Electronic Supporting Information

Liposomes with conjugates of a calix[4]arene and a Gd-DOTA derivative on the outside surface; an efficient potential contrast agent for MRI

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General Remarks

All reagents and anhydrous solvents used during the synthesis were of commercial quality. 5,11,17,23-Tetra-\textit{tert}-butyl-25,27-dihydroxy-26,28-dipropoxy-calix[4]arene (2) and tris-1,4,7-\textit{tert}-butoxycarbonylmethyl-10-carboxymethyl-1,4,7,10-tetraazacyclo-dodecane were synthesised as described in the literature.\(^1\)\(^2\) For the formulation of the liposomes, cholesterol (Avanti polar Inc., Alabaster, AL, USA), DSPC (1,2-diestearoyl-sn-glycero-3-phosphocholine) and DSPE-PEG2000-OMe (1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N-methoxy(polyethyleneglycol)-2000\(\)) (Lipoid AG, Cham, Switzerland) were used without further purification.

Methods

DLS. Dynamic light scattering (DLS) was performed on a Zetasizer NanoZs, Malvern, UK instrument.

Cryo-TEM. A few microliters solution were placed on a quantifoil 3.5/1 holey carbon/coated grid (Quantifoil micro tools GmbH, Jena, Germany). The grids were automatically blotted and vitrified using the vitrobot (FEI, Eindhoven, The Netherlands). Frozen hydrated specimen were observed with a Gatan cryo-stage (Model 626, Gatan, Pleasanton, CA) in a Philips CM10 cryo/electron microscope (Philips, Eindhoven, The Netherlands) operating at 100 keV. Images were recorded under low-dose conditions with a slow scan CCD camera (Gatan, Pleasanton, CA).

NMR. The \(^1\)H NMRD profiles were recorded on a Stelar Smartracer FFC fast-field-cycling relaxometer covering magnetic fields from 2.35\(\times\)10\(^{-4}\) to 0.25 T, which corresponds to a proton Larmor frequency range of 0.01-10 MHz. The temperature was controlled by a VTC90 temperature control unit and fixed by a gas flow. The temperature was determined according to previous calibration with a Pt resistance temperature probe. The longitudinal relaxation times at 20 and 60 MHz were recorded on Bruker Minispec relaxometers (mq20 and mq60). All samples were kept in the probe for at least 10 minutes to equilibrate the temperature prior to the measurement.

HPLC-MS. Samples were analyzed using an Agilent 1200 series HPLC coupled with a XCT 6310 Ultra ion-trap mass spectrometer (Aglient, Santa Clara, CA). All runs were performed on an Agilent Eclipse XDB-C8 column, 150 \(\times\) 2.1 mm, 20 \(\mu\)L injection. Mobile phase A and B were 0.1 % formic acid in water and acetonitrile, respectively. The first 3 minutes were run at 20 % B, then a gradient was initiated to 95 % B in 10 min, followed by a wash out at 95 % B for 7 min. The flow rate was 0.3 mL/min. UV was detected at 254 nm.

Determination of the Gd concentration. Equal volumes of samples (500 \(\mu\)L) and nitric acid were mixed and digested in a microwave oven (Milestone, Analis, Namur, Belgium) and the volume was adjusted to 5 mL with distilled water. The samples were then analyzed by ICP (Jobin Yvon JY38 Plus, Longjumeau, France).

Computations. Least-squares fit and simulations of the \(^1\)H NMRD data were performed by the MicroMath program Scientist version 2.0 (MicroMath Scientific Software, Salt Lake City, Utah, USA).

SEC. Size exclusion chromatography was performed on a Waters Ultrahydrogel 1000 column at a flow of 0.6 ml/min and 25 \(^\circ\)C. Elution was achieved in the standard HEPES buffer. The fractions were detected at 254 nm.

