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Complexes of Yb^{3+} embedded in poly(lactic-co-glycolic acid) (PLGA) nanoparticles as NIR-emitting bioprobes

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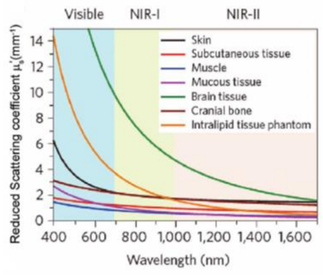
Overview

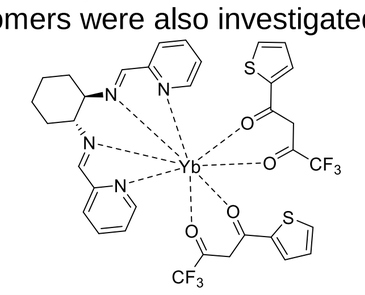
Whereas photosensitization of visible-emitting Eu(III)- and Tb(III)-based complexes is a well-established phenomenon with a large number of current applications,[1] analogous emission from Yb^{3+} and Nd^{3+} in the near-infrared remains relatively unexplored.

Although the luminescence lifetimes of these IR-emitting lanthanide systems are shorter than the Vis-emitting counterparts[2], this should still permit:

- time-gating techniques to be applied (higher signal-to-noise ratios)
- greater tissue penetration
- image resolution in the fluorescence microscopy of biological systems[3].

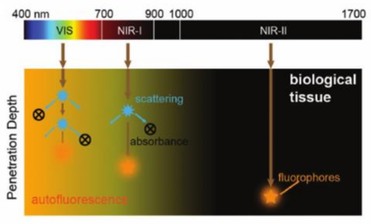
In this regard, we synthesized and investigated the spectroscopic properties of the following complexes [here depicted in the (R,R) stereochemistry; the (S,S) enantiomers were also investigated]

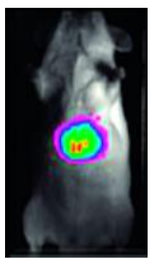




Subsequently, these complexes were embedded in Poly(lactic-co-glycolic acid), leading to nanoparticles characterized by a monodispersed distribution.

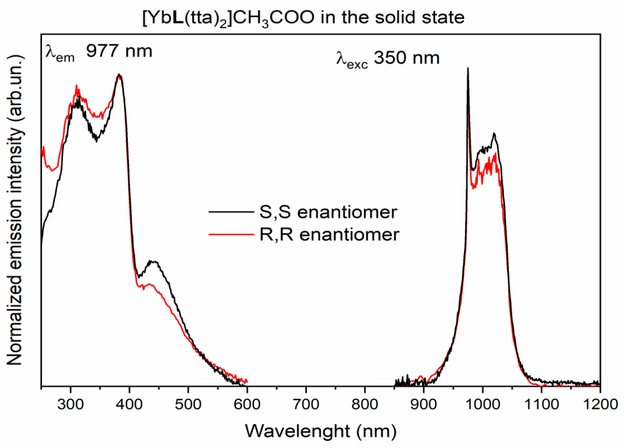
The results of this study and some preliminary evidence reveal that these new complexes are promising candidates for bio-imaging applications.





