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Synthesis, stereocontrol and structural studies of highly luminescent chiral tris-amidepyridyl-triazacyclononane lanthanide complexes†

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The configuration of the remote amide chiral moiety determines the helicity of the metal complex in Ln(III) complexes of nonadentate N_6O_3 ligands based on triazacyclononane. Solution NMR studies revealed the presence of a dominant isomer whose proportion varies from 9 : 1 to 4 : 1 from Ce to Yb and X-ray crystallographic studies at 120 K of the Yb and two enantiomeric Eu complexes confirmed the configuration as *S*-Δ-λ in the major isomer. Global minimisation methods allowed magnetic susceptibility and electronic relaxation times of the lanthanide ions to be estimated by analysis of variable field longitudinal relaxation rate (R_1) data sets. A set of four europium complexes, containing different *para*-substituted pyridinyl-aryl groups, exist as one major isomer (15 : 1), and absorb light strongly *via* an ICT transition in the range 320 to 355 nm (ε = 55 to 65 000 M^{-1} cm^{-1}). The two examples absorbing light at 332 nm, possess overall emission quantum yields of 35 and 37% in aerated water, making these systems as bright as any Eu complex in solution.

Introduction

Triazacyclononane is a small macrocycle that is easily functionalised to generate hexadentate and nonadentate ligands that give rise to thermodynamically and kinetically stable metal complexes of the d and f block elements.[1–6] The ring nitrogen atoms act as donors and have been substituted with carboxylate, phosphonate, phosphinate, phenolate, thiolate and substituted pyridyl moieties to form a large family of well-defined C_3 symmetric complexes. Initial work concentrated on tricarboxymethyl systems[2b,3] and related triphosphinate complexes have also been examined, for example with the late d-block elements and In(III) and Ga(III).[1j,2a] Nine coordinate tris-pyridylcarboxylate triazacyclononane complexes of Ln(III) ions have been reported by Latva, Mazzanti and co-workers,[1d–g] and were shown to exist in the solid state in a tri-capped trigonal prismatic coordination geometry. More recent variants include a series of tri-pyridylphosphinate systems that define an isostructural series across the lanthanide block.[4,5]

The hexadentate or nonadentate complexes in C_3 symmetry exist as Δ or Λ isomers, as revealed by the sign of the NCXY torsion angle, where the nature of X and Y is defined by the constitution of the ligating moiety.[7] A number of strategies exist that allow the preparation of enantiopure complexes. For example, such complexes can be synthesised through incorporation of a remote chiral centre within the ligand framework. Introduction of a stereogenic centre may occur on the macrocyclic ring[8,9] or in the ring N substituent, leading to preferential stabilization of a particular stereoisomer. Complexes with Δ or Λ configuration are formed with partial or total stereocontrol. This approach was recently studied for the ring C-substituted series of lanthanide complexes with pyridyltricarboxylate or triphosphinate donors.[8] Complete stereochemical control has also been achieved in 9-coordinate cationic lanthanide complexes, $[Ln{\cdot}L(H_2O)]^{3+}$, based on 12-N_4 tetraamide ligands in C_4 symmetry. The stereogenic centre at carbon was derived from a precursor enantiopure amine, such as α-methylbenzylamine.[10]

In this work, we have set out to prepare ligand L^1 using a similar stereochemical approach, in order to assess the degree of stereocontrol in lanthanide complex formation. By analogy with recent work, the related ligands $L^{2a–d}$ were also prepared, as the introduction of the aralkynyl moiety greatly enhances the absorption characteristics of the ligand and permits efficient sensitization of Eu emission.[6] Furthermore, these complexes, and their derivatives, are attractive candidates as the basis of probes for circularly polarised emission studies, and this work underpins the development of new luminescent chiral probes.[7,11–13] In addition, their coordination chemistry

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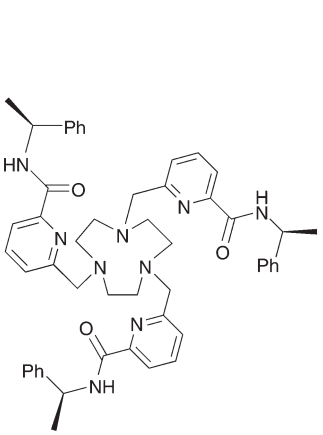
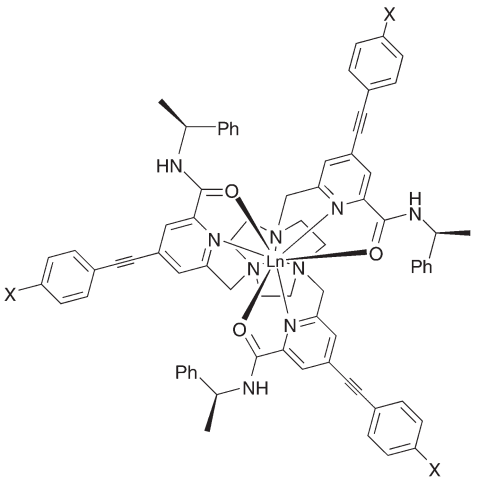
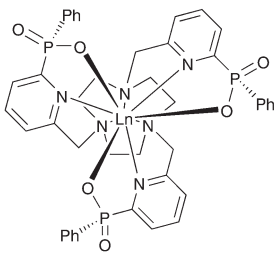
can be directly compared to the kinetically stable triphosphinate, tricarboxylate and tris-diethylcarboxamide analogues, [Ln·L^{3,4,5}],[6,1e,g] allowing us to deepen our understanding of ligand field effects in lanthanide complexes of high symmetry.



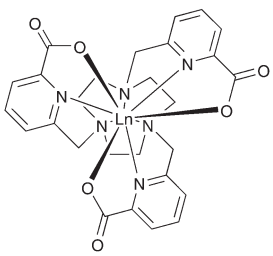
(*S*)-L^1



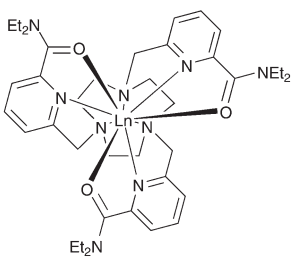
(*S*)-[LnL^{2a}], X = H
[LnL^{2b}], X = CO_2Me
[LnL^{2c}], X = OMe
[LnL^{2d}], X = NHCOMe



[Ln.L^3]



[Ln.L^4]

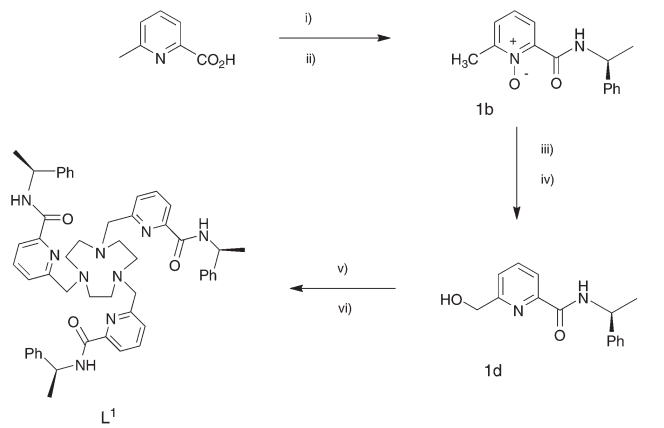


[Ln.L^5]$^{3+}$

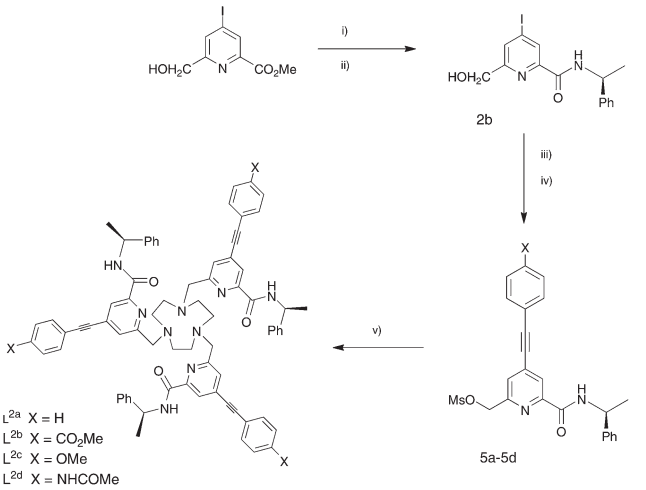
Results and discussion

Ligand and complex synthesis

The parent ligand L^1 was prepared in six steps from commercially available precursors (Scheme 1). The amide coupling reaction of 6-methylpyridine-2-carboxylic acid with *S*-α-methylbenzylamine[14] afforded the desired amide *S*-1a, in good yield. The amide, *S*-1a was treated with *m*CPBA in chloroform to give the *N*-oxide in 83% yield. The *N*-oxide, 1b, was subsequently transformed to a 6-acetoxymethyl-pyridine derivative using acetic anhydride at 120 °C. This rearrangement reaction was followed by ester solvolysis, catalysed by ethoxide, to furnish the alcohol, *S*-1d, in 85% yield. Mesylation under standard conditions gave *S*-1e, which was used directly in the next step without further purification. Alkylation of 9-N_3 was carried out using the crude mesylate in acetonitrile in the presence of K_2CO_3. A mixture of mono-, di- and trialkylated products was obtained and was separated by column chromatography on neutral alumina. The di- and tri-substituted *S*-L^1 ligands were isolated in yields of 22% and 55% respectively. The enantiomeric ligand *R*-L^1 was made by an identical pathway, and their



Scheme 1 (i) *S*-PhCHMeNH$_2$/EDC/DIPEA/HOBt/DMF; (ii) *m*CPBA/$CHCl_3$; (iii) Ac_2O/Δ; (iv) EtOH/cat. NaOEt; (v) MsCl/Et_3N/THF; (vi) K_2CO_3/MeCN/9-N_3.



Scheme 2 (i) NaOH/EtOH/H_2O; (ii) *S*-PhCHMeNH$_2$/EDC/DIPEA/HOBt/DMF-CH_2Cl_2; (iii) Pd(dppf)Cl_2/CuI/NEt_3/X-Ph-CCH/THF; (iv) MsCl/Et_3N/THF; (v) K_2CO_3/MeCN/9-N_3.

lanthanide complexes were made by reaction with one equivalent of the lanthanide triflate salt in dry MeCN. Trituration with cold ether yielded the lanthanide complexes *S*-[LnL^1]-$(CF_3SO_3)_3$ in quantitative yield (Ln = Ce, Pr, Nd, Eu, Gd, Tb, Dy, Ho, Er, Tm, Yb).

For the synthesis of $L^{2a–d}$, a five-step synthetic route was devised (Scheme 2) beginning with preparation of the monohydroxymethyl *p*-iodo mono-carboxylic acid. Formation of the amide bond proved slightly troublesome, but by stirring the coupling reagents, base and amine in a solvent mixture of DCM–DMF (1 : 1) followed by slow, dropwise addition of the carboxylic acid, the amide, *S*-2b, was formed in reasonable yield (58%). The alkynes, *S*-4a–d, were synthesised by a Sonogashira cross-coupling reaction between the *p*-iodopyridyl amide, 2b, and various *p*-substituted aralkynes, using catalytic Pd(dppf)Cl_2 and CuI in degassed THF. Mesylation followed by alkylation of 9-N_3 were carried out using standard conditions to give *S*-$L^{2a–d}$. Complexation with Eu(OTf)$_3$ in acetonitrile at 80 °C gave the triflate salt of the europium complexes, *S*-[Eu$L^{2a–d}$]$(CF_3SO_3)_3$, following trituration with cold ether.

Structural analysis of Eu and Yb complexes of L^1

Crystals of [LnL^1]$(CF_3SO_3)_3$ grew readily from aqueous methanol (1 : 1). The complexes *R*-[EuL^1]$(CF_3SO_3)_3$ and *S*-[EuL^1]-$(CF_3SO_3)_3$ crystallize in the trigonal space group *R*3. Crystallographic analysis of *S*-[YbL^1]$^{3+}$ revealed that it was isostructural with the Eu complexes, strongly suggesting that the series of lanthanide complexes of L^1 would also adopt a common structure, at least from Eu to Yb, as has been verified for [Ln·L^3] and [Ln·L^4]. The anions were slightly disordered, and a severely disordered solvent molecule was present in each structure. The lanthanide ion is coordinated by the three N atoms of the macrocyclic ring, each pyridyl N and the amide O atoms. A C_3 axis passes through the metal atom and the centre of the macrocyclic ring (Fig. 1).

Analysis of the lengths of the lanthanide-donor atom bonds, compared to the values reported for [Ln·L^3][4,5] revealed longer Ln–O and Ln–N_{py} bonds, as expected with a neutral amide donor, and a shorter Ln–N distance, indicating that the Ln ion is sitting closer to the plane of the N_3 ring (Table 1). The complexes each adopted a distorted tricapped trigonal prism structure. The distortion angle is defined by the twist of the mean plane of the 9-N_3 ring with reference to the three bound oxygen atoms of the amide, phosphinate or carboxylate groups (Fig. 2). No significant differences in twist angle were found for the Eu/Yb complexes of L^1, compared to the values for the corresponding complexes of L^3 and L^4.

The crystal structures show that the major diastereoisomer of the complex derived from the enantiopure *S* ligand system

Table 1 Selected mean distances of ligand donor atoms to the lanthanide ion[a] (Å, ±0.01) for [Ln·L^n] (Ln = Eu, Yb, *n* = 1, 3)[b]

[Ln·L^n]	Eu	Yb
Ln·L^1-O	2.40	2.34
Ln·L^3-O	2.33	2.25
Ln·L^1-N	2.63	2.57
Ln·L^3-N	2.68	2.62
Ln·L^1-N_{py}	2.57	2.49
Ln·L^3-N_{py}	2.66	2.62

[a] Effective ionic radii (Å) in 9-coordinate systems are 1.12 (Eu) and 1.04 Å (Yb). [b] Data for [Ln·L^3] are taken from ref. 4 and 5.

