Electronic Supplementary Information for:

Coordination Chemistry of $[Y(pypa)]^-$ and Comparison Immuno-PET Imaging of $[^{44}Sc]$Sc- and $[^{86}Y]$Y-pypa-phenyl-TRC105

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NMR Spectra

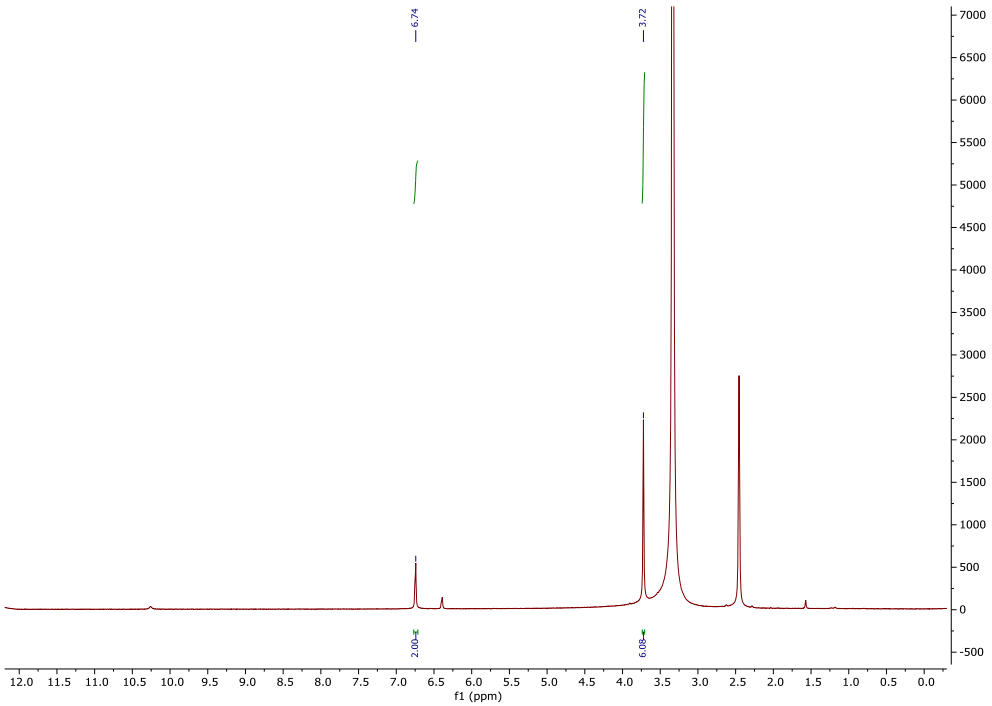

Figure S1. Compound **1** ^{1}H NMR spectrum (400 MHz, 298 K, DMSO-d_6).

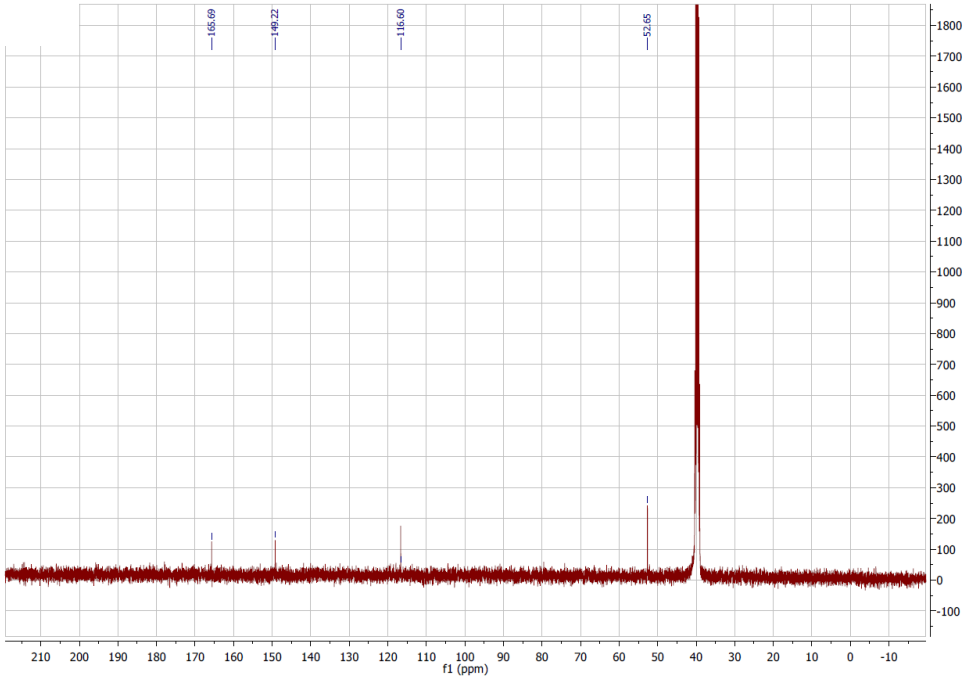

Figure S2. Compound **1** ^{13}C NMR spectrum (100 MHz, 298 K, DMSO-d_6).

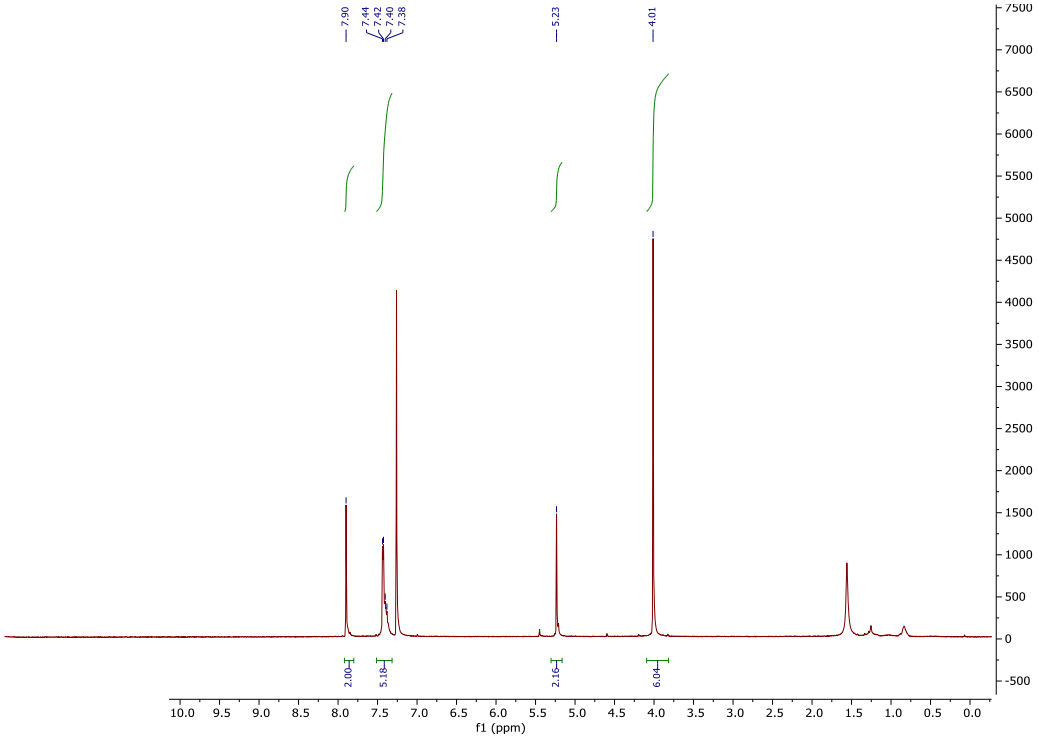

Figure S3. Compound **2** ^{1}H NMR spectrum (400 MHz, 298 K, $CDCl_3$).

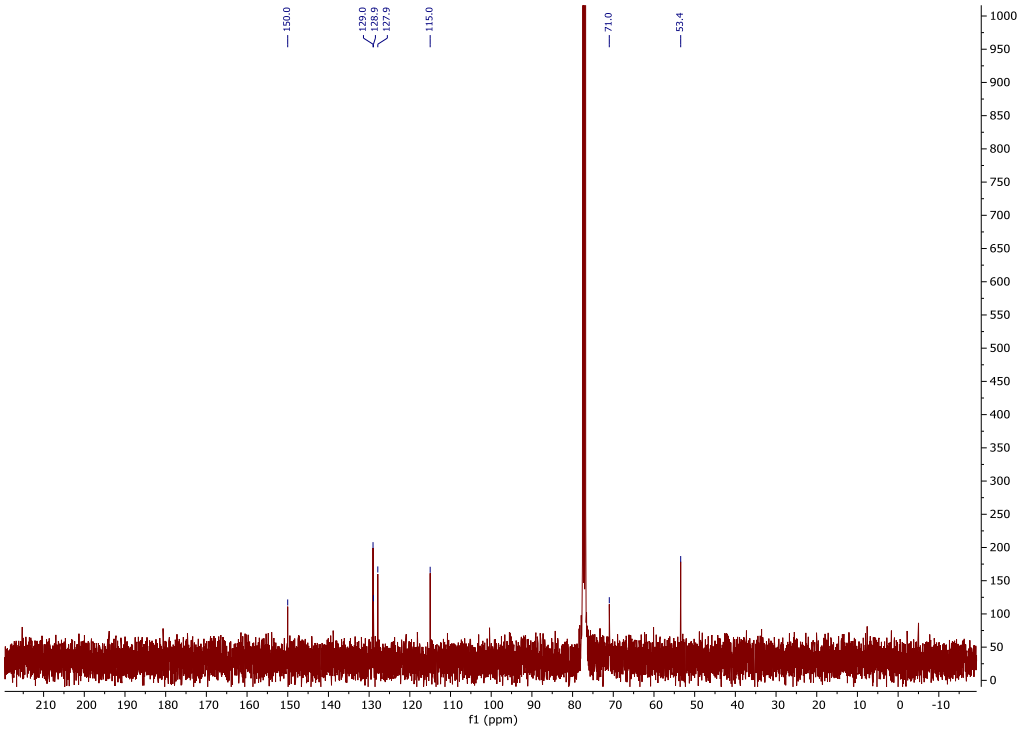

Figure S4. Compound **2** ^{13}C NMR spectrum (100 MHz, 298 K, $CDCl_3$).

