Electronic Supplementary Material (ESI) for ChemComm.

Oligo(aryl-triazole)s CH ··Cl$^-$ Interactions Guide Chloride Efficient and Selective Transmembrane Transport

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1. General materials.

All starting materials were obtained from commercial suppliers and were used without further purification unless otherwise stated. All air- or moisture-sensitive reactions were performed using oven-dried or flame-dried glassware under an inert atmosphere of dry argon. Air- or moisture-sensitive liquids and solutions were transferred via syringe. Tetrahydrofuran (THF) was distilled from sodium benzophenone; dichloromethane was distilled from calcium hydride; triethylamine (TEA) was redistilled and stored over KOH pellets prior to use. Egg yolk phosphatidylcholine (EYPC) was obtained from Avanti Polar lipids as a solution in chloroform (25 mg·mL^{-1}). Lucigenin dye and Trixon-100 were obtained from Sigma-Aldrich and used without further purification.

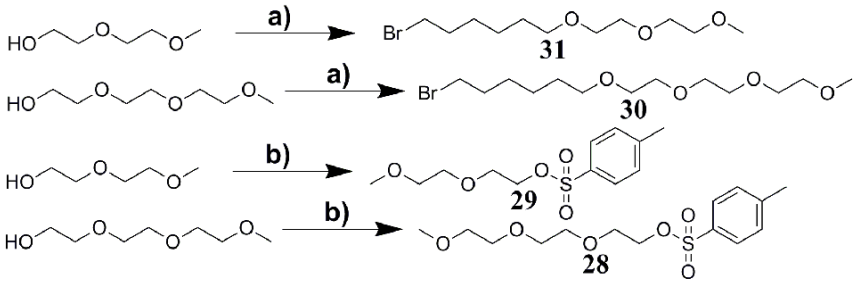
2. Characterizations.

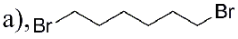
Proton and carbon nuclear magnetic resonance spectra (^{1}H, ^{13}C NMR) were recorded on a Bruker Avance 400 MHz spectrometer. Chemical shifts were reported in parts per million (ppm) downfield from the Me_4Si resonance which was used as the internal standard when recording ^{1}H NMR spectra. Mass spectra were recorded on a Micromass GCTTM and a Micromass LCTTM. Fluorescence measurements were performed on a Varian Cary Eclipses fluorescence spectrometer equipped with a stirrer and a temperature controller (kept at 25 ℃ unless otherwise noted). A

Mini-Extruder used for the preparation of large unilamellar vesicles (LUVs) was purchased from Avanti Polar lipids. The size of EYPC vesicles was determined using a Delsa™ Nano Submicron Particle Size and Zeta Potential Particle Analyzer (Beckman Coulter Inc., USA).

3. Synthesis of compounds.

3.1 Synthetic route for different side substituents:



Regeants and reaction conditions: a),  , NaH, THF; b), TsOCl, TEA, DCM.

Preparation of 31: A 500 mL round bottom flask containing 150 mL of dry THF was cooled to -25 ℃ under nitrogen protection and charged with NaH (60% in mineral oil, 5.00 g, 125.00 mmol) and 1,6-dibromohexane (40.00 g, 163.93 mmol). Freshly distilled diethyleneglycol monomethyl ether (10.00 g, 83.33 mmol) was dissolved in 50 mL of dry THF and added dropwise into the stirred slurry over 20 min. After the addition was complete, the mixture was stirred at ~ -15 ℃ for 24 h and at 0 ℃ for 2 days. The solids were removed by filtration, and the solvent was removed by rotary evaporation to give a light yellow oil, which was purified by column chromatography to afford **31** as a colorless oil. Yield: 60%; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 3.67-3.64 (m, 4 H), 3.61-3.58 (m, 2 H), 3.57-3.55 (m, 2 H), 3.42 (t, J=6.59 Hz, 2 H), 3.36 (t, J=6.84 Hz, 2 H), 3.34 (s, 3 H), 1.90-1.83 (m, 2 H), 1.63-1.58 (m, 2 H), 1.46-1.30 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 71.9, 71.1, 70.6, 70.5, 70.0, 58.9, 33.7, 32.7, 29.4, 27.9, 25.2; LR-MS (ESI-TOF): Calcd. For $C_{11}H_{23}BrO_3Na$ $[M+Na]^+$: 305.0. Found: 305.0.

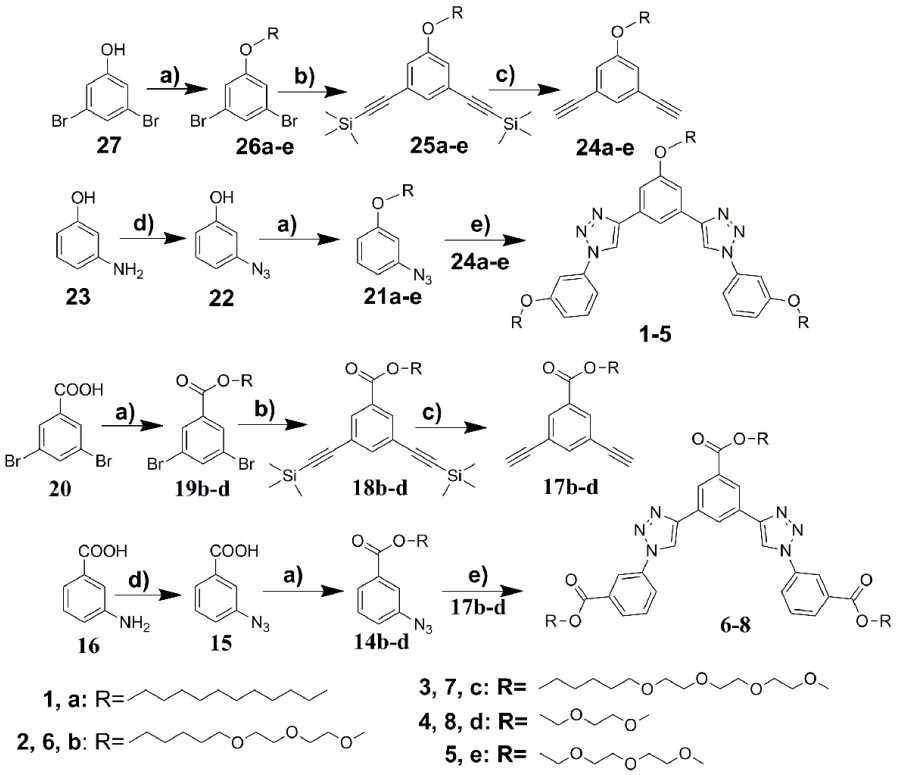
Preparation of 30: This compound was synthesized from 1,6-dibromohexane and triethyleneglycol monomethyl ether using the procedure as described for the synthesis of **31** and purified by column chromatography to give **30** as a colorless oil. Yield:

60%; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 3.71-3.63 (m, 8 H), 3.62-3.52 (m, 4 H), 3.49-3.40 (m, 4 H), 3.39 (s, 3 H), 1.90-1.83 (m, 2 H), 1.65-1.54 (m, 2 H), 1.49-1.31 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 71.9, 71.2, 70.6, 70.5, 70.0, 59.0, 33.9, 33.7, 29.4, 27.9, 25.3; LR-MS (ESI-TOF): Calcd. For $C_{13}H_{27}BrNaO_4$ $[M+Na]^+$: 349.1. Found: 349.1.

Preparation of 29: To a three-necked flask, diethyleneglycol monomethyl ether (6.00 g, 50.00 mmol), sodium hydroxide (7.00 g, 175.00 mmol), THF (35 mL), and water (35 mL) were mixed, and the obtained solution was stirred at 0 ℃. Then, another THF solution (50 mL) of p-toluene sulfonyl chloride (11.40 g, 60.00 mmol) was added dropwise in 2 h, and the reaction mixture was stirred for 12 h at room temperature. The reaction mixture was poured into aqueous hydrochloric acid, and the product was extracted with chloroform. The solvent was evaporated, and the obtained crude product was used for the subsequent synthesis without purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 2.43 (s, 3 H,), 3.33 (s, 3 H), 3.46 (t, J=4.60 Hz, 2 H), 3.56 (t, J=4.58 Hz, 2 H,), 3.67 (t, J=5.25 Hz, 2 H), 4.15 (t, J=4.83 Hz 2 H,), 7.33 (d, J=7.80 Hz, 2 H,), 7.78 (d, J=8.25 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 144.8, 132.8, 129.8, 127.9, 71.7, 70.6, 69.2, 68.6, 59.0, 21.6; LR-MS (ESI-TOF): Calcd. For $C_{12}H_{18}O_5SNa$ $[M+Na]^+$: 297.1. Found: 297.1.

Preparation of 28: This compound was synthesized from triethyleneglycol monomethyl ether and p-toluene sulfonyl chloride using the procedure as described for the synthesis of **29** to give the crude product **28** as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.80 (d, J=8.1 Hz, 2 H), 7.35 (d, J=8.0 Hz, 2 H), 4.20-4.12 (m, 2 H), 3.74-3.65 (m, 2 H), 3.65-3.57 (m, 6 H), 3.54 (dd, J=5.8, 3.2 Hz, 2 H), 3.37 (s, 3 H), 2.45 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 144.8, 132.9, 129.8, 127.9, 71.8, 70.7, 70.5, 70.4, 69.2, 68.6, 59.0, 21.6; LR-MS (ESI-TOF): Calcd. For $C_{14}H_{22}O_6SNa$ $[M+Na]^+$: 341.1. Found: 341.1.

3.2 Synthetic route for compounds 1-8:



Regeants and reaction conditions: a), RBr or TsOR, CH_3CN, K_2CO_3; b), ≡—Si— $Pd(PPh_3)_2Cl_2$,CuI, THF,piperidine; c), TBAF, DCM; d), $NaNO_2$,NaN_3,HCl, H_2O; e), sodium ascorbate, $CuSO_4$ $5H_2O$,THF,H_2O.

