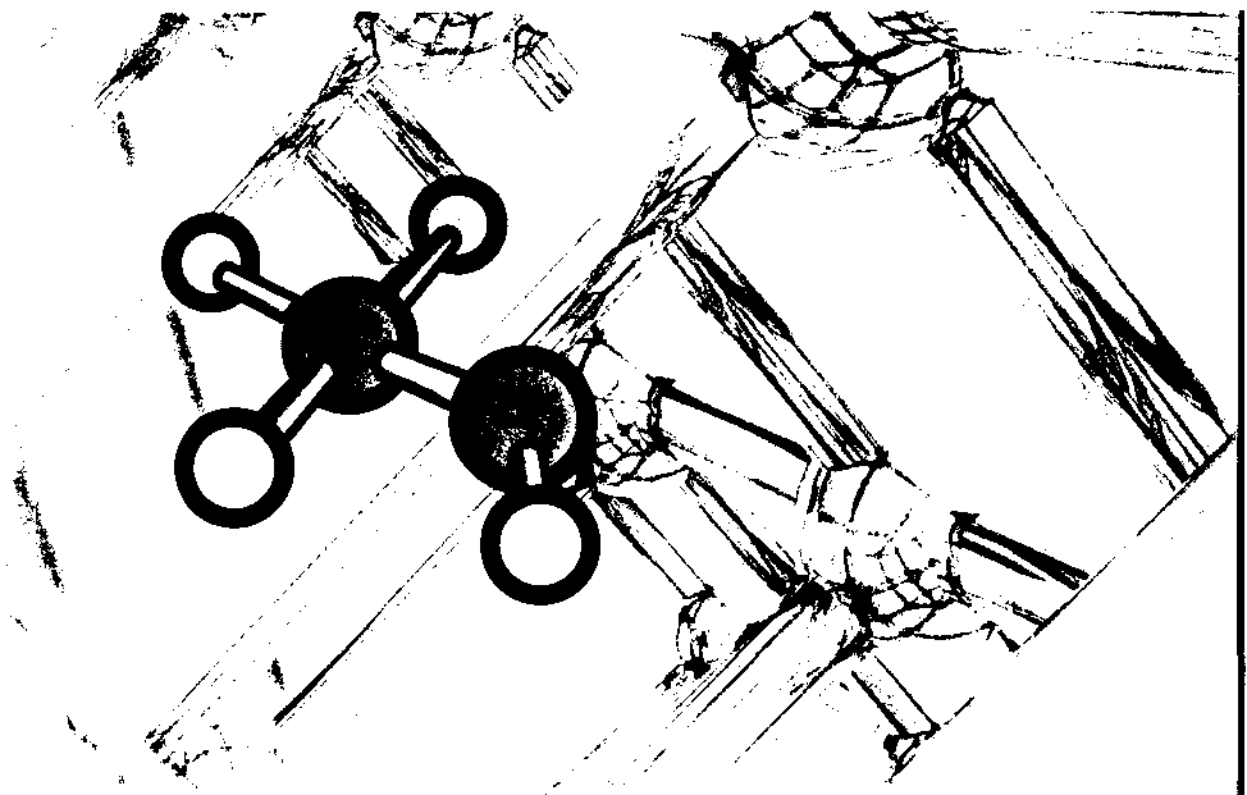

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NEW HETEROGENEOUS CHIRAL VANADIUM(V) *SALEN* CATALYSTS FOR THE STRECKER REACTION

