Phosphinic derivative of DTPA conjugated to a G5 PAMAM dendrimer: an ^{17}O and ^{1}H relaxation study of its Gd(III) complex

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Supplementary information

Equations.

^{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 ω, and of the acidified water reference, $1/T_{1A}$, $1/T_{2A}$ and ω_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, 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]

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

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

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 γ_S is the electron and γ_I is the nuclear gyromagnetic ratio (γ_S = 1.76×1011 rad·s^{-1}·T^{-1}, γ_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), χ is the quadrupolar coupling constant and η is an asymmetry parameter:

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

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

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

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

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.

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

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

For slowly rotating species with internal degrees of freedom, the spectral density functions J are described the Lipari-Szabo approach.[3,4] In this model we distinguish two statistically independent motions; a rapid local motion with a correlation time τ_l and a slower global motion with a correlation time τ_g. Supposing the global molecular reorientation is isotropic, the relevant spectral density functions are expressed as in Eq. **[10]-[13]**, where the general order parameter S^2 describes the degree of spatial restriction of the local motion. If the local motion is isotropic, $S^2=0$; if the rotational dynamics is only governed by the global motion, $S^2=1$.

$$J\left(\omega;\tau_{di}\right)=\left(\frac{S^2\tau_{dig}}{1+\omega^2\tau_{dig}^2}+\frac{\left(1-S^2\right)\tau_{di}}{1+\omega^2\tau_{di}^2}\right) \qquad \textbf{[10]}$$

$$\frac{1}{\tau_{dig}}=\frac{1}{\tau_m}+\frac{1}{\tau_g}+\frac{1}{T_{ie}} \quad ; \quad \frac{1}{\tau_{di}}=\frac{1}{\tau_m}+\frac{1}{\tau^O}+\frac{1}{T_{ie}} \quad ; \quad i=1,2 \qquad \textbf{[11]}$$

$$\frac{1}{\tau^O}=\frac{1}{\tau_g}+\frac{1}{\tau_l^O} \qquad \textbf{[12]}$$

$$J_n\left(\omega\right)=\left(\frac{S^2\tau_g}{1+\left(n\omega\tau_g\right)^2}+\frac{\left(1-S^2\right)\tau^O}{1+\left(n\omega\tau^O\right)^2}\right) \qquad \textbf{[13]}$$

Second sphere contribution to ^{17}O relaxation:

$$\frac{1}{\mathrm{T}_1^{2nd}}\cong\frac{\mathrm{q}^{2nd}}{\mathrm{q}^{1st}}\frac{1}{\mathrm{T}_{1m}^{2nd}}=\frac{\mathrm{q}^{2nd}}{\mathrm{q}^{1st}}\left(\frac{1}{\mathrm{T}_{1dd}^{2nd}}+\frac{1}{\mathrm{T}_{1q}^{2nd}}\right) \qquad \textbf{[14]}$$

$$\frac{1}{\mathrm{T}_{1dd}^{2nd}}=\mathrm{C}_{dd}^{2nd,O}\left(\frac{3\tau_{d1}^{2nd,O}}{1+\left(\omega_I\tau_{d1}^{2nd,O}\right)^2}+\frac{7\tau_{d2}^{2nd,O}}{1+\left(\omega_S\tau_{d2}^{2nd,O}\right)^2}\right) \qquad \textbf{[15]}$$

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

$$\frac{1}{\mathrm{T}_{1q}^{2nd}}=\frac{3\pi^2}{10}\frac{2I+3}{I^2\left(2I-1\right)}\chi^2\left(1+\eta^2/3\right)\left(\frac{0.2\tau^{2nd,O}}{1+\left(\omega_I\tau^{2nd,O}\right)^2}+\frac{0.8\tau^{2nd,O}}{1+\left(2\omega_I\tau^{2nd,O}\right)^2}\right) \qquad \textbf{[16]}$$

$$\frac{1}{\tau^{O,2nd}}=\frac{1}{\tau_g}+\frac{1}{\tau_l^O}\cong\frac{1}{\tau_l^O} \qquad \textbf{[17]}$$

$$\frac{1}{\tau_{di}^{2nd,O}}=k_{ex}^{2nd}+\frac{1}{\tau^{O,2nd}}+\frac{1}{T_{ie}} \qquad \textbf{[18]}$$

^{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. **[19]**, where r_1 is the proton relaxivity:

$$R_1^{obs}=R_1^d+R_1^p=R_1^d+r_1\left[Gd^{3+}\right] \qquad \textbf{[19]}$$

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

$$r_1=r_{1is}+r_{1,2nd}+r_{1os} \qquad \textbf{[20]}$$

Inner sphere ^{1}H relaxation:

