Synthesis and Properties of Shape-Persistent Macrocyclic Amphiphiles with Switchable Amphiphilic Portions

Sigurd Höger,* Anne-Désirée Meckenstock, and Sarah Müller

Abstract: The bidirectional- and convergent-type syntheses of functionalized kinked phenyl – ethynyl oligomers containing ethynyl end groups are described. Key steps in both approaches are the bromo – iodo selectivity of the Hagihara coupling and the possibility to deprotect acetylenes containing different silyl protective groups stepwise. Glaser coupling of the oligomeric bisacetylenes results in the corresponding macrocycles that contain polar and nonpolar side groups in a switchable arrangement.

Keywords: cyclizations · macrocycles · supramolecular chemistry

Introduction

Interest in cyclic structures composed of a shape-persistent molecular backbone together with a well-defined arrangement of functional groups has increased considerably during the last years.[1] This success can be attributed to at least two factors. First, modern synthetic methods for the formation of C–C bonds, as well as progress in protective-group methodology, make the formation of cyclic structures under mild conditions possible, which for years were only available under drastic conditions and in much lower yield.[2] Secondly, increased understanding of the interactions between molecules themselves (*aggregation*) and between different molecules (*complexation*) led to design principles that have enabled the systematic preparation and investigation of these structures.[3]

Usually, cyclic structures with cavities in the nanometer regime are classified by the molecular backbone they are based on, and the most common compounds in this sense are represented by the cyclodextrins.[4] In our ongoing investigations we deal exclusively with functionalized structures, and the nature of the backbone plays only a minor role. It simply acts as the frame for the attachment of the functional groups.[5] Therefore, a classification of the macrocycles based on the orientation of the functional group relative to the molecular backbone seems attractive, since their orientations have a remarkable influence on the properties and on the applications of these compounds (Figure 1).

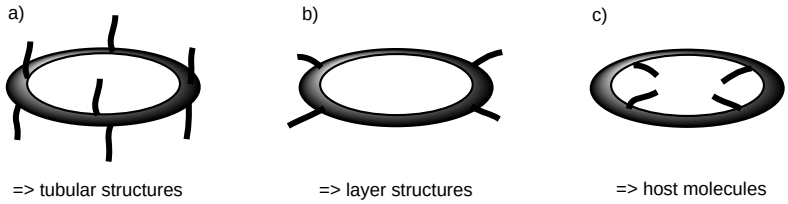

Figure 1. Possible orientations of the polar side groups in common shape-persistent macrocycles and their respective functions or use.

Macrocycles based on three possible functional group orientations have been described in the literature so far. The polar side groups can be arranged perpendicular to the backbone of the macrocycle. As a result, this may lead to interesting aggregation phenomena in the solid state (Figure 1a); the macrocycles may form tubular structures.[1a,b] On the other hand, if the polar groups point to the outside of the ring, these compounds can form two-dimensional, layered structures connected through hydrogen bonds (Figure 1b).[1c] The third group of macrocycles is designed for a completely different purpose. Guest molecules can be complexed by specific interactions with internal substituents that have a functionality and orientation complementary to a specific guest molecule (Figure 1c).[1d,e] If the size of the host compound is in the nanometer regime, biological substrates with molecular weights in the kilodalton regime may be bound. Such large guest molecules can also accomodate several guests and induce a chemical reaction between them.[6]

The large field of organic receptor molecules, natural as well as artificial, can be divided into molecules with highly preorganized binding sites (*lock and key principle*), and molecules with flexible binding sites, which are organized around a specific guest molecule during the act of complexation (*induced-fit mechanism*).[7] The former class of mole-

[*] Dr. S. Höger, A.-D. Meckenstock, Chem.-Ing. S. Müller
Max-Planck-Institut für Polymerforschung
Ackermannweg 10, 55128 Mainz (Germany)
Fax: (+49) 6131-379-100
E-mail: hoeger@mpip-mainz.mpg.de

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cules in general show a higher binding constant to a specific guest molecule,[8] whereas the latter may lead to new insights into enzyme activity.

Here we describe in detail the synthesis of a new class of shape-persistent macrocyclic amphiphiles with nanometer size interiors that are formed by a rigid, noncollapsible molecular backbone. Attached to this backbone are polar and nonpolar side chains. This is done in such a way that *switchable* units can freely rotate, allowing the nonpolar or polar side chains to point into or outside the ring. In order to combine free rotation and stiffness of the backbone, the structures are based on the phenyl–acetylene backbone, as schematically shown in the target structure **M**.[9, 10]

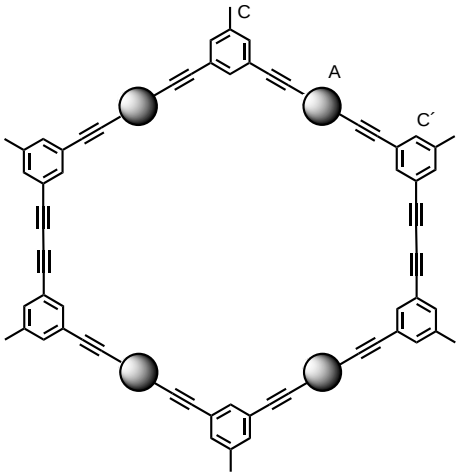
The sides of these shape-persistent macrocyclic amphiphiles are formed by the corner pieces (**C** and **C′**) and by the amphiphilic portions (**A**) of the ring. The former contain additional substituents that influence the solubility and the crystallinity of the macrocycles. Moreover, they also simplify their proton NMR spectra in the aromatic region. The amphiphilic portions are able to rotate and form either more polar or more nonpolar interiors depending on the solvent and the presence of appropriate guest molecules (induced-fit mechanism).[11] In the synthesis described here, all macrocycles contain methyl substituents at the corner pieces, propyloxy groups as the nonpolar and phenolic OH groups as the polar substituents. The use of phenolic OH groups allows further functionalization of these macrocycles, so that a variety of derivatives are available without performing an entire new ring synthesis.[12] However, during the entire synthesis and isolation of the macrocycles these polar groups were protected in the form of their tetrahydropyranyl(THP) ethers.

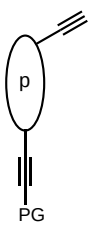
Results and Discussion

Retrosynthesis and synthetic strategy: The synthetic accessibility of shape-persistent macrocycles based on the phenyl–ethynyl backbone has been known for several years. For example, Staab et al. prepared the cyclic hexamer of *m*-phenylacetylene by a sixfold Stephens–Castro coupling of the readily available *m*-iodophenylacetylene in a 4.6% yield.[2a] A completely different approach was investigated by Moore and co-workers during the past several years, cyclizing the appropriate α-alkinyl-ω-iodo precursors to the desired macrocycles in good to excellent yields up to 75%.[2b] Unfortunately, the formation of the starting materials requires a rather time-consuming multistep synthesis.

In the following protocol, the intermolecular Glaser coupling of the bisacetylenes **B** (*half rings*) is used as the cyclization reaction. This coupling method usually results in relatively high yields of cyclic products, but with different ring sizes. Not surprisingly, the number of different rings can be reduced by the use of rigid and large bisacetylene units.[10b,c, 13] Therefore, the use of half rings can be viewed as an intermediate strategy between Staab's and Moore's approach, although in every case a different cyclization reaction is used.

The key to successful synthesis of the cyclic structures **M** relies on an efficient synthetic route to the corresponding ethynyl-terminated phenyl–ethynyl oligomers **B**. Their formation can be performed by two different strategies (Figure 2). Path a) represents a bidirectional-type synthesis, starting from the corner piece **C**; path b) represents a convergent-type strategy, starting from the corner piece **C′**. There has been considerable interest in the preparation of well-defined oligomeric sequences, because they represent ideal models for polymers. The undesired polycondensation to polymeric or oligomeric products can be reduced by the use of either a large excess of one coupling component (*excess approach*), or by the use of monomers that carry properly protected functional groups (*protective-group approach*).[14] To avoid the problems associated with the excess approach, the protective group approach is chosen in the following protocol. An essential requirement for this approach is the use of monoprotected diynes of the general structure **S**.





S

Furthermore, if the aromatic core of these compounds is not symmetrical (as indicated by the elongated shape of the aromatic core in the schematic representation of **S**), the diyne has to be regioselectively protected or the final-

Abstract in German: *Beschrieben wird die zweifach-gerichtete und konvergente Synthese gewinkelter Phenyl–ethinyl Oligomere. Schlüsselschritte sind dabei in beiden Fällen die Brom–Iod Selektivität der Hagihara Kupplung und die Möglichkeit, Bisacetylene mit unterschiedlichen Silylschutzgruppen schrittweise zu entschützen. Die Glaser Kupplung der oligomeren Bisacetylene führt zur Bildung der entsprechenden Makrocyclen mit einer frei drehbaren Anordnung polarer und unpolarer Seitengruppen.*

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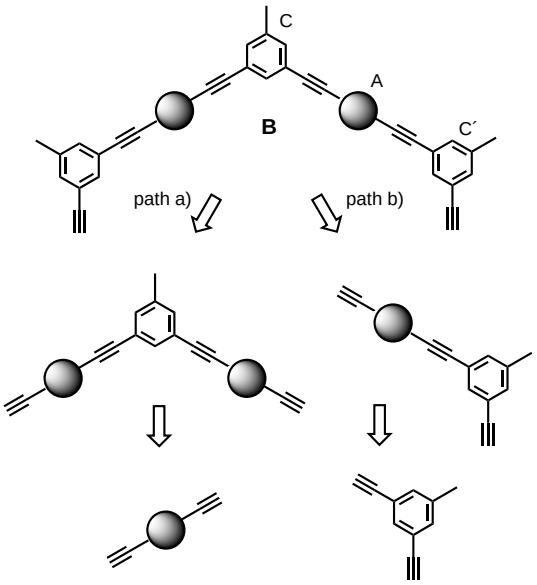
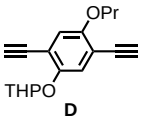


Figure 2. Retrosynthetic pathways to ethynyl end-capped phenyl–ethynyl oligomers: a) bidirectional and b) convergent strategy. In both cases the starting materials need to be bisacetylenes containing *one* protective group.

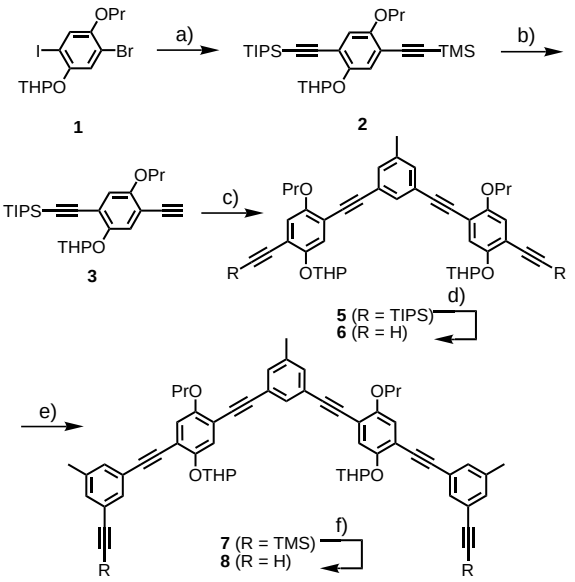
product will be a complex mixture of different isomeric macrocycles. Initial attempts in this direction, the deprotonation of the diyne **D** with EtMgBr and trapping of the acetylide with TMSCl, failed to give satisfactory results.[15]

Therefore, an alternative route to **S** was investigated. The key steps in this synthesis are the selective palladium-catalyzed coupling of a terminal alkyne[16] with an aryl iodide in the presence of an aryl bromide,[17] and the site selective removal of the trimethylsilyl (TMS) group in the presence of a triisopropylsilyl (TIPS) group.[18] During the coupling reaction, the aromatic bromide does not act as a protective group in the common sense, it has not to be transformed into a reactive group prior to the subsequent step.[19] The aryl bromide is reactive under the coupling conditions that are used, but remains unaffected as long as aryl iodide remains in the reaction mixture. Therefore, two regioselective coupling reactions can be performed in a one-pot reaction. For this reason, this type of procedure can be called the *dormant-group strategy*.[20, 21] The starting materials necessary for this approach, 3,5-diiodo toluene,[22] 3-bromo-5-iodo toluene,[23] and the bromo-iodohydroquinone monoalkyl ethers[20] are described in the literature.



