Electronic Supporting Information for


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Experimental: Reagents were obtained from Aldrich and used without further purification. 1,4-bis(2-bromoethoxy)benzene (1) were prepared using literature procedures. All organic solutions were routinely dried by using sodium sulfate (Na$_2$SO$_4$). $^1$H and C NMR spectra were recorded on an ARX 300 MHz Bruker spectrometer in CDCl$_3$ with the use of the residual solvent peak as reference. Equilibration between hydrogen- bonded and nonhydrogen bonded states for a given N-H proton is almost always fast on the NMR time scale and observed proton chemical shifts are weighted averages of the chemical shifts of contributing states. Mass spectrometric studies were performed in the positive ion mode using a quadrupole mass spectrometer (Micromass, Platform II) equipped with a Waters 616HPLC pump.

Synthesis and characterization of compound 2.

Paraformaldehyde (1.50 g, 25 mmol) was added to a solution of 1,4-bis(2-bromoethoxy)benzene (1) (3.28 g, 5 mmol) and 1,4-dimethoxybenzene (2.76 g, 20 mmol) in dry 1,2-dichloroethane (100 ml) under nitrogen atmosphere. Boron trifluoride etherate [(BF$_3$OEt)$_2$, 3 mL, 25 mmol was then added to the solution and the mixture was stirred at room temperature for 1 h. MeOH (50 mL) was poured into the reaction mixture and the solution was concentrated and dissolved in CH$_2$Cl$_2$ (100 mL), then the solution was subjected to silica gel chromatography (2:1 hexanes/ CH$_2$Cl$_2$) to give 2 (520 mg, 11%). $^1$H NMR (300 MHz, CDCl$_3$) δ = 6.78 (t, 8 H), 6.73 (s, 2 H), 4.06 (t, 4 H), 3.79 (s, 1 H), 3.69 (d, 24 H), 3.45 (t, 4 H). $^{13}$C NMR (75 MHz, CDCl$_3$) δ = 150.6, 149.6, 129.1, 128.5, 128.3, 128.2, 127.8, 115.7, 114.3, 113.9, 68.7, 56.1, 55.8, 29.9, 29.7, 29.5. ESI-MS: m/ calcd for C$_{47}$H$_{52}$Br$_2$O$_{10}$ [M+H]$^+$: 937.17, found: 937.20 (100%); MS (HR-ESI TOF), m/z: calculated for C$_{47}$H$_{52}$Br$_2$O$_{10}$NH$_4^+$ [M+NH$_4^+$]: 954.2251, found: 954.2277.
Figure S1. $^1$H NMR spectrum of 2 in CDCl$_3$ at 298K.

Figure S2. $^{13}$C NMR spectrum of 2 in CDCl$_3$ at 298K.
Synthesis and characterization of compound 3.

Sodium azide (193 mg, 3 mol) was added to the solution of 2 (280 mg, 0.3 mmol), in dry DMF (8 ml), after stirring at room temperature for 24 h under nitrogen atmosphere, the mixture was poured into water (80 mL). The precipitate was collected by filtration, and washed with water to yield 3 as white solid (245 mg, 95%), $^1$H NMR (300 MHz, CDCl$_3$) δ = 6.76 (t, 8 H), 6.68 (s, 2 H), 3.84 (t, 4 H), 3.78 (d, 10 H), 3.68 (t, 24 H), 3.37 (t, 4 H). $^{13}$C NMR (75 MHz, CDCl$_3$) δ = 150.8, 150.7, 149.9, 129.4, 128.6, 128.3, 128.2, 115.5, 114.2, 114.1, 113.9, 114.6, 67.4, 55.9, 55.8, 50.7, 29.8, 29.6. ESI-MS: m/z calcd for C$_{47}$H$_{52}$N$_{6}$O$_{10}$Na $[M+Na]^+$: 883.26, found: 883.36 (100%); MS (HR-ESI TOF), m/z: calculated for C$_{47}$H$_{52}$N$_{6}$O$_{10}$NH$_4^+$ [M+NH$_4^+$]: 878.4095, found: 878.4089.

Figure S3. $^1$H NMR spectrum of 3 in CDCl$_3$ at 298K.
Figure S4. $^{13}$C NMR spectrum of 3 in CDCl$_3$ at 298K.

Synthesis and characterization of compound 4.

A suspension of 3 (603 mg, 0.7 mmol) and Pd/C (10%, 150 mg) in methanol was stirred at 50 $^\circ$C under hydrogen atmosphere (60 psi) for 48 h. The resulting mixture was filtered, and the filtrate was concentrated under reduced pressure. The filtrate was purified by crystallization from chloroform to produce 4 as white solid (526 mg, 93%). $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ = 6.74 (t, 8 H), 6.55 (s, 2 H), 3.78 (s, 14 H), 3.65 (t, 24 H), 2.88 (t, 4 H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ = 150.8, 149.8, 128.5, 128.4, 128.2, 115.2, 114.2, 114.0, 70.7, 55.9, 55.8, 41.5. ESI-MS: m/ calcd for C$_{47}$H$_{57}$N$_2$O$_{10}$ [M+H]$^+$: 810.41, found: 810.12 (100%); MS (HR-ESI TOF), m/z: calculated for C$_{47}$H$_{56}$N$_2$O$_{10}$H$^+$ [M+H]$^+$: 809.4019, found: 809.4013.
Figure S5. $^1$H NMR spectrum of 4 in CDCl$_3$ at 298K.

