Electronic Supplementary Information for Dalton Transactions

# Gadolinium(III) Complexes of Mono- and Diethyl Esters of Monophosphonic Acid Analogue of DOTA as Potential MRI Contrast Agents: Solution Structures and Relaxometric Studies

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**Appendix.** Equations used in the analysis of $^{17}$O NMR and $^1$H NMRD data.
**Table S1:** Proton relaxivities ($r_1$ / mM$^{-1}$ s$^{-1}$) of [Gd(do3ap$^{OEt}$)(H$_2$O)]$^-$, $c$(Gd$^{III}$) = 4.7 mM, pH = 6.30, at variable temperature.
**Table S2:** Proton relaxivities ($r_1$ / mM$^{-1}$ s$^{-1}$) of [Gd(do3ap$^{OEt2}$)(H$_2$O)], $c$(Gd$^{III}$) = 4.1 mM, pH = 6.25, at variable temperature.
**Table S3:** Variable temperature reduced transversal and longitudinal $^{17}$O relaxation rates of [Gd(do3ap$^{OEt}$)(H$_2$O)]$^-$, $c$(Gd$^{III}$) = 79 mM, pH = 5.98, $P_m = 1.56\cdot10^{-3}$ at 9.4 T. Reference was acidified H$_2$O, pH = 6.
**Table S4:** Variable temperature reduced transversal and longitudinal $^{17}$O relaxation rates of [Gd(do3ap$^{OEt2}$)(H$_2$O)], $c$(Gd$^{III}$) = 36 mM, pH = 6.2, $P_m = 6.64\cdot10^{-4}$ at 9.4 T. Reference was acidified H$_2$O, pH = 3.71.
**Figure S1.** Variable temperature reduced $^{17}$O chemical shifts of [Gd(do3ap$^{OEt2}$)(H$_2$O)], $c$(Gd$^{III}$) = 36 mM, pH=6.2, $P_m$=6.64·10$^{-4}$ at 9.4 T. Reference was acidified H$_2$O, pH = 3.71.
**Figure S2.** Variable temperature reduced $^{17}$O chemical shifts of [Gd(do3ap$^{OEt}$)(H$_2$O)]$^-$, $c$(Gd$^{III}$) = 79 mM, pH=5.98, $P_m$=1.56·10$^{-3}$ at 9.4 T. Reference was acidified H$_2$O, pH = 6.
**Table S5.** Fitted parameters of [Gd(do3ap$^{OEt2}$)(H$_2$O)] and [Gd(do3ap$^{OEt}$)(H$_2$O)]$^-$. The underlined parameters were fixed during the fitting.
**Figure S3**: Dependence of the chemical shift of $^{31}$P NMR signals of [Eu(do3ap$^{OEt}$)H$_2$O]$^-$ on temperature; pH 6.5
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**Figure S6**: Dependence of fraction of TSAP isomer of [Eu(do3ap$^{OEt2}$)(H$_2$O)] on pH; measured at 3 °C by $^{31}$P NMR.
**Figure S7**: Dependence of fraction of TSAP isomer of [Eu(do3ap$^{OEt2}$)(H$_2$O)] on pH; measured at 3 °C by $^1$H NMR.
**Figure S8**: Temperature dependence of UV-VIS spectra of [Eu(do3ap$^{OEt2}$)(H$_2$O)].
**Figure S9**: Temperature dependence of UV-VIS spectra of [Eu(do3ap$^{OEt}$)(H$_2$O)]$^-$.
**Figure S10**: The contact contributions to the $^{17}$O LIS measurements of [Ln(do3ap$^{OEt}$)(H$_2$O)]$^-$, measured at 9.4 T, 25 °C and pH 7.
**Figure S11**: $^1$H NMRD profile of [Gd(do3ap)(H$_2$O)]$^{2-}$ complex recorded at 37 °C (◆) with fitted line (full line) and calculated contributions from outer-sphere (dashed line) and second-sphere (dotted line) water.

## Appendix.

### $^{17}$O NMR relaxation:

From the measured $^{17}$O NMR relaxation rates and angular frequencies of the paramagnetic solutions, $1/T_1$, $1/T_2$ and $\omega$, and of the acidified water reference, $1/T_{1A}$, $1/T_{2A}$ and $\omega_A$, one can calculate the reduced relaxation rates, $1/T_{1r}$, $1/T_{2r}$ (Eq. **[1]** and **[2]**), where $1/T_{1m}$, $1/T_{2m}$ are the relaxation rates 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.[1,2]

$$\frac{1}{T_{1r}} = \frac{1}{P_m}\left[\frac{1}{T_1} - \frac{1}{T_{1A}}\right] = \frac{1}{T_{1m} + \tau_m} + \frac{1}{T_{1OS}} \qquad \textbf{[1]}$$

$$\frac{1}{T_{2r}} = \frac{1}{P_m}\left[\frac{1}{T_2} - \frac{1}{T_{2A}}\right] = \frac{1}{\tau_m}\frac{T_{2m}^{-2} + \tau_m^{-1}T_{2m}^{-1} + \Delta\omega_m^2}{\left(\tau_m^{-1} + T_{2m}^{-1}\right)^2 + \Delta\omega_m^2} + \frac{1}{T_{2OS}} \qquad \textbf{[2]}$$

The terms $1/T_{1OS}$ and $1/T_{2OS}$ describe relaxation contributions from water molecules not directly bound to the paramagnetic centre. In previous studies it has been shown that $^{17}$O outer-sphere relaxation terms due to water molecules freely diffusing on the surface of Gd-polyaminocarboxylate complexes are negligible. For complexes with phosphate groups relaxation terms due to 2nd-sphere water molecules can however be important for longitudinal relaxation $1/T_{1r}$ and have therefore to be included.

$$\frac{1}{T_{1r}} = \frac{1}{T_{1r}^{1st}} + \frac{1}{T_{1r}^{2nd}} = \frac{1}{T_{1m} + \tau_m} + \frac{1}{T_{1r}^{2nd}} \qquad \textbf{[3]}$$

$$\frac{1}{T_{2r}} = \frac{1}{T_{2r}^{1st}} = \frac{1}{\tau_m}\frac{T_{2m}^{-2} + \tau_m^{-1}T_{2m}^{-1} + \Delta\omega_m^2}{\left(\tau_m^{-1} + T_{2m}^{-1}\right)^2 + \Delta\omega_m^2} \qquad \textbf{[4]}$$

First-sphere contribution to $^{17}$O relaxation:

The $^{17}$O longitudinal relaxation rates in Gd(III) solutions are the sum of the contributions of the dipole-dipole and quadrupolar (in the approximation developed by Halle for non-extreme narrowing conditions) mechanisms as expressed by Eq. **[6]-[7]**, where $\gamma_S$ is the electron and $\gamma_I$ is the nuclear gyromagnetic ratio ($\gamma_S$ = 1.76×1011 rad·s$^{-1}$·T$^{-1}$, $\gamma_I$ = –3.626×10$^7$ rad·s$^{-1}$·T$^{-1}$), $r_{GdO}$ is the effective distance between the electron charge and the $^{17}$O nucleus, $I$ is the nuclear spin (5/2 for $^{17}$O), $\chi$ is the quadrupolar coupling constant and $\eta$ is an asymmetry parameter:

$$\frac{1}{T_{1m}} = \frac{1}{T_{1dd}} + \frac{1}{T_{1q}} \qquad \textbf{[5]}$$

$$\frac{1}{T_{1dd}} = \frac{2}{15}\left(\frac{\mu_0}{4\pi}\right)^2 \frac{\hbar^2\gamma_I^2\gamma_S^2}{r_{GdO}^6} S(S+1)\left[3J(\omega_I;\tau_{d1}) + 7J(\omega_S;\tau_{d2})\right]; \quad J(\omega;\tau) = \frac{\tau}{1+(\omega\tau)^2} \qquad \textbf{[6]}$$

$$\frac{1}{\tau_{d1}} = \frac{1}{\tau_m} + \frac{1}{T_{1e}} + \frac{1}{\tau_{RO}}$$

$$\frac{1}{T_{1q}} = \frac{3\pi^2}{10}\frac{2I+3}{I^2(2I-1)}\chi^2\left(1+\frac{\eta^2}{3}\right)\left[0.2J_1(\omega_I;\tau_{RO}) + 0.8J_2(\omega_I;\tau_{RO})\right]; \quad J_n(\omega;\tau) = \frac{\tau}{1+(n\omega\tau)^2} \qquad \textbf{[7]}$$