Spectroscopic results

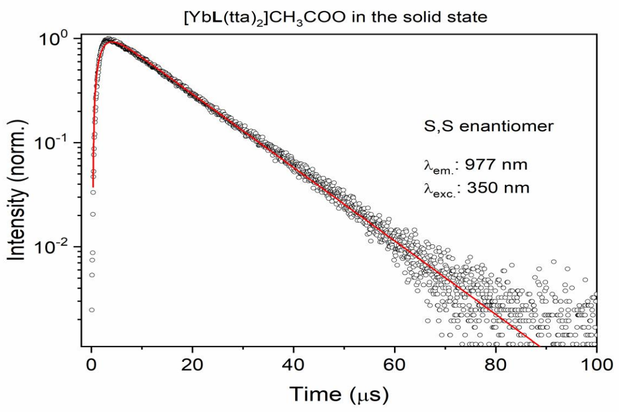
Solid state



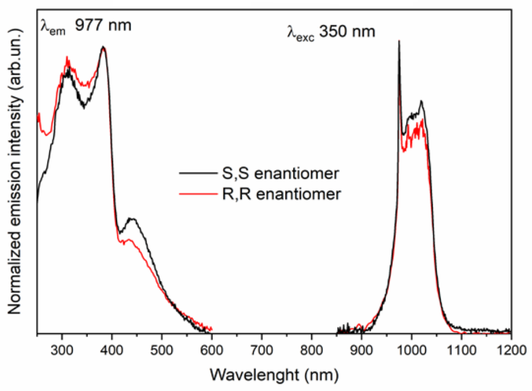
Excitation spectum (left) and emission spectrum (right) of both enantiomers of [YbL $(tta)_2]\cdot CH_3COO$ complex.

Decay curve of the $^2F_{5/2}$ excited state of Yb(III) for $[YbL(tta)_2]\cdot CH_3COO$ (S,S) complex. The decay curve of the R,R enantiomer (not shown) is fully superimposable.

Rise time = 1.49 μs; decay = 12.31 μs



0.44 mM dichloromethane solution



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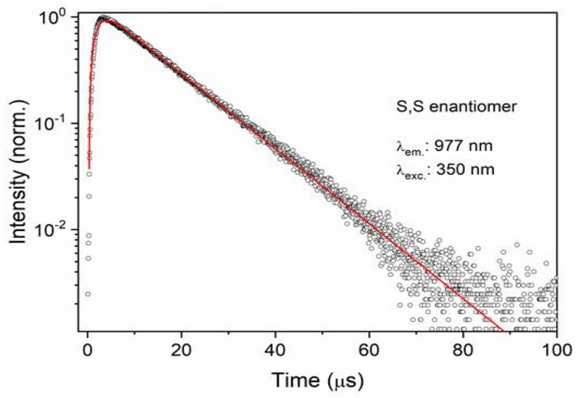
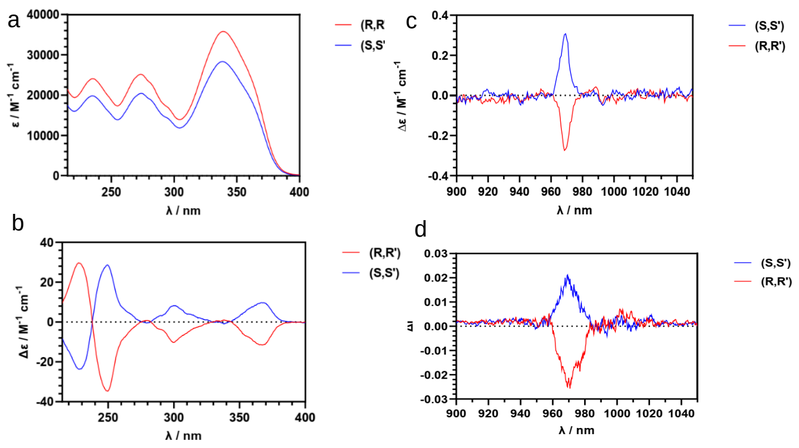
Rise time = 1.45 μs; decay = 15.06 μs.



NIR optical and chiroptical properties



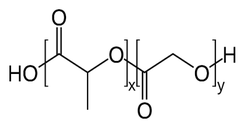
UV absorption (a), ECD (b) NIR-CD (c) NIR-CPL (d) spectra of both the enantiomers of $[YbL(tta)_2]\cdot CH_3COO$ complex in dichloromethane.

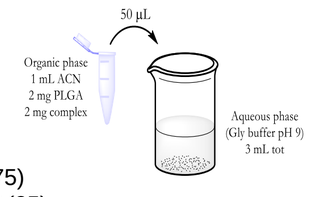
Bands attribution:

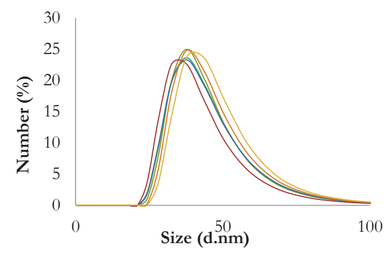
- **250 nm**: pyridine rings
- **270 nm**: conjugated C=N group
- **340 nm**: diketonate-centered singlet-singlet π-π* enolic transition.