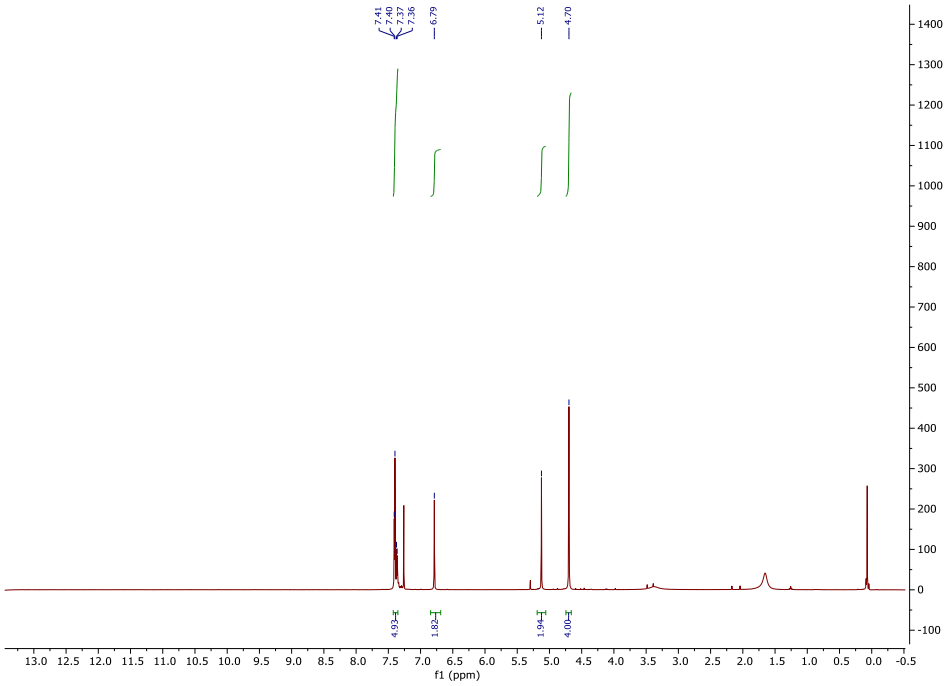

Figure S5. Compound **3** ^{1}H NMR spectrum (400 MHz, 298 K, $CDCl_3$).

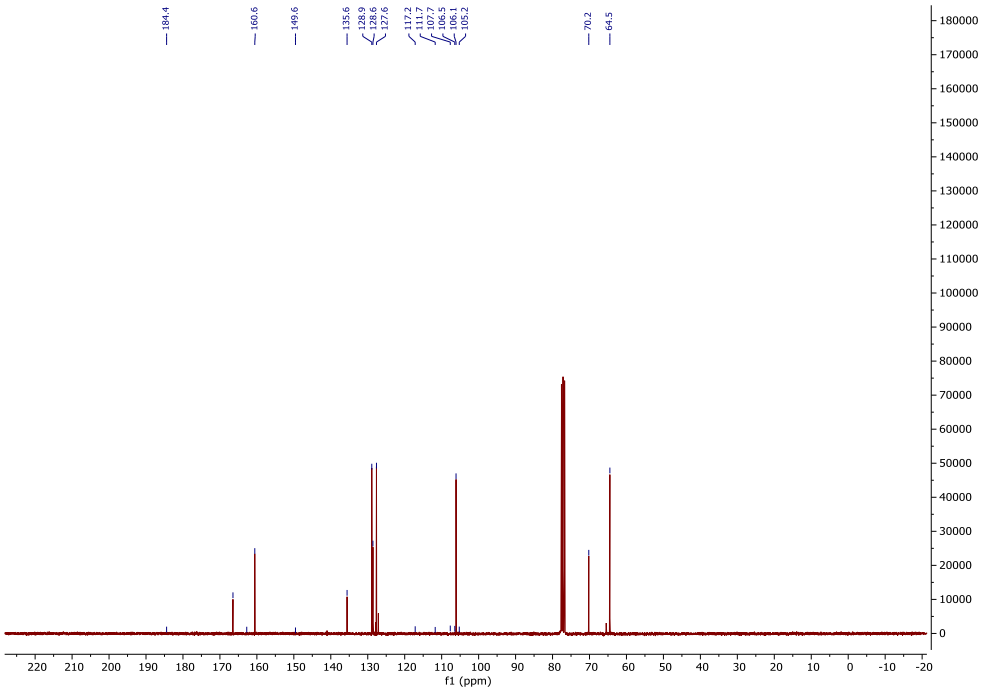

Figure S6. Compound **3** ^{13}C NMR spectrum (100 MHz, 298 K, $CDCl_3$).

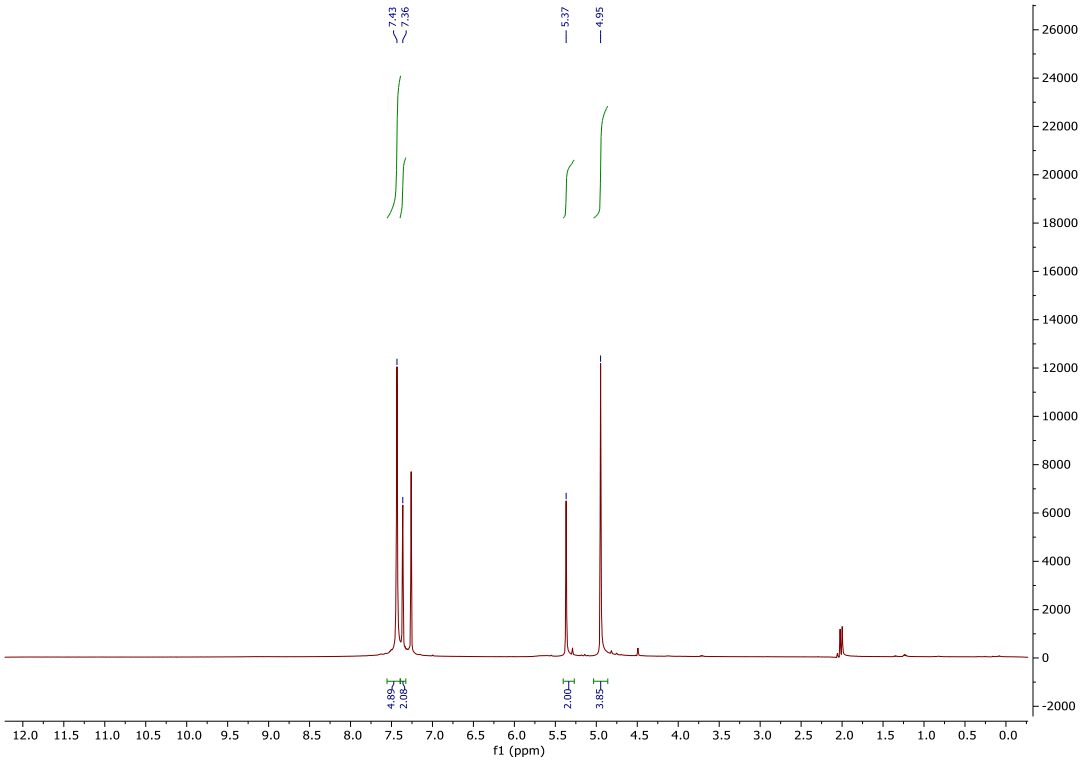

Figure S7. Compound **4** ^{1}H NMR spectrum (400 MHz, 298 K, $CDCl_3$).

