Electronic Supplementary Information (ESI)

Stable and Inert macrocyclic cobalt(II) and nickel(II) complexes with paraCEST response

Paulo Pérez-Lourido,[a] Enikő Madarasi,[b] Fanni Antal,[b] David Esteban-Gómez,[d] Gaoji Wang,[e,‡] Goran Angelovski,[e,f] Carlos Platas-Iglesias,[,d] Gyula Tircsó,[c] and Laura Valencia*[,a]*

[a] Departamento de Química Inorgánica, Facultad de Ciencias, Universidade de Vigo, As Lagoas, Marcosende, 36310 Pontevedra, Spain. E-mail: paulo@uvigo.es
[b] Doctoral School of Chemistry, Faculty of Science and Technology, University of Debrecen, H-4010, Debrecen, Egyetem tér 1, Hungary.
[c] Department of Physical Chemistry, Faculty of Science and Technology, University of Debrecen, H-4010, Debrecen, Egyetem tér 1, Hungary.
[d] Universidade da Coruña, Centro de Investigacións Científicas Avanzadas (CICA) and Departamento de Química, Facultade de Ciencias, 15071, A Coruña, Galicia, Spain. E-mail: carlos.platas.iglesias@udc.es
[e] MR Neuroimaging Agents, Max Planck Institute for Biological Cybernetics, 72076 Tübingen, Germany
[f] Laboratory of Molecular and Cellular Neuroimaging, International Center for Primate Brain Research (ICPBR), Center for Excellence in Brain Science and Intelligence Technology (CEBSIT), Chinese Academy of Sciences (CAS), 20031 Shanghai, PR China.

‡ Current address: School of Chemistry and Chemical Engineering, Jiangsu University, Zhengjiang 212013, PR China.

Contents:

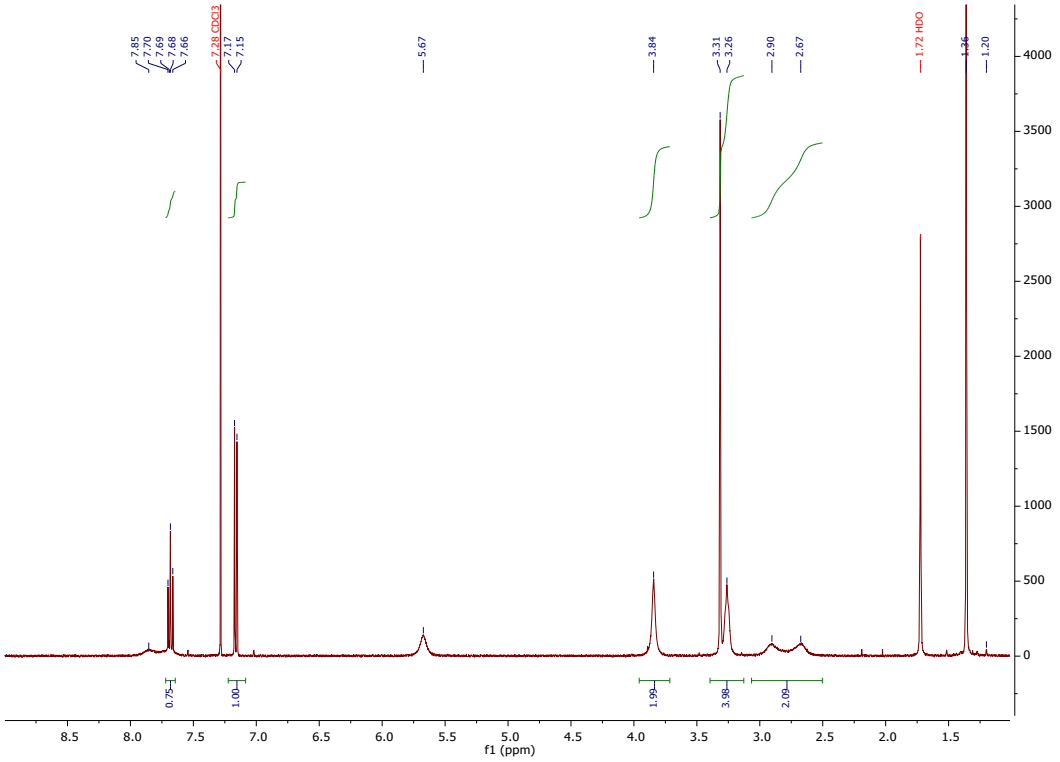

Figure S1. ^{1}H NMR spectrum of compound **2** (400 MHz, $CDCl_3$, 298 K).

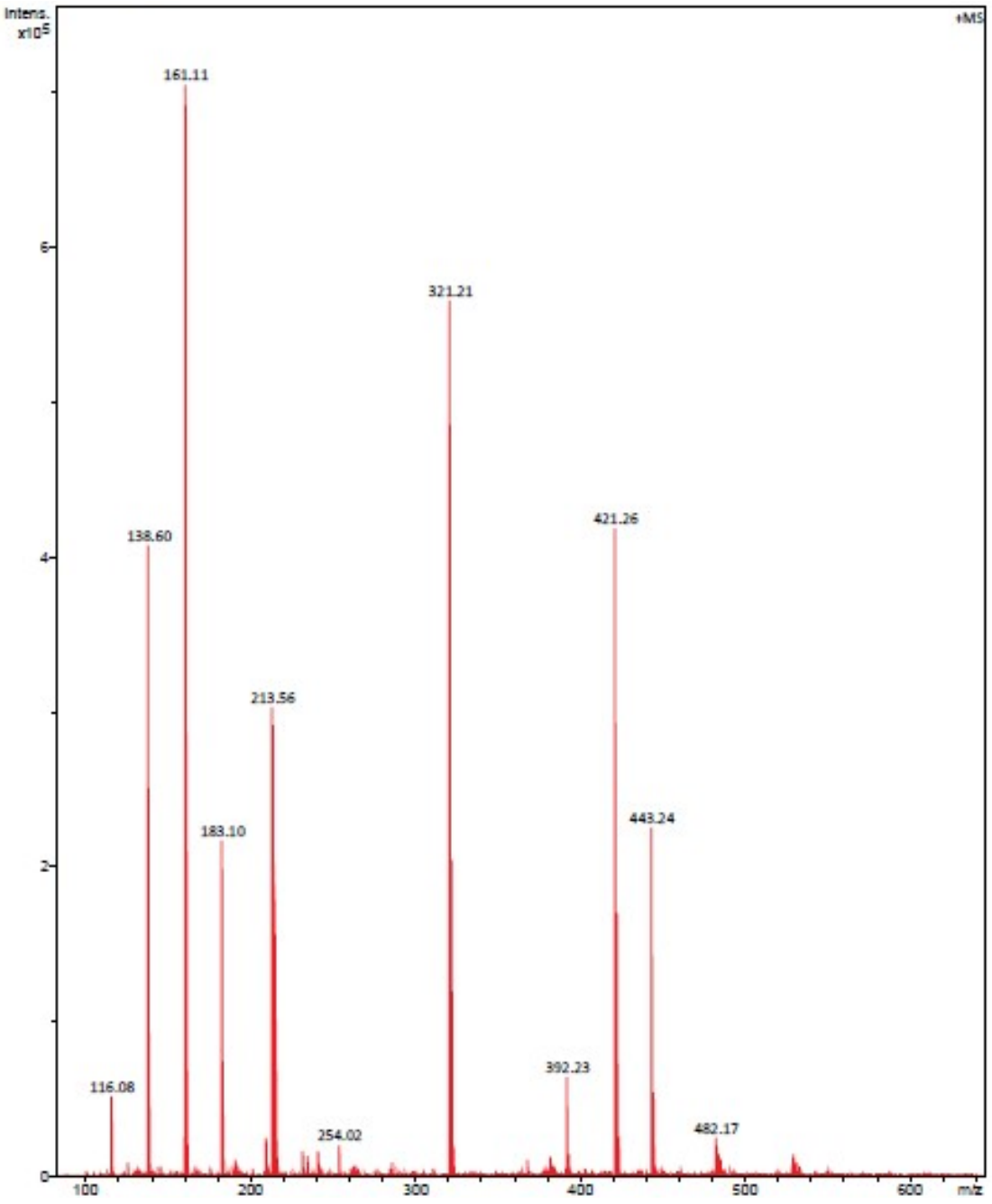

Figure S2. Mass spectrum (ESI^+) of compound **2**.