The inner sphere term is given in Eq. **[21]**, where q^{1st} is the number of inner sphere water molecules.[5]

$$r_{1is}=\frac{1}{1000}\times\frac{q^{1st}}{55.55}\times\frac{1}{T_{1m}^{H}+\tau_m} \qquad \textbf{[21]}$$

The longitudinal relaxation rate of inner sphere protons, $1/T_{1m}{}^{H}$ is expressed by Eq. **[22]**, where r_{GdH} is the effective distance between the electron charge and the ^{1}H nucleus, ω_I is the proton resonance frequency and ω_S is the Larmor frequency of the Gd(III) electron spin.

$$\frac{1}{T_{1m}^{H}}=\frac{2}{15}\left(\frac{\mu_0}{4\pi}\right)^2\frac{\hbar^2\gamma_I^2\gamma_S^2}{r_{GdH}^6}S(S+1)\left[3J(\omega_I;\tau_{d1})+7J(\omega_S;\tau_{d2})\right] \qquad \textbf{[22]}$$

$$J(\omega;\tau_{di})=\left(\frac{S^2\tau_{dig}}{1+\omega^2\tau_{dig}^2}+\frac{(1-S^2)\tau_{di}}{1+\omega^2\tau_{di}^2}\right);\quad i=1,2 \qquad \textbf{[23]}$$

$$\frac{1}{\tau_{dig}}=\frac{1}{\tau_m}+\frac{1}{\tau_g}+\frac{1}{T_{ie}}\;;\quad \frac{1}{\tau_{dig}}=\frac{1}{\tau_m}+\frac{1}{\tau^H}+\frac{1}{T_{ie}}\;;\quad i=1,2 \qquad \textbf{[24]}$$

$$\frac{1}{\tau^{\mathrm{H}}}=\frac{1}{\tau_{\mathrm{g}}}+\frac{1}{\tau_1^{\mathrm{H}}} \qquad \textbf{[25]}$$

The spectral density functions are given by Eq. **[23]**.

Second sphere ^{1}H relaxation:

$$r_1^{2nd}=\frac{1}{1000}\times\frac{q^{2nd}}{55.55}\times\frac{1}{T_{1dd}^{2nd,H}+\tau_m^{2nd}}\cong\frac{1}{1000}\times\frac{q^{2nd}}{55.55}\times\frac{1}{T_{1dd}^{2nd,H}} \qquad \textbf{[26]}$$

$$\frac{1}{T_{1dd}^{2nd,H}}=C_{dd}^{2nd,O}\left(\frac{3\tau_{d1}^{2nd,H}}{1+\left(\omega_I\tau_{d1}^{2nd,H}\right)^2}+\frac{7\tau_{d2}^{2nd,H}}{1+\left(\omega_S\tau_{d2}^{2nd,H}\right)^2}\right) \qquad \textbf{[27]}$$

$$C_{dd}^{2nd,H}=\frac{2}{15}\left(\frac{\mu_0}{4\pi}\right)^2\frac{h^2\gamma_{^1H}^2\gamma_S^2}{\left(r_{GdO}^{2nd}\right)^6}S(S+1) \qquad \textbf{[28]}$$

$$\frac{1}{\tau_{di}^{2nd,H}}=k_{ex}^{2nd}+\frac{1}{\tau^H}+\frac{1}{T_{ie}} \qquad \textbf{[29]}$$

$$\frac{1}{\tau^{\mathrm{H}}}=\frac{1}{\tau_{\mathrm{g}}}+\frac{1}{\tau_1^{\mathrm{H}}} \qquad \textbf{[30]}$$

Outer sphere ^{1}H relaxation:

The outer-sphere contribution can be described by Eq. **[31]** where N_{A} is the Avogadro constant, and J_{os} is its associated spectral density function.[6,7]

$$r_{1os}=\frac{32N_A\pi}{405}\left(\frac{\mu_0}{4\pi}\right)^2\frac{\hbar^2\gamma_S^2\gamma_I^2}{a_{GdH}D_{GdH}}S(S+1)\left[3J_{os}(\omega_I;T_{1e})+7J_{os}(\omega_S;T_{2e})\right] \qquad \textbf{[31]}$$

$$J_{os}(\omega,T_{je})=\mathrm{Re}\left[\frac{1+\frac{1}{4}\left(i\omega\tau_{GdH}+\frac{\tau_{GdH}}{Tje}\right)^{1/2}}{1+\left(i\omega\tau_{GdH}+\frac{\tau_{GdH}}{T_{je}}\right)^{1/2}+\frac{4}{9}\left(i\omega\tau_{GdH}+\frac{\tau_{GdH}}{T_{je}}\right)+\frac{1}{9}\left(i\omega\tau_{GdH}+\frac{\tau_{GdH}}{T_{je}}\right)^{3/2}}\right];\quad j=1,2 \qquad \textbf{[32]}$$

$$\tau_{GdH}=\frac{a_{GdH}^2}{D_{GdH}} \qquad \textbf{[33]}$$

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. **[34]-[35])**, where τ_V is the correlation time for the modulation of the zero-field-splitting interaction.

