SUPPLEMENTARY MATERIAL

STEPWISE SYNTHESIS, CHARACTERIZATION, DNA BINDING PROPERTIES AND CYTOTOXICITY OF DIRUTHENIUM OLIGOPYRIDINE COMPOUNDS CONJUGATED WITH PEPTIDES.

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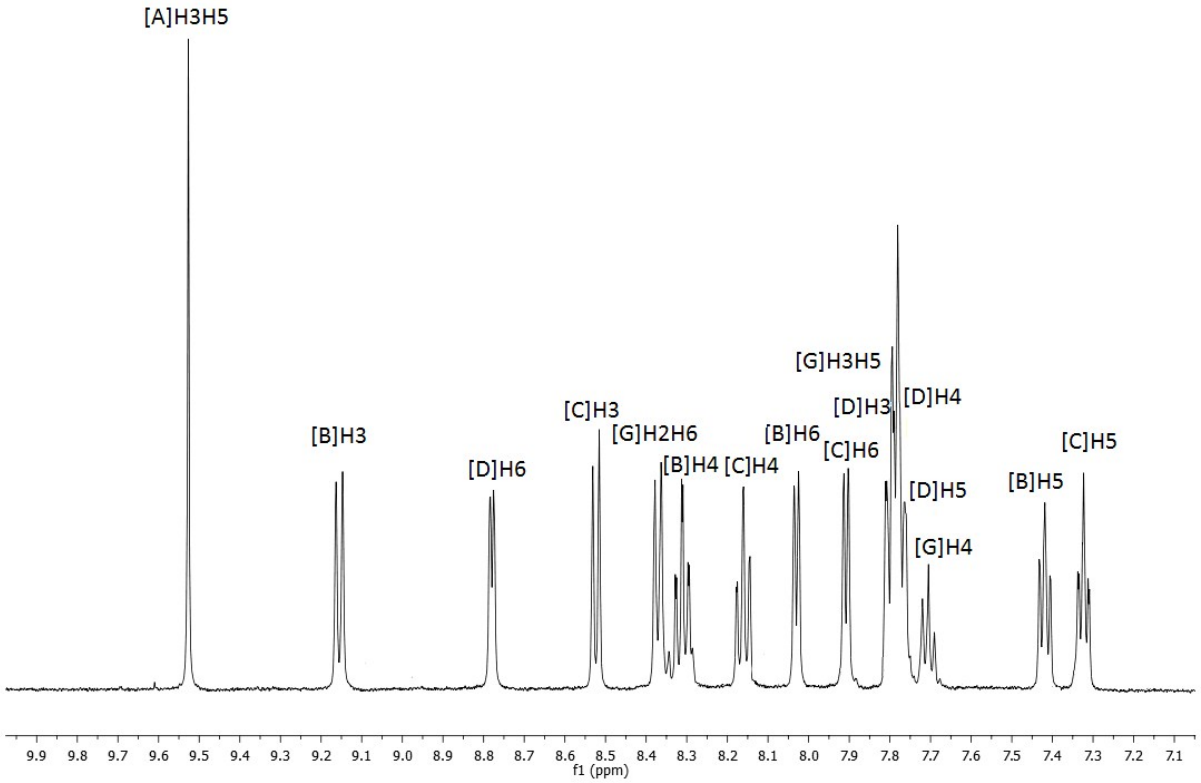

Figure S1. ^{1}H NMR spectrum of complex (**1**) at 298 K in acetone-d_6 with the signal assignments

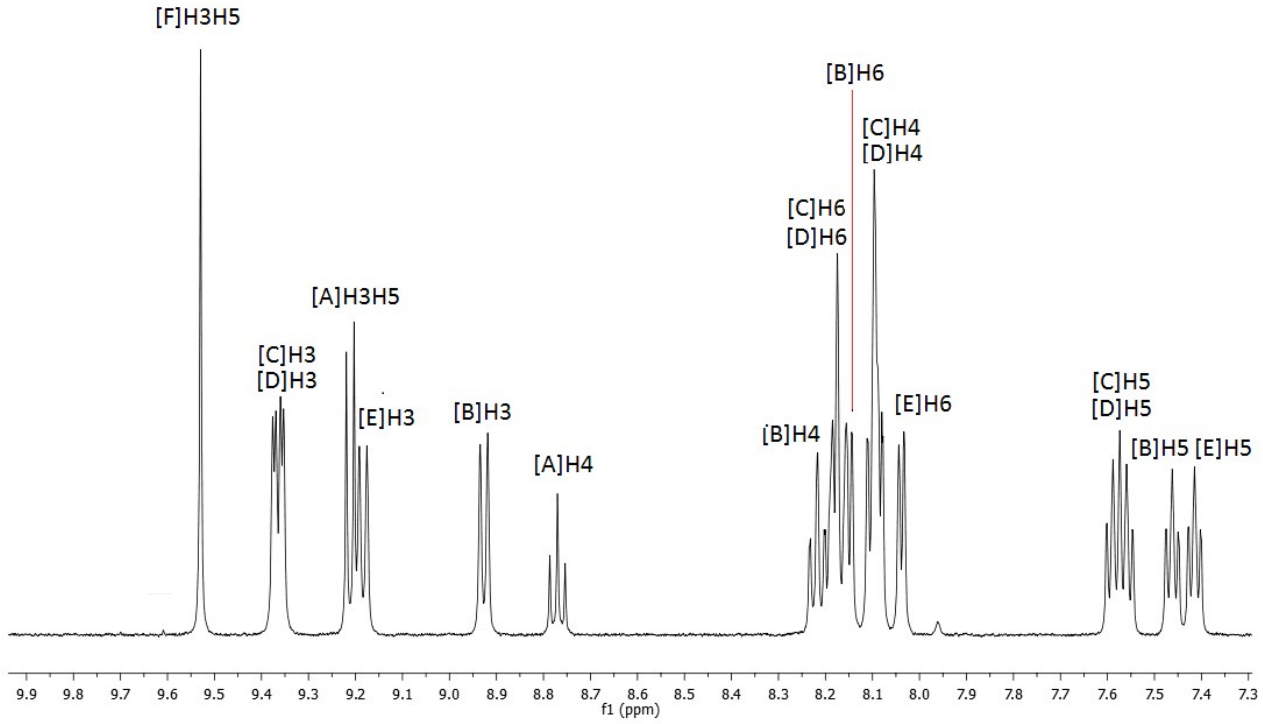

Figure S2. ^{1}H NMR spectrum of complex (**2**) at 298 K in acetone-d_6 with the signal assignments

