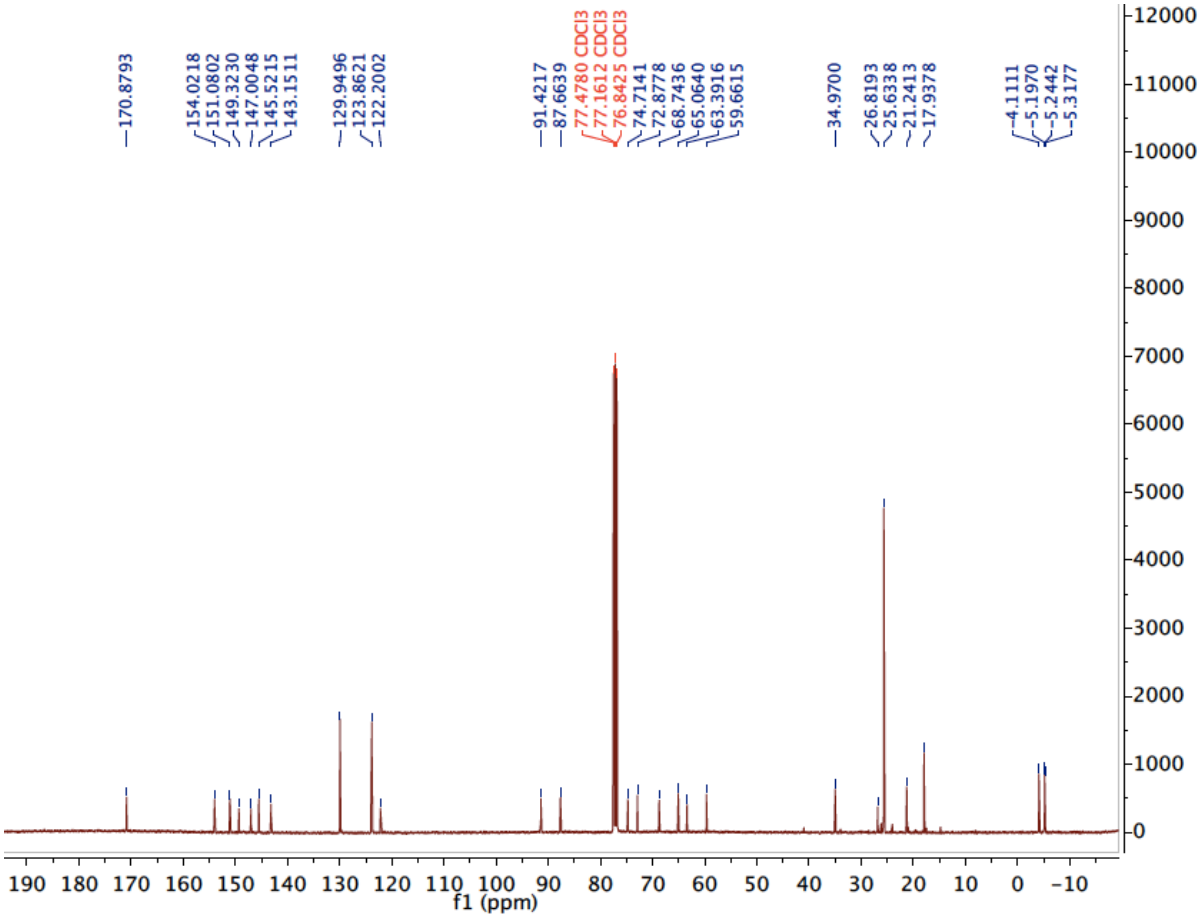

170.5966
153.8978
151.2356
150.2795
149.8019
146.8619
145.6400
141.6346
129.8367
123.7378
121.1385
92.5260
75.9022
75.7119
74.9192
67.8640
64.7843
63.6171
55.6976
34.9771
27.6126
27.1466
26.0215
25.7525
22.8493
20.4915
18.4458
18.2143
-4.1694
-4.8811
-5.3405
-5.5658
f1 (ppm)

