Supporting information

for

Optimising the Relaxivities of Mn^{2+} Complexes by Targeting Human Serum Albumin (HSA)

Attila Forgács,[a] Lorenzo Tei,[a] Zsolt Baranyai,[b] David Esteban-Gómez,[c] Carlos Platas-Iglesias[c] and Mauro Botta[a]**

[a] Dipartimento di Scienze e Innovazione Tecnologica (DiSIT), Università degli Studi del Piemonte Orientale "Amedeo Avogadro", Viale T. Michel 11, I-15121 Alessandria (Italy)

[b] Department of Inorganic and Analytical Chemistry, University of Debrecen, H-4010, Debrecen, Egyetem tér 1. (Hungary)

[c] Universidade da Coruña,Centro de Investigacións Científicas Avanzadas (CICA) and Departamento de Química Fundamental, Facultade de Ciencias, 15071, A Coruña, Galicia, Spain.

1. **^{1}H and ^{13}C NMR spectra of the ligands:**

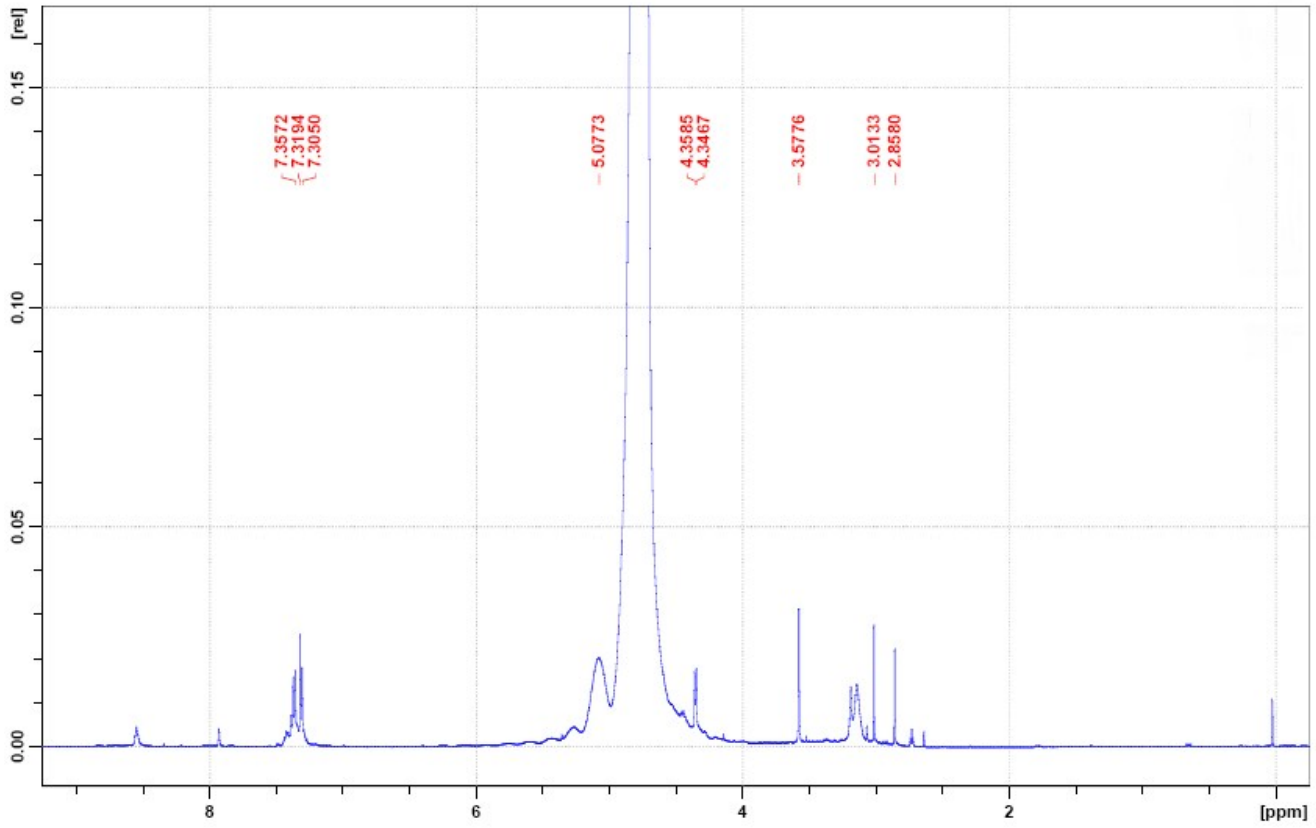

Figure S1. ^{1}H spectrum of 1,4-DO2AMBz

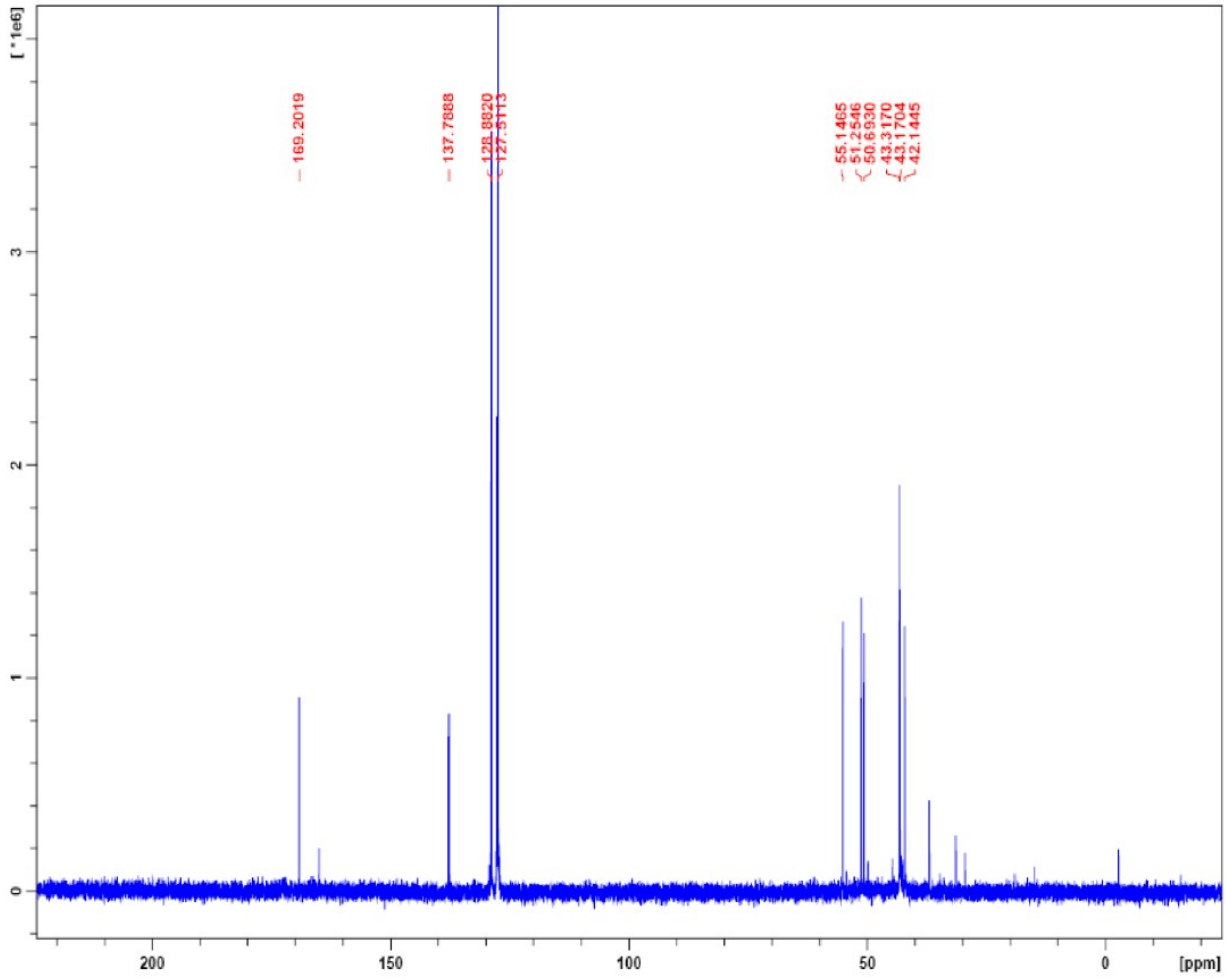

Figure S2. ^{13}C spectrum of 1,4-DO2AMBz

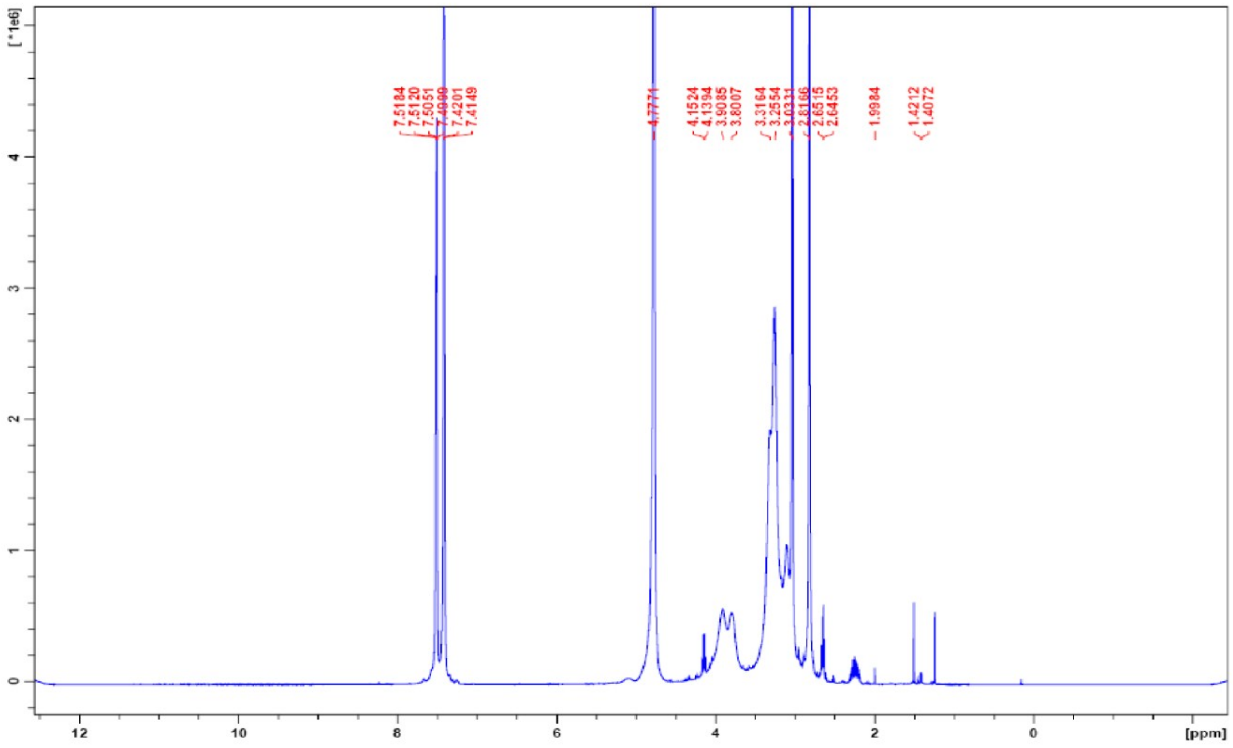

Figure S3. ^{1}H spectrum of 1,4-BzDO2AM

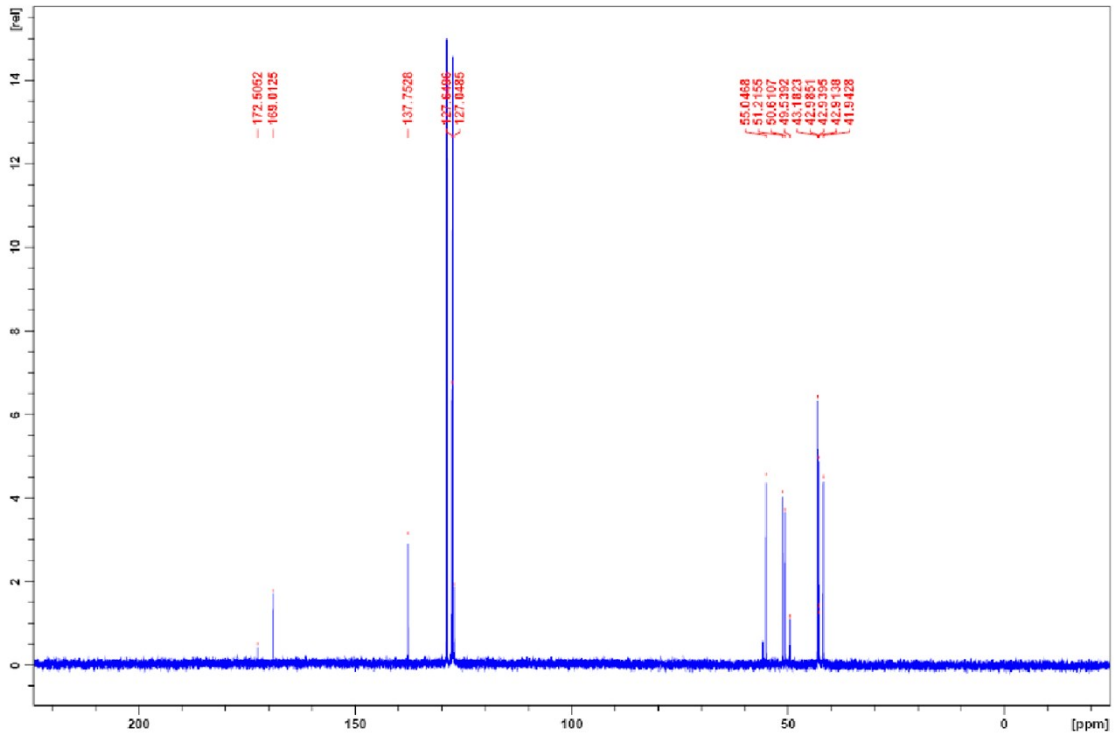

