Supplementary Information:

Axial fluoride binding by lanthanide DTMA complexes alters the local crystal field, resulting in dramatic spectroscopic changes

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Contents:

1 Materials and Methods

1.1 Synthesis of complexes

The ligand DTMA (1,4,7,10-tetrakis[(*N*-methylcarbamoyl)methyl]-1,4,7,10-tetraaza-cyclododecane) and its lanthanide complexes ($LnDTMA(OTf)_3$) were synthesised as previously described.[1] The complexes were characterised by NMR, mass spectrometry and CHN analysis.

1.2 NMR measurements

1.2.1 Instrumentation and parameters

NMR measurements were made using either a Varian Inova-500 (^{1}H = 500 MHz, ^{19}F = 470 MHz), a Bruker Avance-400 (^{1}H = 400 MHz, ^{19}F = 376 MHz), a Bruker AVIII-500 or a Bruker AVIII-400. Wide spectral width spectra were obtained using pulses sufficiently short to ensure reasonably uniform excitation over the observed bandwidth, and with acquisition and recycle times matched to the relaxation characteristics of the lanthanide complexes (repetition time typically 100 ms).
EXSY spectra were recorded at 500 MHz using a gradient selected NOESY sequence with a mixing time of 1 ms.
Y-F HMQC correlation spectra were recorded on the Varian Inova-500 (^{19}F = 470 MHz, ^{89}Y = 25 MHz) and optimized for a coupling of 65 Hz.
Exchange rates were estimated from saturation transfer experiments. The intensities of the free fluoride peaks were recorded in the presence and absence of saturation of the bound fluoride peaks. The rates were then calculated using the following equation:[2]

$$Rate = \frac{1}{T_{1A}}\left(\frac{M_{0A}}{M_A} - 1\right)$$

1.2.2 Titrations

0.005M LnDTMA solutions were titrated with 0.8M NaF in D_2O. A non-dilution method was used where 0.5 mL of the LnDTMA stock solution was put in an NMR tube and a solution of NaF made with the same stock solution was titrated in using a glass microliter syringe. Delay times (d1) were at least 5 times longer than the T_1 of the slowest relaxing peak in order to make integration quantitative. Spectra were phased and baselined before analysis. All titrations were carried out at 298 K.

For ^{1}H titrations of systems in slow exchange, (Eu^{3+}, Y^{3+}, Yb^{3+}), the binding isotherms were obtained by integration of the signals relative to the water-soluble standard DSS (4,4-dimethyl-4-silapentane-1-sulfonic acid). The increasing signals of the fluoride-bound species and the decreasing signals of the original species were both monitored and averaged respectively to give two independent data sets. These were then fit simultaneously in Dynafit[3] to give the association constant K. In the case of LuDTMA, the chemical shifts of 3 clearly defined peaks were monitored as a function of [NaF], after referencing the spectra to H_2O. The 3 data sets were fit simultaneously.

For ^{19}F titrations, the bound fluoride peak was integrated with respect to the triflate peak at around -78 ppm after phasing and baseline correction. For EuDTMA, the pulse width was reduced to 3 μs (ca. 14 °) to ensure excitation across the large chemical shift range.

1.3 Luminescence measurements

1.3.1 Instrumentation and parameters

All luminescence measurements were carried out on a Horiba Fluorolog 3. Spectra of EuDTMA were recorded in fluorescence mode exciting at 394 nm. Exit slits of 0.2

nm were employed when examining the fine structure of ΔJ = 1 band, otherwise a 1 nm slit was used. Lifetime measurements used a delay time of 0.05 ms and a gate time of 1 ms. Lifetimes are quoted with an error of ±10%.
Spectra of YbDTMA were recorded with the same instrument adapted with a Hamamatsu R5509-42 NIR PMT InGaAs detector cooled to -80°C. An excitation wavelength of 265 nm and an exit slit of 5 nm were used; multiple accumulations were necessary.

1.3.2 Titration

EuDTMA (0.001 M) was titrated with 0.8 M NaF in D_2O using the non-dilution methodology described above. Spectra were recorded in fluorescence mode exciting at 394 nm and using 1 nm exit slits. The bands were integrated from 583-604 nm (ΔJ = 1), 605-640 nm (ΔJ = 2) and 680-710 nm (ΔJ = 4) and ratios ΔJ = 2/ΔJ = 1 and ΔJ = 2/ΔJ = 4 gave binding isotherms for fitting.

