Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

On the Reactivity of mRNA Cap0: C–H Oxidative Addition of 7-methylguanosine to Pt^0 and Base Pairing Studies

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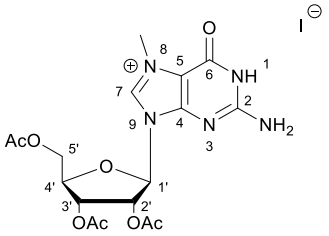
1. Synthetic Procedure

1.1. General considerations

The syntheses of complexes were carried out under an inert atmosphere of N_2 using Schlenk techniques. All ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra were recorded at room temperature on Bruker spectrometers (400 MHz and 800 MHz). Chemical shifts are reported as δ-values in ppm relative to the deuterated solvent peaks: DMSO-d_6 (δH: 2.50; δC: 39.52) and DMF-d_7 (δH: 2.75; δC: 29.76). 2',3',5'-Tri-*O*-acetylguanosine (**MeG$_{Ac}$**),[1] 2',3',5'-tri-*O*-acetylcytidine (**Cy**)[2], 7-methylguanosinium iodide (**7-MeG**)[3] and complex **4**[4] were synthesized according to reported procedures. The syntheses of 7-methyl-2',3',5'-tri-*O*-acetylguanosinium iodide (**7-MeG$_{Ac}$**) and 7,9-dimethylguaninium iodide (**7,9-DMG**) were adapted from previously published procedures.[5,6] All other reagents were purchased from commercial sources and used as received. Elemental analyses were performed by the UniMass Laboratory at Instituto de Tecnologia Química e Biológica, Portugal, using a Leco TruSpec Micro Elemental Analyzer. Mass Spectroscopy measurements were by the UniMass Laboratory at Instituto de Tecnologia Química e Biológica, Portugal.

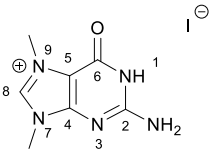
1.2. Compound 7-MeG$_{Ac}$



2',3',5'-Tri-*O*-acetylguanosine (500 mg, 1.22 mmol) was suspended in *N*,*N*-dimethylacetamide (6 mL) and methyl iodide (228 µL, 3.66 mmol) was added, and the reaction mixture was stirred at room temperature for 24h. Addition of Et_2O (200 mL) resulted in the appearance of an oily solid and stirring was kept for ca. 1h. The liquid was then removed, the oil was diluted in MeOH, 200 mL of Et_2O were added and the suspension was stirred for ca. 6h. This process was repeated 2 more times to yield **7-MeG$_{Ac}$** as a light-yellow solid (595 mg, 88%).

^{1}H NMR (400 MHz, DMSO-d_6): δ 11.79 (s, 1H, NH), 9.35 (s, 1H, H-8), 7.24 (br s, 2H, NH_2), 6.18 (d, 1H, H-1', $^3J_{H\text{-}1',\ H\text{-}2'}$ = 4.4 Hz), 5.74 (dd, 1H, H-2', $^3J_{H\text{-}2',\ H\text{-}1'}$ = 4.4 Hz, $^3J_{H\text{-}2',\ H\text{-}3'}$ = 6.0 Hz), 5.54 (dd, H-3', 1H, $^3J_{H\text{-}3',\ H\text{-}2'}$ = 6.0 Hz, $^3J_{H\text{-}3',\ H\text{-}4'}$ = 5.6 Hz), 4.46 (dd, 1H, H-4', $^3J_{H\text{-}4',\ H\text{-}3'}$ = 5.6 Hz, $^3J_{H\text{-}4',\ H\text{-}5'a}$ = 3.6 Hz, $^2J_{H\text{-}4',\ H\text{-}5'b}$ = 6.0 Hz), 4.38 (dd, 1H, H-5'a, $^3J_{H\text{-}5'a,\ H\text{-}4'}$ = 3.6 Hz, $^2J_{H\text{-}5'a,\ H\text{-}5'b}$ = 12.4 Hz), 4.30 (dd, 1H, H-5'b, $^3J_{H\text{-}5'b,\ H\text{-}4'}$ = 6.0 Hz, $^2J_{H\text{-}5'b,\ H\text{-}5'a}$ = 12.4 Hz), 4.02 (s, 3H, 7-NCH_3), 2.10 (s, 3H, CH_3CO), 2.09 (s, 3H, CH_3CO), 2.04 (s, 3H, CH_3CO) ppm.

1.3. Compound 7,9-DMG



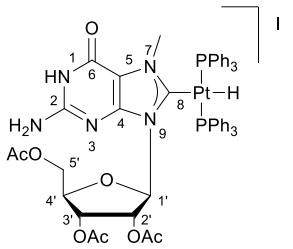
Guanine (1.0 g, 6.6 mmol) was suspended in *N*,*N*-dimethylacetamide (30 mL) and methyl iodide (1.2 mL, 20 mmol) was added, and the solution was stirred at 90 °C for 24h. After cooling-down, addition of Et_2O (200 mL) resulted in the appearance of an oily solid. The reaction mixture was stirred for 6h. The liquid was then removed, 200 mL of Et_2O were added and the suspension was stirred for another 6h. After filtration, the solid was isolated and recrystallized from hot methanol to yield **7,9-DMG** as yellow needles (509 mg, 25%).

^{1}H NMR (400 MHz, DMSO-d_6): δ 11.55 (s, 1H, NH), 9.19 (s, 1H, H-8), 7.11 (br s, 2H, NH_2), 3.97 (s, 3H, 7-NCH_3), 3.68 (s, 3H, 9-NCH_3) ppm.

^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ = 155.5 (C-2), 153.4 (C-6), 149.9 (C-4), 138.5 (C-8), 107.0 (C-5), 35.4 (7-NCH_3), 31.3 (9-NCH_3) ppm.

FTMS–ESI (m/z): $[M + H]^+$ calc. for $C_7H_{10}N_5O$ 180.08799; Found 180.08792.

1.4. Complex 1



Method A: Compound **7-MeG$_{Ac}$** (82.5 mg, 0.15 mmol) and $Pt(PPh_3)_4$ (186 mg, 0.15 mmol) were suspended in degassed toluene (8 mL) and stirred at 100 °C for 16h, after which the formation of a yellow precipitate was observed. The precipitate was filtered and washed with Et_2O (20 mL), and dried under air. The solid was recrystallized from DCM/Et_2O to yield **1** (107 mg, 56%).

Method B: Compound **7-MeG$_{Ac}$** (91.4 mg, 0.17 mmol) and $Pt(PPh_3)_4$ (206 mg, 0.17 mmol) were suspended in degassed DMF (4 mL) and stirred at 100 °C for 2h. After cooling, Et_2O (20 mL) is added to form a precipitate, which was then filtered. The solid was washed profusely with Et_2O and pentane to removed DMF and dried under vacuum to yield **1** (63 mg, 31%).

^{1}H NMR (400 MHz, DMSO-d_6): δ 7.62-7.42 (m, 30H, PPh_3), 6.93 (br s, 2H, NH_2), 6.28 (d, 1H, H-1', $^{3}J_{H\text{-}1',\ H\text{-}2'} \approx 5.6$ Hz), 6.17 (dd, 1H, H-2', $^{3}J_{H\text{-}2',\ H\text{-}1'} = {}^{3}J_{H\text{-}2',\ H\text{-}3'} = 5.6$ Hz), 5.50 (dd, H-3', 1H, $^{3}J_{H\text{-}3',\ H\text{-}2'} = 5.6$ Hz, $^{3}J_{H\text{-}3',\ H\text{-}4'} = 5.2$ Hz), 4.06 (dd, 1H, H-5'a, $^{3}J_{H\text{-}5'a,\ H\text{-}4'} = 4.0$ Hz, $^{2}J_{H\text{-}5'a,\ H\text{-}5'b} = 12.0$ Hz), 3.97 (dd, 1H, H-5'b, $^{3}J_{H\text{-}5'b,\ H\text{-}4'} = 6.4$ Hz, $^{2}J_{H\text{-}5'b,\ H\text{-}5'a} = 12.0$ Hz), 3.40-3.34* (m, 1H, H-4'), 2.86 (s, 3H, 7-NCH_3), 2.08 (s, 3H, 3'-CH_3CO), 1.92 (s, 3H, 5'-CH_3CO), 1.47 (s, 3H, 2'-CH_3CO), -6.20 (t, Pt*H*, $^{2}J_{H,\ P} = 13.0$ Hz, Pt satellites $^{1}J_{H,\ Pt} = 681$ Hz) ppm. *Determined by HSQC and HMBC

$^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6): δ = 181.9 (C-8), 169.8 (5'-CH_3CO), 169.1 (3'-CH_3CO), 168.7 (2'-CH_3CO), 157.6 (C-2 & C-6), 151.2 (C-4), 133.4, 133.2, 131.6, 131.3, 128.7, 129.0 (2×P(C_6H_5)$_3$), 109.4 (C-5), 89.6 (C-1'), 79.2 (C-4'), 70.4 (C-2'), 69.5 (C-3'), 61.8 (C-5'), 35.4 (7-NCH_3), 20.4, 20.4 (3'-CH_3CO & 5'-CH_3CO), 19.6 (2'-CH_3CO) ppm.

$^{31}P\{^{1}H\}$ NMR (162 MHz, DMSO-d_6): δ = 24.00 (s), 23.98 (s) ppm. Pt satellites $^{1}J_{P,\,Pt}$ = 2796 Hz.

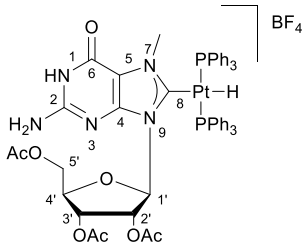
^{1}H NMR (400 MHz, DMF-d_7): δ 7.80-7.41 (m, 32H, PPh_3 & NH_2), 6.43 (d, 1H, H-1', $^{3}J_{H\text{-}1',\,H\text{-}2'} \approx 5.2$ Hz), 6.28 (dd, 1H, H-2', $^{3}J_{H\text{-}2',\,H\text{-}1'} = 5.2$ Hz, $^{3}J_{H\text{-}2',\,H\text{-}3'} = 5.6$ Hz), 5.70 (dd, H-3', 1H, $^{3}J_{H\text{-}3',\,H\text{-}2'} = 5.6$ Hz, $^{3}J_{H\text{-}3',\,H\text{-}4'} = 5.2$ Hz), 4.17 (dd, 1H, H-5'a, $^{3}J_{H\text{-}5'a,\,H\text{-}4'} = 4.0$ Hz, $^{2}J_{H\text{-}5'a,\,H\text{-}5'b} = 12.0$ Hz), 4,09 (dd, 1H, H-5'b, $^{3}J_{H\text{-}5'b,\,H\text{-}4'} = 6.0$ Hz, $^{2}J_{H\text{-}5'b,\,H\text{-}5'a} = 12.0$ Hz), 3.53 (ddd, 1H, H-4', $^{3}J_{H\text{-}4'H\text{-}3'} = 5.2$ Hz, $^{3}J_{H\text{-}4',\,H\text{-}5'a} \approx 4.0$ Hz, $^{3}J_{H\text{-}4',\,H\text{-}5'b} \approx 6.0$ Hz), 3.06 (s, 3H, 7-NCH_3), 2.15 (s, 3H, 3'-CH_3CO), 2.01 (s, 3H, 5'-CH_3CO), 1.61 (s, 3H, 2'-CH_3CO), -6.07 (t, Pt*H*, $^{2}J_{H,\,P} = 13.0$ Hz, Pt satellites $^{1}J_{H,\,Pt} = 680$ Hz) ppm.

$^{13}C\{^{1}H\}$ NMR (100 MHz, DMF-d_7): δ = 183.1, 170.3 (5'-CH_3CO), 169.6 (3'-CH_3CO), 169.4 (2'-CH_3CO), 158.8 (C-2 & C-6), 153.0 (C-4), 134.1, 133.9, 132.6, 132.3, 131.9, 131.6, 129.4, 129.1 (2×P(C_6H_5)$_3$), 110.0 (C-5), 90.5 (C-1'), 80.1 (C-4'), 71.4 (C-2'), 70.3 (C-3'), 62.4 (C-5'), 35.9 (7-NCH_3), 20.4, 20.3 (3'-CH_3CO & 5'-CH_3CO), 19.8 (2'-CH_3CO) ppm.

$^{31}P\{^{1}H\}$ NMR (162 MHz, DMF-d_7): δ = 24.27 (s), 24.26 (s) ppm. Pt satellites $^{1}J_{P,\,Pt} = 2800$ Hz.

Anal. calcd. for $C_{53}H_{52}IN_5O_8P_2Pt$: C, 50.09; H, 4.12; N, 5.51. Found: C, 49.90; H, 4.25; N, 5.47.

1.5. Complex 1-BF_4



Complex **1** (50 mg, 0.039 mmol) was dissolved in dichloromethane (10 mL) and $AgBF_4$ (9.2 mg, 0.047 mmol) was added. The resulting mixture was stirred at room temperature for 45

minutes. The precipitate was filtered through Celite® and washed with dichloromethane. The obtained solution was evaporated under reduced pressure to yield **1-BF_4** (44 mg, 92%).

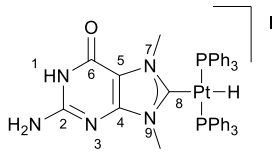
^{1}H NMR (400 MHz, DMSO-d_6): δ 7.60-7.42 (m, 30H, PPh_3), 6.94 (br s, 2H, NH_2), 6.29 (d, 1H, H-1', $^3J_{H\text{-}1',\ H\text{-}2'}$ = 5.6 Hz), 6.17 (dd, 1H, H-2', $^3J_{H\text{-}2',\ H\text{-}1'}$ = 5.6 Hz, $^3J_{H\text{-}2',\ H\text{-}3'}$ = 6.0 Hz), 5.50 (dd, H-3', 1H, $^3J_{H\text{-}3',\ H\text{-}2'}$ = 6.0 Hz, $^3J_{H\text{-}3',\ H\text{-}4'}$ = 5.2 Hz), 4.06 (dd, 1H, H-5'a, $^3J_{H\text{-}5'a,\ H\text{-}4'}$ = 4.4 Hz, $^2J_{H\text{-}5'a,\ H\text{-}5'b}$ = 12 Hz), 3.97 (dd, 1H, H-5'b, $^3J_{H\text{-}5'b,\ H\text{-}4'}$ = 6.0 Hz, $^2J_{H\text{-}5'b,\ H\text{-}5'a}$ = 12 Hz), 3.36* (1H, H-4'), 2.86 (s, 3H, 7-NCH_3), 2.08 (s, 3H, 3'-CH_3CO), 1.92 (s, 3H, 5'-CH_3CO), 1.47 (s, 3H, 2'-CH_3CO), -6.20 (t, Pt*H*, $^2J_{H,\ P}$ = 12.8 Hz, Pt satellites $^1J_{H,\ Pt}$ = 682 Hz) ppm. *Determined by HSQC and HMBC

^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ = 182.5 (C-8), 169.8 (5'-CH_3*C*O), 169.1 (3'-CH_3*C*O), 168.7 (2'-CH_3*C*O), 157.2 (C-2 & C-6), 151.2 (C-4), 133.4, 133.2, 131.6, 131.3, 129.0, 128.7 (2×P(C_6H_5)$_3$), 109.2 (C-5), 89.6 (C-1'), 79.3 (C-4'), 70.3 (C-2'), 69.5 (C-3'), 61.8 (C-5'), 35.5 (7-N*C*H_3), 20.4, 20.4 (3'-*C*H_3CO & 5'-*C*H_3CO), 19.5 (2'-*C*H_3CO) ppm.

^{31}P{^{1}H} NMR (162 MHz, DMSO-d_6): δ = 24.03 (s), 23.99 (s) ppm. Pt satellites $^1J_{P,\ Pt}$ = 2791 Hz.

HRMS (ESI) for $C_{53}H_{52}N_5O_8P_2Pt$ $[M]^+$ calcd. 1143.2933. Found: 1143.2937.
HRMS (ESI) for BF $[M]^-$ calcd. 87.0035 (100.0%), 86.0071 (24.8%). Found: 87.0034 (100.0%), 86.0071 (24.8%).

1.6. Complex 2



Compound **7,9-DMG** (30.7 mg, 0.1 mmol) and $Pt(PPh_3)_4$ (124 mg, 0.1 mmol) were suspended in degassed DMF (2 mL) and stirred at 100 °C for 3h. After cooling, addition of Et_2O (20 mL) results in the appearance of a precipitate. The precipitate was filtered and washed with Et_2O (20 mL) to yield **2** (45 mg, 44%).

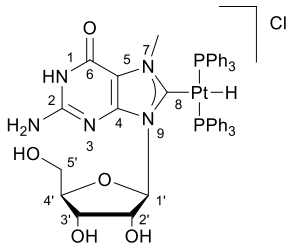
^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 11.48 (br s, 1H, NH), 7.59-7.43 (m, 30H, PPh_3), 6.93 (s, 2H, NH_2), 3.17 (s, 3H, 7-N*CH*$_3$), 2.88 (s, 3H, 9-N*CH*$_3$), -5.91 (t, Pt*H*, $^{2}J_{H,\,P}$ = 12.4 Hz, Pt satellites $^{1}J_{H,\,Pt}$ = 678 Hz) ppm.

^{13}C{^{1}H} NMR (100 MHz, DMSO-*d*$_6$): δ = 182.7 (C-8), 154.4, 153.1 (C-2 & C-6), 151.4 (C-4), 133.2, 131.5, 131.2, 129.1, 128.8 (2×P(C_6H_5)$_3$), 107.9 (C-5), 35.5 (7-N*C*H_3), 31.6 (9-N*C*H_3) ppm.

^{31}P{^{1}H} NMR (162 MHz, DMSO-*d*$_6$): δ = 25.27 (s) ppm. Pt satellites $^{1}J_{P,\,Pt}$ = 2799 Hz.

Anal. calcd. for $C_{43}H_{40}IN_5OP_2Pt$: C, 50.30; H, 3.93; N, 6.82. Found: C, 50.40; H, 4.08; N, 6.83.

1.7. Complex 3



Complex **1** (81.6 mg, 0.642 mmol) was dissolved in a mixture of dichloromethane (0.8 mL) and EtOH (0.6 mL). The solution was stirred for 1 minute and then 12.8 mL of HCl (16.5% in a water/EtOH mixture) were added. After addition of the acidic solution, a white precipitate forms within 5 minutes and the suspension was vigorously stirred for 5 days at room temperature. After evaporation of the dichloromethane and ethanol, the resulting suspension is lyophilized for 3h to remove the water. The resulting solid was suspended in methanol and stirred overnight. After filtration, the filtrate was dried under vacuum and the resulting solid recrystallized in MeOH/Et_2O to yield **3** (40 mg, 60%).

^{1}H NMR (800 MHz, DMSO-*d*$_6$): δ 11.28 (br s, 1H, 1-NH), 7.84-7.21 (m, 30H, PPh_3), 6.87 (br s, 2H, NH_2), 6.06 (d, 1H, H-1', $^{3}J_{H\text{-}1',\,H\text{-}2'}$ = 4.8 Hz), 4.82 (d, 1H, OH-3', $^{3}J_{OH\text{-}3',\,H\text{-}3}$ ≈ 5.6 Hz), 4.58 (ddd, 1H, H-2', $^{3}J_{H\text{-}2',\,H\text{-}1'}$ = 4.8 Hz, $^{3}J_{H\text{-}2',\,OH\text{-}2'}$ = 6.4 Hz, $^{3}J_{H\text{-}2',\,H\text{-}3'}$ = 5.6 Hz), 4.39 (t, 1H, 5'-OH, $^{3}J_{OH\text{-}5',\,H\text{-}5a}$ = $^{3}J_{OH\text{-}5',\,H\text{-}5b}$ = 5.6 Hz), 4.36 (d, 1H, 2'-OH, $^{3}J_{OH\text{-}2',\,H\text{-}2'}$ = 6.4 Hz), 4.14 (ddd, 1H, H-3', $^{3}J_{H\text{-}3',H\text{-}2'}$ ≈ $^{3}J_{H\text{-}3',\,OH\text{-}3'}$ ≈ $^{3}J_{H\text{-}3',\,H\text{-}4'}$ ≈ 5.6 Hz), 3.32* (m, 1H, H-5'a), 3.29 (ddd, 1H, H-4', $^{3}J_{H\text{-}4'H\text{-}3'}$ ≈ $^{3}J_{H\text{-}4',\,H\text{-}5'a}$ ≈ $^{3}J_{H\text{-}4',\,H\text{-}5'b}$ ≈ 4.8 Hz), 3.23 (dt, 1H, H-5'b, $^{3}J_{H\text{-}5'b,\,H\text{-}4'}$ = 4.8 Hz, $^{3}J_{H\text{-}5'b,}$

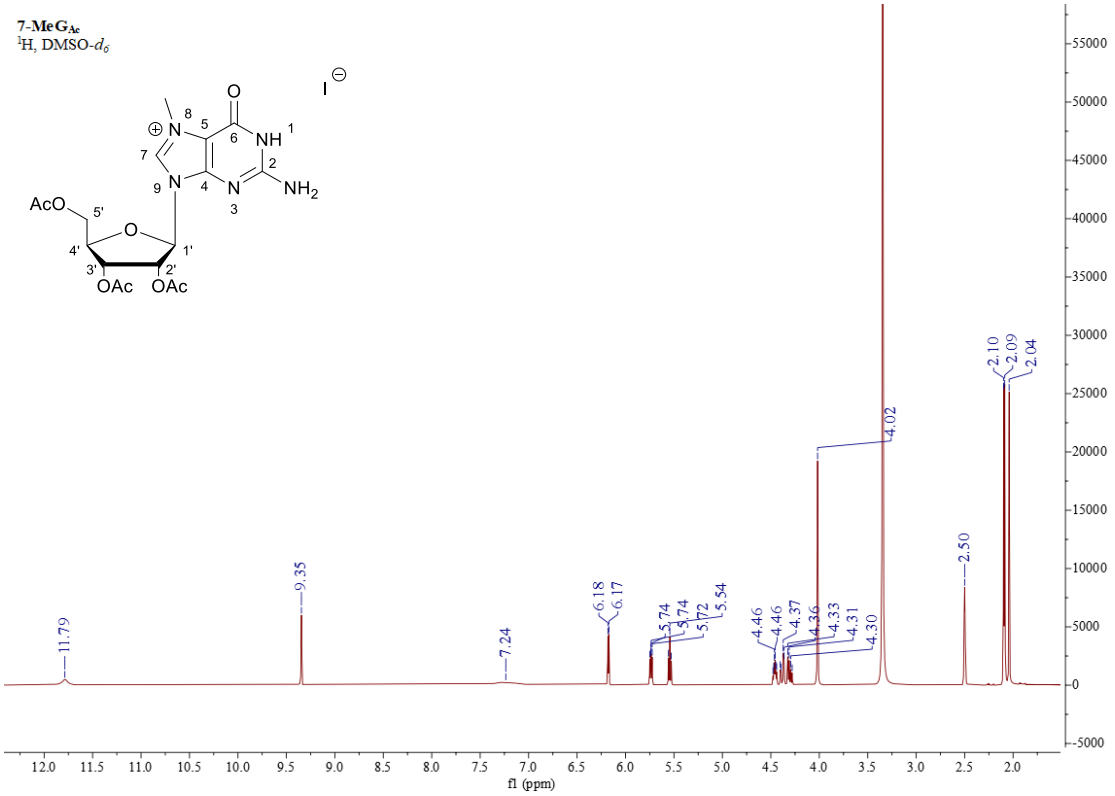
$^{OH\text{-}5'}$ = 5.6 Hz, $^{2}J_{H\text{-}5'b,\ H\text{-}5'a}$ = 11.2 Hz) , -6.36 (t, Pt*H*, $^{2}J_{H,\ P}$ = 12.8 Hz, Pt satellites $^{1}J_{H,\ Pt}$ = 684 Hz) ppm. *Determined by HSQC and HMBC

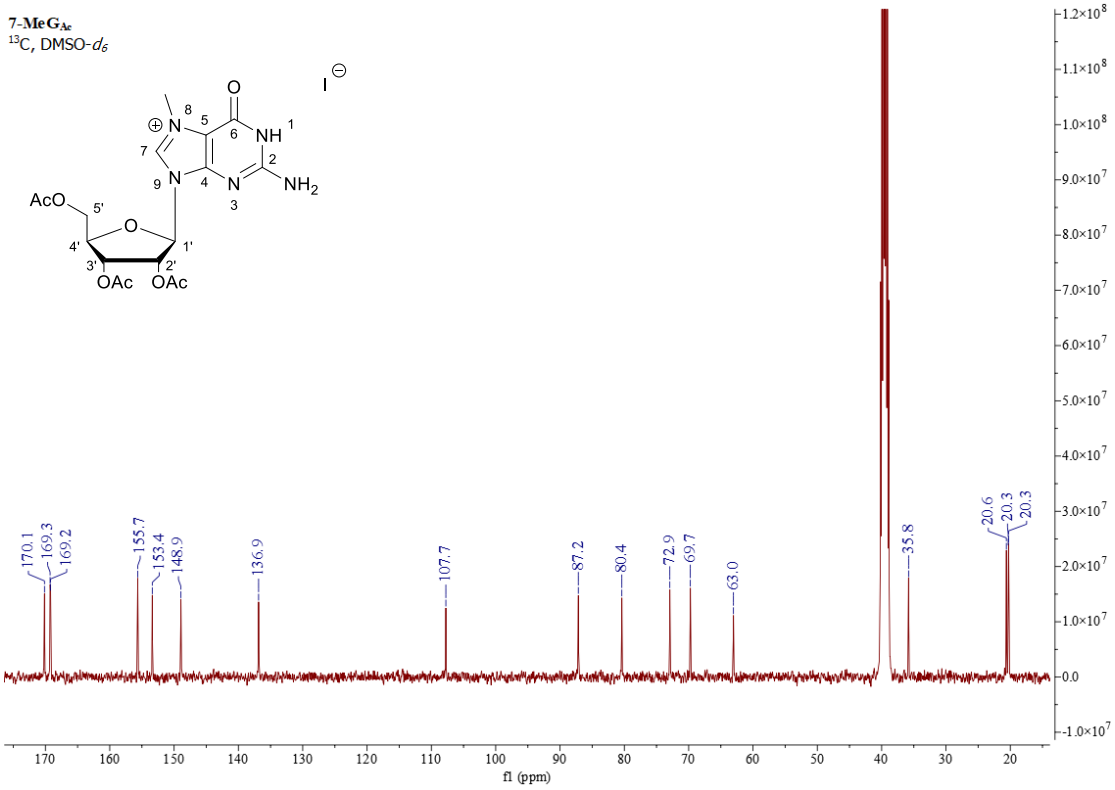
$^{13}C\{^{1}H\}$ NMR (201 MHz, DMSO-d_6): δ = 184.5 (t, C-8, $^{1}J_{C,\ Pt}$ = 8.0 Hz), 153.6 (C-4), 151.9, 150.5 (C-2 & C-6), 133.4, 131.5, 131.4, 131.3, 131.2, 128.8, 128.8 (2×P(C_6H_5)$_3$), 108.9 (C-5), 93.5 (C-1'), 84.6 (C-4'), 70.6 (C-2'), 69.9 (C-3'), 61.4 (C-5'), 35.6 (7-NCH_3) ppm.

