

Electronic Supplementary Material

for

Yb(AAZTA)(H₂O)]⁻: an unconventional ParaCEST MRI probe.

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Synthesis of Yb(AAZTA). The Yb^{III}-complex was readily synthesized by adding stoichiometric amounts of aqueous YbCl₃ to a solution of the starting ligand in water at room temperature, maintaining neutral pH by means of 0.1M NaOH. The pH was then increased to nine to precipitate excess Yb^{III} as hydroxide. The solution was centrifuged (4000 rpm, 3 min, r.t.) and the supernatant filtered through a 0.2 μm filter. The pH was re-adjusted to 7 and the solvent removed *in vacuo* to obtain a colourless solid. The xylenol orange indicator verified the absence of free Yb³⁺. 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. MS (ESI⁻): m/z: found 530.1 [M]⁻; calcd for C₁₄H₁₉N₃O₈Yb [Yb(AAZTA)]⁻: 530.4 [M]⁻.

Relaxometric measurements. The water proton longitudinal relaxation rates of aqueous solutions were measured at 298 K by using a Stellar Spinmaster Relaxometer equipped with a Bruker WP80 NMR electromagnet adapted to variable-field measurements operating in the range of 20–70 MHz. The standard inversion–recovery method was employed (16 experiments, 2 scans) with a typical 90° pulse width of 3.5 μs, and the reproducibility of the T₁ data was ± 0.5%. The temperature was controlled using a Stellar VTC-91 variable temperature unit equipped with a copper-constantan thermocouple (uncertainty of ± 0.1 °C). The concentration of the Yb^{III} and Dy^{III}-chelates was determined by ¹H-NMR (500 MHz) measurements using Evans's method (D. F. Evans, G. V. Fazakerley, R. F. Phillips. J. Chem. Soc. (A), 1971, 1931-1934)

¹H NMR Measurements. [Yb(AAZTA)]⁻ was dissolved either in D₂O or in H₂O, and the pH was adjusted to 7.0 by addition of HCl or KOH and checked with a glass electrode connected to a pH-meter. The spectra were recorded at 14.1 T on a Bruker Avance 600 spectrometer. The temperature was controlled with Bruker thermostating units.

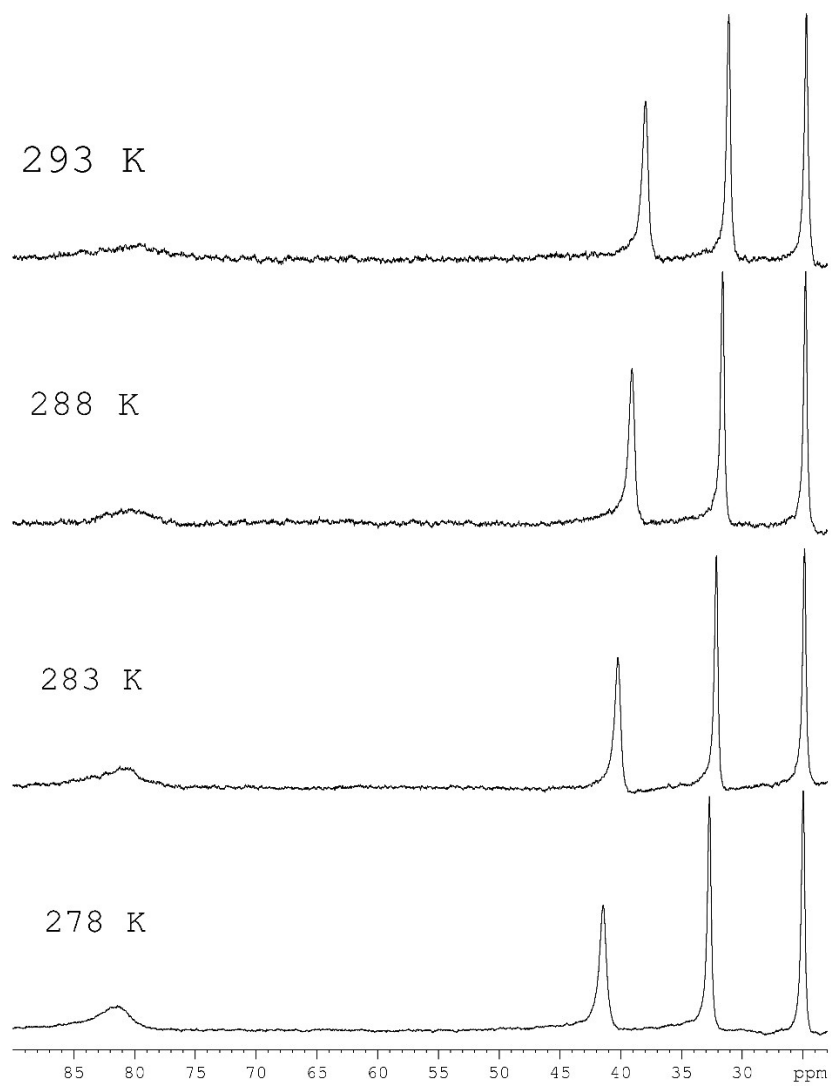


Figure S1: 14.1 T Variable Temperature ^1H NMR spectra (high field region) of a solution 20 mM of $[\text{Yb}(\text{AAZTA})(\text{H}_2\text{O})]^-$ in water.

CEST Measurements

Z-spectra were acquired at 7T on a Bruker Avance 300 spectrometer equipped with a micro-imaging probe. A frequency-offset range of ± 200 ppm was investigated. A typical RARE spin-echo sequence RARE factor=32 with an echo time of 3 ms and a TR value of 5 s was used. An isotropic 64×64 acquisition matrix with a FOV of 10 mm and a slice thickness of 1mm were used. The whole sequence was preceded by a saturation scheme consisting of a continuous rectangular wave pulse 1 s long with a radiofrequency B_2 intensity of $48 \mu\text{T}$. The Z-spectra were interpolated by smoothing splines to identify the zero-offset on a pixel-by-pixel basis of the bulk water and, then, to assess the correct ST% value over the entire range of frequency offsets investigated. Custom-made software, compiled in the Matlab platform (Mathworks Inc., Natick, MA), was used (Stancanello J, Terreno E, Castelli DD, Cabella C, Uggeri F, Aime S. *Contrast Media Mol Imaging*. 2008,4:136-49). The extent of the CEST effect was obtained by comparing the two water signal intensities obtained upon irradiation at $\Delta\omega$ and $-\Delta\omega$ values (bulk water assigned to zero):

$$\text{ST}\% = 1 - \frac{\text{MS}(\Delta\omega)}{\text{MS}(-\Delta\omega)}$$

in which MS refers to the water MR signal intensity.