Electronic Supplementary Information (ESI)

for

Relaxometric and solution NMR structural studies on ditopic lanthanide(III) complexes of a phosphinate analogue of DOTA with a fast rate of water exchange

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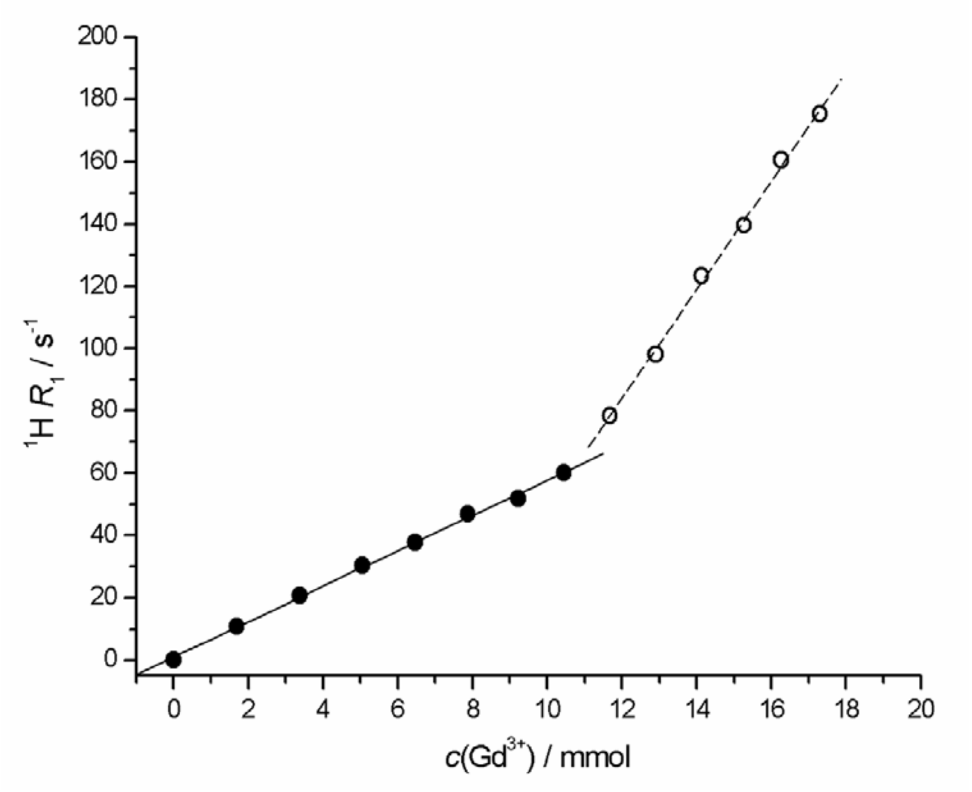


Figure S1. Relaxometric titration of a 5 mM solution of CS(DO3A-$P^{NBn})_2$ with $GdCl_3$. The change in the slope of the curve corresponds to the ratio Gd/L 2:1. The solid line is result of a least-square linear fitting and determines the relaxivity of the $[Gd_2(CS(DO3AP^{NBn})_2)(H_2O)_2]^{2-}$ complex at 400 MHz and 298 K: $^{298}r_1 = 5.67$ s^{-1} mM^{-1}.

