Synthesis of bright water-soluble circularly polarized luminescence emitters as potential sensors

Journal:	*Inorganic Chemistry Frontiers*
Manuscript ID	QI-RES-11-2021-001398.R1
Article Type:	Research Article
Date Submitted by the Author:	31-Dec-2021
Complete List of Authors:	Adewuyi, Joseph; University of Connecticut, Chemistry Schley, Nathan; Vanderbilt University, Chemistry Ung, Gaël; University of Connecticut, Chemistry; University of Connecticut,

ARTICLE

Synthesis of bright water-soluble circularly polarized luminescence emitters as potential sensors

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

Joseph A. Adewuyi,[a] Nathan D. Schley[b] and Gaël Ung*[a]

We describe the synthesis of C_2-symmetrical enantiopure lanthanide complexes (Tb, Eu, Sm, Dy) supported by the decadentate ligand *N*,*N*,*N*′,*N*′-tetrakis[(6-carboxypyridin-2-yl)methyl]-1,2-diaminocyclohexane (tpadac). The chiral tpadac ligand was designed to protect the lanthanide center from coordination of inner-sphere water molecules resulting in air- and water-stable, and highly luminescent complexes in water. The complexes exhibit strong chiroptical properties, with high dissymmetry factors g_{lum} (0.11 to 0.25) and CPL brightness B_{CPL} (up to 245 M^{-1} cm^{-1} for Tb, λ_{exc} 295 nm, λ_{em} 544 nm) in water. These are the first example of aqueous Sm CPL and second example of aqueous Dy CPL reported to date. The lanthanide complexes obtained gave a reversible CPL response to pH ranging from 6.0 to 8.0. In addition, distinctive CPL responses (including a change in CPL sign) towards toxic cations (Pb^{2+}, Cd^{2+}, and Mn^{2+}) were also observed, demonstrating the potential of our complexes to be used as aqueous probes.

Introduction

Circularly polarized luminescence (CPL) spectroscopy is one of the rare techniques responsive to chiral excited state perturbations. Molecules emitting CPL have therefore the potential to become powerful biological probes.[1] CPL spectroscopy is the emission analogue of circular dichroism, and measures the difference between left- and right-handed circularly polarized emissions. CPL can be quantified by two metrics: the dissymmetry factor g_{lum} ($g_{\mathrm{lum}} = 2(I_L - I_R)/(I_L + I_R)$; I_L and I_R being the intensity of left- and right- circularly polarized light, respectively) and CPL brightness B_{CPL} ($B_{\mathrm{CPL}} = \varepsilon \times \Phi \times |g_{\mathrm{lum}}|/2$; ε being molar absorptivity, and Φ the quantum yield of the molecule).[2] The ideal CPL-active biological probe should have the highest g_{lum} and B_{CPL} values possible, and should be soluble and stable in aqueous solution. At the molecular level, lanthanide complexes have been the most successful in obtaining high dissymmetry factors ($0.05 < g_{\mathrm{lum}} < 1$) thanks to their luminescence resulting from $f-f$ transitions.[3] However, a key challenge of lanthanide luminescence in aqueous solution is to overcome luminescence quenching from O−H vibrational overtones from water present in the primary or secondary coordination sphere of the complexes.[4]

To date, the most successful water-stable CPL-emitting lanthanide molecular complexes are derived from polyazacycloalkanes such as 1,4,7-triazacyclononane (TACN) or 1,4,7,10-tetraazacyclododecane (cyclen) coordinated to Eu and/or Tb. Because of the propeller arrangements of the ligands' "arms" (Δ/Λ chirality) and ring inversion of the macrocycle (δ/λ chirality), separation of enantiomerically pure material can be challenging. Several elegant strategies involving either enantiopure ligand "arms",[5] or enantiopure macrocyles[6] have led to impressive results. For example, using europium (λ_{em} = 590 nm), water-soluble complexes supported by triazacyclononane-derived ligands reached g_{lum} of 0.1 to 0.3 and B_{CPL} around 1,000 - 2,000 M^{-1} cm^{-1} (λ_{exc} 340 nm).[5c] Using similar ligands on terbium (λ_{em} = 539 nm), strong metrics were also obtained (g_{lum} up to 0.11, B_{CPL} up to 199 M^{-1} cm^{-1} (λ_{exc} 280 nm).[5b] Despite their strong chiroptical properties, the syntheses of the ligands still require a large number of steps (> 5) however. Other successful terbium-based water-stable CPL-emitting lanthanide molecular complexes utilize enantiopure hexaamines (g_{lum} up to 0.40)[7b], or enantiopure 1,2-diamines (g_{lum} up to 0.20[7c], B_{CPL} up to 314 M^{-1} cm^{-1} (λ_{exc} 340 nm)[7a]), but these systems either require lengthy syntheses[7] or generate mixtures of isomers.[8] The simplification of synthetic methodologies while retaining similar chiroptical properties would therefore be highly desirable.

Herein, we describe the convenient synthesis (3-steps) of enantiopure water-stable lanthanide molecular complexes exhibiting strong chiroptical properties (g_{lum} up to 0.20, B_{CPL} up to 245 M^{-1} cm^{-1} (λ_{exc} 295 nm, λ_{em} 544 nm) for Tb and is amongst the brightest water-soluble Tb complexes reported. Complexes of samarium, europium, and dysprosium with strong chiroptical properties were also synthesized. Furthermore, we show proof-of-principle that these complexes can be utilized as probes responsive to pH and select metal cations in aqueous media.

