Electronic Supplementary Material (ESI) for Chemical Communications

Supplementary Information

'Click cyclic ADP-ribose': a neutral second messenger mimic

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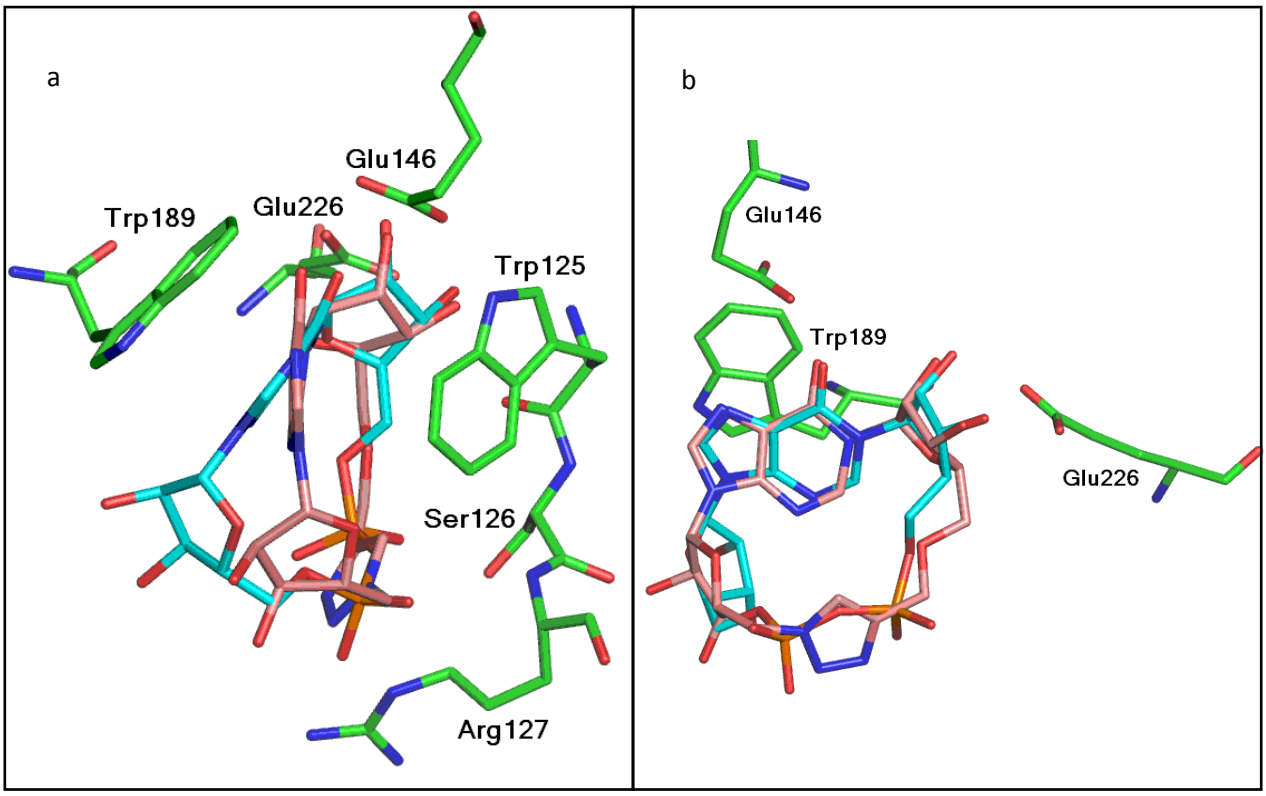


Fig. S1 Compound **3** docked pose in the co-crystal structure of CD38 and cIDPR a) southern ribose pulled out of plane b) overlap of triazole and pyrophosphate groups.

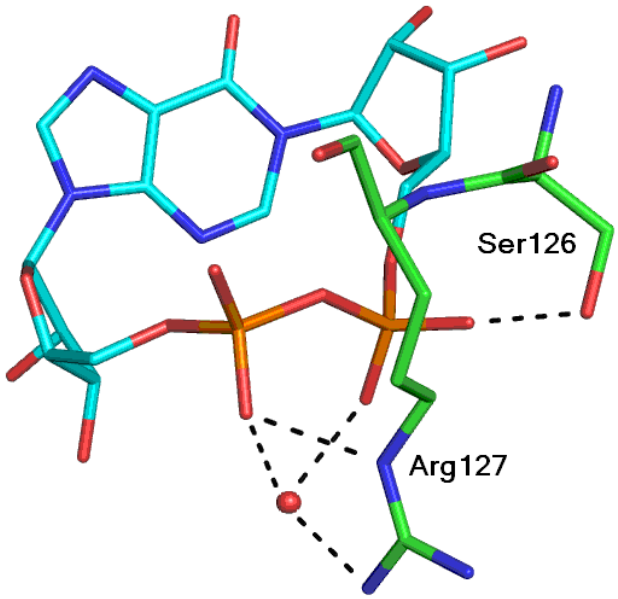


Fig. S2 H-bonds to the pyrophosphate in the crystal structure of cIDPR bound to CD38.

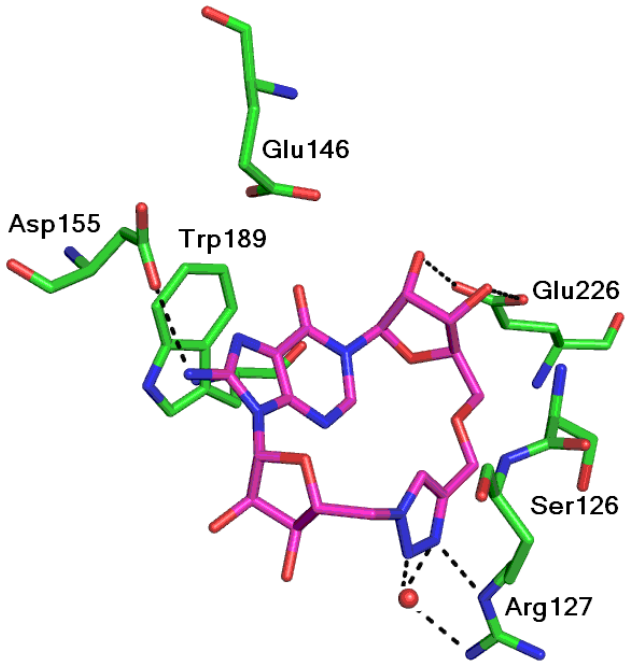


Fig. S3 8-NH_2 group of docked **4** is predicted to H-bond to Asp-155.

Modelling—Compounds **3** and **4** were built and minimised using the Schrödinger software. The 2PGJ structure was passed through the Protein Preparation Wizard of the Schrödinger software after the structure of the ligand in the crystal structure was corrected. Ligands were docked using GOLD with the binding site defined as a sphere of 5Å radius centred on the centroid of the ligand in the binding site. Each ligand was docked 25 times.

Synthesis of Compounds

General Experimental

All reagents and solvents were of commercial quality and were used without further purification, unless described otherwise. Unless otherwise stated, all reactions were carried out under an inert atmosphere of argon. ^{1}H- and ^{13}C chemical shifts (δ) were internally referenced to the residual solvent peak. ^{1}H- and ^{13}C-NMR assignments are based on *g*COSY, *g*HMBC, *g*HSQC, and DEPT-135 experiments. Abbreviations for splitting patterns are as follows: br, broad; s, singlet; d, doublet; t, triplet; m, multiplet etc. Coupling constants are given in Hertz (Hz).

5′-Azido-5′-deoxy-2′,3′-*O*-isopropylideneadenosine 6 - Diphenylphosphoryl azide (2.1 mL, 9.77 mmol) and DBU (2.2 mL, 16.64 mmol) were added dropwise to a suspension of 2′,3′-isopropylidene adenosine (1.5 g, 4.88 mmol) in dioxane (25 mL) and stirring was continued for 3 h. NaN_3 (1.6 g, 24.4 mmol), TBAI (0.18 g, 0.488 mmol) and 15-crown-5 (96 µL, 0.488 mmol) were then added and the solution was refluxed for 4 h. The solvent was removed under reduced pressure and the residue was purified on an Isco chromatographic system (PE:EtOAc, 1:0 → 0:1 v/v) to yield the *title compound* (1.62 g, 100 %) as a pale yellow foam; R_f = 0.47 (DCM:Acetone 1:1 v/v); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.27 (s, 1H, H-8), 7.82 (s, 1H, H-2), 6.02 (d, 1H, *J* = 2.2, H-1′), 5.81 (bs, 2H, NH_2), 5.38 (dd, 1H, *J* = 6.3, 2.2, H-2′), 4.97 (dd, 1H, *J* = 6.3, 3.4, H-3′), 4.29 (dt, 1H, *J* = 3.4, 5.5, H-4′), 3.53-3.44 (m, 2H, H-5′), 1.53 (s, 3H, CH_3) and 1.30 (s, 3H, CH_3) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 155.6, 153.2, 149.1, 139.8, 120.3, 114.7, 90.6, 85.6, 84.0, 82.0, 52.3, 27.0 and 23.7 ppm; HRMS (ES^+) calcd for $C_{13}H_{17}N_8O_3$ 333.1418, found *m/z* $[M+H]^+$ 333.1386.

5′-Azido-5′-deoxy-2′,3′-*O*-isopropylidene-8-bromoadenosine 7 - Adenosine **6** (2.16 g, 6.50 mmol) was taken up in dioxane:NaOAc (0.5 M, pH 4, aq.) (1:1 v/v, 60 mL). Br_2 (0.67 mL, 13.0 mmol) was added and the resulting solution stirred in the dark for 16 h. $Na_2S_2O_3$ (sat. aq.), $NaHCO_3$ (sat. aq.) and DCM were added and the solution stirred vigorously for 30 min. The organic layer was washed with NaCl (sat. aq.), dried (Na_2SO_4) and all solvents evaporated. The residue was purified by column chromatography on silica gel eluting with PE:EtOAc (1:0 → 1:0 v/v) to afford the *title compound* (2.63 mg, 99 %) as a pale yellow foam; R_f = 0.67 (PE:EtOAc, 1:3 v/v); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.28 (s, 1H, H-2), 6.21 (d, 1H, *J* = 1.8, H-1′), 5.96 (bs, 2H, NH_2), 5.68 (dd, 1H, *J* = 6.3, 1.8, H-2′), 5.15 (dd, 1H, *J* = 6.3, 3.7, H-3′), 4.34 (ddd, 1H, *J* = 7.3, 5.8, 3.7, H-4′), 3.51 (dd, 1H, *J* = 12.8, 7.3, H-5′a), 3.45 (dd, 1H, *J* = 12.8, 5.8, H-5′b), 1.61 (s, 3H, CH_3), 1.39 (s, 3H, CH_3) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) 154.4, 153.0, 150.3, 127.5, 120.2, 114.5, 91.2, 86.4, 83.4, 82.4, 52.1, 27.1, 25.3 ppm; HRMS (ESI^+) found *m/z* $[M+H]^+$ 411.0532, 413.0521; $C_{13}H_{16}N_8O_3{}^{79}Br$ requires 411.0523, $C_{13}H_{16}N_8O_3{}^{81}Br$ requires 413.0503.

5′-Azido-5′-deoxy-2′,3′-*O*-isopropylidene-8-bromoinosine 8 - Bromoadenosine **7** (2.23 g, 5.42 mmol) was taken up in acetic acid-water (46 mL, 20:3 v/v). $NaNO_2$ (4.49 g, 65.08 mmol) was added in one portion and the resulting solution stirred for 16 h. All solvents were evaporated and the residue taken up in EtOH and evaporated. The residue was partitioned between $CHCl_3$ and H_2O, and the organic layer washed with

$NaHCO_3$ (sat. aq.), then brine, dried (Na_2SO_4) and evaporated to dryness. The residue was purified by column chromatography on silica gel eluting with PE:EtOAc (1:0 → 1:0 v/v) to afford the *title compound* (2.06 mg, 92 %) as an orange foam; R_f = 0.24 (PE:EtOAc, 1:3 v/v); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 13.08 (bs, 1H, NH), 8.46 (s, 1H, H-2), 6.19 (d, 1H, *J* = 2.0, H-1′), 5.57 (dd, 1H, *J* = 6.4, 2.0, H-2′), 5.08 (dd, 1H, *J* = 6.4, 4.1, H-3′), 4.30 (dd, 1H, *J* = 6.1, 4.2, H-4′), 3.50 (d, 2H, *J* = 6.1, both H-5′), 1.60 (s, 3H, CH_3), 1.39 (s, 3H, CH_3) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) 157.7, 149.5, 146.2, 126.5, 125.5, 114.9, 91.1, 86.1, 83.5, 81.9, 52.0, 27.1, 25.3 ppm; HRMS (ESI$^-$) found *m/z* $[M-H]^-$ 410.0227, 412.0194; $C_{13}H_{13}N_7O_4{}^{79}Br$ requires 410.0218, $C_{13}H_{13}N_7O_4{}^{81}Br$ requires 412.0197.

***N*1-(2″,3″,5″-Tri-*O*-acetyl-β-D-ribofuranosyl)-5′-azido-5′-deoxy-2′,3′-*O*-isopropylidene-8-bromoinosine 9** - Bromoinosine **8** (250 mg, 0.61 mmol) was taken up in DCM (2.5 mL) and DBU (272 µL, 1.82 mmol) added. After 30 minutes, 1,2,3,5-tetra-*O*-acetyl-β-D-ribofuranose (213 mg, 0.67 mmol) was added and the solution cooled to -78 °C. Trimethylsilyl trifluoromethanesulfonate (439 µL, 2.43 mmol) was added dropwise and the solution stirred for a further 45 min before warming to rt. After 1 h, $NaHCO_3$ (sat. aq.) was added and the crude material extracted into DCM (× 3). The combined organic fractions were dried (Na_2SO_4), and solvent evaporated under reduced pressure. The residue was purified by column chromatography on silica gel eluting with PE:EtOAc (1:0 → 0:1 v/v) to afford the *title compound* (369 mg, 91 %) as a colorless glass; R_f = 0.53 (EtOAc:PE 3:1 v/v); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.18 (s, 1H, H-2), 6.32 (d, 1H, *J* = 4.3, H-1″), 6.15 (d, 1H, *J* = 2.2, H-1′), 5.48 (dd, 1H, *J* = 6.4, 2.2, H-2′), 5.43-5.42 (m, 2H, H-2″ and H-3″), 5.03 (dd, 1H, *J* = 6.4, 4.4, H-3′), 4.44-4.36 (m, 3H, H-4" and 2 × H-5″), 4.26 (dt, 1H, *J* = 6.4, 5.9, H-4′), 3.49 (d, 2H, *J* = 5.9, both H-5′), 2.16, 2.11, 2.07 (each s, 3H, 3 × OAc), 1.60 (s, 3H, CH_3), 1.37 (s, 3H, CH_3) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) 170.1, 169.6, 169.5, 154.4, 147.7, 144.4, 126.2, 124.9, 115.1, 90.8, 87.6, 85.5, 83.5, 81.6, 80.4, 74.2, 70.2, 63.0, 51.8, 27.2, 25.3, 20.7, 20.4, 20.3 ppm; HRMS (ESI$^+$) found *m/z* $[M+Na]^+$ 692.0891, 694.0869; $C_{24}H_{28}N_7O_{11}{}^{79}BrNa$ requires 692.0922, $C_{24}H_{28}N_7O_{11}{}^{81}BrNa$ requires 694.0902.

***N*1-(β-D-ribofuranosyl)-5′-azido-5′-deoxy-2′,3′-*O*-isopropylidene-8-bromoinosine 10** - Triacetyl **9** (1.45 g, 2.16 mmol) was taken up in MeOH (10 mL) in a pressure tube. The solution was saturated with NH_3 (g) at 0 °C, then stirred at rt for 12 h. The solvent was evaporated and the residue purified by column chromatography on silica gel eluting with DCM:Acetone (1:0 → 0:1 v/v) to afford the *title compound* (962 mg, 81 %) as a clear oil; R_f = 0.38 (DCM:Acetone 1:1 v/v); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.63 (s, 1H, H-2), 6.11 (d, 1H, *J* = 2.1, H-1′), 6.03 (d, 1H, *J* = 3.8, H-1″), 5.48 (dd, 1H, *J* = 6.4, 2.1, H-2′), 5.14 (bd, 1H, *J* = 3.9, 2′-OH), 5.02 (dd, 1H, *J* = 6.4, 4.2, H-3′), 4.65 (bd, 1H, *J* = 4.6, 3′-OH), 4.47 (m, 1H, H-2″), 4.40 (dd, 1H, *J* = 6.2, 4.7, H-3″), 4.24 (dt, 1H, *J* = 6.2, 4.2, H-4′), 4.18-4.16 (m, 1H, H-4″), 4.02-3.99 (m, 1H, 5′-OH), 3.95-3.86 (m, 2H, both H-5″), 3.45 (d, 2H, *J* = 6.2, both H-5′), 1.57 (s, 3H, CH_3), 1.34 (s, 3H, CH_3) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) 155.7, 148.4, 145.9, 126.5, 124.5, 115.0, 92.2, 91.0, 85.8 (2C), 83.4, 81.7, 75.3, 70.1, 61.5, 51.9, 27.1, 25.3 ppm; HRMS (ESI$^+$) found *m/z* $[M+Na]^+$ 566.0618, 568.0596; $C_{18}H_{22}N_7O_8{}^{79}BrNa$ requires 566.0605, $C_{18}H_{22}N_7O_8{}^{81}BrNa$ requires 568.0585.

