Kinetic and mechanistic study on the reactions of ruthenium(II) chlorophenyl terpyridine complexes with nucleobases, oligonucleotides and DNA

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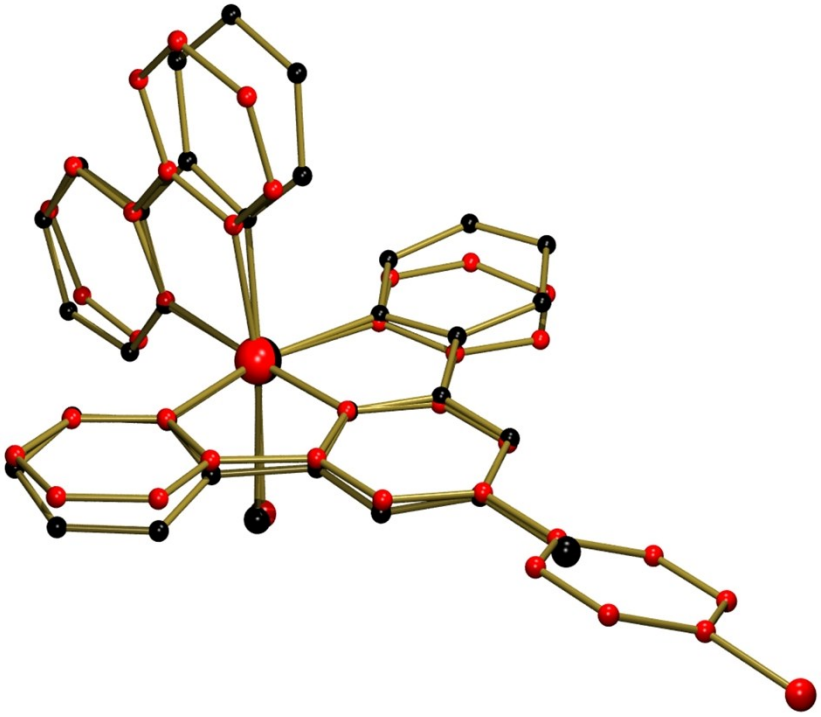


Fig. S1. PLATON[19] drawing showing an overlay of two complexes: [Ru(Cl-Ph-tpy)(bpy)Cl]Cl complex (**3**) (red atoms) and [Ru(Cl-tpy)(bpy)Cl]Cl ($\mathbf{3_{Cl}}$) (black atoms).

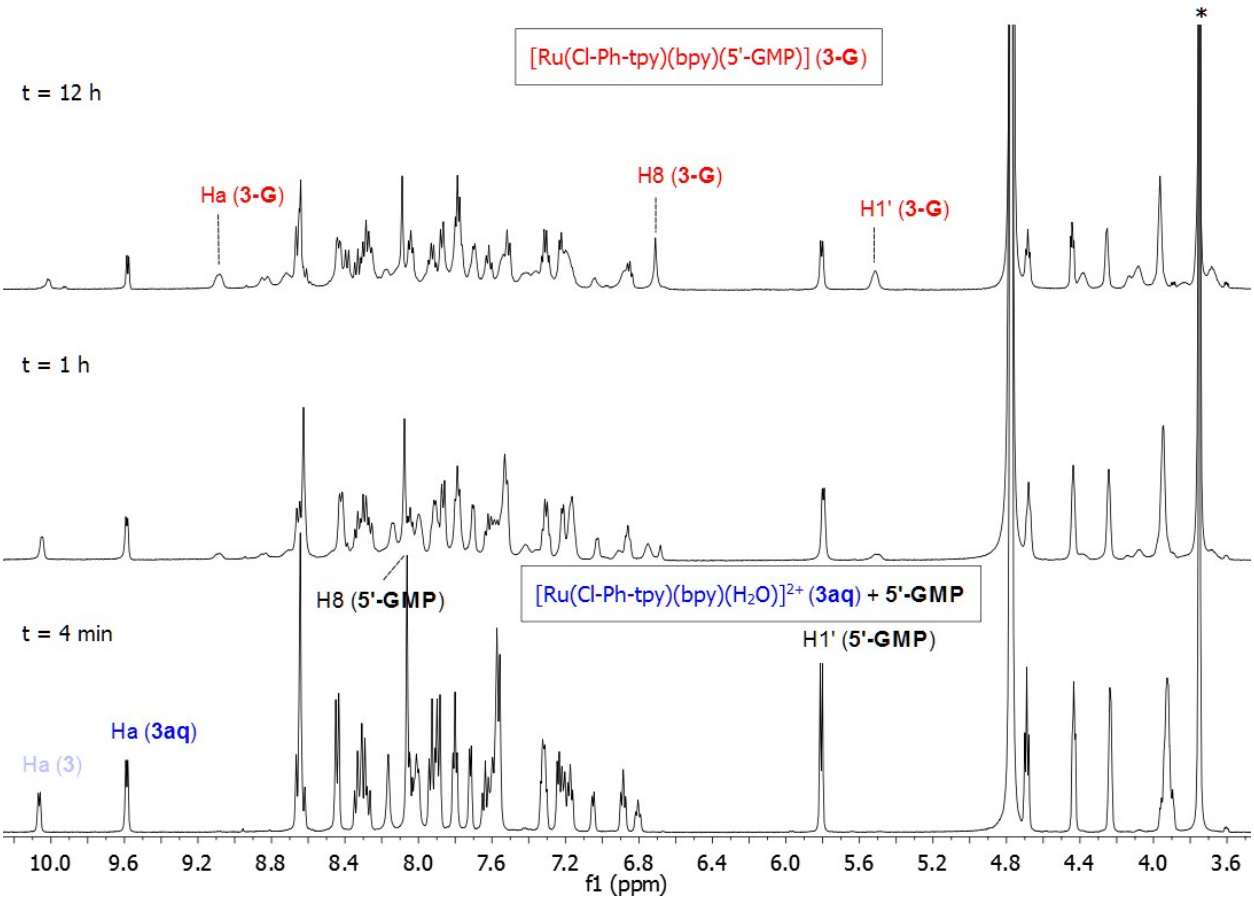


Fig. S2. ^{1}H NMR spectral changes after the addition of 5′-GMP (1.1 equiv.) to an equilibrated solution of [Ru(Cl-Ph-tpy)(bpy)Cl]Cl (**3**; 10 mM)) in D_2O at various reaction times. With * is indicated the reference resonance of 1,4 dixane.

