Supplementary Material (ESI) for Chemical Science

Structurally-simple lipid bilayer transport agents for chloride and bicarbonate

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Supplementary Information

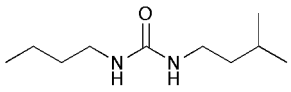
Contents

S1 ***General remarks***

^{1}H NMR (300 MHz) and $^{13}C\{^{1}H\}$ NMR (75 MHz) were determined on a Bruker AV300 spectrometer. Chemical shifts for ^{1}H NMR are reported in parts per million (ppm), calibrated to the solvent peak set. The following abbreviations are used for spin multiplicity: s = singlet, d = doublet, t = triplet, m = multiplet. Chemical shifts for $^{13}C\{^{1}H\}$ NMR are reported in ppm, relative to the central line of a septet at δ = 39.52 ppm for DMSO-d_6. Infrared (IR) spectra were recorded on a Matterson Satellite (ATR). FTIR are reported in wavenumbers (cm^{-1}). HRMS(ES) spectra were recorded using a Bruker Apex III spectrometer and reported as *m/z* (relative intensity). All solvents and starting materials were purchased from commercial sources and used without further purification unless otherwise stated. Dry DCM was obtained by distillation over CaH_2 prior to use. Aniline was distilled prior to use. POPC was supplied by Genzyme. NMR titrations were performed by addition of aliquots of the putative anionic guest as the tetrabutylammonium (TBA) or tetraethylammonium (TEA) salt (0.15 M), in a solution of the receptor (0.01 M) in DMSO-d_6 to 0.01 M solution of the receptor. Chloride concentrations during transport experiments were determined using an Accumet or Cole-Parmer chloride selective electrode.

S2 *Synthetic procedure*

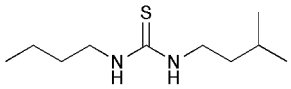
Compound 3[1]



Butylisocyanate (0.44 g, 4.44 mmol) was dissolved in DCM (70 ml) and isopentylamine (0.45 g, 12.2 mmol) was added. The mixture was stirred overnight at room temperature. The solution was washed with 2 x 100 ml water and the organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure to give a solid which was azeotroped with 2 x 50 ml ether to give compound **3** as a fluffy white solid.

Yield: 409 mg (49%); ^{1}H NMR (300 MHz, DMSO-d_6): δ= 5.68 (m, 2H, 2 overlapping NH signals), 2.97 (m, 4H, 2 overlapping CH_2 signals), 1.58 (m, 1H, alkyl CH), 1.29 (m, 6H, 3 overlapping CH_2 signals), 0.87 (m, 9H, 3 overlapping CH_3 signals); ^{13}C NMR (75 MHz, DMSO-d_6): δ= 158.0 (carbonyl C=O), 37.4 (alkyl), 32.2 (alkyl), 25.1 (alkyl), 22.4 (alkyl), 19.5 (alkyl), 13.7 (alkyl); LRMS(ESI+): *m/z* = 209.2 ([M + Na]$^+$); HRMS(ES): [M + Na]$^+$ *m/z*= 209.1630 (calculated), 209.1627 (found); IR (film): ν= 3340 (urea NH stretching), 1630 (carbonyl CO stretching); M_p: 54-55 °C.

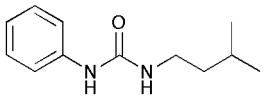
Compound 4



Butyl isothiocyanate (500 mg, 4.34 mmol) was dissolved in 100 ml DCM and *i*-pentylamine (397 mg, 4.56 mmol) was added. The mixture was stirred at room temperature overnight. The solvent was removed under reduced pressure and the oily residue thus obtained was heated to 30 °C under vacuum to remove excess amine. On cooling, this afforded compound **4** as an oily off white solid.

Yield: 434 mg (49%); ^{1}H NMR (300 MHz, $CDCl_3$): δ= 5.80 (br. s, 2H, overlapping NH peaks), 3.41 (br. s, 4H, overlapping CH_2 peaks), 1.53 (complex m, 7H + 8H, 2 x CH_2 + CH + 1/2H_2O), 0.94 (m, 9H, 3 x CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ= 181.9 (thiourea C=S), 43.1 (alkyl), 41.7 (alkyl), 37.7 (alkyl), 30.9 (alkyl), 25.2 (alkyl), 22.4 (alkyl), 19.5 (alkyl), 13.7 (alkyl); LRMS(ESI+): *m/z* = 203.2 ([M+H]$^+$); HRMS(ES): for [M + H]$^+$ *m/z*= 203.1582 (calculated), 203.1582 (found); IR (film): ν= 3250 (thiourea NH stretching); M_p: 52-53.5 °C.

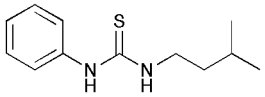
Compound 5[2]



Phenyl isocyanate (200 mg, 1.69 mmol) was dissolved in chloroform (50 ml) and isopentylamine (220 mg, 2.53 mmol) was added. The reaction mixture was stirred overnight at room temperature. The solution was washed with 2 x 100 ml water and the organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure to give a white solid, which was recrystallized from DCM/ hexane (50:50) to give compound **5** as a white crystalline solid.

Yield: 251 mg, 72%; ^{1}H NMR (300 MHz, DMSO-d_6): δ= 8.37 (s, 1H, urea NH), 7.38 (d, 2H, J=8.4 Hz, aromatic CH), 7.20 (t, 2H, J=7.7 Hz, aromatic CH), 6.87 (m, 1H, aromatic CH), 6.07 (t, 1H, J=5.5 Hz, urea NH), 3.10 (q, 2H, J=6.3 Hz, alkyl CH_2), 1.60 (m, 1H, alkyl CH), 1.32 (q, 2H, J=7.0 Hz, alkyl CH_2), 0.89 (d, 6H, J=6.6 Hz, 2 x CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ= 155.1 (carbonyl C=O), 140.6 (aromatic CH), 128.5 (aromatic CH), 120.8 (aromatic CH), 117.5 (aromatic CH), 37.2 (CH_2), 25.1 (alkyl CH or CH_2), 22.4 (alkyl CH or CH_2); IR (film): ν= 3330 (urea NH stretching), 1640 (carbonyl CO stretching); LRMS(ESI+): *m/z* = 207.2 ($[M+H]^+$); HRMS(ES): for $[M + Na]^+$ *m/z*= 229.1317 (calculated), 229.1315 (found); M_p: 111-113 °C.

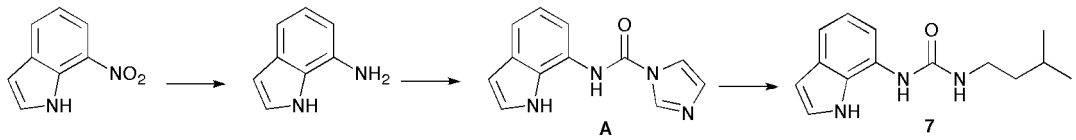
Compound 6[3]



Phenyl isothiocyanate (200 mg, 1.48 mmol) was dissolved in chloroform (50 ml) and isopentylamine (194 mg, 2.22 mmol) was added. The reaction mixture was stirred overnight at room temperature. The solution was washed with 2 x 100 ml water and the organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure to give a white solid, which was recrystallized from DCM/ hexane (50:50) to give compound **6** as a white crystalline solid.

Yield: 159 mg (48%); ^{1}H NMR (300 MHz, DMSO-d_6): δ= 9.40 (br s, 1H, urea NH), 7.68 (br s, 1H, urea NH), 7.40 (m, 2H, aromatic CH), 7.31 (m, 2H, aromatic CH), 7.09 (m, 1H, aromatic CH), 3.48 (q, 2H, J=6.5 Hz, CH_2), 1.60 (m, 1H, alkyl CH), 1.43 (q, 2H, J=7.3 Hz, CH_2), 0.90 (d, 6H, J=6.4 Hz, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ= 180.2 (thiourea C=S), 128.5 (aromatic CH), 124.0 (aromatic CH), 122.9 (aromatic CH), 42.1 (CH_2), 37.4 (CH_2), 25.3 (alkyl CH or CH_2), 22.4 (alkyl CH or CH_2); LRMS(ESI-): *m/z* = 221.2 ($[M-H]^-$); HRMS(ES): for $[M + Na]^+$ *m/z*= 245.1088 (calculated), 245.1089 (found); IR (film): ν= 3320 (urea NH stretching), 3170 (urea NH stretching); M_p: 103-104 °C.

Compound 7



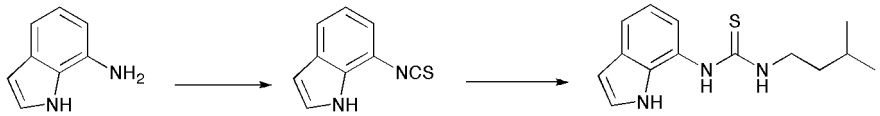
7-Aminoindole was prepared *via* a literature procedure.[1] 7-nitroindole (250 mg, 1.5 mmol) was dissolved in 100 ml ethanol and Pd/C (10% wt., catalytic) was added. The solution was stirred under atmosphere of hydrogen for 2 h. The Pd/C was removed by filtration through celite and the solvent was removed under reduced pressure to give 7-aminoindole as a white solid (assumed 100% yield).

7-aminoindole (1.5 mmol) was dissolved in 75 ml DCM and CDI (750 mg, 4.5 mmol) was added. The mixture was stirred at room temperature overnight under nitrogen. The white precipitate thus formed was isolated by filtration, washed with ice-cold DCM and dried under vacuum to afford intermediate **A** as a white solid which was used without further purification (234 mg).

Intermediate **A** (234 mg) was suspended in 100 ml DCM under nitrogen. Isopentylamine (1.5 g, 17.2 mmol) was added and the reaction mixture was refluxed overnight. On cooling, the crude produce was purified by column chromatography on silica (elution with DCM/ethyl acetate 85:15). This yielded compound **7** as a white solid.

Yield: 163 mg (44% overall yield); ^{1}H NMR (300 MHz, DMSO-d_6): δ= 10.71 (br s, 1H, NH), 8.32 (s, 1H, NH), 7.35 (t, 1H, J=2.6 Hz, aromatic CH), 7.25 (d, 1H, J=7.9 Hz, aromatic CH), 6.93 (m, 1H, aromatic CH), 6.45 (m, 1H, aromatic CH), 6.21 (t, 1H, J=5.3 Hz, NH), 3.22 (m, 2H, CH_2), 1.69 (m, 1H, alkyl CH), 1.43 (q, 2H, J=7.2 Hz, CH_2), 0.97 (d, 6H, J=6.8 Hz, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ= 155.6 (carbonyl C=O), 129.1 (aromatic CH), 127.8 (aromatic CH), 124.9 (aromatic CH), 119.1 (aromatic CH), 114.5 (aromatic CH), 111.8 (aromatic CH), 101.4 (aromatic CH), 37.6 (CH_2), 25.2 (alkyl), 22.4 (alkyl); LRMS(ESI-): *m/z* = 244.2 ([M-H]$^-$); HRMS(ES): for [M + Na]$^+$ *m/z*= 268.1423 (calculated), 268.1423 (found); IR (film): ν= 3390 (indole NH stretching), 3280 (urea NH stretching),1650 (carbonyl CO stretching); M_p: 159-160 °C.

Compound 8

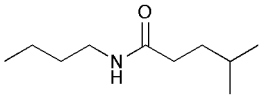


8

7-isothiocyanato-1*H*-indole was prepared *via* a literature procedure.[4] 7-aminoindole (prepared as described above, 1.5 mmol) was dissolved in a 2-phase mixture of DCM (75 ml) and sat. $NaHCO_{3\ (aq)}$ (75 ml) and stirred vigorously. Thiophosgene, (0.171 g, 0.114 ml, 1.5 mmol) was added and the reaction was stirred overnight at room temperature. The organic layer was isolated and washed with 2 x 100 ml water. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure to leave a brown residue. The residue was triturated in hexane to afford 7-isothiocyanato-1*H*-indole as a brown solid which was isolated by filtration. This intermediate was not characterized due to its assumed high reactivity. The isothiocyanate was re-dissolved in 100 ml DCM and *i*-pentylamine (0.131 g, 1.5 mmol) was added. The reaction was stirred at room temperature overnight under nitrogen. The solution was washed with 2 x 100 ml water and the organic layer was dried over $MgSO_4$. The crude mixture was subjected to column chromatography on silica (eluent DCM/MeOH 4%). The solvent was removed to leave an orange residue. Hexane (10 ml) was added causing an off white solid to form which was isolated by filtration and recrystallized from DCM to give compound **8** as a white solid.

Yield: 89 mg (24%); ^{1}H NMR (300 MHz, DMSO-d_6): δ= 10.88 (br s, 1H, NH), 9.20 (br s, 1H, NH), 7.42 (m, 2H, 2 x overlapping aromatic CH), 7.28 (t, 1H, J=2.8 Hz, aromatic CH), 6.97 (m, 2H, 2 x overlapping aromatic CH), 6.46 (dd, 1H, J_1=2.6 Hz, J_2=1.9 Hz, NH), 3.48 (m, 2H, CH_2), 1.56 (m, 1H, alkyl CH), 1.42 (q, 2H, J=6.9 Hz, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6): δ= 180.6 (thiourea C=S), 129.4 (aromatic CH), 125.6 (aromatic CH), 119.0 (aromatic CH), 118.0 (aromatic CH), 42.6 (CH_2), 25.6 (alkyl), 22.5 (alkyl); LRMS(ESI-): *m/z* = 260.2 ([M-H]$^-$), 274.2 ([M.MeOH-H]$^-$); HRMS(ES): for [M + H]$^+$ *m/z*= 262.1378 (calculated), 262.1378 (found) , for [M + Na]$^+$ *m/z*= 284.1197 (calculated), 284.1195 (found); IR (film): ν= 3370 (indole NH stretching), 3310 (urea NH stretching), 3180 (urea NH stretching); M_p: 88-90 °C.

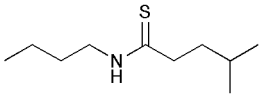
Compound 9[5]



4-methyl valeric acid (461 mg, 3.97 mmol) was activated by reflux in chloroform (100 ml) with CDI (644 mg, 3.97 mmol). After 2 hours, n-butylamine (370 mg, 5 mmol) was added and the reaction was refluxed overnight. On cooling, the product was washed with 2 x 100 ml 0.1 M HCl and 2 x 100 ml sat. $NaHCO_3$. The organic layer was dried over $MgSO_4$ and the solvent removed to give compound **9** as a colourless oil.

Yield: 402 mg, (59%); ^{1}H NMR (300 MHz, DMSO-d_6): δ= 7.71 (br. s, 1H, amide NH), 3.01 (m, 2H, CH_2), 2.05 (m, 2H, CH_2), 1.35 (m, 7H, overlapping alkyl CH + 3 x CH_2), 0.86 (m, 9H, 3 x CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ= 172.0 (thioamide C=S), 38.0 (alkyl), 24.4 (alkyl), 33.5 (alkyl), 31.2 (alkyl), 27.2 (alkyl), 22.2 (alkyl), 19.5 (alkyl), 13.6 (alkyl); LRMS(ESI+): *m/z* = 172.2 ([M + H]$^+$); HRMS(ES): for [M + Na]$^+$ *m/z*= 194.1521 (calculated), 194.1514 (found); IR (film): ν= 3290 (amide NH stretching), 1640 (carbonyl C=O stretching).

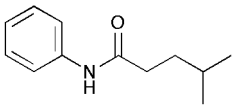
Compound 10



Compound **9** (300 mg, 1.75 mmol) was dissolved in THF and Lawesson's reagent (710 mg, 1.76 mmol) was added. The reaction was refluxed overnight. On cooling, the solvent was removed *in situ* and the oily residue obtained was re-dissolved in DCM. The product was washed with 2 x 100 ml of brine followed by 2 x 100 ml of 0.1 M HCl and 2 x 100 ml sat. $NaHCO_3$. The product was further purified by column chromatography on silica (elution with DCM). This afforded compound **10** as a colourless oil.

Yield: 245 mg (75%); ^{1}H NMR (300 MHz, $CDCl_3$): δ= 7.15 (br.s, 1H, NH), 3.66 (td, 2H, J_1=7.3 Hz, J_2=5.5 Hz, CH_2), 2.66 (m, 2H, CH_2), 1.65 (m, 5H, alkyl CH + 2 x CH_2), 1.41 (m, 2H, CH_2), 0.95 (m, 9H, 3 x CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ= 203.8 (carbonyl CO), 44.8 (alkyl), 43.2 (alkyl), 38.2 (alkyl), 29.2 (alkyl), 27.0 (alkyl), 22.3 (alkyl), 19.6 (alkyl), 13.6 (alkyl); LRMS(ESI+): *m/z* = 188.3 ([M + H]$^+$); HRMS(ES): for [M + Na]$^+$ *m/z*= 210.1292 (calculated), 210.1287 (found); IR (film): ν= 3240 (amide NH stretching).

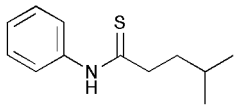
Compound 11[6]



4-methyl valeric acid (500 mg, 4.30 mmol) was activated by reflux in chloroform (100 ml) with CDI (700 mg, 4.30 mmol). After 2 hours, aniline (440 mg, 4.73 mmol) was added and the reaction was refluxed overnight. On cooling the product was washed with 2 x 100 ml water followed by 2 x 100 ml 0.1 M HCl and 2 x 100 ml sat. $NaHCO_3$. The combined organic layers were dried over $MgSO_4$ and the solvent was removed to give an off-white solid. This was triturated in hexane to afford compound **11** as a white solid.

Yield: 623 mg (76%); ^{1}H NMR (300 MHz, DMSO-d_6): δ= 9.86 (s, 1H, NH), 7.59 (d, 2H, J=8.7 Hz, aromatic CH), 7.28 (t, 2H, J=7.9 Hz, aromatic CH), 7.01 (m, 1H, aromatic CH), 2.30 (m, 2H, CH_2), 1.52 (m, 3H, Alkyl CH + CH_2); 0.90 (d, 6H, J=6.4 Hz, 2 x CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ= 171.4 (carbonyl CO), 139.3 (aromatic CH), 128.6 (aromatic CH), 122.8 (aromatic CH), 119.0 (aromatic CH), 34.5 (aromatic CH), 34.0 (aromatic CH), 27.2 (aromatic CH), 22.2 (aromatic CH); LRMS(ESI-): *m/z* = 190.2 ([M – H]$^-$); HRMS(ES): for [M + Na]$^+$ *m/z*= 214.1208 (calculated), 214.1202 (found); IR (film): ν= 3250 (amide NH stretching), 1650 (carbonyl C=O stretching); M_p: 109-110 °C.

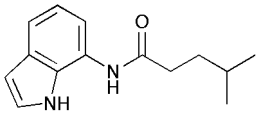
Compound 12[6d]



Compound **11** (300 mg, 1.57 mmol) was dissolved in THF and Lawesson's reagent (634 mg, 1.57 mmol) was added. The reaction was refluxed overnight. On cooling, the solvent was removed *in situ* and the oily residue obtained was re-dissolved in DCM. The product was washed with 2 x 100 ml of brine followed by 2 x 100 ml of 0.1 M HCl and 2 x 100 ml sat. $NaHCO_3$. The organic layer was dried over $MgSO_4$ and the solvent removed to give compound **12** as an off white solid.

Yield: 201 mg (62%); ^{1}H NMR (300 MHz, DMSO-d_6): δ= 11.49 (s, 1H, NH), 7.77 (d, 2H, J=8.1 Hz, aromatic CH), 7.39 (t, 2H, J=7.9 Hz, aromatic CH), 7.22 (m, 1H, aromatic CH), 2.75 (m, 2H, CH_2), 1.64 (m, 3H, alkyl CH + CH_2), 0.92 (d, 6H, J=6.2 Hz, 2 x CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ= 204.3 (thiourea C=S), 139.6 (aromatic CH), 128.4 (aromatic CH), 125.8 (aromatic CH), 123.3 (aromatic CH), 45.1 (alkyl CH_2), 27.1 (alkyl), 22.4 (alkyl); LRMS(ESI-): *m/z* = 206.2 ([M – H]$^-$); HRMS(ES): for [M + H]$^+$ *m/z*= 208.1160 (calculated), 208.1154 (found); IR (film): ν= 3180 (amide NH stretching); M_p: 61-62 °C.

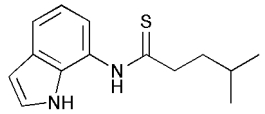
Compound 13



4-methyl valeric acid (276 mg, 2.37 mmol) was activated by reflux in DCM (100 ml) with CDI (400 mg, 2.47 mmol). After 2 hours, 7-aminoindole (402 mg, 2.48 mmol) was added and the reaction was refluxed overnight. On cooling, the product was washed with 300 ml of 0.5 M HCl and 300 ml sat. $NaHCO_3$. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure to give compound **13** as an off-white solid.

Yield: 451 mg (83%); ^{1}H NMR (300 MHz, DMSO-d_6): δ= 10.66 (br. s, 1H, amide NH), 9.64 (s, 1H, indole NH), 7.34 (m, 3H, aromatic CH), 6.92 (m, 1H, aromatic CH), 6.43 (m, 1H, aromatic CH), 2.41 (m, 2H, CH_2), 1.59 (m, 3H, alkyl CH + CH_2), 0.93 (d, 6H, 2 x CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ= 171.3 (carbonyl C=O), 129.0 (aromatic CH), 128.1 (aromatic CH), 125.0 (aromatic CH), 123.6 (aromatic CH), 118.9 (aromatic CH), 116.2 (aromatic CH), 113.3 (aromatic CH), 101.5 (aromatic CH), 34.1 (alkyl), 27.3 (alkyl), 22.3 (alkyl); LRMS(ESI-): *m/z* = 229.3 ([M – H]$^-$); HRMS(ES): for [M + Na]$^+$ *m/z*= 253.1317 (calculated), 253.1311 (found); IR (film): ν= 3330 (amide NH stretching), 3240 (indole NH stretching), 1650 (carbonyl C=O stretching); M_p: 144-145 °C.

Compound 14



Compound **13** (262 mg, 1.14 mmol) was dissolved in THF and Lawesson's reagent (457 mg, 1.14 mmol) was added. The reaction was refluxed overnight. On cooling, the solvent was removed *in situ* and the oily residue obtained was re-dissolved in DCM. The product was washed with 2 x 100 ml of brine followed by 2 x 100 ml of 0.1 M HCl and 2 x 100 ml sat. $NaHCO_3$/brine (50:50). The product was further purified by column chromatography on silica (elution with DCM). Compound **14** was obtained as a white solid.

Yield: 202 mg (73%); ^{1}H NMR (300 MHz, DMSO-d_6): δ= 11.33 (s, 1H, thioamide NH), 10.80 (br. s, 1H, indole NH), 7.48 (d, 1H, J=7.7 Hz, aromatic CH), 7.33 (t, 1H, J=2.7 Hz, aromatic CH), 7.15 (d, 1H, J=7.3 Hz, aromatic CH), 6.99 (m, 1H, aromatic CH), 6.47 (m, 1H, aromatic CH), 2.82 (m, 2H, CH_2), 1.71 (m, 3H, alkyl CH + CH_2), 0.96 (d, 6H, J=6.2 Hz, 2 x CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ= 205.7 (thioamide C=S), 130.6 (aromatic CH), 129.3 (aromatic CH), 125.5 (aromatic CH), 124.2 (aromatic CH), 118.9 (aromatic CH), 118.5 (aromatic CH), 118.3 (aromatic CH), 43.9 (alkyl), 27.3 (alkyl), 22.4 (alkyl); LRMS(ESI-): *m/z* = 245.2 ([M – H]$^-$); HRMS(ES): for [M + H]$^+$ *m/z*= 247.1269 (calculated), 247.1261 (found), for [M + Na]$^+$ *m/z*= 269.1088 (calculated), 269.1061 (found); IR (film): ν= 3320 (amide NH stretching), 3180 (indole NH stretching); M_p: 106-107 °C.

S3 *NMR spectra*

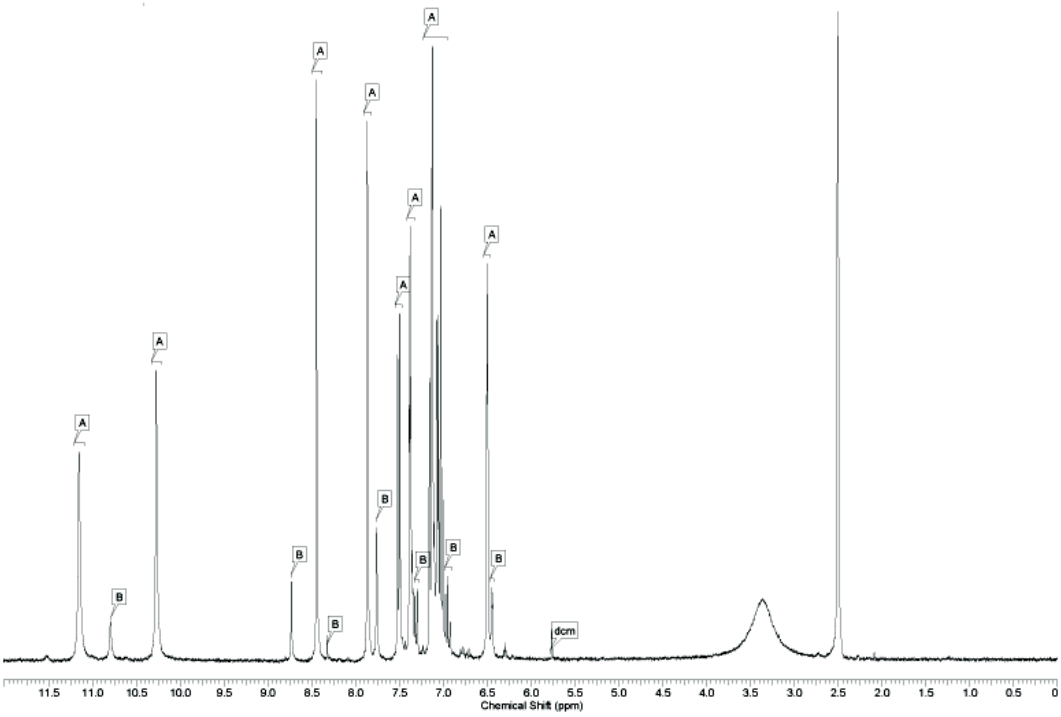


Figure S1 ^{1}H NMR spectrum of intermediate **A** in DMSO-d_6. Peaks associated with **A** are labeled A; minor, undesired products are labeled B. Product was used without further purification.

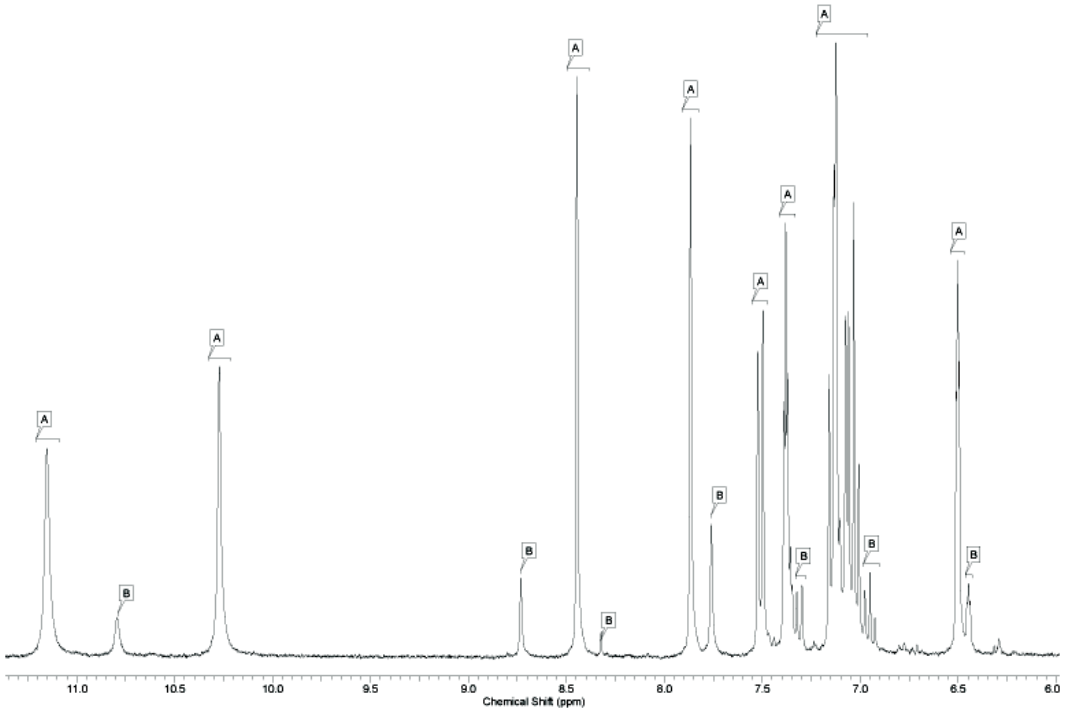


Figure S2 Expanded aromatic region of the ^{1}H NMR spectrum of **A** (recorded in DMSO-d_6)

