Supporting Information

For

Solution properties of the Ln[III] complexes of a novel octadentate chelator with rigidified iminodiacetate arms

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Contents:

1. Protonation and complexation equilibria

The protonation constants of the ligand are defined by Equation (1):

$$K_i^H = \frac{[H_iL]}{[H_{i-1}L][H^+]} \qquad (1)$$

where $i=1, 2 \ldots 4$. These were determined by both pH-potentiometric and ^{1}H-NMR titrations. At different pH values, ^{1}H NMR signals display sharp changes related to the protonation of the ligand. Since the protonation/deprotonation of the different donor atoms is generally fast process on the NMR time scale, the chemical shifts of the observed signals represent a weighted average of the shifts of the different species involved in a specific protonation step (Eq. 2):

$$\delta_{H(obs)} = \sum_i x_i \delta_H^{H_iL} \qquad (2)$$

where, $\delta_{H(obs)}$ is the observed chemical shift of a given signal, x_i and $\delta_H^{H_iL}$ are the molar fraction and the chemical shift of the involved species, respectively (the molar fractions x_i of the different protonated species are expressed with the use of the protonation constants K_i^H).

The stability and protonation constants of the metal complexes formed with the chelating ligands **L1** and EGTA are defined by Equations (3) and (4). The best fitting was obtained by using the model which includes the formation of *ML* and *MHL* species.

$$K_{ML} = \frac{[ML]}{[M][L]} \qquad (3)$$

$$K_{MH_iL} = \frac{[MH_iL]}{[MH_{i-1}L][H^+]} \qquad (4)$$

where $i=1$. The titration data for **L1** and EGTA in the presence of Zn^{2+} and Cu^{2+} indicate base consuming process at pH>9. This process can be interpreted by assuming the coordination of OH$^-$ ion according to Equation (5):

$$K_{MLH_{-1}} = \frac{[ML]}{[M(OH)L][H^+]} \qquad (5)$$

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pH-potentiometric titrations were also made at 2:1 metal-to-ligand ratio in order to examine the possible formation of dinuclear Zn^{2+} and Cu^{2+} complexes. The stability and protonation constants of the dinuclear-, dinuclear-monohydroxo- and dinuclear-dihydroxo-complexes are defined by Equations (6), (7) and (8), respectively.

$$K_{M_2L} = \frac{[M_2L]}{[ML][M]} \qquad (6)$$

$$K_{M_2LH_{-1}} = \frac{[M_2L]}{[M_2(OH)L][H^+]} \qquad (7)$$

$$K_{M_2LH_{-2}} = \frac{[M_2(OH)L]}{[M_2(OH)_2L][H^+]} \qquad (8)$$

As explained in the text, in the presence and absence of Mg^{2+} ion the shape of the titration curve of **L1** is the same (Figure S1). The fitting of the data obtained in these titrations did not give any reasonable result for the stability constant of the Mg^{2+} complex.
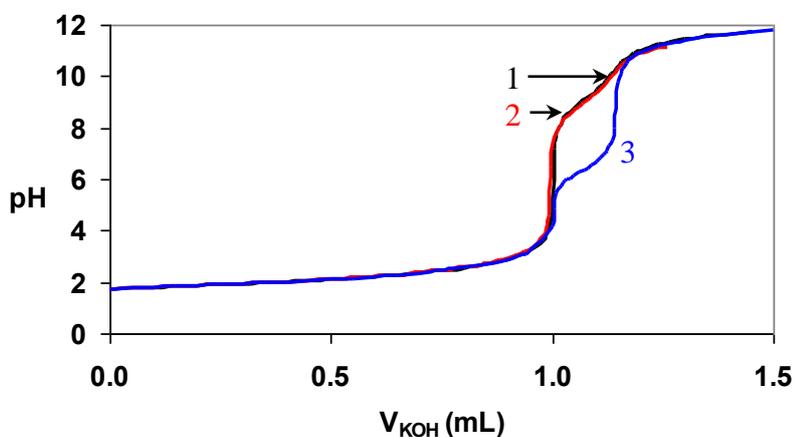