Preparation of 26a-e: The generally process was processed as following. To a solution of **27** in CH_3CN was added 1.4 eq bromoalkane or TsO-ethylene glycol and 6.0 eq K_2CO_3. The mixture was stirred at 70 ^oC for 12 h and then concentrated under reduced pressure. The residue was dissolved in ethyl acetate and washed with brine, dried over anhydrous Na_2SO_4. After removing of the solvent, the crude product was purified by column chromatography on silica gel to afford **26a-e** as colorless transparent crystals or oils.

26a: ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.22 (s, 1 H), 6.97 (s, 2 H), 3.90 (t, J=6.51 Hz, 2 H), 1.83-1.67 (m, 2 H), 1.46-1.39 (m, 2 H), 1.35-1.19 (m, 16 H), 0.88 (t, J=6.73 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 160.3, 126.1, 123.1, 116.9, 63.6, 31.9, 29.6, 29.3, 25.9, 22.7, 14.1; LR-MS (ESI-TOF): Calcd. For $C_{18}H_{29}Br_2O$ $[M+H]^+$: 419.0. Found: 419.0.

26b: ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.22 (t, J=1.7 Hz, 1 H), 6.97 (d, J=1.6 Hz, 2 H), 3.90 (t, J=6.4 Hz, 2 H), 3.65 (td, J=4.5, 2.4 Hz, 4 H), 3.62-3.58 (m, 2 H), 3.58-3.54 (m, 2 H), 3.47 (t, J=6.6 Hz, 2 H), 3.38 (s, 3 H), 1.81-1.72 (m, 2 H), 1.61 (q,

J=6.9 Hz, 2 H), 1.50-1.35 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 160.3, 126.1, 123.0, 116.9, 71.9, 71.2, 70.6, 70.5, 70.1, 68.4, 59.0, 29.5, 28.9, 25.8, 25.7; LR-MS (ESI-TOF): Calcd. For $C_{17}H_{26}Br_2O_4Na$ $[M+Na]^+$: 477.0. Found: 477.0.

26c: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.22 (t, J=1.6 Hz, 1 H), 6.98 (d, J=1.6 Hz, 2 H), 3.91 (t, J=6.4 Hz, 2 H), 3.69-3.48 (m, 8 H), 3.48-3.45 (m, 4 H), 3.47 (t, J= 6.6 Hz, 2 H), 3.38 (s, 3 H), 1.80-1.73 (m, 2 H), 1.60 (q, J=6.8 Hz, 3 H), 1.51-1.35 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 160.3, 126.1, 123.0, 116.9, 71.9, 71.2, 70.5, 70.1, 68.4, 59.0, 29.5, 28.9, 25.8; LR-MS (ESI-TOF): Calcd. For $C_{19}H_{30}Br_2O_5Na$ $[M+Na]^+$: 519.0. Found: 519.0.

26d: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.24 (t, J=1.6 Hz, 1 H), 7.02 (d, J=1.6 Hz, 2 H), 4.13-4.08 (m, 2 H), 3.86-3.81 (m, 2 H), 3.72-3.68 (m, 2 H), 3.60-3.55 (m, 2 H), 3.39 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 159.9, 126.5, 123.0, 117.1, 71.9, 70.8, 69.4, 68.0, 59.1; LR-MS (ESI-TOF): Calcd. For $C_{11}H_{14}Br_2O_3Na$ $[M+Na]^+$: 374.9. Found: 374.9.

26e: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.24 (t, J=1.6 Hz, 1 H), 7.02 (d, J=1.6 Hz, 2 H), 4.13-4.07 (m, 2 H), 3.86-3.81 (m, 2 H), 3.75-3.70 (m, 2 H), 3.69-3.63 (m, 4 H), 3.58-3.53 (m, 2 H), 3.38 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 160.0, 126.5, 123.0, 117.1, 71.9, 70.9, 70.6, 69.4, 68.0, 59.0; LR-MS (ESI-TOF): Calcd. For $C_{13}H_{18}Br_2O_4Na$ $[M+Na]^+$: 420.9. Found: 420.9.

Preparation of 25a-e: The general process was processed as following. For example: Compound **26a** (1.20 g, 2.76 mmol) was dissolved in dry piperidine (25 mL) containing $Pd(PPh_3)_2Cl_2$ (0.10 g, 0.16 mmol), PPh_3 (15.70 mg, 0.06 mmol) and CuI (11.40 mg, 0.06 mmol) and stirred for 5 min, trimethylsilylacetylene (1.80 mL, 13.15 mmol) was then added to above solution and stirred at 60 ^{o}C for 3 h. Dichloromethane was added to the mixture and washed with saturated NH_4Cl, HCl (10%) and NaCl, respectively. The organic phase was dried with $MgSO_4$ and the solvent was removed under vacuum. The crude product was purified by column chromatography on silica gel to afford **25a** as a yellow solid. Yield 87%; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.20 (s, 1 H), 6.96 (s, 2 H), 3.94 (t, J=6.44 Hz, 2 H), 1.84-1.74 (m, 2 H), 1.48-1.41 (m, 2 H), 1.37-1.29 (m, 16 H), 0.91 (t, J=6.70 Hz, 3 H), 0.26 (s, 18 H); ^{13}C NMR (100

MHz, $CDCl_3$) δ ppm 158.7, 128.1, 124.4, 118.3, 104.2, 94.5, 68.3, 32.0, 29.7, 29.6, 29.4, 26.0, 22.8, 14.2, 0.276; LR-MS (ESI-TOF): Calcd. For $C_{28}H_{46}OSi_2$ [M^+]: 454.3. Found: 454.3.

25b: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.17 (t, J=1.3 Hz, 1 H), 6.93 (d, J=1.4 Hz, 2 H), 3.92 (t, J=6.4 Hz, 2 H), 3.65 (dd, J=6.4, 3.3 Hz, 4 H), 3.62-3.58 (m, 2 H), 3.57-3.54 (m, 2 H), 3.47 (t, J=6.6 Hz, 2 H), 3.38 (s, 3 H), 1.75 (dt, J=7.9, 6.3 Hz, 2 H), 1.65-1.55 (m, 2 H), 1.49-1.34 (m, 4 H), 0.23 (s, 18 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 160.3, 126.1, 123.0, 116.9, 71.9, 71.2, 70.6, 70.5, 70.1, 68.5, 59.0, 53.4, 29.5, 28.9, 25.8, 25.7; LR-MS (ESI-TOF): Calcd. For $C_{27}H_{45}O_4Si_2$ [M+H] $^+$: 489.3. Found: 489.3.

25c: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.17 (s, 1 H), 6.93 (s, 2 H), 3.92 (t, J=6.5 Hz, 2 H), 3.69-3.61 (m, 10 H), 3.57-3.54 (m, 2 H), 3.47 (td, J=6.5, 3.3 Hz, 2 H), 3.38 (s, 3 H), 1.75 (p, J=6.6 Hz, 2 H), 1.63-1.57 (m, 2 H), 1.45-1.39 (m, 4 H), 0.23 (s, 18 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 128.1, 124.2, 118.3, 104.2, 94.6, 72.0, 71.4, 70.6, 70.2, 68.1, 59.1, 52.7, 29.6, 29.1, 25.9, -0.1; LR-MS (ESI-TOF): Calcd. For $C_{29}H_{48}NaO_5Si_2$ [M+Na]$^+$: 555.3. Found: 555.3.

25d: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.21 (t, J=1.4 Hz, 1 H), 6.98 (d, J=1.4 Hz, 2 H), 4.16-4.11 (m, 2 H), 3.88-3.83 (m, 2 H), 3.75-3.70 (m, 2 H), 3.62-3.56 (m, 2 H), 3.42 (s, 3 H), 0.25 (s, 18 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 158.3, 128.5, 124.3, 118.5, 94.7, 72.0, 70.9, 69.7, 67.8, 59.2, -0.1; LR-MS (ESI-TOF): Calcd. For $C_{21}H_{33}O_3Si_2$ [M+H]$^+$: 389.2. Found: 389.2.

25e: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.19 (t, J=1.4 Hz, 1 H), 6.95 (d, J=1.3 Hz, 2 H), 4.13-4.08 (m, 2 H), 3.85-3.80 (m, 2 H), 3.75-3.70 (m, 2 H), 3.69-3.63 (m, 4 H), 3.57-3.50 (m, 2 H), 3.38 (s, 3 H), 0.23 (s, 18 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 158.6, 128.7, 124.6, 118.8, 95.1, 72.3, 71.3, 71.0, 69.9, 68.1, 59.4, 54.5, 1.4; LR-MS (ESI-TOF): Calcd. For $C_{23}H_{36}O_4Si_2Na$ [M+ Na]$^+$: 455.2. Found: 455.2.

Preparation of 24a-e: Taking **24a** as example. A 50 mL flask was charged with **25a** (1.00 g, 2.20 mmol), TBAF (3.45 g, 13.20 mmol), THF (20 mL) and the obtained mixture was stirred at RT for 1 h. The solvent was removed under vacuum and the solid obtained was extracted with CH_2Cl_2 (3×50 mL), washed with water (30 mL),

dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was purified by column chromatography to afford **24a** as a white solid. Yield 97%; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.20 (s, 1 H), 7.00 (s, 2 H), 3.93 (t, J=6.53 Hz, 2 H), 3.05 (s, 2 H), 1.79-1.72 (m, 2 H), 1.47-1.37 (m, 2 H), 1.35-1.27 (m, 16 H), 0.88 (t, J=6.69 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 158.5, 128.0, 123.2, 118.8, 82.6, 77.5, 68.2, 31.9, 29.6, 29.3, 25.9, 22.7, 14.1; LR-MS (ESI-TOF): Calcd. For $C_{22}H_{30}O$ $[M+H]^+$: 311.6. Found: 311.6.

