Pyclen-based Ln(III) complexes as fluorescent bioprobes for two-photon microscopy

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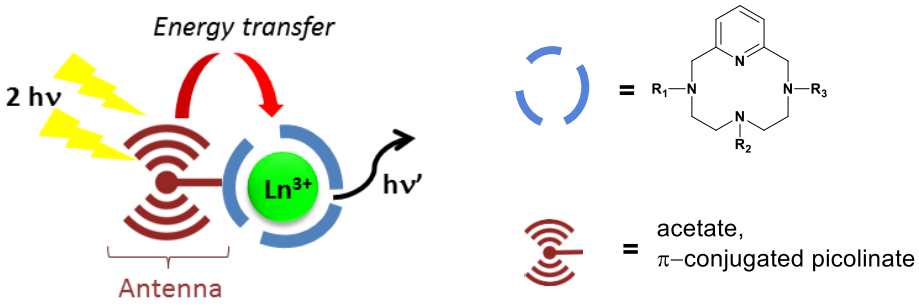
Two-photon (2P) microscopy using lanthanide(III) complexes is of wide interest in optical imaging because it combines the advantages of 2P excitation (NIR excitation in the biological transparency window, 3D resolution) with the sharp emission properties and long excited-state lifetimes of lanthanides.[1] However the conception of 2P-lanthanide luminescent bioprobes (2P-LLBs) combining good photophysical properties, long-term stability in biological media and the ability to be internalized by living cells is still challenging. Polyazamacrocycles such as tacn, cyclen and cyclam are widely studied platforms for metal complexation and their lanthanide(III) complexes have been successfully investigated as LLBs. In particular it is well established that the functionalization with π-conjugated antennae optimizes the 2P absorption cross section of such lanthanide complexes.[2] For example one of our cyclen-based Eu(III) complexes featuring appropriate antennae led to the rapid internalization in living cells and allowed 2P microscopy imaging.[3] Pyclen derivatives (3,6,9,15-tetraazabicyclo[9.3.1]pentadeca-1(15),11,13-triene) are also interesting ligands because they form stable and inert complexes thanks to the rigidity of the macrocycle brought by the pyridine unit.[4] We recently developed a new family of pyclen-based Ln(III) complexes bearing π-conjugated chromophores (Scheme 1). Our optimized strategies of synthesis allowed the regiospecific introduction of different antennae adapted to given lanthanides. The use of the pyclen platform considerably improved the photophysical properties of the complexes, in particular the quantum yields and the brightness. In addition 2P bio-imaging studies of fixed T24-cells stained with our complexes proved to be very promising.



Scheme 1: Pyclen-based Ln(III) complex bearing conjugated antenna optimized for two-photon microscopy.

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