Supplementary Figure S1 | Helical nanotubular assembly of macrocycle 1. The nanotubular assembly of (a) macrocycle 1, which shares the same m-PE core and the amide moiety of 1a and 1b, is optimized based on ab initio calculation. (b) Side view of the resultant helical nanotubular assembly consisting of ten staggered macrocycles. Specifically, to model an infinitely long nanochannel of stacked macrocycles 1, the periodic conditions in all spatial directions for the structural optimization are applied. The supercell of the periodic system consists of three stacked macrocycles based on the optimal stacking angle $\omega$ of $\sim 20^\circ$. The initial dimension of the supercell is 34.0 Å × 34.0 Å × 10.3 Å so that the distance between 1 tubular assembly and its nearest images is sufficiently large ($\sim 10$ Å) to neglect the interaction between 1 tubular assembly and its periodic images. Ab initio optimization is carried out using a density functional theory method, implemented in the CP2K software package. Specifically, the generalized-gradient approximation in the form of Becke-Lee-Yang-Parr (BLYP) functional is used, along with the double-zeta basis sets and dual-space Gaussian pseudopotentials implemented in CP2K software package. To account for the weak interactions among the macrocyclic molecules in the axial direction, the recently developed accurate ab initio parametrization of density functional dispersion correction (DFT-D3) is employed. (c) Top view of the same tube where the 8.63 Å is the (H to H) diameter of the lumen. The van der Waals diameter is 6.4 Å. (d) Detailed structure with two hydrogen-bonded residues from adjacent macrocycles showing the stacking and H-bonding distances.
Supplementary Figure S2. The Eight possible combinations of amide side chain orientations and their corresponding nanotubular assemblies. (Top) Schematic plots of the eight possible tubular assemblies corresponding to the eight combinations of the amide side chain orientations of macrocycle 1. The six helical hydrogen-bonded networks that wrap around each assembly are highlighted in yellow (up-left direction) and/or green (down-right direction). Assembly A, in which all amide side chains adopt the same orientation, has three macrocyclic molecules per unit cell, while each of the other seven tubular assemblies has eighteen macrocycle rings per unit cell. (Bottom) Ab initio density-functional theory optimization of a symmetric dimer based on assembly A, where all hydrogen bonds are oriented in the same direction (left), and an asymmetric dimer of macrocycle 1, in which every other hydrogen bonds are oriented in the same direction (right), shows that the energy difference between the two dimers is about 0.6 kcal/mol. Based on this result, it is expect that all eight types of tubes are nearly degenerate in energy, hence all can be present in bulk samples. Tubular assembly A is selected for ab initio molecular dynamics simulation since it has the smallest unit cell. Our computational results demonstrate that, (i) the orientation of the amide side chains has insignificant energetic effect on the H-bond-mediated tubular assemblies of the macrocycles, and (ii) the interaction of adjacent hydrogen-bonded networks in such an assembly is negligible.
**Supplementary Figure S3 | The AFM image of a sample of 1a and MD simulation of the nanotubular assembly of 1a in chloroform.** (A) AFM images of a sample of 1a nanotubes prepared by depositing a solution in CCl₄ (0.1 mM) onto freshly cleaved mica surface, followed by slow evaporation of solvent in a chamber filled with saturated CCl₄. a, At large scale, long fibers are found to remain stable after removal of CCl₄. b, At increased magnification, additional details can be recognized. These structures remain exceptionally stable under the disturbance of the scanning AFM tip. c, With further increased magnification, parallel nanotubular filaments in a fiber are clearly resolved. (B) Helical nanotubular assembly (in chloroform) consisting of staggered molecules of 1a resulting from MD simulations using GROMACS 3.3.3. The initial structure of the tube was generated by spacing the macrocyclic molecules 4 Å apart along the axial direction but with random rotational angles. In a few ns, the tube adopted the helical configuration. (C) The average inter-planar distance between two stacked macrocycles is about 3.65 Å; the average relative angular displacement between neighboring macrocycles is about 20 degrees, and the helical amplitude and periodicity is 1.5 Å and 69 Å, respectively.
**Supplementary Figure S4 | Synthesis of 1a.** The synthesis of 1a and analogous macrocycles is based on the coupling of the corresponding trimeric precursors under high-dilution condition.
Supplementary Figure S5 | The XRD diffractogram of 1b and the corresponding hexagonal packing. (a) Diffractogram of a solid sample of 1b prepared by evaporating solvent from a CHCl₃ solution. The X-ray diffraction was recorded at the 2-ID-D beamline of the Advanced Photon Source at Argonne National Laboratory using 10.1 keV radiation (λ = 1.2275 Å) on a Newport 6-circle (Kappa) diffractometer. (b) The XRD diffraction pattern revealed by the diffractogram of 1b indicates a highly ordered phase characteristic of columnar assemblies formed by disc-like molecules. The dominant peak at 28.08 Å, along with two other prominent at 16.13 Å and 13.98 Å, with ratios of d-spacings being about (1:1/3:1/2), can be indexed to 100, 110, and 200 reflections of a typical two-dimensional hexagonal lattice, based on which a lattice parameter of a = 32 Å is obtained. Parameter a is the diameter of the column. The very broad peak that ranges from 3 Å to 8 Å and centers at 2θ = 15.5° (~4.2 Å), is often observed with hexagonally packed columnar discotic liquid crystals and can be assigned to the distance between the packed alkyl side chains of 1b. The presence of a very strong peak at 3.53 Å can be attributed to the interplanar reflections between the flat backbones of the macrocyclic molecules, which suggests relatively strong stacking interactions between the backbones of the molecules in the columns, and indicates the existence of periodicity along the columns. The unusually strong reflection at 3.53 Å points to a extraordinary long-range ordering of the molecules within a column, as revealed by a correlation length between 23 nm to 26 nm that is obtained using Scherrer’s equation, which corresponds to a nanotube having ~65 to 73 continuously stacked macrocyclic units. Besides the sharp peak at 3.53 Å, several much less prominent peaks also ride on the broad reflection centered around 4.2 Å. As indicated by their intensities and widths, these small peaks reflect structures that are either much loosely organized or lack long-range repeatability in spatial extension but with relatively high population. For example, the intermolecular hydrogen bonding between the numerous amide groups of stacked macrocycles leads to a loosely organized network consisting of about 5 Å repeating unit on the outer surface of hydrogen-bonded columns. The neighboring benzene rings within a macrocycle constitute a length scale of 7.5 Å although this unit does not repeat in space. The broad peak at 2θ = 23° (3.36 Å) indicates an amorphous structure, which may be attributed to the atomic arrangement of the amide and ester groups of the relatively flexible side chains.
Supplementary Figure S6 | Electron microscopic images of 1a and 1b. Scanning electron micrographs of nanofibers formed by (a) 1a, and (b) 1b. The transmission electron micrographs of nanofibers formed by (c) 1a, and (d) 1b. Samples of 1a and 1b were prepared based on a phase-transfer method by using carbon tetrachloride (CCl₄) and methanol (CH₃OH). The procedure involves the transfer of a larger amount (10:1, v/v) of CH₃OH atop a smaller volume of 1a or 1b (100 µM for both samples) in CCl₄ in a test tube. Within two hours, white fibrous aggregates formed at the interface, and slowly diffused into the upper phase of methanol. The aggregates formed were then transferred and casted onto a solid surface by pipetting. Samples for SEM experiments were prepared by dropping the suspension of the fibrous aggregates in methanol onto aluminium foil, followed by evaporation of solvent in open air. The dried samples were then kept overnight in an oven at 40 °C. Without gold coating, the samples were imaged using a Hitachi S-4800 scanning electron microscope, with an acceleration voltage of 3 kV. Based on the same procedure, samples for TEM measurements were prepared on holey carbon film and imaged using a Tecnai G2 F20 U-TWIN Transmission Electron Microscope, operated at 120 kV or 200 kV.
Extracting the height of individual tubular assemblies and the inter-filament distances from AFM images. The apparent nanotube height decreased as the set-point amplitude ($A_{sp}$) decreased owing to the increased imaging force imposed on the specimen. To estimate the “true” height of the sample of 1a, it is possible to infer this value based on a series of measurements at various imaging forces as described before. Assuming that the imaging force is approximately proportional to the reduced cantilever oscillation amplitude, $\eta = A_0 - A_{sp}$, where $A_0$ is the free amplitude, a plot of the measured height versus $\eta$ can be extrapolated to $\eta = 0$ to obtain the “true” sample height. In this particular case, the measured height varied linearly with $\eta$, yielding a “zero force” height of 3.2 ± 0.1 nm.

