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ARTICLE

Metal and Substituent Influence on the Cytostatic Activity of Cationic Bis-cyclometallated Iridium and Rhodium Complexes with Substituted 1,10-Phenanthrolines as Ancillary Ligands

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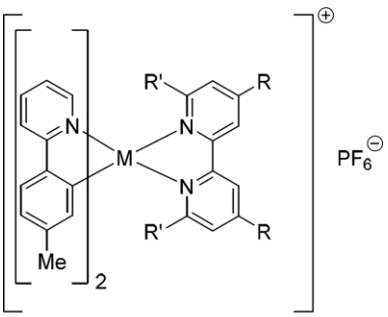
Dedicated to Prof. Manfred Scheer on the Occasion of his 65th Birthday

Abstract. Synthesis and characterization of the new cyclometalated complex salts [Rh(ptpy)$_2$(5.6-dimethyl-1,10-phenanthroline)]PF$_6$ (**1a**) [Rh(ptpy)$_2$(2.9-dimethyl-4.7-diphenyl-1,10- phenanthroline)]PF$_6$ (**2a**), [Rh(ptpy)$_2$(5-amino-1,10-phenanthroline)] PF$_6$ (**3a**), and [M(ptpy)$_2$ (pyrazino-[2.3-f]-1,10-phenanthroline)]PF$_6$ (M = Rh, **4a**; M = Ir, **4b**), (ptpy = 2-(p-tolyl)pyridinato) are described. The molecular structures of compounds **1b** and **4a** in the solid state were determined by single-crystal X-ray diffraction. All these compounds and their already known Iridium counterparts **1b** – **3b** display significant cytotoxicity against human cancer cell lines MCF-7 (human breast adenocarcinoma) and HT-29 (colon adenocarcinoma) with IC$_{50}$ values in the low micromolar range.

Introduction

Since the discovery of the anti-cancer activity of cisplatin (cis-diammine-dichlorido-platinum(II)) more than 50 years ago, numerous transition metal complexes have been tested for their cytostatic activities, both in vitro and in vivo. Among those, cyclometallated iridium and rhodium complexes have evolved as a major object of study in the last decade, as they allow both therapeutic and diagnostic applications.,[1,2] This "theranostic" approach is particularly useful with bis-cyclometallated iridium(III) complexes of the type "[M(C^N)$_2$(N^N)]$^+$", as they show intense phosphorescence, which also allows their use in light-emitting electrochemical cells.[3] It was also shown that modifications of the cyclometallating ligand "C^N" and/or the ancillary ligand "N^N" allowed both fine-tuning of the anticancer and imaging properties.[4]

While the photophysical properties of the Ir^{III} compounds are superior to those of the corresponding Rh^{III} complexes,[5] and therefore make the iridium complexes more useful with regard to diagnostic and phototherapeutic studies, this is not the general case for the antiproliferative properties. For example, while the iridium complex [Ir(ptpy)$_2$(4,4′-dinonyl-2,2′-bipy)]$^+$ (ptpy = *para*-tolyl-pyridinato) was much more effective towards transfected HEK293T cells than its rhodium congener,[6] the rhodium complexes [Rh(phquin)$_2$(4,4′-R$_2$-2,2′-bipy)]$^+$ (phquin = phenylquinolinato) performed much better in MDA-MB-231 cells (R$_2$ = diphenyl) or RAW264.7 cells (R$_2$ = dinonyl) than their iridium counterparts.,[7,8] Besides the nature of the metal, the substituents on the cyclometallating ligands as well as on the ancillary ligand have a great influence on the cancerostatic performance of these complexes. For example, we concentrated our cytostatic studies on the human adenocarcinoma cell lines MCF-7 and HT-29, mostly using the *para*-tolyl-pyridinato cyclometallating ligand and substituted 2,2′-bipyridines as ancillary ligands (Scheme 1).



I: M= Rh, Ir; R= H; R' = Me
II: M= Rh, Ir; R= Cl; R' = H
III: M= Rh, Ir; R= CH_2OH; R' = H;
IVa-c: M= Rh, Ir; R= $(CH_2)_nMe$
n= 1,3,9; R' = H
IVd: M= Rh, Ir; R= ^{t}Bu; R' = H

Scheme 1. Cyclometallated rhodium und iridium complexes with substituted 2,2-bipyridines as ancillary ligands studied by us earlier.

