Supporting Information

New Journal of Chemistry

Synthesis, characterization and cytotoxic activity of cationic half-sandwich Ru(II) complexes stabilized by iminophosphorane N,N,S and N,N,Se tridentate ligands

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1. Mass Spectra (FAB$^+$) for compounds **10** and **11**.

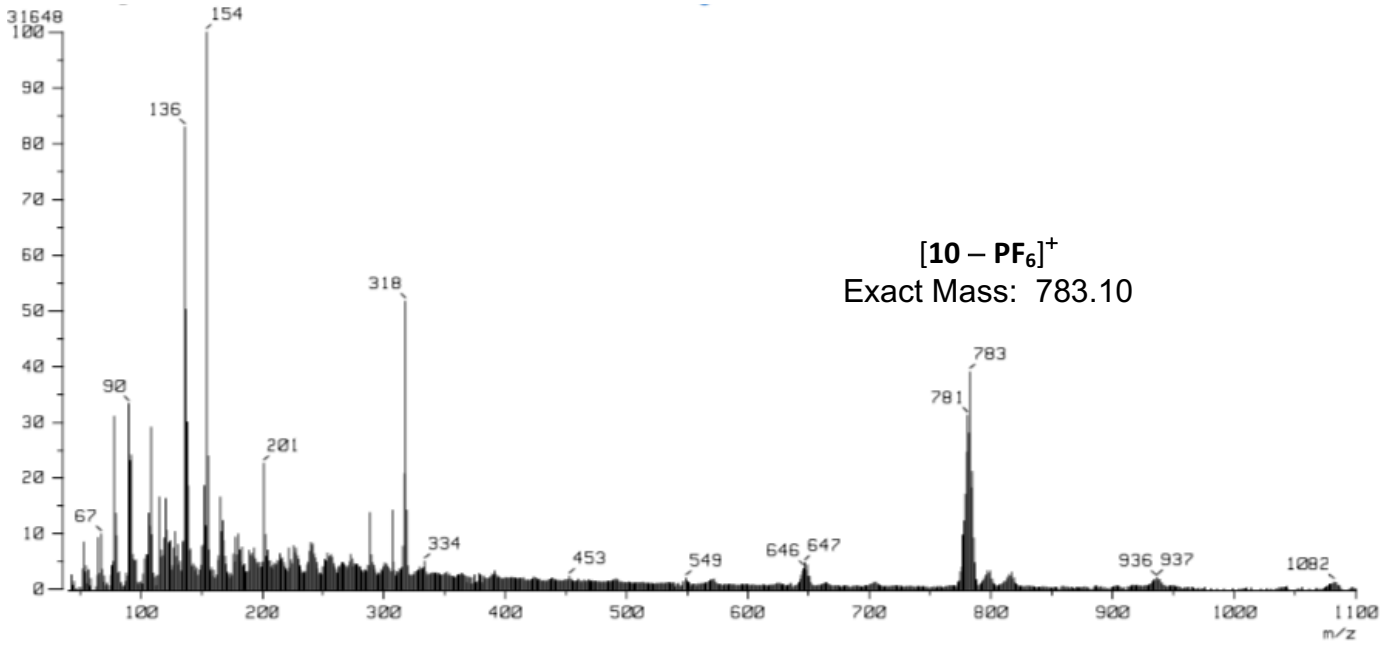


Figure S1. Mass Spectrum (FAB$^+$) for compound **10**.

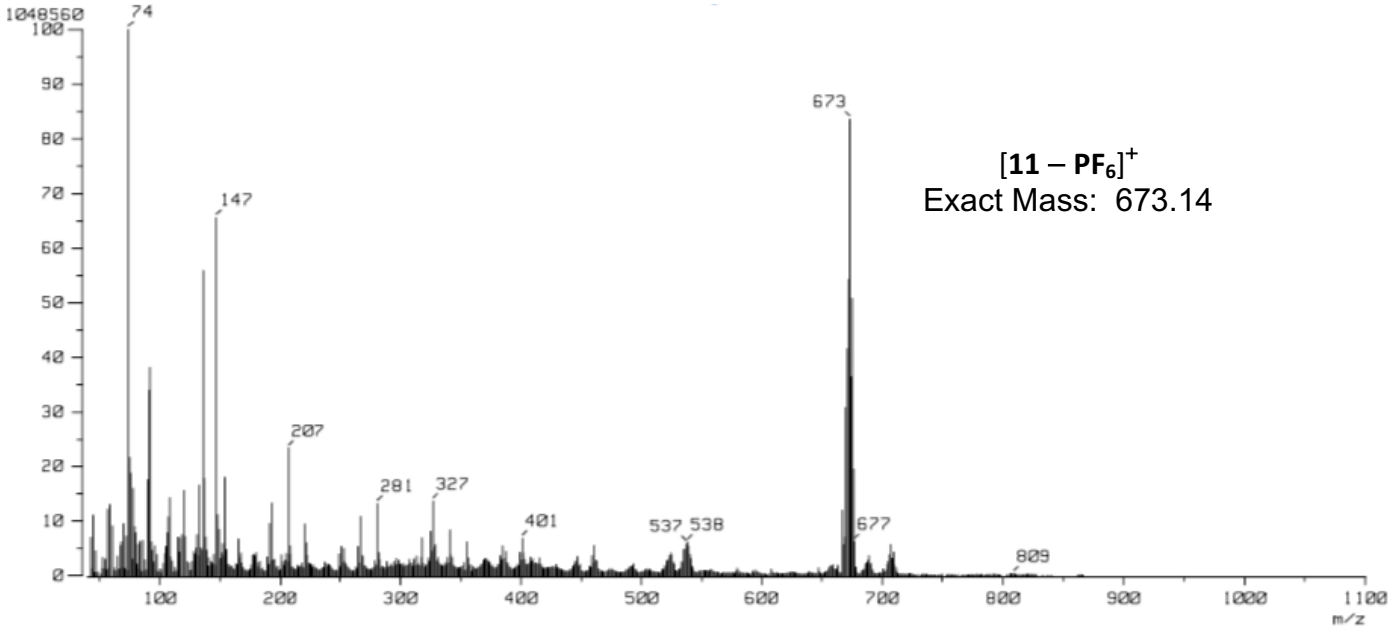


Figure S2. Mass Spectrum (FAB$^+$) for compound **11**.