Synthesis

Scheme S1. i) \(\text{C}_{18}\text{H}_{37}\)-Br, NaH, DMF, 24 h, rt, 48% ii) HNO\(_3\), HOAc, DCM, 2.5 h, rt, 96%, iii) \(\text{NaH}_{2}\text{O}\), Raney-Ni, THF/MeOH, 2 h, reflux, 86%, iv) \(\text{tert}-\text{butyl-DOTA-monoacid, EDC, HOBr, DMF, 9 d, rt, 66%}\), v) TFA/DCM 50:50, overnight, rt, vi) GdCl\(_3\).6\(\times\)2H\(_2\)O, 64% over 2 steps.
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A suspension of 5,11,17,23-tetra(tert-butyl)-25,27-dihydroxy-26,28-dipropoxy-calix[4]arene (2) (1.00 g, 1.36 mmol) and NaH (0.82 g, 20.5 mmol, 60% in mineral oil) in DMF (20 ml) was stirred for 30 min at rt and 1-bromo-octadecane (1.00 g, 2.99 mmol) was added. After 24 h, 2 M HCl was carefully added until no further precipitation occurred. The product was extracted with CHCl₃ and the aqueous phase washed with CHCl₃. The organic phases were combined, dried over Na₂SO₄ and then the solvent was removed. The residue was treated with MeOH and the crude product was filtered off. The pure product (0.80 g, 0.65 mmol, 48%) was obtained by column chromatography (silica gel, hexane).

3¹H NMR (400 MHz, CDCl₃, 25 °C, TMS): δ = 0.88 (6 H, t, J = 7.1 Hz, CH₃), 0.99 (6 H, t, J = 7.6 Hz, CH₂), 1.08 (36 H, s, tert-Bu), 1.26 – 1.38 (60 H, m, CH₂CH₂CH₂CH₂CH₂), 1.98 – 2.08 (8 H, m, OCH₂CH₂), 3.10 (4 H, d, J = 12.5 Hz, ArCH₂Ar), 3.81 (4 H, t, J = 7.6 Hz, OCH₂CH₂), 3.84 (4 H, t, J = 7.6 Hz, OCH₂CH₂), 4.41 (4 H, d, J = 12.5 Hz, ArCH₂Ar), 6.77 (8 H, s, Ar-H). ¹³C NMR (100 MHz, CDCl₃, 25 °C): δ = 10.36, 14.13 (OCH₂CH₂CH₂), 22.70, 23.34, 26.26, 29.37, 29.67, 29.72, 29.76, 29.91, 30.27, 31.07 (CH₂CH₂CH₂, CH₂CH₂CH₃), 31.46 (Ar-CH₂Ar), 31.94, 33.79 (CH₂CH₂CH₂), 75.38, 77.97 (OCH₂CH₂), 124.84, 133.84, 144.09, 153.72, 1543.76 (Ar-C). IR (KBr) ν (cm⁻¹): 2960 (s), 2921 (s), 2851 (s) of CH₂. Elem. analysis: calc.: C, 70.20%; H, 8.93%; N, 4.68%. MS (MALDI, DHB): calc.: m/z = 1237.1 (C₆H₁₂O₂M+H)⁺, found: 1237.1. mp: 62 – 63 °C.


To a solution of 5,11,17,23-tetra-(tert-butyl)-25,27-dioxo-26,28-dipropoxy-calix[4]arene (4) (2.01 g, 1.62 mmol) in DCM (17.5 ml) and glacial acetic acid (17.5 ml) was added fuming nitric acid (5.8 ml) at 0 ºC. The violet solution was stirred for 2.5 h at room temperature until it turned orange. Water was added, the phases separated and the aqeous layer was extracted twice with DCM. The combined organic phases were washed with water and dried over Na₂SO₄. After evaporation of the solvent, the remaining oil was treated with MeOH in an ultrasonic bath and the MeOH was decanted. This procedure was repeated once and the remaining oil was dried in vacuo for 3 h to yield 5a (1.86 g, 1.56 mmol, 96% mmol). An analytically pure sample could be obtained by column chromatography (silica gel, DCM/MeOH 50:1).

5.11.17.23-Tetra(n-butyryloxy)carbomethyl-1,4,7,10-tetrazacyclododec-1-yl-acetamidyl)-25,27-dioxo-26,28-dipropoxy-calix[4]arene (4b) (1.18 g, 0.99 mmol) and N₂H₄·H₂O (5.6 ml) in THF (40 ml) and MeOH (20 ml), Raney nick el was added and the suspensi on stirred at reflux for two hours. The hot mixture was filtered over celite and allowed to cool to rt. DCM and 1 M NaOH were added and the phases separated. The organic phase was dried over Na₂SO₄. After evaporation of the solvent the solid was dried in vacuo for 3 h to yield 5b (0.92 g, 0.85 mmol, 86% mmol).