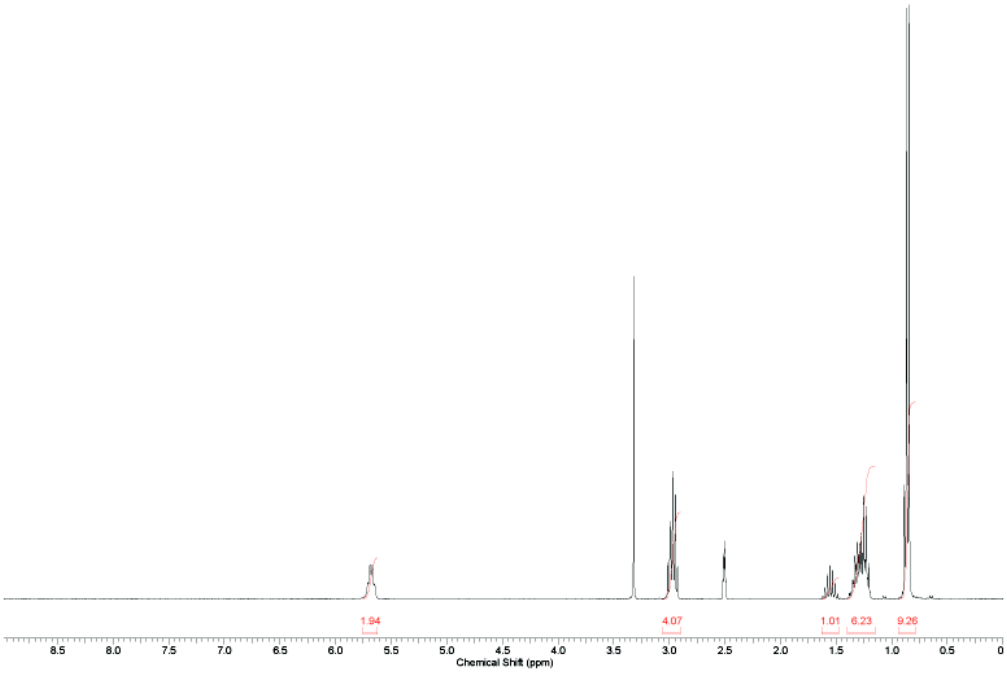


Figure S3 ^{1}H NMR spectrum of compound **3** in DMSO-d_6

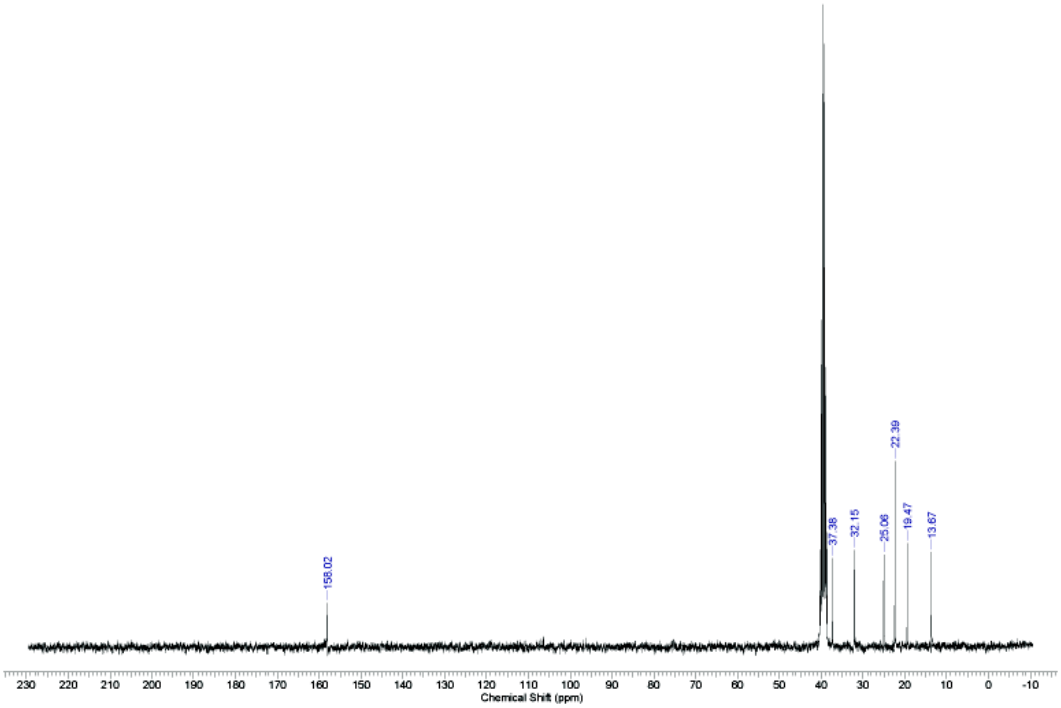


Figure S4 ^{13}C NMR spectrum of compound **3** in DMSO-d_6

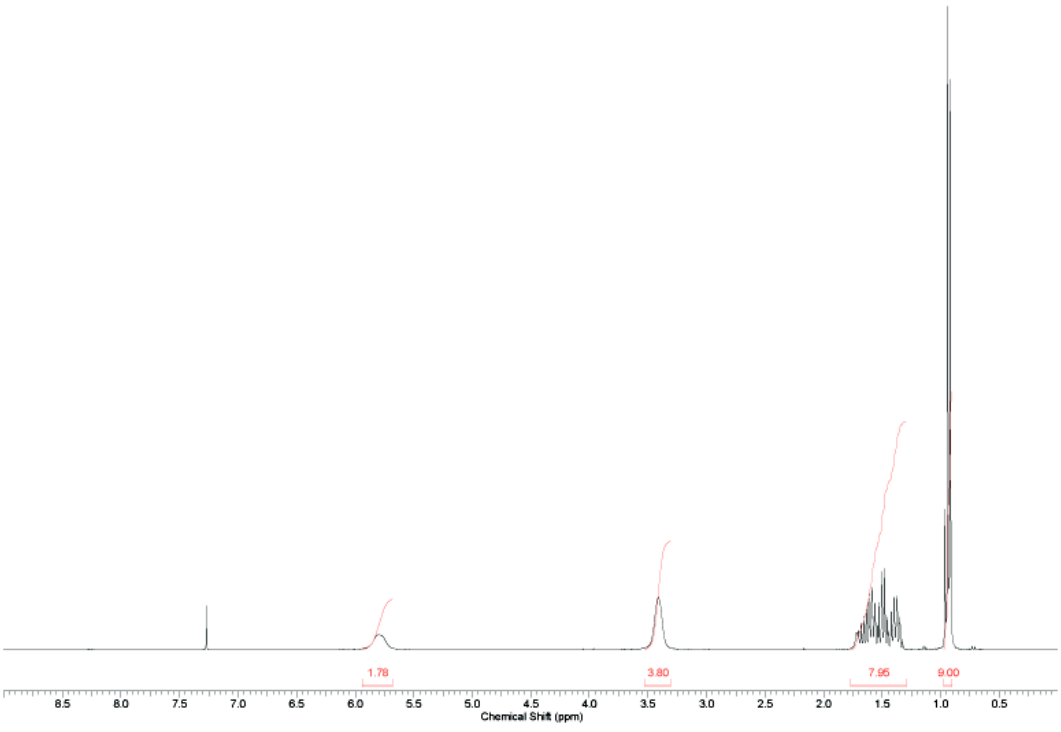


Figure S5 ^{1}H NMR spectrum of compound **4** in $CDCl_3$

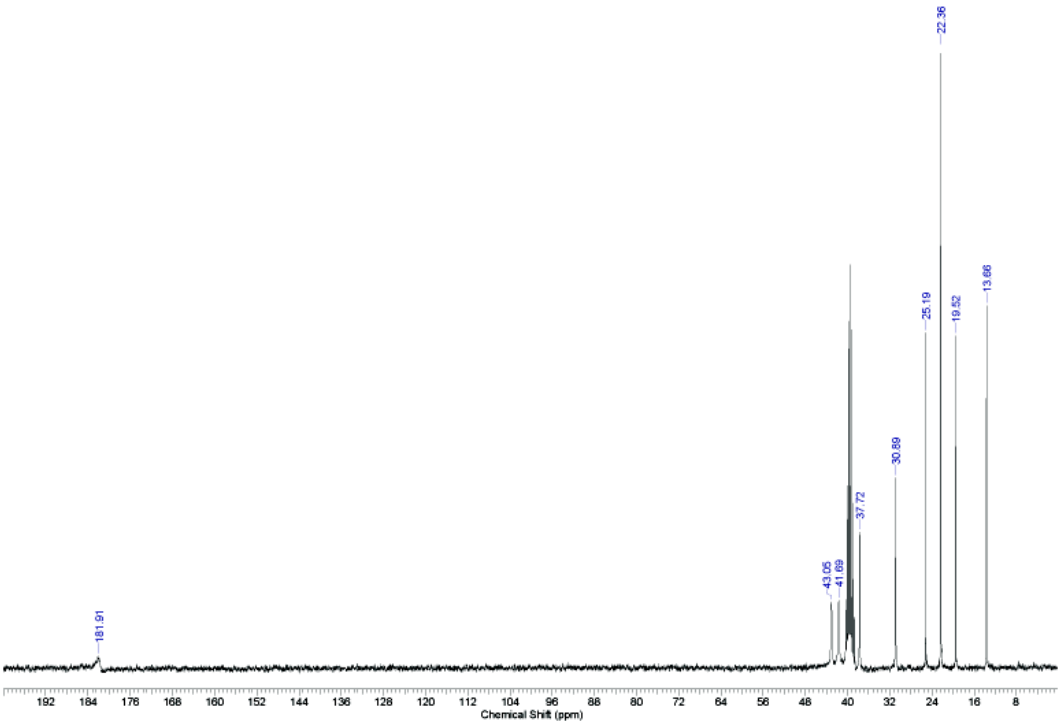


Figure S6 ^{13}C NMR spectrum of compound **4** in DMSO-d_6

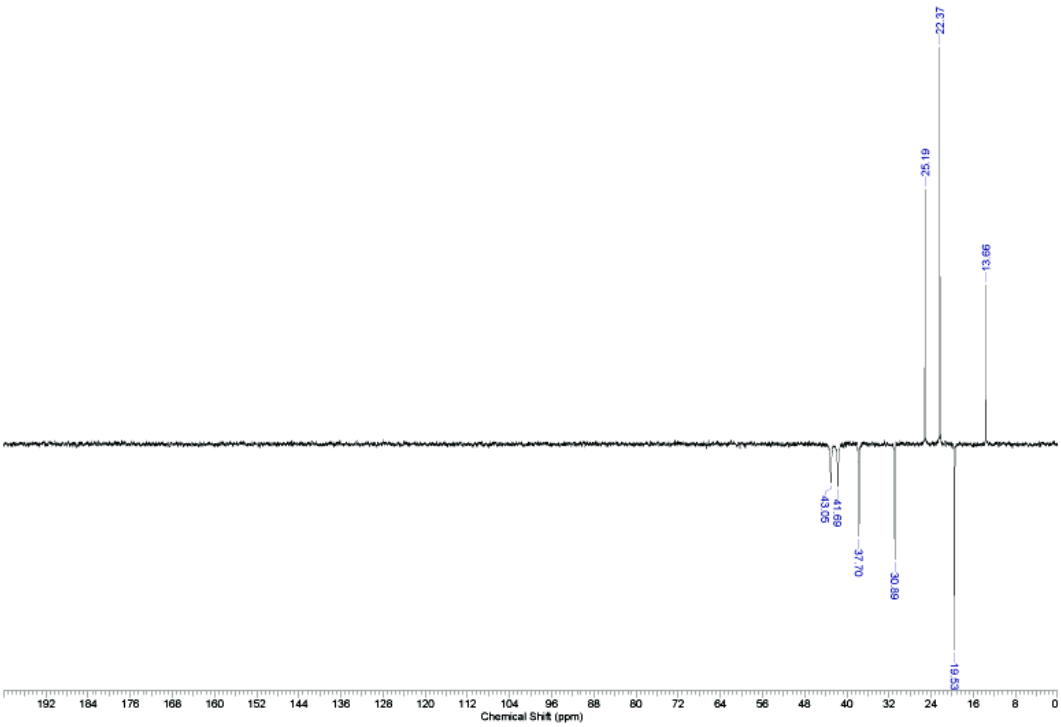


Figure S7 ^{13}C DEPT spectrum of compound **4** in DMSO-d_6

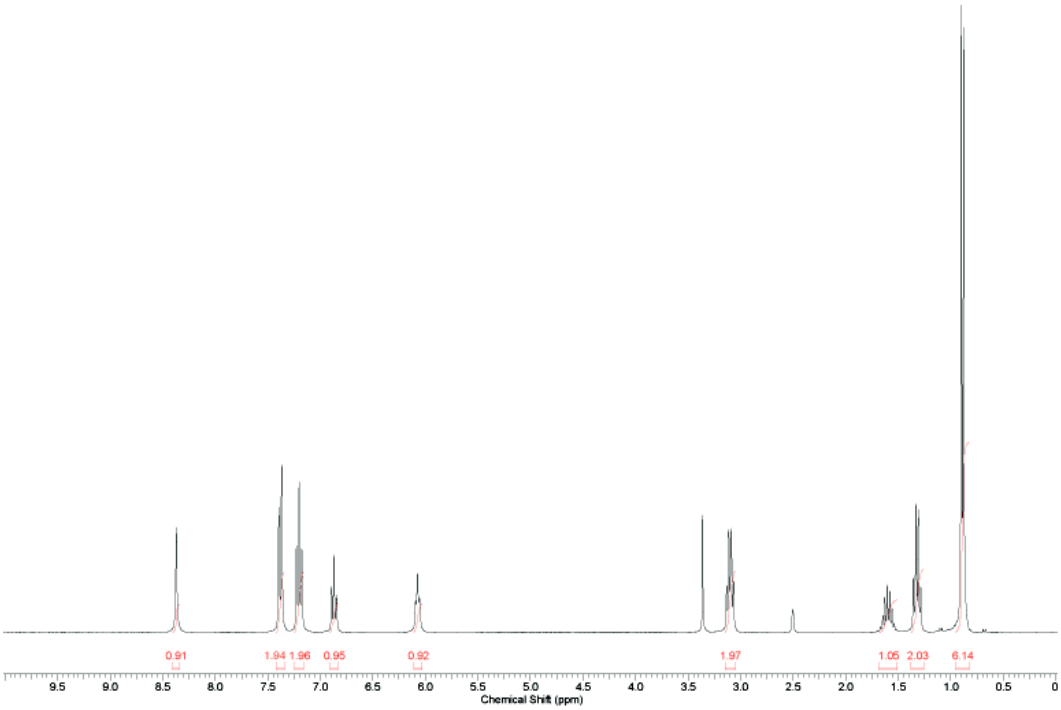


Figure S8 ^{1}H NMR spectrum of compound **5** in DMSO-d_6

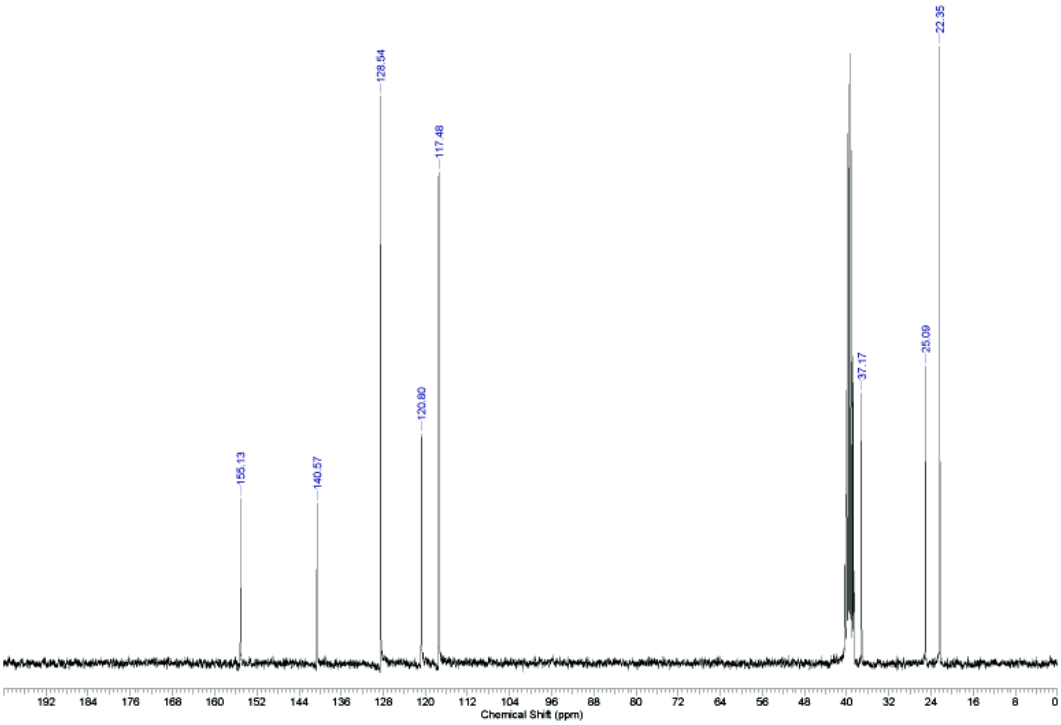


Figure S9 ^{13}C NMR spectrum of compound **5** in DMSO

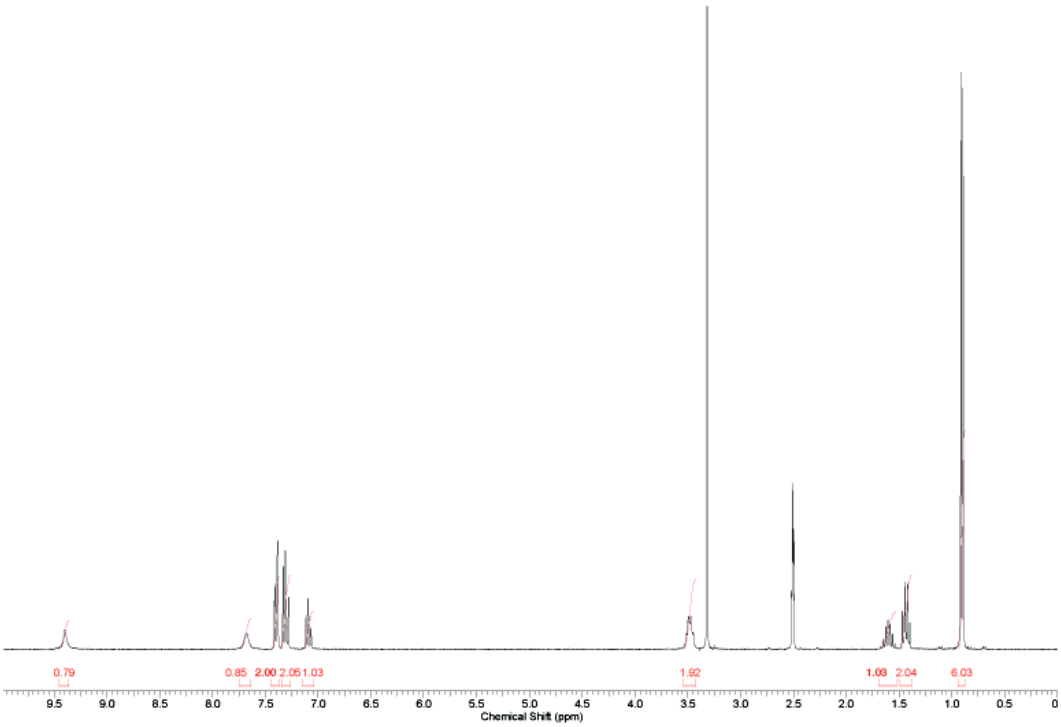


Figure S10 ^{1}H NMR spectrum of compound **6** in DMSO-d_6

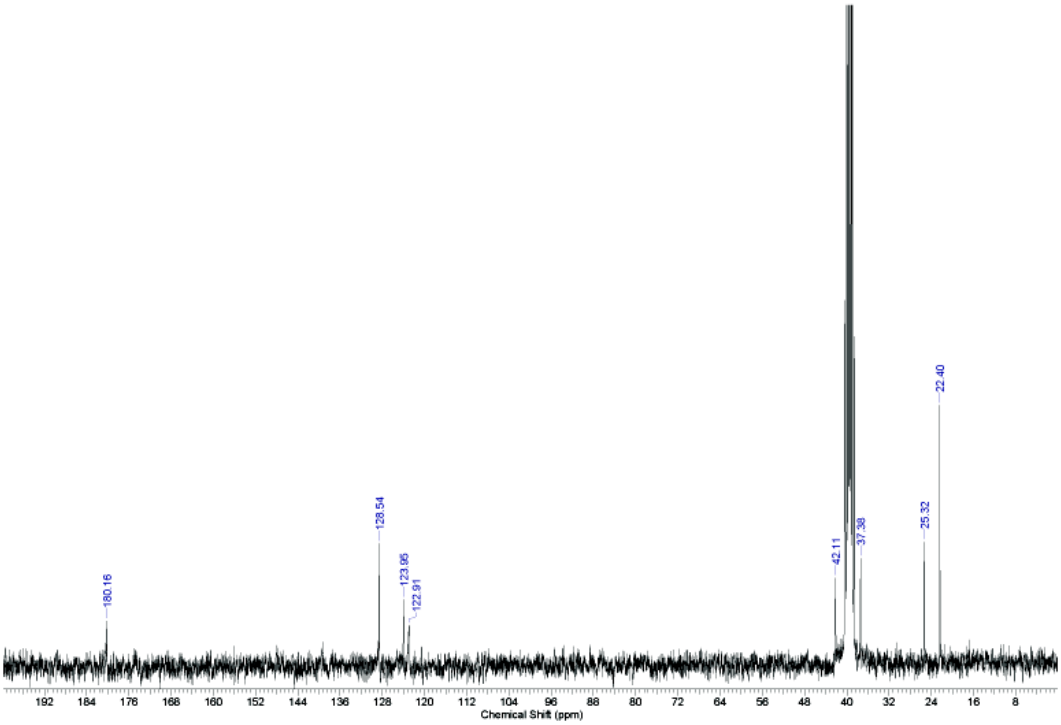


Figure S11 ^{13}C NMR spectrum of compound **6** in DMSO

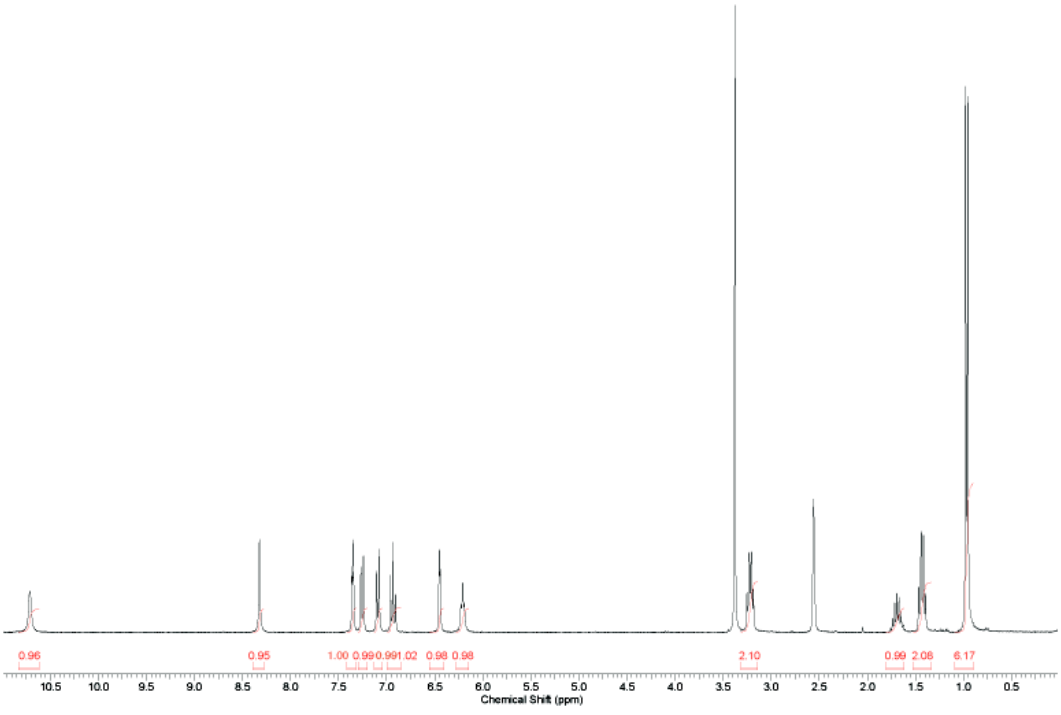


Figure S12 ^{1}H NMR spectrum of compound **7** in DMSO-d_6

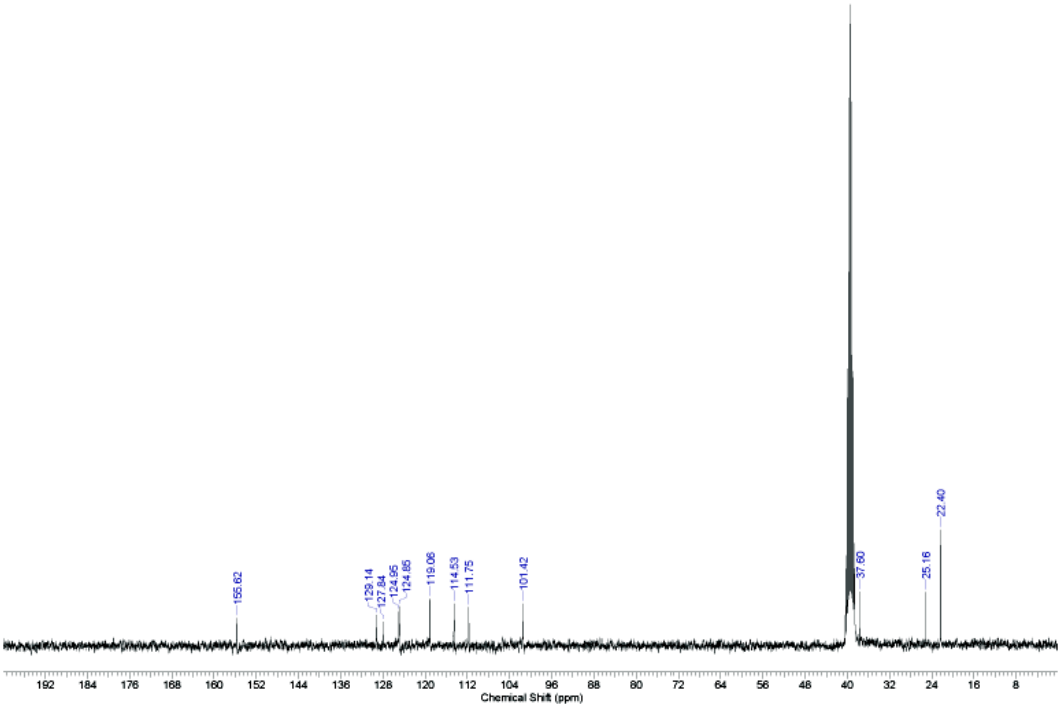


Figure S13 ^{13}C NMR spectrum of compound **7** in DMSO-d_6

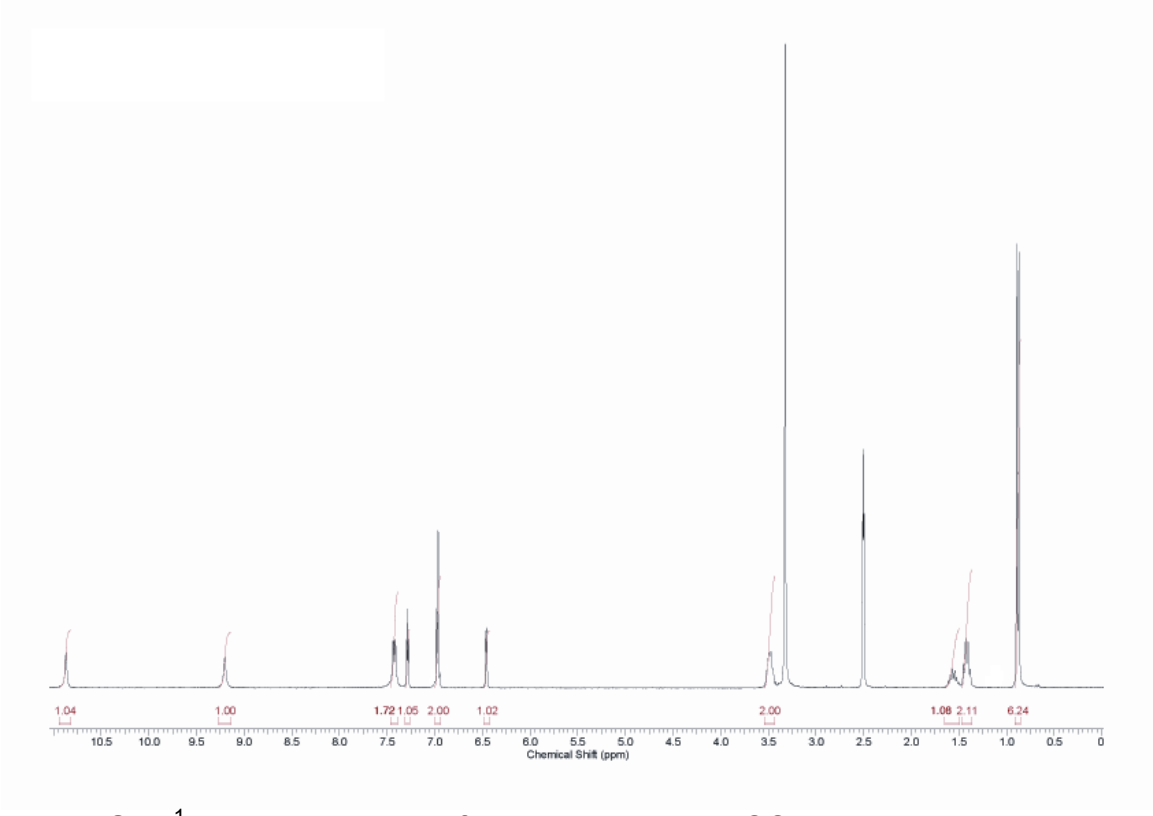


Figure S14 ^{1}H NMR spectrum of compound **8** in DMSO-d_6

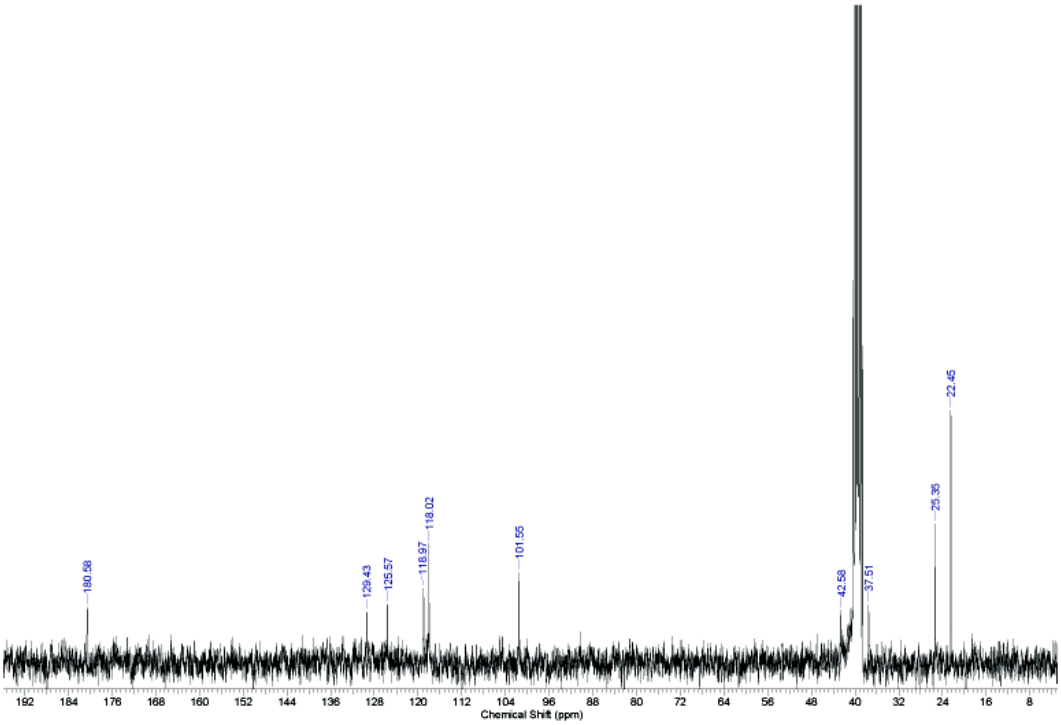


Figure S15 ^{13}C NMR spectrum of compound **8** in DMSO-d_6

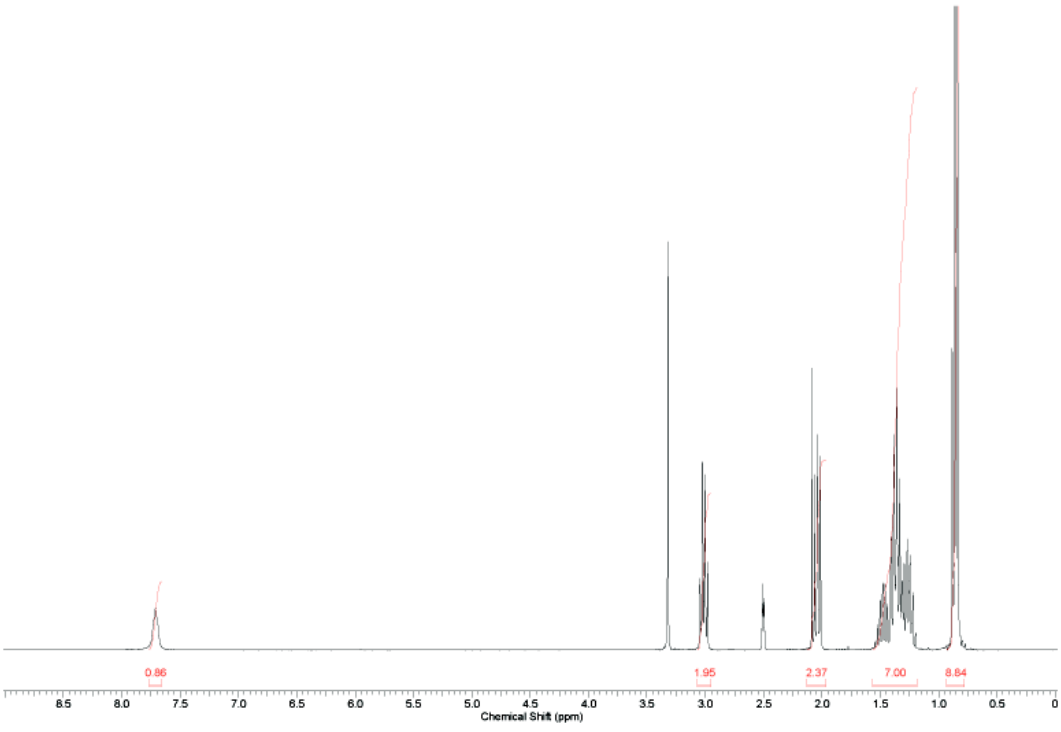


Figure S16 ^{1}H NMR spectrum of compound **9** in DMSO-d_6

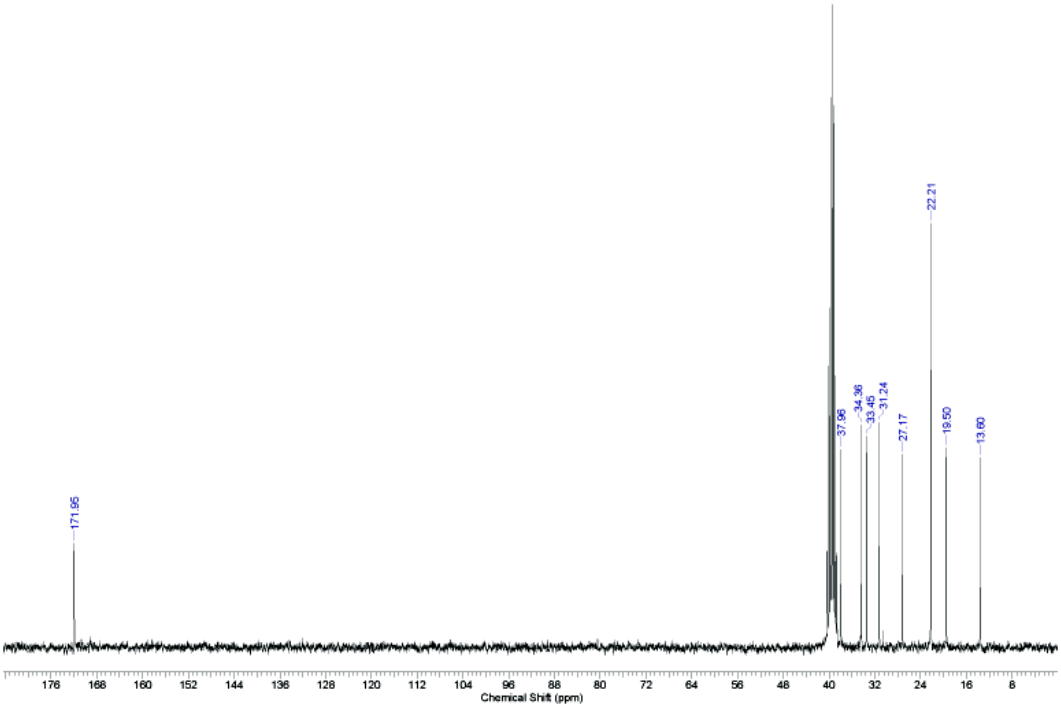


Figure S17 ^{13}C NMR spectrum of compound **9** in DMSO-d_6

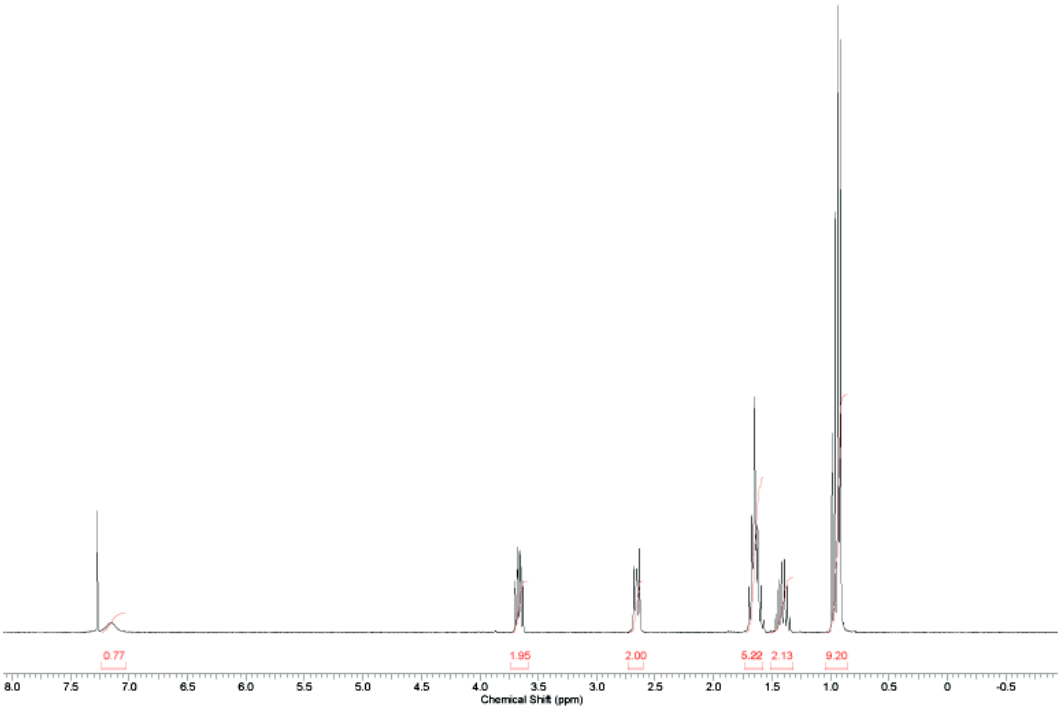


Figure S18 ^{1}H NMR spectrum of compound **10** in $CDCl_3$

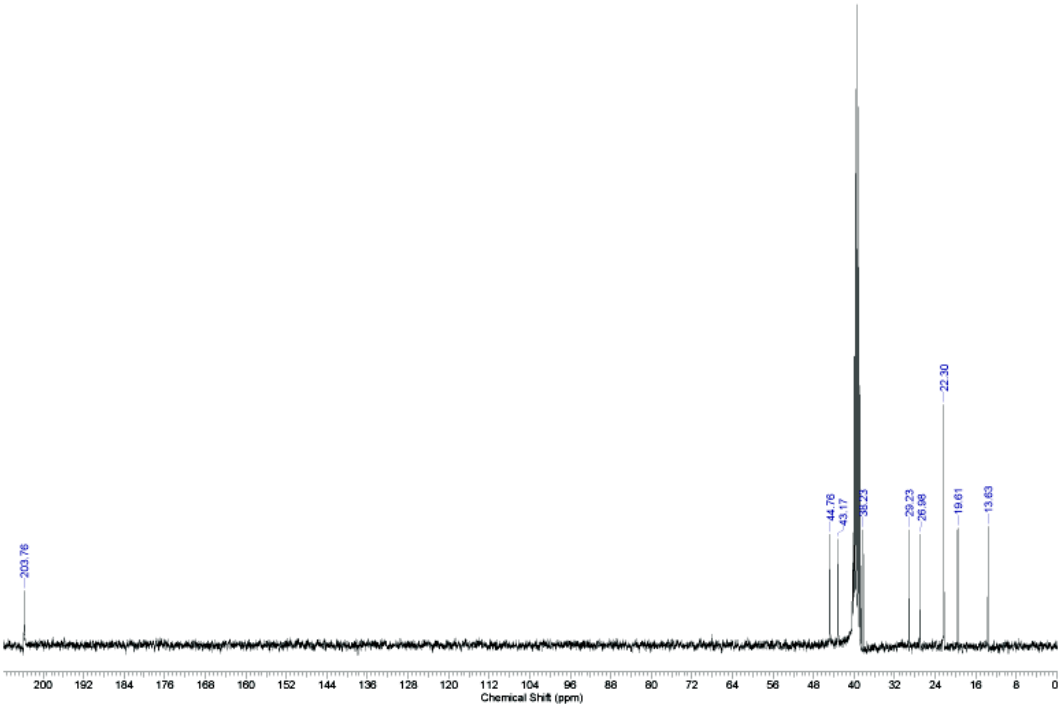


Figure S19 ^{13}C NMR spectrum of compound **10** in DMSO-d_6

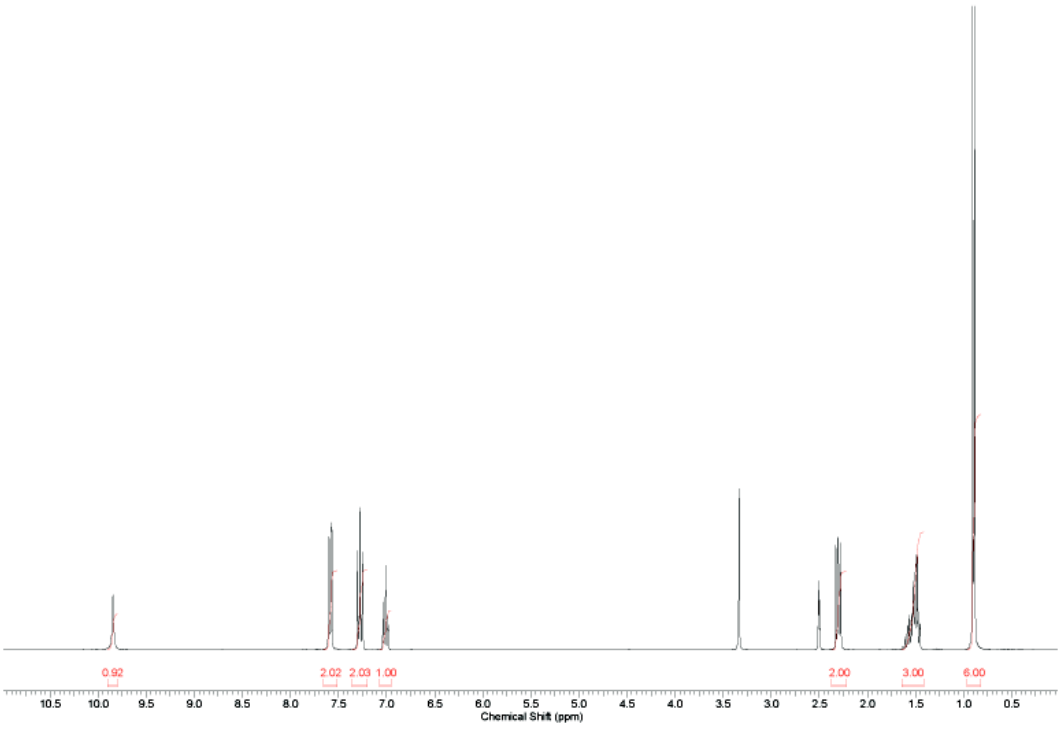


Figure S20 ^{1}H NMR spectrum of compound **11** in DMSO-d_6

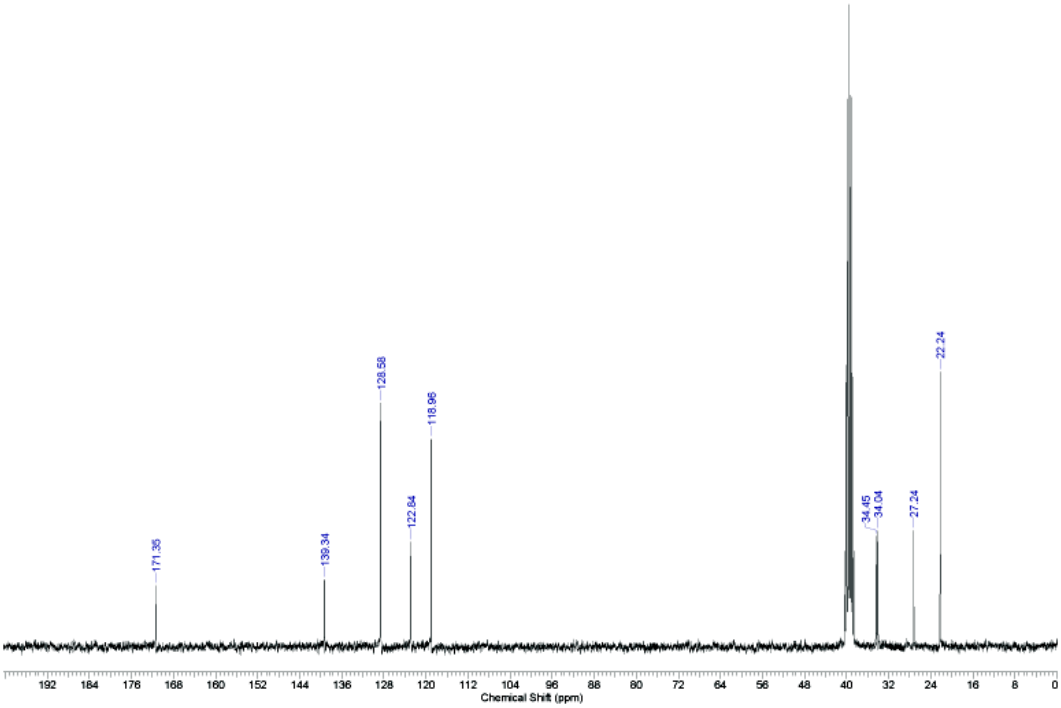


Figure S21 ^{13}C NMR spectrum of compound **11** in DMSO-d_6

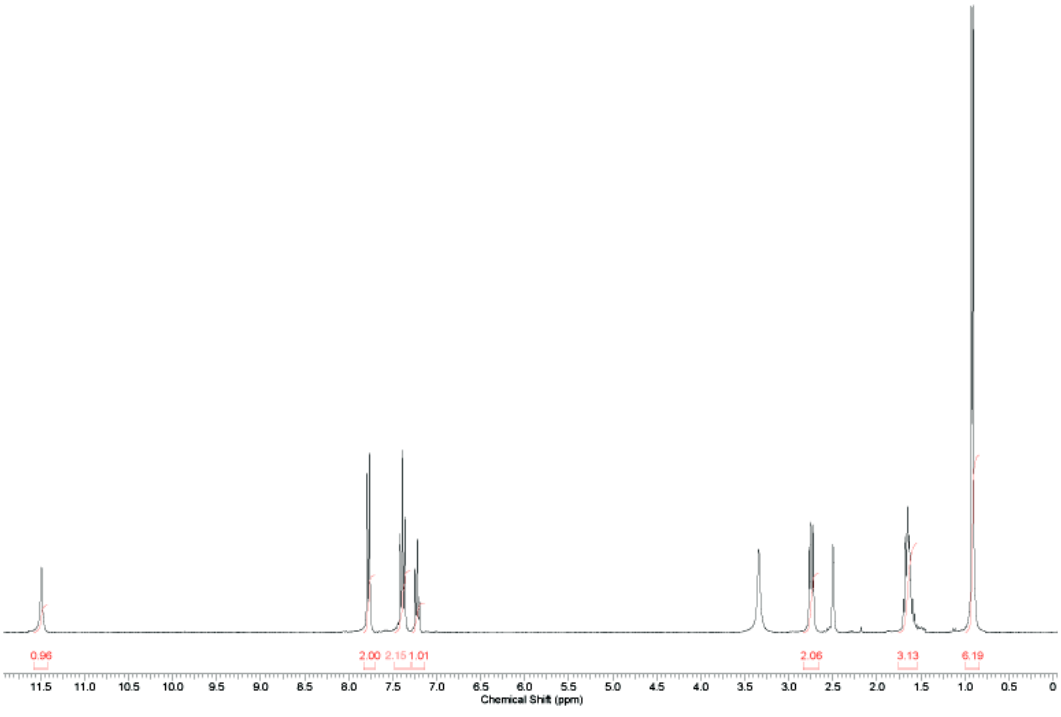


Figure S22 ^{1}H NMR spectrum of compound **12** in DMSO-d_6

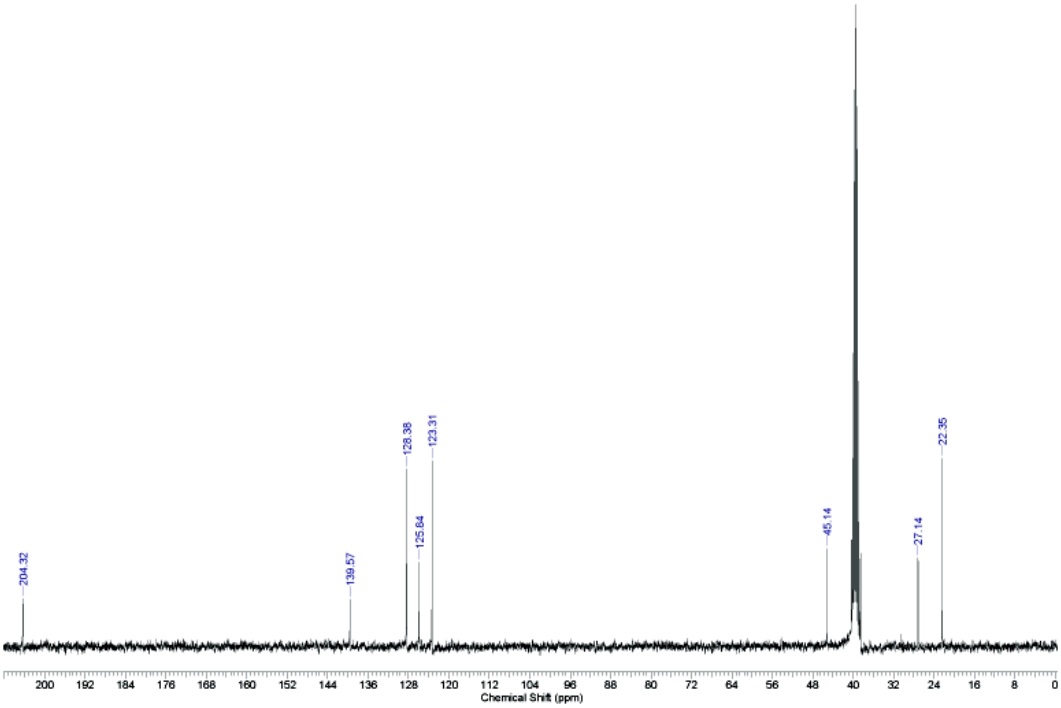


Figure S23 ^{13}C NMR spectrum of compound **12** in DMSO-d_6

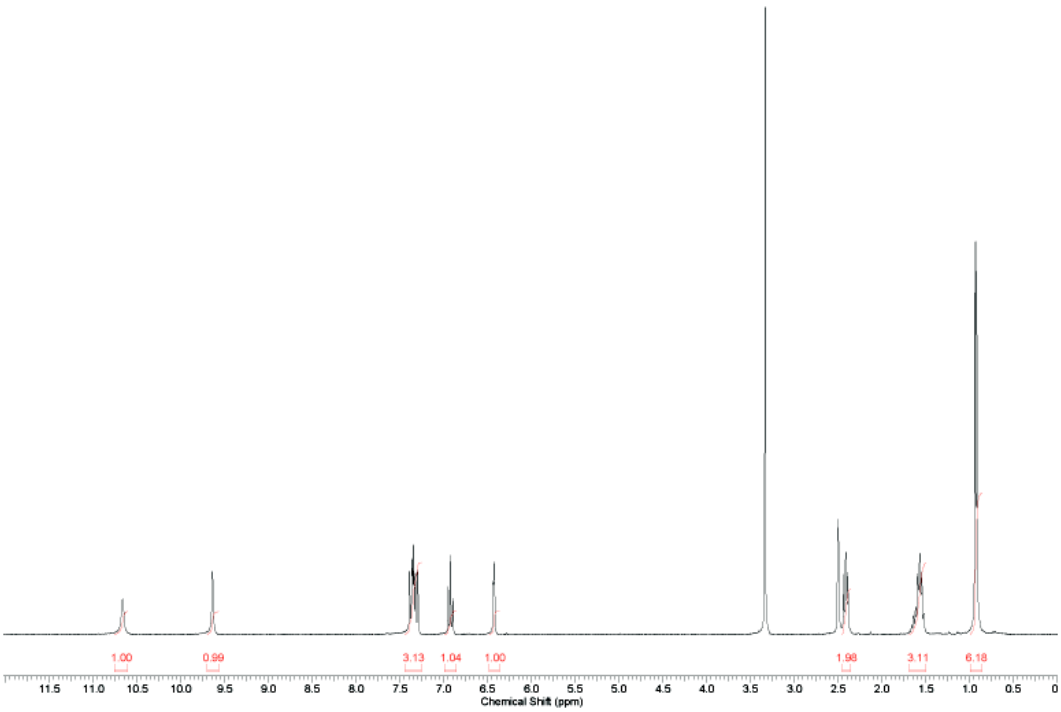


Figure S24 ^{1}H NMR spectrum of compound **13** in DMSO-d_6

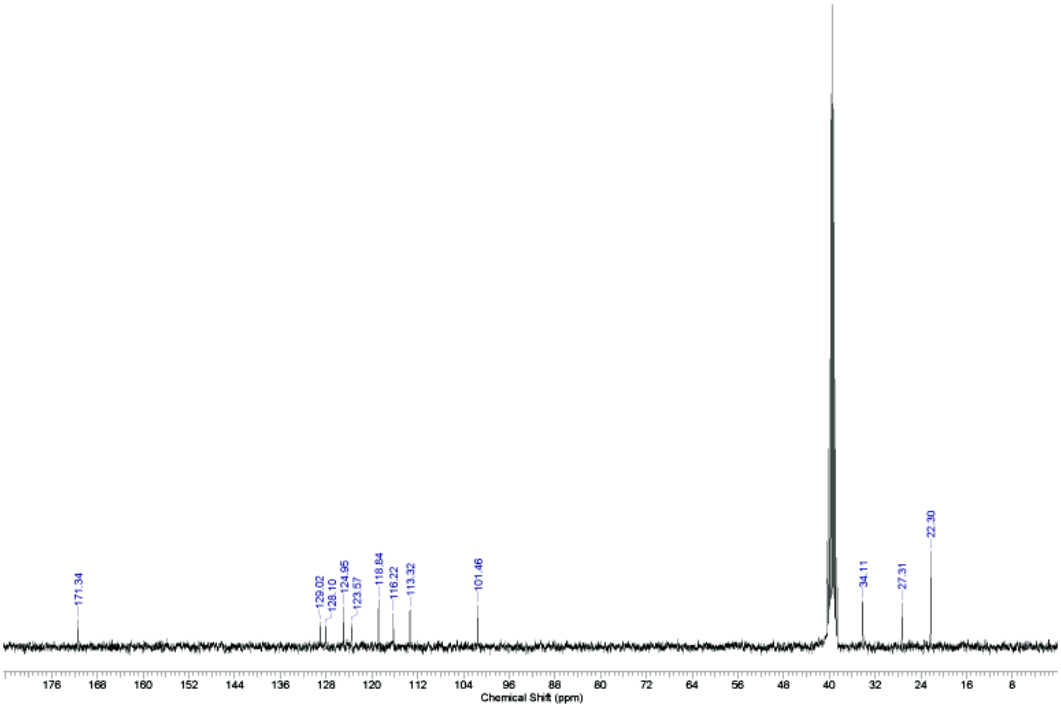


Figure S25 ^{13}C NMR spectrum of compound **13** in DMSO-d_6

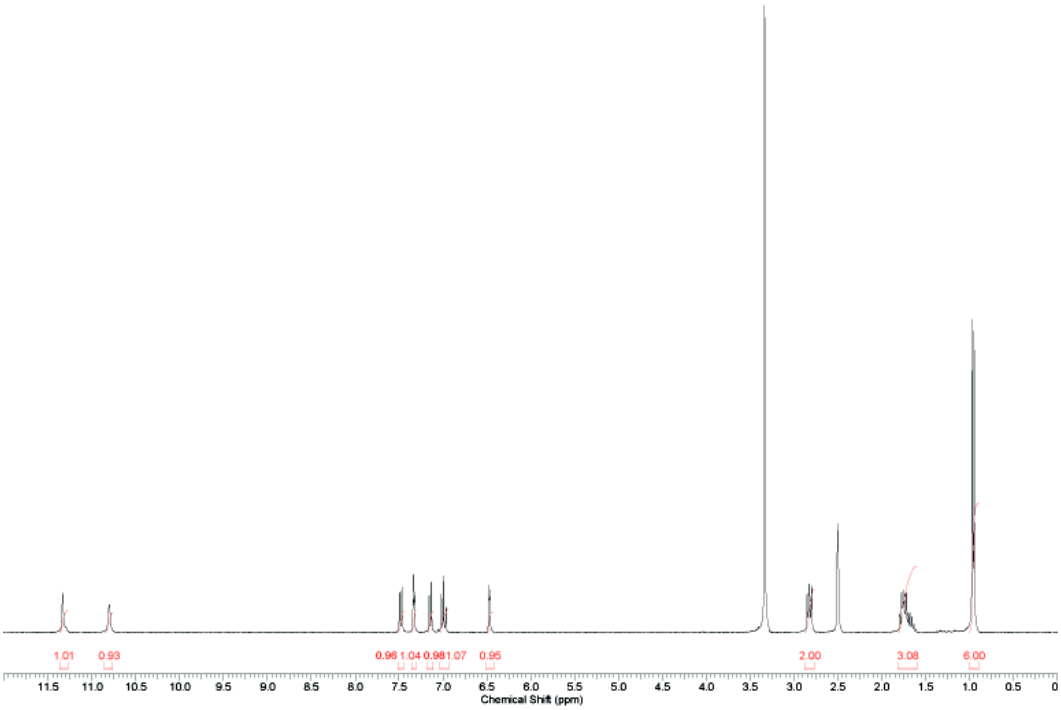


Figure S26 ^{1}H NMR spectrum of compound **14** in DMSO-d_6

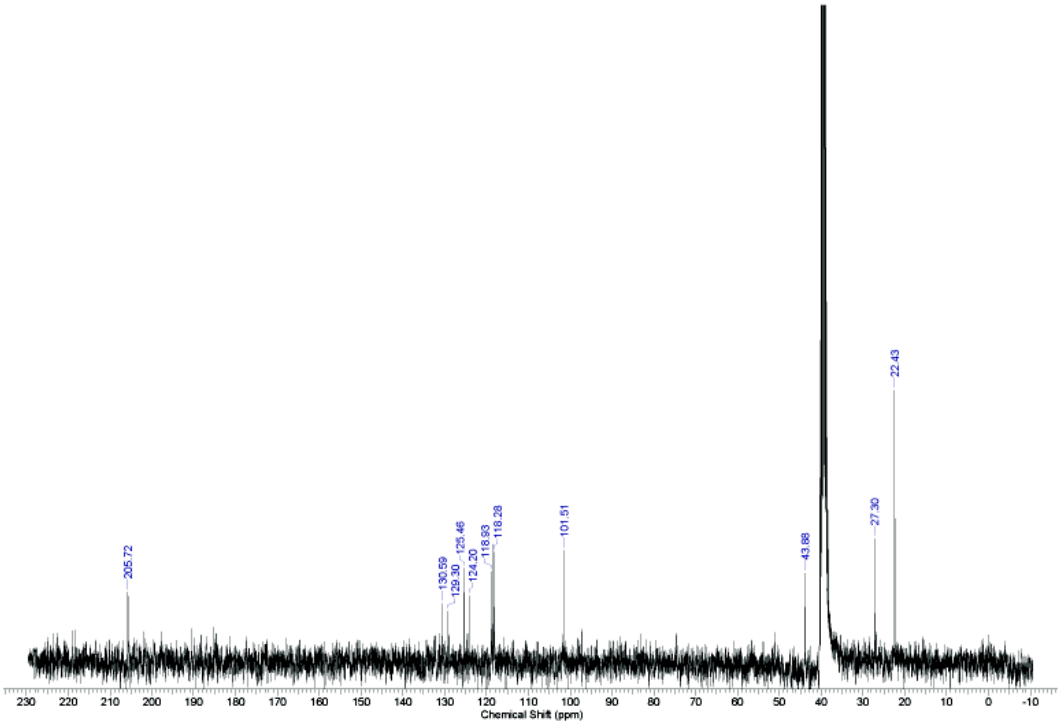


Figure S27 ^{13}C NMR spectrum of compound **14** in DMSO-d_6

S4 *Anion Transport Studies*