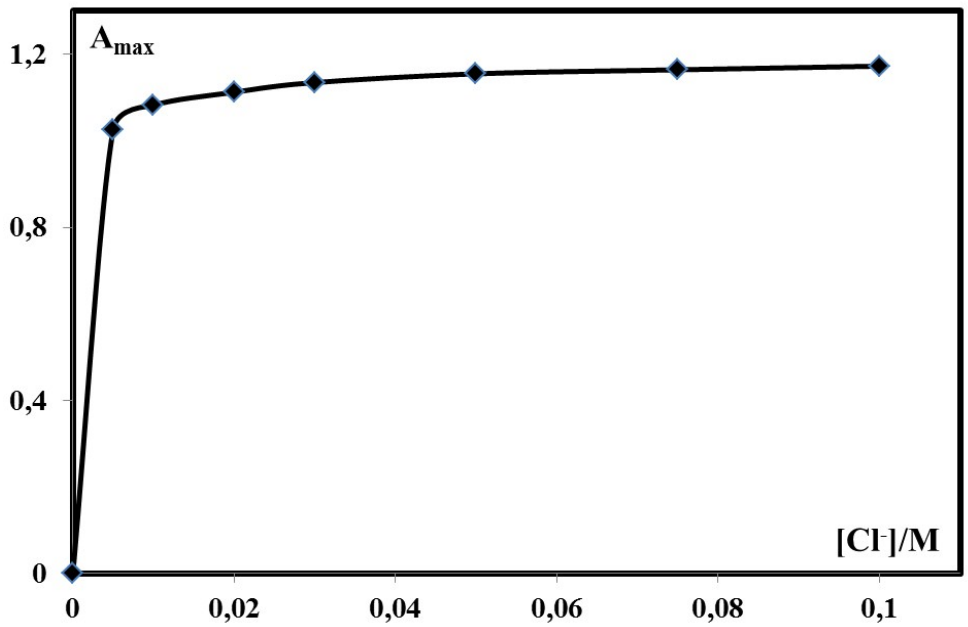
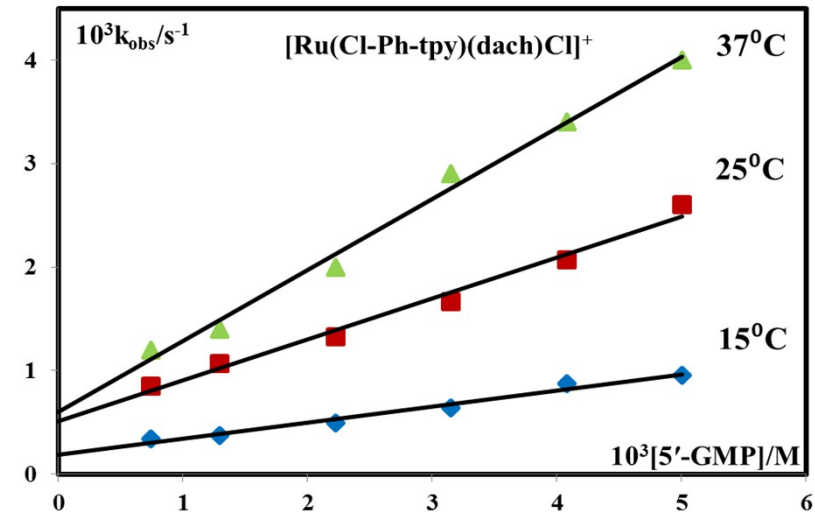
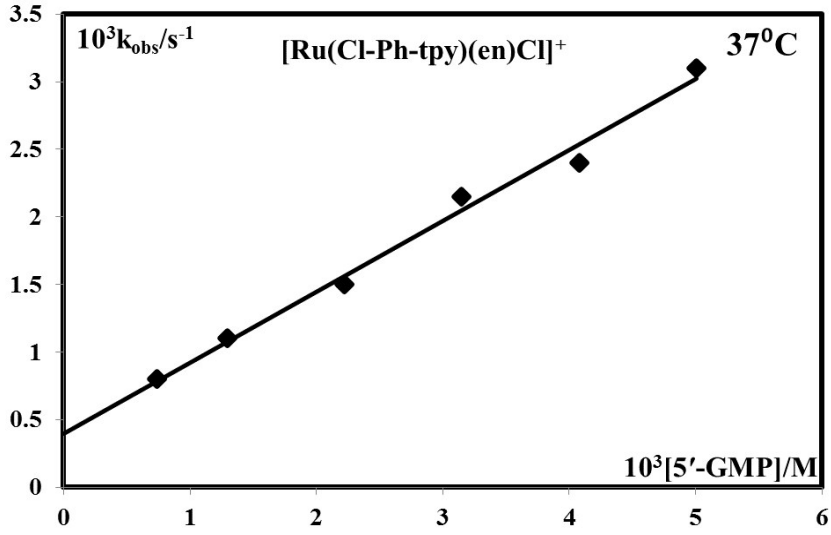


Fig. S3. The change of absorbance at 471 nm of the $[Ru(Cl\text{-}Ph\text{-}tpy)(dach)Cl]^+$ (**2**) complex *vs*. $[Cl^-]$ in 25 mM Hepes buffer at 37 ºC.


$10^3k_{obs}/s^{-1}$
[Ru(Cl-Ph-tpy)(dach)Cl]$^+$
37^{0}C
25^{0}C
15^{0}C
10^3[5′-GMP]/M
0
1
2
3
4
5
6


$10^3k_{obs}/s^{-1}$
[Ru(Cl-Ph-tpy)(en)Cl]$^+$
37^{0}C
10^3[5′-GMP]/M
0
0.5
1
1.5
2
2.5
3
3.5
4
5
6

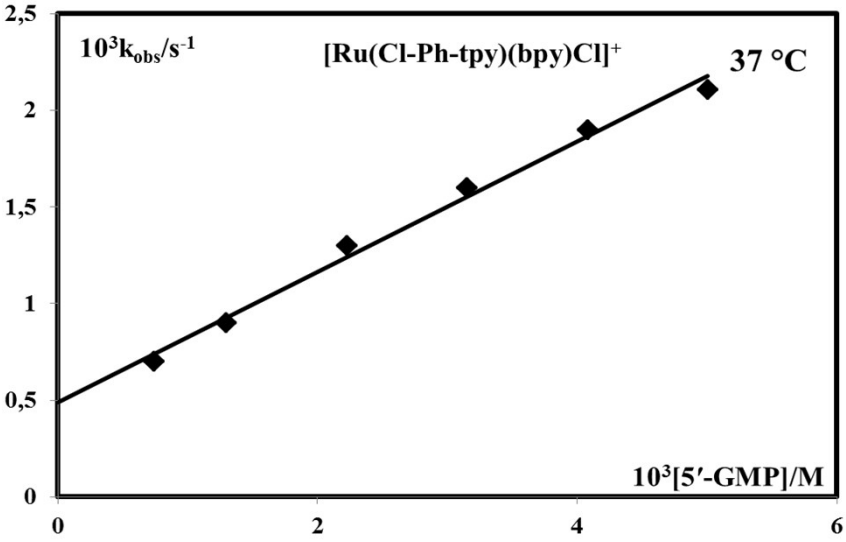

$10^3k_{obs}/s^{-1}$
[Ru(Cl-Ph-tpy)(bpy)Cl]$^+$
37 °C
10^3[5′-GMP]/M
0
0,5
1
1,5
2
2,5
4
6

Fig. S4. *Pseudo*-first-order rate constants, k_{obs}, plotted as a function of ligand concentration and temperature for the substitution reactions of complexes **1 – 3** with 5'-GMP in 25 mM Hepes buffer (50 mM NaCl, pH = 7.2).