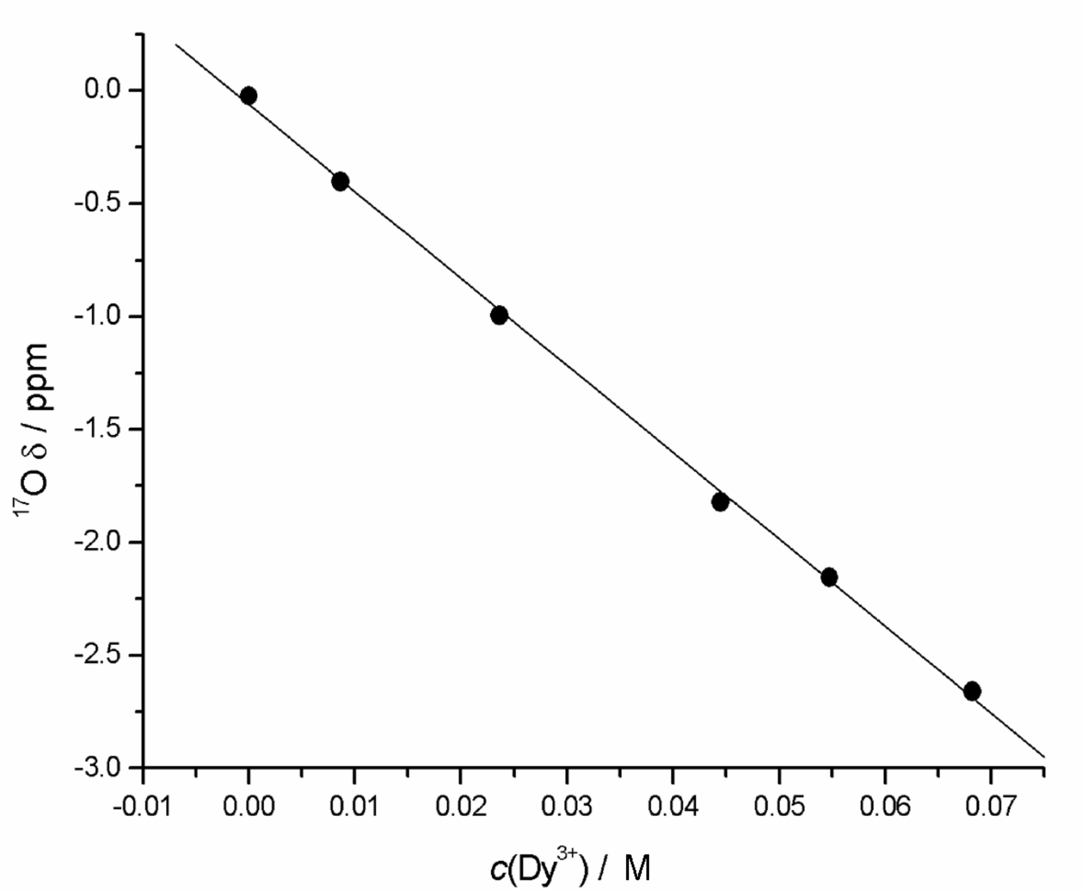


Figure S2. The measurement of the dysprosium-induced ^{17}O chemical shifts during the titration of a solution of CS(DO3A-P^{NBn})$_2$ with $DyCl_3$. The slope of the line is –38.5 ppm M^{-1}. It corresponds to the presence of a single water molecule in the first coordination sphere of the dysprosium(III) complex.

