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Covalent Assembly of Molecular Ladders

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A current challenge for self-assembly is the synthesis of shape-persistent nanostructures with a high degree of structural control. These artificial macromolecules could ultimately approach the sophistication of biomolecules,[1] allowing atomic-level spatial control over multi-nanometer length scales in two and three dimensions, and the construction of molecular objects of size commensurate with top-down nanofabrication. Much like the current use of DNA as a structural element for nanotechnology,[2] a multitopic oligomer-based approach allows, in principle, the formation of complex nonsymmetrical structures by incorporating instructions for self-assembly into sequence. However, in contrast to small-molecule building blocks, the use of linear oligomers as components for nanostructure construction is relatively undeveloped, with a few exceptions.[3−8] Here we show that discrete oligomers are viable building blocks for fully covalent shape-persistent molecular grids. We have found that, using dynamic covalent chemistry (DCC),[9] complimentary *m*-phenylene ethynylene (*m*PE) oligomers will self-assemble into [*n*]-rung molecular ladders ($\mathbf{1}^n$, $n = 3-6$). In the largest case ($\mathbf{1}^6$, Figure 1), the core region is approximately 6.2 × 1.6 nm. In all cases, the desired ladder structure is the only product observed by MALDI mass spectrometry, although gel permeation chromatography (GPC) indicates an increasing fraction of high molecular weight byproducts with increasing *n*. These ladders represent the first step toward larger grids that will be developed as high precision nanofiltration membranes,[10] or as "smart-matrix" grids to position units for solar energy harvesting.[11]

Structures $\mathbf{1}^3-\mathbf{1}^6$ are similar to other reported finite, solution-phase molecular ladders based on zinc porphyrin[5] and aromatic amide[6] oligomers. However, to our knowledge, these are the first examples of molecular ladders directly assembled using DCC.[12] We chose imine formation and exchange reactions for rung construction, as they are well established in the synthesis of organic nanostructures[13] and in particular have been used by us to prepare *m*PE macrocycles.[14] These reactions are fast, and the products can be trapped by irreversible reduction. Furthermore, like a hydrogen bond, the imine bond is *directional*, which prevents homodimerization and could be of future use as a means to larger and more complicated structures.[8]

Oligomers $\mathbf{2}^n$ and $\mathbf{3}^n$ were prepared using a previously reported solid-phase method developed in our laboratory.[15] Ladder formation was carried out at room temperature by stirring a 3 mM chloroform solution of aldehyde-substituted $\mathbf{3}^n$ and a slight (5%) excess of amino-substituted $\mathbf{2}^n$ with scandium(III) triflate[16] (Scheme 1). At no point during the reaction did we observe a precipitate or cloudiness in the reaction mixtures, suggesting that these large ladder structures have good solubility, and that there is no formation of insoluble polymer network byproducts. After 5 h,[17] the reaction mixtures were quenched with sodium triacetoxyborohydride[18] to reduce the imines and facilitate analysis. After workup, the reaction products were analyzed by MALDI mass spectrometry and GPC. In addition, the shorter ladders $\mathbf{1}^3$ and $\mathbf{1}^4$ were isolated by preparatory GPC (57 and 37% yield, respectively) and characterized by ^{1}H NMR.[19]

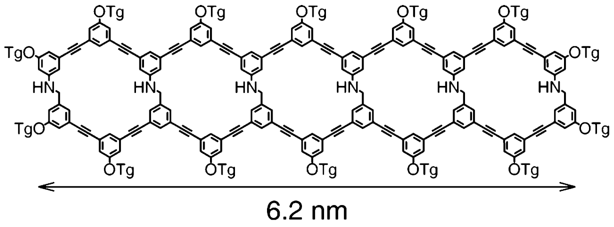
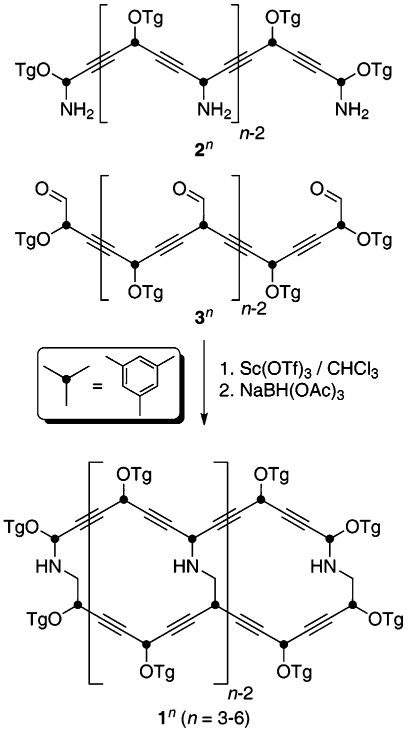


Figure 1. [6]-Rung ladder $\mathbf{1}^6$ (OTg = $O(CH_2CH_2O)_3CH_3$).

