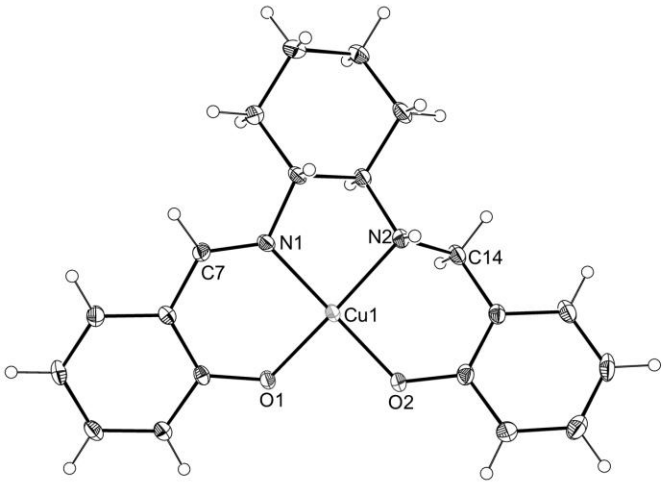
Publications – João Costa Pessoa - 2014

P. Adão, S. Barroso, F. Avecilla, M. C. M. A. Oliveira, J. Costa Pessoa, T. Mukherjee, J. Costa Pessoa, A. Kumar, A. R. Sarkar, *Cu^{II}-salan compounds: synthesis, characterization and evaluation of their potential as oxidation catalysts*,

J. Organom. Chem., 2014, 760, 212-223

http://dx.doi.org/10.1016/j.jorganchem.2013.10.019

The synthesis and characterization of several salan-type Cu^{II} complexes is reported. At room temperature the compounds exhibit low to moderate catalytic activity in sulfoxidations and alkene oxidations, but no activity in oxidative naphthol coupling. Spectroscopic and mass spectrometry studies revealed that in the presence of H_2O_2 the Cu^{II}-salan complexes decompose, significantly faster at 40 ºC than at room temperature. The catalytic activity observed is not attributed to the original Cu^{II}-salan precursors but to their degradation products.



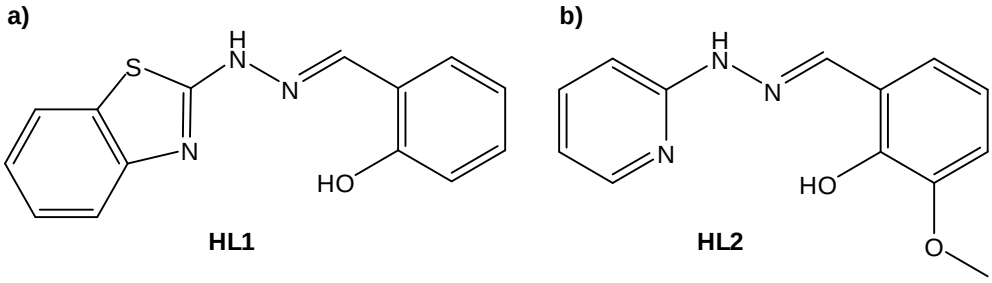
Cu^{II}[sal-(*R,R*-chen)]

I. Machado, M. Fernández, L. Becco, B. Garat, R. F. Brissos, N. Zabarska, P. Gamez, F. Marques, I. Correia, J. Costa Pessoa, D. Gambino, New metal complexes of NNO tridentate ligands: effect of metal center and co-ligand on biological activity

