Electronic Supplementary Information

Double-headed nucleic acids condense the molecular information of DNA to half the number of nucleotides

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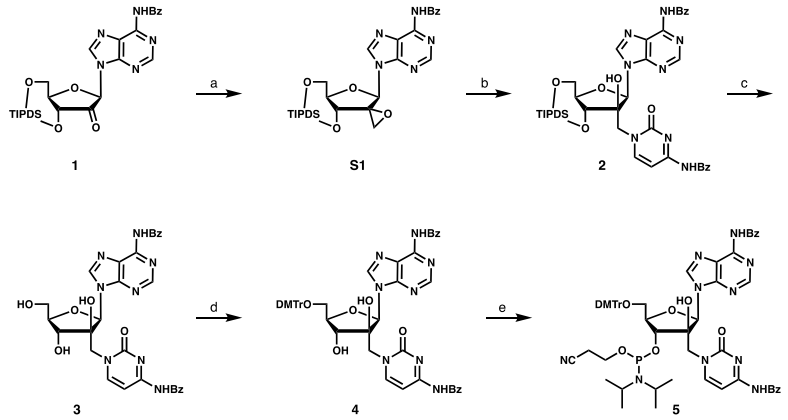
General synthetic details and procedures

All commercial reagents were used as supplied except CH_2Cl_2, which was distilled prior to use, and 4,4'-dimethoxytrityl chloride (DMTrCl), which was reactivated using acetyl chloride in cyclohexane followed by crystallization from Et_2O and exicator drying in the presence of potassium hydroxide. Anhydrous solvents were dried over 3 Å (CH_3CN) or 4 Å (allyl alcohol, CH_2Cl_2, DCE, dioxane, DMSO, DMF, petroleum ether, pyridine, THF) activated molecular sieves. Reactions were carried out under argon or nitrogen atmosphere whenever anhydrous solvents were used. All reactions were monitored using TLC analysis with Merck silica gel plates (60 F_{254}). For visualization, the TLC plates were exposed to UV light (254 nm) and/or immersed in a solution of 5% H_2SO_4 in CH_3OH (v/v) followed by charring. Column chromatography was performed with Silica Gel 60 (particle size 0.040–0.063 µm, Merck). ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectra were recorded at ambient temperature on a Bruker Avance III 400 instrument at 400.12 MHz, 100.62 MHz and 161.97 MHz, respectively. Chemical shift values (δ) are reported in ppm relative to tetramethylsilane ($\delta_{H,C}$: 0.0) or the deuterated solvents ($CDCl_3$: δ_H 7.26, δ_C 77.16; DMSO-d_6: δ_H 2.50, δ_C 39.52) and relative to 85% H_3PO_4 as external standard for ^{31}P NMR. Assignment of NMR signals are based on 2D spectra (^{1}H,^{1}H-COSY, ^{1}H,^{13}C-HSQC, ^{1}H,^{13}C-HMBC) and follow standard nucleoside convention. Regio- and stereochemistry were assigned using ^{1}H,^{13}C-HMBC or ^{1}H,^{1}H-NOESY spectra when appropriate. Signals assigned with a double prime belong to the nucleobase in the 2'-position. High resolution mass spectra (HRMS) were recorded on a Bruker micrOTOF-Q II (ESI) quadrupole time of flight instrument in positive ion mode with an accuracy of ±5 ppm. All phosphoramidites are considered as sensitive intermediate products and were therefore characterized by ^{31}P NMR and HRMS-ESI only.

Preparation of the A_C-monomer



Scheme S1 Reagents and conditions: (a) NaH, trimethylsulfoxonium iodide, DMSO, THF, 0 °C, 40 min; (b) NaHMDS, 4-*N*-benzoylcytosine, THF, DMF, 65 °C, 18 h, 46% over two steps; (c) $Et_3N{\cdot}3HF$, THF, rt, 20 h, 85%; (d) DMTrCl, DMAP, pyridine, rt, 18 h, 50%; (e) 2-cyanoethyl *N*,*N*-diisopropylchlorophosphoramidite, DIPEA, CH_2Cl_2, rt, 18 h, 79%. DMTr = 4,4'-dimethoxytrityl.

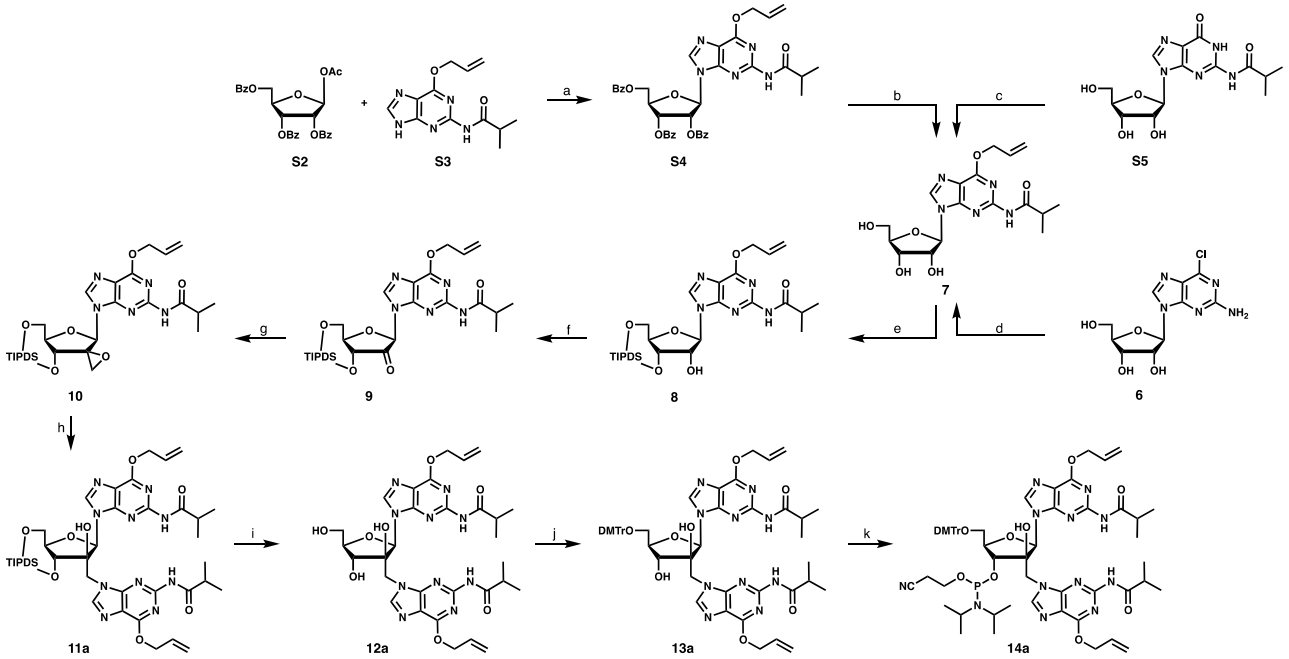
6-*N*-Benzoyl-9-(2′-*C*-(4-*N*-benzoylcytosin-1-yl)methyl-3′,5′-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-D-arabinofuranosyl)adenine (2). A mixture of trimethylsulfoxonium iodide (0.42 g, 1.91 mmol) and NaH (60% in mineral oil, 63 mg, 1.58 mmol) in anhydrous DMSO (8 mL) was stirred for 1 h, after which anhydrous THF (8 mL) was added and the mixture was cooled to 0 °C. A solution of ketone **1**[1-3] (0.77 g, 1.26 mmol) in anhydrous THF (8 mL) was added dropwise at 0 °C, and the mixture was stirred for 40 min at 0 °C. A saturated aqueous solution of NH_4Cl (15 mL), water (20 mL) and EtOAc (60 mL) were added, and the mixture was stirred for 15 min. The phases were separated, and the aqueous phase was extracted with EtOAc (3 × 20 mL). The combined organic phase was dried (Na_2SO_4) and concentrated under reduced pressure to give crude 2′-spiroepoxide **S1**. A mixture of 4-*N*-Benzoylcytosine (0.41 g, 1.88 mmol) and NaHMDS (1.0 M in THF, 1.80 mL, 1.80 mmol) in anhydrous DMF (8 mL) was stirred for 1 h. A solution of the crude epoxide **S1** in anhydrous DMF (8 mL) was added dropwise and the mixture was stirred at 65 °C for 18 h. After cooling to rt, a saturated aqueous solution of NH_4Cl (10 mL), water (20 mL) and CH_2Cl_2 (20 mL) were added, and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (3 × 50 mL) and the combined organic phase was washed with brine (50 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The residue was co-evaporated with anhydrous xylene (20 mL) and purified by silica gel column chromatography (0–4% CH_3OH in CH_2Cl_2, v/v) to give the double-headed nucleoside **2** (0.49 g, 0.58 mmol, 46%) as a yellow foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.11 (s, 1H, NH), 8.62 (s, 1H, H2), 8.24 (s, 1H, H8), 8.00–7.91 (m, 2H, Bz), 7.92–7.84 (m, 2H, Bz), 7.75 (d, J = 7.3 Hz, 1H, H6′′), 7.63–7.54 (m, 2H, Bz), 7.52–7.44 (m, 5H, H5′′, 4 × Bz), 6.55 (s, 1H, 2′OH), 6.40 (s, 1H, H1′), 4.73–4.63 (m, 2H, H3′, H6$_a$′), 4.20 (d, J = 14.6 Hz, 1H, H6$_b$′), 4.10–4.07 (m, 2H, H5′), 3.95 (dt, J = 6.3, 4.5 Hz, 1H, H4′), 1.16–1.05 (m, 28H, TIPDS); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.6 (Bz C=O), 164.5 (Bz C=O), 162.7 (C4′′), 157.8 (C2′′), 152.1 (C2), 151.3 (C4), 150.9 (C6′′), 149.8 (C6), 143.9 (C8), 133.7 (Bz), 133.3 (Bz), 132.8 (Bz), 132.7 (Bz), 129.0 (Bz), 128.8 (Bz), 127.9 (Bz), 127.7 (Bz), 122.9 (C5), 97.3 (C5′′), 86.4 (C1′), 81.8 (C4′), 81.0 (C2′), 79.3 (C3′), 62.2 (C5′), 54.5 (C6′), 17.5, 17.4, 17.3, 17.3, 17.2, 17.1, 17.1, 17.0 (TIPDS), 13.6, 13.3, 12.9, 12.6 (TIPDS); HRMS–ESI m/z 841.3545 $[M + H]^+$; calcd ($C_{41}H_{52}N_8O_8Si_2^+$) 841.3519.

6-*N*-Benzoyl-9-(2′-*C*-(4-*N*-benzoylcytosin-1-yl)methyl-β-D-arabinofuranosyl)adenine (3). Nucleoside **2** (0.39 g, 0.46 mmol) was dissolved in anhydrous THF (7 mL) and $Et_3N{\cdot}3HF$ (0.15 mL, 0.92 mmol) was added. The mixture was stirred for 20 h at rt, then TMS-acetylene (0.17 mL, 1.20 mmol) was added, and the mixture was stirred for 1 h. The solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography (0–5% CH_3OH in CH_2Cl_2) to give nucleoside **3** (232 mg, 0.39 mmol, 85%) as a white powder. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.31 (br s, 1H, NH), 11.19 (br s, 1H, NH), 8.68 (s, 1H, H2), 8.54 (s, 1H, H8), 8.06–8.00 (m, 4H, Bz), 7.96 (d, J = 7.0 Hz, 1H, H6′′), 7.68–7.60 (m, 2H, Bz), 7.57–7.48 (m, 4H, Bz), 7.30 (d, J = 7.0 Hz, 1H, H5′′), 6.40 (s, 1H, 2′OH), 6.37 (s, 1H, H1′), 6.33 (d, J = 3.4 Hz, 1H, 3′OH), 5.57 (t, J = 5.3 Hz, 1H, 5′OH), 4.36 (d, J = 14.3 Hz, 1H, H6$_a$′), 4.09–3.98 (m, 3H, H3′, H4′, H6$_b$′), 3.80–3.68 (m, 2H, H5′); ^{13}C NMR (101 MHz, DMSO-d_6) δ 167.2 (Bz C=O), 165.5 (Bz C=O), 163.2 (C4′′), 157.0 (C2′′), 152.3 (C4), 152.0 (C6′′), 151.4 (C2), 150.0 (C6), 143.3 (C8), 133.4 (Bz), 133.0 (Bz), 132.6 (Bz), 132.3 (Bz), 128.4 (Bz), 128.4 (Bz), 128.4 (Bz), 124.8 (C5), 96.4 (C5′′), 85.1 (C1′), 85.0 (C4′), 80.3 (C2′), 75.7 (C3′), 61.1 (C5′), 49.8 (C6′); HRMS–ESI m/z 599.1960 $[M + H]^+$; calcd ($C_{29}H_{27}N_8O_7^+$) 599.1997.

6-*N*-Benzoyl-9-(2′-*C*-(4-*N*-benzoylcytosin-1-yl)methyl-5′-*O*-(4,4′-dimethoxytrityl)-β-D-arabinofuranosyl)-adenine (4). Nucleoside **3** (0.27 g, 0.45 mmol) was co-evaporated with anhydrous pyridine (2 × 10 mL) and redissolved in anhydrous pyridine (5 mL). DMAP (10 mg, 82 µmol) and DMTrCl (230 mg, 0.68 mmol) was added, and the mixture was stirred at rt for 18 h. Absolute EtOH (3–4 drops) was added and the mixture was concentrated under reduced pressure, redissolved in CH_2Cl_2 (25 mL) and washed with a saturated aqueous solution of $NaHCO_3$ (2 × 25 mL). The combined aqueous phase was extracted with CH_2Cl_2 (2 × 25 mL) and the combined organic phase was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (0–3% CH_3OH in CH_2Cl_2, v/v) to give nucleoside **4** (203 mg, 225 µmol, 50%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.21 (br s, 1H, NH), 8.92 (br s, 1H, NH), 8.68 (s, 1H, H2), 8.50 (s, 1H, H8), 8.06–8.01 (m, 2H, Bz), 7.91–7.86 (m, 2H, Bz), 7.69 (d, *J* = 7.4 Hz, 1H, H6′′), 7.64–7.47 (m, 7H, H5′′, 6 × Bz), 7.38–7.33 (m, 2H, DMTr), 7.32–7.22 (m, 7H, DMTr), 6.83 (d, *J* = 8.9 Hz, 2H, DMTr), 6.82 (d, *J* = 8.9 Hz, 2H, DMTr), 6.51 (s, 1H, H1′), 6.36 (s, 1H, 3′OH), 5.73 (d, *J* = 1.1 Hz, 1H, 2′OH), 4.94 (dd, *J* = 14.4, 1.1 Hz, 1H, H6$_a$′), 4.33 (s, 1H, H4′), 3.89–3.86 (m, 1H, H3′), 3.78 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 3.75 (dd, *J* = 11.2, 2.2 Hz, 1H, H5$_a$′), 3.47 (dd, *J* = 11.2, 2.6 Hz, 1H, H5$_b$′), 3.29 (d, *J* = 14.4 Hz, 1H, H6$_b$′); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2 (Bz C=O), 164.8 (Bz C=O), 162.9 (C4′′), 159.0 (DMTr), 157.6 (C2′′), 152.6 (C2), 152.2 (C4), 152.1 (C6′′), 149.4 (C6), 143.2 (DMTr), 142.8 (C8), 134.5 (DMTr), 134.4 (DMTr), 133.5 (Bz), 133.4 (Bz), 132.9 (Bz), 132.7 (Bz), 130.1 (DMTr), 130.1 (DMTr), 129.2 (Bz), 128.9 (Bz), 128.2 (DMTr), 128.0 (Bz), 127.5 (Bz), 127.5 (DMTr), 122.9 (C5), 113.5 (DMTr), 96.9 (C5′′), 88.8 (DMTr), 85.6 (C1′), 84.3 (C4′), 80.9 (C2′), 75.8 (C3′), 63.9 (C5′), 55.3 (OCH_3), 49.2 (C6′); HRMS–ESI *m*/*z* 923.3095 $[M + Na]^+$; calcd ($C_{50}H_{44}N_8O_9Na^+$) 923.3123.

6-*N*-Benzoyl-9-(2′-*C*-(4-*N*-benzoylcytosin-1-yl)methyl-3′-*O*-(*P*-(2-cyanoethoxy)-*N*,*N*-diisopropylaminophosphinyl)-5′-*O*-(4,4′-dimethoxytrityl)-β-D-arabinofuranosyl)adenine (5). Nucleoside **4** (195 mg, 216 µmol) was co-evaporated with anhydrous DCE (2 × 10 mL) and redissolved in anhydrous CH_2Cl_2 (2 mL). DIPEA (0.23 mL, 1.32 mmol) was added followed by 2-cyanoethyl *N*,*N*-diisopropylchlorophosphoramidite (0.19 mL, 0.85 mmol) and the mixture was stirred for 18 h at rt. CH_3OH (2–3 drops) was added, and the mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (0–3% CH_3OH in CH_2Cl_2, v/v) followed by precipitation from CH_2Cl_2 in anhydrous petroleum ether (150 mL) at 0 °C to give phosphoramidite **5** (187 mg, 170 µmol, 79%) as a white foam. ^{31}P NMR (162 MHz, $CDCl_3$) δ 151.4, 150.6; HRMS–ESI *m*/*z* 1101.4329 $[M + Na]^+$; calcd ($C_{59}H_{62}N_{10}O_{10}PNa^+$) 1101.4383.

Preparation of the G_G-monomer



Scheme S2 Reagents and conditions: (a) i. BSA, CH_3CN, 80 °C, 30 min. ii. TMSOTf, CH_3CN, 80 °C, 5 h, 65%; (b) NaOH, pyridine, EtOH, 0 °C, 30 min, 54%; (c) i. TMS-imidazole, dioxane, rt, 30 min. ii. PPh_3, allyl alcohol, DIAD, dioxane, rt, 18 h. iii. $Et_3N{\cdot}3HF$, dioxane, rt, 15 min, 59%; (d) i. allyl alcohol, NaH, reflux, 60 min. ii. TMSCl, pyridine, rt, 60 min. iii. isobutyryl chloride, pyridine, rt, 18 h. iv. NH_3 (aq), pyridine, rt, 10 min, 61%; (e) $TIPDSCl_2$, pyridine, 0 °C to rt, 18 h, 83%; (f) Dess-Martin periodinane, CH_2Cl_2, 0 °C to rt, 18 h, quant.; (g) NaH, trimethylsulfoxonium iodide, DMSO, THF, 0 °C, 30 min, 60%; (h) NaHMDS, **S3**, THF, DMF, rt, 3 d, 46%; (i) $Et_3N{\cdot}3HF$, THF, rt, 18 h, 93%; (j) DMTrCl, DMAP, pyridine, rt, 18 h, 79%; (k) 2-cyanoethyl *N*,*N*-diisopropylchlorophosphoramidite, DIPEA, CH_2Cl_2, rt, 18 h, 60%. TIPDS = 1,1,3,3-tetraisopropyldisiloxan-1,3-diyl, DMTr = 4,4′-dimethoxytrityl.

6-*O*-Allyl-2′,3′,5′-tri-*O*-benzoyl-2-*N*-isobutyrylguanosine (S4). 1-*O*-Acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (**S2**, 1.26 g, 2.50 mmol) and the protected nucleobase **S3**[4] (1.00 g, 3.83 mmol) were vacuum dried for 16 h and suspended in anhydrous CH_3CN (30 mL). BSA (2.52 mL, 10.2 mmol) was added, and the mixture was stirred at 80 °C for 30 min. After cooling to rt, TMSOTf (1.20 mL, 6.63 mmol) was added, and the mixture was stirred at 80 °C for 5 h. After cooling to rt, a saturated aqueous solution of $NaHCO_3$ (30 mL) was added and the mixture was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic phase was dried ($MgSO_4$) and concentrated under reduced pressure, and the residue was purified by silica gel column chromatography (0–3% CH_3OH in CH_2Cl_2) to give **S4** (1.14 g, 1.62 mmol, 65%) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 1H, NH), 8.01–7.96 (m, 4H, Bz), 7.96–7.92 (m, 3H, Bz, H8), 7.61–7.51 (m, 3H, Bz), 7.43–7.35 (m, 6H, Bz), 6.49 (t, *J* = 5.5 Hz, 1H, H3′), 6.37–6.30 (m, 2H, H1′, H2′), 6.15 (ddt, *J* = 17.1, 10.5, 5.7 Hz, 1H, allyl =CH), 5.48 (dq, *J* = 17.1, 1.2 Hz, 1H, allyl trans =CH_2), 5.31 (dq, *J* = 10.5, 1.2 Hz, 1H, allyl cis =CH_2), 5.10 (dt, *J* = 5.7, 1.2 Hz, 2H, allyl CH_2), 4.94 (dd, *J* = 12.0, 3.8 Hz, 1H, $H5_a$′), 4.89–4.84 (m, 1H, H4′), 4.74 (dd, *J* = 12.0, 4.8 Hz, 1H, $H5_b$′), 3.06 (br s, 1H, iBu CH), 1.28 (d, *J* = 6.9 Hz, 3H, iBu CH_3), 1.26 (d, *J* = 6.9 Hz, 3H, iBu CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.7 (iBu C=O), 166.2, 165.3, 165.1 (Bz C=O), 160.9 (C6), 152.3 (C4), 152.3 (C2), 140.2 (C8), 133.8, 133.6, 133.4 (Bz), 132.2 (allyl =CH), 129.9, 129.8, 129.8, 129.6, 129.4, 128.9, 128.6, 128.5, 128.5 (Bz), 118.9

(allyl =CH_2), 118.7 (C5), 87.5 (C1′), 80.4 (C4′), 74.3 (C2′), 71.6 (C3′), 68.1 (allyl CH_2), 63.5 (C5′), 35.8 (iBu CH), 19.3 (iBu CH_3), 19.2 (iBu CH_3); HRMS–ESI *m/z* 706.2526 $[M + H]^+$; calcd ($C_{38}H_{36}N_5O_9^+$) 706.2508.

6-*O*-Allyl-2-*N*-isobutyrylguanosine (7). Method A: NaH (60% in mineral oil, 0.27 g, 6.75 mmol) was added to anhydrous allyl alcohol (10 mL) and the mixture was stirred for 30 min. 6-Chloroguanosine (**6**, 1.00 g, 3.31 mmol) was added, and the mixture was stirred at reflux for 1 h and then concentrated under reduced pressure. The residue was co-evaporated with anhydrous pyridine (3 × 20 mL), redissolved in anhydrous pyridine (20 mL) and TMSCl (3.57 mL, 28.1 mmol) was added. The mixture was stirred for 1 h at rt, and then isobutyryl chloride (0.70 mL, 6.62 mmol) was added and the mixture was stirred for further 18 h. Water (3 mL) was added, and the mixture was then allowed to cool to rt before NH_4OH (25%, 4 mL) was added. After stirring for 10 min, the mixture was concentrated under reduced pressure and the residue was redissolved in a 1:1 mixture of water and EtOAc (50 mL). The phases were separated, and the aqueous phase was extracted with EtOAc (3 × 30 mL). The combined organic phase was dried ($MgSO_4$), concentrated under reduced pressure and purified by silica gel column chromatography (0–10% CH_3OH in CH_2Cl_2) to give pure **7** (0.79 g, 2.00 mmol, 61%) as a white foam. Method B: 6-*N*-Isobutyrylguanosine (**S5**, 1.00 g, 2.83 mmol) was suspended in anhydrous dioxane (12 mL), and TMS-imidazole (1.66 mL, 11.3 mmol) was added dropwise. The mixture was stirred for 30 min at rt, after which PPh_3 (2.60 g, 9.91 mmol) and allyl alcohol (0.96 mL, 14.1 mmol) were added followed by dropwise addition of DIAD (1.94 mL, 9.9 mmol) over 10 min. The mixture was stirred at rt for 18 h, and then $Et_3N{\cdot}3HF$ (2.31 mL, 14.15 mmol) was added. After stirring for 15 min, the mixture was concentrated under reduced pressure and purified by silica gel column chromatography (0–10% CH_3OH in CH_2Cl_2) to give **7** (0.65 g, 1.66 mmol, 59%) as a white foam containing 2 eq. imidazole. Method C: Nucleoside **S4** (0.99 g, 1.40 mmol) was dissolved in a 1:2 mixture of pyridine and EtOH (12 mL) and the mixture was stirred at 0 °C. A 1.0 M aqueous solution of NaOH (6.3 mL, 6.3 mmol) was added dropwise at 0 °C, and the mixture was stirred for 30 min at 0 °C. DOWEX 50WX8 H^+-form was added and the mixture was stirred for 50 min and filtered. The solid was washed with a 4:1 mixture of pyridine and ethanol (50 mL) and the combined filtrate was evaporated to dryness. The residue was redissolved in a minimum of CH_3OH and triturated in cold Et_2O (400 mL). Precipitated material was collected by filtration and purified by silica gel column chromatography (0–10% CH_3OH in CH_2Cl_2) to give **7** (0.30 g, 0.76 mmol, 54%) as a white foam. Characterization data for **7** were identical for all procedures. Spectral data shown are of the product obtained through method A. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.42 (s, 1H, NH), 8.47 (s, 1H, H8), 6.18 (ddt, *J* = 17.0, 10.5, 5.7 Hz, 1H, allyl =CH), 5.91 (d, *J* = 6.0 Hz, 1H, H1′), 5.53 (br s, 1H, 2′OH), 5.47 (dq, *J* = 17.0, 1.4 Hz, 1H, allyl trans =CH_2), 5.31 (dq, *J* = 10.5, 1.4 Hz, 1H, allyl cis =CH_2), 5.20 (br s, 1H, 3′OH), 5.08 (dq, *J* = 5.7, 1.4 Hz, 2H, allyl CH_2), 4.99 (t, *J* = 5.5 Hz, 1H, 5′OH), 4.58 (q, *J* = 5.7 Hz, 1H, H2′), 4.22–4.15 (m, 1H, H3′), 3.94 (q, *J* = 4.1 Hz, 1H, H4′), 3.69–3.51 (m, 2H, H5′), 2.87 (hept, *J* = 6.5 Hz, 1H, iBu CH), 1.10 (d, *J* = 6.5 Hz, 6H, iBu CH_3); ^{13}C NMR (101 MHz, DMSO-d_6) δ 175.0 (iBu C=O), 159.6 (C6), 153.0 (C4), 152.0 (C2), 141.2 (C8), 132.9 (allyl =CH), 118.7 (allyl =CH_2), 117.3 (C5), 87.1 (C1′), 85.7 (C4′), 73.7 (C2′), 70.5 (C3′), 67.0 (allyl CH_2), 61.4 (C5′), 34.4 (iBu CH), 19.3, 19.3 (iBu CH_3); HRMS–ESI *m/z* 394.1710 $[M + H]^+$; calcd ($C_{17}H_{24}N_5O_9^+$) 394.1721.

6-*O*-Allyl-2-*N*-isobutyryl-3′,5′-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)guanosine (8). Nucleoside **7** (0.74 g, 1.89 mmol) was co-evaporated with anhydrous pyridine (20 mL), redissolved in anhydrous pyridine (12 mL) and the solution was stirred at 0 °C. $TIPDSCl_2$ (0.62 mL, 1.94 mmol) was added dropwise, and the mixture was stirred for 18 h at rt. The reaction mixture was concentrated under reduced pressure and the residue was dissolved in a 1:1 mixture of CH_2Cl_2 and a saturated aqueous solution of $NaHCO_3$ (80 mL). The phases were separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phase was dried ($MgSO_4$), concentrated under reduced pressure and purified by silica gel column chromatography (0–2% CH_3OH in CH_2Cl_2) to give **8** (0.99 g, 1.56 mmol, 83%) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H, H8), 7.85 (s, 1H, NH), 6.13 (ddt, *J* = 17.2, 10.5, 5.7 Hz, 1H, allyl =CH), 5.98 (d, *J* = 1.6 Hz, 1H, H1′), 5.45 (dq, *J* = 17.2, 1.5 Hz, 1H, allyl trans =CH_2), 5.30 (dq, *J* = 10.5, 1.5 Hz, 1H, allyl cis =CH_2), 5.06 (dt, *J* = 5.7, 1.5 Hz, 2H, allyl CH_2), 4.81 (dd, *J* = 7.8, 5.6 Hz, 1H, H3′), 4.48 (dt, *J* = 5.6, 1.6 Hz, 1H, H2′), 4.18 (dd, *J* = 12.2, 4.3 Hz, 1H, $H5_a$′), 4.15–4.09 (m, 1H, H4′), 4.06 (dd, *J* = 12.2, 2.8 Hz, 1H, $H5_b$′), 3.44 (s, 1H, 2′OH), 3.14 (br s, 1H, iBu CH), 1.28 (d, *J* = 6.8 Hz, 3H, iBu CH_3), 1.27 (d, *J* = 6.8 Hz, 3H, iBu CH_3), 1.13–1.00 (m, 28H, TIPDS); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.0 (iBu C=O), 160.7 (C6), 152.2, 152.0 (C2, C4), 139.9 (C8), 132.2 (allyl =CH), 118.8 (allyl =CH_2), 118.7 (C5), 89.5 (C1′), 82.4 (C4′), 75.1 (C2′), 70.8 (C3′), 68.0 (allyl CH_2), 61.8 (C5′), 35.5 (iBu CH), 19.3 (iBu CH_3), 19.3 (iBu CH_3), 17.5, 17.4, 17.3, 17.2, 17.1, 17.1, 17.0, 17.0 (TIPDS CH_3), 13.3, 13.1, 12.9, 12.7 (TIPDS CH); HRMS–ESI *m*/*z* 636.3242 $[M + H]^+$; calcd ($C_{29}H_{50}N_5O_7Si_2^+$) 636.3243.

6-*O*-Allyl-2-*N*-isobutyryl-3′,5′-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)guanosin-2′-one (9). A solution of nucleoside **8** (1.32 g, 2.07 mmol) in anhydrous CH_2Cl_2 (25 mL) was stirred at 0 °C. Dess-Martin periodinane (1.32 g, 3.11 mmol) was added, and the temperature was slowly raised to rt. After stirring for 18 h, saturated aqueous solutions of $Na_2S_2O_3$ (10 mL) and $NaHCO_3$ (10 mL), water (20 mL) and CH_2Cl_2 (20 mL) were added, and the mixture was stirred for 1 h. The phases were separated, and the aqueous phase was extracted with CH_2Cl_2 (2 × 20 mL), dried ($MgSO_4$)* and concentrated to give crude **9** (1.32 g, 2.07 mmol, quant.) as a slightly yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$)* δ 7.84 (s, 1H, H8), 7.71 (br s, 1H, NH), 6.17–6.03 (m, 1H, allyl =CH), 5.70 (s, 1H, H1′), 5.47–5.40 (m, 2H, H3′, trans allyl =CH_2), 5.29 (dq, *J* = 10.5, 1.2 Hz, 1H, allyl cis =CH_2), 5.03 (dt, *J* = 5.6, 1.2 Hz, 2H, allyl CH_2), 4.34 (dd, *J* = 12.0, 5.9 Hz, 1H, $H5_a$′), 4.15 (dd, *J* = 12.0, 2.9 Hz 1H, $H5_b$′), 4.08 (ddd, *J* = 8.8, 5.9, 2.9 Hz, 1H, H4′), 2.82 (br s, 1H, iBu CH), 1.24 (d, *J* = 6.8 Hz, 3H, iBu CH_3), 1.23 (d, *J* = 6.8 Hz, 3H, iBu CH_3), 1.19–1.03 (m, 28H, TIPDS); ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.2 (C2′), 174.4 (iBu C=O), 160.7 (C6), 152.2 (C4), 152.0 (C2), 140.7 (C8), 132.0 (allyl =CH), 118.7 (allyl =CH_2), 118.2 (C5), 80.43 (C1′), 79.7 (C4′), 74.0 (C3′), 68.0 (allyl CH_2), 63.4 (C5′), 36.1 (iBu CH), 19.2, 19.2 (iBu CH_3), 17.5, 17.5, 17.3, 17.1, 17.0, 16.7 (TIPDS), 13.1, 13.0, 12.6, 12.4 (TIPDS); HRMS–ESI *m*/*z* 634.3066 $[M + H]^+$; calcd ($C_{29}H_{48}N_5O_7Si_2^+$) 636.3087.

