ELECTRONIC SUPPLEMENTARY INFORMATION (ESI)

Structurally diverse zinc(II) complexes containing tripodal tetradentate phenoxido-amines with promising antiproliferative effects†

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The authors would like to dedicate this work to Jan Belza, our beloved colleague and friend, who passed away unexpectedly at the age of 31 years.

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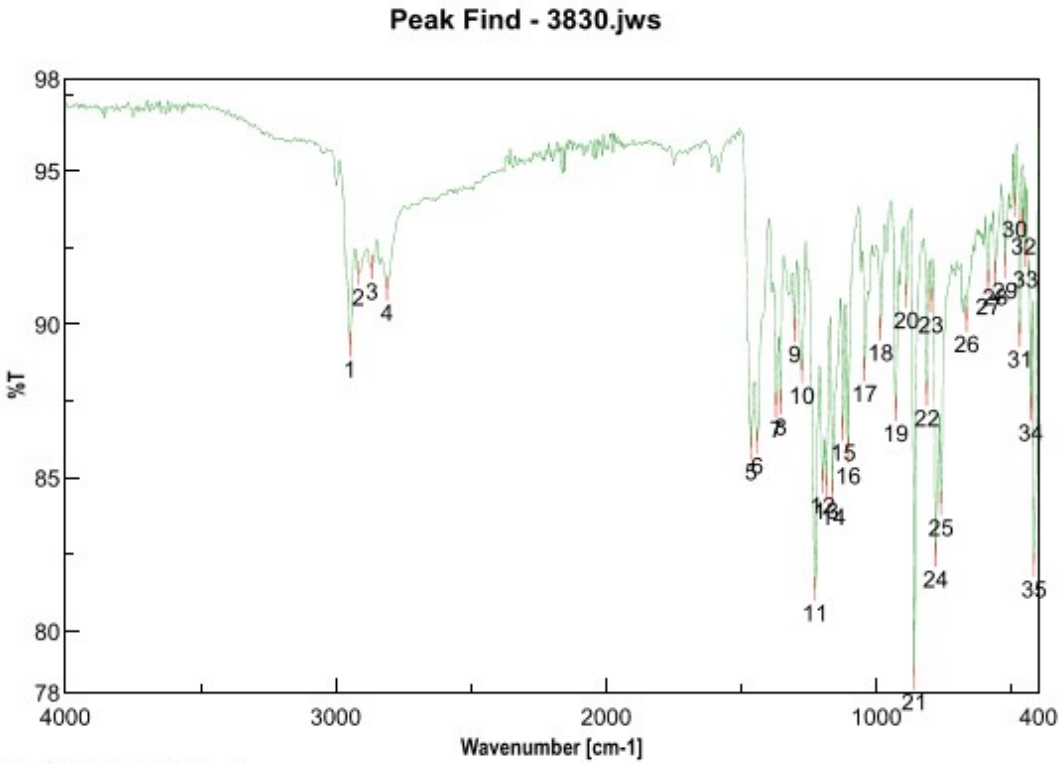
Synthesis of 6,6'-(((2-(Dimethylamino)ethyl)azanediyl)bis(methylene))bis(2-(*tert*-butyl)-4-methylphenol), $\mathbf{H_2L^3}$. A mixture of 2-*tert*-butyl-4-methylphenol (8.213 g, 50 mmol), Et_3N (5.052 g, 50 mmol), 37% HCHO (4.173 g, 50 mmol) and *N*,*N*-dimethylethylenediamine (2.204 g, 25 mmol) was dissolved in methanol (60 mL). The reaction mixture was stirred under gentle reflux for 3 days, then the solution was reduced to half of its volume by a rotary evaporator. The white precipitate, which was obtained was collected by filtration, recrystallized from EtOAc, washed with Et_2O, and air dried (yield: 4.85 g, 47.7 %). Characterization: Anal. Calcd for $C_{28}H_{44}N_2O_2$ (MM = 441.3489 g/mol): C, 76.32; H,10.06; N, 6.36%. Found: C, 76.50; H, 10.24; N, 6.35%. m.p. 167-170° C. ESI-MS (MeOH): *m/z* = 469.3804 (100%), Calcd [$\mathbf{H_2L^3}$+H]$^+$ = 441.34812. IR bands (ATR, cm^{-1}): ~3200 (sh) ν(O-H); 2947 (m), 2917 (vw), 2867 (vw), 2810 (w)

ν(C-H); 1570 (vw) ν(C=N); 1465 (s), 1442 (s), 1371 (s), 1354 (s) ν(C=C, C-N, C-O); 1226 (vs), 1200(s), 1186 (s), 1123 (m), 1105 (m), 1043 (m), 984 (m), 762 (s), 470 (m), 429 (m), 418 (vs). ^{1}H NMR (d_6-DMSO, 400 MHz, δ in ppm): δ = 6.89, 6.76 (s, 1H each, protons-ph); 3.51, 3,17 (s, 2H, N-$\underline{CH_2}$-ph); 2.20, 2.17 (s, 3H, CH_3-N; 8H, N-CH_2-CH_2-N); CH_3-ph); 1.32 (s, 9H, ($\underline{CH_3}$)$_3$C).



[Result of Peak Picking]

No.	Position	Intensity	No.	Position	Intensity
1	2946.7	89	2	2916.81	92
3	2866.67	92	4	2809.78	91
5	1464.67	86	6	1441.53	86
7	1371.14	87	8	1354.75	87
9	1302.68	90	10	1274.72	88
11	1226.5	81	12	1199.51	85
13	1186.01	85	14	1160.94	85
15	1123.33	87	16	1105.01	86
17	1043.3	89	18	984.482	90
19	928.557	87	20	889.987	91
21	860.096	78	22	813.813	88
23	798.385	91	24	781.029	82
25	761.744	84	26	666.285	90
27	586.254	91	28	561.184	92
29	524.543	92	30	488.866	94
31	469.582	90	32	456.082	93
33	448.369	92	34	429.084	87
35	417.513	82			

Fig. S1. IR spectrum of H_2L^3.

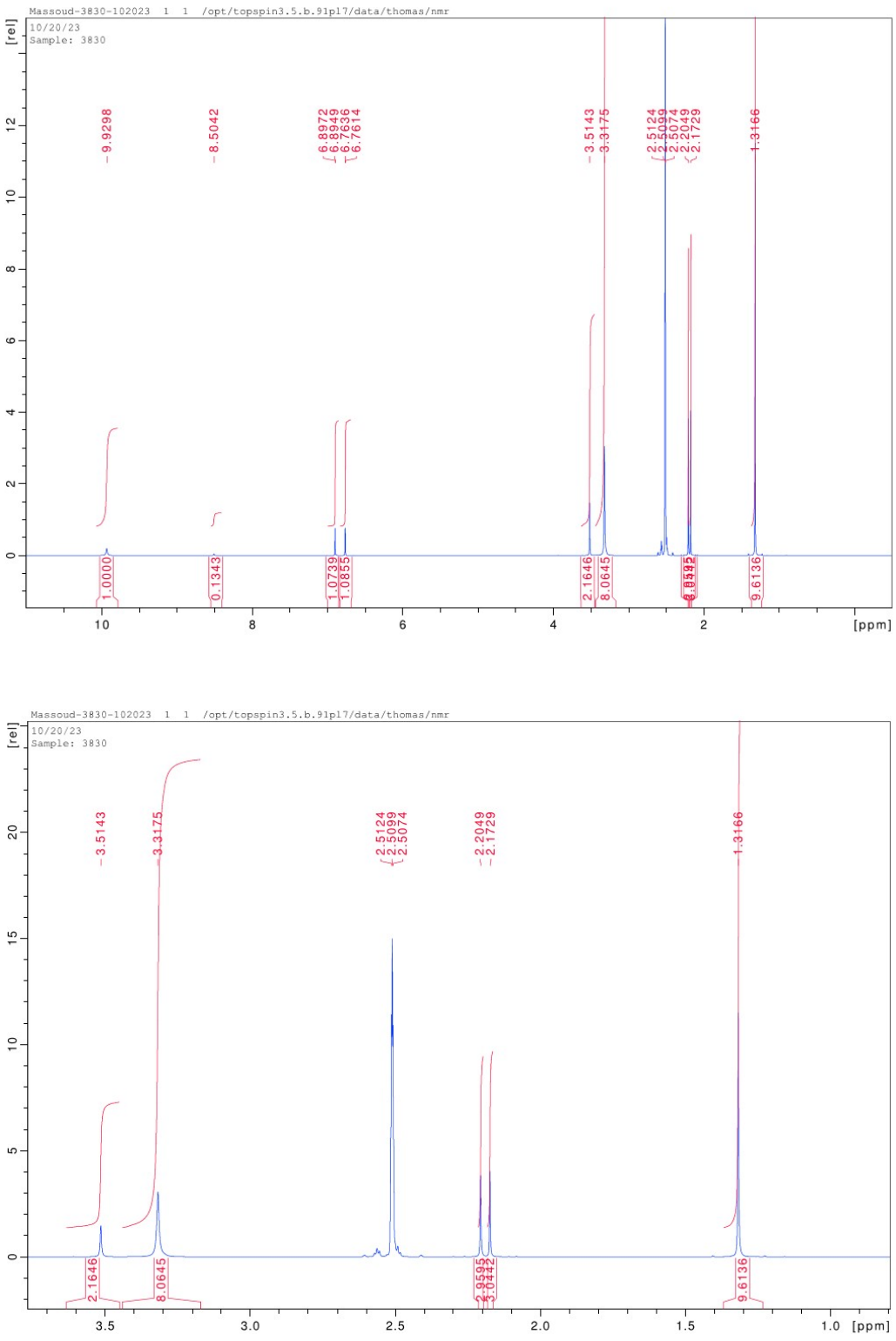


Fig. S2. ^{1}H NMR spectra of H_2L^3 in d_6-DMSO.