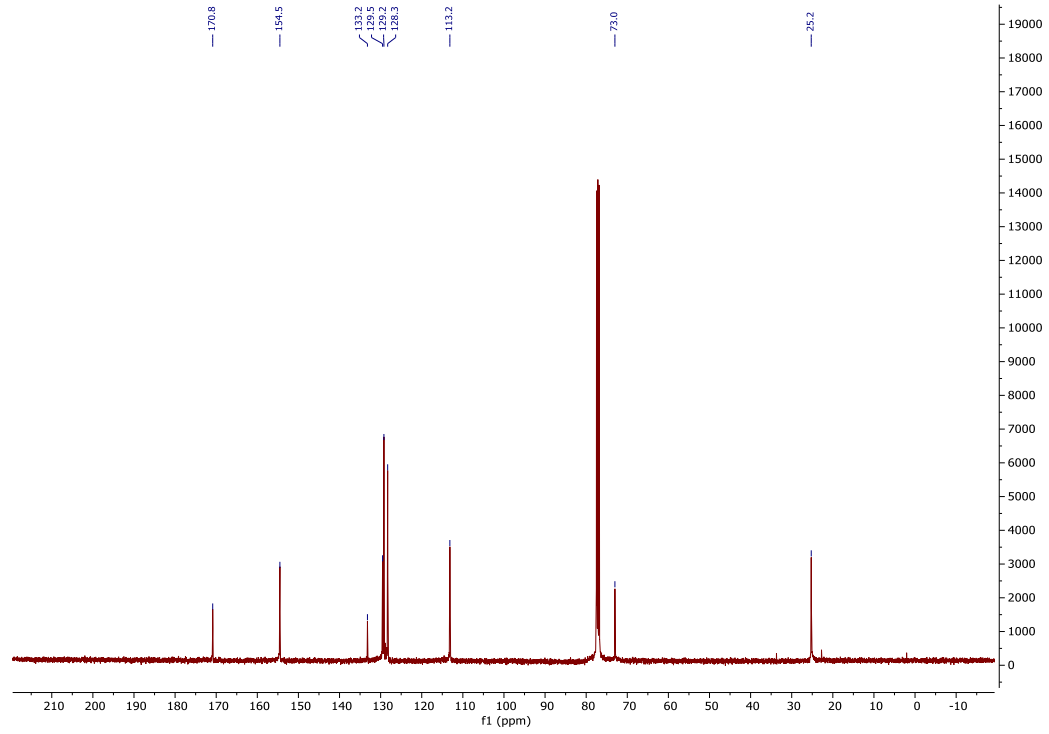

Figure S8. Compound **4** ^{13}C NMR spectrum (100 MHz, 298 K, $CDCl_3$).

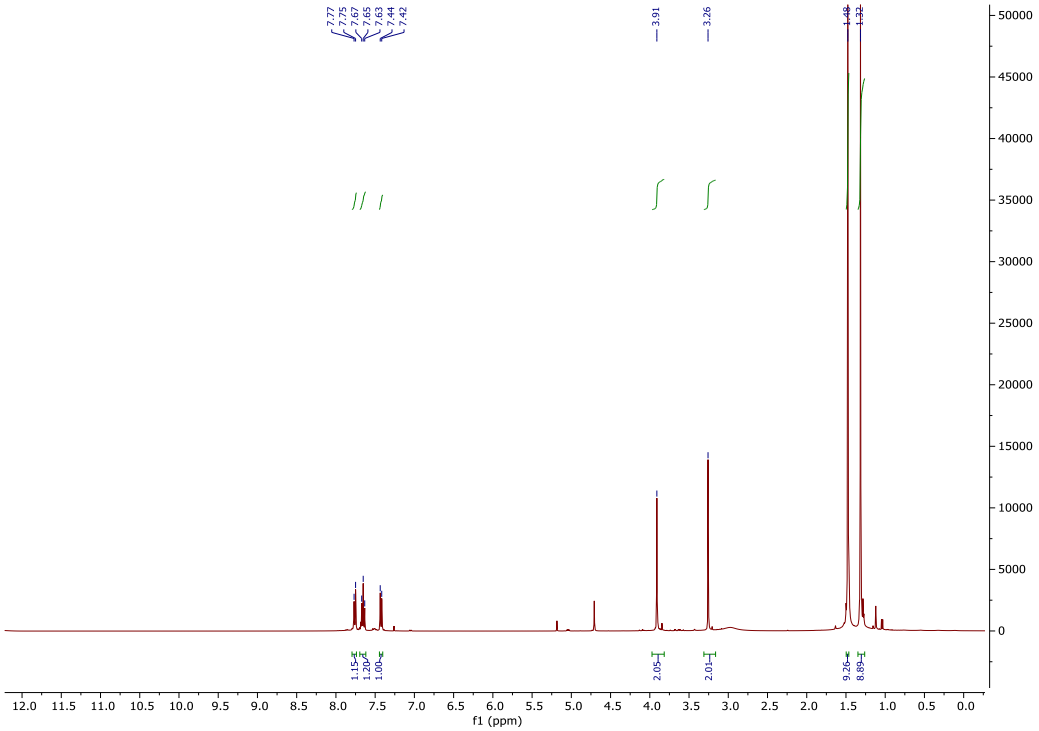

Figure S9. Compound **5** ^{1}H NMR spectrum (400 MHz, 298 K, $CDCl_3$).

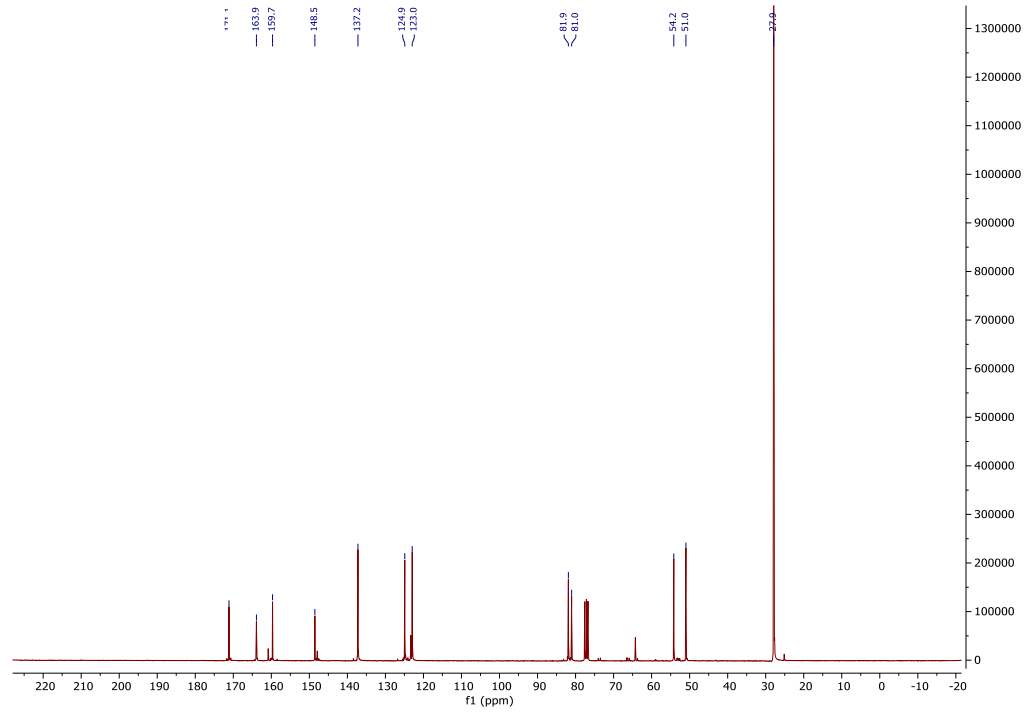

Figure S10. Compound **5** ^{13}C NMR spectrum (100 MHz, 298 K, $CDCl_3$).

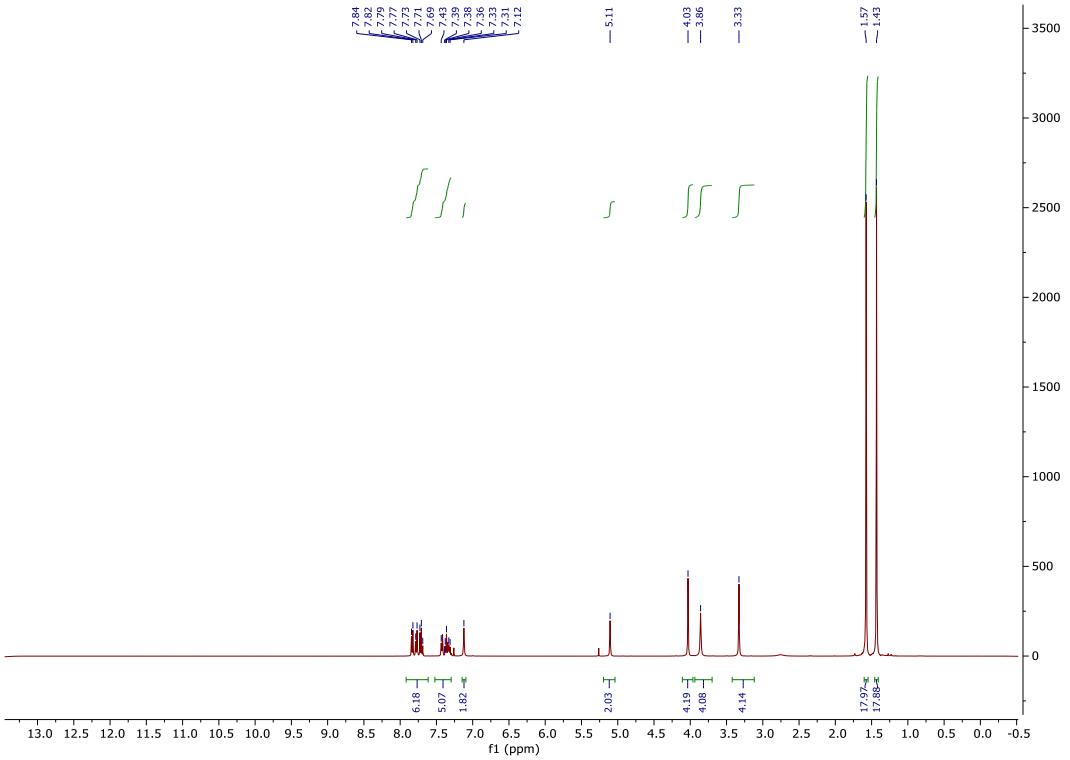

Figure S11. Compound **6** ^{1}H NMR spectrum (400 MHz, 298 K, $CDCl_3$).