For closely packed regions of parallel filaments, the diameter of the filament can be estimated from a 2D Fourier Transform. In the Fourier plot, the periodic structures produce a well-defined diffraction spot, from which this distance can be determined, while the spread of the spot gives an estimate of the variation among the inter-filament distances. The inter-filament distance of 1a nanotubules determined in this way is 3.7 nm ± 0.2 nm.
Supplementary Figure S8 | The SEM image of a sample of 1d prepared directly on a surface. No regular assemblies could be detected for 1d prepared using the same phase-transfer method described above in the legend of Supplementary Fig. S6. The SEM image of 1d was obtained on a sample prepared directly on a surface after CCl₄ evaporation.
Supplementary Figure S9 | The UV and Fluorescence Spectra of 1a and 1b. UV spectra of (A) 1b (5 µM), and (B) 1d (5 µM). The UV spectrum of 1b in carbon tetrachloride shows an absorption maximum at ~275 nm that is significantly blue-shifted from the absorption maxima (at 290 nm) of the spectra recorded in the other three solvents (CHCl₃, DMF, THF). This shift can be attributed to exciton coupling between the conjugated backbones of neighboring macrocycles, which suggests the presence of aggregated structure in carbon tetrachloride. Emission spectra of (C) 1b (5 µM) and (D) 1d (5 µM), in four different solvents (Excitation wavelength = 305 nm). Observation made by fluorescence spectroscopy corroborates that made by UV spectroscopy, which indicates that the emission maximum (at ~425 nm) in carbon tetrachloride undergoes a large red shift from those (at ~350 nm) in the other three solvents (Supplementary Fig. S9C). In contrast, the UV and fluorescence spectra of compound 1d recorded in these four solvents share a similar shape and $\lambda_{\text{max}}$ (Supplementary Figs 9B and 9D), suggesting that the observed shifts in the spectra of 1b in carbon tetrachloride are caused by hydrogen bond mediated aggregation. UV-vis absorption fluorescence spectra were measured on a GBC Cintra 10e spectrophotometer. Fluorescence spectra were measured on a VARIAN Cary Eclipse fluorometer.
Supplementary Figure S10 | The concentration-dependent UV spectra of 1b recorded in CCl₄ at room temperature. Path length = 1 mm. These UV spectra demonstrate that the aggregated structures of 1b remain unchanged from 5 µM to 50 µM in carbon tetrachloride, as indicated by UV spectra having the same shape and unchanged absorption maxima within this concentration range.
Supplementary Figure S11 | CD spectra of 1b and 1c: (a) 1b (30 µM) in CCl₄, (b) 1b in CCl₄ measured at room temperature, and (c) 1c in CCl₄ measured at room temperature. Path length = 1 mm. (d) Thin films of 1b formed by depositing 3, 5, and 7 layers of a 0.5 mM solution in CCl₄ on quartz. The circular dichroism spectra were recorded on a Jasco-J815 CD spectrometer equipped with a Jasco PTC-423S/15 temperature controller. All the measurements were carried out using a 1 mm cuvette in the range between 250 and 400 nm at indicated temperature.
Supplementary Figure S12 | The I-V relationship of 1a channel in planar lipid bilayer. The cis (ground) side contains 1 mL of 1 mM HCl solution and the trans side contains 1 mL of 5 mM HCl solution. The red line is the fitting of a linear equation, enabling measurement of the reverse potential (at 0 pA). The standard deviations for the current measurements obtained at -150mV, 0mV, +150mV, and +200mV are 0.17pA, 0.15pA, 0.19pA, and 0.24pA, respectively.
Supplementary Figure S13 | Single channel conductance traces of 1a. (a) A 20-s single channel conductance recording of 1a in 4.0 M KCl (pH 6.0) at the holding voltage of +200 mV. (b) A 20-s single channel conductance recording of 1a in 4.0 M NaCl (pH 6.0) at the holding voltage of +200 mV. (c) A 20-s single channel conductance recording of 1a in 4.0 M LiCl (pH 6.0) at the holding voltage of +200 mV. No measurable current in 4M NaCl or LiCl was detected.
**Supplementary Figure S14 | MD simulation of 1a nanotube within a lipid bilayer.** Left, schematic plot of 1a nanotube (containing 18 1a molecules) with 10 1a molecules embedded in a POPC lipid bilayer. Right, statistics of the number of 1a molecules in the POPC bilayer (among twenty independent MD simulations).
Supplementary Figure S15 | The relationship between the ratio of 1a to lipid and water permeability. Relative change in the osmotic water permeability coefficient, \((Pf(1a) - Pf)/Pf\), showing a direct dependence on the 1a to lipid ratio. The error bars for the 1:750 and 1:50 measurements are 3 and 18, respectively.
### Supplementary Table S1

The dependence of the open probability on the 1a concentration as measured from single channel electrophysiological measurements.