24b: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.19 (t, J=1.4 Hz, 1 H), 6.99 (s, 2 H), 3.92 (t, J=6.5 Hz, 2 H), 3.68-3.62 (m, 4 H), 3.61-3.58 (m, 2 H), 3.57-3.54 (m, 2 H), 3.49-3.45 (m, 2 H), 3.38 (s, 3 H), 3.07 (s, 2 H), 1.76 (dt, J=8.1, 6.4 Hz, 2 H), 1.61 (q, J=6.9 Hz, 2 H), 1.51-1.35 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 158.6, 128.0, 123.3, 118.8, 82.6, 71.9, 71.3, 70.6, 70.5, 70.1, 59.0, 29.5, 29.0, 25.8; LR-MS (ESI-TOF): Calcd. For $C_{21}H_{28}O_4$ $[M+Na]^+$: 367.2. Found: 367.2

24c: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.20 (s, 1 H), 6.99(s, 2 H), 3.93 (t, J=6.5 Hz, 2 H), 3.70-3.62 (m, 10 H), 3.60-3.54 (m, 2 H), 3.48-3.45 (m, 2 H), 3.38 (s, 1 H), 3.05 (s, 2 H), 1.81-1.74 (m, 2 H), 1.65-1.56 (m, 2 H), 1.48-1.38 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 158.5, 128.0, 123.2, 118.8, 114.3, 82.5, 82.6, 71.9, 70.6, 70.5, 70.0, 68.1, 59.0, 29.5, 29.0, 25.8; LR-MS (ESI-TOF): Calcd. For $C_{23}H_{32}NaO_5$ $[M+Na]^+$: 411.2. Found: 411.2.

24d: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.21 (s, 1H), 7.03(s, 2H), 4.15-4.09 (m, 2H), 3.87-3.82 (m, 2H), 3.73-3.69 (m, 2H), 3.60-3.54 (m, 2H), 3.39 (s, 3H), 3.07 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 158.3, 128.4, 123.3, 118.9, 82.5, 71.9, 70.8, 69.5, 67.7, 59.0; LR-MS (ESI-TOF): Calcd. For $C_{15}H_{17}O_3$ $[M+H]^+$: 245.1. Found: 245.1.

24e: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.21 (d, J=1.5 Hz, 1 H), 7.03 (s, 2 H), 4.11 (t, J=4.8 Hz, 2 H), 3.84 (dd, J=5.6, 3.9 Hz, 2 H), 3.73 (dd, J=6.2, 3.7 Hz, 2 H), 3.70-3.63 (m, 4 H), 3.55 (dd, J=5.8, 3.5 Hz, 2 H), 3.38 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 158.3, 128.4, 123.3, 118.9, 82.5, 71.9, 70.8, 70.6, 70.5, 69.5, 59.0; LR-MS (ESI-TOF): Calcd. For $C_{17}H_{20}O_4Na$ $[M+Na]^+$: 311.1. Found: 311.1.

Preparation of 22: To a vented, stirred solution of 3-Aminophenol **23** (1.64 g,15.00 mmol) in 50 mL 2M HCl at 0 ℃ is syringed sodium nitrite (1.24 g,18.00 mmol) in

water (10 mL) dropwise. The reaction is allowed to proceed for 30 minutes at RT and a solution of NaN_3 (1.46 g, 22.50 mmol) in water (15 mL) is added dropwise. The obtained deep red solution is stirred for a further 2 hours at RT. The reaction is extracted with ethyl acetate (30 mL) and the organic phase was washed with 0.1 M HCl (25 mL), saturated NH_4Cl (25 mL) and brine (25 mL), respectively. The combined organic fractions are dried with Na_2SO_4 and concentrated by rotary evaporation. The crude product is purified by column chromatography (4:1 Hexanes: Ethylacetate) to yield a red oil. Yield: 76%; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.19 (t, J=8.1 Hz, 1 H), 6.61 (ddd, J=12.4, 7.9, 2.2 Hz, 2 H), 6.52 (t, J=2.3 Hz, 1 H), 4.15 (q, J=7.1 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 156.6, 141.4, 130.7 112.1, 111.6, 105.3;

Preparation of 21a-e: The processes were similar as those of **26a-e**.

21a: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.21 (t, J=8.1 Hz, 1 H), 6.67 (dd, J=8.3, 2.4 Hz, 1 H), 6.61 (dd, J=7.9, 2.0 Hz, 1 H), 6.54 (s, 1 H), 3.93 (t, J=6.6 Hz, 2 H), 1.82-1.72 (m, 2 H), 1.44 (p, J=7.0 Hz, 2 H), 1.39-1.21 (m, 16 H), 0.88 (t, J=6.7 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 160.3, 141.3, 130.3, 111.1, 111.0, 105.4, 68.1, 31.4, 29.6, 29.5, 29.3, 29.1, 26.0, 22.7, 14.1; LR-MS (ESI-TOF): Calcd. For $C_{18}H_{29}N_3O$ $[M+Na]^+$: 326.2. Found: 326.2.

21b: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.23 (t, J=8.1 Hz, 1 H), 6.67 (dd, J=8.3, 2.4 Hz, 1 H), 6.62 (dd, J=7.9, 2.2 Hz, 1 H), 6.54 (t, J=2.2 Hz, 1 H), 3.93 (t, J=6.5 Hz, 2 H), 3.67-3.63 (m, 4 H), 3.62-3.58 (m, 2 H), 3.57-3.53 (m, 2 H), 3.47 (t, J=6.6 Hz, 2 H), 3.38 (s, 3 H), 1.78 (dq, J=8.1, 6.6 Hz, 2H), 1.61 (q, J=7.1 Hz, 2 H), 1.52-1.36 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 160.3, 141.1, 130.3, 130.1, 111.1, 105.4, 71.9, 71.3, 70.6, 70.5, 70.1, 68.1, 68.0, 59.0, 29.5, 29.1, 29.0, 25.8; LR-MS (ESI-TOF): Calcd. For $C_{17}H_{27}N_3O_4Na$ $[M+Na]^+$: 360.2. Found: 360.2.

21c: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.23 (t, J=8.1 Hz, 1 H), 6.67 (dd, J=8.3, 2.4 Hz, 1 H), 6.62 (dd, J=7.8, 2.1 Hz, 1 H), 6.54 (s, 1 H), 3.94 (t, J=6.5 Hz, 2 H), 3.67 (s, 2 H), 3.65 (dd, J=5.7, 3.4 Hz, 10 H), 3.47 (t, J=6.7 Hz, 3 H), 3.38 (s, 3 H), 1.77 (dt, J=8.3, 6.4 Hz, 2 H), 1.62 (p, J=6.9 Hz,2 H), 1.52-1.36 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 160.5, 141,1, 130.3, 111.1, 105.4, 71.9, 70.6, 70.5, 70.0, 68.0, 59.0,

29.5, 29.1, 25.8; LR-MS (ESI-TOF): Calcd. For $C_{19}H_{31}N_3O_5Na$ $[M+Na]^+$: 404.2. Found: 404.2.

21d: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.23 (t, J=8.1 Hz, 1 H), 6.70 (dd, J=8.3, 2.4 Hz, 1 H), 6.64 (dd, J=7.9, 2.1 Hz, 1 H), 6.58 (t, J=2.3 Hz, 1 H), 4.16-4.10 (m, 2 H), 3.89-3.83 (m, 2 H), 3.75-3.69 (m, 2 H), 3.61-3.55 (m, 2 H), 3.39 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 159.9, 141.2, 130.4, 111.5, 111.2, 105.7, 71.9, 70.7, 69.6, 67.5, 59.1; LR-MS (ESI-TOF): Calcd. For $C_{11}H_{16}N_3O_3$ $[M+H]^+$: 238.1. Found: 238.1.

21e: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.24 (t, J=8.1 Hz, 1 H), 6.70 (dd, J=8.3, 2.4 Hz, 1 H), 6.64 (dd, J=8.0, 2.1 Hz, 1 H), 6.58 (t, J=2.2 Hz, 1 H), 4.14-4.10 (m, 2 H), 3.88-3.83 (m, 2 H), 3.74-3.72 (m, 2 H), 3.70-3.68 (m, 2 H), 3.61-3.59 (m, 2 H), 3.58-3.54 (m, 2 H), 3.38 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 160.0, 141.2, 129.8, 111.5, 111.2, 105.7, 71.9, 70.8, 70.7, 70.6, 70.5, 69.6, 59.0; LR-MS (ESI-TOF): Calcd. For $C_{13}H_{19}N_3O_4Na$ $[M+Na]^+$: 304.1. Found: 304.1.

Preparation of compounds 1-5: Taking compound **1** as example. A THF: water (V/V= 2/1, 15 mL) solution containing **21a** (0.61 g, 2 mmol), **24a** (0.31 g, 1 mmol), sodium ascorbate (19.81 mg, 0.1 mmol) and copper (II) sulfate pentahydrate (12.45 mg, 0.05 mmol) was stirred at 60 ℃ for 2 h. After removal of the solvents in vacuum, the crude product was purified by column chromatography to afford **1** as yellow solid. Yield: 91%; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.30 (s, 2 H), 8.00 (s, 1 H), 7.51(s, 2 H), 7.44(t, J=8.2 Hz, 2 H), 7.39(s, 2 H), 7.33 (d, J=8.0 Hz, 2 H), 6.99 (d, J=8.3 Hz, 2 H), 4.14 (t, J=6.5 Hz, 2 H), 4.06 (t, J=6.5 Hz, 2 H), 1.89-1.80 (m, 6 H), 1.54-1.45 (m, 6 H), 1.54-1.27 (m, 48 H), 0.88 (t, J=6.6 Hz, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 160.2，147.9, 137.9, 132.0, 130.5, 115.3, 115.2, 112.1, 111.7, 105.7, 68.5, 31.9, 29.6, 29.5, 29.4, 29.3, 29.1, 18.4, 14.1; HR-MS (ESI-TOF): Calcd. For $C_{58}H_{88}N_6O_3Na$ $[M+ Na]^+$: 939.6816. Found: 939.6821.

2： ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.34 (s, 2 H), 8.02 (s, 1 H), 7.51 (s, 2 H), 7.46-7.38 (m, 4 H), 7.37-7.31 (m, 2 H), 6.99 (dd, J=8.3, 2.3 Hz, 2 H), 4.13 (t, J=6.5 Hz, 2 H), 4.05 (t, J=6.4 Hz, 4 H), 3.69-3.64 (m, 12 H), 3.63-3.58 (m, 6 H), 3.56 (dd, J=5.8, 3.5 Hz, 6 H), 3.49 (td, J=6.7, 2.0 Hz, 6 H), 3.38 (s, 9 H), 1.85 (q, J=7.1, 6.0 Hz, 6 H), 1.70 -1.59 (m, 6 H), 1.56-1.41 (m, 12 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm

160.1, 147.8, 137.9, 131.9, 130.5, 118.2, 115.2, 112.1, 111.8, 105.7, 71.9, 70.6, 70.5, 70.1, 68.3, 68.2, 59.0, 29.5, 29.1, 25.9, 25.8; HR-MS (ESI-TOF): Calcd. For $C_{55}H_{82}N_6O_{12}Na$ $[M+ Na]^+$: 1041.5888. Found: 1041.5886.

3: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.33 (s, 2 H), 8.01 (s, 1 H), 7.51 (d, J=1.4 Hz, 2 H), 7.44 (t, J=8.1 Hz, 2 H), 7.40 (t, J=2.2 Hz, 2 H), 7.36-7.31 (m, 2 H), 6.99 (dd, J=8.3, 2.3 Hz, 2 H), 4.14 (t, J=6.5 Hz, 2 H), 4.06 (t, J=6.4 Hz, 4 H), 3.69-3.63 (m, 24 H), 3.61-3.68 (m, 6 H), 3.55 (dd, J=5.8, 3.5 Hz, 6 H), 3.49 (td, J=6.7, 2.4 Hz, 6 H), 3.37 (s, 9 H), 1.88-1.81 (m, 6 H), 1.68-1.61 (m, 6 H), 1.56-1.50 (m, 6 H), 1.48-1.41 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 160.1, 147.8, 137.9, 131.9, 130.5, 118.2, 115.4, 112.1, 111.7, 105.7, 71.9, 70.6, 70.5, 70.0, 68.3, 68.2, 59.0, 29.5, 29.2, 29.1, 25.8; HR-MS (ESI-TOF): Calcd. For $C_{61}H_{94}N_6O_{15}Na$ $[M+ Na]^+$: 1173.6675. Found: 1173.6678.

4: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.32 (s, 2 H), 8.02 (s, 1 H), 7.52 (d, J=1.5 Hz, 2 H), 7.42 (d, J=7.8 Hz, 4 H), 7.38-7.32 (m, 2 H), 7.00 (dd, J=8.1, 2.3 Hz, 2 H), 4.31 (t, J=4.7 Hz, 2 H), 4.24 (t, J=4.8 Hz, 4 H), 3.97-3.88 (m, 6 H), 3.80-3.73 (m, 6 H), 3.61 (dt, J=4.4, 3.0 Hz, 6 H), 3.40 (d, J=1.6 Hz, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 159.8, 147.7, 137.8, 132.0, 130.5, 118.2, 115.7, 115.2, 112.5, 111.9, 105.9, 71.9, 70.8, 70.7, 69.6, 67.8, 59.0; HR-MS (ESI-TOF): Calcd. For $C_{37}H_{47}N_6O_9$ $[M+H]^+$: 719.3405. Found: 719.3403.

5: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.41 (s, 2 H), 8.10 (s, 1 H), 7.54 (s, 2 H), 7.43 (d, J=8.4 Hz, 4 H), 7.36 (d, J=8.0 Hz, 2 H), 7.01 (d, J=8.0 Hz, 2 H), 4.31 (s, 2 H), 4.24 (t, J=4.5 Hz, 4 H), 3.92 (q, J=4.9, 4.2 Hz, 6 H), 3.80-3.75 (m, 6 H), 3.73-3.66 (m, 12 H), 3.57-3.55 (m, 6 H), 3.37 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 159.8, 147.9, 137.9, 132.1, 130.6, 115.2, 112.5, 111.8, 105.9, 71.9, 70.8, 70.6, 70.5, 69.7, 69.6, 67.9, 67.7, 59.0; HR-MS (ESI-TOF): Calcd. For $C_{43}H_{58}N_6O_{12}Na$ $[M+Na]^+$: 873.4010. Found: 873.4013.

Preparation of compound 6-8: The synthetic processes of compounds **6-8** were similar as those of compounds **1-5** except using **20** and **16** as the corresponding original materials.

19b: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.09 (s, 2 H), 7.84 (s, 1 H), 4.32 (t, J=6.7 Hz,

2 H), 3.68-3.63 (m, 4 H), 3.61-3.59 (m, 2 H), 3.57-3.55 (m, 2 H), 3.47 (t, J=6.6 Hz, 2 H), 3.38 (s, 3 H), 1.77 (t, J=7.0 Hz, 2 H), 1.62 (t, J=6.8 Hz, 2 H), 1.50-1.37 (m, J=4.8 Hz, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 164.0, 138.1, 133.6, 131.2, 122.9, 71.9, 70.6, 70.5, 70.1, 65.8, 59.0, 29.4, 28.5, 25.8, 25.7; LR-MS (ESI-TOF): Calcd. For $C_{18}H_{26}Br_2O_5Na$ $[M+Na]^+$: 505.0. Found: 505.0.

19c: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.09 (s , 2 H), 7.84 (s, 1 H), 4.32 (t, J= 6.7 Hz, 2 H), 3.69-3.62 (m, 8 H), 3.61-3.53 (m, 4 H), 3.47 (td, J=6.7, 2.7 Hz, 2 H), 3.38 (s, 4 H), 1.84-1.72 (m, 2 H), 1.61 (q, J=6.8 Hz, 2 H), 1.48-1.40 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 164.0, 138.1, 133.6, 131.2, 122.9, 71.9, 70.6, 70.5, 70.1, 65.9, 59.0, 29.5, 29.0, 25.8, 25.7; LR-MS (ESI-TOF): Calcd. For $C_{20}H_{30}Br_2O_6Na$ $[M+Na]^+$: 549.0. Found: 549.0.

19d: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.12 (s, 2 H), 7.85 (s, 1 H), 4.55-4.42 (m, 2 H), 3.88-3.78 (m, 2 H), 3.74-3.64 (m, 2 H), 3.61-3.53 (m, 2 H), 3.40 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 164.0, 138.2, 133.2, 131.4, 122.9, 77.2, 71.8, 70.5, 69.0, 64.7, 59.1.

18b: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.03 (s, 2 H), 7.73 (s, 1 H), 4.31 (t, J=6.7 Hz, 2 H), 3.67-3.62 (m, 4 H), 3.62-3.54 (m, 4 H), 3.47 (t, J=6.6 Hz, 2 H), 3.38 (s, 3 H), 1.81-1.76 (m, 2 H), 1.65-1.59 (m, 2 H), 1.46-1.39 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 165.4, 139.2, 132.7, 131.0, 123.9, 103.1, 96.2, 72.1, 71.4, 70.8, 70.7, 70.2, 65.6, 59.2, 29.6, 28.8, 25.9. 0.3; LR-MS (ESI-TOF): Calcd. For $C_{28}H_{44}O_5Si_2Na$ $[M+Na]^+$: 539.3. Found: 539.3.

18c: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.02 (s, 2 H), 7.72 (s, 1 H), 4.30 (t, J=6.7 Hz, 2 H), 3.67-3.61 (m, 8 H), 3.60-3.52 (m, 4 H), 3.46 (td, J=6.7, 2.2 Hz, 2 H), 3.37 (s, 3 H), 1.77 (p, J=6.9 Hz, 2 H), 1.60-1.58 (m, 2 H), 1.45-1.39 (m, 4 H), 0.25 (s, 18 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 165.4, 132.7, 131.0, 124.0, 103.1, 96.2, 72.1, 71.4, 70.8, 70.7, 70.2, 65.6, 59.2, 29.6, 28.8, 25.9, 0.3; LR-MS (ESI-TOF): Calcd. For $C_{30}H_{48}O_6Si_2Na$ $[M+Na]^+$: 583.3. Found: 583.3.

18d: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.05 (s, 2 H), 7.72 (s, 1 H), 4.49-4.46 (m, 2 H), 3.70-3.67(m, 2 H), 3.58-3.56 (m, 2 H), 3.39 (s, 3 H), 0.23(s, 18 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 165.4, 132.9, 131.1, 124.0, 103.1, 96.3, 72.0, 70.7, 69.3, 64.6,

59.3, 58.6, 0.19; LR-MS (ESI-TOF): Calcd. For $C_{22}H_{32}O_4Si_2Na$ $[M+Na]^+$: 439.2. Found:439.2.

17b: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.10 (s, 2 H), 7.76 (s, 1 H), 4.32 (t, J=6.7 Hz, 2 H), 3.68-3.63 (m, 4 H), 3.60 (dd, J=5.7, 3.4 Hz, 2 H), 3.56 (dd, J=5.8, 3.5 Hz, 2 H), 3.47 (t, J=6.6 Hz, 2 H), 3.38 (s, 3 H), 3.16 (s, 2 H), 1.81-1.74 (m, 2 H), 1.66-1.59 (m, 2 H), 1.48-1.40 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 165.0, 139.2, 133.1, 131.1, 122.9, 81.6, 78.9, 71.9, 71.2, 70.6, 70.5, 70.0, 59.0, 29.4, 28.5, 25.8; LR-MS (ESI-TOF): Calcd. For $C_{22}H_{28}O_5Na$ $[M+Na]^+$: 395.2. Found: 395.2.

