# SUPPORTING INFORMATION

## Electrochemical, mechanistic and DFT study of amines derived diphosphines containing Ru(II)-cymene complexes with potent *in vitro* cytotoxic activity against HeLa and the triple negative breast cancer cells MDA-MB-231

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**Table S2. NBO charges of atoms (or group) involved in Ru-L bonds.**

**Table S4. $IC_{50}$ values for the two independent experiments using the HeLa and MDA-MB 231 cell lines**

**Table S5. Crystal data and structure refinement for $[1b]BF_4.0.25H_2O$ and $[4b]BF_4$**

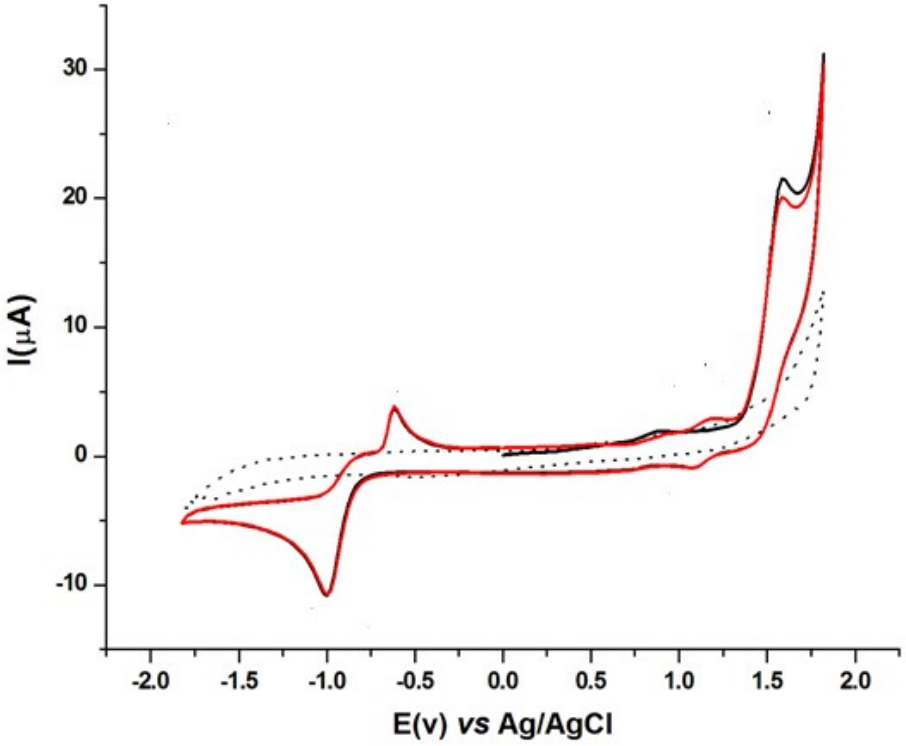


**Fig. S1.** Cyclic voltamogram of **[1a]•$BF_4$**.

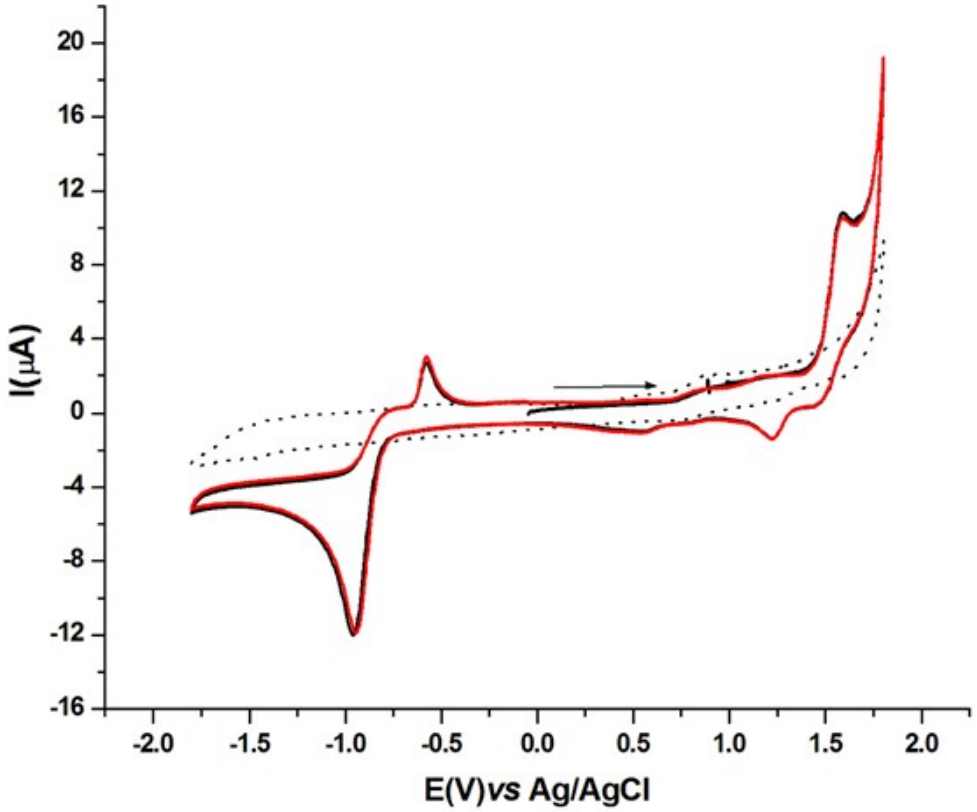


**Fig. S2.** Cyclic voltamogram of **[1c]•$BF_4$**.

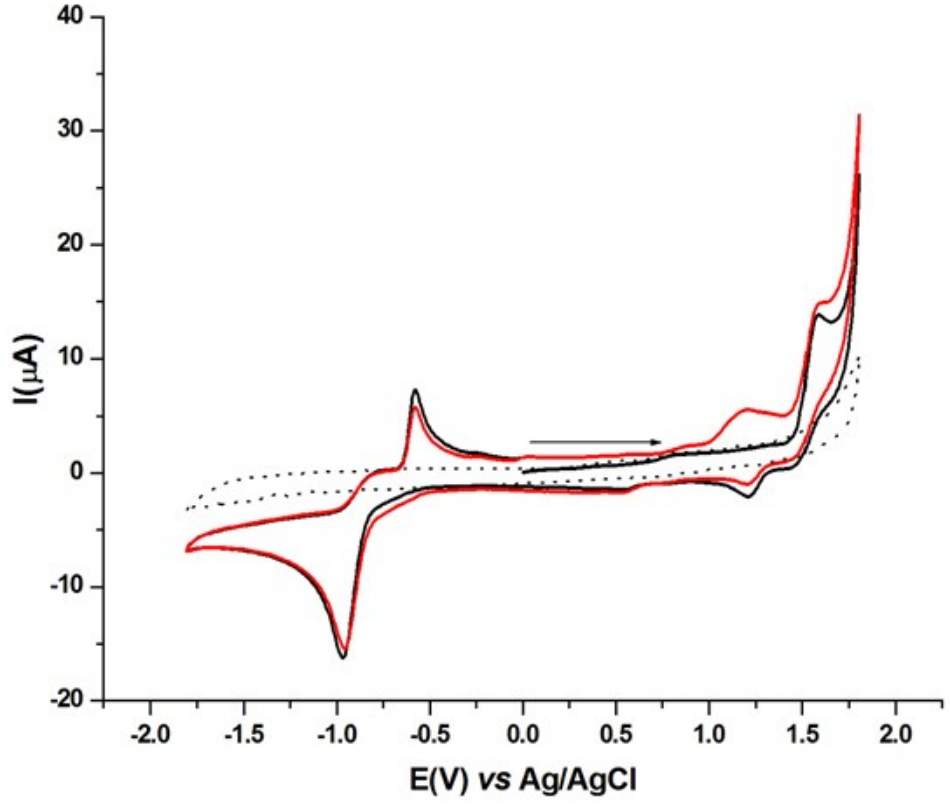


**Fig. S3.** Cyclic voltamogram of **[1d]•$BF_4$**.

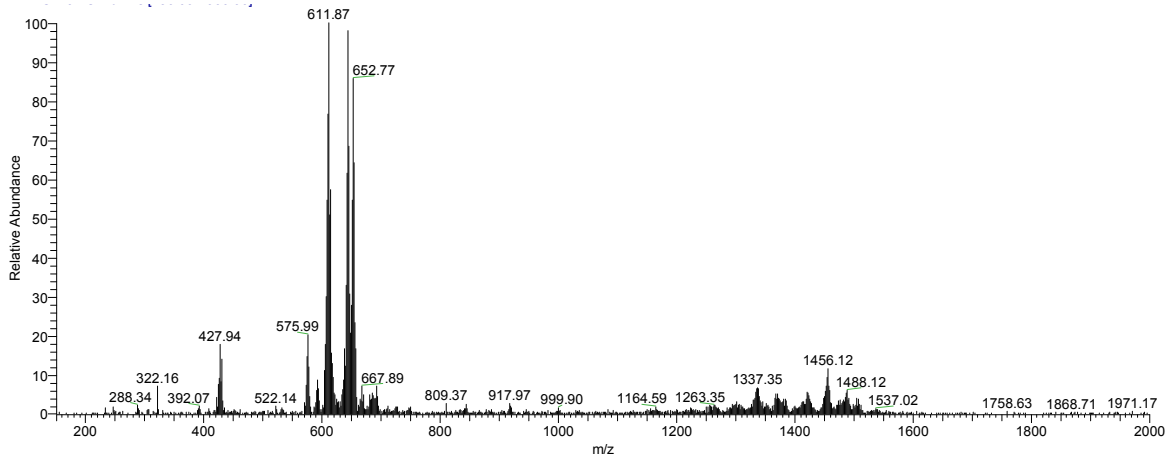


