Electronic Supplementary Material (ESI) for Dalton Transactions.

Analysis of the isomer ratios of polymethylated DOTA complexes and the implications on protein structural studies

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Preparation of M4DOTMA ligand:

The synthesis of *SSSS*-*SSSS*-M4DOTMA was performed using a previously reported method (*1*) with the exception of using *R*-benzyl lactate instead of *S*-benzyl lactate. Tetramethyl cyclen precursor was obtained from J-STAR Research, Inc. (South Plainfield, NJ, USA). The final purification of *SSSS*-*SSSS*-M4DOTMA after deprotection of the tetra-benzyl group, however, was performed using reverse phase HPLC over an Eclipse XDB-C18 column (4.6 x 150 mm; 5 μm). The absorbance was monitored at 210 nm and the solvent system elution started with 100% water in 0.1% TFA followed by a linear gradient to 60% water in 0.1% TFA and 40% acetonitrile in 0.1% TFA over 26 min at a flow rate of 0.5 mL/min (t_R = 13.46 min). The overall yield was 16% and is slightly lower than the literature yield of 26% (*1*). ^{1}H NMR (400 MHz, D_2O at pH 14): δ3.61 (4H, q, J = 7.2 Hz, NC<u>H</u>COOH), 3.09 (4H, m, NC<u>H</u>CH_3), 2.64 (4H, dd, J = 12.8 Hz, NC<u>H</u>$_2$), 2.25 (4H, dd, J = 12.8 Hz, NC<u>H</u>$_2$), 1.16 (12H, d, J = 7.2 Hz, C<u>H</u>$_3$COOH), 0.98 (12H, d, J = 6.4 Hz, NCHC<u>H</u>$_3$). ^{13}C NMR (400 MHz, D_2O at pH 14): δ182.6 (C=O), 60.6 (N<u>C</u>HCOOH), 50.4 (N<u>C</u>HCH_3), 46.9 (N<u>C</u>H_2), 14.5 (<u>C</u>H_3COOH), 12.4 (NCH<u>C</u>H_3). *m/z* (ESI-MS+): calcd for $[C_{24}H_{45}N_4O_8]^+$ $[M+H]^+$ 517.3, found 517.8.

***SSSS*-*SSSS*-M4DOTMA ligand studies.** The ligand *SSSS*-*SSSS*-M4DOTMA was synthesized using the method of Ranganathan and co-workers (*1*) except that (*R*)-benzyl lactate was used instead of (*S*)-benzyl lactate as the starting material for the pendant arms. Alkylation of (*R*)-benzyl

lactate OTf with *SSSS*-M4 cyclen proceeded via an SN_2 reaction, hence a complete inversion of each chiral center of the arm occurred resulting in a single stereoisomer (*SSSS*-*SSSS*-M4DOTMA). The overall yield is 16% and is slightly lower than the literature value (*1*). It is worth mentioning that it is the (δδδδ) helicity of the macrocyclic ring that can afford S-configurations of the methyl group on the ethylene carbon.

The ^{1}H NMR spectrum of *SSSS*-*SSSS*-M4DOTMA is better resolved at highly acidic pH (~1). The ^{1}H NMR spectrum reflects a geometry of 2-fold symmetry, indicative of a hexa-protonated *SSSS*-*SSSS*-M4DOTMA (H_6L^{2+}). Three distinct doublets with a total of 24 protons are observed, which can be attributed to the methyl groups from the arms and the macrocycle (Fig. S1). The acetate and ethylenic protons are found between 2.80 and 4.60 ppm, with the same relative area to each other. On the basis of the COSY spectrum (Fig. S2), the methyl group that appears as a doublet at 1.68 ppm is linked to a quartet at 4.57 ppm that shows no connection to any other signals in the spectrum. These peaks are therefore assigned to the methyl arm protons and CH arm protons, respectively. The doublet at high field (1.18 ppm) has a COSY connection to a poorly resolved peak at 3.56 ppm, which is linked to other ring protons. These signals are thus assigned as the methyl ring and CH ring protons, respectively. The other doublet at 1.38 ppm has two cross-peaks: one is from a quartet at 4.01 ppm that shows no other connections from the spectrum and is attributed to the CH arm protons, and the second cross peak comes from a complex pattern at 3.87 ppm (CH ring protons), which is also connected to a proton from the macrocycle. This doublet is therefore an overlap of two methyl groups from the macrocyclic ring and the pendant arms. The number of protons from this doublet is twice as many as the number of protons from the individual doublets in the spectrum. The geminal coupling between the axial (H_{ax}) and equatorial (H_{eq}) protons from the ethylene bridge of the ring is evident in the COSY spectrum at 3.23 and 2.83 ppm, and at 3.75 and 3.40 ppm. Vicinal coupling between H_{ax} and the CH ring protons can also be deduced in the COSY spectrum (cross peaks at 3.56 and 3.75 ppm, and at 3.87 and 3.23 ppm). Another vicinal coupling at 3.56 and 3.40 ppm, and at 3.87 and 2.83 ppm can be seen as weak cross-peaks (CH ring – H_{eq}). According to the Karplus relationship (*2*), the stronger vicinal coupling is assigned to ax-ax coupling, while the weaker one is assigned to ax-eq or eq-eq coupling. This suggests that the CH ring proton is located in the axial position and the methyl ring group is oriented towards the equatorial position. This is in good agreement with Ranganathan's work, which stated that the ring methyl group is expected to be in the equatorial position as the axial position is too crowded to be occupied by the methyl groups (*1*).

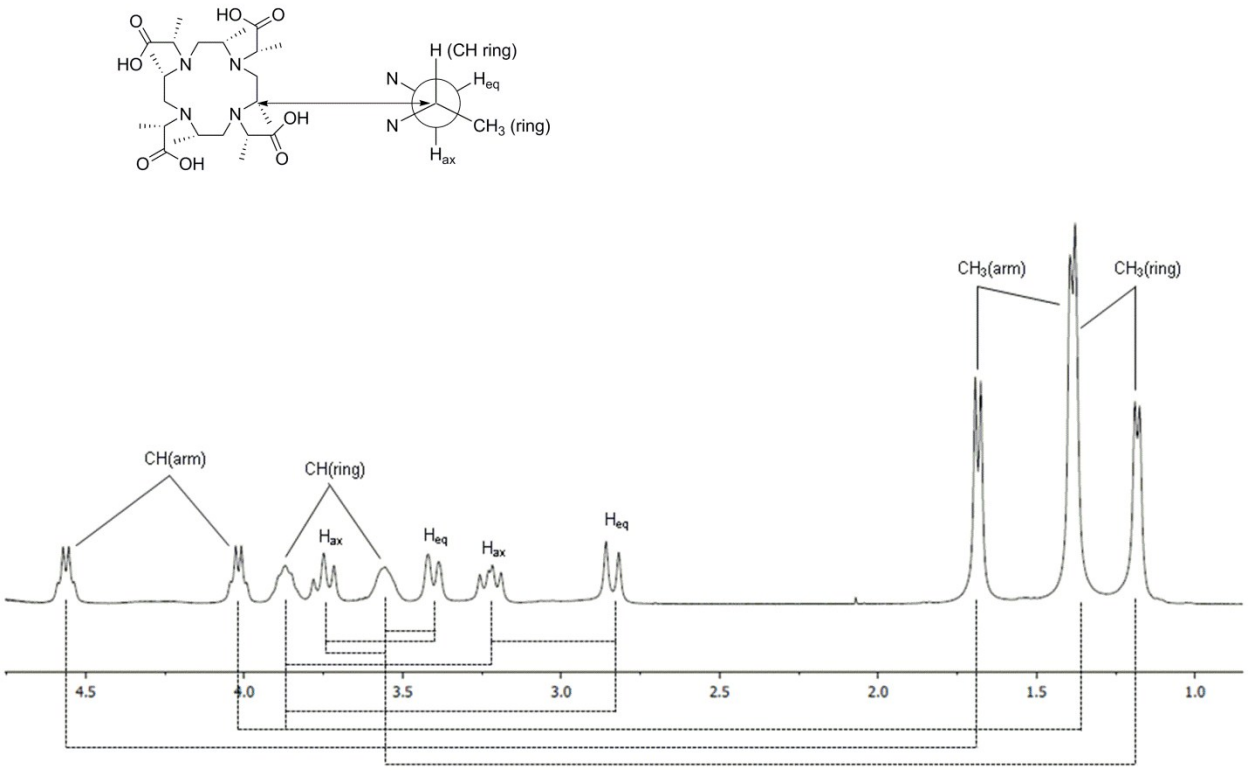


Figure S1. Proton NMR spectrum of *SSSS*-*SSSS*-M4DOTMA recorded at pH 1, 298 K and 400 MHz. The lines underneath the spectrum indicate the couplings determined from 2D COSY spectrum.

The 2-fold symmetry observed from the ^{1}H NMR is corroborated by ^{13}C NMR, which shows 12 distinct resonances (Fig. S3). Here, the methyl protons are displayed as four ^{13}C peaks at 12.2 -15.0 ppm, rather than as 2 peaks for a molecule of four-fold symmetry. Six peaks are observed between 47.5 and 58.5 ppm for the two CH_2 from the ring, and four CH groups from both the ring and acetate arms. The ^{13}C assignments in this

region were based on the DEPT spectrum (Fig. S4). Finally, two carbonyl carbons are found at 172.0 and 177.3 ppm. The ^{1}H-^{13}C HSQC spectrum (Fig. S5) is in good agreement with the COSY spectrum.

Adjusting the pH to highly basic conditions (~14) using LiOD results in a change in symmetry as the methyl groups are resolved into two doublets for both the ring and the arm protons, while only 4 resonances were observed between 2.0 to 4.0 ppm (Fig. S6). On the other hand, the number of signals in the ^{13}C NMR spectrum (Fig. S7) shows 6 resonances, confirming that a four-fold symmetry was achieved.

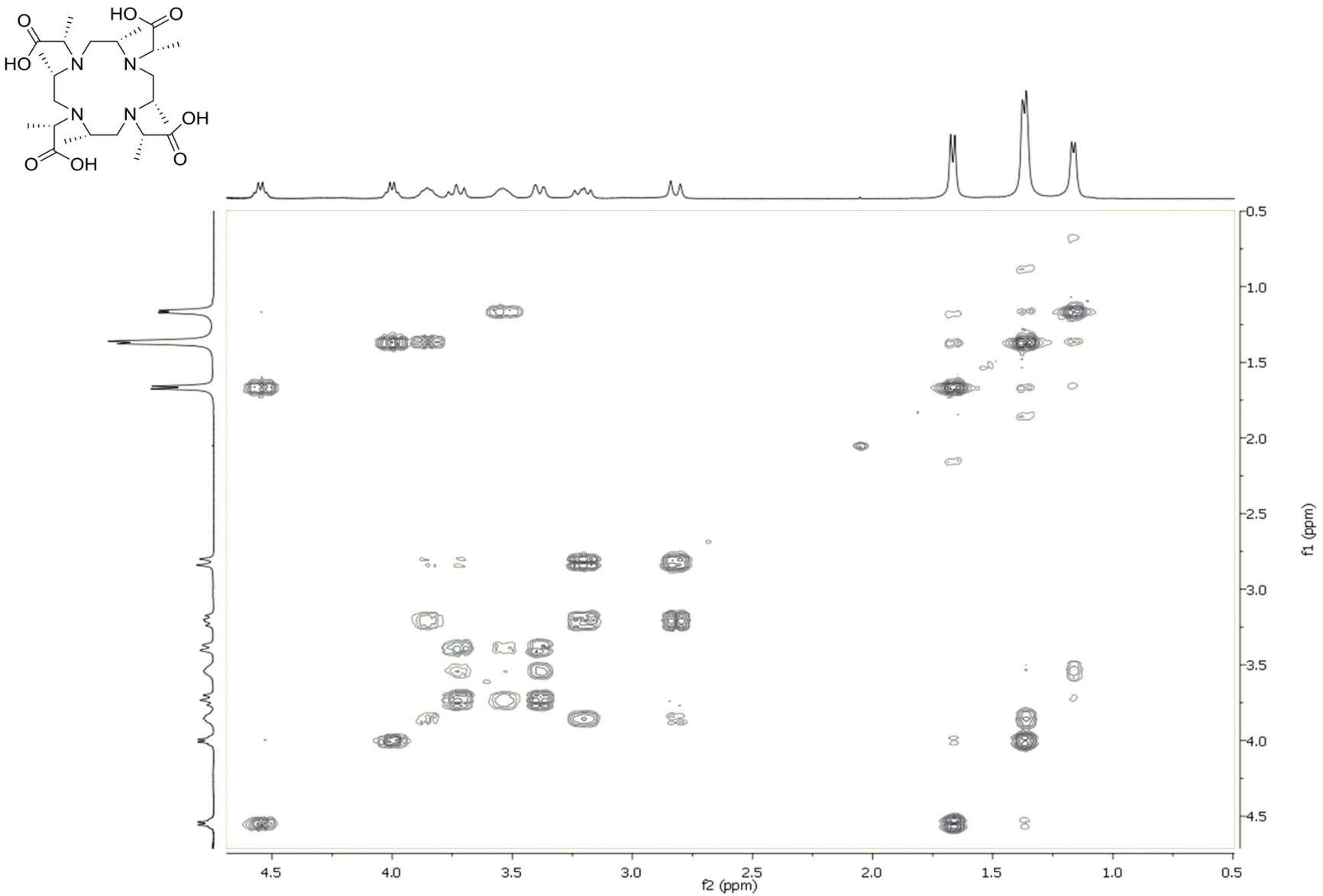
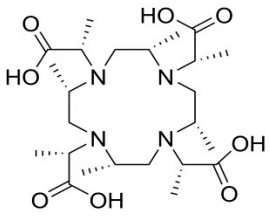


Figure S2. 2D COSY spectrum of *SSSS*-*SSSS*-M4DOTMA in acidic pH (~1) at 298 K and 400 MHz.



