Supporting Information

# Artificial Chloride-Selective Channel: Shape and Function Mimic of the ClC Channel Selective Pore

Wen-Long Huang,<sup>a,b</sup> Xu-Dong Wang,<sup>a,b</sup> Yu-Fei Ao,<sup>a</sup> Qi-Qiang Wang,<sup>a,b,\*</sup> and De-Xian Wang<sup>a,b,\*</sup>

<sup>a</sup> Beijing National Laboratory for Molecular Sciences, CAS Key Laboratory of Molecular Recognition and Function, Institute of Chemistry, CAS, Beijing, 100190, China.

<sup>b</sup> University of Chinese Academy of Sciences, Beijing 100049, China.

E-mail: <u>qiqiangw@iccas.ac.cn</u>, <u>dxwang@iccas.ac.cn</u>

## Contents

1. General information	S2
2. Synthesis procedure	S3
3. NMR titrations	S8
4. Ion transport activity and DPPC assays	S13
5. Planar lipid bilayer experiments	S19
6. Ion selectivity study by planar lipid bilayer experiments	S30
7. Calculation	S38
8. Copies of <sup>1</sup> H and <sup>13</sup> C NMR spectra	S46
9. References	S51

### **1. General Information**

Reagents for synthesis and analysis were purchased from J&K or Sigma-Aldrich. A Mini-Extruder used for vesicle preparation, egg yolk phosphatidylcholine (EYPC), DPPC and 1, 2-diphytanoyl-sn-glycero-3-phosphocholine (DPhPC) were purchased from Avanti Polar Lipids. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on Bruker 400 or 500 MHz NMR spectrometer. Chemical shifts are reported in ppm and referenced to tetramethylsilane (TMS) or the residual solvent resonance. Abbreviations are used in the description of NMR data as follows: chemical shift ( $\delta$ , ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, m = multiplet), coupling constant (*J*, Hz). Melting points are uncorrected. Infrared spectra were recorded on Nicolet-6700 FT-IR spectrometer. Mass spectra were obtained on Bruker APEX-2 (HRMS). Elemental analysis was recorded on Thermo Quest CE Instruments flash EA 1112 analyser. All anhydrous solvents were dried according to standard procedures prior to use. All other major chemicals were obtained from commercial sources and used without further purification.

### 2. Synthesis procedure

#### Synthesis of 5



3<sup>[S1]</sup> (5.11 g, 20 mmol), 4 (17.77 g, 40 mmol) and dried DMF (20 mL) were mixed in a flask. The mixture was heated to 100 °C for 3 h. Then 2-(2-aminoethoxy)ethanol 2 (6.31g, 60 mmol) was added, and the mixture was stirred at 100 °C for 24 h. After cooling to room temperature, DMF was removed by rotary evaporation. The residue dissolved in 100 mL ethyl acetate and 100 mL water, and the two phases were separated. The aqueous phase was extracted with ethyl acetate (2  $\times$ 50 mL). The combined organic phase was washed with brine  $(2 \times 100 \text{ mL})$  and then dried with anhydrous sodium sulfate. After filtration and removal of organic solvent, the residues were chromatographed on a silica gel column (100-200 mesh) with a mixture of dichloromethane and acetone (35:1, v/v) as an eluent to give pure compound 5 as a white solid (4.30 g, 27%). 5: m.p. 77-78 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz)  $\delta$  7.91 (d, J = 8.0 Hz, 1H), 7.87-7.79 (m, 2H), 7.77 (s, 1H), 7.70 (dd, J = 12.9, 8.1 Hz, 2H), 7.36-7.29 (m, 5H), 7.24-7.19 (m, 2H), 7.19-7.13 (m, 3H), 5.27-5.20 (m, 3H), 3.94 (t, J = 5.4 Hz, 2H), 3.76 (t, J = 5.4 Hz, 2H), 3.73-3.67 (m, 2H), 3.67-3.53 (m, 4H), 2.04 (s, 1H);  ${}^{13}C{}^{1}H$  NMR (CDCl<sub>3</sub>, 125 MHz)  $\delta$  168.5, 167.3, 167.2, 166.5, 166.3, 139.0, 138.8, 136.5, 135.9, 135.8, 135.2, 133.0, 132.7, 132.6, 132.2, 128.9, 128.8, 128.7, 128.6, 128.4, 127.2, 125.1, 124.9, 123.9, 123.8, 123.4 (q, J = 286.2 Hz), 72.3, 68.4, 68.0, 65.2 (quint, J = 26.2 Hz), 61.9, 54.1, 38.1, 34.7; IR (KBr) v 3479, 3078, 2920, 2850, 1779, 1717, 1631, 1497, 1386, 1255 cm<sup>-1</sup>; HRMS (ESI<sup>+</sup>): *m/z* calc. for [M+Na]<sup>+</sup> (C<sub>39</sub>H<sub>30</sub>O<sub>8</sub>N<sub>2</sub>F<sub>6</sub>Na<sup>+</sup>) 791.1799, found 791.1793.

### Synthesis of 8



**6**<sup>[S2]</sup> (1.29 g, 4 mmol), TBTU (1.57 g, 4.8 mmol), TEA (809 mg, 8 mmol) and dried DCM (200 mL) were mixed in a flask. After 15 mins, 5 (3.07 g, 4 mmol) was added. The mixture was heated to reflux for 6.5 d. After cooling to room temperature, DCM was removed by rotary evaporation. The residue dissolved in ethyl acetate and then washed with water and brine two times respectively. After removal of organic solvent, EtOH (300 mL) and PPTS (410 mg, 1.6 mmol) were added to the residue. The mixture was heated to reflux for 9 h. After cooling to room temperature, EtOH was removed by rotary evaporation. The residue dissolved in ethyl acetate, washed with water and brine two times respectively, and then dried with anhydrous sodium sulfate. After filtration and removal of organic solvent, the residue was chromatographed on a silica gel column (100-200 mesh) with a mixture of dichloromethane and methanol (120:1, v/v) as an eluent to give pure compound 8 as a white solid (1.73 g, 47%). 8: m.p. 98-99 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz) δ 7.82 (d, J = 8.0 Hz, 1H), 7.79-7.71 (m, 3H), 7.71-7.60 (m, 2H), 7.40-7.28 (m, 5H), 7.24-7.08 (m, 5H), 7.00 (d, J = 2.3 Hz, 2H), 6.55 (br, 2H), 6.38 (t, J = 2.3 Hz, 1H), 5.34-5.17 (m, 3H), 4.36 (t, J = 5.0 Hz, 2H), 3.96 (t, J = 5.5 Hz, 2H), 3.86 (t, J = 5.4 Hz, 2H), 3.80 (t, J = 4.5 Hz, 2H), 3.69-3.49 (m, 2H); <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 125 MHz)  $\delta$  168.9, 167.8, 167.5, 167.0, 166.5, 166.2, 157.3, 138.9, 138.8, 136.4, 136.0, 135.8, 135.0, 132.7, 132.4, 132.0, 128.9, 128.8, 128.78, 128.7, 128.4, 127.2, 125.1, 125.0, 124.0, 123.9, 123.4 (q, J = 286.2 Hz), 109.0, 107.6, 68.7, 68.23, 68.17, 65.2 (quint, J = 26.2 Hz), 64.2, 54.2, 38.2, 34.7; IR (KBr) v 3412, 3078, 2947, 2872, 1779, 1717, 1602, 1454,

1386, 1255, 1212 cm<sup>-1</sup>; HRMS (APCI<sup>-</sup>): m/z calc. for [M-H]<sup>-</sup> (C<sub>46</sub>H<sub>33</sub>O<sub>11</sub>N<sub>2</sub>F<sub>6</sub><sup>-</sup>) 903.1994, found 903.2019.

Synthesis of 9



At room temperature, cyanuric chloride 7 (1.11 g, 6 mmol) and acetone (40 mL) were mixed in a two-neck flask. The solution of 5 (3.07 g, 4 mmol) and 2,4,6-collidine (594 mg, 4.8 mmol) in acetone (40 mL) was then added dropwise within 2 h. The resulting mixture was stirred for 32 h at room temperature. Acetone was removed by rotary evaporation. The residue dissolved in ethyl acetate (200 mL) and washed with water and brine two times respectively, and then dried with anhydrous sodium sulfate. After filtration and removal of organic solvent, the residue was chromatographed on a silica gel column (100-200 mesh) with a mixture of petroleum ether and acetone (4:1, v/v) as an eluent to give pure compound 9 as a white solid (2.74 g, 74%). 9: m.p. 75-76 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 7.90 (d, J = 8.0 Hz, 1H), 7.86-7.80 (m, 2H), 7.77 (s, 1H), 7.70 (t, J = 8.5 Hz, 2H), 7.37-7.28 (m, 5H), 7.24-7.11 (m, 5H), 5.27-5.20 (m, 3H), 4.62 (t, J = 4.5 Hz, 2H), 3.91 (t, J = 5.4 Hz, 2H), 3.88-3.81 (m, 2H), 3.78 (t, J = 5.4 Hz, 2H), 3.66-3.53 (m 2H);  ${}^{13}C{}^{1}H{}$ NMR (CDCl<sub>3</sub>, 125 MHz) δ 172.6, 171.2, 168.6, 167.1, 167.0, 166.5, 166.3, 139.0, 138.8, 136.5, 136.0, 135.8, 135.2, 133.0, 132.7, 132.6, 132.2, 128.9, 128.8, 128.7, 128.6, 128.4, 127.2, 125.1, 124.9, 123.9, 123.8, 123.5 (q, J = 286.2 Hz), 69.1, 68.1, 68.01, 67.98, 65.2 (quint, J = 26.2 Hz), 54.1, 37.7, 34.7; IR (KBr) v 3070, 3028, 2919, 1779, 1720, 1626, 1544, 1511, 1439, 1386, 1255 cm<sup>-1</sup>; HRMS (APCI<sup>+</sup>): *m/z* calc. for  $[M+H]^+$  (C<sub>42</sub>H<sub>30</sub>O<sub>8</sub>N<sub>5</sub>Cl<sub>2</sub>F<sub>6</sub><sup>+</sup>) 916.1370, found 916.1313.

