Supramolecular polymerization of imine-linked macrocycles has been coupled to dynamic imine bond exchange within a series of macrocycles and oligomers. In this way, macrocycle synthesis is driven by supramolecular assembly, either into small aggregates supported by π-π interactions, or high-aspect ratio nanotubes stabilized primarily by electrostatic and solvophobic interactions. For the latter, supramolecular polymerization into nanotubes restricts imine exchange, thereby conferring chemical stability to the assemblies and their constituent macrocycles. Competition in the formation and component exchange among macrocycles favored pyridine-2,6-diimine-linked species due to their rapid synthesis, thermodynamic stability, and assembly into high-aspect ratio nanotubes under the reaction conditions. In addition, the pyridine-containing nanotubes inhibit the formation of similar macrocycles containing benzene-1,3-diimine-linkages, presumably by disrupting their assembly and templation. Finally, we exploit rapid imine exchange within weak, low-aspect ratio macrocycle aggregates to carry out monomer exchange reactions to macrocycles bearing pyridine moieties. Once a pyridine-containing dialdehyde has exchanged into a macrocycle, the macrocycle becomes capable of nanotube formation, which dramatically slows further imine exchange. This kinetic trap provides chemically diverse macrocycles that are not attainable by direct synthetic methods. Together these findings provide new insights into coupling supramolecular polymerization and dynamic covalent bond-forming processes and leverages this opportunity to target asymmetric nanotubes. We envision these findings spurring further research efforts in the synthesis of nanostructures with designed and emergent properties.
Supramolecular Polymerization Provides Non-Equilibrium Product Distributions of Imine-Linked Macrocycles

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Abstract
Supramolecular polymerization of imine-linked macrocycles has been coupled to dynamic imine bond exchange within a series of macrocycles and oligomers. In this way, macrocycle synthesis is driven by supramolecular assembly, either into small aggregates supported by π-π interactions, or high-aspect ratio nanotubes stabilized primarily by electrostatic and solvophobic interactions. For the latter, supramolecular polymerization into nanotubes restricts imine exchange, thereby conferring chemical stability to the assemblies and their constituent macrocycles. Competition in the formation and component exchange among macrocycles favored pyridine-2,6-diimine-linked species due to their rapid synthesis, thermodynamic stability, and assembly into high-aspect ratio nanotubes under the reaction conditions. In addition, the pyridine-containing nanotubes inhibit the formation of similar macrocycles containing benzene-1,3-diimine-linkages, presumably by disrupting their assembly and templation. Finally, we exploit rapid imine exchange within weak, low-aspect ratio macrocycle aggregates to carry out monomer exchange reactions to macrocycles bearing pyridine moieties. Once a pyridine-containing dialdehyde has exchanged into a macrocycle, the macrocycle becomes capable of nanotube formation, which dramatically slows further imine exchange. This kinetic trap provides chemically diverse macrocycles that are not attainable by direct synthetic methods. Together these findings provide new insights into coupling supramolecular polymerization and dynamic covalent bond-forming processes, and leverages this opportunity to target asymmetric nanotubes. We envision these findings spurring further research efforts in the synthesis of nanostructures with designed and emergent properties.

Introduction
Supramolecular polymers are a compelling platform to design nanostructures with diverse functionality, long range order, and dynamic properties that are not attainable via traditional covalent polymerization.\textsuperscript{1-5} Due to the promise of accessing materials with these sought-after properties, the last decade of research has seen an emergence in novel supramolecular polymerization strategies such as ‘sergeant and soldier’ chirality amplification,\textsuperscript{6-9} living supramolecular polymerization,\textsuperscript{10-14} and supramolecular (co)polymerization.\textsuperscript{5,15-18} While these strategies allow access to diverse nanostructures, they all employ a general two-step process in which the building blocks are first isolated as a unimolecular species and polymerized in a second synthetic step. In this process, polymerization is typically induced by altering the solvent composition\textsuperscript{9,22} or changing the temperature of a monomer solution.\textsuperscript{5,24-27} Using this approach, the chemical structure of the building blocks remain fixed and diverse nanostructures emerge from the order in which they assemble. However, supramolecular polymerization under conditions in which the monomers can also undergo structural changes can target highly diverse nanostructures that are kinetically stabilized by the function of supramolecular polymerization.\textsuperscript{28-30}

Using the traditional two-step approach, we have previously isolated imine-linked macrocycles derived from aromatic dialdehydes and a bifunctional aryl amine (DAPB); and studied their aptitude to undergo acid-mediated supramolecular polymerization into high-aspect ratio nanotubes.\textsuperscript{31,32} In the case of macrocycles derived from simple aromatic dialdehydes such as terephthalaldehyde and isophthalaldehyde...
(IDA, MC 1), high concentrations of CF₃CO₂H (>2000 equiv) were required to protonate the imine linkages and drive assembly, while lower acid concentrations catalyzed macrocycle hydrolysis. However, including pyridine moieties (MC 2), which are significantly more basic than the imine linkages allowed macrocycle assembly to occur upon pyridinium formation, even in the presence of sub-stoichiometric acid loadings. Because of the low concentrations of CF₃CO₂H needed for supramolecular polymerization, we hypothesized that pyridine-containing macrocycles would form nanotubes during their covalent synthesis. In this way, the process of supramolecular polymerization and imine-exchange amongst pyridine containing species may interact and influence each other. Furthermore, we hypothesized that the relative strengths of non-covalent interactions supporting the assemblies of MC 1 and MC 2 would have profound effects on their kinetic stability and ability to undergo monomer exchange. Under this hypothesis, the relatively weak π-π interactions supporting MC 1, coupled with the inherent reactivity of IDA and 2,6-pyridinedicarboxaldehyde (DFP), would enable monomer exchange to macrocycles bearing pyridine moieties. This exchange would unlock nanotube formation and provide non-symmetric macrocycles that are inaccessible by direct synthetic methods (Figure 1).

Figure 1. Impacts of pyridine moiety incorporation on macrocycles aptitude to undergo acid-mediated supramolecular polymerization, and the impacts of supramolecular polymerization on imine dynamics.
Results and Discussion

The reactivity of DFP along with the assembly of MC 2 into nanotubes under reaction relevant conditions accelerates the formation of MC 2 relative to MC 1 by at least two orders of magnitude (Figure 2A). The assembly processes of nanotube formation of charged macrocycles and π-π aggregation of neutral macrocycles that each drive macrocyclization cause the relative rates of macrocycle formation to be correlated to the emergence of an x-ray diffraction (XRD) signal. Tracing the emergence of the predominant nanotube diffraction feature via time-resolved XRD (TR-XRD) demonstrates that the formation of MC 2 occurs before the first data point was obtained (2.5 min), while the formation of MC 1 takes over two hours (Figure 2B and 2E). The results of TR-XRD were validated using gel-permeation chromatography (GPC), in which MC 2 demonstrated a single narrow elution band after 2 minutes of reaction time. However, in the case of MC 1, 2 minutes of reaction time yielded linear polymer and as the major product, with a small

Figure 2. Probing the kinetics of the assembly processes that govern the formation of MC 1 and MC 2. (A) Scheme of macrocycle formation. (B) TR-XRD patterns from 0 to 240 minutes depicting the formation and assembly of MC 1. (Inset) Normalized integration of the diffraction signal with respect to time. (C) Atomic force micrograph of the ill-defined aggregates resulting from the formation of MC 1. (D) Scanning electron micrograph of the ill-defined aggregates resulting from the formation of MC 1. (E) TR-XRD patterns from 0 to 10 minutes depicting the rapid formation and assembly of MC 2. Slight decreases in intensity were observed due to x-ray beam damage of the resulting nanotubes. (Inset) Normalized integrations of the diffraction signal with respect to time. (F) Atomic force micrograph of the nanotubes resulting from the formation of MC 2. (G) Scanning electron micrograph of the nanotubes resulting from the formation of MC 2.
secondary peak corresponding to the target macrocycle. At longer times, the GPC signal of the MC 1 experiment narrowed, indicating successful macrocycle formation (See Supporting Information), which is consistent with our previous study on how neutral macrocycles form via linear polyimines. Characterization of the resulting macrocycles by matrix-assisted laser desorption ionization mass spectrometry (MALDI-MS) revealed single peaks corresponding to the target macrocycles (Figures S4 and S23). Furthermore, analysis of the final states of each macrocyclization reaction by atomic force microscopy (AFM), scanning electron microscopy (SEM), and transmission electron microscopy (TEM) demonstrated that MC 2 forms high aspect ratio nanotubes, while MC 1 yield ill-defined aggregates, which is consistent with previous reports (Figures 2C-2D and 2F-2G) (See Supporting Information). Contributing factors to the observed rate acceleration are the inductive nature of the pyridine ring, which increase the rate of imine condensation to yield acyclic products, and supramolecular polymerization, which drives imine-exchange of these undesired intermediates to yield MC 2. A small molecule study in which DFP was condensed with aniline under conditions typical for macrocycle synthesis yielded 2,6-diiminophenylpyridine within the first five minutes of reaction time, which is an order of magnitude faster than the reaction of aniline with IDA (Figure S110-114). The above experiments demonstrate that MC 2 assembles into nanotubes under conditions typical for its synthesis and that its linkages form more rapidly than those of MC 1. These two factors explain the rapid and highly selective formation of MC 2, and we designed follow-up experiments to further explore this interplay.