---

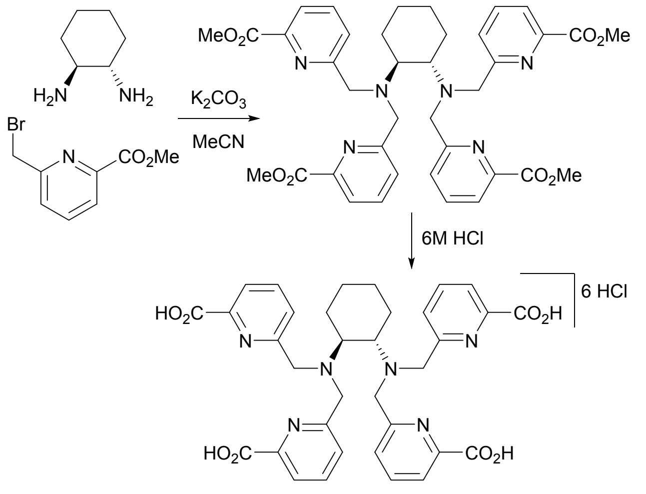
[a] *Department of Chemistry, University of Connecticut, Storrs, Connecticut 06269, United States.*
[b] *Department of Chemistry, Vanderbilt University, Nashville, Tennessee 37235, United States.*

Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

Results and Discussion

Synthesis and Characterization

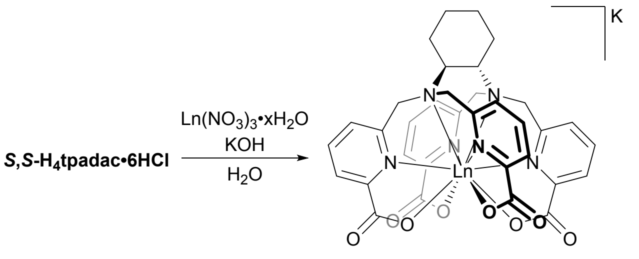
To preclude water coordination to the lanthanide ion, we chose to maximize the coordination number at the metal and designed a decadentate ligand. An achiral ligand derived from ethylene diamine and bearing four methylpicolinate arms was previously synthesized, and the corresponding terbium and europium complexes exhibited strong luminescence in aqueous solution.[9] We chose to introduce chirality through the readily available enantiopure *trans*-1,2-diaminocyclohexane.[10] Tetrasubstitution of (*S*,*S*)-1,2-diaminocyclohexane with 6-(bromomethyl)methylpicolinate afforded the protected ligand, and hydrolysis of the esters under acidic conditions provided the desired (*S*,*S*)-*N*,*N*,*N*′,*N*′-tetrakis[(6-carboxypyridin-2-yl)methyl]-1,2-diaminocyclohexane ligand (*S*,*S*)-H_4tpadac as its hexahydrochloride salt (Fig 1). The compound was obtained as a light brown solid in good overall yield (45% from 1,2-diaminocyclohexane). The synthesis was done analogously for the enantiomer (*R*,*R*)-H_4tpadac and both could be scaled to at least 2.0 g.



S,S-H_4tpadac•6HCl

Figure 1. Synthesis of (*S*,*S*)-*N*,*N*,*N*′,*N*′-tetrakis[(6-carboxypyridin-2-yl)methyl]-1,2-diaminocyclohexane (*S*,*S*-H_4tpadac).

Coordination to the lanthanide ions was performed in basic water using the aqueous lanthanide nitrate salts (Fig 2). After work-up, the complexes were further purified by recrystallisation from water. The complexes were obtained in good yields (60 to 70%) as off-white solids. ^{1}H NMR spectra of the diamagnetic La and the weakly paramagnetic Sm complexes recorded in D_2O showed fifteen resonances with two independent sets of methylpicolinate arms consistent with coordination of the diaminocyclohexane nitrogen atoms, and with a C_2-symmetrical species (Figs S1-S4). Analogously, in the more paramagnetic species (Ln = Eu, Tb, Dy), no more than fifteen broad resonances were observed (Figs S5-S10).



[(S,S-tpadac)Ln][K]

Figure 2. Coordination of *S*,*S*-H_4tpadac to lanthanides. Ln = La, Sm, Eu, Tb, Dy.

Single crystals of [(*S*,*S*-tpadac)Eu][K] were grown by slow evaporation of a saturated aqueous solution.‡ The compound crystallized in the non-centrosymmetric C_2 space group. X-ray diffraction analysis showed the expected coordination number of ten (Fig 3, left), arranged in a distorted sphenocorona (Fig 3, right), with the potassium cation coordinated to the carboxylates. Consistent with our design, no inner-sphere water molecules were found in the solid state. Water could only be found in the secondary coordination sphere, solvating the potassium cation. The complex lies over a crystallographic C_2-axis consistent with what is observed in solution.

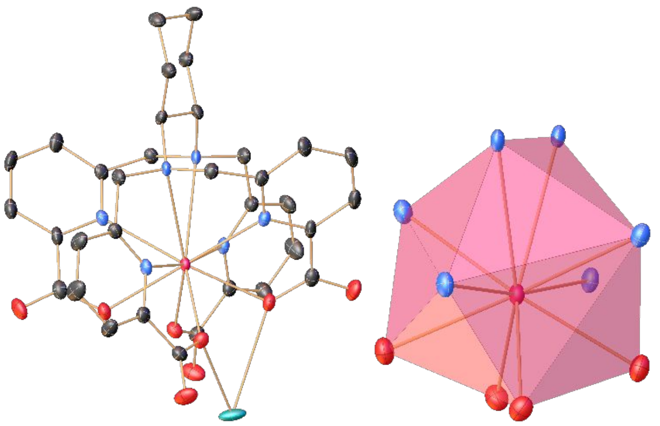


Figure 3. Structure of [(*S*,*S*-tpadac)Eu][K] (left) and coordination polyhedron (right) in the solid state. Thermal ellipsoids are drawn at 50% probability. Hydrogen atoms and co-crystallized water molecules are omitted for clarity. Black: C; Blue: N; Red: O; Teal: K; Pink: Eu.

