Chiral transcription in self-assembled tetrahedral Eu₄L₆ chiral cages displaying sizable circularly polarized luminescence

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Predictable stereoselective formation of supramolecular assembly is generally believed to be an important but complicated process. Here, we show that point chirality of a ligand decisively influences its supramolecular assembly behavior. We designed three closely related chiral ligands with different point chiralities, and observe their self-assembly into europium (Eu) tetrametallic tetrahedral cages. One ligand exhibits a highly diastereoselective assembly into homochiral (either ΔΔΔΔ or ΛΛΛΛ) Eu tetrahedral cages whereas the two other ligands, with two different approaches of loosened point chirality, lead to a significant breakdown of the diastereoselectivity to generate a mixture of (ΔΔΔΔ and ΛΛΛΛ) isomers. The cages are highly emissive (luminescence quantum yields of 16(1) to 18(1)%) and exhibit impressive circularly polarized luminescence properties (|g|: up to 0.16). With in-depth studies, we present an example that correlates the nonlinear enhancement of the chiroptical response to the nonlinearity dependence on point chirality.
The self-assembly formation of lanthanide supramolecular architectures, particularly the relatively simple structures of mononuclear bundles (mononuclear) and dinuclear helicates (dinuclear), has received considerable attention because of their beautiful construction and peculiar spectroscopic and magnetic features. Many pioneering and elegant examples with beautiful architectural formations have been developed by Bünzli, Piguet, and other researchers. However, higher order and sophisticated polynuclear architectures such as tetranuclear tetrahedral edifices and heptanuclear clusters with cavities for potential encapsulation of guests are much less explored due to the difficulty in controlling the topology and coordination geometry. Similar to linear helicates, tetrahedral cages are intrinsically chiral with either a Δ or Λ configuration at each of the four vertices. However, due to the different constraints in metal coordination geometry, tetrahedral cages may result in different combinations of configurations in either (a) a homoconfigurational ΔΔΔΔ- or ΛΛΛΛ-twisted conformation or (b) a blend of heteroconfigurational ΔΔΔΛ-, ΛΛΔΛ-, ΛΛΛΔ-twisted conformers in more complex situations. Manipulation of the formation of either one of these stereoisomers in a predictable manner is key to assessing the properties of these tetrahedral cages for utilization in functional applications such as chiral guest recognition, sensing molecular cargo carriers, and asymmetric catalysis.

Great effort has been devoted to investigating the long-range linker effect and chiral nonlinear effect in order to achieve stereoselective control of tetrahedral cages, but these studies mainly focused on transition metals (M)-related polyhedra, M₄:L₆ or M₄:L₄ (L is either a C₂- or C₃-symmetric ligand), in which the metals usually have well-defined and predictable coordination geometries. In retrospect, studies on lanthanide-based systems

![Fig. 1](image-url)
are scarce as lanthanide ions are known to exhibit variable coordination numbers (from 3 to 12), are kinetically labile and have weak stereoechemical preferences. Hence the rational design of lanthanide tetrahedral cages that possess targeted supramolecular topology with well-defined chirotopic cavities is challenging.

Introducing a predisposed point chiral moiety (point chirality) onto the ligand is a general approach to relay chiral information to an overall stereochemistry of self-assembled tetrahedral cages21–23, but the challenge lies in designing a suitable point chirality to selectively favor formation of one stereoisomeric structure without any depreciation of chiral information. The driving force and formation mechanism behind achieving prominent stereoselectivity for higher order coordination geometry edifices—such as in lanthanide tetrahedral cages—remain unclear and more studies are therefore necessary.

On the other hand, another way of elucidating chiral information is the use of circularly polarized luminescence (CPL), a highly sensitive and powerful tool for evaluating chiral conformational and three-dimensional structural information of the luminescent compound in the excited state, and a complementary technique to that of the ground-state-based circular dichroism (CD)24. However, luminescence from high-order chiral architectures are scarce. CPL spectroscopy studies of mononuclear systems has received considerable attention in recent years, particularly in sensing chemistry25, but the challenge lies in designing a suitable point chirality to selectively favor formation of one stereoisomeric crystallographic results show a tetrahedral connection between the four europium ions, suggesting a tetrahedral cage topology (Supplementary Fig. 1 and Supplementary Table 1). All of the four europium ions are arranged in the same A-configurations, which are same as other reported supramolecular complexes with the same R-chiral moieties and similar pcam coordinating systems14, 34. In our cage, each of the europium can be described to be distorted tricapped trigonal prismatic geometry. At each europium vertex, three pyridyl atoms, which located equatorial plane, are sandwiched by two trigonal faces which consisting of six oxygen atoms of amide units.