1.3.3 Data fitting

All titration data was fit using the Dynafit program[3] to get equilibrium constants, K. An example script is shown below:

```
[task]
data = equil
task = fit
[mechanism]
Eu + F <==> complex1 : K1 assoc
[constants]
K1 = 10 ??
[concentrations]
Eu = 0.005
[equil]
variable F
file ./NMR/EuDTMA_F_1H_new_RT.txt |response complex1 = 45?
file ./NMR/EuDTMA_F_1H_old_RT.txt |response Eu = 47?
[output]
directory ./output/NMR/EuDTMA_F_1H_RT
[end]
```

2 Luminescence lifetimes

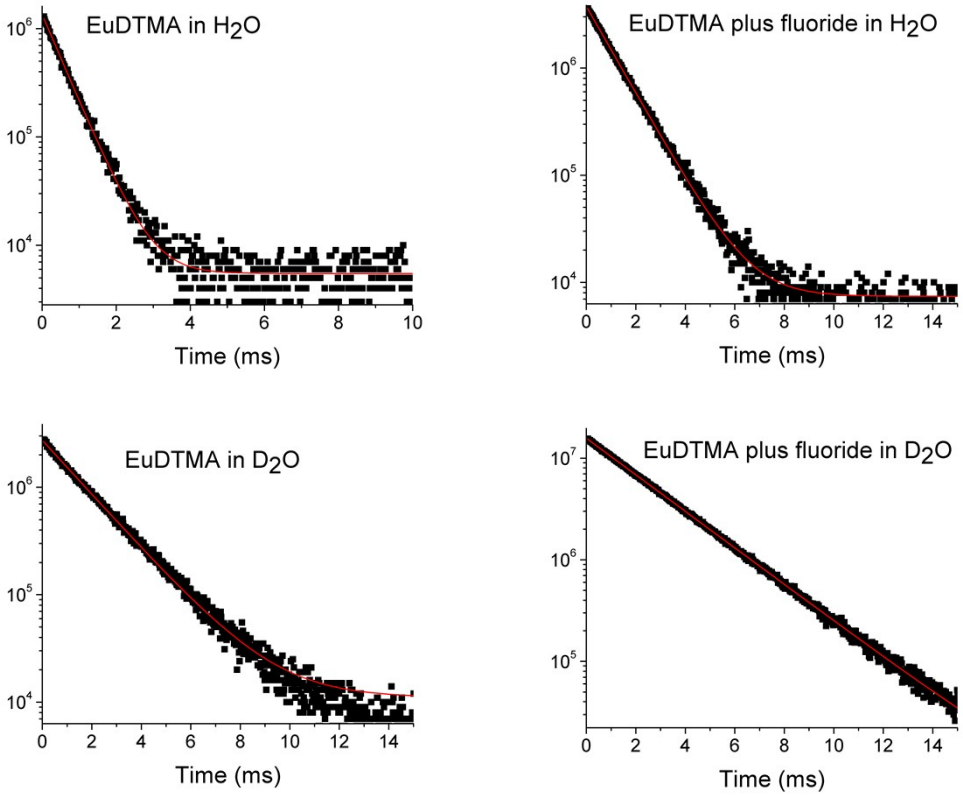

Figure S1. Luminescence decays (λ_{ex} = 394 nm, λ_{em} = 616 nm) of EuDTMA in H_2O and D_2O with and without addition of excess sodium fluoride.

