Metal Template Synthesis of Aromatic Preorganized Ligands for Tuning Stability Constants in Lanthanide Adducts

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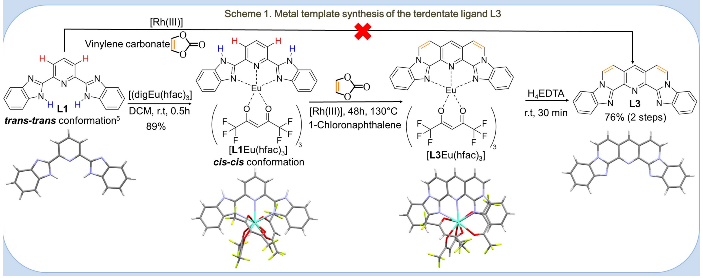
Among the multifactorial parameters affecting the stability and geometry of complexes for a given metal, the structural conformation of ligands displays a crucial influence.[1] A ligand preorganized in an orientation close to the conformation required to complex a metal ion tends to result in increased affinity for the entering guest thanks to the removal of the conformational change energy produced upon complexation.[2] With this in mind, ligand **L3** was synthesized from **L1** *via* a metal template strategy,[3] in which the *cis-cis* bound terdentate ligand in [**L1**Eu(hfac)3] undergoes intermolecular rhodium-catalyzed reactions aiming at intercalating a vinylene carbonate between the N-H groups of the benzimidazole side arms and the C-H units of the central pyridine ring.[4] Comparing the affinity of ligands **L1**, **L2** and **L3** with trivalent lanthanides in both solution (NMR studies) and solid state (X-ray analysis) allowed to determine the relationship of the level of structural preorganization with complexes stability constants.


Scheme 1. Metal template synthesis of the terdentate ligand L3

The *trans-trans* conformation in ligand **L1** leads to the failure of rhodium-catalyzed N-H/C-H activation reaction (red cross in Scheme 1) when **L1** is simply reacted with vinylene carbonate. In order to overcome this limitation, the complexation of **L1** to [(dig)Eu(hfac)3] have been considered for forcing the coordinated terdentate ligand **L1** to accommodate the unfavorable *cis-cis* orientation required for intermolecular rhodium-catalyzed reactions between vinylene carbonate and NH, CH of bound ligand **L1**. As expected, carrying out the rhodium-catalyzed annulation of [**L1**Eu(hfac)3] with vinylene carbonate, followed by demetallation with H4EDTA, finally generates the target ligand **L3** in 76% yield.

Increasing the level of preorganization in ligand scaffold along the **L1→L2→L3** series gives rise to (i) improved binding constants with trivalent lanthanides in CD2Cl2 solution due to the removal of the energy cost for rotating the benzimidazole side arms to reach the high-energy *cis-cis* organization required for metal complexation reaction, and (ii) significant decreased Ln-N affinity in solid state due to a limited match between the lanthanide size and the larger cavity of the rigid terdentate ligand with 5-membered chelate rings.

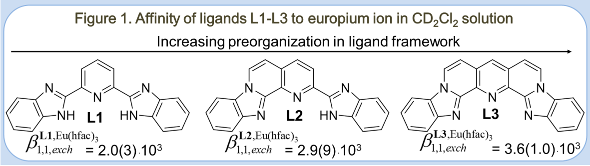


Figure 1. Affinity of ligands L1-L3 to europium ion in CD$_2$Cl$_2$ solution

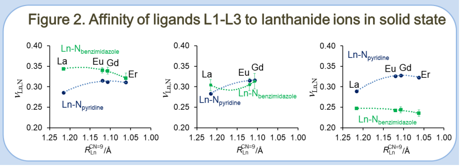


Figure 2. Affinity of ligands L1-L3 to lanthanide ions in solid state

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