### Synthesis of 10



Potassium carbonate (332 mg, 2.4 mmol) and acetonitrile (34 mL) were mixed in a two-neck flask and heated to reflux. The solution of 8 (905 mg, 1 mmol) and 9 (917 mg, 1 mmol) in acetonitrile (34 mL) was then added dropwise within 0.5 h. The resulting mixture was refluxed for another 4 h and cooled to room temperature. Acetonitrile was removed by rotary evaporation. The residue dissolved in ethyl acetate (100 mL) and washed with water and brine two times respectively, and then dried with anhydrous sodium sulfate. After filtration and removal of organic solvent, the residue was chromatographed on a silica gel column (100-200 mesh) with a mixture of dichloromethane and ethyl acetate (10:1, v/v) as an eluent to give pure compound **10** as a white solid (716 mg, 40%). **10:** m.p. 130-131 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz) δ 7.89 (d, J = 8.0 Hz, 2H), 7.85-7.75 (m, 14H), 7.73-7.62 (m, 8H), 7.51 (d, J = 2.2 Hz, 4H), 7.36-7.28 (m, 20H), 7.23-7.10 (m, 20H), 6.94 (t, J = 2.3 Hz, 2H), 5.27-5.20 (m, 12H), 4.61 (t, J = 5.0 Hz, 4H), 4.33 (t, J = 4.7 Hz, 4H), 3.96-3.83 (m, 12H), 3.83-3.71 (m, 12H), 3.67-3.50 (m, 8H); <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 125 MHz) δ174.4, 173.1, 168.5, 167.2, 167.1, 167.0, 166.9, 166.50, 166.48, 166.3, 164.3, 151.9, 139.0, 138.9, 138.74, 138.69, 136.5, 136.0, 135.8, 135.2, 133.1, 133.0, 132.9, 132.8, 132.7, 132.6, 132.5, 132.2, 128.9, 128.8, 128.7, 128.6, 128.3, 127.1, 125.02, 124.99, 124.89, 124.87, 124.0, 123.9, 123.80, 123.78, 123.4 (q, *J* = 286.2 Hz), 121.2, 120.8, 68.4, 68.3, 68.2, 68.1, 67.98, 67.96, 65.2 (quint, *J* = 26.2 Hz), 64.7, 54.05, 54.03, 37.7, 37.6, 34.7; IR (KBr) v 3066, 2921, 1779, 1722, 1717, 1627, 1578, 1558, 1497, 1443, 1386, 1255 cm<sup>-1</sup>; HRMS (ESI<sup>+</sup>): *m/z* calc. for [M+Na]<sup>+</sup> (C<sub>176</sub>H<sub>122</sub>O<sub>38</sub>N<sub>14</sub>F<sub>24</sub>Na<sup>+</sup>) 3517.7553, found 3517.7583. Anal. Calcd. for C<sub>176</sub>H<sub>122</sub>O<sub>38</sub>N<sub>14</sub>F<sub>24</sub> + CHCl<sub>3</sub>: C, 58.79; H, 3.43; N, 5.42. Found: C, 58.65; H, 3.15; N, 5.24.

#### Synthesis of 1



At room temperature, 10 (699 g, 0.2 mmol), 10% Pd/C (80 mg) and THF (100 mL) were mixed in a two-neck flask. The mixture was stirred for 24 h under H<sub>2</sub> balloon. After filtration with siliceousearth, the filtrate was concentrated. The residue was recrystallized with dichloromethane and methanol to give pure compound 1 as a white solid (488 mg, 77%). 1: m.p. 180-181 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz) δ 7.90 (d, J = 8.0 Hz, 2H), 7.84-7.64 (m, 22H), 7.45 (d, J = 1.8 Hz, 4H), 7.24-7.08 (m, 20H), 6.90 (s, 2H), 5.28-5.15 (m, 4H), 4.58 (s, 4H), 4.36-4.23 (m, 4H), 3.98-3.44 (m, 32H); <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 125 MHz) δ 174.2, 173.5, 173.4, 173.21, 173.19, 173.0, 167.3, 167.2, 167.1, 166.40, 166.39, 166.37, 166.3, 166.2, 164.3, 151.8, 139.1, 139.0, 138.8, 138.7, 136.4, 136.0, 135.7, 135.6, 133.0, 132.9, 132.8, 132.7, 132.6, 132.5, 132.4, 132.1, 128.8, 127.2, 125.2, 125.1, 125.0, 124.02, 123.97, 123.8, 123.4 (q, J = 286.2 Hz), 121.2, 120.8, 68.4, 68.3, 68.0, 65.2 (quint, J = 26.2 Hz), 64.7, 53.52, 53.50, 37.8, 37.6, 34.4; IR (KBr) v 3479, 3065, 2946, 1779, 1738, 1733, 1717, 1699, 1625, 1575, 1568, 1497, 1335, 1255, 1211 cm<sup>-1</sup>; HRMS (ESI<sup>-</sup>): m/z calc. for [M-3H]<sup>3-</sup>  $(C_{148}H_{95}O_{38}N_{14}F_{24}^{3-})$  1043.8522, found 1043.8562. Anal. Calcd. for  $C_{148}H_{98}O_{38}N_{14}F_{24}$ : C, 56.68; H, 3.15; N, 6.25. Found: C, 56.39; H, 3.22; N, 6.17.

### 3. NMR titrations<sup>[S3]</sup>

<sup>1</sup>H NMR titrations were performed in CDCl<sub>3</sub> or CD<sub>3</sub>CN at room temperature. The solutions of **1** in CDCl<sub>3</sub> or CD<sub>3</sub>CN, and stock solutions of each guest in CDCl<sub>3</sub> or CD<sub>3</sub>CN were prepared respectively. Aliquots of guest solution were added directly to an NMR tube containing the host solution. All proton signals were referenced to the TMS or solvent residual peak. The association constants *K* were calculated by *Bindfit* v0.5 (for this program, please see: <u>http://app.supramolecular.org/bindfit/</u>). The 1:2 stoichiometry was verified by a Job's plot experiment for binding of **1** with Cl<sup>-</sup> (Figure S3c).

**Table S1.** Association constants *K* of **1** with  $Bu_4N^+Cl^-$  and  $Bu_4N^+Br^-$  calculated by *Bindfit v0.5* with a host-guest stoichiometry of 1:2.

	Bu <sub>4</sub> N <sup>+</sup> Cl <sup>-</sup>	$Bu_4N^+Br^-$
$K_1 (M^{-1})$	$136.3\pm3.7$	$21.3 \pm 1.9$
$K_2 (M^{-1})$	$147.5\pm4.2$	$23.9\pm1.7$



**Figure S1.** <sup>1</sup>H NMR titration of **1** (1 × 10<sup>-3</sup> mol/L in CDCl<sub>3</sub>) upon addition of different amounts of tetrabutylammonium chloride (from bottom to top: 0, 0.2, 0.4, 0.6, 0.8, 1.0, 1.2, 1.4, 1.6, 1.8, 2.0, 2.2, 2.3, 2.5, 2.7, 2.9, 3.1, 3.3, 3.5, 3.7, 3.8, 4.0, 4.2, 4.4, 4.6 × 10<sup>-3</sup> mol/L). Upon addition of chloride, the  $\alpha$ -proton on phenylalanine moiety (H14, H14') moved upfield, indicating interaction of the carboxylic acid site with chloride. Some benzene imide protons (H8-H13, H8'-H13') also shifted upfield, probably a result of shielding effect of the approaching chloride upon anion- $\pi$  contacting with the electron-deficient imide. The continuous downfield movement of the inner proton (H1) within the macrocyclic V-shaped cavity suggested anion- $\pi$  interaction between the triazine and chloride, in line with our previous observations. For clarity, partial spectra are shown.



**Figure S2.** <sup>1</sup>H NMR titration of **1** ( $1 \times 10^{-3}$  mol/L in CDCl<sub>3</sub>) upon addition of different amounts of tetrabutylammonium bromide (from bottom to top: 0, 1.0, 2.0, 3.0, 4.0, 5.0, 10.0, 11.0, 11.5, 12.5, 13.5, 14.5, 15.5, 17.0, 19.0, 21.0, 23.0, 24.0, 25.0, 26.5, 28.0, 30.0, 32.0, 33.5, 35.0 × 10<sup>-3</sup> mol/L). For clarity, partial spectra are shown.