Luminescence and Circularly Polarized Luminescence

Upon excitation at 290 nm, solutions of $[(R,R\text{-tpadac})Ln]^-_{(aq)}[K]^+_{(aq)}$ and $[(S,S\text{-tpadac})Ln]^-_{(aq)}[K]^+_{(aq)}$ (written as solubilized ion pairs) (Ln = Sm, Eu, Tb, Dy) in 0.1 M tris buffer (pH = 7.4) exhibited the expected sharp luminescent features characteristic of each lanthanide (Figs S11-S14). Lifetime measurements (See SI) confirmed the absence of coordinated water molecules in solution (n = 0.11 for Tb, 0.02 for Eu). As a result, moderate to high quantum yields (Sm: 0.2%, Eu: 6.5%, Tb: 47%, Dy: 1.4%) were obtained. These quantum yields are comparable to the achiral analogue (45% for Tb and 7.0% for Eu),[9] and are on the high end of other achiral or chiral emitters.[2a,3]

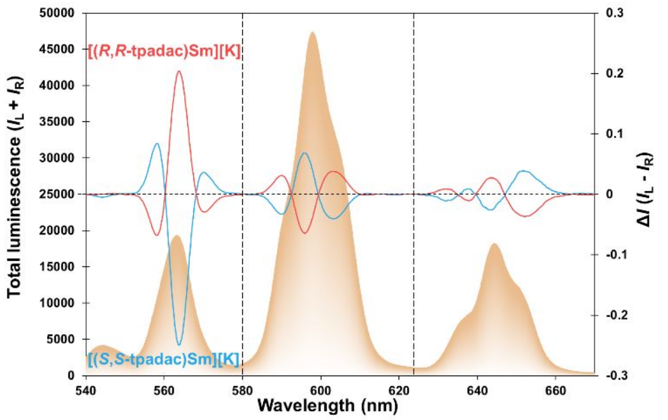


Figure 4. CPL spectra of $[(R,R\text{-tpadac})Sm]^-_{(aq)}[K]^+_{(aq)}$ (red) and $[(S,S\text{-tpadac})Sm]^-_{(aq)}[K]^+_{(aq)}$ (blue) in 0.1 M tris buffer solutions adjusted to pH = 7.4 (5.96 x 10^{-4} mol L^{-1}) at room temperature. Average of 48 scans, 9 minutes per scan. The intensity of each transition (between vertical dashes) has been normalized to reflect their relative g_{lum} values (See Figure S21 for g_{lum} plot). Total luminescence is traced in the background. Excitation at 295 nm. Bandpass: 5 nm.

Circularly polarized luminescence spectra of the $[(R,R\text{-tpadac})Sm]^-_{(aq)}[K]^+_{(aq)}$ and $[(S,S\text{-tpadac})Sm]^-_{(aq)}[K]^+_{(aq)}$ (Fig 4) showed a maximum dissymmetry factor for the $^4G_{5/2} \rightarrow {}^6H_{5/2}$ transition (g_{lum} = 0.25) consistent with its transition type.[11] The maximum B_{CPL} was observed for the $^4G_{5/2} \rightarrow {}^6H_{7/2}$ transition at 0.60 M^{-1} cm^{-1} (λ_{exc} 295 nm, λ_{em} 589 nm). These values are comparable to other lanthanide complexes in any solvent,[2,3,12] but are the first reported examples of samarium complexes emitting CPL in water.

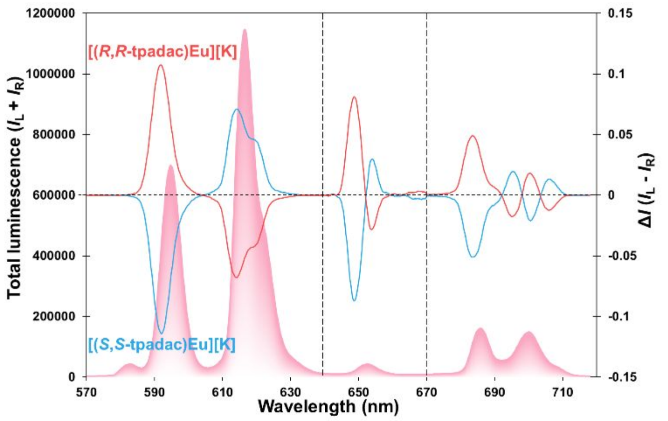


Figure 5. CPL spectra of $[(R,R\text{-tpadac})Eu]^-_{(aq)}[K]^+_{(aq)}$ (red) and $[(S,S\text{-tpadac})Eu]^-_{(aq)}[K]^+_{(aq)}$ (blue) in 0.1 M tris buffer solutions adjusted to pH = 7.4 (6.54 x 10^{-4} mol L^{-1}) at room temperature. Average of 87 scans, 10 minutes per scan. The intensity of each transition (between vertical dashes) has been normalized to reflect their relative g_{lum} values (See Figure S20 for g_{lum} plot). Total luminescence is traced in the background. Excitation at 295 nm. Bandpass: 5 nm.

