Electronic Supplementary Information - Part One

Chloride, carboxylate and carbonate transport by *ortho*-phenylenediamine-based bisureas

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We have previously reported the synthesis of compounds **1**,[1] **3**,[2] **6**[2] and **8**.[2]

1,1'-(4,5-difluoro-1,2-phenylene)bis(3-phenylurea), **2**

4,5-difluoro-2-nitroaniline (0.212g, 1.22mmol) was dissolved in methanol (20mL) with palladium/carbon catalyst (~5mg). The reaction mixture was stirred at room temperature for 4 hours under hydrogen. The catalyst was removed by filtration and the filtrate reduced *in vacuo* to yield a green oil. The oil was dissolved in DCM (20mL) and pyridine (5mL) with phenyl isocyanate (0.265mL, 2.44mmol). The reaction mixture was stirred at room temperature under nitrogen for 2 hours. The resulting precipitate was removed by filtration and sonicated in DCM (200mL) for 1 hour. The suspension was filtered to yield a white solid (0.174g, 37% yield). **Mp:** 196°C; **IR (Golden Gate) ν_{max}/cm^{-1}:** 3330, 3070 (urea NH stretches), 1630, 1600 (urea CO stretches); **LRMS (ES$^+$) m/z:** 405.1 $[M+Na]^+$, 787.4 $[2M+Na]^+$; **HRMS (ES$^+$) m/z:** calc. 405.1134 $[M+Na]^+$, found 405.1131; **^{1}H NMR (400MHz, DMSO-d_6, δ = ppm):** 9.11 (s, 2H, NH), 8.13 (s, 2H, NH), 7.72 (t, J=10.6, 2H, ArCH), 7.48 (d, J=8.60Hz, 4H, ArCH), 7.29 (t, J=7.56Hz, 4H, ArCH), 6.98 (br. t, J=7.60Hz, 2H, ArCH); **^{13}C NMR (100MHz, DMSO-d_6, δ = ppm):** 153.0 (CO), 145.3 (q), 139.5 (q), 128.8 (ArCH), 127.9 (q), 122.0 (ArCH), 118.3 (ArCH), 112.2 (ArCH); **^{19}F NMR (282MHz, DMSO-d_6, δ = ppm):** -143.16 (ArCF)

1,1'-(1,2-phenylene)bis(3-(4-cyanophenyl)urea), **4**

o-Phenylenediamine (0.204g, 1.89mmol) was dissolved in DCM (20mL) and pyridine (5mL) with 4-cyanophenyl isocyanate (0.541g, 3.75mmol). The reaction mixture was stirred at room temperature under nitrogen for 18 hours. The resulting precipitate was removed by filtration and sonicated in DCM (200mL) for 15 minutes. The suspension was filtered to yield a white solid (0.290g, 39% yield). **Mp:** 217-218°C; **IR (Golden Gate) ν_{max}/cm^{-1}:** 3370 (urea NH stretches), 2220 (CN stretch), 1670, 1590 (CO stretches); **LRMS**

(ES^+) m/z: 419.0 $[M+Na]^+$, 815.3 $[2M+Na]^+$; **HRMS (ES^+) m/z:** calc. 419.1227 $[M+Na]^+$, found 419.1227; **^{1}H NMR (400MHz, DMSO-*d*$_6$, δ = ppm):** 9.59 (s, 2H, NH), 8.23 (s, 2H, NH), 7.73 (d, J=8.60Hz, 4H, ArCH), 7.66 (d, J=9.12Hz, 4H, ArCH), 7.61 (m, 2H, ArCH), 7.14 (m, 2H, ArCH); **^{13}C NMR (100MHz, DMSO-*d*$_6$, δ = ppm):** 152.8 (CO), 144.3 (q), 133.3 (ArCH), 131.0 (q), 124.6 (ArCH), 124.4 (ArCH), 119.3 (q), 118.0 (ArCH), 103.3 (CN)

1,1'-(1,2-phenylene)bis(3-(4-(trifluoromethyl)phenyl)urea), **5**

o-Phenylenediamine (0.244g, 2.26mmol)was dissolved in DCM (20mL) with 4-(trifluoromethyl)phenyl isocyanate (0.650mL, 4.55mmol). The reaction mixture was stirred at room temperature under nitrogen for 48 hours. The resulting precipitate was removed by filtration and washed with DCM (2x25mL) to yield a white solid (0.917g, 84% yield). **Mp:** 210°C; **IR (Golden Gate) ν_{max}/cm^{-1}:** 3310 (urea NH stretch), 1560 (urea CO stretch), 1110, 1060 (trifluoromethyl CF stretch); **LRMS (ES^+) m/z:** 505.1 $[M+Na]^+$; **HRMS (ES^+) m/z:** calc. 505.1070 $[M+Na]^+$, found 505.1075; **^{1}H NMR (400MHz, DMSO-*d*$_6$, δ = ppm):** 9.50 (s, 2H, NH), 8.20 (s, 2H, NH), 7.71 (d, 4H, J=8.60Hz, ArCH), 7.65-7.60 (m, 6H, ArCH), 7.13 (dd, J=6.04, 3.52Hz, 2H, ArCH); **^{13}C NMR (100MHz, DMSO-*d*$_6$, δ = ppm):** 153.0 (CO), 143.6 (q), 131.2 (q), 126.1 (ArCH), 124.4 (ArCH), 123.2 (q), 121.8 (CF_3), 117.8 (ArCH); **^{19}F NMR (282MHz, DMSO-*d*$_6$, δ = ppm):** -60.26 (CF_3)

1,1'-(1,2-phenylene)bis(3-(3-nitrophenyl)urea, **7**

o-Phenylenediamine (0.212g, 1.96mmol) was dissolved in DCM (20mL) and pyridine (5mL) with 3-nitrophenyl isocyanate (0.644g, 3.92mmol). The reaction mixture was stirred at room temperature under nitrogen for 24 hours. The resulting precipitate was removed by filtration and sonicated in DCM (200mL) for 15 minutes. The suspension was filtered to yield a yellow solid (0.705g, 82% yield). **Mp:** 206-207°C; **IR (Golden Gate) ν_{max}/cm^{-1}:** 3340, 3270 (urea NH stretches), 1650 (urea CO stretches), 1520 (nitro NO stretch); **LRMS (ES^+) m/z:** 437.2 $[M+H]^+$, 459.1 $[M+Na]^+$; **HRMS (ES^+) m/z:** calc. 459.1024 $[M+Na]^+$, found 459.1025; **^{1}H NMR (400MHz, DMSO-*d*$_6$, δ = ppm):** 9.64 (s, 2H, NH), 8.57 (m, 2H, ArCH), 8.22 (s, 2H, NH), 8.81 (dd, J=8.08, 2.04Hz, 2H, ArCH), 7.74 (dd, J= 8.56, 1.52Hz, 2H, ArCH), 7.63 (m, 2H, ArCH), 7.56 (t, J=8.08, 2H, ArCH), 7.16 (m, 2H, ArCH);

^{13}C NMR (100MHz, DMSO-d_6, δ = ppm): 153.2 (CO), 148.2 (q), 141.2 (q), 131.2 (q), 130.0 (ArCH), 124.6 (ArCH), 124.2 (ArCH), 116.2 (ArCH), 112.1 (ArCH)

1-(4-cyanophenyl)-3-phenylurea, **9**[3]

Aniline (0.379mL, 4.16mmol) and 4-cyanophenyl isocyanate (0.629g, 4.36mmol) were dissolved in DCM (30mL) and pyridine (3mL). The reaction mixture was stirred at room temperature under nitrogen for 18 hours, after which the solvent was removed *in vacuo*. The resulting white solid was sonicated in DCM (25mL) and then isolated by filtration (0.554g, 56% yield). **Mp:** 195-197°C (lit.198°C)[3g]; **^{1}H NMR (400MHz, DMSO-d_6, δ = ppm):** 9.17 (s, 1H, NH), 8.82 (s, 1H, NH), 7.70 (d, J=8.56Hz, 2H, ArCH), 7.65 (d, J=8.08Hz, 2H, ArCH), 7.49 (br.d, J=8.08Hz, 2H, ArCH), 7.29 (m, 2H, ArCH), 6.99 (br. t, J=7.08Hz, 1H, ArCH); **^{13}C NMR (100MHz, DMSO-d_6, δ = ppm):** 152.1 (CO), 144.2 (q), 139.2 (q), 133.2 (ArCH), 128.8 (ArCH), 122.4 (ArCH), 119.3 (q), 118.6 (ArCH), 118.0 (ArCH), 103.3 (CN)

1-phenyl-3-(4-(trifluoromethyl)phenyl)urea, **10**[4, 3d-e]

Aniline (0.343mL, 3.76mmol) and 4-(trifluoromethyl)phenyl isocyanate (0.525mL, 3.68mmol) were dissolved in DCM (50mL) and pyridine (3mL). The reaction mixture was stirred at room temperature under nitrogen for 18 hours, after which the solvent was removed *in vacuo*. The resulting white solid was sonicated in DCM (25mL) and then isolated by filtration (0.597g, 58% yield). **Mp:** 221°C (lit. 225°C)[4a]; **^{1}H NMR (400MHz, DMSO-d_6, δ = ppm):** 9.08 (s, 1H, NH), 8.78 (s, 1H, NH), 7.67 (d, J=8.60Hz, 2H, ArCH), 7.62 (d, J=9.08Hz, 2H, ArCH), 7.47 (dd, J=8.56, 1.04Hz, 2H, ArCH), 7.29 (m, 2H, ArCH), 6.99 (br. t, J=7.60Hz, 1H, ArCH); **^{13}C NMR (100MHz, DMSO-d_6, δ = ppm):** 152.3 (CO), 143.5 (q), 139.3 (q), 128.8 (ArCH), 126.0 (ArCH), 123.2 (q), 122.2 (ArCH), 121.7 (CF_3), 118.5 (ArCH), 117.8 (ArCH); **^{19}F NMR (282MHz, DMSO-d_6, δ = ppm):** -60.20 (CF_3)

1-(4-nitrophenyl)-3-phenylurea, **11**[5,3c-f]

Aniline (0.343mL, 3.76mmol) and 4-nitrophenyl isocyanate (0.648g, 3.95mmol) were dissolved in DCM (50mL) and pyridine (3mL). The reaction mixture was stirred at room temperature under nitrogen for 18 hours, after which the solvent was removed *in vacuo*. The resulting yellow solid was sonicated in DCM (25mL) and then isolated by filtration

(0.722g, 75% yield). **Mp:** 204°C (lit. 207-220°C)[5a]; **^{1}H NMR (400MHz, DMSO-d_6, δ = ppm):** 9.40 (s, 1H, NH), 8.88 (s, 1H, NH), 8.18 (d, J=9.60Hz, 2H, ArCH), 7.69 (d, J=9.08Hz, 2H, ArCH), 7.48 (br. d, J=7.60Hz, 2H, ArCH), 7.30 (m, 2H, ArCH), 7.01 (br. t, J=7.60Hz, 1H, ArCH);**^{13}C NMR (100MHz, DMSO-d_6, δ = ppm):** 151.9 (CO), 146.4 (q), 141.0 (q), 139.0 (q), 128.8 (ArCH), 125.1 (ArCH), 122.5 (ArCH), 118.6 (ArCH), 117.4 (ArCH)

Vesicle studies

General method

A chloroform solution of 1-palmitoyl-2-oleoyl-*sn*-glycero-3-phosphocholine (POPC) (22.32 mg/mL) (Genzyme) was evaporated under reduced pressure to give a thin film. The lipid film was dried under high vacuum for at least 2 hours and rehydrated with the **internal** solution by vortexing. The lipid suspension was then subjected to nine freeze–thaw cycles and twenty-nine extrusions through a 200 nm polycarbonate nucleopore membrane using a LiposoFast Basic extruder (Avestin, Inc.) to obtain unilamellar vesicles. The liposomes underwent dialysis in the **external** solution. The vesicles were diluted to 5mL with the **external** solution to form a stock solution of lipid.

Samples for assay were prepared by diluting lipid stock solution to 5mL (using the **external** solution) to give a solution of 1mM lipid. Chloride efflux was monitored using a chloride selective electrode (Accumet). To initiate the experiment compounds were added as solutions in DMSO, to give a 1:50 compound to lipid ratio (2mol%). At the end of the experiment detergent (octaethylene glycol monododecyl ether) was added to allow the determination of 100% chloride efflux. Experiments were repeated in triplicate and all traces presented are the average of three trials. The chloride electrode was calibrated against sodium chloride solutions of known concentration.

Chloride/nitrate antiport assay

Internal solution: 488mM sodium chloride buffered to pH 7.2 with 5mM sodium phosphate salts.

External solution: 488mM sodium nitrate buffered to pH 7.2 with 5mM sodium phosphate salts.

Compound was added at t=0. Detergent was added at t=5mins.

Chloride/nitrate antiport assay with cholesterol

Internal solution: 488mM sodium chloride buffered to pH 7.2 with 5mM sodium phosphate salts.

External solution: 488mM sodium nitrate buffered to pH 7.2 with 5mM sodium phosphate salts.

To the freeze dried lipid film a chloroform solution of cholesterol was added to achieve a lipid to cholesterol molar ratio of 7:3. The chloroform was removed under reduced pressure to give a thin film. The film was dried under high vacuum for at least 2 hours and vesicles were prepared by the standard method. Compound was added at t=0. Detergent was added at t=5mins.

Chloride/bicarbonate antiport assay

Internal solution: 451mM sodium chloride buffered to pH 7.2 with 20mM sodium phosphate salts.

External solution: 150mM sodium sulphate buffered to pH 7.2 with 20mM sodium phosphate salts.

Compound was added at t=0. A ‘pulse’ of sodium bicarbonate in external solution was added at t=2mins, such that the external concentration of bicarbonate is 40mM. Detergent was added at t=7mins

Chloride/sulphate 'blank' assay

Internal solution: 451mM sodium chloride buffered to pH 7.2 with 20mM sodium phosphate salts.

External solution: 150mM sodium sulphate buffered to pH 7.2 with 20mM sodium phosphate salts.

Compound was added at t=0. Detergent was added at t=7mins.

Chloride/carboxylate antiport assays – pH 7.2

Internal solution: 451mM sodium chloride buffered to pH 7.2 with 20mM sodium phosphate salts.

External solution: 150mM sodium sulphate buffered to pH 7.2 with 20mM sodium phosphate salts.

Compound was added at t=0. A 'pulse' of either sodium maleate or sodium fumarate in external solution was added at t=2mins, such that the external concentration of carboxylate is 40mM. Detergent was added at t=7mins.

Chloride/carboxylate antiport assays – pH 4.0

Internal solution: 451mM sodium chloride buffered to pH 7.2 with 20mM sodium citrate salts.

External solution: 150mM sodium sulphate buffered to pH 7.2 with 20mM sodium citrate salts.

Compound was added at t=0. A 'pulse' of either sodium maleate or sodium fumarate in external solution was added at t=2mins, such that the external concentration of carboxylate is 40mM. Detergent was added at t=7mins.

Chloride/sulphate pH gradient assay

Internal solution: 451mM sodium chloride buffered to pH 4.0 with 20mM sodium citrate salts.

External solution: 150mM sodium sulphate buffered to pH 7.2 with 20mM sodium phosphate salts.

Compound was added at t=0s. Detergent was added at t=5mins.

Lucigenin fluorescence assay for sulphate transport

Internal solution: 100mM sodium chloride and 2mM lucigenin dye buffered to pH 7.2 with 20mM sodium phosphate salts.

External solution: 100mM sodium chloride buffered to pH 7.2 with 20mM sodium phosphate salts.

Vesicles were prepared as described previously. Instead of dialysis, vesicles were purified by size exclusion chromatography using sephadex gel (G-50). Samples for assay were prepared by diluting the lipid stock solution to 3mL (using the **external** solution). Fluorescence spectra were obtained using a Varian Cary Eclipse Fluorescence Spectrophotometer. Lucigenin fluorescence was monitored by excitation at 455nm and emission at 506nm. At t=30s a solution of sodium sulphate was added, such that the external concentration of sulphate was 40mM. At t=1min compounds were added as solutions in methanol, to give a 1:50 compound to lipid ratio (2mol%). Experiments were repeated in triplicate and all traces presented are the average of three trials.

U-tube assays for mobile carrier activity

Source phase: 488mM sodium chloride solution buffered to pH 7.2 with 5mM sodium phosphate salts.

Receiving phase: 488mM sodium nitrate solution buffered to pH 7.2 with 5mM sodium phosphate salts.

The source phase and the receiving phase (7.5mL each) were placed in u-tube apparatus, separated by the organic phase (1mM compound and 1mM tetrabutylammonium hexafluorophosphate in nitrobenzene, 15mL). The organic phase was stirred at room temperature and the chloride concentration in the receiving phase was determined using a chloride selective electrode (Accumet) after 24hrs, 60hrs and 96hrs.

NMR titrations

Known volumes of a 0.15M solution of guest containing 0.01M receptor were added to a solution of 0.01M receptor. 1H NMR spectrum were recorded after each addition. Chemical shifts were calibrated to the solvent peak, and these values were then fitted to a relevant binding model using WinEQNMR 2[7] in order to generate values for the binding constants (**Figures S25-S46**).

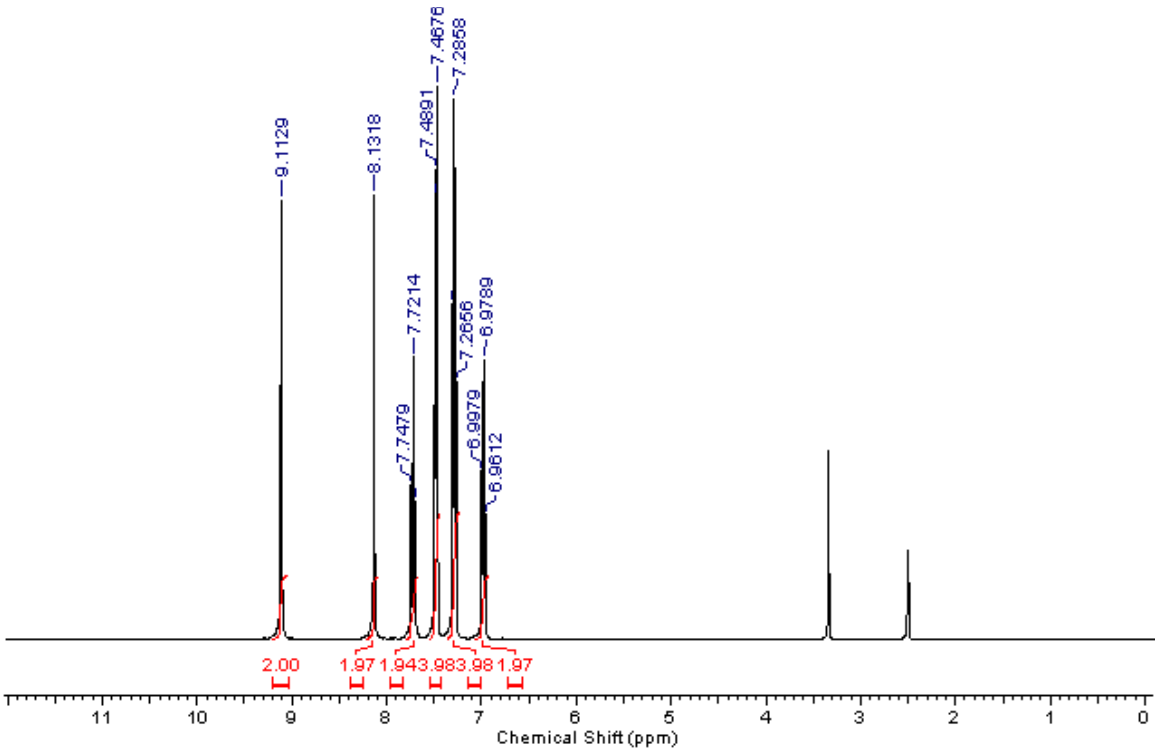

Figure S1: [1]H NMR spectrum of compound **2** in DMSO-d_6.

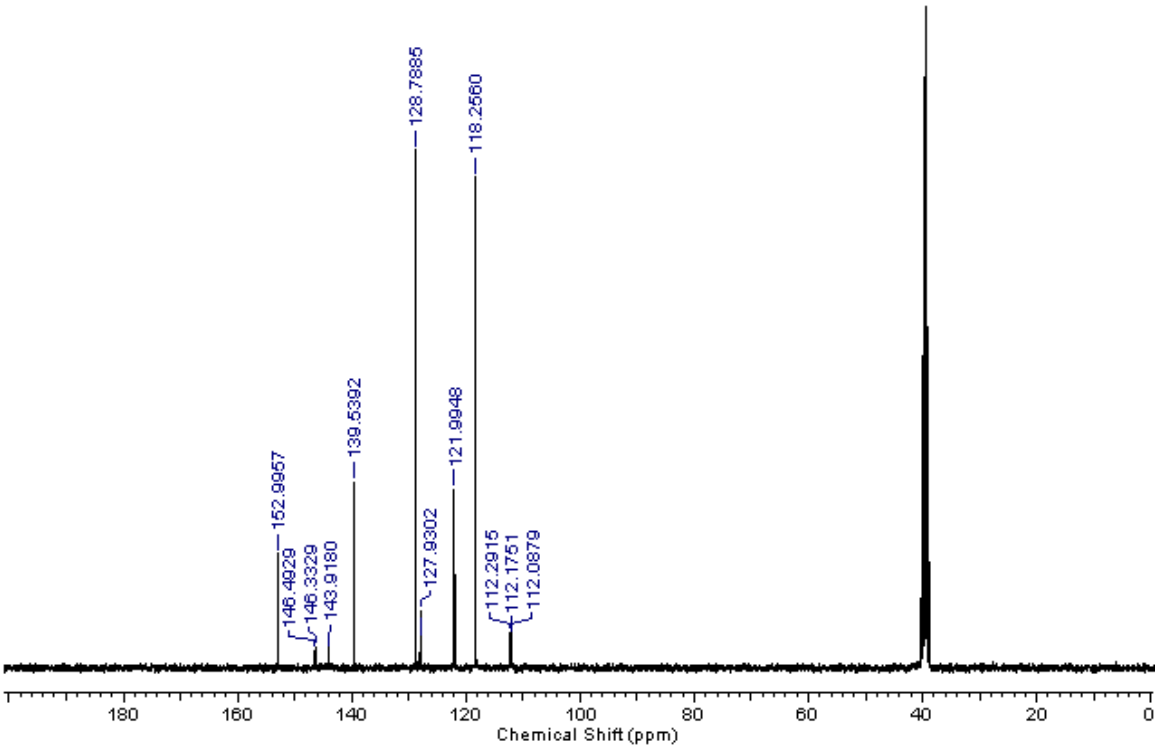

Figure S2: ^{13}C NMR spectrum of compound **2** in DMSO-d_6.

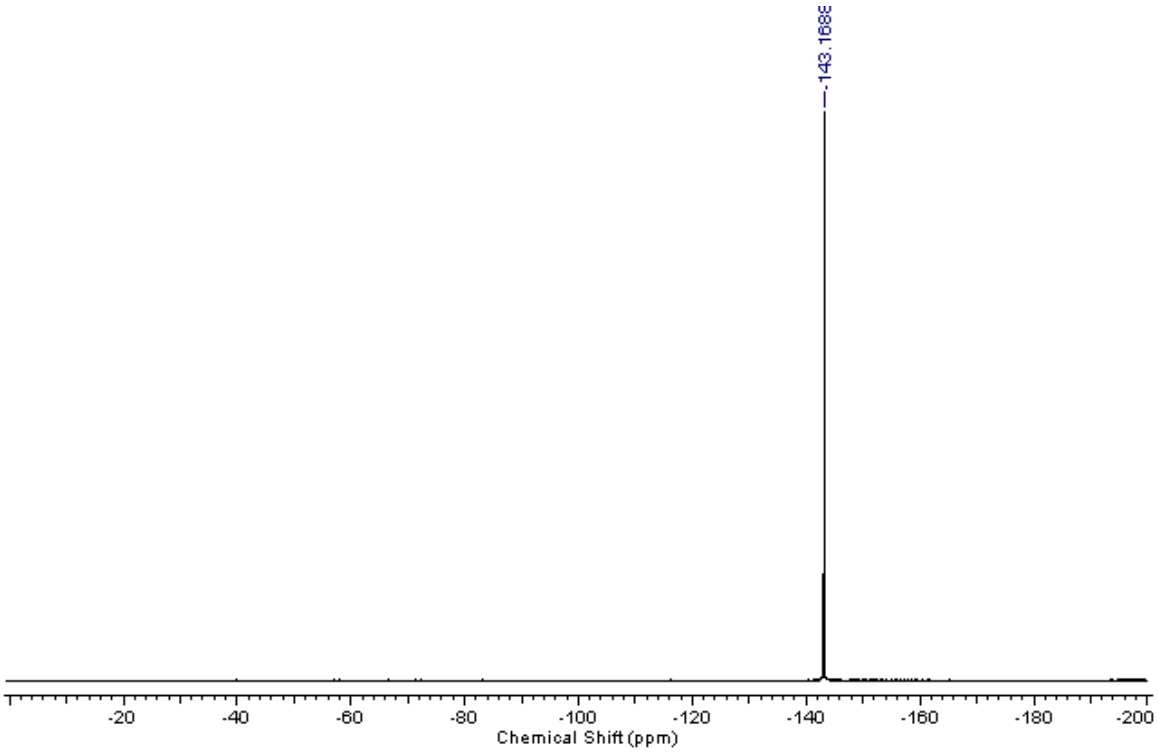

Figure S3: ^{19}F NMR spectrum of compound **2** in DMSO-d_6.

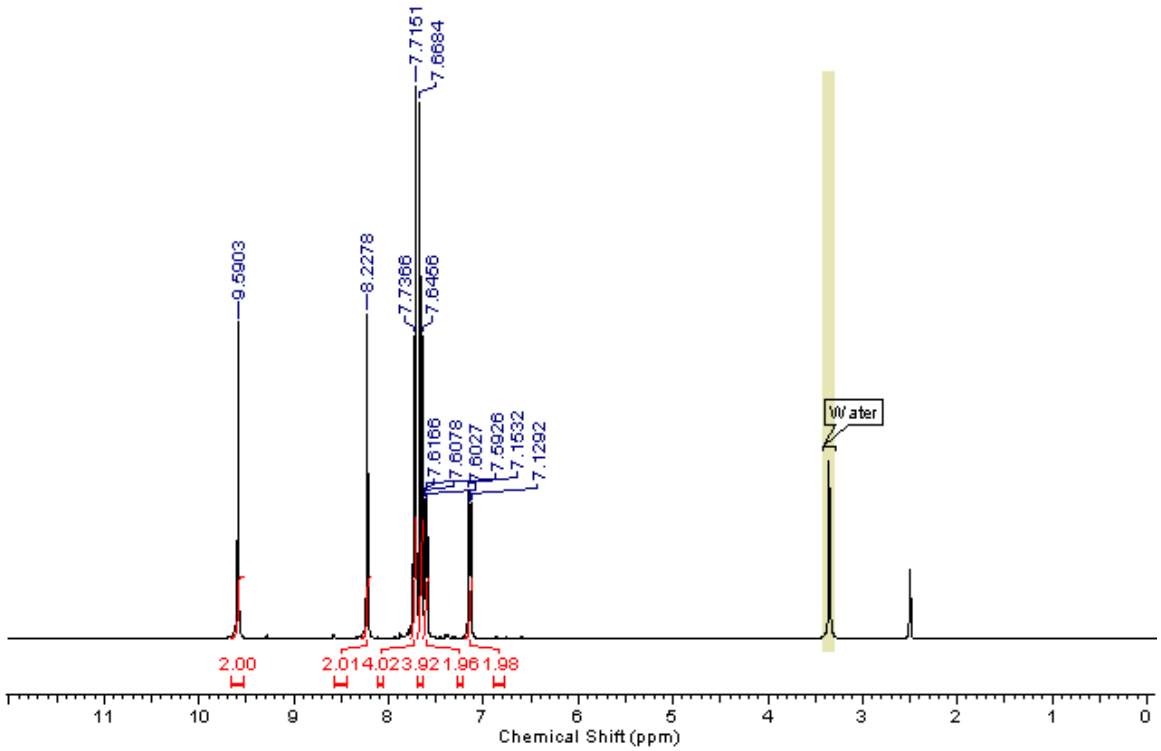

Figure S4: ^{1}H NMR spectrum of compound **4** in DMSO-d_6.