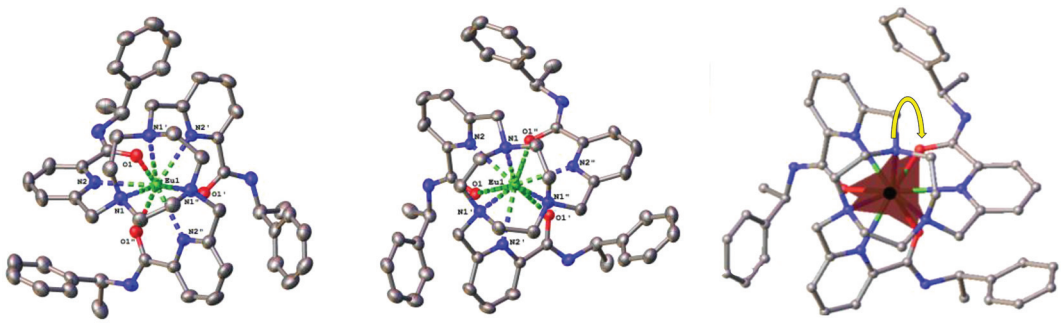


Fig. 1 Views of the structures of the tripositively charged cations of *S*-Δ-(λλλ)-[EuL^1] (*left*) and *R*-Λ-(δδδ)-[EuL^1] (*right*) (120 K), showing the twist angle (23.7°) associated with trigonal prismatic distortion, compared to 19.5° for [Eu·L^3] and 22.3° for [Eu·L^4]. CCDC 965909–965911.

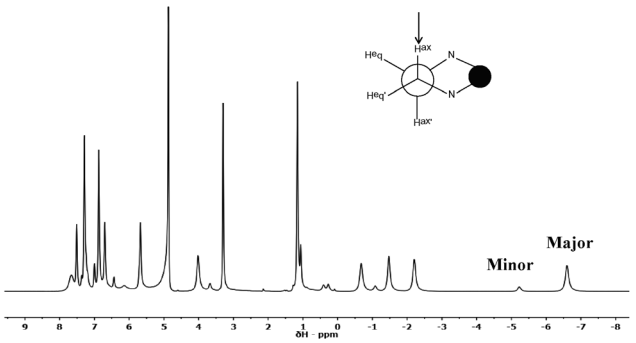


Fig. 2 ^{1}H NMR spectrum of $[EuL^1]^{3+}$ (CD_3OD, 295 K, 9.4 T), showing the two diastereoisomeric species in ratio 7 : 1, examining the most shifted axial ring protons at −6.6 and −5.2 ppm. The major species is assigned as *S*-*Δ*-(*λλλ*), whilst the minor isomer is most likely to be *S*-*Δ*-*δδδ*. Ratios of isomeric species were estimated at 4.7 and 9.4 T by integration and were within ±10%.

had a *Δ* configuration ($NCCN_{py}$ = +36.5°) and a *λ* conformation for each 5-ring chelate derived from the 9-N_3 ring (NCCN = −46.9°). The europium complex derived from the enantiopure *R* ligand system is enantiomeric, with *Λ* helicity and a *δ* LnNCCN chelate ring conformation. The same sense of asymmetric induction was observed in tris-lanthanide Eu complexes of 2,6-picolinamides[11] and in many examples with related 12-N_4 based tetra-amides.[10,15] In each case, the chiral amide moiety is derived from *S*-$PhCHMeNH_2$ or its analogues.

Solution NMR studies

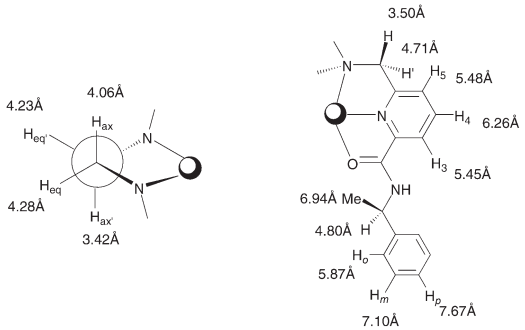
The series of lanthanide complexes of L^1 was examined by proton NMR in CD_3OD, revealing that two C_3 symmetric species were present in each case (Fig. 2). The ratio of these isomers fell from 9 : 1 (Ce) to 4 : 1 (Yb) across the series, consistent with a trend induced by the lanthanide contraction. Proton NMR spectra were obtained in CD_3OD for the crystals isolated and indicated that, in each case, it was the major solution diastereoisomer that had crystallized out of solution. The isomers could also be separated by reverse phase HPLC. Intriguingly, the ratio of isomers for $[Eu{\cdot}L^{2a-d}]^{3+}$ was 15 : 1 (ESI†) suggesting that in these systems the more polarisable pyridine N may have a shorter bond to the lanthanide ion, enhancing the impact of the steric demand of the proximate chiral centre. The isomer ratio observed for $[Yb{\cdot}L^1]$ was invariant with temperature over the range 278 to 353 K (D_2O, 14.1 T) and the variation of the chemical shift followed the expected T^{-2} dependence, consistent with Bleaney's theory of magnetic anisotropy. No evidence was therefore found for chemical exchange between the two isomeric species, on the NMR timescale.

The assignment of each ligand resonance was greatly assisted by the previous studies with $[Ln{\cdot}L^3]$.[5] In addition, longitudinal relaxation rate data (R_1) were measured for each ligand resonance at five magnetic fields, from 4.7 to 16.5 T. Resonances that are closer to the paramagnetic centre relax faster (*via* the r^{-6} dependence of R_1, *vide infra*), allowing a simple internal check of spectral assignments (Tables 2 and 3).

Paramagnetic longitudinal relaxation in these lanthanide complexes arises from rotational and conformational modulation of the electron-nuclear dipolar interaction, as in the equation below,

$$R_1 = \frac{2}{15}\left(\frac{\mu_0}{4\pi}\right)^2 \frac{\gamma_N^2 g_{Ln}^2 \mu_B^2 J(J+1)}{r^6}\left[3\frac{T_{1e}}{1+\omega_N^2 T_{1e}^2} + 7\frac{T_{2e}}{1+\omega_e^2 T_{2e}^2}\right] + \frac{2}{5}\left(\frac{\mu_0}{4\pi}\right)^2 \frac{\omega_N^2 \mu_{eff}^4}{(3k_B T)^2 r^6}\left[3\frac{\tau_r}{1+\omega_N^2 \tau_r^2}\right]$$

Table 2 Proton NMR assignments (δ_H/ppm) of the major isomeric species observed for paramagnetically shifted ligand resonances in $[Ln{\cdot}L^1]^{3+}$ (Ln = Tm, Yb, Eu; 295 K, CD_3OD)[a,b], showing distances to the Eu centre based on X-ray analysis



Ln	H_{ax}	H'_{eq}	H_{eq}	pyCHN	CH_3	C*H*NH	H^o	H^p	H^m	H'_{ex}	H_5	H_4	H_3	pyCH′N
Tm	−79.8	−30.5	−29.0	−22.0	−7.5	+9.3	10.8	10.7	10.4	11.3	19.2	19.6	23.0	+70.4
Yb	−18.8	−6.7	−4.2	−2.8	−1.1	+6.2	7.6	8.2	8.3	8.9	11.4	11.2	11.6	+22.3
Eu	−6.6	−2.2	−1.5	−0.7	+1.2	+4.0	5.7	6.9	6.7	5.1	7.4	7.3	7.5	+7.6

[a] Data for other Ln complexes are given in the Experimental but were not fully assigned due to severe line-broadening of certain protons within 4.5 Å of the metal ion. [b] The isomer ratio was 7 : 1 for $[Eu{\cdot}L^1]^{3+}$, and increased to 15 : 1 for $[Eu{\cdot}L^{2a-d}]^{3+}$. Chemical shift values were more or less unchanged in DMF *vs.* CD_3OD, consistent with encapsulation of the Ln ion by the ligand.

Table 3 Selected relaxation rate data (R_1, s^{-1}), determined at five fields for Yb and Tm complexes of L^1 (CD_3OD, 295 K). Full sets are given (ESI), for the Tb, Dy, Ho and Er analogues

Complex	B_o/T	H_{ax}	H'_{eq}	H_{eq}	pyCHN	H_3	H_4	pyCH′N
$[Yb{\cdot}L^1]^{3+}$	4.7	43(0.5)	34(0.3)	30(0.4)	19(0.1)	7(0.4)	5.0(0.5)	129(2)
	9.4	62(1.2)	48(1.1)	43(0.9)	29(0.5)	12(0.3)	7.3(0.3)	215(3)
	11.7	78(0.6)	63(0.3)	56(0.2)	39(0.2)	15(0.4)	8.6(0.1)	275(9)
	14.1	89(0.3)	73(0.4)	65(0.5)	46(0.3)	17(0.6)	10.1(0.3)	317(3)
	16.4	102(0.1)	83(0.3)	74(0.5)	53(0.4)	21(0.1)	10.7(0.1)	359(1.5)
$[Tm{\cdot}L^1]^{3+}$	4.7	158(2)	130(23)	118(2)	80(1)	31(1)	18(0.5)	566(19)
	9.4	377(9)	327(10)	283(5)	202(6)	75(2)	40(1)	1413(97)
	11.7	479(5)	411(8)	366(4)	256(3)	105(1)	53(1)	1718(20)
	14.1	589(4)	501(5)	443(4)	314(4)	125(2)	63(1)	2088(43)
	16.4	699(5)	580(9)	512(8)	363(3)	149(2)	73(1)	2482(76)

Table 4 Calculated values of magnetic susceptibility[c] (μ_{eff}/μ_B) and electronic relaxation times (T_{1e}, ps) for $[Ln{\cdot}L^n]$ (n = 1, 3, 4), derived from global fitting of the field dependence of longitudinal relaxation rate (R_1) data[a,b] (CD_3OD, 295 K)[d]

	$[Ln{\cdot}L^1]$		$[Ln{\cdot}L^3]$		$[Ln{\cdot}L^4]$	
Ln	μ_{eff}/μ_B	T_{1e}/ps	μ_{eff}/μ_B	T_{1e}/ps	μ_{eff}/μ_B	T_{1e}/ps
Tb	9.59(03)	0.27(03)	9.40(03)	0.21(04)	9.65(02)	0.26(03)
Dy	10.09(03)	0.29(03)	10.21(03)	0.32(03)	10.47(01)	0.28(02)
Ho	10.31(02)	0.21(03)	10.22(01)	0.11(02)	10.44(01)	0.17(02)
Er	8.80(03)	0.22(04)	9.05(02)	0.26(03)	9.23(02)	0.23(03)
Tm	7.77(02)	0.15(03)	7.66(03)	0.09(04)	7.43(01)	0.08(02)
Yb	4.56(04)	0.17(04)	4.36(03)	0.12(06)	4.27(02)	0.09(04)

[a] Values of τ_r estimated simultaneously were: $[Ln{\cdot}L^1]$, 196(1) ps; $[Ln{\cdot}L^3]$ 205(6) ps; $[Ln{\cdot}L^4]$, 132(1) ps. [b] In each case, for every set of resonances considered, the distance r from the proton to the Ln ion was taken from the X-ray crystallographic analysis. [c] Literature μ_{eff} values for the aqua ions are typically as follows: Tb, 9.8; Dy, 10.3; Ho, 10.4; Er, 9.4; Tm, 7.6; Yb, 4.3 BM.[18–20] These values relate to a 'weak' ligand field (less than or close to kT), as is the case here. [d] Data for $[Ln{\cdot}L^4]$ were recorded in D_2O; earlier work has shown that T_{1e} values are independent of solvent viscosity.[17]

where μ_0 is vacuum permeability, g_N is the magnetogyric ratio of the nucleus, g_{Ln} is the Landé factor of the fundamental multiplet J of the free Ln^{3+} ion, μ_B is the Bohr magneton (BM), τ_r is the rotational correlation time, ω_N is the nuclear Larmor frequency, ω_e is the electron Larmor frequency, $(\mu_{eff})^2$ is the square of the effective magnetic moment, T_{1e} and T_{2e} are the relaxation times of the electron spin and r is the electron-nuclear distance. Normally, it is assumed that T_{1e} equals T_{2e}.

Using values of r derived from the X-ray analysis, it is possible to estimate the values of μ_{eff}, τ_r and T_{1e}, by globally minimising the data sets simultaneously. Such an approach has been demonstrated recently to be effective at estimating these variables, especially as the rotational correlation time, τ_r, is not expected to vary significantly from one lanthanide complex to another.[16,17] Data obtained in this manner (Table 4), for $[Ln{\cdot}L^1]$, allowed a comparison to be made with results obtained with $[Ln{\cdot}L^{3,4}]$. The values of T_{1e} and τ_r obtained fell in the range expected for such complexes with rather weak ligand fields (*vide infra* for emission analysis). Furthermore, the estimates of the magnetic susceptibility values were also found to be in reasonable agreement with literature values that are derived from aqua ion or solid-state metal oxide data.[18–20]

Absorption and emission spectral studies

The series of lanthanide complexes of L^1 possess an absorption band at 280 nm, which shifted to the red by up to 75 nm in the complexes of L^{2a-2d}. Indeed, this band was very intense (ε values in MeOH ranged from 63 000 to 69 000 M^{-1} cm^{-1} to about 55 000 M^{-1} cm^{-1} in water) consistent with its ICT character, and in accord with earlier work on related lanthanide complexes with carboxylate or phosphinate donors.[6,1b] The position of the absorption band was particularly sensitive to solvent polarity, and there was a hypsochromic shift in solvents of lower polarity (Table 5). Such behaviour is consistent with the lowering of the energy of the relaxed ICT excited state in more polar protic solvents. The chloride salt complexes of L^{2c} and L^{2d} were the least soluble in water of the four complexes examined.