Figure S1. Titration curve of the H_4**L1** ligand in the absence (1) and in the presence of Mg^{2+} (2) and Ca^{2+} (3) ([H_4**L1**]=[Mg^{2+}]=[Ca^{2+}]=2 mM, [HCl]=16 mM, [KOH]=0.2 M, 0.1 M KCl, 25°C)

2. Kinetic studies

The rates of the transmetallation reactions of [Gd(**L1**)]⁻ and [Gd(EGTA)]⁻ were studied by UV-spectrophotometry with the use of Cu^{2+} and Eu^{3+} as exchanging metal ions. In the presence of excess of the exchanging ion the transmetallation can be treated as a pseudo-first-order process and the reaction rate can be expressed with the Eq. (9), where k_d is a pseudo-first-order rate constant, $[GdL]_t$ and $[GdL]_{tot}$ are the concentrations of the GdL species at time t and the total concentration of the complex, respectively.

$$-\frac{d[GdL]_t}{dt} = k_d[GdL]_{tot} \qquad (9)$$

The rates of the transmetallation reactions were studied at different concentrations of the exchanging ions in the pH range 4.0 – 6.3. The obtained rate constants k_d are presented as a function of the pH in Figures S2, S3, S4 and S5.
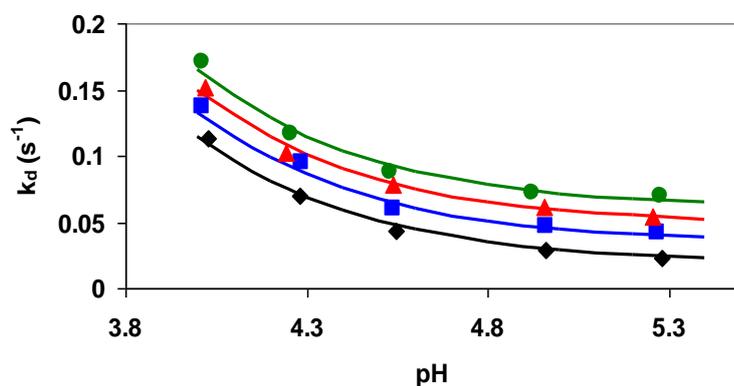

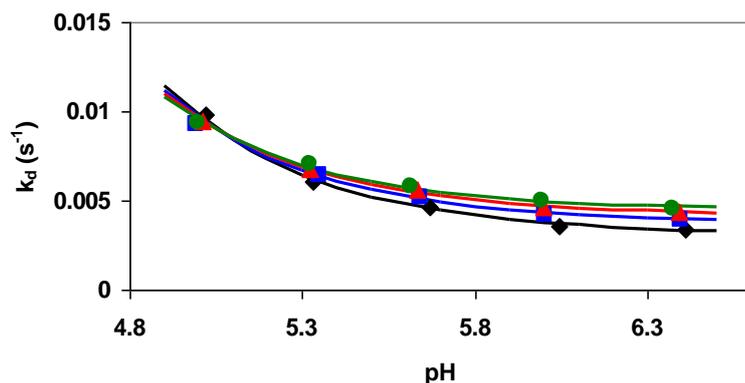**Figure S2.** Pseudo-first order rate constants (k_d) of the metal exchange reactions of [GdL1]⁻ with Cu^{2+} ions as a function of pH ([Gd(L1)⁻]=0.1 mM, [Cu^{2+}]=1 mM (♦), 2 mM (■), 3 mM (▲) and 4 mM (●); 0.1 M KCl, 25 °C)