17c: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.10 (d, J=1.6 Hz, 2 H), 7.76 (t, J=1.7 Hz, 1 H), 4.32 (t, J=6.6 Hz, 2 H), 3.68-3.62 (m, 8 H), 3.61-3.53 (m, 4 H), 3.47 (t, J=6.6 Hz, 2 H), 3.38 (s, 3 H), 3.15 (s, 2 H), 1.81-1.74 (m, 2 H), 1.65-1.58 (m, 2 H), 1.48-1.39 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 165.1, 139.2, 133.2, 131.1, 122.9, 81.7, 79.0, 71.9, 71.2, 70.5, 70.1, 65.6, 59.0, 29.6, 28.6, 25.9; LR-MS (ESI-TOF): Calcd. For $C_{24}H_{32}O_6Na$ $[M+Na]^+$: 439.2. Found:439.2.

17d: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.15 (s, 2 H), 7.78 (s, 1 H), 4.59-4.41 (m, 2 H), 3.86-3.84 (m, 2 H), 3.77-3.74 (m, 2 H), 3.60-3.58 (m, 2 H), 3.41 (s, 3 H), 3.16 (s, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 166.6, 141.0, 135.0, 132.4, 124.6, 80.6, 78.9, 73.5, 72.2, 70.7, 66.2, 60.1; LR-MS (ESI-TOF): Calcd. For $C_{16}H_{16}O_4Na$ $[M+Na]^+$: 295.1. Found: 295.1.

15: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 13.26 (s, 1 H), 7.75 (d, J=7.7 Hz, 1 H), 7.57 (s, 1 H), 7.54 (d, J=7.8 Hz, 1 H), 7.38 (dd, J=8.0, 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 166.9, 140.3, 133.0, 130.8, 126.3, 124.0, 119.8.

14b: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.81 (d, J=7.7 Hz, 1 H), 7.70 (s, 1 H), 7.43 (t, J=7.9 Hz, 1 H), 7.20 (d, J=8.1 Hz, 1 H), 4.32 (t, J=6.7 Hz, 2 H), 3.68-3.63 (m, 4 H), 3.61-3.58 (m, 2 H), 3.57-3.55 (m, 2 H), 3.47 (t, J=6.6 Hz, 2 H), 3.38 (s, 3 H), 1.78 (p, J=6.8 Hz, 2 H), 1.66-1.59 (m, 2 H), 1.48-1.40 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 165.7, 140.5, 132.2, 129.8, 125.9, 123.2, 119.9, 71.9, 71.2, 70.6, 70.5, 70.0, 65.3, 59.0, 29.5, 28.6, 25.8; LR-MS(ESI-TOF): Calcd. For $C_{18}H_{27}N_3O_5Na$ $[M+Na]^+$: 388.2. Found: 388.2.

14c: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.81 (d, J=7.7 Hz, 1 H), 7.69 (s, 1 H), 7.43 (t,

J=7.9 Hz, 1 H), 7.20 (d, J=8.1 Hz, 1 H), 4.32 (t, J=6.7 Hz, 2 H), 3.71-3.62 (m, 8 H), 3.61-3.52 (m, 4 H), 3.47 (t, J=6.6 Hz, 2 H), 3.38 (s, 3 H), 1.83-1.74 (m, 2 H), 1.61 (q, J=7.0 Hz, 2 H), 1.50-1.39 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 165.7, 140.5, 132.2, 129.8, 125.9, 123.2, 119.9, 71.9, 71.2, 70.6, 70.5, 70.2, 65.3, 59.0, 29.5, 28.6, 25.8; LR-MS (ESI-TOF): Calcd. For $C_{20}H_{31}N_3O_6Na$ $[M+Na]^+$: 432.2. Found: 432.2.

14d: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.83 (dt, J=7.8, 1.3 Hz, 1 H), 7.72 (t, J=1.9 Hz, 1 H), 7.43 (t, J=7.9 Hz,1 H), 7.20 (dd, J=8.1, 2.4 Hz, 1 H), 4.51-4.49 (m, 2 H), 3.86-3.83 (m, 2 H), 3.73-3.68 (m, 2 H), 3.60-3.55 (m, 2 H), 3.39 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 165.6, 140.5, 131.8, 129.8, 126.1, 123.4, 120.0, 71.9, 70.6, 69.1, 64.4, 59.1; LR-MS (ESI-TOF): Calcd. For $C_{12}H_{15}N_3O_4Na$ $[M+Na]^+$: 288.1. Found: 288.1.

6: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.76 (s, 1 H), 8.59 (s, 2 H), 8.52 (s, 2 H), 8.45 (s, 2 H), 8.17 (d, J=7.8 Hz, 2 H), 8.15-8.10 (m, 2 H), 7.69 (t, J=7.9 Hz, 2 H), 4.41 (q, J=6.4 Hz, 6 H), 3.66-3.63 (m, 12 H), 3.61-3.59 (m, 6 H), 3.56-3.54 (m, 6 H), 3.51-3.47 (m, 6 H), 3.37 (s, 9 H), 1.88-1.80 (m, 6 H), 1.67-1.60 (m, 6 H), 1.50-1.44 (m, 12 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 165.3, 147.4, 137.0, 132.4, 132.3, 131.2, 130.1, 129.9, 127.0, 126.7, 124.7, 121.1, 118.5, 71.9, 71.2, 70.6, 70.5, 70.0, 65.7, 59.0, 29.5, 28.6, 25.8; HR-MS (ESI-TOF): Calcd. For $C_{58}H_{82}N_6O_{15}Na$ $[M+Na]^+$: 1125.5736. Found: 1125.5841.

7: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.76 (s, 1 H), 8.59(s, 2 H), 8.55 (s, 2 H), 8.46 (s, 2 H), 8.21-8.09 (m, 4 H), 7.69 (t, J=7.9 Hz, 2 H), 4.45-4.36 (m, 6 H), 3.69-3.62 (m, 24 H), 3.59 (dd, J=5.9, 3.8 Hz, 6H), 3.55 (dd, J=5.8, 3.5 Hz, 6 H), 3.50-3.46 (m, 6 H), 3.37 (s, 9 H), 1.88-1.80 (m, 6 H), 1.67-1.60 (m, 6 H), 1.53-1.42 (m, 12 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 165.3, 147.4, 137.0, 132.3, 132.1, 131.2, 130.1, 129.8, 127.0, 126.6, 124.6, 121.1, 118.5, 71.9, 71.2, 70.6, 70.5, 70.0, 65.7, 65.6, 59.0, 29.5, 28.6, 25.8. HR-MS (ESI-TOF): Calcd. For $C_{64}H_{94}N_6O_{18}Na$ $[M+Na]^+$: 1257.6522. Found: 1257.6509.

8: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.77 (s, 1 H), 8.61 (s, 2 H), 8.53 (s, 2 H), 8.48 (s, 2 H), 8.19 (d, J=7.8 Hz, 2 H), 8.13 (d, J=8.2 Hz, 2 H), 7.69 (t, J=7.9 Hz, 2 H), 4.62-4.54 (m, 6 H), 3.95-3.87 (m, 6 H), 3.78-3.70 (m, 6 H), 3.65-3.57 (m, 6 H), 3.40

(d, J=2.0 Hz, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 165.2, 147.4, 132.0, 130.1, 130.0, 126.8, 124.8, 121.2, 118.5, 77.2, 71.9, 70.6, 69.1, 64.7, 64.5, 59.1; HR-MS (ESI-TOF): Calcd. For $C_{40}H_{46}N_6O_{12}Na$ $[M+Na]^+$: 825.3071. Found: 825.3151.

4. Anions Binding assay determined by ^{1}H NMR.

4.1 Job's plot curve for binding stoichiometry.

General procedure using compound **1** as an example: A 10 mM solution of the tetrabutyl ammonium chloride in $CDCl_3$ was mixed with a solution of 10 mM compound **1** in $CDCl_3$ in the ratios shown in Table S1 and each sample was analyzed by ^{1}H-NMR.

Table S1 Sample compositions of Job plot for compound **1**.

Sample NO.	μL of compound **1**	μL of Bu_4NCl solution
1	100	900
2	200	800
3	300	700
4	400	600
5	500	500
6	600	400
7	700	300
8	800	200
9	900	100
10	1000	0

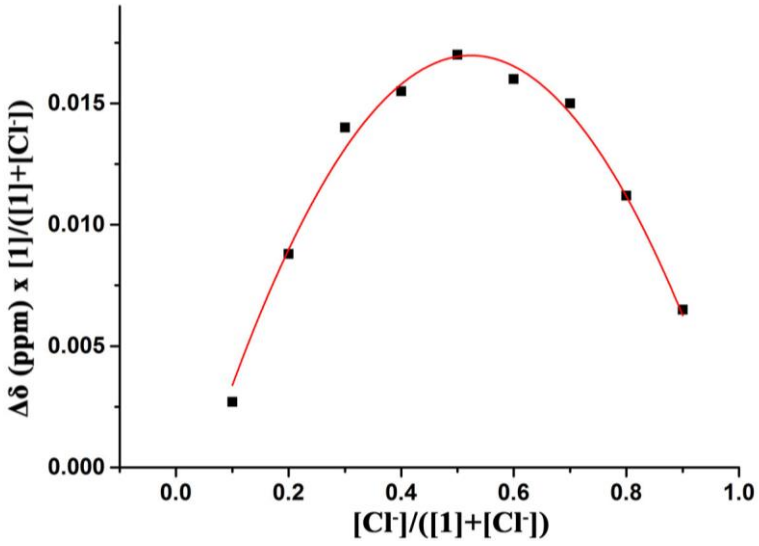


Figure S1 Job analysis of compound **1** with $N(But)_4Cl^-$ at ~8.3 ppm for Hb shift.

4.2 NMR titration for binding constant.

General procedures: The ^{1}H-NMR (CD_3Cl, 400 MHz) titrations were carried out as follows: Taking compound **1** as an example, a solution containing 5.0 mM of compound **1** in CD_3Cl was added aliquots of the corresponding tetra(butyl) ammonium salt while keeping the corresponding compounds' concentration constant. The change in proton Hb shift (Δδ, Hz) was plotted and fitted to a 1:1 model (as the followed exact binding equation Eq.1-8) using Origin 8.0. Only data for Cl^- binding were listed in following figures, and others were summarized as results in Table 1 as shown in main text.