$^{31}P\{^{1}H\}$ NMR (162 MHz, DMSO-d_6): δ = 24.36 (s) ppm. Pt satellites $^{1}J_{P,\ Pt}$ = 2802 Hz.

Anal. calcd. for $C_{47}H_{46}ClN_5O_5P_2Pt$: C, 53.59; H, 4.40; N, 6.65. Found: C, 53.13; H, 4.00; N, 6.21.

2. NMR and MS spectra




7-MeG$_{Ac}$
^{13}C, DMSO-d_6
I$^{\ominus}$
AcO
OAc
OAc
NH$_2$
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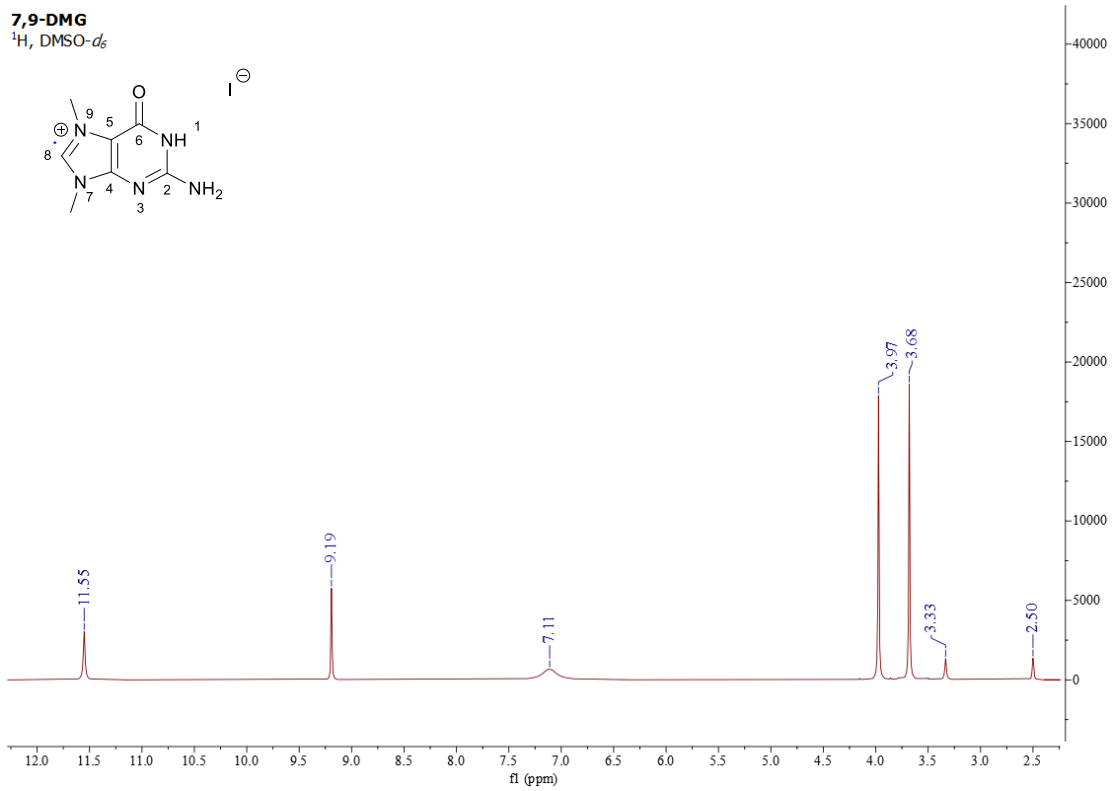
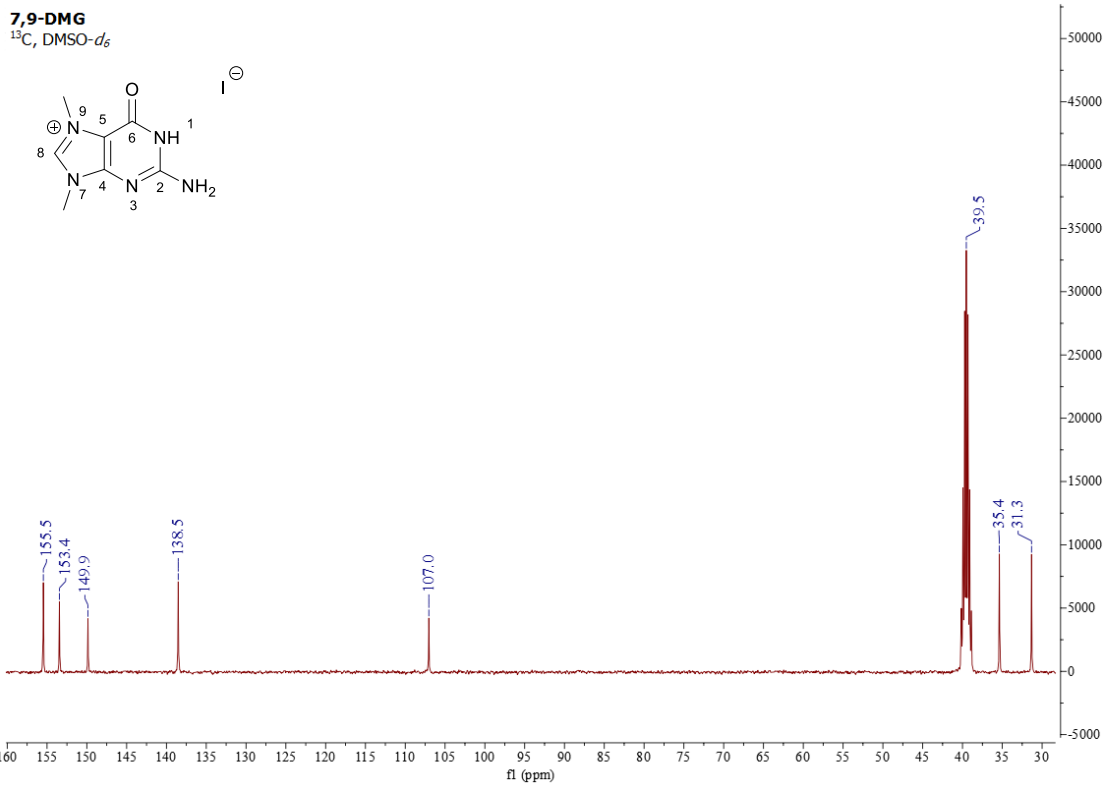
169.3
169.2
155.7
153.4
148.9
136.9
107.7
87.2
80.4
72.9
69.7
63.0
35.8
20.6
20.3
20.3
f1 (ppm)


7,9-DMG
^{1}H, DMSO-d_6
I$^{\ominus}$
NH$_2$
11.55
9.19
7.11
3.97
3.68
3.33
2.50
f1 (ppm)

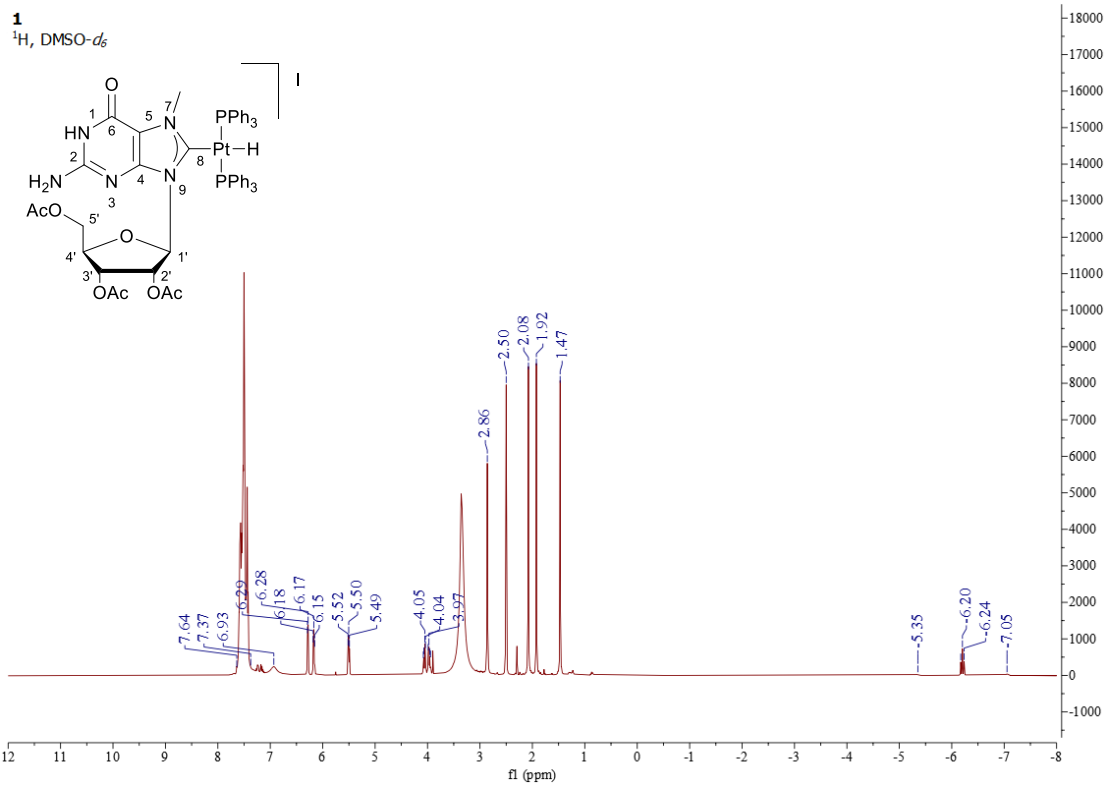
7,9-DMG

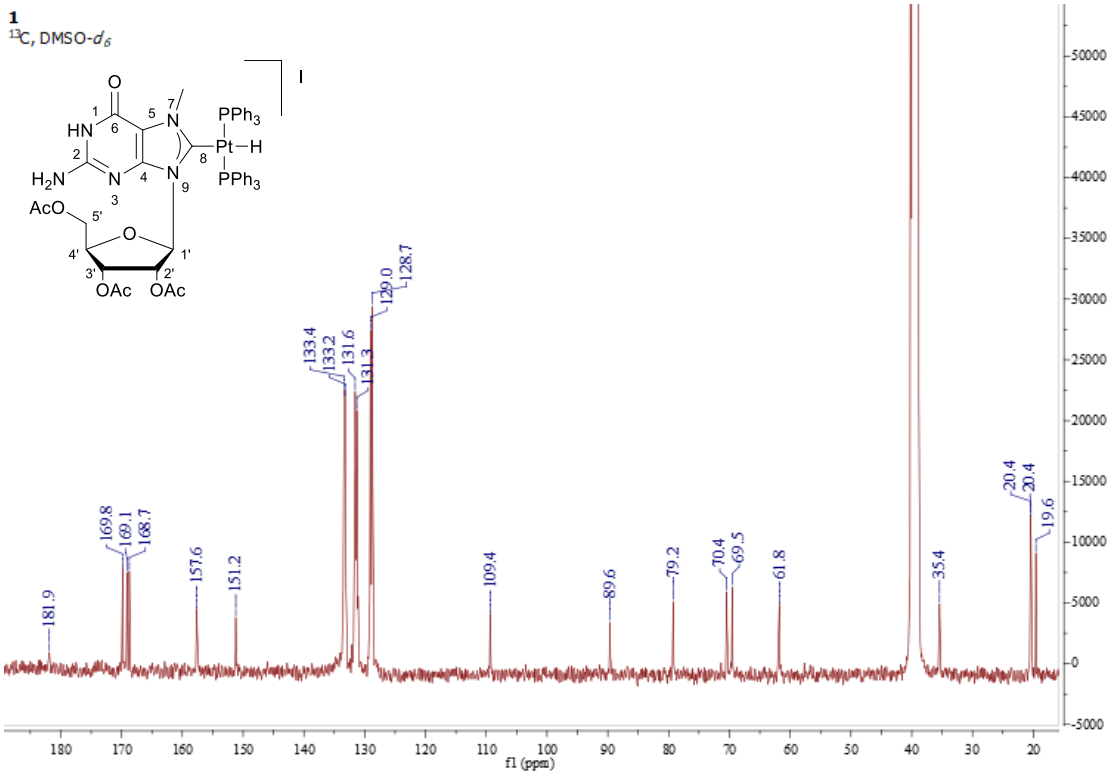
^{13}C, DMSO-d_6



1

^{1}H, DMSO-d_6




1
13C, DMSO-d6
PPh3
Pt—H
PPh3
AcO
OAc
OAc
169.8
169.1
168.7
157.6
151.2
133.4
133.2
131.6
131.3
129.0
128.7
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20.4
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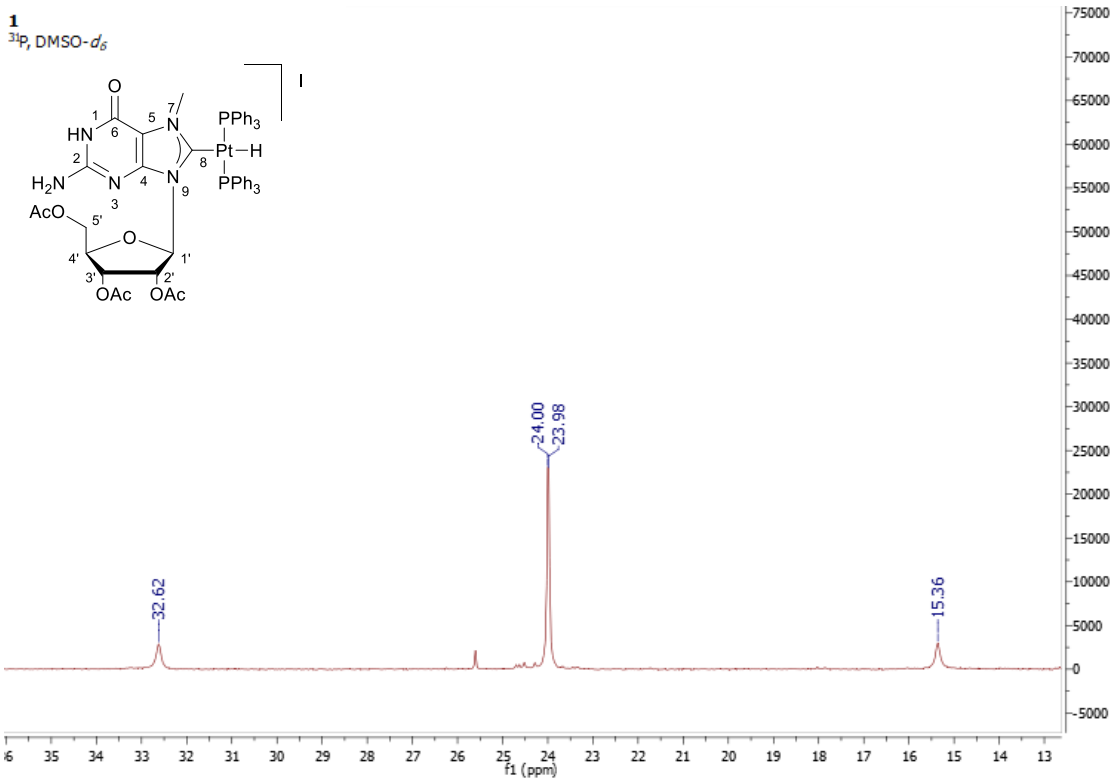
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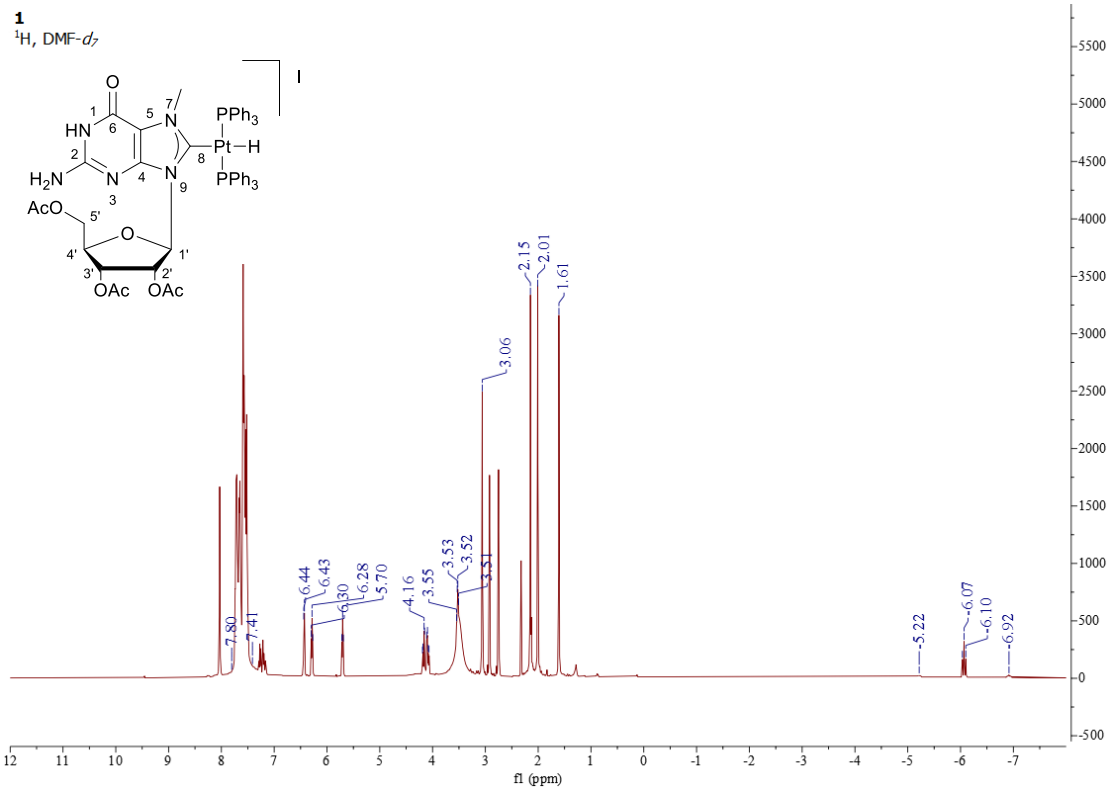
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2.01
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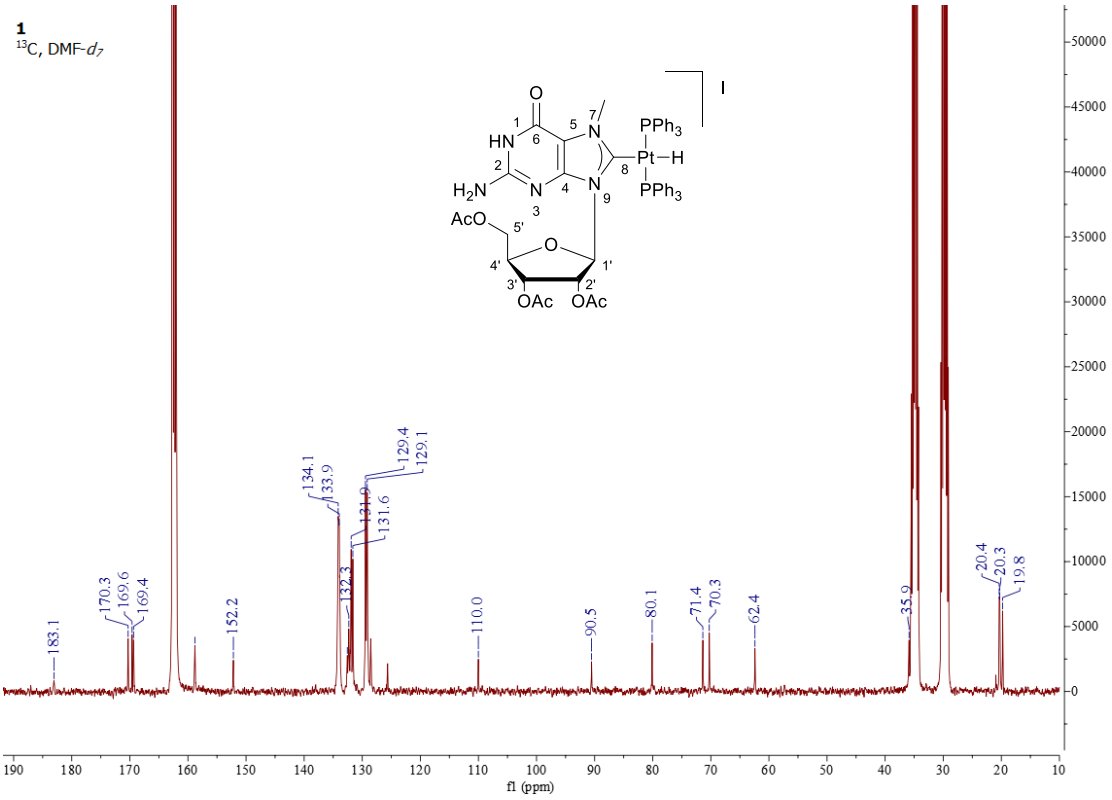
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133.9
132.3
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f1 (ppm)

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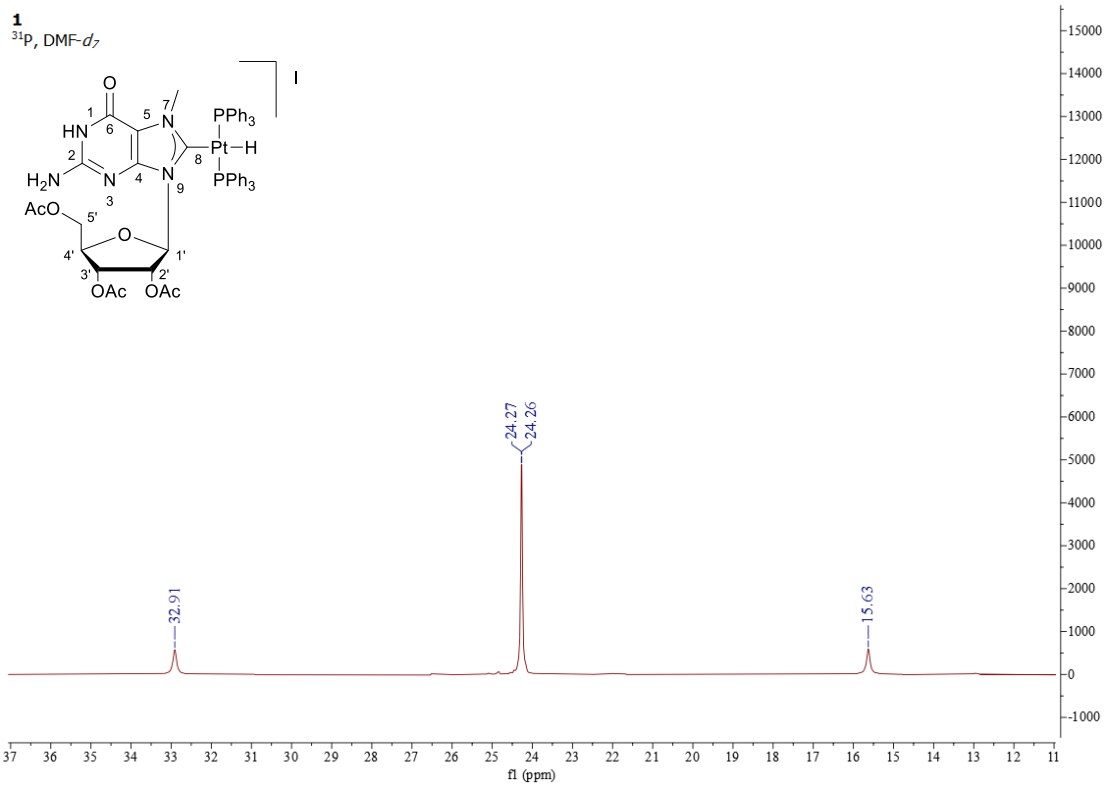