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Figure S3. Pseudo-first order rate constants (k_d) of the metal exchange reactions of [GdL1]⁻ with Eu³⁺ ions as a function of pH ([Gd(L1)⁻]=0.5 mM, [Eu³⁺]=10 mM (♦), 15 mM (■), 20 mM (▲) and 25 mM (●); 0.1 M KCl, 25 °C)
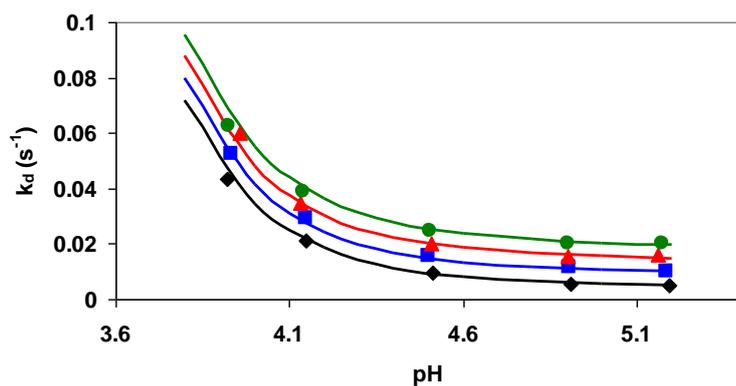
Figure S4. Pseudo-first order rate constants (k_d) of the metal exchange reactions of [Gd(EGTA)]⁻ with Cu²⁺ ions as a function of pH ([Gd(EGTA)⁻] = 0.1 mM, [Cu²⁺] = 1 mM (♦), 2 mM (■), 3 mM (▲) and 4 mM (●); 0.1 M KCl, 25 °C)
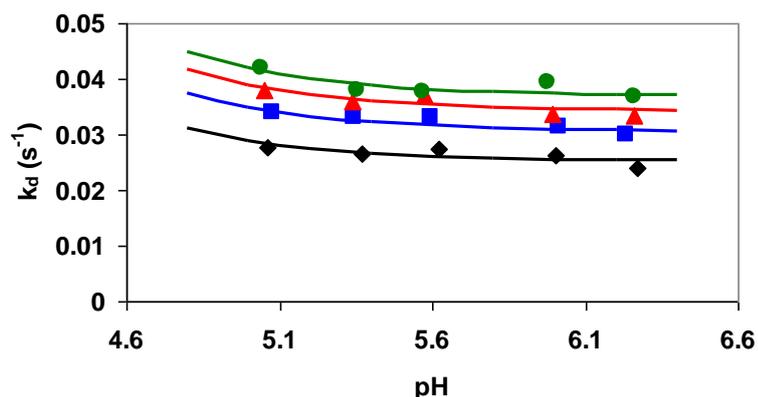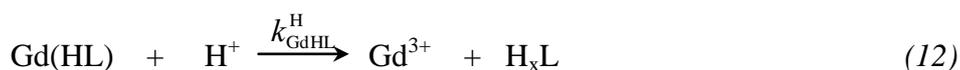
Figure S5. Pseudo-first order rate constants (k_d) of the metal exchange reactions of [Gd(EGTA)]$^-$ with Eu^{3+} ions as a function of pH ([Gd(EGTA)$^-$] = 1.0 mM, [Eu^{3+}] = 20 mM (♦), 30 mM (■), 40 mM (▲) and 50 mM (●); 0.1 M KCl, 25 °C).

These figures show that k_d values exhibit a similar dependence in the reactions with Cu^{2+} and Eu^{3+}. k_d values increase with increase of [H$^+$] and also with increasing [Cu^{2+}] or [Eu^{3+}] at pH > 4.5. The increase in k_d values with increasing H$^+$ concentration can be interpreted in terms of proton assisted dissociation of [Gd(**L1**)]$^-$ and [Gd(EGTA)]$^-$ followed by a fast reaction between free ligand and exchanging metal ions (Cu^{2+} or Eu^{3+}). The dependence of k_d on [H$^+$] can be expressed as a first- and second-order function of [H$^+$] which indicates that the exchange can take place by proton-independent (Eq. 10) and proton assisted (Eqs. 11 and 12) pathways. The proton assisted dissociation of [Gd(**L1**)]$^-$ and [Gd(EGTA)]$^-$ can be explained by the formation of a protonated [Gd(H**L1**)] and [Gd(HEGTA)] complexes, which dissociate through spontaneous (Eq. 11) and proton-assisted (Eq. 12) pathways.