3 ^{1}H NMR of diamagnetic complexes

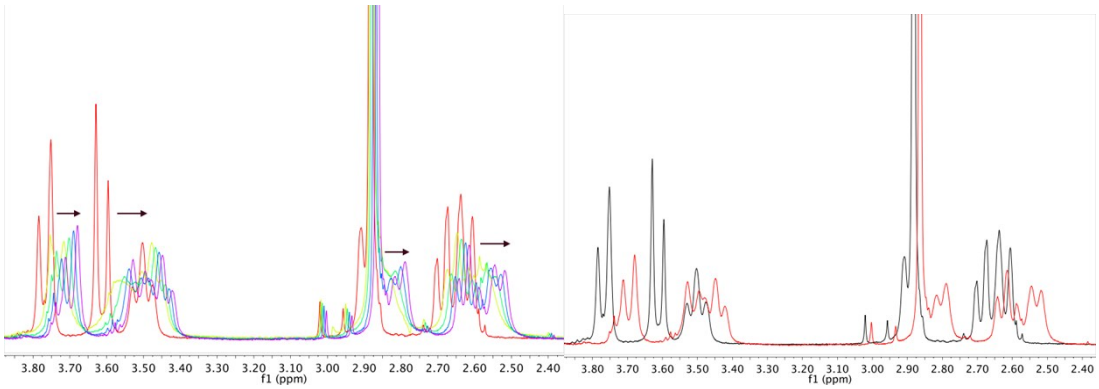

Figure S2. ^{1}H NMR spectra of LuDTMA in D_2O at 298 K recorded at 500MHz. Left: titration with NaF, arrows indicate the direction of change. Right: start (black) and end (red) points of the titration.

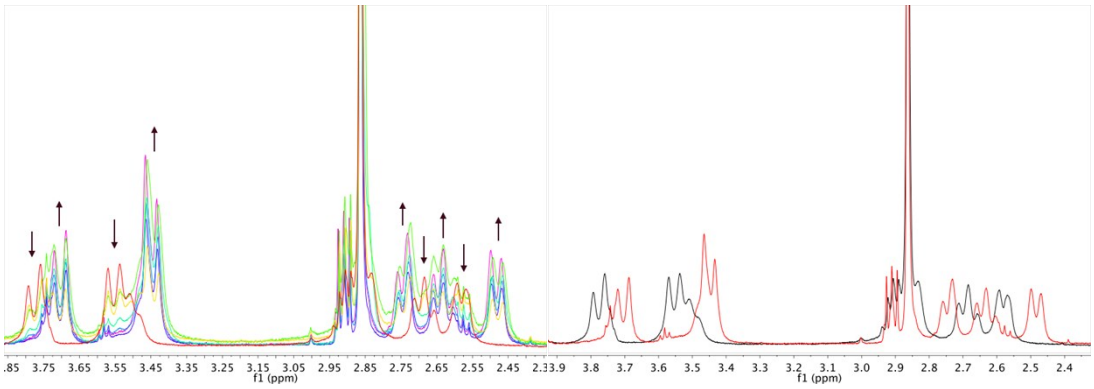

Figure S3. ^{1}H NMR spectra of YDTMA in D_2O at 298 K recorded at 500MHz. Left: titration with NaF, arrows indicate the direction of change. Right: start (black) and end (red) points of the titration.