$$\left(\frac{1}{T_{1e}}\right)^{ZFS}=\frac{1}{25}\Delta^2\tau_v\left\{4S\left(S+1\right)-3\right\}\left(\frac{1}{1+\omega_S^2\tau_v^2}+\frac{4}{1+4\omega_S^2\tau_v^2}\right) \qquad \textbf{[34]}$$

$$\left(\frac{1}{T_{2e}}\right)^{ZFS}=\Delta^2\tau_v\left(\frac{5.26}{1+0.372\omega_S^2\tau_v^2}+\frac{7.18}{1+1.24\omega_S\tau_v}\right) \qquad \textbf{[35]}$$

Temperature dependences of water exchange rates and correlation times:

The exchange rates are supposed to follow the Eyring equation. In Eq. **[36]** $\Delta S^{\ddagger}$ 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. **[37]** $\Delta H^{\ddagger 2nd}$ 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.

$$k_{ex}=\frac{1}{\tau_m}=\frac{k_BT}{h}\exp\left\{\frac{\Delta S^{\ddagger}}{\mathrm{R}}-\frac{\Delta H^{\ddagger}}{RT}\right\}=\frac{k_{ex}^{298}T}{298.15}\exp\left\{\frac{\Delta H^{\ddagger}}{R}\left(\frac{1}{298.15}-\frac{1}{T}\right)\right\} \qquad \textbf{[36]}$$

$$k_{ex}^{2nd}=\frac{k_{ex}^{2nd,298}}{298.14}\exp\left\{\frac{\Delta H^{\ddagger 2nd}}{T}\left(\frac{1}{298.15}-\frac{1}{T}\right)\right\} \qquad \textbf{[37]}$$

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

$$\tau=\tau^{298}\exp\left\{\frac{E_a}{R}\left(\frac{1}{T}-\frac{1}{298.15}\right)\right\} \qquad \textbf{[38]}$$

$$D_{GdH}=D_{GdH}^{298}\exp\left\{\frac{E_{GdH}}{R}\left(\frac{1}{298.15}-\frac{1}{T}\right)\right\} \qquad \textbf{[39]}$$

Table S1: Proton relaxivities (r_1 / $mM^{-1}s^{-1}$) of G5-(Gd(DTTAP))$_{63}$, c(Gd^{III})=5.3 mM, pH=6.25, at variable temperature.

ν (^{1}H)/MHz	5°C	15°C	25°C	37°C	50°C
0.010	22.6	23.2	22.5	20.2	18.1
0.014	22.7	23.4	22.3	20.3	18.1
0.021	22.4	23.4	22.5	20.1	18.0
0.030	22.4	23.4	22.4	20.2	18.1
0.043	22. 5	23.4	22.4	20.3	18.1
0.062	22.5	23.3	22.5	20.3	18.0
0.089	22.5	23.3	22.5	20.1	18.0
0.127	22.5	23.3	22.3	20.1	17.9
0.183	22.4	23.2	22.3	20.1	17.9
0.264	22.3	23.2	22.2	20.1	17.8
0.379	22.0	22.8	21.9	19.8	17.5
0.546	21.8	22.4	21.6	19.4	17.2
0.784	21.1	21.8	21.0	18.8	16.7
1.13	20.6	21.3	20.4	18.2	16.2
1.62	19.9	20.5	19.6	17.7	15.6
2.34	19.1	19.9	18.8	16.7	15.0
3.36	18.5	19.0	18.0	16.2	14.4
4.83	17.9	18.8	17.3	15.6	13.7
6.95	17.5	19.0	17.2	15.5	13.4
10.0	21.4	22.2	21.5	18.8	16.4
11.5	22.8	-	23.0	20.0	17.7
12.0	-	23.9	-	-	-
13.2	23.8	-	24.7	21.6	18.9
13.6	-	24.9	-	-	-
15.2	25.1	-	26.5	23.5	20.3
15.5	-	26.4	-	-	-
17.4	26.0	-	28.3	25.2	22.2
17.6	-	27.6	-	-	-
20	27.6	28.8	30.4	26.8	23.5
30	26.0	29.4	30.6	28.5	24.1
40	24.7	27.9	28.9	27.3	23.5
60	20.6	22.4	23.0	22. 0	19.8
100	14.8	14.8	14.7	14.1	13.2
200	9.10	8.74	8.34	7.83	7.55

Table S2: Proton relaxivities (r_1 / $mM^{-1}s^{-1}$) of $[Gd(DTTAP\text{-}bz\text{-}NH_2)(H_2O)]^{2-}$, $c(Gd^{III})$=4.2 mM, pH=6.75, at variable temperature.