***N*1-(2″,3″-*O*-isopropylidene-β-D-ribofuranosyl)-5′-azido-5′-deoxy-2′,3′-*O*-isopropylidene-8-bromoinosine 11** - To **10** (75 mg, 0.14 mmol) in acetone-2,2-dimethoxypropane (2.5 mL, 4:1 v/v) was added *p*-TsOH (26 mg, 0.14 mmol). After 1 h, DCM and $NaHCO_3$ (sat. aq.) were added, and the organic layer dried (Na_2SO_4) and evaporated to dryness. The residue was taken up in MeOH (5 mL) and DOWEX H^+ resin (25 mg) added. After 30 min the resin was removed by filtration under gravity and the solvent evaporated to obtain the *title compound* (75 mg, 93 %) as a colourless glass; R_f = 0.50 (PE:EtOAc 1:3 v/v); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H, H-2), 6.15 (d, 1H, *J* = 2.2, H-1′), 5.78 (d, 1H, *J* = 2.9, H-1″), 5.47 (dd, 1H, *J* = 6.4, 2.2, H-2′), 5.22 (dd, 1H, *J* = 6.4, 2.9, H-2″), 5.09 (dd, 1H, *J* = 6.4, 3.4, H-3″), 5.03 (dd, 1H, *J* = 6.4, 4.2, H-3′), 4.37 (ddd, 1H, *J* = 3.7, 3.4, 2.5, H-4″), 4.27 (dt, 1H, *J* = 5.9, 4.2, H-4′), 3.93 (dd, 1H, *J* = 12.2, 2.5, H-5″a), 3.83 (dd, 1H, *J* = 12.2, 3.7, H-5″b), 3.49 (d, 2H, *J* = 5.9, both H-5′), 1.60 (s, 3H, CH_3), 1.58 (s, 3H, CH_3), 1.37 (s, 3H, CH_3), 1.35 (s, 3H, CH_3) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) 155.0, 148.1, 146.6, 126.5, 125.6, 115.1, 114.3, 96.6, 90.9, 87.9, 85.6, 83.6, 83.5, 81.7, 80.6, 62.7, 51.9, 27.3, 27.1, 25.3, 25.2 ppm; HRMS (ESI^+) found *m/z* $[M+H]^+$ 584.1096, 586.1091; $C_{21}H_{27}N_7O_8{}^{79}Br$ requires 584.1099, $C_{21}H_{27}N_7O_8{}^{81}Br$ requires 586.1079.

***N*1-(2″,3″-*O*-isopropylidene-5″-*O*-propargyl-β-D-ribofuranosyl)-5′-azido-5′-deoxy-2′,3′-*O*-isopropylidene-8-bromoinosine 12** - To **11** (145 mg, 0.25 mmol) at 0 °C in toluene-dioxane (1.5 mL, 2:1 v/v) was added powdered KOH (28 mg, 0.50 mmol). After 15 min, propargyl bromide (80 %, 55 µL, 0.50 mmol) and TBAI (92 mg, 0.25 mmol) were added, the solution was allowed to warm to rt and stirred for a further 16 h. The reaction mixture was diluted with DCM, washed with H_2O and the organic layer dried (Na_2SO_4) and all solvents evaporated. The residue was purified by column chromatography on silica gel eluting with PE:EtOAc (1:0 → 0:1 v/v) to afford the *title compound* (60 mg, 39 %) as a colourless oil; R_f = 0.66 (EtOAc:PE 3:1 v/v); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.19 (s, 1H, H-2), 6.17 (d, 1H, *J* = 2.1, H-1′), 6.07 (d, 1H, *J* = 1.9, H-1″), 5.48 (dd, 1H, *J* = 6.4, 2.1, H-2′), 5.06 (dd, 1H, *J* = 6.4, 4.2, H-3′), 4.99 (dd, 1H, *J* = 6.3, 1.9, H-2″), 4.93 (dd, 1H, *J* = 6.3, 3.6, H-3″), 4.46 (ddd, 1H, *J* = 5.1, 3.6, 3.3, H-4″), 4.29 (dt, 1H, *J* = 5.8, 4.2, H-4′), 4.21 (dd, 1H, *J* = 15.8, 2.4, propargyl-Ha), 4.16 (dd, 1H, *J* = 15.8, 2.4, propargyl-Hb), 3.89 (dd, 1H, *J* = 10.3, 3.3, H-5″a), 3.78 (dd, 1H, *J* = 10.3, 5.1, H-5″b), 3.50 (d, 2H, *J* = 5.8, both H-5′), 2.46 (t, 1H, *J* = 2.4, alkynyl-H) 1.61 (s, 3H, CH_3), 1.59 (s, 3H, CH_3), 1.37 (s, 3H, CH_3), 1.35 (s, 3H, CH_3) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) 154.7, 148.1, 145.8, 126.1, 125.3, 115.0, 114.2, 94.2, 90.9, 87.1, 85.8, 85.7, 83.7, 81.9, 81.4, 78.8, 75.4, 69.9, 58.6, 52.0, 27.22, 27.20, 25.4, 25.3 ppm; HRMS (ESI^+) found *m/z* $[M+Na]^+$ 644.1053, 646.1062; $C_{24}H_{28}N_7O_8{}^{79}BrNa$ requires 644.1075, $C_{24}H_{28}N_7O_8{}^{81}BrNa$ requires 646.1054.

***N*1-Cyclic-2″,3″-*O*-isopropylidene-8-bromoinosine-5′-deoxy-5′-(4-methyl-1,2,3-triazole)-2′,3′-*O*-isopropylideneribose 13** - To **12** (60 mg, 0.097 mmol) in THF (60 mL) was added DIPEA (50 µL, 0.290 mmol). The solution was degassed with Argon (30 min), CuI (37 mg, 0.193 mmol) added and the solution refluxed at 70 °C for 16 h. All solvents were evaporated, and the residue was purified by column chromatography on silica gel eluting with PE:EtOAc (1:0 → 0:1 v/v) to afford the *title compound* (45 mg, 75 %); R_f = 0.11 (EtOAc:PE 3:1 v/v); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.81 (s, 1H, H-2), 7.15 (s, 1H, triazole-

CH), 6.09 (d, 1H, *J* = 1.2, H-1′), 5.84 (d, 1H, *J* = 1.5, H-1″), 5.21 (t, 1H, *J* = 6.6, H-3′), 5.04 (dd, 1H, *J* = 6.6, 1.2, H-2′), 4.94 (dd, 1H, *J* = 15.1, 1.4, H-5′a), 4.89 (dd, 1H, *J* = 5.6, 1.5, H-2″), 4.82-4.79 (m, 2H, H-3″, H-4″), 4.67 (d, 1H, *J* = 11.0, H-5″a), 4.49 (dd, 1H, *J* = 15.1, 3.2, H-5′b), 4.46 (d, 1H, *J* = 13.8, triazole-CH_2-Ha), 4.28-4.26 (m, 1H, H-4′), 4.25 (d, 1H, *J* = 13.8, triazole-CH_2-Hb), 3.68 (dd, 1H, *J* = 11.0, H-5″b), 1.62 (s, 3H, CH_3), 1.58 (s, 3H, CH_3), 1.39 (s, 3H, CH_3), 1.32 (s, 3H, CH_3) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) 155.1, 148.5, 144.5, 143.7 (2C), 125.7, 124.6, 115.4, 112.6, 97.4, 88.7, 87.5, 87.3, 84.2, 83.6, 81.7, 78.1, 72.2, 63.5, 48.7, 27.5, 26.9, 25.5, 25.0 ppm; HRMS (ESI$^+$) found *m/z* $[M+Na]^+$ 644.1014, 646.1006; $C_{24}H_{28}N_7O_8{}^{79}BrNa$ requires 644.1075, $C_{24}H_{28}N_7O_8{}^{81}BrNa$ requires 646.1054.

***N*1-Cyclic 8-bromoinosine 5′-deoxy-5′-(4-methyl-1,2,3-triazole) ribose 14** - Compound **13** (20 mg, 0.032) was taken up in aqueous TFA (2 mL, 50 %) at 0 °C and then stirred at rt for 3 h. All solvents were evaporated and the residue coevaporated with MeOH (×3). The residue was then purified by column chromatography on silica gel eluting with DCM:MeOH (1:0 → 7:3 v/v) to afford the *title compound* (15 mg, 88 %) as a white amorphous solid; R_f = 0.42 (DCM:MeOH 4:1 v/v); ^{1}H-NMR (500 MHz, d_4-MeOD) δ 8.68 (s, 1H, H-2), 7.88 (s, 1H, triazole-CH), 5.90 (d, 1H, *J* = 2.4, H-1′), 5.86 (s, 1H, H-1″), 4.81 (d, 2H, *J* = 8.5, both H-5′), 4.72 (d, 1H, *J* = 11.1, triazole-CH_2-Ha), 4.65-4.63 (m, 1H, H-3′), 4.61 (d, 1H, *J* = 11.1, triazole-CH_2-Hb), 4.54 (dd, 1H, *J* = 6.3, 2.4, H-2′), 4.34-4.29 (m, 3H, H-2″, H-3″, H-4″), 4.26 (d, 1H, *J* = 11.5, H-5″a), 4.26-4.24 (m, 1H, H-4′), 3.83 (d, 1H, *J* = 11.5, H-5″b) ppm; ^{13}C-NMR (125 MHz, d_4-MeOD) 157.2, 150.5, 146.6 (2C), 127.5, 127.4, 125.1, 94.6, 93.5, 85.7, 82.3, 76.9, 74.1, 69.64, 69.58, 69.3, 65.5, 50.2 ppm; HRMS (ESI$^+$) found *m/z* $[M+Na]^+$ 564.0467, 566.0448; $C_{18}H_{20}N_7O_8{}^{79}BrNa$ requires 564.0449, $C_{18}H_{20}N_7O_8{}^{81}BrNa$ requires 566.0428.

***N*1-Cyclic inosine 5′-deoxy-5′-(4-methyl-1,2,3-triazole) ribose 3** - To **14** (8 mg, 0.015 mmol) in MeOH (2.5 mL) was added Pd/C (1 mg, 10 mol %) and $NaHCO_3$ (6 mg, 0.074 mmol). The resulting suspension was stirred under an atmosphere of H_2 for 8 h, filtered and all solvents evaporated. The residue was purified by semi-preparative reverse phase HPLC eluted at 5 mL/min with acetonitrile:0.1 M TEAB (1:19 → 13:7 v/v) over 25 min. Fractions were analysed by analytical RP-HPLC eluted at 1 mL/min with ion-pair buffer: 0.17% (*m/v*) cetrimide and 45% (*v/v*) phosphate buffer (pH 6.4) in MeOH. Appropriate fractions were collected and evaporated under vacuum to give the *title compound* (2.0 mg, 31 %); ^{1}H-NMR (500 MHz, D_2O) δ 8.53 (s, 1H, H-2), 8.05 (s, 1H, H-8), 7.95 (s, 1H, triazole-CH), 5.90 (s, 1H, H-1″), 5.88 (d, 1H, *J* = 1.6, H-1′), 4.87 (dd, 1H, *J* = 15.7, 2.9, H-5′a), 4.77-4.72 (m, 3H, triazole-CH_2-Ha, H-5′b, H-3′), 4.54 (d, 1H, *J* = 11.3, triazole-CH_2-Hb), 4.46 (dd, 1H, *J* = 6.1, 1.6, H-2′), 4.43-4.39 (m, 2H, H-2″, H-3″), 4.33 (d, 1H, *J* = 7.1, H-4″), 4.30-4.27 (m, 1H, H-4′), 4.21 (dd, 1H, *J* = 12.2, 1.9, H-5″a), 3.84 (dd, 1H, *J* = 12.2, 1.1, H-5″b) ppm; ^{13}C-NMR (125 MHz, D_2O) 157.8, 147.7, 144.5, 143.7, 142.0, 126.7, 123.4, 92.4, 91.1, 84.1, 79.6, 75.4, 73.4, 68.4, 68.1, 67.7, 63.9, 48.5 ppm; HRMS (ESI$^+$) found *m/z* $[M+Na]^+$ 486.1354; $C_{18}H_{21}N_7O_8Na$ requires 486.1344.

***N*1-Cyclic 8-azidoinosine 5′-deoxy-5′-(4-methyl-1,2,3-triazole) ribose 15** - Compound **14** (9.0 mg, 0.016 mmol) was evaporated from dry DMF (4 × 2 mL), taken up in DMF (1 mL) and stirred under Argon. NaN_3

(11 mg, 0.17 mmol) was added and the resulting suspension stirred at 70 °C in the dark for 16 h, after which a second portion of NaN_3 (11 mg, 0.17 mmol) was added and the suspension stirred for a further 16 h, after which full conversion of the starting material to product was observed by HPLC (λ = 255 nm → λ = 277 nm). All solvent was evaporated and the resulting residue co-evaporated with MilliQ (2 × 5 mL). The residue was then taken up in MilliQ (5 mL), filtered through cotton wool, and purified by semi-preparative HPLC (1.1 × 25 cm C_{18} column) eluted with acetonitrile:MilliQ (1:0 → 13:7 v/v) over 25 min. Fractions were analysed by analytical HPLC and appropriate fractions collected and evaporated under vacuum to give the *title compound* (6.0 mg, 71 %); ^{1}H-NMR (500 MHz, d_7-DMF) δ 8.95 (s, 1H, H-2), 8.22 (s, 1H, triazole-CH), 6.07 (s, 1H, H-1″), 5.76 (d, 1H, *J* = 3.1, H-1′), 5.02 (d, 2H, *J* = 2.3, both H-5′), 4.99 (d, 1H, *J* = 10.8, triazole-CH_2-Ha), 4.84 (d, 1H, *J* = 10.8, triazole-CH_2-Hb), 4.75 (dd, 1H, *J* = 7.2, 6.3, H-3′), 4.70 (dd, 1H, *J* = 6.3, 3.1, H-2′), 4.61 (dd, 1H, *J* = 8.2, 4.2, H-3″), 4.48-4.43 (m, 4H, H-2″, H-4′, H-4″, H-5″a), 4.06 (d, 1H, *J* = 11.3, H-5″b) ppm; ^{13}C-NMR (125 MHz, d_7-DMF) 155.3, 148.2, 145.0, 143.8, 143.7, 126.3, 121.9, 92.7, 89.5, 84.1, 81.5, 75.7, 73.1, 68.7, 68.1, 68.0, 65.5, 49.3 ppm; HRMS (ESI$^+$) found *m/z* $[M+Na]^+$ 527.1381; $C_{18}H_{20}N_{10}O_8Na$ requires 527.1358.

***N*1-Cyclic 8-aminoinosine 5′-deoxy-5′-(4-methyl-1,2,3-triazole) ribose 4** - Compound **14** (5.0 mg, 9.2 μmol) was evaporated from dry DMF (4 × 2 mL), taken up in DMF (1 mL) and stirred under Argon. NaN_3 (6 mg, 0.092 mmol) was added and the resulting suspension stirred at 70 °C in the dark for 16 h, after which a second portion of NaN_3 (6 mg, 0.092 mmol) was added and the suspension stirred for a further 16 h, after which full conversion of the starting material to product was observed by HPLC (λ = 255 nm → λ = 277 nm). All solvent was evaporated and the resulting residue co-evaporated with MilliQ (2 × 5 mL). The residue was taken up in EtOH-MilliQ (3 mL, 1:2 v/v), Pd/C (5 mg) added and stirred under an atmosphere of H_2 for 16 h. The suspension was filtered and all solvents evaporated. The residue was purified by semi-preparative HPLC (1.1 × 25 cm C_{18} column) eluted with acetonitrile:0.1 M TEAB (1:0 → 13:7 v/v) over 25 min. Fractions were analysed by analytical HPLC and appropriate fractions collected and evaporated under vacuum to give the *title compound* (1.85 mg, 42 % over 2 steps); ^{1}H-NMR (500 MHz, D_2O) δ 8.33 (s, 1H, H-2), 7.92 (s, 1H, triazole-CH), 5.87 (s, 1H, H-1″), 5.70 (d, 1H, *J* = 1.9, H-1′), 4.83 (dd, 1H, *J* = 15.6, 2.6, H-5′a), 4.76-4.66 (m, 2H, H-5′b, triazole-CH_2-Ha), 4.60 (dd, 1H, *J* = 8.9, 5.2, H-3′), 4.55-4.50 (m, 2H, H-2′, triazole-CH_2-Hb), 4.40-4.37 (m, 2H, H-2″, H-3″), 4.32 (d, 1H, *J* = 6.5, H-4″), 4.24 (d, 1H, *J* = 8.9, H-4′), 4.20 (dd, 1H, *J* = 11.8, 1.6, H-5″a), 3.82 (d, 1H, *J* = 11.8, H-5″b) ppm; ^{13}C-NMR (125 MHz, D_2O) 156.2, 147.5, 143.7, 141.8 (2C), 126.7, 120.1, 92.5, 88.8, 84.2, 79.5, 75.6, 72.9, 68.4, 67.9, 67.8, 64.0, 48.7 ppm; HRMS (ESI$^+$) found *m/z* $[M+Na]^+$ 501.1467; $C_{18}H_{22}N_8O_8Na$ requires 501.1453.