**Figure S3.** Fitting plots of the chemical shifts of proton H1 of **1** with increasing concentration of (a) Bu<sub>4</sub>NCl and (b) Bu<sub>4</sub>NBr using *Bindfit v0.5* program. (c) Job-plot for complex between **1** and Cl<sup>-</sup>.





**Figure S4.** <sup>1</sup>H NMR titration of **1** (1 × 10<sup>-3</sup> mol/L in CD<sub>3</sub>CN) upon addition of different amounts of various cationic salts. (a) NaBPh<sub>4</sub>, from bottom to top: 0, 2.0, 4.0, 6.0, 8.0, 12.0, 19.0, 36.0, 52.0 × 10<sup>-3</sup> mol/L. (b) NaPF<sub>6</sub>, from bottom to top: 0, 2.0, 4.0, 6.0, 8.5, 13.0, 20.0, 37.0, 53.0 × 10<sup>-3</sup> mol/L. (c) KPF<sub>6</sub>, from bottom to top: 0, 2.0, 4.0, 6.0, 7.5, 13.0, 21.0, 37.0, 51.0 × 10<sup>-3</sup> mol/L. In all spectra, the chemical shift changes of the essential protons are very small ( $\Delta\delta < 0.01$  ppm), showing weak binding ability towards the cations. KBPh<sub>4</sub> was not used due to its poor solubility.

### 4. Ion transport activity and DPPC assays <sup>[S3, S4]</sup>

General preparation of Lucigenin or HPTS containing EYPC-LUVs. Egg yolk phosphatidylcholine (EYPC, 25 mg) was dissolved in EtOH/CHCl<sub>3</sub> (2 mL, v/v 1:1). The solution was evaporated under reduced pressure on a rotary evaporator (40 °C) to give a thin film, and the resulting thin film was dried under high vacuum for overnight to remove the residual solvent. The lipid film was hydrated in 1.0 mL buffer solution (10 mM HEPES + 100 mM NaNO<sub>3</sub> + 1 mM Lucigenin, pH = 7.0; 10 mM HEPES + 100 mM NaCl + 1 mM HPTS, pH = 7.0) for 20 mins at room temperature. The suspension was submitted to freeze-thaw for 5 cycles (with liquid nitrogen and 50 °C water bath, respectively), and high-pressure extrusion at room temperature (21 times extrusions through polycarbonate membrane with pore diameter of 100 nm). The LUV suspension was separated from extravesicular Lucigenin or HPTS dye by size exclusion chromatography (Sephadex G-50, mobile phase: 10 mM HEPES + 100 mM NaNO<sub>3</sub>, pH = 7.0; 10 mM HEPES + 100 mM NaCl, pH = 7.0).

General preparation of Lucigenin containing DPPC-LUVs. DPPC (25 mg) was dissolved in MeOH/CHCl<sub>3</sub> (2 mL, v/v 1:1). The solution was evaporated under reduced pressure on a rotary evaporator (50 °C) to give a thin film, and the resulting thin film was dried under high vacuum for overnight to remove the residual solvent. The lipid film was hydrated in 1.0 mL buffer solution (10 mM HEPES + 100 mM NaNO<sub>3</sub> + 1 mM Lucigenin, pH = 7.0) for 20 mins at 50 °C. The suspension was submitted to freeze-thaw for 5 cycles (with liquid nitrogen and 50 °C water bath, respectively), and high-pressure extrusion at 65 °C (21 times extrusions through polycarbonate membrane with pore diameter of 100 nm). The LUV suspension was separated from extravesicular Lucigenin dye by size exclusion chromatography (Sephadex G-50, mobile phase: 10 mM HEPES + 100 mM NaNO<sub>3</sub>, pH = 7.0).

Lucigenin fluorescence assay. 50  $\mu$ L Lucigenin-loaded EYPC-LUV solution was suspended in 1950  $\mu$ L of the buffer solution (10 mM HEPES + 100 mM NaCl,

KCl or NaBr, pH = 7.0) and placed into a quartz cuvette at 25 °C. The intravesicular Lucigenin fluorescence intensity ( $I_t$ ,  $\lambda_{ex} = 369$  nm,  $\lambda_{em} = 505$  nm) was measured over time. THF or the solution of compound **1** or **10** in THF (25 µL) was added at t = 50 s ( $I_0$ ), and then triton X-100 (25 µL, 10% in water) was added at 500 s ( $I_{\infty}$ ). The fluorescence intensity  $I_t$  was normalized to fractional intensity  $I_f$  using equation (S1):

$$I_f = (I_t - I_\infty)/(I_0 - I_\infty) \tag{S1}$$

Where  $I_0$  is the fluorescence intensity after addition of THF or compounds, and  $I_{\infty}$  is the fluorescence intensity after addition of triton X-100.

The effective concentration  $EC_{50}$  and the Hill coefficient *n* were obtained by Hill equation (S2):

$$Y = Y_{\infty} + (Y_0 - Y_{\infty}) / [1 + (c / EC_{50})^n]$$
(S2)

Where *Y* is the  $I_f$  value at 300 s,  $Y_0$  is *Y* in the absence of compound,  $Y_\infty$  is *Y* with excess compound, and *c* is the compound concentration in the cuvette.

The molar ratio of 1 to lipid was obtained through dividing  $EC_{50}$  ( $\mu M$ ) by the concentration ( $\mu M$ ) of lipid in the quartz cuvette.



Figure S5. Evaluation of the ion transport activity of compound 1 and 10 by Lucigenin $\subset$ EYPC-LUV fluorescence assay in KCl buffer solution (the final concentration for 1 and 10 is 2  $\mu$ M.).



Evaluation of  $EC_{5\theta}$  of 1 in different buffer solutions

**Figure S6.** Evaluation of the ion transport activity of **1** in varied concentrations by Lucigenin⊂EYPC-LUV fluorescence assay, and Hill fit of the normalized intensities at 300 s.

Table S2. I	EC50(µM), mol%	of transporter to	lipid and Hill	coefficient n	of 1 in NaCl,
KCl, NaBr	buffer solution.				

		NaCl	KCl	NaBr
	EC <sub>50</sub>	2.00±0.04	1.50±0.05	1.76±0.07
1	mol%	1.49	1.12	1.31
	n	4.3±0.3	3.5±0.3	4.3±0.7

**HPTS assay.**<sup>[S5]</sup> 50 µL HPTS-loaded vesicle solution was suspended in 1950 µL of the buffer solution (solution 1: 10 mM HEPES + 100 mM NaX, X = Cl, Br, I, NO<sub>3</sub>, ClO<sub>4</sub>, pH = 7.0; solution 2: 10 mM HEPES + 100 mM MCl, M = Li, Na, K, Rb, Cs, pH = 7.0) and placed into a quartz cuvette at 25 °C. The intravesicular HPTS fluorescence intensity ( $\lambda_{ex1}$  = 405 nm,  $\lambda_{em}$  = 510 nm,  $I_{t(405)}$ ;  $\lambda_{ex2}$  = 460 nm,  $\lambda_{em}$  = 510 nm,  $I_{t(460)}$ ; ratio fluorescence intensities  $F_t = I_{t(460)}/I_{t(405)}$ ) was measured over time during the addition of base (20 µL NaOH (0.5 M) for creating pH gradient) at t = 50 s, THF or THF solution of 1 (25 µL) at t = 150 s, and 10% Trion X-100 (25 µL) at t = 450 s, respectively. Fluorescence time courses were normalized to fractional emission intensity I<sup>n</sup> using equation (S3):

$$\mathbf{I}^{\mathbf{n}} = (F_t - F_\theta) / (F_\infty - F_\theta)$$
 (S3)

Where  $F_{\theta}$  is the ratio fluorescence intensity after addition of **1**, and  $F_{\infty}$  is ratio fluorescence intensity after addition of Triton X-100. The baseline (THF only)  $I^{n}_{0}$  was then subtracted from  $I^{n}$  to give I (S4):

$$\mathbf{I} = \mathbf{I}^{\mathbf{n}} - \mathbf{I}^{\mathbf{n}}_{0} \tag{S4}$$

The obtained I was further normalized into fractional HPTS emission  $I_F$  using equation (S5)

$$I_F = I / I_{MAX}$$
(S5)

where  $I_{MAX}$  is a reference emission for the varied parameter of interest.

The time axis was normalized according to Equation (S6):

$$t = t - 150$$
 (S6)



Figure S7. (a) Normalized anion transport activities of 1 (2  $\mu$ M) with varied extravesicular anions NaX (10 mM HEPES, 100 mM NaX, X = Cl, Br, I, NO<sub>3</sub>, ClO<sub>4</sub>, pH = 7.0) by HPTS⊂EYPC-LUV fluorescence assay. Background activities without 1 were subtracted after calibration. (b) HPTS assay for anion selectivity. Fractional activity Y was relative to NaCl.



Figure S8. (a) Normalized cation transport activities of 1 (2  $\mu$ M) with varied extravesicular cations MCl (10 mM HEPES, 100 mM MCl, M = Li, Na, K, Rb, Cs, pH = 7.0) by HPTS⊂EYPC-LUV fluorescence assay. Background activities without 1 were subtracted after calibration. (b) HPTS assay for cation selectivity. Fractional activity Y was relative to NaCl.