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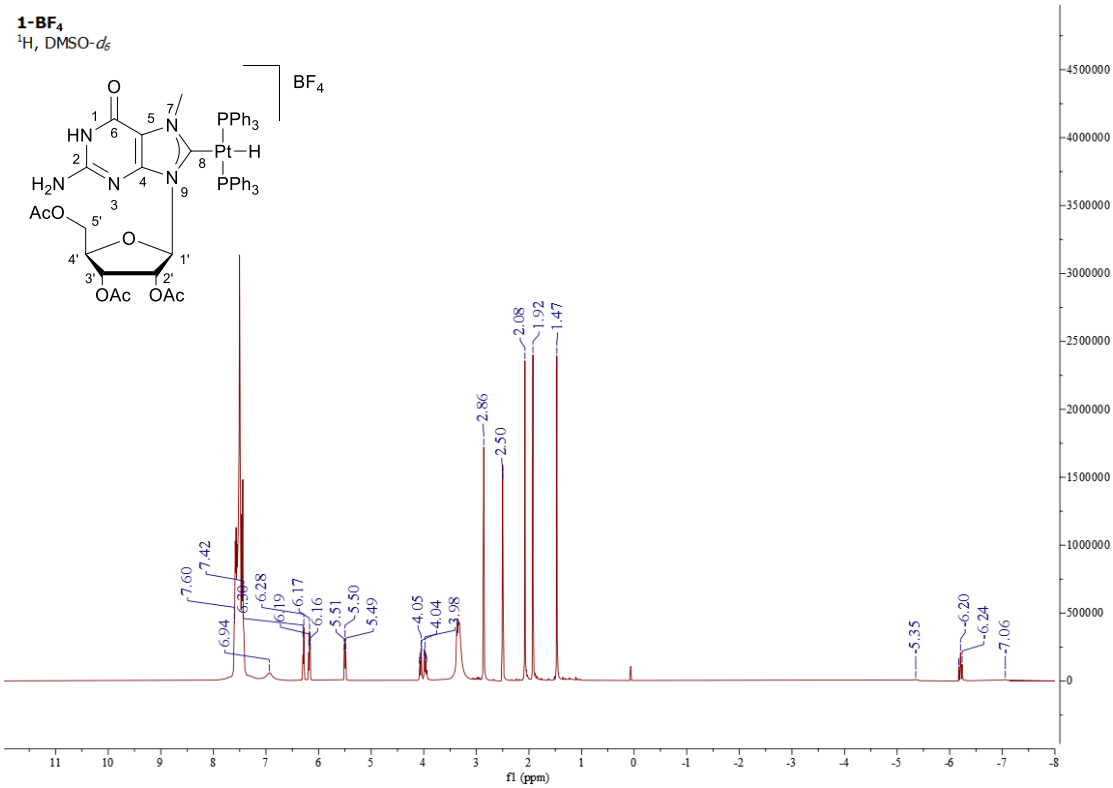

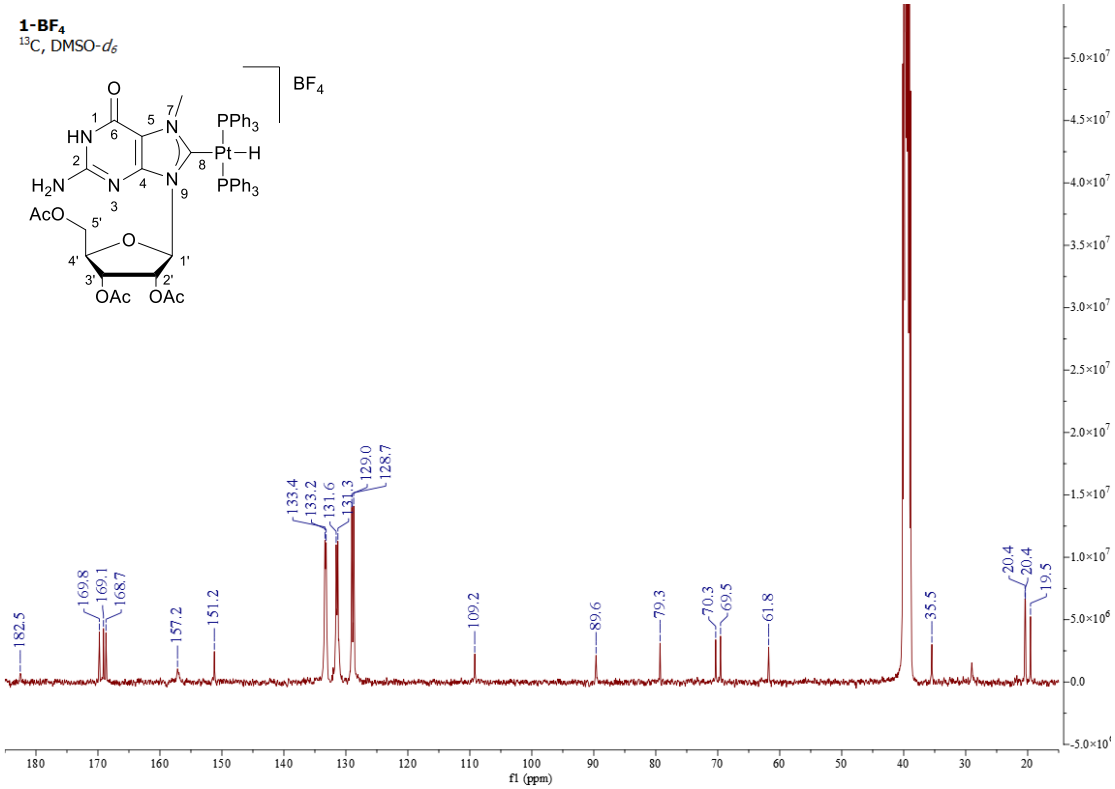
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133.2
131.6
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129.0
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70.3
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20.4
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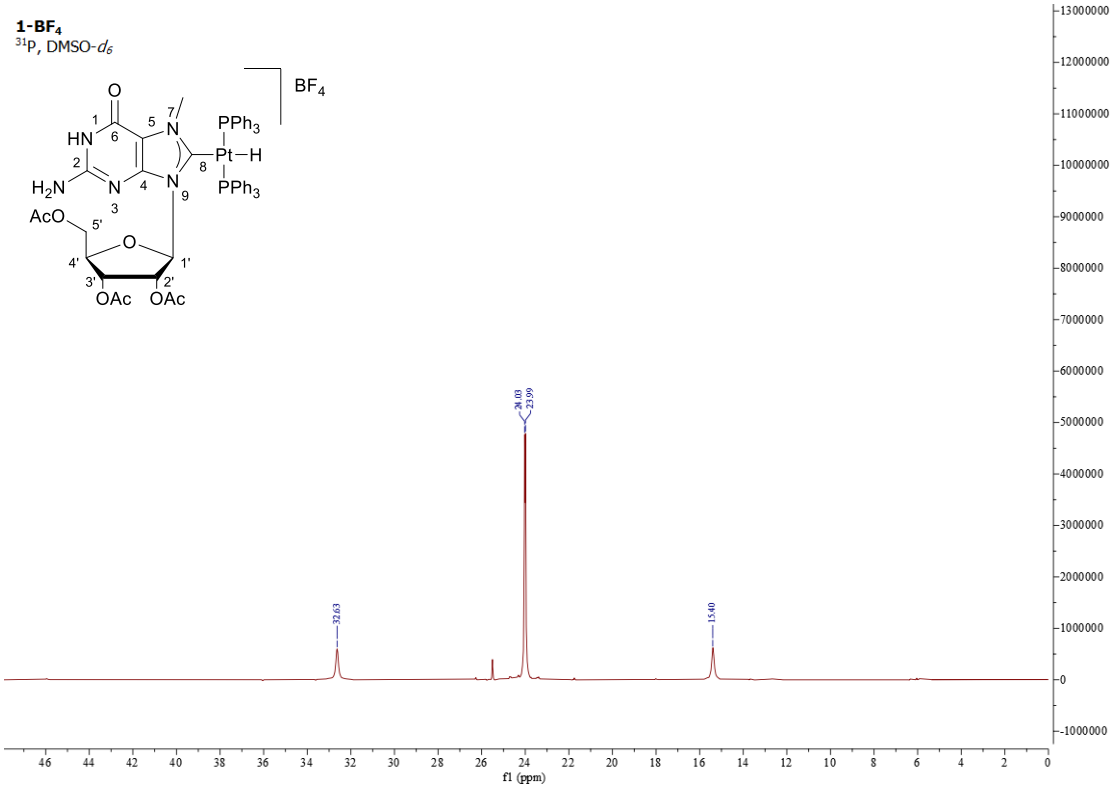
19.5
f1 (ppm)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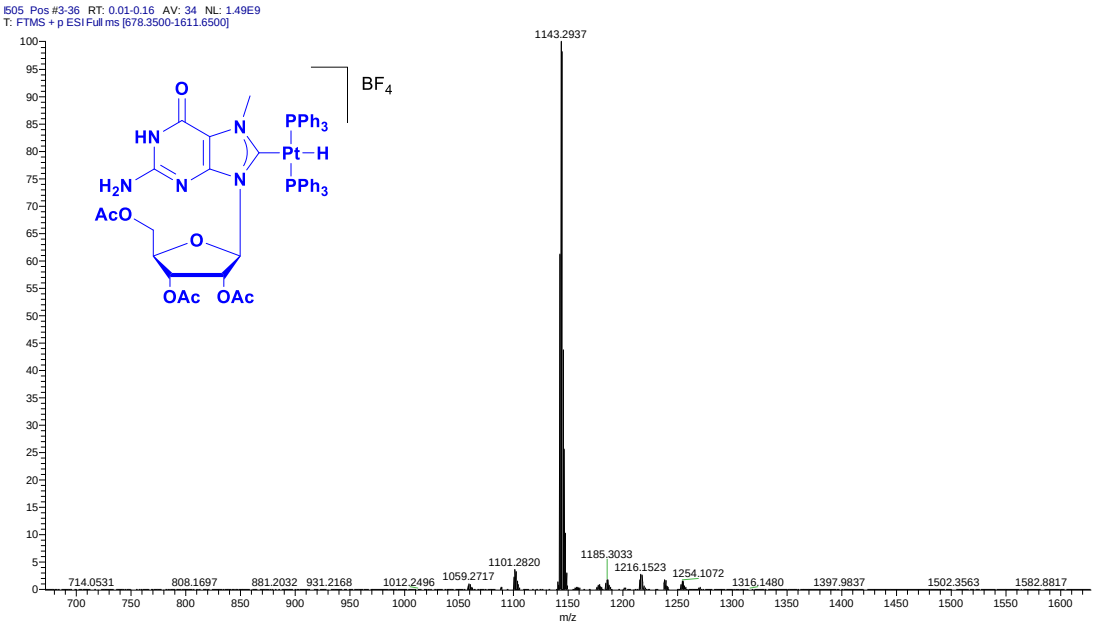
f1 (ppm)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N
PPh3
Pt—H
H2N
N
N
PPh3
AcO
O
OAc OAc
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1185.3033
1216.1523
1254.1072
714.0531
808.1697
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1397.9837
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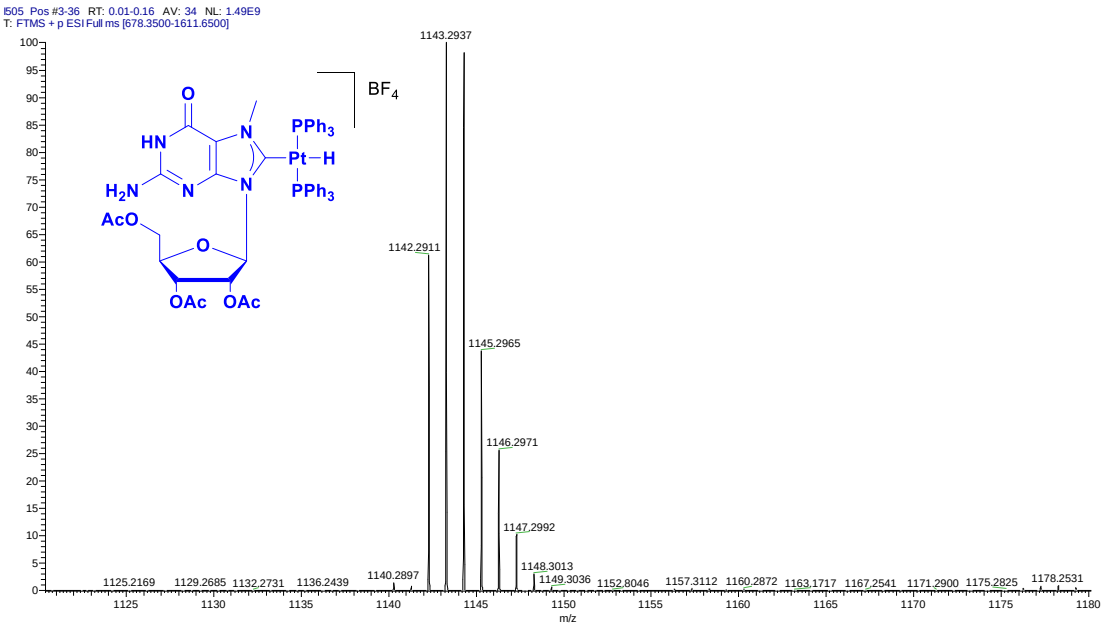
1582.8817
m/z


I505 Pos #3-36 RT: 0.01-0.16 AV: 34 NL: 1.49E9
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1143.2937
BF4
O
HN
N
PPh3
Pt—H
H2N
N
N
PPh3
AcO
O
OAc OAc
1142.2911
1145.2965
1146.2971
1147.2992
1148.3013
1149.3036
1140.2897
1125.2169
1129.2685
1132.2731
1136.2439
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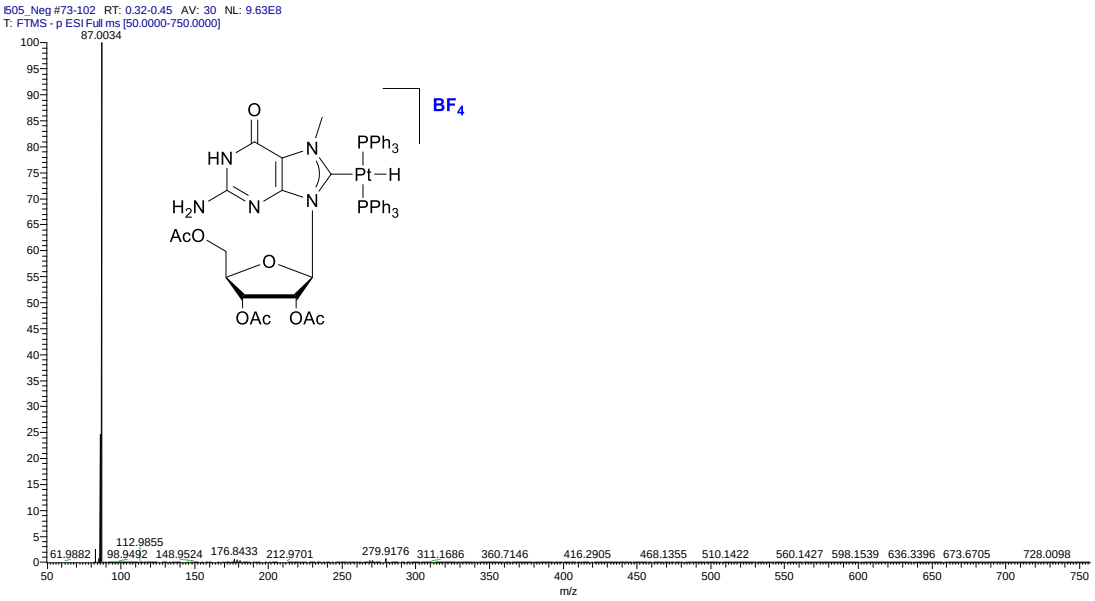
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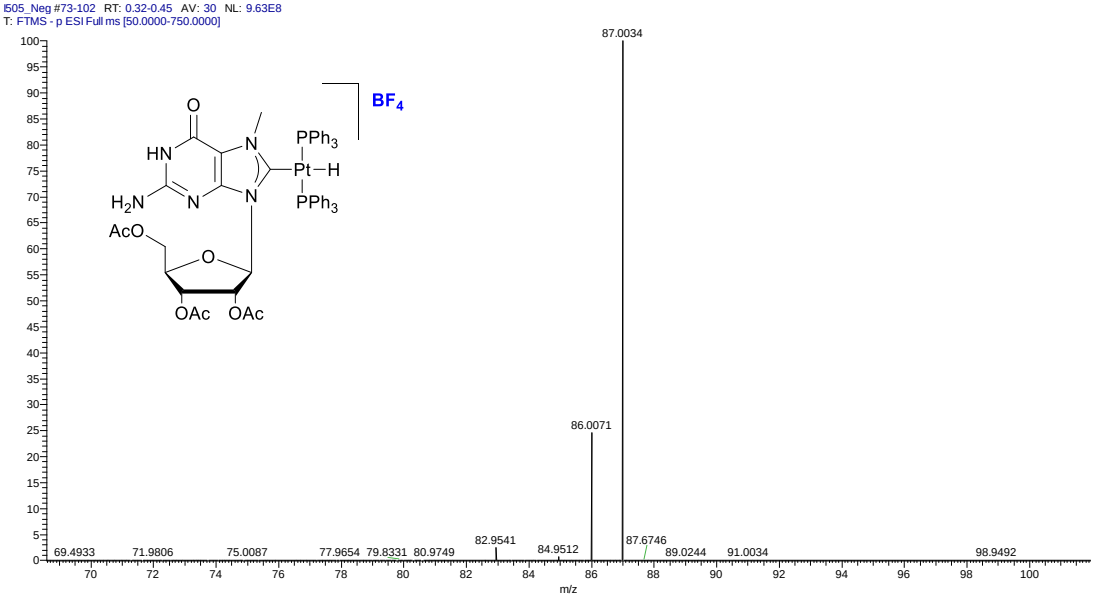
PPh3
Pt—H
H2N
N
N
PPh3
AcO
O
OAc OAc
112.9855
61.9882 98.9492 148.9524 176.8433 212.9701 279.9176 311.1686 360.7146 416.2905 468.1355 510.1422 560.1427 598.1539 636.3396 673.6705 728.0098
m/z


I505_Neg #73-102 RT: 0.32-0.45 AV: 30 NL: 9.63E8
T: FTMS - p ESI Full ms [50.0000-750.0000]
87.0034
BF4
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HN
N
PPh3
Pt—H
H2N
N
N
PPh3
AcO
O
OAc OAc
86.0071
87.6746
82.9541
84.9512
69.4933 71.9806 75.0087 77.9654 79.8331 80.9749 89.0244 91.0034 98.9492
m/z

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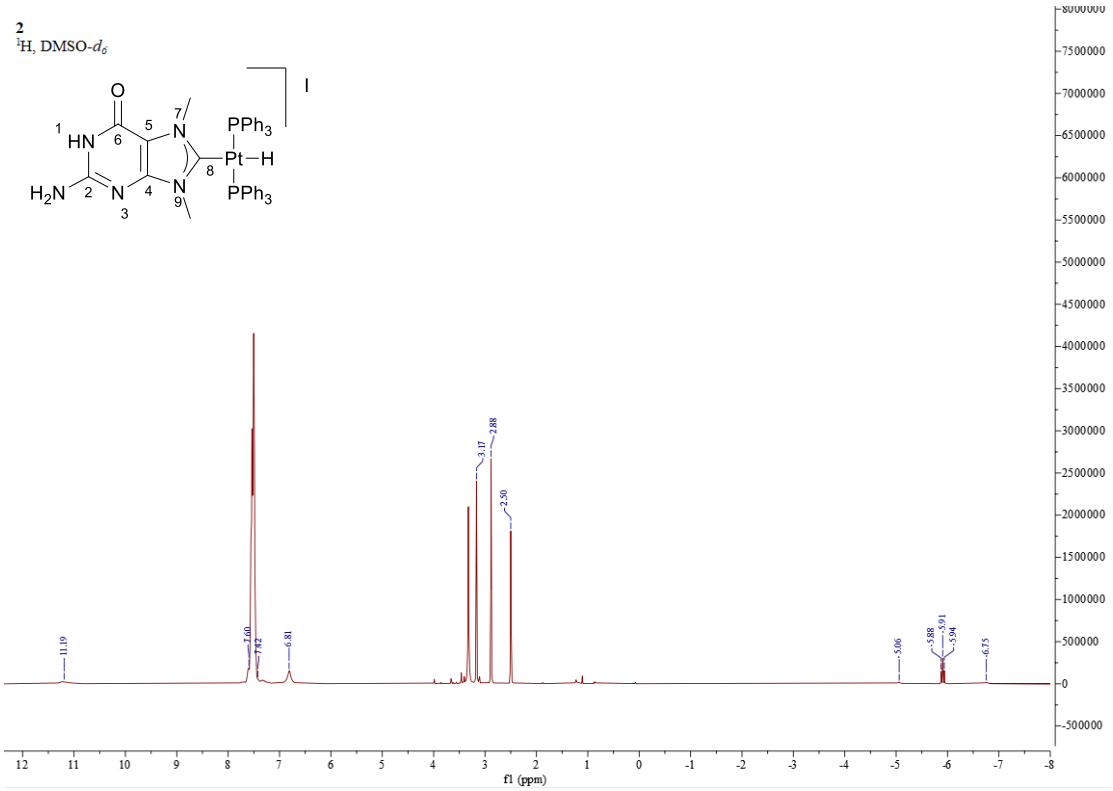

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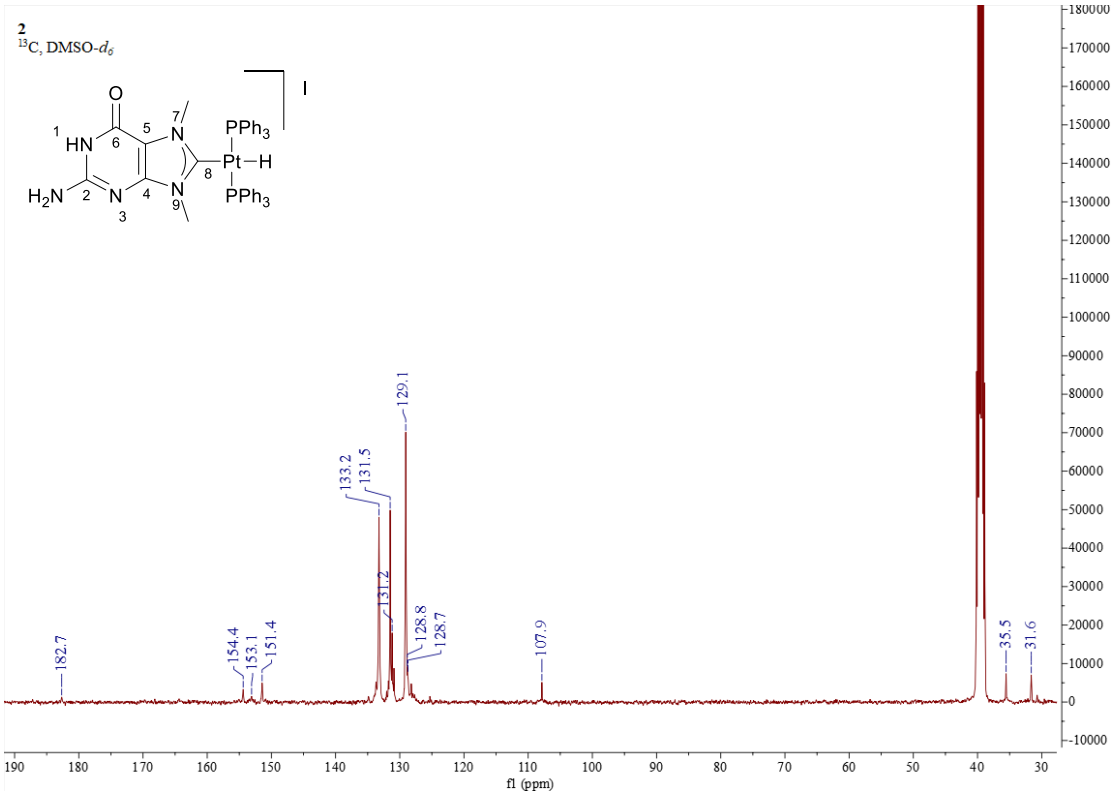