Enzymatic Assay for cADPR Hydrolysis—The inhibition of cADPR hydrolysis by various concentrations of analogue (0–1 mM) was determined by incubating 1 μM cADPR with 1 μg/ml of CD38 for 10 min at 20 – 24 °C in 25 mM sodium acetate, pH 4.5. The reaction was stopped by the addition of 150 mM HCl. The precipitated protein was filtered, and the pH was neutralized with Tris base. After diluting the mixture 20-

fold, the concentration of the unhydrolyzed cADPR present in the diluted reaction mixture was assayed by the fluorimetric cycling assay as described previously.[1]

Preparation of Sea urchin Egg Homogenate (SUH) and Assay for Calcium Release[2]

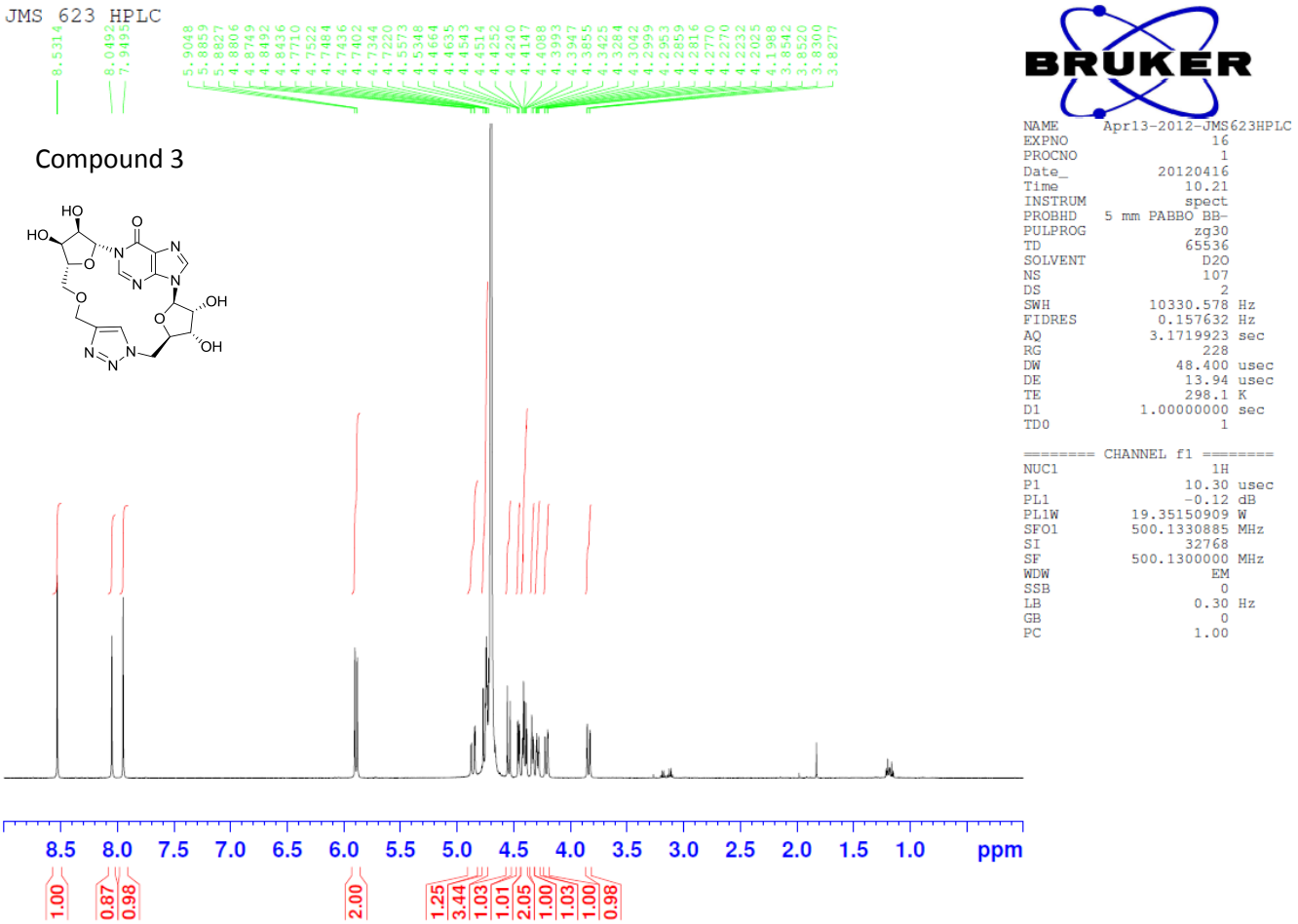
Eggs from the sea urchin *Lytechinus pictus* (Marinus Scientific, Long Beach, CA) were collected into artificial seawater (435 mM NaCl, 40 mM $MgCl_2$, 15 mM $MgSO_4$, 11 mM $CaCl_2$, 10 mM KCl, 2.5 mM $NaHCO_3$, 20 mM Tris and 1mM EDTA, pH 8), following intracoelomic injection of 0.5 M KCl, de-jellied by passing through 100 µm nylon net (Millipore, Watford), then washed to reduce extra-cellular calcium: twice in calcium-free artificial seawater with EGTA (470 mM NaCl, 27 mM $MgCl_2$, 28 mM $MgSO_4$, 10 mM KCl, 2.5 mM $NaHCO_3$, and 1mM EGTA, pH 8), then twice in calcium-free artificial seawater (470 mM NaCl, 27 mM $MgCl_2$, 28 mM $MgSO_4$, 10 mM KCl, and 2.5 mM $NaHCO_3$, pH 8), each time gently spinning down the eggs and discarding the supernatant, re-suspending the eggs at ten times their packed volume.

The eggs were then washed in an ice-cold intra-cellular-like medium (Glu-IM) (250 mM N-methyl glucamine, 250 mM potassium gluconate, 20 mM Hepes, 1 mM $MgCl_2$, pH 7.2), before being re-suspended in an equivalent volume of Glu-IM supplemented with 2 mM ATP, 20 U/ml creatine phosphokinase, 20 U/ml phosphocreatine and protease-inhibitor cocktail tablets (complete™ EDTA-free, Roche, Burgess Hill) one per 50 ml, and then homogenised using a Dounce homogeniser with a tight-fitting pestle. The homogenate was frozen and stored as aliquots at -80°C till required.

For use in the calcium-release assay an aliquot of SUH would be thawed and progressively diluted (approximately doubling the volume each time) over a 3.5 hour period kept at 17°C in Glu-IM supplemented with 1 mM ATP, 10 U/ml creatine phosphokinase, 10 U/ml phosphocreatine to give a final dilution of 1 in 20 (equivalent to 2.5% packed eggs). The fluorescent calcium reporter dye fluo-3 (Life Technologies, Paisley) was added in the final dilution to be at 3 µM. The assays were performed using a Novostar plate reader (BMG Labtech, Aylesbury). The diluted SUEH was placed in wells of a micro plate, 100 µl/well for 98-well plates, 50 or 20 µl/well for 384-well plates and baseline fluorescence recorded. Additions of the compounds being studied were then made at 1%–2.5% volume of SUEH and the subsequent maximum fluorescence recorded, baseline subtracted to give a value for the rise in fluorescence and that value normalised to the rise evoked by 0.5 µM cADPR (an amount that generates a near maximal rise) under the same conditions.

Data was manipulated and plots generated with “Prism” (GraphPad Software, La Jolla, CA).

1. R. M. Graeff, H. C. Lee, *Biochem. J.*, 2002, **361**, 379-384.
2. (a) D. L. Clapper, T. F. Walseth, P. J. Dargie, H. C. Lee, *J. Biol. Chem.*, 1987, **262**, 9561-9568; (b) A. J. Morgan, G. C. Churchill, R. Masgrau, M. Ruas, L. C. Davis, R. A. Billington, S. Patel, M. Yamasaki, J. M. Thomas, A. A. Genazzani, A. Galione, *Methods in cADPR and NAADP research*, CRC Press, Boca Raton, 2006.

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PULPROG                      zg30
TD                          65536
SOLVENT                       D2O
NS                            107
DS                              2
SWH                     10330.578 Hz
FIDRES                   0.157632 Hz
AQ                      3.1719923 sec
RG                            228
DW                         48.400 usec
DE                         13.94 usec
TE                         298.1 K
D1                    1.00000000 sec
TD0                             1

======== CHANNEL f1 ========
NUC1                           1H
P1                         10.30 usec
PL1                        -0.12 dB
PL1W                19.35150909 W
SFO1                500.1330885 MHz
SI                          32768
SF                  500.1300000 MHz
WDW                            EM
SSB                             0
LB                         0.30 Hz
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PC                         1.00
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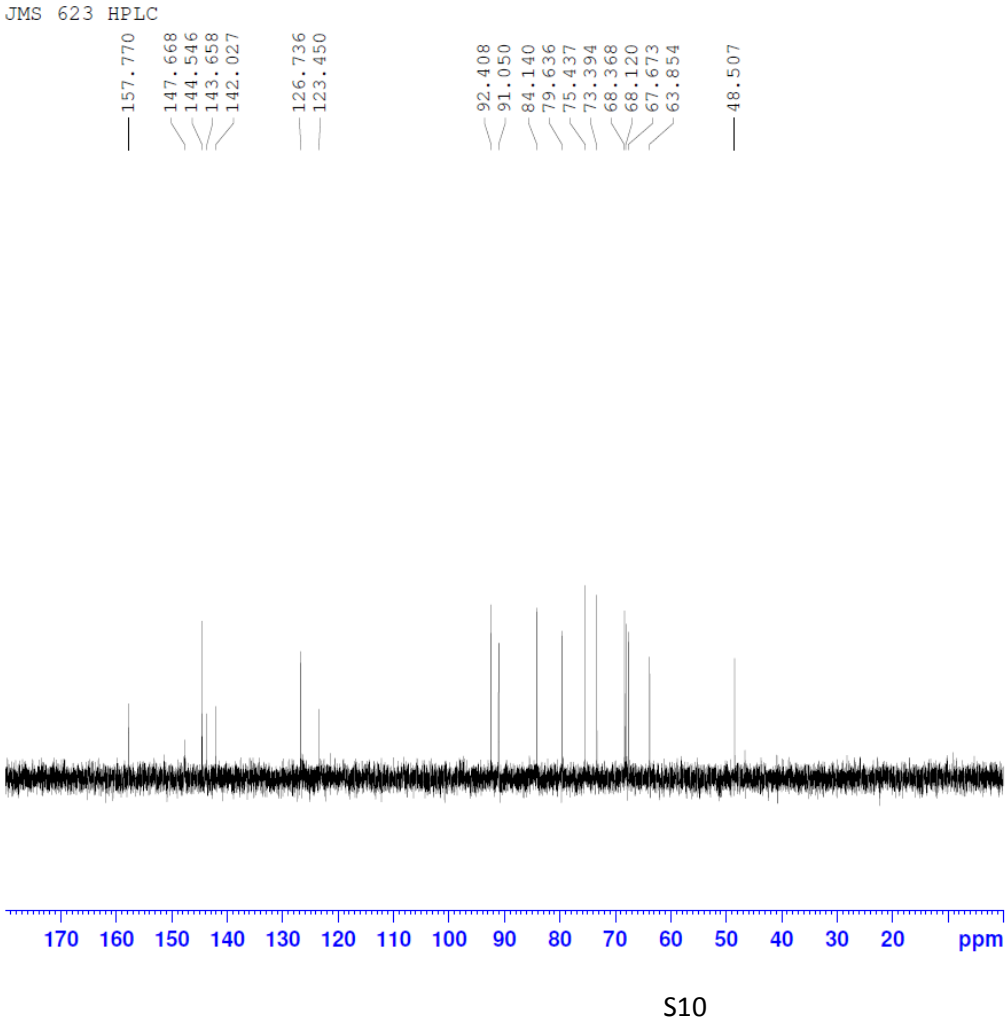


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PROCNO                          1
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PULPROG                  zgpg30
TD                          65536
SOLVENT                       D2O
NS                          10240
DS                              4
SWH                     29761.904 Hz
FIDRES                   0.454131 Hz
AQ                      1.1010548 sec
RG                           2050
DW                         16.800 use
DE                          8.43 use
TE                         298.0 K
D1                    2.00000000 sec
D11                   0.03000000 sec
TD0                             1

======== CHANNEL f1 ========
NUC1                          13C
P1                          9.50 use
PL1                        -0.51 dB
PL1W                99.92730713 W
SFO1                125.7703643 MHz

======== CHANNEL f2 ========
CPDPRG2                  waltz16
NUC2                           1H
PCPD2                      80.00 use
PL2                        -0.12 dB
PL12                       17.94 dB
PL13                       21.00 dB
PL2W                19.35150909 W
PL12W                0.30249262 W
PL13W                0.14952536 W
SFO2                500.1320005 MHz
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SF                  125.7577890 MHz
WDW                            EM
SSB                             0
LB                         1.00 Hz
GB                              0
PC                         1.40
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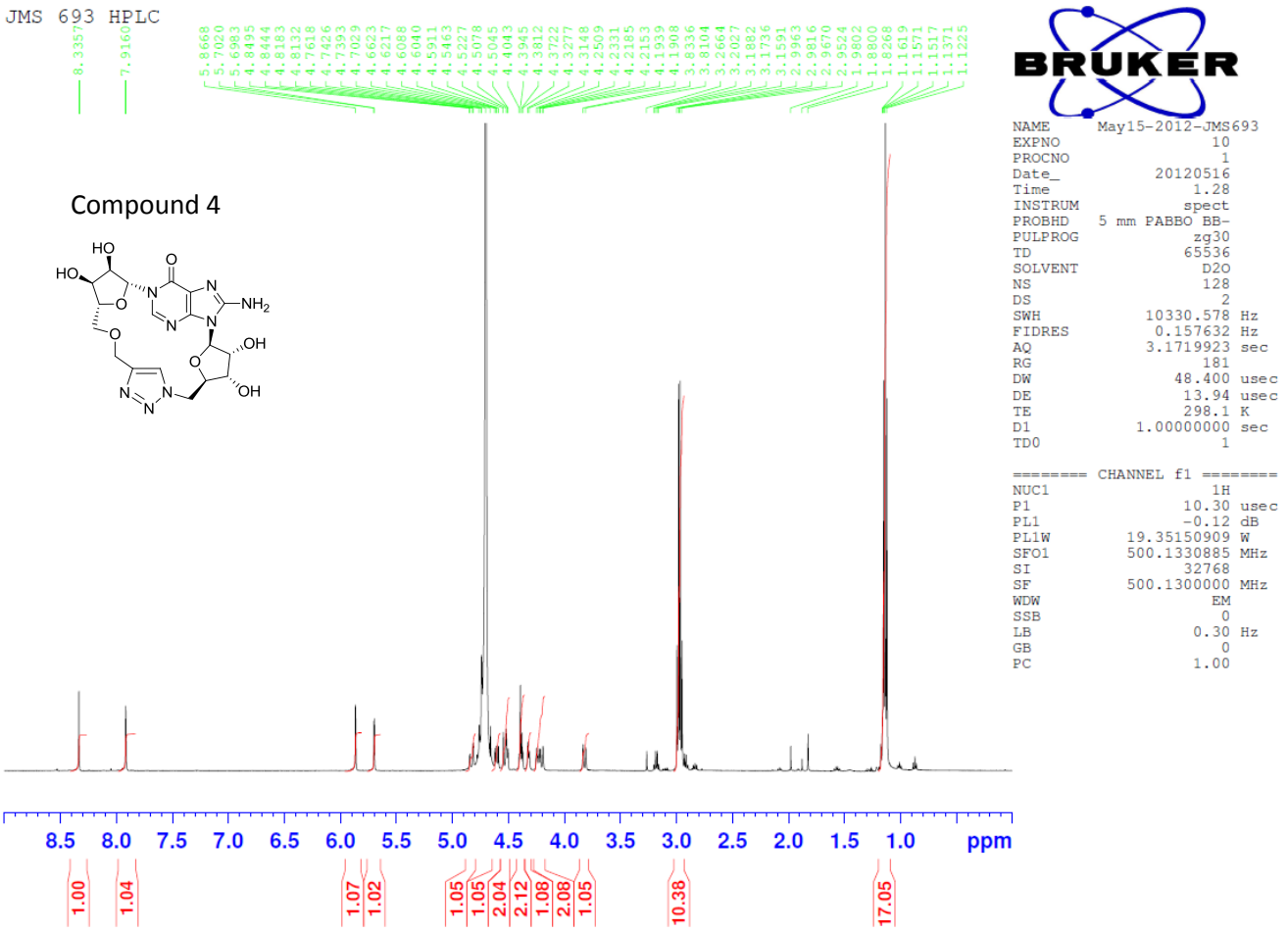