**Compound 32**

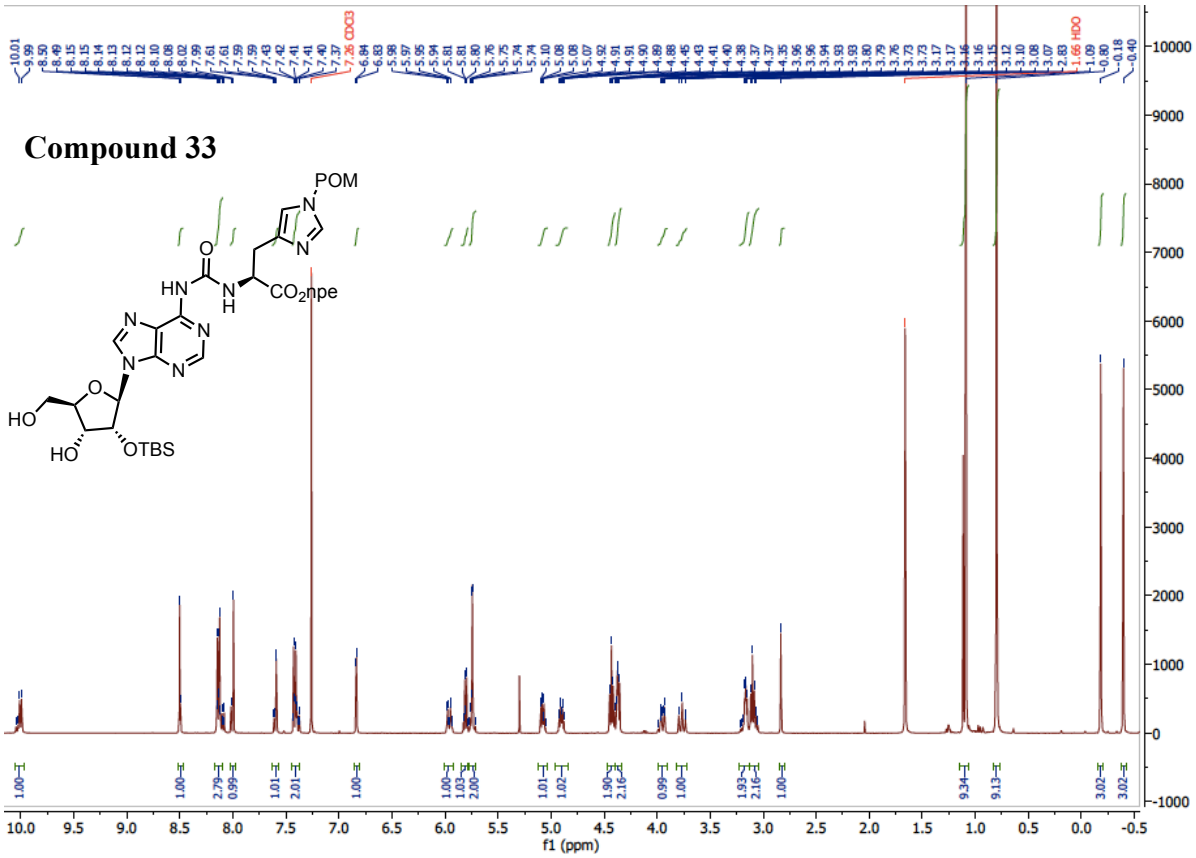


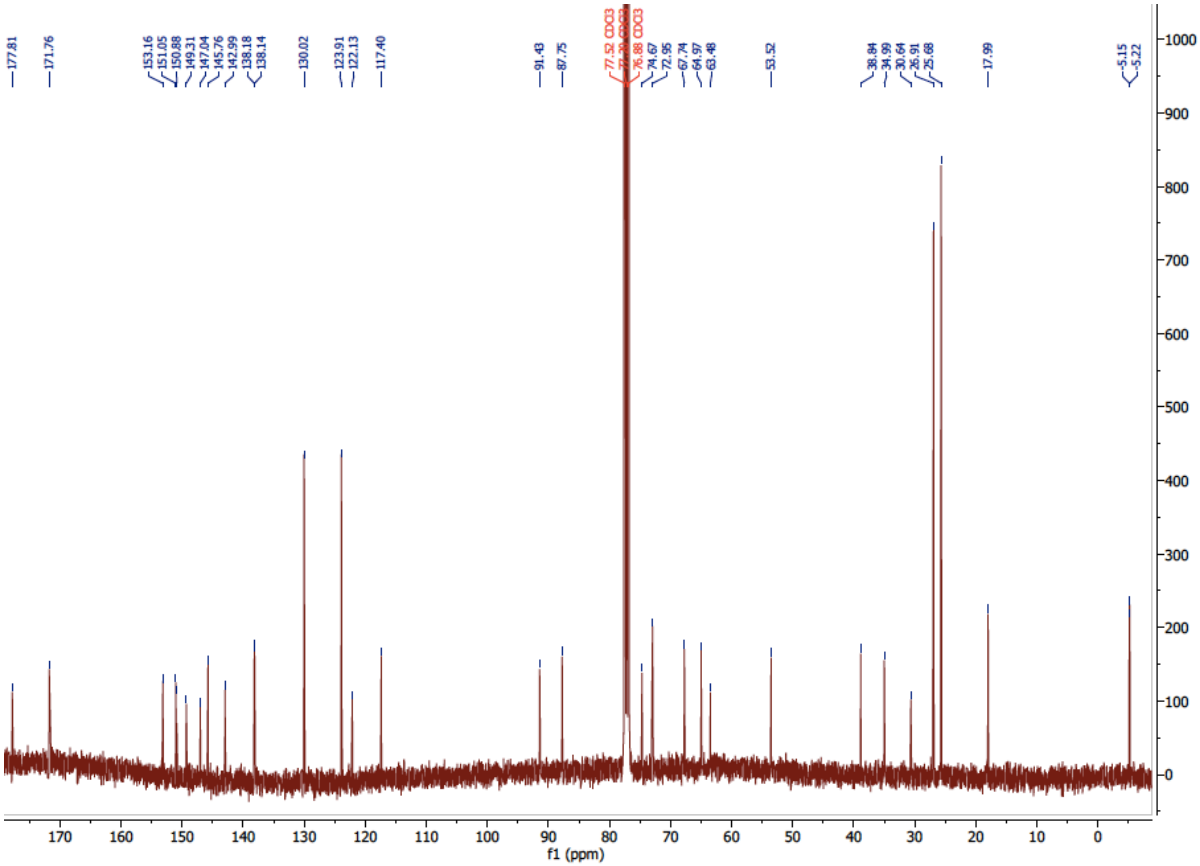




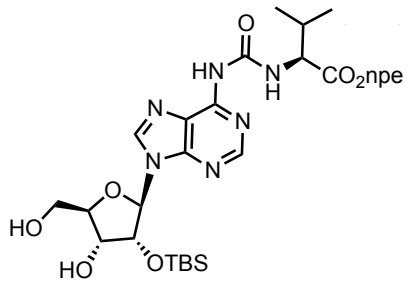


**Compound 33**

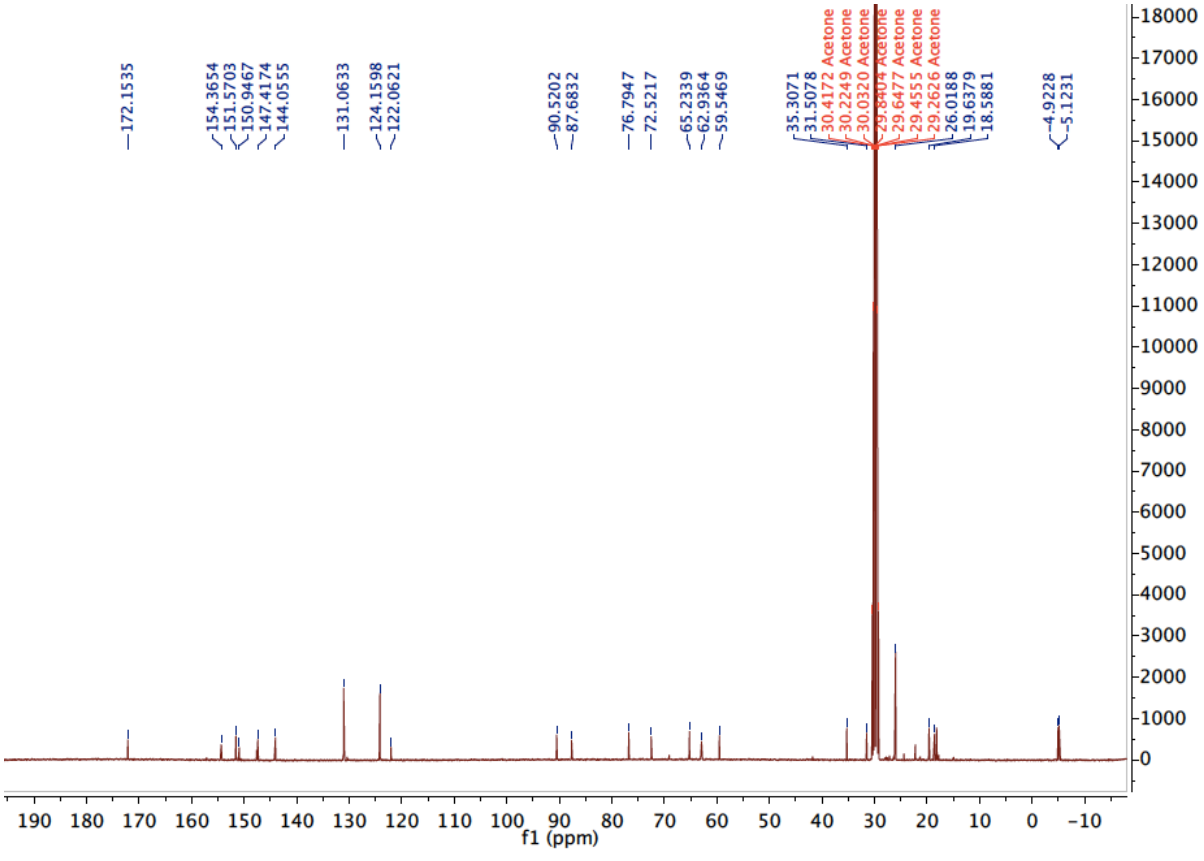


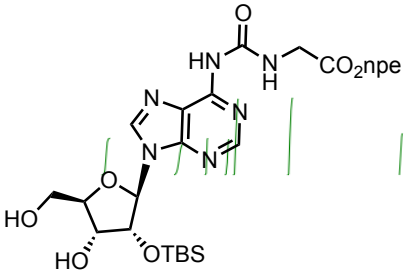
**Compound 34**


O
HN
N
H
CO2npe
N
N
N
N
O
HO
HO
OTBS

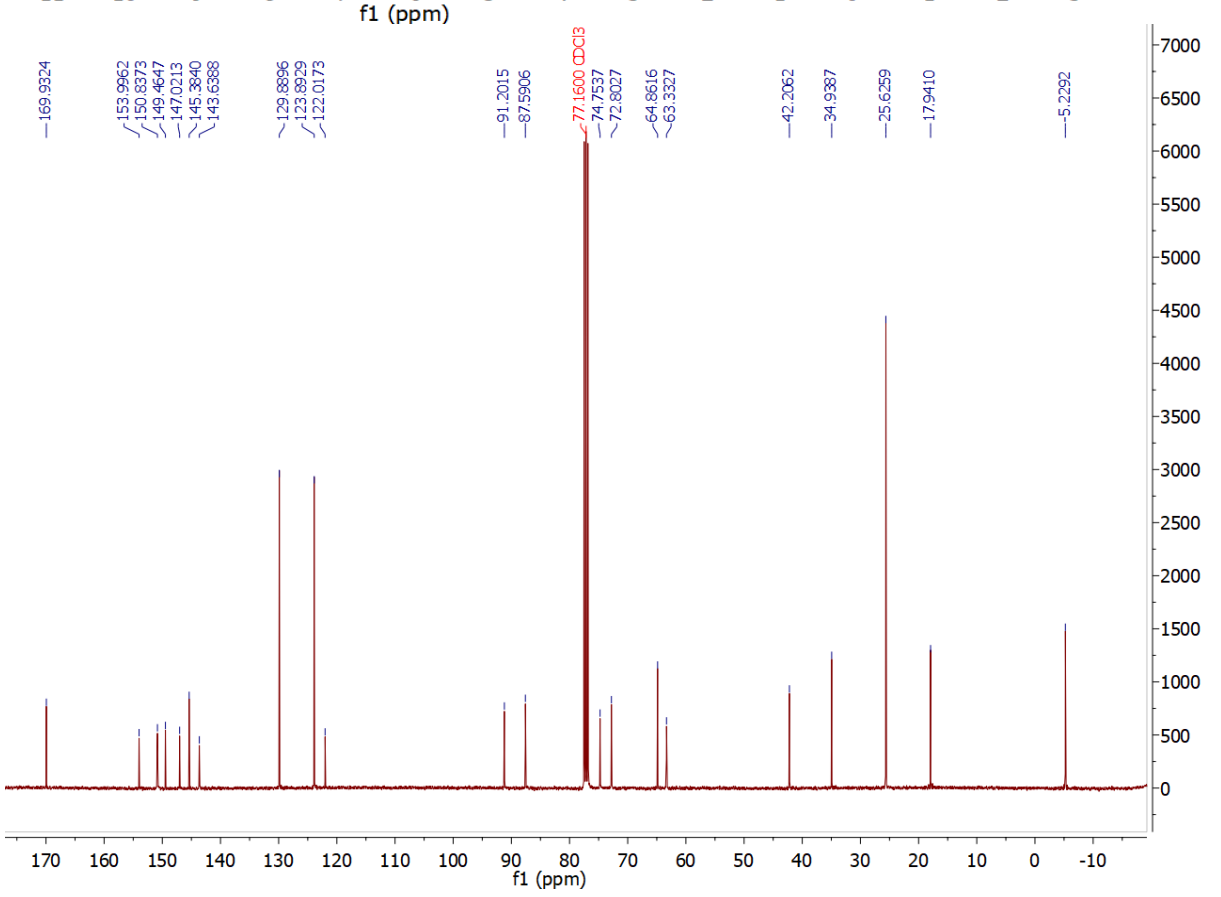

10.0274
10.0069
9.0762
8.7137
8.6203
8.1258
8.1038
7.6075
7.5857
7.1294
6.1145
5.0819
5.0699
4.9973
4.9857
4.9825
4.9706
4.5181
4.5067
4.4905
4.4792
4.4741
4.4636
4.4561
4.4516
4.4481
4.4441
4.4358
4.4237
4.4203
4.4079
4.4039
4.3970
4.3927
4.3860
4.2320
4.2256
4.2192
4.2129
4.0422
4.0323
3.9002
3.8971
3.8913
3.7917
3.7853
3.1834
3.1675
3.1516
2.8819 HDO
2.2369
2.2249
2.0609 Acetone
2.0554 Acetone
2.0499 Acetone
2.0444 Acetone
2.0389 Acetone
1.0037
0.9866
0.9652
0.9479
0.8039
-0.0670
-0.2006
1.00
0.76
1.00
0.90
2.10
2.23
1.00
0.79
1.00
4.57
1.03
0.86
1.01
1.01
2.14
1.09
3.57
3.38
9.54
3.06
3.04
f1 (ppm)


172.1535
154.3654
151.5703
150.9467
147.4174
144.0555
131.0633
124.1598
122.0621
90.5202
87.6832
76.7947
72.5217
65.2339
62.9364
59.5469
35.3071
31.5078
30.4172 Acetone
30.2249 Acetone
30.0320 Acetone
29.6404 Acetone
29.6477 Acetone
29.4555 Acetone
29.2626 Acetone
26.0188
19.6379
18.5881
-4.9228
-5.1231
f1 (ppm)

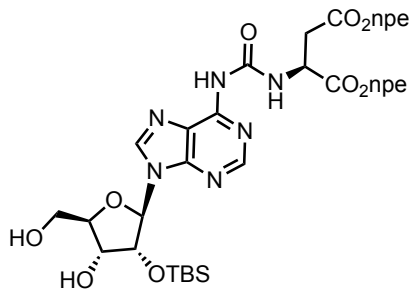
**Compound 35**


O
HN
N
H
CO2npe
N
N
N
N
O
HO
HO
OTBS


9.9314
9.9173
9.9030
8.9130
8.5374
8.2506
8.1438
8.1222
7.4001
7.3785
7.2600 CDCl3
5.8779
5.8599
5.0861
5.0745
5.0682
5.0565
4.4588
4.4422
4.4255
4.3729
4.3600
4.2125
4.1995
4.1865
3.9806
3.9516
3.7823
3.7507
3.1090
3.0924
3.0757
2.9403
0.7849
0.1920
0.3786
1.00
0.84
1.00
0.97
2.07
2.09
1.13
1.04
2.08
2.11
2.12
1.03
1.02
2.10
0.92
9.50
3.10
3.08
f1 (ppm)

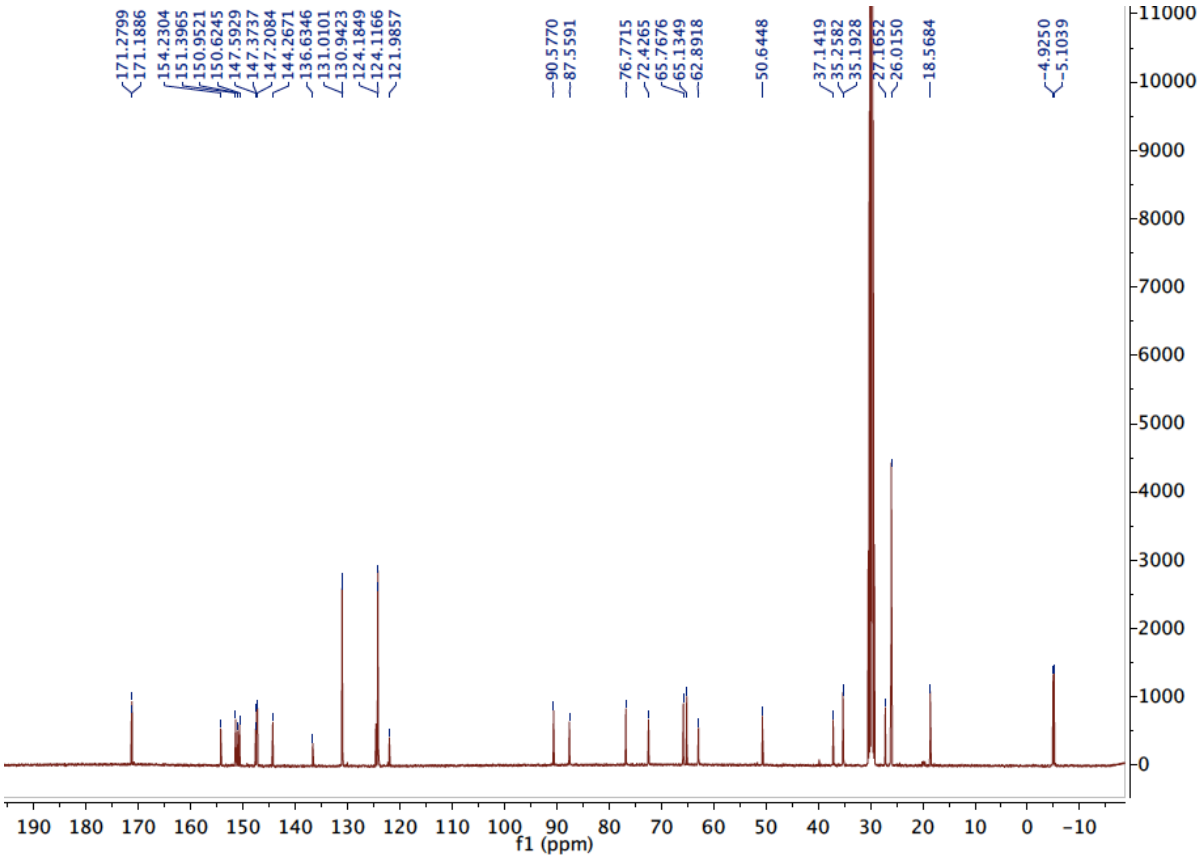

169.9324
153.9962
150.8373
149.4647
147.0213
145.3840
143.6388
129.8896
123.8929
122.0173
91.2015
87.5906
77.1600 CDCl3
74.7537
72.8027
64.8616
63.3327
42.2062
34.9387
25.6259
17.9410
-5.2292
f1 (ppm)