$$GdL \xrightarrow{k_0} Gd^{3+} + H_xL \qquad\qquad (10)$$

$$Gd(HL) \xrightarrow{k_{GdHL}} Gd^{3+} + H_xL \qquad\qquad (11)$$

$$Gd(HL) + H^+ \xrightarrow{k_{GdHL}^{H}} Gd^{3+} + H_xL \qquad\qquad (12)$$

The increase in exchange reaction rate with increasing $[Cu^{2+}]$ or $[Eu^{3+}]$ indicates that the reaction can take place by direct attack of the exchanging metal ion to the complex, via formation of dinuclear intermediates (Eq. 13).
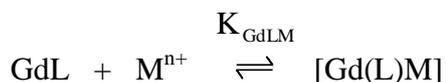
$$GdL \ + \ M^{n+} \ \underset{}{\overset{K_{GdLM}}{\rightleftharpoons}} \ [Gd(L)M]$$

$$K_{GdLM} = \frac{[Gd(L)M]}{[Gd(L)][M^{n+}]} \tag{13}$$

It can be assumed that in the dinuclear intermediate $[Gd(L)M]$, the functional groups of **L1** and EGTA are slowly transferred from the Gd^{3+} to the attacking Cu^{2+} or Eu^{3+} step by step (Eq. 14).

$$[Gd(L)M] \ \xrightarrow{k_{GdLM}} \ Gd^{3+} \ + \ ML \tag{14}$$

At pH < 4.5, the exchanging metal ions attack the protonated $[Gd(H\mathbf{L1})]$ and $[Gd(HEGTA)]$. In case of protonated and dinuclear complexes, the functional groups of **L1** and EGTA are weekly coordinated to the Gd^{3+} ion and they slowly transfer from the Gd^{3+} to the attacking Cu^{2+} and Eu^{3+} ions (Eq. 15).

$$Gd(HL) \ + \ M^{n+} \ \xrightarrow{k_{GdLM}^{H}} \ Gd^{3+} \ + \ ML \ + \ H^{+} \tag{15}$$
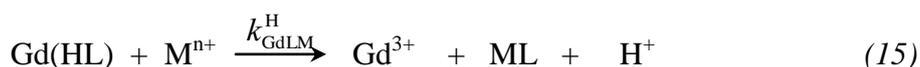
The k_0, k_{GdHL}, k_{GdHL}^{H}, k_{GdLM} and k_{GdLM}^{H} rate constants characterize the dissociation of $[Gd(\mathbf{L1})]^-$ and $[Gd(EGTA)]^-$ via spontaneous, proton-assisted, metal-assisted and proton-metal-assisted (when the exchanging metal attacks the protonated complexes) reaction pathways, respectively. The K_{GdHL} and K_{GdLM} are the protonation constants of the protonated complexes and the stability constant of the mixed dinuclear intermediate complexes, respectively (where $K_{GdHL}=[Gd(HL)]/[Gd(L)][H^+]$, $K_{GdLM}=[Gd(L)M]/[Gd(L)][M]$. The protonation constant of the $[Gd(\mathbf{L1})]^-$ and $[Gd(EGTA)]^-$ complexes were determined by pH-potentiometric titration ($[Gd(\mathbf{L1})]^-$: $\log K_{MHL}= 3.07$; $[Gd(EGTA)]^-$: $\log K_{MHL}= 1.89$ in Table 2) and used for the calculation of the kinetic parameters.

By taking into account all the possible pathways and the rate of the transmetallation of $[Gd(\mathbf{L1})]^-$ and $[Gd(EGTA)]^-$ (Eq. 9), the pseudo-first-order rate constant (k_d) can be defined by Equation (16).

$$-\frac{[\text{GdL}]_t}{dt} = k_0[\text{GdL}] + k_{\text{GdLH}}[\text{Gd(HL)}] + k_{\text{GdHL}}^{\text{H}}[\text{Gd(HL)}][\text{H}^+] + k_{\text{GdLM}}[\text{Gd(L)M}] + k_{\text{GdLM}}^{\text{H}}[\text{Gd(HL)}][\text{M}]$$

$$(16)$$

By taking into account the total concentration of the complex ($[\text{GdL}]_{\text{tot}} = [\text{GdL}] + [\text{Gd(HL)}] + [\text{Gd(L)M}]$) and the equations of protonation and stability constants of the intermediates (K_{GdHL} and K_{GdLM}), the pseudo-first-order rate constant can be expressed as follows:

$$k_d = \frac{k_0 + k_1[\text{H}^+] + k_2[\text{H}^+]^2 + k_3[\text{M}^{n+}] + k_4[\text{M}][\text{H}^+]}{1 + K_{\text{GdHL}}[\text{H}^+] + K_{\text{GdLM}}[\text{M}]}$$