The formation of MC 2 dominates a competition experiment in which both dialdehydes compete for a limited number of amine nucleophiles (Figure 3A). By combining 1 equiv of DAPB with 1 equiv each of DFP and IDA MC 2 is formed in high yield while reaction of IDA with small quantities of DAPB yields acyclic oligomers. In order to ensure that the formation of a small population of MC 1 was not limited by

![Figure 3](image_url)

**Figure 3.** Probing the interplay of kinetic preference and chemical stability of MC 2 through competition and scrambling experiments. (A) Scheme of the competition and scrambling experiments. (B) Representative gel permeation chromatograms of the competition experiment (purple) and the scrambling experiment (blue). (C) Representative MALDI-MS spectra of the results of the competition experiment (purple) and the scrambling experiment (blue). MC 2 was observed as the [M+H]+, [M+Na]+, and [M+K]+ adducts.
availability of the acid catalyst, the reaction was run at an elevated acid loading (10 equiv). The products of this competition reaction were characterized by GPC, MALDI-MS, and 1H NMR spectroscopy. GPC analysis indicated the predominant formation of a single macrocyclic product, as judged by the narrow peak shape whose retention time matched purified samples of MC 2, along with relatively weak signals corresponding to other oligomeric species (Figure S71). MALDI-MS analysis of the same product mixture indicated a strong signal corresponding to the mass of MC 2, along with small oligomers containing IDA and DAPB species that did not react to form macrocycle (Figures 3C and S78-S82). No signal corresponding to MC 1 was observed. 1H NMR spectroscopy of the crude products also indicated the selective formation of MC 2. Similar to the MALDI-MS analysis, no signals in the NMR spectrum corresponding to MC 1 were observed (Figure S83). The formation of nanotubes under the reaction conditions was confirmed by AFM, SEM, and TEM; demonstrating that small oligomers containing IDA moieties did not interrupt the assembly of MC 2 (Figures S84-S86). Lastly, the presence of assembled nanotubes in the reaction solution prior to workup was confirmed by in situ XRD, which yielded a pattern comparable to the direct synthesis of MC 2 (Figure S87). Finally, a small molecule competition study in which IDA (1 equiv), DFP (1 equiv), and aniline (2 equiv) were reacted under conditions typical for macrocycle synthesis exclusively yielded 2,6-diiminophenylpyridine, whereas unreacted IDA remained in solution (Figures S110-S111). Collectively, these results indicate that pyridine-containing macrocycles have two factors that favor their formation relative to benzene-containing derivatives. First, DFP forms imines more rapidly than IDA. Second, pyridine-containing macrocycles undergo supramolecular polymerization as they form, which further drives macrocycle formation over acyclic products. The corresponding process for IDA macrocycles requires 105 higher acid concentrations, such that only more weakly bound assemblies are present during their synthesis.

The most surprising finding of a scrambling experiment was that MC 1 was not formed in detectable amounts, despite there being sufficient DAPB to form a 1:1 mixture of MC 1 and MC 2. This finding suggests that the formation and/or assembly of MC 2 interrupts the templation process required to form MC 1. A scrambling reaction between DAPB (1 equiv), DFP (0.5 equiv), and IDA (0.5 equiv) resulted in the selective formation of MC 2 and small IDA-containing oligomers (Figure 3A). In contrast, both pyridine-2,6-diimine and benzene-1,3-diimine species are formed in the presence of aniline under the same conditions (See Supporting Information). The GPC trace of the scrambling reaction indicated the presence of macrocyclic and oligomeric species. MALDI-MS of the reaction indicated that only MC 2 was formed, and that all identifiable peaks corresponding to oligomers were IDA-containing species (Figures 3B-3C and S60-S66). Furthermore, 1H NMR spectroscopy of the reaction mixture showed resonances corresponding to MC 2, but not MC 1, as well as oligomers containing IDA (Figure S67). Isolation of MC 2 by precipitation into CH2Cl2 resulted in an isolated macrocycle yield of 72-94% with respect to DFP, corresponding to half of the available DAPB reacting to yield macrocycles (Table S3). Similar to the direct synthesis of MC 2 and the previous competition experiment, AFM, SEM, and TEM images confirmed the formation of nanotubes that drive macrocycle formation (Figures S68-S70). Lastly, the in situ XRD pattern of the scrambling reaction demonstrates an extended structure analogous to the direct synthesis of MC 2 (Figure S71). These combined findings indicate that the scrambling experiment, conducted at 25 mM DAPB and 12.5 mM each of DFP and IDA, forms MC 2 with no IDA incorporation, as well as no evidence MC 1 formation. In contrast, when 12.5 mM of DAPB and 12.5 mM of IDA are reacted in the absence of DFP, MC 1 is formed in high yield. This suppression of MC 1 formation in the presence of MC 2 was also observed at four other starting concentrations (12.5 mM, 8.5 mM, 6.40 mM, and 5.10 mM with respect to DAPB) of the scrambling experiment (See Supporting Information). The results of the scrambling experiment, combined with small molecule experiments and concentration dependent controls, suggest that MC 2 nanotubes disrupt formation of MC 1.
MC 1 formation was also inhibited in the presence of a pure sample of MC 2, further validating that MC 2 nanotubes prevent the self-templation necessary for MC 1 formation. Furthermore, MC 2 was stable to the reaction conditions, despite the presence of free aldehydes, amines, and acid catalyst. Independently synthesized MC 2 nanotubes were added to a solution of DAPB (1 equiv), IDA (1 equiv), and CF₃CO₂H (10 equiv) and left undisturbed for 3 days (Figure 4A). Analysis of the reaction by GPC yielded results analogous to the scrambling reaction in which several elution bands were observed corresponding to discrete macrocycles and imine-linked oligomers (Figure 4B). Subsequent analysis by MALDI-MS demonstrated that MC 2 was retained throughout the process by the lack of oligomers containing DFP moieties as well as no evidence of IDA moieties exchanging into MC 2. The MALDI-MS spectrum contained signals corresponding to IDA-containing oligomers with no DFP incorporation, consistent with the results of the scrambling reactions (Figure 4C). These findings demonstrate that either free MC 2 or nanotubes comprised of MC 2 disrupt the formation of MC 1. Although the self-templation of MC 1 is not understood at the molecular level, these experiments and previous studies point to a templation process driving macrocycle formation, which is disrupted upon inclusion of monomeric or assembled MC 2 species (Figure 2B).