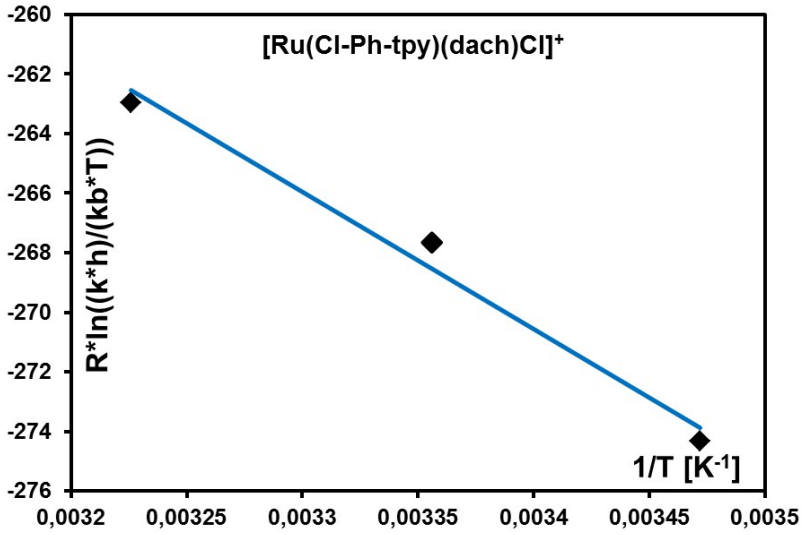


Fig. S5. Eyring plot for the reactions of complex **2** with 5'-GMP, at pH 7.20 in 25 mM Hepes buffer and 50 mM NaCl.

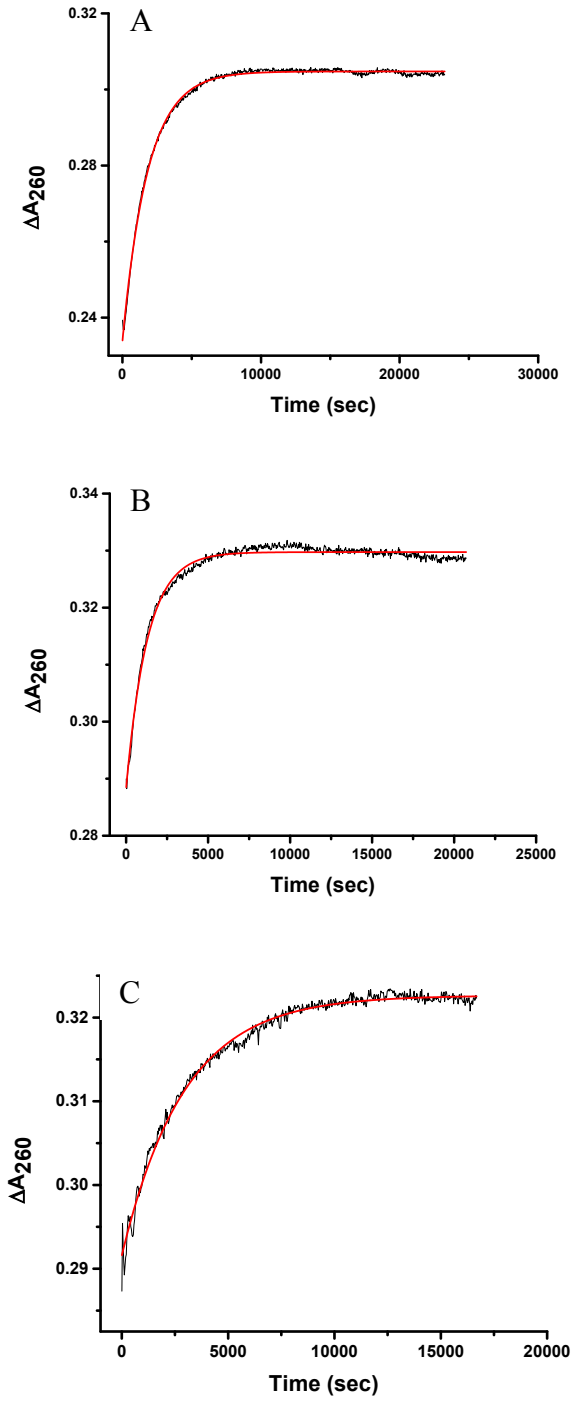


Fig. S6. Absorbance change as a function of time after the addition of complex **1** to DNA-1 (A), DNA-2 (B) and RNA (C) followed at λ = 260 nm. All measurements were conducted with C_1 =

30.0 μM, C_T = 3.0 μM and T = 37 °C in Tris-HCl buffered solution, pH = 7.2. Fits of a single-exponential function to the experimental data is indicated with a solid line (red).

