## **ELECTRONIC SUPPLEMENTARY INFORMATION for**

# Accelerating Water Exchange in Gd<sup>III</sup>-DO3A Derivatives by Favouring the Dissociative Mechanism through Hydrogen Bonding

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### 1. EXPERIMENTAL

All chemicals were purchased from Sigma-Aldrich or Alfa Aesar unless otherwise stated and were used without further purification. The <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded using a Bruker Advance III 500 MHz (11.4 T) spectrometer equipped with 5mm PABBO probes and BVT-3000 temperature control unit. Chemical shifts are reported relative to TMS and were referenced using the residual proton solvent resonances. HPLC analyses and mass spectra were performed on a Waters HPLC-MS system equipped with a Waters 1525 binary pump. Analytical measurements were carried out on a Waters Atlantis RPC18 column (5µm 4.6x100mm) and on a Waters Atlantis prep T3 OBD (5µm 19x100mm) for preparative purposes. Electrospray ionization mass spectra (ESI MS) were recorded using a SQD 3100 Mass Detector (Waters), operating in positive or negative ion mode, with 1% v/v formic acid in methanol as the carrier solvent. Proton relaxation measurements (1 /  $T_1$ ) and the resulting 1 /  $T_1$  NMRD profiles were obtained with a Stelar Smart Tracer loop relaxometer operating in the range between 0.01-10 MHz (0.00024 to 0.25 T). Top magnetic field points (20-70 MHz; 0.37-1.75 T), were obtained using a Stelar Spinmaster console connected to a WP-80 (80 MHz, 2T) magnet.

## 1.1 Synthesis



Scheme S1. Synthesis of DO3A-AP, DO3A-oHAP and DO3A-pHAP.

#### 1-(2-oxo-2-phenylethyl)-4,7,10-tris(tert-butoxycarbonylmethyl)- 1,4,7,10-tetraazacyclododecane (DO3A(tBu)<sub>3</sub>-AP)

A solution in CH<sub>3</sub>CN (5 mL) of DO3A(*t*Bu)<sub>3</sub> (202 mg, 0.388 mmol) and 2-bromoacetophenone (121 mg, 0.583 mmol) was left stirring, under N<sub>2</sub> atmosphere. After 10 min, K<sub>2</sub>CO<sub>3</sub> (272 mg, 1.94 mmol) and KI (17 mg, 0.078 mmol) were added. The reaction mixture was stirred for 3 h at room temperature and then filtered, evaporated in vacuo and then purified by silica gel chromatography (99:1 CH<sub>2</sub>Cl<sub>2</sub>–MeOH) to a ord DO3A(*t*Bu)<sub>3</sub>-AP (216 mg, yield 88%) <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500MHz):  $\delta$ = 7.87 (d, -o-Ph-, J= 7.5 Hz, 2H), 7.55 (t, -*p*-Ph-, J= 7.5 Hz, 1H), 7.44 (t, J= 7.5 Hz -m-Ph, 2H), 2.21-3.97 (m, macrocycle, 16H; m, N<u>CH<sub>2</sub></u>COtBu, 6H), 1.45 (s, -NCH<sub>2</sub>CO<u>tBu</u>, 27 H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125MHz):  $\delta$ = 27.81(-NCH<sub>2</sub>CO<u>tBu</u>), 48.71-52.14 (macrocycle), 55.64 (-N<u>C</u>H<sub>2</sub>COtBu), 60.27 (-N<u>C</u>H<sub>2</sub>COPh), 82.01 (-NCH<sub>2</sub>CO<u>tBu</u>, *C*), 127.60 (m-Ph), 128.72 (o-Ph), 133.69 (p-Ph), 135.65 (C, Ph), 172.84 (-NCH<sub>2</sub><u>CO</u>tBu), 199.62 (NCH<sub>2</sub><u>CO</u>Ph). ESI-MS (m/z): found 633.71 [M+H]<sup>+</sup> (calc for C<sub>34</sub>H<sub>56</sub>N<sub>4</sub>O<sub>7</sub>:633.41).

### 1-(2-oxo-2-phenylethyl)-1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid (DO3A-acetophenone) (DO3A – AP)

DO3A(tBu)<sub>3</sub> –AP (216 mg, 0.34 mmol) was dissolved in a solution of DCM: TFA (1:1/ v:v) and left stirred ar rt, overnight. After evaporation in vacuo, the ligand (DO3A –AP) was obtained in quantitative yield, without further purification. <sup>1</sup>H NMR (D<sub>2</sub>O, 500 MHz):  $\delta$ = 7.97 (d, -*o*-Ph-, J= 7.5 Hz, 2H), 7.67 (t, -*p*-Ph-, J= 7.5 Hz, 1H), 7.54 (t, -o-Ph, J= 7.5 Hz, 2H), 2.42-4.10 (m, macrocycle, 16H; m, N<u>CH<sub>2</sub></u>COtBu, 6H). <sup>13</sup>C NMR (D<sub>2</sub>O, 125MHz): 202.77 (NCH<sub>2</sub>COPh), 180.16 (-NCH<sub>2</sub>COtBu), 136.00 (C, Ph), 133.95 (p-Ph), 128.82 (o-Ph), 127.87 (m-Ph), 58.53 (-N<u>C</u>H<sub>2</sub>COtBu, -N<u>C</u>H<sub>2</sub>COPh), 50.88 (macrocycle), ESI-MS (m/z): found 465.44 [M+H]<sup>+</sup>, 232.63 [M+2H]<sup>2+</sup> (calc for C<sub>22</sub>H<sub>32</sub>N<sub>4</sub>O<sub>7</sub>:465.23).

#### Preparation of Gd(DO3A –AP)

Gd(DO3A-AP) was synthesized by complexometric titration monitoring the change in the longitudinal water proton relaxation rate ( $R_1$ ) as a function of the amount of Gd<sup>3+</sup> added. Knowing the title of the ligand, Gd(DO3A-AP) was also

synthesized on a larger scale by adding dropwise 1 mL of a water solution of  $GdCl_3 \cdot 6H_2O$  (30 mg, 0.08 mmol) to 1 mL water solution of the ligand in slight excess (60 mg, 0.095 mmol) maintaining the pH around 6.5-7 by addition of NaOH 0.1 M. The solution was stirred overnight at room temperature. Possible excess  $Gd^{3+}$  was precipitated as  $Gd(OH)_3$  by raising the pH to 11 and after 2h the precipitate was filtered. Finally, the pH was brought back to 7 and the solution lyophilised to obtain the pure complex as white solid (70 mg). ESI-MS (m/z): found 620.51 [M+H]<sup>+</sup>, 310.54 [M+2H]<sup>2+</sup> (calc for  $GdC_{22}H_{29}N_4O_7$ :619.23).

## Synthesis of 1-(2-(2-methoxyphenyl)-2-oxoethyl)-4,7,10-tris-(t-butoxycarbonylmethyl)-1,4,7,10-tetraazacyclododecane

A solution in CH<sub>3</sub>CN (5 mL) of DO3A(*t*Bu)<sub>3</sub> (200 mg, 0.38 mmol) K<sub>2</sub>CO<sub>3</sub> (160 mg, 1.2 mmol) and 2-bromo-2'methoxyacetophenone (98 mg, 0.42 mmol) was left stirring, under N<sub>2</sub> atmosphere for 3 h at room temperature and then filtered, evaporated in vacuo and then purified by silica gel chromatography (99:1 CH<sub>2</sub>Cl<sub>2</sub>–MeOH) to a  $\Box$  ord (DO3A(*t*Bu)<sub>3</sub> – *o*-MeOAP) (180 mg, yield 70%) <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500MHz):  $\delta$ = 7.80 (d, -*C*<sub>6</sub>-Ph-, 1H), 7.48 (t, -*C*<sub>4</sub>-Ph-, J= 7.5 Hz, 1H), 6.98 (m, *C*<sub>3-5</sub>-Ph, J= 7.5 Hz, 2H), 4.029 (s, -NC<u>H<sub>2</sub>CO-, 2H), 3.89 (s, -OC<u>H<sub>3</sub></u>, 3H), 3.66-2.92 (m, macrocycle, 16H; m, -NC<u>H<sub>2</sub>COOC(CH<sub>3</sub>)<sub>3</sub>, 6H), 1.44 (s, -NCH<sub>2</sub>COOC(C<u>H<sub>3</sub>)<sub>3</sub>, 27H).</u> <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125MHz):  $\delta$ = 201.19 (NCH<sub>2</sub><u>CO</u>Ph), 169.9 (-NCH<sub>2</sub><u>CO</u>OC(CH<sub>3</sub>)<sub>3</sub>, 159.24 (-C<sub>2</sub>-Ph), 134.55 (-*C*<sub>6</sub>-Ph-), 130.60 (-*C*<sub>4</sub>-Ph-), 126.10 (-*C*<sub>1</sub>-Ph-), 120.68 (-*C*<sub>5</sub>-Ph-), 111.64 (-*C*<sub>3</sub>-Ph-), 81.92 (-NCH<sub>2</sub>COOC(CH<sub>3</sub>)<sub>3</sub>), 65.17 (-N<u>C</u>H<sub>2</sub>COPh), 55.89 (-N<u>C</u>H<sub>2</sub>COOC(CH<sub>3</sub>)<sub>3</sub>), 55.64 (-O<u>C</u>H<sub>3</sub>), 52.86-48.55 (macrocycle), 27.92 (-NCH<sub>2</sub>COOC(<u>C</u>H<sub>3</sub>)<sub>3</sub>) ESI-MS (m/z): found 663.47 [M+H]<sup>+</sup> (calc for C<sub>35</sub>H<sub>58</sub>N<sub>4</sub>O<sub>8</sub>:662.87).</u></u>

