Electronic Supplementary Material (ESI) for Inorganic Chemistry Frontiers.

Exploring the use of rigid 18-membered macrocycles with amide pendant arms for Pb(II)-based radiopharmaceuticals

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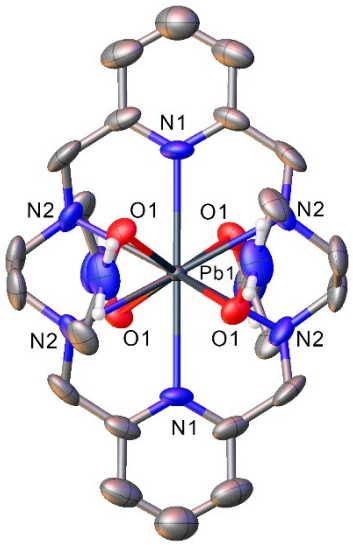


Figure S1: ORTEP views (50%) of the cations present in the crystal structure of **[Pb(PYTAM)](PF$_6$)$_2$.**

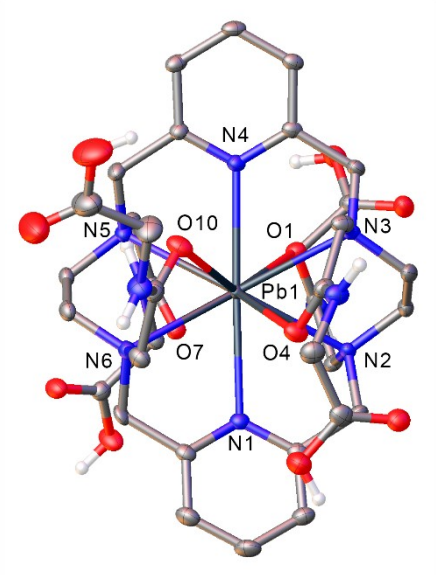
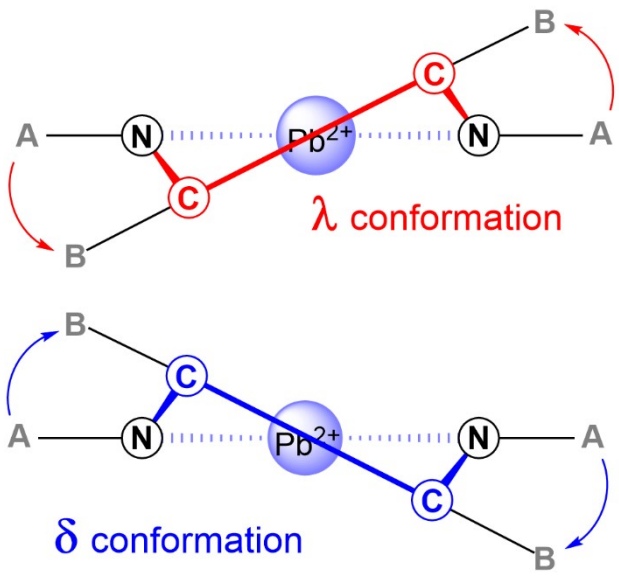


Figure S2: ORTEP views (50%) of the cations present in the crystal structure of **[Pb(H$_4$PYTAMGly)](NO$_3$)$_2$·5H$_2$O.**

Table S1: Natural bond orbital analysis of the Pb 6s^2 lone pair.

	Occupancy	**Coefficients/ Hybrids**	**Natural Electron Configuration**
[Pb(PYTAM)]$^{2+}$	1.97461	s(100.00%) p 0.00(0.00%) d 0.00(0.00%) f 0.00(0.00%)	[core]6s(1.97)6p(0.22)6d(0.02)7p(0.37)
[Pb(H$_4$PYTAMGly)]$^{2+}$	1.97371	s(99.99%) p 0.00(0.00%) d 0.00(0.00%) f 0.00(0.00%)	[core]6s(1.97)6p(0.05)6d(0.02)7p(0.54)



Conformations derived from the spatial arrangement of a chelate ring

Figure S3: Conformations of the five-membered chelate rings formed upon coordination of the ligand ethylenediamine units.

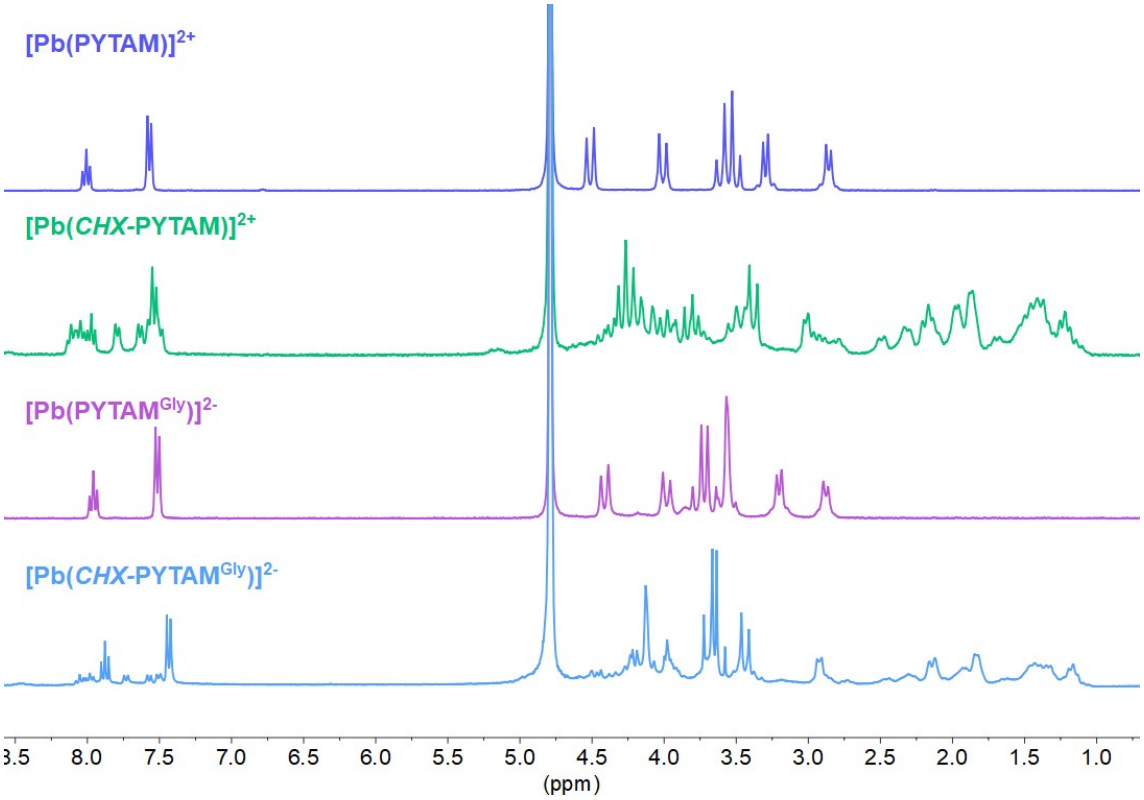


Figure S4: ^{1}H NMR spectra of $[Pb(PYTAM)]^{2+}$ (pD = 1.3), $[Pb(CHX\text{-}PYTAM)]^{2+}$ (pD = 1.5), $[Pb(PYTAMGly)]^{2-}$ (pD = 1.1), $[Pb(CHX\text{-}PYTAMGly)]^{2+}$ (pD = 1.6) recorded in D_2O solution (300 MHz, 298 K).

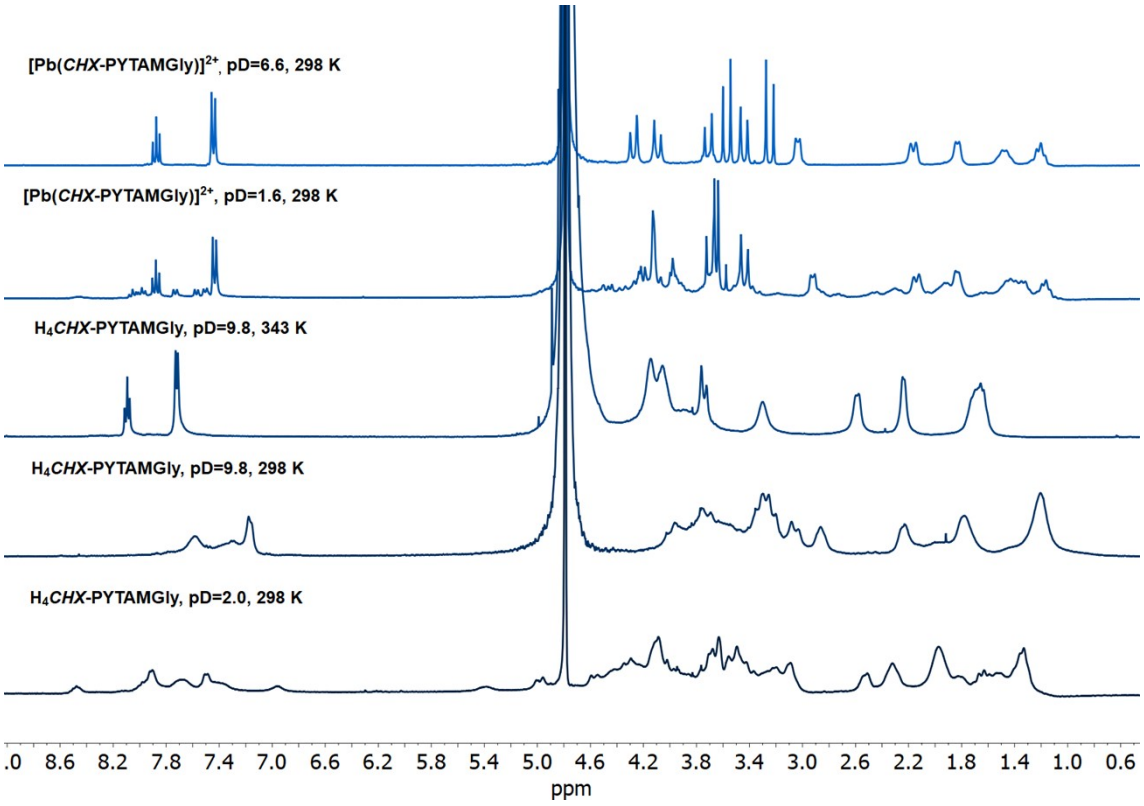


Figure S5: Comparison of the ^{1}H NMR spectra of *CHX*-PYTAMGly and [Pb(*CHX*-PYTAMGly)]$^{2+}$ at different pD values.

Table S2: ^{1}H-NMR chemical shifts (ppm) for the Pb(II) complexes of PYTAM, *CHX*-PYTAM, PYTAMGly^{4-} and *CHX*-PYTAMGly^{4-} (500 MHz, 298 K, D_2O).

	PYTAM	***CHX*-PYTAM**	**PYTAMGly^{4-}**	***CHX*-PYTAMGly^{4-}**
H1	7.96 (t, 2H)	7.91 (t, 2H)	7.89 (t, 2H)	7.90 (t, 2H)
H2	7.51 (d, 4H)	7.47 (d, 4H)	7.46 (d, 4H)	7.47 (d, 4H)
H4eq	3.97 (d, 4H)	4.14 (d, 4H)	3.90 (d, 4H)	4.12 (d, 4H)
H4ax	4.47 (d, 4H)	4.21 (d, 4H)	4.47 (d, 4H)	4.30 (d, 4H)
H5eq	3.57 (d, 4H)	3.77 (d, 4H)	3.47 (d, 4H)	3.73 (d, 4H)
H5ax	3.46 (d, 4H)	3.32(d, 4H)	3.54 (d, 4H)	3.47 (d, 4H)
H7eq	2.81(m, 4H)	-	2.79 (d, 4H)	-
H7ax	3.26 (m, 4H)	2.96 (m, 4H)	3.25 (d, 4H)	3.06 (m, 2H)
H8eq	-	2.13 (m, 4H)	-	2.19 (m, 2H)
H8ax	-	1.46 (m, 4H)	-	1.49 (m, 2H)
H9eq	-	1.81 (m, 4H)	-	1.86 (m, 2H)
H9ax	-	1.16 (m, 4H)	-	1.23 (m, 2H)
H10	-	-	3.59 (d, 4H)	3.60 (d, 2H)
	-	-	3.27(d, 4H)	3.27 (d, 2H)

Table S3: ^{13}C-NMR chemical shifts (ppm) for the Pb(II) complexes of PYTAM, *CHX*-PYTAM, PYTAMGly^{4-} and *CHX*-PYTAMGly^{4-} (126 MHz, 298 K, D_2O).

	PYTAM	***CHX*-PYTAM**	**PYTAMGly^{4-}**	***CHX*-PYTAMGly^{4-}**
C1	139.71	139.59	139.27	139.13
C2	123.34	123.61	123.04	123.29
C3	157.46	157.75	157.53	158.00
C4	57.35	53.39	57.57	53.60
C5	56.04	52.29	56.99	53.40
C6	175.52	175.92	172.67	172.95
C7	52.57	61.48	52.47	61.25
C8	-	23.88		24.12
C9	-	24.79		24.98
C10	-		42.73	43.04
C11	-		175.85	176.10

Table S4: *J* coupling values (Hz) for the Pb(II) complexes of PYTAM, *CHX*-PYTAM, PYTAMGly^{4-} and *CHX*-PYTAMGly^{4-}.

	PYTAM	***CHX*-PYTAM**	**PYTAMGly^{4} -**	***CHX*-PYTAMGly^{4-}**
^{3}J(H1-H2)	7.8	7.8	7.8	7.8
^{2}J(H4eq-H4ax)	15.2	15.0	15.1	14.9
^{2}J(H5eq-H5ax)	16.6	16.7	15.8	15.8
^{2}J(H7eq-H7ax)	10.2	-	10.2	-
^{2}J(H8eq-H8ax)	-	12.5	-	12.2
^{2}J(H10eq-H10ax)	-	-	17.2	17.2
^{3}J(H7ax-H8ax)	-	9.6	-	9.6
^{4}J(H2-Pb)	3.5	-	-	-
^{3}J(H4eq-Pb)	8.8	7.3	8.2	7.9
^{3}J(H5eq-Pb)	7.7	9.4	8.7	11.4
^{3}J(H7eq-Pb)	8.2	-	-	-

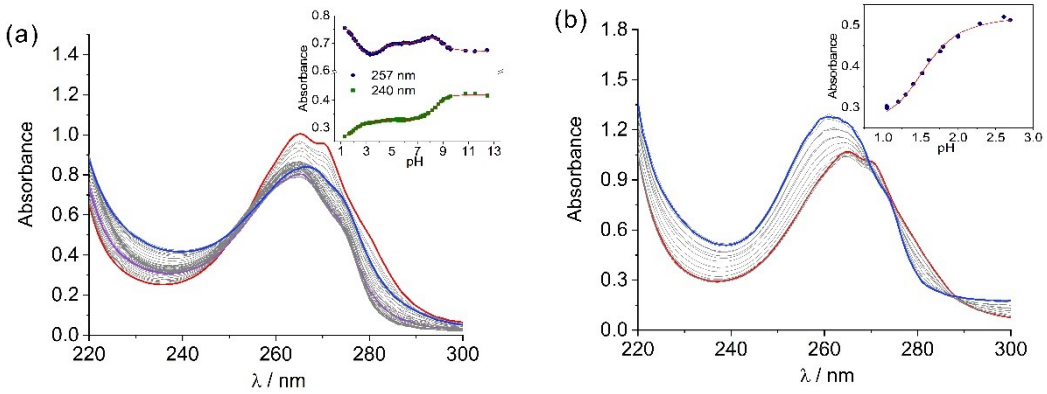


Figure S6: (a) UV-Vis absorption spectra recorded for a solution of *CHX*-PYTAMGly^{4-} (10^{-4} M, I = 0.15 M $NaClO_4$, 25 ºC) at different pH values. The spectra highlighted in red, violet and blue correspond to pH values of 1.30, 5.57 and 8.01, respectively. The inset shows the spectral changes at selected wavelengths and the fits of the data. (b) UV-Vis absorption spectra recorded to monitor the dissociation of the pre-formed Pb(II) complex with *CHX*-PYTAMGly^{4-} (10^{-4} M, I = 0.15 M $NaClO_4$, 25 ºC) at different pH values. The spectra highlighted in red and blue correspond to pH values of 1.05 and 2.69, respectively. The inset shows the spectral changes at 240 nm and the fit of the data.

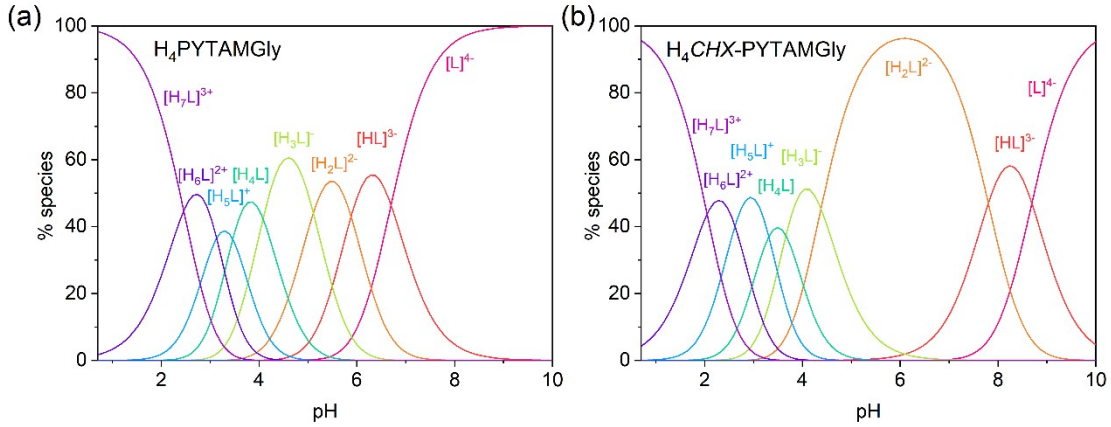


Figure S7: Speciation diagrams for the protonation of PYTAMGly^{4-} and *CHX*-PYTAMGly^{4-} $[L]_{tot}$ = 1 mM (25 °C, I = 0.15 M $NaClO_4$).

Table S5: Radiochemical yields (RCYs) for the [^{203}Pb]Pb(II) radiolabelling reactions after 60 minutes (n=3), room temperature.

Concentration (M)	PYTAM	*CHX*-PYTAM	PYTAMGly^{4-}	*CHX*-PYTAMGly^{4-}	DOTAM
10^{-4}	100 %	97.2 ± 1.2 %	100 %	100 %	100 %
10^{-5}	100 %	86.0 ± 9.5 %	100 %	100 %	100 %
10^{-6}	41.0 ± 0.6 %	64.5 ± 11.4 %	97.6 ± 0.9 %	92.4 ± 0.9 %	100 %
10^{-7}	6.7 ± 3.0 %	14.5 ± 1.4 %	17.5 ± 1.9 %	25.8 ± 9.2	58.4 ± 3.5 %
10^{-8}	0 %	1.2 ± 0.3 %	0 %	0 %	8.9 ± 3.7 %

Table S6: Radiochemical yields (RCYs) for the [^{203}Pb]Pb(II) radiolabelling reactions after 60 minutes (n=3), 80 ºC.

Concentration (M)	PYTAM	*CHX*-PYTAM	PYTAMGly^{4-}	*CHX*-PYTAMGly^{4-}	DOTAM
10^{-4}	100 %	100 %	100 %	100 %	100 %
10^{-5}	100 %	100 %	99.6 ± 0.7 %	100 %	100 %
10^{-6}	100 %	98.2 ± 1.9 %	95.5 ± 2.2 %	100 %	100 %
10^{-7}	63.0 ± 4.2 %	40.4 ± 2.5 %	14.2 ± 6.0 %	11.4 ± 3.7 %	62.7 ± 6.1%
10^{-8}	20.0 ± 6.0 %	5.2 ± 0.8 %	0 %	0 %	11.4 ± 1.7 %

Table S7: Radiochemical yields (RCYs) for the [^{203}Pb]Pb(II) radiolabelling reactions after 30 minutes (n=3), room temperature.

Concentration (M)	PYTAM	*CHX*-PYTAM	PYTAMGly^{4-}	*CHX*-PYTAMGly^{4-}	DOTAM
10^{-4}	100 %	94.7 ± 0.9 %	100 %	100 %	100 %
10^{-5}	100 %	86.7 ± 6.4 %	100 %	100 %	100 %
10^{-6}	29.5 ± 0.5 %	45.7 ± 6.1 %	97.6 ± 0.9 %	79.9 ± 4.5 %	100 %
10^{-7}	4.5 ± 0.5 %	12.2 ± 0.9 %	17.5 ± 1.9 %	14.6 ± 12.1	55.8 ± 4.5 %
10^{-8}	0 %	1.0 ± 0.2 %	0 %	0 %	7.6 ± 1.8 %

Table S8: Radiochemical yields (RCYs) for the [^{203}Pb]Pb(II) radiolabelling reactions after 30 minutes (n=3), 80 ºC.

Concentration (M)	PYTAM	*CHX*-PYTAM	PYTAMGly^{4-}	*CHX*-PYTAMGly^{4-}	DOTAM
10^{-4}	100 %	100 %	100 %	100 %	100 %

10^{-5}	100 %	99.7 ± 0.4 %	100 %	100 %	100 %
10^{-6}	100 %	97.8 ± 2.0 %	95.3 ± 3.1 %	100 %	100 %
10^{-7}	62.3 ± 7.5 %	41.8 ± 3.4 %	7.3 ± 1.7 %	6.1 ± 3.4 %	62.7 ± 6.1%
10^{-8}	17.0 ± 5.2 %	4.8 ± 2.2 %	0 %	0 %	11.4 ± 1.7 %

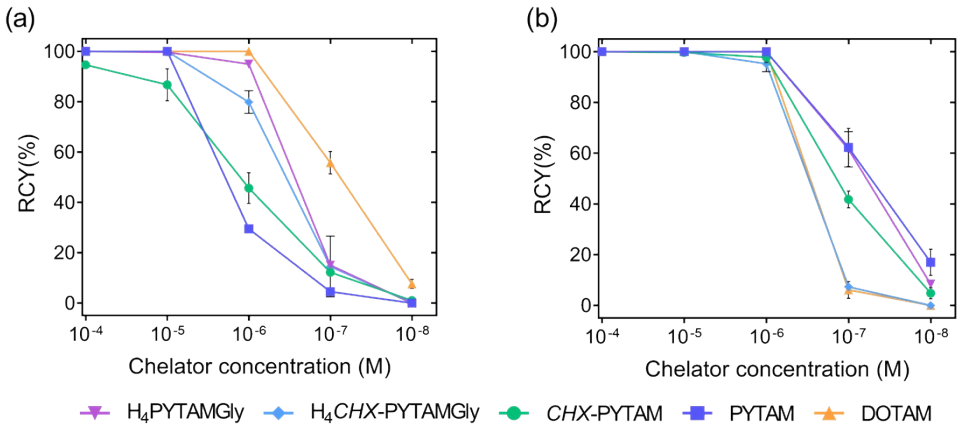


Figure S8: Radiolabelling studies using ^{203}Pb (~150 kBq, 0.1 M NH_4OAc buffer, pH=7.4). (a) Concentration dependent radiolabelling at room temperature after 30 min. (b) Concentration dependent radiolabelling at 80 ºC after 30 min

Table S9: Radiochemical yields (RCYs) for the [^{203}Pb]Pb(II) radiolabelling of CHX-PYTAM at 37 ºC.

Concentration (M)	***CHX*-PYTAM (30 min)**	***CHX*-PYTAM (60 min)**
10^{-4}	98.5 ± 0.4 %	100 %
10^{-5}	97.3 ± 0.5 %	99.6 ± 0.6 %
10^{-6}	73.0 ± 2.3 %	84.0 ± 13.2 %
10^{-7}	21.9 ± 3.2 %	6.5 ± 1.8 %
10^{-8}	3.5 ± 0.1 %	4.9 ± 0.4 %

Table S10: In vitro stability of the ^{203}Pb-labeled chelators at 37 ºC in human serum (n=3).