**Monomer exchange experiments** demonstrate that imines within acid-mediated nanotube assembles are far less dynamic than those in weak assemblies or monomeric species. Due to the stability of the imine linkages of MC 2, through a combination of supramolecular polymerization and the inherent chemistry of pyridine-2,6-diimine moieties, attempts to exchange its DFP moieties for IDA moieties failed. A previously synthesized sample of MC 2 was resuspended in 1,4-dioxane with IDA (10 equiv), and excess CF₃CO₂H (Scheme S6). The reaction mixture was sonicated and held at room temperature for 3 days (Figure 5A). Analysis of the monomer exchange product by GPC confirmed the formation of discrete macrocycles (Figure S88). However, analysis of the solution by MALDI-MS showed full recovery of MC 2, with no incorporation of IDA (Figure 5D). ¹H NMR spectroscopy of product of the attempted monomer exchange demonstrates recovery of MC 2 with no resonances corresponding to IDA-containing species (Figure 5C). Based on the lack of monomer exchange as demonstrated by MALDI-MS and ¹H NMR, we hypothesized that upon exposure to CF₃CO₂H, MC 2 assembled into nanotubes which, along with the inherent stability

**Figure 4.** Control experiment demonstrating the effects of MC 2 nanotubes on the selective synthesis of MC 1. (A) Scheme depicting the control experiment in which previously synthesized MC 2 nanotubes are combined with DAPB, IDA, and CF₃CO₂H under conditions which in the absence of MC 2 nanotubes selectively yields MC 1. (B) Gel permeation chromatogram of the inhibited MC 1 synthesis. (C) MALDI-MS spectra of the results of the inhibited MC 1 synthesis depicting the recovery of MC 2, with no hydrolysis artifacts, and oligomers containing IDA moieties. MC 2 was observed as the [M+H]⁺, [M+Na]⁺, and [M+K]⁺ adducts. (D) Representative gel permeation chromatogram of the direct synthesis of MC 1. (E) Representative MALDI-MS spectra of the direct synthesis of MC 1.
of pyridine-2,6-diimines, prevented reaction of the imine linkages. This hypothesis was supported by AFM, SEM, and TEM, which depicted the formation of nanotubes akin to the direct synthesis of MC 2 (Figures S92-S94). Lastly, the in situ XRD pattern of the failed monomer exchange matches well with that of the direct MC 2 synthesis (Figure S95). Collectively, the inability to exchange the DFP moieties out of nanotubes assembled from MC 2 highlights the chemical persistence and kinetic stability of the imine linkages within the protonation driven molecular assembly.\textsuperscript{32}

Although IDA does not exchange into MC 2 nanotubes, it readily exchanges into macrocycles linked by other substituted isophthalaldehydes. Macrocycles were synthetized using a 5-bromoisophthaldehyde monomer, which assemble similar to MC 1 (Scheme S8) (Figures S106-S107). Monomer exchange of the 5-bromoisophthaldehyde linked macrocycles with IDA resulted in the formation of macrocyclic species, as evident by the narrow elution band in the corresponding GPC trace (Scheme S9) (Figure S108). MALDI-MS depicts scrambling of the linkages, such that peaks were observed corresponding to macrocycles containing 0, 1, 2, or 3 5-bromoisophthaldehyde moieties (Figure S109). These observations indicate that IDA can exchange into macrocycles that contain similar linkages. IDA’s inability to exchange into MC 2 under similar conditions arises either from the increased stability of the pyridine-2,6-diimine moiety or the kinetic persistence of macrocycles in acid-mediated assemblies.

![Figure 5](image.png)

**Figure 5.** Monomer exchange of imine-linked macrocycles. (A) Monomer exchange of MC 2 with IDA. (B) Monomer exchange of MC 1 with DFP. (C) \textsuperscript{1}H NMR spectra of macrocycles resulting from each monomer exchange. (D) MALDI-MS comparison of the macrocycles resulting from each monomer exchange.

When the previous exchange experiment was run in reverse, DFP was able to exchange into MC 1 (Figure 5B). However, the major product of the exchange is a macrocycle containing only one pyridine-2,6-diimine moiety, despite DFP being used in 10-fold excess with respect to MC 1. MALDI-MS of the products revealed the presence of macrocycles containing a mixture of IDA and DFP subunits (Figure 5D). The spectrum clearly shows no evidence of remaining MC 1 or the fully exchanged MC 2. However, the relative amounts of singly and doubly exchanged macrocycles are not clear. \textsuperscript{1}H NMR spectroscopy of the reaction indicated that 86% of the macrocycles contained a single pyridine moiety and 14% contained two pyridine moieties (Figures 5C and S101). Given the rapid and complete formation of MC 2 from DAPB and DFP,
even in the presence of IDA, coupled with the thermodynamic preference for pyridine-2,6-diimine linkages; the selective formation of singly and doubly exchanged macrocycles under these conditions strongly suggest that incorporation of a single pyridine unit drives nanotube formation in the presence of CF₃CO₂H and results in a kinetic trap en route to the thermodynamically favored MC 2. Indeed, nanotubes were observed in these exchange experiments by AFM, SEM, and TEM (Figures S102-S104). The results of the three monomer exchange experiments highlight the diminished reactivity of imine linkages within acid-mediated assemblies. Furthermore, supramolecular polymerization into nanotubes served as a kinetic trap in the full conversion of MC 1 to MC 2, which allows access to non-symmetric macrocycles.

Conclusions
In conclusion, we have developed a system in which supramolecular polymerization is coupled to dynamic covalent bond-forming processes in the synthesis of imine-linked macrocycles. We have demonstrated that the formation of MC 2 is kinetically favored relative to MC 1, and its imine linkages are stabilized as a function of acid-mediated supramolecular polymerization and the inherent chemistry of the linkage itself. These three factors led to the selective synthesis of MC 2 dominating a competition experiment with MC 1. Additionally, the mere presence of nanotubes assembled from MC 2 proved to interrupt the synthesis of MC 1, presumably by disrupting the self-templation that guides its selective synthesis. Lastly, monomer exchange experiments demonstrated that once a pyridine-containing dialdehyde exchanged into MC 1 macrocycle, the macrocycle became capable of nanotube formation, which dramatically slowed further imine exchange, and resulted in the kinetic trapping of chemically diverse macrocycles not attainable by direct synthetic methods. These findings highlight the complex interplay of covalent and non-covalent synthesis that can give rise to complex dynamic reaction networks and stimuli responsive materials.

ASSOCIATED CONTENT
Supporting Information. The Supporting Information is available free of charge on the ChemRxiv Preprint Server:

   Experimental procedures and additional characterization data (PDF)

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Notes
The authors declare no competing financial interests.

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Supramolecular Polymerization Provides Non-Equilibrium Product Distributions of Imine-Linked Macrocycles

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A. Materials and Instrumentation.

I. Materials

Reagents were purchased from commercial grade suppliers and used without further purification. All measurements presented ≤3 mg were delivered via a stock solution of the appropriate monomer. Anhydrous solvents (Toluene, THF, DMF, DCM) were obtained from a solvent purification system (JC Meyer System). Reaction progress was monitored by thin layer chromatography (TLC) carried out on EMD 250 μm silica gel 60-F254 plates. Visualization was performed by UV light irradiation.

II. Instrumentation.

Nuclear Magnetic Resonance (NMR). Isolated \(^1\)H and \(^{13}\)C NMR spectra were acquired on a Bruker AvanceIII-500 MHz spectrometer with a CryoProbe 5mm DCH w/ Z-Gradient, or on a 400 MHz Agilent DD MR-400 spectrometer using an AutoX 5mm probe w/ Z-Gradient. All kinetic NMR experiments were carried out on a Bruker AvanceIII HB Nanobay-400 MHz spectrometer using a BBFO Smart probe w/ Z-Gradient. All spectra were recorded at 25°C unless specified otherwise. All spectra were calibrated using residual solvent as an internal reference (CDCl\(_3\): 7.26 ppm for \(^1\)H NMR, 77.00 for \(^{13}\)C NMR; THF-d8: 3.58, 1.73 ppm for \(^1\)H NMR, 67.57, 25.37 ppm for \(^{13}\)C NMR).

Infrared Spectroscopy (IR). Infrared spectra were recorded on a Nicolet iS10 FT-IR spectrometer equipped with a diamond ATR attachment and are uncorrected.

Matrix Assisted Laser Desorption Ionization Time of Flight (MALDI-TOF) Mass Spectrometry. MALDI-TOF mass spectra were recorded on a Bruker AutoFlex III with a 2,5-dihydroxybenzoic acid (DHB) matrix. All measurements were taken in reflectron positive (RP) mode.