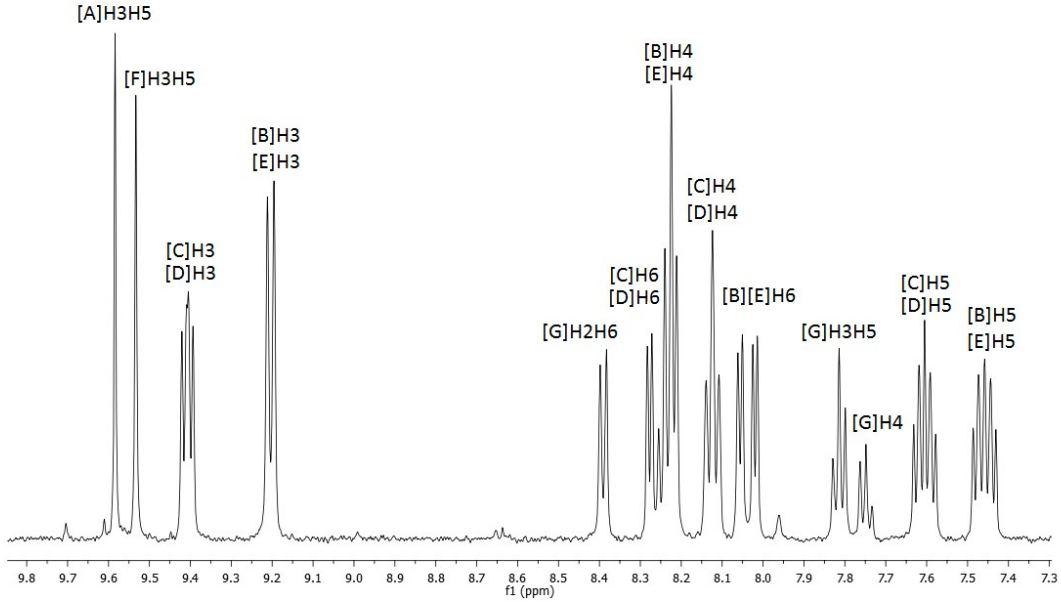

Figure S3. ^{1}H NMR spectrum of complex (**3**) at 298 K in acetone-d_6 with the signal assignments

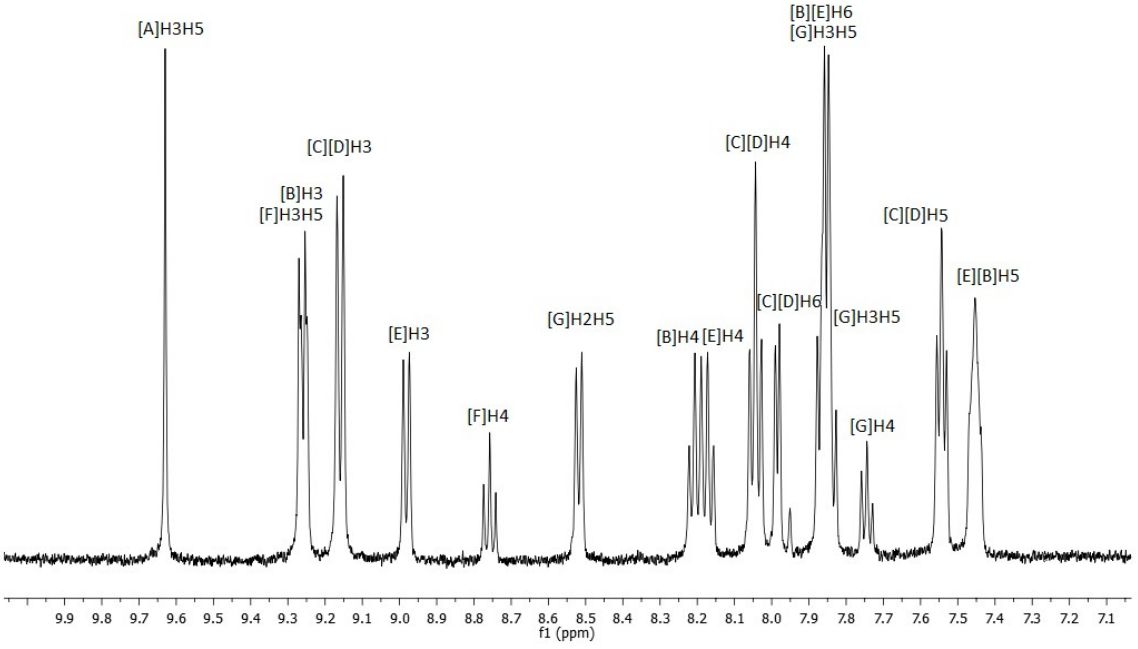

Figure S4. ^{1}H NMR spectrum of complex (**4**) at 298 K in dmso-d_6 with the signal assignments