ν (^{1}H)/MHz	5°C	25°C	37°C	50°C
0.010	14.0	9.58	8.02	6.26
0.014	14.0	9.56	8.07	6.26
0.021	14.0	9.63	7.99	6.30
0.030	13.8	9.61	7.93	6.26
0.043	13.9	9.64	8.15	6.25
0.062	13.9	9.61	8.06	6.22
0.089	14.0	9.56	8.04	6.22
0.127	14.0	9.59	8.05	6.25
0.183	13.9	9.59	8.04	6.22
0.264	14.0	9.58	8.07	6.25
0.379	13.9	9.53	8.11	6.25
0.546	13.5	9.56	7.98	6.18
0.784	13.7	9.48	7.99	6.17
1.13	13.5	9.37	7.85	6.15
1.62	13.2	9.27	7.86	6.07
2.34	12.7	9.11	7.68	6.00
3.36	12.3	8.76	7.49	5.87
4.83	11.6	8.27	7.20	5.64
6.95	10.9	7.81	6.72	5.36
10.0	11.1	7.27	5.97	4.80
10.0	11.0	-	-	-
11.6	10.9	7.08	5.68	4.55
13.4	10.8	6.87	5.39	4.34
15.5	10.8	6.62	5.20	4.09
18	10.8	6.44	4.97	3.93
20	10.7	6.34	5.02	4.08
30	10.6	6.34	4.75	3.76
40	10.6	6.22	4.60	3.61
60	10.6	6.23	4.51	3.46
100	10.3	6.08	4.43	3.42
200	9.48	5.88	4.26	3.32
400	7.92	5.49	4.19	3.24

Table S3: Proton relaxivities (r_1 / mM^{-1}s^{-1}) of [Gd(DTTAP-bz-NO$_2$)(H$_2$O)]$^{2-}$, c(Gd^{III})=3.8 mM, pH=6.59, at variable temperature.

ν (^{1}H)/MHz	5°C	25°C	37°C	50°C
0.010	14.2	10.1	8.22	6.82
0.014	14.2	10.1	8.24	6.84
0.021	14.3	10.1	8.24	6.81
0.030	14.3	10.1	8.21	6.84
0.043	14.2	10.1	8.22	6.80
0.062	14.2	10.1	8.24	6.81
0.089	14.2	10.1	8.22	6.80
0.127	14.2	10.1	8.21	6.81
0.183	14.2	10.1	8.19	6.79
0.264	14.1	10.1	8.18	6.79
0.379	14.1	10.1	8.20	6.78
0.546	14.0	10.1	8.15	6.74
0.784	13.8	9.99	8.13	6.75
1.13	13.6	9.81	8.04	6.68
1.623	13.3	9.67	7.96	6.59
2.34	12.8	9.43	7.72	6.48
3.36	12.4	9.07	7.48	6.26
4.83	11.6	8.58	7.08	5.94
6.95	11.0	7.77	6.54	5.49
10.0	10.9	7.58	6.07	5.16
11.5	10.7	7.27	5.84	4.93
13.2	10.8	7.04	5.61	4.68
15.2	10.6	6.87	5.34	4.45
17.4	10.6	6.72	5.16	4.31
20	10.7	6.76	5.24	4.34
30	10.2	6.34	4.74	3.76
40	10.2	6.27	4.60	3.61
60	10.3	6.23	4.51	3.47
100	9.90	6.01	4.45	3.39
200	9.36	5.84	4.32	3.32
400	8.23	5.46	4.23	3.23

Table S4: Variable temperature reduced transverse and longitudinal ^{17}O relaxation rates of G5-(Gd(DTTAP))$_{63}$, c(Gd^{III})=39 mM, pH=5.69, P$_m$=7.95·10^{-4} at 9.4 T. Reference was G5-(Y(DTTAP))$_{63}$, c(Y^{III})=34 mM, pH=5.83.

t / °C	T / K	1000/T / K^{-1}	T_1 (Gd)/s	T_1 (Y)/s	T_2(Gd)/s	T_2(Y)/s	ln(1/T_{1r})	ln(1/T_{2r})
5.4	278.6	3.59	2.41E-03	2.80E-03	9.15E-04	2.00E-03	11.19	13.52
10.7	283.9	3.52	2.91E-03	3.39E-03	8.38E-04	2.47E-03	11.02	13.81
18.3	291.5	3.43	3.47E-03	4.31E-03	6.80E-04	3.24E-03	11.16	14.20
23.6	296.8	3.37	3.93E-03	5.02E-03	6.87E-04	3.92E-03	11.15	14.23
30.3	303.5	3.30	4.59E-03	6.11E-03	7.02E-04	5.00E-03	11.13	14.25
40.2	313.4	3.19	5.60E-03	7.83E-03	9.25E-04	6.77E-03	11.07	13.98
49.2	322.4	3.10	6.73E-03	9.62E-03	1.16E-03	8.62E-03	10.93	13.75
59.7	332.9	3.00	7.99E-03	1.19E-02	1.66E-03	1.10E-02	10.86	13.38
70.5	343.7	2.91	9.62E-03	1.47E-02	2.49E-03	1.40E-02	10.72	12.94
81.3	354.5	2.82	1.17E-02	1.78E-02	3.76E-03	1.71E-02	10.51	12.47

