Electronic Supplementary Material (ESI) for Inorganic Chemistry Frontiers

Towards the Quantification of Ion Binding Using Electrospray Mass Spectrometry

Jennifer S. Mathieson, Geoffrey J. T. Cooper, Leroy Cronin*

University of Glasgow, School of Chemistry, Joseph Black Building, University Avenue, Glasgow, G12 8QQ, U.K.

All reagents were used as received from commercial sources, without further purification. The ligand *cis,cis*-1,3,5-triaminocyclohexane was synthesised according to literature methods.[21]

1H and 13C NMR spectra were recorded at room temperature, unless otherwise stated, on a Bruker DPX-400 spectrometer in d_6-DMSO and $CDCl_3$. Mass spectra were obtained using a Bruker Microtof-Q in ESI mode in methanol and chloroform.

The ^{1}H NMR and MS studies were undertaken in two different solvents. Due to proton exchange in 1H NMR experiments d_6-DMSO had to be used to observe the amide shift, whilst methanol was used in the mass spectrometry studies. d_6-DMSO was the NMR solvent of choice for the experiment with receptor **1**, even though it is a polar aprotic solvent and therefore a good hydrogen-bond acceptor, due to its ability to solvate both the neutral ligand and the negatively charged anion. Methanol was used to solvate receptor **1** and anion in the mass spectrometry experiments as the solvent was evaporated off prior to entering the capillary and so would not interfere with the results.

Synthesis of receptor (**1**) –

Cis-tach (100 mg, 0.77 mmol) was dissolved in MeOH (20 mL) and to this triethylamine (545 mg, 5.39 mmol) was added. Acetic anhydride (236 mg, 2.31 mmol) was then added and the reaction refluxed for 24 hrs. The resulting solution was then concentrated in vacuo to give a white solid. The excess triethylamine was then removed by redissolving the solid in water and then again concentrating in vacuo to give the final product. ^{1}H NMR (d_6-DMSO): δ/ppm 1.02 (m, 3H), 1.78 (m, 9H), 1.93 (m, 3H), 3.58 (m, 3H), 7.92 (d, NH); ^{13}C NMR (D_2O): δ/ppm 23.2 (CH_3), 36.3 (CH_2), 45.3 (CH), 181.5 (C=O); IR (Golden Gate) *v* /cm-1 3410(w), 3279(m), 3063(w), 2939(w), 2854(w), 1635(m), 1597(m), 1543(s), 1373(s), 1296(m), 1172(w), 1134(w), 1064(w), 1018(w), 972(w), 925(w), 802(w), 709(s), 671(s), 640(s). ESI-MS (-ve) *m/z* 254 [M-H]

MS parameters –

The experiments were carried out at 30°C at concentrations of 10^{-5} mol L^{-1} in methanol using a Bruker MicrOTOF-Q instrument. The calibration solution used was Agilent ESI-L low concentration tuning mix solution, Part No. G1969-85000, enabling calibration between approximately 50 m/z and 2000 m/z. Samples were dissolved in CH_3OH and introduced into the MS at a dry gas temperature of 30 °C.

For **1** reacted with KCl/ KBr/ KI -

The ion polarity for all MS scans recorded was negative, with the voltage of the capillary tip set at 4500 V, end plate offset at -500 V, funnel 1 RF at 400 Vpp and funnel 2 RF at 400 Vpp, hexapole RF at 400 Vpp, ion energy 5 eV, collision energy at 10 eV, collision cell RF at 200 Vpp, transfer time at 100.0 µs and the pre-pulse storage time at 10.0 µs. Each spectrum was collected for 2 mins.

For 12-crown-4 reacted with Li and Na –

The ion polarity for all MS scans recorded was negative, with the voltage of the capillary tip set at 4000 V, end plate offset at -500 V, funnel 1 RF at 200 Vpp and funnel 2 RF at 400 Vpp, hexapole RF at 400 Vpp, ion energy 5 eV, collision energy at 10 eV, collision cell RF at 200 Vpp, transfer time at 100.0 µs and the pre-pulse storage time at 10.0 µs. Each spectrum was collected for 2 mins.

For 2,2'-bipyridine reacted with $Co(NO_3)_2.6H_2O$ -

The ion polarity for all MS scans recorded was negative, with the voltage of the capillary tip set at 4500 V, end plate offset at -500 V, funnel 1 RF at 300 Vpp and funnel 2 RF at 400 Vpp, hexapole RF at 400 Vpp, ion energy 5 eV, collision energy at 5 eV, collision cell RF at 100 Vpp, transfer time at 100.0 µs and the pre-pulse storage time at 10.0 µs. Each spectrum was collected for 2 mins.

