Electronic Supplementary Material (ESI) for Dalton Transactions.

Supporting Information

Synthesis, characterization and anticancer mechanism studies of fluorinated cyclometalated ruthenium(II) complexes

Ya Wen,[a] Cheng Ouyang,[a] Quanwen Li,[b] Thomas W. Rees,[a] Kangqiang Qiu,*[a] Liangnian Ji[a] and Hui Chao*[a,c]

[a] *MOE Key Laboratory of Bioinorganic and Synthetic Chemistry, School of Chemistry, Sun Yat-Sen University, Guangzhou, 510275, P. R. China*

[b] *School of Materials Science and Engineering, Nankai University, Tianjin 300350, P. R. China.*

[c] *MOE Key Laboratory of Theoretical Organic Chemistry and Functional Molecule, School of Chemistry and Chemical Engineering, Hunan University of Science and Technology, Xiangtan, 400201, P. R. China*

Email: ceschh@mail.sysu.edu.cn (H. Chao), qiukq3@mail.sysu.edu.cn (K. Qiu).

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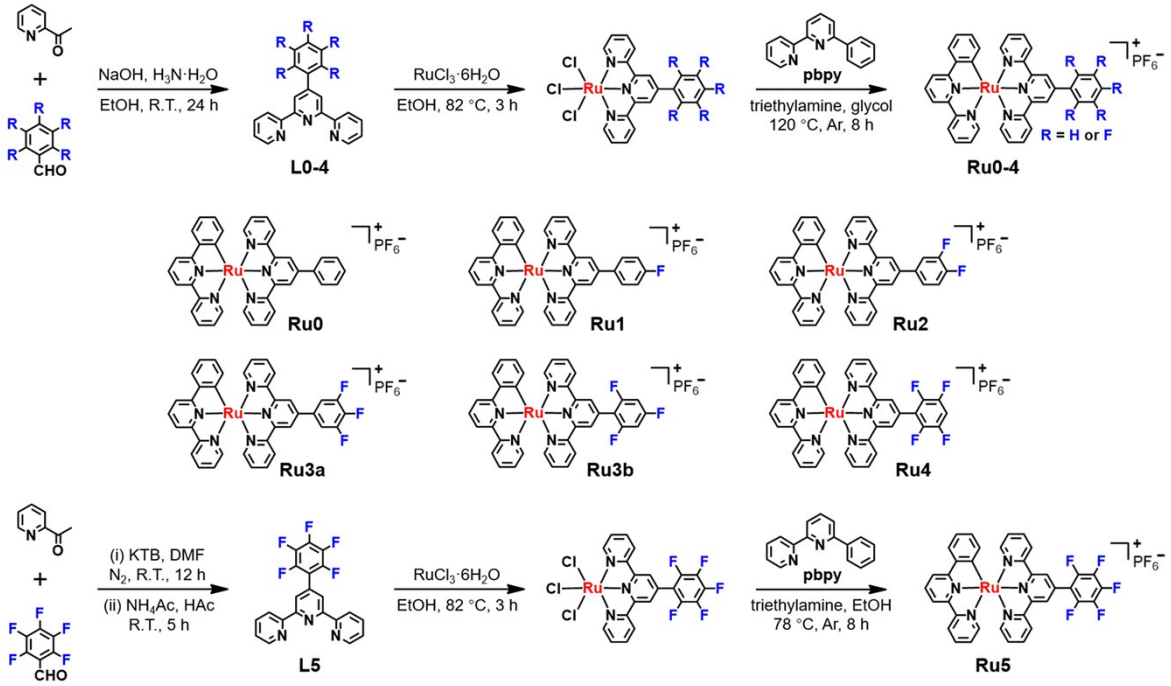

Scheme S1. Synthetic route to **Ru0-5**.

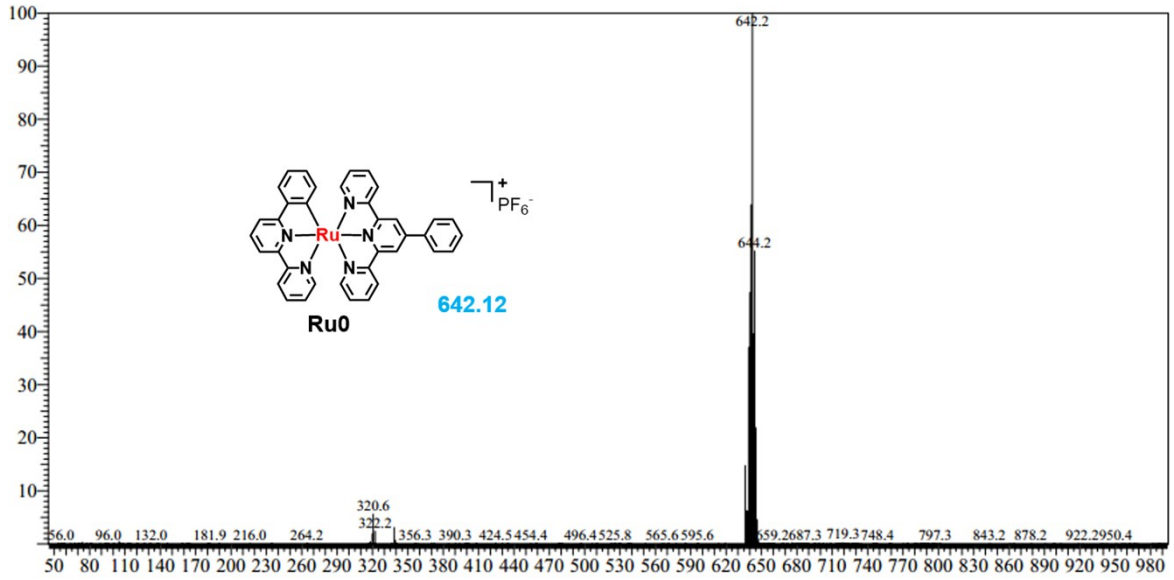

Fig. S1 ES-MS spectrum of complex **Ru0**.

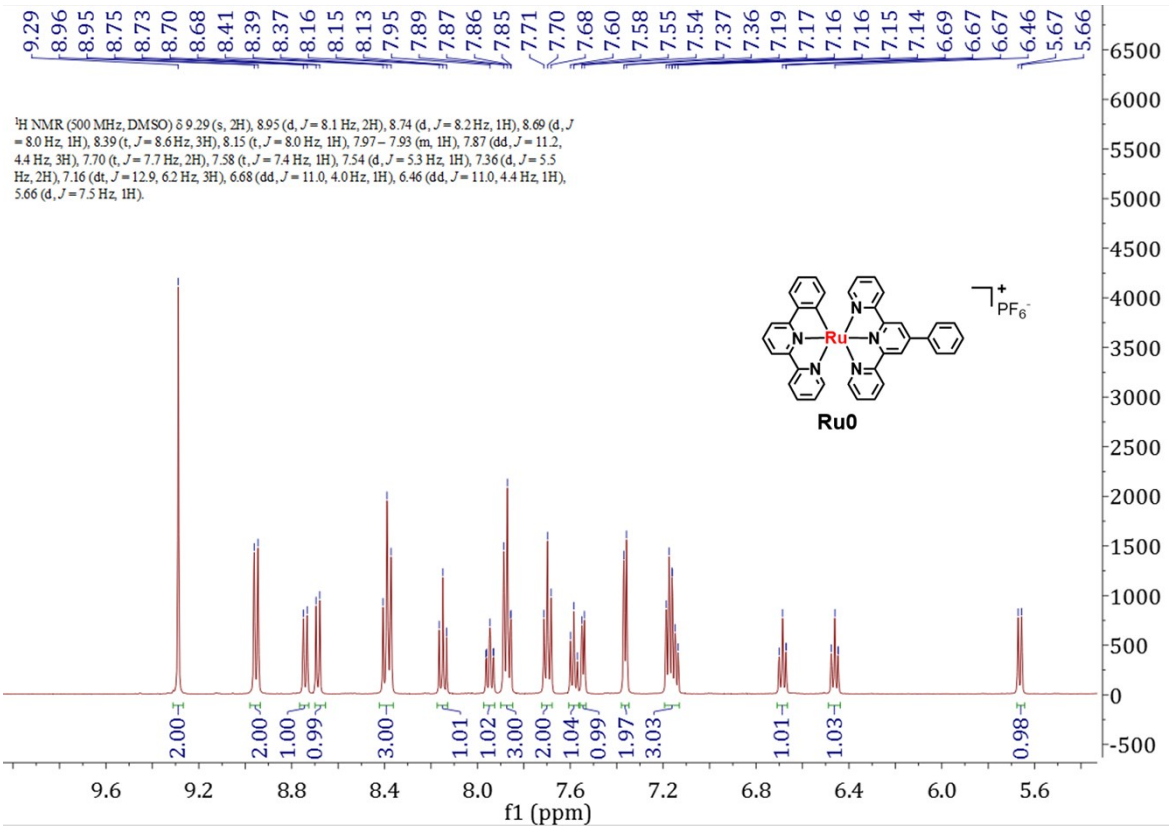

Fig. S2 ^{1}H NMR spectrum of complex **Ru0** in d_6-DMSO.

