Supplementary Information

New Tris-3,4-HOPO lanthanide complexes as potential imaging probes: complex stability and magnetic properties

Ana C. Mendonça, André F. Martins, Andrea Melchior, Sérgio M. Marques, Sílvia Chaves, Sandrine Villette, Stéphane Petoud, Pier Luigi Zanonato, Marilena Tolazzi, Célia S. Bonnet, Éva Tóth, Plinio Di Bernardo, Carlos F.G.C. Geraldes and M. Amélia Santos

a Centro de Química Estrutural, Instituto Superior Técnico, Universidade Técnica de Lisboa, Av. Rovisco Pais 1, 1049-001 Lisboa, Portugal.
b Department of Life Sciences, Faculty of Science and Technology, University of Coimbra, P.O. Box 3046, 3001-401 Coimbra, Portugal.
c Center of Neurosciences and Cell Biology, Largo Marquês de Pombal, University of Coimbra, Portugal
d Coimbra Chemistry Center, Rua Larga, University of Coimbra, 3004-535 Coimbra, Portugal
e Centre de Biophysique Moléculaire, CNRS, Rue Charles Sadron, 45071 Orléans, France.
f Dipartimento di Scienze Chimiche, Università di Padova, Via Marzolo 1, 35131 Padova, Italy
g Dipartimento di Chimica, Fisica e Ambiente, Università di Udine, Via del Cotonificio 108, 33100 Udine, Italy
Figure S1. UV-Vis absorption spectra variations of the ligand solutions (C<sub>L, start</sub> = 1.3×10<sup>-5</sup> M) along the titration with acid (HCl 0.1 M) or base (KOH 0.1M) in the ranges of pH 0.98-2.36 (a) and 3.19-10.6 (b). In (a) the red arrow indicates the (small) increase of absorbance on going from pH 0.98 to 2.36. In (b) arrow 1 indicates an increase of absorbance (pH ~3-5) at 280 nm followed by nearly constant values corresponding to a large pH change and a sharp decrease (arrow 2) at pH > 9. Arrow 3 evidences the marked increase of absorbance at 304 nm at pH > 9 corresponding to the decrease of absorbance at 280 nm. Data at 244, 280 and 304 nm are plotted in Figure 3.
**Figure S2.** UV-Vis absorption spectra variations of a solution of the ligand L in the presence of La$^{3+}$, along the titration with base (pH = 3.07-10.6, $C_L = 1.3 \times 10^{-5}$ M, $C_L/C_{La^{3+}} = 1.01$).
**Figure S3.** Temperature dependence of the $r_1$ (20 MHz) relaxivity of the complex Gd-(NTP(PrHP)3) at pH 7.1.

**Figure S4.** pH dependence of the $r_1$ (20 MHz) relaxivity of the complex Gd-(NTP(PrHP)3) at 37ºC.
**Figure S5.** Evolution of the relative water proton paramagnetic relaxation rate $R_1^p(t)/R_1^p(0)$ (20 MHz, pH 7.1, 37 °C) versus time for 0.75 mM Gd-(NTP(PrHP)$_3$), in 10 mM phosphate buffer solution, in the absence (empty circles) and in the presence (full circles) of an equimolar amount of Zn$^{2+}$ ions.
Table S1. Stability constants for formation of Zn$^{2+}$ - L complexes, Zn$_m$H$_h$L$_l$ (25 °C, $I = 0.1$ M KCl)

<table>
<thead>
<tr>
<th></th>
<th>log $\beta_{mhl}$</th>
<th>log $\beta_{151}$</th>
<th>log $\beta_{141}$</th>
<th>log $\beta_{131}$</th>
<th>log $\beta_{121}$</th>
<th>log $\beta_{111}$</th>
<th>log $\beta_{302}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zn$^{2+}$-L</td>
<td>42.87±0.05</td>
<td>38.46±0.05</td>
<td>34.02±0.07</td>
<td>29.26±0.09</td>
<td>22.11±0.08</td>
<td>38.92±0.06</td>
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</table>

Table S2. Initial volume and concentrations of the reagents in cell. Titrant: KOH 51.71 mM for all titrations. $V_f = V$ added final before precipitation occurred.

<table>
<thead>
<tr>
<th>Titration</th>
<th>$V$, mL</th>
<th>$C_L$, mM</th>
<th>$C_M$, mM</th>
<th>$C_{H}$, mM</th>
<th>$V_f$, mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>H_1</td>
<td>85.0</td>
<td>0.2036</td>
<td>---</td>
<td>7.112</td>
<td></td>
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<tr>
<td>H_2</td>
<td>25.5</td>
<td>0.5851</td>
<td>---</td>
<td>9.004</td>
<td></td>
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<tr>
<td>H_3</td>
<td>4.924</td>
<td>2.098</td>
<td>---</td>
<td>17.77</td>
<td></td>
</tr>
</tbody>
</table>

|       |         |           |           |             |           |           |           |           |
| La_1   | 25.50   | 0.398     | 0.375     | 8.538       | 3.92      |
| La_2   | 25.50   | 0.4069    | 0.1819    | 8.346       | 3.60      |
| La_3   | 4.092   | 1.090     | 0.3736    | 17.389      | 1.40      |