6-*O*-Allyl-2-*N*-isobutyryl-3′,5′-*O*-(tetraisopropyldisiloxane-1,3-diyl)guanosine-2′(*S*)-spiroepoxide (10). NaH (60% in mineral oil, 57 mg, 1.43 mmol) was added to a stirred suspension of trimethylsulfoxonium iodide (0.52 g, 2.36 mmol) in anhydrous DMSO (4 mL). After stirring for 1 h at rt, anhydrous THF (4 mL) was added

*Extensive drying times (60 min) were needed to push the equilibrium between 2′-ketone and 2′-hydrate towards the ketone form, however, signals arising from the 2′-hydrate can still be observed in the spectra of **9**. A short drying time (5 min) resulted in a 3:1 mixture of **9** and the corresponding 2′-hydrate.

and the mixture was cooled to 0 °C. A solution of **9** (0.75 g, 1,18 mmol) in anhydrous THF (4 mL) was added dropwise at 0 °C and the mixture was stirred for 30 min at 0 °C. A saturated aqueous solution of NH_4Cl (10 mL), water (20 mL) and CH_2Cl_2 (20 mL) were added, and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (2 × 20 mL) and the combined organic phase was dried ($MgSO_4$), concentrated under reduced pressure and purified by silica gel column chromatography (20–40% EtOAc in petroleum ether, v/v) to give the epoxide **10** (0.46 g, 0.71 mmol, 60%) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (s, 1H, H8), 7.79 (s, 1H, NH), 6.25 (s, 1H, H1'), 6.12 (ddt, *J* = 17.2, 10.5, 5.7 Hz, 1H, allyl CH), 5.45 (dq, *J* = 17.2, 1.2 Hz, 1H, allyl trans =CH_2), 5.29 (dq, *J* = 10.5, 1.2 Hz, 1H, allyl cis =CH_2), 5.05 (dq, *J* = 5.7, 1.2 Hz, 2H, allyl CH_2), 4.77 (d, *J* = 8.6 Hz, 1H, H3'), 4.20-4.06 (m, 2H, H5'), 3.99 (dt, *J* = 8.6, 3.5 Hz, 1H, H4'), 3.29 (d, *J* = 5.3 Hz, 1H, $H6_a$'), 3.13 (br s, 1H, iBu CH), 3.00 (d, *J* = 5.3 Hz, 1H, $H6_b$'), 1.27 (d, *J* = 6.9 Hz, 6H, iBu CH_3), 1.16–0.98 (m, 28H, TIPDS); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.0 (iBu C=O), 160.6 (C6), 153.1 (C4), 152.1 (C2), 140.0 (C8), 132.2 (allyl =CH), 118.7 (allyl =CH_2), 117.9 (C5), 81.2 (C4'), 80.4 (C1'), 69.8 (C3'), 67.9 (allyl CH_2), 65.8 (C2'), 61.7 (C5'), 49.1 (C6'), 35.5 (iBu CH), 19.3 (iBu CH_3), 19.3 (iBu CH_3), 17.4, 17.4, 17.3, 17.3, 17.0, 17.0, 16.9, 16.8 (TIPDS CH_3), 13.3, 13.1, 12.8, 12.6 (TIPDS CH); HRMS–ESI *m/z* 648.3269 $[M + H]^+$; calcd ($C_{30}H_{50}N_5O_7Si_2^+$) 648.3243.

6-*O*-Allyl-2-*N*-isobutyryl-9-(2'-*C*-(6-*O*-allyl-2-*N*-isobutyrylguanin-9-yl)methyl-3',5'-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-D-arabinofuranosyl)guanine (11a) and 6-*O*-allyl-2-*N*-isobutyryl-9-(2'-*C*-(6-*O*-allyl-2-*N*-isobutyrylguanin-7-yl)methyl-3',5'-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-D-arabinofuranosyl)guanine (S6). NaHMDS (1.0 M in THF, 0.13 mL, 0.13 mmol) was added to a stirred suspension of 6-*O*-allyl-2-*N*-isobutyryl-guanine (**S3**, 0.33 g, 1.26 mmol) in anhydrous DMF (3 mL) and the mixture was stirred for 1 h. A solution of nucleoside **10** (0.42 g, 0.65 mmol) in anhydrous DMF (2 mL) was added, and the mixture was stirred for 3 days at rt. A saturated aqueous solution of NH_4Cl (20 mL) was added followed by water (100 mL) and CH_2Cl_2 (100 mL). The phases were separated, and the aqueous phase was extracted with CH_2Cl_2 (100 mL). The combined organic phase was washed with brine (2 × 100 mL), dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (20–100% EtOAc in petroleum ether, v/v) to give the desired *N*9 double-headed nucleoside **11a** (0.27 g, 0.30 mmol, 46%) and the *N*7-isomer (**S6**, 159 mg, 175 µmol, 27%) as white foams. **11a**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H, H8), 7.85 (s, 1H, H8''), 7.70 (s, 1H, NH), 7.66 (s, 1H, NH), 7.58 (s, 1H, 2'OH), 6.16–6.01 (m, 3H, H1', 2 × allyl =CH), 5.44 (dq, *J* = 17.2, 1.4 Hz, 1H, allyl trans =CH_2), 5.42 (dq, *J* = 17.2, 1.4 Hz, 1H, allyl trans =CH_2), 5.31 (dq, *J* = 10.5, 1.4 Hz, 1H, allyl cis =CH_2), 5.29 (dq, *J* = 10.5, 1.4 Hz, 1H, allyl cis =CH_2), 5.01–4.84 (m, 5H, $H6_a$', 2 × allyl CH_2), 4.70 (d, *J* = 5.0 Hz, 1H, H3'), 4.35 (d, *J* = 15.1 Hz, 1H, $H6_b$'), 4.14–4.10 (m, 2H, H5'), 3.94 (q, *J* = 6.2 Hz, 1H, H4'), 2.84 (br s, 1H, iBu), 2.66 (hept, *J* = 6.7 Hz, 1H, iBu CH), 1.37–1.30 (m, 12H, iBu CH_3), 1.15–1.08 (m, 28H, TIPDS); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.1, 174.8 (iBu C=O), 160.1 (C6''), 159.8 (C6), 152.4 (C4''), 151.4 (C4), 151.1 (C2), 150.8 (C2''), 143.5 (C8''), 142.5 (C8), 132.4, 132.1 (allyl =CH), 118.7, 118.5 (allyl =CH_2), 117.8 (C5''), 116.7 (C5), 85.7 (C1'), 83.2 (C4'), 81.4 (C3'), 80.7 (C2'), 68.1, 67.8 (allyl CH_2), 64.0 (C5'), 50.2 (C6'), 36.8, 36.2 (iBu CH), 19.4, 19.3 (iBu CH_3), 17.6, 17.4, 17.4, 17.4, 17.3, 17.4, 17.2, 17.1 (TIPDS CH_3), 13.5, 13.4, 13.0, 12.7 (TIPDS CH); HRMS–ESI *m/z* 909.4440 $[M + H]^+$; calcd ($C_{42}H_{65}N_{10}O_9Si_2^+$) 909.4469. **S6**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24–8.13 (m, 2H, H8'', NH), 7.81 (br s, 1H, NH), 7.72–7.63 (m, 2H, H8, 2'OH), 6.27–6.12 (m, 1H, allyl =CH),

6.09–5.98 (m, 1H, allyl =CH), 5.90 (s, 1H, 1H'), 5.58 (d, *J* = 17.2 Hz, 1H, allyl trans =CH_2), 5.46–5.35 (m, 2H, allyl cis =CH_2, allyl trans =CH_2), 5.29–5.24 (m, 1H, allyl cis =CH_2), 5.05–4.88 (m, 5H, $H6_a$', 2 × allyl CH_2), 4.73 (d, *J* = 1.9 Hz, 1H, H3'), 4.62 (d, *J* = 15.1 Hz, 1H, $H6_b$'), 4.14–4.03 (m, 3H, H4', H5'), 3.23 (br s, 1H, iBu CH), 2.68 (hept, *J* = 6.7 Hz, 1H, iBu CH), 1.36 (d, *J* = 6.7 Hz, 3H, iBu CH_3), 1.30 (d, *J* = 6.7 Hz, 3H, iBu CH_3), 1.24 (d, *J* = 6.7 Hz, 6H, iBu CH_3), 1.14–1.04 (m, 28H, TIPDS); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 176.6, 175.0 (iBu C=O), 162.1 (C4''), 160.5 (C6), 155.4 (C6''), 151.4 (C2''), 151.0 (C2), 150.7 (C4), 148.9 (C8''), 142.2 (C8), 131.8, 131.8 (allyl =CH), 120.0, 118.9 (allyl =CH_2), 117.6 (C5), 109.0 (C5''), 87.7 (C1'), 84.3 (C4'), 79.8 (C2'), 79.1 (C3'), 68.2, 68.1 (allyl CH_2), 63.3 (C5'), 50.2 (C6'), 36.9, 35.0 (iBu CH), 19.4, 19.3, 19.3, 19.2 (iBu CH_3), 17.5, 17.4, 17.4, 17.2, 17.2, 17.1, 17.0 (TIPDS CH_3), 13.6, 13.5, 13.0, 12.6 (TIPDS CH); HRMS–ESI *m/z* 909.4490 $[M + H]^+$; calcd ($C_{42}H_{65}N_{10}O_9Si_2^+$) 909.4469.

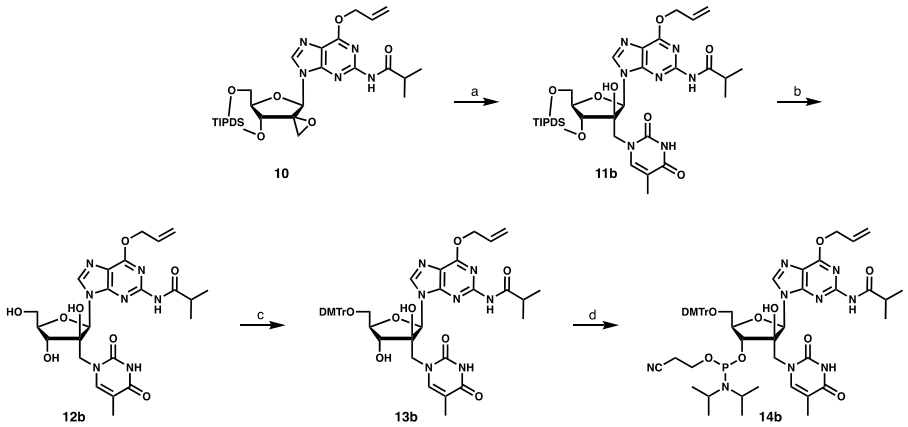
6-*O*-Allyl-2-*N*-isobutyryl-9-(2'-*C*-(6-*O*-allyl-2-*N*-isobutyrylguanin-9-yl)methyl-β-D-arabinofuranosyl)guanine (12a). Nucleoside **11a** (0.40 g, 0.44 mmol) was dissolved in anhydrous THF (6 mL), and $Et_3N{\cdot}3HF$ (0.22 mL, 1.35 mmol) was added. The mixture was stirred for 18 h, and then TMS-acetylene (0.50 mL, 3.51 mmol) was added. After stirring for 1 h, the mixture was concentrated under reduced pressure and the residue was purified by silica gel column chromatography (0–5% CH_3OH in CH_2Cl_2, v/v) to give nucleoside **12a** (0.27 g, 0.41 mmol, 93%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.65 (br s, 1H, NH), 8.28 (br s, 1H, NH), 8.25 (s, 1H, H8), 7.70 (s, 1H, H8''), 7.08 (d, *J* = 4.2 Hz, 1H, 3'OH), 6.93 (br s, 1H, 2'OH), 6.86 (br s, 1H, 5'OH), 6.35 (s, 1H, H1'), 6.13–5.95 (m, 2H, 2 × allyl =CH), 5.42 (dq, *J* = 17.4, 1.4 Hz, 1H, allyl trans =CH_2), 5.37 (dq, *J* = 17.4, 1.4 Hz, 1H, allyl trans =CH_2), 5.27 (dq, *J* = 10.5, 1.4 Hz, 1H, allyl cis =CH_2), 5.23 (dq, *J* = 10.5, 1.4 Hz, 1H, allyl cis =CH_2), 5.05–4.85 (m, 5H, $H6_a$', 2 × allyl CH_2), 4.41 (s, 1H, H4'), 4.07 (d, *J* = 10.9 Hz, 1H, $H5_a$'), 3.94–3.80 (m, 3H, H3', $H5_b$', $H6_b$'), 3.07 (s, 1H, iBu CH), 2.73 (hept, *J* = 6.9 Hz, 1H, iBu CH), 1.31 (d, *J* = 6.9 Hz, 3H, iBu CH_3), 1.30 (d, *J* = 6.9 Hz, 3H, iBu CH_3), 1.25 (d, *J* = 6.9 Hz, 6H, iBu CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 176.3, 175.3 (iBu C=O), 160.5 (C6''), 160.2 (C6), 152.8 (C4), 152.4 (C4''), 152.0, 151.7 (C2, C2''), 144.5 (C8''), 141.9 (C8), 132.1, 131.9 (allyl =CH), 119.1, 119.0 (allyl =CH_2), 117.6 (C5''), 117.4 (C5), 87.0 (C1'), 86.5 (C4'), 79.9 (C2'), 76.6 (C3'), 68.0, 67.9 (allyl CH_2), 61.6 (C5'), 43.3 (C6'), 36.8, 35.7 (iBu CH), 19.5, 19.4, 19.3, 19.3 (iBu CH_3); HRMS–ESI *m/z* 667.2943 $[M + H]^+$; calcd ($C_{30}H_{39}N_{10}O_8^+$) 667.2947.

6-*O*-Allyl-2-*N*-isobutyryl-9-(2'-*C*-(6-*O*-allyl-2-*N*-isobutyrylguanin-9-yl)methyl-5'-*O*-(4,4'-dimethoxytrityl)-β-D-arabinofuranosyl)guanine (13a). Nucleoside **12a** (0.60 g, 0.90 mmol) was co-evaporated with anhydrous pyridine (2 × 15 mL) and redissolved in anhydrous pyridine (10 mL). DMAP (10 mg, 82 μmol) and DMTrCl (1.20 g, 3.54 mmol) were added, and the mixture was stirred for 18 h at rt. Absolute EtOH (3–4 drops) was added and the mixture was concentrated under reduced pressure, redissolved in CH_2Cl_2 (50 mL) and washed with a saturated aqueous solution of $NaHCO_3$ (2 × 50 mL). The combined aqueous phase was extracted with CH_2Cl_2 (2 × 50 mL) and the combined organic phase was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (0–3% CH_3OH in CH_2Cl_2, v/v) to give nucleoside **13a** (0.69 g, 0.71 mmol, 79%) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.14 (br s, 2H, 2 × NH), 7.95 (br s, 1H, H8), 7.62 (br s, 1H, H8''), 7.33 (d, *J* = 7.4 Hz, 2H, DMTr), 7.25–7.17 (m, 6H, DMTr), 7.11 (t, *J* =

7.3 Hz, 1H, DMTr), 6.84 (d, *J* = 4.2 Hz, 1H, 3′OH), 6.72 (d, *J* = 8.9 Hz, 2H, DMTr), 6.70 (d, *J* = 8.9 Hz, 2H, DMTr), 6.42 (s, 1H, H1′), 6.12–5.94 (m, 2H, 2 × allyl =CH), 5.79 (br s, 1H, 2′OH), 5.42–5.36 (m, 2H, 2 × allyl trans $=CH_2$), 5.29–5.22 (m, 2H, 2 × allyl cis $=CH_2$), 5.05–4.87 (m, 5H, 2 × allyl CH_2, $H6_a$′), 4.46 (br s, 1H, H4′), 3.90 (d, *J* = 14.3 Hz, 1H, $H6_b$′), 3.73–3.61 (m, 7H, 2 × DMTr OCH_3, H3′), 3.53 (d, *J* = 9.6 Hz, 1H, $H5_a$′), 3.43 (dd, *J* = 9.6, 4.7 Hz, 1H, $H5_b$′), 3.12 (br s, 1H, iBu CH), 2.63 (hept, *J* = 7.0 Hz, 1H, iBu CH), 1.32–1.25 (m, 12H, iBu CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 176.1, 174.8 (Bz C=O), 160.4, 160.3 (C6, C6′′), 158.7, 158.6 (DMTr), 152.7 (C4), 152.5 (C4′′), 151.9, 151.6 (C2, C2′′), 144.5 (C8′′), 143.7 (DMTr), 142.0 (C8), 135.2, 135.0 (DMTr), 132.1, 131.7 (allyl =CH), 130.2, 130.0, 128.2, 128.0, 127.1 (DMTr), 119.3, 119.2 (allyl $=CH_2$), 117.7, 117.4 (C5, C5′′), 113.2 (DMTr), 87.7 (DMTr), 85.9 (C1′), 85.2 (C4′), 80.3 (C2′), 75.9 (C3′), 68.2, 68.1 (allyl CH_2), 64.3 (C5′), 55.2, 55.2 (DMTr OCH_3), 43.7 (C6′), 37.0, 35.5 (iBu CH), 19.4, 19.4, 19.3, 19.3 (iBu CH_3); HRMS–ESI *m*/*z* 991.4027 $[M + Na]^+$; calcd ($C_{51}H_{56}N_{10}O_{10}Na^+$) 991.4073.

6-*O*-Allyl-2-*N*-isobutyryl-9-(2′-*C*-(6-*O*-allyl-2-*N*-isobutyrylguanin-9-yl)methyl-3′-*O*-(*P*-(2-cyanoethoxy)-*N*,*N*-diisopropylaminophosphinyl)-5′-*O*-(4,4′-dimethoxytrityl)-β-D-arabinofuranosyl)guanine (14a). Nucleoside **13a** (110 mg, 114 µmol) was co-evaporated with anhydrous DCE (2 × 5 mL) and redissolved in anhydrous CH_2Cl_2 (2 mL). DIPEA (0.12 mL, 0.69 mmol) was added followed by 2-cyanoethyl *N*,*N*-diisopropylchlorophosphoramidite (0.10 mL, 0.45 mmol) and the mixture was stirred for 18 h at rt under argon. CH_3OH (2–3 drops) was added, and the mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (0–3% CH_3OH in CH_2Cl_2, v/v) followed by precipitation from CH_2Cl_2 in anhydrous petroleum ether (100 mL) at 0 °C to give phosphoramidite **14a** (80 mg, 68 µmol, 60%) as a white foam. ^{31}P NMR (162 MHz, $CDCl_3$) *δ* 151.3, 149.8; HRMS–ESI *m*/*z* 1191.5126 $[M + Na]^+$; calcd ($C_{60}H_{73}N_{12}O_{11}PNa^+$) 1191.5152.

Preparation of the G_T-monomer



Scheme S3 Reagents and conditions: (a) K_2CO_3, thymine, DMF, rt, 18 h, 73%; (b) $Et_3N{\cdot}3HF$, THF, rt, 3 h, 89%; (c) DMTrCl, DMAP, pyridine, rt, 48 h, 74%; (k) 2-cyanoethyl *N*,*N*-diisopropylchlorophosphoramidite, DIPEA, CH_2Cl_2, rt, 18 h, 87%. DMTr = 4,4′-dimethoxytrityl.

6-*O*-Allyl-2-*N*-isobutyryl-9-(3′,5′-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-2′-*C*-(thymin-1-yl)methyl-β-D-arabinofuranosyl)guanine (11b). K_2CO_3 (0.25 g, 1.81 mmol) was added to a suspension of thymine (230 mg, 1.82 mmol) in anhydrous DMF (3 mL), and the suspension was stirred for 15 min. A solution of epoxide **10** (0.78 g, 1.20 mmol) in anhydrous DMF (10 mL) was added dropwise at rt, and the resulting suspension was stirred for 18 h. A saturated aqueous solution of NH_4Cl (10 mL), water (50 mL) and CH_2Cl_2 (50 mL) was added, and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (2 × 50 mL), and the combined organic phase was washed with brine (100 mL), dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (50–100% EtOAc in petroleum ether, v/v) to give the double-headed nucleoside **11b** (0.68 g, 0.87 mmol, 73%) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (s, 1H, NH), 8.05 (s, 1H, NH), 7.98 (s, 1H, H8), 7.35–7.30 (m, 2H, H6′′, 2′OH), 6.11–5.97 (m, 2H, H1′, allyl =CH), 5.39 (dq, J = 17.3, 1.3 Hz, 1H, allyl trans =CH_2), 5.27 (dq, J = 10.5, 1.3 Hz, 1H, allyl cis =CH_2), 4.98–4.87 (m, 2H, allyl CH_2), 4.69–4.62 (m, 2H, H3′, H6$_a$′), 4.07–3.98 (m, 3H, H4′, H5′), 3.83 (d, J = 14.8 Hz, 1H, H6$_b$′), 2.66 (hept, J = 6.4 Hz, 1H, iBu CH), 1.74 (d, J = 0.8 Hz, 3H, C5′′-CH_3), 1.29 (d, J = 6.4 Hz, 3H, iBu CH_3), 1.28 (d, J = 6.4 Hz, 3H, iBu CH_3), 1.12–1.04 (m, 28H, TIPDS); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.5 (iBu C=O), 163.7 (C4′′), 160.9 (C6), 151.6 (C2′′), 151.5 (C4), 150.9 (C2), 143.5 (C8), 142.8 (C6′′), 131.9 (allyl =CH), 118.8 (allyl =CH_2), 118.6 (C5), 109.7 (C5′′), 88.1 (C1′), 83.2 (C4′), 80.7 (C2′), 79.2 (C3′), 68.2 (allyl CH_2), 63.2 (C5′), 51.0 (C6′), 36.7 (iBu CH), 19.4, 19.2 (iBu CH_3), 17.5, 17.4, 17.4, 17.3, 17.2, 17.2, 17.1, 17.0 (TIPDS CH_3), 13.5, 13.4, 13.0, 12.5 (TIPDS CH), 12.1 (C5′′-CH_3); HRMS–ESI m/z 774.3682 $[M + H]^+$; calcd ($C_{35}H_{56}N_7O_9Si_2^+$) 774.3673.

6-*O*-Allyl-2-*N*-isobutyryl-9-(2′-*C*-(thymin-1-yl)methyl-β-D-arabinofuranosyl)guanine (12b). Nucleoside **11b** (0.68 g, 0.88 mmol) was dissolved in anhydrous THF (10 mL), and then $Et_3N{\cdot}3HF$ (0.43 mL, 2.64 mmol) was added. The mixture was stirred for 3 h and TMS-acetylene (1.00 mL, 7.03 mmol) was added. After stirring for 1 h, the mixture was concentrated under reduced pressure and the residue was purified by silica gel column chromatography (0–7% CH_3OH in CH_2Cl_2, v/v) to give nucleoside **12b** (0.41 g, 0.78 mmol, 89%) as a white foam. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.25 (s, 1H, NH), 10.35 (s, 1H, NH), 8.30 (s, 1H, H8), 7.27 (d, J = 1.1 Hz, 1H, H6′′), 6.35 (s, 1H, 2′OH), 6.19 (ddt, J = 17.2, 10.4, 5.8 Hz, 1H, allyl =CH), 6.11 (s, 1H, H1′), 5.96 (d, J = 3.8 Hz, 1H, 3′OH), 5.54–5.45 (m, 2H, 5′OH, allyl trans =CH_2), 5.32 (dd, J = 10.4, 1.3 Hz, 1H, allyl cis =CH_2), 5.12–5.02 (m, 2H, allyl CH_2), 4.03 (d, J = 14.7 Hz, 1H, H6$_a$′), 3.99 (dd, J = 3.8, 1.5 Hz, 1H, H3′), 3.96 (dt, J = 4.9, 1.5 Hz, 1H, H4′), 3.86 (d, J = 14.7 Hz, 1H, H6$_b$′), 3.68 (t, J = 4.9 Hz, 2H, H5′), 2.87 (hept, J = 6.7 Hz, 1H, iBu CH), 1.62 (d, J = 1.1 Hz, 3H, C5′′-CH_3), 1.10 (d, J = 6.7 Hz, 6H, iBu CH_3); ^{13}C NMR (101 MHz, DMSO-d_6) δ 175.0 (iBu C=O), 163.8 (C4′′), 159.5 (C6), 152.9 (C4), 152.1 (C2), 151.9 (C2′′), 142.4 (C6′′), 141.9 (C8), 132.9 (allyl =CH), 118.7 (allyl =CH_2), 116.4 (C5), 108.2 (C5′′), 85.6 (C4′), 85.2 (C1′), 79.8 (C2′), 76.2 (C3′), 66.9 (allyl CH_2), 61.5 (C5′), 47.5 (C6′), 34.3 (iBu CH), 19.2 (iBu CH_3), 11.7 (C5′′-CH_3); HRMS–ESI m/z 532.2133 $[M + H]^+$; calcd ($C_{23}H_{30}N_7O_8^+$) 532.2150.

6-*O*-Allyl-2-*N*-isobutyryl-9-(5′-*O*-(4,4′-dimethoxytrityl)-2′-*C*-(thymin-1-yl)methyl-β-D-arabinofuranosyl)-guanine (13b). Nucleoside **12b** (0.36 g, 0.68 mmol) was co-evaporated with anhydrous pyridine (2 × 20 mL) and redissolved in anhydrous pyridine (10 mL). DMAP (15 mg, 123 μmol) and DMTrCl (0.35 g, 1.03 mmol)

were added, and the mixture was stirred at rt for 48 h. Absolute EtOH (3–4 drops) was added and the mixture was concentrated under reduced pressure, redissolved in CH_2Cl_2 (25 mL) and washed with a saturated aqueous solution of $NaHCO_3$ (2 × 25 mL). The combined aqueous phase was extracted with CH_2Cl_2 (2 × 25 mL) and the combined organic phase was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (0–5% CH_3OH in CH_2Cl_2, v/v) to give nucleoside **13b** (0.43 g, 0.50 mmol, 74%) as a white foam containing 0.4 eq pyridine. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.08 (br s, 1H, NH), 10.35 (br s, 1H, NH), 8.21 (s, 1H, H8), 7.36–7.18 (m, 9H, DMTr), 6.94 (d, *J* = 1.1 Hz, 1H, H6''), 6.81 (d, *J* = 8.9 Hz, 2H, DMTr), 6.79 (d, *J* = 8.9 Hz, 2H, DMTr), 6.60 (s, 1H, H1'), 6.13 (ddt, *J* = 17.2, 10.5, 5.5 Hz, 1H, allyl =CH), 5.90 (br s, 1H, 3'OH), 5.64 (br s, 1H, 2'OH), 5.47 (dq, *J* = 17.2, 1.3 Hz, 1H, allyl trans =CH_2), 5.33 (dq, *J* = 10.5, 1.3 Hz, 1H, allyl cis =CH_2), 5.07 (dt, *J* = 5.5, 1.3 Hz, 2H, allyl CH_2), 4.70 (d, *J* = 14.8 Hz, 1H, $H6_a$'), 4.18 (s, 1H, H4'), 3.95 (s, 1H, H3'), 3.86 (br s, 1H, iBu CH), 3.77 (s, 3H, DMTr OCH_3), 3.76 (s, 3H, DMTr OCH_3), 3.68 (dd, *J* = 11.1, 1.6 Hz, 1H, $H5_a$'), 3.42 (dd, *J* = 11.1, 2.0 Hz, 1H, $H5_b$'), 3.06 (d, *J* = 14.8 Hz, 1H, $H6_b$'), 1.87 (s, 3H, 5''-CH_3), 1.30 (d, *J* = 6.8 Hz, 3H, iBu CH_3), 1.30 (d, *J* = 6.8 Hz, 3H, iBu CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.1† (iBu C=O), 163.4 (C4''), 160.4 (C6), 159.0, 159.0 (DMTr), 154.3 (C2''), 153.1 (C4), 152.5 (C2), 143.1 (DMTr), 142.3 (C6''), 141.5 (C8), 134.4, 134.2 (DMTr), 132.1 (allyl =CH), 130.2, 130.1, 128.2, 128.1, 127.5 (DMTr), 118.6 (allyl =CH_2), 117.4 (C5), 113.4, 113.4 (DMTr), 111.5 (C5''), 88.9 (DMTr), 85.4 (C1'), 84.2 (C4'), 81.0 (C2'), 75.9 (C3'), 67.9 (allyl CH_2), 63.8 (C5'), 55.3 (DMTr OCH_3), 47.2 (C6'), 33.9 (iBu CH), 19.2 (iBu CH_3), 19.2 (iBu CH_3), 12.2 (C5''-CH_3); HRMS–ESI *m/z* 834.3403 $[M + H]^+$; calcd ($C_{44}H_{48}N_7O_{10}^+$) 834.3457.

6-*O*-Allyl-2-*N*-isobutyryl-9-(3'-*O*-(*P*-(2-cyanoethoxy)-*N*,*N*-diisopropylaminophosphinyl)-5'-*O*-(4,4'-dimethoxytrityl)-2'-*C*-(thymin-1-yl)methyl-β-D-arabinofuranosyl)guanine (14b). Nucleoside **13b** (0.27 g, 0.32 mmol) was co-evaporated with anhydrous DCE (2 × 10 mL) and redissolved in anhydrous CH_2Cl_2 (2 mL). DIPEA (0.33 mL, 1.89 mmol) was added followed by 2-cyanoethyl *N*,*N*-diisopropylchlorophosphoramidite (0.28 mL, 1.25 mmol) and the mixture was stirred for 18 h at rt. CH_3OH (2–3 drops) was added and the mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (0–3% CH_3OH in CH_2Cl_2, v/v) followed by precipitation from CH_2Cl_2 in anhydrous petroleum ether (200 mL) at 0 °C to give phosphoramidite **14b** (0.29 g, 0.28 mmol, 87%) as a white foam. ^{31}P NMR (162 MHz, $CDCl_3$) δ 151.3, 149.7; HRMS–ESI *m/z* 1034.4488 $[M + H]^+$; calcd ($C_{53}H_{65}N_9O_{11}P^+$) 1034.4536.

Oligonucleotide synthesis

Oligonucleotide synthesis was carried out on an automated DNA synthesizer (Expedite Nucleic Acid Synthesis System, Model 8909) following the phosphoramidite approach. The synthesis was performed on a 0.2–0.5 µmol scale by using the amidites **5**, **14a** and **14b** as well as the previously reported phosphoramidite equivalents of $\mathbf{U_G}$,[4] $\mathbf{U_A}$,[5] $\mathbf{C_C}$[6] and $\mathbf{A_T}$[7] and the corresponding commercial 2-cyanoethyl phosphoramidites of the natural deoxynucleosides. The synthesis followed the regular protocol for the DNA synthesizer. For modified amidites, however, manual couplings (~10 µmol in 0.2 mL anhydrous CH_3CN and 0.3 mL activator solution)

†Clearly observed in ^{1}H,^{13}C–HMBC spectrum.

with a prolonged coupling time of 15 min were used. 4,5-Dicyanoimidazole was used as the activator. Oligonucleotides containing $\mathbf{G_G}$, $\mathbf{G_T}$ or $\mathbf{U_G}$ were treated with a mixture of $Pd(PPh_3)_4$ (20 mg), PPh_3 (20 mg) and $Et_2NH_2{\cdot}HCO_3$ (20 mg) in anhydrous DCE (1 mL) at rt for 24 h followed by sequential washings with CH_2Cl_2 (5 mL), acetone (5 mL) and water (5 mL). The 5′-*O*-DMTr oligonucleotides were removed from the solid support by treatment with concentrated aqueous ammonia (28%, 1 mL) at rt for 72 h. After reversed-phase HPLC purification, appropriate fractions were combined, evaporated and detritylated by treatment with an 80% aqueous solution of acetic acid for 30 min. Then, aqueous solutions of sodium acetate (3 M, 15 µL) and sodium perchlorate (5 M, 15 µL) were added, followed by acetone (1 mL). The pure oligonucleotides were precipitated over night at −20 °C. After centrifugation at 12,000 rpm for 10 min at 4 °C, the supernatant was removed, and the pellet was washed with cold acetone (2 × 1 mL), dried for 30 min at 35 °C and dissolved in Milli-Q® water (1 mL). The concentrations of the purified oligonucleotides were determined by optical density at 260 nm, and the purity was obtained by ion-exchange chromatography. For all oligonucleotides, mass spectra (Table 1) were recorded on a MALDI-TOF mass spectrometer, and the obtained m/z values were within ±2 amu of the calculated masses. Neither branching nor capping at the unprotected 2′-hydroxyl was observed for any of the synthesized oligonucleotides.

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MALDI-TOF MS data and analytical HPLC profiles for synthesized oligonucleotides

Analytical anion-exchange HPLC (IE-HPLC) was performed using a Merck-Hitachi Lachrom system equipped with a Dionex DNAPac® PA100 Analytical Oligonucleotide column (13 µm, 250 mm × 4 mm) heated to 60 °C. Elution was performed with an 10% isocratic hold of C, starting with a fixed 2% solution of A in B, followed by a linear gradient to a 30% solution of A in B in 23 min at a flow rate of 2.0 mL/min. A = H_2O; B = $NaClO_4$ (1.0 M); C = TrisCl (0.25 M), pH 8.0.