$$(17)$$

where, k_0, and $k_1 = k_{\text{GdHL}} \cdot K_{\text{GdHL}}$, $k_2 = k_{\text{GdHL}}^{\text{H}} \cdot K_{\text{GdHL}}$, $k_3 = k_{\text{GdLM}} \cdot K_{\text{GdLM}}$ and $k_4 = k_{\text{GdLM}}^{\text{H}} \cdot K_{\text{GdHL}}$ characterize the spontaneous, proton-, metal- and proton-metal-assisted dissociation of [Gd(**L1**)]$^-$ and [Gd(EGTA)]$^-$, respectively. Rate constants, protonation and stability constants have been calculated by fitting the k_d values to the Eq. (17).

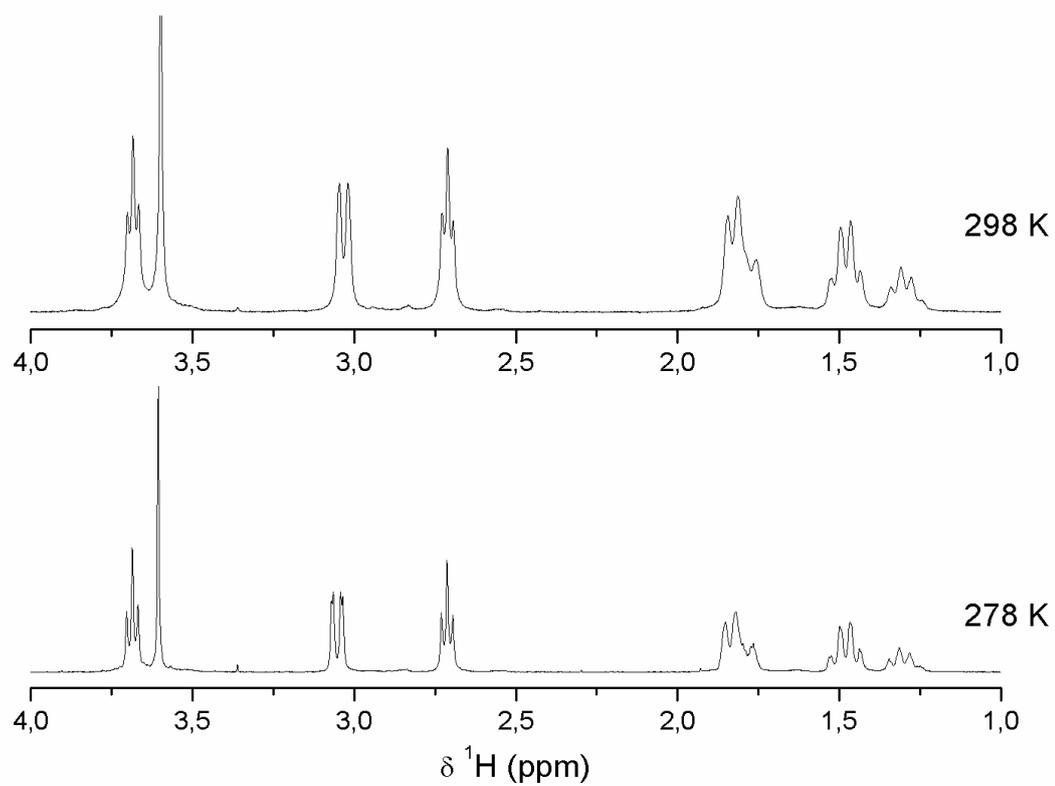## 3. Variable temperature ^{1}H and ^{13}C NMR spectra

