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A High-Yield, One-Step Synthesis of *o*-Phenylene Ethynylene Cyclic Trimer via Precipitation-Driven Alkyne Metathesis

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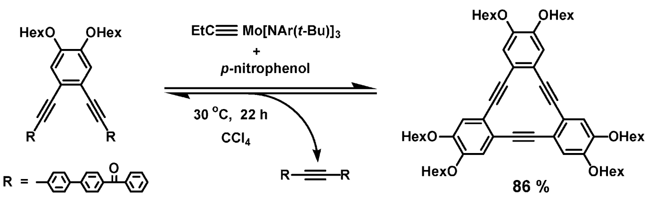
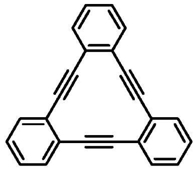


A shape-persistent, conjugated *o*-phenylene ethynylene cyclic trimer was prepared in one step from tetrasubstituted benzene monomer **4** in 86% isolated yield through precipitation-driven alkyne metathesis. The template-free, selective generation of the molecular triangle **5** is a thermodynamically favored process and under equilibrium control. A novel tetrameric macrocycle **7** was generated via scrambling metathesis between tricycle **5** and hexacycle **6** using this dynamic covalent chemistry.

There has been growing interest in shape-persistent, arylene ethynylene macrocycles as building blocks for molecular materials and supramolecular chemistry.[1] These macrocycles have rigid, noncollapsible hydrocarbon backbones and are able to organize in solution, the molten phase, and solid state (noncovalent nanotubes, discotic liquid crystals, guest−host complexes, etc.). Among these structures, the conjugated cyclic trimer comprising three *o*-phenylene ethynylene units (**1**) has attracted great interest.[2] Macrocycle **1** and its derivatives are structural units of *graphyne*.[2a] The distance from the center of the 12-membered dehydroannulene to the center of the carbon−carbon triple bonds is about 1.2 Å, which provides a suitable geometry for π-alkylene/transition-metal bonding interactions.[2c] The metal can be either in or out of the plane of the macrocycle. The interesting structural and conducting properties of the transition-metal complexes derived from **1** have been extensively explored.[2b−d]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Although there have been a series of phenylene ethynylene trimeric macrocycles reported to date, their preparation is mainly restricted to cross-coupling approaches, and usually only low yields are obtained.[3,4] The primary disadvantage of the coupling approach is that the product distribution is kinetically determined. Since these irreversible reactions do not have the ability to correct undesired bond formations, oligomer growth that overshoots the length of target macrocycles cannot contribute to the yield of the desired product.

On the other hand, given the successful examples of dynamic covalent chemistry in organic synthesis,[5] we envisioned a one-step approach to arylene ethynylene macrocycles from monomers could be accomplished via reversible alkyne metathesis. By utilizing molybdenum catalyst that is both functional group tolerant and active near room temperature,[6] we have accomplished one-step, gram-scale synthesis of hexameric phenylene ethynylene macrocycles.[7] Macrocycle formation is a thermodynamically favored process under equilibrium control.[8]

Recently, Vollhardt et al. synthesized trimeric phenylene ethynylene macrocycles through alkyne metathesis catalyzed by Schrock's catalyst.[9] Although the un-

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(7) Zhang, W.; Moore, J. S. *J. Am. Chem. Soc.* **2004**, *126*, 12796. Bunz previously reported the synthesis of hexameric macrocycles via alkyne metathesis. Under their conditions, which required high temperature (150 °C), the desired products were obtained in only 0.5−6% yields. Ge, P.-H.; Fu, W.; Herrmann, W. A.; Herdtweck, E.; Campana, C.; Adams, R. D.; Bunz, U. H. F. *Angew. Chem., Int. Ed.* **2000**, *39*, 3607−3610.

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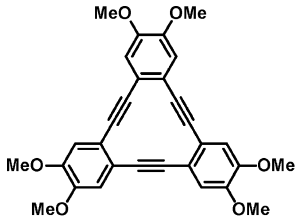
substituted cyclic product **1** can be obtained in 54% yield at 80 °C, methoxy substituted analogue **2** was only obtained in 28% yield even after 140 h, with 20% catalyst loading. To further improve the synthesis of trimeric phenylene ethynylene macrocycles and also to explore the scope of our newly developed synthetic protocol, we now report the efficient, one-step preparation of an alkoxy subsituted *o*-phenylene ethynylene cyclic trimer using the precipitation-driven alkyne metathesis.[7] Under equilibrium control, the thermodynamically favored cyclic trimer **5** was obtained in high yield.