In the transverse relaxation the scalar contribution, $1/T_{2sc}$, is dominating, Eq. **[8]**. $1/\tau_{s1}$ is the sum of the exchange rate constant and the electron spin relaxation rate.

$$\frac{1}{T_{2m}} \cong \frac{1}{T_{2SC}} = \frac{S(S+1)}{3}\left(\frac{A}{\hbar}\right)^2 \tau_{S1} \qquad \textbf{[8]}$$

$$\frac{1}{\tau_{S1}} = \frac{1}{\tau_m} + \frac{1}{T_{1e}} \qquad \textbf{[9]}$$

Second-sphere contribution to $^{17}$O relaxation:

$$\frac{1}{T_1^{2nd}} \cong \frac{q^{2nd}}{q^{1st}}\frac{1}{T_{1m}^{2nd}} = \frac{q^{2nd}}{q^{1st}}\left(\frac{1}{T_{1dd}^{2nd}}+\frac{1}{T_{1q}^{2nd}}\right) \qquad \textbf{[10]}$$

$$\frac{1}{T_{1dd}^{2nd}} = C_{dd}^{2nd,O}\left(\frac{3\tau_{d1}^{2nd,O}}{1+\left(\omega_I\tau_{d1}^{2nd,O}\right)^2}+\frac{7\tau_{d2}^{2nd,O}}{1+\left(\omega_S\tau_{d2}^{2nd,O}\right)^2}\right) \qquad \textbf{[11]}$$

$$C_{dd}^{2nd,O} = \frac{2}{15}\left(\frac{\mu_0}{4\pi}\right)^2\frac{h^2\gamma_{^{17}O}^2\gamma_S^2}{\left(r_{GdO}^{2nd}\right)^6}S(S+1)$$

$$\frac{1}{T_{1q}^{2nd}} = \frac{3\pi^2}{10}\frac{2I+3}{I^2(2I-1)}\chi^2\left(1+\eta^2/3\right)\left(\frac{0.2\tau^{2nd,O}}{1+\left(\omega_I\tau^{2nd,O}\right)^2}+\frac{0.8\tau^{2nd,O}}{1+\left(2\omega_I\tau^{2nd,O}\right)^2}\right) \qquad \textbf{[12]}$$

$$\frac{1}{\tau^{O,2nd}} = \frac{1}{\tau_g}+\frac{1}{\tau_1^O} \cong \frac{1}{\tau_1^O} \qquad \textbf{[13]}$$

$$\frac{1}{\tau_{di}^{2nd,O}} = k_{ex}^{2nd}+\frac{1}{\tau^{O,2nd}}+\frac{1}{T_{ie}} \qquad \textbf{[14]}$$

## $^1$H NMRD:

The measured longitudinal proton relaxation rate, $R_1^{obs}$ is the sum of a paramagnetic and a diamagnetic contribution as expressed in Eq. **[15]**, where $r_1$ is the proton relaxivity:

$$R_1^{obs} = R_1^d + R_1^p = R_1^d + r_1\left[Gd^{3+}\right] \qquad \textbf{[15]}$$

The relaxivity is here given by the sum of inner-sphere, second-sphere and outer-sphere contributions:

$$r_1 = r_{1is} + r_{1,2nd} + r_{1os} \qquad \textbf{[16]}$$

Inner-sphere $^1$H relaxation:

The inner-sphere term is given in Eq. **[17]**, where $q^{1st}$ is the number of inner-sphere water molecules.[3]

$$r_{1is} = \frac{1}{1000}\times\frac{q^{1st}}{55.55}\times\frac{1}{T_{1m}^H+\tau_m} \qquad \textbf{[17]}$$

The longitudinal relaxation rate of inner-sphere protons, $1/T_{1m}^H$ is expressed by Eq. **[18]**, where $r_{GdH}$ is the effective distance between the electron charge and the $^1$H nucleus, $\omega_I$ is the proton resonance frequency and $\omega_S$ is the Larmor frequency of the Gd(III) electron spin.

$$\frac{1}{T_{1m}^H} = \frac{2}{15}\left(\frac{\mu_0}{4\pi}\right)^2\frac{\hbar^2\gamma_I^2\gamma_S^2}{r_{GdH}^6}S(S+1)\left[3J(\omega_I;\tau_{d1})+7J(\omega_S;\tau_{d2})\right] \qquad \textbf{[18]}$$

$$J(\omega;\tau_{di}) = \left(\frac{S^2\tau_{dig}}{1+\omega^2\tau_{dig}^2}+\frac{\left(1-S^2\right)\tau_{di}}{1+\omega^2\tau_{di}^2}\right);\quad i=1,2 \qquad \textbf{[19]}$$

$$\frac{1}{\tau_{dig}} = \frac{1}{\tau_m}+\frac{1}{\tau_g}+\frac{1}{T_{ie}}\ ;\quad \frac{1}{\tau_{dig}} = \frac{1}{\tau_m}+\frac{1}{\tau^H}+\frac{1}{T_{ie}}\ ;\quad i=1,2 \qquad \textbf{[20]}$$

$$\frac{1}{\tau^H} = \frac{1}{\tau_g}+\frac{1}{\tau_1^H} \qquad \textbf{[21]}$$

The spectral density functions are given by Eq. **[19]**.

Second-sphere $^1$H relaxation:

$$r_1^{2nd} = \frac{1}{1000} \times \frac{q^{2nd}}{55.55} \times \frac{1}{T_{1dd}^{2nd,H} + \tau_m^{2nd}} \cong \frac{1}{1000} \times \frac{q^{2nd}}{55.55} \times \frac{1}{T_{1dd}^{2nd,H}} \qquad \textbf{[22]}$$

$$\frac{1}{T_{1dd}^{2nd,H}} = C_{dd}^{2nd,O} \left( \frac{3\tau_{d1}^{2nd,H}}{1+\left(\omega_I \tau_{d1}^{2nd,H}\right)^2} + \frac{7\tau_{d2}^{2nd,H}}{1+\left(\omega_S \tau_{d2}^{2nd,H}\right)^2} \right) \qquad \textbf{[23]}$$

$$C_{dd}^{2nd,H} = \frac{2}{15}\left(\frac{\mu_0}{4\pi}\right)^2 \frac{h^2 \gamma_{{}^1H}^2 \gamma_S^2}{\left(r_{GdO}^{2nd}\right)^6} S(S+1) \qquad \textbf{[24]}$$

$$\frac{1}{\tau_{di}^{2nd,H}} = k_{ex}^{2nd} + \frac{1}{\tau^H} + \frac{1}{T_{ie}} \qquad \textbf{[25]}$$

$$\frac{1}{\tau^H} = \frac{1}{\tau_g} + \frac{1}{\tau_l^H} \qquad \textbf{[26]}$$