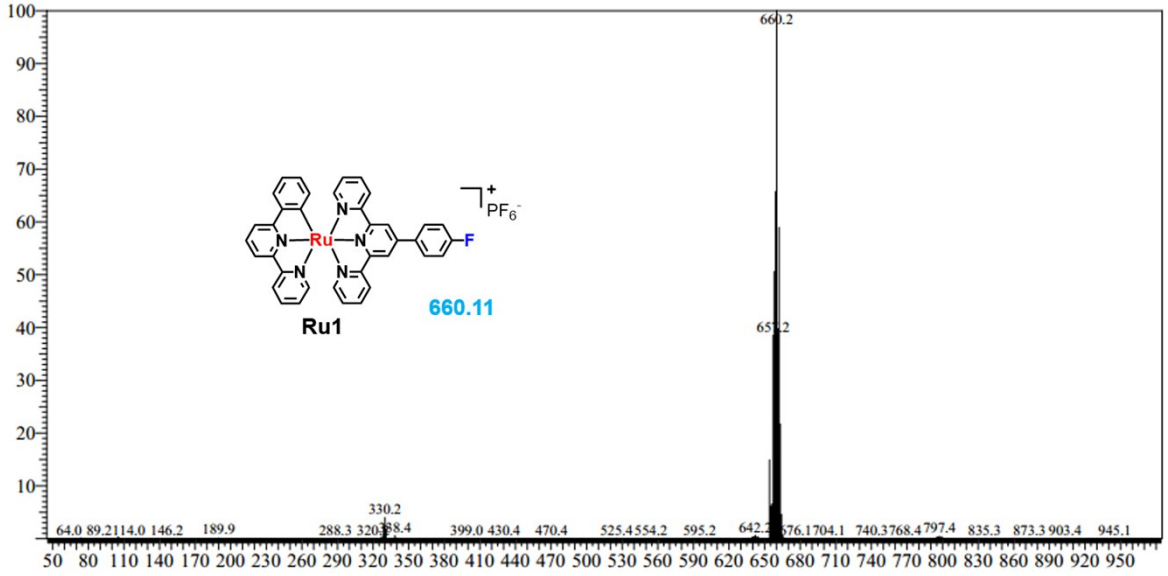

Fig. S3 ES-MS spectrum of complex **Ru1**.

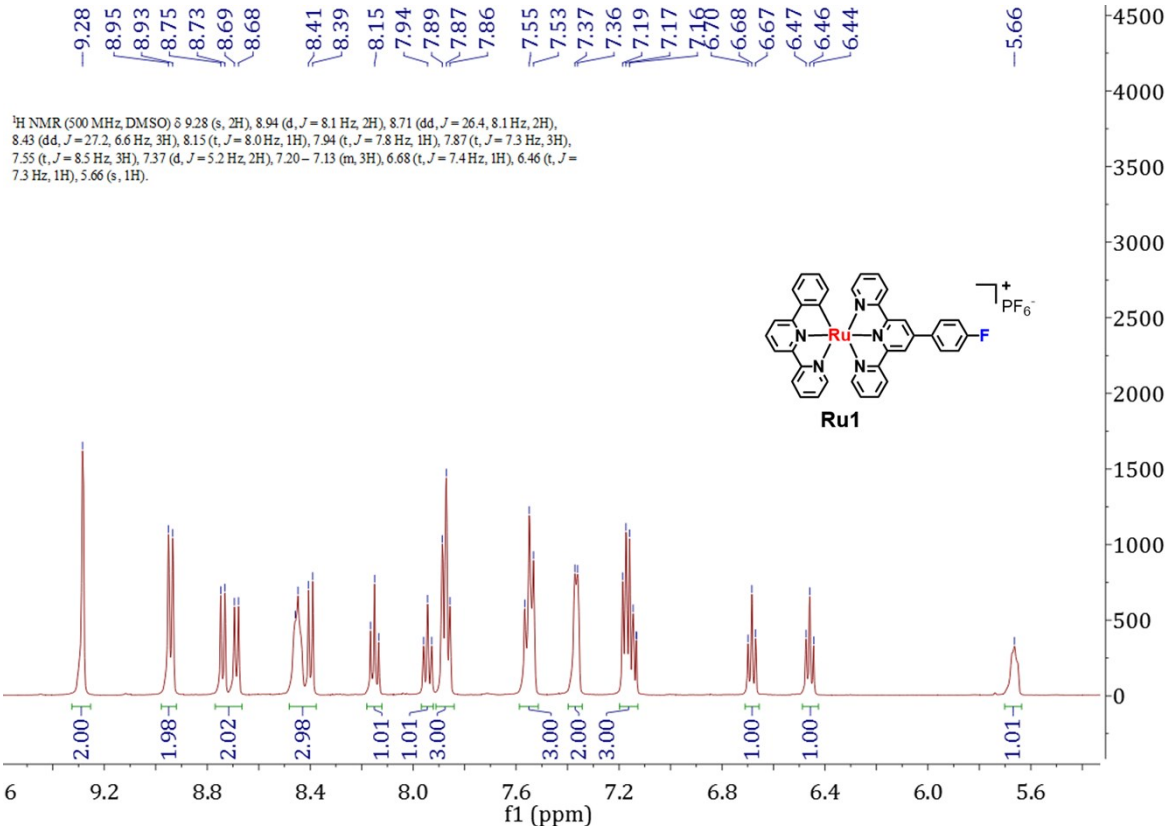

Fig. S4 ^{1}H NMR spectrum of complex **Ru1** in d_6-DMSO.

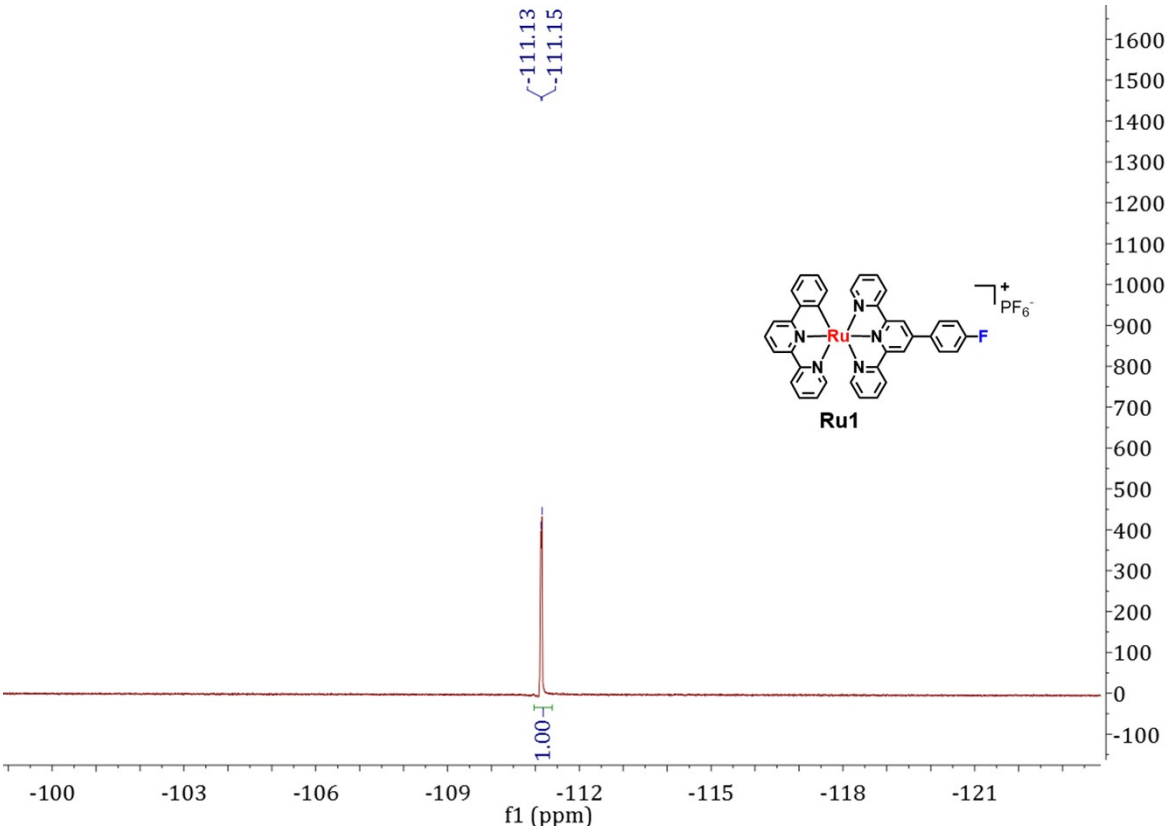

Fig. S5 ^{19}F NMR spectrum of the complex **Ru1**.

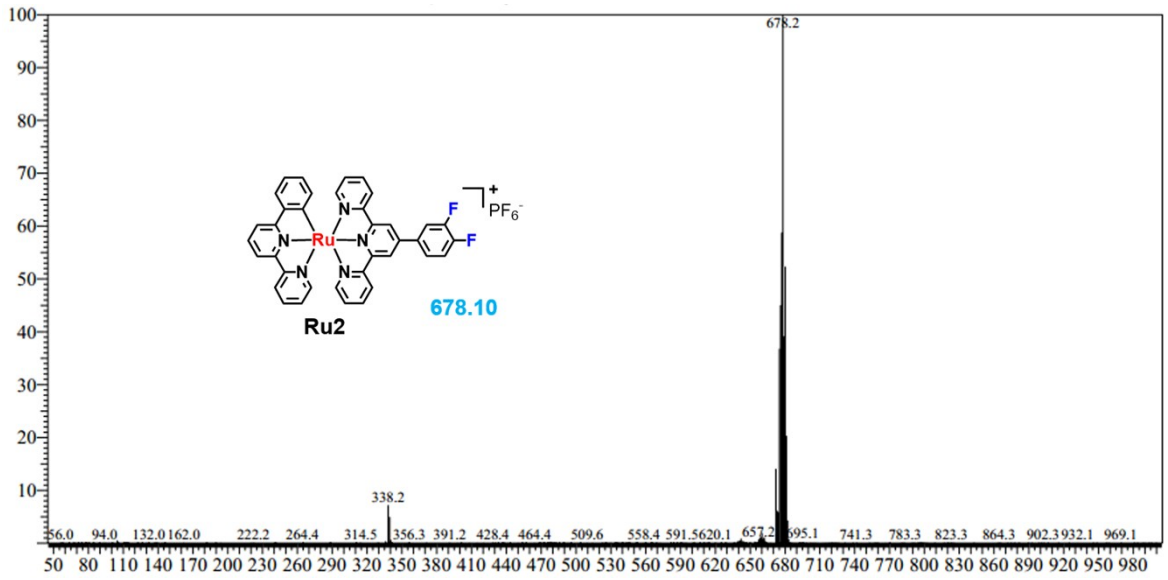

Fig. S6 ES-MS spectrum of complex **Ru2**.

