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ARTICLE

Supporting Information to:

Solution thermodynamics, computational and relaxometric studies of ditopic DO3A-based Mn(II) complexes

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Protonation and complexation equilibria

The protonation constants of ligands, defined by Equation (1):

$$K_{\mathrm{i}}^{\mathrm{H}} = \frac{[\mathrm{H_iL}]}{[\mathrm{H_{i-1}L}][\mathrm{H^+}]} \tag{1}$$

where i=1, 2 …8, The protonation constants of ligands of **L1** have also been investigated with ^{1}H-NMR titrations by recording the chemical shift of the non-labile protons as a function of pH. The ^{1}H-NMR titration and the fits of the experimental data points are shown in Figure S1.

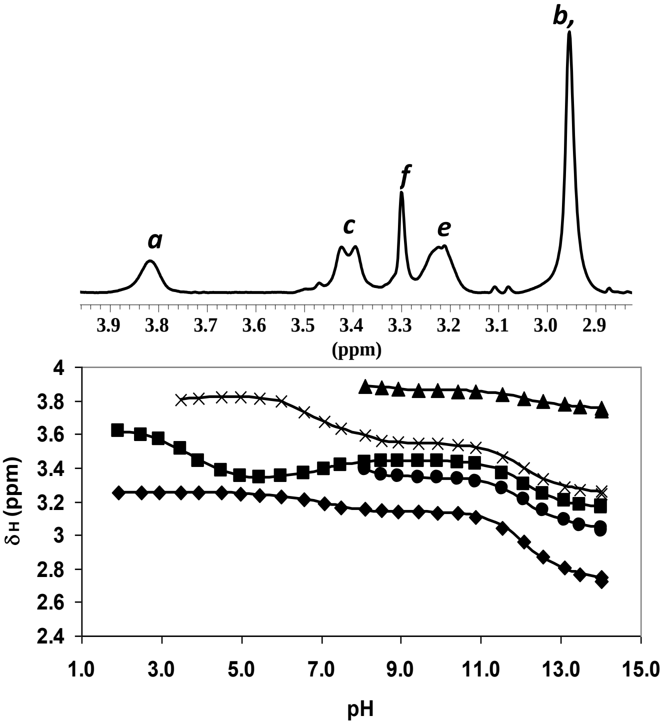

Figure S1. ^{1}H-NMR spectrum at pH=12.02 and ^{1}H-NMR titration curve of **L1** ligand.

(a (▲); b,d (♦); c (×); e (•) and f(■); 400 MHz, 0.1 M KCl, 25°C)

The ^{1}H-NMR titration curve displays sharp changes at different pH values, which are related to the protonation of the ligand. Since the protonation/deprotonation of the different donor atoms is generally fast process on the NMR time scale, the chemical shifts of the observed signals represent a weighted average of the shifts of the different species involved in a specific protonation step (Eq. 2) [Pagado, J. M.; Goldberg, D. E.; Fernelius, W. C., *J. Phys. Chem.*, 1961, **65**, 1062]:

$$\delta_{H(obs)} = \sum x_i \delta_H^{H_iL} \tag{2}$$

where, $\delta_{H(obs)}$ is the observed chemical shift of a given signal, x_i and $\delta_H^{H_iL}$ are the molar fraction and the chemical shift of the involved species, respectively. The observed chemical shifts have been fitted with Eq. 2 (the molar fractions x_i of the different protonated species are expressed with the use of the protonation constants K_i^H).

The protonation and stability constants of the Mn(II)-complexes formed with **L1** and **L2** ligands have been calculated from the titration curves obtained at 1:1 and 2:1 metal to ligand concentration ratios. The best fitting was obtained by using the model which includes the formation of MnL, $MnHL$, MnH_2L, MnH_3L, MnH_4L, Mn_2L, Mn_2H_1L and Mn_2H_2L species. The stability and protonation constants of the metal complexes formed with **L1** and **L2** ligands have been defined by Equations (3) - (6).

$$K_{\mathrm{MnL}} = \frac{[\mathrm{MnL}]}{[\mathrm{Mn}^{2+}][\mathrm{L}]} \tag{3}$$

$$K_{\mathrm{MnH_iL}} = \frac{[\mathrm{MnH_iL}]}{[\mathrm{MnH_{i-1}L}][\mathrm{H}^+]} \tag{4}$$

$$K_{\mathrm{Mn_2L}} = \frac{[\mathrm{Mn_2L}]}{[\mathrm{MnL}][\mathrm{Mn}^{2+}]} \tag{5}$$

$$K_{\mathrm{Mn_2H_iL}} = \frac{[\mathrm{Mn_2H_iL}]}{[\mathrm{Mn_2H_{i-1}L}][\mathrm{H}^+]} \tag{6}$$

where *i*=1, 2, …4. The pH-potentiometric titration curves of the H_6**L1**, H_6**L2** ligands and Mn(II)-**L1**, Mn(II)-**L2** systems are shown in Figure S2 and S3.