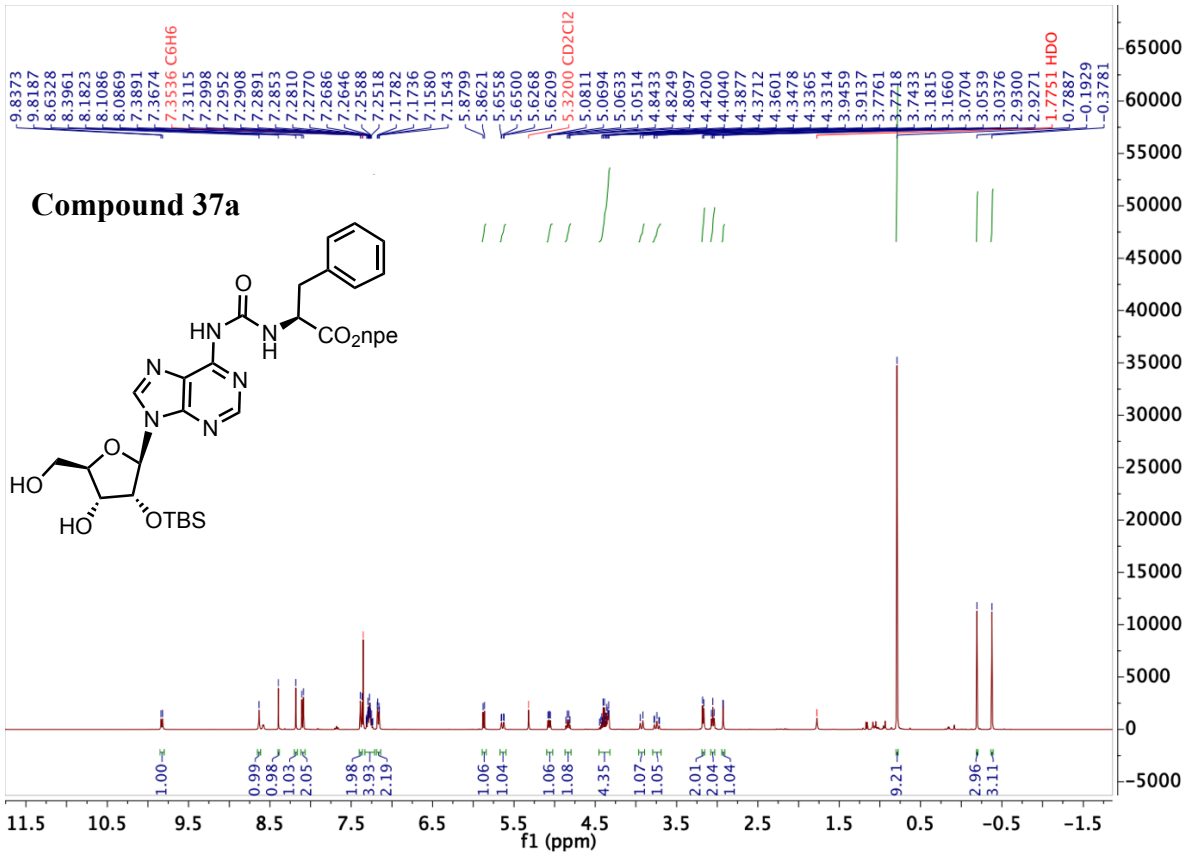
**Compound 36**

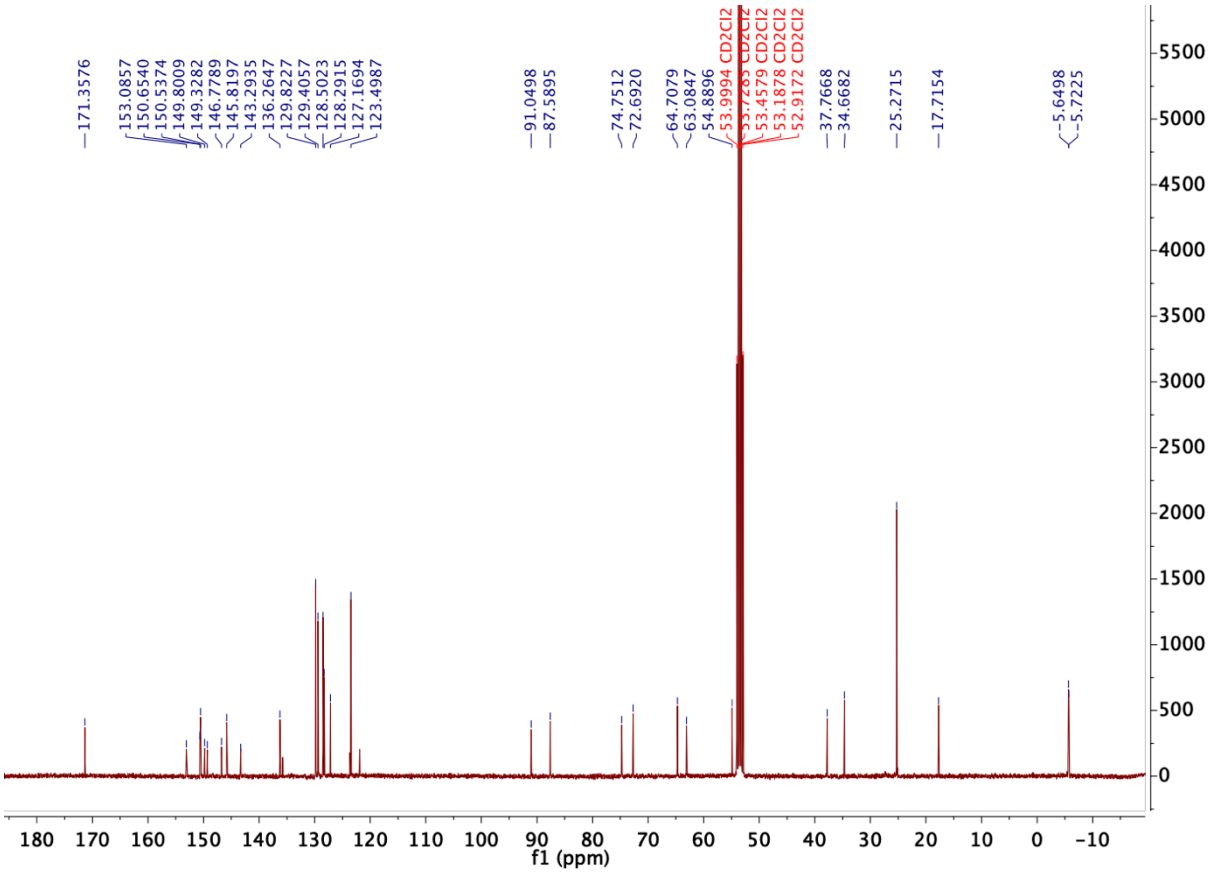




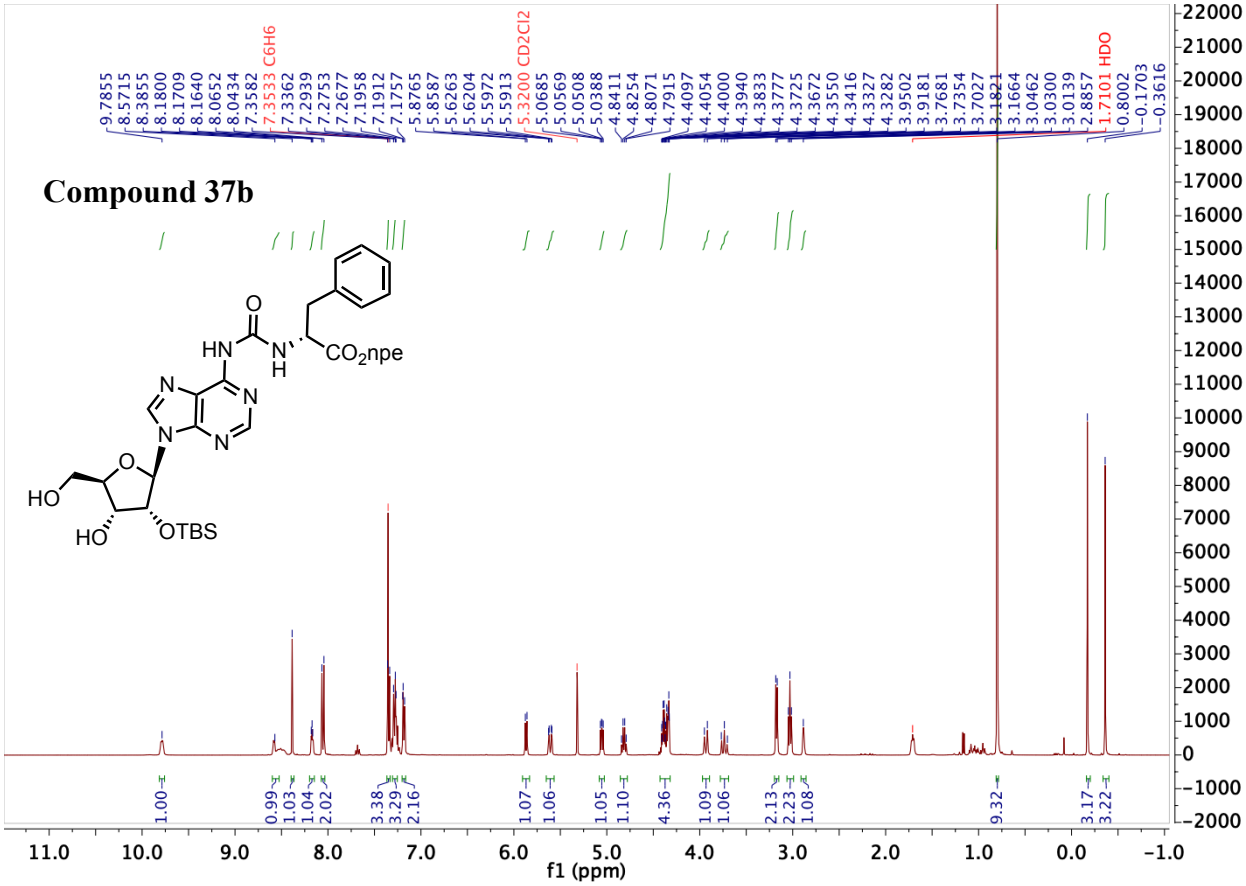


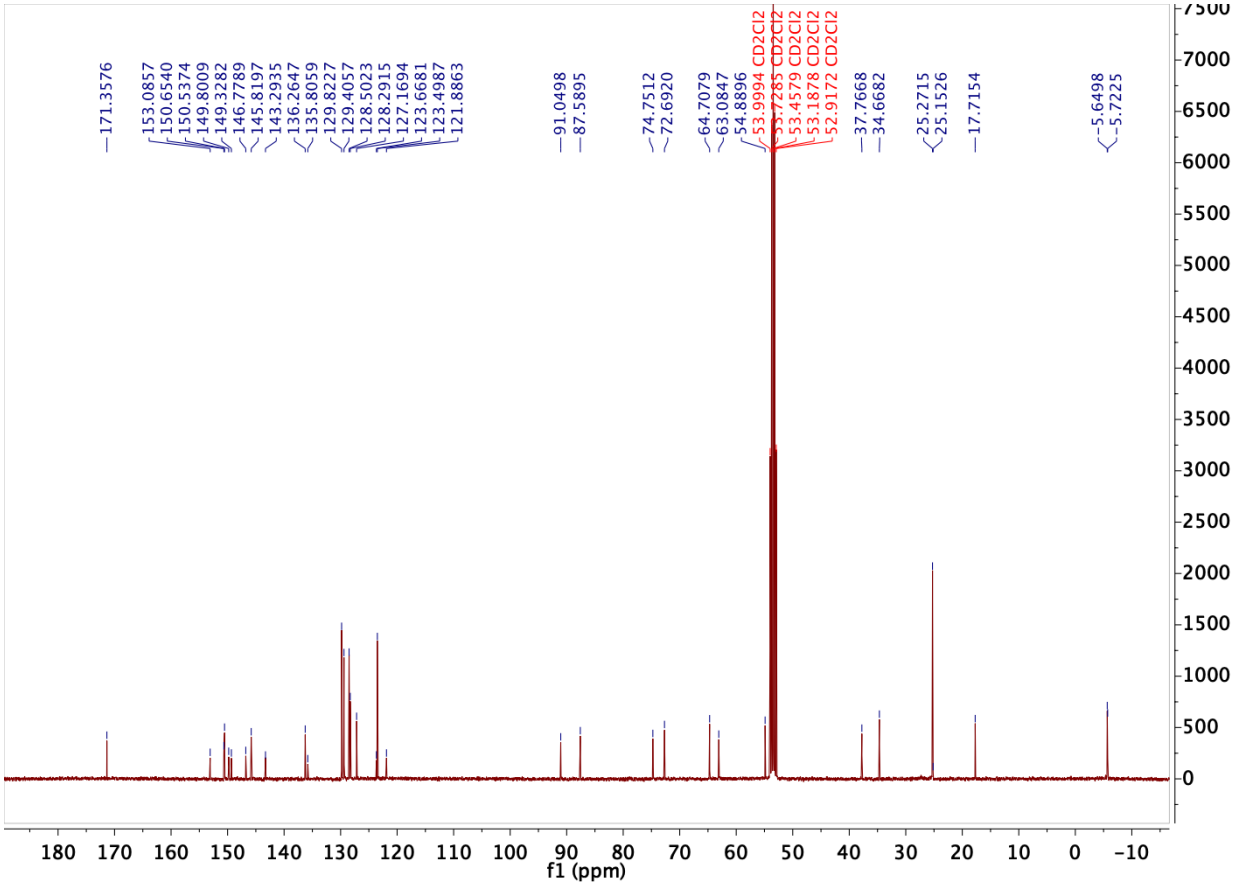



Compound 37a
HN
O
N
H
CO2npe
HO
HO
OTBS
f1 (ppm)

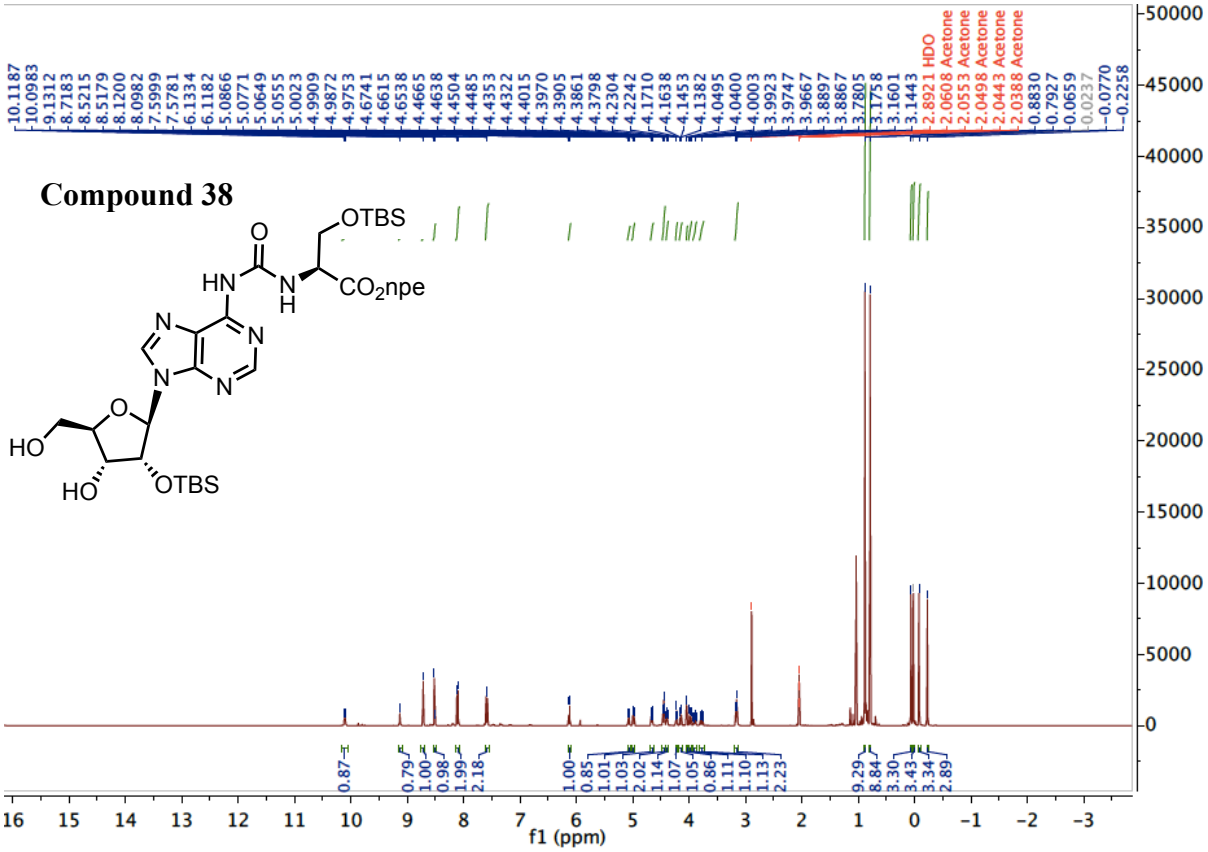

f1 (ppm)

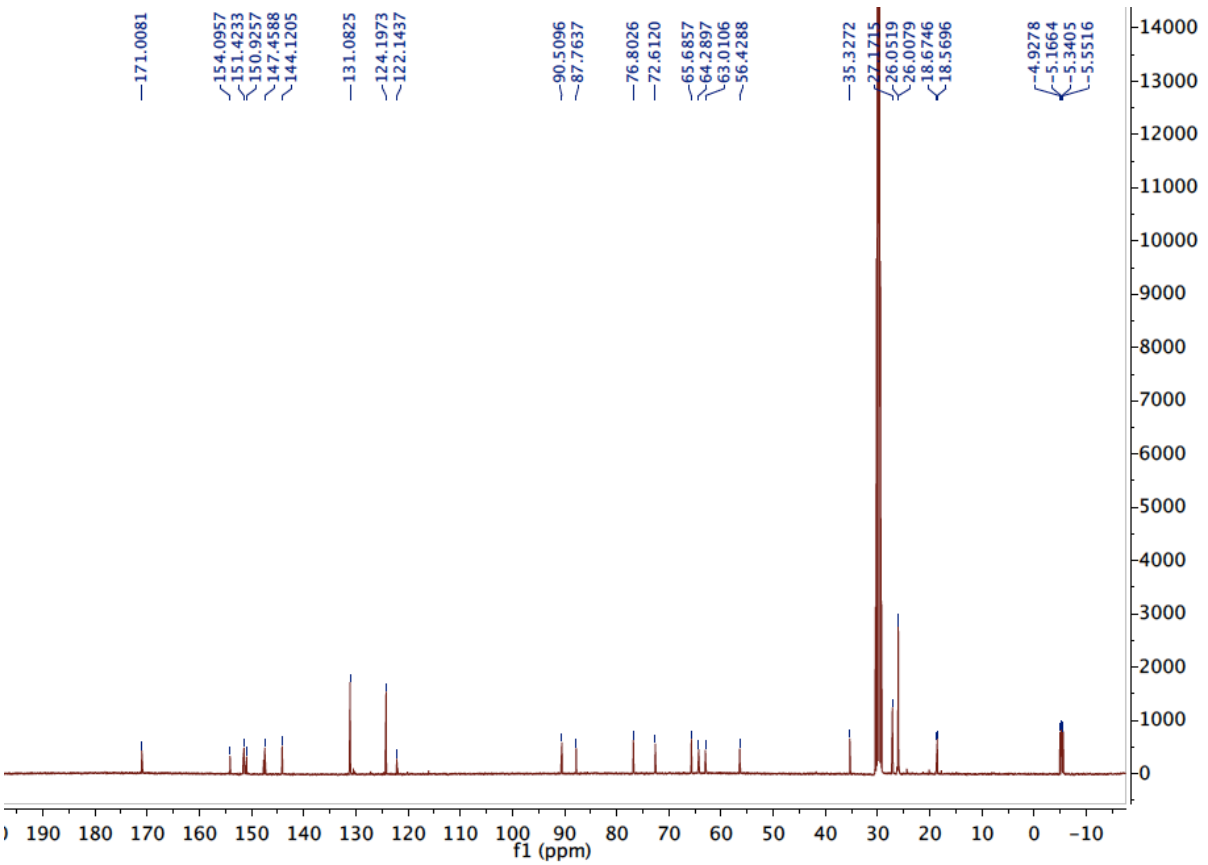
**Compound 37b**



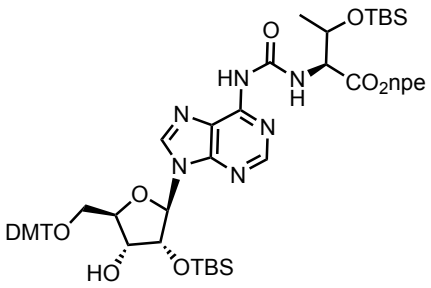



**Compound 38**

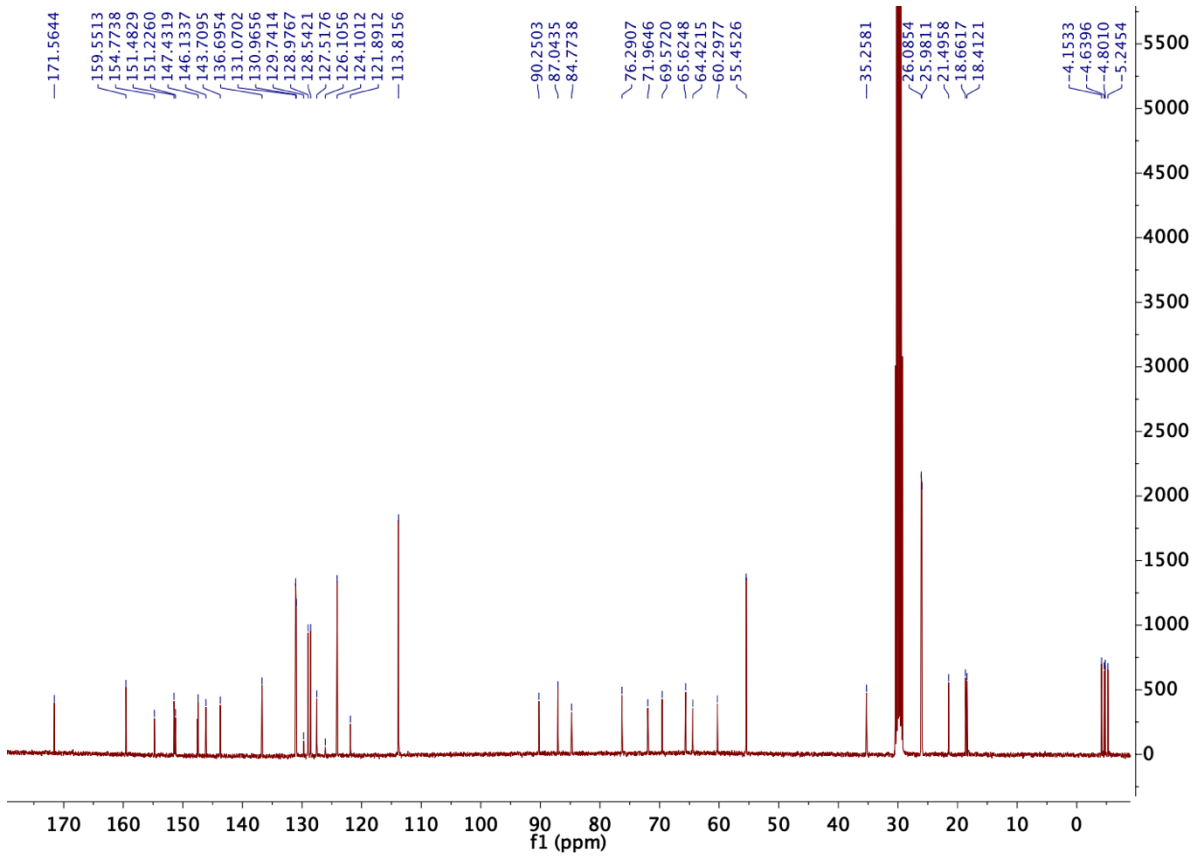


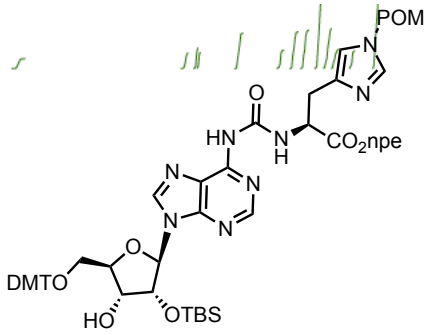
**Compound 39**


OTBS
O
HN
N
H
CO2npe
N
N
N
N
O
DMTO
HO
OTBS


8.9466
8.5607
8.4027
8.0231
8.0014
7.5382
7.5166
7.5081
7.5041
7.4865
7.4838
7.3826
7.3760
7.3705
7.3657
7.3601
7.3535
7.2641
7.2598
7.2445
7.1935
6.8484
6.8434
6.8397
6.8340
6.8314
6.8261
6.8220
6.8174
6.1692
6.1581
5.1649
4.5650
4.5615
4.5499
4.5455
4.5345
4.5306
4.4102
4.3947
3.7541
3.4849
3.4769
3.1344
3.1189
2.8742
2.8686
2.0609 Acetone
2.0554 Acetone
2.0499 Acetone
2.0444 Acetone
2.0389 Acetone
1.2811
1.2656
0.9158
0.9084
0.9011
0.8594
0.8518
0.8448
0.0907
0.0641
-0.0255
-0.0377
1.01
0.73
1.01
0.99
2.01
4.12
4.26
3.91
4.26
1.00
1.02
3.22
2.13
1.06
0.73
6.42
2.05
2.08
3.33
9.66
9.85
3.05
3.10
2.85
3.10
f1 (ppm)

