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14. ABSTRACT

The central goal of our research program is to exert unprecedented control over macroscopic properties in polymeric materials by tuning their structure at the molecular level. We aim to create new synthetic methods for precision control of copolymer sequence, a goal which has been called the “Holy Grail” of polymer science. One strategy involves a macromolecular template that is programmed to direct sequence-controlled chain growth polymerization. We will synthesize a ?-conjugated “parent” polymer by iterative exponential growth (IEG), attach cyclic olefin “daughter” monomers, and then polymerize the daughter monomers via ring-opening metathesis

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Final Report: STIR: Sequence-Controlled Polymerization on Facially Amphiphilic Templates at Interfaces

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Enter List of papers submitted or published that acknowledge ARO support from the start of the project to the date of this printing. List the papers, including journal references, in the following categories:

(a) Papers published in peer-reviewed journals (N/A for none)

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Number of Presentations: 0.00

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Patents Submitted

Patents Awarded

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NAME	PERCENT_SUPPORTED	Discipline
Abhirup Dutta	0.10	
FTE Equivalent:	**0.10**	
Total Number:	**1**	

Names of Post Doctorates

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Total Number:	

Names of Faculty Supported

NAME	PERCENT_SUPPORTED	National Academy Member
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FTE Equivalent:	**0.10**	
Total Number:	**1**	

Names of Under Graduate students supported

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Utthara Ramesbabu	0.10	Materials Science and Engineering
FTE Equivalent:	**0.10**	
Total Number:	**1**	

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NAME

Abhirup Dutta, M.Eng. 2016

Total Number: 1

Names of personnel receiving PHDs

NAME

Total Number:

Names of other research staff

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FTE Equivalent:

Total Number:

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Sequence-Controlled Polymerization on Facially Amphiphilic Templates at Interfaces

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Materials Science & Engineering, Rensselaer Polytechnic Institute (Troy, NY)

1. Foreword

The central goal of our research program is to exert unprecedented control over macroscopic properties in polymeric materials by tuning their structure at the molecular level. We aim to create new synthetic methods for precision control of chain length and copolymer sequence, a goal which has been called the "Holy Grail" of polymer science.[1] One canonical strategy involves a macromolecular template that is programmed to direct sequence-controlled chain growth polymerization. We will synthesize a π-conjugated "parent" polymer by organometallic iterative exponential growth (IEG),[2] attach cyclic olefin "daughter" monomers via dynamic covalent bonds, and then polymerize the daughter monomers via ring-opening metathesis polymerization (Figure 1). This method is intended to ***transfer sequence information*** from a copolymer made by stepwise methods to an olefin copolymer ***for which no stepwise synthesis exists***. Dynamic covalent bonding of daughter monomers to parent chain enables facile detachment of the daughter polymer, regeneration of the template, and re-attachment of a subsequent batch of daughter monomer. Hence, a continuous multi-batch process can theoretically produce a stream of daughter polymer product from a small amount of the cost- and labor-intensive parent polymer. Control of sequence in synthetic polymers is expected to enable unprecedented control of polymer properties, single chain folding, and self-assembly, hence leading to transformative materials to enable a broad range of technologies of interest to the Army Research Office.

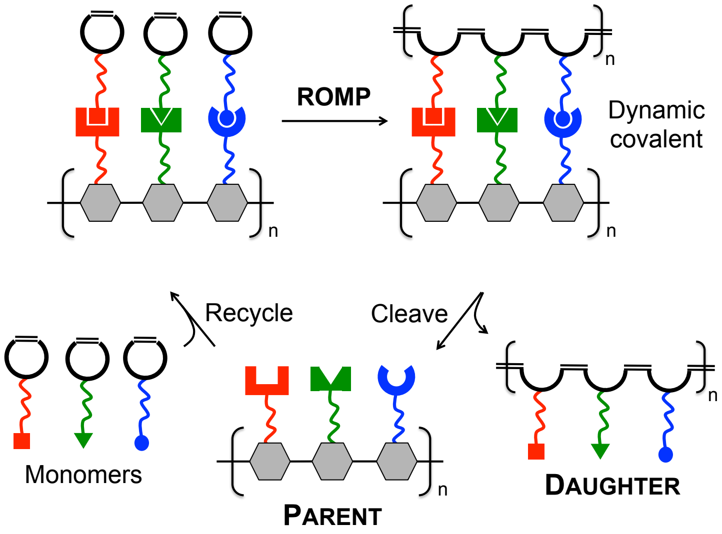

Figure 1. Template polymerization of daughter monomers in the side chains of a parent polymer, followed by liberation the daughter, and finally replenishing the template for further batches of template polymerization.

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4. Statement of the Problem Studied

The central goal of our research program is to exert unprecedented control over macroscopic properties in polymeric materials by tuning their structure at the molecular level. We aim to create new synthetic methods for precision control of chain length and copolymer sequence, a goal that has been called the “Holy Grail” of polymer science. One canonical strategy involves a macromolecular template that is programmed to direct sequence-controlled chain growth polymerization. One canonical strategy involves a macromolecular template that is programmed to direct sequence-controlled chain growth polymerization. We have synthesized a π-conjugated “parent” polymer by organometallic iterative exponential growth plus side chain functionality (IEG+), attached cyclic olefin “daughter” monomers via covalent bonds, and then polymerized the daughter monomers via ring-opening metathesis polymerization (Figure 2).