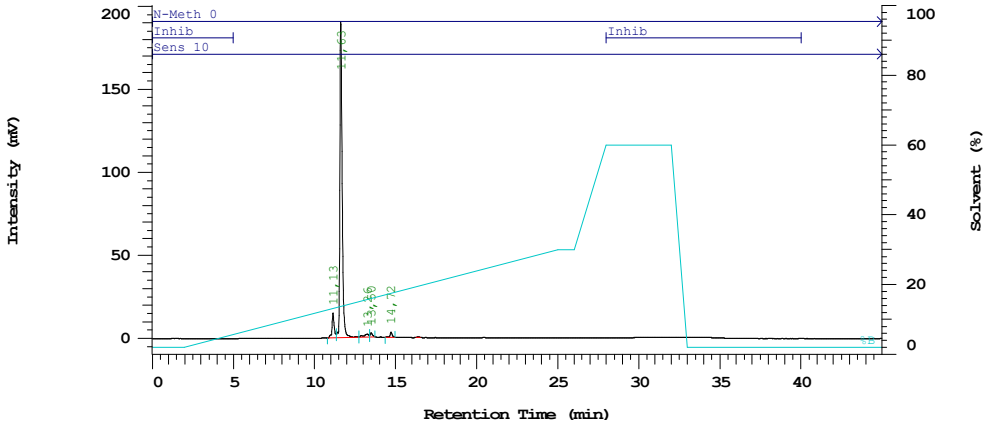


Fig. S1 HPLC profile for ON1 with the sequence 5′-d(CGCT **A_C** CTACGC).

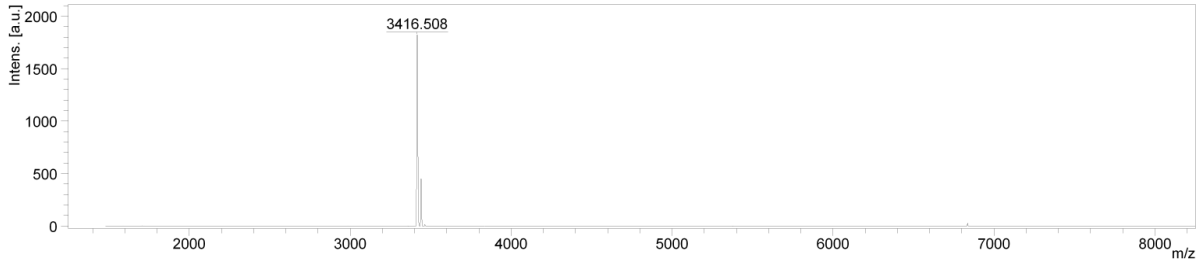


Fig. S2 MALDI-TOF mass spectrum for ON1 with the sequence 5′-d(CGCT **A_C** CTACGC).

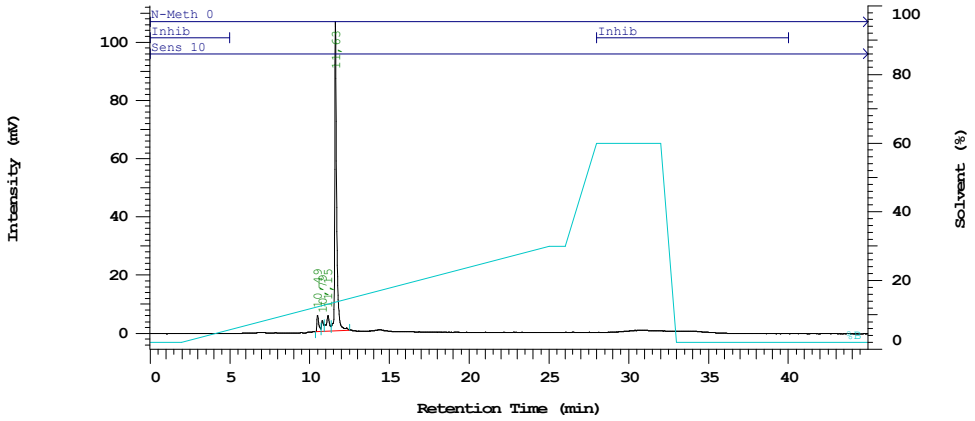


Fig. S3 HPLC profile for ON2 with the sequence 5′-d(GCGTA **G_G** TAGCG).

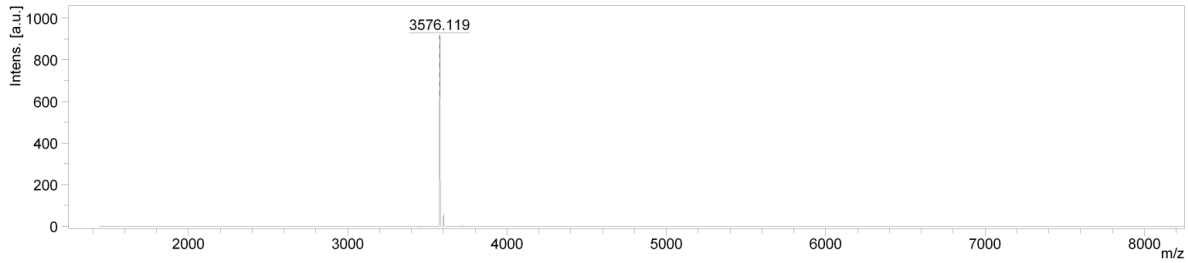


Fig. S4 MALDI-TOF mass spectrum for ON2 with the sequence 5′-d(GCGTA **G_G** TAGCG).

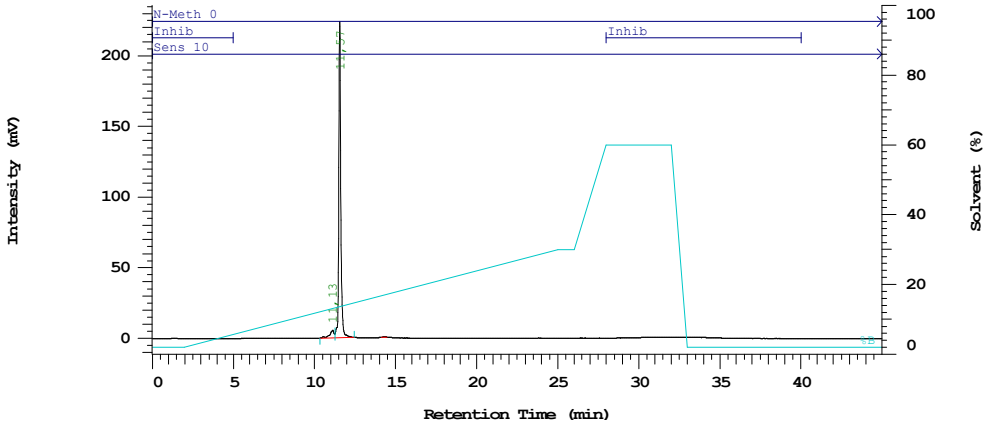


Fig. S5 HPLC profile for ON3 with the sequence 5′-d(GCGTAG **G_T** AGCG).

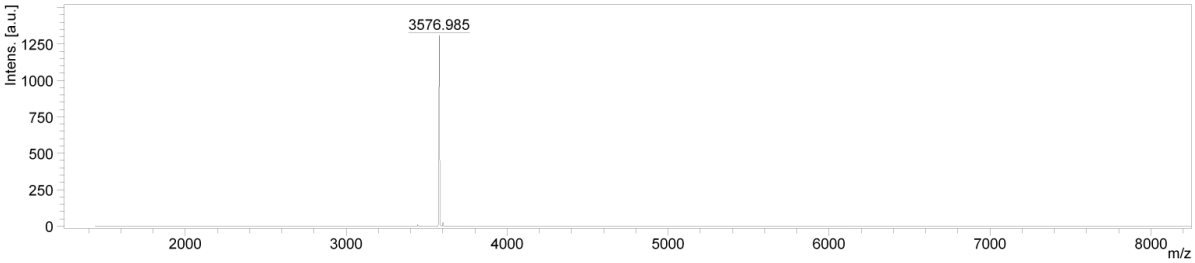


Fig. S6 MALDI-TOF mass spectrum for ON3 with the sequence 5′-d(GCGTAG **G_T** AGCG).

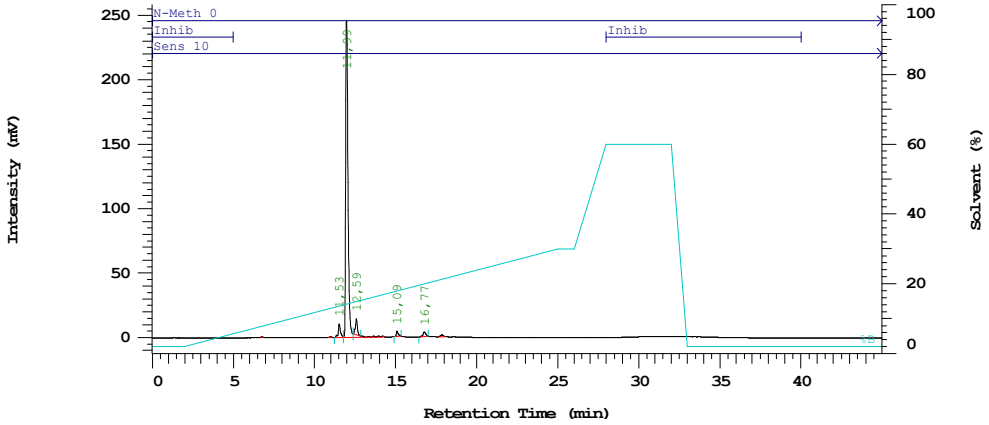


Fig. S7 HPLC profile for ON4 with the sequence 5′-d(CGCTA **C_C** TACGC).

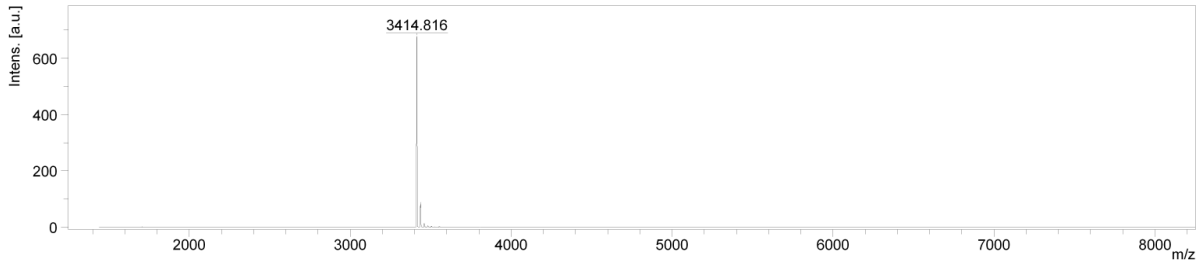


Fig. S8 MALDI-TOF mass spectrum for ON4 with the sequence 5′-d(CGCTA **C_C** TACGC).

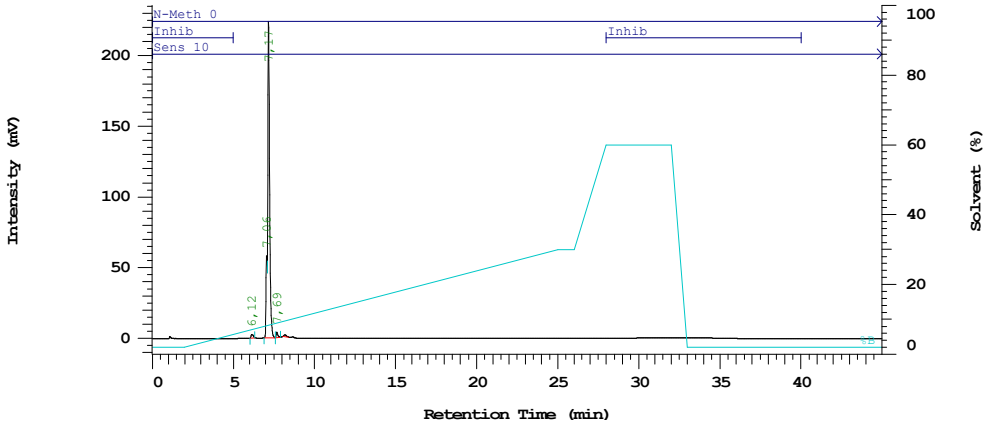


Fig. S9 HPLC profile for ON5 with the sequence 5′-d(**$U_AC_CA_CA_TA_C$**).

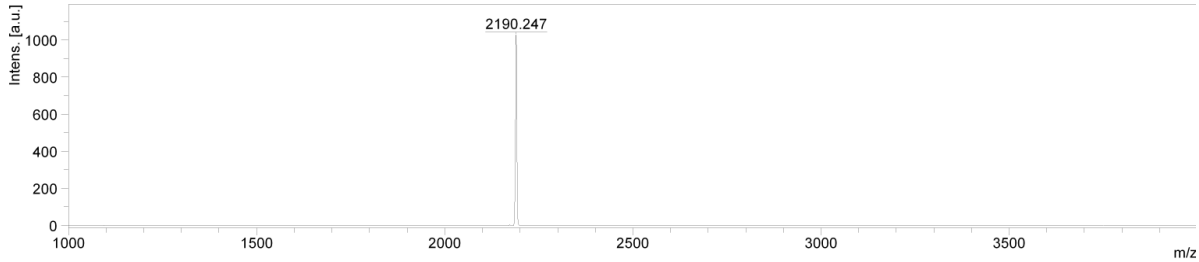


Fig. S10 MALDI-TOF mass spectrum for ON5 with the sequence 5′-d(**$U_AC_CA_CA_TA_C$**).

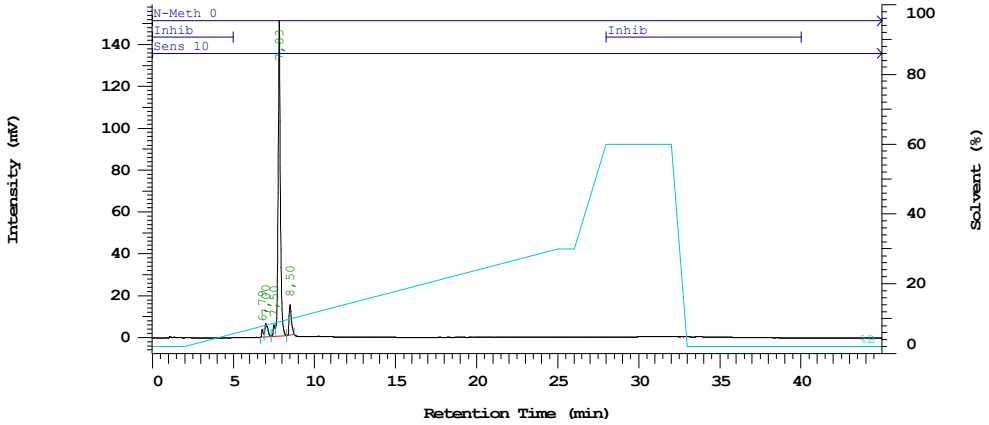


Fig. S11 HPLC profile for ON6 with the sequence 5′-d(**$G_TA_TG_TG_GU_A$**).

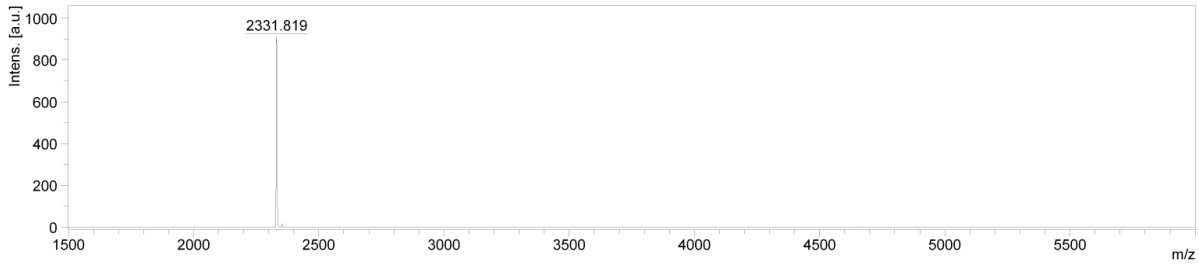


Fig. S12 MALDI-TOF mass spectrum for ON6 with the sequence 5′-d(**$G_TA_TG_TG_GU_A$**).

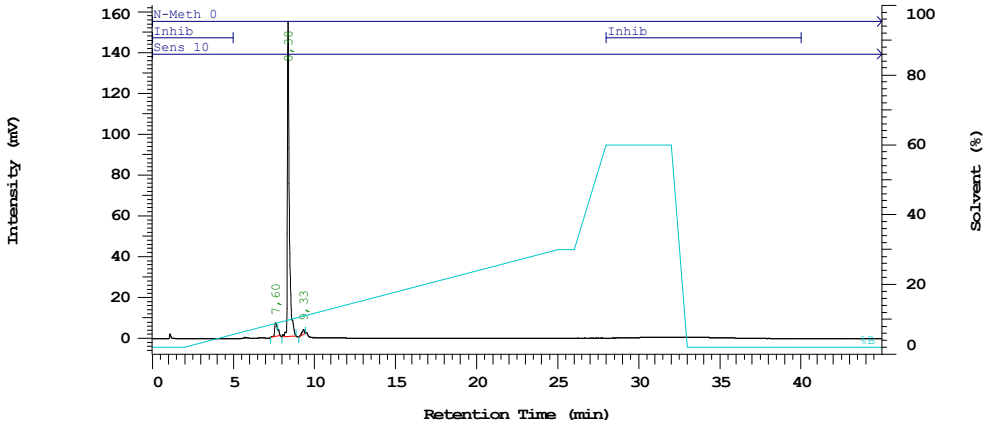


Fig. S13 HPLC profile for ON7 with the sequence 5′-d(G **$U_AU_GU_GG_T$** A).

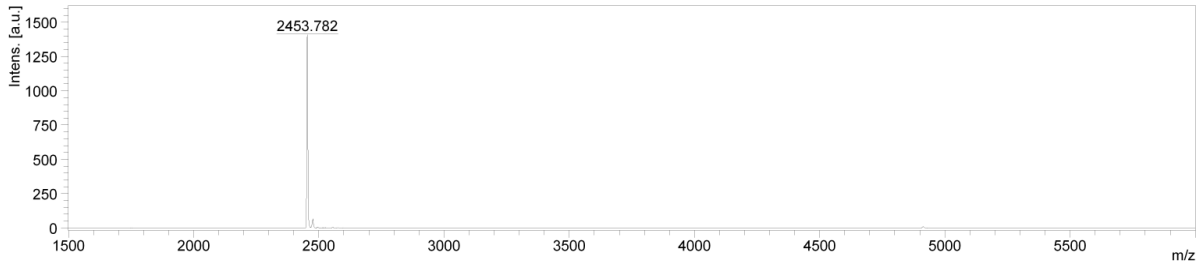


Fig. S14 MALDI-TOF mass spectrum for ON7 with the sequence 5′-d(G **$U_AU_GU_GG_T$** A).

Thermal denaturation experiments and UV melting curves

UV melting experiments were carried out on a PerkinElmer 35 UV/Vis spectrophotometer. The samples were comprised of a medium salt buffer containing 2.5 mM Na_2HPO_4, 5 mM NaH_2PO_4, 100 mM NaCl, and 0.1 mM EDTA at pH = 7.0 with 1.5 µM concentrations of the two complementary sequences. Before measuring, the oligonucleotides were annealed by heating the samples to 75 °C followed by controlled cooling to 10 °C. The absorbance at 260 nm was recorded as a function of the temperature (10 °C to 75 °C, 1 °C/min) by means of a PTP-6 Peltier Temperature Programmer (Fig. S17). The melting temperatures (T_m) were determined as the local maximum of the first derivatives of the absorbance vs. temperature curves. For each melting temperature, a clear and well-defined maximum was found, and the process of denaturation was reversible upon cooling. All determinations are averages of at least duplicates within ±0.5 °C. All melting temperatures have been adjusted by –2.4 °C to account for the residual error of the spectrophotometer that was determined using multiple known references. In Fig. S15, the structure of measured dsRNA and DNA·RNA hybrids and RNA·DhNA hybrids (D12–D17) are presented together with the results of the thermal stability measurements. In the experiments with varying NaCl concentrations (Fig. S16), the buffer contained 2.5 mM Na_2HPO_4, 5 mM NaH_2PO_4, and 0.1 mM EDTA, and then a 5 M aqueous solution of NaCl were added to the 485 µL samples sequentially in aliquots of 5 µL, 5 µL and 15 µL to reach NaCl concentrations of 50 mM, 100 mM and 250 mM, respectively. To reach 500 mM NaCl, 7.3 mg solid NaCl was added to the 250 mM samples. Concentration deviations due to the additional volume of the NaCl solution aliquots were kept within ±3%.

In Fig. S17C+D, we observed two unexpectedly low melting temperatures (red lines) for both a native and a modified mismatch duplex. To ensure correct measurement, the commercial mismatch sequence was measured alone, which showed no melting ruling out observable competing secondary structures. It was also measured against its fully matching complementary sequence, which gave an expected melting temperature of 47.0 °C. Therefore, we attribute the stability decrease to an inherent characteristic of the specific oligonucleotide sequence, which may or may not arise from its central palindromic hexamer.

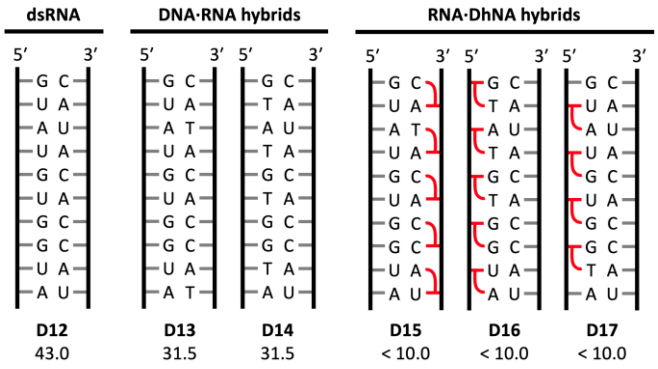


Fig. S15 Structures and melting temperatures (T_m, °C) of dsRNA, DNA·RNA hybrids and RNA·DhNA hybrids.

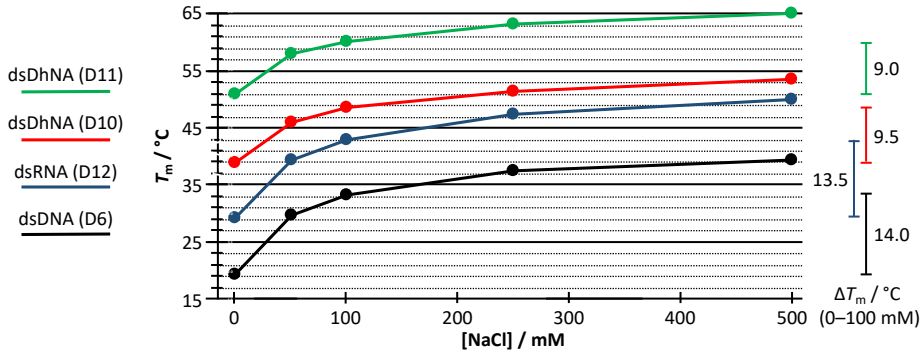
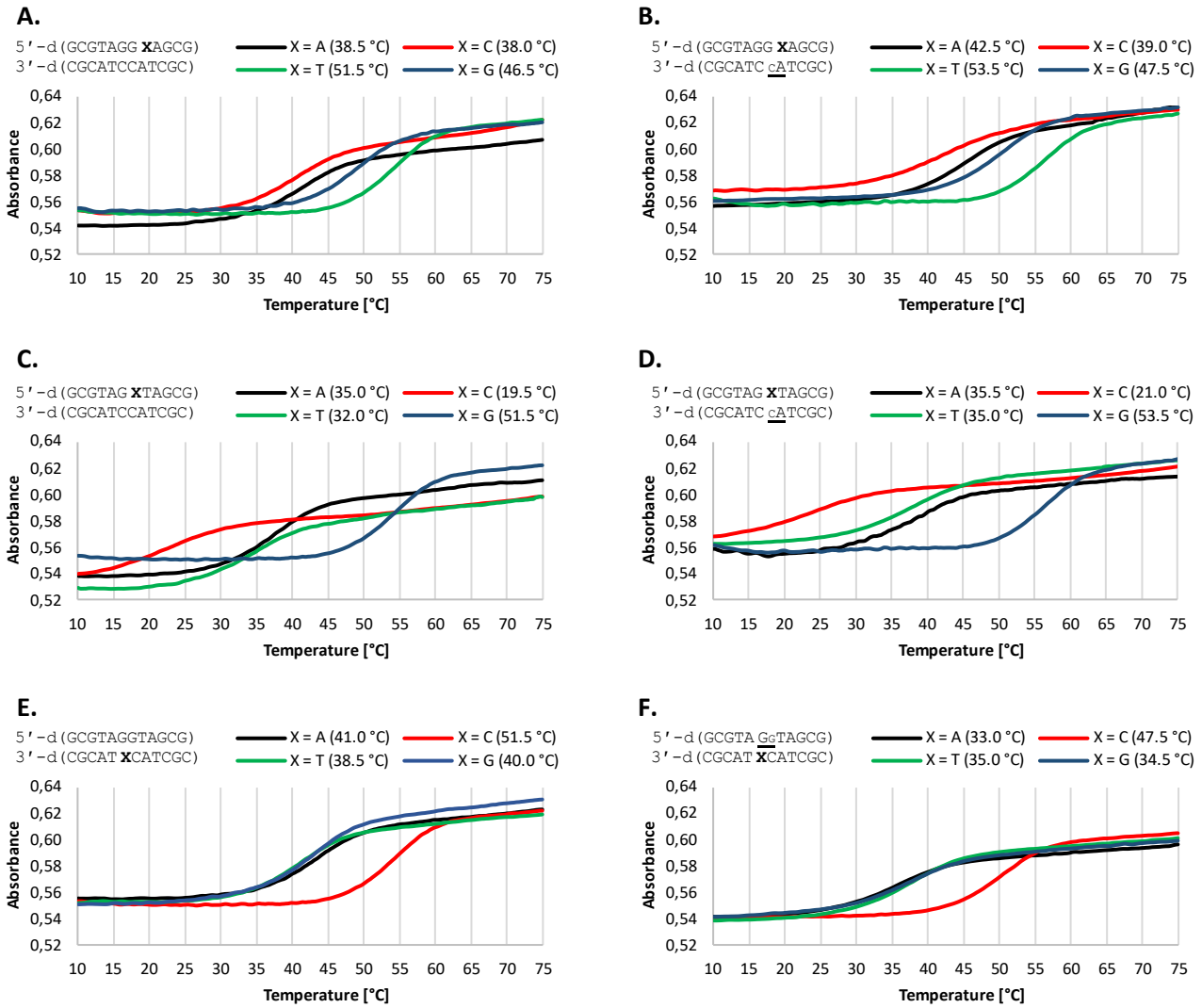
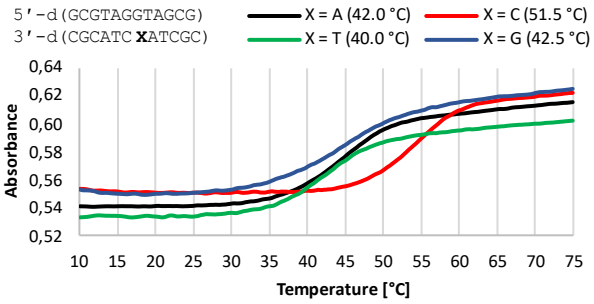


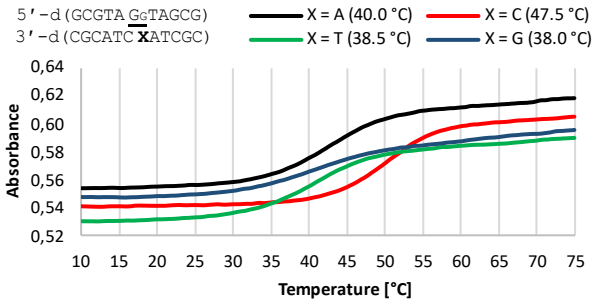
Fig. S16 Melting temperatures (T_m, °C) of duplexes D6 and D10–D12 at varying (0–500 mM) NaCl concentrations (referring to Fig. 4 and Fig. S15, ESI†).



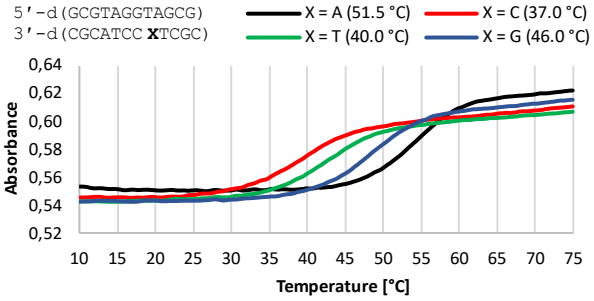
G.


5′-d(GCGTAGGTAGCG)
3′-d(CGCATC XATCGC)
X = A (42.0 °C)
X = C (51.5 °C)
X = T (40.0 °C)
X = G (42.5 °C)
Absorbance
Temperature [°C]

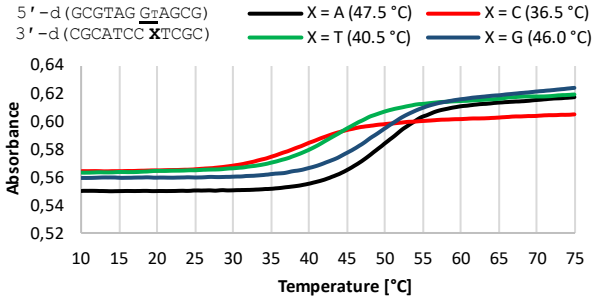
H.


5′-d(GCGTA GGTAGCG)
3′-d(CGCATC XATCGC)
X = A (40.0 °C)
X = C (47.5 °C)
X = T (38.5 °C)
X = G (38.0 °C)
Absorbance
Temperature [°C]

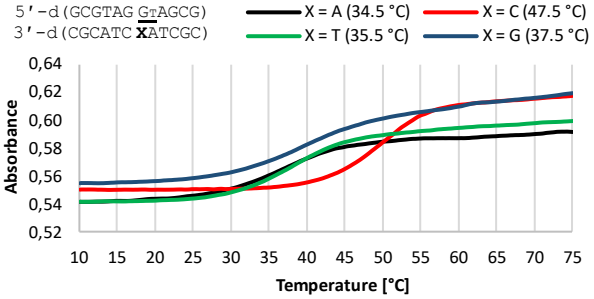
I.


5′-d(GCGTAGGTAGCG)
3′-d(CGCATCC XTCGC)
X = A (51.5 °C)
X = C (37.0 °C)
X = T (40.0 °C)
X = G (46.0 °C)
Absorbance
Temperature [°C]

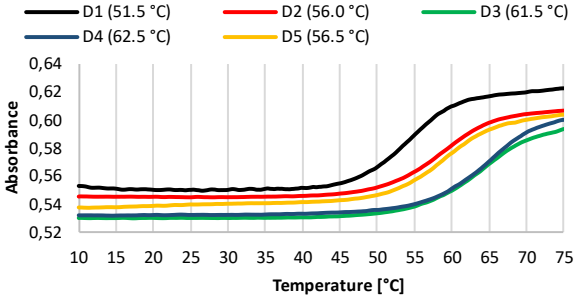
J.


5′-d(GCGTAG GTAGCG)
3′-d(CGCATCC XTCGC)
X = A (47.5 °C)
X = C (36.5 °C)
X = T (40.5 °C)
X = G (46.0 °C)
Absorbance
Temperature [°C]

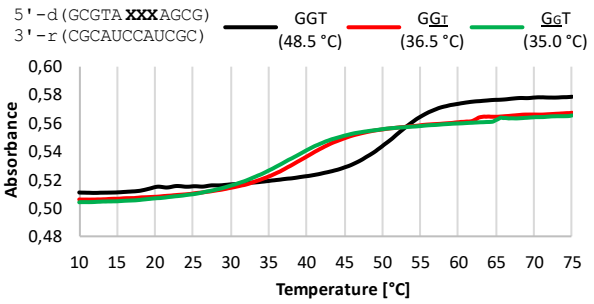
K.


5′-d(GCGTAG GTAGCG)
3′-d(CGCATC XATCGC)
X = A (34.5 °C)
X = C (47.5 °C)
X = T (35.5 °C)
X = G (37.5 °C)
Absorbance
Temperature [°C]

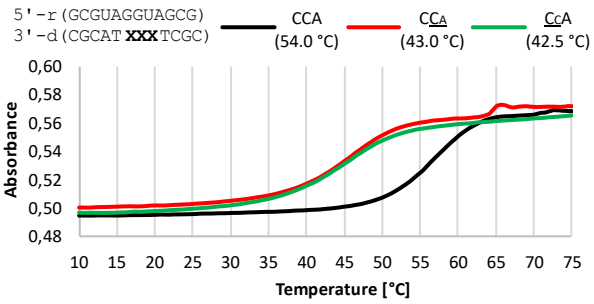
L.