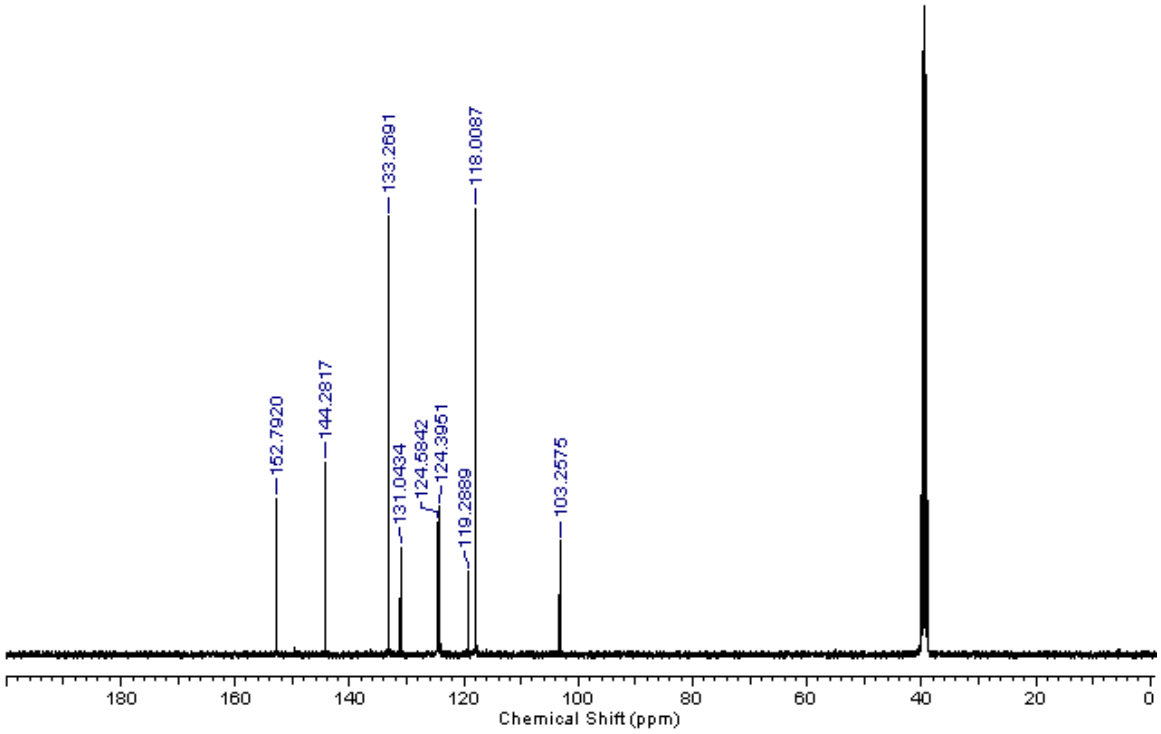

Figure S5: ^{13}C NMR spectrum of compound **4** in DMSO-d_6.

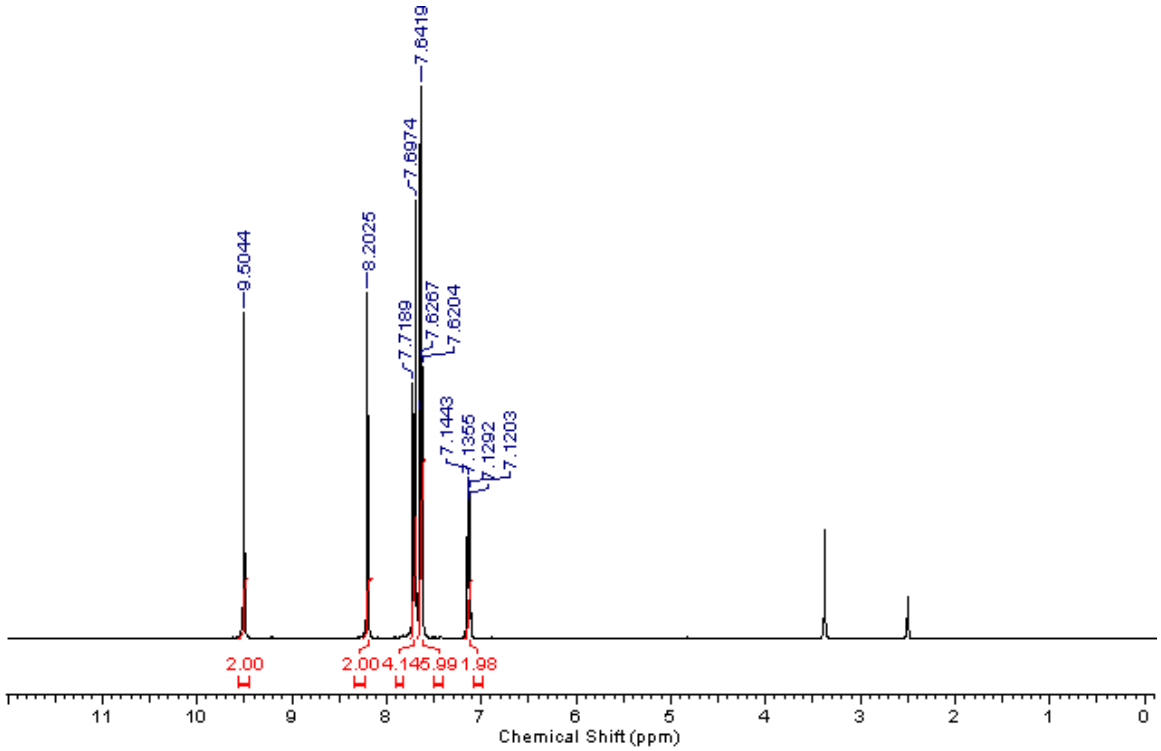

Figure S6: ^{1}H NMR spectrum of compound **5** in DMSO-d_6.

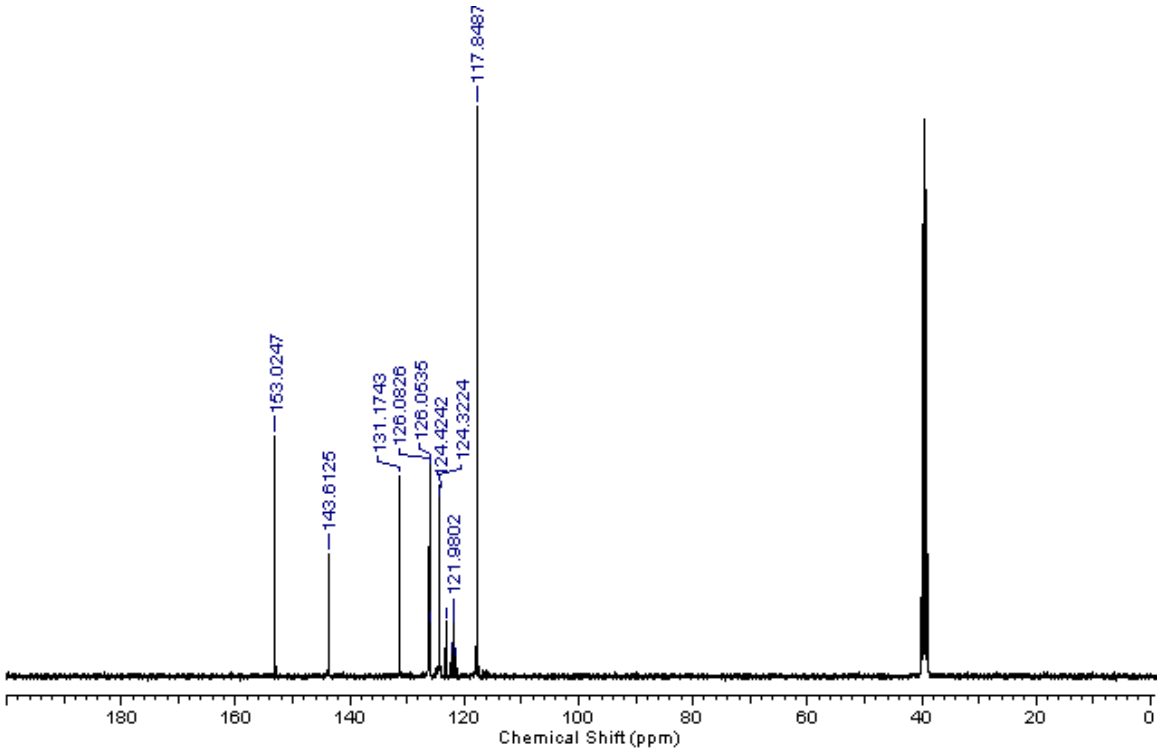

Figure S7: ^{13}C NMR spectrum of compound **5** in DMSO-d_6.

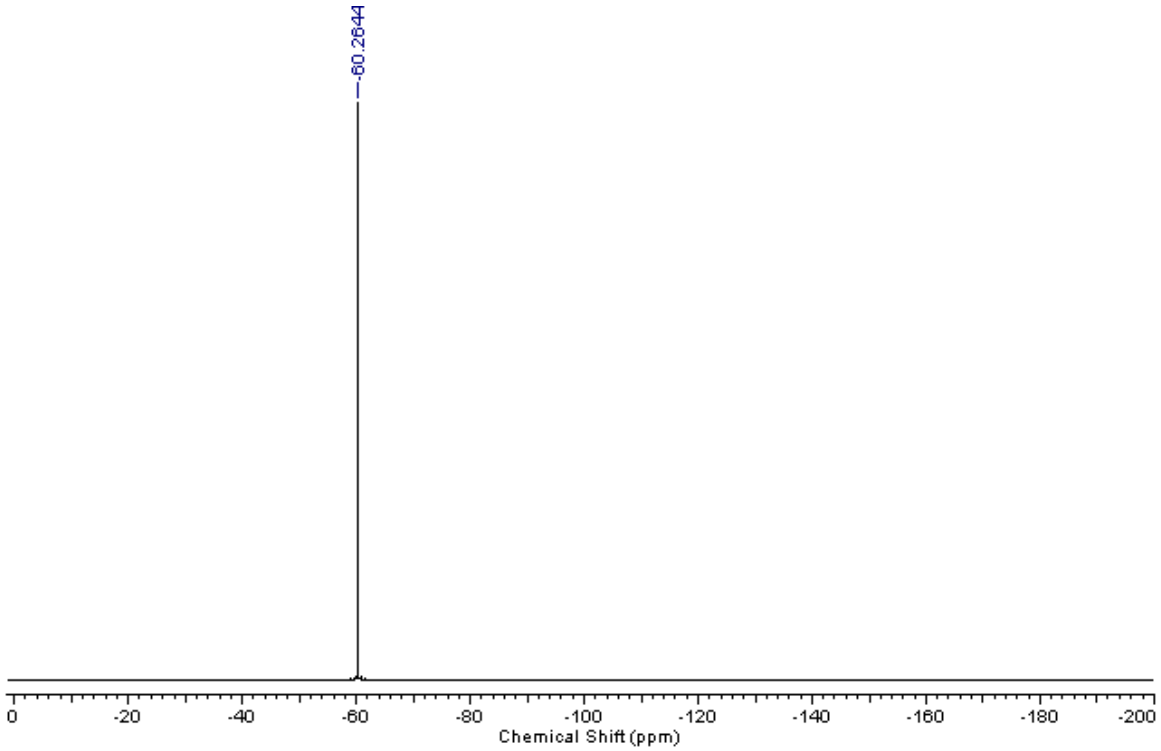

Figure S8: ^{19}F NMR spectrum of compound **5** in DMSO-d_6.

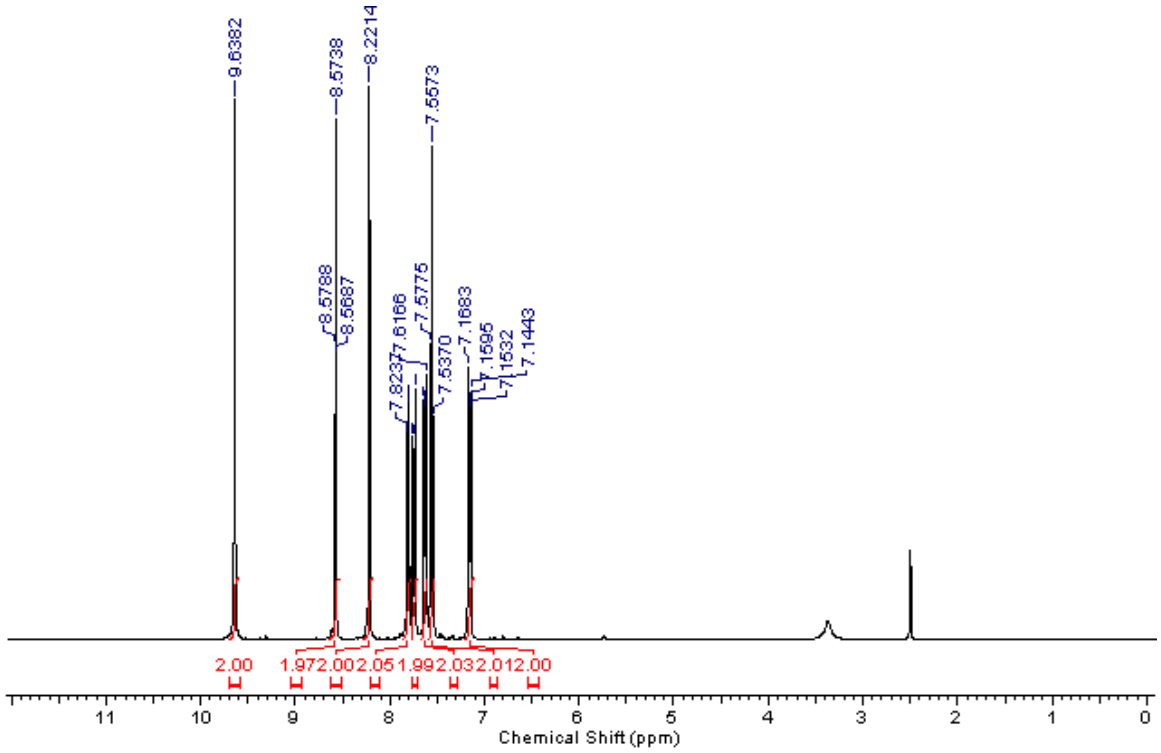

Figure S9: ^{1}H NMR spectrum of compound **7** in DMSO-d_6.

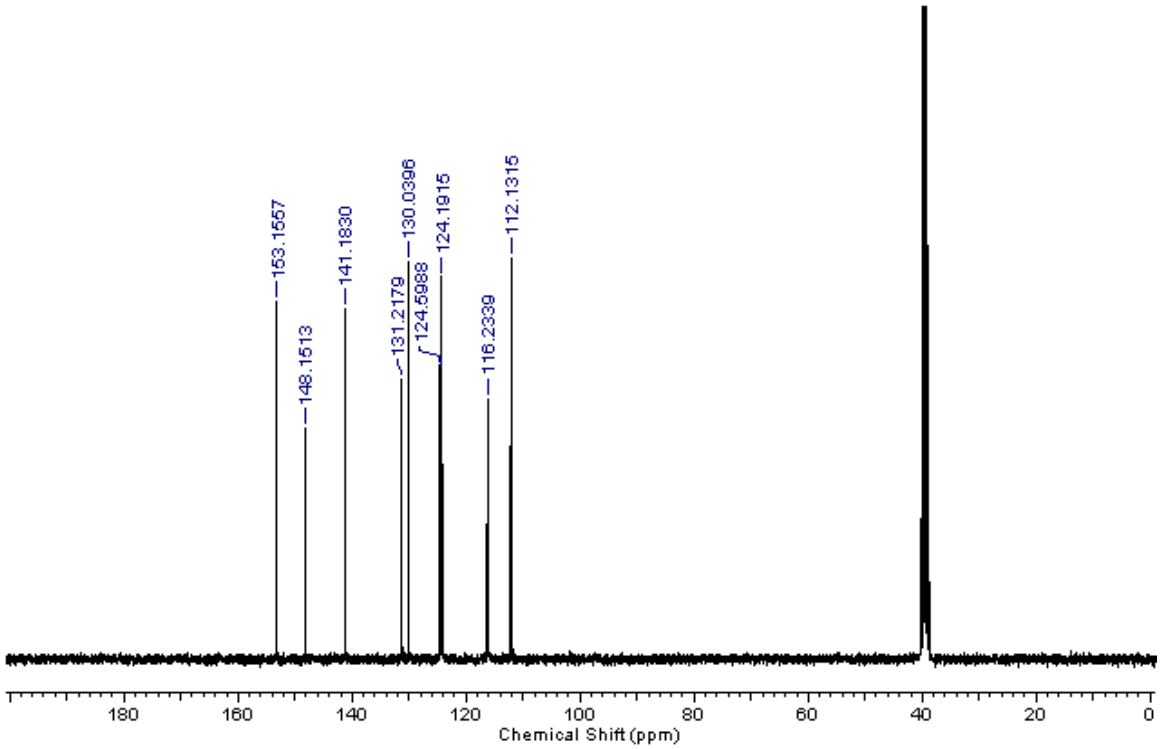

Figure S10: ^{13}C NMR spectrum of compound **7** in DMSO-d_6.

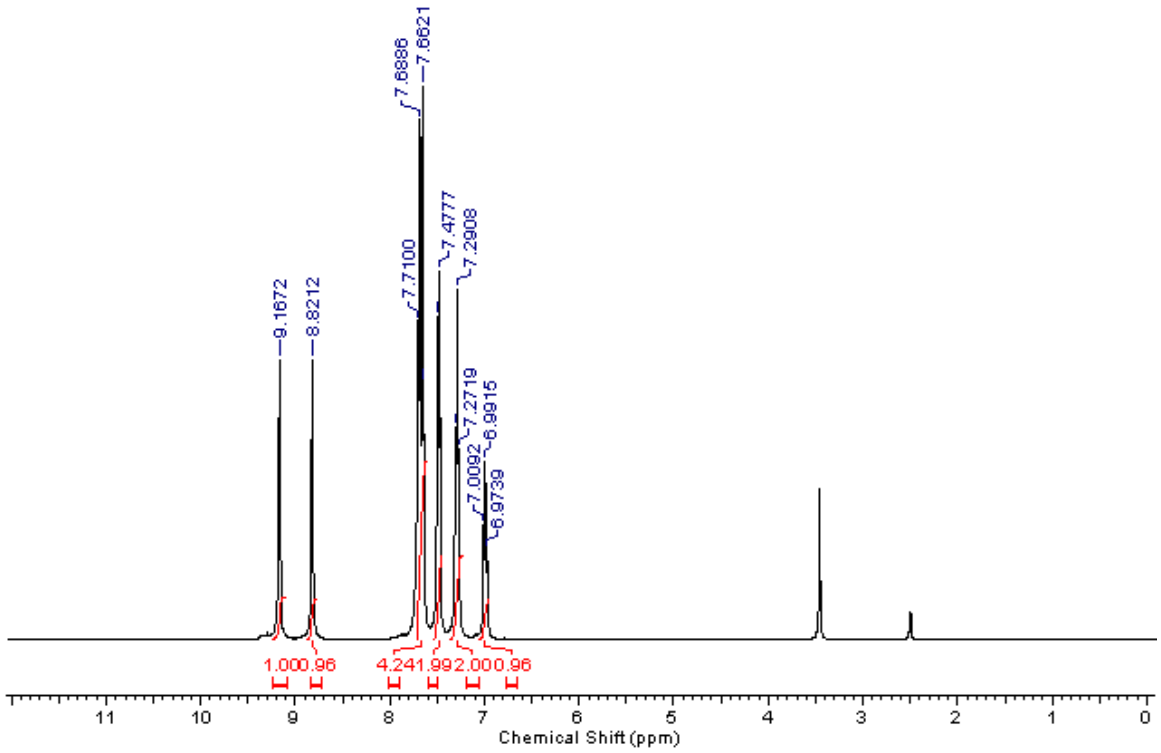

Figure S11: ^{1}H NMR spectrum of compound **9** in DMSO-d_6.

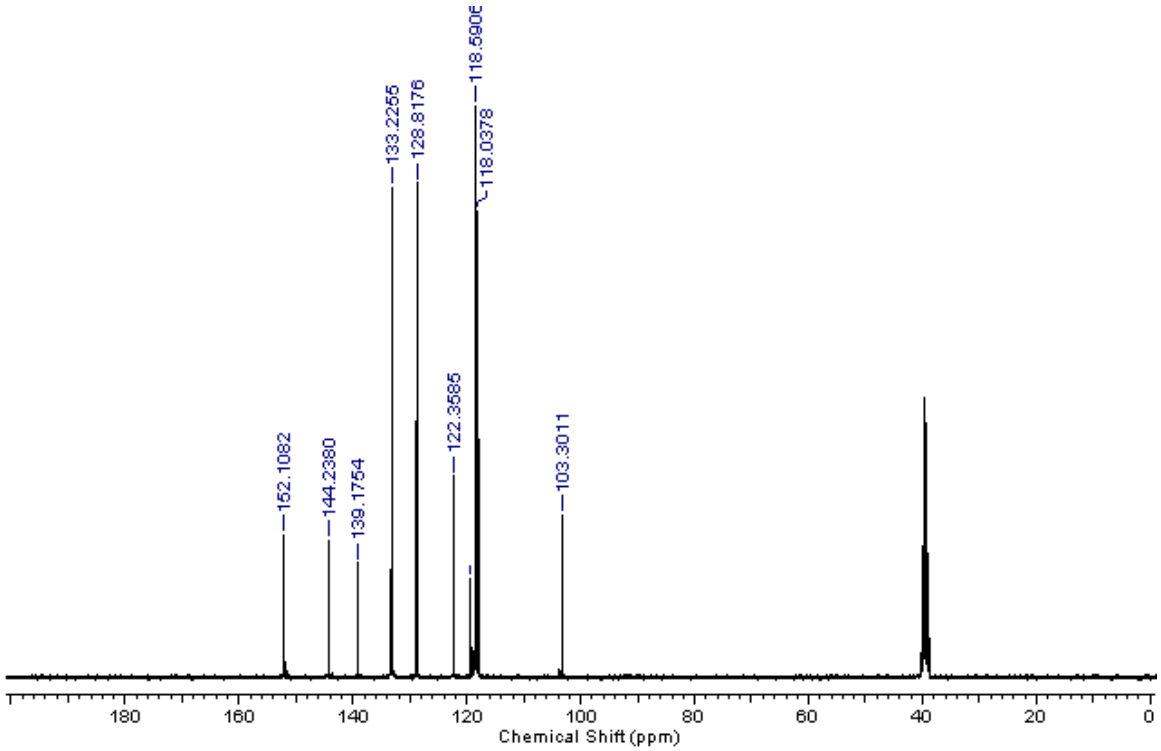

Figure S12: ^{13}C NMR spectrum of compound **9** in DMSO-d_6.

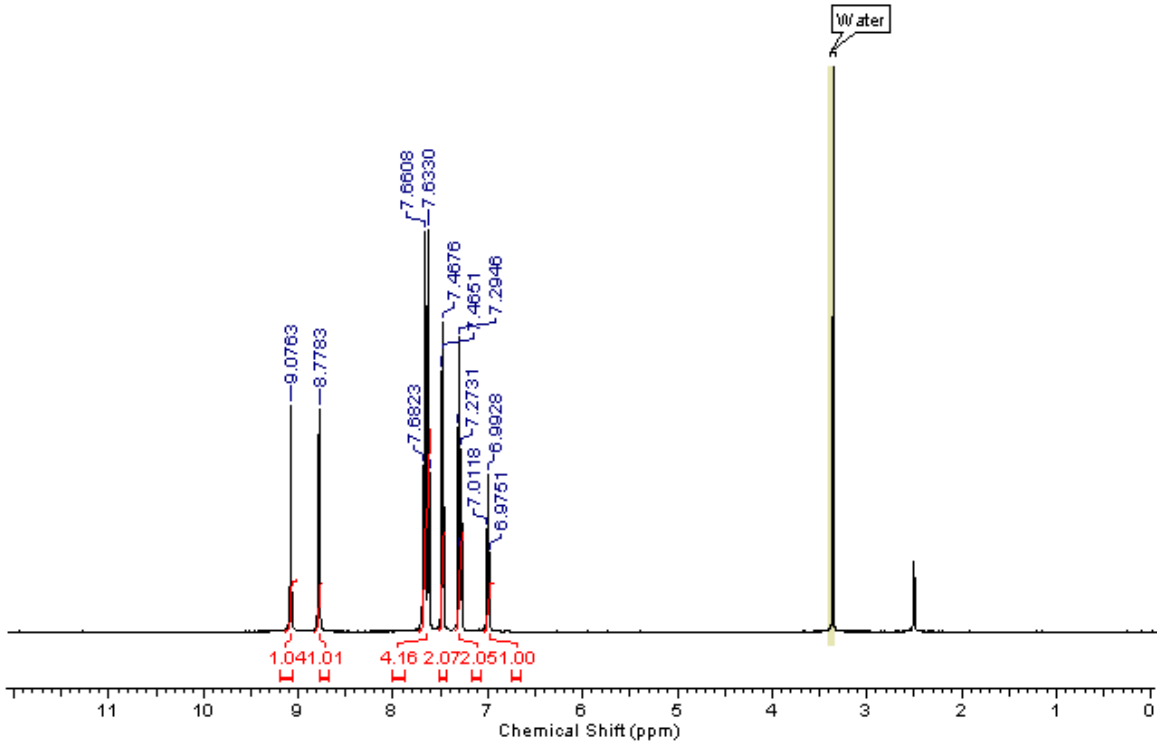

Figure S13: ^{1}H NMR spectrum of compound **10** in DMSO-d_6.

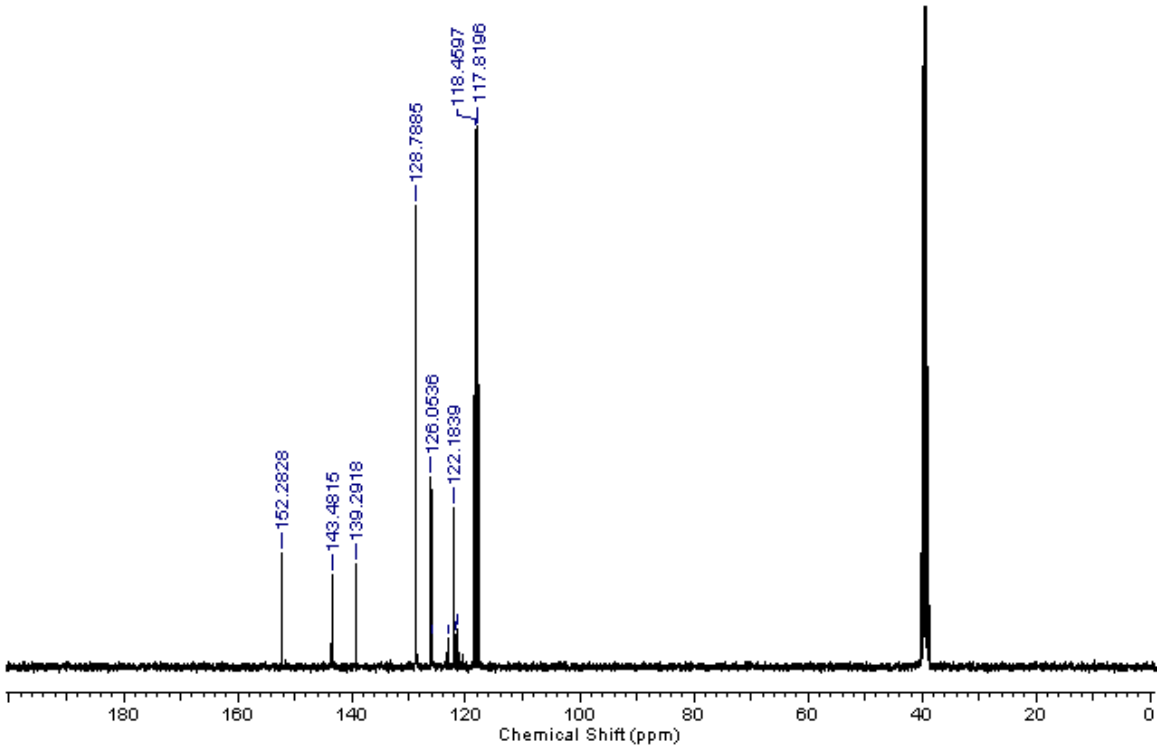

Figure S14: ^{13}C NMR spectrum of compound **10** in DMSO-d_6.

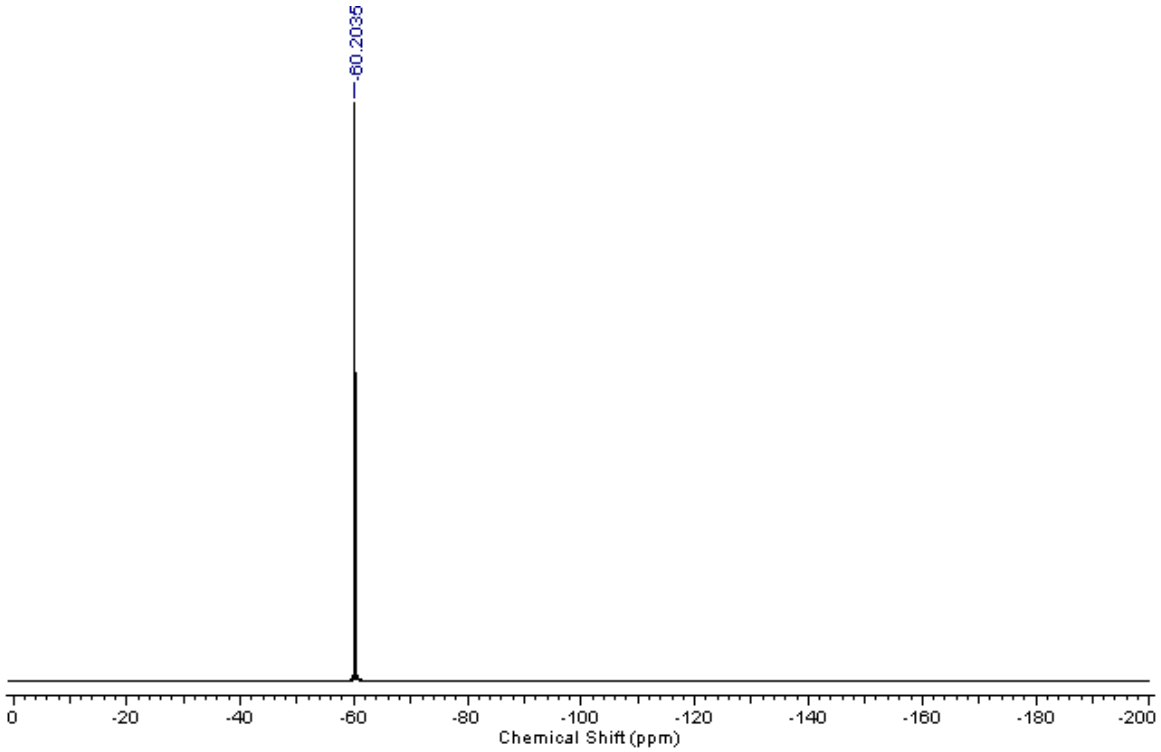

Figure S15: ^{19}F NMR spectrum of compound **10** in DMSO-d_6.