S4.1 Experimental details

Preparation of Vesicles

A lipid film of 1-palmitoyl-2-oleoyl-*sn*-glycero-3-phosphocholine (POPC) and cholesterol (0% or 30%) was formed from a chloroform solution under reduced pressure and dried under vacuum for at least 6 hours. The lipid film was rehydrated by vortexing with a metal chloride (MCl) salt solution (489 mM MCl, 5 mM phosphate buffer at pH 7.2). The lipid suspension was then subjected to seven freeze-thaw cycles and allowed to age for 30 min at room temperature before extruding 25 times through a 200 nm polycarbonate membrane. The resulting unilamellar vesicles were dialyzed against the external medium to remove unencapsulated MCl salts.

Chloride Transport Assays

Unilamellar POPC vesicles containing NaCl, prepared as described above, were suspended in 489 mM $NaNO_3$ or 162 mM Na_2SO_4 solution buffered to pH 7.2 with sodium phosphate salts. The lipid concentration per sample was 1 mM. A DMSO solution of the carrier molecule (10 mM) was added to start the experiment and the chloride efflux was monitored using a chloride sensitive electrode. At 5 min, the vesicles were lysed with 50 μl of polyoxyethylene(8)lauryl ether (0.232 mM in 7:1 water:DMSO v/v) and a total chloride reading was taken at 7 min. In the case of the external anion being sulfate, the experiment was extended such that the vesicles were lysed at 20 min and total chloride reading taken at 22 min.

Bicarbonate Transport Assay

Unilamellar POPC vesicles containing 489 mM NaCl solution buffered to pH 7.2 with 20 mM sodium phosphate salts, prepared as described above, were suspended in 162 mM Na_2SO_4 solution buffered to pH 7.2 with sodium phosphate salts. The lipid concentration per sample was 1 mM. A DMSO solution of the carrier molecule (10 mM) was added to start the experiment and chloride efflux was monitored using a chloride sensitive electrode. At 2 min, $NaHCO_3$ solution (1.2 M in 162 mM Na_2SO_4 buffered to pH 7.2 with 20 mM sodium phosphate salts) was added so that the outer solution contained 40 mM $NaHCO_3$. At 8 min, the vesicles were lysed with 50 μl of polyoxyethylene(8)lauryl ether (0.232 mM in 7:1 water:DMSO v/v) and a total chloride reading was taken at 10 min.

S4.2 Additional membrane transport studies

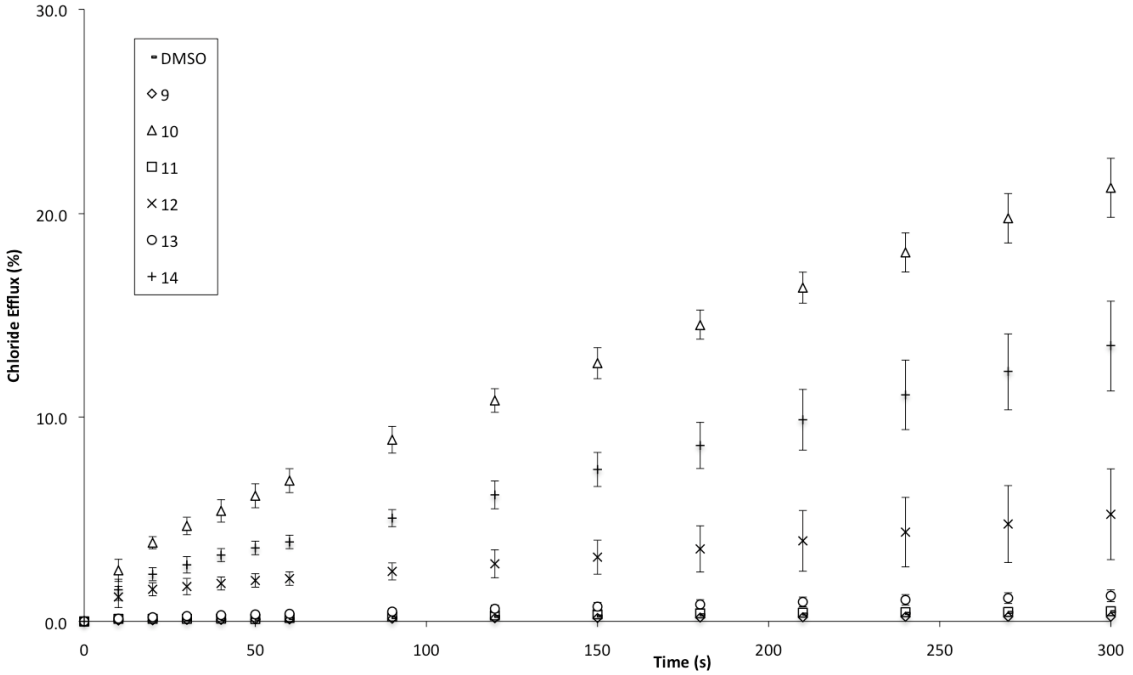


Figure S28 Chloride efflux promoted by 0.02 molar equiv of receptors **9-14** from unilamellar POPC vesicles loaded with 489mM NaCl buffered to pH 7.2 with sodium phosphate salts. The vesicles were dispersed in 489mM $NaNO_3$ buffered to pH 7.2 with 5mM sodium phosphate salts. Each point represents the average of three trials.