|       |         |           |           |             |           |           |           |           |
| Pr_1   | 25.50   | 0.3966    | 0.369     | 8.529       | 3.94      |
| Pr_2   | 25.5    | 0.3729    | 0.183     | 8.306       | 3.60      |
| Pr_3   | 4.890   | 1.072     | 0.334     | 17.793      | 1.40      |

|       |         |           |           |             |           |           |           |           |
| Gd_1   | 25.50   | 0.378     | 0.371     | 8.501       | 3.84      |
| Gd_2   | 25.50   | 0.3719    | 0.1863    | 8.3013      | 3.52      |
| Gd_3   | 4.894   | 1.078     | 0.331     | 17.950      | 1.42      |

|       |         |           |           |             |           |           |           |           |
| Er_1   | 25.50   | 0.3899    | 0.3702    | 8.376       | 3.80      |
| Er_2   | 25.50   | 0.2586    | 0.1857    | 7.627       | 3.40      |
| Er_3   | 4.925   | 1.087     | 0.3270    | 17.712      | 1.44      |

|       |         |           |           |             |           |           |           |           |
| Lu_1   | 25.50   | 0.3940    | 0.3769    | 8.477       | 3.84      |
| Lu_2   | 25.50   | 0.3950    | 0.182     | 8.394       | 3.56      |
| Lu_3   | 4.876   | 1.104     | 0.351     | 18.120      | 1.40      |
Equations used for the analysis of $^{17}$O NMR and NMRD data

NMRD and $^{17}$O NMR data have been analysed within the framework of the Solomon-Bloembergen-Morgan theory.

$^{17}$O NMR spectroscopy

From the measured $^{17}$O NMR relaxation rates and angular frequencies of the paramagnetic solutions, $1/T_2$ and $\omega$, and of the acidified water reference, $1/T_{2A}$ and $\omega_A$, one can calculate the reduced relaxation rates and chemical shifts, $1/T_2r$ and $\Delta \omega_r$, which may be written as in Equations (A1)-(A2), where, $1/T_{2m}$ is the relaxation rate of the bound water and $\Delta \omega_m$ is the chemical shift difference between bound and bulk water, $\tau_m$ is the mean residence time or the inverse of the water exchange rate $k_{ex}$ and $P_m$ is the mole fraction of the bound water.  

$$\frac{1}{T_{2r}} = \frac{1}{P_m} \left[ \frac{1}{T_2} - \frac{1}{T_{2A}} \right] = \frac{1}{\tau_m} \frac{T_{2m}^{-2} + \tau_m^{-1} T_{2m}^{-1} + \Delta \omega_m^2}{(\tau_m^{-1} + T_{2m}^{-1})^2 + \Delta \omega_m^2} + \frac{1}{T_{2os}}$$  \hspace{1cm} (A1)

$$\Delta \omega_r = \frac{1}{P_m} (\omega - \omega_A) = \frac{\Delta \omega_m}{(1 + \tau_m T_{2m}^{-1})^2 + \tau_m^2 \Delta \omega_m^2} + \Delta \omega_{os}$$  \hspace{1cm} (A2)

Previous studies have shown that outer sphere contributions to the $^{17}$O relaxation rates are negligible.  

In equation (A2) the chemical shift of the bound water molecule, $\Delta \omega_m$, depends on the hyperfine interaction between the Gd$^{3+}$ electron spin and the $^{17}$O nucleus and is directly proportional to the scalar coupling constant, $\frac{A}{\hbar}$, as expressed in Equation (A3).

$$\Delta \omega_m = \frac{g_L \mu_B S(S+1)B A}{3k_B T} \frac{1}{\hbar}$$  \hspace{1cm} (A3)

The isotopic Landé g factor is equal to 2.0 for the Gd$^{3+}$, B represents the magnetic field, and $k_B$ is the Boltzmann constant.

The outer-sphere contribution to the chemical shift is assumed to be linearly related to $\Delta \omega_m$ by a constant $C_{os}$ [Equation (A4)].

$$\Delta \omega_{os} = C_{os} \Delta \omega_m$$  \hspace{1cm} (A4)

In the transverse relaxation, the scalar contribution, $1/T_{2sc}$, is the most important [Equation (A9)]. $1/\tau_{s1}$ is the sum of the exchange rate constant and the electron spin relaxation rate.
\[ \frac{1}{T_{2m}} = \frac{1}{T_{2sc}} = \frac{S(S+1)}{3} \left( \frac{A}{\hbar} \right)^2 \tau_{s1} \quad (A5) \]

\[ \frac{1}{\tau_{s1}} = \frac{1}{\tau_m} + \frac{1}{T_{1e}} \quad (A6) \]

The exchange rate is supposed to obey the Eyring equation. In equation (A7) \( \Delta S^\ddagger \) and \( \Delta H^\ddagger \) are the entropy and enthalpy of activation for the water exchange process, and \( k_{ex}^{298} \) is the exchange rate at 298.15 K.