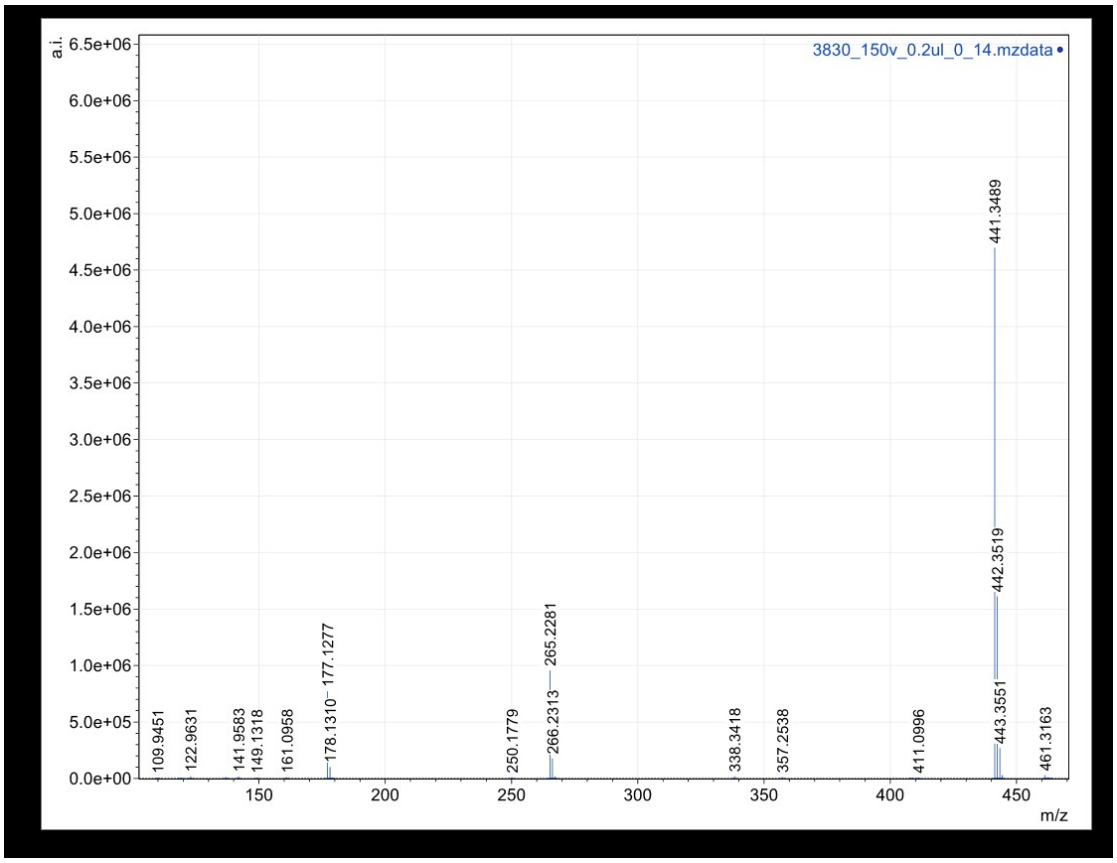
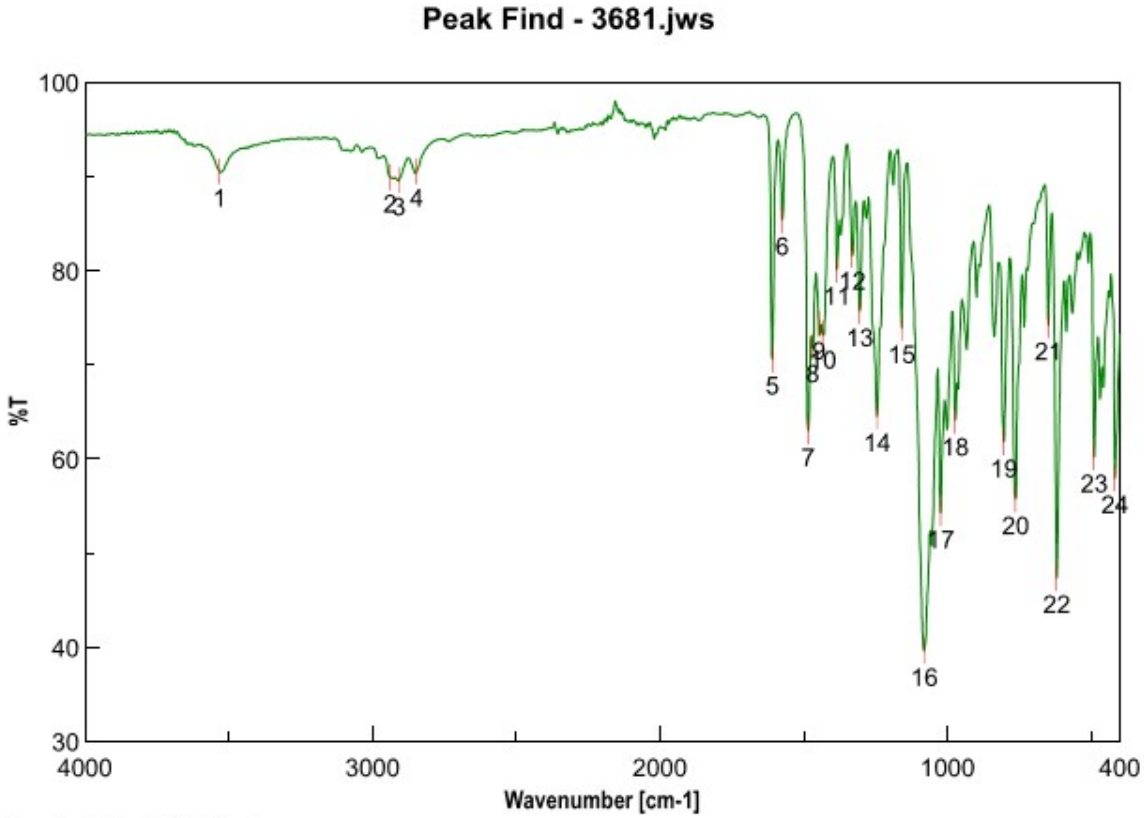


Fig. S3. ESI-MS of $\mathbf{H_2L^3}$ in CH_3OH.



[Result of Peak Picking]

No.	Position	Intensity	No.	Position	Intensity
1	3531.99	90	2	2938.98	90
3	2908.13	90	4	2846.42	90
5	1609.31	71	6	1574.59	85
7	1484.92	63	8	1469.49	72
9	1447.31	74	10	1433.82	73
11	1384.64	80	12	1331.61	82
13	1305.57	76	14	1244.83	64
15	1159.01	74	16	1080.91	40
17	1024.02	54	18	972.912	64
19	804.171	62	20	763.673	56
21	649.893	74	22	620.002	47
23	489.831	60	24	417.513	58

Fig. S4. IR spectrum of $[Zn_2(L^1)_2](ClO_4)_2$ (**1**)

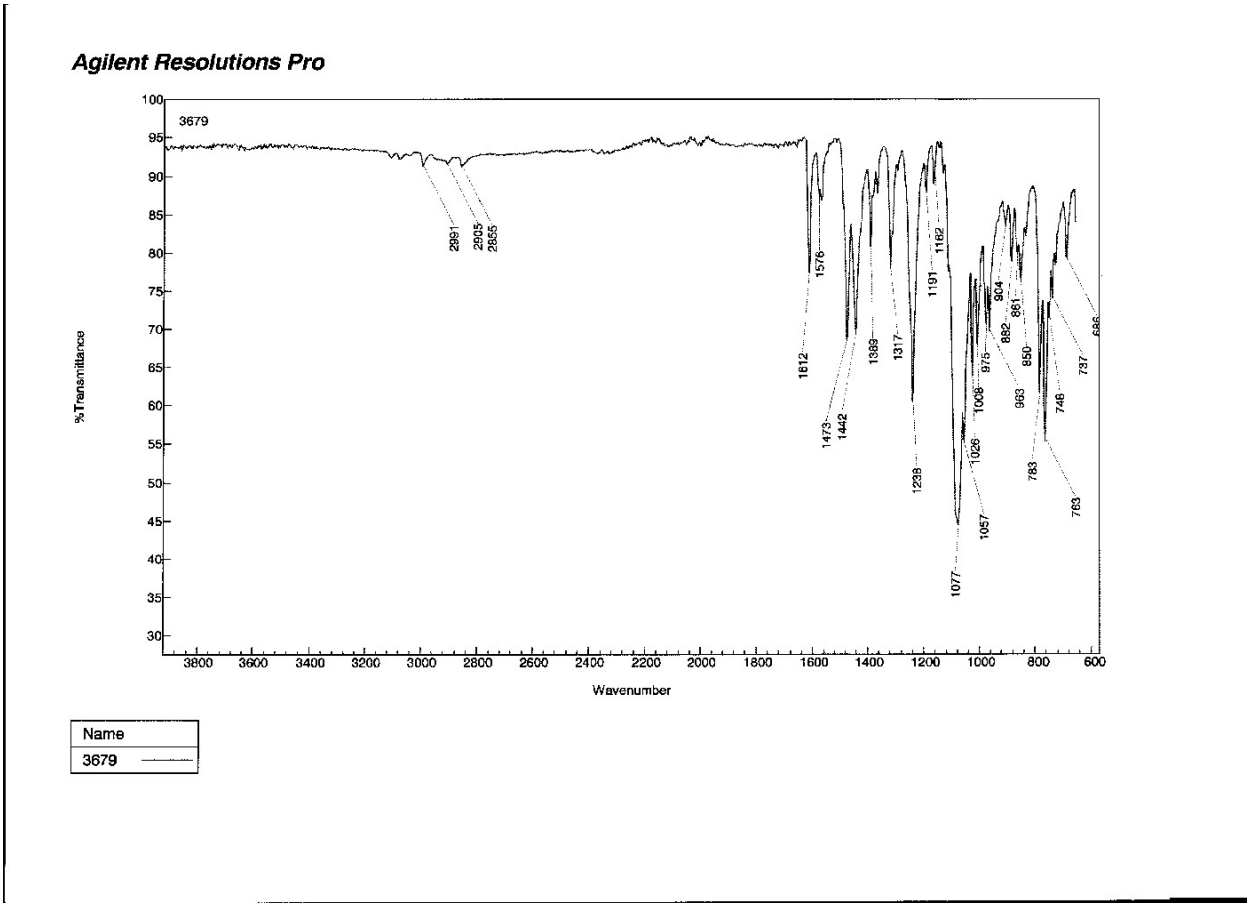
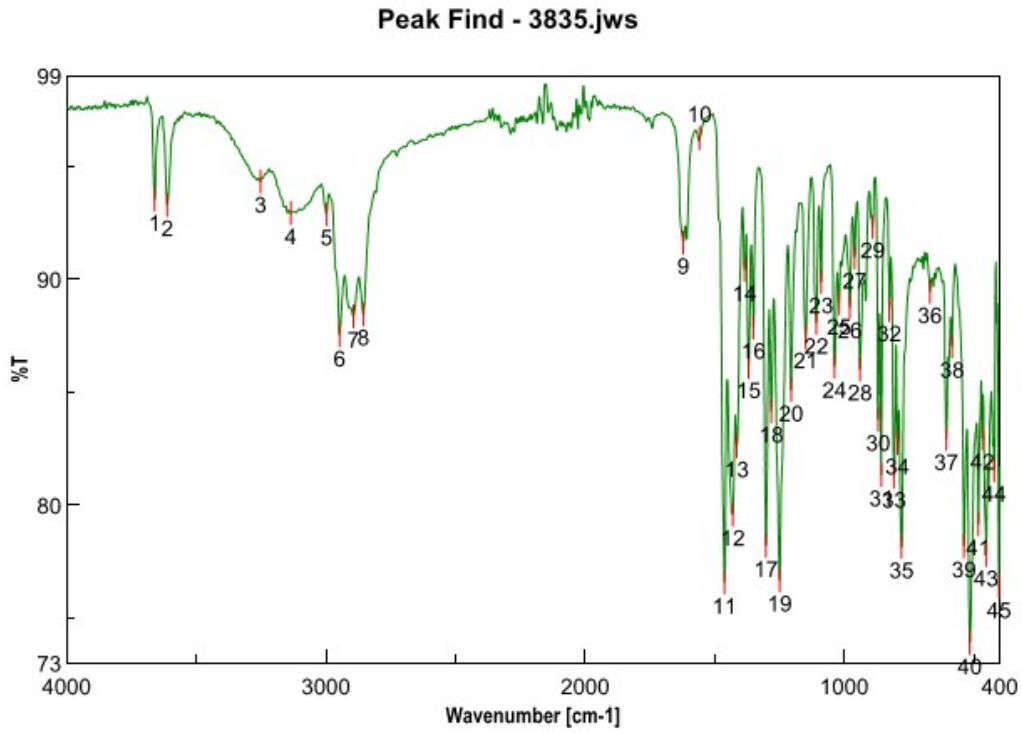