Table 5 Solvatochromism[a] data observed with $[Eu{\cdot}L^{2a-d}]^{3+}$ (295 K)

	λ_{max}/nm				
Solvent	E_T^{30} normalised	$[Eu{\cdot}L^{2a}]$	$[Eu{\cdot}L^{2b}]$	$[Eu{\cdot}L^{2c}]$	$[Eu{\cdot}L^{2d}]$
H_2O	1.00	332[b]	328[b]	356	352
MeOH	0.76	332	328	355	352
EtOH	0.65	331	327	355	349
^{i}PrOH	0.55	320	324	336	344
DMF	0.40	308	316	332	336

[a] E_T^{30} values are based on Reichardt's normalised solvent polarity scale. [b] Europium emission was an order of magnitude greater in water for these complexes, compared to organic solvents or to $[Eu{\cdot}L^{2c-2d}]$.

The aralkynyl chromophore acts as an efficient sensitiser of europium emission, and quantum yields in methanol were 5 (±3)% for the complexes with ligands L^{2a-d} (Table 6). The europium emission spectrum for all of the complexes was very similar (Fig. 3), and almost identical to the behaviour of [Eu·L[3,4]] and their extended chromophore analogues, consistent with time-averaged C_3 symmetry.[5,6]

The lower quantum yields and emission lifetimes for [Eu·L^{2c}] and [Eu·L^{2d}] (Table 6) suggested that the intramolecular energy transfer step from the relaxed excited ICT state may be partially reversible, and therefore is thermally activated. As the temperature was lowered, the emission intensity increased by a factor of 5 over the range 295 to 235 K, in accord with this premise, and consistent with a suppression of thermally activated back energy transfer from the excited Eu $^5D_0$ state to the ICT excited state. The phosphorescence spectrum of [GdL^{2d}], recorded at 85 K in a glass of ether–isopentane–ethanol (5 : 5 : 2), showed a very broad band at low temperature, centred at 450 nm (530 nm shoulder), consistent with the intermediacy of an excited state with predominant ICT character, rather than a ligand centred triplet excited state.[1b]

Table 6 Photophysical data for the complexes *S*-[EuL^{2a-d}]Cl_3 (295 K, MeOH)[a,b]

Complex	λ_{max}/nm	ε/M^{-1} cm^{-1}	τ/ms	ϕ_{em}
[EuL^{2a}]$^{3+}$	332	69 000	0.80	0.08
[EuL^{2b}]$^{3+}$	328	63 000	0.81	0.03
[EuL^{2c}]$^{3+}$	355	65 000	0.49	0.04
[EuL^{2d}]$^{3+}$	352	65 000	0.54	0.03

[a] In water at pH 6.5, emission lifetimes for [Eu·L^{2a}] and [Eu·L^{2b}] were 0.81 (1.10 ms in D_2O, hence the hydration state,[26] q = 0) and 0.80 ms, and overall quantum yields 35% and 37% respectively whilst for [Eu·L^{2c}] and [Eu·L^{2d}], corresponding values were 0.49 and 0.46 ms, with quantum yields of 2%, in each case. Extinction coefficients in water were lower: 55(±4) mM^{-1} cm^{-1}. [b] For the parent complexes in water: [TbL^1]: λ_{max} = 280 nm, ε = 15 400 M^{-1} cm^{-1}, τ = 1.87 ms, ($\tau(D_2O)$ = 2.12 ms), ϕ_{em} = 50%; [EuL^1]: λ_{max} = 280 nm, ε = 15 500 M^{-1} cm^{-1}, τ = 0.98 ms, ($\tau(D_2O)$ = 1.42 ms), ϕ_{em} = 7%. In comparison, [EuL^5] has an overall emission quantum yield of 0.2% in water, with a lifetime of 1.01 ms, (λ_{max} = 281 nm, ε = 20 500 M^{-1} cm^{-1}).[1e]

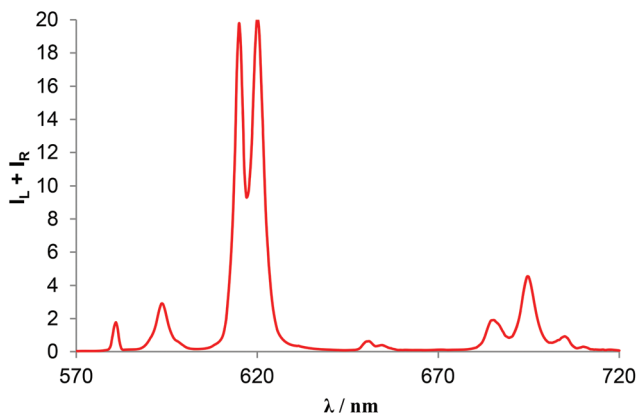


Fig. 3 Emission spectrum of *S*-[EuL^{2c}]$(CF_3SO_3)_3$ (MeOH, 295 K, λ_{exc} = 355 nm).

In water at pH 6.5, the emission quantum yields for the Eu complexes of L^{2a} and L^{2b} (X = H and CO_2Me) were 35 and 37% respectively (Table 6). These are amongst the highest values reported for sensitized emission of any europium complex in aqueous solution, and compare to 39% for a closely related tris-phenylphosphinate, based on [Eu·L^3], that possesses the same core chromophore as the L^2 series of ligands used here.[6] Emission intensities were unchanged in 0.1 M NaCl solution and in 0.1 M HEPES buffer at pH 7.4. The emission intensities of solutions of [Eu·L^{2c}]$^{3+}$ and [Eu·L^{2a}]$^{3+}$, in the presence of a thousand fold excess of EDTA at pH 6.5, were monitored as a function of time over a period of 7 days; after an initial 15% reduction, no significant change in intensity was observed in each case, consistent with the high kinetic stability of these systems with respect to dissociative ligand exchange.

The absorption and emission spectral behaviour of the complexes of L^{2c} and L^{2d}, absorbing at longer wavelength in protic solvents, were also sensitive to the apparent pH. In an 80/20 ^{i}PrOH–water mixture, as the apparent pH was varied, both the absorbance at 348 nm and the europium emission spectral form varied (Fig. 4). The spectral changes observed were completely reversible. The emission spectral changes were particularly striking and led to the appearance of additional transitions, consistent with a lowering of the symmetry around the Eu ion, and a change in the Eu coordination environment. These changes were most apparent in the ΔJ = 1 transitions around 595 nm, which evolved from a broad single manifold, to a set of three distinct transitions. For Eu complexes, three transitions are symmetry-allowed in systems lacking a C_n symmetry axis. The absorption spectral change was characterized by a shift to the blue at higher pH, moving the primary absorption band from 355 to 328 nm (Fig. 5). Values of the apparent pK_a for the ground and excited states, derived by iterative fitting of the observed spectral changes to a two-state equilibrium, were estimated to be 9.1 in each case.

Taken, together, this behaviour is consistent with deprotonation of one amide NH proton, reversibly generating an

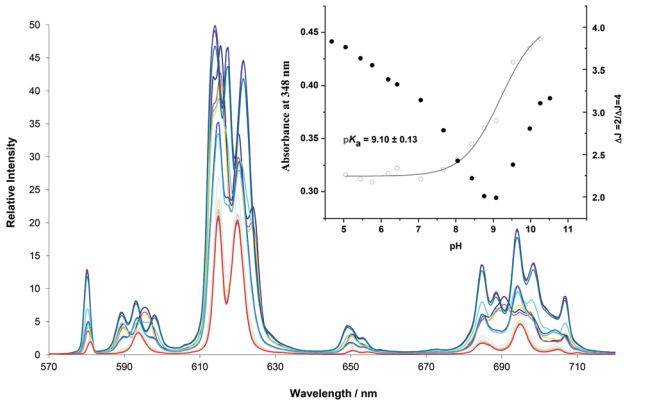


Fig. 4 Variation of the Ln(III) emission spectrum as a function of pH for *S*-[EuL^{2c}]Cl_3 (iPrOH–H_2O 80 : 20 v/v, 5 μM complex, 298 K, λ_{exc} 348 nm). *Top right*: absorbance changes at 348 nm with pH (filled circles), and variation of the ΔJ = 2/ΔJ = 4 relative emission intensity ratio with pH (open circles) (pK_a 9.10 (±0.13)).

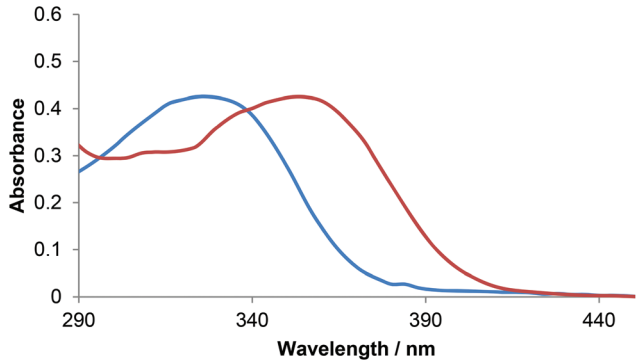


Fig. 5 UV-absorption spectra of *S*-[EuL^{2c}]Cl$_3$ in iPrOH–H$_2$O (80 : 20 v/v) at an apparent pH of 10.3 (blue) and pH 4.4 (red).

amide enolate in which the anionic oxygen is coordinated to the europium centre. Indeed, in several examples of 12-N$_4$ lanthanide tetra-amide complexes, similar pK_a values (range 7.9 to 11.1) have been associated with amide deprotonation in aqueous media.[21–23]

Chiroptical spectral behaviour

Circularly polarized luminescence spectroscopy is a sensitive means of interrogating the excited state chirality of lanthanide complexes.[7,24] The CPL spectra of the *Δ* and *Λ* complexes of [Ln·L^1] were examined and showed mirror image behaviour (Fig. 6). Furthermore, when the sign and magnitude of the CPL transitions for *Δ*-[Tb·L^1] and *Δ*-[Tb·L^3] were compared[4] they were very similar, in accord with their common configuration. In the latter case, the absolute configuration at each phosphorus is *S*, as is the case with this amide complex.

The CPL spectra of the *Δ* and *Λ* complexes of [Tb·L^1]$^{3+}$ and [Eu·L^{2d}]$^{3+}$ were also recorded (Fig. 6 and 7). With these examples, CPL spectroscopy allowed the two components of the $\Delta J = 1$ manifold in the Eu spectrum to be more clearly resolved. Analysis of the energies of these transitions allows an estimate to be made of the second order crystal field term, B_0^2.[25] For [Eu·L^1]$^{3+}$, for example, the splitting of the two

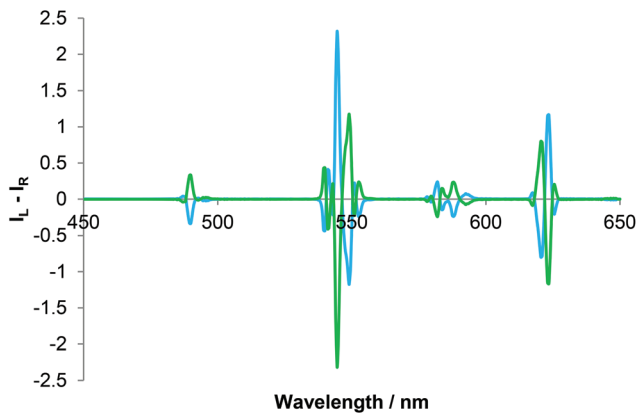


Fig. 6 Circularly polarized luminescence emission spectra for *S*-*Δ* (green) and *R*-*Λ* (blue) [Tb·L^1] (λ_{exc} 280 nm; H$_2$O, pH 6.5, 295 K; *Δ*-complex: g_{em} (539) +0.11; g_{em}(623) −0.35).

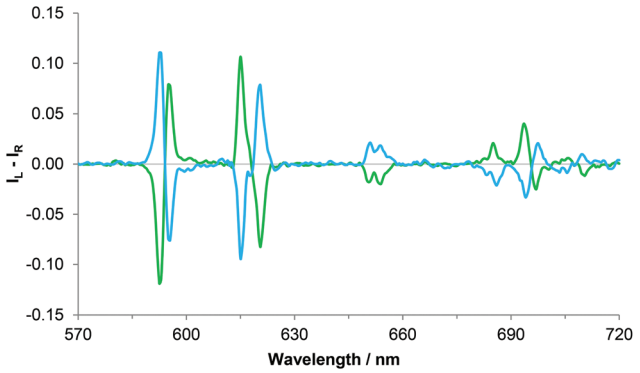


Fig. 7 Circularly polarized luminescence emission spectra for *S*-*Δ* (green) and *R*-*Λ* (blue) [Eu·L^{2d}] (λ_{exc} 348 nm; pH 5, water, 295 K).

transitions was found to be 70 cm^{-1}, corresponding to a B_0^2 value of +233 cm^{-1}, compared to +110 cm^{-1} for [Eu·L^3] and +75 cm^{-1} for [Eu·L^4].[17] As this parameter also determines the magnitude of the dipolar shift in NMR, this trend was also reflected in the relative shifts of the ligand protons, best illustrated in the ^{1}H NMR chemical shift data for the Yb complexes of ligands L$^{1–3}$ (Table 2 and ref. 5). Thus, the most shifted ring proton (H$_{ax}$, see Fig. 2) resonates at −18.8, −13.8 and −4.8 ppm for [YbL^1], [Yb·L^3] and [Yb·L^4] respectively, and the total spectral width is 30, 24 and 14 ppm in that sequence. These examples also highlight the fact that the sign of B_0^2 in these C_3 symmetric complexes is positive and opposite to that of the multitudinous C_4 12-N$_4$ analogues, explaining the different sense of the NMR shifts observed.

Summary and conclusions

Structural determinations using crystallographic, NMR and CPL methods have shown that the configuration of the stereogenic centre in the remote amide moiety determines the helicity of the metal complex in this new range of Ln(III) complexes of nonadentate N$_6$O$_3$ ligands based on triazacyclononane. The NMR studies revealed the presence of a dominant isomer in solution that was isolated by crystallization. The proportion of the major isomer present in solution was 9 : 1 for Ce and Pr, 7 or 6 : 1 from Nd to Tm and 4 : 1 for Yb. The level of remote stereocontrol in complex formation is inferior to that created by C-substitution of the 9-N$_3$ ring. In that case, even the introduction of a single methyl substituent led to preferential formation of one (>96%) enantiomeric complex.[8]

In four analogous europium complexes, containing *para*-substituted pyridinyl-aryl groups, stereocontrol is higher and the complex exists as one major isomer in solution in a ratio of 15 : 1. Each complex absorbs light strongly *via* an ICT transition in the range 320 to 355 nm (ε = 55 000 M^{-1} cm^{-1} in water) that is strongly solvatochromic. Two examples absorbing light around 332 nm, albeit with a broad transition that extends to 365 nm, possess overall emission quantum yields at Eu of 35 and 37% in aerated water. These values are amongst

the highest ever observed for sensitised europium emission in water, rendering them particularly 'bright' complexes. Such behaviour augurs well for the use of analogues of these systems as the basis of CPL probes, in which the sign, intensity and form of selected CPL transitions can be used to probe the local chiral environment.