Job plot analysis of **1** reacted with KCl/ KBr/ KI using ESI-MS–

Standard solutions (0.02 M) of **1** and the salt (KCl/KBr/KI) were made up in methanol and 18-crown-6 (2 g, 7.56 mmol) dissolved in each solution to remove any unwanted Na still present. Varying ratios of each solution were then taken and mixed together (with the overall concentration remaining the same) e.g. 1 mL of **1** solution mixed with 9 mL of the salt solution, 2 mL of **1** solution mixed with 2 mL of the salt solution, 3mL of **1** solution mixed with 7 mL of the salt solution….9mL of **1** solution mixed with 1 mL of the salt solution. ESI-MS of the reaction mixtures was then observed and the intensity of the corresponding peak recorded. The recorded change in intensity multiplied by the mole fraction ([Host]/[Host]+[Guest]) was then plotted against mole fraction to give a maximum value at 0.5 mole fraction and therefore a stoichiometry of 1:1 (**1**:A). ESI-MS (-ve) **1**:Cl *m/z* 290.1, **1**:Br *m/z* 334.1, **1**:I *m/z* 382.1.

Job plot analysis of **1** reacted with KCl/ KBr/ KI using ^{1}H NMR -

Standard solutions (0.02 M) of **1** and the salt (KCl/KBr/KI) were made up in d_6-DMSO. Varying ratios of each solution were then taken and mixed together (with the overall concentration remaining the same) e.g. 1 mL of **1** solution mixed with 9 mL of the salt solution, 2 mL of **1** solution mixed with 2 mL of the salt solution, 3mL of **1** solution mixed with 7 mL of the salt solution….9mL of **1** solution mixed with 1 mL of the salt solution. ^{1}H NMR experiments were carried out for each of the mixtures and the free receptor. A plot of Δδ (where Δδ = the shift of the receptor-(shift of the receptor + guest) multiplied by the mole fraction was then plotted against mole fraction (where the mole fraction is [Host]/[Host]+[Guest]).

Job plot analysis of **2** using ESI-MS–

Standard solutions (0.02 M) of 2,2′-bipyridine and $Co(NO_3)_2.6H_2O$ were made up in methanol. Varying ratios of each solution were then taken and mixed together (with the overall concentration remaining the same) e.g. 1 mL of the 2,2′-bipyridine solution mixed with 9 mL of the salt solution, 2 mL of the 2,2′-bipyridine solution mixed with 2 mL of the salt solution, 3mL of the 2,2′-bipyridine solution mixed with 7 mL of the salt solution….9mL of the 2,2′-bipyridine solution mixed with 1 mL of the salt solution. ESI-MS of the reaction mixtures was then observed and the intensity of the corresponding peak recorded. The recorded change in intensity multiplied by the mole fraction ([Host]/[Host]+[Guest]) was then plotted against mole fraction to give a maximum value at 0.67 mole fraction and therefore a stoichiometry of 2:1 (Receptor: Metal). ESI-MS (+ve) $[Co(C_{10}H_8N_2)_2(NO_3)]^+$ *m/z* 433.1.

Job plot analysis of 12-crown-4 reacted with Li using ESI-MS–

Standard solutions (0.02 M) of 12-crown-4 and LiCl were made up in chloroform. Varying ratios of each solution were then taken and mixed together (with the overall concentration remaining the same) e.g. 1 mL of 12-crown-4 solution mixed with 9 mL of the salt solution, 2 mL of 12-crown-4 solution mixed with 2 mL of the salt solution, 3mL of 12-crown-4 solution mixed with 7 mL of the salt solution….9mL of 12-crown-4 solution mixed with 1 mL of the salt solution. ESI-MS of the reaction mixtures was then observed and the intensity of the corresponding peak recorded. The recorded change in intensity multiplied by the mole fraction ([Host]/[Host]+[Guest]) was then plotted against mole fraction to give a maximum value at 0.5 mole fraction and therefore a stoichiometry of 1:1 (12-crown-4:Li). ESI-MS (-ve) $[C_8H_{16}O_4Li]^+$ *m/z* 183.1.

