

Supplementary Information

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

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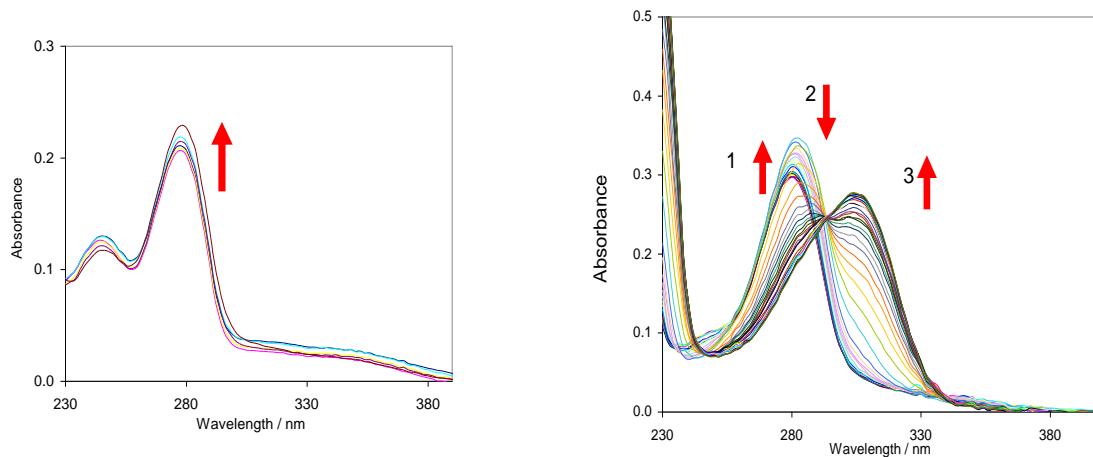
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(b)

Figure S1. UV-Vis absorption spectra variations of the ligand solutions ($C_{L, \text{start}} = 1.3 \times 10^{-5} \text{ M}$) 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.

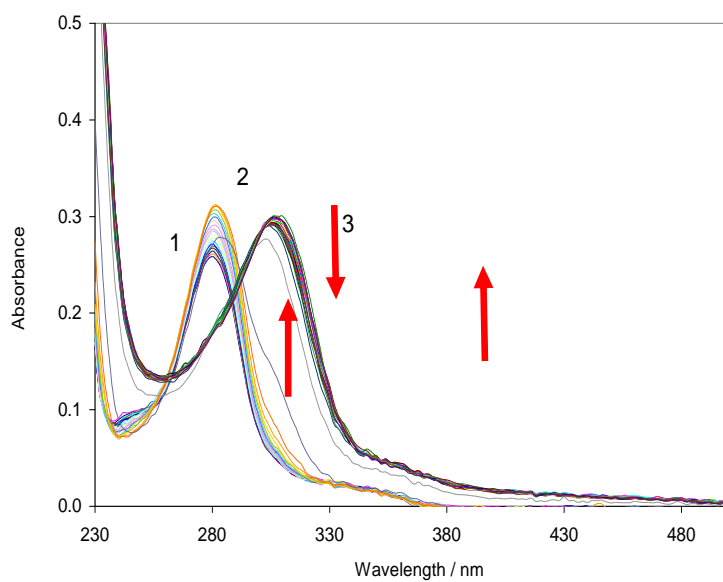


Figure S2. UV-Vis absorption spectra variations of a solution of the ligand L in the presence of La^{3+} , along the titration with base (pH = 3.07-10.6, $C_L = 1.3 \times 10^{-5}$ M, $C_L/C_{\text{La}^{3+}} = 1.01$).