Copolymers with statistical sequence distributions (*e.g.* block, gradient, random) have been extensively studied due to their unique and interesting physical properties.[3] Such control of microstructure is rudimentary, however, when compared to the sophisticated structure and function of ribosomally translated proteins. We aim to creatively mimic one essential feature of protein synthesis – use of a ***template parent polymer to encode a sequence of comonomers*** into a daughter polymer – in a fully synthetic scheme.[4] In the context of synthetic chemistry, this objective presents a “chicken-and-the-egg” problem: in order to obtain a sequence defined daughter polymer, a sequence-defined parent polymer must first be synthesized. One approach is to circumvent the issue altogether through the use of a preexisting biopolymer (peptide or DNA) as the template.[5] The alternative, more challenging and also more ***chemically diverse approach***, is to synthesize a fully abiotic template by iterative coupling methods. Iterative divergent-convergent coupling, or ***iterative exponential growth*** (IEG), is a key strategy to obtain precisely defined π-conjugated polymers.[2a] For example, stepwise synthesis of poly(3-hexyl thiophene) by Stille coupling yields gram-scale amounts of P3HT with a ***single peak in the MALDI*** spectra.[6] Recently, Johnson and coworkers combined IEG with orthogonal side chain functionality (IEG+),[2b] which is conceptually similar to our method to synthesize the parent template polymer. Going beyond the precision synthesis of the parent polymer, we will direct the sequence-specific translation of parent to daughter polymer. Specifically, we will functionalize the pendant side chains of precisely defined π-conjugated polymers with olefin daughter monomers. Subsequently, the daughter monomers in the parent side chains will be polymerized by ROMP, and the resulting daughter polymer then liberated from the template via dynamic covalent bonding.

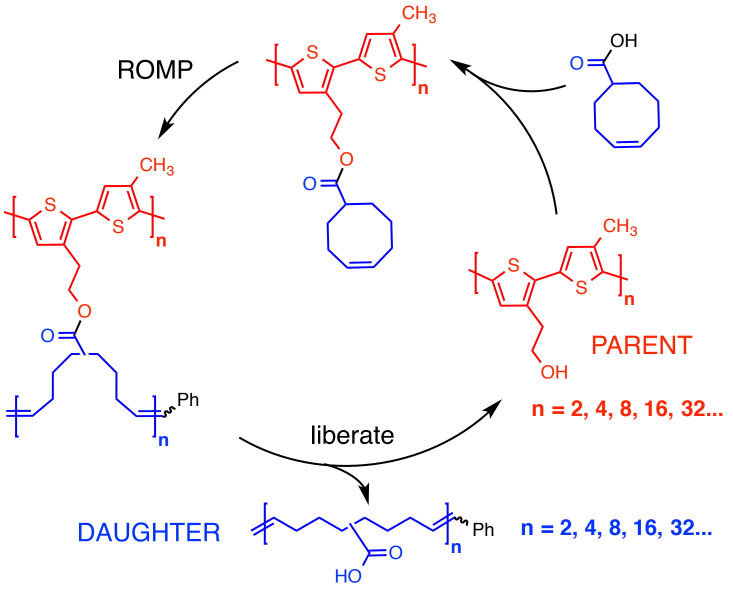


Figure 2. ROMP of COE templated by a polythiophene (T-ROMP).

5. Summary of Most Important Results

We succeeded in ***developing the first template polymerization methodology*** for ROMP performed on the side chains of a parent π-conjugated polymer. Specifically, cyclooctenes and norbornenes were covalently attached to the side chains of precisely defined oligomers of thiophene prepared by iterative exponential growth (n = 2, 4, 8, 16…) with side chain functionality, followed by attachment of cyclic olefins, and finally ROMP to yield daughter polymer. The resulting materials exhibit a single peak by MALDI and their fragmentation was examined by ms/ms. Reaction conditions were optimized to yield daughter polymers that replicate the precise molecular weight of the parent polymer. This ***proof-of-principle*** bolsters the ***feasibility of precision template strategies*** toward sequence-control in fully synthetic materials.

5.1. Template "parent". For the parent polymer, we targeted alternating polythiophenes with pendant functional groups on every other thiophene unit. In this initial study, silyl-protected hydroxyl groups were employed as the functional group handle for further modifications after the organometallic coupling. We selected Stille coupling due to the excellent functional group tolerance, which enables complex multistep synthesis. Following the iterative Stille couplings, the protecting groups are cleaved in mild conditions to give hydroxyl groups for further functionalization.

5.2. Daughter monomer. A *cis*-cyclooctene bearing a pendant carboxylic acid group, was synthesized on the multigram scale, in three steps, following literature procedures with minor modifications. The details of the synthetic procedures are given in the supporting information (Appendix A). Briefly, commercially available cyclooctadiene (COD) was brominated and purified by distillation, followed by nucleophilic substitution with cyanide anion, and finally oxidation to the carboxylic acid product. The final product is purified by distillation and the clear, colorless oil slowly solidifies upon standing at 4 °C. Each step gave moderate to good yields. This monomer was then covalently attached to the polythiophene template using simple carbodiimide coupling chemistry, in excellent yield.

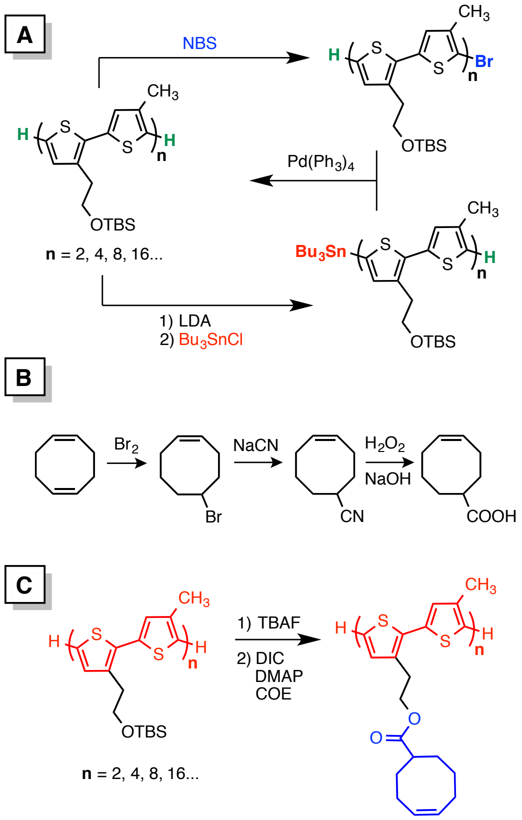


Figure 3. (A) iterative exponential growth of the template, (B) synthesis of the daughter monomer, and (C) attachment of the daughter monomer to the side chains of the parent.