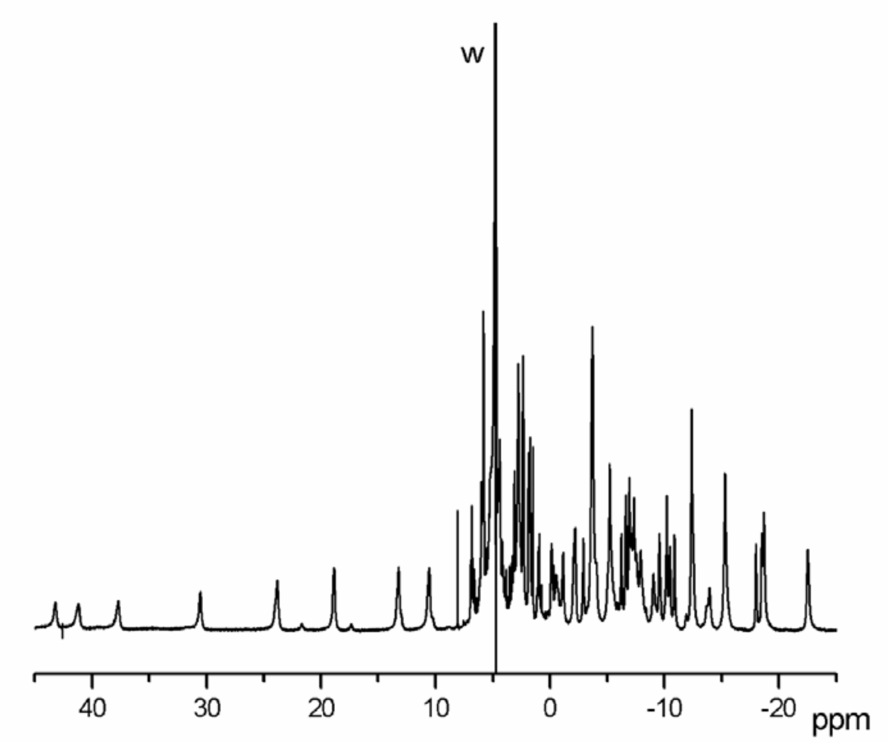


Figure S3. ^{1}H NMR spectrum of the $[Eu_2(CS(DO3A\text{-}PNBn)_2)(H_2O)_2]^{2-}$ complex at 400 MHz and 273 K.

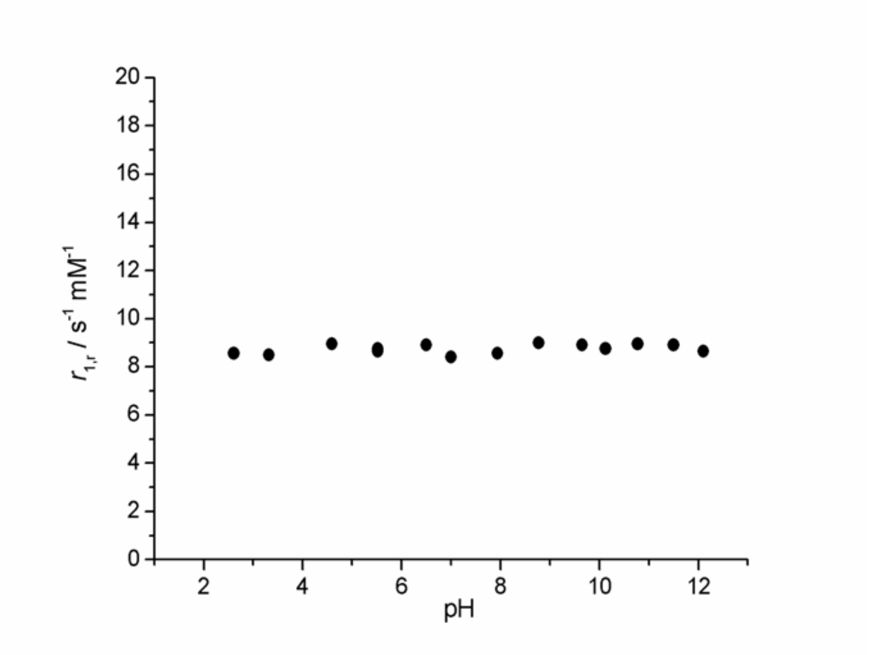


Figure S4 The relaxivity of the $[GdY(CS(DO3A\text{-}P^{NBn})_2)(H_2O)_2]^{2-}$ complex as a function of pH at 20 MHz and 25 °C.