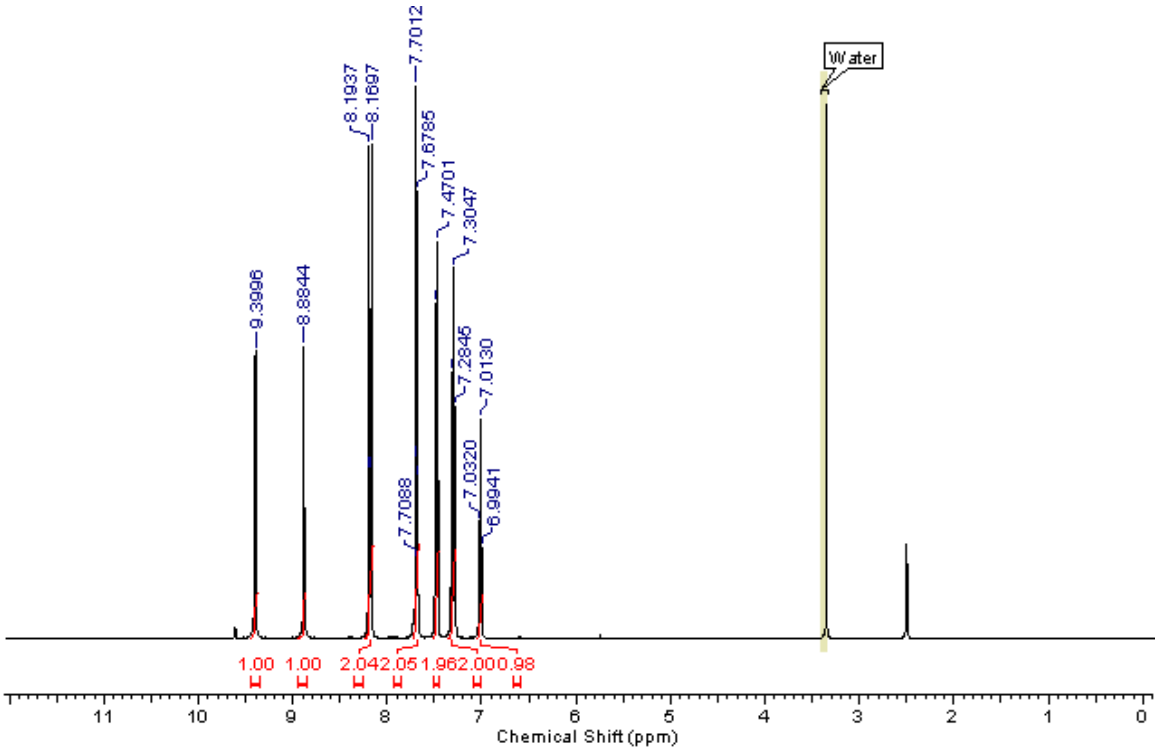

Figure S16: ^{1}H NMR spectrum of compound **11** in DMSO-d_6.

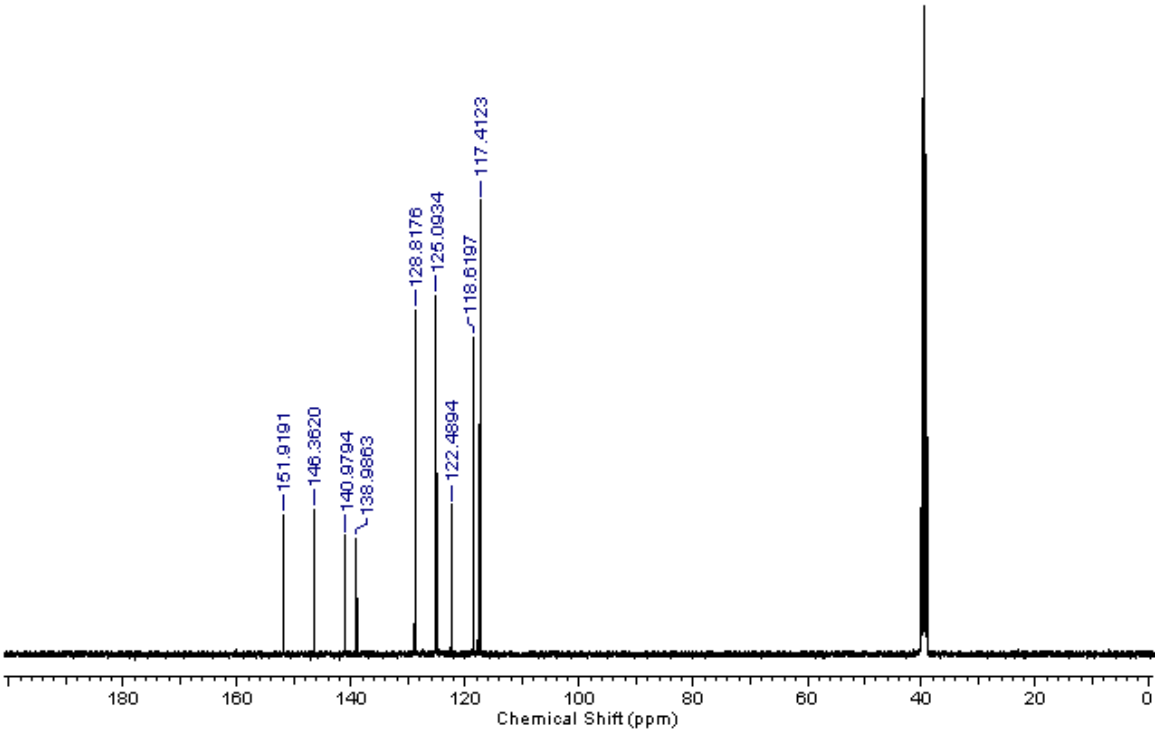

Figure S17: ^{13}C NMR spectrum of compound **11** in DMSO-d_6.

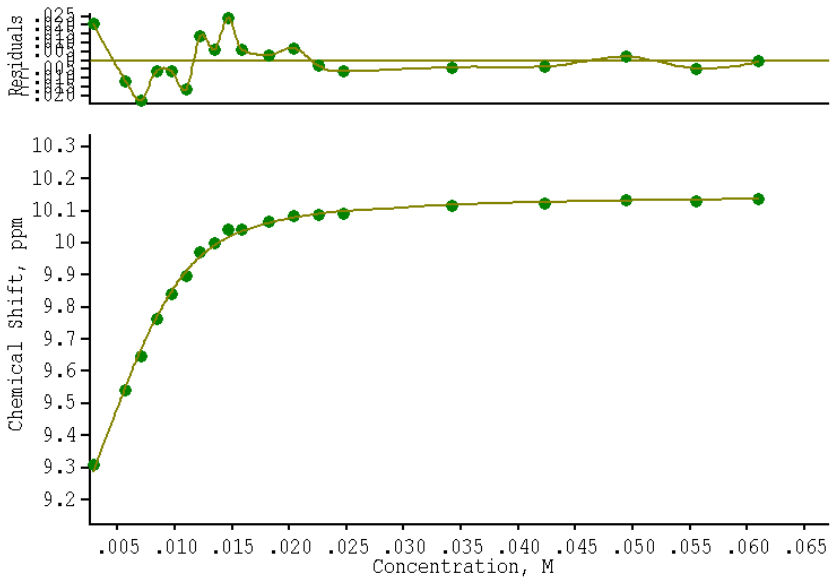

Figure S18: NMR titration of compound **1** with $TEAHCO_3$ in 0.5% H_2O/DMSO-d_6.

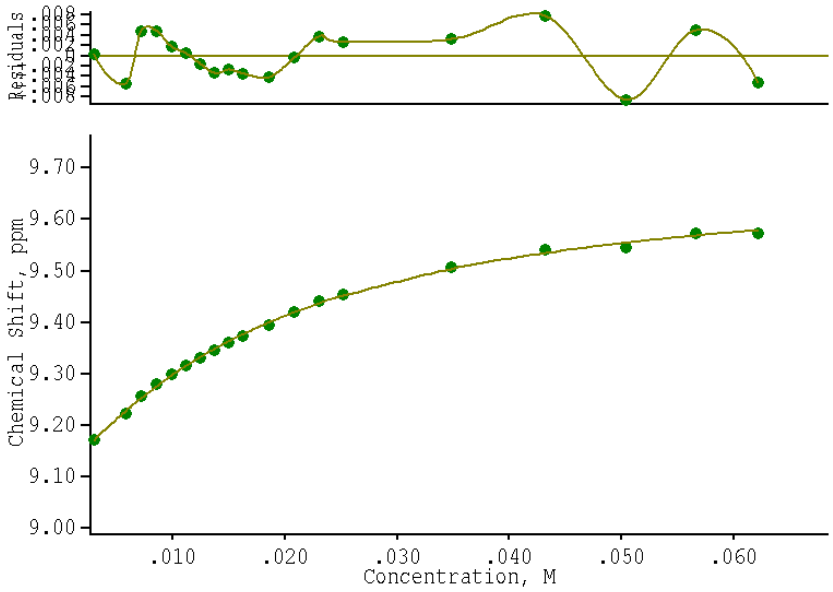

Figure S19: NMR titration of compound **2** with TBACl in 0.5% H_2O/DMSO-d_6.

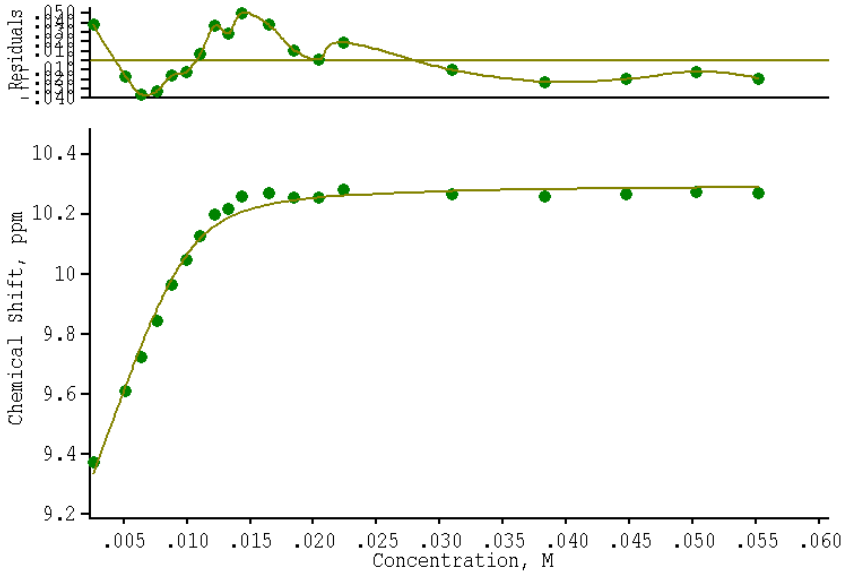

Figure S20: NMR titration of compound **3** with $TEAHCO_3$ in 0.5% H_2O/DMSO-d_6.

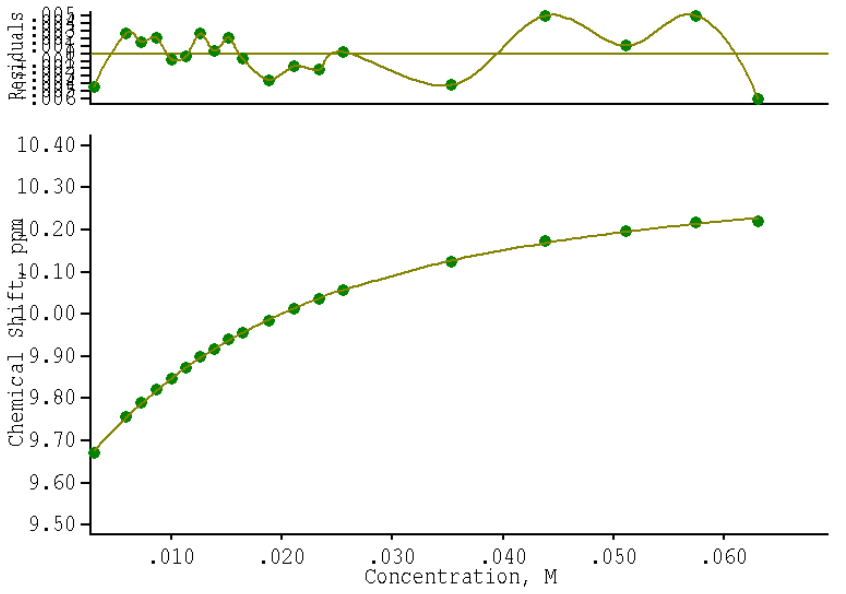

Figure S21: NMR titration of compound **4** with TBACl in 0.5% H_2O/DMSO-d_6.

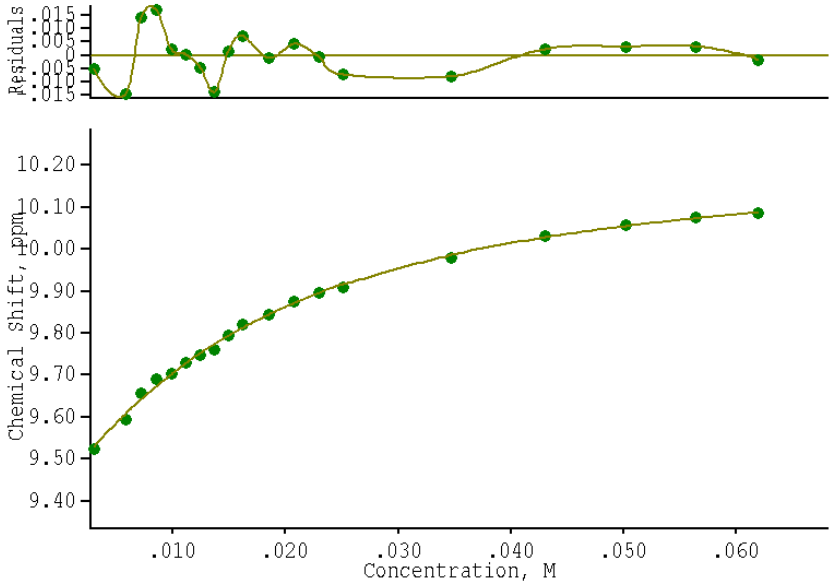

Figure S22: NMR titration of compound **5** with TBACl in 0.5% H_2O/DMSO-d_6.

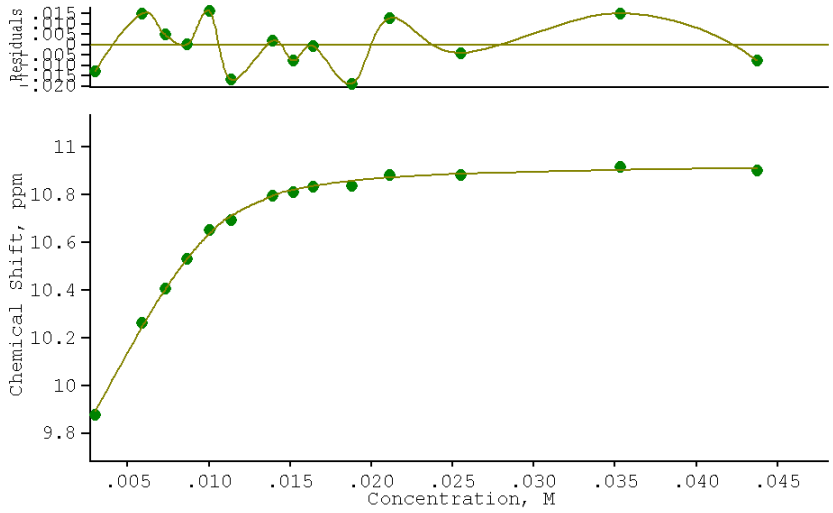

Figure S23: NMR titration of compound **5** with $TEAHCO_3$ in 0.5% H_2O/DMSO-d_6.

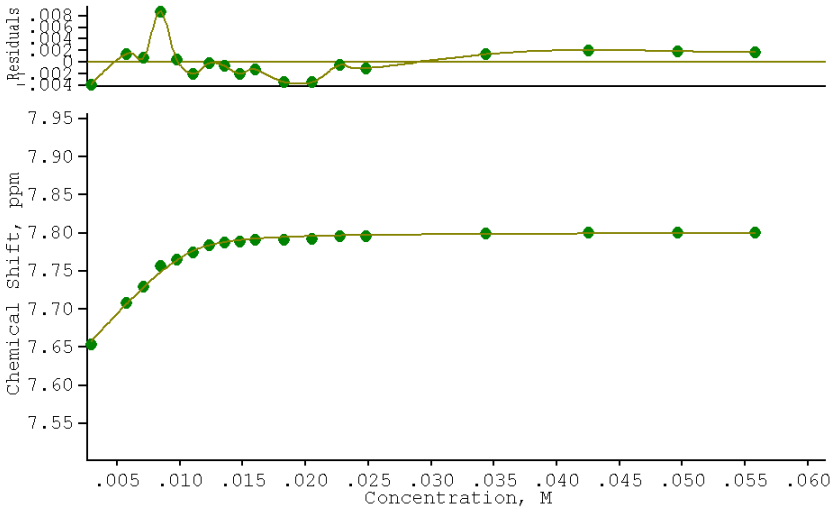

Figure S24: NMR titration of compound **6** with $TEAHCO_3$ in 0.5% H_2O/DMSO-d_6.

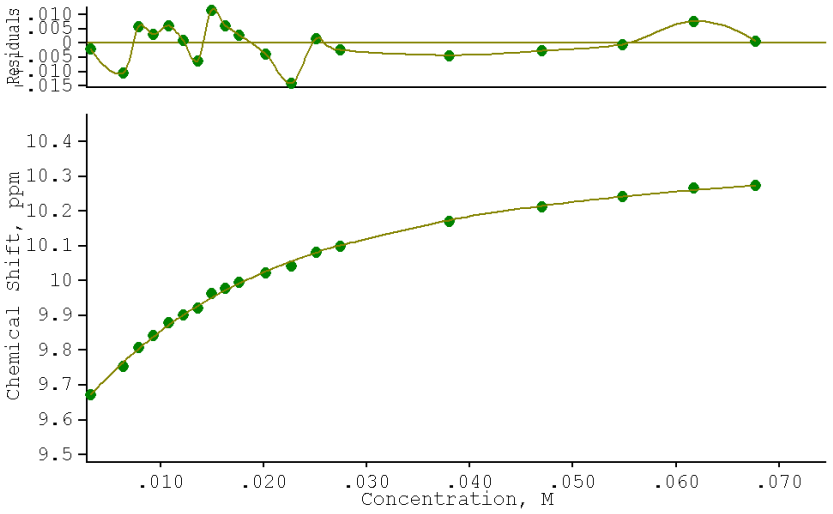

Figure S25: NMR titration of compound **7** with TBACl in 0.5% H_2O/DMSO-d_6.

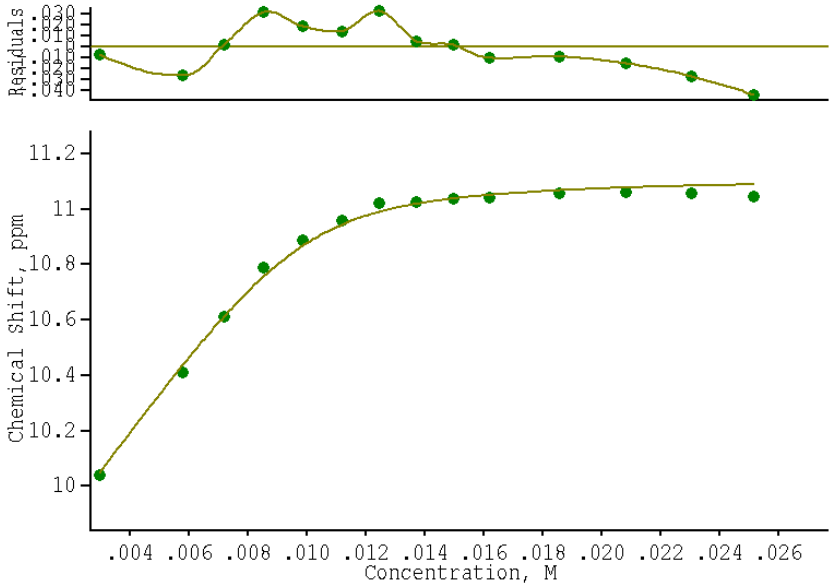

Figure S26: NMR titration of compound **7** with $TEAHCO_3$ in 0.5% H_2O/DMSO-d_6.

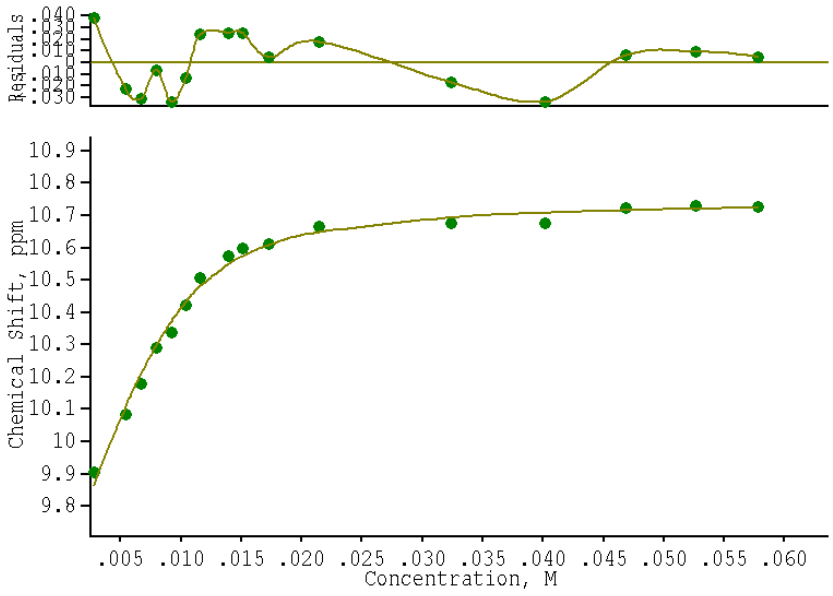

Figure S27: NMR titration of compound **8** with $TEAHCO_3$ in 0.5% H_2O/DMSO-d_6.

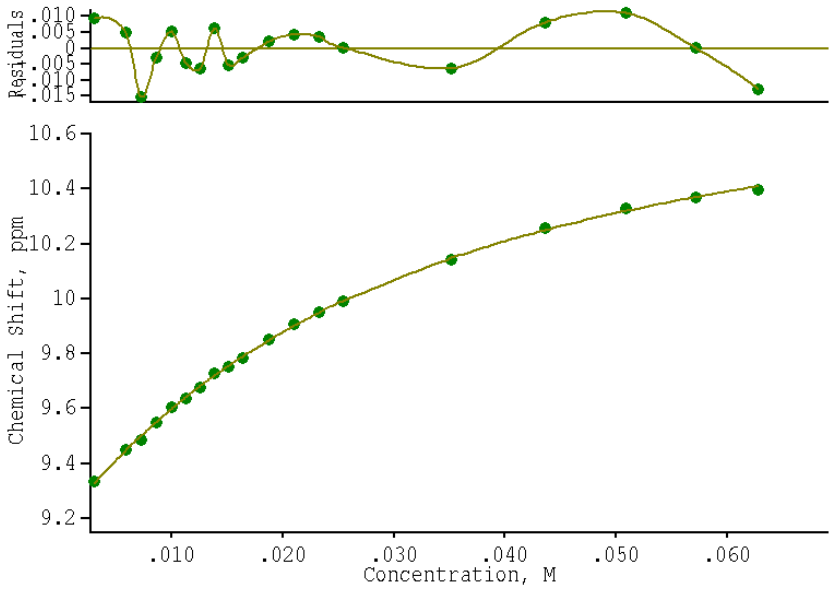

Figure S28: NMR titration of compound **9** with TBACl in 0.5% H_2O/DMSO-d_6.

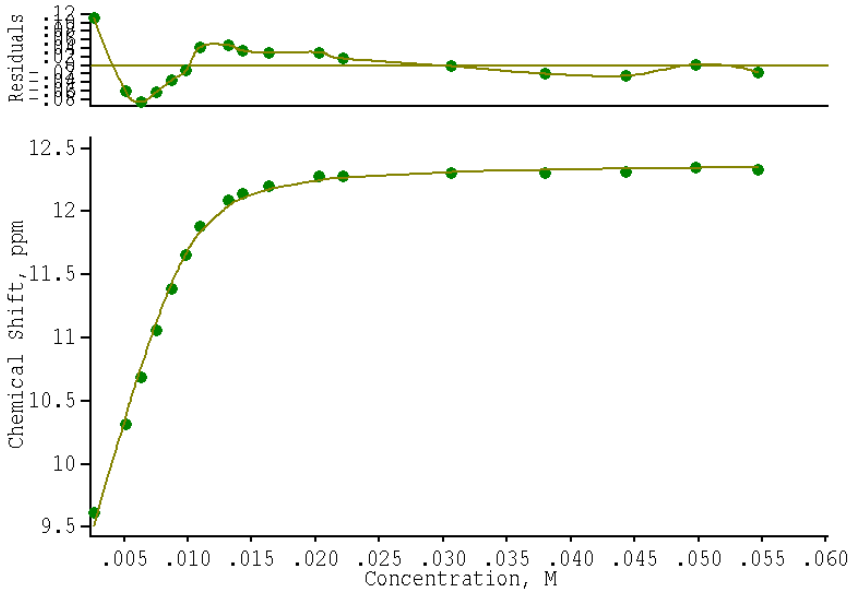

Figure S29: NMR titration of compound **9** with $TEAHCO_3$ in 0.5% H_2O/DMSO-d_6.

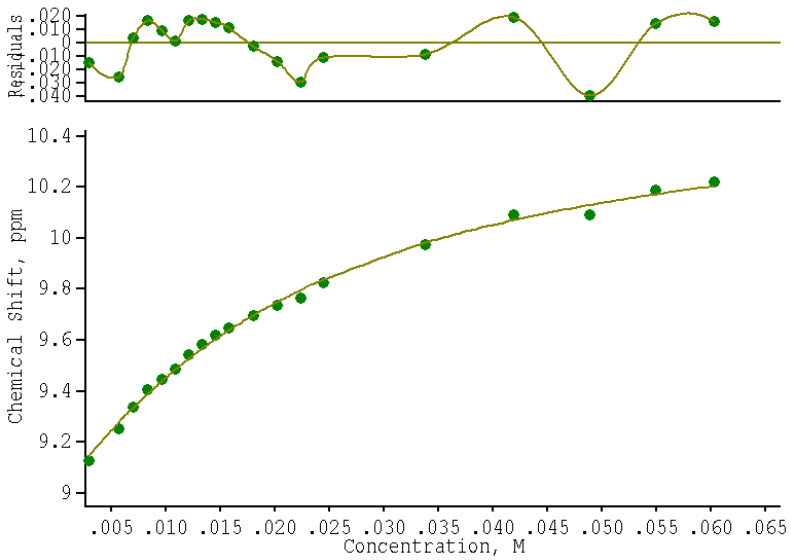

Figure S30: NMR titration of compound **10** with TBACl in 0.5% H_2O/DMSO-d_6.

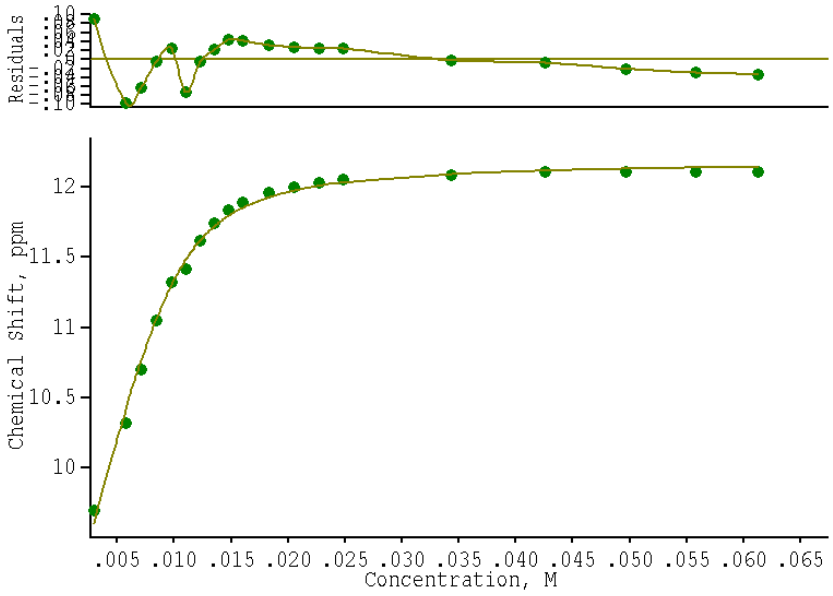

Figure S31: NMR titration of compound **10** with $TEAHCO_3$ in 0.5% H_2O/DMSO-d_6.

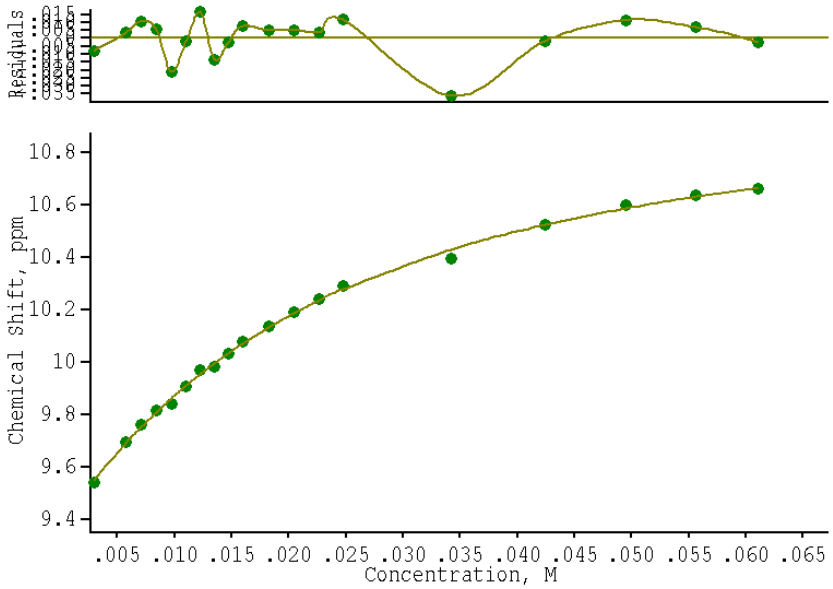

Figure S32: NMR titration of compound **11** with TBACl in 0.5% H_2O/DMSO-d_6.