The tetrahedral stoichiometry of the species was further supported by high resolution ESI-MS analysis (Supplementary Figs. 2–7). Interestingly, these kind of tetrahedral cages possess a number of characteristics. For instance, [Eu₄(L(SS)₃)(OTf)₁₂] exhibits three clusters of peaks which correspond to three different species with 4+, 5+, and 6+ charge states (Supplementary Fig. 2a). In each of the clusters, the peaks were found to correspond to the species with a consecutive loss of one triflate anion and one proton cation to account for the overall charge state. For example, in the group of 4+ charge, the peaks with m/z = 1564.2017, 1526.7125, 1489.2229, 1451.4837, and 1414.2432 can be assigned to molecular species of [[[Eu₄(L(SS)₃)₃](OTf)₉]⁻–(H₂O)]⁰ with m = 4, n = 0; m = 5, n = 1; m = 6, n = 2; m = 7, n = 3 and m = 8, n = 4, respectively (Supplementary Fig. 2b). The assignments were verified by comparing to the corresponding isotopic distributions of the simulated and experimental results. Similar phenomena of subsequent loss of triflates and protons were also observed for the groups with 5+ and 6+ charges. The corresponding yttrium complexes, [Y₄(L(SS)₃)₃](OTf)₁₂ (L = L₁–L₃), were also analyzed for comparison. From Electrospray ionization mass spectrometers (ESI-MS) analysis, this also verified the formation of tetrahedral cages with similar trflate(s) and proton (s) subtraction patterns when compare to the corresponding isostuctural Eu counterparts (Supplementary Figs. 5–7).

Results

Ligand synthesis. Previously, we have developed a system of stereoselective formation of lanthanide bimetallic triple helicates with chiral ligands in which chiral moieties of the ligands are connected with a linear rod-like benzidine-based biphenyl linker31. Based on these designs, we conceived different ligand building blocks to engineer supramolecular assemblies of a higher hierarchical order. The three pairs of chiral bis-tridentate ligands L₁–L₃ are based on the diagonal 2,6-diamoantranoinquanie unit, (Fig. 1a), in which L₂ has a smaller point chirality relative to L₁, and L₃ has an extended point chirality from the coordinating unit. Utilization of this type of linker for potential guest encapsulated-tetrahedral cage formation was first demonstrated with transition metals a few years ago;22 here we aim to engineer a similar topology of luminescent supramolecular assemblies with lanthanide ions: Ln₄L₆ tetrahedral cages (Fig. 1b, c).

The three ligands (L₁–L₃) were synthesized in two steps using general HATU peptide coupling reactions35 sourced from commercially available pyridyl dicarboxylic acid, chiral amines, and 2,6-diamoantranoinquanie. ¹³C NMR spectra of the ligands show a total of 19 aromatic and carbonyl carbon signals for L₁ and L₃, and 14 signals for L₂, indicating a dynamically average C₂-symmetric nature of these ligands in solution.

NMR characterization of tetrahedral cages. ¹H and ¹³C NMR experiments were performed to characterize the supramolecular tetrahedral cages. For [Eu₄(L₁¹⁸R)(OTf)₁₂], the integrations are equivalent to the corresponding ligand in C₃-symmetric nature (Supplementary Fig. 8). As all resonances are affected by slight paramagnetic broadening, the diagnosis of the presence of the total number of species was not confidently concluded. Even though ¹H NMR experiments were performed at a different range of temperatures, e.g., over a span of 108 K, the resonances were still too broad to confidently verify the number of species present (Supplementary Fig. 9a). However by further analysis, a plot of δ vs. 1/T shows good linearity and implies the consistent presence of a single species in each temperature regime (Supplementary Fig. 9b)36. No obvious coalescence nor decomposition was observed upon increasing the temperature to 346 K showing that the cage is relatively thermally stable32. This hypothesis of the existence of a single species is also further supported by diffusion
Cotton effect is observed (Supplementary Fig. 11). A total of 20 resonancestwo sets of resonances (Supplementary Figs. 14 and 16). The L2 ppm based, (Supplementary Fig. 16a and 17)) were found. The L3 L2/L3 = 0.93 and 1.13 ppm based, (Supplementary Figs. 21a) and 21b) were found. The NMR shows splitting into two sets of resonances, indicating a high probability of the formation of two supramolecular species where isomerization are extremely slow in the NMR timescale. However, we postulate that these two species should possess a very similar supramolecular structure as shown by one dominant D value found in the DOSY measurement (Supplementary Fig. 18). In addition, the two species seem to be in some extent of dynamic motion as verified with variable temperature 1H NMR experiments. For [Eu4(L2)6](OTf)12, the two sets of resonances for aromatic protons (a–c and e–g) show coalescence at 267 and 283 K. However, no obvious coalescence can be observed for the rest of the protons (i, j, and l) even upon increasing temperature to 346 K (Supplementary Fig. 19). For [Eu4(L3)6](OTf)12, only pyridyl protons (e–g) show coalescence at 325 and 346 K when increasing in temperature. For the other aromatic protons (b–c), two set of resonances still could not be resolved even at very low temperature (238 K). For the aliphatic protons (i and j), no obvious coalescence in this span of temperature was observed (Supplementary Fig. 20). Absence or presence of coalescence at different temperatures may indicate different extent of dynamic motion occurring for different type of protons of ligands in the same cage. For each ligand, the respective diamagnetic counterparts, yttrium cages ([Y4(L2/L3)6](OTf)12), were examined which also exhibited two sets of resonances (Supplementary Fig. 21), suggesting the existence of two supramolecular species. The ratios of ~1: 1.15(5) for L2 (0.86 and 0.55 ppm based, (Supplementary Fig. 21a)) and ~1: 1.06(4) for L3 (0.93 and 1.13 ppm based, (Supplementary Fig. 21b)) were found.