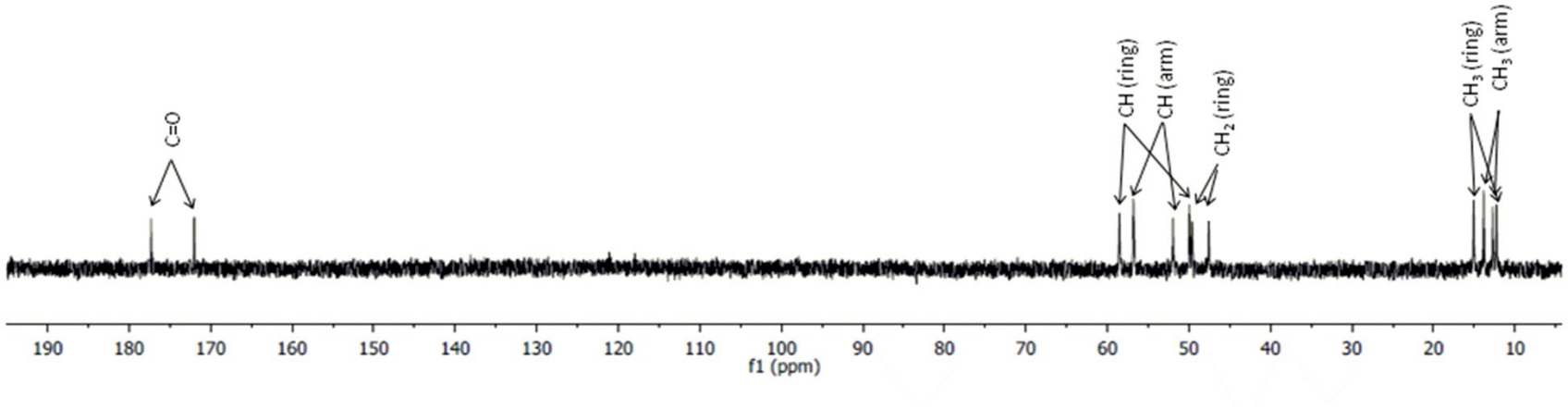
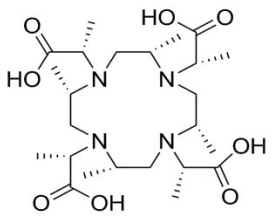


Fig. S3. ^{13}C NMR spectrum of *SSSS*-*SSSS*-M4DOTMA in acidic pH (~1) at 298K and 400 MHz.



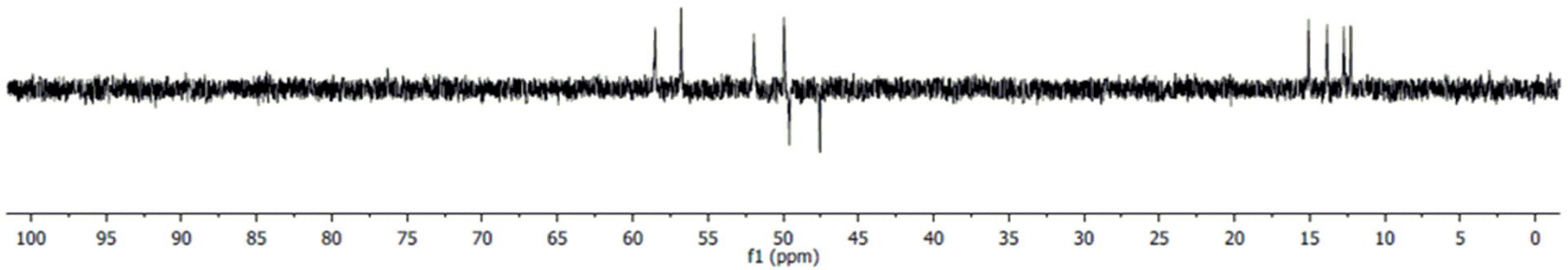


Fig. S4. (C)DEPT spectrum of *SSSS*-*SSSS*-M4DOTMA in acidic pH (~1) at 298 K and 400 MHz.

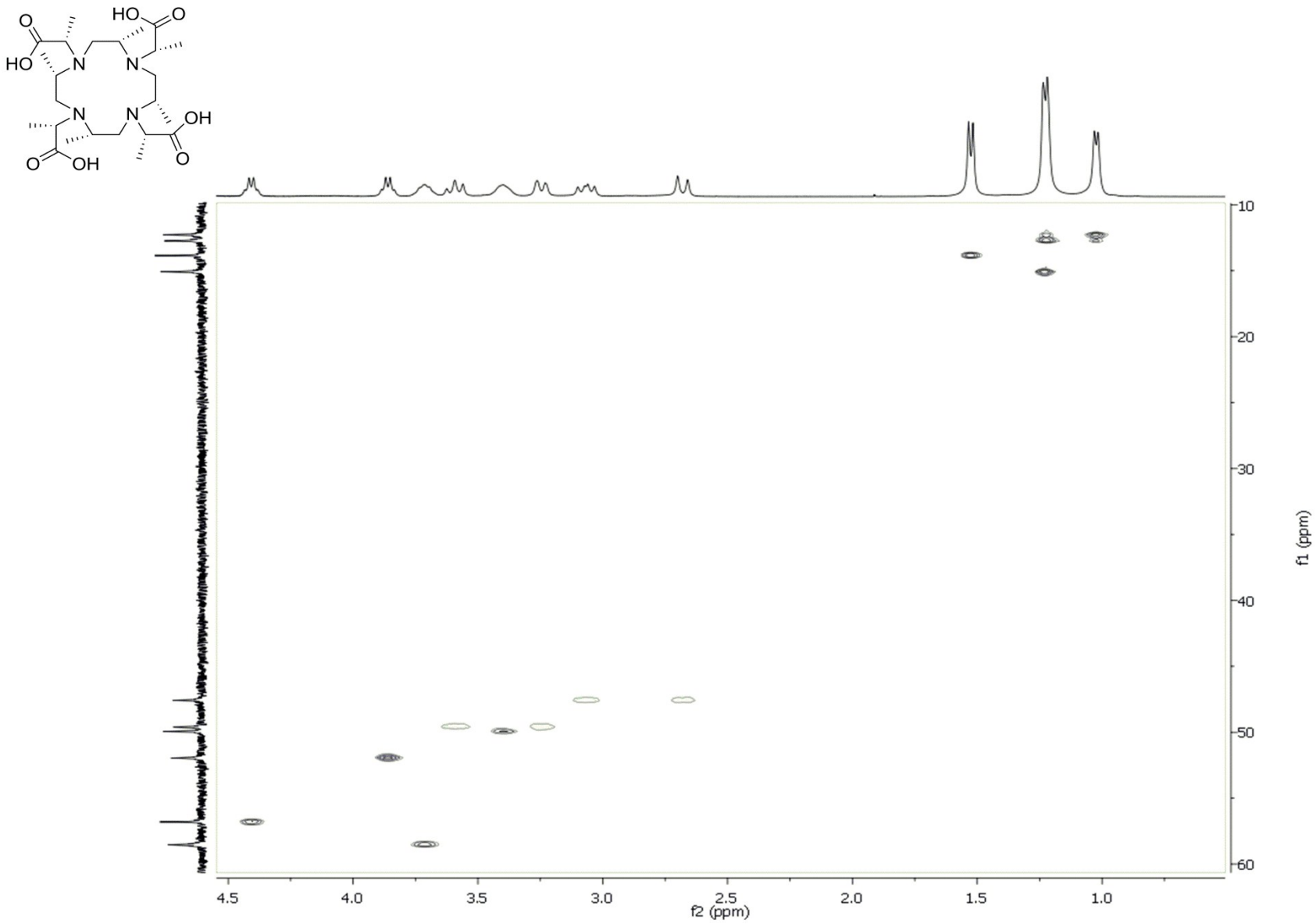


Fig. S5. HSQC spectrum of *SSSS*-*SSSS*-M4DOTMA in acidic pH (~1) at 298 K and 400 MHz.

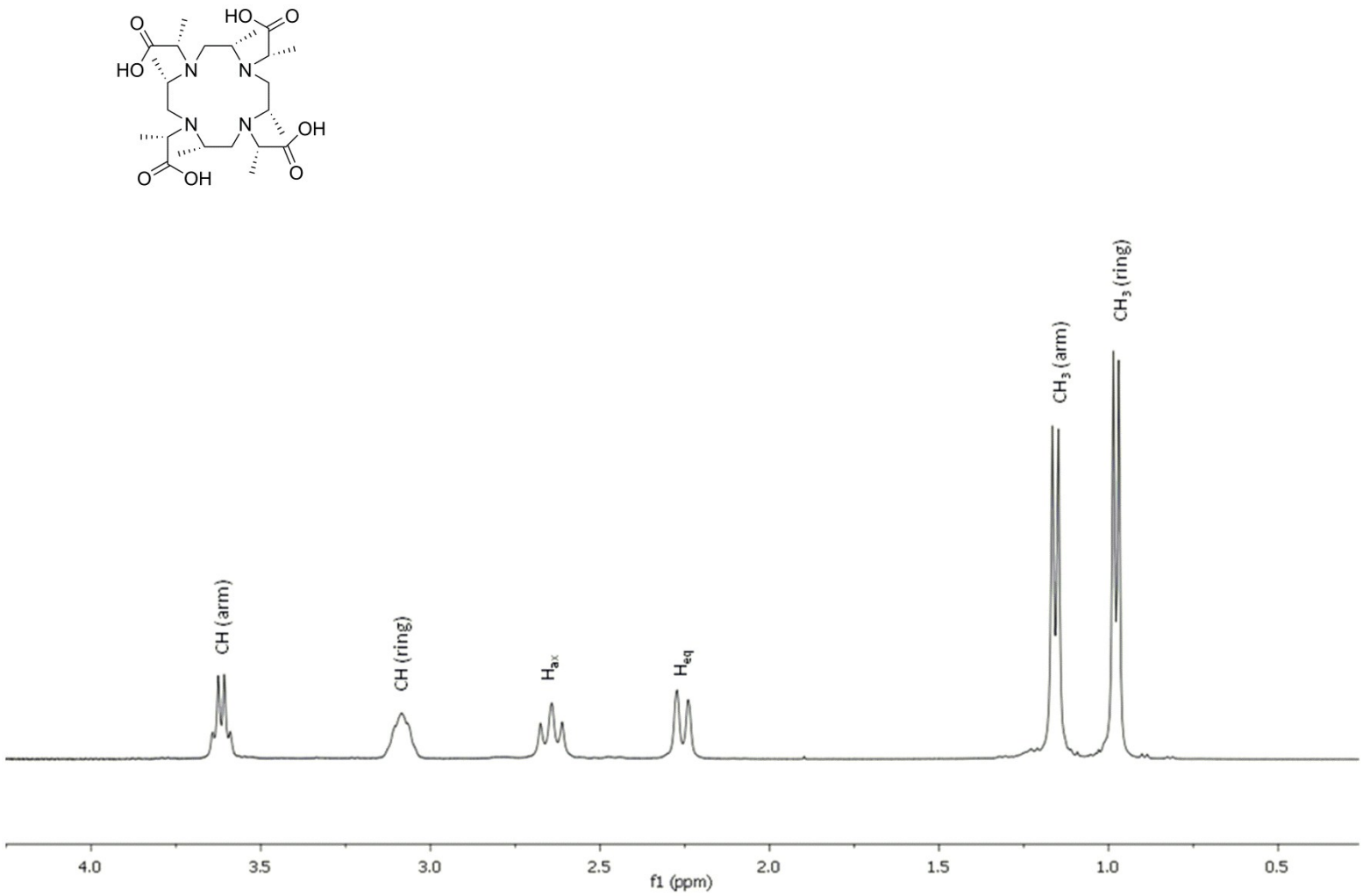
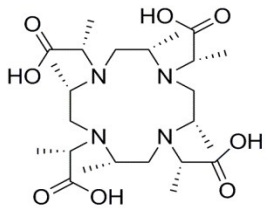


Fig. S6. ^{1}H NMR spectrum of *SSSS*-*SSSS*-M4DOTMA at highly basic pH (~14) at 298 K and 400 MHz.