Outer-sphere $^1$H relaxation:

The outer-sphere contribution can be described by Eq. **[27]** where $N_A$ is the Avogadro constant, and $J_{os}$ is its associated spectral density function.[4,5]

$$r_{1os} = \frac{32 N_A \pi}{405}\left(\frac{\mu_0}{4\pi}\right)^2 \frac{\hbar^2 \gamma_S^2 \gamma_I^2}{a_{GdH} D_{GdH}} S(S+1)\left[3J_{os}\left(\omega_I; T_{1e}\right) + 7J_{os}\left(\omega_S; T_{2e}\right)\right] \qquad \textbf{[27]}$$

$$J_{os}\left(\omega, T_{je}\right) = \mathrm{Re}\left[ \frac{1 + \frac{1}{4}\left(i\omega\tau_{GdH} + \frac{\tau_{GdH}}{Tje}\right)^{1/2}}{1 + \left(i\omega\tau_{GdH} + \frac{\tau_{GdH}}{T_{je}}\right)^{1/2} + \frac{4}{9}\left(i\omega\tau_{GdH} + \frac{\tau_{GdH}}{T_{je}}\right) + \frac{1}{9}\left(i\omega\tau_{GdH} + \frac{\tau_{GdH}}{T_{je}}\right)^{3/2}} \right]; \quad j = 1,2 \qquad \textbf{[28]}$$

$$\tau_{GdH} = \frac{a_{GdH}^2}{D_{GdH}} \qquad \textbf{[29]}$$

$a_{GdH}$ is the distance of closes approach and $D_{GdH}$ is the diffusion coefficient for the diffusion of a water proton relative to the Gd(III) complex.

Electron spin relaxation:

The longitudinal and transverse electronic relaxation rates, $1/T_{1e}$ and $1/T_{2e}$ are described by Solomon-Bloembergen-Morgan theory modified by Powell (Eqs. **[30]-[31]**), where $\tau_V$ is the correlation time for the modulation of the zero-field-splitting interaction.

$$\left(\frac{1}{T_{1e}}\right)^{ZFS} = \frac{1}{25}\Delta^2 \tau_v \left\{4S(S+1) - 3\right\}\left(\frac{1}{1+\omega_S^2\tau_v^2} + \frac{4}{1+4\omega_S^2\tau_v^2}\right) \qquad \textbf{[30]}$$

$$\left(\frac{1}{T_{2e}}\right)^{ZFS} = \Delta^2 \tau_v \left(\frac{5.26}{1+0.372\omega_S^2\tau_v^2} + \frac{7.18}{1+1.24\omega_S\tau_v}\right) \qquad \textbf{[31]}$$

Temperature dependences of water exchange rates and correlation times:

The exchange rates are supposed to follow the Eyring equation. In Eq. **[32]** $\Delta S^{\ddagger}$ 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. In Eq. **[33]** $\Delta H^{\ddagger 2nd}$ is the enthalpy of activation for the second sphere water exchange process and $k_{ex}^{2nd,298}$ is the corresponding exchange rate at 298 K.

$$k_{ex} = \frac{1}{\tau_m} = \frac{k_B T}{h}\exp\left\{\frac{\Delta S^{\ddagger}}{\mathrm{R}} - \frac{\Delta H^{\ddagger}}{RT}\right\} = \frac{k_{ex}^{298} T}{298.15}\exp\left\{\frac{\Delta H^{\ddagger}}{R}\left(\frac{1}{298.15} - \frac{1}{T}\right)\right\} \quad \textbf{[32]}$$

$$k_{ex}^{2nd} = \frac{k_{ex}^{2nd,298}}{298.14}\exp\left\{\frac{\Delta H^{\ddagger 2nd}}{T}\left(\frac{1}{298.15} - \frac{1}{T}\right)\right\} \quad \textbf{[33]}$$

All correlation times and the diffusion constant are supposed to obey an Arrhenius law:

$$\tau = \tau^{298}\exp\left\{\frac{E_a}{R}\left(\frac{1}{T} - \frac{1}{298.15}\right)\right\} \quad \textbf{[34]}$$

$$D_{GdH} = D_{GdH}^{298}\exp\left\{\frac{E_{GdH}}{R}\left(\frac{1}{298.15} - \frac{1}{T}\right)\right\} \quad \textbf{[35]}$$

**Table S1:** Proton relaxivities ($r_1$ / mM$^{-1}$ s$^{-1}$) of [Gd(do3ap$^{OEt}$)($H_2O$)]$^-$, $c$(Gd$^{III}$) = 4.7 mM, pH = 6.30, at variable temperature.

| ν($^1$H) /MHz | 5 °C | 25 °C | 37 °C | 50 °C |
|---|---|---|---|---|
| 0.010 | 17.0 | 10.9 | 8.53 | 6.39 |
| 0.014 | 17.0 | 10.9 | 8.53 | 6.41 |
| 0.021 | 17.0 | 10.9 | 8.50 | 6.41 |
| 0.030 | 17.0 | 10.9 | 8.51 | 6.36 |
| 0.043 | 17.1 | 10.8 | 8.48 | 6.38 |
| 0.062 | 16.9 | 10.8 | 8.50 | 6.40 |
| 0.089 | 17.0 | 10.9 | 8.51 | 6.40 |
| 0.13 | 16.9 | 10.8 | 8.48 | 6.36 |
| 0.18 | 16.9 | 10.8 | 8.49 | 6.40 |
| 0.26 | 16.9 | 10.9 | 8.40 | 6.39 |
| 0.38 | 16.9 | 10.8 | 8.43 | 6.36 |
| 0.55 | 16.7 | 10.7 | 8.36 | 6.31 |
| 0.78 | 16.5 | 10.6 | 8.34 | 6.24 |
| 1.1 | 16.0 | 10.4 | 8.16 | 6.17 |
| 1.6 | 15.4 | 10.1 | 7.93 | 5.99 |
| 2.3 | 14.3 | 9.52 | 7.56 | 5.79 |
| 3.4 | 12.6 | 8.58 | 6.92 | 5.44 |
| 4.8 | 10.9 | 7.57 | 6.12 | 4.93 |
| 7.0 | 9.61 | 6.51 | 5.15 | 4.17 |
| 10 | 8.75 | 5.48 | 4.45 | 3.64 |
| 11 | 8.47 | 5.15 | 4.08 | 3.41 |
| 13 | 8.30 | 4.94 | 3.79 | 3.17 |
| 15 | 8.15 | 4.69 | 3.61 | 2.97 |
| 17 | 8.08 | 4.56 | 3.51 | 2.91 |
| 20 | 8.12 | 4.53 | 3.49 | 2.81 |
| 30 | 8.09 | 4.50 | 3.32 | 2.69 |
| 40 | 7.88 | 4.41 | 3.19 | 2.55 |
| 60 | 8.11 | 4.33 | 3.09 | 2.44 |
| 100 | 7.58 | 4.16 | 2.98 | 2.29 |
| 200 | 7.24 | 4.04 | 2.88 | 2.23 |
| 400 | 6.68 | 3.76 | 2.67 | 2.12 |

**Table S2:** Proton relaxivities ($r_1$ / mM$^{-1}$ s$^{-1}$) of [Gd(do3ap$^{\mathrm{OEt2}}$)($H_2O$)], $c$(Gd$^{\mathrm{III}}$) = 4.1 mM, pH = 6.25, at variable temperature.