We found that the performance of bis-hydroxymethyl complexes of series **III** was inferior compared to the other tested structures with both metals and towards both cell lines, but

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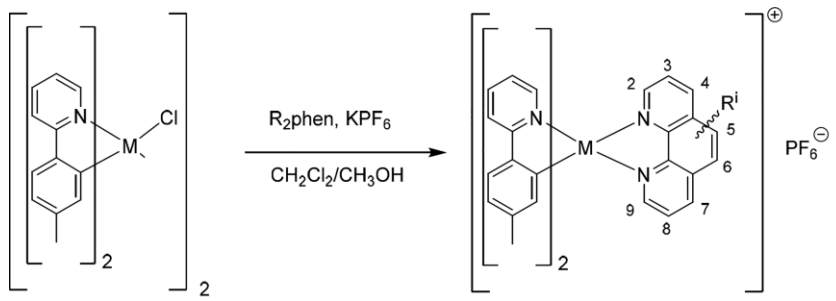

	1a/b	2a/b	3a/b	4a/b	5a/b
$R^{2/9}$	H	Me	H	H	Me
$R^{4/7}$	H	Ph	H	H	Cl
R^{5}	Me	H	NH_2	N=CH	H
R^{6}	Me	H	H	N=CH	H

Scheme 2. Synthesis of compounds **1a/b** – **4a/b**.

were still comparable to cisplatin (IC_{50} values ca. 10–12 μM vs. 10–23 μM). Slightly better performance was shown by the *tert*-butyl complexes **IVd** (IC_{50} values ca. 7μM towards HT-29 and ca. 9 μM towards MCF-7 for both metals). In case of 6,6′-dimethyl-substituted complexes **I** the iridium complex performed 15–18 times better than the rhodium complex, with both compounds being more effective towards HT-29 by a factor of 2.5 to 3.5. The chlorido-substituted compounds **II** had a very good performance towards HT-29 for both metals (IC_{50} values of ca. 0.5 μM), while they were less effective towards MCF-7 by a factor of 2.5 to 5.5, with a slightly superior performance of the iridium complex. The best results were obtained with complexes carrying *n*-alkyl substituents in the 4, 4'-positions, showing no differences between the metals and the two cell lines (all IC_{50} values 0.12–0.19 μM).[9]

Herein, we now report a systematic structure-activity (SAR) study on isostructural bis-cyclometalated Rh and Ir complexes, using the 1,10-phenanthroline ligand with substituents of differing steric demand and electronic properties.

Results and Discussion

The reactions of the chloride-bridged precursor complexes $[M(ptpy)_2(\mu\text{-}Cl)]_2$ (M = Rh, Ir) with substituted phenanthrolines in a refluxing CH_2Cl_2/MeOH mixture followed by metathetic exchange with PF_6^- for chloride yielded the title compounds **1a**–**4a** (M = Rh) and **1b**–**4b** (M = Ir) (Scheme 2). The analytical data of the chloro-substituted compounds **5a/b** corresponds to the values we described previously.[10]

All compounds are obtained as yellow crystals in yields of ca. 40 % and were characterized by elemental analyses, mass spectrometry, ^1H NMR and ^{13}C NMR spectroscopy. The iridium complexes **1b** – **3b** have been reported before, prepared by the same method and were obtained in yields of 50–60 %.[11–13] They had been prepared in the context of studies towards biological labeling reagents, particular as G-quadruplex-selective probes and STAT3 inhibitors. A rhodium complex closely related to **2a** with phenylpyridinato instead of the tolylpyridinato cyclometallating ligands had also been reported before and was shown to have strong *anti*-proliferative activity against A2058 melanoma cells.[14] A phenylpyridinato analog of the iridium pyrazino-phenanthroline complex **4b** had originally been studied as potential luminescent nucleic acid intercalator,[15] but was recently also suggested for a potential use in LEDs.[16]

Crystals of compounds **1b** and **4a** were studied by X-ray structure analysis. orte representations of both compounds are depicted in Figure 1 and Figure 2.