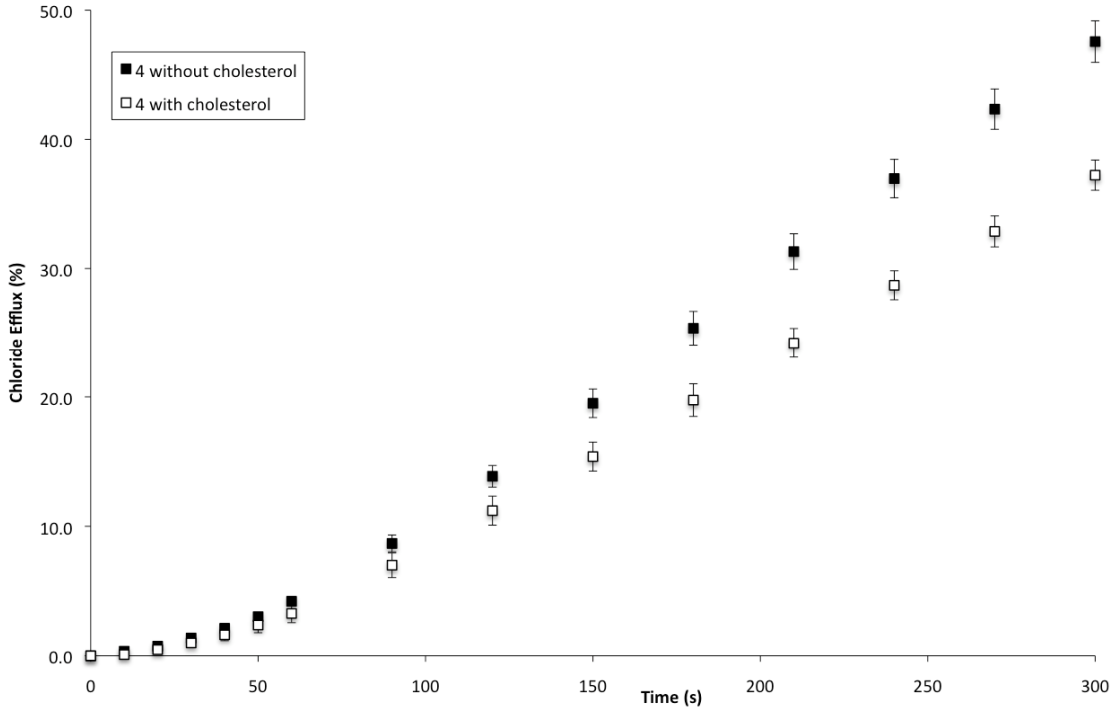


Figure S29 Chloride efflux promoted by 0.02 molar equiv of receptor **4** from unilamellar POPC vesicles and unilamellar POPC/cholesterol (7:3) vesicles, loaded with 489mM NaCl buffered to pH 7.2 with sodium phosphate salts. The vesicles were dispersed in 489mM $NaNO_3$ buffered to pH 7.2 with 5mM sodium phosphate salts. Each point represents the average of three trials.

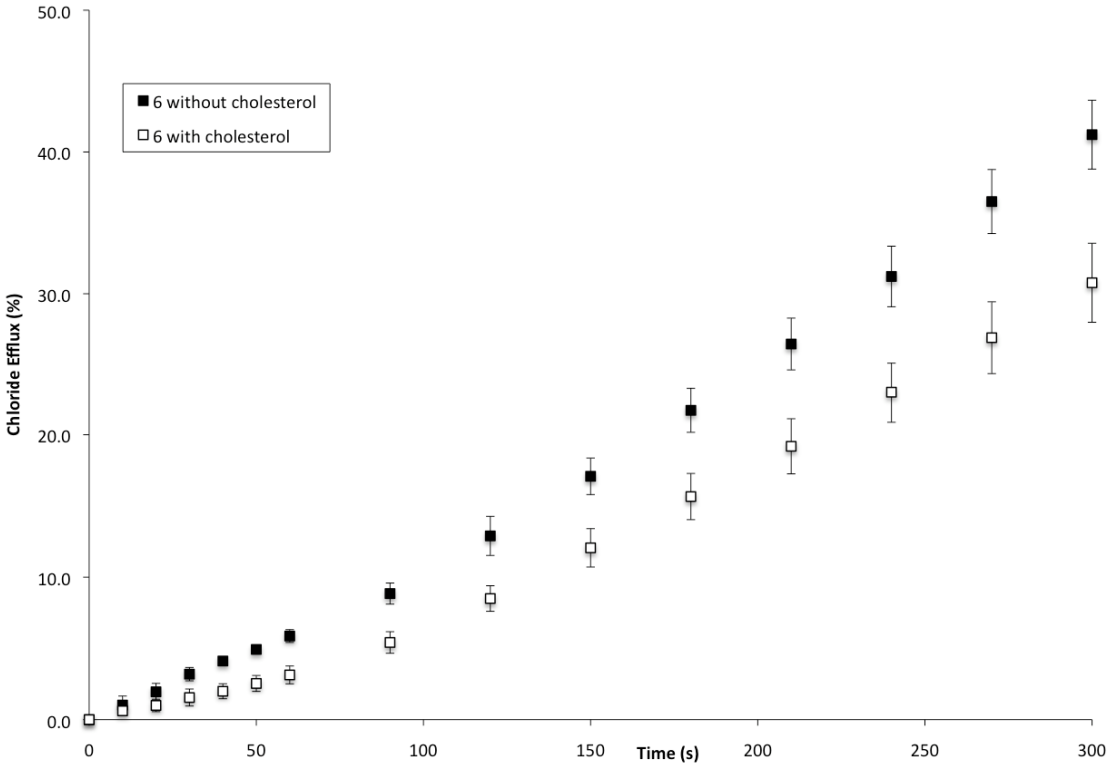


Figure S30 Chloride efflux promoted by 0.02 molar equiv of receptor **6** from unilamellar POPC vesicles and unilamellar POPC/cholesterol (7:3) vesicles, loaded with 489mM NaCl buffered to pH 7.2 with sodium phosphate salts. The vesicles were dispersed in 489mM $NaNO_3$ buffered to pH 7.2 with 5mM sodium phosphate salts. Each point represents the average of three trials.

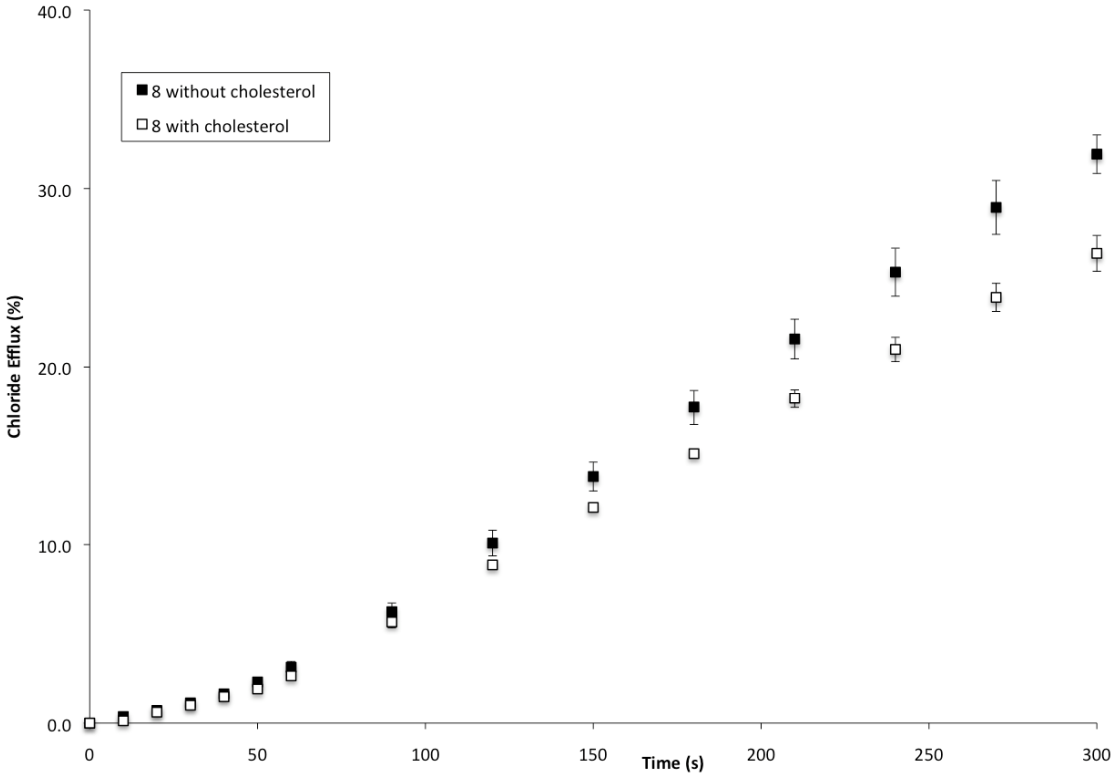


Figure S31 Chloride efflux promoted by 0.02 molar equiv of receptor **8** from unilamellar POPC vesicles and unilamellar POPC/cholesterol (7:3) vesicles, loaded with 489mM NaCl buffered to pH 7.2 with sodium phosphate salts. The vesicles were dispersed in 489mM $NaNO_3$ buffered to pH 7.2 with 5mM sodium phosphate salts. Each point represents the average of three trials.

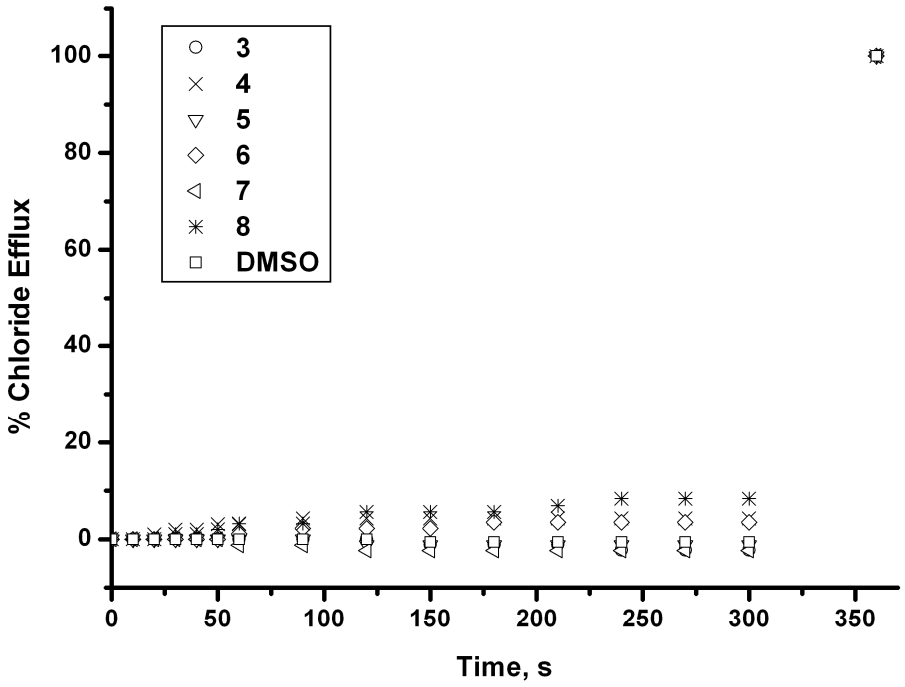


Figure S32 Chloride efflux promoted by 0.02 molar equiv of receptors **3**-**8** and from unilamellar POPC vesicles loaded with 500 mM NaCl buffered to pH 7.2 with sodium phosphate salts. The vesicles were dispersed in 167 mM Na_2SO_4 buffered to pH 7.2 with 5 mM sodium phosphate salts. At the end of the experiment, detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride release. Each point represents the average of three trials

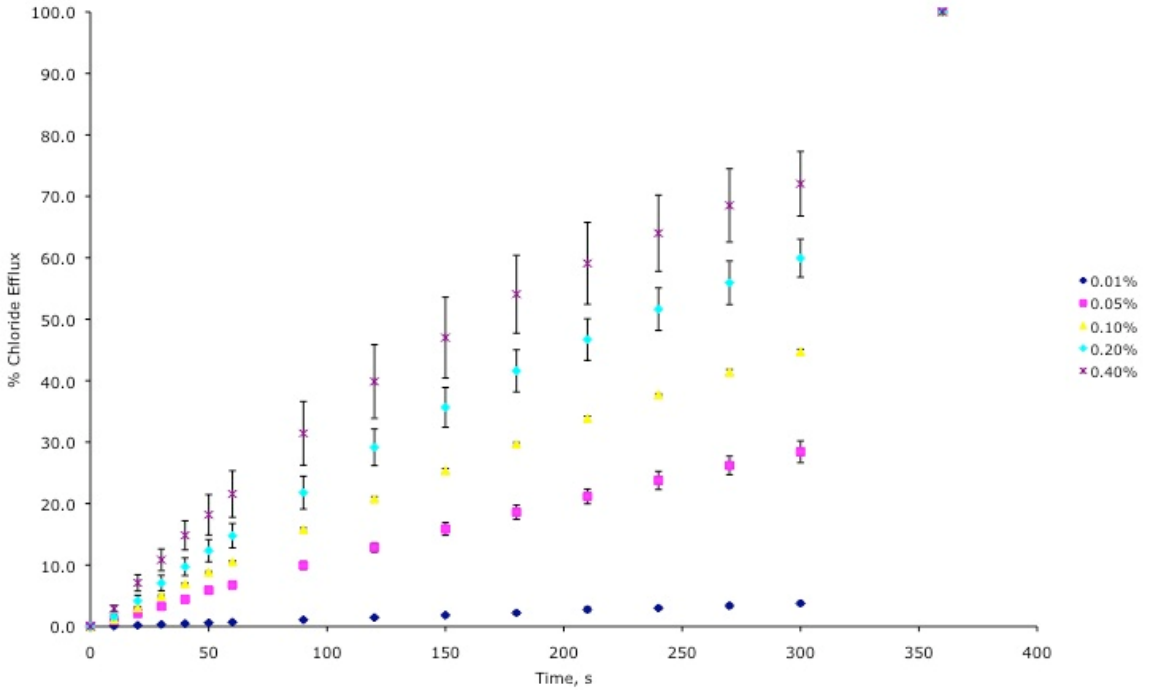


Figure S33 Chloride efflux promoted by addition of various molar% (with respect to lipid) of receptor **4** from unilamellar POPC vesicles loaded with 489 mM NaCl buffered to pH 7.2 with sodium phosphate salts. The vesicles were dispersed in 489 mM $NaNO_3$ buffered to pH 7.2 with sodium phosphate salts. At the end of the experiment, detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride release. Each point represents the average of three trials.

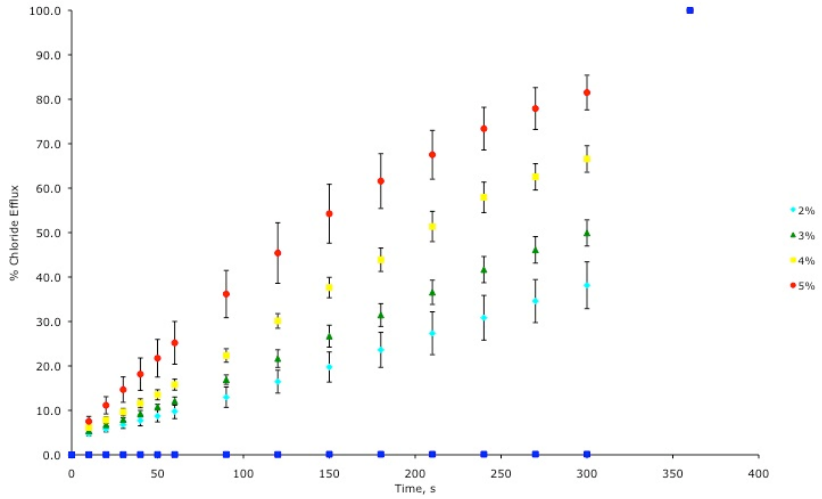


Figure S34 Chloride efflux promoted by addition of various molar% (with respect to lipid) of receptor **6** from unilamellar POPC vesicles loaded with 489 mM NaCl buffered to pH 7.2 with sodium phosphate salts. The vesicles were dispersed in 489 mM $NaNO_3$ buffered to pH 7.2 with sodium phosphate salts. At the end of the experiment, detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride release. Each point represents the average of three trials.

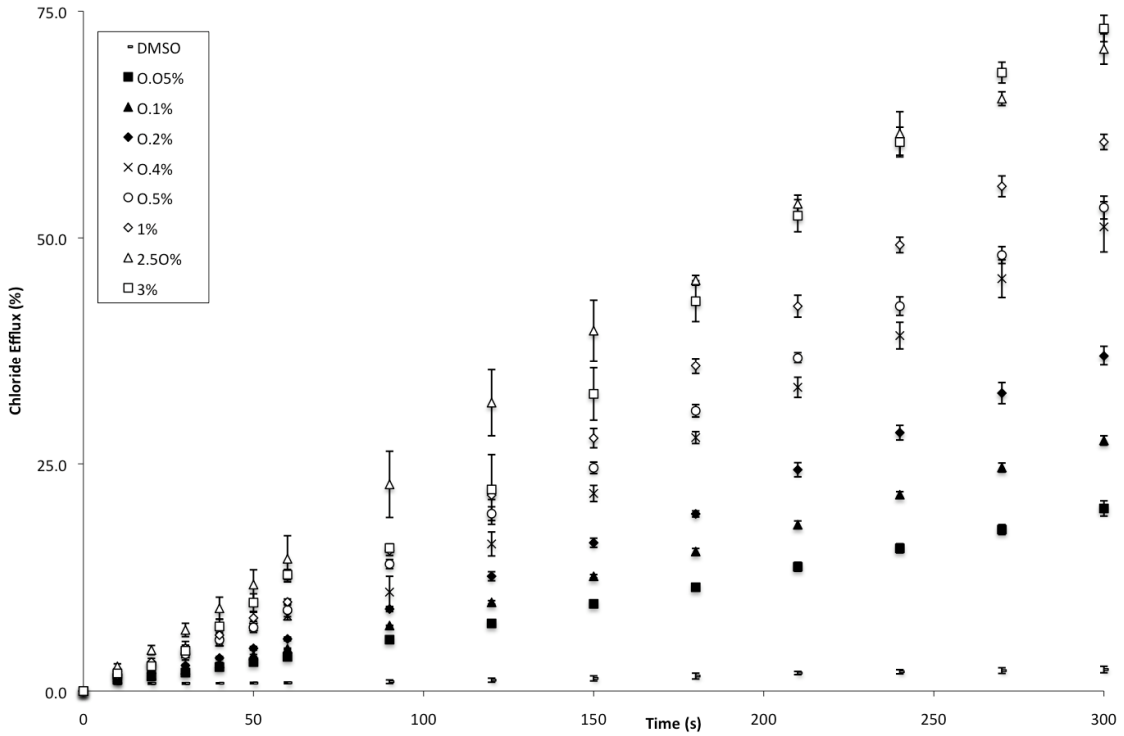


Figure S35 Chloride efflux promoted by addition of various molar% (with respect to lipid) of receptor **4** from unilamellar POPC vesicles loaded with 489mM NaCl buffered to pH 7.2 with 20mM sodium phosphate salts upon addition of a $NaHCO_3$ pulse to make the extravesicular bicarbonate concentration 40mM. The vesicles were dispersed in 167mM Na_2SO_4 buffered at pH 7.2 with 20mM sodium phosphate salts. Each point represents an average of 3 trials.

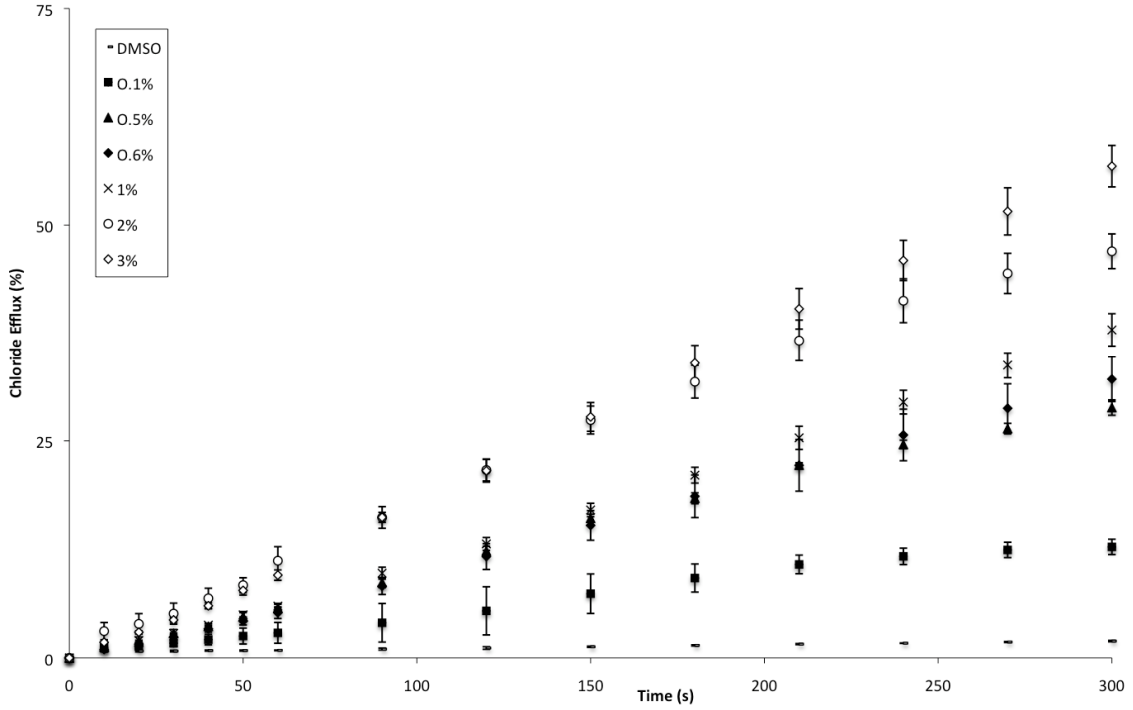


Figure S36 Chloride efflux promoted by addition of various molar% (with respect to lipid) of receptor **6** from unilamellar POPC vesicles loaded with 489mM NaCl buffered to pH 7.2 with 20mM sodium phosphate salts upon addition of a $NaHCO_3$ pulse to make the extravesicular bicarbonate concentration 40mM. The vesicles were dispersed in 167mM Na_2SO_4 buffered at pH 7.2 with 20mM sodium phosphate salts. Each point represents an average of 3 trials.

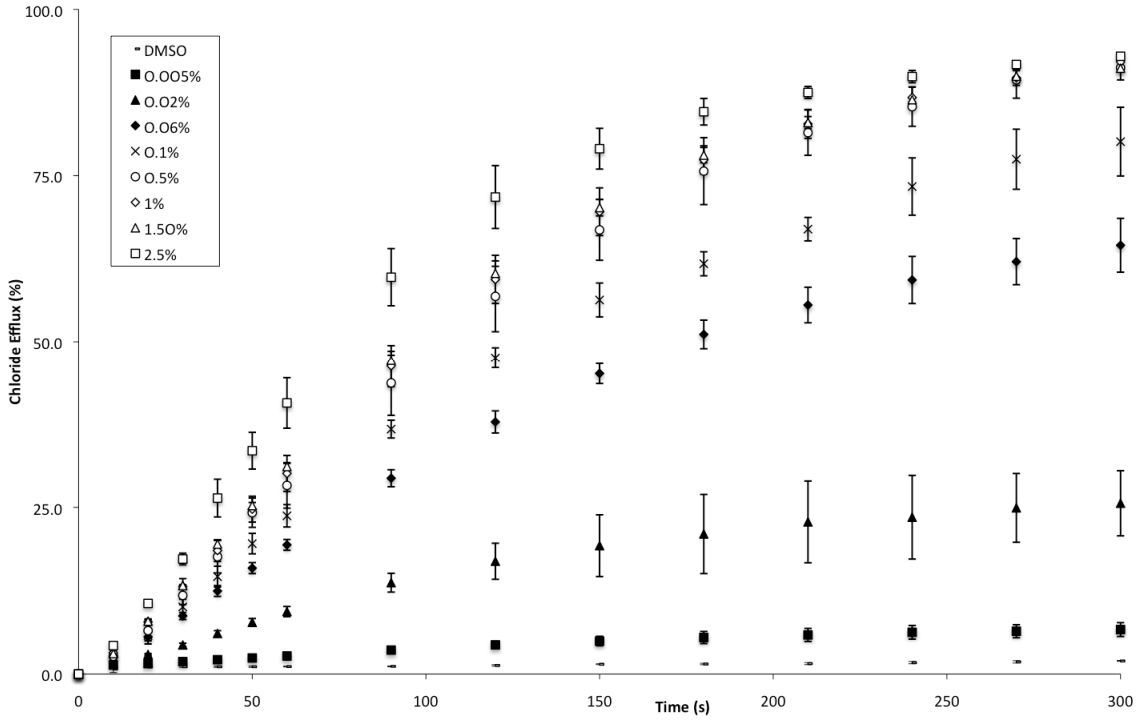


Figure S37 Chloride efflux promoted by addition of various molar% (with respect to lipid) of receptor **8** from unilamellar POPC vesicles loaded with 489mM NaCl buffered to pH 7.2 with 20mM sodium phosphate salts upon addition of a $NaHCO_3$ pulse to make the extravesicular bicarbonate concentration 40mM. The vesicles were dispersed in 167mM Na_2SO_4 buffered at pH 7.2 with 20mM sodium phosphate salts. Each point represents an average of 3 trials.

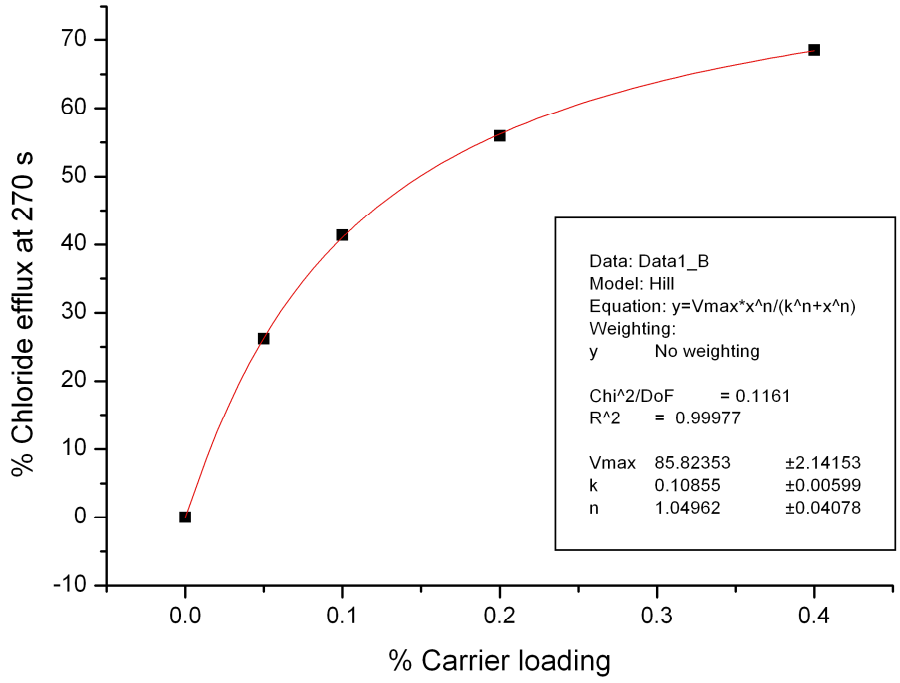


Figure S38 Hill plot for chloride release mediated by receptor **4** from unilamellar POPC vesicles loaded with 489 mM NaCl buffered to pH 7.2 with sodium phosphate salts. The vesicles were dispersed in 489 mM $NaNO_3$ buffered to pH 7.2 with 5 mM sodium phosphate salts. Chloride efflux was measured at 270 s.

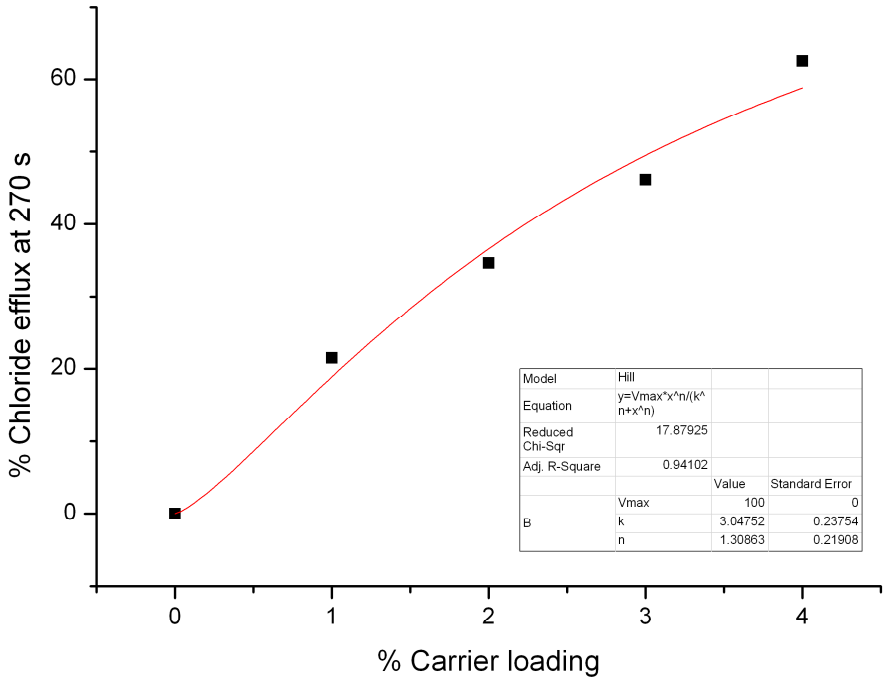


Figure S39 Hill plot for chloride release mediated by receptor **6** from unilamellar POPC vesicles loaded with 489 mM NaCl buffered to pH 7.2 with sodium phosphate salts. The vesicles were dispersed in 489 mM $NaNO_3$ buffered to pH 7.2 with 5 mM sodium phosphate salts. Chloride efflux was measured at 270 s.