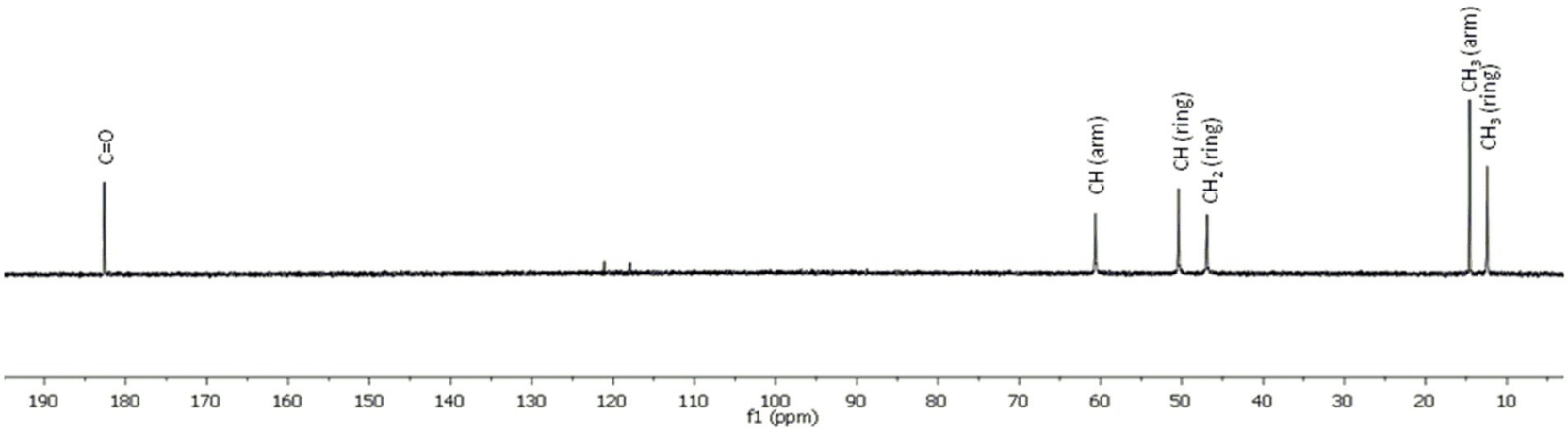
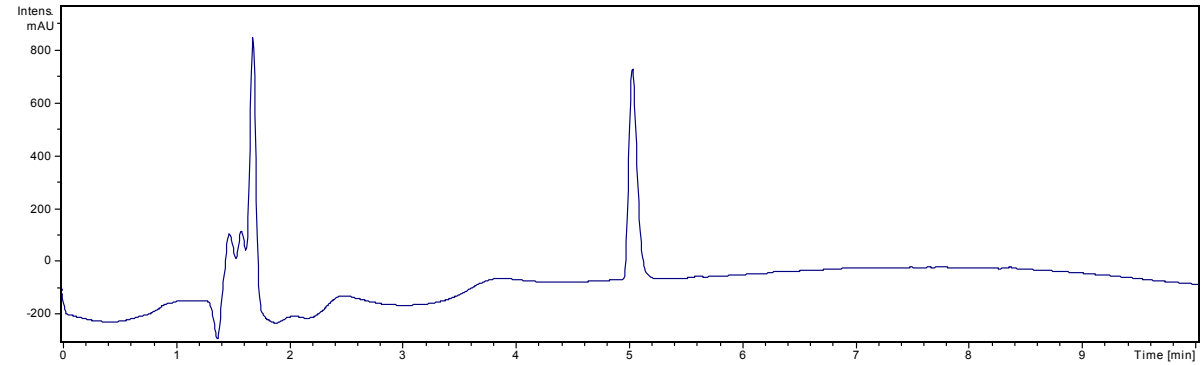
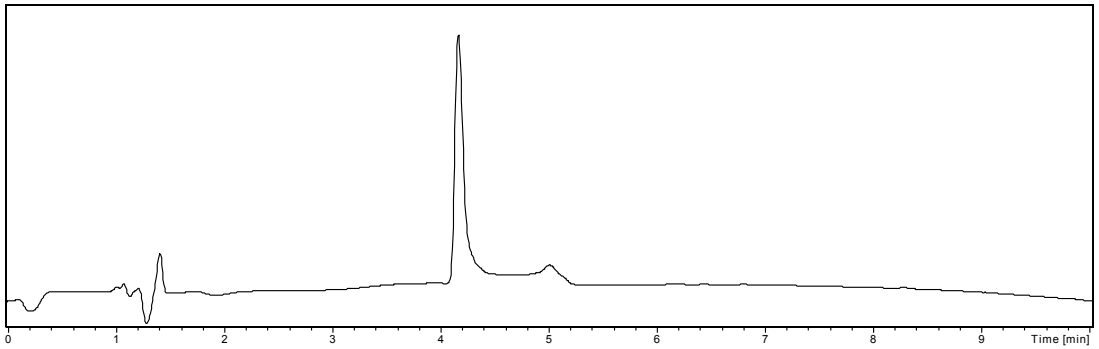


Fig. S7. ^{13}C NMR spectrum of *SSSS*-*SSSS*-M4DOTMA at highly basic pH (~14) at 298 K and 400 MHz.

a. Yb- *SSSS*-*SSSS*-M4DOTMA



b. Eu- *SSSS*-*SSSS*-M4DOTMA



c. Pr- *SSSS*-*SSSS*-M4DOTMA

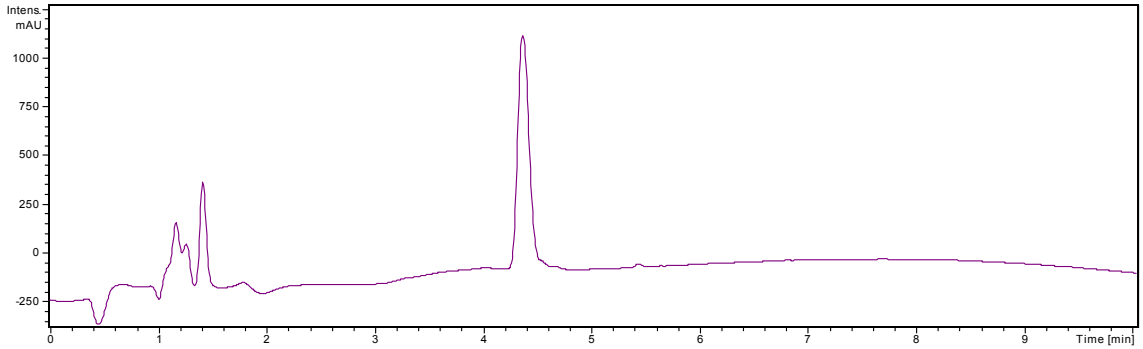


Fig. S8. HPLC chromatogram of (a) Yb- *SSSS*-*SSSS*-M4DOTMA, (b) Eur- *SSSS*-*SSSS*-M4DOTMA, and (c) Pr- *SSSS*-*SSSS*-M4DOTMA observed at 210 nm, 298 K, and pH 6.5.

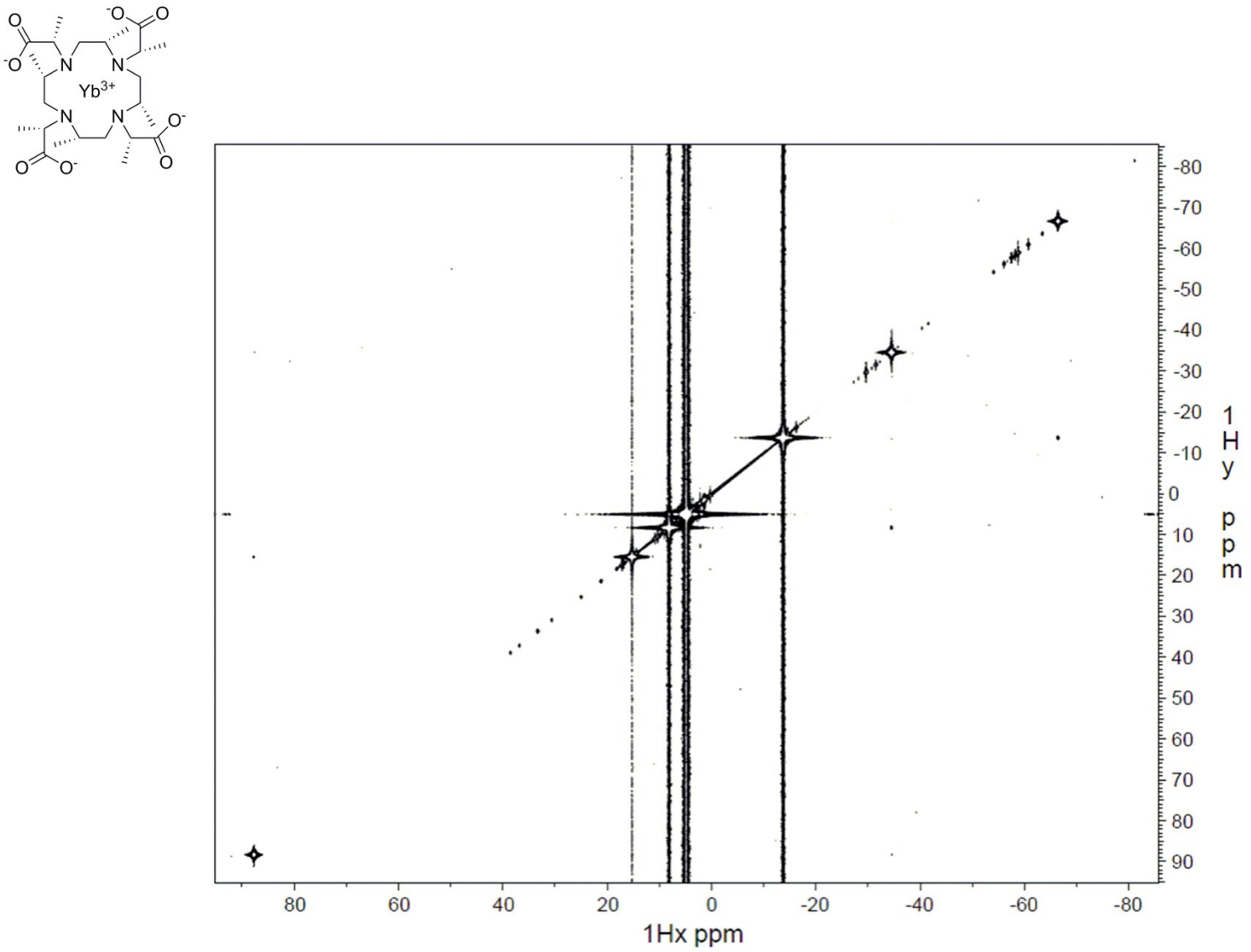


Fig. S9. 2D COSY spectrum of Yb- *SSSS*-*SSSS*-M4DOTMA at 298 K and 600 MHz.

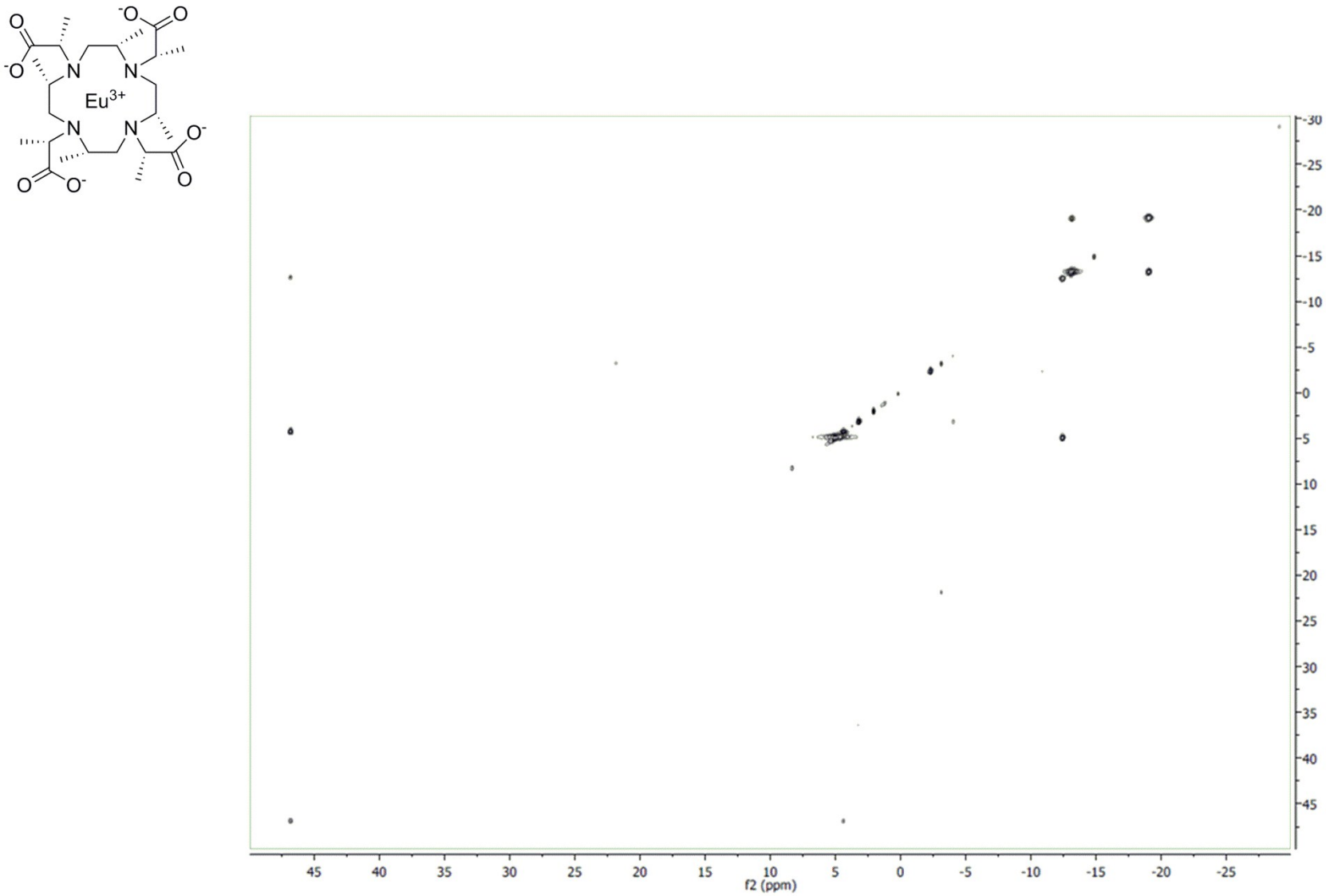


Fig. S10. 2D COSY spectrum of Eu- *SSSS*-*SSSS*-M4DOTMA at 298 K and 400 MHz.