Table S5: Variable temperature reduced transverse and longitudinal ^{17}O relaxation rates of G5-(Gd(DTTAP))$_{63}$, c(Gd^{III})=39 mM, pH=5.69, P$_m$=7.95·10^{-4} at 4.7 T. Reference was G5-(Y(DTTAP))$_{63}$, c(Y^{III})=34 mM, pH=5.83.

t / °C	T / K	1000/T / K^{-1}	T_1 (Gd)/s	T_1 (Y)/s	T_2(Gd)/s	T_2(Y)/s	ln(1/T_{1r})	ln(1/T_{2r})
6.0	279.2	3.58	2.05E-03	2.68E-03	8.98E-04	1.93E-03	11.89	13.53
10.3	283.5	3.53	2.31E-03	3.14E-03	9.12E-04	2.30E-03	11.88	13.63
14.3	287.5	3.48	2.48E-03	3.52E-03	7.81E-04	2.67E-03	11.92	13.95
18.8	292.0	3.43	2.74E-03	4.11E-03	8.41E-04	3.13E-03	11.94	13.91
24.1	297.3	3.36	3.15E-03	4.88E-03	8.52E-04	3.83E-03	11.86	13.95
29.6	302.8	3.30	3.57E-03	5.64E-03	8.47E-04	4.58E-03	11.77	14.01
37.2	310.4	3.22	4.23E-03	6.94E-03	1.06E-03	5.90E-03	11.66	13.78
47.9	321.1	3.11	5.27E-03	8.86E-03	1.27E-03	7.90E-03	11.48	13.63
58.7	331.9	3.01	6.52E-03	1.14E-02	1.81E-03	1.05E-02	11.32	13.26
71.1	344.3	2.90	8.58E-03	1.45E-02	2.72E-03	1.35E-02	10.99	12.82
81.8	355.0	2.82	1.09E-02	1.74E-02	3.86E-03	1.68E-02	10.66	12.43

Table S6: Variable temperature reduced transverse and longitudinal ^{17}O relaxation rates of $[Gd(DTTAP\text{-}bz\text{-}NH_2)(H_2O)]^{2-}$, $c(Gd^{III})$=46 mM, pH=5.51, $P_m=8.19\cdot10^{-4}$ at 9.4 T. Reference was acidified H_2O, pH=3.3.

t / °C	T / K	1000/T / K^{-1}	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})
5.8	279.0	3.58	3.28E-03	3.99E-03	7.85E-04	4.02E-03	11.09	14.04
12.5	285.7	3.50	4.16E-03	5.02E-03	6.68E-04	5.00E-03	10.82	14.27
19.6	292.8	3.42	5.15E-03	6.17E-03	6.47E-04	6.26E-03	10.58	14.34
29.1	302.3	3.31	6.63E-03	7.95E-03	7.12E-04	7.95E-03	10.33	14.26
39.2	312.4	3.20	8.60E-03	1.02E-02	9.70E-04	1.03E-02	9.99	13.95
45.9	319.1	3.13	9.95E-03	1.16E-02	1.29E-03	1.16E-02	9.76	13.65
55.4	328.6	3.04	1.20E-02	1.39E-02	1.77E-03	1.39E-02	9.58	13.31
59.9	333.1	3.00	1.30E-02	1.51E-02	2.14E-03	1.50E-02	9.49	13.10
64.5	337.7	2.96	1.40E-02	1.64E-02	2.56E-03	1.63E-02	9.47	12.90
75.4	348.6	2.87	1.70E-02	1.95E-02	4.10E-03	1.94E-02	9.12	12.37
85.7	358.9	2.79	1.96E-02	2.25E-02	5.92E-03	2.25E-02	8.99	11.93

Table S7: Variable temperature reduced transverse and longitudinal ^{17}O relaxation rates of $[Gd(DTTAP\text{-}bz\text{-}NO_2)(H_2O)]^{2-}$, $c(Gd^{III})$=32 mM, pH=5.91, $P_m=5.73\cdot10^{-4}$ at 9.4 T. Reference was acidified H_2O, pH=3.3.