5.3. Control Experiments. Before delving into the template polymerization studies, we first examined the reactivity of model monomers attached to single thiophene units, *i.e.* without any polythiophene template. This effort is required because of the sensitivity of ROMP to the steric and electronic nature of the monomer substrates, as well as reaction conditions (time, temperature, solvent, and concentration). Owning to the time and labor-intensive nature of the template synthesis, it is prudent to first optimize polymerization conditions for batch polymerizations and copolymerizations for model monomers, and then apply the principles learned to the template process.

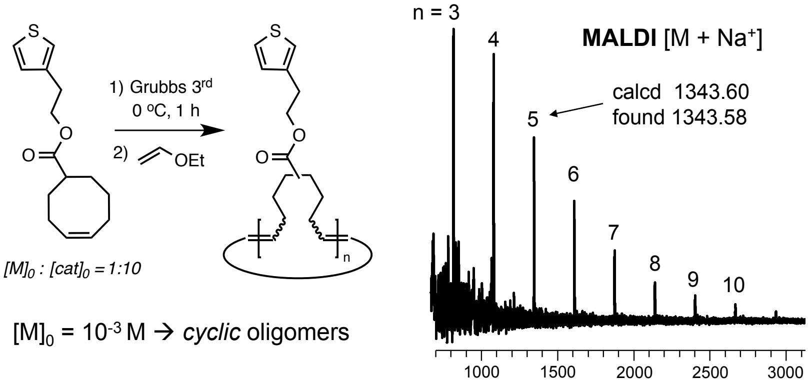


Figure 4. Polymerization of cyclooctene (COE) attached to a single thiophene unit (no template effect, negative control experiment) in dilute DCM solution. The MALDI data shows cyclic oligomers with a broad distribution of molecular weights.

The COE monomer attached to a single thiophene unit (which does not have any template effect) was subjected to ROMP conditions in dilute solution. Specifically, ROMP was performed in anhydrous DCM under nitrogen atmosphere at 0 °C for 1 h, with a monomer to catalyst ratio of 10:1, at concentrations varying from 10^{-3} to 10^{-1} M. We observed a broad distribution of MALDI peaks indicating a disperse population of cyclic oligomers (from n = 3 to 11). The important metric for success of this control experiment is the absence of linear oligomers bearing styrenyl end groups derived from the Grubbs catalyst. This is important because the conditions are sufficiently dilute to yield only cyclic oligomers, suggesting that this concentration regime is appropriate for template synthesis in which we aim to avoid inter-template reactivity. We found that an initial monomer concentration of 10^{-3} M satisfies this requirement for the homopolymerization of COE.

Next, we examined copolymerization of COE with other cyclic olefin models monomers. We hypothesized that using a high ring strain monomer at the alpha position of a template would favor initiation at the alpha site, followed by propagation of lower ring strain monomer along the backbone of the template. To test the feasibility of this idea, we first needed to confirm cross-propagation proceeds for a given pair of high/low ring strain monomers. Our first attempt involved a cyclobutene comonomer, which unfortunately failed. Although the cyclobutene route was unsuccessful, norbornene works very well. Again, we started with a control experiment – batch copolymerization of norbornene and cyclooctene in a 1:1 ratio. Fortunately, these two monomers indeed cross-propagate efficiently. We observed a series of peaks in the ESI ms indicative of NBE/COE cyclic co-oligomers, which proves the monomer pair is capable of efficient cross-propagation (Figure 5).

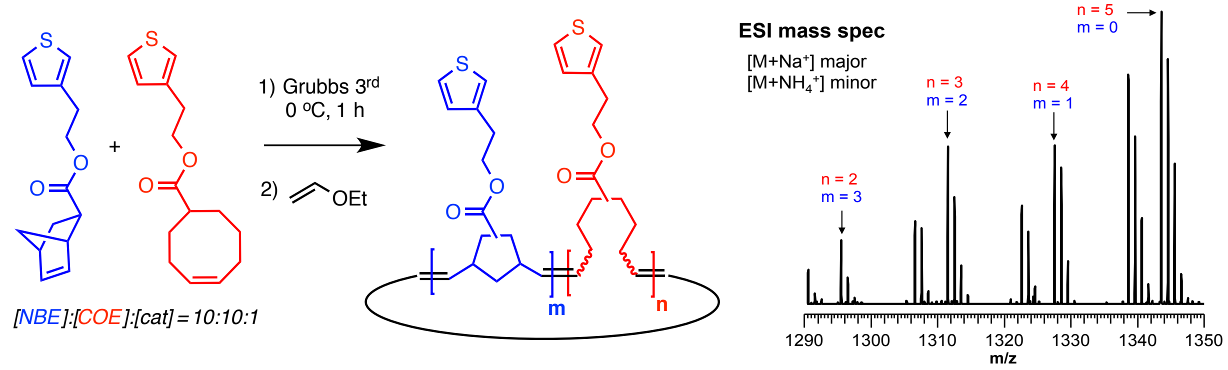


Figure 5. Copolymerization of cyclooctene (COE) and norbornene (NBE) coupled to single thiophene units (no template effect) yields cyclic co-oligomers with a broad distribution of MW and composition.