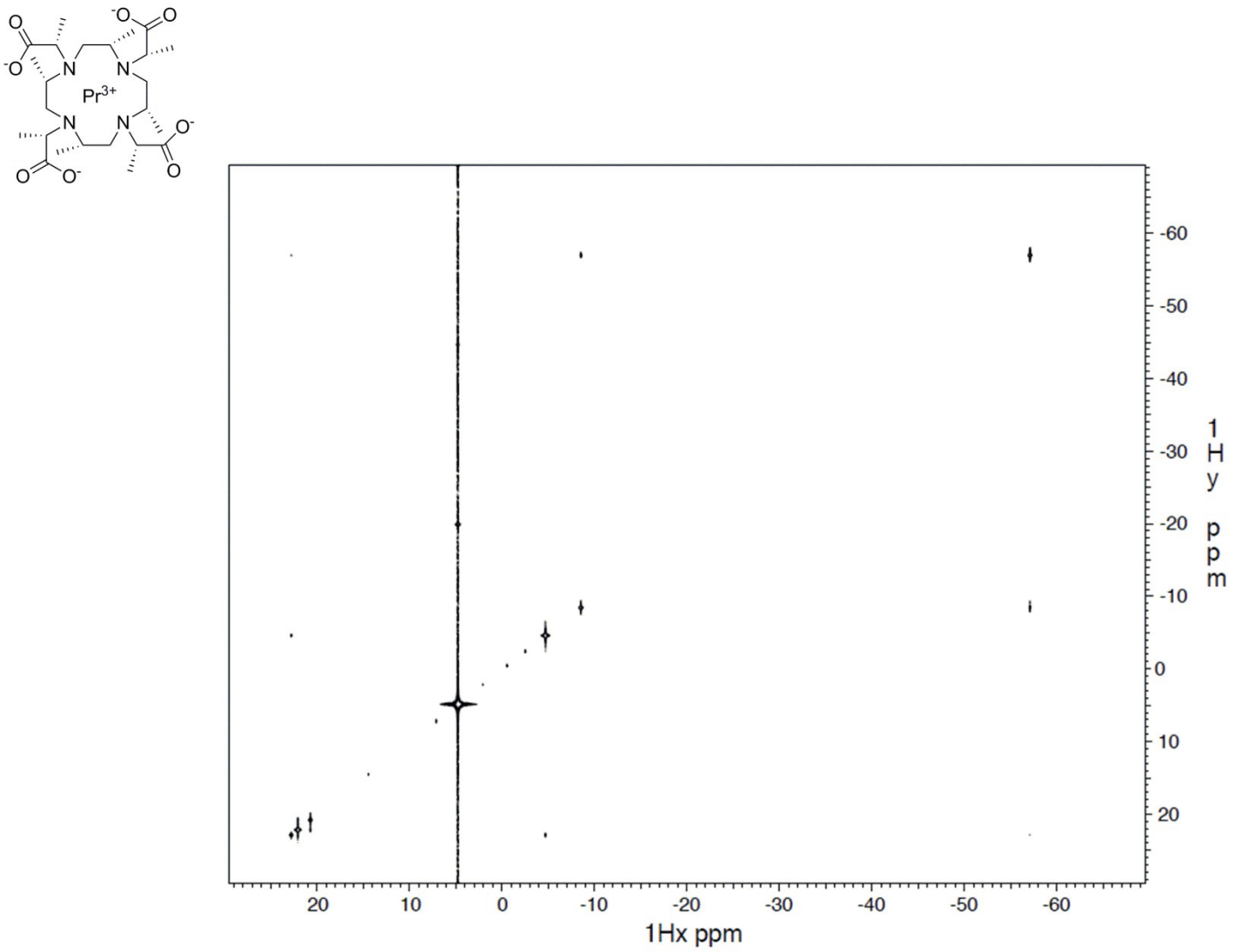


Fig. S11. 2D COSY spectrum of the major isomer of Pr- *SSSS*-*SSSS*-M4DOTMA at 298 K and 600 MHz.

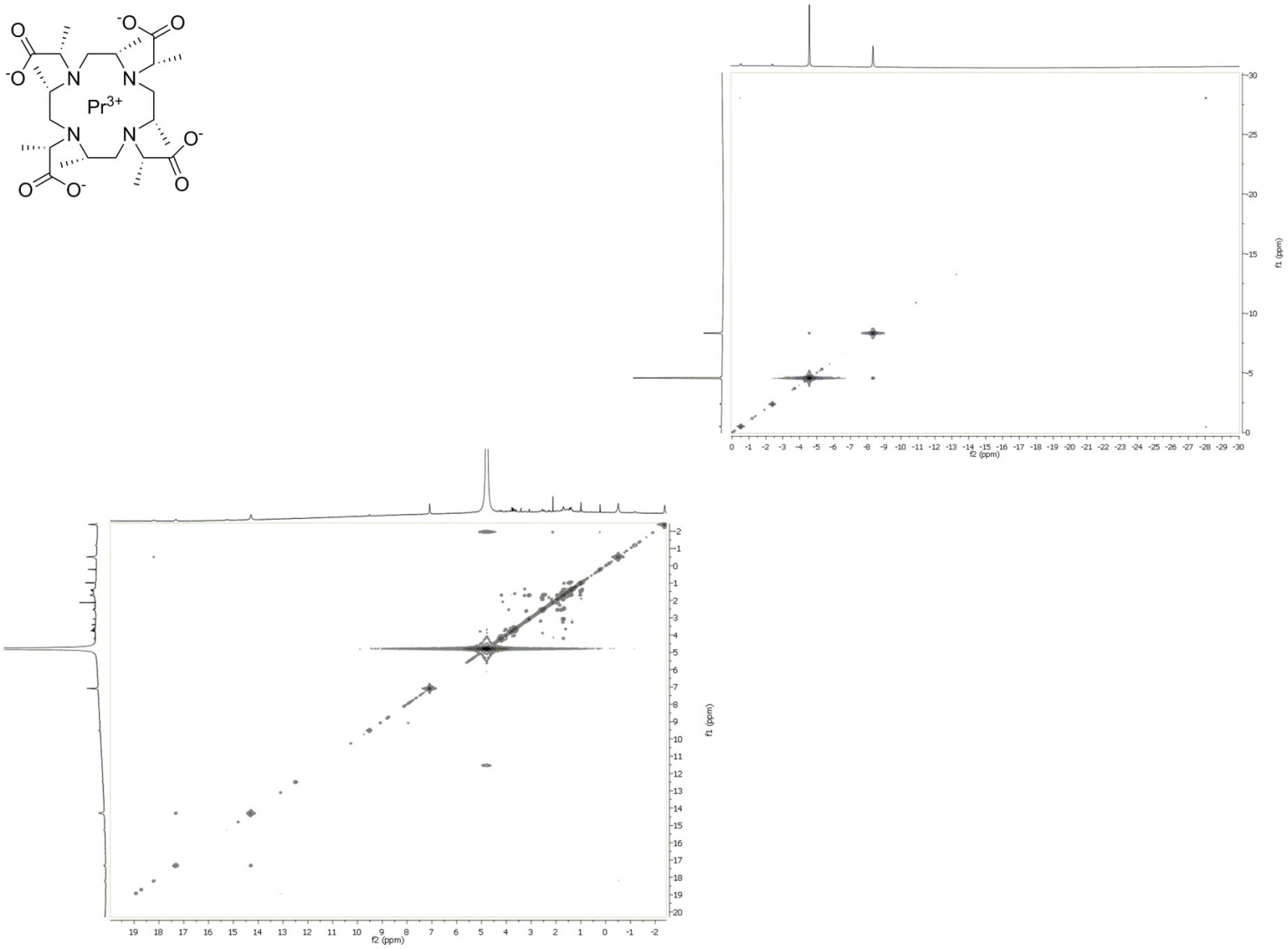
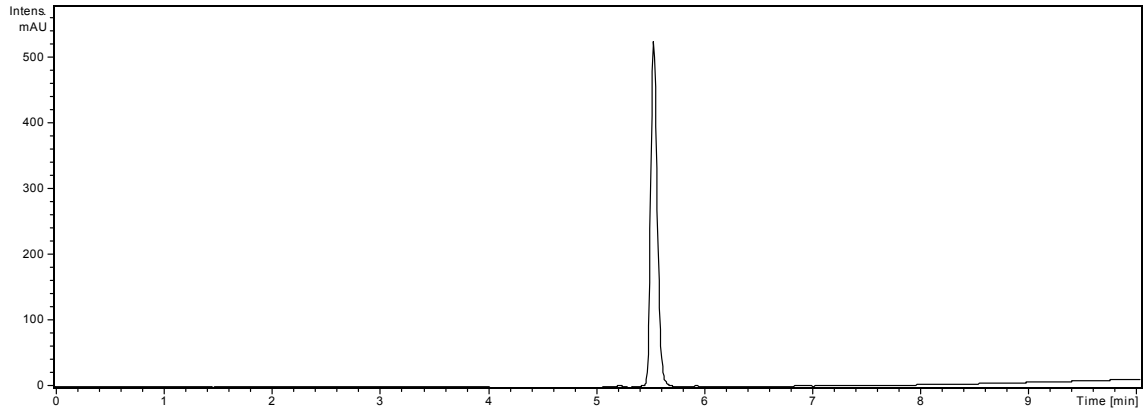
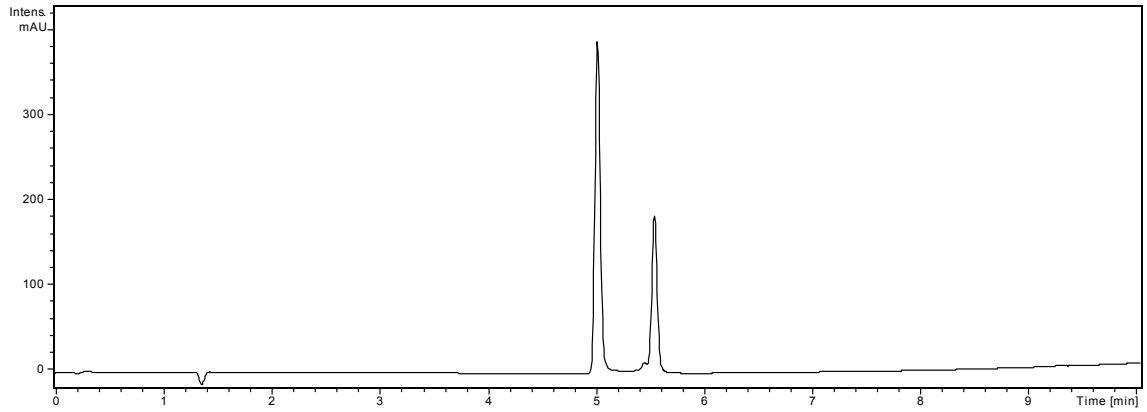


Figure S12. 2D COSY spectrum of the minor isomer of Pr-*SSSS*-*SSSS*-M4DOTMA at 303 K and 600 MHz.

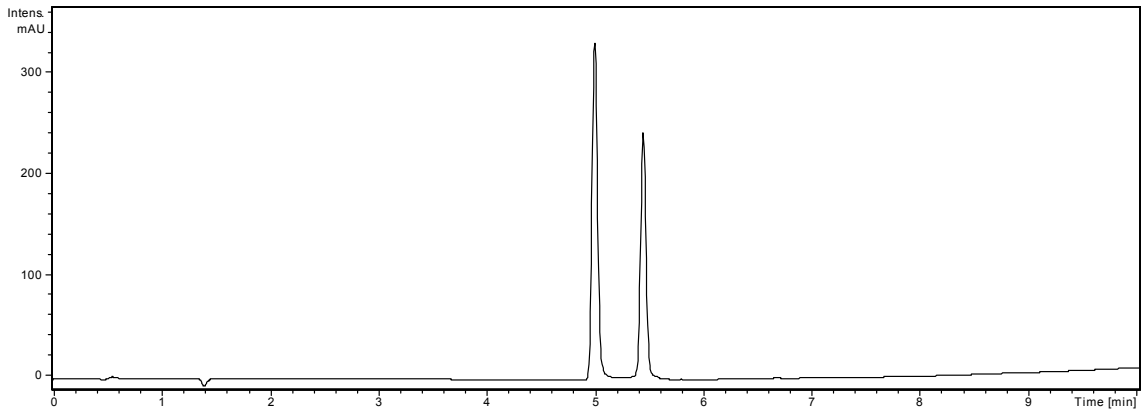
a.


Intens.
mAU
500
400
300
200
100
0
0
1
2
3
4
5
6
7
8
9
Time [min]

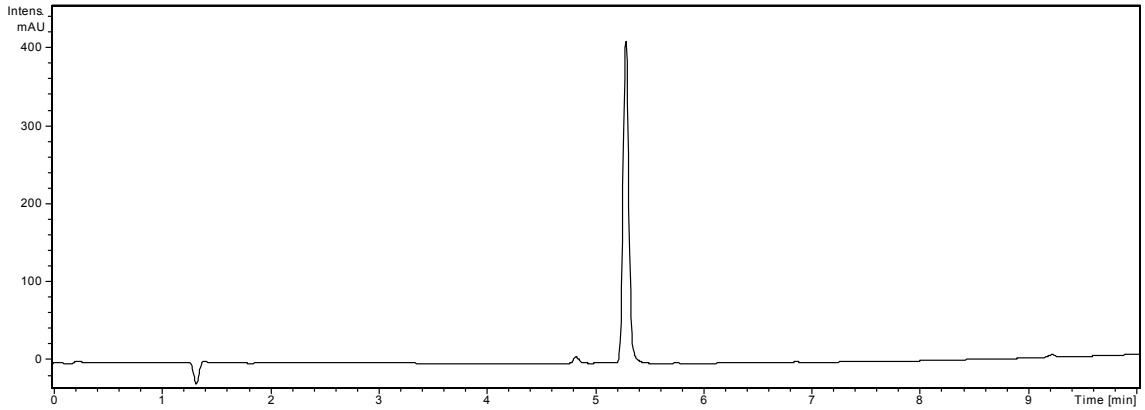
b.