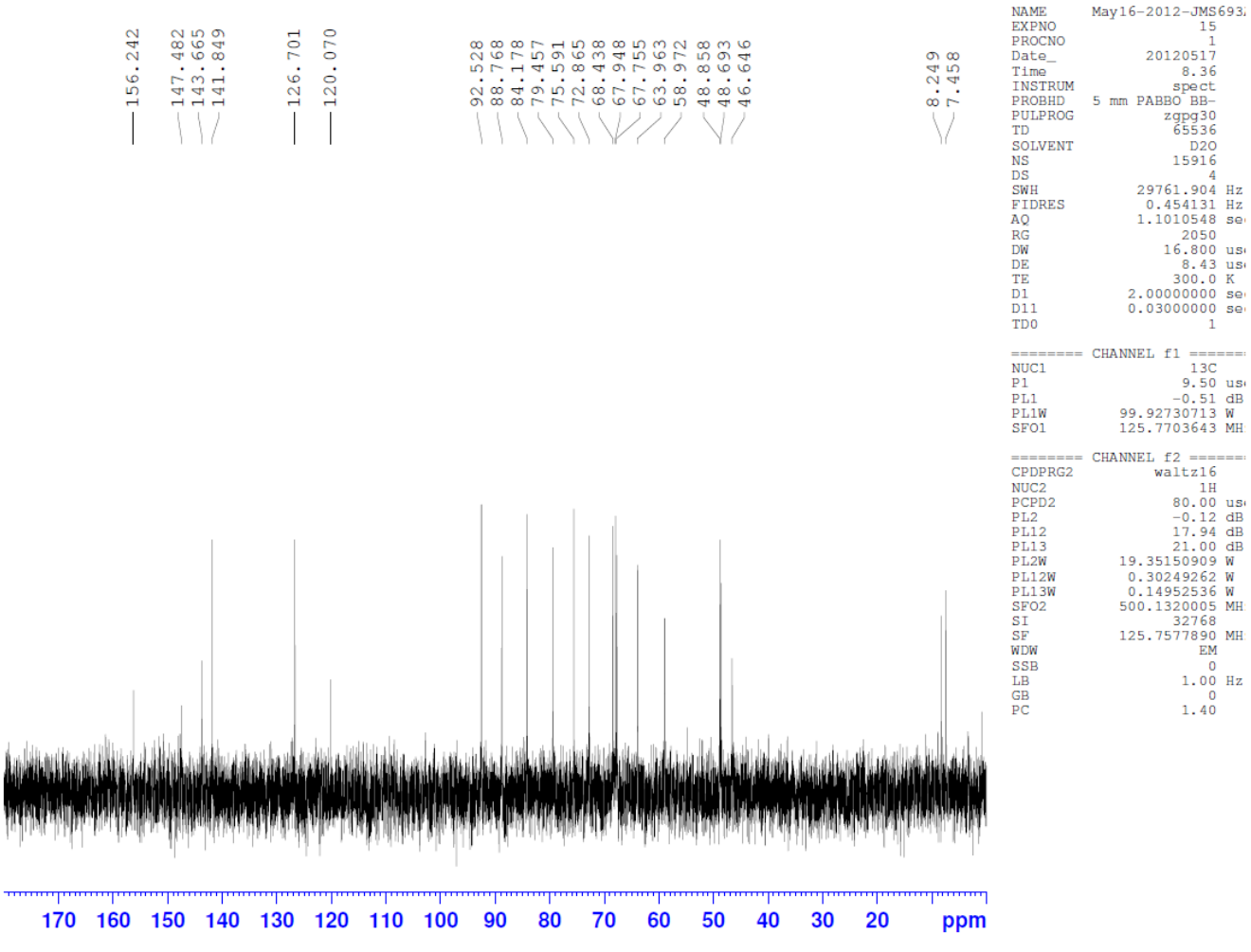

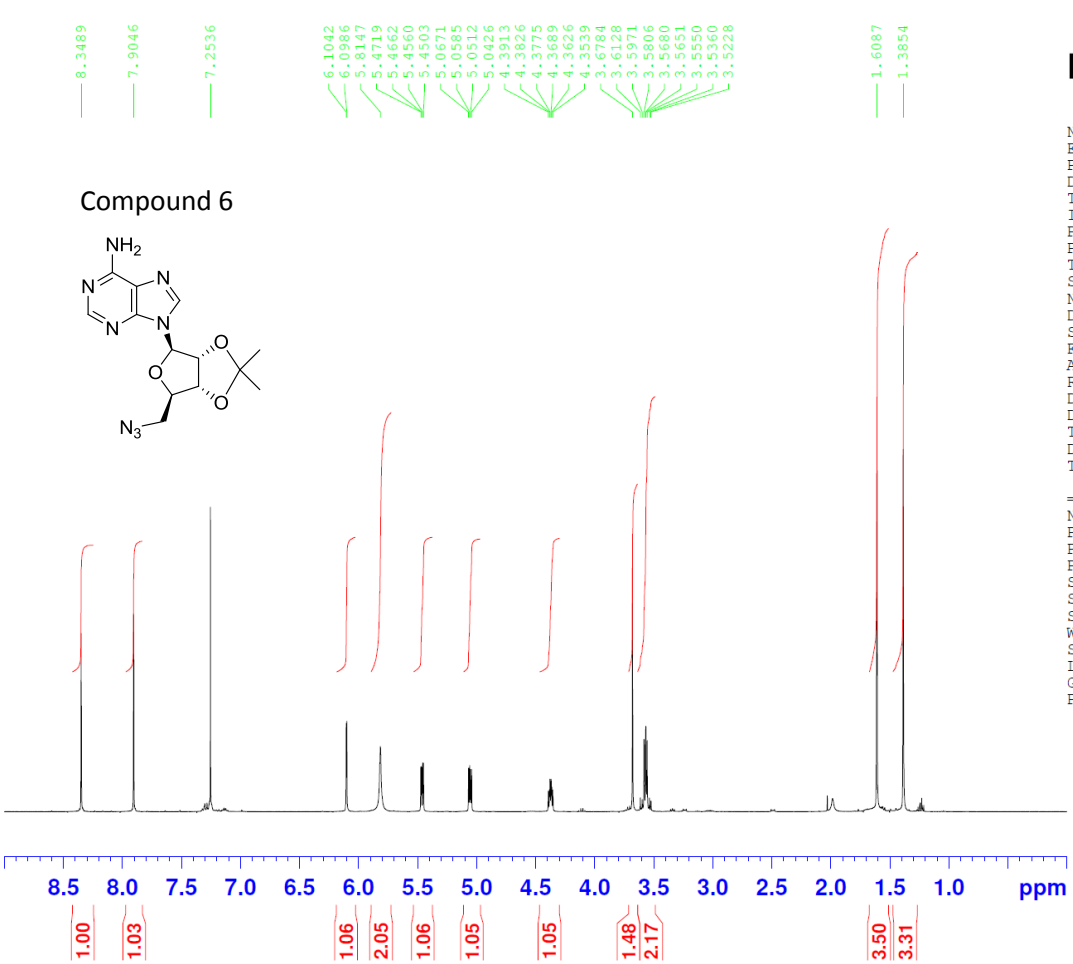


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PROCNO                          1
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PULPROG                      zg30
TD                          65536
SOLVENT                     CDCl3
NS                             16
DS                              2
SWH                      8223.685 Hz
FIDRES                   0.125483 Hz
AQ                       3.9846387 sec
RG                            203
DW                          60.800 usec
DE                          17.24 usec
TE                          298.0 K
D1                    1.00000000 sec
TD0                             1

======== CHANNEL f1 ========
NUC1                           1H
P1                          13.00 usec
PL1                          0.00 dB
PL1W                 9.74611950 W
SFO1                400.0424704 MHz
SI                          65536
SF                  400.0399837 MHz
WDW                            EM
SSB                             0
LB                           0.20 Hz
GB                              0
PC                           1.00
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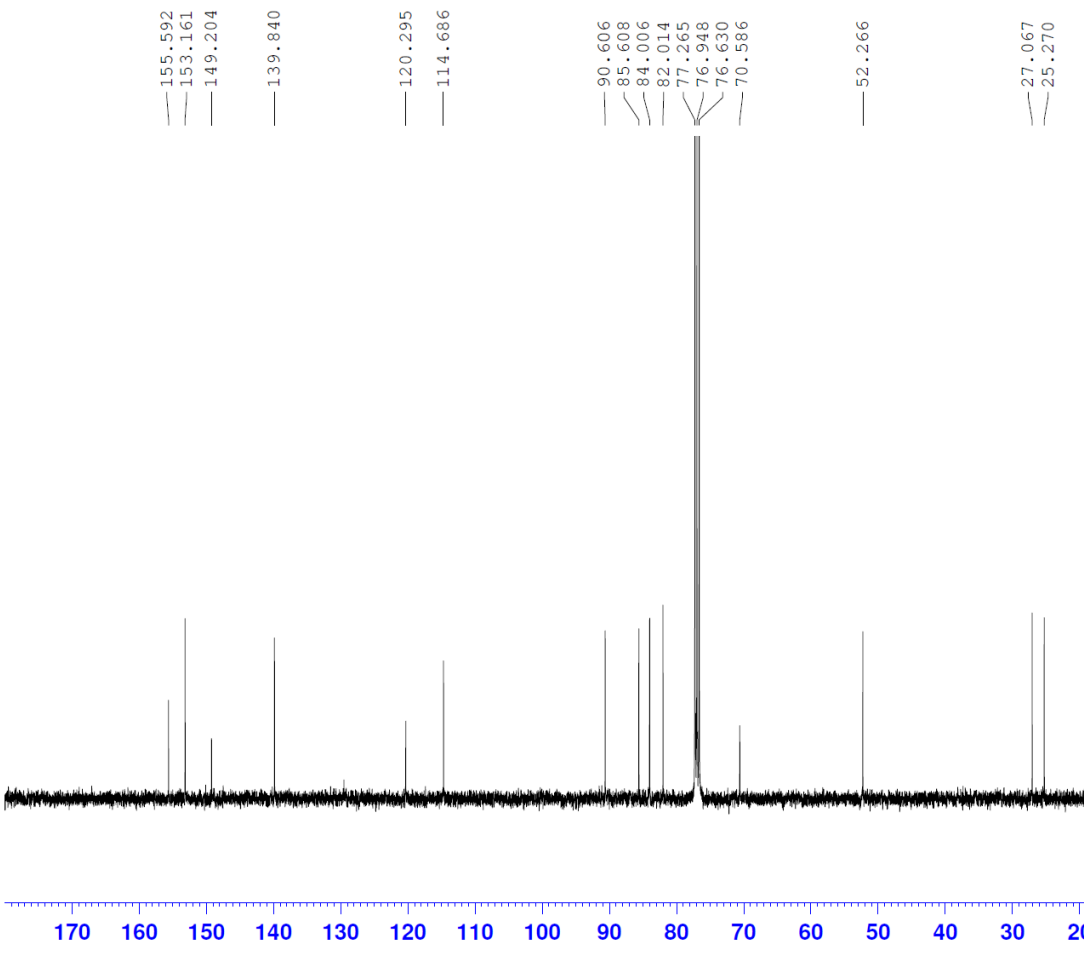


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PROCNO                          1
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PULPROG                   zgpg30
TD                          65536
SOLVENT                     CDCl3
NS                            512
DS                              4
SWH                     24038.461 Hz
FIDRES                   0.366798 Hz
AQ                       1.3631988 sec
RG                           2050
DW                          20.800 usec
DE                           6.50 usec
TE                          298.0 K
D1                    2.00000000 sec
D11                   0.03000000 sec
TD0                             1

======== CHANNEL f1 ========
NUC1                          13C
P1                           8.75 usec
PL1                         -2.00 dB
PL1W                58.91986084 W
SFO1               100.6001970 MHz

======== CHANNEL f2 ========
CPDPRG2                   waltz16
NUC2                           1H
PCPD2                       80.00 usec
PL2                          0.00 dB
PL12                        15.78 dB
PL13                        19.00 dB
PL2W                 9.74611950 W
PL12W                0.25753233 W
PL13W                0.12269637 W
SFO2               400.0416002 MHz
SI                          65536
SF                 100.5901380 MHz
WDW                            EM
SSB                             0
LB                           1.00 Hz
GB                              0
PC                           1.40
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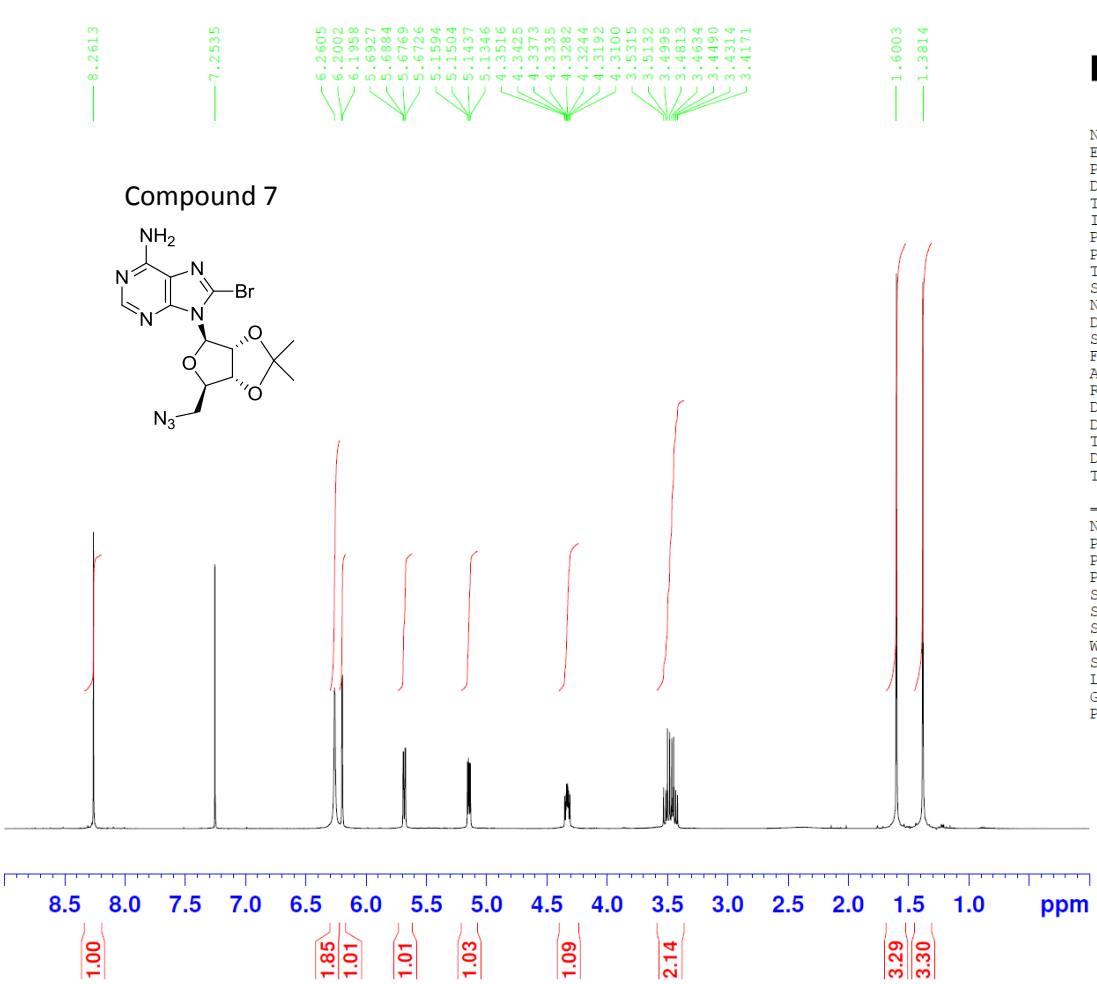


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PROCNO                          1
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PULPROG                     zg30
TD                         65536
SOLVENT                    CDCl3
NS                             16
DS                              2
SWH                     8223.685 Hz
FIDRES                  0.125483 Hz
AQ                     3.9846387 sec
RG                          80.6
DW                         60.800 usec
DE                         17.24 usec
TE                         298.0 K
D1                    1.00000000 sec
TD0                             1