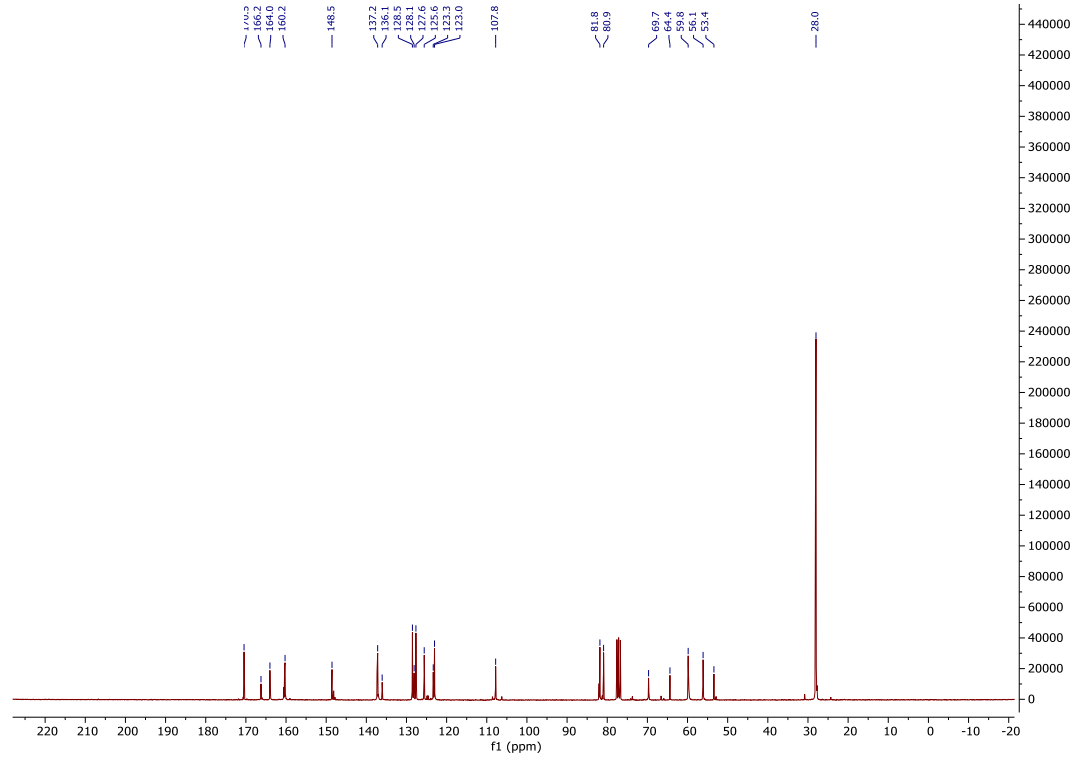

Figure S12. Compound **6** ^{13}C NMR spectrum (100 MHz, 298 K, $CDCl_3$).

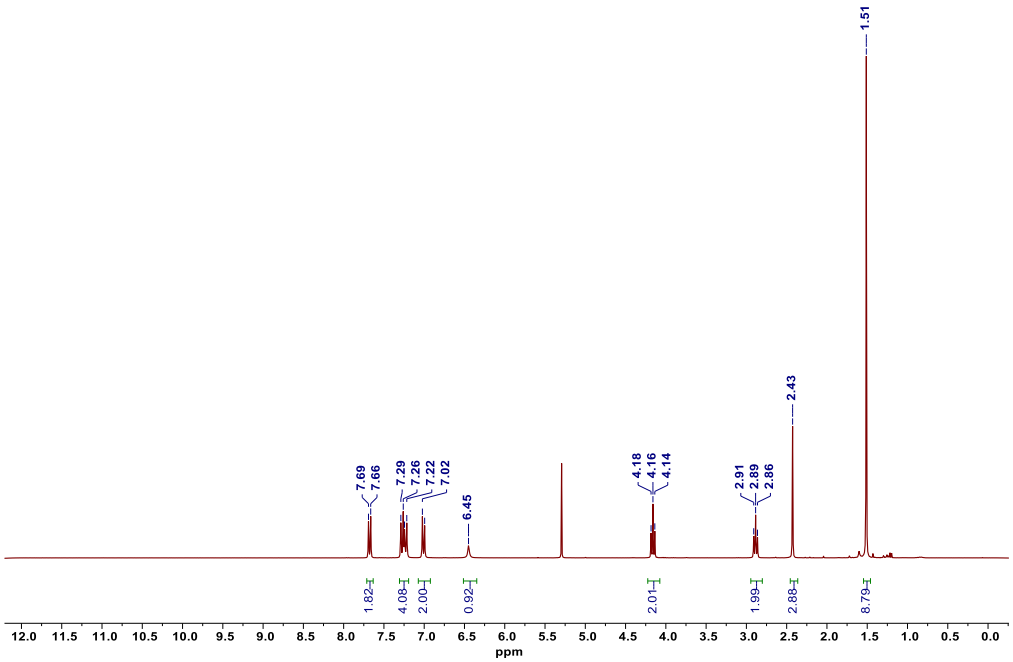

Figure S13. Compound **8** ^{1}H NMR spectrum (400 MHz, 298 K, $CDCl_3$).

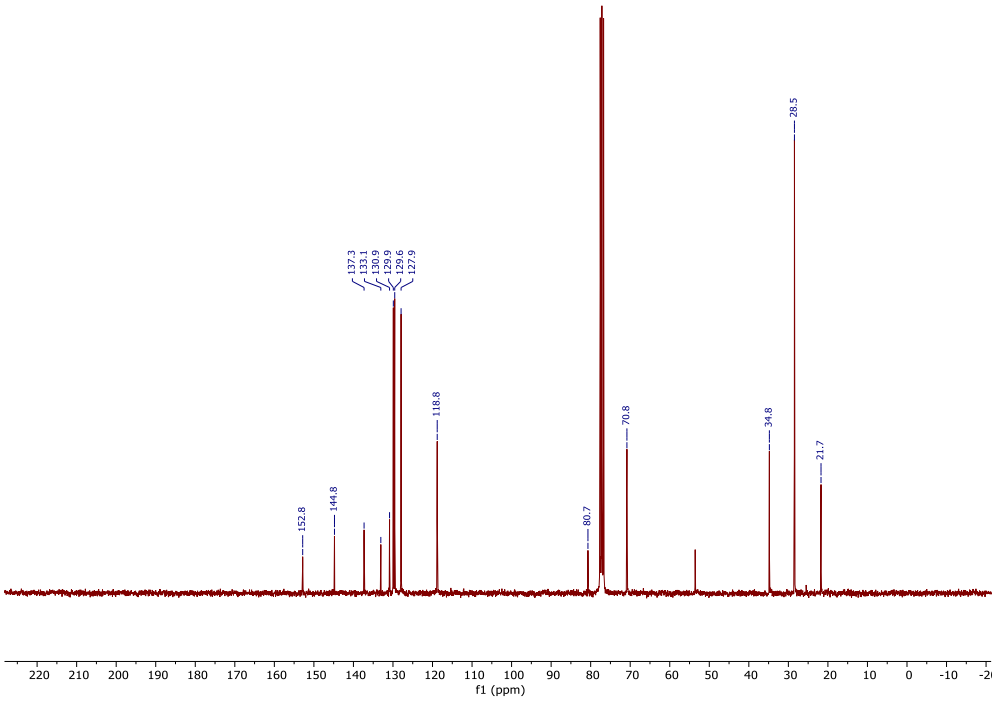

Figure S14. Compound **8** ^{13}C NMR spectrum (100 MHz, 298 K, $CDCl_3$).