Intens.
mAU
300
200
100
0
0
1
2
3
4
5
6
7
8
9
Time [min]

c.


Intens.
mAU
300
200
100
0
0
1
2
3
4
5
6
7
8
9
Time [min]

d.


Intens.
mAU
400
300
200
100
0
0
1
2
3
4
5
6
7
8
9
Time [min]

e.

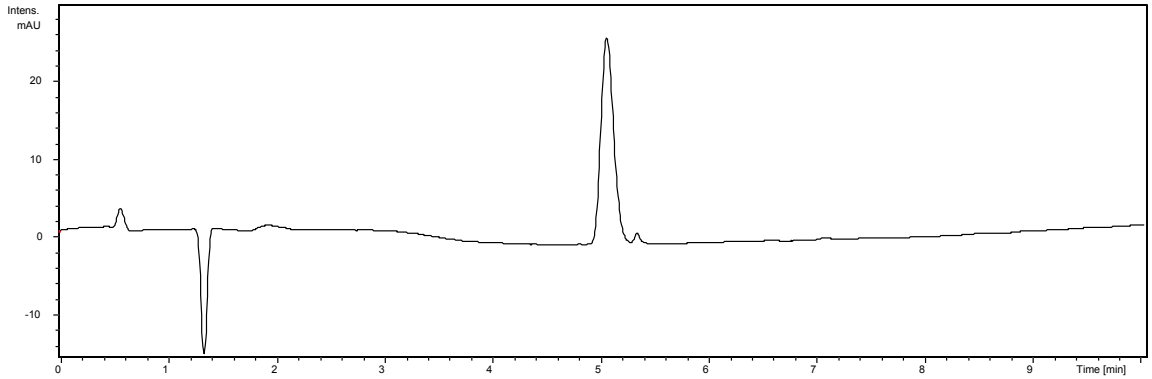


Fig. S13. HPLC chromatogram of (a) the ligand, *SSSS*-*SSSS*-M8SPy, (b) Dy- *SSSS*-*SSSS*-M8SPy, (c) Ho- *SSSS*-*SSSS*-M8SPy, (d) Yb- *SSSS*-*SSSS*-M8SPy, and (e) Pr-*SSSS*-*SSSS*-M8SPy observed at 254 nm, 298 K and pH 6.5.

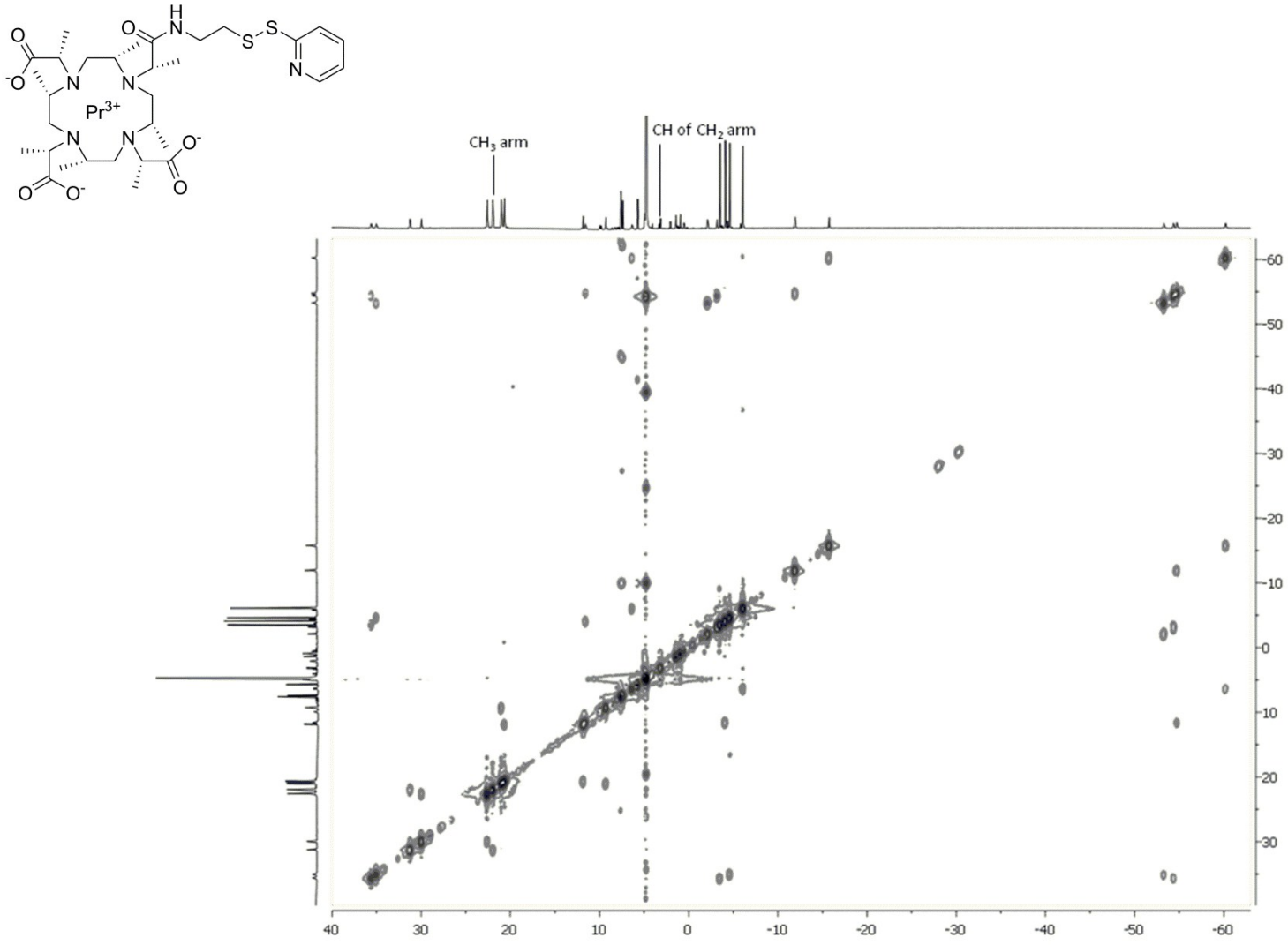


Fig. S14. 2D COSY spectrum of Pr- *SSSS*-*SSSS*-M8SPy at 298 K and 600 MHz.

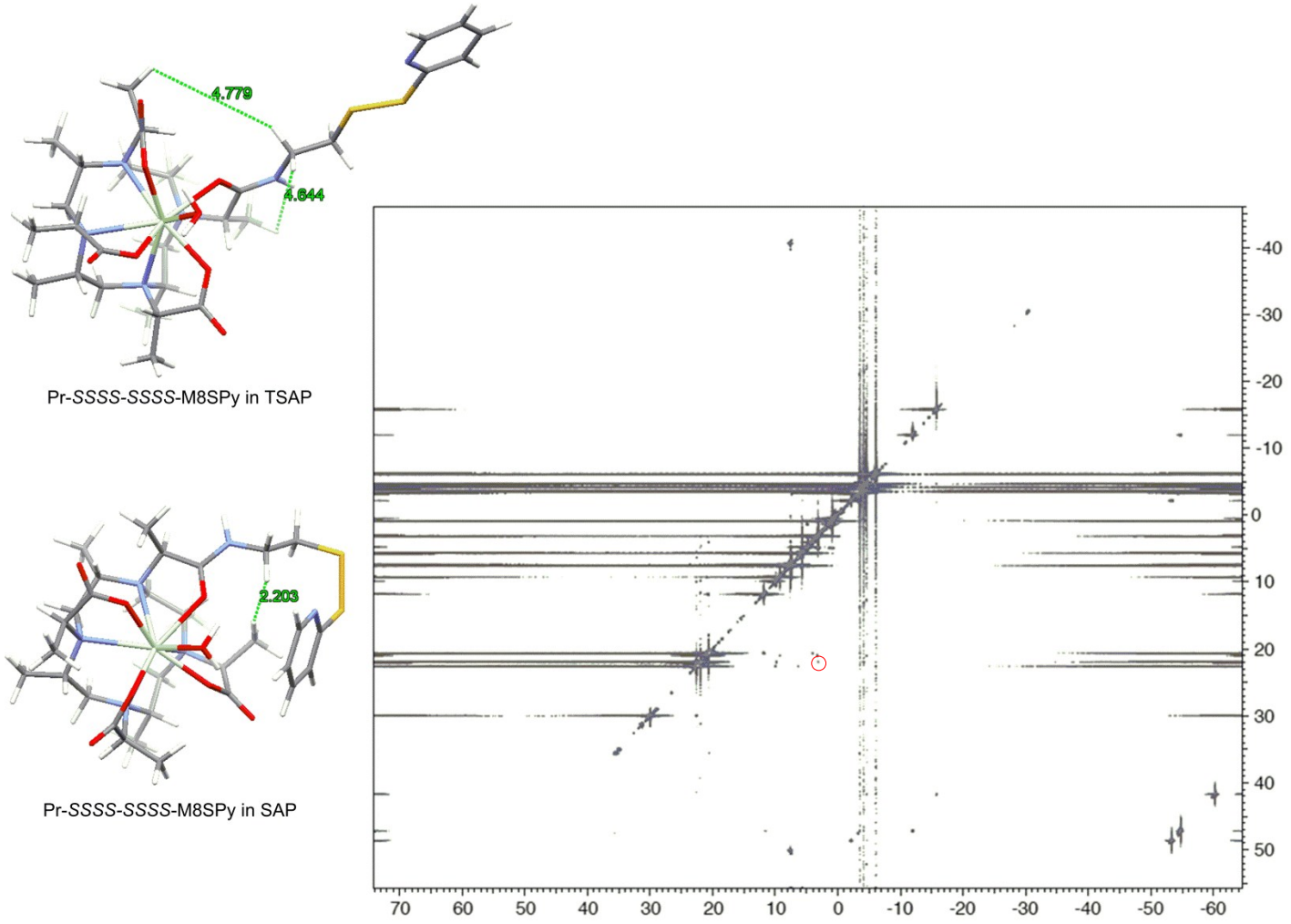


Fig. S15. 2D NOESY spectrum of Pr- *SSSS-SSSS*-M8SPy at 298 K and 600 MHz. The red circle shows the NOE observed between the CH_2 proton (3.15 ppm) of the pendant arm bearing the pyridine ring and the protons from one of the CH_3 arms (21.98 ppm), which can only be present in the SAP isomer. To the left are the geometry optimized structures of Pr-*SSSS-SSSS*-M8SPy in TSAP (top) and SAP (bottom).

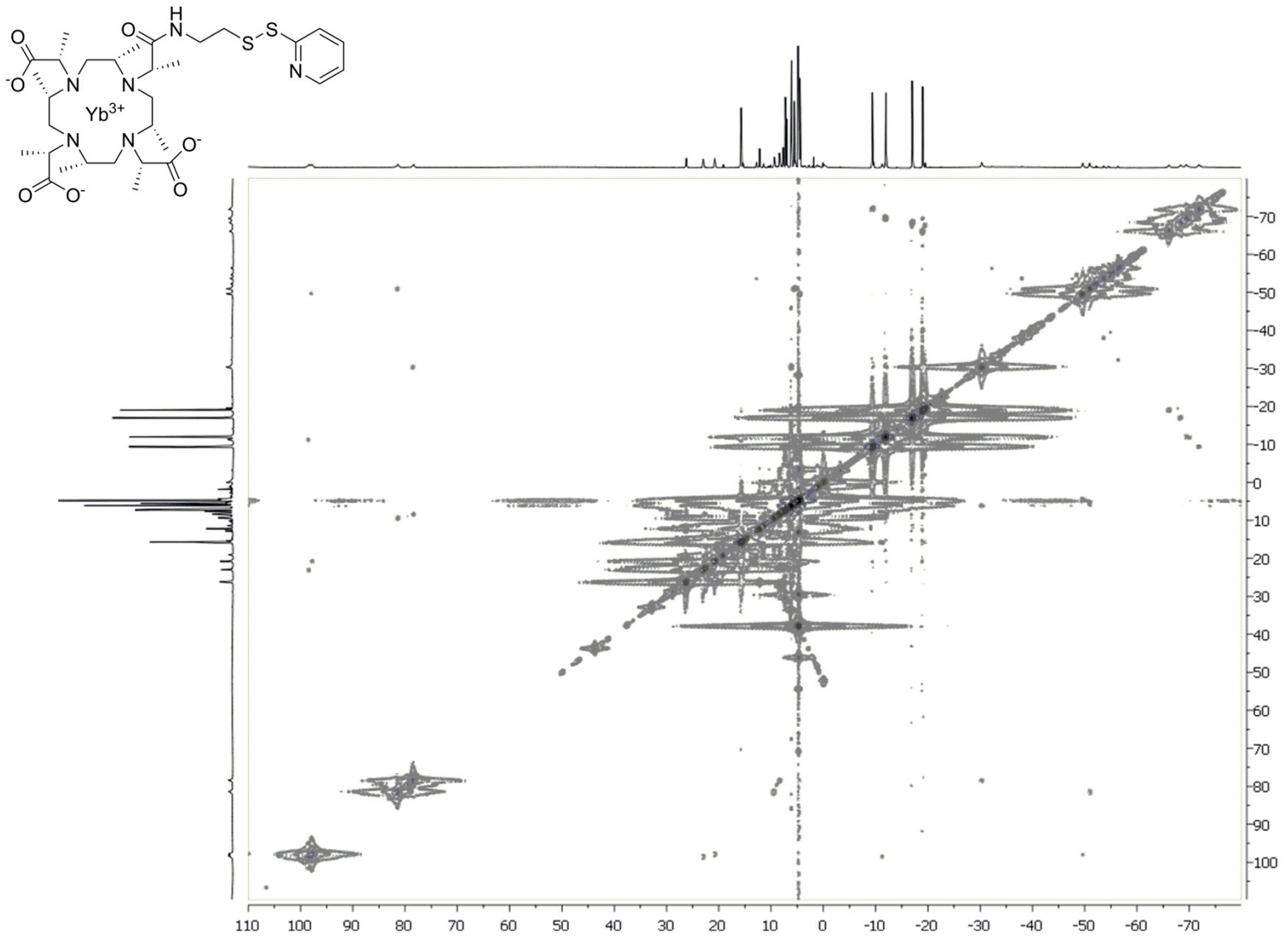


Fig. S16. 2D COSY spectrum of Yb-*SSSS*-*SSSS*-M8SPy at 298 K and 600 MHz.