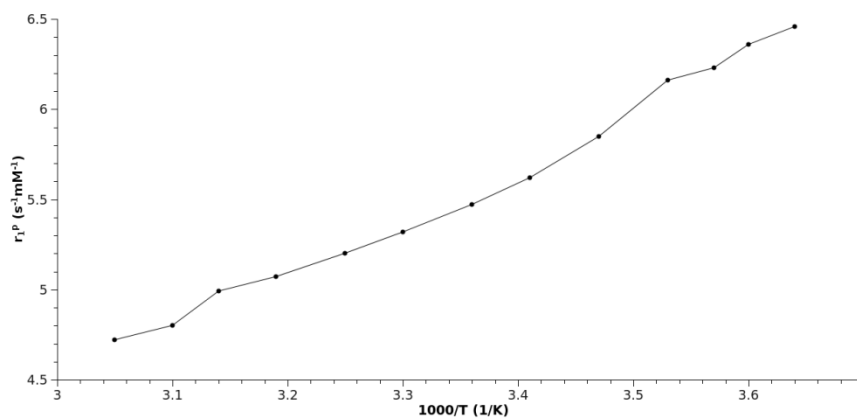


Figure S3. Temperature dependence of the r_1 (20 MHz) relaxivity of the complex Gd-(NTP(PrHP)₃) at pH 7.1.

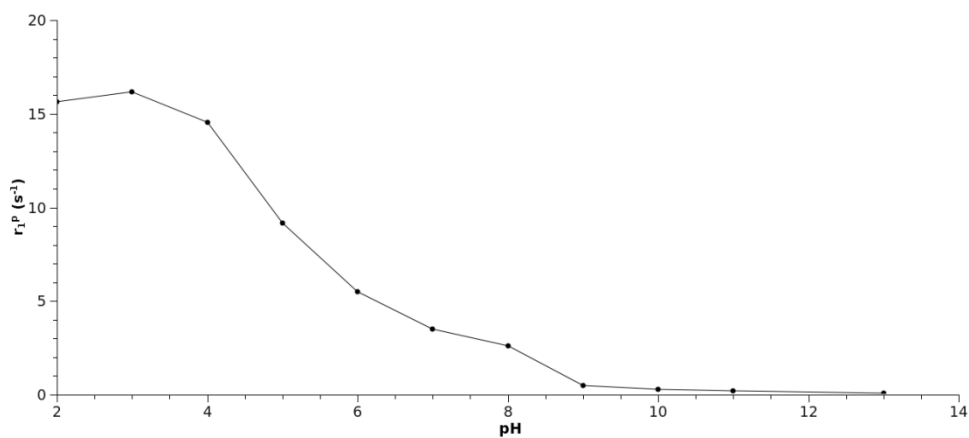


Figure S4. pH dependence of the r_1 (20 MHz) relaxivity of the complex Gd-(NTP(PrHP)₃) at 37°C.

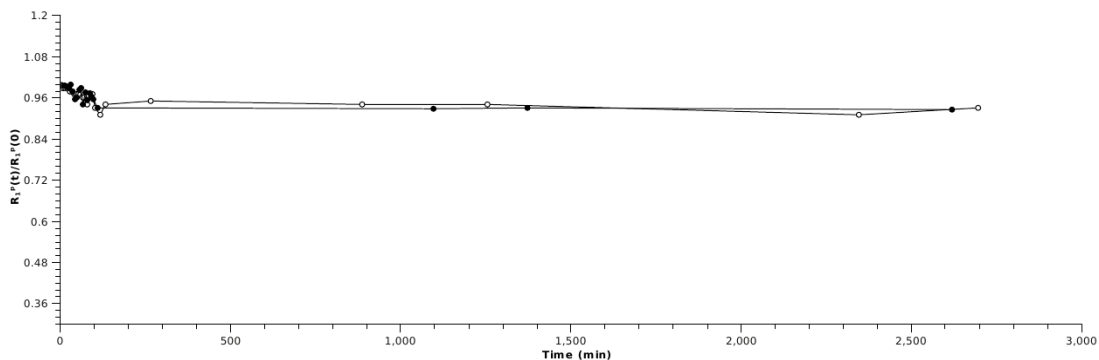


Figure S5. Evolution of the relative water proton paramagnetic relaxation rate $R_1^p(t)/R_1^p(0)$ (20 MHz, pH 7.1, 37 °C) versus time for 0.75 mM Gd-(NTP(PrHP)₃), in 10 mM phosphate buffer solution, in the absence (empty circles) and in the presence (full circles) of an equimolar amount of Zn²⁺ ions.

Table S1. Stability constants for formation of Zn^{2+} - L complexes, $Zn_mH_hL_l$ (25 °C, $I = 0.1$ M KCl)

$\log \beta_{mhl}$	$\log \beta_{151}$	$\log \beta_{141}$	$\log \beta_{131}$	$\log \beta_{121}$	$\log \beta_{111}$	$\log \beta_{302}$
Zn^{2+} -L	42.87±0.05	38.46±0.05	34.02±0.07	29.26±0.09	22.11±0.08	38.92±0.06

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.