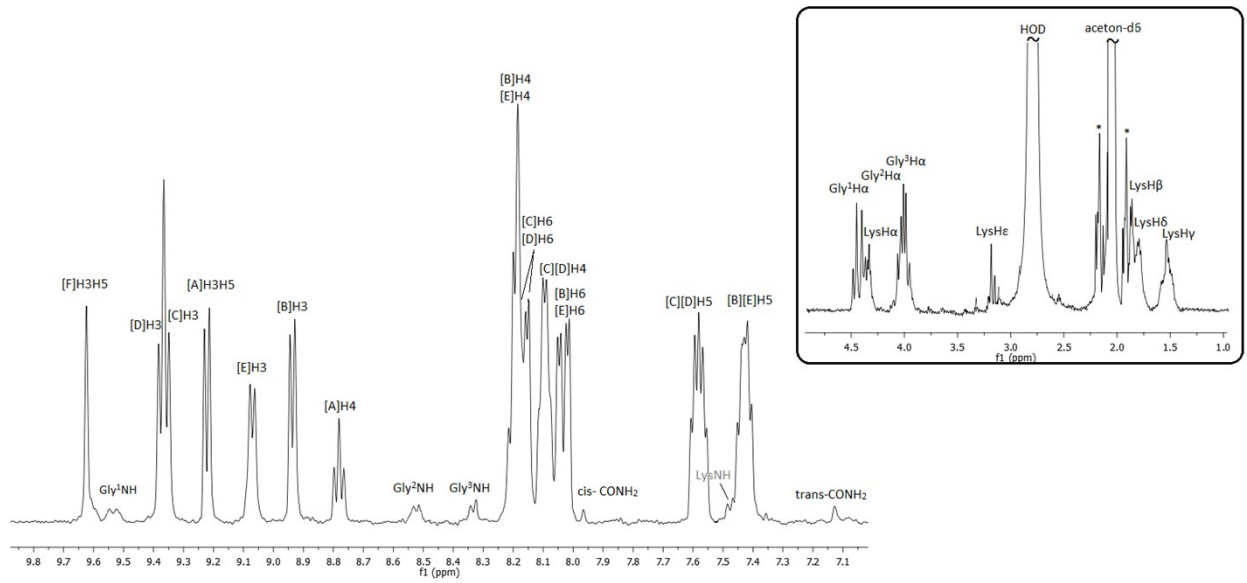

Figure S5. ^{1}H NMR spectrum of complex (**5**) at 298 K in aceton-d_6 with the signal assignments

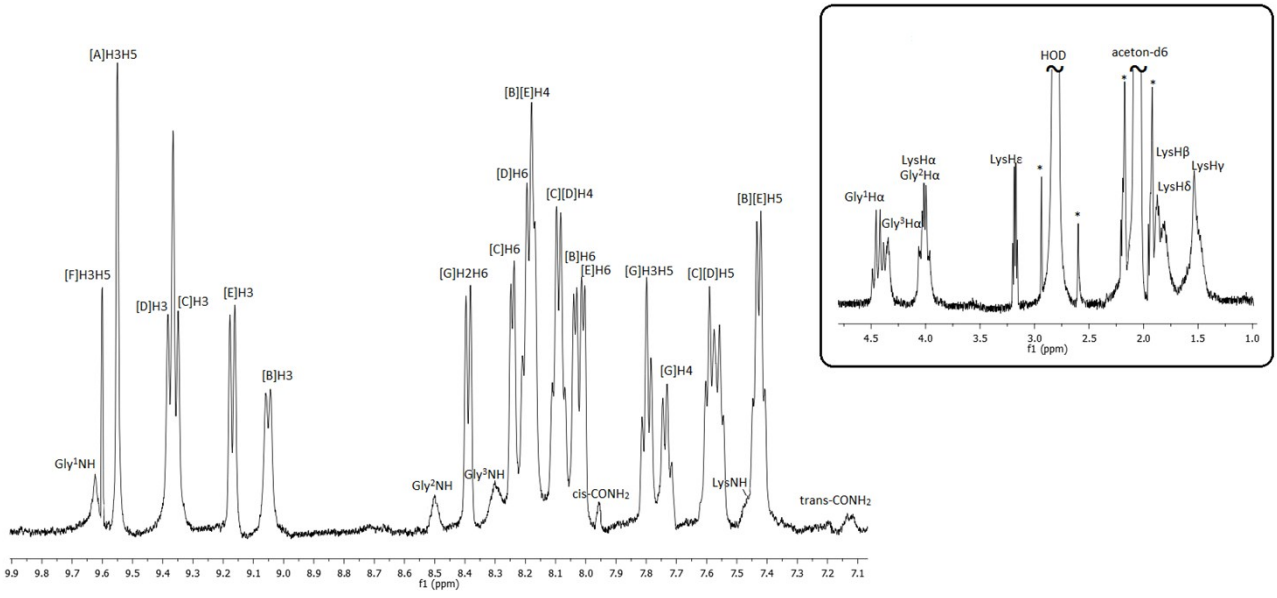

Figure S6. ^{1}H NMR spectrum of complex (**6**) at 298 K in aceton-d_6 with the signal assignments

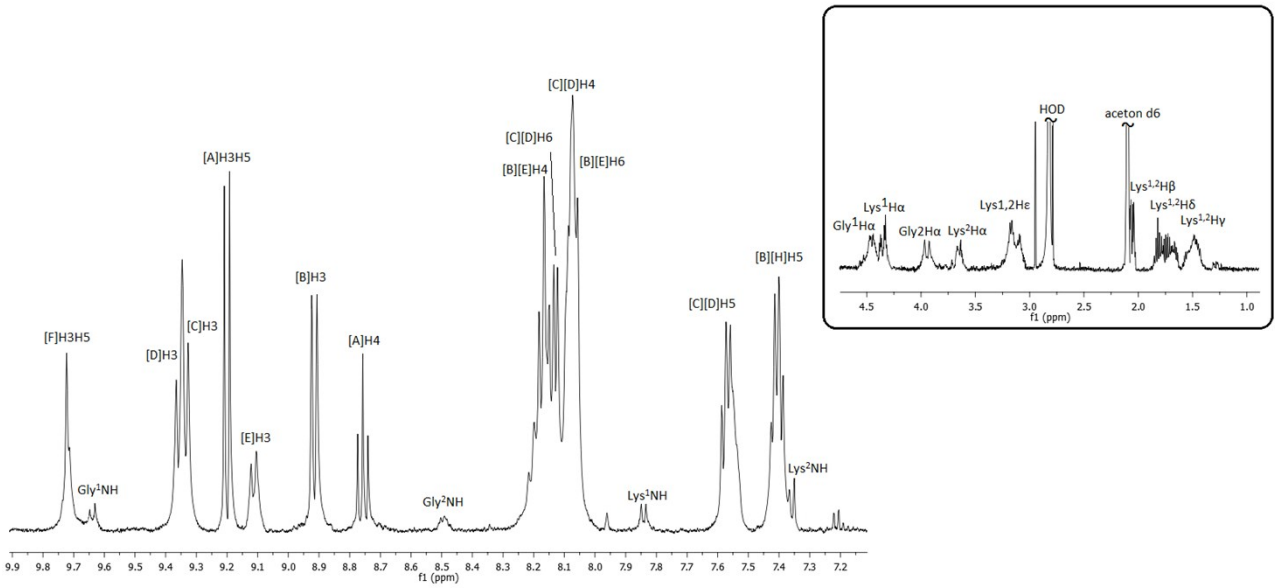

Figure S7. ^{1}H NMR spectrum of complex (**6**) at 298 K in aceton-d_6 with the signal assignments