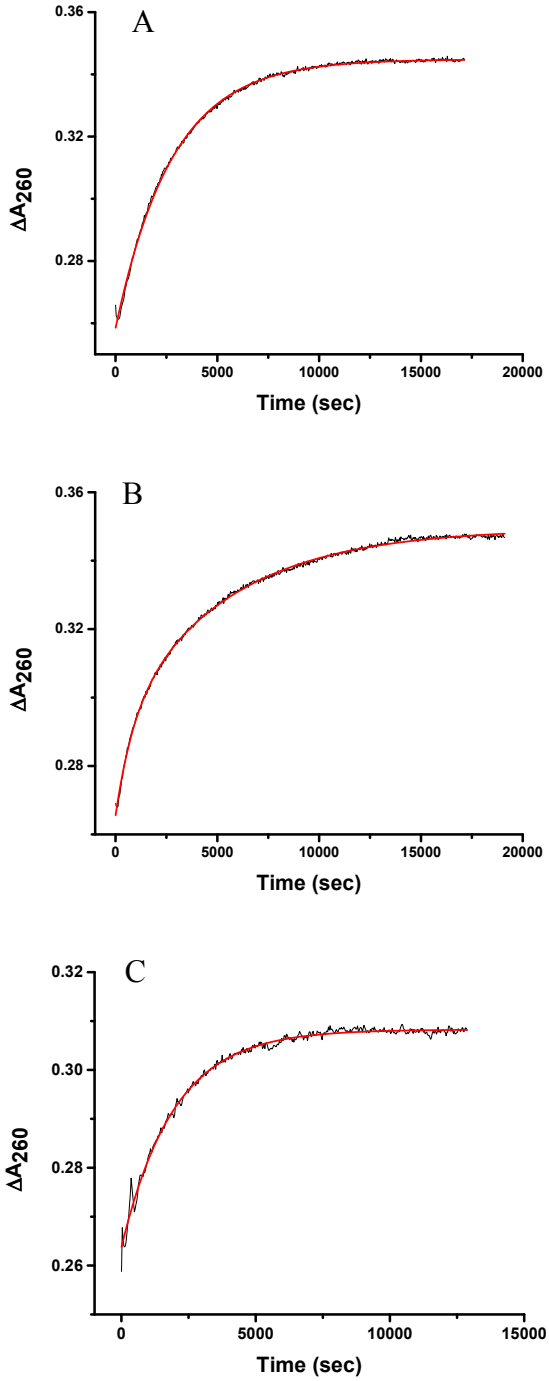


Fig. S7. Absorbance change as a function of time after the addition of complex **2** to DNA-1 (A), DNA-2 (B) and RNA (C) followed at λ = 260 nm. All measurements were conducted with $C_{\mathbf{2}}$ = 30.0 μM, C_T = 3.0 μM and T = 37 °C in Tris-HCl buffered solution, pH = 7.2. Fits of a single-exponential function to the experimental data is indicated with a solid line (red).

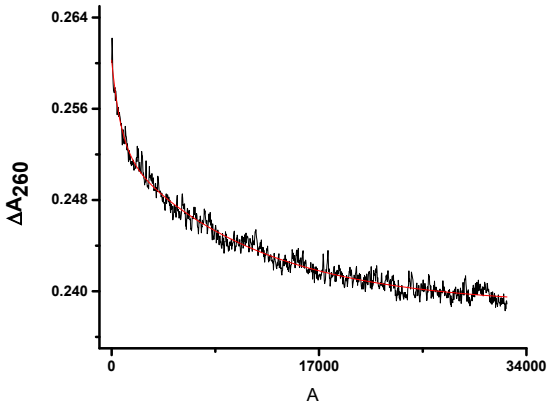


Fig. S8. Absorbance change as a function of time after the addition of complex **3** to DNA-1 followed at λ = 260 nm. All measurements were conducted with $C_{\mathbf{3}}$ = 30.0 μM, C_T = 3.0 μM and T = 37 °C in Tris-HCl buffered solution, pH = 7.2. Fits of a single-exponential function to the experimental data is indicated with a solid line (red).

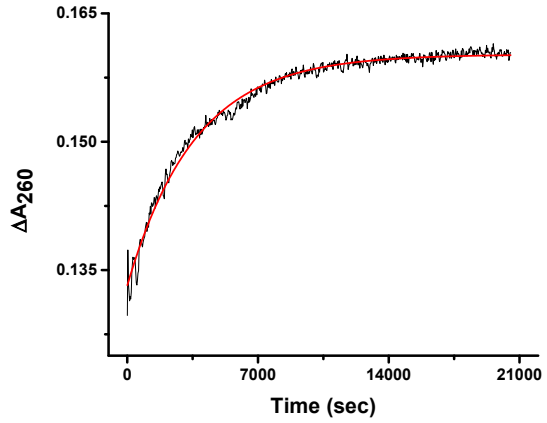
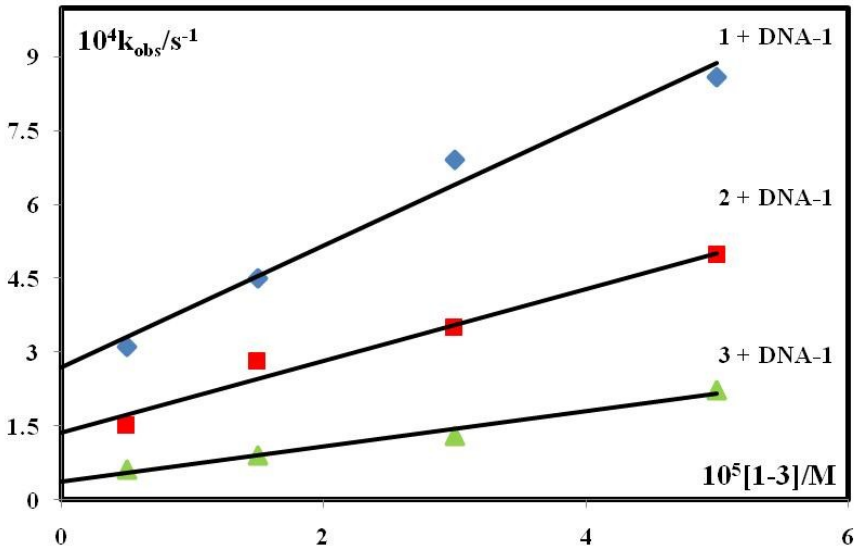
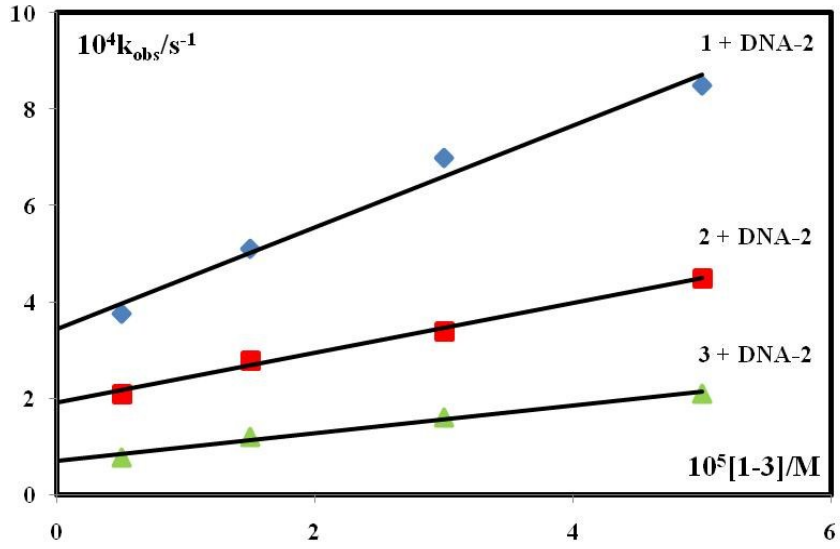


Fig. S9. Absorbance change as a function of time after the addition of complex **3** to RNA followed at λ = 260 nm. All measurements were conducted with $C_{\mathbf{3}}$ = 30.0 μM, C_{T} = 3.0 μM and T = 37 °C in Tris-HCl buffered solution, pH = 7.2. Fits of a single-exponential function to the experimental data is indicated with a solid line (red).