For the above tetrahedral cages, concentration and solvent effects were also investigated. The results suggest that tetrahedral to helicate conversion which was observed in other similar tetrahedral cages36 cannot be observed (Supplementary Figs. 22–33).

**Chiral optical measurements.** Measurement of solution CD was performed for [Eu4(L1)6](OTf)12 (L = L1–L3). Similar to the NMR observation, the cage of L1 also exhibited very different and
distinct phenomena in the CD measurements when compared with the cages formed with L2 and L3. In general, [Eu4(L1SS)n] (OTf)12 resulted in a very strong exciton coupling with peaks at 352, 306, 279 (shoulder), 255, and 211 nm (Fig. 2a). A predicted mirror image of the spectra was also observed for the opposite chiral isomer L1RR, indicating their enantiomeric nature. In addition, the corresponding Y cages also resulted in CD spectra very similar to those of the Eu cages (Supplementary Fig. 34).

On the other hand, the other two cages, [Eu4(L1)b](OTf)12 (L = L2 or L3) resulted in significant attenuation of the Cotton effect when compared with [Eu4(L1)](OTf)12 (Fig. 2a). Generally, the extent of signal depletion from L2 [96(1)% (352 nm), 95(1)% (306 nm), 94(1)% (279 nm), and 91(5)% (211 nm)] was greater than that from L3 [85(1)% (352 nm), 83(1)% (306 nm), 79(1)% (279 nm), and 84(4)% (211 nm)]. Signal attenuation was observed for the corresponding Y cages of L2 or L3 (Supplementary Fig. 34). The similarity in the CD phenomena between Eu and Y cages indicated that the supramolecular behavior of the tetrahedral cages was similar.

The enantiomeric nature of the supramolecular tetrahedral cages was also proved by the corresponding CPL spectra. CPL of supramolecular chiral f-tetrametallic tetrahedral cages has not been reported previously. For [Eu4(L1)b](OTf)12, mirroring CPL spectra were observed for the corresponding complexes of L1RR and L1SS isomers, confirming their enantiomeric property (Fig. 2b, Supplementary Fig. 35a). For the other two Eu cages with L2 or L3, the CPL response decreased significantly with [Eu4(L2)b](OTf)12 exhibiting the weakest signals (Fig. 2b). This trend matches and supports the results derived from the CD studies. This observation can be attributed to the different overall screw sense of the different cages arising from the Eu ions contortion, which in turn is controlled by the stereoselective controlling ability of the ligand strands. This can be assumed as CPL reveals chiral information directly at the emitting Eu center.
and provides a better insight to the supramolecular chirality instead of CD data which only concerns the absorption of the chiral ligand. In terms of the degree of CPL response, \([\text{Eu}_4(\text{L}_1)_{6}]^{(\text{OTf})_{12}}\) was found to have the two highest luminescent dissymmetry factors, \(g_{\text{lum}}(591 \text{ nm}) = -0.16(1)\) and \(+0.16(1)\) which is comparable in magnitude \((-0.19\) and \(+0.19\)) to the corresponding monomeric complexes with the same chiral group at the same \(^5\text{D}_0 \rightarrow ^7\text{F}_1\) transition (Supplementary Fig. 35b(i); Supplementary Table 2) \(^{37}\). The \(g_{\text{lum}}(704 \text{ nm})\) values for the \(^5\text{D}_0 \rightarrow ^7\text{F}_4\) transition was found to be \(-0.16(2)\) and \(+0.16(1)\), which is lower than reported values \((-0.24\) and \(+0.24\)) of the monomeric complexes. Very weak \(g_{\text{lum}}(591.0 \text{ nm})\) was observed for \([\text{Eu}_4(\text{L}_3)_{6}]^{(\text{OTf})_{12}}\) \((+0.04(2)\) and \(-0.03(2)\)), whereas no reasonable dissymmetry factors were found for \([\text{Eu}_4(\text{L}_2)_{6}]^{(\text{OTf})_{12}}\) (Supplementary Fig. 35b(ii–iii); Supplementary Table 2), affirming the extremely weak signals.

