Supplemental Information

for

Contrast agents possessing high temperature sensitivity

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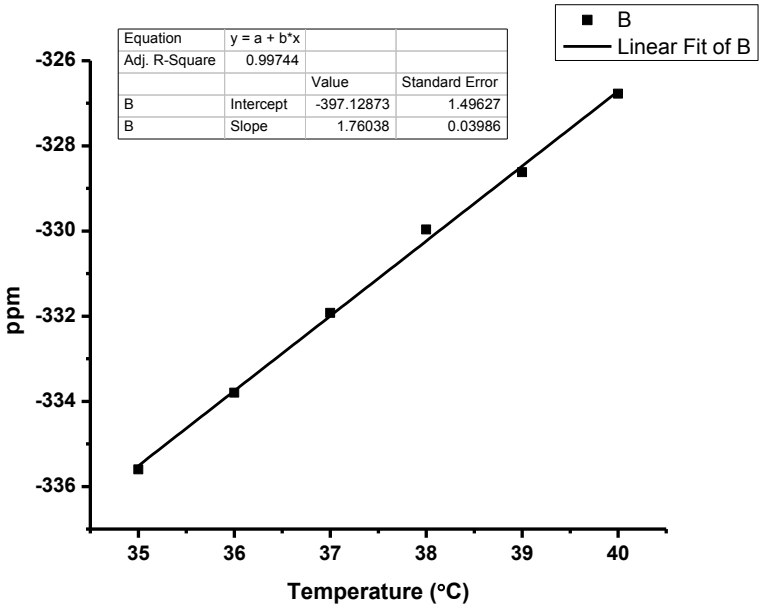
S1. Tetrapropargyl DOTAM (**1**)

To a stirred solution of cyclen (38 mg, 0.22 mmol) and DIPEA (154 µL, 4 mmol) in 5 mL acetonitrile, *N*-(propargyl) chloroacetamide (**6**) (131 mg, 1 mmol) was added in one portion and then refluxed overnight. The product was precipitated with 5 mL H_2O and filtered as a white solid (66 mg, 0.11 mmol), yield 54%. ^{1}H NMR (400 MHz, DMSO-d6): δ 7.57 (4H, m); 3.05 (8H, m); 2.22 (10H, m); 1.79 (14H, s); 1.67 (4H, s,). HRMS (ESI-TOF) m/z calc $C_{28}H_{40}N_8O_4$ $(M+H)^+$,553.3251, found 553.2574.

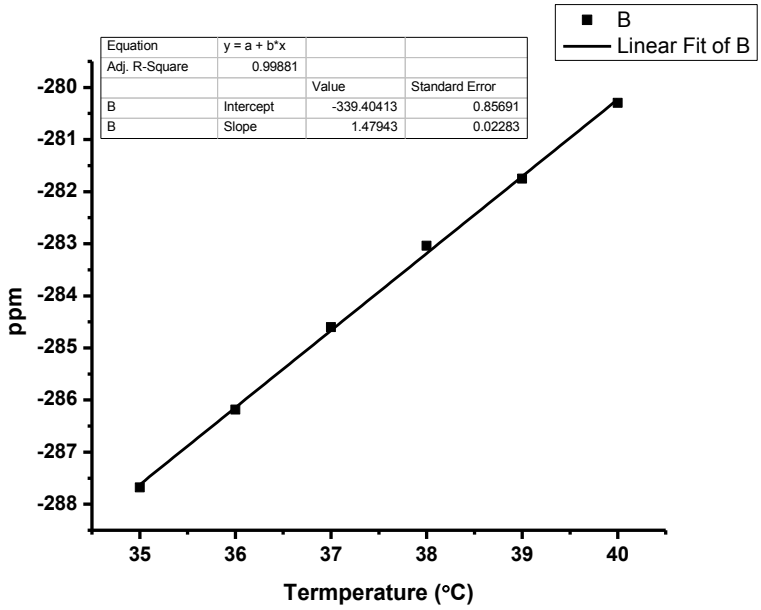
S2. Metallated Tetrapropargyl DOTAM (**Ln(1)**)

Tetrapropargyl DOTAM (**1**) (55 mg, 0.1 mmol) was added to a stirred solution of dioxane:H_2O (4 mL) containing one of the following lanthanides at 1.1 eq: $TbCl_3$, $DyCl_3$, $TmCl_3$. The progress of the metallation of **1** was monitored by UPLC/MS and upon completion the solvent was removed under reduced pressure. The solid was then taken in 1 mL H_2O and passed through a column of size exclusion gel. The fractions collected were tested against xylenol orange for the presence of free metals. Fractions identified as containing the metallated ligand were found not to contain free metal ions. HRMS (ESI-TOF) m/z: $C_{28}H_{40}N_8O_4Tb$ $(M+COOH)^+$, calc 757.2481, found 757.3318; $C_{28}H_{40}N_8O_4Dy$ $(M+COOH)^+$, calc 756.2627, found 756.3125; $C_{28}H_{40}N_8O_4Tm$ $(M+COOH)^+$, calc 767.2570, found 767.3286.