Complexes embedded in PLGA nanoparticles

The $[YbL(tta)_2]\cdot CH_3COO$ complex embedded in Poly(lactic-co-glycolic acid) (PLGA) polymer was prepared by modified ultra small method at 20°C.[4]

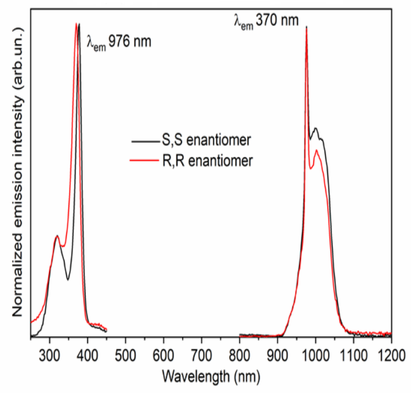






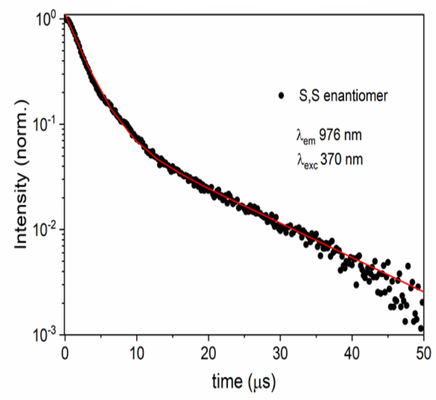
x = number of units of lactic acid (75)
y = number of units of glycolic acid (25)

- Dynamic Light Scattering measurements point out a hydrodynamic diameter of around 40-45 nm for both the enantiomers
- The value of the zeta-potential falls in the -20/-25 mV range.



Excitation spectra (left) and emission spectra (right) in aqueous solution of both enantiomers of $[YbL(tta)_2]\cdot CH_3COO$ complex embedded in PLGA nanoparticles.

Decay curve in aqueous solution of the $^2F_{5/2}$ excited state of Yb(III) in $[YbL(tta)_2]\cdot CH_3COO$ complex embedded in PLGA nanoparticles (λ_{exc}=362 nm-TTA).
[t_1 = 2.44 μs; t_2 = 13.3 μs]



Conclusions & Outlooks

The polymer that makes up the nanoparticles can ensure water solubility to the complexes and, at the same time, protect it from ligand hydrolysis/water coordination. For this reason, the value of the decay time of the excited state of Yb (III) is comparable to that observed for the same Yb (III) complexes dissolved in an organic solvent. Taken together, the **stability** and the good **water solubility** of the encapsulated complexes along with their **efficient antenna effect** candidate the $[YbL_2(tta)_2]\cdot CH_3COO$ complex as a potential NIR optical probe for *in vitro* bioimaging applications. Biological studies are ongoing to evaluate cytotoxicity against human cancer cell lines.

References

[1] Zhou, X.; Wang, H.; Jiang, S.; Xiang, G.; Tang, X.; Luo X.; Li, L.; Zhou, X.; Inorg. Chem. 2019, 58, 6, 3780–3788.
[2] Wang, L.; Zhao, Z.; Wei, C.; Wei, H.; Liu, Z.; Bian, Z.; Huang, C.; Ad. Opt. Mat. 2021, 7, 11, 1801256 .
[3] Cho, U.; Riordan, D.P.; Ciepla, P.; Kocherlakota, P.C.; Chen, J.K.; Harbury, P.B.; Nat Chem Biol. 2018; 14, 1, 15–21.
[4] Reisch, A.; Runser, A.; Arntz, Y.; Mely, Y.; Klymchenko, A.S.; ACS Nano 2015; 9, 5, 5104–5116.

Acknowledgments

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