New strong extrafunctionalizable tris(3,4-HP) and bis(3,4-HP) metal sequestering agents. Synthesis, solution and *in vivo* metal chelation

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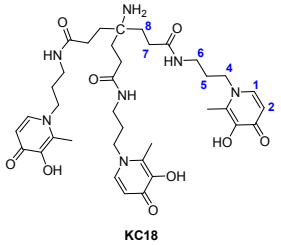
SUPPLEMENTARY INFORMATION

Table 1S. ^{1}H and ^{13}C NMR titration of KC18



KC18

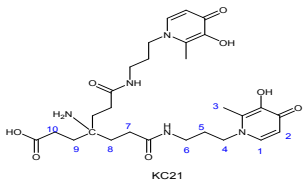
^{1}H Chemical shifts (ppm) of KC18 ligand *vs* pH

	HN	**2**	**1**	**4**	**6**	**3**	**7 e 8**	**5**
1.61	8.050	7.948	7.021	4.265	3.181	2.488	2.136	1.970
2.01	8.052	7.942	7.005	4.261	3.177	2.486	2.139	1.973
2.38	8.042	7.890	6.928	4.224	3.176	2.461	2.133	1.956
2.60	8.037	7.862	6.884	4.203	3.174	2.447	2.131	1.948
2.80	8.030	7.815	6.820	4.175	3.167	2.427	2.127	1.938
3.00	8.029	7.800	6.796	4.168	3.167	2.422	2.129	1.935
3.28	8.021	7.733	6.693	4.120	3.155	2.389	2.124	1.918
3.58	8.017	7.686	6.652	4.168	3.150	2.368	2.121	1.907
4.00	8.014	7.651	6.576	4.074	3.148	2.359	2.118	1.903
4.53	8.013	7.577	6.463	4.028	3.147	2.328	2.119	1.884
4.80	8.011	7.589	6.475	4.027	3.139	2.328	2.114	1.883
5.10	8.009	7.553	6.426	4.010	3.137	2.317	2.112	1.877
5.23	8.010	7.549	6.422	4.008	3.136	2.316	2.112	1.875
5.30	8.009	7.540	6.407	4.005	3.136	2.315	2.112	1.874
5.50	8.009	7.542	6.412	4.004	3.142	2.314	2.115	1.874
6.10	8.008	7.534	6.403	3.998	3.132	2.309	2.109	1.870
6.50	8.007	7.534	6.404	4.000	3.138	2.311	2.113	1.872
7.20	8.006	7.535	6.404	4.000	3.134	2.309	2.110	1.873
7.89	8.012	7.525	6.399	3.998	3.138	2.309	2.111	1.873
8.21	8.008	7.530	6.401	3.999	3.136	2.308	2.108	1.870
8.50	8.010	7.530	6.401	3.999	3.138	2.310	2.112	1.871
8.77	8.010	7.519	6.397	4.000	3.140	2.310	2.115	1.873
8.87	8.008	7.511	6.392	3.997	3.138	2.306	2.111	1.870
9.12	7.997	7.500	6.389	3.997	3.138	2.305	2.112	1.871
9.31		7.483	6.381	3.992	3.135	2.301	2.110	1.867
9.40		7.482	6.381	3.995	3.138	2.303	2.115	1.871
9.55		7.470	6.377	3.994	3.137	2.302	2.117	1.871
9.80		7.419	6.353	3.982	3.131	2.291	2.117	1.864
9.95		7.414	6.352	3.983	3.132	2.292	2.117	1.866
10.03		7.395	6.344	3.981	3.131	2.289	2.119	1.866
10.20		7.337	6.319	3.971	3.127	2.280	2.127	1.862
10.50		7.322	6.312	3.969	3.127	2.276	2.123	1.862
10.74		7.336	6.319	3.972	3.127	2.279	2.122	1.862
11.00		7.301	6.304	3.965	3.124	2.274	2.125	1.860

^{13}C shifts (ppm) of KC18 ligand *vs* pH

pH	2	1	4	6	3	7 e 8	5
1.61	138.435	111.060	54.414	36.391	12.231	30.159	28.713
2.01	138.470	111.083	54.488	36.457	12.236	30.196	28.713
2.38	138.429	111.269	54.162	36.434	12.172	30.159	28.831
2.60	138.360	111.446	54.037	36.421	12.091	30.150	28.800
2.80	138.379	111.556	53.798	36.471	12.026	30.133	28.786
3.00	138.404	111.406	53.637	36.476	11.981	30.167	28.777
3.28	138.430	111.657	53.330	36.546	11.869	30.040	28.791
3.58	138.456	111.910	53.099	36.565	11.747	30.170	28.829
4.00	138.411	112.161	52.938	36.594	11.752	30.112	28.795
4.53	138.392	112.276	52.538	36.602	11.564	30.167	28.890
4.80	138.389	112.334	52.664	36.542	11.537	30.170	28.950
5.10	138.318	112.379	52.483	36.594	11.526	30.181	28.911
5.23	138.397	112.418	52.357	36.620	11.522	30.269	28.922
5.30	138.364	112.374	52.399	36.607	11.530	30.208	29.002
5.50	138.347	112.390	52.397	36.600	11.473	30.174	28.974
6.10	138.299	112.402	52.391	36.585	11.521	30.192	28.922
6.50	138.292	112.422	52.357	36.630	11.493	30.173	28.937
7.20	138.334	112.456	52.467	36.655	11.497	30.193	28.955
7.89	138.193	112.392	52.355	36.622	11.502	30.178	28.981
8.21	138.187	112.394	52.429	36.648	11.519	30.226	29.003
8.50	138.269	112.399	52.367	36.569	11.506	30.192	28.954
8.77	138.118	112.336	52.321	36.620	11.526	30.164	29.007
8.87	137.953	112.360	52.406	36.634	11.558	30.199	28.922
9.12	137.727	112.338	52.390	36.627	11.555	30.255	28.919
9.31	137.468	112.260	52.468	36.574	11.577	30.168	28.988
9.40	137.458	112.281	52.405	36.575	11.588	30.160	29.000
9.55	137.252	112.213	52.489	36.655	11.626	30.173	28.981
9.80	136.383	112.089	52.524	36.635	11.699	30.222	28.978
9.95	136.305	112.049	52.555	36.662	11.736	30.204	29.018
10.03	135.938	111.998	52.470	36.615	11.755	30.212	29.008
10.20	135.050	111.871	52.574	36.636	11.872	30.224	29.090
10.50	134.805	111.803	52.647	36.682	11.897	30.235	29.068
10.74	134.964	111.849	52.574	36.680	11.894	30.181	29.048
11.00	134.493	111.788	52.632	36.698	11.927	30.229	29.094

Table 2S. ^{1}H and ^{13}C NMR titration of KC21



^{1}H Chemical shifts (ppm) of KC21 ligand *vs* pH

pH	HN	2	1	4	6	3	5	8
1.84	8.079	7.942	7.013	4.269	3.189	2.491	2.002	1.885
2.08	8.076	7.929	6.992	4.263	3.189	2.486	2.000	1.884
2.15	8.079	7.939	7.009	4.269	3.190	2.491	2.004	1.884
2.37	8.065	7.898	6.943	4.243	3.189	2.473	1.995	1.879
2.60	8.051	7.857	6.880	4.221	3.187	2.457	1.989	1.860
2.98	8.027	7.785	6.770	4.180	3.183	2.427	1.972	1.853
3.42	8.002	7.698	6.638	4.127	3.170	2.386	1.964	1.847
4.23	7.990	7.612	6.504	4.074	3.163	2.351	1.940	1.804
4.86	7.993	7.574	6.444	4.050	3.164	2.338	1.925	1.832
4.90	7.993	7.576	6.446	4.052	3.165	2.339	1.925	1.825
5.77	7.993	7.562	6.426	4.043	3.164	2.334	1.925	1.824
6.58	7.993	7.561	6.424	4.042	3.162	2.333	1.925	1.819
6.79	7.992	7.561	6.423	4.040	3.161	2.333	1.924	1.822
7.41	7.992	7.559	6.423	4.041	3.162	2.333	1.925	1.808
7.64	7.992	7.559	6.422	4.039	3.160	2.332	1.924	1.819
7.83	7.986	7.554	6.420	4.038	3.166	2.331	1.921	1.745
8.14	7.983	7.555	6.421	4.039	3.167	2.332	1.921	1.749
8.42	7.965	7.547	6.415	4.034	3.161	2.326	1.920	1.720
8.76		7.543	6.415	4.035	3.164	2.329	1.922	1.675
9.03		7.525	6.408	4.032	3.163	2.326	1.919	1.610
9.30		7.499	6.392	4.017	3.151	2.313	1.917	1.564
9.95		7.446	6.369	4.005	3.144	2.302	1.908	1.548
10.09		7.413	6.358	4.005	3.148	2.300	1.908	1.550
10.22		7.386	6.347	3.997	3.146	2.294	1.900	1.543
10.76		7.318	6.318	3.985	3.140	2.283	1.899	1.547
11.17		7.352	6.314	3.985	3.138	2.281	1.898	1.546
11.72		7.226	6.277	3.965	3.131	2.267	1.891	1.555

