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

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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 $245 \text{ M}^{-1} \text{ cm}^{-1}$ 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.

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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} ($g_{lum} = 2(I_L - I_R)/(I_L + I_R)$; I_L and I_R being the intensity of left- and right-circularly polarized light, respectively) and CPL brightness B_{CPL} ($B_{CPL} = \epsilon \times \Phi \times |g_{lum}|/2$; 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 ($0.05 < g_{lum} < 1$) 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 macrocycles⁶ have led to impressive results. For example, using europium ($\lambda_{em} = 590 \text{ nm}$), water-soluble complexes supported by triazacyclononane-derived ligands reached g_{lum} of 0.1 to 0.3 and B_{CPL} around $1000\text{--}2000 \text{ M}^{-1} \text{ cm}^{-1}$ (λ_{exc} 340 nm).^{5c} Using similar ligands on terbium ($\lambda_{em} = 539 \text{ nm}$), strong metrics were also obtained (g_{lum} up to 0.11, B_{CPL} up to $199 \text{ M}^{-1} \text{ cm}^{-1}$ (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 $314 \text{ M}^{-1} \text{ cm}^{-1}$ (λ_{exc} 340 nm)^{7a}), but these systems either require lengthy syntheses⁷ or generate mixtures of isomers.⁸ The simplification of synthetic methodologies while retaining similar chiroptical properties would therefore be highly desirable.

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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 $245\text{ M}^{-1}\text{ cm}^{-1}$ (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.

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*)-H₄tpadac 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*)-H₄tpadac and both could be scaled to at least 2.0 g.

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 recrystal-

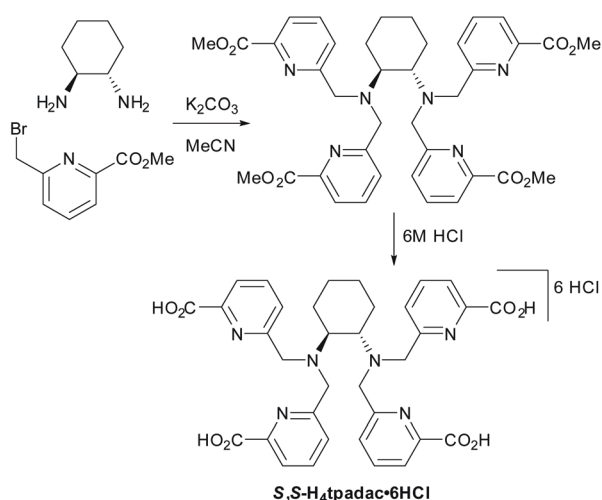


Fig. 1 Synthesis of (*S,S*)-*N,N,N',N'*-tetrakis[(6-carboxypyridin-2-yl)methyl]-1,2-diaminocyclohexane (*S,S*)-H₄tpadac.

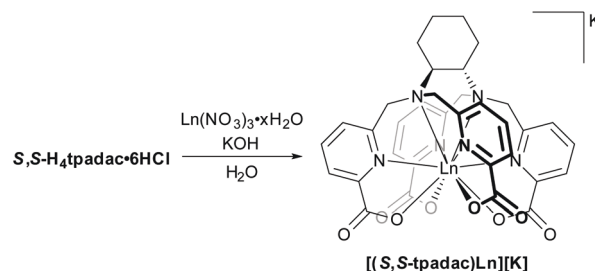


Fig. 2 Coordination of (*S,S*)-H₄tpadac to lanthanides. Ln = La, Sm, Eu, Tb, Dy.

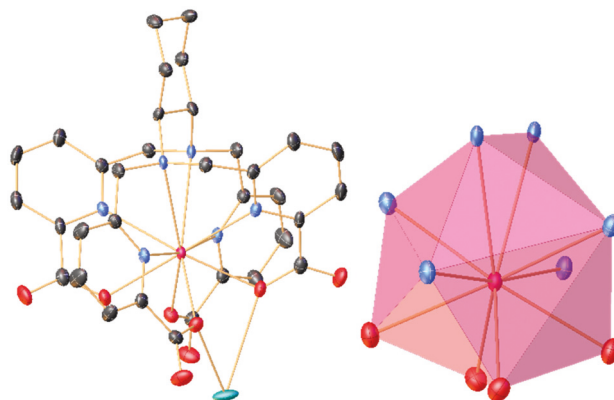


Fig. 3 Structure of [(*S,S*)-tpadac)Eu][K] (left) and coordination polyhedron (right) in the solid state. Thermal ellipsoids are drawn at 50% probability. Hydrogen atoms and co-crystallized water molecules are omitted for clarity. Black: C; blue: N; red: O; teal: K; pink: Eu.