4 ^{1}H NMR of paramagnetic complexes

4.1 Bleaney plots

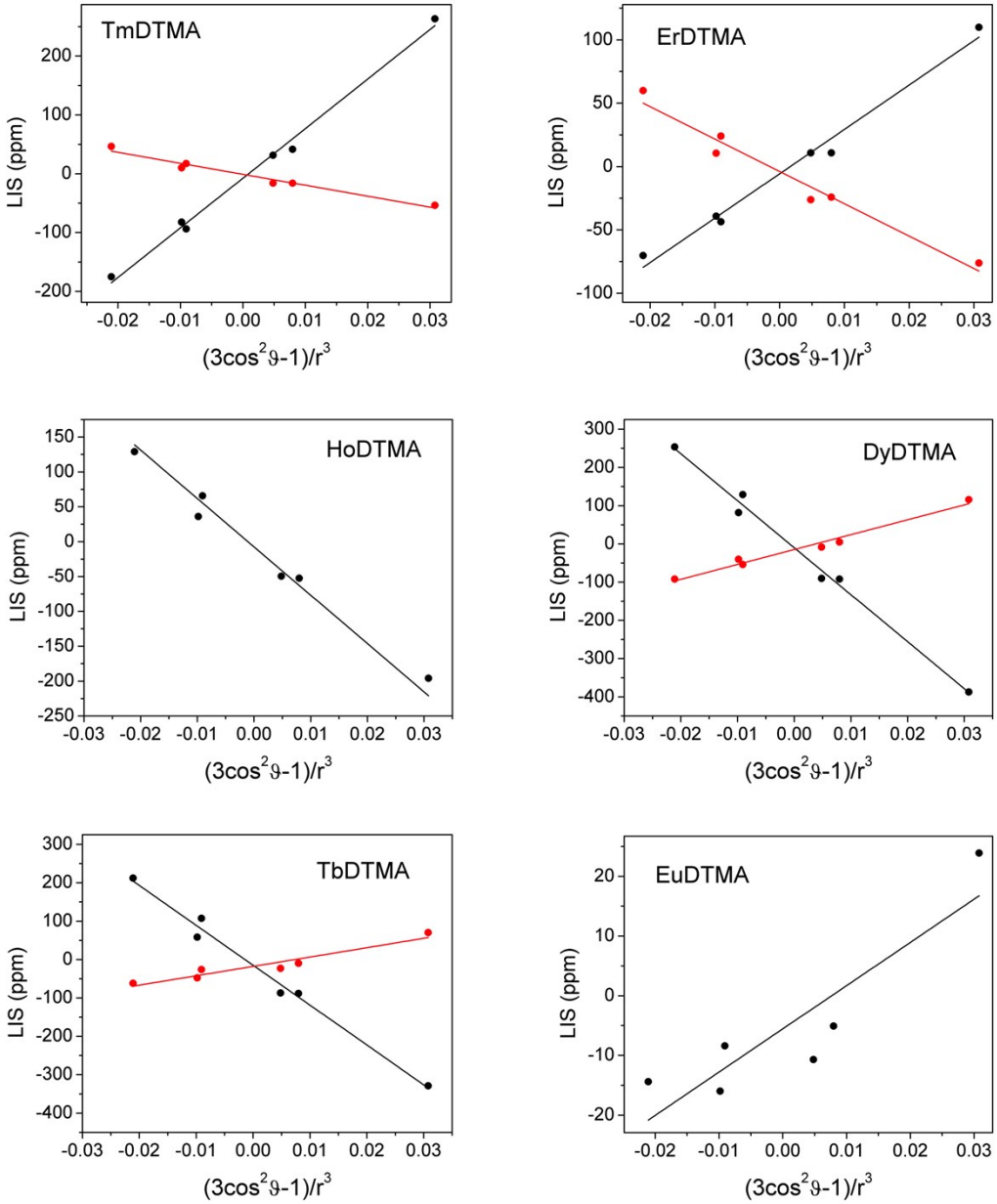

Figure S4. Plots of the experimental lanthanide induced shifts against $(3\cos^2\vartheta-1)/r^3$ for LnDTMA proton resonances in the absence (black) and presence (red) of an excess of sodium fluoride in D_2O, using coordinates from the crystal structure of DyDTMA.[1] R^2 values for linear fits all ≥0.9 except for EuDTMA. Fluoride data for HoDTMA cannot be extracted due to the very small chemical shift range resulting in overlap of peaks.

4.2 Results from Reilley plots

Table S1. Calculated shifts (ppm) for YbDTMA-OH_2 based on F and G values extracted from the Reilley plots.

Proton	δ_P (C^DG)	δ_C (<S_Z>F)	Total calc. LIS	Expt. LIS	Diff.
Axial 1	99.40	2.14	101.54	97.7	-3.84
Axial 2	-34.52	-1.16	-35.68	-35.2	0.48
Eq. 1	17.92	-1.68	16.24	15.8	-0.44
Eq. 2	15.34	-2.14	13.20	12.9	-0.30
Amide 1	-27.42	-2.73	-30.15	-29.7	0.45
Amide 2	-64.35	-1.10	-65.45	-64.0	1.45
Methyl	-9.23	0.35	-8.88	-9.1	-0.22

Table S2. Calculated shifts (ppm) for YbDTMA-F based on F and G values extracted from the Reilley plots.