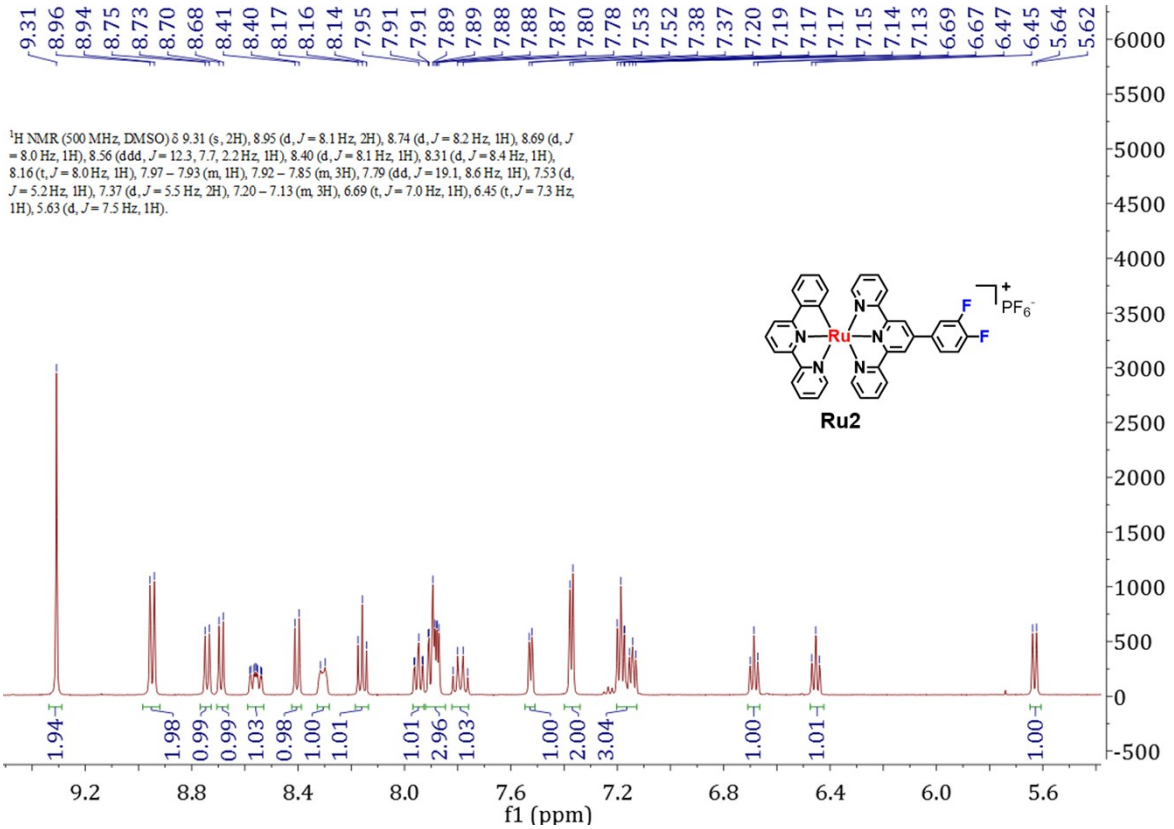

Fig. S7 ^{1}H NMR spectrum of complex **Ru2** in d_6-DMSO.

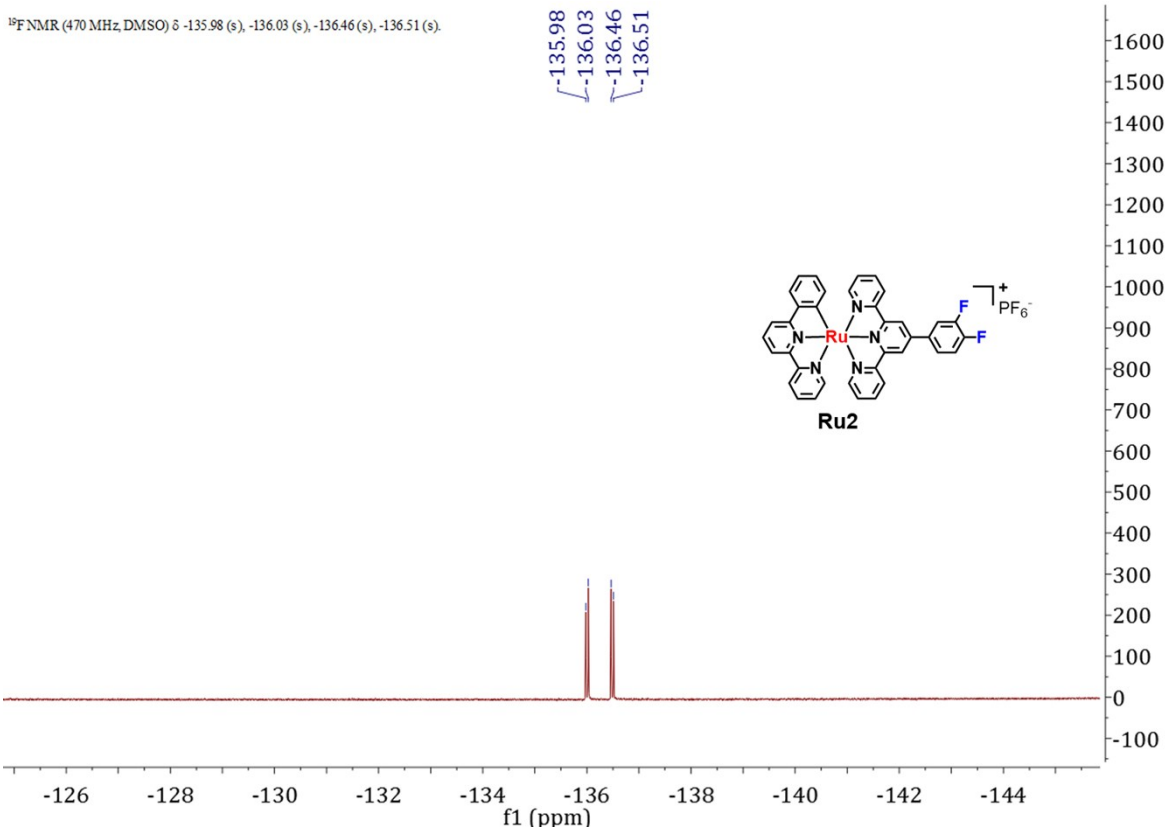

Fig. S8 ^{19}F NMR spectrum of the complex **Ru2**.

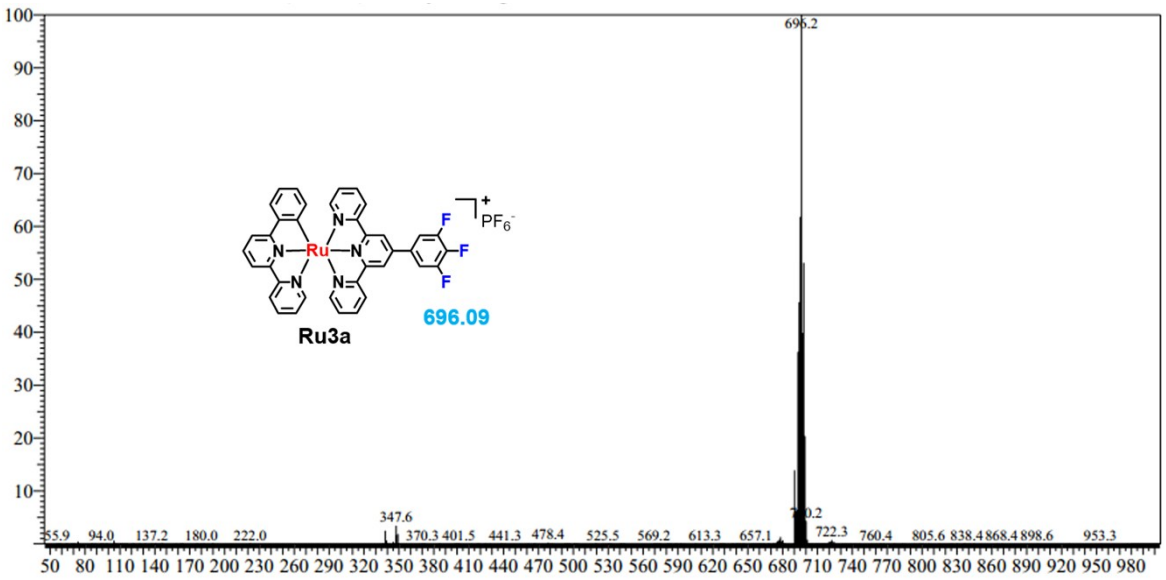

Fig. S9 ES-MS spectrum of complex **Ru3a**.