^{13}C Chemical shifts (ppm) of KC21 ligand *vs* pH

pH	2	1	4	6	3	5	8
1.84	138.476	111.102	54.281	36.403	12.207	28.702	30.723
2.08	138.441	111.149	54.284	36.406	12.166	28.739	30.743
2.15	138.441	111.104	54.333	36.388	12.210	28.77	30.878
2.37	138.451	111.317	54.140	36.388	12.118	28.803	30.738
2.60	138.374	111.389	53.991	36.447	12.078	28.752	30.716
2.98	138.478	111.660	53.704	36.552	11.955	28.735	30.785
3.42	138.480	111.925	53.282	36.621	11.794	28.771	30.809
4.23	138.422	112.307	52.797	36.633	11.631	28.744	30.976
4.86	138.469	112.403	52.535	36.657	11.557	28.817	30.965
4.90	138.404	112.398	52.531	36.720	11.560	28.831	30.963
5.77	138.430	112.454	52.487	36.699	11.541	28.798	31.014
6.58	138.440	112.441	52.452	36.762	11.538	28.834	31.069
6.79	138.447	112.419	52.437	36.684	11.520	28.852	30.976
7.41	138.432	112.455	52.490	36.698	11.531	28.844	31.184
7.64	138.392	112.456	52.466	36.746	11.533	28.852	31.249
7.83	138.368	112.454	52.467	36.644	11.540	28.860	31.791
8.14	138.385	112.445	52.462	36.664	11.523	28.814	31.899
8.42	138.365	112.452	52.438	36.634	11.552	28.863	32.262
8.76	138.142	112.398	52.487	36.666	11.559	28.867	32.768
9.03	137.915	112.332	52.591	36.643	11.590	28.858	33.440
9.30	137.597	112.276	52.488	36.588	11.570	28.969	34.003
9.95	136.804	112.197	52.526	36.566	11.677	28.996	34.287
10.09	136.039	112.043	52.628	36.601	11.756	28.964	34.449
10.22	135.685	111.981	52.594	36.651	11.798	28.963	34.446
10.76	134.671	111.839	52.684	36.645	11.923	29.032	34.622
11.17	134.397	111.781	52.727	36.675	11.925	29.078	34.668
11.72	132.948	111.519	52.784	36.582	12.089	29.121	34.738

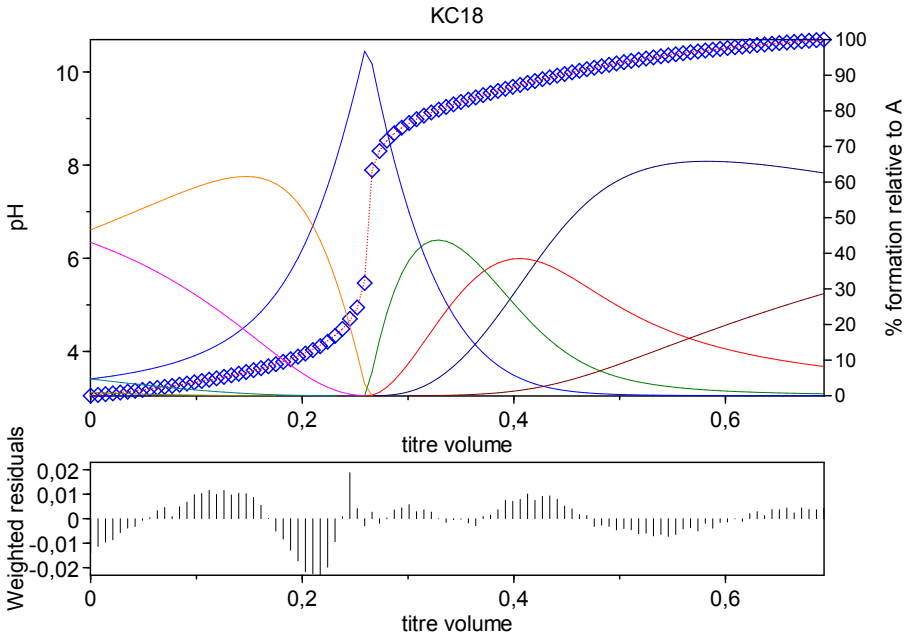


Figure 1S. Potentiometric titration of KC18 (HyperQuad screenshot)

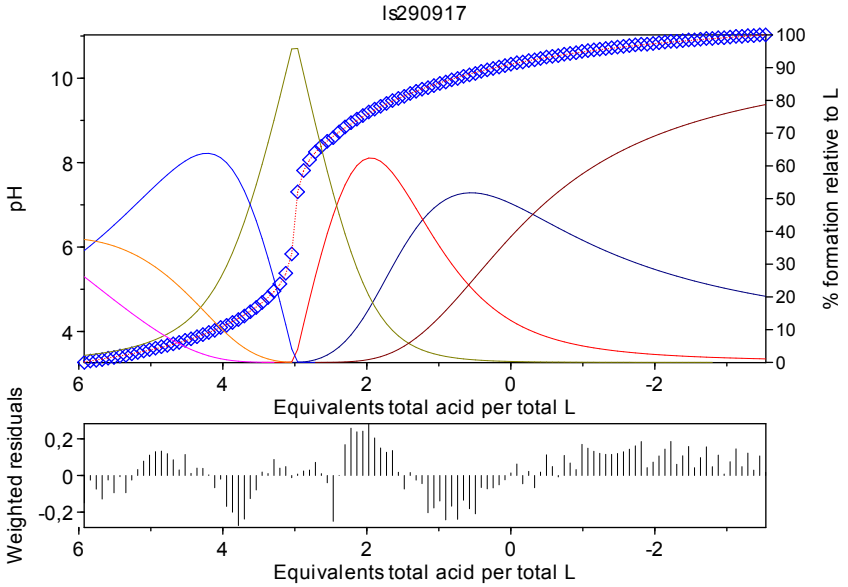


Figure 2S. Potentiometric titration of KC21 (HyperQuad screenshot)

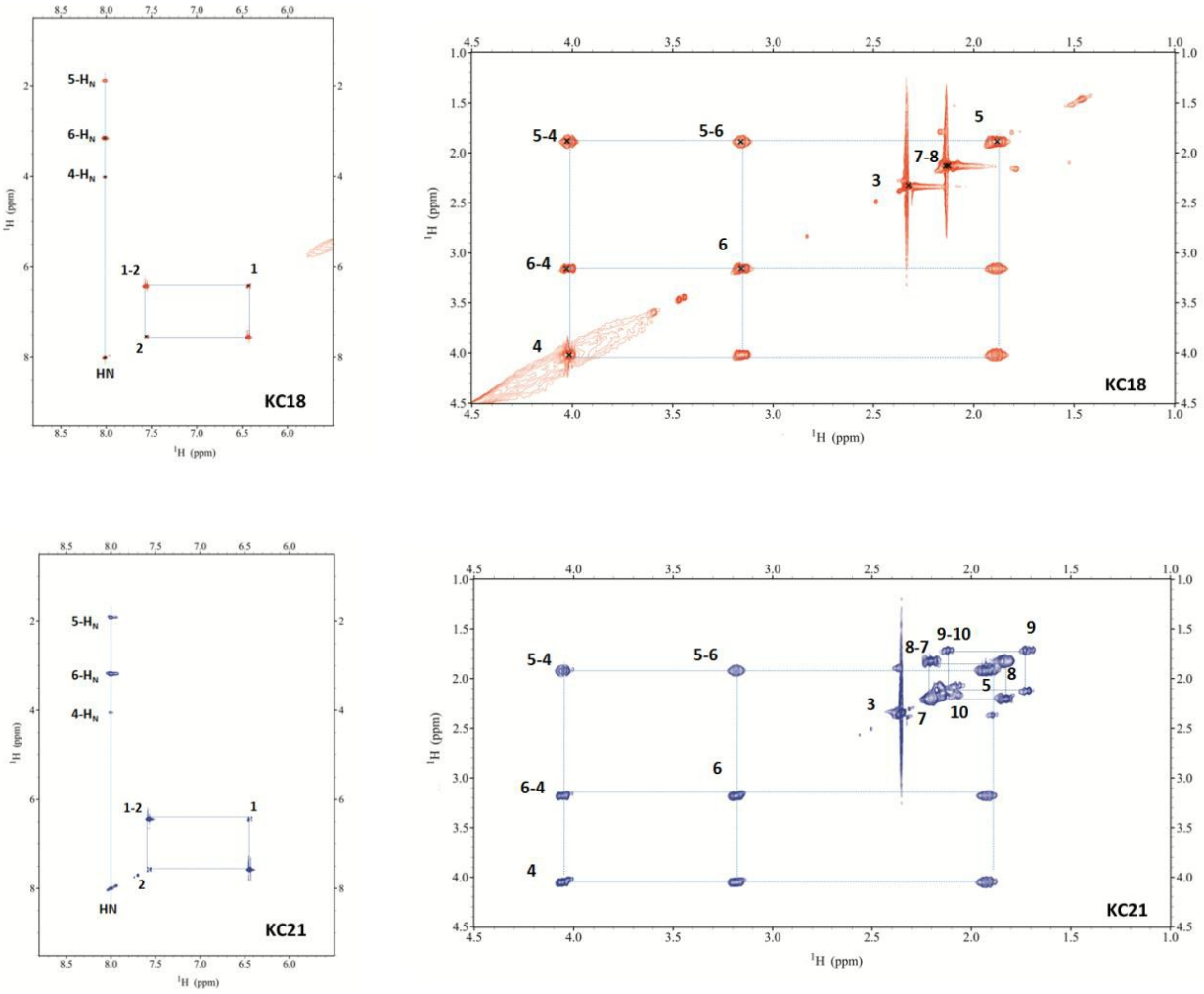


Figure 3S. Aromatic (left) and aliphatic (right) region of 1H-1H TOCSY spectra for KC18 and KC21 ligands with the relative proton and correlation assignments.