Figure S4. ^{13}C spectrum of 1,4-BzDO2AM

2. Relaxometric data

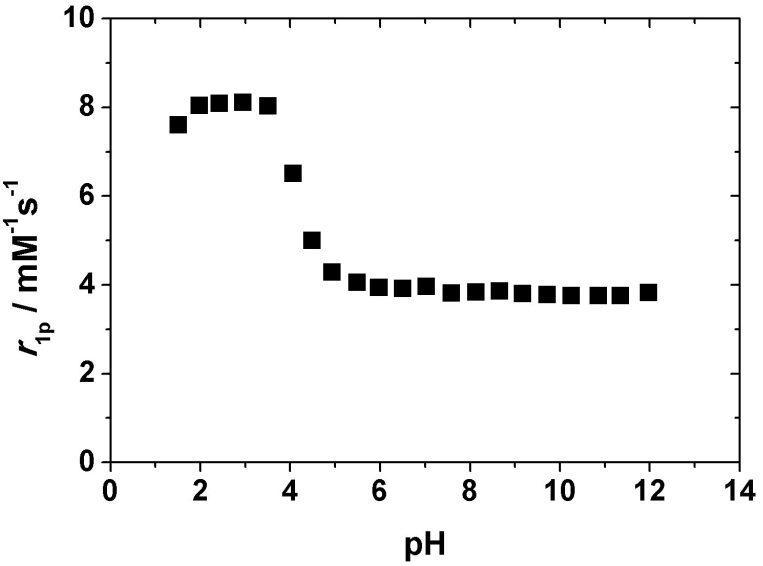

Figure S5. Plot of the relaxivity (20 MHz; 25 ºC) of [Mn(1,4-BzDO2AM)]$^{2+}$ as a function of pH

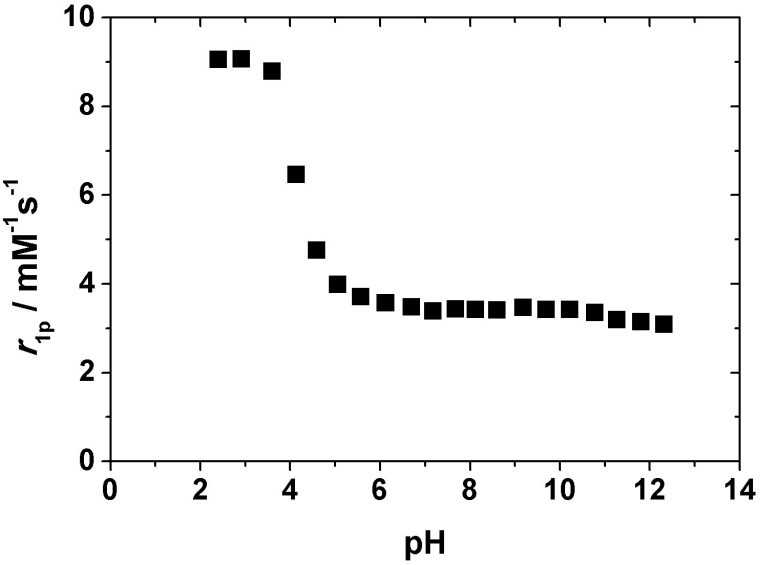

Figure S6. Plot of the relaxivity (20 MHz; 25 ºC) of [Mn(1,4-DO2AMBz)]$^{2+}$ as a function of pH.