lisation from water. The complexes were obtained in good yields (60 to 70%) as off-white solids. ¹H NMR spectra of the diamagnetic La and the weakly paramagnetic Sm complexes recorded in D₂O 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 (Fig. S1–S4†). Analogously, in the more paramagnetic species (Ln = Eu, Tb, Dy), no more than fifteen broad resonances were observed (Fig. S5–S10†).

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.

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

Luminescence and circularly polarized luminescence

Upon excitation at 290 nm, solutions of $[(R,R\text{-tpadac})\text{Ln}]^{-}(\text{aq})[\text{K}]^{+}(\text{aq})$ and $[(S,S\text{-tpadac})\text{Ln}]^{-}(\text{aq})[\text{K}]^{+}(\text{aq})$ (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 (Fig. S11–S14†). Lifetime measurements (see ESI†) confirmed the absence of co-ordinated 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}

Circularly polarized luminescence spectra of the $[(R,R\text{-tpadac})\text{Sm}]^{-}(\text{aq})[\text{K}]^{+}(\text{aq})$ and $[(S,S\text{-tpadac})\text{Sm}]^{-}(\text{aq})[\text{K}]^{+}(\text{aq})$ (Fig. 4) showed a maximum dissymmetry factor for the ${}^4\text{G}_{5/2} \rightarrow {}^6\text{H}_{5/2}$ transition ($g_{\text{lum}} = 0.25$) consistent with its transition type.¹¹ The maximum B_{CPL} was observed for the ${}^4\text{G}_{5/2} \rightarrow {}^6\text{H}_{7/2}$ transition at $0.60 \text{ M}^{-1} \text{ cm}^{-1}$ ($\lambda_{\text{exc}} 295 \text{ nm}$, $\lambda_{\text{em}} 589 \text{ nm}$). 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.

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

The $[(R,R\text{-tpadac})\text{Tb}]^{-}(\text{aq})[\text{K}]^{+}(\text{aq})$ and $[(S,S\text{-tpadac})\text{Tb}]^{-}(\text{aq})[\text{K}]^{+}(\text{aq})$ showed moderate dissymmetry factors ($|g_{\text{lum}}| \leq 0.20$) (Fig. 6), but are amongst the brighter Tb CPL emitters in water to date ($B_{\text{CPL}} = 245 \text{ M}^{-1} \text{ cm}^{-1}$ ($\lambda_{\text{exc}} 295 \text{ nm}$, $\lambda_{\text{em}} 544 \text{ nm}$) for the ${}^5\text{D}_4 \rightarrow {}^7\text{F}_5$ transition), owing to their strong quantum yields.

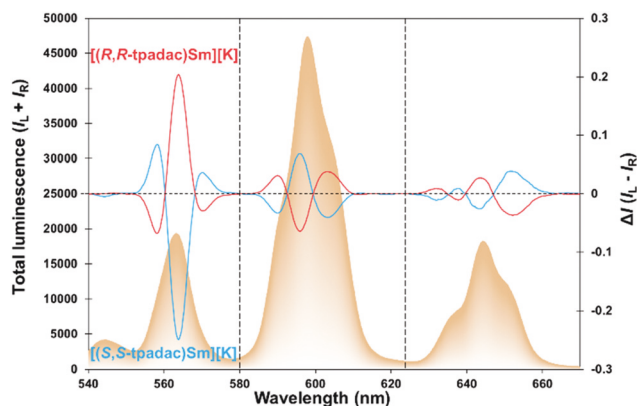


Fig. 4 CPL spectra of $[(R,R\text{-tpadac})\text{Sm}]^{-}(\text{aq})[\text{K}]^{+}(\text{aq})$ (red) and $[(S,S\text{-tpadac})\text{Sm}]^{-}(\text{aq})[\text{K}]^{+}(\text{aq})$ (blue) in 0.1 M tris buffer solutions adjusted to pH = 7.4 ($5.96 \times 10^{-4} \text{ mol L}^{-1}$) at room temperature. 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 Fig. S21† for g_{lum} plot). Total luminescence is traced in the background. Excitation at 295 nm. Bandpass: 5 nm.