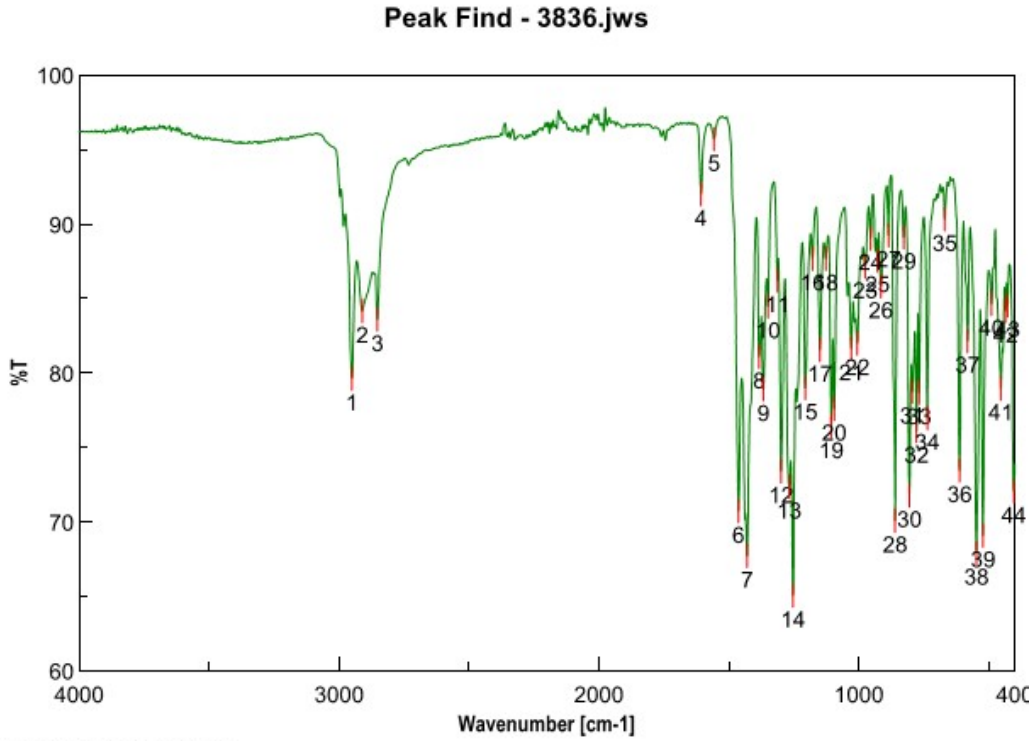
Fig. S5. IR spectrum of $[Zn_2(L^2)_2](ClO_4)_2$ (**2**)



[Result of Peak Picking]

No.	Position	Intensity	No.	Position	Intensity
1	3660.23	94	2	3611.05	93
3	3252.36	94	4	3134.72	93
5	2997.8	93	6	2946.7	88
7	2893.66	88	8	2855.1	88
9	1620.88	92	10	1558.2	96
11	1461.78	77	12	1429.96	80
13	1414.53	83	14	1384.64	90
15	1369.21	86	16	1350.89	88
17	1301.72	78	18	1281.47	84
19	1249.65	77	20	1205.29	85
21	1149.37	87	22	1107.9	88
23	1089.58	90	24	1037.52	86
25	1020.16	89	26	978.697	89
27	960.377	91	28	939.163	86
29	890.952	92	30	868.774	84
31	857.204	81	32	826.348	89
33	808.028	81	34	794.528	83
35	779.101	78	36	669.178	89
37	606.503	83	38	584.325	87
39	538.042	78	40	515.865	74
41	483.081	79	42	467.653	83
43	452.225	78	44	421.37	82
45	403.05	76			

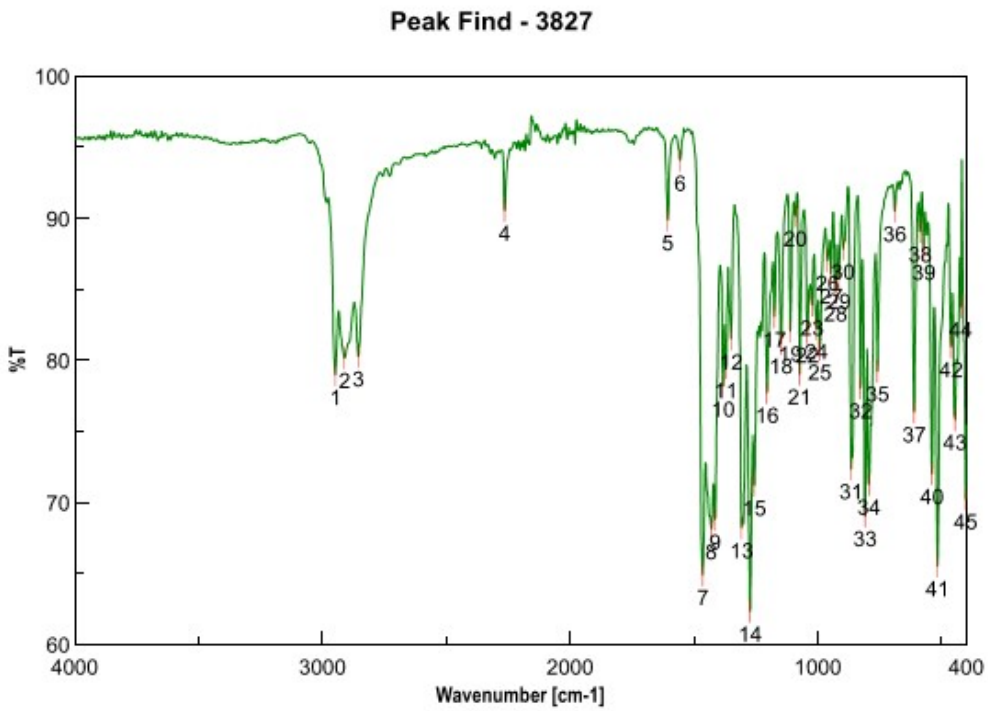
Fig. S6. IR spectrum of $[Zn(L^3)(H_2O)]\cdot CH_3OH$ (**3**).



[Result of Peak Picking]

No.	Position	Intensity	No.	Position	Intensity
1	2950.55	80	2	2911.02	84
3	2852.2	84	4	1607.38	92
5	1557.24	96	6	1463.71	71
7	1429.96	68	8	1383.68	81
9	1367.28	79	10	1348.96	84
11	1313.29	86	12	1298.82	73
13	1267.97	72	14	1253.5	65
15	1206.26	79	16	1178.29	88
17	1149.37	82	18	1127.19	88
19	1105.98	76	20	1094.4	78
21	1028.84	82	22	1005.7	82
23	975.804	87	24	954.591	89
25	928.557	88	26	915.058	86
27	886.131	89	28	860.096	70
29	827.312	89	30	805.135	72
31	794.528	79	32	778.136	76
33	767.53	79	34	736.674	77
35	669.178	90	36	612.288	73
37	581.433	82	38	547.685	68
39	522.615	69	40	489.831	85
41	453.19	79	42	435.834	84
43	427.155	85	44	403.05	72

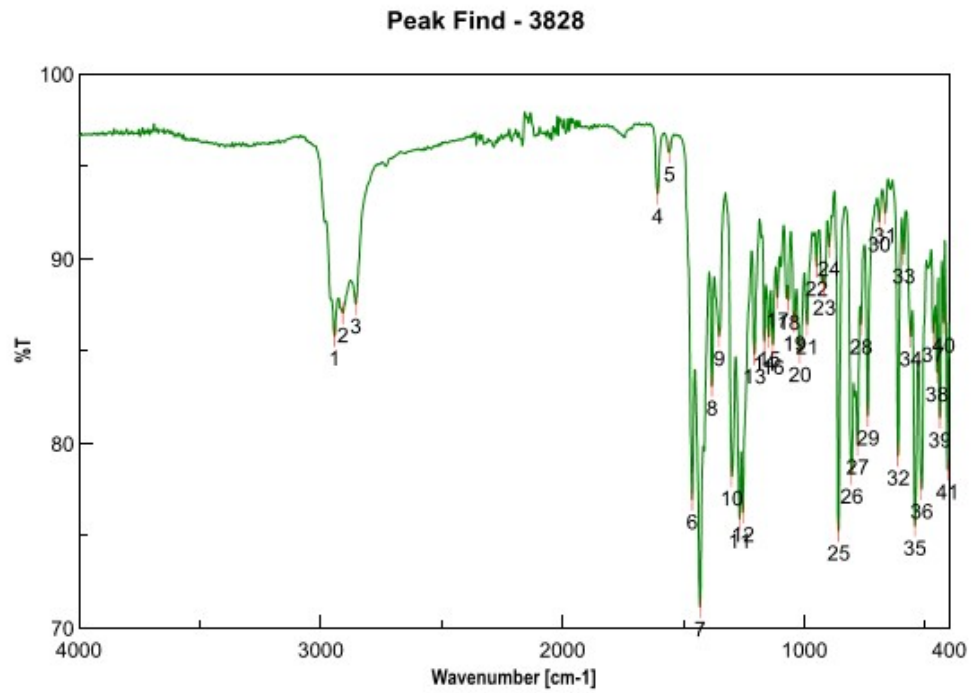
Fig. S7. IR spectrum of [Zn(L^4)] (**4**)**.**



[Result of Peak Picking]

No.	Position	Intensity	No.	Position	Intensity
1	2947.66	79	2	2911.02	80
3	2855.1	80	4	2264.02	91
5	1606.41	90	6	1556.27	94
7	1464.67	65	8	1429.96	68
9	1415.49	69	10	1382.71	78
11	1371.14	79	12	1349.93	81
13	1307.5	68	14	1272.79	62
15	1256.4	71	16	1205.29	78
17	1174.44	83	18	1148.4	81
19	1110.8	82	20	1091.51	90
21	1073.19	79	22	1042.34	82
23	1024.02	84	24	1005.7	82
25	992.196	81	26	960.377	87
27	945.913	86	28	928.557	85
29	915.058	86	30	897.701	88
31	865.882	72	32	827.312	78
33	808.992	69	34	793.564	71
35	758.852	79	36	689.427	90
37	611.324	76	38	587.218	89
39	572.755	88	40	539.007	72
41	516.829	65	42	461.868	81
43	445.476	76	44	423.298	84
45	403.05	70			

Fig. S8. IR spectrum of [Zn(L^5)] (**5**).



[Result of Peak Picking]

No.	Position	Intensity	No.	Position	Intensity
1	2942.84	86	2	2908.13	87
3	2855.1	88	4	1607.38	93
5	1558.2	96	6	1463.71	77
7	1431.89	71	8	1381.75	83
9	1352.82	86	10	1299.79	78
11	1267.97	76	12	1254.47	76
13	1206.26	85	14	1165.76	86
15	1146.47	86	16	1130.08	85
17	1110.8	88	18	1065.48	88
19	1041.37	87	20	1018.23	85
21	989.304	86	22	949.77	90
23	916.986	89	24	897.701	91
25	858.168	75	26	804.171	78
27	780.065	80	28	765.601	86
29	737.639	81	30	690.391	92
31	666.285	92	32	612.288	79
33	589.147	90	34	560.22	86
35	542.863	76	36	514.901	77
37	467.653	86	38	452.225	84
39	439.69	81	40	424.263	86
41	408.835	79			

Fig. S9. IR spectrum of [Zn(L^6)] (**6**).