D

Two-directional diyne synthesis: The key compound in the synthesis of the half rings by this approach is the mono-protected bisacetylene **3**, containing the propyloxy group as the nonpolar side chain and the THP protected phenol OH group as polar unit (Scheme 1). The THP-protected bromo-iodohydroquinone monopropyloxy ether **1** is treated with 1.1 equivalents of TIPS-acetylene for two days at room temperature and an additional two days at 55 °C. Subsequently, two equivalents of TMS-acetylene are added and the mixture is stirred for an additional four days at the same temperature. The use of $[PdCl_2(PPh_3)_2]$ and CuI, together

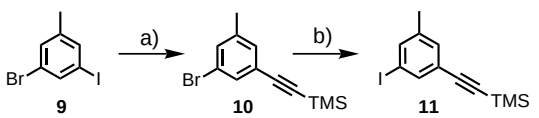


Scheme 1. a) 1. TIPS-acetylene, $[PdCl_2(PPh_3)_2]$, PPh_3, CuI, piperidine; 2. TMS-acetylene (82%); b) NaOH, MeOH, THF (95%); c) **4**, $[PdCl_2(PPh_3)_2]$, PPh_3, CuI, piperidine (94%); d) Bu_4NF, THF (82%); e) **11**, $[PdCl_2(PPh_3)_2]$, PPh_3, CuI, piperidine (86%); f) NaOH, MeOH, THF (92%).

with an additional two equivalents PPh_3 per palladium atom in piperidine, turned out to give a high bromo–iodo selectivity. The formation of the isomeric compound with switched position of the TIPS and TMS groups is not detectable in the ^1H NMR spectrum.[24] Therefore, this protocol continues to be used for all palladium catalyzed C–C coupling reactions in this work. After chromatography, **2** is obtained in good yields, even when the reaction is performed on a 20–30 g scale. Deprotection of the TMS group is accomplished by stirring a solution of **2** in MeOH/THF with a few drops of 1N NaOH at room temperature for 30 minutes to form **3** in nearly quantitative yield (alternatively, this deprotection can be performed by stirring **2** with an excess of a weak base, like K_2CO_3, in the same solvent, as described later in the convergent diyne synthesis).

Palladium-catalyzed coupling of **3** with 3,5-diiodotoluene (**4**), and desilylation of **5** by reaction with Bu_4NF in THF at room temperature gave **6**. The separation of **6** from the triisopropylsilanol is troublesome and can only be performed by repeated chromatography. Treatment of **6** with a small excess of 3-iodo-5-(2-trimethylsilyethynyl)toluene (**11**) yields **7** which is desilylated by stirring in MeOH/THF (1:1) with a few drops of 1N NaOH at room temperature for two hours to give **8**.

The preparation of **11** again relies on the selective coupling of 3-bromo-5-iodotoluene (**9**) with 1.1 equivalents TMS-acetylene to give bromo-5-(2-trimethylsilyethynyl)toluene (**10**; Scheme 2). In order to facilitate the Pd-catalyzed

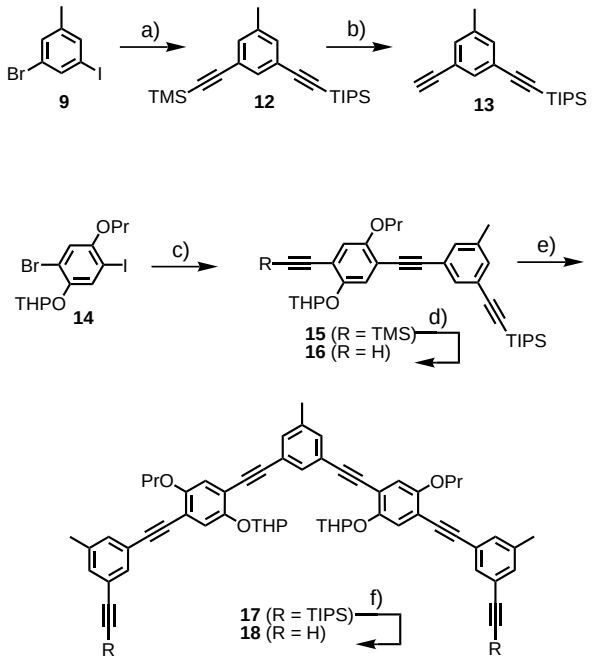


Scheme 2. a) TMS-acetylene, $[PdCl_2(PPh_3)_2]$, PPh_3, CuI, piperidine (85%); b) 1. *n*BuLi; 2. 1,2-diiodoethane, THF (99%).

coupling reaction with **6**, **10** is converted to the iodo derivative **11** by halogen–metal exchange and subsequent reaction with diiodoethane.

Convergent diyne synthesis: The convergent-type synthesis of the half rings has some advantages over the bidirectional-type synthesis described above. First, the number of steps is reduced. Second, column chromatographic purification of the intermediates is easier to perform due to fewer tailing problems.[25] And finally, the separation of the products from the triisopropylsilanol produced during the fluoride-induced deprotection is much easier.

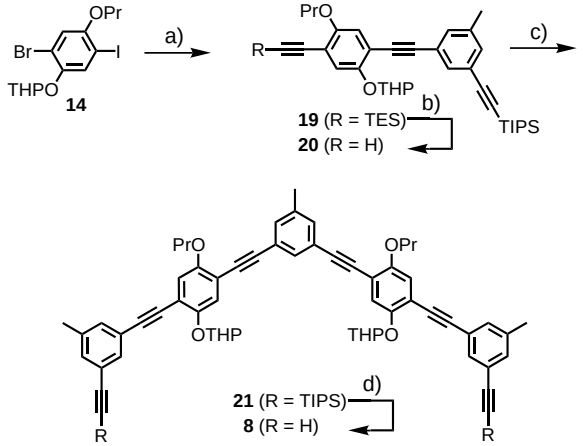
Reaction of **9** with 1.1 equivalents TIPS-acetylene and subsequent addition of an excess of TMS-acetylene under the conditions used above, gives the mixed protected bisacetylene **12** in high yields (Scheme 3). Compound **12** can be purified by vacuum destillation and is therefore easily available in large



Scheme 3. a) 1. TIPS-acetylene, $[PdCl_2(PPh_3)_2]$, PPh_3, CuI, piperidine; 2. TMS-acetylene (89%); b) K_2CO_3, MeOH, THF (95%); c) 1. **13**, $[PdCl_2(PPh_3)_2]$, PPh_3, CuI, piperidine; 2. TMS-acetylene (88%); d) K_2CO_3, MeOH, THF (93%); e) **4**, $[PdCl_2(PPh_3)_2]$, PPh_3, CuI, piperidine (92%); f) Bu_4NF, THF (96%).

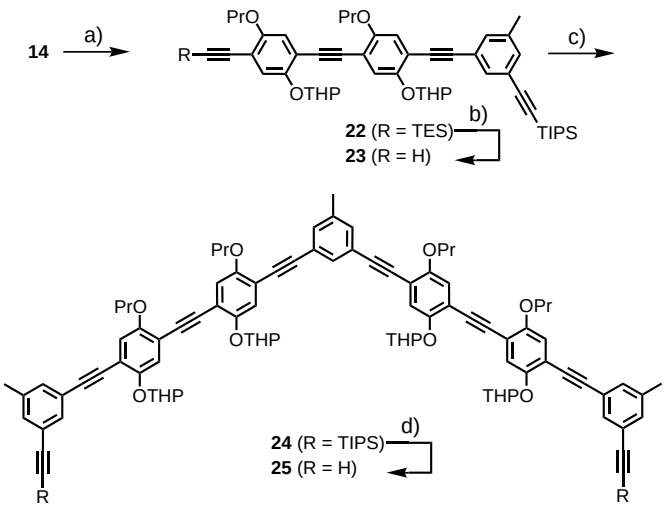
quantities. Deprotection of the TMS group is performed by stirring **12** with potassium carbonate in methanol/THF (1:1) overnight. Palladium-catalyzed coupling of **13** with **14** (the isomer of **1**) and subsequent coupling with TMS-acetylene, again in a one-pot procedure, gives the mixed protected compound **15**. Base-induced deprotection of the TMS group and coupling with **4** gives, after fluoride-induced deprotection, the half ring **18** in good yield. In this case, the separation of the product and the triisopropylsilanol byproduct can be easily performed by treating the reaction mixture with petroleum ether. The byproduct dissolves, and the diyne is separated by filtration. This large diyne **18** is an isomer of **8**, such that the positions of the propyloxy and the tetrahydropyranyloxy groups at the amphiphilic portions of the ring are switched.

In order to prepare the diyne **8** by a convergent-type synthesis, one might use the isomeric starting material **1**. As shown in Scheme 4, it is also possible to perform the reaction with compound **14** (which is easier to prepare) in a reaction sequence analogous to the preparation of **18**, by simply switching the order of the addition of the acetylenes to this compound. In this reaction sequence, triethylsilyl(TES)-acetylene instead of TMS-acetylene is used because it is less volatile and therefore easier to handle in a stoichiometric reaction.



Scheme 4. a) 1. TES-acetylene, $[PdCl_2(PPh_3)_2]$, PPh_3, CuI, piperidine; 2. **13** (86%); b) K_2CO_3, MeOH, THF (93%); c) **4**, $[PdCl_2(PPh_3)_2]$, PPh_3, CuI, piperidine (91%); d) Bu_4NF, THF (90%).

In order to prepare bisacetylenes with enlarged amphiphilic portions, one can make use of the geometric structure of the monoprotected bisacetylene **13**: two alkynes are in *meta* positions, and one of them is protected by a TIPS group. The same structural element is found in compound **20**. Following the procedure outlined in Scheme 4, and replacing **13** by **20** gives, by an otherwise identical order of steps, the enlarged diyne **25** (Scheme 5), a phenyl–ethynyl oligomer containing



Scheme 5. a) 1. TES-acetylene, $[PdCl_2(PPh_3)_2]$, PPh_3, CuI, piperidine; 2. **20** (75%); b) K_2CO_3, MeOH, THF (88%); c) **4**, $[PdCl_2(PPh_3)_2]$, PPh_3, CuI, piperidine (93%); d) Bu_4NF, THF (95%).

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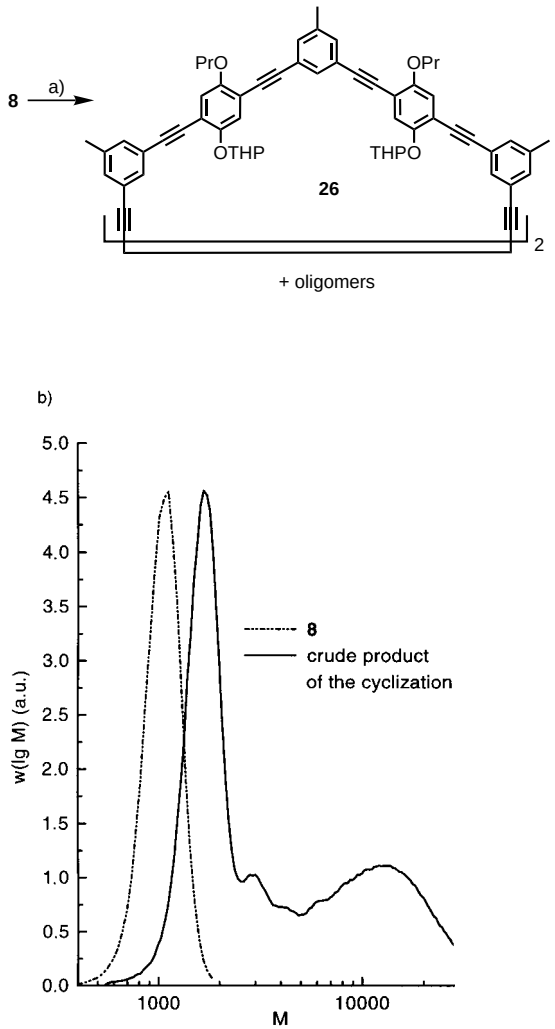
seven aromatic units and ethynyl end groups. It is interesting to note that the deprotection of **22** takes more than two weeks, even though it readily dissolves in the solvent mixture that is used to perform this reaction.

Compounds **8** and **18** are slighly yellow, while **25** is bright yellow. They are stable at room temperature for several months without detectable decomposition. Nevertheless, they are usually stored under an argon atmosphere in the dark to protect them from acidic conditions and sunlight.