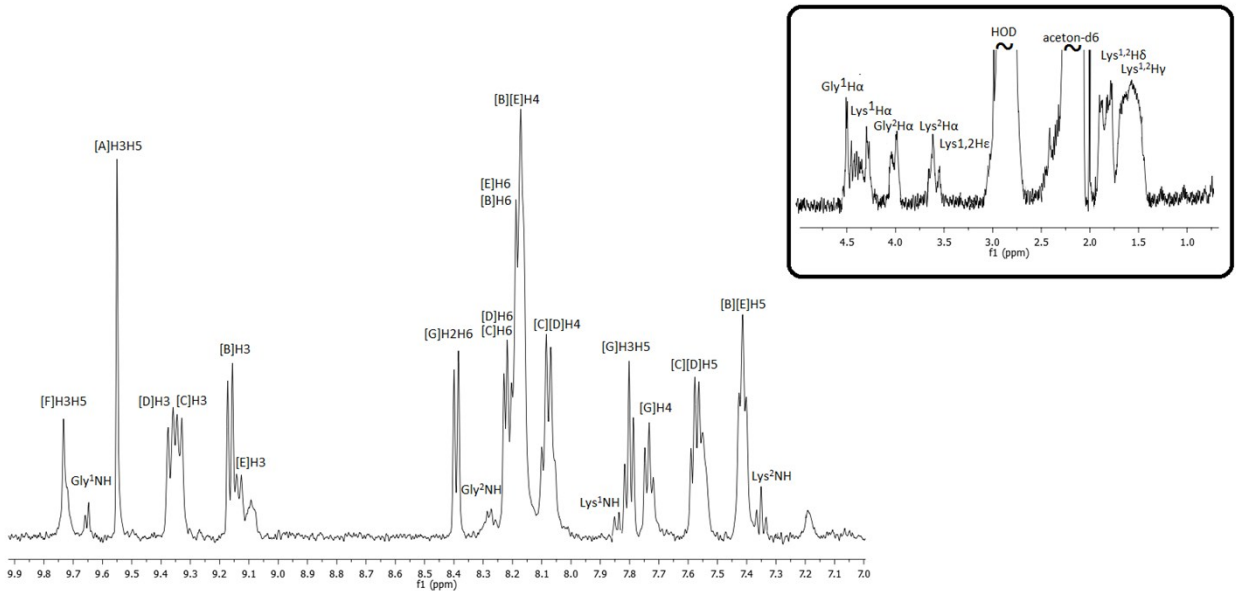

Figure S8. ^{1}H NMR spectrum of complex (**8**) at 298 K in aceton-d_6 with the signal assignments

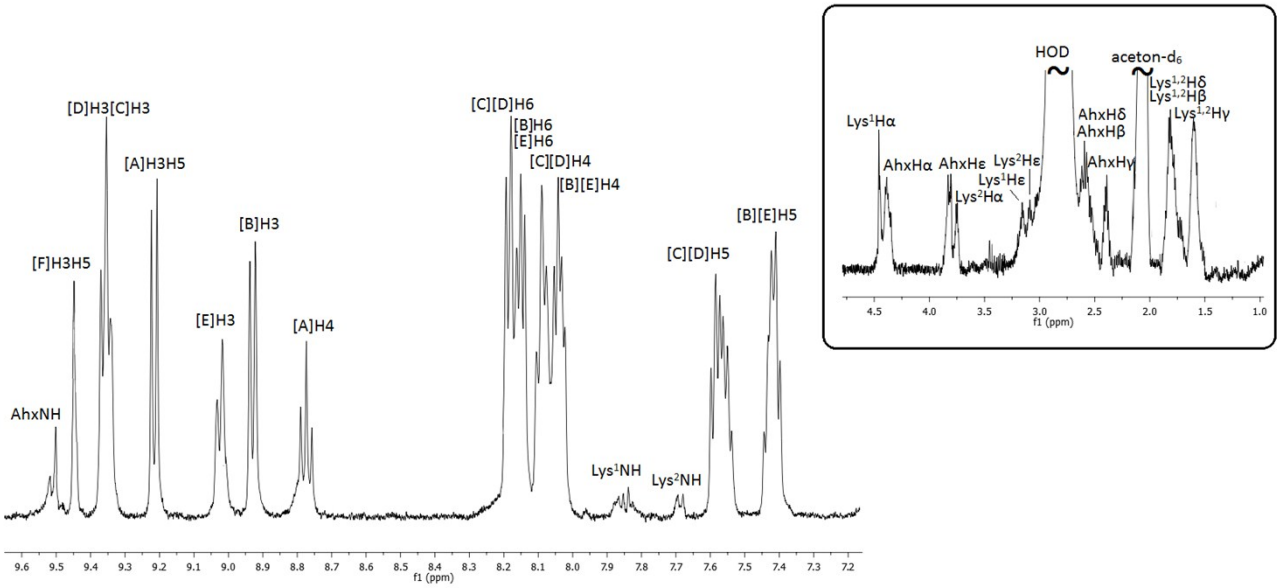

Figure S9. ^{1}H NMR spectrum of complex (**9**) at 298 K in aceton-d_6 with the signal assignments