# Synthesis of 1-(2-(2-hydroxyphenyl)-2-oxoethyl)- 1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid (DO3A-oHAP)

DO3A(*t*Bu)<sub>3</sub>-oMAP (90 mg, 0.14 mmol) was dissolved in a solution of MeOH: HBr (aq) (1:1/ v:v) into a microwave tube, and placed in a CEM Discover Microwave Synthesizer. The sample was heated at 60 °C with stirring for 15 min (70 W, 18 psi). The reaction mixture was concentrated in vacuum and then purified by preparative HPLC-MS (Waters Atlantis prep T3 OBD 5µm 19x100 mm) with the following method. A: TFA 0.1% in H<sub>2</sub>O; B: MeOH; flow 20 mL/min; 0-2 min: 100% A, 3-12 min: from 0 to 100% B, 12-13 min 100% B, 13-14 min 100 % A (tr= 7.6 min), to obtain (DO3A-*o*-HyAP) (34 mg, 0.07 mmol, 50%).<sup>1</sup>H NMR (D<sub>2</sub>O, 500MHz):  $\delta$ = 7.87 (d, -C<sub>6</sub>-Ph-, J=7.5 Hz, 1H), 7.67 (t, -C<sub>4</sub>-Ph-, J= 7.5, 1H), 7.10 (m, -C<sub>3-5</sub>-Ph, 2H), 4.09-3.25 (m, macrocycle, 16H; m, N<u>CH<sub>2</sub></u>COOH, 6H, N<u>CH<sub>2</sub></u>CO-, 2H ). <sup>13</sup>C NMR (D<sub>2</sub>O, 125Hz):  $\delta$ = 203.58 (NCH<sub>2</sub><u>CO</u>Ph), 174.33 (-NCH<sub>2</sub><u>CO</u>OH), 160.22 (-C<sub>2</sub>-Ph), 130.68 (-C<sub>6</sub>-Ph-), 129.75 (-C<sub>4</sub>-Ph-), 120.98 (-C<sub>1</sub>-Ph-), 120.29 (-C<sub>5</sub>-Ph-), 117.88 (-C<sub>3</sub>-Ph-), 55.74 (-N<u>C</u>H<sub>2</sub>COPh), 54.34 (-N<u>C</u>H<sub>2</sub>COOH), 53.43-48.27 (macrocycle). ESI-MS (m/z): found 481.50 [M+H]<sup>+</sup>, 241.33 [M+2H]<sup>2+</sup> (calc for C<sub>22</sub>H<sub>32</sub>N<sub>4</sub>O<sub>6</sub>:480.52).

#### Preparation of Gd(DO3A-oHAP)

Gd(DO3A-*o*HAP) was prepared with same procedure reported for Gd(DO3A-AP) using a slight excess of ligand (34 mg, 0.07 mmol) and (21 mg, 0.56 mmol) of GdCl<sub>3</sub>·6H<sub>2</sub>O to obtain 69 mg of final complex. ESI-MS (m/z): found 636.30 [M+H]<sup>+</sup>, 317.48 [M+2H]<sup>2+</sup> (calc for GdC<sub>22</sub>H<sub>29</sub>N<sub>4</sub>O<sub>7</sub>:635.12).

# Synthesis of 1-(2-(4-methoxyphenyl)-2-oxoethyl)-4,7,10-tris-(t-butoxycarbonylmethyl)-1,4,7,10-tetraazacyclododecane (DO3A(*t*Bu)<sub>3</sub>-*p*MAP).

DO3A(tBu)<sub>3</sub>–*p*MAP was prepared following the same procedure as for the synthesis of DO3A(*t*Bu)<sub>3</sub>-*o*MAP (200 mg, 0.3 mmol, 78%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500MHz):  $\delta$ = 7.86 (d, -*C*<sub>2-6</sub>-Ph-, J= 8.8 Hz, 2H), 6.91 (d, *C*<sub>3-5</sub>-Ph, J= 8.8 Hz, 2H), 4.03 (s, -NC*H*<sub>2</sub>CO-, 2H), 3.85 (s, -OC*H*<sub>3</sub>, 3H), 3.62-2.66 (m, macrocycle, 16H; m, -NC*H*<sub>2</sub>COOC(CH<sub>3</sub>)<sub>3</sub>, 6H), 1.43 (s, -NCH<sub>2</sub>COOC(C*H*<sub>3</sub>)<sub>3</sub>, 27H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125MHz):  $\delta$ = 197.72 (NCH<sub>2</sub><u>CO</u>Ph), 169.92 (-NCH<sub>2</sub><u>CO</u>OC(CH<sub>3</sub>)<sub>3</sub>, 163.84 (-C<sub>4</sub>-Ph), 129.82 (-*C*<sub>2-6</sub>-Ph-), 128.68 (-*C*<sub>1</sub>-Ph-), 113.8 (-*C*<sub>3-5</sub>-Ph-), 81.90 (-NCH<sub>2</sub>COOC(CH<sub>3</sub>)<sub>3</sub>), 59.77 (-N<u>C</u>H<sub>2</sub>COPh), 55.78 (-N<u>C</u>H<sub>2</sub>COOC(CH<sub>3</sub>)<sub>3</sub>), 55.53 (-O<u>C</u>H<sub>3</sub>), 52.98-48.96 (macrocycle), 27.85 (-NCH<sub>2</sub>COOC(<u>C</u>H<sub>3</sub>)<sub>3</sub>) ESI-MS (m/z): found 663.87 [M+H]<sup>+</sup> (calc for C<sub>35</sub>H<sub>58</sub>N<sub>4</sub>O<sub>8</sub>:662.87).

## Synthesis of 1-(2-(4-hydroxyphenyl)-2-oxoethyl)- 1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid (DO3ApHAP).

DO3A–*p*HAP was prepared following the same procedure as for the synthesis of (DO3A–*p*HAP) (29 mg, 0.06 mmol, 42%). <sup>1</sup>H NMR (D<sub>2</sub>O, 500MHz): δ=7.93 (d, -C<sub>2-6</sub>-Ph, J=8.8 Hz, 2H), 7.01 (d,  $C_{3^-5}$ -Ph, J= 8.8 Hz, 2H), 4.13-3.17 (m, macrocycle, 16H; m, -NC<u>*H*</u><sub>2</sub>COOH, 6H, -NC<u>*H*</u><sub>2</sub>CO-, 2H). <sup>13</sup>C NMR (D<sub>2</sub>O, 125Hz): δ= 190.8 (NCH<sub>2</sub><u>CO</u>Ph), 174.06 (-NCH<sub>2</sub><u>CO</u>OH), 164.62 (-C<sub>4</sub>-Ph), 130.83 (-C<sub>2-6</sub>-Ph-), 126.37 (-C<sub>1</sub>-Ph-), 114.41 (-C<sub>3-5</sub>-Ph-), 59.42 (-N<u>C</u>H<sub>2</sub>COPh), 54.35 (-N<u>C</u>H<sub>2</sub>COOC(CH<sub>3</sub>)<sub>3</sub>), 53.39-48.27 (macrocycle). ESI-MS (m/z): found 481.72 [M+H]<sup>+</sup>, 241.35 [M+2H]<sup>2+</sup> (calc for C<sub>23</sub>H<sub>34</sub>N<sub>4</sub>O<sub>8</sub>:480.55).

#### Preparation of Gd(DO3A-pHAP)

Gd(DO3A-*p*HAP) was prepared with same procedure reported for Gd(DO3A-AP) using a slight excess of ligand (50 mg, 0.10 mmol) and (30 mg, 0.8 mmol) of GdCl<sub>3</sub>·6H<sub>2</sub>O to obtain 55 mg of final complex. ESI-MS (m/z): found 636.26 [M+H]<sup>+</sup>, 318.55 [M+2H]<sup>2+</sup> (calc for GdC<sub>22</sub>H<sub>29</sub>N<sub>4</sub>O<sub>7</sub>:635.12).

### 1.2 UV-Vis measurements

UV analyses were carried out on a Jasco V-550 dual-lamp (deuterium) and visible (Xenon) spectrophotometer, scanning from 700 nm to 200 nm. Solutions at known concentration of the complexes were prepared (0.1 M NaCl, 298 K) and the UV-vis spectra were recorded at different pH intervals (pH 6-11 for the free ligands and pHs 4-10 for Gd complexes). In case of GdDO3A-*o*HAP and GdDO3A-*p*HAP the Molar Extinction Coefficient was determined by measuring the absorbance of solution at different concentrations (Table S1).