Job plot analysis of 12-crown-4 reacted with Li using ^{1}H NMR -

Standard solutions (0.02 M) of 12-crown-4 and LiCl were made up in $CDCl_3$. Varying ratios of each solution were then taken and mixed together (with the overall concentration remaining the same) e.g. 1 mL of 12-crown-4 solution mixed with 9 mL of the salt solution, 2 mL of 12-crown-4 solution mixed with 2 mL of the salt solution, 3mL of 12-crown-4 solution mixed with 7 mL of the salt solution….9mL of 12-crown-4 solution mixed with 1 mL of the salt solution. ^{1}H NMR experiments were carried out for each of the mixtures and the free receptor. A plot of Δδ (where Δδ = the shift of the receptor-(shift of the receptor + guest) multiplied by the mole fraction was then plotted against mole fraction (where the mole fraction is [Host]/[Host]+[Guest]).

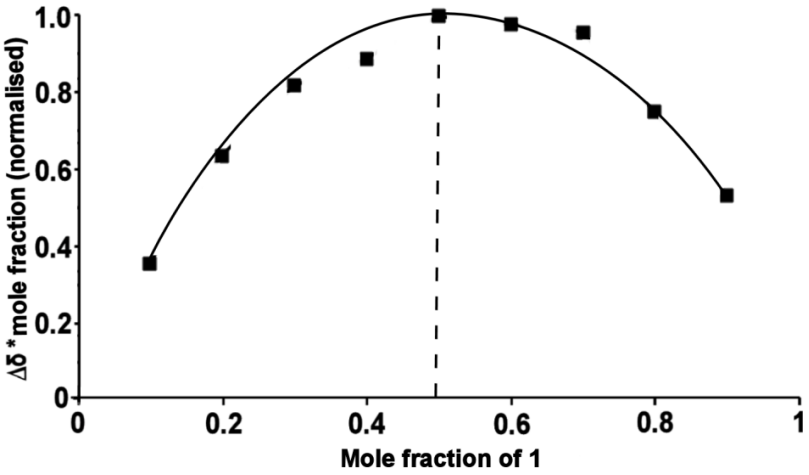
Job plot analysis of 12-crown-4 reacted with Na using ESI-MS–

Standard solutions (0.02 M) of 12-crown-4 and NaCl were made up in chloroform. Varying ratios of each solution were then taken and mixed together (with the overall concentration remaining the same) e.g. 1 mL of 12-crown-4 solution mixed with 9 mL of the salt solution, 2 mL of 12-crown-4 solution mixed with 2 mL of the salt solution, 3mL of 12-crown-4 solution mixed with 7 mL of the salt solution….9mL of 12-crown-4 solution mixed with 1 mL of the salt solution. ESI-MS of the reaction mixtures was then observed and the intensity of the corresponding peak recorded. The recorded change in intensity multiplied by the mole fraction ([Host]/[Host]+[Guest]) was then plotted against mole fraction to give a maximum value at 0.5 mole fraction and therefore a stoichiometry of 1:1 (12-crown-4:Li). ESI-MS (-ve) $[C_8H_{16}O_4Li]^+$ *m/z* 199.1.

Job plot analysis of 12-crown-4 reacted with Na using ^{1}H NMR -

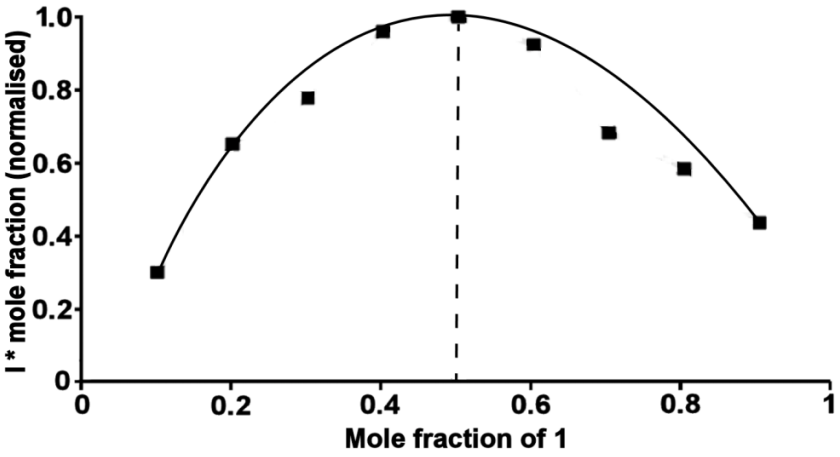
Standard solutions (0.02 M) of 12-crown-4 and NaCl were made up in $CDCl_3$. Varying ratios of each solution were then taken and mixed together (with the overall concentration remaining the same) e.g. 1 mL of 12-crown-4 solution mixed with 9 mL of the salt solution, 2 mL of 12-crown-4 solution mixed with 2 mL of the salt solution, 3mL of 12-crown-4 solution mixed with 7 mL of the salt solution….9mL of 12-crown-4 solution mixed with 1 mL of the salt solution. ^{1}H NMR experiments were carried out for each of the mixtures and the free receptor. A plot of Δδ (where Δδ = the shift of the