3. Kinetic data

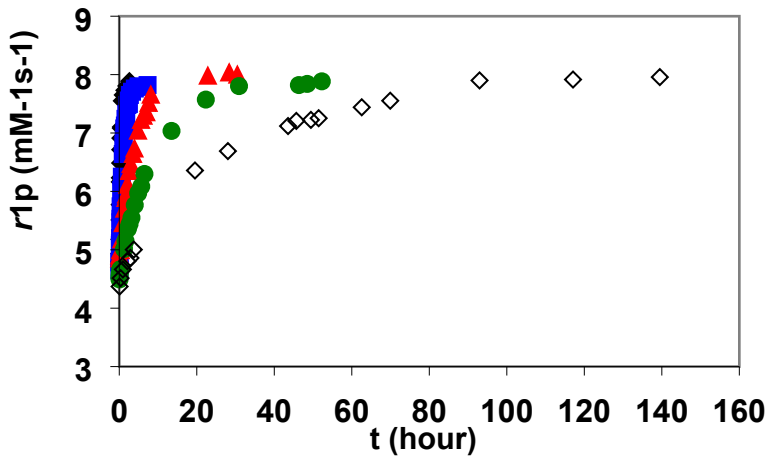

Figure S7. Relaxivity values of $[Mn(1,4\text{-BzDO2AM})]^{2+}$ obtained at pH=4.5 (◆), 5.0 (O), 5.5 (□), 6.0 (ஜ) and 6.5 (❋) in the presence of 40 fold Zn^{2+} excess ([MnL]=0.0005 M, 0.1 M KCl, 20 MHz, 298 K)

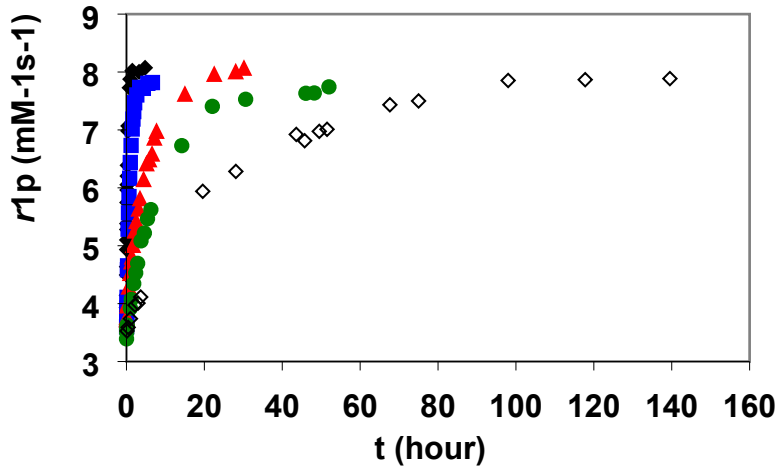

Figure S8. Relaxivity values of $[Mn(1,4\text{-DO2AMBz})]^{2+}$ obtained at pH=4.5 (◆), 5.0 (O), 5.5 (□), 6.0 (ஜ) and 6.5 (❋) in the presence of 40 fold Zn^{2+} excess ([MnL]=0.0005 M, 0.1 M KCl, 20 MHz, 298 K)