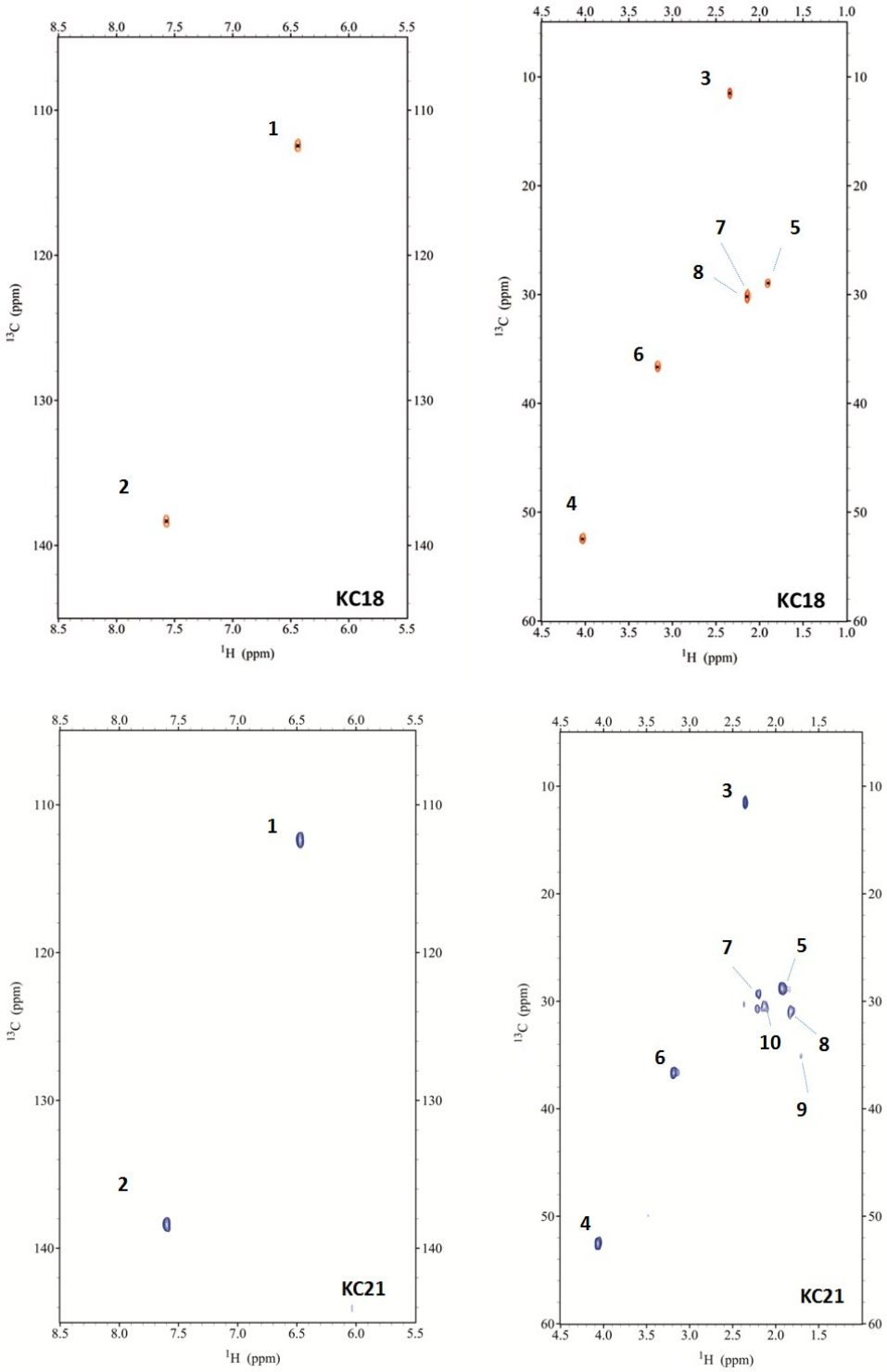
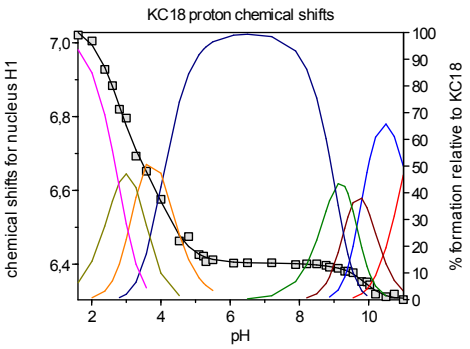
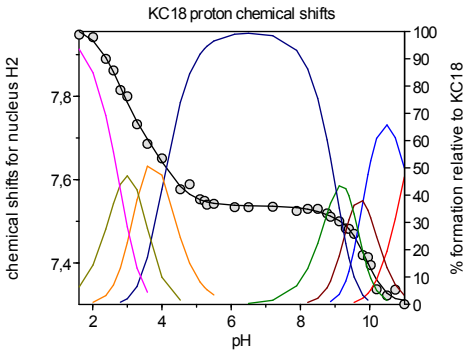
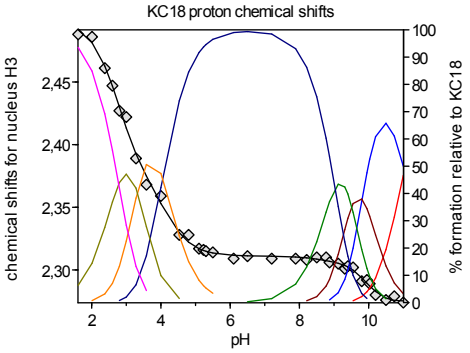
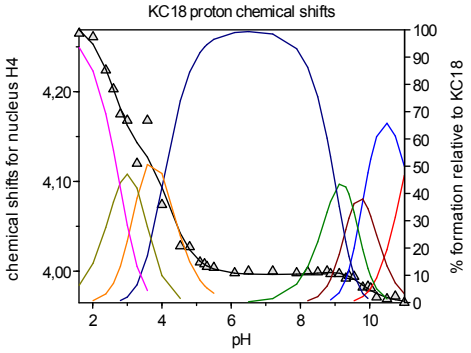


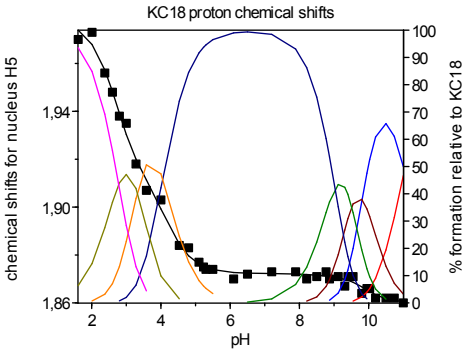
Figure 4S. Aromatic (left) and aliphatic (right) region of ^{1}H-^{13}C HSQC spectra for KC18 and KC21 ligands with the relative H-C correlation assignments.

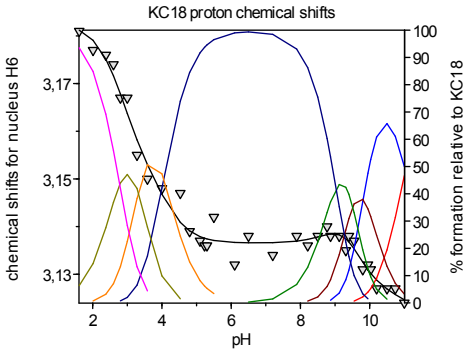

KC18 proton chemical shifts
chemical shifts for nucleus H1
% formation relative to KC18
pH

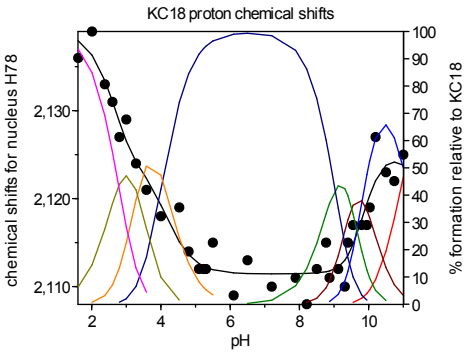

KC18 proton chemical shifts
chemical shifts for nucleus H2
% formation relative to KC18
pH

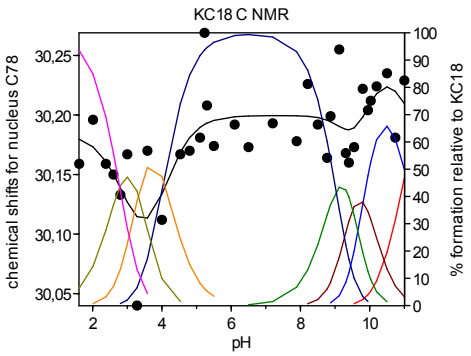

KC18 proton chemical shifts
chemical shifts for nucleus H3
% formation relative to KC18
pH