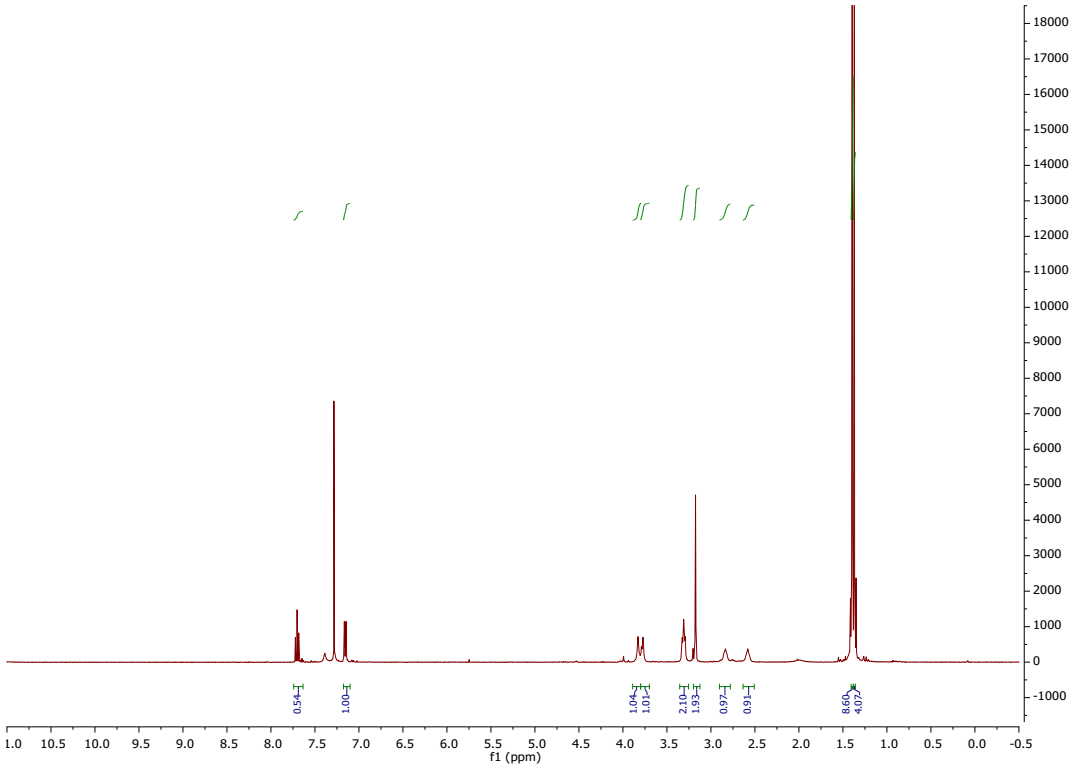

Figure S3. ^{1}H NMR spectrum of compound **3** (400 MHz, $CDCl_3$, 298 K).

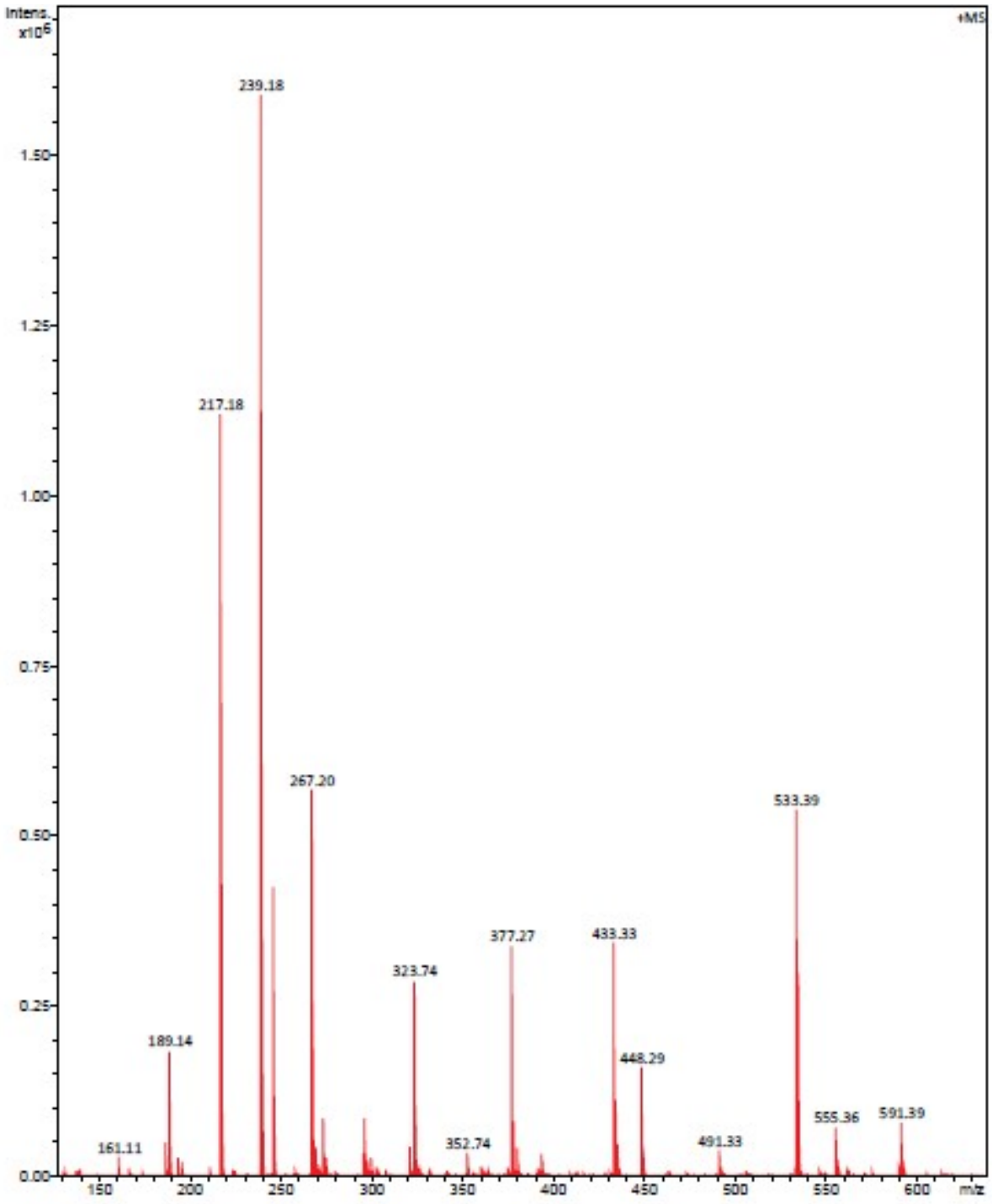
Intens.
x10^6
+MS
239.18
217.18
267.20
533.39
377.27
433.33
323.74
189.14
448.29
555.36
591.39
161.11
352.74
491.33
1.50
1.25
1.00
0.75
0.50
0.25
0.00
150
200
250
300
350
400
450
500
550
600
m/z

Figure S4. Mass spectrum (ESI$^+$) of compound **3**.