From these spectroscopic data, we can preliminarily conclude that only one diastereomer tetrahedral cage is formed from \(\text{L}_1\text{RR/SS}\), whereas two diastereomers are formed with \(\text{L}_2\text{RR/SS}\) or \(\text{L}_3\text{RR/SS}\), resulting in the opposite CD and CPL signals and hence the weaker optical properties (Fig. 2c).

**Chiral amplification.** Strong supramolecular stereoselective control of \(\text{L}_1\) can be reflected in a series of nonlinear enhancing experiments (Fig. 3a, Supplementary Fig. 36). First of all, a pronounced deviation from linearity of CD intensity was observed for the supramolecular tetrahedral formation \([\text{L}_1\text{RR}]_n(\text{L}_\text{achiral})_{6−n}\text{Eu}_4(\text{OTf})_{12}\) \((n = 0–6)\) when there was a continuous subcomponent substitution of the achiral component \((\text{L}_\text{achiral})\), with the chiral component(s) \(\text{L}_1\text{RR}\). Due to the chiral inducing ability of \(\text{L}_1\text{RR}\), an original racemic mixture of \(\text{ΔΔΔΔ}−\text{and ΔΔΔΛ}−\text{[L}_1\text{RR}]_{6−n}\text{Eu}_4(\text{OTf})_{12}\), probably swapping from \(\text{ΔΔΔΔ}−\text{to ΔΔΔΛ}/\text{ΔΔΔΛ}/\text{ΛΛΛΛ}−\text{or ΛΛΛΛ}−\text{to ΔΔΔΛ}/\text{ΔΔΔΛ}/\text{ΔΔΔΔ}−\text{diastereomers cooperatively by substitution with an increasing amount of L}_1\text{RR}, led to the enhancement of the nonlinear effect. The addition of around 17% of \(\text{L}_1\text{RR}\) can induce ~40% of CD signal (354 nm) that arises from \([\text{L}_1\text{RR}]_{6−n}\text{Eu}_4(\text{OTf})_{12}\).

For the tetrahedral cages of \(\text{L}_2\) or \(\text{L}_3\), it is assumed that they behaved like achiral \(\text{L}_\text{achiral}\) ligand as the CD and CPL observed were very weak. Due to these observed phenomena, it was therefore interesting to further explore whether \(\text{L}_1\) can also facilitate prominent supramolecular inducing ability in

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**Fig. 4** \(^1\text{H} \)NMR titrations of \(\text{L}_1\) or \(\text{L}_2\) with \(\text{Eu}(\text{OTf})_3\) to form tetrahedral cage. **a** Variation in \(^1\text{H} \)NMR spectra of titrating \(\text{L}_1\text{SS}\) \((1.23 \times 10^{-3} \text{ M in 72:23:5, v/v/v, of CDCl}_3/\text{CD}_3\text{CN}/\text{CD}_3\text{OD})\) with \(\text{Eu}(\text{OTf})_3\) \((0.0904 \text{ M in 67:33, v/v, of CD}_3\text{CN/CD}_3\text{OD})\) at 298 K. (Ligand is shown in black. Tetrahedral cage is shown in magenta. New species is shown in blue. Solid arrow and dash arrow indicate CH\(_3\)– from the cage and ligand, respectively; peaks that are marked as i, ii, iii, iv are from the residual solvents of CHCl\(_3\), MeOH, H\(_2\)O, and MeCN, respectively.) **b** Variation in \(^1\text{H} \)NMR spectra of titrating \(\text{L}_2\text{SS}\) \((1.37 \times 10^{-3} \text{ M in 58:40:2, v/v/v, of CDCl}_3/\text{CD}_3\text{CN/CD}_3\text{OD})\) with \(\text{Eu}(\text{OTf})_3\) \((0.136 \text{ M in CD}_3\text{OD})\) at 298 K. (Ligand is shown in black. Tetrahedral cage is shown in magenta. New species is shown in blue. Solid arrow and dash arrow indicate CH\(_3\)– from the cage and ligand, respectively; peaks that are marked as i, ii, iii, iv are from the residual solvents of CHCl\(_3\), MeOH, H\(_2\)O, and MeCN, respectively.)
the tetrahedral cages based on L2 and L3. The following results showed that nonlinear enhancements were also observed for each of the supramolecular tetrahedral formation \( ([\text{L}1^{\text{RR}}]_n)_6 \cdot \text{Eu(OTf)}_2 \) (\( n = 0 \)–6) between the strong supramolecular chiral inducing ligand L1\(^{\text{RR}}\) and the weak chiral inducing ability of L2 or L3. However, a slightly different extent of nonlinear effect was found in the formation of tetrahedral cages with the use of L2\(^{\text{RR}}\) and L2\(^{\text{SS}}\), with L2\(^{\text{SS}}\) resulted in a lesser extent of nonlinear enhancement than L2\(^{\text{RR}}\) (Fig. 3d, Supplementary Fig. 37a, b). On the other hand, L3\(^{\text{RR}}\) and L3\(^{\text{SS}}\) brought about a very similar extent of nonlinear effect (Fig. 3e, Supplementary Fig. 37c, d). We believe this is a unique way of correlating the extent of the chirality effect with the nonlinear enhancement using the soldier and sergeant model.