5.11.17.23-Tetra(4,7,10-tert-butoxy carbonylmethyl)-1,4,7,10-tetrazacyclododec-1-yl-acetamidyl)-25,27-dioxo-26,28-dipropoxy-calix[4]arene (4c)

Under inert atmosphere, a suspension of tris-4,7,10-tert-butoxy carbonylmethyl-1,4,7,10-tetrazacyclododecane (1.55 g, 2.71 mmol), DIPEA (30 mg, 0.21 mmol) and EDC (520 mg, 2.71 mmol) in DMF (20 ml) was stirred for 0.5 h at ambient temperature. A solution of 5,11,17,23-tetramino-25,27-dioxidotetraacetic acid (350 mg, 0.326 mmol) in DCM (5 ml) was added. After 2 d stirring at rt, another portion of tris-4,7,10-tert-butoxy carbonylmethyl-1,4,7,10-tetrazacyclododecane (388 mg, 678 µmol) was activated with HOBT (93 mg, 0.68 mmol), EDC (130 mg, 0.68 mmol) and DIPEA (0.33 ml) in DMF, and added to the mixture. After 3 d, EDC (0.50 g, 2.61 mmol) and DIPEA were added and the reaction was continued for another 4 d. Thereafter, the solvent was removed in high vacuo, and the residue purified by ultrafiltration using a membrane with a cut-off of 1 kDa. The solvent was changed from a 0.05 M NH₄HCOO buffer in MeOH to pure MeOH. After evaporation of the solvent, the residue was freeze-dried from benzene to yield a slightly brown powder of the conjugate (710 mg, 216 µmol, 66%). No 1³C-NMR data could be obtained because the compound decomposes during the long measurements.
1H NMR (400 MHz, dmso-d6, 100 °C, TMS): δ = 0.88 (6 H, t, J = 6.4 Hz, CH₃), 0.98 (6 H, t, J = 7.2 Hz, CH₃), 1.28 (60 H, CH₂CH₂CH₃), 1.42, 1.47 (108 H, 2 s, tert-Bu), 1.81 – 1.87 (8 H, m, OCH₂CH₃), 2.26 – 2.97 (64 H, m, N-CH₂CH₂), 3.04 (4 H, d, J = 13.2 Hz, ArCH₂Ar), 3.16, 3.18 (32 H, 2 s, N-CH₂-CO), 3.80 (4 H, t, J = 7.2 Hz, OCH₂CH₃), 3.88 (4 H, d, J = 13.2 Hz, ArCH₂Ar), 4.38 (4 H, t, J = 6.8 Hz, OCH₂CH₃), 4.40 (4 H, d, J = 12.6 Hz, ArCH₂Ar), 6.97 (4 H, br. s, Ar-H), 7.12 (4 H, br. s, Ar-H), 9.66 (2 H, br. s, NH), 9.77 (2 H, br. s, NH). ESI-MS: calc.: m/z = 809.3 (C₁₈₂H₃₁₂N₂O₃₂+4H-tBu)⁴⁺, found: 809.8.


5,11,17,23-Tetrakis(tris-4,7,10-tert-butoxycarbonylmethyl-1,4,7,10-tetrazacyclododec-1-yl-acetamidyl)-25,27-dioctadecoxy-26,28-dipropoxy-calix[4]arene (500 mg, 155 μmol) was dissolved in DCM/TFA 50:50 (20 ml) and stirred overnight. After the liquids were removed, the crude product was lyophilized from water to yield the title compound as its TFA salt (556 mg). The compound was not purified further since the TFA as well as inorganic impurities can easily be removed after complexation by ultrafiltration. The NMR spectra were recorded in the presence of pyridine in order to obtain better spectra.

1H NMR (400 MHz, dmso-d6, 100 °C, TMS): δ = 0.90 (6 H, t, J = 7.5 Hz, CH₃), 0.99 (6 H, t, J = 7.5 Hz, CH₃), 1.26 - 1.48 (60 H, CH₂CH₂CH₃), 1.89 (8 H, sext, J = 7.2 Hz, OCH₂CH₃), 2.93 – 3.16 (64 H, m, N-CH₂CH₂), 4 H, ArCH₂Ar), 3.59- 3.67 (32 H, br s, N-CH₂-CO), 3.81 (4 H, d, J = 12.6 Hz, ArCH₂Ar), 4.40 (4 H, d, J = 12.6 Hz, ArCH₂Ar), 6.97 (4 H, br. s, Ar-H), 7.12 (4 H, br. s, Ar-H), 9.66 (2 H, br. s, NH), 9.77 (2 H, br. s, NH). ESI-MS: calc.: m/z = 657.4 (C₁₃₄H₂₁₆N₂O₃₂+4H)⁴⁺, found: 657.4.