**Fig. S4.** ESI-MS of **[2b]•$BF_4$**.in MeOH.

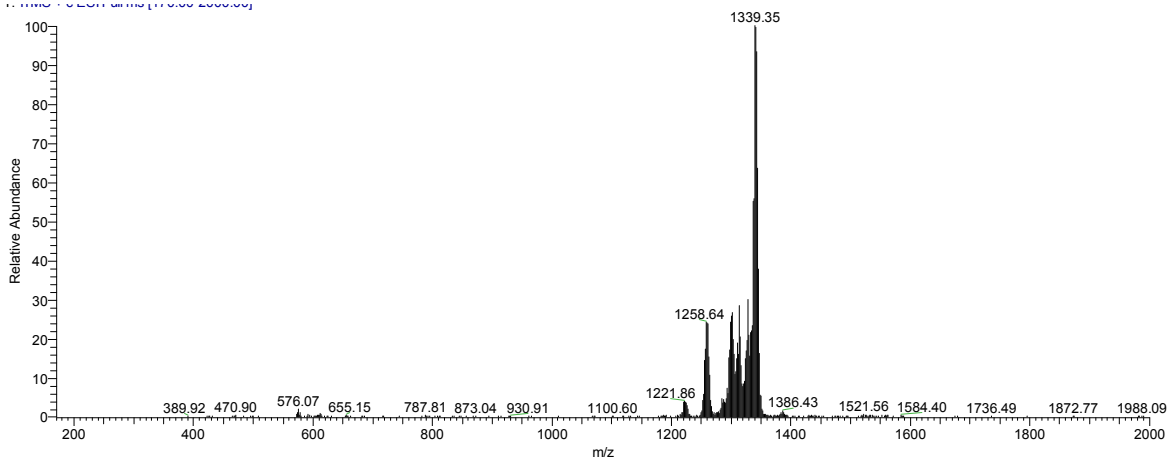


**Fig. S5.** ESI-MS of **[3b]•$BF_4$**.in $CH_2Cl_2$.

**Table S1.** Selected metric parameters (Experimental and calculated) for **[1a]•$PF_6$**, **[1b]•$BF_4$**, **[1c]•$BF_4$** and **[1d]•$PF_6$** (the molecular structures of **[1a]•$PF_6$**, **[1c]•$BF_4$** and **[1d]•$PF_6$** were published elsewhere [1]).