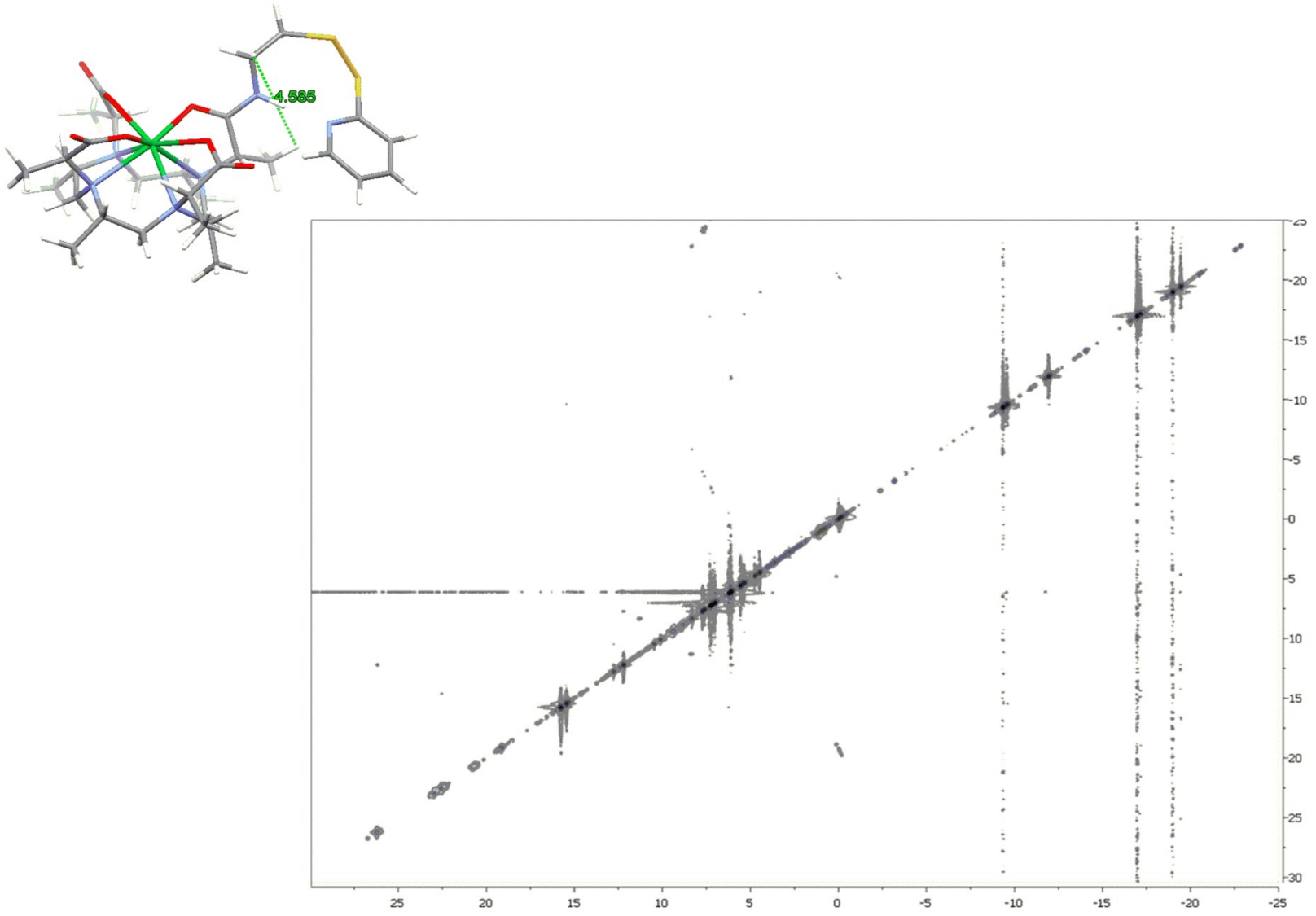


Fig. S17. 2D NOESY spectrum of Yb- *SSSS*-*SSSS*-M8SPy at 298 K and 600 MHz, and the geometry optimized structure of Yb-*SSSS*-*SSSS*-M8SPy in TSAP.

Table S1. Calculated distances for the isomers of Pr-DOTA, Pr- *SSSS*-*SSSS*-M4DOTMA and Yb- *SSSS*-*SSSS*-M4DOTMA

	Pr-DOTA		Pr- *SSSS*-*SSSS*-M4DOTMA		Yb- *SSSS*-*SSSS*-M4DOTMA	
	SAP	TSAP	SAP	TSAP	SAP	TSAP
Ln N	2.732 (2.720)[a]	2.735	2.782	2.756	2.647	2.605
Ln O	2.426 (2.453)	2.439	2.412	2.430	2.248	2.261
Ln Ow	2.650 (2.529)	2.677	2.646	2.696	-	-

[a]Values in parenthesis represent the distances from the X-ray structure of Na[PrDOTA(H_2O)] (*3*)

Table S2. Coordinates of the geometry optimized SAP Pr-DOTA

Atomic Number	Coordinates (Angstroms) X	Y	Z
59	-0.001366	0.001057	-0.608400
7	0.604969	-1.972904	1.182034
6	-0.637509	-2.506710	1.783529
1	-0.407912	-3.144255	2.655061
1	-1.113504	-3.155252	1.040599
6	-1.596495	-1.416825	2.216749
1	-2.464856	-1.883056	2.714544
1	-1.121993	-0.780706	2.971812
7	-2.056017	-0.547624	1.111879
6	-2.593957	0.715695	1.664476
1	-3.253750	0.515493	2.526395
1	-3.222340	1.176469	0.895670
6	1.486674	-1.443567	2.244808
1	1.949272	-2.278802	2.799921
1	0.860773	-0.908842	2.967832
6	1.296460	-3.026160	0.416394
1	0.527885	-3.629592	-0.084258
1	1.852051	-3.703826	1.085176
6	2.216028	-2.522578	-0.698176
8	1.918306	-1.379272	-1.205660
8	3.139548	-3.261954	-1.072128

6	-3.080813	-1.236153	0.306304
1	-3.638606	-0.467769	-0.244695
1	-3.804858	-1.762321	0.949739
6	-2.540074	-2.192758	-0.758470
8	-1.362894	-1.934829	-1.209433
8	-3.280555	-3.106046	-1.153006
7	-0.611582	2.111794	1.005408
6	0.624413	2.695147	1.572459
1	0.386675	3.397072	2.390742
1	1.103118	3.287192	0.785949
6	1.583852	1.646168	2.097089
1	2.451929	2.153409	2.553683
1	1.108638	1.078884	2.904841
7	2.043723	0.683246	1.073071
6	2.579728	-0.526854	1.734604
6	3.068394	1.299558	0.210979
1	3.625484	0.486912	-0.273361
1	3.792839	1.879607	0.805923
6	2.517744	2.161659	-0.927487
8	1.345091	1.855822	-1.354606
8	-1.901876	1.299479	-1.325785
6	-2.198662	2.486643	-0.934852
6	-1.295457	3.092003	0.142678
6	-1.504608	1.674961	2.099801
1	-1.972533	2.553979	2.577603
1	-0.885660	1.203860	2.871706
1	-0.522298	3.653743	-0.397360
1	-1.863833	3.821716	0.742559
8	-3.113806	3.191608	-1.389167
8	3.248431	3.051272	-1.391527
1	3.237397	-0.254094	2.577949
1	3.208796	-1.054026	1.009799
8	0.063662	-0.612697	-3.185824
1	0.937890	-1.041247	-3.180923

1	-0.559197	-1.356950	-3.086226

Table S3. Coordinates of the geometry optimized TSAP Pr-DOTA.

Atomic Number	Coordinates (Angstroms) X	Y	Z
59	-0.002888	-0.002324	-0.538987
7	-1.459019	-1.412652	1.297477
6	-2.536388	-0.566229	1.855312
1	-3.013470	-1.068355	2.714374
1	-3.309761	-0.468934	1.084990
6	-2.053316	0.805283	2.274552
1	-2.887747	1.362883	2.734340
1	-1.285545	0.713503	3.052046
7	-1.472437	1.565009	1.152514
6	-0.646697	2.685248	1.653215
1	-1.177154	3.225022	2.456422
1	-0.525487	3.397454	0.828901
6	-0.620515	-1.962666	2.380131
1	-1.145673	-2.782550	2.900062
1	-0.474837	-1.174163	3.128081
6	-2.066203	-2.489988	0.500762
1	-2.836294	-3.029481	1.077263
1	-1.289563	-3.222120	0.245014
6	-2.655007	-1.986105	-0.818432
8	-2.201462	-0.856677	-1.241250
8	-3.486974	-2.697505	-1.399380
6	-2.519081	2.104382	0.270447
1	-3.079692	2.917108	0.762050
1	-3.240788	1.308235	0.047129
6	-1.956862	2.589184	-1.068942
8	-0.815321	2.101482	-1.408856
8	-2.637259	3.380583	-1.738197

7	1.509132	1.578986	1.104130
6	2.606981	0.790794	1.704880
1	3.109003	1.372205	2.497202
1	3.356461	0.621150	0.923456
6	2.142313	-0.534793	2.267329
1	2.992465	-1.047004	2.750257
1	1.400214	-0.369095	3.057393
7	1.528420	-1.400524	1.242046
6	0.717965	-2.461344	1.879556
6	2.552880	-2.029561	0.394489
1	3.127238	-2.786054	0.955277
1	3.266746	-1.260835	0.072474
6	1.968157	-2.652149	-0.875319
8	0.808375	-2.218977	-1.233479
8	2.147617	0.725422	-1.373342
6	2.621122	1.891765	-1.105291
6	2.084403	2.555733	0.166644
6	0.711788	2.242587	2.152089
1	1.252580	3.113228	2.562097
1	0.597744	1.537955	2.984435
1	2.879166	3.152155	0.645357
1	1.299066	3.258068	-0.140655
8	3.438612	2.520120	-1.793964
8	2.647670	-3.491534	-1.482608
1	1.275274	-2.922056	2.713365
1	0.565805	-3.250613	1.134540
8	-0.222834	-0.529528	-3.154754
1	0.208899	-1.398888	-3.050146
1	-1.173553	-0.737372	-3.090537

Table S4. Coordinates of the geometry optimized SAP Pr- *SSSS*-*SSSS*-M4DOTMA.