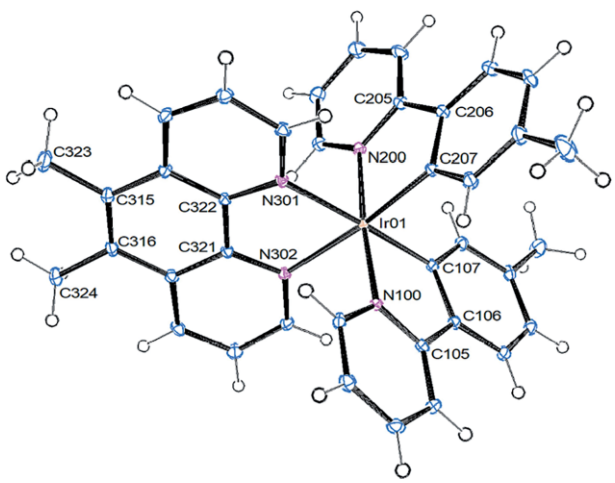

Figure 1. Molecular structure of the cation of **1b.** Thermal ellipsoids are at the 30 % probability level.

Compound **1b** crystallizes in the centrosymmetric space group $P2_1/n$, compound **4a** in the triclinic space group $P\bar{1}$. **4a** crystallizes with 1.5 CH_2Cl_2 molecules per formula unit,

Table 1. Selected bond parameters /Å,° of **1b** and **4a**.

	$M–N_{phen}$	$M–N_{C^\wedge N}$	$M–C_{C^\wedge N}$	$(N–M–N)_{phe}$	$(N–M–C)_{C^\wedge N}$
1b	2.140(2), 2.144(2)	2.049(2), 2.052(2)	2.009(2), 2.014(2)	78.85(7)	80.35(8), 80.19(8
4a	2.150(4), 2.159(4)	2.040(5), 2.041(5)	1.9936(6), 1.933(6)	75.05(16)	81.1(2), 81.3(2)

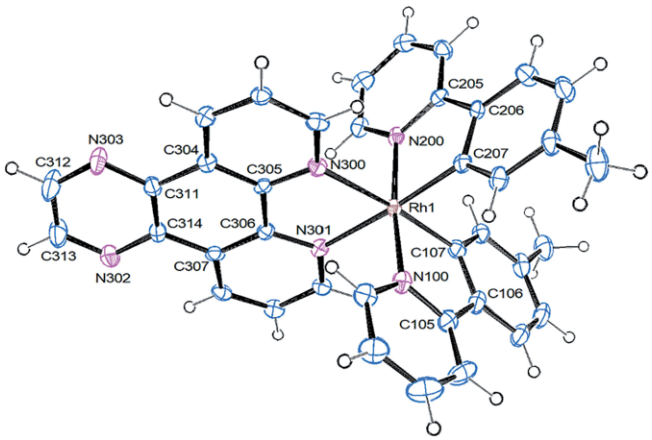

Figure 2. Molecular structure of **4a**. Thermal ellipsoids are at the 30 % probability level.

whereby the carbon atom of the "half" solvent molecule is disordered over two positions (with the consequence that the attached two hydrogen atoms had to be left out of the refinement). In both compounds, the PF_6 anions are involved in non-classical hydrogen bonds with some aromatic C–H bonds. As usual, both the Δ_M and Λ_M enantiomers are found in the crystal, and the nitrogen atoms of the cyclometallating ligands are in mutual *trans* configuration in both compounds. Also in both compounds, the bond lengths from the metal to the phenanthroline nitrogen atoms are longer than those to the ptpy nitrogen atoms and the N–M–C chelate angles are slightly larger than the N–M–N chelate angle. Selected bond parameters around the central metal atoms are collected in Table 1.

Biological Activity

To estimate the impact of our compounds on cancerous cells, the presented complexes were subjected to an MTT assay, measuring the metabolic activity of the treated cells which allows for a correlation to cell viability. The human cell lines HT-29 (colorectal adenocarcinoma) and MCF-7 (breast adenocarcinoma) served as test organisms in this study and the resulting IC_{50} values are summarized in Table 2.