======== CHANNEL f1 ========
NUC1                           1H
P1                         13.00 usec
PL1                         0.00 dB
PL1W                    9.74611950 W
SFO1                  400.0424704 MHz
SI                         65536
SF                    400.0399837 MHz
WDW                            EM
SSB                             0
LB                          0.20 Hz
GB                              0
PC                           1.00
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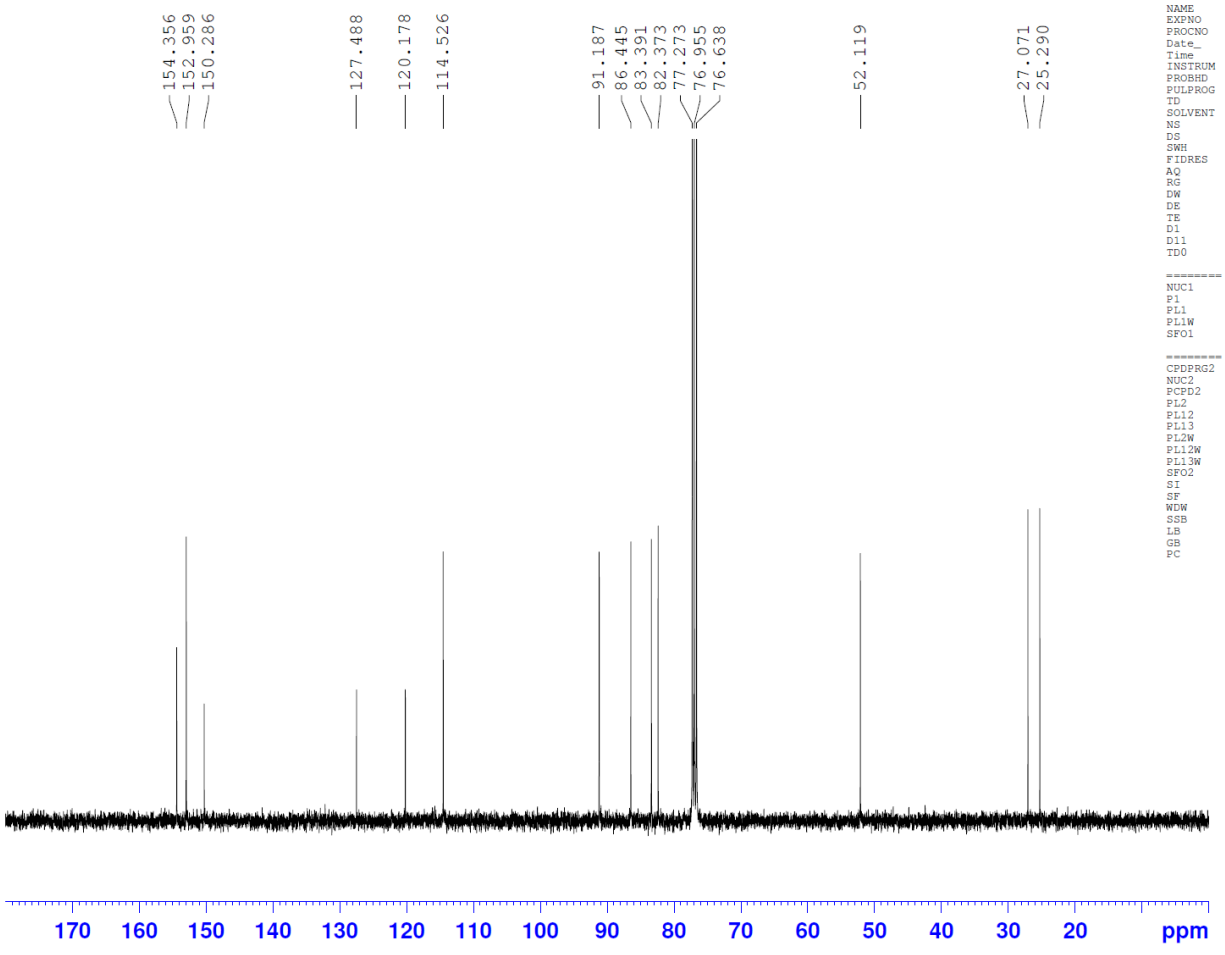


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PROCNO                          1
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PULPROG                  zgpg30
TD                         65536
SOLVENT                    CDCl3
NS                            512
DS                              4
SWH                    24038.461 Hz
FIDRES                  0.366798 Hz
AQ                     1.3631988 sec
RG                           2050
DW                         20.800 usec
DE                          6.50 usec
TE                         298.0 K
D1                    2.00000000 sec
D11                   0.03000000 sec
TD0                             1

======== CHANNEL f1 ========
NUC1                           13C
P1                          8.75 usec
PL1                        -2.00 dB
PL1W                   58.91986084 W
SFO1                  100.6001970 MHz

======== CHANNEL f2 ========
CPDPRG2                 waltz16
NUC2                           1H
PCPD2                      80.00 usec
PL2                         0.00 dB
PL12                       15.78 dB
PL13                       19.00 dB
PL2W                    9.74611950 W
PL12W                   0.25753233 W
PL13W                   0.12269637 W
SFO2                  400.0416002 MHz
SI                         65536
SF                    100.5901380 MHz
WDW                            EM
SSB                             0
LB                          1.00 Hz
GB                              0
PC                           1.40
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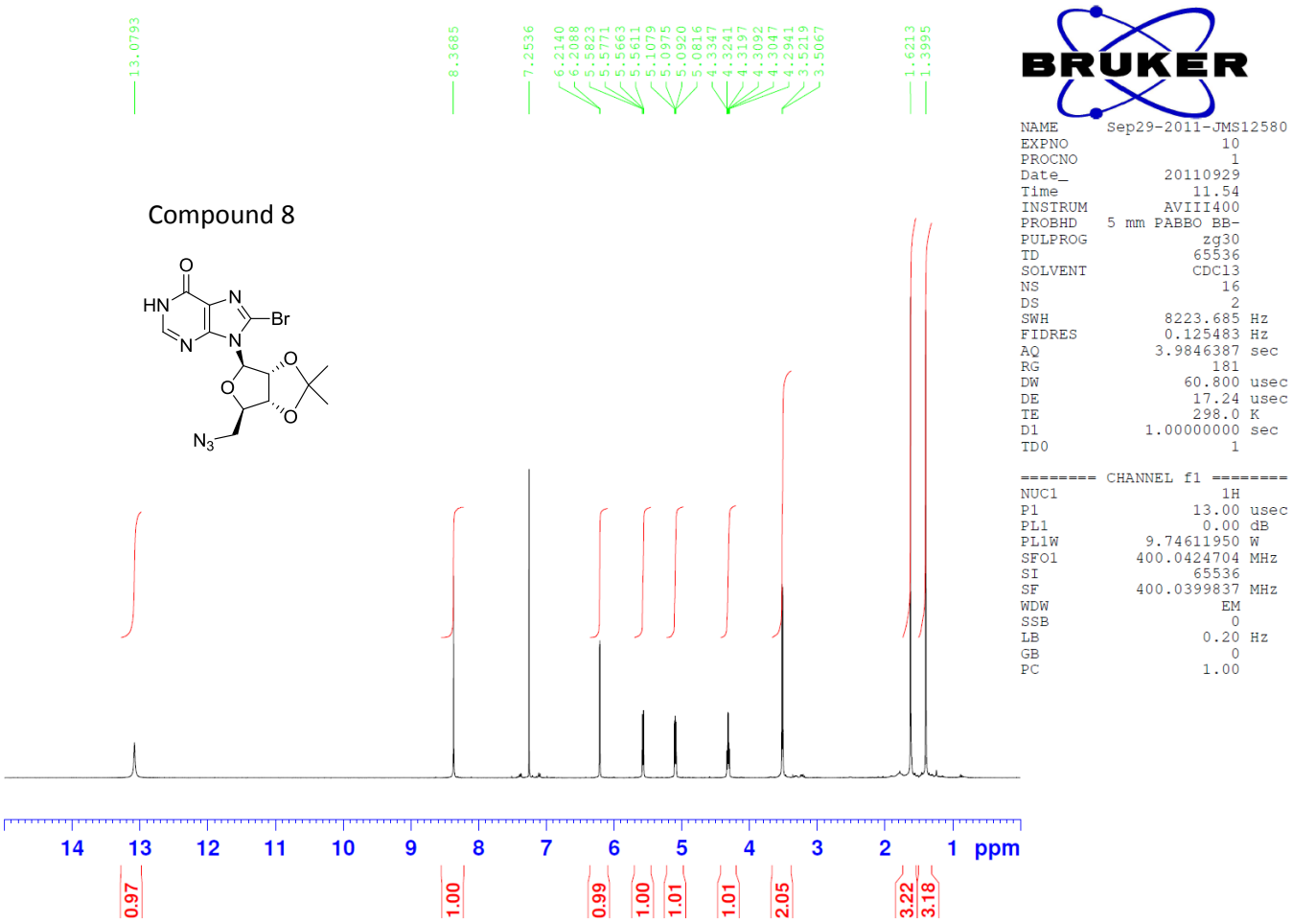
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4.3241
4.3197
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4.3047
4.2941
3.5219
3.5067
1.6213
1.3995
Compound 8
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Br
N
N
O
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N3
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PROCNO 1
Date_ 20110929
Time 11.54
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TD 65536
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SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 181
DW 60.800 usec
DE 17.24 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.00 usec
PL1 0.00 dB
PL1W 9.74611950 W
SFO1 400.0424704 MHz
SI 65536
SF 400.0399837 MHz
WDW EM
SSB 0
LB 0.20 Hz
GB 0
PC 1.00
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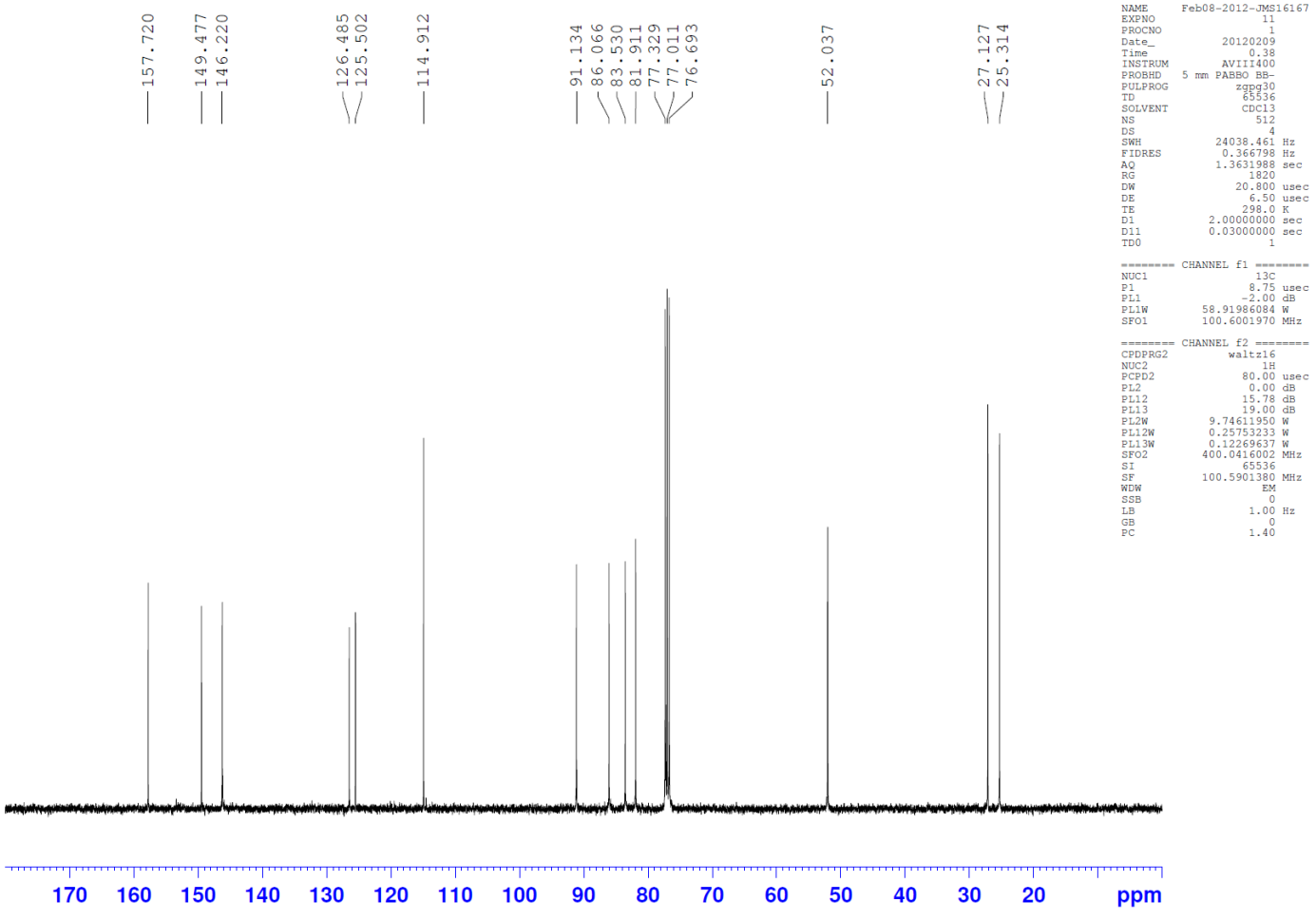
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27.127
25.314
NAME Feb08-2012-JMS16167
EXPNO 11
PROCNO 1
Date_ 20120209
Time 0.38
INSTRUM AVIII400
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 512
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631988 sec
RG 1820
DW 20.800 usec
DE 6.50 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.75 usec
PL1 -2.00 dB
PL1W 58.91986084 W
SFO1 100.6001970 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 0.00 dB
PL12 15.78 dB
PL13 19.00 dB
PL2W 9.74611950 W
PL12W 0.25753233 W
PL13W 0.12269637 W
SFO2 400.0416002 MHz
SI 65536
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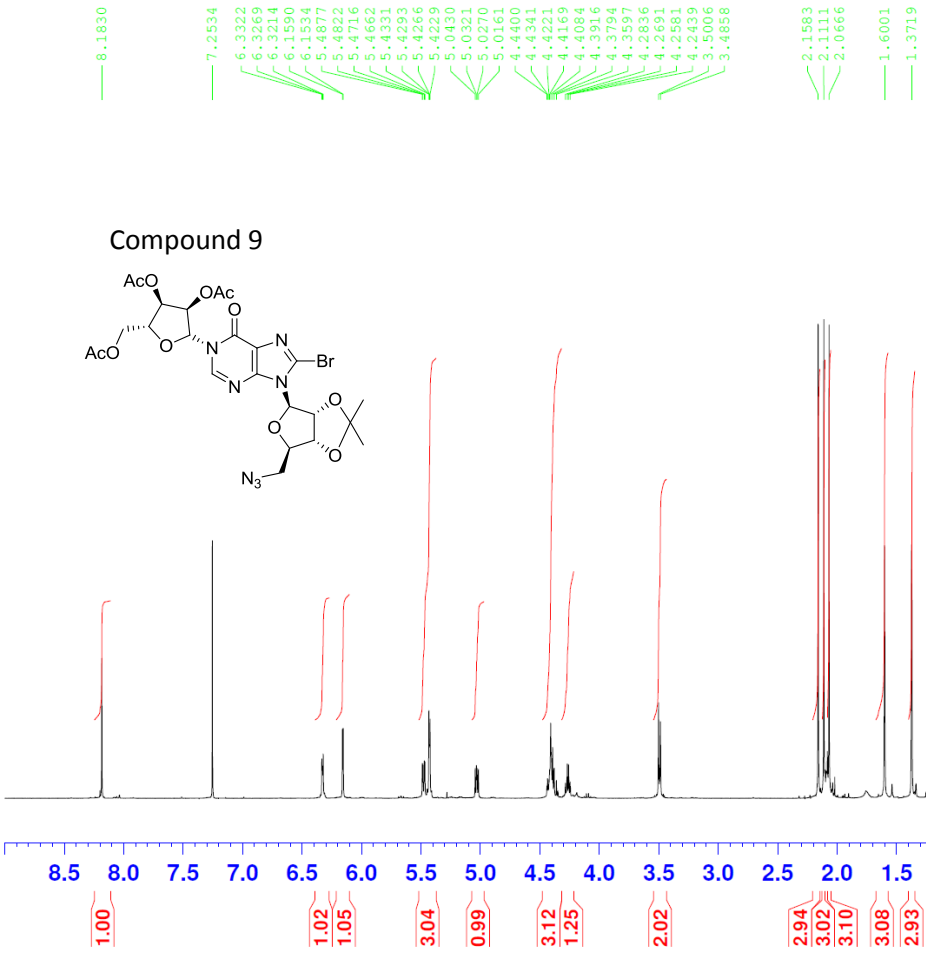
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