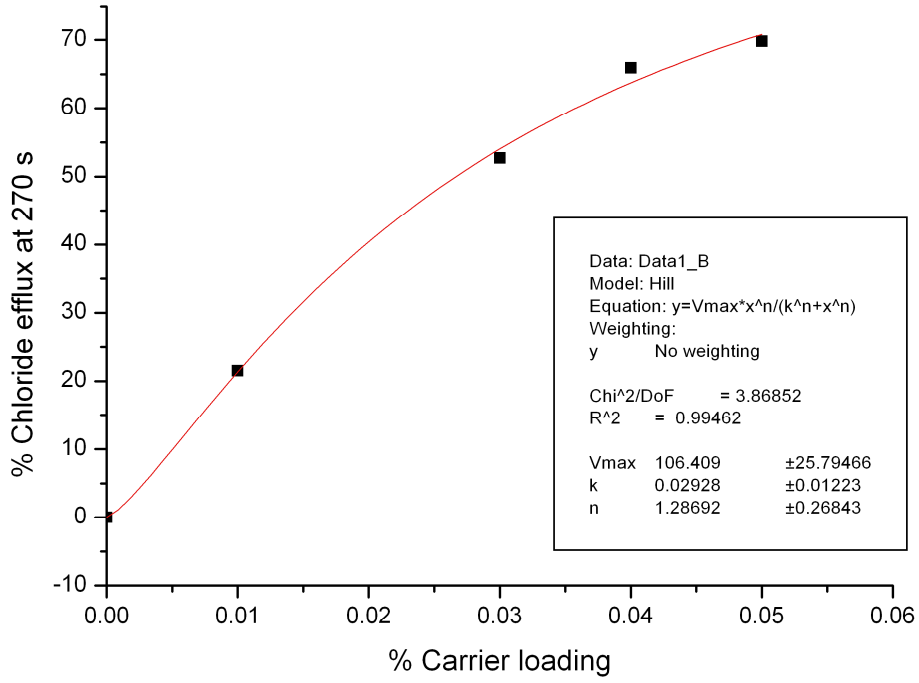


Figure S40 Hill plot for chloride release mediated by receptor **8** from unilamellar POPC vesicles loaded with 489 mM NaCl buffered to pH 7.2 with sodium phosphate salts. The vesicles were dispersed in 489 mM $NaNO_3$ buffered to pH 7.2 with 5 mM sodium phosphate salts. Chloride efflux was measured at 270 s.

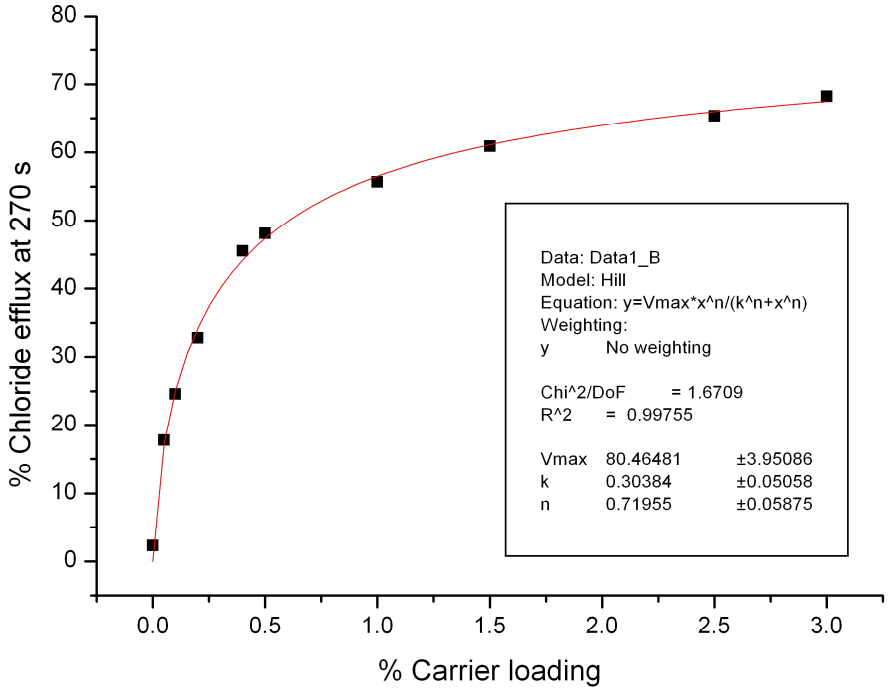


Figure S41 Hill plot for chloride release mediated by receptor **4** from unilamellar POPC vesicles loaded with 489mM NaCl buffered to pH 7.2 with 20mM sodium phosphate salts upon addition of a $NaHCO_3$ pulse to make the extravesicular bicarbonate concentration 40mM. The vesicles were dispersed in 167mM Na_2SO_4 buffered at pH 7.2 with 20mM sodium phosphate salts. Each point represents an average of 3 trials at t=390s (270s after bicarbonate pulse).

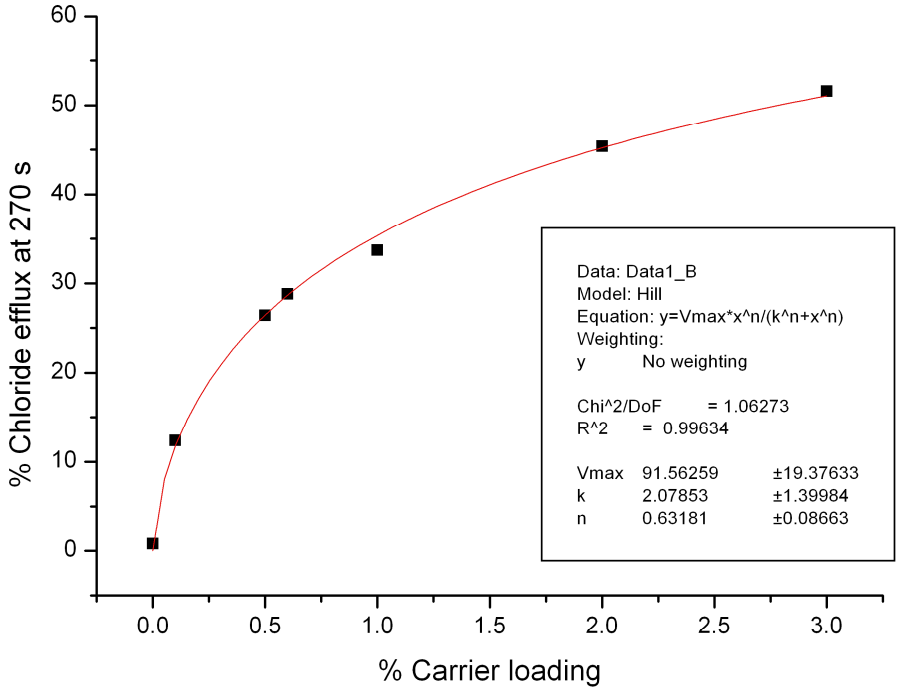


Figure S42 Hill plot for chloride release mediated by receptor **6** from unilamellar POPC vesicles loaded with 489mM NaCl buffered to pH 7.2 with 20mM sodium phosphate salts upon addition of a $NaHCO_3$ pulse to make the extravesicular bicarbonate concentration 40mM. The vesicles were dispersed in 167mM Na_2SO_4 buffered at pH 7.2 with 20mM sodium phosphate salts. Each point represents an average of 3 trials at t=390s (270s after bicarbonate pulse).

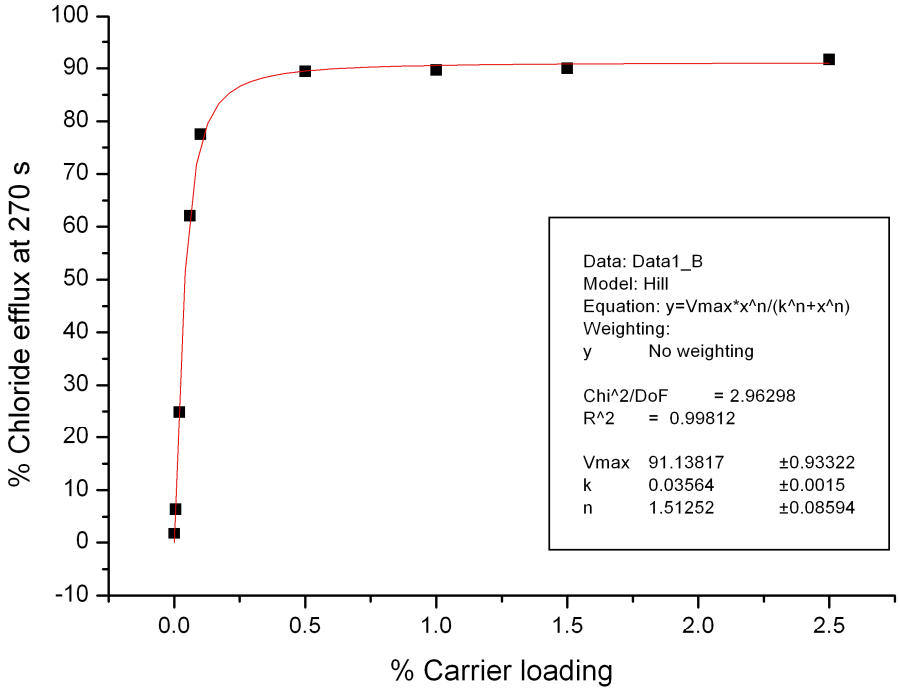


Figure S43 Hill plot for chloride release mediated by receptor **8** from unilamellar POPC vesicles loaded with 489mM NaCl buffered to pH 7.2 with 20mM sodium phosphate salts upon addition of a $NaHCO_3$ pulse to make the extravesicular bicarbonate concentration 40mM. The vesicles were dispersed in 167mM Na_2SO_4 buffered at pH 7.2 with 20mM sodium phosphate salts. Each point represents an average of 3 trials at t=390s (270s after bicarbonate pulse).

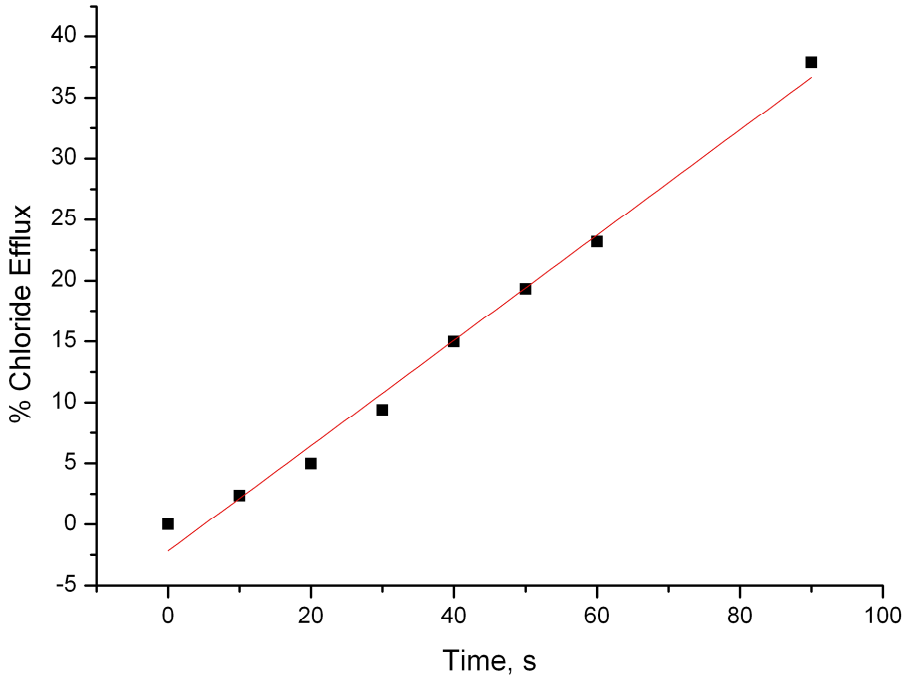


Figure S44 Chloride efflux promoted by 0.02 molar equiv of receptor **4** from unilamellar POPC vesicles loaded with 489mM NaCl buffered to pH 7.2 with sodium phosphate salts. The vesicles were dispersed in 489mM $NaNO_3$ buffered to pH 7.2 with 5mM sodium phosphate salts. Each point represents the average of three trials. The data for the first 90s after the bicarbonate pulse was fitted to a straight line of the form y=mx+c, where $m \propto k_{initial}$ = 0.431 $\%s^{-1}$ (4% error).

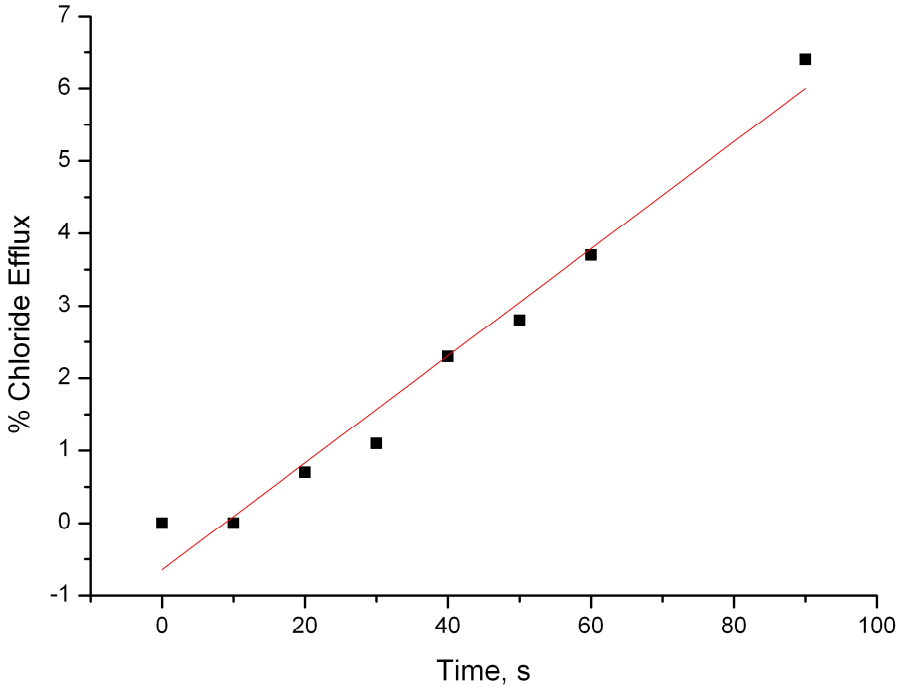


Figure S45 Chloride efflux promoted by 0.02 molar equiv of receptor **6** from unilamellar POPC vesicles loaded with 489mM NaCl buffered to pH 7.2 with sodium phosphate salts. The vesicles were dispersed in 489mM $NaNO_3$ buffered to pH 7.2 with 5mM sodium phosphate salts. Each point represents the average of three trials. The data for the first 90s after the bicarbonate pulse was fitted to a straight line of the form y=mx+c, where $m \propto k_{initial}$ = 0.074 $\%s^{-1}$ (6% error).

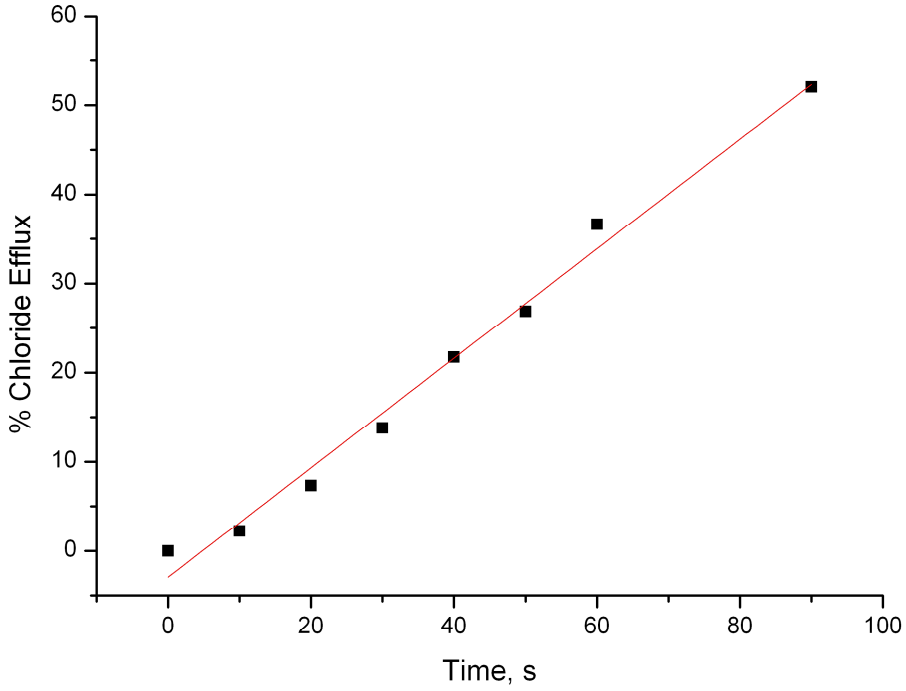


Figure S46 Chloride efflux promoted by 0.02 molar equiv of receptor **8** from unilamellar POPC vesicles loaded with 489mM NaCl buffered to pH 7.2 with sodium phosphate salts. The vesicles were dispersed in 489mM $NaNO_3$ buffered to pH 7.2 with 5mM sodium phosphate salts. Each point represents the average of three trials. The data for the first 90s after the bicarbonate pulse was fitted to a straight line of the form y=mx+c, where $m \propto k_{initial}$ = 0.614 $\%s^{-1}$ (4% error).

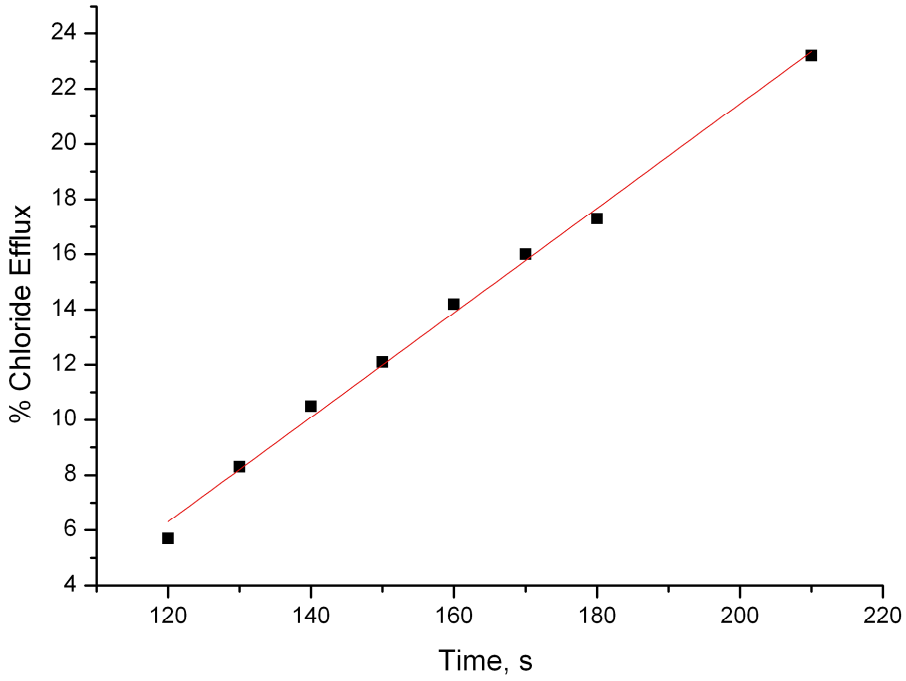


Figure S47 Chloride efflux promoted by 0.02 molar equiv of receptor **4** from unilamellar POPC vesicles loaded with 489mM NaCl buffered to pH 7.2 with 20mM sodium phosphate salts upon addition of a $NaHCO_3$ pulse to make the extravesicular bicarbonate concentration 40mM. The vesicles were dispersed in 167mM Na_2SO_4 buffered at pH 7.2 with 20mM sodium phosphate salts. Each point represents an average of 3 trials. The data for the first 90s after the bicarbonate pulse was fitted to a straight line of the form y=mx+c, where $m \propto k_{initial}$ = 0.277 $\%s^{-1}$ (6% error).

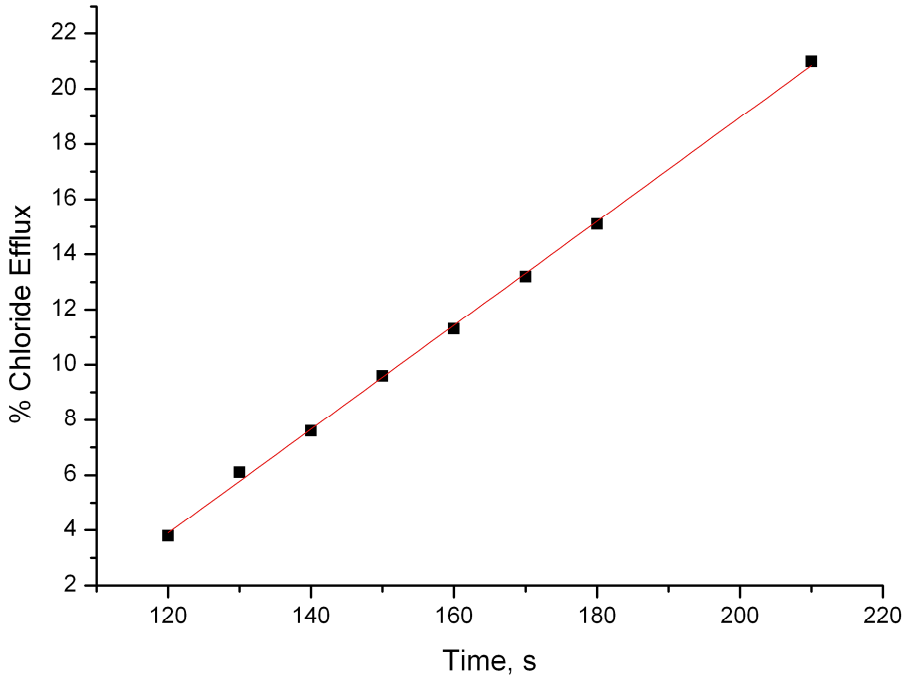


Figure S48 Chloride efflux promoted by 0.02 molar equiv of receptor **6** from unilamellar POPC vesicles loaded with 489mM NaCl buffered to pH 7.2 with 20mM sodium phosphate salts upon addition of a $NaHCO_3$ pulse to make the extravesicular bicarbonate concentration 40mM. The vesicles were dispersed in 167mM Na_2SO_4 buffered at pH 7.2 with 20mM sodium phosphate salts. Each point represents an average of 3 trials. The data for the first 90s after the bicarbonate pulse was fitted to a straight line of the form y=mx+c, where $m \propto k_{initial}$ = 0.188 $\%s^{-1}$ (1% error).

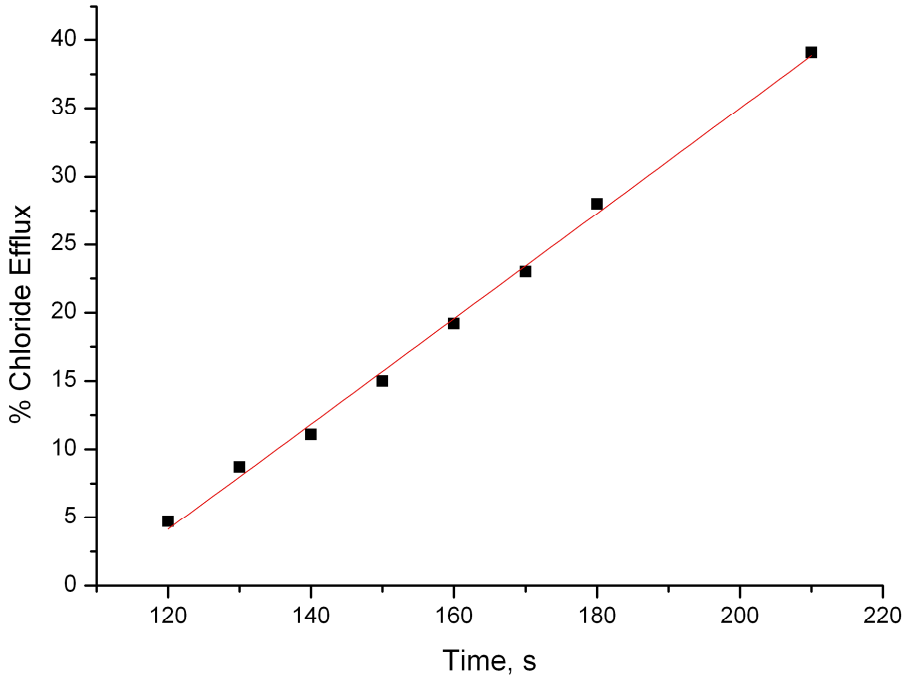
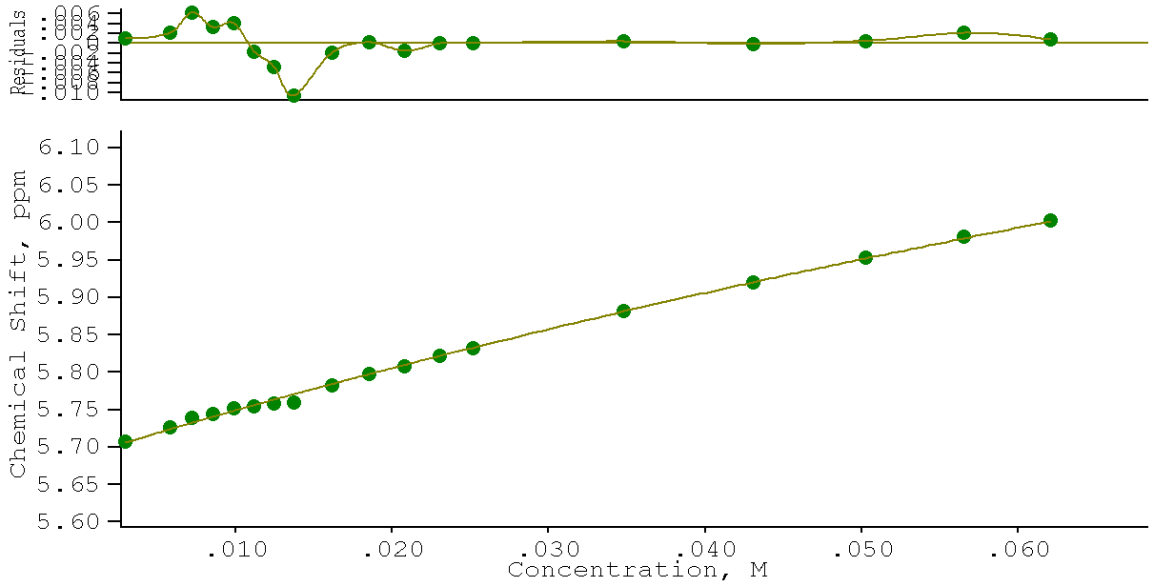


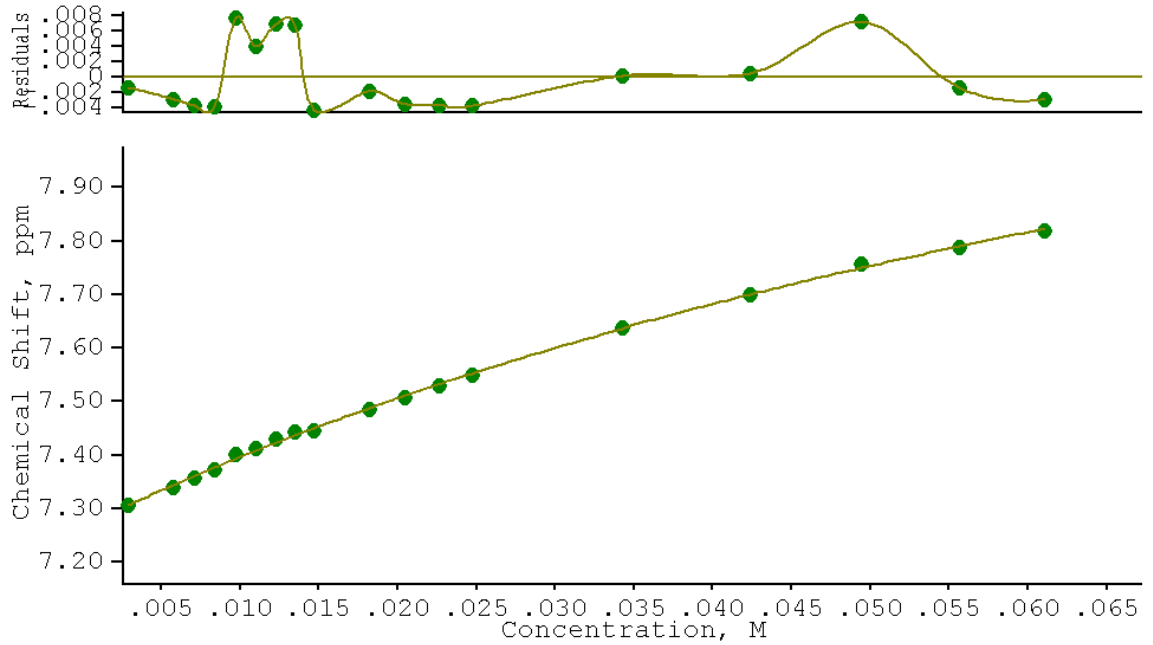
Figure S49 Chloride efflux promoted by 0.02 molar equiv of receptor **8** from unilamellar POPC vesicles loaded with 489mM NaCl buffered to pH 7.2 with 20mM sodium phosphate salts upon addition of a $NaHCO_3$ pulse to make the extravesicular bicarbonate concentration 40mM. The vesicles were dispersed in 167mM Na_2SO_4 buffered at pH 7.2 with 20mM sodium phosphate salts. Each point represents an average of 3 trials. The data for the first 90s after the bicarbonate pulse was fitted to a straight line of the form y=mx+c, where $m \propto k_{initial}$ = 0.386 $\%s^{-1}$ (2% error).

S5 ^{1}H NMR titration binding curves



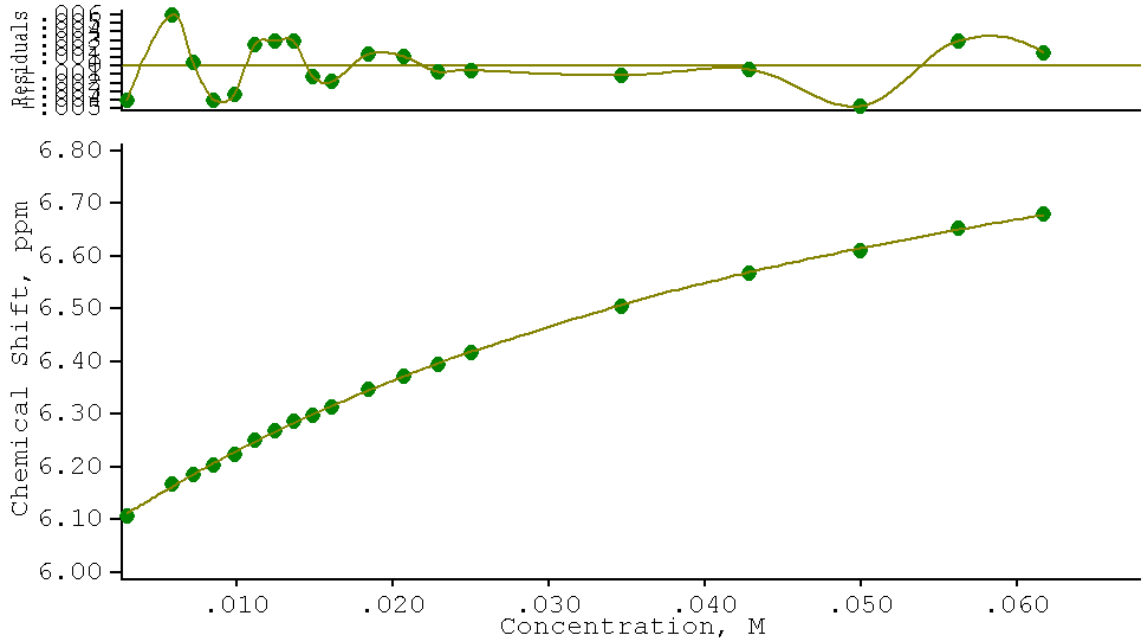
K_a = <10M^{-1} Error = N.A.