Time (h)	**PYTAM**	***CHX*-PYTAM**	**PYTAMGly^{4-}**	***CHX*-PYTAMGly^{4-}**	**DOTAM**
0	100 %	100 %	100 %	98.0 ± 0.7 %	100 %
24	100 %	100 %	100 %	97.8 ± 1.4 %	100 %
48	98.9 ± 0.9 %	100 %	100 %	97.5 ± 0.5 %	100 %
72	97.9 ± 1.5 %	100 %	99.6 ± 0.7 %	96.5 ± 0.9 %	100 %

Table S11: Stability of the ^{203}Pb-labeled chelators prepared at 80 ºC in a 20-fold excess EDTA (n=3).

Time (h)	**PYTAM**	***CHX*-PYTAM**	**PYTAMGly^{4-}**	***CHX*-PYTAMGly^{4-}**	**DOTAM**
0	100 %	100 %	100 %	100 %	100 %
0.0833	100 %	100 %	100 %	88.2 ± 8.9 %	100 %
0.5	100 %	100 %	100 %	76.2 ± 8.5 %	100 %
1	100 %	100 %	100 %	73.3 ± 10.1 %	100 %
2	100 %	100 %	100 %	71.6 ± 6.4 %	100 %
24	100 %	100 %	100 %	60.0 ± 4.0 %	100 %
48	100 %	100 %	100 %	56.3 ± 5.7 %	100 %
72	100 %	100 %	100 %	52.9 ± 6.7 %	100 %

Table S12: Stability of the ^{203}Pb-labeled chelators prepared at room temperature in a 20-fold excess EDTA (n=3).

Time (h)	PYTAM	*CHX*-PYTAM	PYTAMGly^{4-}	*CHX*-PYTAMGly^{4-}	DOTAM
0	100 %	100 %	100 %	99.1 ± 0.9 %	100 %
0.0833	100 %	99.7 ± 0.5 %	100 %	92.5 ± 3.9 %	100 %
0.5	100 %	100 %	100 %	89.5 ± 4.8 %	100 %
1	100 %	99.8 ± 0.2 %	99.0 ± 1.0 %	88.1 ± 7.7 %	100 %
2	100 %	100 %	98.2 ± 0.4 %	84.3 ± 9.1 %	100 %
24	100 %	98.6 ± 1.1 %	97.7 ± 1.1 %	69.2 ± 3.1 %	100 %
48	100 %	99.8 ± 0.4 %	97.8 ± 0.3 %	64.0 ± 6.8 %	100 %
72	98.7 ± 0.3 %	97.8 ± 1.1 %	98.0 ± 1.4 %	65.5 ± 5.2 %	100 %

Table S13: Stability of the ^{203}Pb-labeled chelators prepared at 80 ºC in a 20-fold excess Pb(II)(n=3).

Time (h)	PYTAM	*CHX*-PYTAM	PYTAMGly^{4-}	*CHX*-PYTAMGly^{4-}	DOTAM
0	100 %	100 %	100 %	100 %	100 %
0.0833	99.7 ± 0.4 %	100 %	83.8 ± 1.5 %	94.9 ± 4.1 %	100 %
0.5	97.6 ± 0.3 %	100 %	39.4 ± 3.0 %	89.3 ± 5.0 %	100 %
1	96.8 ± 0.1 %	100 %	34.3 ± 4.6 %	89.1 ± 4.1 %	100 %
2	93.2 ± 0.7 %	100 %	13.5 ± 2.0 %	82.3 ± 4.7 %	100 %
24	66.0 ± 1.6 %	100 %	7.1 ± 1.1 %	70.8 ± 5.1 %	100 %
48	54.9 ± 3.5 %	95.9 ± 0.3 %	6.5 ± 1.3 %	56.1 ± 4.4 %	100 %
72	37.0 ± 2.0 %	93.2 ± 0.6 %	6.1 ± 1.0 %	54.3 ± 1.5 %	100 %

Table S14: Stability of the ^{203}Pb-labeled chelators prepared at room temperature in a 20-fold excess Pb(II) (n=3).

Time (h)	PYTAM	*CHX*-PYTAM	PYTAMGly^{4-}	*CHX*-PYTAMGly^{4-}	DOTAM
0	100 %	100 %	100 %	100 %	100 %
0.0833	98.6 ± 0.4 %	99.7 ± 0.5 %	69.4 ± 4.3 %	92.2 ± 4.9 %	100 %
0.5	97.2 ± 0.2 %	98.0 ± 1.9 %	26.5 ± 1.0 %	82.6 ± 4.5 %	100 %
1	96.6 ± 0.2 %	98.0 ± 0.7 %	12.7 ± 1.0 %	81.9 ± 4.6 %	100 %
2	96.4 ± 0.6 %	95.9 ± 0.8 %	5.1 ± 0.3 %	76.4 ± 7.8 %	100 %
24	66.1 ± 1.5 %	93.6 ± 1.0 %	5.5 ± 1.5 %	51.9 ± 3.6 %	100 %
48	43.7 ± 8.2 %	92.9 ± 1.7 %	4.6 ± 0.4 %	42.7 ± 1.9 %	100 %
72	25.0 ± 2.4 %	90.5 ± 1.5 %	4.1 ± 0.5 %	24.7 ± 2.2 %	100 %

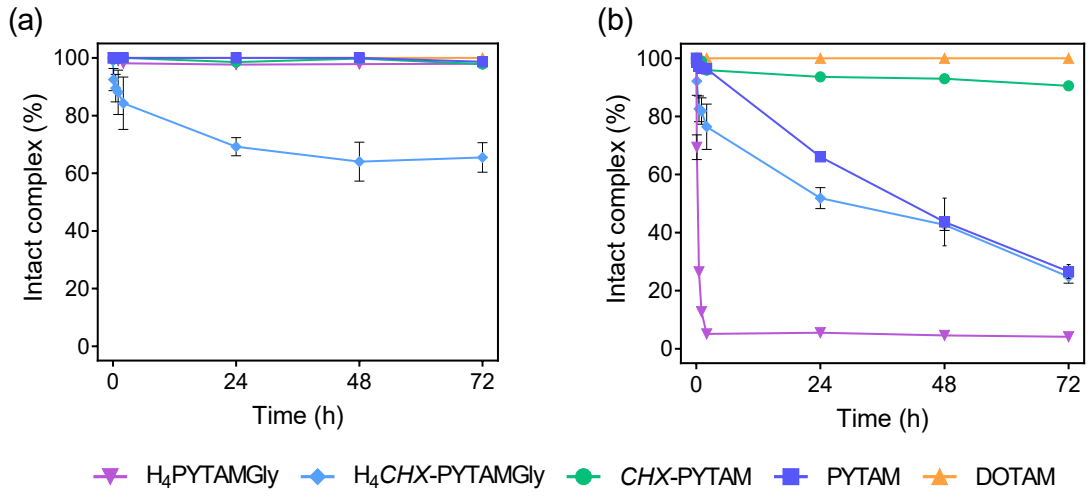


Figure S9 Challenging studies of the ^{203}Pb-labelled complexes prepared at room temperature. (a) Excess EDTA challenge (20 equiv.). (b) Excess cold Pb(II) challenge (20 equiv.).

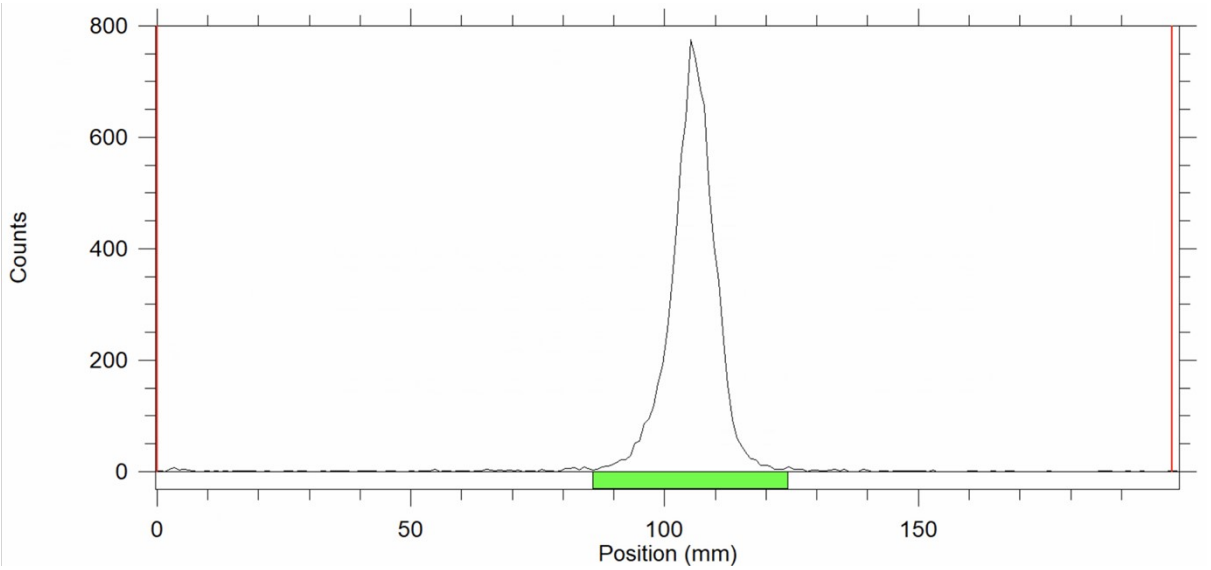


Figure S10: Negative control showing no radiolabelling with [^{203}Pb]Pb(II).

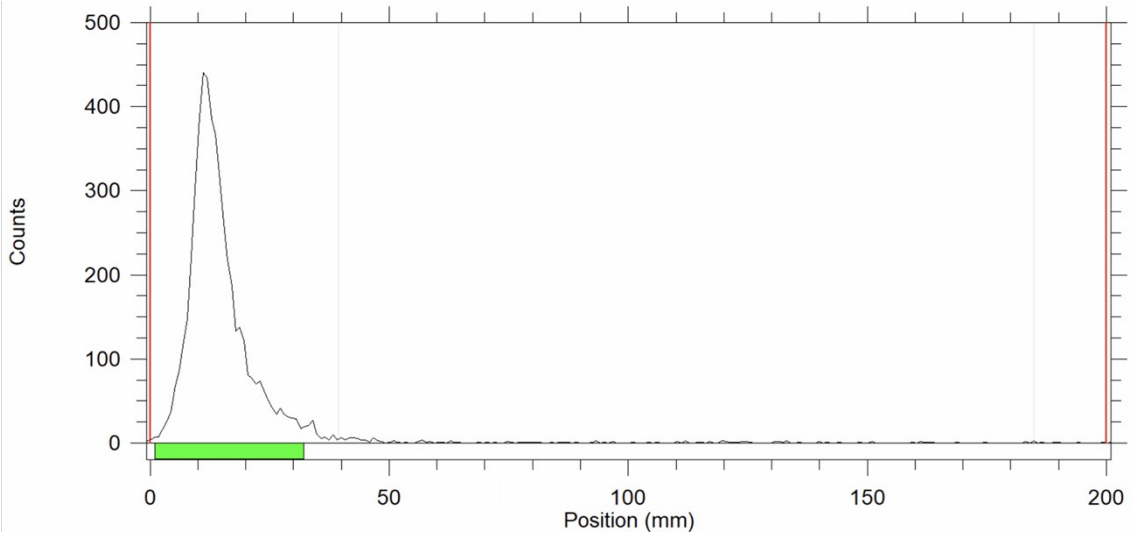


Figure S11: Example of iTLC showing quantitative radiolabelling of PYTAM with [^{203}Pb]Pb(II).

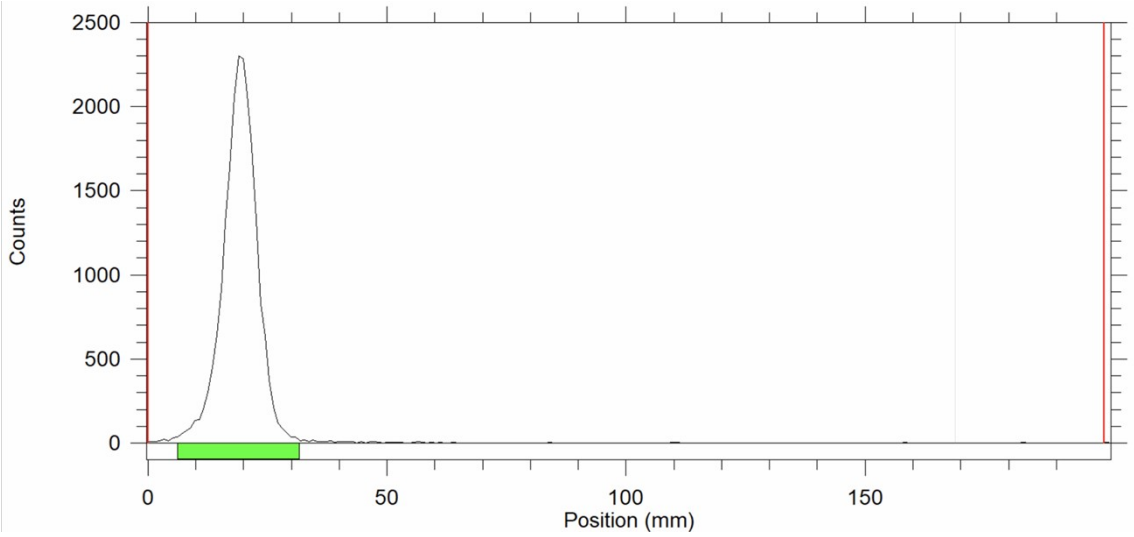


Figure S12: Example of iTLC showing quantitative radiolabelling of *CHX*-PYTAM with [^{203}Pb]Pb(II).

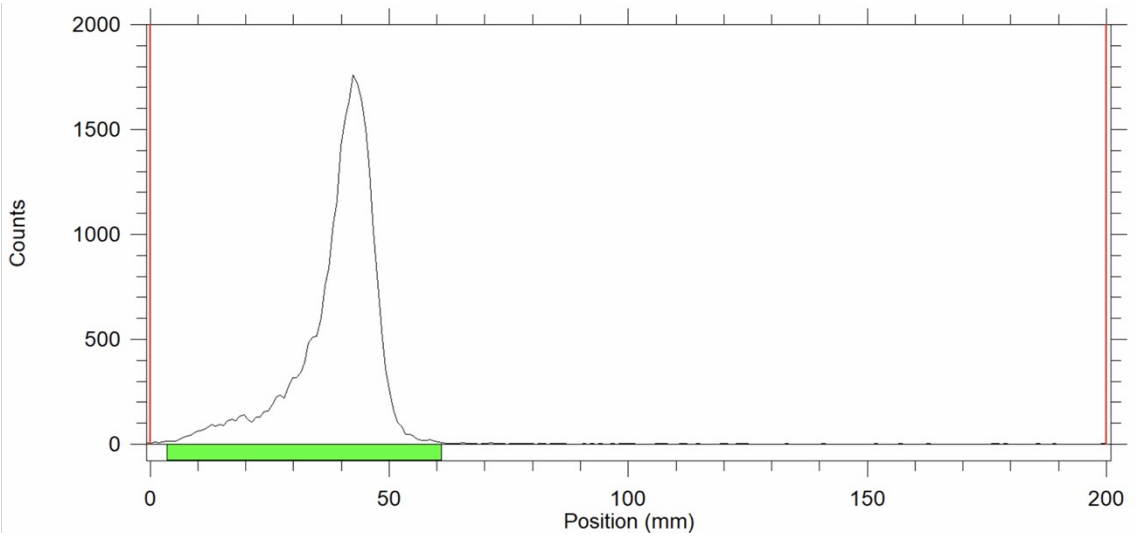


Figure S13: Example of iTLC showing quantitative radiolabelling of H_4PYTAMGly with [^{203}Pb]Pb(II).

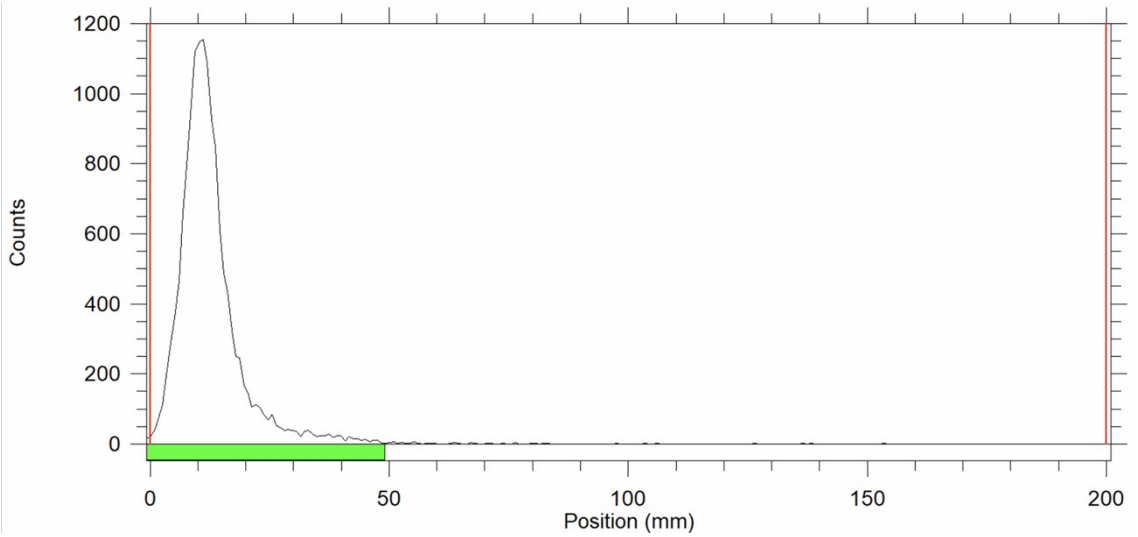


Figure S14: Example of iTLC showing quantitative radiolabelling of H_4*CHX*-PYTAMGly with [^{203}Pb]Pb(II).

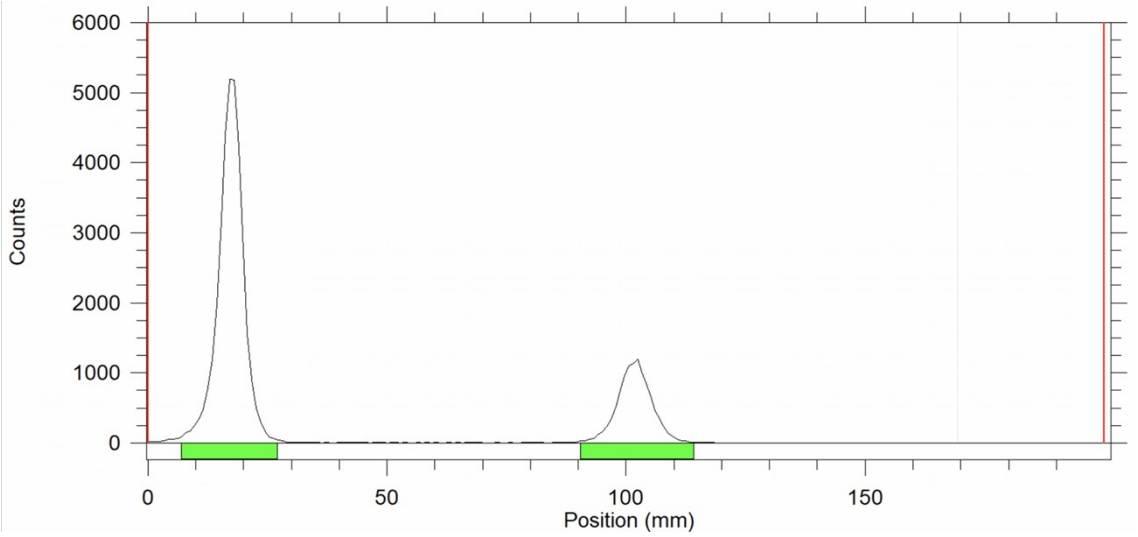


Figure S15: Example of iTLC showing ~75% radiolabelling of *CHX*-PYTAM with [^{203}Pb]Pb(II).

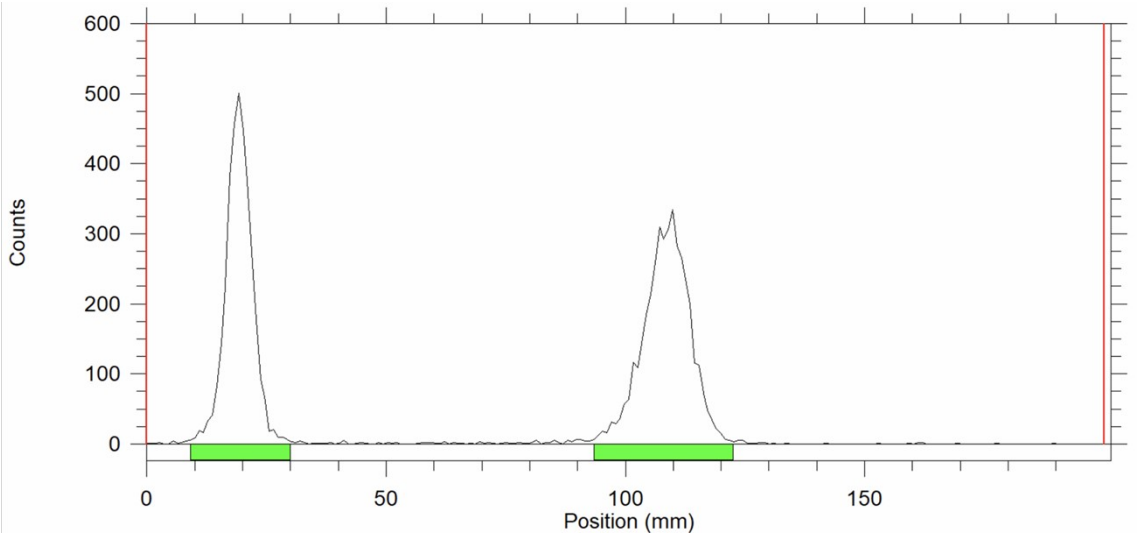


Figure S16: Example of iTLC showing ~45% radiolabelling of PYTAM with [^{203}Pb]Pb(II).

Table S15: MPLC purification method A

Column volumes (CV)	Time (min:s)	Flow rate (mL/min)	%A (H_2O)	%B (CH_3CN)
0.00	0:00	15	100	0
4.00	5:28	15	100	0
4.62	6:19	15	90	10
4.67	6:23	15	90	10
6.13	8:23	15	65	35
6.17	8:26	15	65	35
6.22	8:29	15	64	36
7.17	9:47	15	64	36
11.01	15:02	15	0	100
17.01	23:13	15	0	100

Table S16: MPLC purification method B

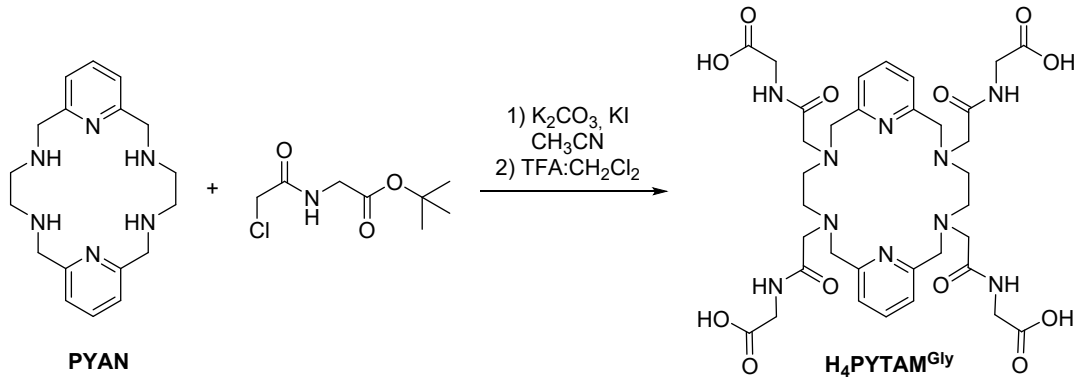
Column volumes (CV)	Time (min:s)	Flow rate (mL/min)	%A (H_2O)	%B (CH_3CN)
0.00	0	15	100	0
6.00	8:12	15	100	0
7.93	10:43	15	73	27
9.23	12:41	15	73	27
13.59	16:43	15	0	100
19.59	18:49	15	0	100

Table S17: MPLC purification method C

Column volumes (CV)	Time (min:s)	Flow rate (mL/min)	%A (H_2O)	%B (CH_3CN)
0.00	0	15	100	0
6.00	8:12	15	100	0
8.43	11:31	15	59	41
9.84	13:27	15	59	41
13.39	18:18	15	0	100
19.39	26:30	15	0	100

Table S18: HPLC conditions for the purification of the chelators (A = H_2O+0.1%TFA, B = CH_3CN+0.1%TFA)

Chelator	Conditions	Retention time (min)
PYTAM	Isocratic 95% A (8 min)	5.91
CHX-PYTAM	85 to 65% A (10 min)	6.37
H_4PYTAM-Gly	Isocratic 95% A (2 min) and gradient from 95 to 50% (16 min)	8.62
H_4*CHX*-PYTAMGly	90 to 70% A (25 min)	15.11



Scheme S1: Synthesis of **H_4PYTAMGly**.