Table 2. Antiproliferative activities of the studied compounds.

Compound	IC_{50} [μM] HT-29	IC_{50} [μM] MCF-7
1a	1.53 ± 0.58	1.02 ± 0.25
2a	0.51 ± 0.11	0.47 ± 0.07
3a	0.47 ± 0.05	0.75 ± 0.06
4a	1.66 ± 0.08	1.57 ± 0.36
1b	1.33 ± 0.45	0.52 ± 0.16
2b	0.48 ± 0.26	0.43 ± 0.14
3b	0.61 ± 0.10	0.78 ± 0.25
4b	1.76 ± 0.27	1.44 ± 0.41
5a [10]	0.5 ± 0.1	1.0 ± 0.3
5b [10]	0.2 ± 0.1	0.3 ± 0.1

Both tested cell lines were found to be susceptible towards the tested complexes in the low micromolar or even in the nanomolar concentration range. The most striking deviations were observed for compounds with substituents at 5 and 6 position, i.e. compounds **1** and **4**, which show an approximately threefold lower activity against HT-29 (**1a**: 1.53 μM, **4a** 1.66 μM) and MCF-7 (**1a**: 1.02 μM, **4a**: 1.57 μM) cells compared to the compounds without a functional substitution at these positions. The remaining compounds of series **2** and **3** show IC_{50} values between 0.47 μM and 0.75 μM against both cell lines.

Considering the error limits, no significant differences in activity of individual compounds against the two tested cell lines were observed (except for **1b**, which was performing better towards MCF-7 by about a factor of 2). All rhodium compounds show the same activities as the corresponding iridium complexes, except for the chloro-substituted compounds **5**, where the iridium compound performs better by a factor of ca. 3. Despite of the described minor differences in activity, the presented complexes obviously represent highly active candidate compounds that can further be fine-tuned in future studies.

Conclusions

Five new bis-cyclometallated rhodium and iridium complexes with differently substituted 1,10-phenanthroline ligands were prepared in moderate yields (40–46 %) and were studied together with three other closely related complexes for their proliferative activities. Despite of the differences in activity, it can be stated that all complexes show a significantly higher activity than the clinical drug cisplatin on both cell lines (IC_{50} for cisplatin: 10.4 μM for HT-29 and 23.1 μM for MCF-7). At least with the phenanthroline ligands of this study, there seems to be no drastic effect neither of the nature of the metal atom nor the kind of substituents. However, introducing functional substituents in 5 and 6 position of the phenanthroline moiety caused a significant decrease in anti-cancer activity. Thus, modulation of lipophilicity as well as functional modification should rather be conducted in the remaining positions as the antiproliferative activity seems to be less affected. An interesting task for future studies might be the separation of the Λ, Δ enantiomers and studying the effect of the chirality on the proliferative activity.

Experimental Section

All manipulations were performed in an atmosphere of dry nitrogen using conventional Schlenk techniques. 1,10-phenanthroline ligands were purchased from Aldrich and used as received. $[\{M(\mu\text{-}Cl)(C^\wedge N)_2\}_2]$ (M = Rh, Ir) were prepared by adequately modified literature methods.[17] NMR spectra were usually recorded in CD_2Cl_2 using a Jeol Eclipse 400 instrument operating at 400 MHz

(^{1}H) and 100 MHz (^{13}C) respectively and also using Jeol Eclipse 270. Chemical shifts are given in ppm, referenced to the solvent signals at δ = 5.30 (^{1}H) or 53.8 ppm (^{13}C). Mass spectra were measured using a Jeol Mstation JMS 700 spectrometer. Elemental analyses (C, H, N) were performed by the Microanalytical Laboratory of the Department of Chemistry, LMU Munich, using a Heraeus Elementar Vario EL instrument.

Crystals of **1b** and **4a** suitable for an X-ray diffraction study were grown from CH_2Cl_2/$CHCl_3$/hexane solutions. **1b** was measured on a Bruker D8 venture instrument, while **4a** was examined on an Oxford xcalibur2 instrument. The structures were solved with SHELXT and refined with SHELXL 2018/3, graphics were produced with Ortep3 for windows, and tested for residual solvent with Platon, all programs included in Wingx.[18] Details of the crystal data, data collection, structure solution, and refinement parameters are summarized in Table 3.