Experimental

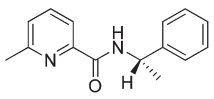
Details of the general procedures, and instrumentation used are given in the ESI.†

Crystal structure determinations of *Δ* and *Λ*-[EuL^1] and *Δ*-[Yb·L^1]

Crystals of [**EuL^1**] suitable for single crystal structure determination were grown by slow evaporation of a CH_3OH solution. The crystals of Eu-complexes are shattered by flash-freezing, so they were gradually cooled at the rate of 120° per hour from 250 K to 120 K. The X-ray single crystal data for all compounds were collected at 120 K on a Bruker SMART CCD 6000 diffractometer (graphite monochromator, MoK_α, λ = 0.71073 Å) equipped with a Cryostream (Oxford Cryosystems) open-flow nitrogen cryostat. The structures were solved by direct methods and refined by full-matrix least squares on F^2 for all data using Olex2[27] and SHELXTL[28] software. In all compounds the counterions are linked by N–H···O hydrogen bonds and triflate anions are disordered over two positions. All non-disordered non-hydrogen atoms were refined anisotropically, disordered atoms were refined isotropically with fixed SOF = 0.5. Hydrogen atoms in Eu-complexes were found in the difference Fourier maps and refined isotropically while H-atoms in Yb-complex were placed in the calculated positions and refined in riding mode. The structures of all complexes contain small amounts of severely disordered solvent molecules (av. 15 electrons per independent part of unit cell) that could not be reliably modelled and have been taken into account using the MASK procedure of the Olex2 programme package. The absolute configuration of the compounds was established by measurements of anomalous dispersion effects. CCDC 965909–965911.

Ligand syntheses

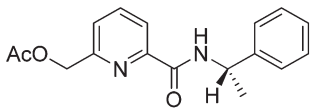
(*S*)-6-Methyl-*N*-(1-phenylethyl)picolinamide (*S*-1a).



6-Methylpyridine-2-carboxylic acid (1.00 g, 7.29 mmol), HOBt·H_2O (1.48 g, 10.9 mmol), EDC (1.70 g, 10.94 mmol) and DIPEA (3.17 mL, 18.2 mmol) were dissolved in anhydrous DMF (20 mL). (*S*)-(−)-α-Methylbenzyl amine (0.93 mL, 7.29 mmol) was added dropwise to the solution and the mixture was stirred at rt for 22 h under an argon atmosphere. Water was added (25 mL) and the mixture extracted with EtOAc (3 × 10 mL). The organic layers were combined and washed successively with water (1 × 10 mL) and brine (1 × 10 mL), dried over $MgSO_4$ and the solvent removed under reduced pressure. The crude mixture was purified by flash column chromatography (silica, gradient elution starting from 30% EtOAc in hexane to 60% EtOAc in hexane) to afford compound ***S*-1a** as a yellow oil (1.32 g, 75%). TLC analysis R_f 0.24 (silica, 30% EtOAc in hexane); ^{1}H NMR (295 K, 400 MHz, $CDCl_3$) δ_H 8.38 (1H, d, ^3J 7.5, NH), 7.94 (1H, d, ^3J 7.5, py-H^3), 7.64 (1H, t, ^3J 7.5, py-H^4), 7.41 (2H, d, ^3J 7.5, Ph-H^o), 7.35 (2H, t, ^3J 7.5, Ph-H^m), 7.27–7.25 (2H, m, Ph-H^p, py-H^5) 5.26 (1H, dq, ^3J 7, ^3J 7.5 C*H*CH$_3$), 2.49 (3H, s, py-CH_3), 1.56 (3H, d, ^3J 7, CHCH_3); ^{13}C NMR (295 K, 100 MHz, $CDCl_3$) δ_C 163.4 (*C*=O), 157.0 (py-C^6), 149.1 (py-C^2), 143.3 (Ph-C^i), 137.4 (py-C^4), 128.5 (Ph-C^m), 127.2 (Ph-C^p), 126.2 (Ph-C^o), 125.8 (py-C^5), 119.3 (py-C^3), 48.6 (*C*HCH$_3$), 24.1 (py-CH_3), 21.9 (CH*C*H$_3$); *m*/*z* (HRMS$^+$) 241.1334 ($C_{15}H_{17}ON_2$ requires 241.1335).

(*S*)-6-Methyl-2-((1-phenylethyl)carbamoyl)pyridine 1-oxide (*S*-1b). *m*-CPBA (1.89 g, 10.9 mmol) was added to a stirred solution of amide ***S*-1a** (1.32 g, 5.49 mmol) in anhydrous $CHCl_3$ (16 mL). The resulting solution was stirred at rt for 18 h under an argon atmosphere. The solution was washed with $NaHCO_3$ (aq.) (0.5 M, 25 mL) and extracted with DCM (3 × 20 mL). The organic layers were combined, dried over $MgSO_4$ and the solvent removed under reduced pressure. The crude mixture was purified by flash column chromatography (silica, gradient elution starting from 40% EtOAc in hexane to 70% EtOAc in hexane) to yield compound ***S*-1b** as a white crystalline solid (1.17 g, 83%). TLC analysis R_f 0.21 (silica, 60% EtOAc in hexane); m.p. 70–71 °C; ^{1}H NMR (295 K, 400 MHz, $CDCl_3$) δ_H 11.91 (1H, d, ^3J 7.5, NH), 8.34 (1H, dd, ^3J 8, ^4J 2, py-H^3), 7.40 (2H, m, Ph-H^o), 7.38 (1H, dd, ^3J 8, ^4J 2, py-H^5), 7.34 (3H, m, Ph-H^m, Ph-H^p), 7.25–7.23 (1H, m, py-H^4), 5.31 (1H, dq, ^3J 7, ^3J 7.5 C*H*CH$_3$), 2.57 (3H, s, py-CH_3), 1.62 (3H, d, ^3J 7, CHCH_3); ^{13}C NMR (295 K, 100 MHz, $CDCl_3$) δ_C 159.4 (*C*=O), 150.3 (py-C^6), 143.5 (Ph-C^i), 141 (py-C^2), 128.9 (Ph-C), 128.1 (py-C^5), 127.4 (py-C^4), 127.1 (py-C^3), 126.5 (Ph-C), 126.4 (Ph-C^o), 49.8 (*C*HCH$_3$), 22.8 (CH*C*H$_3$), 18.4 (py-CH$_3$); *m*/*z* (HRMS$^+$) 257.1280 ($C_{15}H_{17}N_2O_2$ requires 257.1290).

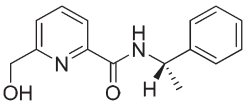
(*S*)-(2-((1-Phenylethyl)carbamoyl)pyrdin-2-yl)methyl acetate (*S*-1c).



The *N*-oxide ***S*-1b** (700 mg, 2.73 mmol) was dissolved in acetic anhydride (14 mL) and the solution was heated to 120 °C for 24 h with stirring. The reaction progress was monitored by LCMS and TLC (silica, 50% EtOAc in hexane, R_f(product) 0.38, R_f(reactant) 0.16). The solvent was removed under reduced pressure and the residue purified by column chromatography (silica, gradient elution starting from 20% EtOAc in hexane to 70% EtOAc in hexane) to give ***S*-1c** as dark yellow oil (476 mg, 59%). TLC analysis R_f 0.38 (silica, 50% EtOAc in hexane); ^{1}H NMR (295 K, 400 MHz, $CDCl_3$) δ_H 8.26 (1H, d, ^3J 7.5, NH), 8.14 (1H, d, ^3J 8, py-H^3), 7.86 (1H, t, ^3J 8, py-H^4), 7.48 (1H, d, ^3J 8,

py-H^5), 7.42–7.25 (5H, m, Ph-H), 5.36–5.28 (1H, dq, ^3J 7, ^3J 7.5, C*H*CH$_3$), 5.24 (2H, s, py-CH$_2$), 2.16 (3H, s, COCH$_3$), 1.63 (3H, d, ^3J 7, CHC*H*$_3$); ^{13}C NMR (295 K, 100 MHz, CDCl$_3$) δ_C 170.6 (*C*OCH$_3$), 163.2 (*C*ONH), 154.7 (py-C^2), 149.7 (py-C^6), 143.4 (Ph-C^i), 138.3 (py-C^4), 128.8 (Ph-C^m), 127.5 (Ph-C^p), 126.4 (Ph-C^o), 124.1 (py-C^5), 121.6 (py-C^3), 66.5 (py-*C*H$_2$), 49.0 (*C*HCH$_3$), 22.2 (CH*C*H$_3$), 21.0 (CO*C*H$_3$); *m*/*z* (HRMS$^+$) 299.1373 [M + H]$^+$ (C$_{17}$H$_{19}$N$_2$O$_3$ requires 299.1396).

(*S*)-6-(Hydroxymethyl)-*N*-(1-phenylethyl)picolinamide (*S*-1d).



The ester, ***S*-1c**, (350 mg, 1.16 mmol) was dissolved in anhydrous CH$_3$CH$_2$OH (12 mL). A small amount of sodium metal (~5 mg) was added and the solution stirred at 40 °C under argon for 2 h. The solution was concentrated under reduced pressure and the residue dissolved in DCM (100 mL). The sodium salts were extracted by washing with water (1 × 25 mL) and the aqueous layer was re-extracted with DCM (3 × 20 mL). The organic layers were combined, dried over MgSO$_4$, filtered and the solvent removed under reduced pressure. The crude residue was purified by column chromatography (silica, gradient elution starting from 40% EtOAc 100% EtOAc) to yield compound ***S*-1d** as a white solid (330 mg, 85%). TLC analysis R_f 0.35 (silica, 70% EtOAc in hexane); m.p. 152–154 °C; ^{1}H NMR (295 K, 400 MHz, CDCl$_3$) δ_H 8.21 (1H, s, ^3J 7.5, NH), 8.16 (1H, d, ^3J 7.5, py-H^3), 7.89 (1H, t, ^3J 7.5, py-H^4), 7.49 (1H, d, ^3J 7.5, py-H^5), 7.43–7.25 (5H, m, Ph-H), 5.37–5.30 (1H, dq, ^3J 7, ^3J 7.5, C*H*CH$_3$), 4.83 (2H, s, py-CH$_2$), 2.91 (1H, br s, OH), 1.64 (3H, d, ^3J 7, CHC*H*$_3$); ^{13}C NMR (295 K, 100 MHz, CDCl$_3$) δ_C 163.1 (CONH), 158.4 (py-C^6), 149.1 (py-C^2), 143.2 (Ph-C^i), 138.7 (py-C^4), 128.9 (Ph-C^m), 127.6 (Ph-C^p), 126.4 (Ph-C^o), 123.5 (py-C^5), 121.7 (py-C^3), 64.6 (py-CH$_2$), 49.1 (*C*HCH$_3$), 22.1 (CH*C*H$_3$); *m*/*z* (HRMS$^+$) 257.1282 [M + H]$^+$ (C$_{15}$H$_{17}$N$_2$O$_2$ requires 257.1290).

(*S*)-(6-((1-Phenylethyl)carbamoyl)pyridine-2-yl)methyl methane sulfonate (*S*-1e). The alcohol, ***S*-1d**, (227 mg, 0.886 mmol) was dissolved in anhydrous THF (5.5 mL) and NEt$_3$ (0.37 mL, 2.66 mmol) was added. The mixture was stirred at 5 °C, methanesulfonyl chloride (0.12 mL, 1.49 mmol) was added and the reaction stirred at rt for 30 minutes and monitored by TLC (silica, 100% ethyl acetate, R_f(product) 0.63, R_f(reactant) 0.53). The solvent was removed under reduced pressure and the residue dissolved in DCM (25 mL) and washed with saturated aqueous NaCl solution (15 mL). The aqueous layer was re-extracted with DCM (3 × 10 mL) and the organic layers were combined, dried over MgSO$_4$, filtered and the solvent removed under reduced pressure to leave compound ***S*-1e**, as a bright yellow oil, which was used directly in the next step without further purification. TLC analysis R_f 0.63 (silica, 100% ethyl acetate); ^{1}H NMR (295 K, 400 MHz, CDCl$_3$) δ_H 8.25 (1H, d, ^3J 8, NH), 8.19 (1H, d, ^3J 8, py-H^5), 7.91 (1H, t, ^3J 8, py-H^4), 7.59 (1H, d, ^3J 8, py-H^3), 7.42–7.26 (5H, m, Ph-H), 6.36 (2H, s, py-CH$_2$), 5.34–5.28 (1H, dq, ^3J 7, ^3J 8, C*H*CH$_3$), 3.07 (3H, s, SO$_2$C*H*$_3$), 1.63 (3H, d, ^3J 7, CHC*H*$_3$); ^{13}C NMR (295 K, 100 MHz, CDCl$_3$) δ_C 162.8 (*C*ONH), 152.5 (py-C^6), 149.9 (py-C^2), 143.3 (Ph-C^i), 138.7 (py-C^4), 128.8 (Ph-C^m), 127.5 (Ph-C^p), 126.4 (Ph-C^o), 124.6 (py-C^3), 122.4 (py-C^5), 70.8 (py-CH$_2$), 49.0 (*C*HCH$_3$), 38.3 (OSO$_2$*C*H$_3$), 22.1 (CH*C*H$_3$); *m*/*z* [HRMS]$^+$ 335.1066 [M + H]$^+$ (C$_{16}$H$_{19}$N$_2$O$_4$S requires 335.1060).