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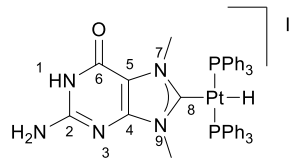

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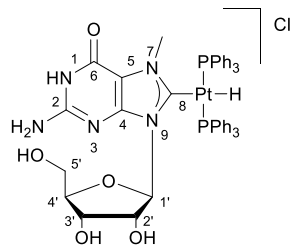

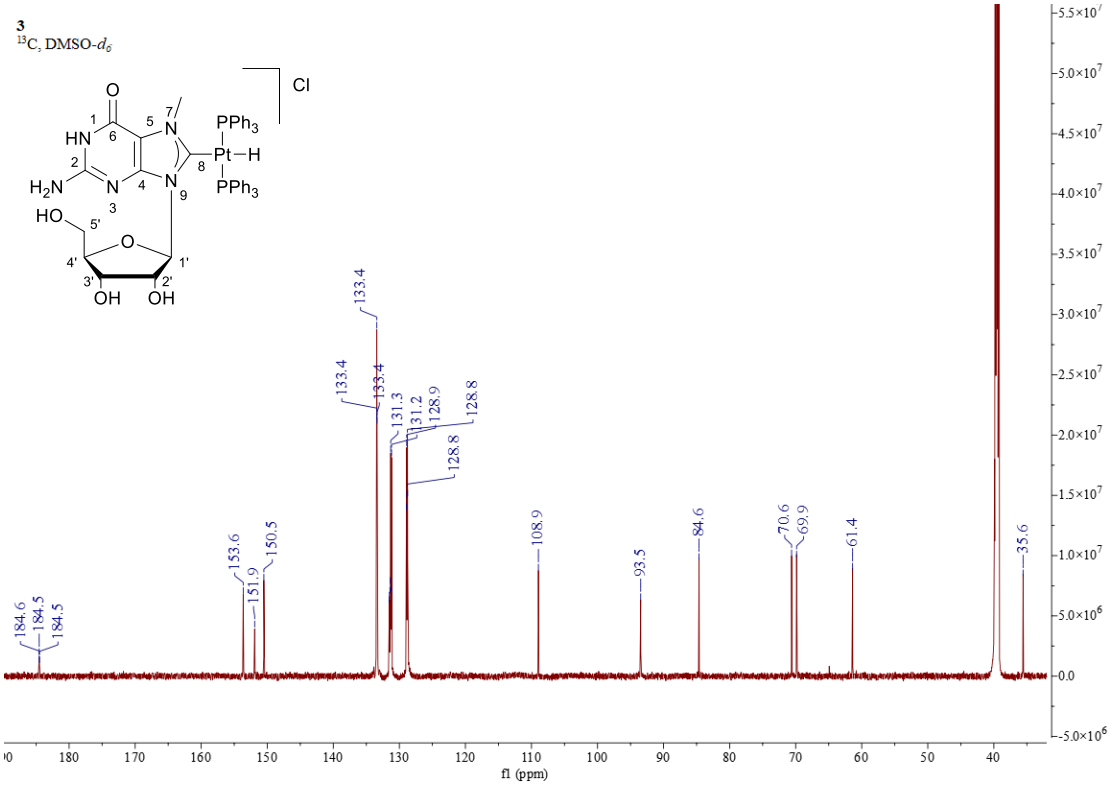
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13C, DMSO-d6
Cl
PPh3
Pt—H
PPh3
HO
OH
OH
133.4
133.4
133.4
131.3
131.2
128.9
128.8
128.8
153.6
151.9
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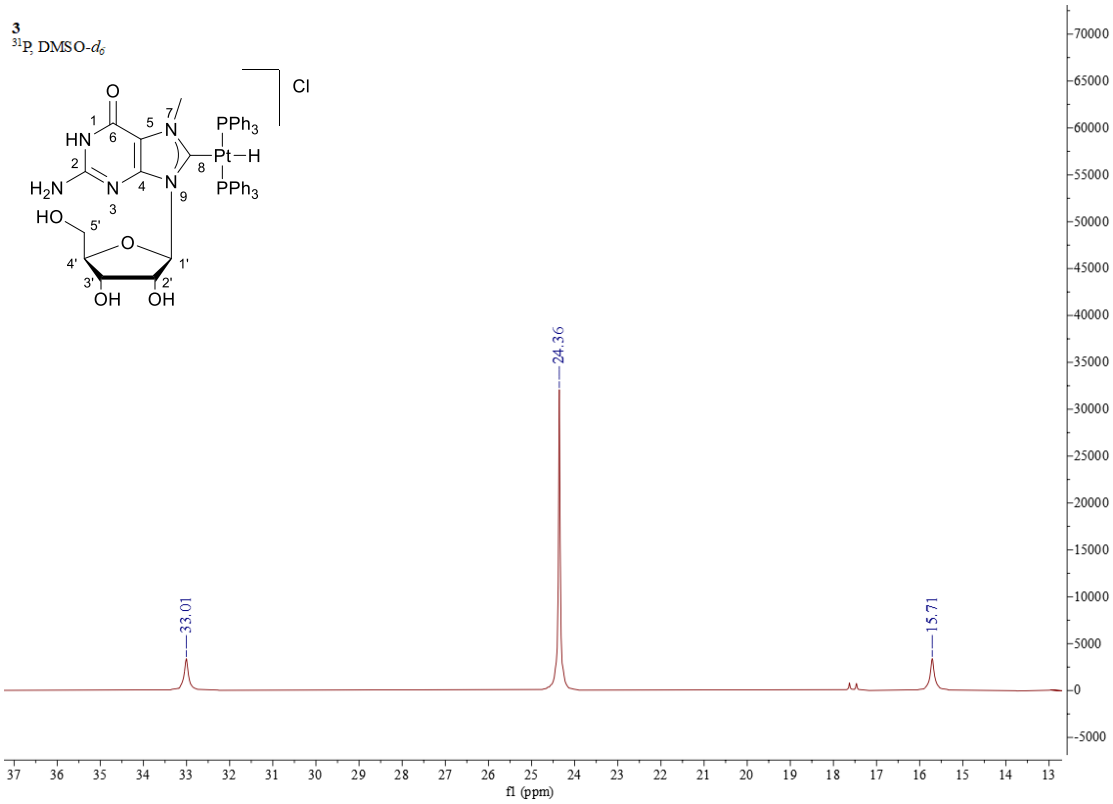
70.6
69.9
61.4
35.6
f1 (ppm)


3
31P, DMSO-d6
Cl
PPh3
Pt—H
PPh3
HO
OH
OH
24.36
33.01
15.71
f1 (ppm)

3. Crystallographic details for complex 3

Table S1. Crystal data and structure refinement for complex **3**.

Empirical formula	C47 H46 Cl N5 O5 P2 Pt	
Formula weight	1053.37	
Temperature	110(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21	
Unit cell dimensions	a = 14.8090(7) Å	α= 90°.
	b = 9.7032(4) Å	β= 113.307(2)°.
	c = 18.6573(9) Å	γ = 90°.
Volume	2462.2(2) $Å^3$	
Z	2	
Density (calculated)	1.421 Mg/m^3	
Absorption coefficient	3.016 mm^{-1}	
F(000)	1056	
Crystal size	0.360 x 0.260 x 0.200 mm^3	
Theta range for data collection	1.499 to 28.330°.	
Index ranges	-19<=h<=19, -12<=k<=9, -24<=l<=24	
Reflections collected	37856	
Independent reflections	10029 [R(int) = 0.0810]	
Completeness to theta = 25.242°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7457 and 0.3228	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	10029 / 8 / 544	
Goodness-of-fit on F^2	1.052	
Final R indices [I>2sigma(I)]	R1 = 0.0424, wR2 = 0.1048	
R indices (all data)	R1 = 0.0483, wR2 = 0.1071	
Absolute structure parameter	0.122(9)	
Extinction coefficient	n/a	
Largest diff. peak and hole	3.422 and -3.557 $e.Å^{-3}$	

Table S2. Chemical Selected Bond lengths [Å] and angles [°] for complex **3**.

Pt(1)-H(1)	1.68386(6)	N(3)-C(2)	1.328(11)
C(8)-Pt(1)	2.036(9)	C(1')-N(9)	1.472(12)
C(8)-N(7)	1.339(11)	C(1')-O(4')	1.428(8)
C(8)-N(9)	1.388(10)	C(2')-C(1')	1.501(11)
C(12)-N(7)	1.472(10)	C(2')-O(2')	1.414(10)
C(2)-N(1)	1.357(11)	C(2')-C(3')	1.555(11)
C(2)-N(11)	1.344(11)	C(3')-O(3')	1.418(9)
N(3)-C(4)	1.361(10)	C(4')-C(3')	1.535(11)
C(4)-N(9)	1.370(11)	C(4')-O(4')	1.435(9)
C(5)-C(4)	1.376(11)	C(4')-C(5')	1.511(11)
C(5)-N(7)	1.399(11)	C(5')-O(5')	1.425(9)
C(5)-C(6)	1.404(12)	P(2)-Pt(1)	2.2886(19)
C(6)-O(10)	1.232(10)	P(1)-Pt(1)	2.2888(19)
C(6)-N(1)	1.362(11)		

4. Measurement of the stability of 7-MeG$_{Ac}$ by ^{1}H NMR.

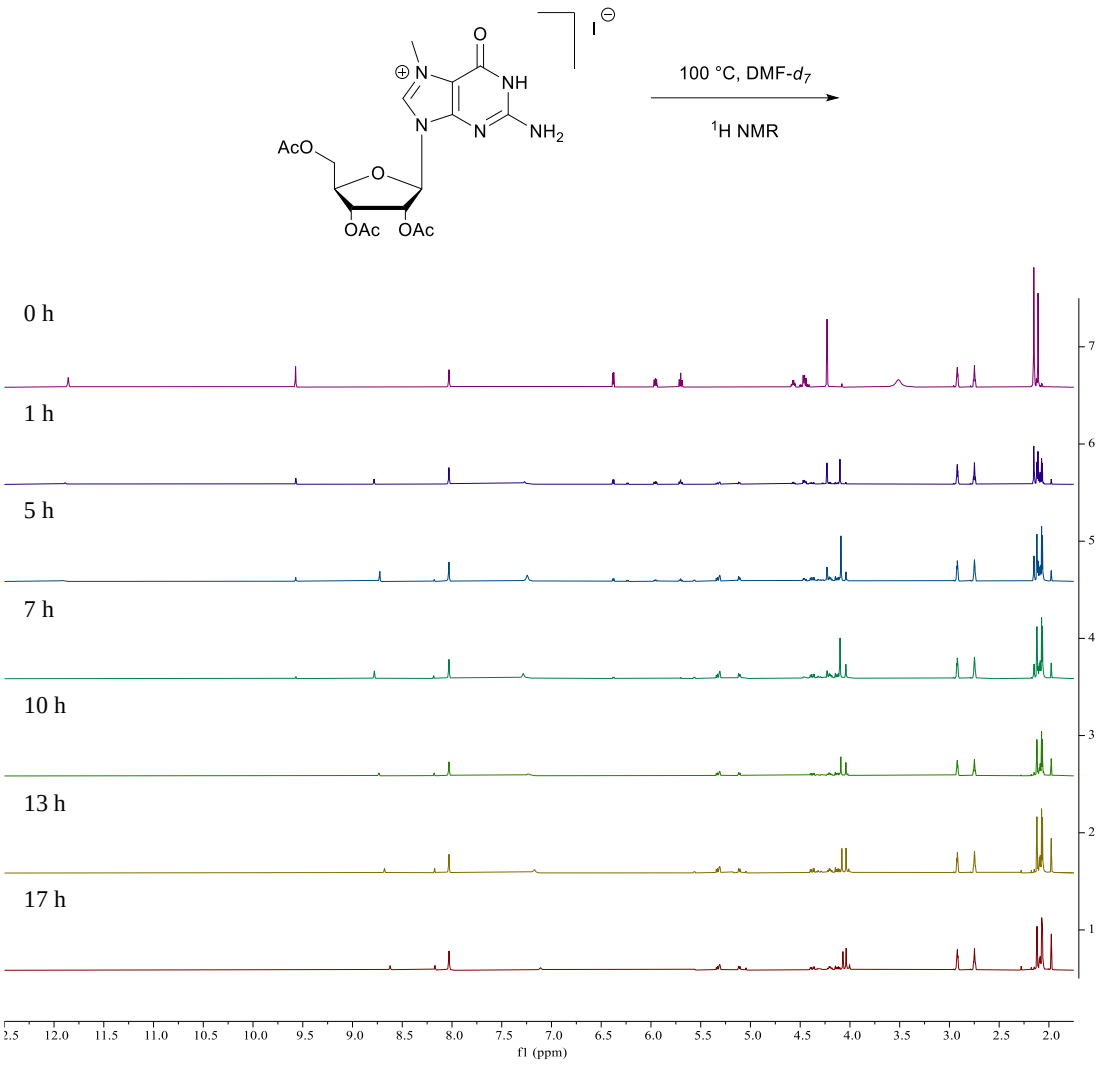


Figure S1. ^{1}H NMR spectrum of **7-MeG$_{Ac}$** in deuterated DMF after heating at 100 °C for different time periods (0 h, 1 h, 5 h, 7 h, 10 h, 13 h and 17 h).

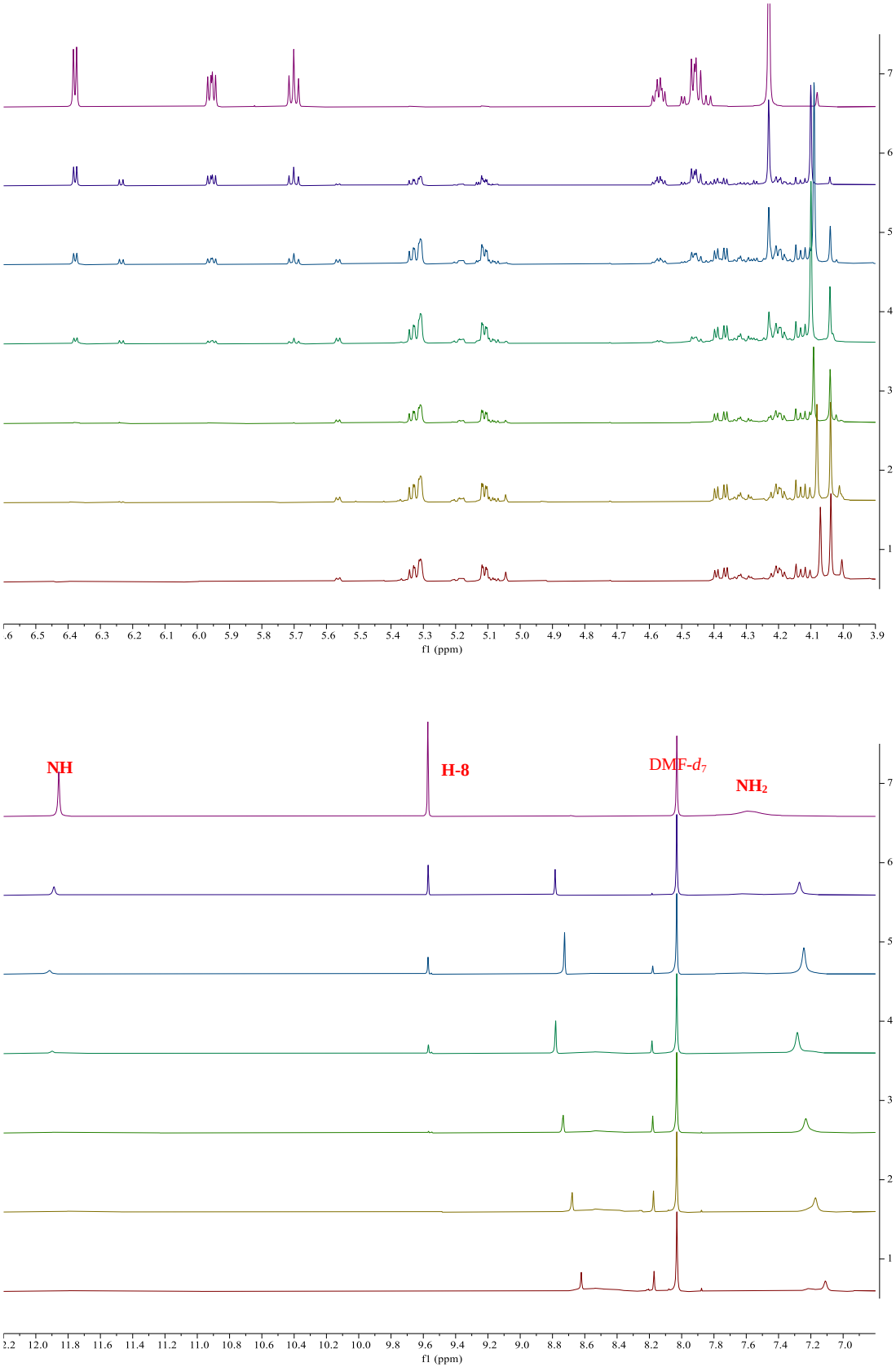


Figure S2. Selected areas (6.6 to 3.9 and 12.2 to 6.8 ppm) of the ^{1}H NMR spectrum of **7-MeG$_{Ac}$** in deuterated DMF, covering the ribose signals and the NH, H-8 and NH_2 groups, after heating at 100 °C for different time periods (0 h, 1 h, 5 h, 7 h, 10 h, 13 h and 17 h).

5. Measurement of the stability of complex 1 by ^{1}H NMR.

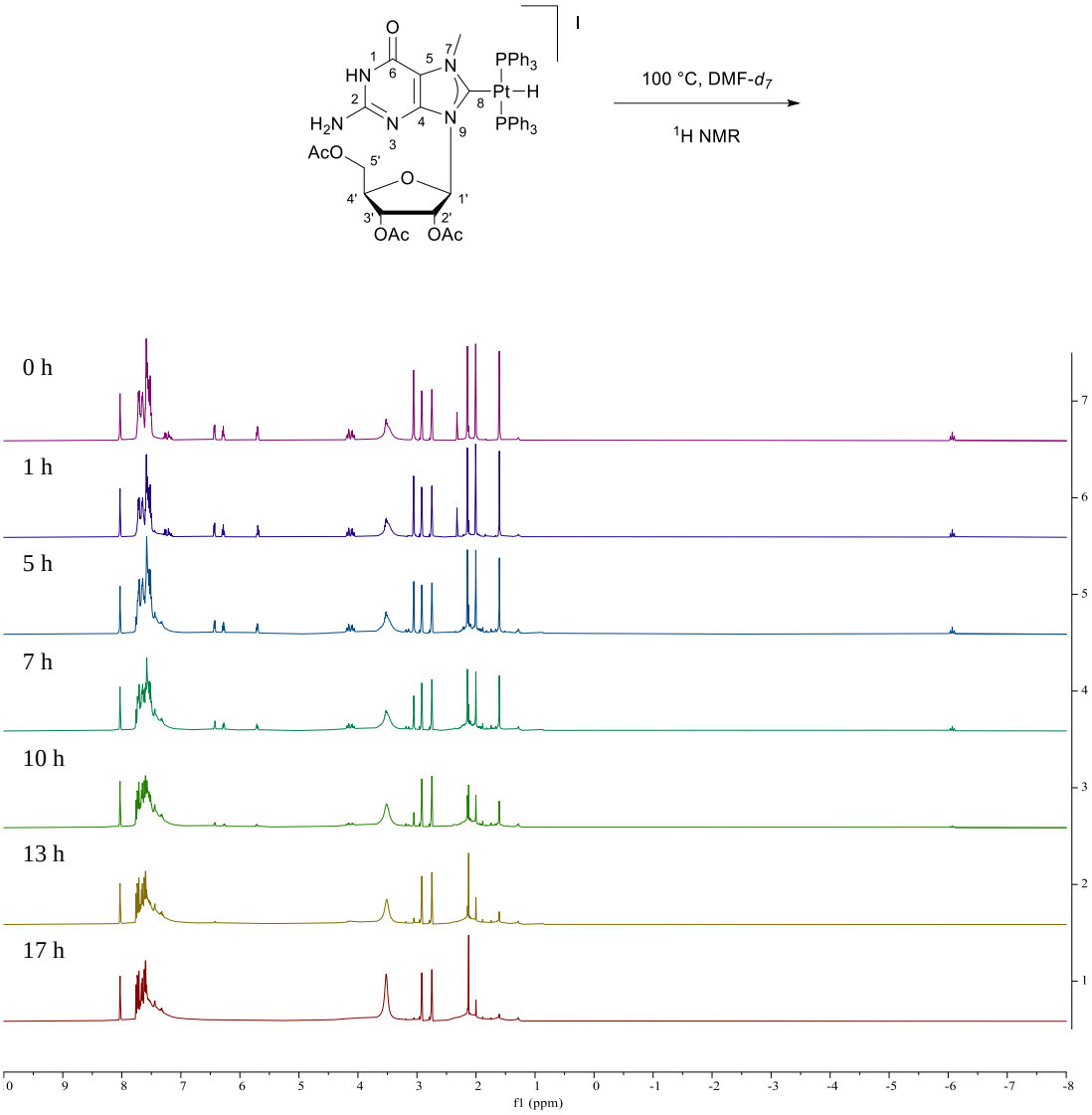


Figure S3. ^{1}H NMR spectrum of complex **1** in deuterated DMF after heating at 100 °C for different time periods (0 h, 1 h, 5 h, 7 h, 10 h, 13 h and 17 h).