Gel Permeation Chromatography (GPC). Gel permeation chromatography (GPC) was performed in stabilized, HPLC-grade tetrahydrofuran using an Agilent 1260 Infinity II system with variable-wavelength diode array (254, 450, and 530 nm) and refractive index detectors, guard column (Agilent PLgel; 5μm; 50 x 7.5 mm), and three analytical columns (Agilent PLgel; 5μm; 300 x 7.5 mm; 105, 104, and 103 Å pore sizes). The instrument was calibrated with narrow dispersity polystyrene standards between 640 Da and 2300 kDa (Polymer Standards Service GmbH). All runs were performed at 1.0 mL/min flow rate and 40 °C. All samples were dissolved in THF (1 mg/mL) and sonicated for 10 minutes before being filtered through a 0.45 μm syringe filter (PTFE membrane). All chromatograms were obtained using the refractive index detector.

Atomic Force Microscopy (AFM). Atomic force microscopy (AFM) was conducted using the facilities at the Northwestern Atomic and Nanoscale Characterization Experiment Center (NUANCE) on a SPIID Bruker FastScan AFM under the non-contact mode in air. AFM samples
were prepared by drop casting reaction mixtures onto silicon native oxide substrates and allowed to dry for 4 hours before imaging.

**Scanning Electron Microscopy (SEM).** Scanning electron microscopy (SEM) was conducted using the facilities at Northwestern’s Electron Probe Instrumentation Center (EPIC) on an SEM Hitachi SU8030 microscope with an accelerating voltage of 15 kV. SEM samples were prepared by drop casting reaction mixtures onto silicon native oxide substrates and allowed to dry for 4 hours. The samples were then mounted onto a flat aluminum sample holder and coated with 3 nm of Osmium before images were taken.

**Transmission Electron Microscopy (TEM).** Transmission electron microscopy (TEM) images were obtained using the facilities at Northwestern’s Atomic and Nanoscale Characterization Experimental Center (NUANCE) using a JEOL ARM300F GrandARM TEM operating at 300 kV, equipped with a Gatan OneView-IS camera. Samples were prepared by drop casting 4 μL of the macrocyclization reaction solution onto a lacy carbon copper grid (Ted Pella 01885-F). The samples sat on the grids in ambient conditions for ~10 seconds, and then were wicked dry with filter paper.

**In-Situ Wide-Angle X-Ray Scattering (WAXS).** Wide-Angle X-Ray Scattering (WAXS) patterns were collected simultaneously at sector 5-ID-D of the Advanced Photon Source at Argonne National Laboratory. A beam energy of 17.0 KeV was used for all experiments. Patterns were collected with single 10 second frames on a series of 3 Pilatus 2D detectors which were then radially integrated. All samples were conducted in 0.5 mm borosilicate capillaries with a wall thickness of 0.01 nm available from Charles Supper Scientific. For the time resolved XRD experiments, patterns were baselined and then background subtracted from the starting time pattern to produce corrected patterns. The predominant diffraction pattern was then integrated and plotted against the time of each pattern.

**Sonication.** Sonication was performed with a Branson 3510 ultrasonic cleaner with a power output of 100 W and a frequency of 42 kHz.

**Centrifugation.** Centrifugation was performed with a Fisherbrand Mini-Centrifuge operating at 6000 rpm.
B. Synthetic Procedures

Scheme S1. Overall synthesis of S1 (DAPB).

Synthesis of S1:
S1 was prepared using a reported procedure.$^{1,2}$ All characterization of synthetic intermediates were consistent with previous reports. (A) Pd(PPh)$_3$, K$_2$CO$_3$, PhMe:EtOH:H$_2$O (3:1:1), 115°C; (B) Boc$_2$O, PhMe, 90°C; (C) Pd(OAc)$_2$, SPhos, K$_3$PO$_4$, PhMe:H$_2$O (10:1), 80°C; (D) TsCl, Et$_3$N, CH$_2$Cl$_2$; r.t.; (E) K$_2$CO$_3$, DMF, 100°C, then CF$_3$CO$_2$H, CH$_2$Cl$_2$, r.t. (2 steps).
Scheme S2. Synthesis of MC 1 and Corresponding Dilution Experiments.

Synthesis of MC 1:
S1 (3 mg, 0.006 mmol) and isophthalaldehyde (IDA) (0.84 mg, 0.006 mmol, 1.0 equiv) were combined in 1,4-dioxane (0.243 mL, 25 mM with respect to S1) and sonicated until completely dissolved. 20 μL of a 0.2 M solution of CF3CO2H in 1,4-dioxane (0.003 mmol, 0.5 equiv) was then added. The solution immediately turned yellow and a precipitate began to form. The solution was then left undisturbed at room temperature for 36 h. After 36 h, the reaction mixture was neutralized with Et3N (0.5 mL) and poured into Et2O (c.a. 2 mL). The precipitate was isolated by centrifugation and subsequently rinsed with additional Et2O (3x2 mL). The resulting solid was dried under high vacuum at room temperature to yield MC 1 (2.8 mg, 78%) as a light-yellow solid. For all kinetic traces of MC 1 formation, the acid loading was reduced to 0.05 equivalents.

Table S1. Concentrations used to probe dilution effects on MC 1 synthesis.

| Concentration of S1 (mM) | Volume Dioxane (mL) | Yield (mg) | Yield (%) |
|-------------------------|----------------------|------------|-----------|
| 25.00                   | 0.153                | 2.80       | 78%       |
| 12.50                   | 0.397                | 3.10       | 86%       |
| 8.50                    | 0.626                | 2.70       | 75%       |
| 6.40                    | 0.861                | 2.60       | 72%       |
| 5.10                    | 1.103                | 2.40       | 67%       |
| 3.40                    | 1.691                | 2.50       | 69%       |
Scheme S3. Synthesis of MC 2 and Corresponding Dilution Experiments.

Synthesis of MC 2:

S1 (3 mg, 0.006 mmol) and 2,6-pyridinedicarboxaldehyde (0.84 mg, 0.006 mmol, 1.0 equiv) were combined in 1,4-dioxane (0.243 mL, 25 mM with respect to S1) and sonicated until completely dissolved. 20 μL of a 0.2 M solution of CF₃CO₂H in 1,4-dioxane (0.003 mmol, 0.5 equiv) was then added. The solution immediately turned yellow and a precipitate began to form. The solution was then left undisturbed at room temperature for 36 h. After 36 h., the reaction mixture was neutralized with Et₃N (0.5 mL) and poured into Et₂O (c.a. 2 mL). The precipitate was isolated by centrifugation and subsequently rinsed with additional Et₂O (3x2 mL). The resulting solid was dried under high vacuum at room temperature to yield the desired MC 2 (3.1 mg, 86%) as a light brown solid. For all kinetic traces of MC 2 formation, the acid loading was reduced to 0.05 equivalents.

Table S2. Concentrations used to probe dilution effects on MC 2 synthesis.

| Concentration of S1 (mM) | Volume Dioxane (mL) | Yield (mg) | Yield (%) |
|--------------------------|---------------------|------------|-----------|
| 25.00                    | 0.153               | 3.10       | 86%       |
| 12.50                    | 0.397               | 3.40       | 94%       |
| 8.50                     | 0.626               | 3.00       | 83%       |
| 6.40                     | 0.861               | 3.10       | 86%       |
| 5.10                     | 1.103               | 3.10       | 86%       |
| 3.40                     | 1.691               | 3.10       | 86%       |
Scheme S4. Scrambling Experiments Between MC 1 and MC 2.

![Scheme S4. Scrambling Experiments Between MC 1 and MC 2.](image)

Macrocycle Scrambling Experiment:

S1 (3 mg, 0.006 mmol) and a 1:1 mixture of isophthalaldehyde:2,6-pyridinedicarboxaldehyde (0.84 mg, 0.006 mmol, 1.0 equiv) were combined in 1,4-dioxane (0.243 mL, 25 mM with respect to S1) and sonicated until completely dissolved. 40 μL of a 2.0 M solution of CF$_3$CO$_2$H in 1,4-dioxane (0.060 mmol, 10.0 equiv) was then added. The solution immediately turned yellow and a precipitate began to form. The solution was then left undisturbed at room temperature for 36 h. After 36 h., the reaction mixture was neutralized with Et$_3$N (0.5 mL) and poured into Et$_2$O (c.a. 2 mL). The precipitate was isolated by centrifugation and subsequently rinsed with additional Et$_2$O (3x2 mL). The resulting solid was dried under high vacuum at room temperature to yield the desired macrocycles (1.7 mg, 47%) as a light brown solid.