Both $[(R,R\text{-tpadac})Eu]^-_{(aq)}[K]^+_{(aq)}$ and $[(S,S\text{-tpadac})Eu]^-_{(aq)}[K]^+_{(aq)}$ emitted CPL, though, as is observed for other C_2-symmetrical europium CPL emitters,[8,12b,12c] relatively low dissymmetry factors ($g_{lum} \leq 0.11$) and brightnesses ($B_{CPL} \leq 12.5$ M^{-1} cm^{-1}, λ_{exc} 295 nm, λ_{em} 589 nm, 620 nm) were observed (Fig 5).

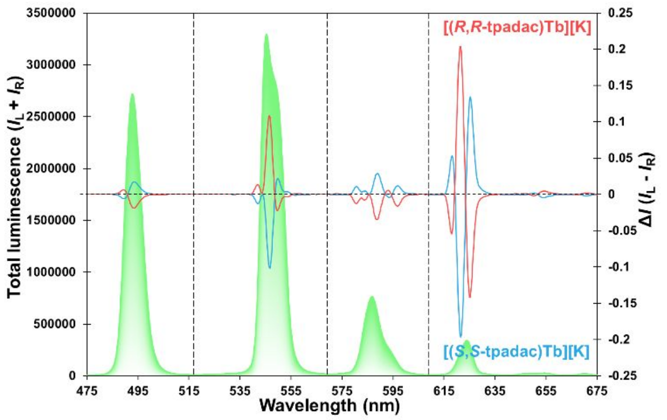


Figure 6. CPL spectra of $[(R,R\text{-tpadac})Tb]^-_{(aq)}[K]^+_{(aq)}$ (red) and $[(S,S\text{-tpadac})Tb]^-_{(aq)}[K]^+_{(aq)}$ (blue) in 0.1 M tris buffer solutions adjusted to pH = 7.4 (6.13 x 10^{-4} mol L^{-1}) at room temperature. Average of 60 scans, 12 minutes per scan. The intensity of each transition (between vertical dashes) has been normalized to reflect their relative g_{lum} values (See Figure S19 for g_{lum} plot). Total luminescence is traced in the background. Excitation at 295 nm. Bandpass: 2.4 nm.

The $[(R,R\text{-tpadac})Tb]^-_{(aq)}[K]^+_{(aq)}$ and $[(S,S\text{-tpadac})Tb]^-_{(aq)}[K]^+_{(aq)}$ showed moderate dissymmetry factors ($|g_{lum}| \leq 0.20$) (Fig 6), but are amongst the brighter Tb CPL emitters in water to date (B_{CPL} = 245 M^{-1} cm^{-1} (λ_{exc} 295 nm, λ_{em} 544 nm) for the $^5D_4 \rightarrow {}^7F_5$ transition), owing to their strong quantum yields.

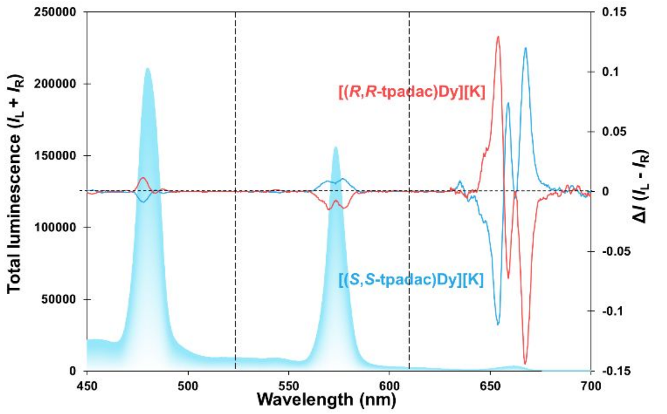


Figure 7. CPL spectra of $[(R,R\text{-tpadac})Dy]^-_{(aq)}[K]^+_{(aq)}$ (red) and $[(S,S\text{-tpadac})Dy]^-_{(aq)}[K]^+_{(aq)}$ (blue) in 0.1 M tris buffer solutions adjusted to pH = 7.4 (6.13 x 10^{-4} mol L^{-1}) at room temperature. Average of 31 scans, 20 minutes per scan. The intensity of each transition (between vertical dashes) has been normalized to reflect their relative g_{lum} values (See Figure S22 for g_{lum} plot). Total luminescence is traced in the background. Excitation at 295 nm. Bandpass: 5 nm.

The dysprosium complexes $[(R,R\text{-tpadac})Dy]^-_{(aq)}[K]^+_{(aq)}$ and $[(S,S\text{-tpadac})Dy]^-_{(aq)}[K]^+_{(aq)}$ also exhibited CPL with a maximum dissymmetry factor ($|g_{lum}|$ = 0.14) and brightness (B_{CPL} = 0.68 M^{-1} cm^{-1}, λ_{exc} 295 nm, λ_{em} 668 nm) for the magnetic-dipole allowed $^4F_{9/2} \rightarrow {}^6H_{11/2}$ transition (Fig 7). The dissymmetry factor is comparatively lower than the only other reported aqueous CPL emitter to date, a C_4-symmetrical DOTA-derived complex with $|g_{lum}|$ = 0.41,[5a] but is on par with other non-aqueous C_2-symmetrical dysprosium emitters.[12]

Utility as sensors

Because of the ability in CPL spectroscopy to observe potential changes of sign within luminescent transitions, individual Stark levels can be resolved more accurately. This advantageous feature can be exploited to obtain more sensitive sensors than when using standard non-polarized fluorescence spectroscopy. We were therefore interested in exploring the chiroptical behaviour of our complexes towards various stimuli. We focused our studies on the brighter [(*S*,*S*-tpadac)Tb][K] and [(*S*,*S*-tpadac)Eu][K] complexes, and selected the transitions that combined high luminescence intensity and high dissymmetry factors: $^5D_4 \rightarrow {}^7F_5$ (Tb), $^5D_4 \rightarrow {}^7F_3$ (Tb), $^5D_0 \rightarrow {}^7F_1$ (Eu), and $^5D_0 \rightarrow {}^7F_2$ (Eu).

