Tuning the photophysical properties of luminescent lanthanide complexes through regioselective antenna fluorination†

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Carbostyrils monofluorinated in the 3, 5, or 6 positions were synthesised from olefinic precursors via a photochemical isomerisation-cyclisation route, and incorporated into octadentate cyclen triacetate ligands that formed luminescent complexes with Tb(III) and Eu(III). The photophysical properties of the emitters were strongly dependent on the position of the fluorination.

The luminescence of the trivalent lanthanide (Ln) ions is applied in diverse biological and industrial settings ranging from the monitoring of the components of living cells to the thermometric analysis of materials.1,2 Ln(III) luminescence is often sensitised by a light-harvesting antenna to avoid the need for direct excitation of the Laporte-forbidden 4f–4f transitions.3 Optimisation of energy transfer (EnT) to the Ln(III) and elimination of processes that quench the antenna and Ln(III) excited states are essential for bright emitters.

Photoinduced electron transfer (PeT) from the excited antenna to Ln(III) is feasible for several Lns,4,5 and for Eu(III) emission it can be an effective luminescence quenching process.6 PeT is suppressed when the antenna is less reducing. Antenna substitution with electron-withdrawing groups (e.g. with CF3, Fig. 1)4,5 or protonation7,8 can increase the Eu(III) luminescence quantum yield, but may have unintended consequences on the antenna excited state energies.5,9,10 Ln sensitisation commonly takes place via the antenna singlet (S1) and triplet excited states (T1). Even subtle changes to the antenna may alter the S1 and T1 energies and EnT. In the previous examples both antenna trifluoromethylation4,5 and protonation proved detrimental to Tb(III) emission.6

Here, we have prepared three monofluorinated 7-aminocarbostyril regioisomers. Electronegative fluorine was expected to decrease PeT by making the antenna less reducing, a strategy that complements the use of C–F bonds to replace the more efficiently quenching C–H oscillators.11 Fluorination has additional potential benefits. Fluorine is a hydrogen isostere conferring metabolic stability, H-bond acceptor ability, and altered lipophilicity on pharmaceuticals.12 Diagnostic applications of fluorinated probes include multimodal13 and responsive14 systems.19F-MRI is a promising low-background technique,15 and 18F is an attractive PET label.16,17

Fluorinated carbostyrils were incorporated into do3a (1,4,7,10-tetraazacyclododecane-1,4,7-triacetate)-based octadentate ligands to enable comparison with previously reported structures.4,5 The Eu(III), Tb(III), and Gd(III) chelates of the ligands were characterised using 1H NMR spectroscopy, cyclic voltammetry, and UV-vis absorption and steady-state and time-resolved emission spectroscopies. Our results show fluorination meaningfully impacts the antenna and Ln(III) photophysical properties, and substitution at a remote antenna position could even influence the excited state behaviour of the Ln(III).

Fluorinated antennae were synthesised as shown in Scheme 1 and Schemes S1–S6 (ESI†). The procedures were

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Fig. 1 Decreased PeT quenching of Eu(III) luminescence through antenna substitution with electron-withdrawing group(s) (EWG), and its effects on the S1 and T1 energies.
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robust, scalable (e.g. 466 mg of CSF was obtained in one experiment), and reproducible. Olefins S were prepared from commercially available starting materials as the Z isomers with excellent selectivity due to the steric clash between the ester group and the aromatic ring.18 The stereochemical assignment was based on the JHH = 33–38 Hz and JHH = 15–16 Hz coupling constants. The key photochemical olefin isomerisation-cyclisation was carried out by irradiating a 100 mM solution in MeOH or EtOH with 254 nm-UV light, giving CSF, CSF, and CSF in good to excellent yield. Regioisomer identities were confirmed by 1D and 2D NMR spectroscopy and single-crystal X-ray crystallography (Fig. S1–S6 and Tables S1–S3, ESI†). The key photochemical olefin isomerisation-cyclisation was carried out by irradiating a 100 mM solution in MeOH or EtOH with 254 nm-UV light, giving CSF, CSF, and CSF in good to excellent yield. Regioisomer identities were confirmed by 1D and 2D NMR spectroscopy and single-crystal X-ray crystallography (Fig. S1–S6 and Tables S1–S3, ESI†). The analogous CSF could not be accessed via similar routes due to the instability of the intermediates (Schemes S3–S5, ESI†). CS/CSF was acetylated with Ac2O or chloroacetyl chloride to yield reference compounds AcCS/AcCSF, or the reactive antennae 6, respectively. 6 were incorporated into LnL (Ln = Gd, Eu, Tb) using procedures previously developed for similar compounds. Synthetic details, compound characterisations, and the attempted syntheses of CSF are given in the ESI.1 Analytical data were fully consistent with the assigned structures.