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PROCNO                        1
Date_                  20111005
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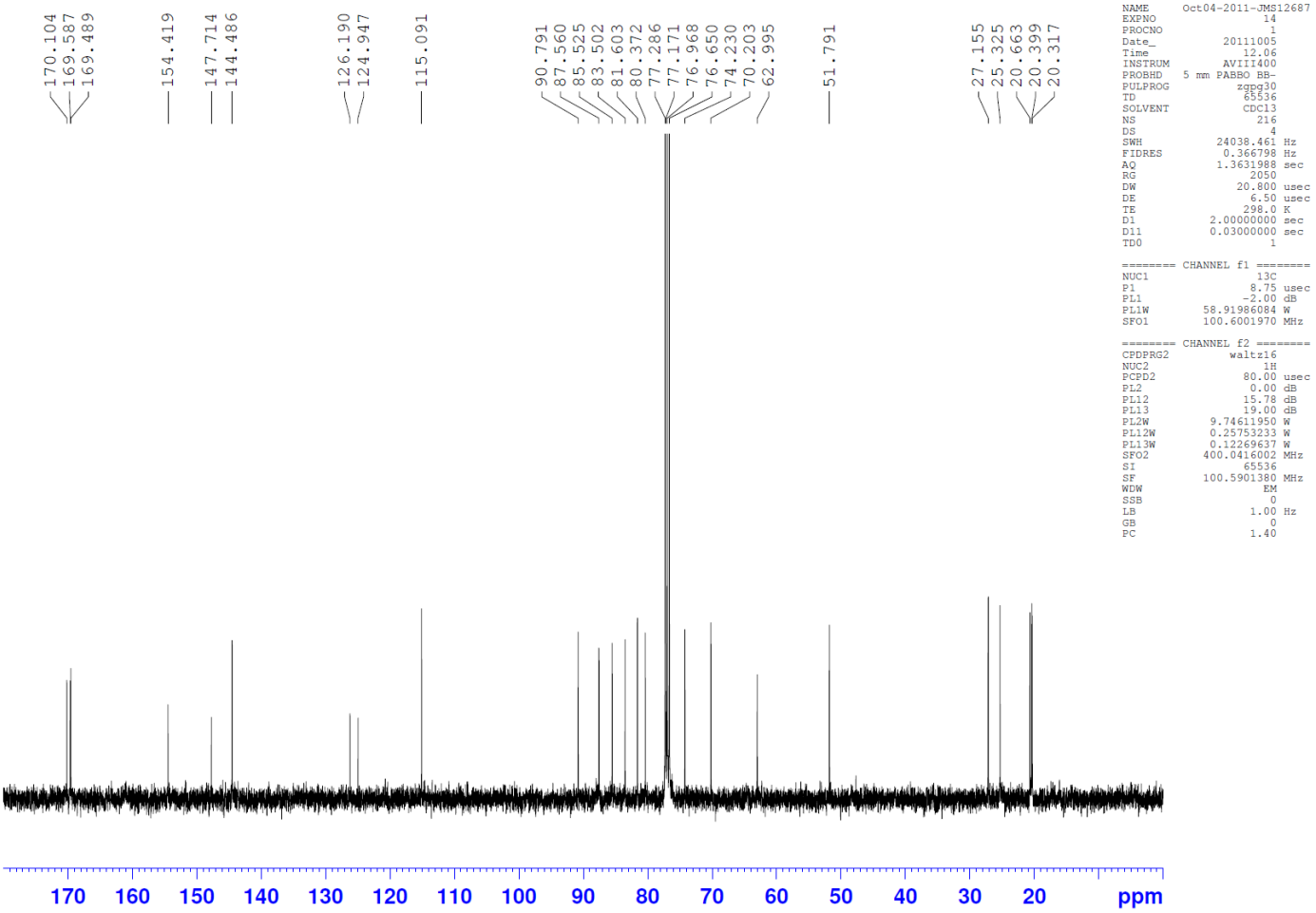
PULPROG                   zg30
TD                       65536
SOLVENT                  CDCl3
NS                           16
DS                            2
SWH                    8223.685 Hz
FIDRES                 0.125483 Hz
AQ                     3.9846387 sec
RG                         114
DW                      60.800 usec
DE                      17.24 usec
TE                      298.0 K
D1                   1.00000000 sec
TD0                           1

======== CHANNEL f1 ========
NUC1                         1H
P1                      13.00 usec
PL1                      0.00 dB
PL1W                 9.74611950 W
SFO1                400.0424704 MHz
SI                       65536
SF                  400.0399837 MHz
WDW                         EM
SSB                          0
LB                       0.20 Hz
GB                           0
PC                        1.00
```

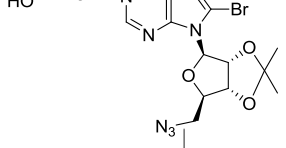



```
NAME        Oct04-2011-JMS12687
EXPNO                        14
PROCNO                        1
Date_                  20111005
Time                      12.06
INSTRUM                AVIII400
PROBHD    5 mm PABBO BB-
PULPROG                 zgpg30
TD                       65536
SOLVENT                  CDCl3
NS                          216
DS                            4
SWH                   24038.461 Hz
FIDRES                 0.366798 Hz
AQ                     1.3631988 sec
RG                         2050
DW                      20.800 usec
DE                       6.50 usec
TE                      298.0 K
D1                   2.00000000 sec
D11                  0.03000000 sec
TD0                           1

======== CHANNEL f1 ========
NUC1                        13C
P1                       8.75 usec
PL1                     -2.00 dB
PL1W                58.91986084 W
SFO1               100.6001970 MHz

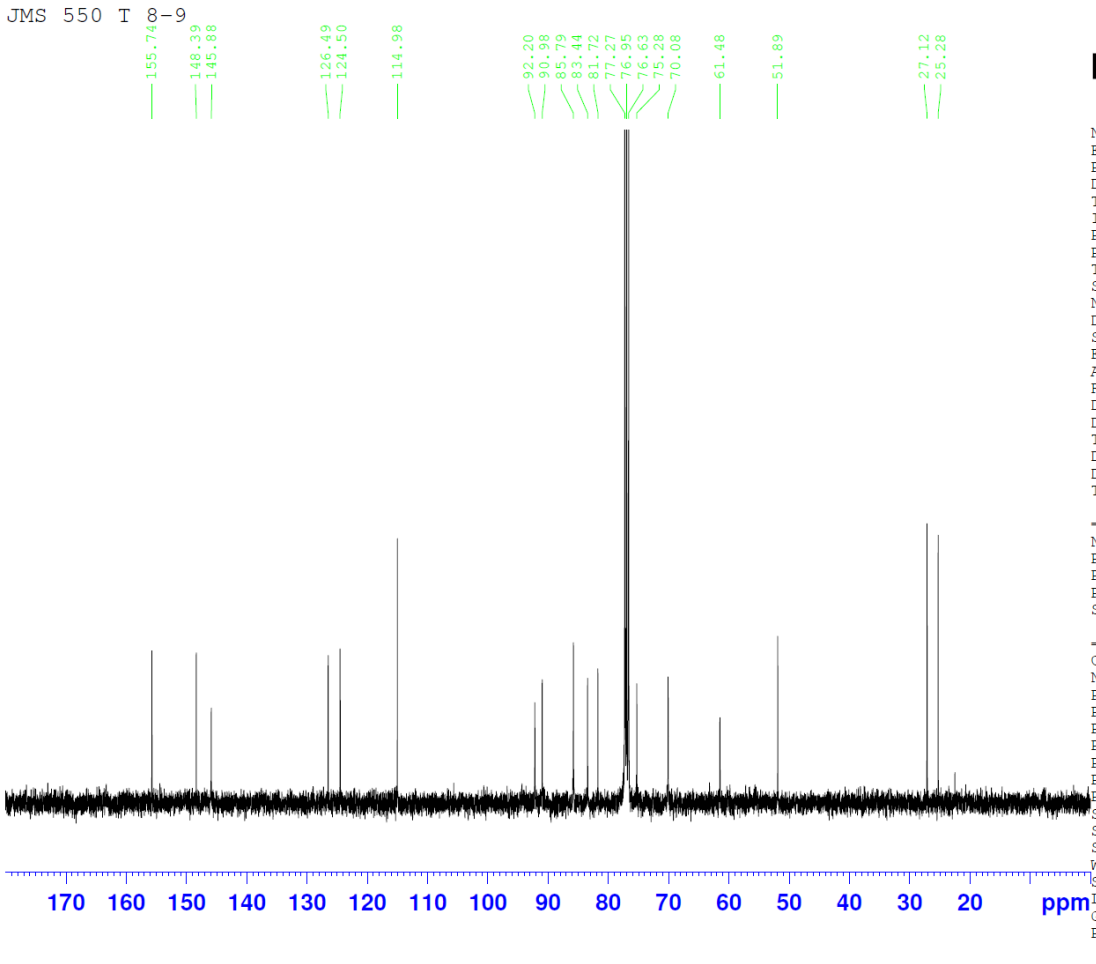
======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                         1H
PCPD2                   80.00 usec
PL2                      0.00 dB
PL12                    15.78 dB
PL13                    19.00 dB
PL2W                 9.74611950 W
PL12W                0.25753233 W
PL13W                0.12269637 W
SFO2               400.0416002 MHz
SI                       65536
SF                 100.5901380 MHz
WDW                         EM
SSB                          0
LB                       1.00 Hz
GB                           0
PC                        1.40
```

Compound 10




```
NAME          Oct26-2011-JMS18252
EXPNO                          10
PROCNO                          1
Date_                    20111027
Time                         8.14
INSTRUM                 AVIII400
PROBHD          5 mm PABBO BB-
PULPROG                      zg30
TD                          65536
SOLVENT                     CDCl3
NS                             16
DS                              2
SWH                    8223.685 Hz
FIDRES                 0.125483 Hz
AQ                     3.9846387 sec
RG                          90.5
DW                        60.800 usec
DE                        17.24 usec
TE                        298.0 K
D1                    1.00000000 sec
TD0                             1

======== CHANNEL f1 ========
NUC1                           1H
P1                        13.00 usec
PL1                        0.00 dB
PL1W                9.74611950 W
SFO1               400.0424704 MHz
SI                          65536
SF                 400.0399837 MHz
WDW                            EM
SSB                             0
LB                         0.20 Hz
GB                              0
PC                         1.00
```

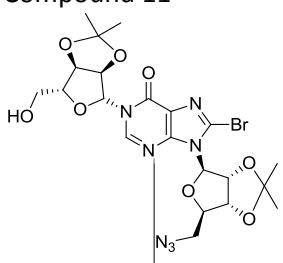



```
NAME          Oct07-2011-JMS12763
EXPNO                          11
PROCNO                          1
Date_                    20111007
Time                        23.00
INSTRUM                 AVIII400
PROBHD          5 mm PABBO BB-
PULPROG                    zgpg30
TD                          65536
SOLVENT                     CDCl3
NS                           1024
DS                              4
SWH                   24038.461 Hz
FIDRES                 0.366798 Hz
AQ                     1.3631988 sec
RG                           1820
DW                        20.800 usec
DE                         6.50 usec
TE                        298.0 K
D1                    2.00000000 sec
D11                   0.03000000 sec
TD0                             1

======== CHANNEL f1 ========
NUC1                          13C
P1                         8.75 usec
PL1                       -2.00 dB
PL1W               58.91986084 W
SFO1              100.6001970 MHz

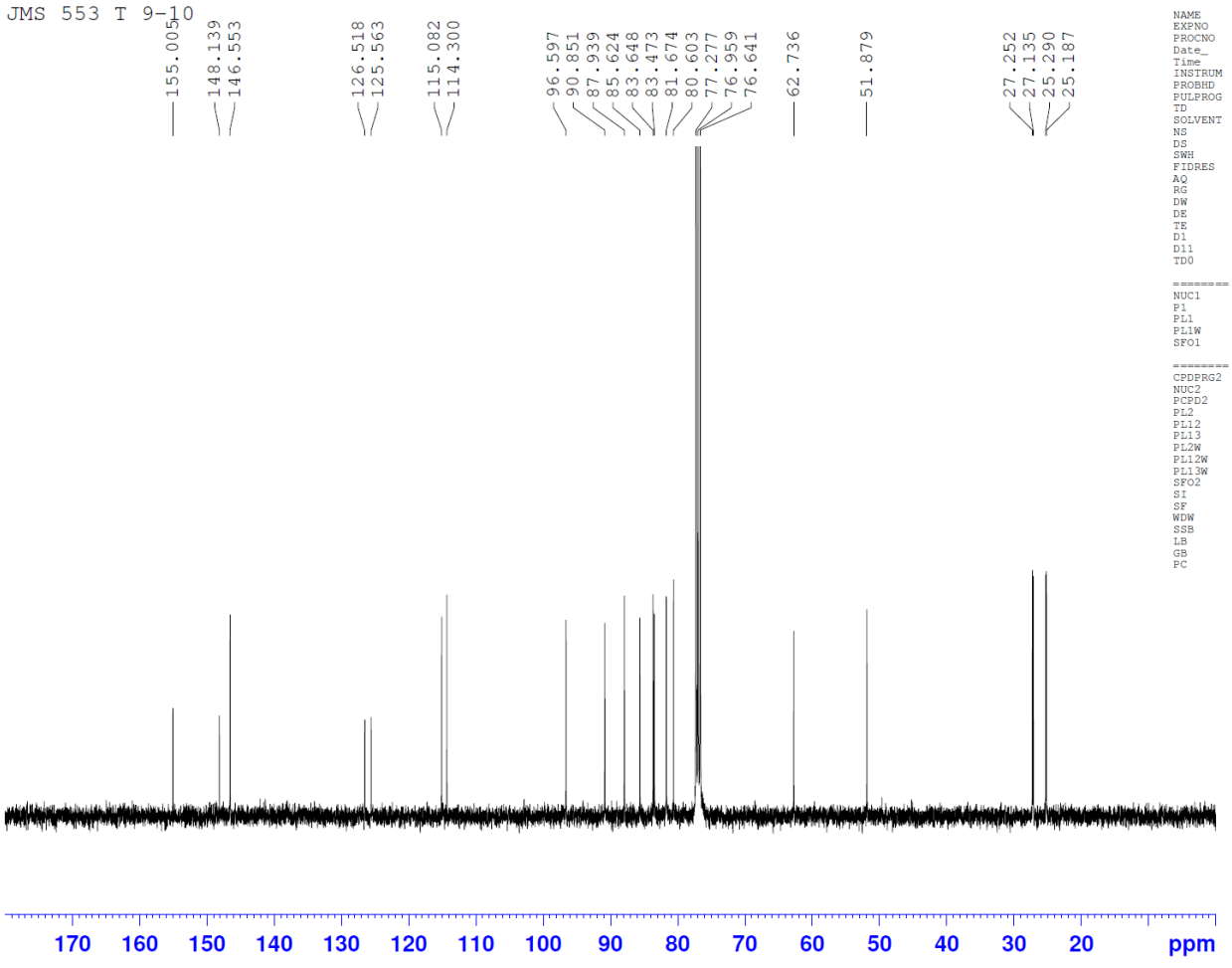
======== CHANNEL f2 ========
CPDPRG2                 waltz16
NUC2                           1H
PCPD2                     80.00 usec
PL2                        0.00 dB
PL12                      15.78 dB
PL13                      19.00 dB
PL2W                9.74611950 W
PL12W               0.25753233 W
PL13W               0.12269637 W
SFO2               400.0416002 MHz
SI                          65536
SF                 100.5901380 MHz
WDW                            EM
SSB                             0
LB                         1.00 Hz
GB                              0
PC                         1.40
```

Compound 11




```
NAME          Oct10-2011-JMS12788
EXPNO                          11
PROCNO                          1
Date_                    20111010
Time                        16.36
INSTRUM                  AVIII400
PROBHD    5 mm PABBO BB-
PULPROG                     zg30
TD                         65536
SOLVENT                    CDCl3
NS                             16
DS                              2
SWH                     8223.685 Hz
FIDRES                  0.125483 Hz
AQ                     3.9846387 sec
RG                            144
DW                         60.800 usec
DE                         17.24 usec
TE                         298.0 K
D1                   1.00000000 sec
TD0                             1