5,11,17,23-Tetrakis(tris-4,7,10-tert-butoxycarbonylmethyl-1,4,7,10-tetrazacyclododec-1-yl-acetamidyl)-25,27-dioctadecoxy-26,28-dipropoxy-calix[4]arene (500 mg) as obtained above was dissolved in water and GdCl₃·6H₂O (326 mg, 860 μmol) was added in small portions. After each addition, the pH was adjusted to 4 to 4.5 using aqueous NaOH during which a solid precipitated. As soon as this solid was dissolved again, a new portion of GdCl₃·6H₂O was added and the procedure repeated. After complete addition, the solution was stirred overnight. The Gd(III)-complex was purified by ultrafiltration (1 kDa membrane, solvent: water) and obtained after lyophilisation as a white powder (296 mg, 64% yield). ESI-MS: calc.: m/z = 1641.10 (C₁₃₄H₂₀₄Gd₄N₂O₃₂+2Na)⁴⁺, found: 1640.80.

Figure S1. HPLC-MS analysis of 5,11,17,23-Tetrakis(tris-4,7,10-tert-butoxycarbonylmethyl-1,4,7,10-tetrazacyclododec-1-yl-acetamidyl)-25,27-dioctadecoxy-26,28-dipropoxy-calix[4]arene: a) HPLC-UV detection, b) HPLC-EIC detection c) MS for the area from 12 to 14.5 min shows (M+3H)³⁺ peak at 1098.2, (M+4H)⁴⁺ at 823.8, (M+4H-tBu)⁴⁺ at 809.8 and (M+4H-2tBu)⁴⁺ at 795.9.
Figure S2. HPLC-MS analysis of 5,11,17,23-Tetrakis(tris-4,7,10-carboxymethyl-1,4,7,10-tetrazacyclododec-1-yl-acetamidyl)-25,27-dioctadecoxy-26,28-dipropoxy-calix[4]arene: a) HPLC-UV detection, b) HPLC-EIC detection c) The major peak of UV trace shows four times charged parent ion at 657.4 plus its sodium adduct.

Preparation of liposomes

a) Addition of 1 during the extrusion. DSPC (104 mg, 132 μmol), DSPE-PEG2000-OMe (38.54, 14 μmol), and cholesterol (33.36 mg, 86.3 μmol) were dissolved in chloroform (6 ml). After evaporation of the solvent, the film was resuspended in HEPES buffer (6 ml). Calixarene 1 (36.3 mg, 11.2 μmol) was dissolved in 3 ml of this suspension, the mixture was initially extruded at 65 °C first through a 200 nm filter (13 times) and then through a 100 nm filter (13 times). Then the temperature of the extrusion was optimized to minimize the amount of bicelles formed. This was achieved for an extrusion temperature of 85°C. The loading efficiency of 1 was 100%.

b) Addition of 1 prior to the lipidic film preparation. DSPC, DSPE-PEG2000-OMe, cholesterol and 1 were dissolved in a mixture of chloroform (2 ml) and methanol (2 ml). Two formulations were prepared with a total amount of compounds of 50 μmol and with the following ratios: DSPC/DSPE-PEG2000-OMe/cholesterol/1 2.42/0.2/1.32/0.06 (containing 1.5 mol% 1) and a second formulation: 2.28/0.2/1.32/0.2 (containing 5 mol% 1). The solutions were vacuum-dried to get a thin lipidic film. The film was then hydrated and broken with a HEPES/NaCl buffer (10 mM, 135 mM NaCl, pH=7.4), resulting in a suspension of multi-lamellar layers of lipids. This mixture was extruded through polycarbonate membrane filters with a porosity of 200 nm (10 times) and 100 nm (10 times), using a Lipofast extruder (Avestin, Canada). The temperature during the extrusion was set at 55°C.
Characterization of liposomes

All liposomes prepared had an average hydrodynamic diameter of about 100 nm as determined by DLS.

**Figure S3.** (A) Liposomes with 0 mol% of 1 (blank); (B) 5 mol% 1 present during the lipid film preparation (method b); (C) 8.8 mol% 1 present during the extrusions at (method a).

**Figure S4.** Characterisation of the liposome formulation with 8.8 mol% 1 present during the extrusion at 85 °C: DLS spectra at 25 °C (top left), DSC heating trace of a blank liposome formulation (solid line) and of the liposomes (dashed line, top right), cryo-TEM (down left) and SEC (down right).