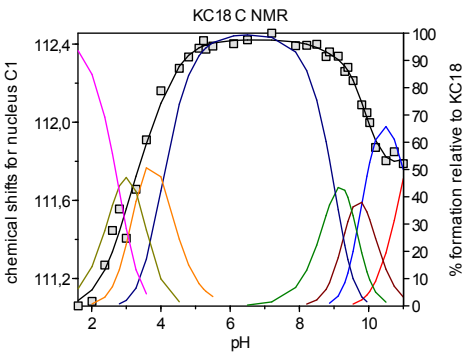

KC18 proton chemical shifts
chemical shifts for nucleus H4
% formation relative to KC18
pH

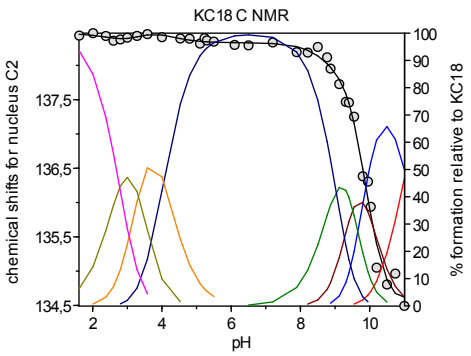

KC18 proton chemical shifts
chemical shifts for nucleus H5
% formation relative to KC18
pH


KC18 proton chemical shifts
chemical shifts for nucleus H6
% formation relative to KC18
pH


KC18 proton chemical shifts
chemical shifts for nucleus H78
% formation relative to KC18
pH


KC18 C NMR
chemical shifts for nucleus C78
% formation relative to KC18
pH


KC18 C NMR
chemical shifts for nucleus C1
% formation relative to KC18
pH


KC18 C NMR
chemical shifts for nucleus C2
% formation relative to KC18
pH

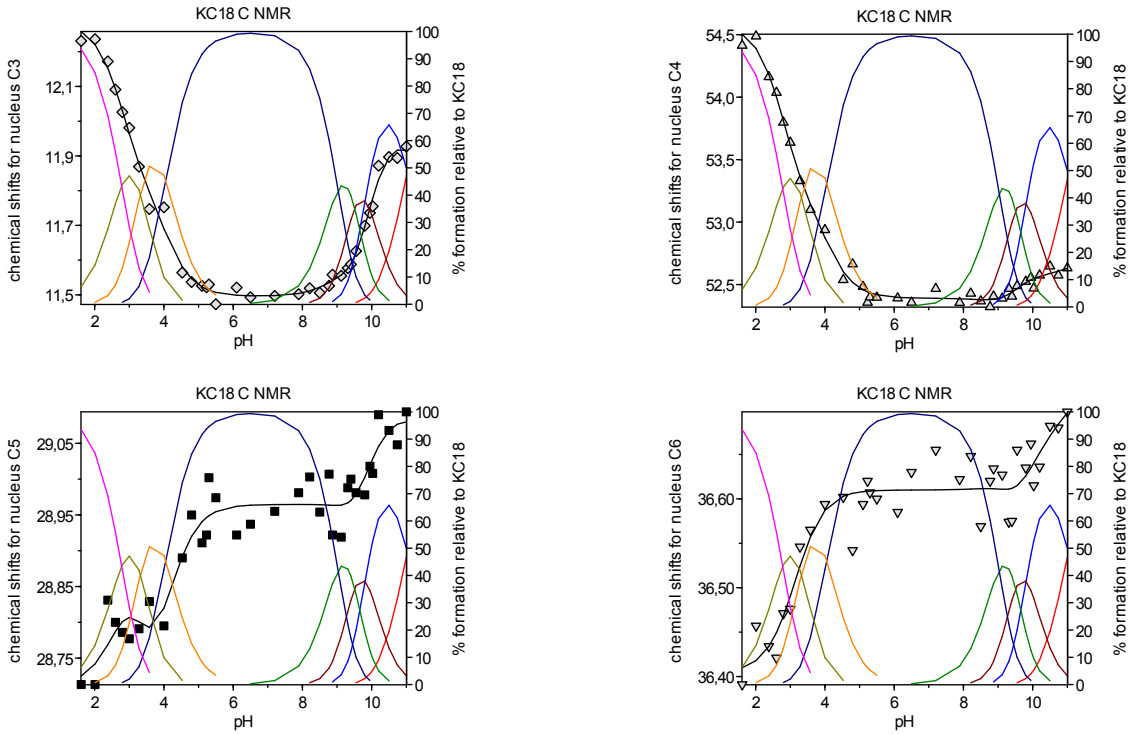


Figure 5S. Trend of chemical shifts of KC18 *vs* pH, overlapping speciation plots (HypNMR).

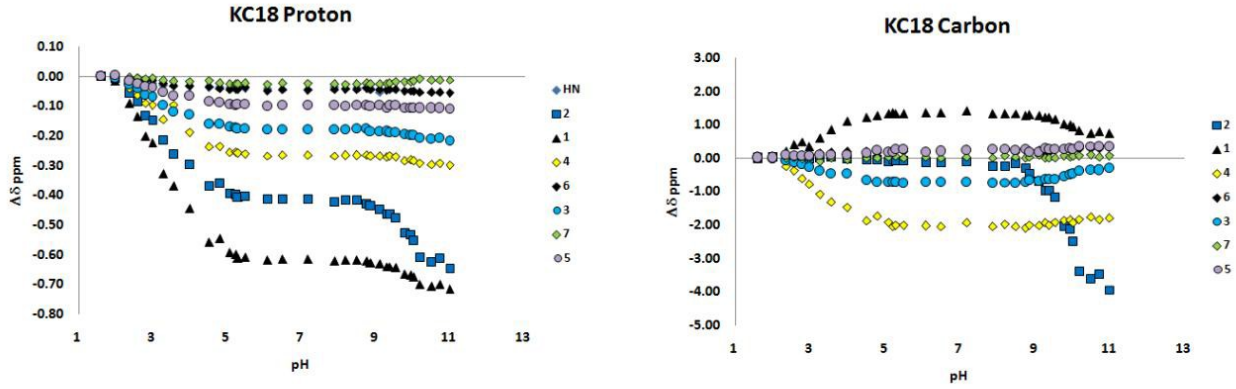


Figure 6S. Trend of ^{1}H (left) and ^{13}C (right) chemical shifts *vs* pH for KC18 ligand calculated using the formula $\Delta\delta = \delta_{pHi} - \delta_{pH0}$ ppm. δ_{pH0} is the value of the proton or carbon chemical shift at the first value of pH whereas δ_{pHi} are the subsequent values at the following pH's.

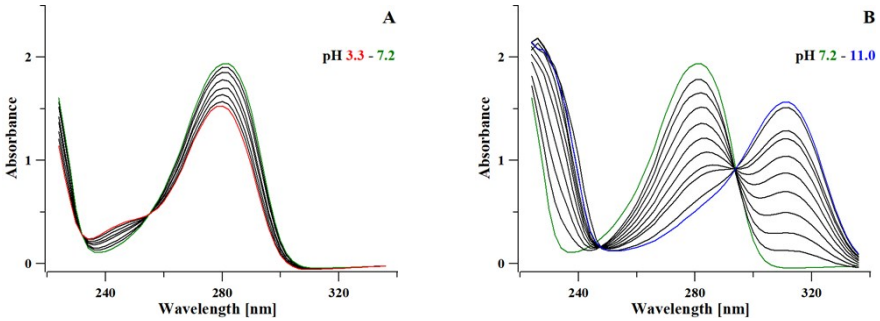


Figure 7S. Representative spectra (0.2 cm optical path) collected during the titration of KC21 ligand 10^{-3} M with NaOH 0.1 M (A) from pH 3.3 to 7.2; (B) from pH 7.2 to 11.0