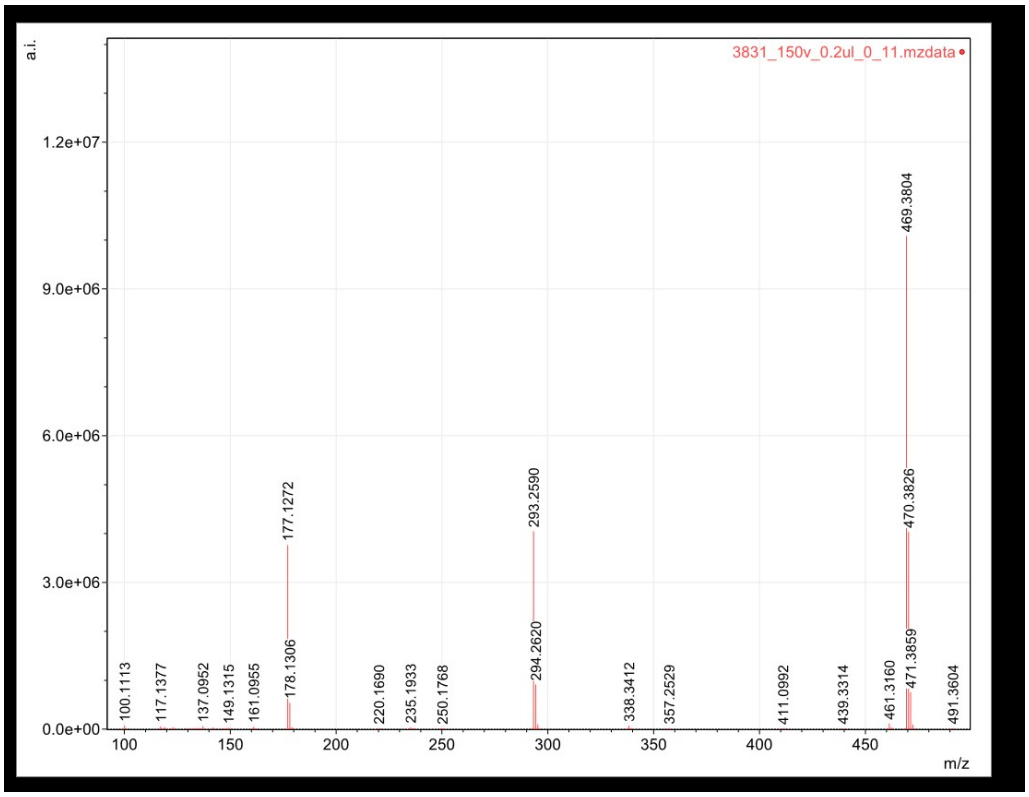


Fig. S10. ESI-MS of $\mathbf{H_2L^4}$ in CH_3OH.

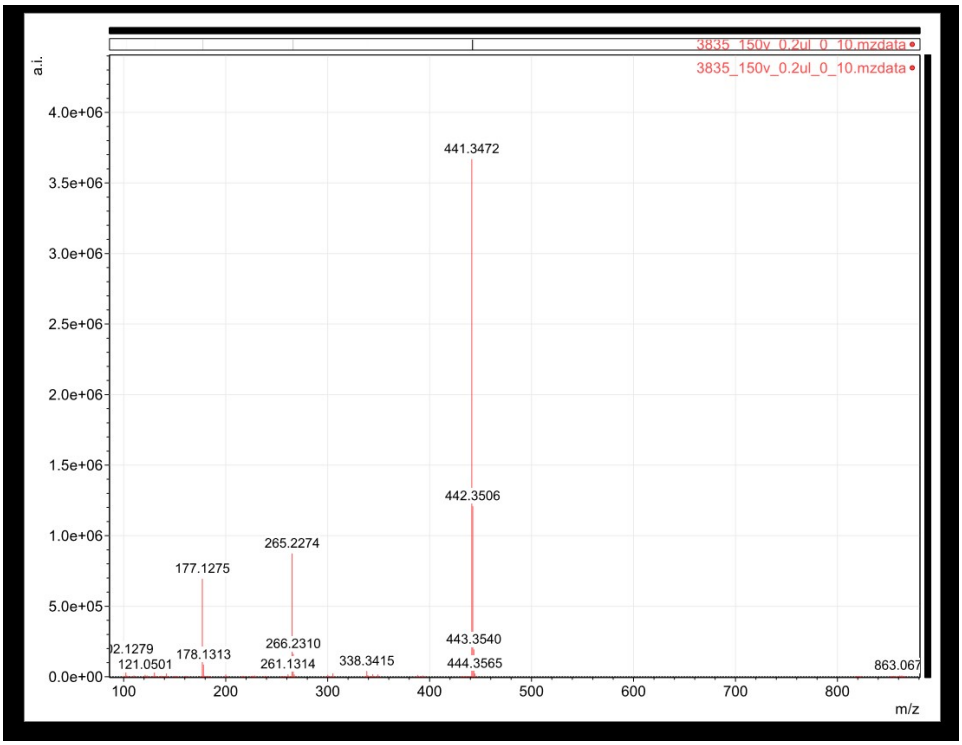


Fig. S11. ESI-MS of complex **3** in CH_3CN.

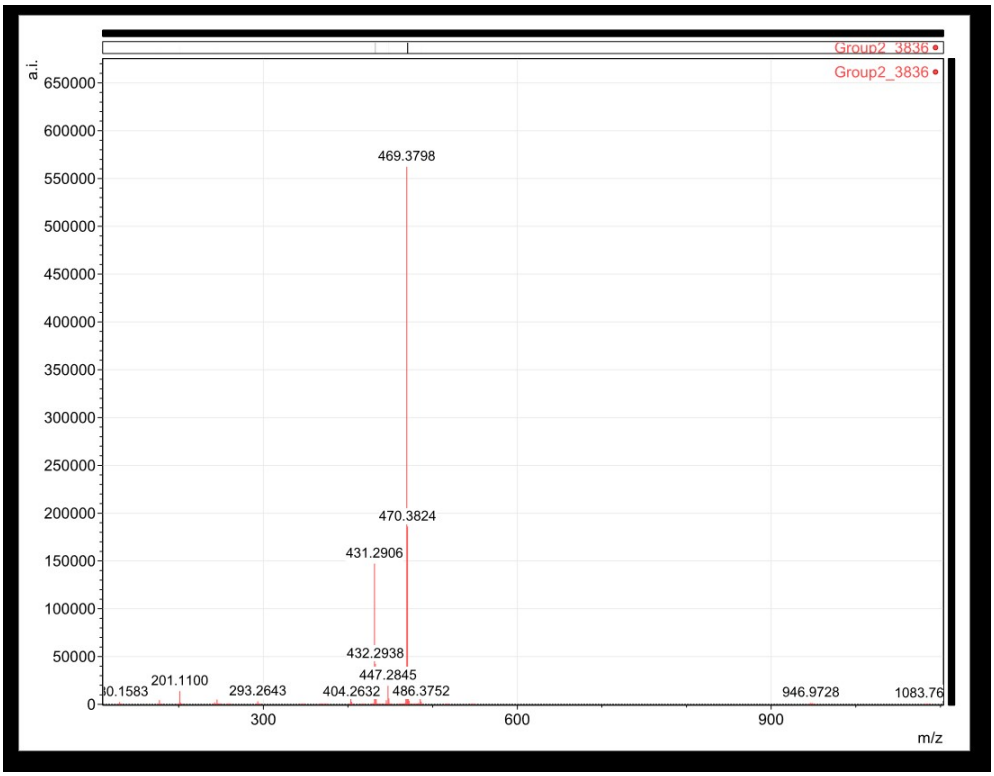


Fig. S12. ESI-MS of complex **4** in CH_3CN.

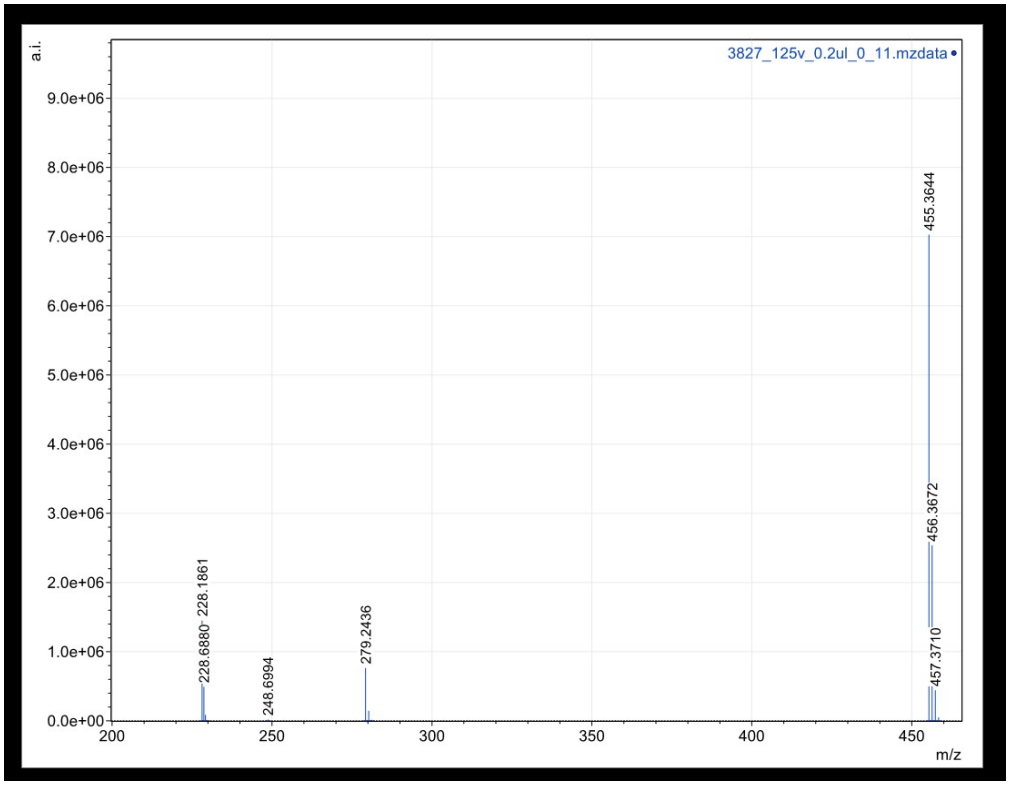


Fig. S13. ESI-MS of complex **5** in CH_3CN.

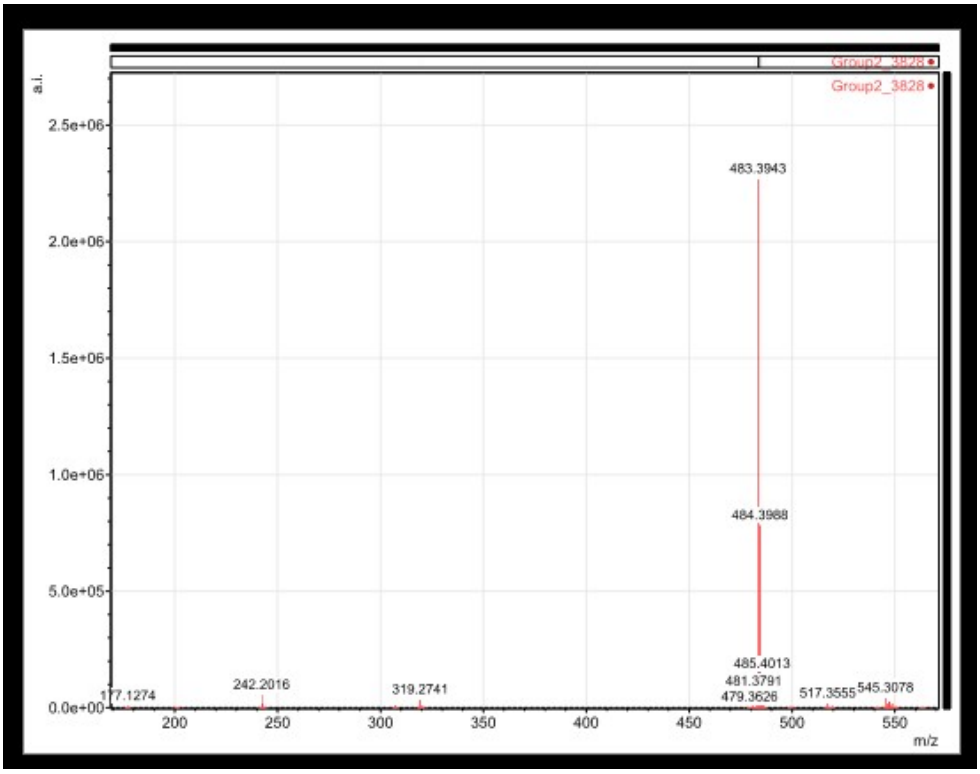


Fig. 14. ESI-MS of complex **6** in CH_3CN.