Table S3. Concentrations used to probe dilution effect on macrocycle scrambling reactions. Yields are established assuming S1 could react fully to yield macrocycles. Macrocycles were isolated by precipitating the solid yielded from the reaction into CH$_2$Cl$_2$ and drying under high vacuum.

| Concentration of S1 (mM) | Volume Dioxane (mL) | Yield (mg) | Yield (%) |
|-------------------------|---------------------|------------|-----------|
| 25.00                   | 0.153               | 1.70       | 47%       |
| 12.50                   | 0.397               | 1.50       | 42%       |
| 8.50                    | 0.626               | 1.40       | 39%       |
| 6.40                    | 0.861               | 1.30       | 36%       |
| 5.10                    | 1.103               | 1.40       | 39%       |
Scheme S5. Competition Experiments Between MC 1 and MC 2.

Macrocycle Competition Experiment:

S1 (3 mg, 0.006 mmol) and a 1:1 mixture of isophthalaldehyde:2,6-pyridinedicarboxaldehyde (1.68 mg, 0.012 mmol, 2.0 equiv) were combined in 1,4-dioxane (0.243 mL, 25 mM with respect to S1) and sonicated until completely dissolved. 40 μL of a 2.0 M solution of CF₃CO₂H in 1,4-dioxane (0.060 mmol, 10.0 equiv) was then added. The solution immediately turned yellow and a precipitate began to form. The solution was then left undisturbed at room temperature for 36 h. After 36 h., the reaction mixture was neutralized with Et₃N (0.5 mL) and poured into Et₂O (c.a. 2 mL). The precipitate was isolated by centrifugation and subsequently rinsed with additional Et₂O (3x2 mL). The resulting solid was dried under high vacuum at room temperature to yield the desired macrocycles (3.1 mg, 86%) as a light brown solid.

Table S4. Concentrations used to probe dilution effect on macrocycle competition reactions.

| Concentration of S1 (mM) | Volume Dioxane (mL) | Yield (mg) | Yield (%) |
|--------------------------|---------------------|------------|-----------|
| 25.00                    | 25.00               | 3.10       | 86%       |
| 12.50                    | 12.50               | 3.30       | 92%       |
| 8.50                     | 8.50                | 3.20       | 89%       |
| 6.40                     | 6.40                | 3.40       | 94%       |
| 5.10                     | 5.10                | 3.30       | 92%       |
Scheme S6. Monomer Exchange Experiments Beginning with MC 2.

**Macrocycle Monomer Exchange Experiment:**

MC 2 (15 mg, 0.008 mmol) was sonicated in 1,4-dioxane (4 mL) until completely dispersed. After dispersion of the original macrocycle, isophthalaldehyde (11.3 mg, 0.080 mmol, 10.0 equiv) and CF$_3$CO$_2$H (2.0 M in dioxane, 160 μL, 10 equiv) was then added. The solution was then allowed to sit undisturbed at room temperature for 3 days. After 3 days, the reaction mixture was neutralized with Et$_3$N (2 mL) and poured into Et$_2$O (c.a. 10 mL). The precipitate was isolated by centrifugation and subsequently rinsed with Et$_2$O (3x10 mL). The resulting solid was dried under high vacuum at room temperature to yield the desired macrocycle (14.7 mg, 98%) as a light brown solid.
Scheme S7. Monomer Exchange Experiments Beginning with MC 1.

Macrocycle Monomer Exchange Experiment:

MC 1 (15 mg, 0.008 mmol) was sonicated in 1,4-dioxane (4 mL) until completely dispersed. After dispersion of the original macrocycle, pyridine-2,6-dicarboxaldehyde (11.3 mg, 0.080 mmol, 10.0 equiv) and CF$_3$CO$_2$H (2.0 M in dioxane, 160 μL, 10 equiv) was then added. The solution was then allowed to sit undisturbed at room temperature for 3 days. After 3 days, the reaction mixture was neutralized with Et$_3$N (2 mL) and poured into Et$_2$O (c.a. 10 mL). The precipitate was isolated by centrifugation and subsequently rinsed with Et$_2$O (3x10 mL). The resulting solid was dried under high vacuum at room temperature to yield the desired macrocycle (14.1 mg, 96%) as a light brown solid.
Scheme S8. Synthesis of 5-Br-IDA Macrocycles.

Synthesis of 5-Br-IDA Macrocycles:

S1 (25 mg, 0.055 mmol) and 5-bromoisophthalaldehyde (11 mg, 0.055 mmol, 1.0 equiv) were combined in 1,4-dioxane (2.2 mL, 25 mM with respect to S1) and sonicated until completely dissolved. 12.5 μL of a 2 M solution of CF₃CO₂H in 1,4-dioxane (0.028 mmol, 0.5 equiv) was then added. The solution immediately turned yellow and a precipitate began to form. The solution was then left undisturbed at room temperature for 36 h. After 36 h., the reaction mixture was neutralized with Et₃N (1.0 mL) and poured into Et₂O (c.a. 5 mL). The precipitate was isolated by centrifugation and subsequently rinsed with additional Et₂O (3x5 mL). The resulting solid was dried under high vacuum at room temperature to yield the desired 5-Br-IDA macrocycle (26 mg, 84%) as a light-yellow solid.
Scheme S9. Monomer Exchange Control Experiment Beginning with 5-Br-IDA Macrocycles.

Macrocycle Monomer Exchange Experiment:

A sample of 5-Br-IDA macrocycles (13.1 mg, 0.007 mmol) were sonicated in 1,4-dioxane (4 mL) until completely dispersed. After dispersion of the original macrocycle, isophthalaldehyde (2.6 mg, 0.021 mmol, 3.0 equiv) and CF₃CO₂H (2.0 M in dioxane, 140 μL, 10 equiv) was added. The solution was then allowed to sit undisturbed for 3 days at room temperature. After 3 days, the reaction mixture was neutralized with Et₃N (2 mL) and poured into Et₂O (c.a. 10 mL). The precipitate was isolated by centrifugation and subsequently rinsed with Et₂O (3x10 mL). The resulting solid was dried under high vacuum at room temperature to yield the desired macrocycle (10.6 mg, 81%) as a yellow solid.
C. $^1$H and $^{13}$C NMR Spectra

Figure S1. $^1$H NMR (CDCl$_3$, 500 MHz, 298 K) of S1.

Figure S2. $^{13}$C NMR (CDCl$_3$, 126 MHz, 298 K) of S1.
D. Dilution Experiments Macrocycle and Nanotube Characterization

I. Characterization of MC 1

Figure S3. GPC of MC 1, synthesized at 25 mM, in THF showing a single narrow elution band corresponding to successful macrocyclization.

Figure S4. MALDI-MS of MC 1, synthesized at 25 mM, showing the desired [M+H]⁺ adduct (m/z=1771.68).
**Figure S5.** FT-IR spectra of MC 1 synthesized at 25 mM with respect to S1. The observations made in this spectra are consistent with previous reports.\textsuperscript{1,2}

**Figure S6.** \textsuperscript{1}H NMR (THF-\textit{d}_8, 500 MHz, 298 K) of MC 1.
Figure S7. GPC of MC 1, synthesized at 12.5 mM, in THF showing a single narrow elution band corresponding to successful macrocyclization.

Figure S8. GPC of MC 1, synthesized at 8.5 mM, in THF showing a single narrow elution band corresponding to successful macrocyclization.
Figure S9. GPC of MC 1, synthesized at 6.4 mM, in THF showing a single narrow elution band corresponding to successful macrocyclization.

Figure S10. GPC of MC 1, synthesized at 5.1 mM, in THF showing a single narrow elution band corresponding to successful macrocyclization.
Figure S11. GPC of MC 1, synthesized at 3.4 mM, in THF showing a single narrow elution band corresponding to successful macrocyclization.

Figure S12. Overlaid GPC traces from all diluted syntheses of MC 1, showing no concentration dependence on macrocycle formation.
Figure S13. MALDI-MS of MC 1, synthesized at 12.5 mM, showing the desired [M+H]^+ adduct (m/z=1771.67).