receptor-(shift of the receptor + guest) multiplied by the mole fraction was then plotted against mole fraction (where the mole fraction is [Host]/[Host]+[Guest]).



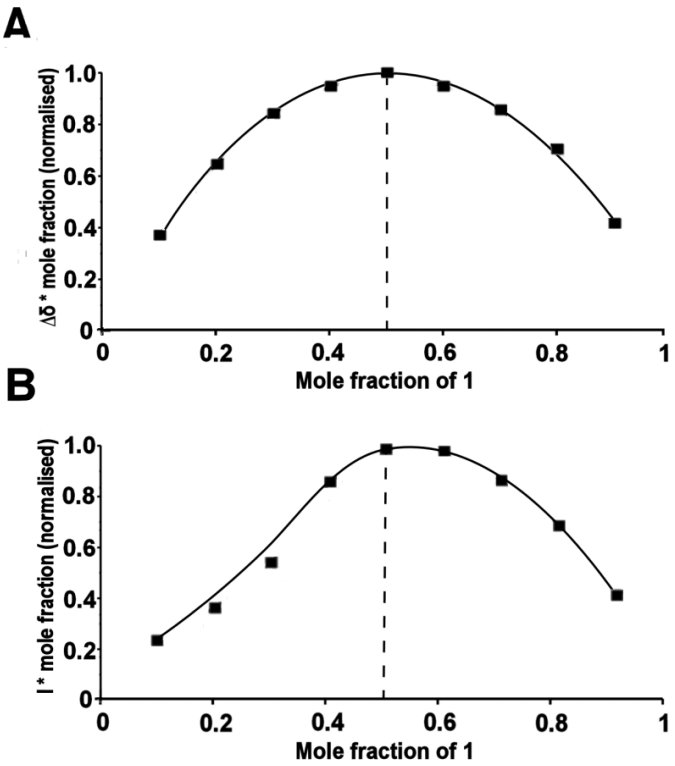
Mole fraction	Shift/ppm	Δδ	Δδ* mole fraction
receptor	7.89785	-	
0.1	7.87590	0.02195	0.002195
0.2	7.87790	0.01995	0.003990
0.3	7.88065	0.01720	0.00516
0.4	7.88385	0.01400	0.005600
0.5	7.88520	0.01265	0.006325
0.6	7.88755	0.01030	0.006180
0.7	7.88920	0.00865	0.006055
0.8	7.89195	0.00590	0.004720
0.9	7.89415	0.00370	0.003330

Figure S1. ^{1}H NMR (d_6-DMSO) job plot of **1** + Cl showing a 1:1 (R:Cl^-) stoichiometry and tabulated NMR data of **1** + KCl showing the actual shift (ppm) of the NH peak, Δδ (where Δδ = the shift of the receptor-(shift of the receptor + guest)) and Δδ multiplied by mole fraction.