We first examined the response of our complexes to changes in pH and opted for a range of pH (6.0 to 8.0) that could be relevant to biological applications (physiological pH = 7.4) or potential diagnosis (tumour cells pH = 6.4-7.0). Titration of a solution of $[(S,S\text{-tpadac})\text{Tb}]^-_{(aq)}[\text{K}]^+_{(aq)}$ in tris buffer adjusted by incremental addition of 1 M HCl yielded a response in both CPL and dissymmetry factors (Fig 8). These decreases could be attributed to partial protonation of the ligand, resulting in a loss of the C_2-symmetry. There was also a decrease in total emission intensity (Figure S25) as the pH was gradually reduced from 8.0 to 6.0. We attribute this to partial protonation of the carboxylate oxygens at low pH, leading to the formation of less emissive species due to either quenching through O–H vibrations, or distortion of the ligand arrangement around the metal centre. From the changes in emission intensity, the *p*Ka value was calculated to be 6.99 (Figure S28b).

An observation of the lifetime of the complex during the pH titration with careful consideration to excite the Tb metal directly at 488 nm revealed a gradual increase in lifetime from 2.38 ms at pH 8.0 to a peak value of 2.67 ms at pH 7.4 and then a steady decrease to 1.79 ms as the pH approached 6.0. This observation is consonant with the g_{lum} changes at 544 nm (Fig 8 insert) where there is also an initial increase in g_{lum} up to maximum value of −0.11 at pH 7.4 from which the value then declines to −0.08 at pH 6.0.

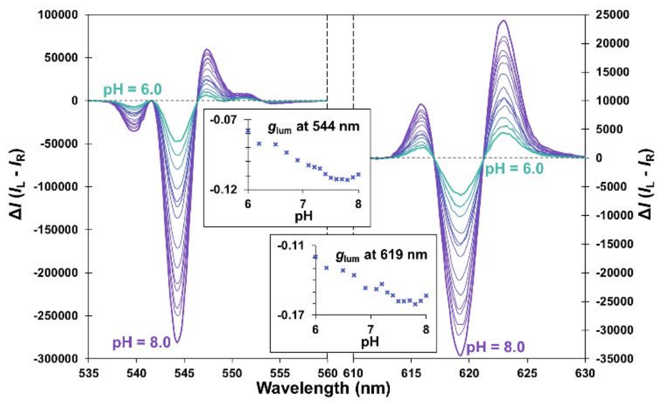


Figure 8. CPL response of $[(S,S\text{-tpadac})\text{Tb}]^-_{(aq)}[\text{K}]^+_{(aq)}$ to pH ranging from 8.0 to 6.0. Inserts show dissymmetry factors changes at 544 and 619 nm. Excitation at 295 nm. Bandpass: 2.4 nm.

To determine if our system can be described as "sensors" or "activity-based probes",[13] we tested the reversibility of our system. When the pH was reversed back to 8.0, the initial g_{lum} value was recovered (Figure S28 inset). The Δ*I* plot is not fully reversible as expected from the increased dilution from the titration. This highlights the significance of observing both g_{lum} and Δ*I* when utilizing CPL. We also tested the detection limit, and report that the complex is sensitive to these pH changes at a minimum concentration limit of 5 µM (Figure S28).

Analogous titration of $[(S,S\text{-tpadac})\text{Eu}]^-_{(aq)}[\text{K}]^+_{(aq)}$ yielded a similar response (Fig S26 and S27). Luminescence quenching was more pronounced in the europium case compared to terbium, consistent with the sensitivity of europium luminescence to the increased presence of O–H vibrational overtones at low pH. This is detrimental to the sensing ability of the europium complex, as CPL detection is less reliable at low luminescence intensity. We thus decided to do our follow-up studies with the terbium complex.

Following these promising results, we were interested in examining the response of our sensors to other stimuli. Due to the anionic charge of our complexes, we examined their responses towards cations. We selected Pb^{2+}, Cd^{2+}, and Mn^{2+} as proof-of-principle due to their notorious detrimental effects to aquatic environments, and human health.[14]

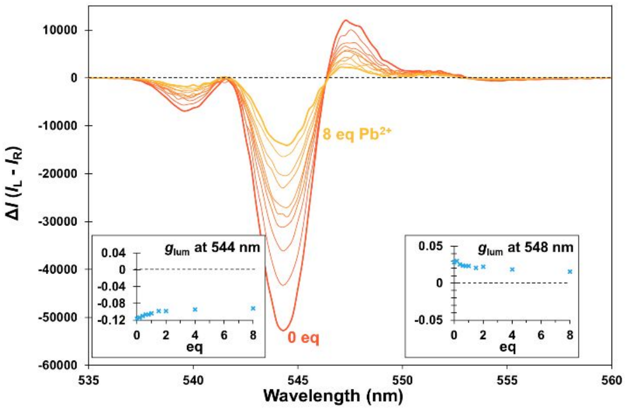


Figure 9. CPL response of $[(S,S\text{-tpadac})\text{Tb}]^-_{(aq)}[\text{K}]^+_{(aq)}$ (6.13×10^{-5} mol L^{-1}) to increasing addition of Pb^{2+} (6.13×10^{-3} mol L^{-1}). Inserts show dissymmetry factor changes at 544 and 548 nm. Excitation at 295 nm. Bandpass: 2.4 nm.