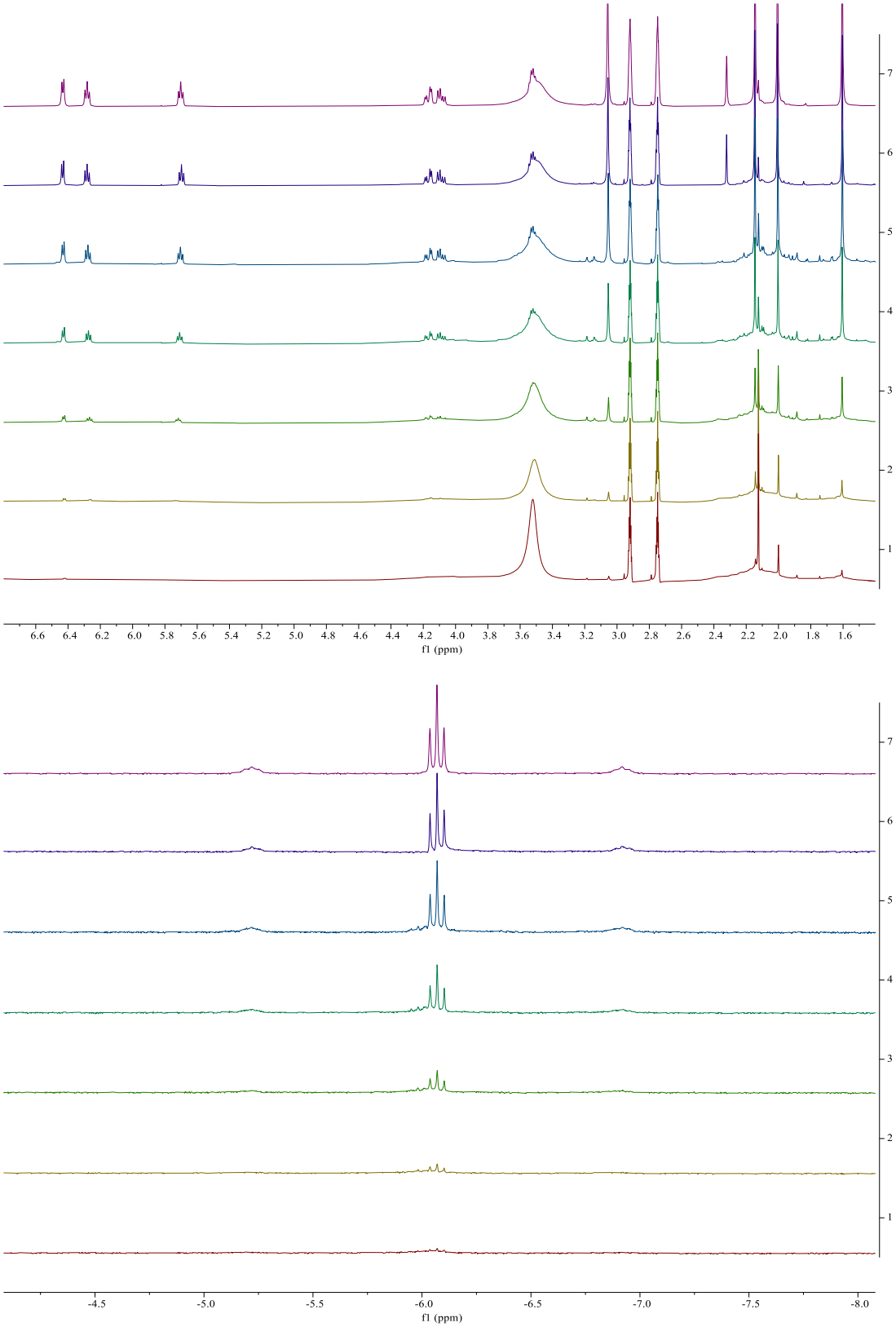
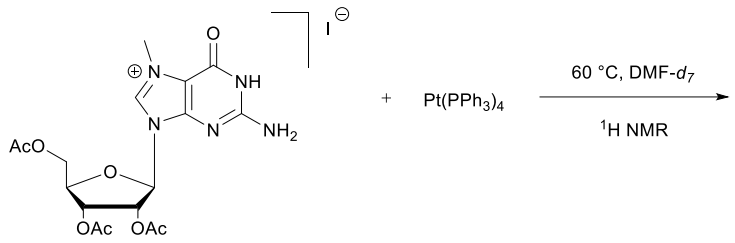
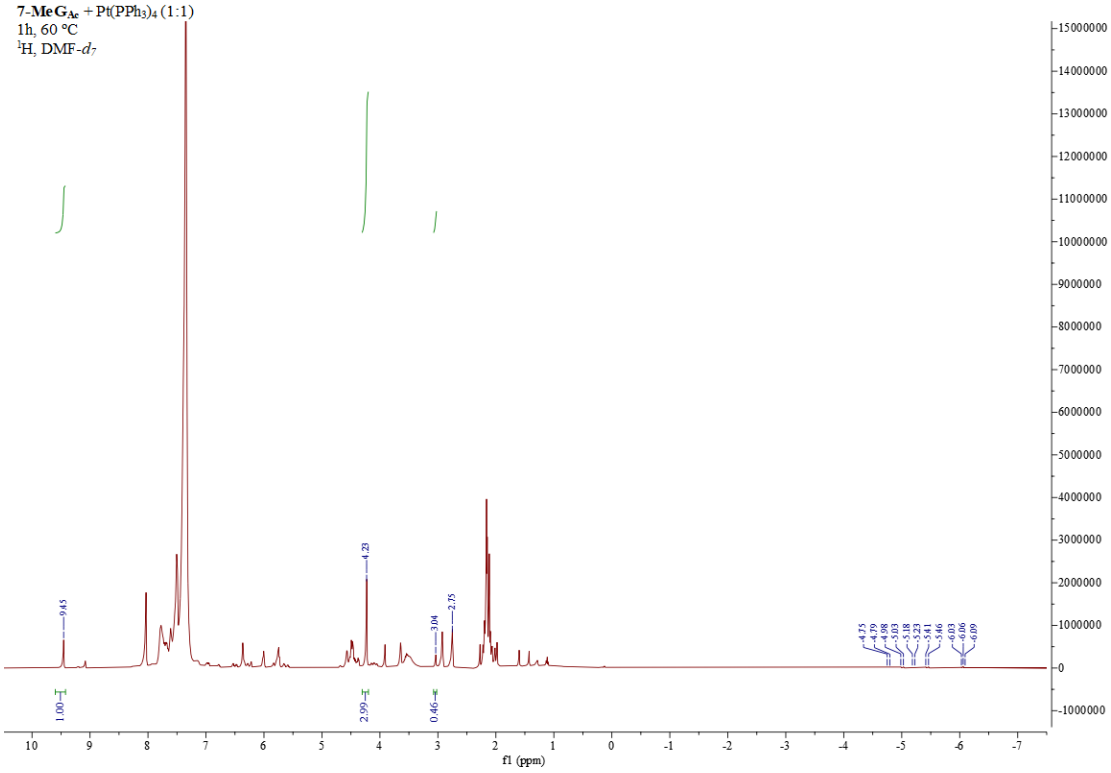


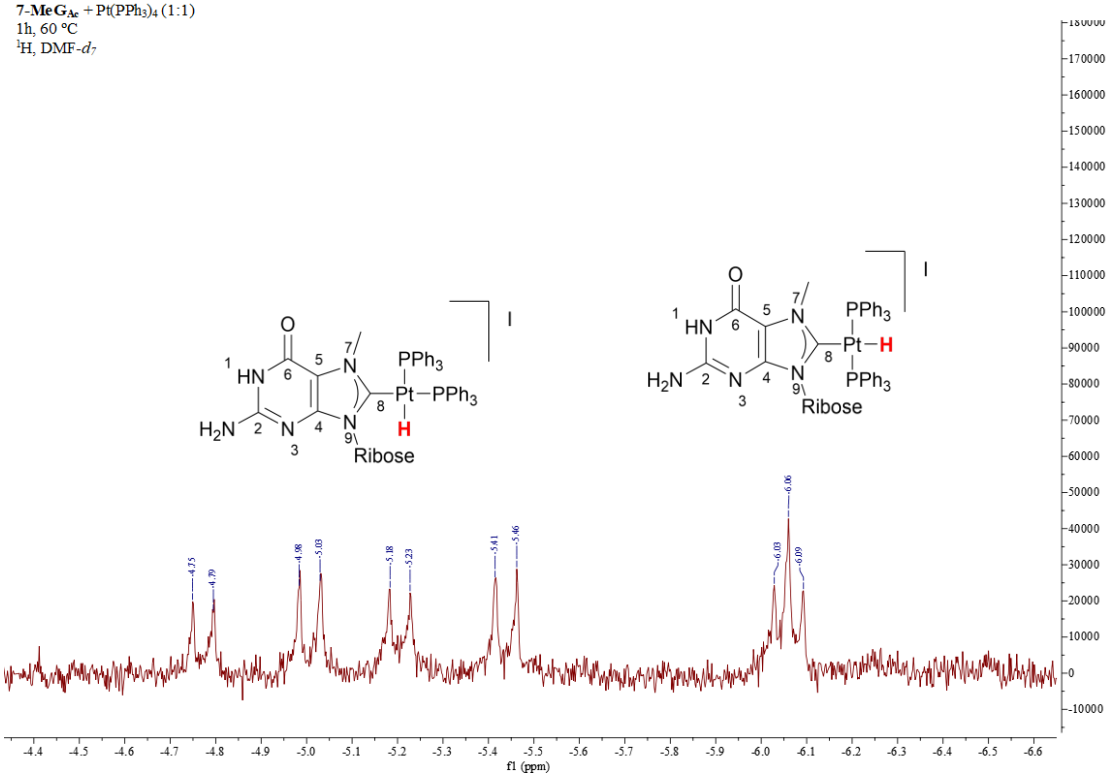
Figure S4. Selected areas (6.8 to 1.4 and -4.1 to -8.1 ppm) of the ^{1}H NMR spectrum of complex **1** in deuterated DMF, covering the guanosine (middle) and the hydride ligands (bottom), after heating at 100 °C for different time periods (0 h, 1 h, 5 h, 7 h, 10 h, 13 h and 17 h).

6. ^{1}H NMR study of the C-H activation of 7-methylguanosinium iodide with $Pt(PPh_3)_4$



7-MeG$_{Ac}$

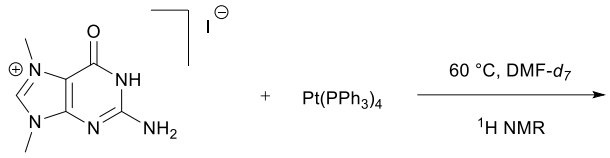




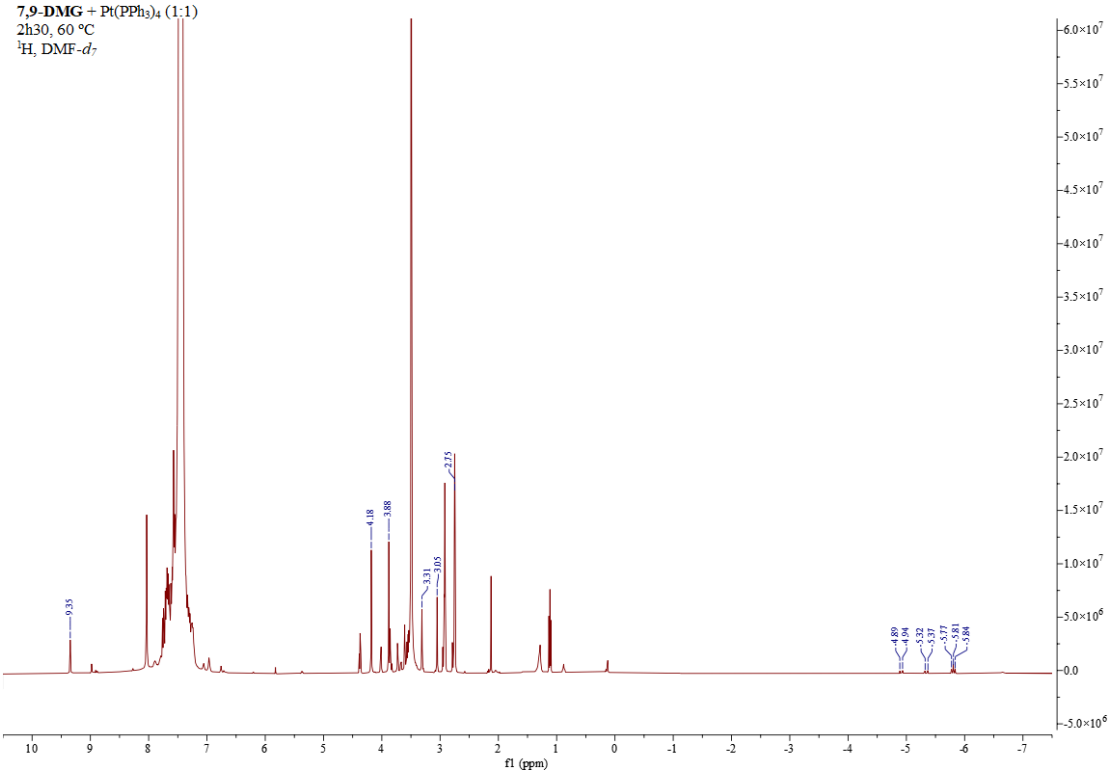
x

Figure S5. ^{1}H NMR spectrum (top) and selected area (-4.33 till -6.65 ppm) covering the hydride region (bottom) of activation reaction of 7-methyl-tri-*O*-acetylguanosinium iodide (**7-MeG$_{Ac}$**) with Pt(PPh$_3$)$_4$ in deuterated DMF, at 60 °C for 1 hour.

7. ^{1}H NMR study of C-H activation of 7,9-dimethylguaninium iodide by $Pt(PPh_3)_4$



7,9-DMG



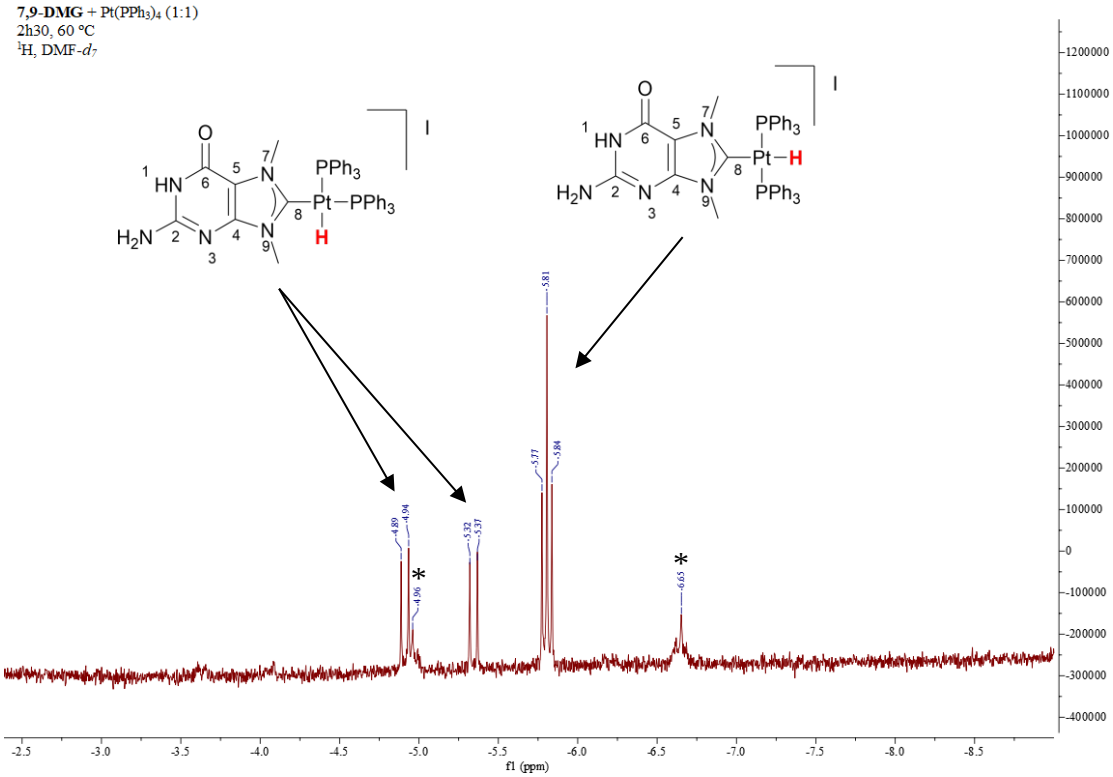
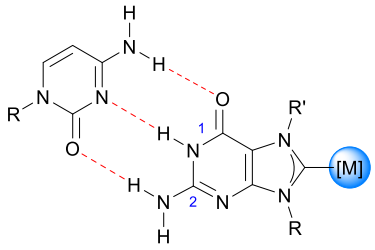


Figure S6. ^{1}H NMR spectrum (top) and selected area (-2.38 to -9.0 ppm) covering the hydride region (bottom) of the activation reaction of the 7,9-dimethylguanosinium iodide (**7,9-DMG**) with $Pt(PPh_3)_4$ in deuterated DMF, at 60 °C for 2h30. * Pt satellites for the *trans* isomer hydride signal.

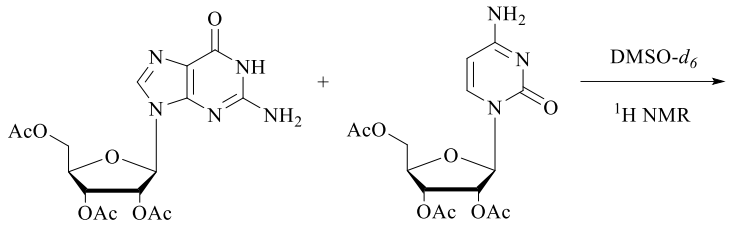
8. ^{1}H NMR studies on Watson-Crick base-pairs

Table S3. Base-pairing interactions measured using ^{1}H NMR in DMSO-d_6 for complexes **1**–**4** and ligand precursors in the presence of increasing amounts of 2',3',5'-tri-*O*-acetylcytidine (**Cy$_{Ac}$**) and cytidine (**Cy**)[a].

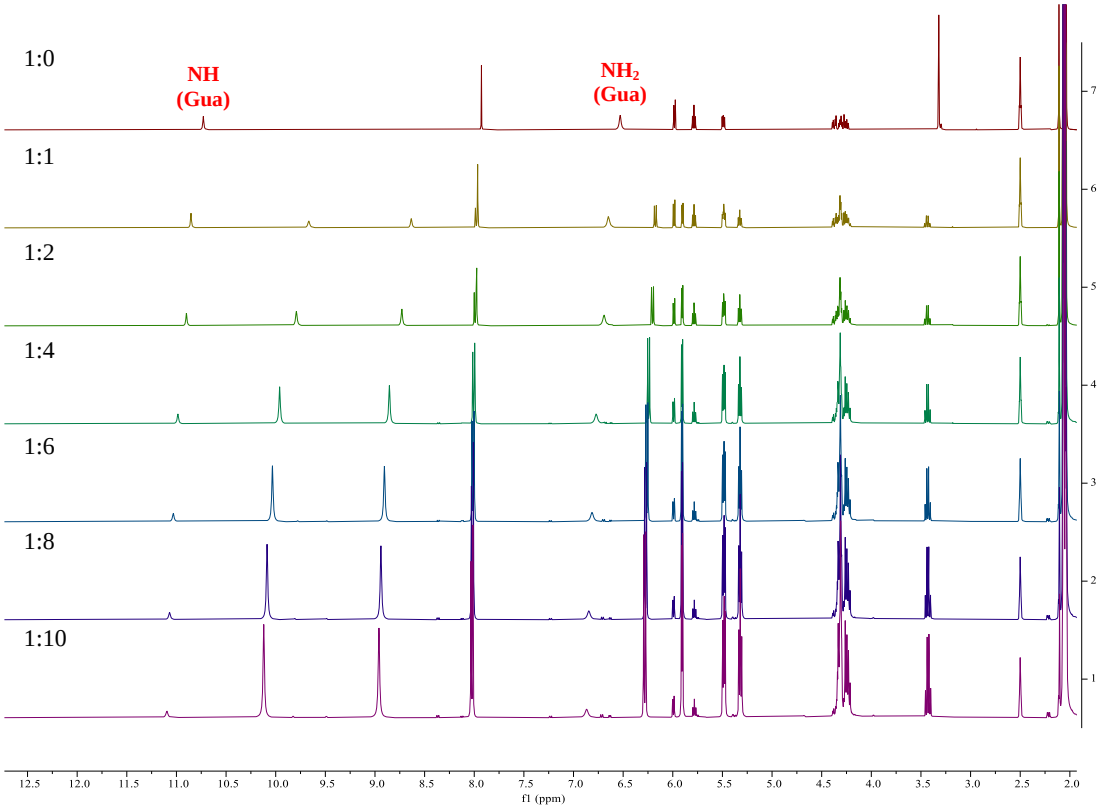


Compound[b]	Group	**Cy** (equiv.) 0	1	2	4	6	8	10	$\Delta\delta_{max}$ / ppm
G$_{Ac}$	1-NH	10.73	10.85 (10.90)	10.90 (11.06)	10.99 (11.34)	11.03 (11.56)	11.07 (11.70)	11.10 (11.98)	0.37 (1.26)
	NH_2	6.53	6.65 (6.61)	6.69 (6.69)	6.77 (6.82)	6.81 (6.93)	6.85 (7.00)	6.87 (7.13)	0.34 (0.60)
7-MeG$_{Ac}$	1-NH	11.78	11.96 (11.90)	12.11 (12.00)	12.15 (12.19)	12.17 (12.31)	12.18 (12.44)	12.19 (12.42)	0.41 (0.65)
	NH_2	7.22	7.41 (7.25)	7.57 (7.34)	7.61 (7.44)	7.63 (7.51)	7.64 (7.57)	7.65 (7.58)	0.43 (0.36)
1	1-NH	n.d.	11.40 (n.d.)	11.47 (n.d.)	11.53 (n.d.)	11.58 (n.d.)	11.60 (n.d.)	11.62 (n.d.)	0.22* (-)
	NH_2	6.87	6.98 (6.85)	7.05 (6.83)	7.11 (6.81)	7.15 (6.78)	7.18 (6.76)	7.19 (6.74)	0.32 (-0.14)
4	1-NH	11.16 (11.17)	11.22 (11.23)	11.25 (11.29)	11.29 (11.40)	11.31 (11.50)	11.33 (11.61)	11.34 (11.70)	0.17 (0.53)
	NH_2	6.85 (6.86)	6.90 (6.88)	6.92 (6.90)	6.96 (6.94)	6.98 (6.97)	6.99 (7.01)	6.99 (7.05)	0.15 (0.19)
1-BF$_4$	1-NH	n.d	11.41 (n.d.)	11.49 (n.d.)	11.55 (n.d.)	11.59 (n.d.)	11.61 (n.d.)	11.62 (n.d.)	0.21[c] (-)
	NH_2	6.94	7.00 (6.87)	7.07 (6.87)	7.14 (6.87)	7.17 (6.87)	7.18 (6.87)	7.20 (6.86)	0.26 (-0.08)
3	1-NH	11.23 (11.21)	11.31 (11.30)	11.35 (11.40)	11.40 (11.57)	11.42 (11.74)	11.44 (11.88)	11.45 (12.01)	0.21 (0.80)
	NH_2	6.83 (6.81)	6.92 (6.84)	6.96 (6.89)	7.01 (6.97)	7.03 (7.04)	7.05 (7.11)	7.06 (7.20)[d]	0.23 (0.39)
2	1-NH	11.19	(11.31)	(11.42)	(11.64)	(11.87)	(11.97)	(12.12)	(0.93)
	NH_2	6.81	(6.87)	(6.93)	(7.04)	(7.15)	(n.d)	(7.29)	(0.48)
7-MeG	1-NH	11.69	-	-	-	-	-	(12.51)	(0.82)
	NH_2	7.21	-	-	-	-	-	(7.64)	(0.43)
G	1-NH	(10.61)	(10.85)	-	-	-	-	(11.80)	(1.19)
	NH_2	(6.44)	(6.55)	-	-	-	-	(7.00)	(0.56)

[a] the values between parentheses correspond to the experiment with unprotected cytidine.
[b] [guanosine derivative] = 20 mM.
[c] since the signal for the NH group of **1** is not detected (n.d.) before the addiction of the cytidine derivative, the $\Delta\delta_{max}$ corresponds to the difference between the chemical shifts of this NH group for 1 and 10 equivalents of 2',3',5'-tri-*O*-acetylcytidine.
[d] estimated value – the signal corresponding to the NH_2 group of guanosine is under the NH_2 signal of cytidine. Since no shoulder is observed in these signals, the estimated value corresponds to the average of the two cytidine peaks.