**Luminescence measurements.** The luminescent nature of the newly synthesized Eu tetrahedral cages was investigated in solution states (Supplementary Figs. 38–43). Generally, all the Eu tetrahedral cages exhibited characteristic narrow line-like emission bands with peaks at 595, 616/619, 650, 688, and 696/705 nm corresponding to energy decay from the first excited state \( \Phi_{\text{D0}} \) to the \( \Phi_2 \) (J = 0, 1, 2, 3, 4) ground state multiplet–multiplet. The quantum yields (\( \Phi_{\text{D0}} \)) of these supramolecular tetrahedral cages relative to quinine sulphate were determined to be 0.16(1)–0.17 (1) for \([\text{Eu}(\text{L}1)_6](\text{OTf})_{12}\), 0.18(1) for \([\text{Eu}(\text{L}2)_6](\text{OTf})_{12}\) and \([\text{Eu}(\text{L}3)_6](\text{OTf})_{12}\) (Supplementary Table 3). Long excited state decays (\( \tau = 1.6 \) ms) in solution were measured at the \( \Phi_{\text{D0}} \rightarrow \Phi_2 \) transition. Low temperature (77 K) emission of the \([\text{Gd}4(\text{L}1^{\text{SS}})_6](\text{OTf})_{12}\) complex was measured as well as the lifetime (0.3 \( \mu \)s), revealing the triplet state, which confirmed energy sensitization was via the “antenna” mechanism. (Supplementary Fig. 44).

**UV and NMR titrations.** The solution state formation behavior of these supramolecular tetrahedral cages was examined by titration experiments. First, UV–Vis titration of L1\(^{\text{RR}}\) with Eu(OTf)\(_3\) in a solvent mixture of CHCl\(_3\)/MeCN/MeOH (73:24:3, v/v/v) showed a smooth evolution of a new absorption band centering at 320 nm for the supramolecular complex and simultaneous progressive disappearance of absorption bands at 281, 315, and 353 nm for the ligand (Supplementary Fig. 45a). An end point \(-0.69\) was observed at four wavelengths in a plot showing the changes of molar absorptivity as a function of total equivalents of Eu(OTf)\(_3\) (Supplementary Fig. 45b), which is consistent to the formation of a \([\text{Eu}(\text{L}1^{\text{RR}})_6](\text{OTf})_{12}\) species in solution. In the \(^1\)H NMR titration, upon addition of Eu(OTf)\(_3\), no signal at 2.56 ppm in the aliphatic region progressively emerged at the expense of the signal at 1.75 ppm (\( \Delta \Phi_L \) of L1\(^{\text{SS}}\) (Fig. 4a). After addition of 0.70 equiv. Eu(OTf)\(_3\), all the signals from the ligand disappeared, and one set of signals, which was most likely due to the stereoselective formation of one supramolecular species, was observed. Another new species, corresponding to a signal 0.76 ppm, evolved after further addition of Eu(OTf)\(_3\).

For the ligand L2, an end point of \(-0.69\) was observed with UV–Vis titrations (Supplementary Fig. 46). This projected that the formation of a \([\text{Eu}(\text{L}2^{\text{SS}})_6](\text{OTf})_{12}\) supramolecular species, a M\(_4\)L\(_6\) cage was proposed. However, the species seemed to be more sensitive to a further addition of Eu(OTf)\(_3\) as observed with the absence of plateau immediately after the end point. \(^1\)H NMR titrations also showed a complete disappearance of signals from L2\(^{\text{SS}}\), after addition of 0.70 equiv. Eu(OTf)\(_3\) (Fig. 4b). However, two sets of signals (0.07, 0.95, 2.84, and 2.94 ppm for CH\(_2\)- of complex), in \(-1:1.06\) ratio, appeared at the expense of signals from L2\(^{\text{SS}}\) (1.02 and 1.36 ppm for CH\(_3\)- of L2\(^{\text{SS}}\)). Two closely related supramolecular species were likely to be formed stereoselectively in a little bias. With continuous addition of Eu(OTf)\(_3\), a noticeable transformation to another new species was observed. For L3, no UV–Vis titration could be performed due to the limited solubility. However, some meaningful results were obtained from the \(^1\)H NMR titration of L3\(^{\text{SS}}\) with Eu(OTf)\(_3\). Although no end point could be concluded, similar to L2\(^{\text{SS}}\), the formation of two supramolecular species are proposed as shown by the presence of two sets of signals simultaneously (Supplementary Fig. 47). Another new complex was also observed when more Eu(OTf)\(_3\) was added, again formed at the expense of the original supramolecular species due to the decrease in the signals of the original species.