Atomic Number	Coordinates (Angstroms) X	Y	Z

59	-0.023389	0.016976	-0.990870
7	2.001269	0.886924	0.729509
6	2.687102	-0.304145	1.317812
6	3.640720	0.035094	2.460340
1	3.276024	-0.737439	0.505054
6	1.695251	-1.363442	1.780181
1	2.272627	-2.141307	2.309311
1	1.022912	-0.935630	2.532258
7	0.878791	-1.984870	0.713233
6	-0.312550	-2.666753	1.309743
6	0.034827	-3.624625	2.446458
1	-0.754320	-3.253135	0.500291
6	1.362748	1.687500	1.798739
1	2.131944	2.258954	2.347041
1	0.925409	1.002987	2.534456
6	2.939341	1.777819	-0.026946
6	4.089414	1.063453	-0.730634
1	3.371751	2.508873	0.678577
6	2.204678	2.571744	-1.120844
8	1.240723	1.959171	-1.709157
8	2.620135	3.705351	-1.409067
6	1.756595	-2.922845	-0.062847
6	1.031758	-4.075424	-0.751736
1	2.498705	-3.354372	0.631087
6	2.536730	-2.192405	-1.171776
8	1.917807	-1.238501	-1.768508
8	3.671521	-2.605959	-1.460556
7	-2.013694	-0.857772	0.736163
6	-2.695045	0.324430	1.347423
6	-3.637557	-0.031301	2.493997
1	-3.292264	0.768157	0.546361
6	-1.698841	1.378150	1.813367
1	-2.272226	2.152278	2.352221
1	-1.022623	0.943314	2.558231

7	-0.888066	2.006691	0.745955
6	0.305467	2.685185	1.340705
6	-1.771010	2.948060	-0.020899
6	-1.054375	4.113820	-0.695488
1	-2.517321	3.366240	0.676649
6	-2.542841	2.220751	-1.138084
8	-1.915443	1.279870	-1.744824
8	-1.254449	-1.893421	-1.715599
6	-2.221253	-2.511659	-1.139526
6	-2.954583	-1.738811	-0.028652
6	-1.364963	-1.672997	1.788392
1	-2.129804	-2.251171	2.335642
1	-0.921369	-0.998382	2.529393
6	-4.112359	-1.016549	-0.710555
1	-3.379001	-2.483339	0.667620
8	-2.639730	-3.639436	-1.447746
8	-3.682760	2.625720	-1.421659
6	-0.034686	3.630145	2.490295
1	0.739671	3.281499	0.534465
1	-4.659706	-1.746914	-1.315902
1	-4.824008	-0.588883	0.003832
1	-3.752852	-0.220514	-1.372073
1	1.762300	-4.622780	-1.356997
1	0.600794	-4.788824	-0.041084
1	0.238590	-3.710761	-1.413554
1	4.634426	1.801923	-1.328258
1	4.805593	0.621592	-0.029561
1	3.721025	0.279611	-1.401844
1	-1.789442	4.663777	-1.292927
1	-0.626953	4.821050	0.023448
1	-0.259943	3.763122	-1.363213
1	4.285327	-0.821752	2.684176
1	4.288490	0.881937	2.204908
1	3.102296	0.293092	3.380703

1	-0.884864	4.275848	2.240671
1	-0.288180	3.085487	3.408225
1	0.820254	4.276735	2.715674
1	-4.280034	0.822080	2.736384
1	-4.287722	-0.874330	2.232001
1	-3.090655	-0.302775	3.405426
1	-0.820068	-4.270911	2.672767
1	0.880619	-4.270386	2.182613
1	0.298281	-3.090239	3.367610
8	0.398704	0.127188	-3.600683
1	0.798006	1.016030	-3.578673
1	1.169538	-0.469773	-3.569866

Table S5. Coordinates of the geometry optimized TSAP Pr-*SSSS*-*SSSS*-M4DOTMA.

Atomic Number	Coordinates (Angstroms) X	Y	Z
70	-0.000002	-0.000037	0.786645
7	-0.843262	-1.974397	-0.775634
6	0.335616	-2.668204	-1.374759
6	-0.012798	-3.624424	-2.511081
1	0.781854	-3.253299	-0.565674
6	1.375245	-1.663278	-1.844941
1	2.169351	-2.222936	-2.367866
1	0.931268	-0.999736	-2.596481
7	1.962340	-0.833587	-0.769265
6	2.672945	0.340974	-1.359707
6	3.641665	-0.015984	-2.482474
1	3.249379	0.782093	-0.541445
6	-1.684765	-1.389944	-1.842137
1	-2.259744	-2.182637	-2.350653
1	-1.032243	-0.957432	-2.609463
6	-1.706067	-2.881709	0.055785

6	-1.007772	-4.087309	0.678295
1	-2.513112	-3.267723	-0.590637
6	-2.381951	-2.115602	1.207789
8	-1.778358	-1.071825	1.641784
8	-3.441297	-2.573413	1.667932
6	2.864464	-1.709459	0.055950
6	4.061069	-1.016812	0.701994
1	3.258301	-2.503988	-0.601069
6	2.089692	-2.401674	1.191555
8	1.049671	-1.799262	1.636773
8	2.538880	-3.473001	1.632636
7	0.843245	1.974378	-0.775607
6	-0.335631	2.668194	-1.374725
6	0.012787	3.624444	-2.511020
1	-0.781891	3.253261	-0.565632
6	-1.375233	1.663259	-1.844942
1	-2.169330	2.222913	-2.367884
1	-0.931231	0.999720	-2.596471
7	-1.962350	0.833575	-0.769275
6	-2.672976	-0.340985	-1.359702
6	-2.864450	1.709491	0.055916
6	-4.061152	1.016936	0.701881
1	-3.258190	2.504061	-0.601112
6	-2.089679	2.401630	1.191572
8	-1.049687	1.799174	1.636799
8	1.778383	1.071739	1.641752
6	2.381963	2.115540	1.207790
6	1.706105	2.881665	0.055782
6	1.684711	1.389913	-1.842128
1	2.259670	2.182603	-2.350671
1	1.032166	0.957387	-2.609427
6	1.007906	4.087330	0.678277
1	2.513163	3.267614	-0.590662
8	3.441347	2.573296	1.667899

8	-2.538807	3.472983	1.632649
6	-3.641727	0.015974	-2.482442
1	-3.249396	-0.782095	-0.541428
1	1.744956	4.618993	1.288717
1	0.636559	4.793234	-0.072032
1	0.178037	3.786794	1.325961
1	4.585976	-1.760023	1.310860
1	4.776523	-0.634751	-0.033653
1	3.749612	-0.195510	1.355475
1	-1.744773	-4.619012	1.288761
1	-0.636386	-4.793203	-0.072003
1	-0.177912	-3.786697	1.325956
1	-4.586022	1.760181	1.310739
1	-4.776605	0.634963	-0.033812
1	-3.749805	0.195589	1.355356
1	0.841504	-4.271884	-2.736468
1	-0.860342	-4.268264	-2.248654
1	-0.274083	-3.089468	-3.432421
1	-4.271427	0.872069	-2.213638
1	-3.117215	0.267458	-3.412445
1	-4.302692	-0.831212	-2.694922
1	-0.841521	4.271893	-2.736412
1	0.860314	4.268294	-2.248561
1	0.274102	3.089511	-3.432365
1	4.302621	0.831203	-2.694977
1	4.271375	-0.872076	-2.213686
1	3.117126	-0.267474	-3.412460

Table S6. Coordinates of the geometry optimized SAP Yb-*SSSS*-*SSSS*-M4DOTMA.

Atomic Number	Coordinates (Angstroms) X	Y	Z
70	-0.000002	-0.000037	0.786645

7	-0.843262	-1.974397	-0.775634
6	0.335616	-2.668204	-1.374759
6	-0.012798	-3.624424	-2.511081
1	0.781854	-3.253299	-0.565674
6	1.375245	-1.663278	-1.844941
1	2.169351	-2.222936	-2.367866
1	0.931268	-0.999736	-2.596481
7	1.962340	-0.833587	-0.769265
6	2.672945	0.340974	-1.359707
6	3.641665	-0.015984	-2.482474
1	3.249379	0.782093	-0.541445
6	-1.684765	-1.389944	-1.842137
1	-2.259744	-2.182637	-2.350653
1	-1.032243	-0.957432	-2.609463
6	-1.706067	-2.881709	0.055785
6	-1.007772	-4.087309	0.678295
1	-2.513112	-3.267723	-0.590637
6	-2.381951	-2.115602	1.207789
8	-1.778358	-1.071825	1.641784
8	-3.441297	-2.573413	1.667932
6	2.864464	-1.709459	0.055950
6	4.061069	-1.016812	0.701994
1	3.258301	-2.503988	-0.601069
6	2.089692	-2.401674	1.191555
8	1.049671	-1.799262	1.636773
8	2.538880	-3.473001	1.632636
7	0.843245	1.974378	-0.775607
6	-0.335631	2.668194	-1.374725
6	0.012787	3.624444	-2.511020
1	-0.781891	3.253261	-0.565632
6	-1.375233	1.663259	-1.844942
1	-2.169330	2.222913	-2.367884
1	-0.931231	0.999720	-2.596471
7	-1.962350	0.833575	-0.769275

6	-2.672976	-0.340985	-1.359702
6	-2.864450	1.709491	0.055916
6	-4.061152	1.016936	0.701881
1	-3.258190	2.504061	-0.601112
6	-2.089679	2.401630	1.191572
8	-1.049687	1.799174	1.636799
8	1.778383	1.071739	1.641752
6	2.381963	2.115540	1.207790
6	1.706105	2.881665	0.055782
6	1.684711	1.389913	-1.842128
1	2.259670	2.182603	-2.350671
1	1.032166	0.957387	-2.609427
6	1.007906	4.087330	0.678277
1	2.513163	3.267614	-0.590662
8	3.441347	2.573296	1.667899
8	-2.538807	3.472983	1.632649
6	-3.641727	0.015974	-2.482442
1	-3.249396	-0.782095	-0.541428
1	1.744956	4.618993	1.288717
1	0.636559	4.793234	-0.072032
1	0.178037	3.786794	1.325961
1	4.585976	-1.760023	1.310860
1	4.776523	-0.634751	-0.033653
1	3.749612	-0.195510	1.355475
1	-1.744773	-4.619012	1.288761
1	-0.636386	-4.793203	-0.072003
1	-0.177912	-3.786697	1.325956
1	-4.586022	1.760181	1.310739
1	-4.776605	0.634963	-0.033812
1	-3.749805	0.195589	1.355356
1	0.841504	-4.271884	-2.736468
1	-0.860342	-4.268264	-2.248654
1	-0.274083	-3.089468	-3.432421
1	-4.271427	0.872069	-2.213638

1	-3.117215	0.267458	-3.412445
1	-4.302692	-0.831212	-2.694922
1	-0.841521	4.271893	-2.736412
1	0.860314	4.268294	-2.248561
1	0.274102	3.089511	-3.432365
1	4.302621	0.831203	-2.694977
1	4.271375	-0.872076	-2.213686
1	3.117126	-0.267474	-3.412460

Table S7. Coordinates of the geometry optimized TSAP Yb-*SSSS*-*SSSS*-M4DOTMA.

Atomic Number	Coordinates (Angstroms) X	Y	Z
70	-0.000002	0.000001	0.765088
7	-0.204949	2.113263	-0.749431
6	-1.577029	2.198483	-1.349749
6	-1.722042	3.131534	-2.553628
1	-2.223815	2.567702	-0.541402
6	-2.064592	0.825109	-1.795190
1	-3.046797	0.951475	-2.279437
1	-1.393961	0.462285	-2.586953
7	-2.106594	-0.202865	-0.747282
6	-2.195806	-1.576442	-1.345411
6	-3.133033	-1.720431	-2.546114
1	-2.563898	-2.220861	-0.534826
6	0.825019	2.068280	-1.794583
1	0.956413	3.049906	-2.279012
1	0.462886	1.398537	-2.587398
6	0.033773	3.203624	0.244897
6	-0.091618	4.637555	-0.245607
1	1.066400	3.052572	0.587413
6	-0.822459	2.945740	1.499558
8	-1.112227	1.714558	1.731136

8	-1.151289	3.903289	2.214932
6	-3.194235	0.038143	0.250184
6	-4.629592	-0.081966	-0.237646
1	-3.039561	1.070069	0.593084
6	-2.937053	-0.819321	1.503772
8	-1.708252	-1.124931	1.730875
8	-3.894043	-1.133637	2.226440
7	0.204947	-2.113263	-0.749433
6	1.577029	-2.198484	-1.349749
6	1.722042	-3.131536	-2.553627
1	2.223813	-2.567703	-0.541401
6	2.064594	-0.825110	-1.795190
1	3.046799	-0.951479	-2.279436
1	1.393965	-0.462286	-2.586954
7	2.106595	0.202864	-0.747282
6	2.195807	1.576441	-1.345410
6	3.194237	-0.038144	0.250184
6	4.629593	0.081975	-0.237646
1	3.039569	-1.070073	0.593077
6	2.937052	0.819307	1.503781
8	1.708251	1.124924	1.730879
8	1.112215	-1.714555	1.731136
6	0.822451	-2.945738	1.499558
6	-0.033776	-3.203625	0.244895
6	-0.825019	-2.068281	-1.794585
1	-0.956414	-3.049907	-2.279014
1	-0.462886	-1.398539	-2.587400
6	0.091618	-4.637557	-0.245606
1	-1.066404	-3.052574	0.587408
8	1.151296	-3.903286	2.214927
8	3.894047	1.133645	2.226433
6	3.133033	1.720431	-2.546114
1	2.563899	2.220860	-0.534826
1	-0.307778	-5.308021	0.520228

1	-0.478405	-4.809703	-1.166116
1	1.133754	-4.928498	-0.416095
1	-5.296456	0.319170	0.530394
1	-4.802473	0.489264	-1.157189
1	-4.924371	-1.123044	-0.407984
1	0.307777	5.308021	0.520227
1	0.478407	4.809699	-1.166115
1	-1.133753	4.928497	-0.416099
1	5.296461	-0.319164	0.530389
1	4.802475	-0.489248	-1.157194
1	4.924367	1.123056	-0.407977
1	-2.785295	3.275812	-2.774362
1	-1.281130	4.116310	-2.392987
1	-1.259541	2.701365	-3.450762
1	4.115719	1.275509	-2.383792
1	2.703686	1.261959	-3.445681
1	3.281807	2.783740	-2.763459
1	2.785295	-3.275815	-2.774360
1	1.281130	-4.116311	-2.392985
1	1.259543	-2.701368	-3.450762
1	-3.281809	-2.783739	-2.763458
1	-4.115719	-1.275507	-2.383791
1	-2.703687	-1.261960	-3.445682

Table S8. Coordinates of the geometry optimized SAP Pr-*SSSS*-*SSSS*-M8Spy

Atomic Number	Coordinates (Angstroms) X	Y	Z
59	0.931593	-0.192871	-0.677406
7	-0.041206	-0.355896	2.050806
6	-0.370733	0.988486	2.592718
6	-0.619786	1.012433	4.101477
1	-1.299428	1.289562	2.098098