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Sonogashira cross-coupling[10] of 1,2-diethynyl-4,5-dihexyloxybenzene (**3**)[11] and 4-benzoyl-4′-bromobiphenyl gave the desired tetrasubstituted benzene monomer **4** (Scheme 1). The metathesis reaction of **4** was performed in CCl_4 catalyzed by a molybdenum alkylidyne catalyst[6] (10 mol % loading) generated in situ from the corresponding molybdenum triamide and *p*-nitrophenol. The reaction mixture was stirred for 22 h at 30 °C, during which time the precipitation of the byproduct diarylacetylene drove the reaction to completion. After removal of the precipitate, the filtrate was concentrated and the macrocyclic product was purified by column chromatography, affording triangular cycle **5** as a yellow solid with 86% isolated yield.

The obtained cyclic trimer **5** was fully characterized by ^{1}H NMR, ^{13}C NMR, FAB-MS, GPC, and elemental analysis, which unambiguously demonstrate the desired cyclic trimer. The ^{1}H NMR spectrum of **5** revealed the presence of only one type of aromatic proton (δ 6.72) and the ^{13}C NMR spectrum showed a unique signal coresponding to the acetylene carbon (δ 91.8), which are consistent with D_{3h} symmetry for the trianular structure. FAB mass spectrometry showed the molecular ion at *m/z* = 900.6269 (calcd 900.6268), supporting the structure of cyclic trimer **5**. GPC trace of macrocycle **5** (Figure 1) showed the monodisperse product distribution (PD = 1.00) and a M_n of 1090, further supporting the generation of the target structure. Finally, the elemental analysis result is also consistent with the expected composition of **5**.[12]

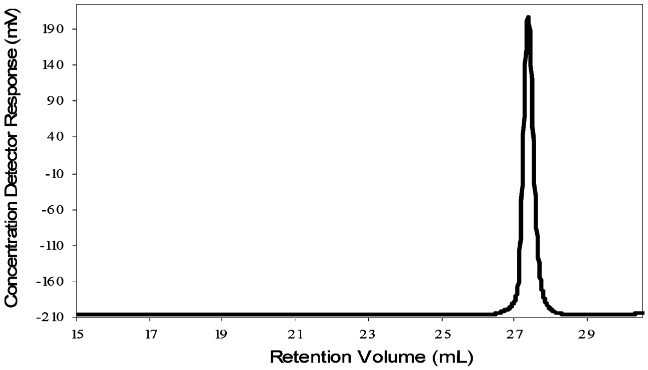


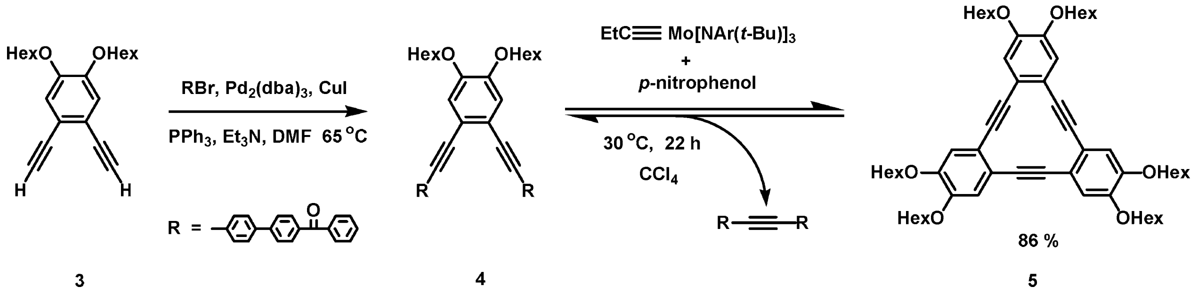
FIGURE 1. GPC trace of purified cyclic trimer **5** (THF, 25 °C).