**DPPC assay.** 50  $\mu$ L Lucigenin-loaded DPPC-LUV solution was suspended in 1950  $\mu$ L of NaCl buffer solution (10 mM HEPES + 100 mM NaCl, pH = 7.0) and placed into a quartz cuvette at 25 °C. The intravesicular Lucigenin fluorescence intensity ( $I_t$ ,  $\lambda_{ex}$  = 369 nm,  $\lambda_{em}$  = 505 nm) was measured over time at 25 °C. THF or the solution of compound **1** in THF (25  $\mu$ L) was added at t = 50 s ( $I_0$ ), and then triton X-100 (25 µL, 10% in water) was added at 300 s ( $I_{\infty}$ ). The fluorescence intensity  $I_t$  was normalized to fractional intensity  $I_f$  using equation (S7):

$$I_f = (I_t - I_\infty)/(I_0 - I_\infty)$$
(S7)

Where  $I_0$  is the fluorescence intensity after addition of THF or compound, and  $I_{\infty}$  is the fluorescence intensity after addition of triton X-100.

For DPPC assay at 45 °C, the intravesicular Lucigenin fluorescence intensity was measured over time at 45 °C. The other processes are the same as that mentioned above.

### **DPPC test results**



**Figure S9.** Cl<sup>-</sup> transport by **1** in Lucigenin-loaded DPPC-LUV at 25 °C and 45 °C, the molar ratio of **1** to lipid is 1:112.

### 5. Planar lipid bilayer experiments<sup>[S6]</sup>

The chloroform solution of 1,2-diphytanoyl-sn-glycero-3-phosphocholine (DPhPC, 25 mg/mL, 10 µL) was evaporated using nitrogen gas and dissolved in *n*-decane (25  $\mu$ L). 0.5  $\mu$ L of the *n*-decane solution was painted onto the aperture of the Delrin cup (diameter =  $200 \mu m$ , Warner Instruments) and the *n*-decane was removed with nitrogen gas. In a traditional planar lipid bilayer conductance measurement experiment, the chamber (cis side) and the Delrin cup (trans side) were filled with 1.0 M KCl aqueous solution (1.0 mL). Ag-AgCl electrodes were placed into the two solutions with the trans side grounded. Planar lipid bilayer was formed by painting  $0.5 \ \mu L$  of the above mentioned *n*-decane solution around the pretreated aperture. The formation of planar lipid bilayer was confirmed by capacitance value ranging from 80 to 120 pF. THF or compound 1 in THF (0.5 µL) was added to the *cis* chamber to reach a final concentration of around 10<sup>-7</sup> M, and the solution was stirred for about five minutes. Then the baseline and current signals were recorded at different holding potentials in a Faraday cage, amplified with BC-535 bilayer clamp amplifier (Warner Instruments), low-pass filtered with an 8-pole Bessel filter at 1 kHz (LPF-8, Warner Instruments), A-D converted (1550B, Axon Instruments), and sampled with a sample interval at 10 kHz by Clampex 10.6, The data were analyzed by Clampfit 10.6 with a digital filter at 100 Hz. All the measurements were performed at room temperature (ca. 25 °C).



**Figure S10.** Schematic diagram of the planar lipid bilayer experiments. Experimental conditions: DPhPC in *n*-decane (10 mg/mL); *cis/trans* = 1.0 M/1.0 M KCl solution(1 mL/1 mL); applied voltages: 150 mV, 100 mV, 60 mV, 0 mV, -60 mV, -100 mV, -150 mV; addition: 0.5  $\mu$ L THF solution of channel molecule **1** (1 mM), final concentration is 0.5  $\mu$ M.



**Figure S11.** Current traces of channel molecule 1 at 150 mV in symmetrical KCl solutions (*cis/trans* = 1.0 M/1.0 M), final concentration is 0.5  $\mu$ M. Top, full spectra; bottom, enlarged spectra.



Figure S12. Current traces of channel molecule 1 at 100 mV in symmetrical KCl solutions (*cis/trans* = 1.0 M/1.0 M), final concentration is 0.5  $\mu$ M. Top, full spectra; bottom, enlarged spectra.



**Figure S13.** Current traces of channel molecule **1** at 60 mV in symmetrical KCl solutions (*cis/trans* = 1.0 M/1.0 M), final concentration is 0.5  $\mu$ M. Top, full spectra; bottom, enlarged spectra.



**Figure S14.** Current trace of channel molecule **1** at 0 mV in symmetrical KCl solutions (*cis/trans* = 1.0 M/1.0 M), final concentration is  $0.5 \mu$ M. Full spectra.



**Figure S15.** Current traces of channel molecule 1 at -60 mV in symmetrical KCl solutions (*cis/trans* = 1.0 M/1.0 M), final concentration is 0.5  $\mu$ M. Top, full spectra; bottom, enlarged spectra.



**Figure S16.** Current traces of channel molecule 1 at -100 mV in symmetrical KCl solutions (*cis/trans* = 1.0 M/1.0 M), final concentration is 0.5  $\mu$ M. Top, full spectra; bottom, enlarged spectra.



**Figure S17.** Current traces of channel molecule 1 at -150 mV in symmetrical KCl solutions (*cis/trans* = 1.0 M/1.0 M), final concentration is 0.5  $\mu$ M. Top, full spectra; bottom, enlarged spectra.

	Current (pA)							
Entry	150	100	60	0	-60	-100	-150	<i>g</i> (pS)
	(mV)	(mV)	(mV)	(mV)	(mV)	(mV)	(mV)	
1	3.04	2.04	0.82	0	-0.79	-1.94	-3.20	19.8±1.0
2	3.18	1.96	0.79	0	-0.90	-2.00	-3.25	20.0±1.0
3	3.53	2.10	0.79	0	-0.81	-2.31	-3.36	21.7±1.0
4	-	1.77	1.02	0	-0.80	-1.94	-3.05	18.7±1.0
5	3.14	2.0	0.70	0	-0.94	-2.18	-3.77	21.5±1.0
6	3.60	2.01	1.02	0	-1.22	-2.19	-3.78	23.0±1.0

**Table S3.** The current under the corresponding voltage and slope conductance g in symmetrical KCl solutions (*cis/trans* = 1.0 M/1.0 M, the final concentration of **1** is 0.5  $\mu$ M).



**Figure S18.** Current trace of channel molecule **1** at 100 mV in symmetrical KCl solutions (*cis/trans* = 1.0 M/1.0 M), final concentration is 0.05  $\mu$ M. Full spectra.



**Figure S19.** Current trace of channel molecule **1** at 80 mV in symmetrical KCl solutions (*cis/trans* = 1.0 M/1.0 M), final concentration is 0.05  $\mu$ M. Full spectra.



**Figure S20.** Current trace of channel molecule **1** at 60 mV in symmetrical KCl solutions (*cis/trans* = 1.0 M/1.0 M), final concentration is  $0.05 \mu$ M. Full spectra.



**Figure S21.** Current trace of channel molecule **1** at 40 mV in symmetrical KCl solutions (*cis/trans* = 1.0 M/1.0 M), final concentration is  $0.05 \mu$ M. Full spectra.



**Figure S22.** Current trace of channel molecule **1** at 20 mV in symmetrical KCl solutions (*cis/trans* = 1.0 M/1.0 M), final concentration is  $0.05 \mu$ M. Full spectra.



**Figure S23.** Current trace of channel molecule 1 at 0 mV in symmetrical KCl solutions (*cis/trans* = 1.0 M/1.0 M), final concentration is  $0.05 \mu$ M. Full spectra.



**Figure S24.** Current trace of channel molecule 1 at -20 mV in symmetrical KCl solutions (*cis/trans* = 1.0 M/1.0 M), final concentration is  $0.05 \mu$ M. Full spectra.



**Figure S25.** Current trace of channel molecule **1** at -40 mV in symmetrical KCl solutions (*cis/trans* = 1.0 M/1.0 M), final concentration is  $0.05 \mu$ M. Full spectra.



**Figure S26.** Current trace of channel molecule 1 at -60 mV in symmetrical KCl solutions (*cis/trans* = 1.0 M/1.0 M), final concentration is  $0.05 \mu$ M. Full spectra.



**Figure S27.** Current trace of channel molecule 1 at -80 mV in symmetrical KCl solutions (*cis/trans* = 1.0 M/1.0 M), final concentration is 0.05  $\mu$ M. Full spectra.



**Figure S28.** Current trace of channel molecule **1** at -100 mV in symmetrical KCl solutions (*cis/trans* = 1.0 M/1.0 M), final concentration is  $0.05 \mu$ M. Full spectra.

<u>0.05</u> μl	).05 μM).											
					C	urrent (p	A)					
Entry	100 (mV)	80 (mV)	60 (mV)	40 (mV)	20 (mV)	0 (mV)	-20 (mV)	-40 (mV)	-60 (mV)	-80 (mV)	-100 (mV)	g (pS)
1	2.00	1.40	0.93	0.57	0.23	0	-0.19	-0.59	-0.81	-1.17	-1.96	17.2± 2.2
2	2.29	2.06	1.54	0.74	0.36	0	-0.48	-0.83	-1.32	-1.41	-1.73	21.1± 2.2
3	2.16	1.01	-	-	-	0	-0.21	-0.33	-0.65	-0.88	-1.75	16.0± 2.7

**Table S4.** The current under the corresponding voltage and slope conductance g in symmetrical KCl solutions (*cis/trans* = 1.0 M/1.0 M, the final concentration of **1** is 0.05  $\mu$ M).