Cyclization: The cyclization of the bisacetylenes is performed by a modified Eglinton–Glaser coupling under the conditions introduced by Breslow.[26] The high dilution conditions, necessary to obtain a high yield of the cyclized dimer, are obtained by adding a pyridine solution of the diyne with a syringe pump over 96 hours to a slurry of CuCl and $CuCl_2$ in pyridine at room temperature (pseudo-high-dilution conditions). This procedure avoids the use of extremely large solvent volumes, and amounts of about 1.5 g of the diyne are cyclized in 300 mL of pyridine.

The workup is performed after stirring for an additional 2 to 4 days at room temperature. Scheme 6 shows the gel-permeation chromatography (GPC) results of the bisacetylene **8** (dotted line) and the crude reaction product of its cyclization (solid line). No signals attributable to alkyne protons are observed in the ^{1}H NMR spectrum. According to the GPC data, the crude product of this reaction contains mostly cyclized dimer (depending on the batch, 60–65% yield), along with small amounts of cyclic trimer and tetramer, and cyclic or noncyclic oligomers and polymers.[27] Purification of **26** is rather simple and is achieved by recrystallization of the crude reaction mixture from dichloromethane. By this procedure macrocycle **26** is obtained in 45% isolated yield in the form of slightly yellow crystals, which were unstable when removed from the mother liquor.[28] The reason for this purification method is the restricted flexibility of the macrocyclic dimer, which reduces its solubility compared with the higher macrocycles and polymers (for entropic reasons). The cyclization of the bisacetylenes **18** and **25** under identical conditions gives the corresponding macrocycles **27** and **28**. In these cases the crude product of the reaction mixtures contains about 50–55% and 45–50% cyclic dimer, respectively. These results show that not only the size of the bisacetylenes, but also the arrangement of the functional groups has an influence on the outcome of the cyclization. Again, in these cases the isolation of the macrocycles is based on their restricted solubility compared with the higher oligomers and polymers, and **27** and **28** were isolated in 38% and 34% yield, respectively.

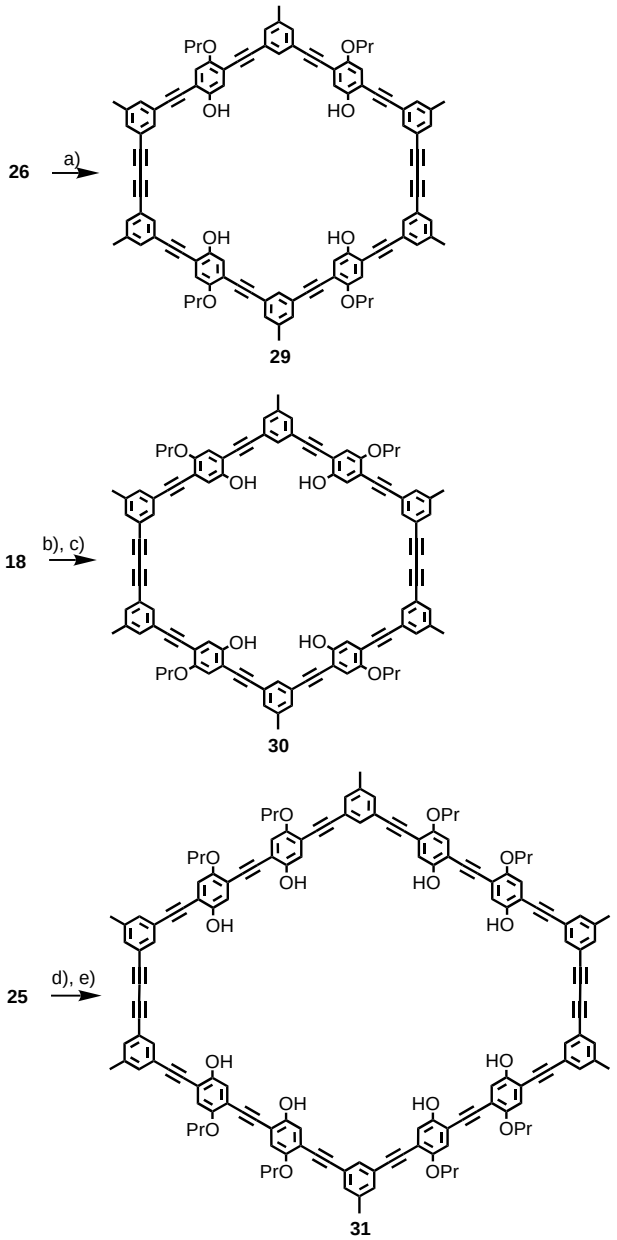


Scheme 6. a) $CuCl/CuCl_2$, pyridine; b) GPC of **8** and of the crude product of the cyclization.

Compound **26** is soluble in chlorinated organic solvents up to about 2–5 mg mL^{-1} at room temperature. It is interesting to note that **27** is much less soluble in CH_2Cl_2 than **26**, indicating that the orientation of the functional groups has a strong influence on the solubility of these compounds. Compound **28** shows a much higher solubility than **26** and **27** in chlorinated solvents. One might speculate that on the one hand the amount of switchable units relative to the molecular weight is much higher, and that on the other hand **28** is an even more complex mixture of stereoisomers than **26** and **27**. While **26** and **27** are stable for at least several months and can be isolated in analytically pure form, **28** always contains a small amount of the (partly) free phenolic macrocycle, as observed by ^{1}H NMR spectroscopy.

After isolation of the THP-protected macrocycles, deprotection is performed by stirring a suspension of the rings in acidic MeOH/$CHCl_3$ at room temperature to give the amphiphilic products **29**–**31** in nearly quantitative yield (Scheme 7). The macrocycles **29** and **30** are slightly yellow solids; **31** is a bright yellow solid. All macrocyclic amphiphiles are only sparingly soluble in chlorinated solvents. Compounds **29** and **30** are soluble in THF and pyridine to an amount of about 4–8 mg mL^{-1}; **31** is only marginally soluble in THF ($\ll$1 mg mL^{-1}), but readily dissolves in pyridine ($>$20 mg mL^{-1}). Although all amphiphiles can be handled under atmospheric conditions for a short period of time, they turn brown after longer exposure to light and air. However, if they are kept under an argon atmosphere in the dark, they are stable for at least several months.

NMR spectra: Figure 3 shows as an example the ^{1}H NMR spectrum of **29**. As mentioned before, the use of toluene



Scheme 7. a) *p*-TsOH, MeOH, $CHCl_3$ (98%); b) $CuCl/CuCl_2$, pyridine (38%); c) *p*-TsOH, MeOH, $CHCl_3$ (98%); d) $CuCl/CuCl_2$, pyridine (34%); e) *p*-TsOH, MeOH, $CHCl_3$ (93%).

corner pieces instead of benzene corner pieces has the advantage that the diminished coupling of the aromatic protons gives a much clearer spectrum. Compounds **29** and **30** do not exhibit any concentration dependence in the ^{1}H NMR spectra recorded in pyridine or THF, neither does **31** in pyridine. Therefore, there is no evidence for self-association of these compounds resulting from $\pi-\pi$ stacking or through hydrogen bonding.[29, 30] However, the chemical shifts of the ^{1}H NMR spectra of these compounds strongly depend on the solvent used to record the spectra. The most sensitive absorptions in this sense show the aromatic protons of the amphiphilic portions *ortho* to the phenol OH groups. For example, the chemical shift of this proton in **29** changes from $\delta = 6.93$ in THF to $\delta = 7.05$ in $C_2D_2Cl_4$.[31]

UV spectra: Figure 4 shows the UV spectra of the macrocycles **29**–**31**. Despite the fact that they are built up by an extended molecular backbone containing aromatic and acetylenic moieties, these compounds are only slightly yellow to bright yellow. The reason for this is the interruption of the conjugation by the *meta*-substituted corner pieces of the ring.

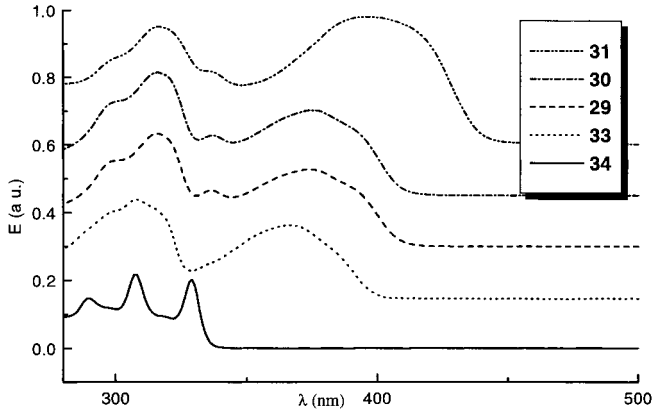


Figure 4. UV spectra of **34** (THF, $\lambda_{max} = 329$ nm, $\varepsilon = 31000$), **33** (THF, $\lambda_{max} = 367$ nm, $\varepsilon = 37000$), **29** (THF, $\lambda_{max} = 374$ nm, $\varepsilon = 143000$), **30** (THF, $\lambda_{max} = 374$ nm, $\varepsilon = 148000$), **31** (DMF, $\lambda_{max} = 397$ nm, $\varepsilon = 244000$).

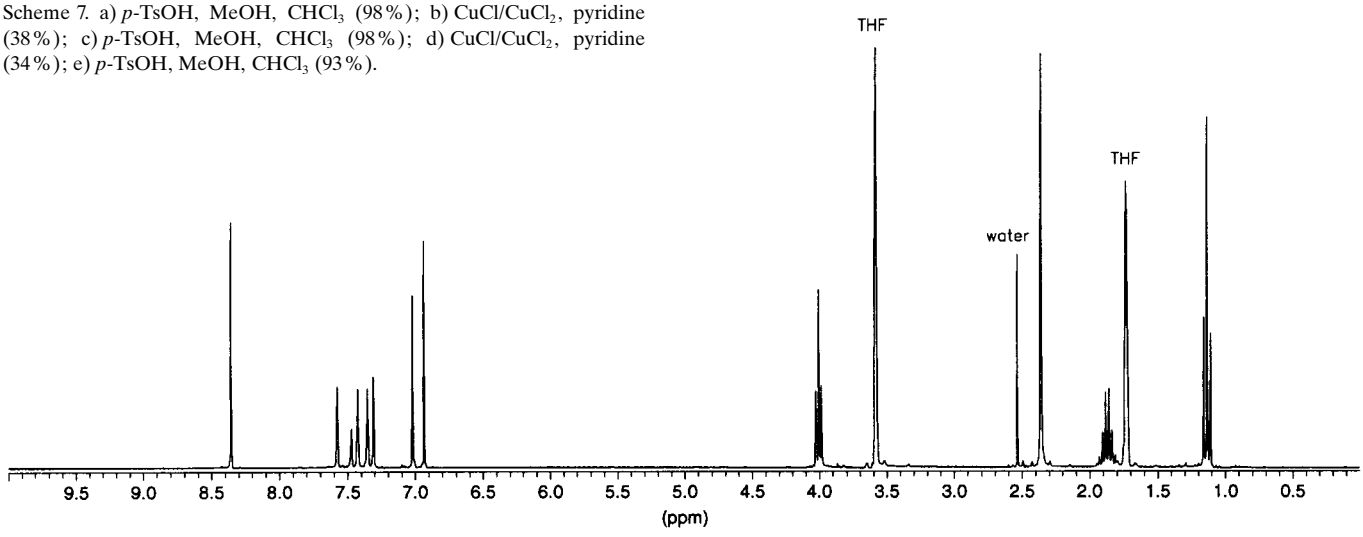


Figure 3. ^{1}H NMR spectrum of **29** (300 MHz; in $[D_8]$THF).