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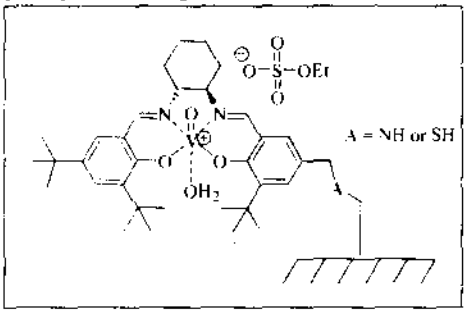
The addition of cyanide to imines (Strecker reaction) using a chiral catalyst constitutes one of the most direct and viable strategies for the asymmetric synthesis of chiral α-amino acids derivatives, which are important building blocks in a variety of biologically-interesting natural products. Homogeneous metal complexes with chiral ligands are currently the most widely used and versatile enantioselective catalysts. Metallic salen complexes, such as aluminium(III) and vanadium(V) salen, proved to be very efficient homogeneous catalysts for the Strecker reaction.[1,2] In spite of the good results achieved with these homogeneous catalysts (excellent enantioselectivities conjugated with high yields), if they were transformed into heterogeneous systems, environmental and experimental advantages would be obtained, since the separation of the catalyst would be done by simple filtration, avoiding the production of wastes and leading to economic benefits, due to their reuse.[3]



As a part of an ongoing project, herein, we present the preparation of five new heterogeneous catalysts resulting from the immobilization of vanadium(V) salen complexes to solids supports, namely a polystyrene polymer and an amorphous silica, using several anchoring strategies. The solid catalysts were characterized by analytical and spectroscopic techniques and tested in a Strecker type reaction, the asymmetric addition of hydrogen cyanide (generated *in situ* from TMSCN) to *N*-benzyl benzylimine.[2]

[1] J. F. Larrow, E. N. Jacobsen; *Topics Organomet. Chem.*, 6 (2004) 123.

[2] J. Blacker, L. A. Clutterbuck, M. R. Crampton, C. Grosjean, M. North; *Tetrahedron: Assymetry*, 17 (2006) 1449.

[3] C. Baleizão, H. Garcia; *Chem. Rev.*, 106 (2006) 3987.

NEW HYDROXYPYRIMIDINONE-SULFONAMIDES AS BI-TARGET LIGANDS FOR ENZYME INHIBITION

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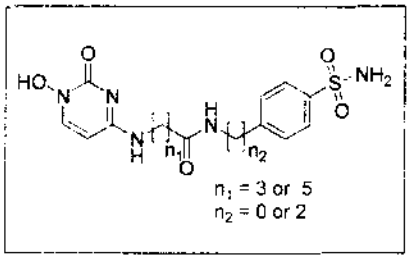
Hydroxypyrimidinones are endocyclic hydroxamic acids with high affinity for hard metal ions, with potential application either as metal decontaminants for environmental and biological purposes or as inhibitors of zinc-containing enzymes, such as matrix metalloproteinases (MMP), since the hydroxamate is one of the preferred metal-binding group for the MMP inhibitors (MMPi). On the other hand, arylsulfonamides are specific inhibitors of other zinc-containing enzymes, the carbonic anhydrases (CAs). Both types of enzymes have isoforms involved in carcinogenesis and tumor invasion processes and they are currently the target of drug design [1]. Having this in mind and trying to explore potential hybrid drugs aimed at combining CA and MMP inhibition roles, we have designed new inhibitors by attaching a sulfonamide moiety to a hydroxypirimidone [2]. Recently, we prepared a new hydroxypyrimidinone-sulfonamide, 4-[2-(4-sulfamoyl-phenyl)-ethylamino]1-hydroxy-2(*1H*)-pyrimidinone [3], which showed inhibitory activity in micromolar range against several MMPs. Following this preliminary work and aiming at further exploring the bi-targeting ability of these hybrid compounds, we have developed a new series of hydroxyprimidinone-sulfonamide compounds, having different spacers between these two functional groups. Herein, we present the synthesis and characterization of these new compounds as well as some preliminary results of bioassays to assess the inhibitory activity against several CAs. The results show that all these sulfonamide-containing compounds present good CA inhibitory capacity (IC50 in the nanomolar range) for the three isoforms (I, II and IX).



[1] C.M. Overall, O. Kleifeld, *Natural Rev. Cancer* (2006) 227.

[2] M.A. Esteves, A. Cachudo, C. Ribeiro, S. Chaves, A. Rossello, M.A. Santos, *Metal Ions in Biology and Medicine* 9 (2006) 35.

[3] S. Chaves, S.M. Marques, A. Cachudo, M.A. Esteves, M.A. Santos, *Eur. J. Inorg. Chem.* (2006) 3853.