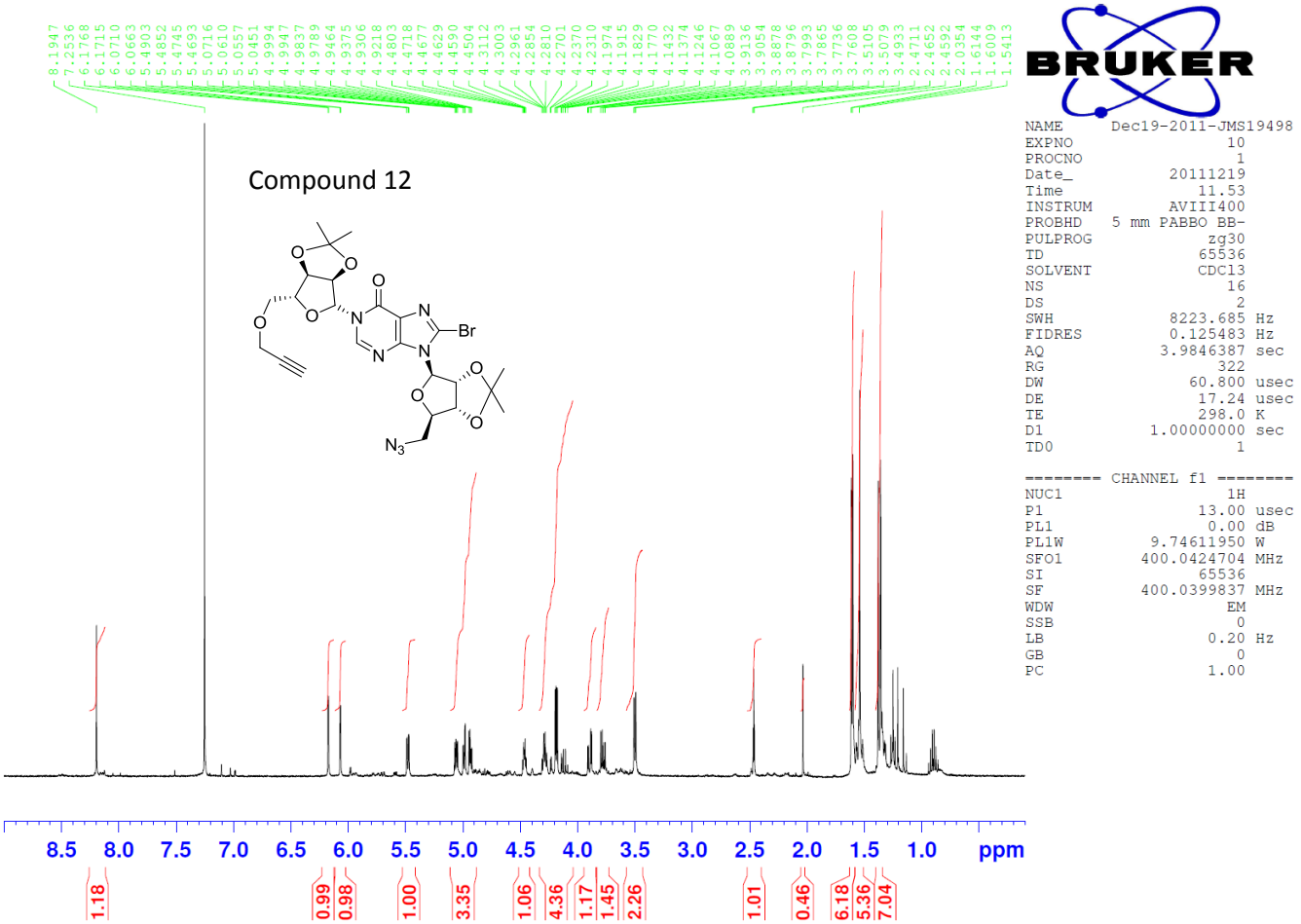
======== CHANNEL f1 ========
NUC1                           1H
P1                         13.00 usec
PL1                         0.00 dB
PL1W                 9.74611950 W
SFO1                400.0424704 MHz
SI                         65536
SF                  400.0399837 MHz
WDW                           EM
SSB                            0
LB                          0.20 Hz
GB                             0
PC                          1.00
```




```
NAME          Oct10-2011-JMS12788
EXPNO                          12
PROCNO                          1
Date_                    20111011
Time                         7.04
INSTRUM                  AVIII400
PROBHD    5 mm PABBO BB-
PULPROG                  zgpg30
TD                         65536
SOLVENT                    CDCl3
NS                            512
DS                              4
SWH                    24038.461 Hz
FIDRES                  0.366798 Hz
AQ                     1.3631988 sec
RG                           2050
DW                         20.800 usec
DE                          6.50 usec
TE                         298.0 K
D1                   2.00000000 sec
D11                  0.03000000 sec
TD0                             1

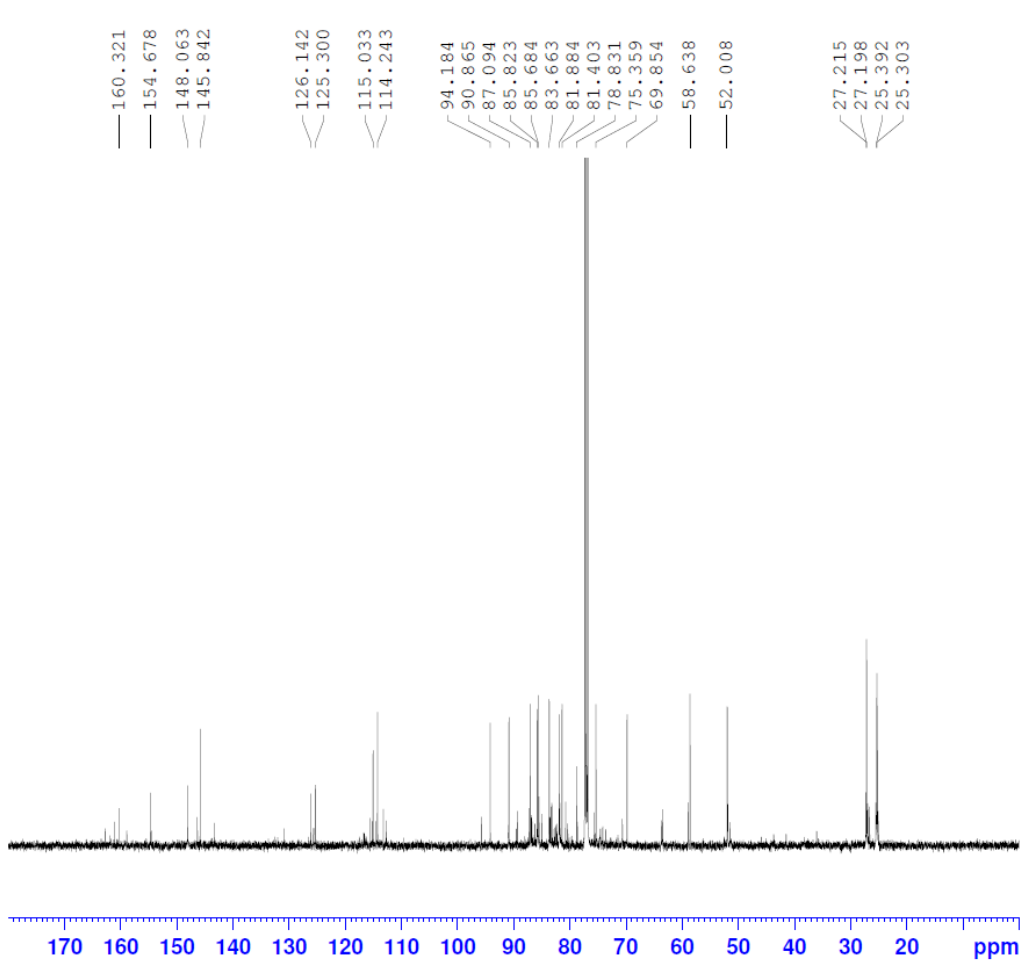
======== CHANNEL f1 ========
NUC1                           13C
P1                          8.75 usec
PL1                        -2.00 dB
PL1W                58.91986084 W
SFO1               100.6001970 MHz

======== CHANNEL f2 ========
CPDPRG2                 waltz16
NUC2                           1H
PCPD2                      80.00 usec
PL2                         0.00 dB
PL12                       15.78 dB
PL13                       19.00 dB
PL2W                 9.74611950 W
PL12W                0.25753233 W
PL13W                0.12269637 W
SFO2               400.0416002 MHz
SI                         65536
SF                 100.5901380 MHz
WDW                           EM
SSB                            0
LB                          1.00 Hz
GB                             0
PC                          1.40
```




```
NAME          Dec19-2011-JMS19498
EXPNO                          10
PROCNO                          1
Date_                    20111219
Time                        11.53
INSTRUM                  AVIII400
PROBHD     5 mm PABBO BB-
PULPROG                      zg30
TD                          65536
SOLVENT                     CDCl3
NS                             16
DS                              2
SWH                      8223.685 Hz
FIDRES                   0.125483 Hz
AQ                       3.9846387 sec
RG                            322
DW                         60.800 usec
DE                         17.24 usec
TE                         298.0 K
D1                      1.00000000 sec
TD0                             1

======== CHANNEL f1 ========
NUC1                           1H
P1                         13.00 usec
PL1                         0.00 dB
PL1W                 9.74611950 W
SFO1                 400.0424704 MHz
SI                          65536
SF                   400.0399837 MHz
WDW                            EM
SSB                             0
LB                          0.20 Hz
GB                              0
PC                           1.00
```

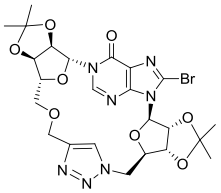



```
NAME          Oct05-2012-JMS743T12
EXPNO                          11
PROCNO                          1
Date_                    20121005
Time                        12.27
INSTRUM                     spect
PROBHD     5 mm PABBO BB-
PULPROG                   zgpg30
TD                          65536
SOLVENT                     CDCl3
NS                           1024
DS                              4
SWH                  29761.904 Hz
FIDRES                   0.454131 Hz
AQ                       1.1010548 sec
RG                           2050
DW                         16.800 usec
DE                          8.43 usec
TE                         298.0 K
D1                      2.00000000 sec
D11                     0.03000000 sec
TD0                             1

======== CHANNEL f1 ========
NUC1                          13C
P1                          9.50 usec
PL1                        -0.51 dB
PL1W                99.92730713 W
SFO1                125.7703643 MHz

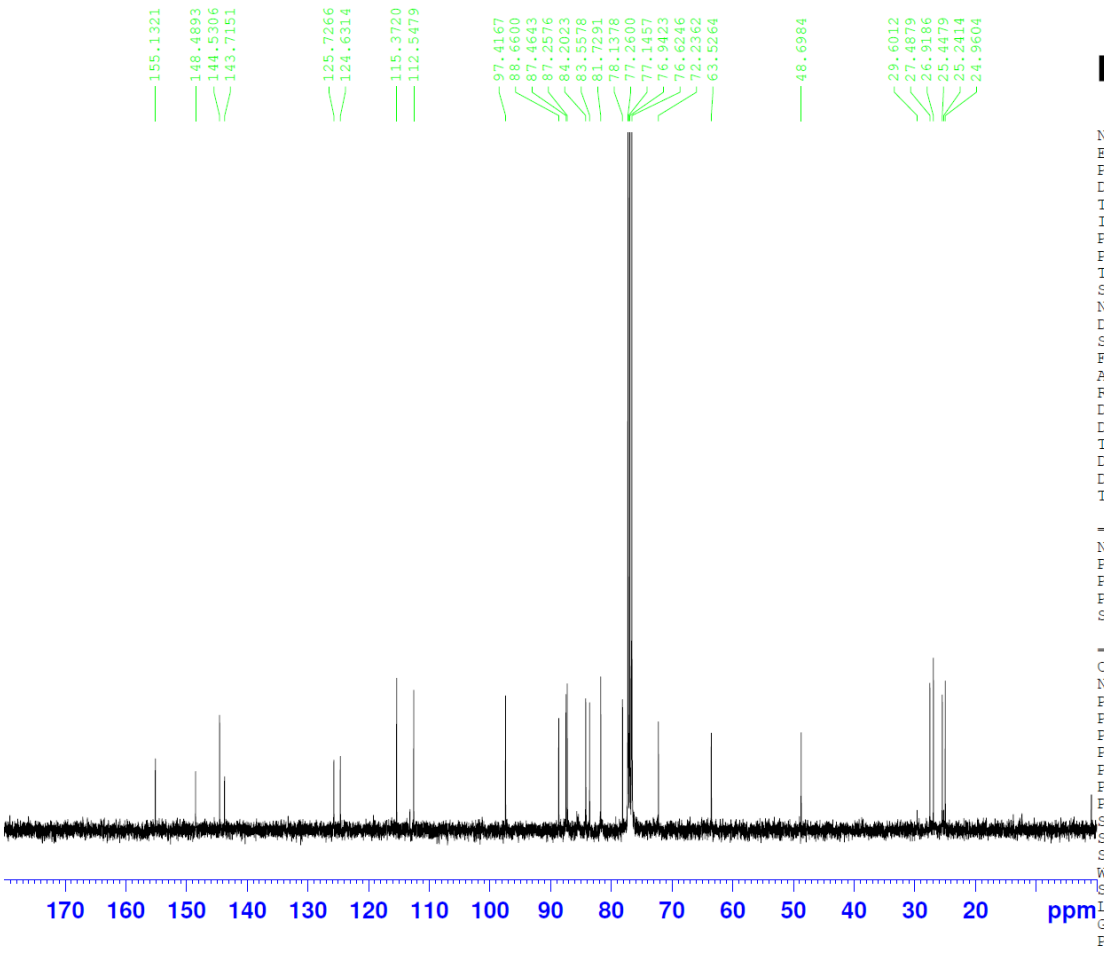
======== CHANNEL f2 ========
CPDPRG2                  waltz16
NUC2                           1H
PCPD2                      80.00 usec
PL2                        -0.12 dB
PL12                       17.94 dB
PL13                       21.00 dB
PL2W                19.35150909 W
PL12W                0.30249262 W
PL13W                0.14952536 W
SFO2                500.1320005 MHz
SI                          32768
SF                  125.7577890 MHz
WDW                            EM
SSB                             0
LB                          1.00 Hz
GB                              0
PC                           1.40
```

Compound 13




```
NAME        Jan23-2012-JMS15903
EXPNO                        10
PROCNO                        1
Date_                  20120123
Time                      14.52
INSTRUM                AVIII400
PROBHD    5 mm PABBO BB-
PULPROG                   zg30
TD                       65536
SOLVENT                  CDC13
NS                          16
DS                           2
SWH                   8223.685 Hz
FIDRES                0.125483 Hz
AQ                    3.9846387 sec
RG                         161
DW                      60.800 usec
DE                      17.24 usec
TE                      300.0 K
D1                  1.00000000 sec
TD0                          1

======== CHANNEL f1 ========
NUC1                        1H
P1                       13.00 usec
PL1                       0.00 dB
PL1W                9.74611950 W
SFO1               400.0424704 MHz
SI                       65536
SF                 400.0399837 MHz
WDW                         EM
SSB                          0
LB                        0.20 Hz
GB                           0
PC                        1.00
```



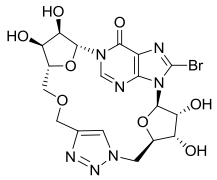

```
NAME        Jan23-2012-JMS15903
EXPNO                        11
PROCNO                        1
Date_                  20120123
Time                      20.03
INSTRUM                AVIII400
PROBHD    5 mm PABBO BB-
PULPROG                 zgpg30
TD                       65536
SOLVENT                  CDC13
NS                        1024
DS                           4
SWH                  24038.461 Hz
FIDRES                0.366798 Hz
AQ                    1.3631988 sec
RG                        1820
DW                      20.800 usec
DE                       6.50 usec
TE                      300.0 K
D1                  2.00000000 sec
D11                 0.03000000 sec
TD0                          1

======== CHANNEL f1 ========
NUC1                       13C
P1                        8.75 usec
PL1                      -2.00 dB
PL1W               58.91986084 W
SFO1              100.6001970 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                        1H
PCPD2                    80.00 usec
PL2                       0.00 dB
PL12                     15.78 dB
PL13                     19.00 dB
PL2W                9.74611950 W
PL12W               0.25753233 W
PL13W               0.12269637 W
SFO2               400.0416002 MHz
SI                       65536
SF                 100.5901380 MHz
WDW                         EM
SSB                          0
LB                        1.00 Hz
GB                           0
PC                        1.40
```

JMS 617

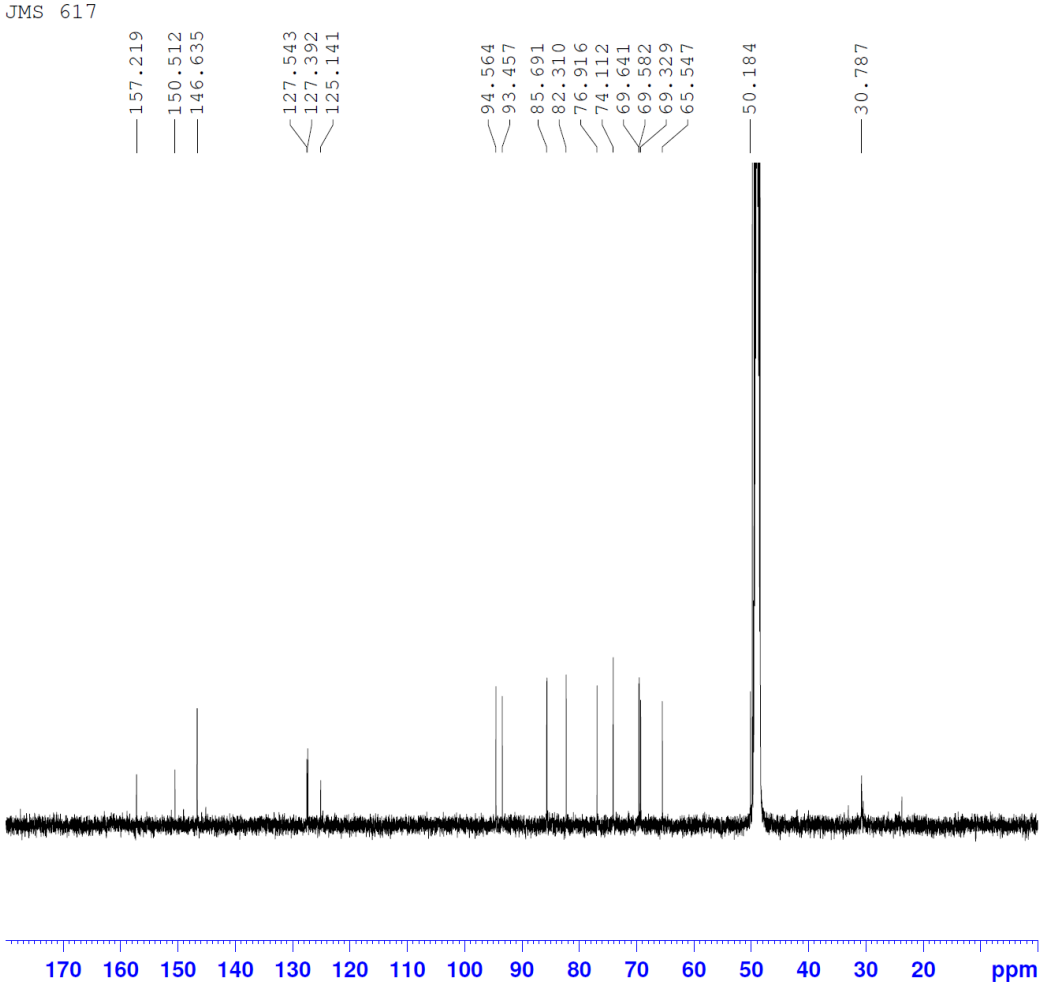
Compound 14