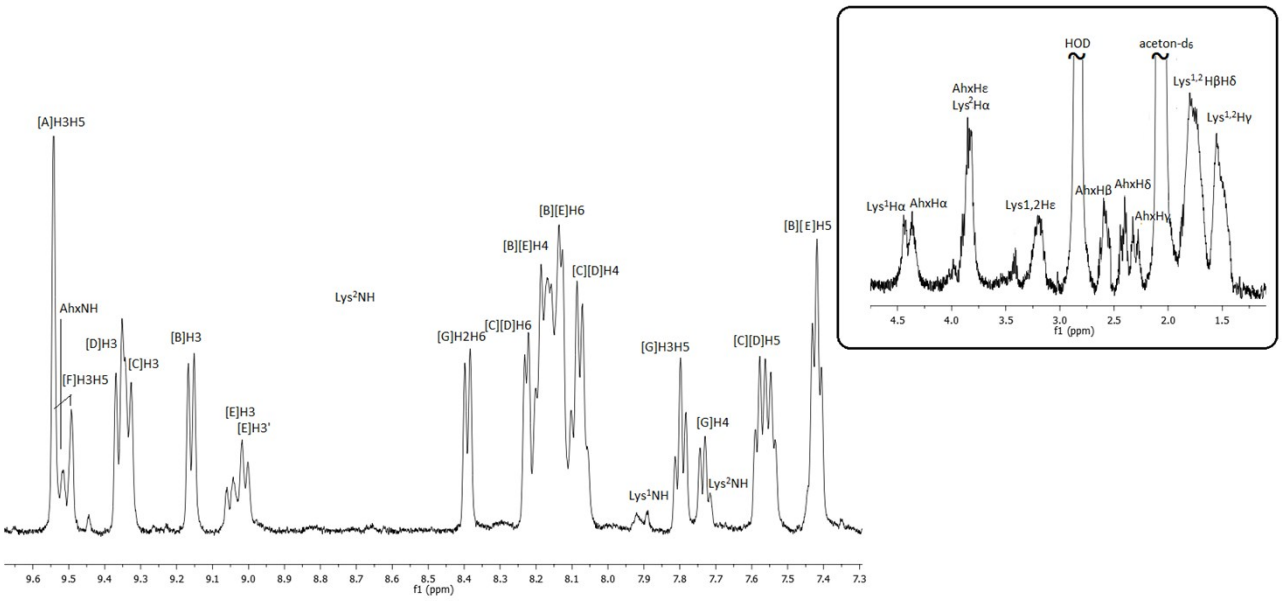

Figure S10. ^{1}H NMR spectrum of complex (**10**) at 298 K in aceton-d_6 with the signal assignments

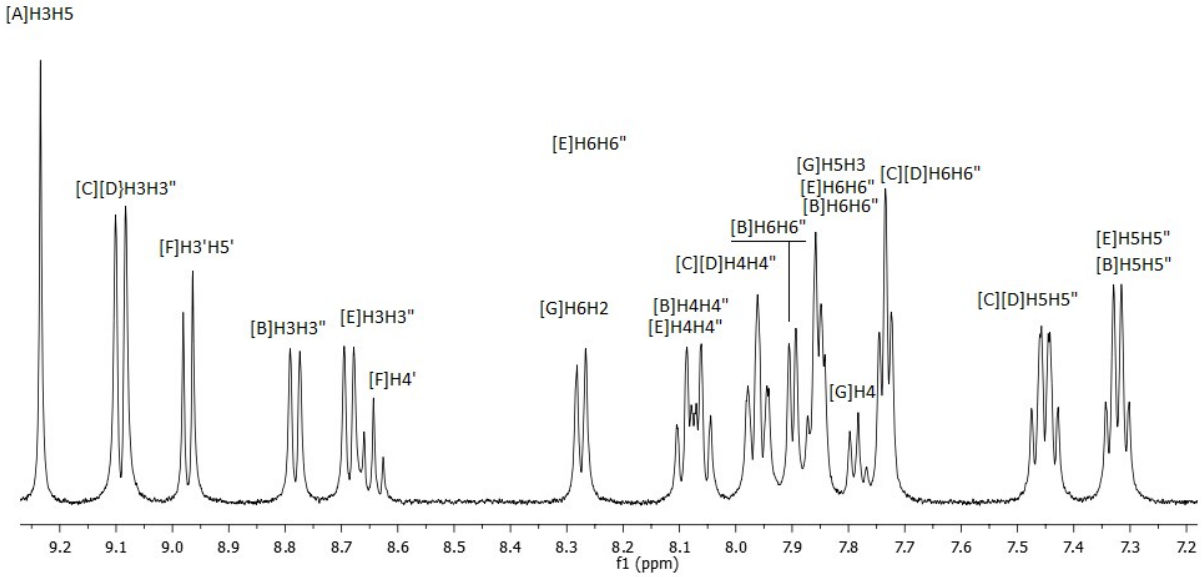

Figure S11. ^{1}H NMR spectrum of complex (**4**) in H_2O:D_2O 9:1, 100 mM phosphates pH = 7.0, 298 K, with the signal assignments

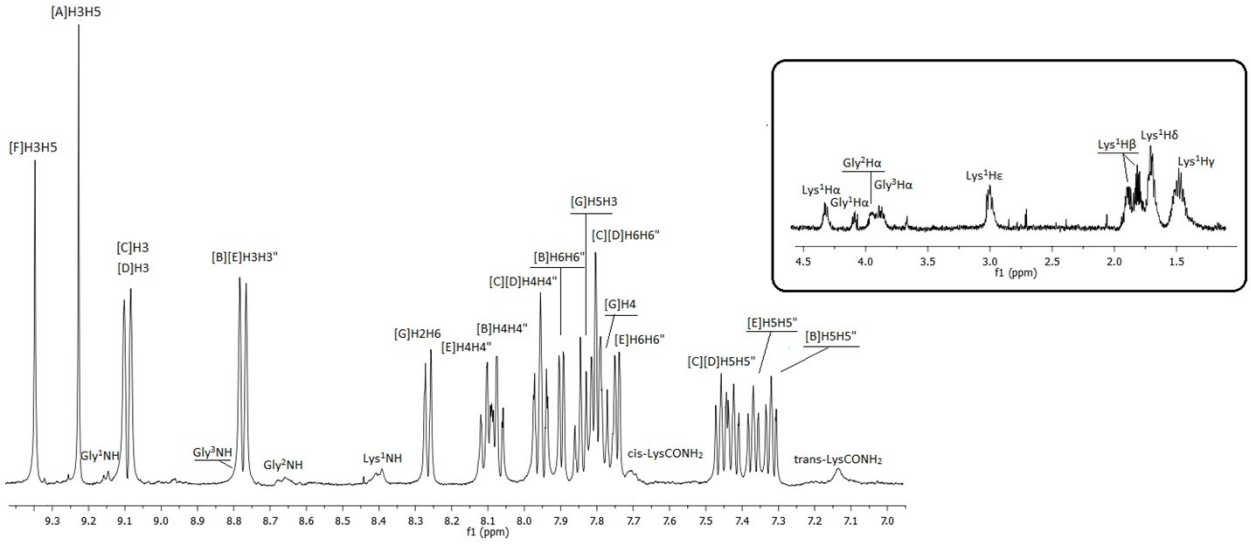

Figure S12. ^{1}H NMR spectrum of complex (**5**) in H_2O:D_2O 9:1, 100 mM phosphates pH = 7.0, 298 K, with the signal assignments