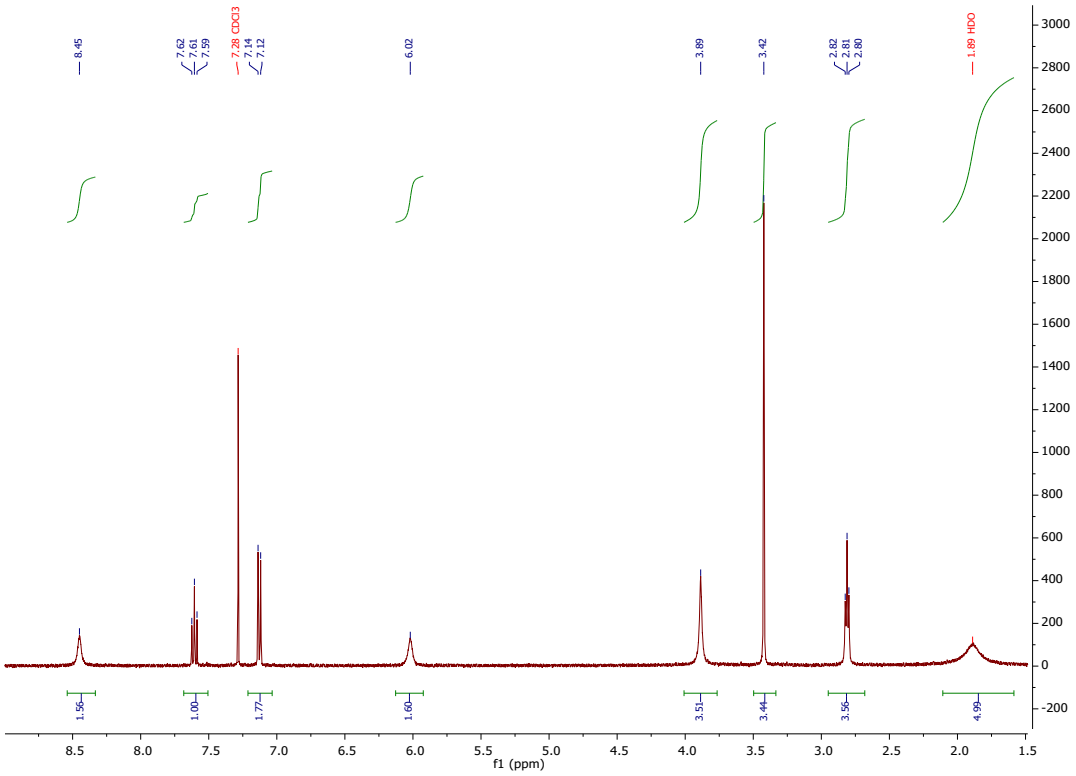

Figure S5. ^{1}H NMR spectrum of 3,9-PC2AM^H (400 MHz, $CDCl_3$, 298 K).

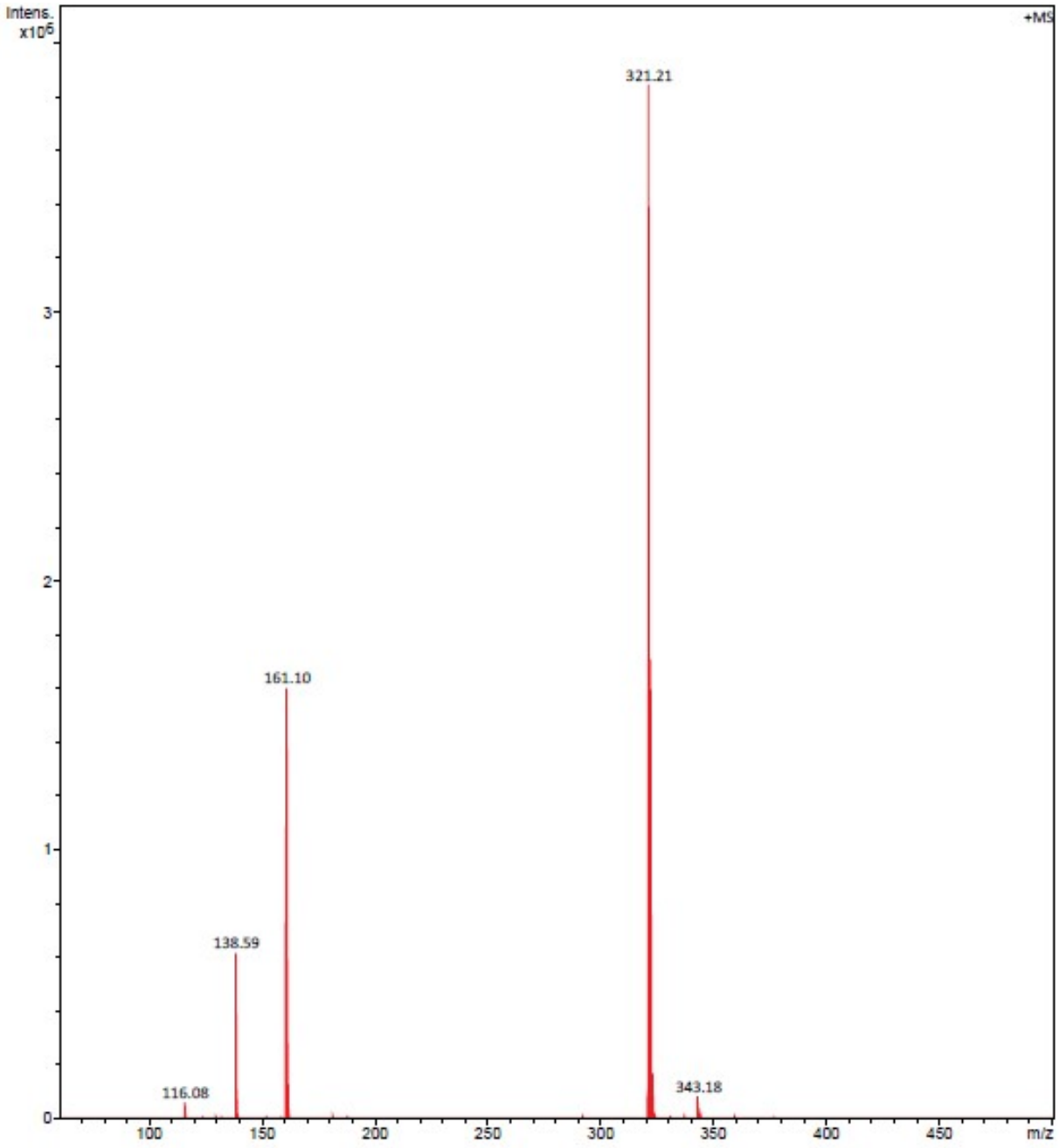

Figure S6. Mass spectrum (ESI^+) of 3,9-$PC2AM^H$.

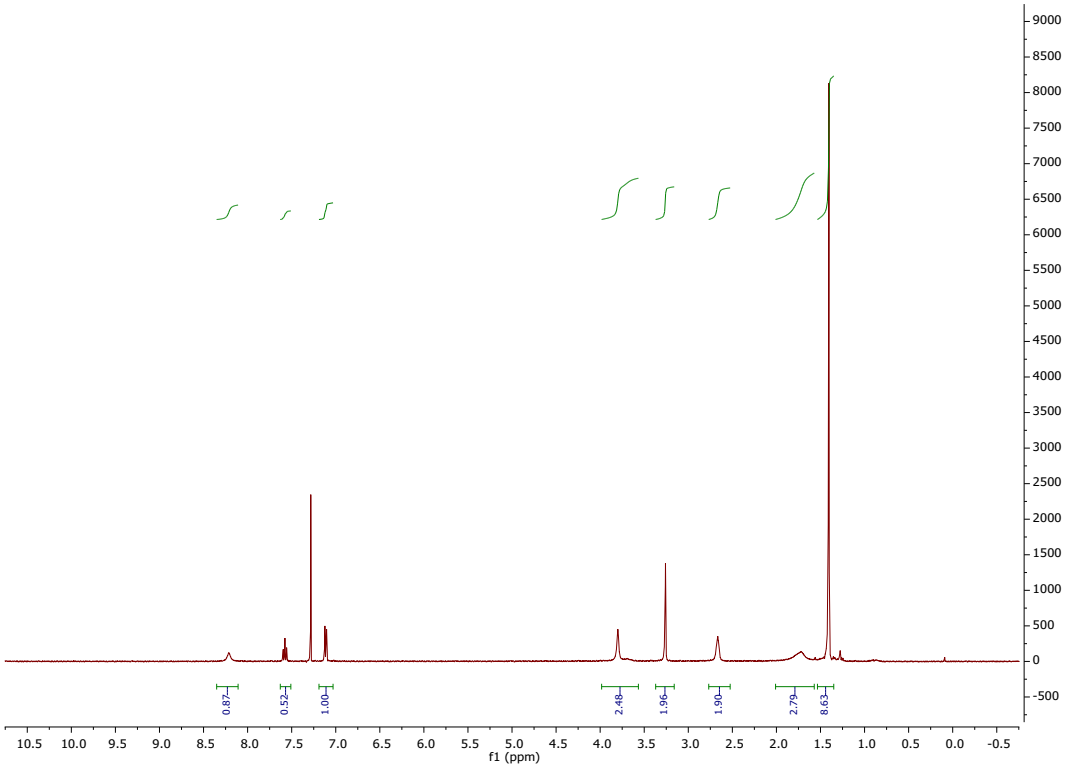

Figure S7. ^{1}H NMR spectrum of 3,9-PC2AM^{tBu} (400 MHz, $CDCl_3$, 298 K).