Titration of up to 8 equivalents of $Pb(OAc)_2$ in a solution of $[(S,S\text{-tpadac})\text{Tb}]^-_{(aq)}[\text{K}]^+_{(aq)}$ in tris buffer generated a response in both CPL and dissymmetry factors (Fig 9). The Δ*I* maxima for the $^5D_4 \rightarrow {}^7F_5$ transition between 535 and 560 nm decreased with addition of Pb^{2+}, concomitant with a slight decrease in $|g_{\text{lum}}|$ at 544 and 548 nm. These changes are reversible, as the initial g_{lum} values were recovered upon addition of 16 equivalents of dipotassium EDTA as a chelator for Pb (Figure S35).

A similar response was observed for the same transition when titrating up to 8 equivalents of $Cd(OAc)_2$ (Fig 10). The decrease of both Δ*I* and $|g_{\text{lum}}|$ was noticeably smaller for Cd^{2+} when compared to Pb^{2+}, suggesting that specific speciation quantification could be developed with this technology in the future. Cadmium sensing was also reversible, as addition of 8 equivalents of dipotassium EDTA were enough to reverse the response. (Figure S36).

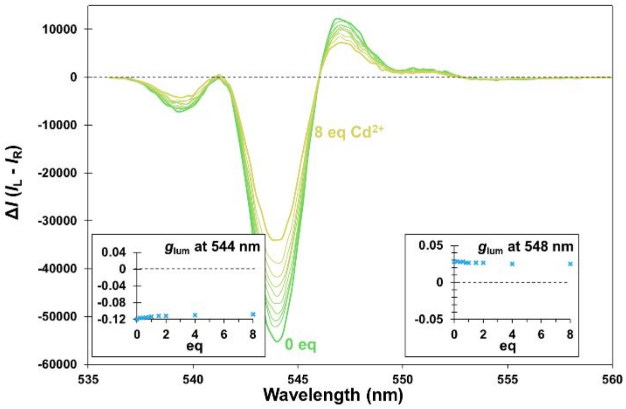


Figure 10. CPL response of [(*S*,*S*-tpadac)Tb]$^{-}_{(aq)}$[K]$^{+}_{(aq)}$ (6.13 x 10^{-5} mol L^{-1}) to increasing addition of Cd^{2+} (6.13 x 10^{-3} mol L^{-1}). Inserts show dissymmetry factor changes at 544 and 548 nm. Excitation at 295 nm. Bandpass: 2.4 nm.

Titration of up to 8 equivalents of $MnBr_2$ yielded a more striking difference (Fig 11). A drastic decrease of CPL was observed after addition of 0.4 equivalent, and more importantly, a sign inversion was observed at 548 nm (Fig 11 right insert). A sign inversion was also observed at 544 nm (Fig 11 left insert), but only after addition of more than 2 equivalents. A CPL sign inversion from an emissive transition should be due to a significant change of direction in either magnetic or electric dipole transition moment vectors.[15] This suggests that the interaction between [(*S*,*S*-tpadac)Tb]$^{-}_{(aq)}$[K]$^{+}_{(aq)}$ and the manganese ion is covalent enough to either flip the electric dipole transition moment (by adding two positive charges) or flip the magnetic dipole transition moment (by incorporating a highly paramagnetic ion). In contrast, the interaction between [(*S*,*S*-tpadac)Tb]$^{-}_{(aq)}$[K]$^{+}_{(aq)}$ and lead or cadmium ions are more ionic, thus do not drastically change the CPL response. We note that the pH of the solutions remained unchanged before and after the metal titrations. Additionally, the tris buffer does not interfere with the metal ions at the titration's metal concentration.[16] The emission quenching upon addition of manganese was postulated to be due to energy transfer from Tb excited state to manganese. This was confirmed by lifetime measurements as the lifetime of the complex decreased from 2.67 ms to 0.061 ms after addition of 8 equivalents of manganese. Since the response to Mn^{2+} was so striking with Tb, we chose to examine how the analogous europium complex would behave and performed a titration of [(*S*,*S*-tpadac)Eu]$^{-}_{(aq)}$[K]$^{+}_{(aq)}$ against Mn^{2+}, and, even with diminished luminescence and resolution, a similarly diagnostic CPL sign inversion at 597 nm was observed (Fig S32).

It is important to note that the Mn response, both in terms of quenching and CPL fingerprint, is reversible after addition of 16 equivalents of dipotassium EDTA chelator (Figure S34). Due to the quenching of Tb luminescence by Mn, the sensing concentration limit for the complex against Mn is 60 µM whereas for Pb, Cd and pH, the complex is effective for sensing at concentrations of 5 µM (Figures S28, S34-S36).