| ν($^1$H) /MHz | 5 °C | 25 °C | 37 °C | 50 °C |
|---|---|---|---|---|
| 0.010 | 13.5 | 8.83 | 6.938 | 5.92 |
| 0.014 | 13.5 | 8.85 | 6.920 | 5.92 |
| 0.0208 | 13.5 | 8.80 | 6.945 | 5.93 |
| 0.030 | 13.5 | 8.80 | 6.925 | 5.89 |
| 0.043 | 13.5 | 8.79 | 6.917 | 5.93 |
| 0.062 | 13.5 | 8.80 | 6.900 | 5.91 |
| 0.089 | 13.5 | 8.78 | 6.932 | 5.92 |
| 0.13 | 13.5 | 8.81 | 6.890 | 5.94 |
| 0.18 | 13.4 | 8.80 | 6.891 | 5.90 |
| 0.26 | 13.4 | 8.79 | 6.904 | 5.87 |
| 0.38 | 13.4 | 8.80 | 6.885 | 5.84 |
| 0.55 | 13.4 | 8.76 | 6.866 | 5.84 |
| 0.78 | 13.3 | 8.71 | 6.818 | 5.79 |
| 1.1 | 12.9 | 8.60 | 6.746 | 5.72 |
| 1.6 | 12.4 | 8.34 | 6.612 | 5.64 |
| 2.3 | 11.8 | 8.04 | 6.358 | 5.41 |
| 3.4 | 10.8 | 7.47 | 5.976 | 5.14 |
| 4.8 | 9.76 | 6.79 | 5.502 | 4.75 |
| 7.0 | 8.52 | 5.97 | 4.787 | 4.21 |
| 10 | 8.19 | 5.30 | 4.152 | 3.62 |
| 11 | 7.83 | 4.94 | 3.893 | 3.33 |
| 13 | 7.66 | 4.72 | 3.671 | 3.12 |
| 15 | 7.53 | 4.56 | 3.529 | 2.97 |
| 17 | 7.53 | 4.47 | 3.446 | 2.93 |
| 20 | 7.49 | 4.43 | 3.435 | 2.87 |
| 30 | 7.40 | 4.52 | 3.296 | 2.70 |
| 40 | 7.38 | 4.35 | 3.198 | 2.55 |
| 60 | 7.38 | 4.28 | 3.100 | 2.42 |
| 100 | 6.91 | 4.28 | 3.142 | 2.31 |
| 200 | 6.59 | 3.96 | 2.897 | 2.10 |
| 400 | 5.89 | 3.87 | 2.799 | 2.01 |

**Table S3:** Variable temperature reduced transversal and longitudinal $^{17}$O relaxation rates of $[Gd(do3ap^{OEt})(H_2O)]^-$, $c(Gd^{III})$ = 79 mM, pH = 5.98, $P_m = 1.56\cdot10^{-3}$ at 9.4 T. Reference was acidified $H_2O$, pH = 6.

| $t$ / °C | $T$ / K | 1000/$T$ / K$^{-1}$ | $P_m$ | $T_1$ (Gd)/s | $T_1$ ($H_2O$)/s | $T_2$(Gd)/s | $T_2$($H_2O$)/s | ln(1/$T_{1r}$) | ln(1/$T_{2r}$) |
|---|---|---|---|---|---|---|---|---|---|
| 8.3 | 281.5 | 3.55 | 1.56E-03 | 3.03E-03 | 3.58E-03 | 4.97E-04 | 3.22E-03 | 10.38 | 13.90 |
| 15.7 | 288.9 | 3.46 | 1.56E-03 | 4.01E-03 | 4.72E-03 | 5.00E-04 | 3.85E-03 | 10.08 | 13.93 |
| 24.9 | 298.1 | 3.36 | 1.56E-03 | 5.25E-03 | 6.07E-03 | 7.62E-04 | 4.73E-03 | 9.71 | 13.47 |
| 34.1 | 307.3 | 3.25 | 1.56E-03 | 6.83E-03 | 7.94E-03 | 9.10E-04 | 5.28E-03 | 9.48 | 13.28 |
| 43.3 | 316.5 | 3.16 | 1.56E-03 | 8.42E-03 | 9.94E-03 | 1.33E-03 | 6.47E-03 | 9.36 | 12.86 |
| 52.6 | 325.8 | 3.07 | 1.56E-03 | 1.03E-02 | 1.23E-02 | 2.20E-03 | 7.74E-03 | 9.26 | 12.25 |
| 61.8 | 335.0 | 2.99 | 1.56E-03 | 1.24E-02 | 1.46E-02 | 3.36E-03 | 8.50E-03 | 8.98 | 11.66 |
| 71.0 | 344.2 | 2.91 | 1.56E-03 | 1.45E-02 | 1.71E-02 | 4.98E-03 | 1.10E-02 | 8.83 | 11.16 |
| 80.2 | 353.4 | 2.83 | 1.56E-03 | 1.69E-02 | 1.89E-02 | 7.40E-03 | 1.37E-02 | 8.33 | 10.59 |

**Table S4:** Variable temperature reduced transversal and longitudinal $^{17}$O relaxation rates of $[Gd(do3ap^{OEt2})(H_2O)]$, $c(Gd^{III})$ = 36 mM, pH = 6.2, $P_m = 6.64\cdot10^{-4}$ at 9.4 T. Reference was acidified $H_2O$, pH = 3.71.

| $t$ / °C | $T$ / K | 1000/$T$ / K$^{-1}$ | $P_m$ | $T_1$ (Gd)/s | $T_1$ ($H_2O$)/s | $T_2$(Gd)/s | $T_2$($H_2O$)/s | ln(1/$T_{1r}$) | ln(1/$T_{2r}$) |
|---|---|---|---|---|---|---|---|---|---|
| 4.3 | 277.5 | 3.60 | 6.64E-04 | 3.51E-03 | 3.80E-03 | 1.40E-03 | 3.27E-03 | 10.40 | 13.33 |
| 9.2 | 282.4 | 3.54 | 6.64E-04 | 4.19E-03 | 4.52E-03 | 1.31E-03 | 3.80E-03 | 10.19 | 13.53 |
| 15.0 | 288.2 | 3.47 | 6.64E-04 | 5.00E-03 | 5.38E-03 | 1.19E-03 | 4.47E-03 | 9.98 | 13.74 |
| 20.3 | 293.5 | 3.41 | 6.64E-04 | 5.94E-03 | 6.36E-03 | 1.17E-03 | 5.20E-03 | 9.72 | 13.81 |
| 25.0 | 298.2 | 3.35 | 6.64E-04 | 6.65E-03 | 7.21E-03 | 1.13E-03 | 5.82E-03 | 9.78 | 13.89 |
| 30.7 | 303.9 | 3.29 | 6.64E-04 | 7.66E-03 | 8.34E-03 | 1.14E-03 | 6.72E-03 | 9.68 | 13.91 |
| 36.0 | 309.2 | 3.23 | 6.64E-04 | 8.60E-03 | 9.39E-03 | 1.15E-03 | 7.42E-03 | 9.60 | 13.91 |
| 44.5 | 317.7 | 3.15 | 6.64E-04 | 1.05E-02 | 1.14E-02 | 1.43E-03 | 8.71E-03 | 9.34 | 13.69 |
| 56.0 | 329.2 | 3.04 | 6.64E-04 | 1.32E-02 | 1.42E-02 | 2.07E-03 | 1.07E-02 | 8.94 | 13.28 |
| 66.1 | 339.3 | 2.95 | 6.64E-04 | 1.56E-02 | 1.69E-02 | 3.00E-03 | 1.19E-02 | 8.85 | 12.84 |
| 75.6 | 348.8 | 2.87 | 6.64E-04 | 1.83E-02 | 1.95E-02 | 4.70E-03 | 1.34E-02 | 8.55 | 12.24 |
| 84.6 | 357.8 | 2.80 | 6.64E-04 | 2.09E-02 | 2.24E-02 | 6.45E-03 | 1.51E-02 | 8.52 | 11.80 |

**Figure S1.** Variable temperature reduced $^{17}O$ chemical shifts of [Gd(do3ap$^{OEt2}$)($H_2O$)], *c*($Gd^{III}$) = 36 mM, pH=6.2, $P_m$=6.64·$10^{-4}$ at 9.4 T. Reference was acidified $H_2O$, pH = 3.71.