Figure S14. MALDI-MS of MC 1, synthesized at 8.5 mM, showing the desired [M+H]^+ adduct (m/z=1771.74).
Figure S15. MALDI-MS of MC 1, synthesized at 6.4 mM, showing the desired [M+H]$^+$ adduct ($m/z$=1771.64).

Figure S16. MALDI-MS of MC 1, synthesized at 5.1 mM, showing the desired [M+H]$^+$ adduct ($m/z$=1771.68).
**Figure S17.** MALDI-MS of MC 1, synthesized at 3.4 mM, showing the desired [M+H]$^+$ adduct ($m/z$=1771.66).

**Figure S18.** Atomic force microscopy image of a drop cast aliquot of from the MC 1 reaction at 3.4 mM showing a lack high-aspect ratio assemblies but rather ill-defined aggregates.
Figure S19. Scanning electron microscopy images of a drop cast aliquot of from the MC 1 reaction at 3.4 mM showing no formation of high-aspect ratio assemblies but rather ill-defined aggregates.

Figure S20. Transmission electron microscopy images of a drop cast aliquot of from the MC 1 reaction at 25 mM showing the formation of low aspect ratio aggregates, like what has been previously reported in the literature.¹
Figure S21. *In-Situ* WAXS pattern of the **MC 1** reaction run at 25 mM.
II. Characterization of MC 2

**Figure S22.** GPC of MC 2, synthesized at 25 mM, in THF showing a single narrow elution band corresponding to successful macrocyclization.

**Figure S23.** MALDI-MS of MC 2, synthesized at 25 mM, showing the desired [M+H]+, [M+Na]+, and [M+K]+ adducts. (m/z = 1774.61 [M+H]+; m/z = 1796.40 [M+Na]+; m/z = 1813.94 [M+K]+).
Figure S24. FT-IR spectra of MC 2 synthesized at 25 mM with respect to S1. The observations made in this spectra are consistent with previous reports.\textsuperscript{1,2}

Figure S25. \textsuperscript{1}H NMR (THF-\textit{d}_8, 500 MHz, 298 K) of MC 2.
**Figure S26.** GPC of MC 2, synthesized at 12.5 mM, in THF showing a single narrow elution band corresponding to successful macrocyclization.

**Figure S27.** GPC of MC 2, synthesized at 8.5 mM, in THF showing a single narrow elution band corresponding to successful macrocyclization.
**Figure S28.** GPC of MC 2, synthesized at 6.4 mM, in THF showing a single narrow elution band corresponding to successful macrocyclization.

**Figure S29.** GPC of MC 2, synthesized at 5.1 mM, in THF showing a single narrow elution band corresponding to successful macrocyclization.
Figure S30. GPC of MC 2, synthesized at 3.4 mM, in THF showing a single narrow elution band corresponding to successful macrocyclization.

Figure S31. Overlaid GPC traces from all diluted syntheses of MC 2, showing no concentration dependence on macrocycle formation.
Figure S32. MALDI-MS of MC 2, synthesized at 12.5 mM, showing the desired [M+H]^+, [M+Na]^+, and [M+K]^+ adducts. (m/z=1774.61 [M+H]^+; m/z= 1796.44 [M+Na]^+; m/z= 1813.92 [M+K]^+).

Figure S33. MALDI-MS of MC 2, synthesized at 8.5 mM, showing the desired [M+H]^+, [M+Na]^+, and [M+K]^+ adducts. (m/z=1774.64 [M+H]^+; m/z= 1796.72[M+Na]^+; m/z= 1813.64 [M+K]^+).
**Figure S34.** MALDI-MS of MC 2, synthesized at 6.4 mM, showing the desired [M+H]$^+$, [M+Na]$^+$, and [M+K]$^+$ adducts. ($m/z$=1774.66 [M+H]$^+$; $m/z$= 1796.48 [M+Na]$^+$; $m/z$= 1813.90 [M+K]$^+$).

**Figure S35.** MALDI-MS of MC 2, synthesized at 5.1 mM, showing the desired [M+H]$^+$, [M+Na]$^+$, and [M+K]$^+$ adducts. ($m/z$=1774.62 [M+H]$^+$; $m/z$= 1796.44 [M+Na]$^+$; $m/z$= 1813.86 [M+K]$^+$). Peaks around $m/z$=1000 do not correspond to reaction of DFP or S1 but are instrument artifacts observed in control samples. Furthermore MC 2 formation was confirmed by $^1$H NMR.
Figure S36. MALDI-MS of MC 2, synthesized at 3.4 mM, showing the desired \([\text{M+H}]^+, [\text{M+Na}]^+,\) and \([\text{M+K}]^+\) adducts. ($m/z=1774.62$ [M+H]$^+$; $m/z=1796.50$ [M+Na]$^+$; $m/z=1813.86$ [M+K]$^+$).

Figure S37. Atomic force microscopy images of a drop cast aliquot of from the MC 2 reaction at 3.4 mM showing the formation of high-aspect ratio nanotubes.
Figure S38. Scanning electron microscopy images of a drop cast aliquot of from the MC 2 reaction at 3.4 mM showing the formation of high-aspect ratio nanotubes.

Figure S39. Transmission electron microscopy images of a drop cast aliquot of from the MC 2 reaction at 25 mM showing the formation of high-aspect ratio nanotubes.
Figure S40. *In-Situ* WAXS pattern of the MC 2 reaction run at 25 mM.
E. Kinetic Experiments Characterization
I. Characterization of MC 1 Kinetics

Figure S41. GPC trace of the MC 1 reaction after 2 minutes depicting the presence of varying imine-linked structures.

Figure S42. GPC trace of the MC 1 reaction after 15 minutes depicting successful macrocyclization.
**Figure S43.** GPC trace of the **MC 1** reaction after 30 minutes depicting successful macrocyclization.

**Figure S44.** GPC trace of the **MC 1** reaction after 60 minutes depicting successful macrocyclization.
Figure S45. GPC trace of the MC 1 reaction after 120 minutes depicting successful macrocyclization.

Figure S46. GPC traces of all MC 1 reaction kinetic data. Overall, the GPC kinetic traces are consistent with previous reports of macrocycle formation, but shown different time dependences than the TR-XRD data due to having more catalyst added and being run at a higher concentration.
II. Characterization of MC 2 Kinetics

Figure S47. GPC trace of the MC 2 reaction after 2 minutes depicting successful macrocyclization.

Figure S48. GPC trace of the MC 2 reaction after 15 minutes depicting successful macrocyclization.
Figure S49. GPC trace of the MC 2 reaction after 30 minutes depicting successful macrocyclization.

Figure S50. GPC trace of the MC 2 reaction after 60 minutes depicting successful macrocyclization.
Figure S51. GPC trace of the MC 2 reaction after 120 minutes depicting successful macrocyclization.

Figure S52. GPC traces of all MC 2 reaction kinetic data. Overall, the GPC kinetic traces are consistent with previous reports of macrocycle formation, but shown different time dependences than the TR-XRD data due to having more catalyst added and being run at a higher concentration.
Figure S53. GPC trace of the MC 2 reaction at 3.4 mM, with 0.005 equivalents of CF₃CO₂H, after 2 minutes of reaction time, thereby highlighting the polymeric intermediate in the formation of the desired macrocycle.
F. Scrambling Experiment Characterization

Figure S54. GPC trace of the scrambling experiment at 25 mM, showing the formation of macrocycles as well as small oligomers.

Figure S55. GPC trace of the scrambling experiment at 12.5 mM, showing the formation of macrocycles as well as small oligomers.
Figure S56. GPC trace of the scrambling experiment at 8.5 mM, showing the formation of macrocycles as well as small oligomers.

Figure S57. GPC trace of the scrambling experiment at 6.4 mM, showing the formation of macrocycles as well as small oligomers.
**Figure S58.** GPC trace of the scrambling experiment at 5.1 mM, showing the formation of macrocycles as well as small oligomers.