D1 (51.5 °C)
D2 (56.0 °C)
D3 (61.5 °C)
D4 (62.5 °C)
D5 (56.5 °C)
Absorbance
Temperature [°C]

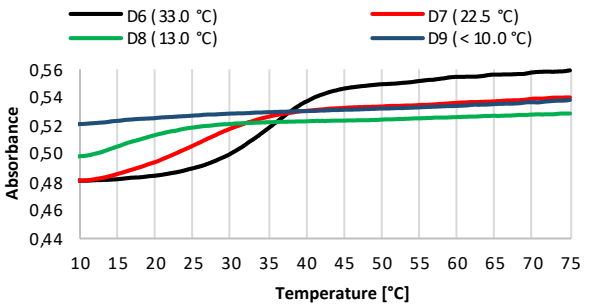
M.


5′-d(GCGTA XXXAGCG)
3′-r(CGCAUCCAUCGC)
GGT (48.5 °C)
GGT (36.5 °C)
GGT (35.0 °C)
Absorbance
Temperature [°C]

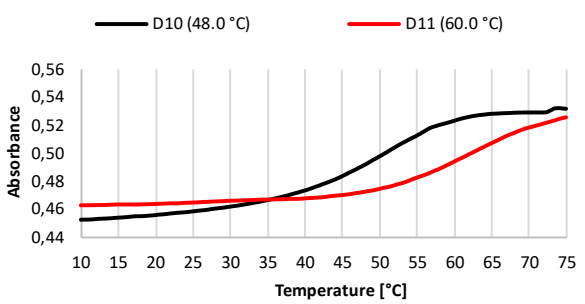
N.


5′-r(GCGUAGGUAGCG)
3′-d(CGCAT XXXTCGC)
CCA (54.0 °C)
CCA (43.0 °C)
CCA (42.5 °C)
Absorbance
Temperature [°C]

O.


D6 (33.0 °C)
D7 (22.5 °C)
D8 (13.0 °C)
D9 (< 10.0 °C)
Absorbance
Temperature [°C]

P.


D10 (48.0 °C)
D11 (60.0 °C)
Absorbance
Temperature [°C]

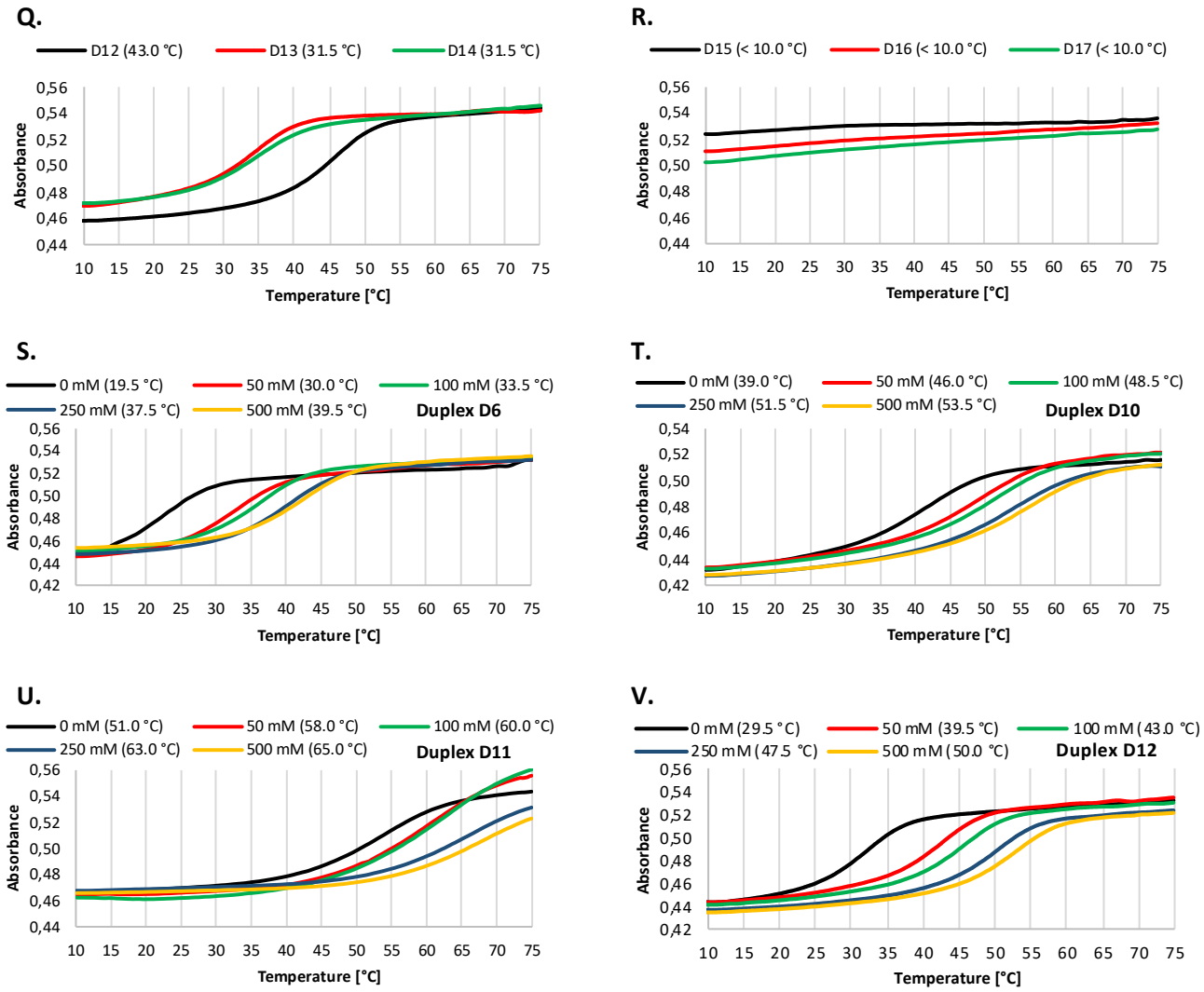


Fig. S17A–V Melting curves and melting temperatures (T_m, °C) for all measure duplexes. Underlined dinucleotides indicate double-headed nucleotides and for simplicity, only one melting curve is shown for each duplex.

Circular dichroism spectroscopy

CD spectra were recorded at 20 °C on a Jasco J-715 spectropolarimeter as an average of 5 scans from 200–350 nm. Measurements were performed using a split width of 2.0 nm, a scan speed of 50 nm/min and in quartz optical cells with an optical path length of 5.0 mm. The samples contained 1.5 µM concentrations of each strand (duplex or single measurement) in a medium salt buffer (2.5 mM Na_2HPO_4, 5 mM NaH_2PO_4, 100 mM NaCl, and 0.1 mM EDTA, pH 7.0) and before the measuring, the oligonucleotides were annealed by heating the samples to 75 °C followed by controlled cooling.

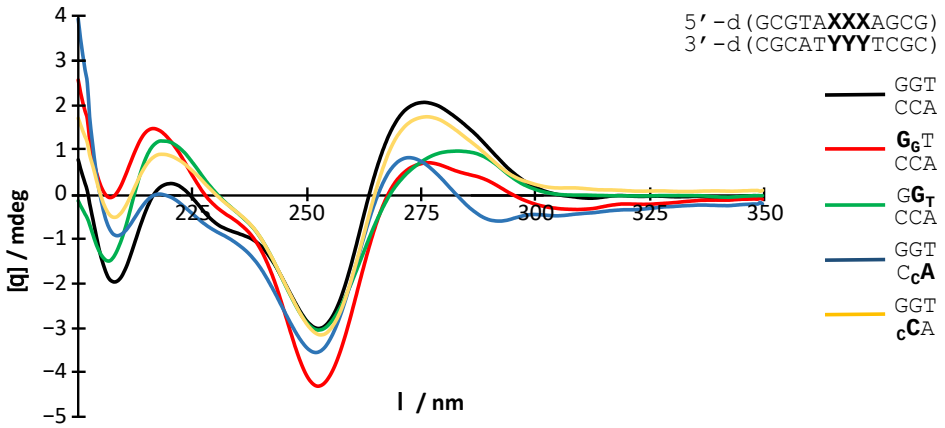


Fig. S18 CD spectra of the full match duplexes of Fig. 2.

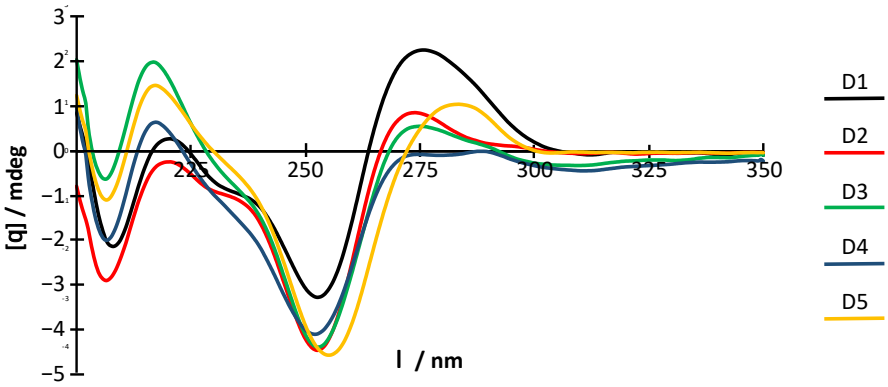


Fig. S19 CD spectra of duplexes D1–D5 of Fig. 3.

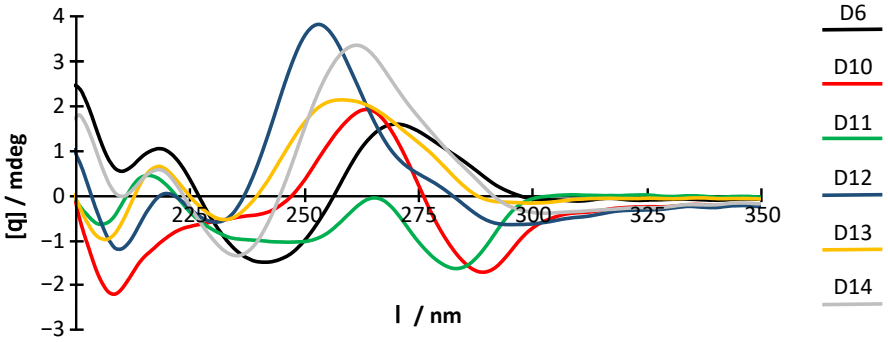
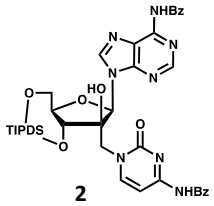


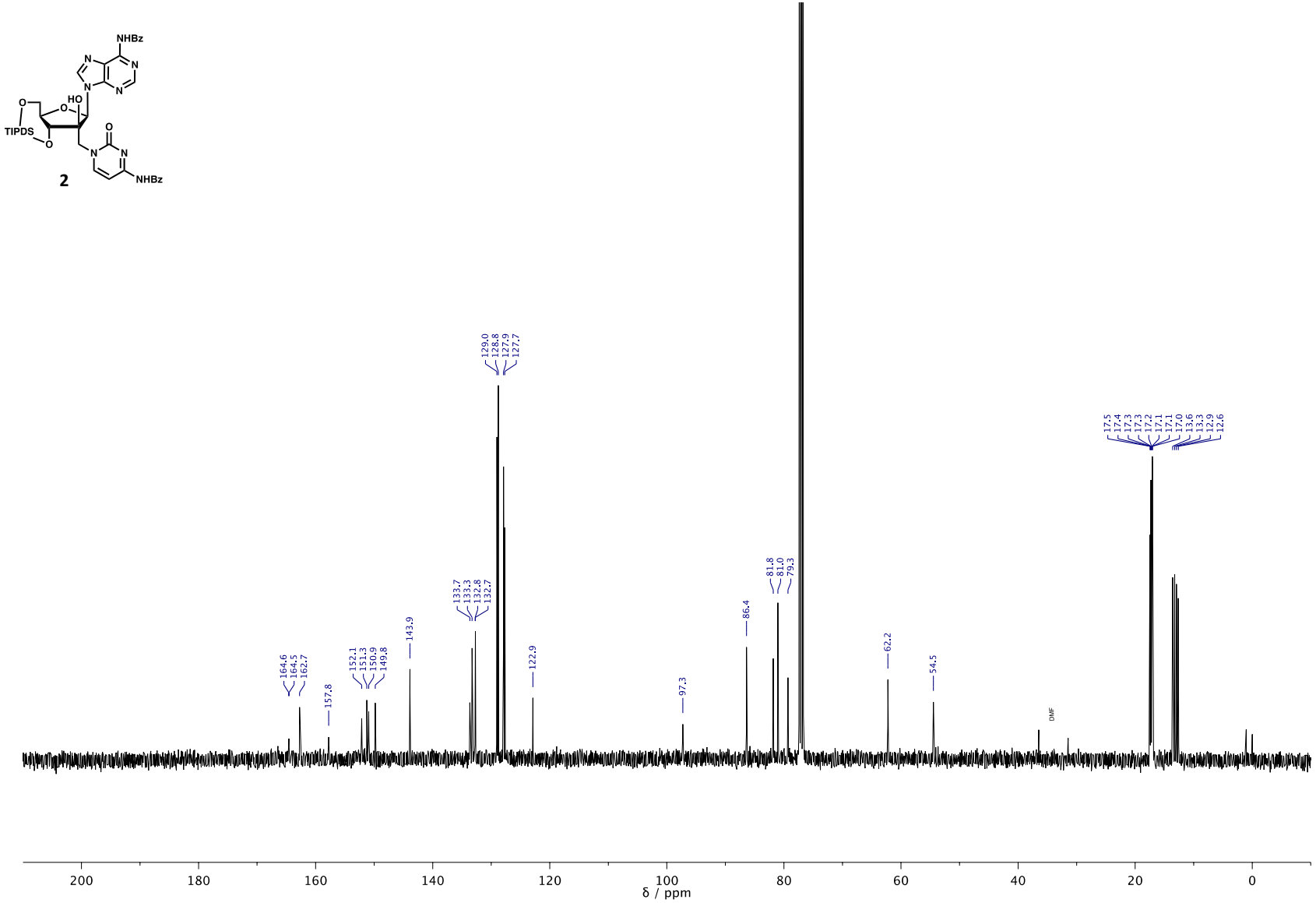
Fig. S20 CD spectra of duplexes D6, and D10–D14 (referring to Fig. 4 and Fig. S15).

Selected NMR spectra

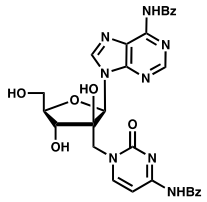


2

Spectrum S1 400 MHz ^{1}H NMR spectrum of compound **2** in $CDCl_3$.

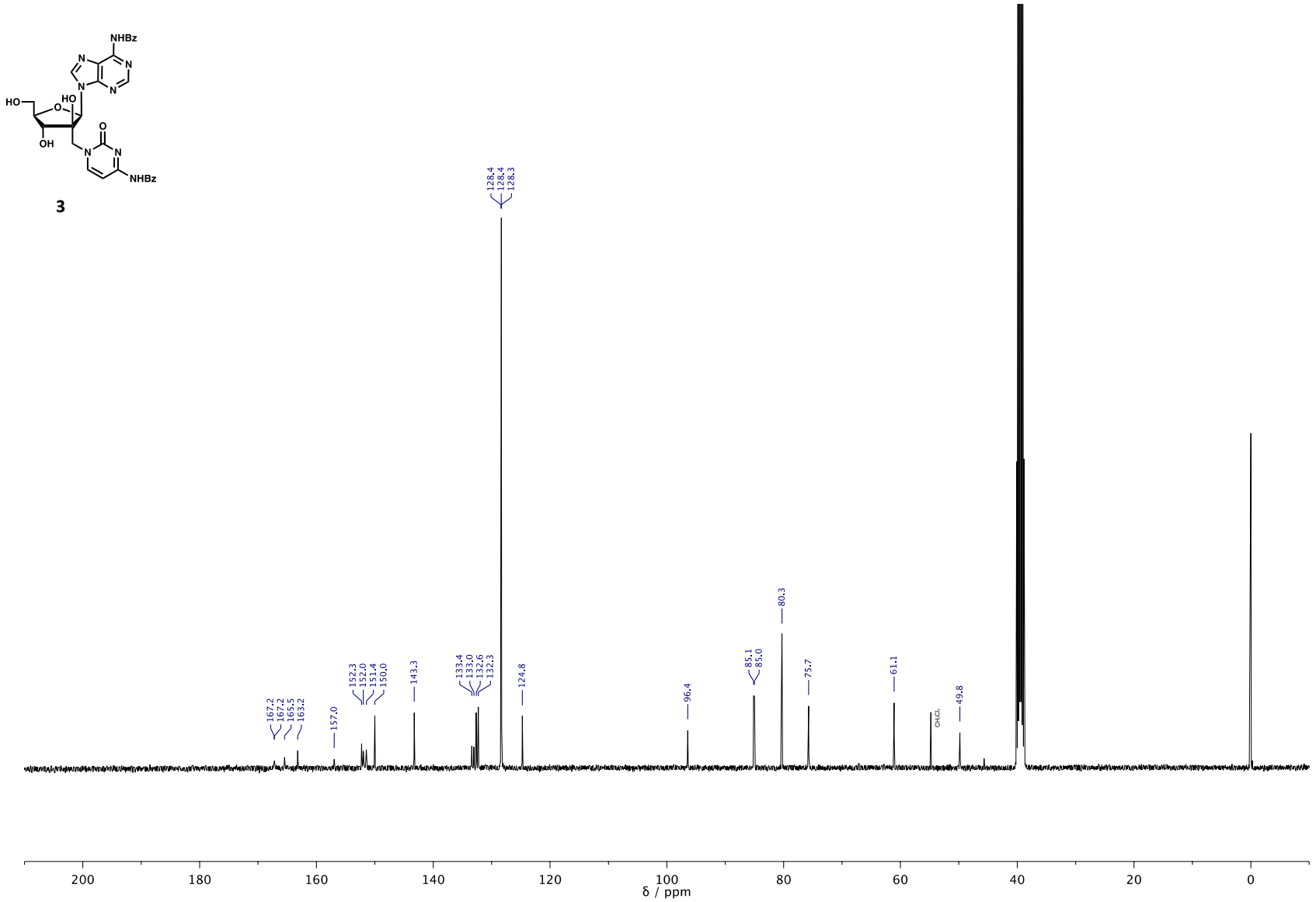


Spectrum S2 101 MHz ^{13}C NMR spectrum of compound **2** in $CDCl_3$.

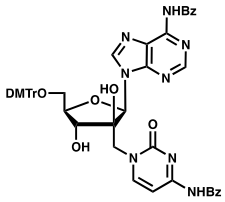


3

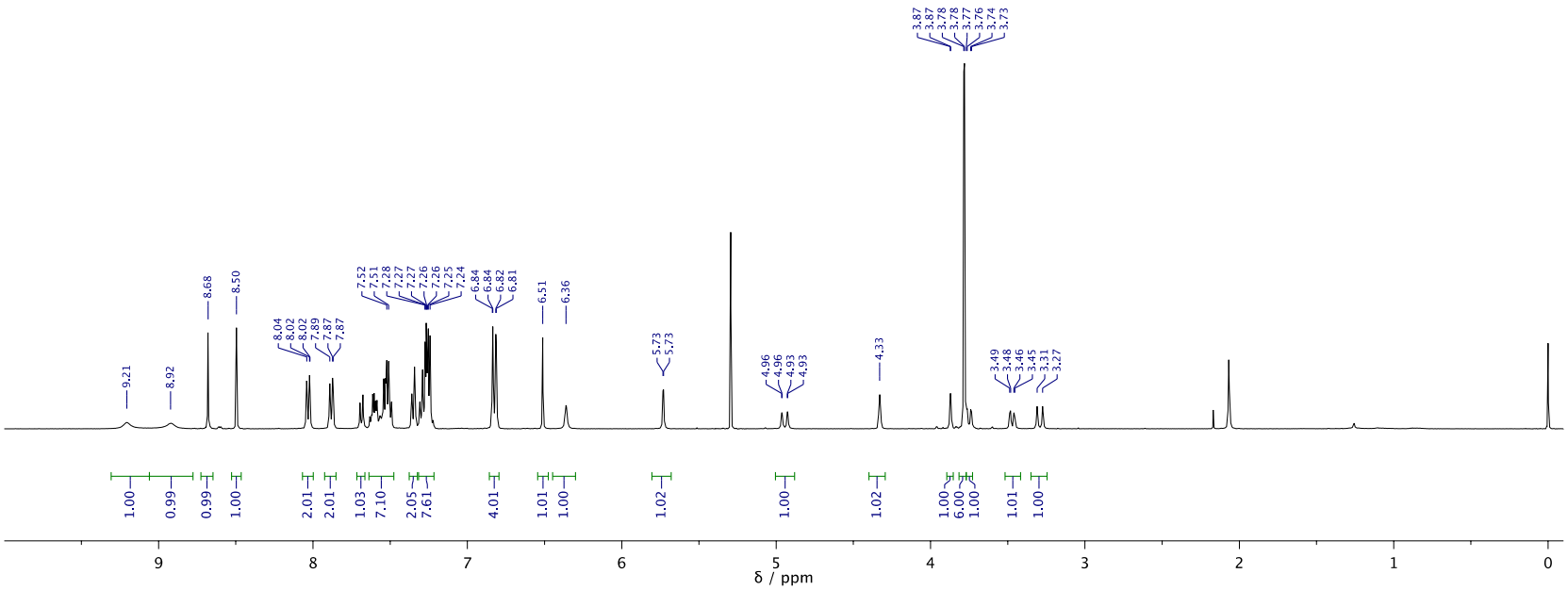
Spectrum S3 400 MHz ^{1}H NMR spectrum of compound **3** in DMSO-d_6.



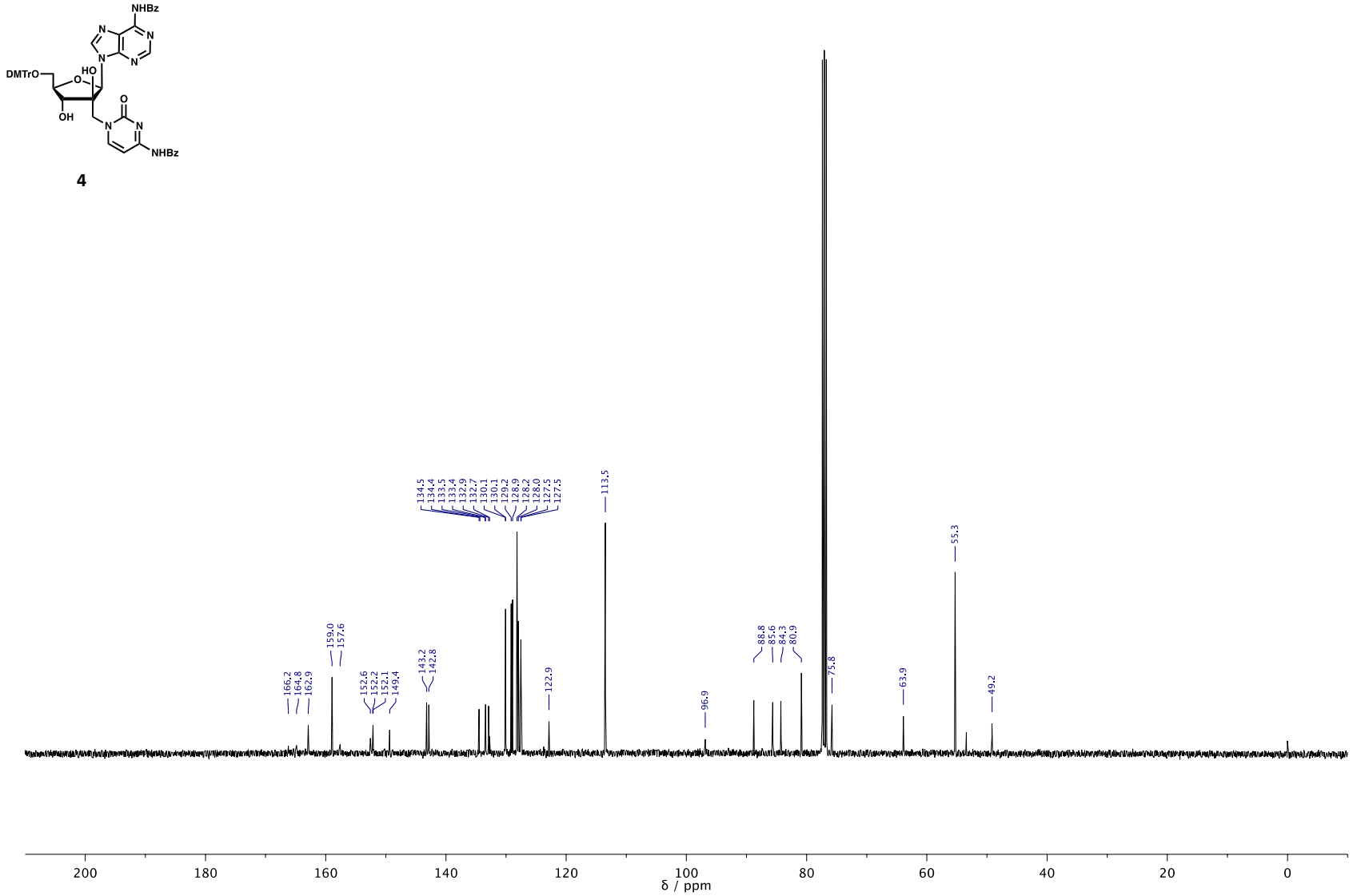
Spectrum S4 101 MHz ^{13}C NMR spectrum of compound **3** in DMSO-d_6.



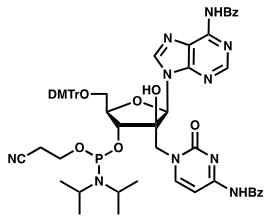
4



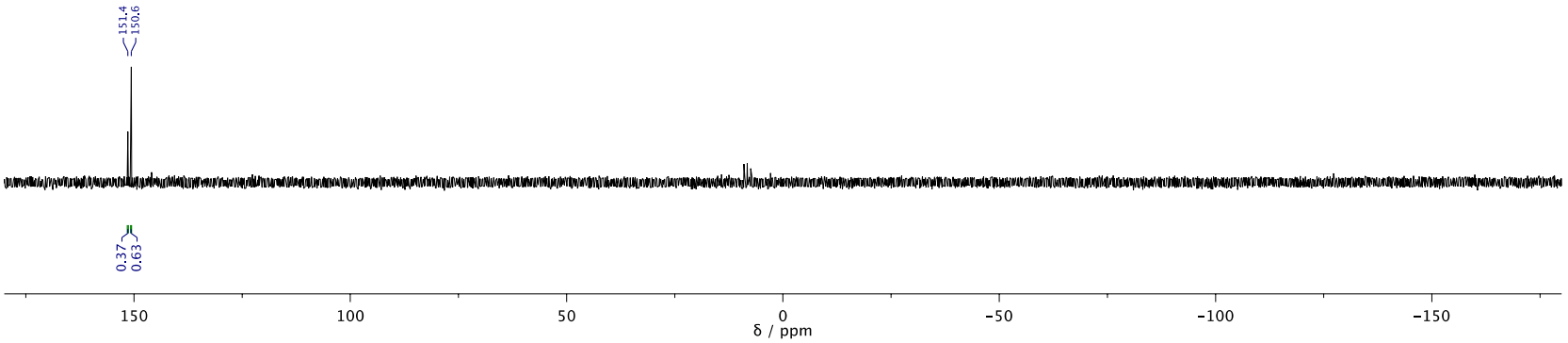
Spectrum S5 400 MHz ^{1}H NMR spectrum of compound **4** in $CDCl_3$.



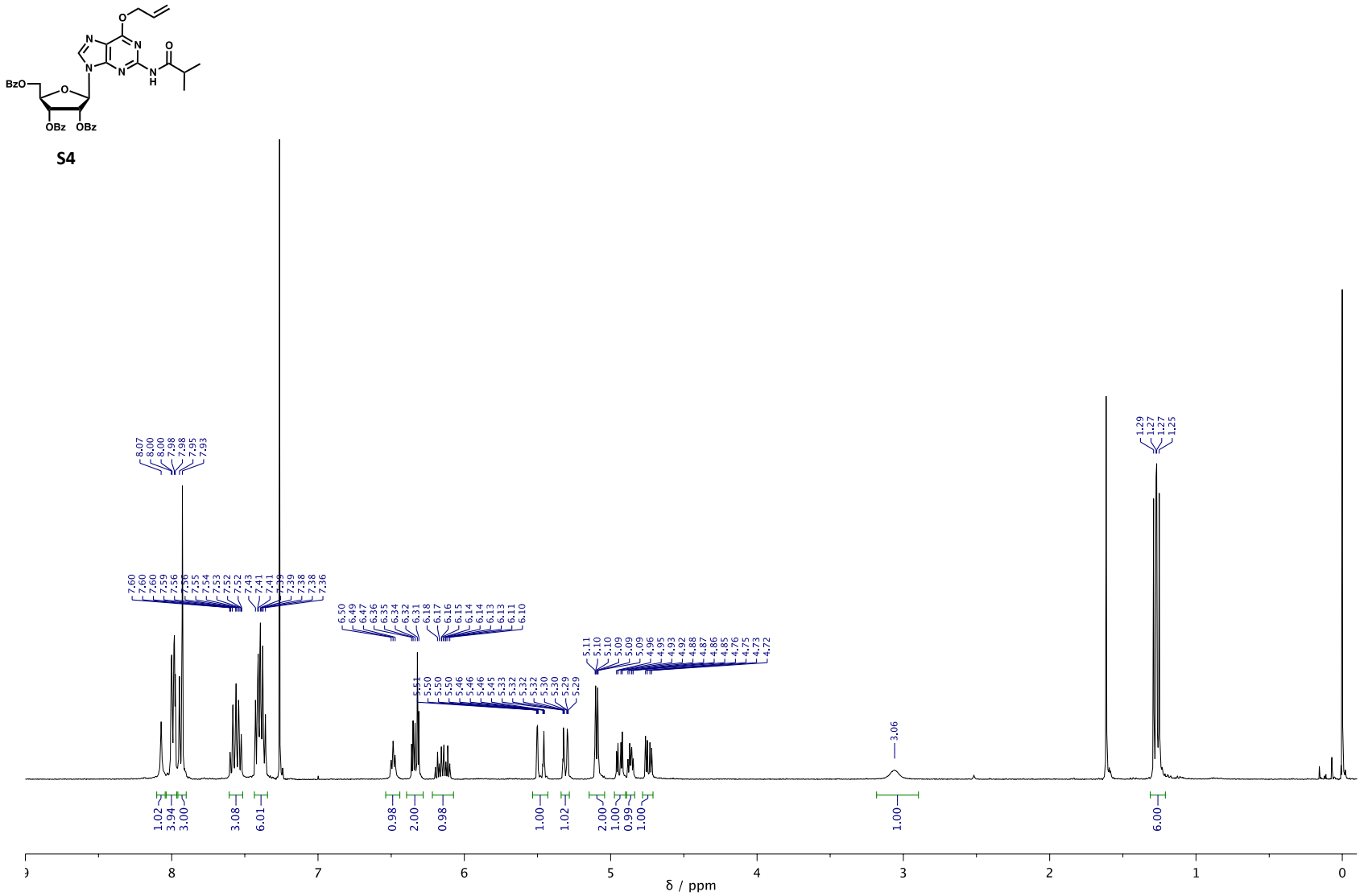
Spectrum S6 101 MHz ^{13}C NMR spectrum of compound **4** in $CDCl_3$.