Table S1, Mola	r extinction coefficients f	or GdDO3A-oHAF	and GdDO3A-pHA	P at acidic and basic	nН
					P' ''

	ε <sub>HA</sub> (M <sup>-1</sup> cm <sup>-1</sup> )	ε <sub>A-</sub> (M <sup>-1</sup> cm <sup>-1</sup> )
GdDO3A-oHAP	5222 ±14 (340 nm, pH 4.5)	9204 ±11 (393 nm, pH 9.9)
GdDO3A- <i>p</i> HAP	24254±140 (306 nm, pH 4.0)	33936±118 (354 nm, pH 8.8)



**Fig. S1**. (A) Deprotonation scheme for GdDO3A-AP. (B) Spectral data analysis and  $pK_a$  determination. (A) UV spectra ( $\lambda$  = 225–400 nm) of GdDO3A-AP in different aqueous solutions ranging from pH 6 to 13 (0.1 M NaCl, 298 K). The absorbances are normalized to zero for  $\lambda$  = 600 nm. Inset: plot of the total absorbance difference vs pH to determine the  $pK_a$ . The total absorbance difference is the sum of the absolute absorbance difference values at the chosen wavelengths (i.e. 265 and 290 nm). The  $pK_a$  value was worked out by nonlinear regression.<sup>1</sup>



**Fig. S2**. Spectral data analysis and  $pK_a$  determination for DO3A-oHAP and GdDO3A-oHAP. (A) UV spectra ( $\lambda = 200-450$  nm) of DO3A-oHAP in different aqueous solutions ranging from pH 4.3 to 10.9 (0.1 M NaCl, 298 K). The absorbances are normalized to zero for  $\lambda = 600$  nm. Insert: plot of the total absorbance difference vs pH to determine the  $pK_a$ . The total absorbance difference is the sum of the absolute absorbance difference values at the chosen wavelengths (i.e. 320 and 367 nm). The  $pK_a$  value was worked out by nonlinear regression using eq. 1S reported in ref 1. (B) UV spectra ( $\lambda = 250-500$  nm) of GdDO3A-oHAP in different aqueous solutions ranging from pH 4.5 to 9.9 (0.1 M NaCl, 298 K). The absorbances are normalized to zero for  $\lambda = 600$  nm. Insert: plot of the total absorbance difference vs pH to determine the  $pK_a$ . The total absorbance difference is the sum of the absolute absorbance difference vs pH to determine the  $pK_a$ . The total absorbance difference is the sum of the absolute absorbance difference vs pH to determine the  $pK_a$ . The total absorbance difference is the sum of the absolute absorbance difference vs pH to determine the  $pK_a$ . The total absorbance difference is the sum of the absolute absorbance difference values at the chosen wavelengths (i.e. 336 and 396 nm). (C) Deprotonation scheme for DO3A-oHAP. (D) Deprotonation scheme for GdDO3A-oHAP.



**Fig. S3.** Spectral data analysis and  $pK_a$  determination for DO3A-*p*HAP and GdDO3A-*p*HAP. (A) UV spectra ( $\lambda = 200-400$  nm) of DO3A-*p*HAP in different aqueous solutions ranging from pH 4.1 to 10.2 (0.1 M NaCl, 298 K). The absorbances are normalized to zero for  $\lambda = 600$  nm. Insert: plot of the total absorbance difference vs pH to determine the  $pK_a$ . The total absorbance difference is the sum of the absolute absorbance difference values at the chosen wavelengths (*i.e.* 279 and 327 nm). The  $pK_a$  value was worked out by nonlinear regression using eq. 1S reported in ref 1. (B) UV spectra ( $\lambda = 250-500$  nm) of GdDO3A-*o*HAP in different aqueous solutions ranging from pH 4.5 to 9.9 (0.1 M NaCl, 298 K). The absorbances are normalized to zero for  $\lambda = 600$  nm. Insert: plot of the total absorbance difference vs pH to determine the  $pK_a$ . The total absorbance difference is the sum of the absolute absorbance difference values at the chosen wavelengths (*i.e.* 279 and 327 nm). C) Deprotonation scheme for DO3A-*p*HAP. (D) Deprotonation scheme for GdDO3A-*p*HAP.

## 1.3 X-ray crystallography

Despite the several attempts, the Gd complex of DO3A-oHAP forms only very thin laminae slowly grown from water at 4 °C. Many among them were checked and finally the data collection was carried out on a very thin lamina (0.20x0.10x0.02 mm<sup>3</sup>). A full redundant dataset was collected with a 200 s per frame to obtain a good statistic and carry out the best possible absorption correction. The automatic assignment of the space group suggested a C2/m symmetry, but the structure cannot be solved except for the localization of Gd and its first coordination sphere. Clearly, the C lattice is consistent with the pseudo-symmetry of the metallic centre but it is not obeyed by the full complex, especially by the phenol group dramatically lowering the local symmetry. This feature, together with the crystal morphology and problems of absorption give exception to systematic extinction in all space groups and the automatic symmetry analysis failed. A careful analysis of the systematic extinctions suggested other possible lower symmetry space groups with a preference for P21/c. The structure solution was then attempted in all the possible monoclinic and triclinic space groups. P21/a, P21/n, P21/m, P2, Pm gave no or very disorder solutions, while P21/c, P21, Pc, P-1, and P1 converged to the same crystal structure and packing, but high correlation coefficients among symmetry related molecules were observed using the Pc, P21, P-1, P1 space groups. The analysis of the symmetry and the obtained agreement factors confirmed P21/c as the best solution with a stable refinement. The disordered crystal structure is shown Fig. S4 together with the Gd coordination sphere. The complex forms intermolecular hydrogen bonds with other complexes in the trans conformation and assisted by water in the cis conformation (Fig. S5). The crystal packing is rather peculiar with a 2D arrangement of Gd-complexes with large 1D voids disposed perpendicular to the 2D net (Fig. S6 top). The voids are filled by a net of H-bonded water molecules (Fig. S6 bottom). This structure explains the morphology of the crystal, with one preferred direction of growth. These voids are imposed by the molecular structure with phenyl groups exposed as flags standing up from the pseudo-spherical bulky and rigid GdDO3A moiety. No close packing is evidently possible. Phenolic hydrogen atoms were not assigned for two reasons: on one hand, the pH during crystallization is close to the  $pK_a$  of this hydroxyl, and both phenol and phenolate can be present; on the other hand, the complexity of the H-bond net, coupled to the disorder makes the assignment on the base of the geometry unreliable. The typical twinning law observed when a mirror plane perpendicular to the b axis emulates a monoclinic C lattice<sup>2</sup> was suggested by the checkcif and implemented in the refinement. In this way, the 77 exceptions to systematic extinctions were reduced to three. This twinning confirms the above-described uncertainty between C2/m and P21/c space group when looking to the raw data.

As a final consideration, the low crystal quality, related to the feature of the crystal structure, allowed the solution of a crystal structure with some important alert on the checkcif: some atoms are refined isotropically, some anisotropic displacement parameters are on the limit of acceptance and agreement factors are not of "acta crystallografica" quality. However, the check done about space group assignation and the identification of a twinning law eliminating most of the exception to systematic extinctions, suggest that the structure is reliable enough to allow extracting some interesting chemical information, i.e. Gd coordination, 2-hydroxyacetophenone conformation and the features of the observed H-bond network.



**Fig. S4**: The Gd-complex from X-ray crystallography, highlighting the phenyl disorder and the co-crystallized water molecules (top); the molecular structure of the major *trans* conformation viewed along Gd-water bond (bottom left) and Gd centre coordination with the rotation calculated as average of the four equivalent O-Gd-N moieties (bottom right).



**Fig. S5**: Intramolecular H-bond between the phenolic OH and a water molecule in interaction with the coordinated water (top) and intermolecular H-bond between the phenolic OH and the acetate group of another Gd-complex (bottom), with highlighted the O...O distances involved in the hydrogen bonds.



**Fig. S6**: The porous crystal packing with the 1D void channels (yellow) filled by seven H-bonded water molecules, within the 2D net formed by the Gd-complexes (top) and the molecular view of the crystal packing highlighting the role of the phenyl groups Inn creating the voids (bottom).

## 1.3 <sup>1</sup>H NMR spectroscopic study on Eu<sup>III</sup> complexes.

To get more insight into the structural and dynamic properties of Ln-DO3A-AP, LnDO3A-*o*HAP and LnDO3A-*p*HAP complexes, the Eu<sup>III</sup> complexes were investigated by using <sup>1</sup>H NMR spectroscopy at three temperatures (283, 298 and 310K). In case of EuDO3A-*o*HAP, the <sup>1</sup>H NMR spectra were recorded at two different pH, *i.e.* 3.5 and 9.5, in order to obtain the spectra of the fully protonated and fully deprotonated species. The solution structure of these DO3A-acetophenone-like complexes is expected to resemble that of the corresponding LnDOTA analogues (DOTA = 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid).<sup>3</sup> The latter complexes are characterized by the presence of two different coordination isomers defined by the same conformation of the macrocyclic ring but with different orientation of the side arms (*i.e.*, capped square-antiprismatic geometry, SAP, and capped twisted square antiprismatic geometry, TSAP). These isomers exhibit two different sets of signals in the paramagnetic <sup>1</sup>H NMR spectra with relative population that is affected by the size of the Ln<sup>III</sup> ion. The substitution of one acetic arm with phenacyl or 2'-hydroxyphenacyl moieties reduces the

symmetry removing the proton equivalence, although the carbonyl oxygen is expected to coordinate the metal ion and therefore the rigidity of the system should be maintained. The <sup>1</sup>H NMR spectra of EuDO3A-AP and EuDO3A-*p*HAP at pH 7 and EuDO3A-oHAP at pH 3.5 and 9.5 at 283 K (Figure S5-S8) show one predominant set of signals (70-80%) and another set present in ca. 20-30% amount. The chemical shifts of the four predominant axial ring protons are in the range 25-40 ppm, suggesting the presence of SAP isomers. By comparing the integral of the two set of signals of axial ring-protons, the ratio between the SAP and TSAP isomers for EuDO3A-*o*HAP at basic pH, a ratio SAP/TSAP of 73:18 was found together with a small amount of a third set of signal (*ca.* 9%) at low field (> 20 ppm), suggesting the presence of the second TSAP isomer in exchange. For EuDO3A-*p*HAP the SAP/TSAP ratio is 72/28.