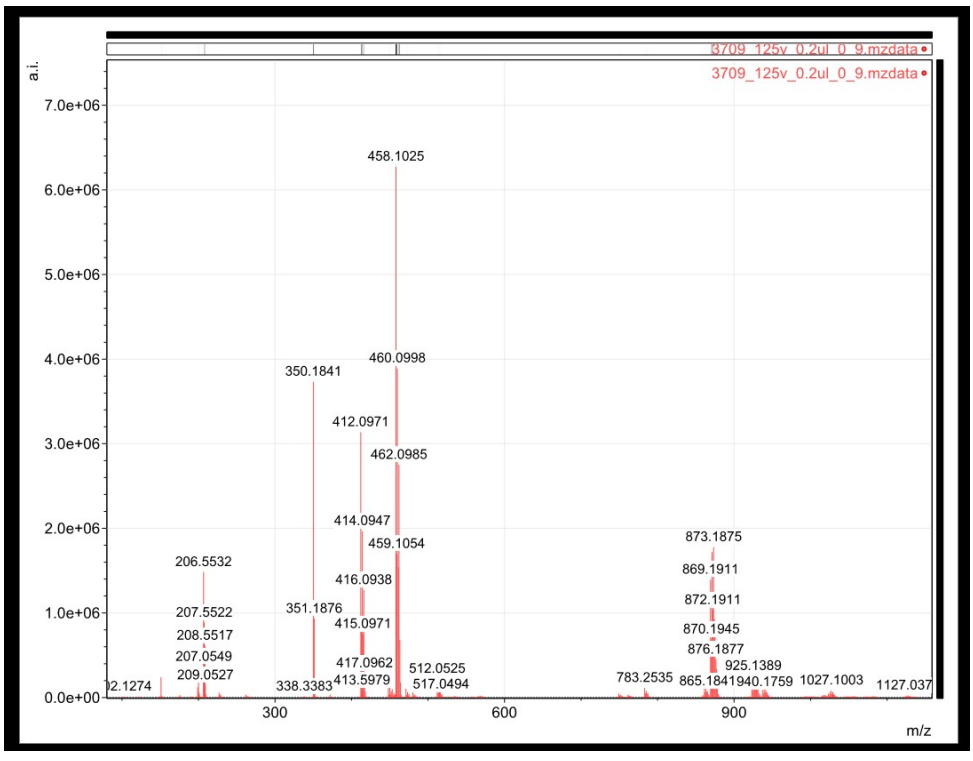


Fig. S15. ESI-MS of **1** in CH_3CN.

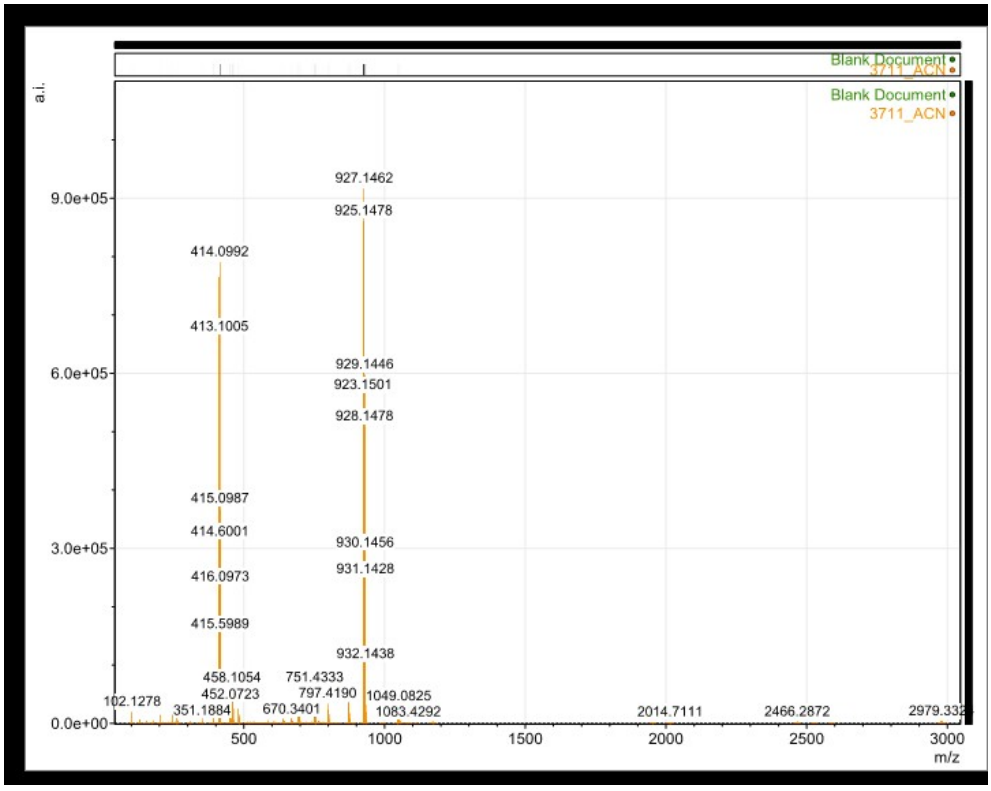
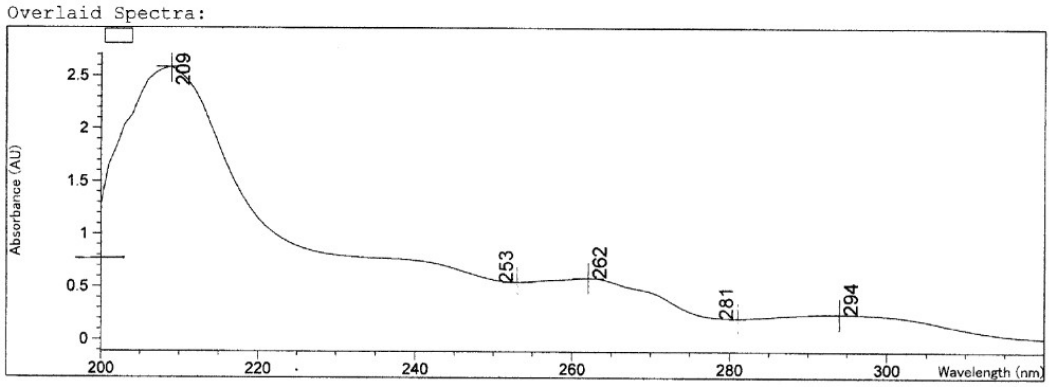
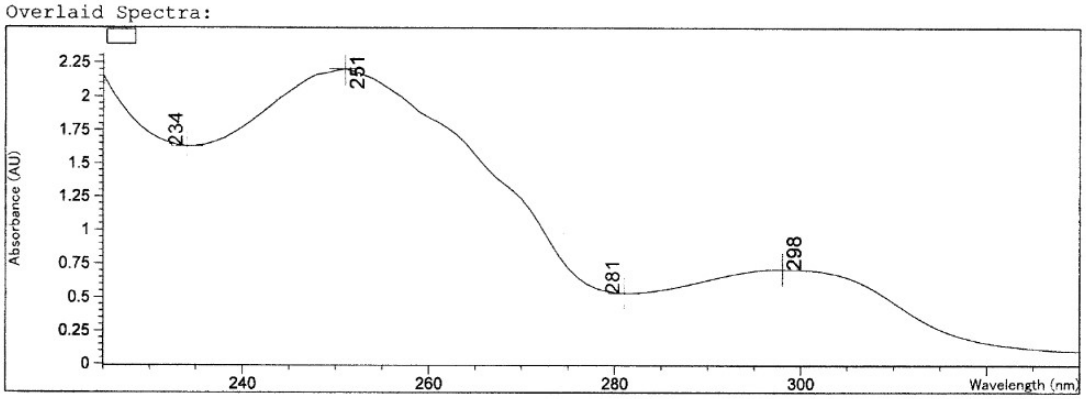


Fig. S16. ESI-MS of complex **2** in a CH_3CN/HCOOH (1:1) mixture.

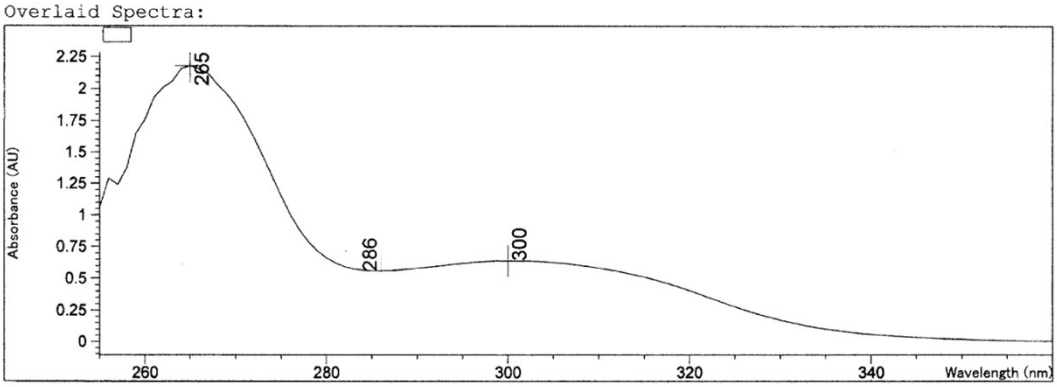


#	Name	Peaks(nm)	Abs(AU)	Valleys(nm)	Abs(AU)
1		209.0	2.58380	281.0	0.20472
1		262.0	0.58635	253.0	0.54402
1		294.0	0.24630	***	***

Fig. S17. UV spectrum of **1** (3.64 x 10^{-5} M) in MeOH.

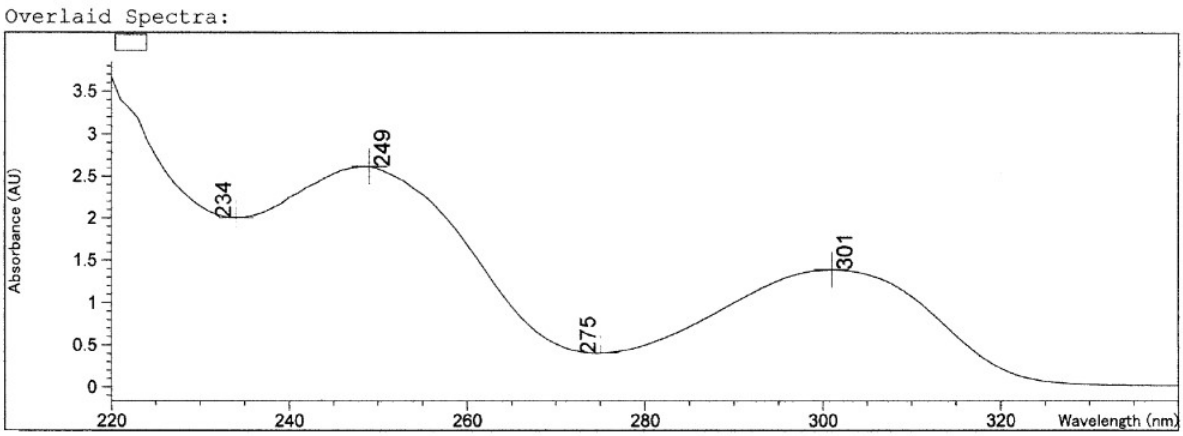


#	Name	Peaks(nm)	Abs(AU)	Valleys(nm)	Abs(AU)
1		251.0	2.20330	281.0	0.53069
1		298.0	0.70912	234.0	1.62720
1		***	***	***	***



#	Name	Peaks(nm)	Abs(AU)	Valleys(nm)	Abs(AU)
1		265.0	2.17680	286.0	0.55923
1		300.0	0.63994	***	***
1		***	***	***	***

Fig. S18. UV spectrum of **2** in CH_3CN (8.994 x 10^{-5} M) (*top*) and in DMSO (1.04 x 10^{-4} M) (*bottom*).