2. ^{31}P-{^{1}H}, ^{1}H and ^{13}C NMR spectra for compound **6**

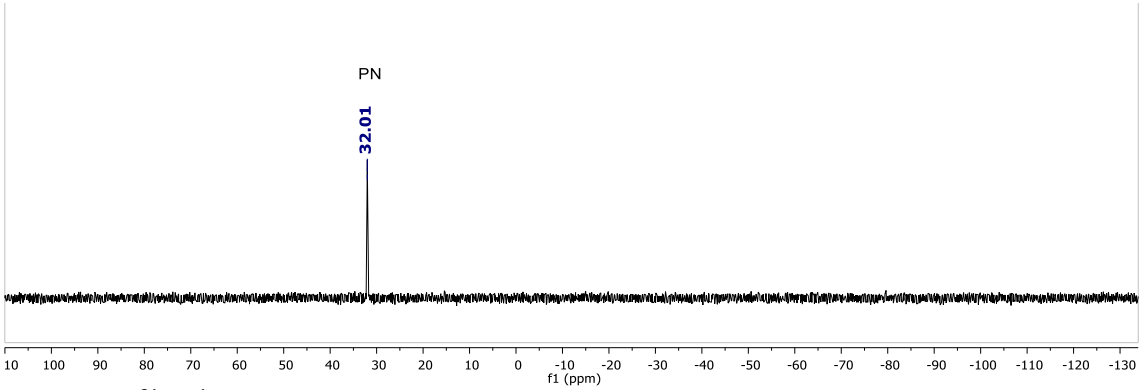


Figure S3.^{31}P-{^{1}H} NMR spectrum for compound **6** in $CDCl_3$ (202 MHz).

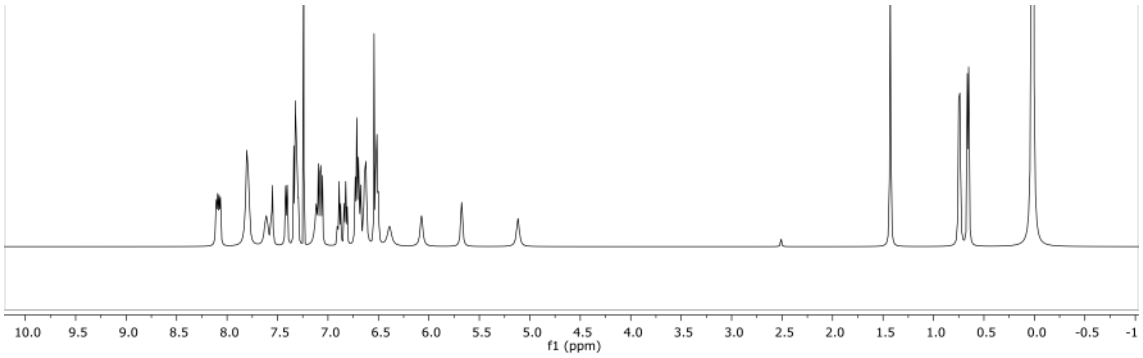
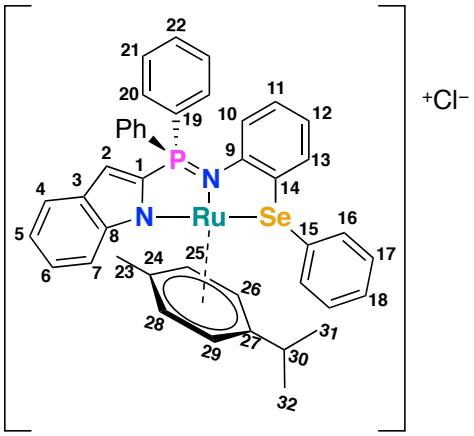
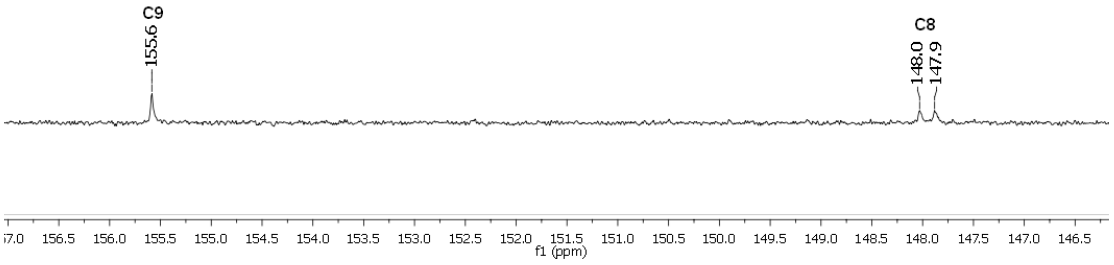


Figure S4.^{1}H NMR spectrum for compound **6** in $CDCl_3$ (500 MHz).