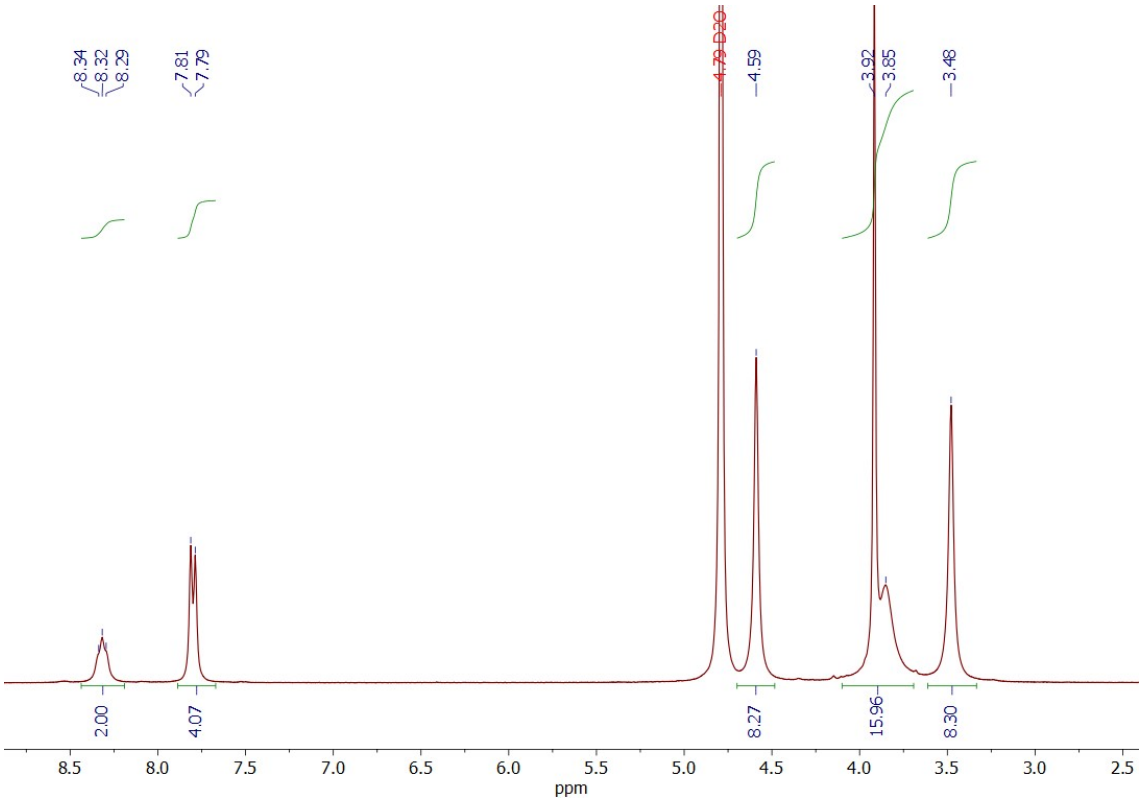


Figure S17: ^{1}H NMR spectrum of compound **H_4PYTAMGly** (300 MHz, D_2O, pD= 2.00, 298 K).

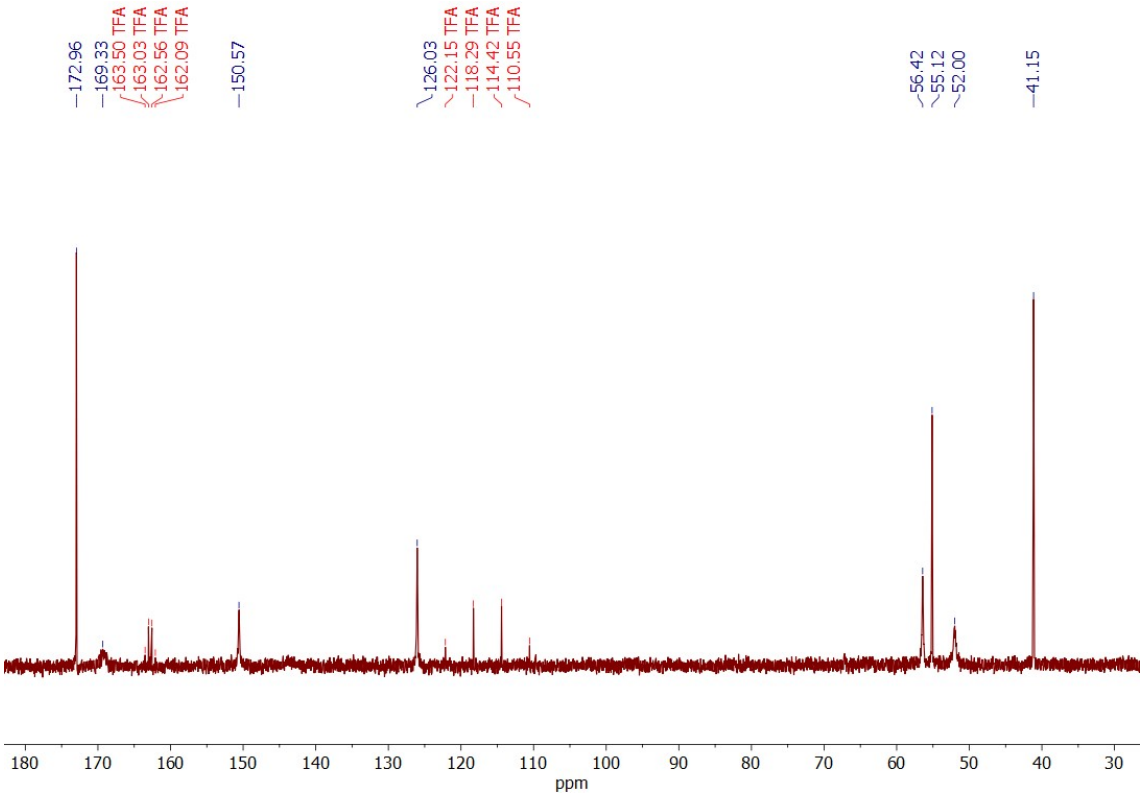


Figure S18: ^{13}C NMR spectrum of compound **H_4PYTAMGly.** (75 MHz, D_2O, pD= 2.00, 298 K).

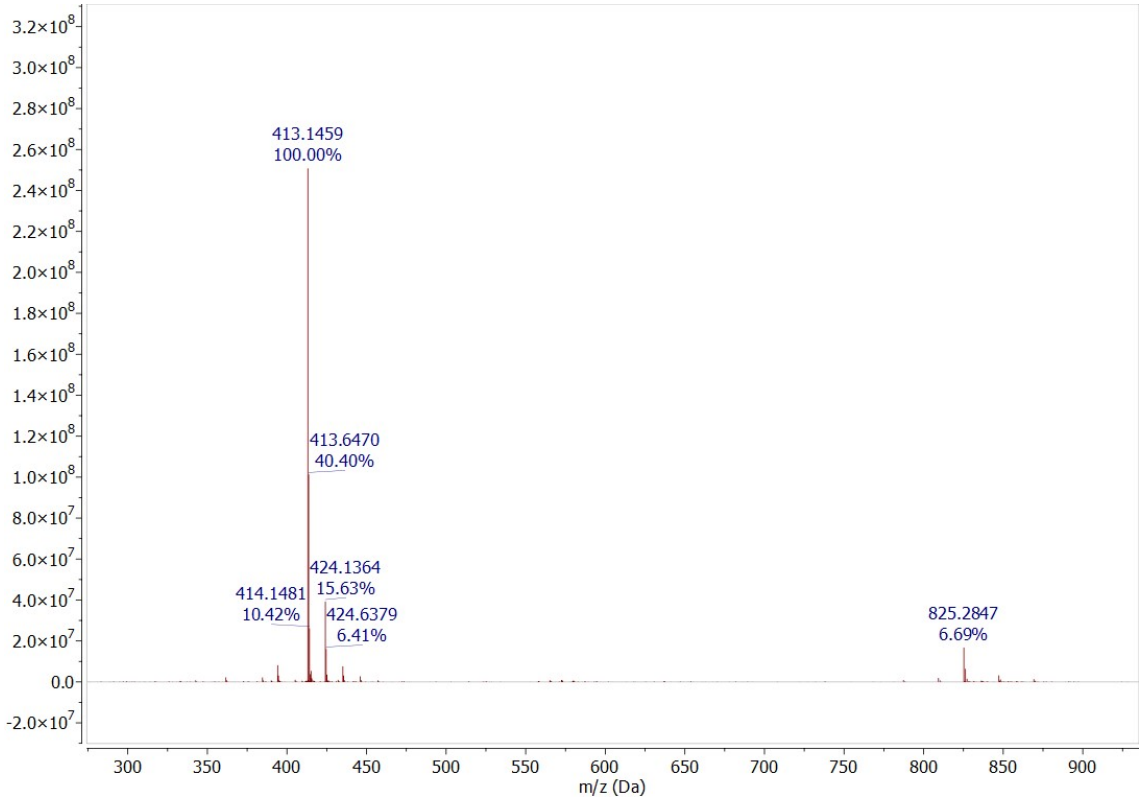
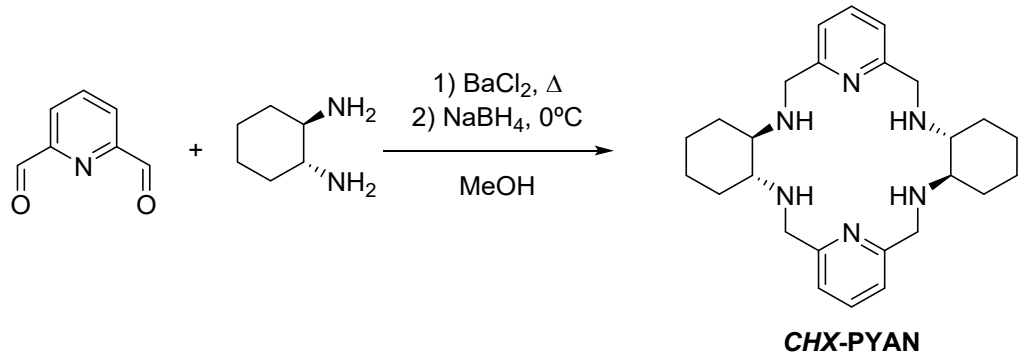


Figure S19: Experimental high resolution mass spectrum (ESI^+) of compound **H_4PYTAMGly**.



***CHX*-PYAN**

Scheme S2: Synthesis of ***CHX*-PYAN**.

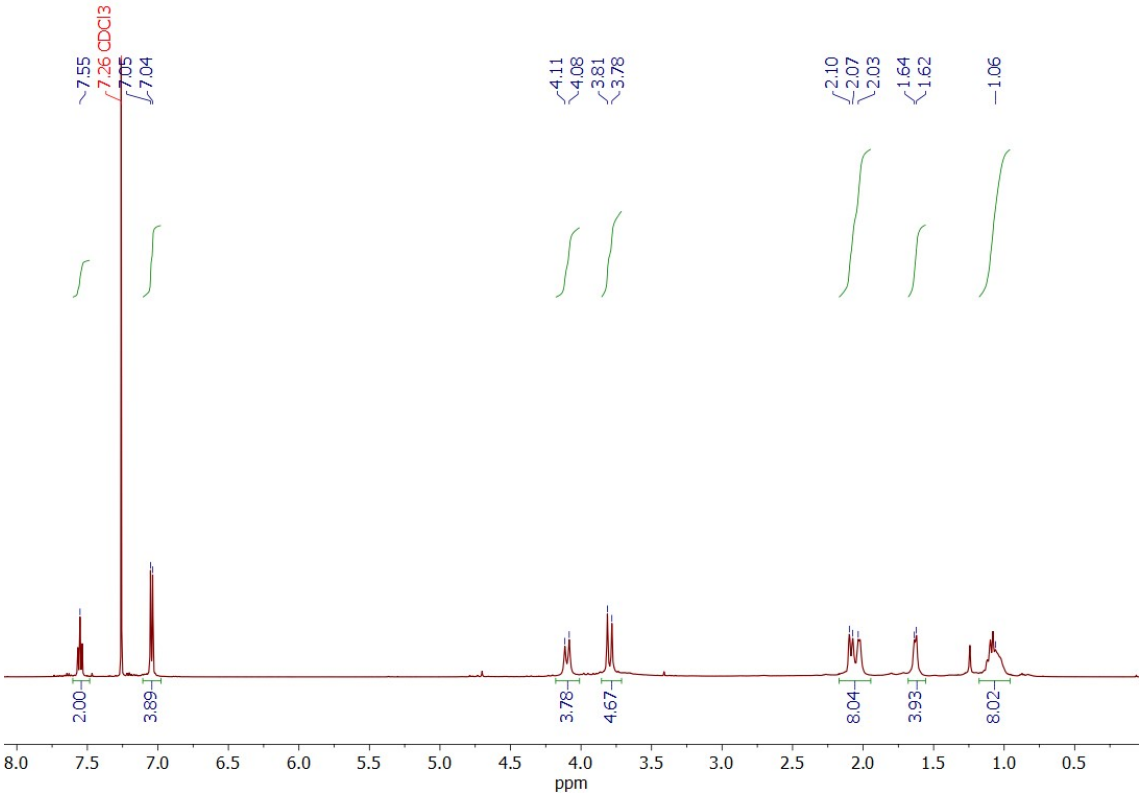


Figure S20: ^{1}H NMR spectrum of ***CHX-PYAN*** (500 MHz, $CDCl_3$, 298 K).

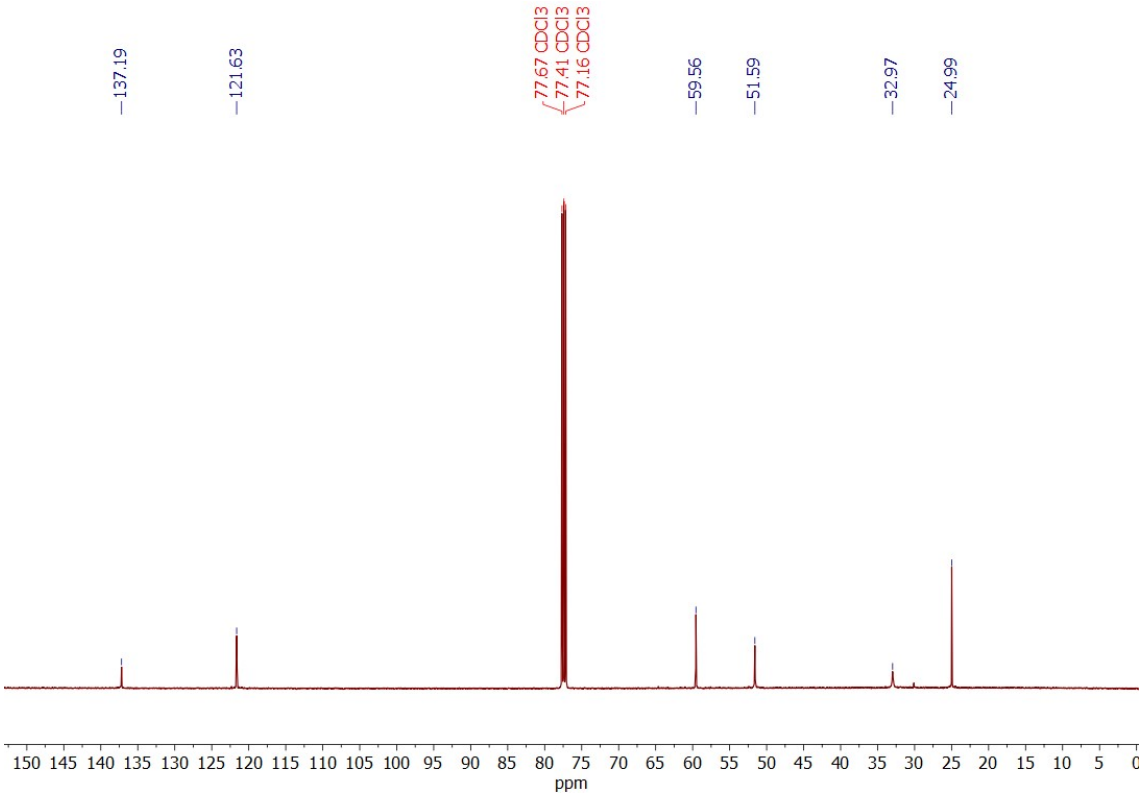


Figure S21: ^{13}C NMR spectrum of ***CHX-PYAN*** (126 MHz, $CDCl_3$, 298 K).

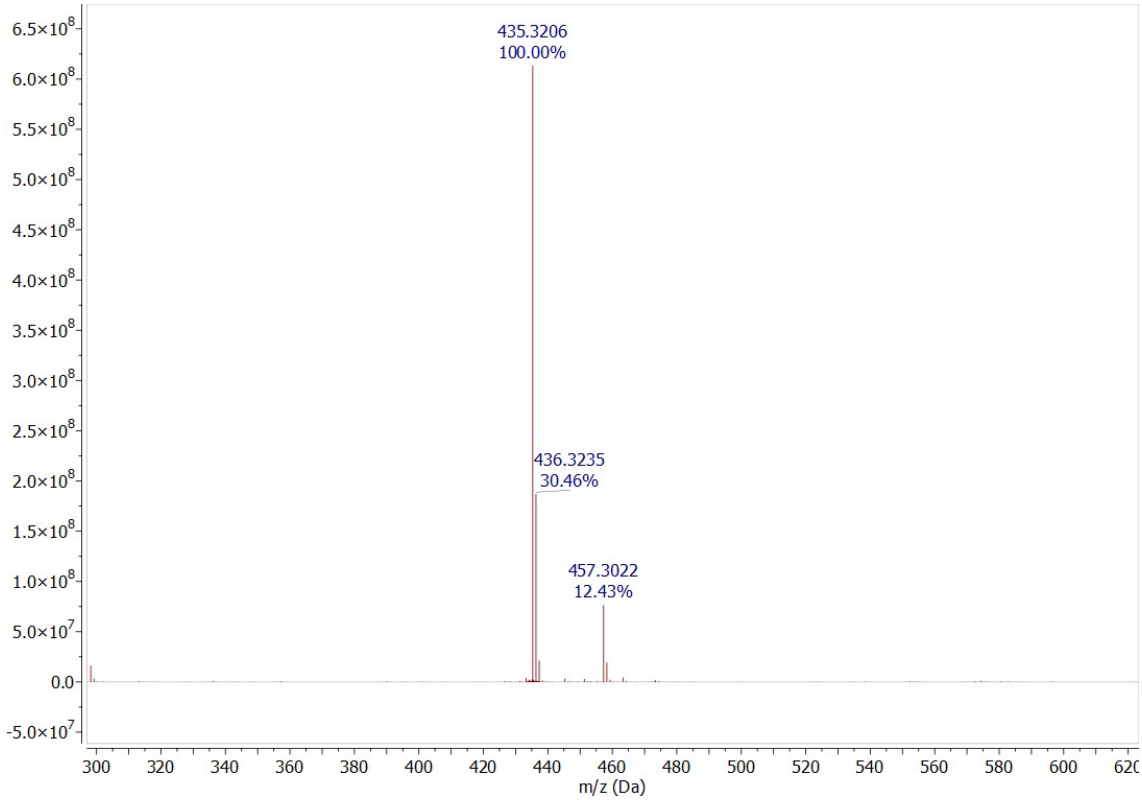
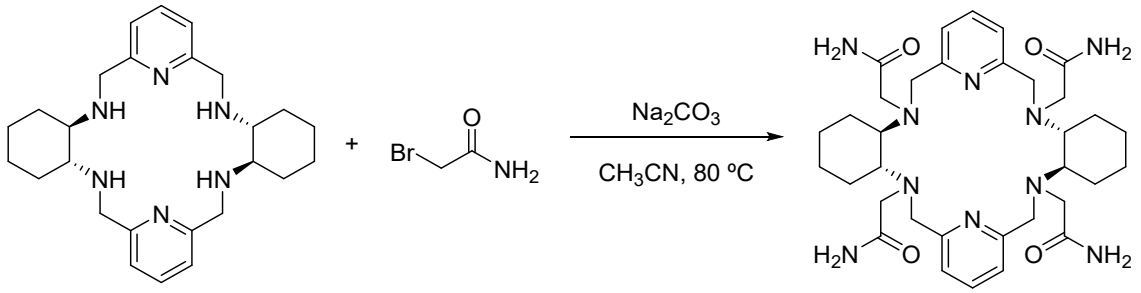


Figure S22: Experimental high resolution mass spectrum (ESI^+) of ***CHX-PYAN.***



Scheme S3: Synthesis of ***CHX*-PYTAM**

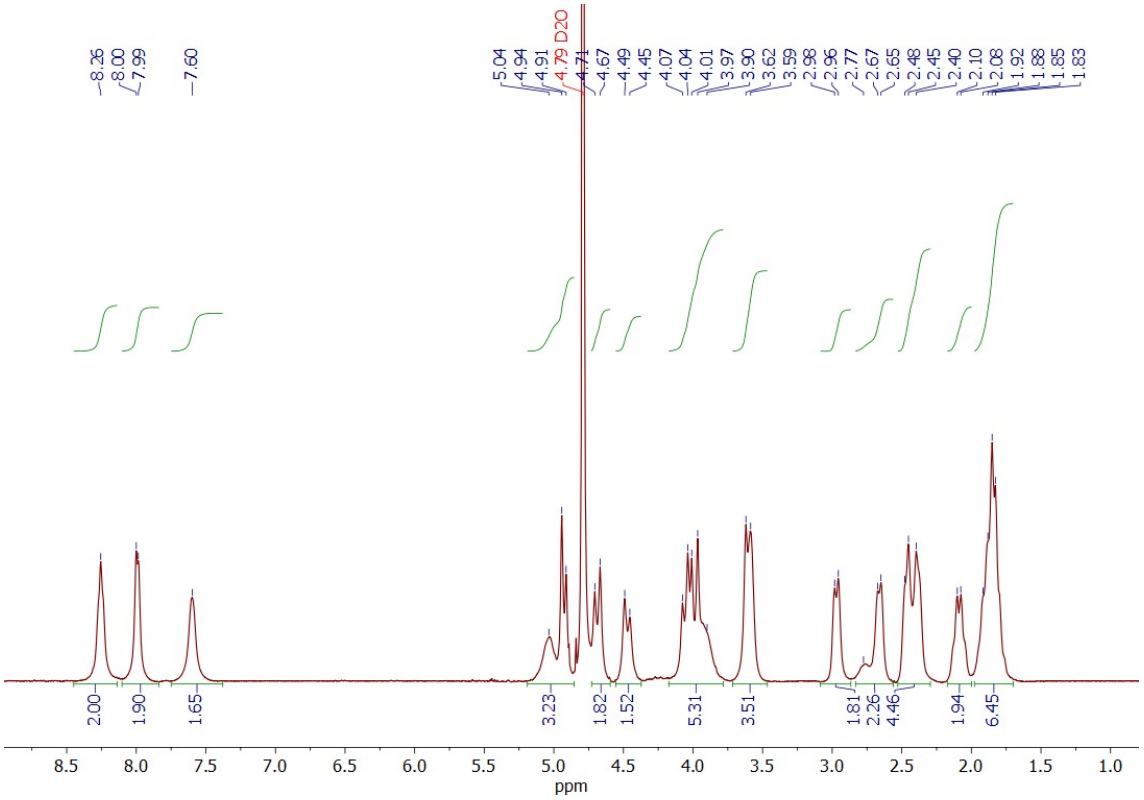


Figure S23: ^{1}H NMR spectrum of compound ***CHX*-PYTAM** (400 MHz, D_2O, pD= 1.74, 343.15 K).