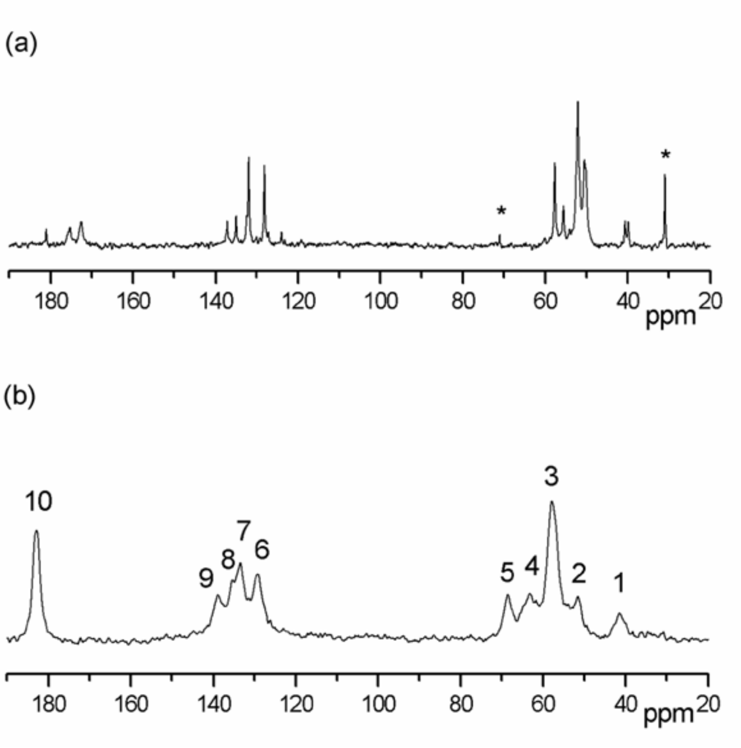
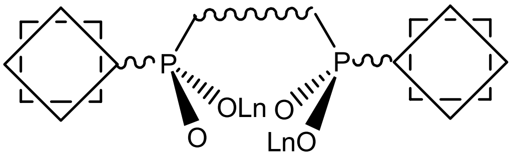
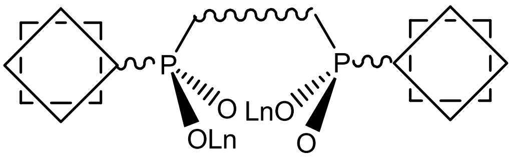
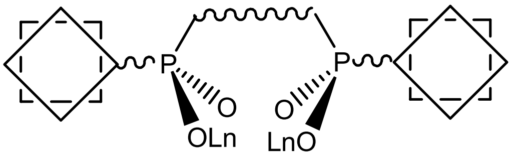
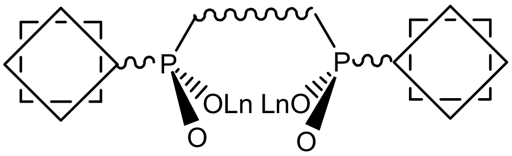
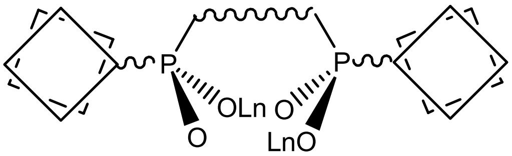
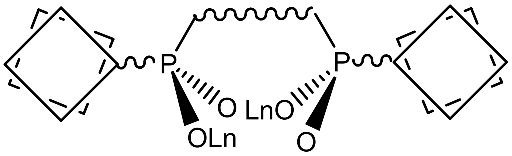
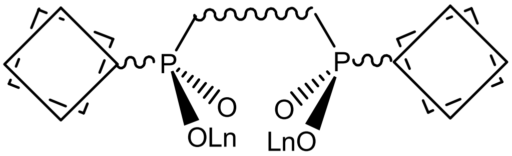
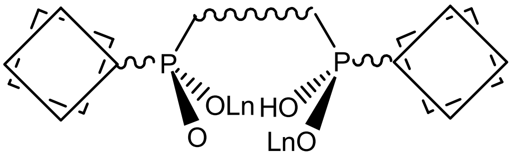
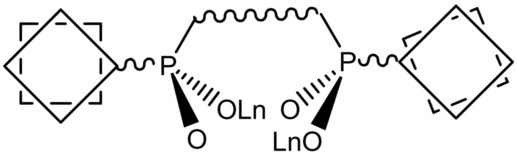


Figure S5. ^{13}C NMR spectrum of CS(DO3A-P^{NBn})$_2$ (a) and of [GdY(CS(DO3A-P^{NBn})$_2$)(H$_2$O)$_2$]$^{2-}$ (b) at 9.4 T and 298 K. The resonances were assigned in the order of increasing chemical shift. The asterisks label the signals of *t*-BuOH present in the deuterium oxide solution as an internal standard.