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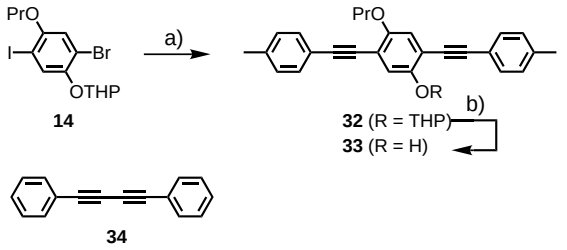
In order to understand the UV spectra in more detail, they are compared with the UV spectra of **33** and **34** (Scheme 8). Compound **33** displays the longest linear conjugated π-electron fragment of **29** and **30**. As a result, there is only a small shift in the longest wavelength absorption maxima in going from **33** to **29** and **30**, the latter show practically identical spectra. The molar absorption coefficients of these



Scheme 8. a) 4-tolylacetylene, $[PdCl_2(PPh_3)_2]$, PPh_3, CuI, piperidine (76%); b) *p*-TsOH, MeOH, CH_2Cl_2 (71%).

bands in **29** and **30** compared with **33** correspond well with the number of fragments per ring. Not surprisingly, if the π system is more extended, as in **31**, a bathochromic shift of the longest wavelength absorption maxima occurs. In addition, all macrocycles show an absorption band at 336 nm, whose origin is the presence of the diacetylene unit, as a comparison with the spectrum of **34** shows. For that band a slight red shift of 7 nm is also observed.

Conclusion

The combination of the bromo–iodo selectivity in the Pd-catalyzed Hagihara coupling and of the possibility to deprotect a TMS-protected acetylene in the presence of a TIPS-protected acetylene is a powerful tool for the preparation of monoprotected bisacetylenes. Further coupling reactions in a convergent or bidirectional manner lead to large phenyl–ethynyl oligomers containing ethynyl end groups (half rings), which are then used in the copper-catalyzed Eglington–Glaser coupling to yield shape-persistent macrocycles in good yields. The isolation and purification of these compounds, due to their restricted solubility, is quite simple and can be performed by recrystallization or extraction. The ^{1}H NMR spectra of these compounds are well-structured due to the fact that the coupling of the protons at the corner pieces are diminished by additional methyl substituents. Although all phenyl–ethynyl oligomers as well as all macrocycles are highly unsaturated compounds, they are only slightly yellow to bright yellow, depending on their size. The interruption of the effective conjugation length by the *meta*-substituted corner pieces is proved by comparison of the UV spectra of the rings with the absorption behavior of model compounds.

Experimental Section

General methods: Commercially available chemicals were used as received. THF was distilled from potassium prior to use. Piperidine and pyridine were distilled from CaH_2 and stored under argon. ^{1}H NMR and ^{13}C NMR spectroscopy: spectra were recorded on Bruker AC300 (300 MHz for proton, 75.48 MHz for carbon). UV spectra were recorded on a Perkin–Elmer Lambda 3 instrument. Thin-layer chromatography was performed on aluminum plates precoated with Merck 5735 silica gel 60 F_{254}. Column chromatography was performed with Merck silica gel 60 (230–400 mesh). Radial chromatography was performed with Merck silica gel 60 PF_{254} containing $CaSO_4$. The gel permeation chromatograms were measured in THF (flow rate 1 mL min^{-1}) at room temperature, with a combination of three styragel columns (porosity 10^3, 10^5, and 10^6) and a UV detector operating at $\lambda = 254$ nm. The molecular weight was obtained from polystyrene calibrated SEC columns. The matrix-assisted laser desorption ionization time-of-flight measurements were carried out on a Bruker reflex spectrometer (Bruker, Bremen), incorporating a 337 nm nitrogen laser with a 3 ns pulse duration (10^6–10^7 W cm^{-1}, 100 μm spot diameter). The instrument was operated in a linear mode with an accelerating potential of 33.65 kV. The mass scale was calibrated with polystyrene ($M_p = 4700$), with a number of resolved oligomers. Samples were prepared by dissolving the macrocycle in THF at a concentration of 10^{-4} mol l^{-1}. 10 μl of this solution and 10 μl of a 10^{-3} mol l^{-1} silver trifluoroacetate solution were added to 10 μl of a 0.1 mol l^{-1} matrix solution, dissolved in THF. In all cases 1,8,9-trihydroxyanthracene (Aldrich, Steinheim) was used as matrix. 1 μl of this mixture was applied to the multistage target and airdried. Microanalyses were performed by the University of Mainz.

5-Bromo-2-iodo-4-propyloxy-1-(tetrahydro-2*H*-pyran-2-yloxy)benzene (**1**): 3,4-Dihydro-2*H*-pyran (42.1 g, 500 mmol) was added to a solution of 3-bromo-5-iodo-4-propyloxyphenol (35.7 g, 100 mmol) and of *p*-toluenesulfonic acid (100 mg) in CH_2Cl_2 (100 mL) at 0 °C. The solution was stirred for 1 h at this temperature, and subseqently for 1 h at room temperature before being poured into ether (500 mL) and 10% aqueous sodium hydroxide (200 mL). The organic phase was separated and washed with 10% aqueous sodium hydroxide, water, and brine, and dried over $MgSO_4$. Evaporation of the solvent yielded a slightly yellow oil, which was filtered through a short column of silica gel (height 6 cm, diameter 12 cm) with hexanes/ether (10:1) as the eluent. The solvent was removed and the residue recrystallized twice from ethanol to give 39.7 g (90.0%) of **1** as colorless crystals. ^{1}H NMR (CD_2Cl_2): $\delta = 7.30$ (s, 1H), 7.28 (s, 1H), 5.35 (t, $J = 2.9$ Hz, 1H), 3.92 (t, $J = 6.5$ Hz, 2H), 3.91–3.82 (m, 1H), 3.65–3.55 (m, 1H), 2.20–1.55 (m, 8H), 1.05 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (CD_2Cl_2): $\delta =$ 151.63, 150.93, 124.18, 120.72, 112.83, 98.32, 86.13, 72.20, 62.36, 30.64, 25.63, 23.00, 18.87, 10.67; $C_{14}H_{18}BrIO_3$ (441.10): calcd C 38.12, H 4.11; found C 38.33, H 4.07.

4-Propyloxy-1-(tetrahydro-2*H*-pyran-2-yloxy)-2-(2-triisopropylsilylethynyl)-5-(2-trimethylsilylethynyl)benzene (**2**): $[Pd(PPh_3)_2Cl_2]$ (1.4 g) and CuI (500 mg) were added to a solution of **1** (22.1 g, 50.0 mmol), triisopropylsilylacetylene (9.75 g, 53.5 mmol), and PPh_3 (1.4 g) in piperidine (150 mL) at 0 °C. The mixture was allowed to reach room temperature and was stirred for 2 days, and for an additional two days at 55 °C. Then trimethylsilylacetylene (9.75 g, 99.3 mmol) was added and the mixture stirred for an additional 4 days at the same temperature. After the reaction mixture cooled down to room temperature, ether (600 mL) and water (300 mL) were added. The organic phase was seperated and extracted with water, 10% acetic acid, water, 10% aqueous sodium hydroxide, water, and brine, and dried over $MgSO_4$. Evaporation of the solvent yielded a brown oily residue which was chromatographed over silica gel with hexanes/ether (10:1) as the eluent ($R_f = 0.50$) to give **2** (21.03 g, 82%) as a slightly yellow waxy solid. ^{1}H NMR (CD_2Cl_2): $\delta = 7.14$ (s, 1H), 6.89 (s, 1H), 5.40 (t, $J =$ 3.1 Hz, 1H), 4.00–3.86 (m, 1H), 3.93 (t, $J = 6.3$ Hz, 2H), 3.63–3.54 (m, 1H), 2.15–1.50 (m, 8H), 1.14 (s, 21H), 1.07 (t, $J = 7.4$ Hz, 3H), 0.25 (s, 9H); ^{13}C NMR (CD_2Cl_2): $\delta = 155.13$, 152.17, 121.13, 117.86, 115.76, 114.48, 103.32, 101.38, 100.38, 97.85, 96.83, 71.53, 62.25, 30.70, 25.69, 23.13, 18.87, 11.80, 10.69, −0.02; $C_{30}H_{48}O_3Si_2$ (512.88): calcd C 70.26, H 9.43; found C 70.23, H 9.45.

5-Ethynyl-4-propyloxy-1-(tetrahydro-2*H*-pyran-2-yloxy)-2-(2-triisopropylsilylethynyl)benzene (**3**): Compound **2** (20.5 g, 40.0 mmol) was dissolved in THF/MeOH (1:1; 160 mL). NaOH (1N, 6 mL) was added, and the solution stirred at room temperature for 45 min. The mixture was poured into ether (600 mL) and water (400 mL), the organic layer was extracted with water and brine, and dried over $MgSO_4$. Evaporation of the solvent and chromatography over silica gel with hexanes/ether (10:1) as the eluent ($R_f = 0.32$) gave **3** (16.8 g, 95%) as a slightly yellow oil. ^{1}H NMR (CD_2Cl_2):

$\delta = 7.21$ (s, 1H), 6.92 (s, 1H), 5.41 (t, $J = 3.1$ Hz, 1H), 4.02–3.87 (m, 1H), 3.95 (t, $J = 6.5$ Hz, 2H), 3.63–3.54 (m, 1H), 3.36 (s, 1H), 2.13–1.50 (m, 8H), 1.15 (s, 21H), 1.05 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (CD_2Cl_2): $\delta = 155.20$, 152.14, 121.91, 117.58, 116.19, 113.24, 103.24, 98.02, 96.95, 82.59, 80.23, 71.48, 62.31, 30.72, 25.70, 23.04, 18.98, 18.90, 11.83, 10.64; $C_{27}H_{40}O_3Si$ (440.70): calcd C 73.59, H,9.15; found C 73.26, H 9.17.

3,5-Bis-{2-[2-propyloxy-5-(tetrahydro-2*H*-pyran-2-yloxy)-4-(2-triisopropylsilylethynyl)phenyl]ethynyl}toluene (**5**): $[Pd(PPh_3)_2Cl_2]$ (950 mg) and CuI (400 mg) were added to a solution of **3** (15.4 g, 35.0 mmol), **4** (5.41 g, 15.7 mmol), and PPh_3 (950 mg) in piperidine (100 mL). The solution was stirred for 1 h at room temperature and then overnight at 35 °C. The mixture was poured into ether (500 mL) and water (250 mL). The organic phase was separated and extracted with water, 10% acetic acid, water, 10% aqueous sodium hydroxide, water, and brine. Drying over $MgSO_4$ and evaporation of the solvent yielded a yellow residue, which was chromatographed over silica gel with CH_2Cl_2/hexanes (1:1) as the eluent ($R_f = 0.54$) to give **5** (14.4 g, 94%) as a slightly yellow solid. ^{1}H NMR (CD_2Cl_2): $\delta =$ 7.49–7.47 (m, 1H), 7.34–7.32 (m, 2H), 7.25 (s, 2H), 6.96 (s, 2H), 5.44 (t, $J =$ 3.1 Hz, 2H), 4.03–3.91 (m, 2H), 4.00 (t, $J = 6.5$ Hz, 4H), 3.66–3.55 (m, 2H), 2.37 (s, 3H), 2.16–1.53 (m, 16H), 1.16 (s, 42H), 1.11 (t, $J = 7.3$ Hz, 6H); ^{13}C NMR (CD_2Cl_2): $\delta = 154.79$, 152.36, 139.07, 132.53, 131.73, 124.09, 121.15, 117.85, 115.80, 114.50, 103.50, 98.08, 96.03, 94.39, 86.54, 71.67, 62.38, 30.79, 25.75, 23.20, 21.22, 19.04, 18.92, 11.88, 10.75; $C_{61}H_{84}O_6Si_2$ (969.51): calcd C 75.75, H 8.73; found C 75.84, H 8.34.

3,5-Bis-{2-[4-ethynyl-2-propyloxy-5-(tetrahydro-2*H*-pyran-2-yloxy)phenyl]ethynyl}toluene (**6**): A solution of Bu_4NF in THF (1M, 60 mL, 60 mmol) was added to a solution of **5** (13.57 g, 14.0 mmol) in THF (70 mL). The mixture was stirred for 2 h at room temperature and then poured into ether (500 mL) and water (300 mL). The organic layer was extracted with water and brine, and dried over $MgSO_4$. Evaporation of the solvent yielded a slightly brown oil, which was purified by repeated chromatography over silica gel with hexanes/CH_2Cl_2 (1:3) as the eluent ($R_f = 0.53$) to give **6** (7.54 g, 82%) as a slightly yellow solid. ^{1}H NMR (CD_2Cl_2): $\delta = 7.51-7.49$ (m, 1H), 7.36–7.34 (m, 2H), 7.25 (s, 2H), 7.00 (s, 2H), 5.43 (t, $J = 3.3$ Hz, 2H), 4.01–3.90 (m, 2H), 3.99 (t, $J = 6.5$ Hz, 4H), 3.66–3.57 (m, 2H), 3.42 (s, 2H), 2.37 (s, 3H), 2.16–1.54 (m, 16H), 1.11 (t, $J = 7.4$ Hz, 6H); ^{13}C NMR (CD_2Cl_2): $\delta = 154.77$, 152.34, 139.06, 132.57, 131.75, 123.96, 121.33, 117.67, 114.87, 114.43, 98.11, 94.48, 86.27, 82.66, 80.27, 71.48, 62.41, 30.71, 25.71, 23.09, 21.21, 19.02, 10.71; $C_{43}H_{44}O_6$ (656.87): calcd C 78.67, H 6.75; found C 78.50, H 6.83.