$10^4k_{obs}/s^{-1}$
1 + DNA-1
2 + DNA-1
3 + DNA-1
10^5[1-3]/M
9
7.5
6
4.5
3
1.5
0
0
2
4
6


$10^4k_{obs}/s^{-1}$
1 + DNA-2
2 + DNA-2
3 + DNA-2
10^5[1-3]/M
10
8
6
4
2
0
0
2
4
6

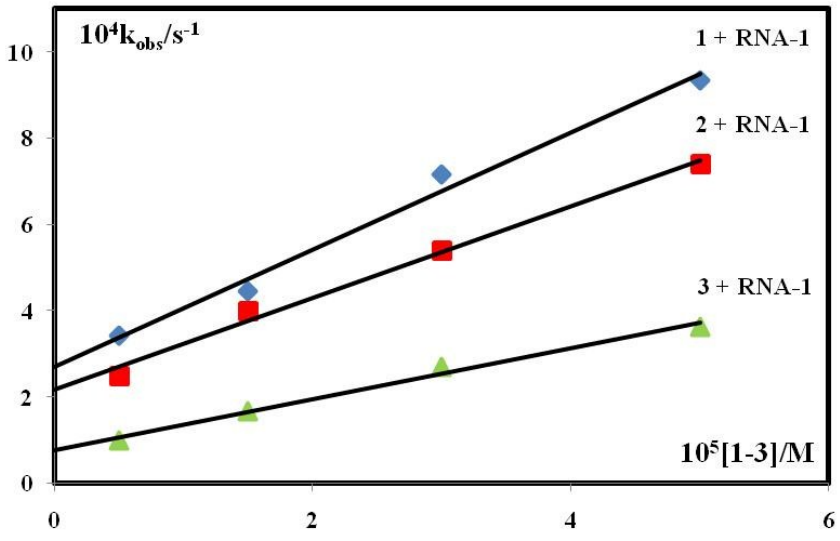

$10^4k_{obs}/s^{-1}$
1 + RNA-1
2 + RNA-1
3 + RNA-1
10^5[1-3]/M
10
8
6
4
2
0
0
2
4
6

Fig. S10. Observed *pseudo*-first order rate constants, k_{obs}, plotted as a function of complex concentration in the interval of 5 – 50 μM together with linear regression lines allowing for determination of $k_{2,app}$ from the slope.

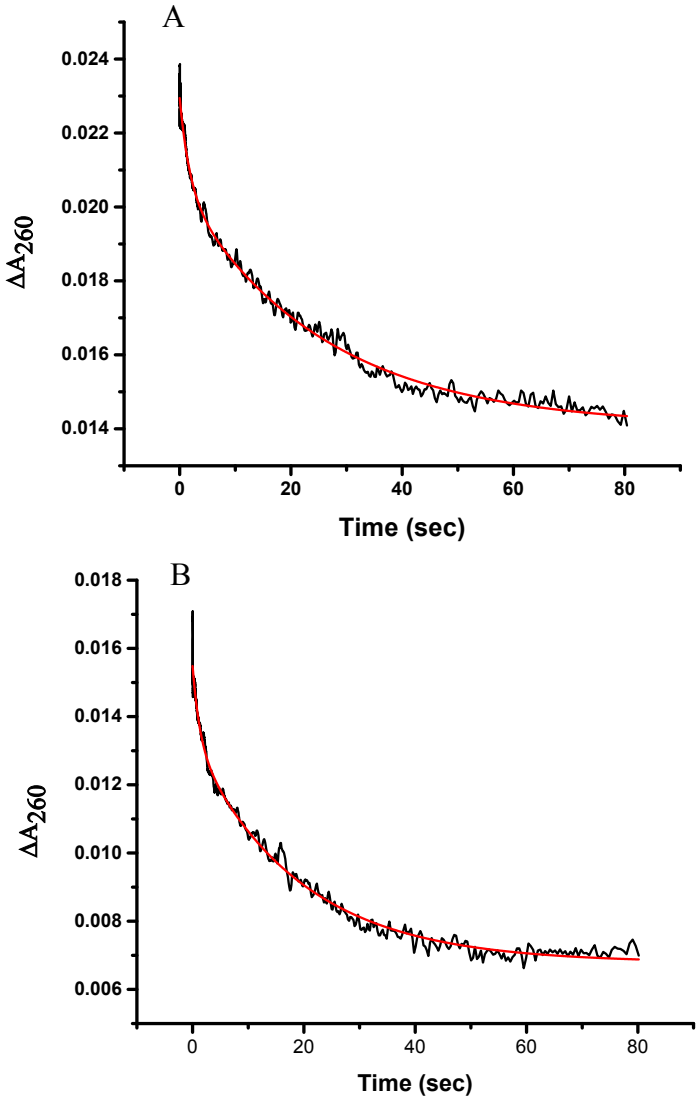


Fig. S11. Absorbance change as a function of time after the addition of complex **1** to CT DNA (A) and HT DNA (B) followed at λ = 260 nm. All measurements were conducted with C_1 = 30.0 μM, C_T = 50.0 μM and T = 37 °C in Tris-HCl buffered solution, pH = 7.2. Fits of a single-exponential function to the experimental data is indicated with a solid line (red).