### **1.4 Relaxometric measurements**

The water proton longitudinal relaxation rates as a function of the magnetic field strength were measured in non-deuterated aqueous solutions on a Fast Field-Cycling Stelar SmarTracer relaxometer (Stelar s.r.l., Mede (PV), Italy) over a continuum of magnetic field strengths from 0.00024 to 0.25 T (corresponding to 0.01–10 MHz proton Larmor frequencies). The relaxometer operates under computer control with an absolute uncertainty in  $1/T_1$  of ±1%. Additional longitudinal relaxation data in the range 20–70 MHz were obtained on a Stelar Relaxometer connected to a Bruker WP80 NMR electromagnet adapted to variable-field measurements. The exact concentration of Gd<sup>III</sup> was determined by measurement of bulk magnetic susceptibility shifts of a *t*BuOH signal or by inductively coupled plasma mass spectrometry (ICP-MS, Element-2,

Thermo-Finnigan, Rodano (MI), Italy). Sample digestion was performed with concentrated HNO<sub>3</sub> (70%, 2 mL) under microwave heating at 160°C for 20 min (Milestone MicroSYNTH Microwave lab station equipped with an optical fibre temperature control and HPR-1000/6 M six position high pressure reactor, Bergamo, Italy). The <sup>1</sup>H  $T_1$  relaxation times were acquired by the standard inversion recovery method with typical 90° pulse width of 3.5 µs, 16 experiments of 4 scans. The temperature was controlled with a Stelar VTC-91 airflow heater equipped with a calibrated copper-constantan thermocouple (uncertainty of ±0.1 °C). Variable-temperature <sup>17</sup>O NMR measurements were recorded on a Bruker Avance III spectrometer (11.7 T) equipped with a 5 mm probe and standard temperature control unit. Aqueous solutions of the complexes containing 2.0% of the <sup>17</sup>O isotope (Cambridge Isotope) were used. The observed transverse relaxation rates were calculated from the signal width at half-height.



Fig. S11 pH dependence of the solvent longitudinal relaxivity for GdDO3A-oHAP (top) and GdDO3A-pHAP (bottom) at 298 K and 20 MHz.



**Fig S12.** <sup>1</sup>H NMRD profiles recorded at 298 (black) and 310 K (red) for (A) GdDO3A-*o*HAP at pH 4; (B) GdDO3A-*o*HAP at pH 9; (C) GdDO3A-AP at pH 7 and (D) GdDO3A-*p*HAP at pH 7.



**Fig S13.** Transverse <sup>17</sup>O relaxation rates measured at 11.74 T for GdDO3A-AP (pH 7, 18.5 mM) (left) and for GdDO3AoHAP (pH 4, 12.8 mM) (right). The red and blue lines represent the calculated contributions of the isomeric species SAP and TSAP, respectively.



**Fig S14.** Reduced transverse <sup>17</sup>O relaxation rates (A, C) and chemical shifts (B, D) measured at 11.74 T (pH 7) for GdDO3A-AP (top) and GdDO3A-*p*HAP (bottom).



**Fig S15.** Reduced transverse <sup>17</sup>O relaxation rates (A, C) and chemical shifts (B, D) measured at 11.74 T (pH 7) for GdDO3A-oHAP at pH 4 (top) and GdDO3A-oHAP at pH 9 (bottom).

## 2. <sup>1</sup>H and <sup>13</sup>C NMR spectra of ligands











Fig. S18b <sup>13</sup>C NMR spectrum of DO3A-pHAP



## 3. HPLC chromatograms and ESI-MS spectra of ligands and complexes











Fig. S21a. HPLC-MS chromatogram of DO3A-pHAP





Fig. S22a. HPLC-MS chromatogram of GdDO3A-AP







Fig. S23a. HPLC-MS chromatogram of GdDO3A-oHAP



Fig. S23b. ESI-MS spectrum of GdDO3A-oHAP









#### 4. DFT calculations

DFT calculations were performed within the hybrid meta-GGA approximation with the M062X exchange-correlation functional<sup>4</sup> and the Gaussian 09 package (Revision D.01).<sup>5</sup> Full geometry optimizations were carried out in aqueous solution by using the large-core relativistic effective core potential (LCRECP) of Dolg *et al.* and the associated (7s6p5d)/[5s4p3d]-GTO valence basis set for the Gd.<sup>6</sup> This LCRECP includes 46+4f<sup>7</sup> electrons in the core for Gd and treats explicitely the outermost 11 electrons (5s, 5p, 5d and 6s). The standard 6-311G(d,p) basis set was used for the ligand atoms. All calculations were conducted on a pseudo-singlet state configuration, as the LCRECP includes the 4f electrons in the core. The stationary points found on the potential energy surfaces as a result of the geometry optimizations have been tested to represent energy minima rather than saddle points via frequency analysis. Bulk solvent effects (water) were evaluated by using the polarizable continuum model (PCM), in particular with the integral equation formalism (IEFPCM) variant as implemented in Gaussian 09.<sup>7</sup> Molecular graphics were generated using USCF Chimera (version 1.8).<sup>8</sup> The transition states characterising the dissociative water exchange mechanisms were located with the synchronous transit-guided quasi-Newton approach.<sup>9</sup> Frequency analysis confirmed the nature of the transition states (1 imaginary frequency). Frequency calculations provided zero-point energies (ZPEs), enthalpies (*H*) and free energies (*G*) at 298.15 K and 1 atm.

Center	Atomic	Coordinates (Angstroms)		
Number	Number	Х	Y	Z
1	7	2.261029	-1.898502	0.479601
2	6	3.620660	-1.383377	0.762017
3	6	3.595566	-0.064056	1.524805
4	7	2.869520	1.014220	0.816943
5	6	2.517715	2.100358	1.759307
6	6	1.342948	1.740976	2.654751
7	7	0.090759	1.482019	1.909111
8	6	-0.847804	0.737432	2.779073
9	6	-0.520049	-0.745610	2.848627
10	7	-0.519704	-1.430157	1.532667
11	6	0.197312	-2.723089	1.665969
12	6	1.711459	-2.550708	1.689522
13	6	2.297607	-2.853152	-0.643099
14	6	0.931827	-3.069804	-1.303724
15	8	0.151333	-2.042685	-1.286644
16	8	0.676197	-4.143440	-1.823929
17	6	3.690709	1.550961	-0.284881
18	6	3.671795	0.677540	-1.548431
19	8	4.662182	0.659114	-2.267271
20	8	2.568599	0.061721	-1.765867
21	6	-0.522364	2.743936	1.448096
22	6	-0.156427	3.168256	0.021439
23	8	-0.690518	4.195133	-0.408886
24	8	0.624057	2.415003	-0.640895
25	6	-1.897984	-1.668959	1.075476
26	6	-2.499944	-0.460901	0.382188
27	8	-1.758723	0.400992	-0.072078
28	1	2.933814	-2.430069	-1.424138
29	1	2.711289	-3.820319	-0.337481
30	1	4.725549	1.719878	0.031585

Table S2. Optimized Cartesian Coordinates for GdDO3A-AP (SAP isomer, Charge 0,0 imaginary frequencies).

31	1	3.258418 2.50757	'0 -0.588780		
32	1	-0.297989 3.57410	2.128217		
33	1	-1.607331 2.63039	1.434501		
.34	1	-1.894506 -2.45760	0.314798		
35	- 1	-2536102 -200271	6 1 001220		
35	1		1 0 105416		
20	1	4.143400 -1.23033			
37	1	4.194053 -2.11414	1.346820		
38	1	4.629971 0.24859	1.719432		
39	1	3.129051 -0.21244	2.498599		
40	1	3.379543 2.35500	2.390029		
41	1	2.270025 2.98389	0 1.171450		
42	1	1.186255 2.55662	3.372676		
4.3	1	1.579801 0.85485	3,243494		
<u>л</u> д д	- 1	-0.832536 1 14142	2 799531		
15	1		2 2 108120		
45	1		2.400429		
46		0.465176 -0.87906	3.292/03		
47	Ţ	-1.233902 -1.23462	3.524117		
48	1	-0.096974 -3.36859	0.840449		
49	1	-0.106293 -3.23156	2.589960		
50	1	2.002472 -1.95899	2.557278		
51	1	2.170103 -3.53949	0 1.821220		
52	8	-1.347462 3.03181	8 -2.855595		
53	1	-1 059135 3 56110	-2 086832		
50	1		2.000002		
54			2 -2.039020		
55	04		-0.550255		
56	8	-0.41/584 0.4/9/8	37 -2.514828		
57	1	-1.175694 -0.12229	1 -2.635337		
58	6	-3.965609 -0.33188	30 0.247331		
59	6	-4.835913 -1.37115	0.588550		
60	6	-4.475115 0.86979	-0.257802		
61	6	-6.205375 -1.20718	0.423346		
62	1	-4.457735 -2.31249	0.967117		
63	-	-5 843197 1 03302	-0.408912		
64	6		-0.069016		
65	1		-0.009040		
65	1		0.000340		
66	1	-6.2385/3 1.96519	94 -0.792464		
67	1	-7.777110 0.12059	-0.189683		
68	1	-2.303924 3.12325	6 -2.881134		
69	8	-2.246808 -1.59703	3 -2.309705		
70	1	-1.409745 -2.03260	9 -2.041029		
71	1	-2.613567 -2.12528	-3.023420		
72	1	-3.786014 1.66233	-0.524062		
E(RM062	$(x) = -1866 \ 704^{\circ}$	3336 Hartree			
	1000.701	Jost Marciec			
Zero-po	oint correction	= 0.596813			
Thermal	correction to	Energy = 0.634174			
Thermal correction to Enthalpy = $0.635118$					
Thermal	correction to	Gibbs Free Energy = $0.530233$			
Sum of	electronic and	$z_{ero-point}$ Energies = -1866 107520	)		
Sum of	electronic and	thermal Energies $-1866$ 070160	,		
Sum of	oloctronic and	thermal Enthalping $= 1066.060216$			
SUII OI	electronic and	$\operatorname{chermat} \operatorname{Enchatptes} = -1866.069216$	0.1		
Sum of electronic and thermal Free Energies = $-1866.174101$					