Solution structures of EuL were studied by paramagnetic 1H and 19F NMR spectroscopy. In CD3OD at r.t. the 1H NMR spectra of EuL, EuL, EuL, and EuL, were similar (Fig. S7–S10, ESI†). The major isomer had square antiprismic geometry (4 peaks at > 32 ppm). Trace amounts of the twisted square antiprismic isomer were also present (signals at 12–16 ppm). 19F NMR spectra supported this interpretation, showing a single peak at −133.8, −118.8, and −134.1 ppm for EuL, EuL, and EuL, respectively (Fig. S11–S13, ESI†). These data are consistent with the ligands imposing similar geometries on the Ln(n) ions in solution, and is similar to what has been observed for other do3a-complexes carrying carboxylate antennae.6 This was expected as fluorine is small, and the fluorination sites are quite distant from the Ln(n).

The photophysical properties of CS and CSF were recorded in acetonitrile due to their low aqueous solubility. The lowest-energy bands in the absorption spectra were assigned to π-π* transitions, and were located at 320–360 nm with λmax = 335, 332, and 339 nm for CSF, CSF, and CSF, respectively (Fig. S18–S22, ESI†), non-fluorinated CS had λmax = 337 nm. CS, CSF, and CSF excitation at λmax resulted in fluorescence emission maxima at λem = 384, 400, 387, and 382 nm, respectively (Table 1 and Fig. S23–S27, ESI†). CSF had the highest fluorescence quantum yield, φFL = 56%. Fluorination in the 5-position had minimal effect on φFL, compared to CS (φFL = 25 and 27%, respectively), while substitution in the 6-position lowered φFL to 10%. CSF fluorescence lifetimes (τFL) mirrored the observations made for φFL (Table 1). CSF had the longest τFL (2.84 ns), and CSF the shortest, τFL = 0.41 ns. CS and CSF had very similar τFL, 1.15 and 1.09 ns, respectively (Table S5 and Fig. S49–S56, ESI†).

LnL absorption spectra were collected in aqueous solutions (0.01 M PIPES buffer, pH = 6.5). Absorption maxima were blue-shifted relative to the corresponding CS with λmax = 325, 327, 337, and 330 nm for LnL, LnL, LnL, and LnL, respectively (Fig. 2 and Fig. S28–S32, ESI†). In aqueous PIPES buffer (10 mM), pH 6.5, at 10 μM complex concentrations.

Table 1 Photophysical properties of CS, CSF, and GdL. a, b

| Compound | λmax (nm) | λem (nm) | S1 (cm−1) | τFL (ns) | φFL (%) |
|----------|-----------|-----------|------------|----------|---------|
| CS       | 337       | 384       | —          | —        | 27      | 1.15 (5) |
| CSF      | 335       | 400       | —          | —        | 56      | 2.84 (6) |
| CSF      | 332       | 387       | —          | —        | 25      | 1.09 (2) |
| CSF      | 339       | 382       | —          | —        | 10      | 0.41 (6) |
| GdL      | 330       | 369       | 28700     | 22500    | 7.6     | 0.34 (3) |
| GdL      | 325       | 364       | 29200     | 22100    | 13      | 0.60 (5) |
| GdL      | 327       | 367       | 28900     | 22400    | 6.1     | 0.44 (8) |
| GdL      | 337       | 380       | 28100     | 22300    | 5.9     | 0.36 (4) |