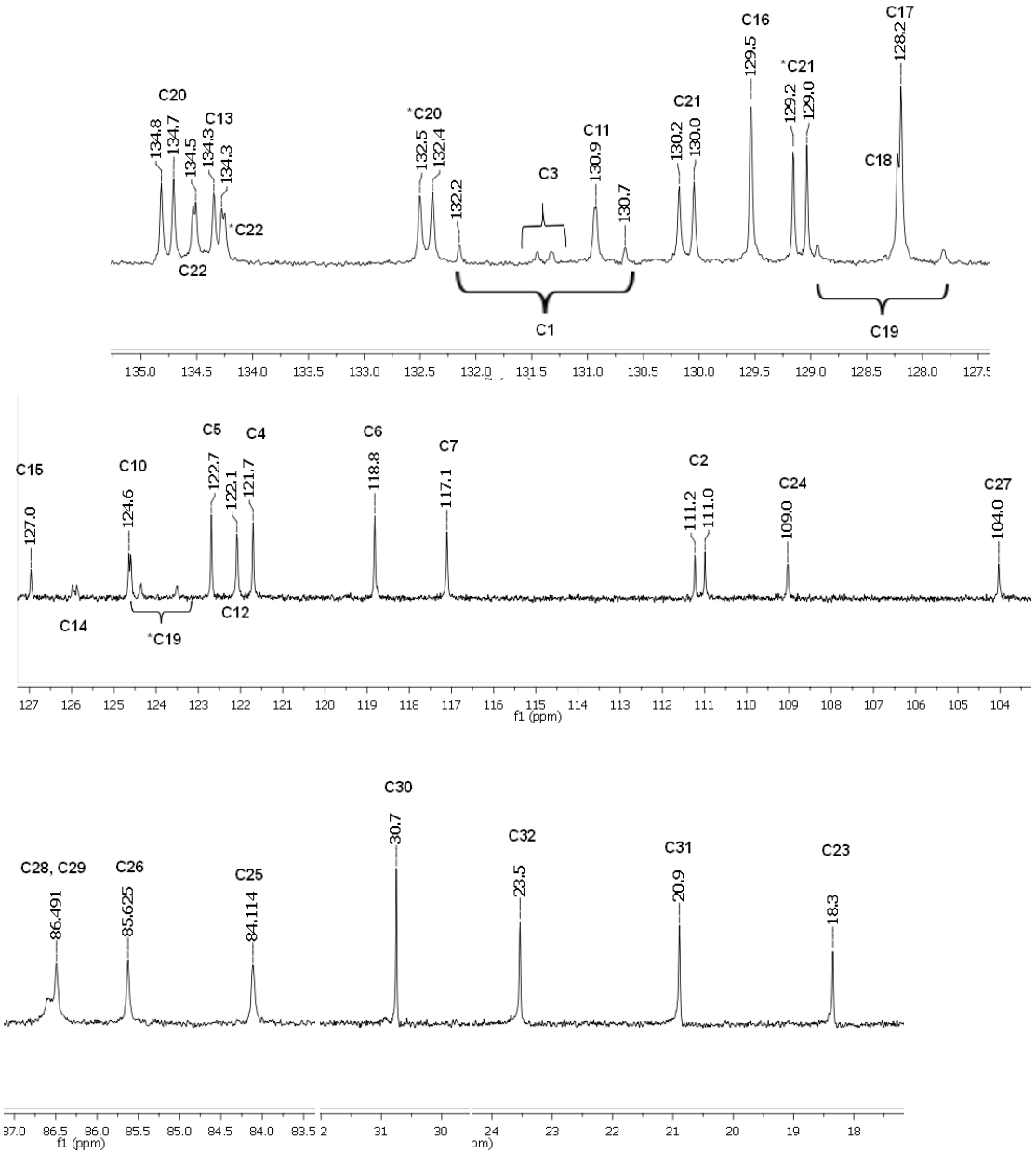


Figure S5. ^{13}C NMR spectrum for compound **6** in $CDCl_3$ (125 MHz).

3. ^{31}P-{^{1}H} spectra for compound **9, 10** and **12**

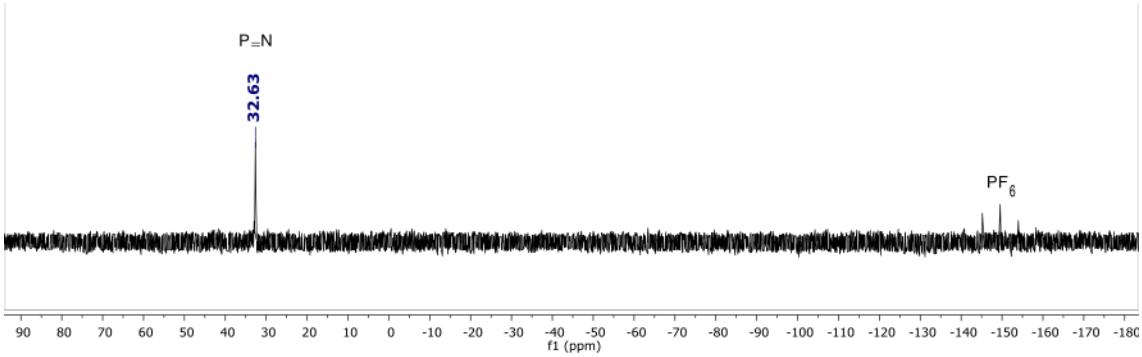


Figure S6.^{31}P-{^{1}H} NMR spectrum for compound **9** in $CDCl_3$ (202 MHz).

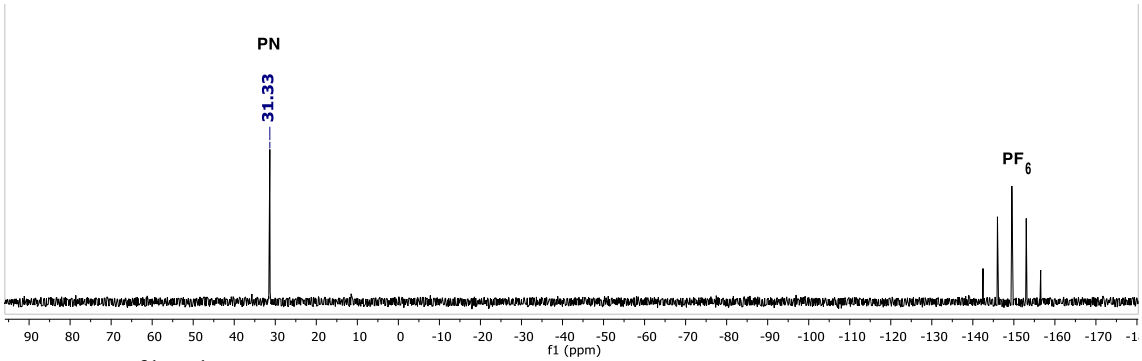


Figure S7.^{31}P-{^{1}H} NMR spectrum for compound **10** in $CDCl_3$ (202 MHz).

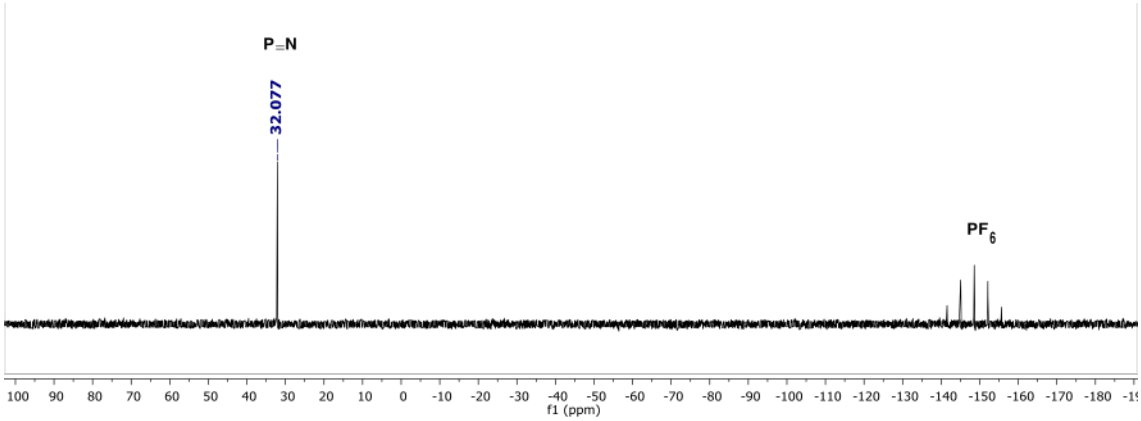


Figure S8. ^{31}P-{^{1}H} NMR spectrum for compound **12** in $CDCl_3$ (202 MHz).