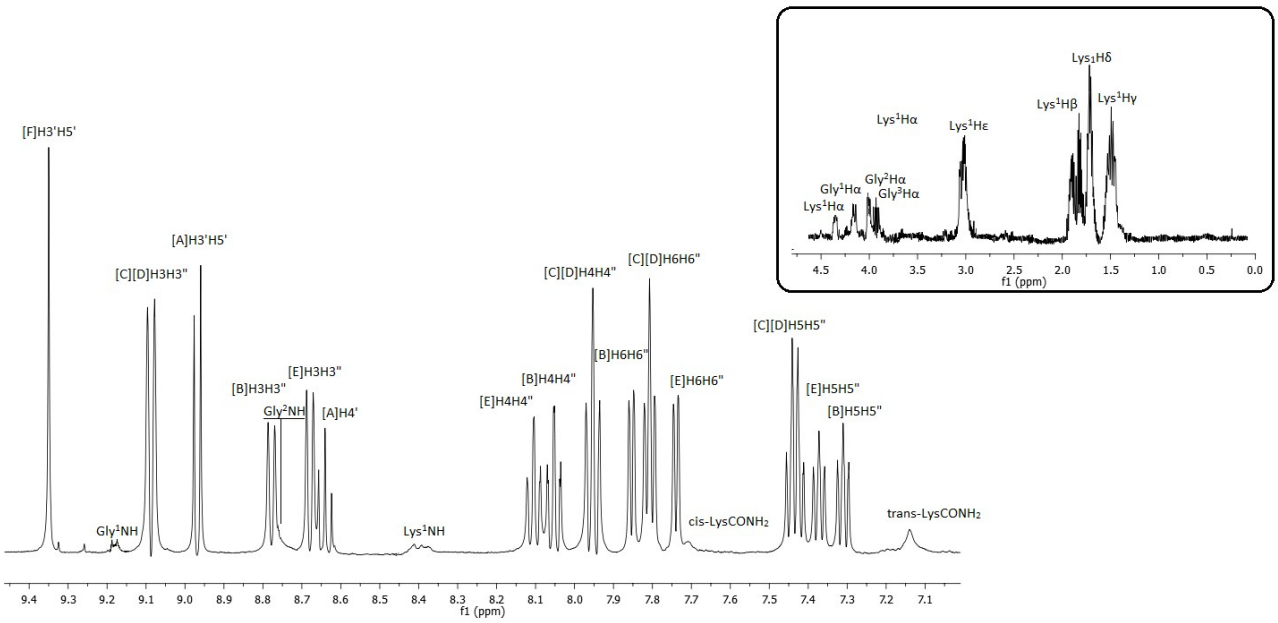

Figure S13. ^{1}H NMR spectrum of complex (**6**) in H_2O:D_2O 9:1, 100 mM phosphates pH = 7.0, 298 K, with the signal assignments

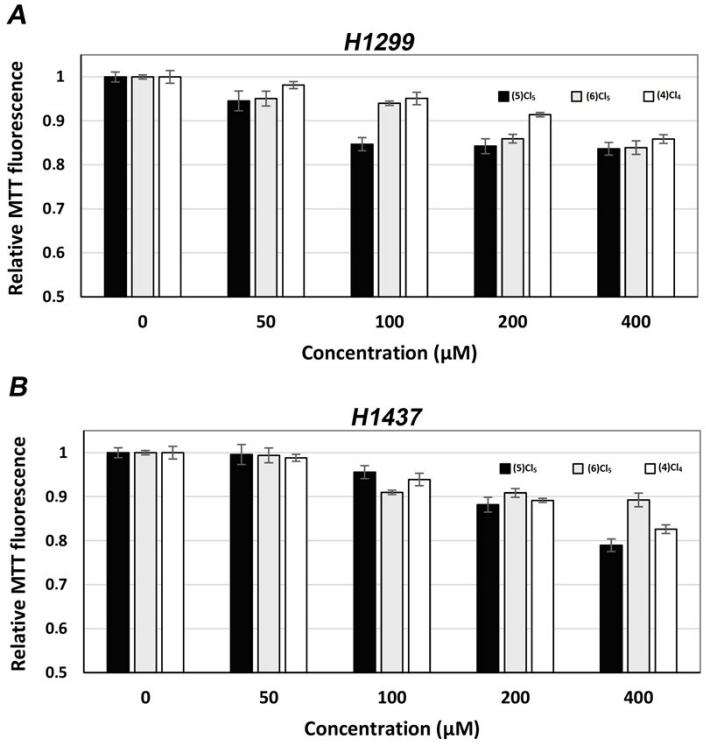

Figure S14. Figure 13. MTT assay on H1299 and H1437. Cell viability was assessed by the trypan blue exclusion test in H1299 (A) or H1437 (B) cells. 5x104 lung cancer cells were seeded in a 24-well-plate and treated with (**5**)Cl_5, (**6**)Cl_5 or (**4**)Cl_4 (50, 100, 200, 300 or 400 µM). Viability tests were performed 24h post-treatment. Fluorescence values were normalized to those of non-treated cells.

Table S1: Crystallographic data for complexes [(trpy)Ru(tppz)Ru(trpy-CO_2H)]$(PF_6)_4$, (**2**)$(PF_6)_4$; [(ptrpy)Ru(tppz)Ru(trpy-CO_2H)]$(PF_6)_4$, (**3**)$(PF_6)_4$; [(ptrpy)Ru(tppz)Ru(trpy-CO_2H)]$(PF_6)_4$, (**4**)$(PF_6)_4$

	(**2**)$(PF_6)_4$	(**3**)$(PF_6)_4$	(**4**)$(PF_6)_4$
Formula	$C_{55}H_{36}N_{12}O_2Ru_2(PF_6)_4$	$C_{61}H_{41}N_{12}O_2Ru_2(PF_6)_4$	$C_{60}H_{42}N_{12}Ru_2(PF_6)_4$
FW	1678.98	1756.08	1713.08
T (K)	100(3)	100(3)	100(3)
Crystal system	monoclinic	monoclinic	monoclinic
Space group	*C*2/c	*C*2/c	*C*2/c
a (Å)	23.5727(8)	23.830(2)	14.9492(14)
b (Å)	17.0533(5)	17.0667(16)	33.781(3)
c (Å)	18.1277(7)	18.275(2)	15.9327(11)
β (°)	104.936(4)	105.189(11)	97.180(8)
V (Å^3)	7041.0(4)	7172.8(13)	7982.9(12)
Z	4	4	4
ρ_{calcd} (g cm^{-3})	1.584	1.626	1.425
final *R* indices [$I>2\sigma(I)$]	*R*1 = 0.0450	*R*1 = 0.0525	*R*1 = 0.0721
	*wR*2 = 0.1130	*wR*2 = 0.1347	*wR*2 = 0.1311
R indices (all data)	*R*1 = 0.0509	*R*1 = 0.0762	*R*1 = 0.1637
	*wR*2 =0.1156	*wR*2 =0.1533	*wR*2 =0.1868

Table S2: ^{1}H NMR chemical shifts (δ) in ppm of the complexes (**4**), (**5**) and (**6**) in aqueous (H_2O:D_2O, 9:1) buffer phosphates (100 mM, pH = 7.0) at 298 K [a].