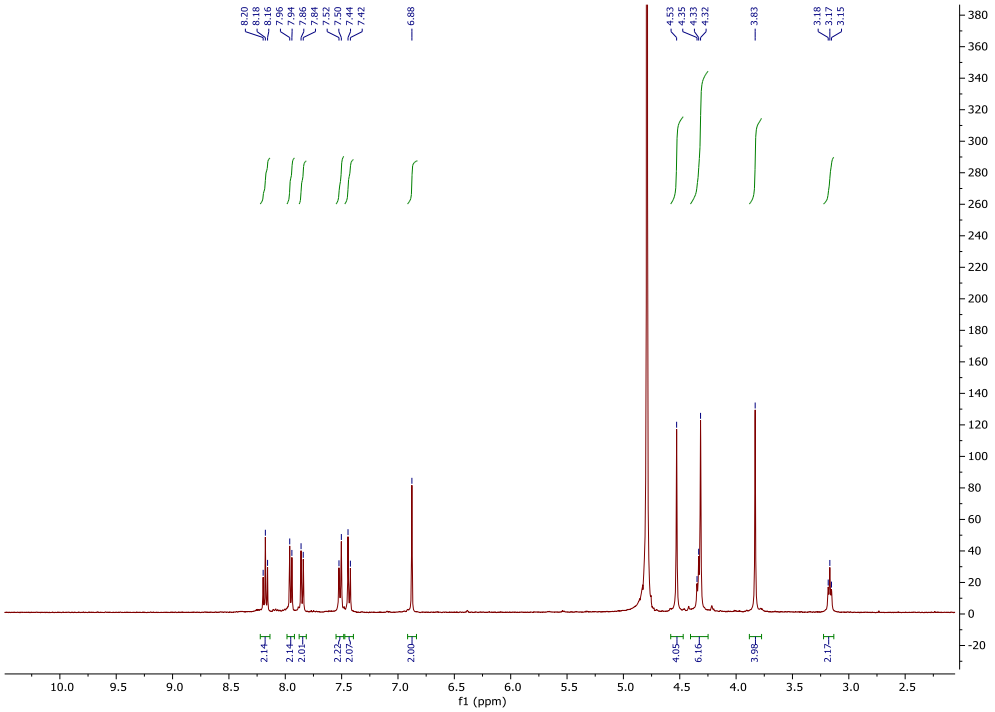

Figure S15. Compound **10** ^{1}H NMR spectrum (400 MHz, 298 K, D_2O).

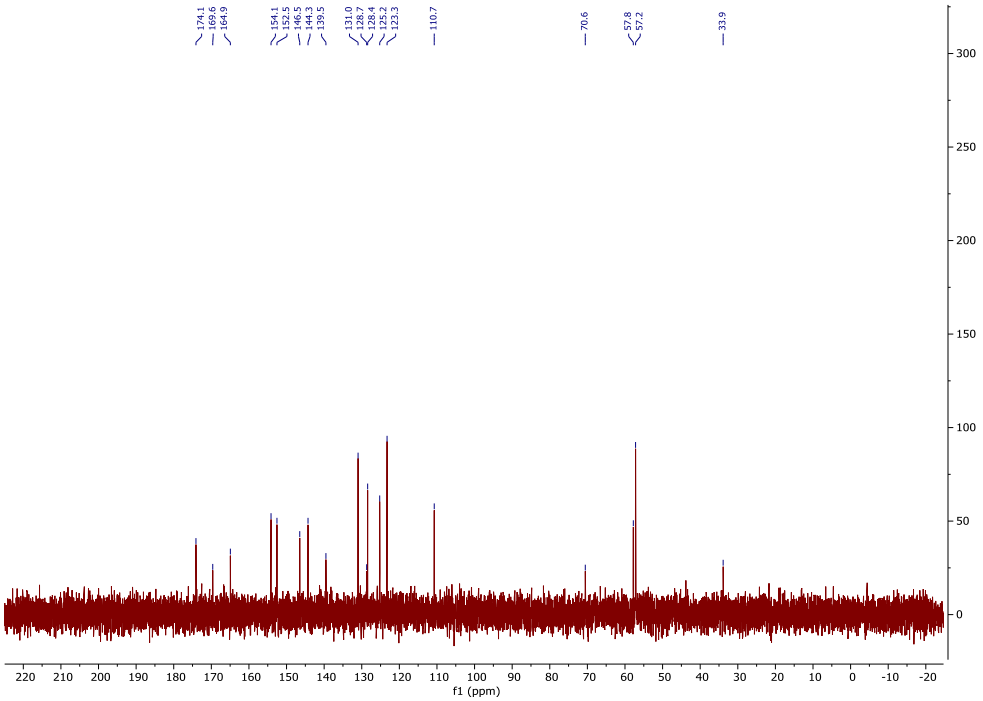

Figure S16. Compound **10** ^{13}C NMR spectrum (100 MHz, 298 K, D_2O).

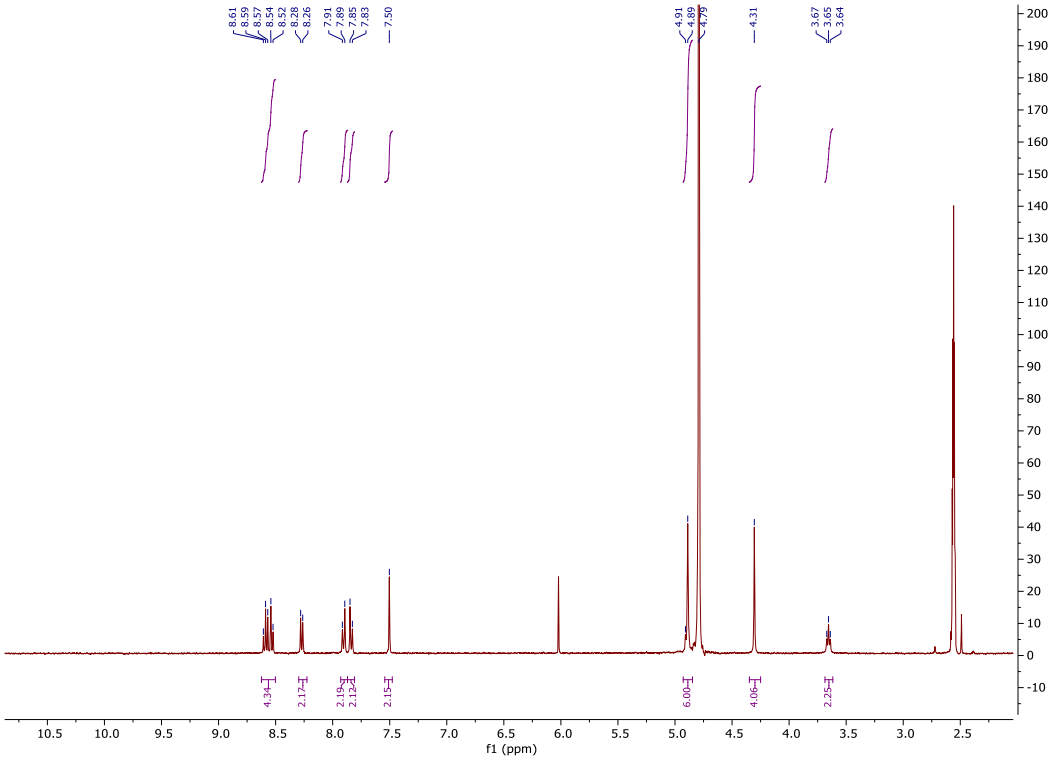

Figure S17. Compound **11** ^{1}H NMR spectrum (400 MHz, 298 K, D_2O/CD_3CN 1:1).

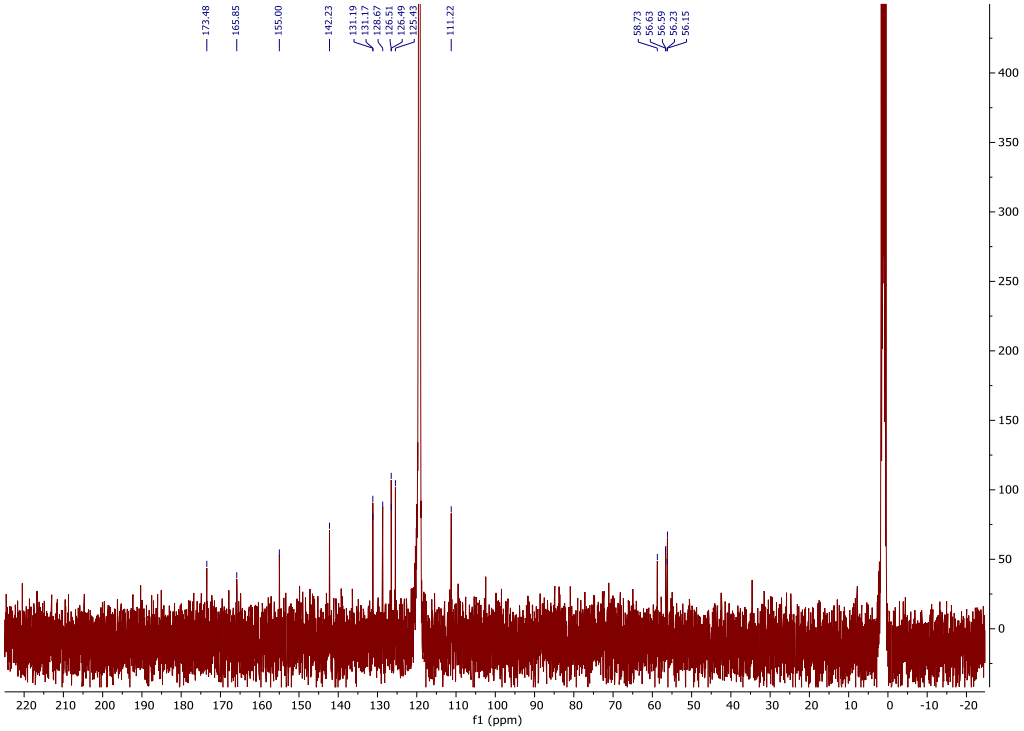

Figure S18. Compound **11** ^{13}C NMR spectrum (100 MHz, 298 K, D_2O/CD_3CN 1:1).