4. ^{31}P-{^{1}H}, ^{1}H and ^{13}C NMR spectra for compound **11**

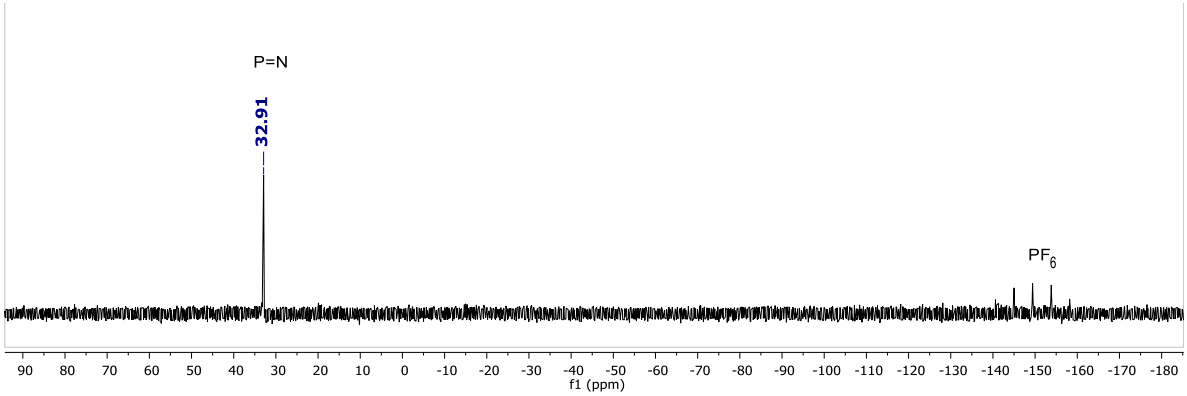
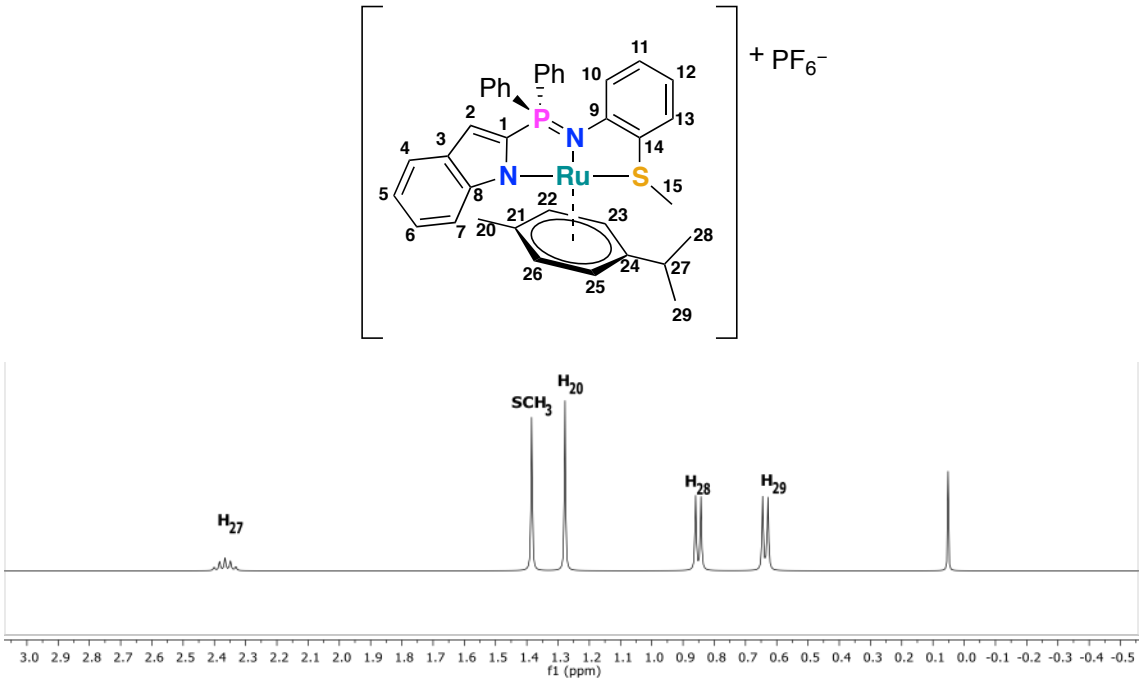


Figure S9.^{31}P-{^{1}H} NMR spectrum for compound **11** in $CDCl_3$ (202 MHz).



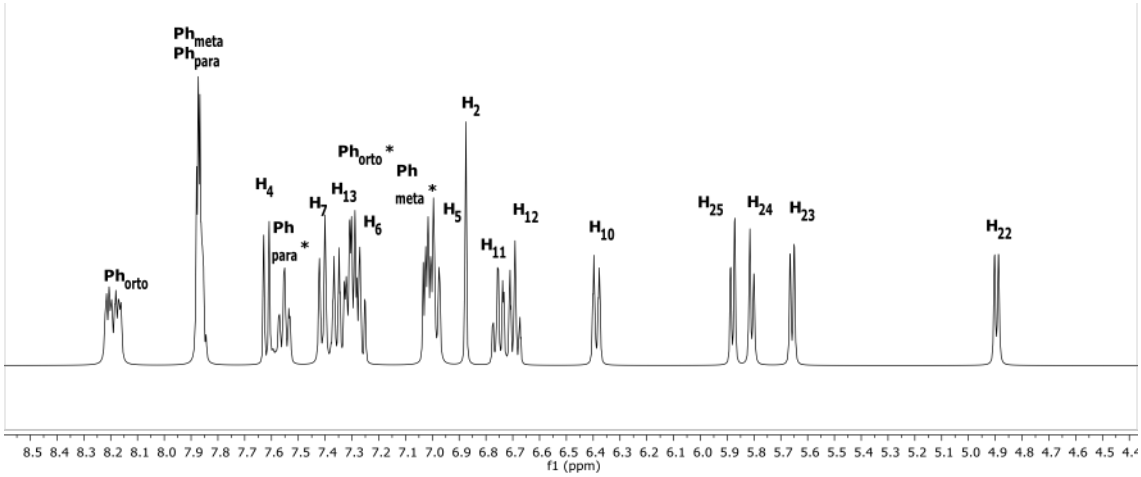


Figure S10. ^{1}H NMR spectra for compound **11** in $CDCl_3$ (500 MHz).