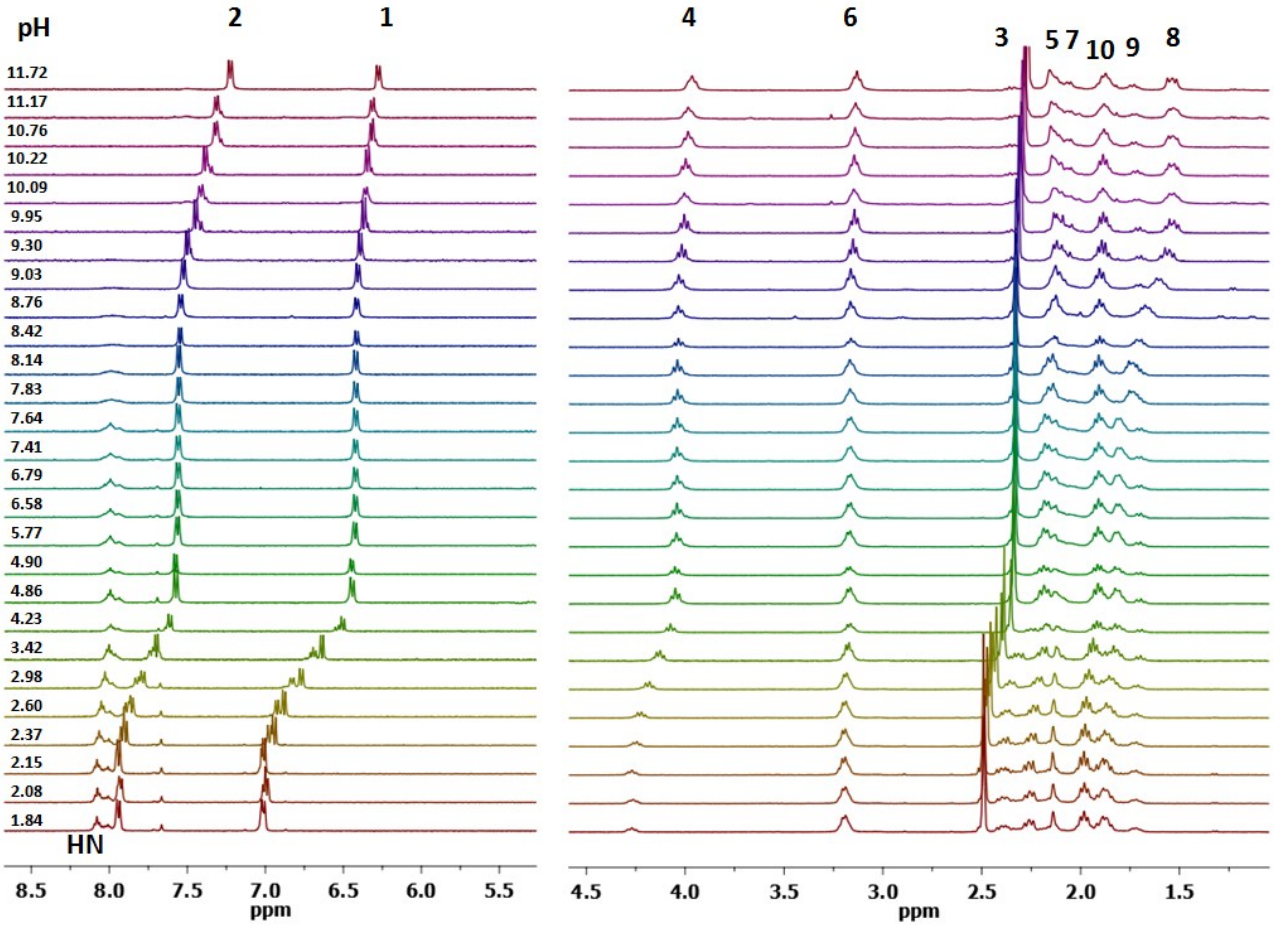
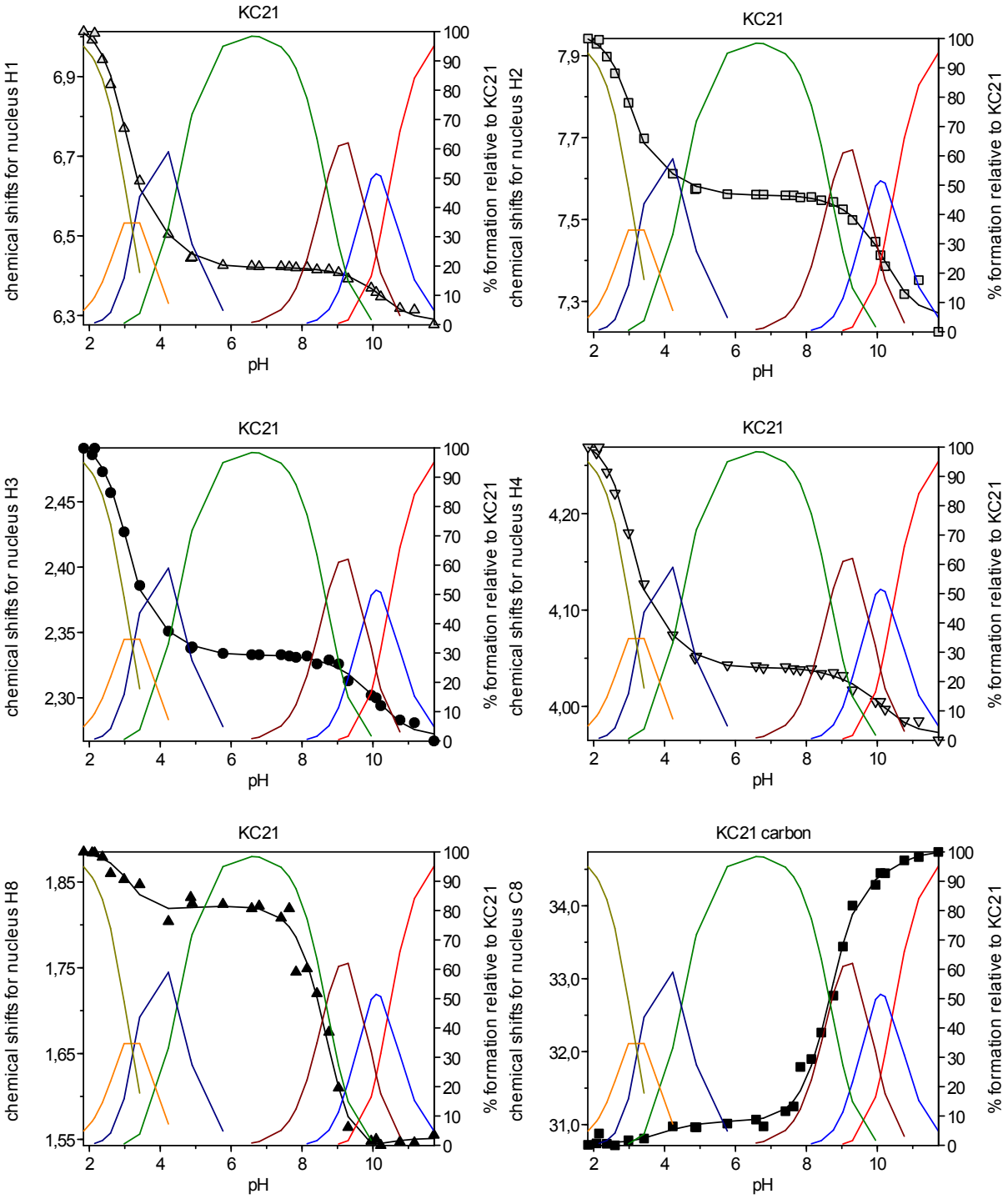


Figure 8S. ^{1}H NMR spectra of KC21 ligand as a function of pH.


KC21
chemical shifts for nucleus H1
% formation relative to KC21
pH
KC21
chemical shifts for nucleus H2
% formation relative to KC21
pH
KC21
chemical shifts for nucleus H3
% formation relative to KC21
pH
KC21
chemical shifts for nucleus H4
% formation relative to KC21
pH
KC21
chemical shifts for nucleus H8
% formation relative to KC21
pH
KC21 carbon
chemical shifts for nucleus C8
% formation relative to KC21
pH

