EurJOC European Journal of Organic Chemistry

FULL PAPER

DOI: 10.1002/ejoc.201200655

Studies Toward the Synthesis of Phenylacetylene Macrocycle Based Rotaxane Precursors as Building Blocks for Organic Nanotubes

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Keywords: Macrocycles / Rotaxanes / Cross-coupling / Synthetic methods / Nanotubes

Synthetic efforts toward the preparation of rotaxane precursors based on phenylacetylene macrocycles (PAM) are described. The aim of this study was to determine the optimal structural parameters to prepare high-molecular-weight rotaxane precursors through a strategy involving two Sonogashira couplings to attach bulky blockers on the PAM core. PAMs with different sizes and functions were prepared and coupled to different blockers to assess whether or not the resulting structure adopts a rotaxane-like conformation in which the rigid rod forms after the Sonogashira coupling threads through the PAM.

Introduction

The preparation of nanoarchitectures with finite size and shape is a key aspect for the development of nanoscience. Although the development of inorganic nanoarchitectures has benefited from a great deal of attention from materials scientists in the past two decades, lesser efforts have been devoted to preparing their organic counterparts. Most of the physical methods frequently used to prepare inorganic nanoarchitectures, like nanoparticles, carbon nanotubes, nanocrystals and so on, do not offer the same level of control and precision with regard to size and shape as organic synthetic methods do at the molecular level. Moreover, the versatility of organic synthesis allows the fine-tuning of physical properties through precise chemical alterations of the nanoarchitectures, opening the way to their use in various applications ranging from electronics to biomedical areas. Recent examples include the preparation of monodisperse organic nanocapsules from dendrimers,[1] well-defined graphene sheets and nanoribbons,[2] ion channels[3] and semiconducting nanowires.[4]

Among the organic nanoarchitectures reported so far, the organic nanotube is undoubtedly the molecular architecture that attracted the most attention owing to its internal cavity that makes it a good candidate for host–guest chemistry,[5] scaffolding[6] and site isolation.[7] Although interesting examples and proof-of-concept have been reported for each of these applications, an efficient, reliable and versatile method to prepare stable organic nanotubes is still lacking. Most of the methods reported so far to prepare organic nanotubes rely on self-assembly, under very specific conditions, of carefully designed building blocks. However, because the interactions (H-bonding, van der Waals, hydrophobic and π–π interactions) that keep these building blocks together are rather weak, many of the supramolecular architectures reported to date are kinetically unstable. The most well-known examples of supramolecular nanotubes are made from cyclic oligopeptides,[8] cyclic oligosaccharides,[9] calixarene,[10] phenylacetylene foldamers[11] and block copolymers.[12] One way to increase the strength and kinetic stability of supramolecular nanotubes is to covalently link the building blocks to one another once the nanotube is formed by using specific reactions conducted under self-assembly conditions. The reactions that have been used for nanotube stabilization include photochemical and thermal cross-linking,[13] alkene metathesis,[14] ring-opening metathesis,[14,15] atom transfer radical polymerization,[16] nucleophilic substitution reaction[17] and metal–ligand coordination.[18]

One of the major drawbacks of supramolecular chemistry to self-assemble the building blocks of nanotubes is that specific functional groups have to be used to direct and drive the self-assembly process, thus limiting the scope of this strategy in terms of chemical diversity. Therefore, the next logical step toward the preparation of monodisperse and well-defined nanotubes is to develop a versatile strategy that will not only allow control of the nanotubes' shape but also its function. The most obvious approach to obtain such control is to grow nanotubes by using traditional covalent chemistry from polymerizable building blocks. Recently, Zimmerman et al. reported an elegant way to prepare organic nanotubes from porphyrin-cored dendrimers by using this strategy.[14] Although their approach is synthetically demanding and mostly leads to short nanotubes,

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Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201200655.

we believe that the covalent approach ought to be further explored to extend its scope and understand its limitations. Therefore, we decided to investigate a new strategy of covalent growth of the nanotubes' architecture involving a phenylacetylene macrocycle (PAM) containing rotaxane precursor as the building blocks. Our strategy (Figure 1) is similar to the strategy developed by Zimmerman et al.; it consists of preparing a polymerizable rotaxane precursor (**I**) in which the macrocycle is a PAM and the rigid rod is an oligophenyleneethynylene (OPE). The PAM structure has been chosen for its shape-persistency, which is expected to provide a rigid scaffold to the nanotubes that would help preventing the nanotube from collapsing, as observed by Zimmerman for a more flexible nanotube wall.[14] This rotaxane precursor will undergo a polymerization reaction through its reactive end to give the rotaxane precursor polymer (**II**) before cross-linkable units are attached to the outer part of the macrocycles (**III**). Then, the macrocycles will be covalently linked to each other, and the interior of the macrocycle will be removed to leave a void inside the nanotube structure (**IV**). By using this strategy, the PAM will stay within the nanotube structure meaning that the diameter of the nanotube could be tuned by changing the size of the macrocycle used to template the assembly.

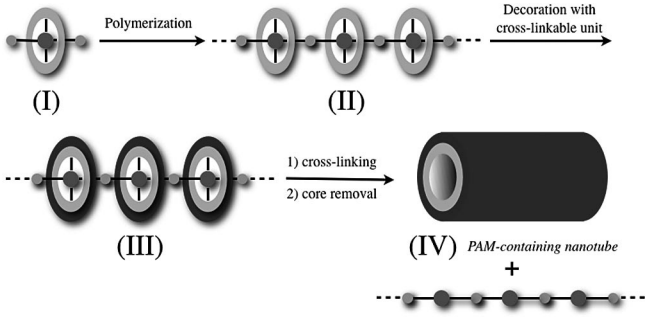


Figure 1. Strategy for the preparation of PAM-based nanotubes inspired by Zimmerman et al.[14]

However, before undertaking the preparation of such nanotubes, many structural parameters of the rotaxane precursor need to be optimized to ensure that the growth of the nanotube works efficiently. The most important question to answer is whether or not the rigid rod of the rotaxane precursor seen in structures **I** and **II** passes through the macrocycle, because steric congestion might arise from these structures. Figure 2 shows two possible conformations for the rotaxane precursor. Depending on the diameter of the nanotube and the steric congestion in the interior of the macrocycle, one of the two isomers could be formed preferentially. Consequently, the first step toward the preparation of an organic nanotube through the rotaxane precursor strategy is to prepare [2]rotaxanes that are blocked at both ends with bulky moieties to assess whether or not the OPE rigid rod can pass through the macrocycle. To the best of our knowledge, only Höger et al. have reported the preparation of a PAM-based polymer with a rotaxane-like architecture.[19] However, the primary objective of their study was the photophysical characterization of the polymer so no study of any relationship between structure and properties was undertaken.

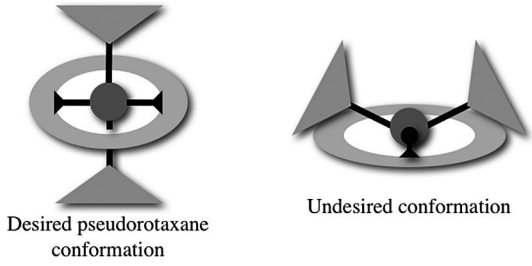


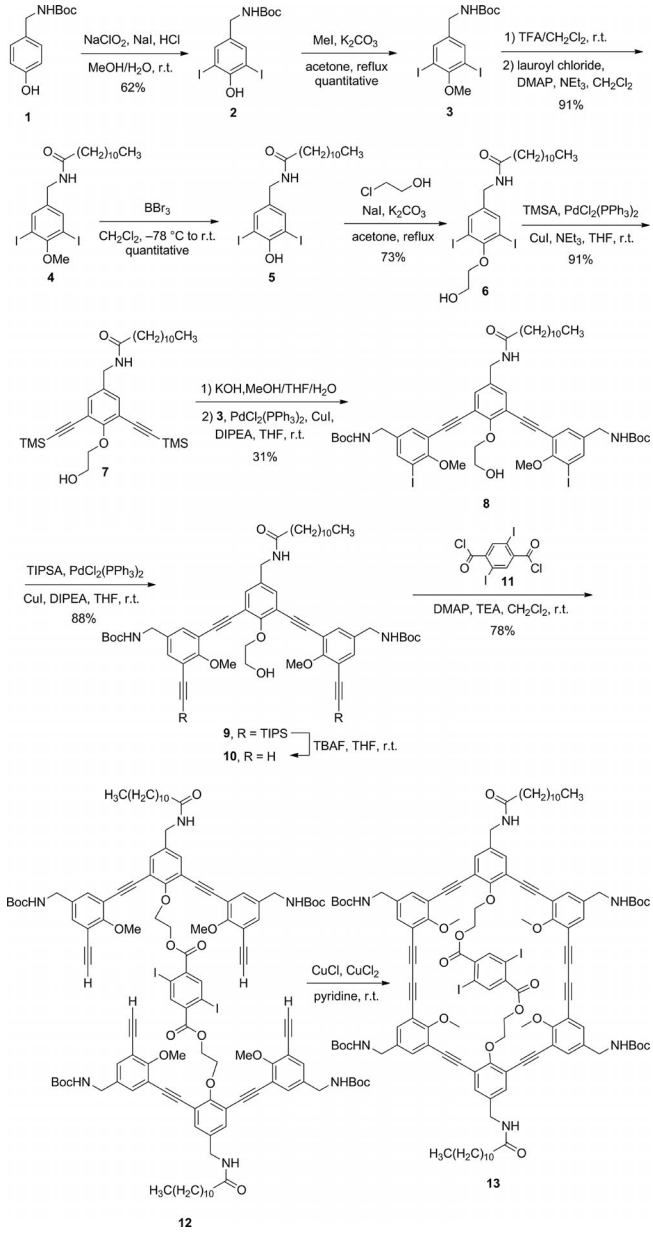
Figure 2. Possible conformations for the rotaxane precursor obtained after the coupling of PAM to the blockers.

Herein, we report synthetic efforts toward the preparation of PAM-containing [2]rotaxanes as building blocks for rigid organic nanotubes. The synthesis of PAMs, blockers and rotaxane precursors with different sizes and functions is presented. The rotaxane architecture is not only interesting as a potential building block for organic nanotubes, but also as supramolecular scaffold for the development molecular machines,[20] photochemical devices[22] and actuators.[21] All the structure-related optimizations reported here were conducted with the sole goal of preparing rotaxane building blocks for further nanotube synthesis.

Results and Discussion

The first step toward the preparation of a PAM-containing rotaxane precursor is the synthesis of a macrocycle containing reactive functions at its core. We chose two aryl iodides as a polymerizable unit, because they can react with terminal alkynes in Sonogashira coupling reactions to a give rigid phenyleneethynylene-based polymer backbone. The synthesis of the first PAM is depicted in Scheme 1. Because functional groups are needed inside the PAM to prepare the rotaxane precursor, we used the template approach developed by Höger et al. to prepare our macrocycle.[23] This method allows the preparation of macrocycles in higher yields than through traditional ring-closing reactions under very dilute conditions. Our strategy was to prepare the half-PAM before connecting it to the template and closing the macrocycle by an Eglinton coupling. Protected amino groups were added on four out of six phenyl units to allow the covalent attachment of cross-linkable units required for the preparation of the nanotubes' wall (Figure 1, Steps II→III). Compound **1**[24] was diiodinated in 62% yield (compound **2**) by using a known method for phenols, followed by a methylation reaction to protect the phenol group to give **3**. Protection of the phenol group was necessary, because attempts to acylate the benzylic amine group selectively from the phenol were unsuccessful or poor-yielding. Next, the di-*tert*-butyl dicarbonate (Boc) group was removed with trifluoroacetic acid (TFA) in dichloromethane, and the resulting benzylic amine treated with lauroyl chlor-

ide and (dimethylamino)pyridine (DMAP) as the catalyst to give **4** in 91% yield. The phenol group was then deprotected in very high yield by using boron tribromide (compound **5**) and treated with chloroethanol in the presence of sodium iodide to give **6**. By using standard Sonogashira coupling reaction conditions two (trimethylsilyl)acetylene (TMSA) moieties were installed in excellent yield (compound **7**). The alkynes were then deprotected under alkaline conditions and immediately coupled to **3** by standard Sonogashira coupling to give half-macrocycle **8** in 31% yield. The free alkyne intermediate was not isolated owing to its apparent instability under ambient conditions. The relatively low yield obtained for the formation of **8** is attributed to the formation of a significant number of oligomers even though a large excess (3 equiv.) of the diiodo derivative was used to minimize the occurrence of AA/BB-type polycondensation reactions. Acetylene groups were then installed on **8** by using (triisopropylsilyl)acetylene (TIPSA) followed by deprotection by using tetrabutylammonium fluoride (TBAF) in THF. The alkynes were deprotected prior to the coupling of the half-macrocycle on the diiodo-containing template molecule, because the ester groups were very sensitive in the presence of TBAF. Thus, deprotected analog **10** of **9** was coupled to **11**[25] by using DMAP as the catalyst to provide the macrocycle precursor **12** in good yield. Finally, the ring-closure reaction was performed under Eglinton conditions over 11 d to produce the final PAM **13**. The yield of this reaction was very low relative to those usually obtained for this kind of templated ring-closure reaction. Because the reactivity of the terminal alkyne is unlikely to be a limiting factor, we attributed this low yield to high steric hindrance in the inner part of the macrocycle and to the poor solubility of the resulting material. Because of the very small quantity of macrocycle obtained, we did not attempt to prepare the corresponding rotaxane precursor. Instead, we decided to prepare a very similar macrocycle with a larger diameter. The synthetic pathway used to prepare a larger macrocycle is presented in Scheme 2.