**Figure S59.** GPC of all scrambling experiments showing the formation of macrocycles as well as small oligomers regardless of reaction concentration.
Figure S60. MALDI-MS of the scrambling reaction at 25 mM showing the formation of the MC 2 ([M+H]$^+$ m/z=1774.24, [M+Na]$^+$ m/z=1796.42, [M+K]$^+$ m/z=1813.90), as well as oligomers corresponding to IDA monomer incorporation ([2•S1+ IDA+H]$^+$ m/z=1083.64).

Figure S61. MALDI-MS of the scrambling reaction at 12.5 mM showing the formation of the MC 2 ([M+H]$^+$ m/z=1774.28, [M+Na]$^+$ m/z=1796.56, [M+K]$^+$ m/z=1813.88).
Figure S62. MALDI-MS of the scrambling reaction at 8.5 mM showing the formation of the MC2 ([M+H]+ m/z=1774.28, [M+Na]+ m/z=1796.47, [M+K]+ m/z=1813.85), as well as oligomers corresponding to IDA monomer incorporation ([2•S1+ IDA+H]+ m/z=1083.64, [2•S1+ IDA+Na]+ m/z=1105.63).

Figure S63. MALDI-MS of the scrambling reaction at 6.4 mM showing the formation of the MC2 ([M+H]+ m/z=1774.34, [M+Na]+ m/z=1796.44, [M+K]+ m/z=1813.90), as well as oligomers corresponding to IDA monomer incorporation ([2•S1+ IDA+H]+ m/z=1083.82, [2•S1+ IDA+Na]+ m/z=1105.93).
Figure S64. MALDI-MS of the scrambling reaction at 5.1 mM showing the formation of the MC 2 ([M+H]+ m/z=1774.30, [M+Na]+ m/z=1796.50, [M+K]+ m/z=1813.85).

Figure S65. MALDI-MS of the scrambling reaction at 3.4 mM showing the formation of the MC 2 ([M+H]+ m/z=1774.26, [M+Na]+ m/z=1796.42, [M+K]+ m/z=1813.92), as well as oligomers corresponding to IDA monomer incorporation ([2•S1+ IDA+H]+ m/z=1083.90, [2•S1+ IDA+Na]+ m/z=1105.90).
Figure S66. MALDI-MS of a 1:1 mixture of MC 1 and MC 2, showing that when both macrocycles are present, they can both be detected.

Figure S67. $^1$H NMR (THF-\textit{d}$_8$, 500 MHz, 298 K) of the scrambling experiment showing the formation of the MC 2 and oligomers containing IDA moieties. Oligomers containing IDA moieties were removed by precipitating the solid into CH$_2$Cl$_2$, after which the $^1$H NMR spectra was analogous to that of the direct MC 2 synthesis.
**Figure S68.** Atomic force microscopy images of a drop cast aliquot of from the scrambling macrocyclization reaction at 3.4 mM showing the formation of high-aspect ratio nanotubes, further supporting the formation of MC 2 which have previously demonstrated self-assembly ability.

**Figure S69.** Scanning electron microscopy images of a drop cast aliquot of from the scrambling macrocyclization reaction at 3.4 mM showing the formation of high-aspect ratio nanotubes, further supporting the formation of MC 2 which have previously demonstrated self-assembly ability.
Figure S70. Transmission electron microscopy images of a drop cast aliquot of from the scrambling macrocyclization reaction at 25 mM showing the formation of high-aspect ratio nanotubes, further supporting the formation of MC 2 which have previously demonstrated self-assembly ability.

Figure S71. In-Situ WAXS pattern of the scrambling reaction run at 25 mM.
G. Competition Experiment Characterization

**Figure S72.** GPC trace of the competition experiment at 25 mM, showing mainly the formation of macrocycles as well as low quantities of small oligomers.

![GPC trace of the competition experiment at 25 mM](image)

**Figure S73.** GPC trace of the competition experiment at 12.5 mM, showing mainly the formation of macrocycles as well as low quantities of small oligomers.

![GPC trace of the competition experiment at 12.5 mM](image)
Figure S74. GPC trace of the competition experiment at 8.5 mM, showing mainly the formation of macrocycles as well as low quantities of small oligomers.

Figure S75. GPC trace of the competition experiment at 6.4 mM, showing mainly the formation of macrocycles as well as low quantities of small oligomers.
Figure S76. GPC trace of the competition experiment at 5.1 mM, showing mainly the formation of macrocycles as well as low quantities of small oligomers.

Figure S77. GPC traces of all competition experiments showing the formation of macrocycles as evident by the narrow elution band at ~26 minutes.
Figure S78. MALDI-MS of the competition reaction at 25 mM showing the formation of the MC 2 ([M+H]^+ m/z=1774.28, [M+Na]^+ m/z=1796.52, [M+K]^+ m/z=1813.81) as well as a small oligomer corresponding to the reaction of IDA monomers ([S1+2IDA+H]^+ m/z=725.37).

Figure S79. MALDI-MS of the competition reaction at 12.5 mM showing the formation of the MC 2 ([M+H]^+ m/z=1774.32, [M+Na]^+ m/z=1796.50, [M+K]^+ m/z=1813.92) as well as a small oligomer corresponding to the reaction of IDA monomers ([S1+2IDA+H]^+ m/z=725.35).
Figure S80. MALDI-MS of the competition reaction at 8.5 mM showing the formation of the MC2 ([M+H]+ m/z=1774.61, [M+Na]+ m/z=1796.44, [M+K]+ m/z=1813.90).

Figure S81. MALDI-MS of the competition reaction at 6.4 mM showing the formation of the MC2 ([M+H]+ m/z=1774.54, [M+Na]+ m/z=1796.48, [M+K]+ m/z=1813.93) as well as a small oligomer corresponding to the reaction of IDA monomers ([S1+2•IDA+H]+ m/z=725.39 and [S1+2•IDA+Na]+ m/z=748.36).
Figure S82. MALDI-MS of the competition reaction at 5.1 mM showing the formation of the MC 2 ([M+H]^+ m/z=1774.62, [M+Na]^+ m/z=1796.48, [M+K]^+ m/z=1813.90).

Figure S83. ^1^H NMR (THF-d8, 500 MHz, 298 K) of the macrocycles resulting of the competition experiment. Small oligomers containing IDA moieties were removed from the sample prior to analysis.
Figure S84. Atomic force microscopy images of a drop cast aliquot of from the competition macrocyclization reaction at 5.1 mM showing the formation of high-aspect ratio nanotubes, further supporting the formation of MC 2 which have previously demonstrated self-assembly ability.

Figure S85. Scanning electron microscopy images of a drop cast aliquot of from the competition macrocyclization reaction at 5.1 mM showing the formation of high-aspect ratio nanotubes, further supporting the formation of MC 2 which have previously demonstrated self-assembly ability.
**Figure S86.** Transmission electron microscopy images of a drop cast aliquot of from the competition macrocyclization reaction at 25 mM showing the formation of high-aspect ratio nanotubes, further supporting the formation of MC 2 which have previously demonstrated self-assembly ability.

**Figure S87.** *In-Situ* WAXS pattern of the competition reaction run at 25 mM.
H. Monomer Exchange Experiments Characterization

I. Monomer Exchange of MC 2

**Figure S88.** GPC trace of the monomer exchange reaction beginning with the MC 2 depicting the formation of macrocycles.

**Figure S89.** MALDI-MS of the monomer exchange reaction beginning with the MC 2, showing full recovery of the initial MC 2 ([M+H]+ m/z=1774.64, [M+Na]+ m/z=1796.51).
Figure S90. FT-IR spectra of the macrocycles resulting from the attempted monomer exchange reaction beginning with **MC 2**.

Figure S91. $^1$H NMR (THF-$d_8$, 500 MHz, 298 K) of the macrocycles resulting from the attempted monomer exchange reaction beginning with **MC 2**. Rather than observing intercalation of the IDA moieties into **MC 2**, full recovery of **MC 2** was demonstrated.
Figure S92. Atomic force microscopy images of a drop cast aliquot of from the monomer exchange reaction beginning with MC 2, showing the formation of high-aspect ratio nanotubes as seen in previous MC 2 samples.

Figure S93. Scanning electron microscopy images of a drop cast aliquot of from the monomer exchange reaction beginning with MC 2, showing the formation of high-aspect ratio nanotubes as seen in previous MC 2 samples.
Figure S94. Transmission electron microscopy images of a drop cast aliquot of from the monomer exchange reaction beginning with MC 2, showing the formation of high-aspect ratio nanotubes as seen in previous MC 2 samples.