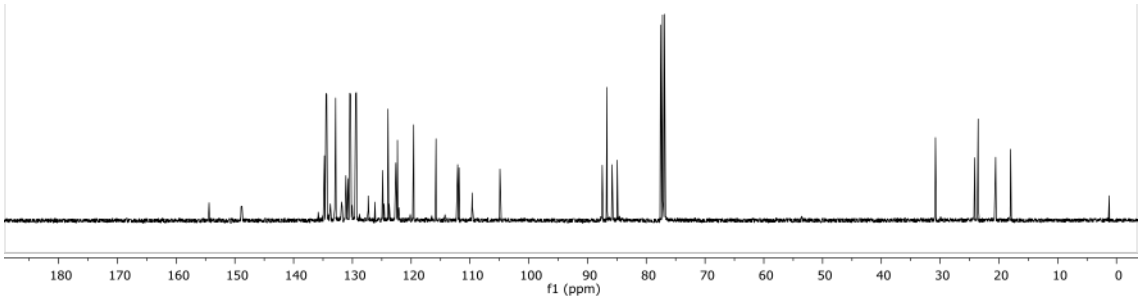


Figure S11. ^{13}C NMR spectra for compound **11** in $CDCl_3$ (125 MHz).

5. Solubility of Ru(II) compounds

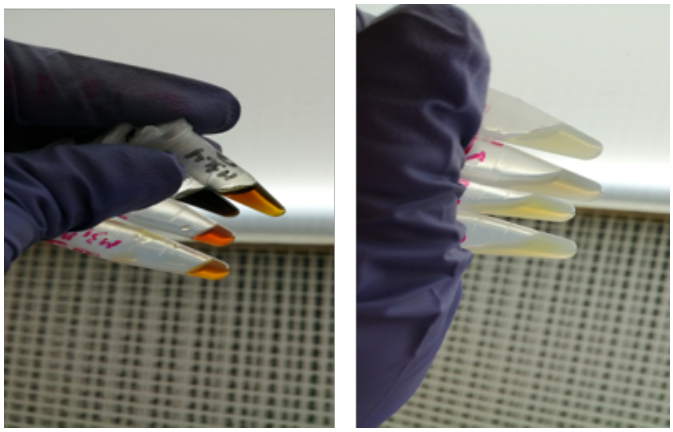


Figure S12. Solubility of Ru compounds. A) Dissolved in DMSO: Tween 80 solution (1:1 v/v) and B) further diluted with MilliQ® water

6. Stability of compound **11** in DMSO+H_2O

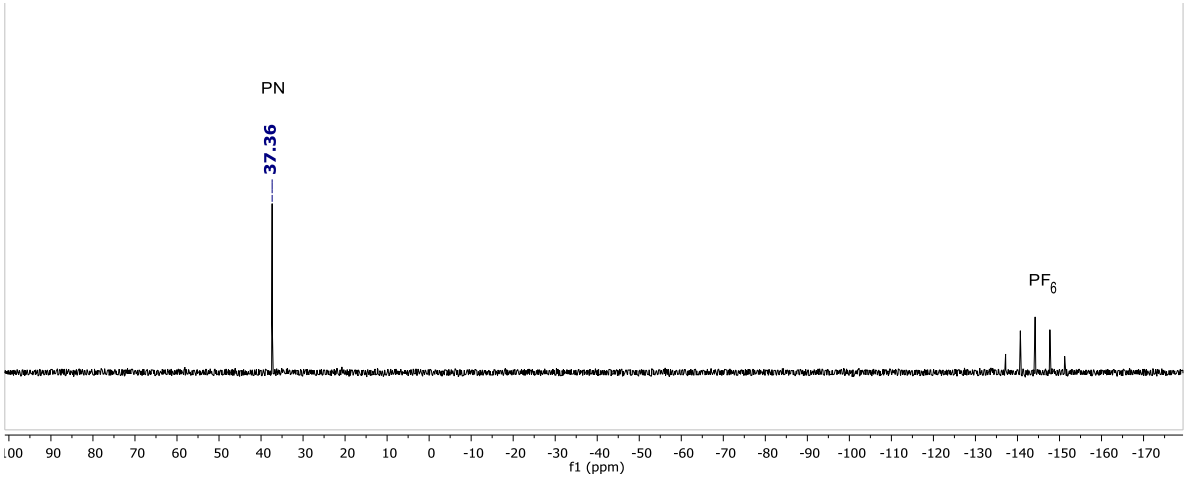


Figure S13. ^{31}P-{^{1}H} NMR spectrum for the precipitate formed by adding H_2O to a DMSO solution of compound **11** (CH_2Cl_2, 202 MHz).

7. Stability of compounds **9** and **10** in stock solutions containing polysorbate 80.

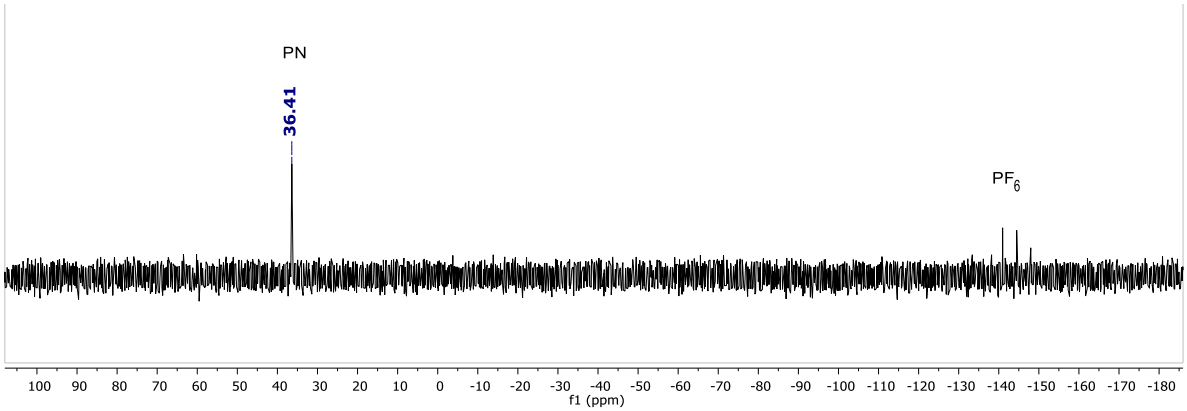


Figure S14. ^{31}P-{^{1}H} NMR spectrum for aliquot of the stock solution of compound **9** (DMSO+Tween 80+H_2O), after the cytotoxic assay was completed (202 MHz).

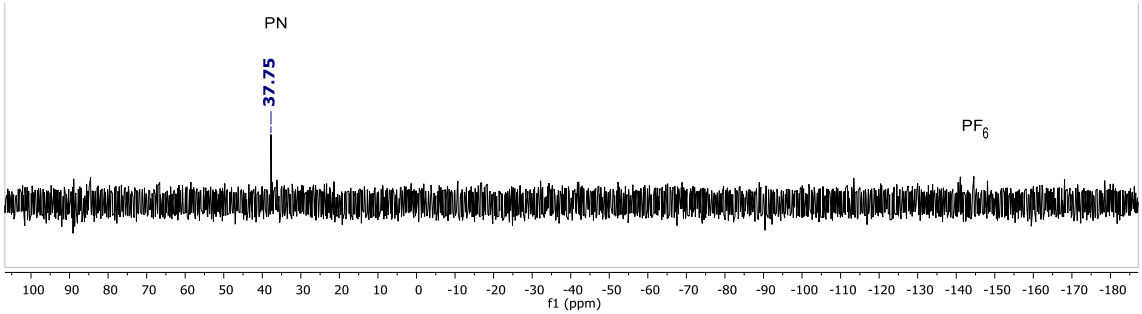


Figure S15. ^{31}P-{^{1}H} NMR spectrum for aliquot of the stock solution of compound **10** (DMSO+Tween 80+H_2O), after the cytotoxic assay was completed (202 MHz).