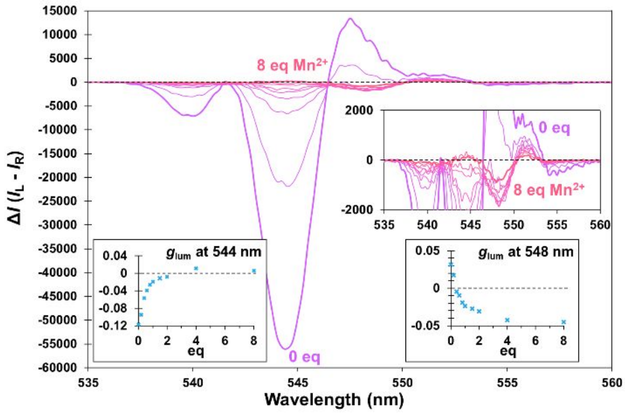


Figure 11. CPL response of [(*S*,*S*-tpadac)Tb]$^{-}_{(aq)}$[K]$^{+}_{(aq)}$ (6.13 x 10^{-5} mol L^{-1}) to increasing addition of Mn^{2+} (6.13 x 10^{-3} mol L^{-1}). Inserts show a magnification for clarity and dissymmetry factor changes at 544 and 548 nm. Excitation at 295 nm. Bandpass: 2.4 nm.

Conclusions

We have developed an expedient and scalable synthesis of enantiopure lanthanide complexes that emit CPL in aqueous solutions. Complexes of four lanthanides emitting in the visible were investigated, and their luminescent and chiroptical properties were comparable to other more elaborate platforms. Additionally, we report the first examples of aqueous samarium CPL. The strong chiroptical properties of the terbium complexes allowed us to examine their viability as potential sensors. At a concentration of 5 µM, our complexes were reversibly responsive to variations in pH, and provided unique CPL responses (including a drastic change in CPL sign) when exposed to different divalent metals even at micromolar concentrations. These changes were reversible in the presence of a competing chelating ligand. The Tb complex is responsive towards the metal ions chosen (Pb^{2+}, Cd^{2+}, Mn^{2+}) over K^{+} with prominent response for Mn over Pb and Cd. These results show the potential of our simple, easily accessible complexes for future sensing applications, and open the gates for the design of other simple CPL-based sensors. For example, longer excitation wavelengths can be achieved by substitution at the para-position of the pyridine ring,[17] and given the response of our complexes to manganese, sensing of other paramagnetic metals can be envisioned.

Author Contributions

We strongly encourage authors to include author contributions and recommend using CRediT for standardised contribution descriptions. Please refer to our general author guidelines for more information about authorship.

Conflicts of interest

"There are no conflicts to declare".

Acknowledgements

We thank the University of Connecticut for partial support of this work. This material is based upon work supported by the National Science Foundation under grant no. CHE-2041084. We thank a reviewer for their valuable comments and suggestions.

Notes and references

‡ CCDC 2118661 contain the supplementary crystallographic data for this paper.

1 (a) R. Farshchi, M. Ramsteiner, J. Herfort, A. Tahraoui and H. T. Grahn. Optical communication of spin information between light emitting diodes. *Appl. Phys. Lett.*, 2011, **98**, 162508-1-162508-3; (b) J. F. Sherson, H. Krauter, R. K. Olsson, B. Julsgaard, K. Hammerer, I. Cirac and E. S. Polzik. Quantum teleportation between light and matter. *Nature,* 2006, **443**, 557-560.

2 (a) L. Arrico, L. Di Bari and F. Zinna. Quantifying the overall efficiency of circularly polarized emitters. *Chem. Eur. J.*, 2020, **27**, 2920-2934; (b) Y. Nagata and T. Mori. Irreverent nature of dissymmetry factor and quantum yield in circularly polarized luminescence of small organic molecules. *Front. Chem.*, 2020, **8**, 448.

3 (a) F. Zinna and L. Di Bari. Lanthanide circularly polarized luminescence: bases and applications. *Chirality,* 2015, **27,** 1-13; (b) R. Carr, N. H. Evans and D. Parker. Lanthanide complexes as chiral probes exploiting circularly polarized luminescence. *Chem. Soc. Rev.,* 2012, **41**, 7673-7686; (c) G. Muller. Luminescent chiral lanthanide (III) complexes as potential molecular probes. *Dalton Trans.,* 2009, **44**, 9692-9707.

4 A. Beeby, I. M. Clarkson, R. S. Dickins, S. Faulkner, D. Parker, L. Royle, A. S. de Sousa, J. A. G. Williams and M. Woods. Non-radiative deactivation of the excited states of europium, terbium, ytterbium complexes by proximate energy matched OH, NH and CH oscillators: an improved luminescence method for establishing solution hydration states. *J. Chem. Soc., Perkin Trans. 2*, 1999, 493-504.

5 (a) R. S. Dickins, J. A. K. Howard, C. L. Maupin, J. M. Moloney, D. Parker, J. P. Riehl and G. Siligardi. Synthesis, time-resolved luminescence, NMR spectroscopy, Circular dichroism, and circularly polarized luminescence studies of enantiopure macrocyclic lanthanide tetraamide complexes. *Chem. Eur. J.*, 1999, **5,** 1095-1105; (b) E. R. Neil, A. M. Funk, D. S. Yufit and D. Parker. Synthesis, stereocontrol and structural studies of highly luminescent chiral tris-amidepyridyl-triazacyclononane lanthanide complexes. *Dalton Trans.*, 2014, **43**, 5490-5504; (c) A. T. Frawley, H. V. Linford, M. Starck, R. Pal and D. Parker. Enantioselective cellular localisation of europium (III) coordination complexes. *Chem. Sci.*, **2018**, 9, 1042-1049

6 (a) L. Dai, J. Zhang, Y. Chen, L. E. Mackenzie, R. Pal and G.-L. Law. Synthesis of water-soluble chiral DOTA lanthanide complexes with predominantly twisted square antiprism isomers and circularly polarized luminescence. *Inorg. Chem.*, 2019, **58**, 12506-15210; (b) L. Dai, W. Lo, I. D. Coates, R. Pal and G.-L. Law. New class of bright and highly stable chiral cyclen europium complexes for circularly polarized luminescence applications. *Inorg. Chem.*, 2016, **55**, 9065-9070.