**Figure S29.** Current traces of channel molecule 1 at 150 mV in symmetrical KCl solutions (*cis/trans* = 1.0 M/1.0 M), final concentration is 1.0  $\mu$ M. Top, full spectra; bottom, enlarged spectra.



**Figure S30.** Current traces of channel molecule **1** at 100 mV in symmetrical KCl solutions (*cis/trans* = 1.0 M/1.0 M), final concentration is 1.0  $\mu$ M. Top, full spectra; bottom, enlarged spectra.



**Figure S31.** Current traces of channel molecule 1 at 60 mV in symmetrical KCl solutions (*cis/trans* = 1.0 M/1.0 M), final concentration is 1.0  $\mu$ M. Top, full spectra; bottom, enlarged spectra.



**Figure S32.** Current trace of channel molecule **1** at 0 mV in symmetrical KCl solutions (*cis/trans* = 1.0 M/1.0 M), final concentration is  $1.0 \mu$ M. Full spectra.



**Figure S33.** Current trace of channel molecule 1 at -60 mV in symmetrical KCl solutions (*cis/trans* = 1.0 M/1.0 M), final concentration is  $1.0 \mu$ M. Full spectra.



**Figure S34.** Current traces of channel molecule 1 at -100 mV in symmetrical KCl solutions (*cis/trans* = 1.0 M/1.0 M), final concentration is 1.0  $\mu$ M. Top, full spectra; bottom, enlarged spectra.



**Figure S35.** Current traces of channel molecule 1 at -150 mV in symmetrical KCl solutions (*cis/trans* = 1.0 M/1.0 M), final concentration is 1.0  $\mu$ M. Top, full spectra; bottom, enlarged spectra.

**Table S5.** The current under the corresponding voltage and slope conductance g in symmetrical KCl solutions (*cis/trans* = 1.0 M/1.0 M, the final concentration of **1** is  $1.0 \mu$ M).

Current (pA)							_	
Entry	150	100	60	0	-60	-100	-150	<i>g</i> (pS)
	(mV)	(mV)	(mV)	(mV)	(mV)	(mV)	(mV)	
1	3.28	2.09	0.79	0	-0.88	-2.00	-3.39	20.9±1.1
2	3.10	1.86	0.73	0	-0.81	-1.92	-3.01	19.2±1.0
3	3.09	2.07	0.67	0	-	-2.21	-3.02	20.2±1.0

### 6. Ion selectivity study by planar lipid bilayer experiments

Conditions for anion/cation selectivity experiments were that: cis chamber 1.0 M KCl aqueous solution (1 mL), trans chamber 0.5 M or 0.25 M KCl aqueous solution (1 mL); holding potentials changing between -100 mV and +100 mV; the final concentration of **1** is 0.5  $\mu$ M.



Figure S36. Current traces of channel molecule 1 at 100 mV in KCl solutions (cis/trans = 1.0 M/0.25 M). Top, full spectra; bottom, enlarged spectra.



Figure S37. Current traces of channel molecule 1 at 60 mV in KCl solutions (cis/trans = 1.0 M/0.25 M). Top, full spectra; bottom, enlarged spectra.



Figure S38. Current traces of channel molecule 1 at 20 mV in KCl solutions (cis/trans = 1.0 M/0.25 M). Top, full spectra; bottom, enlarged spectra.



**Figure S39.** Current traces of channel molecule 1 at 0 mV in KCl solutions (*cis/trans* = 1.0 M/0.25 M). Top, full spectra; bottom, enlarged spectra.



Figure S40. Current traces of channel molecule 1 at -20 mV in KCl solutions (cis/trans = 1.0 M/0.25 M). Top, full spectra; bottom, enlarged spectra.



Figure S41. Current traces of channel molecule 1 at -60 mV in KCl solutions (cis/trans = 1.0 M/0.25 M). Top, full spectra; bottom, enlarged spectra.



Figure S42. Current traces of channel molecule 1 at -100 mV in KCl solutions (cis/trans = 1.0 M/0.25 M). Top, full spectra; bottom, enlarged spectra.



Figure S43. Current traces of channel molecule 1 at 100 mV in KCl solutions (cis/trans = 1.0 M/0.5 M). Top, full spectra; bottom, enlarged spectra.



Figure S44. Current traces of channel molecule 1 at 20 mV in KCl solutions (cis/trans = 1.0 M/0.5 M). Top, full spectra; bottom, enlarged spectra.



Figure S45. Current traces of channel molecule 1 at 0 mV in KCl solutions (*cis/trans* = 1.0 M/0.5 M). Top, full spectra; bottom, enlarged spectra.



Figure S46. Current traces of channel molecule 1 at -20 mV in KCl solutions (cis/trans = 1.0 M/0.5 M). Top, full spectra; bottom, enlarged spectra.



Figure S47. Current traces of channel molecule 1 at -60 mV in KCl solutions (cis/trans = 1.0 M/0.5 M). Top, full spectra; bottom, enlarged spectra.



Figure S48. Current traces of channel molecule 1 at -100 mV in KCl solutions (cis/trans = 1.0 M/0.5 M). Top, full spectra; bottom, enlarged spectra.

	cis/trans=1.0 M	/0.25 M KCl	cis/trans=1.0 M/0.5 M KCl		
Entry	Reversal voltage	P /P b	Reversal voltage	P /P b	
	$V_{r}$ (mV)	Cl- K+	$V_{r}(mV)$	Cl- K+	
1	12.89	2.38	4.12	1.63	
2	10.12	1.95	4.48	1.70	
3	12.47	2.31	4.72	1.75	
4	8.78	1.78	5.22	1.87	
5	7.11	1.59	4.52	1.71	
6	7.54	1.64	4.21	1.64	

**Table S6.** Reversal voltage  $V_r$  and permeability ratio  $P_{Cl}/P_K^+$ .

7 7.50	1.63	4.40	1.68
--------	------	------	------

a, obtained after correcting the potential caused by chloride concentration gradient; b, calculated from the equation derived from Goldman-Hodgin-Katz equation:

 $P_{\text{Cl}}/P_{\text{K}}^{+} = [a_{\text{K}, cis} - a_{\text{K}, trans} \exp(-V_{\text{r}}F/\text{RT})]/[a_{\text{Cl}, cis} \exp(-V_{\text{r}}F/\text{RT}) - a_{\text{Cl}, trans}]$ 

where  $a_{K, cis}$  and  $a_{K, trans}$  are the activities of K<sup>+</sup> in the *cis* and the *trans* chambers,  $a_{Cl, cis}$  and  $a_{Cl, trans}$  the same for Cl<sup>-</sup>.

Conditions for anion/anion selectivity experiments were that: cis chamber 1.0 M KCl aqueous solution (1 mL), trans chamber 1.0 M KBr aqueous solution (1 mL); holding potentials changing between -100 mV and +200 mV; the final concentration of **1** is 0.5  $\mu$ M.



Figure S49. Current traces of channel molecule 1 at 200 mV in KCl and KBr solutions (cis/trans = 1.0 M KCl/1.0 M KBr).



Figure S50. Current traces of channel molecule 1 at 150 mV in KCl and KBr solutions (cis/trans = 1.0 M KCl/1.0 M KBr).



**Figure S51.** Current traces of channel molecule **1** at 50 mV in KCl and KBr solutions (*cis/trans* = 1.0 M KCl/1.0 M KBr).



Figure S52. Current traces of channel molecule 1 at 0 mV in KCl and KBr solutions (cis/trans = 1.0 M KCl/1.0 M KBr).



Figure S53. Current traces of channel molecule 1 at -50 mV in KCl and KBr solutions (cis/trans = 1.0 M KCl/1.0 M KBr).



**Figure S54.** Current traces of channel molecule **1** at -100 mV in KCl and KBr solutions (*cis/trans* = 1.0 M KCl/1.0 M KBr).

	cis/trans=1.0 M KCl/1.0 M KBr				
Entry	Reversal voltage $V_r(mV)$	$P_{\rm Cl}/P_{\rm Br}^{a}$			
1	78.62	21.32			
2	79.36	21.94			
3	83.06	25.34			
4	81.08	23.46			
5	81.64	23.98			
6	80.35	22.81			
7	78.20	20.97			

**Table S7.** Reversal voltage  $V_r$  and permeability ratio  $P_{Cl}/P_{Br}$ .

a, calculated from:  $V_r = \{RTln(P_A[A]/P_B[B])\}/zF$ 

### 7. Calculation

Geometry optimizations were carried out with the Accelrys Material Studio 7.0 suite by DMol<sup>3</sup> code at LDA PWC/DNP level, and the orbital cut off was set at fine quality. A self-consistent field procedure was performed with a convergence criterion of 10<sup>-6</sup> Ha. We calculated Frequency analysis and electrostatic potential using DFT method based on B3LYP/6-31G level.

Cartesian coordinates (Å) of the optimized structure.