Proton	(**4**)	(**5**)	(**6**)
[A]H3'H5'	9.23	9.23	8.97
[C][D] H3H3"	9.09	9.09	9.08
[F]H3'H5'	8.97	9.35	9.35
[B]H3H3"	8.78	8.78	8.68
[E]H3H3"	8.68	8.78	8.78
[F]4'	8.61	-	-
[A]H4'	-	-	8.64
[G]H6H2	8.27	8.27	-
[E]H4H4"	8.08	8.10	8.10
[B]H4H4"	8.07	8.08	8.06
[C][D]H4H4"	7.96	7.96	7.95
[B]H6H6''	7.90	7.90	7.85
[E]H6H6"	7.86	7.74	7.74
[G]H5H3	7.85	7.86	-
[G]H4	7.79	7.77	-
[C][D]H6H6"	7.73	7.79, 7.81	7.81
[C][D]H5H5"	7.45	7.46, 7.42	7.43
[E]H5H5"	7.32	7.37	7.37
[B]H5H5"	7.32	7.32	7.31
$Lys^{1}H\alpha$	-	4.30	4.30
$Lys^{1}H\beta$	-	1.89, 1.84	1.89, 1.84
$Lys^{1}H\gamma$	-	1.49	1.49
$Lys^{1}H\delta$	-	1.71	1.71
$Lys^{1}H\varepsilon$	-	3.02	3.02
$Gly^{1}H\alpha$	-	4.10	4.07
$Gly^{2}H\alpha$	-	3.93	3.93
$Gly^{3}H\alpha$	-	3.88	3.88
$Gly^{1}NH$	-	9.15	9.16
Gly^{2} NH	-	8.67	8.67
Gly^{3} NH	-	8.77	8.77
$Lys^{1}NH$	-	8.39	8.39
cis-$Lys^{1}CONH_2$	-	7.69	7.71
trans-$Lys^{1}CONH_2$	-	7.13	7.14

[a] The proton numbering and the designation of the ligand rings are based in Fig. 2.

Table S3. ^{1}H NMR (500 MHz) resonances (ppm) of the free d(5′-CGCGAATTCGC-3′)$_2$ in 100 mM phosphate buffer (pH 7.0), H_2O:D_2O 9:1, at 298 K.

Base	H8/H6	H5/H2/ T-CH_3	H1′	H2′	H2′′	H3′	H4′	N3H/N1H	NH_2(b)	NH_2(nb)
C1	7.60	5.88	5.72	1.94	2.39	4.67	4.03			
G2	7.92		5.88	2.61	2.68	4.94	4.31	13.02		
C3	7.25	5.35	5.58	1.82	2.26	4.78	4.12		8.41	6.42
G4	7.83		5.41	2.63	2.75	4.96	4.29	12.68		
A5	8.09	7.21	5.97	2.67	2.90	5.03	4.43			
A6	8.09	7.60	6.13	2.59	2.90	4.98	4.44			
T7	7.09	1.26	5.88	1.94	2.53	4.79	4.18	13.65		
T8	7.35	1.51	6.08	2.15	2.53	4.87	4.17	13.78		
C9	7.44	5.60	5.65	2.04	2.40	4.84	4.12		8.40	6.80
G10	7.89		5.82	2.62	2.67	4.96	4.34	12.91		
C11	7.31	5.42	5.72	1.87	2.30	4.79	4.18		8.37	6.55
G12	7.92		6.13	2.36	2.62	4.65	4.14			

Table S4: ^{1}H NMR chemical shifts (δ) in ppm of the complexes (**4**), (**5**) and (**6**) upon addition to the oligonucleotide duplex d(CGCGAATTCGCG)$_2$ at 1:1 molar ratio, in aqueous buffer phosphates (100 mM, pH = 7.0) at 298 K [a].

Proton	(**4**)	(**5**)	(**6**)
[A]H3'H5'	**9.03 (-0.20)**	**9.10 (-0.13)**	8.96 (-0.01)
[C][D] H3H3"	9.08 (-0.01)	9.12 (+0.03)	9.05 (+0.03)
[F]H3'H5'	8.93 (-0.04)	9.34 (-0.01)	9.34 (-0.01)
[B]H3H3"	**8.60 (-0.18)**	**8.72 (-0.06)**	8.67 (-0.01)
[E]H3H3"	8.65 (-0.03)	8.78 (0.00)	8.78 (0.00)
[F]4'	8.60 (-0.01)	-	-
[A]H4'	-	-	8.68 (+0.04)
[G]H6H2	**8.00 (-0.27)**	**8.12 (-0.15)**	-
[E]H4H4"	8.05 (-0.03)	8.14 (+0.04)	8.16 (+0.06)
[B]H4H4"	8.00(-0.07)	8.05 (-0.03)	8.08 (+0.02)
[C][D]H4H4"	7.95 (+0.01)	8.02 (+0.06)	8.01 (+0.06)
[B]H6H6''	**7.80 (-0.10)**	7.98 (+0.08)	7.87 (+0.02)
[E]H6H6"	7.79 (-0.07)	7.76 (+0.02)	7.75 (+0.01)
[G]H5H3	**7.52 (-0.33)**	**7.72 (-0.14)**	-
[G]H4	**7.32 (-0.47)**	**7.42 (-0.35)**	-
[C][D]H6H6"	7.71 (+0.02)	7.80, 7.82 (+0.01)	7.831 (+0.02)
[C][D]H5H5"	7.45 (0.00)	7.53, 7.49 (+0.07)	7.50 (+0.07)
[E]H5H5"	7.31 (+0.01)	7.41 (+0.04)	7.39 (+0.02)
[B]H5H5"	7.29(-0.03)	7.36 (+0.04)	7.33 (+0.02)
Lys^{1}Hα	-	4.33 (+0.03)	4.31 (+0.01)
Lys^{1}Hβ	-	1.90, 1.85 (+0.01)	1.90, 1.87 (+0.02)
Lys^{1}Hγ	-	1.48 (-0.01)	1.52 (+0.03)
Lys^{1}Hδ	-	1.72 (+0.01)	1.73 (+0.02)
Lys^{1}Hε	-	3.05 (+0.03)	3.04 (+0.02)
Gly^{1}Hα	-	4.15 (-0.05)	4.14 (+0.04)
Gly^{2}Hα	-	3.96 (+0.03)	3.93 (0.00)
Gly^{3}Hα	-	3.88 (0.00)	3.85 (-0.03)
Gly^{1}NH	-	9.12 (-0.03)	9.13 (-0.03)
Gly^{2} NH	-	8.72 (+0.05)	8.62 (-0.05)
Gly^{3} NH	-	8.72 (-0.05)	8.75 (-0.02)
Lys^{1}NH	-	8.41 (+0.02)	8.32 (-0.07)