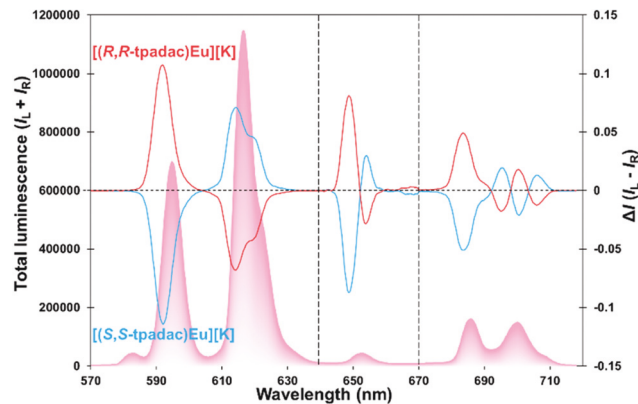


Fig. 5 CPL spectra of $[(R,R\text{-tpadac})\text{Eu}]^{-}(\text{aq})[\text{K}]^{+}(\text{aq})$ (red) and $[(S,S\text{-tpadac})\text{Eu}]^{-}(\text{aq})[\text{K}]^{+}(\text{aq})$ (blue) in 0.1 M tris buffer solutions adjusted to pH = 7.4 ($6.54 \times 10^{-4} \text{ mol L}^{-1}$) at room temperature. 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 Fig. S20† for g_{lum} plot). Total luminescence is traced in the background. Excitation at 295 nm. Bandpass: 5 nm.

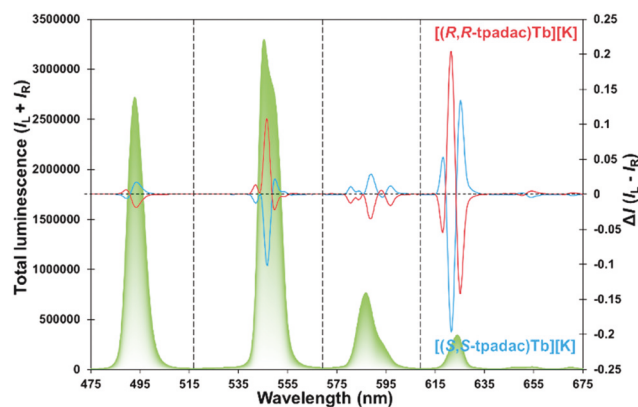


Fig. 6 CPL spectra of $[(R,R\text{-tpadac})\text{Tb}]^{-}(\text{aq})[\text{K}]^{+}(\text{aq})$ (red) and $[(S,S\text{-tpadac})\text{Tb}]^{-}(\text{aq})[\text{K}]^{+}(\text{aq})$ (blue) in 0.1 M tris buffer solutions adjusted to pH = 7.4 ($6.13 \times 10^{-4} \text{ mol L}^{-1}$) at room temperature. 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 Fig. S19† for g_{lum} plot). Total luminescence is traced in the background. Excitation at 295 nm. Bandpass: 2.4 nm.

The dysprosium complexes $[(R,R\text{-tpadac})\text{Dy}]^{-}(\text{aq})[\text{K}]^{+}(\text{aq})$ and $[(S,S\text{-tpadac})\text{Dy}]^{-}(\text{aq})[\text{K}]^{+}(\text{aq})$ also exhibited CPL with a maximum dissymmetry factor ($|g_{\text{lum}}| = 0.14$) and brightness ($B_{\text{CPL}} = 0.68 \text{ M}^{-1} \text{ cm}^{-1}$, $\lambda_{\text{exc}} 295 \text{ nm}$, $\lambda_{\text{em}} 668 \text{ nm}$) for the magnetic-dipole allowed ${}^4\text{F}_{9/2} \rightarrow {}^6\text{H}_{11/2}$ 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 $|g_{\text{lum}}| = 0.41$,^{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