| | **[1a]$^+$** | | **[1b]$^+$** | | **[1c]$^+$** | | **[1d]$^+$** | |
|---|---|---|---|---|---|---|---|---|
| | Calcd. | Exp. | Calcd. | Exp. | Calcd. | Exp. | Calcd. | Exp. |
| **Bond Lengths (Å)** | | | | | | | | |
| Ru-P1 | 2.361 | 2.3043(8) | 2.360 | 2.3074(12) | 2.362 | 2.2884(9) | 2.362 | 2.3077(6) |
| Ru-P2 | 2.356 | 2.3020(8) | 2.358 | 2.3116(11) | 2.345 | 2.3010(9) | 2.345 | 2.2948(6) |
| Ru-Cl | 2.416 | 2.3813(8) | 2.419 | 2.3815(10) | 2.421 | 2.3933(9) | 2.421 | 2.3763(7) |
| P1-N1 | 1.718 | 1.692(3) | 1.719 | 1.698(4) | 1.723 | 1.710(3) | 1.722 | 1.711(2) |
| P2-N1 | 1.710 | 1.697(3) | 1.713 | 1.702(3) | 1.724 | 1.703(3) | 1.723 | 1.7102(19) |
| Ru-C(cym)$^{avg}$ | 2.333 | 2.275 | 2.335 | 2.251 | 2.337 | 2.250 | 2.337 | 2.258 |

| Bond Angles (°) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| P2-Ru-P1 | 69.0 | 68.81(3) | 68.8 | 68.68(4) | 69.4 | 69.03(3) | 69.3 | 69.18(2) |
| P1-Ru-Cl | 89.4 | 87.68(3) | 90.8 | 86.15(4) | 86.8 | 85.57(3) | 86.8 | 84.35(3) |
| P2-Ru-Cl | 85.7 | 86.26(3) | 90.5 | 85.72(4) | 86.1 | 82.90(3) | 86.1 | 82.93(3) |
| P2-N-P1 | 102.4 | 100.32(14) | 102.0 | 100.03(19) | 102.0 | 99.27(14) | 102.0 | 99.60(11) |

**Table S2.** NBO charges of atoms (or group) involved in Ru-L bonds.

| **Atoms** | **NBO Charges** | | | |
|---|---|---|---|---|
| | **$Ru^0$** | **$Ru^{1+}$** | **$Ru^{2+}$** | **$Ru^{3+}$** |
| Ru | 0.0198 | 0.0648 | 0.1975 | 0.3627 |
| Cl | -0.7399 | -0.7050 | -0.5000 | -0.276 |
| N* | -1.1423 | -1.1395 | -1.1382 | -1.147 |
| P | 1.3640 | 1.4035 | 1.4980 | 1.5503 |
| P | 1.3620 | 1.4536 | 1.5058 | 1.5557 |
| *p*-cym | -0.5050 | 0.0091 | 0.2574 | 0.4998 |

*N of P-$N^R$-P ligand. $Ru^0$ = $[Ru^0Cl(p\text{-cym})(P\text{-}N^R\text{-}P)]^-$, $Ru^{1+}$ = $[Ru^{1+}Cl(p\text{-cym})(P\text{-}N^R\text{-}P)]$, $Ru^{2+}$ = $[Ru^{2+}Cl(p\text{-cym})(P\text{-}N^R\text{-}P)]^+$, $Ru^{3+}$ = $[Ru^{3+}Cl(p\text{-cym})(P\text{-}N^R\text{-}P)]^{2+}$. R = $CH_2Ph$

**Table S3.** NBO charges of atoms (or group) involved in Ru-L bonds for the proposed complexes formed after electron-transfer processes (CV).

| **Atoms** | **NBO Charges** | |
|---|---|---|
| | **$[Ru^0(p\text{-cym})(P\text{-}N^{CH2Ph}\text{-}P)]$** | **$[Ru^{3+}Cl(CH_3CN)_3(P\text{-}N^{CH2Ph}\text{-}P)]^{2+}$** |
| Ru | -0,19066 | 0,53290 |
| Cl | - | -0,2712 |
| N* | -1,13551 | -1,1451 |
| P | 1,37133 | 1,51269 |
| P | 1,37120 | 1,51079 |
| *p*-cym | -0,21338 | - |