[a] The proton numbering and the designation of the ligand rings are based in Fig. 2.

Table S5. Changes in d(5′-CGCGAATTCGC-3′)$_2$ chemical shifts upon addition of (**4**) in molar ratio 1:1 [(δ ppm),100 mM phosphate buffer (*p*H 7.0), H_2O:D_2O = 9:1, 298 K.

Base	H8/H6	H5/H2/ T-CH_3	H1′	H2′	H2′′	N3H/N1H	NH_2(b)	NH_2(nb)
C1	(-0.01)	(-0.01)	(-0.02)	(-0.01	(-0.01)			
G2	(+0.01)		(-0.01)	(-0.01	(+0.01)	(-0.01)		
C3	(-0.01)	(+0.01)	(0.00)	(+0.01)	(+0.01)		(-0.01)	(-0.01)
G4	(+0.01)		(0.00)	(0.00)	2.75	(+0.01)		
A5	(-0.01)	(+0.01)	**(-0.03)**	**(-0.03)**	**(-0.03)**			
A6	(-0.01)	(-0.01)	**(-0.05)**	**(-0.04)**	**(-0.07)**			
T7	**(-0.03)**	(0.00)	**(-0.03)**	**(-0.03)**	**(-0.05)**	**(-0.06)**		
T8	**(-0.03)**	(-0.01)	**(-0.04)**	**(-0.06)**	**(-0.05)**	**(-0.06)**		
C9	(0.00)	(0.00)	**(-0.03)**	**(-0.06)**	**(-0.03)**		(-0.01)	(0.00)
G10	(-0.01)		(-0.01)	(-0.02)	(-0.02)	(-0.00)		
C11	(0.00)	(-0.01)	(0.00)	(-0.01)	(-0.01)		(0.00)	(0.00)
G12	(-0.01)		(-0.01)	(-0.01)	(-0.02)			

Table S6. Changes in d(5′-CGCGAATTCGC-3′)$_2$ chemical shifts upon addition of (**5**) in molar ratio 1:1 [(δ ppm),100 mM phosphate buffer (*p*H 7.0), H_2O:D_2O = 9:1, 298 K.

Base	H8/H6	H5/H2/ T-CH_3	H1′	H2′	H2′′	N3H/N1H	NH_2(b)	NH_2(nb)
C1	(-0.01)	(-0.01)	(-0.02)	(-0.01	(-0.01)			
G2	(+0.01)		(-0.01)	(-0.01	(+0.01)	(-0.01)		
C3	(-0.02)	(0.00)	(-0.01)	(+0.01)	(+0.01)		(-0.01)	(-0.01)
G4	(0.00)		(0.00)	(0.00)	(0.00)	(+0.01)		
A5	(-0.01)	(+0.01)	**(-0.03)**	(-0.01)	(-0.02)			
A6	(-0.01)	(-0.01)	**(-0.05)**	(-0.00)	(-0.02)			
T7	(-0.01)	(0.00)	**(-0.06)**	(-0.02)	(-0.01)	**(-0.06)**		
T8	(-0.02)	(-0.01)	**(-0.07)**	(-0.01)	(0.00)	**(-0.04)**		
C9	(0.00)	(0.00)	(-0.01)	(-0.02)	(-0.01)		(-0.01)	(0.00)
G10	(-0.01)		(-0.01)	(-0.02)	(-0.02)	(-0.00)		
C11	(0.00)	(-0.01)	(0.00)	(-0.01)	(-0.01)		(0.00)	(0.00)
G12	(0.00)		(-0.01)	(-0.01)	(-0.02)			

Table S7. Changes in d(5′-CGCGAATTCGC-3′)$_2$ chemical shifts upon addition of (**6**) in molar ratio 1:1 [(δ ppm),100 mM phosphate buffer (*p*H 7.0), H_2O:D_2O = 9:1, 298 K.

Base	H8/H6	H5/H2/ T-CH_3	H1′	H2′	H2′′	N3H/N1H	NH_2(b)	NH_2(nb)
C1	(0.00)	(0.00)	(-0.01)	(+0.01)	(-0.01)			
G2	(+0.01)		(-0.01)	(-0.01)	(-0.01)	(-0.01)		
C3	(-0.01)	(0.00)	(-0.01)	(-0.01)	(+0.01)		(+0.01)	(0.00)
G4	(0.00)		(0.00)	(0.00)	(0.00)	(0.00)		
A5	(0.00)	(-0.01)	(-0.02)	(-0.01)	(+0.01)			
A6	(-0.01)	(-0.01)	(-0.01)	(-0.00)	(-0.02)			
T7	(-0.01)	(-0.01)	(-0.02)	(-0.02)	(-0.01)	(-0.01)		
T8	(-0.01)	(-0.01)	(-0.01)	(-0.01)	(0.00)	(-0.01)		
C9	(0.00)	(0.00)	(-0.01)	(-0.01)	(-0.01)		(-0.01)	(0.00)
G10	(-0.01)		(0.00)	(0.00)	(-0.02)	(0.00)		
C11	(0.00)	(-0.01)	(0.00)	(0.00)	(-0.01)		(0.00)	(0.00)
G12	(0.00)		(-0.01)	(-0.01)	(-0.02)			