<table>
<thead>
<tr>
<th>1a (µM)</th>
<th>Open probability (P₀)</th>
<th>Standard deviation of P₀</th>
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<td>3×10⁻³</td>
</tr>
<tr>
<td>20</td>
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Supplementary methods

Synthetic Procedures. Chemicals were purchased from commercial sources and used as received. Reactions requiring an inert gas were all under nitrogen. Silicagel for analytical thin layer chromatography (TLC) and column chromatography (200–300 mesh) were purchased from Qingdao Haiyang Chemical Co., Ltd & Speical Silicagel Factory. The 1H NMR spectra were recorded at 400 or 500 MHz and 13C NMR spectra were measured at 100 or 125 MHz on a Bruker AV400 or AV500 spectrometer at ambient temperature using deuterated solvents purchased from Beijing Chongxi High-Tech Incubator Co.,Ltd. Chemical shifts are reported in parts per million downfield from TMS (tetramethylsilane). Coupling constant in 1H NMR are expressed in Hertz. MS (MALDI-TOF) spectra were performed on a ZAB-HS instrument. ESI mass spectra were performed on a Quattro microTM API instrument. Elemental analyses were performed on a vario EL instrument. HRMS mass spectra were performed on a LCT Premier XE instrument. Melting points were measured on a microscope hot stage melting point apparatus.

3,5-Diiodobenzoic acid (2). To an ice-cooled, stirred suspension of 3, 5-diaminobenzoic (6g, 39.47 mmol) in 25% sulfuric acid (135 mL) was added dropwise an aqueous solution of sodium nitrite (5.79g, 82.89 mmol). After 2h, urea (6.0g, 100 mol) was added, and then the solution was added slowly to an ice-cooled solution of potassium iodide (32.76 g, 197.37 mol) in water (100 mL). After 48h at r.t, the suspension was filtered off and dried. The crude product was purified by column chromatography (petroleum ether:acetone = 15:1) to give a desired product (5.5 g, 38 %).

Butyl 2-(3, 5-diiodobenzamido) propanoate (1a-1). 3, 5-diiodobenzoic acid (5.57 g, 15.0 mmol) and SOCl2 (15 mL) was added to a 100 mL round-bottomed flask. The resulting suspension was heated to reflux for 5 h. Excess SOCl2 was removed in vacuo to give a yellow solid which was dissolved in 50 mL CH2Cl2 and added to a dry flask containing NEt3 (5 mL) and butyl 2-aminopropanoate (2.98 g, 16.0 mmol) at 0 °C. The mixture was stirred for 8 h at room temperature, filtered, and the filtrate was concentrated in vacuo to afford the crude product which was purified by column gel chromatography (petroleum ether:acetone = 15:1) to give the desired product (3.6 g, 81%) as a yellow oil. 1H NMR (400 MHz, CDCl3) δ8.16 (s, 1H), 8.05 (d, J = 1.4 Hz, 2H), 6.77 (s, 1H), 4.73 (m, 1H), 4.19 (m, 2H), 1.65 (m, 2H), 1.50 (d, J = 4.6 Hz, 3H), 1.39 (m, 2H), 0.95 (t, J = 7.4 Hz, 3H); 13C NMR (100 MHz, CDCl3) δ173.0, 163.8, 148.1, 137.3, 135.4, 94.8, 65.7, 48.8, 30.5, 19.1, 18.6, 13.7. MS (EI) m/z 441.15; HRMS (ESI) m/z calcd for C14H13I3NO2: C, 33.56; H, 3.42; I, 50.65; N, 2.80; O, 9.58; Found: C, 33.67; H, 3.546; N, 2.748.

Butyl 2-(3, 5-bis((trimethylsilyl)ethynyl)benzamido) propanoate (1a-2). Under nitrogen protection, 1a-1 (5.0 g, 9.6 mmol), Pd(PPh3)4Cl2 (0.34 g, 0.48 mmol) and CuI (0.091 g, 0.48 mmol) were added to a dry 100 mL flask, followed by addition of THF (50 mL) and NEt3 (5 mL) via syringe, then trimethylsilylethylene (6.8 mL, 48 mmol) was added in one portion. The mixture was stirred over night at room temperature. The crude mixture was filtered through a silica gel plug and concentrated in vacuo. The concentrate was purified by column gel chromatography (petroleum ether:acetone = 20:1) to give the desired product (3.6 g, 81%) as a white solid, mp 130.4-136.0 °C. 1H NMR (400 MHz, CDCl3) δ7.87 (d, J = 1.5 Hz, 2H), 7.72 (t, J = 1.5 Hz, 1H), 6.73 (d, J = 7.0 Hz, 1H), 4.76 (m, 1H), 4.20 (m, 2H), 3.15 (s, 2H), 1.67 (m, 2H), 1.52 (d, J = 7.1 Hz, 3H), 1.40 (m, 2H), 0.95 (t, J = 7.4 Hz, 3H); 13C NMR (100 MHz, CDCl3) δ173.1, 165.0, 138.1, 134.6, 130.4, 124.2, 103.2, 96.5, 65.8, 48.9, 30.7, 19.2, 18.9, 13.8, 0.1. MS (EI) m/z 442.2234; found 442.2244.