O
NH
N
N
N
NH2
AcO
O
OAc OAc
+
NH2
N
N
O
AcO
O
OAc OAc
DMSO-d6
1H NMR

G_{Ac}


1:0
NH
(Gua)
NH2
(Gua)
1:1
1:2
1:4
1:6
1:8
1:10
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0
f1 (ppm)
7
6
5
4
3
2
1

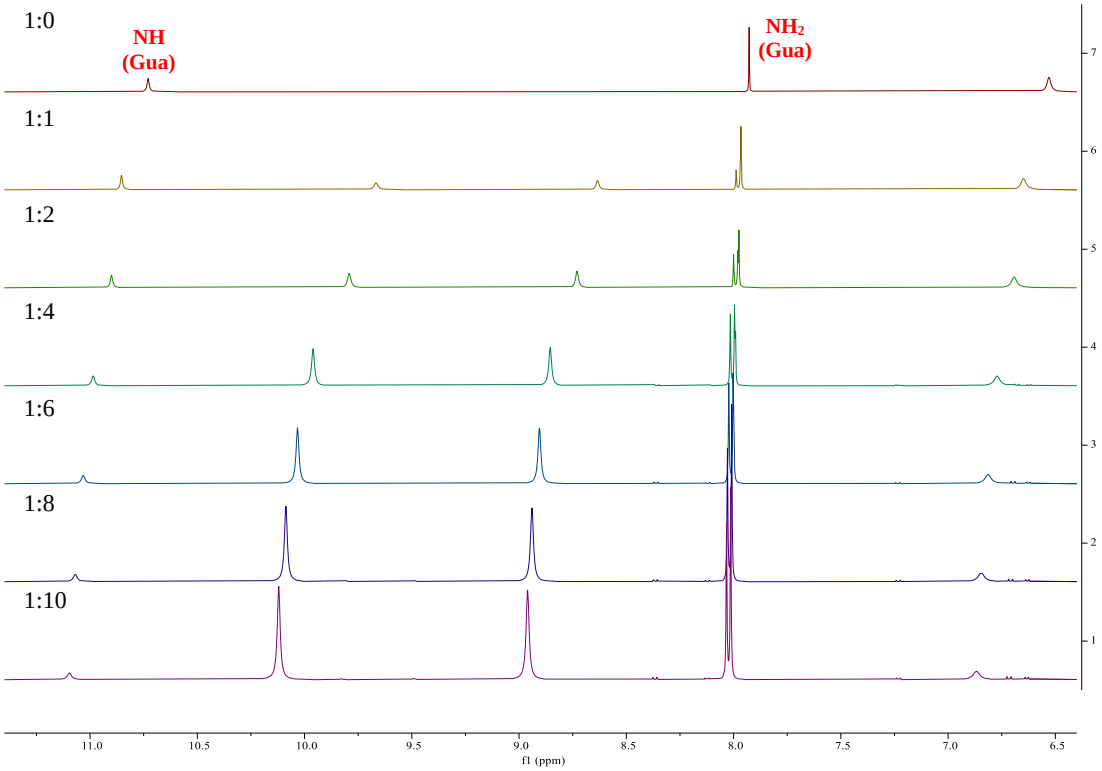
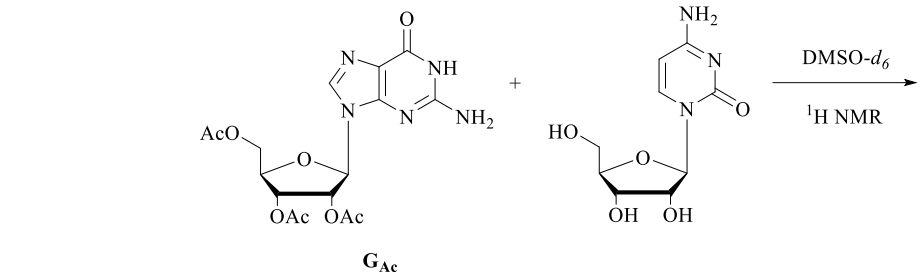
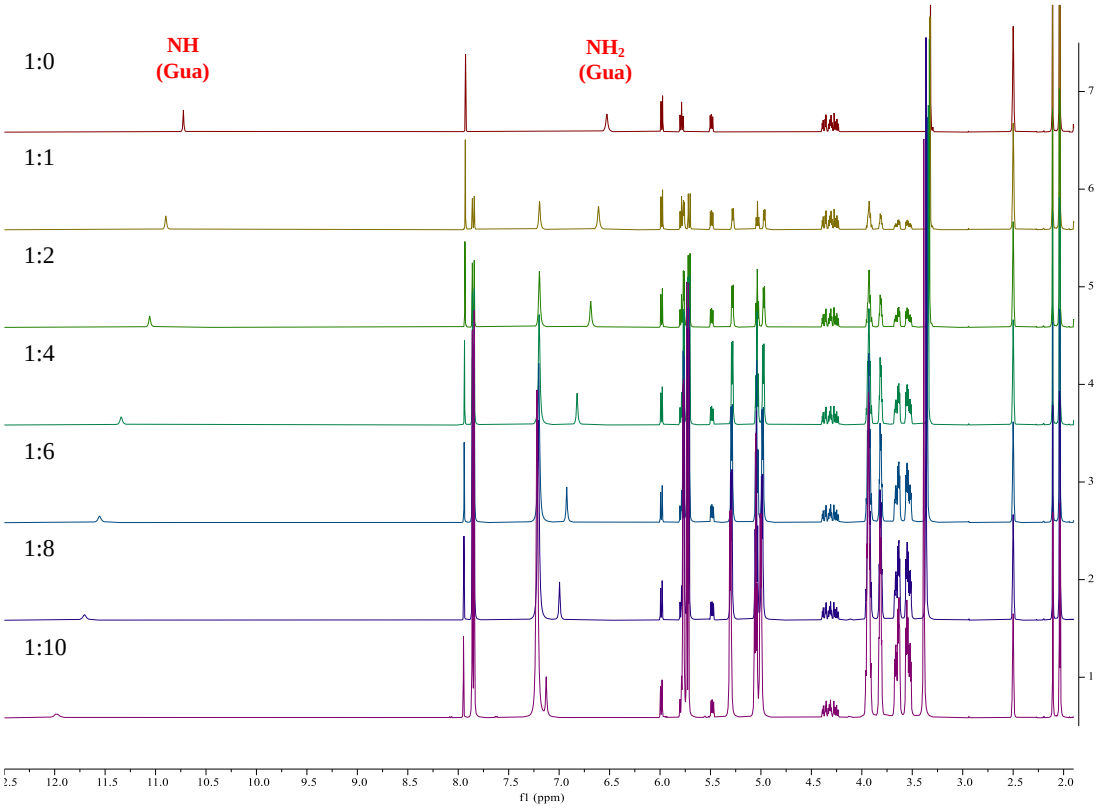


Figure S7. ^{1}H NMR spectrum (top) and selected area covering the NH and NH_2 groups (11.4 to 6.4) of compound $\mathbf{G_{Ac}}$ in deuterated DMSO at room temperature and in presence of different concentrations of $\mathbf{Cy_{Ac}}$ (0, 1, 2, 4, 6, 8 and 10 equivalents in respect with the amount of the guanosine derivative $\mathbf{G_{Ac}}$). $c_{\text{compound } \mathbf{G_{Ac}}}$ = 0.02M.


AcO
OAc
OAc
O
N
NH
N
N
NH2
+
HO
OH
OH
NH2
N
N
O
DMSO-d6
1H NMR

G_{Ac}


NH
(Gua)
NH2
(Gua)
1:0
1:1
1:2
1:4
1:6
1:8
1:10
f1 (ppm)

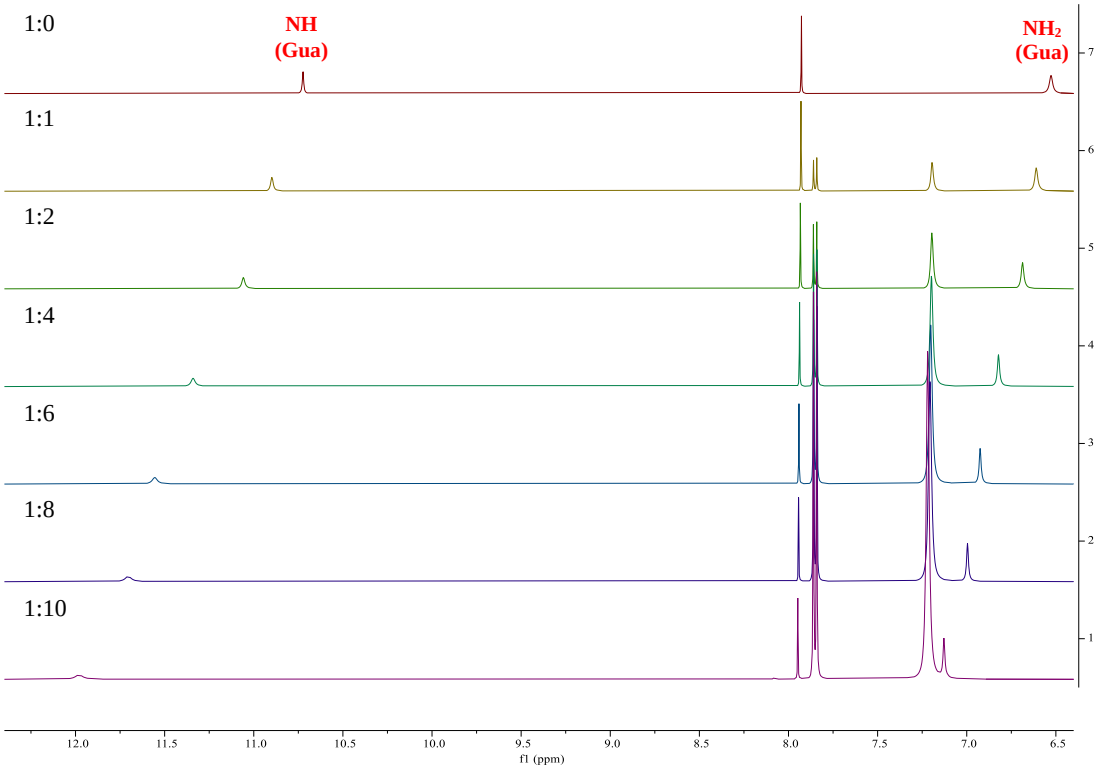
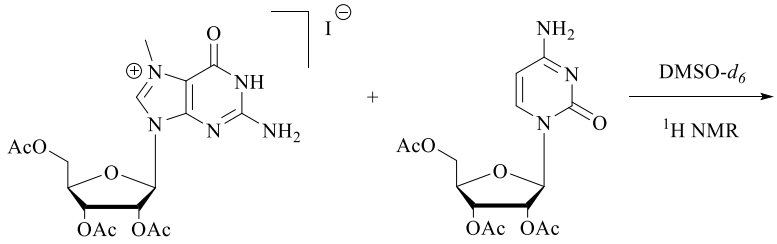
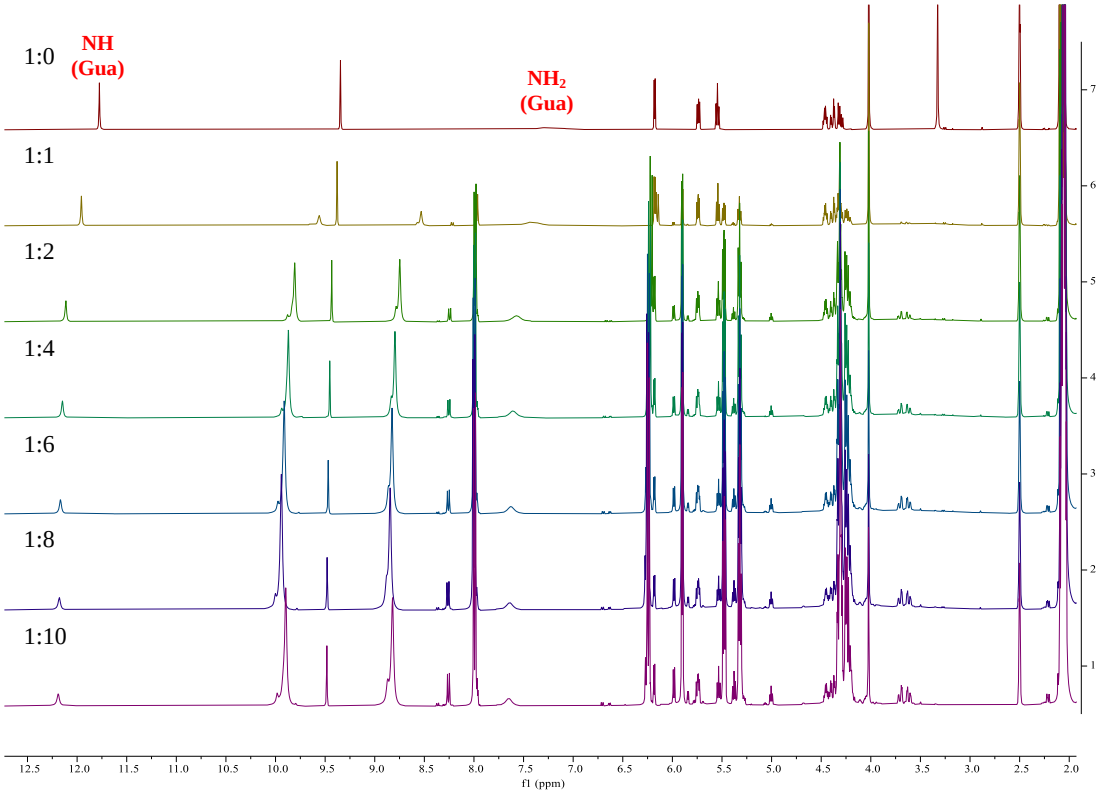


Figure S8. ^{1}H NMR spectrum (top) and selected area covering the NH and NH_2 groups (12.4 to 6.4) of compound $\mathbf{G_{Ac}}$ in deuterated DMSO at room temperature and in presence of different concentrations of **Cy** (0, 1, 2, 4, 6, 8 and 10 equivalents in respect with the amount of the guanosine derivative $\mathbf{G_{Ac}}$). $c_{\text{compound } \mathbf{G_{Ac}}}$ = 0.02M.


I
O
NH
N
N
N
NH2
AcO
O
OAc
OAc
+
NH2
N
N
O
AcO
O
OAc
OAc
DMSO-d6
1H NMR

7-MeG$_{Ac}$


1:0
NH
(Gua)
NH2
(Gua)
1:1
1:2
1:4
1:6
1:8
1:10
12.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
f1 (ppm)

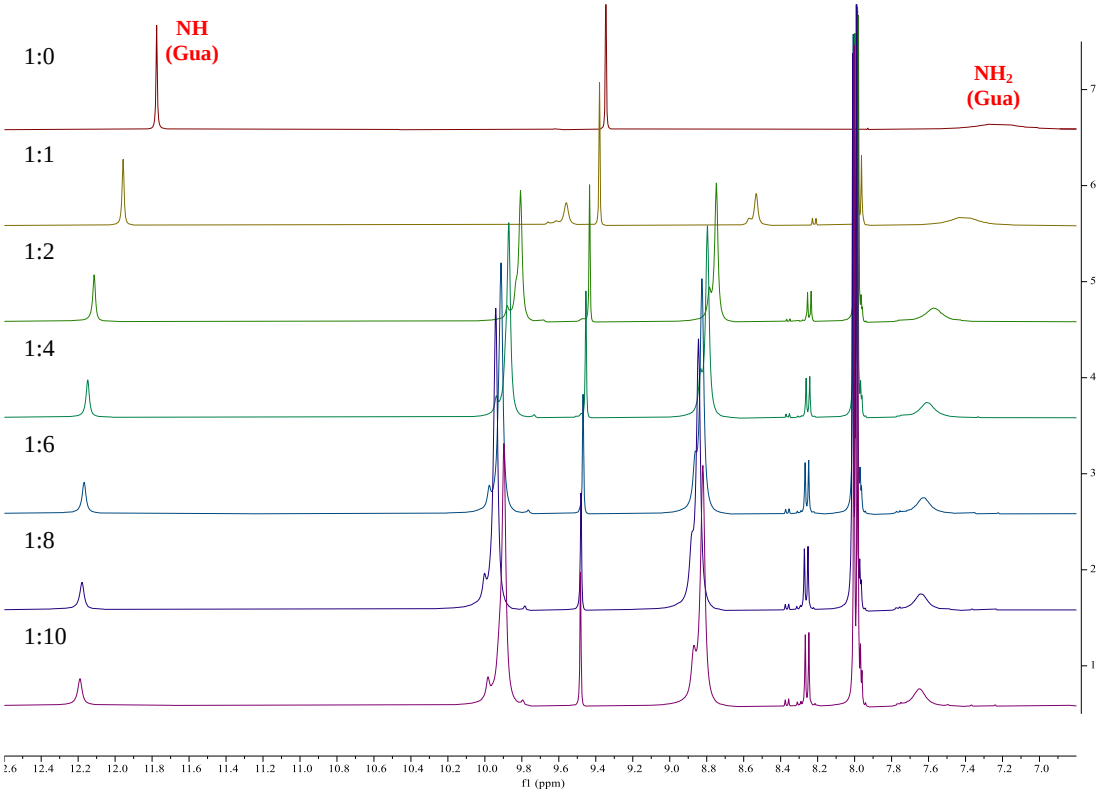
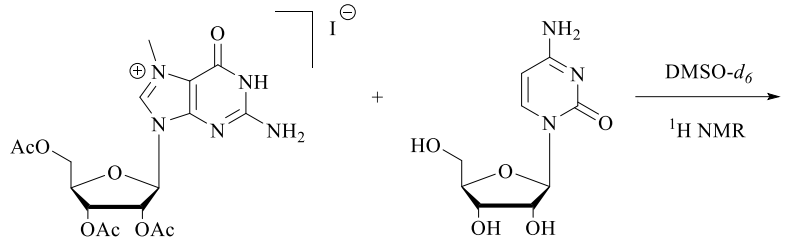
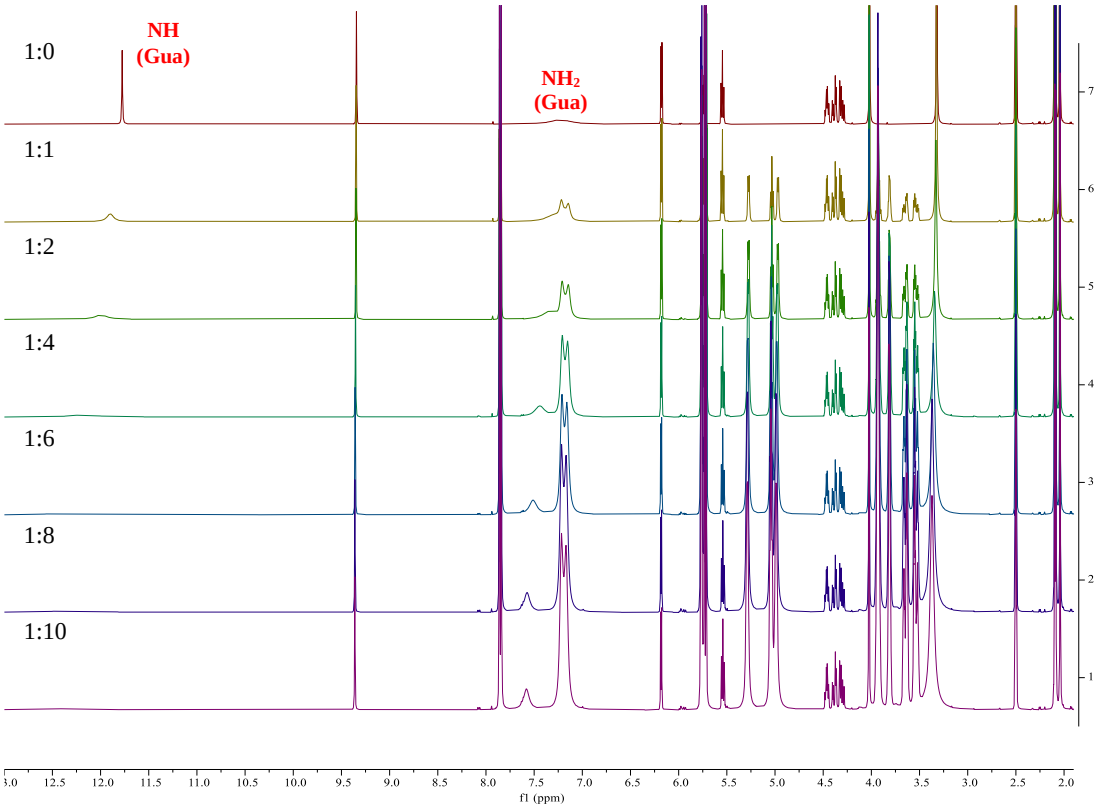


Figure S9. ^{1}H NMR spectrum (top) and selected area covering the NH and NH_2 groups (12.6 to 6.8) of compound **7-MeG$_{Ac}$** in deuterated DMSO at room temperature and in presence of different concentrations of **Cy$_{Ac}$** (0, 1, 2, 4, 6, 8 and 10 equivalents in respect with the amount of the guanosine derivative **7-MeG$_{Ac}$**). $c_{\text{compound 7-MeG}_{Ac}}$ = 0.02M.


I
NH2
DMSO-d6
1H NMR
AcO
OAc
OAc
HO
OH
OH

7-MeGAc


NH
(Gua)
NH2
(Gua)
1:0
1:1
1:2
1:4
1:6
1:8
1:10
f1 (ppm)

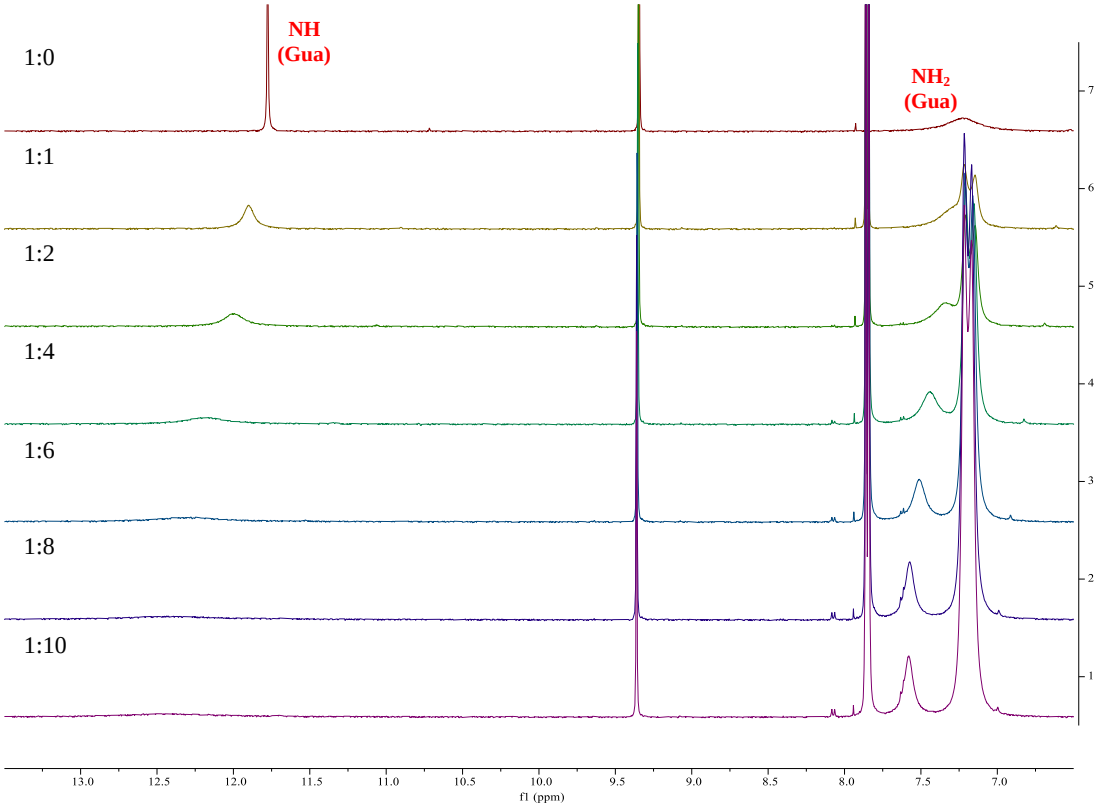
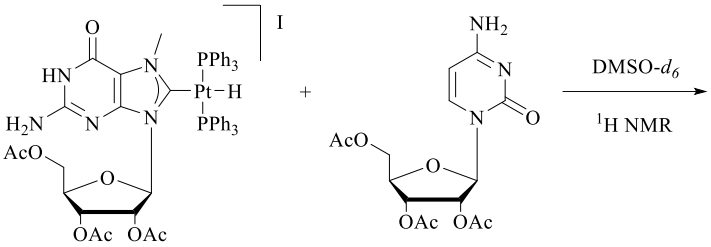
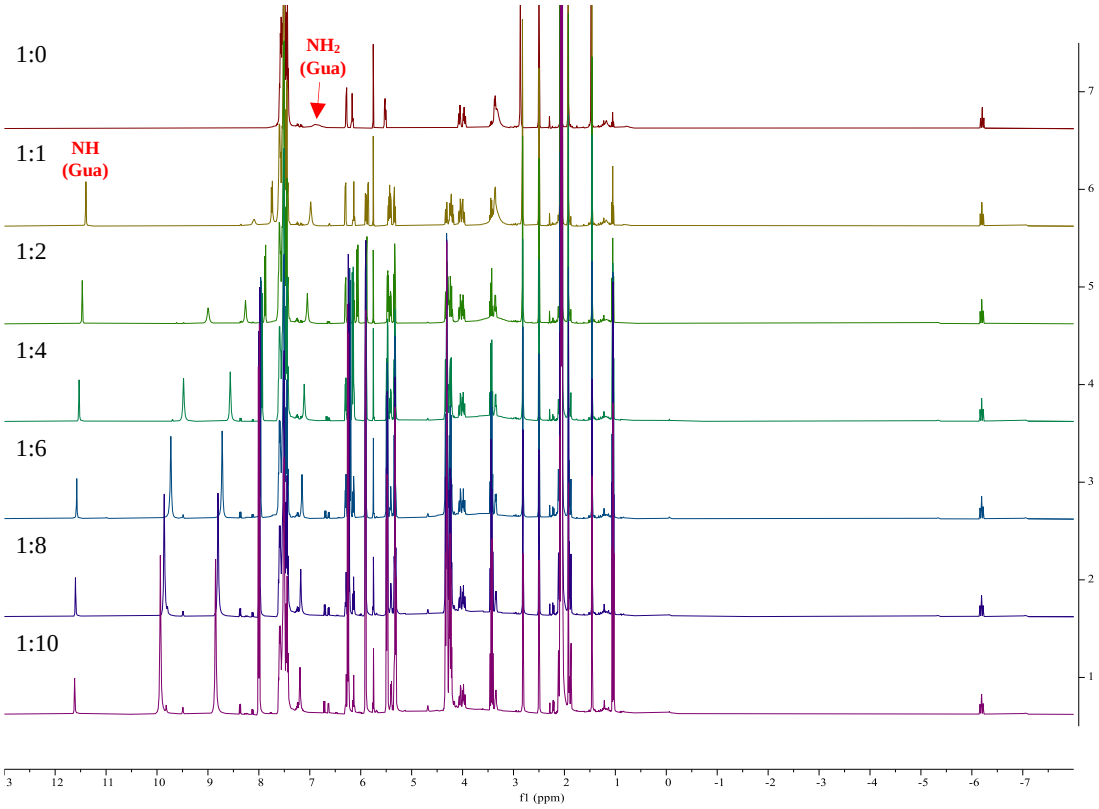


Figure S10. ^{1}H NMR spectrum (top) and selected area covering the NH and NH_2 groups (13.5 to 6.5) of compound **7-MeG$_{Ac}$** in deuterated DMSO at room temperature and in presence of different concentrations of **Cy** (0, 1, 2, 4, 6, 8 and 10 equivalents in respect with the amount of the guanosine derivative **7-MeG$_{Ac}$**). $c_{\text{compound 7-MeG}_{Ac}}$ = 0.02M.