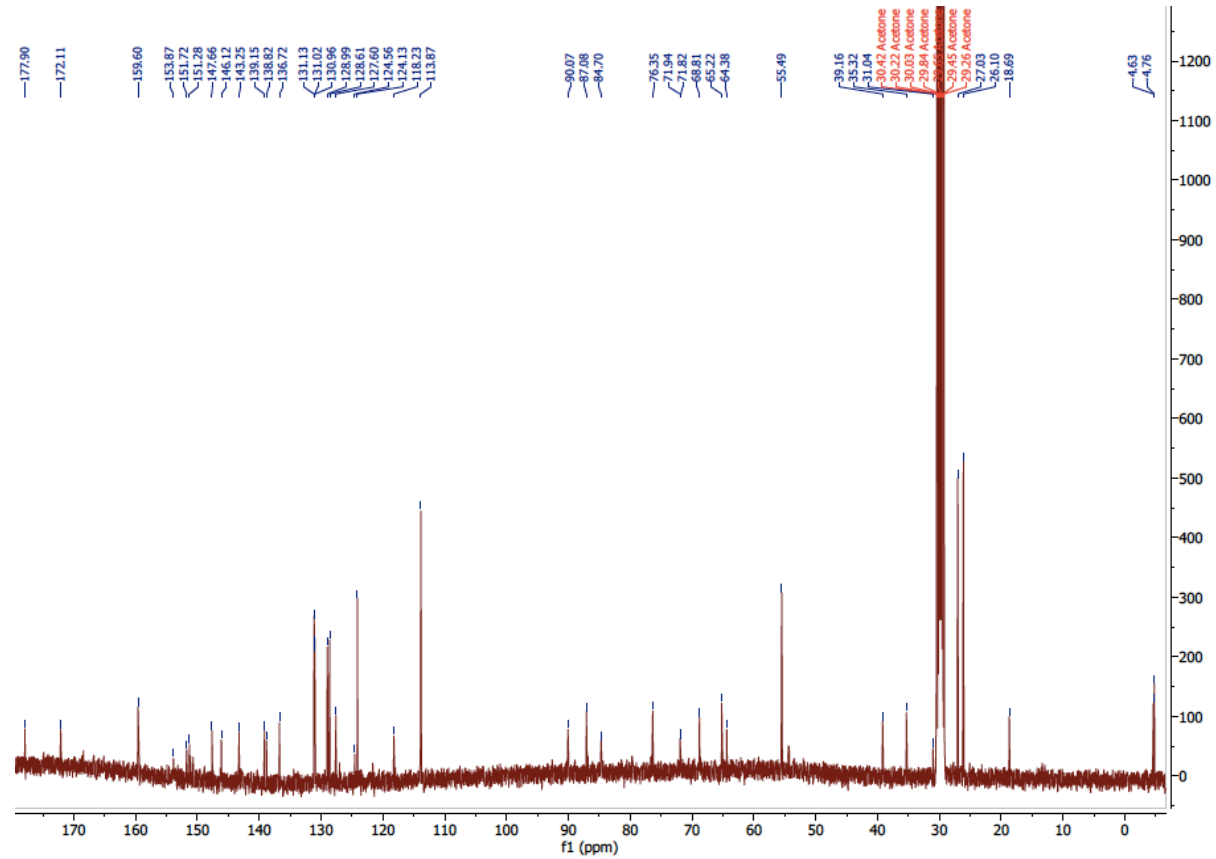

171.5644
159.5513
154.7738
151.4829
151.2260
147.4319
146.1337
143.7095
136.6954
131.0702
130.9656
129.7414
128.9767
128.5421
127.5176
126.1056
124.1012
121.8912
113.8156
90.2503
87.0435
84.7738
76.2907
71.9646
69.5720
65.6248
64.4215
60.2977
55.4526
35.2581
26.0854
25.9811
21.4958
18.6617
18.4121
-4.1533
-4.6396
-4.8010
-5.2454
f1 (ppm)