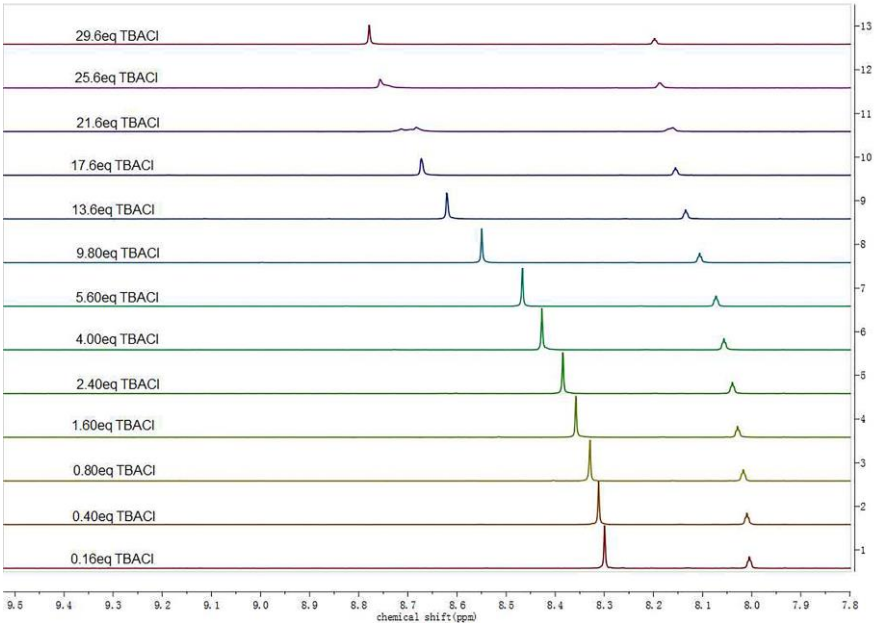


Figure S2 Titration experiment of compound **1** with $N(But)_4Cl$.

From the Job plots a 1:1 stoichiometry between our compounds and tetra(butyl) ammonium salts was found. Hence, the equilibrium constant for the host-guest complexation is given by Eq. 1 and expanded by Eq. 2-3 giving Eq.4.

$$K_a = \frac{[HG]}{[H][G]} \quad \text{(Eq.1)}$$

$$[\mathrm{H}] = [H]_0 - [HG] \quad \text{(Eq. 2)}$$

$$[\mathrm{G}] = [G]_0 - [HG] \quad \text{(Eq.3)}$$

$$K_a = \frac{[HG]}{[H]_0[G]_0 - [HG]([H]_0 + [G]_0 + [HG]^2} \quad \text{(Eq. 4)}$$

Eq. 4 can be rearranged to the second order equation with [HG] as the unknown, and then deduced to Eq. 5.

$$[\mathrm{HG}] = \frac{1}{2}\left\{\left([G]_0 + [H]_0 + \frac{1}{K_a}\right) - \sqrt{\left([G]_0 + [H]_0 + \frac{1}{K_a}\right)^2 - 4[H]_0[G]_0}\right\} \quad \text{(Eq. 5)}$$

From the titration NMR spectra, the complexation was fast on the chemical shift time scale, and therefore the observed signal δ_{obs} is as a weighted average of the signals δ_H and δ_{HG} as express in Eq. 6 with the molar fractions χ_H and χ_{HG} as the weighting factors, which can be further deduced as Eq. 7. Then, δ_{obs}-δ_H is denoted as $\Delta\delta$, δ_{HG}-δ_H is denoted as $\Delta\delta_{max}$, and with these notations, Eq. 8 is obtained as the final exact fitting equation.[1]

$$\delta = \delta_H \chi_H + \delta_{HG} \chi_{HG} \quad \text{Eq. 6}$$

$$\delta = \delta_H + (\delta_{HG} - \delta_H)\frac{[HG]}{[H]_0} \quad \text{Eq. 7}$$

$$\Delta\delta = \frac{\Delta\delta_{\max}}{2[H]_0}\left\{\left([G]_0 + [H]_0 + \frac{1}{K_a}\right) - \sqrt{\left([G]_0 + [H]_0 + \frac{1}{K_a}\right)^2 - 4[H]_0[G]_0}\right\} \quad \text{Eq. 8}$$

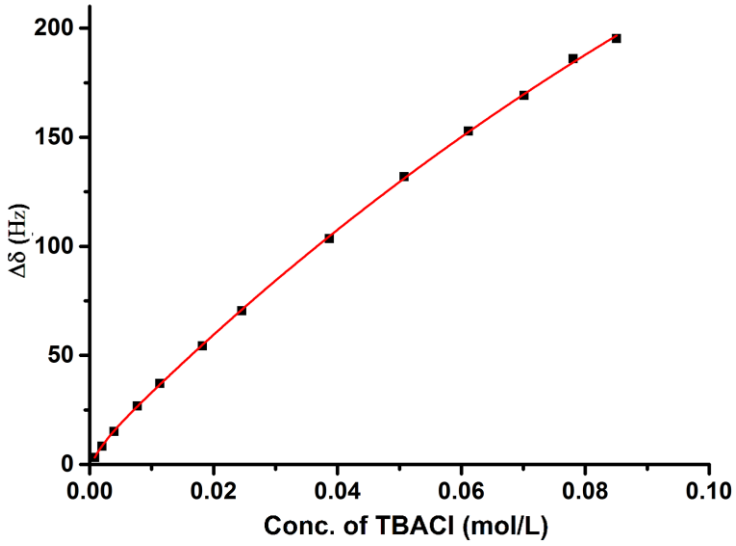


Figure S3 Binding constant determination of 5 mM compound **1** with $N(But)_4Cl$. K = 6.4 (±0.1) M^{-1} with $\Delta\delta_{max}$ = 656.4 Hz.

5. Anion transport.

5.1 Preparation of POPC Vesicles.

A solution of 360 μL EYPC (EYPC, 25 mg/mL, 9 mg) in deacidified chloroform was mixed with 100 μL of cholesterol (10 mg/mL, 1 mg) in deacidified chloroform.

The solvents were evaporated by a slow stream of nitrogen, followed by drying under vacuum for 12 hours. Then the lipid membrane was rehydrated by overtaxing with a 500 μL of salt solution containing of 225 mM $NaNO_3$ and 1 mM N,N′-Dimethyl-9,9′-biacridinium dinitrate (Lucigenin) in 5 mM phosphate buffer (PB, pH=7.2). Then, the suspension was 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 excess Lucigenin was separated from the vesicles by size exclusion column chromatography (SephadexG-25) using 225 mM $NaNO_3$ PB solution (5 mM, pH=7.2) as eluent. The vesicles were further diluted to reach a total lipid concentration of 0.4 mM, assuming 100% retention of lipid during the gel filtration process.

5.2 Lucigenin vesicle fluorescence assay.

In a typical experiment, 3 mL of stock EYPC liposomes (0.4 mM) as prepared above were transferred to a quartz cuvette. The temperature was set at 25 ℃, and the sample was left stirring for 2 min in the fluorescence spectrometer in order for the sample to reach the set temperature. The spectrometer used a 368 nm excitation wavelength and measured the fluorescence at 506 nm. At 50 s and 100 s after the start of the measurement, a 100 μL of PB solution containing of 4 M NaCl and 225 mM $NaNO_3$ and 10 μL THF solution containing transporters in different concentrations were respectively added. After 800s, 100 μL of 5% Triton-X detergent was added to lyse the liposomes. All transport experiments were done in triplicate, and the initial data (initial plateaus and drop by quenching of external Lucigenin) before the addition of transporter (before 100s) were removed. The 3 runs were normalized, averaged and plotted. The concentrated experiments were not stopped until the activity achieved maximum or the appearance of precipitation.

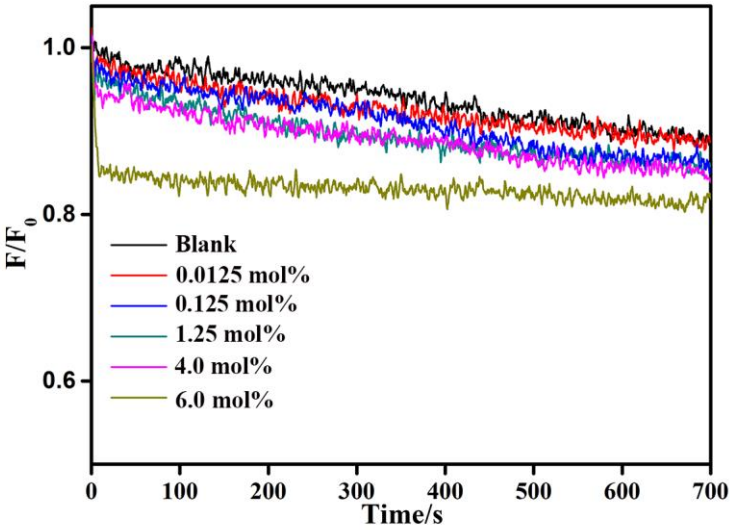


Figure S4 Chloride transport by compound **1** at different molar ratio of transporter to lipid ratios.

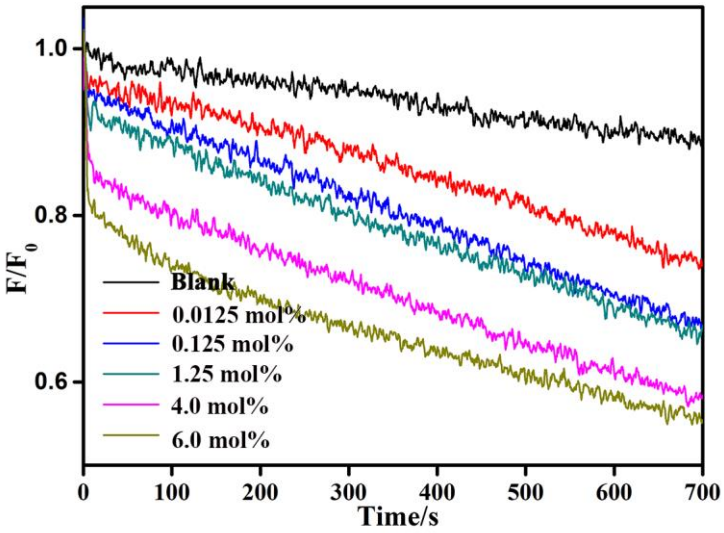


Figure S5 Chloride transport by compound **2** at different molar ratio of transporter to lipid ratios.

