

Supporting Information

for

Synthesis of a bifunctional monophosphinic acid DOTA analogue ligand and its lanthanide(III) complexes. A gadolinium(III) complex endowed with an optimal water exchange rate for MRI applications

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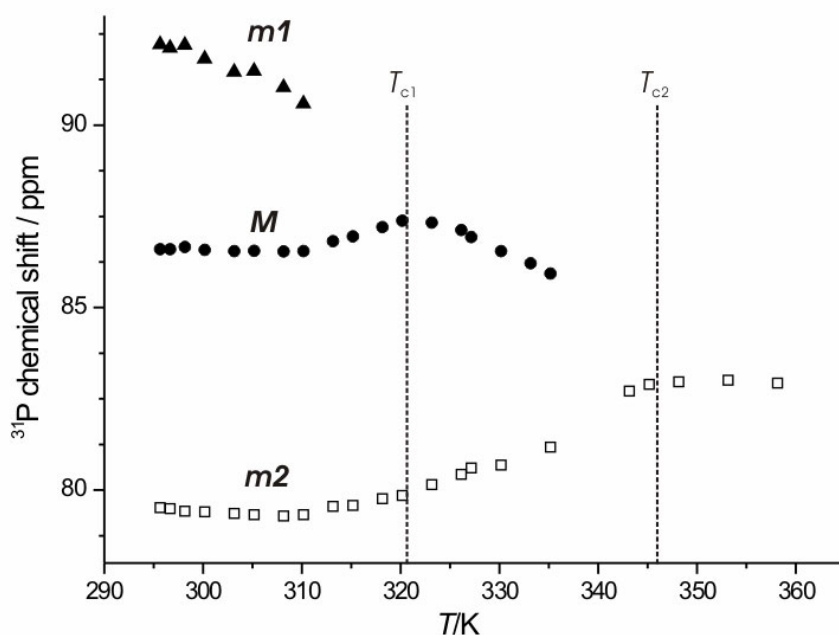


Figure S1. ³¹P dynamic-NMR study of [Eu(H₂O)DO3A^{ABn}]⁻. Dashed lines assigned as T_{c1}, T_{c2} correspond to coalescence point of *m1* and *M* isomers (▲, ●) and *M*, *m1* and *m2* isomer (□) respectively. Coalescence points were obtained from by DNMR simulation.

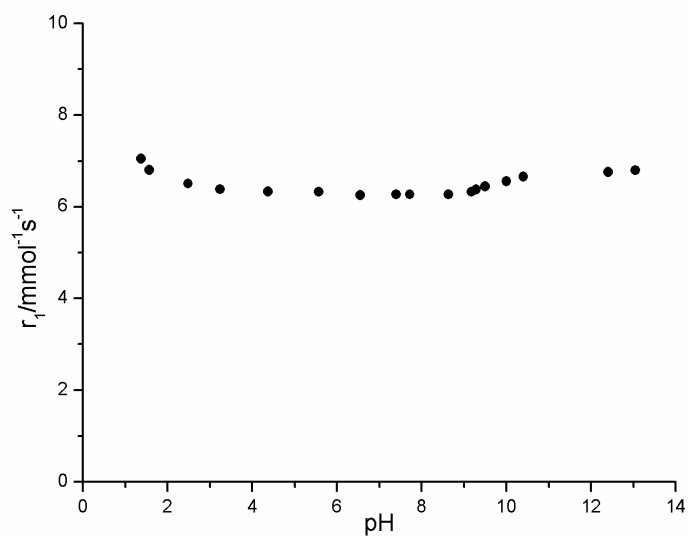


Figure S2. The dependence of the water proton relaxivity of $[\text{Gd}(\text{H}_2\text{O})(\text{DO3AP}^{\text{ABn}})]^-$ on pH (10 MHz, 25 °C).

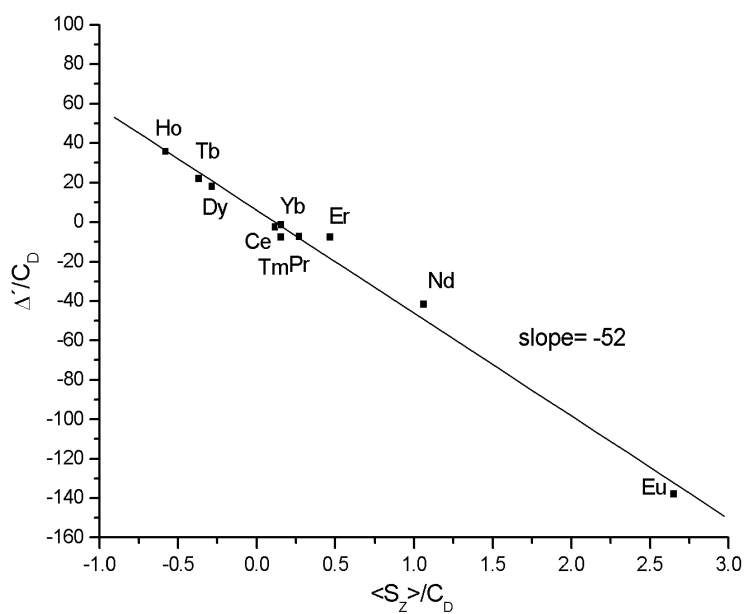


Figure S3. The separation of contact contribution to ^{17}O chemical shift of water measured in presence of $[\text{Ln}(\text{H}_2\text{O})(\text{DO3AP}^{\text{ABn}})]^-$ complexes.