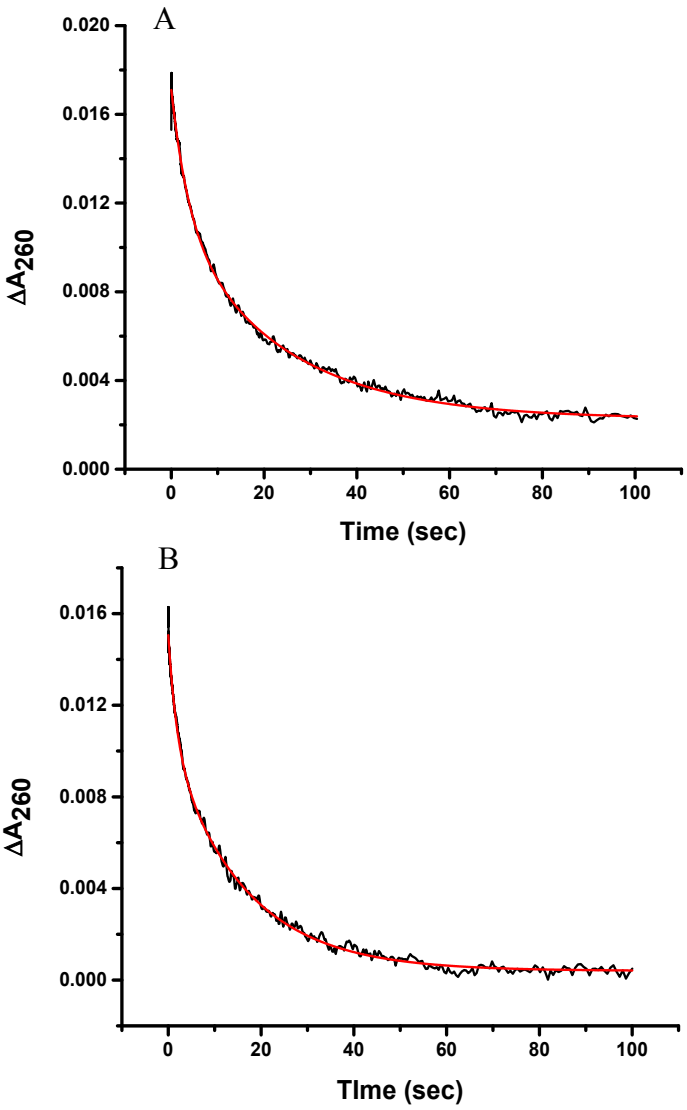
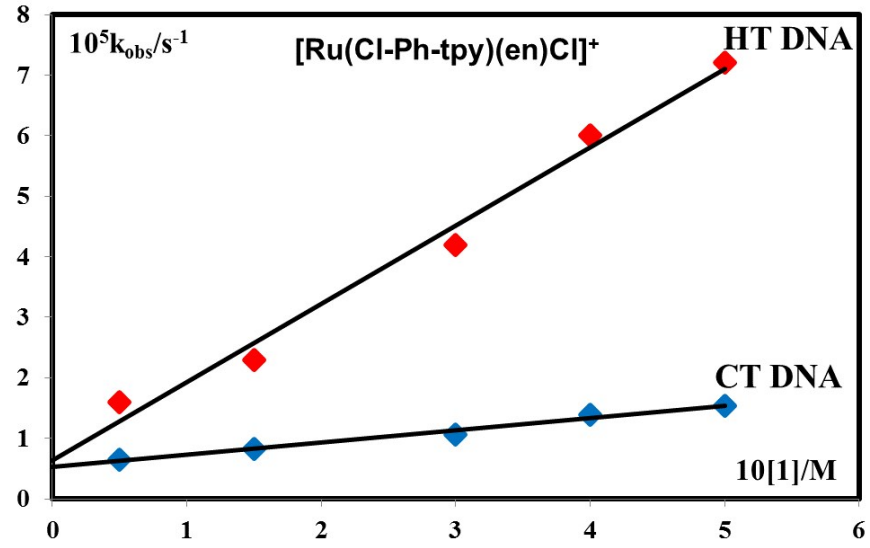
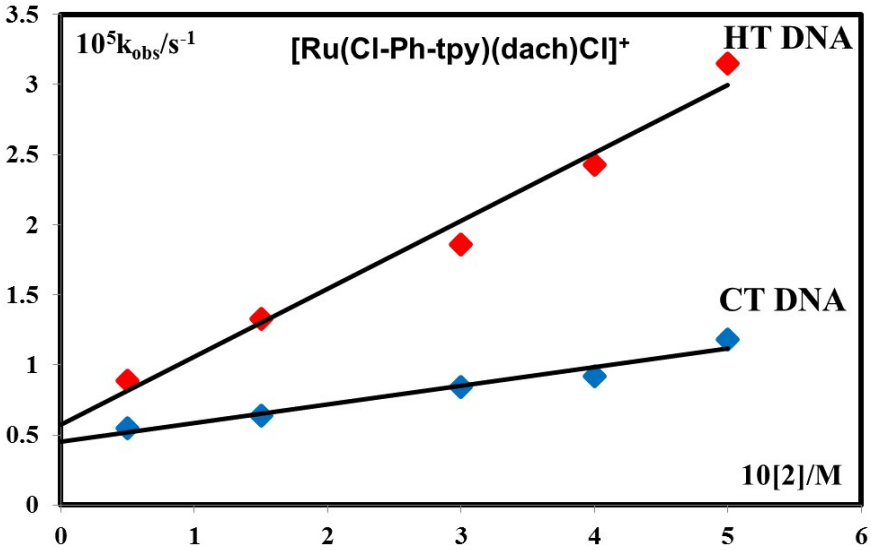


Fig. S12. Absorbance change as a function of time after the addition of complex **2** to CT DNA (A) and HT DNA (B) followed at λ = 260 nm. All measurements were conducted with C_2 = 30.0 μM, C_T = 50.0 μM and T = 37 °C in Tris-HCl buffered solution, pH = 7.2. Fits of a single-exponential function to the experimental data is indicated with a solid line (red).


$10^5k_{obs}/s^{-1}$
[Ru(Cl-Ph-tpy)(en)Cl]+
HT DNA
CT DNA
10[1]/M
0
1
2
3
4
5
6
7
8


$10^5k_{obs}/s^{-1}$
[Ru(Cl-Ph-tpy)(dach)Cl]+
HT DNA
CT DNA
10[2]/M
0
0.5
1
1.5
2
2.5
3
3.5
4
5
6