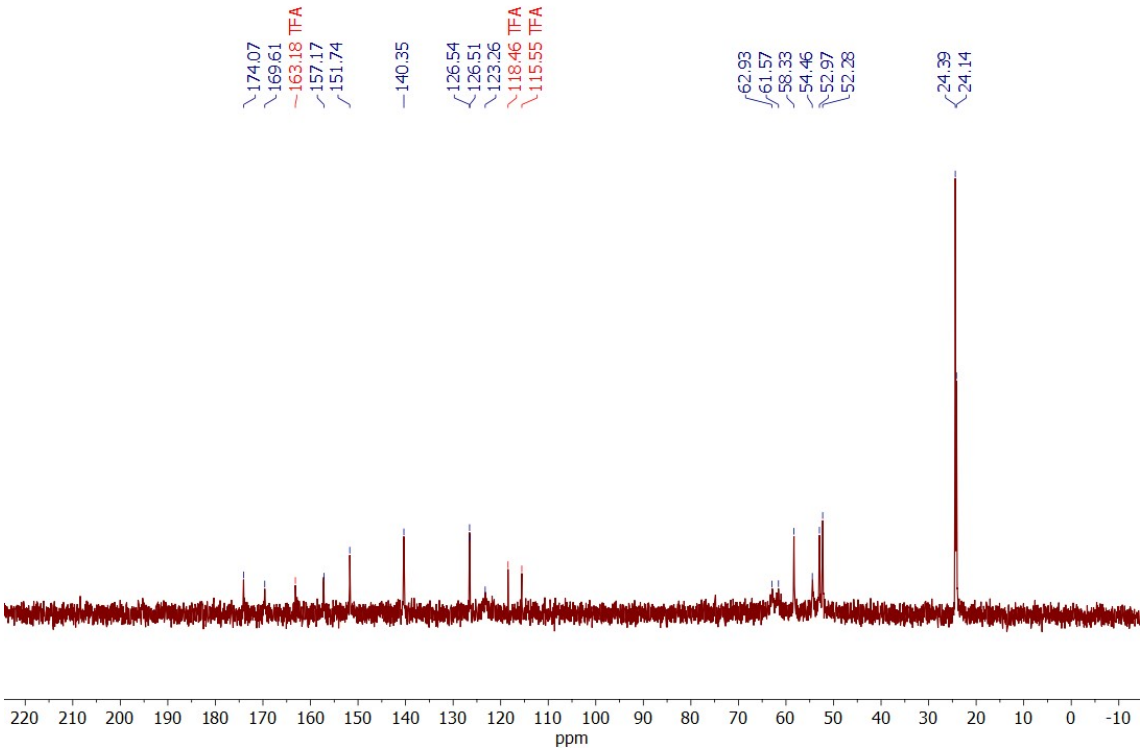


Figure S24: ^{13}C NMR spectrum of compound ***CHX*-PYTAM** (101 MHz, D_2O, pD= 1.74, 343.15 K).

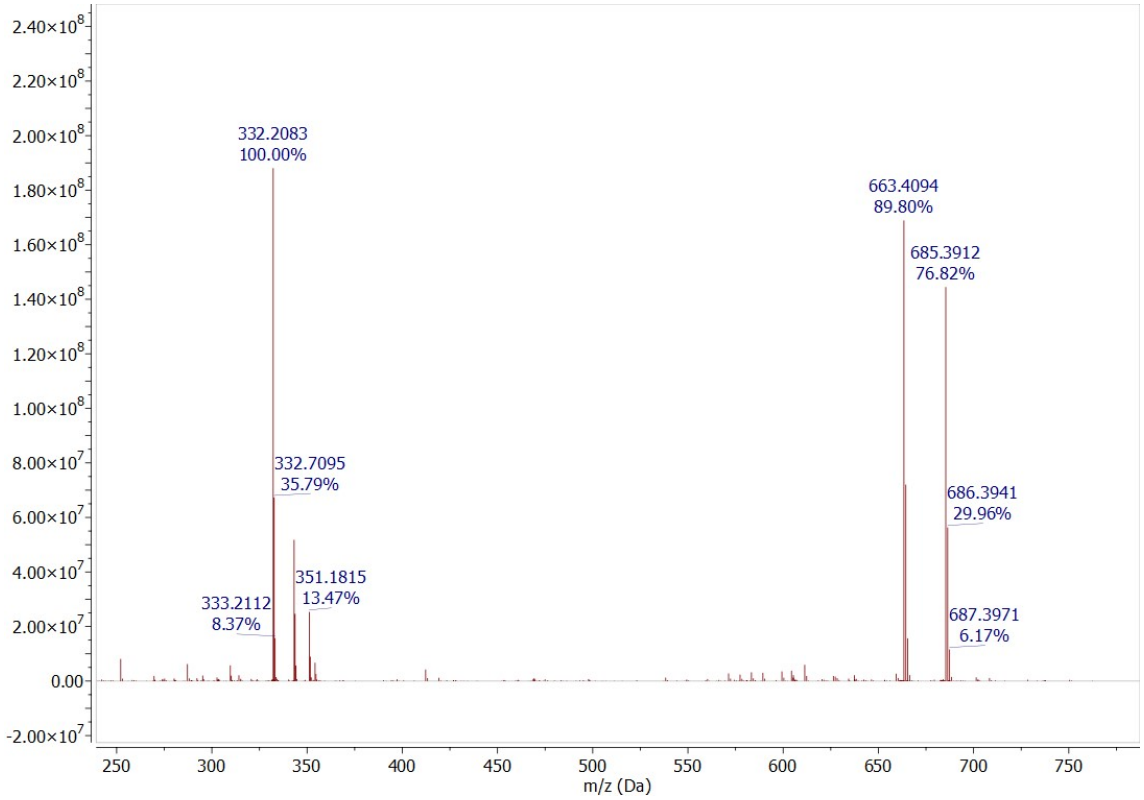
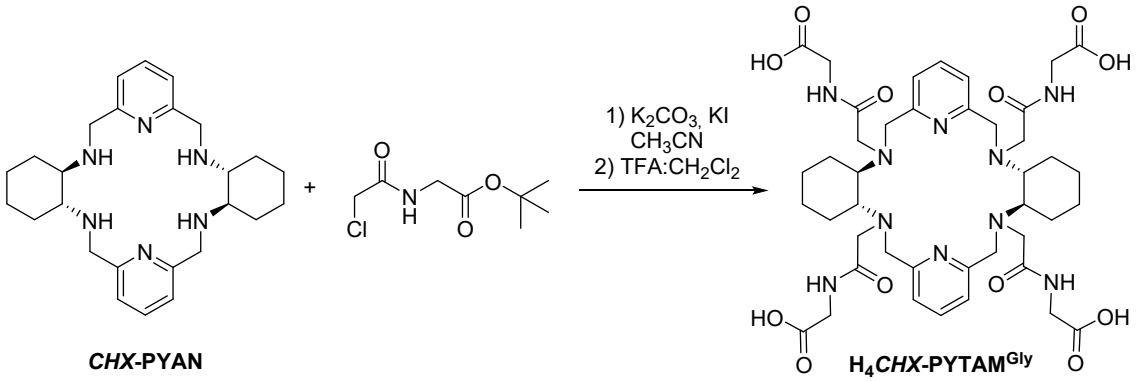


Figure S25: Experimental high resolution mass spectrum (ESI^+) of compound ***CHX*-PYTAM.**



Scheme S4: Synthesis of **H_4*CHX*-PYTAMGly**

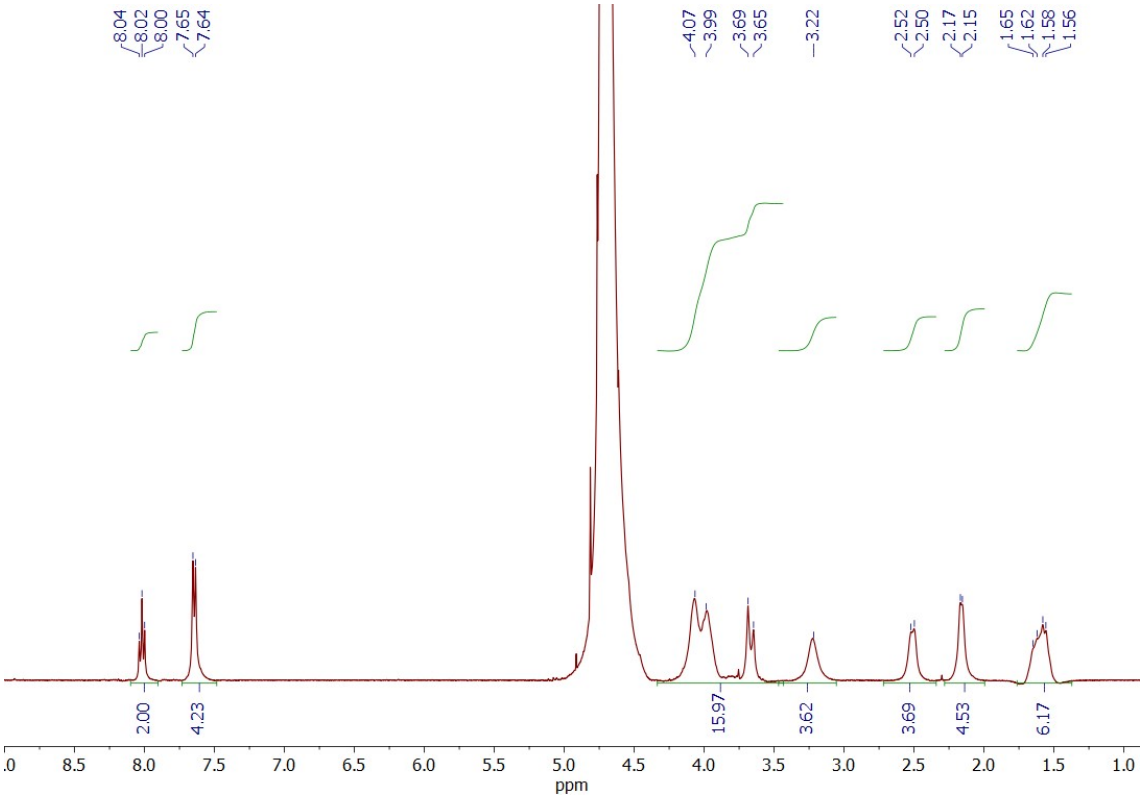


Figure S26: ^{1}H NMR spectrum of compound **H_4*CHX*-PYTAMGly** (400 MHz, D_2O, pD= 9.8, 343.15 K).

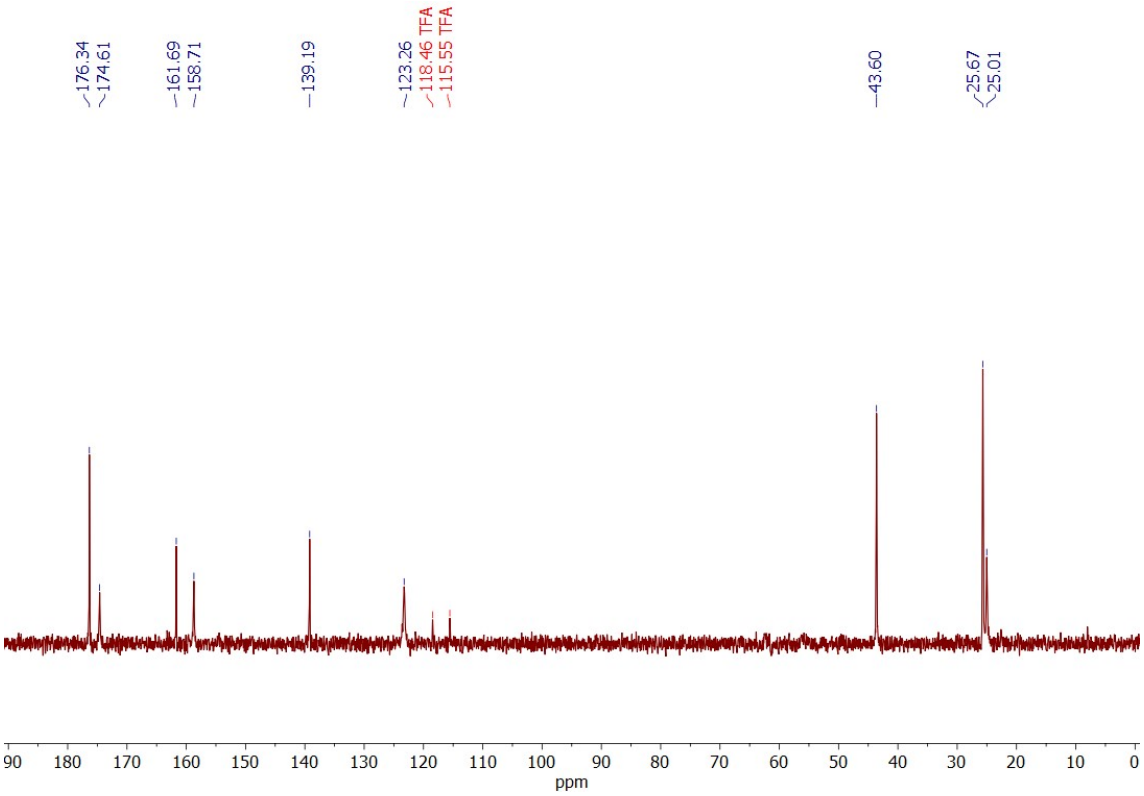


Figure S27: ^{13}C NMR spectrum of compound **H_4*CHX*-PYTAMGly** (400 MHz, D_2O, pD= 9.8, 343.15 K).

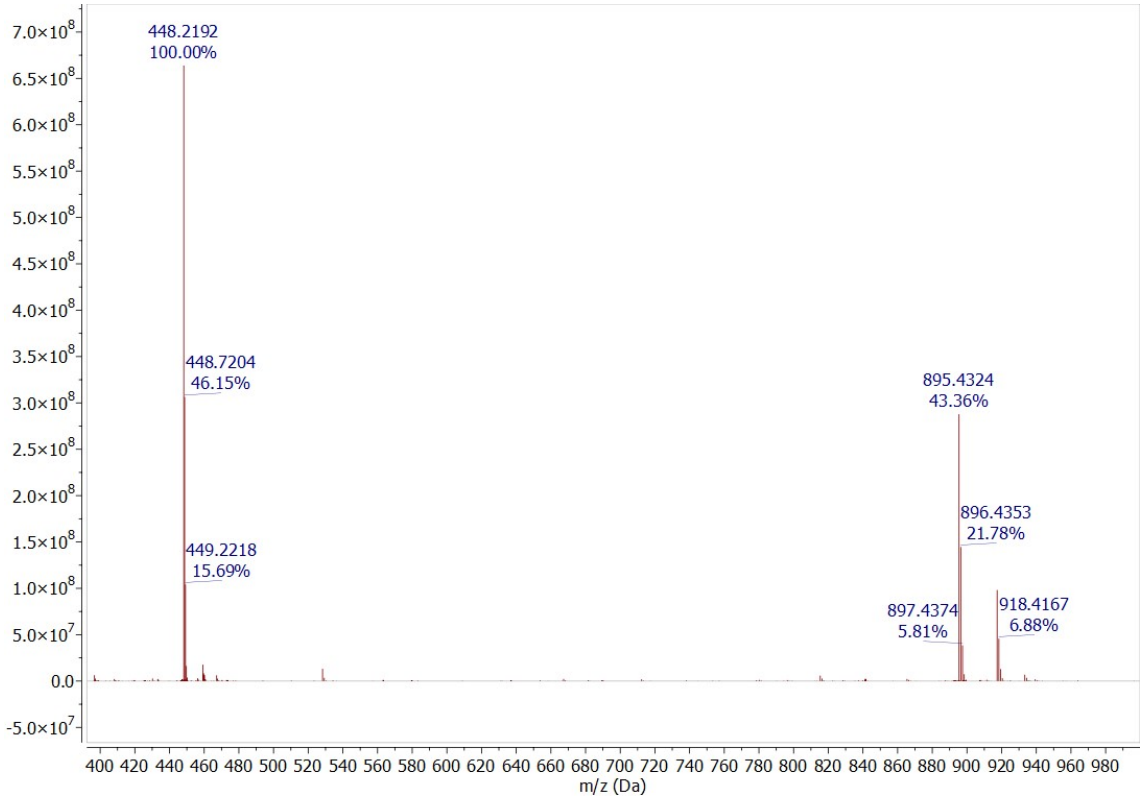
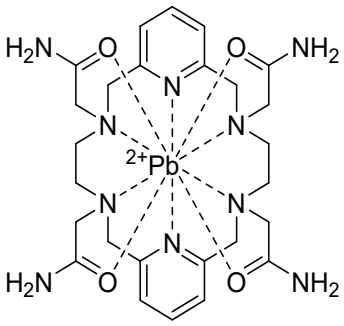


Figure S28: Experimental high resolution mass spectrum (ESI^+) of compound **H_4*CHX*-PYTAMGly**



Scheme S5: Structure of $[Pb(PYTAM)]^{2+}$

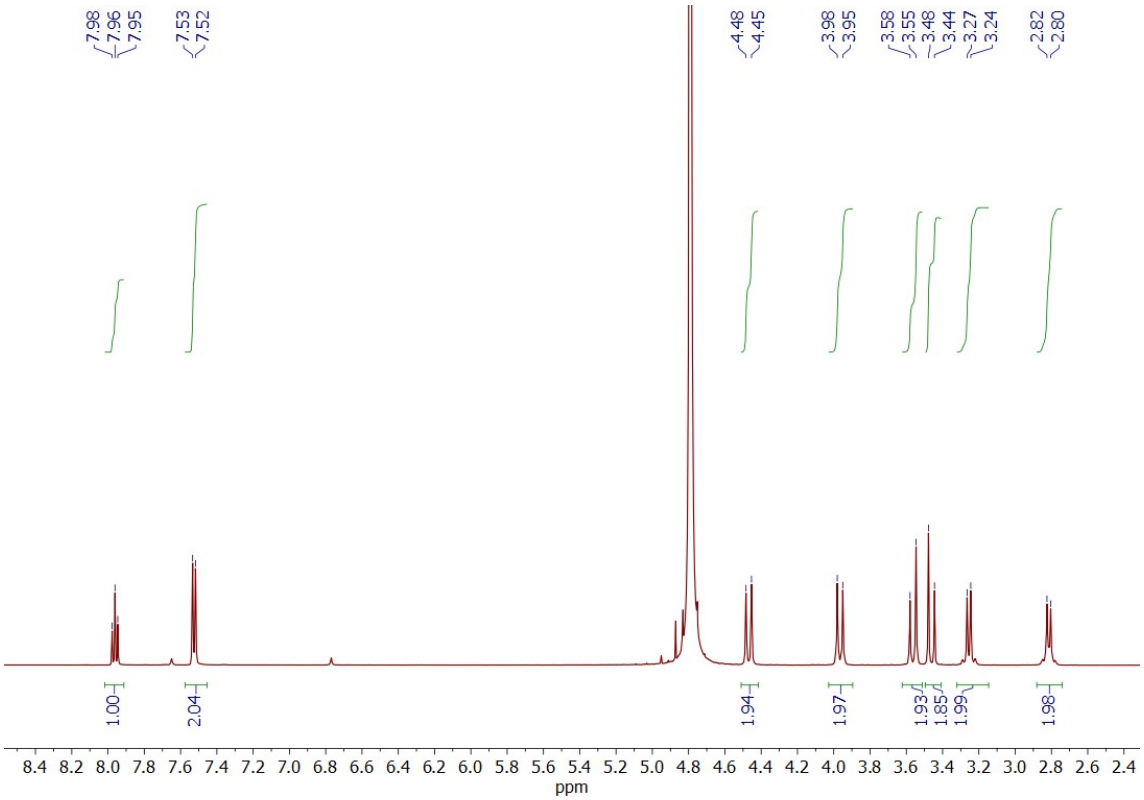


Figure S29: ^{1}H NMR spectrum of complex **$[Pb(PYTAM)]^{2+}$** (500 MHz, D_2O, pD= 6.5, 298 K).

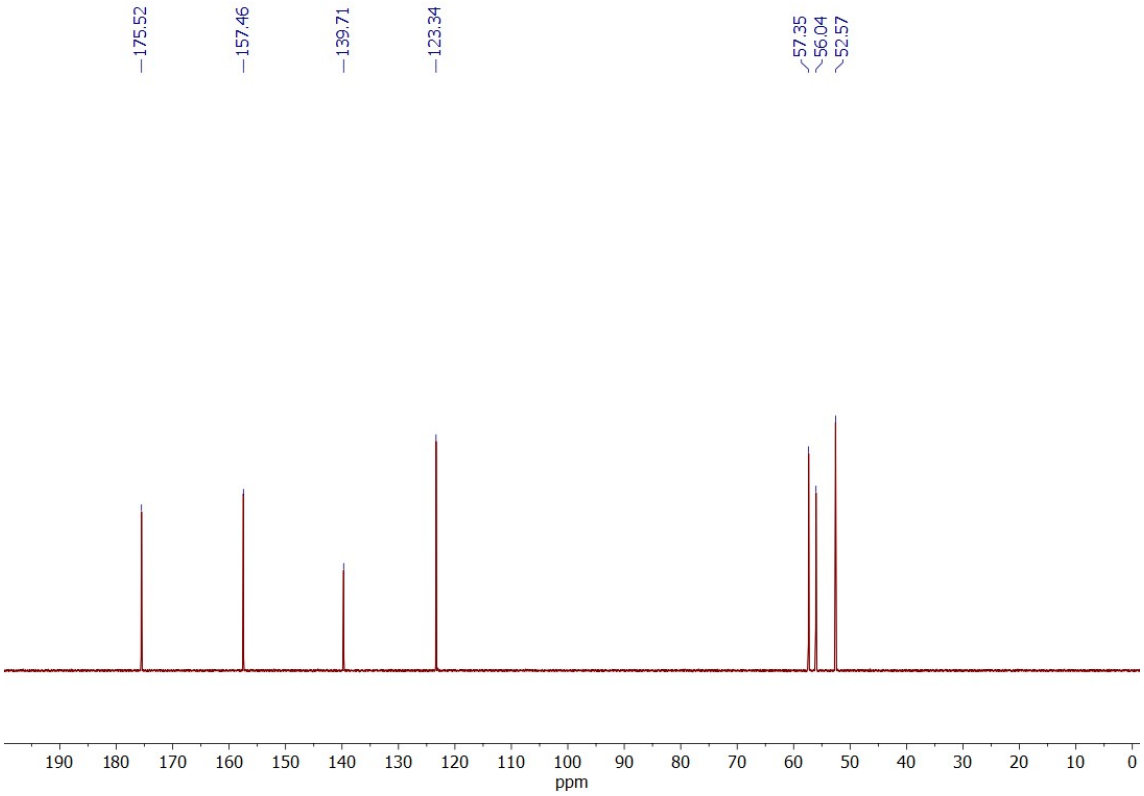


Figure S30: ^{13}C NMR spectrum of complex **[Pb(PYTAM)]$^{2+}$** (126 MHz, D_2O, pD= 6.5, 298 K).