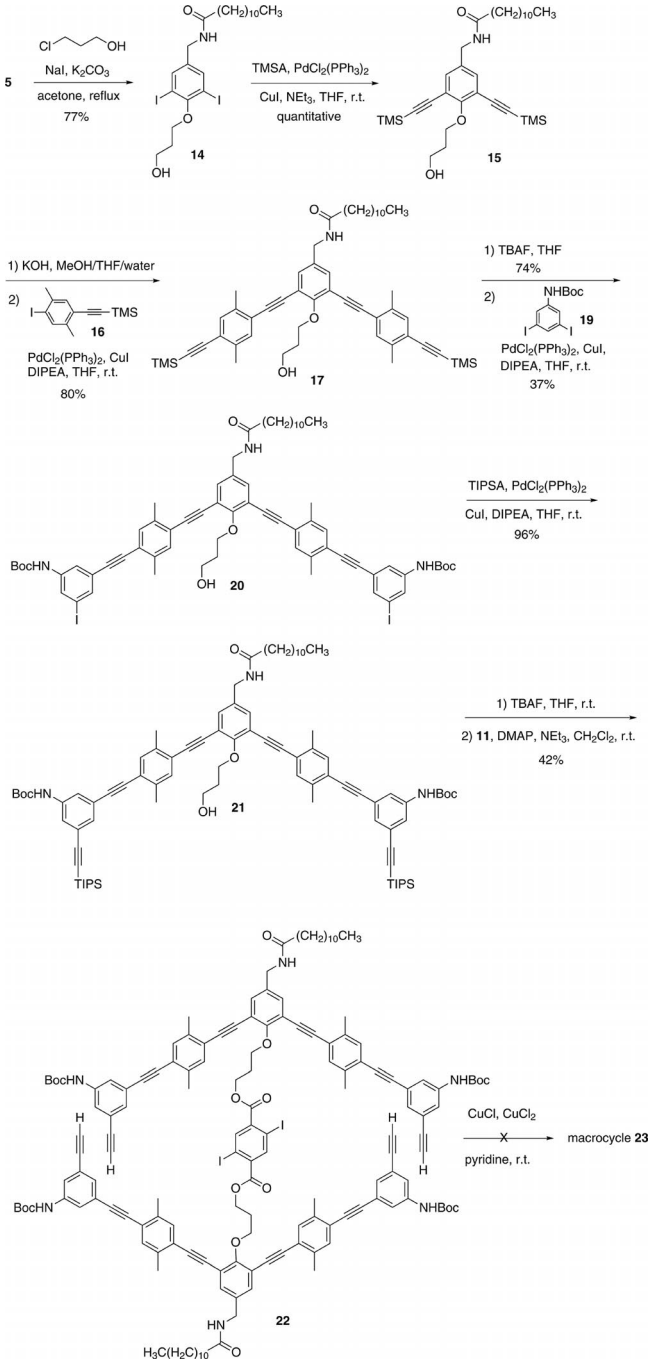


Scheme 1. Synthesis of PAM **13**.

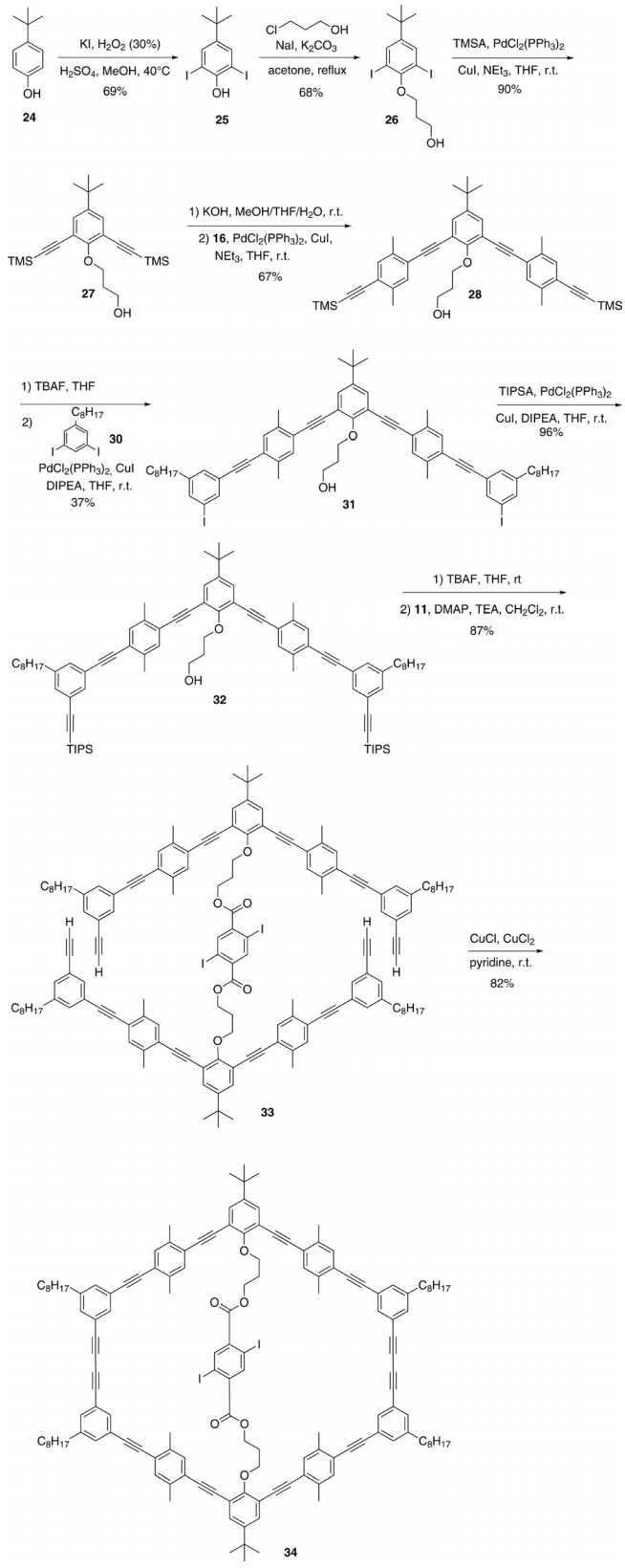
The strategy used to increase the macrocycle diameter was to add a 1,4-dimethylphenyl unit on each side on the half-macrocycle. To further increase the chance of success for the ring-closure reaction, we removed the methoxy group pointing inside the macrocycle cavity. Also, for the larger macrocycle, a spacer that was a little longer (propyl rather than ethyl) was used to link the half-macrocycle to the templating unit. Starting from **5**, a propanol chain was attached by using the same conditions described for the synthesis of **6** (Scheme 1) to give **14** in 77% yield. A Sonogashira coupling/alkyne deprotection sequence involving TMSA, compound **16** (obtained from 1,4-diiodo-*p*-xylene[26]), compound **19**[27] and TIPSA gave half-macrocycle **21** in 21% overall yield. The two alkynes were then deprotected with TBAF, and the resulting compound was treated with **11** to give macrocycle precursor **22**. Unexpectedly, **22** was very sparingly soluble in common organic solvents. An attempt at a ring-closure reaction gave only insoluble materials, which likely contained small amounts of macrocycle **23**. The poor solubility of **22** and **23** was likely owing to the presence of six amide groups that can participate in intermolecular H-bonding interactions. Recently, we showed that H-bonding could be used to direct the assembly of PAM in different solvents.[28]

Because the primary purpose of this study is to assess whether or not a rotaxane can be formed by using a PAM as macrocyclic unit and a rigid OPE as the rod, we replaced the four amide groups on each corner of the PAM by straight alkyl chains and the two other amide groups with *tert*-butyl groups to improve the solubility of the final structure. As shown in Scheme 3, we started with the commercially available 4-*tert*-butylphenol (**24**) that was iodinated by using a known procedure.[29]

After a propyl connector was installed on the phenol, successive Sonogashira coupling/alkyne deprotection steps involving TMSA, **16**, **30**[24] and TIPSA gave half-macrocycle



Scheme 2. Synthesis of PAM **23**.

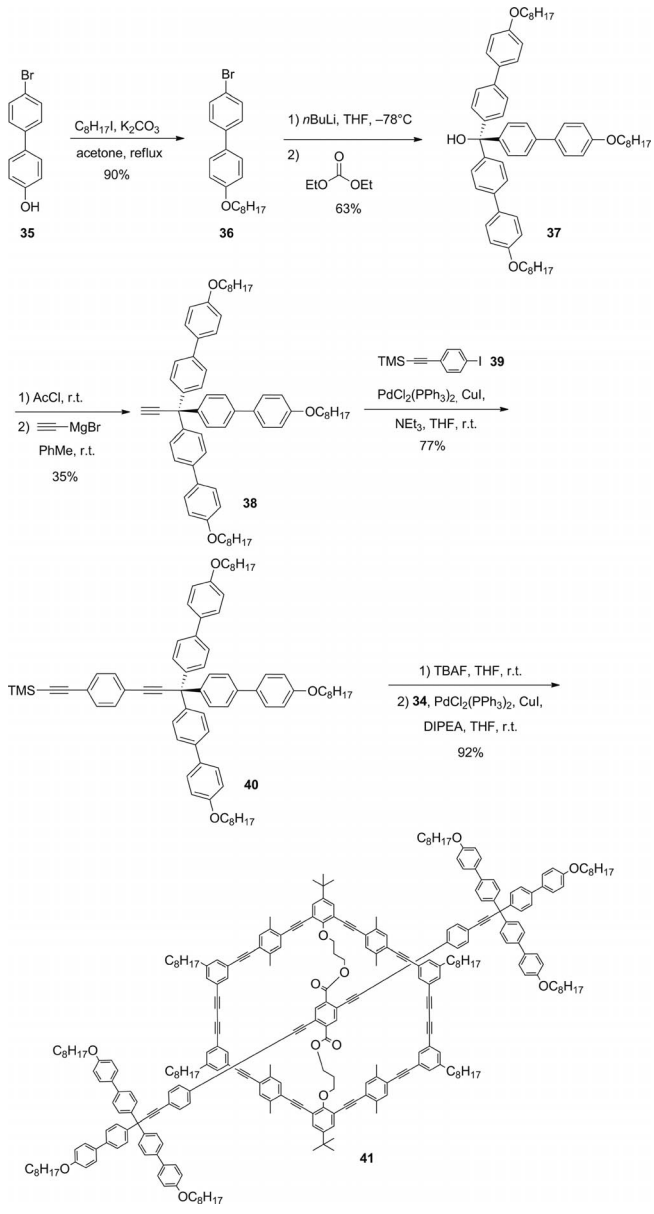


Scheme 3. Synthesis of PAM **34**.

32 in 16% overall yield. The compound was then coupled to **11** in excellent yield. Unlike **22**, **33** is readily soluble in common organic solvents. Finally, an Eglinton ring closure reaction was performed over 11 d to yield soluble PAM **34** in very good yield (82%) after purification by flash chromatography. This result supports our hypothesis regarding the steric hindrance and poor solubility issues for **13**.

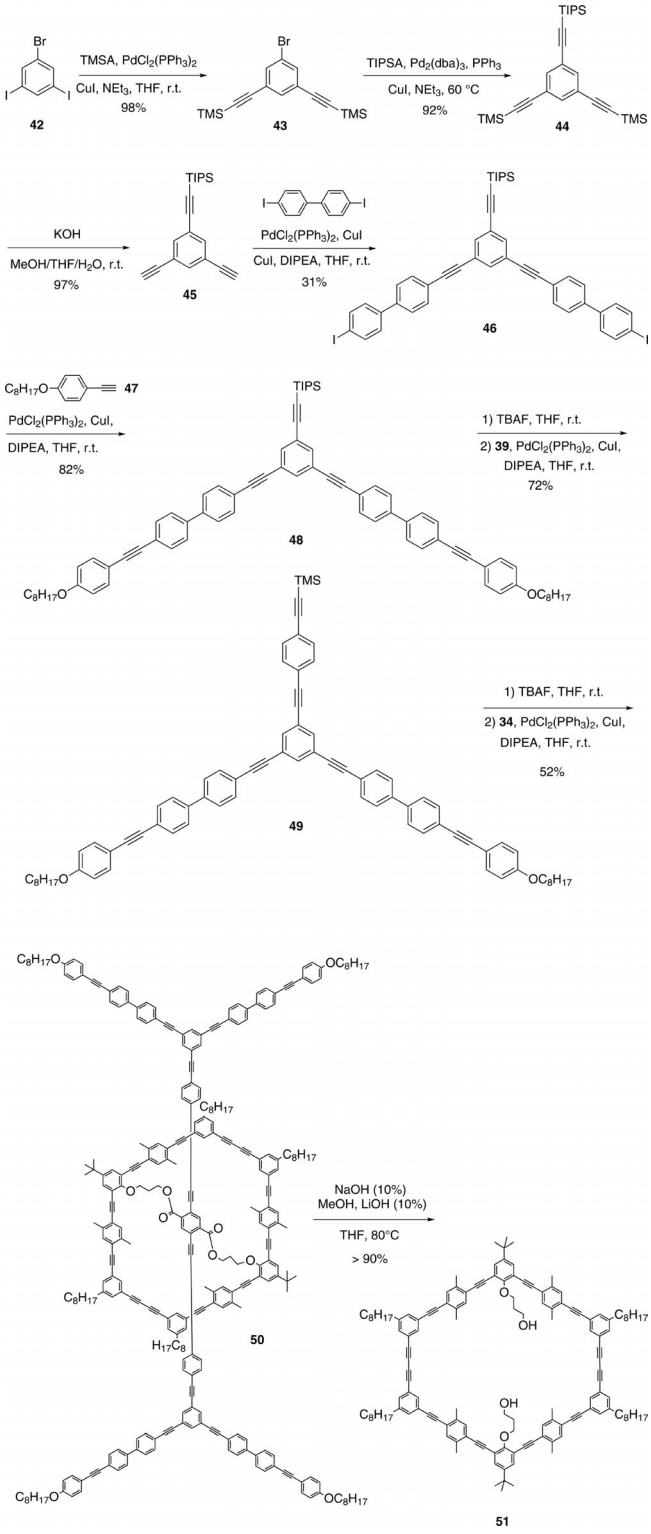
With PAM **34** in hand, we undertook the synthesis of a blocker that is bulky enough to prevent the macrocycle from threading off the rotaxane structure. By using molecular modeling to aid design, we calculated the inner diameter of **34** at its narrowest point to be 20.9 Å. Therefore, a tris(biphenylyl)methane-based conical-shaped blocker with a larger diameter at its widest point should ensure the

macrocycle stays mechanically interlocked within the rotaxane structure. The synthesis of target structure **40** is presented in Scheme 4. Starting from commercially available 4′-bromo-1,1′-biphenyl-4-ol (**35**), the hydroxy group was treated with iodooctane under standard nucleophilic substitution conditions to give **36** in 90% yield. Next, **36** was treated with *n*-butyllithium at –78 °C followed by diethyl carbonate to provide tris(biphenylyl)methanol derivative **37** in 63% yield. Compound **37** was treated with acetyl chloride followed by ethynylmagnesium bromide to give **38** that was further coupled to **39**[30] to give blocker **40** in 27% overall yield. After deprotection of the alkyne, the blocker was coupled to PAM **33** by Sonogashira coupling to give rotaxane precursor **41** in 92% yield after purification by flash chromatography. Compound **41** is readily soluble in common organic solvents including THF, chloroform, dichloromethane and toluene.