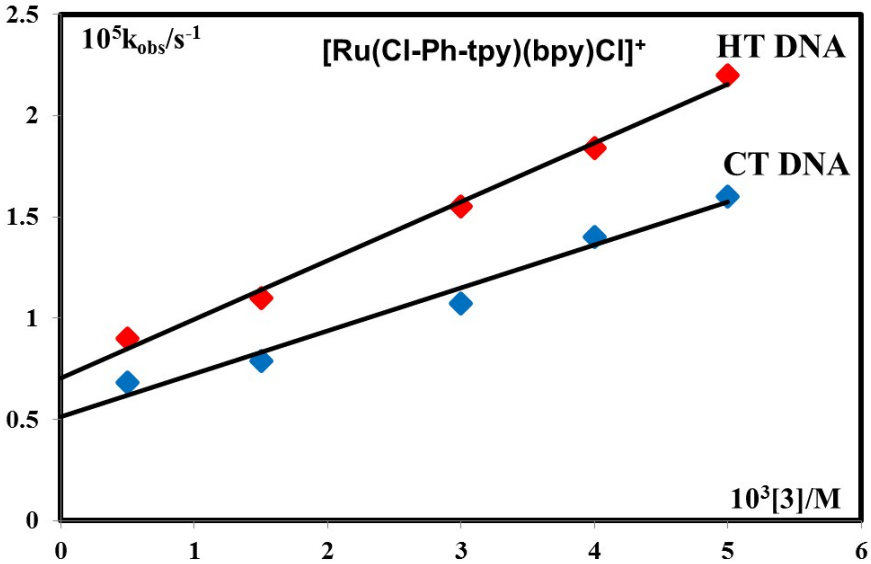

$10^5k_{obs}/s^{-1}$
[Ru(Cl-Ph-tpy)(bpy)Cl]+
HT DNA
CT DNA
10^3[3]/M
0
0.5
1
1.5
2
2.5
3
4
5
6

Fig. S13. Observed *pseudo*-first order rate constants, k_{obs}, plotted as a function of complex concentration in the interval of 5 – 50 μM together with linear regression lines allowing for determination of k_2 from the slope.

Table S1. Selected geometrical parameters for **3** and $\mathbf{3_{Cl}}$.

Bond length [°]		
	3	$\mathbf{3_{Cl}}$*
Ru1—N1	2.078(3)	2.067 (3)
Ru1—N2	1.956(3)	1.953 (3)
Ru1—N3	2.065(3)	2.064 (3)
Ru1—N4	2.089(3)	2.079 (3)
Ru1—N5	2.035(3)	2.032 (3)
Ru1—Cl1	2.4078(9)	2.4205 (9)
Bond angles [°]		
N2—Ru1—N4	176.36(11)	177.28(12)
N2—Ru1—N1	79.55(11)	79.45(12)
N4—Ru1—N1	100.27(11)	101.42(12)
N2—Ru1—N3	79.16(11)	79.62(12)
N4—Ru1—N3	100.93(11)	99.35(12)
N1—Ru1—N3	158.70(10)	158.84(12)
N2—Ru1—N5	97.83(11)	99.50(12)
N4—Ru1—N5	78.55(11)	78.06(12)
N1—Ru1—N5	95.40(11)	84.91(12)
N3—Ru1—N5	86.88(12)	95.53(12)
N2—Ru1—Cl1	89.30(8)	88.44(9)
N4—Ru1—Cl1	94.33(8)	93.99(9)
N1—Ru1—Cl1	89.78(8)	96.82(8)
N3—Ru1—Cl1	90.58(8)	85.66(8)
Torsion angles [°]		
Ru1—N1—C5—C4	175.8 (2)	
Ru1—N1—C5—C6	-4.1 (3)	
Ru1—N2—C6—C7	-178.0 (2)	
Ru1—N2—C6—C5	2.1 (4)	
Ru1—N2—C10—C9	178.1 (2)	
Ru1—N2—C10—C11	-2.3 (4)	
Ru1—N3—C11—C12	175.1 (3)	
Ru1—N3—C11—C10	-3.4 (4)	

***** Data obtained from reference [10].

Table S2. Observed *pseudo*-first order rate constants as a function of complex concentration for the reaction between complex [Ru(Cl-Ph-tpy)(en)Cl]Cl (**1**) and 5'-GMP (**L**) in 25 mM Hepes buffer (50 mM NaCl, pH = 7.2) at 37 ºC.

t (ºC)	$C_{\mathbf{L}}$ [10^{-3} M]	k_{obs} [10^{-3} s^{-1}]
37.0	5.00	3.10(3)
	4.10	2.40(2)
	3.15	2.15(3)
	2.20	1.50(3)
	1.30	1.10(2)
	0.75	0.80(3)

Table S3. Observed *pseudo*-first order rate constants as a function of complex concentration and temperature for the reaction between complex [Ru(Cl-Ph-tpy)(dach)Cl]Cl (**2**) and 5'-GMP (**L**) in 25 mM Hepes buffer (50 mM NaCl, pH = 7.2).

t (ºC)	C_L [10^{-3} M]	k_{obs} [10^{-3} s^{-1}]
15.0	5.00	0.96(2)
	4.10	0.88(3)
	3.15	0.64(2)
	2.20	0.50(3)
	1.30	0.37(3)
	0.75	0.34(3)
25.0	5.00	2.60(3)
	4.10	2.07(3)
	3.15	1.67(2)
	2.20	1.33(3)
	1.30	1.07(3)
	0.75	0.85(3)
37.0	5.00	4.00(3)
	4.10	3.40(2)
	3.15	2.90(3)
	2.20	2.00(3)
	1.30	1.40(3)
	0.75	1.20(3)

Table S4. Observed *pseudo*-first order rate constants as a function of complex concentration for the reaction between complex [Ru(Cl-Ph-tpy)(bpy)Cl]Cl (**3**) and 5'-GMP (**L**) in 25 mM Hepes buffer (50 mM NaCl, pH = 7.2) at 37 ºC.

t ºC	$C_{\mathbf{L}}$ [10^{-3} M]	k_{obs} [10^{-3} s^{-1}]
37.0	5.00	2.11(2)
	4.10	1.90(3)
	3.15	1.70(2)
	2.20	1.40(3)
	1.30	0.90(3)
	0.75	0.60(3)

Table S5. Observed *pseudo*-first order rate constants as a function of complex concentration for the reaction between complex [Ru(Cl-Ph-tpy)(en)Cl]Cl (**1**) and DNA-1 in Tris-HCl buffer (50 mM NaCl, pH = 7.2).

t ºC	$C_{\mathbf{1}}$ [10^{-5} M]	k_{obs}[10^{-4} s^{-1}]
37.0	5.0	8.60(3)
	3.0	6.90(3)
	1.5	4.50(2)
	0.5	3.10(3)

Table S6. Observed *pseudo*-first order rate constants as a function of complex concentration for the reaction between complex [Ru(Cl-Ph-tpy)(en)Cl]Cl (**1**) and DNA-2 in Tris-HCl buffer (50 mM NaCl, pH = 7.2).

t ºC	C_1 [10^{-5} M]	k_{obs} [10^{-4} s^{-1}]
37.0	5.0	8.50(2)
	3.0	7.00(2)
	1.5	5.10(3)
	0.5	3.75(3)