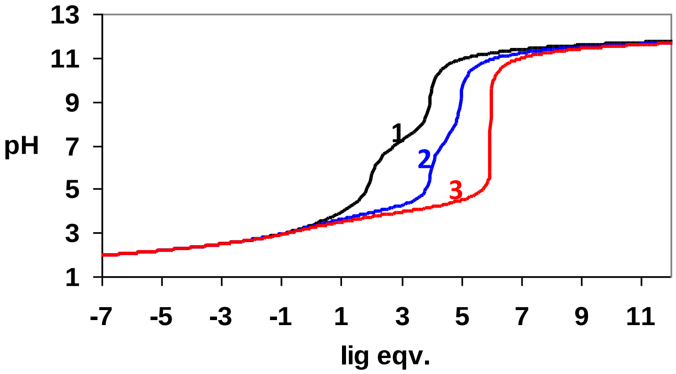

Figure S2. Titration curve of the H_6**L1** ligand in the absence (**1**) and in the presence of one (**2**) and two (**3**) equivalent of Mn(II). ([H_6**L1**]=2.0 mM (**1**); [H_6**L1**]=[Mn^{2+}]=2.0 mM (**2**); [H_6**L1**]=2.0 mM, [Mn^{2+}]=4.0 mM (**3**); [HCl]=0.014 M, 0.1 M KCl, 25°C).

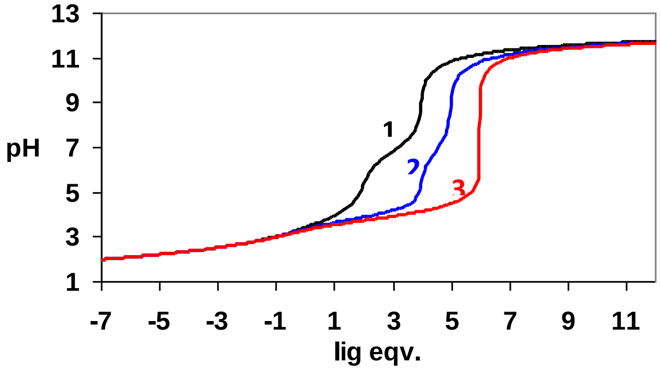

Figure S3. Titration curve of the H_6**L2** ligand in the absence (**1**) and in the presence of one (**2**) and two (**3**) equivalent of Mn(II). ([H_6**L2**]=2.0 mM (**1**); [H_6**L2**]=[Mn^{2+}]=2.0 mM (**2**); [H_6**L2**]=2.0 mM, [Mn^{2+}]=4.0 mM (**3**); [HCl]=0.014 M, 0.1 M KCl, 25°C).

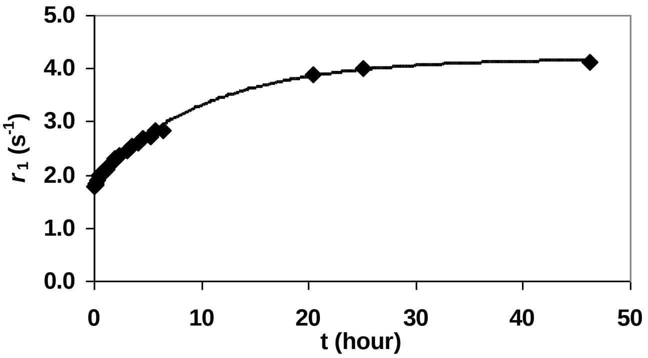

Figure S4. The relaxivity (r_{1p}) values of the Mn_2**L1** - Zn^{2+} reacting system as a function of time. ([Mn_2**L1**]=0.5 mM; [Zn^{2+}]=10 mM, pH=4.6, [*N*,*N*-dimethyl-piperazine]=0.01 M, 20 MHz, 0.1 M KCl, 25°C).