Table 3. Experimental details of the crystal structure determinations.

	1b	**4a**
Empirical formula	$C_{38}H_{32}F_6IrN_4P$	$C_{39.5}H_{30}Cl_3F_6N_6PRh$
Formula weight	881.84	942.92
Temperature /K	100(2)	100(2)
Crystal system	monoclinic	triclinic
Space group	$P2_1/n$	$P\bar{1}$
Unit cell dimensions		
a /Å	9.51000(4)	8.8154(5)
b /Å	13.8467(6)	13.0895(9)
c /Å	15.4480(11)	17.6440(10)
α /°	90	70.918(6)
β /°	97.6540(10)	80.957(4)
γ /°	90	85.968(5)
Volume /Å^3	3321.2(2)	1899.8(2)
Z	4	2
Density (calcd.) /g·cm^{-3}	1.764	1.648
Absorption coefficient / mm^{-1}	4.138	0.772
F(000)	1736	948
Crystal size /mm^3	0.06 × 0.04 × 0.02	0.348 × 0.108 × 0.09
Theta range for data collection /°	2.614 to 30.517	4.289 to 25.026
Index ranges	$-13 \le h \le 13$ $-19 \le k \le 19$ $36 \le l \le 35$	$-10 \le h \le 10$ $-9 \le k \le 15$ $-19 \le l \le 20$
Reflections collected	67573	10061
Independent reflections	10133 [R(int) = 0.0509]	6636 [R(int) = 0.0339]
Max. and min. transmission	0.7461 and 0.6879	1 and 0.93559
Data / restraints / parameters	10133 / 0 / 455	6636 / 1 / 516
Goodness-of-fit on F^2	1.048	1.045
Final R indices [$I > 2\sigma(I)$]	R_1 = 0.0217, wR_2 = 0.0450	R_1 = 0.0599, wR_2 = 0.1362
R indices (all data)	R_1 = 0.0291, wR_2 = 0.0485	R_1 = 0.0825, wR_2 = 0.1590
Largest diff. peak and hole /e·Å^{-3}	0.721 and –0.625	1.386 and –1.187

Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre, CCDC, 12 Union Road, Cambridge CB21EZ, UK. Copies of the data can be obtained free of charge on quoting the depository numbers CCDC-1969175 (**1b**) and CCDC-1969176 (**4a**) (Fax: +44-1223-336-033; E-Mail: deposit@ccdc.cam.ac.uk, http://www.ccdc.cam.ac.uk)

For biological experiments on human cancer cell lines, Dulbecco's Modified Eagle's Medium (DMEM), containing 10 % fetal calf serum, 1 % penicillin and streptomycin, was used as growth medium. MCF-7 (breast adenocarcinoma) or HT-29 (colorectal adenocarcinoma) cells were detached from the wells with trypsin and EDTA (0.25 %), harvested by centrifugation and resuspended again in fresh cell culture medium. The assays were carried out on 96 well plates with 6000 (3000) cells per well for MCF-7 (HT-29, respectively). After 24 h of incubation at 37 °C and 10 % CO_2, the cells were treated with serial dilutions of the compounds 1–4 (DMSO concentration: 0.5 %) with a final volume of 200 µL per well. For a negative control, one series of cells was left untreated. The cells were incubated for 48 h followed by adding 50 µL MTT (2.5 mg·mL^{-1}). After an incubation time of 2 h, the medium was removed and 200 µL DMSO were added. The formazan crystals were dissolved, and the absorption was measured at 550 nm, using a reference wavelength of 620 nm. Each test was repeated in quadruplicates in at least two independent experiments for each cell line

Synthesis of Compounds 1–4

General Procedure: To a solution of [{M(µ-Cl)(ptpy)$_2$}$_2$] (M = Rh, Ir) (0.15 mmol) in 25 mL of a mixture of CH_2Cl_2/MeOH/H_2O (1:1:0.5) the phenanthroline ligand (0.3 mmol) was added and the mixture refluxed with stirring for 3 h. After cooling to room temperature KPF_6 (0.5 mmol) was added and stirred for 20 minutes. The solvent was removed to dryness in vacuo and the residue dissolved in dichloromethane and chromatographed on alumina with CH_2Cl_2/acetone (9:1) as the eluent. The resulting solution was evaporated to dryness and the residue was redissolved in 5 mL of dichloromethane or chloroform and the product was precipitated by slow diffusion of isohexane.