Proton	δ_P (C^DG)	δ_C (<S_Z>F)	Total calc. LIS	Expt. LIS	Diff.
Axial 1	-23.60	-1.66	-25.26	-25	0.26
Axial 2	8.18	-0.06	8.12	7.7	-0.42
Eq. 1	-4.41	-2.01	-6.43	-6.2	0.23
Eq. 2	-3.29	-2.72	-6.01	-5.7	0.31
Amide 1	6.77	-1.04	5.74	6.0	0.26
Amide 2	20.14	1.43	21.58	21.6	0.02
Methyl	2.06	0.14	2.20	2.3	0.10

Table S3. Calculated % pseudocontact shift for each proton (calculated with absolute values of the shifts)

Ln	Ax. 1		Ax. 2		Eq. 1		Eq. 2		Am. 1		Am. 2		Me	
	No F^-	+ F^-	No F^-	+ F^-	No F^-	+ F^-	No F^-	+ F^-	No F^-	+ F^-	No F^-	+ F^-	No F^-	+ F^-
Pr	95	86	93	99	82	49	76	35	82	74	96	86	92	87
Nd	84	61	77	95	54	19	44	12	53	42	87	61	74	63
Sm	95	84	92	98	80	44	72	31	79	71	96	84	90	85
Eu	74	47	65	91	40	12	31	7	39	29	79	47	61	49
Tb	94	82	90	98	77	41	69	28	76	68	95	82	89	83
Dy	95	85	92	98	81	47	75	33	81	73	96	85	91	86
Ho	90	74	86	97	68	31	59	20	67	57	92	74	84	76
Er	92	78	88	98	73	35	64	23	72	62	94	78	87	79
Tm	97	92	96	99	89	62	84	48	88	83	98	92	95	92
Yb	98	93	97	99	91	69	88	55	91	87	98	93	96	94