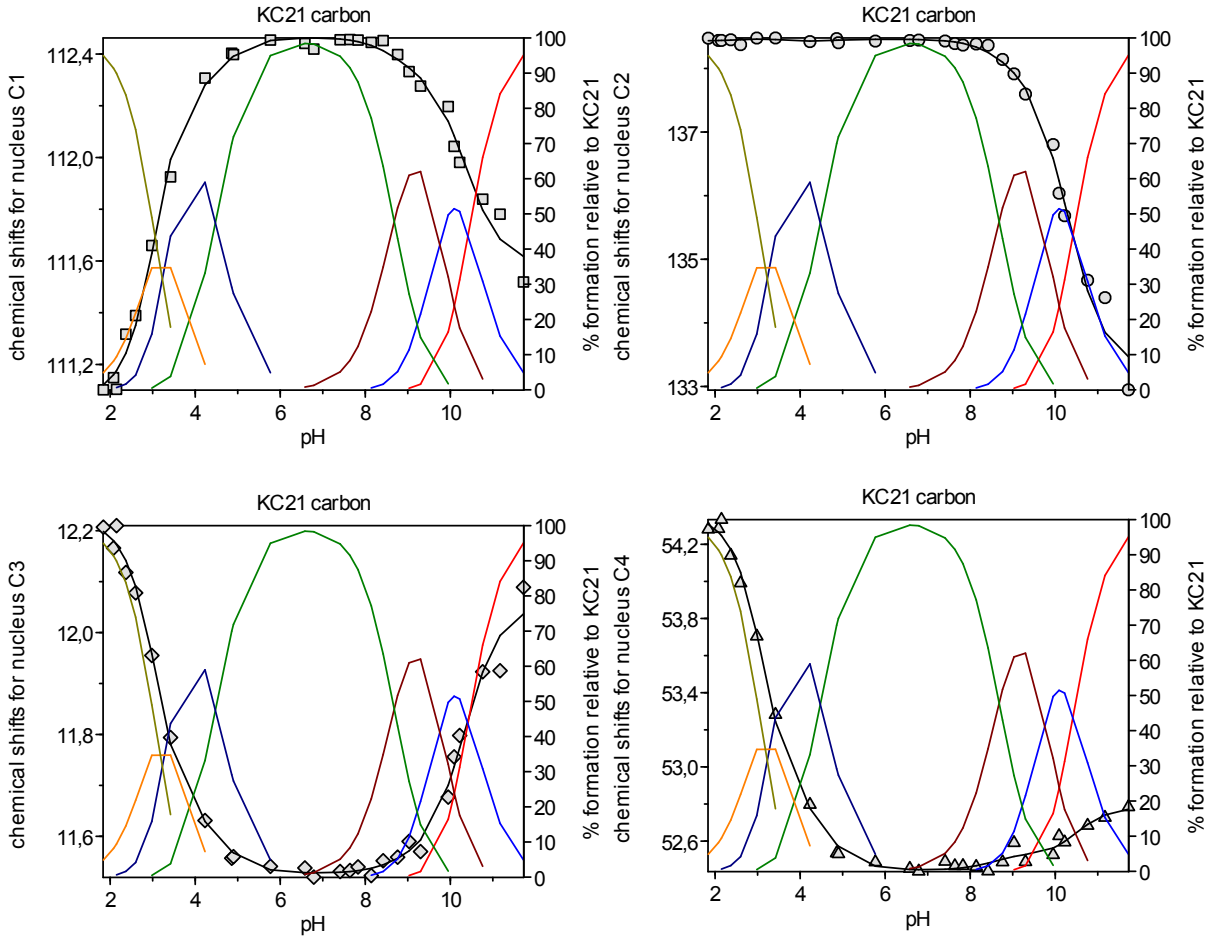


Figure 9S. Trend of chemical shifts of KC21 *vs* pH, overlapping speciation plots (HypNMR).

Figure 10S. Trend of ^{1}H (left) and ^{13}C (right) chemical shifts *vs* pH for KC21 ligand calculated using the formula $\Delta\delta = \delta_{pHi} - \delta_{pH0}$ ppm; where δ_{pH0} is the value of the proton or carbon chemical shift at the first value of pH whereas δ_{pHi} are the subsequent values at the following pH's.

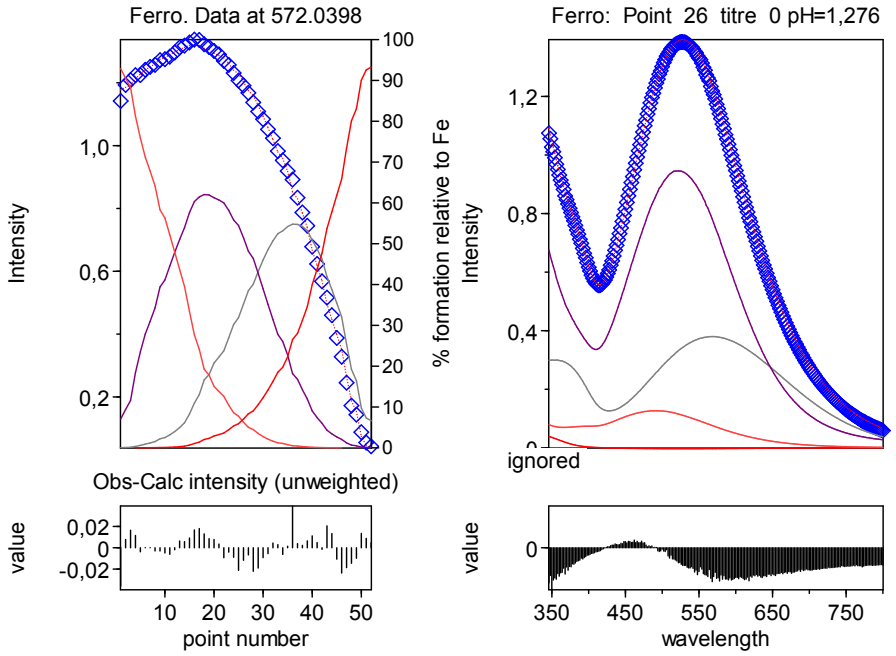


Fig. 11S. Representative HypSpec screenshot from the spectrophotometric titration of the system Fe^{3+}-KC18.

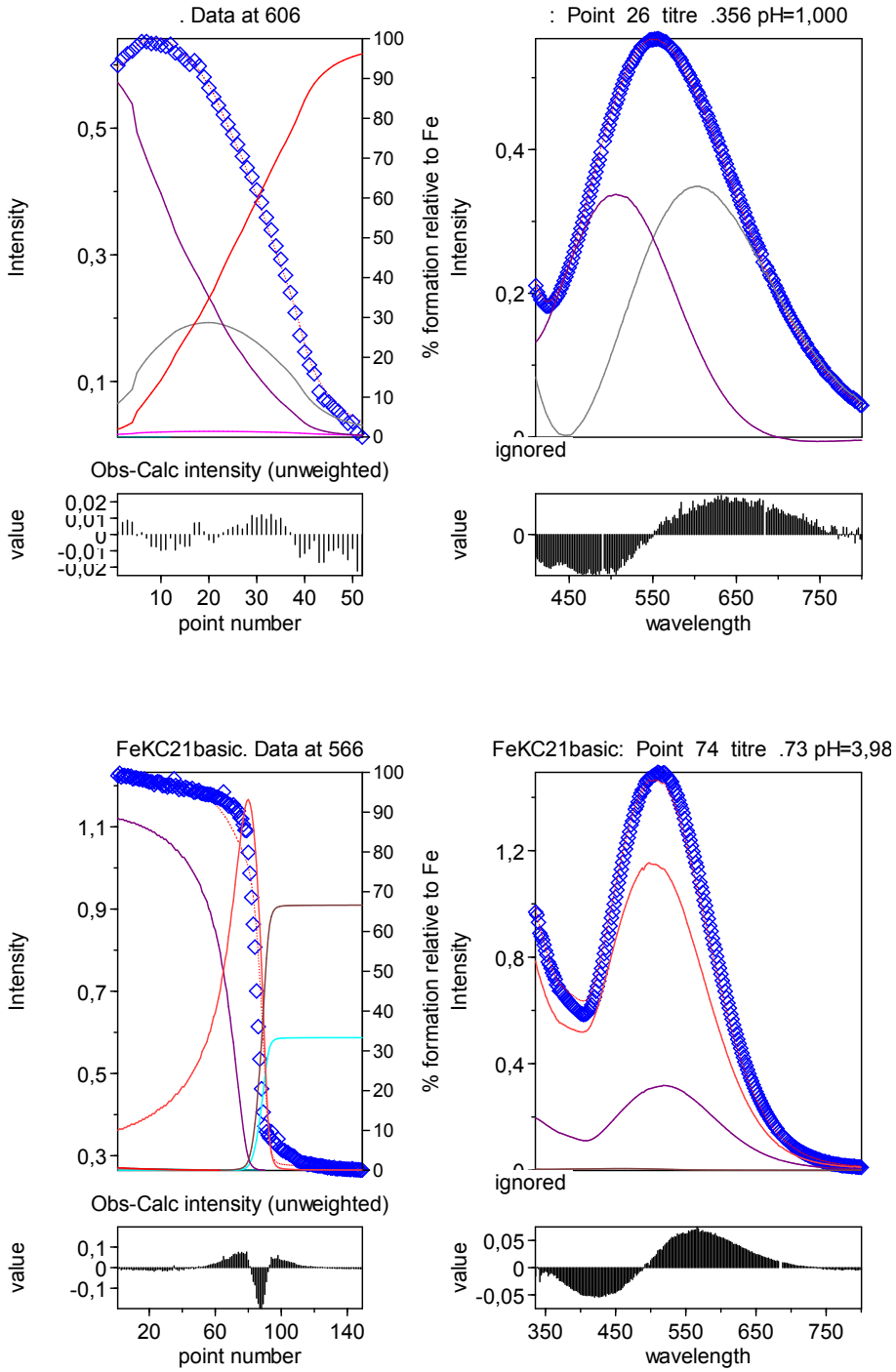


Fig. 12S. Representative HypSpec screenshots from the spectrophotometric titrations of the system Fe^{3+}-KC21.