It is reasonable to speculate that the high ring strain NBE monomer is consumed firstly, followed by cross-propagation and subsequent consumption of COE, to form blocky co-oligomers in this condition. Importantly, this phenomenon will be exploited in our template polymerization efforts (*vide infra*); a template bearing a single NBE unit at the alpha position, with all remaining sites bearing COE monomers will putatively enable exclusive initiation at the alpha position, followed by end-to-end polymerization of the COEs.

5.4. Templated Ring-Opening Metathesis (T-ROM). After immobilization of COE on the thiophene template, the cyclic monomers are then polymerized using T-ROM with the Grubb's 3rd generation catalyst. Optimization of the T-ROM reaction conditions was key to success: in order to ensure quantitative ***intra-template propagation***, with no detectable ***inter-template*** reactions, we found that dilute conditions (10^{-3} M in DCM) and low temperatures (0 °C) were required. For example, the simplest template, with just two COEs, is shown in Figure 6:

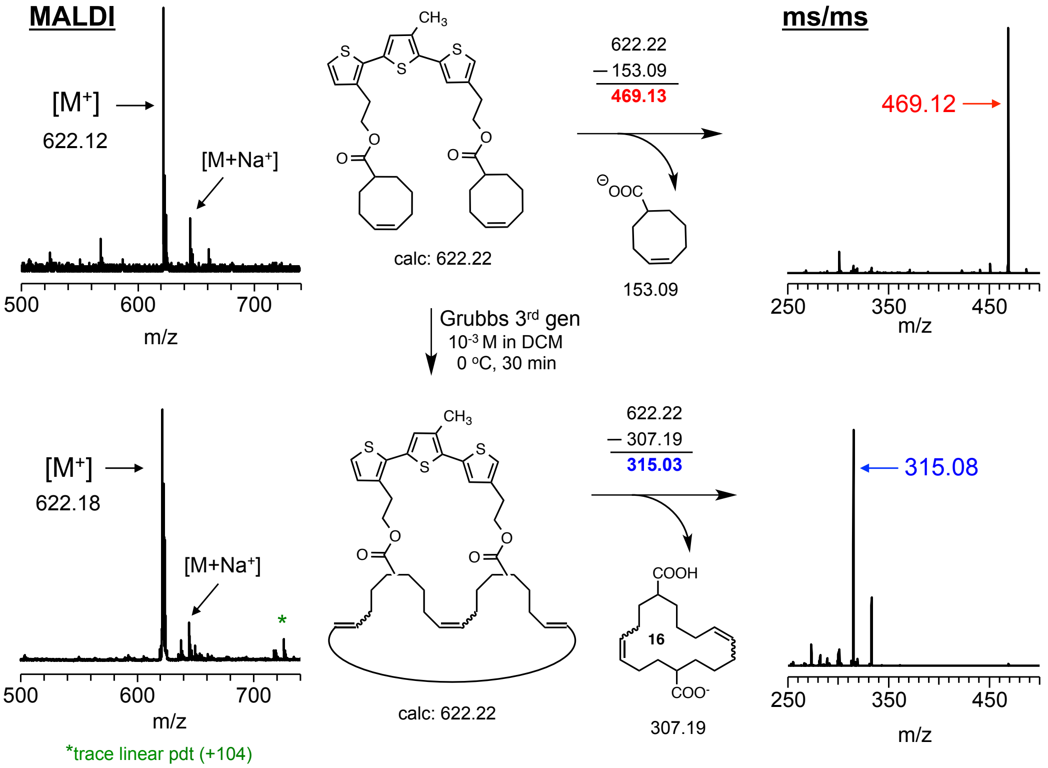


Figure 6. The first example of template ring-opening metathesis (T-ROM) confined to the side chains of a π-conjugated thiophene trimer bearing two COE units. After treatment with the Grubbs catalyst, MALDI shows a single predominant molecular ion with the same mass as the starting material. Fragmentation in ms/ms further reveals that the template product is in fact the 16 membered macrocycle shown (as a mixture of regioisomers and diastereomers). The asterisk indicates trace amount of linear dimer product with styrenyl end group.

Upon subjecting the template to the T-ROM conditions described above, NMR spectra of the crude product revealed complete conversion of the COE olefinic protons (δ 5.7 ppm) to their ring-opened analogue (δ 5.3 ppm). The MALDI spectra of the resulting product exhibited a single major peak with the same exact mass as the starting compound. This evidence suggests that the two COE monomers underwent T-ROM to give a 16-membered ring immobilized on the template. Indeed, this hypothesis was confirmed by MALDI ms/ms, which showed fragmentation product consistent with loss of the 16-membered carbon macrocycle bearing two carboxylic groups.

No traces of any higher degrees of polymerization were detected by MALDI or GPC, confirming that the ***dilute conditions forbid inter-template metathesis*** in our optimized conditions. Interestingly, there is a trace amount of linear dimer evident by NMR and MALDI (green asterisk in Figure 6). This minor product is the dimer of COE with a styrenyl end group (m/z M+104) derived from the Grubb's 3rd generation catalyst. The observation can be rationalized either kinetically or thermodynamically. That is, perhaps the templates undergo linear TROM rapidly but the subsequent ring-closing to give the macrocycle is sluggish on the time scale of the experiment, or perhaps the cyclic and linear products rapidly establish an equilibrium to minimize free energy. We are currently exploring the extent to which the relative abundance of cyclic versus linear product can be tuned by optimization of the time, temperature and concentration in the reaction conditions to distinguish between these two possibilities.