**Compound 40**

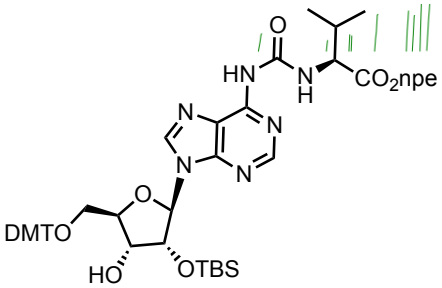






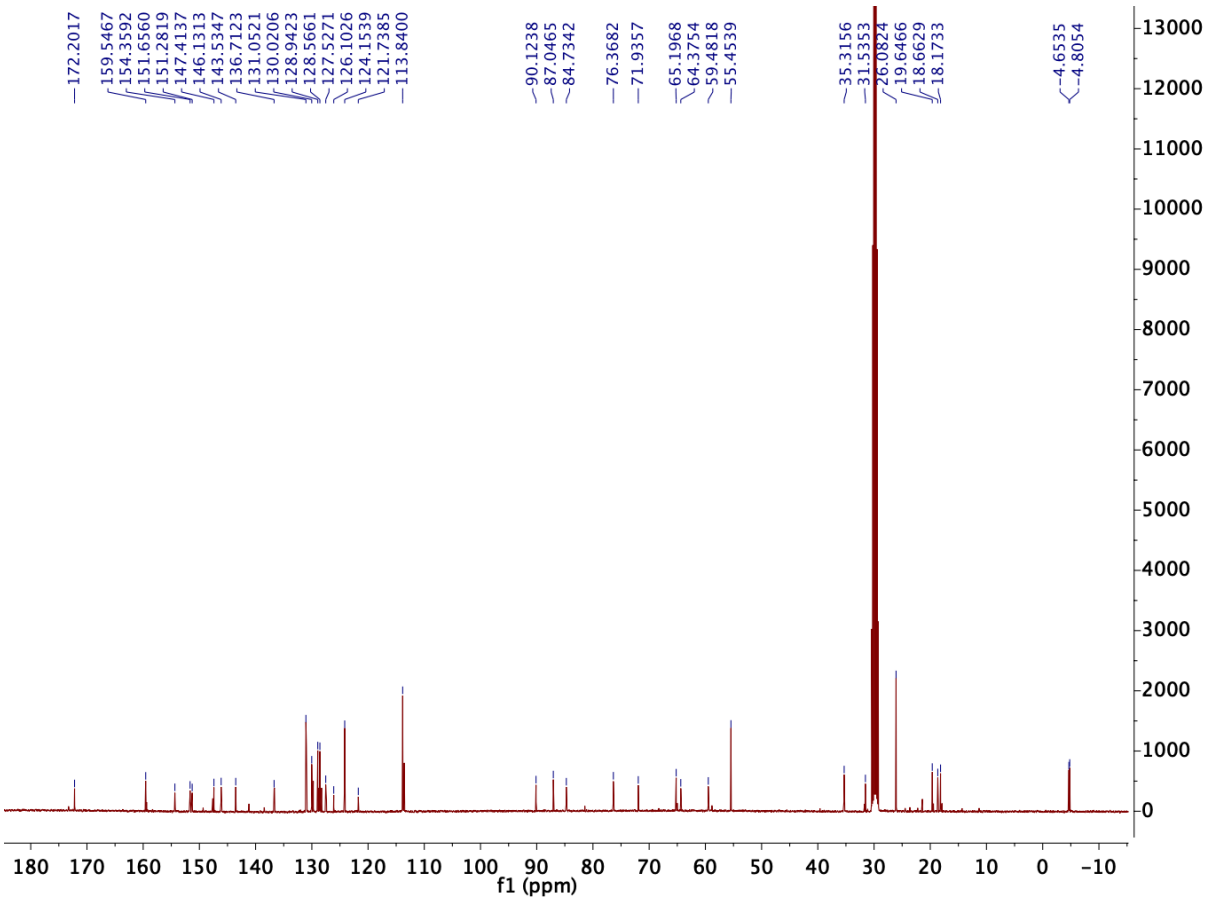


**Compound 41**

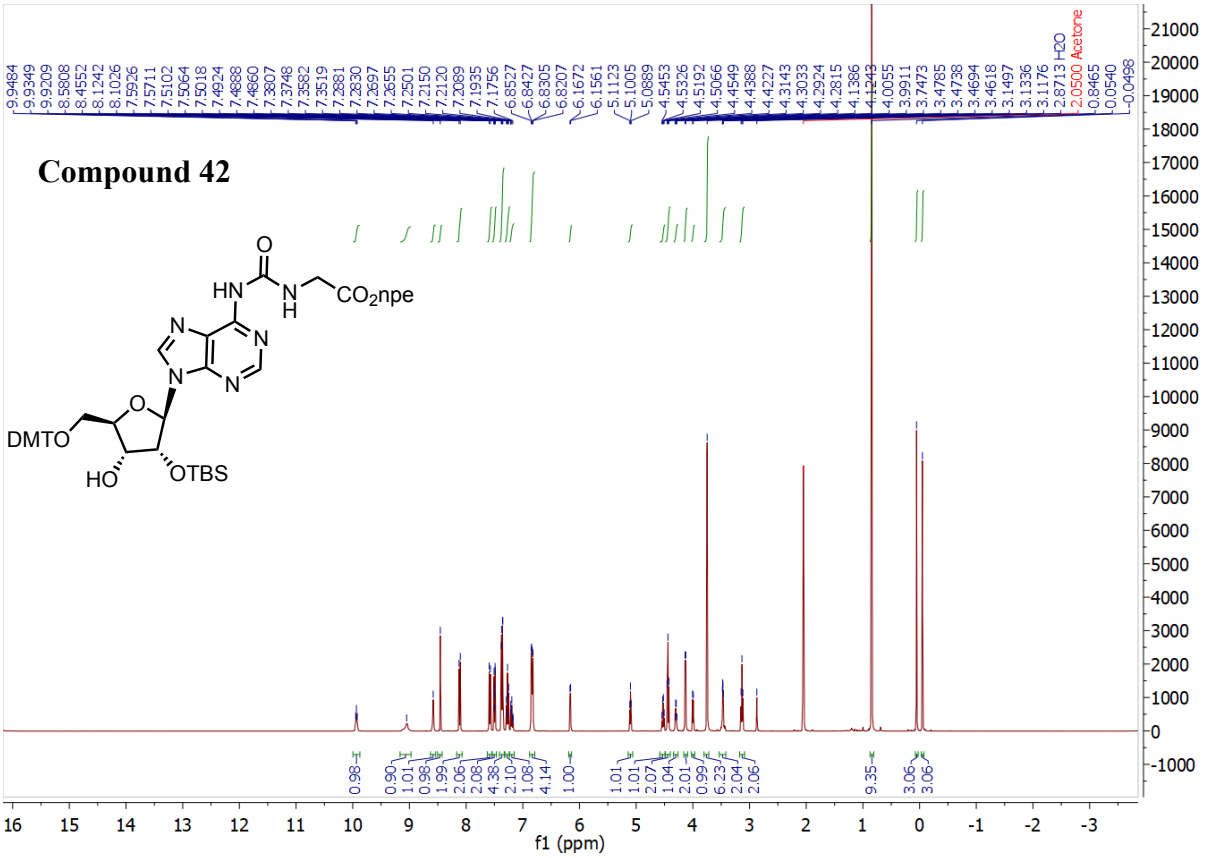






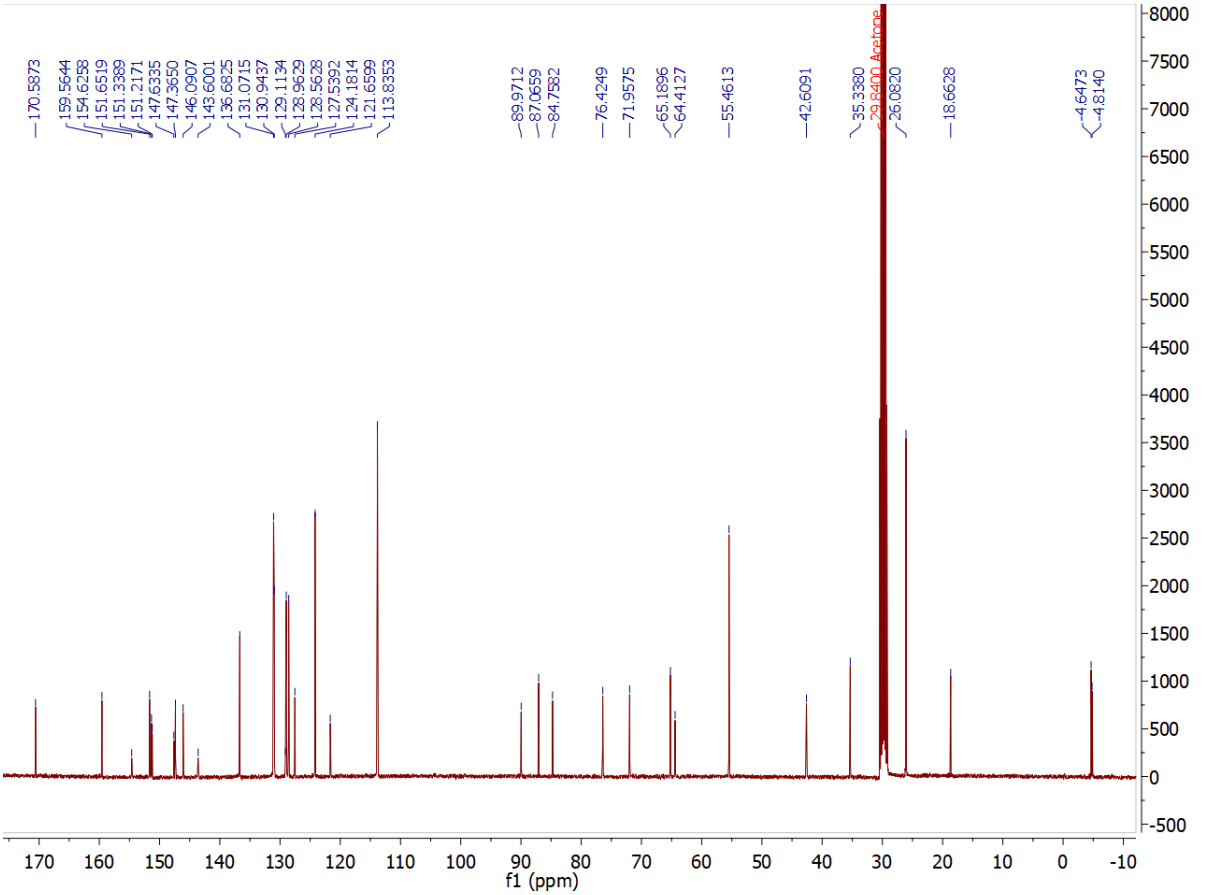


**Compound 42**

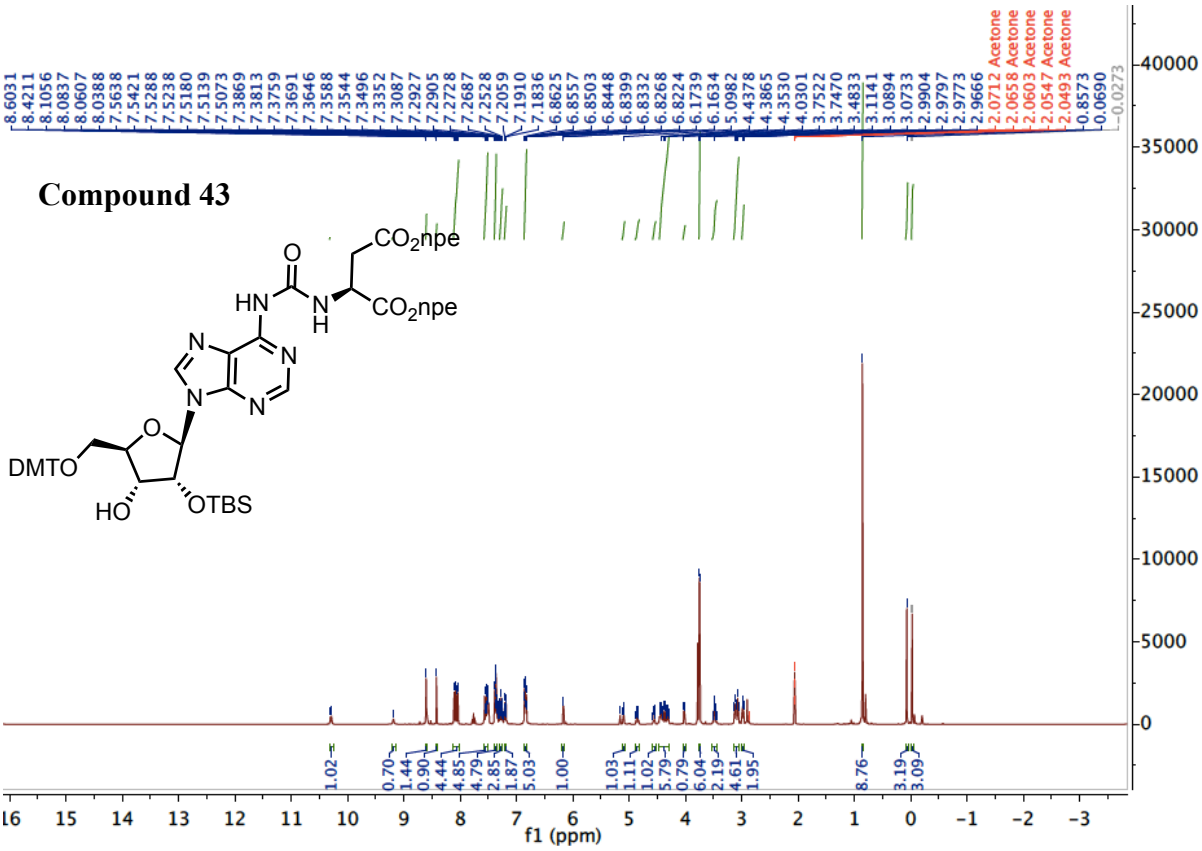


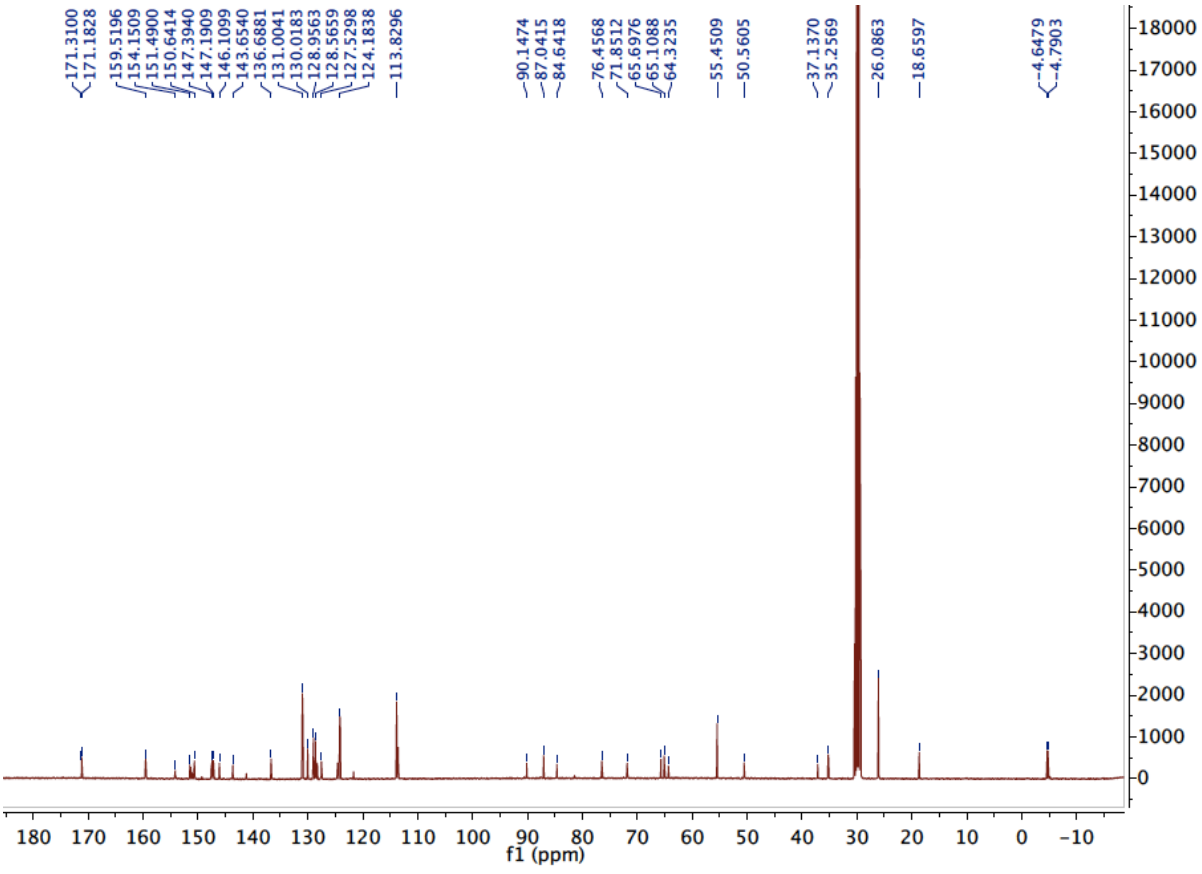


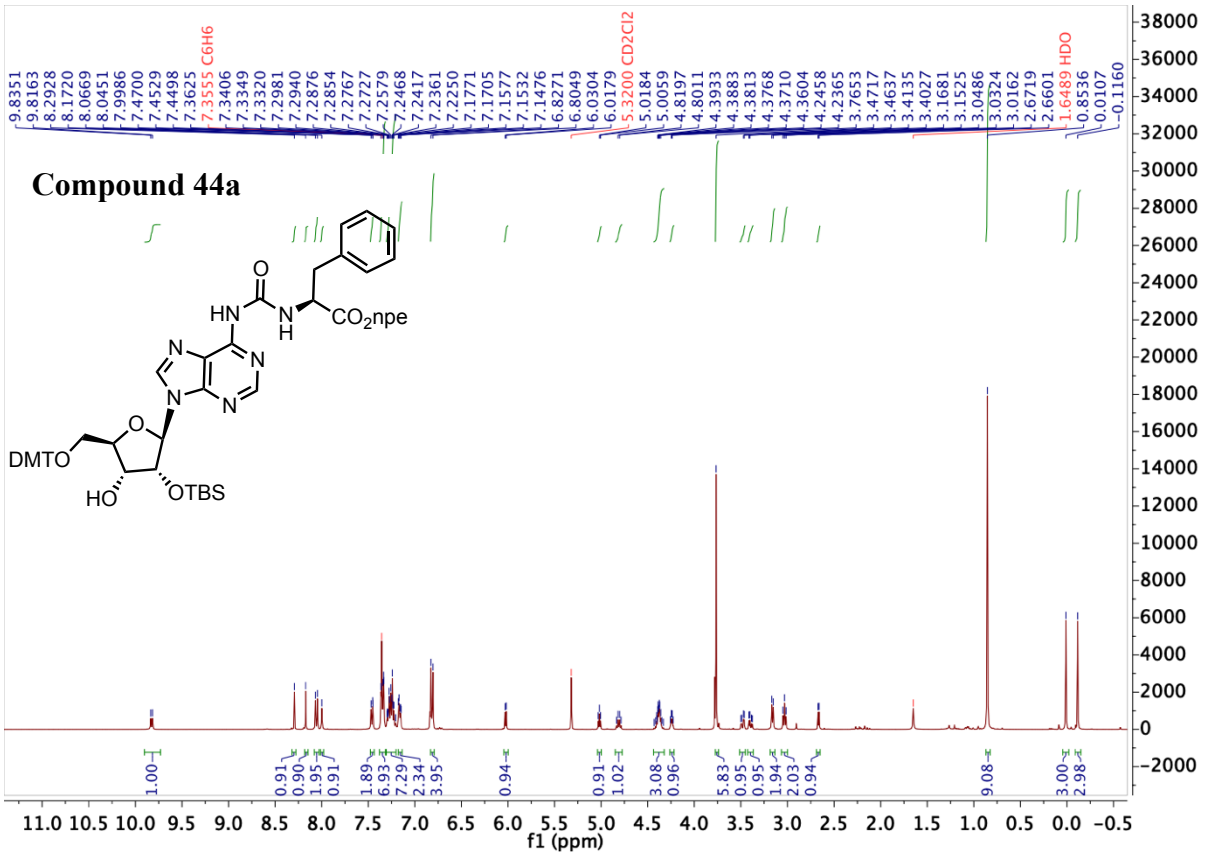


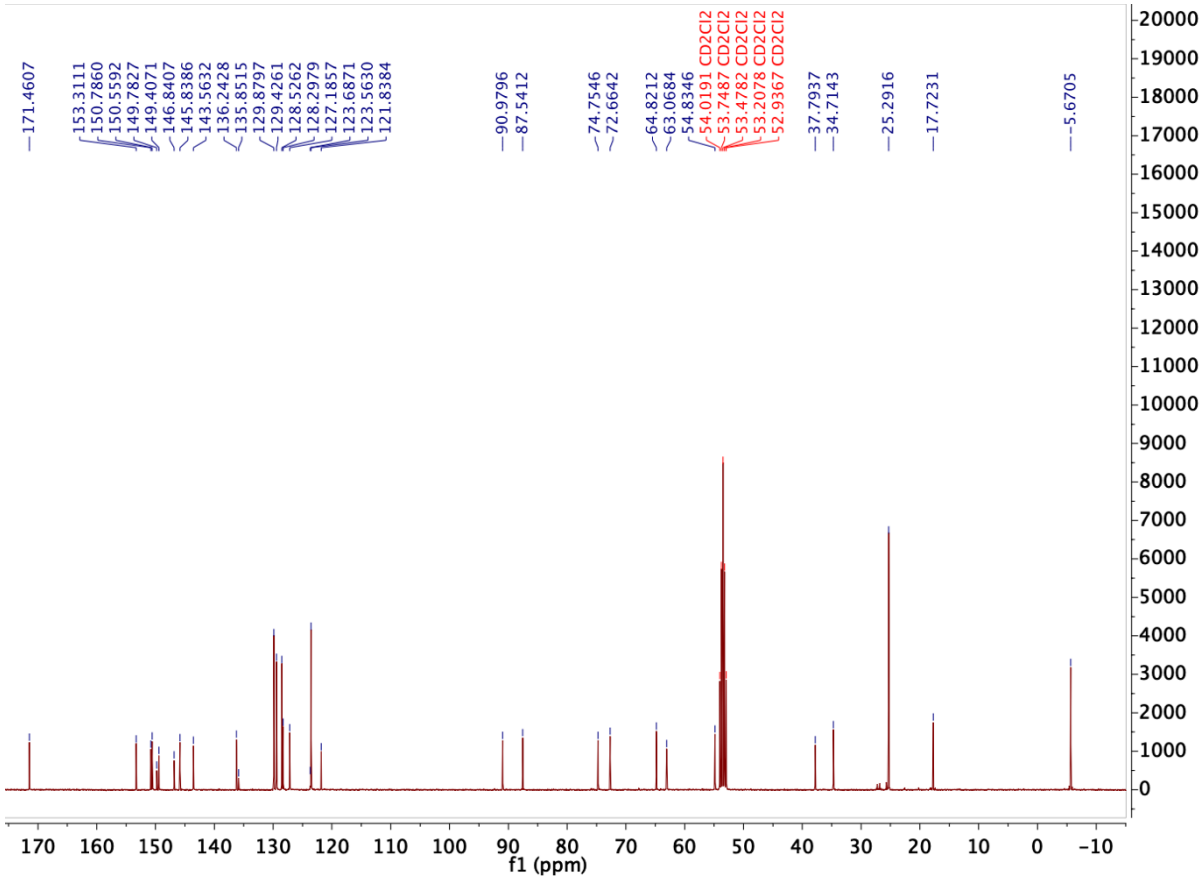


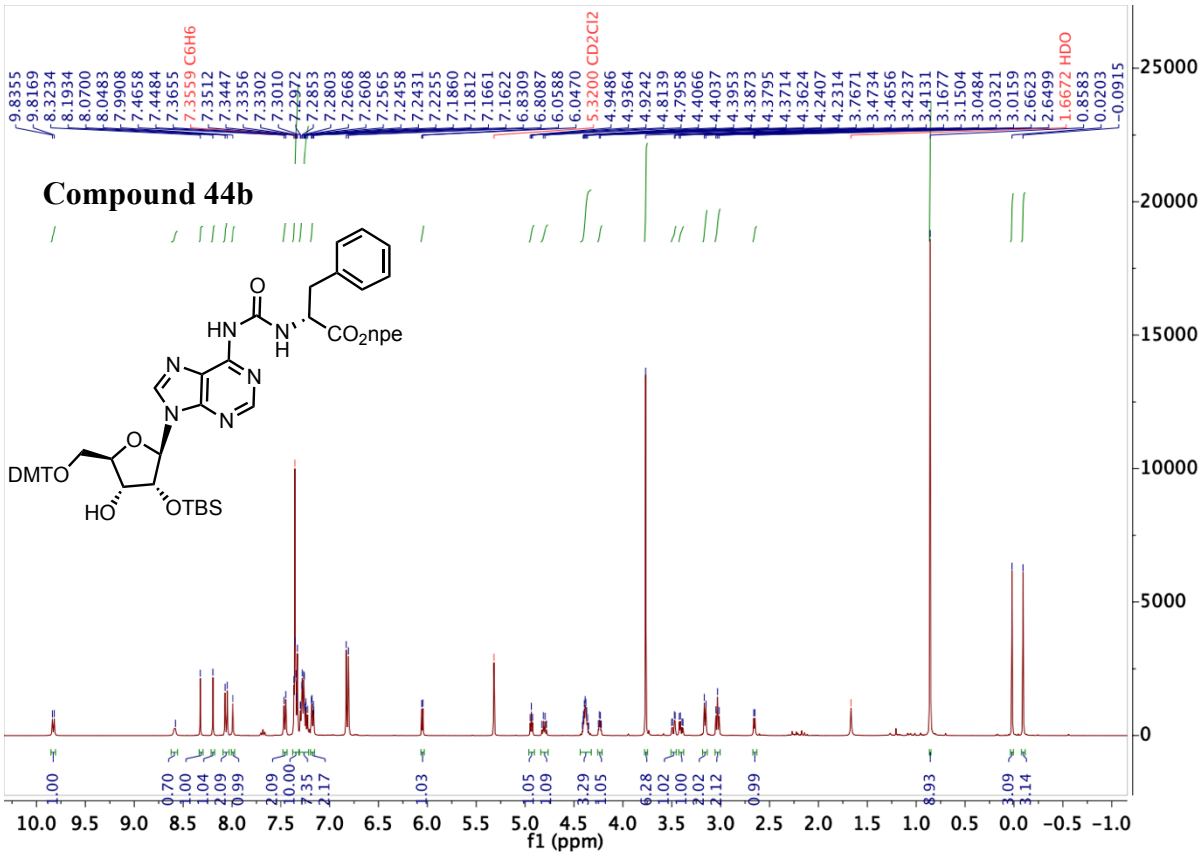
**Compound 43**

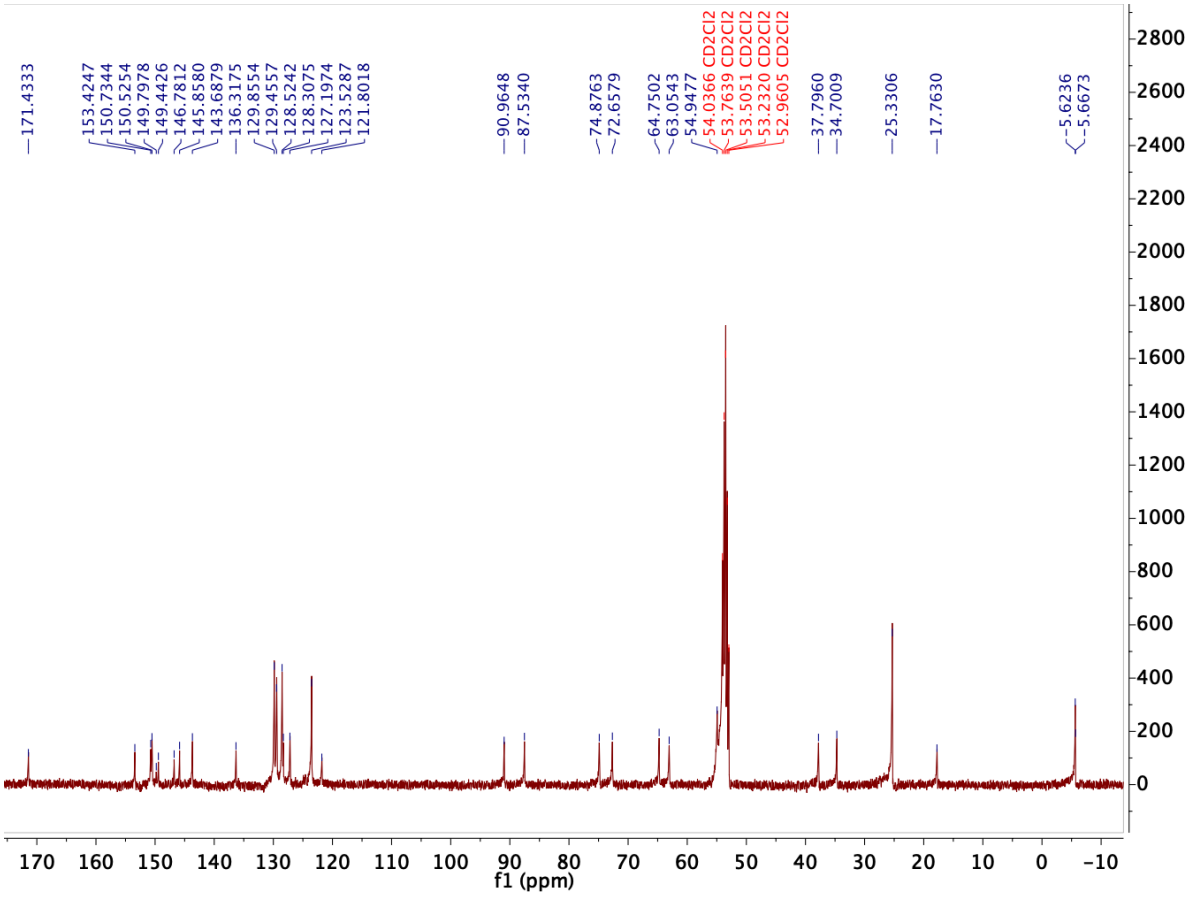

8.6031
8.4211
8.1056
8.0837
8.0607
8.0388
7.5638
7.5421
7.5288
7.5238
7.5180
7.5139
7.5073
7.3869
7.3813
7.3759
7.3691
7.3646
7.3588
7.3544
7.3496
7.3352
7.3087
7.2927
7.2905
7.2728
7.2687
7.2528
7.2059
7.1910
7.1836
6.8625
6.8557
6.8503
6.8448
6.8399
6.8332
6.8268
6.8224
6.1739
6.1634
5.0982
4.4378
4.3865
4.3530
4.0301
3.7522
3.7470
3.4833
3.1141
3.0894
3.0733
2.9904
2.9797
2.9773
2.9666