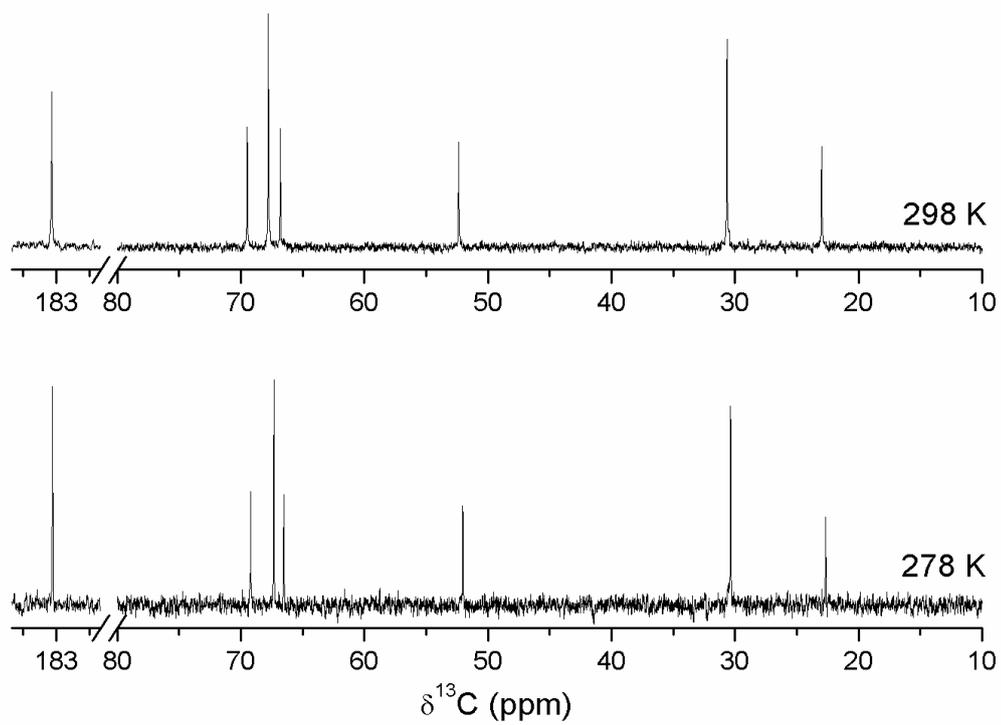**Figure S6.** VT ^{1}H NMR spectra for [La(**L1**)]$^-$ at 9.4 T.