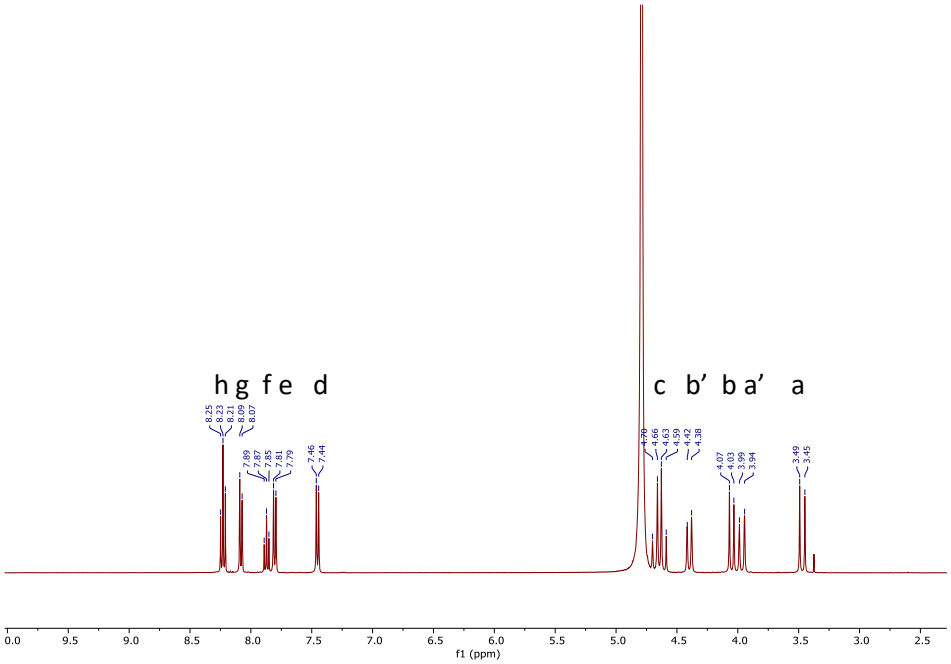

Figure S19 [Y(pypa)]$^{-}$ ^{1}H NMR spectrum (400 MHz, 298 K, D_2O)

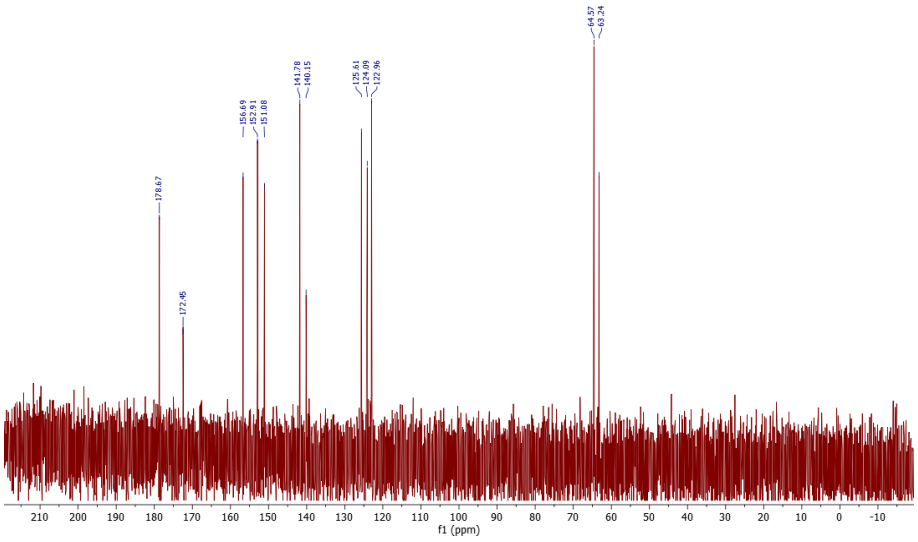

Figure S20 [Y(pypa)]$^{-}$ ^{13}C NMR spectrum (100 MHz, 298 K, D_2O)

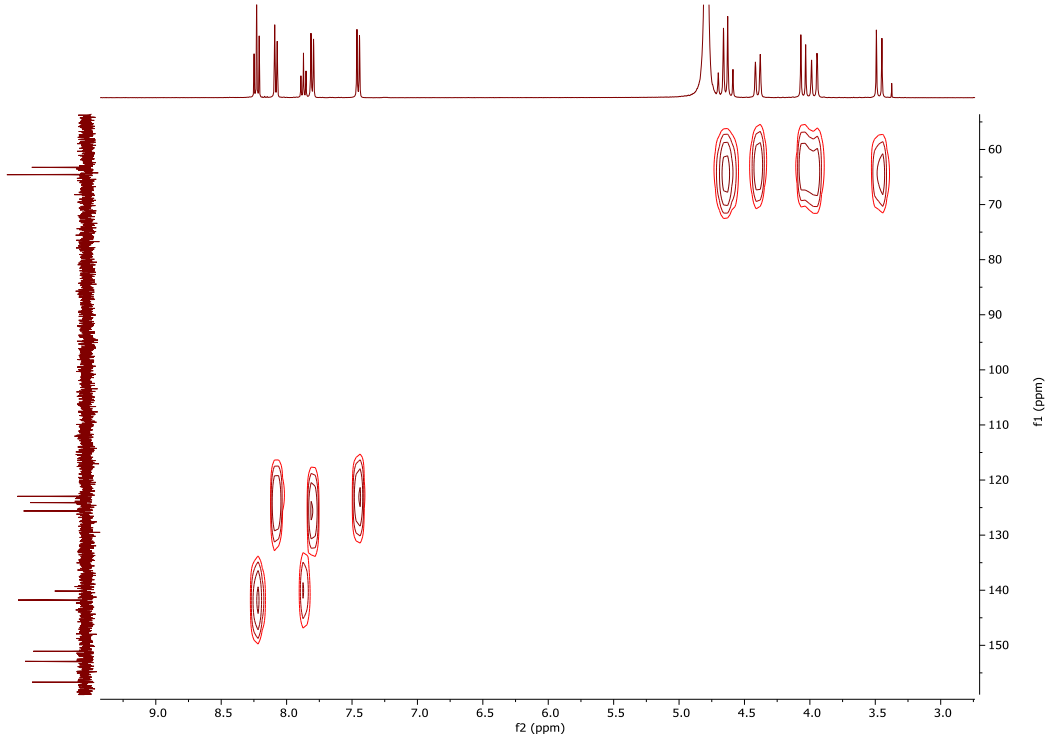

Figure S21 [Y(pypa)]$^{-}$ ^{1}H-^{13}C HSQC spectrum (400/100 MHz, 298 K, D_2O)

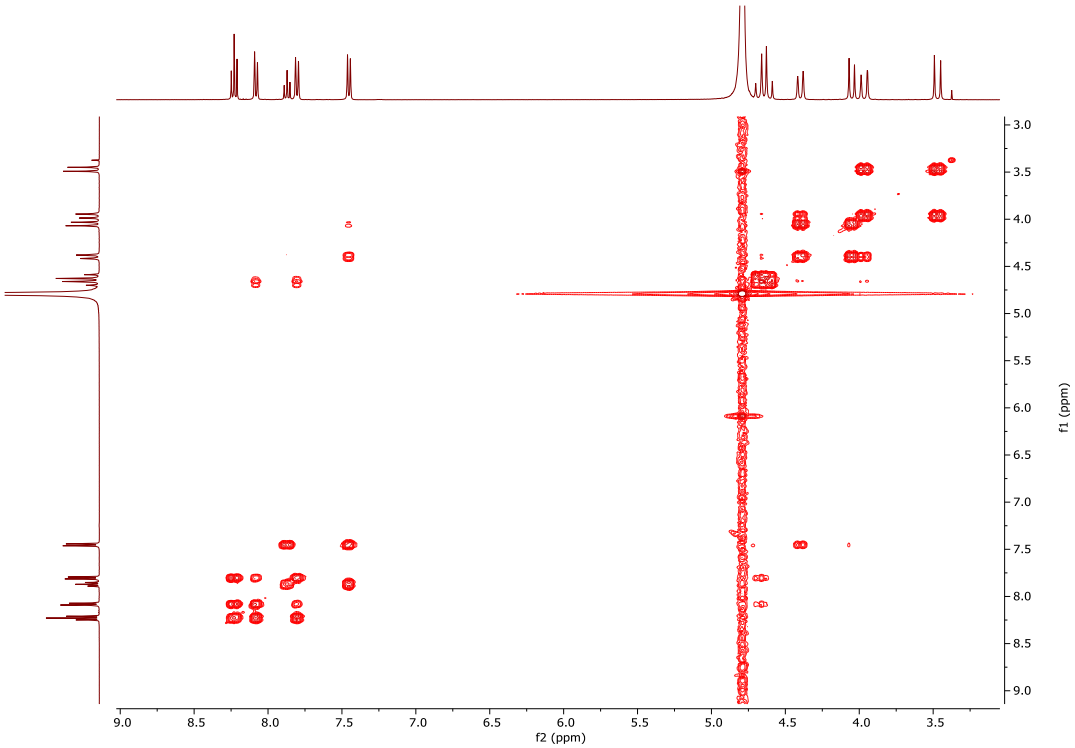

Figure S22 [Y(pypa)]$^{-}$ ^{1}H-^{1}H COSY spectrum (100/100 MHz, 298 K, D_2O)