Inorg. Chim. Acta, 2014, 420, 39-46

http://dx.doi.org/10.1016/j.ica.2013.10.022

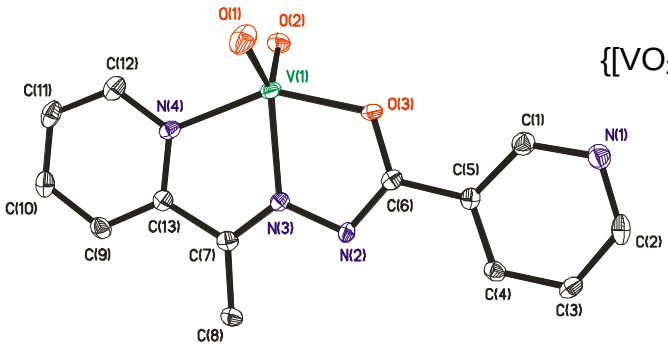
New complexes $[V^{V}O_2(L1)]$, $[V^{V}O_2(L2)]$, $[V^{IV}O(L1\text{-}H)(phen))]$ and $[Ga^{III}(L2)_2](NO_3)$ were synthesized, their stability investigated in DMSO and in aqueous - DMSO medium. The cytotoxicity on three tumor lines that show different sensitivity to cisplatin was evaluated. All the compounds evidenced antiproliferative activity towards ovarian A2780, breast MCF7 and prostate PC3 human carcinoma cell lines in the μM range. The highest cytotoxic activity, in molar units, is shown by $[Ga^{III}(L2)_2](NO_3)$ (IC_{50}: 1.7 μM) and $[V^{IV}O(L1\text{-}H)(phen)]$ (IC_{50}: 2.7 μM) against the ovarian cancer cells. With the exception of $[V^{V}O_2(L1)]$, the cytotoxic activity of the ligands and complexes is similar to that of cisplatin in A2780 cells and surpass cisplatin in the other tumor cell lines. In respect to the activity on *Trypanosoma cruzi*, $[V^{IV}O(L1\text{-}H)(phen)]$ showed a ten-fold decrease of IC_{50} in respect to HL1 and an IC_{50} value (10.74 μM) of the same order of that of the antitrypanosomal drug Nifurtimox (IC_{50}: 6.0 μM). HL2 showed significant growth inhibitory effect on the parasite (IC_{50}: 23.55 μM) and its coordination to Ga(III) lead to a 2-fold increase in activity in molar units (IC_{50}: 14.19 μM). AFM images show effects that suggest DNA as a potential target.



HL1 **HL2**

M. R. Maurya, N. Chaudhary, A. Kumar, F. Avecilla, J. Costa Pessoa,
Polystyrene bound dioxidovanadium(V) complexes of 2-acetylpyridine derived ligands for catalytic oxidations
Inorg. Chim. Acta, 2014, 420, 24-38
http://dx.doi.org/10.1016/j.ica.2013.11.021

Three neat complexes [$V^{V}O_2$(acpy-bhz)] (**1**) [$V^{V}O_2$(acpy-inh)] (**2**) and [$V^{V}O_2$(acpy-nah] (**3**) and the corresponding polymer-supported (PS) dioxidovanadium(V) complexes having monobasic tridentate ONN donor ligands, abbreviated herein as PS-im[$V^{V}O_2$(acpy-bhz)] (**4**) PS-im[$V^{V}O_2$(acpy-inh)] (**5**) and PS-im[$V^{V}O_2$(acpy-nah] (**6**) were isolated. Polymer-supported as well neat complexes are used as catalyst precursors for the oxidative bromination of styrene and *trans*-stilbene using 30 % aqueous H_2O_2 as an oxidant, the compounds acting as functional models of vanadium dependent haloperoxidases. It is also shown that all these compounds are catalyst precursors for the catalytic oxidation of benzoin by peroxide. An outline of the mechanism is proposed and plausible intermediates involved in the catalytic processes are proposed/established by UV-Vis and ^{51}V NMR studies.



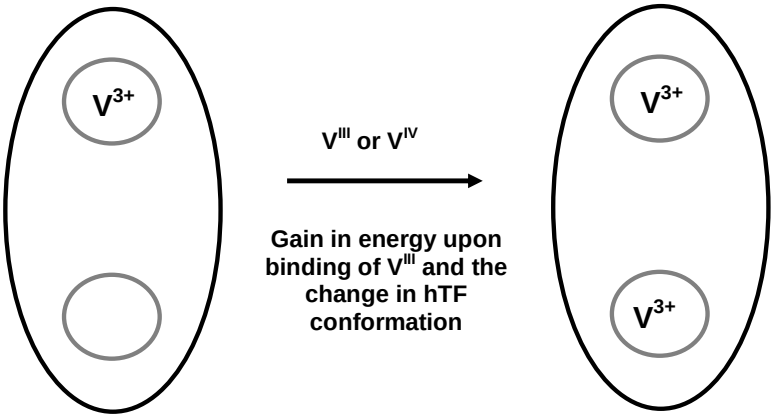
{[VO_2(acpy-nah)]·DMSO (**3**·DMSO)}

S. Mehtab, G. Gonçalves, S. Roy, A. I. Tomaz, T. Santos-Silva, M.F.A. Santos, M.J. Romão, T. Jakusch, T. Kiss, J. Costa Pessoa, *Interaction of vanadium(IV) with human serum apo-transferrin*