a In acetonitrile at 10 μM concentration. b In aqueous PIPES buffer (10 mM), pH 6.5, at 10 μM complex concentrations. c Δν = 332 nm (CSF), 331 nm (CSF), 338 nm (CSF), 335 nm (GdL), 325 nm (GdL). d Calculated from the 0–0 transitions of the Gd-complexes recorded at 77 K. e Relative to quinine sulfate (Φ = 0.59) in H2SO4 (0.05 M).23
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Fig. 2 Normalised absorption (grey, 298 K), excitation [blue, \( \lambda_{\text{em}} = 380 \text{ nm} \) (GdL\(6^\text{F} \)), \( \lambda_{\text{em}} = 364 \text{ nm} \) (GdL\(3^\text{F} \)), \( \lambda_{\text{em}} = 546 \text{ nm} \) (Tb), \( \lambda_{\text{em}} = 615 \text{ nm} \) (Eu), 298 K], steady-state emission at 298 K [black, \( \lambda_{\text{em}} = 335 \text{ nm} \) (LnL\(6^\text{F} \)), \( \lambda_{\text{em}} = 325 \text{ nm} \) (LnL\(3^\text{F} \))], steady-state emission at 77 K [purple, \( \lambda_{\text{em}} = 335 \text{ nm} \) (LnL\(6^\text{F} \)), \( \lambda_{\text{em}} = 325 \text{ nm} \) (LnL\(3^\text{F} \))], and time-resolved emission [green (Tb), red (Eu), \( \lambda_{\text{em}} = 335 \text{ nm} \) (LnL\(6^\text{F} \)), \( \lambda_{\text{em}} = 325 \text{ nm} \) (LnL\(3^\text{F} \))], 298 K spectra of LnL\(6^\text{F} \).

Exitation of TbL and EuL at \( \lambda_{\text{max}} \) yielded green and red Ln(III) luminescence, respectively (Fig. 2 and Fig. S37–S44, ESI,† Table 2), with residual antenna fluorescence. TbL had slightly lower \( \Phi_{\text{L}} \) than the analogous GdL likely due to some antenna S1-mediated EnT to Tb(III). EuL had drastically diminished \( \Phi_{\text{L}} \), which may be due to a combination of EnT from S1, and depopulation of S1 by PeT. AcCS\(6^\text{F} \), oxidation potentials (\( E_{\text{ox}} \)) were found by cyclic voltammetry as +1.73, +1.86, and +1.77 V (vs. NHE, for AcCS\(3^\text{F} \), AcCS\(5^\text{F} \), and AcCS\(6^\text{F} \), respectively); only 5-fluorination made antenna oxidation more difficult than in AcCS (\( E_{\text{ox}} = +1.81 \) V). PeT was calculated to be slightly less thermodynamically favoured in EuL\(3^\text{F} \), and EuL\(6^\text{F} \) than in EuL\(1^\text{H} \), and more favoured in EuL\(3^\text{F} \) (\( \Delta G(PeT) = -1.01, -1.14, -0.98, \) and −0.97 eV, for EuL\(1^\text{H} \), EuL\(3^\text{F} \), EuL\(5^\text{F} \), and EuL\(6^\text{F} \)), respectively (see ESI† for details). Thus, the effects of fluorination on the antenna S1, T1 and \( E_{\text{ox}} \), and in turn on \( \Delta G(PeT) \) can be difficult to predict.