Center Atomic Number Number		Coor X	dinates (Ang Y	stroms) Z
1	 7	2.393627	-1.806523	0.442937
2	6	3.741991	-1.232005	0.669305
3	6	3.688985	0.105066	1.401271
4	7	2.909145	1.141308	0.684254
5	6	2.550338	2.248092	1.601917
6	6	1.429539	1.877552	2.559340
7	7	0.164112	1.526591	1.873713
8	6	-0.700892	0.765183	2.804195
9	6	-0.292941	-0.694186	2.899714
10	7	-0.349894	-1.405551	1.600432
11	6	0.402864	-2.680038	1.713173
12	6	1.912653	-2.470661	1.676288
13	6	2.421483	-2.768063	-0.677121
14	6	1.040968	-3.028238	-1.290820
15	8	0.234443	-2.018333	-1.267191
16	8	0.790470	-4.115576	-1.781159
17	6	3.679936	1.668733	-0.459357
18	6	3.629295	0.770080	-1.703396
19	8	4.579857	0.769582	-2.471032
20	8	2.537403	0.109705	-1.850207
21	6	-0.535366	2.738595	1.398787
22	6	-0.265007	3.135881	-0.056551
23	8	-0.860727	4.131742	-0.473190
2.4	8	0.505723	2.390384	-0.742689
25	6	-1.751034	-1.674824	1.229915
26	6	-2.387161	-0.532797	0.460662
27	8	-1.666636	0.286498	-0.101051
28	1	3.019583	-2.333275	-1.481172
29	1	2.871556	-3.720290	-0.378015
30	1	4.721995	1.862078	-0.184434
31	1	3.222666	2.612717	-0.766421
32	1	-0.327670	3.602013	2.040940
33	1	-1.612691	2.568064	1.438233
34	1	-1.794435	-2.521848	0.537731
35	1	-2.345963	-1.934052	2.111701
36	1	4.230089	-1.111180	-0.297138
37	1	4.360709	-1.925078	1.252706
38	1	4.715258	0.457993	1.564657
39	1	3.247352	-0.036502	2.387818
40	1	3.426156	2.562297	2.183899
41	1	2.240065	3.096148	0.991435
42	1	1.260698	2.718268	3.244030
43	1	1.729256	1.032733	3.178726
44	1	-0.671868	1.205641	3.808612
45	1	-1.734293	0.842504	2.465835
46	1	0.724800	-0.766395	3.280548
47	1	-0.936855	-1.197950	3.631907
48	1	0.093487	-3.335267	0.900635
49	1	0.147616	-3.191006	2.650144

 Table S3. Optimized Cartesian Coordinates for the TS of GdDO3A-AP (SAP isomer, Charge 0, 1 imaginary frequency).

50	1	2.227436	-1.871804	2.530589
51	1	2.400210	-3.447477	1.787748
52	8	-2.349520	2.879377	-2.477524
53	1	-1.828071	3.413328	-1.851293
54	1	-1.883281	1.107461	-2.798012
55	64	0.756272	0.090556	-0.346207
56	8	-1.520401	0.273698	-3.137001
57	1	-1.976004	-0.438754	-2.663798
58	6	-3.853545	-0.403038	0.362407
59	6	-4.728888	-1.326537	0.940791
60	6	-4.357768	0.685669	-0.360455
61	6	-6.100480	-1.157971	0.799019
62	1	-4.355864	-2.181048	1.490670
63	6	-5.727309	0.851087	-0.493104
64	6	-6.598248	-0.070054	0.087737
65	1	-6.780012	-1.873733	1.243871
66	1	-6.120111	1.692856	-1.049728
67	1	-7.668734	0.059746	-0.017130
68	1	-3.240674	3.236134	-2.445008
69	8	-2.374057	-2.120229	-1.850739
70	1	-1.410183	-2.282438	-1.770265
71	1	-2.719776	-2.809573	-2.423607
72	1	-3.661755	1.381356	-0.816542

E(RM062X) = -1866.6865072 Hartree Zero-point correction = 0.594456 Thermal correction to Energy = 0.632349 Thermal correction to Enthalpy = 0.633293 Thermal correction to Gibbs Free Energy = 0.526224 Sum of electronic and zero-point Energies = -1866.092051 Sum of electronic and thermal Energies = -1866.054159 Sum of electronic and thermal Enthalpies = -1866.053215 Sum of electronic and thermal Free Energies = -1866.160283

Table S4. Optimized Cartesian Coordinates for GdDO3A-oHAP (SAP isomer, Charge -1, 0 imaginary frequencies).

Center	Atomic	Coo:	Coordinates (Angstroms)		
Number	Number	Х	Y	Z	
		-1.948386	-2.332661	0.039608	
2	6	-3.406526	-2.105391	0.162202	
3	6	-3.877048	-0.919139	-0.670573	
4	7	-3.215406	0.351975	-0.305727	
5	6	-3.393834	1.350157	-1.385242	
6	6	-2.461233	1.111418	-2.565901	
7	7	-1.025357	1.164072	-2.208273	
8	6	-0.219177	0.494581	-3.255887	
9	6	-0.282439	-1.020300	-3.161214	
10	7	0.240251	-1.539058	-1.880501	
11	6	-0.220283	-2.936046	-1.683142	
12	6	-1.671026	-3.024334	-1.238189	
13	6	-1.440946	-3.107694	1.189006	
14	6	0.020366	-2.816839	1.560290	
15	8	0.601042	-1.873324	0.933499	
16	8	0.524306	-3.478583	2.471094	

17	6	-3.757905	0.867254	0.966156
18	6	-3.173883	0.183740	2.214910
19	8	-3.878920	0.087332	3.210998
20	8	-1.953630	-0.196461	2.113720
21	6	-0.575629	2.558048	-2.045156
22	6	-0.743747	3.132879	-0.634742
23	8	-0.506687	4.338391	-0.489870
24	8	-1 049179	2 326197	0 294086
25	e e	1 717210	-1 493829	-1 837098
25	6	2 274809	-0 303473	-1 05/303
20	8	1 /0823/	0.505475	_0 778783
27	0	-2 016202	-2 021200	-0.770793
20	1	-2.010295	-2.031209	1 025061
29	1	-1.562048	-4.100/03	1.035661
30	1	-4.851011	0.800437	0.992134
31		-3.4/0285	1.91/896	1.051427
32		-1.061/54	3.228835	-2.762824
33	1	0.498472	2.601668	-2.237995
34	1	2.084080	-2.397994	-1.353844
35	1	2.138596	-1.478883	-2.851230
36	1	-3.645388	-1.940051	1.211626
37	1	-3.963881	-2.997046	-0.153075
38	1	-4.964860	-0.819346	-0.557276
39	1	-3.693026	-1.111584	-1.727736
40	1	-4.429673	1.341100	-1.749008
41	1	-3.208036	2.337093	-0.963666
42	1	-2.681171	1.855509	-3.342643
43	1	-2.667230	0.136453	-3.007159
44	1	-0.550945	0.805215	-4.255151
45	1	0.815223	0.817188	-3.141544
46	1	-1.312537	-1.358698	-3.269785
47	1	0.276080	-1.450982	-4.002821
48	1	0.414198	-3.399661	-0.931320
49	1	-0.104351	-3.510861	-2.611416
50	- 1	-2,322581	-2,601379	-2.002660
51	1	-1 942588	-4 085255	-1 154068
52	8	0 134700	4 475531	2 350178
53	1	-0.363855	4 443858	1 520127
54	1	1 781745	1 076969	1 526373
55	64	-0 649349		0 174016
56	8	0.049349	0.000752	1 946647
57	1	1 276002	-0 020118	2 165671
50	-	3 656948	_0 320373	-0 640840
50	6	1 552469	-0.320373	-0.040040
59	6	4.555400	-1.234470	-1.223990
6U C1	6	4.125598	0.589039	0.381067
61	6	5.8//388	-1.309395	-0.8/440/
62	l	4.191040	-1.931332	-1.989081
63	6	5.519292	0.484088	0./16681
64	6	6.353/41	-0.418/86	0.114/4/
65		6.545759	-2.018360	-1.344867
66	1	5.881830	1.160436	1.482287
67	1	7.398817	-0.454118	0.404423
68	8	3.392438	1.422622	1.005381
69	8	2.243125	3.847319	0.599095
70	1	1.016846	4.236760	2.027705
71	1	1.527045	3.919271	-0.042202
72	8	2.490423	-1.453985	2.997162