С	-1.08	-1.2194	-6.3151
С	-0.9976	0.1535	-6.364
С	0.0511	0.8394	-5.784
С	1.0073	0.1233	-5.0924
С	0.9387	-1.2489	-4.9812
С	-0.108	-1.916	-5.6078
0	-1.9891	0.8939	-6.9869
0	2.0568	0.8409	-4.5361
С	1.932	1.1848	-3.2483
С	-2.9523	1.3374	-6.1641
Ν	-3.7493	2.2605	-6.6575
Ν	-4.8194	2.2534	-4.5344
С	-3.9656	1.3031	-4.193
Ν	-2.9907	0.8215	-4.9406
Ν	0.9236	0.678	-2.5633
С	0.9141	1.0406	-1.2863
Ν	1.7699	1.8381	-0.6848
Ν	2.8488	2.0194	-2.7911
0	-4.1206	0.807	-2.9586
С	-3.0855	0.02	-2.475
0	-0.077	0.5624	-0.5188
С	-3.0357	-1.3357	-2.7187
С	-1.9936	-2.0722	-2.1667
С	-1.0101	-1.4587	-1.4012
С	-1.078	-0.0972	-1.213
С	-2.1193	0.6538	-1.7192
С	6.3713	10.314	-2.8816
С	6.0739	11.7422	-3.0999
С	4.836	11.8446	-3.7131
С	4.2988	10.4797	-3.9041
С	6.868	12.8379	-2.8642
С	6.3924	14.0864	-3.2682

С	5.1399	14.1867	-3.8765
С	4.3418	13.0697	-4.1009
0	3.26	10.1259	-4.4196
0	7.3574	9.7968	-2.4032
0	3.5243	3.1865	-0.9355
С	4.3857	3.9631	-1.7642
С	3.9608	5.3987	-1.6217
0	4.699	6.1507	-2.5402
С	4.5024	7.5275	-2.3821
С	5.24	8.1973	-3.5109
С	2.7009	2.3198	-1.5039
С	5.5033	16.6275	-2.0316
С	6.5095	16.6099	-3.0011
С	6.8616	17.7915	-3.6531
С	6.1958	18.9405	-3.3019
C	5.2051	18.9559	-2.335
С	4.8369	17.798	-1.6866
С	6.4094	20.3189	-3.7777
Ν	5.4924	21.0971	-3.0767
C	4.7521	20.352	-2.1599
0	3.9295	20.8097	-1.3965
0	7.2037	20.7419	-4.5901
С	5.5108	22.5276	-3.1034
C	-7.6548	10.8706	-3.1872
С	-7.6397	12.2659	-3.6677
С	-6.6633	12.3837	-4.642
С	-6.0134	11.0664	-4.809
С	-8.4348	13.3226	-3.2934
C	-8.2288	14.5456	-3.9329
С	-7.2481	14.6574	-4.9211
C	-6.4489	13.5806	-5.2877
0	-5.1048	10.746	-5.5462
0	-8.3526	10.3582	-2.3399
0	-5.3553	3.736	-6.1839
С	-6.1127	4.4316	-5.1958
С	-6.3352	5.8245	-5.716
0	-6.4467	6.6662	-4.6003
С	-6.6528	8.0036	-4.9593
С	-6.3405	8.8319	-3.7391
С	-4.6352	2.7072	-5.7711
С	-7.1244	17.1241	-3.0932
С	-8.3733	17.0624	-3.7153
С	-8.9372	18.2176	-4.259
С	-8.2241	19.3861	-4.1493

С	-6.9879	19.4422	-3.5296
С	-6.4097	18.3125	-2.9946
С	-8.5907	20.7396	-4.6104
Ν	-7.5293	21.5684	-4.1913
С	-6.5218	20.8324	-3.5962
0	-5.4477	21.3063	-3.2422
0	-9.5775	21.0868	-5.2126
С	-7.4263	23.0125	-4.3174
С	-2.1255	-12.3029	-2.2332
С	-3.2572	-13.2449	-2.3602
С	-4.3524	-12.5454	-2.8359
С	-3.9648	-11.1321	-3.0025
С	-3.3439	-14.591	-2.0863
С	-4.5637	-15.2154	-2.3191
С	-5.6642	-14.5179	-2.8222
С	-5.5622	-13.1505	-3.0773
0	-4.6202	-10.2018	-3.4205
0	-0.975	-12.5284	-1.9181
0	-1.0055	-4.1409	-1.7345
С	-0.7105	-5.4825	-2.1163
С	-1.7709	-6.4458	-1.6651
0	-1.3637	-7.703	-2.1358
С	-2.2902	-8.7221	-1.8677
С	-1.8427	-9.8793	-2.7165
С	-6.9771	-15.2654	-2.9799
С	-6.7724	-16.6869	-3.4739
С	-5.8602	-16.8895	-4.5124
C	-5.6485	-18.1445	-5.0713
C	-6.3731	-19.1947	-4.5577
C	-7.2881	-18.9971	-3.5383
C	-7.5175	-17.7596	-2.9841
C	-6.3823	-20.6239	-4.9342
Ν	-7.3287	-21.2219	-4.0759
С	-7.932	-20.2839	-3.2606
0	-8.8599	-20.5336	-2.4993
0	-5.7327	-21.1827	-5.7844
С	-7.7096	-22.6212	-3.9955
С	0.5746	-11.2076	-4.5888
С	1.5826	-12.2102	-4.1945
C	2.8121	-11.5825	-4.1058
C	2.621	-10.1489	-4.3905
С	1.4456	-13.5485	-3.9051
С	2.5951	-14.2444	-3.5543
С	3.8454	-13.6231	-3.4931