It is noteworthy that at higher concentrations (above 10^{-2} M) or longer reaction times (hours), substantial extents of secondary metathesis do occur. In fact, at 10^{-1} M, an insoluble but solvent-swollen (cross-linked) gel was obtained in a few minutes. These observations highlight the ***necessity of careful optimization of the T-ROM*** conditions.

Encouraged by the observation of NBE/COE co-oliogomers by MALDI (Fig. 5), we proceeded to synthesize a thiophene template containing one NBE unit and one COE unit in the side chains. The previously optimized polymerization conditions were employed to yield a parent-daughter product, which is the linear hetero-dimer of NBE and COE attached by two ester linkages to the template. NMR confirmed complete disappearance of olefinic signals for COE and NBE monomers, replaced by a feature corresponding to the ring-opened olefins (δ 5.3 ppm), and MALDI showed a single predominant peak corresponding to the linear heterodimer (m/z 806). Combined, these data support the applicability of the NBE/COE pair for T-ROMP.

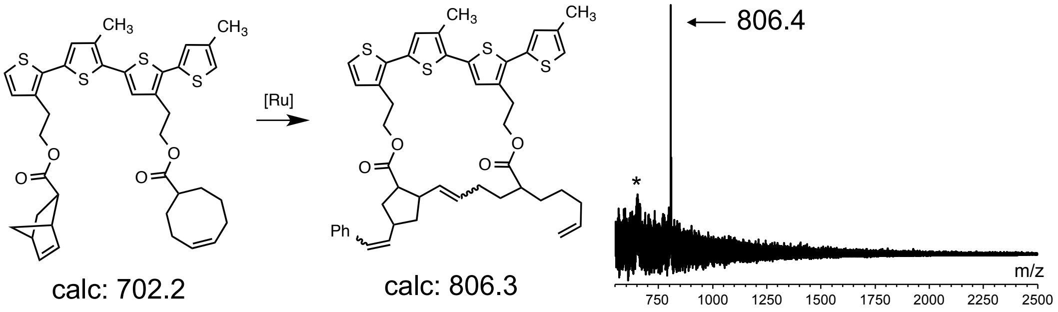


Figure 7. Templated copolymerization of NBE and COE on a model tetramer of thiophene. Both the linear and macrocyclic products are observed by MALDI, after completed monomer conversion confirmed by NMR.

Importantly, judicious optimization of the T-ROM conditions (10^{-3} M in DCM, 0 °C, **10 min**) was again critical for success. When the reaction is run for 10 min, the sole product shown in Figure 7 is obtained. If allowed to react for 30 min or longer, higher MW products corresponding to undesired metathesis between multiple templates start to appear in the MALDI spectra (see supporting info Figure S5). Hence, not only ***dilute conditions*** but also ***short reaction times*** are required in order to access the desired daughter dimer as the sole product.

5.5. Molecular Modeling. In parallel with our synthetic efforts, we are also exploring molecular models of our template parent and daughter polymers to gain insights into the chemical design principles. While it can be difficult to view the complexity of the proposed structures as 2D drawings: the 3D energy minimized conformations of both the unreacted template and the putative metathesis products are used to assess the length scale commensurability and the feasibility of a given template/daughter pair. For example, Figure 8 shows a molecular models for the linear hetero-dimer product of T-ROM (structure in Fig. 7). From these simulations, we can potently visualize the extended chain conformation of the relatively rigid thiophene backbone as well as the configurational freedom available to the daughter oligomer while still attached to the template. The models also provide an excellent method to evaluate the length scale commensurability of the daughter and parent polymer.

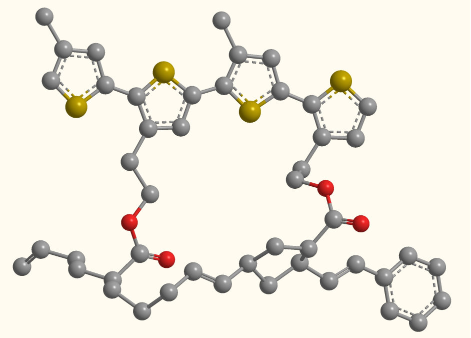


Figure 8. Molecular model of the linear hetero-dimer from T-ROM.

Furthermore, we use these simulations to predict the outcomes for T-ROM on longer templates. For example, Figure 9 shows snapshots from a molecular dynamics simulation on the n = 4 template after T-ROM, with a comparison of the linear and macrocyclic species. Clearly, the macrocyclization would induce substantially unfavorable bending strain on the parent thiophene backbone. Hence, we hypothesize that linear daughter polymers will predominate for templates of 4 units and higher. This prediction is in contrast to the observed predominance of macrocyclic product in the case of the n = 2 template, for which the thiophene backbone does not need to bend in order for the cyclization to occur.

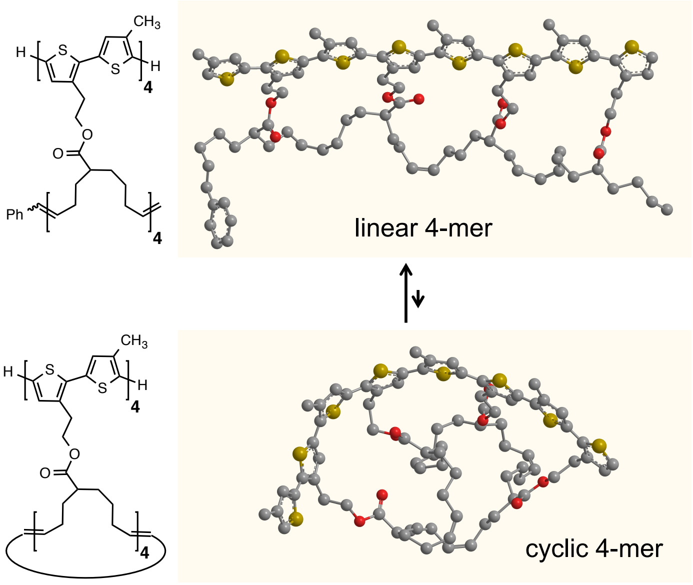


Figure 9. Molecular models of the putative daughter polymer of COE attached to the n=4 template.