[Rh(ptpy)$_2$(5,6-dimethyl-1,10-phenanthroline)]PF$_6$ (1a): Yield: 110 mg (46.3 %). $C_{38}H_{32}N_4F_6PRh$: calcd. C, 57.59; H, 4.07; N, 7.07 %; found: C, 57.48; H, 4.24; N, 6.96 %. **MS** (FAB$^+$): m/z = 647.4 [M$^+$] complex cation. **^{1}H NMR** (400 MHz): δ = 8.74 (dd, J = 1.2 / 8.6 Hz, 2 H), 8.31 (dd, J = 1.2 Hz/ 4.8 Hz, 2 H), 7.88 (d, J = 8 Hz, 2 H), 7.77 (m, 4 H), 7.70 (d, J = 7.6 Hz, 2 H), 7.22 (dd, J = 1.2 / 5.4 Hz, 2 H), 6.97 (dd, J = 0.8 / 8 Hz, 2 H), 6.80 (dt, J = 1.6 / 6.4 Hz, 2 H), 6.20 (s, 2 H), 2.78 (s, 6 H), 2.13 (s, 6 H) ppm.

[Ir(ptpy)$_2$(5,6-dimethyl-1,10-phenanthroline)]PF$_6$ (1b): Reported[11]: **^{1}H NMR** (400 MHz,): δ = 8.72 (dd, J = 2 / 12.4 Hz, 2 H), 8.27 (dd, J = 1.6/ 7.4 Hz, 2 H), 7.88 (d, J = 12 Hz, 2 H), 7.77 (m, 6 H), 7.24 (d, J = 8 Hz, 2 H), 6.94 (dd, J = 2 / 9.8 Hz, 2 H), 6.77 (dt, J = 2/ 9.8 Hz, 2 H), 6.20 (s, 2 H), 2.84 (s, 6 H), 2.16 (s, 6 H) ppm.

[Rh(ptpy)$_2$(2,9-dimethyl-4,7-diphenyl-1,10-phenanthroline)]PF$_6$ (2a): Yield: 120 mg (42.3 %). $C_{50}H_{40}N_4F_6PRh$: calcd. C, 63.57; H, 4.27; N, 5.93; found: C, 63.76; H, 4.68; N, 5.64 %. **MS** (FAB+): m/z = 799.5 [M$^+$] complex cation. **^{1}H NMR** (270 MHz): δ = 7.96 (s, 1 H), 7.87 (m, 5 H), 7.56 (m, 18 H), 6.91 (m, 4 H), 6.05 (s, 2 H), 2.21 (s, 6 H), 2.07 (s, 6 H) ppm.

[Ir(ptpy)$_2$(2,9-dimethyl-4,7-diphenyl-1,10-phenanthroline)]PF$_6$ (2b): Reported[12]. **^{1}H NMR** (270 MHz): δ = 8.00 (s, 1 H), 7.85 (m, 5 H), 7.59 (m, 18 H), 6.86 (m, 4 H), 5.98 (s, 2 H), 2.17 (s, 6 H), 2.07 (s, 6 H) ppm.

[Rh(ptpy)$_2$(5-amino-1,10-phenanthroline)]PF$_6$ (3a): Yield: 100 mg (42.8 %). $C_{36}H_{29}N_5F_6PRh$: calcd. C, 5′55.47; H, 3.75; N, 8.98 %, found: C, 55.48; H, 3.81; N, 8.80 %. **MS** (FAB$^+$): m/z = 634.9 [M$^+$] complex cation. **^{1}H NMR** (270 MHz): δ = 8.64 (dd, J = 1.2/ 8.4 Hz,, 2 H), 8.27 (dd, J = 1.2/ 4.8 Hz, 2 H), 8.23 (dd, J = 1.2/ 8.4 Hz, 2 H),

7.99 (dd, *J* = 1.2/ 5 Hz, 2 H), 7.87 (m, 2 H), 7.75 (m, 2 H), 7.68 (m, 2 H), 7.54 (m, 2 H), 7.26 (m, 2 H), 7.17 (s, 1 H), 6.96 (m, 2 H), 6.82 (m, 2 H), 6.48 (d, 2 H), 5.00 (s, 2 H), 2.14 (s, 3 H), 2.13 (s, 3 H) ppm.