Table S1. The complete set of the possible isomers of $[Ln_2(CS(DO3A\text{-}P^{NBn})_2)(H_2O)_2]^{2-}$ complexes.

Schematic structure of isomer	Abbreviation	N° of ^{31}P NMR signals	Relative intensity of the NMR signal
	M_R-M_R	**1**	**2**
	M_S-M_S	**1**	**2**
 	M_S-M_R = = M_R-M_S	**2**	**2**
	m_R-m_R	**1**	**2**
	m_S-m_S	**1**	**2**
 	m_S-m_R = = m_R-m_S	**2**	**2**
	M_R-m_R	**2**	**1**

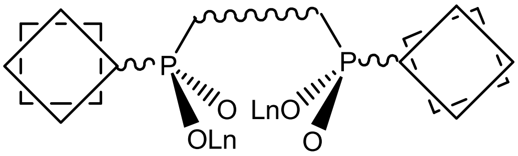
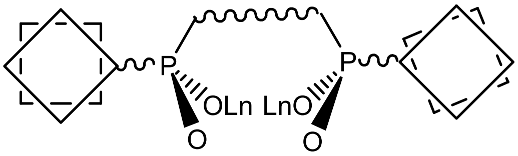
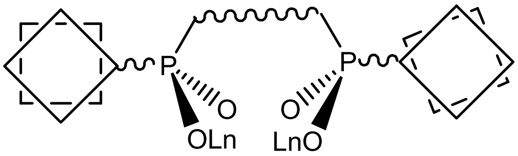
	**M_{S}-m_{S}**	**2**	**1**
	**M_{R}-m_{S}**	**2**	**1**
	**M_{S}-m_{R}**	**2**	**1**
Total	**10 species**	**16 NMR signals**	

Table S2. ^{13}C NMR T_1 relaxation times of the $[GdY(CS(DO3A\text{-}P^{NBn})_2)(H_2O)_2]^{2-}$ complex measured at 9.4 T and 298 K. The resonances were assigned in the order of increasing chemical shift – see the spectra in Fig. S4.

Assignment	Peak	T_1 / ms
$–P–\underline{C}H_2–C_6H_4$	1	9.7 ± 0.5
ring $–\underline{C}H_2–$	2	15 ± 1
	3	14.6 ± 0.2
	4	14.9 ± 0.7
$–N–\underline{C}H_2–P–$ and $–N–\underline{C}H_2–CO_2H$	5	16.3 ± 0.5
phenyl CH and C	6	4.1 ± 0.3
	7	6.2 ± 0.4
	8	6.1 ± 0.3
	9	4.1 ± 0.4
C=O and C=S	10	14.6 ± 0.5

Equations used for the multiparametrical fitting of ^{1}H and ^{17}O relaxometric data in Scientist form. The description of a given equation is provided directly in the script:

// Fit of NMRD and 17O T2 data

```
IndVars: T,B
DepVars: R1h,R2o
Params:delta,Hm,tm0,tr0,Hr,tv0,Hv,acc,ro,rh,n,a,trsf,rsf,Hmss,tm0ss,n1,gl
```