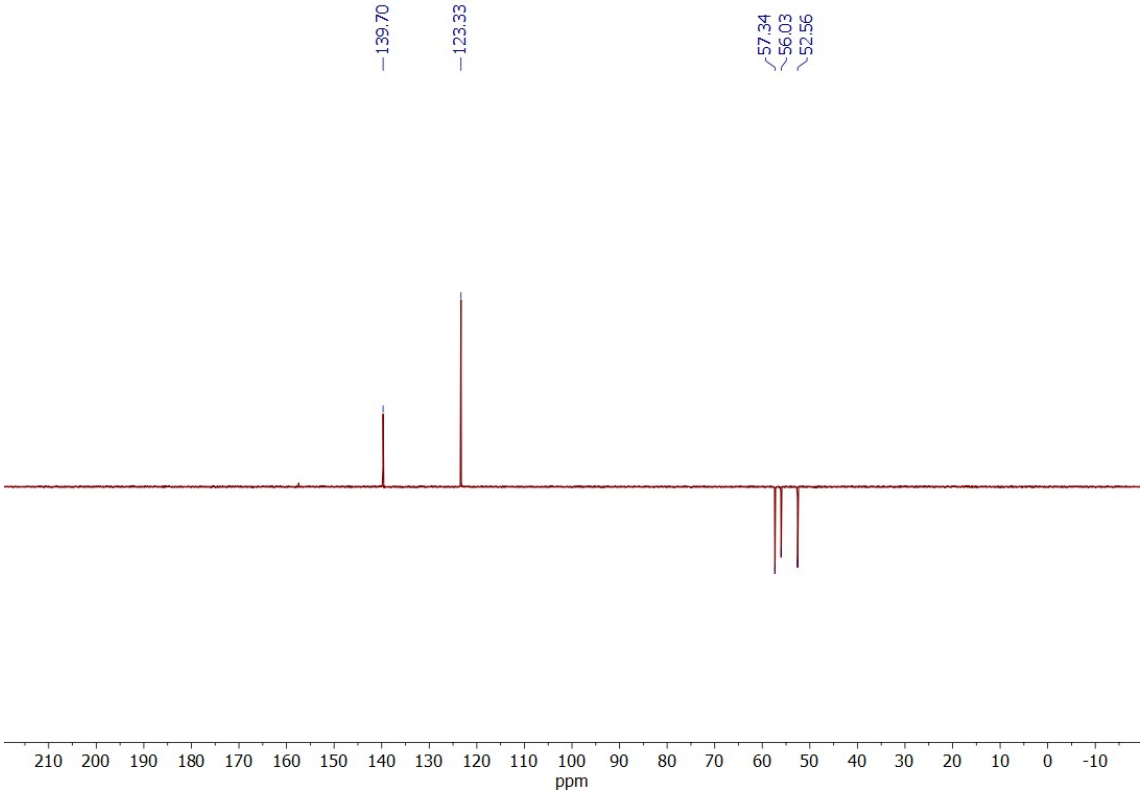


Figure S31: DEPT spectrum of complex **[Pb(PYTAM)]$^{2+}$** (126 MHz, D_2O, pD= 6.5, 298 K).

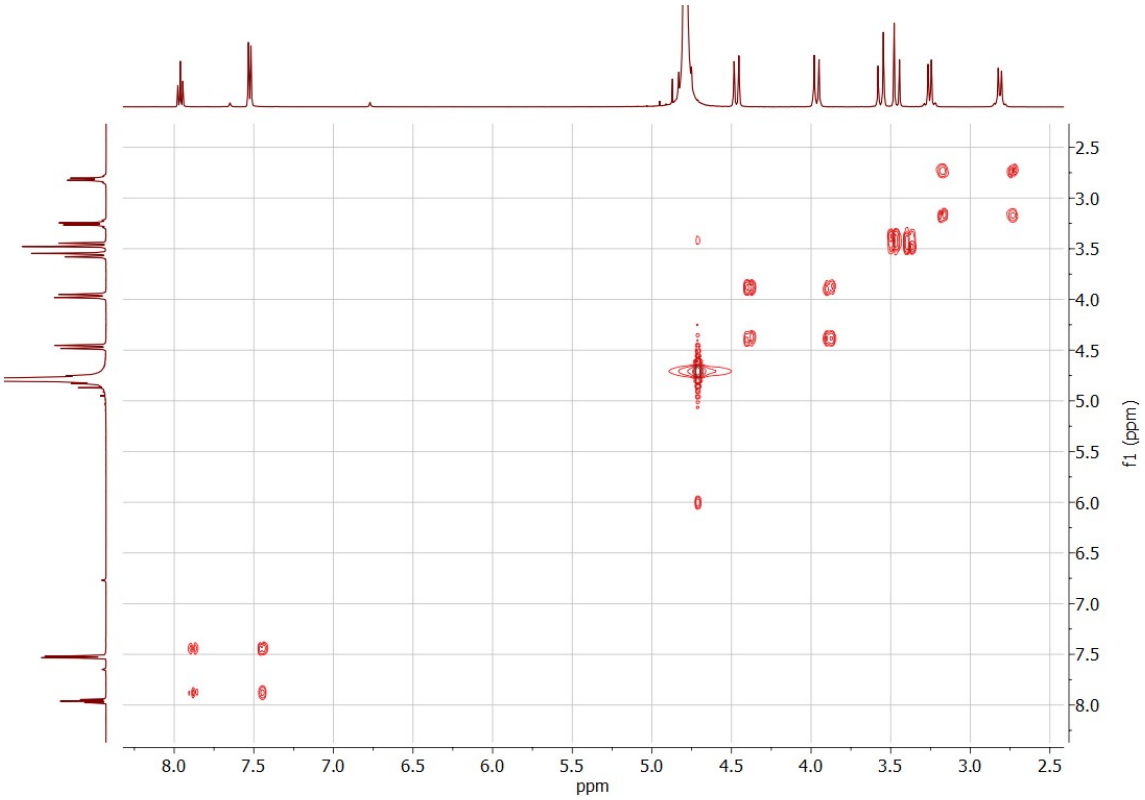


Figure S32: COSY NMR spectrum of complex **[Pb(PYTAM)]**$^{2+}$ (500 MHz, D_2O, pD= 6.5, 298 K).

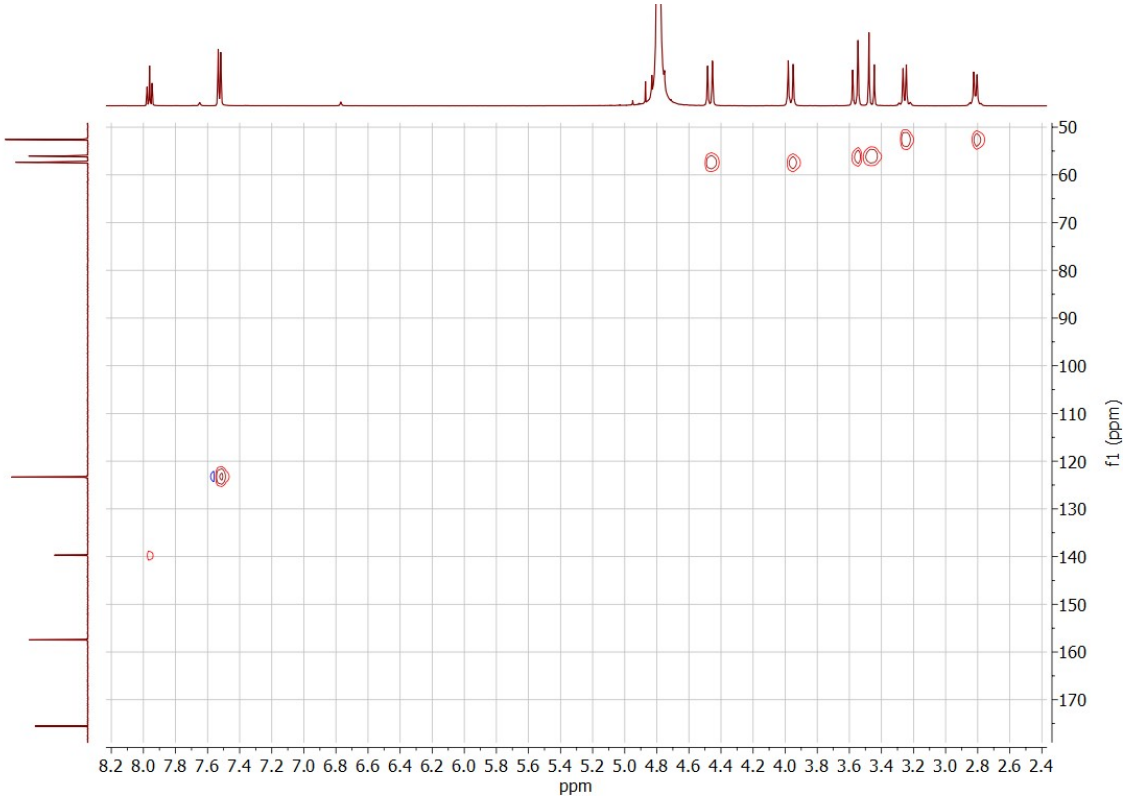


Figure S33: HSQC NMR spectrum of complex **[Pb(PYTAM)]**$^{2+}$ (D_2O, pD= 6.5, 298 K).

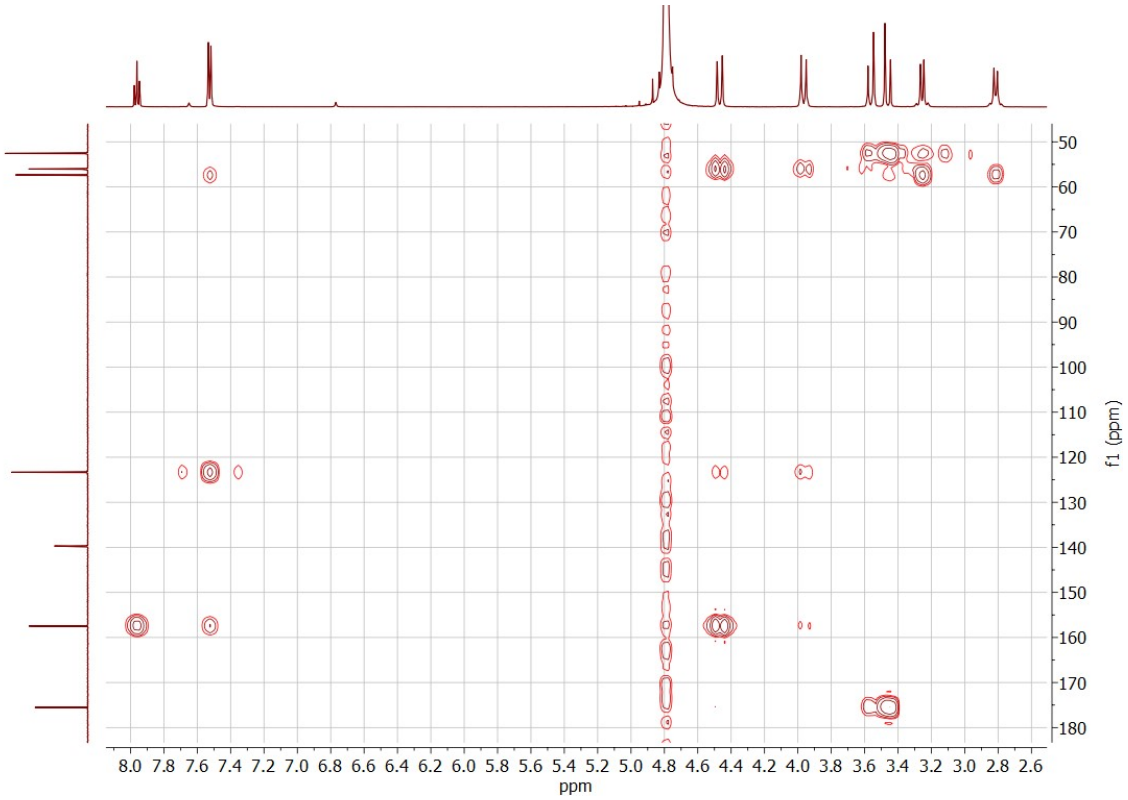


Figure S34: HMBC NMR spectrum of complex **[Pb(PYTAM)]$^{2+}$** (D_2O, pD= 6.5, 298 K).

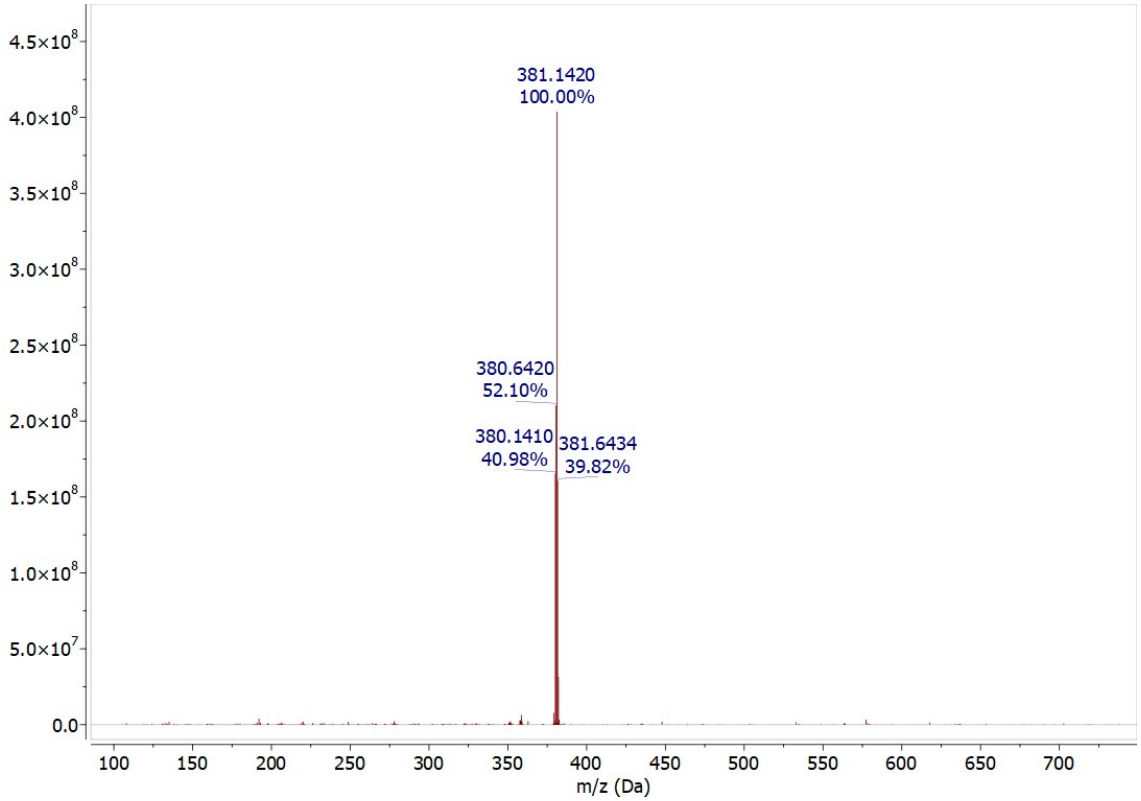
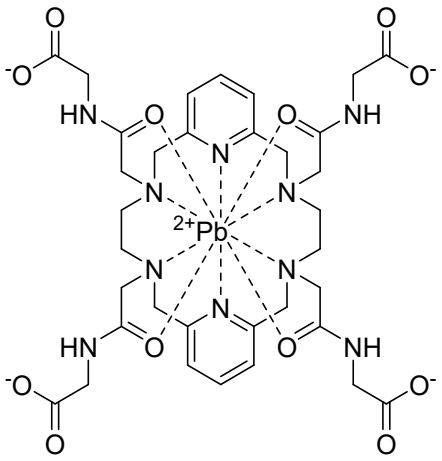


Figure S35: Experimental high resolution mass spectrum (ESI$^+$) of compound **[Pb(PYTAM)]$^{2+}$**



Scheme S6: Structure of $[Pb(PYTAMGly)]^{2-}$

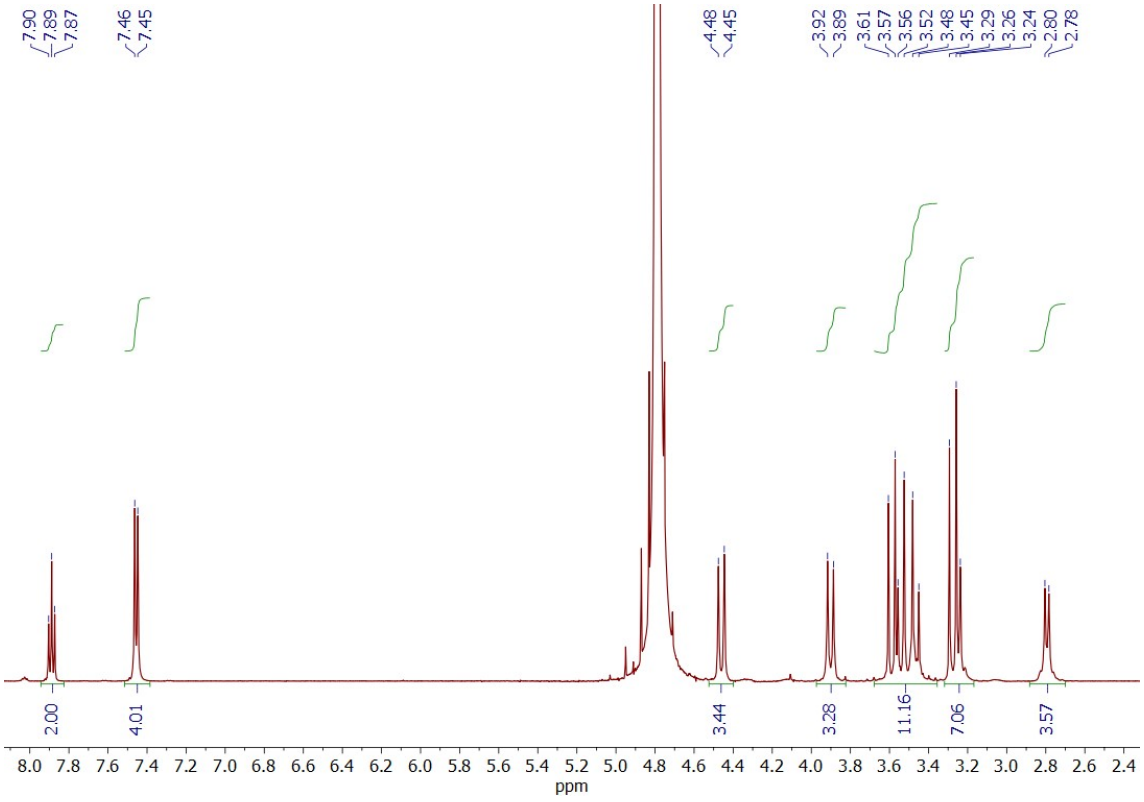


Figure S36: ^{1}H NMR spectrum of complex **$[Pb(PYTAMGly)]^{2-}$** (500 MHz, D_2O, pD= 6.8, 298 K).

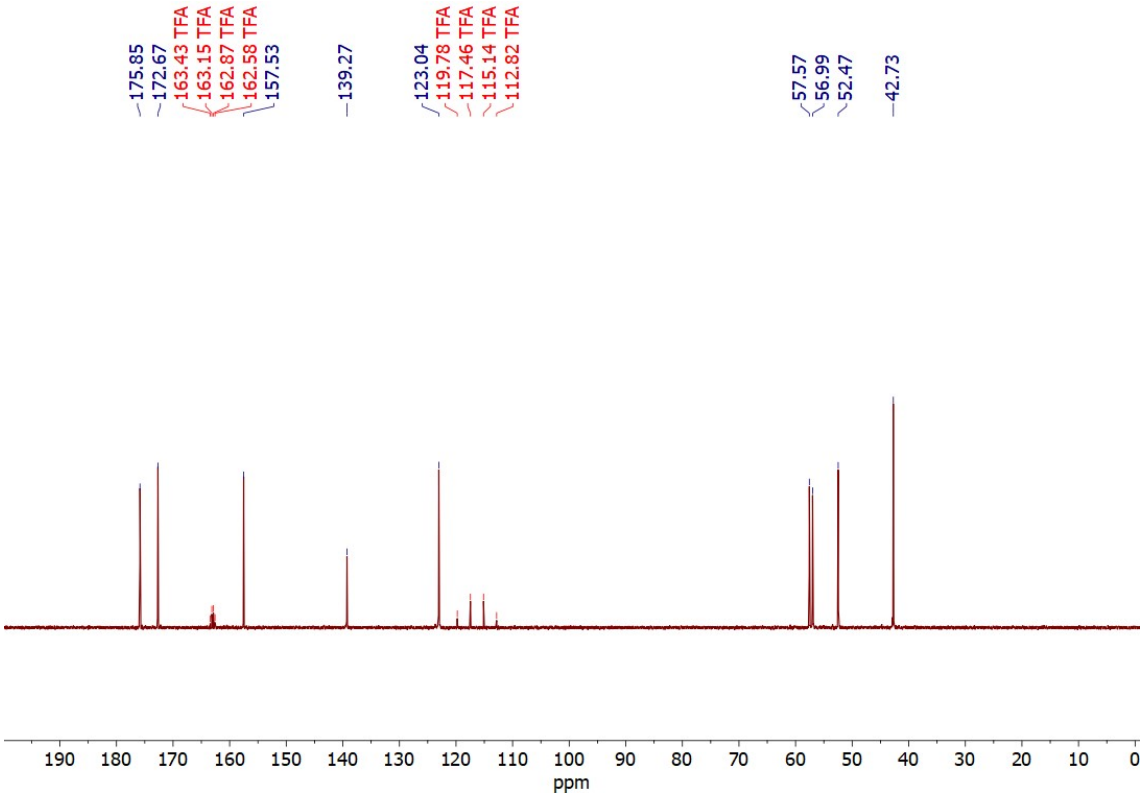


Figure S37: ^{13}C NMR spectrum of complex **[Pb(PYTAMGly)]$^{2-}$** (126 MHz, D_2O, pD= 6.8, 298 K).

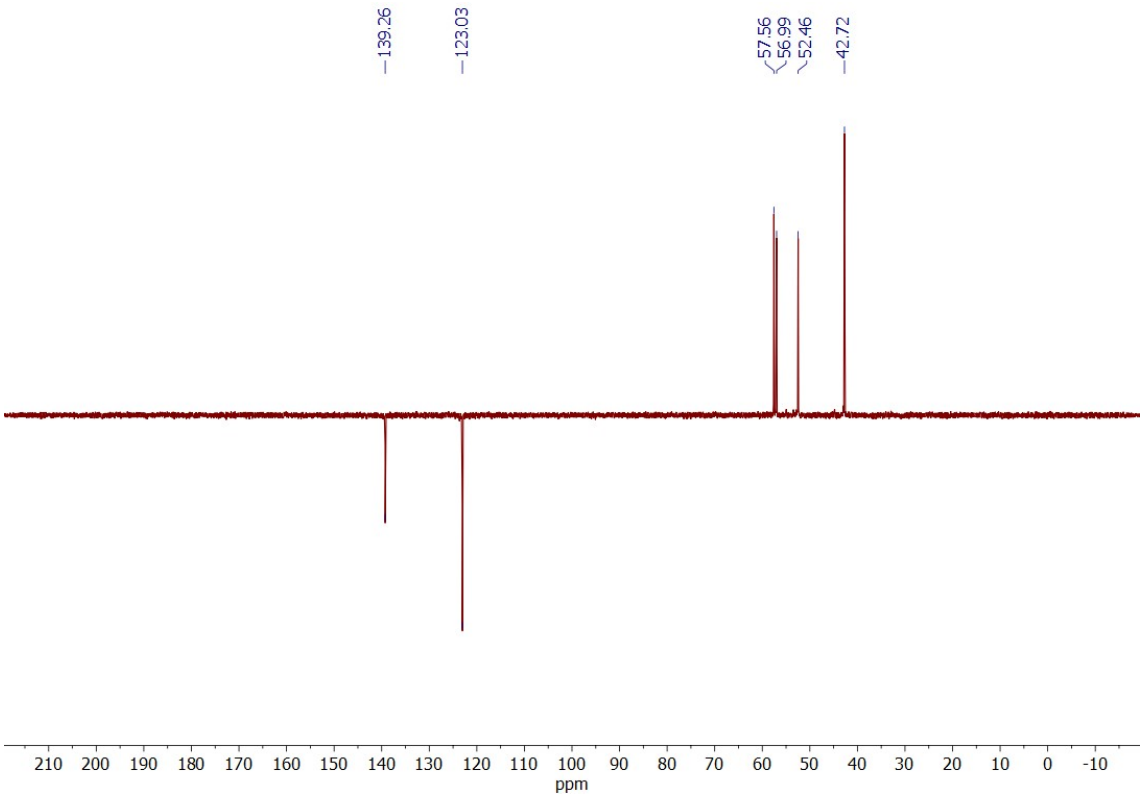


Figure S38: DEPT spectrum of complex **[Pb(PYTAMGly)]$^{2-}$** (126 MHz, D_2O, pD= 6.8, 298 K).