While these initial models are rather preliminary, we are now working to identify the appropriate collaborators to pursue rigorous molecular dynamics simulations to shed light on the conformational energy minimizations. Moreover, we are exploring how density functional theory may shed light on the nature of the reactivity in these systems. We expect that theoretical framework will compliment our experimental chemistry efforts and enable rapid progress in this new and exciting field.

5.6. Ongoing Experiments. The longest template we have synthesized and purified to date is the 8-mer of thiophene, containing 4 pendant COE monomers. We are currently performing further iterative Stille couplings to give longer polythiophenes (n= 16, 32, 64…). The procedures for synthesis and purification require independent optimization for each template length. For example, the 4-mer is readily purified by silica gel chromatography, whereas the 8-mer requires size exclusion chromatography to isolate the analytically pure template. Additionally, solubility constraints on longer templates have led us to slightly modify our chemical design platform. Longer alkyl side chains (methyl is replaced with hexyl or ethylhexyl) on the alternating thiophene units, as well as bulkier protecting groups (tert-butyldimethyl silyl ether is replaced with tert-butyldiphenyl silyl ether) on the functional thiophene units, are employed to enhance solubility. Ultimately, we are confident that we can approach high molecular polymers with precisely defined chain length and comonomer sequence following rigorous optimization.

6. Bibliography

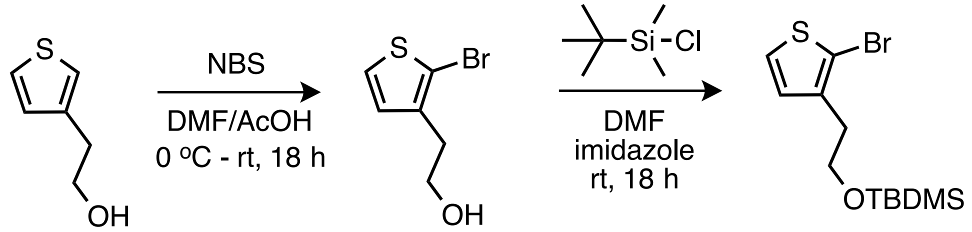
1. Lutz, J.-F., Sequence-controlled polymerizations: the next Holy Grail in polymer science? *Polym Chem-Uk* **2010,** *1* (1), 55-62.
2. (a) Wang, C. Y.; Glorius, F., Controlled Iterative Cross-Coupling: On the Way to the Automation of Organic Synthesis. *Angew Chem Int Edit* **2009,** *48* (29), 5240-5244; (b) Barnes, J. C.; Ehrlich, D. J. C.; Gao, A. X.; Leibfarth, F. A.; Jiang, Y. V.; Zhou, E.; Jamison, T. F.; Johnson, J. A., Iterative exponential growth of stereo- and sequence-controlled polymers. *Nature Chemistry* **2015,** *7* (10), 810-815.
3. Braunecker, W. A.; Matyjaszewski, K., Controlled/living radical polymerization: Features, developments, and perspectives. *Prog. Polym. Sci.* **2007,** *32* (1), 93-146.
4. (a) Sugiyama, J.; Yokozawa, T.; Endo, T., Production of Polymers from Polymers - Novel Template Polymerization Via Radical Ring-Opening Isomerization. *J. Am. Chem. Soc.* **1993,** *115* (5), 2041-2042; (b) Ida, S.; Terashima, T.; Ouchi, M.; Sawamoto, M., Selective Radical Addition with a Designed Heterobifunctional Halide: A Primary Study toward Sequence-Controlled Polymerization upon Template Effect. *J. Am. Chem. Soc.* **2009,** *131* (31), 10808-+; (c) Hibi, Y.; Tokuoka, S.; Terashima, T.; Ouchi, M.; Sawamoto, M., Design of AB divinyl "template monomers" toward alternating sequence control in metal-catalyzed living radical polymerization. *Polym Chem-Uk* **2011,** *2* (2), 341-347; (d) Nickels, P.; Dittmer, W. U.; Beyer, S.; Kotthaus, J. P.; Simmel, F. C., Polyaniline nanowire synthesis templated by DNA. *Nanotechnology* **2004,** *15* (11), 1524-1529; (e) Chen, W.; Schuster, G. B., Precise Sequence Control in Linear and Cyclic Copolymers of 2,5-Bis(2-thienyl)pyrrole and Aniline by DNA-Programmed Assembly. *J. Am. Chem. Soc.* **2013,** *135* (11), 4438-4449; (f) South, C. R.; Weck, M., Template-enhanced ring-opening metathesis polymerization. *Macromolecules* **2007,** *40* (5), 1386-1394.
5. (a) Tang, H. W.; Chen, L. L.; Xing, C. F.; Guo, Y. G.; Wang, S., DNA-Templated Synthesis of Cationic Poly(3,4-ethylenedioxythiophene) Derivative for Supercapacitor Electrodes. *Macromol Rapid Comm* **2010,** *31* (21), 1892-1896; (b) Uemura, S.; Shimakawa, T.; Kusabuka, K.; Nakahira, T.; Kobayashi, N., Template photopolymerization of dimeric aniline by photocatalytic reaction with Ru(bpy)(3)(2+) in the presence of DNA. *J Mater Chem* **2001,** *11* (2), 267-268; (c) Ruiz-Carretero, A.; Janssen, P. G. A.; Kaeser, A.; Schenning, A. P. H. J., DNA-templated assembly of dyes and extended pi-conjugated systems. *Chem Commun* **2011,** *47* (15), 4340-4347; (d) Chen, W.; Schuster, G. B., DNA-Programmed Modular Assembly of Cyclic and Linear Nanoarrays for the Synthesis of Two-Dimensional Conducting Polymers. *J Am Chem Soc* **2012,** *134* (2), 840-843; (e) Milnes, P. J.; McKee, M. L.; Bath, J.; Song, L. J.; Stulz, E.; Turberfield, A. J.; O'Reilly, R. K., Sequence-specific synthesis of macromolecules using DNA-templated chemistry. *Chem Commun* **2012,** *48* (45), 5614-5616; (f) McKee, M. L.; Milnes, P. J.; Bath, J.; Stulz, E.; Turberfield, A. J.; O'Reilly, R. K., Multistep DNA-Templated Reactions for the Synthesis of Functional Sequence Controlled Oligomers. *Angew Chem Int Edit* **2010,** *49* (43), 7948-7951.
6. Koch, F. P. V.; Smith, P.; Heeney, M., "Fibonacci's Route" to Regioregular Oligo(3-hexylthiophene)s. *J Am Chem Soc* **2013,** *135* (37), 13695-13698.