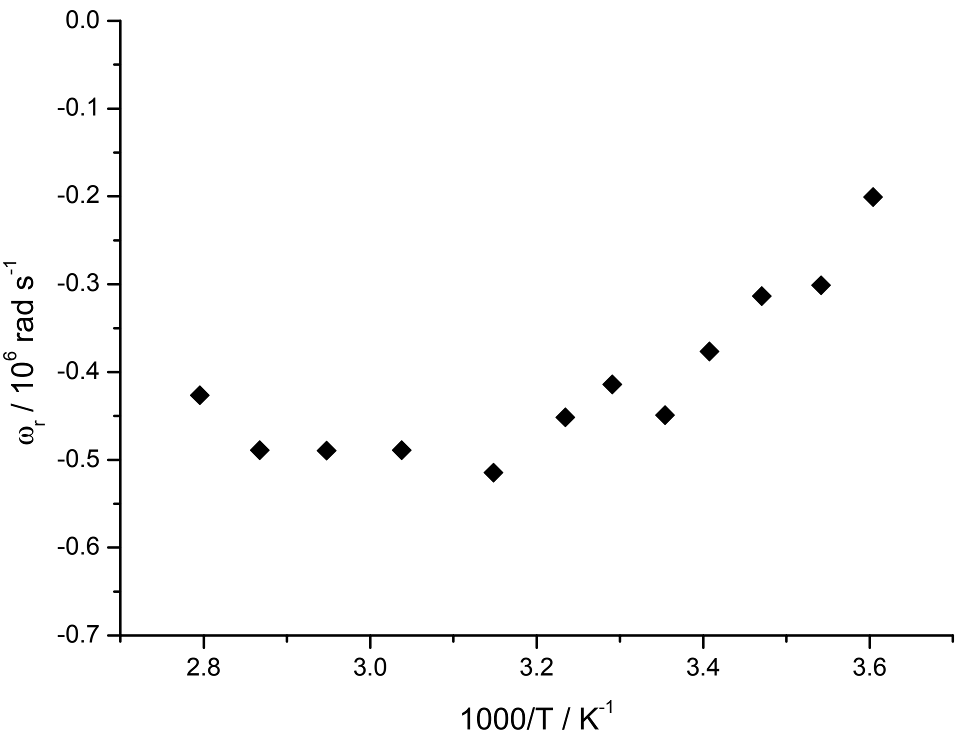


**Figure S2.** Variable temperature reduced $^{17}O$ chemical shifts of [Gd(do3ap$^{OEt}$)($H_2O$)]$^-$, *c*($Gd^{III}$) = 79 mM, pH=5.98, $P_m$=1.56·$10^{-3}$ at 9.4 T. Reference was acidified $H_2O$, pH = 6.

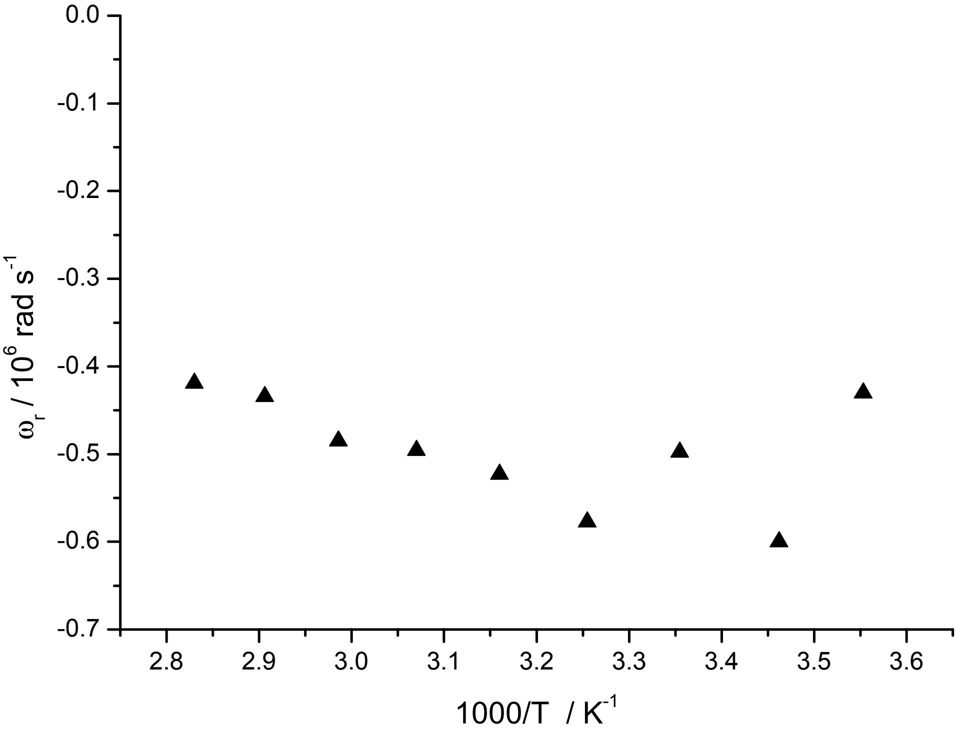


**Table S5.** Fitted parameters of [Gd(do3ap$^{\mathrm{OEt2}}$)($H_2O$)] and [Gd(do3ap$^{\mathrm{OEt}}$)($H_2O$)]$^-$. The underlined parameters were fixed during the fitting.

| Parameter | [Gd(do3ap$^{\mathrm{OEt2}}$)($H_2O$)] | [Gd(do3ap$^{\mathrm{OEt}}$)($H_2O$)]$^-$ |
|---|---|---|
| $k_{ex}^{298}$ [$10^6$ s$^{-1}$] | 4.4±0.3 | 20±5 |
| $\Delta H^\ddagger$ [kJ mol$^{-1}$] | 56.8±2 | 61.4±5 |
| $\Delta S^\ddagger$ [J mol$^{-1}$ K$^{-1}$] | +72.7±0.5 | +100.9±0.6 |
| $A/\hbar$ [$10^6$ rad s$^{-1}$] | $\underline{-3.3}$ | $\underline{-3.3}$ |
| $\tau_R^{298}$(O) [ps] | 77±8 | 84±9 |
| $E_R$ [kJ mol$^{-1}$] | $\underline{20}$ | $\underline{22}$ |
| $\tau_V^{298}$ [ps] | 11.4±1.5 | 8.7±1.2 |
| $E_V$ [kJ mol$^{-1}$] | $\underline{1}$ | $\underline{1}$ |
| $\Delta^2$[$10^{20}$ s$^{-2}$] | $\underline{0.55}$ | 0.42±0.07 |
| $D^{298}_{GdH}$ [$10^{-10}$ m$^2$ s$^{-1}$] | 25±3 | 25±2 |
| $E_{DGdH}$ [kJ mol$^{-1}$] | 28±1 | 22±1 |
| $\delta g_L^2$ [$10^{-2}$] | $\underline{1.7}$ | 3.3±0.1 |
| $\tau_R^{298}$(H)/ $\tau_R^{298}$(O) | 0.77±0.11 | 0.79±0.10 |
| $r_{GdO}$ [Å] | $\underline{2.5}$ | $\underline{2.5}$ |
| $r_{GdH}$ [Å] | $\underline{3.1}$ | $\underline{3.1}$ |
| $r_{GdHouter}$ [Å] | $\underline{3.65}$ | $\underline{3.65}$ |
| $\chi(1+\eta^2/3)^{1/2}$ [MHz] | $\underline{7.58}$ | $\underline{7.58}$ |
| $q$ | $\underline{1}$ | $\underline{1}$ |
| $q_{2nd}$ | $\underline{1}$ | $\underline{1}$ |
| $\tau_M{}^{298}{}_{2nd}$ [ps] | $\underline{50}$ | $\underline{50}$ |
| $\Delta H^\ddagger_{2nd}$ [kJ mol$^{-1}$] | $\underline{30}$ | $\underline{30}$ |