#	Name	Peaks(nm)	Abs(AU)	Valleys(nm)	Abs(AU)
1		249.0	2.61770	275.0	0.40479
1		301.0	1.38960	234.0	2.00040
1		***	***	***	***

Fig. S19. UV spectrum of **4** in CH_3CN (2.067×10^{-4} M).

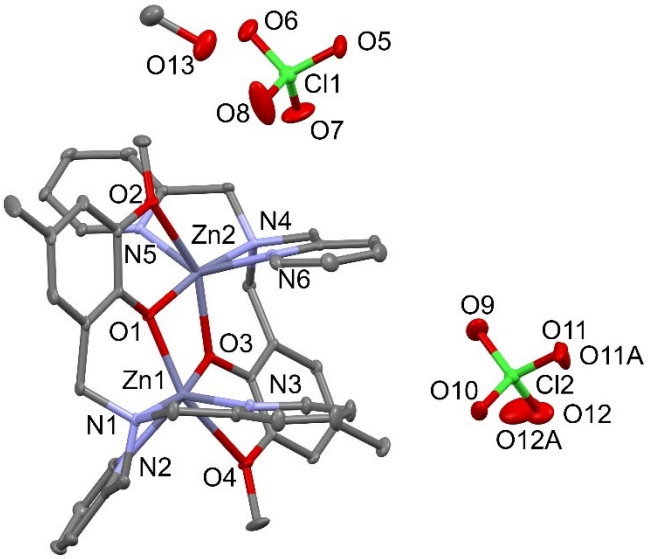


Fig. S20: ORTEP view of **1** showing also disordered parts of the complex.

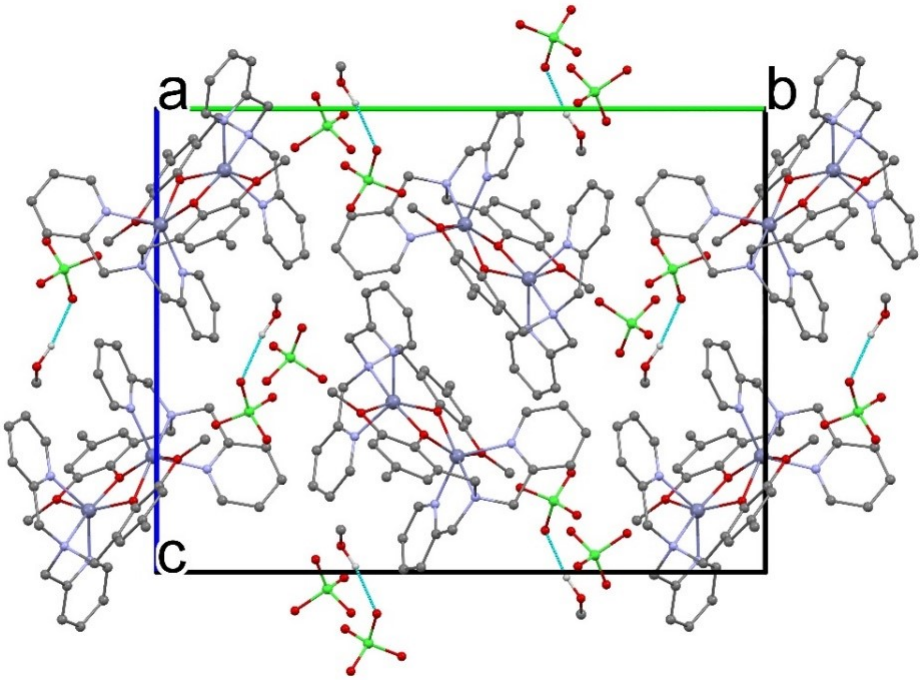


Fig. S21. Packing plot of **1**.

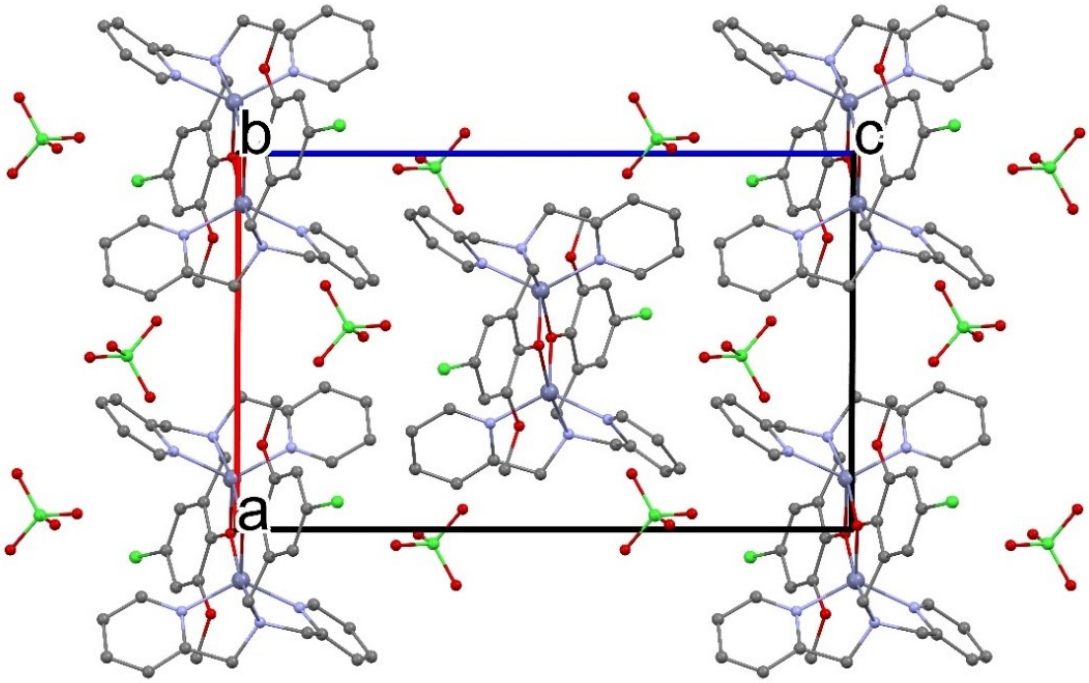


Fig. S22. Packing plot of **2**.

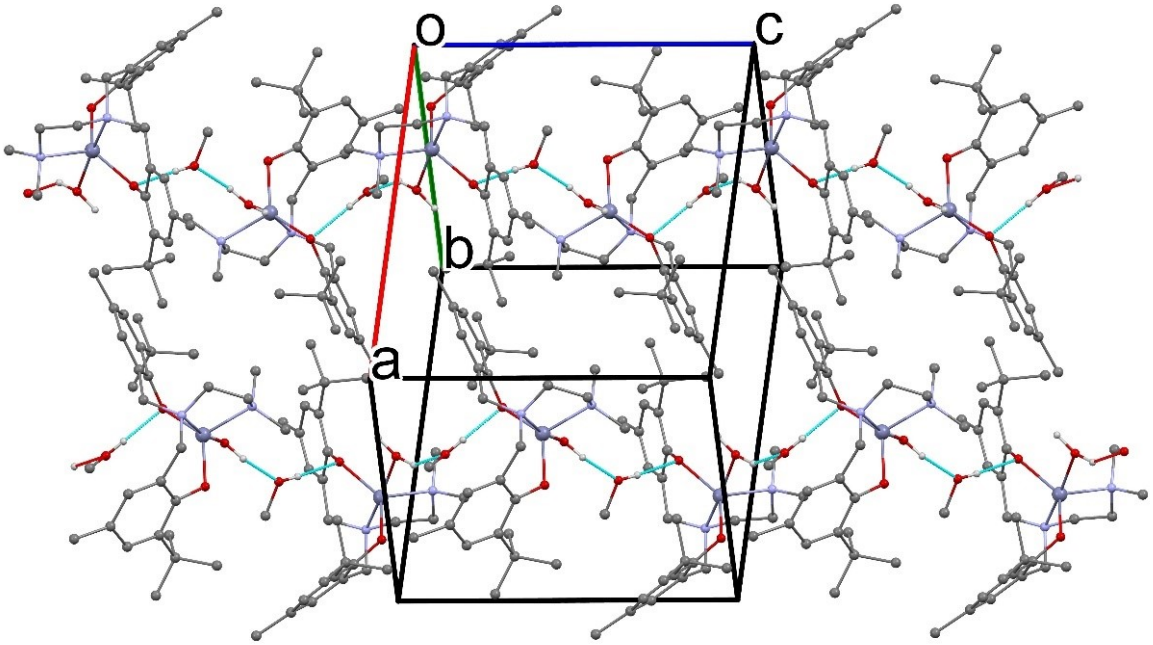


Fig. S23. Packing plot of **3**.

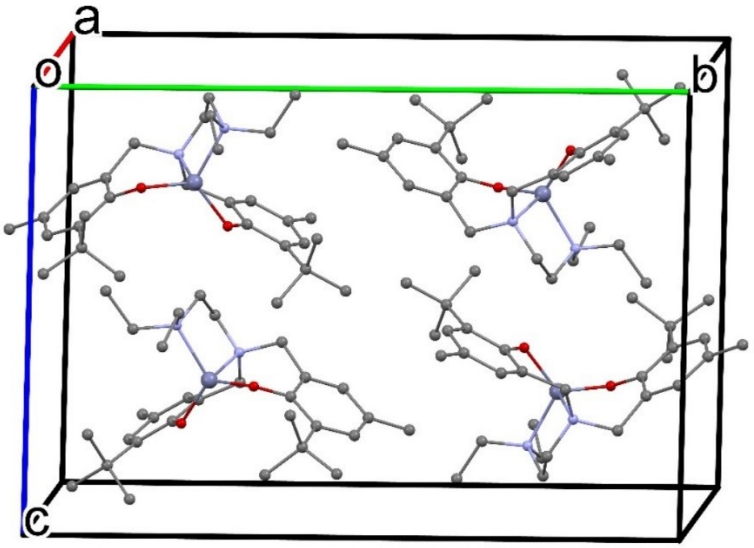


Fig. S24. Packing plot of **4**.

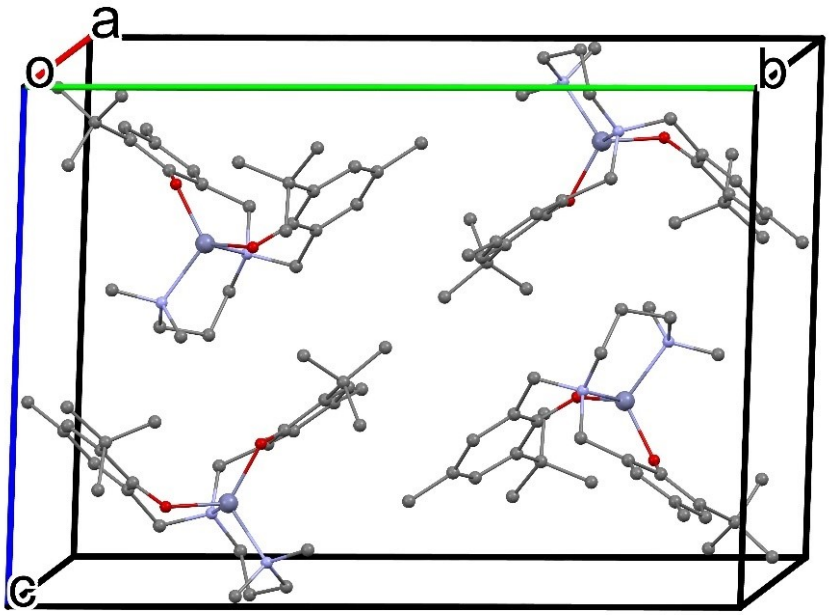


Fig. S25. Packing plot of **5**.