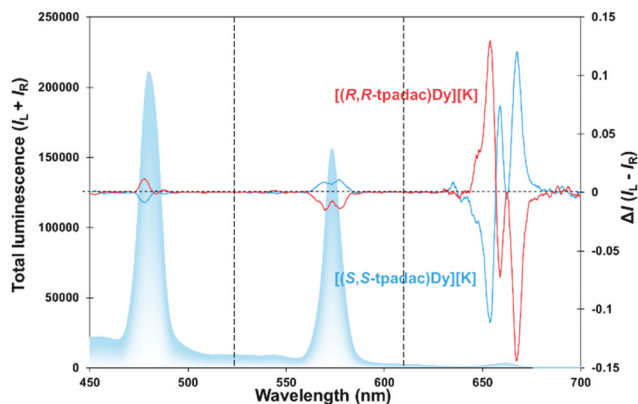


Fig. 7 CPL spectra of $[(R,R\text{-tpadac})\text{Dy}]^{-}(\text{aq})[\text{K}]^{+}(\text{aq})$ (red) and $[(S,S\text{-tpadac})\text{Dy}]^{-}(\text{aq})[\text{K}]^{+}(\text{aq})$ (blue) in 0.1 M tris buffer solutions adjusted to pH = 7.4 ($6.13 \times 10^{-4} \text{ mol L}^{-1}$) at room temperature. 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 Fig. S22† for g_{lum} plot). Total luminescence is traced in the background. Excitation at 295 nm. Bandpass: 5 nm.

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 $[(S,S\text{-tpadac})\text{Tb}][\text{K}]$ and $[(S,S\text{-tpadac})\text{Eu}][\text{K}]$ complexes, and selected the transitions that combined high luminescence intensity and high dissymmetry factors: $^5\text{D}_4 \rightarrow ^7\text{F}_5$ (Tb), $^5\text{D}_4 \rightarrow ^7\text{F}_3$ (Tb), $^5\text{D}_0 \rightarrow ^7\text{F}_1$ (Eu), and $^5\text{D}_0 \rightarrow ^7\text{F}_2$ (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 $[(S,S\text{-tpadac})\text{Tb}]^{-}(\text{aq})[\text{K}]^{+}(\text{aq})$ in tris buffer adjusted by incremental addition of 1 M HCl yielded a response in both CPL and dissymmetry factors (Fig. 8). These

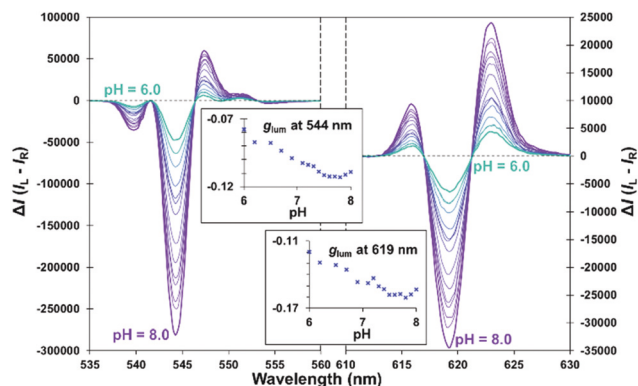


Fig. 8 CPL response of $[(S,S\text{-tpadac})\text{Tb}]^{-}(\text{aq})[\text{K}]^{+}(\text{aq})$ to pH ranging from 8.0 to 6.0. Inserts show dissymmetry factors changes at 544 and 619 nm. Excitation at 295 nm. Bandpass: 2.4 nm.

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 (Fig. 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 pK_a value was calculated to be 6.99 (Fig. 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.

To determine if our system can be best 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 (Fig. S28† inset). The ΔI plot is not fully reversible as expected from the increased dilution from the titration. This highlights the significance of observing both g_{lum} and ΔI 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 (Fig. S28†).

Analogous titration of $[(S,S\text{-tpadac})\text{Eu}]^{-}(\text{aq})[\text{K}]^{+}(\text{aq})$ 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

Titration of up to 8 equivalents of $\text{Pb}(\text{OAc})_2$ in a solution of $[(S,S\text{-tpadac})\text{Tb}]^{-}(\text{aq})[\text{K}]^{+}(\text{aq})$ in tris buffer generated a response in both CPL and dissymmetry factors (Fig. 9). The ΔI maxima for the $^5\text{D}_4 \rightarrow ^7\text{F}_5$ 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 (Fig. S35†).