Butyl 2-(3, 5-diethylbenzamido) propanoate (1a-3). Tetrabutylammonium fluoride (5.87 g, 22.5 mmol) was added to a solution of 1a-2 (3.44 g, 7.5 mmol) in THF (50 mL) at room temperature. The solution was stirred for 0.5 h, and the solvent was removed in vacuo to leave a brown residue. The residue was purified by column gel chromatography (petroleum ether:acetone = 5:1) to give the desired product (1.22 g, 51%) as a white solid, mp 135.0-136.0 °C. 1H NMR (400 MHz, CDCl3) δ7.87 (d, J = 1.5 Hz, 2H), 7.72 (t, J = 1.5 Hz, 1H), 6.73 (d, J = 7.0 Hz, 1H), 4.76 (m, 1H), 4.20 (m, 2H), 3.15 (s, 2H), 1.67 (m, 2H), 1.52 (d, J = 7.1 Hz, 3H), 1.40 (m, 2H), 0.95 (t, J = 7.4 Hz, 3H); 13C NMR (100 MHz, CDCl3) δ173.1, 165.0,
Compound 1a-4. Under nitrogen protection, 1a-3 (0.32 g, 1.0 mmol), Pd\(_2\)(dba)\(_3\) (0.092 g, 0.1 mmol), CuI (0.023 g, 0.12 mmol) and PPh\(_3\) (0.18 g, 0.72 mmol) were added to a dry 100 mL flask, followed by addition of THF (100 mL) and NEt\(_3\) (20 mL) via syringe. The solution was stirred at room temperature for 15 h. The mixture was poured into water, extracted with ethyl ether, washed with saturated aqueous solution of NH\(_4\)Cl, brine and water, dried over anhydrous Na\(_2\)SO\(_4\) and concentrated in vacuo. The crude product was purified by silicon gel column chromatography (petroleum ether/THF = 4:1) to obtain the desired product (0.3 g, 30%) as a yellow solid. \(^1\)H NMR (400 MHz, DMF) \(\delta\) 8.13 (s, 2H), 8.01 (s, 2H), 7.93 (d, \(J = 0.9\) Hz, 2H), 7.89 (s, 2H), 7.79 (s, 1H), 6.87 (d, \(J = 7.2\) Hz, 1H), 6.80 (d, \(J = 7.0\) Hz, 2H), 4.79 (m, 3H), 4.22 (m, 6H), 1.66 (m, 6H), 1.55 (m, 9H), 1.41 (m, 6H), 0.96 (m, 9H). \(^13\)C NMR (100 MHz, DMF) \(\delta\) 173.2, 173.1, 165.1, 164.5, 142.9, 137.2, 136.5, 135.9, 134.9, 130.6, 130.4, 130.4, 124.5, 124.0, 123.7, 103.1, 96.9, 89.5, 89.2, 65.8, 49.0, 48.9, 30.8, 19.2, 18.9, 13.9, 0.1. HRMS (ESI) m/z calcd for [M+Na]\(^+\): 297.41; Anal. Calcd for C\(_{18}\)H\(_{14}\)NO\(_3\): C, 72.71; H, 6.44; N, 4.71; O, 16.14; Found: C, 71.60; H, 6.580; N, 4.505.

Compound 1a-5. Under nitrogen protection, 1a-4 (0.47 g, 0.45 mmol), Pd(PPh\(_3\))\(_2\)Cl (0.016 g, 0.023 mmol) and CuI (0.005 g, 0.023 mmol) were added to a dry 100 mL flask, followed by addition of THF (50 mL) and NEt\(_3\) (10 mL) via syringe, then trimethylsilylethylene (0.32 mL, 2.25 mmol) was added in one portion. The mixture was stirred over night at room temperature. The crude mixture was filtered through a silica gel plug and concentrated in vacuo. The concentrate was purified by silicon gel column chromatography (petroleum ether/acetone = 5:1) to give the desired product (0.38 g, 85%) as a yellow oil. \(^1\)H NMR (400 MHz, DMF) \(\delta\) 7.92 (d, \(J = 1.5\) Hz, 2H), 7.90 (t, \(J = 1.6\) Hz, 2H), 7.85 (t, \(J = 1.6\) Hz, 2H), 7.80 (t, \(J = 1.5\) Hz, 1H), 7.77 (t, \(J = 1.5\) Hz, 2H), 7.20 (d, \(J = 7.3\) Hz, 1H), 6.77 (d, \(J = 7.3\) Hz, 2H), 4.79 (m, 3H), 4.21 (m, 6H), 1.66 (m, 6H), 1.56 (m, 9H), 1.42 (m, 6H), 0.96 (m, 9H), 0.27 (s, 18H). \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 173.2, 165.3, 165.2, 138.7, 137.4, 135.1, 134.9, 130.6, 130.4, 130.4, 124.5, 124.0, 123.7, 103.1, 96.9, 89.5, 89.2, 65.8, 49.0, 48.9, 30.8, 19.2, 18.9, 13.9, 0.1. HRMS (ESI) m/z calcd for [M+Na]\(^+\): 1006.4470; found 1006.4482; MS (MALDI-TOF): 1006.7 [M+Na]\(^+\).

Compound 1a-6. Tetrabutylammonium fluoride (0.27 g, 1.04 mmol) was added to a solution of 1a-5 (0.34 g, 0.35 mmol) in THF (50 mL) at room temperature. The solution was stirred for 1 h, and the solvent was removed in vacuo to leave a brown residue. The residue was purified by silicon gel column chromatography (petroleum ether/acetone = 3:1) to give the desired product (0.16 g, 60%) as a white solid. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.45 (s, 12H), 8.07 (s, 6H), 4.62 (m, 6H), 4.12 (m, 12H), 1.62 (m, 12H), 1.56 (m, 18H), 1.38 (m, 12H), 0.90 (t, \(J = 7.4\) Hz, 18H). \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 138.2, 134.7, 130.8, 123.2, 81.6, 79.1, 65.6, 48.7, 30.5, 19.0, 18.6, 13.6. MS (EI) m/z 297.41; Anal. Calcd for C\(_{18}\)H\(_{14}\)NO\(_3\): C, 72.71; H, 6.44; N, 4.71; O, 16.14; Found: C, 71.60; H, 6.580; N, 4.505.

Macrocycles 1b, 1c, and 1d were prepared based on the same procedures as shown in Supplementary Fig. S4.

Macrocyclic 1b. \(^1\)H NMR (400 MHz, DMF) \(\delta\) 8.17 (d, \(J = 6.8\) Hz, 6H), 8.27 (s, 12H), 8.11 (s, 6H), 4.65 (m, 6H), 4.15 (m, 12H), 1.63 (m, 12H), 1.56 (d, \(J = 7.3\) Hz, 12H), 1.35-1.25 (m, 60H), 0.82 (t, \(J = 6.2\) Hz, 18H).
$^{13}$C NMR (100 MHz, DMF) $\delta$ 172.7, 164.8, 137.2, 135.4, 130.8, 123.4, 89.2, 64.8, 49.3, 31.8, 28.6, 25.9, 22.5, 16.6, 13.7. MS (MALDI-TOF): 1986.7 [M+Na]$^+$. 