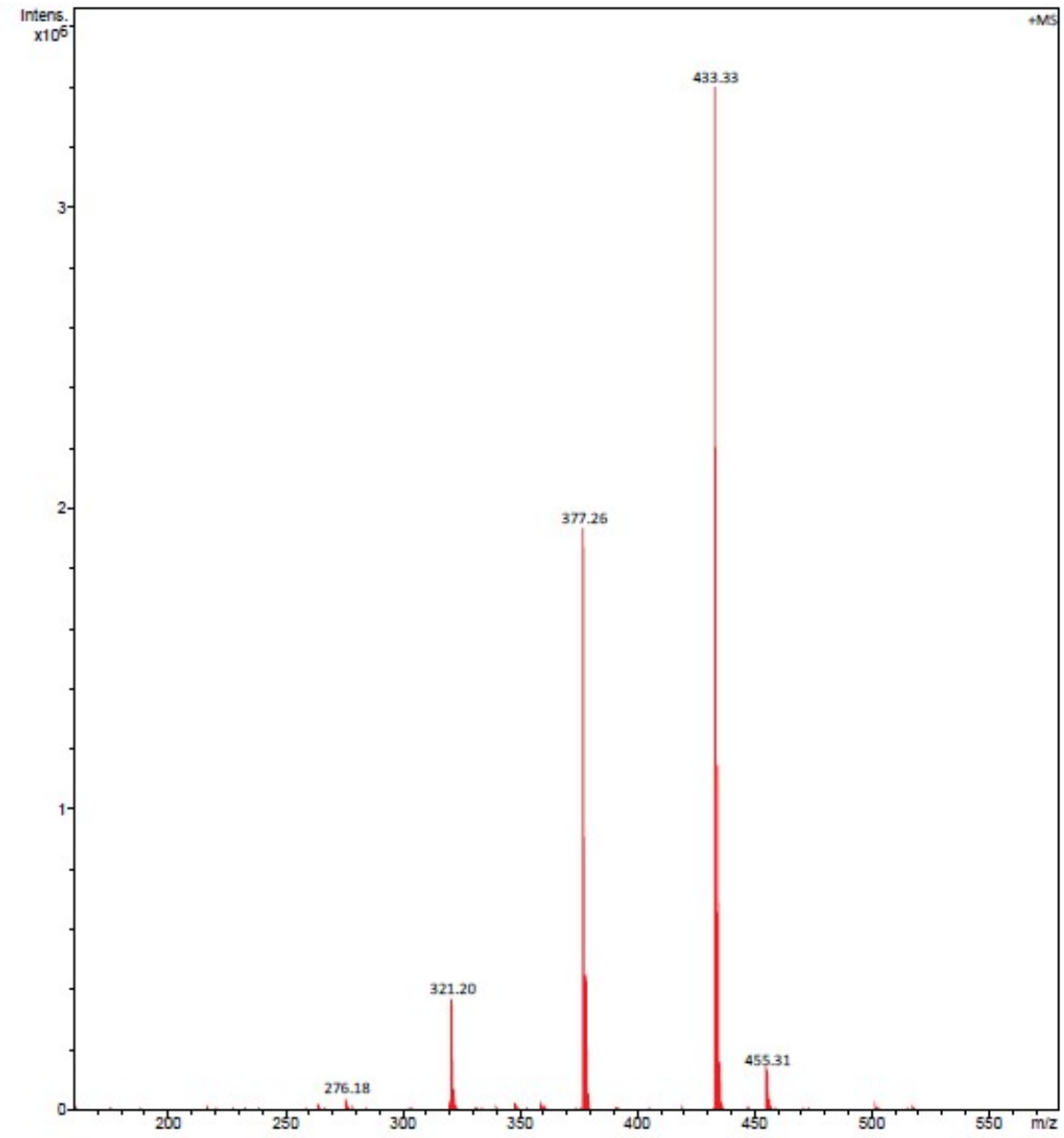

Figure S8. Mass spectrum (ESI^+) of 3,9-PC2AM^{tBU}.

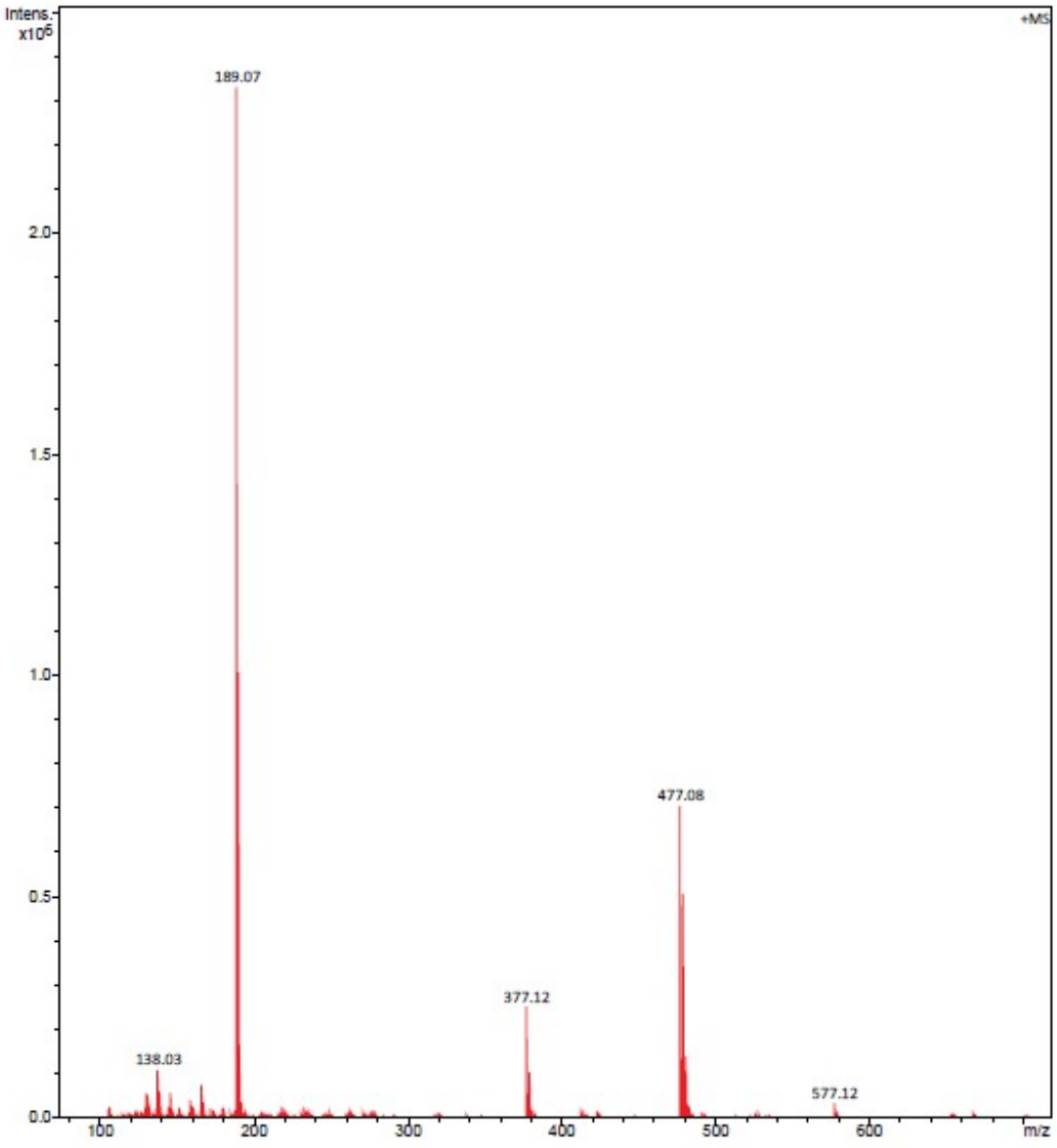

Figure S9. Mass spectrum (ESI^+) of $[Ni(3,9\text{-}PC2AM^H)](ClO_4)_2$.