Scheme 4. Synthesis of **41**.

On the basis of NMR analysis, it was impossible to determine whether or not **41** adopted a threaded structure in which the OPE passes through the macrocycle. Thus, we moved on to the hydrolysis of the ester groups linking the macrocycle and the OPE. If **41** is a threaded rotaxane precursor then the product of the hydrolysis reaction would be a [2]rotaxane. If not, the hydrolysis reaction would lead to two distinct compounds – a macrocycle with two alcohol-terminating chains lying inside the cavity, and a free OPE with two carboxylic acid groups in its center. Unfortunately, the hydrolysis reaction performed by using a mixture of sodium hydroxide and lithium hydroxide in a mixture of MeOH, H_2O and THF gave no trace of the desired rotaxane. Two explanations could account for this result. Compound **41** might not present itself as a threaded compound but as a structure in which the OPE is parallel to the macrocycle (see Figure 2), or **41** is in fact a threaded rotaxane precursor but the blockers were not bulky enough to prevent the macrocycle unthreading (even though molecular modeling suggests otherwise). Because the former hypothesis is difficult to verify by using standard analytical tools, we decided to test the latter by preparing a second rotaxane precursor with the same macrocycle, but with larger blockers. According to molecular modeling, this new blocker has a diameter of 33.9 Å at its largest point (Scheme 5) that is expected to be large enough to avoid the macrocycle, which has an internal cavity of 20.9 Å, to thread off the OPE rod. The synthesis of the blockers is depicted in Scheme 5. Starting from 3,5-diiodobromobenzene (**42**),[24] a double chemoselective Sonogashira coupling was performed with TMSA under standard Sonogashira coupling at room temperature to provide **43** in 98% yield. Then, another Sonogashira coupling reaction to install TIPSA was performed on the bromine atom by using the more active $Pd_2(dba)_3$ catalyst and triphenylphosphane as the ligand at 60 °C to give **44**. The TMS-protected alkynes were deprotected selectively under alkaline conditions (**45**) and then treated with an excess of 4,4′-diiodobiphenyl to give **46** in low yield (31%). Again, the excess of 4,4′-diiodobiphenyl used for this reaction was not enough to avoid the formation of polycondensation reactions leading to oligomeric materials. Compound **46** was subsequently coupled to **47**[31] in 82% before the TIPS-protected alkyne was deprotected with TBAF and coupled to **39** by a Sonogashira coupling reaction to give TMS-protected blocker **49**. Rotaxane precursor **50** was finally prepared by deprotecting the alkyne by using TBAF and coupling the resulting compound to PAM **34** in 52% overall yield over two steps. The hydrolysis of the ester groups was performed under the same conditions as previously described. Unfortunately, PAM **51** was recovered in 90% yield. The remaining 10% consisted of a mixture of compounds that were inseparable by using standard purification techniques. The presence of a very small amount of the desired rotaxane cannot be completely ruled out but the yield would be very low. This result suggests that compound **50** was actually not threaded but that the macrocycle attached to the OPE was lying parallel to it (see Figure 2).



Scheme 5. Synthesis of rotaxane precursor **50**.

In light of these results, our strategy for the preparation of PAM-based rotaxanes has some limitations. Our strategy does not rely on supramolecular interactions to drive the OPE rod to fit inside the PAM cavity as is the case, for example, with ammonium crown ether rotaxanes under thermodynamic control.[20a] Because the PAMs and blockers that were prepared are large molecular architectures, steric effects might play a very important role leading to the kinetically most favorable products. In addition, the linker used to attach both half-macrocycles might be too flexible owing to the presence of sp^3 carbon atoms, allowing the two iodo positions on the core to be on the same side of the macrocycle. A more rigid linker with only sp^2 carbon atoms might be better to ensure rotaxane precursor formation. However, our initial analysis suggests that the synthesis of such a linker and its introduction to the half-macrocycles would be time-consuming without guarantee of success. Finally, in order to ensure an efficient ring closure reaction along with efficient rotaxane precursor formation, relatively large PAMs have to be prepared, resulting in a difficult and time-consuming synthetic process. Although this strategy has never been tried before, we believe that other more efficient and synthetically less demanding strategies need to be explored. As a plausible alternative, the preparation of a rotaxane starting from a preformed rigid rod and a non-covalently-bound macrocycle followed by the capping of the rotaxane precursor could be envisioned (Figure 3).[32]

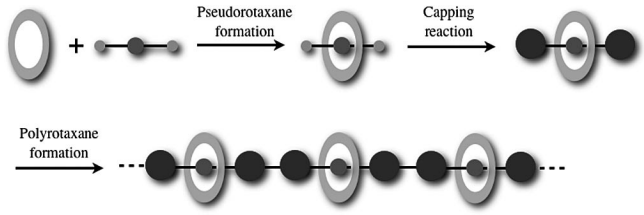


Figure 3. Proposed strategy for the preparation of PAM-based polyrotaxane.

Conclusions

Several attempts to obtain PAM-containing rotaxanes through a rotaxane precursor strategy have been unsuccessful, even though several structural parameters such as the size of the macrocycles and blockers and the length of the rigid rods were optimized. For the soluble structures tested, the macrocycle prefers to stack parallel to the rigid rod rather than encircle it. Nonetheless, the influence of the structural parameters on the reactivity and solubility of the molecular architectures reported in this study have been highlighted and will guide us in developing a new strategy.

Experimental Section

General Methods: Solvents used for organic synthesis (tetrahydrofuran, dichloromethane, dimethylformamide, toluene) were dried and purified with a Solvent Purifier System (Vacuum Atmosphere Co., Hawthorne, USA). Other solvents were used as received. Tetrahydrofuran (THF), triethylamine (TEA) and diisopropylethylamine (DIPEA) used for Sonogashira reactions were degassed for 30 min prior to use. Pyridine used for Eglinton reactions was degassed for 30 min prior to use. All anhydrous and air-sensitive reactions were performed in oven-dried glassware under posi-

tive argon pressure. All silica used came from SiliCycle Inc. (Quebec, Canada): analytical thinlayer chromatography (TLC) was performed with silica gel 60 F_{254}, 0.25 mm pre-coated TLC plates. Preparative TLC was performed with 60 F_{254}, 2000 μm pre-coated TLC plates. Compounds were visualized by using 254 nm and/or 365 nm UV wavelength and/or aqueous sulfuric acid solution of ammonium heptamolybdate tetrahydrate (10 g in 100 mL of H_2SO_4 and 900 mL of H_2O). Flash column chromatography was performed on 230–400 mesh silica gel R10030B. NMR spectroscopic data were recorded at 400 MHz (^1H) and 100 MHz (^{13}C). Signals are reported as m (multiplet), s (singlet), d (doublet), dd (doublet of doublet), t (triplet), q (quadruplet), br. m (broad multiplet) and br. s (broad singlet). The chemical shifts are reported (δ) relative to the residual solvent peak. HRMS data were recorded with an Agilent 6210 time-of-flight (TOF) LC-MS apparatus equipped with an ESI or APPI ion source (Agilent Technologies, Toronto, Canada). IR spectra were recorded by using a Nicolet Magna 850 Fourier transform infrared spectrometer (Thermo Scientific, Madison, WI) with a liquid-nitrogen-cooled narrowband mercury cadmium telluride (MCT) detector and a Golden Gate ATR accessory (Spacac Ltd., London, UK). Each spectrum was obtained from 64 scans (data resolution 4 cm^{-1}).

Compound 2: A 3 L round-bottomed flask equipped with a magnetic stir bar was charged with MeOH (900 mL) and H_2O (900 mL). Compound **1** (10.0 g, 44.8 mmol), $NaClO_2$ (16.2 g, 179 mmol) and NaI (26.9 g, 179 mmol) were added. Next, concentrated HCl (20 mL) was added over 2 min. The reaction mixture was stirred at room temperature for 10 min, neutralized with $NaHSO_3$ and diluted with ethyl acetate. The aqueous layer was extracted four times with ethyl acetate. The organic layers were combined and washed with $NaHSO_3$. The organic layer was dried with Na_2SO_4, the solvent was removed under reduced pressure and the crude product was recrystallized first from EtOH/H_2O followed by a second recrystallization from ethyl acetate/H_2O. The solid was collected by filtration, washed with 2-propanol and dried under vacuum to afford desired compound **2** (13.3 g, 62% yield) as a white solid. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.59 (s, 2 H), 5.73 (br. s, 1 H), 4.82 (br. s, 1 H), 4.17 (d, J = 5.2 Hz, 2 H), 1.46 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 155.9, 152.9, 138.4, 135.2, 82.4, 80.1, 42.7, 28.5 ppm. HRMS (ESI-TOF): calcd. for $C_{12}H_{15}I_2NO_3$ [M^+] 474.9141; found 474.9139. FTIR (ATR): $\tilde{\nu}$ = 3362 (w), 3053 (br. w), 1669 (s), 1534 (s), 1365 (m), 1156 (s) cm^{-1}.

Compound 3: A 100 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **2** (2.00 g, 4.21 mmol), acetone (20 mL), iodomethane (0.52 mL, 8.42 mmol) and K_2CO_3 (1.74 g, 12.6 mmol). The reaction mixture was stirred at reflux temperature overnight, cooled to room temperature, diluted with CH_2Cl_2 and washed with H_2O. The aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure to afford desired compound **3** (2.04 g, quantitative yield) as a white solid. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.65 (s, 2 H), 5.08 (br. s, 1 H), 4.19 (d, J = 4.6 Hz, 2 H), 3.82 (s, 3 H), 1.46 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 157.9, 155.8, 138.9, 138.7, 90.6, 79.9, 60.7, 42.6, 28.4 ppm. FTIR (ATR): $\tilde{\nu}$ = 3309 (br. m), 1682 (s), 1530 (s), 1413 (m), 1290 (s), 1160 (s), 988 (s), 857 (m) cm^{-1}. HRMS data for **3** could not be obtained in either ESI or APPI mode.

Compound 4: A 500 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **3** (10.0 g, 20.5 mmol), CH_2Cl_2 (200 mL) and trifluoroacetic acid (70 mL). The reaction mixture was stirred for 2 h, and the solvent was removed under reduced pressure. Then, CH_2Cl_2 (70 mL) and 1,8-diazabicyclo[5.4.0]undec-7-ene (3.7 mL, 24.6 mmol) were added to the flask under argon. 4-(Dimethylamino)pyridine (0.501 g, 4.10 mmol), Et_3N (11.4 mL, 8.20 mmol) and dodecanoyl chloride (5.1 mL, 21.5 mmol) were added, and the reaction mixture was stirred at room temperature overnight before being neutralized with H_2O. The aqueous layer was extracted three times with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$, filtered, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography on silica gel (CH_2Cl_2) to afford desired compound **4** (10.6 g, 91% yield) as a white solid. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.65 (s, 2 H), 5.84 (m, 1 H), 4.32 (d, J = 5.9 Hz, 2 H), 3.83 (s, 3 H), 2.23 (t, J = 7.6 Hz, 2 H), 1.66 (m, 2 H), 1.35–1.21 (br. m, 16 H), 0.88 (t, J = 6.7 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 173.3, 157.9, 138.9, 138.5, 90.5, 60.7, 41.3, 36.7, 31.9, 29.6, 29.6, 29.6, 29.5, 29.4, 29.3, 25.7, 22.7, 14.1 ppm. HRMS (ESI-TOF): calcd. for $C_{20}H_{31}I_2NO_2$ [M + H]$^+$ 572.0517; found 572.0524. FTIR (ATR): $\tilde{\nu}$ = 3276 (br. m), 2915 (m), 1624 (s), 1547 (s), 1249 (m), 996 (s) cm^{-1}.