2.0712 Acetone
2.0658 Acetone
2.0603 Acetone
2.0547 Acetone
2.0493 Acetone
0.8573
0.0690
-0.0273
1.02
0.70
1.44
0.90
4.44
4.85
4.79
2.85
1.87
5.03
1.00
1.03
1.11
1.02
5.79
0.79
6.04
2.19
4.61
1.95
8.76
3.19
3.09
f1 (ppm)

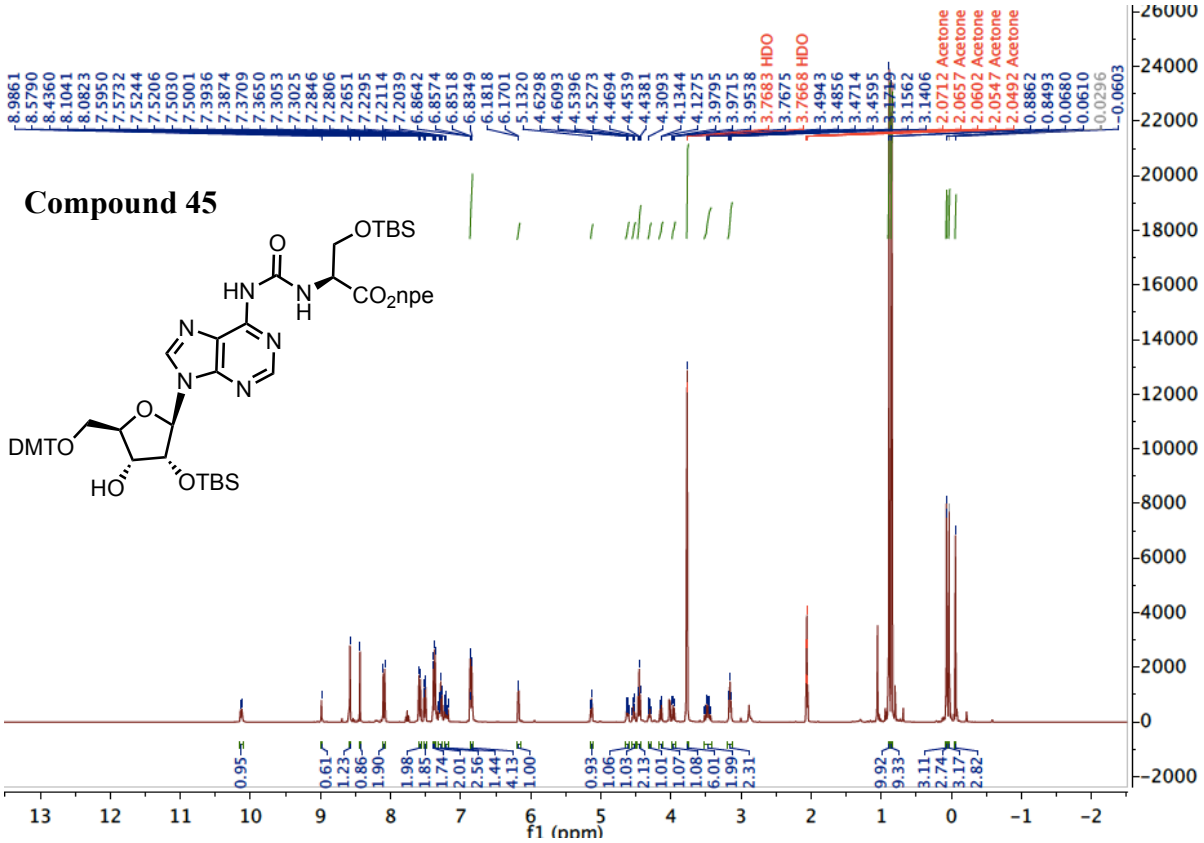

171.3100
171.1828
159.5196
154.1509
151.4900
150.6414
147.3940
147.1909
146.1099
143.6540
136.6881
131.0041
130.0183
128.9563
128.5659
127.5298
124.1838
113.8296
90.1474
87.0415
84.6418
76.4568
71.8512
65.6976
65.1088
64.3235
55.4509
50.5605
37.1370
35.2569
26.0863
18.6597
-4.6479
-4.7903
f1 (ppm)

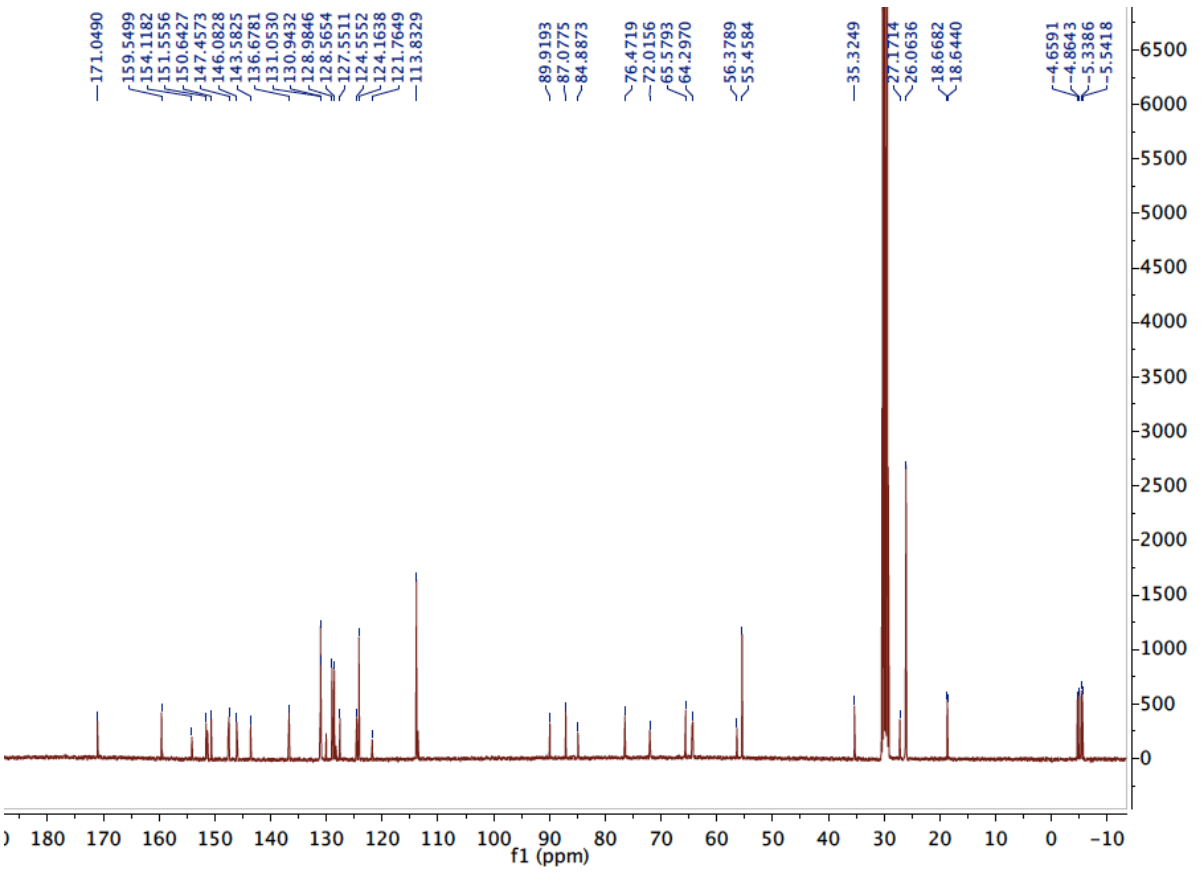

Compound 44a
DMTO
HO
OTBS
HN
N
H
CO2npe
f1 (ppm)


f1 (ppm)

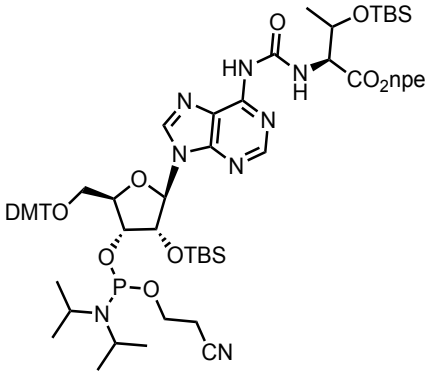

Compound 44b
DMTO
HO
OTBS
HN
N
H
CO2npe
f1 (ppm)


f1 (ppm)

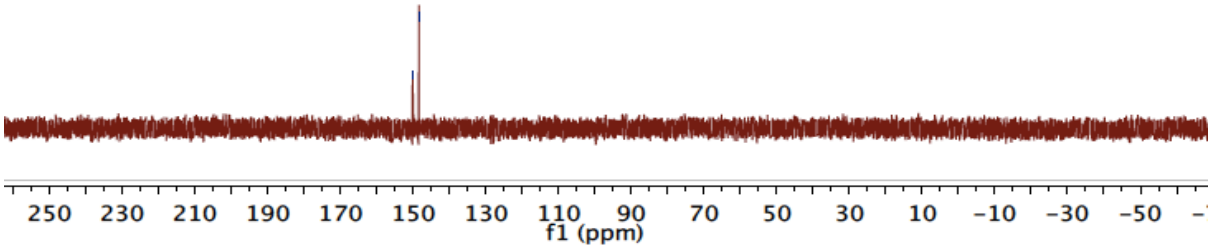

Compound 45
OTBS
HN
O
N
H
CO2npe
N
N
N
N
O
DMTO
HO
OTBS
f1 (ppm)


f1 (ppm)