3-Bromo-5-(2-trimethylsilylethynyl)toluene (**10**): $[Pd(PPh_3)_2Cl_2]$ (400 mg) and CuI (180 mg) were added to a solution of **9** (11.35 g, 38.2 mmol), trimethylsilylacetylene (4.27 g, 43.4 mmol), and PPh_3 (400 mg) in piperidine (70 mL) at 0 °C. The mixture was allowed to reach room temperature, stirred for 2 days, and was then poured into ether (300 mL) and water (200 mL). The organic phase was separated and extracted with water, 10% acetic acid, water, 10% aqueous sodium hydroxide, water, and brine. Drying over $MgSO_4$ and evaporation of the solvent yielded a slightly brown residue, which was chromatographed over silica gel with hexanes as the eluent ($R_f = 0.40$) to give **10** (8.7 g, 85%) as a colorless liquid. ^{1}H NMR (CD_2Cl_2): $\delta = 7.42-7.39$ (m, 1H), 7.32–7.29 (m, 1H), 7.23–7.20 (m, 1H), 2.30 (s, 3H), 0.25 (s, 9H); ^{13}C NMR (CD_2Cl_2): $\delta = 140.71$, 132.78, 131.94, 131.58, 125.20, 122.12, 103.79, 95.75, 21.08, −0.06; $C_{12}H_{15}BrSi$ (267.24): calcd C 53.93, H, 5.66; found C 53.58, H 5.47.

3-Iodo-5-(2-trimethylsilylethynyl)toluene (**11**): A solution of *n*BuLi in hexane (1.6M, 16.5 mL, 26.4 mmol) was added to a solution of **10** (6.7 g, 25.1 mmol) in THF (100 mL) at −78 °C under argon. The solution was stirred for 15 min at this temperature and then a solution of 1,2-diiodoethane (7.5 g, 26.6 mmol) in THF (50 mL) was added dropwise. The solution was stirred for an additional 45 min at −78 °C, and then warmed to room temperature (the solution changed its color from slighly yellow to dark brown). The mixture was poured into ether (400 mL) and water (200 mL), and the organic layer was extracted with sodium thiosulfate solution, water, and brine. Drying over $MgSO_4$ and evaporation of the solvent yielded **11** (7.8 g, 99%) as a nearly colorless oil. An analytical sample was prepared by column chromatograpy over silica gel with hexanes as the eluent ($R_f = 0.51$). ^{1}H NMR (CD_2Cl_2): $\delta = 7.63-7.60$ (m, 1H), 7.53–7.50 (m, 1H), 7.26–7.22 (m, 1H), 2.27 (s, 3H), 0.24 (s, 9H); ^{13}C NMR (CD_2Cl_2): $\delta = 140.62$, 138.72, 137.86, 132.15, 125.21, 103.62, 95.75, 93.75, 20.92, −0.06; $C_{12}H_{15}ISi$ (314.24): calcd C 45.87, H 4.81; found C 45.72, H 4.76.

3,5-Bis-[2-(4-{2-[3-methyl-5-(2-trimethylsilylethynyl)-phenyl]ethynyl}-2-propyloxy-5-{tetrahydro-2*H*-pyran-2-yloxy}phenyl)ethynyl]toluene (**7**): Compound **7** was prepared by the procedure described for **5**, by adding $[Pd(PPh_3)_2Cl_2]$ (300 mg) and CuI (150 mg) to a solution of **11** (6.91 g, 22.0 mmol), **5** (3.28 g, 10.0 mmol), and PPh_3 (300 mg) in piperidine (100 mL). The yellow crude product was chromatographed over silica gel with CH_2Cl_2/hexanes (1:1) as the eluent ($R_f = 0.39$) to give **7** (8.85 g, 86%) as a slightly yellow solid. ^{1}H NMR (CD_2Cl_2): $\delta = 7.51-7.49$ (m, 1H), 7.45–7.42 (m, 2H), 7.36–7.34 (m, 2H), 7.34–7.31 (m, 2H), 7.28–7.26 (m, 4H), 7.03 (s, 2H), 5.49 (t, $J = 2.9$ Hz, 2H), 4.06–3.97 (m, 2H), 4.02 (t, $J = 6.5$ Hz, 4H), 3.68–3.60 (m, 2H), 2.38 (s, 3H), 2.34 (s, 6H), 2.21–1.57 (m, 16H), 1.13 (t, $J = 7.4$ Hz, 6H), 0.26 (s, 18H); ^{13}C NMR (CD_2Cl_2): $\delta = 154.94$, 151.79, 139.07, 139.04, 132.85, 132.56, 132.22, 131.73, 124.04, 123.86, 123.83, 121.42, 116.91, 115.55, 114.45, 104.57, 98.12, 95.03, 94.53, 94.30, 86.59, 86.46, 71.48, 62.36, 30.78, 25.75, 23.12, 21.22, 21.17, 19.00, 10.73, −0.03; $C_{67}H_{72}O_6Si_2$ (1029.57): calcd C 78.16, H 7.06; found C 78.23, H 6.97.

3,5-Bis-(2-{4-[2-(3-ethynyl-5-methylphenyl)ethynyl]-2-propyloxy-5-(tetrahydro-2*H*-pyran-2-yloxy)phenyl}ethynyl)toluene (**8**): From **7**: Compound **8** was prepared by the procedure described for **3**, by adding NaOH (1N, 10 mL) to a solution of **7** (8.24 g, 8.0 mmol) in THF/MeOH (1:1, 150 mL). Compound **8** (6.5 g, 92%) was obtained after 2 h as a slightly yellow solid. An analytical sample was prepared by chromatography over silica gel with hexanes/CH_2Cl_2 (1:3) as the eluent ($R_f = 0.56$). ^{1}H NMR (CD_2Cl_2): $\delta =$ 7.52–7.49 (m, 1H), 7.48–7.45 (m, 2H), 7.37–7.34 (m, 4H), 7.32–7.29 (m, 2H), 7.28 (s, 2H), 7.04 (s, 2H), 5.49 (t, $J = 2.9$ Hz, 2H), 4.06–3.97 (m, 2H), 4.02 (t, $J = 6.5$ Hz, 4H), 3.68–3.59 (m, 2H), 3.16 (s, 2H), 2.38 (s, 3H), 2.35 (s, 6H), 2.20–1.58 (m, 16H), 1.13 (t, $J = 7.4$ Hz, 6H); ^{13}C NMR (CD_2Cl_2): $\delta = 154.93$, 151.79, 139.15, 133.11, 132.93, 132.55, 132.36, 131.73, 124.01, 123.95, 122.76, 121.40, 116.89, 115.46, 114.49, 98.10, 94.57, 94.14, 86.69, 86.45, 83.17, 77.76, 71.47, 62.35, 30.78, 25.75, 23.11, 21.21, 21.16, 19.00, 10.73; $C_{61}H_{56}O_6$ (885.11): calcd C 82.75, H 6.39; found C 82.63, H 6.46.

From **21**: Compound **8** was prepared by the procedure described for **6**, by adding a solution of Bu_4NF in THF (1M, 9 mL, 9 mmol) to a solution of **21** (2.6 g, 2.2 mmol) in THF (20 mL). The crude product of the reaction was treated 3 times with methanol (30 mL, containing a few drops of pyridine) to give **8** (1.75 g, 90%) as a yellow solid.

3-(2-Triisopropylsilylethynyl)-5-(2-trimethylsilylethynyl)toluene (**12**): Compound **12** was prepared by the procedure described for **2**, with **9** (17.8 g; 60 mmol), triisopropylsilylacetylene (12.03 g; 66 mmol), $[PdCl_2(PPh_3)_2]$(250 mg), PPh_3 (250 mg), CuI (120 mg), piperidine (150 mL), and trimethylsilylacetylene (10.8 g; 110 mmol). After workup the brown residue was filtered over a short column of silica gel with hexanes as the eluent. Purification was performed by vacuum destillation (b.p. 165–170 °C; 10^{-4} Torr) to give 19.7 g (89%) of **12** as a slightly yellow oil. ^{1}H NMR (CD_2Cl_2): $\delta = 7.39-7.36$ (m, 1H), 7.28–7.25 (m, 1H), 7.25–7.22 (m, 1H), 2.30 (s, 3H), 1.14 (s, 21H), 0.25 (s, 9H); ^{13}C NMR (CD_2Cl_2): $\delta = 138.86$, 133.06, 132.85, 132,76, 124.03, 123.67, 106.71, 104.64, 94.86, 91.36, 21.12, 18.89, 11.81, 0.03; $C_{23}H_{36}Si_2$ (368.71): calcd C 74.92, H 9.84; found C 74.86, H 9.75.

3-Ethynyl-5-(2-triisopropylsilylethynyl)toluene (**13**): Compound **12** (15 g; 50 mmol) was dissolved in MeOH/THF (1:1, 150 mL), K_2CO_3 (13.8 g, 100 mmol) was added, and the mixture was stirred overnight. The mixture was poured into ether (300 mL) and water (200 mL), and the organic layer was extracted with water and brine. Drying over $MgSO_4$ and evaporation of the solvent yielded **13** (14.1 g, 95%) as a nearly colorless oil. An analytical sample was prepared by column chromatograpy over silica gel with hexanes as the eluent ($R_f = 0.78$). ^{1}H NMR (CD_2Cl_2): $\delta = 7.58-7.55$ (m, 1H), 7.47–7.44 (m, 1H), 7.44–7.41 (m, 1H), 3.27 (s, 1H), 2.47 (s, 3H), 1.29 (s, 21H); ^{13}C NMR (CD_2Cl_2): $\delta = 138.96$, 133.38, 133.05, 132.97, 124.11, 122.57, 106.55, 91.57, 83.21, 77.61, 21.10, 18.86, 11.78; $C_{20}H_{28}Si$ (296.53): calcd C 81.01, H 9.52; found C 80.98, H 9.50.

2-Bromo-5-iodo-4-propyloxy-1-(tetrahydro-2*H*-pyran-2-yloxy)benzene (**14**): Compound **14** was prepared by the procedure described for **1**, with 3,4-dihydro-2*H*-pyran (42.1 g, 500 mmol), 5-bromo-3-iodo-4-propyloxyphenol (35.7 g, 100 mmol) and *p*-toluenesulfonic acid (100 mg) in CH_2Cl_2 (100 mL). Recrystallization from ethanol gave 36.1 g (82%) of **14** as colorless crystals. ^{1}H NMR (CD_2Cl_2): $\delta = 7.55$ (s, 1H), 7.00 (s, 1H), 5.33 (t, $J = 3.0$ Hz, 1H), 3.93–3.83 (m, 1H), 3.90 (t, $J = 6.5$ Hz, 2H), 3.63–3.55 (m, 1H), 2.11–1.48 (m, 8H), 1.07 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (CD_2Cl_2): $\delta =$ 153.72, 148.56, 128.05, 116.85, 113.85, 98.37, 85.02, 72.07, 62.36, 30.54, 25.57,

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22.91, 18.82, 10.81; $C_{14}H_{18}BrIO_3$ (441.10): calcd C 38.12, H 4.11; found C 38.25, H 4.08.