6,6′,6″-((1,4,7-Triazacyclononane-1,4,7-triyl)tris(methylene))-tris(*N*-((*S*)-1-phenylethyl)picolinamide (*S*-L^1)

1,4,7-Triazacyclononane (55 mg, 0.427 mmol) and the mesylate, ***S*-1e**, (428 mg, 1.28 mmol) were dissolved in anhydrous CH$_3$CN (19.5 mL) and K$_2$CO$_3$ (59 mg, 0.427 mmol) was added. The mixture was stirred under argon at 78 °C. After 21 h the reaction was cooled and filtered to remove excess potassium salts. The solvent was removed under reduced pressure and the crude material purified by column chromatography (alumina, gradient elution starting from 100% CH$_2$Cl$_2$ to 5% CH$_3$OH in CH$_2$Cl$_2$) to give ***S*-L^1** as a yellow glassy solid (180 mg, 55%); TLC analysis R_f 0.21 (alumina, CH$_2$Cl$_2$: CH$_3$OH 1%); ^{1}H NMR (295 K, 400 MHz, CDCl$_3$) δ_H 8.53 (3H, d, ^3J 7, CONH), 8.08 (3H, d, ^3J 7.5, py-H^3), 7.77 (3H, t, py-H^4), 7.51 (3H, d, ^3J 7, py-H^5), 7.43–7.17 (15H, m, Ph-H), 5.35 (3H, dq, ^3J 7, ^3J 7.5, C*H*CH$_3$), 3.78 (6H, s, py-CH$_2$), 2.79 (12H, s, *ring* Hs), 1.62 (9H, d, ^3J 7, CHC*H*$_3$); ^{13}C NMR (295 K, 100 MHz, CDCl$_3$) δ_C 163.7 (*C*ONH), 159.3 (py-C^2), 149.5 (py-C^6), 143.6 (Ph-C^i), 137.9 (py-C^4), 128.8 (Ph-C^m), 127.5 (Ph-C^p), 126.6 (Ph-C^o), 125.9 (py-C^5), 120.9 (py-C^3), 64.6 (py-CH$_2$), 56.3 (*ring* Cs), 49.0 (*ring* Cs), 46.0 (*C*HCH$_3$), 22.05 (CH*C*H$_3$); *m*/*z* (HRMS$^+$) 844.4683 [M + H]$^+$ (C$_{51}$H$_{58}$N$_9$O$_3$ requires 844.4663).

***S*-[EuL^1](CF$_3$SO$_3$)$_3$.** Europium(III) triflate (14 mg, 0.024 mmol) was added to a solution of ligand, ***S*-L^1**, (19 mg, 0.024 mmol) in anhydrous acetonitrile (2 mL) and the mixture heated at reflux for 20 h. The solution was concentrated under vacuum and cold diethyl ether (2 mL) was added dropwise to the solution. The resulting white solid was filtered and dried *in vacuo* to yield ***S*-[EuL^1](CF$_3$SO$_3$)$_3$** as a white solid (20 mg, 85%). ^{1}H NMR (295 K, 400 MHz, CD$_3$OD) δ_H major diastereoisomer 7.6 (pyCH′N), 7.5 (py-H^3), 7.4 (py-H^5), 7.3 (py-H^4), 6.9 (Ph-H^p), 6.7 (Ph-H^m), 5.7 (Ph-H^o), 5.1 (NCH′$_{ax}$), 4.0 (C*H*CH$_3$), 1.2 (CHC*H*$_3$), −0.7 (pyCHN), −1.5 (NCH$_{eq}$), −2.2 (NCH′$_{eq}$), −6.6 (NCH$_{ax}$); *m*/*z* HRMS$^+$ 992.3646 [M − 2H]$^+$ (C$_{51}$H$_{55}$N$_9$O$_3$^{151}Eu requires 992.3626). τ(H$_2$O) = 0.98 ms, τ(D$_2$O) = 1.42 ms (q = 0) and ϕ_{em} (H$_2$O) = 7%. t_R = 5.63 min.

Crystals of the europium complex were grown by slow evaporation of aqueous methanol (1 : 1 v/v) and examined by X-ray crystallography.

Crystal data: C$_{51}$H$_{57}$EuN$_9$O$_3$ × 3CF$_3$SO$_3$, M_r = 1443.22, trigonal (*R*3); a = 21.6392(5) Å, c = 11.4683(4) Å, V = 4650.6(2) Å^3, Z = 3; μ = 1.205 mm^{-1}, D_{calc} = 1.546 mg mm^{-3}, T = 120 K; 62 469 reflections were measured ($2.18 \leq 2\Theta \leq 62.06$), 5722 independent reflections (R_{int} = 0.0336), R_1 = 0.0412 (5684 $I \geq 2\sigma(I)$), ωR_2 = 0.1043 (all data), GOOF = 1.026. Flack parameter −0.0013 (11), Hooft parameter 0.004(5), CCDC 965909.

***S*-[CeL^1](CF$_3$SO$_3$)$_3$.** An analogous method to that for ***S*-[EuL^1]$^{3+}$** using cerium(III) triflate (7 mg, 0.012 mmol) and the ligand ***S*-L^1** (10 mg, 0.012 mmol) in dry acetonitrile (2 mL) was followed to yield ***S*-[CeL^1](CF$_3$SO$_3$)$_3$** as a white solid (10 mg, 85%). ^{1}H NMR (295 K, 400 MHz, CD$_3$OD) δ_H major diastereoisomer

9.6 (py-H^3), 9.4 (py-H^4), 8.4 (py-H^5), 7.7 (Ph-H), 7.6 (Ph-H), 6.2 (NCH′$_{ax}$), 4.5 (C*H*CH$_3$), 4.1 (pyCHN), 1.6 (NCH′$_{eq}$), 1.3 (CHC*H*$_3$), 0.3 (NCH$_{eq}$), −1.0 (NCH$_{ax}$); *m*/*z* (HRMS$^+$) 981.3506 [M − 2H]$^+$ ($C_{51}H_{55}N_9O_3{}^{140}$Ce requires 981.3482).

***S*-[PrL^1](CF$_3$SO$_3$)$_3$.** An analogous method to that for ***S*-[EuL^1]$^{3+}$** using praseodymium(III) triflate (7 mg, 0.012 mmol) and the ligand ***S*-L^1** (10 mg, 0.012 mmol) in dry acetonitrile (2 mL) was followed to yield ***S*-[PrL^1](CF$_3$SO$_3$)$_3$**, as a white solid (10 mg, 85%). ^{1}H NMR (295 K, 400 MHz, CD$_3$OD) δ_H major diastereoisomer 11.1 (py-H^3), 10.5 (py-H^4), 10.1 (py-H^5), 9.4 (NCH′$_{ax}$), 8.4 (Ph-H), 8.2 (Ph-H), 8.1 (Ph-H), 6.4 (pyCHN), 4.1 (C*H*CH$_3$), 1.6 (NCH$_{eq}$), 1.1 (CHC*H*$_3$), 0.5 (pyCH′N), −1.3 (NCH′$_{eq}$), −5.5 (NCH$_{ax}$); *m*/*z* HRMS$^+$ 982.3493 [M − 2H]$^+$ ($C_{51}H_{55}N_9O_3{}^{141}$Pr requires 982.3499).

***S*-[NdL^1](CF$_3$SO$_3$)$_3$.** An analogous method to that for ***S*-[EuL^1]$^{3+}$** using neodymium(III) triflate (7 mg, 0.012 mmol) and the ligand ***S*-L^1** (10 mg, 0.012 mmol) in dry acetonitrile (2 mL) was followed to yield **[NdL^1]$^{3+}$**, as a white solid (9 mg, 72%). ^{1}H NMR (295 K, 400 MHz, CD$_3$OD) δ_H major diastereoisomer 10.2 (py-H^3), 9.3 (py-H^4), 8.9 (py-H^5), 7.5 (Ph-H), 7.2 (pyCHN), 6.4 (Ph-H), 5.8 (NCH$_{ax}$), 5.3 (C*H*CH$_3$), 4.1 (NCH′$_{ax}$), 2.7 (NCH$_{eq}$), 2.6 (NCH′$_{eq}$), 1.6 (CHC*H*$_3$), 0.4 (pyCH′N); *m*/*z* (HRMS$^+$) 983.3505 [M − 2H]$^+$ ($C_{51}H_{55}N_9O_3{}^{142}$Nd requires 983.3530).

***S*-[TbL^1](CF$_3$SO$_3$)$_3$.** An analogous method to that for ***S*-[EuL^1]$^{3+}$** using terbium(III) triflate (10 mg, 0.017 mmol) and the ligand ***S*-L^1** (15 mg, 0.017 mmol) in dry acetonitrile (2 mL) was followed to yield ***S*-[TbL^1](CF$_3$SO$_3$)$_3$**, as a white solid (16 mg, 92%). ^{1}H NMR (295 K, 400 MHz, CD$_3$OD) δ_H major diastereoisomer; partial assignment: 57.5 (NCH$_{ax}$), 29.9 (NCH′$_{eq}$), 23.9 (NCH$_{eq}$), 8.6 (CHC*H*$_3$), 5.8 (C*H*CH$_3$), 4.5 (Ph-H^m), 2.0 (Ph-H^o), −3.2 (py-H^4), −4.4 (py-H^5), −11.0 (py-H^3), −12.4 (NCH′$_{ax}$), −45.5 (pyCH′N); *m*/*z* HRMS$^+$ 1000.369 [M − 2H]$^+$ ($C_{51}H_{55}N_9O_3{}^{159}$Tb requires 1000.368). τ(H$_2$O) = 1.87 ms, τ(D$_2$O) = 2.12 ms and ϕ_{em} (H$_2$O) = 50%.

***S*-[DyL^1](CF$_3$SO$_3$)$_3$.** An analogous method to that for ***S*-[EuL^1]$^{3+}$** using dysprosium(III) triflate (11 mg, 0.017 mmol) and the ligand ***S*-L^1** (15 mg, 0.017 mmol) in dry acetonitrile (2 mL) was followed to yield ***S*-[DyL^1](CF$_3$SO$_3$)$_3$**, as a white solid (15 mg, 88%). ^{1}H NMR (295 K, 400 MHz, CD$_3$OD) δ_H major diastereoisomer, partial assignment: 22.5 (NCH′$_{ax}$), 18.2, 11.1, 7.0, 6.5 (Ph-H), 6.2 (Ph-H), 5.6, 5.0 (py-H^4), 3.0 (py-H^5), 1.9 (py-H^3), −1.5, −3.7 (pyCHN), −4.8, −14.0, 18.0; *m*/*z* HRMS$^+$ 1002.371 [M − 2H]$^+$ ($C_{51}H_{55}N_9O_3{}^{161}$Dy requires 1002.370). τ(H$_2$O) = 0.04 ms and ϕ_{em} (H$_2$O) = 1.2%.

***S*-[HoL^1](CF$_3$SO$_3$)$_3$.** An analogous method to that for ***S*-[EuL^1]$^{3+}$** using holmium(III) triflate (8 mg, 0.013 mmol) and the ligand ***S*-L^1** (11 mg, 0.013 mmol) in dry acetonitrile (2 mL) was followed to yield ***S*-[HoL^1](CF$_3$SO$_3$)$_3$**, as a white solid (13 mg, 99%). ^{1}H NMR (295 K, 400 MHz, CD$_3$OD) δ_H major diastereoisomer, partial assignment: 47.3 (NCH$_{ax}$), 23.3 (NCH′$_{eq}$), 22.6 (NCH$_{eq}$), 11.9, 10.2, 9.8, 7.2 (CHC*H*$_3$), 5.8 (C*H*CH$_3$), 5.5 (Ph-H^m), 5.1 (Ph-H^o), 0.5 (py-H^5), −0.4 (py-H^4), −3.7 (NCH′$_{ax}$), −5.5 (py-H^3), −32.0 (pyCH′N); *m*/*z* HRMS$^+$ 1006.374 [M − 2H]$^+$ ($C_{51}H_{55}N_9O_3{}^{165}$Ho requires 1006.373).

***S*-[ErL^1](CF$_3$SO$_3$)$_3$.** ^{1}H NMR (295 K, 400 MHz, CD$_3$OD) δ_H major diastereoisomer 12.8, 8.2 (py-H^3), 8.0 (py-H^5), 7.9 (py-H^4), 7.5 (Ph-H^p), 6.9 (Ph-H^m), 6.1 (Ph-H^o), 3.6, 1.9 (C*H*CH$_3$), 1.8 (pyCHN), 0.9 (CHC*H*$_3$), −5.0 (NCH$_{eq}$), −5.1 (NCH′$_{eq}$), −8.8 (NCH$_{ax}$); *m*/*z* HRMS$^+$ 1009.380 [M − 2H]$^+$ ($C_{51}H_{55}N_9O_3{}^{168}$Er requires 1009.377).

***S*-[TmL^1](CF$_3$SO$_3$)$_3$.** ^{1}H NMR (295 K, 400 MHz, CD$_3$OD) δ_H major diastereoisomer 70.4 (pyCH′N), 23.0 (py-H^3), 19.6 (py-H^4), 19.2 (py-H^5), 11.3 (NCH′$_{ax}$), 10.8 (Ph-H^o), 10.7 (Ph-H^p), 10.4 (Ph-H^m), 9.3 (C*H*CH$_3$), −7.5 (CHC*H*$_3$), −22.0 (pyCHN), −29.0 (NCH$_{eq}$), −30.5 (NCH′$_{eq}$), −79.8 (NCH$_{ax}$); *m*/*z* HRMS$^+$ 1010.375 [M − 2H]$^+$ ($C_{51}H_{55}N_9O_3{}^{169}$Tm requires 1010.376).