I
PPh3
Pt−H
PPh3
HN
H2N
N
N
N
O
AcO
O
OAc OAc
+
NH2
N
N
O
AcO
O
OAc OAc
DMSO-d6
1H NMR

1


1:0
NH2
(Gua)
1:1
NH
(Gua)
1:2
1:4
1:6
1:8
1:10
f1 (ppm)

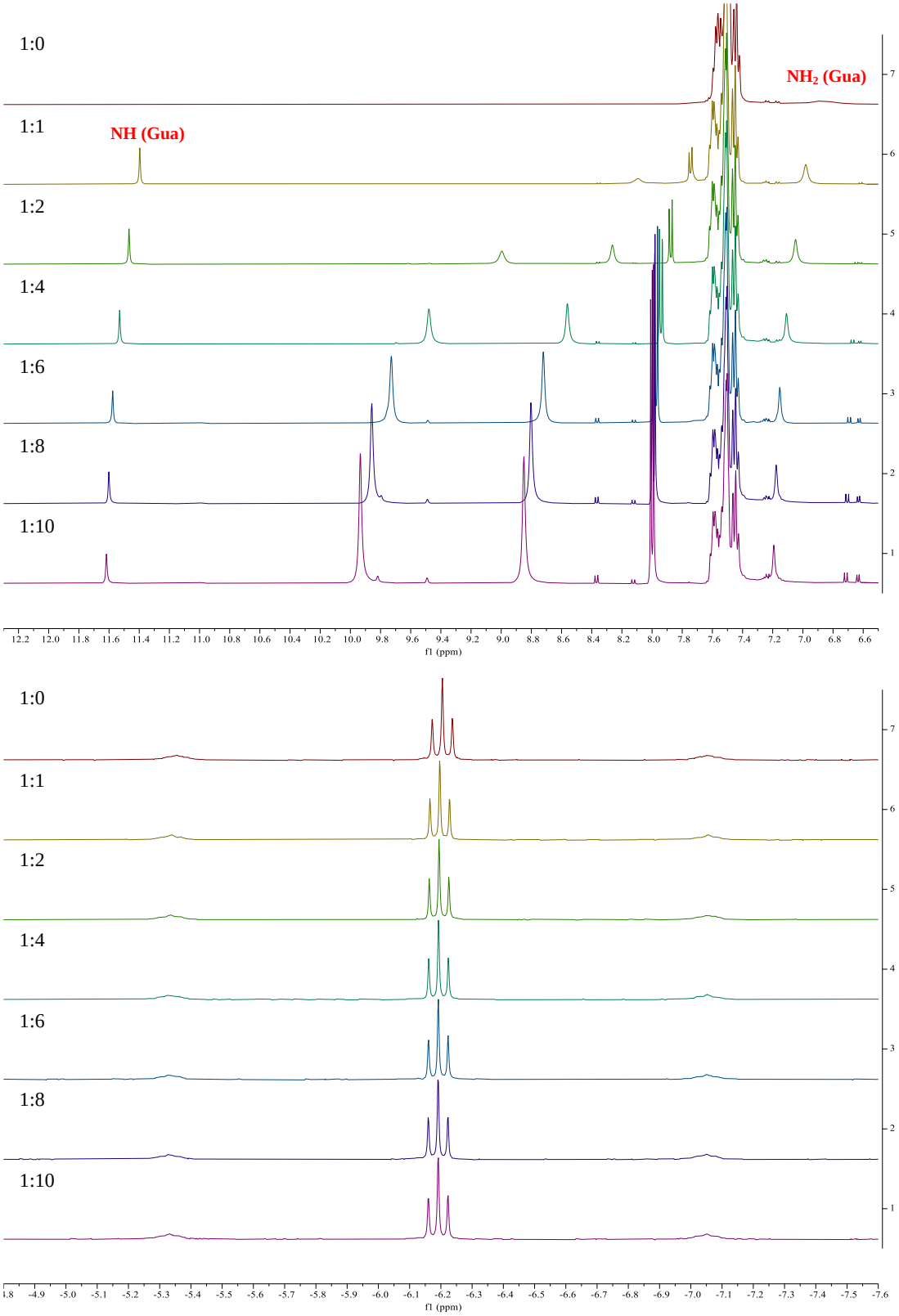
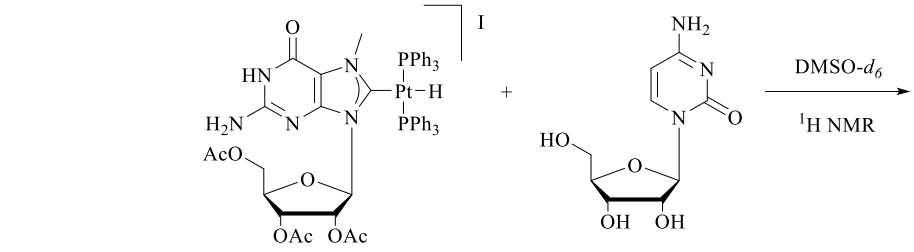
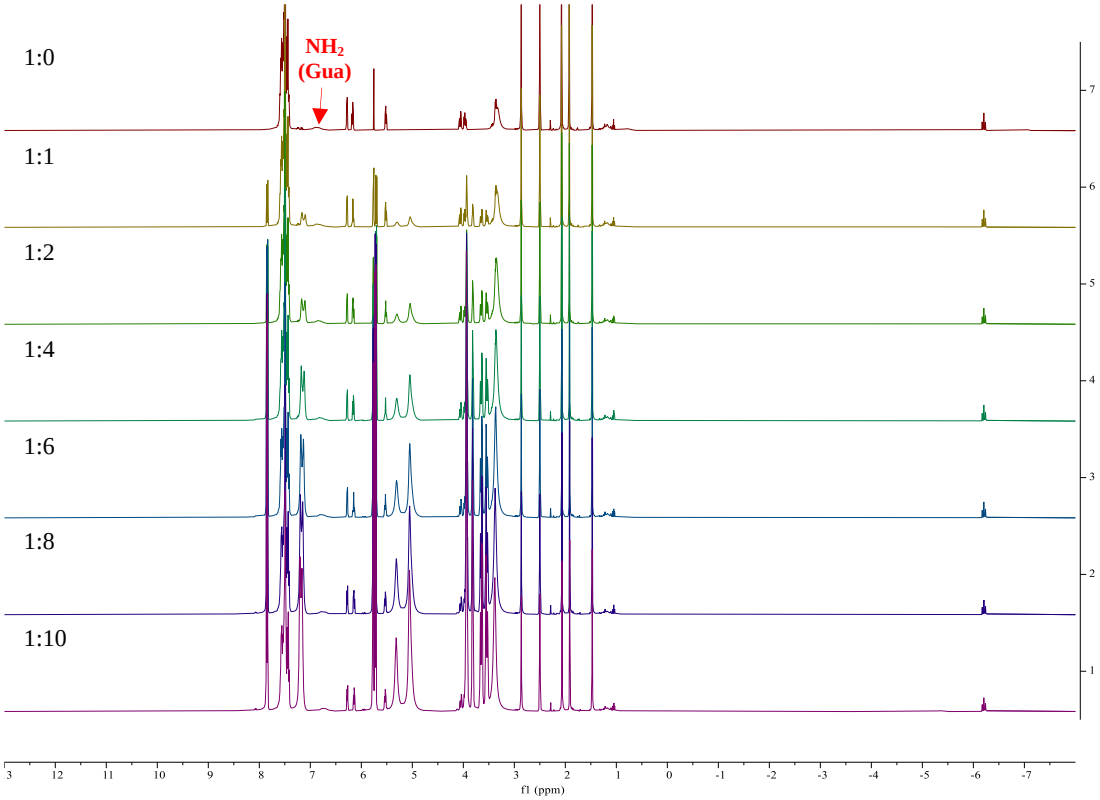


Figure S11. ^{1}H NMR spectrum (top) and selected areas (12.3 to 6.5 ppm; -4.8 to -7.6 ppm) covering the NH and NH_2 groups (middle) and the hydride ligand (bottom) of complex **1** in deuterated DMSO at room temperature and in presence of different concentrations of **Cy$_{Ac}$** (0, 1, 2, 4, 6, 8 and 10 equivalents in respect with the amount of the guanosine derivative **1**). $c_{complex\ 1}$ = 0.02M


I
PPh3
Pt−H
PPh3
HN
H2N
N
N
O
AcO
O
OAc OAc
+
NH2
N
N
O
HO
O
OH OH
DMSO-d6
1H NMR

1


1:0
NH2
(Gua)
1:1
1:2
1:4
1:6
1:8
1:10
f1 (ppm)

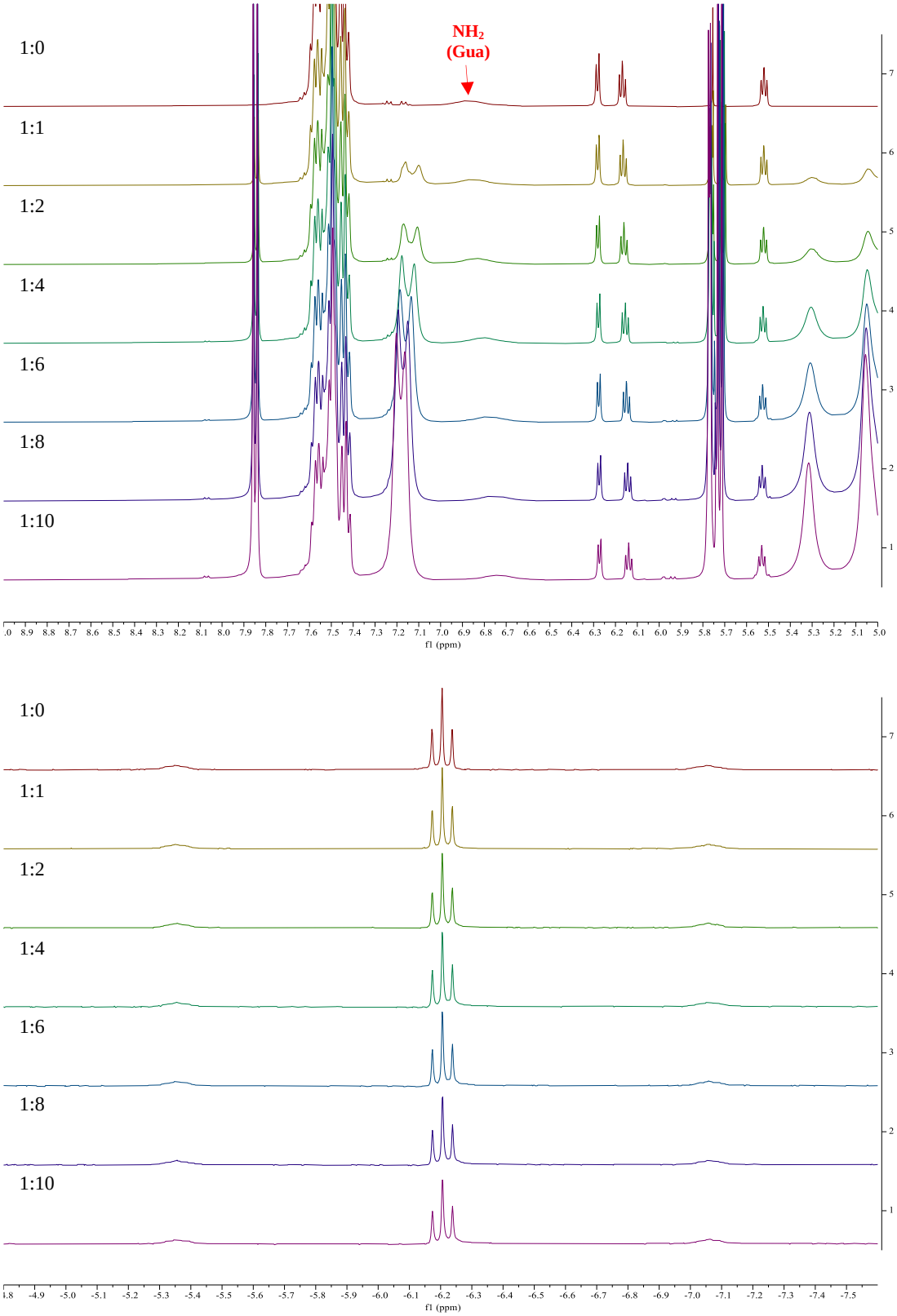
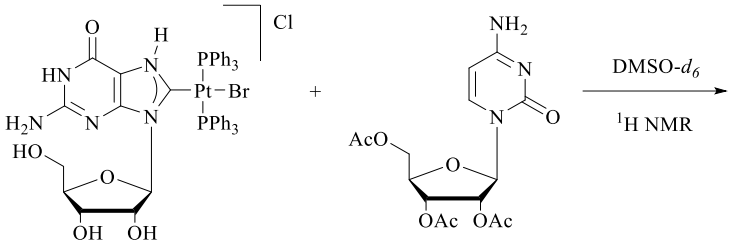
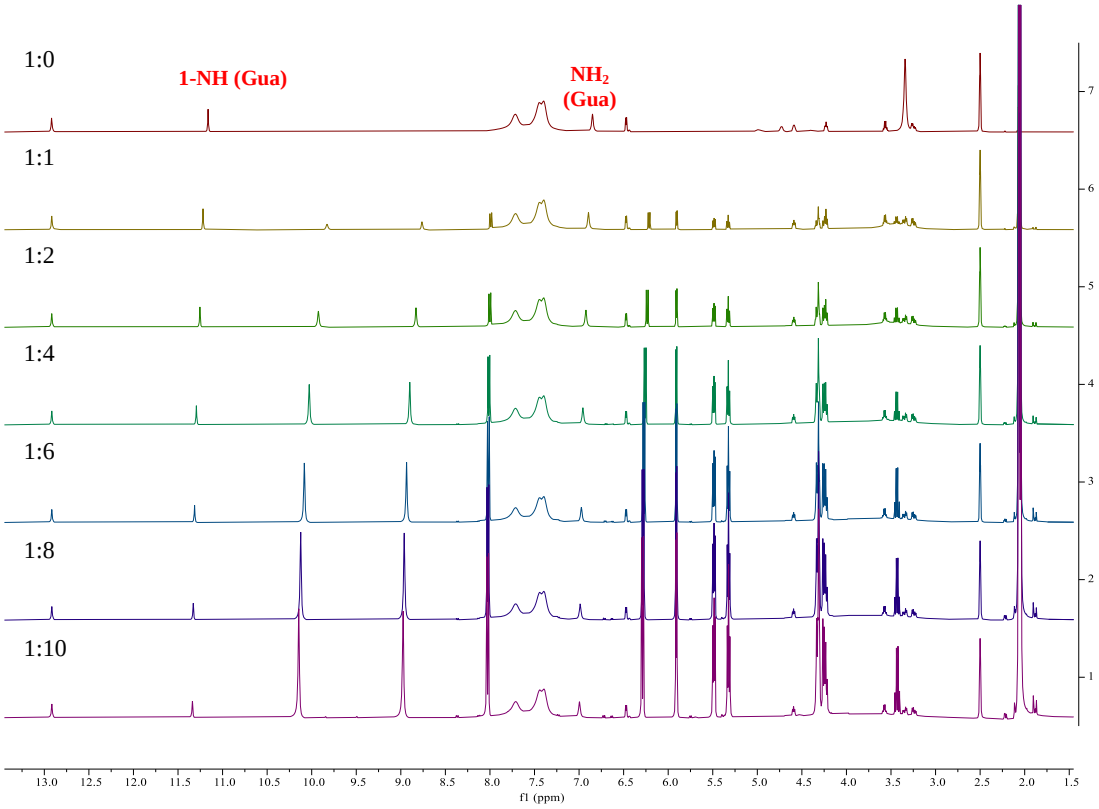


Figure S12. ^{1}H NMR spectrum (top) and selected areas (9.0 to 5.0 ppm; -4.8 to -7.6 ppm) covering the NH_2 groups (middle) and the hydride ligand (bottom) of complex **1** in deuterated DMSO at room temperature and in presence of different concentrations of **Cy** (0, 1, 2, 4, 6, 8 and 10 equivalents in respect with the amount of the guanosine derivative **1**). $c_{complex\ 1}$ = 0.02M.


Cl
PPh3
Pt−Br
PPh3
HN
H2N
HO
OH
OH
NH2
AcO
OAc
OAc
DMSO-d6
1H NMR

4


1:0
1-NH (Gua)
NH2
(Gua)
1:1
1:2
1:4
1:6
1:8
1:10
f1 (ppm)

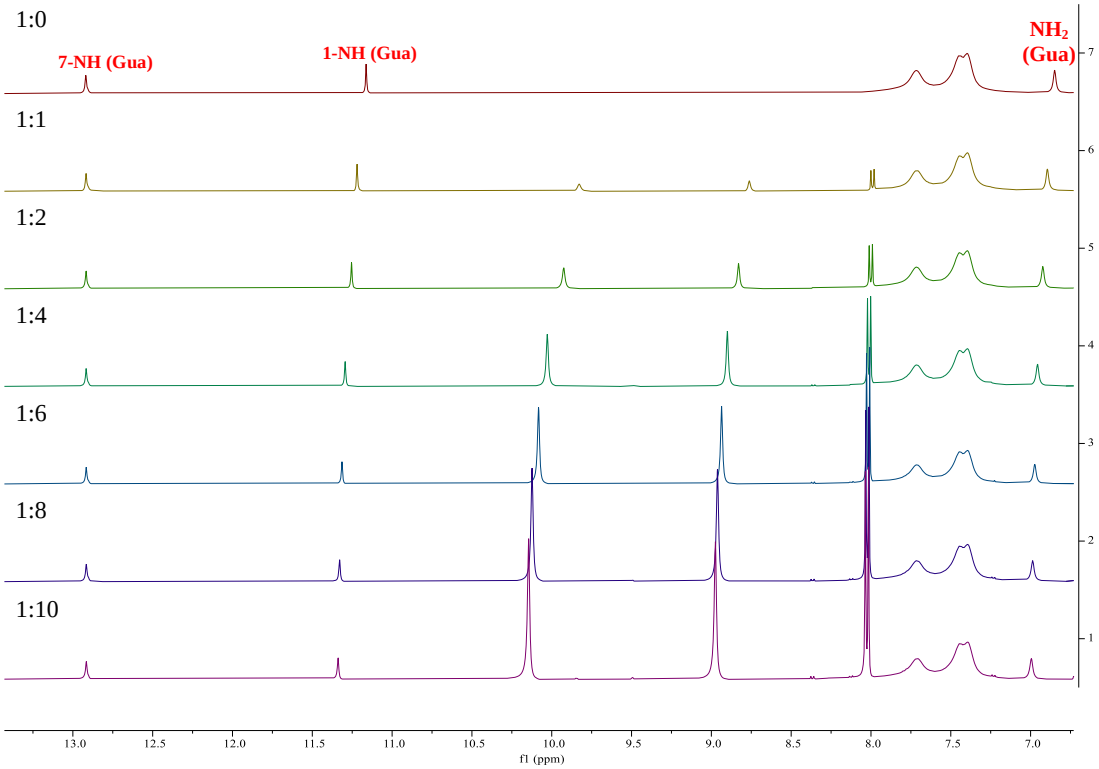
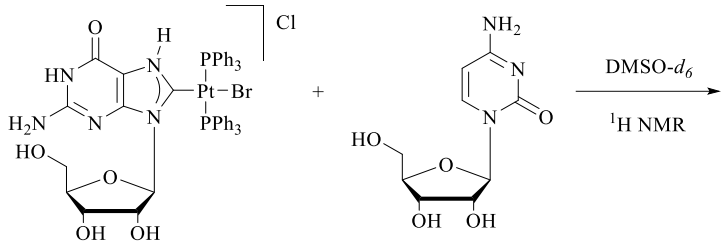
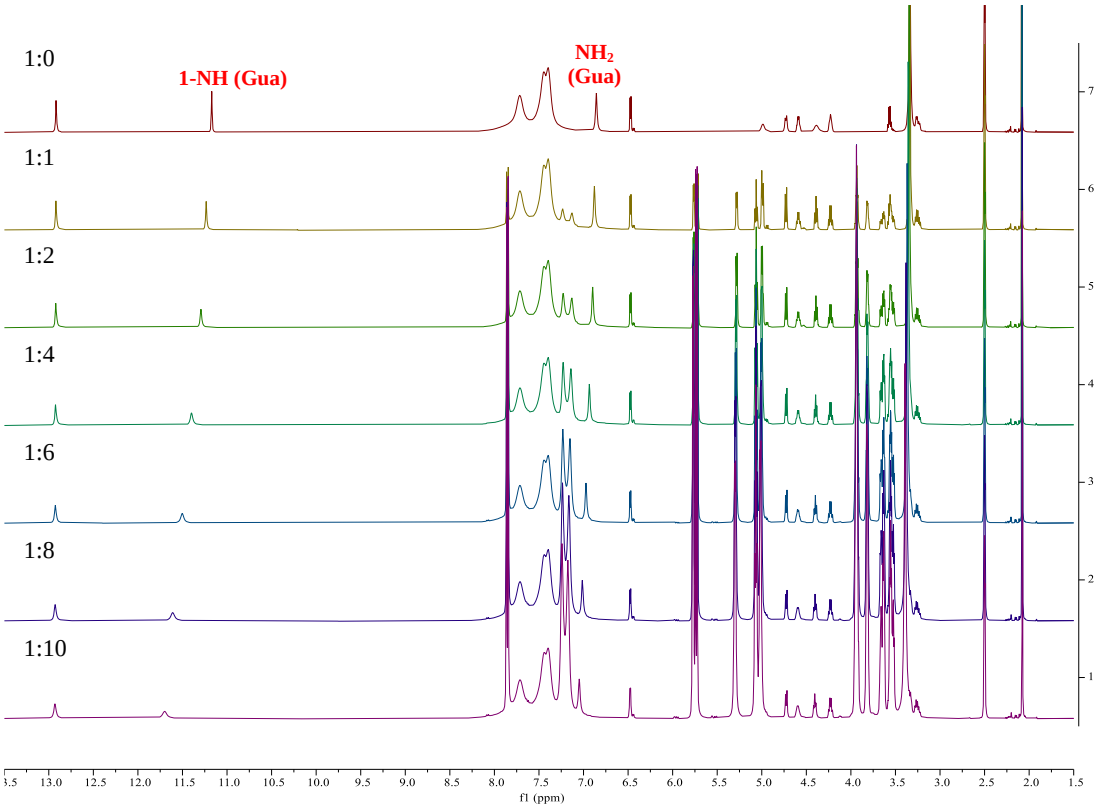


Figure S13. ^{1}H NMR spectrum (top) and selected area (13.5 to 6.5 ppm) covering the NH and NH_2 groups (bottom) of complex **4**, previously published by our group,[S4] in deuterated DMSO at room temperature and in presence of different concentrations of **Cy_{Ac}** (0, 1, 2, 4, 6, 8 and 10 equivalents in respect with the amount of the guanosine derivative **4**). $c_{complex\ 4}$ = 0.02M


Cl
PPh3
Pt−Br
PPh3
NH2
DMSO-d6
1H NMR

4


1:0
1-NH (Gua)
NH2
(Gua)
1:1
1:2
1:4
1:6
1:8
1:10
f1 (ppm)