5-{2-[3-Methyl-5-(2-triisopropylsilylethynyl)phenyl]ethynyl}-4-propyloxy-1-{tetrahydro-2*H*-pyran-2-yloxy}-2-{2-trimethylsilylethynyl}benzene (15): Compound **15** was prepared by the procedure described for **2**, with **14** (6.62 g; 15.0 mmol), **13** (4.90 g; 16.5 mmol), $[PdCl_2(PPh_3)_2]$ (150 mg), PPh_3 (150 mg), CuI (75mg), piperidine (60 mL), and trimethylsilylacetylene (3.0 g; 30.5 mmol). Purification was performed by column chromatography (silica gel) with hexanes/CH_2Cl_2 (2:1) as the eluent ($R_f = 0.44$) to give **15** (8.83 g; 88%) as a slightly yellow oil. ^{1}H NMR (CD_2Cl_2): $\delta = 7.46-7.43$ (m, 1H), 7.31–7.29 (m, 1H), 7.29–7.26 (m, 1H), 7.20 (s, 1H), 6.94 (s, 1H), 5.44 (t, $J = 2.9$ Hz, 1H), 4.05–3.95 (m, 1H), 3.97 (t, $J = 6.5$ Hz, 2H), 3.64–3.55 (m, 1H), 2.33 (s, 3H), 2.13–1.55 (m, 8H), 1.14 (s, 21H), 1.10 (t, $J = 7.4$ Hz, 3H), 0.26 (s, 9H); ^{13}C NMR (CD_2Cl_2): $\delta = 154.96$, 152.25, 138.96, 132.80, 132.56, 132.42, 124.12, 123.89, 121.73, 117.10, 115.88, 114.56, 106.82, 101.55, 100.45, 98.14, 94.50, 91.42, 86.38, 71.46, 62.22, 30.74, 25.80, 23.14, 21.18, 18.88, 11.81, 10.73, 0.04; $C_{39}H_{54}Si_2O_3$ (627.03): calcd C 74.71, H 8.68; found C 74.75, H 8.89.

2-Ethynyl-5-{2-[3-methyl-5-(2-triisopropylsilylethynyl)phenyl]ethynyl}-4-propyloxy-1-{tetrahydro-2*H*-pyran-2-yloxy}benzene (16): Compound **16** was prepared by the procedure described for **13**, with **15** (6.27 g; 10.0 mmol), K_2CO_3 (4.14 g, 30 mmol), and MeOH/THF (1:1, 100 mL). Purification was performed by column chromatography (silica gel) with hexanes/CH_2Cl_2 (1:2) as the eluent ($R_f = 0.54$) to give **16** (5.16 g; 93%) as a slightly yellow solid. ^{1}H NMR (CD_2Cl_2): $\delta = 7.47-7.44$ (m, 1H), 7.32–7.29 (m, 1H), 7.29–7.27 (m, 1H), 7.23 (s, 1H), 6.98 (s, 1H), 5.42 (t, $J = 3.1$ Hz, 1H), 4.01–3.91 (m, 1H), 3.98 (t, $J = 6.5$ Hz, 2H), 3.65–3.55 (m, 1H), 3.39 (s, 1H), 2.34 (s, 3H), 2.12–1.55 (m, 8H), 1.15 (s, 21H), 1.10 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (CD_2Cl_2): $\delta = 154.82$, 152.37, 138.97, 132.82, 132.55, 132.42, 124.11, 123.82, 121.26, 117.69, 114.89, 114.43, 106.79, 98.13, 94.50, 91.43, 86.25, 82.61, 80.27, 71.50, 62.43, 30.74, 25.72, 23.11, 21.16, 19.03, 18.86, 11.79, 10.70; $C_{36}H_{46}O_3Si$ (554.84): calcd C 77.93, H 8.36; found C 77.85, H 8.39.

3,5-Bis-[2-(4-{2-[3-methyl-5-(2-triisopropylsilylethynyl)phenyl]ethynyl}-5-propyloxy-2-{tetrahydro-2*H*-pyran-2-yloxy}phenyl)ethynyl]toluene (17): Compound **17** was prepared by the procedure described for **5**, by adding $[Pd(PPh_3)_2Cl_2]$ (80 mg) and CuI (40 mg) to a solution of **16** (4.54 g, 8.18 mmol), **4** (1.28 g, 3.72 mmol), and PPh_3 (80 mg) in piperidine (50 mL). Chromatography over silica gel with CH_2Cl_2/hexanes (1:1) as the eluent ($R_f = 0.52$) gave **17** (4.10 g, 92%) as a slightly yellow solid. ^{1}H NMR (CD_2Cl_2): $\delta = 7.51-7.48$ (m, 1H), 7.47–7.44 (m, 2H), 7.37–7.34 (m, 2H), 7.33–7.30 (m, 2H), 7.29–7.26 (m, 2H), 7.26 (s, 2H), 7.03 (s, 2H), 5.48 (t, $J =$ 3.0 Hz, 2H), 4.05–3.96 (m, 2H), 4.02 (t, $J = 6.3$ Hz, 4H), 3.68–3.59 (m, 2H), 2.38 (s, 3H), 2.34 (s, 6H), 2.19–1.57 (m, 16H), 1.15 (s, 42H), 1.12 (t, $J = 7.6$ Hz, 6H); ^{13}C NMR (CD_2Cl_2): $\delta = 155.02$, 151.85, 139.21, 138.97, 132.79, 132.60, 132.55, 132.42, 131.65, 124.11, 124.08, 123.89, 121.39, 116.96, 115.55, 114.51, 106.81, 98.16, 94.58, 94.36, 91.42, 86.68, 86.48, 71.50, 62.38, 30.83, 25.78, 23.15, 21.29, 21.17, 19.06, 18.87, 11.80, 10.73; $C_{79}H_{96}O_6Si_2$ (1197.80): calcd C 79.22, H 8.01; found C 78.82, H 7.99.

3,5-Bis-(2-{4-[2-(3-ethynyl-5-methylphenyl)ethynyl]-5-propyloxy-2-[tetrahydro-2*H*-pyran-2-yloxy]phenyl}ethynyl)toluene (18): Compound **18** was prepared by the procedure described for **6**, by adding a solution of Bu_4NF in THF (1M, 9 mL, 9 mmol) to a solution of **17** (2.6 g, 2.2 mmol) in THF (20 mL). The crude product of the reaction was treated 3 times with methanol (30 mL, containing a few drops of pyridine) to give **18** (1.87 g, 96%) as a slightly yellow solid. An analytical sample was prepared by column chromatography with hexanes/CH_2Cl_2 (1:4) as the eluent ($R_f =$ 0.65). ^{1}H NMR (CD_2Cl_2): $\delta = 7.55-7.52$ (m, 1H), 7.50–7.47 (m, 2H), 7.39–7.35 (m, 4H), 7.32–7.29 (m, 2H), 7.29 (s, 2H), 7.06 (s, 2H), 5.51 (t, $J =$ 2.9 Hz, 2H), 4.11–3.97 (m, 2H), 4.03 (t, $J = 6.5$ Hz, 4H), 3.71–3.61 (m, 2H), 3.16 (s, 2H), 2.40 (s, 3H), 2.36 (s, 6H), 2.21–1.59 (m, 16H), 1.14 (t, $J =$ 7.3 Hz, 6H); ^{13}C NMR (CD_2Cl_2): $\delta = 154.96$, 151.81, 139.18, 139.06, 133.04, 132.97, 132.59, 132.42, 131.64, 124.08, 124.03, 122.73, 121.43, 116.90, 115.59, 114.42, 98.11, 94.41, 94.37, 86.74, 86.66, 83.27, 77.81, 71.43, 62.33, 30.81, 25.78, 23.14, 21.29, 21.16, 19.05, 10.75; $C_{61}H_{56}O_6$ (885.11): calcd C 82.78, H 6.38; found C 82.41, H 6.32.

2-{2-[3-Methyl-5-(2-triisopropylsilylethynyl)phenyl]ethynyl}-4-propyloxy-1-{tetrahydro-2*H*-pyran-2-yloxy}-5-{2-triethylsilylethynyl}benzene (19): Compound **19** was prepared by the procedure described for **2**, with **14** (7.95 g; 18.0 mmol), triethylsilylacetylene (2.80 g; 20.0 mmol), $[PdCl_2(PPh_3)_2]$ (150 mg), PPh_3 (150 mg), CuI (75 mg), piperidine (60 mL), and **13** (6.52 g; 22.0 mmol). Purification was performed by column chromatography (silica gel) with hexanes/CH_2Cl_2 (2:1) as the eluent ($R_f = 0.66$) to give **19** (10.4 g; 86%) as a slightly yellow solid. ^{1}H NMR (CD_2Cl_2): $\delta = 7.46-7.43$ (m, 1H), 7.31–7.24 (m, 2H), 7.16 (s, 1H), 6.97 (s, 1H), 5.46 (t, $J = 3.1$ Hz, 1H), 4.04–3.91 (m, 1H), 3.95 (t, $J = 6.3$ Hz, 2H), 3.64–3.56 (m, 1H), 2.34 (s, 3H), 2.17–1.55 (m, 8H), 1.14 (s, 21H), 1.06 (t, $J = 7.8$ Hz, 9H), 1.05 (t, $J = 6.8$ Hz, 3H), 0.69 (q, $J = 7.8$ Hz, 6H); ^{13}C NMR (CD_2Cl_2): $\delta = 155.52$, 151.68, 139.04, 132.83, 132.56, 132.32, 124.19, 123.86, 121.76, 116.77, 115.63, 114.70, 106.78, 102.56, 98.26, 98.03, 94.30, 91.52, 86.60, 71.45, 62.30, 30.79, 25.79, 23.14, 21.19, 18.95, 18.87, 11.81, 10.75, 7.70, 4.88; $C_{42}H_{60}Si_2O_3$ (669.11): calcd C 75.39, H 9.04; found C 75.25, H 9.04.

5-Ethynyl-2-{2-[3-methyl-5-(2-triisopropylsilylethynyl)phenyl]ethynyl}-4-propyloxy-1-{tetrahydro-2*H*-pyran-2-yloxy}benzene (20): Compound **20** was prepared by the procedure described for **13**, with **19** (6.70 g; 10.0 mmol), K_2CO_3 (4.14 g, 30 mmol), and MeOH/THF (1:1, 100 mL). Purification was performed by column chromatography (silica gel) with hexanes/CH_2Cl_2 (1:2) as the eluent ($R_f = 0.54$) to give **20** (5.16 g; 93%) as a slightly yellow solid. ^{1}H NMR (CD_2Cl_2): $\delta = 7.46-7.43$ (m, 1H), 7.31–7.27 (m, 2H), 7.21 (s, 1H), 6.99 (s, 1H), 5.44 (t, $J = 3.1$ Hz, 1H), 4.03–3.94 (m, 1H), 3.97 (t, $J = 6.5$ Hz, 2H), 3.64–3.55 (m, 1H), 3.37 (s, 1H), 2.34 (s, 3H), 2.15–1.55 (m, 8H), 1.14 (s, 21H), 1.06 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (CD_2Cl_2): $\delta = 155.43$, 151.67, 139.04, 132.88, 132.56, 132.33, 124.18, 123.76, 122.25, 116.76, 116.07, 113.30, 106.76, 98.12, 94.39, 91.53, 86.36, 82.73, 80.20, 71.43, 62.32, 30.76, 25.74, 23.01, 21.18, 18.96, 18.85, 11.79, 10.63; $C_{36}H_{46}O_3Si$ (554.84): calcd C 77.93, H 8.36; found C 77.80, H 8.38.

3,5-Bis-[2-(4-{2-[3-methyl-5-(2-triisopropylsilylethynyl)phenyl]ethynyl}-2-propyloxy-5-{tetrahydro-2*H*-pyran-2-yloxy}phenyl)ethynyl]toluene (21): Compound **21** was prepared by the procedure described for **5**, by adding $[Pd(PPh_3)_2Cl_2]$ (90 mg) and CuI (45 mg) to a solution of **20** (5.24 g, 9.44 mmol), **4** (1.51 g, 4.39 mmol), and PPh_3 (90 mg) in piperidine (60 mL). Chromatography over silica gel with CH_2Cl_2/hexanes (1:1) as the eluent ($R_f = 0.68$) gave **21** (4.78 g, 91%) as a yellow solid. ^{1}H NMR (CD_2Cl_2): $\delta =$ 7.50–7.48 (m, 1H), 7.47–7.44 (m, 2H), 7.35–7.33 (m, 2H), 7.33–7.30 (m, 2H), 7.30–7.27 (m, 2H), 7.26 (s, 2H), 7.02 (s, 2H), 5.49 (t, $J = 3.0$ Hz, 2H), 4.06–3.96 (m, 2H), 4.02 (t, $J = 6.5$ Hz, 4H), 3.68–3.58 (m, 2H), 2.37 (s, 3H), 2.34 (s, 6H), 2.19–1.57 (m, 16H), 1.14 (s, 42H), 1.12 (t, $J = 7.6$ Hz, 6H); ^{13}C NMR (CD_2Cl_2): $\delta = 154.99$, 151.85, 139.08, 139.04, 132.83, 132.56, 132.32, 131.76, 124.16, 124.06, 123.84, 121.41, 116.88, 115.60, 114.49, 106.75, 98.10, 94.56, 94.40, 91.51, 86.62, 86.50, 71.52, 62.35, 30.80, 25.78, 23.14, 21.23, 21.19, 18.98, 18.85, 11.77, 10.75; $C_{79}H_{96}O_6Si_2$ (1197.80): calcd C 79.22, H 8.01; found C 78.85, H 8.08.

