Anticancer rhenium di- and tricarbonyl complexes and synthesis of new α-diimine rhenium dicarbonyl complexes

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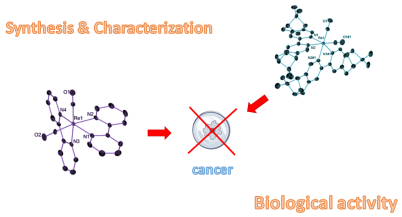
In our effort to discover novel selective and non-toxic agents effective against CRC, we synthesized a series of rhenium(I) tricarbonyl-based complexes with increased lipophilicity. Two of these novel compounds were discovered to possess remarkable anticancer, anti-angiogenic and antimetastatic activity in vivo (zebrafish-human HCT-116 xenograft model), being effective at very low doses (1-3 µM). At doses as high as 250 µM the complexes did not provoke toxicity issues encountered in clinical anticancer drugs (cardio-, hepato-, and myelotoxicity). In vivo assays showed that the two compounds exceed the anti-tumor and anti-angiogenic activity of clinical drugs cisplatin and sunitinib malate, and display a large therapeutic window.[1]



In another study, we reported a rhenium(II) dicarbonyl complex, which displayed better cytotoxicity against MCF-7 breast cancer cells than cisplatin.[2] We investigated later new synthetic routes to aerobically stable and substitutionally labile α-diimine rhenium(I) dicarbonyl complexes. The molecules were prepared in high yield from the *cis–cis–trans*-$[Re(CO)_2(^tBu_2bpy)Br_2]^-$ anion (where $^tBu_2$bpy is 4,4′-di-*tert*-butyl-2,2′-bipyridine), which could be isolated from the one electron reduction of the corresponding 17-electron complex. Ligand substitution of Re(I) complexes proceeded via pentacoordinate intermediates capable of Berry pseudorotation. In addition to the *cis–cis–trans*-complexes, *cis–cis–cis*- (all *cis*) isomers were also formed. $[Re(CO)_2(^tBu_2bpy)Br(L)]$ complexes may be considered as synthons for the preparation of a variety of new stable diamagnetic dicarbonyl rhenium *cis*-$[Re(CO)_2]^+$ complexes, offering a convenient entry in the chemistry of the core.[3]

[1] Joachim Delasoie, Aleksandar Pavic, Noémie Voutier, Sandra Vojnovic, Aurélien Crochet, Jasmina Nikodinovic-Runic, Fabio Zobi, *Eur. J. Med. Chem.*, **2020**, 204, 112583.
[2] Jérémie Rossier, Daniel Hauser, Emmanuel Kottelat, Barbara Rothen-Rutishauser, Fabio Zobi, *Dalton Trans.*, **2017**, 7, 2159.
[3] Kevin Schindler, Aurélien Crochet, Fabio Zobi, *RSC Adv.*, **2021**, 13, 7511.