Compound 5: A 500 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **4** (10.6 g, 18.6 mmol) and CH_2Cl_2 (190 mL) under argon. Next, the mixture was cooled to –78 °C. A solution of BBr_3 in CH_2Cl_2 (1.0 M, 74 mL, 74.4 mmol) was added dropwise to the reaction mixture. The reaction mixture was stirred at –78 °C to room temperature overnight, cooled to 0 °C, neutralized with MeOH and diluted with H_2O. The reaction mixture was warmed at room temperature and acidified to pH = 5. The aqueous layer was extracted three times with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduce pressure to afford desired compound **5** (10.4 g, quantitative yield) as a white solid. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.59 (s, 2 H), 5.69 (br. s, 1 H), 4.30 (d, J = 5.9 Hz, 2 H), 2.21 (t, J = 7.6 Hz, 2 H), 1.65 (m, 2 H), 1.56 (br. s, 1 H), 1.35–1.21 (br. m, 16 H), 0.88 (t, J = 6.7 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 173.1, 153.0, 138.7, 134.7, 82.3, 41.4, 36.8, 32.0, 29.7, 29.6, 29.5, 29.4, 29.4, 29.3, 25.7, 22.7, 14.2 ppm. HRMS (ESI-TOF): calcd. for $C_{19}H_{29}I_2NO_2$ [M^+] 557.0288; found 557.0287. FTIR (ATR): $\tilde{\nu}$ = 3447 (br. m), 3293 (br. m), 2915 (s), 2849 (s), 1623 (s), 1546 (s), 1250 (m), 997 (s) cm^{-1}.

Compound 6: A 100 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **5** (12.2 g, 21.9 mmol), acetone (30 mL), NaI (16.5 g, 110 mmol), 2-chloroethanol (4.4 mL, 65.7 mmol) and K_2CO_3 (9.08 g, 65.7 mmol). The reaction mixture was stirred at reflux temperature overnight, cooled to room temperature and then filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (acetone/CH_2Cl_2, 1:49) to afford desired compound **6** (9.66 g, 73% yield) as a white solid. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.68 (s, 2 H), 5.80 (br. s, 1 H), 4.33 (d, J = 5.5 Hz, 2 H), 4.14 (m, 2 H), 4.04 (m, 2 H), 2.32 (t, J = 5.9 Hz, 1 H), 2.31 (t, J = 7.2 Hz, 2 H), 1.66 (m, 2 H), 1.35–1.21 (br. m, 16 H), 0.88 (t, J = 5.8 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 173.2, 156.3, 139.1, 138.7, 90.9, 74.3, 65.2, 41.4, 36.7, 32.0, 29.7, 29.6, 29.4, 29.4, 29.4, 25.7, 22.7, 14.2 ppm. FTIR (ATR): $\tilde{\nu}$ = 3287 (br. m), 2315 (s), 2849 (s), 1626 (s), 1535 (m), 1021 (w) cm^{-1}. HRMS data for **6** could not be obtained in either ESI or APPI mode.

Compound 7: A 250 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **6** (9.60 g, 16.0 mmol), degassed THF (80 mL), degassed TEA (8.9 mL, 64.0 mmol), $PdCl_2(PPh_3)_2$ (0.449 g, 0.640 mmol), CuI (0.244 g, 1.28 mmol) and (trimethylsilyl)acetylene (5.8 mL, 41.6 mmol) un-

der argon. The reaction mixture was stirred at room temperature overnight, diluted with CH_2Cl_2, washed with NH_4Cl, and the aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (acetone/CH_2Cl_2, 1:99) to afford desired compound **7** (10.6 g, 91% yield) as brown solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.29 (s, 2 H), 6.38 (t, J = 5.7 Hz, 1 H), 4.35 (t, J = 4.2 Hz, 2 H), 4.28 (d, J = 5.8 Hz, 2 H), 3.80 (m, 2 H), 3.08 (t, J = 6.7 Hz, 1 H), 2.20 (t, J = 7.6 Hz, 2 H), 1.63 (m, 2 H), 1.35–1.21 (br. m, 16 H), 0.88 (t, J = 6.7 Hz, 3 H), 0.25 (s, 18 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 173.2, 160.3, 134.1, 133.2, 117.4, 100.4, 100.2, 75.8, 61.4, 42.1, 36.5, 31.8, 29.5, 29.5, 29.4, 29.3, 29.3, 29.2, 25.6, 22.6, 14.6, –0.3 ppm. HRMS (ESI-TOF): calcd. for $C_{31}H_{51}NO_3Si_2$ $[M + H]^+$ 542.3480; found 542.3485. FTIR (ATR): $\tilde{\nu}$ = 3281 (br. m), 2922 (m), 2160 (m), 1651 (m), 1247 (m), 837 (s) cm^{-1}.

Compound 8: A 100 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **7** (4.50 g, 8.30 mmol), THF (20 mL), MeOH (20 mL) and KOH (2.5 M, 10 mL). The reaction mixture was stirred for 1 h, acidified to pH = 7 and diluted with CH_2Cl_2. The aqueous layer was extracted three times with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was then removed under reduced pressure. A 100 mL round-bottomed flask equipped with a magnetic stir bar was charged with the crude product (3.38 g, 8.30 mmol), degassed THF (30 mL), degassed DIPEA (11.6 mL, 66.4 mmol), $PdCl_2(PPh_3)_2$ (0.117 g, 0.166 mmol), CuI (0.126 g, 0.664 mmol) and compound **2** (12.2 g, 24.9 mmol) under argon. The reaction mixture was stirred at room temperature overnight, diluted with CH_2Cl_2, washed with NH_4Cl, and the aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (CH_2Cl_2 then acetone/CH_2Cl_2, 1:9) to afford desired compound **8** (2.87 g, 31% yield) as brown oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.66 (d, J = 1.4 Hz, 2 H), 7.36 (d, J = 8.3 Hz, 4 H), 6.91 (br. s, 1 H), 5.61 (br. s, 2 H), 4.43 (t, J = 4.2 Hz, 2 H), 4.39 (d, J = 5.8 Hz, 2 H), 4.22 (d, J = 5.3 Hz, 4 H), 3.94 (s, 6 H), 3.90 (t, J = 4.1 Hz, 2 H), 2.29 (t, J = 7.6 Hz, 2 H), 1.68 (m, 2 H), 1.46 (s, 18 H), 1.35–1.21 (br. m, 17 H), 0.86 (t, J = 6.8 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 173.5, 159.5, 159.2, 156.0, 138.8, 136.9, 134.6, 133.4, 133.0, 117.2, 117.0, 91.8, 90.0, 89.7, 79.8, 76.3, 61.7, 61.3, 43.0, 42.2, 36.6, 31.9, 29.6, 29.6, 29.5, 29.4, 29.3, 28.4, 25.7, 22.7, 19.0, 14.1 ppm. HRMS (ESI-TOF): calcd. for $C_{51}H_{67}I_2N_3O_9$ $[M^+]$: 1119.2967; found 1119.2921. FTIR (ATR): $\tilde{\nu}$ = 3307 (br. w), 2925 (m), 1690 (s), 1645 (s), 1246 (s), 1162 (s), 871 (m) cm^{-1}.

Compound 9: A 25 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **8** (2.03 g, 1.81 mmol), degassed THF (6 mL), degassed DIPEA (2.5 mL, 14.5 mmol), $PdCl_2(PPh_3)_2$ (0.025 g, 0.063 mmol), CuI (0.028 g, 0.15 mmol) and (triisopropylsilyl)acetylene (2.0 mL, 9.05 mmol) under argon. The reaction mixture was stirred at room temperature overnight, diluted with CH_2Cl_2, washed with NH_4Cl, and the aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (acetone/CH_2Cl_2, 1:19) to afford desired compound **9** (1.95 g, 88% yield) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.35 (m, 6 H), 6.35 (br. s, 1 H), 5.24 (br. s, 2 H), 4.49 (t, J = 4.1 Hz, 2 H), 4.39 (d, J = 5.7 Hz, 2 H), 4.23 (d, J = 4.8 Hz, 4 H), 4.05 (s, 6 H), 3.90 (br. s, 2 H), 3.36 (br. s, 1 H), 2.26 (t, J = 7.6 Hz, 2 H), 1.67 (t, J = 6.8 Hz, 2 H), 1.47 (s, 18 H), 1.35–1.21 (br. m, 16 H), 1.14 (s, 42 H), 0.87 (t, J = 6.8 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 173.3, 161.2, 159.6, 156.0, 134.6, 134.3, 133.7, 133.1, 132.5, 117.6, 117.2, 102.1, 96.5, 90.3, 89.4, 79.7, 76.4, 61.8, 61.4, 43.5, 42.3, 36.7, 31.9, 29.6, 29.6, 29.5, 29.4, 29.3, 28.4, 25.7, 22.7, 18.7, 14.1, 11.3 ppm. HRMS (ESI-TOF): calcd. for $C_{73}H_{109}N_3O_9Si_2$ $[M^+]$ 1227.7702; found 1227.7693. FTIR (ATR): $\tilde{\nu}$ = 3333 (br. w), 2925 (m), 2864 (m), 1691 (m), 1465 (s), 1242 (s), 1164 (s), 881 (s) cm^{-1}.

Compound 10: A 10 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **9** (0.940 g, 0.765 mmol), THF (4 mL) and tetrabutylammonium fluoride (1.0 M in THF, 1.9 mL, 1.91 mmol). The reaction mixture was stirred at room temperature for 30 min, diluted with CH_2Cl_2, washed with water, and the aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (acetone/CH_2Cl_2, 1:19) to afford desired compound **10** (0.730 g, quantitative yield) as a pale yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.38 (s, 2 H), 7.35 (s, 4 H), 6.62 (br. s, 1 H), 5.41 (br. s, 2 H), 4.47 (t, J = 3.9 Hz, 2 H), 4.38 (d, J = 5.6 Hz, 2 H), 4.23 (d, J = 4.8 Hz, 4 H), 4.05 (s, 6 H), 3.90 (br. s, 2 H), 3.40 (br. s, 1 H), 3.30 (s, 2 H), 2.27 (t, J = 7.6 Hz, 2 H), 1.67 (m, 2 H), 1.47 (s, 18 H), 1.35–1.21 (br. m, 16 H), 0.86 (t, J = 6.7 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 173.4, 161.3, 159.6, 156.0, 134.8, 134.4, 133.6, 133.2, 117.4, 117.1, 116.2, 102.1, 90.0, 89.6, 82.2, 79.7, 79.1, 76.3, 61.8, 61.6, 61.6, 43.4, 42.3, 36.7, 31.9, 29.6, 29.6, 29.5, 29.4, 29.3, 28.4, 25.7, 22.7, 14.1 ppm. HRMS (ESI-TOF): calcd. for $C_{55}H_{69}N_3O_9$ $[M^+]$ 915.5034; found 915.5029. FTIR (ATR): $\tilde{\nu}$ = 3299 (br. m), 2925 (m), 1961 (s), 1523 (s), 1242 (s), 1164 (s), 876 (w) cm^{-1}.

Compound 12: A 10 mL round-bottomed flask equipped with a magnetic stir bar was charged with the compound **11** (0.149 g, 0.327 mmol), CH_2Cl_2 (2.5 mL), 4-(dimethylamino)pyridine (0.008 g, 0.065 mmol), TEA (0.80 mL, 5.76 mmol) and compound **10** (0.660 g, 0.720 mmol) under argon. The reaction mixture was stirred at room temperature overnight, diluted with CH_2Cl_2 and washed with water. The aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (CH_2Cl_2, then acetone/CH_2Cl_2, 2:23). The crude product was then passed through a preparative GPC in $CHCl_3$ (column: Jordi gel DVB 250 × 22.0 mm, 2 µm, 500 Å with a guard column: Jordi gel DVB, 50 × 22 mm, 5 µm at 5.0 mL/min) to afford desired compound **12** (0.563 g, 78% yield) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.02 (s, 2 H), 7.40 (s, 4 H), 7.34 (s, 4 H), 7.31 (s, 4 H), 6.15 (br. s, 2 H), 5.16 (br. s, 4 H), 4.77 (m, 4 H), 4.73 (m, 4 H), 4.38 (d, J = 5.7 Hz, 4 H), 4.20 (d, J = 5.0 Hz, 8 H), 4.04 (s, 12 H), 3.29 (s, 4 H), 2.24 (t, J = 7.6 Hz, 4 H), 1.65 (m, 4 H), 1.45 (s, 36 H), 1.35–1.21 (br. m, 32 H), 0.86 (t, J = 6.8 Hz, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 173.3, 164.1, 161.5, 159.7, 155.9, 142.7, 137.4, 134.5, 134.3, 133.5, 133.1, 133.0, 117.5, 117.0, 116.3, 93.1, 90.2, 89.5, 82.2, 79.7, 79.2, 61.6, 61.5, 43.5, 42.3, 36.7, 31.9, 29.6, 29.6, 29.5, 29.4, 29.3, 28.4, 25.7, 22.7, 14.1 ppm. HRMS (ESI-TOF): calcd. for $C_{118}H_{138}I_2N_6O_{20}$ $[M^+]$ 2212.8055; found 2212.8083. FTIR (ATR): $\tilde{\nu}$ = 3295 (br. w), 2925 (m), 1695 (s), 1391 (m), 1238 (s), 1164 (s), 1042 (m), 876 (m) cm^{-1}.