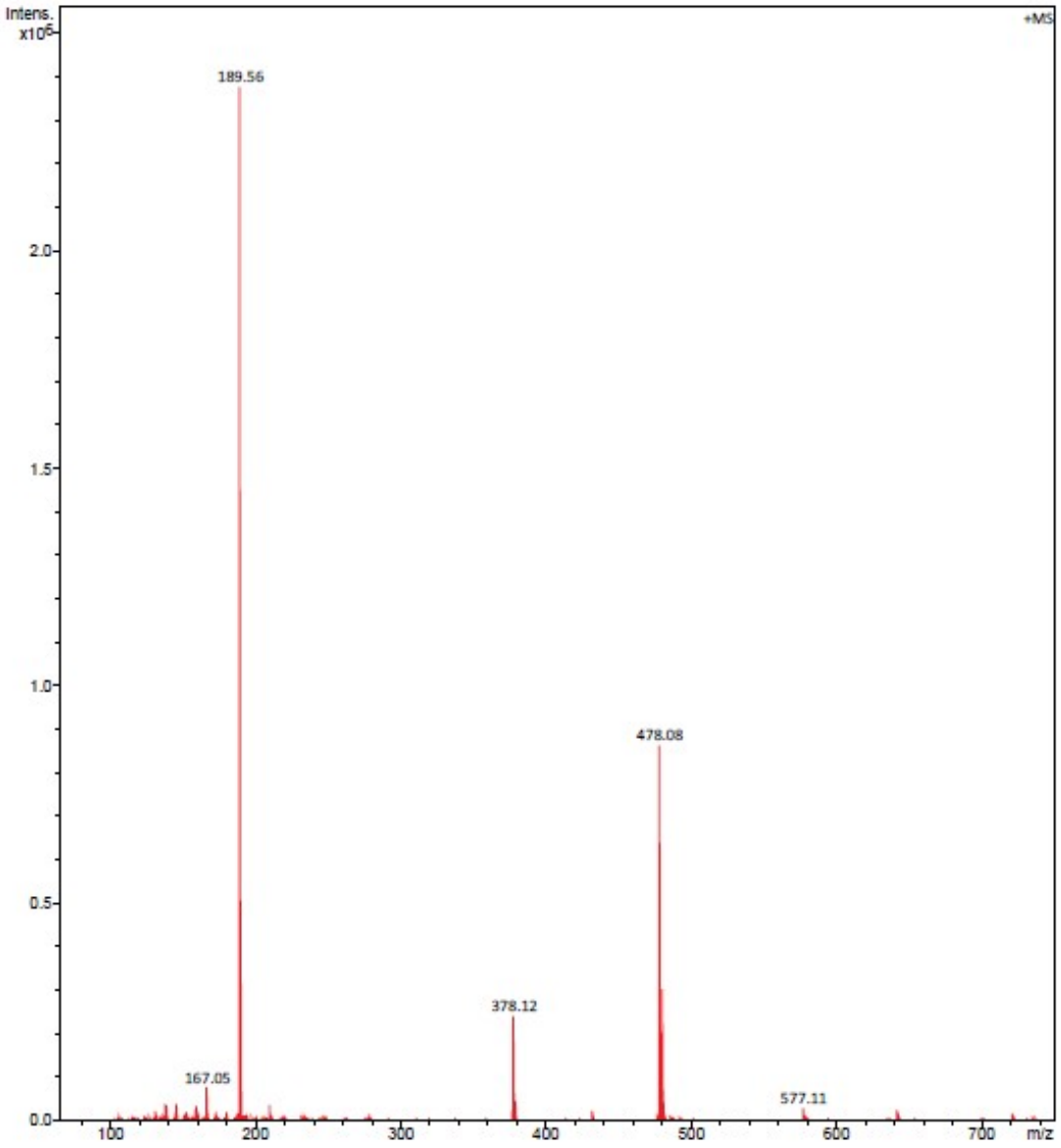

Figure S10. Mass spectrum (ESI$^+$) of [Co(3,9-PC2AM^H)(H_2O)](ClO_4)$_2$·4.5H_2O.

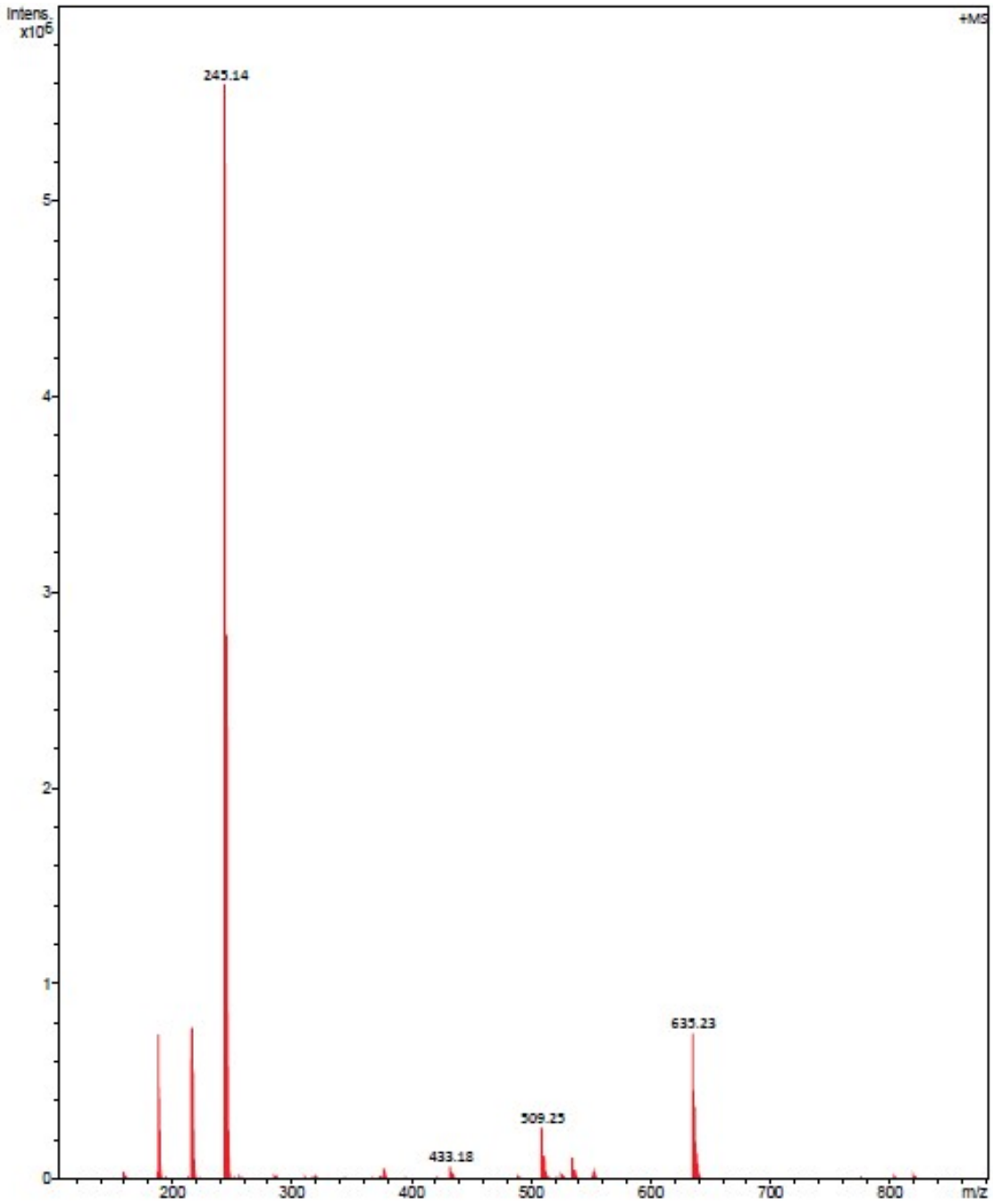

Figure S11. Mass spectrum (ESI$^+$) of [Ni(3,9-PC2AM^{tBU})]$(PF_6)_2$.