**Macrocycle 1c.** $^1$H NMR (400 MHz, DMF) $\delta$ 8.98 (s, 4H), 8.91 (s, 2H), 8.13 (s, 12H), 8.00 (d, $J = 10.7$ Hz, 4H), 4.50 (dd, $J = 13.6, 6.8$ Hz, 6H), 4.05 – 3.93 (m, 12H), 2.71 (d, $J = 4.1$ Hz, 12H), 1.47 (d, $J = 2.8$ Hz, 18H), 1.42–1.36 (m, 12H), 1.23 (dd, $J = 7.1, 1.9$ Hz, 12H). $^1$C NMR (101 MHz, DMF) $\delta$ 172.95, 172.88, 165.08, 135.67, 132.65, 131.70, 130.99, 129.04, 123.72, 123.52, 123.39, 92.79, 89.28, 88.64, 64.60, 49.31, 49.24, 30.76, 19.04, 16.73, 13.40. MS: m/z (MALDI-TOF): 3307.2 [2M+Na]$^+$. 

**Macrocycle 1d.** $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.78-7.53 (18H), 4.30+4.01 (m, 12H), 4.20 (m, 12H), 3.16+3.10+3.09 (18H), 1.71-1.63 (m, 12H), 1.30-1.28 (m, 60H), 0.87 (m, 18H); $^1$C NMR (100 MHz, CDCl$_3$) $\delta$ 170.1, 168.8, 143.7, 136.6, 136.2, 130.0, 123.7, 89.3, 65.6, 49.3, 38.8, 31.8, 29.2, 28.6, 25.9, 22.6, 14.0. MS (MALDI-TOF): 1985.5 [M+Na]$^+$. 

**XRD.** The XRD diffraction pattern revealed by the diffractogram of 1b indicates a highly ordered phase characteristic of disc-like molecules (Supplementary Fig. S5). Specifically, the dominant peak at 28.08 Å, along with two other prominent at 16.13 Å and 13.98 Å, with ratios of $d$-spacings being about (1:1/$\sqrt{3}$:1/2), can be indexed to 100, 110, and 200 reflections of a typical two-dimensional hexagonal lattice, based on which a lattice parameter of $a = 32$ Å is obtained (Supplementary Fig. S5b). Parameter $a$ is the diameter of the column which, assuming partially (~8%) collapsed or interdigitated side chains, is consistent with the molecular dimension of 1b. In addition, the very broad peak that ranges from 3 Å to 8 Å and centers at $2\theta = 15.5^\circ$ (~4.2 Å), is often observed with hexagonally packed columnar discotic liquid crystals and can be assigned to the distance between the packed alkyl side chains of 1b. The presence of a very strong peak at 3.53 Å can be attributed to the interplanar reflections between the flat backbones of the macrocyclic molecules, which suggests relatively strong stacking interactions between the backbones of the molecules in the columns, and indicates the existence of periodicity along the columns. The unusually strong reflection at 3.53 Å points to a extraordinary long-range ordering of the molecules within a column, as revealed by a correlation length between 23 nm to 26 nm that is obtained using Scherrer’s equation, which corresponds to a nanotube having ~65 to 73 continuously stacked macrocyclic units.

Besides the sharp peak at 3.53 Å, several much less prominent peaks also ride on the broad reflection centered around 4.2 Å. As indicated by their intensities and widths, these small peaks reflect structures that are either much loosely organized or lack long-range repeatability in spatial extension but with relatively high population. For example, the intermolecular hydrogen bonding between the numerous amide groups of stacked macrocycles leads to a loosely organized network consisting of about 5 Å repeating unit on the outer surface of hydrogen-bonded columns. The neighboring benzene rings within a macrocycle constitute a length scale of 7.5 Å although this unit does not repeat in space. The broad peak at $2\theta = 23^\circ$ (3.36 Å) indicates an amorphous structure, which may be attributed to the atomic arrangement of the amide and ester groups of the relatively flexible side chains.

**SEM and TEM.** Samples of 1a and 1b were prepared based on a phase-transfer method by using carbon tetrachloride (CCl$_4$) and methanol (CH$_3$OH). The procedure involves the transfer of a larger amount (10:1, v/v) of CH$_3$OH atop a smaller volume of 1a or 1b (100 M for both samples) in CCl$_4$ in a test tube. Within two hours, white fibrous aggregates formed at the interface, and slowly diffused into the upper phase of methanol. The aggregates formed were then transferred and casted onto a solid surface by pipetting. Samples for SEM experiments were prepared by dropping the suspension of the fibrous aggregates in methanol onto aluminium foil, followed by evaporation of solvent in open air. The dried samples were then kept overnight in an oven at 40 °C. Without gold coating, the samples were imaged using a Hitachi S-4800 scanning electron microscope, with an acceleration voltage of 3 kV. Based on the same procedure, samples for TEM
measurements were prepared on holey carbon film and imaged using a Tecnai G2 F20 U-TWIN Transmission Electron Microscope, operated at 120 kV or 200 kV.

No regular assemblies could be detected for 1d prepared using the above phase-transfer method (Supplementary Fig. S8).

**AFM.** The sample was prepared following a method described previously. Briefly, 10 µL of a stock solution of sample (1a, 1b) in CCl$_4$ at 0.1 mM was deposited onto a freshly cleaved mica surface, and then the specimen was placed in an environment with saturated CCl$_4$ vapor for overnight incubation. AFM images were recorded using a Nanoscope 3D multimode SPM (Veeco Instruments Inc., Santa Barbara, Ca) in air with the tapping mode, using RTESP probes (40 N/m, 300 kHz, Veeco Probes, Camarillo, Ca). Typical scan speeds were between 1 m/s to 15 µm/s, depending on the scan size, and the typical cantilever free amplitude was 35 nm. The piezo-scanner was calibrated using a standard 1x1 µm$^2$ grid, prior to imaging the sample.

The apparent nanotube height decreased as the set-point amplitude (A$_{sp}$) decreased owing to the increased imaging force imposed on the specimen. To estimate the "true" height of the sample of 1a, it is possible to infer this value based on a series of measurements at various imaging forces as described before. In this, assuming that the imaging force is approximately proportional to the reduced cantilever oscillation amplitude, $|\sigma| = A_0 - A_{sp}$, where $A_0$ is the free amplitude, a plot of the measured height versus $|\sigma|$ can be extrapolated to $|\sigma| = 0$ to obtain the “true” sample height. In this particular case, the measured height varied linearly with $|\sigma|$ (see Supplementary Fig. S7), yielding a “zero force” height of 3.2 ± 0.1 nm.