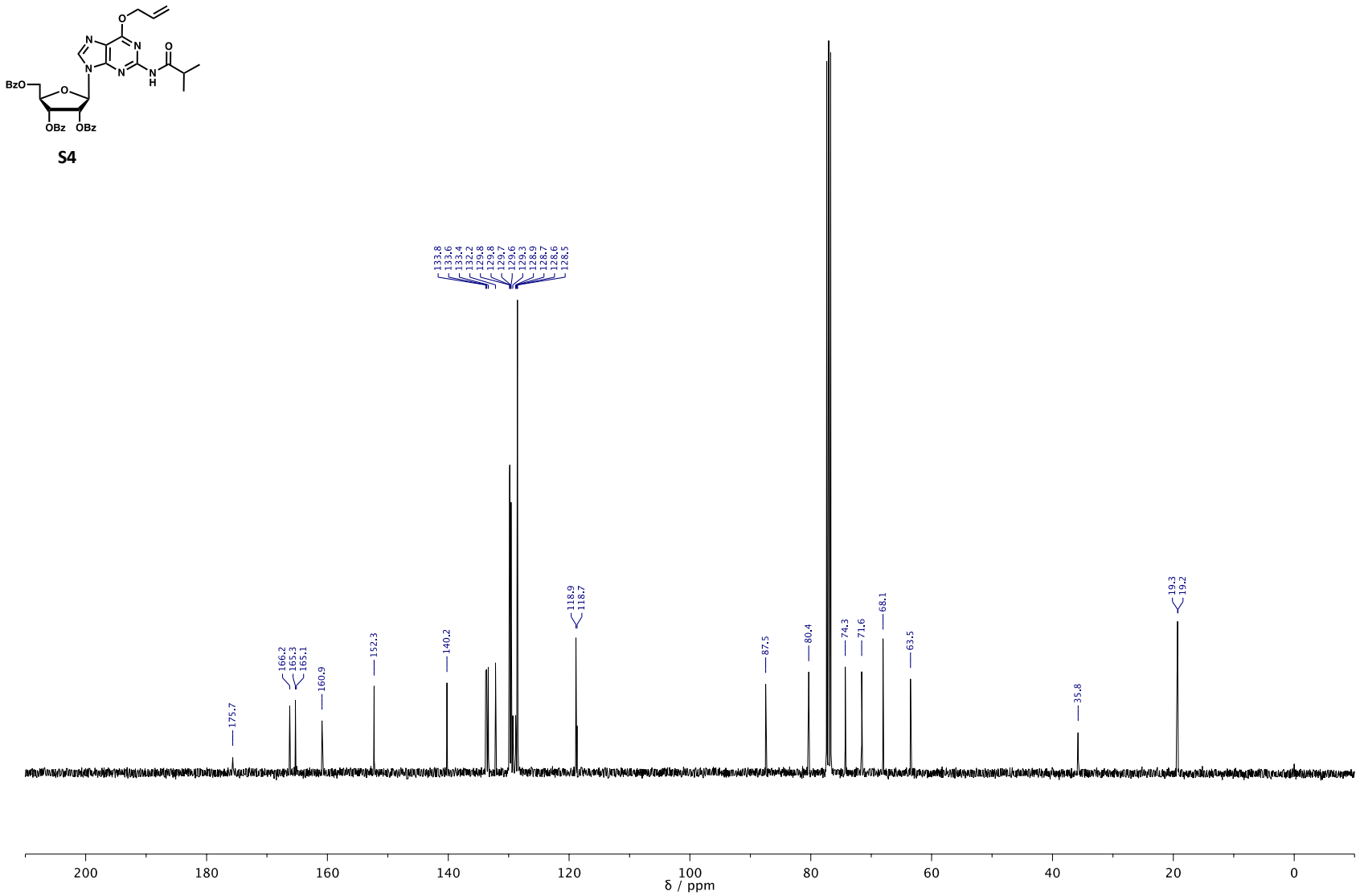
5



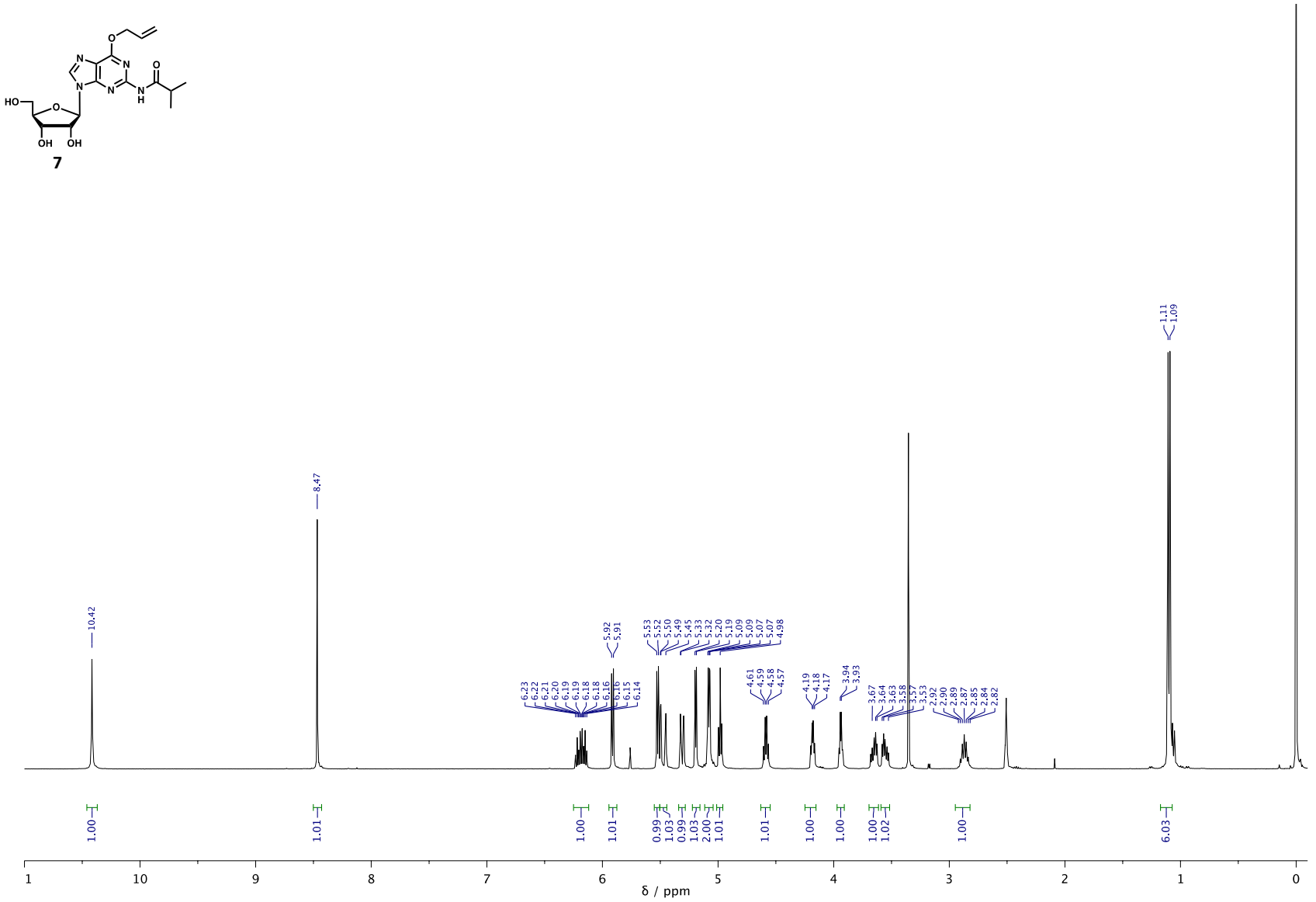
Spectrum S7 162 MHz ^{31}P NMR spectrum of compound **5** in $CDCl_3$.



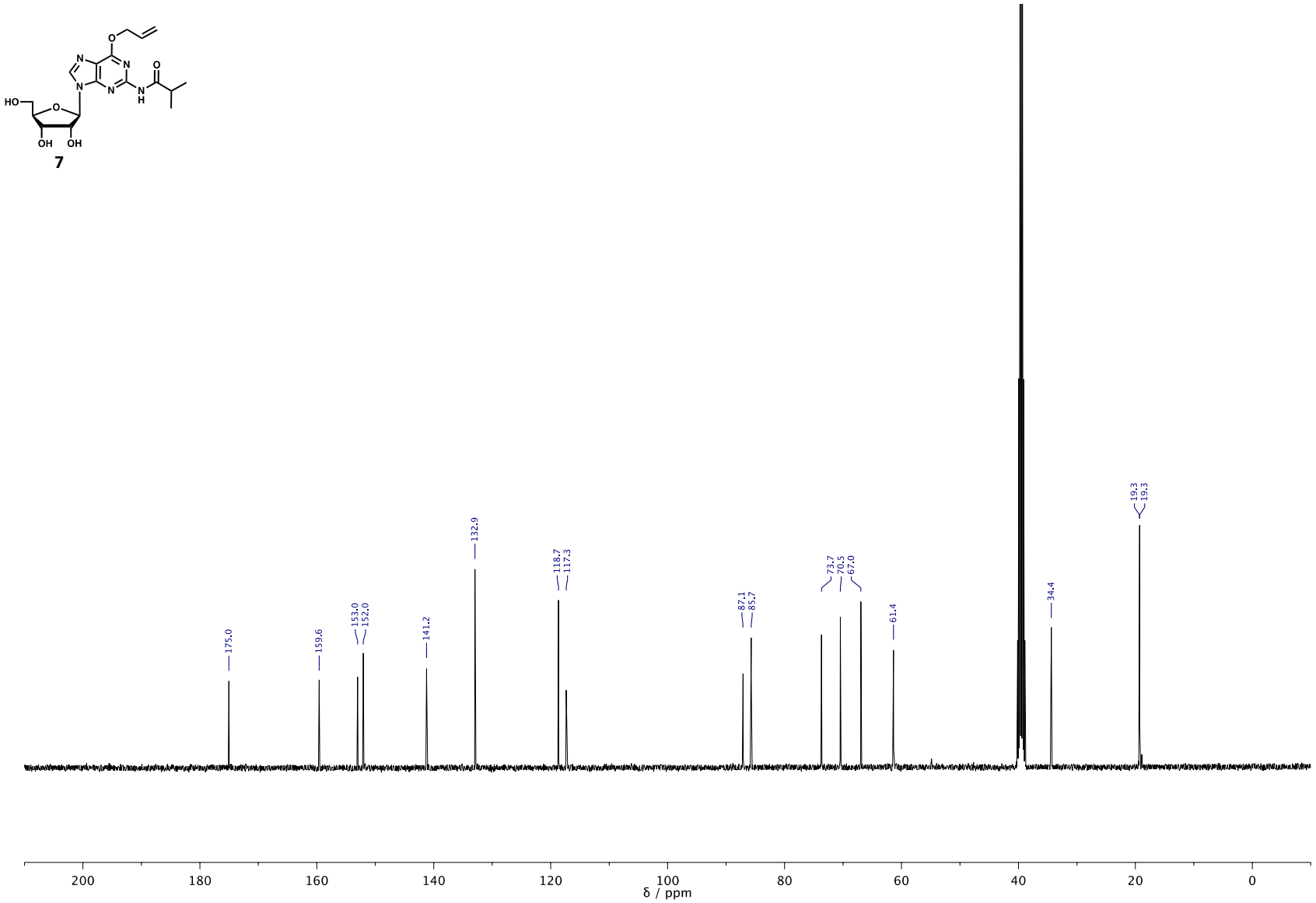
Spectrum S8 400 MHz ^{1}H NMR spectrum of compound **S4** in $CDCl_3$.



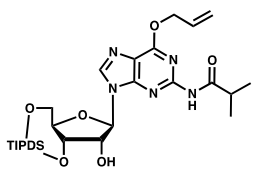
Spectrum S9 101 MHz ^{13}C NMR spectrum of compound **S4** in $CDCl_3$.



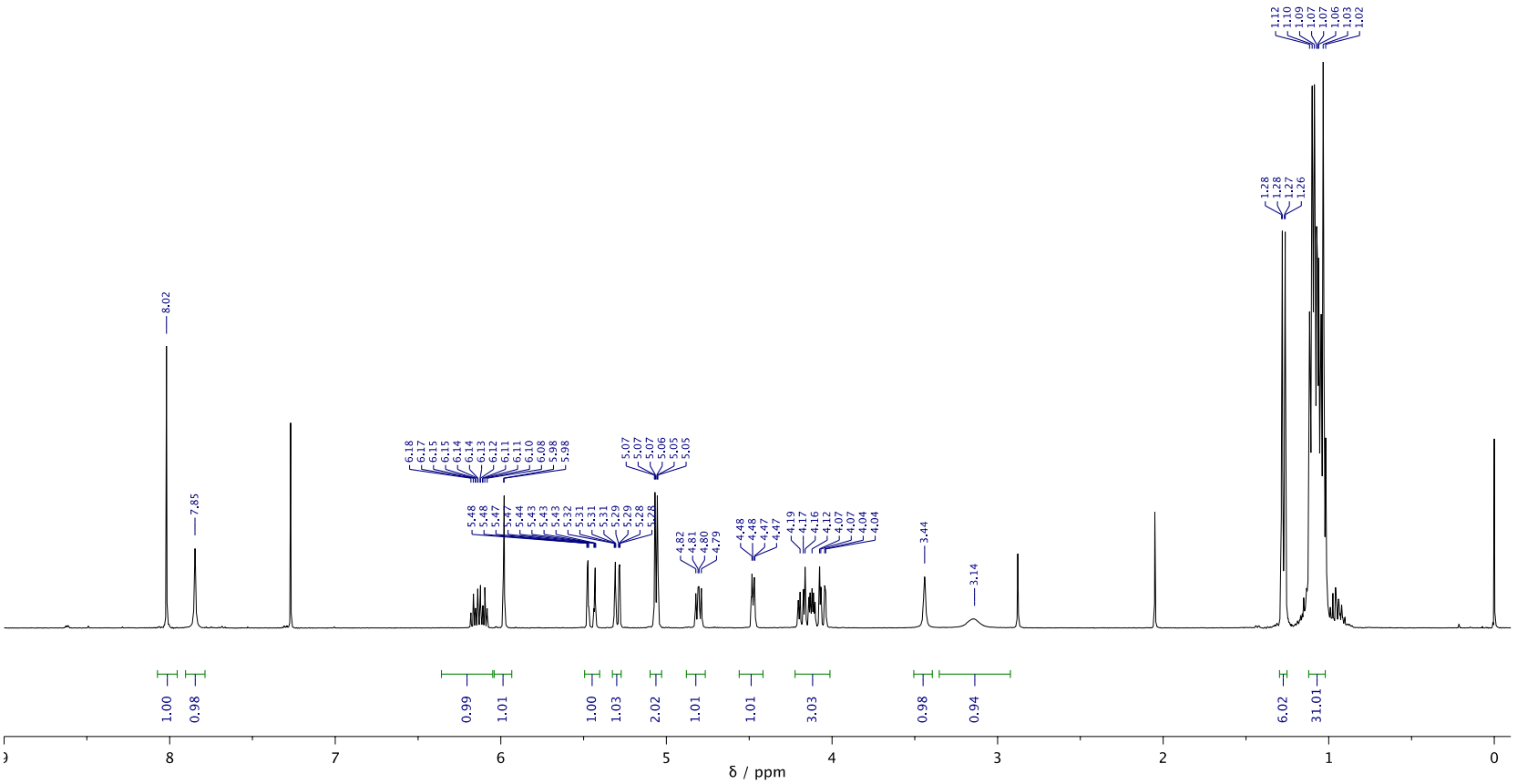
Spectrum S10 400 MHz ^{1}H NMR spectrum of compound **7** in DMSO-d_6.



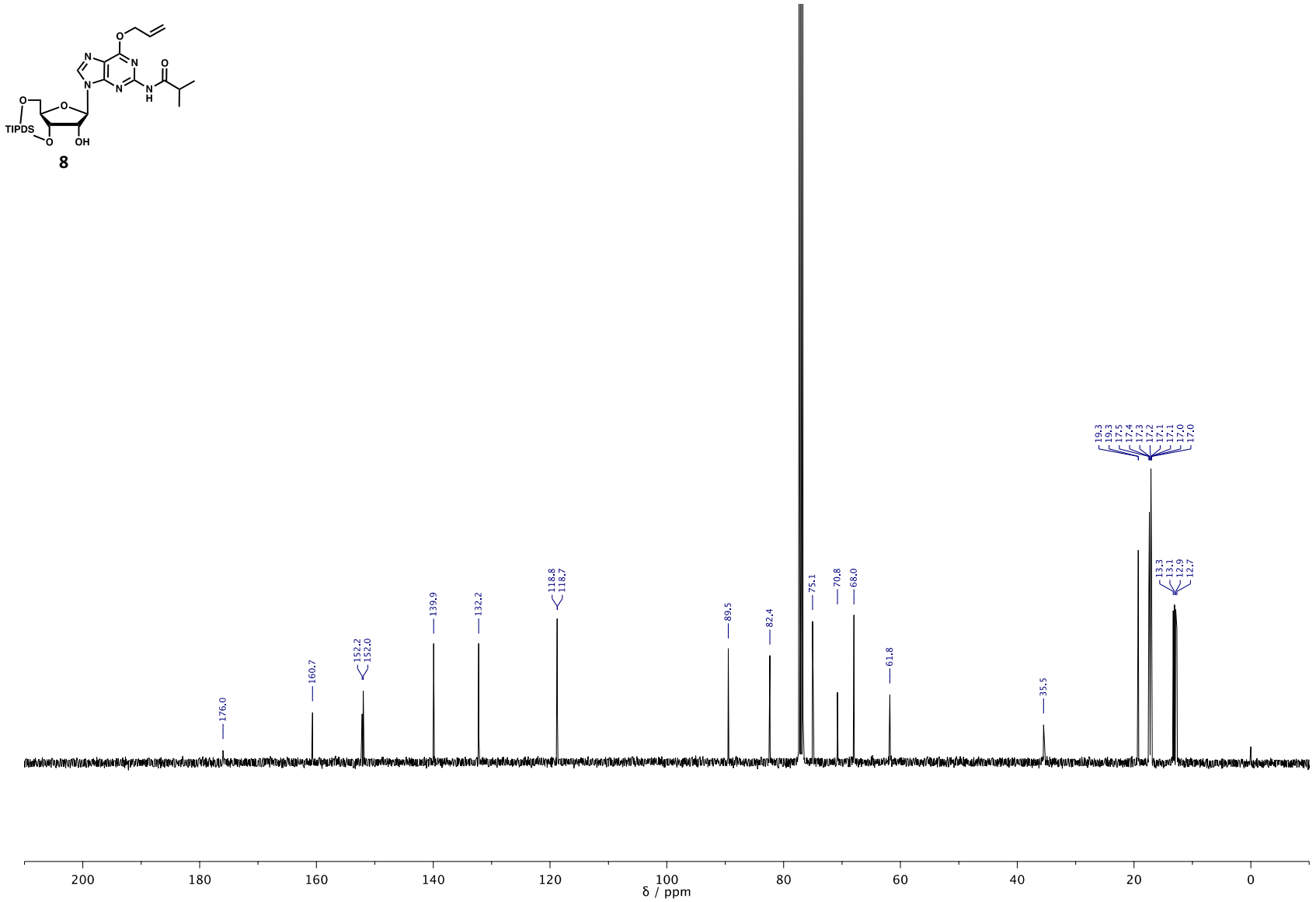
Spectrum S11 101 MHz ^{13}C NMR spectrum of compound **7** in DMSO-d_6.



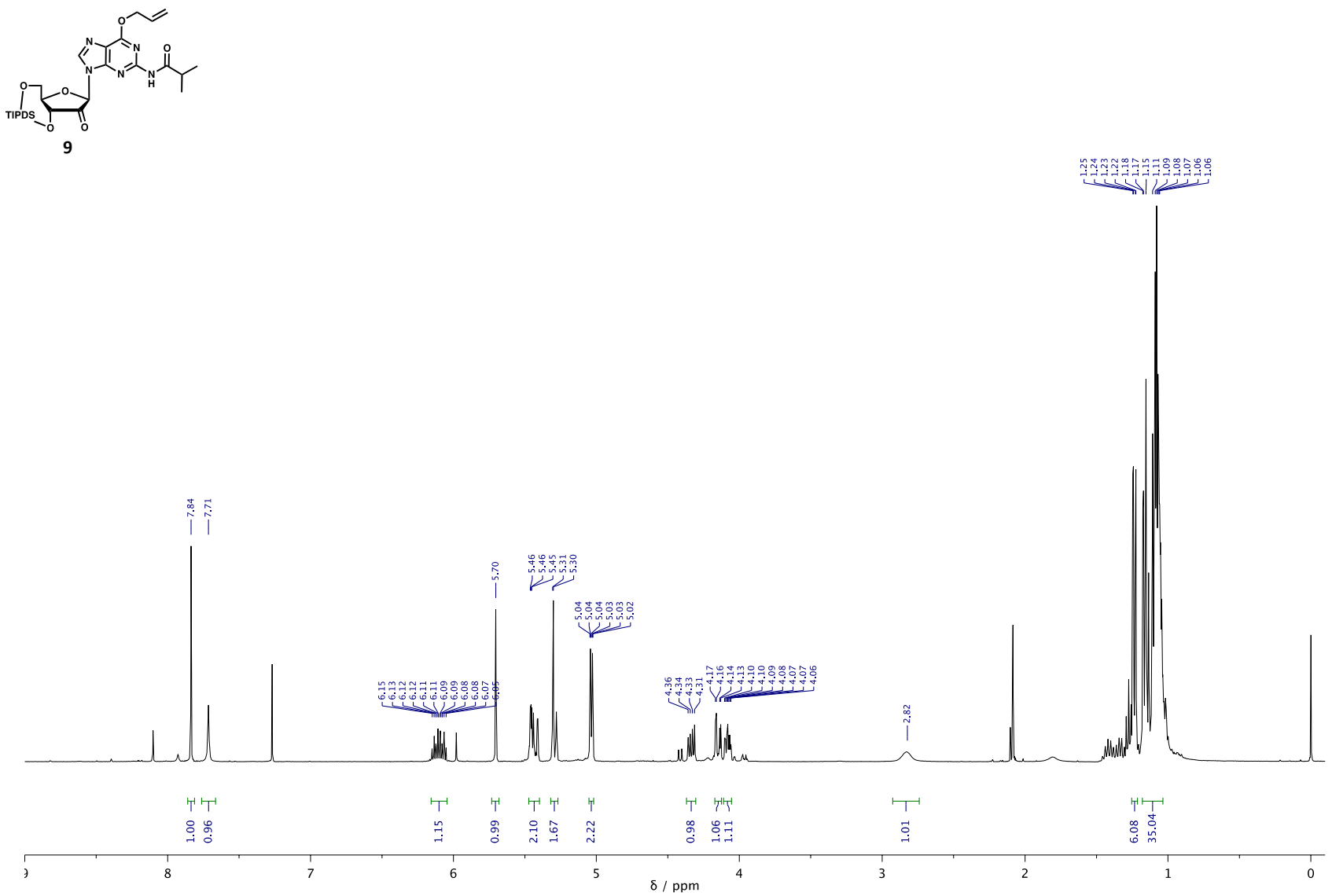
8



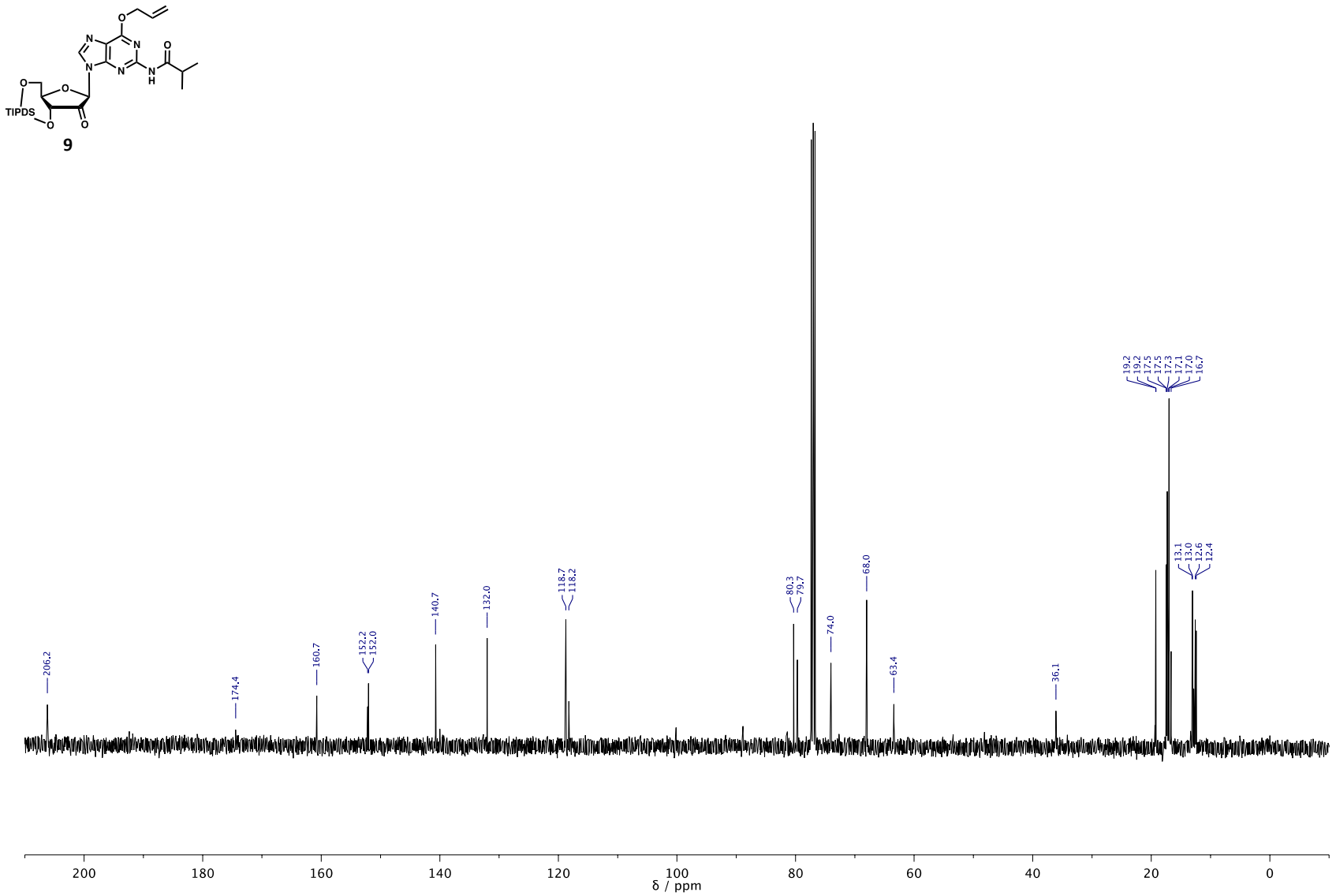
Spectrum S12 400 MHz ^{1}H NMR spectrum of compound **8** in $CDCl_3$.



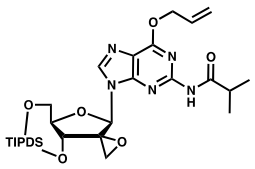
Spectrum S13 101 MHz ^{13}C NMR spectrum of compound **8** in $CDCl_3$.



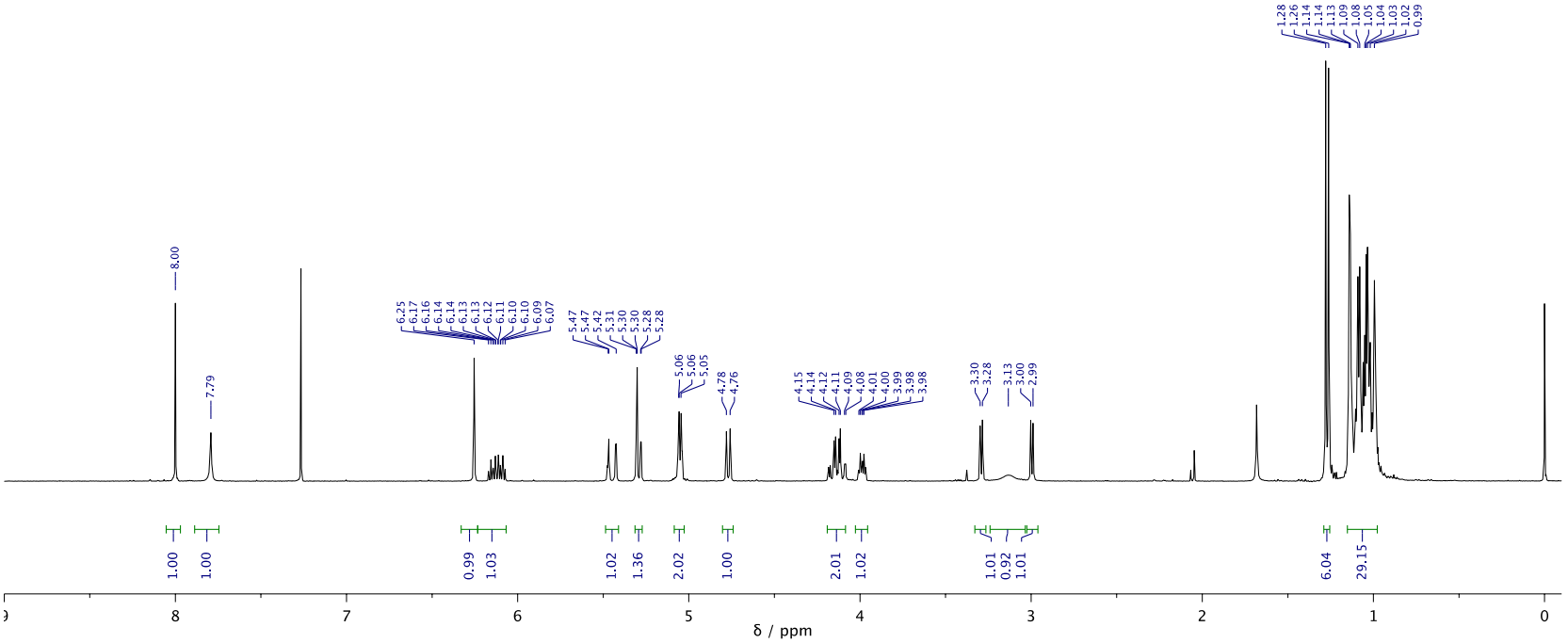
Spectrum S14 400 MHz ^{1}H NMR spectrum of compound **9** in $CDCl_3$.



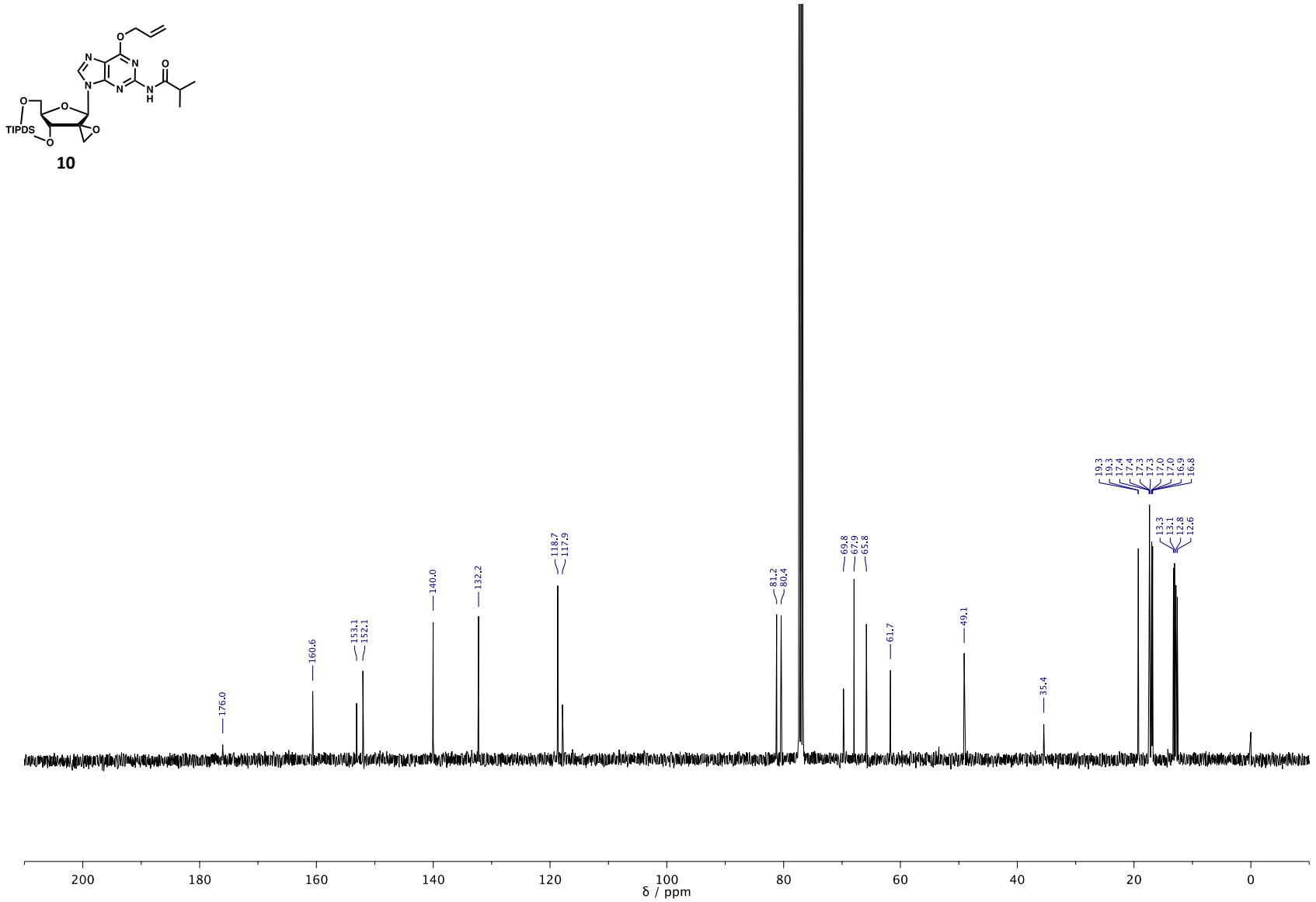
Spectrum S15 101 MHz ^{13}C NMR spectrum of compound **9** in $CDCl_3$.