Equations:

// Equations used for the fit of NMRD and 17O T2 data in Scientist format

IndVars: T,B

DepVars: R2o,R1h

Params:delta,Hm,tm0,Hr,tr0,Hv,tv0,acc,ro,rh,n,a,trsf,rsf,Hmss,tm0ss,n1

// 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 - Δ² trace of ZFS matrix

// tm0 - water residence time at 298°K

// Hm - water exchange free energy

// tr0 - rotation correlation time at 298°K

// Hr - rotation free energy

// tv0 - correlation time of modulation of ZFS matrix

// Hv - modulation of ZFS free energy

// acc - hyperfine Gd-O coupling constant A/hbar

// ro - Gd-O distance at m

// rh - Gh-H distance at m

// n number of water molecule coordinated at Gd

// conc - milimolar concentration for unreduced 17O data

// s - multiplicity of Gd - fixed to 3.5

// a - shortest distance from outer sphere to gadolinium - for OS contribution

// D - diffusion coefficient at 298 K

// n1 - number of water molecules in the second sphere

// rsf - Gd-SF distance

// trsf - rotation correlation time of the second sphere

// Hmss - water exchange free energy for the second sphere contribution

// tm0ss - water residence time at 298 K for the second sphere

// Physical constants implicitly used

// univ - universal gas 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 - electronic 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=-0.133557*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)*T/298.15)*exp((Hr/univ)*(0.003354-(1/T)))⁻¹

tv=((tv0⁻¹)*T/298.15)*exp((Hv/univ)*(0.003354-(1/T)))⁻¹

// **Electronic relaxation**

T1e=((1/25)*delta*tv*(4*s²+4*s-3)*((1/(1+ws²*tv²))+4/(1+4*ws²*tv²)))⁻¹

T2e=((0.02*(4*s²+4*s-3)*tv*delta*(3+(5/(1+(ws²*tv²)))+(2/(1+(4*ws²*tv²))))))⁻¹

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)*acc²*(te1+(te2/(1+ws²*te2²)))

// **R2 dipolar - pseudocontact contribution for 17O**

dip1=((1/15)*4.535671e-45*s*(s+1))/(ro⁶)

dip2=4*tc1

dip3=(13*tc2)/(1+ws²*tc2²)

dip4=(3*tc1)/(1+wo²*tc1²)

dip=dip1*(dip2+dip3+dip4)

// **R2 dipolar Curie contribution for 17O**

dip7=(1/5)*(wo²*7.397e-107*7.94⁴)/(9*1.9063324e-46*T²*ro⁶)

dip8=4*tr+(3*tr)/(1+wo²*tr²)

cur=dip7*dip8

// **Total dipolar contribution to R2 of 17O**

diptot=dip+cur

// **Total R2 relaxation**

T2m=(cont+diptot)⁻¹

// **Radial frequency difference of bound and free water at rad/s**

dwm=sz*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+dwm²

denom=(tm⁻¹+T2m⁻¹)²+dwm²

scam=num/denom

pm=n*1e-3/55.56

R2o=pm*scam/tm

// **R1 dipolar - pseudocontact 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-3/55.6)/(T1M+TM)
// Calculus for difusion 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 contrubution 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 Freeds
model
COST3=3.68e-20*S*(S+1)
R1OS=(COST3/(A*D))*((3*JI)+(7*JS))
// Aime´s and Bota´s 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-3/55.6)/(T1MSF+tmss)
// Overall R1 proton relaxivity
R1h=R1IN+R1OS+R1SF
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-3/55.6)/(T1M+TM)
// Calculus for difusion 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 contrubution 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 Freeds model

$$COST3=3.68e-20*S*(S+1)$$

$$R1OS=(COST3/(A*D))*((3*JI)+(7*JS))$$

// Aime's and Bota's second sphere contribution to 1H R1 relaxivity; only dipolar R1 contribution

$$TC1SF=(T1E^(-1)+TRSF^(-1))^(-1)$$

$$TC2SF=(T2E^(-1)+TRSF^(-1))^(-1)$$

$$COST2SF=(5.16963e-43/RSF^6)$$

$$R1DIPSF=(COST2SF*((7*TC2SF/(1+WS^2*TC2SF^2)))+(3*TC1SF/(1+Wh^2*TC1SF^2))))$$

$$T1MSF=(R1DIPSF)^(-1)$$

$$R1SF=(N1*1e-3/55.6)/(T1MSF+tmss)$$

// Overall R1 proton relaxivity

$$R1h=R1IN+R1OS+R1SF$$