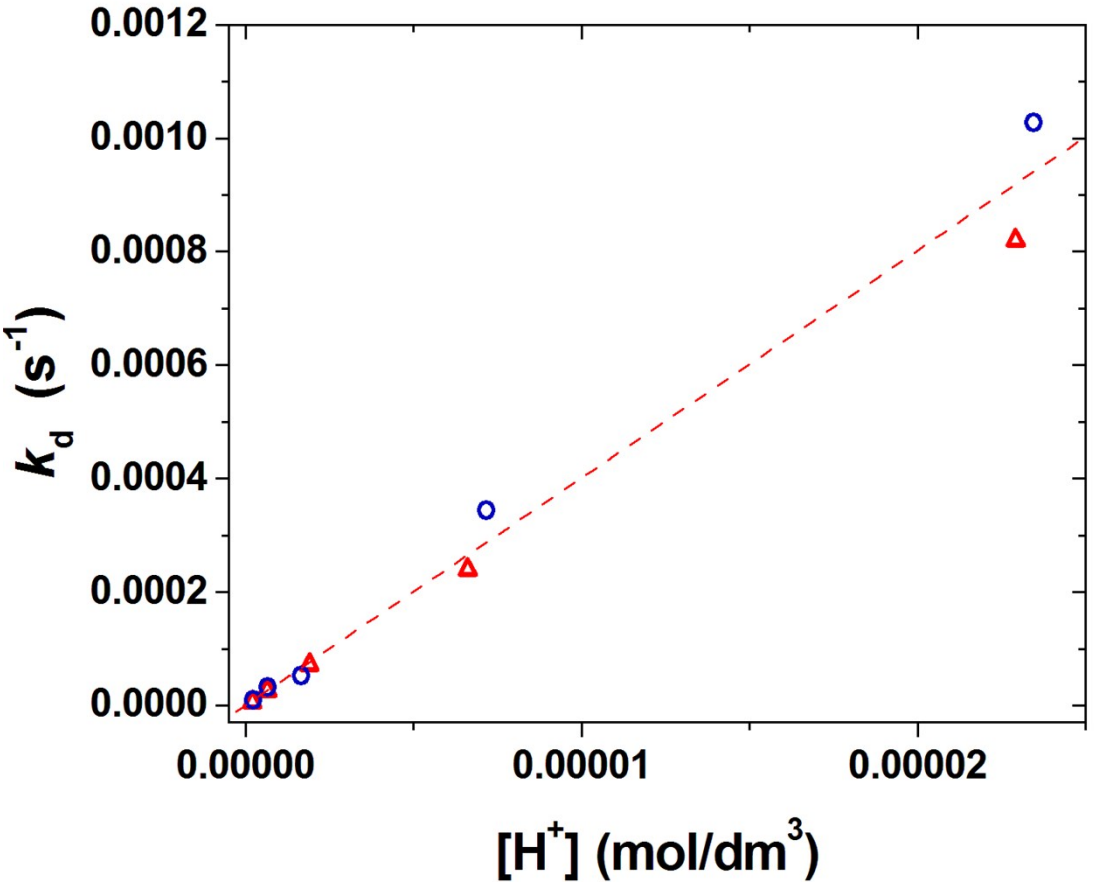

Figure S9. k_d values obtained for the transmetallation reactions of $[Mn(1,4\text{-DO2AMNz})]^{2+}$ with Zn^{2+} ([MnL]=0.5 mM, $[Zn^{2+}]$=10 mM (blue circles) and 20 mM (red triangles), 0.1 M KCl, 25°C).

Table S1. $[Mn(1,4\text{-DO2AMBz})(H_2O)]^{2+}\cdot 2H_2O$, M062X/tzvp, aqueous solution (0 Imaginary Frequencies)

Center Number	Atomic Number		Coordinates (Angstroms) X	Y	Z
1	7	0	-0.710841	-2.899816	-0.218801
2	6	0	-1.846907	-3.703445	-0.695150
3	6	0	-2.399742	-3.091970	-1.974795
4	7	0	-2.835476	-1.705263	-1.736002
5	6	0	-4.185650	-1.585675	-1.175749
6	6	0	-4.381441	-0.190853	-0.605176
7	7	0	-3.379179	0.150657	0.429437
8	6	0	-3.639846	-0.552733	1.699582
9	6	0	-2.444862	-0.495680	2.639710
10	7	0	-1.218563	-1.045205	2.019253
11	6	0	-1.191973	-2.516948	2.166502
12	6	0	-0.287277	-3.201791	1.154859
13	6	0	-3.335816	1.600038	0.616098
14	6	0	-2.258019	2.238985	-0.242924
15	8	0	-1.392829	1.549768	-0.810967
16	6	0	-0.014404	-0.425177	2.573132
17	1	0	-2.619198	-3.707146	0.077428
18	1	0	-1.561007	-4.744583	-0.870692
19	1	0	-1.613492	-3.064996	-2.731638
20	1	0	-3.215915	-3.709398	-2.361646
21	1	0	-4.308775	-2.346515	-0.404549
22	1	0	-4.956800	-1.772312	-1.928577
23	1	0	-4.269309	0.533219	-1.415943
24	1	0	-5.395784	-0.083997	-0.204036
25	1	0	-3.871633	-1.590886	1.464125
26	1	0	-4.517383	-0.136005	2.207426
27	1	0	-2.249473	0.535472	2.927476
28	1	0	-2.692085	-1.034386	3.560420
29	1	0	-2.212034	-2.880532	2.037751
30	1	0	-0.883541	-2.787431	3.182620
31	1	0	0.745089	-2.862970	1.269191
32	1	0	-0.294496	-4.278206	1.354321
33	1	0	-4.303976	2.069575	0.413884
34	1	0	-3.083920	1.846249	1.648587
35	1	0	-0.251117	0.580516	2.927181
36	1	0	0.380279	-0.982498	3.430254
37	8	0	0.860371	-0.315069	0.322952
38	25	0	-1.258708	-0.654896	-0.404725
39	6	0	1.083941	-0.232041	1.542390
40	7	0	-2.246433	3.561361	-0.304240
41	7	0	2.282393	0.083246	2.015089
42	6	0	3.387040	0.445467	1.139222
43	1	0	3.022090	1.164554	0.404204
44	1	0	4.129330	0.952093	1.756168
45	6	0	-1.193389	4.299713	-0.983332