Figure S50 NMR titration of compound **3** with TBACl in 0.5% H_2O/DMSO-d_6 following NH at 5.68ppm.



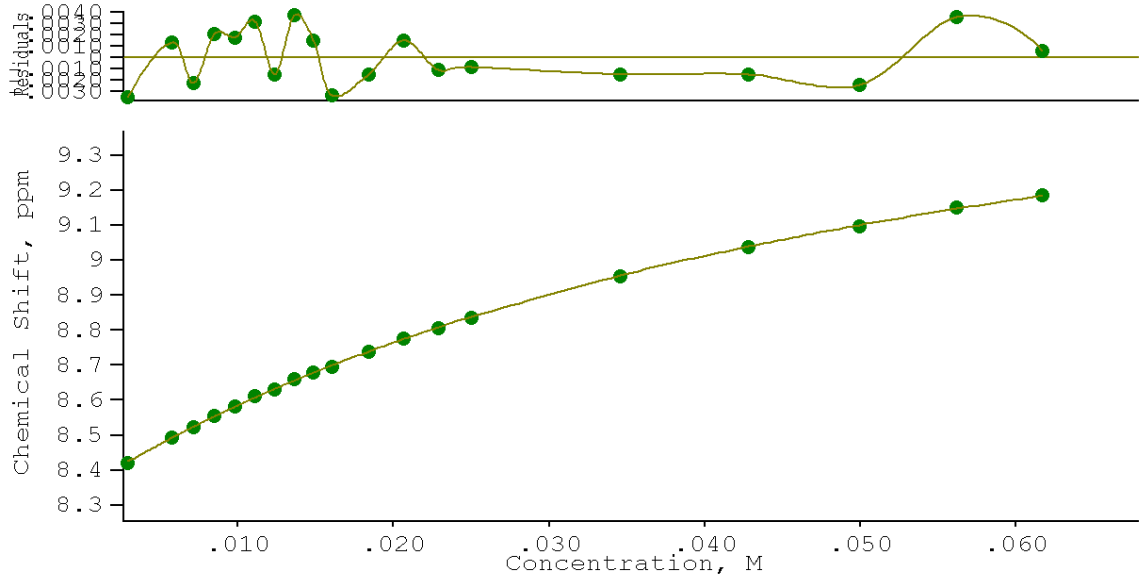
K_a = 10M^{-1} Error = 10%

Figure S51 NMR titration of compound **4** with TBACl in 0.5% H_2O/DMSO-d_6 following NH at 7.25ppm.



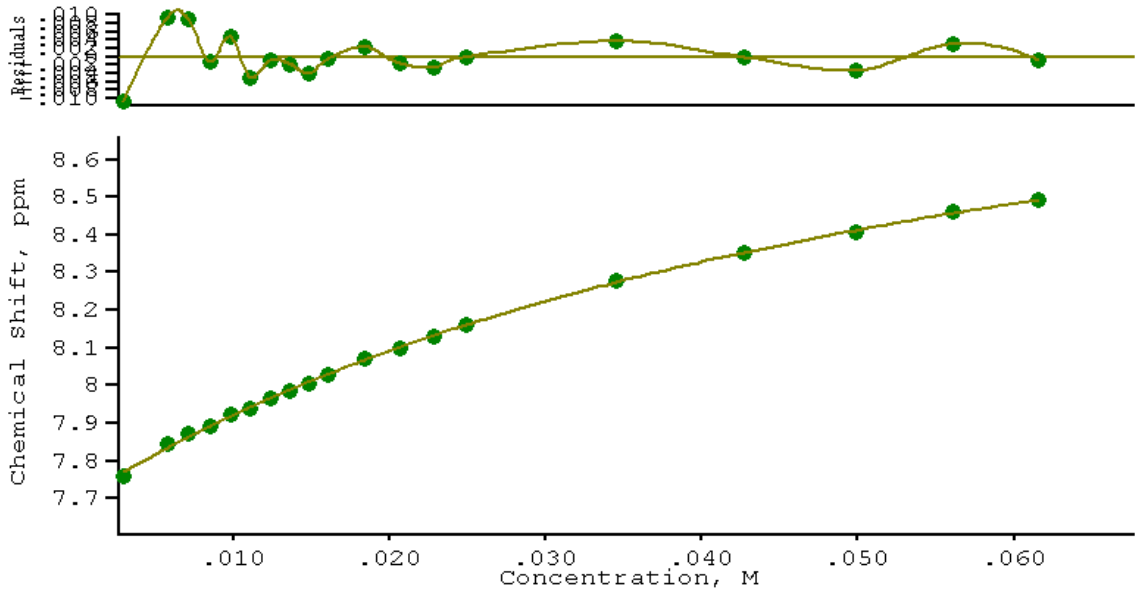
K_a = 21M^{-1} Error = <1%

Figure S52 NMR titration of compound **5** with TBACl in 0.5% H_2O/DMSO-d_6 following NH at 6.05ppm.



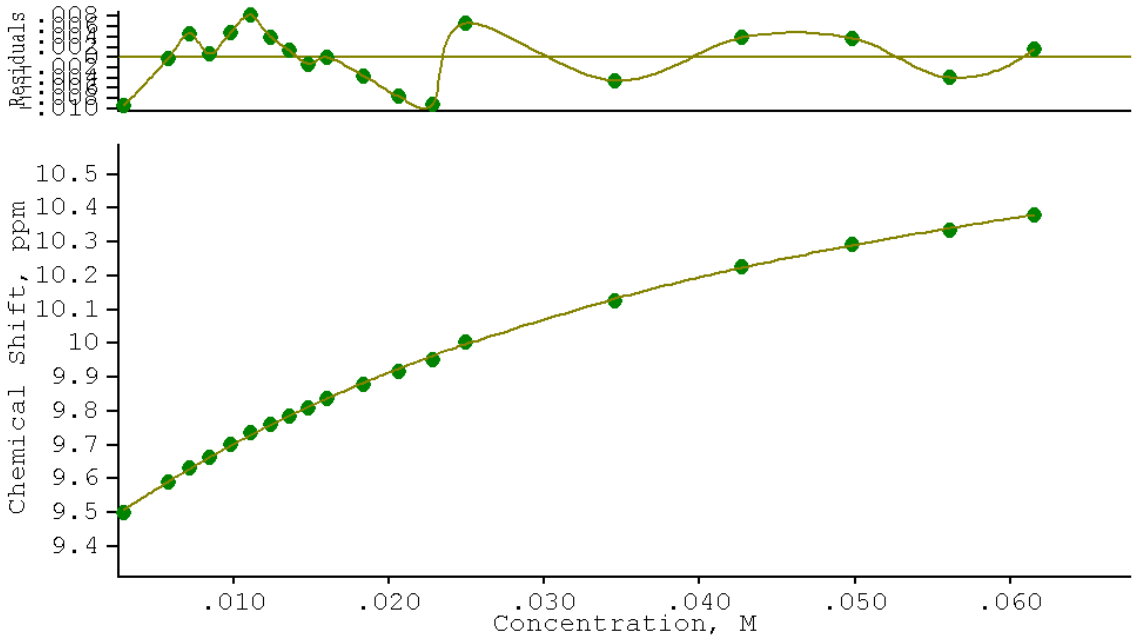
K_a = 22M^{-1} Error = <1%

Figure S53 NMR titration of compound **5** with TBACl in 0.5% H_2O/DMSO-d_6 following NH at 8.34ppm.



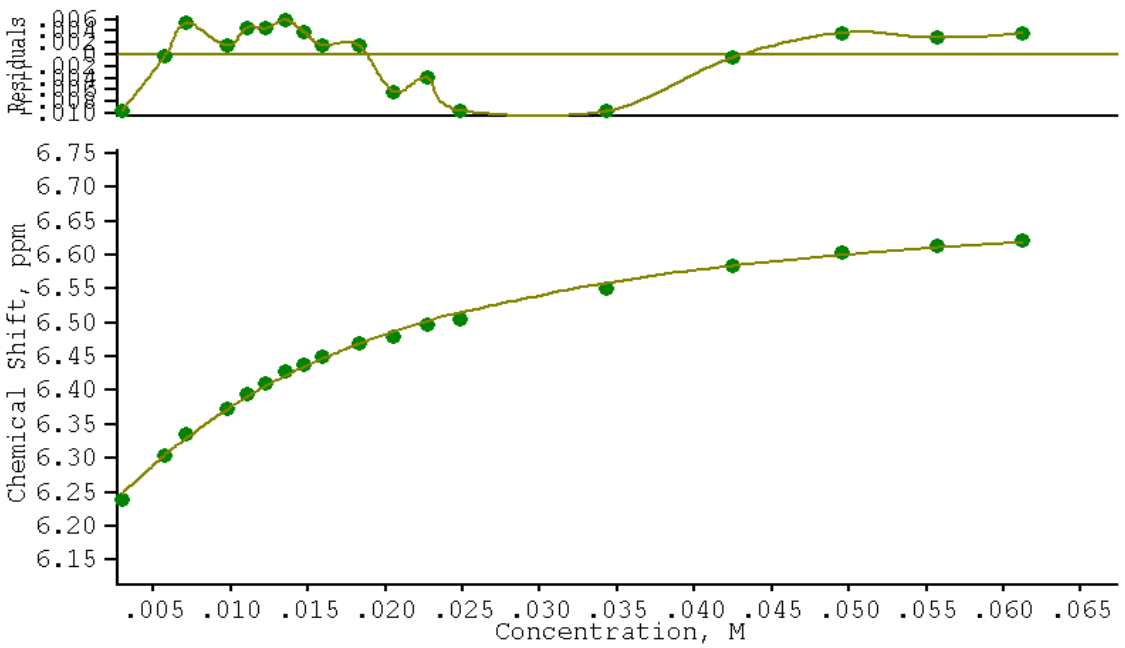
K_a = 22M^{-1} Error = 5%

Figure S54 NMR titration of compound **6** with TBACl in 0.5% H_2O/DMSO-d_6 following NH at 7.68ppm.



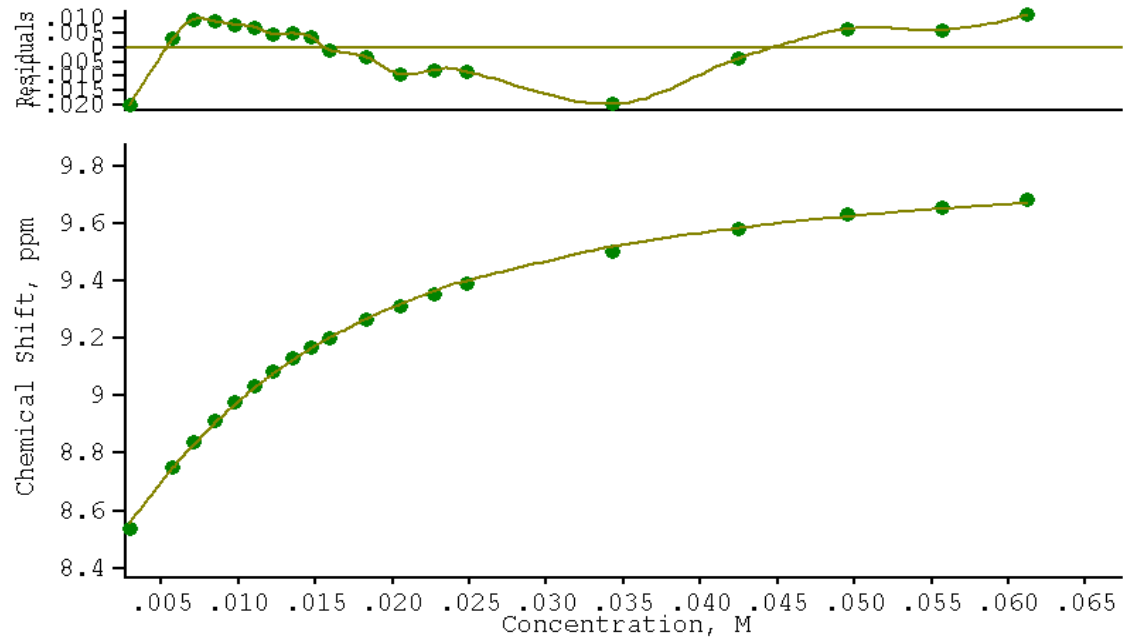
K_a = 26M^{-1} Error = 4%

Figure S55 NMR titration of compound **6** with TBACl in 0.5% H_2O/DMSO-d_6 following NH at 9.40ppm.



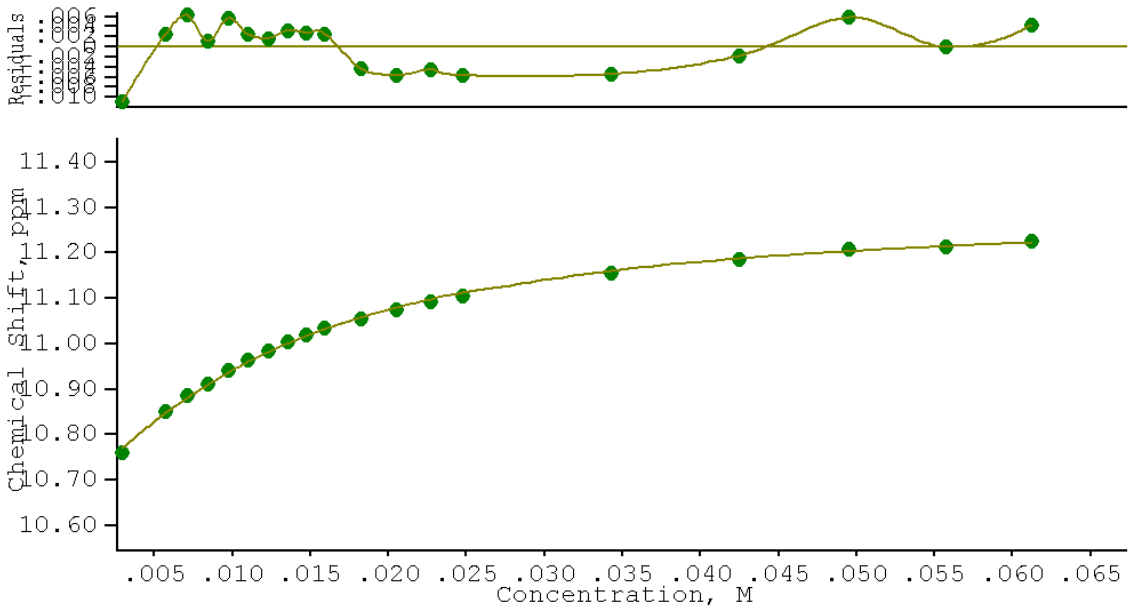
K_a = 96M^{-1} Error = 6%

Figure S56 NMR titration of compound **7** with TBACl in 0.5% H_2O/DMSO-d_6 following NH at 6.15ppm.



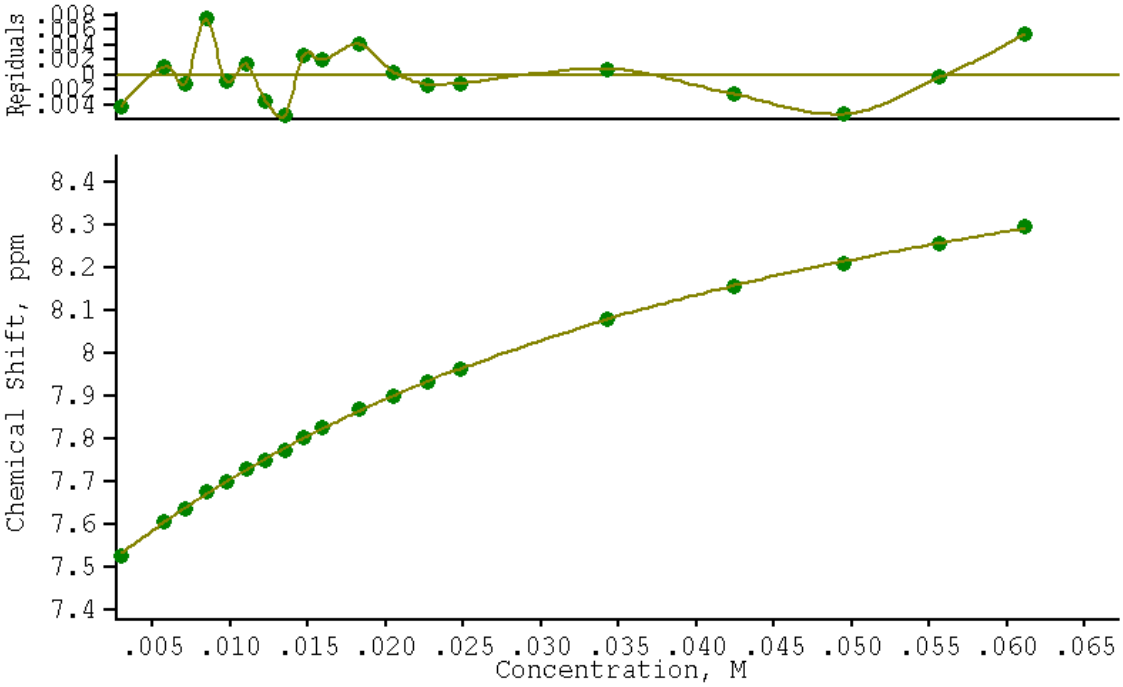
K_a = 128M^{-1} Error = 4%

Figure S57 NMR titration of compound **7** with TBACl in 0.5% H_2O/DMSO-d_6 following NH at 8.26ppm.



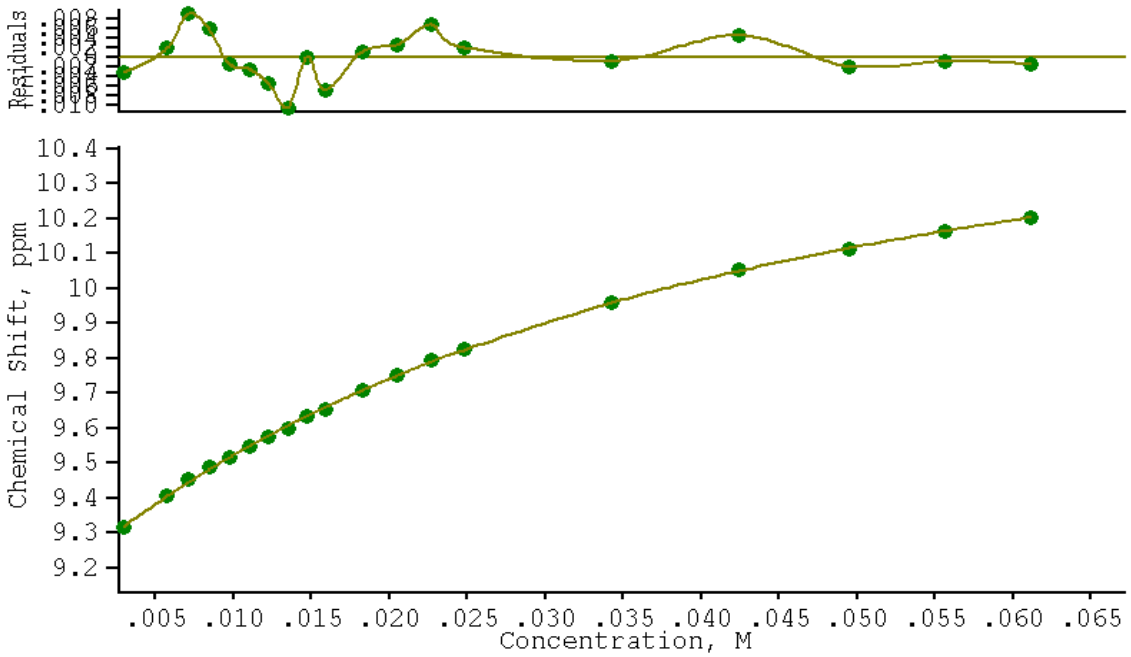
K_a = 126M^{-1} Error = 4%

Figure S58 NMR titration of compound **7** with TBACl in 0.5% H_2O/DMSO-d_6 following NH at 10.65ppm.



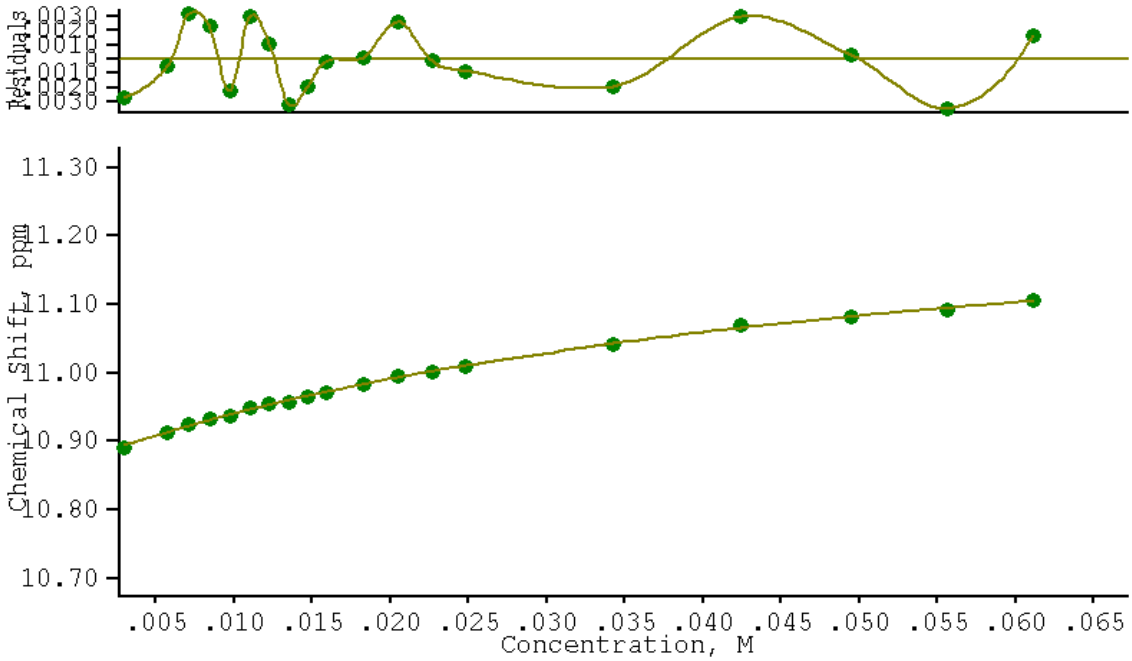
K_a = 28M^{-1} Error = 3%

Figure S59 NMR titration of compound **8** with TBACl in 0.5% H_2O/DMSO-d_6 following NH at 7.42ppm.



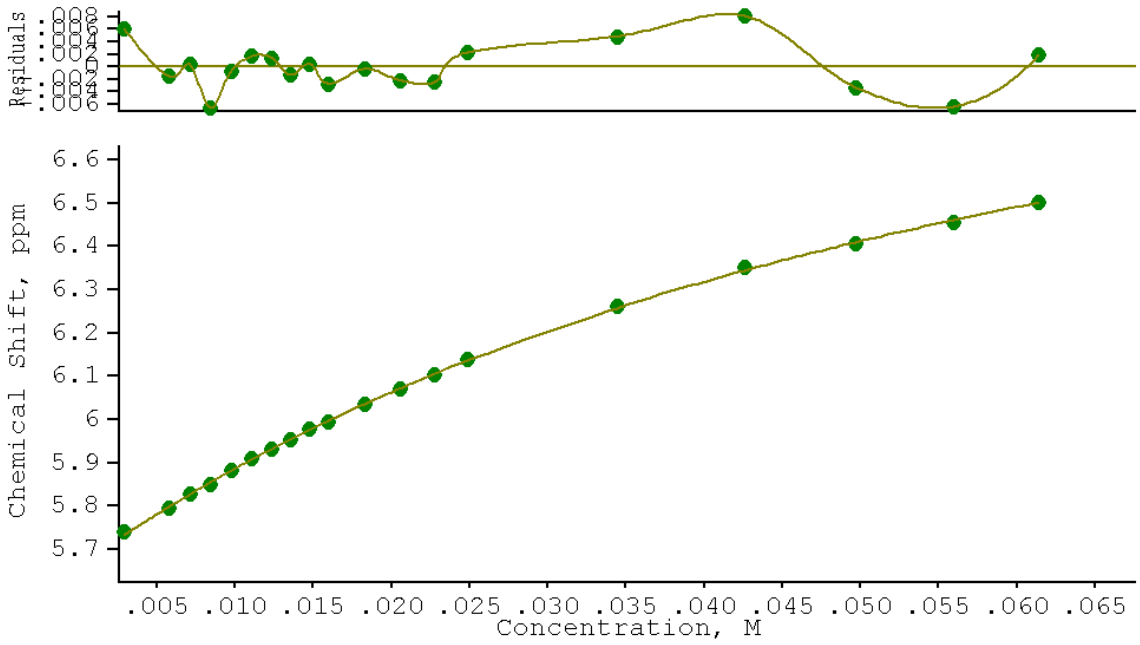
K_a = 29M^{-1} Error = 4%

Figure S60 NMR titration of compound **8** with TBACl in 0.5% H_2O/DMSO-d_6 following NH at 9.21ppm.



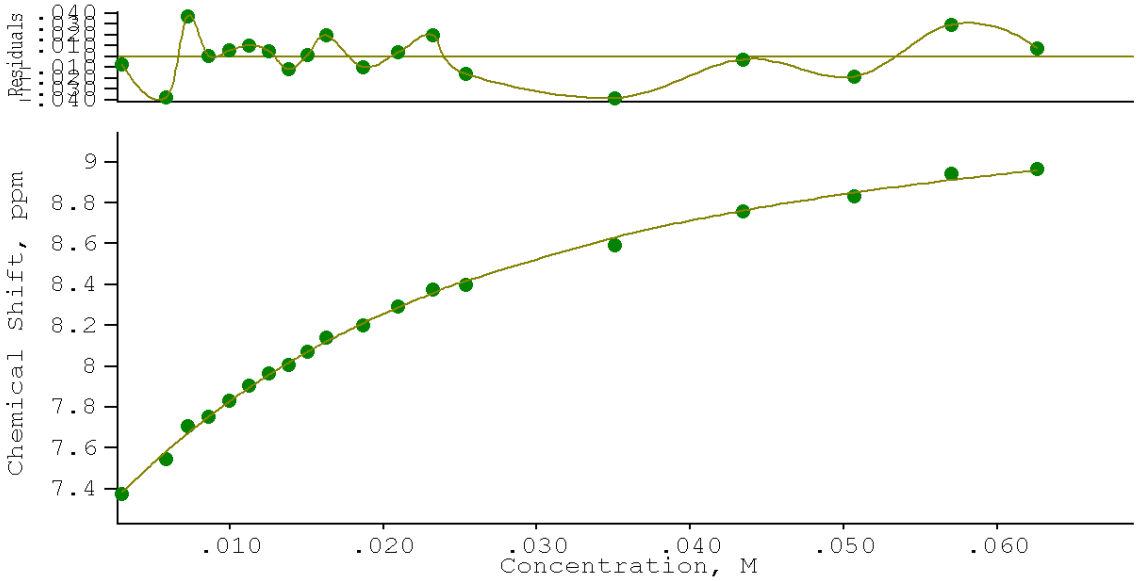
K_a = 24M^{-1} Error = 7%

Figure S61 NMR titration of compound **8** with TBACl in 0.5% H_2O/DMSO-d_6 following NH at 10.87ppm.



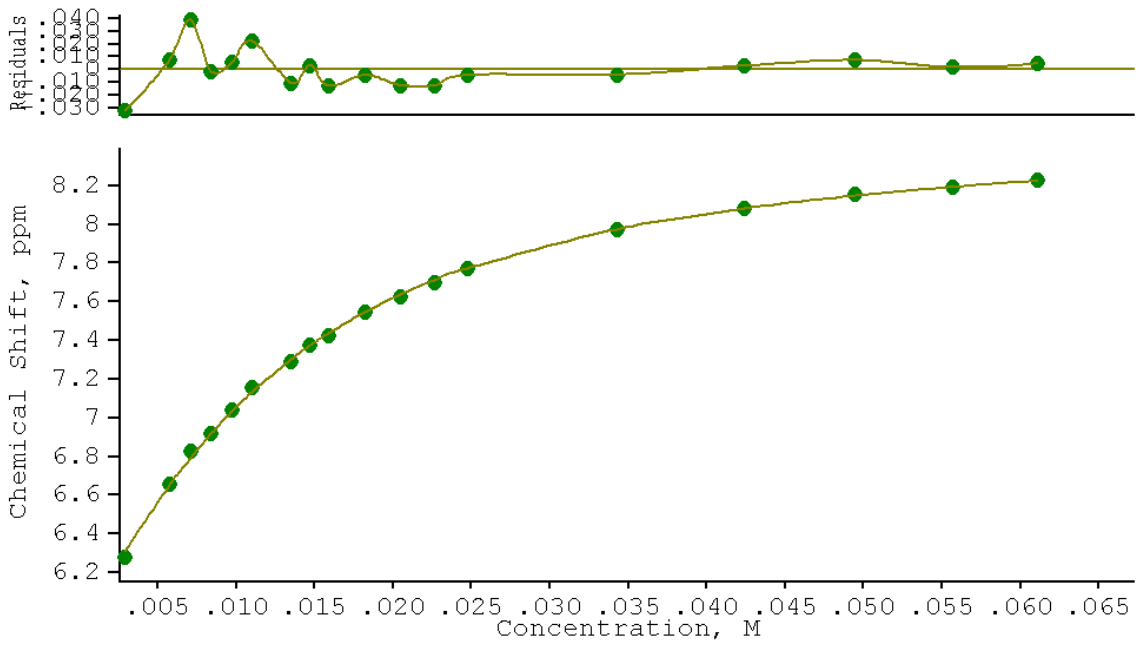
K_a = 18M^{-1} Error = 4%

Figure S62 NMR titration of compound **3** with $TEAHCO_3$ in 0.5% H_2O/DMSO-d_6 following NH at 5.69ppm.



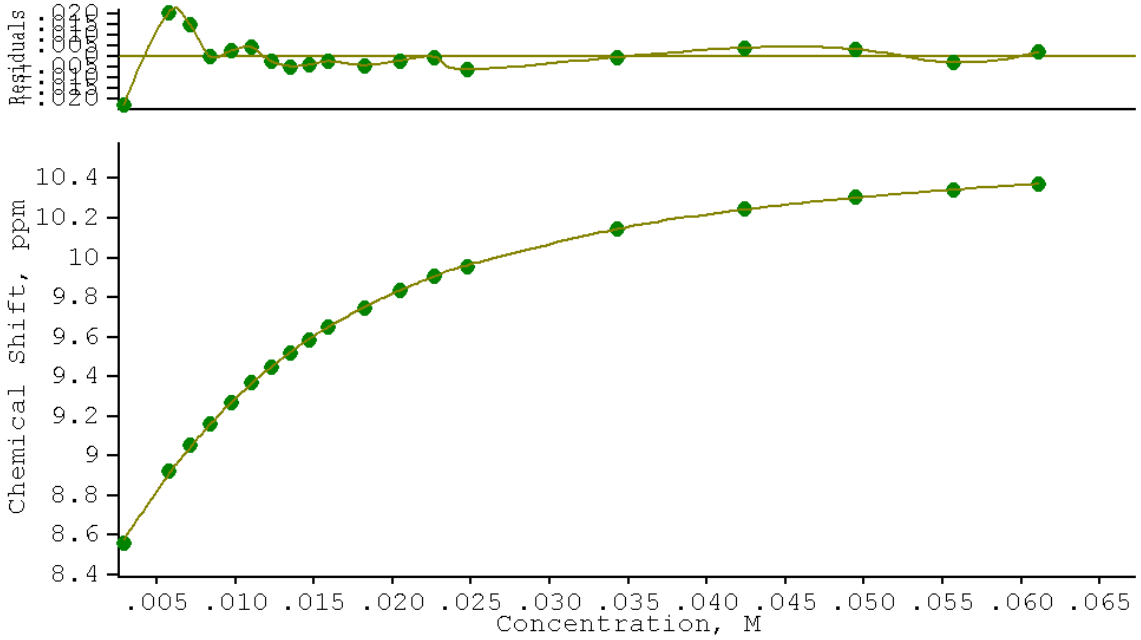
K_a = 58M^{-1} Error = 7%

Figure S63 NMR titration of compound **4** with $TEAHCO_3$ in 0.5% H_2O/DMSO-d_6 following NH at 7.26ppm.