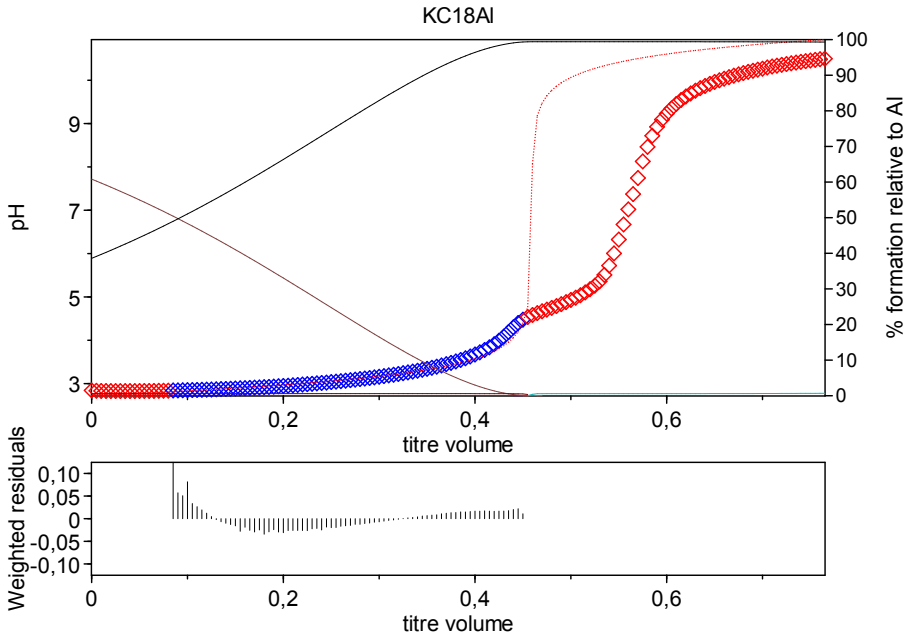


Figure 13S. Potentiometric titration of the system KC18-Al^{3+} (HyperQuad screenshot)

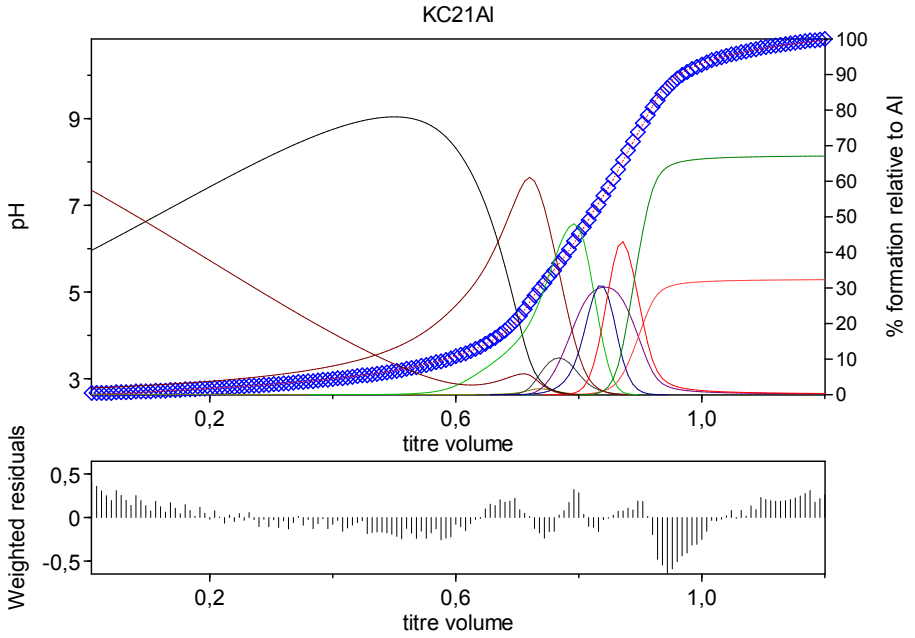


Figure 14S. Potentiometric titration of the system KC21-Al^{3+} (HyperQuad screenshot)

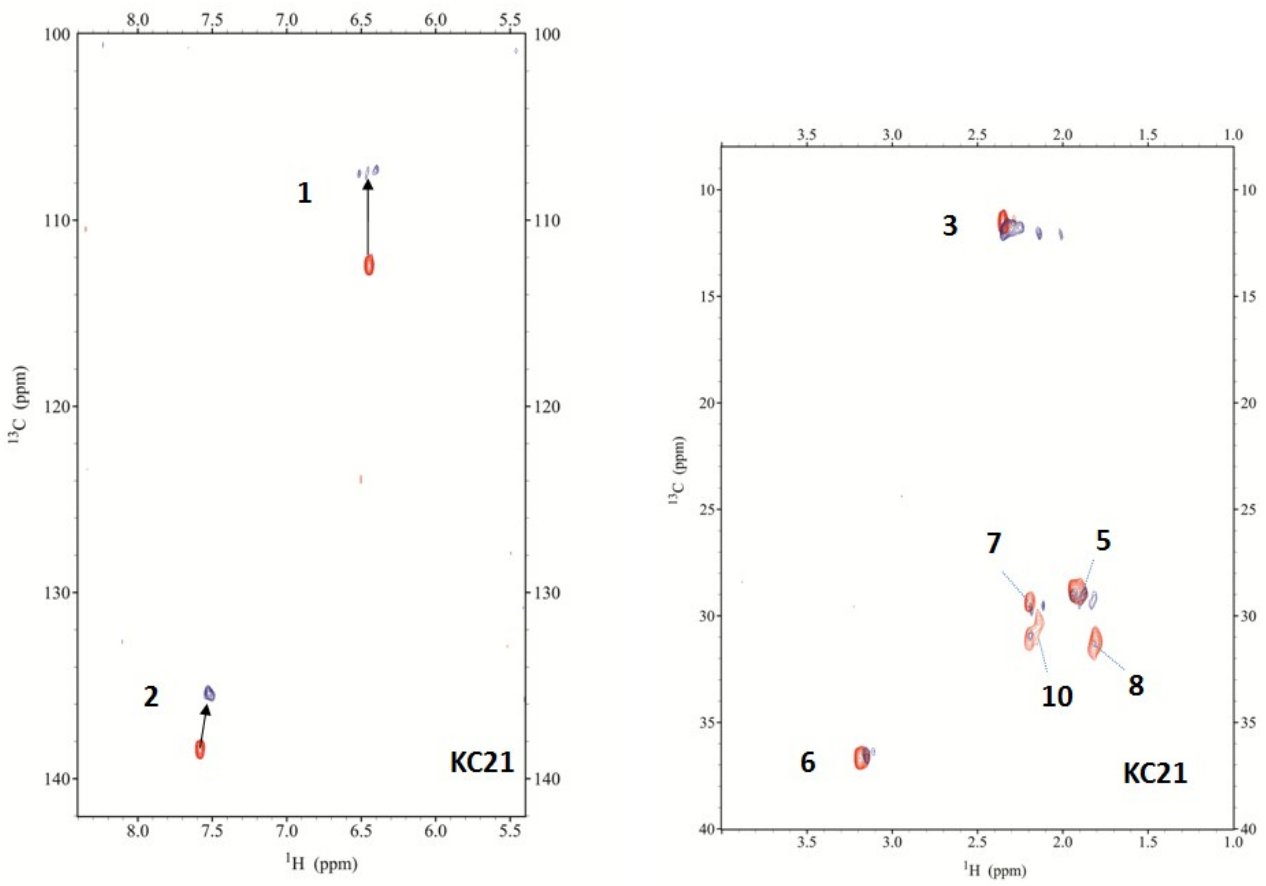


Fig. 15S. Aromatic (left) and aliphatic (right) region of ^{1}H-^{13}C HSQC spectra for KC21:Al^{3+} system at 1:1 molar ratio at pH 7.5.

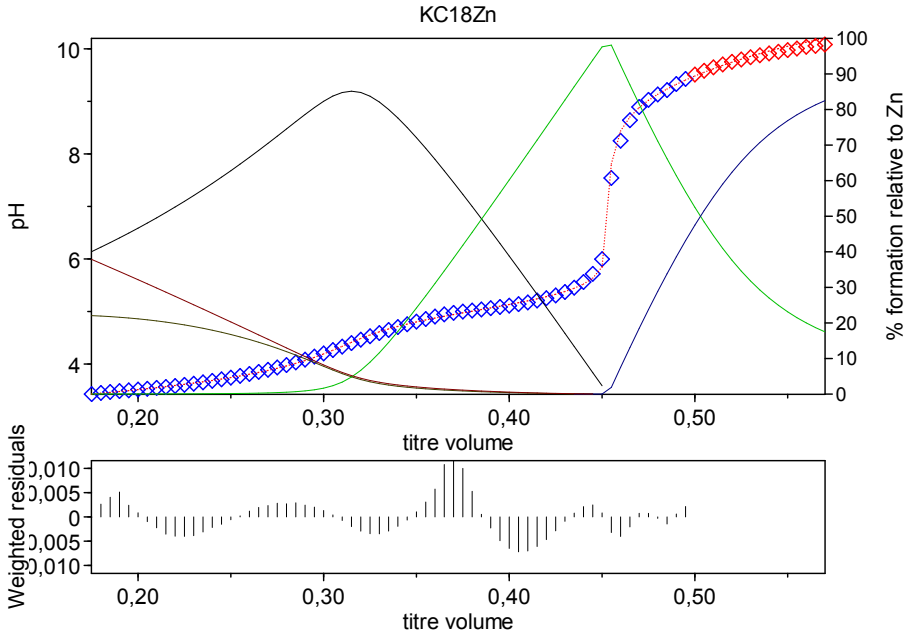


Fig. 16S. Potentiometric titration of the system KC18-Zn^{2+} (HyperQuad screenshot)