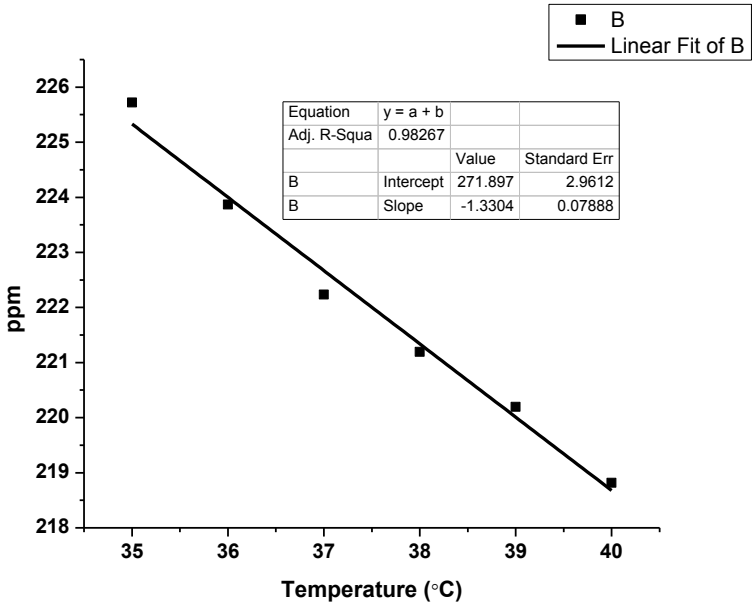
S3. Temperature vs. δ (ppm) **Dy(1)** H_4



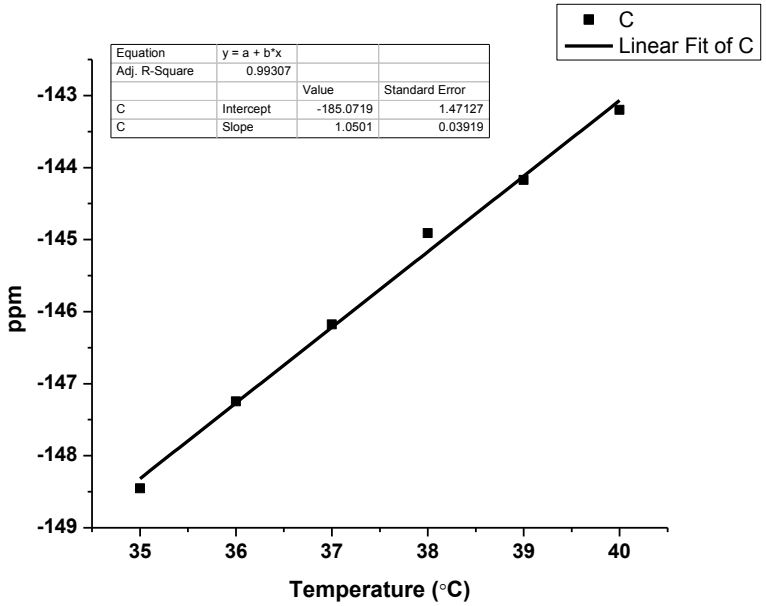
S4. Temperature vs. δ (ppm) **Tb(1)** H_4



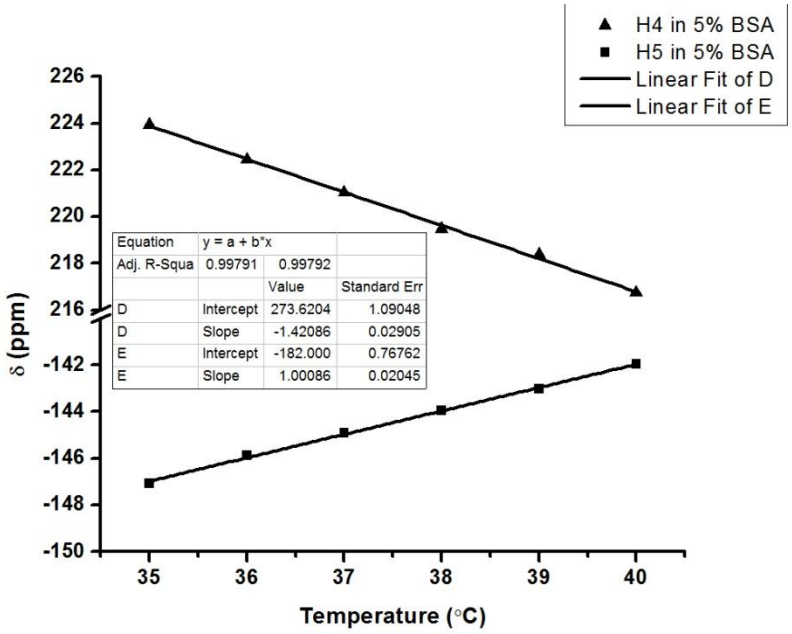
S5. Temperature vs. δ (ppm) **Tm(1)** H_4