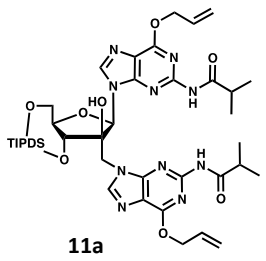
10



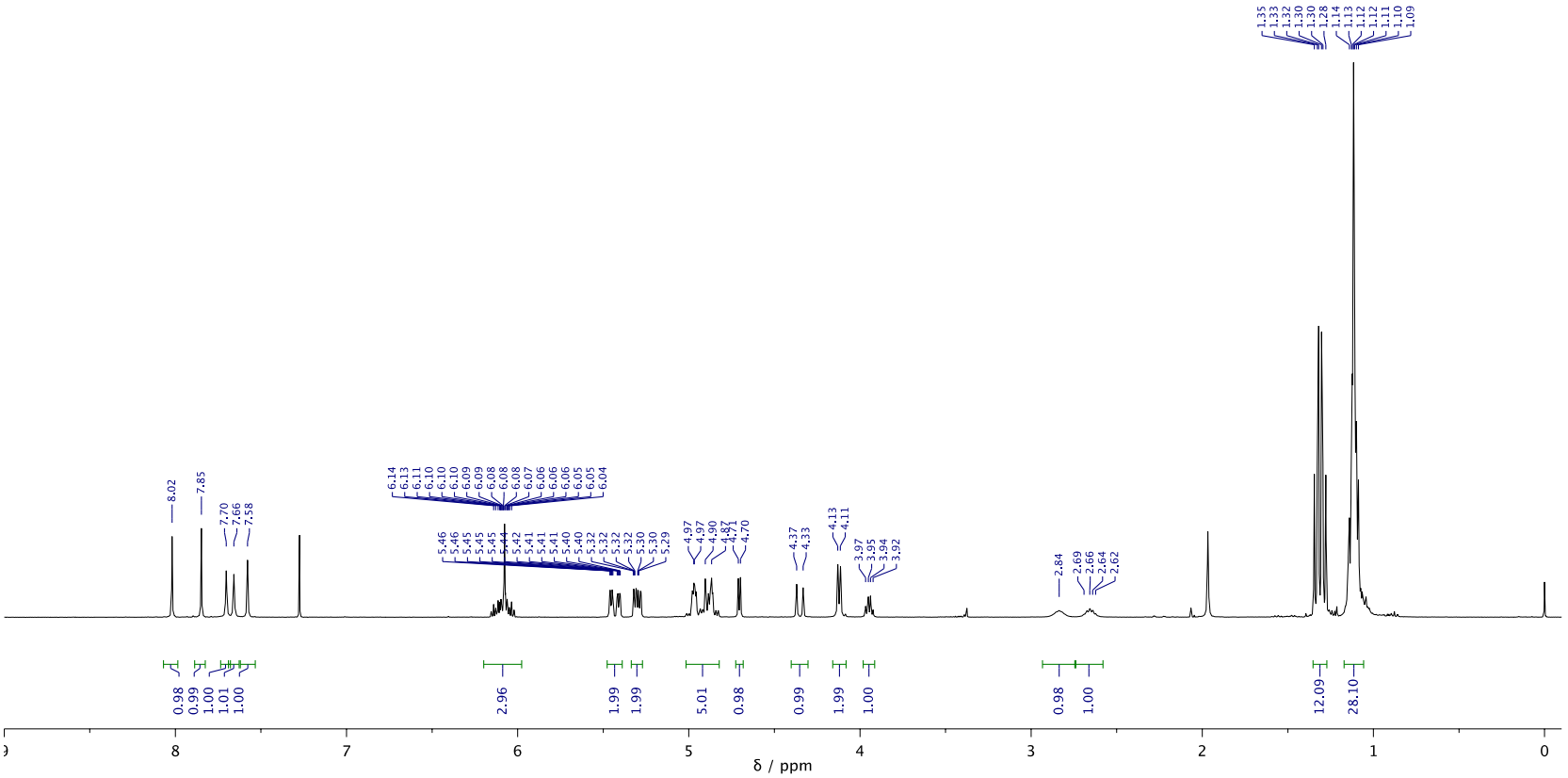
Spectrum S16 400 MHz ^{1}H NMR spectrum of compound **10** in $CDCl_3$.



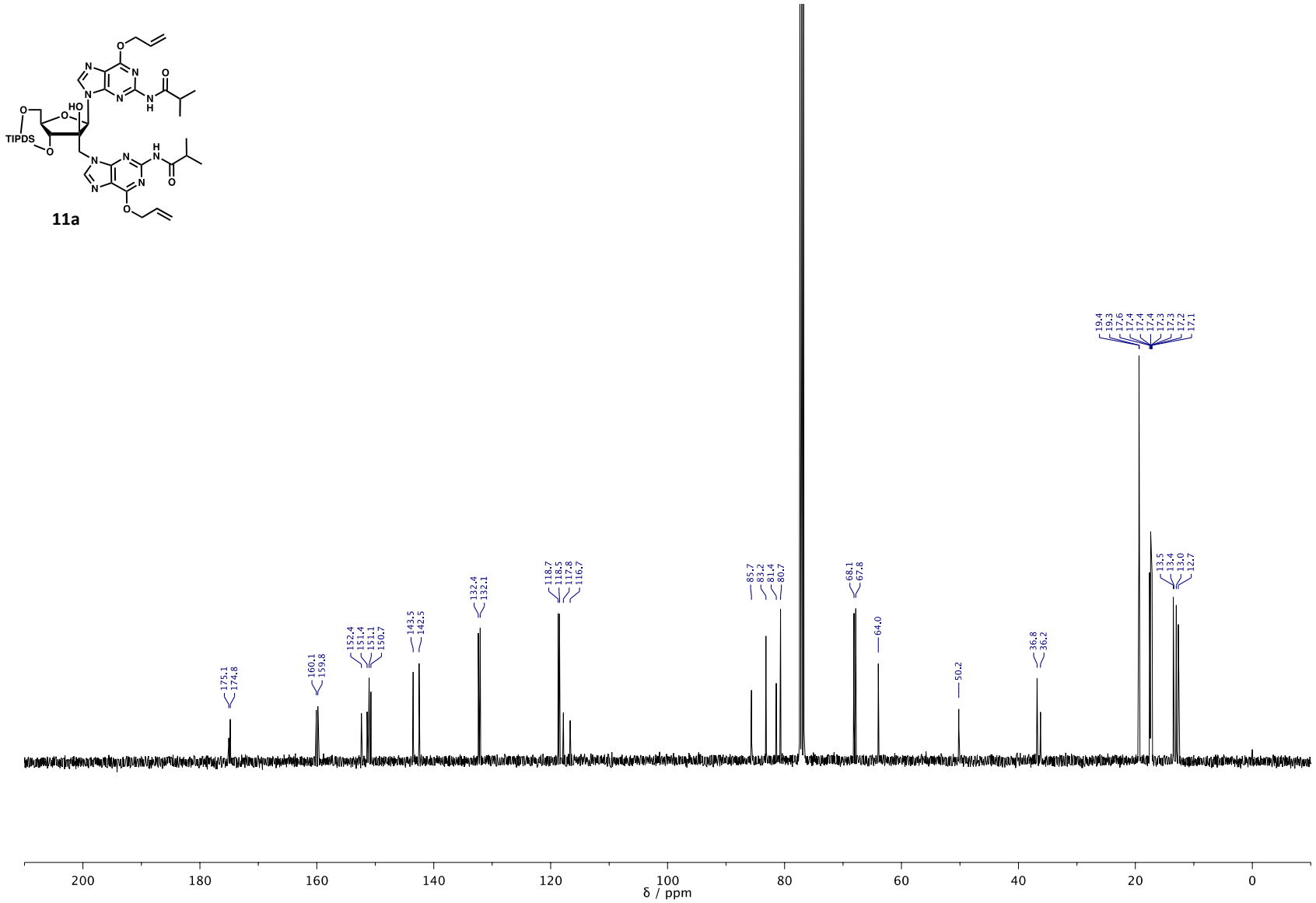
Spectrum S17 101 MHz ^{13}C NMR spectrum of compound **10** in $CDCl_3$.



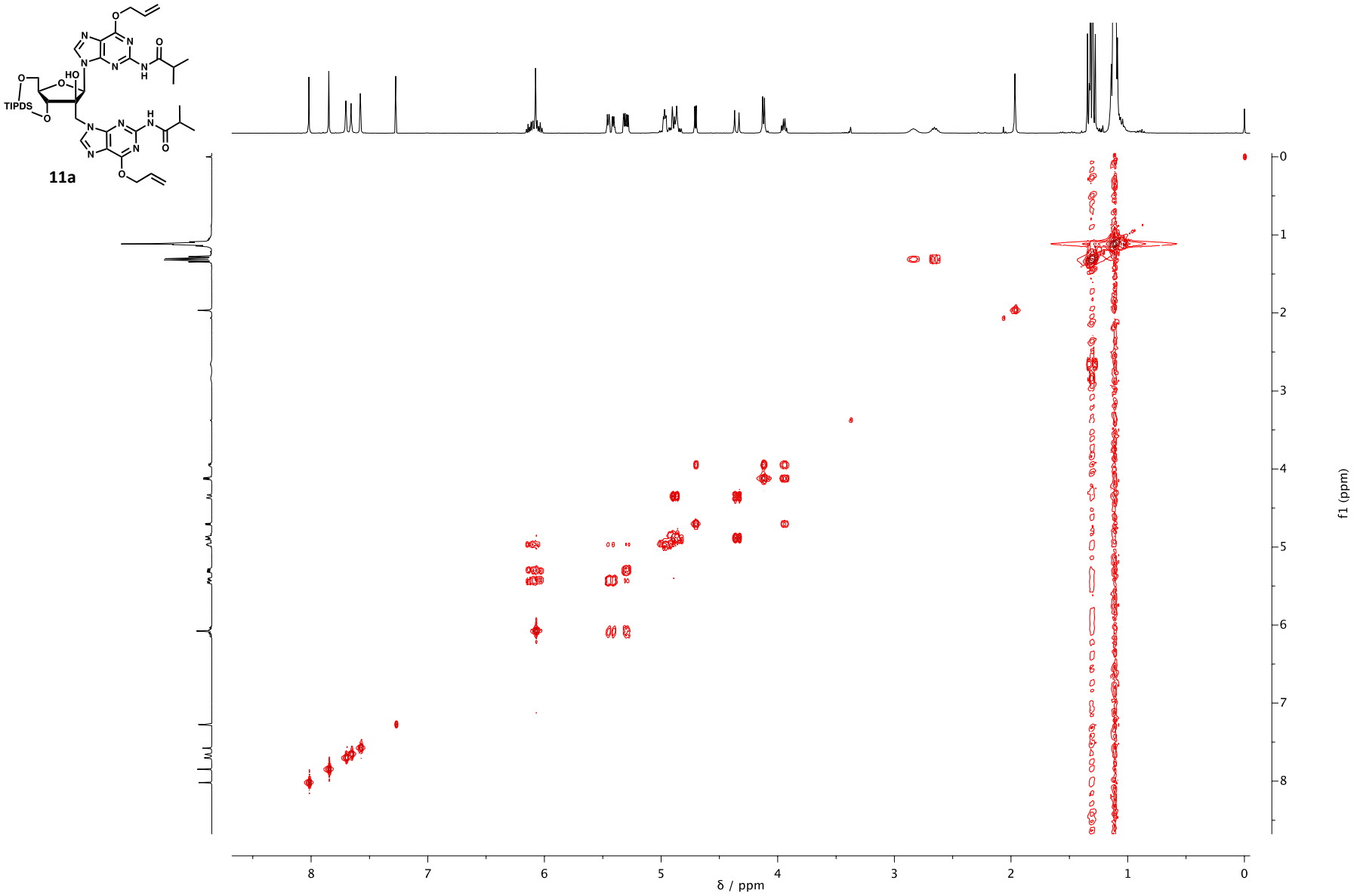
11a



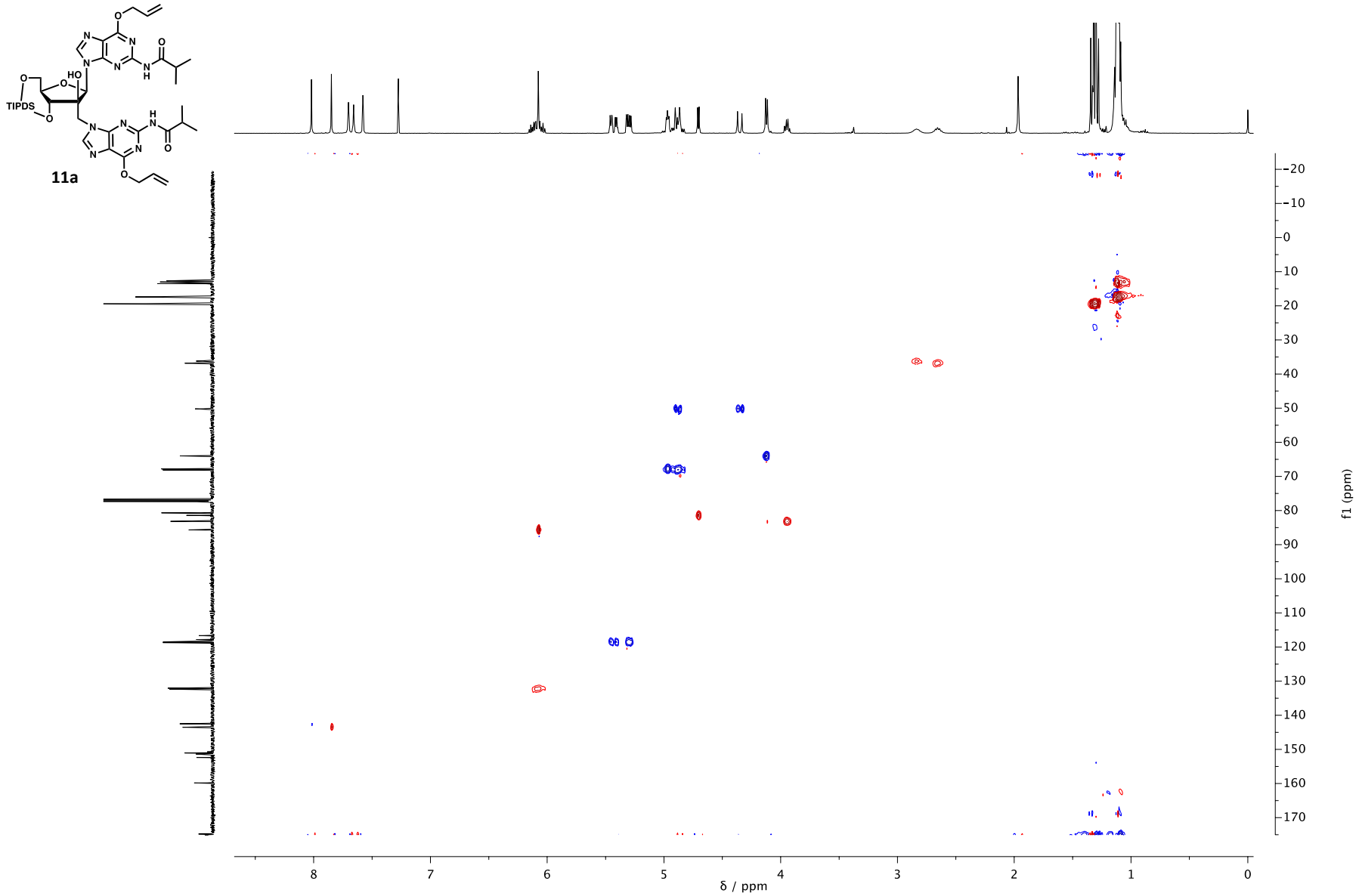
Spectrum S18 400 MHz ^{1}H NMR spectrum of compound **11a** in $CDCl_3$.



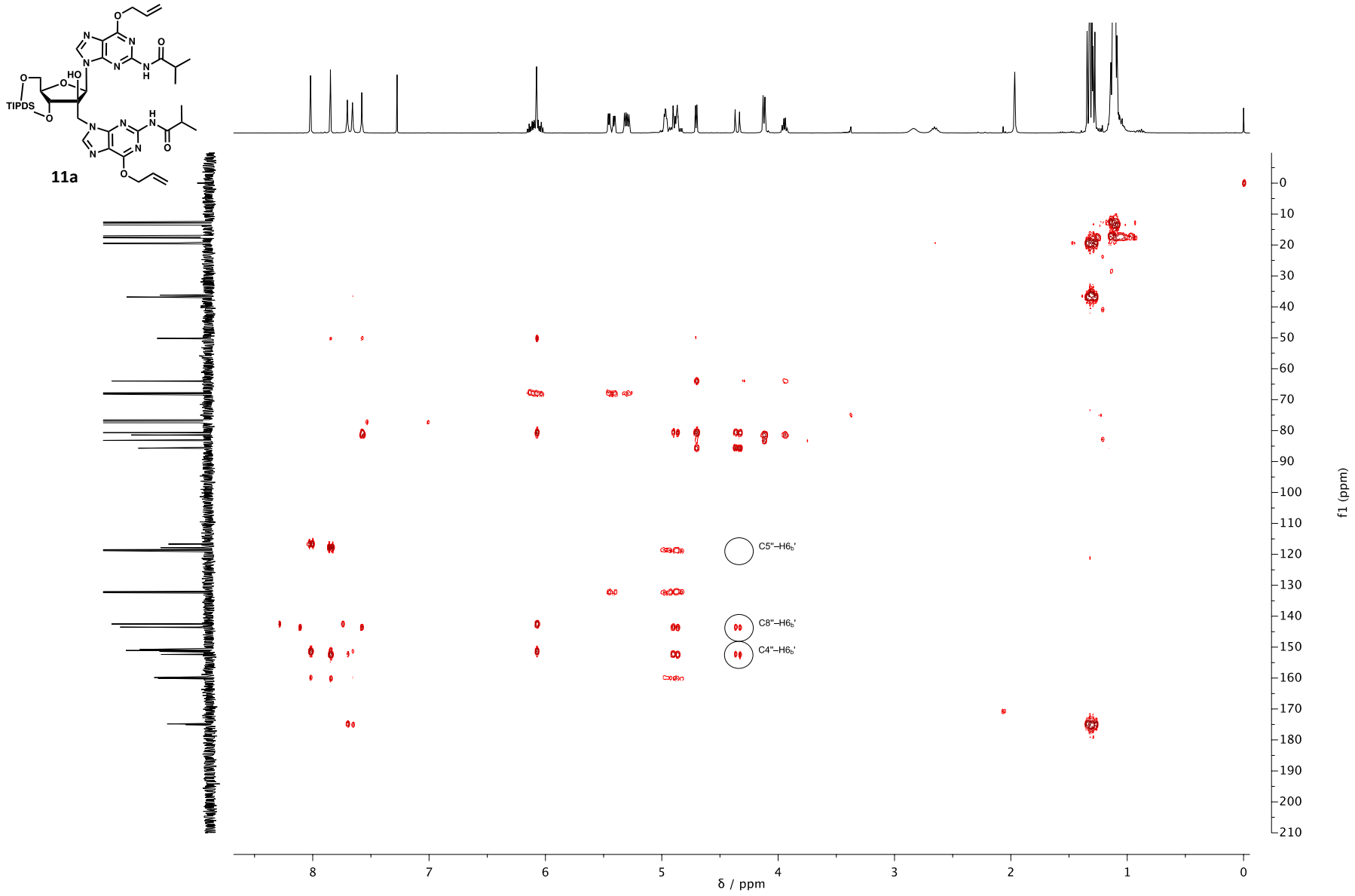
Spectrum S19 101 MHz ^{13}C NMR spectrum of compound **11a** in $CDCl_3$.



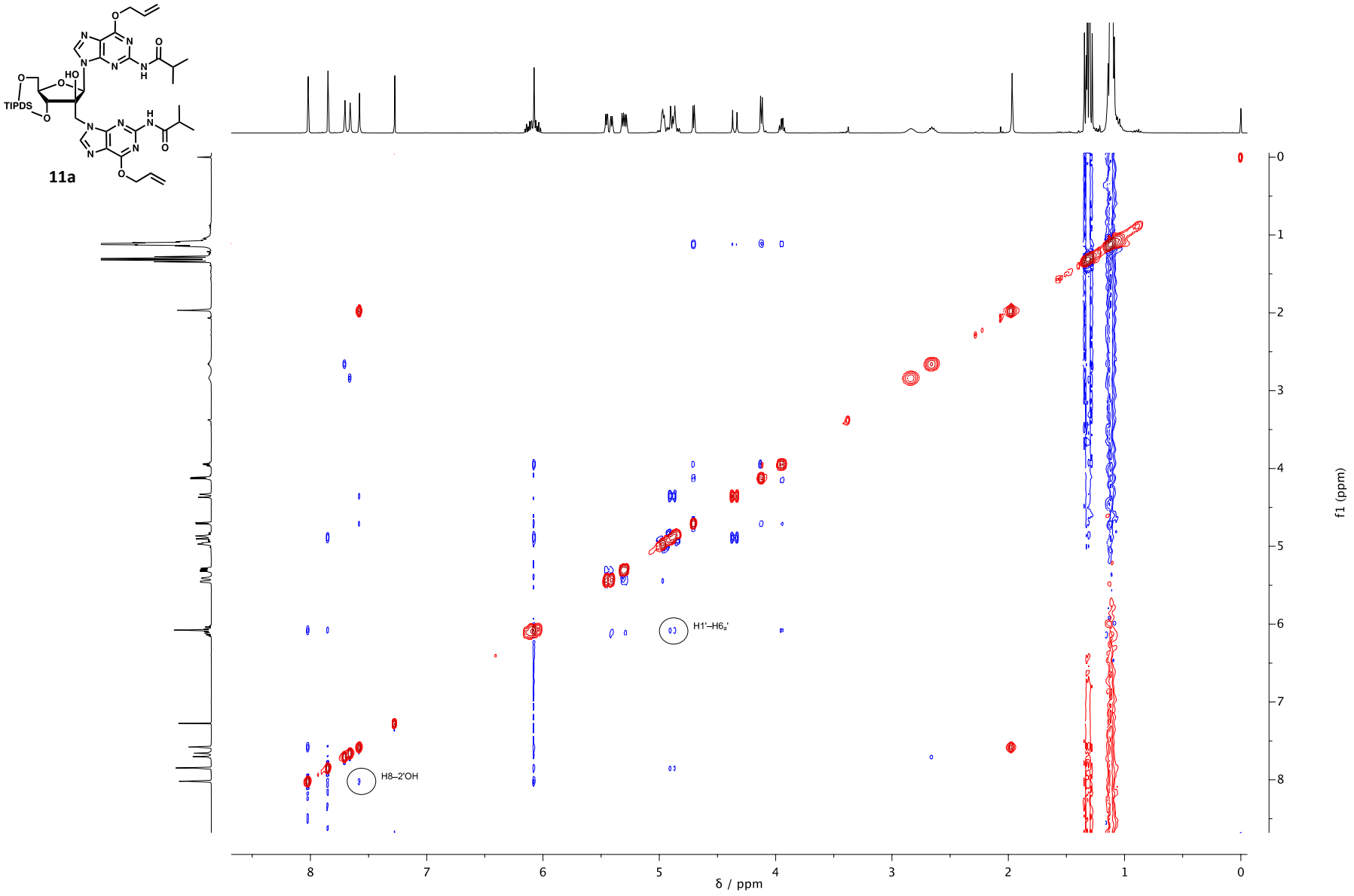
Spectrum S20 $^{1}H,^{1}H$-COSY spectrum of compound **11a** in $CDCl_3$.



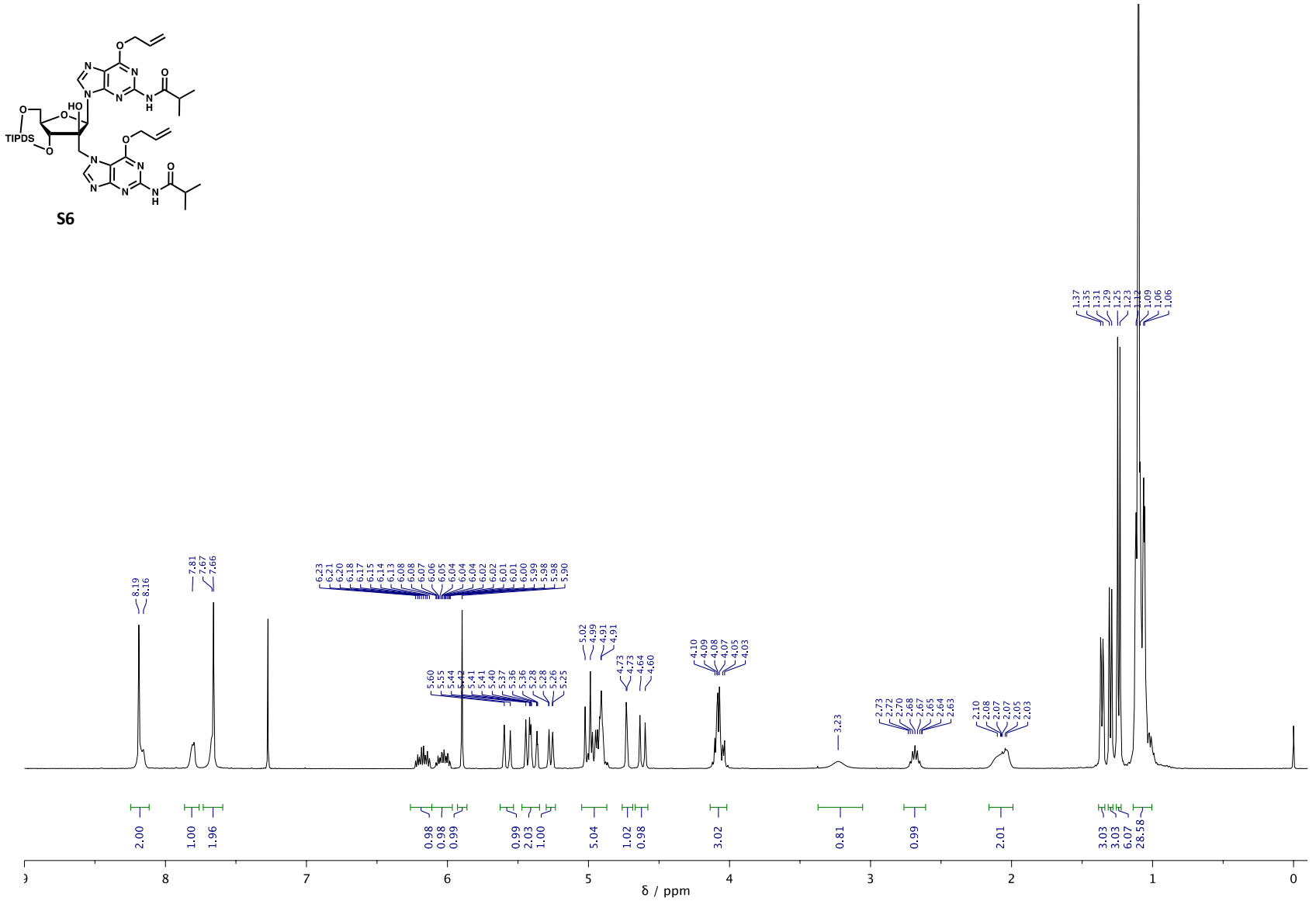
Spectrum S21 $^{1}H,^{13}C$-HSQC spectrum of compound **11a** in $CDCl_3$.



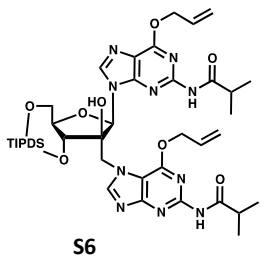
Spectrum S22 $^{1}H,^{13}C$-HMBC spectrum of compound **11a** in $CDCl_3$.



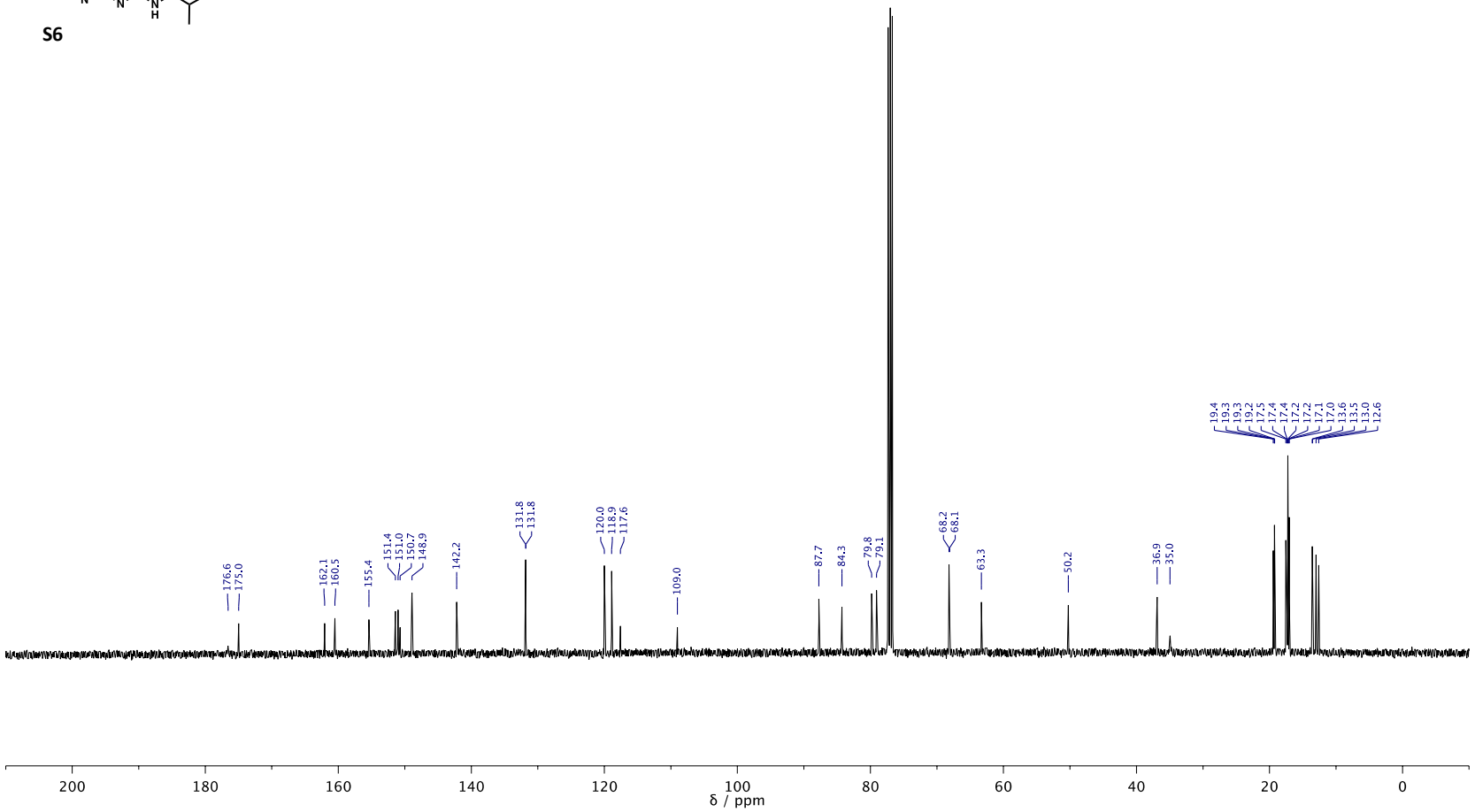
Spectrum S23 $^{1}H,^{1}H$-NOESY spectrum of compound **11a** in $CDCl_3$.