C	3.9581	-12.2586	-3.7578
0	3.4348	-9.2516	-4.391
0	-0.6063	-11.3747	-4.8262
0	-1.0727	-3.9343	-6.2705
С	-1.4312	-5.2931	-6.0095
С	-0.3204	-6.271	-6.2793
0	-0.9349	-7.5358	-6.2572
С	-0.0356	-8.6084	-6.2275
С	0.6634	-8.7043	-4.8826
С	5.0283	-14.4645	-3.0443
С	5.0302	-15.8357	-3.6974
С	4.6849	-15.9126	-5.0483
С	4.722	-17.112	-5.7492
С	5.1252	-18.2325	-5.0617
С	5.4796	-18.1617	-3.7257
С	5.4427	-16.9826	-3.0178
С	5.2662	-19.6297	-5.5188
Ν	5.7485	-20.3357	-4.3966
С	5.8468	-19.5128	-3.2906
0	6.1549	-19.9052	-2.1705
0	5.0275	-20.0906	-6.6089
C			
C	6.1366	-21.7344	-4.317
C C	6.1366 -1.9042	-21.7344 -3.5038	-4.317 -2.4951
C O	6.1366 -1.9042 -2.5575	-21.7344 -3.5038 -4.04	-4.317 -2.4951 -3.3699
C O C	6.1366 -1.9042 -2.5575 -0.2206	-21.7344 -3.5038 -4.04 -3.3707	-4.317 -2.4951 -3.3699 -5.4098
C C O C O	6.1366 -1.9042 -2.5575 -0.2206 0.3801	-21.7344 -3.5038 -4.04 -3.3707 -3.981	-4.317 -2.4951 -3.3699 -5.4098 -4.5447
C O C O C	6.1366 -1.9042 -2.5575 -0.2206 0.3801 -9.1254	-21.7344 -3.5038 -4.04 -3.3707 -3.981 15.7437	-4.317 -2.4951 -3.3699 -5.4098 -4.5447 -3.6735
C C O C C C	6.1366 -1.9042 -2.5575 -0.2206 0.3801 -9.1254 7.2795	-21.7344 -3.5038 -4.04 -3.3707 -3.981 15.7437 15.3179	-4.317 -2.4951 -3.3699 -5.4098 -4.5447 -3.6735 -3.2122
C C O C C C C N	6.1366 -1.9042 -2.5575 -0.2206 0.3801 -9.1254 7.2795 -6.6667	-21.7344 -3.5038 -4.04 -3.3707 -3.981 15.7437 15.3179 10.2141	-4.317 -2.4951 -3.3699 -5.4098 -4.5447 -3.6735 -3.2122 -3.9228
C C O C C C N N	6.1366 -1.9042 -2.5575 -0.2206 0.3801 -9.1254 7.2795 -6.6667 5.2705	-21.7344 -3.5038 -4.04 -3.3707 -3.981 15.7437 15.3179 10.2141 9.6231	-4.317 -2.4951 -3.3699 -5.4098 -4.5447 -3.6735 -3.2122 -3.9228 -3.3882
C C O C C C N N N	6.1366 -1.9042 -2.5575 -0.2206 0.3801 -9.1254 7.2795 -6.6667 5.2705 -2.6412	-21.7344 -3.5038 -4.04 -3.3707 -3.981 15.7437 15.3179 10.2141 9.6231 -11.0555	-4.317 -2.4951 -3.3699 -5.4098 -4.5447 -3.6735 -3.2122 -3.9228 -3.3882 -2.5771
C C O C C C N N N N N	6.1366 -1.9042 -2.5575 -0.2206 0.3801 -9.1254 7.2795 -6.6667 5.2705 -2.6412 1.2555	-21.7344 -3.5038 -4.04 -3.3707 -3.981 15.7437 15.3179 10.2141 9.6231 -11.0555 -9.9936	-4.317 -2.4951 -3.3699 -5.4098 -4.5447 -3.6735 -3.2122 -3.9228 -3.3882 -2.5771 -4.6549
C C O C C C N N N N N C	6.1366 -1.9042 -2.5575 -0.2206 0.3801 -9.1254 7.2795 -6.6667 5.2705 -2.6412 1.2555 4.7276	-21.7344 -3.5038 -4.04 -3.3707 -3.981 15.7437 15.3179 10.2141 9.6231 -11.0555 -9.9936 24.5381	-4.317 -2.4951 -3.3699 -5.4098 -4.5447 -3.6735 -3.2122 -3.9228 -3.3882 -2.5771 -4.6549 -4.4206
C C O C C C N N N N N N C C	6.1366 -1.9042 -2.5575 -0.2206 0.3801 -9.1254 7.2795 -6.6667 5.2705 -2.6412 1.2555 4.7276 5.4112	-21.7344 -3.5038 -4.04 -3.3707 -3.981 15.7437 15.3179 10.2141 9.6231 -11.0555 -9.9936 24.5381 25.4639	-4.317 -2.4951 -3.3699 -5.4098 -4.5447 -3.6735 -3.2122 -3.9228 -3.3882 -2.5771 -4.6549 -4.4206 -5.1978
C C O C O C C N N N N N N N C C C	6.1366 -1.9042 -2.5575 -0.2206 0.3801 -9.1254 7.2795 -6.6667 5.2705 -2.6412 1.2555 4.7276 5.4112 5.0646	-21.7344 -3.5038 -4.04 -3.3707 -3.981 15.7437 15.3179 10.2141 9.6231 -11.0555 -9.9936 24.5381 25.4639 26.8049	-4.317 -2.4951 -3.3699 -5.4098 -4.5447 -3.6735 -3.2122 -3.9228 -3.3882 -2.5771 -4.6549 -4.4206 -5.1978 -5.1722
C C O C O C C C N N N N N N C C C C C C	6.1366 -1.9042 -2.5575 -0.2206 0.3801 -9.1254 7.2795 -6.6667 5.2705 -2.6412 1.2555 4.7276 5.4112 5.0646 4.029	-21.7344 -3.5038 -4.04 -3.3707 -3.981 15.7437 15.3179 10.2141 9.6231 -11.0555 -9.9936 24.5381 25.4639 26.8049 27.2396	-4.317 -2.4951 -3.3699 -5.4098 -4.5447 -3.6735 -3.2122 -3.9228 -3.3882 -2.5771 -4.6549 -4.4206 -5.1978 -5.1722 -4.3593
C C O C O C C C N N N N N N N N C C C C	6.1366 -1.9042 -2.5575 -0.2206 0.3801 -9.1254 7.2795 -6.6667 5.2705 -2.6412 1.2555 4.7276 5.4112 5.0646 4.029 3.339	-21.7344 -3.5038 -4.04 -3.3707 -3.981 15.7437 15.3179 10.2141 9.6231 -11.0555 -9.9936 24.5381 25.4639 26.8049 27.2396 26.3237	-4.317 -2.4951 -3.3699 -5.4098 -4.5447 -3.6735 -3.2122 -3.9228 -3.3882 -2.5771 -4.6549 -4.4206 -5.1978 -5.1722 -4.3593 -3.5791
C C O C O C C C C C C C C C C C C C C C	6.1366 -1.9042 -2.5575 -0.2206 0.3801 -9.1254 7.2795 -6.6667 5.2705 -2.6412 1.2555 4.7276 5.4112 5.0646 4.029 3.339 3.6854	-21.7344 -3.5038 -4.04 -3.3707 -3.981 15.7437 15.3179 10.2141 9.6231 -11.0555 -9.9936 24.5381 25.4639 26.8049 27.2396 26.3237 24.9827	-4.317 -2.4951 -3.3699 -5.4098 -4.5447 -3.6735 -3.2122 -3.9228 -3.3882 -2.5771 -4.6549 -4.4206 -5.1978 -5.1722 -4.3593 -3.5791 -3.6143
C C O C O C C C C C C C C C C C C C C C	6.1366 -1.9042 -2.5575 -0.2206 0.3801 -9.1254 7.2795 -6.6667 5.2705 -2.6412 1.2555 4.7276 5.4112 5.0646 4.029 3.339 3.6854 5.0948	-21.7344 -3.5038 -4.04 -3.3707 -3.981 15.7437 15.3179 10.2141 9.6231 -11.0555 -9.9936 24.5381 25.4639 26.8049 27.2396 26.3237 24.9827 23.0915	-4.317 -2.4951 -3.3699 -5.4098 -4.5447 -3.6735 -3.2122 -3.9228 -3.3882 -2.5771 -4.6549 -4.4206 -5.1978 -5.1722 -4.3593 -3.5791 -3.6143 -4.4547
C C O C O C C C C C C C C C C C C C C C	6.1366 -1.9042 -2.5575 -0.2206 0.3801 -9.1254 7.2795 -6.6667 5.2705 -2.6412 1.2555 4.7276 5.4112 5.0646 4.029 3.339 3.6854 5.0948 6.8699	-21.7344 -3.5038 -4.04 -3.3707 -3.981 15.7437 15.3179 10.2141 9.6231 -11.0555 -9.9936 24.5381 25.4639 26.8049 27.2396 26.3237 24.9827 23.0915 22.9699	-4.317 -2.4951 -3.3699 -5.4098 -4.5447 -3.6735 -3.2122 -3.9228 -3.3882 -2.5771 -4.6549 -4.4206 -5.1978 -5.1722 -4.3593 -3.5791 -3.6143 -4.4547 -2.6006
C C O C O C C C C C C C C C C C C C C C	6.1366 -1.9042 -2.5575 -0.2206 0.3801 -9.1254 7.2795 -6.6667 5.2705 -2.6412 1.2555 4.7276 5.4112 5.0646 4.029 3.339 3.6854 5.0948 6.8699 7.5501	-21.7344 -3.5038 -4.04 -3.3707 -3.981 15.7437 15.3179 10.2141 9.6231 -11.0555 -9.9936 24.5381 25.4639 26.8049 27.2396 26.3237 24.9827 23.0915 22.9699 22.3118	-4.317 -2.4951 -3.3699 -5.4098 -4.5447 -3.6735 -3.2122 -3.9228 -3.3882 -2.5771 -4.6549 -4.4206 -5.1978 -5.1722 -4.3593 -3.5791 -3.6143 -4.4547 -2.6006 -1.8506
C C O C O C C C C C C C C C C C C C C C	6.1366 -1.9042 -2.5575 -0.2206 0.3801 -9.1254 7.2795 -6.6667 5.2705 -2.6412 1.2555 4.7276 5.4112 5.0646 4.029 3.339 3.6854 5.0948 6.8699 7.5501 7.2147	-21.7344 -3.5038 -4.04 -3.3707 -3.981 15.7437 15.3179 10.2141 9.6231 -11.0555 -9.9936 24.5381 25.4639 26.8049 27.2396 26.3237 24.9827 23.0915 22.9699 22.3118 24.1788	-4.317 -2.4951 -3.3699 -5.4098 -4.5447 -3.6735 -3.2122 -3.9228 -3.3882 -2.5771 -4.6549 -4.4206 -5.1978 -5.1722 -4.3593 -3.5791 -3.6143 -4.4547 -2.6006 -1.8506 -3.0489
C C O C C C C C C C C C C C C C C C C C	6.1366 -1.9042 -2.5575 -0.2206 0.3801 -9.1254 7.2795 -6.6667 5.2705 -2.6412 1.2555 4.7276 5.4112 5.0646 4.029 3.339 3.6854 5.0948 6.8699 7.5501 7.2147 -6.4959	-21.7344 -3.5038 -4.04 -3.3707 -3.981 15.7437 15.3179 10.2141 9.6231 -11.0555 -9.9936 24.5381 25.4639 26.8049 27.2396 26.3237 24.9827 23.0915 22.9699 22.3118 24.1788 23.3482	-4.317 -2.4951 -3.3699 -5.4098 -4.5447 -3.6735 -3.2122 -3.9228 -3.3882 -2.5771 -4.6549 -4.4206 -5.1978 -5.1722 -4.3593 -3.5791 -3.6143 -4.4547 -2.6006 -1.8506 -3.0489 -5.488