For closely packed regions of parallel filaments, the diameter of the filament can be estimated from a 2D Fourier Transform. In the Fourier plot, the periodic structures produce a well-defined diffraction spot, from which this distance can be determined, while the spread of the spot gives an estimate of the variation among the inter-filament distances. The inter-filament distance of 1a nanotubules determined in this way is 3.7 nm ± 0.2 nm.

**UV and Fluorescence Spectroscopy.** UV-vis absorption fluorescence spectra were measured on a GBC Cintra 10e spectrophotometer, and fluorescence spectra were measured on a VARIAN Cary Eclipse fluorometer. As shown in Supplementary Fig. S9A, the UV spectrum of 1b in carbon tetrachloride shows an absorption maximum at ~275 nm that is significantly blue-shifted from the absorption maxima (at 290 nm) of the spectra recorded in the other three solvents (CHCl$_3$, DMF, THF). This shift can be attributed to exciton coupling between the conjugated backbones of neighboring macrocycles, which suggests the presence of aggregated structure in carbon tetrachloride. The observation made by UV spectroscopy is corroborated by fluorescence spectroscopy, which indicates that the emission maximum (at ~425 nm) in carbon tetrachloride undergoes a large red shift from those (at ~350 nm) in the other three solvents (Supplementary Fig. S9C). In contrast, the UV and fluorescence spectra of compound 1d recorded in these four solvents share a similar shape and $\lambda_{\text{max}}$ (Supplementary Figs S9B and S9D), suggesting that the observed shifts in the spectra of 1b in carbon tetrachloride are caused by hydrogen bond mediated aggregation. The aggregated structures of 1b remain unchanged from 5 mM to 50 mM in carbon tetrachloride, as indicated by UV spectra having the same shape and unchanged absorption maxima within this concentration range (Supplementary Fig. S10).

**CD Spectroscopy.** The circular dichroism spectra were recorded on a Jasco-J815 CD spectrometer equipped with a Jasco PTC-423S/15 temperature controller. All the measurements were carried out using a 1 mm cuvette in the range between 250 and 400 nm at indicated temperature.

**IR Spectroscopy.** The FT-IR spectra were acquired using an IR spectrometer (Vertex 70, Bruker Optics) with a MCT detector, which are collected as transmission with the monomer, trimer and 1a dissolved in CCl$_4$ (2 mM) onto ATR (Attenuated total reflectance). A total of 250 scans for both sample and background were operated in the range of 4000-1000 cm$^{-1}$ with 4 cm$^{-1}$ resolution.
Liposome assay to measure proton transport. In order to study the proton permeability of lipid membranes by target compounds 1a and 1b, solutions of LUVs with entrapped pH sensitive, fluororescent dye 8-Hydroxypyrene-1, 3, 6-trisulfonic acid (HPTS) dissolved at neutral pH were pulsed with an aliquot of a HCl (2.0 M) solution. If the target compound forms transmembrane pores, the fluorescence intensity of HPTS will be quenched by the influx of protons through the pores.

HPTS (0.1 mM) encapsulated within LUVs depicts a signature emission spectrum (green line) at 520 nm (data not shown). In contrast, compound 1a and 1b (30 µM in THF, blue line) do not emit at the same wavelength (data not shown). Therefore, in this study, HPTS is a suitable indicator for monitoring change of membrane proton permeability caused by the target compounds 1a and 1b.

A solution of LUVs in HEPES buffer pH = 7.2 (final volume 2 mL, LUV concentration 50 µM) was acidified by adding 40 µL of HCl (2.0 M) and then incubated at room temperature for one minute in a cuvette, to which 1a (5 µM and 10 µM), 1b (5 µM and 10 µM), or 1c (10 µM) from stock solution (1 mM) in THF, or Triton (600 µL, 100 mM TritonX-100 in HEPES buffer) was added to reach the final concentrations shown. Changes in fluorescence intensity were monitored over a period of 70 minutes. Total lysis of the LUVs was achieved in the presence of 30 mM Triton X-100. The experiments were carried out at room temperature on a Perkin Elmer LS 55 luminescence spectrometer set at an excitation wavelength of 450 nm and an emission wavelength of 520 nm with an excitation slit of 15.0 nm and emission slit of 20 nm, respectively.

The reduction in the fluorescence emission of HPTS after adding 1a is an indication that there is significant proton influx into the vesicle, leading to the acidification of the vesicle interior. The leveling off of the emission at later times is a consequence of the reversal potential at equilibrium, a result of this proton influx, which impedes further net ion translocation, as described below.

Owing to the small size of the vesicles, the translocation of ions into the vesicles, down their concentration gradient, significantly alters both the membrane potential and the vesicular proton concentration (pH). As more ions enter the vesicle, the magnitude of the potential increases until the potential equals the reversal potential (which by definition is the voltage, associated with the concentration gradient, at which there is no net ion translocation).

The membrane potential at any net ion influx can be obtained from

\[ V = \frac{Q}{C} \]

where Q is the net charge of the ions translocated and C is the capacitance, which can be obtained from the typical areal capacitance of 1µF/cm² for bilayer membranes and the surface area of the vesicles of 100 nm diameter. The reversal potential is given by

\[ V_{rev} = \left(\frac{RT}{F}\right) \ln \left(\frac{\left[\frac{c}{c_i}\right]}{\left[\frac{c}{c_i}\right]} \right) \]

where R is the gas constant, T is the temperature, F is Faraday’s constant, \(\frac{c}{c_i}\) is the permeability ratio obtained from single channel measurements, and \(\frac{c}{c_i}\) is the intra-vesicular and extra-vesicular concentration, respectively, of ion \(\mathbf{X}\). In this calculation, we only consider the permeability ratio of the channel, and not of the lipid bilayer itself, since during the time course of our experiments, the rate of proton flux is determined only by the ion transport through the channel.
As a simple example, with the ion concentrations used in the present experiment ([H^+]_o = 40 mM, [Cl^-]_o = 185 mM, [Cl^-]_i = 145 mM) and excluding the effect of HEPES, the translocation of 10 protons inside the vesicle would produce a membrane potential of 5 mV whereas the reversal potential associated with this concentration gradient would be 157 mV. Hence protons would continue to flow into the vesicle causing an increase in the membrane potential and, with an increase of the intra-vesicular proton concentration, a decrease in the reverse potential. This would continue until the membrane potential equals the reversal potential, at which point there would be no further net translocations. When this occurs, the intra-vesicular pH would be 3.2, significantly lower than the original pH (7.2), but still higher than the extra-vesicular pH of 1.4, which explains why the fluorescence never reaches the level of that of Triton even at long times. The effect of HEPES does not fundamentally alter this phenomenon. Calculating the effects of HEPES, which has pKa values of 3 and 7.55, is complicated. However by directly measuring an extra-vesicular pH of 4.3 (50 µM) under these conditions, an intra-vesicular pH of 4.6 (25 µM) at equilibrium is expected, again significantly lower than the original pH of 7.2, leading to the reduced fluorescence as observed in Fig. 3.