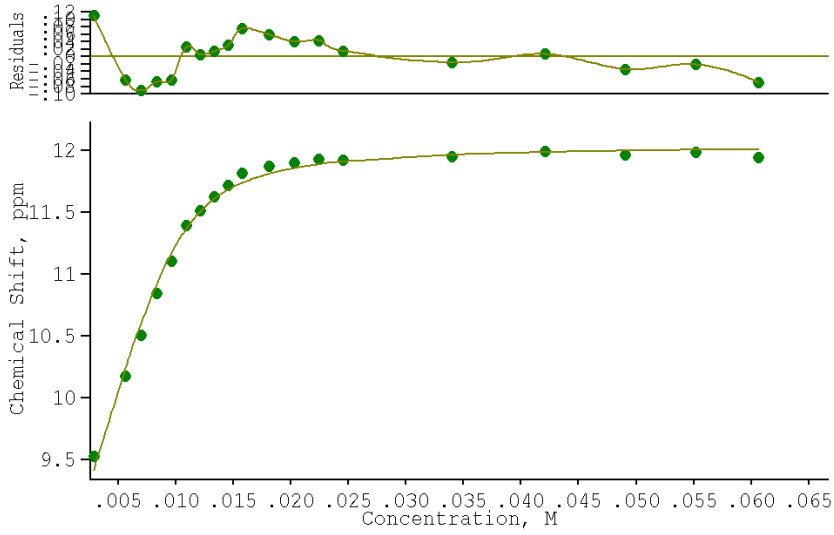

Figure S33: NMR titration of compound **11** with $TEAHCO_3$ in 0.5% H_2O/DMSO-d_6.

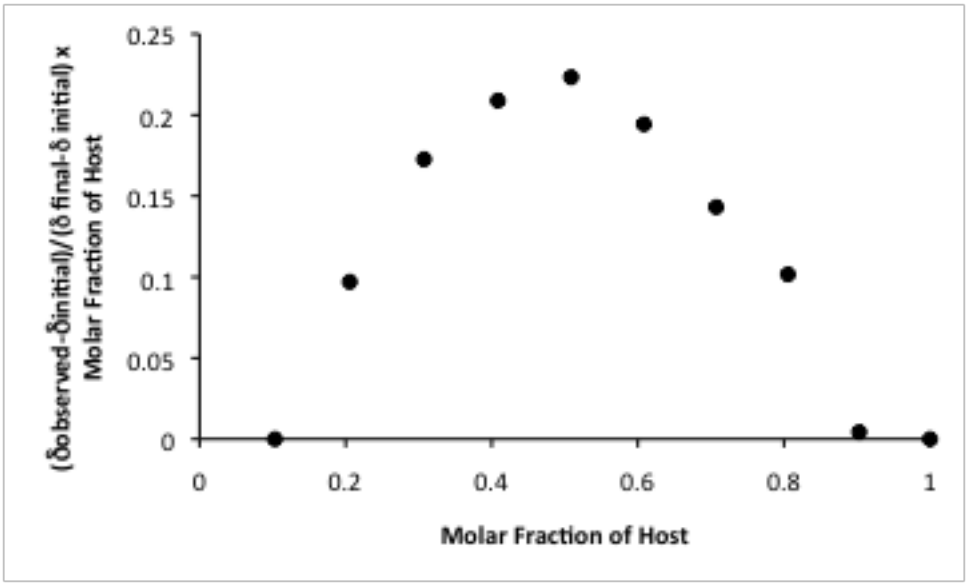

Figure S34: Job plot for compound **2** with $TEAHCO_3$ in 0.5% H_2O/DMSO-d_6.

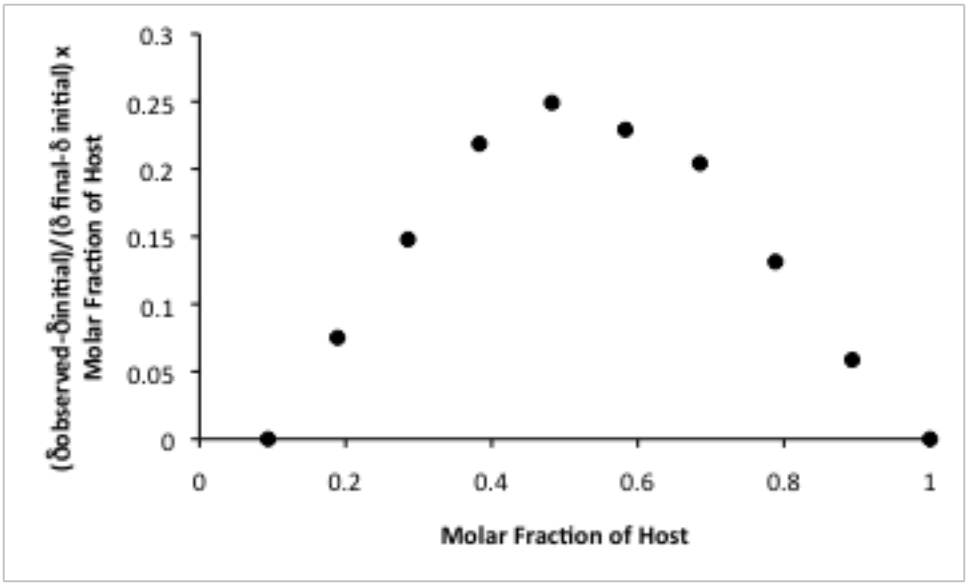

Figure S35: Job plot for compound **4** with $TEAHCO_3$ in 0.5% H_2O/DMSO-d_6.

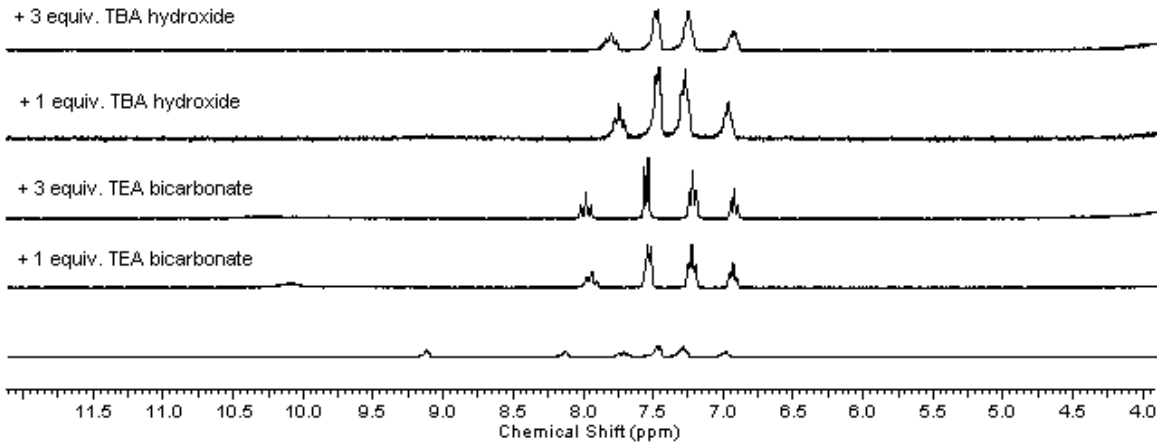

Figure S36: NMR spectra upon addition of TEA bicarbonate (1 and 3 equivalents) or TBA hydroxide (1 and 3 equivalents) to a solution of compound **2** in 0.5% H_2O/DMSO-d_6.

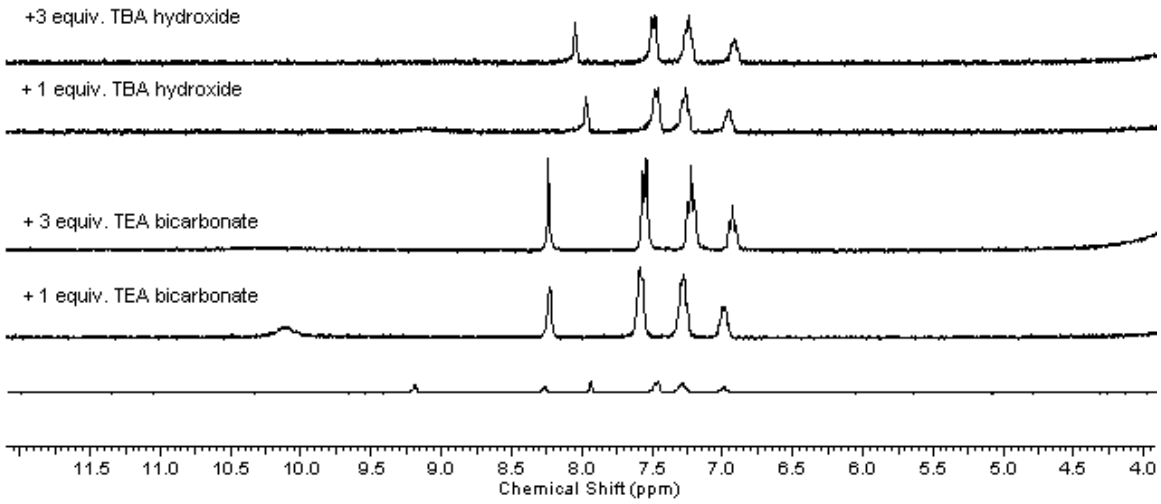

Figure S37: NMR spectra upon addition of TEA bicarbonate (1 and 3 equivalents) or TBA hydroxide (1 and 3 equivalents) to a solution of compound **3** in 0.5% H_2O/DMSO-d_6.

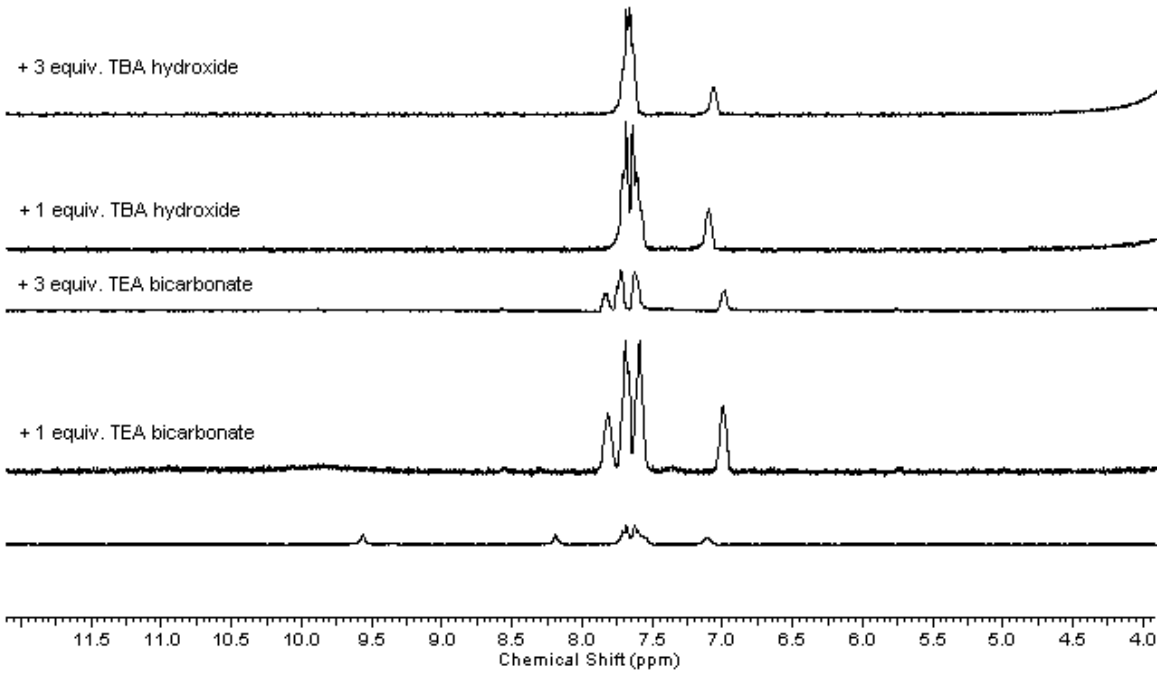

Figure S38: NMR spectra upon addition of TEA bicarbonate (1 and 3 equivalents) or TBA hydroxide (1 and 3 equivalents) to a solution of compound **4** in 0.5% H_2O/DMSO-d_6.

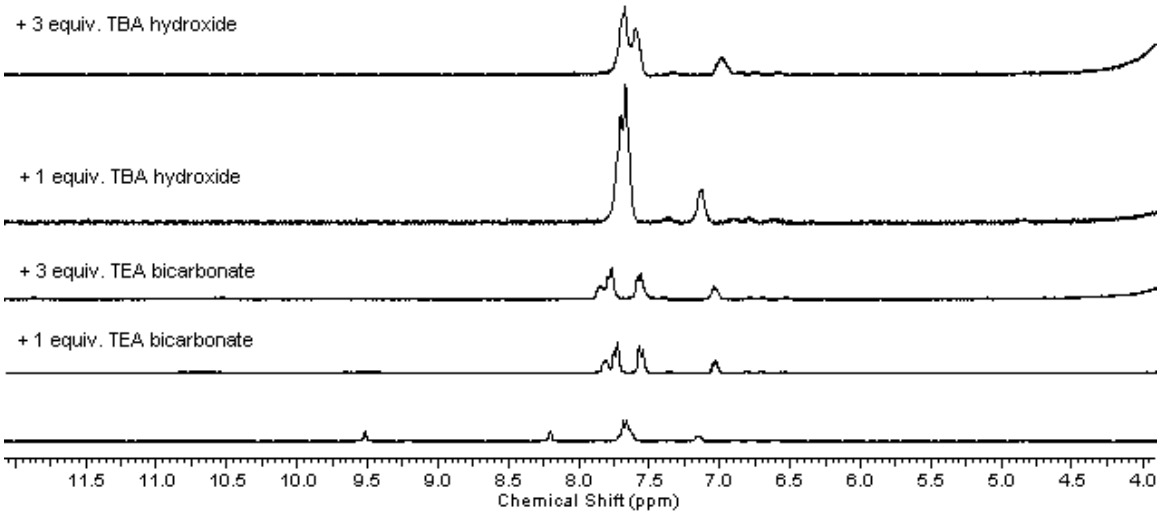

Figure S39: NMR spectra upon addition of TEA bicarbonate (1 and 3 equivalents) or TBA hydroxide (1 and 3 equivalents) to a solution of compound **5** in 0.5% H_2O/DMSO-d_6.

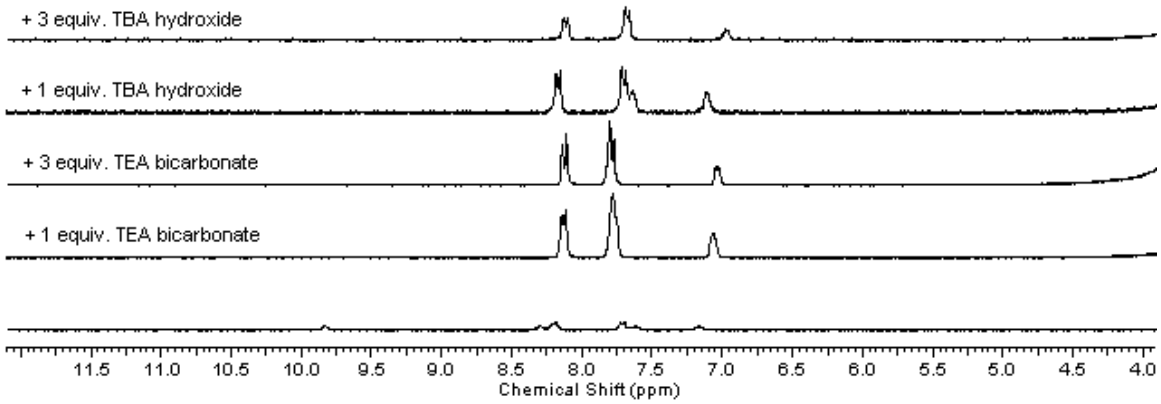

Figure S40: NMR spectra upon addition of TEA bicarbonate (1 and 3 equivalents) or TBA hydroxide (1 and 3 equivalents) to a solution of compound **6** in 0.5% H_2O/DMSO-d_6.

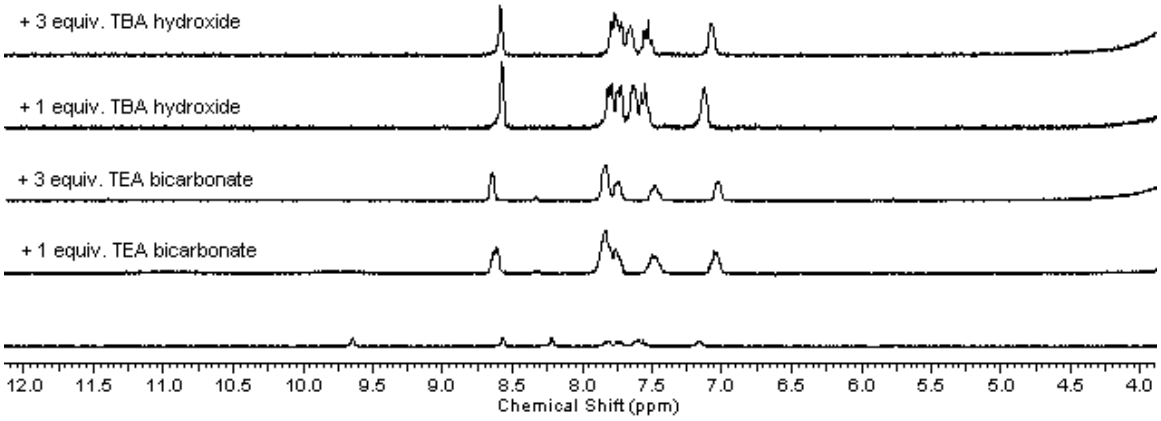

Figure S41: NMR spectra upon addition of TEA bicarbonate (1 and 3 equivalents) or TBA hydroxide (1 and 3 equivalents) to a solution of compound **7** in 0.5% H_2O/DMSO-d_6.

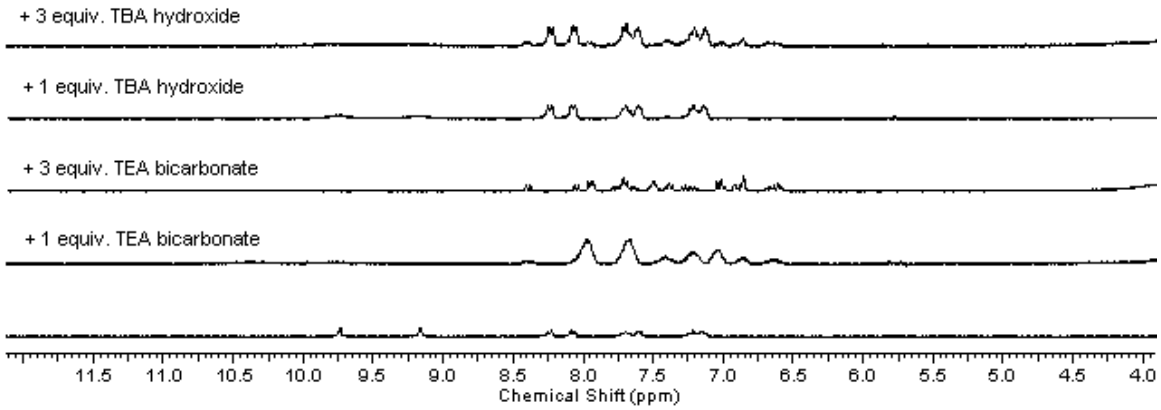

Figure S42: NMR spectra upon addition of TEA bicarbonate (1 and 3 equivalents) or TBA hydroxide (1 and 3 equivalents) to a solution of compound **8** in 0.5% H_2O/DMSO-d_6.

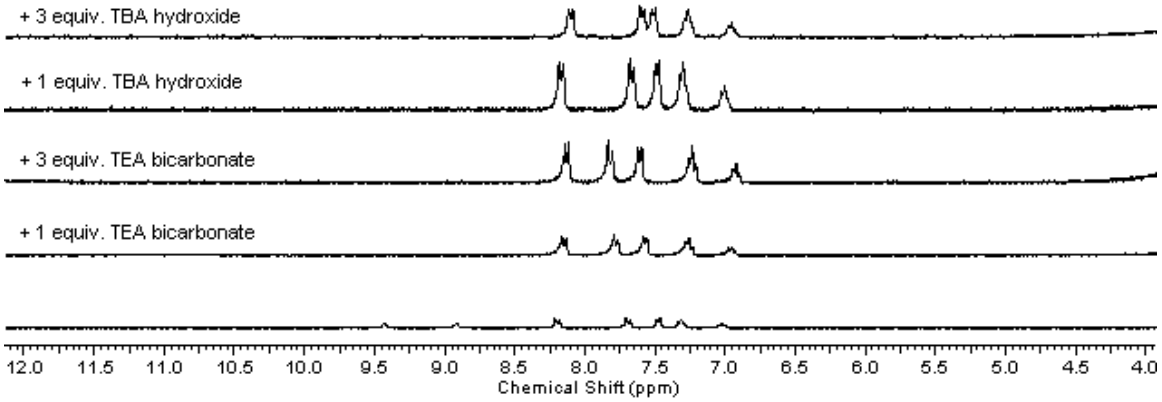

Figure S43: NMR spectra upon addition of TEA bicarbonate (1 and 3 equivalents) or TBA hydroxide (1 and 3 equivalents) to a solution of compound **11** in 0.5% H_2O/DMSO-d_6.

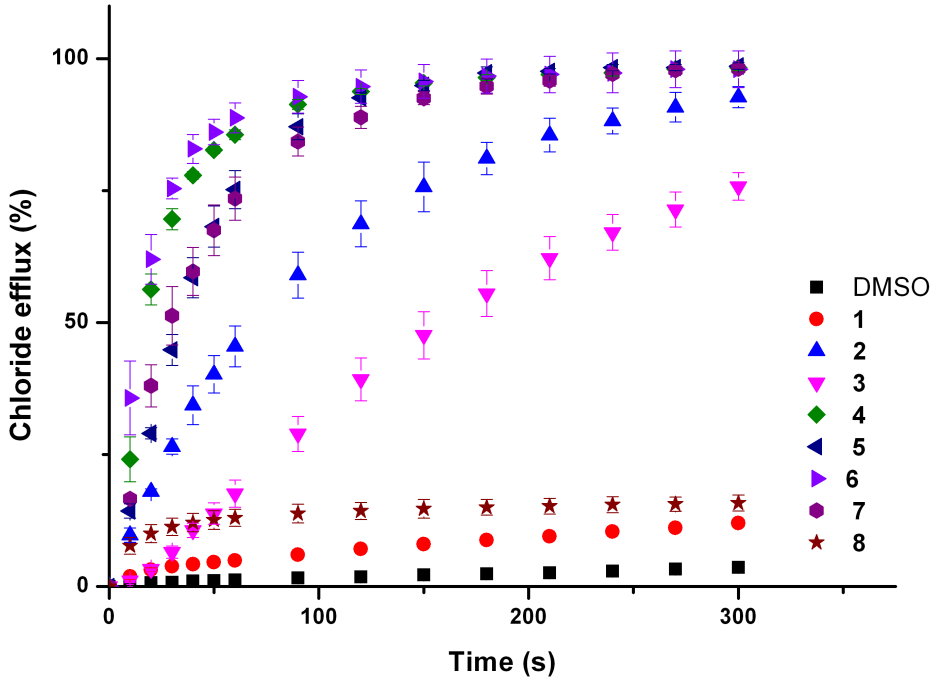

Figure S44: Chloride efflux promoted by a DMSO solution of compounds **1-8** (2mol% carrier to lipid) from unilamellar POPC vesicles loaded with 488mM NaCl buffered to pH 7.2 with 5mM sodium phosphate salts. The vesicles were dispersed in 488mM $NaNO_3$

buffered to pH 7.2 with 5mM sodium phosphate salts. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials. DMSO was used as a control.

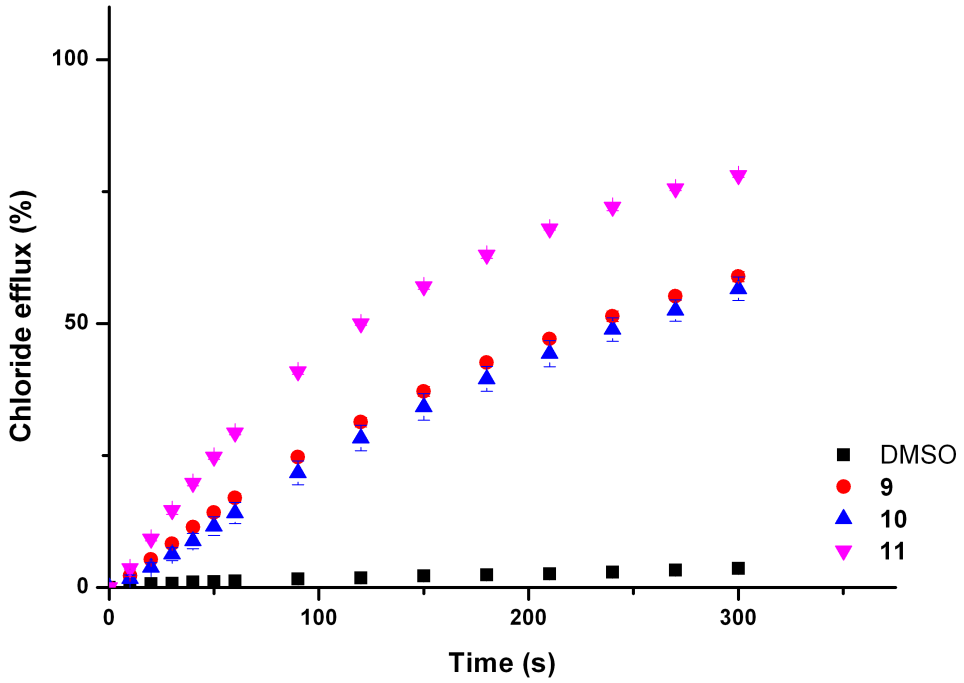

Figure S45: Chloride efflux promoted by a DMSO solution of compounds **9-11** (2mol% carrier to lipid) from unilamellar POPC vesicles loaded with 488mM NaCl buffered to pH 7.2 with 5mM sodium phosphate salts. The vesicles were dispersed in 488mM $NaNO_3$ buffered to pH 7.2 with 5mM sodium phosphate salts. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials. DMSO was used as a control.

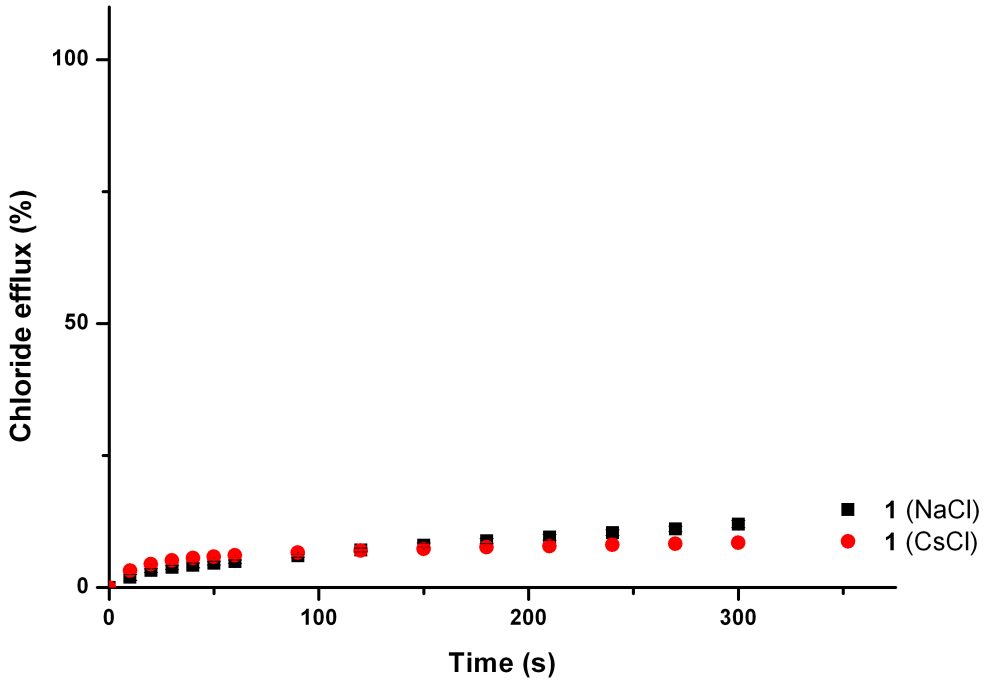

Figure S46: Chloride efflux promoted by a DMSO solution of compound **1** (2mol% carrier to lipid) from unilamellar POPC vesicles loaded with either 488mM NaCl or 488mM CsCl buffered to pH 7.2 with 5mM sodium phosphate salts. The vesicles were dispersed in 488mM $NaNO_3$ buffered to pH 7.2 with 5mM sodium phosphate salts. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials. DMSO was used as a control.