	73	1		2.	842858	-1.405331	2.100463
	74	1		1.	876066	-2.208290	2.927649
	75	1		2.	597237	2.939535	0.547935
E (RM	062X) = -2	017.9022	2463 Har	 tree			
Zero	-point cor	rection	= 0.613	394			
Ther	mal correc	tion to	Energy	= 0.654190	)		
Ther	mal correc	tion to	Enthalp	y = 0.6551	.35		
Ther	mal correc	tion to	Gibbs F	ree Energy	v = 0.54	2738	
Sum o	of electro	nic and	zero-po	int Energi	.es = -2	017.288852	
Sum o	of electro	nic and	thermal	Energies	= -2017	.248056	
Sum o	of electro	nic and	thermal	Enthalpie	es = -20	17.247112	
Sum o	of electro	nic and	thermal	Free Ener	gies =	-2017.359508	}

Table S5. Optimized Cartesian Coordinates for the TS of GdDO3A-oHAP (SAP isomer, Charge -1, 1 imaginary

frequency).	
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Center	Atomic	Coor	dinates (Ang	stroms)
Number	Number	Х	Y	Z
1	7	1.899973	-2.317050	-0.125941
2	6	3.372881	-2.150751	-0.098141
3	6	3.813493	-1.063640	0.877922
4	7	3.243169	0.268682	0.573389
5	6	3.330152	1.154342	1.758781
6	6	2.259935	0.851240	2.797900
7	7	0.878888	1.018209	2.287357
8	6	-0.075314	0.308803	3.171616
9	6	-0.049344	-1.193582	2.962683
10	7	-0.436918	-1.586249	1.589730
11	6	-0.019316	-2.988906	1.347541
12	6	1.467715	-3.109972	1.047149
13	6	1.471623	-2.974918	-1.375876
14	6	-0.016327	-2.761771	-1.674151
15	8	-0.488290	-1.617022	-1.342838
16	8	-0.662319	-3.658876	-2.209854
17	6	3.947005	0.880715	-0.571316
18	6	3.484831	0.352248	-1.938237
19	8	4.281171	0.348823	-2.865800
20	8	2.254667	-0.010378	-1.996121
21	6	0.513062	2.444960	2.201645
22	6	0.783984	3.110724	0.851336
23	8	0.512312	4.304038	0.743349
24	8	1.221415	2.359051	-0.087025
25	6	-1.897717	-1.462229	1.399561
26	6	-2.342403	-0.169090	0.714147
27	8	-1.468567	0.669258	0.416444
28	1	2.011042	-2.508911	-2.203864
29	1	1.693722	-4.046950	-1.363476
30	1	5.032230	0.765865	-0.481034
31	1	3.710064	1.947214	-0.580551
32	1	0.995441	3.035065	2.989259
33	1	-0.564530	2.541943	2.344548
34	1	-2.244211	-2.271806	0.753375
35	1	-2.417117	-1.567545	2.359052