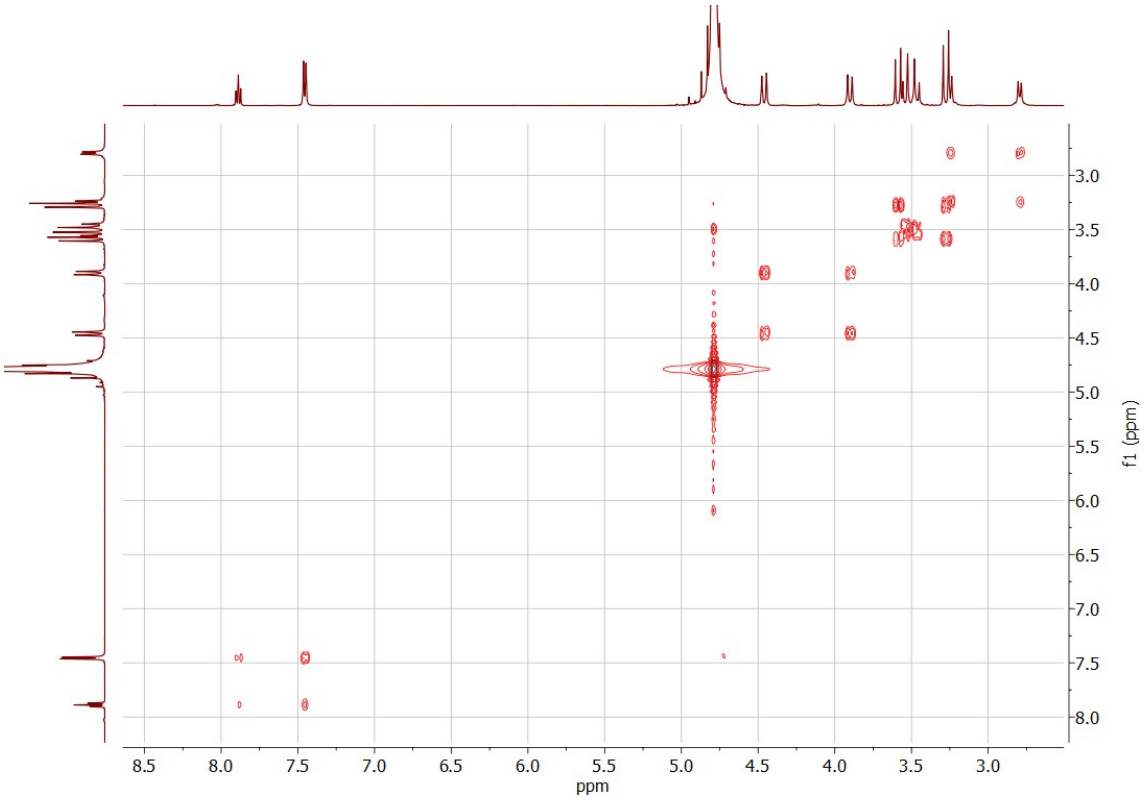


Figure S39: COSY NMR spectrum of complex **[Pb(PYTAMGly)]$^{2-}$** (500 MHz, D_2O, pD= 6.8, 298 K).

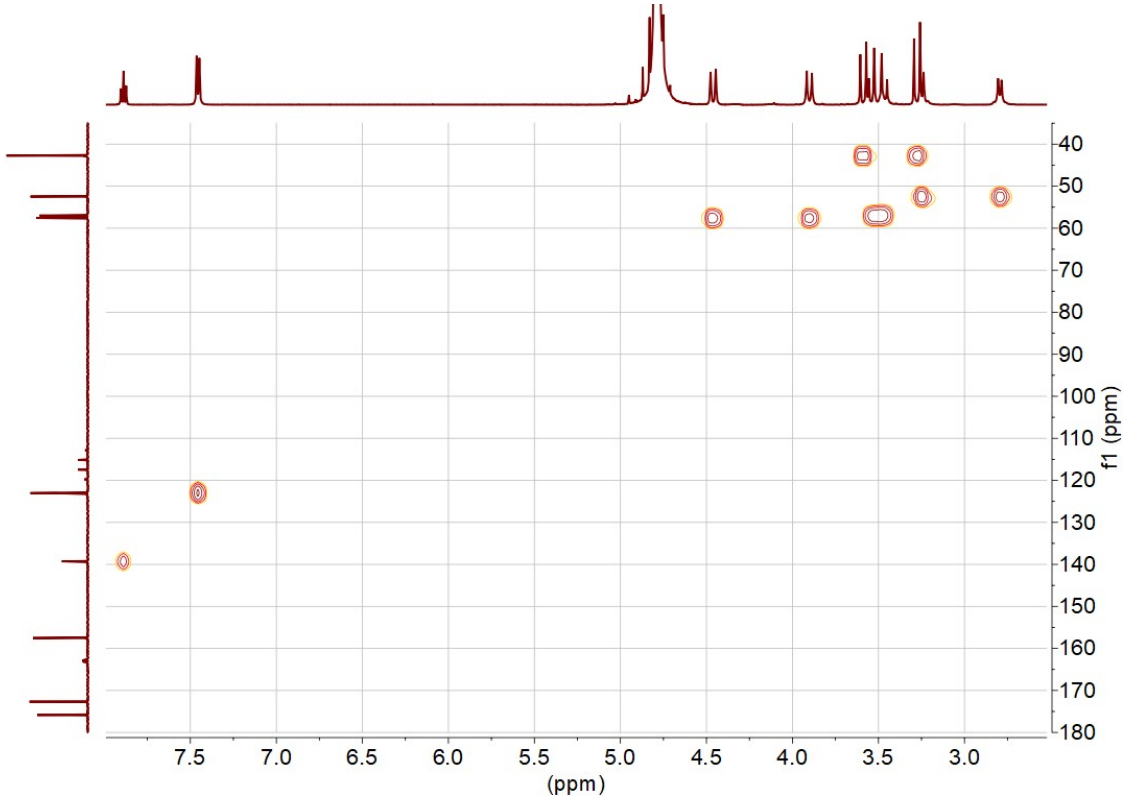


Figure S40: HSQC NMR spectrum of complex **[Pb(PYTAMGly)]$^{2-}$** (D_2O, pD= 6.8, 298 K).

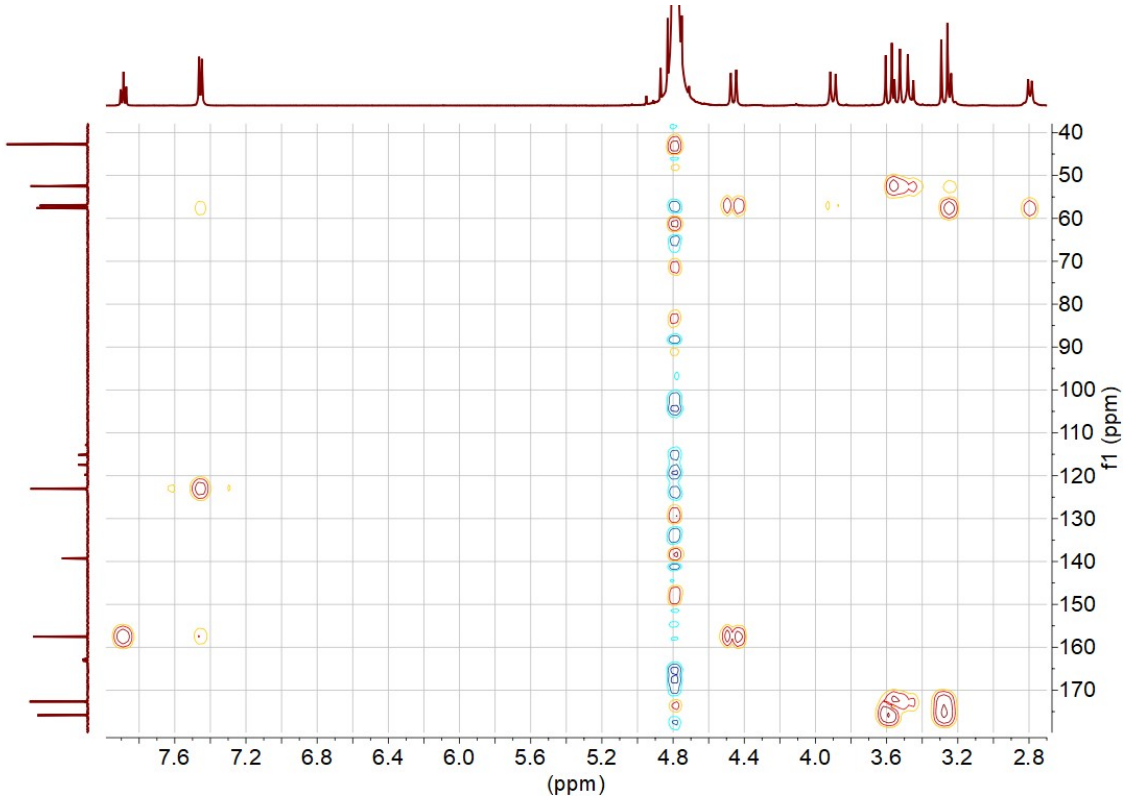


Figure S41: HMBC NMR spectrum of complex **[Pb(PYTAMGly)]$^{2-}$** (D_2O, pD= 6.8, 298 K).

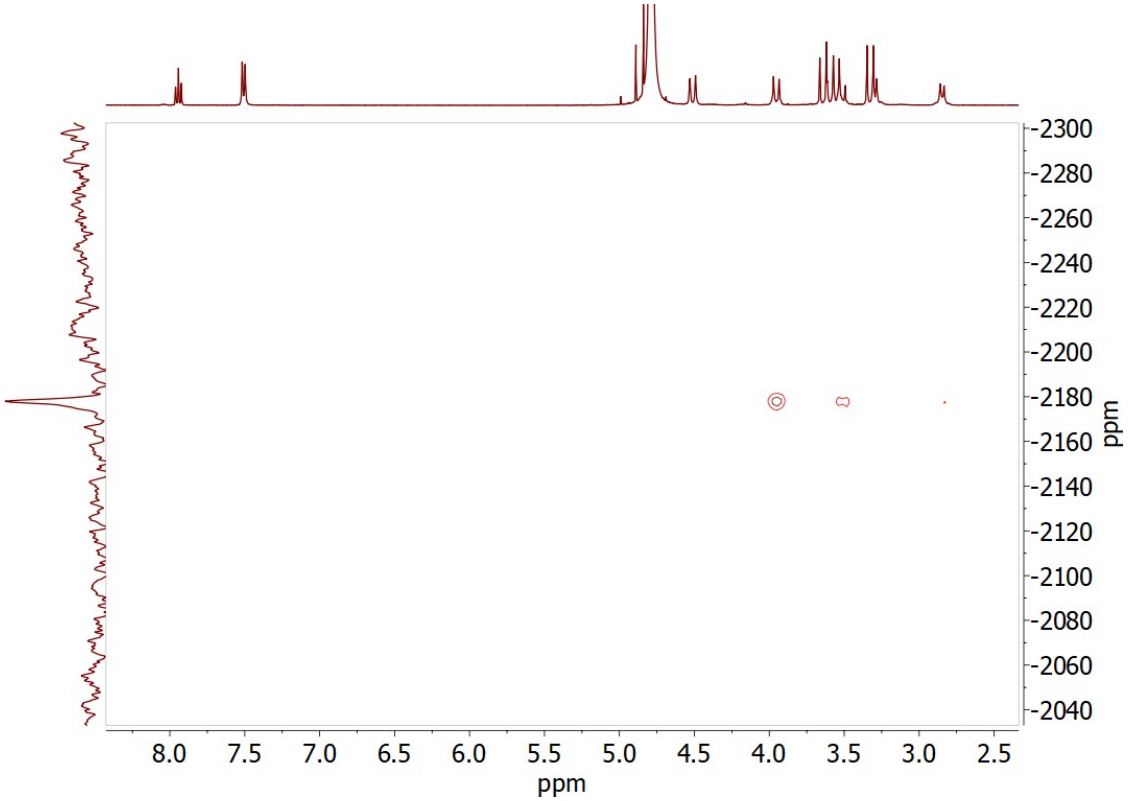


Figure S42: HMQC NMR ^{1}H-^{207}Pb spectrum of complex **[Pb(PYTAMGly)]$^{2-}$** (D_2O, pD= 6.8, 298 K).

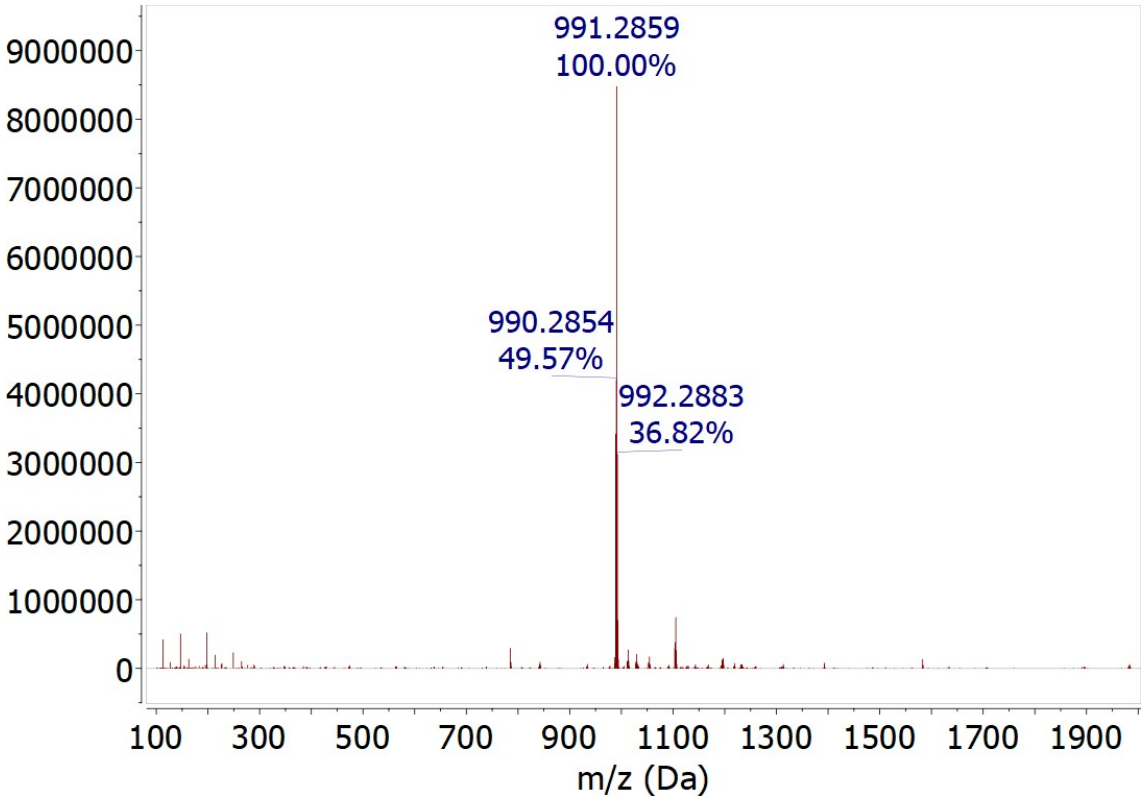
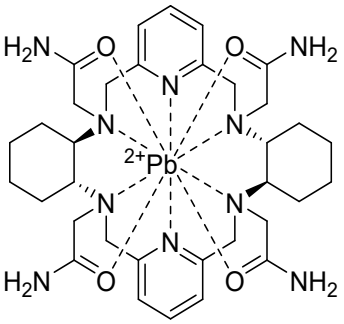


Figure S43: Experimental high resolution mass spectrum (ESI^-) of compound **$[Pb(HPYTAMGly)]^-$**



Scheme S7: Structure of [Pb(*CHX*-PYTAM)]$^{2+}$

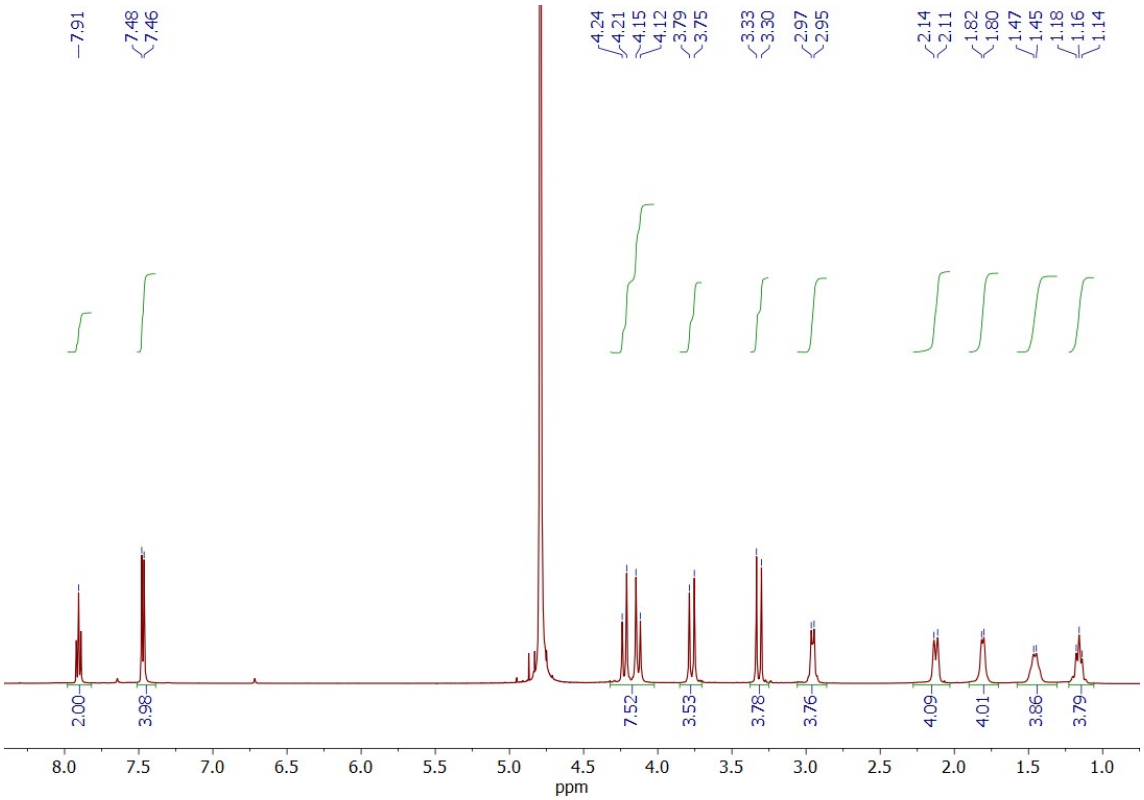


Figure S44: ^{1}H NMR spectrum of complex **[Pb(*CHX*-PYTAM)]$^{2+}$** (500 MHz, D_2O, pD= 7.4, 298 K).

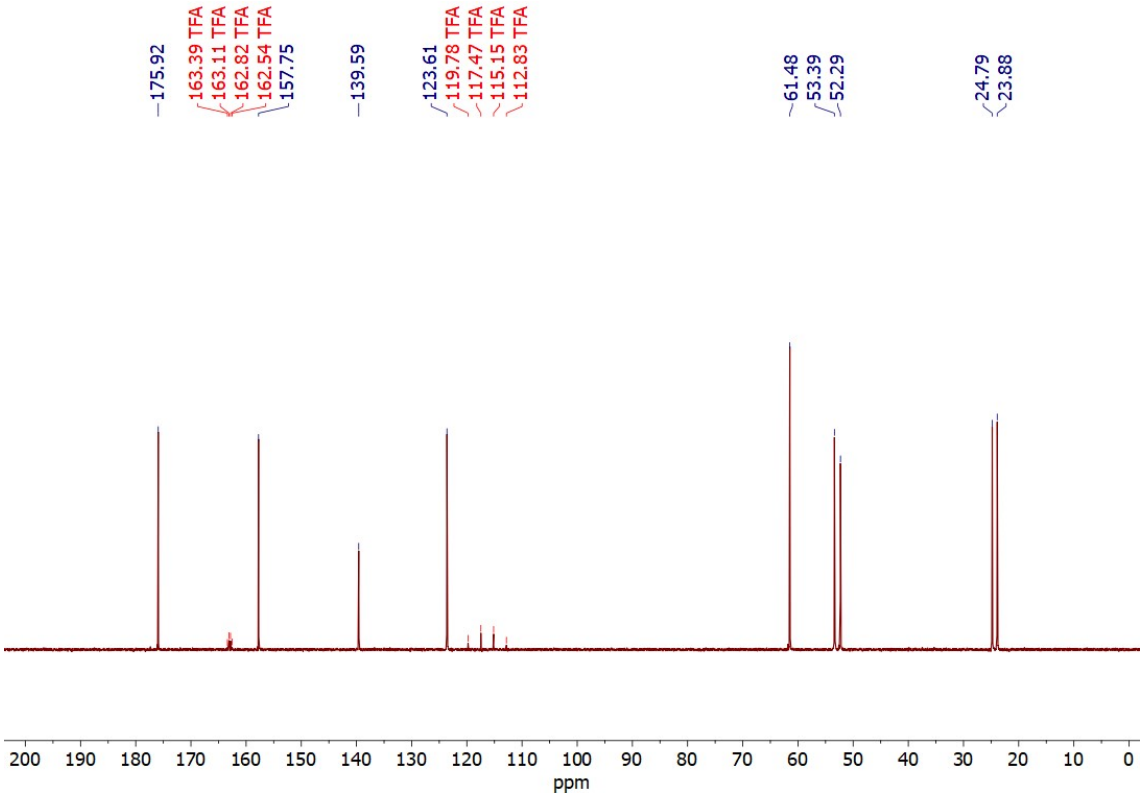


Figure S45: ^{13}C NMR spectrum of complex **[Pb(*CHX*-PYTAM)]$^{2+}$** (126 MHz, D_2O, pD= 7.4, 298 K).

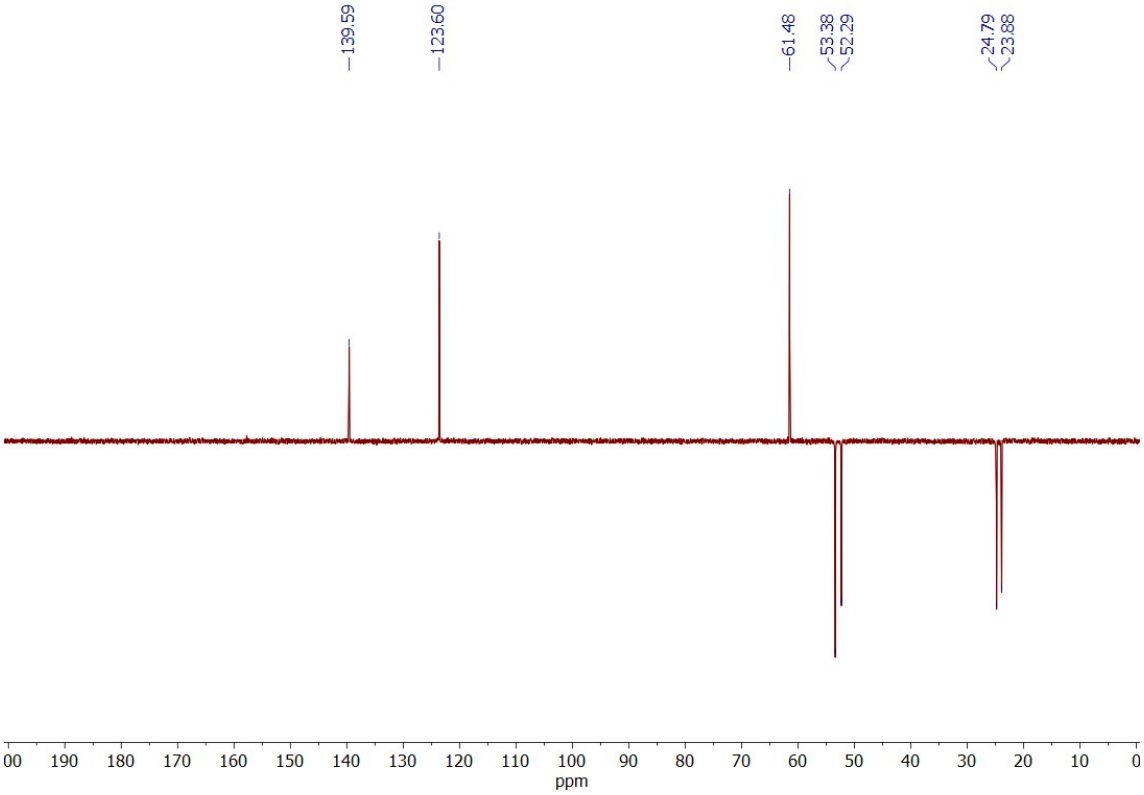


Figure S46: DEPT spectrum of complex **[Pb(*CHX*-PYTAM)]$^{2+}$** (126 MHz, D_2O, pD= 7.4, 298 K).