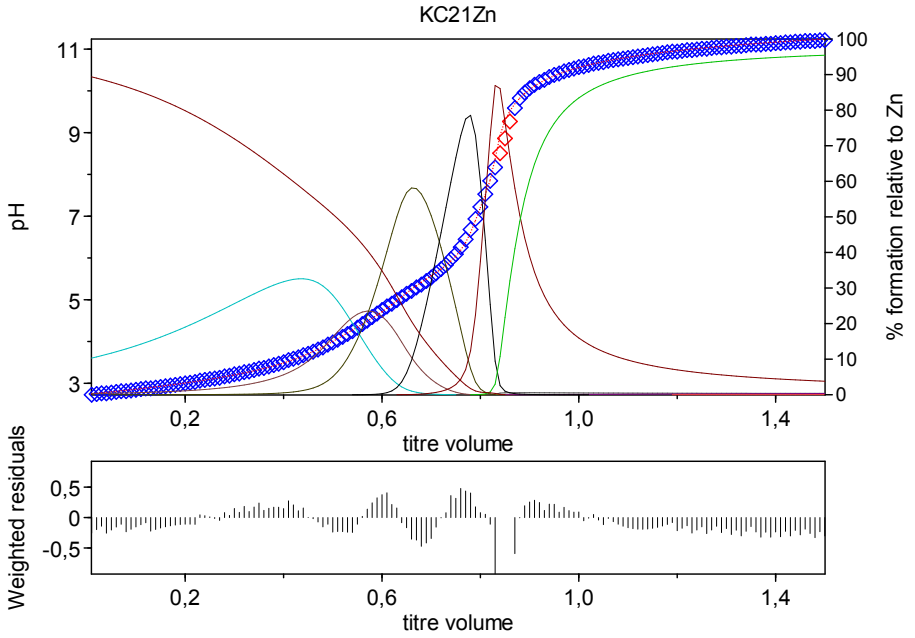


Fig. 17S. Potentiometric titration of the system KC21-Zn^{2+} (HyperQuad screenshot)

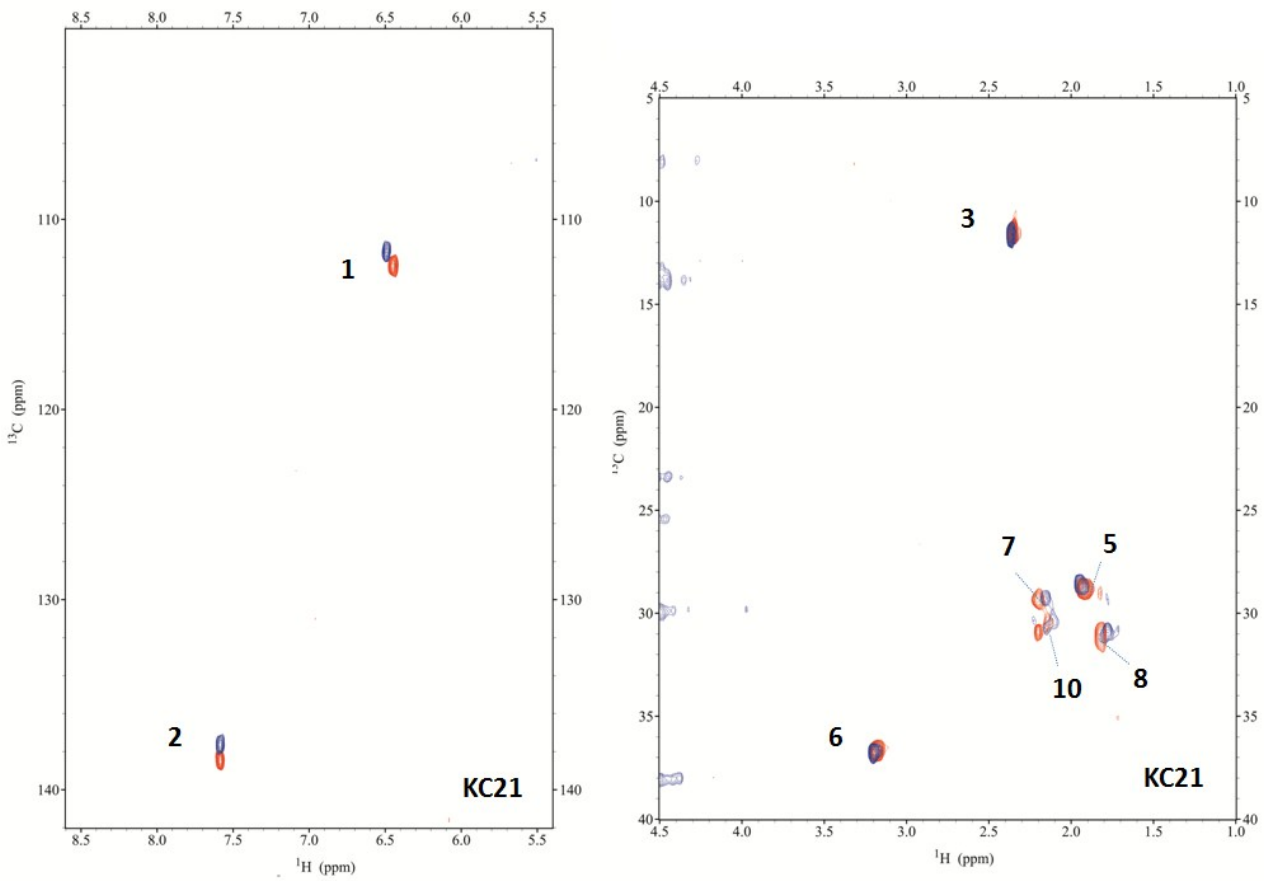


Figure 18S. Aromatic (left) and aliphatic (right) region of 1H-^{13}C HSQC spectra for KC21:Zn^{2+} system at 1:1 molar ratio at pH 5.8.

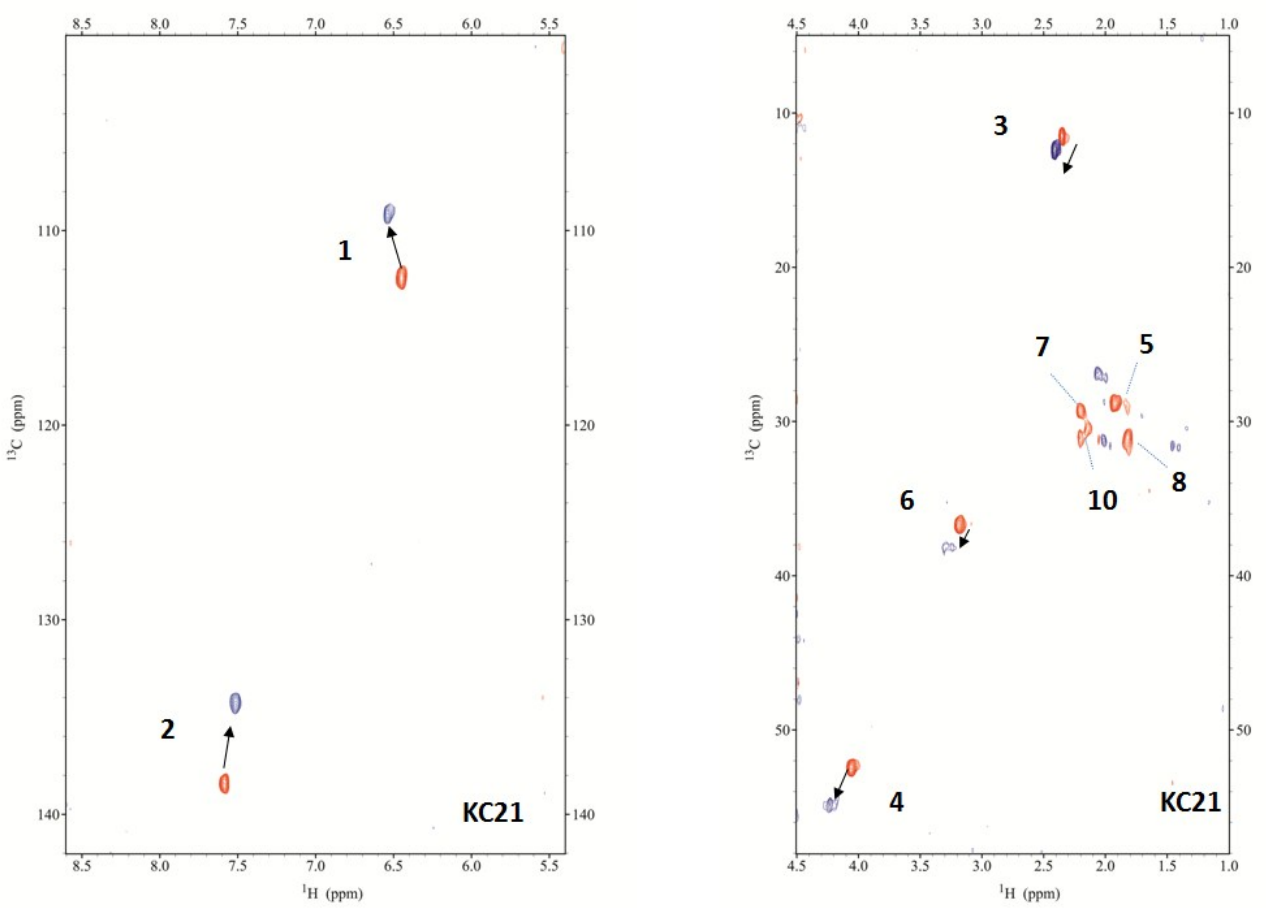


Figure 19S. Aromatic (left) and aliphatic (right) region of ^{1}H-^{13}C HSQC spectra for KC21:Zn^{2+} system at 1:1 molar ratio at pH 7.5.