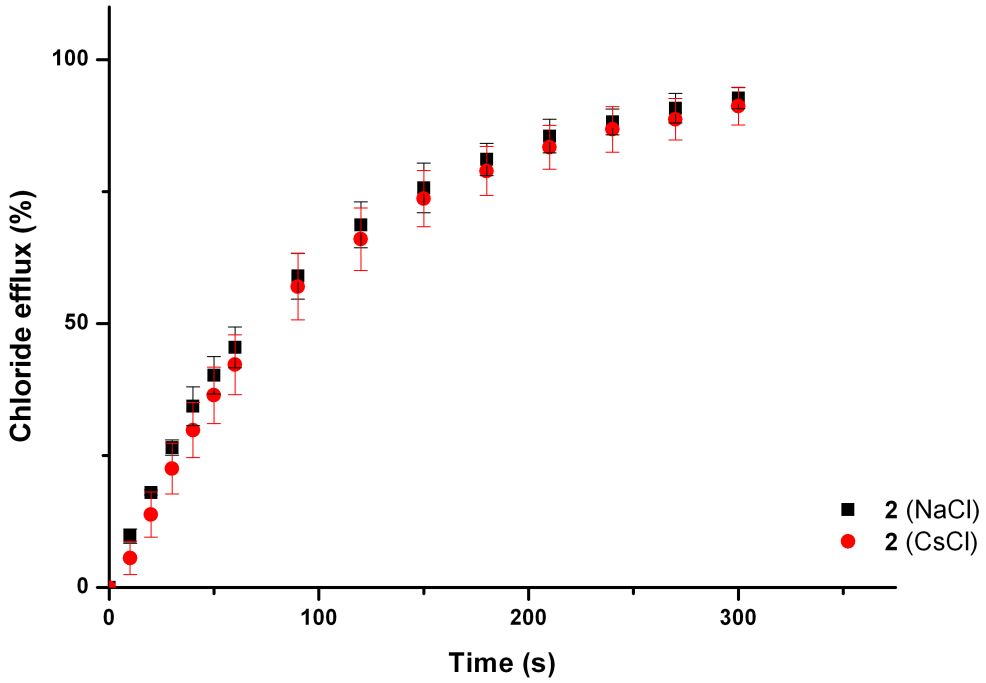

Figure S47: Chloride efflux promoted by a DMSO solution of compound **2** (2mol% carrier to lipid) from unilamellar POPC vesicles loaded with either 488mM NaCl or 488mM CsCl buffered to pH 7.2 with 5mM sodium phosphate salts. The vesicles were dispersed in 488mM $NaNO_3$ buffered to pH 7.2 with 5mM sodium phosphate salts. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials. DMSO was used as a control.

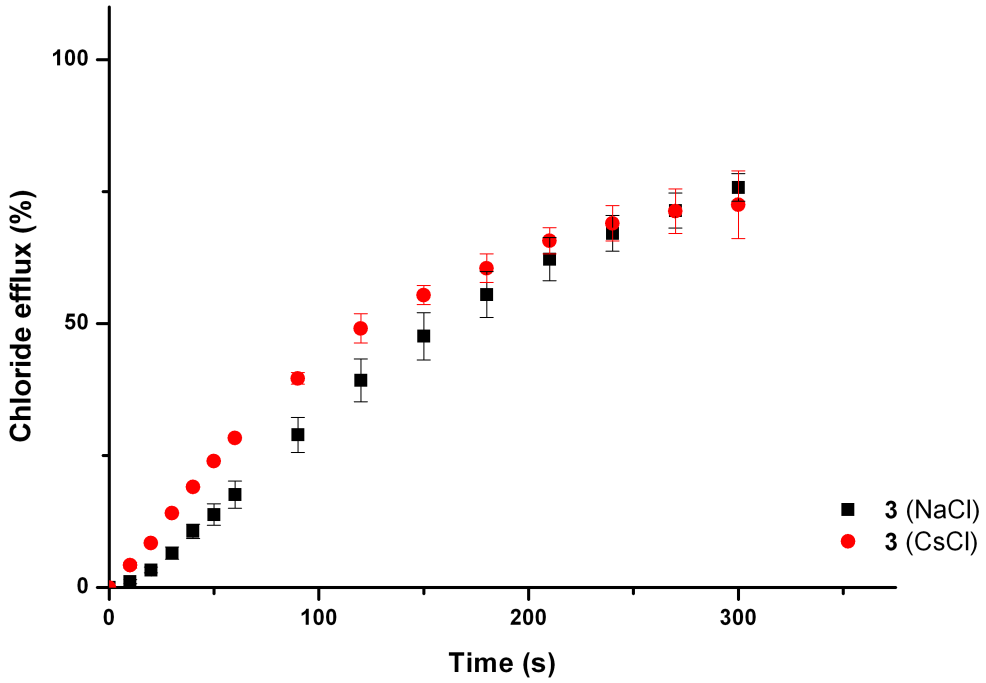

Figure S48: Chloride efflux promoted by a DMSO solution of compound **3** (2mol% carrier to lipid) from unilamellar POPC vesicles loaded with either 488mM NaCl or 488mM CsCl buffered to pH 7.2 with 5mM sodium phosphate salts. The vesicles were dispersed in 488mM $NaNO_3$ buffered to pH 7.2 with 5mM sodium phosphate salts. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials. DMSO was used as a control.

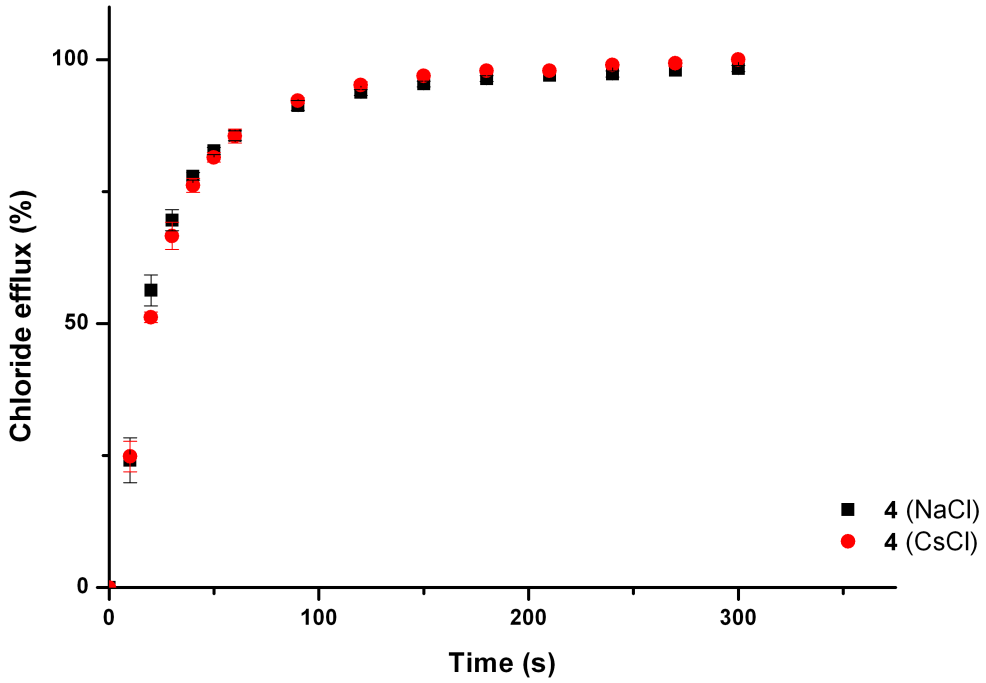

Figure S49: Chloride efflux promoted by a DMSO solution of compound **4** (2mol% carrier to lipid) from unilamellar POPC vesicles loaded with either 488mM NaCl or 488mM CsCl buffered to pH 7.2 with 5mM sodium phosphate salts. The vesicles were dispersed in 488mM $NaNO_3$ buffered to pH 7.2 with 5mM sodium phosphate salts. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials. DMSO was used as a control.

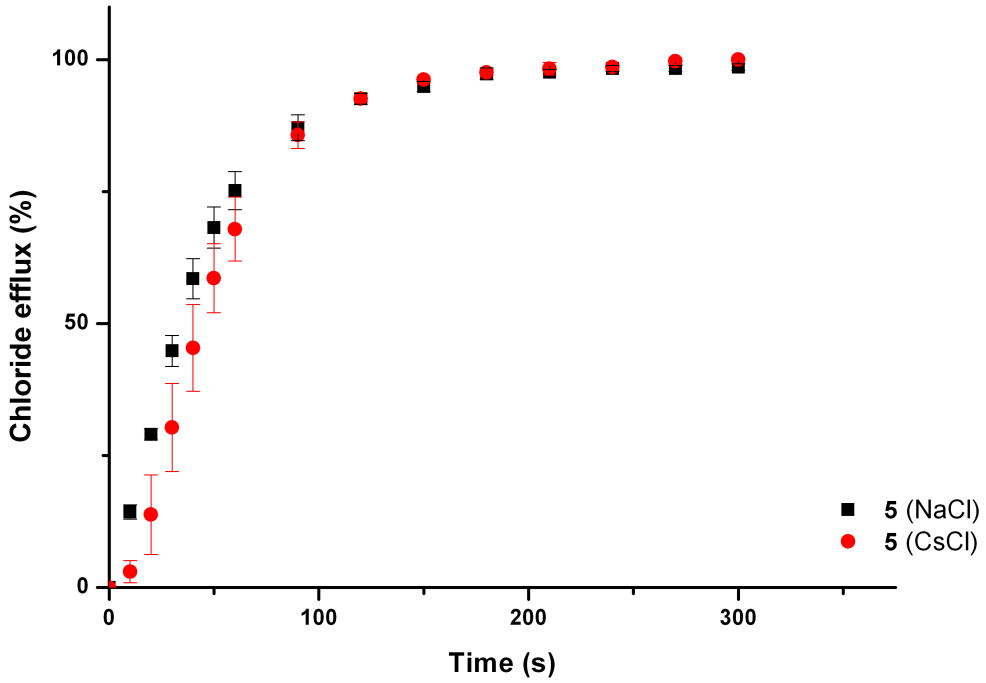

Figure S50: Chloride efflux promoted by a DMSO solution of compound **5** (2mol% carrier to lipid) from unilamellar POPC vesicles loaded with either 488mM NaCl or 488mM CsCl buffered to pH 7.2 with 5mM sodium phosphate salts. The vesicles were dispersed in 488mM $NaNO_3$ buffered to pH 7.2 with 5mM sodium phosphate salts. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials. DMSO was used as a control.

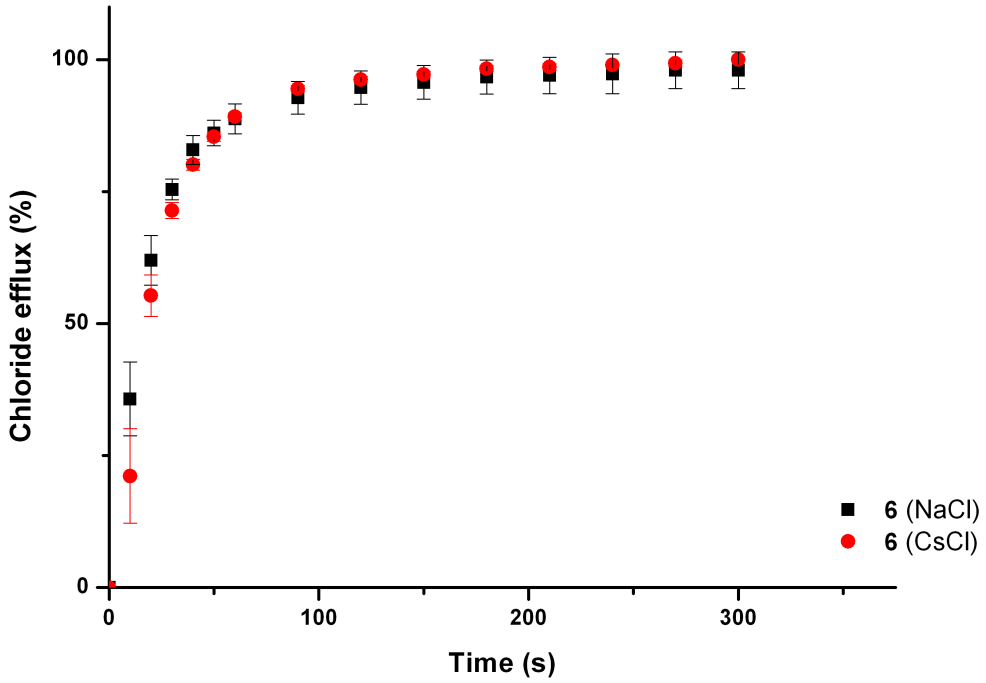

Figure S51: Chloride efflux promoted by a DMSO solution of compound **6** (2mol% carrier to lipid) from unilamellar POPC vesicles loaded with either 488mM NaCl or 488mM CsCl buffered to pH 7.2 with 5mM sodium phosphate salts. The vesicles were dispersed in 488mM $NaNO_3$ buffered to pH 7.2 with 5mM sodium phosphate salts. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials. DMSO was used as a control.

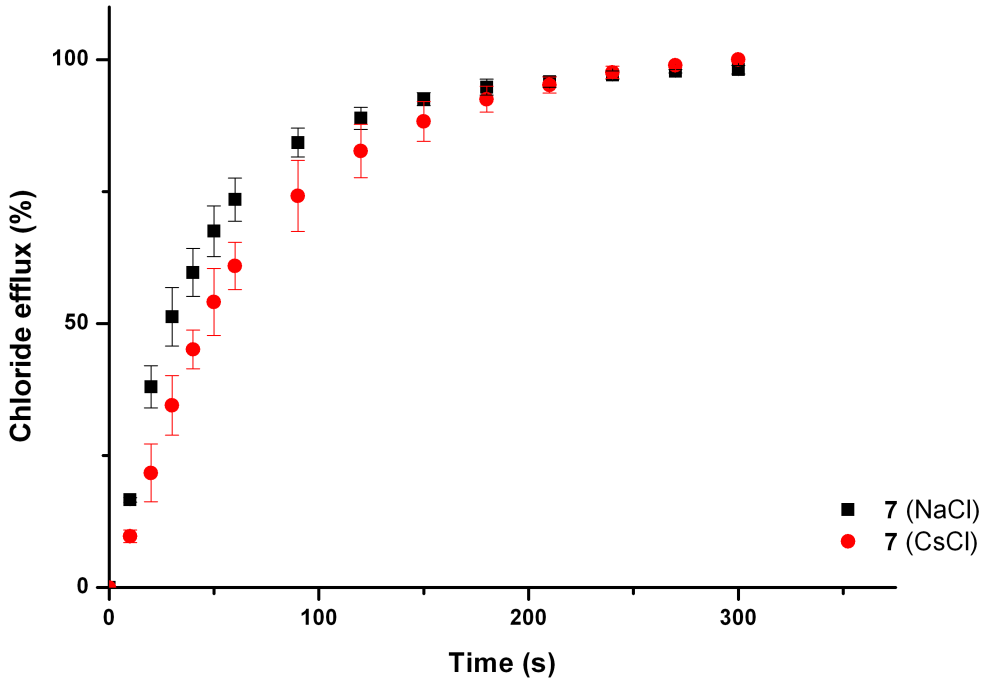

Figure S52: Chloride efflux promoted by a DMSO solution of compound **7** (2mol% carrier to lipid) from unilamellar POPC vesicles loaded with either 488mM NaCl or 488mM CsCl buffered to pH 7.2 with 5mM sodium phosphate salts. The vesicles were dispersed in 488mM $NaNO_3$ buffered to pH 7.2 with 5mM sodium phosphate salts. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials. DMSO was used as a control.

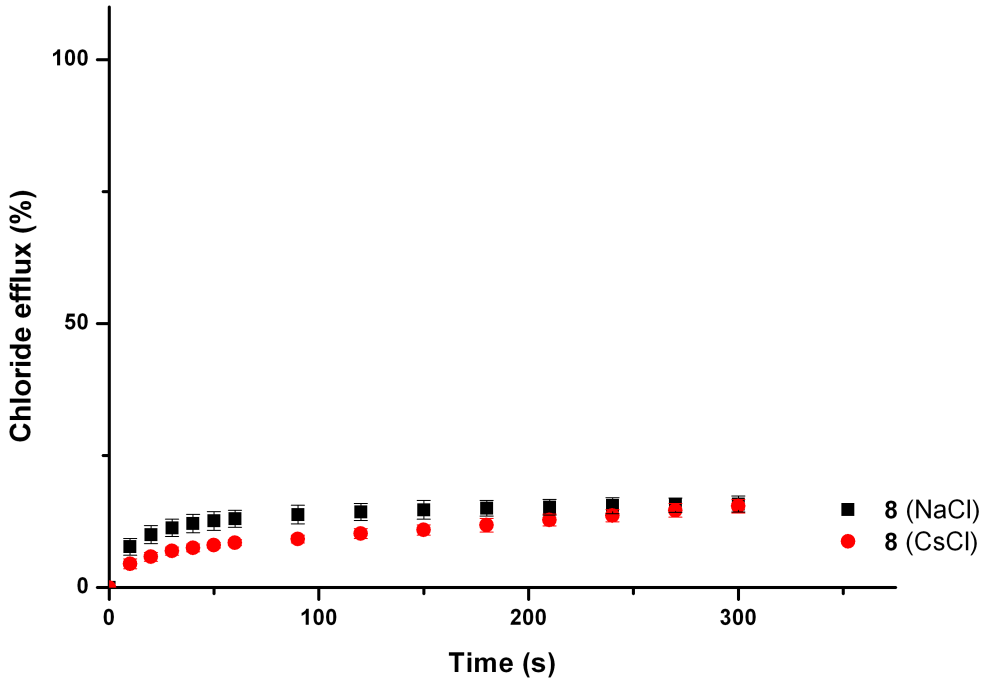

Figure S53: Chloride efflux promoted by a DMSO solution of compound **8** (2mol% carrier to lipid) from unilamellar POPC vesicles loaded with either 488mM NaCl or 488mM CsCl buffered to pH 7.2 with 5mM sodium phosphate salts. The vesicles were dispersed in 488mM $NaNO_3$ buffered to pH 7.2 with 5mM sodium phosphate salts. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials. DMSO was used as a control.

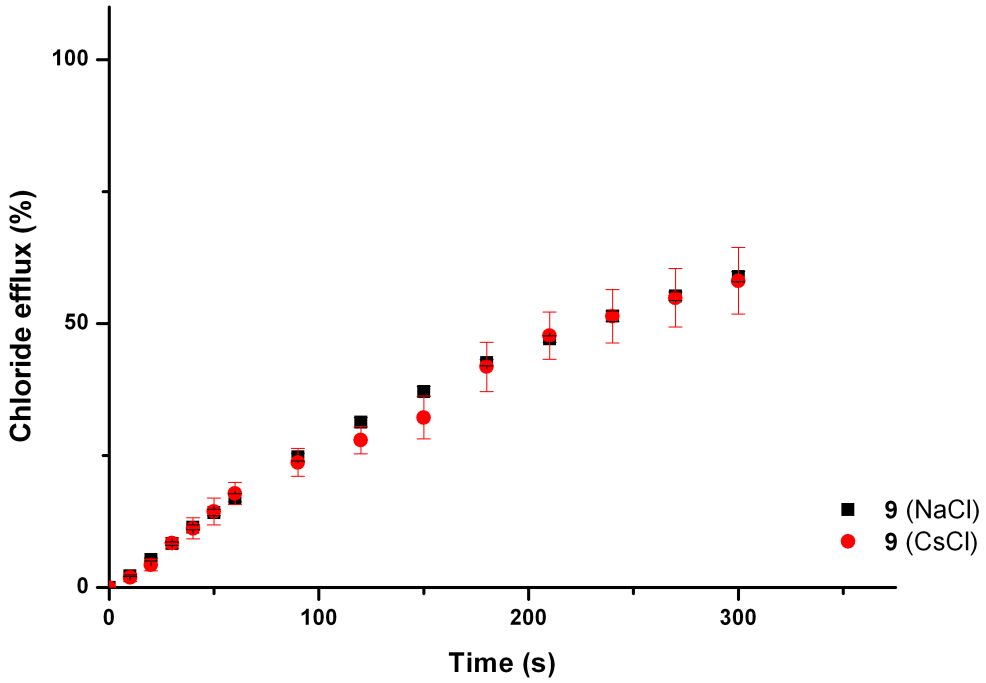

Figure S54: Chloride efflux promoted by a DMSO solution of compound **9** (2mol% carrier to lipid) from unilamellar POPC vesicles loaded with either 488mM NaCl or 488mM CsCl buffered to pH 7.2 with 5mM sodium phosphate salts. The vesicles were dispersed in 488mM $NaNO_3$ buffered to pH 7.2 with 5mM sodium phosphate salts. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials. DMSO was used as a control.

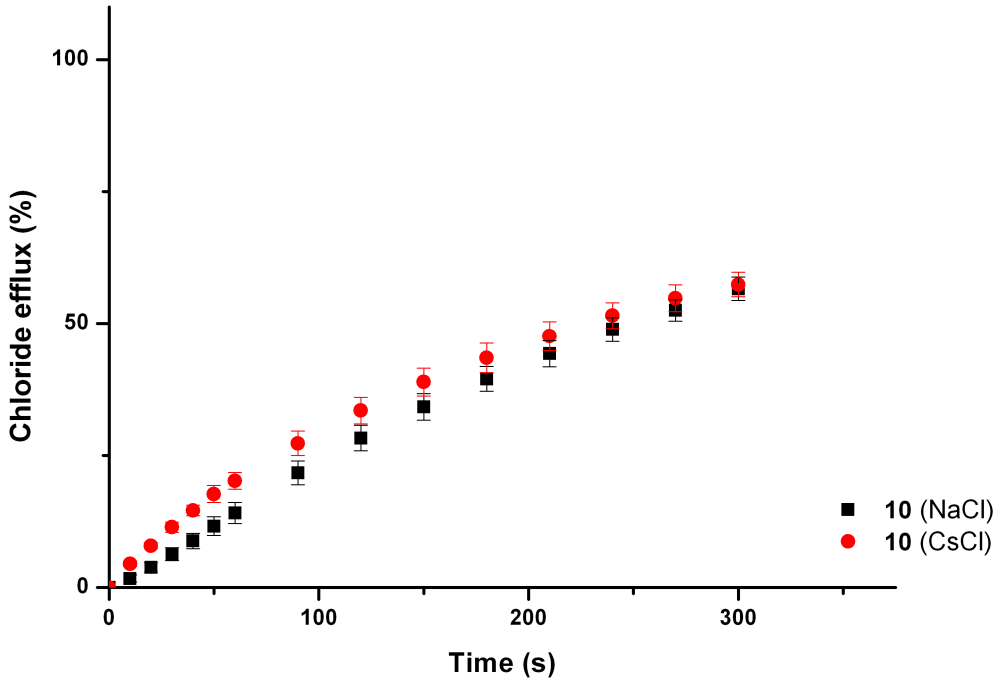

Figure S55: Chloride efflux promoted by a DMSO solution of compound **10** (2mol% carrier to lipid) from unilamellar POPC vesicles loaded with either 488mM NaCl or 488mM CsCl buffered to pH 7.2 with 5mM sodium phosphate salts. The vesicles were dispersed in 488mM $NaNO_3$ buffered to pH 7.2 with 5mM sodium phosphate salts. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials. DMSO was used as a control.

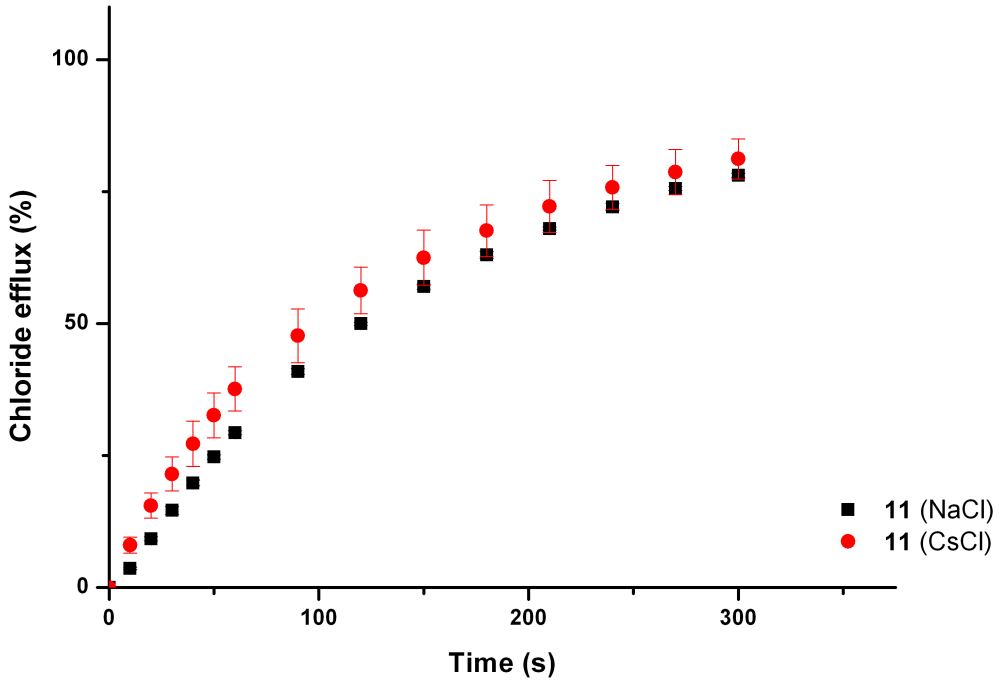

Figure S56: Chloride efflux promoted by a DMSO solution of compound **11** (2mol% carrier to lipid) from unilamellar POPC vesicles loaded with either 488mM NaCl or 488mM CsCl buffered to pH 7.2 with 5mM sodium phosphate salts. The vesicles were dispersed in 488mM $NaNO_3$ buffered to pH 7.2 with 5mM sodium phosphate salts. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials. DMSO was used as a control.

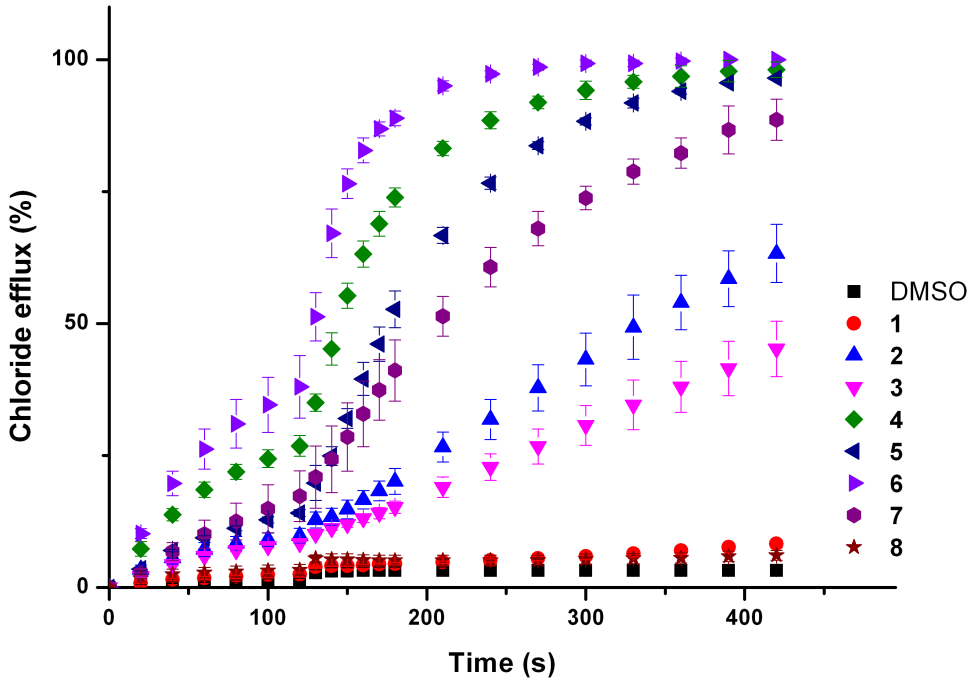

Figure S57: Chloride efflux promoted by a DMSO solution of compounds **1-8** (2mol% carrier to lipid) from unilamellar POPC vesicles loaded with 451mM NaCl buffered to pH 7.2 with 20mM sodium phosphate salts. The vesicles were dispersed in 150mM Na2SO4 buffered to pH 7.2 with 20mM sodium phosphate salts. At t=20s a solution of sodium bicarbonate was added such that the external concentration of bicarbonate was 40mM. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials. DMSO was used as a control.

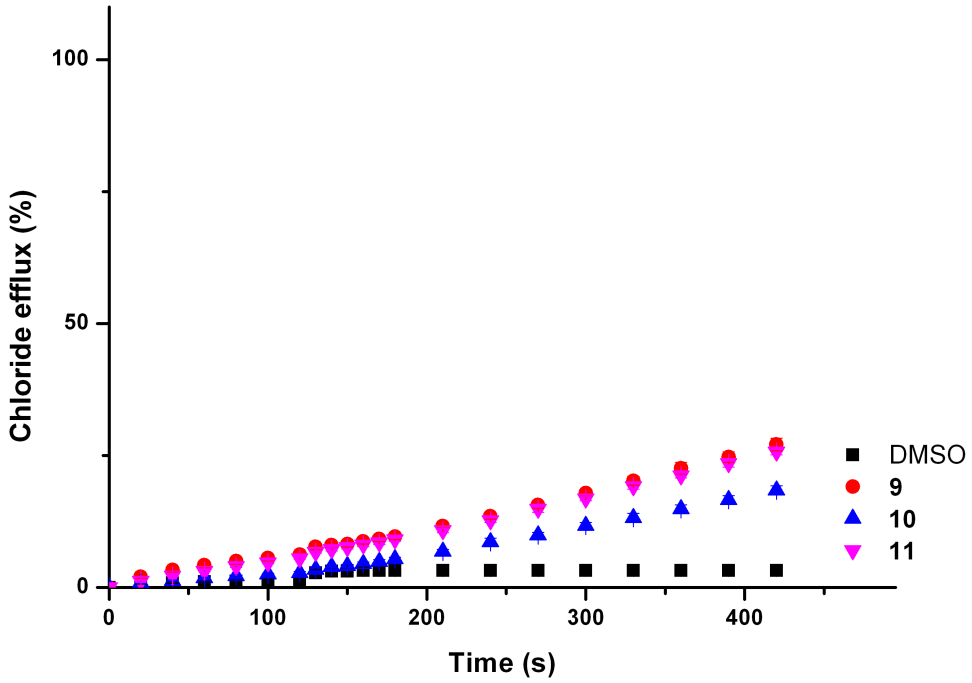

Figure S58: Chloride efflux promoted by a DMSO solution of compounds **9-11** (2mol% carrier to lipid) from unilamellar POPC vesicles loaded with 451mM NaCl buffered to pH 7.2 with 20mM sodium phosphate salts. The vesicles were dispersed in 150mM Na2SO4 buffered to pH 7.2 with 20mM sodium phosphate salts. At t=20s a solution of sodium bicarbonate was added such that the external concentration of bicarbonate was 40mM. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials. DMSO was used as a control.