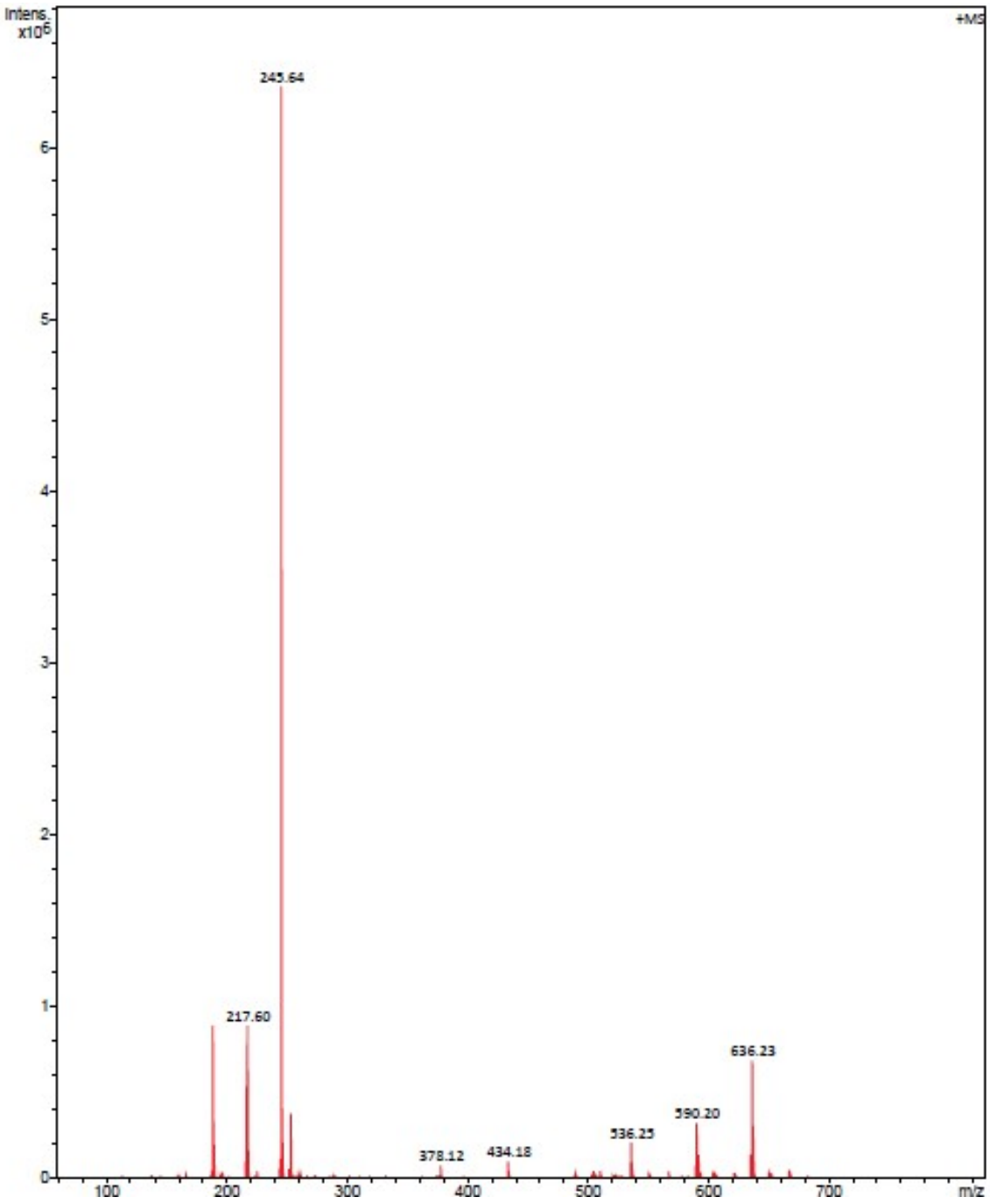

Figure S12. Mass spectrum (ESI$^+$) of [Co(3,9-PC2AM^{tBU})](PF_6)$_2$·1.875H_2O.

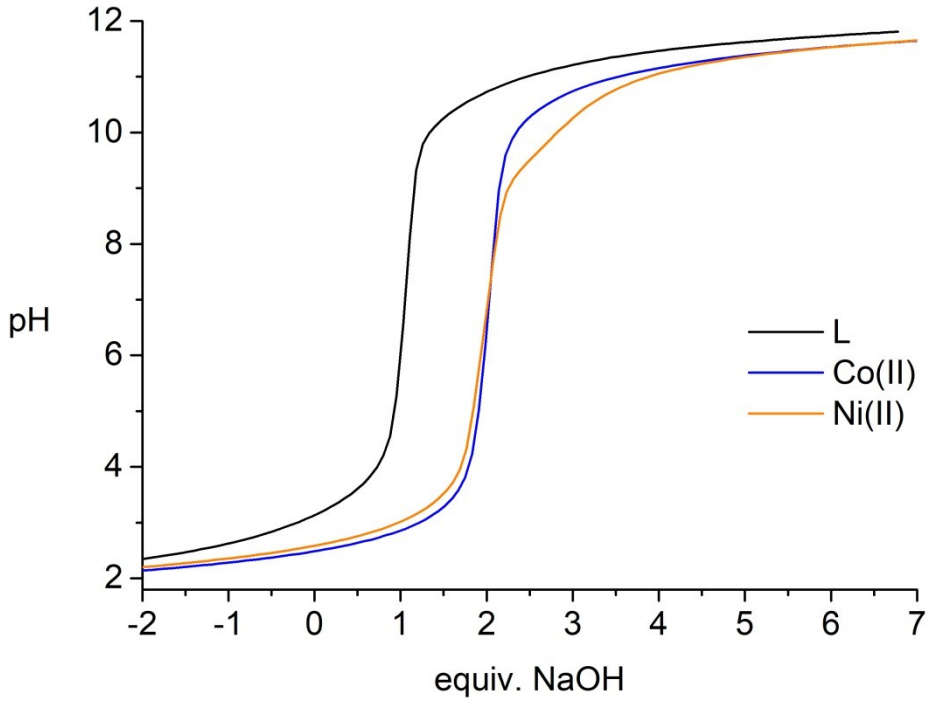

Figure S13. Potentiometric titrations of the 3,9-PC2AM^{H} ligand (2.5 mM) in the absence and in the presence of one equivalent of Co(II) or Ni(II) (0.15 M NaCl, 25°C).

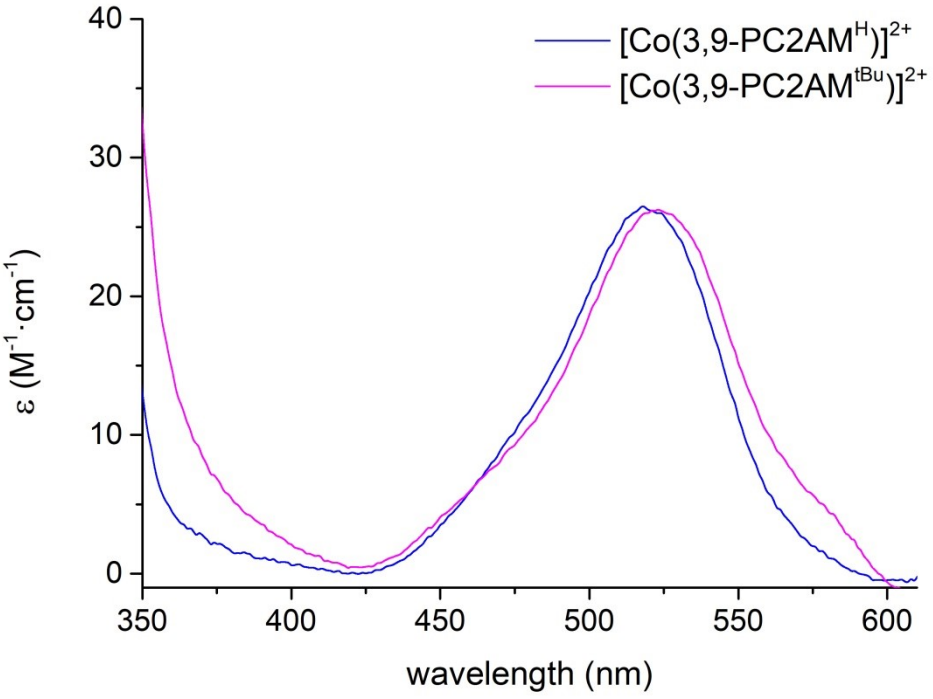

Figure S14. Absorption spectra of the Co(II) complexes recorded in aqueous solution (2 mM, 0.15 M NaCl, 25 ºC, pH 7.0).