Compound 13: A 250 mL round-bottomed flask equipped with a magnetic stir bar was charged with CuCl (2.51 g, 25.4 mmol), $CuCl_2$ (0.569 g, 4.23 mmol) and degassed pyridine (85 mL). To this

suspension was added a solution of compound **12** (0.375 mg, 0.169 mmol) in degassed pyridine (25 mL) at room temperature under argon over 96 h. After completion of the addition, the mixture was stirred for an additional 7 d and then poured into a mixture of CH_2Cl_2 and water. The organic layer was extracted successively with water, NH_4OH (25%), water, acetic acid (10%), water, aqueous sodium hydroxide (10%) and brine. The organic layers were dried with $MgSO_4$, the solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (acetone/CH_2Cl_2, 1:9) to afford compound **13** (19 mg, 5% yield) as a beige solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.63 (s, 2 H), 7.45–7.17 (br. m, 12 H), 5.61 (br. s, 2 H), 5.34 (br. s, 4 H), 4.59 (br. s, 4 H), 4.31 (br. s, 4 H), 4.16–3.90 (br. m, 24 H), 2.36 (m, 4 H), 1.75 (m, 4 H), 1.53 (s, 36 H), 1.42–1.14 (br. m, 32 H), 0.86 (t, J = 6.8 Hz, 6 H) ppm. FTIR (ATR): $\tilde{\nu}$ = 3328 (br. w), 2924 (m), 1691 (m), 1520 (m), 1241 (s), 1164 (s), 1039 (m), 998 (w) cm^{-1}. ^{13}C NMR spectroscopic data for **13** could not be obtained owing to its low solubility. HRMS data for **13** could not be obtained in either ESI or APPI mode.

Compound 14: A 50 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **5** (8.60 g, 15.4 mmol), acetone (20 mL), NaI (11.5 g, 77 mmol), 3-chloropropanol (3.9 mL, 46.2 mmol) and K_2CO_3 (6.38 g, 46.2 mmol). The reaction mixture was stirred at reflux temperature overnight, cooled to room temperature and then filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (CH_2Cl_2) to afford desired compound **14** (7.31 g, 77% yield) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.67 (s, 2 H), 5.76 (br. s, 1 H), 4.33 (d, J = 5.9 Hz, 2 H), 4.11 (t, J = 5.6 Hz, 2 H), 3.99 (q, J = 5.6 Hz, 2 H), 2.33 (t, J = 7.5 Hz, 2 H), 2.14 (m, 2 H), 2.00 (t, J = 5.8 Hz, 1 H), 1.66 (m, 2 H), 1.35–1.21 (br. m, 16 H), 0.88 (t, J = 6.4 Hz, 3 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 100 MHz): δ = 172.3, 156.3, 139.9, 138.3, 91.6, 70.8, 58.0, 35.3, 33.2, 31.3, 29.1, 29.0, 29.0, 28.8, 28.8, 28.8, 28.6, 25.3, 22.1, 14.0 ppm. FTIR (ATR): $\tilde{\nu}$ = 3287 (br. m), 2915 (s), 2849 (s), 1645 (s), 1552 (s), 1042 (s), 924 (m) cm^{-1}. HRMS data for **14** could not be obtained in either ESI or APPI mode.

Compound 15: A 250 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **14** (7.20 g, 11.7 mmol), degassed THF (60 mL), degassed TEA (6.5 mL, 46.8 mmol), $PdCl_2(PPh_3)_2$ (0.328 g, 0.468 mmol), CuI (0.178 g, 0.936 mmol) and (trimethylsilyl)acetylene (4.2 mL, 30.4 mmol) under argon. The reaction mixture was stirred at room temperature overnight, diluted with CH_2Cl_2, washed with NH_4Cl, and the aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (acetone/CH_2Cl_2, 1:99) to afford desired compound **15** (6.51 g, quantitative yield) as a red oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.30 (s, 2 H), 5.82 (br. s, 1 H), 4.33 (m, 4 H), 3.96 (q, J = 5.7 Hz, 2 H), 2.35 (t, J = 5.5 Hz, 1 H), 2.21 (t, J = 7.6 Hz, 2 H), 2.03 (m, 2 H), 1.64 (m, 2 H), 1.35–1.21 (br. m, 16 H), 0.88 (t, J = 6.8 Hz, 3 H), 0.26 (s, 18 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 173.2, 160.7, 134.0, 133.6, 117.8, 100.3, 99.9, 72.4, 61.1, 42.5, 36.8, 32.7, 32.0, 29.7, 29.7, 29.6, 29.5, 29.5, 29.4, 25.8, 22.8, 14.2, –0.1 ppm. HRMS (APPI-TOF): calcd. for $C_{32}H_{53}NO_3Si_2$ [M + H]$^+$ 556.3637; found 5556.3638. FTIR (ATR): $\tilde{\nu}$ = 3281 (br. w), 2923 (m), 2853 (m), 2158 (w), 1646 (m), 1248 (s), 842 (s) cm^{-1}.

Compound 17: A 100 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **15** (4.98 g, 8.96 mmol), THF (20 mL), MeOH (20 mL) and KOH 2.5 M (10 mL). The reaction mixture was stirred for 1 h, acidified to pH = 7 and diluted with CH_2Cl_2. The aqueous layer was extracted three times with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was then removed under reduced pressure. A 100 mL round-bottomed flask equipped with a magnetic stir bar was charged with the crude product (3.69 g, 8.96 mmol), degassed THF (40 mL), degassed DIPEA (10.8 mL, 61.8 mmol), $PdCl_2(PPh_3)_2$ (0.217 g, 0.309 mmol), CuI (0.118 g, 0.618 mmol) and compound **16** (6.34 g, 19.3 mmol) under argon. The reaction mixture was stirred at room temperature for 48 h, diluted with CH_2Cl_2, washed with NH_4Cl, and the aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (acetone/CH_2Cl_2, 1:49) to afford desired compound **17** (5.00 g, 80% yield) as a brown solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.30 (s, 2 H), 7.29 (s, 2 H), 7.27 (s, 2 H), 6.44 (t, J = 5.6 Hz, 1 H), 4.39 (t, J = 5.8 Hz, 2 H), 4.31 (d, J = 5.6 Hz, 2 H), 3.89 (t, J = 5.4 Hz, 2 H), 2.52 (br. s, 1 H), 2.40 (s, 6 H), 2.37 (s, 6 H), 2.20 (t, J = 7.5 Hz, 2 H), 2.05 (m, 2 H), 1.63 (m, 2 H), 1.35–1.21 (br. m, 16 H), 0.87 (t, J = 6.9 Hz, 3 H), 0.27 (s, 18 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 173.4, 159.0, 137.7, 137.0, 134.2, 132.9, 132.6, 132.4, 123.2, 122.6, 117.8, 103.7, 99.8, 92.9, 90.0, 72.6, 60.7, 42.2, 36.6, 32.8, 31.9, 29.6, 29.6, 29.5, 29.4, 29.3, 29.3, 25.8, 22.7, 20.0, 19.9, 14.1, 0.0 ppm. HRMS (APPI-TOF): calcd. for $C_{52}H_{69}NO_3Si_2$ [M + H]$^+$ 812.4889; found 812.4887. FTIR (ATR): $\tilde{\nu}$ = 3289 (br. w), 2924 (m), 2148 (m), 1652 (s), 1450 (s), 1248 (s), 840 (s), 760 (s) cm^{-1}.

Compound 18: A 100 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **17** (4.89 g, 7.30 mmol), THF (40 mL) and tetrabutylammonium fluoride in THF (1.0 M, 18.3 mL, 18.3 mmol). The reaction mixture was stirred at room temperature for 30 min, diluted with CH_2Cl_2, washed with water, and the aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (acetone/CH_2Cl_2, 1:19) to afford desired compound **18** (3.64 g, 74%) as a purplish solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.38 (s, 2 H), 7.37 (s, 2 H), 7.34 (s, 2 H), 5.86 (t, J = 5.0 Hz, 1 H), 4.44 (t, J = 5.7 Hz, 2 H), 4.39 (d, J = 5.7 Hz, 2 H), 3.93 (q, J = 5.5 Hz, 2 H), 3.35 (s, 2 H), 2.45 (s, 6 H), 2.41 (s, 6 H), 2.23 (t, J = 7.6 Hz, 2 H), 2.15 (t, J = 5.6 Hz, 1 H), 2.08 (m, 2 H), 1.65 (m, 2 H), 1.35–1.21 (br. m, 16 H), 0.87 (t, J = 6.7 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 173.2, 159.3, 138.0, 137.3, 134.3, 133.4, 133.0, 132.7, 123.0, 122.3, 118.1, 92.9, 90.0, 82.3, 72.8, 61.0, 42.4, 36.8, 32.8, 31.9, 29.7, 29.6, 29.5, 29.4, 29.3, 25.8, 22.7, 20.1, 20.0, 14.2 ppm. HRMS (APPI-TOF): calcd. for $C_{46}H_{53}NO_3$ [M + H]$^+$ 667.4025; found 667.4043. FTIR (ATR): $\tilde{\nu}$ = 3279 (br. m), 2919 (m), 1621 (s), 1532 (s), 1441 (s), 1146 (m), 886 (s) cm^{-1}.

Compound 20: A 100 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **18** (3.64 g, 5.44 mmol), degassed THF (30 mL), degassed DIPEA (7.6 mL, 43.5 mmol), $PdCl_2(PPh_3)_2$ (0.077 g, 0.11 mmol), CuI (0.083 g, 0.44 mmol) and compound **19** (7.25 g, 16.3 mmol) under argon. The reaction mixture was stirred at room temperature overnight, diluted with CH_2Cl_2, washed with NH_4Cl, and the aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (acetone/CH_2Cl_2, 1:49) to afford desired compound **20** (2.61 g, 37% yield) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.79 (s, 2 H), 7.52 (s, 2 H), 7.47 (s, 2 H),

7.36 (s, 2 H), 7.36 (s, 2 H), 7.31 (s, 2 H), 6.70 (s, 2 H), 6.02 (t, J = 5.7 Hz, 1 H), 4.45 (t, J = 5.7 Hz, 2 H), 4.39 (d, J = 5.5 Hz, 2 H), 3.96 (m, 2 H), 2.46 (s, 6 H), 2.43 (s, 6 H), 2.33 (br. s, 1 H), 2.25 (t, J = 7.5 Hz, 2 H), 2.10 (m, 2 H), 1.68 (m, 2 H), 1.52 (s, 18 H), 1.35–1.21 (br. m, 16 H), 0.87 (t, J = 6.8 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 173.3, 159.2, 152.3, 139.5, 137.5, 137.3, 134.5, 134.2, 132.9, 132.8, 132.7, 127.0, 125.6, 122.9, 122.8, 120.3, 118.0, 93.7, 93.1, 92.8, 90.2, 89.4, 81.2, 72.8, 61.0, 42.4, 36.8, 32.8, 31.9, 29.7, 29.6, 29.5, 29.4, 29.4, 29.4, 28.3, 25.8, 22.7, 20.1, 20.1, 14.2 ppm. HRMS (APPI-TOF): calcd. for $C_{68}H_{77}I_2N_3O_7$ $[M + H]^+$ 1302.3924; found 1302.3926. FTIR (ATR): $\tilde{\nu}$ = 3280 (br. w), 2924 (m), 1702 (m), 1566 (s), 1259 (s), 1153 (s), 1033 (s), 851 (m) cm^{-1}.

Compound 21: A 25 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **20** (0.500 g, 0.384 mmol), degassed THF (5 mL), degassed DIPEA (0.54 mL, 3.07 mmol), $PdCl_2(PPh_3)_2$ (0.005 g, 0.0077 mmol), CuI (0.006 g, 0.031 mmol) and (triisopropylsilyl)acetylene (0.43 mL, 1.92 mmol) under argon. The reaction mixture was stirred at room temperature overnight, diluted with CH_2Cl_2, washed with NH_4Cl, and the aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (acetone/CH_2Cl_2, 1:19) to afford desired compound **21** (0.519 g, 96% yield) as a brown solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.56 (s, 2 H), 7.46 (s, 2 H), 7.36 (s, 2 H), 7.35 (s, 2 H), 7.32 (s, 2 H), 7.30 (s, 2 H), 6.85 (s, 2 H), 6.19 (t, J = 5.5 Hz, 1 H), 4.44 (t, J = 5.5 Hz, 2 H), 4.39 (d, J = 5.2 Hz, 2 H), 3.96 (m, 2 H), 2.46 (s, 6 H), 2.44 (s, 6 H), 2.25 (t, J = 7.5 Hz, 2 H), 2.10 (m, 2 H), 1.67 (m, 2 H), 1.52 (s, 18 H), 1.35–1.21 (br. m, 17 H), 1.13 (s, 42 H), 0.87 (t, J = 6.8 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 173.4, 159.2, 152.6, 138.6, 137.4, 137.2, 134.2, 134.2, 132.8, 132.8, 132.6, 132.6, 129.6, 129.5, 124.4, 124.1, 123.0, 122.7, 121.5, 121.1, 118.0, 105.9, 93.8, 93.1, 91.4, 90.1, 89.6, 80.9, 72.7, 60.9, 42.4, 36.7, 32.8, 31.9, 29.6, 29.6, 29.5, 29.4, 29.3, 28.3, 28.3, 25.8, 22.7, 20.1, 20.1, 18.7, 14.1 ppm. HRMS (APPI-TOF): calcd. for $C_{90}H_{119}N_3O_7Si_2$ $[M^+]$ 1409.8587; found 1409.8566. FTIR (ATR): $\tilde{\nu}$ = 3296 (br. w), 2923 (m), 1420 (m), 1264 (s), 1229 (s), 1155 (s), 867 (m) cm^{-1}.