// Parameters and variables used

```
// T - temperature at K
// B - used field at MHz
// R2o - 17O transversal relaxivity at ms-1 (unreduced)
// R1h- 1H longitudinal relaxivity at ms-1/mmol (reduced)
// delta - squared ZFS matrix
// tm0 - water residence time at 298°K
// Hm - water exchange activation energy
// tr0 - rotation correlation time at 298°K
// Hr -activation energy of rotation
// tv0 - electronic correlation time of ZFS splitting
// Hv - activation energy of electronic relaxation
// acc - hyperfine Gd-O coupling constant A/hbar
// ro - Gd-O distance
// rh - Gh-H distance
// n number of water molecule coordinated to Gd
// s - multiplicity of Gd  - fixed to 3.5
// a - shortest distance form outer sphere to gadolinium - for OS contribution
// D - diffusion coefficient at 298°K
// n1 - number of water molecules at second sphere
// rsf - Gd-SS distance
// trsf - rotation correlation time of the second sphere
// Hmss - water exchange activation energy for second sphere contribution
// tm0ss - second-sphere water residence time at 298°K
// gl - squared deviation tensor of Lande g-factor
```

// Physical constants implicitly used

```
// univ - universal gass constant R = 8.31441
// μB - Bohr magneton μB = 9.274e-24
// μ0 - vacuum magnetic susceptibility μ0 = 4πe-7
// h - Planck constant h = 6.62617e-34
// hbar = 1.0546e-34
// NA - Avogadro constant NA = 6.023e23
// k - Boltzman constant k = 1.38066e-23
// γo - gyromagnetic ratio of 17O γo = -3.626e7
// γh - gyromagnetic ration of 1H  γh = 2.675e8
// gs - elektrononic gyromagnetic ratio gs = 1.75977e11
```

// Notes

```
// magnetic field  is in Larmor frequencies - omegas (Wo a WS) are calculated as 2*pi*B*ratio of gyros
```

// **BMS equations** :