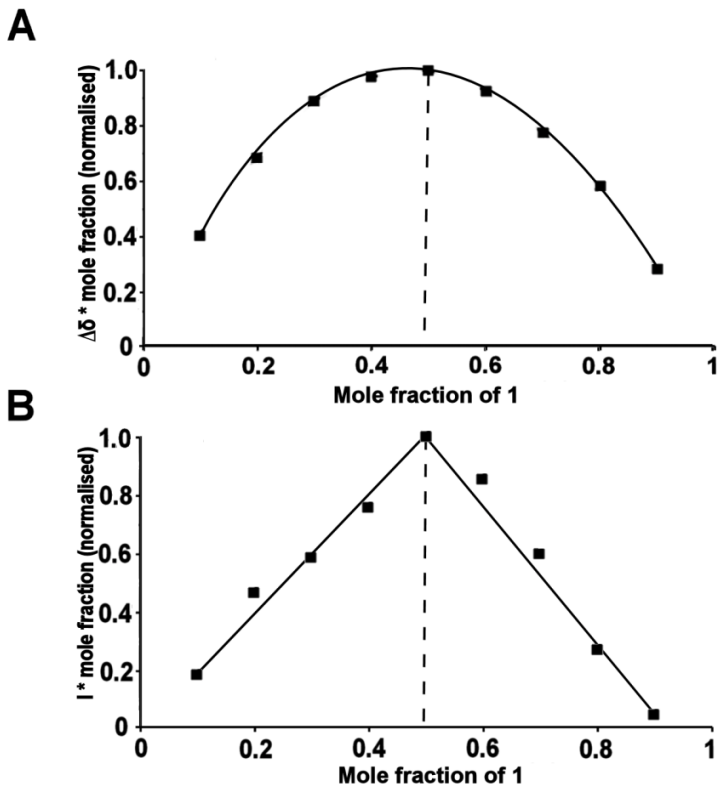
Mole fraction	Intensity	I * mole fraction
0.1	36721	3672
0.2	40305	8061
0.3	32062	9619
0.4	29719	11888
0.5	24742	12371
0.6	19025	11415
0.7	12064	8445
0.8	9020	7216
0.9	5983	5385

Figure S2. MS (CH_3OH) job plot of **1** + Cl showing a 1:1 (**1**:Cl^-) stoichiometry and tabulated MS data of **1** + KCl showing the intensity of the $[C_6H_{12}N_3(C_2H_3O)_3Cl]^-$ (290.1 *m/z*) peak and intensity multiplied by mole fraction.



Mole fraction	Shift/ppm	Δδ	Δδ* mole fraction	Intensity	I * mole fraction
receptor	7.89665	-	-	-	-
0.1	7.82770	0.06895	0.006895	36699	3670
0.2	7.83640	0.06025	0.012050	28179	5636
0.3	7.84425	0.05240	0.015720	27950	8385
0.4	7.85250	0.04415	0.017660	33559	13424
0.5	7.85935	0.03730	0.018650	31006	15503
0.6	7.86715	0.02950	0.017700	25583	15350
0.7	7.87385	0.02280	0.015960	19380	13566
0.8	7.88025	0.01640	0.013120	13445	10756
0.9	7.88800	0.00865	0.007850	7242	6518

Figure S3. A. ^{1}H NMR (d_6-DMSO) job plot of **1** + Br showing a 1:1 (**1**:Br^-) stoichiometry; B. MS (methanol) job plot of **1** + Br showing a 1:1 (**1**:Br^-) stoichiometry; tabulated data from NMR and MS experiments.



Mole fraction	Shift/ppm	Δδ	Δδ* mole fraction	Intensity	I * mole fraction
receptor	7.88545	-	-	-	-
0.1	7.82055	0.06490	0.006490	3557	356
0.2	7.83020	0.05525	0.011050	4446	890
0.3	7.83740	0.04805	0.014415	3723	1117
0.4	7.84590	0.03955	0.015820	3599	1440
0.5	7.85305	0.03240	0.016200	3810	1905
0.6	7.86045	0.02500	0.015000	2717	1630
0.7	7.86755	0.01790	0.012530	1636	1145
0.8	7.87370	0.01175	0.009400	652	522
0.9	7.88045	0.00500	0.004500	98	88

Figure S4. A. ^{1}H NMR (d_6-DMSO) job plot of **1** + I showing a 1:1 (**1**:I$^-$) stoichiometry; B. MS (methanol) job plot of **1** + I showing a 1:1 (**1**:I$^-$) stoichiometry; tabulated data from NMR and MS experiments.