**Table 2** Photophysical properties of LnL\(6^\text{F} \) (Ln = Eu, Tb) and \( \tau_{\text{rad}}, \Phi_{\text{rad}}^L, \Phi_{\text{rad}}^{\text{sen}} \) and \( \eta_{\text{sen}} \) EuL\(6^\text{F} \)

| LnL\(6^\text{F} \) | \( \Phi_{\text{L}}^\text{en} \) (%) | \( \tau_{\text{B}} \) (ns) | \( \Phi_{\text{rad}}^L \) (%) | \( \tau_{\text{rad}} \) (ms) | \( \Phi_{\text{rad}}^{\text{sen}} \) (%) | \( \eta_{\text{sen}} \) (%) |
|-----------------|---------------------|-----------------|-----------------|-----------------|---------------------|-----------------|
| TbL\(1^\text{H} \) | 5.1 (67%) | 0.21(4) | 22.5 | — | — | — |
| TbL\(3^\text{F} \) | 8.1 (63%) | 0.39(2) | 5.6 | — | — | — |
| TbL\(5^\text{F} \) | 4.6 (75%) | 0.36(3) | 21.7 | — | — | — |
| TbL\(6^\text{F} \) | 4.6 (75%) | 0.25(4), 2.40(3) | 16.7 | — | — | — |
| EuL\(1^\text{H} \) | 0.261 (3.4%) | — | 4.34 | 5.18\(a \), 4.73\(b \) | 11.9\(f \), 13.1\(h \) | 36.2\(f \) |
| EuL\(3^\text{F} \) | 0.680 (5.3%) | 0.93(6), 0.42(5) | 1.09 | 9.25\(e \), 5.10\(b \) | 6.7\(f \), 12.3\(h \) | 16.1\(f \) |
| EuL\(5^\text{F} \) | 0.814 (13%) | 0.47(6), 1.76(5) | 5.05 | 5.25\(e \), 5.11\(b \) | 11.5\(f \), 11.8\(h \) | 43.4\(f \) |
| EuL\(6^\text{F} \) | 0.207 (3.5%) | 0.20(1), 2.85(3) | 5.10 | 5.28\(e \), 5.19\(b \) | 11.6\(f \), 11.8\(h \) | 43.8\(f \) |

\( a \) LnL\(1^\text{H} \) = 10 \( \mu \)M in 10 mM PIPES buffered H\(2\)O, pH 6.5. \( b \) Determined using the method in ref. 26, \( \ln _{\text{rad}}/\ln _{\text{exc}} \); integral ratio of total Eu-centred corrected emission spectrum (570–800 nm) and \( D_{\text{LnL}} \rightarrow T_2 \) band (582–603 nm), \( \text{AMU} = 14.65 \text{ s}^{-1} \), \( n = 1.333 \) (refractive index).\( ^{27} \) \( \tau_{\text{B}} = \tau_{\text{rad}} \).

\( ^* \) Relative to quinine sulfate (\( \Phi = 0.59 \)) in H\(2\)SO\(4 \) (0.05 M).\( ^{23,24} \) In parentheses; compared to GdL analogue. \( ^* \) Biexponential fit better based on \( \chi^2 \).

\( ^{a} \) Too short to measure. \( ^{b} \) Calculated from the steady-state emission spectra. \( ^{h} \) Calculated from the time-resolved emission spectra.

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The Ln(n) luminescence lifetimes ($\tau_{1230}$) were measured by time-resolved emission spectroscopy. The decays were monoexponential. $\tau_{1230}$ values varied for Ln = Tb but were almost identical for all EuL5F ($\approx 0.61$ ms) (Table S4, ESI†). The number of Ln(n)-bound water molecules ($q$) were $q = 1$ for EuL5F. Deviations for TbL5F from $q = 1$ could be due to BET, which makes this method inapplicable,\textsuperscript{24,25} or the result of the typical error of $q \pm 0.5$.