5 ^{19}F NMR

5.1 ^{19}F Spectra

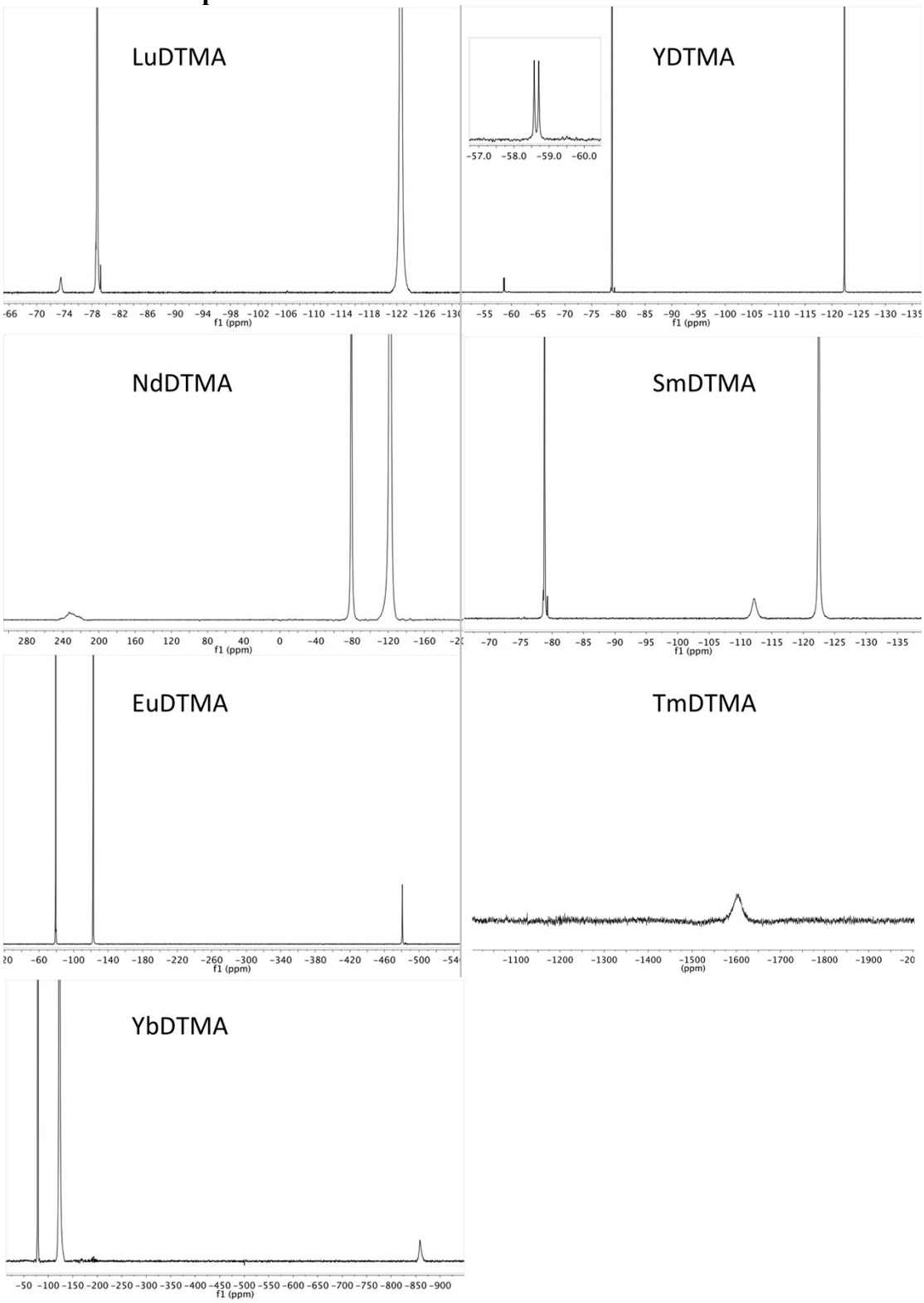

Figure S5. ^{19}F NMR spectra of Lu^{3+}, Y^{3+}, Nd^{3+}, Sm^{3+}, Eu^{3+}, Tm^{3+} and Yb^{3+} lanthanide complexes of DTMA in D_2O with addition of excess sodium fluoride recorded at either 400 or 500 MHz. The NdDTMA spectrum was recorded at 278 K, the others at 298 K. The inset for YDTMA shows the fine structure of the bound fluoride peak.

5.2 Results from Reilley plots

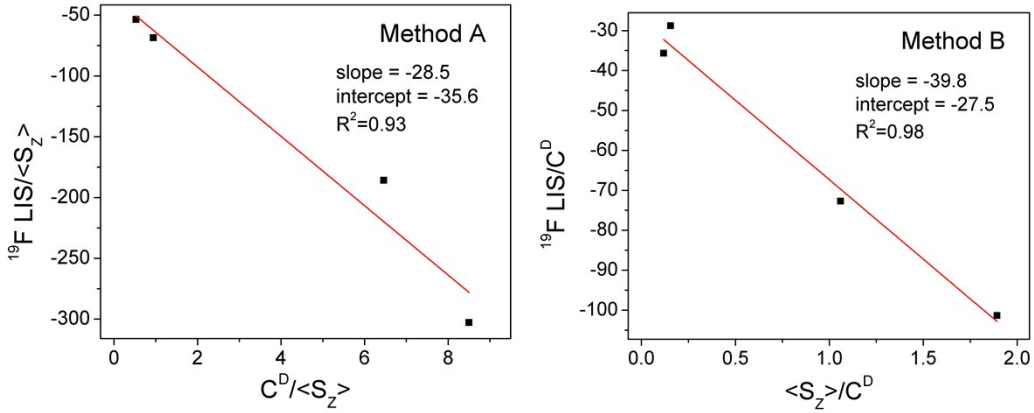

Figure S6. Reilley plots for bound fluoride peaks of Nd, Eu, Tm and Yb DTMA complexes using both methods.

Table S4. Calculated ^{19}F pseudocontact and contact shift contributions, the total calculated LIS, calculated observed shift and the percentage pseudocontact shift (using absolute values), based on F and G values from the Reilley plots and using the Lu analogue to approximate δ_D.