Scheme 1



MALDI spectra of the crude products are shown in Figure 2. Remarkably, in each case, the spectra are dominated by peaks assigned to $\mathbf{1}^3-\mathbf{1}^6$ (both M^+ and $M + Na^+$ ions are observed). The desired ladder structures are the only reasonable products corresponding to the observed molecular weights (the instrument is accurate to 0.05−0.1%). We do not observe any signals corresponding to out-of-register $\mathbf{2}^n\cdot\mathbf{3}^n$ adducts (which would occur at +18 au for each unreacted NH_2/CHO pair), or higher molecular weight polymers (i.e., $(\mathbf{2}^n)_x(\mathbf{3}^n)_y$, with $x + y > 2$). The small features at twice the desired molecular weight are assigned to gas phase aggregate dimers of $\mathbf{1}^n$ (i.e., $[\mathbf{1}^n{}_2\cdot Na^+]$), which have been observed for other shape-persistent macrocycles.[20]

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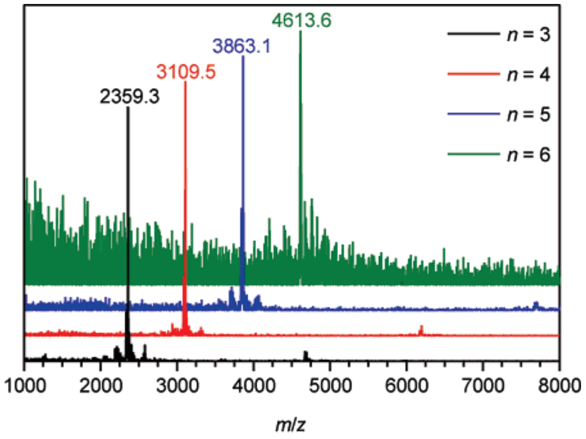

Figure 2. MALDI spectra of $\mathbf{1}^3$–$\mathbf{1}^6$ (TCNQ matrix). Calculated molecular weights: [$\mathbf{1}^3$ + Na$^+$] 2358.7; [$\mathbf{1}^4$ + Na$^+$] 3110.6; [$\mathbf{1}^5$ + Na$^+$] 3862.4; [$\mathbf{1}^6$ + Na$^+$] 4614.3.

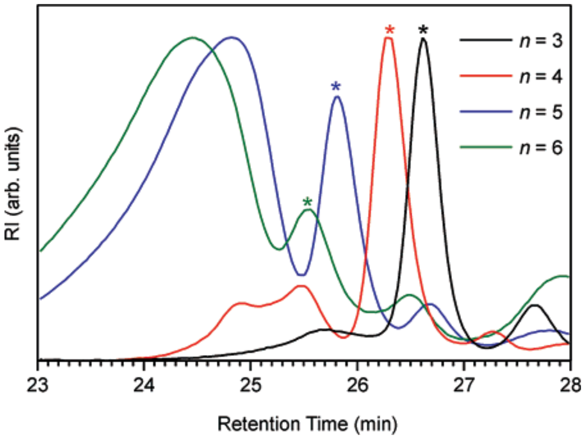

Figure 3. GPC traces for crude $\mathbf{1}^3$–$\mathbf{1}^6$. The traces are normalized to the height of the largest peak. The target ladder structures are labeled with the $*$ symbol. $\mathbf{1}^3$, $t_r = 26.6$ min, $M_n = 2080$, PDI = 1.03; $\mathbf{1}^4$, $t_r = 26.3$ min, $M_n = 2720$, PDI = 1.03; $\mathbf{1}^5$, $t_r = 25.8$ min, $M_n = 4050$, PDI = 1.02; $\mathbf{1}^6$, $t_r = 25.6$ min, $M_n = 4740$, PDI = 1.02 (polystyrene standards).

In contrast to the clean MALDI spectra, GPC of the product mixtures suggests the formation of high molecular weight byproducts (Figure 3). For $\mathbf{1}^3$ and $\mathbf{1}^4$, the desired molecular ladders are formed in high yield (71 and 62%, respectively, by deconvolution[19] of the GPC traces). However, for the larger $\mathbf{1}^5$ and $\mathbf{1}^6$, the yields are much lower (17 and 10%), and broad peaks are observed at high molecular weight. We believe that these are high molecular weight species which have widely varying molar mass and thus do not contribute to a unique MALDI signal.[21] It is unlikely that aggregation of $\mathbf{1}^5$ and $\mathbf{1}^6$ contributes to these features as the GPC trace of $\mathbf{1}^5$ is concentration independent,[19] and the literature[22] suggests that aggregates bound by weak intermolecular forces should yield a single asymmetric (tailing) GPC peak, in contrast to the distinct product/byproduct peaks that have been observed here.

There are two possible explanations for the trend toward higher molecular weight byproducts with increasing *n*. The equilibrium distribution may be less populated by the desired [*n*]-rung ladder as *n* increases. Alternatively, the longer oligomers $\mathbf{1}^5$ and $\mathbf{1}^6$ may be prone to misassembly, the products of which are kinetically trapped by multiple imine bonds. The GPC trace was essentially unchanged when the formation of $\mathbf{1}^5$ was carried out at elevated temperature (75 °C, in a sealed tube).[19] This suggests that the system may not be kinetically trapped at large *n*. Further studies to probe the mechanism are underway, as is the development of strategies to overcome these limitations.

To summarize, we have demonstrated the self-assembly of [*n*]-rung molecular ladders $\mathbf{1}^n$ using DCC to cross-link discrete *m*PE oligomers. Despite their large aromatic surface, these structures show good solubility under the reaction conditions. MALDI spectra of the unpurified products are remarkably clean and provide direct evidence for the formation of the desired ladder structures $\mathbf{1}^n$. However, GPC traces suggest that, as the oligomer length increases, the yield decreases as a greater proportion of higher molecular weight material is observed. Nevertheless, these structures demonstrate the utility of discrete oligomers as components for two-dimensional nanostructure assembly.

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Supporting Information Available: Experimental procedures for the synthesis of $\mathbf{2}^n$ and $\mathbf{3}^n$ and the self-assembly of $\mathbf{1}^n$, ^{1}H NMR spectra of $\mathbf{1}^3$ and $\mathbf{1}^4$, deconvoluted GPC traces, concentration dependence of the GPC trace of $\mathbf{1}^5$, and formation of $\mathbf{1}^5$ at 75 °C. This material is available free of charge via the Internet at http://pubs.acs.org.

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