***S*-[YbL^1](CF$_3$SO$_3$)$_3$.** ^{1}H NMR (295 K, 400 MHz, CD$_3$OD) δ_H major diastereoisomer 22.3 (pyCH′N), 11.6 (py-H^3), 11.4 (py-H^5), 11.2 (py-H^4), 8.9 (NCH′$_{ax}$), 8.3 (Ph-H^m), 8.2 (Ph-H^p), 7.6 (Ph-H^o), 6.2 (C*H*CH$_3$), −1.1 (CHC*H*$_3$), −2.8 (pyCHN), −4.2 (NCH$_{eq}$), −6.7 (NCH′$_{eq}$), −18.8 (NCH$_{ax}$); *m*/*z* HRMS$^+$ 1012.382 [M − 2H]$^+$ ($C_{51}H_{55}N_9O_3{}^{171}$Yb requires 1012.379). Crystals of the ytterbium complex were grown by slow evaporation of aqueous methanol (1 : 1 v/v) and examined by X-ray crystallography.

Crystal data: $C_{54}H_{57}F_9N_9O_{12}S_3Yb$, M_r = 1464.30, trigonal (*R*3); *a* = 21.836(2), *c* = 11.1868(17) Å, *V* = 4619.5(10) Å^3, *Z* = 3; μ = 1.713 mm^{-1}, D_{calc} = 1.579 mg mm^{-3}, *T* = 120 K; 65 596 reflections measured (2.16 ≤ 2Θ ≤ 62.06), 5472 independent reflections (R_{int} = 0.0398), R_1 = 0.0437 (5432 $I \geq 2\sigma(I)$), ωR_2 = 0.1116 (all data), GOOF = 1.053, Flack parameter −0.018(11), Hooft parameter 0.003(3). CCDC 965911.

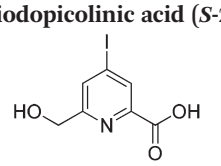
R*-L^1** and ***R*-L^2** were synthesised in an analogous manner to the ***S series starting from *R*-(+)-α-methylbenzyl amine.

***R*-[EuL^1](CF$_3$SO$_3$)$_3$.** ^{1}H NMR (295 K, 400 MHz, CD$_3$OD) δ_H major diastereoisomer 7.6 (pyCH′N), 7.5 (py-H^3), 7.4 (py-H^5), 7.3 (py-H^4), 6.9 (Ph-H^p), 6.7 (Ph-H^m), 5.7 (Ph-H^o), 5.1 (NCH′$_{ax}$) 4.0 (C*H*CH$_3$), 1.2 (CHC*H*$_3$), −0.7 (pyCHN), −1.5 (NCH$_{eq}$), −2.2 (NCH′$_{eq}$), −6.6 (NCH$_{ax}$); *m*/*z* [HRMS]$^+$ 992.3674 [M − 2H]$^+$ ($C_{51}H_{55}N_9O_3{}^{151}$Eu requires 992.3626). Crystals of the europium complex were grown by slow evaporation of aqueous methanol (1 : 1 v/v) and examined by X-ray crystallography.

Crystal data $C_{51}H_{57}EuN_9O_3 \times 3CF_3SO_3$, M_r = 1443.22, trigonal (*R*3); *a* = 21.6423(8), *c* = 11.5027 Å, *V* = 4665.9 Å^3, *Z* = 3; μ = 1.201 mm^{-1}, D_{calc} = 1.541 mg mm^{-3}, *T* = 120 K; 29 561 reflections were measured (3.76 ≤ 2Θ ≤ 62), 6082 independent reflections (R_{int} = 0.0267), R_1 = 0.0281 (6077 $I \geq 2\sigma(I)$), ωR_2 = 0.0740 (all data), GOOF = 1.029, Flack parameter −0.012(7), Hooft parameter -0.009(2). CCDC 965910.

***R*-[TbL^1](CF$_3$SO$_3$)$_3$.** ^{1}H NMR (295 K, 400 MHz, CD$_3$OD) δ_H major diastereoisomer, partial assignment: 57.5 (NCH$_{ax}$), 29.9 (NCH′$_{eq}$), 23.9 (NCH$_{eq}$), 8.6 (CHC*H*$_3$), 5.8 (C*H*CH$_3$), 4.5 (Ph-H^m), 2.0 (Ph-H^o), −3.2 (py-H^4), −4.4 (py-H^5), −11.0 (py-H^3), −12.4 (NCH′$_{ax}$), −45.5 (pyCH′N); *m*/*z* [HRMS]$^+$ 1000.368 [M − 2H]$^+$ ($C_{51}H_{55}N_9O_3{}^{159}$Tb requires 1000.368).

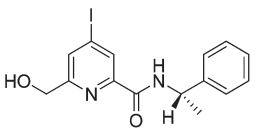
6-(Hydroxymethyl)-4-iodopicolinic acid (*S*-2a)



Methyl 6-(hydroxymethyl)-4-iodopicolinate (200 mg, 0.683 mmol) was dissolved in a 1 : 1 v/v mixture of ethanol–

water (6 mL) and NaOH (2 M, 0.5 mL) was added dropwise. The solution was stirred at room temperature for 1 h. The ethanol was removed under reduced pressure and the aqueous layer was acidified to pH = 4 using a 2 M HCl solution until a white precipitate was formed. The solid was extracted into EtOAc (4 × 50 mL), dried over $MgSO_4$ and concentrated under reduced pressure to yield the compound ***S*-2a** as a white solid (168 mg, 88%) which was used in the next step without further purification. TLC analysis R_f 0.08 (silica, 15% CH_3OH in CH_2Cl_2); m.p. >190 °C (dec.); ^{1}H NMR (295 K, 400 MHz, MeOD) δ_H 8.38 (1H, s, py-H^3), 8.16 (1H, s, py-H^5), 4.72 (2H, s, py-CH_2); ^{13}C NMR (295 K, 100 MHz, MeOD) δ_C 166 (*C*OOH), 164 (py-C^6), 149 (py-C^2), 134 (py-C^5), 133 (py-C^3), 108 (py-C^4), 64.7 (py-CH_2); *m*/*z* (HRMS$^+$) 279.9478 $[M + H]^+$ ($C_7H_7NO_3{}^{127}I$ requires 279.9471).

(*S*)-6-(Hydroxymethyl)-4-iodo-*N*-(1-phenylethyl)picolinamide (*S*-2b)

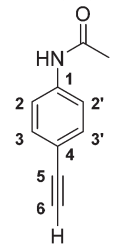


$HOBt{\cdot}H_2O$ (442 mg, 3.27 mmol), EDC (507 mg, 3.27 mmol), DIPEA (0.76 mL, 4.36 mmol) and (*S*)-(−)-α-methylbenzyl amine (0.30 mL, 2.40 mmol) were dissolved in anhydrous 1 : 1 DMF–DCM (4 mL). The carboxylic acid, ***S*-2a**, (608 mg, 2.18 mmol in 1 mL DMF) was added slowly and dropwise to the solution and the mixture stirred at rt for 22 h under an argon atmosphere. The solvent was removed under reduced pressure, water was added to the crude residue and the mixture extracted with EtOAc (4 × 40 mL). The organic layers were combined and washed successively with water (1 × 40 mL) and brine (1 × 40 mL), dried over $MgSO_4$ and the solvent removed under reduced pressure. The crude mixture was purified by flash column chromatography (silica, gradient elution starting from 20% EtOAc in hexane to 50% EtOAc in hexane) to afford ***S*-2b** as a yellow oil (510 mg, 61%). TLC analysis R_f 0.38 (silica, 50% EtOAc in hexane); ^{1}H NMR (295 K, 400 MHz, $CDCl_3$) δ_H 8.48 (1H, s, py-H^3), 8.08 (1H, d, ^3J 8.5, NH), 7.92 (1H, s, py-H^5), 7.39–7.38 (2H, m, Ph-H^o), 7.36–7.34 (2H, m, Ph- H^m), 7.29–7.27 (1H, m, Ph-H^p), 5.32 (1H, dq, ^3J 8.5, ^3J 7, C*H*CH_3), 4.76 (2H, s, py-CH_2), 1.62 (3H, d, ^3J 7, CH*C*H_3); ^{13}C NMR (295 K, 100 MHz, $CDCl_3$) δ_C 161.9 (*C*ONH), 159.5 (py-C^6), 149.3 (py-C^2), 143.0 (Ph-C^i), 132.6 (py-C^5), 130.9 (py-C^3), 128.9 (Ph-C^m), 127.6 (Ph-C^p), 126.4 (Ph-C^o), 108.0 (py-C^4), 64.3 (py-*C*H_2), 49.1 (*C*HCH$_3$), 21.9 (CH*C*H$_3$); *m*/*z* (HRMS$^+$) 383.0271 $[M + H]^+$ ($C_{15}H_{16}N_2O_2I^{127}$ requires 383.0257).

(4-(Trimethylsilyl)ethynyl)acetanilide (3a) CAS: 81854-47-9

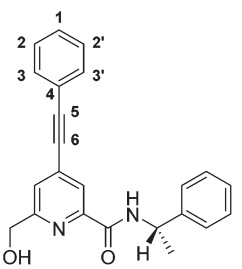
4-((Trimethylsilyl)ethynyl)aniline (200 mg, 1.06 mmol) was dissolved in anhydrous CH_2Cl_2 (3 mL) and acetic anhydride (0.12 mL, 1.27 mmol) was added dropwise. The solution was stirred at room temperature under an argon atmosphere for 2 h. The reaction mixture was washed with saturated aqueous Na_2CO_3 solution (10 mL) and extracted into CH_2Cl_2 (2 × 10 mL). The organic layers were combined, dried over $MgSO_4$, filtered and the solvent removed under reduced pressure to yield the compound **3a** as a pale brown solid. TLC analysis R_f 0.32 (silica, 50% EtOAc in hexane); m.p. 152–153 °C; ^{1}H NMR (295 K, 400 MHz, $CDCl_3$) δ_H 7.47–7.40 (4H, m, Ar-H), 2.17 (3H, s, COCH_3), 0.24 (9H, s, Si(CH_3)$_3$); ^{13}C NMR (295 K, 100 MHz, $CDCl_3$) δ_C 168.3 (*C*OCH$_3$), 138.2 (Ar-C), 132.9 (Ar-C), 119.3 (Ar-C), 118.9 (Ar-C), 104.9 (alkyne C), 93.8 (alkyne C), 24.9 (CO*C*H$_3$), 0.1 (Si(*C*H$_3$)$_3$); *m*/*z* (HRMS$^+$) 232.1148 $[M + H]^+$ ($C_{13}H_{18}NOSi$ requires 232.1158).

N-(4-Ethynylphenyl)acetamide (3b) CAS: 35447-83-7



(4-(Trimethylsilyl)ethynyl)acetanilide (213 mg, 0.921 mmol) was dissolved in anhydrous THF (3.5 mL) and triethylammonium trihydrofluoride (1.50 mL, 9.21 mmol) was added. The mixture was stirred at 35 °C under argon for 48 h. The solvent was removed under vacuum to give an off-white solid which was purified by column chromatography (silica, gradient elution starting from 100% hexane to 40% EtOAc in hexane) to afford compound **3b** as a white solid (104 mg, 71%). TLC analysis R_f 0.31 (silica, 40% EtOAc in hexane); ^{1}H NMR (295 K, 400 MHz, $CDCl_3$) δ_H 7.64 (1H, s, NH), 7.48 (2H, d, ^3J 8.5, Ar-H$^{2,2'}$), 7.43 (2H, d, ^3J 8.5, Ar-H$^{3,3'}$), 3.04 (1H, s, H^6), 2.17 (3H, s, COCH_3); ^{13}C NMR (295 K, 100 MHz, $CDCl_3$) δ_C 168.7 (*C*OCH$_3$), 138.5 (Ar-C^1), 133.0 (Ar-C$^{3,3'}$), 119.5 (Ar-C$^{2,2'}$), 117.8 (C^4), 83.5 (C^5), 76.8 (C^6), 24.8 (CO*C*H$_3$); *m*/*z* (HRMS$^+$) 160.0751 $[M + H]^+$ ($C_{10}H_{10}NO$ requires 160.0762); m.p. 115–117 °C (lit. 115–119 °C).[29]

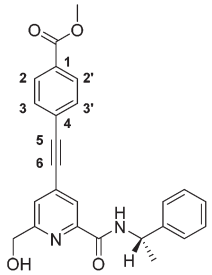
(*S*)-6-(Hydroxymethyl)-*N*-(1-phenylethyl)-4-(phenylethynyl)-picolinamide (*S*-4a)



General Sonogashira cross coupling reaction. The compound ***S*-2b** (100 mg, 0.262 mmol) was dissolved in anhydrous THF (2 mL) and the solution was degassed (freeze–thaw cycle) three times. Phenylacetylene (40 μL, 0.393 mmol) and triethylamine (0.18 mL, 1.31 mmol) were added and the solution was degassed (freeze–thaw cycle) once more. [1,1-Bis(diphenylphosphino)ferrocene]dichloropalladium(II) (19 mg, 26 μmol) and CuI (10 mg, 52 μmol) were added and the resulting brown

solution was stirred at 65 °C under argon for 24 h. The solvent was removed under reduced pressure and the resulting brown oil was purified by column chromatography (silica, gradient elution starting from 100% CH_2Cl_2 to 2% CH_3OH in CH_2Cl_2 in 0.2% increments) to give the compound ***S*-4a** as a yellow oil (91 mg, 98%). TLC analysis R_f 0.32 (silica, 1% CH_3OH in CH_2Cl_2); ^{1}H NMR (295 K, 400 MHz, $CDCl_3$) δ_H 8.19 (1H, br s, py-H^3), 8.15 (1H, d, ^3J 9, CONH), 7.57–7.54 (3H, m, Ar-H$^{3,3'}$, py-H^5), 7.42–7.27 (8H, m, Ar-H^1, Ar-H$^{2,2'}$, Ph-H), 5.35 (1H, dq, ^3J 9, ^3J 7, C*H*CH$_3$), 4.80 (2H, s, py-CH$_2$), 1.63 (3H, d, ^3J 7 CHC*H*$_3$); ^{13}C NMR (295 K, 100 MHz, $CDCl_3$) δ_C 162.9 (CONH), 159.1 (py-C^6), 149.2 (py-C^2), 143.1 (Ph-C^i), 134.0 (C^4), 132.1 (Ar-C), 129.6 (Ar-C), 128.8 (Ph-C), 128.6 (Ph-C), 127.5 (py-C^5), 126.4 (Ph-C), 124.9 (py-C^4), 123.4 (py-C^3), 121.9 (C^1), 95.4 (C^5), 86.5 (C^6), 64.7 (py-CH$_2$), 49.0 (*C*HCH$_3$), 21.9 (CH*C*H$_3$); *m*/*z* (HRMS$^+$) 357.1608 [M + H]$^+$ ($C_{23}H_{21}N_2O_2$ requires 357.1603).