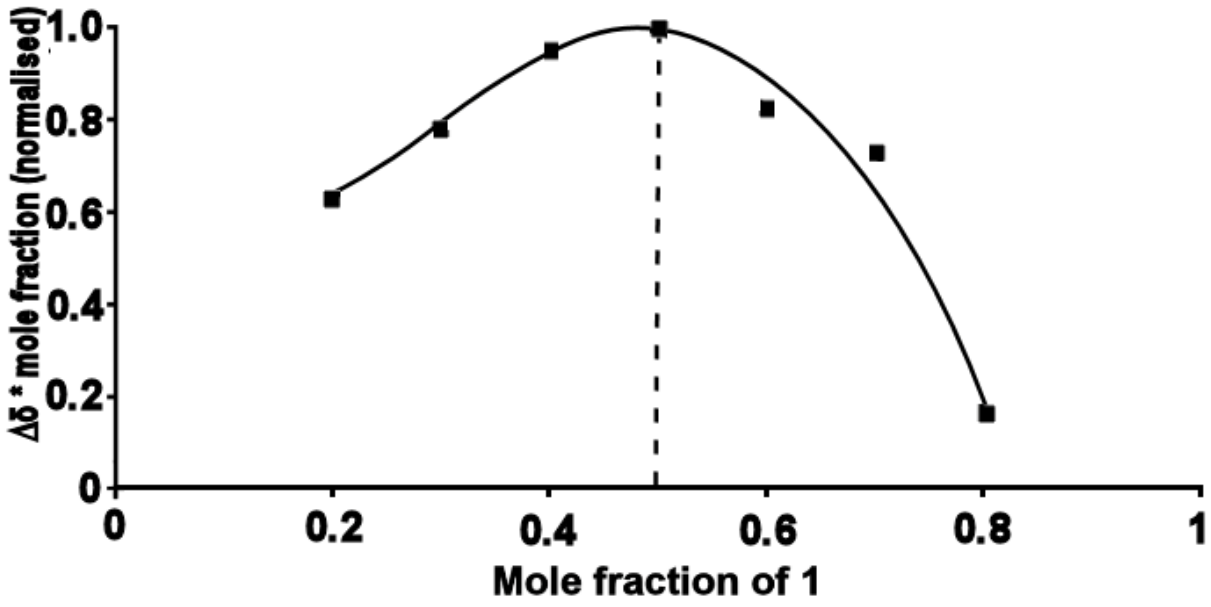
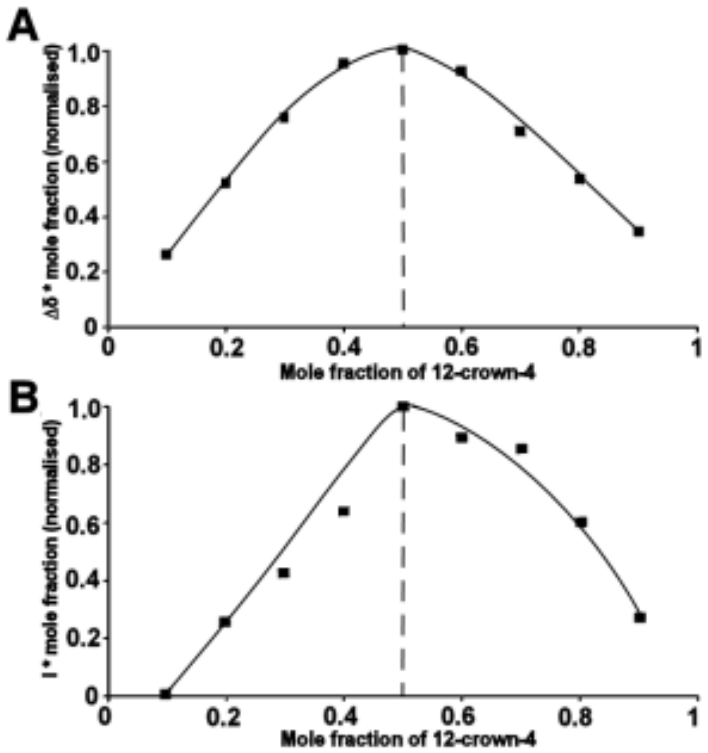
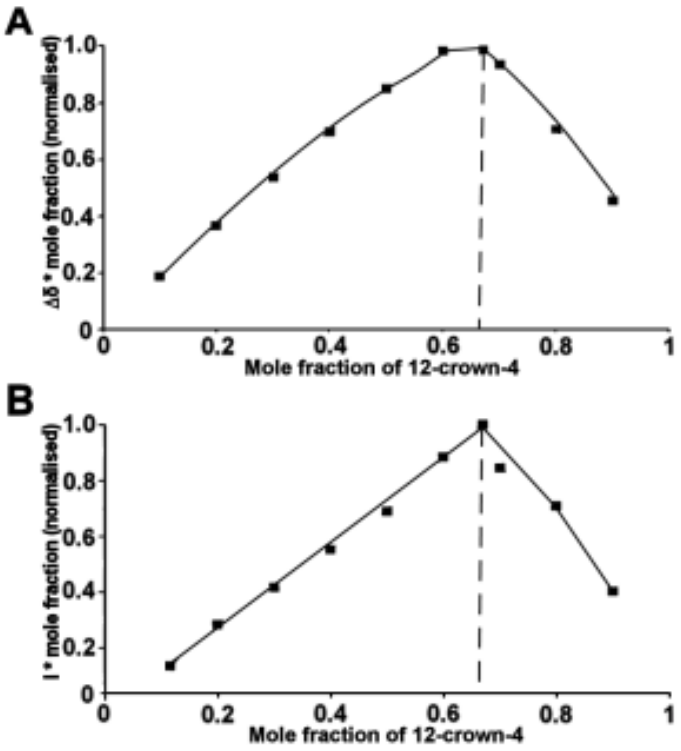