We note that macrocycle Ib directly added to solutions of LUVs containing entrapped HPTS did not lead to any change of fluorescence intensity (data not shown). However, upon an acid pulse, the fluorescence intensity of HPTS entrapped in LUVs prepared from lipids (PS and POPC) containing pre-mixed Ib showed a rapid reduction that levels off over times (data not shown).

**Single Channel Electrophysiology.** Single channel activity is examined in 1 mM HCl solution and only 1a produced measurable currents (Fig. 3b). The single channel conductance histogram (N=262) is fitted to the Gaussian function:

\[
f(x) = \frac{A}{\sqrt{2\pi} \sigma} e^{-\frac{(x-x_c)^2}{2\sigma^2}}
\]  

(1)

The results indicate that the mean conductance (x_c) of 1a is 4.8, and the standard deviation (\sigma) of 1a conductance is 1.9 pS. We found that the open-close kinetics of 1a channel in the bilayer follows the function of first order decay. The single channel lifetime histogram (N=262) is fitted to the first-order exponential decay equation:

\[
f(x) = A_t e^{-x/t}
\]  

(2)

These results indicate that the lifetime (t) of 1a channel is 148 ± 6 ms. Furthermore, the I-V relationship of 1a channel is determined to be linear when the holding voltage is changed from -200 mV to +200 mV. The data is well fitted to the linear equation:

\[y = A + Bx\]  

(3)

The 1a channel is highly selective of protons as determined by the reversal potential\(^{12}\). As described in the standard procedure, two different ionic concentrations were used: 1 mM HCl solution in cis and 5 mM HCl in trans. Potentials between -200 mV to +200 mV were applied and the channel current was recorded (Supplementary Fig. S12).

The result indicates that the reversal potential is -75.2 mV (Supplementary Fig. S12). After correcting the Nernst potential of chloride (-35 mV), the reversal potential of 1a in asymmetrical HCl solution (cis 1 mM, trans 5 mM) is -40.2 mV, the magnitude of which is very close to the Nernst potential of proton
Based on the reversal potential, the ion permeability ratio of proton and chloride could be calculated by the Goldman-Hodgkin-Katz equation:

\[ V_{rev} = \frac{k_B T}{e} \ln \left( \frac{P_H [C]}{P_H [C] + P_{Cl} [Cl]} \right) \]  

The calculated permeability ratio of \( P_H/P_{Cl} \) is about 3,328. Therefore the 1a channel is highly proton-selective.

In addition to the reversal potential experiments, we also performed the single channel conductance recording of 1a in the solution of 1 mM HCl + 150 mM NaCl, 1 mM HCl + 150 mM KCl and 1 mM HCl + 150 mM LiCl. When channel activity is detected in 1 mM HCl solution at +200 mV, either NaCl, KCl, or LiCl is added to both sides of lipid bilayer to a final concentration of 150 mM. The values of all of the latter conductance are nearly the same as that of 1 mM HCl solution, which is about 6 pS (data not shown). Therefore, proton is the key factor attributes for channel observation in planar lipid bilayer.

Compound 1a was also found to have well defined conductance (Fig. 4a) in 4.0 M KCl solution (pH 6.0). The mean conductance of 1a in 4.0 M KCl (pH 6.0) is 5.8 ± 0.1 pS (N = 895) and the lifetime of 1a in 4.0 M KCl (pH 6.0) is 350 ± 10 ms (N = 895). Furthermore, we found that the I-V relationship of 1a in 4.0 M KCl (pH 6.0) is also linear.

According to the CRC handbook of Chemistry and Physics, the activity coefficients of 4.0 M KCl and 1 mM HCl are 0.593 and 0.965, respectively, so the effective concentrations of KCl and HCl are 2.372 M and 0.963 mM, respectively. Together with the conductance of 1a in 1 mM HCl (4.8 pS) and in 4.0 M KCl (5.8 pS), the \( H^+ \) permeability is ~2,000 times of that for \( K^+ \). Furthermore, no measurable current in 4M NaCl or LiCl was detected (Supplementary Fig. S13).

The traces of 1a single-channel recordings have two well-defined states, i.e., the open state and closed state, in both 1 mM HCl and 4 M KCl (pH 6.0). Each state can be fitted into the Gaussian equation (1), with mean values of 0 pA and 1.14 pA respectively. \( P_0 \) is defined as the open probability, and thus \((1-P_0)\) is the closed probability. The ratio \( P_0/(1-P_0) \) equals to the ratio of the areas of the open state to the closed state, namely, \( A_2/A_1 \), which is 0.056. Thus the open probability \( P_0 \) is determined to be 5.3%.

In 4M KCl and +200mV, the lifetime of the open state was found to be 350 ms. Based on the analysis of closed events of ten independent single-channel recording experiments under these conditions, the lifetime of the closed state was found to be about 6500 ms. From the rates of closed state and open state, we obtained the open probability \( P_0 = \tau_0/(\tau_0+\tau_c) = 0.051 = 5.1\% \), which is consistent with the all-points data.

Furthermore, based on the Boltzmann equation: \( P_0/P_c = \exp(-\Delta \mu/k_B T) \), the free energy difference \( \mu_o - \mu_c \) between the open state and the closed state can be estimated, which is about 3 k_B T (7-8 kJ/mol). The open probability of the 1a channel was found to be correlated with 1a concentration (solution) (Table S1 and Fig. 4b). The data shown in Table S1 were fitted to the Hill equation (5):

\[ \log (P_0/(1-P_0)) = n \log ([1a])-log (K) \]  

where \( n \) is the Hill coefficient, [1a] is the 1a concentration, K is a constant related to the rate constants of the process.