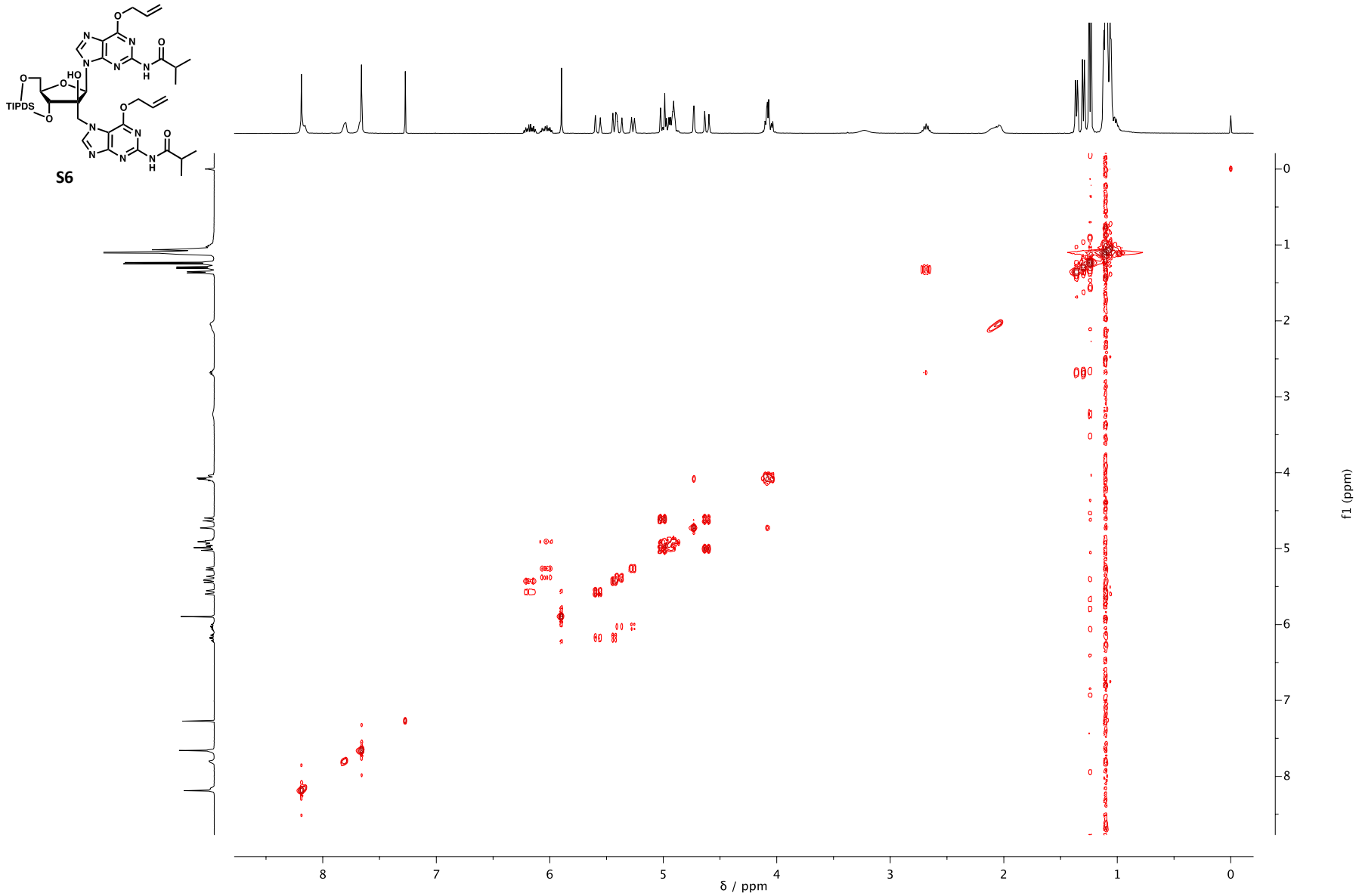
Spectrum S24 400 MHz ^{1}H NMR spectrum of compound **S6** in $CDCl_3$.



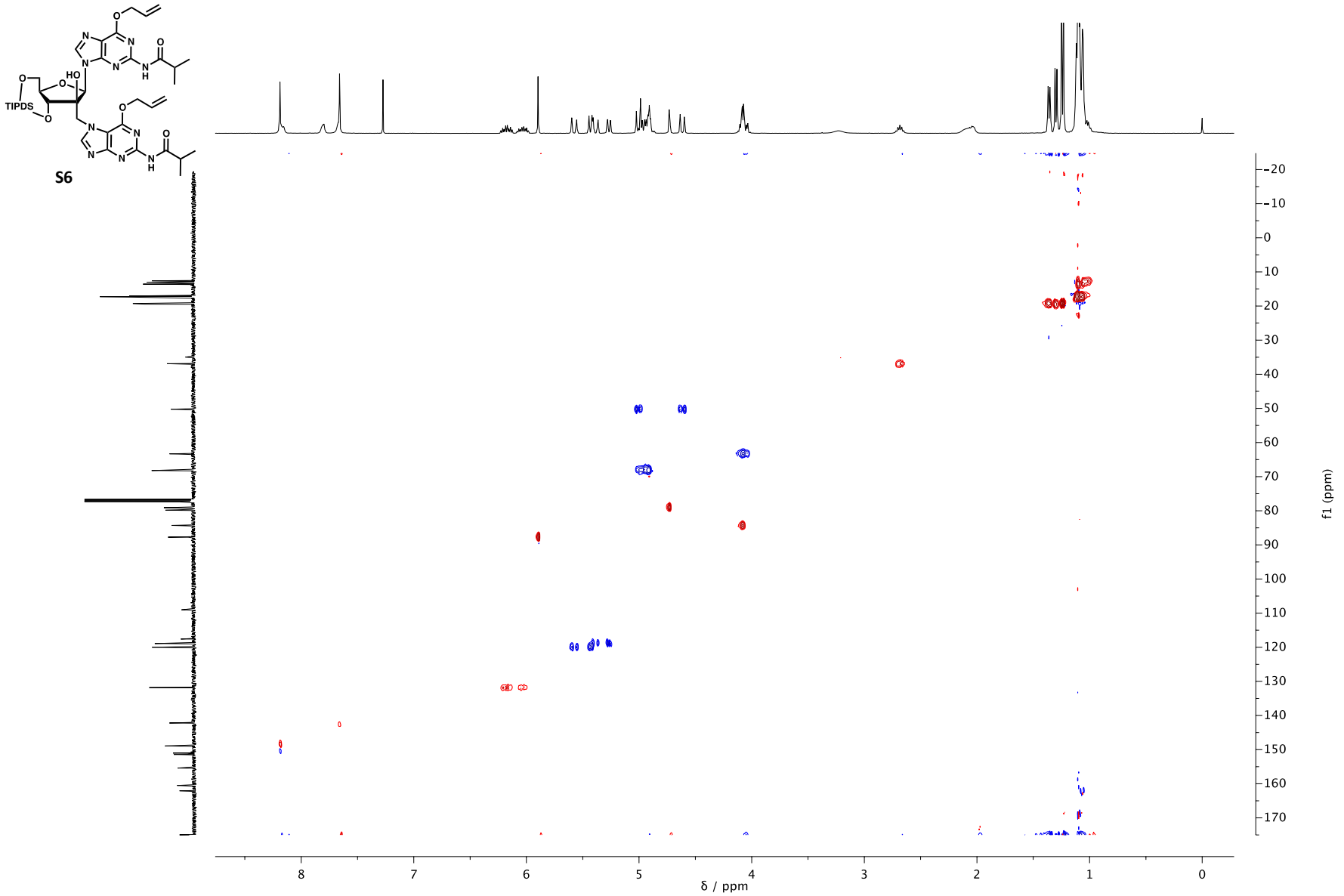
S6



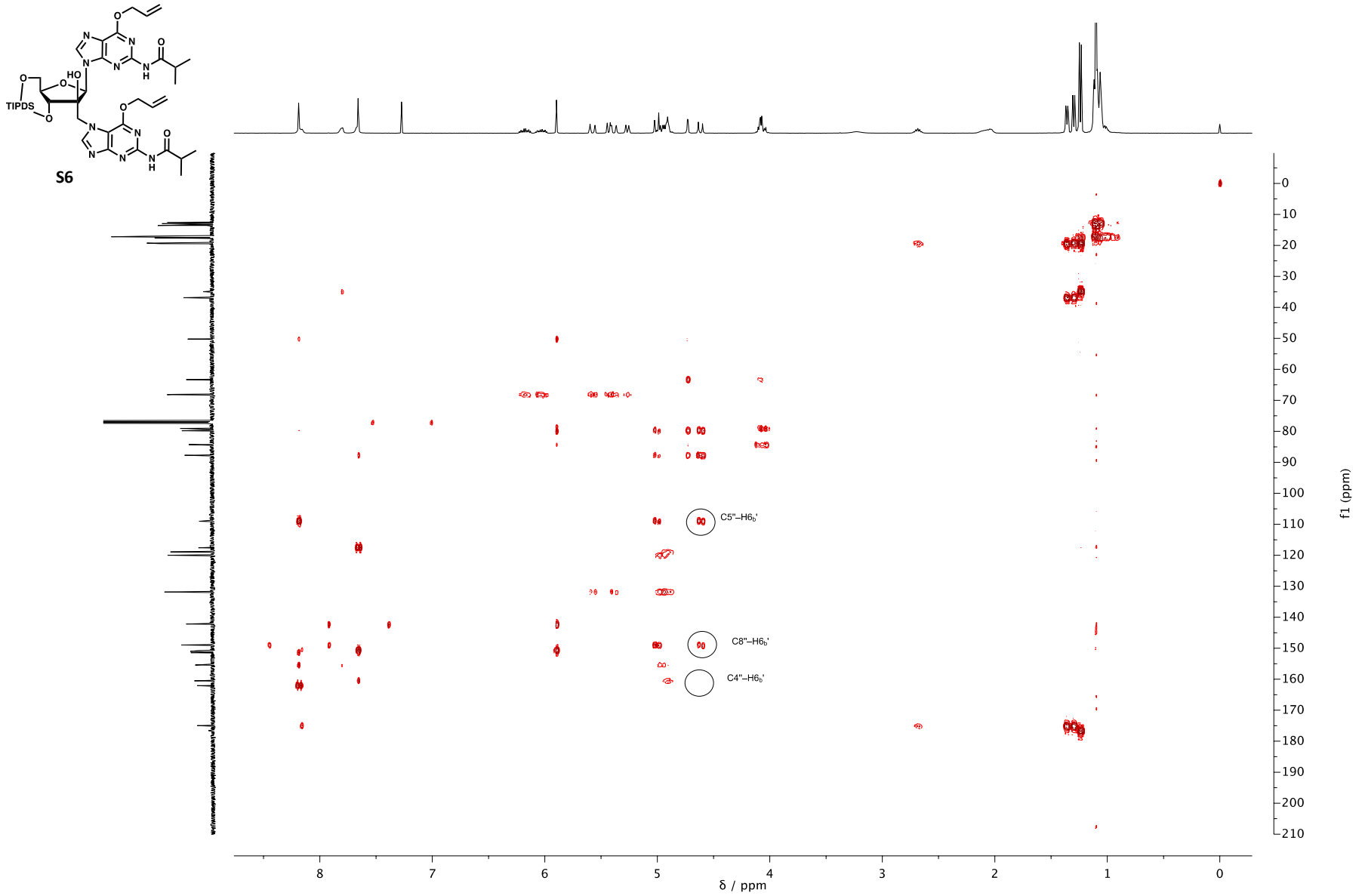
Spectrum S25 101 MHz ^{13}C NMR spectrum of compound **S6** in $CDCl_3$.



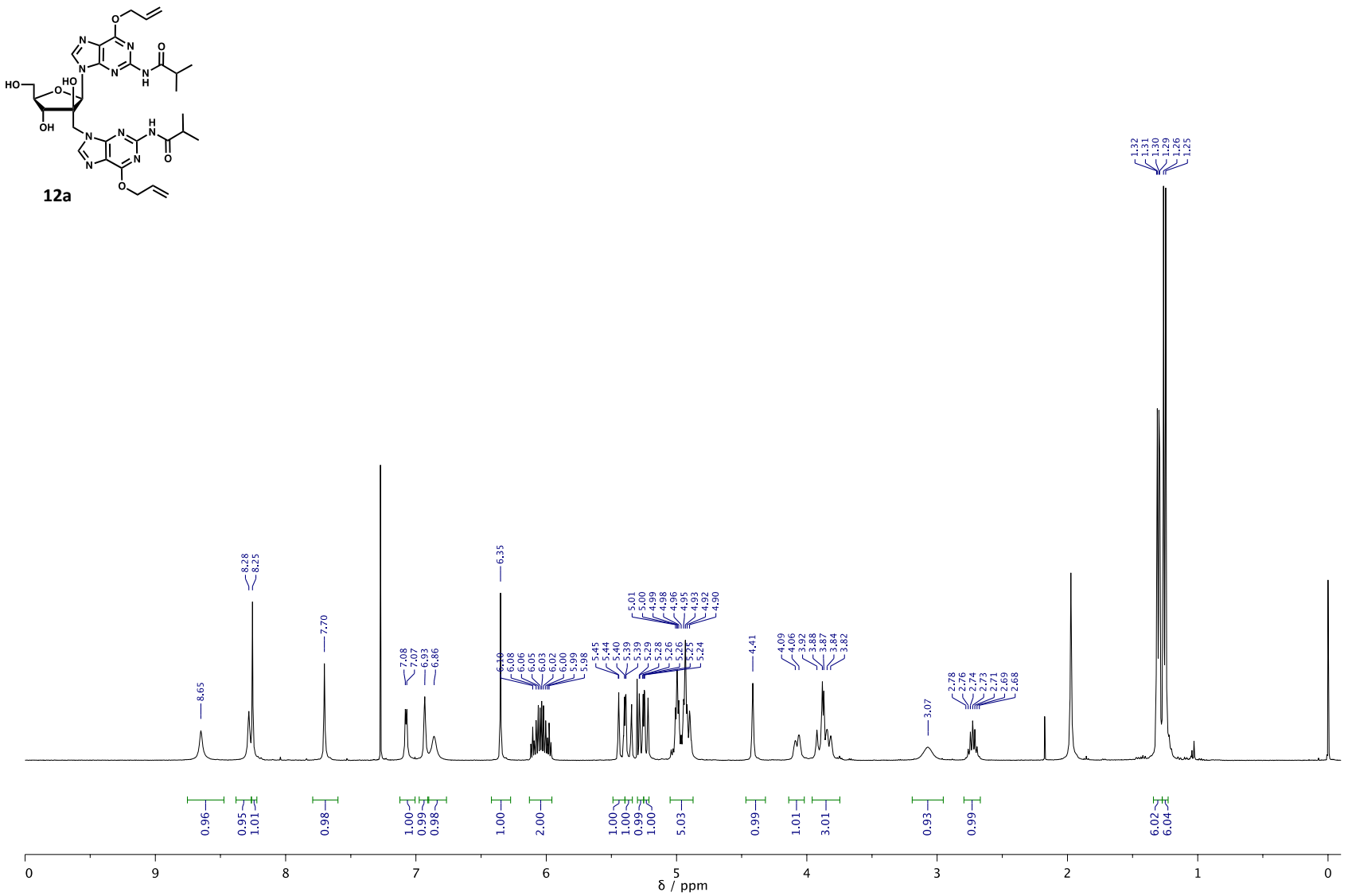
Spectrum S26 ^{1}H,^{1}H-COSY spectrum of compound **S6** in $CDCl_3$.



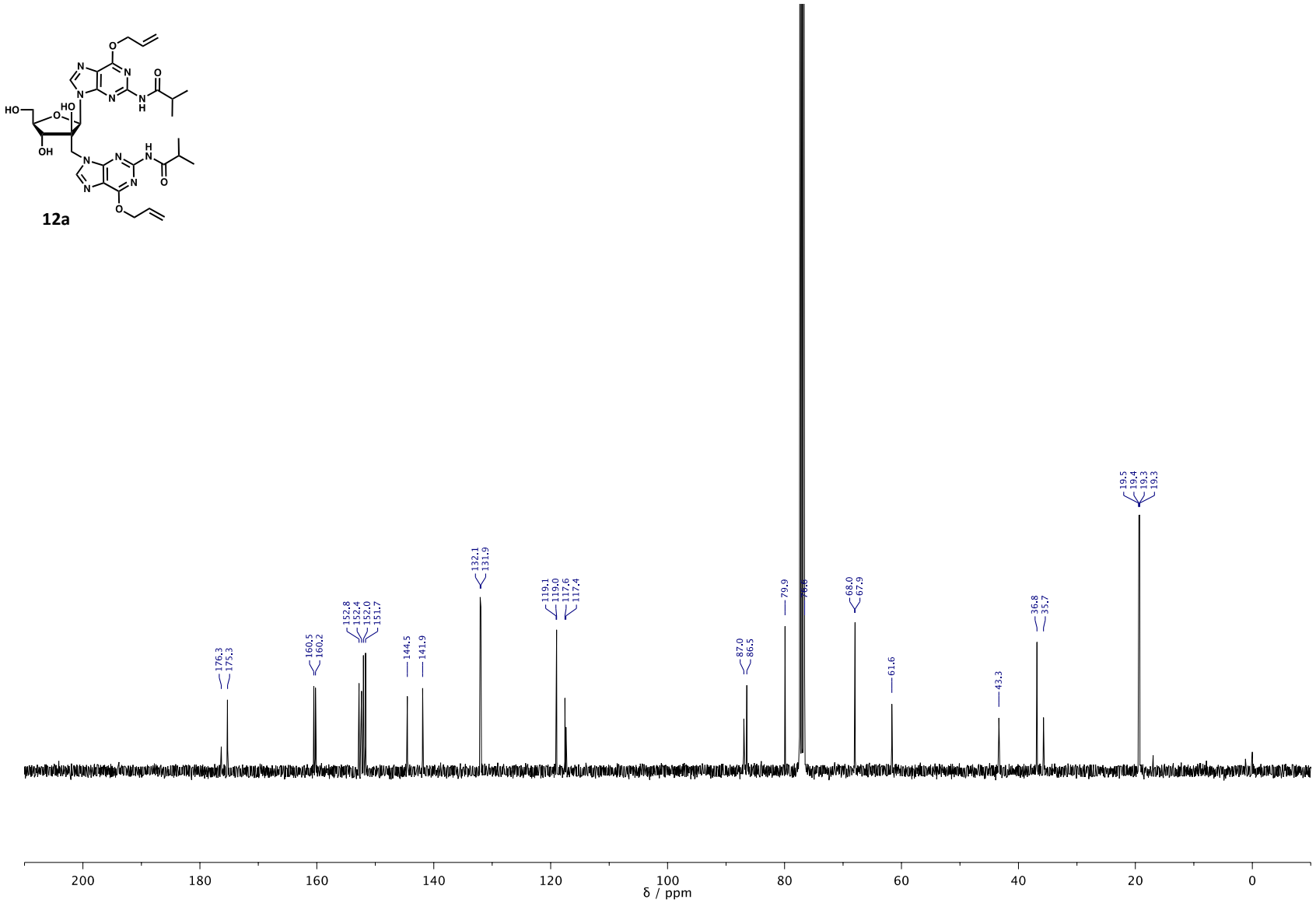
Spectrum S27 $^{1}H,^{13}C$-HSQC spectrum of compound **S6** in $CDCl_3$.



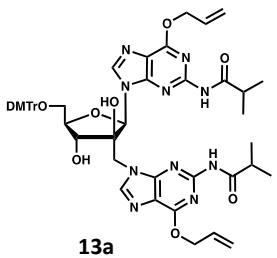
Spectrum S28 $^{1}H,^{13}C$-HMBC spectrum of compound **S6** in $CDCl_3$.



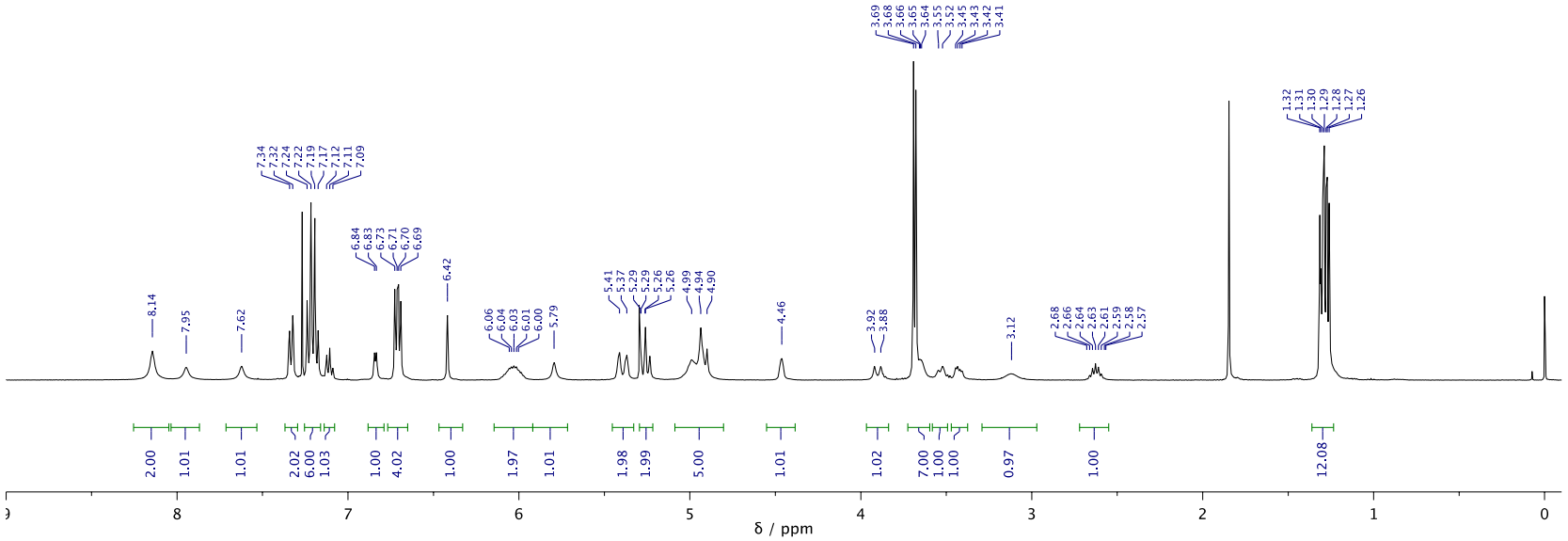
Spectrum S29 400 MHz ^{1}H NMR spectrum of compound **12a** in $CDCl_3$.



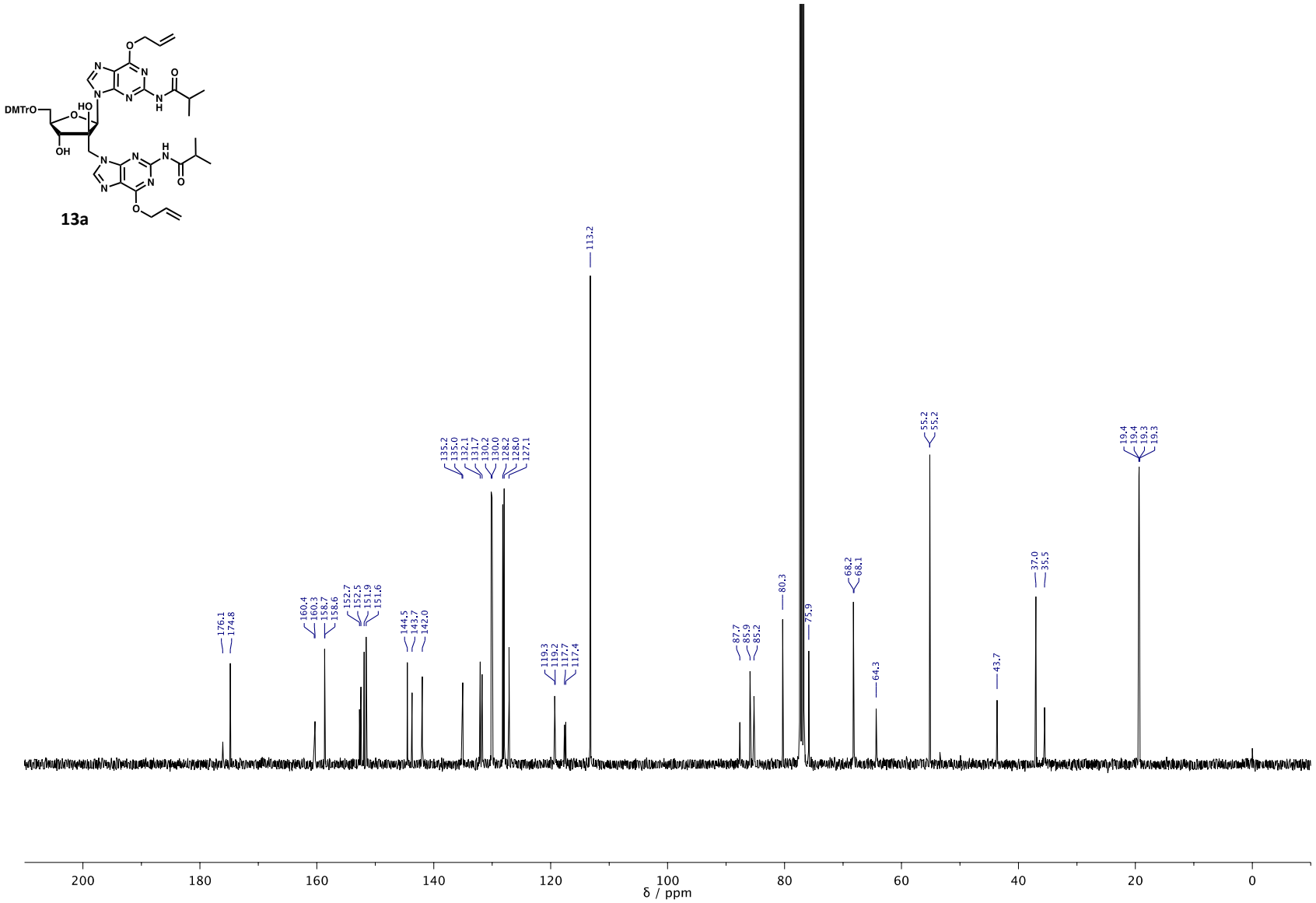
Spectrum S30 101 MHz ^{13}C NMR spectrum of compound **12a** in $CDCl_3$.



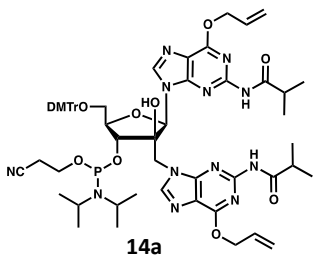
13a



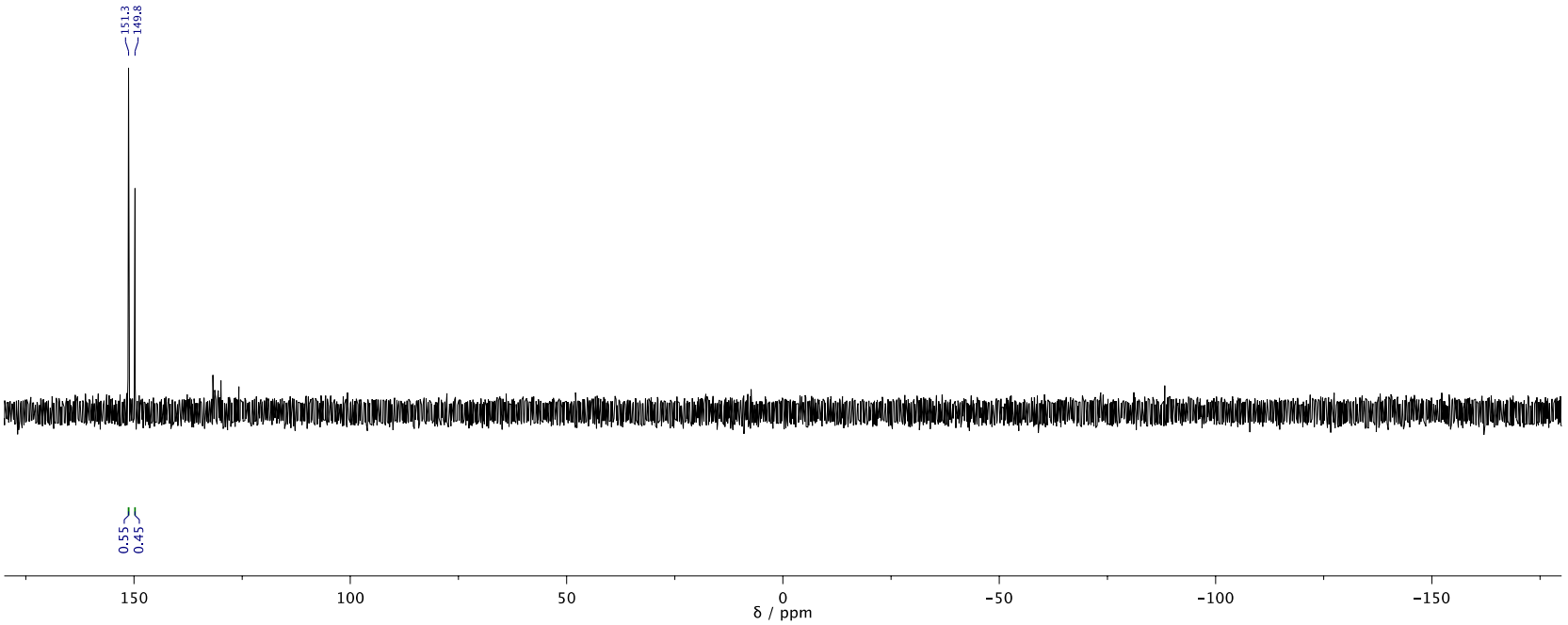
Spectrum S31 400 MHz ^{1}H NMR spectrum of compound **13a** in $CDCl_3$.



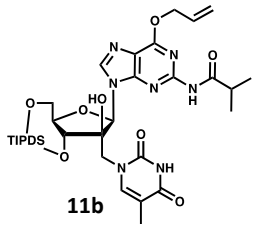
Spectrum S32 101 MHz ^{13}C NMR spectrum of compound **13a** in $CDCl_3$.

