Supporting Information

For

Solution properties of the Ln$^{III}$ complexes of a novel octadentate chelator with rigidified iminodiacetate arms

Lorenzo Tei$^{[a]}$, Zsolt Baranyai$^{[b]}$, Claudio Cassino$^{[a]}$, Marianna Fekete$^{[a]}$, Ferenc K. Kálmán$^{[b]}$ and Mauro Botta$^{[a]}$

$^{a}$Dipartimento di Scienze ed Innovazione Tecnologica, Università del Piemonte Orientale “Amedeo Avogadro” Viale T. Michel 11, I-15121, Alessandria, Italy;

$^{b}$Department of Inorganic and Analytical Chemistry, University of Debrecen, H-4010, Debrecen, Egyetem tér 1., Hungary

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1. Protonation and complexation equilibria

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

\[
K_i^H = \frac{[H_iL]}{[H_{i-1}L][H^+]} \tag{1}
\]

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):

\[
\delta_{H_{(obs)}} = \sum x_i \delta_{H_i}^L \tag{2}
\]

where, \( \delta_{H_{(obs)}} \) is the observed chemical shift of a given signal, \( x_i \) and \( \delta_{H_i}^L \) 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 \( L_1 \) 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.

\[
K_{ML} = \frac{[ML]}{[M][L]} \tag{3}
\]

\[
K_{MHL} = \frac{[MH[L]]}{[MH_{i-1}L][H^+]} \tag{4}
\]

where \( i = 1 \). The titration data for \( L_1 \) 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):

\[
K_{MLH_4} = \frac{[ML]}{[M(OH)L][H^+]} \tag{5}
\]
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.

$$K_{\text{ML}} = \frac{[\text{ML}]}{[M][L]}$$  \hspace{1cm} (6)

$$K_{\text{M(2OH)L}_{1,1}} = \frac{[\text{M(2OH)L}]}{[\text{M(2OH)L}][\text{H}^+]$$  \hspace{1cm} (7)

$$K_{\text{M(2OH)L}_{2,2}} = \frac{[\text{M(2OH)L}]}{[\text{M(2OH)L}][\text{H}^+]$$  \hspace{1cm} (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 $[\text{Gd(L1)}]^{-}$ and $[\text{Gd(EGTA)}]^{-}$ 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, $[\text{GdL}]_t$ and $[\text{GdL}]_{tot}$ are the concentrations of the GdL species at time $t$ and the total concentration of the complex, respectively.

$$\frac{-d[\text{GdL}]}{dt} = k_d [\text{GdL}]_{tot}$$

(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](image.png)

**Figure S2.** Pseudo-first order rate constants ($k_d$) of the metal exchange reactions of $[\text{GdL1}]^{-}$ with Cu$^{2+}$ ions as a function of pH ($[\text{Gd(L1)}^{-}]=0.1$ mM, $[\text{Cu}^{2+}]=1$ mM (◇), 2 mM (■), 3 mM (▲) and 4 mM (●); 0.1 M KCl, 25 °C)
Figure S3. Pseudo-first order rate constants \((k_d)\) of the metal exchange reactions of \([\text{GdL}_1]^-\) with \(\text{Eu}^{3+}\) ions as a function of pH \(([\text{Gd(L}_1]^-]=0.5 \text{ mM, } [\text{Eu}^{3+}]=10 \text{ mM (}), 15 \text{ mM (■), 20 mM (▲) and 25 mM (●); 0.1 M KCl, 25 ^\circ\text{C}})\)

Figure S4. Pseudo-first order rate constants \((k_d)\) of the metal exchange reactions of \([\text{Gd(EGTA)}]^-\) with \(\text{Cu}^{2+}\) ions as a function of pH \(([\text{Gd(EGTA)}^-]=0.1 \text{ mM, } [\text{Cu}^{2+}]=1 \text{ mM (}), 2 \text{ mM (■), 3 mM (▲) and 4 mM (●); 0.1 M KCl, 25 ^\circ\text{C}})\)
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 \( ([Gd(EGTA)]^- = 1.0 \text{ mM}, \ [Eu^{3+}] = 20 \text{ mM (●)}, 30 \text{ mM (■)}, 40 \text{ mM (▲)} \) 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 \([Gd(HL1)]\) and \([Gd(HEGTA)]\) complexes, which dissociate through spontaneous (Eq. 11) and proton-assisted (Eq. 12) pathways.