In the blank sample A, unilamellar vesicles are visible along with a small amount of disk-like micelles (bicelles). If 1 is present during the lipid film preparation (method b), a high content of bicelles as well as some multilamellar vesicles are formed (B). The preparation of liposomes following method a leads to good inclusion and a minor formation of aggregates other than liposomes. Therefore, this procedure was optimized. Liposomes finally obtained in this way were characterized as depicted in Figure S4.
Permeability measurements

The water permeability of the liposomal membranes was determined following a method described by Terreno and co-workers. Equation 1 was used for the determination of the water permeability, $P_w$. Gd-HPDO3A was removed by ultra-centrifugation for 1 h at 4°C (Beckman L7, rotor 50Ti, 40Krpm, 266000 g). The pellet was separated from the supernatant, resuspended in 10 ml buffer and the centrifugation repeated.

$$P_w = \frac{1000 \cdot d_{inner} \cdot r_1^{overall} \cdot r_1^{inner} \cdot [Gd]^{inner}}{6(r_1^{inner} - r_1^{overall})}$$

$d_{inner}$ is the inner diameter of the liposomes as determined by DLS assuming a thickness of the bilayer of 5 nm, $r_1^{overall}$ is the relaxivity of Gd-HPDO3A in the liposomes, $r_1^{inner}$ is the relaxivity of Gd-HPDO3A in pure buffer and $[Gd]^{inner}$ the Gd concentration inside the liposomes (equals the Gd concentration of the solution that is used to hydrate the lipid film).

Calculations of the relaxivities of liposomal systems

Model applied. The relaxation rates of the liposomal systems were evaluated with a two-step model that considers the system as an aqueous solution of Gd-chelates with water molecules that exchange with the bulk water outside the liposomes. The relaxivity of the whole system, assuming that free exchange of water between the interior and the exterior of the liposomes were possible, $r_1^{overall}$, was calculated with the set of commonly used equations to evaluate NMRD profiles. To take into account local motions, the Lipari-Szabo approach was followed. Then, if the membrane is limiting the relaxivity, the overall relaxivity of the system can be given by eqs 2 and 3.

$$r_{1,in} = \frac{f_{in} \cdot r_1}{v_{in}}$$

$$r_{1,out} = (1 - f_{in}) \cdot r_1$$

Here, $r_{1,in}$ and $r_{1,out}$ are the contributions of the in- and outside water to the relaxivity, respectively, $f_{in}$ is the fraction of chelates that is inside the cavities of the liposomes, and $v_{in}$ is the volume fraction of the water that is inside the liposomes ($v_1 << 1$). Then the overall relaxivity $r_1$ of the system is given by:

$$r_1 = r_{1,overall} + \frac{v_{in}}{(1 - f_{in}) + \tau_{lip}}$$

where $\tau_{lip}$ is the residence time of water in the interior of the liposomes.

Results of simulations of the relaxivity as function of $f_{in}$. These simulations were performed with a set of parameters estimated based on the results of a previously studied low molecular weight calix[4]arene-Gd-DOTA conjugate (see Table S1). The calculated curve of $r_1$ as a function of $f_{in}$ is displayed in Fig. S3.

Table S1. Values of parameters used in the simulations of the relaxivity as function of $f_{in}^a$ 

<table>
<thead>
<tr>
<th>parameter</th>
<th>value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\tau_2^{298}$ (μs)</td>
<td>1.0</td>
</tr>
<tr>
<td>$\Delta H$ (kJ mol$^{-1}$)</td>
<td>17.7</td>
</tr>
<tr>
<td>$\tau_1^{298}$ (ms)</td>
<td>0.906</td>
</tr>
<tr>
<td>$\tau_2^{298}$ (ns)</td>
<td>4.3</td>
</tr>
<tr>
<td>$E_1$ (kJ mol$^{-1}$)</td>
<td>8.58</td>
</tr>
<tr>
<td>$E_2$ (kJ mol$^{-1}$)</td>
<td>8.58</td>
</tr>
<tr>
<td>$S_2$</td>
<td>0.25</td>
</tr>
<tr>
<td>$\tau_2^{298}$ (ps)</td>
<td>41.5</td>
</tr>
<tr>
<td>$E_1$ (kJ mol$^{-1}$)</td>
<td>1</td>
</tr>
<tr>
<td>$\Delta$ (10$^{-6}$ s$^{-1}$)</td>
<td>1.06</td>
</tr>
<tr>
<td>$\delta Gd$</td>
<td>0.021</td>
</tr>
<tr>
<td>$D_{Gd}^{298}$ (10$^{-9}$ m$^2$ s$^{-1}$)</td>
<td>2.0</td>
</tr>
<tr>
<td>$E_{DGdH}$ (kJ mol$^{-1}$)</td>
<td>22</td>
</tr>
</tbody>
</table>