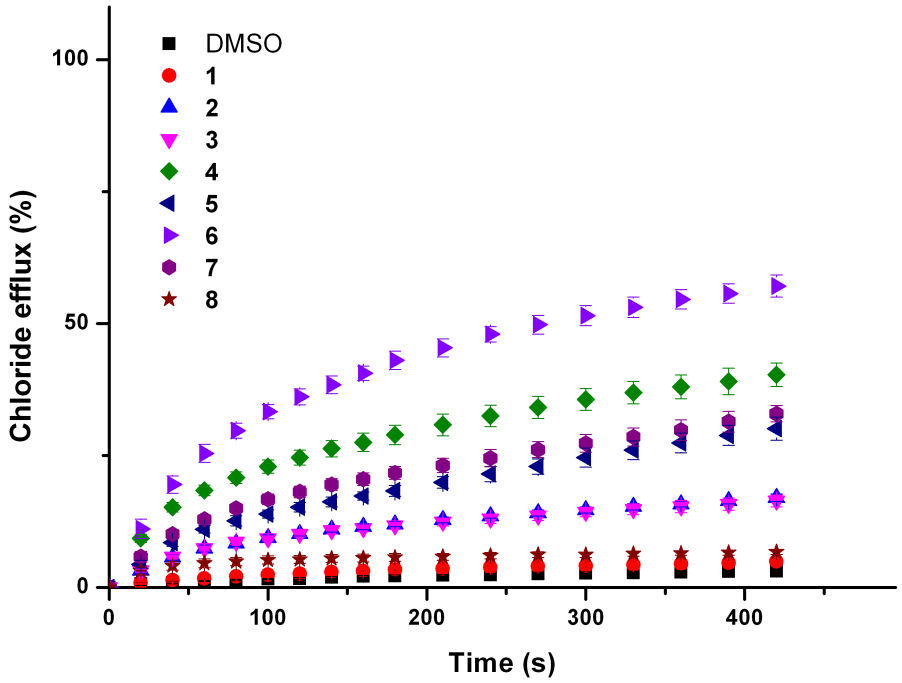

Figure S59: Chloride efflux promoted by a DMSO solution of compounds **1-8** (2mol% carrier to lipid) from unilamellar POPC vesicles loaded with 451mM NaCl buffered to pH 7.2 with 20mM sodium phosphate salts. The vesicles were dispersed in 150mM Na2SO4 buffered to pH 7.2 with 20mM sodium phosphate salts. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials. DMSO was used as a control.

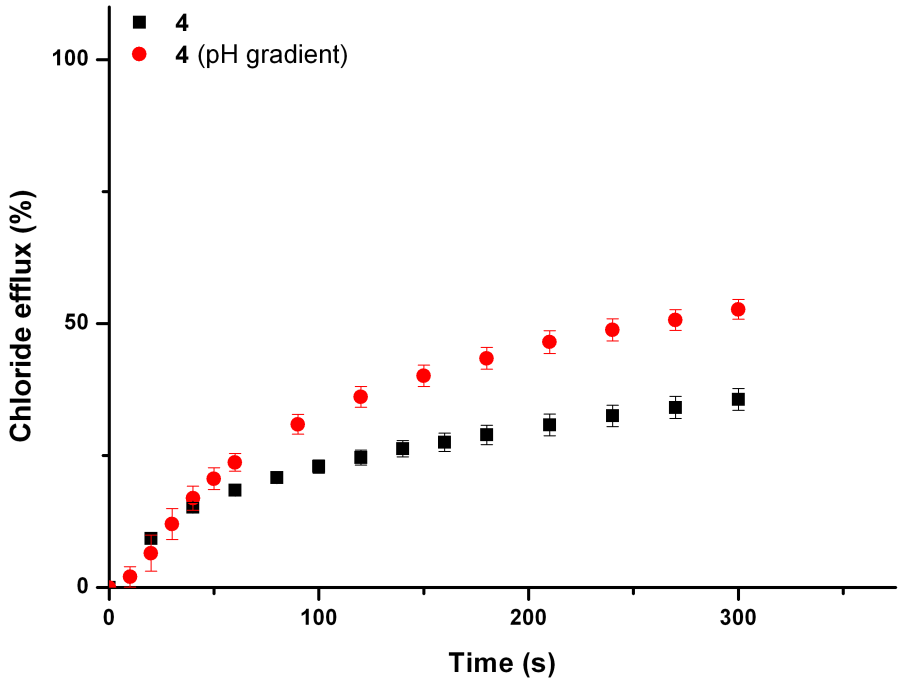

Figure S60: Chloride efflux promoted by a DMSO solution of compound **4** (2mol% carrier to lipid) from unilamellar POPC vesicles loaded with either 451mM NaCl buffered to pH 7.2 with 20mM sodium phosphate salts or 451mM NaCl buffered to pH 4.0 with 20mM sodium citrate salts. The vesicles were dispersed in 150mM Na_2SO_4 buffered to pH 7.2 with 20mM sodium phosphate salts. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials. DMSO was used as a control.

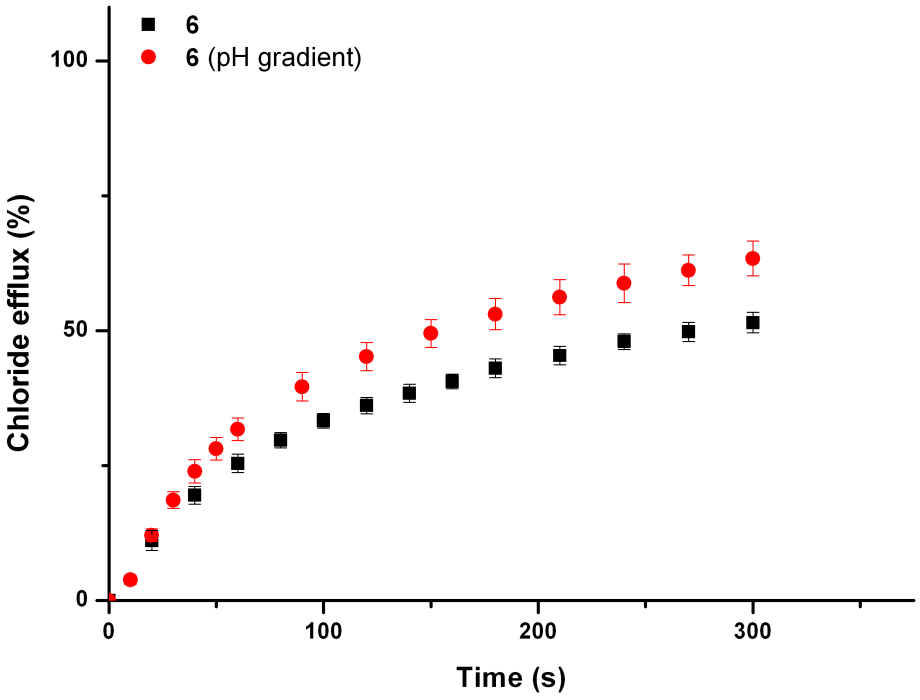

Figure S61: Chloride efflux promoted by a DMSO solution of compound **6** (2mol% carrier to lipid) from unilamellar POPC vesicles loaded with either 451mM NaCl buffered to pH 7.2 with 20mM sodium phosphate salts or 451mM NaCl buffered to pH 4.0 with 20mM sodium citrate salts. The vesicles were dispersed in 150mM Na_2SO_4 buffered to pH 7.2 with 20mM sodium phosphate salts. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials. DMSO was used as a control.

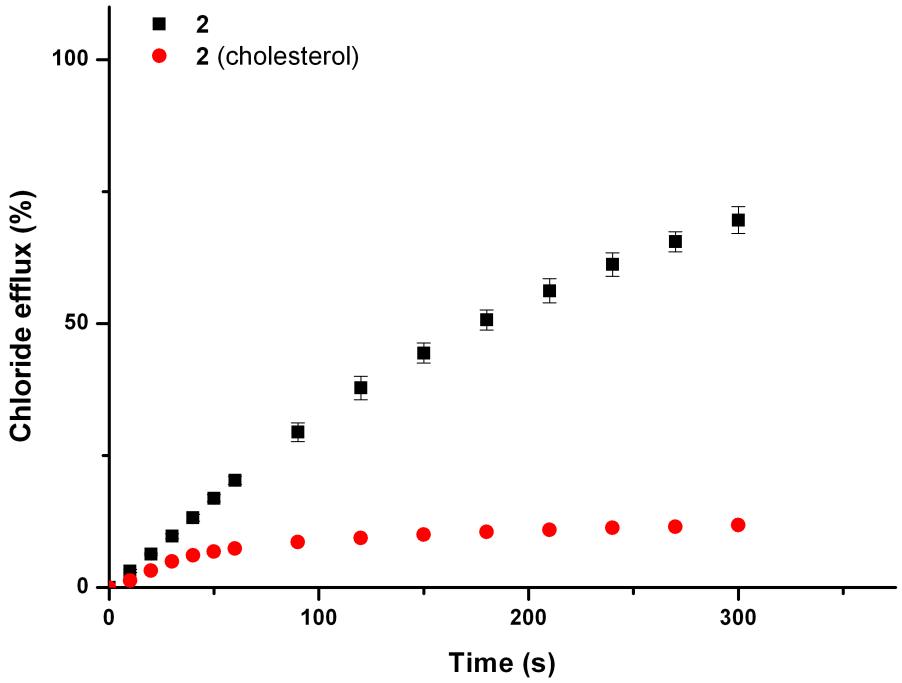

Figure S62: Chloride efflux promoted by a DMSO solution of compound **2** (2mol% carrier to lipid) from unilamellar vesicles comprising of either POPC or POPC/cholesterol (7:3 molar ratio), loaded with 488mM NaCl buffered to pH 7.2 with 5mM sodium phosphate salts. The vesicles were dispersed in 488mM $NaNO_3$ buffered to pH 7.2 with 5mM sodium phosphate salts. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials. DMSO was used as a control.

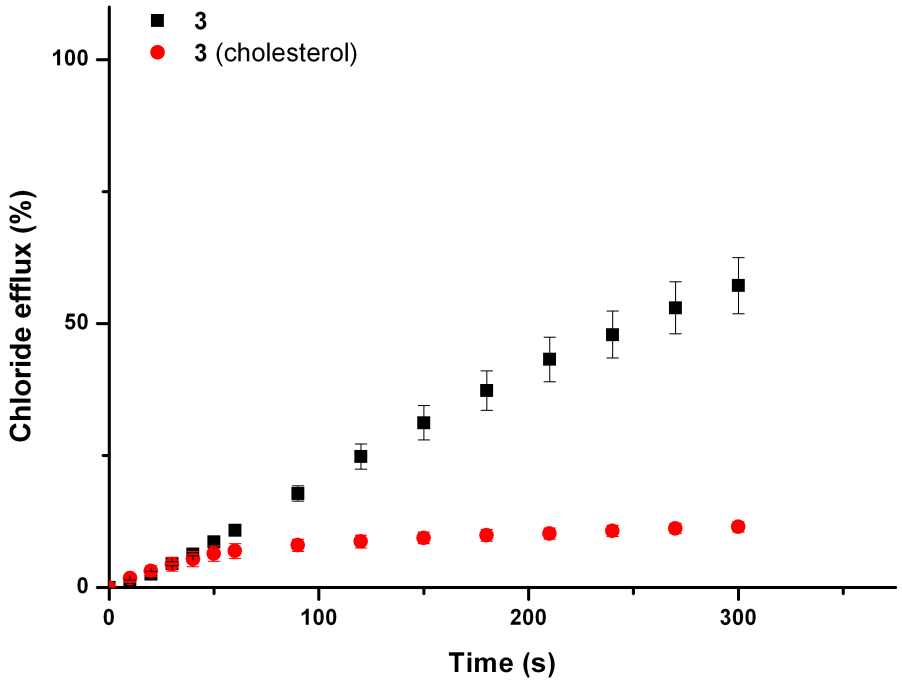

Figure S63: Chloride efflux promoted by a DMSO solution of compound **3** (2mol% carrier to lipid) from unilamellar vesicles comprising of either POPC or POPC/cholesterol (7:3 molar ratio), loaded with 488mM NaCl buffered to pH 7.2 with 5mM sodium phosphate salts. The vesicles were dispersed in 488mM $NaNO_3$ buffered to pH 7.2 with 5mM sodium phosphate salts. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials. DMSO was used as a control.

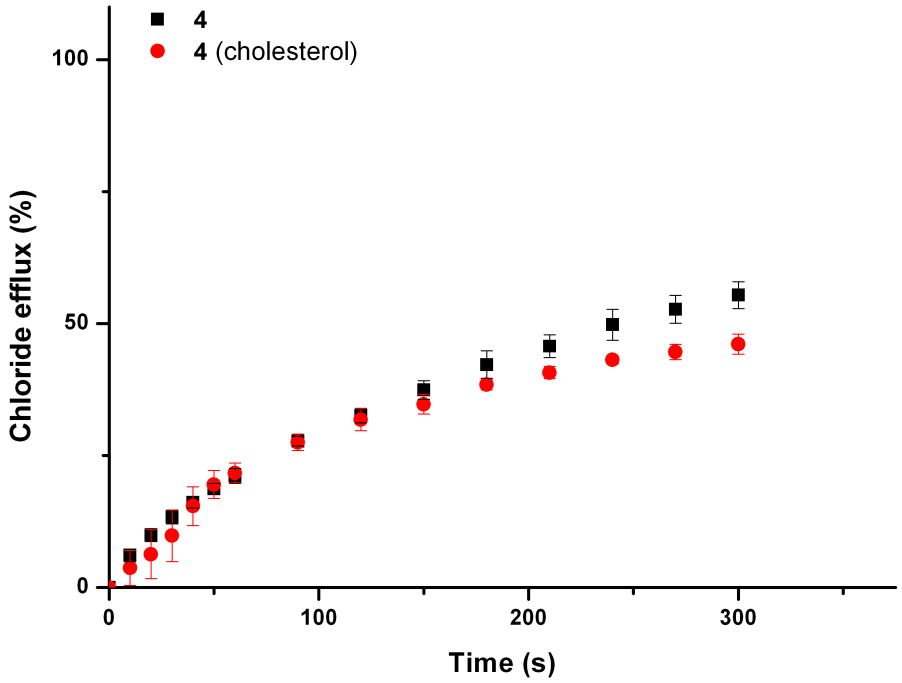

Figure S64: Chloride efflux promoted by a DMSO solution of compound **4** (2mol% carrier to lipid) from unilamellar vesicles comprising of either POPC or POPC/cholesterol (7:3 molar ratio), loaded with 488mM NaCl buffered to pH 7.2 with 5mM sodium phosphate salts. The vesicles were dispersed in 488mM $NaNO_3$ buffered to pH 7.2 with 5mM sodium phosphate salts. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials. DMSO was used as a control.

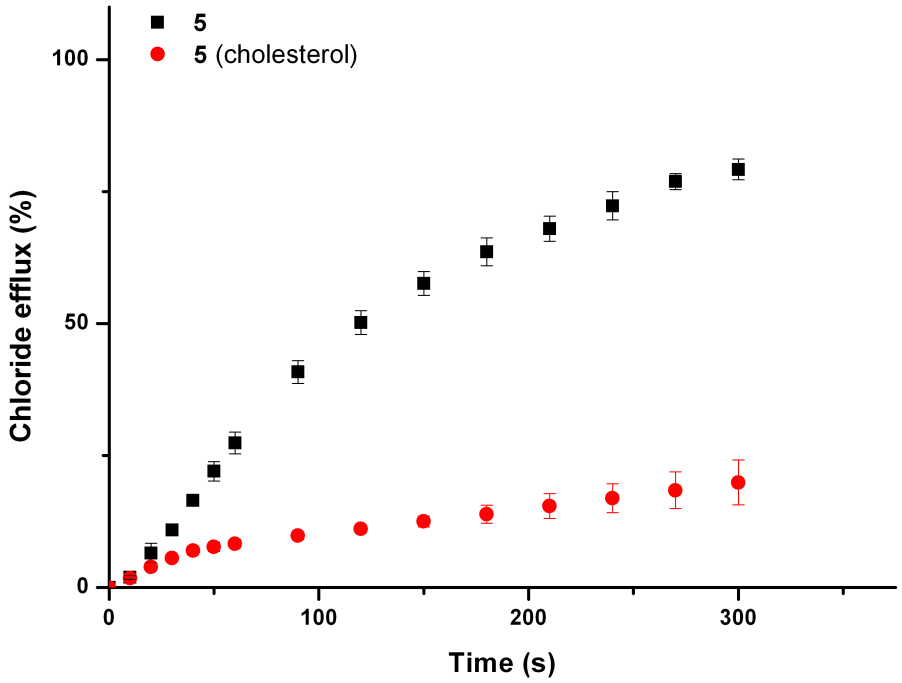

Figure S65: Chloride efflux promoted by a DMSO solution of compound **5** (2mol% carrier to lipid) from unilamellar vesicles comprising of either POPC or POPC/cholesterol (7:3 molar ratio), loaded with 488mM NaCl buffered to pH 7.2 with 5mM sodium phosphate salts. The vesicles were dispersed in 488mM $NaNO_3$ buffered to pH 7.2 with 5mM sodium phosphate salts. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials. DMSO was used as a control.

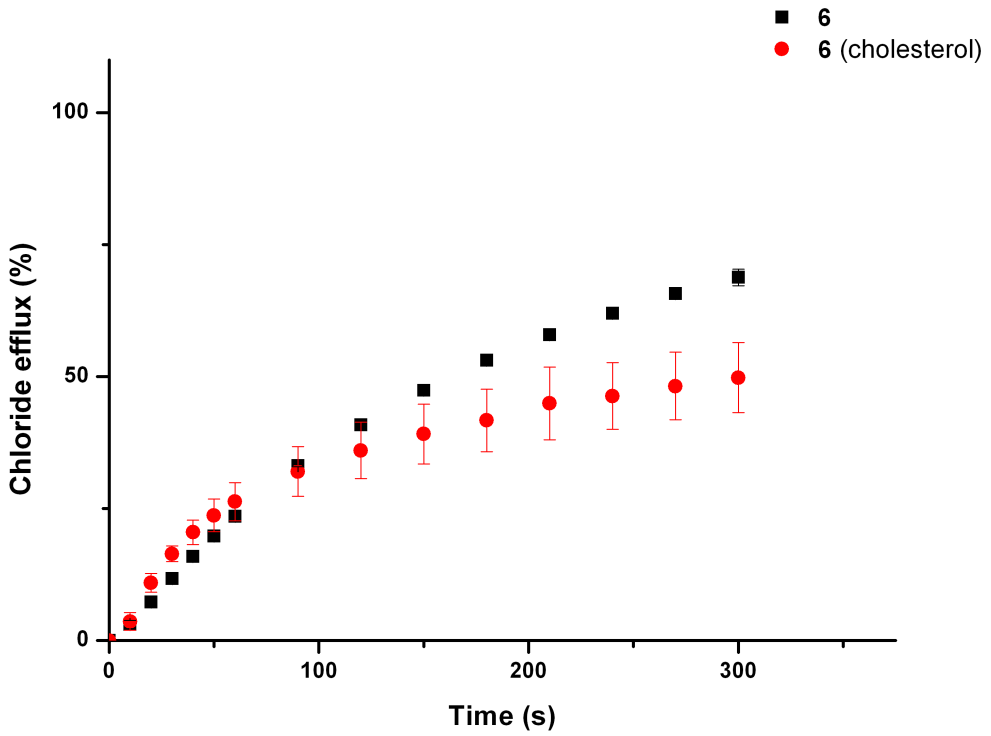

Figure S66: Chloride efflux promoted by a DMSO solution of compound **6** (2mol% carrier to lipid) from unilamellar vesicles comprising of either POPC or POPC/cholesterol (7:3 molar ratio), loaded with 488mM NaCl buffered to pH 7.2 with 5mM sodium phosphate salts. The vesicles were dispersed in 488mM $NaNO_3$ buffered to pH 7.2 with 5mM sodium phosphate salts. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials. DMSO was used as a control.

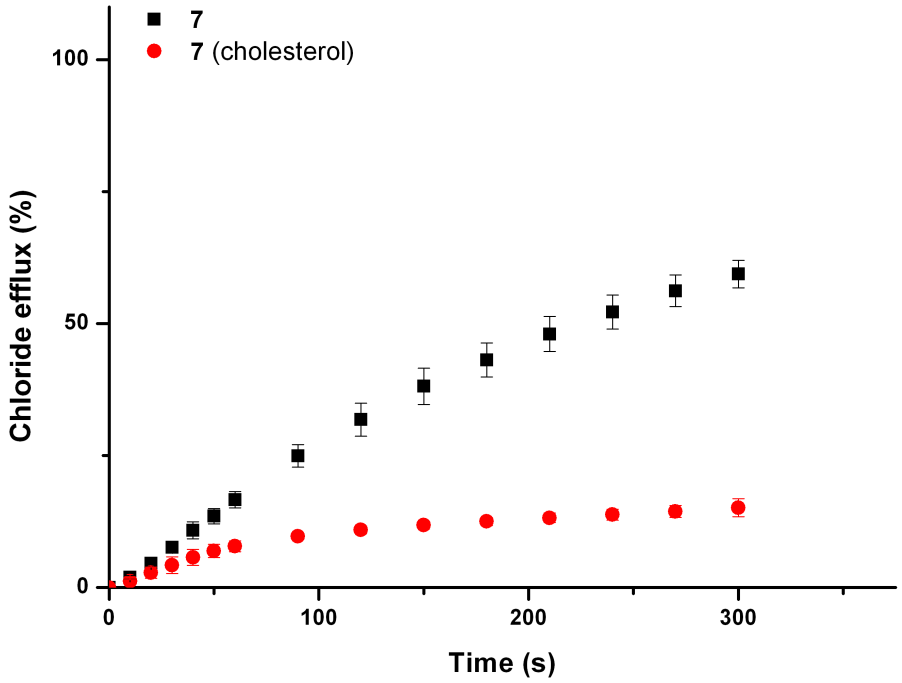

Figure S67: Chloride efflux promoted by a DMSO solution of compound **7** (2mol% carrier to lipid) from unilamellar vesicles comprising of either POPC or POPC/cholesterol (7:3 molar ratio), loaded with 488mM NaCl buffered to pH 7.2 with 5mM sodium phosphate salts. The vesicles were dispersed in 488mM $NaNO_3$ buffered to pH 7.2 with 5mM sodium phosphate salts. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials. DMSO was used as a control.

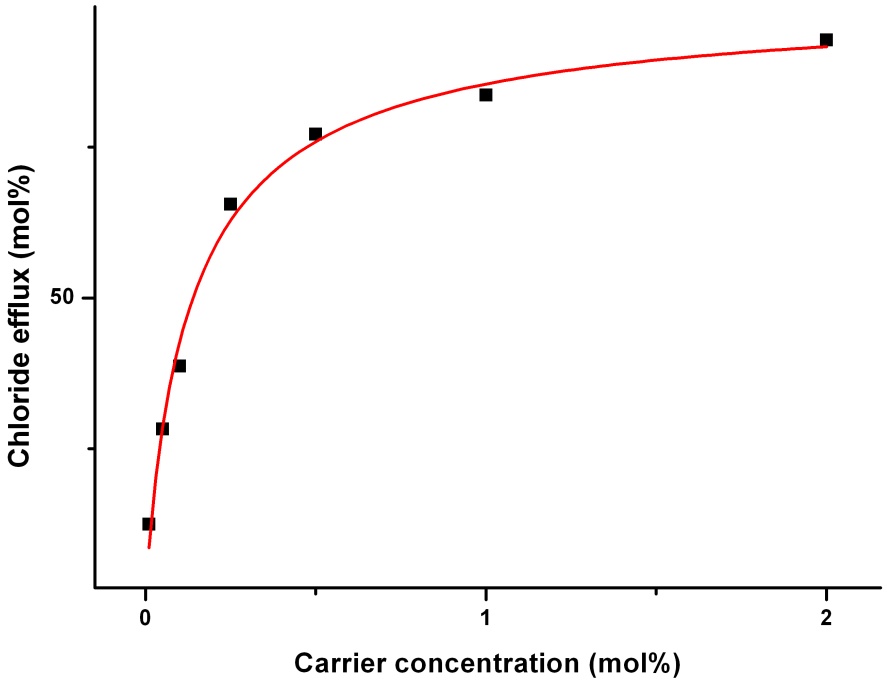

Figure S68: Hill plot of chloride efflux promoted by varying concentrations of compound **2** from unilamellar POPC vesicles loaded with 488mM NaCl buffered to pH 7.2 with 5mM sodium phosphate salts. The vesicles were dispersed in 488mM $NaNO_3$ buffered at pH 7.2 with 5mM sodium phosphate salts. Each point represents an average of 3 trials.

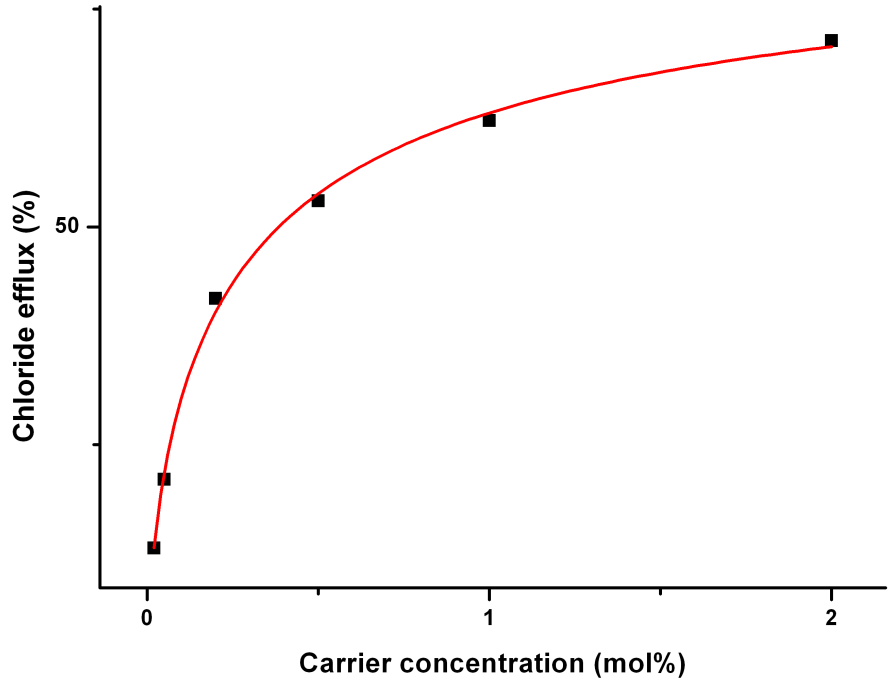

Figure S69: Hill plot of chloride efflux promoted by varying concentrations of compound **3** from unilamellar POPC vesicles loaded with 488mM NaCl buffered to pH 7.2 with 5mM sodium phosphate salts. The vesicles were dispersed in 488mM $NaNO_3$ buffered at pH 7.2 with 5mM sodium phosphate salts. Each point represents an average of 3 trials.

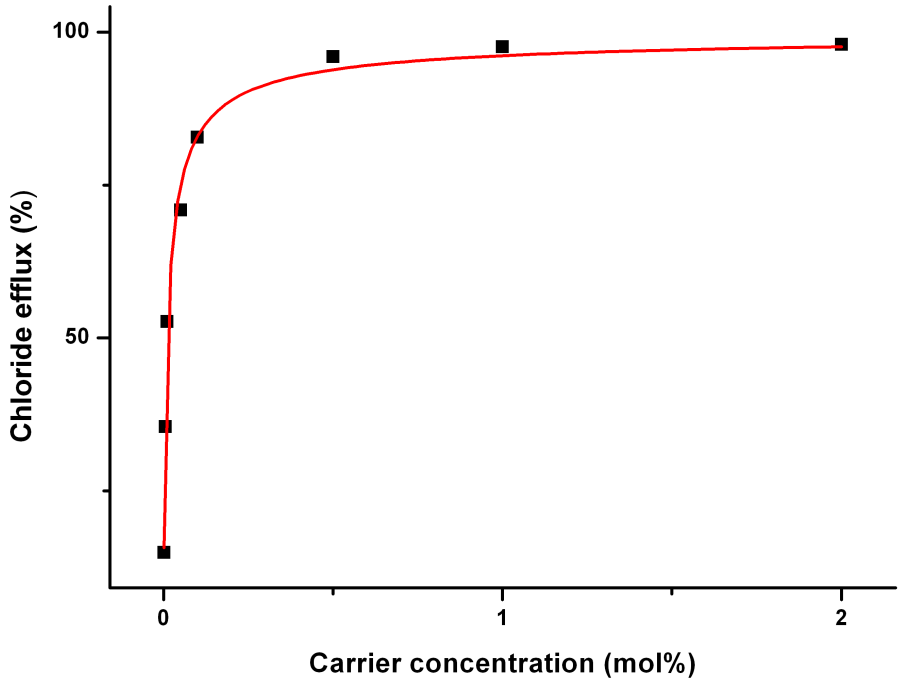

Figure S70: Hill plot of chloride efflux promoted by varying concentrations of compound **4** from unilamellar POPC vesicles loaded with 488mM NaCl buffered to pH 7.2 with 5mM sodium phosphate salts. The vesicles were dispersed in 488mM $NaNO_3$ buffered at pH 7.2 with 5mM sodium phosphate salts. Each point represents an average of 3 trials.