```
NAME        Dec22-2011-JMS617
EXPNO                  10
PROCNO                  1
Date_            20111222
Time                13.04
INSTRUM             spect
PROBHD    5 mm PABBO BB-
PULPROG              zg30
TD                  65536
SOLVENT              MeOD
NS                    128
DS                      0
SWH           10330.578 Hz
FIDRES         0.157632 Hz
AQ            3.1719923 sec
RG                    161
DW               48.400 usec
DE                6.50 usec
TE               293.3 K
D1            2.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                 10.30 usec
PL1                -0.12 dB
PL1W         19.35150909 W
SFO1         500.1330885 MHz
SI                  32768
SF           500.1300139 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

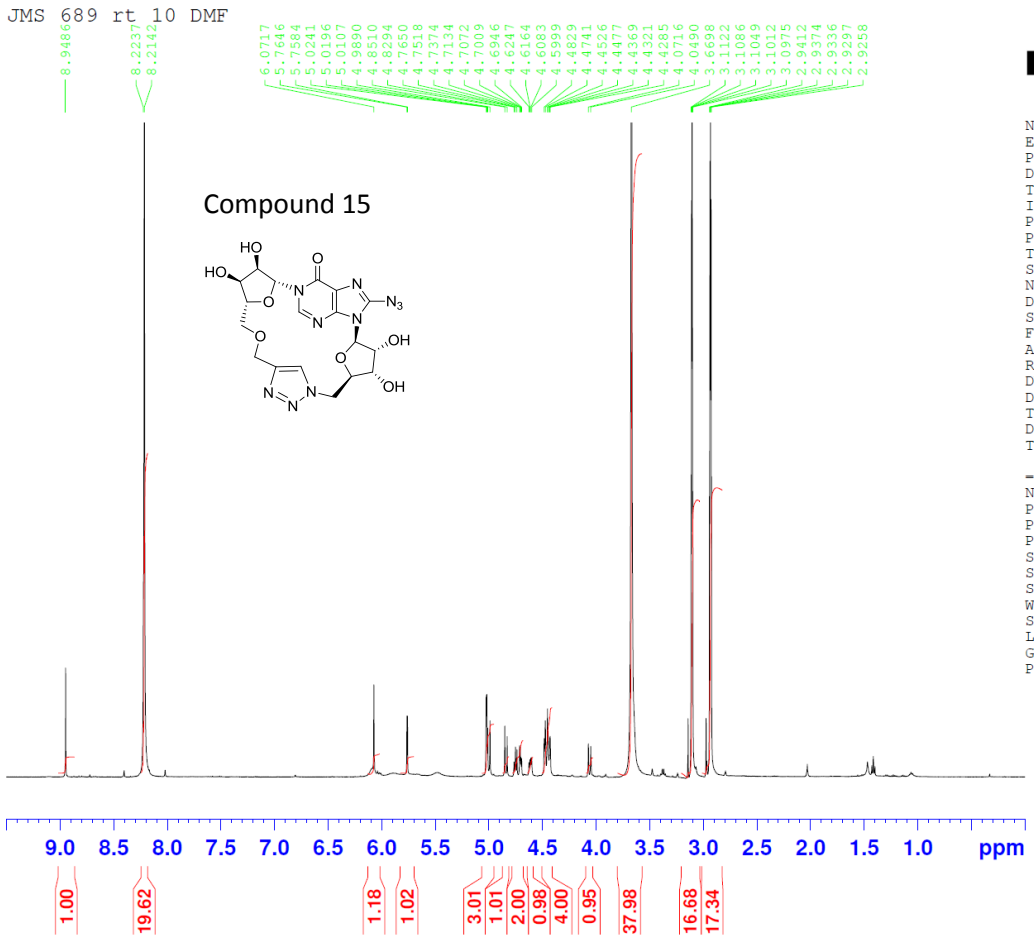
JMS 617




```
NAME        Dec22-2011-JMS61
EXPNO                  11
PROCNO                  1
Date_            20111223
Time                10.21
INSTRUM             spect
PROBHD    5 mm PABBO BB-
PULPROG           zgpg30
TD                  65536
SOLVENT              MeOD
NS                  40960
DS                      4
SWH           29761.904 H
FIDRES         0.454131 H
AQ            1.1010548 s
RG                   2050
DW               16.800 u
DE                8.43 u
TE               293.1 K
D1            2.00000000 s
D11           0.03000000 s
TD0                     1

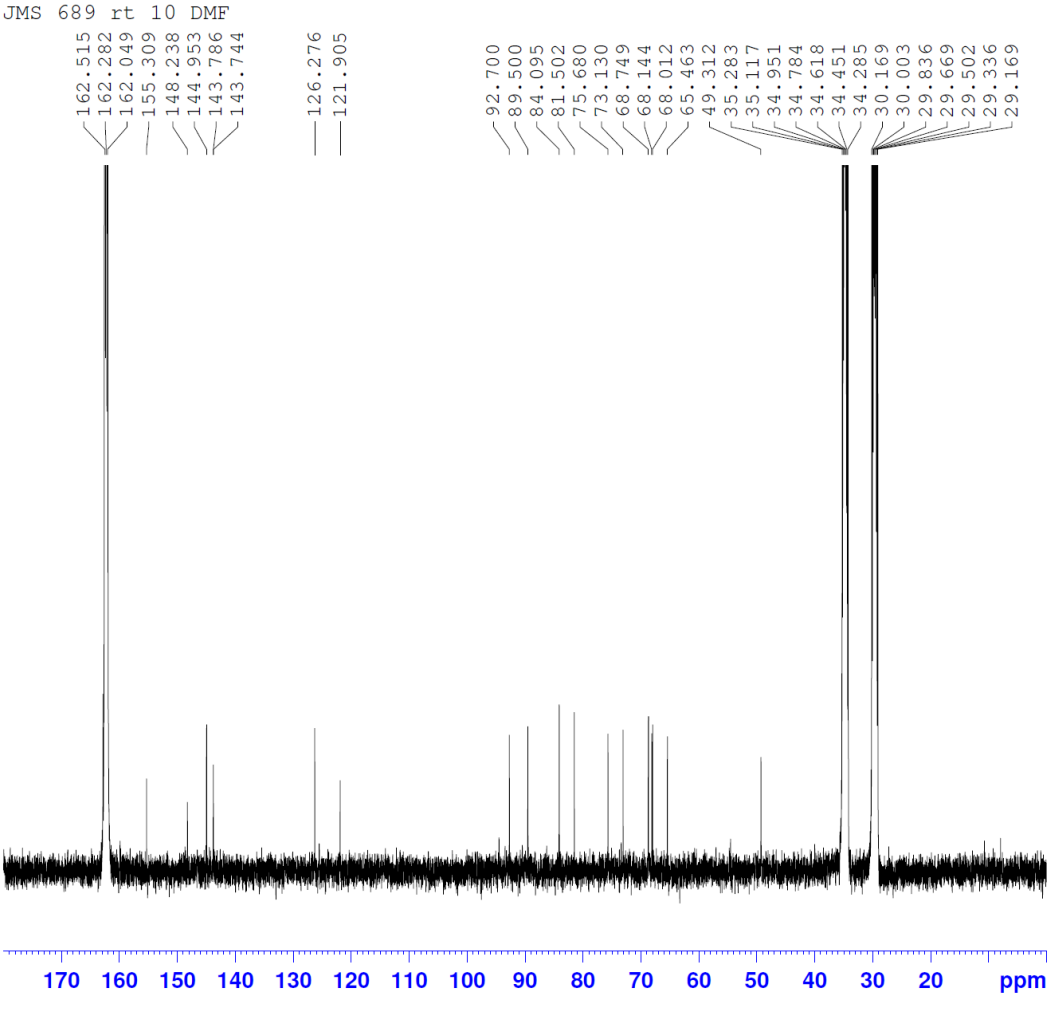
======== CHANNEL f1 =====
NUC1                  13C
P1                  9.50 u
PL1                -0.51 d
PL1W         99.92730713 W
SFO1         125.7703643 M

======== CHANNEL f2 =====
CPDPRG2          waltz16
NUC2                   1H
PCPD2              80.00 u
PL2                -0.12 d
PL12               17.94 d
PL13               21.00 d
PL2W         19.35150909 W
PL12W         0.30249262 W
PL13W         0.14952536 W
SFO2         500.1320005 M
SI                  32768
SF           125.7576104 M
WDW                   EM
SSB                    0
LB                  1.00 H
GB                     0
PC                  1.40
```




```
NAME      JMS 689 rt 10 DMF
EXPNO                    20
PROCNO                    1
Date_              20120430
Time                  16.35
INSTRUM               spect
PROBHD    5 mm PABBO BB-
PULPROG                zg30
TD                    65536
SOLVENT                 DMF
NS                      128
DS                        2
SWH              10330.578 Hz
FIDRES            0.157632 Hz
AQ               3.1719923 sec
RG                      256
DW                 48.400 usec
DE                 13.94 usec
TE                   297.9 K
D1              1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                 10.30 usec
PL1                 -0.12 dB
PL1W          19.35150909 W
SFO1          500.1330885 MHz
SI                    32768
SF            500.1300000 MHz
WDW                      EM
SSB                       0
LB                 0.30 Hz
GB                        0
PC                     1.00
```

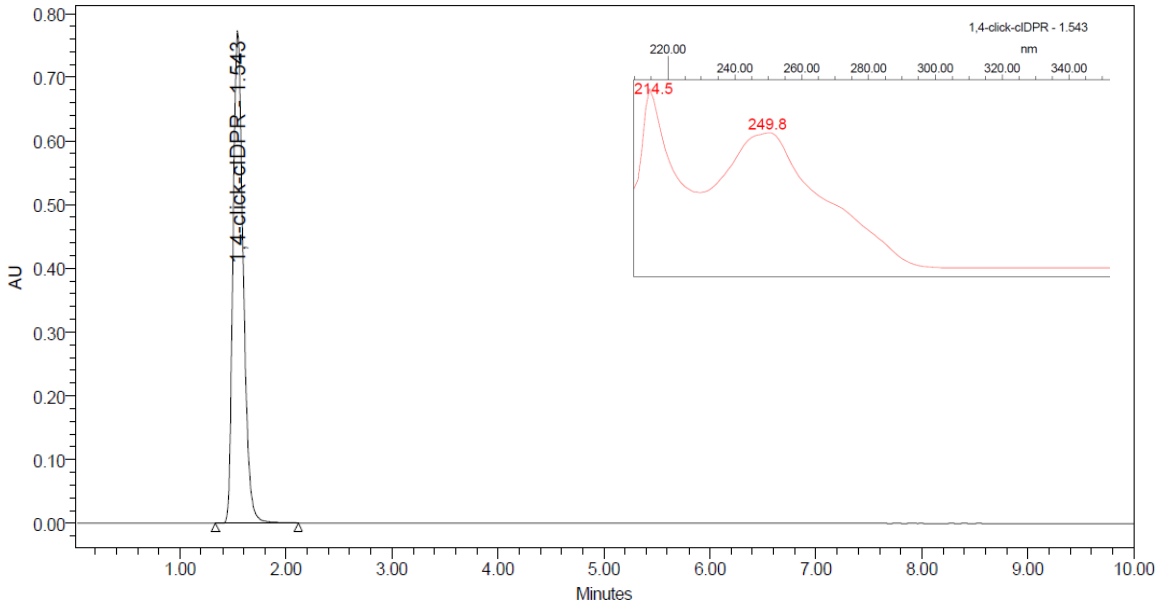



```
NAME      JMS 689 rt 10 DMI
EXPNO                    24
PROCNO                    1
Date_              20120501
Time                   8.12
INSTRUM               spect
PROBHD    5 mm PABBO BB-
PULPROG             zgpg30
TD                    65536
SOLVENT                 DMF
NS                    16064
DS                        4
SWH              29761.904 H
FIDRES            0.454131 H
AQ               1.1010548 s
RG                     2050
DW                 16.800 u
DE                  8.43 u
TE                   298.0 K
D1              2.00000000 s
D11             0.03000000 s
TD0                       1

======== CHANNEL f1 ======
NUC1                    13C
P1                  9.50 u
PL1                -0.51 d
PL1W          99.92730713 W
SFO1         125.7703643 M

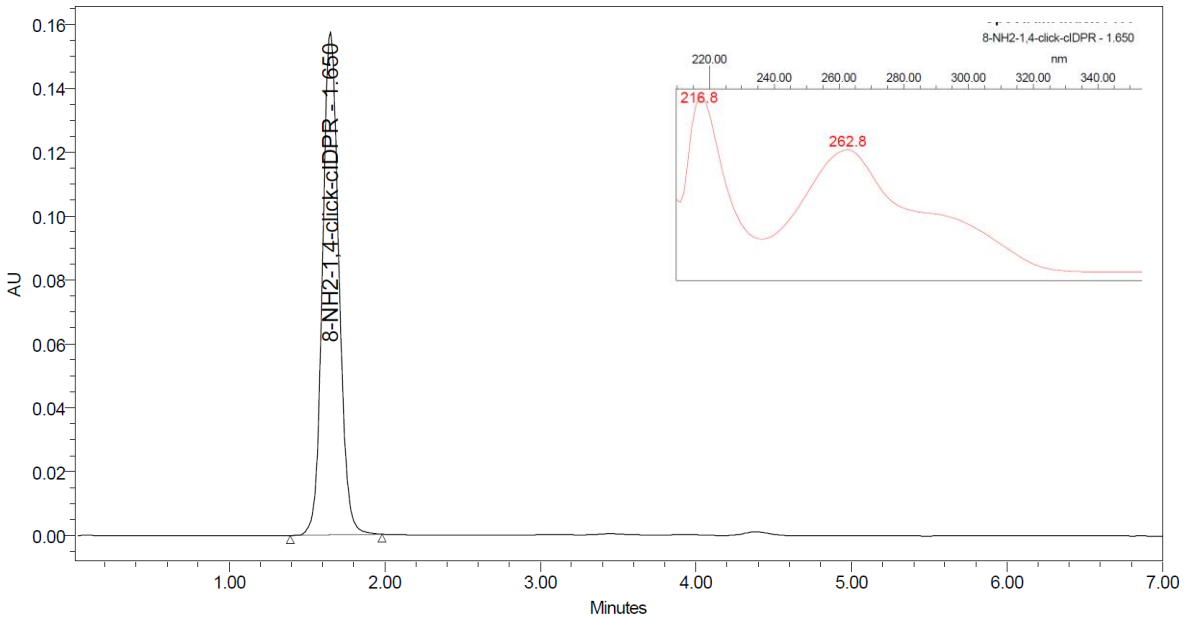
======== CHANNEL f2 ======
CPDPRG2           waltz16
NUC2                     1H
PCPD2               80.00 u
PL2                 -0.12 d
PL12                17.94 d
PL13                21.00 d
PL2W          19.35150909 W
PL12W          0.30249262 W
PL13W          0.14952536 W
SFO2          500.1320005 M
SI                    32768
SF           125.7577890 M
WDW                      EM
SSB                       0
LB                 1.00 H
GB                        0
PC                     1.40
```

HPLC trace for compound **3**



	Peak Name	RT	Area	% Area	Height
1	1,4-click-cIDPR	1.543	5164776	100.00	772677

HPLC trace for compound **4**



	Peak Name	RT	Area	% Area	Height
1	8-NH2-1,4-click-cIDPR	1.650	1135929	100.00	157412