$^a$v$_{in}$ = 0.059 as estimated from the volume and the concentration of the liposomes, Larmor frequency = 0.01 MHz.
Meaning of symbols: \( \tau^{298}_M \), residence time of water in first coordination sphere of Gd(III) at 298 K; \( \Delta H \), the enthalpy of activation of the corresponding water exchange process; \( \tau^{298}_g \), the global rotational correlation time at 298 K in the Lipari-Szabo approach; \( E_g \), the corresponding activation energy; \( \tau^{298}_l \), the global rotational correlation time at 298 K in the Lipari-Szabo approach; \( E_l \), the corresponding activation energy; \( S^2 \), order parameter in the Lipari-Szabo approach, \( S^2=1 \) for perfectly rigid compounds and 0 for fully flexible compounds; \( \tau^{298}_v \), is the correlation time for the modulation of the zero field splitting (ZFS); \( \Delta^2 \), the trace of the square of the ZFS tensor; \( \delta_{Gd} \), a factor involved in a correction for the spin rotation; \( D^{298}_{Gd} \), the diffusion coefficient for water at 298 K; \( E_{DGdH} \), the corresponding activation energy.

Estimated from the Debye-Stokes-Einstein equation from the radius of the liposomes.

**Figure S5.** The relaxivity as a function of the fraction of the chelates that are in the interior of the liposomes, as calculated with eqs 2-4; • 25 °C, ■ 55 °C, other parameters see Table S1.

**Best-fit parameters of NMRD profiles of liposomes 1.** The fits were performed with the model described above, assuming that \( f_{in} = 0 \). The results are compiled in Table S2. For comparison, the best-fit parameters of the previously reported NMRD profiles of the corresponding tetrapropyl derivative in the monomeric (5) are included.  

**Table S2.** Best-fit parameters of NMRD profiles of liposomes 1; see Fig. 2 (main text), comparison with best fit parameters of the corresponding tetrapropyl derivative in the monomeric form (5). Underlined values were fixed during the fitting procedure.

<table>
<thead>
<tr>
<th></th>
<th>8% included in liposomes</th>
<th>1</th>
<th>5²</th>
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</thead>
<tbody>
<tr>
<td>( \tau^{298}_M ) (μs)</td>
<td>1.05 ± 0.03</td>
<td>1.28</td>
<td></td>
</tr>
<tr>
<td>( \Delta H ) (kJ mol⁻¹)</td>
<td>25.2</td>
<td>17.7</td>
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<tr>
<td>( \tau^{298}_g ) (ms)</td>
<td>0.906 ± 0.001 b</td>
<td>0.39×10⁻⁶</td>
<td></td>
</tr>
<tr>
<td>( \tau^{298}_l ) (ns)</td>
<td>3.5 ± 0.3</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>( E_g ) (kJ mol⁻¹)</td>
<td>25.4</td>
<td>8.58</td>
<td></td>
</tr>
<tr>
<td>( E_l ) (kJ mol⁻¹)</td>
<td>25.4</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>( S^2 )</td>
<td>0.22 ± 0.03</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>( \tau^{298}_v ) (ps)</td>
<td>51.3 ± 1.0</td>
<td>45.9</td>
<td></td>
</tr>
<tr>
<td>( \Delta^2 ) (10⁻⁹ s⁻²)</td>
<td>0.8 ± 0.2</td>
<td>1.07</td>
<td></td>
</tr>
<tr>
<td>( \delta_{Gd} )</td>
<td>1.0 ± 0.2</td>
<td>0.021</td>
<td></td>
</tr>
<tr>
<td>( D^{298}_{GdH} ) (10⁻⁹ m² s⁻¹)</td>
<td>2.0</td>
<td>2.0</td>
<td></td>
</tr>
<tr>
<td>( E_{DGdH} ) (kJ mol⁻¹)</td>
<td>22</td>
<td>22</td>
<td></td>
</tr>
</tbody>
</table>

Ref. 6

Value calculated for 100 nm spheres using the Debye-Stokes-Einstein equation.
Supplementary Material (ESI) for Chemical Communications
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References