Figure S95. In-Situ WAXS pattern of the monomer exchange reaction beginning with the MC 2.
II. Monomer Exchange of MC 1

Figure S96. GPC trace of the monomer exchange reaction beginning with the MC 1, showing a narrow elution band corresponding to the formation of macrocycles.

Figure S97. MALDI-MS of the monomer exchange reaction beginning with MC 1, showing neither the retainment of the MC 1, nor the full conversion to the MC 2 (m/z=1772.18). A full comparison of the MALDI-MS spectra of MC 1, MC 2, and this linker exchange can be found in the main text (Figure 5D).
Figure S98. FT-IR spectra of the macrocycles resulting from the attempted monomer exchange reaction beginning with MC 1.

Figure S99. $^1$H NMR (THF-$d_8$, 500 MHz, 298 K) of the mixture of macrocycles resulting from the monomer exchange reaction beginning with MC 1.
Figure S100. Comparison of $^1$H NMR spectra from the isolated MC 2, the isolated MC 1, and the result of the monomer exchange reaction beginning with MC 1.

Figure S101. Quantification of monomer exchange via $^1$H NMR. Furthermore, the small secondary peaks ~7.1 ppm and ~7.4 ppm correspond to species bearing two pyridine moieties and match with the assignment of 14% of macrocycles existing as such.
Figure S102. Atomic force microscopy images of a drop cast aliquot of from the monomer exchange reaction beginning with MC 1, showing the formation of high-aspect ratio nanotubes.

Figure S103. Scanning electron microscopy images of a drop cast aliquot of from the monomer exchange reaction beginning with MC 1, showing the formation of high-aspect ratio nanotubes.
Figure S104. Transmission electron microscopy images of a drop cast aliquot of from the monomer exchange reaction beginning with MC 1, showing the formation of high-aspect ratio nanotubes.

Figure S105. In-Situ WAXS pattern of the monomer exchange reaction beginning with the MC 1.
III. Synthesis and Monomer Exchange of 5-Br-MC 1

Figure S106. GPC trace of the synthesized 5-Br-IDA MC, showing a single narrow elution band corresponding to successful macrocyclization.

Figure S107. MALDI-MS of 5-Br-IDA MC, showing the desired [M+H]+ adduct (m/z=2005.72).
Figure S108. GPC trace of the macrocycles resulting from monomer exchange of the 5-Br-IDA MC with IDA. The narrow elution band corresponds to macrocycle products.

Figure S109. MALDI-MS of the monomer exchange reaction beginning with 5-Br-MC 1, showing the statistical incorporation of IDA monomers into the system ([3•S1+3•IDA+H]⁺ m/z=1771.74, [3•S1+3•IDA+Na]⁺ m/z=1794.86, [3•S1+2•IDA+1•5-Br-IDA+H]⁺ m/z=1848.92, [3•S1+2•IDA+1•5-Br-IDA+Na]⁺ m/z=1871.89, [3•S1+1•IDA+2•5-Br-IDA+H]⁺ m/z=1927.83, [3•S1+1•IDA+2•5-Br-IDA+Na]⁺ m/z=1950.82, [3•S1+3•5-Br-IDA+H]⁺ m/z=2005.75, [3•S1+3•5-Br-IDA+Na]⁺ m/z=2028.71).
I. Small Molecule $^1$H NMR Studies

I. Small Molecule Competition $^1$H NMR Study

Scheme S10. Scheme of small molecule competition study between IDA, DFP, and Aniline under conditions typical for macrocycle synthesis.

Small Molecule Competition Study:
Aniline (0.025 g, 0.27 mmol), IDA (0.018 g, 0.13 mmol), and DFP (0.018 g, 0.13 mmol) were dissolved in previously dried CDCl$_3$ to a final concentration of 20 mM with respect to aniline. A 1,4-dichlorobenzene (0.015 g) was added to the solution. CF$_3$CO$_2$H (34 uL of a 2M solution in CDCl$_3$, 0.5 equiv) was added to the solution, a 1 mL aliquot was placed into an NMR tube and the tube was inverted 3-4 times to ensure proper mixing of the solution. The reaction mixture was then monitored over the course of two hours via $^1$H NMR spectrometry. HRMS of the reaction mixture after 120 minutes confirmed the presence of a pyridine-2,6-diimine species and unreacted isophthalaldehyde.

Figure S110. Stacked $^1$H NMR spectra (400 MHz, CDCl$_3$, 298 K) of the small molecule competition study over the course of two hours. No appreciable changes in the spectra are observed from 5 min. to 2 h. of reaction time indicating that the rapidly formed pyridine-2,6-diimine species is both kinetically and thermodynamically favored.
Figure S11. Normalized integrations of the aldehydic protons of both IDA and DFP, along with the integrations of the imine C-H proton with respect to the included 1,4-dichlorobenzene internal standard. The results of the small molecule competition study indicate that DFP is rapidly consumed due to its enhanced electrophilicity relative to IDA, and that the resulting pyridine-2,6-diimine species is thermodynamically favored relative to the benzene-1,3-diimine analogue.
II. Small Molecule Scrambling $^1$H NMR Study

Scheme S11. Scheme of small molecule scrambling study between IDA, DFP, and Aniline under conditions typical for macrocycle synthesis.

Small Molecule ‘Scrambling’ Study:
Aniline (0.025 g, 0.27 mmol), IDA (0.009 g, 0.07 mmol), and DFP (0.009 g, 0.07 mmol) were dissolved in previously dried CDCl$_3$ to a final concentration of 20 mM with respect to aniline. A 1,4-dichlorobenzene (0.02 g) was added to the solution. CF$_3$CO$_2$H (16 uL of a 2M solution in CDCl$_3$, 0.5 equiv) was added to the solution, a 1 mL aliquot was placed into an NMR tube and inverted 3-4 times to ensure proper mixing of the solution. The reaction mixture was then monitored over the course of two hours via $^1$H NMR spectrometry. HRMS of the reaction mixture after 120 minutes confirmed the presence of both pyridine-2,6-diimine and benzene-1,3-diimine species.

Figure S112. Stacked $^1$H NMR spectra (400 MHz, CDCl$_3$, 298 K) of the small molecule ‘scrambling’ study over the course of two hours. Consumption of the pyridine-2,6-dicarboxaldehyde monomer mainly occurred prior to the first spectra being recorded, and the consumption of isophthalaldehyde began at ~45 min of reaction time. At elevated reaction times, two aldehydic species are observed, one in which IDA had reacted with 1 equiv of aniline and one in which IDA had not reacted with aniline. Resonances corresponding to the DFP aldehydes were almost completely consumed upon the first measurement. Integration relative to an internal standard yielded that the IDA imine resonance corresponded to structures with both one and two imines, which was further corroborated by mass spectrometry (Figure S113).
Figure S113. Mass spectrum of the results of the small molecule ‘scrambling’ reaction yielding peaks 135.3 ([IDA+H]+), 210.3 ([IDA+1•Aniline+H]+), 285.4 ([IDA+2•Aniline+H]+), 286.5 ([DFP+2•Aniline+H]+) matching with the changes observed via ¹H NMR.

Figure S114. Normalized integrations of the aldehydic protons of both IDA and DFP, along with the integrations of the imine C-H protons with respect to the included 1,4-dichlorobenzene internal standard. The results of the small molecule scrambling study indicate that both imines can be formed in solution, albeit at different reaction times. These results contradict the macrocycle competition study in which both MC 2 and MC 1 could not both be formed under reaction relevant conditions. These results suggest that an antagonistic effect exists between the kinetically favored MC 2 nanotubes and the kinetically sluggish MC 1 species.
J. References

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Low-Aspect Ratio Aggregates
Benzene Based Monomer

High-Aspect Ratio Nanotubes
Pyridine Based Monomer

Pyridine Inclusion Unlocks Assembly Into Nanotubes

Weak π-π Interactions
Rapid Imine Exchange

Robust Ionic Interactions
No Imine Exchange

Strauss2019_SADynamics_TOC.jpg (483.52 KiB)