IL-32

Piano-Stool Ruthenium(II) Complexes with 1-Pyrenylphosphines Presenting Delayed Cytotoxic Activity

Arnald Grabulosa,[1,2] Laia Rafols,[1] Dana Josa,[1,2] Patrick Gamez[1,2,3]

[1]*Departament de Química Inorgànica i Orgànica, Secció de Química Inorgànica, Universitat de Barcelona, 08028, Barcelona Spain*

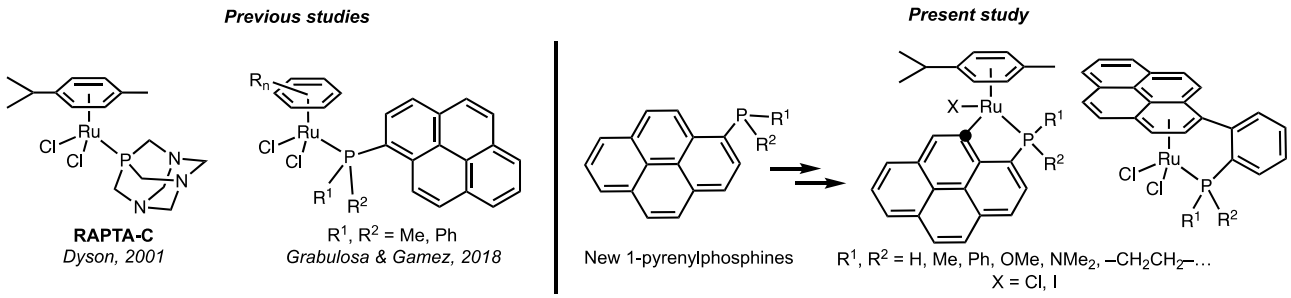
[2]*Institut de Nanociència i Nanotecnologia (IN²UB), 08028, Barcelona, Spain*

[3]*Institució Catalana de Recerca i Estudis Avançats (ICREA), 08010, Barcelona, Spain*

e-mail: arnald.grabulosa@qi.ub.es

The remarkable chemotherapeutic properties of cisplatin are shadowed by its severe side effects and the frequent appearance of tumoral resistance, but these limitations have also spurred tremendous efforts to find more efficient and less toxic drugs based on alternative metals.[1] In this context, ruthenium stands as one of the more promising metals because the reduced toxicity, increased selectivity and antimetastic activity observed by several ruthenium compounds.[2]

Two decades ago, Dyson described that Ru(II) complexes with η^6-coordinated arenes bearing a PTA phosphine were particularly active, RAPTA-C being the most well-known example.[3] These results inspired our own research and a few years ago we uncovered a family of Ru(II)-arene complexes with 1-pyrenylphosphine ligands.[4a] These complexes were very cytotoxic against several tumor cell lines and clear Structure Activity Relationships (SARs) were elucidated. More recently, the synthesis of 1-pyrenylphosphines and their derived complexes has been expanded[4b] but the active species have remained elusive.



In this contribution we will firstly present the synthesis of 1-pyrenylphosphines including the parent 1-pyrenylphosphine, a phosphirane, a phosphonite and several tertiary phosphines. The preparation of several types of organometallic, Ru(II)-η^6-arene complexes will be subsequently considered. Finally, the cytotoxicity of the complexes will be discussed, paying particular attention to the activation mechanism, which involves the ruthenation of the phosphine.

References

[1] E. Boros, P. J. Dyson and G. Gasser, *Chem*, 2020, **6**, 41-60

[2] A. Bergamo and G. Sava, *Dalton Trans.* **2011**, *40*, 7817.

[3] C. S. Allardyce, P. J. Dyson, D. J. Ellis and S. L. Heath, *Chem. Commun.*, **2001**, 1396-1397.

[4] (*a*) R. F. Brissos, P. Clavero, A. Gallen, A. Grabulosa, L. A. Barrios, A. B. Caballero, L. Korrodi-Gregório, R. Pérez-Tomás, G. Muller, V. Soto-Cerrato and P. Gamez, *Inorg. Chem.*, **2018**, *57*, 14786. (*b*) L. Rafols, S. Torrente, D. Aguilà, V. Soto-Cerrato, R. Pérez-Tomás, P. Gamez and A. Grabulosa, *Organometallics*, **2020**, *39*, 2959-2971.