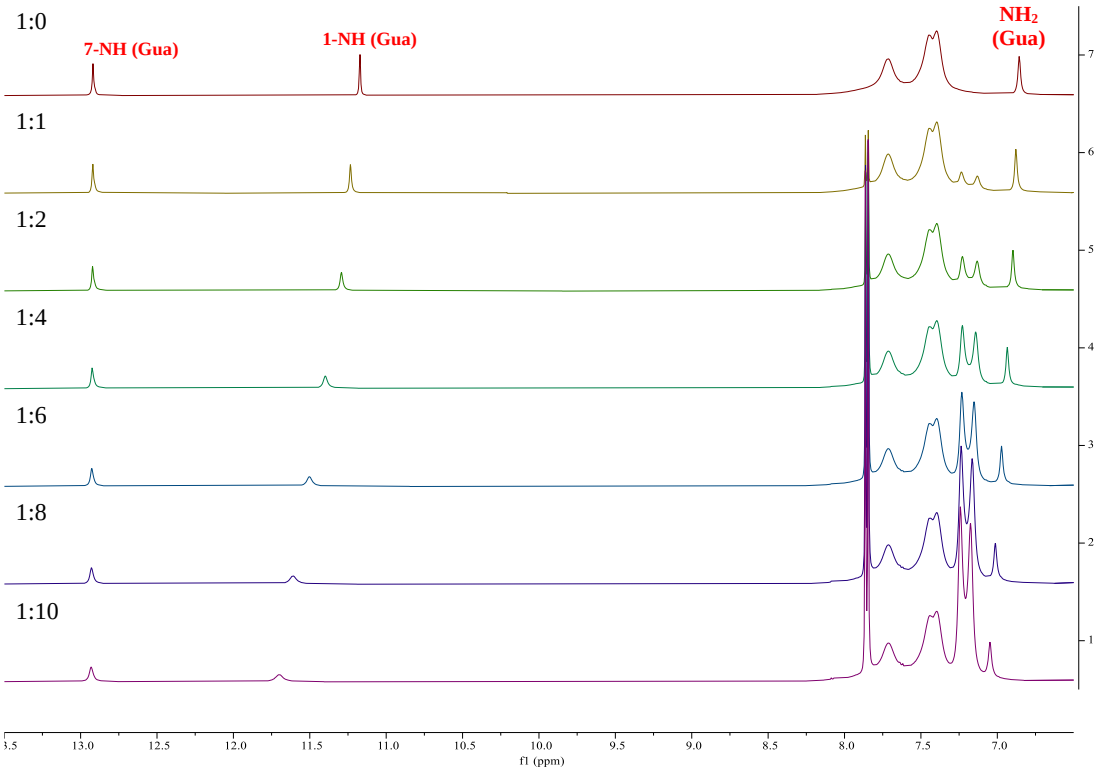
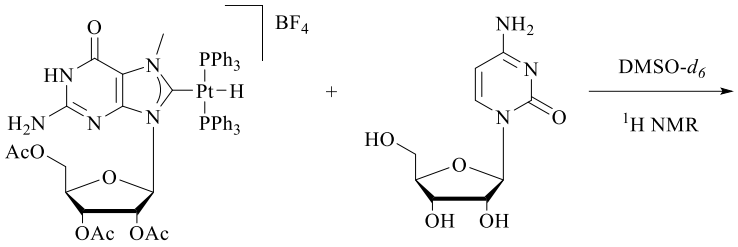
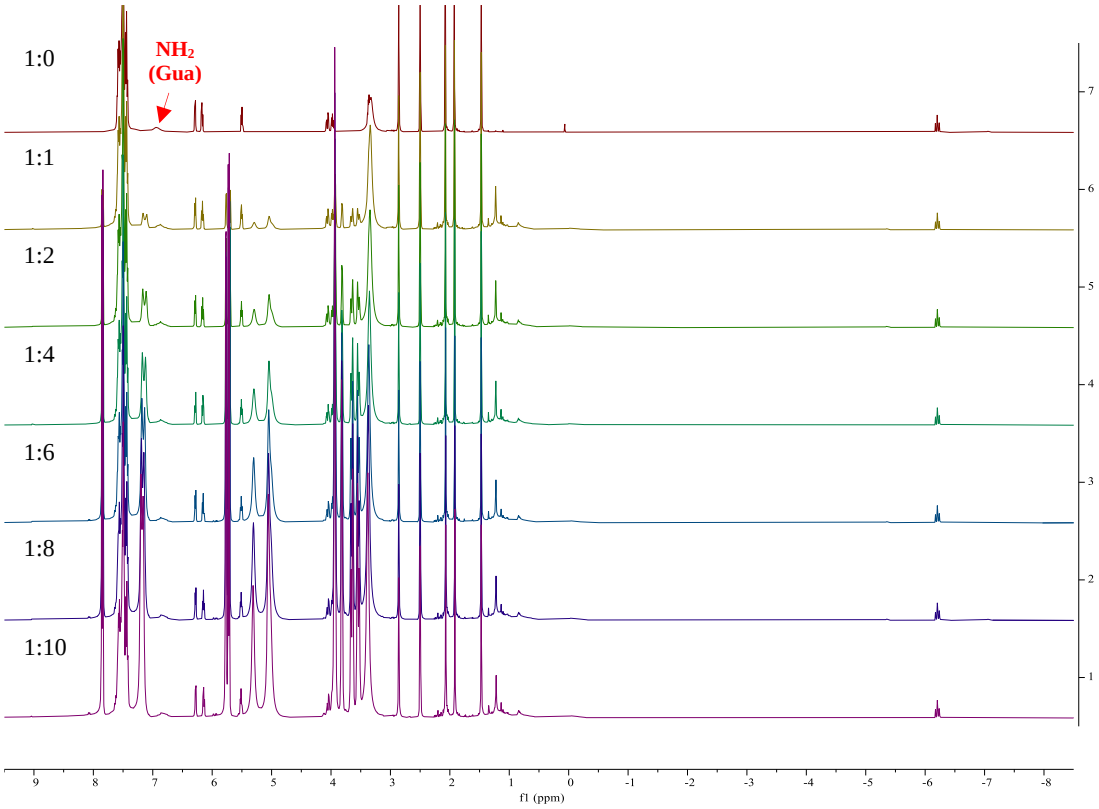


Figure S14. ^{1}H NMR spectrum (top) and selected area (13.5 to 6.5 ppm) covering the NH and NH_2 groups (bottom) of complex **4**, previously published by our group,[S4] in deuterated DMSO at room temperature and in presence of different concentrations of **Cy** (0, 1, 2, 4, 6, 8 and 10 equivalents in respect with the amount of the guanosine derivative **4**). $c_{complex\ 4}$ = 0.02M


BF4
PPh3
Pt−H
PPh3
HN
H2N
N
N
N
O
AcO
O
OAc
OAc
+
NH2
N
N
O
HO
O
OH
OH
DMSO-d6
1H NMR

1-BF_4


1:0
NH2
(Gua)
1:1
1:2
1:4
1:6
1:8
1:10
f1 (ppm)

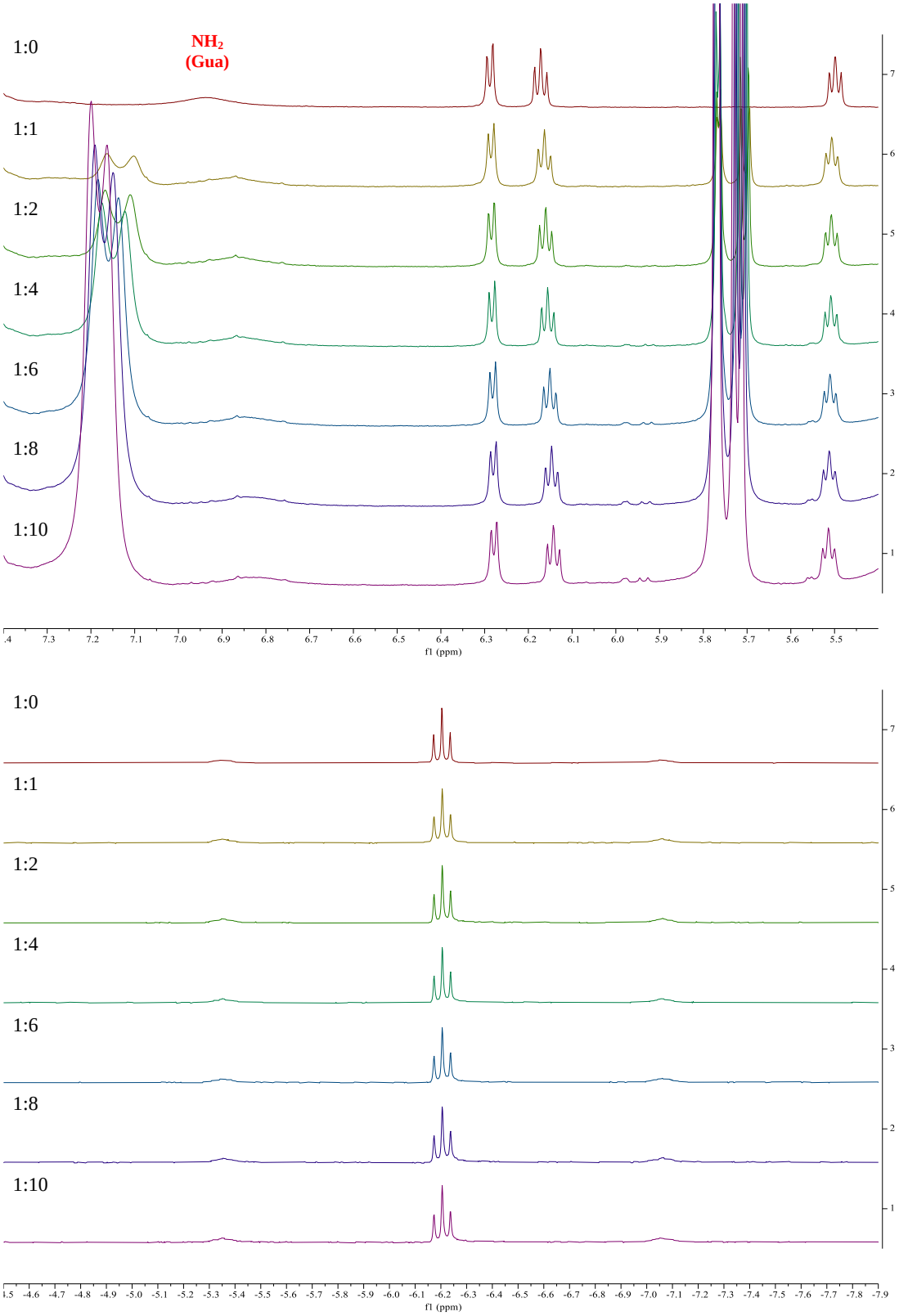
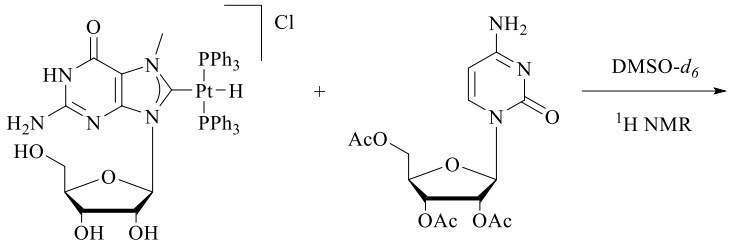
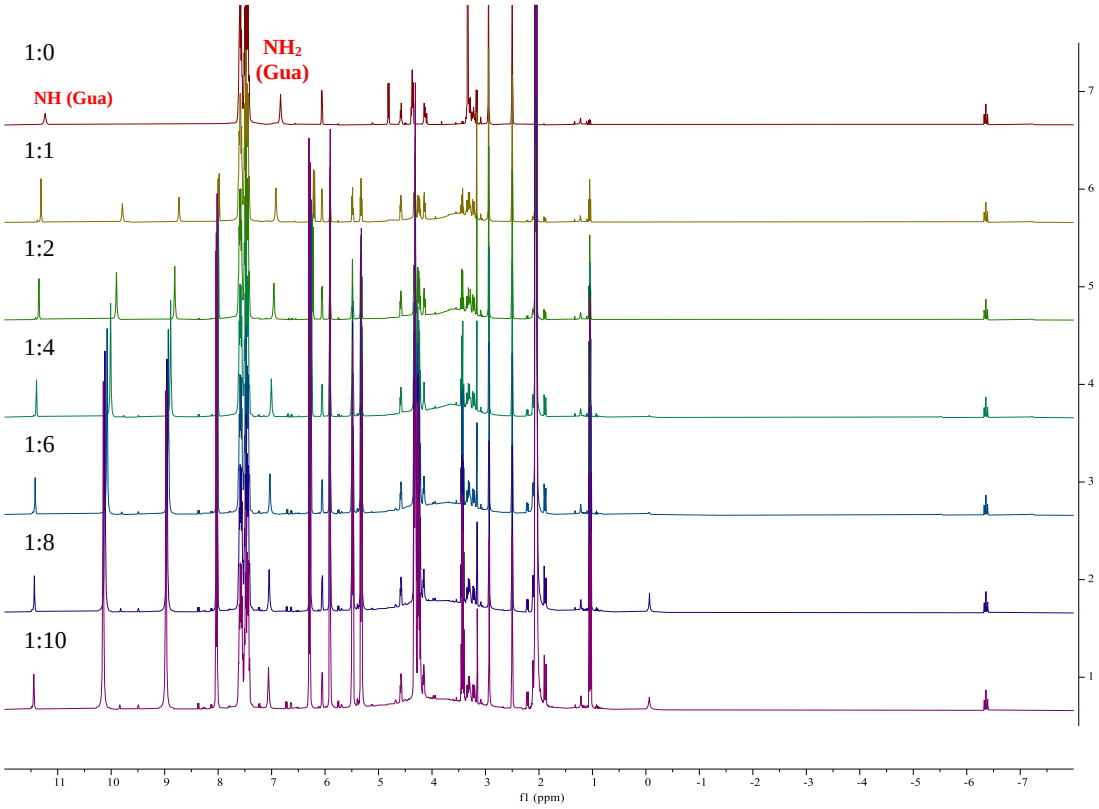


Figure S15. ^{1}H NMR spectrum (top) and selected areas covering the NH_2 and hydride groups (7.4 to 5.4 and -4.5 to -7.9 ppm, respectively) of complex **1-BF$_4$**, in deuterated DMSO at room temperature and in presence of different concentrations of **Cy** (0, 1, 2, 4, 6, 8 and 10 equivalents in respect with the amount of the guanosine derivative **1-BF$_4$**). $c_{\text{complex 1-BF}_4}$ = 0.02M


Cl
PPh3
Pt–H
PPh3
HN
H2N
N
HO
O
OH
OH
NH2
AcO
OAc
OAc
DMSO-d6
1H NMR

3


1:0
NH (Gua)
NH2
(Gua)
1:1
1:2
1:4
1:6
1:8
1:10
f1 (ppm)

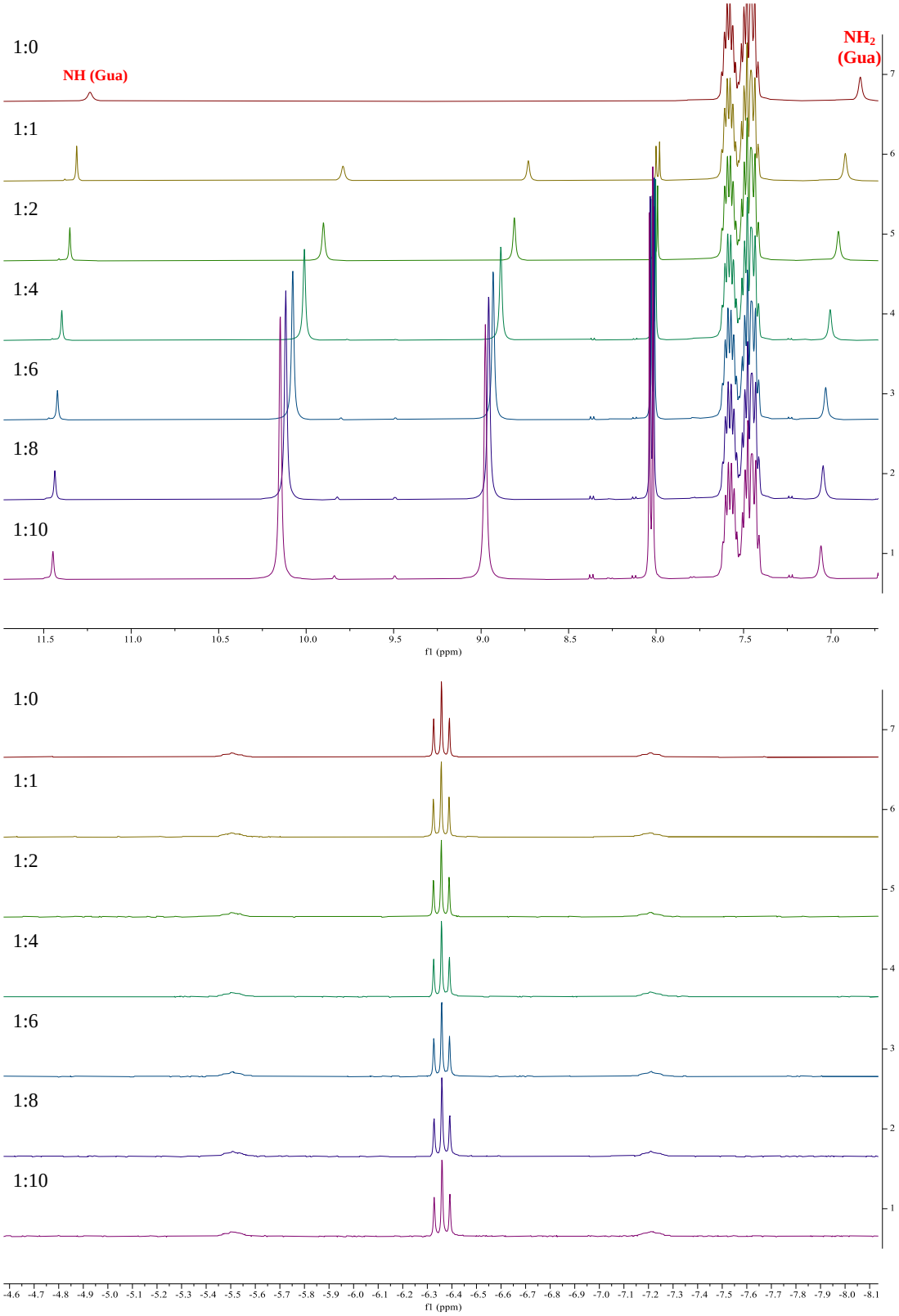
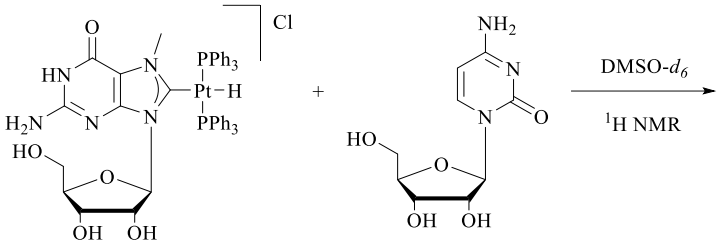
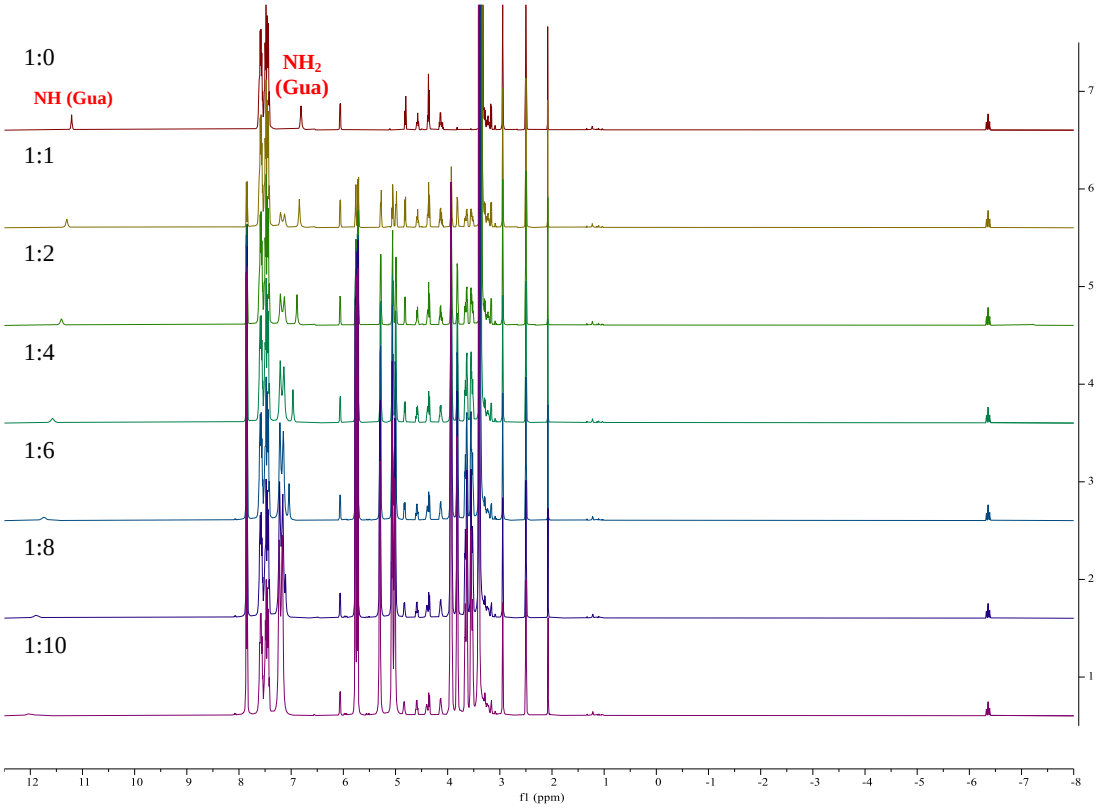


Figure S16. ^{1}H NMR spectrum (top) and selected areas covering the NH_2 and hydride groups (11.73 to 7.73 and -4.57 to -8.13 ppm, respectively) of complex **3**, in deuterated DMSO at room temperature and in presence of different concentrations of $\mathbf{Cy_{Ac}}$ (0, 1, 2, 4, 6, 8 and 10 equivalents in respect with the amount of the guanosine derivative **3**). $c_{complex\ 3}$ = 0.02M


Cl
PPh3
Pt−H
PPh3
HN
H2N
HO
OH
OH
NH2
HO
OH
OH
DMSO-d6
1H NMR

3


1:0
NH (Gua)
NH2
(Gua)
1:1
1:2
1:4
1:6
1:8
1:10
f1 (ppm)

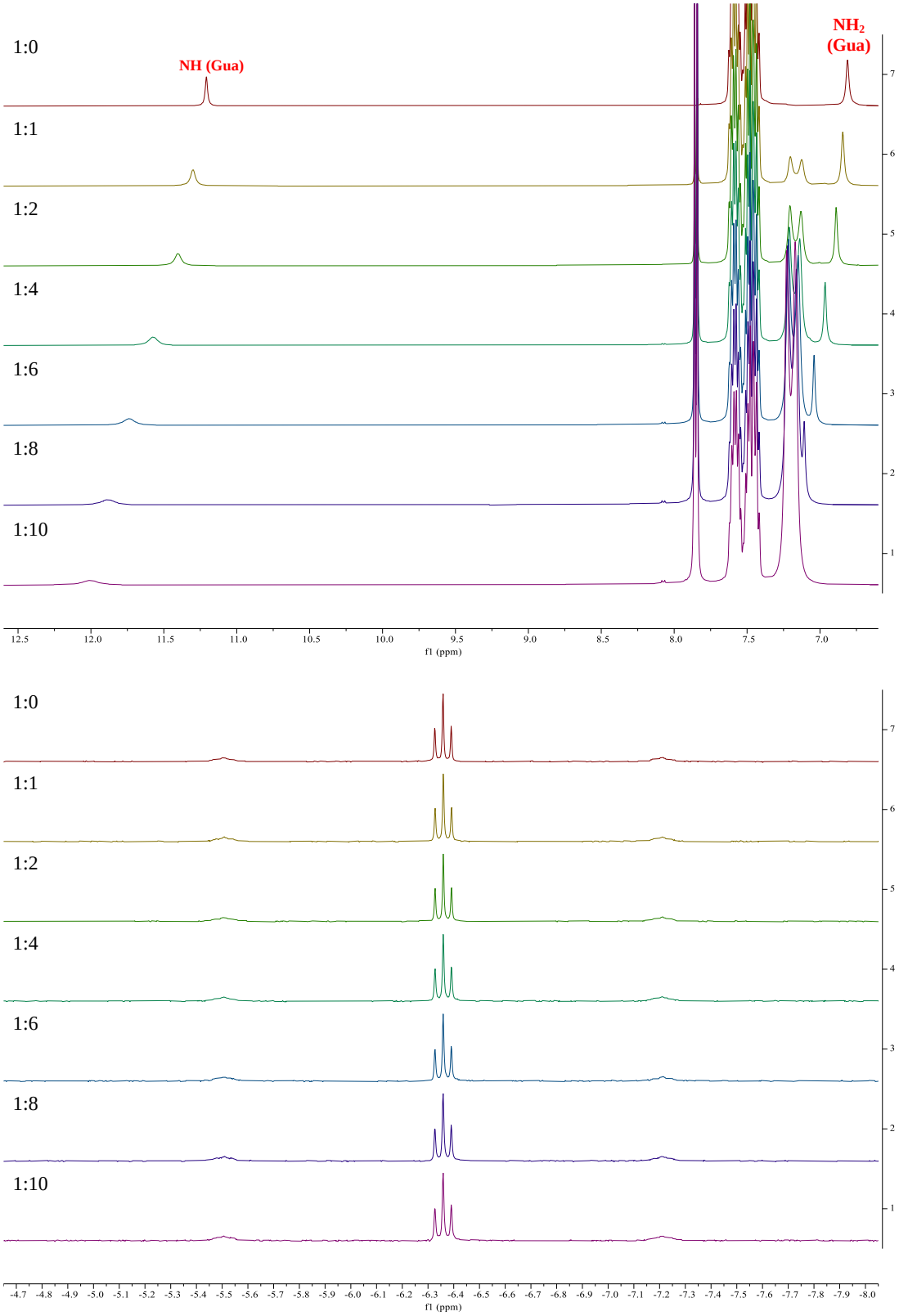


Figure S17. ^{1}H NMR spectrum (top) and selected areas covering the NH_2 and hydride groups (12.6 to 6.6 and -4.65 to -8.05 ppm, respectively) of complex **3**, in deuterated DMSO at room temperature and in presence of different concentrations of **Cy** (0, 1, 2, 4, 6, 8 and 10 equivalents in respect with the amount of the guanosine derivative **3**). $c_{complex\ 3}$ = 0.02M

9. References

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