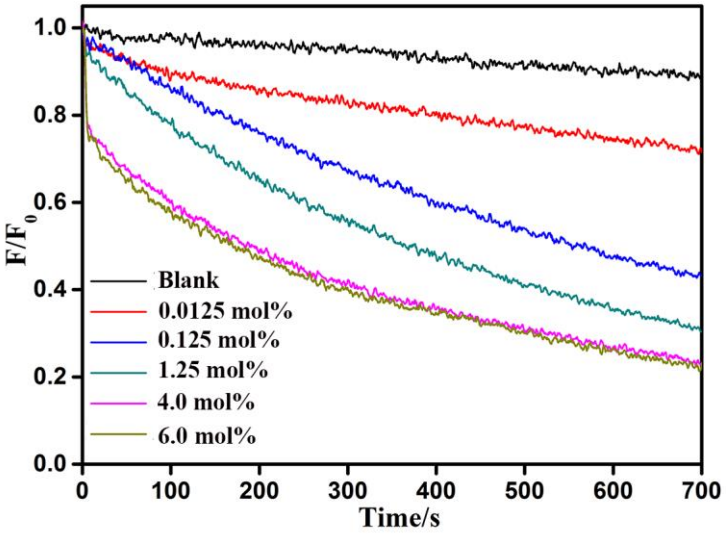


Figure S6 Chloride transport by compound **3** at different molar ratio of transporter to lipid ratios.

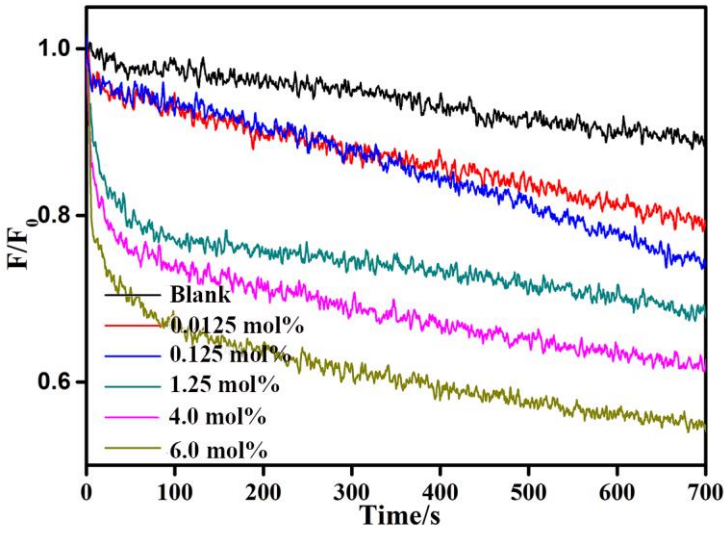


Figure S7 Chloride transport by compound **4** at different molar ratio of transporter to lipid ratios.

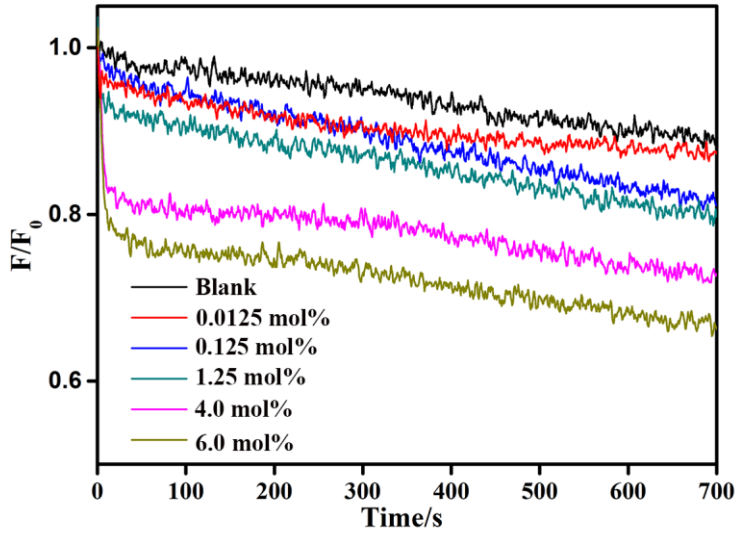


Figure S8 Chloride transport by compound **5** at different molar ratio of transporter to lipid ratios.

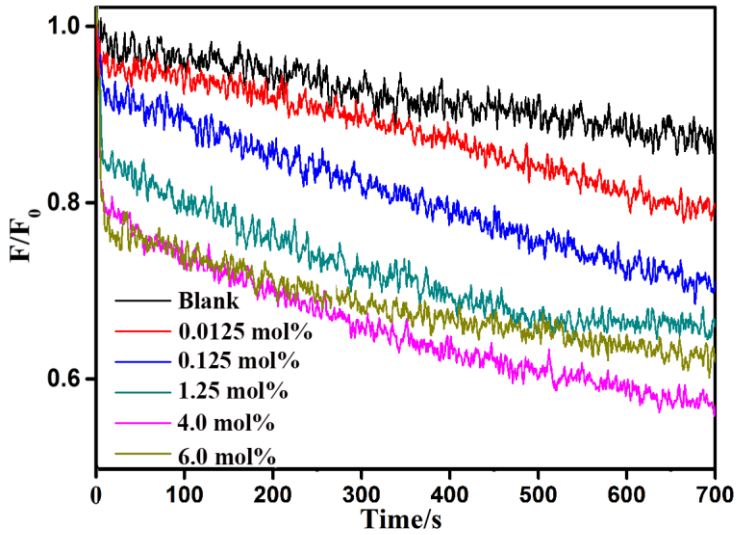


Figure S9 Chloride transport by compound **6** at different molar ratio of transporter to lipid ratios.

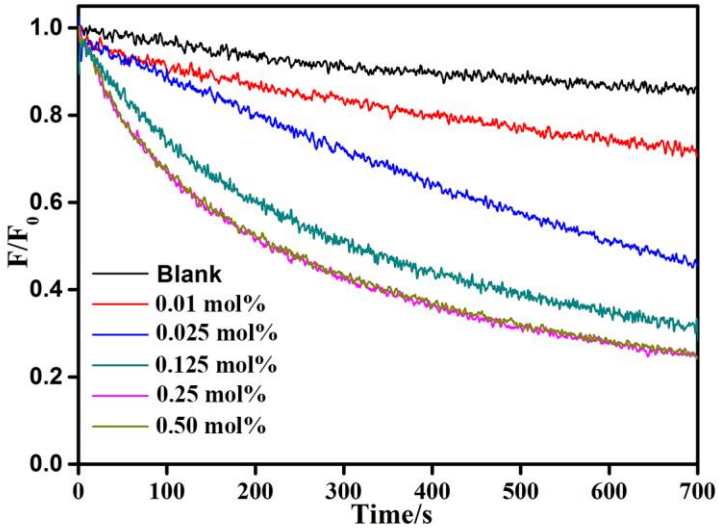


Figure S10 Chloride transport by compound **7** at different molar ratio of transporter to lipid ratios.

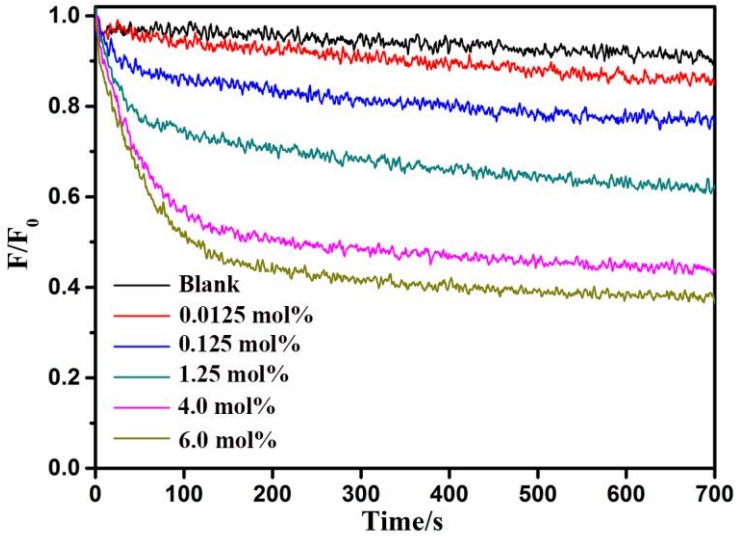


Figure S11 Chloride transport by compound **8** at different molar ratio of transporter to lipid ratios.

5.3 The calculation of initial rates k_{ini} for compounds.

Initial rates were obtained from fluorescence-decay curves (0-700 s) by fitting their inverse (F_0/F) to a double exponential decay function:[2-3]

$$\frac{F_0}{F} = y - ae^{-bt} - ce^{-dt}$$

Differentiating this gives $\frac{d(\frac{F_0}{F})}{dt} = abe^{-bt} - cde^{-dt}$ and substituting t = 0 obtains the initial rate I = ab + cd

The k_{ini} in Table 2 is the specific initial rate which defined as initial slope of F_0/F vs time t (I), devided by the transporter/lipid ratio and averaged over a range of experiments at different ratios.

When we calculated the k_{ini} of the compounds, it was found the linear range of initial rate vs transporter/lipid molar ratio was very narrow for compounds **1-6**. When the burst drop appeared, the initial rate was hard to evaluate, so the k_{ini} of compounds **1-6** was calculated at the concentrations before the appearance of burst drop.