t / °C	T / K	1000/T / K^{-1}	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})
5.8	279.0	3.58	3.43E-03	3.99E-03	1.07E-03	4.02E-03	11.16	13.99
12.5	285.7	3.50	4.39E-03	5.02E-03	9.24E-04	5.00E-03	10.81	14.25
19.6	292.8	3.42	5.39E-03	6.17E-03	8.37E-04	6.26E-03	10.63	14.41
29.1	302.3	3.31	6.93E-03	7.95E-03	9.13E-04	7.95E-03	10.38	14.34
39.2	312.4	3.20	8.95E-03	1.02E-02	1.20E-03	1.03E-02	10.05	14.07
45.9	319.1	3.13	1.02E-02	1.16E-02	1.50E-03	1.16E-02	9.93	13.83
55.4	328.6	3.04	1.24E-02	1.39E-02	2.09E-03	1.39E-02	9.63	13.47
59.9	333.1	3.00	1.35E-02	1.51E-02	2.45E-03	1.50E-02	9.53	13.30
64.5	337.7	2.96	1.46E-02	1.64E-02	3.02E-03	1.63E-02	9.47	13.06
75.4	348.6	2.87	1.75E-02	1.95E-02	4.63E-03	1.94E-02	9.20	12.57
85.7	358.9	2.79	2.04E-02	2.25E-02	6.66E-03	2.25E-02	9.01	12.13

Table S8. Calculation of the number of chelating groups per dendrimer.

	G5-(Gd(DTTAP))$_{63}$
n = number of mols of chelate per gram of product obtained from complexometric titration	9.89×10^{-4}
Total percentage of C obtained from elemental analysis	48.9
Percentage of carbon in the chelate (DTTAP-bz-NCS = $C_{21}H_{29}N_4O_{10}S$) calculated from n	24.9
Percentage of carbon in PAMAM skeleton	48.9-24.9 = 24.0
Formula of PAMAM skeleton	G5-(NH$_2$)$_{128}$ $C_{1262}H_{2528}N_{506}O_{252}$
***x* = number of chelate bound on the dendrimer**	**63**
Percentage of substituted amino groups	49%
Total percentage of N calculated by using ***x***	16.6
Total percentage of N obtained by elemental analysis	17.3
Total percentage of S calculated by using ***x***	3.1
Total percentage of S obtained by elemental analysis	2.8
Total percentage of P calculated by using ***x***	3.0
Total percentage of P obtained by elemental analysis	2.7

Figure S1. Variable temperature reduced ^{17}O chemical shifts of $[Gd(DTTAP\text{-}bz\text{-}NO_2)(H_2O)]^{2-}$, c(Gd^{III})=32 mM, pH=5.91, $P_m=5.73\cdot10^{-4}$ at 9.4 T. Reference was acidified H_2O, pH=3.3.

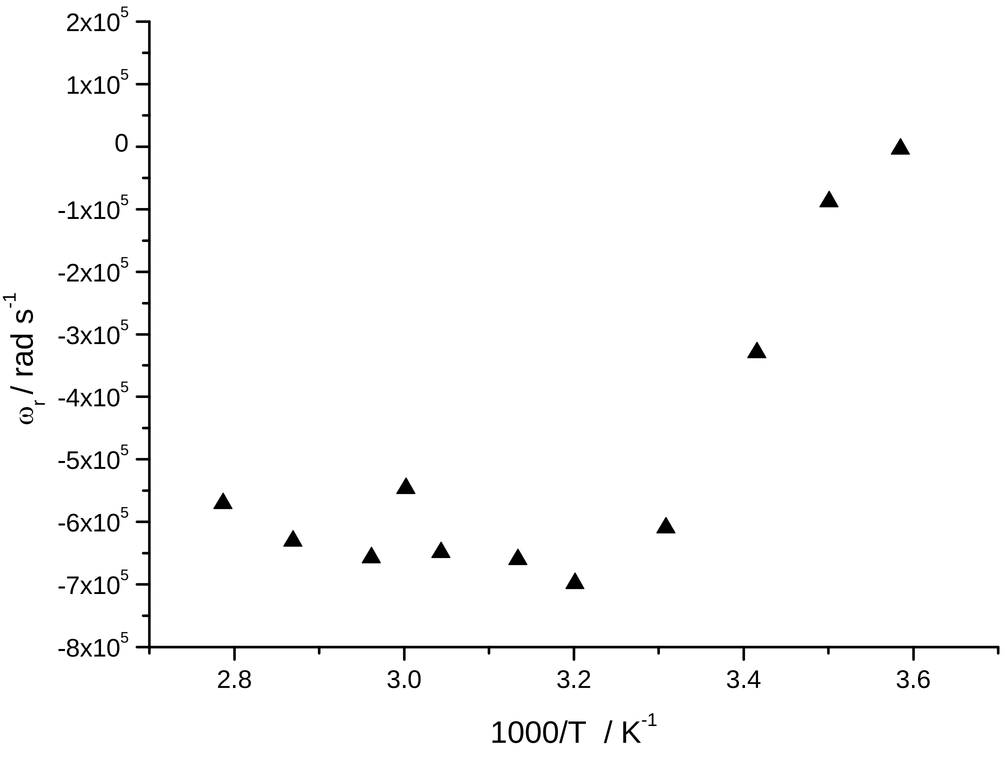

Figure S2. Variable temperature reduced ^{17}O chemical shifts of $[Gd(DTTAP\text{-}bz\text{-}NH_2)(H_2O)]^{2-}$, c(Gd^{III})=46 mM, pH=5.51, $P_m=8.19\cdot10^{-4}$ at 9.4 T. Reference was acidified H_2O, pH=3.3.