0	-5.2356	22.9665	-5.3077
С	-8.6331	25.1556	-4.0318
С	-8.7985	25.5347	-2.703
С	-8.6675	26.8602	-2.3217
С	-8.368	27.8261	-3.2706
С	-8.2017	27.4579	-4.5969
С	-8.3308	26.131	-4.9759
С	-8.7612	23.718	-4.4184
С	-7.6581	-15.2238	-1.5999
F	-8.9368	-15.6231	-1.6473
F	-7.0105	-16.0272	-0.7445
F	-7.6432	-13.994	-1.0887
С	-7.909	-14.5915	-4.006
F	-8.412	-13.4323	-3.5621
F	-8.9386	-15.3819	-4.3099
F	-7.2406	-14.3399	-5.1393
С	-9.0335	-22.8186	-4.7423
0	-9.1302	-23.4694	-5.7517
0	-10.0692	-22.1978	-4.1868
C	-6.8915	-24.9425	-3.8686
С	-6.356	-25.2743	-2.6276
С	-6.6143	-26.5066	-2.0491
С	-7.4147	-27.4262	-2.7099
С	-7.9505	-27.1058	-3.9477
С	-7.692	-25.8718	-4.524
С	-6.6404	-23.5891	-4.4517
С	4.9368	-14.5518	-1.5095
F	3.93	-15.3615	-1.1529
F	6.0591	-15.0331	-0.9547
F	4.7067	-13.3561	-0.9719
C	6.3758	-13.8194	-3.4171
F	7.3883	-14.6631	-3.2124
F	6.3843	-13.4866	-4.7152
F	6.6267	-12.7118	-2.7082
C	7.3794	-23.5556	-5.4355
C	8.7602	-23.4187	-5.327
C	9.5688	-24.524	-5.118
C	9.0013	-25.7855	-5.0144
C	7.6265	-25.9314	-5.118
С	6.8193	-24.8237	-5.325
С	6.5247	-22.3473	-5.6441
С	5.0262	-22.527	-3.6169
0	4.3684	-23.3692	-4.1738
0	4.8421	-22.1986	-2.3427

С	-9.782	15.6842	-2.28
F	-8.8544	15.4377	-1.3451
F	-10.3678	16.8417	-1.9724
F	-10.7158	14.7283	-2.1926
С	-10.2345	15.677	-4.7403
F	-11.252	16.5083	-4.4747
F	-10.7399	14.4483	-4.8369
F	-9.737	16.0086	-5.939
С	8.0584	15.3268	-4.5424
F	8.5623	14.1251	-4.8237
F	7.2406	15.6671	-5.5476
F	9.0811	16.1927	-4.531
С	8.2937	15.2436	-2.0522
F	7.6683	14.9009	-0.918
F	9.2631	14.3431	-2.2711
F	8.8867	16.4191	-1.8509
Н	-1.9188	-1.7469	-6.7728
Н	0.1039	1.9294	-5.8374
Н	1.6685	-1.8175	-4.399
Н	-3.7753	-1.8355	-3.349
Н	-0.174	-2.0367	-1.0039
Н	-2.1597	1.7341	-1.5591
Н	7.8538	12.7013	-2.4132
Н	4.7907	15.1718	-4.2006
Н	3.3704	13.152	-4.5957
Н	4.3115	3.6321	-2.8112
Н	5.414	3.8132	-1.4041
Н	4.1359	5.7547	-0.5853
Н	2.87	5.4829	-1.8203
Н	4.9048	7.873	-1.4059
Н	3.4224	7.7842	-2.4202
Н	4.7697	7.9376	-4.4727
Н	6.2858	7.8487	-3.5069
Н	5.2464	15.6929	-1.5235
Н	7.6573	17.8442	-4.3992
Н	4.062	17.8082	-0.9157
Н	-9.2038	13.1744	-2.5317
Н	-7.1122	15.6217	-5.4205
Н	-5.6846	13.6736	-6.0637
Н	-5.5392	4.4843	-4.2566
Н	-7.0459	3.8855	-4.9872
Н	-7.2384	5.8904	-6.3565
Н	-5.4627	6.114	-6.3381
Н	-7.7009	8.177	-5.2851

Н	-5.982	8.2964	-5.7927
Н	-5.2699	8.7348	-3.4949
Н	-6.9356	8.4786	-2.8811
Н	-6.7039	16.2066	-2.6704
Н	-9.9155	18.2284	-4.745
Н	-5.4336	18.3537	-2.5045
Н	-2.4856	-15.1428	-1.6939
Н	-4.6697	-16.2827	-2.1029
Н	-6.4	-12.5533	-3.4454
Н	0.2539	-5.7165	-1.6451
Н	-0.5882	-5.5268	-3.2107
Н	-2.7506	-6.1629	-2.0993
Н	-1.8614	-6.4435	-0.559
Н	-3.3146	-8.411	-2.1544
Н	-2.2921	-8.9883	-0.7899
Н	-0.8126	-10.1661	-2.4472
Н	-1.8538	-9.5715	-3.7755
Н	-5.2984	-16.0305	-4.8914
Н	-4.9391	-18.2977	-5.8888
Н	-8.2672	-17.6465	-2.198
Н	0.4644	-14.0294	-3.9299
Н	2.5261	-15.3099	-3.3151
Н	4.9041	-11.7164	-3.6891
Н	-2.269	-5.5059	-6.6882
Н	-1.7891	-5.3676	-4.9687
Н	0.4637	-6.1724	-5.5057
Н	0.1419	-6.0724	-7.2698
Н	0.7083	-8.533	-7.0481
Н	-0.6384	-9.5169	-6.3841
Н	-0.0706	-8.4747	-4.0867
Н	1.4946	-7.9856	-4.7894
Н	4.3719	-14.9988	-5.5619
Н	4.4469	-17.1701	-6.8056
Н	5.7383	-16.9685	-1.9661
Н	6.2414	25.1202	-5.8236
Н	5.6128	27.5208	-5.7911
Н	3.7571	28.2983	-4.3344
Н	2.516	26.657	-2.9411
Н	3.1274	24.2623	-3.004
Н	5.9011	22.9079	-5.1833
Н	4.2237	22.4986	-4.7857
Н	8.0881	24.3736	-2.6415
Н	-5.1415	22.4868	-4.4294
Н	-9.0484	24.7727	-1.9555

Н	-8.809	27.1437	-1.2751
Н	-8.2703	28.8742	-2.9745
Н	-7.9712	28.2159	-5.3507
Н	-8.1834	25.8262	-6.0168
Н	-9.1427	23.6142	-5.4453
Н	-9.4804	23.2182	-3.7497
Н	-9.7685	-21.6756	-3.3829
Н	-5.7141	-24.5513	-2.1107
Н	-6.1802	-26.754	-1.0764
Н	-7.6183	-28.401	-2.2583
Н	-8.5812	-27.8274	-4.4744
Н	-8.1301	-25.6004	-5.4896
Н	-6.6325	-23.6219	-5.5517
Н	-5.6561	-23.2168	-4.1246
Н	9.2093	-22.4235	-5.4267
Н	10.6529	-24.4015	-5.0448
Н	9.6372	-26.6606	-4.8547
Н	7.1735	-26.9232	-5.034
Н	5.7309	-24.9244	-5.3844
Н	5.6106	-22.6004	-6.2018
Н	7.0764	-21.6006	-6.2375
Н	5.4555	-21.4432	-2.0881
Н	7.0171	-21.7503	-3.6449
Н	-6.9144	23.3467	-3.3935
Н	4.7767	22.8369	-2.3312
Н	-7.9169	-22.799	-2.9219

# 8. Copies of <sup>1</sup>H and <sup>13</sup>C NMR spectra



Figure S55. <sup>1</sup>H NMR spectrum of 1.



Figure S56. <sup>13</sup>C NMR spectrum of 1.



Figure S57. <sup>1</sup>H NMR spectrum of 5.



Figure S58. <sup>13</sup>C NMR spectrum of 5.





Figure S60. <sup>13</sup>C NMR spectrum of 8.



Figure S61. <sup>1</sup>H NMR spectrum of 9.



Figure S62. <sup>13</sup>C NMR spectrum of 9.



Figure S63. <sup>1</sup>H NMR spectrum of 10.



Figure S64. <sup>13</sup>C NMR spectrum of 10.

### 9. References

[S1] Boyle, T. P.; Bremner, J. B.; Brkic, Z.; Coates, J. A. V.; Dalton, N. K.; Deadman, J.; Keller, P. A.; Morgan, J.; Pyne, S. G.; Rhodes, D. I.; Robertson, M. J. Preparation of Biaryl-Based Peptides for the Treatment of Infection, AU: WO2006074501 (A1). 2006-07-20.

[S2] Hou, B.-Y.; Wang, D.-X.; Yang, H.-B.; Zheng, Q.-Y.; Wang, M.-X. Synthesis and Structure of Upper-Rim 1,3-Alternate Tetraoxacalix[2]arene[2]triazine Azacrowns and Change of Cavity in Response to Fluoride Anion, *J. Org. Chem.* 2007, 72, 5218-5226.

[S3] Huang, W.-L.; Wang, X.-D.; Li, S.; Zhang, R.; Ao, Y.-F.; Tang, J.; Wang, Q.-Q.;
Wang, D.-X. Anion Transporters Based on Noncovalent Balance Including Anion-π,
Hydrogen, and Halogen Bonding, *J. Org. Chem.* 2019, *84*, 8859-8869.

[S4] Wang, X.-D.; Li, S.; Ao, Y.-F.; Wang, Q.-Q.; Huang, Z.-T.; Wang, D.-X.
Oxacalix[2]arene[2]triazine Based Ion-Pair Transporters, *Org. Biomol. Chem.* 2016, 14, 330-334.

[S5] Gorteau, V.; Bollot, G.; Mareda, J.; Matile, S. Rigid-Rod Anion- $\pi$  Slides for Multiion Hopping Across Lipid Bilayers, *Org. Biomol. Chem.* **2007**, *5*, 3000-3012.

[S6] Chui, J. K. W.; Fyles, T. M. Ionic Conductance of Synthetic Channels: Analysis, Lessons, and Recommendations, *Chem. Soc. Rev.* **2012**, *41*, 148-175.