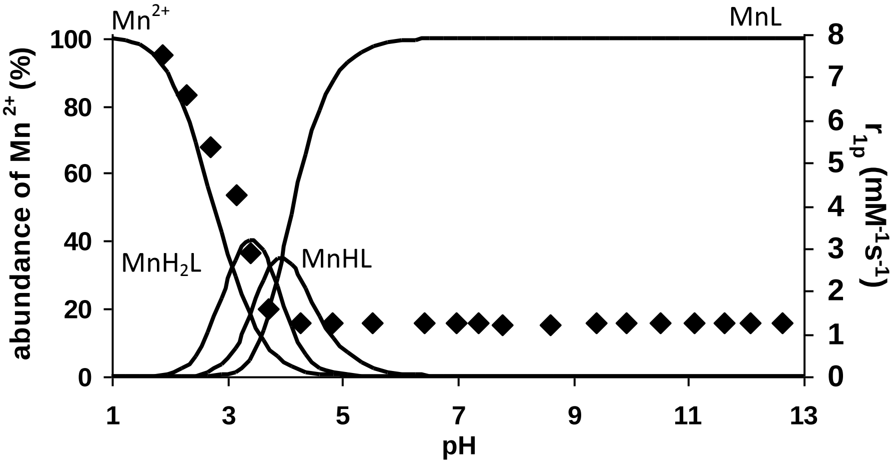

Figure S5. Species distribution and relaxivity values of the Mn(II) - DOTA system as a function of pH ([Mn^{2+}]=[DOTA]=1.0 mM, 0.1 M KCl, 20 MHz, 25°C)

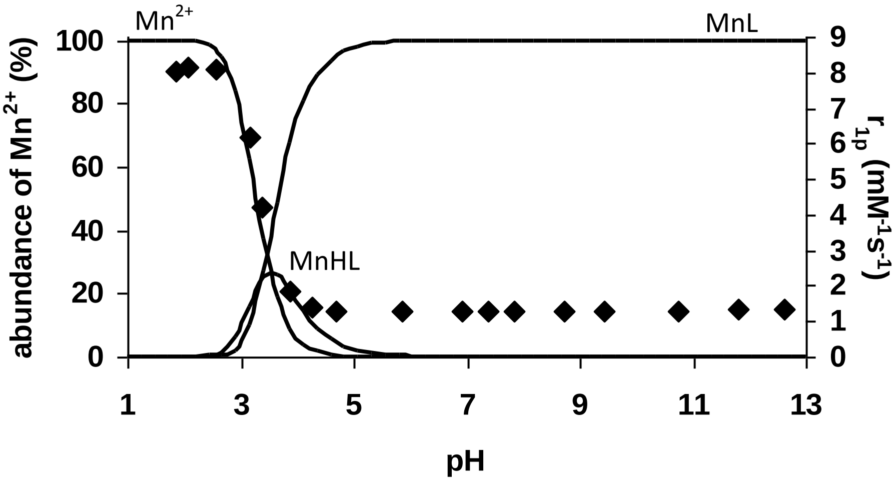

Figure S6. Species distribution and relaxivity values of the Mn(II) - DO3A system as a function of pH ([Mn^{2+}]=[DO3A]=1.0 mM, 0.1 M KCl, 20 MHz, 25°C)

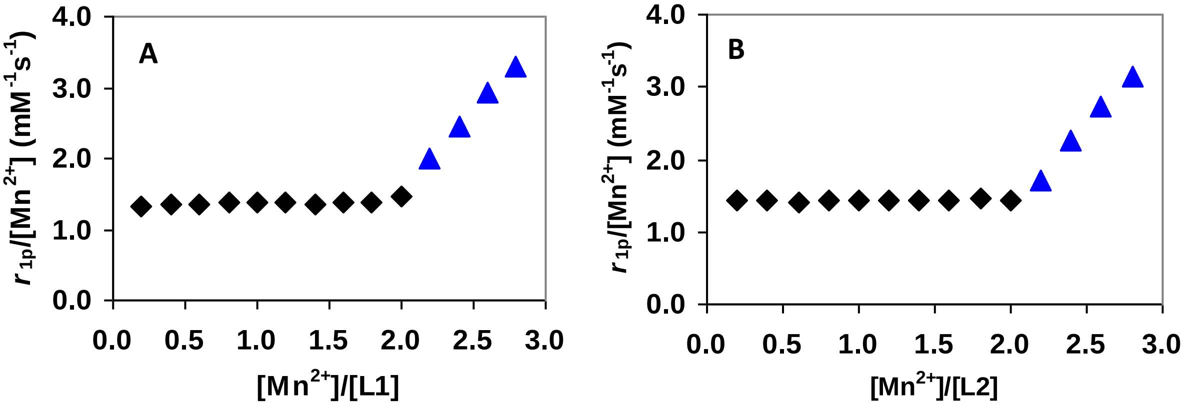

Figure S7. Relaxivity values of the Mn^{2+} - **L1** (**A**) and Mn^{2+} - **L2** (**B**) systems as a function of $[Mn^{2+}]/[L]$ ($[Mn^{2+}]=[L]=1.0$ mM, pH=6.5, 0.1 M KCl, 20 MHz, 25°C)