2-[2-(4-{2-[3-Methyl-5-(2-triisopropylsilylethynyl)phenyl]ethynyl}-2-propyloxy-5-{tetrahydro-2*H*-pyran-2-yloxy}phenyl)ethynyl]-4-propyloxy-1-{tetrahydro-2*H*-pyran-2-yloxy}-5-{2-triethylsilylethynyl}benzene (22): Compound **22** was prepared by the procedure described for **2**, with **14** (2.80 g; 5.6 mmol), triethylsilylacetylene (0.88 g; 6.2 mmol), $[PdCl_2(PPh_3)_2]$ (60 mg), PPh_3 (60 mg), CuI (30 mg), piperidine (20 mL), and **20** (2.90 g; 5.2 mmol). Purification was performed by column chromatography (silica gel) with hexanes/CH_2Cl_2 (1:3) as eluent ($R_f = 0.62$), and then by radial chromatography with hexanes/CH_2Cl_2 (1:1) as eluent ($R_f = 0.27$) to give **22** (3.62 g; 75%) as a yellow solid. ^{1}H NMR (CD_2Cl_2): $\delta = 7.47-7.45$ (m, 1H), 7.34–7.31 (m, 1H), 7.31–7.28 (m, 1H), 7.27 (s, 1H), 7.18 (s, 1H), 7.03 (s, 1H), 6.98 (s, 1H), 5.49–5.44 (m, 2H), 4.04–3.95 (m, 2H), 4.02 (t, $J = 6.7$ Hz, 2H), 3.96 (t, $J = 6.3$ Hz, 2H), 3.66–3.56 (m, 2H), 2.34 (s, 3H), 2.20–1.58 (m, 16H), 1.15 (s, 21H), 1.13–1.03 (m, 15H), 0.70 (q, $J = 8.01$ Hz, 6H); ^{13}C NMR (CD_2Cl_2): $\delta = 155.50$, 154.74, 151.89, 151.39, 139.04, 132.83, 132.55, 132.30, 124.16, 123.82, 121.97, 121.54, 116.89, 116.04, 115.56, 114.71, 114.51, 106.74, 102.60, 98.19, 98.12, 98.10, 94.44, 91.79, 91.59, 91.51, 86.60, 71.49, 71.35, 62.31, 30.81, 30.74, 25.77, 23.10, 23.05, 21.19, 18.98, 18.85, 11.78, 10.73, 10.69, 7.69, 4.86; $C_{58}H_{78}O_6Si_2$ (927.42): calcd C 75.12, H 8.48; found C 74.93, H 8.33.

5-Ethynyl-2-[2-(4-{2-[3-methyl-5-(2-triisopropylsilylethynyl)phenyl]ethynyl}-2-propyloxy-5-{tetrahydro-2*H*-pyran-2-yloxy}phenyl)ethynyl]-4-propyloxy-1-{tetrahydro-2*H*-pyran-2-yloxy}benzene (23): Compound **23** was prepared by the procedure described for **13**, with **22** (2.65 g; 2.9 mmol), K_2CO_3 (1.75 g, 12.7 mmol), and MeOH/THF (2:3, 50 mL). The mixture was stirred for 30 days at room temperature. Purification was performed by column chromatography (silica gel) with hexanes/CH_2Cl_2 (1:3) as the eluent ($R_f = 0.41$) to give **23** (1.9 g; 88%) as a yellow solid. ^{1}H NMR (CD_2Cl_2): $\delta = 7.48-7.45$ (m, 1H), 7.33–7.30 (m, 1H), 7.30–7.28 (m, 1H), 7.27 (s, 1H), 7.22 (s, 1H), 7.03 (s, 1H), 7.01 (s, 1H), 5.49–5.42 (m, 2H),

4.04 – 3.94 (m, 2H), 4.02 (t, $J = 6.5$ Hz, 2H), 3.97 (t, $J = 6.7$ Hz, 2H), 3.65 – 3.56 (m, 2H), 3.39 (s, 1H), 2.35 (s, 3H), 2.21 – 1.56 (m, 16H), 1.15 (s, 21H), 1.09 (t, $J = 7.4$ Hz, 3H), 1.06 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (CD_2Cl_2): $\delta =$ 155.34, 154.73, 151.84, 151.36, 139.03, 132.82, 132.53, 132.30, 124.13, 123.77, 122.47, 121.51, 116.84, 116.48, 115.62, 114.56, 113.09, 106.70, 98.18, 98.13, 94.45, 91.66, 91.53, 91.50, 86.55, 82.69, 80.22, 71.44, 71.34, 62.29, 30.78, 30.71, 25.74, 23.03, 22.97, 21.18, 18.83, 11.75, 10.69, 10.59; $C_{52}H_{64}O_6Si$ (813.16): calcd C 76.81, H 7.93; found C 76.80, H 7.81.

3,5-Bis-(2-{4-[2-(4-{2-[3-methyl-5-(2-triisopropylsilylethynyl)phenyl]-ethynyl}-2-propyloxy-5-{tetrahydro-2*H*-pyran-2-yloxy}phenyl)ethynyl]-2-propyloxy-5-[tetrahydro-2*H*-pyran-2-yloxy]phenyl}ethynyl)toluene (24): Compound **24** was prepared by the procedure described for **5**, by adding $[Pd(PPh_3)_2Cl_2]$ (35 mg) and CuI (18 mg) to a solution of **23** (1.74 g, 2.14 mmol), **4** (0.33 g, 0.97 mmol), and PPh_3 (35 mg) in piperidine (25 mL). Chromatography over silica gel with CH_2Cl_2/hexanes (2:1) as the eluent ($R_f = 0.40$) gave **24** (1.55 g, 93 %) as a yellow solid. ^{1}H NMR (CD_2Cl_2): $\delta =$ 7.51 – 7.48 (m, 1H), 7.47 – 7.44 (m, 2H), 7.36 – 7.33 (m, 2H), 7.33 – 7.30 (m, 2H), 7.30 – 7.27 (m, 2H), 7.27 (s, 4H), 7.03 (s, 2H), 7.02 (s, 2H), 5.51 – 5.43 (m, 4H), 4.05 – 3.95 (m, 4H), 4.03 (t, $J = 6.5$ Hz, 4H), 4.02 (t, $J = 6.5$ Hz, 4H), 3.67 – 3.56 (m, 4H), 2.37 (s, 3H), 2.35 (s, 6H), 2.26 – 1.56 (m, 32H), 1.14 (s, 42H), 1.12 (t, $J = 7.6$ Hz, 6H), 1.10 (t, $J = 7.4$ Hz, 6H); ^{13}C NMR (CD_2Cl_2): $\delta = 155.00$, 154.75, 151.90, 151.60, 139.04, 132.83, 132.57, 132.32, 131.78, 124.17, 124.09, 123.83, 121.66, 121.53, 117.02, 116.87, 116.05, 115.57, 114.72, 114.36, 106.75, 98.21, 98.16, 94.56, 94.47, 91.86, 91.74, 91.51, 86.66, 86.58, 71.46, 62.35, 62.30, 30.82, 30.79, 25.78, 23.14, 23.07, 21.20, 19.07, 19.00, 18.87, 11.75, 10.76; $C_{111}H_{132}O_{12}Si_2$ (1714.43): calcd C 77.76, H 7.76; found C 77.71, H 7.83.

3,5-Bis-{2-[4-(2-{4-[2-(3-ethynyl-5-methylphenyl)ethynyl]-2-propyloxy-5-[tetrahydro-2*H*-pyran-2-yloxy]phenyl}ethynyl)-2-propyloxy-5-(tetrahydro-2*H*-pyran-2-yloxy)phenyl]ethynyl}-toluene (25): Compound **25** was prepared by the procedure described for **6**, by adding a solution of Bu_4NF in THF (1M, 3.7 mL, 3.7 mmol) to a solution of **24** (1.49 g, 0.86 mmol) in THF (40 mL). The crude product of the reaction was treated 3 times with methanol (30 mL, containing a few drops of pyridine) to give **25** (1.14 g, 95 %) as a yellow solid. An analytical sample was prepared by radial chromatography with CH_2Cl_2 as the eluent ($R_f = 0.28$). ^{1}H NMR (CD_2Cl_2): $\delta =$ 7.52 – 7.49 (m, 1H), 7.48 – 7.45 (m, 2H), 7.38 – 7.34 (m, 4H), 7.32 – 7.29 (m, 2H), 7.29 (s, 2H), 7.28 (s, 2H), 7.05 (s, 2H), 7.04 (s, 2H), 5.52 – 5.47 (m, 2H), 5.47 (t, $J = 3.1$ Hz, 2H), 4.07 – 3.95 (m, 4H), 4.04 (t, $J = 6.5$ Hz, 4H), 4.03 (t, $J = 6.5$ Hz, 4H), 3.72 – 3.57 (m, 4H), 3.16 (s, 2H), 2.38 (s, 3H), 2.35 (s, 6H), 2.21 – 1.59 (m, 32H), 1.13 (t, $J = 7.4$ Hz, 6H), 1.11 (t, $J = 7.6$ Hz, 6H); ^{13}C NMR (CD_2Cl_2): $\delta =$ 154.97, 154.73, 151.87, 151.59, 139.16, 139.06, 133.13, 132.93, 132.53, 132.36, 131.74, 124.05, 123.96, 122.77, 121.65, 121.57, 117.02, 116.96, 116.01, 115.47, 114.77, 114.34, 98.22, 94.53, 94.19, 91.84, 91.67, 86.71, 86.53, 83.16, 77.77, 71.48, 68.16, 62.34, 30.81, 30.76, 25.75, 23.11, 23.04, 21.22, 21.17, 19.01, 10.71; $C_{93}H_{92}O_{12}$ (1401.75): calcd C 79.69, H 6.62; found C 79.31, H 6.68.

THP-protected macrocycle 26: A solution of **8** (1.5 g, 1.7 mmol) in pyridine (50 mL) was added to a suspension of CuCl (12 g, 121.2 mmol) and $CuCl_2$ (2.4 g, 17.8 mmol) in pyridine (250 mL) over 96 h at room temperature. After the completion of the addition, the mixture was allowed to stir for an additional 4 days and then was poured into CH_2Cl_2 (500 mL) and water (300 mL). The organic phase was extracted with water, 25 % NH_3 solution (in order to remove the copper salts), water, 10 % acetic acid, water, 10 % aqueous sodium hydroxide, and brine, and dried over $MgSO_4$. After evaporation of the solvent to about 30 to 40 mL, the coupling products were precipitated by the addition of methanol (200 mL) and collected by filtration (1.45 g). Recrystallization from CH_2Cl_2 gave of **26** (0.675 g, 45 %) as a slightly yellow solid. ^{1}H NMR ($C_2D_2Cl_4$): $\delta =$ 7.50 – 7.48 (m, 4H), 7.48 – 7.46 (m, 2H), 7.30 – 7.27 (m, 4H), 7.27 – 7.24 (m, 8H), 7.18 (s, 4H), 6.94 (s, 4H), 5.44 – 5.39 (m, 4H), 4.04 – 3.94 (m, 4H), 3.95 (t, $J = 6.5$ Hz, 8H), 3.64 – 3.54 (m, 4H), 2.28 (s, 18H), 2.15 – 1.45 (m, 32H), 1.06 (t, $J = 7.4$ Hz, 12H); ^{13}C NMR ($C_2D_2Cl_4$): $\delta =$ 154.82, 151.57, 139.05, 138.74, 133.35, 133.13, 132.92, 132.42, 132.27, 123.98, 123.77, 122.11, 121.45, 117.13, 115.37, 114.57, 98.04, 94.79, 94.06, 87.08, 86.51, 81.40, 71.48, 62.36, 30.64, 25.64, 23.01, 21.46, 18.85, 10.96; $C_{122}H_{108}O_{12}$ (1766.19): calcd C 82.97, H 6.16; found C 82.80, H 6.05.