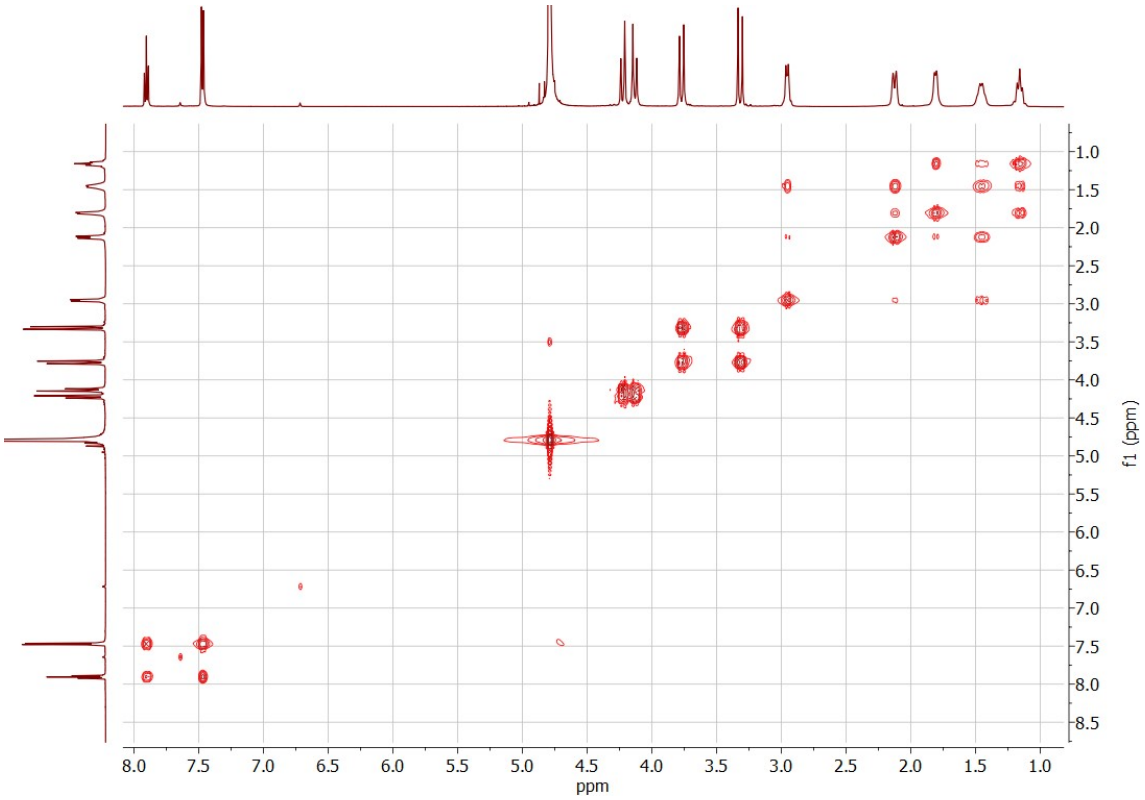


Figure S47: COSY NMR spectrum of complex **[Pb(*CHX*-PYTAM)]$^{2+}$** (500 MHz, D_2O, pD= 7.4, 298 K).

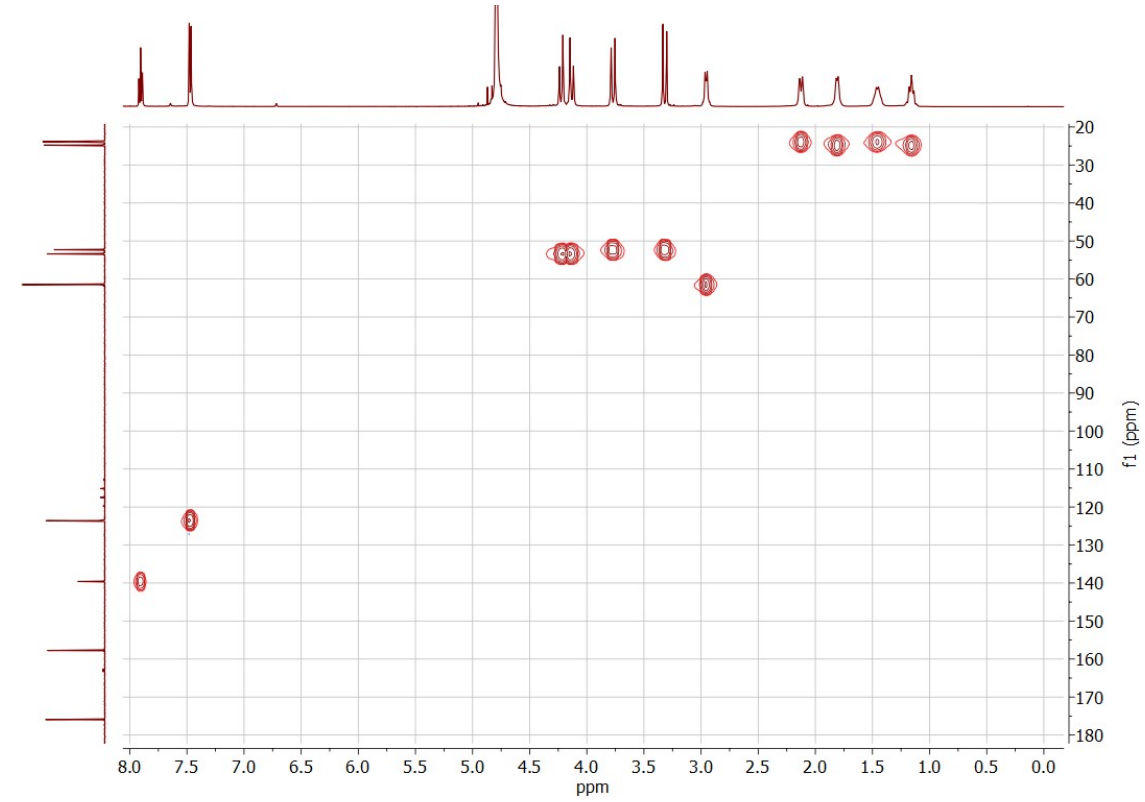


Figure S48: HSQC NMR spectrum of complex **[Pb(*CHX*-PYTAM)]$^{2+}$** (D_2O, pD= 7.4, 298 K).

Figure S49: HMBC NMR spectrum of complex **[Pb(*CHX*-PYTAM)]$^{2+}$** (D_2O, pD= 7.4, 298 K).

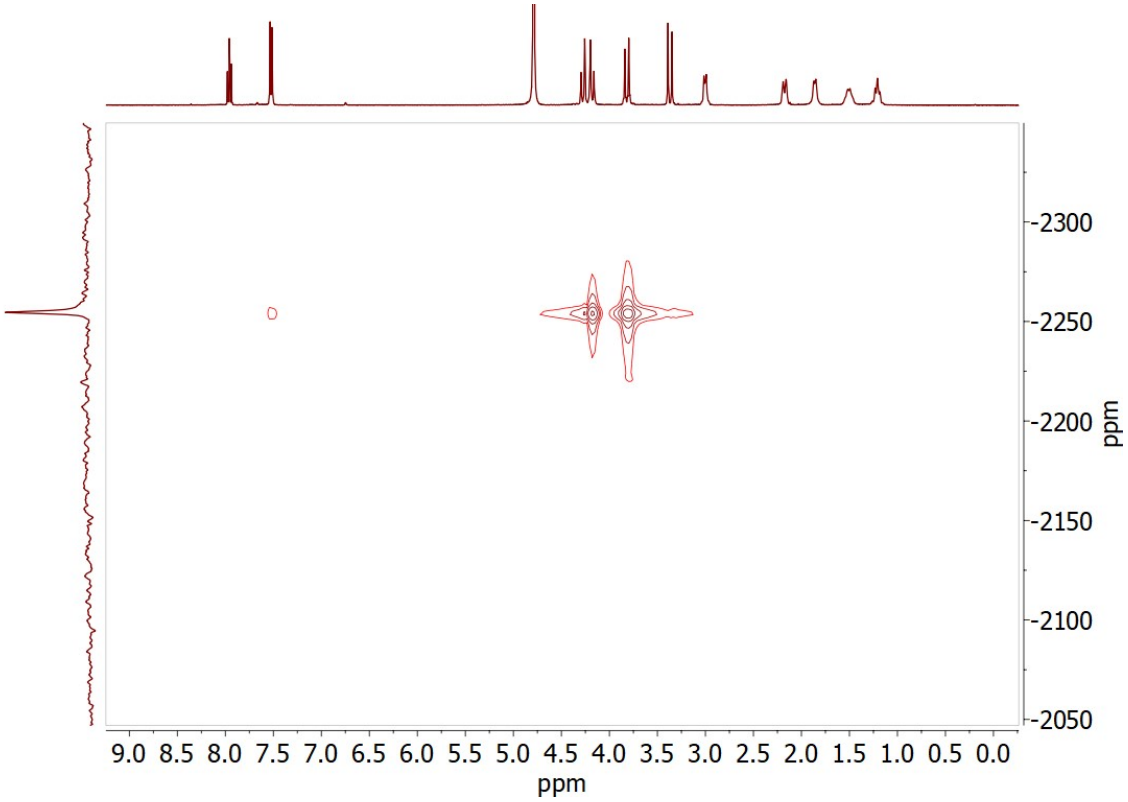


Figure S50: HMQC NMR ^{1}H-^{207}Pb spectrum of complex **[Pb(*CHX*-PYTAM)]$^{2+}$** (D_2O, pD= 7.4, 298 K).

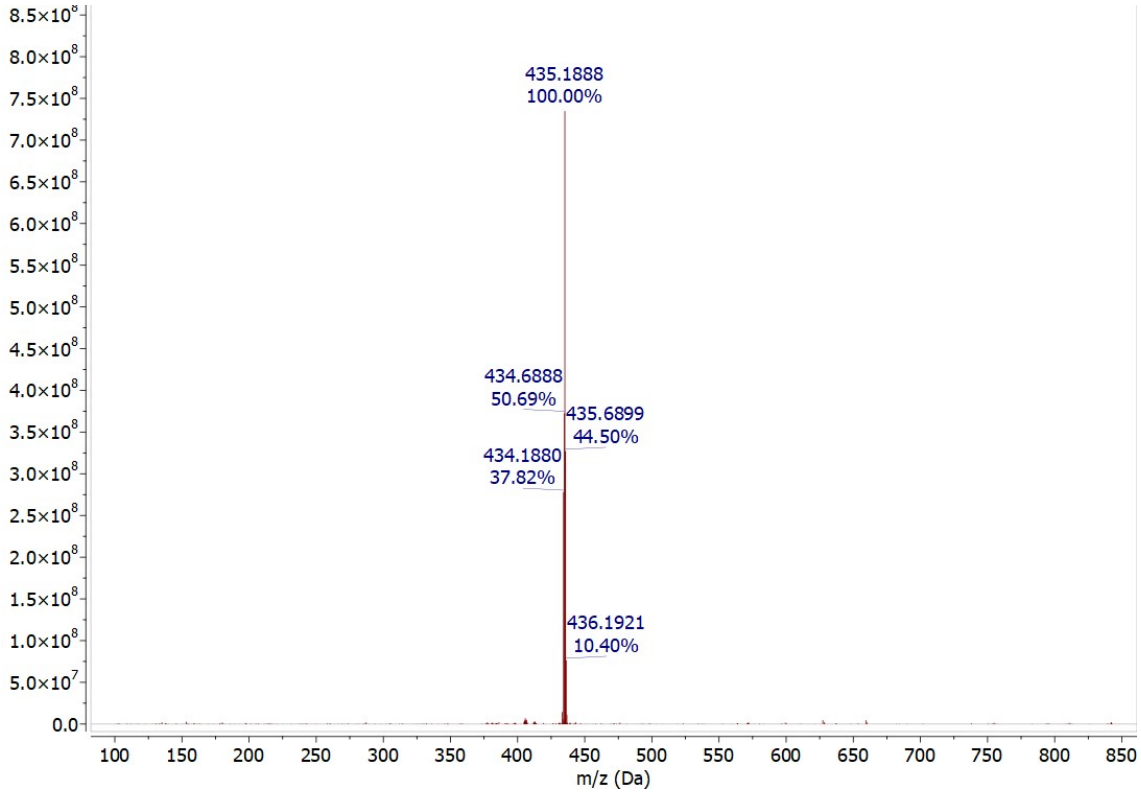
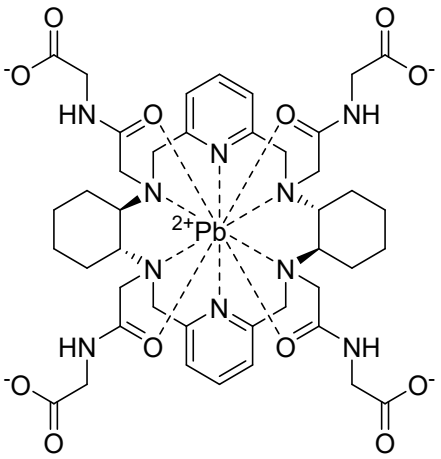


Figure S51: Experimental high resolution mass spectrum (ESI^+) of compound **[Pb(*CHX*-PYTAM)]$^{2+}$**



Scheme S8: Structure of [Pb(*CHX*-PYTAMGly)]$^{2-}$

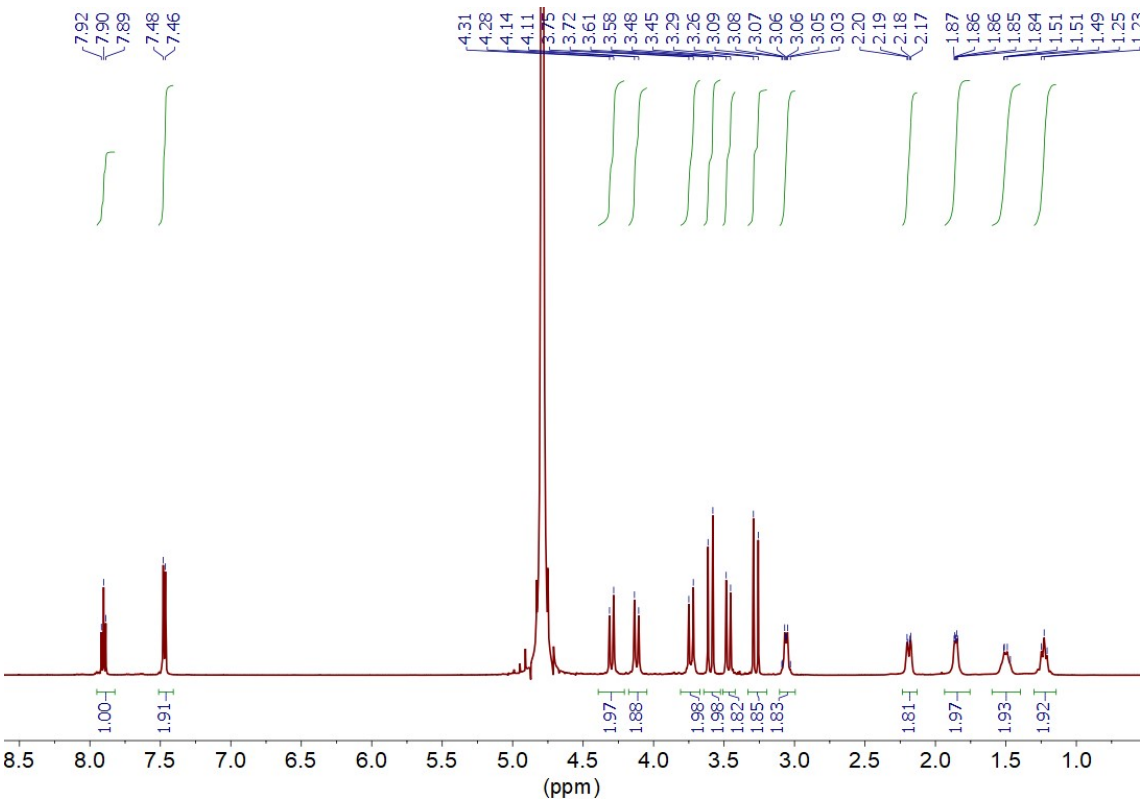


Figure S52: ^{1}H NMR spectrum of complex **[Pb(*CHX*-PYTAMGly)]$^{2-}$** (500 MHz, D_2O, pD= 6.3, 298 K).

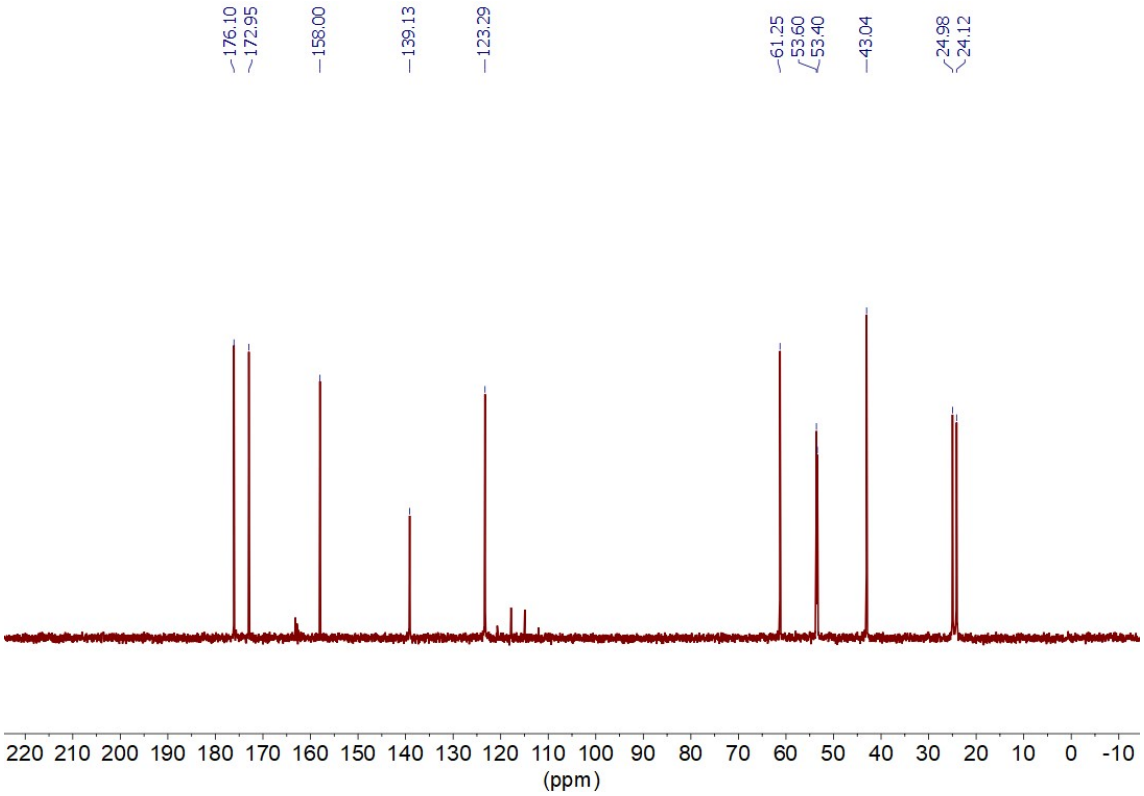


Figure S53: ^{13}C NMR spectrum of complex **[Pb(*CHX*-PYTAMGly)]$^{2-}$** (126 MHz, D_2O, pD= 6.3, 298 K).

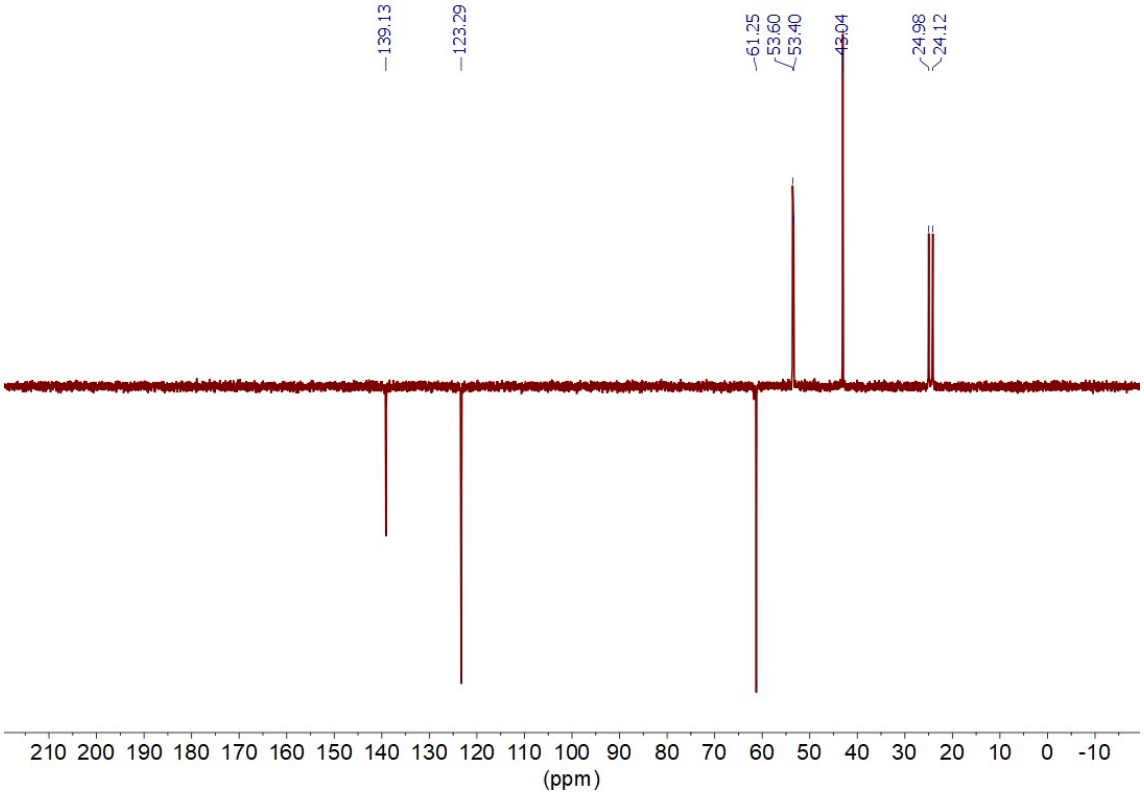


Figure S54: DEPT spectrum of complex **[Pb(*CHX*-PYTAMGly)]$^{2-}$** (126 MHz, D_2O, pD= 6.3, 298 K).

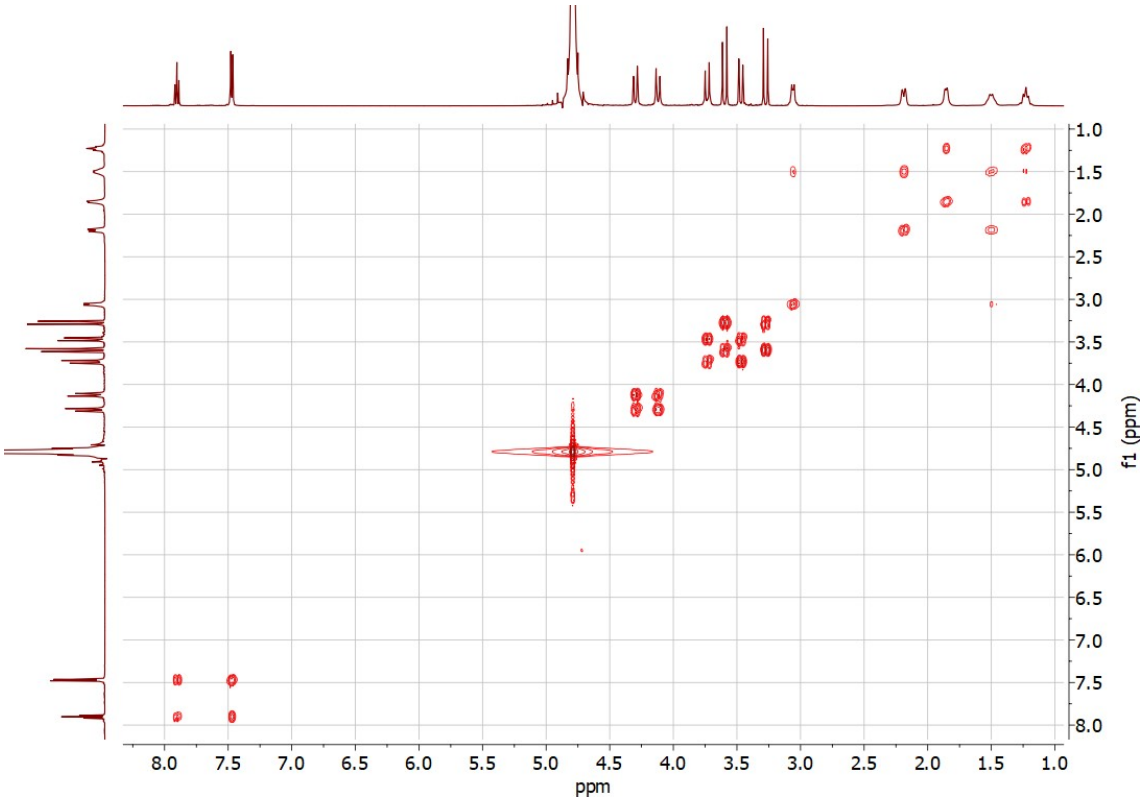


Figure S55: COSY NMR spectrum of complex **[Pb(*CHX*-PYTAMGly)]$^{2-}$** (500 MHz, D_2O, pD= 6.3, 298 K).