(*S*)-Methyl 4-((2-(hydroxymethyl)-6-(1-phenylethylcarbamoyl)-pyridin-4-yl)ethynyl)benzoate (*S*-4b)



The compound ***S*-4b** was obtained as a yellow oil (97 mg, 89%) according to the general cross coupling procedure. TLC analysis R_f 0.19 (silica, 1% CH_3OH in CH_2Cl_2); ^{1}H NMR (295 K, 400 MHz, $CDCl_3$) δ_H 8.21 (1H, br s, py-H^5), 8.13 (1H, d, ^3J 7, CONH), 8.04 (2H, d, ^3J 8, Ar-H$^{2,2'}$), 7.62–7.60 (3H, m, Ar-H$^{3,3'}$, py-H^3), 7.42–7.28 (5H, m, Ph-H), 5.35 (1H, dq, ^3J 7, ^3J 7, C*H*CH$_3$), 4.82 (2H, s, py-CH$_2$), 3.94 (3H, s, CO$_2$C*H*$_3$), 2.80 (1H, br s, OH), (1.64, 3H, d, ^3J 7, CHC*H*$_3$); ^{13}C NMR (295 K, 100 MHz, $CDCl_3$) δ_C 166.4 (*C*O$_2$Me), 162.8 (*C*ONH), 159.4 (py-C^2), 149.4 (py-C^6), 143.0 (Ph-C^i), 133.4 (Ar-C^4), 132.0 (Ar-C$^{3,3'}$), 130.7 (Ar-C^1), 129.7 (Ar-C$^{2,2'}$), 128.8 (Ph-C^m), 127.6 (Ph-C^p), 126.4 (Ph-C^o), 125.0 (py-C^3), 123.4 (py-C^5), 94.1 (C^5), 89.0 (C^6), 64.7 (py-CH$_2$), 52.5, 49.0 (*C*HCH$_3$), 21.9 (CH*C*H$_3$); *m*/*z* (HRMS$^+$) 415.1643 [M + H]$^+$ ($C_{25}H_{23}N_2O_4$ requires 415.1658).

(*S*)-6-(Hydroxymethyl)-4-((4-methoxyphenyl)-*N*-(1-phenylethyl)-picolinamide (*S*-4c)

The compound ***S*-4c** was obtained as a yellow oil (190 mg, 94%) according to the general cross coupling procedure. TLC analysis R_f 0.18 (silica, 1% CH_3OH in CH_2Cl_2); ^{1}H NMR (295 K, 400 MHz, $CDCl_3$) δ_H 8.17 (1H, br s, py-H^3), 8.12 (1H, d, ^3J 7.5, CONH), 7.53 (1H, br s, py-H^5), 7.49 (2H, dt, ^4J 2, ^3J 9, Ar-H$^{3,3'}$), 7.42–7.35 (4H, m, Ph-H^o, Ph-H^m), 7.29–7.27 (1H, m, Ph-H^p), 6.90 (2H, dt, ^4J 2, ^3J 9, Ar-H$^{2,2'}$), 5.36 (1H, dq, ^3J 7.5, ^3J 7, C*H*CH$_3$), 4.80 (2H, s, py-CH$_2$), 3.84 (3H, s, OC*H*$_3$), 2.77 (1H, br s, OH), 1.64 (3H, d, ^3J 7, CHC*H*$_3$); ^{13}C NMR (295 K, 100 MHz, $CDCl_3$) δ_C 162.9 (*C*ONH), 160.7 (Ar-C^1), 158.7 (py-C^6), 149.4 (py-C^2), 143.2 (Ph-C^i), 134.5 (Ar-C^4), 133.8 (Ar-C$^{3,3'}$), 128.9 (Ph-C), 127.6 (Ph-C), 126.4 (Ph-C) 124.7 (py-C^5), 123.4 (py-C^3), 114.4 (Ar-C$^{2,2'}$), 114.0 (py-C^4), 96.0 (C^5), 85.6 (C^6), 64.7 (py-*C*H$_2$), 55.5 (O*C*H$_3$), 49.0 (*C*HCH$_3$), 22.0 (CH*C*H$_3$); *m*/*z* (HRMS$^+$) 387.1701 [M + H]$^+$ ($C_{24}H_{23}N_2O_3$ requires 387.1709).

(*S*)-4-((4-Acetamidophenyl)ethynyl)-6-(hydroxymethyl)-*N*-(1-phenylethyl)picolinamide (*S*-4d)

The compound ***S*-4d** was obtained as a yellow oil (122 mg, 68%) according to the general cross coupling procedure. TLC analysis R_f 0.49 (silica, 5% CH_3OH in CH_2Cl_2); m.p. >200 °C (dec.); ^{1}H NMR (295 K, 400 MHz, d^6-DMSO) δ_H 10.19 (1H, s, N*H*OAc), 9.01 (1H, d, ^3J 8.5, CON*H*), 7.89 (1H, br s, py-H^3), 7.68–7.67 (3H, m, py-H^5, Ar-H$^{3,3'}$), 7.59–7.57 (2H, m, Ar-H$^{2,2'}$), 7.42–7.33 (4H, m, Ph-H^o, Ph-H^m), 7.24 (1H, t, ^3J 7, Ph-H^p), 5.59 (1H, br t, ^3J 6.5, OH), 5.21 (1H, dq, ^3J 8.5, ^3J 7, C*H*CH$_3$), 4.68 (2H, d, ^3J 6.3, py-CH$_2$), 2.07 (3H, s, NHCOC*H*$_3$), 1.54 (3H, d, ^3J 7, CHC*H*$_3$); ^{13}C NMR (295 K, 100 MHz, d^6-DMSO) δ_C 168.7 (NH*C*OCH$_3$), 162.4 (*C*ONH), 161.6 (py-C^6), 149.5 (py-CH$_2$), 144.1 (C^i), 140.7 (Ar-C^1), 132.7 (Ar-C$^{2,2'}$), 128.3 (C^m), 126.8 (C^p), 126.2 (C^o), 123.9 (py-C^5), 121.3 (py-C^3), 118.8 (Ar-C$^{3,3'}$), 114.9 (Ar-C^4), 94.7 (C^5), 85.9 (C^6), 63.6 (py-*C*H$_2$), 48.2 (*C*HCH$_3$), 24.1 (NHCO*C*H$_3$), 21.9 (CH*C*H$_3$); *m*/*z* (HRMS$^+$) 414.1803 [M + H]$^+$ ($C_{25}H_{24}N_3O_3$ requires 414.1818).

(*S*)-(6-(1-Phenylethylcarbamoyl)-4-(phenylethynyl)pyridin-2-yl)-methyl methanesulfonate (*S*-5a)

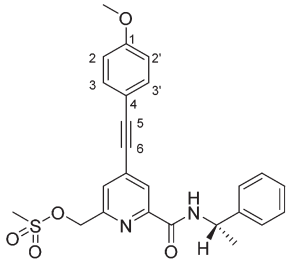
General mesylation procedure. The compound ***S*-4a** (91 mg, 0.256 mmol) was dissolved in anhydrous THF (2 mL) and NEt_3 (0.12 mL, 0.896 mmol) was added. The mixture was stirred at 5 °C and methanesulfonyl chloride (30 μL, 0.383 mmol) was added and the reaction stirred at rt for 30 minutes and monitored by TLC. The solvent was removed under reduced pressure and the residue dissolved in CH_2Cl_2 (15 mL) and washed with NaCl solution (saturated, 15 mL). The aqueous layer was re-extracted with CH_2Cl_2 (3 × 15 mL) and the organic layers were combined, dried over $MgSO_4$, filtered and the solvent removed under reduced pressure to yield the compound ***S*-5a**, as a bright yellow oil (111 mg, 99%), which was used directly in the next step without further purification. TLC analysis R_f = 0.75 (silica, 100% EtOAc); ^{1}H NMR (295 K, 400 MHz, $CDCl_3$) δ_H 8.25 (1H, d, ^4J 2, py-H^5), 8.22 (1H, d, ^3J 9, CON*H*), 7.65 (1H, d, ^4J 2, py-H^3), 7.58–7.56 (2H, m, Ar-H), 7.43–7.27 (8H, m, Ar-H, Ph-H), 5.35 (2H, s, py-CH$_2$), 5.33 (1H, dq, ^3J 9, ^3J 7, C*H*CH$_3$), 3.10 (3H, s, SO$_2$C*H*$_3$), 1.64 (3H, d, ^3J 7, CHC*H*$_3$); *m*/*z* (HRMS)$^+$ 435.1374 [M + H]$^+$ ($C_{24}H_{23}N_2O_4S$ requires 435.1379).

(*S*)-Methyl 4-((2-((methylsulfonyloxy)methyl)-6-(1-phenylethylcarbamoyl)pyridin-4-yl)ethynyl)benzoate (*S*-5b)

The compound ***S*-5b** was obtained as a yellow oil (101 mg, 88%) according to the general mesylation procedure. TLC analysis R_f 0.75 (silica, 100% EtOAc); ^{1}H NMR (295 K, 400 MHz, $CDCl_3$) δ_H 8.27 (1H, br s, py-H^5), 8.21 (1H, d, ^3J 8.5, CON*H*), 8.06 (2H, d, ^3J 8.5, Ar-H$^{2,2'}$), 7.67 (1H, br s, py-H^3), 7.63 (2H, d, ^3J 8.5, Ar-H$^{3,3'}$), 7.43–7.35 (4H, m, Ph-H^o, Ph-H^m), 7.28 (1H, t,

^3J 7, Ph-H^p), 5.36 (2H, s, py-CH$_2$), 5.33 (1H, dq ^3J 8.5, ^3J 7, C*H*CH$_3$), 3.94 (3H, s, CO$_2$C*H*$_3$), 3.11 (3H, s, SO$_2$CH$_3$), 1.64 (3H, d, ^3J 7, CHC*H*$_3$); ^{13}C NMR (295 K, 100 MHz, CDCl$_3$) δ_C 166.4 (*C*O$_2$CH$_3$), 162.2 (*C*ONH), 153.0 (py-C^6), 150.2 (py-C^2), 143.1 (Ph-C^i), 134.0 (Ar-C^4), 132.1 (Ar-C$^{3,3'}$), 130.9 (Ar-C^1), 129.8 (Ar-C$^{2,2'}$), 128.9 (Ph-C^m), 127.6 (Ph-C^p), 126.4 (Ph-C^o), 125.9 (py-C^3), 124.4 (py-C^5), 94.9 (C^5), 88.5 (C^6), 70.2 (py-*C*H$_2$), 52.5 (CO$_2$*C*H$_3$), 49.1 (*C*HCH$_3$), 38.4 (SO$_2$*C*H$_3$), 22.1 (CH*C*H$_3$); *m*/*z* (HRMS)$^+$ 493.1421 [M + H]$^+$ ($C_{26}H_{25}N_2O_6S$ requires 493.1433).

(*S*)-(4-((4-Methoxyphenyl)ethynyl-6-((1-phenylethylcarbamoyl)-pyridine-2-yl)methyl methane sulfonate (*S*-5c)



The compound ***S*-5c** was obtained as a yellow oil (165 mg, 98%) according to the general mesylation procedure. TLC analysis R_f 0.78 (silica, 100% EtOAc); ^{1}H NMR (295 K, 400 MHz, CDCl$_3$) δ_H 8.23 (1H, br s, py-H^5), 8.12 (1H, br s, CONH), 7.62 (1H, br s, py-H^3), 7.51 (2H, d, ^3J 8.5, Ar-H$^{3,3'}$), 7.42–7.28 (5H, m, Ph-H), 6.91 (2H, d, ^3J 8.5, Ar-H$^{2,2'}$), 5.34 (2H, s, py-CH$_2$), 5.32 (1H, t, ^3J 7, C*H*CH$_3$), 3.85 (3H, s, OC*H*$_3$), 3.10 (OSO$_2$C*H*$_3$), 1.64 (3H, d, ^3J 7, CHC*H*$_3$); ^{13}C NMR (295 K, 100 MHz, CDCl$_3$) δ_C 162.5 (*C*ONH), 160.8 (Ar-C^1), 152.7 (py-C^2), 150.1 (py-C^6), 143.2 (Ph-C^i), 135.0 (Ar-C^4), 133.9 (Ar-C$^{3,3'}$), 128.9 (Ph-C), 127.6 (Ph-C), 126.4 (Ph-C) 125.7 (py-C^3), 124.2 (py-C^5), 114.4 (Ar-C$^{2,2'}$), 96.7 (C^5), 85.4 (C^6), 70.4 (py-*C*H$_2$), 55.5 (O*C*H$_3$), 49.1 (*C*HCH$_3$), 38.4 (OSO$_2$*C*H$_3$), 22.1 (CH*C*H$_3$).

(*S*)-(4-((4-Acetamidophenyl)ethynyl)-6-(1-phenylethylcarbamoyl)pyridin-2-yl)methyl methanesulfonate (*S*-5d)

The compound ***S*-5d** was obtained as a yellow oil (110 mg, 84%) according to the general mesylation procedure. TLC analysis R_f 0.51 (silica, 100% EtOAc); ^{1}H NMR (295 K, 400 MHz, d^3-acetonitrile) δ_H 8.50 (1H, s, N*H*COCH$_3$), 8.45 (1H, d, ^3J 8.5, CON*H*), 8.05 (1H, d, ^4J 2, py-H^5), 7.67 (1H, d, ^4J 2, py-H^3), 7.61 (2H, dt, ^3J 9, ^4J 2, Ar-H$^{3,3'}$), 7.52 (2H, dt, ^3J 9, ^4J 2, Ar-H$^{2,2'}$), 7.39–7.21 (5H, m, Ph-H), 5.33 (2H, s, py-CH$_2$), 5.18 (1H, dq, ^3J 8.5, ^3J 7, C*H*CH$_3$), 3.12 (3H, s, SO$_2$C*H*$_3$), 2.04 (3H, s, NHCOC*H*$_3$), 1.53 (3H, d, ^3J 7, CHC*H*$_3$)H; *m*/*z* (HRMS$^+$) 492.1594 [M + H]$^+$ ($C_{26}H_{26}N_3O_5S$ requires 492.1593).