Compound 22: A 10 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **21** (0.408 g, 0.289 mmol), THF (1.5 mL) and tetrabutylammonium fluoride in THF (1.0 M, 0.72 mL, 0.723 mmol). The reaction mixture was stirred at room temperature for 30 min, diluted with CH_2Cl_2, washed with water, and the aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure. A 10 mL round-bottomed flask equipped with a magnetic stir bar was charged with the crude product (0.317 g, 0.289 mmol), compound **11** (0.053 g, 0.12 mmol), CH_2Cl_2 (0.4 mL), 4-(dimethylamino)pyridine (0.003 g, 0.023 mmol), TEA (0.13 mL, 0.936 mmol) under argon. The reaction mixture was stirred at room temperature overnight, diluted with CH_2Cl_2 and washed with water. The aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (EtOAc/toluene, 7:43) to afford desired compound **22** (0.127 g, 42% yield) as a brown solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.09 (s, 2 H), 7.54 (s, 4 H), 7.46 (s, 4 H), 7.36 (s, 4 H), 7.30 (s, 4 H), 7.27 (s, 4 H), 7.18 (s, 4 H), 6.71 (s, 4 H), 6.01 (br. s, 2 H), 4.60 (m, 4 H), 4.45 (m, 4 H), 4.40 (m, 4 H), 3.05 (s, 4 H), 2.44 (s, 12 H), 2.39 (s, 12 H), 2.28 (m, 8 H), 1.68 (m, 4 H), 1.52 (s, 36 H), 1.35–1.21 (br. m, 32 H), 0.87 (m, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 173.3, 164.1, 159.4, 152.5, 142.7, 138.7, 138.0, 137.5, 137.2, 134.1, 132.8, 132.8, 132.6, 132.6, 129.6, 129.6, 124.3, 123.0, 122.9, 122.8, 121.5, 121.1, 118.1, 93.6, 93.2, 92.8, 90.1, 88.9, 82.6, 81.1, 77.9, 70.8, 63.4, 42.5, 36.8, 31.9, 29.7, 29.7, 29.6, 29.6, 29.4, 28.3, 25.8, 22.7, 20.2, 20.2, 14.2 ppm. FTIR (ATR): $\tilde{\nu}$ = 3296 (br. w), 2923 (m), 1720 (m), 1597 (m), 1432 (m), 1229 (s), 1155 (s), 867 (m) cm^{-1}. HRMS data for **22** could not be obtained in either ESI or APPI mode.

Compound 25: A 1 L round-bottomed flask equipped with a magnetic stir bar was charged with MeOH (330 mL) and concentrated H_2SO_4 (7.1 mL, 133 mmol). Then, 4-*tert*-butylphenol (10.0 g, 66.6 mmol) and KI (22.1 g, 133 mmol) were added to the reaction mixture. Finally, H_2O_2 (30%, 27.2 mL, 266 mmol) was added. The reaction mixture was stirred at 40 °C for 2 h, cooled to room temperature, diluted with CH_2Cl_2. The organic layer was washed with $NaHSO_3$ (0.1 M), washed with H_2O, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (EtOAc/hexanes, 1:49) to afford desired compound **25** (18.6 g, 69% yield) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.64 (s, 2 H), 5.58 (s, 1 H), 1.26 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 151.2, 147.5, 136.4, 82.2, 34.0, 31.3 ppm. HRMS (APPI-TOF): calcd. for $C_{10}H_{12}I_2O$ $[M^+]$ 401.8978; found 401.8984. FTIR (ATR): $\tilde{\nu}$ = 3472 (br. m), 2962 (s), 1545 (w), 1460 (s), 1274 (m), 1154 (m) cm^{-1}.

Compound 26: A 100 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **25** (9.00 g, 22.4 mmol), acetone (30 mL), NaI (13.4 g, 89.6 mmol), 3-chloropropanol (3.7 mL, 44.8 mmol) and K_2CO_3 (9.29 g, 67.2 mmol). The reaction mixture was stirred at reflux overnight, cooled to room temperature and then filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (EtOAc/hexanes, 1:9) to afford desired compound **26** (7.01 g, 68% yield) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.72 (s, 2 H), 4.09 (t, J = 5.8 Hz, 2 H), 3.98 (t, J = 6.0 Hz, 2 H), 2.88 (br. s, 1 H), 2.14 (m, 2 H), 1.26 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 155.1, 151.4, 137.2, 90.7, 71.3, 60.7, 34.3, 32.6, 31.3 ppm. HRMS (APPI-TOF): calcd. for $C_{13}H_{18}I_2O_2$ $[M + H]^+$ 460.9469; found 460.9466. FTIR (ATR): $\tilde{\nu}$ = 3344 (br. m), 2960 (s), 1531 (w), 1443 (s), 1265 (s), 1047 (m) cm^{-1}.

Compound 27: A 250 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **26** (7.00 g, 15.2 mmol), degassed THF (75 mL), degassed TEA (8.5 mL, 60.8 mmol), $PdCl_2(PPh_3)_2$ (0.427 g, 0.608 mmol), CuI (0.232 g, 1.22 mmol) and (trimethylsilyl)acetylene (5.5 mL, 39.5 mmol) under argon. The reaction mixture was stirred at room temperature overnight, diluted with CH_2Cl_2, washed with NH_4Cl, and the aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (EtOAc/hexanes, 1:9) to afford desired compound **27** (5.49 g, 90% yield) as a brown solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.40 (s, 2 H), 4.33 (t, J = 5.6 Hz, 2 H), 3.97 (q, J = 5.2 Hz, 2 H), 2.46 (t, J = 5.5 Hz, 1 H), 2.03 (m, 2 H), 1.28 (s, 9 H), 0.27 (s, 18 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 159.2, 146.4, 131.4, 116.7, 101.1, 98.6, 72.2, 61.1, 34.3, 32.6, 31.1, –0.1 ppm. FTIR (ATR): $\tilde{\nu}$ = 3464 (br. w), 2956 (m), 2152 (m), 1246 (m), 1000 (m), 835 (s) cm^{-1}. HRMS data for **27** could not be obtained in either ESI or APPI mode.

Compound 28: A 250 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **27** (5.40 g,

13.5 mmol), THF (35 mL), MeOH (35 mL) and KOH (2.5 M, 14 mL). The reaction mixture was stirred for 1 h, acidified to pH = 7 and diluted with CH_2Cl_2. The aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was then removed under reduced pressure. A 100 mL round-bottomed flask equipped with a magnetic stir bar was charged with the crude product (3.46 g, 13.5 mmol), degassed THF (70 mL), degassed TEA (14.9 mL, 107 mmol), $PdCl_2(PPh_3)_2$ (0.376 g, 0.536 mmol), CuI (0.204 g, 0.536 mmol) and compound **16** (10.4 g, 31.7 mmol) under argon. The reaction mixture was stirred at room temperature for 48 h, diluted with CH_2Cl_2, washed with NH_4Cl, and the aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (CH_2Cl_2/hexanes, 1:3) to afford desired compound **28** (5.93 g, 67% yield) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.49 (s, 2 H), 7.39 (s, 2 H), 7.31 (s, 2 H), 4.44 (t, J = 5.7 Hz, 2 H), 3.91 (t, J = 5.7 Hz, 2 H), 2.47 (s, 6 H), 2.40 (s, 6 H), 2.25 (br. s, 1 H), 2.07 (m, 2 H), 1.33 (s, 9 H), 0.27 (s, 18 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 157.8, 146.7, 137.8, 137.1, 132.9, 132.6, 130.9, 123.1, 122.9, 117.2, 103.8, 99.7, 92.2, 90.7, 72.7, 61.0, 34.3, 32.8, 31.2, 20.1, 20.0, 0.0 ppm. HRMS (APPI-TOF): calcd. for $C_{43}H_{52}O_2Si_2$ [M + H]$^+$ 657.3579; found 657.3608. FTIR (ATR): $\tilde{\nu}$ = 3421 (br. w), 2956 (m), 2147 (m), 1452 (m), 1247 (m), 837 (s), 758 (m) cm^{-1}.

Compound 29: A 100 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **28** (3.50 g, 5.33 mmol), THF (30 mL) and tetrabutylammonium fluoride in THF (1.0 M, 13.3 mL, 13.3 mmol). The reaction mixture was stirred at room temperature for 30 min, diluted with CH_2Cl_2 and washed with water. The aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (CH_2Cl_2/hexanes, 3:7) to afford desired compound **29** (2.58 g, 94%) as an orange oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.49 (s, 2 H), 7.40 (s, 2 H), 7.35 (s, 2 H), 4.43 (t, J = 5.7 Hz, 2 H), 3.93 (q, J = 5.7 Hz, 2 H), 3.34 (s, 2 H), 2.48 (s, 6 H), 2.42 (s, 6 H), 2.13 (t, J = 5.7 Hz, 1 H), 2.08 (m, 2 H), 1.34 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 157.9, 146.8, 138.0, 137.2, 133.4, 132.7, 131.1, 123.3, 122.1, 117.1, 92.0, 90.8, 82.4, 82.2, 72.8, 61.2, 34.4, 32.8, 31.3, 20.1, 20.0 ppm. HRMS (APPI-TOF): calcd. for $C_{37}H_{36}O_2$ [M + H]$^+$ 513.2788; found 513.2790. FTIR (ATR): $\tilde{\nu}$ = 3455 (br. w), 3299 (m), 2950 (m), 2101 (w), 1451 (m), 1222 (m), 1034 (s), 884 (s) cm^{-1}.

Compound 31: A 100 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **29** (2.58 g, 5.02 mmol), degassed THF (25 mL), degassed DIPEA (7.0 mL, 40.2 mmol), $PdCl_2(PPh_3)_2$ (0.070 g, 0.10 mmol), CuI (0.077 g, 0.40 mmol) and compound **30** (6.68 g, 15.1 mmol) under argon. The reaction mixture was stirred overnight at room temperature, diluted with CH_2Cl_2, washed with NH_4Cl, and the aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (CH_2Cl_2/hexanes, 3:7) to afford desired compound **31** (1.54 g, 27% yield) as a dark oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.70 (s, 2 H), 7.50 (s, 4 H), 7.43 (s, 2 H), 7.36 (s, 2 H), 7.30 (s, 2 H), 4.45 (t, J = 5.6 Hz, 2 H), 3.95 (m, 2 H), 2.53 (t, J = 7.4 Hz, 4 H), 2.50 (s, 6 H), 2.47 (s, 6 H), 2.23 (br. s, 1 H), 2.10 (m, 2 H), 1.59 (m, 4 H), 1.35 (s, 9 H), 1.35–1.21 (br. m, 20 H), 0.89 (t, J = 6.4 Hz, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 157.8, 146.7, 145.1, 137.4, 137.3, 137.2, 132.7, 132.7, 131.0, 130.8, 125.0, 123.0, 122.8, 117.1, 93.8, 93.2, 92.2, 90.9, 89.1, 72.7, 61.1, 35.3, 34.3, 32.8, 31.9, 31.2, 31.1, 29.4, 29.2, 22.7, 20.1, 14.2 ppm. HRMS (APPI-TOF): calcd. for $C_{65}H_{74}I_2O_2$ [M + H]$^+$ 1141.3851; found 1141.3842. FTIR (ATR): $\tilde{\nu}$ = 3408 (br. w), 2924 (s), 2854 (m), 1553 (m), 1454 (m), 884 (m), 770 (s) cm^{-1}.

Compound 32: A 25 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **31** (1.54 g, 1.35 mmol), degassed THF (6 mL), degassed DIPEA (1.64 mL, 9.44 mmol), $PdCl_2(PPh_3)_2$ (0.017 g, 0.024 mmol), CuI (0.018 g, 0.094 mmol) and (triisopropylsilyl)acetylene (1.08 mL, 5.90 mmol) under argon. The reaction mixture was stirred at room temperature overnight, diluted with CH_2Cl_2, washed with NH_4Cl, and the aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (CH_2Cl_2/hexanes, 1:3) to afford desired compound **32** (1.40 g, 96% yield) as a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.50 (s, 2 H), 7.47 (s, 2 H), 7.43 (s, 2 H), 7.39 (s, 2 H), 7.30 (s, 2 H), 7.26 (s, 2 H), 4.46 (t, J = 5.6 Hz, 2 H), 3.96 (m, 2 H), 2.58 (t, J = 7.4 Hz, 4 H), 2.51 (s, 6 H), 2.49 (s, 6 H), 2.19 (br. s, 1 H), 2.10 (m, 2 H), 1.62 (m, 4 H), 1.35 (s, 9 H), 1.35–1.21 (br. m, 20 H), 1.14 (s, 42 H), 0.89 (t, J = 6.4 Hz, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 157.8, 146.8, 143.3, 137.5, 137.3, 132.8, 132.7, 132.4, 132.0, 131.5, 131.0, 123.7, 123.3, 123.1, 122.9, 117.2, 106.5, 94.2, 92.3, 90.8, 90.8, 88.4, 72.8, 61.2, 35.6, 34.4, 32.9, 31.9, 31.3, 31.3, 29.5, 29.3, 29.3, 22.7, 20.2, 18.7, 14.2, 11.3 ppm. HRMS (APPI-TOF): calcd. for $C_{87}H_{116}O_2Si_2$ [M + H]$^+$ 1249.8587; found 1249.8613. FTIR (ATR): $\tilde{\nu}$ = 2924 (s), 2862 (s), 2154 (w), 1586 (m), 1462 (m), 1264 (w), 882 (m) cm^{-1}.