Titration	V, mL	C_L , mM	C_M , mM	C_H , mM	V_f , mL
H_1	85.0	0.2036	---	7.112	
H_2	25.5	0.5851	---	9.004	
H_3	4.924	2.098	---	17.77	
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 ω , and of the acidified water reference, $1/T_{2A}$ and ω_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, τ_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.^{1,2}

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

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

Previous studies have shown that outer sphere contributions to the ^{17}O relaxation rates are negligible.³

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).⁴

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

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)].⁵

$$\Delta\omega_{os} = C_{os} \Delta\omega_m \quad (\text{A4})$$

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.

$$\frac{1}{T_{2m}} = \frac{1}{T_{2sc}} = \frac{S(S+1)}{3} \left(\frac{A}{\hbar} \right)^2 \tau_{sl} \quad (\text{A5})$$

$$\frac{1}{\tau_{sl}} = \frac{1}{\tau_m} + \frac{1}{T_{1e}} \quad (\text{A6})$$

The exchange rate is supposed to obey the Eyring equation. In equation (A7) ΔS^\ddagger and ΔH^\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.

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

NMRD

The measured longitudinal proton relaxation rate, $R_1^{obs} = 1/T_1^{obs}$, is the sum of a paramagnetic and a diamagnetic contribution as expressed in Equation (A12), where r_l is the proton relaxivity:

$$R_1^{obs} = R_1^d + R_1^p = R_1^d + r_l [Gd^{3+}] \quad (\text{A8})$$

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

$$r_l = r_{1is} + r_{1os} \quad (\text{A9})$$

The inner sphere term is given in Equation (A14), where q is the number of inner sphere water molecules.⁶

$$r_{1is} = \frac{1}{1000} \times \frac{q}{55.55} \times \frac{1}{T_{1m}^H + \tau_m} \quad (\text{A10})$$

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 ^1H nucleus, ω_l is the proton resonance frequency and ω_s is the Larmor frequency of the Gd^{3+} electron spin.

$$\frac{1}{T_{1m}^H} = \frac{2}{15} \left(\frac{\mu_0}{4\pi} \right)^2 \frac{\hbar^2 \gamma_l^2 \gamma_s^2}{r_{GdH}^6} S(S+1) \times [3J(\omega_l; \tau_{d1}) + 7J(\omega_s; \tau_{d2})] \quad (\text{A11})$$

$$\frac{1}{T_{1e}} = \frac{1}{T_{1e}} + \frac{1}{T_{1e}} + \frac{1}{T_{1e}} \quad \text{for } i=1,2 \quad (\text{A12})$$

where τ_{RH} is the rotational correlation time of the Gd-H_{water} vector.

The rotational correlation time, τ_{RH} is assumed to have simple exponential temperature dependence with an E_R activation energy as given in equation (A13).

$$\tau_{RH} = \tau_{RH} \exp\left(\frac{E_R}{RT}\right) \quad (\text{A13})$$

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).^{8,9}

$$r_{1os} = \frac{32N_A\pi}{405} \left(\frac{\mu_0}{4\pi}\right)^2 \frac{\hbar^2\gamma_S^2\gamma_I^2}{a_{GdH}D_{GdH}} S(S+1) [3J_{os}(\omega_I, T_{1e}) + 7J_{os}(\omega_S, T_{2e})] \quad (\text{A14})$$

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

$j = 1,2$

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

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

$$\left(\frac{1}{T_{2e}}\right)^{ZFS} = \Delta^2 \tau_v \left(\frac{5.26}{1 + 0.372\omega_S^2 \tau_v^2} + \frac{7.18}{1 + 1.24\omega_S^2 \tau_v^2} \right) \quad (\text{A17})$$

$$\tau_v = \tau_v^{298} \exp \left[\frac{E_v}{R} \left(\frac{1}{T} - \frac{1}{298.15} \right) \right] \quad (\text{A18})$$

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 $E_{D_{\text{GdH}}}$, as given in Equation (A19). D_{GdH}^{298} is the diffusion coefficient at 298.15K.

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

References for Equations

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