6	0.687331	2.029678	2.253439
1	0.411839	2.958686	2.788352
1	1.646965	1.723184	2.684873
7	0.895917	2.313309	0.822254
6	2.232170	2.954766	0.617641
6	2.485460	4.147808	1.537158
1	2.240949	3.326504	-0.407073
6	1.061552	-0.960192	2.824989
1	0.691258	-1.286725	3.814439
1	1.812115	-0.186112	3.031413
6	-1.209081	-1.296047	2.089958
6	-2.583793	-0.648918	1.986923
1	-1.176335	-1.851265	3.044336
6	-1.169960	-2.347926	0.955620
8	-0.583176	-1.973957	-0.129200
8	-1.752913	-3.414096	1.144755
6	-0.228179	3.150388	0.323616
6	0.079428	4.033545	-0.888325
1	-0.564107	3.813487	1.148448
6	-1.406974	2.265931	-0.070486
8	-1.254998	1.129830	-0.542865
7	-2.634176	2.812168	0.077080
7	3.433325	0.880008	-0.253823
6	4.350261	-0.211760	0.192623
6	5.733092	0.275795	0.615423
1	4.482803	-0.859887	-0.676440
6	3.736602	-1.052090	1.310181
1	4.514028	-1.761511	1.647188
1	3.532371	-0.411774	2.178197
7	2.503328	-1.786224	0.958654
6	1.741359	-2.163964	2.181741
6	2.890516	-2.978074	0.123979
6	1.883885	-4.120000	0.106171
1	3.852443	-3.366135	0.501881

6	3.113013	-2.550920	-1.340483
8	2.224515	-1.713430	-1.783179
8	1.519363	1.497968	-2.134131
6	2.627346	2.162669	-2.238230
6	3.843180	1.491809	-1.567073
6	3.375453	1.951557	0.756489
1	4.310784	2.540764	0.734622
1	3.341970	1.492738	1.754003
6	4.450006	0.525280	-2.574111
1	4.577839	2.290710	-1.360137
8	2.769908	3.241622	-2.805335
8	4.048989	-3.022513	-1.972115
6	2.578428	-2.901026	3.223884
1	0.954654	-2.844105	1.842475
1	4.596869	1.074689	-3.510289
1	5.429992	0.145083	-2.263722
1	3.793391	-0.327908	-2.776681
1	-0.847005	4.519398	-1.215711
1	0.788214	4.829829	-0.642527
1	0.479033	3.453880	-1.727561
1	-3.325360	-1.452043	2.018192
1	-2.819303	0.036344	2.809361
1	-2.708663	-0.121114	1.032754
1	2.244918	-4.863733	-0.612491
1	1.787368	-4.625557	1.074186
1	0.892124	-3.786474	-0.217621
1	-1.097616	1.951857	4.402082
1	-1.273704	0.190634	4.414351
1	0.314416	0.924363	4.670173
1	3.157768	-3.710729	2.765402
1	3.285445	-2.233103	3.732878
1	1.935000	-3.346694	3.990466
1	6.423005	-0.569793	0.708138
1	6.154013	0.964814	-0.126379

1	5.715134	0.794886	1.582747
1	3.355543	4.714907	1.189958
1	1.630308	4.835207	1.549651
1	2.681772	3.844751	2.573530
8	-0.724277	-0.821374	-2.569321
1	-1.041204	-1.591400	-2.055189
1	-1.446092	-0.178951	-2.481594
6	-3.848871	2.164633	-0.397276
6	-4.978631	2.288572	0.608114
1	-3.594706	1.113646	-0.561415
1	-4.152737	2.570074	-1.372344
1	-2.692710	3.769797	0.399621
16	-6.454003	1.334675	0.107693
1	-5.326563	3.327440	0.699208
1	-4.657320	1.955562	1.602944
16	-5.905337	-0.568309	0.623315
6	-3.521101	-2.293941	-2.802675
6	-4.272493	-1.130146	-2.931667
7	-4.980016	-0.584116	-1.934336
6	-4.960300	-1.217341	-0.767854
6	-4.231074	-2.383518	-0.515276
6	-3.486528	-2.920210	-1.557220
1	-2.951598	-2.675938	-3.646417
1	-4.310846	-0.594456	-3.881704
1	-4.206458	-2.846561	0.468643
1	-2.866110	-3.794067	-1.368630

Table S9. Coordinates of the geometry optimized TSAP Pr-*SSSS*-*SSSS*-M8Spy

Atomic	Coordinates (Angstroms)		
Number	X	Y	Z

7	2.411555	-0.725525	1.332115
6	3.139874	-1.149672	0.141443
6	4.602357	-1.356651	0.485579
1	3.013335	-0.397131	-0.649120
1	2.667031	-2.070650	-0.212480
1	2.766002	0.114139	1.777454
16	5.489780	-1.898903	-1.019322
1	4.718975	-2.108334	1.275057
1	5.065756	-0.416016	0.806365
16	7.430825	-1.887714	-0.375698
6	8.661784	2.452911	-0.477176
6	7.332341	2.047848	-0.472167
7	6.945724	0.767160	-0.445883
6	7.900842	-0.157084	-0.445063
6	9.269764	0.133376	-0.449942
6	9.647932	1.468244	-0.461770
1	8.916657	3.509445	-0.495314
1	6.524930	2.780975	-0.484371
1	10.008026	-0.665973	-0.460986
1	10.702806	1.736959	-0.474390
59	-1.132401	-0.083053	-0.545604
7	-3.683729	0.694434	-1.020717
6	-3.840064	2.153469	-0.733153
6	-5.280840	2.668578	-0.742106
1	-3.278447	2.667173	-1.525779
6	-3.243641	2.535222	0.621158
1	-3.486256	3.597842	0.796330
1	-3.790394	1.986817	1.403491
7	-1.817844	2.267973	0.821936
6	-1.466142	2.305021	2.272562
6	-2.158977	3.390223	3.100208
1	-0.390259	2.517230	2.309212
6	-4.625898	-0.115891	-0.243749

1	-5.653900	-0.027044	-0.635442
1	-4.670742	0.303972	0.772120
6	-3.720073	0.380984	-2.489088
6	-5.030524	0.584571	-3.231055
1	-3.449350	-0.684329	-2.548766
6	-2.560776	1.127076	-3.187460
8	-1.449626	1.121035	-2.504859
8	-2.732074	1.634680	-4.284446
6	-0.905440	3.149485	0.014550
6	-0.996714	4.641749	0.270065
1	-1.159343	2.942415	-1.036066
6	0.530879	2.613498	0.249428
8	0.659495	1.348083	0.006543
8	1.406077	3.355435	0.686460
7	-1.082327	-0.202237	2.340249
6	-1.754215	-1.476257	2.744770
6	-2.104767	-1.597424	4.232346
1	-1.051339	-2.274086	2.474947
6	-3.067413	-1.684946	1.982377
1	-3.576280	-2.548360	2.444835
1	-3.723131	-0.827331	2.190629
7	-2.978607	-1.836694	0.529247
6	-4.304538	-1.606500	-0.127090
6	-2.360287	-3.144296	0.132276
6	-3.086335	-4.419611	0.529025
1	-1.375459	-3.139884	0.620802
6	-2.060686	-3.132636	-1.384806
8	-1.583705	-2.002611	-1.818533
8	0.458397	-1.672378	0.662745
6	1.084040	-0.918723	1.433000
6	0.383684	-0.173104	2.566058
6	-1.738550	0.962882	2.944646
1	-1.486625	1.060222	4.017568
1	-2.822415	0.782440	2.917373

6	0.904814	-0.634966	3.928218
1	0.676646	0.877026	2.439008
8	-2.257951	-4.138716	-2.049391
6	-5.503906	-2.266250	0.558072
1	-4.203405	-2.033153	-1.135092
1	1.984408	-0.462069	3.991017
1	0.439028	-0.073684	4.745968
1	0.738429	-1.704532	4.097485
1	-0.418343	5.167492	-0.495709
1	-2.026089	5.019887	0.224728
1	-0.548529	4.911130	1.231175
1	-4.965524	0.071766	-4.194667
1	-5.895832	0.176061	-2.694005
1	-5.208128	1.638974	-3.460677
1	-2.411087	-5.264962	0.371234
1	-3.396129	-4.429084	1.581935
1	-3.956003	-4.606252	-0.107581
1	-5.285110	3.763469	-0.703654
1	-5.832442	2.368040	-1.634067
1	-5.838884	2.311452	0.133614
1	-5.332209	-3.316465	0.799047
1	-5.769706	-1.747871	1.488842
1	-6.378872	-2.216616	-0.099334
1	-2.406114	-2.626743	4.456283
1	-1.278721	-1.346447	4.899151
1	-2.950990	-0.950500	4.497294
1	-1.684712	3.464325	4.085280
1	-2.094826	4.374249	2.629881
1	-3.220318	3.166237	3.267066
8	0.720542	-0.645856	-2.332949
1	0.199979	-1.407850	-2.653861
1	0.452087	0.081710	-2.923021

Table S10. Coordinates of the geometry optimized TSAP Yb-*SSSS*-*SSSS*-M8Spy

Atomic Number	Coordinates (Angstroms) X	Y	Z
70	-0.604999	1.229829	-0.842054
7	-1.023774	1.896681	1.628223
6	0.293584	2.172417	2.291047
6	0.276843	2.198652	3.820966
1	0.594622	3.163645	1.923603
6	1.343406	1.145823	1.878312
1	2.271032	1.362954	2.435265
1	1.016067	0.156825	2.235519
7	1.590667	1.042507	0.438320
6	2.303409	-0.229036	0.095619
6	3.450184	-0.614451	1.031308
1	2.710043	-0.072091	-0.912994
6	-1.760042	0.843621	2.329418
1	-2.170939	1.207243	3.287556
1	-1.042569	0.055136	2.602924
6	-1.838486	3.148053	1.469107
6	-2.175262	3.926437	2.728949
1	-2.777777	2.812721	1.012396
6	-1.179120	4.051760	0.400191
8	-0.565553	3.413872	-0.538231
8	-1.294072	5.269718	0.504109
6	2.293663	2.250335	-0.126623
6	3.692935	2.544591	0.380278
1	1.640402	3.098397	0.119961
6	2.246334	2.135745	-1.667534
8	1.131889	1.659168	-2.119619

8	3.220745	2.469843	-2.332691
7	0.198566	-1.276822	-0.849584
6	-0.864954	-2.275436	-0.520301
6	-0.375978	-3.659633	-0.090139
1	-1.442573	-2.407364	-1.445486
6	-1.785223	-1.746773	0.571722
1	-2.546851	-2.517555	0.791322
1	-1.197325	-1.643767	1.495495
7	-2.398081	-0.443435	0.292246
6	-2.902950	0.194322	1.550881
6	-3.429242	-0.541809	-0.778705
6	-4.785583	-1.123708	-0.386307
1	-2.999526	-1.195319	-1.548533
6	-3.561746	0.822418	-1.456425
8	-2.900477	1.802561	-1.049204
8	-1.293268	0.096885	-2.658580
6	-0.706841	-0.966429	-3.089892
6	0.569943	-1.351347	-2.307566
6	1.337262	-1.407143	0.063492
1	1.922400	-2.320741	-0.139322
1	0.928155	-1.543279	1.077263
6	1.170306	-2.657665	-2.788510
1	1.286585	-0.535278	-2.468747
8	-1.109175	-1.694810	-4.001593
6	-3.620101	-0.737624	2.532662
1	-3.601866	0.973595	1.220961
1	1.541511	-2.519365	-3.808381
1	2.016249	-2.984188	-2.169457
1	0.425239	-3.458430	-2.837054
1	3.973809	3.547982	0.048008
1	3.763440	2.523983	1.475982
1	4.436364	1.863391	-0.045256
1	-2.909267	4.694211	2.470357
1	-2.607876	3.295422	3.516876

1	-1.306452	4.458500	3.129764
1	-5.408272	-1.252220	-1.277622
1	-4.675236	-2.113818	0.071759
1	-5.337935	-0.475409	0.303302
1	1.221750	2.612523	4.190422
1	-0.530645	2.804696	4.233932
1	0.183259	1.186966	4.238149
1	-4.370005	-1.376270	2.064184
1	-2.909478	-1.391116	3.055113
1	-4.128138	-0.140648	3.298359
1	-1.217385	-4.362129	-0.083779
1	0.384611	-4.062683	-0.762435
1	0.044628	-3.648400	0.923668
1	4.032275	-1.429290	0.586420
1	4.135652	0.211721	1.225959
1	3.075564	-0.974297	1.999053
7	-4.415436	0.892444	-2.474779
6	-4.542433	2.072074	-3.306064
6	-5.992577	2.328735	-3.665833
1	-3.928014	1.947575	-4.208970
1	-4.138885	2.922781	-2.746372
1	-4.677439	0.011282	-2.944292
16	-6.778835	1.133596	-4.815891
1	-6.073467	3.275897	-4.214034
1	-6.618360	2.413774	-2.770298
16	-7.547224	-0.384250	-3.653471
6	-4.658316	-3.843346	-4.018783
6	-4.234000	-2.517343	-4.030750
7	-5.091295	-1.491029	-3.914965
6	-6.394086	-1.749188	-3.822453
6	-6.917851	-3.045799	-3.810709
6	-6.022180	-4.106107	-3.896156
1	-3.933175	-4.648045	-4.113666
1	-3.177798	-2.242908	-4.124186

1	-7.992020	-3.210073	-3.754678
1	-6.391964	-5.130442	-3.892446

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