High-Resolution Mass Spectra

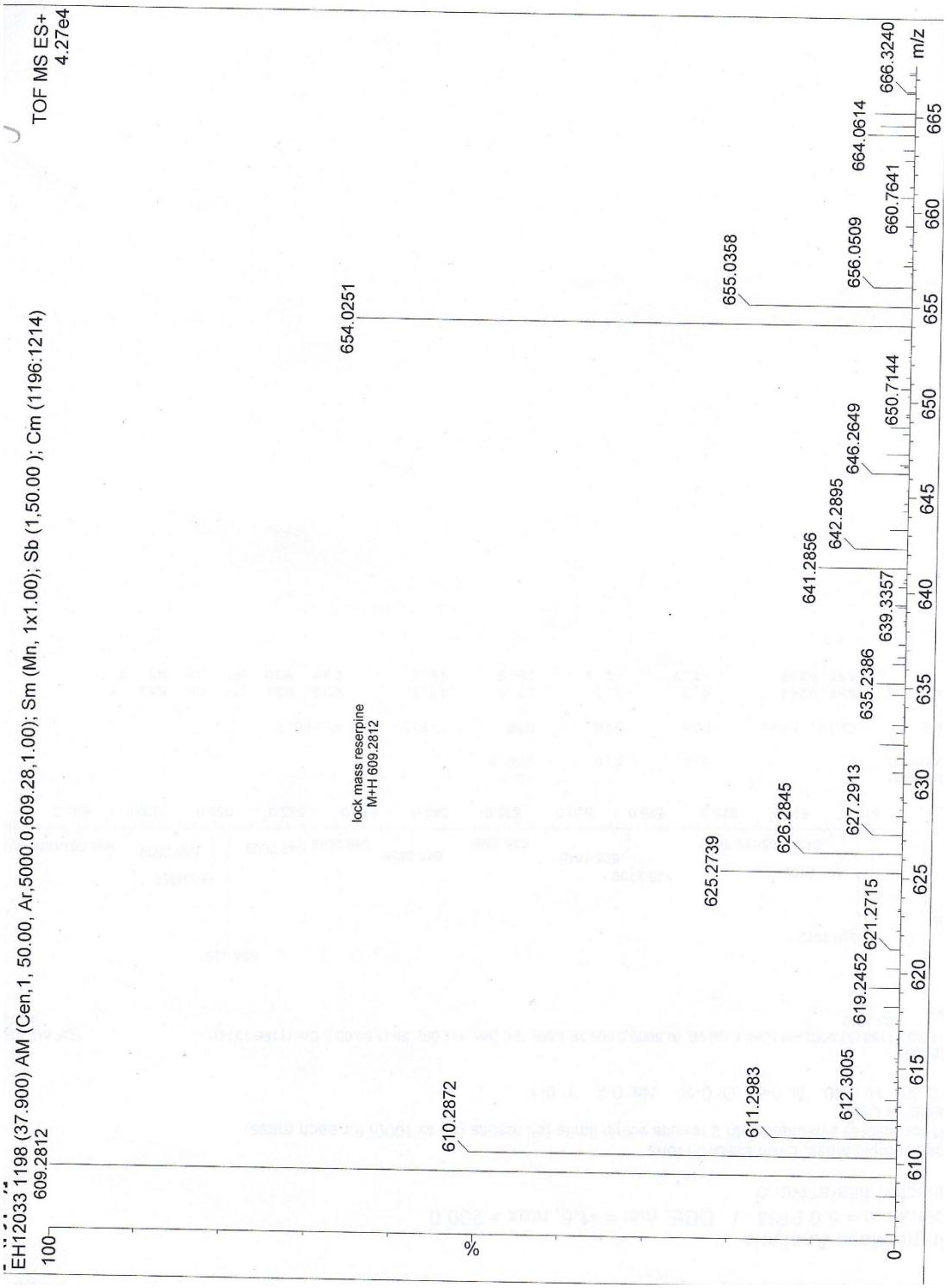

Figure S23. [Y(pypa)]$^-$ high-resolution mass spectrum.

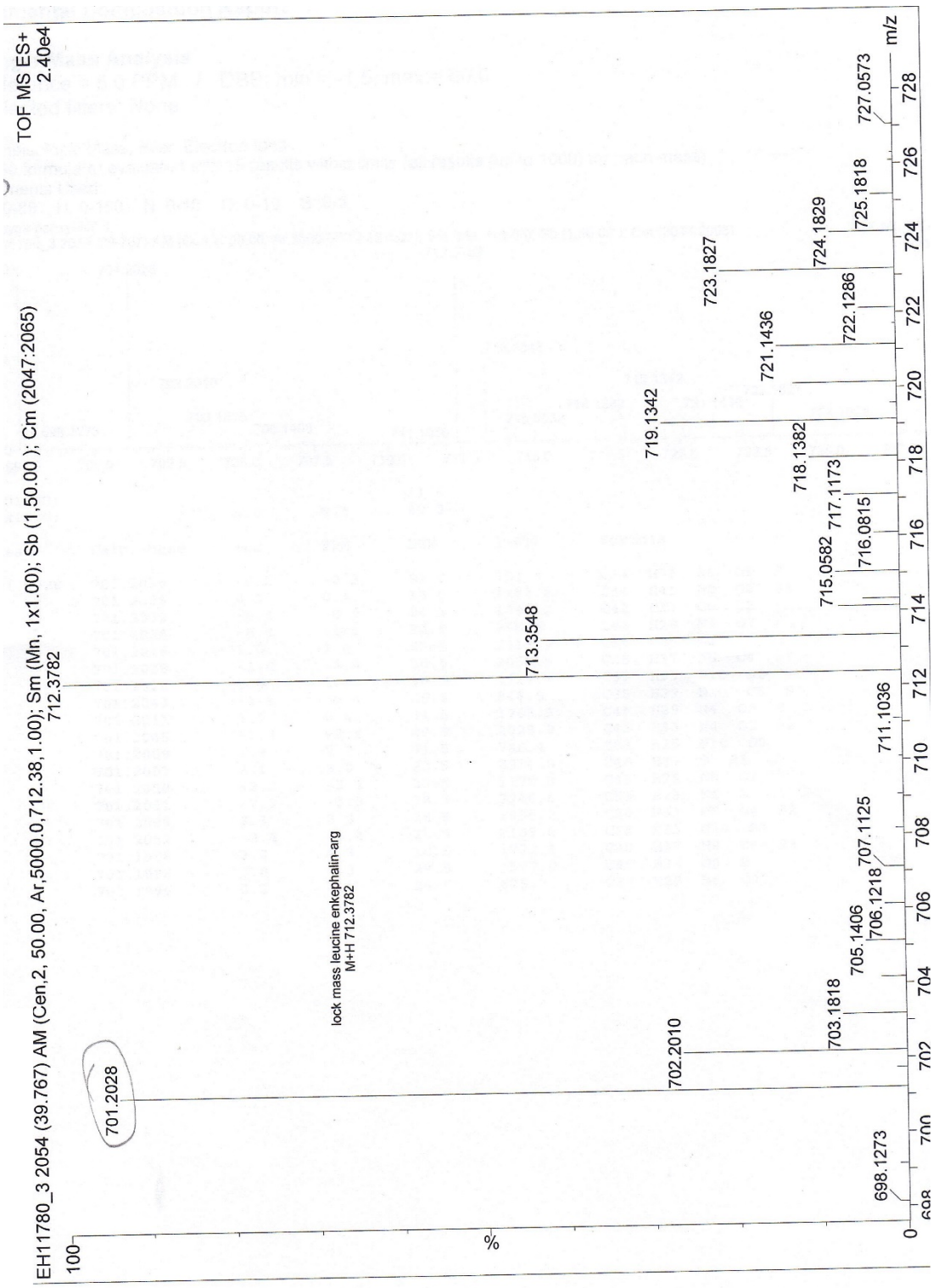

Figure S24. H_4pypa-phenyl-NCS high-resolution mass spectrum.

DFT Calculation

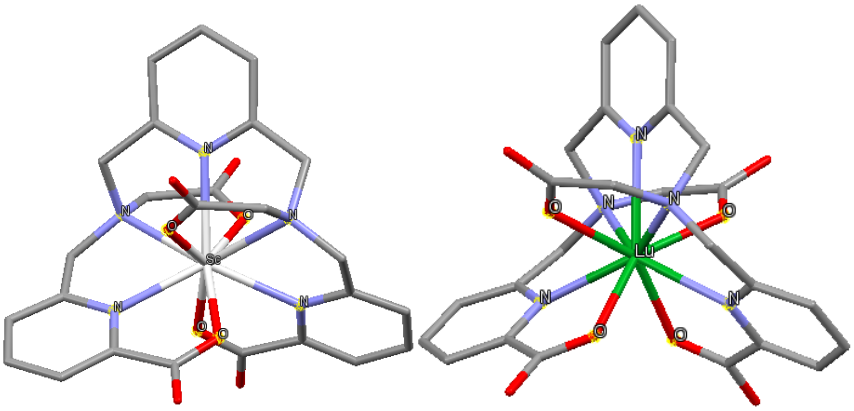

Figure S25. DFT calculated geometry for the $[Sc(pypa)]^-$ (left) and $[Lu(pypa)]^-$ (right) anions.