Table S7. Observed *pseudo*-first order rate constants as a function of complex concentration for the reaction between complex [Ru(Cl-Ph-tpy)(en)Cl]Cl (**1**) and RNA in Tris-HCl buffer (50 mM NaCl, pH = 7.2).

t ºC	C_1 [10^{-5} M]	k_{obs} [10^{-4} s^{-1}]
37.0	5.0	9.34(3)
	3.0	7.15(3)
	1.5	4.45(2)
	0.5	3.41(3)

Table S8. Observed *pseudo*-first order rate constants as a function of complex concentration for the reaction between complex [Ru(Cl-Ph-tpy)(dach)Cl]Cl (**2**) and DNA-1 in Tris-HCl buffer (50 mM NaCl, pH = 7.2).

t ºC	C_2 [10^{-5} M]	k_{obs} [10^{-4} s^{-1}]
37.0	5.0	4.97(2)
	3.0	3.50(3)
	1.5	2.80(2)
	0.5	1.50(3)

Table S9. Observed *pseudo*-first order rate constants as a function of complex concentration for the reaction between complex [Ru(Cl-Ph-tpy)(dach)Cl]Cl (**2**) and DNA-2 in Tris-HCl buffer (50 mM NaCl, pH = 7.2).

t ºC	C_2 [10^{-5} M]	k_{obs} [10^{-4} s^{-1}]
37.0	5.0	4.50(3)
	3.0	3.40(2)
	1.5	2.80(2)
	0.5	2.10(3)

Table S10. Observed *pseudo*-first order rate constants as a function of complex concentration for the reaction between complex [Ru(Cl-Ph-tpy)(dach)Cl]Cl (**2**) and RNA in Tris-HCl buffer (50 mM NaCl, pH = 7.2).

t ºC	C_2 [10^{-5} M]	k_{obs} [10^{-4} s^{-1}]
37.0	5.0	7.40(2)
	3.0	5.40(3)
	1.5	4.00(3)
	0.5	2.50(3)

Table S11. Observed *pseudo*-first order rate constants as a function of complex concentration for the reaction between complex [Ru(Cl-Ph-tpy)(bpy)Cl]Cl (**3**) and DNA-1 in Tris-HCl buffer (50 mM NaCl, pH = 7.2).

t ºC	C_3 [10^{-5} M]	10^4 k_{obs}/s^{-1}
37.0	5.0	2.23(3)
	3.0	1.30(3)
	1.5	0.89(3)
	0.5	0.61 (2)

Table S12. Observed *pseudo*-first order rate constants as a function of complex concentration for the reaction between complex [Ru(Cl-Ph-tpy)(bpy)Cl]Cl (**3**) and DNA-2 in Tris-HCl buffer (50 mM NaCl, pH = 7.2).

t ºC	C_3 [10^{-5} M]	k_{obs} [10^{-4} s^{-1}]
37.0	5.0	2.10(2)
	3.0	1.60(2)
	1.5	1.20(3)
	0.5	0.78(3)

Table S13. Observed *pseudo*-first order rate constants as a function of complex concentration for the reaction between complex [Ru(Cl-Ph-tpy)(bpy)Cl]Cl (**3**) and RNA in Tris-HCl buffer (50 mM NaCl, pH = 7.2).

t ºC	C_3 [10^{-5} M]	k_{obs} [10^{-4} s^{-1}]
37.0	5.0	3.63(3)
	3.0	2.70(3)
	1.5	1.65(3)
	0.5	0.98(3)

Table S14. Observed *pseudo*-first order rate constants as a function of complex concentration for the reaction between complex [Ru(Cl-Ph-tpy)(en)Cl]Cl (**1**) and CT DNA in Tris-HCl buffer (50 mM NaCl, pH = 7.2).

t ºC	C_1 [10^{-5} M]	k_{obs} [10^{-1} s^{-1}]
37.0	5.00	1.54(2)
	4.00	1.39(3)
	3.00	1.07(3)
	1.50	0.83(2)
	0.50	0.65(3)

Table S15. Observed *pseudo*-first order rate constants as a function of complex concentration for the reaction between complex [Ru(Cl-Ph-tpy)(en)Cl]Cl (**1**) and HT DNA in Tris-HCl buffer (50 mM NaCl, pH = 7.2).

t ºC	C_1 [10^{-5} M]	k_{obs} [10^{-1} s^{-1}]
37.0	5.00	7.20(3)
	4.00	6.00(3)
	3.00	4.20(3)
	1.50	2.29(3)
	0.50	1.60(3)

Table S16. Observed *pseudo*-first order rate constants as a function of complex concentration for the reaction between complex [Ru(Cl-Ph-tpy)(dach)Cl]Cl (**2**) and CT DNA in Tris-HCl buffer (50 mM NaCl, pH = 7.2).

t ºC	C_2 [10^{-5} M]	k_{obs} [10^{-1} s^{-1}]
37.0	5.00	1.18(3)
	4.00	0.92(3)
	3.00	0.84(2)
	1.50	0.64(3)
	0.50	0.55(3)

Table S17. Observed *pseudo*-first order rate constants as a function of complex concentration for the reaction between complex [Ru(Cl-Ph-tpy)(dach)Cl]Cl (**2**) and HT DNA in Tris-HCl buffer (50 mM NaCl, pH = 7.2).

t ºC	C_2 [10^{-5} M]	k_{obs} [10^{-1} s^{-1}]
37.0	5.00	3.15(2)
	4.00	2.43(3)
	3.00	1.86(3)
	1.50	1.33(3)
	0.50	0.89(3)

Table S18. Observed *pseudo*-first order rate constants as a function of complex concentration for the reaction between complex [Ru(Cl-Ph-tpy)(bpy)Cl]Cl (**3**) and CT DNA in Tris-HCl buffer (50 mM NaCl, pH = 7.2).

t ºC	C_3 [10^{-5} M]	k_{obs} [10^{-3} s^{-1}]
37.0	5.00	1.60(2)
	4.00	1.40(2)
	3.00	1.07(2)
	1.50	0.79(3)
	0.50	0.68(3)

Table S19. Observed *pseudo*-first order rate constants as a function of complex concentration for the reaction between complex [Ru(Cl-Ph-tpy)(bpy)Cl]Cl (**3**) and HT DNA in Tris-HCl buffer (50 mM NaCl, pH = 7.2).

t ºC	C_3 [10^{-5} M]	k_{obs} [10^{-3} s^{-1}]
37.0	5.00	2.20(3)
	4.00	1.84(3)
	3.00	1.55(3)
	1.50	1.10(3)
	0.50	0.90(2)