$\begin{array}{cccccccccccccccccccccccccccccccccccc$	36	1	3.710811	-1.911401	-1.105552
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	37	1	3.858596	-3.092744	0.185961
391 $3.520140$ $-1.337462$ $1.891543$ 401 $4.316658$ $1.066513$ $2.231238$ 411 $3.224002$ $2.182637$ $1.414998$ 421 $2.418557$ $1.503124$ $3.666476$ 431 $2.372487$ $-0.171851$ $3.155703$ 441 $0.136495$ $0.530340$ $4.22541$ 451 $-1.076423$ $0.683052$ $2.956180$ 461 $0.947647$ $-1.584900$ $3.162993$ 471 $-0.720122$ $-1.663344$ $.692258$ 481 $-0.602609$ $-3.386913$ $0.518672$ 491 $-0.249338$ $-3.612839$ $2.220674$ 501 $2.047843$ $-2.785513$ $1.910627$ 511 $1.708671$ $-4.169318$ $0.889670$ 528 $0.894279$ $3.428291$ $-2.670448$ 531 $1.230189$ $3.122893$ $-1.813766$ 541 $-2.178073$ $1.036195$ $-1.979453$ 5564 $0.756853$ $0.048652$ $-0.193034$ 568 $-1.615365$ $0.56794$ $-2.623462$ 571 $-1.481698$ $-0.320401$ $-2.266471$ 586 $-3.736907$ $0.007474$ $0.1414795$ 596 $-4.692996$ $-0.920253$ $0.923731$ 606 $-4.186409$ $1.123372$ $-0.398108$ 616 $-6.036098$ $-0.771086$ $-0.77036653$ <	38	1	4.909752	-1.010834	0.874071
401 $4.316658$ $1.066513$ $2.231238$ $41$ 1 $3.224002$ $2.182637$ $1.414998$ $42$ 1 $2.418557$ $1.503124$ $3.666476$ $43$ 1 $2.372487$ $-0.171851$ $3.155703$ $44$ 1 $0.136495$ $0.530340$ $4.22541$ $45$ 1 $-1.076423$ $0.683052$ $2.956180$ $46$ 1 $0.947647$ $-1.584900$ $3.162993$ $47$ 1 $-0.720122$ $-1.665384$ $3.692258$ $48$ 1 $-0.602609$ $-3.386913$ $0.518672$ $49$ 1 $-0.249338$ $-3.612839$ $2.220674$ $50$ 1 $2.047843$ $-2.785513$ $1.910627$ $51$ 1 $1.708671$ $-4.169318$ $0.889670$ $52$ 8 $0.894279$ $3.428291$ $-2.670448$ $53$ 1 $1.230189$ $3.122893$ $-1.813766$ $54$ 1 $-2.178073$ $1.036195$ $-1.979453$ $55$ $64$ $0.756853$ $0.49652$ $-0.193034$ $56$ 8 $-1.615365$ $0.567994$ $-2.2623462$ $57$ 1 $-1.481698$ $-0.320401$ $-2.266471$ $58$ 6 $-3.736907$ $0.007474$ $0.414795$ $59$ 6 $-4.692996$ $-0.920253$ $0.923731$ $60$ 6 $-4.186409$ $1.123372$ $-0.398108$ $61$ 6 $-6.492502$ $0.344365$ $-0.030123$ $65$ 1 $-6.740338$ <t< td=""><td>39</td><td>1</td><td>3.520140</td><td>-1.337462</td><td>1.891543</td></t<>	39	1	3.520140	-1.337462	1.891543
411 $3.224002$ $2.182637$ $1.414998$ 421 $2.418557$ $1.503124$ $3.66676$ 431 $2.372487$ $-0.171851$ $3.155703$ 441 $0.136495$ $0.530340$ $4.225441$ 451 $-1.076423$ $0.683052$ $2.956180$ 461 $0.947647$ $-1.584900$ $3.162993$ 471 $-0.720122$ $-1.665384$ $3.692258$ 481 $-0.602609$ $-3.386913$ $0.518672$ 491 $-0.249338$ $-3.612839$ $2.220674$ 501 $2.047843$ $-2.785513$ $1.910627$ 511 $1.708671$ $-4.169318$ $0.889670$ 528 $0.894279$ $3.428291$ $-2.670448$ 531 $1.230189$ $3.122893$ $-1.813766$ 541 $-2.178073$ $1.036195$ $-1.979453$ 5564 $0.756853$ $0.048652$ $-0.193034$ 568 $-1.615365$ $0.567994$ $-2.623462$ 571 $-1.481698$ $-0.220401$ $-2.266471$ 586 $-3.76907$ $0.007474$ $0.414795$ 596 $-4.692996$ $-0.920253$ $0.923731$ 606 $-4.186409$ $1.123372$ $-0.398108$ 616 $-6.36098$ $-0.771086$ $0.717006$ 621 $-4.354311$ $-1.77245$ $1.498966$ 636 $-5.615201$ $1.246649$ $-0.558663$ <td< td=""><td>40</td><td>1</td><td>4.316658</td><td>1.066513</td><td>2.231238</td></td<>	40	1	4.316658	1.066513	2.231238
421 $2.418557$ $1.503124$ $3.666476$ $43$ 1 $2.372487$ $-0.171851$ $3.155703$ $44$ 1 $0.136495$ $0.530340$ $4.225441$ $45$ 1 $-1.076423$ $0.683052$ $2.956180$ $46$ 1 $0.947647$ $-1.584900$ $3.162993$ $47$ 1 $-0.720122$ $-1.665384$ $3.692258$ $48$ 1 $-0.602609$ $-3.386913$ $0.518672$ $49$ 1 $-0.249338$ $-3.612839$ $2.220674$ $50$ 1 $2.047843$ $-2.785513$ $1.910627$ $51$ 1 $1.708671$ $-4.169318$ $0.889670$ $52$ 8 $0.894279$ $3.428291$ $-2.670448$ $53$ 1 $1.230189$ $3.122893$ $-1.813766$ $54$ 1 $-2.178073$ $1.036195$ $-1.979453$ $55$ $64$ $0.756853$ $0.048652$ $-0.193034$ $56$ 8 $-1.615365$ $0.567994$ $-2.623462$ $57$ 1 $-1.481698$ $-0.320401$ $-2.226471$ $58$ 6 $-3.736907$ $0.007474$ $0.414795$ $59$ 6 $-4.929966$ $-0.920253$ $0.923731$ $60$ 6 $-4.186409$ $1.12372$ $-0.398108$ $61$ 6 $-6.492502$ $0.344365$ $-0.030123$ $65$ 1 $-7.57541$ $0.477746$ $-0.398108$ $61$ 6 $-6.492502$ $0.92026$ $-1.143079$ $67$ 1 $-7.595987$	41	1	3.224002	2.182637	1.414998
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	42	1	2.418557	1.503124	3.666476
441 $0.136495$ $0.530340$ $4.225441$ $45$ 1 $-1.076423$ $0.683052$ $2.956180$ $46$ 1 $0.947647$ $-1.584900$ $3.162933$ $47$ 1 $-0.720122$ $-1.665384$ $3.692258$ $48$ 1 $-0.602609$ $-3.386913$ $0.518672$ $49$ 1 $-0.249338$ $-3.612839$ $2.220674$ $50$ 1 $2.047843$ $-2.785513$ $1.910627$ $51$ 1 $1.708671$ $-4.169318$ $0.889670$ $52$ 8 $0.894279$ $3.428291$ $-2.670448$ $53$ 1 $1.230189$ $3.122893$ $-1.813766$ $54$ 1 $-2.178073$ $1.036195$ $-1.979453$ $55$ $64$ $0.756853$ $0.048652$ $-0.1930346$ $57$ 1 $-1.481698$ $-0.320401$ $-2.266471$ $58$ 6 $-3.736907$ $0.007474$ $0.414795$ $59$ 6 $-4.692996$ $0.920253$ $0.923731$ $60$ 6 $-4.186409$ $1.123372$ $-0.398108$ $61$ 6 $-6.036098$ $-0.771086$ $0.717006$ $62$ 1 $-4.354311$ $-1.772245$ $1.499896$ $63$ 6 $-5.615201$ $1.246649$ $-0.558663$ $64$ 6 $-6.492502$ $0.344365$ $-0.030123$ $65$ 1 $-0.559987$ $2.092026$ $-1.143079$ $67$ 1 $-7.557541$ $0.473766$ $-0.980734$ $69$ 8 $-3.421307$	43	1	2.372487	-0.171851	3.155703
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	44	1	0.136495	0.530340	4.225441
461 $0.947647$ $-1.584900$ $3.162993$ $47$ 1 $-0.720122$ $-1.665384$ $3.692258$ $48$ 1 $-0.602609$ $-3.386913$ $0.518672$ $49$ 1 $-0.249338$ $-3.612839$ $2.220674$ $50$ 1 $2.047843$ $-2.785513$ $1.910627$ $51$ 1 $1.708671$ $-4.169318$ $0.889670$ $52$ 8 $0.894279$ $3.422891$ $-2.670448$ $53$ 1 $1.230189$ $3.122893$ $-1.813766$ $54$ 1 $-2.178073$ $1.036195$ $-1.979453$ $55$ $64$ $0.756853$ $0.048652$ $-0.193034$ $56$ 8 $-1.615365$ $0.567994$ $-2.623462$ $57$ 1 $-1.481698$ $-0.320401$ $-2.266471$ $58$ 6 $-3.736977$ $0.007474$ $0.414795$ $59$ 6 $-4.692996$ $-0.920253$ $0.923731$ $60$ 6 $-4.186409$ $1.123372$ $-0.398108$ $61$ 6 $-6.336098$ $-0.771086$ $0.17006$ $62$ 1 $-4.554311$ $-1.772245$ $1.499896$ $63$ 6 $-5.615201$ $1.246649$ $-0.558663$ $64$ 6 $-6.740338$ $-1.486630$ $1.120417$ $66$ 1 $-7.557541$ $0.477746$ $-0.189580$ $68$ 8 $-3.421307$ $1.943706$ $-0.980734$ $69$ 8 $-1.518593$ $3.901690$ $-1.303705$ $70$ 1 $-0.9524$	45	1	-1.076423	0.683052	2.956180
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	46	1	0.947647	-1.584900	3.162993
481 $-0.602609$ $-3.386913$ $0.518672$ $49$ 1 $-0.249338$ $-3.612839$ $2.220674$ $50$ 1 $2.047843$ $-2.785513$ $1.910627$ $51$ 1 $1.708671$ $-4.169318$ $0.889670$ $52$ 8 $0.894279$ $3.428291$ $-2.670448$ $53$ 1 $1.230189$ $3.122893$ $-1.813766$ $54$ 1 $-2.178073$ $1.036195$ $-1.979453$ $55$ $64$ $0.756853$ $0.048652$ $-0.193034$ $56$ 8 $-1.615365$ $0.567994$ $-2.623462$ $57$ 1 $-1.481698$ $-0.320401$ $-2.266471$ $58$ 6 $-3.736907$ $0.007474$ $0.414795$ $59$ 6 $-4.622996$ $-0.920253$ $0.923731$ $60$ 6 $-4.06098$ $-0.771086$ $0.717066$ $62$ 1 $-4.354311$ $-1.772245$ $1.499896$ $63$ 6 $-5.615201$ $1.246649$ $-0.558663$ $64$ 6 $-6.492502$ $0.344365$ $-0.030123$ $65$ 1 $-7.557541$ $0.477746$ $-0.189580$ $68$ 8 $-3.421307$ $1.943706$ $-0.980734$ $69$ 8 $-1.518593$ $3.901690$ $-1.303705$ $70$ 1 $-0.052457$ $4.103384$ $-0.545512$ $72$ 8 $-3.22049$ $-3.017944$ $-1.222507$ $73$ 1 $-2.402557$ $-3.200718$ $-1.663257$ $74$ 1 $-2.40$	47	1	-0.720122	-1.665384	3.692258
491 $-0.249338$ $-3.612839$ $2.220674$ $50$ 1 $2.047843$ $-2.785513$ $1.910627$ $51$ 1 $1.708671$ $-4.169318$ $0.889670$ $52$ 8 $0.894279$ $3.428291$ $-2.670448$ $53$ 1 $1.230189$ $3.122893$ $-1.813766$ $54$ 1 $-2.178073$ $1.036195$ $-1.979453$ $55$ $64$ $0.756853$ $0.048652$ $-0.193034$ $56$ 8 $-1.615365$ $0.567994$ $-2.262462$ $57$ 1 $-1.481698$ $-0.320401$ $-2.26474$ $58$ 6 $-3.736907$ $0.007474$ $0.414795$ $59$ 6 $-4.692996$ $-0.920253$ $0.923731$ $60$ 6 $-4.186409$ $1.123372$ $-0.398108$ $61$ 6 $-6.036098$ $-0.771086$ $0.717006$ $62$ 1 $-4.354311$ $-1.772245$ $1.499896$ $63$ 6 $-5.615201$ $1.246649$ $-0.558663$ $64$ 6 $-6.740338$ $-1.486630$ $1.120417$ $65$ 1 $-7.557541$ $0.477746$ $-0.189580$ $68$ 8 $-3.421307$ $1.943706$ $-0.980734$ $69$ 8 $-1.518593$ $3.901690$ $-1.303705$ $70$ 1 $-0.922457$ $4.103384$ $-0.545512$ $72$ 8 $-3.250489$ $-3.017944$ $-1.222507$ $73$ 1 $-2.402557$ $-3.200718$ $-1.663257$ $75$ 1 $-2.1$	48	1	-0.602609	-3.386913	0.518672
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	49	1	-0.249338	-3.612839	2.220674
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	50	1	2.047843	-2.785513	1.910627
528 $0.894279$ $3.428291$ $-2.670448$ $53$ 1 $1.230189$ $3.122893$ $-1.813766$ $54$ 1 $-2.178073$ $1.036195$ $-1.979453$ $55$ $64$ $0.756853$ $0.048652$ $-0.193034$ $56$ 8 $-1.615365$ $0.567994$ $-2.623462$ $57$ 1 $-1.481698$ $-0.320401$ $-2.266471$ $58$ 6 $-3.736907$ $0.007474$ $0.414795$ $59$ 6 $-4.692996$ $-0.920253$ $0.923731$ $60$ 6 $-4.186409$ $1.123372$ $-0.398108$ $61$ 6 $-6.036098$ $-0.771086$ $0.717006$ $62$ 1 $-4.354311$ $-1.772245$ $1.499896$ $63$ 6 $-5.615201$ $1.246649$ $-0.558663$ $64$ 6 $-6.740338$ $-1.486630$ $1.120417$ $66$ 1 $-5.959987$ $2.092026$ $-1.143079$ $67$ 1 $-7.557541$ $0.477746$ $-0.189580$ $68$ 8 $-3.421307$ $1.943706$ $-0.980734$ $69$ 8 $-1.518593$ $3.901690$ $-1.303705$ $70$ 1 $-0.034446$ $3.596883$ $-2.444348$ $71$ 1 $-0.952457$ $4.103384$ $-0.545512$ $72$ 8 $-3.250489$ $-3.017944$ $-1.222507$ $73$ 1 $-2.402557$ $-3.200718$ $-1.663257$ $75$ 1 $-2.113020$ $3.181040$ $-1.029216$	51	1	1.708671	-4.169318	0.889670
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	52	8	0.894279	3.428291	-2.670448
541 $-2.178073$ $1.036195$ $-1.979453$ $55$ $64$ $0.756853$ $0.048652$ $-0.193034$ $56$ $8$ $-1.615365$ $0.567994$ $-2.623462$ $57$ $1$ $-1.481698$ $-0.320401$ $-2.266471$ $58$ $6$ $-3.736907$ $0.007474$ $0.414795$ $59$ $6$ $-4.692996$ $-0.920253$ $0.923731$ $60$ $6$ $-4.186409$ $1.123372$ $-0.398108$ $61$ $6$ $-6.036098$ $-0.771086$ $0.717006$ $62$ $1$ $-4.354311$ $-1.772245$ $1.499896$ $63$ $6$ $-5.615201$ $1.246649$ $-0.558663$ $64$ $6$ $-6.740338$ $-1.486630$ $1.120417$ $66$ $1$ $-5.959987$ $2.092026$ $-1.143079$ $67$ $1$ $-7.557541$ $0.477746$ $-0.189580$ $68$ $8$ $-3.421307$ $1.943706$ $-0.980734$ $69$ $8$ $-1.518593$ $3.901690$ $-1.303705$ $70$ $1$ $-0.034446$ $3.596883$ $-2.444348$ $71$ $1$ $-0.952457$ $4.103384$ $-0.545512$ $72$ $8$ $-3.250489$ $-3.017944$ $-1.222507$ $73$ $1$ $-2.402557$ $-3.200718$ $-1.663257$ $75$ $1$ $-2.113020$ $3.181040$ $-1.029216$	53	1	1.230189	3.122893	-1.813766
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	54	1	-2.178073	1.036195	-1.979453
568 $-1.615365$ $0.567994$ $-2.623462$ $57$ 1 $-1.481698$ $-0.320401$ $-2.266471$ $58$ 6 $-3.736907$ $0.007474$ $0.414795$ $59$ 6 $-4.692996$ $-0.920253$ $0.923731$ $60$ 6 $-4.186409$ $1.123372$ $-0.398108$ $61$ 6 $-6.036098$ $-0.771086$ $0.717006$ $62$ 1 $-4.354311$ $-1.772245$ $1.499896$ $63$ 6 $-5.615201$ $1.246649$ $-0.558663$ $64$ 6 $-6.740338$ $-1.486630$ $1.120417$ $66$ 1 $-5.959987$ $2.092026$ $-1.143079$ $67$ 1 $-7.557541$ $0.477746$ $-0.189580$ $68$ 8 $-3.421307$ $1.943706$ $-0.980734$ $69$ 8 $-1.518593$ $3.901690$ $-1.303705$ $70$ 1 $-0.034446$ $3.596883$ $-2.444348$ $71$ 1 $-0.952457$ $4.103384$ $-0.545512$ $72$ 8 $-3.250489$ $-3.017944$ $-1.222507$ $73$ 1 $-2.402557$ $-3.200718$ $-1.663257$ $75$ 1 $-2.113020$ $3.181040$ $-1.029216$	55	64	0.756853	0.048652	-0.193034
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	56	8	-1.615365	0.567994	-2.623462
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	57	1	-1.481698	-0.320401	-2.266471
596 $-4.692996$ $-0.920253$ $0.923731$ $60$ 6 $-4.186409$ $1.123372$ $-0.398108$ $61$ 6 $-6.036098$ $-0.771086$ $0.717006$ $62$ 1 $-4.354311$ $-1.772245$ $1.499896$ $63$ 6 $-5.615201$ $1.246649$ $-0.558663$ $64$ 6 $-6.492502$ $0.344365$ $-0.030123$ $65$ 1 $-6.740338$ $-1.486630$ $1.120417$ $66$ 1 $-5.959987$ $2.092026$ $-1.143079$ $67$ 1 $-7.557541$ $0.477746$ $-0.189580$ $68$ 8 $-3.421307$ $1.943706$ $-0.980734$ $69$ 8 $-1.518593$ $3.901690$ $-1.303705$ $70$ 1 $-0.952457$ $4.103384$ $-0.545512$ $72$ 8 $-3.250489$ $-3.017944$ $-1.222507$ $73$ 1 $-2.402557$ $-3.200718$ $-1.663257$ $75$ 1 $-2.113020$ $3.181040$ $-1.029216$	58	6	-3.736907	0.007474	0.414795
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	59	6	-4.692996	-0.920253	0.923731
61 $6$ $-6.036098$ $-0.771086$ $0.717006$ $62$ 1 $-4.354311$ $-1.772245$ $1.499896$ $63$ $6$ $-5.615201$ $1.246649$ $-0.558663$ $64$ $6$ $-6.492502$ $0.344365$ $-0.030123$ $65$ 1 $-6.740338$ $-1.486630$ $1.120417$ $66$ 1 $-5.959987$ $2.092026$ $-1.143079$ $67$ 1 $-7.557541$ $0.477746$ $-0.189580$ $68$ 8 $-3.421307$ $1.943706$ $-0.980734$ $69$ 8 $-1.518593$ $3.901690$ $-1.303705$ $70$ 1 $-0.952457$ $4.103384$ $-0.545512$ $72$ 8 $-3.250489$ $-3.017944$ $-1.222507$ $73$ 1 $-2.402557$ $-3.200718$ $-1.663257$ $75$ 1 $-2.113020$ $3.181040$ $-1.029216$	60	6	-4.186409	1.123372	-0.398108
621 $-4.354311$ $-1.772245$ $1.499896$ $63$ 6 $-5.615201$ $1.246649$ $-0.558663$ $64$ 6 $-6.492502$ $0.344365$ $-0.030123$ $65$ 1 $-6.740338$ $-1.486630$ $1.120417$ $66$ 1 $-5.959987$ $2.092026$ $-1.143079$ $67$ 1 $-7.557541$ $0.477746$ $-0.189580$ $68$ 8 $-3.421307$ $1.943706$ $-0.980734$ $69$ 8 $-1.518593$ $3.901690$ $-1.303705$ $70$ 1 $-0.034446$ $3.596883$ $-2.444348$ $71$ 1 $-0.952457$ $4.103384$ $-0.545512$ $72$ 8 $-3.250489$ $-3.017944$ $-1.222507$ $73$ 1 $-2.402557$ $-3.200718$ $-1.663257$ $75$ 1 $-2.113020$ $3.181040$ $-1.029216$	61	6	-6.036098	-0.771086	0.717006
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	62	1	-4.354311	-1.772245	1.499896
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	63	6	-5.615201	1.246649	-0.558663
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	64	6	-6.492502	0.344365	-0.030123
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	65	1	-6.740338	-1.486630	1.120417
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	66	1	-5.959987	2.092026	-1.143079
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	67	1	-7.557541	0.477746	-0.189580
69       8       -1.518593       3.901690       -1.303705         70       1       -0.034446       3.596883       -2.444348         71       1       -0.952457       4.103384       -0.545512         72       8       -3.250489       -3.017944       -1.222507         73       1       -3.346145       -2.061637       -1.277038         74       1       -2.402557       -3.200718       -1.663257         75       1       -2.113020       3.181040       -1.029216	68	8	-3.421307	1.943706	-0.980734
70       1       -0.034446       3.596883       -2.444348         71       1       -0.952457       4.103384       -0.545512         72       8       -3.250489       -3.017944       -1.222507         73       1       -3.346145       -2.061637       -1.277038         74       1       -2.402557       -3.200718       -1.663257         75       1       -2.113020       3.181040       -1.029216	69	8	-1.518593	3.901690	-1.303705
71       1       -0.952457       4.103384       -0.545512         72       8       -3.250489       -3.017944       -1.222507         73       1       -3.346145       -2.061637       -1.277038         74       1       -2.402557       -3.200718       -1.663257         75       1       -2.113020       3.181040       -1.029216	70	1	-0.034446	3.596883	-2.444348
72       8       -3.250489       -3.017944       -1.222507         73       1       -3.346145       -2.061637       -1.277038         74       1       -2.402557       -3.200718       -1.663257         75       1       -2.113020       3.181040       -1.029216	71	1	-0.952457	4.103384	-0.545512
73       1       -3.346145       -2.061637       -1.277038         74       1       -2.402557       -3.200718       -1.663257         75       1       -2.113020       3.181040       -1.029216	72	8	-3.250489	-3.017944	-1.222507
74         1         -2.402557         -3.200718         -1.663257           75         1         -2.113020         3.181040         -1.029216	73	1	-3.346145	-2.061637	-1.277038
75 1 -2.113020 3.181040 -1.029216	74	1	-2.402557	-3.200718	-1.663257
	75	1	-2.113020	3.181040	-1.029216