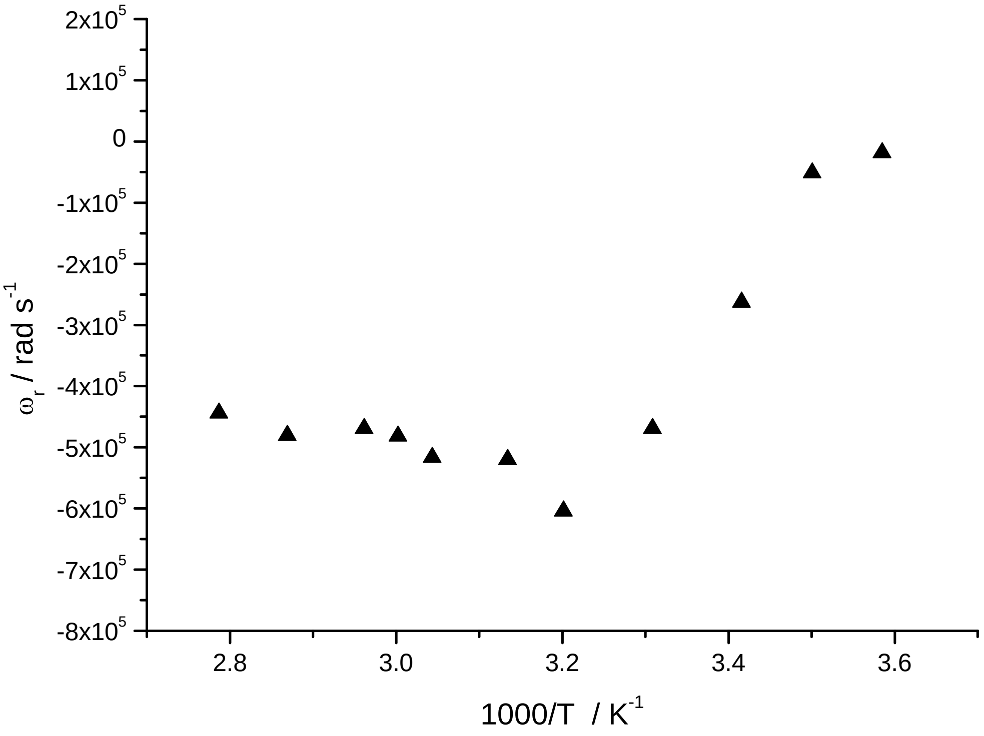

Figure S3. Variable temperature reduced ^{17}O chemical shifts of G5-(Gd(DTTAP))$_{63}$, c(Gd^{III})=39 mM, pH=5.69, $P_m=7.95\cdot10^{-4}$ at 4.7 T (○) and 9.4 T (▲). Reference was G5-(Y(DTTAP))$_{63}$, c(Y^{III})=34 mM, pH=5.83.

