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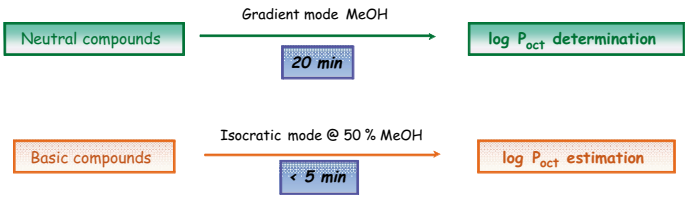
High-Throughput log *P* Determination by Ultraperformance Liquid Chromatography: A Convenient Tool for Medicinal Chemists

Y. Henchoz, D. Guillarme, S. Rudaz, J. L. Veuthey, and P. A. Carrupt*, *J. Med. Chem.* **2008**, *51*, 396
School of Pharmaceutical Sciences, University of Geneva and University of Lausanne

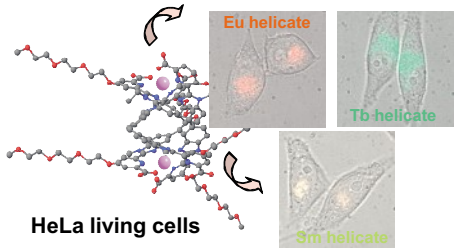
Precise knowledge of the physicochemical properties of new chemical entities is essential in early steps of drug design and discovery. Among these properties, lipophilicity is important to understand permeation mechanisms. In this article, a very fast strategy for log *P* measurements is presented, thanks to the recent advances in chromatographic sciences such as the launch of ultraperformance liquid chromatography (UPLC). Using this method, high-throughput log *P* measurements of therapeutic compounds in both isocratic and gradient modes were achieved. As UPLC columns are highly stable in basic pH conditions, this approach also allowed a direct lipophilicity estimation of basic compounds in their neutral form.



A Versatile Ditopic Ligand System for Sensitizing the Luminescence of Bimetallic Lanthanide Bio-Imaging Probes

A.-S. Chauvin*, S. Comby, B. Song, C. D. B. Vandevyver*, and J.-C. G. Bünzli*, *Chem. Eur. J.* **2008**, *14*, 1726
EPFL – SB – ISIC – LCSL

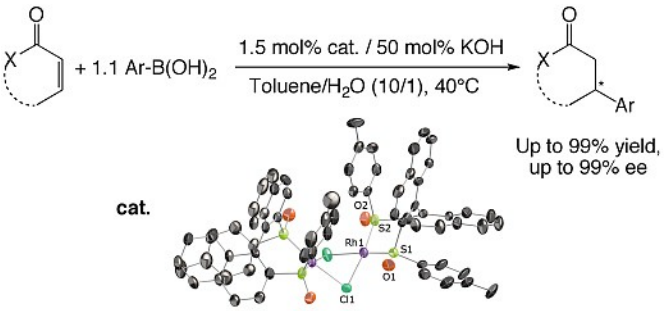
A novel homoditopic ligand, H_2L^{C2} has been tailored to self-assemble with lanthanide ions (Ln^{III}), forming neutral bimetallic helicates of $[Ln_2(L^{C2})_3]$ composition. The latter are water-soluble, pH resistant (down to pH 3), thermodynamically stable and kinetically inert *versus* both ligand exchange and trans-metallation. The ligand sensitizes the visible and/or NIR luminescence of a variety of Ln^{III} ions, *e.g.* Sm^{III} (Q = 0.38%), Eu^{III} (21%), Tb^{III} (11%), Yb^{III} (0.15%). The helicates permeate into the cytoplasm of HeLa cells by endocytosis and bright images of cancerous cell lines are obtained with small incubation concentrations. Finally, the polyoxyethylene substituents lend themselves to derivatization, opening the way to *in cellulo* targeting experiments.



A Chiral Bis-Sulfoxide Ligand in Late-Transition Metal Catalysis; Rhodium-Catalyzed Asymmetric Addition of Arylboronic Acids to Electron-Deficient Olefins

R. Mariz, X. Luan, M. Gatti, A. Linden, and R. Dorta*, *J. Am. Chem. Soc.* **2008**, *130*, 2172
Institute of Organic Chemistry, University of Zurich

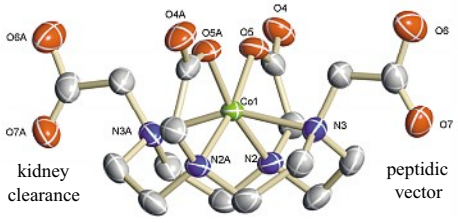
This paper describes the one-step preparation of a chiral bis-sulfoxide with a binaphthyl backbone. The compound can be used as an effective ligand in asymmetric late-transition metal catalysis. The ligand, named *p*-tol-BINASO, reacts readily with $[RhCl(C_2H_4)_2]_2$ and the resulting complex was isolated in high yield and structurally characterized by X-ray diffraction. The dimeric $[\{p\text{-tol-BINASO}\}RhCl]_2$ precatalyst shows both excellent reactivity and selectivity in the asymmetric 1,4-addition of arylboronic acids to cyclic α,β-unsaturated ketones and esters.



Metal-Ion-Dependent Biological Properties of a Chelator-Derived Somatostatin Analogue for Tumour Targeting

A. Heppeler, J.-P. André, I. Buschmann, X. Wang, J.-C. Reubi, M. Hennig, T.-A. Kaden, and H. R. Maecke*, *Chem. Eur. J.* **2008**, *14*, 3026
University Hospital of Basel, Universidade do Minho, University of Bern, F. Hoffman-La Roche Ltd, University of Basel

Somatostatin-based radioligands have been shown to have sensitive imaging properties for neuroendocrine tumours and their metastases. The potential of a novel derivative, named [^{55}Co(dotatoc)], as a radiopharmaceutical agent for PET was evaluated. ^{57}Co was used as a surrogate of the positron emitter ^{55}Co and the pharmacokinetics of [^{57}Co(dotatoc)] investigated by using two nude mouse models. Studies have revealed that this analogue presents the highest affinity ever found for the sst2 receptor subtype and a very high rate of internalization. The structural features of the (radio)metal complex determine its *in vivo* properties.



Prepared by Martina Austeri, Renaud Bach, Nathalie Mehanna, Roman Novikov, Ankit Sharma, Franck Torricelli, Jérôme Lacour
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