Inorg. Chim. Acta, 2014, 420, 60-68

http://dx.doi.org/10.1016/j.ica.2013.11.025

Binding of vanadium ions and complexes to serum proteins and how vanadium might be transported in blood and up-taken by cells is revised and discussed, namely the two main types of binding proposed for transport of $V^{IV}O(carrier)_2$ complexes. New results, obtained by circular dichroism (CD), EPR and gel electrophoresis, regarding the binding of vanadium to hTF in the oxidation states +5 and +3 are also presented. Namely, evidences for the binding of V^{V}-species to diferric-transferrin, designated by $(Fe^{III})_2$hTF, as well as to $(Al^{III})_2$hTF, are presented and discussed, the possibility of up-take of vanadate by cells through $(Fe^{III})_2$hTF endocytosis being suggested. It is also confirmed that V^{III} binds strongly to hTF, forming di-vanadium(III)-transferrin, designated by $(V^{III})_2$hTF, and gel electrophoresis experiments indicate that $(V^{III})_2$hTF corresponds to a 'closed conformation' similar to $(Fe^{III})_2$hTF.



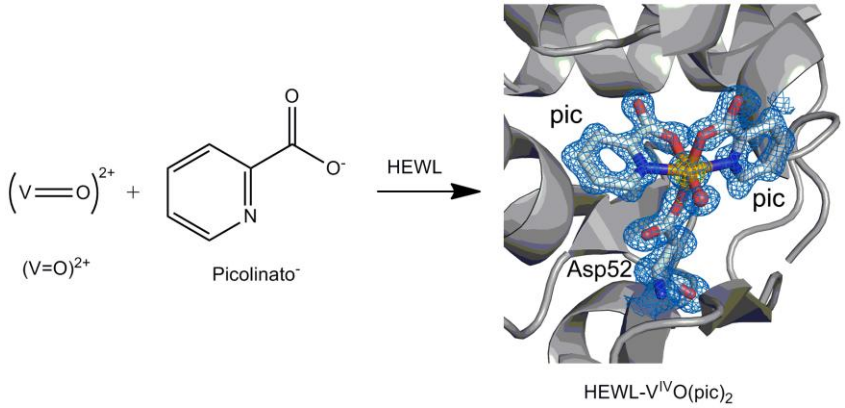
Schematic explanation of the reduction process where the driving force is the formation of the highly stable $(V^{III})_2$hTF

M.F.A. Santos, I. Correia, A.R. Oliveira, E. Garribba, J. Costa Pessoa, T. Santos-Silva, *Vanadium Complexes as Prospective Therapeutics: Structural Characterization of a V(IV) Lysozyme Adduct*

Eur. J. Inorg. Chem., 2014, 3293-3297

http://dx.doi.org/10.1002/ejic.201402408

To further understand their binding to blood serum proteins and interactions with membrane or cytosolic proteins studies of the interaction of vanadium picolinate complexes with the protein hen egg white lysozyme (HEWL) are reported. Crystals of HEWL-$V^{IV}O$(pic)2, where pic is picolinato ligand, were obtained and studied by X-ray crystallography. It is shown that the $V^{IV}O(pic)_2$ complex covalently binds to the COO^- of the side chain of Asp52 of HEWL. For the crystals of HEWL-$V^{IV}O$(pic)2 adducts a reasonably strong EPR signal was observed, confirming the presence of $V^{IV}O$-species, this being the first example of a $V^{IV}O$-protein adduct characterized by X-ray diffraction analysis. A relatively long V^{IV}=O bond distance (~1.82 Å) was obtained from the X-ray diffraction data collected, but EPR and DFT results allowed to confirm the carboxylate binding of Asp52 of HEWL to the $V^{IV}O(pic)_2$ moiety and to predict that the V=O bond should be ~1.60 Å. The explanation for the long V^{IV}=O bond obtained in the X-ray study, further confirmed by analysis of several sub-sets of the collected data, is that during the exposure of the HEWL-$V^{IV}O$(pic)2 crystals to the intense X-ray beam, reduction of V^{IV} to V^{III} took place progressively, and thus a bond distance intermediate between V^{IV}=O and V^{III}–O was obtained.