TbL5F and TbL4H had the highest Tb-centred luminescence quantum yields ($\phi_{\text{Ln}}$) = 21.7% and 22.5%, respectively, values identical within experimental error). The low $\phi_{\text{Ln}}$ of TbL5F is presumably the result of BET. EuL5F and EuL5H had $\phi_{\text{Ln}}$ = 5%, which is higher than most Eu(n) complexes with similar structures, i.e. uncharged do3a-based emitters with secondary amide-linked carbostyril antenna, including EuL4H ($\phi_{\text{Ln}}$ = 4.34%). EuL5F, however, had low $\phi_{\text{Ln}}$ = 1.09%. Unlike TbL5F, EuL5F does not suffer from BET, therefore, an alternative explanation for the poor performance of this emitter was necessary.

$\phi_{\text{Ln}}$ is the product of the intrinsic quantum yield of the Ln(n) ($\phi_{\text{Ln}}^{\text{obs}}$) and the Ln(n) sensitisation efficiency ($\eta_{\text{sens}}$ eqn (1)), i.e. the efficiency of Ln(n) excited state population. For Eu$\mu$(n) $\phi_{\text{Ln}}^{\text{obs}}$ can be determined from the corrected emission spectrum.\textsuperscript{26}

$$\phi_{\text{Ln}} = \eta_{\text{sens}} \cdot \phi_{\text{Ln}}^{\text{obs}} = \eta_{\text{sens}} \frac{\tau_{\text{obs}}}{\tau_{\text{rad}}}$$

In EuL5F and EuL4H $\eta_{\text{sens}}$ is increased compared to EuL4H, presumably due to a combination of the small adjustments in spectral overlap and PeT quenching. EuL4H had markedly lower $\eta_{\text{sens}}$ and $\phi_{\text{Ln}}^{\text{obs}}$ than the other EuL (Table 2). The steady-state and time-resolved EuL5F emission spectra have different shapes. Eu(n) spectra are sensitive to coordination environment, and these differences indicate the presence of several emissive species.\textsuperscript{21} The signal of the slow-decaying component dominating the time-resolved spectrum resembles the EuL5F/EuL4H/EuL4H spectra. Contribution from the fast-decaying species modifies the steady-state EuL5F spectrum. If $\tau_{\text{obs}}$ is assumed unchanged, the steady-state spectral shape yields a lower overall $\phi_{\text{Ln}}^{\text{obs}}$ (Table 2). The spectrum of TbL5F is similarly time-dependent, but not those of Eu/TbL5F and Eu/TbL4F. The reasons for the diminished $\eta_{\text{sens}}$ of EuL5F are unclear. PeT is more favoured in EuL5F than in EuL3F and EuL6F, and EuL6F have much lower $\phi_t$ than the corresponding GdL5F, which is consistent with PeT quenching. The $h_{\text{t}}$ of EuL5F and GdL5F, however, cannot be compared directly. The biexponential decay of the EuL5F antenna fluorescence suggested the presence of additional emitters to those seen in GdL5F. Further work is therefore needed to understand the effect of fluorination on EuTf and PeT.

In conclusion, monofluorinated 7-aminocarbostyrils, obtained via a photochemical cyclisation, were competent sensitizers of Eu(n) and Tb(n) emission. The position of the fluorine had a dramatic impact on the antenna and Ln(n) photophysical properties, rendering the emission oxygen-sensitive (TbL3F, TbL4H), and increasing (EuL3F, EuL6F), or decreasing $\phi_{\text{Ln}}^{\text{obs}}$ (TbL3F, TbL4H, EuL5F) compared to non-fluorinated LnL4H. 5-Fluorination improved Eu(n) emission without negatively impacting Tb(n) luminescence. Remote fluorination influenced the excited-state behaviour of LnL4H. Work towards the 4-fluorinated isomer, and ligands containing other EWGs than fluorine is ongoing.

D. K. did all experiments except the crystallographic analysis, which was done by A. O. K. E. B. designed the project, secured funding, and supervised the work. All authors contributed to data analysis and manuscript writing.

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Conflicts of interest
There are no conflicts to declare.

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