The reversibility of macrocycle **5** formation was demonstrated by a scrambling experiment, in which a 1:2 mixture of two different phenylene ethynylene macrocycles (**5** and **6**[13]) was subjected to metathesis (eq 1). The reaction was conducted in CCl_4 at 30 °C for 22 h followed by FD-MS analysis (Figure 2). A tetrameric macrocycle, presumably structure **7** (*m/z* = 1200) having two *o*-disubstituted units from **5** (*m/z* = 900) and two *m*-disubstituted units from **6** (*m/z* = 1800) was observed, demonstrating the reversibility of macrocycle formation.

This template-free,[14,15] selective generation of triangular cycle **5** via precipitation-driven alkyne metathesis is thus confirmed to be a thermodynamically controlled process.[8] The initial growth of the oligomers is driven by the poor solubility of the diarylacetylene byproduct. Once the chains are sufficiently long, the oligomers can transform into corresponding cyclic oligomers ($n \geq 3$) through intramolecular metathesis with nearly complete removal of end groups. At this point, open-chain and macrocyclic intermediates can equilibrate leading predominantly to the thermodynamically more stable trimeric macrocycles.

In conclusion, the cyclic trimer **5** has been successfully synthesized by using precipitation-drivien alkyne metathesis. The selective generation of cyclic trimer is a thermodynamically favored process and under equilibrium control. The successful synthesis of **5** as well as generation of a tetracycle via scrambling metathesis of tricycle **5** and hexacycle **6** further demonstrates the general scope of the one-step protocol for arylene ethynylene macrocycle preparation and the importance of dynamic covalent chemistry in constructing thermodynamically favored molecular architectures in high yields.

SCHEME 1. Synthesis of *o*-Phenylene Ethynylene Cyclic Trimer 5



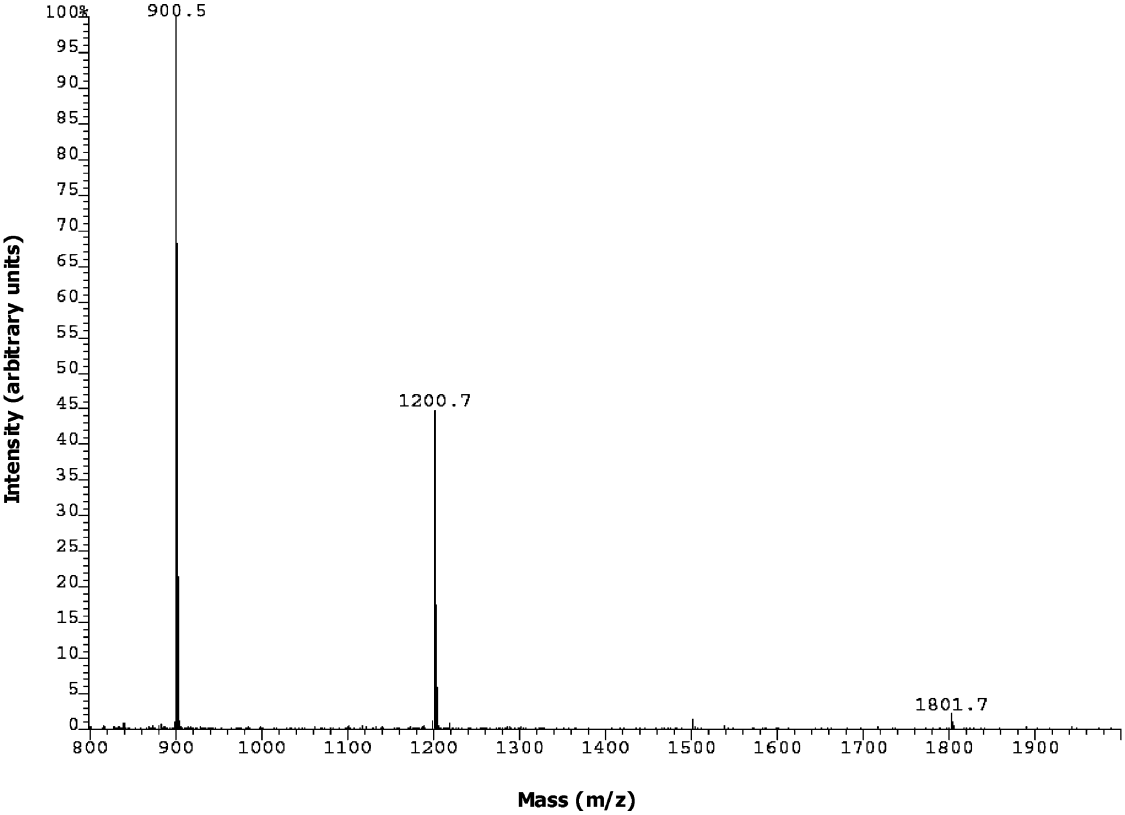
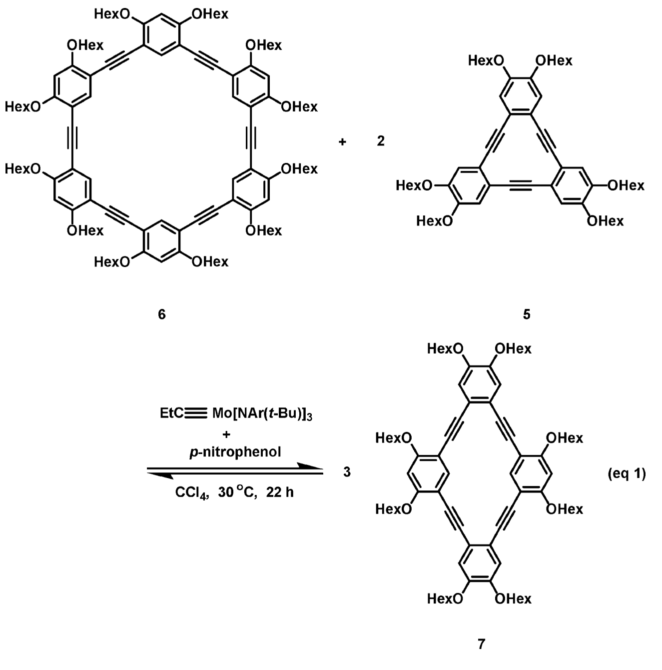