Ln	**δ_P (C^DG)**	**δ_C ($\langle S_Z \rangle F$)**	**Total LIS**	**Calc δ_{obs}**	**% δ_P**
Pr	308	111	419	345	73
Nd	118	168	285	211	41
Sm	20	-8	11	-63	70
Eu	-112	-285	-397	-471	28
Tb	2408	-1201	1207	1133	67
Dy	2800	-1077	1723	1649	72
Ho	1092	-854	238	164	56
Er	-924	-580	-1504	-1578	61
Tm	-1484	-310	-1794	-1868	83
Yb	-616	-98	-714	-788	86

6 Titration data

6.1 ^{1}H Titrations: binding isotherms

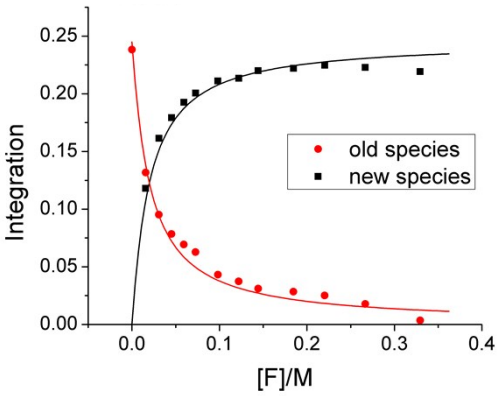

Figure S6. Binding isotherms and fits for titration of EuDTMA with NaF monitoring ^{1}H NMR integrals relative to DSS.

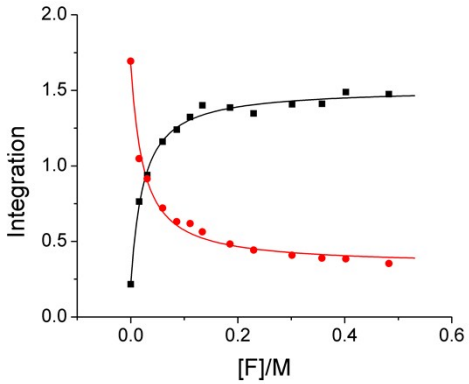

Figure S7. Binding isotherms and fits for titration of YDTMA with NaF monitoring ^{1}H NMR integrals relative to DSS.

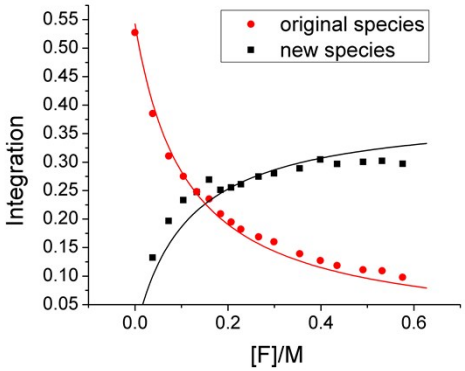

Figure S8. Binding isotherms and fits for titration of YbDTMA with NaF monitoring ^{1}H NMR integrals relative to DSS.

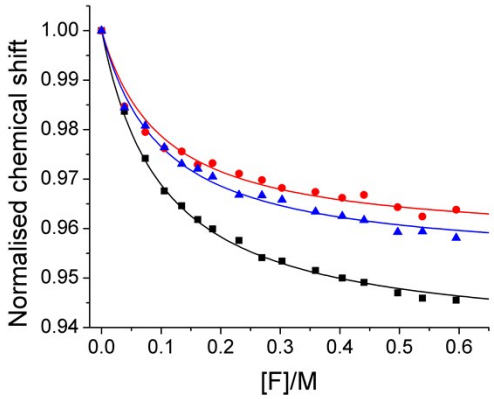

Figure S9. Binding isotherms and fits for titration of LuDTMA with NaF monitoring ^{1}H NMR chemical shifts of three peaks relative to water. Shifts are normalised by subtraction to give an initial shift of 1.

6.2 ^{19}F Titrations: binding isotherms

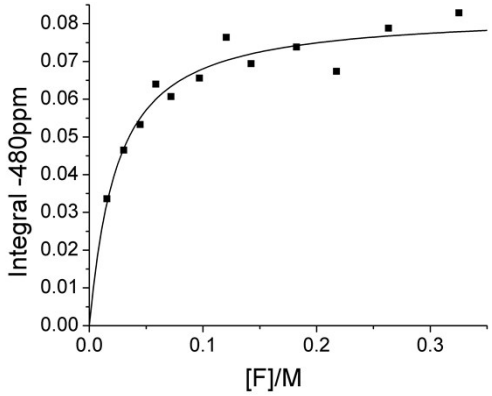

Figure S10. Binding isotherm and fit for titration of EuDTMA with NaF monitoring the^{19}F NMR integral of the bound fluoride peak relative to the triflate peak.