\[
\begin{align*}
GdL & \xrightarrow{k_d} Gd^{3+} + H_3L \\
Gd(HL) & \xrightarrow{k_{GdHL}} Gd^{3+} + H_3L \\
Gd(HL) + H^+ & \xrightarrow{k_{GdHL}^H} Gd^{3+} + H_3L
\end{align*}
\]
The increase in exchange reaction rate with increasing \([\text{Cu}^{2+}]\) or \([\text{Eu}^{3+}]\) 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).

\[
\begin{align*}
\text{GdL} + \text{M}^{n+} & \rightleftharpoons [\text{Gd(L)M}] \\
K_{\text{GdLM}} &= \frac{[\text{Gd(L)M}]}{[\text{Gd(L)}][\text{M}^{n+}]} \\
\end{align*}
\] (13)

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

\[
\begin{align*}
[\text{Gd(L)M}] & \rightarrow \text{Gd}^{3+} + \text{ML} \\
\end{align*}
\] (14)

At pH < 4.5, the exchanging metal ions attack the protonated \([\text{Gd(HL1)}]\) and \([\text{Gd(HEGTA)}]\). In case of protonated and dinuclear complexes, the functional groups of \(\text{L1}\) and EGTA are weekly coordinated to the \(\text{Gd}^{3+}\) ion and they slowly transfer from the \(\text{Gd}^{3+}\) to the attacking \(\text{Cu}^{2+}\) and \(\text{Eu}^{3+}\) ions (Eq. 15).

\[
\begin{align*}
\text{Gd(HL)} + \text{M}^{n+} & \stackrel{k_{\text{GdHL}}^H}{\longrightarrow} \text{Gd}^{3+} + \text{ML} + \text{H}^+ \\
\end{align*}
\] (15)

The \(k_0\), \(k_{\text{GdHL}}\), \(k_{\text{GdHL}}^H\), \(k_{\text{GdLM}}\) and \(k_{\text{GdLM}}^H\) rate constants characterize the dissociation of \([\text{Gd(L1)}]^-\) and \([\text{Gd(EGTA)}]^-\) via spontaneous, proton-assisted, metal-assisted and proton-metal-assisted (when the exchanging metal attacks the protonated complexes) reaction pathways, respectively. The \(K_{\text{GdHL}}\) and \(K_{\text{GdLM}}\) are the protonation constants of the protonated complexes and the stability constant of the mixed dinuclear intermediate complexes, respectively (where \(K_{\text{GdHL}}=[\text{Gd(HL)}]/[\text{Gd(L)}][\text{H}^+], K_{\text{GdLM}}=[\text{Gd(L)M}]/[\text{Gd(L)}][\text{M}]\). The protonation constant of the \([\text{Gd(L1)}]^-\) and \([\text{Gd(EGTA)}]^-\) complexes were determined by pH-potentiometric titration (\([\text{Gd(L1)}]^-\): \(\log K_{\text{MHL}}= 3.07\); \([\text{Gd(EGTA)}]^-\): \(\log K_{\text{MHL}}= 1.89\) 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 \([\text{Gd(L1)}]^-\) and \([\text{Gd(EGTA)}]^-\) (Eq. 9), the pseudo-first-order rate constant \(k_d\) can be defined by Equation (16).
\[
- \frac{[\text{GdL}]}{dt} = k_0 [\text{GdL}] + k_{\text{GdHL}} [\text{Gd(HL)}] + k_{\text{GdL}}^H [\text{Gd(L)}][H^+] + k_{\text{GdL}} [\text{Gd(L)}][\text{M}] + k_{\text{GdL}}^H [\text{Gd(HL)}][\text{M}]
\]  

(16)

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

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

(17)

where, \( k_0 \), and \( k_1 = k_{\text{GdHL}} \cdot K_{\text{GdHL}} \), \( k_2 = k_{\text{GdHL}}^H \cdot K_{\text{GdHL}} \), \( k_3 = k_{\text{GdL}} \cdot K_{\text{GdL}} \) and \( k_4 = k_{\text{GdL}}^H \cdot K_{\text{GdHL}} \) 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 $[\text{Lu}(\text{L1})]^{-}$ 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).