46	1	0	-1.508374	5.341271	-1.025168
47	1	0	-1.121457	3.940551	-2.012662
48	8	0	-0.204395	-0.662726	-2.419613
49	1	0	0.218044	0.202228	-2.604458
50	1	0	0.530017	-1.302943	-2.413365
51	8	0	0.791487	1.870494	-2.493593
52	1	0	1.678089	2.153379	-2.244123
53	1	0	0.227134	2.046848	-1.722183
54	1	0	-2.791543	-1.194776	-2.613667
55	1	0	0.087063	-3.055871	-0.833082
56	8	0	1.841198	-2.255754	-1.541527
57	1	0	2.723134	-2.576334	-1.768148
58	1	0	1.971389	-1.574090	-0.862103
59	1	0	-2.969185	4.076653	0.177474
60	1	0	2.415274	0.124775	3.015301
61	6	0	0.167943	4.191906	-0.321109
62	6	0	0.361930	3.605087	0.924379
63	6	0	1.269567	4.698130	-1.010253
64	6	0	1.638814	3.521888	1.472335
65	1	0	-0.481072	3.215143	1.482457
66	6	0	2.542933	4.616747	-0.465401
67	1	0	1.127713	5.149422	-1.986502
68	6	0	2.731693	4.025209	0.780136
69	1	0	1.774581	3.060748	2.443367
70	1	0	3.388989	5.012905	-1.012693
71	1	0	3.725085	3.955574	1.205276
72	6	0	4.010469	-0.736329	0.429614
73	6	0	4.595287	-0.543225	-0.820178
74	6	0	4.029825	-2.005017	1.002758
75	6	0	5.194542	-1.604208	-1.488141
76	1	0	4.571929	0.440219	-1.276448
77	6	0	4.624436	-3.068467	0.333613
78	1	0	3.575063	-2.164986	1.973501
79	6	0	5.207077	-2.871242	-0.913695
80	1	0	5.642665	-1.444840	-2.460742
81	1	0	4.629571	-4.052400	0.785097
82	1	0	5.669738	-3.699665	-1.434706

E(UM062X) = -2872.74012486 Hartree
Zero-point correction = 0.717568
Thermal correction to Energy = 0.756863
Thermal correction to Enthalpy = 0.757808
Thermal correction to Gibbs Free Energy = 0.647603
Sum of electronic and zero-point Energies = -2872.022557
Sum of electronic and thermal Energies = -2871.983262
Sum of electronic and thermal Enthalpies = -2871.982317
Sum of electronic and thermal Free Energies = -2872.092522

Table S2. [Mn(1,4-BzDO2AM)(H_2O)]$^{2+}$·2H_2O, M062X/tzvp, aqueous solution (0 Imaginary Frequencies)

Center Number	Atomic Number		Coordinates (Angstroms) X	Y	Z
1	7	0	1.577213	0.846537	-0.680020
2	6	0	0.879071	1.942050	-1.377810
3	6	0	-0.392203	2.367273	-0.657202
4	7	0	-1.368223	1.265693	-0.521580
5	6	0	-2.067723	1.014916	-1.795271
6	6	0	-2.747766	-0.343175	-1.810176
7	7	0	-1.780212	-1.453972	-1.680807
8	6	0	-1.128306	-1.738641	-2.971307
9	6	0	0.147301	-2.543803	-2.787237
10	7	0	1.081326	-1.885752	-1.854795
11	6	0	1.800710	-0.795698	-2.544781
12	6	0	2.506597	0.143792	-1.584245
13	6	0	-2.462377	-2.645170	-1.181715
14	6	0	-2.573020	-2.605182	0.331967
15	8	0	-1.884413	-1.780593	0.977441
16	6	0	2.030258	-2.843062	-1.280935
17	1	0	0.640476	1.605734	-2.385809
18	1	0	1.532313	2.812976	-1.496543
19	1	0	-0.145367	2.705298	0.350116
20	1	0	-0.832603	3.220357	-1.185935
21	1	0	-1.339238	1.073101	-2.603525
22	1	0	-2.810449	1.793910	-1.995936
23	1	0	-3.451323	-0.415367	-0.979457
24	1	0	-3.331458	-0.452055	-2.731657
25	1	0	-0.910664	-0.788236	-3.455902
26	1	0	-1.805298	-2.283351	-3.639873
27	1	0	-0.092007	-3.526421	-2.384064
28	1	0	0.612375	-2.706688	-3.766353
29	1	0	1.083072	-0.243722	-3.150671
30	1	0	2.540720	-1.213709	-3.238113
31	1	0	3.206561	-0.425055	-0.968200
32	1	0	3.109363	0.854317	-2.161058
33	1	0	-3.450933	-2.753085	-1.639926
34	1	0	-1.893056	-3.540873	-1.436023
35	1	0	1.597243	-3.845572	-1.299834
36	1	0	2.952396	-2.879212	-1.867957
37	8	0	1.547656	-1.816153	0.831799
38	25	0	-0.138402	-0.697543	-0.037447
39	6	0	2.331950	-2.529827	0.178955
40	7	0	-3.375807	-3.467603	0.931939
41	7	0	3.427922	-3.045603	0.718943
42	6	0	3.799444	-2.708019	2.089616
43	1	0	4.871428	-2.514633	2.117266
44	1	0	3.257457	-1.821545	2.405745
45	1	0	3.570359	-3.540462	2.757279