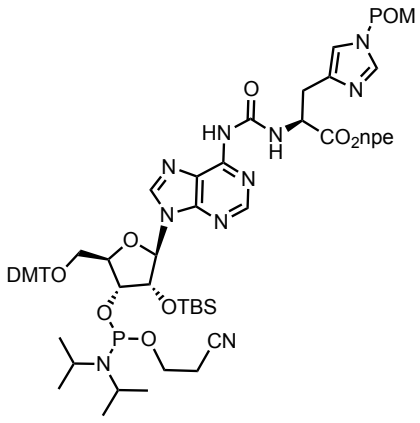
**Compound 46**



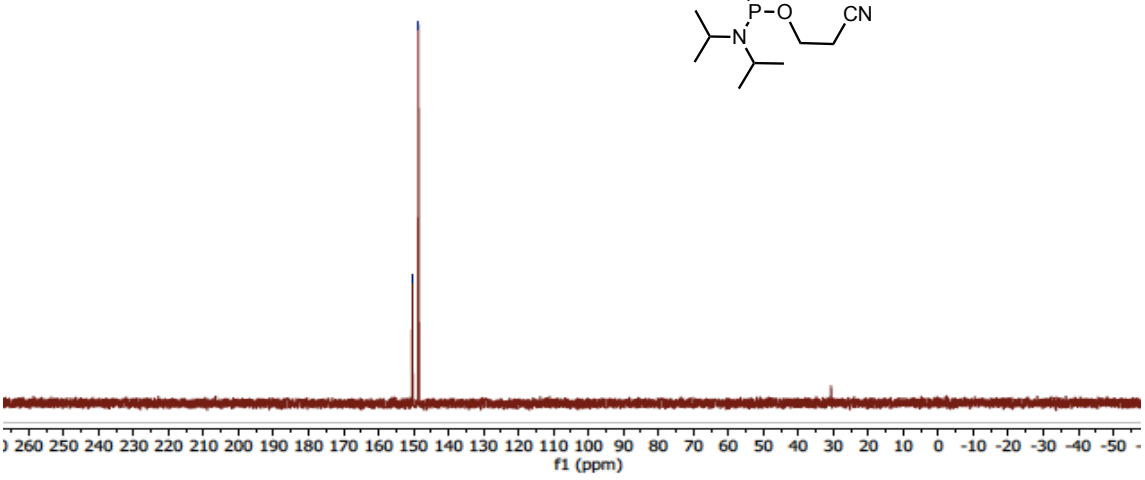


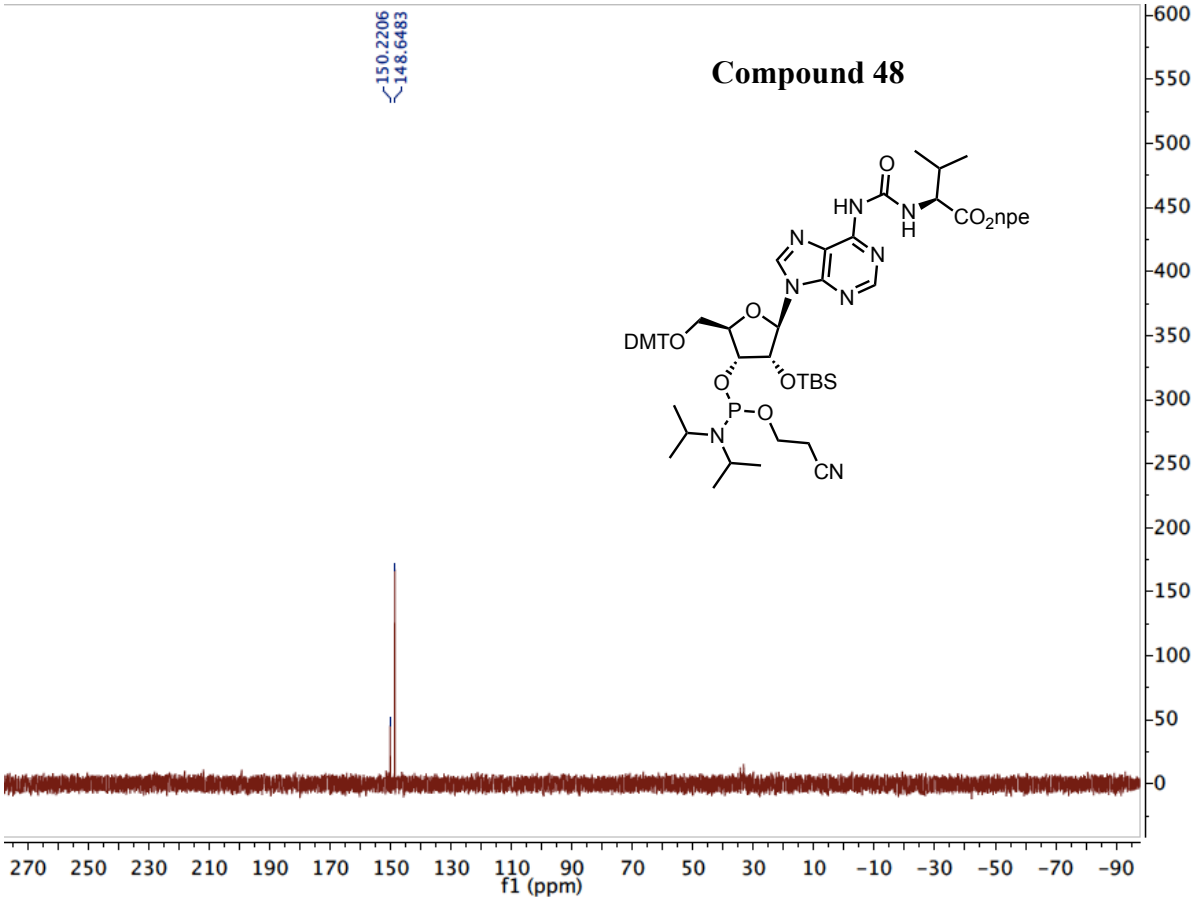


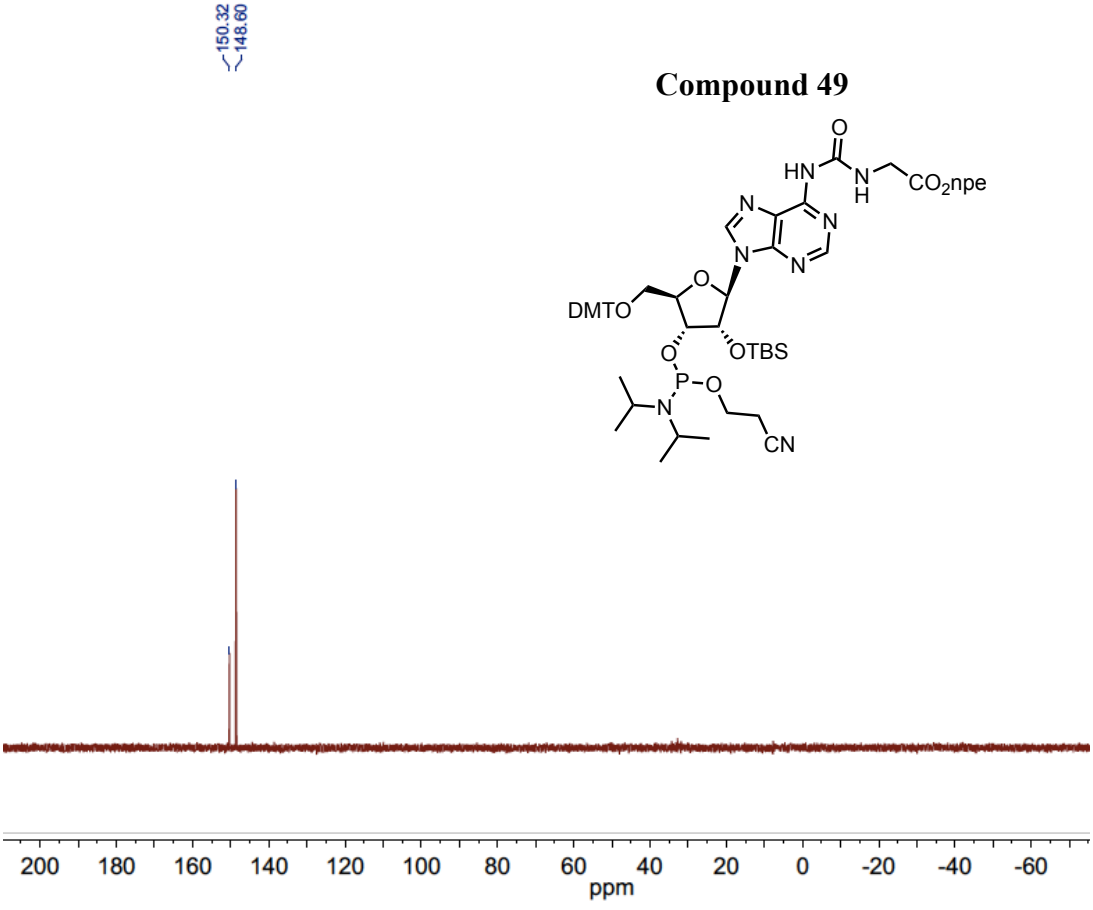

**Compound 47**

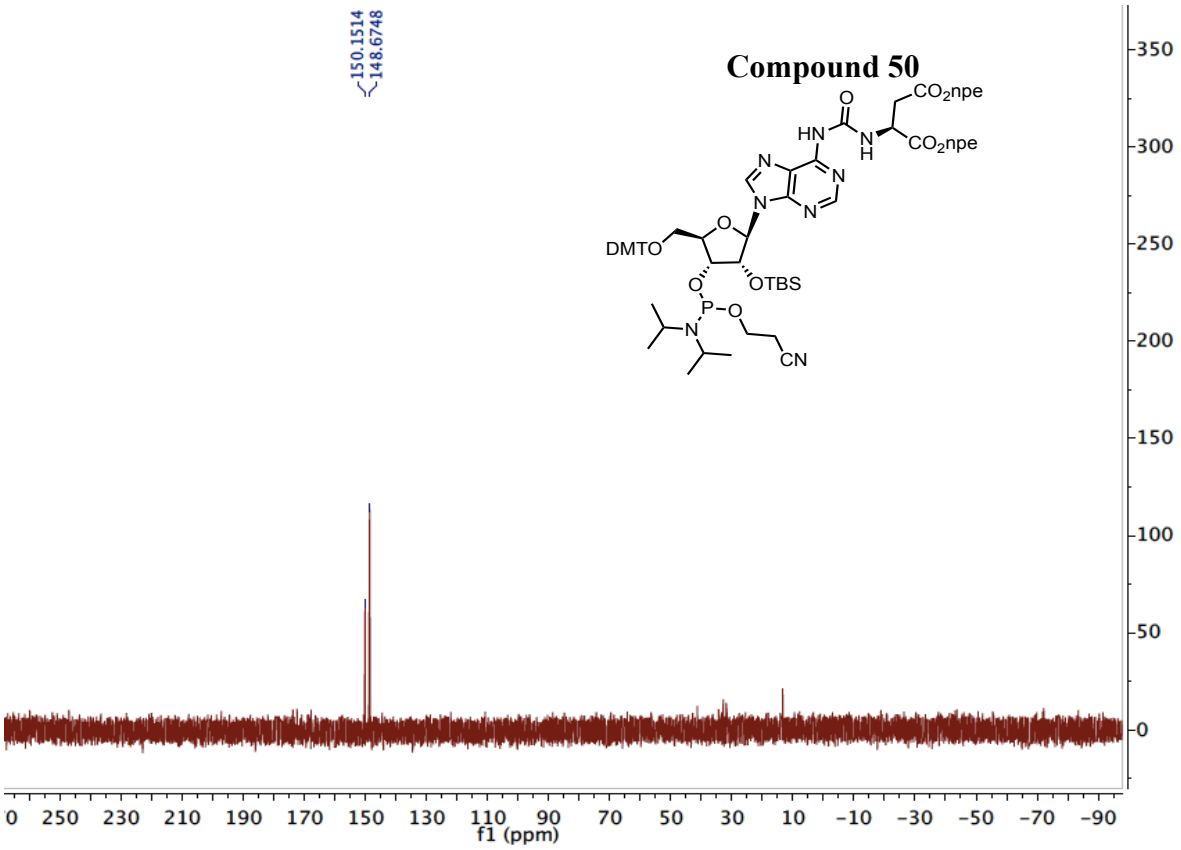


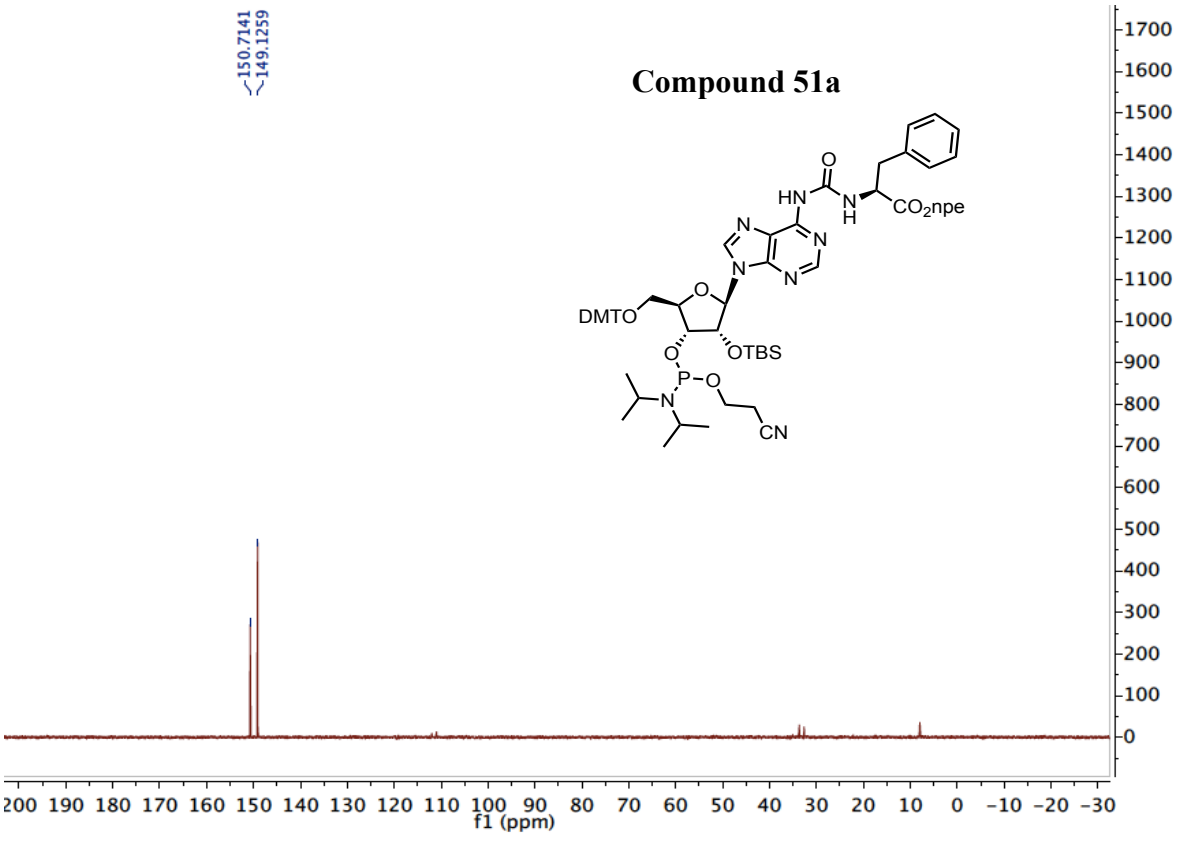




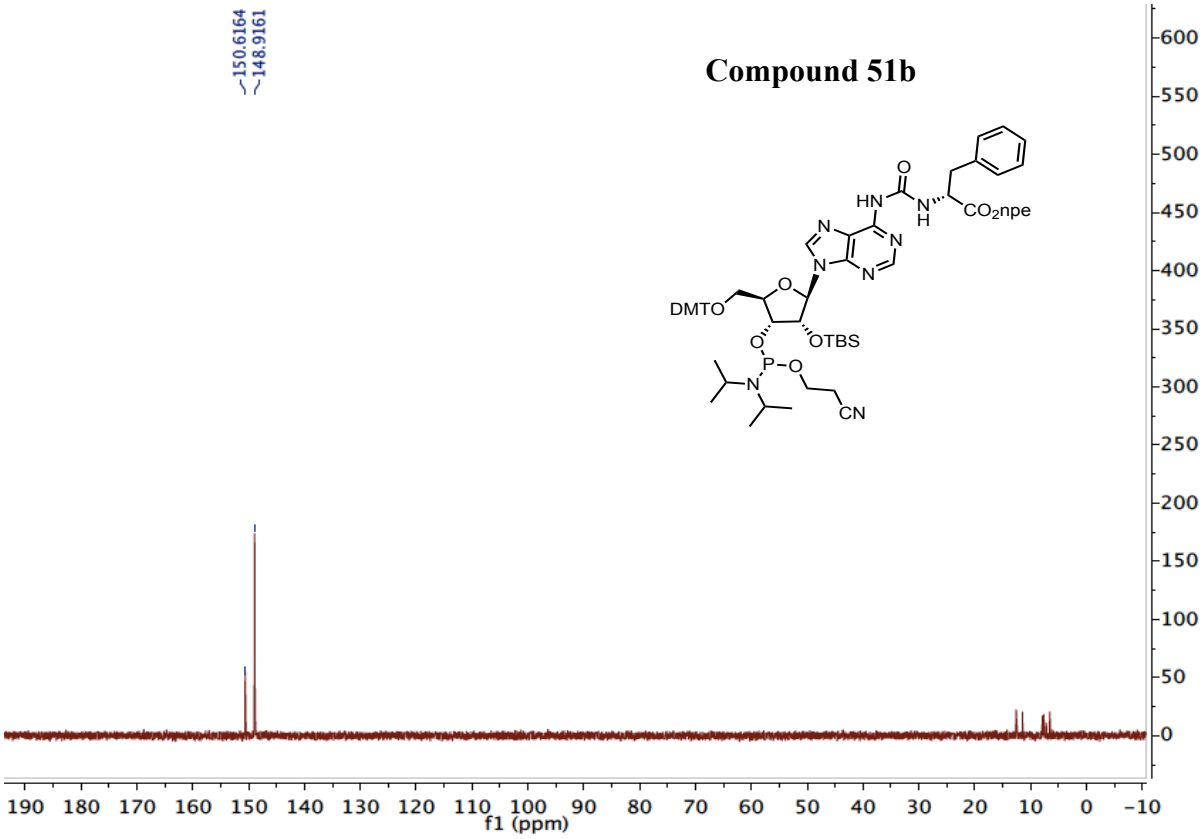

150.2206
148.6483
Compound 48
HN
O
N
H
CO2npe
N
N
N
N
O
DMTO
O
OTBS
P
O
N
CN
600
550
500
450
400
350
300
250
200
150
100
50
0
270 250 230 210 190 170 150 130 110 90 70 50 30 10 -10 -30 -50 -70 -90
f1 (ppm)


150.32
148.60
Compound 49
HN
O
N
H
CO2npe
N
N
N
N
O
DMTO
O
OTBS
P
O
N
CN
200 180 160 140 120 100 80 60 40 20 0 -20 -40 -60
ppm