Compound 33: A 5 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **32** (0.250 g, 0.200 mmol), THF (1 mL) and tetrabutylammonium fluoride in THF (1.0 M, 0.50 mL, 0.500 mmol). The reaction mixture was stirred at room temperature for 30 min, diluted with CH_2Cl_2 and washed with water. The aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure. A 5 mL round-bottomed flask equipped with a magnetic stir bar was charged with the crude product (0.187 g, 0.200 mmol), compound **11** (0.041 g, 0.091 mmol), CH_2Cl_2 (1 mL), 4-(dimethylamino)pyridine (0.002 g, 0.018 mmol) and TEA (0.22 mL, 1.60 mmol) under argon. The reaction mixture was stirred at room temperature overnight, diluted with CH_2Cl_2 and washed with water. The aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (CH_2Cl_2/hexanes, 1:1) to afford desired compound **33** (0.179 g, 87% yield) as a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.11 (s, 2 H), 7.51 (s, 4 H), 7.48 (s, 4 H), 7.36 (s, 4 H), 7.32 (s, 8 H), 7.26 (s, 4 H), 4.60 (t, J = 6.0 Hz, 4 H), 4.46 (t, J = 5.5 Hz, 4 H), 3.05 (s, 4 H), 2.56 (t, J = 7.6 Hz, 8 H), 2.48 (s, 12 H), 2.43 (s, 12 H), 2.28 (m, 4 H), 1.59 (m, 8 H), 1.35 (s, 18 H), 1.35–1.21 (br. m, 40 H), 0.88 (t, J = 6.7 Hz, 12 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 164.0, 157.9, 146.7, 143.4, 142.8, 137.8, 137.4, 137.2, 132.8, 132.7, 132.6, 132.4, 132.0, 131.9, 131.0, 123.5, 122.9, 122.3, 117.2, 93.9, 92.9, 92.3, 90.9, 88.6, 83.1, 77.4, 70.6, 63.5, 35.5, 34.4, 31.9, 31.2, 31.2, 29.4, 29.3, 29.2, 22.7, 20.2, 20.2, 14.2, 11.3 ppm. HRMS (APPI-TOF): calcd. for $C_{146}H_{152}I_2O_6$ [M$^+$] 2254.9678; found 2254.9684. FTIR (ATR): $\tilde{\nu}$ = 3293 (br. m), 2924 (s), 2854 (m), 1731 (m), 1586 (m), 1455 (m), 1233 (m), 1045 (m), 880 (m), 772 (s) cm^{-1}.

Compound 34: A 25 mL round-bottomed flask equipped with a magnetic stir bar was charged with CuCl (0.387 g, 3.91 mmol),

$CuCl_2$ (0.075 g, 0.56 mmol) and degassed pyridine (8 mL). To this suspension was added a solution of compound **33** (0.075 g, 0.56 mmol) in degassed pyridine (2 mL) at room temperature under argon over 96 h. After completion of the addition, the mixture was stirred for an additional 7 d and then poured into a mixture of CH_2Cl_2/water. The organic layer was extracted successively with water, NH_4OH (25%), water, acetic acid (10%), water, aqueous sodium hydroxide (10%) and brine. The organic layers were dried with $MgSO_4$, the solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel ($CHCl_3$). The crude product was suspended in hexanes and then filtered to afford compound **34** (103 mg, 82% yield) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.39 (s, 2 H), 7.62 (s, 4 H), 7.52 (s, 4 H), 7.51 (s, 4 H), 7.41 (s, 4 H), 7.34 (s, 4 H), 7.26 (s, 4 H), 4.81 (t, J = 8.2 Hz, 4 H), 4.41 (m, 4 H), 2.73 (t, J = 4.6 Hz, 4 H), 2.60 (t, J = 7.1 Hz, 8 H), 2.56 (s, 12 H), 2.54 (s, 12 H), 1.71–1.49 (br. m, 8 H), 1.39–1.17 (br. m, 58 H), 0.89 (m, 12 H) ppm. FTIR (ATR): $\tilde{\nu}$ = 2920 (m), 1728 (m), 1583 (m), 1453 (m), 1275 (m), 1225 (s), 1045 (s), 874 (s) cm^{-1}. ^{13}C NMR spectroscopic data for **34** could not be obtained owing to its low solubility. HRMS data for **34** could not be obtained in either ESI or APPI mode.

Compound 36: A 100 mL round-bottomed flask equipped with a magnetic stir bar was charged with 4-bromo-4′-hydroxybiphenyl (5.00 g, 20.1 mmol), acetone (25 mL), 1-iodooctane (10.9 mL, 60.3 mmol) and K_2CO_3 (14.0 g, 101 mmol). The reaction mixture was stirred at reflux overnight, cooled to room temperature and then filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (CH_2Cl_2/hexanes, 1:19) to afford desired compound **36** (6.53 g, 90% yield) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.52 (d, J = 8.4 Hz, 2 H), 7.45 (d, J = 8.6 Hz, 2 H), 7.39 (d, J = 8.4 Hz, 2 H), 6.94 (d, J = 8.6 Hz, 2 H), 3.97 (t, J = 6.5 Hz, 2 H), 1.79 (m, 2 H), 1.46 (m, 2 H), 1.38–1.24 (br. s, 8 H), 0.89 (t, J = 6.5 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 159.0, 139.8, 132.2, 131.8, 128.3, 127.9, 120.7, 114.9, 68.1, 31.9, 29.4, 29.3, 26.1, 22.7, 14.2 ppm. HRMS (APPI-TOF): calcd. for $C_{20}H_{25}BrO$ [M + H]$^+$ 360.1162; found 360.1107. FTIR (ATR): $\tilde{\nu}$ = 2920 (m), 2853 (m), 1604 (m), 1472 (m), 1287 (m), 1253 (m), 996 (m), 810 (s) cm^{-1}.

Compound 37: A 250 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **36** (6.47 g, 17.9 mmol) and THF (60 mL) under argon. The reaction mixture was cooled to –78 °C. Then, *n*-butyllithium in hexanes (1.6 M, 12.2 mL, 18.2 mmol) was added dropwise. The reaction mixture was stirred for 1 h, and diethyl carbonate (0.70 mL, 5.77 mmol) was added dropwise. The reaction mixture was warmed to room temperature and stirred overnight, neutralized with saturated $NaHCO_3$ and extracted three times with diethyl ether. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (EtOAc/hexanes, 1:19) to afford desired compound **37** (3.16 g, 63% yield) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.49 (d, J = 8.5 Hz, 12 H), 7.36 (d, J = 8.3 Hz, 6 H), 6.93 (d, J = 8.7 Hz, 6 H), 3.97 (t, J = 6.5 Hz, 6 H), 2.99 (s, 1 H), 1.79 (m, 6 H), 1.46 (m, 6 H), 1.38–1.24 (br. s, 24 H), 0.89 (t, J = 6.6 Hz, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 158.8, 145.2, 139.7, 132.9, 128.4, 128.0, 126.2, 114.8, 81.7, 68.1, 31.9, 29.4, 29.3, 29.3, 26.1, 22.7, 14.2 ppm. HRMS (APPI-TOF): calcd. for $C_{61}H_{76}O_4$ [M + H]$^+$ 873.5816; found 873.5807. FTIR (ATR): $\tilde{\nu}$ = 3454 (br. w), 2922 (m), 1607 (w), 1495 (s), 1245 (s), 1176 (m), 817 (s) cm^{-1}.

Compound 38: A 50 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **37** (1.50 g, 1.72 mmol) and acetyl chloride (20 mL) under argon. The reaction mixture was stirred overnight and, the solvent was removed under reduced pressure. A 100 mL round-bottomed flask equipped with a magnetic stir bar was charged with the crude product (1.53 g, 1.72 mmol), toluene (15 mL) and ethynylmagnesium bromide in THF (0.5 M, 35 mL, 17.2 mmol) under argon. The reaction mixture was stirred overnight, neutralized with water and extracted three times with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (toluene/hexanes, 7:13) to afford desired compound **38** (0.536 g, 35% yield) as a yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.48 (m, 12 H), 7.38 (d, J = 8.3 Hz, 6 H), 6.92 (d, J = 8.7 Hz, 6 H), 3.93 (t, J = 6.5 Hz, 6 H), 2.70 (s, 1 H), 1.76 (m, 6 H), 1.44 (m, 6 H), 1.38–1.24 (br. s, 24 H), 0.88 (t, J = 6.4 Hz, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 158.8, 143.1, 139.4, 132.8, 129.8, 129.4, 128.0, 126.6, 126.3, 114.7, 89.7, 68.0, 31.9, 29.4, 29.3, 29.3, 26.1, 22.7, 14.2 ppm. HRMS (APPI-TOF): calcd. for $C_{63}H_{76}O_3$ [M + H]$^+$ 881.5867; found 881.5873. FTIR (ATR): $\tilde{\nu}$ = 2921 (m), 2853 (m), 1605 (m), 1493 (s), 1242 (s), 1175 (m), 806 (s) cm^{-1}.

Compound 40: A 10 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **38** (0.393 g, 0.446 mmol), degassed THF (2 mL), degassed TEA (0.25 mL, 1.78 mmol), $PdCl_2(PPh_3)_2$ (0.006 g, 0.0089 mmol), CuI (0.003 g, 0.018 mmol) and compound **39** (0.268 g, 0.892 mmol) under argon. The reaction mixture was stirred at room temperature overnight, diluted with CH_2Cl_2, washed with NH_4Cl, and the aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (toluene/hexanes, 1:3) to afford desired compound **40** (0.362 g, 77% yield) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.51 (d, J = 8.5 Hz, 12 H), 7.48–7.39 (br. m, 10 H), 6.93 (d, J = 8.8 Hz, 6 H), 3.95 (t, J = 6.4 Hz, 6 H), 1.77 (m, 6 H), 1.45 (m, 6 H), 1.38–1.24 (br. s, 24 H), 0.88 (t, J = 6.4 Hz, 9 H), 0.25 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 158.9, 143.6, 139.5, 132.9, 131.9, 131.6, 129.6, 128.1, 126.4, 123.8, 122.8, 114.9, 104.9, 97.7, 96.1, 85.1, 68.1, 55.2, 32.0, 29.5, 29.4, 29.4, 26.2, 22.8, 14.3, 0.1 ppm. HRMS (APPI-TOF): calcd. for $C_{74}H_{88}O_3Si$ [M + H]$^+$ 1053.6575; found 1053.6575. FTIR (ATR): $\tilde{\nu}$ = 2914 (m), 2854 (m), 2456 (w), 1607 (m), 1494 (s), 1244 (s), 1172 (m), 840 (s), 817 (m) cm^{-1}.

Compound 41: A 5 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **40** (0.146 g, 0.139 mmol), THF (1 mL), MeOH (1 mL) and KOH 2.5 M (0.14 mL). The reaction mixture was stirred for 1 h, acidified to pH = 7 and diluted with CH_2Cl_2. The aqueous layer was extracted three times with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was then removed under reduced pressure. A 5 mL round-bottomed flask equipped with a magnetic stir bar was charged with the crude product (0.137 g, 0.139 mmol), degassed THF (2 mL), degassed DIPEA (0.30 mL, 1.85 mmol), $PdCl_2(PPh_3)_2$ (0.0003 g, 0.00046 mmol), CuI (0.0002 g, 0.00092 mmol) and compound **34** (0.052 g, 0.0236 mmol) under argon. The reaction mixture was stirred at room temperature for 48 h, diluted with CH_2Cl_2, washed with NH_4Cl, and the aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel ($CHCl_3$/hexanes, 3:2) to afford desired compound **41** (0.084 g, 92% yield) as a yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.32 (s, 2 H), 7.63–7.18 (br. m, 68

H), 6.93 (d, J = 8.5 Hz, 12 H), 4.90 (t, J = 7.3 Hz, 4 H), 4.43 (br. s, 4 H), 3.98 (t, J = 6.6 Hz, 12 H), 2.61 (br. s, 4 H), 2.58–2.41 (br. m, 32 H), 1.80 (m, 12 H), 1.58 (m, 8 H), 1.47 (m, 12 H), 1.41–1.18 (br. m, 106 H), 0.89 (br. m, 30 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 165.2, 158.8, 157.3, 147.1, 143.7, 143.6, 139.4, 139.2, 137.8, 137.4, 134.7, 134.6, 133.0, 132.9, 132.7, 132.0, 131.8, 131.5, 131.2, 129.6, 128.1, 126.5, 126.4, 126.3, 124.4, 123.9, 123.1, 123.0, 122.4, 122.0, 117.8, 114.9, 114.9, 97.8, 96.8, 93.9, 92.4, 91.1, 89.3, 89.2, 85.1, 81.6, 74.4, 70.7, 68.2, 64.5, 55.4, 35.6, 34.5, 32.0, 32.0, 31.4, 31.2, 29.8, 29.6, 29.5, 29.4, 29.4, 29.4, 26.2, 26.2, 22.8, 20.3, 20.2, 14.3 ppm. FTIR (ATR): $\tilde{\nu}$ = 2923 (s), 2852 (s), 1494 (s), 1467 (m), 1247 (s), 1042 (m), 819 (m) cm^{-1}. HRMS data for **41** could not be obtained in either ESI or APPI mode.

Compound 43: A 100 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **42** (4.00 g, 9.79 mmol), degassed THF (50 mL), degassed TEA (5.4 mL, 39.1 mmol), $PdCl_2(PPh_3)_2$ (0.275 g, 0.390 mmol), CuI (0.750 g, 0.390 mmol) and (trimethylsilyl)acetylene (2.8 mL, 20.5 mmol) under argon. The reaction mixture was stirred at room temperature overnight, diluted with CH_2Cl_2, washed with NH_4Cl (3×) and dried with Na_2SO_4. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (hexanes) to afford compound **43** (3.41 g, 98% yield) as a colorless oil. ^{1}H NMR ($CDCl_3$): δ = 7.53 (s, 2 H), 7.49 (s, 1 H), 0.23 (s, 18 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 134.7, 134.2, 125.3, 121.9, 102.6, 96.8, 0.01 ppm. HRMS (APPI-TOF): calcd. for $C_{16}H_{21}BrSi_2$ [M + H]$^+$ 349.0438; found 349.0454. FTIR (ATR): $\tilde{\nu}$ = 2960 (m), 2160 (m), 1550 (m), 1249 (m), 842 (m) cm^{-1}.