**Discussion**

The significant differences in NMR, CD, and CPL observations arising from the tetrahedral cage formation with ligands L1 vs. L2 or L3 can be associated to the different extent of stereoisomer formation. The resultant CD and CPL responses depend on the relative population of the two diastereomers, which in turn relies on the supramolecular stereoselective controlling ability of the ligand. Based on this hypothesis, a single tetrahedral isomer, either \([\Delta \Phi_{\text{L}}\Delta \Phi_{\text{L}}\Delta \Phi_{\text{L}}\Delta \Phi_{\text{L}}\text{Eu}_4\text{L}_4\text{L}_4\text{L}_4\text{L}_4\text{OTf})_{12}\) or \([\Lambda \Phi_{\text{L}}\Lambda \Phi_{\text{L}}\Lambda \Phi_{\text{L}}\Lambda \Phi_{\text{L}}\text{Eu}_4\text{L}_4\text{L}_4\text{L}_4\text{L}_4\text{OTf})_{12}\), is proposed to be the major form of L1; this is also justified by the single set of signals observed in \(^{13}\)C NMR and other NMR studies. The results also affirm the strong chiral inducing ability of this ligand is key to the formation of this pure stereoisomer supramolecular tetrahedral cage.

On the other hand, we have also shown that the tetrahedral cage formation process is extremely sensitive to any slight structural changes in the ligands. Significant deterioration effects on the diastereoselectivity were observed for L2 and L3. When compared with L1, L3 differs only in a slightly extended point chirality from the metal center, whereas L2 incorporated a less sterically bulky chiral moiety and in both cases very weak CD and CPL responses were obtained. In each case, two species observed based on NMR is proposed to be the co-existing diastereomeric mixtures of \([\Delta \Phi_{\text{L}}\Delta \Phi_{\text{L}}\Delta \Phi_{\text{L}}\Delta \Phi_{\text{L}}\text{Eu}_4\text{L}_4\text{L}_4\text{L}_4\text{L}_4\text{OTf})_{12}\) and \([\Lambda \Phi_{\text{L}}\Lambda \Phi_{\text{L}}\Lambda \Phi_{\text{L}}\Lambda \Phi_{\text{L}}\text{Eu}_4\text{L}_4\text{L}_4\text{L}_4\text{L}_4\text{OTf})_{12}\) with either a \( \Delta \) or \( \Lambda \) helical wrapping of the binding strands at each europium ion. The two diastereomers induced opposite CD and CPL signals in each corresponding wavelength and resulted in a weaker overall intensity of the optical signals. Furthermore, we know that L3 resulted in a slightly better supramolecular stereoselective control than L2, a phenomenon that was also reflected from the isomeric ratio in the NMR and a slightly stronger intensity in both CD and CPL for L3. Although preliminary, this suggests that steric effects have a greater influence on the diastereoselectivity for these europium tetrahedral cages than the location of point chirality.

Variable temperature \(^1\)H NMR studies also support the above hypothesis. Although different extents of dynamic motion for different protons such as antracenyl, pyridyl, aliphatic, and aromatic were found in \([\text{Eu}(\text{L}2)_6](\text{OTf})_{12}\) and \([\text{Eu}(\text{L}3)_6](\text{OTf})_{12}\), the dynamic motion for the pyridyl protons can be used to directly illustrate whether interconversion between \( \Delta \) or \( \Lambda \) occurred at the Eu center. As a higher temperature was required for the pyridyl protons of \([\text{Eu}(\text{L}3)_6](\text{OTf})_{12}\) to achieve dynamic equilibrium/coalescence, this implies that L3 possesses less rotational freedom to interconvert between \( \Delta \) or \( \Lambda \) compared to L2.

Absolution configuration of the four europium ions can be inferred by CPL analysis. For \([\text{Eu}(\text{L}1)_6](\text{OTf})_{12}\), a very similar CPL spectrum was observed when the corresponding monomeric complexes with the same chiral substituent were compared\(^{37}\). This implies that the absolution configurations (\( \Delta / \Lambda \)) or helical twists (\( P / M \)) at the Eu ions of the supramolecular complexes are the same as those of the monomeric complexes\(^{34, 38}\). Hence, a \( \Lambda \),...
ΔΔΔΔ and ΔΔΔΔΔ configuration is proposed for [Eu₄(L₁RR)₆] (OTf)₁₂ and [Eu₄(L₃RR)₆](OTf)₁₂ respectively. A similar correlation of the CPL results associating to the absolute configuration has been successfully employed to Eu(III) triple stranded helicates in prior reports 39.