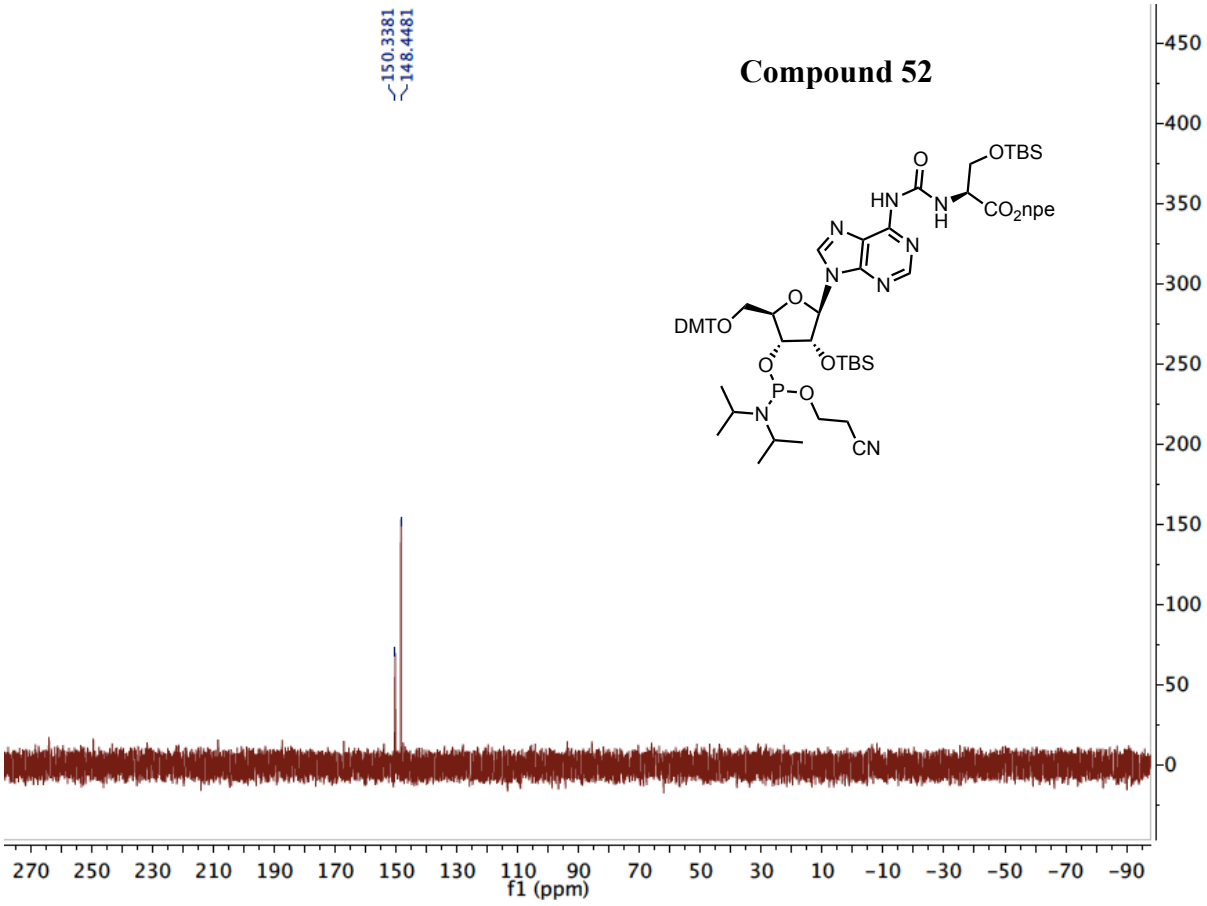

150.1514
148.6748
Compound 50
CO2npe
HN
O
N
H
CO2npe
N
N
N
N
DMTO
O
OTBS
O
P
O
N
CN
350
300
250
200
150
100
50
0
250 230 210 190 170 150 130 110 90 70 50 30 10 -10 -30 -50 -70 -90
f1 (ppm)


150.7141
149.1259
Compound 51a
HN
O
N
H
CO2npe
N
N
N
N
DMTO
O
OTBS
O
P
O
N
CN
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30
f1 (ppm)

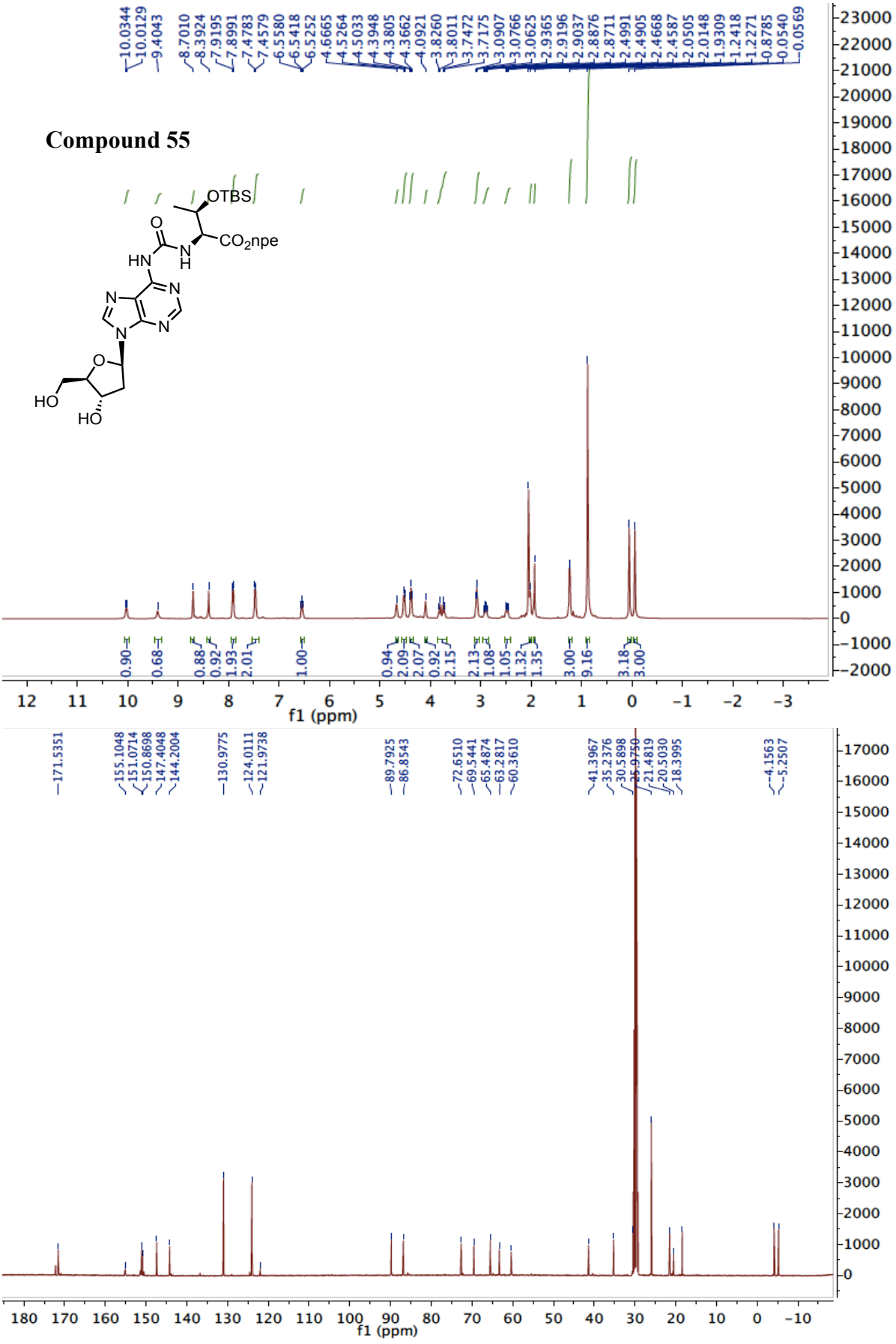
**Compound 51b**



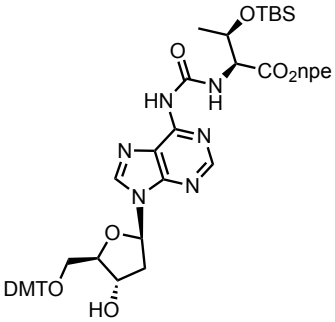

**Compound 52**



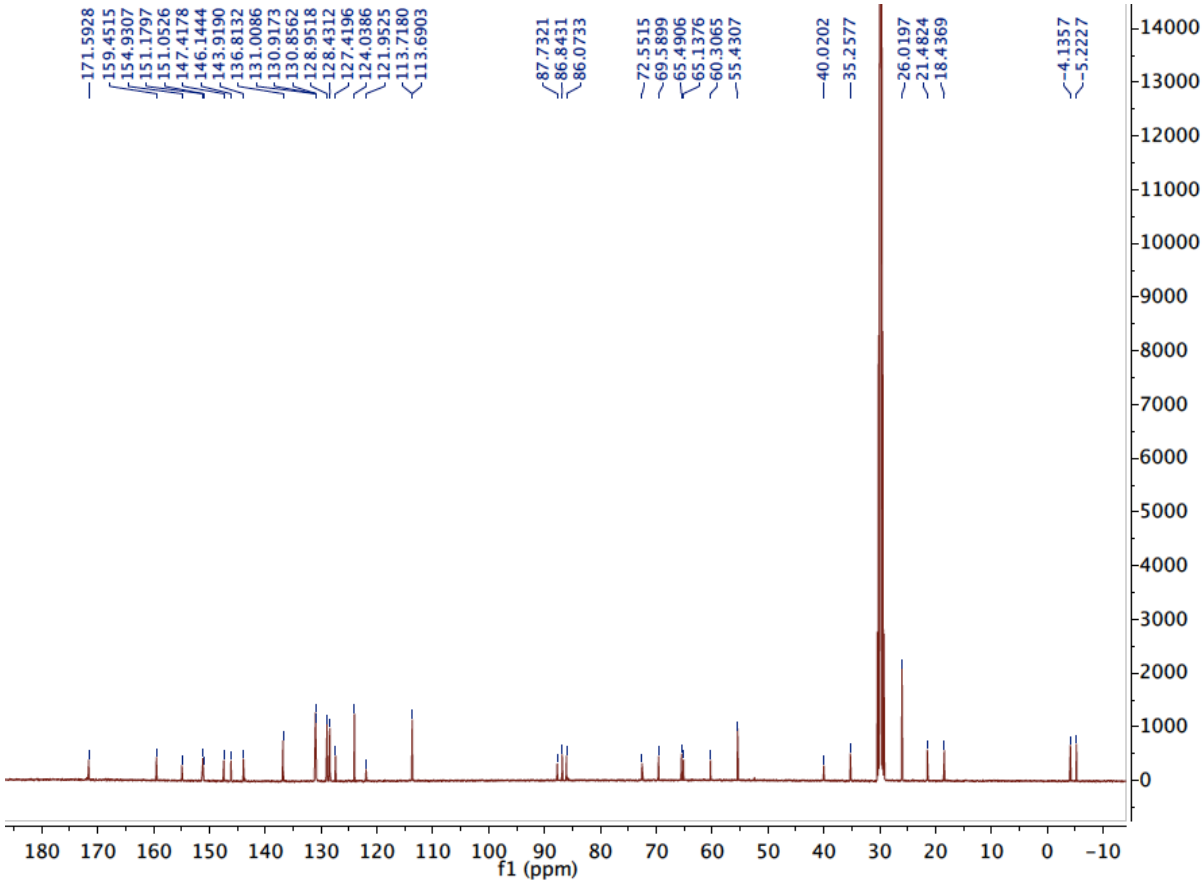
**Compound 55**

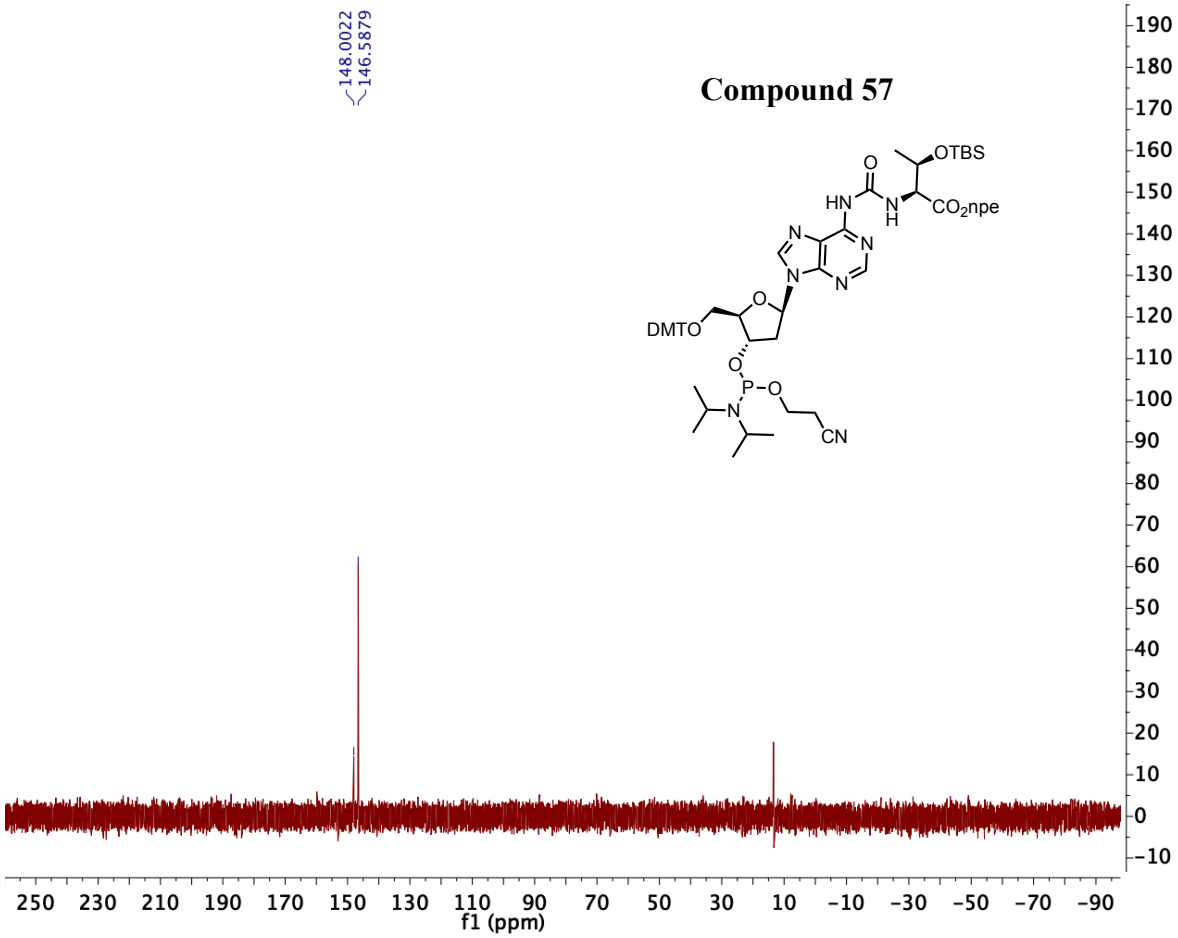


**Compound 56**


OTBS
O
CO2npe
HN
N
H
N
N
N
N
O
DMTO
HO


8.9750
8.5245
8.3414
7.9718
7.9670
7.9551
7.9500
7.5178
7.5128
7.5011
7.4960
7.4294
7.4252
7.4079
7.4048
7.3080
7.3044
7.2857
7.2821
7.2245
7.2074
7.1881
7.1698
7.1522
6.7993
6.7938
6.7821
6.7769
6.7695
6.7641
6.7528
6.7472
6.5507
4.5714
4.5560
4.5486
4.5444
4.5258
4.5217
4.4234
4.4080
4.3924
4.2118
3.7401
3.7319
3.4233
3.4087
3.3653
3.3553
3.1227
3.1075
3.0918
2.8781 HDO
2.0606 Acetone
2.0551 Acetone
2.0496 Acetone
2.0441 Acetone
2.0385 Acetone
1.2940
1.2784
0.9287
0.1060
-0.0148
-0.0221
0.87
0.61
0.96
0.87
1.84
1.83
1.95
4.03
3.11
3.97
1.00
1.00
0.88
1.84
1.88
1.00
6.13
0.96
1.00
2.90
0.98
3.40
8.88
2.94
2.89
f1 (ppm)


171.5928
159.4515
154.9307
151.1797
151.0526
147.4178
146.1444
143.9190
136.8132
131.0086
130.9173
130.8562
128.9518
128.4312
127.4196
124.0386
121.9525
113.7180
113.6903
87.7321
86.8431
86.0733
72.5515
69.5899
65.4906
65.1376
60.3065
55.4307
40.0202
35.2577
26.0197
21.4824
18.4369
4.1357
-5.2227
f1 (ppm)


148.0022
146.5879
Compound 57
OTBS
HN
N
H
O
CO2npe
DMTO
O
P
N
CN
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
250 230 210 190 170 150 130 110 90 70 50 30 10 -10 -30 -50 -70 -90
f1 (ppm)

## 6. References

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