E(RM062X) = -2017.8947611 Hartree Zero-point correction = 0.612954 Thermal correction to Energy = 0.653343 Thermal correction to Enthalpy = 0.654287 Thermal correction to Gibbs Free Energy = 0.543542 Sum of electronic and zero-point Energies = -2017.281807 Sum of electronic and thermal Energies = -2017.241418 Sum of electronic and thermal Enthalpies = -2017.240474 Sum of electronic and thermal Free Energies = -2017.351219

#### 5. Additional References

- (1) C. H. R. Martínez, C, Dardonville, ACS Med. Chem. Lett. 2013, 4, 142-145
- (2) M. Bolte and M. Kettner, Acta Cryst., C54, 1998, 963-964
- (3) S. Aime, M. Botta, M. Fasano, M. P. M. Marques, C. F. G. C. Geraldes, D. Pubanz, A. E. Merbach, *Inorg. Chem.* 1997, **36**, 2059-2068.
- (4) Y. Zhao and D. G. Truhlar, *Theor. Chem. Accounts*, 2008, **120**, 215.
- (5) M. J. Frisch et al. Gaussian, Inc., Wallingford CT, 2009.
- (6) M. Dolg, H. Stoll, A. Savin, H. Preuss. *Theor. Chim. Acta*, 1989, **75**, 173.
- (7) J. Tomasi, B. Mennucci, R. Cammi, *Chem. Rev.*, 2005, **105**, 2999.
- (8) Pettersen, E. F., Goddard, T. D., Huang, C. C., Couch, G. S., Greenblatt, D. M., Meng, E. C. Ferrin, T. E. J. Comput. Chem., 2004, 25, 1605-1612.
- (9) (a) C. Peng and H. B. Schlegel, *Israel J. of Chem.*, 1993, **33**, 449; (b) C. Peng, P. Y. Ayala, H. B. Schlegel and M. J. Frisch, *J. Comp. Chem.*, 1995, **16**, 49.