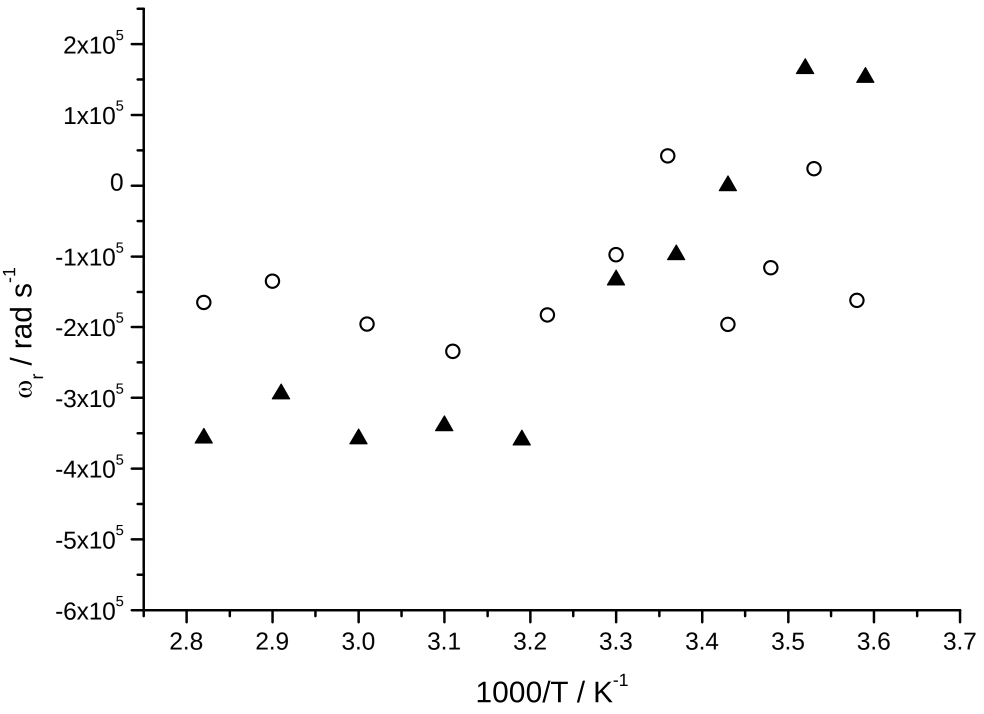

Table S9. Fitted parameters of G5-(Gd(DTTAP))$_{63}$. The underlined parameters were fixed during the fitting.

Parameter	G5-(Gd(DTTAP))$_{63}$
k_{ex}^{298} [10^6 s^{-1}]	5.0±0.2
$\Delta H^{\ddagger}$ [kJ mol^{-1}]	56.2±1.0
$\Delta S^{\ddagger}$ [J mol^{-1}K^{-1}]	+71.9±3
$A/\hbar$ [10^6 rad s^{-1}]	$\underline{-3.8}$
τ_{gO}^{298} [ps]	4417±340
E_{gO} [kJ mol^{-1}]	21±2
τ_{lO}^{298} [ps]	71±3
E_{lO} [kJ mol^{-1}]	21±2
S^2	0.28±0.01
τ_V^{298} [ps]	21±2
E_V [kJ mol^{-1}]	5.5±5.4
Δ^2[10^{20} s^{-2}]	0.62±0.11
δg_L^2 [10^{-2}]	1.7±0.1
r_{GdO} [Å]	$\underline{2.5}$
$r_{GdHouter}$ [Å]	$\underline{3.5}$
$\chi(1+\eta^2/3)^{1/2}$ [MHz]	$\underline{7.58}$
q	$\underline{1}$
q_{2nd}	$\underline{2}$
$\tau_M{}^{298}{}_{2nd}$ [ps]	$\underline{50}$
$\Delta H^{\ddagger}{}_{2nd}$ [kJ mol^{-1}]	$\underline{35.0}$
$r^{2nd}{}_{GdH}$ [Å]	$\underline{3.5}$
$r^{2nd}{}_{GdO}$ [Å]	$\underline{4.1}$

Table S10. Fitted parameters of [Gd(DTTAP-bz-NO_2)(H_2O)]$^{2-}$ and [Gd(DTTAP-bz-NH_2)(H_2O)]$^{2-}$. The underlined parameters were fixed during the fitting.

Parameter	[Gd(DTTAP-bz-NH_2)(H_2O)]$^{2-}$	[Gd(DTTAP-bz-NO_2)(H_2O)]$^{2-}$
k_{ex}^{298} [10^6 s^{-1}]	8.9±1.3	8.3±0.6
$\Delta H^{\ddagger}$ [kJ mol^{-1}]	48.1±3	48.5±2
$\Delta S^{\ddagger}$ [J $mol^{-1}K^{-1}$]	+49.8±10	+50.3±8
$A/\hbar$ [10^6 rad s^{-1}]	-3.8	-3.8
τ_{RO}^{298} [ps]	116±2	117±10
E_R [kJ mol^{-1}]	20.5±0.8	18±1
τ_V^{298} [ps]	28.2±0.5	26.3±0.4
E_V [kJ mol^{-1}]	1	1
Δ^2[10^{20} s^{-2}]	0.403±0.003	0.40±0.01
D^{298}_{GdH} [$10^{-10}m^2s^{-1}$]	25±2	25±2
E_{DGdH} [kJ mol^{-1}]	30±1	30±1
δg_L^2 [10^{-2}]	3.3±0.6	2.8±0.5
$\tau_{RH}^{298}/\ \tau_{RO}^{298}$	0.81±0.04	0.85±0.08
r_{GdO} [Å]	2.5	2.5
r_{GdH} [Å]	3.1	3.1
$r_{GdHouter}$ [Å]	3.5	3.5
$\chi(1+\eta^2/3)^{1/2}$ [MHz]	7.58	7.58
q	1	1
q_{2nd}	2	2
$\tau_M{}^{298}{}_{2nd}$ [ps]	50	50
$\Delta H^{\ddagger}_{2nd}$ [kJ mol^{-1}]	35.0	35.0
r^{2nd}_{GdH} [Å]	3.5	3.5
r^{2nd}_{GdO} [Å]	4.1	4.1

References for equations.

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