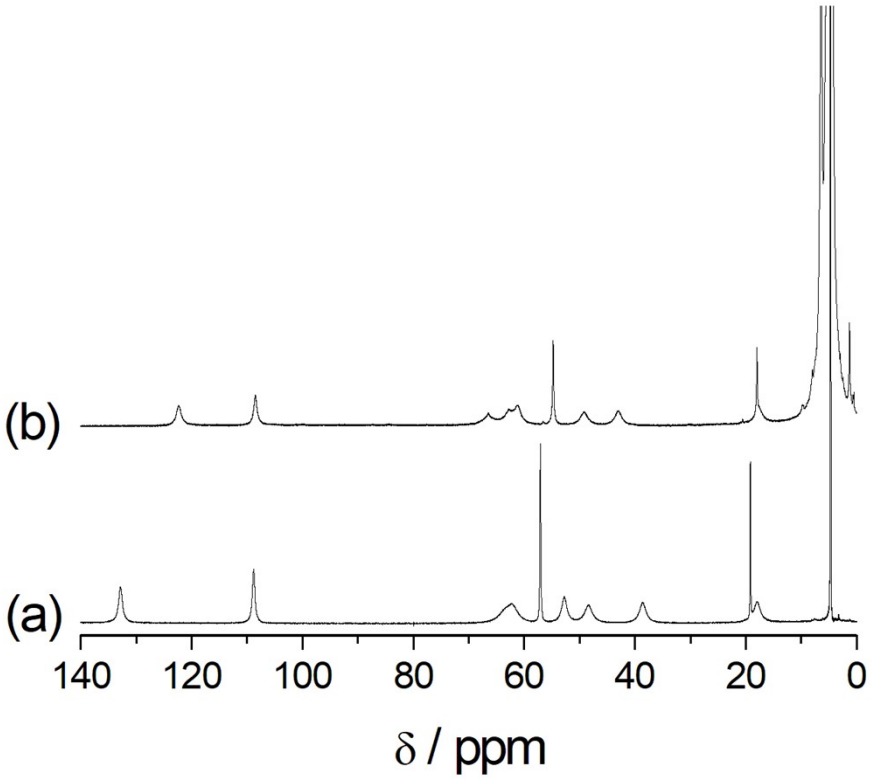

Figure S15. ^{1}H NMR spectra of (a) $[Co(PC2AM^{H})(H_2O)]^{2+}$ and (b) $[Co(PC2AM^{tBu})(H_2O)]^{2+}$ (D_2O, pH 7.0, 300 MHz).

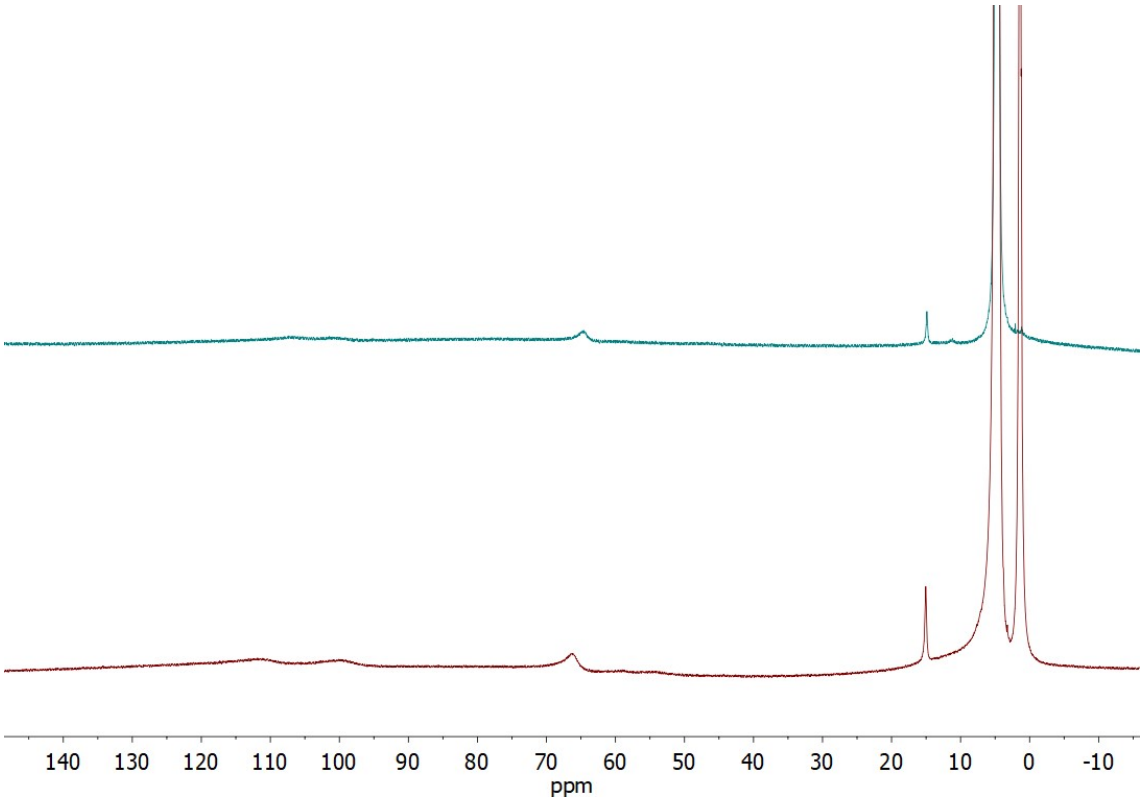

Figure S16. 1H NMR spectra of $[Ni(PC2AM^{H})]^{2+}$ (top) and $[Ni(PC2AM^{tBu})]^{2+}$ (bottom) recorded at 25 ºC in D_2O solution (400 MHz).

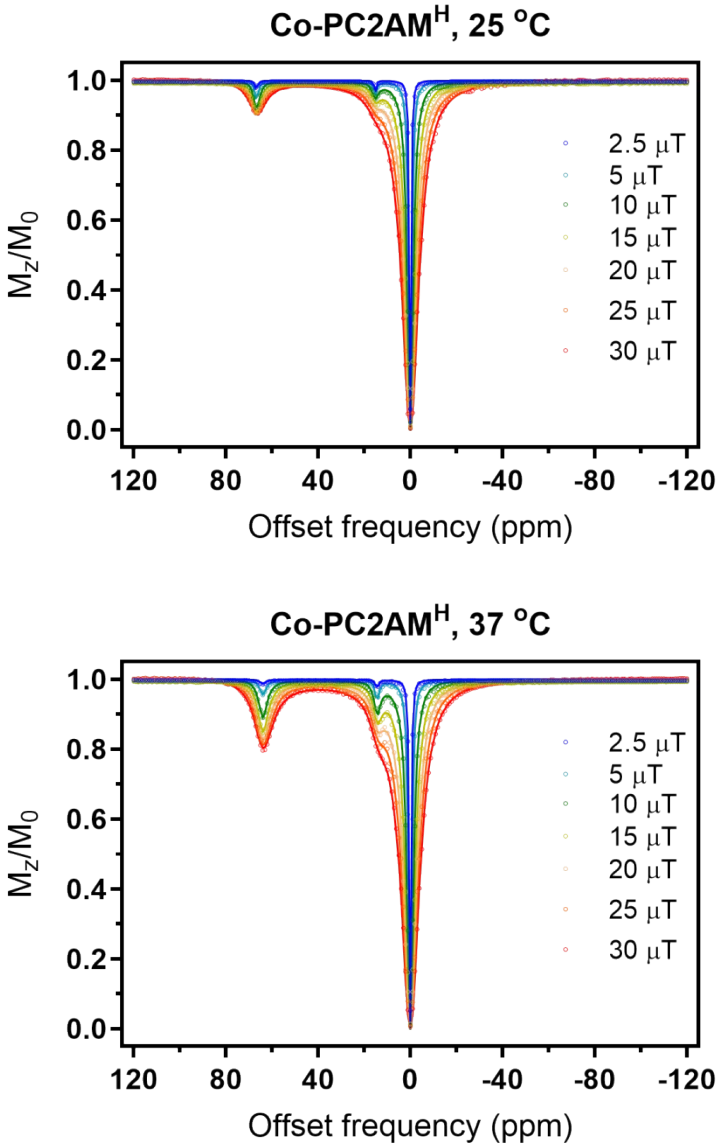

Figure S17. CEST spectra of 20 mM $[Co(PC2AM^{H})(H_2O)]^{2+}$ (50 mM HEPES, pH 7.4, 300 MHz) recorded at 25 ºC (top) 37 ºC (bottom) with a saturation time of 2 s and varying saturation powers.