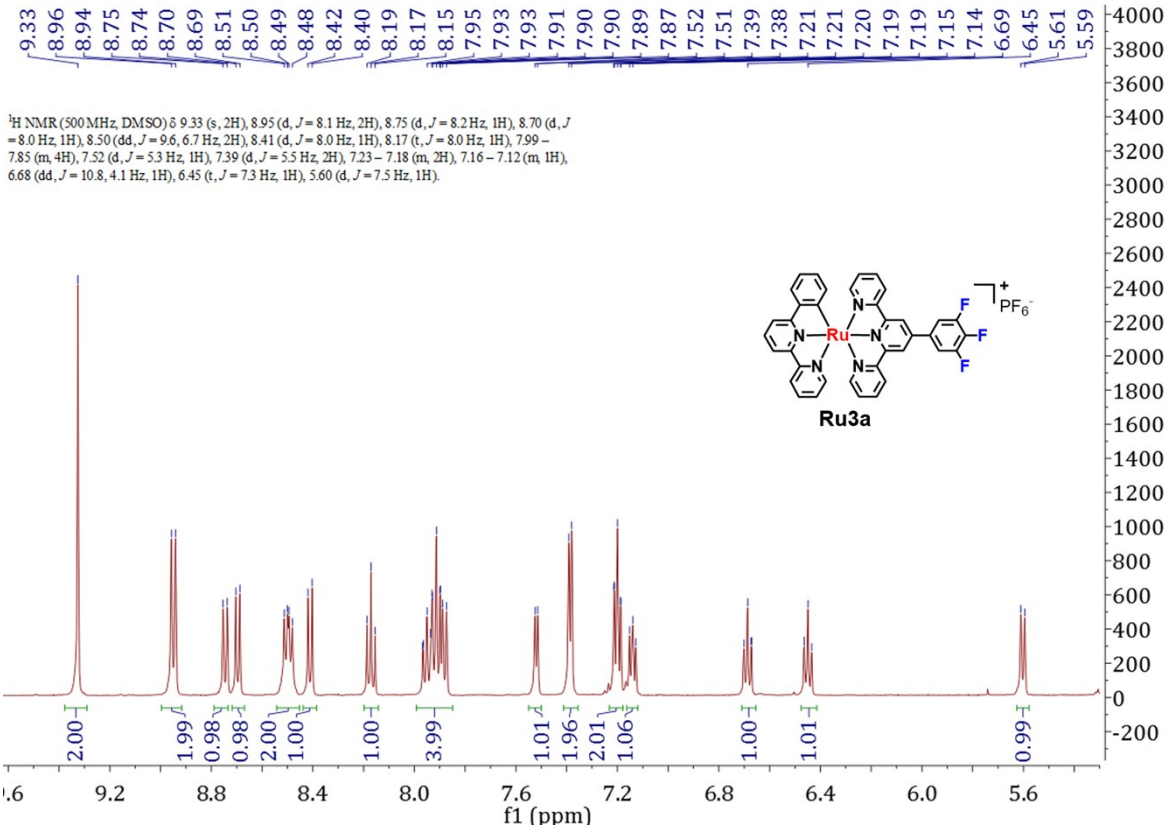

Fig. S10 ^{1}H NMR spectrum of complex **Ru3a** in d_6-DMSO.

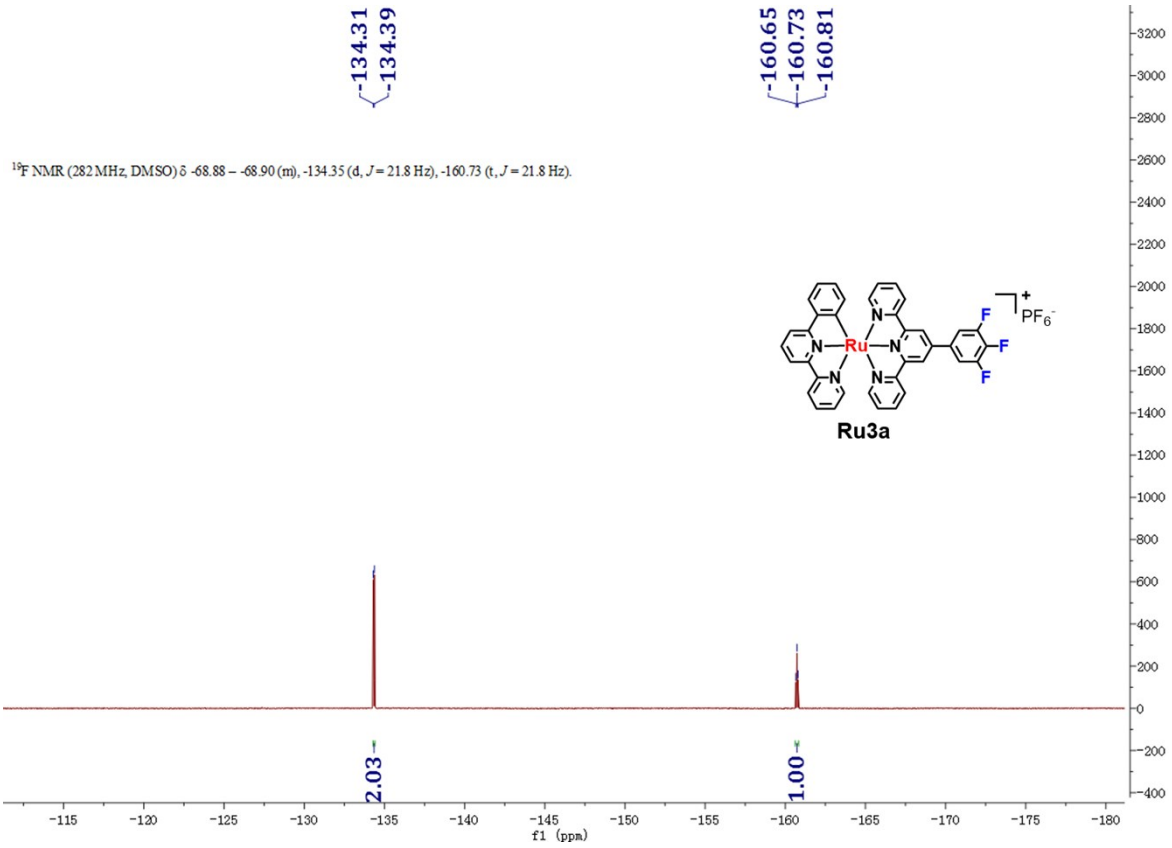

Fig. S11 ^{19}F NMR spectrum of the complex **Ru3a**.

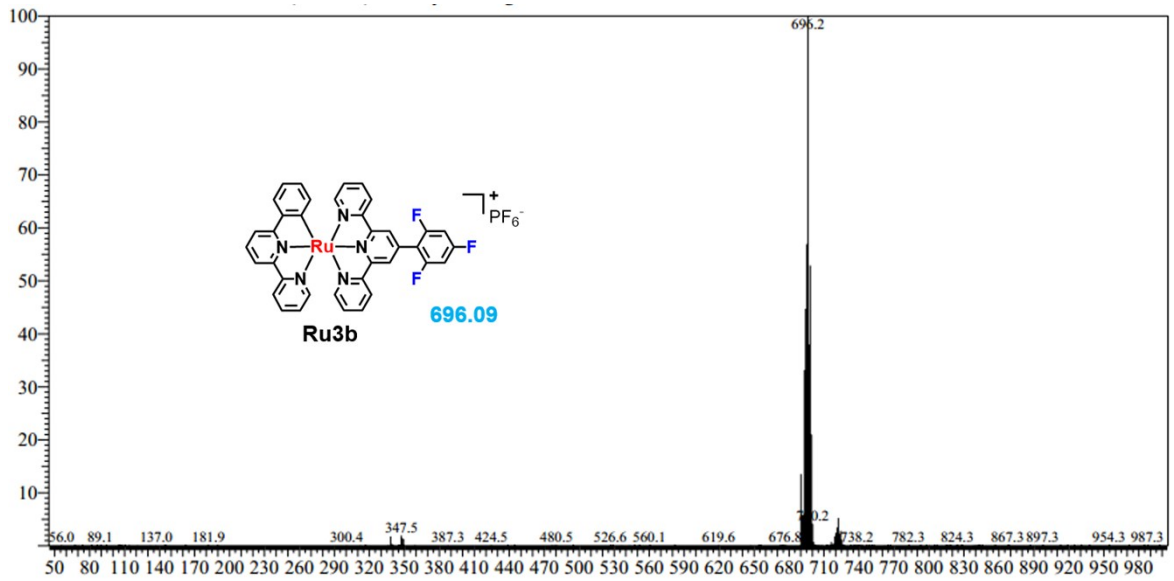

Fig. S12 ES-MS spectrum of complex **Ru3b**.