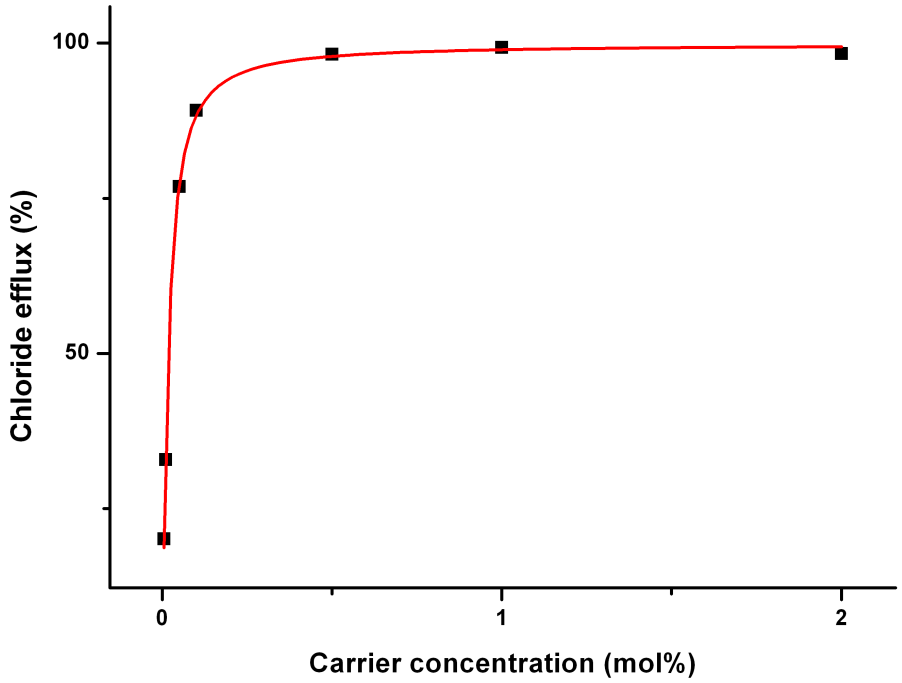

Figure S71: Hill plot of chloride efflux promoted by varying concentrations of compound **5** from unilamellar POPC vesicles loaded with 488mM NaCl buffered to pH 7.2 with 5mM sodium phosphate salts. The vesicles were dispersed in 488mM $NaNO_3$ buffered at pH 7.2 with 5mM sodium phosphate salts. Each point represents an average of 3 trials.

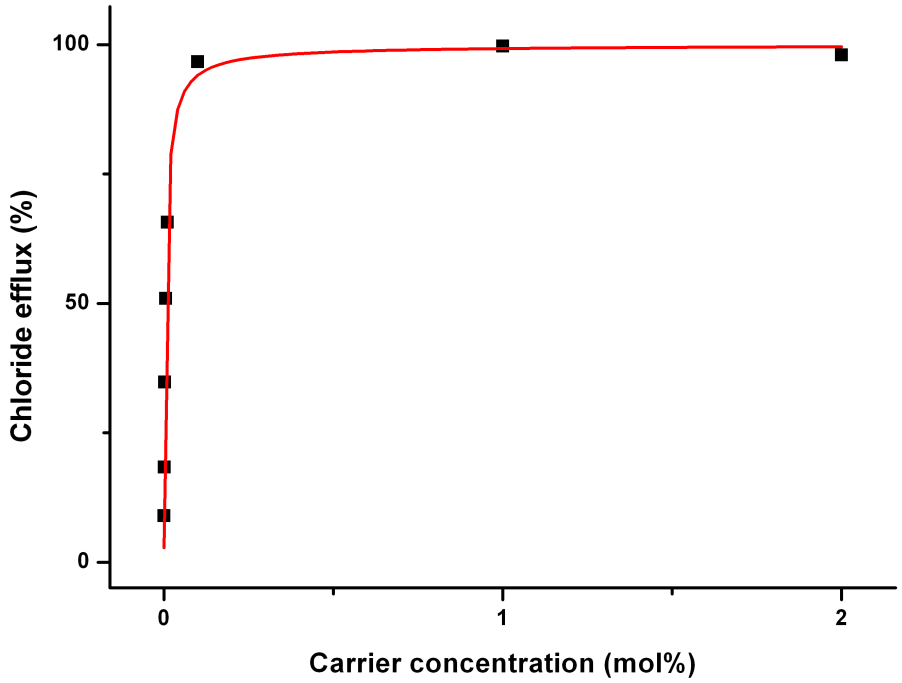

Figure S72: Hill plot of chloride efflux promoted by varying concentrations of compound **6** from unilamellar POPC vesicles loaded with 488mM NaCl buffered to pH 7.2 with 5mM sodium phosphate salts. The vesicles were dispersed in 488mM $NaNO_3$ buffered at pH 7.2 with 5mM sodium phosphate salts. Each point represents an average of 3 trials.

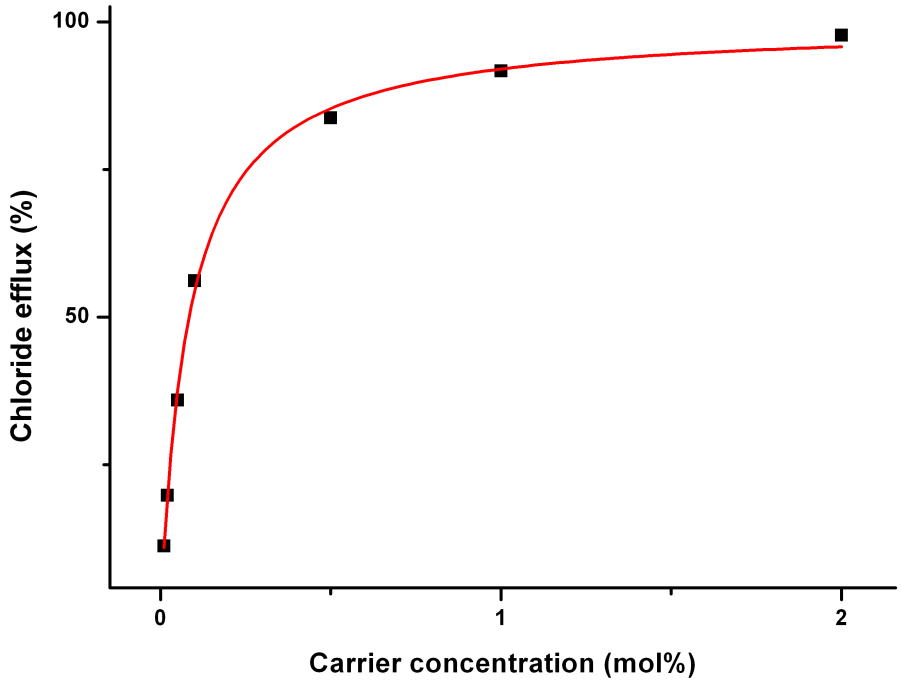

Figure S73: Hill plot of chloride efflux promoted by varying concentrations of compound **7** from unilamellar POPC vesicles loaded with 488mM NaCl buffered to pH 7.2 with 5mM sodium phosphate salts. The vesicles were dispersed in 488mM $NaNO_3$ buffered at pH 7.2 with 5mM sodium phosphate salts. Each point represents an average of 3 trials.

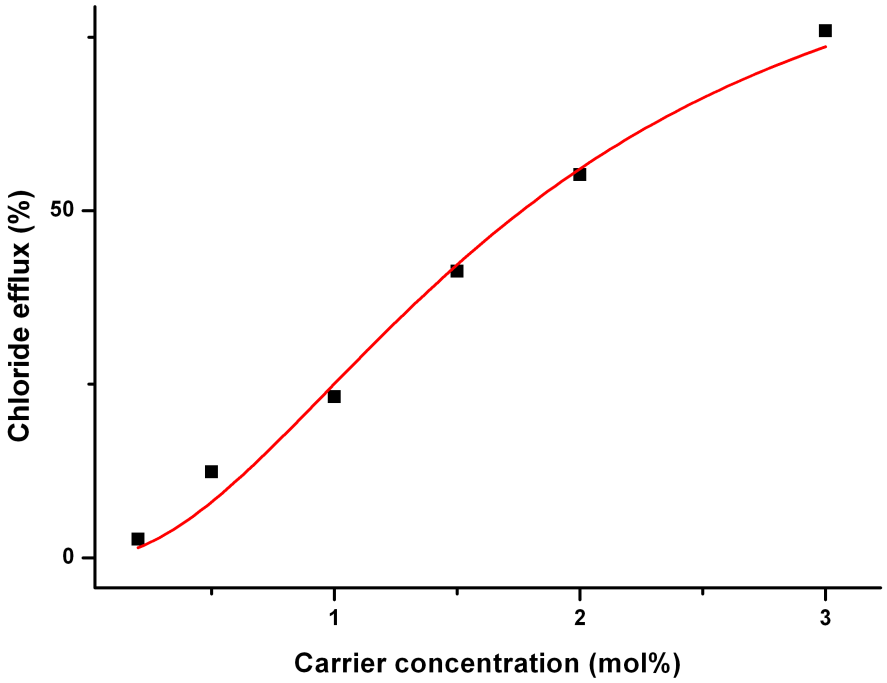

Figure S74: Hill plot of chloride efflux promoted by varying concentrations of compound **9** from unilamellar POPC vesicles loaded with 488mM NaCl buffered to pH 7.2 with 5mM sodium phosphate salts. The vesicles were dispersed in 488mM $NaNO_3$ buffered at pH 7.2 with 5mM sodium phosphate salts. Each point represents an average of 3 trials.

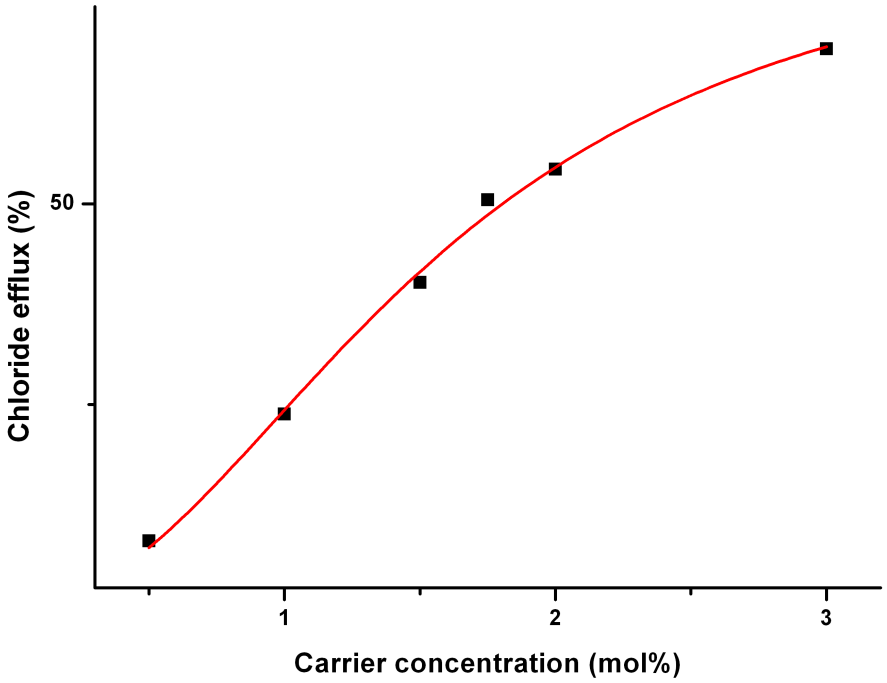

Figure S75: Hill plot of chloride efflux promoted by varying concentrations of compound **10** from unilamellar POPC vesicles loaded with 488mM NaCl buffered to pH 7.2 with 5mM sodium phosphate salts. The vesicles were dispersed in 488mM $NaNO_3$ buffered at pH 7.2 with 5mM sodium phosphate salts. Each point represents an average of 3 trials.

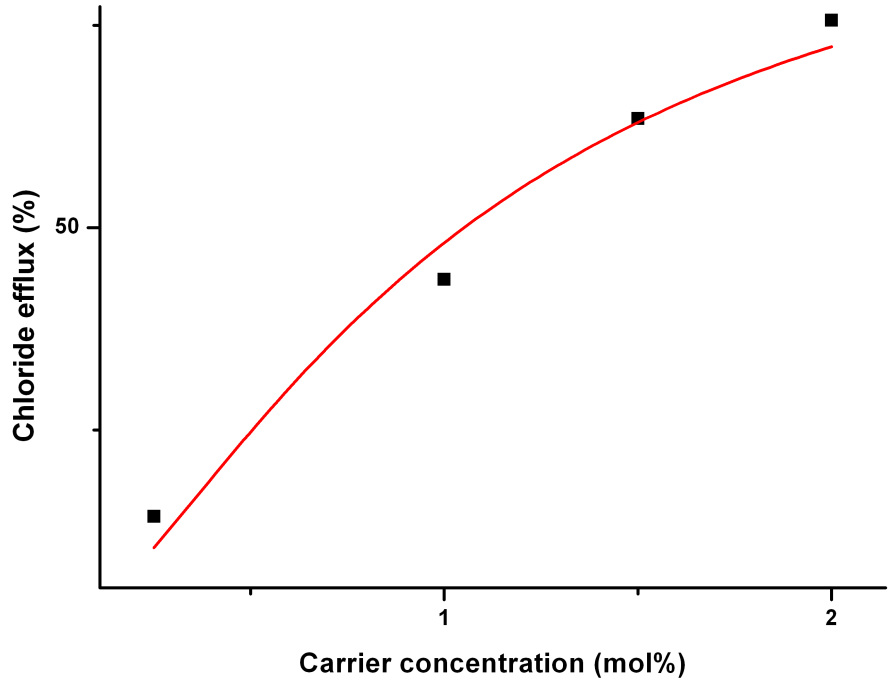

Figure S76: Hill plot of chloride efflux promoted by varying concentrations of compound **11** from unilamellar POPC vesicles loaded with 488mM NaCl buffered to pH 7.2 with 5mM sodium phosphate salts. The vesicles were dispersed in 488mM $NaNO_3$ buffered at pH 7.2 with 5mM sodium phosphate salts. Each point represents an average of 3 trials.

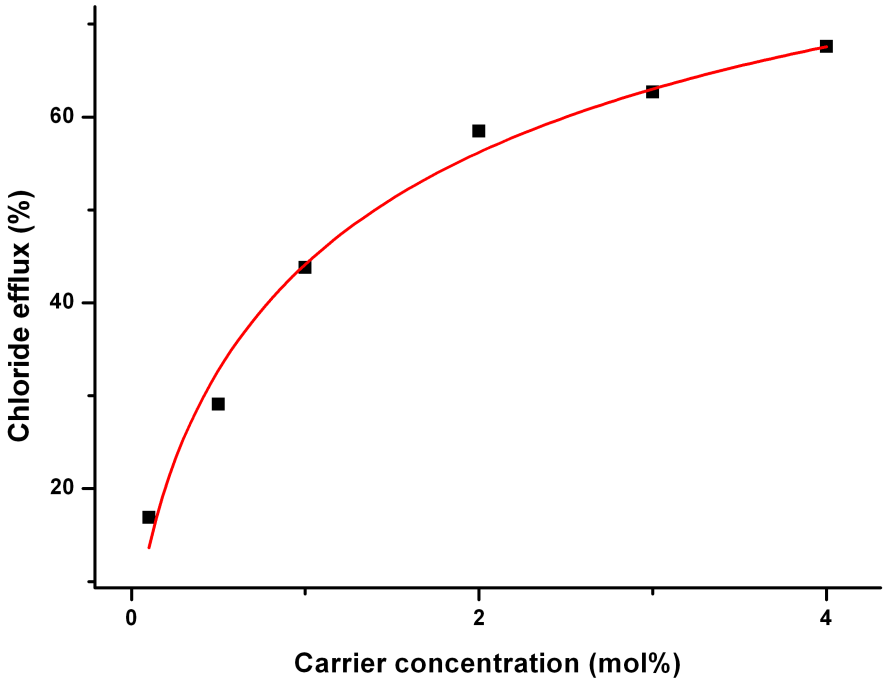

Figure S77: Hill plot of chloride efflux promoted varying concentrations of compound **2** from unilamellar POPC vesicles loaded with 451mM NaCl buffered to pH 7.2 with 20mM sodium phosphate salts upon addition of a bicarbonate 'pulse', bringing the external concentration of bicarbonate to 40mM. The vesicles were dispersed in 150mM Na_2SO_4 buffered to pH 7.2 with 20mM sodium phosphate salts. Each point represents an average of 3 trials.

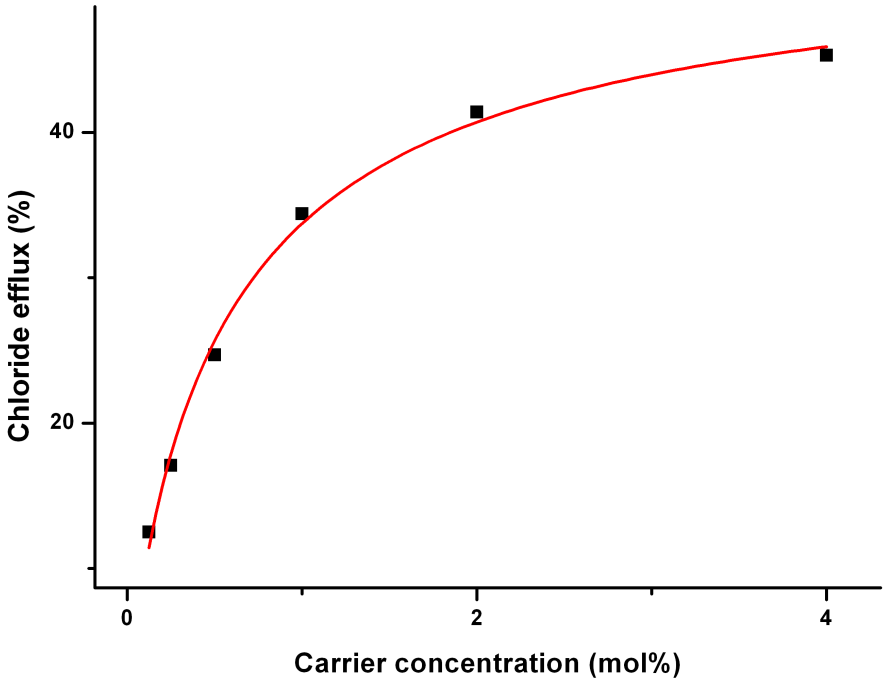

Figure S78: Hill plot of chloride efflux promoted varying concentrations of compound **3** from unilamellar POPC vesicles loaded with 451mM NaCl buffered to pH 7.2 with 20mM sodium phosphate salts upon addition of a bicarbonate 'pulse', bringing the external concentration of bicarbonate to 40mM. The vesicles were dispersed in 150mM Na_2SO_4 buffered to pH 7.2 with 20mM sodium phosphate salts. Each point represents an average of 3 trials.

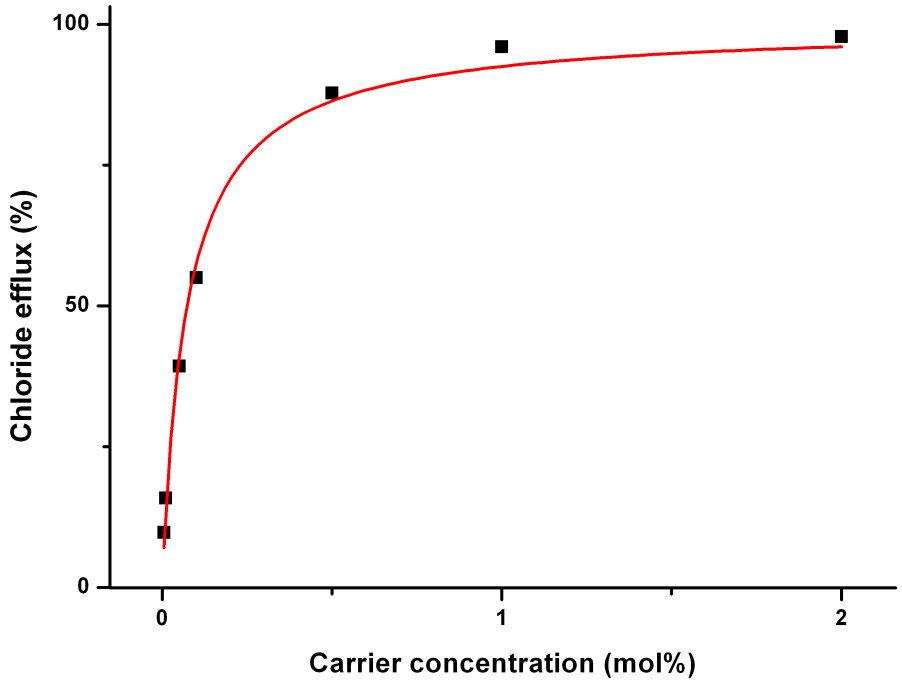

Figure S79: Hill plot of chloride efflux promoted varying concentrations of compound **4** from unilamellar POPC vesicles loaded with 451mM NaCl buffered to pH 7.2 with 20mM sodium phosphate salts upon addition of a bicarbonate 'pulse', bringing the external concentration of bicarbonate to 40mM. The vesicles were dispersed in 150mM Na_2SO_4 buffered to pH 7.2 with 20mM sodium phosphate salts. Each point represents an average of 3 trials.

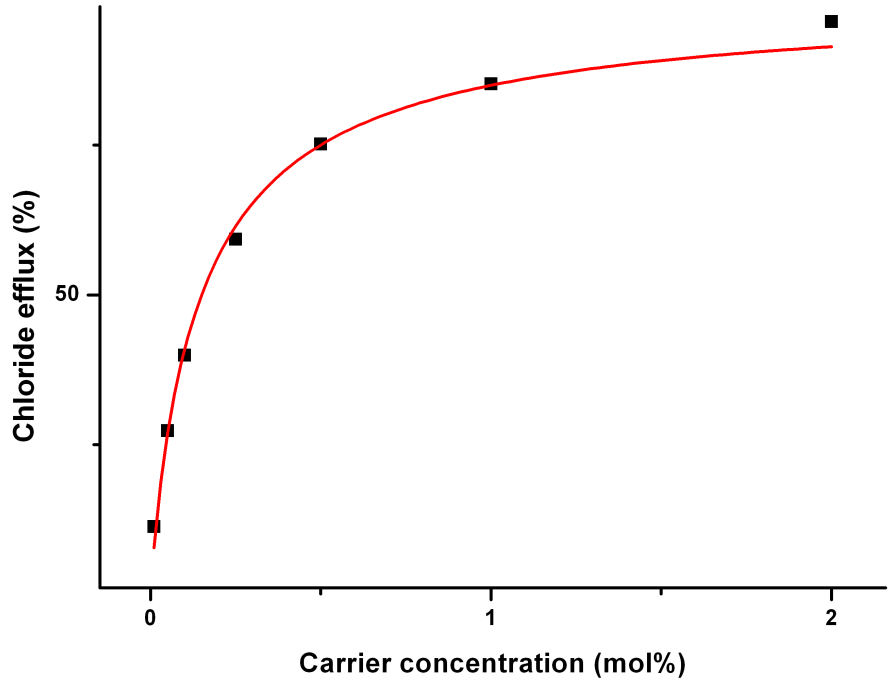

Figure S80: Hill plot of chloride efflux promoted varying concentrations of compound **5** from unilamellar POPC vesicles loaded with 451mM NaCl buffered to pH 7.2 with 20mM sodium phosphate salts upon addition of a bicarbonate 'pulse', bringing the external concentration of bicarbonate to 40mM. The vesicles were dispersed in 150mM Na_2SO_4 buffered to pH 7.2 with 20mM sodium phosphate salts. Each point represents an average of 3 trials.

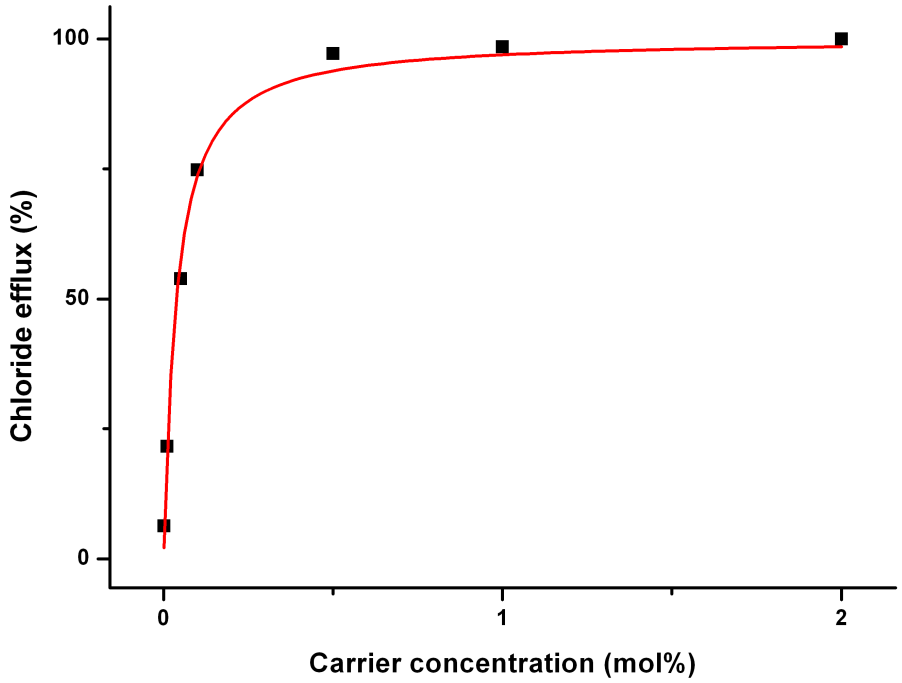

Figure S81: Hill plot of chloride efflux promoted varying concentrations of compound **6** from unilamellar POPC vesicles loaded with 451mM NaCl buffered to pH 7.2 with 20mM sodium phosphate salts upon addition of a bicarbonate 'pulse', bringing the external concentration of bicarbonate to 40mM. The vesicles were dispersed in 150mM Na_2SO_4 buffered to pH 7.2 with 20mM sodium phosphate salts. Each point represents an average of 3 trials.

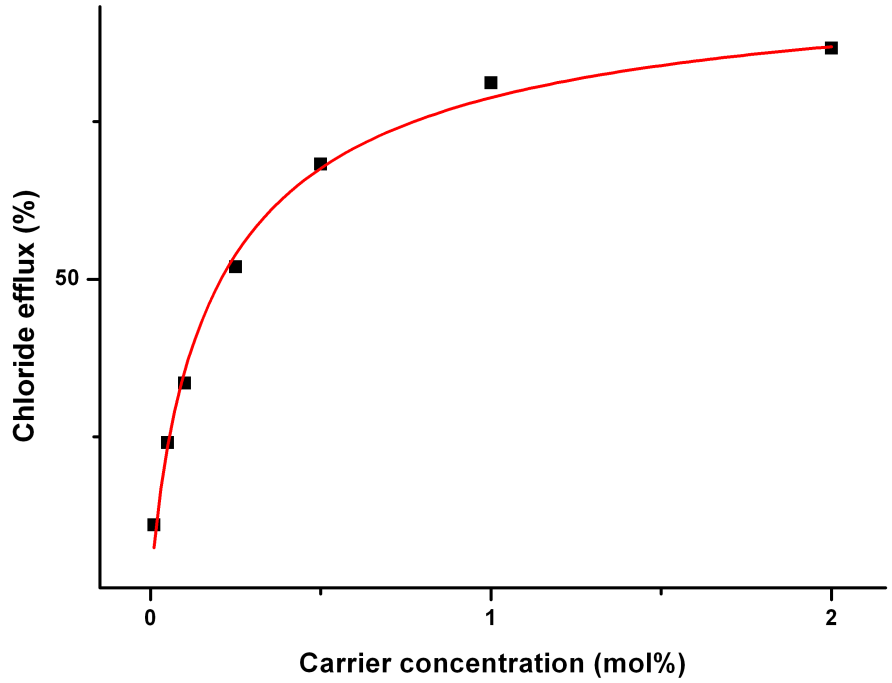

Figure S82: Hill plot of chloride efflux promoted varying concentrations of compound **7** from unilamellar POPC vesicles loaded with 451mM NaCl buffered to pH 7.2 with 20mM sodium phosphate salts upon addition of a bicarbonate 'pulse', bringing the external concentration of bicarbonate to 40mM. The vesicles were dispersed in 150mM Na_2SO_4 buffered to pH 7.2 with 20mM sodium phosphate salts. Each point represents an average of 3 trials.