// **Definitions of constants**

```
s=3.5
univ=8.31441
sz=31.5
```

// **Definition of omegas**

```
wh=6.28e6*B
ws=658.21*wh
```

```
wo=-0.1355514*wh
// Eyring equations
tm=((tm0^(-1)*T/298.15)*exp((Hm/univ)*(0.003354-(1/T))))^(-1)
tmss=((tm0ss^(-1)*T/298.15)*exp((Hmss/univ)*(0.003354-(1/T))))^(-1)
tr=((tr0^(-1))*exp((Hr/univ)*(0.003354-(1/T))))^(-1)
tv=((tv0^(-1))*exp((Hv/univ)*(0.003354-(1/T))))^(-1)
// Electronic relaxation-ZFS
T1eZFS=((1/25)*delta*tv*(4*s^2+4*s-3)*((1/(1+ws^2*tv^2))+(4/(1+4*ws^2*tv^2))))^(-1)
T2eZFS=(delta*tv*((5.26/(1+(0.372*ws^2*tv^2)))+(7.18/(1+(1.24*ws^2*tv^2)))))^(-1)
// Spin rotation term - optional
TeSR=(dg/(9*tr))^(-1)
// Powell's terms of Gd-Gd interaction - optional (need to set new parameter RGd)
// R1ed=((CONST*(2*dipe1+8*dipe2))/rgd^6)
// R2ed=((CONST*(dipe0+5*dipe1+2*dipe2))/rgd^6)
// CONST=3.3597e+23
// dipe0=tr
// dipe1=tr/(1+ws^2*tr^2)
// dipe2=tr/(1+4*ws^2*tr^2)
// Total electronic relaxation
T1e=(T1eZFS^(-1)+TeSR^(-1)+R1ed)^(-1)
T2e=(T2eZFS^(-1)+TeSR^(-1)+R2ed)^(-1)
// Total correlation times
tc1=(T1e^(-1)+tr^(-1)+tm^(-1))^(-1)
tc2=(T2e^(-1)+tr^(-1)+tm^(-1))^(-1)
te1=(T1e^(-1)+tm^(-1))^(-1)
te2=(T2e^(-1)+tm^(-1))^(-1)
// R2 scalar - contact contribution for 17O
//cont=(1/3)*s*(s+1)*acc^2*(te1+(te2/(1+ws^2*te2^2)))
cont=(1/3)*s*(s+1)*acc^2*(te1)
// R2 dipolar – pseudo-contact contribution for 17O
dip1=((1/15)*4.535671e-45*s*(s+1))/(ro^6)
dip2=4*tc1
dip3=(13*tc2)/(1+ws^2*tc2^2)
dip4=(3*tc1)/(1+wo^2*tc1^2)
dip=dip1*(dip2+dip3+dip4)
// R2 dipolar Curie contribution for 17O
dip7=(1/5)*(wo^2*7.397e-107*7.94^4)/(9*1.9063324e-46*T^2*ro^6)
dip8=4*tr+(3*tr)/(1+wo^2*tr^2)
cur=dip7*dip8
// Total dipolar contribution to R2 of 17O
diptot=dip+cur
// Total R2 relaxation - optional
//T2m=(cont+diptot)^(-1)
T2m=(cont)^(-1)
// Radial frequency difference of bound and free water at rad/s
dwm=2*s*(s+1)*9.274e-24/(3*1.38066e-23*T)*acc*(B*1E6*6.28/2.675E8)
// Overall reduced T2 relaxation of 17O
num=(T2m^(-2))+(T2m*tm)^(-1)+dwm^2
denom=(tm^(-1)+T2m^(-1))^2+dwm^2
scam=num/denom
pm=n*1e-3/55.55
R2o=pm*scam/tm
// R1 dipolar – pseudo-contact contribution for 1H
COST2=5.16963e-43/rh^6
R1DIP=(COST2*((7*TC2/(1+WS^2*TC2^2))+(3*TC1/(1+Wh^2*TC1^2))))
// Total inner sphere milimolar contribution to 1H relaxivity
T1M=(R1DIP)^(-1)
R1IN=(N*1E-3/55.55)/(T1M+TM)
// Calculus for diffusion coefficient according to J.C.Hindman
B1=3.118150E-04
```

```
B2=5.062560E+03
B3=1.547920E+02
B4=1.629310E+03
D=(1E-4)/((B1*EXP(B2/T))+(B3*EXP(B4/T)))
// Freed model of outer sphere contribution to 1H relaxivity
TAU=A^2/D
// Spectral density function J(i) for proton spins
AI=TAU/T1e
CI=[0,1]*wh*tau
z2I=ai+ci
JI=RE((1+0.25*(z2I^0.5))/(1+z2I^0.5+(4/9)*z2I+(1/9)*(z2I^1.5)))
// Spectral density function J(s) for gadolinium electron states
AS=TAU/T2e
CS=[0,1]*ws*tau
z2S=aS+cS
JS=RE((1+0.25*(z2S^0.5))/(1+z2S^0.5+(4/9)*z2S+(1/9)*(z2S^1.5)))
// Calculation of outer sphere contribution to 1H relaxivity according to Freed’s model
COST3=3.68e-20*S*(S+1)
R1OS=(COST3/(A*D))*((3*JI)+(7*JS))
// Second sphere contribution to 1H R1 relaxivity; only dipolar R1 contribution
TC1SF=(T1E^(-1)+TRSF^(-1))^(-1)
TC2SF=(T2E^(-1)+TRSF^(-1))^(-1)
COST2SF=(5.16963e-43/RSF^6)
R1DIPSF=(COST2SF*((7*TC2SF/(1+WS^2*TC2SF^2))+(3*TC1SF/(1+Wh^2*TC1SF^2))))
T1MSF=(R1DIPSF)^(-1)
R1SF=(N1*1e-3/55.55)/(T1MSF+tmss)
// Overall R1 proton relaxivity
R1h=R1IN+R1OS+R1SF
// Estimation of parameter - combination of Merbach’s DOTA parameters and estimation
// for the second sphere
```