S6. Temperature vs. δ (ppm) **Tm(1)** H_5



S7. Temperature vs. δ (ppm) **Tm(1)** H_4 , H_5 in 5% BSA

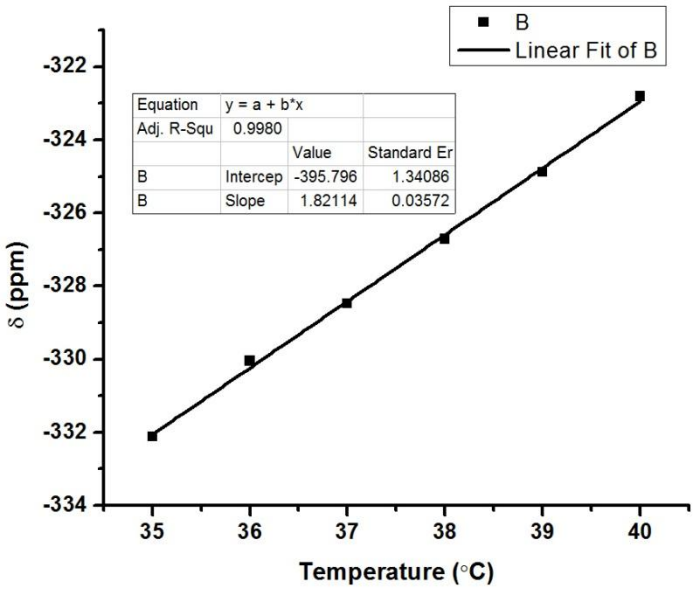


S8.

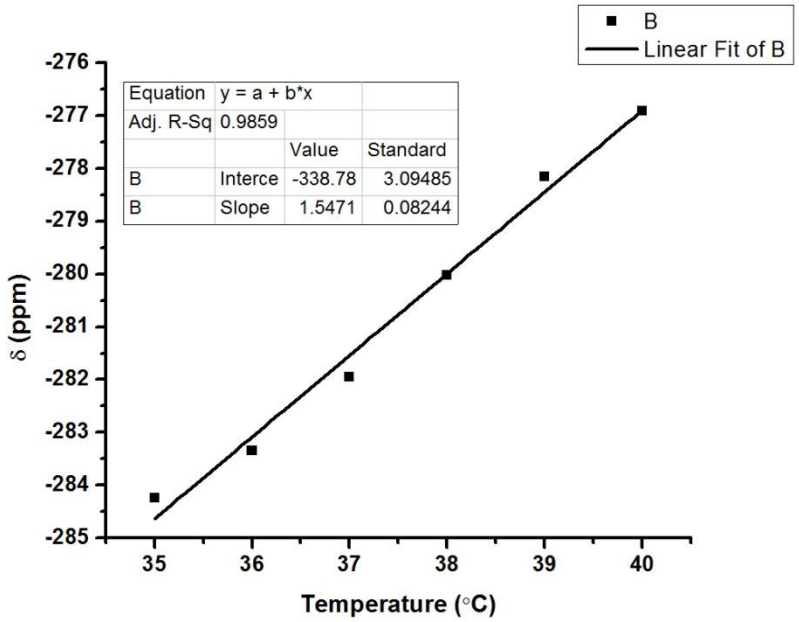
Table S1. δ (ppm) vs. pH of Tm(**1**) H_5