For the chiral amplification experiment, a nonlinear effect of CD response with % of chiral ligand, L₁RR, was observed for the supramolecular tetrahedral formation \([\{(\text{L}_{1}\text{RR})_n (\text{L}_{1}\text{RR})_{6-n}\text{Eu}_4(\text{OTf})_{12}\}]_n\), \(n = 0-6\). A similar nonlinear enhancement of chiral response has been reported for subcomponent substitution in transitional metal-based M₃L₆ cage 39 or hydrogen-bonded assembly 39. However, this phenomenon is rarely known for lanthanide supramolecular complexes. This observation may imply that the presence of prominent cooperative stereochemical coupling between each stereogenic metal center may be the major factor leading to the nonlinear enhancement induced by \(\text{L}_{1}\text{RR}\). For opposite isomers \(\text{L}_{2}\text{SS}\) and \(\text{L}_{3}\text{SS}\), this resulted in a different extent of nonlinearity, whereas \(\text{L}_{1}\text{RR}\) and \(\text{L}_{3}\text{RR}\) led to a similar nonlinear effect. It is postulated that these observations may be attributed to the different relative positions of asymmetric centers for \(\text{L}_{2}\) and \(\text{L}_{3}\). In supramolecular cage formation with \(\text{L}_{1}\text{RR}\) and \(\text{L}_{2}\), which possess the same relative position of asymmetric centers, their asymmetric methyl substituents may be located at a very close spatial arrangement from the nearby ligands at the same vertex, therefore leading to sensitivity to the \((\text{R})\) - and \((\text{S})\)-configuration for \(\text{L}_{2}\). On the contrary, the relative position of asymmetric centers for \(\text{L}_{3}\) is one carbon away from the metal centers at each vertex compared with \(\text{L}_{1}\text{RR}\) in the formation of the supramolecular cage. The difference in steric bulkiness from the chiral center may not be significant, hence resulting in similar nonlinear effect for \(\text{L}_{1}\text{RR}\) or \(\text{L}_{3}\text{SS}\).

Observations from UV–Vis absorption and NMR titrations suggest specific formation of one (for \(\text{L}_{1}\)) or two very similar supramolecular species (for \(\text{L}_{2}\) and \(\text{L}_{3}\)) in solution state by titrating Eu(OTf)₃ to a solution of each corresponding \(\text{L}\). In UV–Vis titration, the simultaneous growth of a new absorption band and the decrease in the absorption for \(\text{L}\) suggest the existence of only the uncoordinated ligand and its supramolecular cage(s) (Supplementary Figs. 45 and 46), which corroborates with NMR titrations in which a single set of signals from \(\text{L}_{1}\) (Fig. 4a) and two sets of chemical shifts from \(\text{L}_{2}\) (Fig. 4b) and \(\text{L}_{3}\) (Supplementary Figs. 47) were observed. The similarity of the two species observed for \(\text{L}_{2}\) or \(\text{L}_{3}\) is supported by the similar observation of one dominant diffusion coefficient from the DOSY analyses. In UV–Vis and NMR titrations, end-points of ~0.7 Eu/L were also observed, further supporting the topology of the tetrahedral cage, \([\text{Eu}(\text{L}_{1})_n](\text{OTf})_{12}\).

The relative quantum yields (φₑₒ) of the supramolecular tetrahedral cages were found to be surprisingly high, ranging from 16(1) to 18(1)%. To the best of our knowledge, these values are the highest among the rarely reported \(\text{L}_{1}\text{RR}\). In contrast, the experimentally observed quantum yields are smaller than the theoretical values 39 of lanthanide complexes, therefore two standards matching the excitation and emission regions separately were used to cross-check the quantum yields of our complexes.

Syntheses.

All the new compounds were fully characterized. Experiment details and characterization are given in Supplementary Methods.

Luminescence measurements. Single-photon luminescence spectra were recorded using an Edinburgh Instrument FLS920 spectrophotometer that was equipped with a Xe900 continuous xenon lamp, a µPL920 microsecond flashlamp and single-photon counting Photomultiplier Tube. The excitation and emission spectra recorded on the FLS920 were corrected with the correction file from the F900 software. Unless otherwise noted, all measurements were performed in triplicates.

Quantum yield measurements. An ideal quantum yield standard should exhibit similar excitation and emission regions with the sample of interest, however, the Stokes shifts of commonly used organic fluorophores are smaller than the Richardson shifts 42 of lanthanide complexes, therefore two standards matching the excitation and emission regions separately were used to cross-check the quantum yields of our complexes.