| | | |
|---|---|---|
| $r^{2nd}_{GdH}$ [Å] | 3.5 | 3.5 |
| $r^{2nd}_{GdO}$ [Å] | 4.1 | 4.1 |

**Figure S3**: Dependence of the chemical shift of $^{31}$P NMR signals of $[Eu(do3ap^{OEt})H_2O]^-$ on temperature; pH 6.5

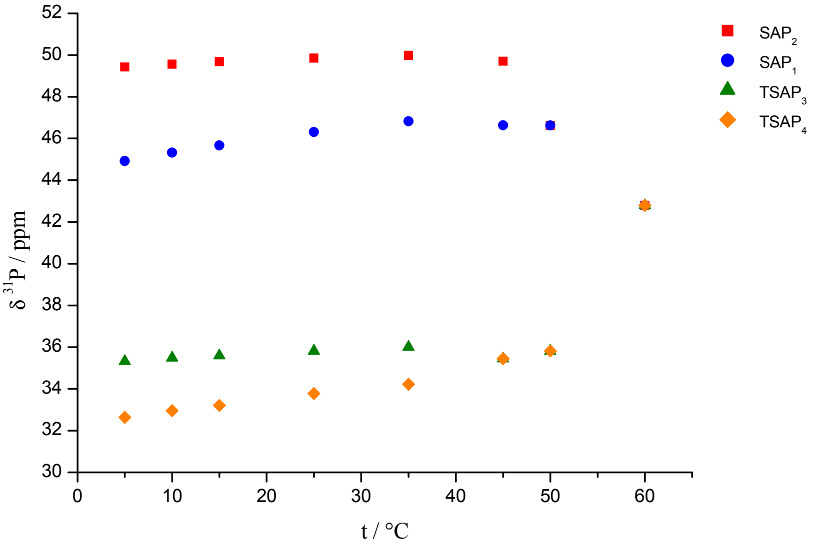


**Figure S4**: Dependence of fraction TSAP isomer of $[Eu(do3ap^{OEt})(H_2O)]^-$ on pH; measured at 3 °C by $^{31}$P NMR

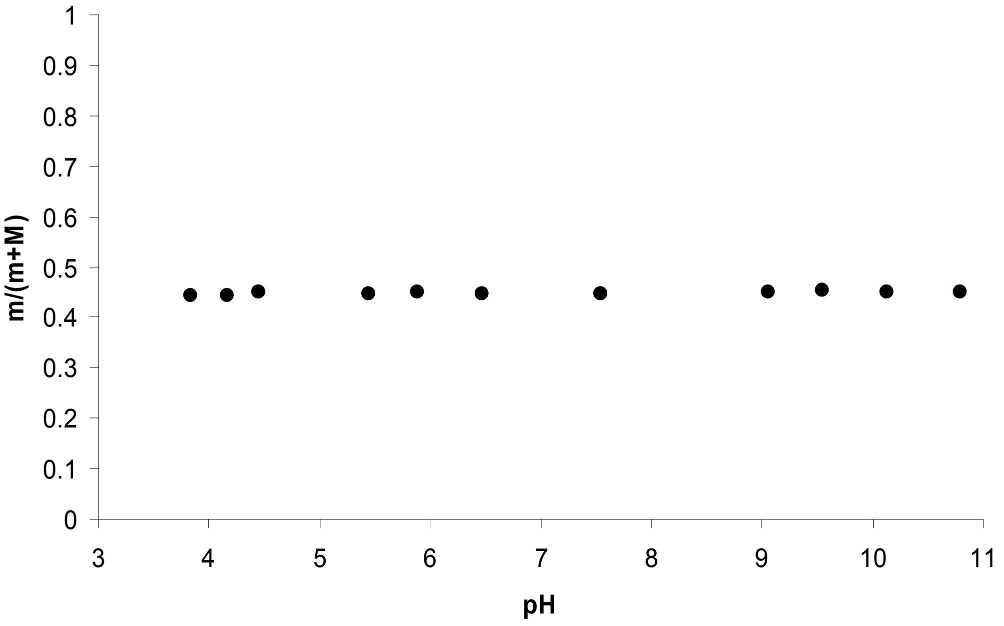


**Figure S5**: Dependence of fraction TSAP isomer of $[Eu(do3ap^{OEt})(H_2O)]^-$ on pH; measured at 3 °C by $^1$H NMR

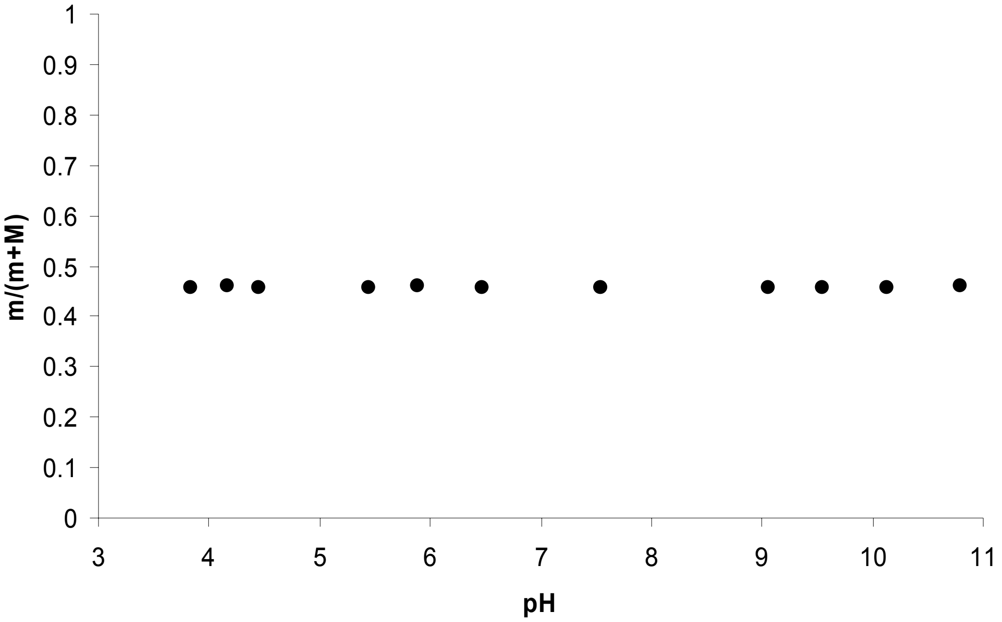


**Figure S6**: Dependence of fraction TSAP isomer of [Eu(do3ap$^{OEt2}$)($H_2O$)] on pH; measured at 3 °C by $^{31}$P NMR.