7. Appendix A - Supporting Information

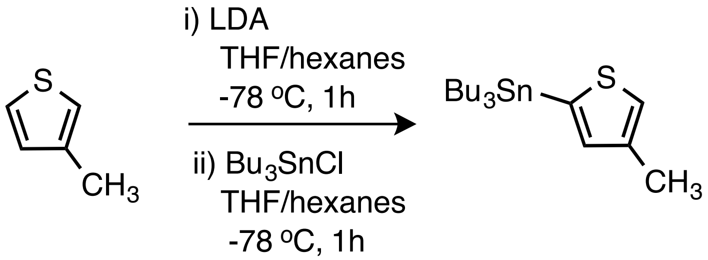
Materials and Methods.

Reactants and reagents including 3-thiophene ethanol, 3-methyl thiophene, N-bromo succinimide (NBS), tert-butyldimethylsilyl chloride, imidazole, tributyltin chloride, n-butyllithium (1.6M in hexanes), diisopropylamine, tetrakis triphenylphosphine palladium, cyclooctadiene, exo-3 norbornyl carboxylic acid, diisopropyl carbodiimide, and 4-dimethyl aminopyridine were purchased from Sigma-Aldrich as *ACS Reagent Plus* grade and used without further purification, except where noted otherwise. Toluene and dichloromethane were purchased from Sigma-Aldrich and purified over an MBraun SPS, followed by three freeze/pump/thaw cycle and were stored in flasks sealed by a Teflon valve (Chemglass AF-0093-05) in a nitrogen-filled glovebox (MBraun Unilab Pro). All reactions were carried out under inert gas atmosphere under strictly anhydrous conditions, except where noted otherwise. Standard Schlenk line techniques using an inert gas/vacuum double manifold were employed for all reagent manipulations.

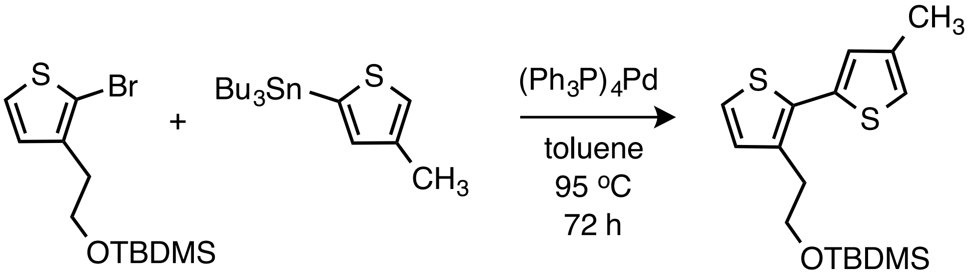
Synthetic Procedures.



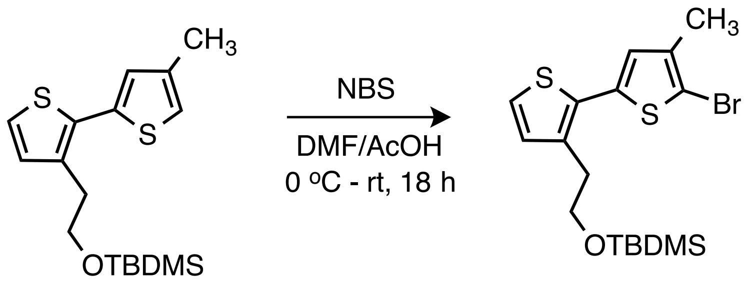
(2-(2-bromothiophen-3-yl)ethoxy)(*tert*-butyl)dimethylsilane (1). (a) In a 200 mL oven-dried Schlenk flask under nitrogen, 3-thiopheneethanol (10 mL, 89 mmol) was dissolved in anhydrous THF (100mL). The flask was cooled to 0 °C in the dark and recrystallized NBS (15.7 g, 89 mmol) was added in one portion under a gentle positive flow of nitrogen. The solution was allowed to warm to rt overnight. The reaction was quenched with saturated aq. sodium carbonate, and the crude reaction mixture was extracted with 3×50mL EtOAc, followed by washing with DI water and brine, drying over magnesium sulfate, and evaporation under reduced pressure to give a orange/brown oil. The crude oil was purified by vacuum distillation and by silica gel chromatography (hexanes:EtOAc, 9:1→2:1) to give the intermediate (10.6g, 57%). **(b)** Imidazole (8.6 g, 126 mmol, 2.5 equiv.) and tert-butyldimethyl silyl chloride (9.2 g, 60.8 mmol, 1.2 equiv.) were dissolved in DMF (100 mL) and the neat intermediate **1(a)** (10.5 g, 50.7 mmol, 1 equiv.) was added in a single portion. After the reaction mixture was stirred at 35 °C overnight, it was quenched with saturated aq. sodium carbonate, and the crude reaction mixture was extracted with 3×100mL EtOAc, followed by washing with 3×100mL DI water and brine, drying over magnesium sulfate, and evaporation under reduced pressure. The crude yellow oil was purified by distillation (75 °C, 0.15 torr) to give the title product (13.2g, 81%).