Taking compound **7** as example:

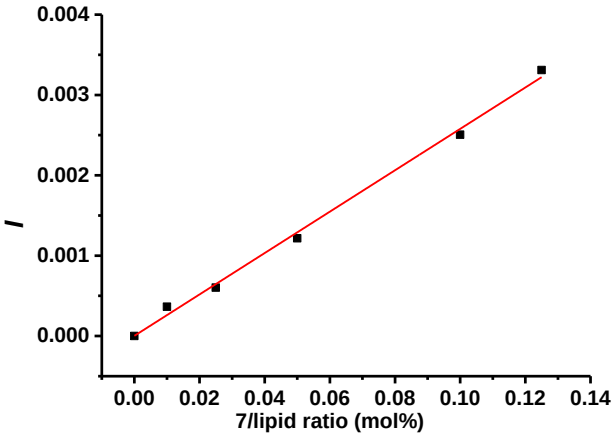


Figure S12 Plot of the initial rate for Cl^- transport against the molar ratio of compound **7** relative to lipid.

The linear relationship between k_{ini} and transporter/lipid molar ratio over the range of 0.01 to 0.125 mol% supports the carrier mechanism transport for compound **7**.

5.4 Cl^- selective electrode assay.

POPC vesicles (5 mL) were prepared as described above in which 489 mM NaCl in 5 mM PB (pH = 7.2) was used as inside solution of vesicles and 489 mM $NaNO_3$ or 162 mM Na_2SO_4 in 5 mM PB as suspension solution. The lipid concentration was quantified at 1 mM for experiments and a chloride selective electrode (EAInstruments Ltd) was used for monitoring. At 50 s, a 10 μL THF solution of transporter at certain concentrations was added to the solution, and at 755 s, the vesicles were lysed with

100 μL 5% Triton-X detergent to determine the final chloride concentration as 100% chloride efflux. Each point represents the average of three trials; THF also was used as a control experiment.

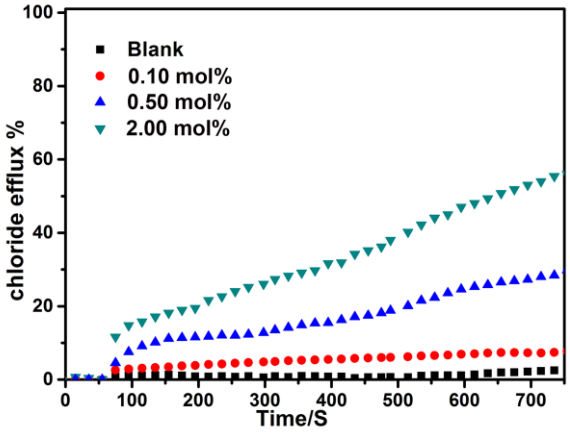


Figure S13 Chloride efflux promoted by compound **3** at different concentrations.

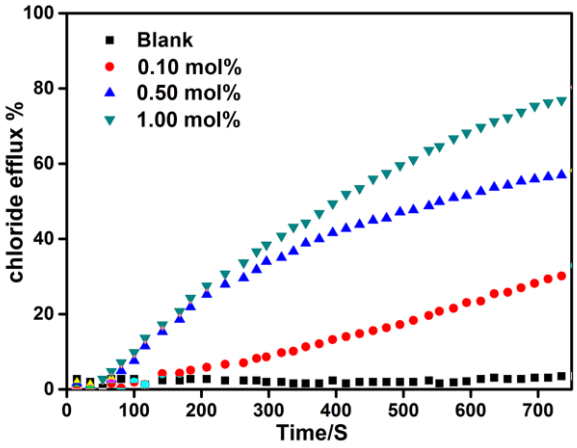


Figure S14 Chloride efflux promoted by compound **7** at different concentrations.

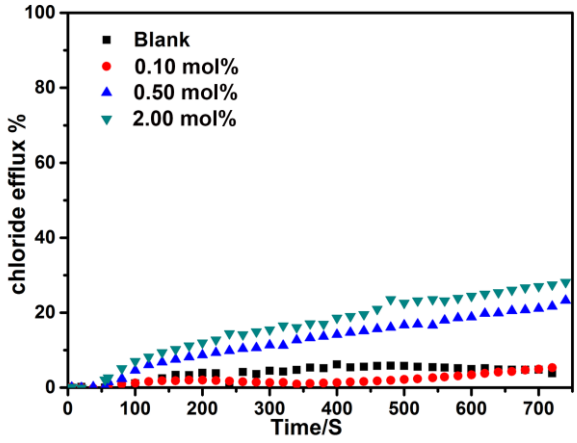


Figure S15 Chloride efflux promoted by compound **8** at different concentrations.

6. Anion selectivity.

6.1 Lucigenin vesicle fluorescence assay.

To test the anion selective transport by the trimmers, transport experiments for compound **7** at 0.25 mol% were repeated with SO_4^{2-} and HCO_3^- as counter ions. The general procedure was followed, in which all 225 mM $NaNO_3$ solution were replaced by either 225 mM Na_2SO_4 or 225 mM $NaHCO_3$ (pH = 8.4)

6.2 Cl^- selective electrode assay.

For HCO_3^- selectivity assay, the process was similar as that for SO_4^{2-} except a solution of $NaHCO_3$ was added at 200s to give a final concentration of 40 mM. Each point represents the average of three trials; THF also was used as a control experiment.

7. Anion transport mechanism: carrier or channel?

7.1 The effect of different level of cholesterol in vesicle.

Changing the amount of cholesterol, in the EYPC/cholesterol membrane, also changes the fluidity of the membrane, which should affect carriers through a change in their mobility. A transmembrane channel, however, should not be affected as they span the whole membrane. Increasing the amount of cholesterol will decrease the fluidity of the membrane and thereby decrease the transport rate of a carrier. Vesicles were prepared as before, but with 10 wt%, 20 wt% of cholesterol.

7.2 U-tube experiments.

In a U-tube experiment the lipid bilayer is substituted with bulk organic phase. The organic phase consisted of 10 mL chloroform and contained 1mM of carrier. A blank chloroform was used as for a control. To one side of the U-tube was added a receiving phase of 488 mM $NaNO_3$ that was buffered to pH 7.2 with 5 mM phosphate salts (5 mL, pH = 7.2). And to another side was added a donating phase containing 488 mM NaCl with 5 mM phosphate salts (5 mL, pH = 7.2). The chloroform phase was stirred at 250 rpm throughout the experiment to ensure efficient diffusion of any carrier-ion complex to the receiving phase. The change in chloride concentration of the receiving phase was monitored with a chloride-selective electrode. Measurements

were then taken every 24 hours for 5 days. The experiments were conducted at room temperature and the data represented the average of 3 trials. The results were shown as below and exhibited that chloride transport through a bulk organic layer is possible, indicating that the compounds function as mobile carriers.

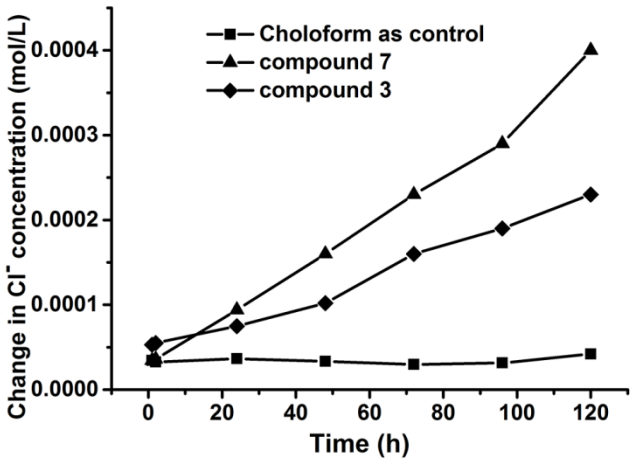


Figure S16 The change in the chloride concentration of the receiving aqueous phase as a function of time from U-tube experiment in chloroform. The concentration for compounds in chloroform was 1 mM.

7.3 Self-assembly of compound 3 induced by anions.

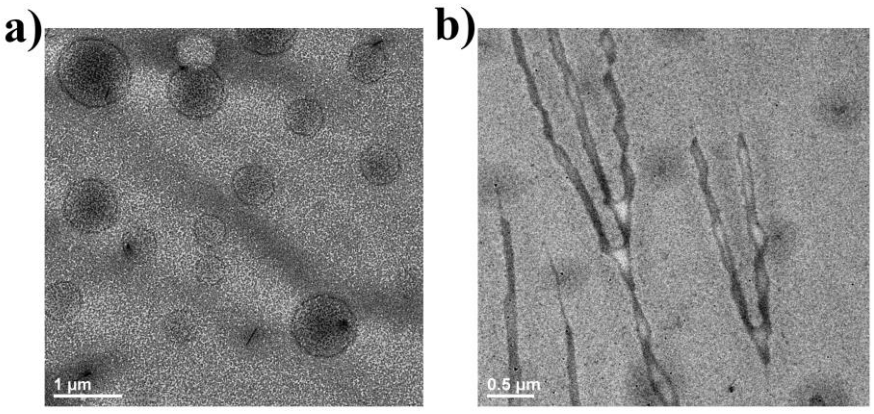


Figure S17 The TEM images of self-assembled compound **3** induced by a) Cl^- (in the presence of TBACl) and b) NO_3^- (in the presence of $TBANO_3$) in $CHCl_3$, a solvent mimic the membrane phase.

References:

1. P. Thordarson, *Chem. Soc. Rev.*, 2011, **40**, 1305-1323.

2. H. Li, H. Valkenier, L. W. Judd, P. R. Brotherhood, S. Hussain, J. A. Cooper, O. Jurček, H. A. Sparkes, D. N. Sheppard, and A. P. Davis, *Nat. Chem.*, 2016, **8**, 24-32.
3. H. Valkenier, L. W. Judd, H. Li, S. Hussain, D. N. Sheppard and A. P. Davis, *J. Am. Chem. Soc.*, 2014, **136**, 12507-12512.