Figure S6. $^{13}$C NMR spectrum of 4 in CDCl$_3$ at 298K.
Synthesis and characterization of compound 5.

4-Aminobenzo-15-crown-5 ether (84.99 mg, 0.3 mol) was dissolved in dry chloroform (10 mL), then 1,1'-thiocarbonyldi-2,2'-pyridone (69.6 mg, 0.3 mmol) was added. The solution was stirred overnight under room temperature. Subsequently, compound 4 (81 mg, 0.1 mmol) was added to the solution. The solution was stirred under room temperature. Using TLC to monitor the reaction process and after completion, the solution was washed with water, evaporation. The product was purified after a chromatography column (silica gel, preparing the column using CHCl₃ containing 3volume% triethylamine; eluent, CHCl₃) to give 5 (51 mg, 35%). ¹H NMR (300 MHz, CDCl₃) δ = 7.68 (s, 1 H), 6.74 (m, 12 H), 6.56 (d, 4 H), 4.14 (s, 4 H), 4.03 (d, 4 H), 3.94 (d, 4 H), 3.87 (d, 6 H), 3.78 (s, 10 H), 3.75 (t, 24 H), 3.64 (s, 8 H), 3.60 (s, 6 H), 3.44 (d, 8 H). ¹³C NMR (75 MHz, CDCl₃) δ = 181.2, 150.8, 149.7, 148.3, 128.8, 128.3, 127.9, 127.7, 118.4, 114.9, 114.5, 114.3, 114.0, 111.4, 70.9, 70.3, 69.3, 69.2, 69.1, 68.7, 67.1, 55.8, 45.8, 44.9, 29.7. ESI-MS: m/ calcld for C₇₇H₉₅N₄O₂₀S₂ [M+H]⁺: 1460.60, found: 1460.74 (73%); calcld for C₇₇H₉₄N₄O₂₀S₂Na [M+Na]⁺: 1482.58, found: 1482.71 (100%); calcld for C₇₇H₉₄N₄O₂₀S₂Na₂ [M+2Na]⁺: 752.78, found: 752.79 (100%); MS (HR-ESI TOF), m/z: calculated for C₇₇H₉₄N₄O₂₀S₂H⁺ [M+H]⁺: 1459.5963, found: 1459.5981.
Figure S7. $^1$H NMR spectrum of 5 in CDCl$_3$ at 298K.

Figure S8. $^{13}$C NMR spectrum of 5 in CDCl$_3$ at 298K.
Synthesis and characterization of control compound 6.

Compound 4 (81 mg, 0.1 mmol) was dissolved in dry chloroform (10 mL), then isothiocyanatobenzene (400 μl, 0.4 mol) was added. The solution was stirred overnight under room temperature at N₂ atmosphere using TLC to monitor the reaction process and after completion, the product was purified after a chromatography column (silica gel, preparing the column using CHCl₃ containing 1 volume% triethylamine; eluent, CHCl₃) to give 6 (45 mg, 42%). ¹H NMR (300 MHz, CDCl₃) δ = 7.34 (t, 4 H), 7.24 (d, 4 H), 6.69 (d, 10 H), 6.46 (s, 2 H), 3.79 (s, 8 H), 3.70 (s, 10 H), 3.58 (m, 18 H), 3.39 (s, 6 H). ¹³C NMR (75 MHz, CDCl₃) δ = 180.8, 151.1, 150.9, 150.7, 149.7, 130.1, 129.1, 128.4, 128.1, 127.8, 124.8, 114.9, 114.1, 65.9, 56.3, 56.1, 55.8, 44.9, 29.7. ESI-MS: m/z calcld for C₆₁H₆₆N₄O₁₀S₂ [M+H]⁺: 1079.43, found: 1079.57 (100%); MS (HR-ESI TOF), m/z: calculated for C₆₁H₆₆N₄O₁₀S₂H⁺ [M+H]⁺: 1079.4299, found: 1079.4297.

Figure S9. ¹H NMR spectrum of 6 in CDCl₃ at 298K.
Figure S10. $^1$C NMR spectrum of 6 in CDCl$_3$ at 298K.

Figure S11. $^1$H NMR spectral in the presence of 125 mM of KCF$_3$SO$_3$ against the concentration of 5 in CDCl$_3$ at 293 for K.
Figure S12. $^1$H NMR spectral in the presence of 125 mM of NaCF$_3$SO$_3$ ion against the concentration of 5 in CDCl$_3$ at 293 for K.