8. Determination of the vehicle's NOAEL

Table S1. Preparation of different concentrations of the vehicle DMSO: Tween 80 to determine the NOAEL on cancer and normal cell lines

Mixture of DMSO: Tween 80 solution (1:1 v/v)[a]				
Dilution No.	DMSO in stock (%v/vH_2O)	Tween 80 in stock (%w/vH_2O)	DMSO in the assay (%v/v_{assay})	Tween 80 in the assay (%w/v_{assay})
-	100	0	NT	NT
1	50	5	NT	NT
2	1.25	0.125	NT	NT
3	0.625	0.0625	0.0625	0.00625
4	0.3125	0.03125	0.03125	0.003125
5	0.15625	0.015625	0.015625	0.0015625
6	0.078125	0.0078125	0.0078125	0.00078125
7	0.0390625	0.00390625	0.00390625	0.000390625
8	0.01953125	0.001953125	0.001953125	0.000195313
9	0.009765625	0.000976563	0.000976563	0.0000976563
10	0.004882813	0.000488281	0.000488281	0.0000488281
11	0.002441406	0.000244141	0.000244141	0.0000244141

[a]Initial concentrations of DMSO (100%v/v) and Tween 80® solution (10% w/v aqueous solution)
NT: Not tested in the SRB assay

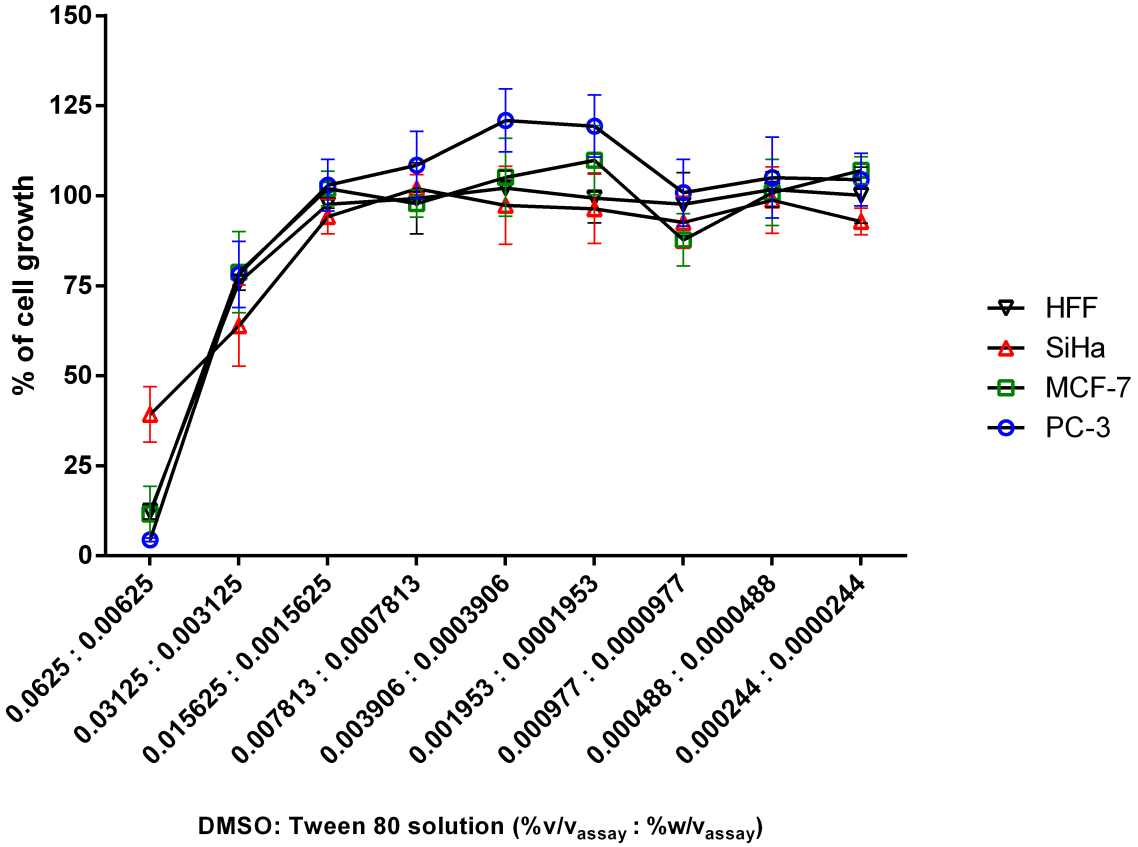


Figure S16. Determination of the Non Observable Adverse Level (NOAEL) of the vehicle DMSO: Tween 80 ® solution

9. Crystallography data for **6**, **9** and **10**.

Table S2. Crystal data and structure refinement for **6**

Identification code	RuSePhCl
Empirical formula	$C_{43}H_{40}Cl_3N_2PRuSe$
Formula weight	902.12
Temperature/K	99.98(12)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	12.1571(3)
b/Å	16.3864(4)
c/Å	20.0229(5)
α/°	90
β/°	94.020(2)
γ/°	90
Volume/Å^3	3978.96(17)
Z	4
ϱ_{calc}g/cm^3	1.506
μ/mm^{-1}	1.584
F(000)	1824.0
Crystal size/mm^3	0.4 × 0.36 × 0.15
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.374 to 58.438
Index ranges	-16 ≤ h ≤ 16, -21 ≤ k ≤ 22, -25 ≤ l ≤ 25
Reflections collected	34326
Independent reflections	9574 [R_{int} = 0.0330, R_{sigma} = 0.0349]
Data/restraints/parameters	9574/0/463
Goodness-of-fit on F^2	1.054
Final R indexes [I>=2σ (I)]	R_1 = 0.0295, wR_2 = 0.0609
Final R indexes [all data]	R_1 = 0.0390, wR_2 = 0.0642
Largest diff. peak/hole / e Å^{-3}	1.06/-1.72

Note: The compound crystallized as solvate. The crystal structure contains two solvent voids, but only in one case the atom positions corresponding to dichloromethane could be clearly identified. In the second void, corresponding to a calculated volume of 73 Ang3, the solvent is disordered. Since the disorder could not be resolved, the solvent mask instruction implemented in OLEX was employed in the final refinement cycle.