Figure S7. VT ^{13}C NMR spectra for [La(**L1**)]$^-$ at 9.4 T.
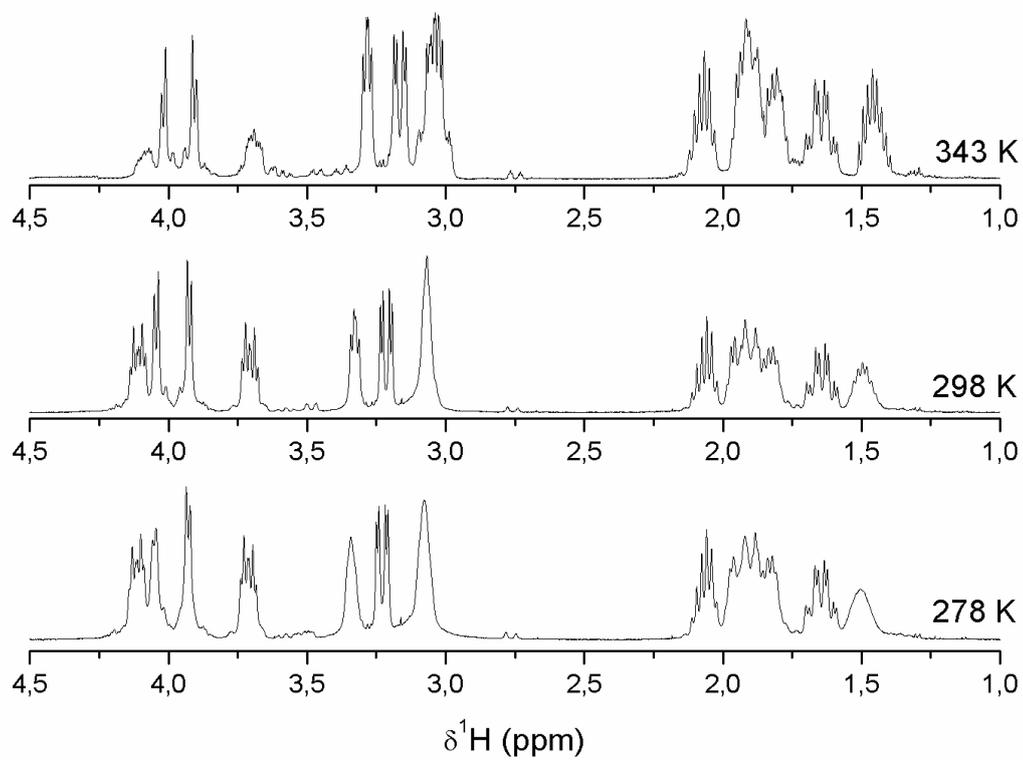
Figure S8. VT ^{1}H NMR spectra for [Lu(**L1**)][-] at 9.4 T.
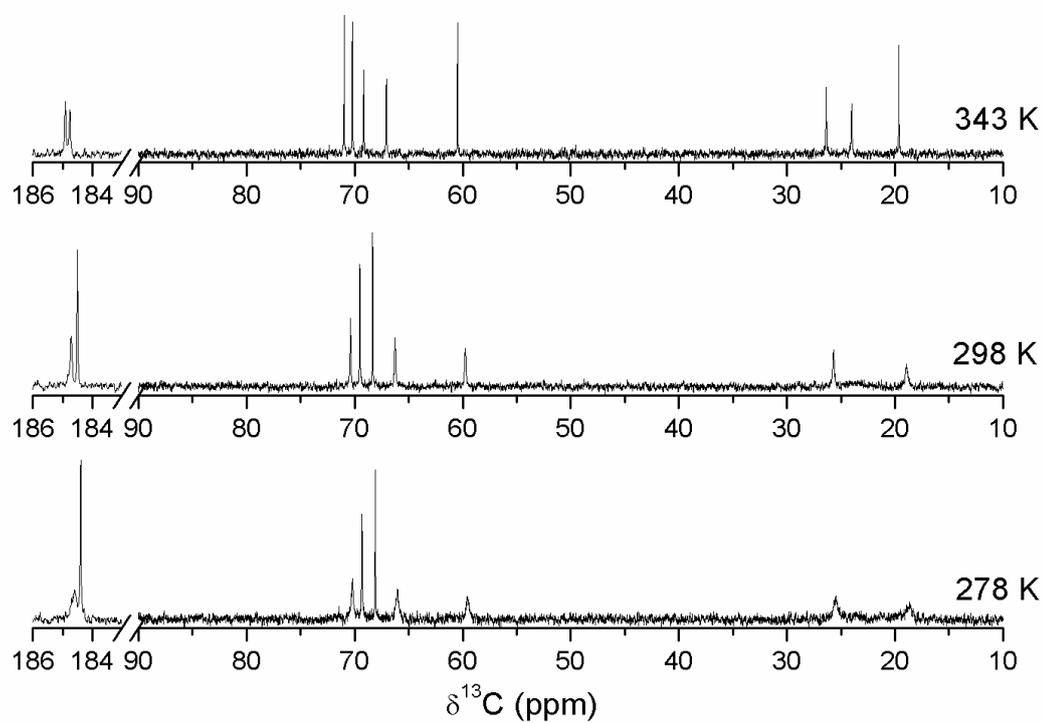
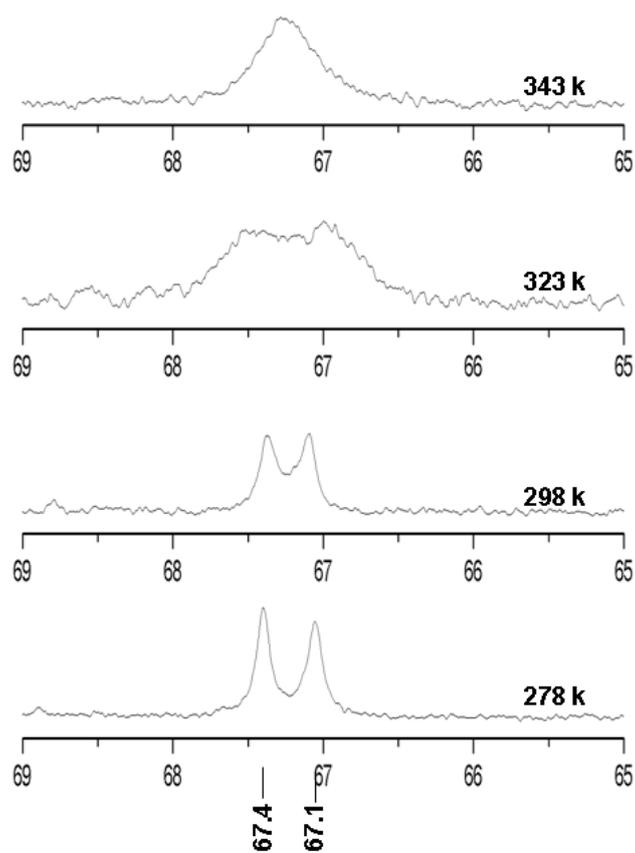**Figure S9.** VT ^{13}C NMR spectra for [Lu(**L1**)]$^-$ at 9.4 T.