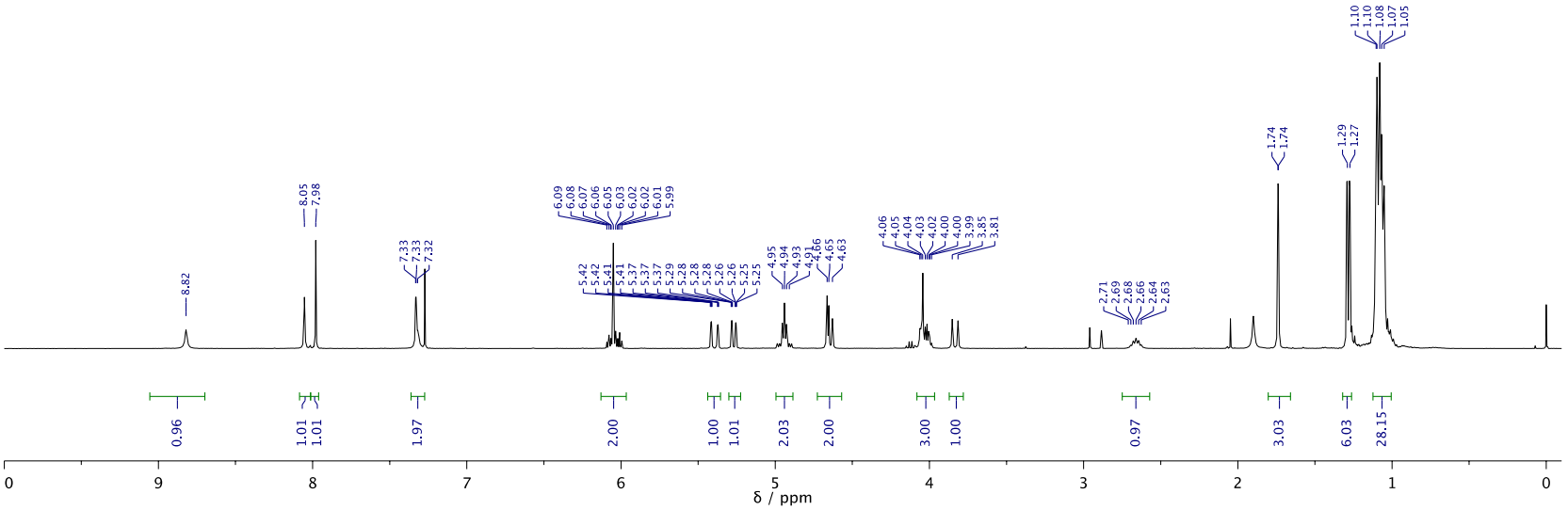


14a

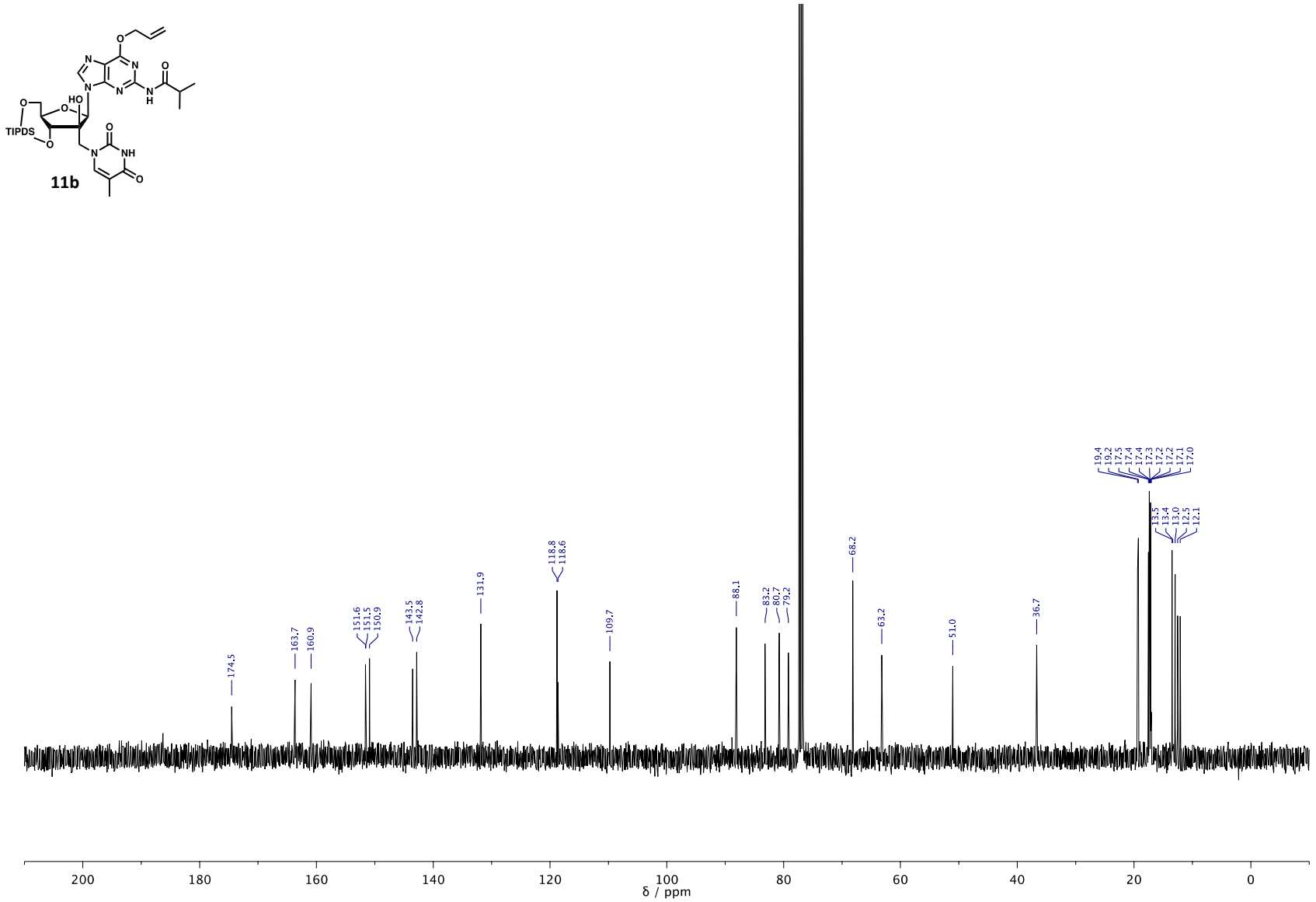


Spectrum S33 162 MHz ^{31}P NMR spectrum of compound **14a** in $CDCl_3$.

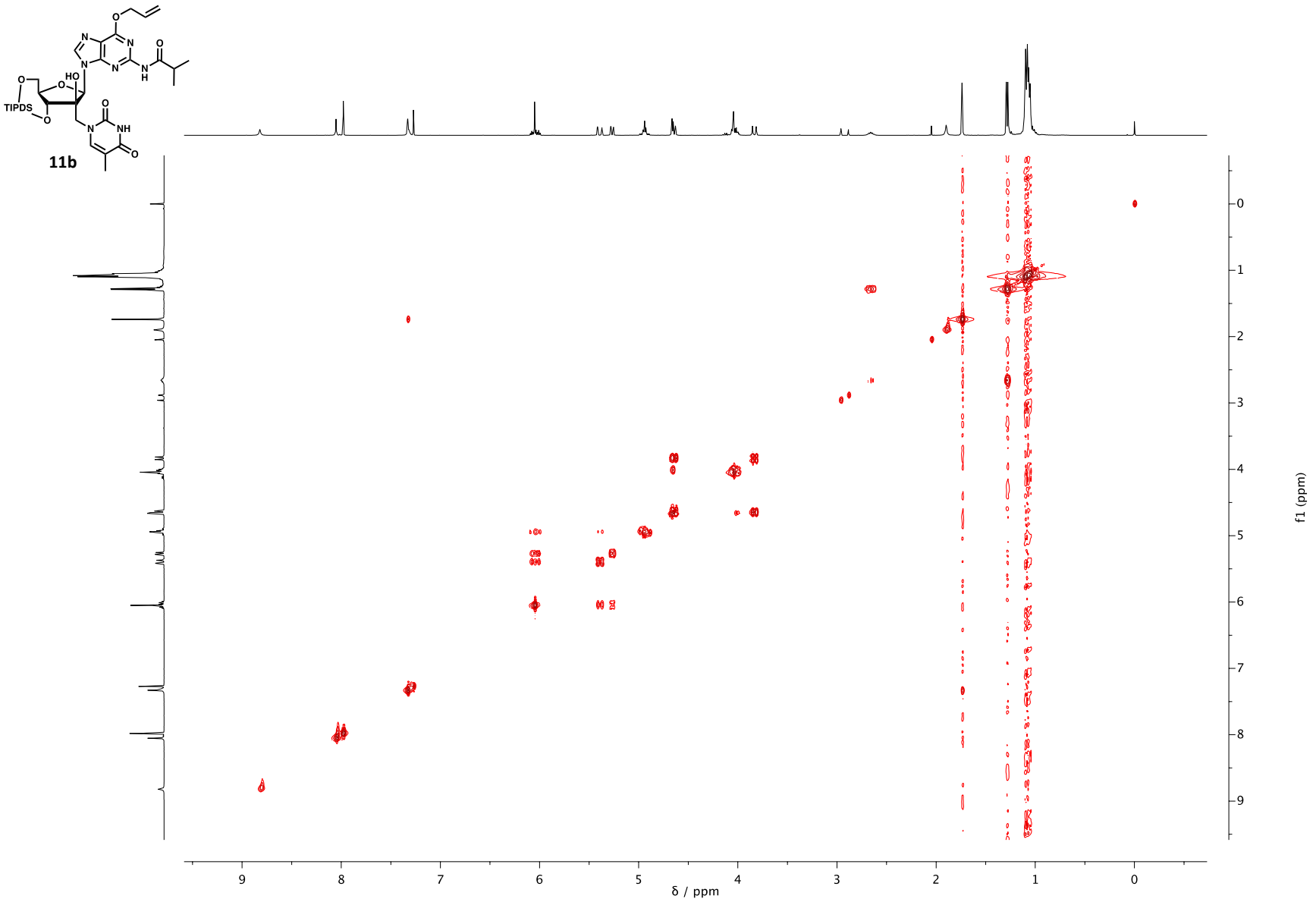




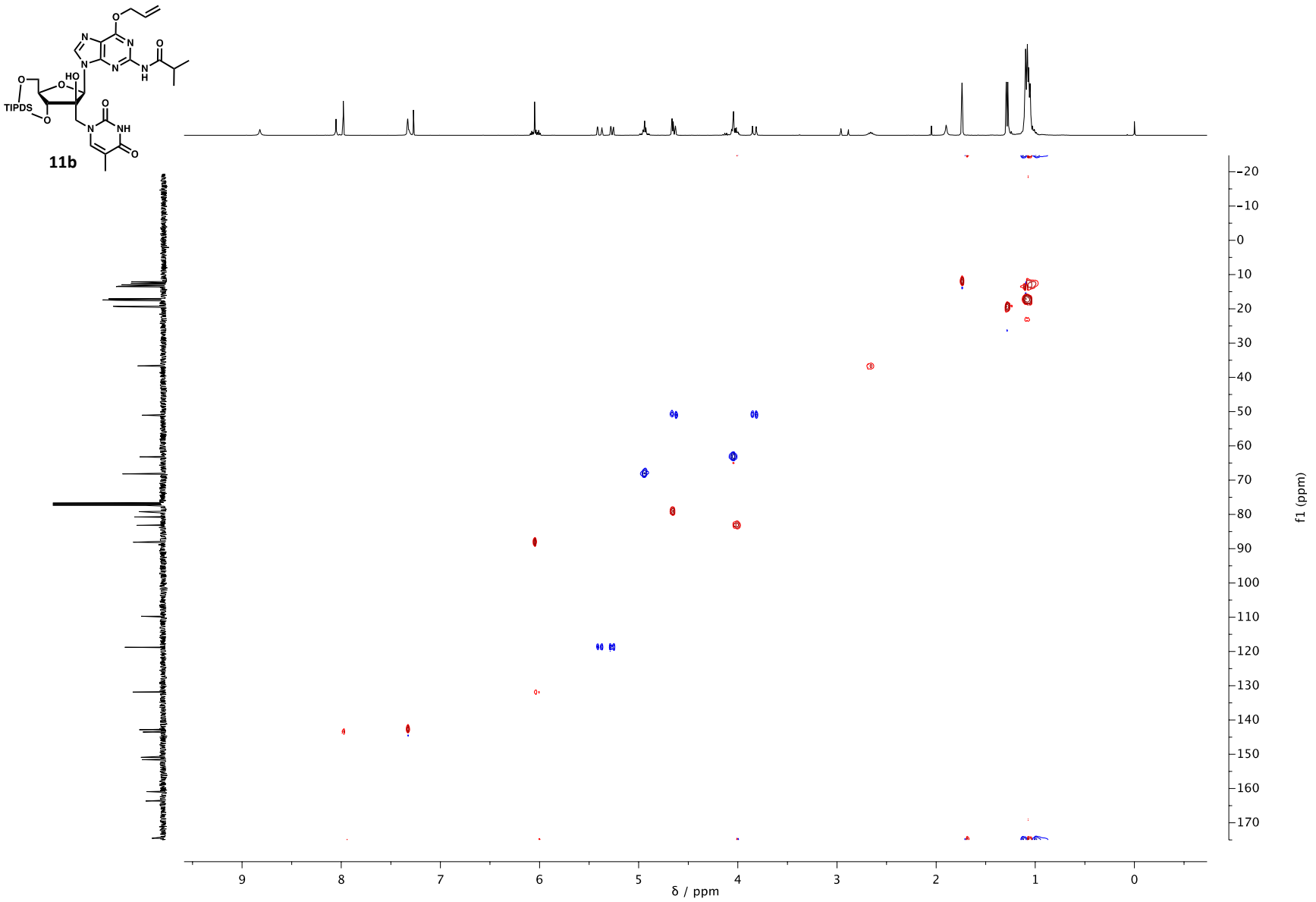
Spectrum S34 400 MHz ^{1}H NMR spectrum of compound **11b** in $CDCl_3$.



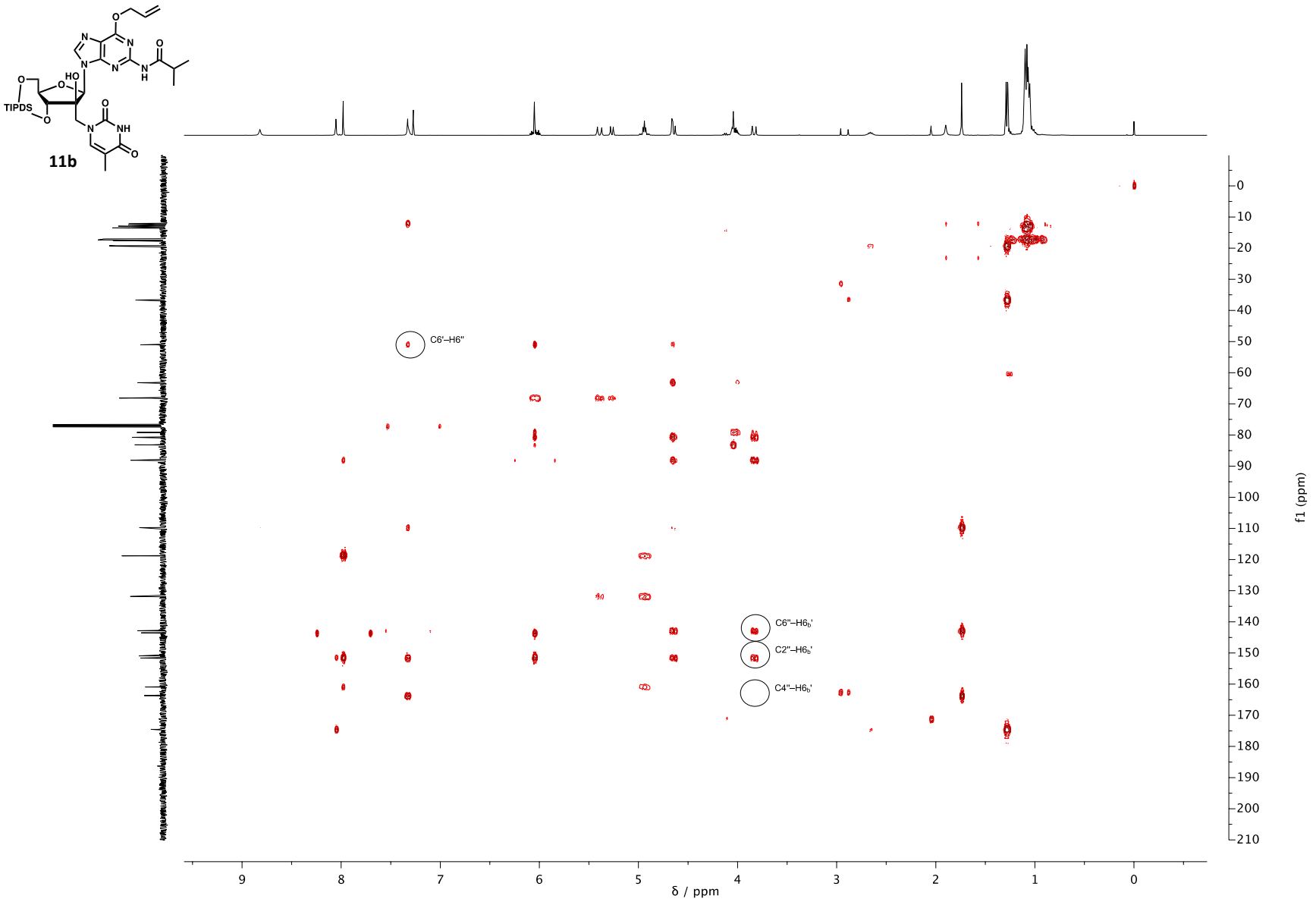
Spectrum S35 101 MHz ^{13}C NMR spectrum of compound **11b** in $CDCl_3$.



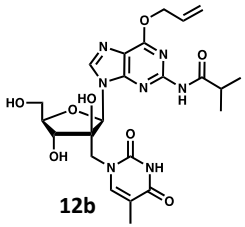
Spectrum S36 $^{1}H,^{1}H$-COSY spectrum of compound **11b** in $CDCl_3$.



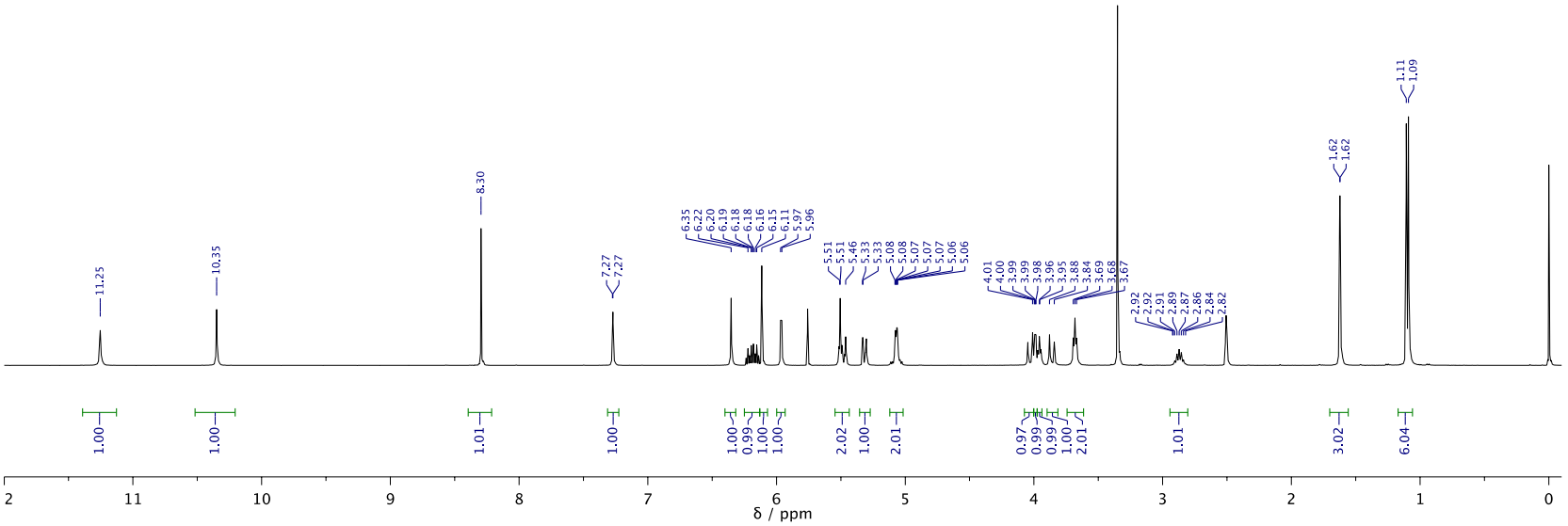
Spectrum S37 $^{1}H,^{13}C$-HSQC spectrum of compound **11b** in $CDCl_3$.



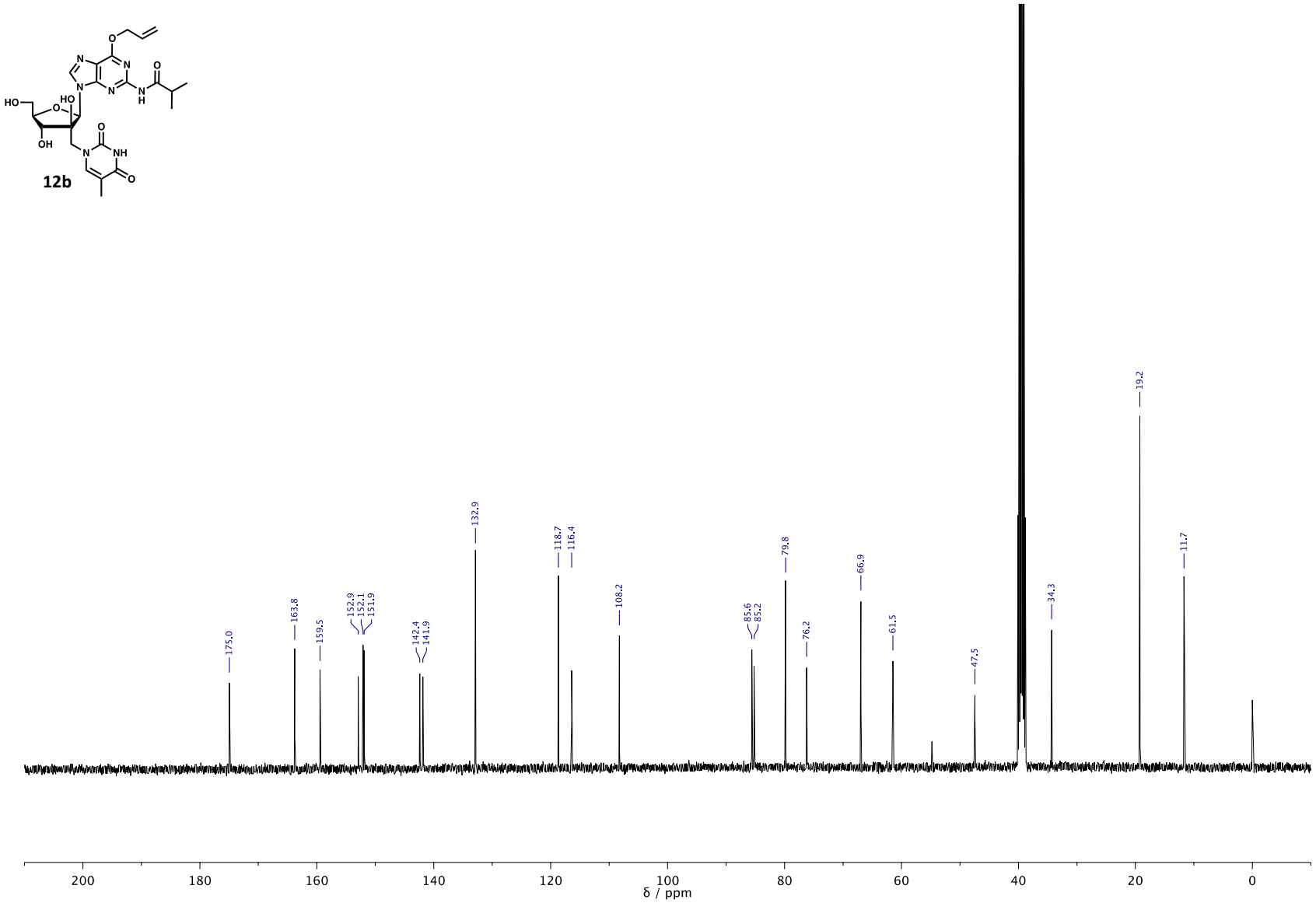
Spectrum S38 $^{1}H,^{13}C$-HMBC spectrum of compound **11b** in $CDCl_3$.



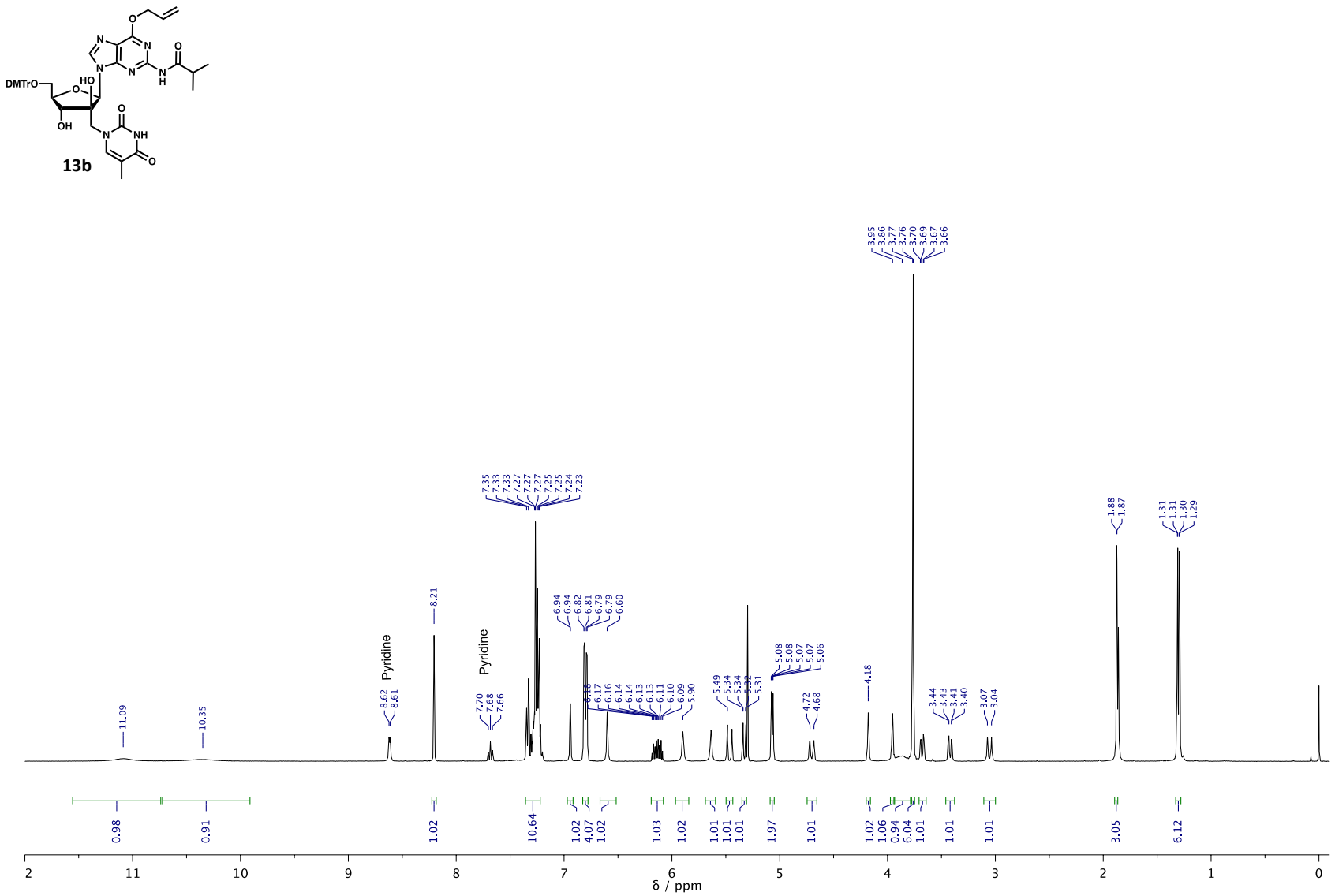
12b



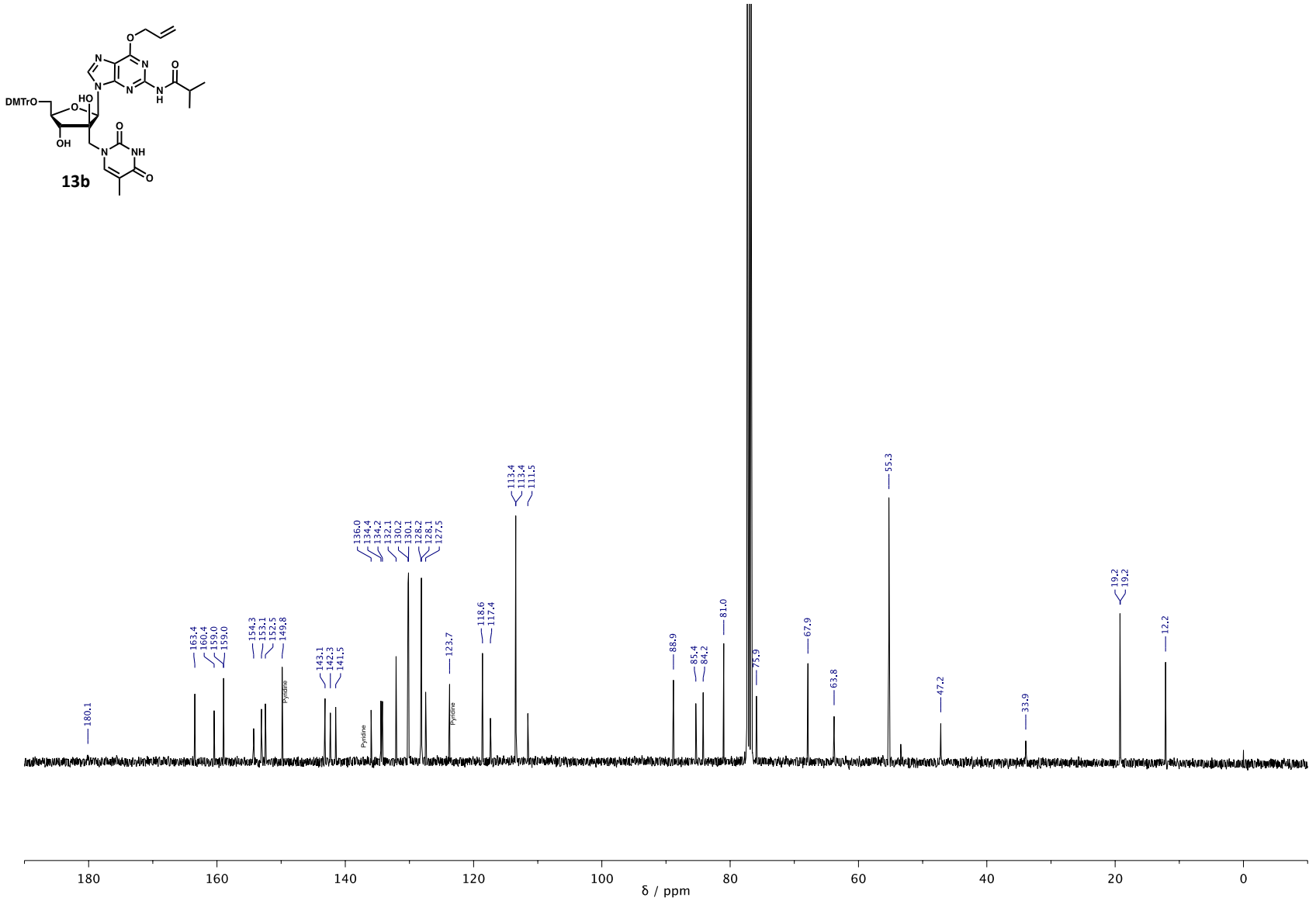
Spectrum S39 400 MHz ^{1}H NMR spectrum of compound **12b** in DMSO-d_6.



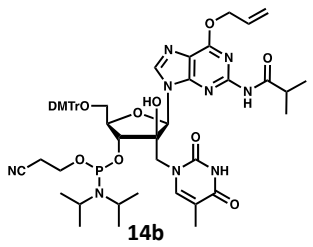
Spectrum S40 101 MHz ^{13}C NMR spectrum of compound **12b** in DMSO-d_6.



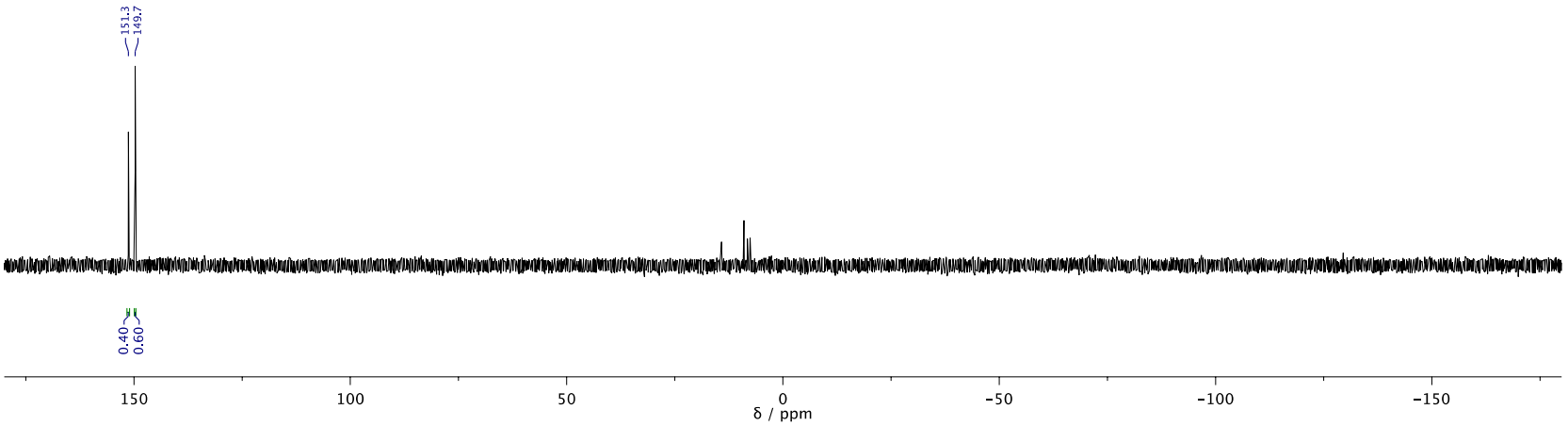
Spectrum S41 400 MHz ^{1}H NMR spectrum of compound **13b** in $CDCl_3$.



Spectrum S42 101 MHz ^{13}C NMR spectrum of compound **13b** in $CDCl_3$.



14b



Spectrum S43 162 MHz ^{31}P NMR spectrum of compound **14b** in $CDCl_3$.