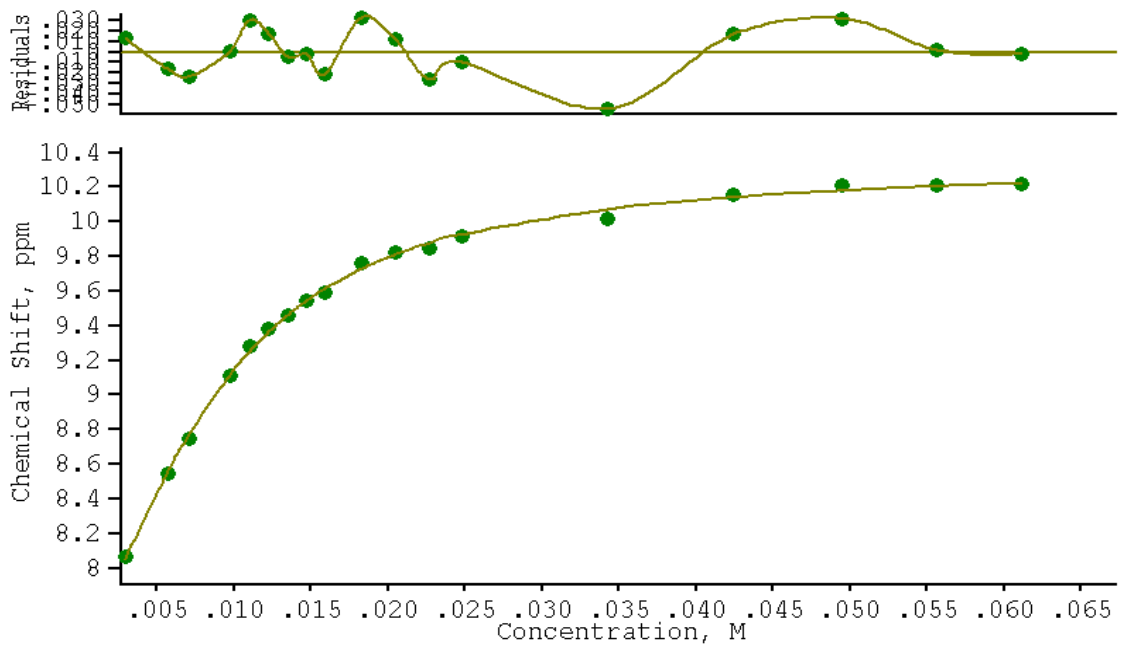
K_a = 135M^{-1} Error = 4%

Figure S64 NMR titration of compound **5** with $TEAHCO_3$ in 0.5% H_2O/DMSO-d_6 following NH at 6.05ppm.



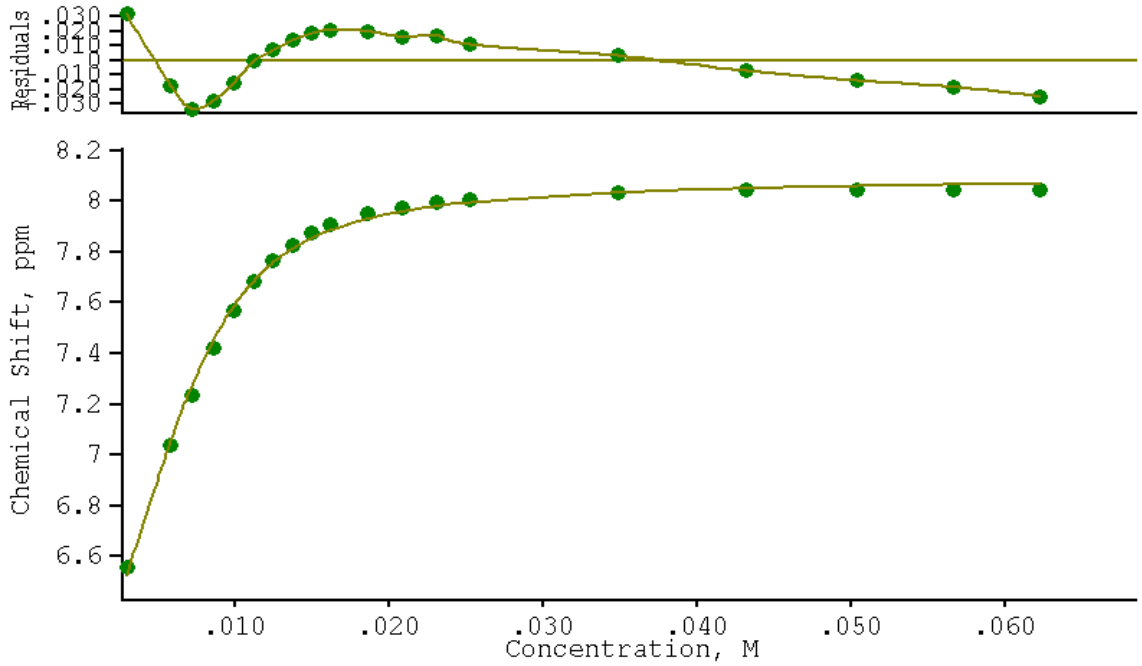
K_a = 143M^{-1} Error = 2%

Figure S65 NMR titration of compound **5** with $TEAHCO_3$ in 0.5% H_2O/DMSO-d_6 following NH at 8.35ppm.



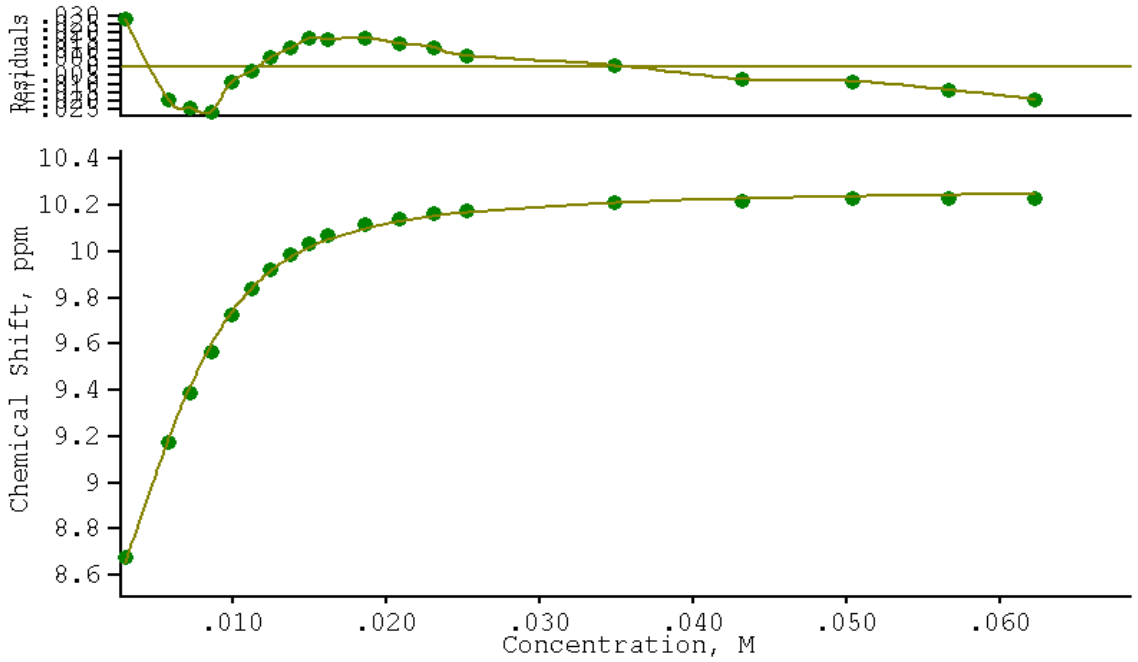
K_a = 343M^{-1} Error = 5%

Figure S66 NMR titration of compound **6** with $TEAHCO_3$ in 0.5% H_2O/DMSO-d_6 following NH at 7.68ppm.



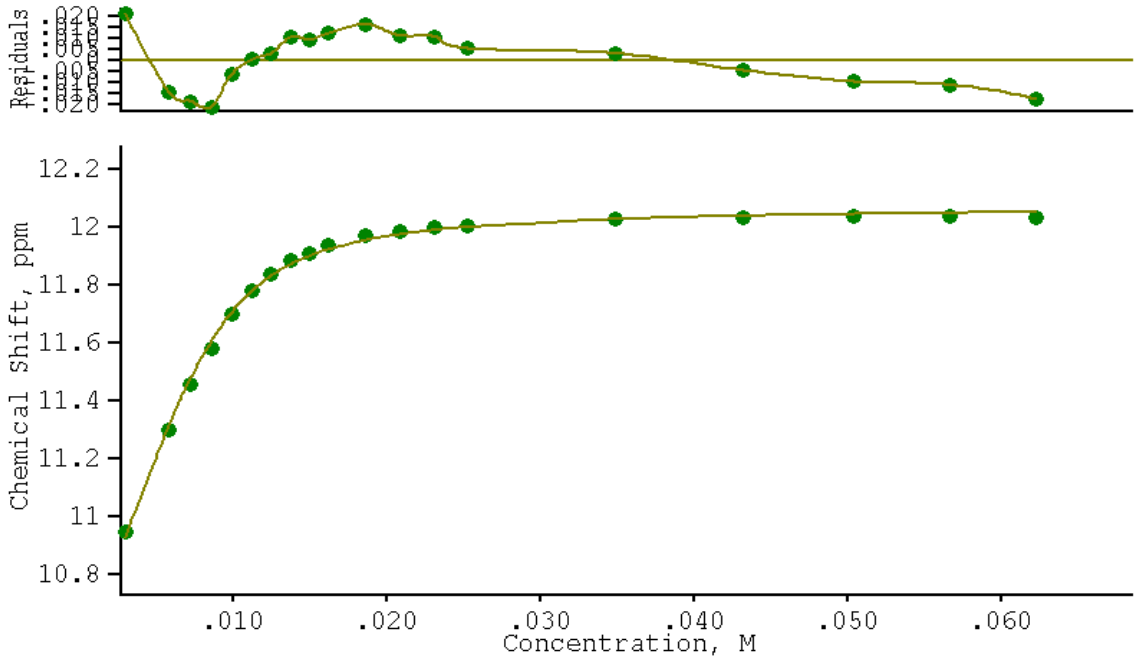
K_a = 1170M^{-1} Error = 7%

Figure S67 NMR titration of compound **7** with $TEAHCO_3$ in 0.5% H_2O/DMSO-d_6 following NH at 6.15ppm.



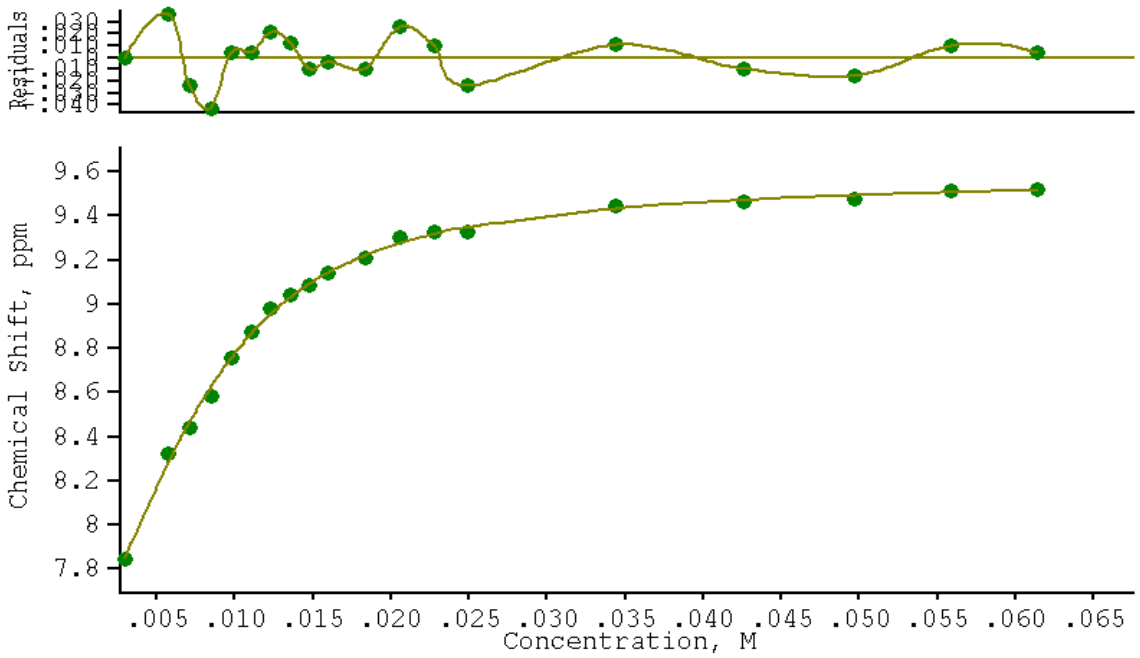
K_a = 1104M^{-1} Error = 5%

Figure S68 NMR titration of compound **7** with $TEAHCO_3$ in 0.5% H_2O/DMSO-d_6 following NH at 8.26ppm.



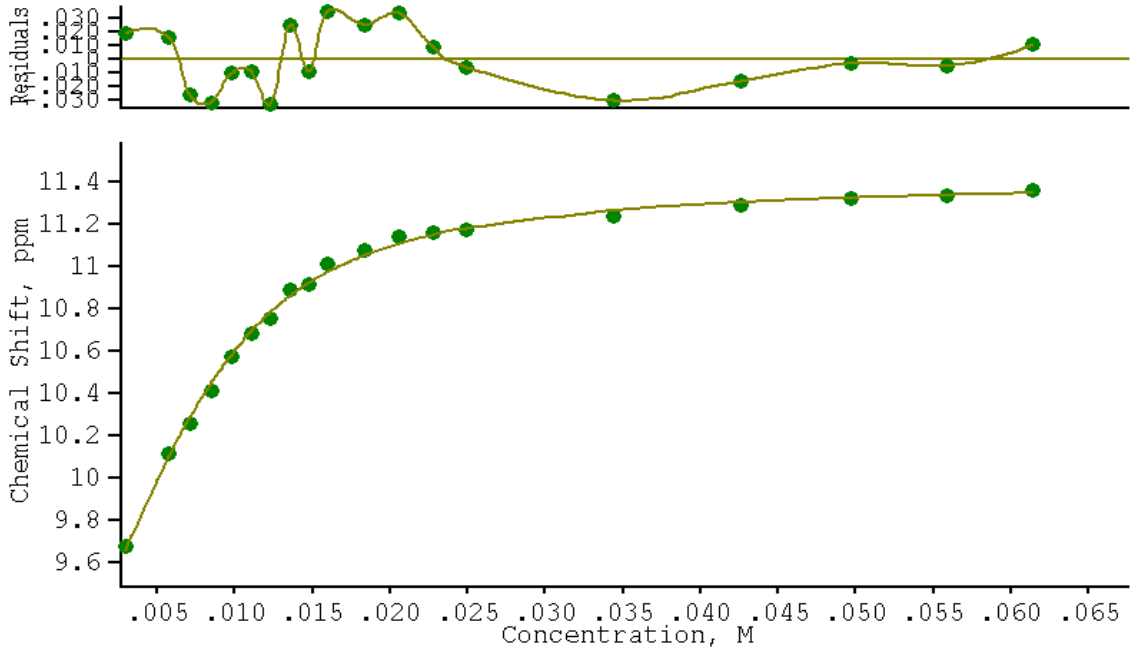
K_a = 1228M^{-1} Error = 6%

Figure S69 NMR titration of compound **7** with $TEAHCO_3$ in 0.5% H_2O/DMSO-d_6 following NH at 10.65ppm.



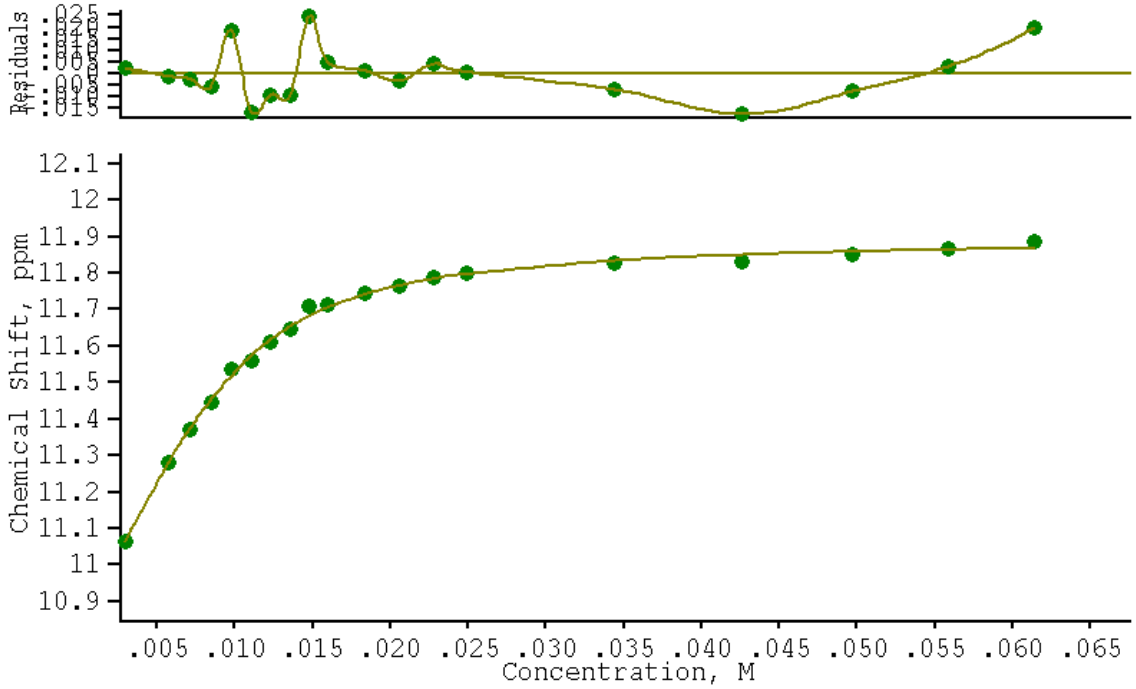
K_a = 516M^{-1} Error = 5%

Figure S70 NMR titration of compound **8** with $TEAHCO_3$ in 0.5% H_2O/DMSO-d_6 following NH at 7.42ppm.



K_a = 526M^{-1} Error = 6%

Figure S71 NMR titration of compound **8** with $TEAHCO_3$ in 0.5% H_2O/DMSO-d_6 following NH at 9.21ppm.



K_a = 613M^{-1} Error = 7%

Figure S72 NMR titration of compound **8** with $TEAHCO_3$ in 0.5% H_2O/DMSO-d_6 following NH at 10.87ppm.

S6 *Job's Plot Analyses*

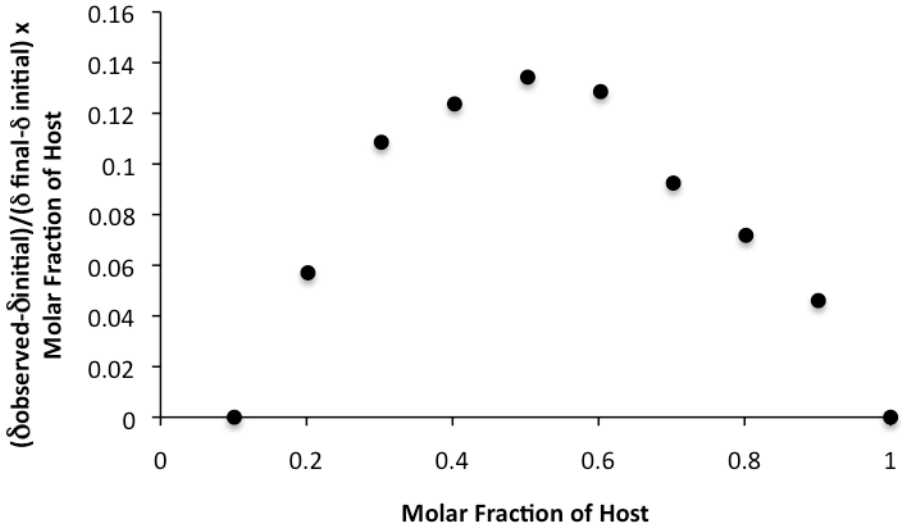


Figure S73 Job plot of compound **3** with TBACl in 0.5% H_2O/DMSO-d_6 following NH at 5.68ppm

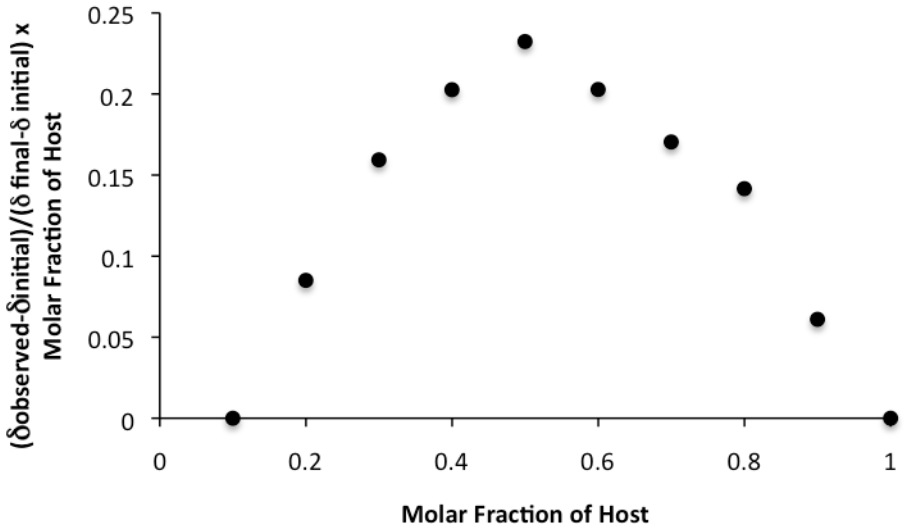


Figure S74 Job plot of compound **4** with TBACl in 0.5% H_2O/DMSO-d_6 following NH at 7.25ppm

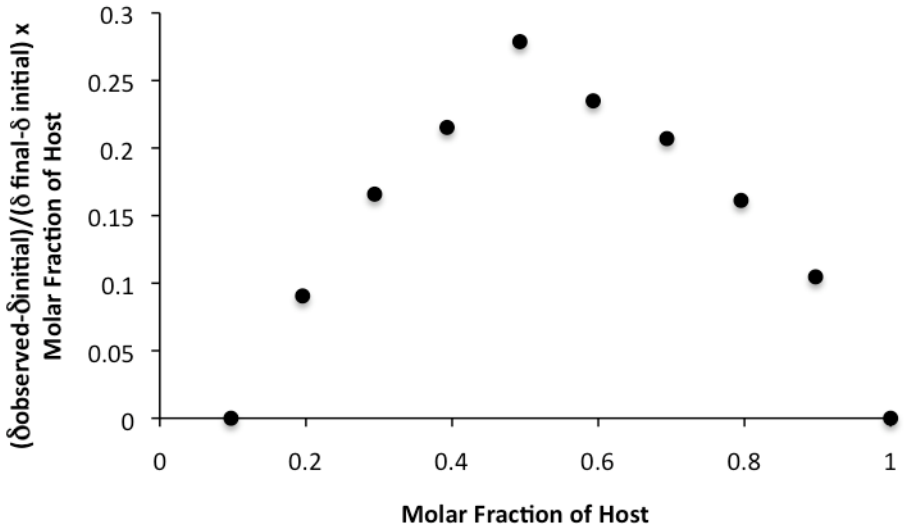


Figure S75 Job plot of compound **5** with TBACl in 0.5% H_2O/DMSO-d_6 following NH at 6.05ppm

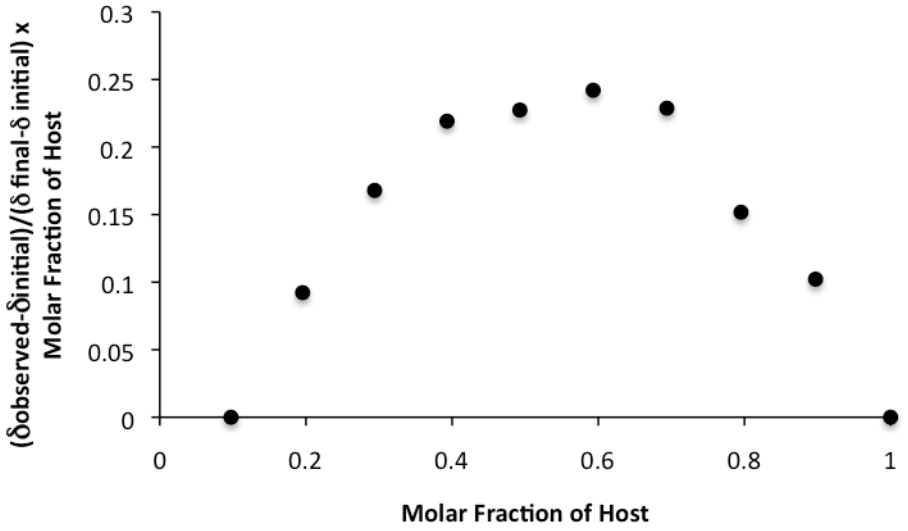


Figure S76 Job plot of compound **5** with TBACl in 0.5% H_2O/DMSO-d_6 following NH at 8.35ppm

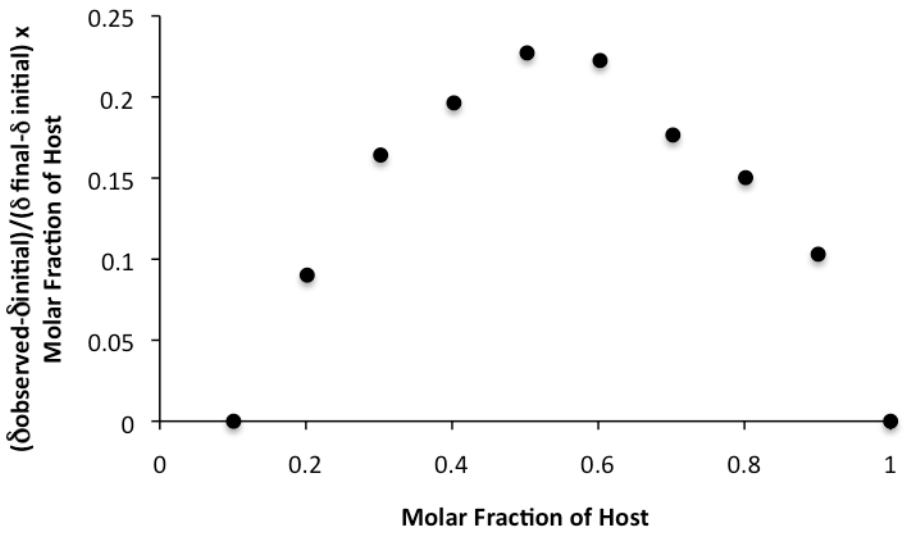


Figure S77 Job plot of compound **6** with TBACl in 0.5% H_2O/DMSO-d_6 following NH at 7.68ppm

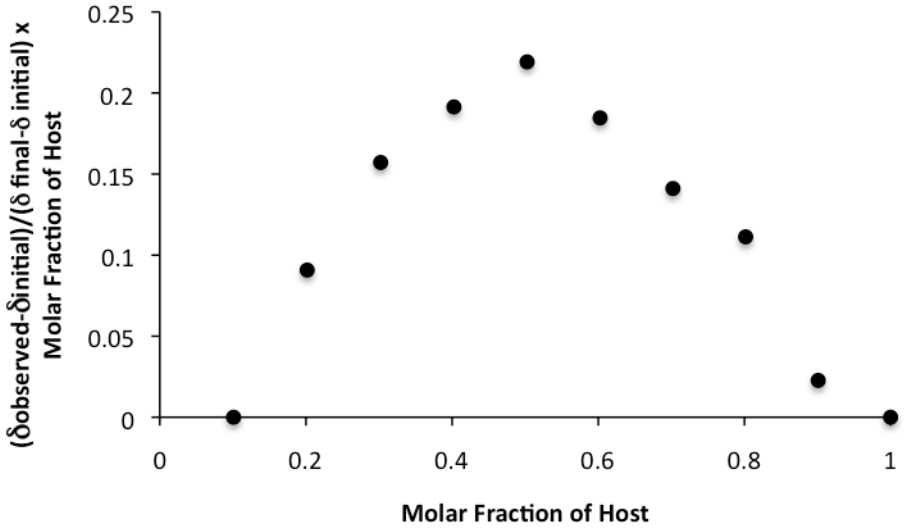


Figure S78 Job plot of compound **6** with TBACl in 0.5% H_2O/DMSO-d_6 following NH at 9.42ppm

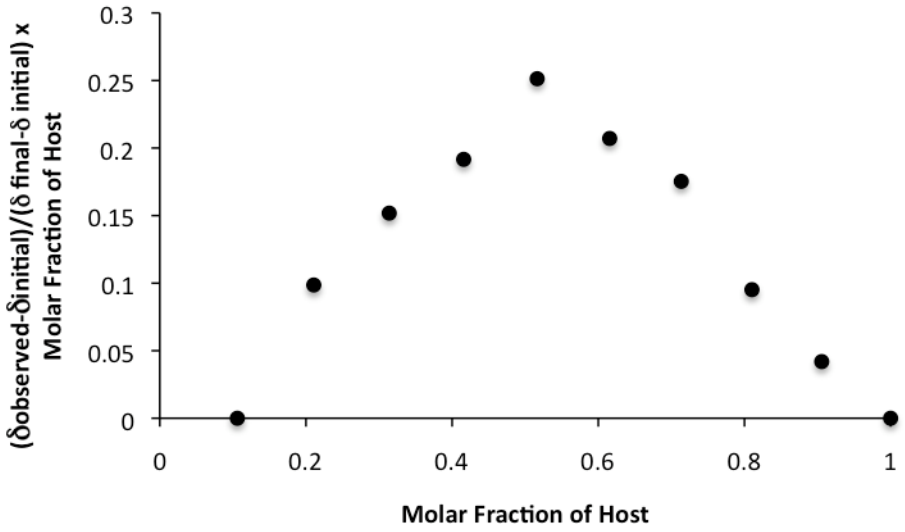


Figure S79 Job plot of compound **7** with TBACl in 0.5% H_2O/DMSO-d_6 following NH at 6.17ppm

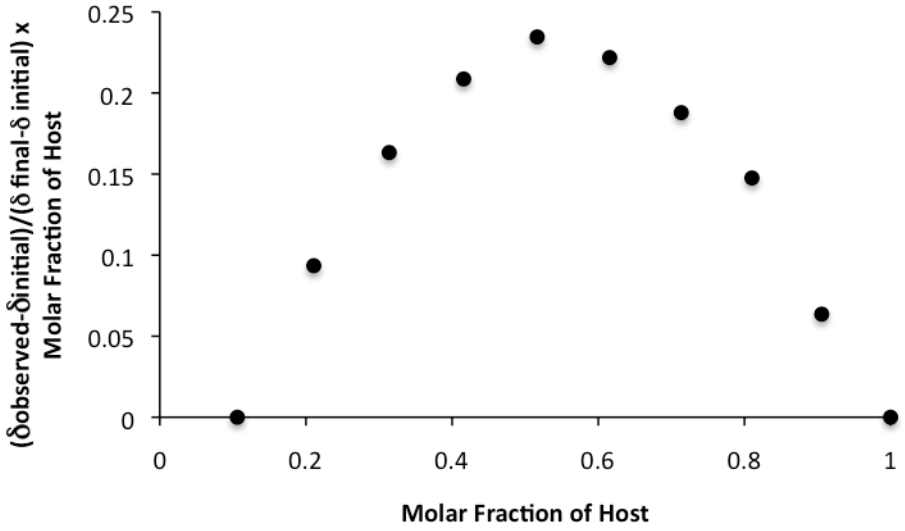


Figure S80 Job plot of compound **7** with TBACl in 0.5% H_2O/DMSO-d_6 following NH at 8.28ppm