Table S3. Crystal data and structure refinement for **9**

Identification code	RuSPh
Empirical formula	$C_{42}H_{38}F_6N_2P_2RuS$
Formula weight	879.81
Temperature/K	100.0(3)
Crystal system	triclinic
Space group	P-1
a/Å	10.3583(4)
b/Å	11.4739(4)
c/Å	17.6428(6)
α/°	102.881(3)
β/°	93.052(3)
γ/°	111.451(4)
Volume/Å^3	1881.39(13)
Z	2
ϱ_{calc}g/cm^3	1.553
μ/mm^{-1}	0.622
F(000)	896.0
Crystal size/mm^3	0.19 × 0.14 × 0.11
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.356 to 58.332
Index ranges	-12 ≤ h ≤ 14, -14 ≤ k ≤ 15, -23 ≤ l ≤ 23
Reflections collected	16349
Independent reflections	8671 [R_{int} = 0.0332, R_{sigma} = 0.0608]
Data/restraints/parameters	8671/0/490
Goodness-of-fit on F^2	1.029
Final R indexes [I>=2σ (I)]	R_1 = 0.0372, wR_2 = 0.0698
Final R indexes [all data]	R_1 = 0.0465, wR_2 = 0.0740
Largest diff. peak/hole / e Å^{-3}	0.57/-0.68

Table S4. Crystal data and structure refinement for **10**

Identification code	RuSePh
Empirical formula	$C_{42}H_{38}F_6N_2P_2RuSe$
Formula weight	926.71
Temperature/K	99.9(5)
Crystal system	triclinic
Space group	P-1
a/Å	10.3258(3)
b/Å	11.4664(5)
c/Å	17.7014(7)
α/°	102.299(3)
β/°	92.894(3)
γ/°	111.556(4)
Volume/Å^3	1885.31(13)
Z	2
ϱ_{calc}g/cm^3	1.632
μ/mm^{-1}	1.530
F(000)	932.0
Crystal size/mm^3	0.26 × 0.23 × 0.15
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.318 to 58.354
Index ranges	$-13 \le h \le 12$, $-14 \le k \le 15$, $-22 \le l \le 23$
Reflections collected	16267
Independent reflections	8622 [R_{int} = 0.0389, R_{sigma} = 0.0633]
Data/restraints/parameters	8622/0/490
Goodness-of-fit on F^2	1.030
Final R indexes [I>=2σ (I)]	R_1 = 0.0391, wR_2 = 0.0778
Final R indexes [all data]	R_1 = 0.0483, wR_2 = 0.0826
Largest diff. peak/hole / e Å^{-3}	0.93/-0.79

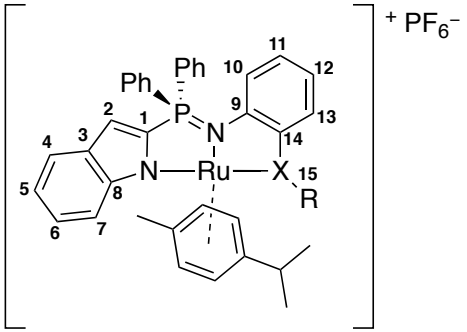


Table S5. ^{13}C NMR data (ppm) for iminophosphorane ligand moieties of compounds **1*-4***, **6**, **9-12** ($CDCl_3$). * Data taken from reference [1]

Compound	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15/*ipso***	**o (XPh)**	**m (XPh)**	**p (XPh)**	***i* $(Ph)_2$**	**o $(Ph)_2$**	**m $(Ph)_2$**	**p $(Ph)_2$**
1 * (J= Hz)	131.2 (11)	111.8 (16)	128.4 (13)	121.7	120.6	124.4	112.3	138.1 (9)	149.9	121.1 (10)	118.5	128.1	126.2	132.0 (11)	137.1	130.2	129.1	132.1	129.7 *(99)*	132.6 *(10.7)*	128.8 (12)	132.3 *(3)*
9 (J= Hz)	130.9 *(145.2)*	111.6 *(23.1)*	131.4 *(14.0)*	121.8	118.8	122.5	115.8	147.3 (14.8)	155.6	124.9	131.2	122.7	134.5	127.4 (8.4)	126.9	128.2	128.4	128.6	127.5 *(115.7)* 123.8 *(85)*	132.5 (11)	130.2 *(13)* 129.4 *(10.7)*	134.8 134.7
2 (J= Hz)	129.3 (6)	112.4 (20.4)	128.5	121.8	120.8	124.6	112.2	138.4 (8)	150.7	120.7 (10.8)	119.0	129.5	126.8	130.3 (34)	130.7	135.6	127.9	129.5	131.2 *(93)*	132.6 *(11)*	128.9 *(13.2)*	132.4
6 (J= Hz)	131.4 *(148)*	111.1 *(24)*	131.3 *(12)*	121.7	118.8	122.6	117.1	147.9 *(14)*	155.5	124.6 *(4)*	130.9	122.0	134.3	125.9 *(10)*	126.9	129.5	128.1	128.2	128.3 *(112.3)* 124.4 *(85)*	134.7 *(11)* 132.4 *(11)*	130.1 *(13.3)* 129.0 *(12.2)*	134.5 *(2.3)* 134.2 *(2.7)*
10 (J= Hz)	131.7 *(148.2)*	111.1 *(23.8)*	131.5 *(12.7)*	121.9	118.8	122.1	116.3	147.9 *(15)*	155.5	125.1 *(4.5)*	131.3	122.7	134.1	125.6 *(10.2)*	126.5	129.2	128.4	128.4	127.0 *(132.6)* 123.7 *(86)*	134.8 *(11)* 132.5 *(11.3)*	130.2 *(13)* 129.1 *(13)*	134.5 *(2.5)* 134.3 *(2.6)*
3 * (J= Hz)	132.4 *(2.0)*	112.0 *(15.0)*	128.5	121.7	120.7	124.4	112.3	138.2 *(8.3)*	147.0	119.7 *(9.3)*	118.8	124.6	123.7	133.6 *(22.6)*	14.6	—	—	—	130.9 *(100)*	132.6 *(10.8)*	128.8 *(12.5)*	132.2 *(2.9)*
11 (J= Hz)	131.8	111.9	133.8	122.3	119.4	123.9	115.7	148.8	154.3	124.8 *(4.6)*	130.7	122.5	131.1	130.1 *(13.7*)	24.1	—	—	—	126.7 *(114.8)* 124.1 *(86.5)*	134.43 *(10.6)* 132.91 *(10.6)*	130.38 *(13.6)* 129.39 *(12.3)*	134.77 *(2.9)* 134.57 *(2.74)*
4* (J= Hz)	132.4 *(3.0)*	112.4 *(16.0)*	128.4 *(12)*	121.8	120.8	124.6	112.3	138.3 *(5.3)*	148.3	119.3 *(15)*	119.0	125.4	126.2	133.5 *(15)*	4.5	—	—	—	130.8 *(102)*	132.6 *(10.4)*	128.9 *(12.5)*	132.3 *(2.9)*
12 (J= Hz)	133.6 *(146)*	111.66 *(28.0)*	131.53 *(12.3)*	122.1	119.46	123.7	115.82	148.8 *(14.8)*	154.2	125.01 *(4.6)*	130.4	122.3	132.4	127.44 *(9.6)*	13.72	—	—	—	127.1 *(113.5)* 124.09 *(86.2)*	134.35 *(10.5)* 132.83 *(11.6)*	130.31 *(13.3)* 129.32 *(12.1)*	134.68 *(2.7)* 134.47 *(2.3)*