LUV preparation for HPTS experiments

The vesicles (LUVs) were prepared using egg yolk L-α-phosphatidylcholine (EYPC choloform solution, 800 μL, 20 mg) and the appropriate amount of 5 or 6 dissolved in a CHCl$_3$/MeOH mixture. The solution was evaporated without heating and dried overnight under high vacuum. The resulting thin film was hydrated in 400 μL of buffer (10 mM sodium phosphate, PH 6.4, 100 mM NaCl) containing 10 μM HPTS (8-hydroxypyrrole-1,3,6-trisulfonic acid trisodium salt). During hydration, the suspension was submitted to eight freeze-thaw cycles (Liquid nitrogen, water at room temperature). The obtained white suspension was extruded 21 times through a 0.1 μm polycarbonate membrane, in order to transform the large multilamellar liposome suspension (LMVs) into large unilamellar vesicles.
(LUVs) with an average diameter of 100 nm. The LUVs suspension was separated from extra-vesicular HPTS dye by using size exclusion chromatography (SEC, stationary phase Sephadex G-50, mobile phase: phosphate buffer with 100 mm NaCl), diluted with mobile phase to give 2.8 mL of stock solution. The stock solution has to be used within two weeks after its preparation.

**Cation transport experiments**

We used a ratio data collection method. 100 mL of stock vesicle solution was suspended in 1.88 mL of the corresponding buffer (containing 100 mm of the analyzed cation) and placed into a quartz fluorimetric cell. The emission of HPTS at 510 nm was monitored at two excitation wavelengths (403 and 460 nm) simultaneously. An experiment takes 600 s, with two main events: at 50s, 29 mL of aqueous NaOH (0.5 m) was added, resulting in a pH increase of about one unit in the extravesicular media. Finally, at 505 s, when the curve is stabilized, the monitoring was stopped by lysing the vesicles with detergent (40 mL of 5% aqueous Triton X-100), in order to equilibrate the intravesicular and the extravesicular solution. The value of transport was obtained as a ratio of the emission intensities monitored at 460 and 403 nm, and normalized to 100% of transport (fluorescence curves are a $I/I_0$ ratio function on time, between 0 and 1). We calculated the first-order rate constant from the slopes of the plot of $\ln ([H^+_{\text{in}}]-[H^+_{\text{out}}])$ versus time, where $[H^+_{\text{in}}]$ and $[H^+_{\text{out}}]$ are the intravesicular and extravesicular proton concentrations, respectively. The $[H^+_{\text{out}}]$ was assumed to be constant during the experiment (pH 7.4), while $[H^+_{\text{in}}]$ values were calculated for each point from the HPTS emission intensity with excitation at 403 nm (using the calibration equation $[H^+_{\text{in}}] = 1.1684*\log(I/I_0) + 6.9807$). Then we determined the fractional activity ($Y$), the highest value of $I/I_0$ before lysing the vesicles with detergent. After considering this value (at 500 s), we expressed $Y$ function on time.

To calculate $EC_{50}$ and Hill coefficient $n$, we use three parameters, $Y$- activity, $EC_{50}$ and Hill number,
expressed \( Y \) as a function of time, and we performed fittings using the equation: \( Y = \frac{1}{1+(EC_{50}/[C])^n} \).

This equation can be linearized in the following form:

\[
\log\left[\frac{Y}{1-Y}\right] = n \log(C) - n \log(EC_{50})
\]

where \( Y \) is the activity of the channels, \( n \) is the hill number and \( \log(C) \) is the 10 base logarithm of the molar concentration of monomer.

**Figure S13.** The Hill plot of compound 5 using in the transport of \( K^+ \) cations.

**Figure S14.** \( K^+ \) cations transport activity of 5 plotting its concentration.
Figure S15. The Hill plot of compound 5 using in the transport of Na\textsuperscript{+} cations.

Figure S16. Na\textsuperscript{+} cations transport activity of 5 plotting its concentration.

Figure S17. Transport of Li\textsuperscript{+} cations using compound 5 as determined in a pH gradient assay.
Figure S18. The Hill plot of compound 5 using in the transport of Li$^+$ cations.

Figure S19. Li$^+$ cations transport activity of 5 plotting its concentration.

Figure S20. Transport of Rb$^+$ cations using compound 5 as determined in a pH gradient assay.
Figure S21. The Hill plot of compound 5 using in the transport of Rb\(^+\) cations.

Figure S22. Rb\(^+\) cations transport activity of 5 plotting its concentration.

Figure S23. Transport of Cs\(^+\) cations using compound 5 as determined in a pH gradient assay.
Figure S24. The Hill plot of compound 5 using in the transport of Cs⁺ cations.

Figure S25. Cs⁺ cations transport activity of 5 plotting its concentration.

Figure S26. Transport of Li⁺ cations using compound 6 as determined in a pH gradient assay.
Figure S27. Transport of Na$^+$ cations using compound 6 as determined in a pH gradient assay.

Figure S28. Transport of K$^+$ cations using compound 6 as determined in a pH gradient assay.

Figure S29. Transport of Rb$^+$ cations using compound 6 as determined in a pH gradient assay.
Figure S30. Transport of Cs⁺ cations using compound 6 as determined in a pH gradient assay.