pH	ppm
6.00	-144.99
6.98	-144.94
8.22	-144.92
9.22	-145.10

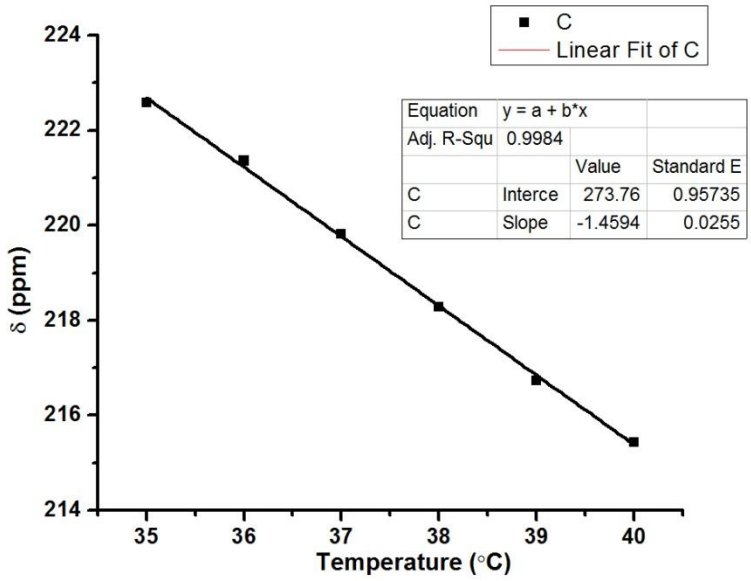
S9. Chemical shift versus temperature for Dy(**1**) H_4 in the presence of 1 mM Ca^{2+}



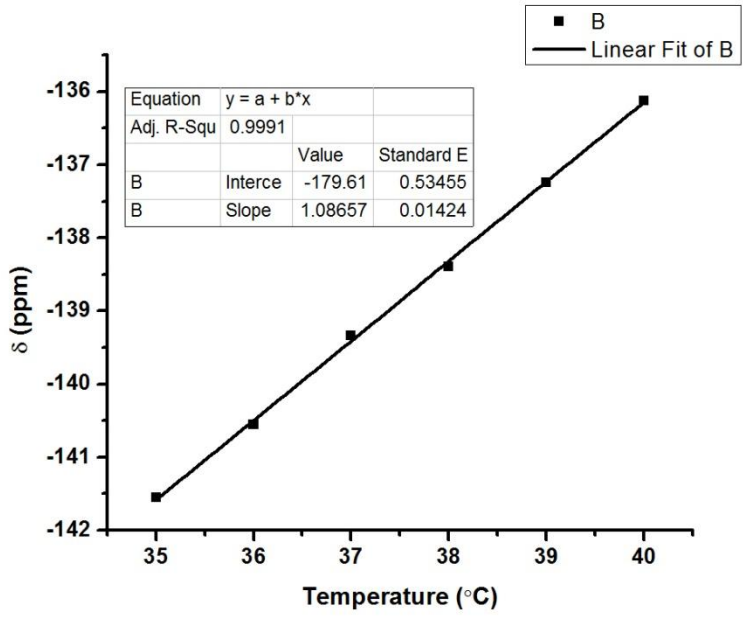
S10. Chemical shift versus temperature for Tb(**1**) H_4 in the presence of 1 mM Ca^{2+}



S11. Chemical shift versus temperature for Tm(**1**) H_4 in the presence of 1 mM Ca^{2+}



S12. Chemical shift versus temperature for Tm(**1**) H_5 in the presence of 1 mM Ca^{2+}



S13.

Table S2. Temperature coefficients measured at 1 mM Ca^{2+} with 10 mM Ln^{3+} (**1**) in D_2O.

	Tb^{3+} H_4	Tm^{3+} H_4	Tm^{3+} H_5	Dy^{3+} H_4
C_T(ppm/˚C)	1.55	1.46	1.09	1.82

S14. The NMR experiments were preformed on a 600 MHz Varian vertical bore magnet. ^{1}H experiments of Ln^{3+} complexes were done in deuterated water. Temperature dependence studies were done in distilled water using the variable temperature (VT) control supplied, which was first calibrated using glycol. Temperature calibration experiments of Ln complexes were done at 20 mM in a range of 35˚C – 40˚C in triplicate and averaged. Parameters used, 100 scans, Tm: relaxation delay = 0.8 sec, observed pulse = 20˚, sweep width = -170 to 250 ppm, acquisition time = 1.0 sec, overall time = 3:05. Tb: relaxation delay = 0.8 sec, observed pulse = 20˚, sweep width = -325 to 250 ppm, acquisition time = 0.76 sec, overall time = 2:41. Dy: relaxation delay = 0.8 sec, observed pulse = 20˚, sweep width = -250 to 150 ppm, acquisition time = 0.9 sec, overall time = 2:55.

Parameters used in 5% BSA study, 16 scans, Tm: relaxation delay = 0.8 sec, observed pulse = 20˚, sweep width = -170 to 250 ppm, acquisition time = 1.0 sec, overall time = 34 s.
FIDs were then line broadened 30 Hz, phased corrected and baseline subtracted.

T_1 measurements were obtained using an inversion recovery method using sixteen delay values at 35 ºC.