Figure S5. A. ^{1}H NMR (d_3-CD_3OH) job plot of **1** + KCl showing a 1:1 (**1**:I) stoichiometry



Mole fraction	Shift/ppm	Δδ	Δδ* mole fraction	Intensity	I * mole fraction
receptor	3.6180	-	-	-	-
0.1	3.7697	0.1517	0.01517	5695	570
0.2	3.7678	0.1498	0.02996	65000	13000
0.3	3.7625	0.1445	0.04335	71339	21402
0.4	3.7544	0.1364	0.05456	80000	32000
0.5	3.7325	0.1145	0.05725	99998	49999
0.6	3.7061	0.0881	0.05286	74339	44603
0.7	3.6758	0.0578	0.04046	60961	42673
0.8	3.6564	0.0384	0.03072	37602	30082
0.9	3.6401	0.0221	0.01989	15225	13703

Figure S6. A. ^{1}H NMR ($CDCl_3$) job plot of 12-crown-4 + Li showing a 1:1 (12-crown-4:Li) stoichiometry; B. MS ($CHCl_3$) job plot of 12-crown-4 + Li showing a 1:1 (12-crown-4:Li) stoichiometry; tabulated data from NMR and MS experiments.



Mole fraction	Shift/ppm	Δδ	Δδ* mole fraction	Intensity	I * mole fraction
receptor	3.6148	-	-	-	-
0.1	3.6618	0.0470	0.00470	25249	2525
0.2	3.6607	0.0459	0.00918	42949	8590
0.3	3.6595	0.0447	0.001341	43869	13161
0.4	3.6583	0.0435	0.01740	44650	17860
0.5	3.6571	0.0423	0.02115	45068	22534
0.6	3.6556	0.0408	0.02448	48598	29159
0.67	3.6515	0.0367	0.02458	49580	33219
0.7	3.6481	0.0333	0.02331	39821	27875
0.8	3.6369	0.0221	0.01768	28944	23155
0.9	3.6274	0.0126	0.01134	14137	12723

Figure S7. A. ^{1}H NMR ($CDCl_3$) job plot of 12-crown-4 + Na showing a 2:1 (12-crown-4:Na) stoichiometry; B. MS ($CHCl_3$) job plot of 12-crown-4 + Na showing a 2:1 (12-crown-4:Na) stoichiometry; tabulated data from NMR and MS experiments.

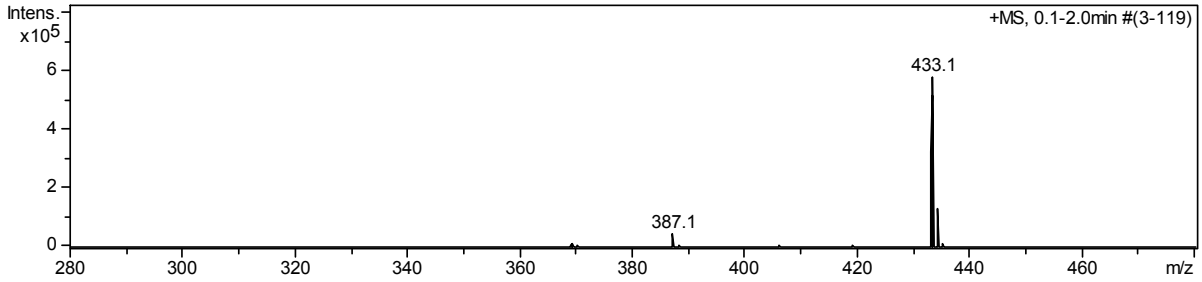


Figure S8. Full MS of $Co(NO3)_2$ in the presence of 2,2'-bipyridine.