Table S6. ^{1}H NMR data (ppm) for iminophosphorane moiety of compounds **1*-4***, **6**, **9-12** ($CDCl_3$). * Data taken from reference [1]

	2	4	5	6	7	10	11	12	13	15/ ipso (XPh)	m (XPh)	p (XPh)	o $(Ph)_2$	m $(Ph)_2$	p $(Ph)_2$	NH
1* (J= Hz)	6.71 *(4)*	7.59 *(8)*	7.12 *(8.0)*	7.25/7.29	7.36/7.41	6.58 (8)	6.65 *(8/8)*	6.90 *(7.6/7.6/1.4)*	7.17-7.21	7.36/7.42	7.26/7.29	7.17/7.21	7.74/7.79	7.44/7.48	7.54/7.57	9.19
9 (J= Hz)	6.69/6.7	7.36 (7.5)	6.69/6.79	6.95	7.01	6.59/6.64	6.86	6.77	7.25	6.54/6.55	6.59/6.64	6.69/6.74	8.12/8.15 7.38/7.44	7.80/7.86 7.28/7.32	7.80/7.86 7.56/7.64	None
2* (J= Hz)	6.59	7.61 *(8.0)*	7.12	7.27	7.42	6.49 *(7.2)*	6.54 *(7.2/8.0)*	6.81 *(8.0)*	6.78	7.64/7.72	7.27/7.35	7.52/7.54	7.80/7.85	7.41/7.47	7.64/7.72	9.4
6 (J= Hz)	6.54	7.41 *(7.5)*	6.76/6.73	6.89 *(7.5/7.5)*	6.67/6.72	7.33	6.82 *(7.0/7.0)*	7.05/7.11	7.61	6.50/6.25	6.72/6.67	6.38/6.62	8.06/8.10 7.38/7.44	7.75/7.83 7.28/7.32	7.75/7.83 7.56/7.64	None
10 (J= Hz)	6.73/6.79	7.37 (8.0)	6.73/6.79	7.15 *(8.0/8.0)*	7.06 *(8.0)*	6.56	6.95 (7.5/7.5)	6.87 (7.5/7.5)	7.08 (7.5/7.5)	6.40/6.42	6.53/6.55	6.72/6.79	8.07/8.13 7.40/7.45	7.79/7.83 7.30/7.33	7.79/7.83 7.53/7.60	None
3* (J= Hz)	6.78 3.6	7.61 (8.0)	7.26 (8.0/7.2)	7.12 (7.2/8)	7.42 (7.47)	6.43 (8.8)	6.71/6.74	6.71/6.74	7.03/7.05	2.47			7.81/7.87	7.42/7.47	7.51/7.55	9.69
11 (J= Hz)	6.85	7.64 *(8.0)*	7.03	7.30	7.41 *(8.0)*	6.38 *(8.0)*	6.77 *(7.0/8.0/1)*	6.69 *(7.0/7.6)*	7.35 *(7.6)*	1.27			8.16/8.22 7.52/7.32	7.85/7.8 6.97/7.03	7.85/7.87 7.55	None
4* (J= Hz)	6.80	7.61 *(8.0)*	7.26 *8.0/7.2)*	7.09/7.14	7.42 7.46	6.41 *6.6*	6.91/6.77	6.91/6.77	7.09/7.14	2.28			7.2/7.87	7.42/7.46	7.51/7.53	9.53
12 (J= Hz)	6.84	7.60 (8.0)	6.94/7.01	7.25/7.30	7.37 *(8.0)*	6.46 *(8.0)*	6.76 *(7.0/8.0)*	6.65 *(8.0/8.0)*	7.41 *(8.0)*	1.02			8.16/8.20 7.25/7.30	7.84/7.87 6.94/7.01	7.84/7.87 7.51/7.55	None

Table S7. ^{1}H and ^{13}C NMR data (ppm) for Cymene moiety of complexes **6**, **9-12** ($CDCl_3$)

	Me (iPr)		**Me(iPr)**		**Me**		**CH (iPr)**		**CH**		**CH**		**CH**		**CH**		**C***	**C***
	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C	^{13}C	^{13}C
9 (J= Hz)	0.69 (6.0)	20.30	0.88 (7.0)	23.70	1.34	18.1	2.49	30.50	4.71 (5.0)	87.26	5.73 (5.0)	85.22	5.98	86.91	5.98	85.31	105.80	108.80
6 (J= Hz)	0.66 (6.5)	20.80	0.74 (6.0)	23.50	1.43	18.30	2.51	30.70	5.11	86.60	5.67	84.10	6.08	85.60	6.40	86.50	104.00	109.00
10 (J= Hz)	0.67 (7.0)	20.70	0.78 (6.5)	23.40	1.39	18.10	2.41	30.80	4.95 (5.5)	86.10	5.69 (6.0)	84.10	5.92	85.10	5.92	84.90	103.80	108.80
11 (J= Hz)	0.63 (6.8)	18.00	0.85 (7.2)	23.52	1.38	17.00	2.36	30.77	4.89 (6.0)	87.40	5.65 (5.6)	84.90	5.80 (6.0)	86.60	5.87 (6.8)	85.81	104.90	109.60
12 (J= Hz)	0.64 (7.0)	20.51	0.84 (7.0	23.80	1.38	18.10	2.39	30.00	4.88 (5.5)	86.50	5.56 (6.0)	84.10	5.78 (6.0)	85.30	5.86 (6.0)	84.60	104.20	108.30

[1] C. G. Martínez-De-León, A. Rodríguez-Álvarez, A. Flores-Parra and J-M. Grévy, *Inorg. Chim. Acta*, 2019, **495**, 118945.