Figure S10. VT ^{13}C NMR spectra for [Y(**L1**)]⁻ at 9.4 T; magnification of the region of the –CH carbons.
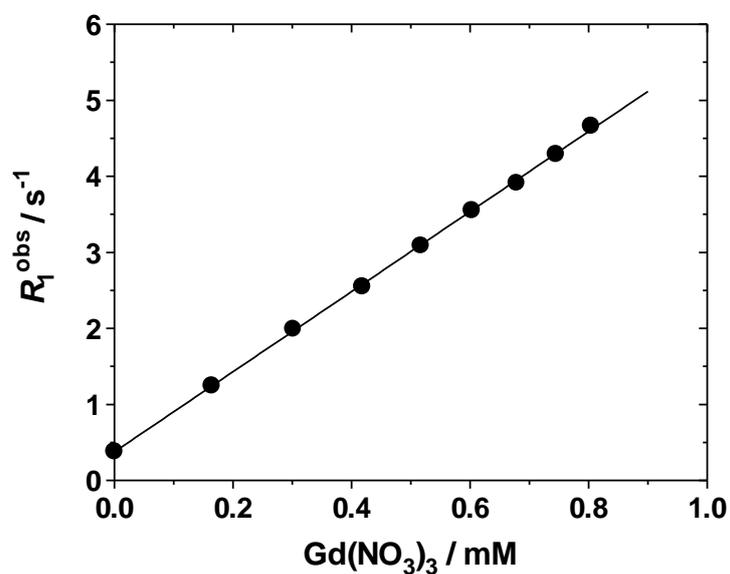
4. Relaxometric properties

Figure S11. Variation of the relaxation rate, at 20 MHz and 298 K, of a 0.8 mM solution of **L1** following stepwise additions of a stock solution of $Gd(NO_3)_3$. A large and non linear increase of R_1 indicates that the Gd/**L1** ratio is higher than one. In that case a further small addition of ligand restores the 1:1 molar ratio and the R_1 value returns to the straight line. The slope of the line (5.2 mM^{-1} s^{-1}; R=0.9998) corresponds to the r_{1p} value of [Gd(**L1**)]$^-$.
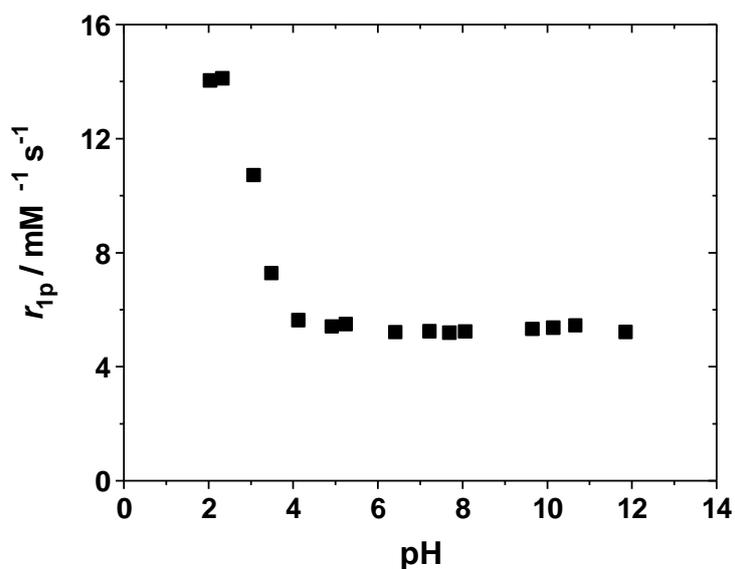

Figure S12. Plot of R_1 of [Gd(**L1**)]$^-$ on pH variation (20 MHz, 298 K).