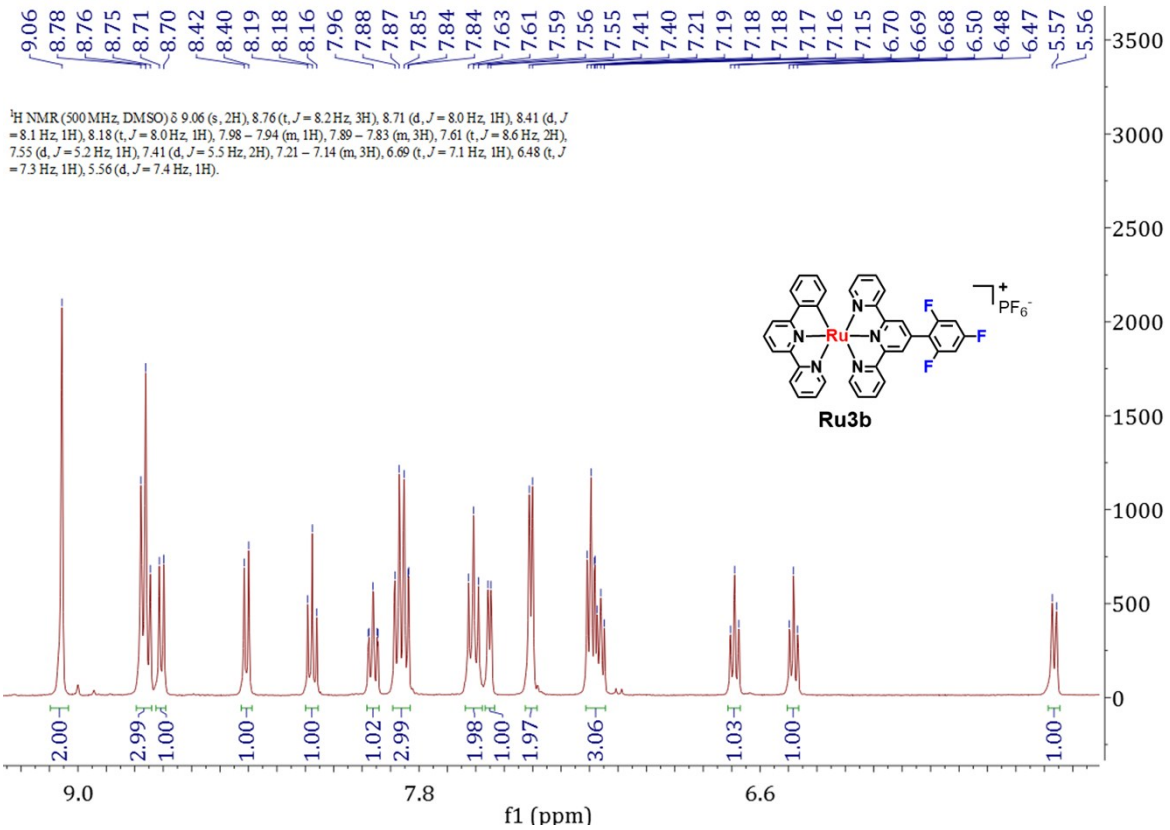

Fig. S13 ^{1}H NMR spectrum of complex **Ru3b** in d_6-DMSO.

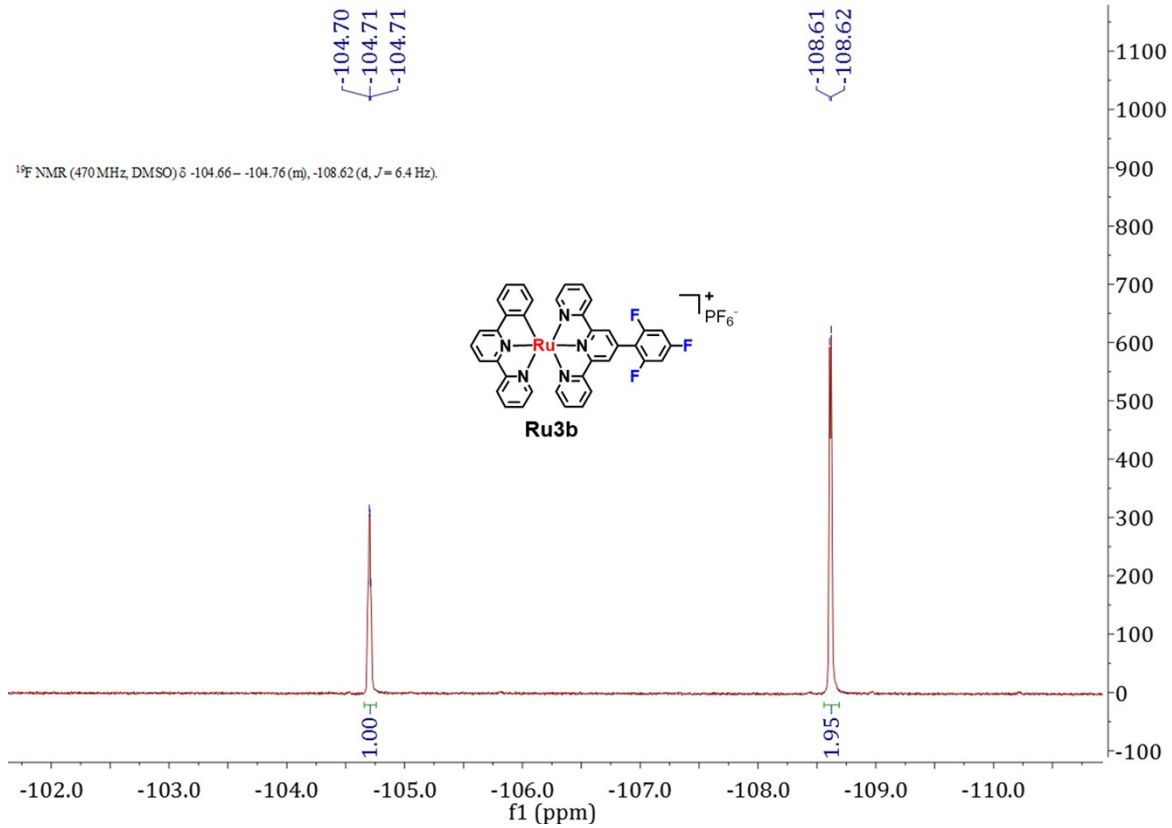

Fig. S14 ^{19}F NMR spectrum of the complex **Ru3b**.

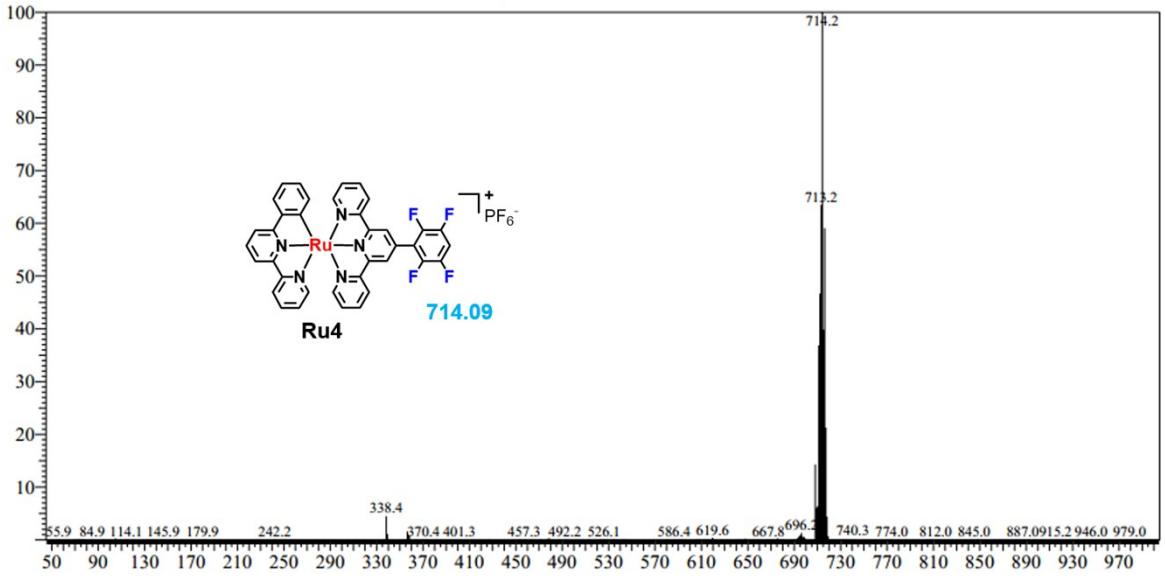

Fig. S15 ES-MS spectrum of complex **Ru4**.

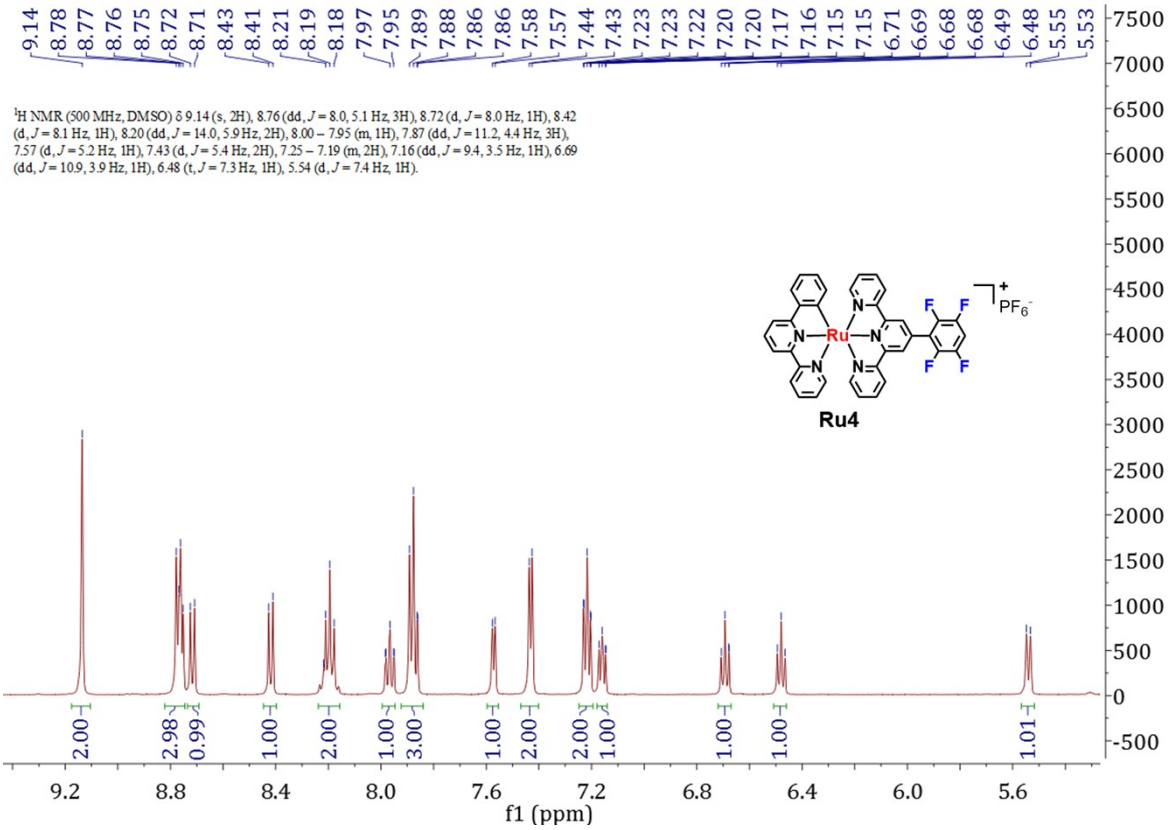

Fig. S16 ^{1}H NMR spectrum of complex **Ru4** in d_6-DMSO.