A Hill coefficient of \( n = 9 \pm 3 \) was obtained (Fig. 4b), suggesting a stoichiometry of nine 1a monomers in each assembled channel, a result consistent with MD simulations (below). With these data, an EC50 = 30 µM (at the point \( P_0 = 1-P_0 = 0.5 \)) was estimated from the fitted red line (Fig. 4b). However, we should indicate that above about 20µM, 1a precipitates quickly. As such, EC50 concentration is not experimentally accessible through direct addition to aqueous solution.
**MD Simulations.** The 3D structures of 1a nanotube was constructed by using the molecular builder package in Molecular Operating Environment (MOE 2008). The constructed structure was then parameterized by MMFF94x force field, subjected to a 2000-step energy minimization using the steepest descent approach, followed by a 2000-step conjugate-gradient energy minimization. Next, a systematic search for the side-chain conformation in vacuum using the stimulated annealing approach with the macrocycles (the atoms in the benzene ring and C-C triple bond) fixed. During the conformation search, totally 2 million configurations of the side-chains were obtained and recorded in a conformation database.

Molecular dynamics (MD) simulations of 1a nanotube in vacuum, chloroform solvent, and a POPC lipid bilayer were performed. The force field parameters for 1a, chloroform, and the POPC lipid bilayer were generated using the Paratool Plugin package (version 1.4) in VMD. Initially, the lipid bilayer was consisted of 256 POPC molecules. The lipid bilayer was equilibrated at room temperature for 100 ns in our MD simulations. The 1a nanotube was then inserted into the equilibrated bilayer by superposing the mass centers of the nanotube and the POPC bilayers. Molecules of the lipid bilayer within 3 Å to atoms of 1a nanotube were removed. The combined system was then relaxed for 10 ns in the MD simulation with all atoms of 1a nanotube fixed. The final combined system for next-stage MD simulation contained 208 POPC molecules (see below).

MD simulations of 1a nanotube in vacuum and chloroform solvent were performed using GROMACS 3.3.3 package, and those in the POPC lipid bilayer were performed using NAMD 2.7. Periodic boundary conditions were applied in all spatial directions. Constant-pressure and constant-temperature (NPT) ensemble was selected. In the MD simulations, all bonds were constrained by using the LINear Constraint Solver (LINCS) algorithm. The temperature and pressure were controlled by the Berendsen thermostat and barostate with a coupling time of 0.1 ps and 1.0 ps, respectively. The particle mesh Ewald algorithm was employed to treat electrostatic interactions with an interpolation order of 4 and a grid spacing of 0.12. The van der Waals (vdW) interactions were treated with a cut-off of 12 Å. The integration step was set to 1 fs.

To investigate dynamic behavior of the 1a nanotube in vacuum and in chloroform, MD simulations were performed for systems containing 5-, 10-, and 40- 1a molecules. We found that 1a molecules can self-assemble into a nanotube in vacuum and chloroform, similar to those shown in the AFM images (Supplementary Fig. S3). In chloroform, the inner (vdW) diameter of the 1a nanotube is ~6.4 Å. The average inter-planar distance between two stacked 1a macrocycles is ~3.65 Å, the average relative angular displacement between neighboring molecules is ~ 20 degrees. At 0 K, six hydrogen bonds can form between two neighboring 1a molecules. However, in our MD simulations, only three hydrogen bonds can form on average at room temperature due to thermal fluctuations.

As mentioned above, the final combined system for the nanotube in the bilayer containing 208 POPC molecules and 16 1a molecules were used in a 10 ns MD simulation. We independently prepared twenty such systems and performed independent MD simulations. In 17 of the twenty systems, the stable 1a nanotube that was embedded in the POPC bilayer contained ten 1a molecules (Supplementary Fig. S14).

Lastly, we constructed a new system with ten 1a molecules embedded in the POPC lipid bilayer (having 208 POPC molecules) to study water permeability and ion sensitivity (for K+ and Cl-). To simplify the simulations, we fixed all the 1a atoms during the MD simulations. We found that water molecules can spontaneously enter into the lumen of the 1a nanotube, and form a structured water wire (data not shown). Additionally, when K+ ion is present and the system is under an external potential of 1 V, K+ can enter the 1a nanotube within 10 ns.

**Stopped-flow experiments.** Phospholipids POPC (1-Palmitoyl-2-Oleoyl-sn-Glycero-3-Phosphocholine)/PS (L-(-Phosphatidylserine) lipids (from Avanti Polar Lipids, Alabaster, Al) in an 80/20 (w/w) ratio were first dissolved in chloroform with/without 1a or 1c. Several different lipid/1a ratios have been used. The solvent was then evaporated using a rotary evaporator under vacuum for one hour, after which the lipid film was placed in a buffer (100 mM HEPES, 145 mM NaCl, pH7.2, 5 mM carboxyfluorescein; final
concentration of lipids = 2 mg/mL). The solution was hydrated in a water bath for one hour followed by extrusion through a 0.1-µm polycarbonate membrane (Avanti Polar Lipids, Alabaster, AL) to produce a homogeneous solution of large unilamellar vesicles (LUVs). LUVs were then separated from the extra-vesicular fluorescent dye by gel filtration using Sephadex G-50 (GE Healthcare), pre-equilibrated with HEPES buffer. The size of LUV was measured by DLS particle analyzer (Nano ZS90, Malvern, U.K.). The measured sizes of LUVs with and without 1a or 1c were around 130 nm.

The coefficient of osmotic water permeability, $P_f$, was determined by rapidly increasing the extra-vesicular osmolality in a stopped-flow fluorometer. For the case where the molar lipid/1a = 50/1, the $P_f$ was found to increase ($P_f = 0.0051\pm0.0008$ cm/s, n = 3) when compared with control liposomes ($P_f = 0.0044$ cm/s). As the number ratio of 1a to the lipid was 1:50, and there were approximately 3000 1a molecules in each vesicle (diameter = 130 nm) and if we assume 10 1a molecules forming each pore, there are about 300 channels per LUV. As 1a readily assembled into long nanotubes in chloroform, some of these may not get incorporated into the LUVs. Therefore, this can only be considered as the upper limit. Taking this estimate and the measured kinetics of these channels (see above), the estimated osmotic water permeability of each 1a channel, when open, is $p_f = 2.6 (\pm 0.4) \times 10^{-14}$ cm$^3$/s (n = 3). For the well-studied aquaporin, $p_f = 11.7 \times 10^{-14}$ cm$^3$/s. Therefore, the water conductance of the 1a nanapore is about 22% of the aquaporin. This is the estimated lower limit of the 1a channel.

**Supplementary References**