Standard 1:43 Quinine sulfate in 0.1 M sulfuric acid (Φ = 0.577, λₑₒ = 350 nm). Standard 2:43 Ca₃[Eu(dpa)₂] in 0.1 M Tris-HCl (Φ = 0.240, λₑₒ = 279 nm).

Absorption and emission spectra of the standard were measured at five or more absorbances within 0.1 in a 10 mm fluorescent quartz cuvette. A graph of integrated fluorescence intensity vs absorbance was plotted to give a straight line with gradient. The above procedure was repeated for the \([\text{Eu}(\text{L}_{1})_n](\text{OTf})_{12}\). The related quantum yields were calculated according to the Eq. (1).

\[
\Phi = \Phi_0 \left( \frac{1}{\text{Grad}_{\lambda_{ex}}} - \frac{1}{\text{Grad}_{\lambda_{em}}} \right) \left( \frac{\eta_2}{\eta_1} \right)
\]

Where ST and X are standard sample and test sample, respectively. Grad is the refractive index of the solvent. Three independent samples were measured and the errors were then estimated.

Circular dichroism. CD measurements were performed with a Jasco J-810 spectropolarimeter. Hellma quartz cuvettes (1 mm path length) were employed. All spectra were baseline subtracted with the blank solvent. Three independent samples of \([\text{Eu}(\text{L}_{1})_n](\text{OTf})_{12}\) and \([\text{Y}(\text{L}_{1})_n](\text{OTf})_{12}\) were measured.
Circularly polarized luminescence. CPL measurements were conducted on a custom-built spectrometer (in Durham University) with a laser light source (Emergent Photonics Ltd, Q-switched Nd:YAG laser, 1064 nm) coupled to an Acton SP2150 monochromator (600 g/nm, 300 nm Blaze) that allows selection of the excitation wavelengths (6 nm FWHM band-pass). The collection of the emitted light was aided by a Lock-In Amplifier (Hinds Instruments Signaloc 2100) and Photostatic Modulator (Hinds Instruments PEM-90 controller and Hinds Instruments Series 80A) with the use of a 5-cm path length quartz cuvette. The differentiated light was focused onto an Acton SP2150 monochromator (1200 g/nm, 500 nm Blaze) equipped with a high sensitivity cooled Photo Multiplier Tube [H11723-20 Extended red-multalkali PMT based photomultiplier (5 V, coated)] in a range of 370–720 nm (0.5 nm spectral intervals) using a five spectral average sequence and 500 µs integration time. Three independent samples of [Eu(Ln)](OTf)3 were measured.

Chiral amplification. The stock solutions of Lchiral (0.00123 M) and LR1 (0.00123 M) solution B were prepared in a solvent mixture of CH2Cl2/MeOH/MeCN = 73:23:4. The stock solution of Eu(OTf)3 (0.00659 M) was prepared in MeOH. For each experiment, a total volume of 8 ml solution was mixed from each component. For each experiment, triplicate measurements were performed to estimate the error. In AmpliChem, a total volume of 1.5 mL of each solution was added and then mixed thoroughly. An aliquot of 1.5 mL of each solution was stored in a 60 °C water bath for 24 h. After cooling at room temperature for 2 h, the solutions were checked by CD spectroscopy directly without any further dilution. In the experiments, triplicate measurements were performed to estimate the error.

Single crystal X-ray diffractions. Data for [Eu(L1L2)],6(OTf)12 were collected on beamline 11.3.1 at the Advanced Light Source, using a Bruker D8 diffractometer equipped with a PHOTON II CPAD detector operating in shutterless mode. The crystal was coated in protective oil prior to being mounted on a MiTeGen kapton loop. A total volume of 8 ml solution was mixed from each component. For each experiment, triplicate measurements were performed to estimate the error. The thermal ellipsoids of the majority of the pendant ethylbenzene groups have been re

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Author contributions
G.-L.L. conceived and supervised the project. G.-L.L. also supervised and assisted with the photophysical measurements. C.-T.Y. performed the synthesis of the compounds and the majority of the measurements. K.H.Y. performed the circular dichroism measurements. R.P. performed the CPL measurements. D.Y. collected and solved the preliminary crystal structure. W.-S.L. performed some of the luminescent measurements. S.-C.Y. performed some of the NMR measurements. M.Y.-M.W. performed some of the MS experiments. D.E.S., L.J.M., S.J.T. and D.K.S. are responsible for the collection and solving and optimization of the final crystal structures. H.Y.W. was involved with the crystal structural analysis work. W.-T.W., C.-T.Y. and G.-L.L. co-wrote the manuscript.

Additional information

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