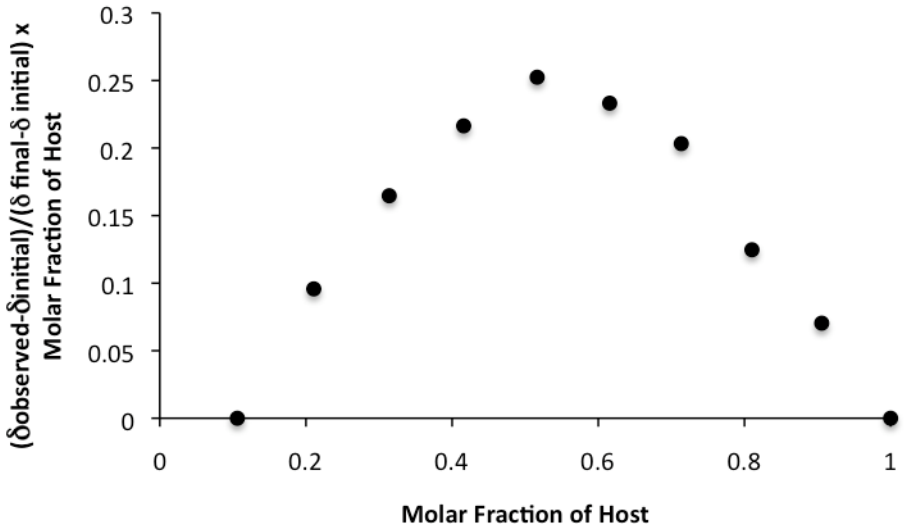


Figure S81 Job plot of compound **7** with TBACl in 0.5% H_2O/DMSO-d_6 following NH at 10.66ppm

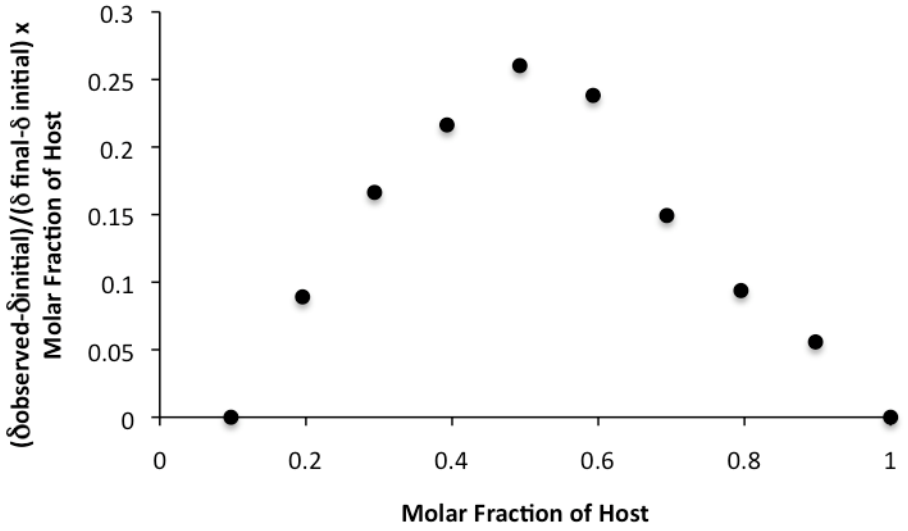


Figure S82 Job plot of compound **8** with TBACl in 0.5% H_2O/DMSO-d_6 following NH at 9.20ppm

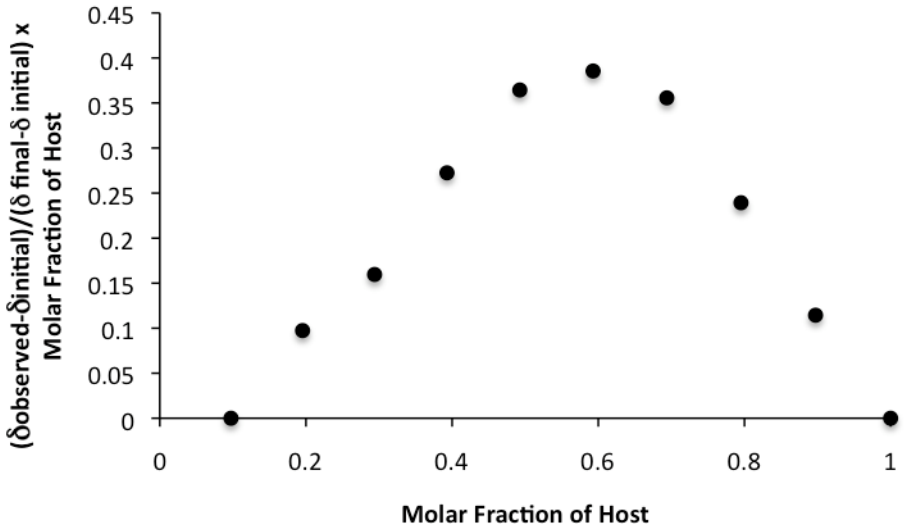


Figure S83 Job plot of compound **8** with TBACl in 0.5% H_2O/DMSO-d_6 following NH at 10.87ppm

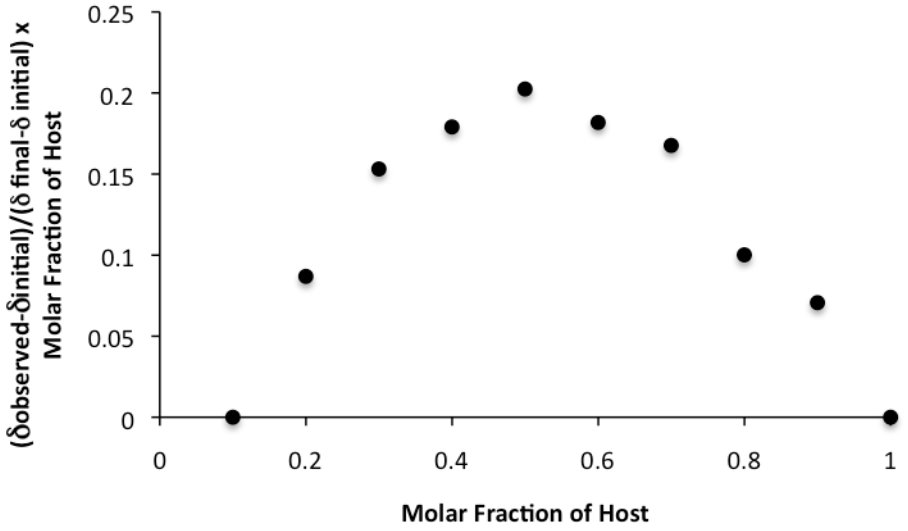


Figure S84 Job plot of compound **3** with $TEAHCO_3$ in 0.5% H_2O/DMSO-d_6 following NH at 5.69ppm

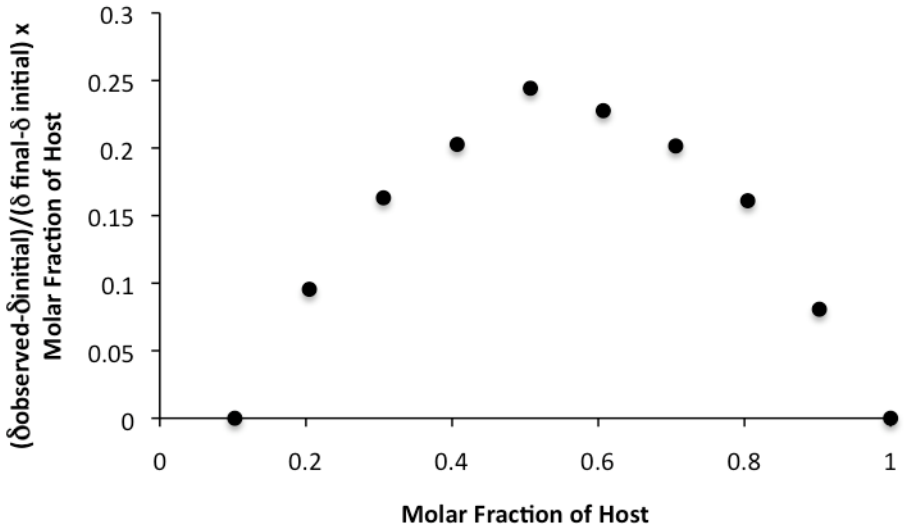


Figure S85 Job plot of compound **4** with $TEAHCO_3$ in 0.5% H_2O/DMSO-d_6 following NH at 7.26ppm

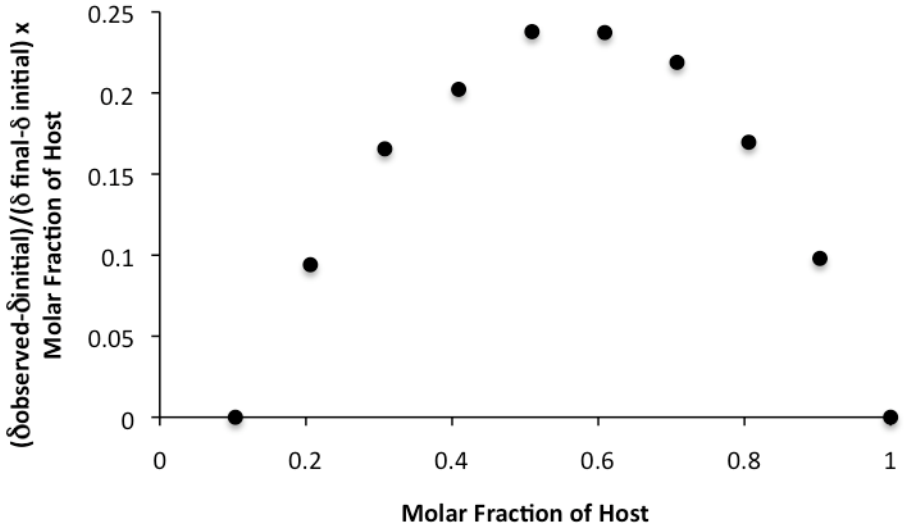


Figure S86 Job plot of compound **5** with $TEAHCO_3$ in 0.5% H_2O/DMSO-d_6 following NH at 6.05ppm

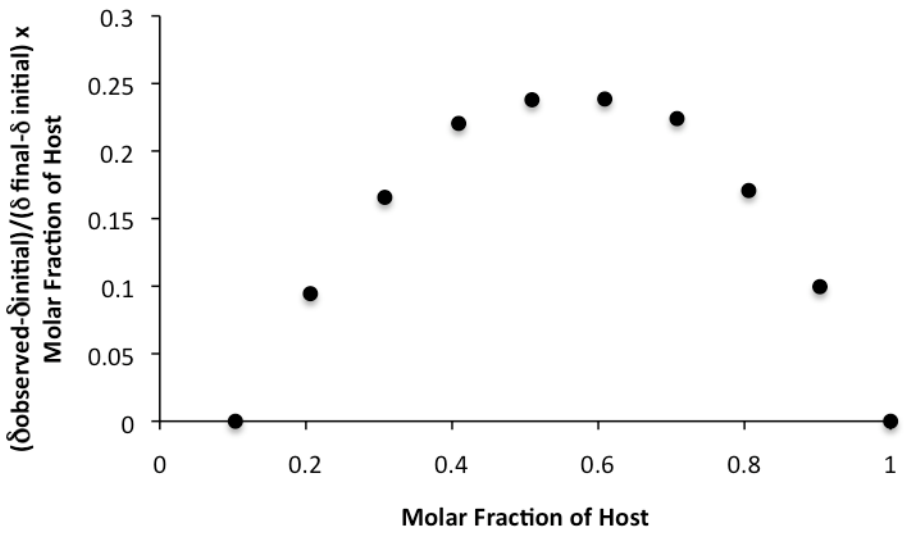


Figure S87 Job plot of compound **5** with $TEAHCO_3$ in 0.5% H_2O/DMSO-d_6 following NH at 8.34ppm

S7 *X-ray Crystallography*

Crystals of compound **5** suitable for X-ray crystallography were grown by slow evaporation of a solution of **5** in DMSO. The resulting structure obtained and relevant structural data are listed below.

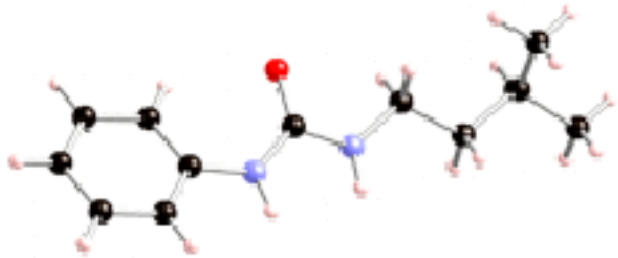


Figure S88 X-ray crystal structure of compound **5**

References

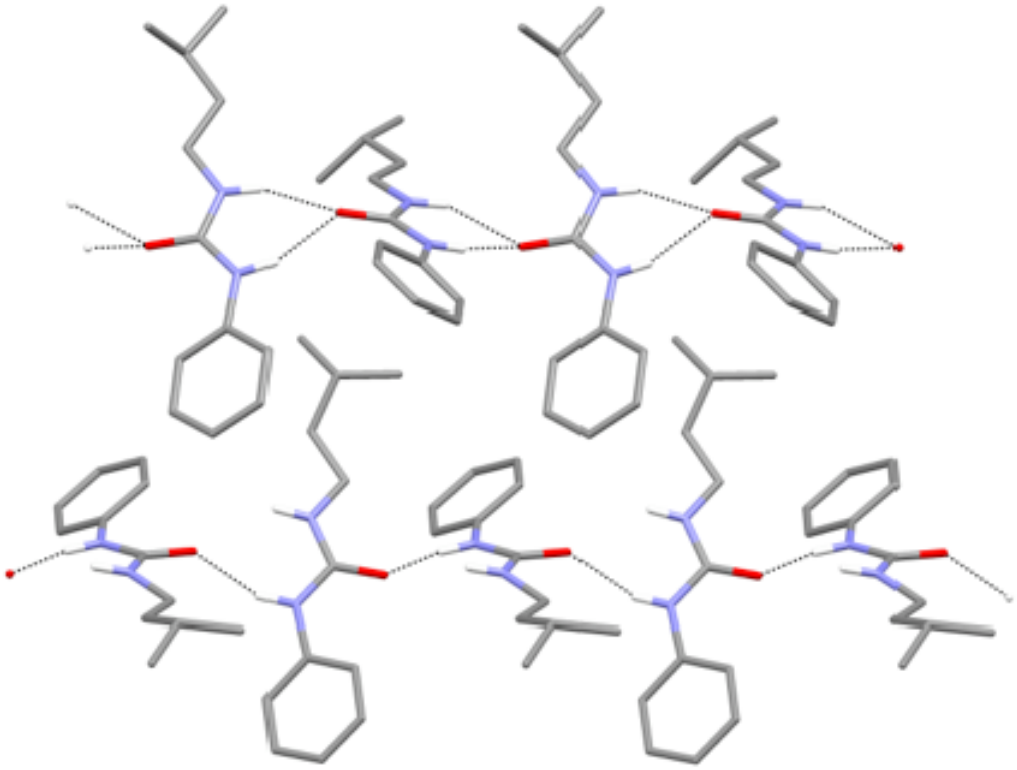


Figure S89 Hydrogen bonding chains of compound **5** showing the different twists

Table S1. Crystal data and structure refinement details for compound **5**.

CCDC Deposition number	791977
Empirical formula	$C_{12}H_{18}N_2O$
Formula weight	206.28
Temperature	120(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	*Pccn*
Unit cell dimensions	a = 21.8777(7) Å
	b = 24.4332(8) Å
	c = 8.9667(2) Å
Volume	4793.1(2) Å^3
Z	16
Density (calculated)	1.143 Mg / m^3
Absorption coefficient	0.074 mm^{-1}
F(000)	1792
Crystal	Block; Colourless
Crystal size	$0.20 \times 0.10 \times 0.04$ mm^3
θ range for data collection	2.91 – 25.02°
Index ranges	$-26 \le h \le 26$, $-29 \le k \le 29$, $-10 \le l \le 9$
Reflections collected	55376
Independent reflections	4234 [R_{int} = 0.1849]
Completeness to θ = 25.02°	99.9 %
Absorption correction	Semi–empirical from equivalents
Max. and min. transmission	0.9971 and 0.9854
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4234 / 189 / 287
Goodness-of-fit on F^2	1.153
Final R indices [$F^2 > 2\sigma(F^2)$]	$R1$ = 0.1143, $wR2$ = 0.1725
R indices (all data)	$R1$ = 0.1841, $wR2$ = 0.2013
Largest diff. peak and hole	0.247 and –0.261 e Å^{-3}

Diffractometer: *Nonius KappaCCD* area detector (ϕ scans and ω scans to fill *asymmetric unit*). **Cell determination:** DirAx (Duisenberg, A.J.M.(1992). J. Appl. Cryst. 25, 92-96.) **Data collection:** Collect (Collect: Data collection software, R. Hooft, Nonius B.V., 1998). **Data reduction and cell refinement**: *Denzo* (Z. Otwinowski & W. Minor, *Methods in Enzymology* (1997) Vol. **276**: *Macromolecular Crystallography*, part A, pp. 307–326; C. W. Carter, Jr. & R. M. Sweet, Eds., Academic Press). **Absorption correction**: Sheldrick, G. M. SADABS - Bruker Nonius area detector scaling and absorption correction - V2.10 S**tructure solution**: *SHELXS97* (G. M. Sheldrick, Acta Cryst. (1990) A**46** 467–473). S**tructure refinement**: *SHELXL97* (G. M. Sheldrick (1997), University of Göttingen, Germany). **Graphics:** Cameron - A Molecular Graphics Package. (D. M. Watkin, L. Pearce and C. K. Prout, Chemical Crystallography Laboratory, University of Oxford, 1993).

Special details: All hydrogen atoms were placed in idealised positions and refined using a riding model. The carbon chain is modelled as disordered over 2 positions.

Table S2. Hydrogen bonds [Å and °].

D–H···*A*	*d*(*D*–H)	*d*(H···*A*)	*d*(*D*···*A*)	∠(*DHA*)
N2A–H2A···O1^{i}	0.88	2.19	2.895(4)	136.4
N2B–H2B···O1^{i}	0.88	2.11	2.895(4)	149.0
N1–H1A···O1^{i}	0.88	1.95	2.788(4)	158.0
N4–H4A···O2^{ii}	0.88	2.16	2.933(4)	146.5
N3–H3A···O2^{ii}	0.88	2.01	2.844(4)	158.1

Symmetry transformations used to generate equivalent atoms:
(i) x,–y+1/2,z+1/2 (ii) –x+1/2,y,z–1/2

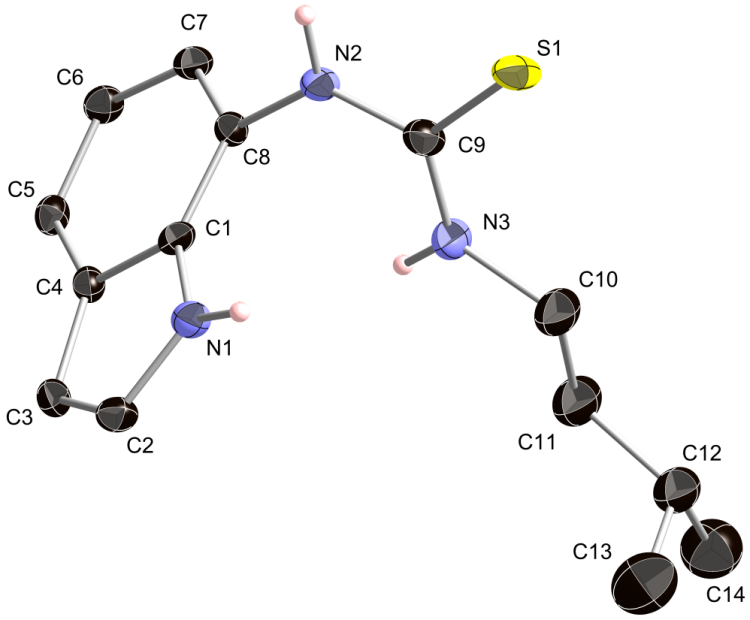


Figure S90 The X-ray crystal structure of compound **8**. Thermal ellipsoids are at the 35% probability level, selected hydrogens have been omitted for clarity.

Table S3. Crystal data and structure refinement details for compound **8**.

CCDC Deposition number	793790
Empirical formula	$C_{14}H_{19}N_3S$
Formula weight	261.38
Temperature	120(2) K
Wavelength	0.71073 Å
Crystal system	Tetragonal
Space group	$I4_1/a$
Unit cell dimensions	a = 29.2158(5) Å
	c = 7.5897(2) Å
Volume	6478.3(2) Å^3
Z	16
Density (calculated)	1.072 Mg / m^3
Absorption coefficient	0.189 mm^{-1}
$F(000)$	2240
Crystal	Needle; Colourless
Crystal size	$0.23 \times 0.03 \times 0.03$ mm^3
θ range for data collection	$3.10 - 25.02°$
Index ranges	$-23 \le h \le 24$, $0 \le k \le 34$, $0 \le l \le 9$
Reflections collected	2849
Independent reflections	2849 [R_{int} = 0.0000]
Completeness to θ = 25.02°	99.9 %
Absorption correction	Semi–empirical from equivalents
Max. and min. transmission	0.9944 and 0.9579
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2849 / 0 / 165
Goodness-of-fit on F^2	1.059
Final R indices [$F^2 > 2\sigma(F^2)$]	$R1$ = 0.0815, $wR2$ = 0.1815
R indices (all data)	$R1$ = 0.1060, $wR2$ = 0.1930
Largest diff. peak and hole	0.592 and –0.314 e Å^{-3}

Diffractometer: *Nonius KappaCCD* area detector (ϕ scans and ω scans to fill *asymmetric unit*). **Cell determination:** DirAx (Duisenberg, A.J.M.(1992). J. Appl. Cryst. 25, 92-96.) **Data collection:** Collect (Collect: Data collection software, R. Hooft, Nonius B.V., 1998). **Data reduction and cell refinement**: *Denzo* (Z. Otwinowski & W. Minor, *Methods in Enzymology* (1997) Vol. **276**: *Macromolecular Crystallography*, part A, pp. 307–326; C. W. Carter, Jr. & R. M. Sweet, Eds., Academic Press). **Absorption correction**: Sheldrick, G. M. SADABS - Bruker Nonius area detector scaling and absorption correction - V2.10 S**tructure solution**: *SHELXS97* (G. M. Sheldrick, Acta Cryst. (1990) A**46** 467–473). S**tructure refinement**: *SHELXL97* (G. M. Sheldrick (1997), University of Göttingen, Germany). **Graphics:** Cameron - A Molecular Graphics Package. (D. M. Watkin, L. Pearce and C. K. Prout, Chemical Crystallography Laboratory, University of Oxford, 1993).

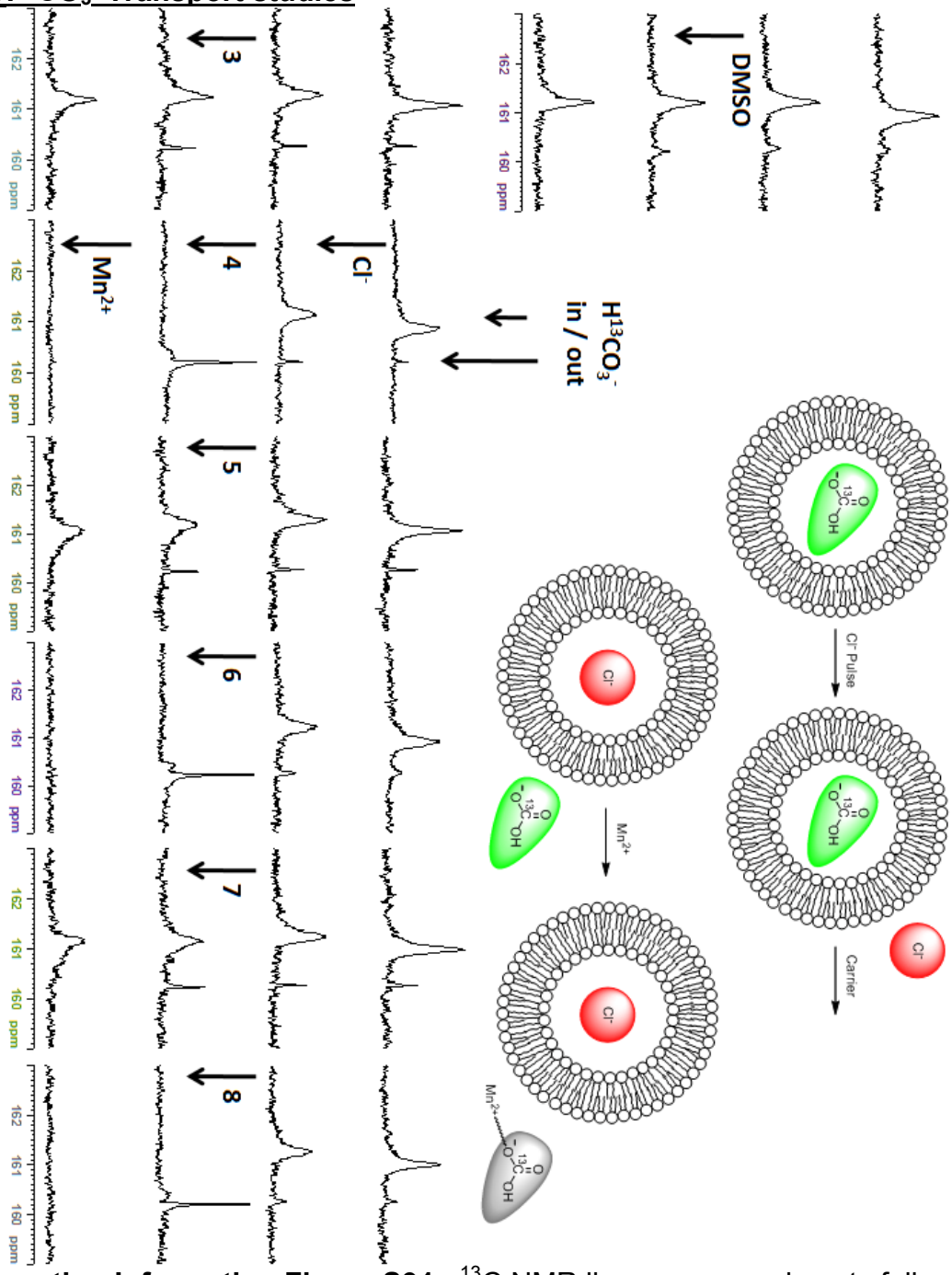
Special details: All hydrogens were identified in the difference map and subsequently placed in idealised positions and refined using a riding model. An unidentified (probably Et2O) disordered solvent is present in channels running along the c direction. This was treated using the Squeeze algorithm (SQUEEZE - Sluis, P. v.d. & Spek, A. L. (1990) Acta Cryst. A46, 194-201.). This has left a void of 252.00 A**3.

Table S4. Hydrogen bonds [Å and °] in the solid-state structure of compound **5**.

D–H···*A*	*d*(*D*–H)	*d*(H···*A*)	*d*(*D*···*A*)	∠(*DHA*)
N1–H1···S1^{i}	0.88	2.55	3.292(3)	142.3
N2–H2A···S1^{ii}	0.88	2.47	3.263(3)	150.5

Symmetry transformations used to generate equivalent atoms:
(i) –x+3/2,–y+3/2,–z–1/2 (ii) –x+3/2,–y+3/2,–z+1/2

S8 $H^{13}CO_3^-$ Transport studies



Supporting Information Figure S91. ^{13}C NMR liposome experiments following exchange of $H^{13}CO_3^-$ for Cl^- promoted by 0.04 molar equiv. of receptors **3-8**. a) before and b) after addition of a 50 mM NaCl pulse to EYPC vesicles containing 100 mM $NaH^{13}CO_3$ buffered to pH 7.4 with 20 mM HEPES, dispersed in 75 mM Na_2SO_4 buffered to pH 7.4 with 20 mM HEPES; c) spectra 5 min after addition of **3-8** and DMSO; d) following addition of 0.5 mM $MnCl_2$, a paramagnetic line broadening agent that only affects external bicarbonate.

General Experimental for ^{13}C NMR Liposome Assays. ^{13}C NMR spectra were recorded on a Bruker AVIII-600 operating at 150.92 MHz. Deuterated solvents were purchased from Cambridge Isotope Labs. Phospholipids used to prepare liposomes were purchased from Avanti Polar Lipids. High-pressure extrusion was performed on the Avanti mini-extruder using a 5.0 mm polycarbonate membrane. Dialysis was performed using a #2 Spectra/Por dialysis membrane. ^{13}C labeled sodium bicarbonate was purchased from Sigma/Isotec. All other chemicals were purchased from Sigma, Aldrich, Fisher, Fluka or Acros and used without further purification.

Preparation of Liposomes for ^{13}C NMR Anion Transport Assay. A stock solution of egg-yolk phosphatidylcholine (EYPC) in $CHCl_3$ (280 mg in 14 mL) was evaporated under reduced pressure to produce a thin film that was dried *in vacuo* overnight. The lipid film was hydrated with a 2 mL solution containing 20 mM HEPES (pH 7.4) and 100 mM $NaH^{13}CO_3$ in a 9:1 H_2O/D_2O mixture. Freeze/thaw cycles were repeated at 6 times until no solids were visible. The frozen solution was warmed to 30-35 ^oC before each freeze cycle. The mixture was placed on a vortexer every 3 cycles for 30 s to facilitate hydration. The cloudy solution was extruded in 2 separate 1 mL batches through a 5.0 mm polycarbonate membrane 17 times. In order to exchange external $NaH^{13}CO_3$ with Na_2SO_4, this solution was placed in dialysis tubing and stirred in a 9:1 H_2O/D_2O solution containing of 20 mM HEPES and 75 mM Na_2SO_4 at pH 7.4 for 4 hr. Stock solutions of liposomes were stored in the refrigerator and used within 24 hr. for transport assays. Liposome stock solution concentration was determined assuming 90% retention of lipid throughout preparation process.

^{13}C NMR Anion Transport Assays. ^{13}C NMR spectra were recorded on a Bruker AVIII-600 operating at 150.92 MHz, with chemical shifts reported in ppm. The instrument was locked on 9:1 H_2O/D_2O. Experimental conditions were: temperature, 27 °C; acquisition time, 0.93 s; spectrum width 35,211 Hz; relaxation delay, 0.2 s; number of scans, 196. For each experiment, an initial ^{13}C NMR spectrum of a 520 µL of the liposome solution was acquired. This solution consisted of EYPC liposomes containing 100 mM $NaH^{13}CO_3$ buffered to pH 7.4

with 20 mM HEPES, dispersed in 75 mM Na_2SO_4 buffered to pH 7.4 with 20 mM HEPES. A NaCl pulse followed, resulting in final extravesicular concentrations of 41 mM lipid and 50 mM NaCl. The ^{13}C NMR of this liposome mixture was taken, followed by the addition of a solution of **3-8** (in DMSO, 15 µL) or 15 µL of DMSO. Ligands **3-8** were added to give a 0.04 molar equiv. to lipid ratio and another spectrum was taken approxiamately 5 min after addition of the compounds **3-8** or the DMSO blank. A ^{13}C NMR of the ligand containing mixture was acquired before and 5 min after the addition 3 µL of a solution of $MnCl_2$ (0.5 mM final Mn^{2+} concentration).

S9 *References*

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