[Ir(ptpy)$_2$(5-amino –1,10-phenanthroline)]PF$_6$ (3b): Reported[13]. **^{1}H NMR** (270 MHz): δ = 8.63 (dd, *J* = 2/ 12.8 Hz,, 2 H), 8.29 (dd, *J* = 2/ 7.6 Hz, 2 H), 8.231 (dd, *J* = 2/ 12.4 Hz, 2 H), 7.96 (dd, *J*/ = 7.2 Hz, 2 H), 7.87 (d, *J* = 11.6, 2 H), 7.77 (m, 2 H), 7.67 (m, 4 H), 7.65 (m, 2 H), 7.28 (m, 2 H), 7.20 (s, 1 H), 6.93 (m, 2 H), 6.79 (m, 2 H), 6.19 (d, 2 H), 5.07 (s, 2 H), 2.16 (s, 3 H), 2.15 (s, 3 H). **^{13}C{^{1}H} NMR** (270 MHz): δ = 168.0, 167.9, 150.9, 150.5, 150.4, 150.1, 148.4 (2), 146.8, 143.7, 141.7, 141.2, 141.0, 137.8, 135.4, 133.7, 133.1, 132.7, 132.6, 132.5, 126.3, 125.5, 124.8, 124.7, 124.6, 123.7, 122.5 (2), 119.4, 119.3, 104.8, 21.6 (Me-ptpy) ppm.

[Rh(ptpy)$_2$(pyrazino-[2.3-f]-1,10-phenanthroline)]PF$_6$ (4a): Yield: 100 mg (40.8 %). $C_{38}H_{28}N_6F_6PRh$: calcd. C, 55.90; H, 3.46; N, 10.29 %; found: C, 55.88; H, 3.40; N, 10.31 %. **MS** (FAB$^+$): *m*/*z* = 671.5 [M$^+$] complex cation. **^{1}H NMR** (400 MHz): δ = 9.73 (dd, *J* = 2.4/ 10.4 Hz, 2 H), 9.17 (s, 2 H), 8.46 (dd, *J* = 2.4/ 7.4 Hz, 2 H), 7.95 (m, 4 H), 7.75 (m, 4 H), 7.35 (d, *J* = 8.4 Hz, 2 H), 7.00 (dd, *J* = 1.2/ 11.8 Hz, 2 H), 6.86 (dt, *J* = 2/ 7.4 Hz, 2 H), 6.22 (s, 2 H), 2.16 (s, 6 H) ppm.

[Ir(ptpy)$_2$(pyrazino[2.3-f]-1,10-phenanthroline)]PF$_6$ (4b): Yield: 110 mg (40.5 %). $C_{38}H_{28}N_6F_6PIr$: calcd. C, 50.38; H, 3.12; N, 9.28 %; found: C, 49.93; H, 3.19; N, 9.06 %. MS (FAB+): *m*/*z* = 761.5 [M$^+$] complex cation. **^{1}H NMR** (400 MHz): δ = 9.69 (dd, *J* = 2.4/ 12.2 Hz, 2 H), 9.20 (s, 2 H), 8.43 (dd, *J* = 2/ 7.4 Hz, 2 H), 7.94 (dd, *J* = 2.4/ 7.4 Hz, 2 H), 7.69 (m, 4 H), 7.75 (m, 4 H), 7.37 (dd, *J* = 1.2/ 7.6 Hz, 2 H), 6.95 (dd, *J* = 1.6/ 11.6 Hz, 2 H), 6.81 (dt, *J* = 2.4/ 10 Hz, 2 H), 6.21 (s, 2 H), 2.18 (s, 6 H) ppm.

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Keywords: Cyclometallate complexes; Rhodium; Iridium; Phenanthrolines; Cytostatic activity

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