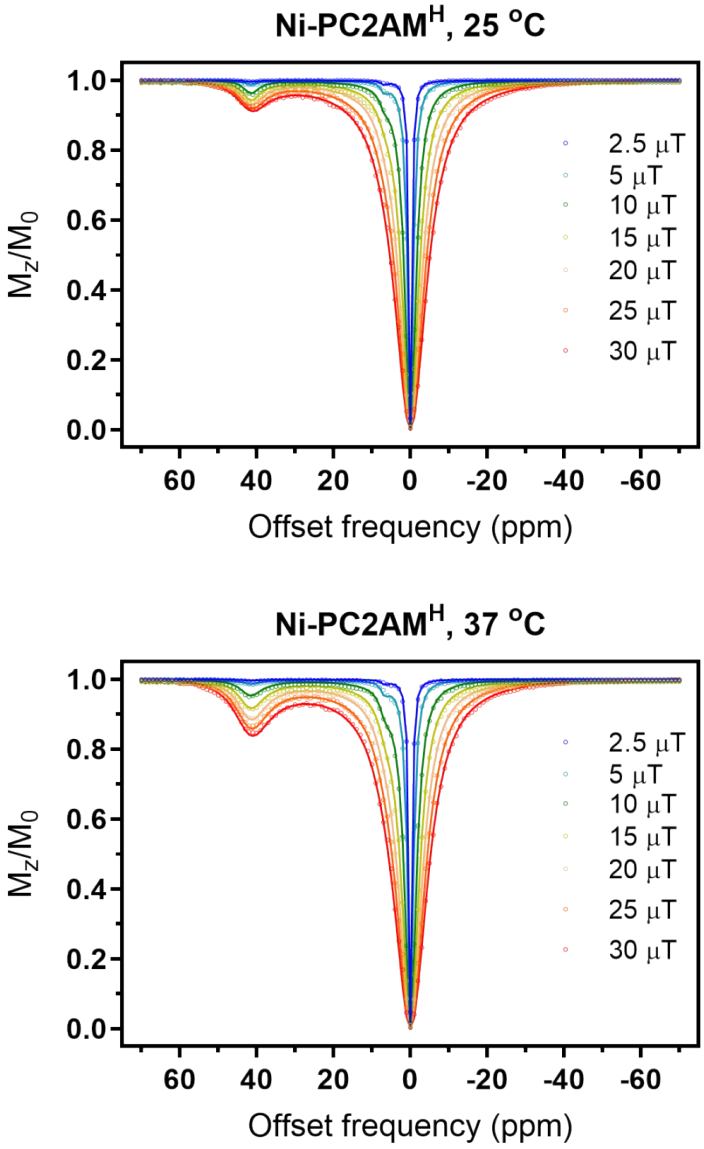

Figure S18. CEST spectra of 15 mM [Ni(PC2AM^{H})(H_2O)]$^{2+}$ (50 mM HEPES, pH 7.4, 300 MHz) recorded at 25 (top) and 37 ºC (bottom) with a saturation time of 2 s and varying saturation powers.

Table S1. Paramagnetic shifts (σ^{para}, ppm) of $[Co(PC2AM^{H})(H_2O)]^{2+}$ computed using the *A*-tensors obtained with different functionals (contributions of ZFS and g-tensors neglected).

	B3LYP	**BH&HLYP**	**PBE0**	**PBE30**
%HF exchange	20	50	25	30
H1	-11.39	-15.48	-13.54	-12.73
H2	-29.12	-14.38	-34.92	-28.20
H3ax	17.52	21.60	15.35	18.99
H3eq	-114.9	-74.63	-129.18	-107.22
H4A	-21.29	-7.79	-24.24	-17.93
H4B	-25.70	-10.93	-29.96	-22.76
H5A	-75.61	-54.18	-80.15	-90.02
H5B	-94.34	-70.54	-95.64	-70.87
H6ax	3.19	1.46	3.82	3.30
H6eq	-154.19	-110.8	-172.63	-147.52
NH_{cis} [a]	-1.88	-2.52	-2.80	-2.17
NH_{trans}[a]	-55.00	-42.33	-62.30	-53.91

[a] Amide protons in cis and trans with respect to the amide O atom.

Table S2. Cartesian coordinates (Å) used for the calculation of ^{1}H NMR chemical shifts of $[Co(PC2AM^{H})(H_2O)]^{2+}$.

Co	0.48058900	0.15801800	-0.29784500
C	-1.95684700	-1.67530900	-0.64033900
C	-3.27261000	-2.11765000	-0.61868100
C	-4.28154200	-1.19578000	-0.37300200
C	-3.94827100	0.13033800	-0.15585400
C	-2.60960500	0.50117500	-0.20821900
C	-2.19879500	1.93047900	-0.05029200
C	-0.56609800	2.13358500	1.77799900
C	-0.45422300	0.75597000	2.41531600
C	0.89724600	-1.32394500	2.26202100
C	0.06780200	-2.28988100	1.42177900
C	-0.78558300	-2.59813600	-0.84200100
C	-0.20178000	3.25896400	-0.32540300
C	1.28769600	3.06672300	-0.51142400
C	1.60335700	-2.75977000	-0.43259200
C	2.76267800	-1.80293000	-0.25789700
N	-1.62989900	-0.38248200	-0.45264500
N	-0.77181200	2.06198000	0.30995200
N	0.69329900	0.06528700	1.80202400
N	0.34585800	-2.11220500	-0.03134700
N	2.01114800	4.16142400	-0.66244300
N	3.95605600	-2.31965700	-0.03113700
O	1.76074900	1.92728400	-0.58750000
O	2.55250500	-0.58222500	-0.35734100
O	0.59630700	-0.06334000	-2.38712100
H	-0.13330600	0.27183300	-2.92431100
H	1.39302600	0.36174600	-2.73232400
H	-3.49190800	-3.16700400	-0.76553400
H	-5.31563100	-1.51452000	-0.33395500
H	-4.70568300	0.87277700	0.05954400
H	-2.35777100	2.42789300	-1.00950400
H	-2.84188500	2.43519200	0.67732600
H	-1.36679800	2.71095500	2.25102000
H	0.36978000	2.66889000	1.95483000
H	-0.32790200	0.86537500	3.49699900
H	-1.35348600	0.16410700	2.24358600
H	0.62651400	-1.43801800	3.31591600
H	1.95958900	-1.55092200	2.17779700
H	0.26233100	-3.32200500	1.73117100
H	-0.99316500	-2.09357600	1.57728000
H	-1.06194800	-3.62840000	-0.59495000
H	-0.47845800	-2.57298200	-1.88983300
H	-0.42800100	4.17644900	0.22766600
H	-0.62115600	3.36457600	-1.32784000
H	1.55417600	-2.98670200	-1.49987700
H	1.76637500	-3.70351700	0.09736600
H	1.53198400	0.59401300	2.02834300
H	2.99744700	4.09607400	-0.86588200
H	1.60663600	5.07958700	-0.57129800
H	4.76690600	-1.72094500	0.02121700
H	4.09684700	-3.31453800	0.04346700