A similar response was observed for the same transition when titrating up to 8 equivalents of $\text{Cd}(\text{OAc})_2$ (Fig. 10). The decrease of both ΔI and $|g_{\text{lum}}|$ was noticeably smaller for Cd^{2+} when compared to Pb^{2+} , suggesting that specific speciation

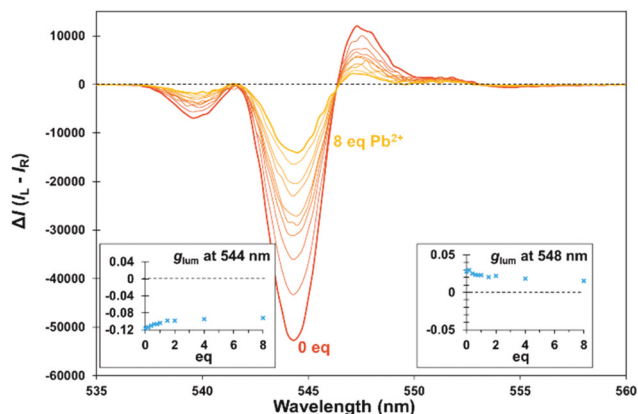


Fig. 9 CPL response of $[(S,S\text{-tpadac})\text{Tb}]^{-}(\text{aq})[\text{K}]^{+}(\text{aq})$ ($6.13 \times 10^{-5} \text{ mol L}^{-1}$) to increasing addition of Pb^{2+} ($6.13 \times 10^{-3} \text{ mol L}^{-1}$). Inserts show dissymmetry factor changes at 544 and 548 nm. Excitation at 295 nm. Bandpass: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

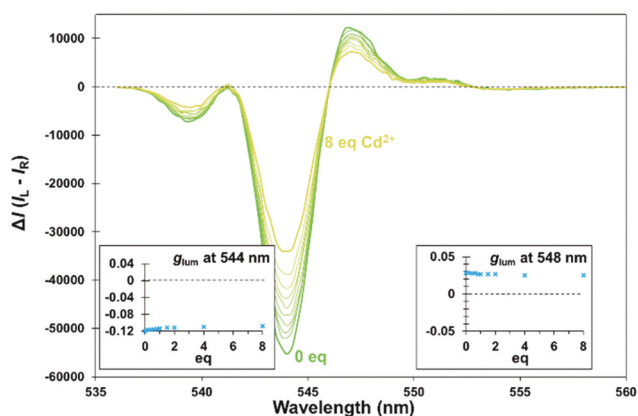


Fig. 10 CPL response of $[(S,S\text{-tpadac})\text{Tb}]^{-}(\text{aq})[\text{K}]^{+}(\text{aq})$ ($6.13 \times 10^{-5} \text{ mol L}^{-1}$) to increasing addition of Cd^{2+} ($6.13 \times 10^{-3} \text{ mol L}^{-1}$). Inserts show dissymmetry factor changes at 544 and 548 nm. Excitation at 295 nm. Bandpass: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

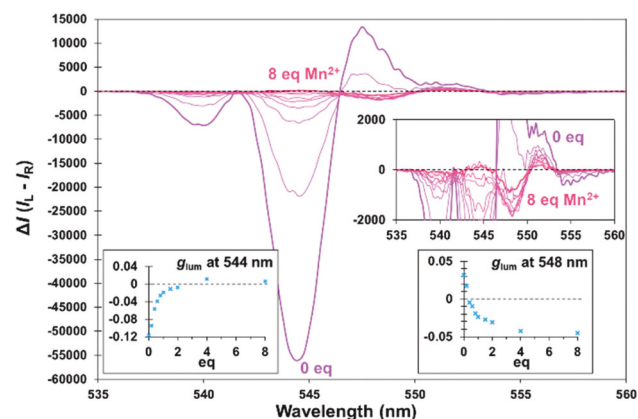


Fig. 11 CPL response of $[(S,S\text{-tpadac})\text{Tb}]^{-}(\text{aq})[\text{K}]^{+}(\text{aq})$ ($6.13 \times 10^{-5} \text{ mol L}^{-1}$) to increasing addition of Mn^{2+} ($6.13 \times 10^{-3} \text{ mol L}^{-1}$). Inserts show a magnification for clarity and dissymmetry factor changes at 544 and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

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 (Fig. S36†).

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 $[(S,S\text{-tpadac})\text{Tb}]^{-}(\text{aq})[\text{K}]^{+}(\text{aq})$ 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 $[(S,S\text{-tpadac})\text{Tb}]^{-}(\text{aq})[\text{K}]^{+}(\text{aq})$ 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 $[(S,S\text{-tpadac})\text{Eu}]^{-}(\text{aq})[\text{K}]^{+}(\text{aq})$ 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 (Fig. 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 (Fig. S28 and S34–S36†).

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 luminescence 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.

Conflicts of interest

There are no conflicts to declare.

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