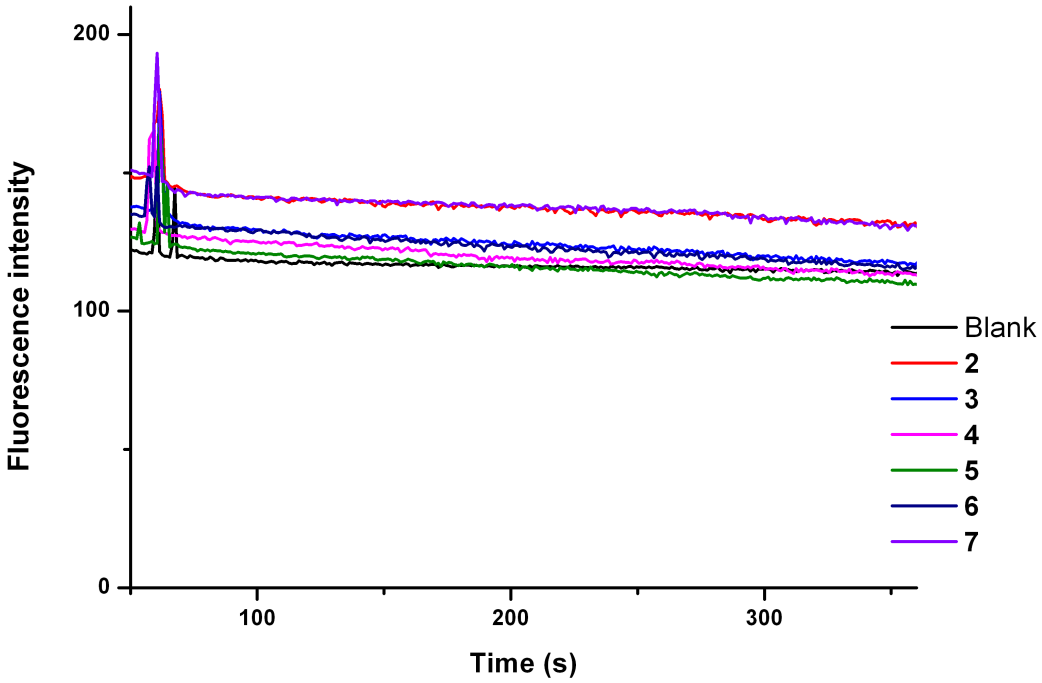

Figure S83: Lucigenin fluorescence intensity of unilamellar POPC vesicles containing 100mM sodium chloride and 2mM lucigenin dye buffered to pH 7.2 with 20mM sodium phosphate salts upon addition of compounds **2**-**7**. Vesicles were suspended in a solution containing 100mM sodium chloride buffered to pH 7.2 with 20mM sodium phosphate salts. A sulphate 'pulse' was added at t=30s such that the external concentration of sulphate was 40mM. Compounds (2mol%) were added as solutions in methanol at t=60s. Experiments were repeated in triplicate and all traces presented are the average of three trials.

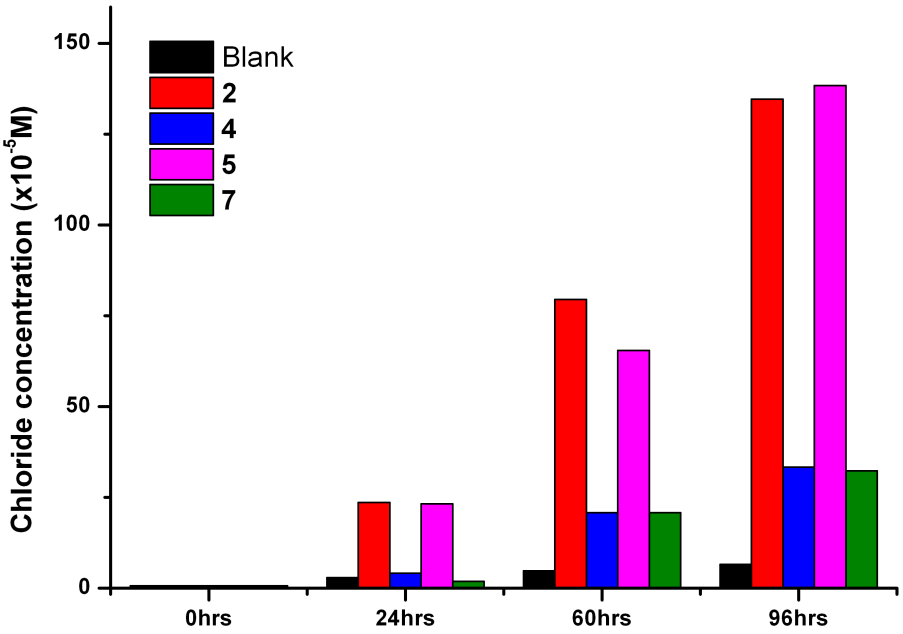

Figure 84: Chloride concentration in the aqueous receiving phase for a series of U-tube experiments for compounds **2**, **4**, **5** and **7**. The source phase was loaded with sodium chloride (488mM buffered to pH 7.2 with 5mM sodium phosphate salts) and the receiving phase was loaded with sodium nitrate (488mM buffered to pH 7.2 with sodium phosphate salts). The carrier (1mM) was dissolved in a nitrobenzene organic phase.

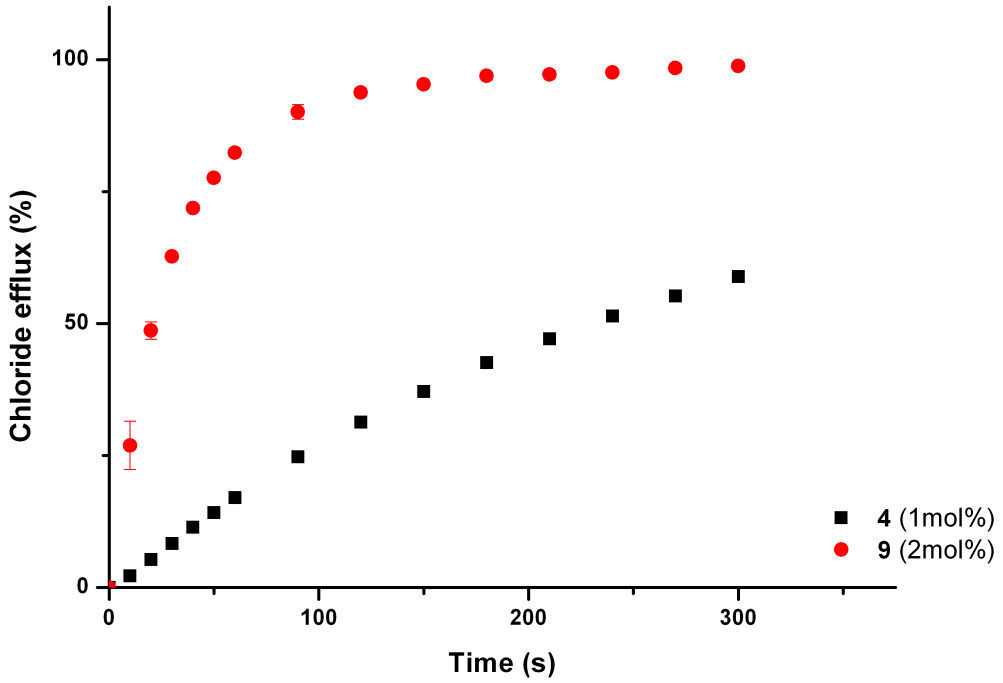

Figure S85: Chloride efflux promoted by DMSO solutions of **4** (1mol% carrier to lipid) and **9** (2mol% carrier to lipid) from unilamellar POPC vesicles loaded with 488mM NaCl buffered to pH 7.2 with 5mM sodium phosphate salts. The vesicles were dispersed in 488mM $NaNO_3$ buffered to pH 7.2 with 5mM sodium phosphate salts. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials

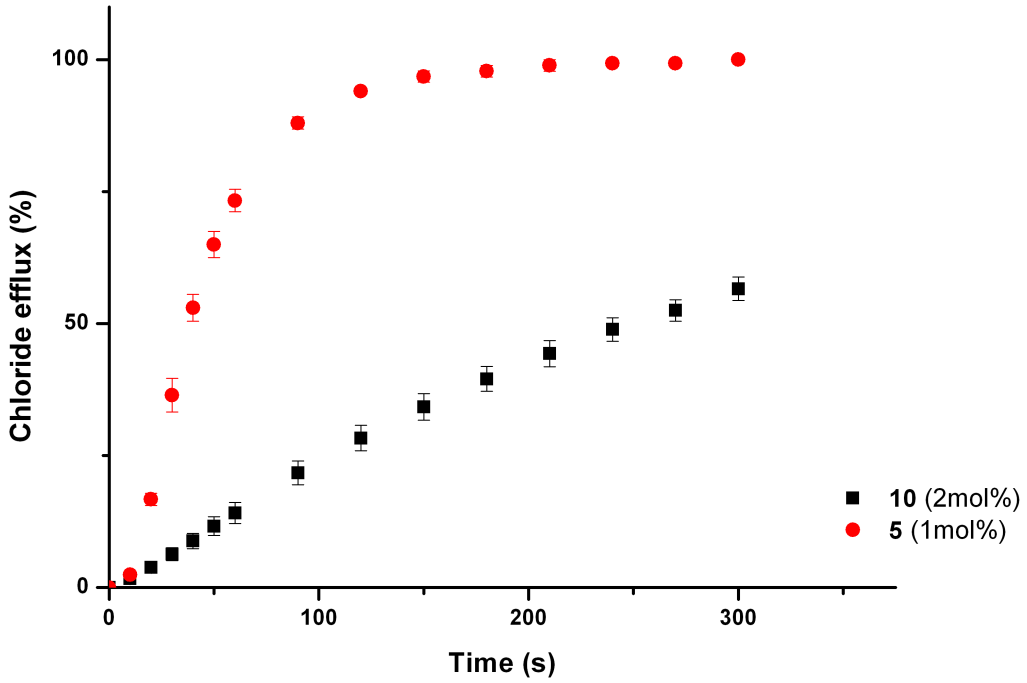

Figure S86: Chloride efflux promoted by DMSO solutions of **5** (1mol% carrier to lipid) and **10** (2mol% carrier to lipid) from unilamellar POPC vesicles loaded with 488mM NaCl buffered to pH 7.2 with 5mM sodium phosphate salts. The vesicles were dispersed in 488mM $NaNO_3$ buffered to pH 7.2 with 5mM sodium phosphate salts. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials

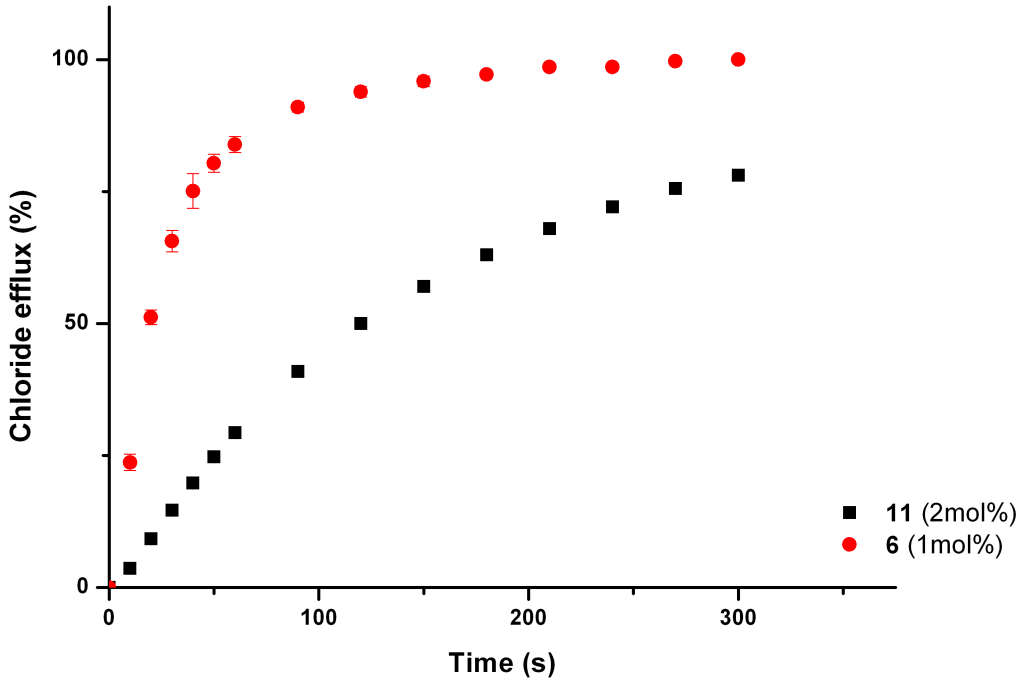

Figure S87: Chloride efflux promoted by DMSO solutions of **6** (1mol% carrier to lipid) and **11** (2mol% carrier to lipid) from unilamellar POPC vesicles loaded with 488mM NaCl buffered to pH 7.2 with 5mM sodium phosphate salts. The vesicles were dispersed in 488mM $NaNO_3$ buffered to pH 7.2 with 5mM sodium phosphate salts. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials

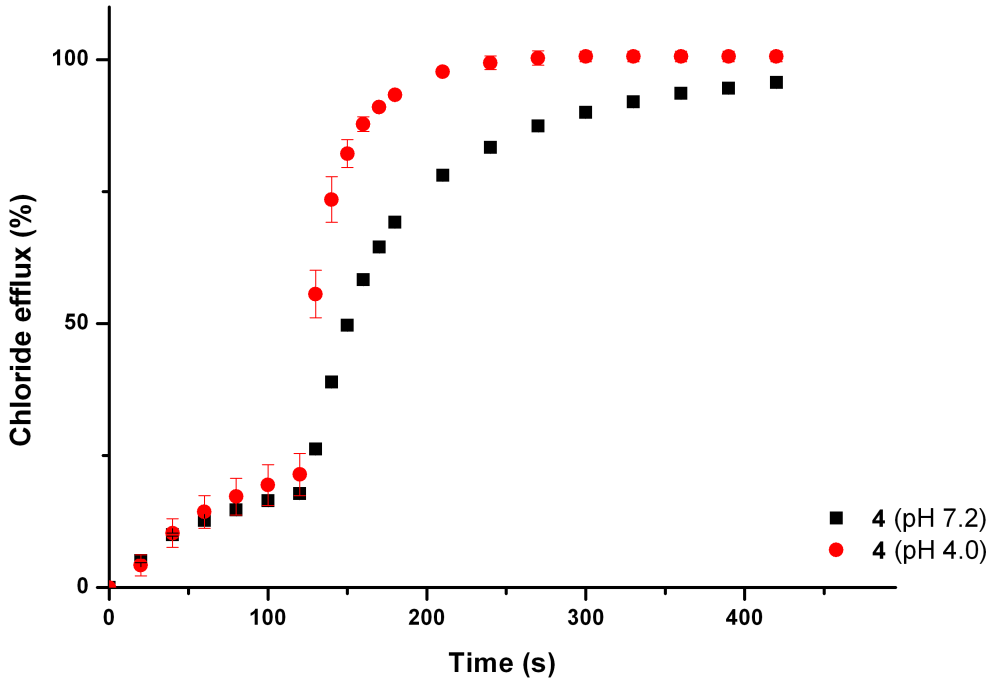

Figure S88: Chloride efflux promoted by a DMSO solution of compound **4** (2mol% carrier to lipid) from unilamellar POPC vesicles loaded with either; i) 451mM NaCl buffered to pH 7.2 with 20mM sodium phosphate salts and dispersed in 150mM Na_2SO_4 buffered to pH 7.2 with 20mM sodium phosphate salts, or ii) 451mM NaCl buffered to pH 4.0 with 20mM sodium citrate salts and dispersed in150mM Na_2SO_4 buffered to pH 4.0 with 20mM sodium phosphate salts. At t=120s a solution of sodium maleate was added such that the external concentration of maleate was 20mM. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials. DMSO was used as a control.

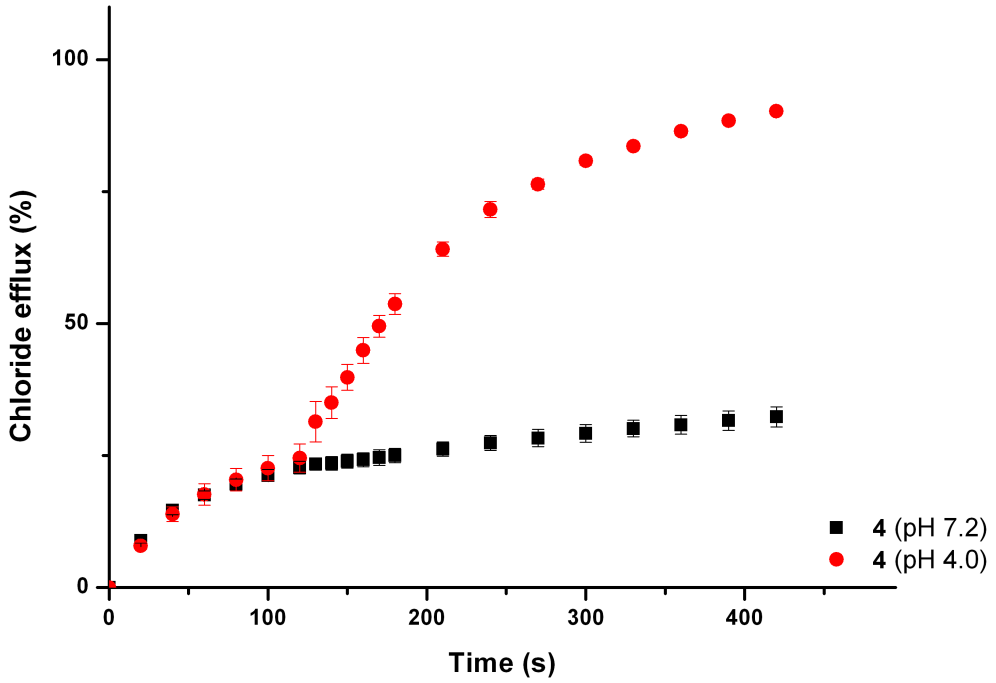

Figure S89: Chloride efflux promoted by a DMSO solution of compound **4** (2mol% carrier to lipid) from unilamellar POPC vesicles loaded with either; i) 451mM NaCl buffered to pH 7.2 with 20mM sodium phosphate salts and dispersed in 150mM Na_2SO_4 buffered to pH 7.2 with 20mM sodium phosphate salts, or ii) 451mM NaCl buffered to pH 4.0 with 20mM sodium citrate salts and dispersed in150mM Na_2SO_4 buffered to pH 4.0 with 20mM sodium phosphate salts. At t=120s a solution of sodium fumarate was added such that the external concentration of fumarate was 20mM. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials. DMSO was used as a control.

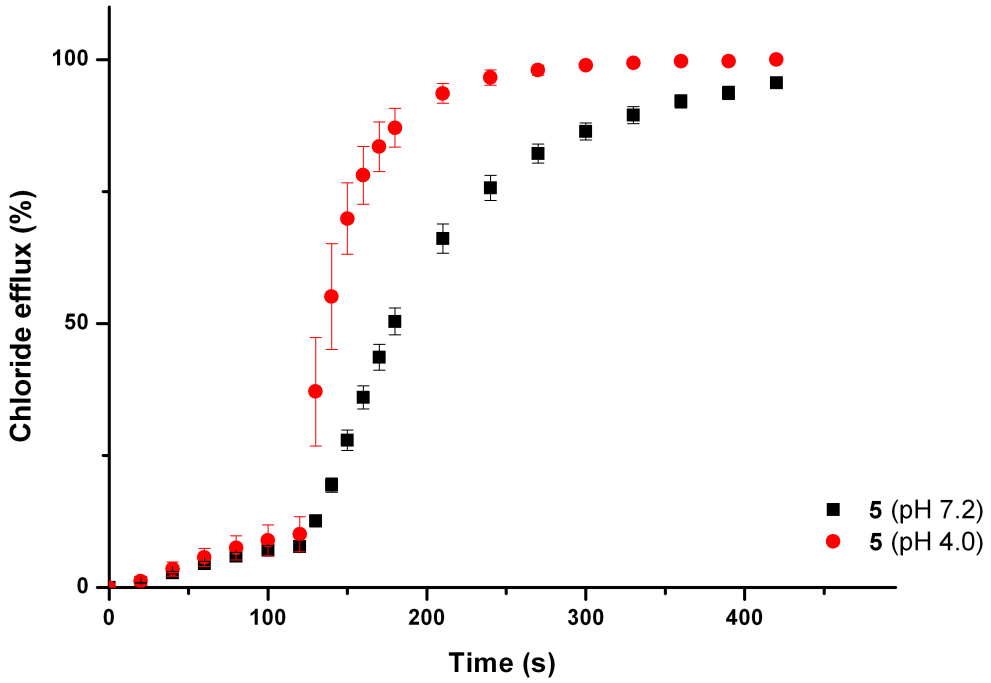

Figure S90: Chloride efflux promoted by a DMSO solution of compound **5** (2mol% carrier to lipid) from unilamellar POPC vesicles loaded with either; i) 451mM NaCl buffered to pH 7.2 with 20mM sodium phosphate salts and dispersed in 150mM Na_2SO_4 buffered to pH 7.2 with 20mM sodium phosphate salts, or ii) 451mM NaCl buffered to pH 4.0 with 20mM sodium citrate salts and dispersed in150mM Na_2SO_4 buffered to pH 4.0 with 20mM sodium phosphate salts. At t=120s a solution of sodium maleate was added such that the external concentration of maleate was 20mM. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials. DMSO was used as a control.

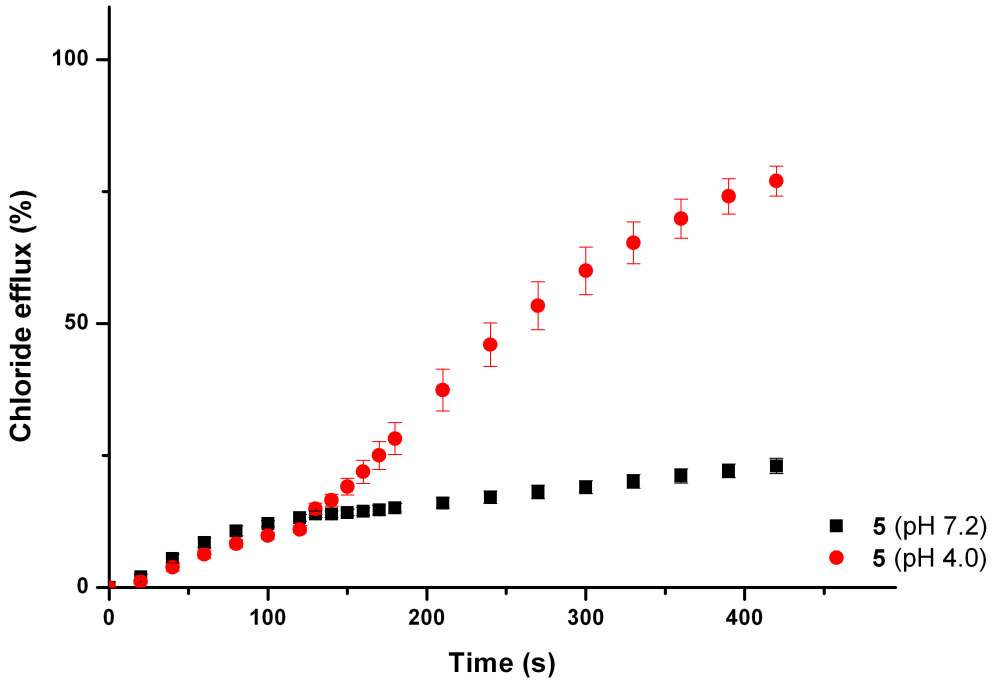

Figure S91: Chloride efflux promoted by a DMSO solution of compound **5** (2mol% carrier to lipid) from unilamellar POPC vesicles loaded with either; i) 451mM NaCl buffered to pH 7.2 with 20mM sodium phosphate salts and dispersed in 150mM Na_2SO_4 buffered to pH 7.2 with 20mM sodium phosphate salts, or ii) 451mM NaCl buffered to pH 4.0 with 20mM sodium citrate salts and dispersed in150mM Na_2SO_4 buffered to pH 4.0 with 20mM sodium phosphate salts. At t=120s a solution of sodium fumarate was added such that the external concentration of fumarate was 20mM. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials. DMSO was used as a control.

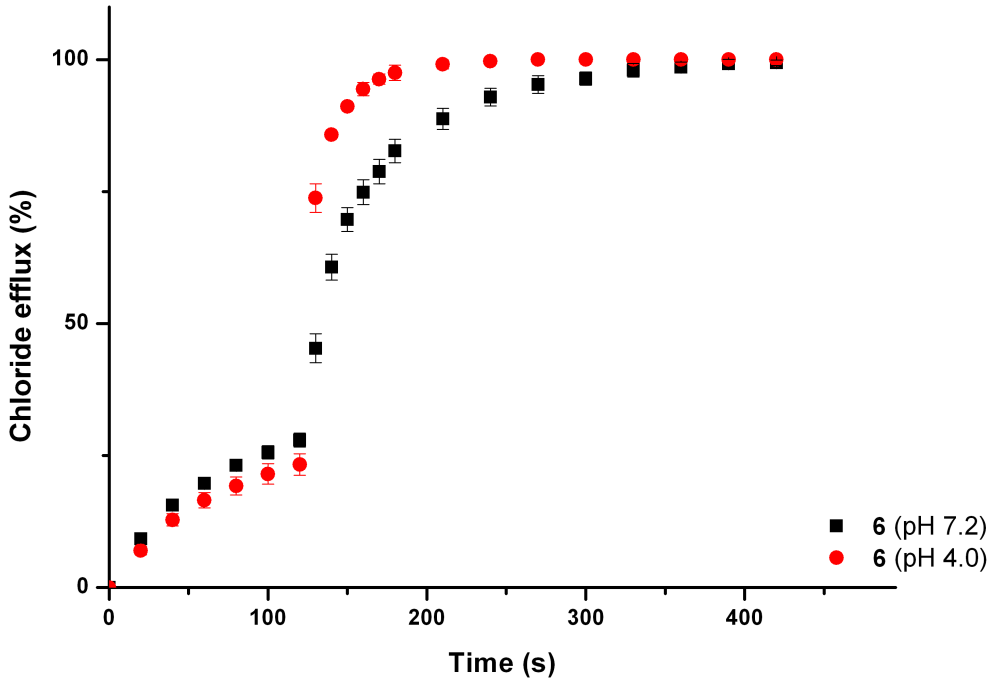

Figure S92: Chloride efflux promoted by a DMSO solution of compound **6** (2mol% carrier to lipid) from unilamellar POPC vesicles loaded with either; i) 451mM NaCl buffered to pH 7.2 with 20mM sodium phosphate salts and dispersed in 150mM Na_2SO_4 buffered to pH 7.2 with 20mM sodium phosphate salts, or ii) 451mM NaCl buffered to pH 4.0 with 20mM sodium citrate salts and dispersed in150mM Na_2SO_4 buffered to pH 4.0 with 20mM sodium phosphate salts. At t=120s a solution of sodium maleate was added such that the external concentration of maleate was 20mM. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials. DMSO was used as a control.

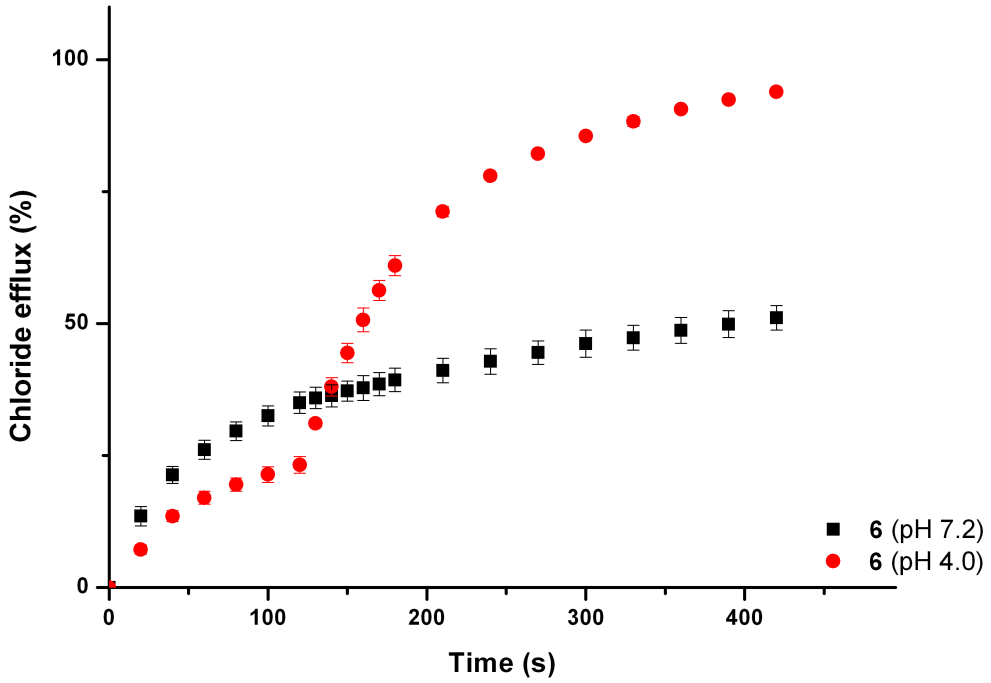

Figure S93: Chloride efflux promoted by a DMSO solution of compound **6** (2mol% carrier to lipid) from unilamellar POPC vesicles loaded with either; i) 451mM NaCl buffered to pH 7.2 with 20mM sodium phosphate salts and dispersed in 150mM Na_2SO_4 buffered to pH 7.2 with 20mM sodium phosphate salts, or ii) 451mM NaCl buffered to pH 4.0 with 20mM sodium citrate salts and dispersed in150mM Na_2SO_4 buffered to pH 4.0 with 20mM sodium phosphate salts. At t=120s a solution of sodium fumarate was added such that the external concentration of fumarate was 20mM. At the end of the experiment detergent was added to lyse the vesicles and calibrate the ISE to 100% chloride efflux. Each point represents an average of three trials. DMSO was used as a control.

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