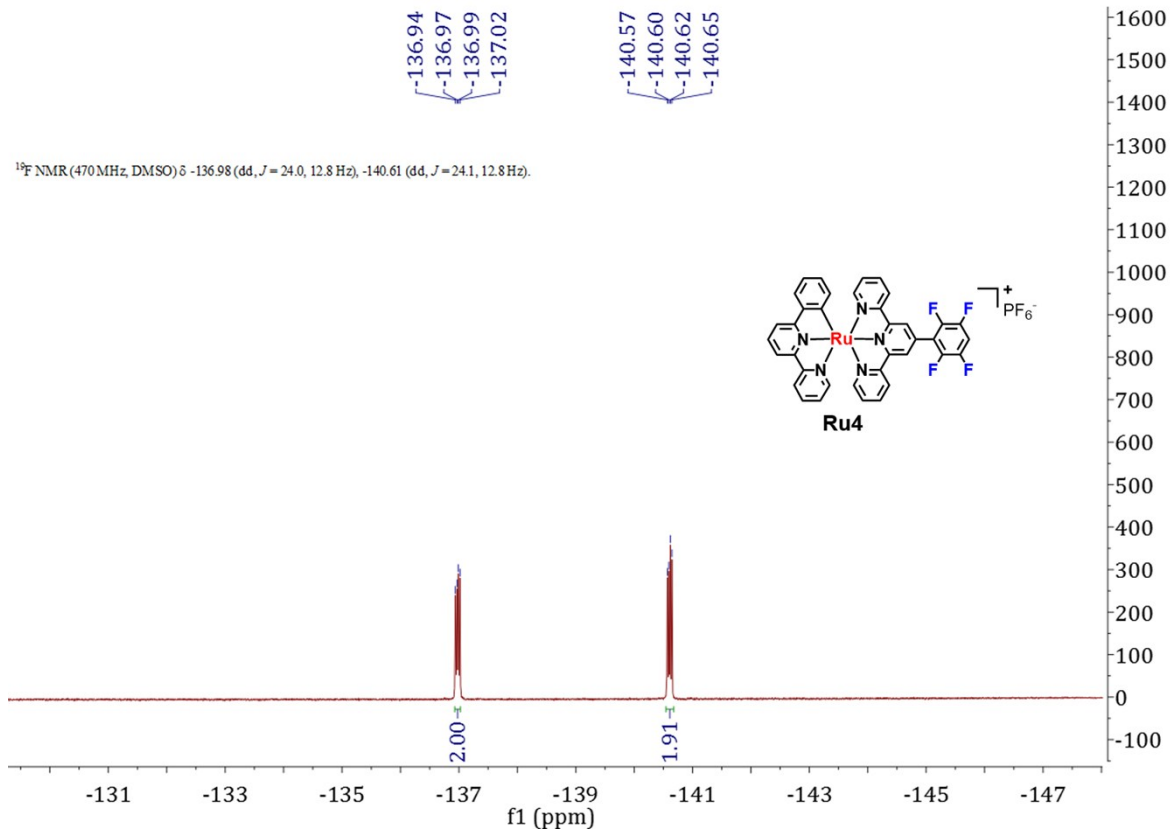

Fig. S17 ^{19}F NMR spectrum of the complex **Ru4**.

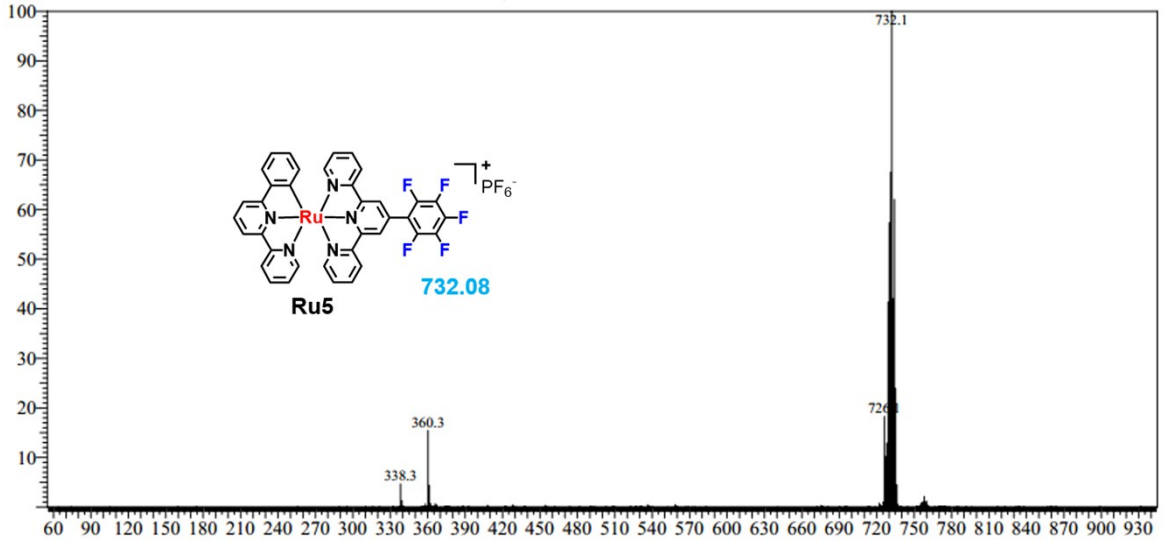

Fig. S18 ES-MS spectrum of complex **Ru5**.

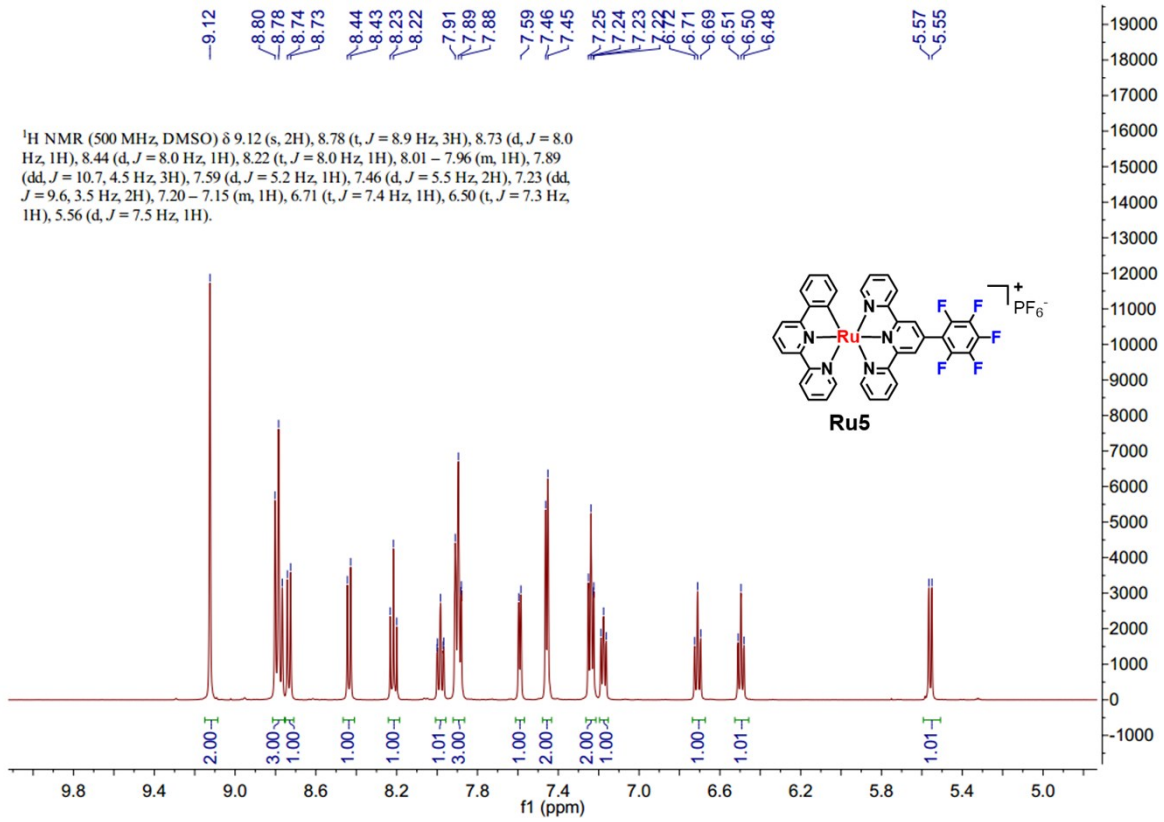

Fig. S19 [1]H NMR spectrum of complex **Ru5** in d_6-DMSO.