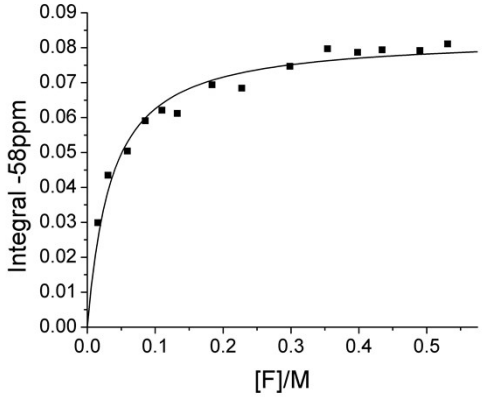

Figure S11. Binding isotherm and fit for titration of YDTMA with NaF monitoring the^{19}F NMR integral of the bound fluoride peak relative to the triflate peak.

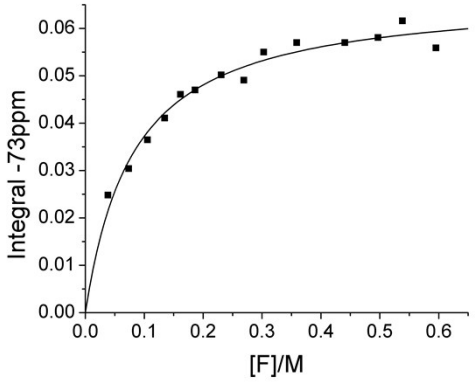

Figure S12. Binding isotherm and fit for titration of LuDTMA with NaF monitoring the^{19}F NMR integral of the bound fluoride peak relative to the triflate peak.

6.3 Luminescence titration: EuDTMA

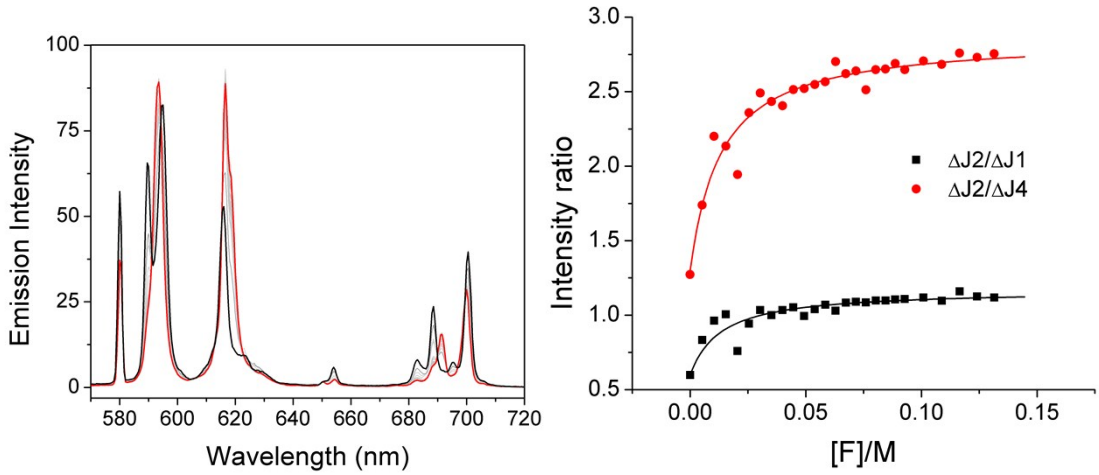

Figure S13. Left: Changes to the EuDTMA emission spectrum on addition of fluoride: 0 M NaF (black), 0.13 M (127 equiv.) NaF (red), intermediate concentrations (grey). Right: Binding isotherms and fits using the intensity ratios ΔJ = 2/ΔJ = 1 and ΔJ = 2/ΔJ = 4.

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[1] S. Aime, A. Barge, J. I. Bruce, M. Botta, J. A. K. Howard, J. M. Moloney, D. Parker, A. S. de Sousa, and M. Woods, *J. Am. Chem. Soc.*, 1999, **121**, 5762–5771.
[2] R. L. Jarek, R. J. Flesher, and S. K. Shin, *J. Chem. Educ.*, 1997, **74**, 978–982.
[3] P. Kuzmič, *Anal. Biochem.*, 1996, **237**, 260-273.