7 (a) M. Seitz, E. G. Moore, A. J. Ingram, G. Muller and K. N. Raymond. Enantiopure, octadentate ligands as sensitizers for europium and terbium circularly polarized luminescence in aqueous solution. *J. Am. Chem. Soc.*, 2007, **129**, 15468-15470; (b) M. Seitz, K. Do, A. J. Ingram. E. G. Moore, G. Muller and K. N. Raymond. Circularly polarized luminescence in enantiopure europium and terbium complexes with modular, all-oxygen donor ligands. *Inorg. Chem.*, 2009, **48**, 8469-8479; (c) A. P. S. Samuel, J. L. Lunkley, G. Muller and K. N. Raymond. Strong circularly polarized luminescence from highly emissive terbium complexes in aqueous solution. *Eur. J. Inorg. Chem.*, 2010, 3343-3347.

8 M. Leonzio, A. Melchoir, G. Faura, M. Tolazzi, F. Zinna, L. Di Bari and F. Piccinelli. Strong circularly polarized emission from water-stable Eu(III)- and Tb(III)-based complexes: a structural and spectroscopic study. *Inorg. Chem.*, 2017, **56**, 4413-4421.

9 N. Chatterton, Y. Bretonniere, J. Pecaut and M. Mazzanti. An efficient design for the rigid assembly of four bidentate chromophores in water-stable highly luminescent lanthanide complexes. *Angew. Chem. Int. Ed.*, 2005, **44**, 7595-7598.

10 F. Piccinelli, C. Nardon, M. Bettinelli, A. Melchior, M. Tolazzi, F. Zinna, L. Di Bari. Lanthanide-based complexes containing a chiral *trans*-1,2-diaminocyclohexane (DACH) backbone: spectroscopic properties and potential applications. *ChemPhotoChem,* DOI:10.1002/cptc.202100143

11 F. Chauveau, P. Doppelt and J. Lefebvre. Selection rules for lanthanide optical activity. *Inorg. Chem.*, 1980, **19**, 2806-2812.

12 (a) M. Deng, N. D. Schley and G. Ung. High circularly polarized luminescence brightness of analogues of Shibasaki's lanthanide complexes. *Chem Commun.*, 2020, **56**, 14813-14816; (b) D. Schnable, K. Freedman, K. M. Ayers, N. D. Schley, M. Kol and G. Ung. Synthesis of enantiopure lanthanide complexes supported by hexadentate *N*,*N'*-bis(methylbipyridyl)bipyrrolidine and their circularly polarized luminescence. *Inorg. Chem*., 2020, **59**, 8498-8504; (c) K. Ayers, N. D. Schley and G. Ung. Circularly polarized luminescence from enantiopure C2-symmetrical tetrakis(2-pyridylmethyl)-1,2-diaminocyclohexane lanthanide complexes. *Inorg. Chem.*, 2020, **59**, 7657-7665.

13 D. Parker, J. D. Fradgley, K.-L. Wong. The design of responsive luminescent lanthanide probes and sensors. *Chem. Soc. Rev.*, 2021, **50**, 8193-8213.

14 (a) H. N. Kim, W. X. Ren, J. S. Kim and J. Yoon. Fluorescent and colorimetric sensors for detection of lead, cadmium, and mercury ions. *Chem. Soc. Rev.*, 2012, **41**, 3210-3244; (b) T. Eicher and E. Avery. Toxic encephalopathies. *Neurologic Clinics*, 2005, **23**, 353-376; (c) D. Ding, J. Roth and R. Salvi. Manganese is toxic to spiral ganglion neurons and hair cells in vitro. *Neurotoxicology*, 2011, **32**, 233-241; (d) V. Bencko and M. Cikrt. Manganese: a review of occupational and environmental toxicology. *J. Hyg. Epidemiol. Microbiol. Immunol.* 1984, **28**, 139-48.

15 (a) F. S. Richardson. Theory of optical activity in the ligand-field transitions of chiral transition metal complexes. *Chem. Rev.*, 1979, **79**, 17-36; (b) J. P. Riehl and F. S. Richardson. Circularly polarized luminescence spectroscopy. *Chem. Rev.*, 1986, **86**, 1-16.

16 (a) A. S. Mildvan and M. Cohn. Magnetic resonance studies of the interaction of the manganous ion with bovine serum albumin. *Biochemistry*, 1963, **2**, 910-919; (b) H. Jouve, H. Jouve, E. Melgar and B. Lizarraga. A study of the binding of Mn^{2+} to bovine pancreatic deoxyribonuclease I and to deoxyribonucleic acid by electron paramagnetic resonance. *J. Bio. Chem.*, 1975, **250**, 6631-6635.

17 M. Starck, J. D. Fradgley, D. F. De Rosa, A. S. Batsanov, M. Papa, M. J. Taylor, J. E. Lovett, J. C. Lutter, M. J. Allen, D. Parker. Versatile para-substituted pyridine lanthanide coordination complexes allow late stage tailoring of complex function. *Chem. Eur. J.*, 2021, **27**, 17921-17927.