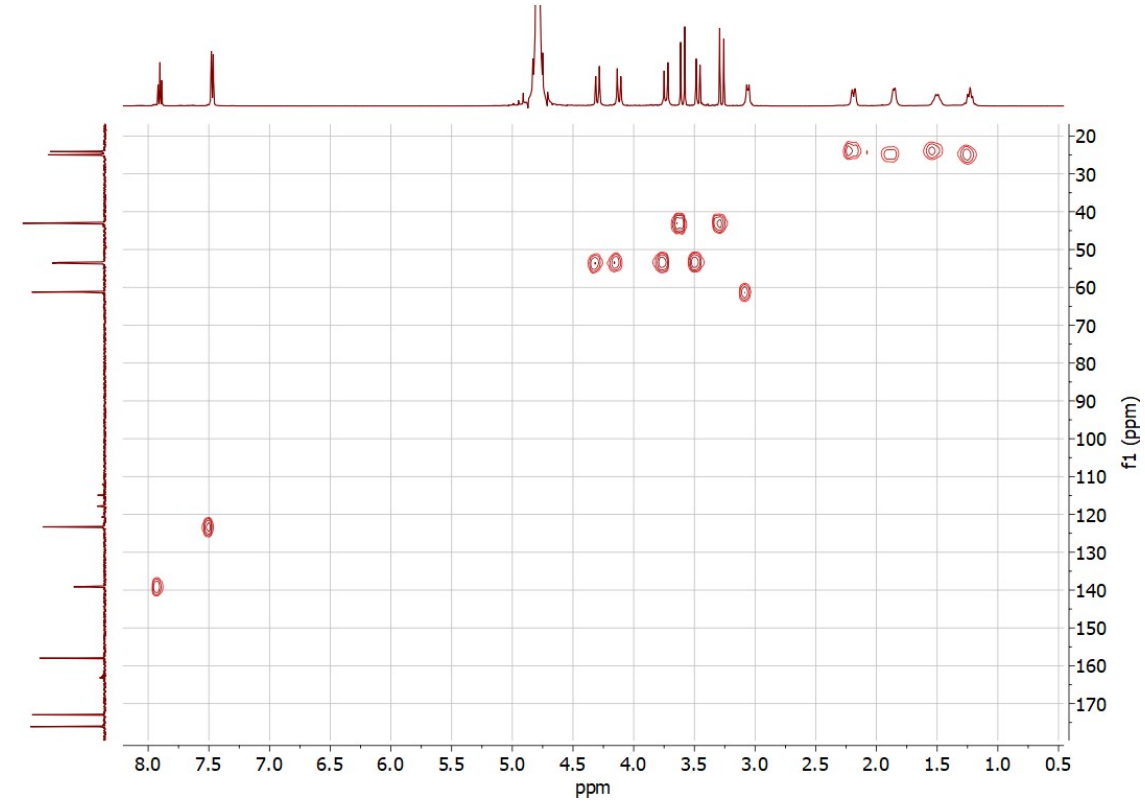


Figure S56: HSQC NMR spectrum of complex **[Pb(*CHX*-PYTAMGly)]$^{2-}$** (D_2O, pD= 6.3, 298 K).

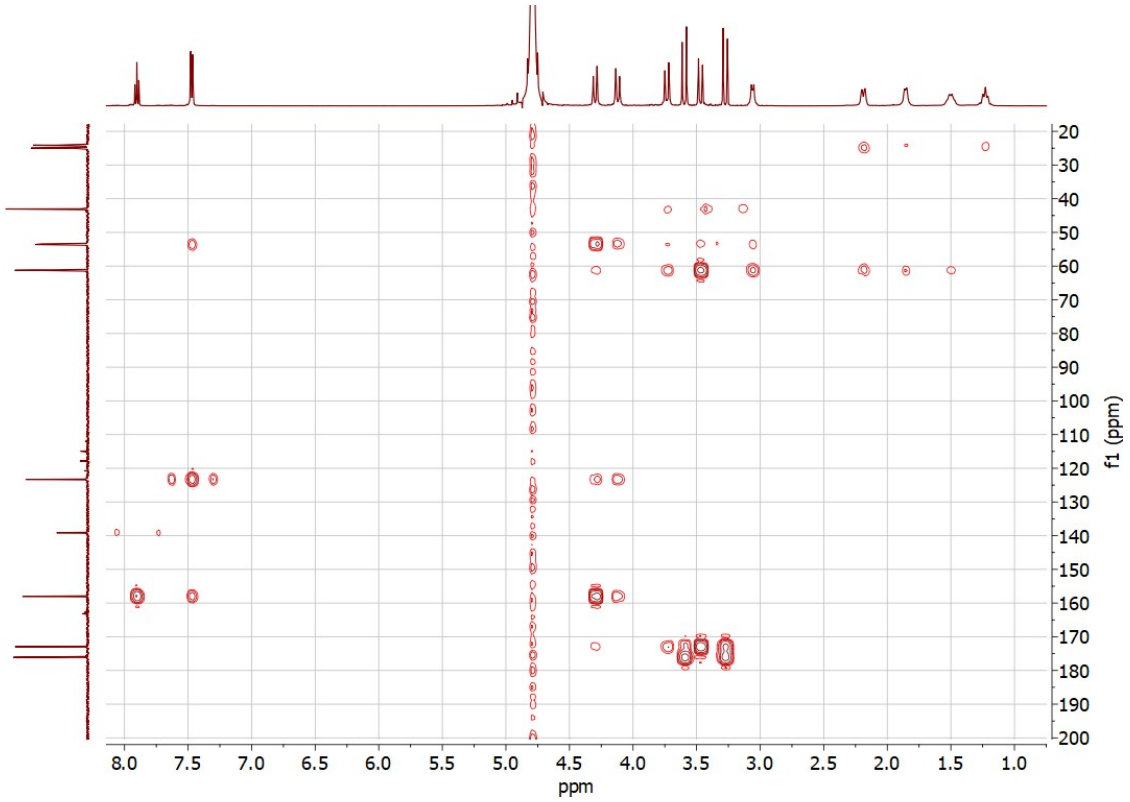


Figure S57: HMBC NMR spectrum of complex **[Pb(*CHX*-PYTAMGly)]$^{2-}$** (D_2O, pD= 6.3, 298 K).

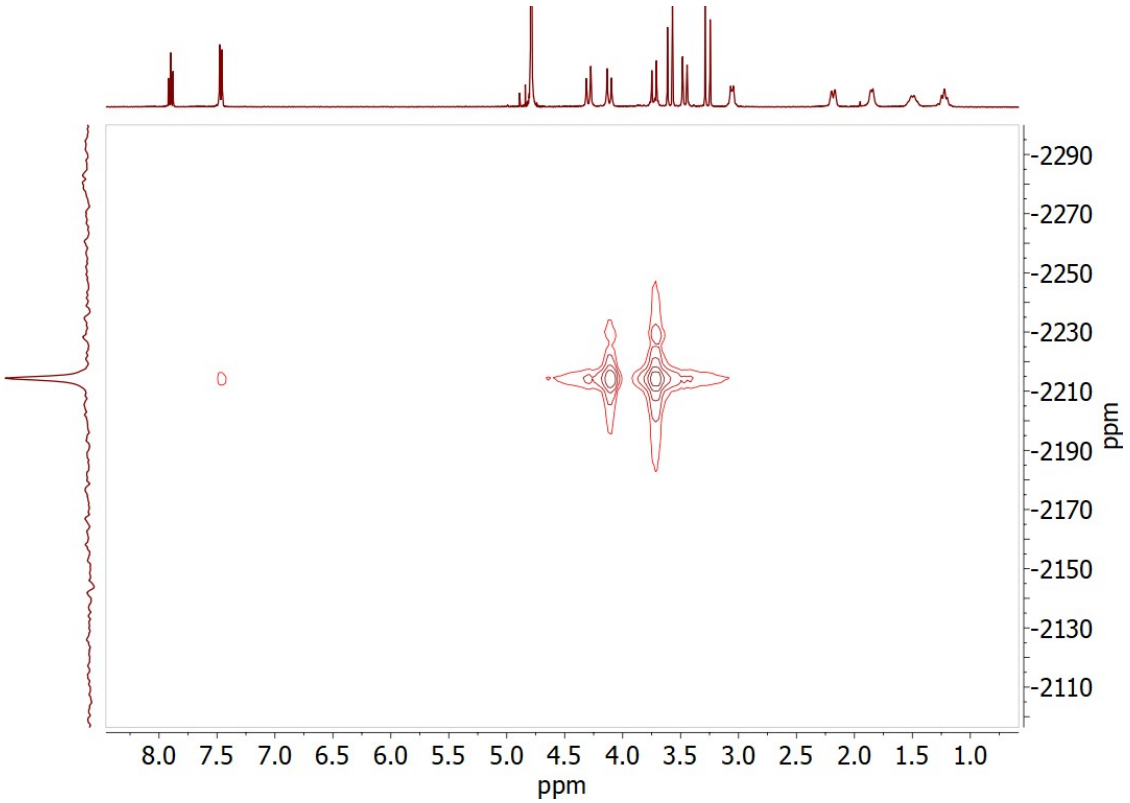


Figure S58: HMQC NMR ^{1}H-^{207}Pb spectrum of complex **[Pb(*CHX*-PYTAMGly)]$^{2-}$** (D_2O, pD= 6.3, 298 K).

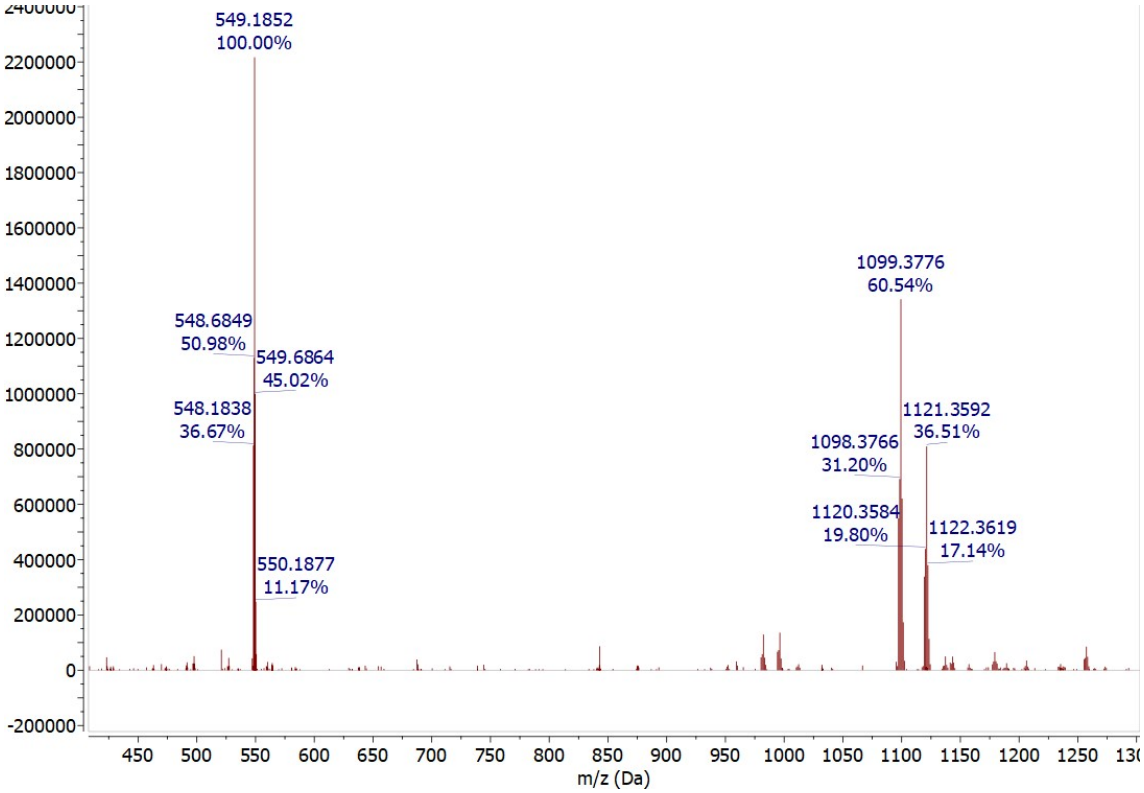


Figure S59: Experimental high resolution mass spectrum (ESI$^-$) of compound **[Pb(*CHX*-PYTAMGly)]$^{2-}$**.

Table S19: Crystal Data and Structure Refinement Details for **[Pb(PYTAM)](PF$_6$)$_2$ and [Pb(H$_4$PYTAMGly)](NO$_3$)$_2$**

	[Pb(PYTAM)](PF$_6$)$_2$	**[Pb(H$_4$PYTAMGly)](NO$_3$)$_2$**
Empirical formula	$C_{26}H_{38}N_{10}O_4F_{12}P_2Pb$	$C_{34}H_{56}Br_{0.09}N_{11.91}O_{22.72}Pb$
Molecular weight MW	1051.79	1209.79
Crystal system	Orthorhombic	Monoclinic
Space group	Fddd	$P2_1/c$
a/Å	13.5776(7)	22.1973(11)
b/Å	16.3882(9)	10.1543(5)
c/Å	32.7592(15)	20.7147(10)
β/º		99.397(2)
Volume (Å^3)	7289.3(6)	4606.4(4)
Z	8	4
ρ_{calc} (g/cm^3)	1.917	1.744
μ (mm^{-1})	4.828	3.841
θ range	2.05º - 28.30º	1.86-28.303
R_{int}	0.0402	0.0349
Measured reflections	40984	107981
Independent reflections / unique (I >2σ (I)	2280 / 2125	11459 / 10652
Goodness-of-fit on F^2	1.162	1.051
R_1	0.0342	0.0231
wR_2 (all data)	0.0876	0.0530
Larg. diff. peak and hole (eÅ^{-3})	1.26 and -0.97	1.44 and -0.89

Table S20: Cartesian coordinates (Å) of **[Pb(PYTAM)]$^{2+}$**with optimized hydrogen positionss obtained with DFT calculations.

Center Number	Atomic Number	Coordinates (Angstroms) X	Y	Z
1	82	-0.000000	0.000000	0.000003
2	8	2.362497	0.841300	1.224204
3	7	0.886602	-1.222600	2.276302
4	7	-0.000000	-2.645997	0.000004
5	7	4.346196	-0.147398	1.645405
6	6	0.148000	-3.315894	1.165201
7	6	3.000593	-0.140899	1.596203
8	6	2.331308	-1.425013	2.051808
9	6	0.668001	-0.360401	3.449704
10	6	0.191397	-2.512605	2.417216
11	6	0.135801	-4.710796	1.186507
12	6	0.000000	-5.372501	0.000005
13	8	-2.362497	-0.841300	1.224204
14	7	-0.886602	1.222600	2.276302
15	7	0.000000	2.645997	0.000004
16	7	-4.346196	0.147398	1.645405
17	6	-0.148000	3.315894	1.165201
18	6	-3.000593	0.140899	1.596203
19	6	-2.331308	1.425013	2.051808
20	6	-0.668001	0.360401	3.449704
21	6	-0.191397	2.512605	2.417216
22	6	-0.135801	4.710796	1.186507
23	6	-0.000000	5.372501	0.000005
24	8	-2.362496	0.841300	-1.224194
25	7	-0.886603	-1.222599	-2.276292
26	7	-4.346196	-0.147399	-1.645394
27	6	-0.147999	-3.315895	-1.165191
28	6	-3.000593	-0.140900	-1.596194
29	6	-2.331308	-1.425013	-2.051798
30	6	-0.668001	-0.360401	-3.449694
31	6	-0.191397	-2.512603	-2.417304
32	6	-0.135800	-4.710797	-1.186497
33	8	2.362496	-0.841300	-1.224194
34	7	0.886603	1.222599	-2.276292
35	7	4.346196	0.147399	-1.645394
36	6	0.147999	3.315895	-1.165191
37	6	3.000593	0.140900	-1.596194
38	6	2.331308	1.425013	-2.051798
39	6	0.668001	0.360401	-3.449694
40	6	0.191397	2.512603	-2.417304
41	6	0.135800	4.710797	-1.186497
42	1	0.247323	5.245783	-2.121049
43	1	4.859878	-0.658882	-1.326013
44	1	4.865178	-0.942975	1.980014
45	1	1.474392	-0.371443	-3.474562
46	1	0.741743	0.942206	-4.379373
47	1	-0.839352	2.290714	-2.705707
48	1	0.630650	3.114397	-3.224911
49	1	2.459774	2.162225	-1.255466
50	1	2.837104	1.812821	-2.946623
51	1	4.865182	0.943013	-1.979911
52	1	-0.247323	-5.245783	-2.121049
53	1	-4.859878	0.658882	-1.326013
54	1	0.839352	-2.290714	-2.705707
55	1	-0.630650	-3.114397	-3.224911
56	1	-1.474392	0.371443	-3.474562
57	1	-0.741743	-0.942206	-4.379373
58	1	-2.459774	-2.162225	-1.255466
59	1	-2.837104	-1.812821	-2.946623
60	1	-4.865182	-0.943013	-1.979911

61	1	-0.000000	6.457499	0.000006
62	1	-4.859880	-0.658884	1.326027
63	1	-0.247328	5.245781	2.121059
64	1	0.839368	2.290706	2.705608
65	1	-0.630601	3.114393	3.224844
66	1	-1.474412	-0.371424	3.474561
67	1	-0.741728	0.942202	4.379386
68	1	-2.459751	2.162151	1.255378
69	1	-2.837100	1.812908	2.946578
70	1	-4.865178	0.942975	1.980014
71	1	0.000000	-6.457499	0.000006
72	1	4.859880	0.658884	1.326027
73	1	0.247328	-5.245781	2.121059
74	1	-0.839368	-2.290706	2.705608
75	1	0.630601	-3.114393	3.224844
76	1	1.474412	0.371424	3.474561
77	1	0.741728	-0.942202	4.379386
78	1	2.459751	-2.162151	1.255378
79	1	2.837100	-1.812908	2.946578

Table S21: Cartesian coordinates (Å) of **[Pb(H$_4$PYTAMGly)]$^{2+}$** with optimized hydrogen positions obtained with DFT calculations.

Center Number	Atomic Number	Coordinates (Angstroms) X	Y	Z
1	82	0.028922	-0.036492	-0.078988
2	6	0.005211	3.429957	-0.567099
3	6	-0.438985	4.748177	-0.426687
4	6	-0.986827	5.132860	0.787124
5	6	-1.043924	4.221649	1.833343
6	6	-0.557983	2.942138	1.630171
7	6	-0.576363	1.891070	2.732853
8	6	-1.082141	-0.428495	3.290259
9	6	0.275313	-1.115888	3.279844
10	6	-0.127692	-2.977614	1.750460
11	6	-0.063078	-3.491018	0.320370
12	6	-0.170838	-4.855879	0.051113
13	6	-0.171910	-5.282488	-1.266479
14	6	-0.073888	-4.339762	-2.288566
15	6	0.029364	-2.997712	-1.951152
16	6	0.179878	-1.940793	-3.033442
17	6	-0.153943	0.397148	-3.647294
18	6	1.166655	1.063960	-3.293157
19	6	0.463000	2.944968	-1.928655
20	6	-2.615003	0.840512	1.918917
21	6	-3.198245	-0.402694	1.253496
22	6	2.052824	-1.936987	1.874903
23	6	2.800605	-0.609168	1.839864
24	6	4.920821	0.506816	2.242453
25	6	4.683688	1.288524	3.519398
26	6	-1.976779	-0.883165	-2.709821
27	6	-2.673472	0.317888	-2.101525
28	6	-4.698484	1.552265	-1.766963
29	6	-4.121463	2.936434	-1.998124
30	6	2.542773	1.823176	-1.455204
31	6	3.274427	0.493557	-1.295927
32	6	5.455025	-0.542448	-0.954824
33	6	5.833391	-1.278982	-2.225652
34	7	-0.042061	2.560425	0.445836
35	7	-1.210592	0.633076	2.262965
36	7	0.609008	-1.716372	1.968062
37	7	0.043855	-2.591790	-0.670530
38	7	-0.525849	-0.685602	-2.710455
39	7	1.171609	1.649551	-1.930284

40	7	-4.520721	-0.539326	1.413077
41	7	4.101204	-0.684569	2.158194
42	7	-3.946801	0.512829	-2.451252
43	7	4.598494	0.600116	-1.193115
44	8	-2.502962	-1.185997	0.609913
45	8	2.259177	0.451330	1.512338
46	8	3.813563	1.038033	4.326799
47	8	5.512781	2.296808	3.629641
48	8	-2.115245	1.060797	-1.284485
49	8	-3.664580	3.289628	-3.075556
50	8	-4.205293	3.694464	-0.938171
51	8	2.664171	-0.588449	-1.213103
52	8	5.428595	-0.977671	-3.324793
53	8	6.659661	-2.293921	-2.060846
54	8	-6.746127	-3.437587	1.521847
55	6	-5.265334	-1.654167	0.885777
56	6	-5.962722	-2.444503	1.950969
57	8	-5.853214	-2.212632	3.129176
58	1	-4.562108	-2.300286	0.355345
59	1	-6.006219	-1.313675	0.154733
60	1	-6.742724	-3.508131	0.555029
61	1	6.911086	-2.422209	-1.133609
62	1	-3.874635	4.583019	-1.155191
63	1	5.308715	2.786542	4.444190
64	1	5.033835	1.491707	-1.376915
65	1	4.462721	-1.542461	2.547280
66	1	-4.389297	-0.052448	-3.158655
67	1	-5.000726	0.094829	2.034923
68	1	4.938743	-1.239747	-0.293261
69	1	6.363642	-0.205515	-0.453818
70	1	2.510775	2.287101	-0.465891
71	1	3.122757	2.488030	-2.112687
72	1	-4.744282	1.347399	-0.698486
73	1	-5.717569	1.549123	-2.155338
74	1	-2.216559	-1.740791	-2.075268
75	1	-2.376114	-1.091524	-3.712224
76	1	4.694285	1.166875	1.405272
77	1	5.972352	0.229576	2.178759
78	1	2.270745	-2.455286	0.937143
79	1	2.432983	-2.562061	2.694801
80	1	-2.684793	1.657026	1.196117
81	1	-3.219674	1.118658	2.793511
82	1	-0.435136	2.827788	-2.537817
83	1	1.070090	3.726460	-2.406407
84	1	1.969144	0.330612	-3.340810
85	1	1.385039	1.831852	-4.047499
86	1	-0.955623	1.135891	-3.634042
87	1	-0.091958	0.019941	-4.676742
88	1	1.241064	-1.701345	-3.128446
89	1	-0.157484	-2.356129	-3.991474
90	1	-0.085867	-4.641842	-3.327963
91	1	-0.252706	-6.336631	-1.501049
92	1	-0.246515	-5.565208	0.865818
93	1	-1.177219	-2.788518	1.981226
94	1	0.223208	-3.764488	2.430886
95	1	1.055522	-0.394666	3.518777
96	1	0.286380	-1.877006	4.071651
97	1	-1.865952	-1.163542	3.110043
98	1	-1.259836	-0.019287	4.293243
99	1	0.450388	1.654073	3.014367
100	1	-1.096118	2.289982	3.612284
101	1	-1.470395	4.497788	2.789265
102	1	-1.362151	6.140171	0.920884
103	1	-0.378069	5.437915	-1.258948