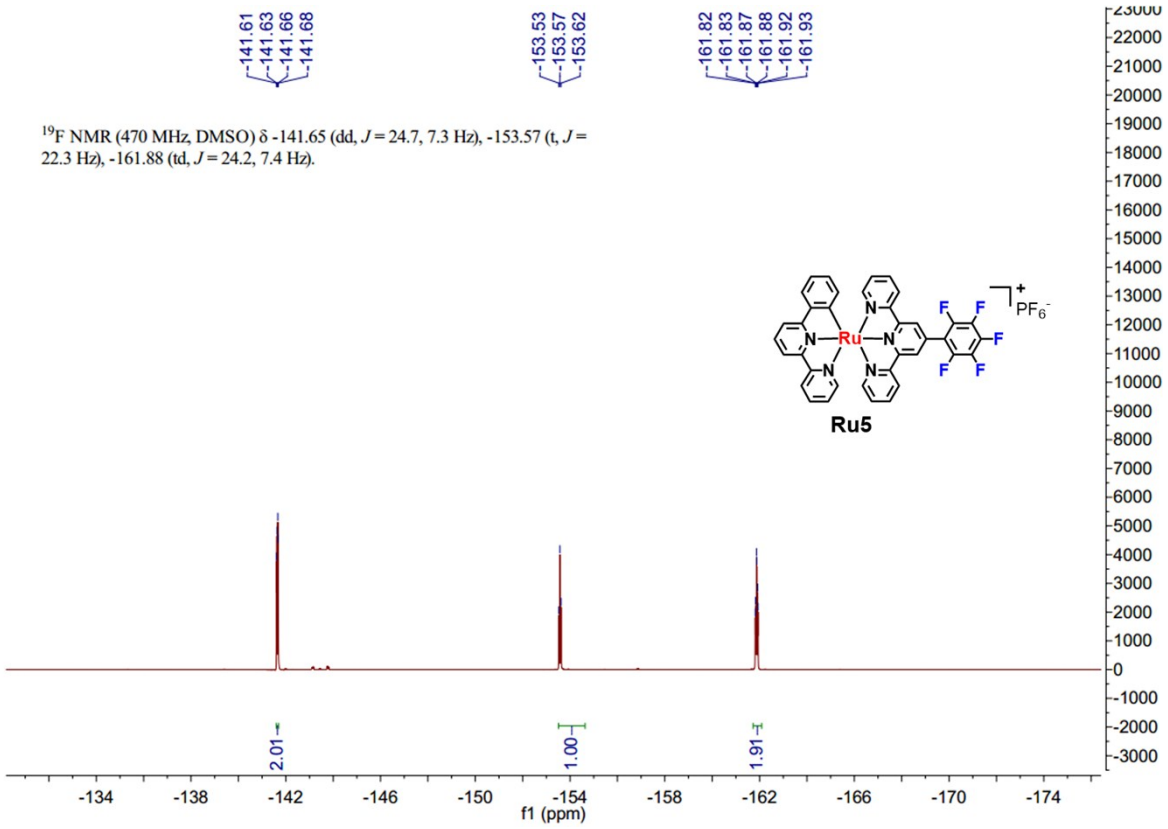

Fig. S20 ^{19}F NMR spectrum of the complex **Ru5**.

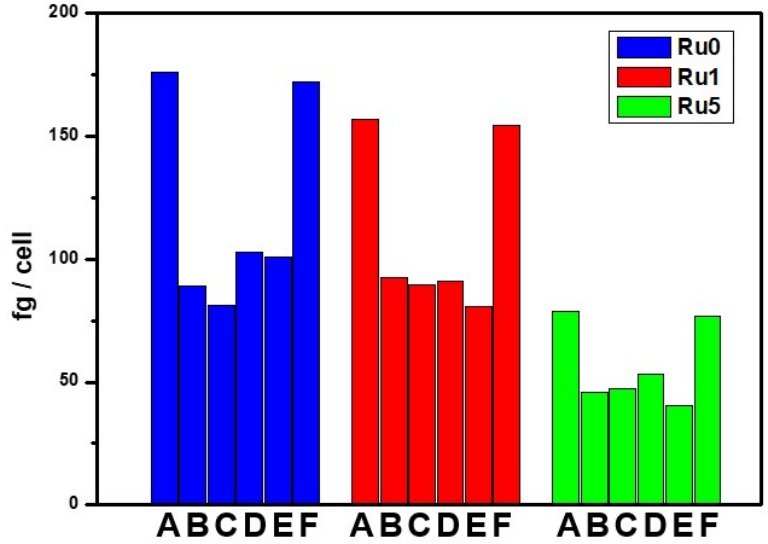

Fig. S21 ICP-MS data of A549R cells incubated with **Ru0**, **Ru1** and **Ru5** (1.0 μM) at different conditions. (A) Control cells without adding inhibitor at 37 °C; (B) Cells were incubated at 4 °C; (C) 50 mM NH_4Cl; (D) 50 μM chloroquine; (E) 50 mM 2-deoxy-D-glucose and 5 μM oligomycin; (F) High K^+-HBSS (170 mM K^+).

Table S1 Crystallographic Data for **Ru0** and **Ru1**

Complexes	**Ru0**	**Ru1**
Empirical formula	$C_{42.5}H_{32.5}F_6N_6PRu$	$C_{39}H_{28}F_7N_6PRu$
Formula weight	873.28	845.71
Temperature /K	293(2)	150.00(10)
Wavelength/Å	0.71073	0.71073
Crystal system	Monoclinic	Monoclinic
a / Å	8.4069(3)	8.7662(2)
b / Å	21.1667(9)	18.5608(4)
c / Å	21.7727(7)	21.9662(5)
β/°	99.448(3)	99.627(2)
V / Å^3	3821.8(2)	3523.74(14)
Z	4	4
ρ_{cald}/g.cm^{-3}	1.518	1.594
Absorption coefficient /mm^{-1}	0.522	0.567
F (000)	1770	1704
θ range for data collection /°	3.377 to 27.496	3.243 to 27.499
Data / restraints / parameters	8503 / 18 / 516	7990 / 0 / 488
Goodness-of-fit on F^2	1.030	1.032
R_1, wR_2 indices [$I>2\sigma(I)$]	0.0417, 0.0895	0.0313, 0.0706
R_1, wR_2 indices (all data)	0.0580, 0.0960	0.0382, 0.0739
Largest diff. peak and hole /*e*. Å^{-3}	0.761 and -0.431	0.831 and -0.463

Table S2 Crystallographic Data for **Ru2** and **Ru3a**

Complexes	**Ru2**	**Ru3a**
Empirical formula	$C_{37}H_{24}F_{9.50}N_{5.25}P_{1.25}Ru$	$C_{37}H_{23}F_{10.50}N_{5.25}P_{1.25}Ru$
Formula weight	862.40	880.39
Temperature /K	293(2)	293(2)
Wavelength/Å	0.71073	0.71073
Crystal system	Tetragonal	Tetragonal
a / Å	24.0261(4)	23.9804(9)
b / Å	24.0261(4)	23.9804(9)
c / Å	25.2884(7)	25.2619(14)
β/°	90	90
V / Å^3	14597.8(6)	14527.1(14)
Z	16	16
ρ_{cald}/g.cm^{-3}	1.570	1.610
Absorption coefficient /mm^{-1}	0.568	0.577
F (000)	6896	7024
θ range for data collection /°	3.222 to 27.496	3.336 to 27.493
Data / restraints / parameters	8333 / 6 / 489	8098 / 6 / 498
Goodness-of-fit on F^2	1.027	1.084
R_1, wR_2 indices [$I>2\sigma(I)$]	0.0577, 0.1454	0.0835, 0.2108
R_1, wR_2 indices (all data)	0.0849, 0.1639	0.1083, 0.2343
Largest diff. peak and hole /*e*. Å^{-3}	1.496 and -1.298	1.950 and -1.405

Table S3 Crystallographic Data for **Ru3b** and **Ru4**

Complexes	**Ru3b**	**Ru4**
Empirical formula	$C_{44}H_{31}F_9N_5PRu$	$C_{46}H_{33}F_{10}N_6PRu$
Formula weight	932.78	991.82
Temperature /K	293(2)	150.00(10)
Wavelength/Å	0.71073	0.71073
Crystal system	Monoclinic	Monoclinic
a / Å	12.4892(5)	26.7258(8)
b / Å	9.0100(3)	8.8028(3)
c / Å	17.9682(8)	18.4875(6)
β/°	105.056(4)	107.270(3)
V / Å^3	1952.51(14)	4153.3(2)
Z	2	4
ρ_{cald}/g.cm^{-3}	1.587	1.586
Absorption coefficient /mm^{-1}	0.526	0.504
F (000)	940	2000
θ range for data collection /°	3.378 to 25.998	3.524 to 27.498
Data / restraints / parameters	6343 / 38 / 542	7419 / 20 / 579
Goodness-of-fit on F^2	1.075	1.041
R_1, wR_2 indices [$I>2\sigma(I)$]	0.0468, 0.1142	0.0351, 0.0872
R_1, wR_2 indices (all data)	0.0579, 0.1220	0.0373, 0.0897
Largest diff. peak and hole /*e*. Å^{-3}	1.206 and -0.677	0.453 and -0.618

Table S4 Crystallographic Data for **Ru5**

Complexes	**Ru5**
Empirical formula	$C_{44}H_{29}F_{11}N_5PRu$
Formula weight	968.76
Temperature /K	293(2)
Wavelength/Å	0.71073
Crystal system	Monoclinic
a / Å	27.1180(7)
b / Å	9.1320(2)
c / Å	35.8913(9)
β/°	106.414(3)
V / Å^3	8525.9(4)
Z	8
ρ_{cald}/g.cm^{-3}	1.509
Absorption coefficient /mm^{-1}	0.492
F (000)	3888
θ range for data collection /°	3.185 to 27.494
Data / restraints / parameters	9509 / 0 / 560
Goodness-of-fit on F^2	1.028
R_1, wR_2 indices [$I>2\sigma(I)$]	0.0340, 0.0716
R_1, wR_2 indices (all data)	0.0483, 0.0789
Largest diff. peak and hole /*e*. Å^{-3}	0.392 and -0.411