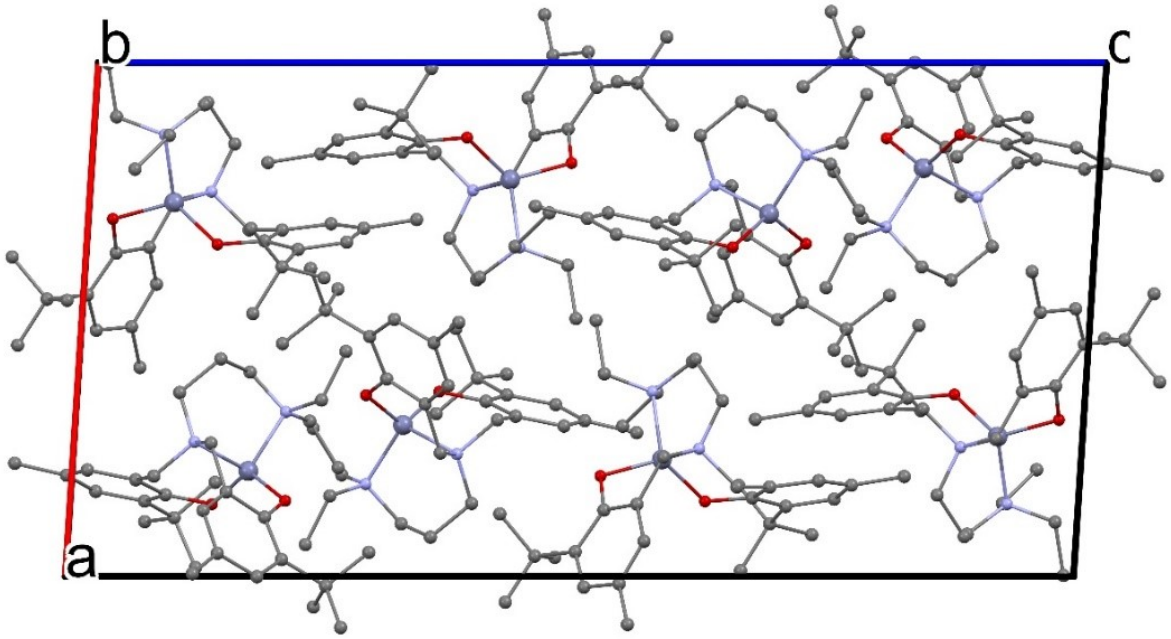


Fig. S26. Packing plot of **6.**

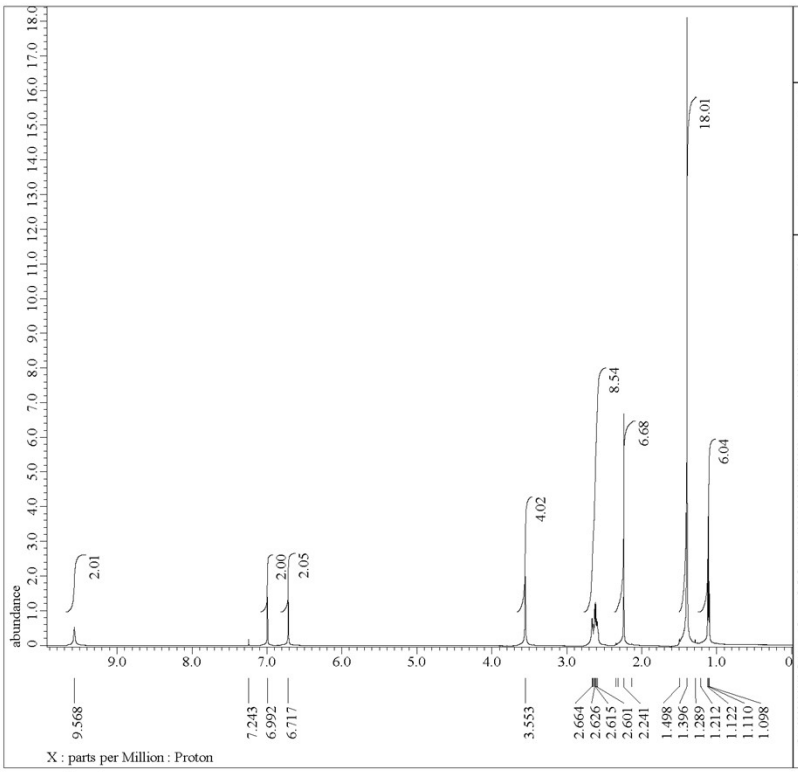


Fig. S27. ^{1}H NMR spectrum of free H_2L^4 measured in $CDCl_3$.

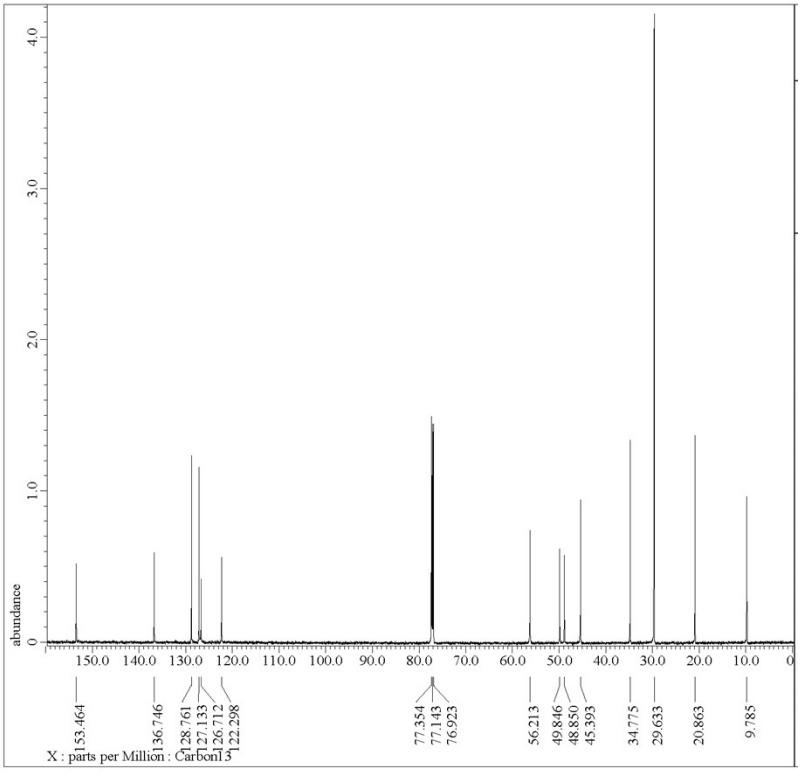


Fig. S28. ^{13}C NMR spectrum of free H_2L^4 measured in $CDCl_3$.

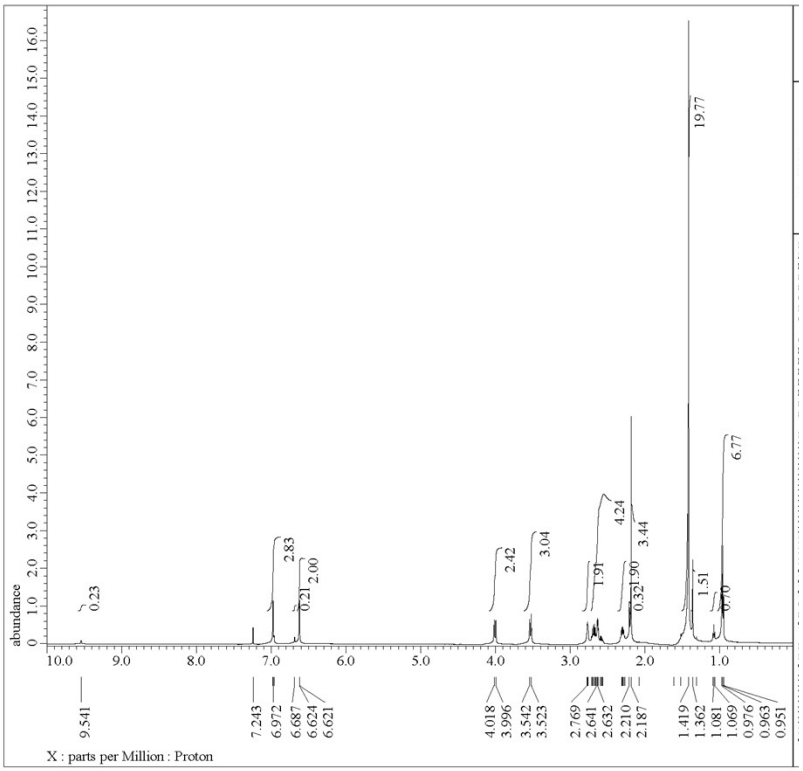


Fig. S29. ^{1}H NMR spectrum of **[Zn(L^4)]** (**4**) measured in $CDCl_3$ immediately after the sample dissolution.

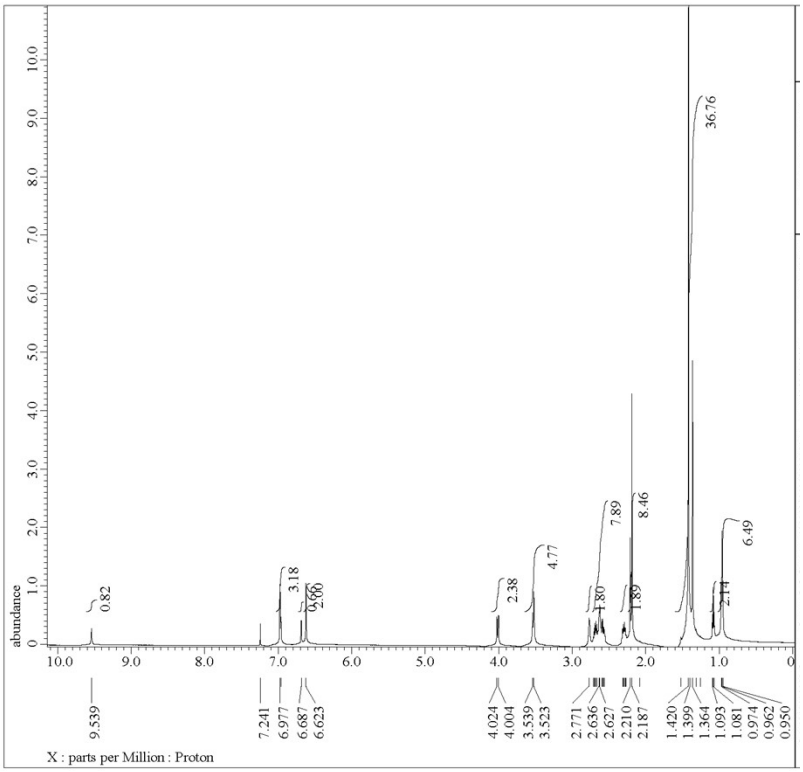


Fig. S30. ^{1}H NMR spectrum of **[Zn(L^4)]** (**4**) measured in $CDCl_3$ 22 h after the sample dissolution.