THP-protected macrocycle 27: Compound **27** was prepared by the procedure described for **26**, by adding of **18** (1.5 g, 1.7 mmol) in pyridine (50 mL) to a suspension of CuCl (12 g, 121.2 mmol) and $CuCl_2$ (2.4 g, 17.8 mmol) in pyridine (250 mL) over 96 h at room temperature. The crude product was extracted with warm CH_2Cl_2, and the residue recrystallized from $C_2H_2Cl_4$ to give of **27** (0.57 g, 38 %) as a slightly yellow solid. ^{1}H NMR ($C_2D_2Cl_4$): $\delta =$ 7.50 – 7.46 (m, 6H), 7.31 – 7.29 (m, 4H), 7.29 – 7.23 (m, 8H), 7.17 (s, 4H), 6.94 (s, 4H), 5.44 – 5.38 (m, 4H), 4.03 – 3.92 (m, 4H), 3.94 (t, $J = 6.5$ Hz, 8H), 3.64 – 3.53 (m, 4H), 2.30 (s, 6H), 2.28 (s. 12H), 2.12 – 1.41 (m, 32H), 1.05 (t, $J = 7.4$ Hz, 12H); ^{13}C NMR ($C_2D_2Cl_4$): $\delta =$ 154.86, 151.51, 138.97, 133.42, 133.3 – 133.1 (several signals; not resolved), 132.9 – 132.7 (several signals; not resolved), 132.27, 124.02, 123.77, 122.04, 121.57, 117.09, 115.66, 114.27, 98.05, 94.49, 94.31, 86.90, 86.70, 81.44, 71.46, 62.36, 30.63, 25.63, 23.01, 21.44, 18.85, 10.96; $C_{122}H_{108}O_{12}$ (1766.19): calcd C 82.97, H 6.16; found C 82.64, H 6.01.

THP-protected macrocycle 28: Compound **28** was prepared by the procedure described for **26**, by adding of **25** (1.2 g, 0.85 mmol) in pyridine (25 mL) to a suspension of CuCl (6 g, 60.6 mmol) and $CuCl_2$ (1.2 g, 8.9 mmol) in pyridine (150 mL) over 96 h at room temperature. The crude product was extracted with ethyl acetate, and the residue filtered through a short column of silica gel with CH_2Cl_2/THF (100:1) as the eluent to give 0.41 g (34 %) of **28** as a yellow solid. ^{1}H NMR ($C_2D_2Cl_4$): $\delta =$ 7.51 – 7.43 (m, 6H), 7.31 – 7.23 (m, 12H), 7.18 (s, 8H), 6.94 (s, 8H), 5.45 – 5.39 (m, 4H), 5.39 – 5. 35 (m, 4H), 4.02 – 3.89 (m, 8H), 3.95 (t, $J = 6.5$ Hz, 8H), 3.93 (t, $J =$ 6.1 Hz, 8H), 3.63 – 3.52 (m, 8H), 2.29 (s, 18H), 2.10 – 1.40 (m, 64H), 1.04 (t, $J = 7.4$ Hz, 12H), 1.03 (t, $J = 7.3$ Hz, 12H); ^{13}C NMR ($C_2D_2Cl_4$): $\delta =$ 154.83, 154.64, 151.64, 151.35, 139.06, 138.71, 133.29, 133.18, 132.99, 132.30, 123.97, 123.79, 122.10, 121.74, 121.57, 117.27, 117.13, 116.01, 115.39, 114.79, 114.37, 98.21, 98.10, 94.71, 94.11, 92.02, 91.67, 87.06, 86.56, 81.44, 71.43, 62.35, 62.28, 30.67, 30.58, 25.63, 22.99, 22.93, 21.45, 18.89, 18.80, 10.92; $C_{186}H_{180}O_{24}$ (2799.46): calcd C 79.80, H 6.48; found C 80.74, H 6.04.

Macrocycle 29: A suspension of **26** (300 mg, 0.17 mmol) in oxygen-free $CHCl_3$ (30 mL) and oxygen-free methanol (10 mL) containing *p*-TsOH (10 – 15 mg) was stirred for 2 days at room temperature under an argon atmosphere. Oxygen-free methanol (100 mL) was added, and the yellow precipitate was collected by filtration and vacuum dried to give **29** (239 mg, 98 %) as a slightly yellow solid. ^{1}H NMR ([D$_8$]THF): $\delta =$ 8.35 (s, 4H), 7.59 – 7.56 (m, 4H), 7.48 – 7.46 (m, 2H), 7.43 – 7.41 (m, 4H), 7.36 – 7.33 (m, 4H), 7.32 – 7.29 (m, 4H), 7.01 (s, 4H), 6.93 (s, 4H), 4.00 (t, $J = 6.3$ Hz, 8H), 2.36 (s, 18H), 1.95 – 1.77 (m, 8H), 1.13 (t, $J = 7.4$ Hz, 12H); ^{13}C NMR ([D$_8$]THF): 153.88, 153.11, 139.66, 139.25, 133.63, 133.44, 132.97, 132.51, 132.27, 125.03, 124.81, 122.65, 120.20, 117.19, 115.71, 112.05, 94.33, 94.16, 87.44, 86.92, 81.47, 74.38, 71.66, 23.53, 20.84, 10.84; UV (THF): λ_{max} (ε) = 374 nm (143 000); MALDI-TOF: 1429.3 $[M]^+$, 1539.1 $[M+Ag]^+$, 1646.4 $[M+2Ag]^+$; $C_{102}H_{76}O_8$ (1429.72): calcd C 85.69, H 5.36; found C 85.44, H 5.32.

Macrocycle 30: Compound **30** was prepared by the procedure described for **29**, with **27** (300 mg, 0.17 mmol) giving **30** (240 mg, 98 %) as a slightly yellow solid. ^{1}H NMR ([D$_8$]THF): $\delta =$ 8.35 (s, 4H), 7.60 – 7.57 (m, 2H), 7.57 – 7.47 (m, 4H), 7.40 – 7.37 (m, 4H), 7.37 – 7.33 (m, 8H), 7.02 (s, 4H), 6.94 (s, 4H), 4.00 (t, $J = 6.3$ Hz, 8H), 2.36 (s, 18H), 1.98 – 1.78 (m, 8H), 1.13 (t, $J = 7.4$ Hz, 12H); ^{13}C NMR ([D$_8$]THF): 153.92, 153.05, 139.70, 139.21, 133.49, 133.02, 132.77, 132.14, 125.14, 124.67, 122.69, 120.23, 117.16, 115.29, 112.45, 94.71, 93.77, 87.44, 86.93, 81.52, 74.43, 71.66, 23.51, 20.84, 10.81; UV (THF): λ_{max} (ε) = 374 nm (148 000); MALDI-TOF: 1429.4 $[M]^+$, 1537.8 $[M+Ag]^+$, 1644.0 $[M+2Ag]^+$; $C_{102}H_{76}O_8$ (1429.72): calcd C 85.69, H 5.36; found C 85.30, H 5.42.

Macrocycle 31: Compound **31** was prepared by the procedure described for **29**, with **28** (250 mg, 0.09 mmol) giving **31** (180 mg, 93 %) as a yellow solid. ^{1}H NMR ([D$_7$]DMF): $\delta =$ 10.06 (br s, 8H), 7.69 – 7.65 (m, 4H), 7.56 – 7.49 (m, 10H), 7.45 – 7.41 (m, 4H), 7.23 (s, 4H), 7.17 (s, 4H), 7.16 (s, 4H), 7.13 (s, 4H), 4.09 (t, $J = 6.4$ Hz, 8H), 4.08 (t, $J = 6.5$ Hz, 8H), 2.42 (s, 12H), 2.41 (s, 6H), 1.13 (t, $J = 7.4$ Hz, 24H); ^{13}C NMR ([D$_7$]DMF): 153.42, 153.38, 153.23, 153.22, 140.20, 139.98, 133.8 – 133.5 (several signals, not resolved), 133.4 – 133.2 (several signals, not resolved), 132.5 – 131.8 (several signals, not resolved), 124.68, 124.31, 122.02, 119.96, 119.94, 119.86, 117.66, 117.30, 115.70, 114.58, 112.74, 111.63, 94.14, 93.77, 92.44, 91.85, 88.10, 87.16, 81.81, 74.23, 71.63, 71.49, 23.21, 23.17, 20.84, 20.76, 10.78, 10.73; UV (DMF): λ_{max} (ε) = 397 nm (244 000); MALDI-TOF: 2126.6 $[M]^+$, 2234.5 $[M+Ag]^+$; $C_{146}H_{116}O_{16}$ (2126.52): calcd C 82.46, H 5.50; found C 82.18 H 5.31.

4-Propyloxy-1-[tetrahydro-2*H*-pyran-2-yloxy]-2,5-bis-[2-(4-tolyl)ethynyl]-benzene (32): Compound **32** was prepared by the procedure described for **5**, by adding $[Pd(PPh_3)_2Cl_2]$ (100 mg) and CuI (50 mg) to a solution of **14** (3.30 g, 7.5 mmol), 4-tolylacetylene (2.33 g, 20.0 mmol), and PPh_3 (100 mg) in piperidine (40 mL). The mixture was stirred overnight at 65 °C. The

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yellow-brown crude product was chromatographed over silica gel with CH_2Cl_2/hexanes (1:1) as the eluent ($R_f = 0.41$), dissolved in warm CH_2Cl_2, and precipitated by the addition of MeOH to give **32** (2.65 g, 76%) as a slightly yellow solid. ^{1}H NMR (CD_2Cl_2): $\delta = 7.46$ and 7.43 (AA′BB′ pattern, 2H each), 7.26 (s, 1H), 7.22 and 7.19 (AA′BB′ pattern, 2H each), 7.03 (s, 1H), 5.50 (t, $J = 3.0$ Hz, 1H), 4.09–3.99 (m, 1H), 4.02 (t, $J = 6.5$ Hz, 2H), 3.68–3.59 (m, 1H), 2.39 (s, 6H), 2.21–1.58 (m, 8H), 1.13 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (CD_2Cl_2): $\delta = 154.87$, 151.66, 139.23, 139.13, 131.76, 131.73, 129.65, 129.58, 121.37, 120.74, 120.69, 116.79, 115.71, 114.50, 98.09, 95.32, 95.19, 85.72, 85.60, 71.44, 62.29, 30.80, 25.78, 23.15, 21.64, 18.99, 10.74; $C_{32}H_{32}O_3$ (464.60): calcd C 82.73, H 6.94; found C 82.46, H 6.77.

4-Propyloxy-2,5-bis-[2-(4-tolyl)ethynyl]phenol (**33**): A solution of **32** (2.15 g, 4.63 mmol) in CH_2Cl_2 (30 mL) and methanol (10 mL) containing *p*-TsOH (10–15 mg) was stirred at room temperature under an argon atmosphere overnight. The mixture was poured into ether (200 mL) and water (100 mL). The organic phase was extracted with water and brine. Drying over $MgSO_4$ and evaporation of the solvent yielded a yellow-brown residue, which was chromatographed over silica gel with CH_2Cl_2/hexanes (1:1) as the eluent ($R_f = 0.31$) to give **33** (1.25 g, 71%) as a slightly yellow solid. ^{1}H NMR (CD_2Cl_2): $\delta = 7.50–7.41$ (m, 4H), 7.26–7.18 (m, 4H), 7.07 (s, 1H), 6.96 (s, 1H), 5.58 (br s, 1H), 3.99 (t, $J = 6.5$ Hz, 2H), 2.39 (s, 3H), 2.38 (s, 3H), 1.95–1.82 (m, 2H), 1.12 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (CD_2Cl_2): 153.83, 150.74, 139.92, 139.21, 131.85, 131.81, 129.73, 129.57, 120.67, 119.54, 119.02, 115.87, 115.59, 110.64, 97.92, 95.53, 85.36, 83.04, 71.64, 23.16, 21.67, 21.63, 10.74; UV (THF): λ_{max} (ε) = 367 nm (37000); $C_{27}H_{24}O_2$ (380.49): calcd C 85.23, H 6.36; found C 85.12, H 6.23.

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