46	6	0	4.322588	-3.961887	0.016159
47	1	0	3.782619	-4.566606	-0.706786
48	1	0	5.124792	-3.416513	-0.483878
49	1	0	4.758315	-4.634274	0.752379
50	6	0	-3.498728	-3.422070	2.387718
51	1	0	-2.511659	-3.323296	2.835775
52	1	0	-4.128059	-2.584842	2.695559
53	1	0	-3.950821	-4.348425	2.728114
54	6	0	-4.243319	-4.384373	0.190090
55	1	0	-5.166020	-3.887587	-0.113181
56	1	0	-3.734147	-4.777780	-0.685675
57	1	0	-4.487595	-5.220658	0.838282
58	8	0	0.013167	0.195174	2.010191
59	1	0	-0.737376	0.089788	2.628924
60	1	0	0.830363	0.034187	2.522276
61	8	0	-2.317433	-0.332160	3.301837
62	1	0	-2.367668	-1.027691	2.622671
63	1	0	-2.370097	-0.772933	4.156092
64	8	0	2.285433	0.030771	3.606185
65	1	0	2.644320	0.896462	3.830681
66	1	0	2.218311	-0.443038	4.442557
67	6	0	2.301783	1.319344	0.532175
68	1	0	1.578624	1.813709	1.177783
69	1	0	2.639738	0.424271	1.058851
70	6	0	-2.321739	1.542584	0.589311
71	1	0	-1.718598	1.713836	1.478554
72	1	0	-2.900914	0.636851	0.770221
73	6	0	3.473245	2.241742	0.279547
74	6	0	3.297136	3.625343	0.252745
75	6	0	4.758549	1.730429	0.096951
76	6	0	4.370982	4.476186	0.020088
77	1	0	2.311678	4.043301	0.429751
78	6	0	5.835184	2.576299	-0.136174
79	1	0	4.923014	0.659647	0.151836
80	6	0	5.642170	3.952131	-0.180704
81	1	0	4.215913	5.547613	0.003829
82	1	0	6.825987	2.161563	-0.273567
83	1	0	6.480587	4.613518	-0.359365
84	6	0	-3.251215	2.716057	0.374845
85	6	0	-2.851799	4.008521	0.714942
86	6	0	-4.528552	2.529465	-0.152931
87	6	0	-3.699330	5.090508	0.514139
88	1	0	-1.873620	4.168583	1.154337
89	6	0	-5.380699	3.608063	-0.354641
90	1	0	-4.864617	1.528269	-0.401352
91	6	0	-4.965460	4.892404	-0.024354
92	1	0	-3.375011	6.086887	0.786897
93	1	0	-6.369523	3.445431	-0.764829
94	1	0	-5.629043	5.733975	-0.178100

E(UM062X) = -3029.9135992 Hartree
Zero-point correction = 0.829510

Thermal correction to Energy = 0.875495
Thermal correction to Enthalpy = 0.876439
Thermal correction to Gibbs Free Energy = 0.749986
Sum of electronic and zero-point Energies = -3029.084089
Sum of electronic and thermal Energies = -3029.038104
Sum of electronic and thermal Enthalpies = -3029.037160
Sum of electronic and thermal Free Energies = -3029.163614