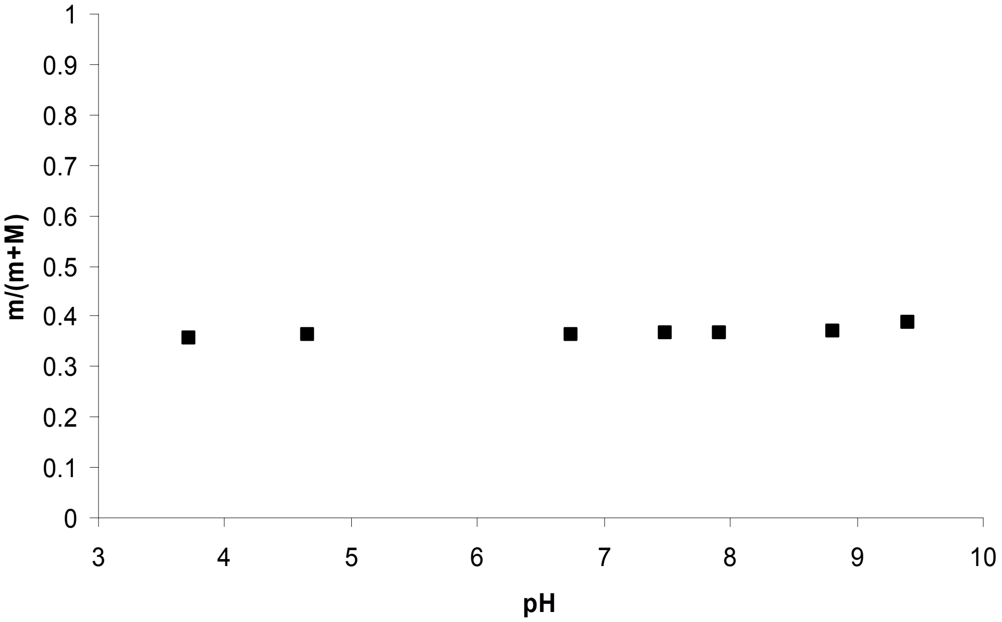


**Figure S7**: Dependence of fraction TSAP isomer of [Eu(do3ap$^{OEt2}$)($H_2O$)] on pH; measured at 3 °C by $^1$H NMR.

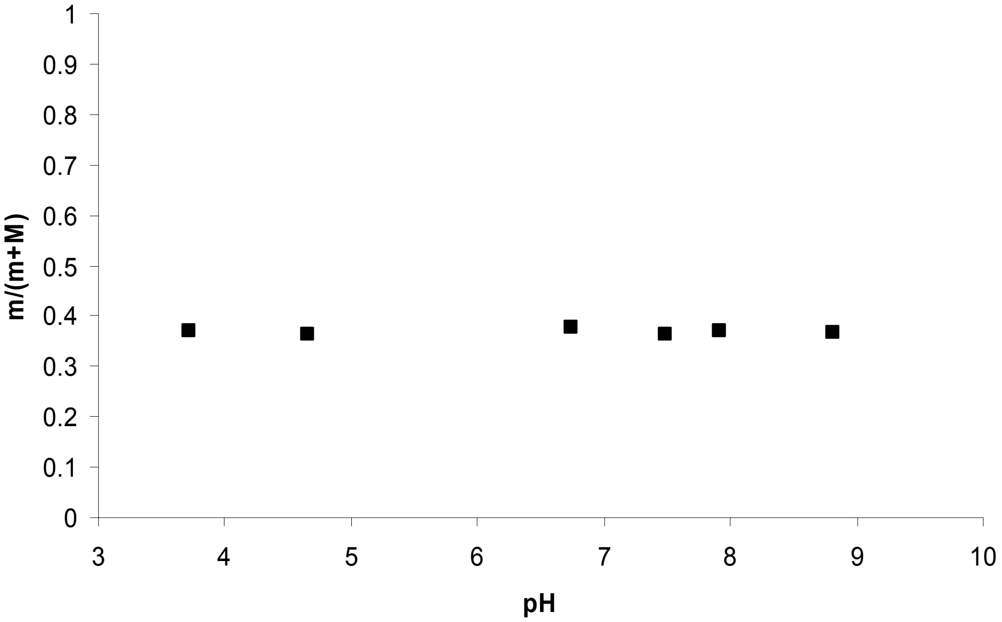


**Figure S8**: Temperature dependence of UV-Vis spectra of [Eu(do3ap$^{OEt2}$)($H_2O$)].

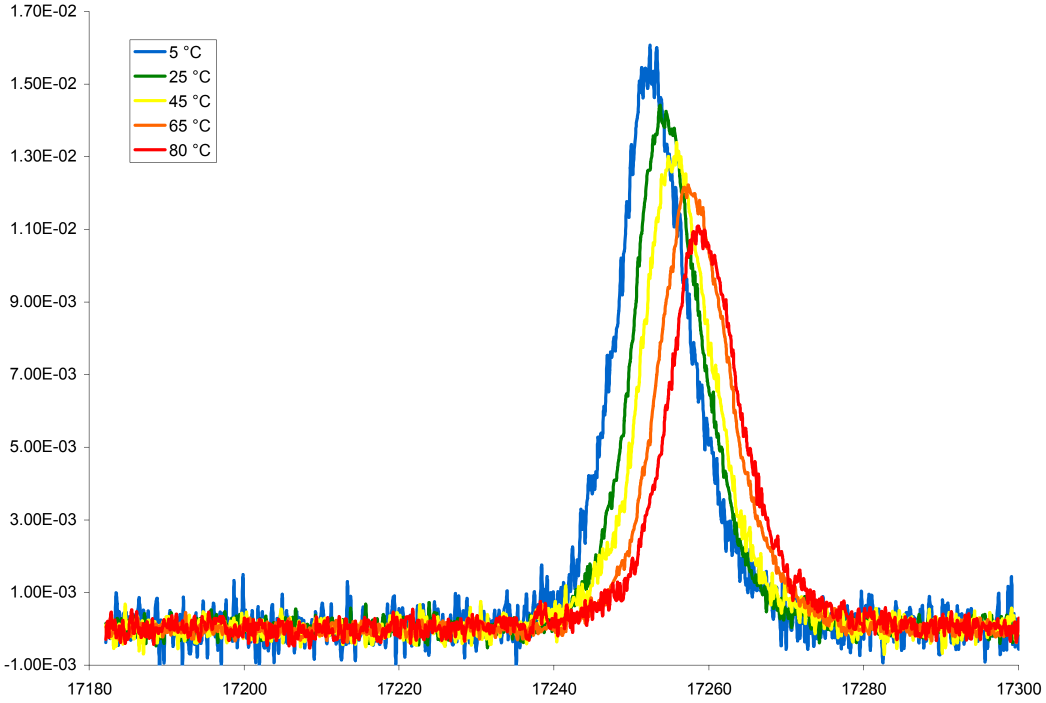


**Figure S9**: Temperature dependence of UV-Vis spectra of [Eu(do3ap$^{OEt}$)($H_2O$)]$^{-}$.

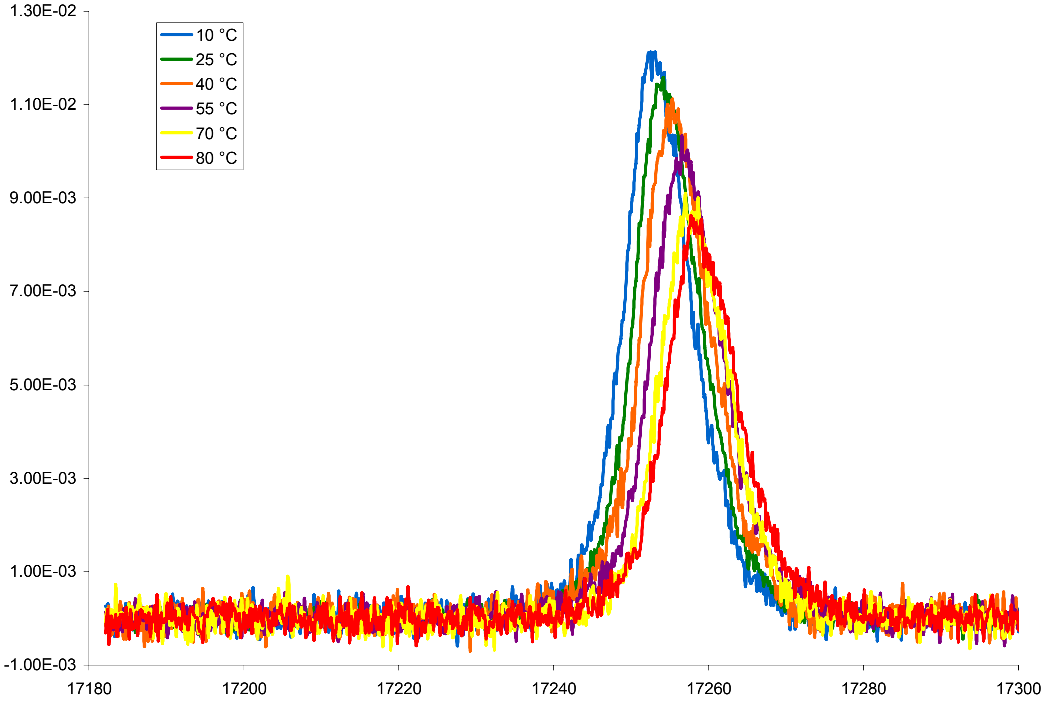