FIGURE 2. FD-MS of crude product from scrambling metathesis of macrocycle **5** and **6**.



Experimental Section

Macrocycle (5). In an argon-filled glovebox, a solution of molybdenum triamide[6] (7.5 mg, 0.011 mmol) and *p*-nitrophenol (4.7 mg, 0.034 mmol) in CCl_4 (1.0 mL) was added to a solution of monomer **4** (94.3 mg, 0.11 mmol) in CCl_4 (2.1 mL). The flask was sealed and removed from the glovebox. The resulting mixture was stirred for 22 h at 30 °C. After removal of the precipitate by vacuum filtration, the filtrate was concentrated in vacuo and the macrocyclic product was purified by column chromatography (*n*-hexane/CH_2Cl_2, 3/2, v/v) to give macrocycle **5** as a yellow solid (28.9 mg, 86%): mp 125−126 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.72 (s, 6H), 3.95 (t, $J = 7.6$ Hz, 12H), 1.80 (m, 12H), 1.30−1.50 (m, 36H), 0.90 (t, $J = 6.4$ Hz, 18H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.0, 119.6, 115.5, 91.8, 68.9, 31.5, 29.0, 25.6, 22.5, 14.0; MS (FAB) *m/z* 900.7 (66), 816.6 (15), 731.5 (7), 307.1 (20), 154.1 (100); HR-MS ($C_{60}H_{84}O_6$) calcd 900.6268, found 900.6269; TLC $R_f = 0.34$ (*n*-hexane/CH_2Cl_2, 1/1, v/v); GPC

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(12) See the Experimental Section for detailed characterization data.

(13) Macrocycle **6** was synthesized from the corresponding *m*-dialkoxybenzene monomer via precipitation-driven alkyne metathesis (see the Supporting Information for details). On MALDI-MS of the metathesis product, only hexameric (*m/z* = 1800) and pentameric (*m/z* = 1500) macrocycles were observed. Such a macrocycle mixture was subjected to the subsequent scrambling metathesis experiment without further separation.

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1090 (M_n), 1.00 (M_w/M_n). Anal. Calcd for $C_{60}H_{54}O_4$ (900.6): C, 79.96; H, 9.39. Found: C, 79.87; H, 9.44.

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Supporting Information Available: Characterization data for compound **3**, **4**, and precursors to **6**; experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

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