Compound 44: A 100 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **43** (33.7 g, 9.64 mmol), degassed TEA (50 mL), $Pd_2(dba)_3$ (0.353 g, 0.386 mmol), CuI (0.074 g, 0.39 mmol), PPh_3 (0.506 g, 1.93 mmol) and (triisopropylsilyl)acetylene (4.3 mL, 19.3 mmol) under argon. The reaction mixture was stirred at 60 °C for 48 h, cooled to room temperature, diluted with CH_2Cl_2, washed with NH_4Cl, and the aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (hexanes) to afford desired compound **44** (4.02 g, 92% yield) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.48 (br. m, 3 H), 1.11 (s, 21 H), 0.23 (s, 18 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 135.1, 135.1, 124.1, 123.7, 105.3, 103.3, 95.7, 92.2, 18.8, 11.4, 0.0 ppm. FTIR (ATR): $\tilde{\nu}$ = 2958 (s), 2865 (s), 2163 (m), 1250 (s), 843 (s) cm^{-1}. HRMS data for **44** could not be obtained in either ESI or APPI mode.

Compound 45: A 100 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **44** (4.02 g, 8.92 mmol), THF (20 mL), MeOH (20 mL) and KOH 2.5 M (10 mL). The reaction mixture was stirred for 1 h, acidified to pH = 7 and diluted with CH_2Cl_2. The aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was then removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (hexanes) to afford desired compound **45** (2.66 g, 97% yield) as a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.55 (s, 2 H), 7.53 (s, 1 H), 3.09 (s, 2 H), 1.12 (s, 21 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 135.7, 135.2, 124.4, 122.9, 104.9, 92.8, 81.9, 78.6, 18.8, 11.4 ppm. HRMS (APPI-TOF): calcd. for $C_{21}H_{26}Si$ [M + H]$^+$ 307.1877; found 307.1879. FTIR (ATR): $\tilde{\nu}$ = 3301 (m), 2943 (s), 2865 (s), 2160 (w), 1579 (m), 967 (m), 881 (s) cm^{-1}.

Compound 46: A 10 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **45** (0.102 g, 0.333 mmol), degassed THF (4 mL), degassed DIPEA (0.46 mL, 2.66 mmol), $PdCl_2(PPh_3)_2$ (0.005 g, 0.0067 mmol), CuI (0.005 g, 0.0027 mmol) and 4,4′-diiodobiphenyl (0.406 g, 0.999 mmol) under argon. The reaction mixture was stirred at room temperature overnight, diluted with CH_2Cl_2, washed with NH_4Cl, and the aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (CH_2Cl_2/hexanes, 1:9) to afford desired compound **46** (0.089 g, 31% yield) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.77 (d, J = 8.0 Hz, 4 H), 7.65 (s, 1 H), 7.56 (br. m, 10 H), 7.33 (d, J = 8.0 Hz, 4 H), 1.15 (s, 21 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 140.2, 139.9, 138.1, 134.7, 134.2, 132.4, 129.0, 127.0, 124.4, 124.0, 122.3, 105.3, 93.7, 92.5, 90.4, 88.9, 18.8, 11.4 ppm. HRMS (APPI-TOF): calcd. for $C_{45}H_{40}I_2Si$ [M + H]$^+$ 863.1061; found 863.1042. FTIR (ATR): $\tilde{\nu}$ = 2937 (m), 2860 (m), 1577 (m), 1478 (m), 1000 (m), 879 (m), 809 (s) cm^{-1}.

Compound 48: A 10 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **46** (0.309 g, 0.358 mmol), degassed THF (4 mL), degassed DIPEA (0.50 mL, 2.86 mmol), $PdCl_2(PPh_3)_2$ (0.005 g, 0.0072 mmol), CuI (0.005 g, 0.0029 mmol) and compound **47** (0.458 g, 1.99 mmol) under argon. The reaction mixture was stirred at room temperature overnight, diluted with CH_2Cl_2, washed with NH_4Cl, and the aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (CH_2Cl_2/hexanes, 1:9) to afford desired compound **48** (0.314 g, 82% yield) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.67 (s, 2 H), 7.65 (s, 1 H), 7.59 (d, J = 7.8 Hz, 16 H), 7.47 (d, J = 8.7 Hz, 4 H), 6.87 (d, J = 8.7 Hz, 4 H), 3.97 (t, J = 6.5 Hz, 4 H), 1.79 (m, 4 H), 1.46 (m, 4 H), 1.38–1.24 (br. m, 16 H), 1.15 (s, 21 H), 0.89 (t, J = 6.4 Hz, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 159.4, 140.6, 139.6, 134.7, 134.3, 133.2, 132.3, 132.1, 127.0, 127.0, 124.4, 124.0, 123.2, 122.1, 115.1, 114.7, 105.4, 92.4, 90.8, 90.5, 88.9, 88.0, 68.2, 32.0, 29.5, 29.4, 29.3, 26.2, 22.8, 18.8, 14.3, 11.4 ppm. FTIR (ATR): $\tilde{\nu}$ = 2919 (m), 2852 (m), 2164 (w), 1598 (m), 1503 (s), 1247 (s), 1174 (s), 829 (s) cm^{-1}. HRMS data for **48** could not be obtained in either ESI or APPI mode.

Compound 49: A 10 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **48** (0.280 g, 0.262 mmol), THF (3 mL) and tetrabutylammonium fluoride in THF (1.0 M, 0.34 mL, 0.341 mmol). The reaction mixture was stirred at room temperature for 30 min, diluted with CH_2Cl_2, washed with water. The aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure. A 10 mL round-bottomed flask equipped with a magnetic stir bar was charged with the crude product (0.239 g, 0.262 mmol), degassed THF (3 mL), degassed DIPEA (0.36 mL, 2.08 mmol), $PdCl_2(PPh_3)_2$ (0.004 g, 0.0052 mmol), CuI (0.002 g, 0.010 mmol) and compound **39** (0.312 g, 1.04 mmol) under argon. The reaction mixture was stirred at room temperature overnight, diluted with CH_2Cl_2, washed with NH_4Cl, and the aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (CH_2Cl_2/hexane, 1:3) to afford desired compound **49** (0.204 g, 72% yield) as a pale yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.67 (s, 1 H), 7.65 (s, 2 H), 7.58 (d, J = 9.0 Hz, 16 H), 7.46 (br. m, 8 H), 6.86 (d, J = 8.6 Hz, 4 H), 3.95 (t, J = 6.5 Hz, 4 H), 1.78 (m, 4 H), 1.45 (m, 4 H), 1.38–1.24 (br. m, 16 H), 0.89

(t, J = 6.4 Hz, 6 H), 0.26 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 159.4, 140.6, 139.6, 134.7, 134.3, 133.2, 132.3, 132.1, 131.6, 127.0, 127.0, 124.2, 124.0, 123.5, 123.2, 123.0, 122.0, 115.1, 114.7, 104.7, 96.7, 90.8, 90.7, 90.3, 89.9, 88.8, 88.0, 68.2, 32.0, 29.5, 29.4, 29.4, 26.2, 22.8, 18.8, 14.3, 0.1 ppm. HRMS (APPI-TOF): calcd. for $C_{79}H_{74}O_2Si$ $[M + H]^+$ 1083.5531; found 1083.5534. FTIR (ATR): $\tilde{\nu}$ = 2921 (m), 2853 (m), 1508 (s), 1247 (s), 820 (s) cm^{-1}.

Compound 50: A 5 mL round-bottomed flask equipped with a magnetic stir bar was charged with compound **49** (0.100 g, 0.0923 mmol), THF (2 mL) and tetrabutylammonium fluoride in THF (1.0 M, 0.12 mL, 0.120 mmol). The reaction mixture was stirred at room temperature for 30 min, diluted with CH_2Cl_2 and washed with water. The aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure. A 10 mL round-bottomed flask equipped with a magnetic stir bar was charged with the crude product (0.094 g, 0.0923 mmol), degassed THF (2 mL), degassed DIPEA (0.26 mL, 1.48 mmol), $PdCl_2(PPh_3)_2$ (0.0003 g, 0.00037 mmol), CuI (0.0001 g, 0.00074 mmol) and compound **34** (0.042 g, 0.0185 mmol) under argon. The reaction mixture was stirred at room temperature for 48 h, diluted with CH_2Cl_2, washed with NH_4Cl, and the aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel ($CHCl_3$/hexanes, 3:2) to afford desired compound **50** (0.039 g, 52% yield) as a yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.34 (s, 2 H), 7.68–7-45 (br. m, 66 H), 7.40 (s, 4 H), 7.30 (s, 4 H), 7.21 (s, 4 H), 6.88 (d, J = 8.6 Hz, 8 H), 4.89 (t, J = 7.9 Hz, 4 H), 4.44 (br. s, 4 H), 3.97 (t, J = 6.4 Hz, 8 H), 2.67 (br. s, 4 H), 2.57–2.47 (br. m, 32 H), 1.79 (m, 8 H), 1.56 (m, 8 H), 1.46 (m, 8 H), 1.41–1.17 (br. m, 90 H), 0.88 (br. m, 24 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 159.3, 157.1, 143.6, 140.4, 139.5, 137.7, 137.3, 134.4, 133.2, 133.1, 132.8, 132.7, 132.2, 132.2, 131.9, 131.9, 131.8, 131.7, 131.7, 131.4, 131.4, 131.1, 126.9, 126.9, 126.8, 123.8, 123.8, 123.7, 123.1, 123.0, 123.0, 122.9, 122.9, 122.0, 121.9, 117.6, 115.0, 114.5, 94.9, 92.3, 91.0, 90.6, 90.4, 89.0, 89.0, 88.8, 87.8, 81.5, 74.3, 68.1, 35.5, 35.5, 34.4, 31.9, 31.8, 31.2, 31.1, 31.1, 29.7, 29.6, 29.7, 29.5, 29.4, 29.4, 29.3, 29.2, 26.0, 22.7, 22.7, 20.6, 20.1, 14.1 ppm. FTIR (ATR): $\tilde{\nu}$ = 2921 (s), 2852 (m), 1729 (w), 1581 (m), 1509 (s), 1247 (m), 821 (m) cm^{-1}. HRMS data for **50** could not be obtained in either ESI or APPI mode.

Compound 51: A 15 mL round heavy-wall pressure vessel equipped with a magnetic stir bar was charged with compound **50** (0.030 g, 0.00746 mmol), THF (5 mL), LiOH 10% (0.02 mL), and NaOH 10% in MeOH (0.07 mL). The reaction mixture was stirred at 80 °C for 48 h, cooled to room temperature and acidified to pH = 6. The organic layer was washed with water. The aqueous layer was extracted three times with $CHCl_3$. The organic layers were combined, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel ($CHCl_3$) to afford desired compound **51** (0.014 g, 90%) as a pale yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.57 (s, 4 H), 7.49 (s, 4 H), 7.46 (s, 4 H), 7.39 (s, 4 H), 7.34 (s, 4 H), 7.30 (s, 4 H), 4.45 (t, J = 5.7 Hz, 4 H), 3.98 (m, 4 H), 2.60 (t, J = 7.5 Hz, 8 H), 2.53 (s, 12 H), 2.49 (s, 12 H), 2.13 (m, 4 H), 1.79 (m, 2 H), 1.63 (m, 8 H), 1.38–1.22 (br. m, 58 H), 0.89 (t, J = 6.3 Hz, 12 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 143.8, 137.7, 137.4, 132.9, 132.9, 123.9, 123.1, 123.0, 122.0, 117.4, 93.9, 92.4, 90.9, 89.0, 81.3, 74.2, 61.3, 35.7, 34.5, 33.0, 32.0, 32.0, 31.4, 31.3, 29.6, 29.4, 29.3, 26.2, 22.8, 20.3, 20.3, 14.3 ppm. FTIR (ATR): $\tilde{\nu}$ = 2923 (s), 2854 (m), 1581 (m), 1494 (m), 1455 (m), 1380 (m), 1000 (s), 878 (s), 808 (s) cm^{-1}. HRMS data for **51** could not be obtained in either ESI or APPI mode.

Supporting Information (see footnote on the first page of this article): ^{1}H and ^{13}C NMR spectra for new compounds.

Acknowledgments

This work was supported by the National Science and Engineering Council (NSERC) through a Discovery Grant. K. C. thanks the Fonds de Recherche du Québec – Nature et Technologies for a PhD scholarship. We are also grateful for professional support from the Centre québécois sur les matériaux fonctionnels (CQMF) and the Centre de recherche sur les matériaux avancés (CERMA).

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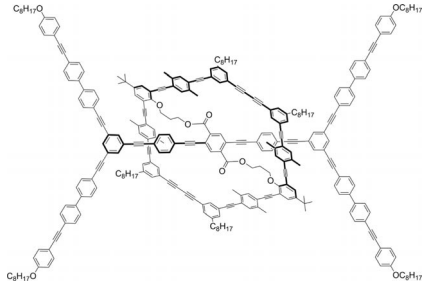
Received: May 15, 2012
Published Online: ■

Phenylacetylene Macrocycles

Synthetic efforts towards phenylacetylene macrocycle based rotaxane precursors are presented. Macrocycles with different sizes and functional groups have been prepared and attached to bulky blockers through a Sonogashira coupling reaction. Hydrolysis of the ester groups that bind the macrocycle to the rigid rod was undertaken to assess whether or not the rotaxane precursor conformation has been obtained.



Keywords: Macrocycles / Rotaxanes / Cross-coupling / Synthetic methods / Nanotubes