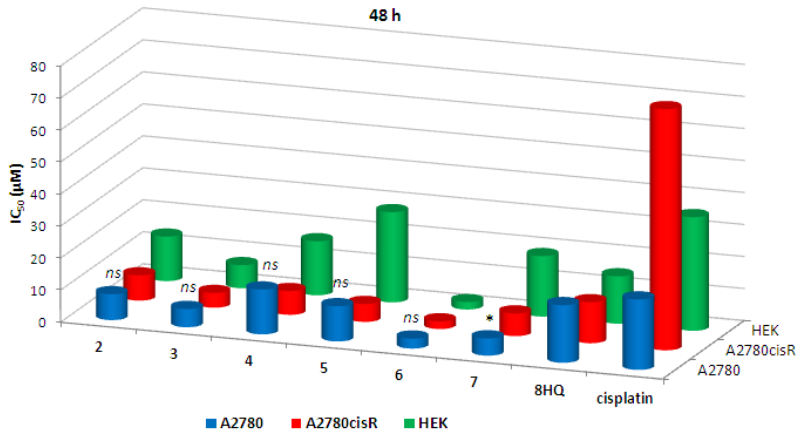


I. Correia, P. Adão, S. Roy, M. Wahba, C. Matos, M.R. Maurya, F. Marques, F.R. Pavan, C.Q.F. Leite, F. Avecilla, J. Costa Pessoa, *Hydroxyquinoline derived vanadium(IV and V) and copper(II) complexes as potential anti-tuberculosis and anti-tumor agents*

J. Inorg. Biochem. 2014, 141, 83-93

http://dx.doi.org/10.1016/j.jinorgbio.2014.07.019

Several vanadium and copper complexes were synthesized containing 8-hydroxyquinoline (8HQ) and a ligand such as picolinato (pic^-), dipicolinato ($dipic^{2-}$) or a Schiff base. The biological activity of the compounds was assessed through the minimal inhibitory concentration (MIC) of the compounds against *Mycobacterium Tuberculosis* (Mtb) and the cytotoxic activity against the cisplatin sensitive/resistant ovarian cells A2780/A2780cisR and the non-tumorigenic HEK cells (IC_{50} values). Almost all tested vanadium complexes were very active against Mtb and the MICs were comparable to, or better than, the MICs of drugs, such as streptomycin. The activity of the complexes against the A2780 cell line was dependent on incubation time presenting IC_{50} values in the 3–14 μM (at 48 h). In these conditions, the complexes were significantly more active than cisplatin (22 μM), in the A2780 cells and even surpassing its activity in the cisplatin-resistant cells A2780cisR (2.4–8 μM *vs.* 75.4).



S. Gama, I. Rodrigues, F. Marques, E. Palma, I. Correia, M.F.N.N. Carvalho, J. Costa Pessoa, A. Cruz, S. Mendo, I.C. Santos, F. Mendes, I. Santos, A.Paulo,

New ternary Bipyridine-Terpyridine Copper(II) complexes as self-activating chemical nucleases

RSC Adv., 2014, 4, 61363-61377

DOI: 10.1039/c4ra12085j

New ternary terpyridine–bipyridine–Cu(II) complexes carrying pendant cyclic amines were developed as self-activating chemical nucleases with potential applications as therapeutic agents. The new complexes present an impressive plasmid DNA cleaving ability, which triggers double-strand DNA breaks in the absence of any exogenous agents, via an oxidative mechanism. The binding affinity towards duplex DNA was determined using UV-Vis and fluorescence spectroscopic titrations. These studies showed that the tested complexes bind moderately (in the order of 10^4 M^{-1}) to duplex DNA. The copper complexes displayed high cytotoxicity against ovarian carcinoma A2780 cells (4-fold cisplatin activity), surpassing the resistance on the cisplatin-resistant cell line (A2780cisR) with lower resistance factors. Cellular uptake studies showed that the ternary complexes were able to enter the cell with a significant localization in the cytoskeleton.