**Figure S10**: The contact contributions to the $^{17}$O LIS measurements of $[Ln(do3ap^{OEt})(H_2O)]^-$, measured at 9.4 T, 25 °C and pH 7.

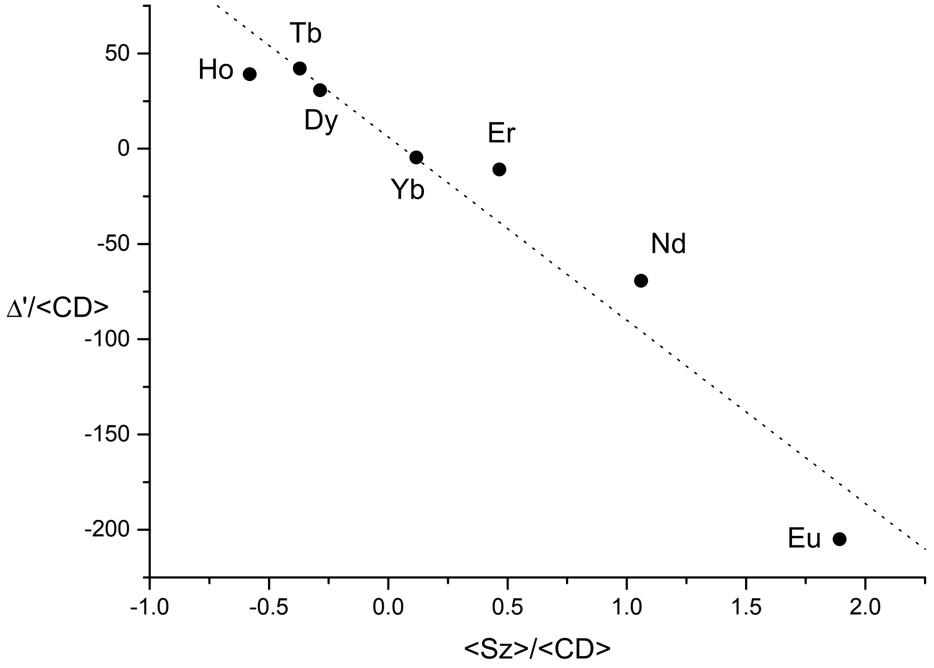
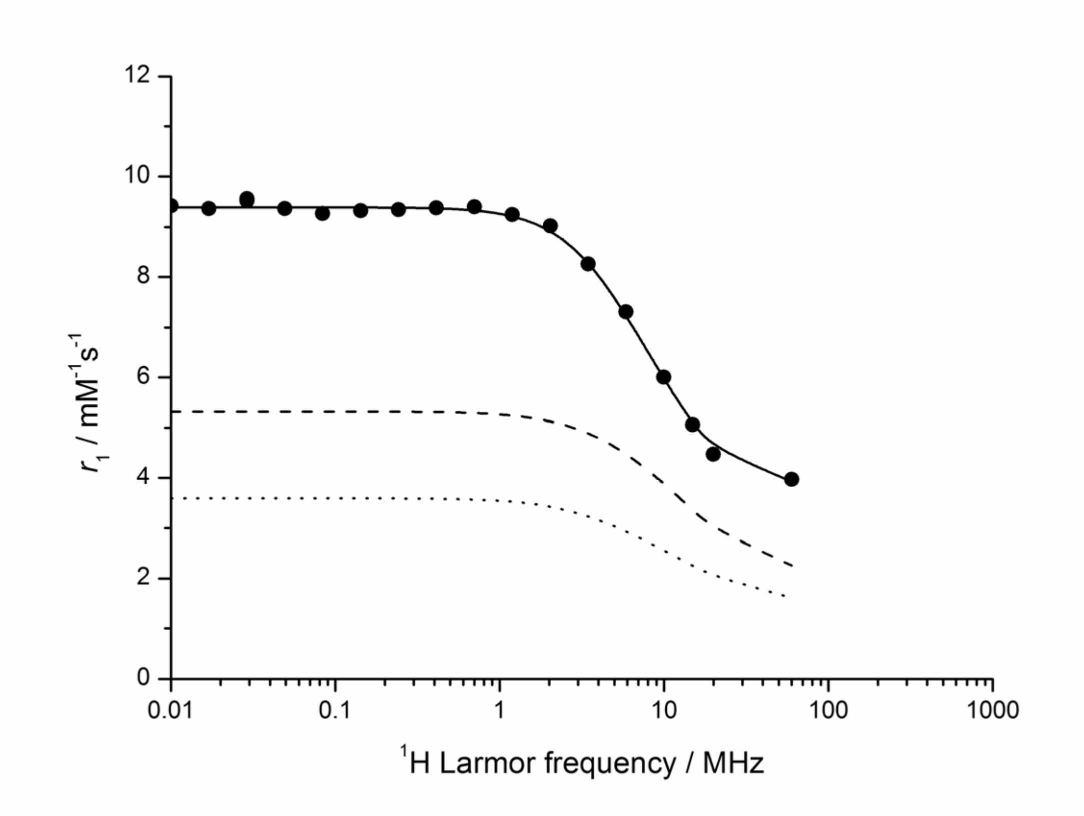


**Figure S11**: $^1$H NMRD profile of $[Gd(do3ap)(H_2O)]^{2-}$ complex recorded at 37 °C (●) with fitted line (full line) and calculated contributions from outer-sphere (dotted line) and second-sphere (dashed line) water.



**References for equations.**

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