\[ \frac{1}{\tau_m} = k_{ex} = \frac{k_a T}{h} \exp \left\{ \frac{\Delta S^\ddagger}{R} - \frac{\Delta H^\ddagger}{RT} \right\} = \frac{k_{ex}^{298} T}{298.15} \exp \left\{ \frac{\Delta H^\ddagger}{R} \left( \frac{1}{298.15} - \frac{1}{T} \right) \right\} \quad (A7) \]

**NMRD**

The measured longitudinal proton relaxation rate, \( R_{1}\text{obs} \) = \( 1/T_{1}\text{obs} \), is the sum of a paramagnetic and a diamagnetic contribution as expressed in Equation (A12), where \( r_i \) is the proton relaxivity:

\[ R_{1}\text{obs} = R_{1}^d + R_{1}^\text{p} = R_{1}^d + r_i \{ \text{Gd}^{3+} \} \quad (A8) \]

The relaxivity can be divided into an inner and an outer sphere term as follows:

\[ r_i = r_{1is} + r_{1os} \quad (A9) \]

The inner sphere term is given in Equation (A14), where \( q \) is the number of inner sphere water molecules.

\[ r_{1is} = \frac{1}{1000} \times \frac{q}{55.55} \times \frac{1}{T^{1H}_{1m} + \tau_m} \quad (A10) \]

The longitudinal relaxation rate of inner sphere protons, \( 1/T_{1m}^{H} \) is expressed by Equation (A11), where \( r_{GdH} \) is the effective distance between the electron charge and the \(^1\text{H} \) nucleus, \( \omega_I \) is the proton resonance frequency and \( \omega_S \) is the Larmor frequency of the \( \text{Gd}^{3+} \) electron spin.

\[ \frac{1}{T^{H}_{1m}} = \frac{2}{15} \left( \frac{\mu_0}{4\pi} \right)^2 \frac{\hbar^2 \gamma_I^2 \gamma_S^2}{r_{GdH}^6} S(S+1) \times [3I(\omega_I;\tau_{d1}) + 7I(\omega_S;\tau_{d2})] \quad (A11) \]
The rotational correlation time, $\tau_{RH}$, is assumed to have simple exponential temperature dependence with an $E_R$ activation energy as given in equation (A13).

$$\tau_{RH} \propto \exp(-\frac{E_R}{RT}) \quad \text{(A13)}$$

The outer-sphere contribution can be described by Equation (A14) where $N_A$ is the Avogadro constant, and $J_{os}$ is its associated spectral density function as given by Equation (A15).

$$r_{1os} = \frac{32N_A}{405} \rho_0^2 \left( \frac{\hbar}{4\pi} \right)^2 a_{GdH}^2 D_{GdH}^2 S(S+1) [3J_{os}(\omega_1, T_{1e}) + 7J_{os}(\omega_2, T_{2e})] \quad \text{(A14)}$$

$$J_{os}(\omega, T_{je}) = \text{Re} \left[ \frac{1 + 14 \left( i\omega_\tau_{GdH} + \frac{\tau_{GdH}}{T_{je}} \right)^{1/2}}{1 + \left( i\omega_\tau_{GdH} + \frac{\tau_{GdH}}{T_{je}} \right)^{1/2}} + 49 \left( i\omega_\tau_{GdH} + \frac{\tau_{GdH}}{T_{je}} \right)^{1/2} + 19 \left( i\omega_\tau_{GdH} + \frac{\tau_{GdH}}{T_{je}} \right)^{3/2} \right] \quad \text{(A15)}$$

The longitudinal and transverse electronic relaxation rates, $1/T_{1e}$ and $1/T_{2e}$, are expressed by Equation (A16)-(A17), where $\tau_v$ is the electronic correlation time for the modulation of the zero-field-splitting interaction, $E_v$ the corresponding activation energy and $\Delta^2$ is the mean square zero-field-splitting energy. We assumed a simple exponential dependence of $\tau_v$ versus $1/T$ as written in Equation (A18).

$$\left( \frac{1}{T_{1e}} \right)^{\text{ZFS}} = \frac{1}{25} \Delta^2 \tau_v \left( 4S(S+1) - 3 \right) \left( \frac{1}{1 + \omega_\tau^2} + \frac{4}{1 + 4\omega_\tau^2} \right) \quad \text{(A16)}$$

$$\left( \frac{1}{T_{2e}} \right)^{\text{ZFS}} = \Delta^2 \tau_v \left( \frac{5.26}{1 + 0.372\omega_\tau^2} + \frac{7.18}{1 + 1.24\omega_\tau^2} \right) \quad \text{(A17)}$$
The diffusion coefficient for the diffusion of a water proton away from a Gd$^{III}$ complex, $D_{GdH}$, is assumed to obey an exponential law versus the inverse of the temperature, with an activation energy $E_{DGdH}$, as given in Equation (A19). $D_{GdH}^{298}$ is the diffusion coefficient at 298.15K.

$$D_{GdH} = D_{GdH}^{298} \exp \left( \frac{E_{DGdH}}{R} \left( \frac{1}{T} - \frac{1}{298.15} \right) \right)$$  \hspace{1cm} (A19)

References for Equations