Table S5 Selected bond lengths (Å) and bond angles (°) for **Ru0**

Bond	Dist. (Å)	Bond	Dist. (Å)
Ru(1)-N(1)	2.018(2)	Ru(1)-N(2)	2.144(2)
Ru(1)-N(3)	2.061(2)	Ru(1)-N(4)	1.950(2)
Ru(1)-N(5)	2.059(2)	Ru(1)-C(1)	2.032(3)
Angle	(°)	Angle	(°)
N(1)-Ru(1)-N(2)	76.72(9)	N(1)-Ru(1)-N(3)	98.32(9)
N(1)-Ru(1)-N(5)	103.26(9)	N(1)-Ru(1)-C(1)	80.00(10)
N(3)-Ru(1)-N(2)	88.67(9)	N(4)-Ru(1)-N(1)	176.19(9)
N(4)-Ru(1)-N(2)	105.98(9)	N(4)-Ru(1)-N(3)	79.18(9)
N(4)-Ru(1)-N(5)	79.14(9)	N(4)-Ru(1)-C(1)	97.32(10)
N(5)-Ru(1)-N(2)	98.59(9)	N(5)-Ru(1)-N(3)	158.27(9)
C(1)-Ru(1)-N(2)	156.70(10)	C(1)-Ru(1)-N(3)	95.82(10)
C(1)-Ru(1)-N(5)	85.59(9)		

Table S6 Selected bond lengths (Å) and bond angles (°) for **Ru1**

Bond	Dist. (Å)	Bond	Dist. (Å)
Ru(1)-N(1)	2.0213(17)	Ru(1)-N(2)	2.1592(17)
Ru(1)-N(3)	2.0503(16)	Ru(1)-N(4)	1.9490(16)
Ru(1)-N(5)	2.0621(16)	Ru(1)-C(1)	2.033(2)
Angle	(°)	Angle	(°)
N(1)-Ru(1)-N(2)	76.58(7)	N(1)-Ru(1)-N(3)	101.90(7)
N(1)-Ru(1)-N(5)	99.93(7)	N(1)-Ru(1)-C(1)	79.89(8)
N(3)-Ru(1)-N(2)	93.38(6)	N(4)-Ru(1)-N(1)	175.82(7)
N(4)-Ru(1)-N(2)	107.40(7)	N(4)-Ru(1)-N(3)	79.36(7)
N(4)-Ru(1)-N(5)	78.74(7)	N(4)-Ru(1)-C(1)	96.19(7)
N(5)-Ru(1)-N(2)	93.34(6)	N(5)-Ru(1)-N(3)	158.10(7)
C(1)-Ru(1)-N(2)	156.31(8)	C(1)-Ru(1)-N(3)	88.76(7)
C(1)-Ru(1)-N(5)	93.37(7)		

Table S7 Selected bond lengths (Å) and bond angles (°) for **Ru2**

Bond	Dist. (Å)	Bond	Dist. (Å)
Ru(1)-N(1)	2.024(4)	Ru(1)-N(2)	2.125(4)
Ru(1)-N(3)	2.057(3)	Ru(1)-N(4)	1.949(3)
Ru(1)-N(5)	2.051(3)	Ru(1)-C(1)	2.085(4)
Angle	(°)	Angle	(°)
N(1)-Ru(1)-N(2)	77.49(15)	N(1)-Ru(1)-N(3)	105.67(14)
N(1)-Ru(1)-N(5)	96.14(14)	N(1)-Ru(1)-C(1)	78.54(16)
N(3)-Ru(1)-N(2)	93.86(13)	N(4)-Ru(1)-N(1)	174.73(14)
N(4)-Ru(1)-N(2)	105.16(14)	N(4)-Ru(1)-N(3)	78.85(13)
N(4)-Ru(1)-N(5)	79.40(14)	N(4)-Ru(1)-C(1)	98.90(16)
N(5)-Ru(1)-N(2)	89.93(13)	N(5)-Ru(1)-N(3)	158.17(13)
C(1)-Ru(1)-N(2)	155.93(16)	C(1)-Ru(1)-N(3)	90.53(14)
C(1)-Ru(1)-N(5)	94.74(14)		

Table S8 Selected bond lengths (Å) and bond angles (°) for **Ru3a**

Bond	Dist. (Å)	Bond	Dist. (Å)
Ru(1)-N(1)	2.024(5)	Ru(1)-N(2)	2.116(5)
Ru(1)-N(3)	2.055(4)	Ru(1)-N(4)	1.946(4)
Ru(1)-N(5)	2.044(5)	Ru(1)-C(1)	2.097(6)
Angle	(°)	Angle	(°)
N(1)-Ru(1)-N(2)	77.8(2)	N(1)-Ru(1)-N(3)	105.64(19)
N(1)-Ru(1)-N(5)	96.22(19)	N(1)-Ru(1)-C(1)	77.9(2)
N(3)-Ru(1)-N(2)	93.46(18)	N(4)-Ru(1)-N(1)	174.9(2)
N(4)-Ru(1)-N(2)	104.8(2)	N(4)-Ru(1)-N(3)	78.74(19)
N(4)-Ru(1)-N(5)	79.50(19)	N(4)-Ru(1)-C(1)	99.6(2)
N(5)-Ru(1)-N(2)	89.75(19)	N(5)-Ru(1)-N(3)	158.10(19)
C(1)-Ru(1)-N(2)	155.6(2)	C(1)-Ru(1)-N(3)	90.51(18)
C(1)-Ru(1)-N(5)	95.48(19)		

Table S9 Selected bond lengths (Å) and bond angles (°) for **Ru3b**

Bond	Dist. (Å)	Bond	Dist. (Å)
Ru(1)-N(1)	2.012(9)	Ru(1)-N(2)	2.177(7)
Ru(1)-N(3)	2.056(6)	Ru(1)-N(4)	1.950(9)
Ru(1)-N(5)	2.053(6)	Ru(1)-C(1)	2.026(8)
Angle	(°)	Angle	(°)
N(1)-Ru(1)-N(2)	76.6(3)	N(1)-Ru(1)-N(3)	102.6(3)
N(1)-Ru(1)-N(5)	97.9(3)	N(1)-Ru(1)-C(1)	80.8(4)
N(3)-Ru(1)-N(2)	90.0(2)	N(4)-Ru(1)-N(1)	174.8(4)
N(4)-Ru(1)-N(2)	108.1(3)	N(4)-Ru(1)-N(3)	79.8(3)
N(4)-Ru(1)-N(5)	79.6(3)	N(4)-Ru(1)-C(1)	94.5(4)
N(5)-Ru(1)-N(2)	96.6(2)	N(5)-Ru(1)-N(3)	159.4(2)
C(1)-Ru(1)-N(2)	157.3(3)	C(1)-Ru(1)-N(3)	92.3(3)
C(1)-Ru(1)-N(5)	89.1(3)		

Table S10 Selected bond lengths (Å) and bond angles (°) for **Ru4**

Bond	Dist. (Å)	Bond	Dist. (Å)
Ru(1)-N(1)	2.163(4)	Ru(1)-N(2)	2.015(5)
Ru(1)-N(3)	2.072(4)	Ru(1)-N(4)	1.946(5)
Ru(1)-N(5)	2.066(4)	Ru(1)-C(1)	2.030(5)
Angle	(°)	Angle	(°)
N(1)-Ru(1)-N(2)	76.99(19)	N(1)-Ru(1)-N(3)	94.32(15)
N(1)-Ru(1)-N(5)	92.02(15)	N(1)-Ru(1)-C(1)	155.74(17)
N(3)-Ru(1)-N(2)	98.80(17)	N(4)-Ru(1)-N(1)	105.34(19)
N(4)-Ru(1)-N(2)	176.7(3)	N(4)-Ru(1)-N(3)	78.77(16)
N(4)-Ru(1)-N(5)	79.54(16)	N(4)-Ru(1)-C(1)	98.9(2)
N(5)-Ru(1)-N(2)	102.85(17)	N(5)-Ru(1)-N(3)	158.30(14)
C(1)-Ru(1)-N(2)	78.9(2)	C(1)-Ru(1)-N(3)	91.53(16)
C(1)-Ru(1)-N(5)	91.16(17)		

Table S11 Selected bond lengths (Å) and bond angles (°) for **Ru5**

Bond	Dist. (Å)	Bond	Dist. (Å)
Ru(1)-N(1)	2.157(2)	Ru(1)-N(2)	2.0234(17)
Ru(1)-N(3)	2.0663(18)	Ru(1)-N(4)	1.9479(17)
Ru(1)-N(5)	2.0614(18)	Ru(1)-C(1)	2.055(2)
Angle	(°)	Angle	(°)
N(1)-Ru(1)-N(2)	76.45(7)	N(1)-Ru(1)-N(3)	96.04(7)
N(1)-Ru(1)-N(5)	89.59(7)	N(1)-Ru(1)-C(1)	155.89(8)
N(3)-Ru(1)-N(2)	102.30(7)	N(4)-Ru(1)-N(1)	108.52(7)
N(4)-Ru(1)-N(2)	174.81(7)	N(4)-Ru(1)-N(3)	78.91(7)
N(4)-Ru(1)-N(5)	79.41(7)	N(4)-Ru(1)-C(1)	95.58(8)
N(5)-Ru(1)-N(2)	99.41(7)	N(5)-Ru(1)-N(3)	158.28(7)
C(1)-Ru(1)-N(2)	79.47(8)	C(1)-Ru(1)-N(3)	87.89(7)
C(1)-Ru(1)-N(5)	95.50(8)		