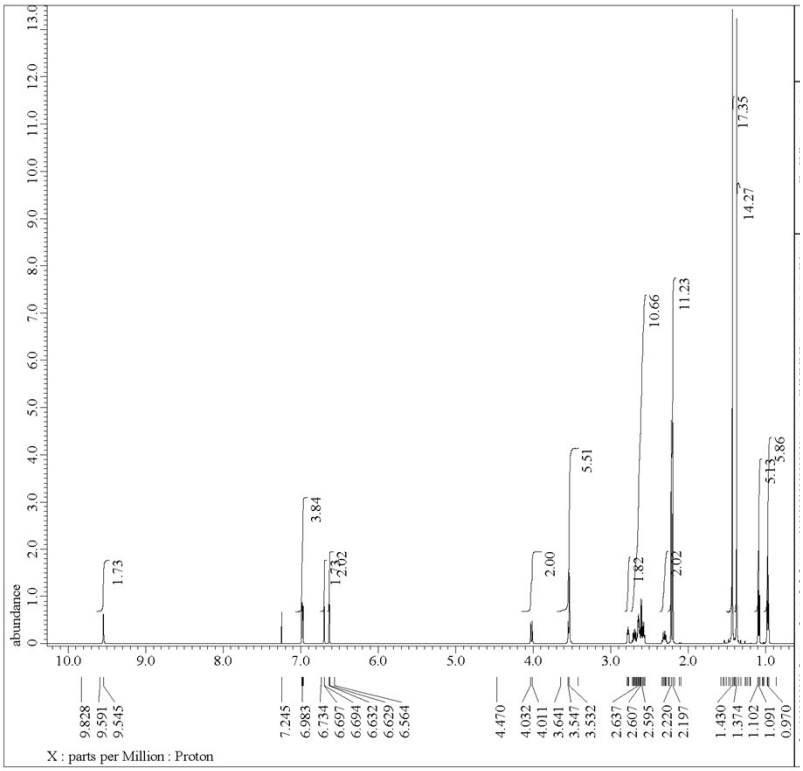


Fig. S31. ^{1}H NMR spectrum of **[Zn(L^{4})]** (**4**) measured in $CDCl_3$ 6 days after the sample dissolution.

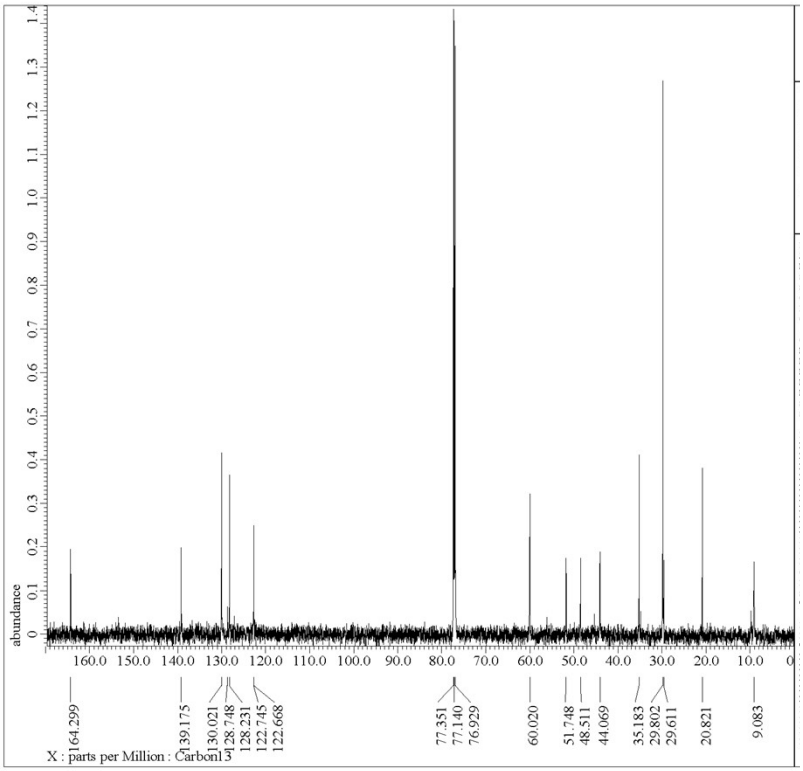


Fig. S32. ^{13}C NMR spectrum of **[Zn(L^{4})]** (**4**) measured in $CDCl_3$ immediately after the sample dissolution.

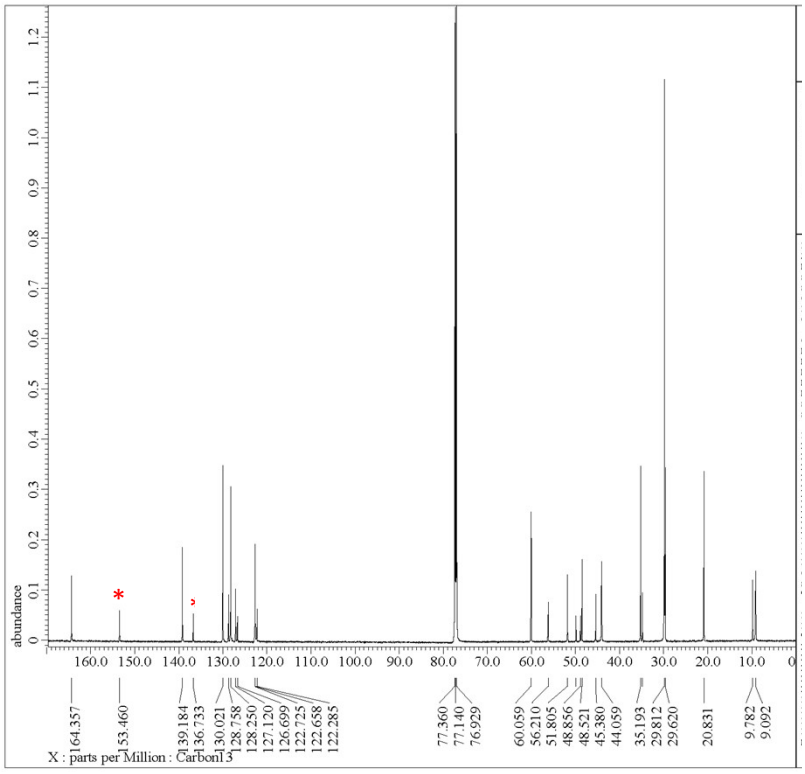


Fig. S33. ^{13}C NMR spectrum of **[Zn(L^4)]** (**4**) measured in $CDCl_3$ 22 h after the sample dissolution. *The selected signals belonging to the free H_2L^4 ligand.

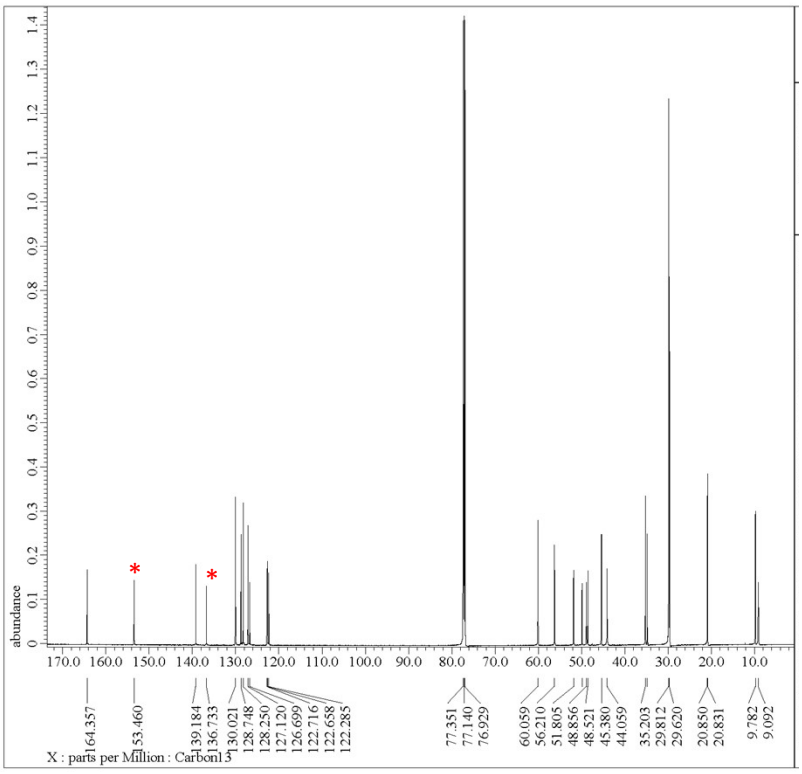


Fig. S34. ^{13}C NMR spectrum of **[Zn(L^4)]** (**4**) measured in $CDCl_3$ 6 days after the sample dissolution. *The selected signals belonging to the free H_2L^4 ligand.

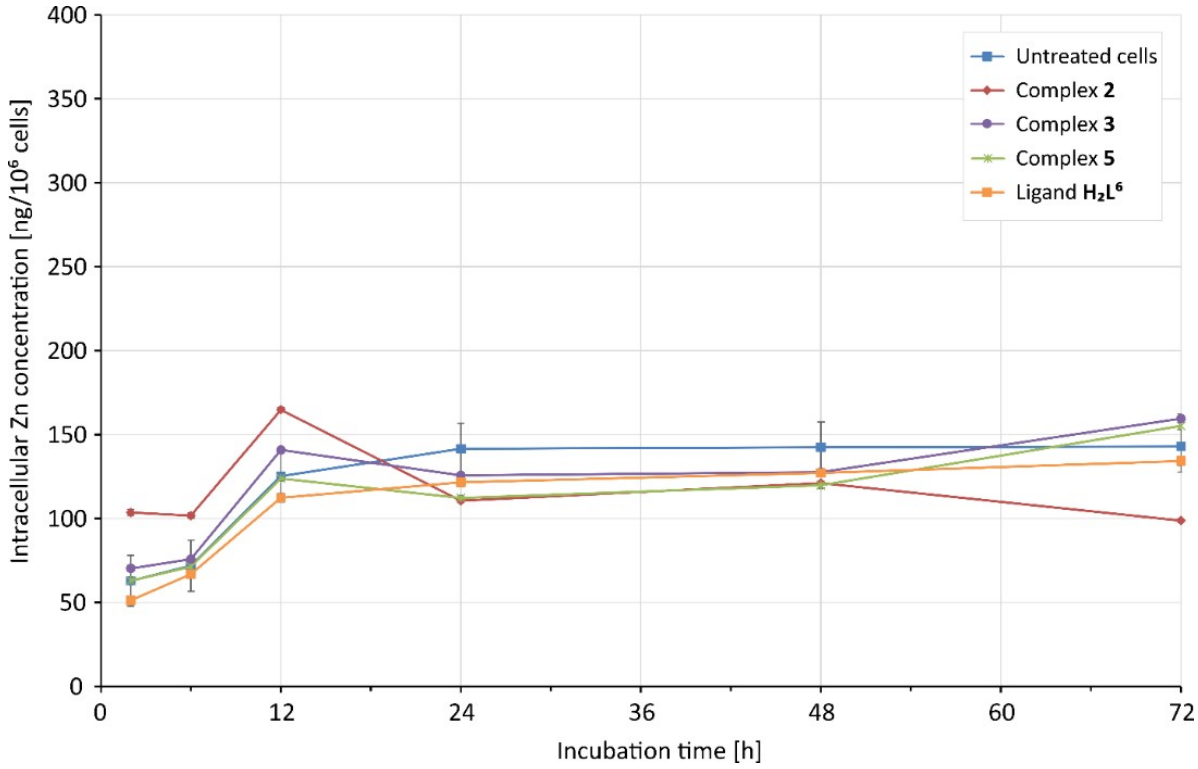


Fig. S35. The effect of complexes **2**, **3**, and **5**, and ligand $\mathbf{H_2L^6}$ on intracellular levels of zinc in A2780 cells incubated with half-toxic concentrations of the compounds for 2, 6, 12, 24, 48, and 72 h. The determined values are averages from three parallel determinations ± standard deviation.