Solution Thermodynamics

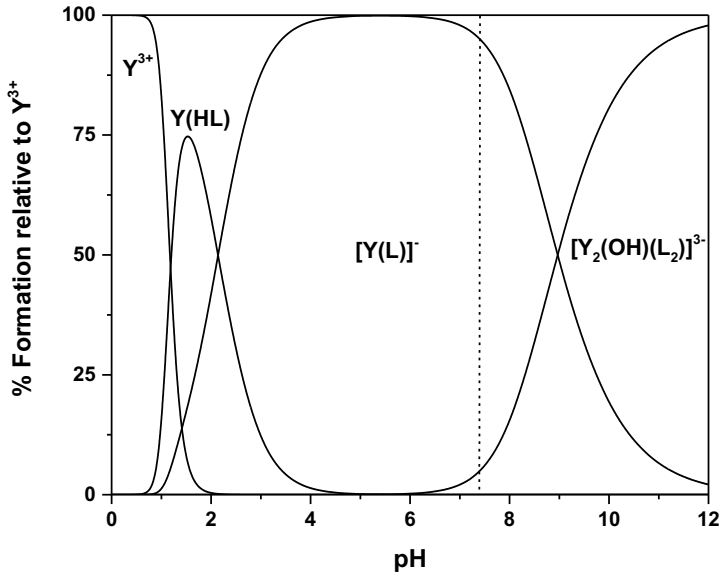

Figure S26. Distribution diagram of the Y^{3+}-H_4pypa system calculated with stability constants in Table 3, $[L] = [Y^{3+}] = 1 \times 10^{-3}$ M. Dashed line indicates physiological pH (7.4).

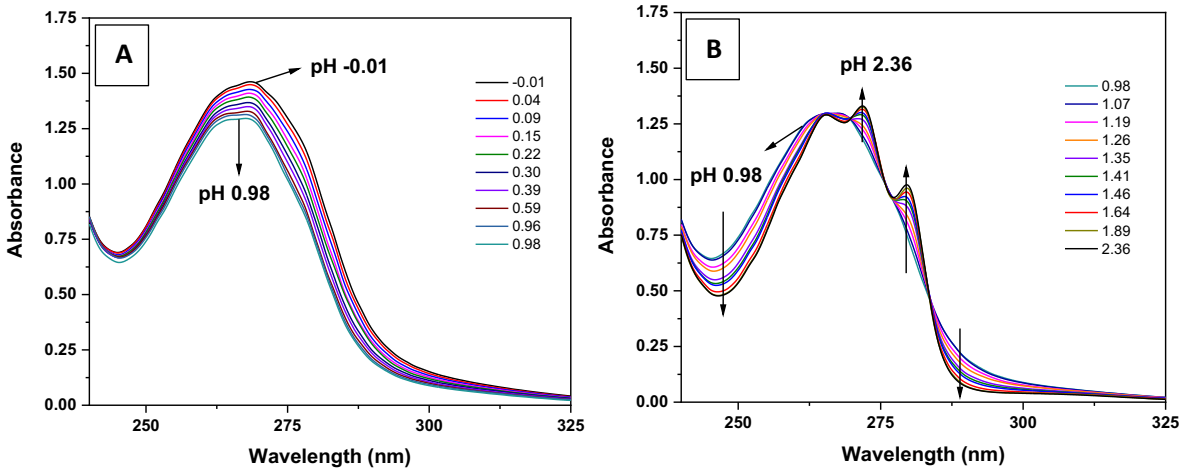

Figure S27. (A) and **(B)** Representative spectra of the in-batch UV-titration of the Y^{3+}-pypa system as the pH is raised. [L] = [Y^{3+}] = 1.33 × 10^{-4} M at 25 °C, l = 1 cm. The ionic strength was maintained constant (*I* = 0.16 M) when possible by addition of different amounts of NaCl.

Radiolabeling and Mouse Serum Challenge

Table S1. Radiochemical yield% of [^{86}Y][Y(pypa)]$^{-}$ at pH=7.

Final concentration	RCY % (n = 3)							
	7 min		15 min		30 min		60 min	
[-log(L)]	Avg.	St.dev.	Avg.	St.dev.	Avg.	St.dev.	Avg.	St.dev.
4	95	3	98	0	97	1	97	0
5	96	0	96	1	97	1	97	1
6	83	2	88	3	92	1	93	1
7	15	2	16	5	23	2	26	2
ESA (EoB) GBq/μmol	79		85		98		105	

Table S2. Intact percentage of [^{86}Y][Y(pypa)]$^{-}$ in mouse serum.

Time	% intact (n=3)	
(h)	Avg.	St.dev.
0.5	97	1
4	97	1
24	97	1
48	97	0

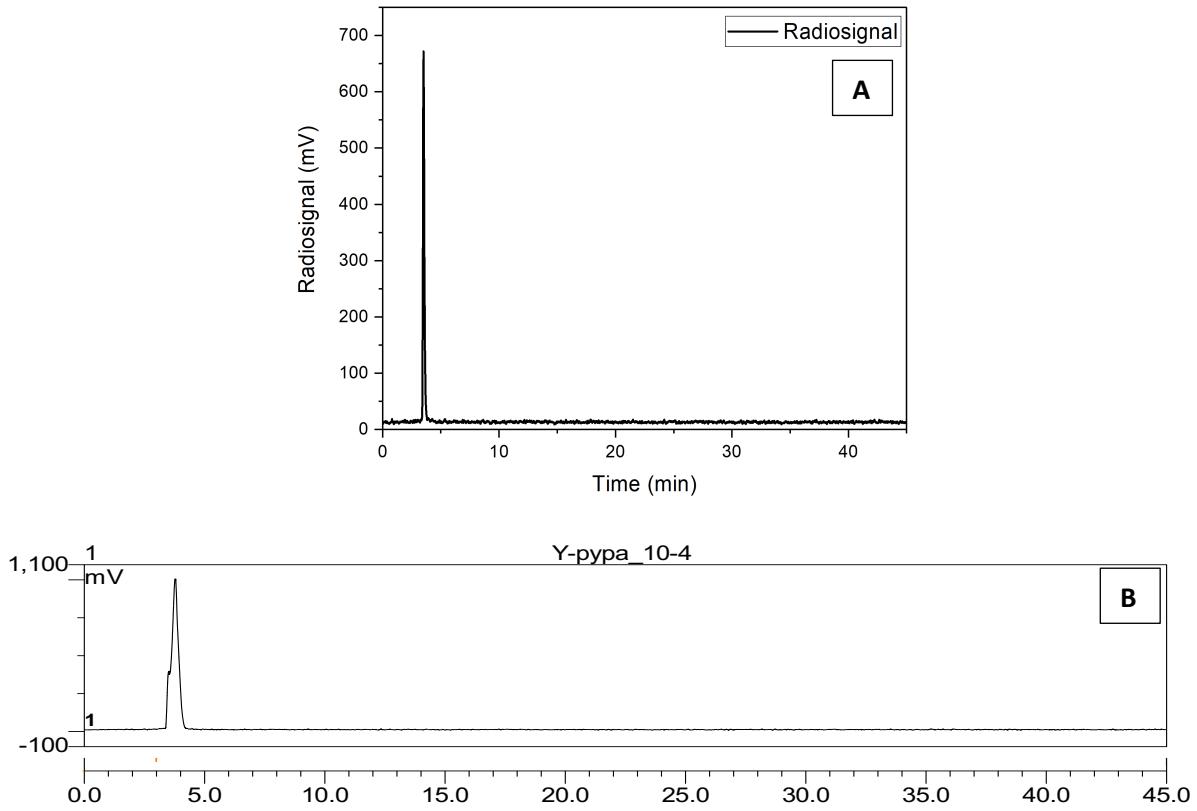

Figure S28. Radio-HPLC chromatographs of **(A)** uncomplexed yttrium-86 (t_R = 3.5 min) and **(B)** [^{86}Y][Y(pypa)]$^-$ (t_R = 3.5 min) (A: H_2O/0.1%TFA B:ACN/0.1%TFA, 5-65% B over 32 min, 1 mL/min)

Biodistribution Studies

Table S3. *Ex Vivo* Quantification of both ^{44}Sc- and ^{86}Y-labeled H_4pypa-phenyl-TRC105 at 18 h and 48 h p.i., respectively (n = 3).

***Ex Vivo* Quantification**	**[^{44}Sc][Sc(pypa-phenyl-TRC105)] 18 h**		**[^{86}Y][Y(pypa-phenyl-TRC105)] 48 h**	
Organs	**Avg.**	**St.dev.**	**Avg.**	**St.dev.**
Blood	23.75	1.61	10.31	0.78
Skin	1.48	0.23	3.53	1.46
Muscle	1.69	0.22	0.59	0.04
Bone	3.76	0.20	7.72	0.99
Heart	4.83	0.29	3.02	0.22
Lung	12.88	0.20	7.71	2.83
Liver	7.75	0.34	7.56	1.26
Kidney	8.96	0.06	5.04	2.12
Spleen	9.90	0.32	6.15	1.23
Pancreas	2.33	0.34	0.90	0.22
Stomach	3.31	0.35	0.96	0.13
Intestine	5.95	0.19	1.84	0.14
4T1 tumor	16.07	3.40	11.21	1.93
Brain	0.82	0.06	0.46	0.03