6,6′,6″-(1,4,7-Triazacyclononane-1,4,7-triyl)tris(methylene)tris-(*N*-((*S*)-1-phenylethyl)-4-(phenylethynyl)picolinamide) (*S*-L^{2a})

General alkylation procedure. 1,4,7-Triazacyclononane trihydrochloride (20 mg, 0.085 mmol) and the mesylate, ***S*-5a**, (111 mg, 0.256 mmol) were dissolved in anhydrous CH$_3$CN (4.5 mL) and K$_2$CO$_3$ (71 mg, 0.512 mmol) was added. The mixture was stirred under argon at 78 °C. After 24 h the reaction was cooled and filtered to remove excess potassium salts. The solvent was removed under reduced pressure and the crude material purified by column chromatography (silica, gradient elution starting from 100% CH$_2$Cl$_2$ to 10% CH$_3$OH in CH$_2$Cl$_2$) to give ***S*-L^{2a}** as a yellow glassy solid (35 mg, 36%). TLC analysis R_f 0.42 (silica, 5% CH$_3$OH in CH$_2$Cl$_2$); ^{1}H NMR (295 K, 400 MHz, CDCl$_3$) δ_H 8.21 (3H, br s, py-H^3), 7.51 (6H, d, ^3J 7, Ar-H$^{3,3'}$), 7.42–7.33 (15H, m, py-H^5, Ar-H^1, Ar-H$^{2,2'}$, Ph-H^o), 7.24 (6H, m, Ph-H^m), 7.16 (3H, t, ^3J 7.2, Ph-H^p), 5.34 (3H, q, ^3J 6.5, C*H*CH$_3$), 3.87 (6H, s, py-CH$_2$), 2.84 (12H, br s, *ring Hs*), 1.63 (9H, d, ^3J 6.5, CHC*H*$_3$); ^{13}C NMR (295 K, 100 MHz, CDCl$_3$) δ_C 163.1 (CONH), 159.4 (py-C^6), 149.8 (py-C^2), 143.3 (Ph-C^i), 133.4 (Ar-C^4), 132.1 (Ar-C), 129.5 (Ar-C), 128.7 (Ph-C^m), 127.4 (Ph-C^p), 127.1 (py-C^5), 126.4 (Ph-C^o), 122.9 (py-C^3), 122.0 (Ar-C^1), 94.8 (C^5), 86.8 (C^6), 64.1 (py-CH$_2$), 56.2 (*ring Cs*), 48.9 (*C*HCH$_3$), 21.9 (CH*C*H$_3$); *m*/*z* (HRMS$^+$) 1144.562 [M + H]$^+$ ($C_{75}H_{70}N_9O_3$ requires 1144.560).

Trimethyl 4,4′,4″-(*S*,*S*)-6,6′,6″-(1,4,7-triazacyclononane-1,4,7-triyl)tris(methylene)tris(2-((*S*)-1-phenylethylcarbamoyl)-pyridine-6,4-diyl)tris(ethyne-2,1-diyl)tribenzoate (*S*-L^{2b})

The compound ***S*-L^{2b}** was obtained as a yellow oil (58 mg, 55%) according to the general alkylation procedure. TLC analysis R_f 0.47 (silica, 5% CH$_3$OH in CH$_2$Cl$_2$); ^{1}H NMR (295 K, 700 MHz, CDCl$_3$) δ_H 8.41 (3H, d, ^3J 6, CON*H*), 8.17 (3H, br s, py-H^3), 8.02 (6H, d, ^3J 8.5, Ar-H$^{2,2'}$), 7.64 (3H, br s, py-H^5), 7.56 (6H, d, ^3J 8.5, Ar-H$^{3,3'}$), 7.38–7.36 (6H, m, Ph-H^o), 7.2–7.25 (6H, m, Ph-H^m), 7.20 (3H, t, ^3J 7, Ph-H^p), 5.33 (3H, dq, ^3J 6, ^3J 7, C*H*CH$_3$), 3.93 (9H, s, CO$_2$C*H*$_3$), 3.81 (6H, m, py-CH$_2$), 2.83 (12H, br s, *ring Hs*), 1.60 (9H, d, ^3J 7, CHC*H*$_3$); ^{13}C NMR (295 K, 100 MHz, CDCl$_3$) δ_C 166.4 (*C*O$_2$CH$_3$), 163.0 (*C*ONH), 159.6 (py-C^6), 149.9 (py-C^2), 143.3 (C^i), 132.9 (Ar-C^4), 132.0 (Ar-C$^{3,3'}$), 130.7 (Ar-C^1), 129.8 (Ar-C$^{2,2'}$), 128.7 (Ph-C^m), 127.5 (Ph-C^p), 127.1 (py-C^5), 126.4 (Ph-C^o), 123.0 (py-H^3), 93.7 (C^5), 89.3 (C^6), 64.1 (py-CH$_2$), 56.1 (*ring Cs*), 52.5 (CO$_2$*C*H$_3$), 48.9 (*C*HCH$_3$), 21.9 (CH*C*H$_3$); *m*/*z* (HRMS$^+$) 1318.623 [M + H]$^+$ ($C_{78}H_{76}N_9O_6$ requires 1318.627).

6,6′,6″-((1,4,7-Triazacyclononane-1,4,7-triyl)tris(methylene))-tris(4-((4-methoxyphenyl)ethynyl)-*N*-((*S*)-1-phenylethyl)-picolinamide) (*S*-L^{2c})

The compound ***S*-L^{2c}** was obtained as a yellow oil (42 mg, 28%) according to the general alkylation procedure. TLC analysis R_f 0.68 (silica, 7% CH$_3$OH in CH$_2$Cl$_2$); ^{1}H NMR (295 K, 400 MHz, CDCl$_3$) δ_H 8.47 (3H, d, ^3J 8.5, CON*H*), 8.13 (3H, br s, py-H^3), 7.45 (6H, d, ^3J 9, Ar-H$^{3,3'}$), 7.38–7.18 (18H, m, Ph-H, py-H^5), 6.87 (6H, d, ^3J 9, Ar-H$^{2,2'}$), 5.33 (3H, dq, ^3J 8.5, ^3J 6.5, C*H*CH$_3$), 3.82 (9H, s, OC*H*$_3$), 3.80–3.75 (6H, m, py-CH$_2$), 2.85–2.79 (12H, m, *ring Hs*), 1.60 (9H, d, ^3J 6.5, CHC*H*$_3$); ^{13}C NMR (295 K, 100 MHz, CDCl$_3$) δ_C 163.0 (*C*ONH), 160.4 (Ar-C^1), 159.1 (py-C^6), 149.5 (py-C^2), 143.2 (Ph-C^i), 133.6 (Ar-C^4), 133.5 (Ar-C$^{3,3'}$), 128.5 (Ph-C), 127.2 (Ph-C), 126.7 (Ph-C), 126.2 (py-C^5), 122.6 (py-C^3), 114.2 (Ar-C$^{2,2'}$), 113.9 (py-C^4), 95.0 (C^5), 85.7 (C^6), 63.9 (py-*C*H$_2$), 56.0 (*ring Cs*), 55.3 (O*C*H$_3$), 48.7 (*C*HCH$_3$), 21.8 (CH*C*H$_3$); *m*/*z* (HRMS$^+$) 1234.592 [M + H]$^+$ ($C_{78}H_{76}N_9O_6$ requires 1234.592).

6,6′,6″-(1,4,7-Triazacyclononane-1,4,7-triyl)tris(methylene)-tris(4-((4-acetamidophenyl)ethynyl)-*N*-((*S*)-1-phenylethyl)-picolinamide) (*S*-L^{2d})

The compound ***S*-L^{2d}** was obtained as a yellow oil (50 mg, 43%) according to the general alkylation procedure. TLC analysis R_f 0.63 (silica, 15% CH_3OH in CH_2Cl_2); ^{1}H NMR (295 K, 400 MHz, CD_3OD) δ_H 7.94 (3H, s, py-H^3), 7.58 (6H, d, ^3J 8.5, Ar-H$^{3,3'}$), 7.54 (3H, s, py-H^5), 7.36–7.16 (21H, m, Ph-H, Ar-H$^{2,2'}$), 5.20 (1H, s, C*H*CH$_3$), 4.04 (6H, br s, py-CH$_2$), 3.02 (12H, br s, ring Hs), 2.10 (9H, s, NHCOC*H*$_3$), 1.53 (9H, d, ^3J 6.5, CHC*H*$_3$); ^{13}C NMR (295 K, 100 MHz, CD_3OD) δ_C 171.6 (NH*C*OCH$_3$), 164.7 (*C*ONH), 151.4 (py-C^6), 144.4 (C^i), 141.5 (py-C^2), 135.4 (Ar-C^4), 133.8 (Ar-C$^{3,3'}$), 129.7 (Ph-C^o), 128.5 (py-C^5), 127.3 (Ph-C^m), 124.2 (py-C^4), 123.0 (py-C^3), 120.6 (Ar-C$^{2,2'}$), 117.6 (Ar-C^1), 86.6 (C^5), 79.1 (C^6), 64.6 (py-CH$_2$), 50.4 (*C*HCH$_3$), 24.1 (NHCOC*H*$_3$), 22.1 (CH*C*H$_3$); *m*/*z* (HRMS$^+$) 1315.621 [M + H]$^+$ ($C_{81}H_{76}N_{12}O_6$ requires 1315.624).

R*-L^{2d}** was synthesised in an analogous manner to the ***S series starting from *R*-(+)-α-methylbenzyl amine.

S-[EuL^{2a}](CF$_3$SO$_3$)$_3$

General complexation procedure. Europium(III) triflate (9 mg, 0.015 mmol) was added to a solution of ligand, ***S*-L^{2a}**, (18 mg, 0.015 mmol) in anhydrous acetonitrile (2 mL) and the mixture heated at reflux for 20 h. The solution was concentrated under vacuum and cold diethyl ether (2 mL) was added dropwise to the solution. The resulting solid was isolated and dried *in vacuo* to yield ***S*-[EuL^{2a}](CF$_3$SO$_3$)$_3$** as a yellow glassy solid (10 mg, 50%). ^{1}H NMR (295 K, 200 MHz, CD_3OD) δ_H major diastereoisomer, partial assignment: 7.7 (pyCH′N), 7.6, 7.4, 7.1, 7.0, 5.9, 4.1, 3.5, 1.2 (CHC*H*$_3$), 0.8, −1.5 (NCH$_{eq}$), −2.1 (NCH′$_{eq}$), −6.5 (NCH$_{ax}$); *m*/*z* (HRMS)$^+$ 1292.455 [M − 2H]$^+$ ($C_{75}H_{67}N_9O_3{}^{151}$Eu requires 1292.456). t_R = 8.4 min.

S-[EuL^{2b}](CF$_3$SO$_3$)$_3$

The complex ***S*-[EuL^{2b}](CF$_3$SO$_3$)$_3$** was obtained according to the general complexation procedure, using the ligand ***S*-L^{2b}**, as a white solid (10 mg, 52%). ^{1}H NMR (295 K, 400 MHz, CD_3OD) δ_H (major isomer, partial assignment: 8.2, 7.8, 7.4, 7.3, 7.0, 6.1, 5.1, 3.9, 1.2 (CHC*H*$_3$), 0.8, −1.6 (NCH$_{eq}$), −2.5 (NCH′$_{eq}$), −6.7 (NCH$_{ax}$); *m*/*z* (HRMS)$^+$ 734.7366 [M − H]$^{2+}$ ($C_{81}H_{72}N_9O_9{}^{151}$Eu requires 734.7418). t_R = 8.8 min.

S-[EuL^{2c}] (CF$_3$SO$_3$)$_3$

The complex ***S*-[EuL^{2c}](CF$_3$SO$_3$)$_3$** was obtained according to the general complexation procedure, using the ligand ***S*-L^{2c}**, as a white solid (20 mg, 70%). ^{1}H NMR (295 K, 400 MHz, CD_3OD) δ_H (major diastereoisomer, partial assignment: 7.6 (pyCH′N), 7.5, 7.3, 7.1, 7.0, 6.7, 5.8, 4.2, 3.9, 3.5, 2.0, 1.1 (CHC*H*$_3$), −0.8 (pyCHN), −1.5 (NCH$_{eq}$), −2.0 (NCH′$_{eq}$), −6.5 (NCH$_{ax}$); *m*/*z* (HRMS$^+$) 1382.492 [M − 2H]$^+$ ($C_{78}H_{73}N_9O_6{}^{151}$Eu requires 1382.488). t_R = 8.4 min.

S-[EuL^{2d}] (CF$_3$SO$_3$)$_3$

The complex ***S*-[EuL^{2d}](CF$_3$SO$_3$)$_3$** was obtained according to the general complexation procedure, using the ligand ***S*-L^{2d}**, as a yellow glassy solid (8 mg, 72%). ^{1}H NMR (295 K, 200 MHz, CD_3OD) δ_H major diastereoisomer, partial assignment 7.8, 7.6, 7.4, 7.1, 7.0, 6.9, 5.9, 4.1, 2.2, 1.2 (CHC*H*$_3$), 0.7, −1.5 (NCH$_{eq}$), −2.2 (NCH′$_{eq}$), −6.6 (NCH$_{ax}$); *m*/*z* (HRMS)$^+$ 1463.523 [M − 2H]$^+$ ($C_{81}H_{76}N_{12}O_6{}^{151}$Eu) requires 1463.520). t_R = 8.0 min.

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