*N of P-$N^R$-P ligand

**Table S4.** $IC_{50}$ values for the two independent experiments using the HeLa and MDA-MB 231 cell lines

| Complexo | Hela 1° entry | Hela 2° entry | Hela média | Hela ESD | MDA-MB 231 1° entry | MDA-MB 231 2° entry | MDA-MB média | MDA-MB 231 ESD |
|---|---|---|---|---|---|---|---|---|
| **1b.$PF_6$** | 8.75 | 8.83 | 8.79 | 0.0032 | 6.56 | 6.60 | 6.58 | 0.02828 |
| **1b.$BF_4$** | 11.93 | 10.69 | 11.31 | 0.66468 | 6.44 | 6.31 | 6.37 | 0.091 |
| **1d.$PF_6$** | 13.80 | 13.12 | 13.46 | 0.48083 | 10.60 | 9.96 | 10.30 | 0.45255 |
| **1c.$PF_6$** | 14.57 | 14.64 | 14.60 | 0.0495 | 13.60 | 13.35 | 13.47 | 0.17678 |
| **1a.$BF_4$** | 14.70 | 14.64 | 14.67 | 0.0424 | 14.16 | 14.25 | 14.20 | 0.06364 |
| **1c.$BF_4$** | 15.58 | 15.83 | 15.22 | 0.39598 | 11.36 | 10.42 | 10.90 | 0.66468 |
| **1a.$PF_6$** | 15.67 | 15.86 | 15.76 | 0.13435 | 15.90 | 15.82 | 15.86 | 0.05657 |
| **1d.$BF_4$** | 15.87 | 14.95 | 15.41 | 0.65054 | 6.95 | 7.05 | 7.0 | 0.07071 |

**Table S5.** Crystal data and structure refinement for **[1b]$BF_4$.0.25$H_2O$ and [4b]$BF_4$**

| Complex | **[1b]$BF_4$** | **[4b]$BF_4$** |
|---|---|---|
| Empirical formula | $C_{41}H_{41}BClF_4NP_2Ru$•0.25$H_2O$ | $C_{66}H_{60}BCl_3F_4N_4P_4Ru_2$ |
| Formula weight | 837.52 | 1428.36 |
| Temperature | 293(2) K | 296(2) K |
| Wavelength | 0.71070 Å | 0.71073 Å |
| Crystal system, Space group | Triclinic, P-1 | Monoclinic, P21/c |
| Unit cell dimensions | a = 10.7960(6) Å α = 96.965(3)°<br>b = 12.2360(7) Å β = 91.221(3)°<br>c = 15.3090(5) Å γ = 97.427(2)° | a = 10.8878(5) Å α = γ = 90°<br>b = 19.1910(9) Å β = 98.354(2)°<br>c = 31.0546(13) Å |
| Volume | 1989.15(17) $A^3$ | 6419.9(5) $A^3$ |
| Z, Density (calculated) | 2, 1.398 $Mg/m^3$ | 4, 1.478 $Mg/m^3$ |
| Absorption coefficient | 0.591 $mm^{-1}$ | 0.750 $mm^{-1}$ |
| F(000) | 857 | 2896 |
| Crystal size | 0.260 x 0.220 x 0.200 mm | 0.20 x 0.15 x 0.10 mm |
| Theta range for data | 2.988 to 26.471° | 2.19 to 27.98° |

| | | |
|---|---|---|
| collection | | |
| Index ranges | $-13 \leq h \leq 13$, $-15 \leq k \leq 15$, $-18 \leq l \leq 19$ | $-14 \leq h \leq 13$, $-25 \leq k \leq 21$, $-40 \leq l \leq 40$ |
| Reflections collected | 42574 | 54349 |
| Independent reflections | 8172 [R(int) = 0.0580] | 15422 [R(int) = 0.1291] |
| Completeness to θ | 99.6 % | 99.6 % |
| Absorption correction | Gaussian | Semi-empirical from equivalents |
| Max. and min. Transmission | 0.915 and 0.858 | 0.9387 and 0.8744 |
| Refinement method | Full-matrix least-squares on $F^2$ | Full-matrix least-squares on $F^2$ |
| Final R indices [I>2sigma(I)] | R1 = 0.0515, wR2 = 0.1359 | R1 = 0.0665, wR2 = 0.1038 |
| R indices (all data) | R1 = 0.0735, wR2 = 0.1483 | R1 = 0.1663, wR2 = 0.1165 |
| Largest diff. peak and hole | 0.613 and -0.816 e.$A^{-3}$ | 0.641 and -0.490 e. $A^{-3}$ |

## References

[1] J.P. da Silva, I.C. Silva, F.R. Pavan, D.F. Back, M.P. de Araujo, Bis(diphenylphosphino)amines-containing ruthenium cymene complexes as potential anti-Mycobacterium tuberculosis agents, Journal of Inorganic Biochemistry, 173 (2017) 134-140.