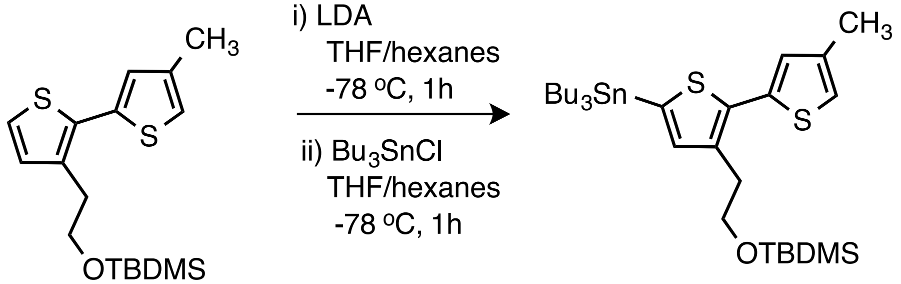
tributyl(4-methyl thiophen-2-yl) stannane (2). First, lithium diisopropyl amide (LDA) was prepared by mixing diisopropyl amine (7.15 mL, 51 mmol) with hexane (50 mL) and THF (50 mL) in a 250 mL oven-dried Schlenk flask, cooling to -78 °C, and injecting *n*-BuLi (2.5M solution, 20 mL, 50 mmol). Then, 3-methylthiophene (5 mL, 51 mmol) in THF (100 mL) was added dropwise via cannula transfer. After 30 min, tributyltin chloride (13.8 mL, 51 mmol) was injected via syringe and the reaction mixture was stirred for 1 h at -78 °C. Upon warming to rt overnight, the reaction was quenched with saturated aq. sodium carbonate, and the crude reaction mixture was extracted with 3×50mL EtOAc, followed by washing with DI water and brine, drying over magnesium sulfate, and evaporation under reduced pressure. The crude brown oil was purified by vacuum distillation (0.1 torr, 73 °C) to yield the pure product as a clear, colorless oil (15.3 g, 78 %).



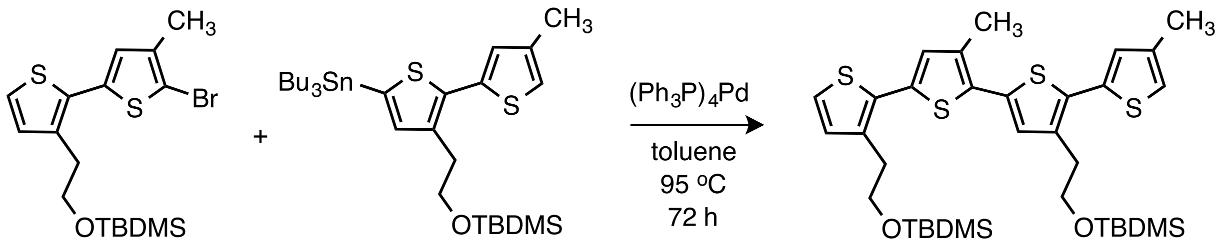
Stille Coupling, bithiophene parent “monomer” (3). In a 200 mL storage flask with a Teflon valve seal, **1** (1 g, 3.1 mmol) and **2** (1.33 g, 3.4 mmol) were dissolved in toluene (50 mL) and subjected to 3× freeze/pump/thaw/cycles. $Pd(Ph_3P)_4$ (36 mg, 0.031 mmol) as a slurry in toluene (1mL) was added and subjected to another 3× freeze/pump/thaw/cycles. The reaction vessel was sealed under vacuum with a Teflon valve, and then heated to 95 °C for 24-72 h, or until the appearance of a black precipitate. The reaction mixture was cooled to rt, diluted with 50mL THF, and stirred with 1M NaOH aq (100 mL) for 1 hr. The organic layer was washed with water and brine, dried over sodium sulfate, filtered, and concentrated under reduced pressure. Purification by silica gel column chromatography (hexane:toluene, 9:1, $R_f = 0.35$) gave the title cmpd as a colorless oil (477 mg, 45%).



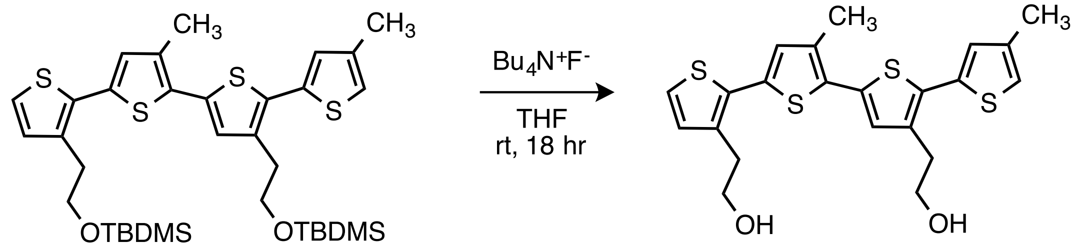
Bromination of bithiophene parent "monomer" (4). Same procedure as for **1(a)**. Amounts: Bithiophene **3** (477 mg, 1.4 mmol), NBS (0.25 g, 1.4 mmol), DMF (5 mL), AcOH (5 mL). Silica gel (EtOAc:toluene, 4:1), obtained 300 mg (49%).



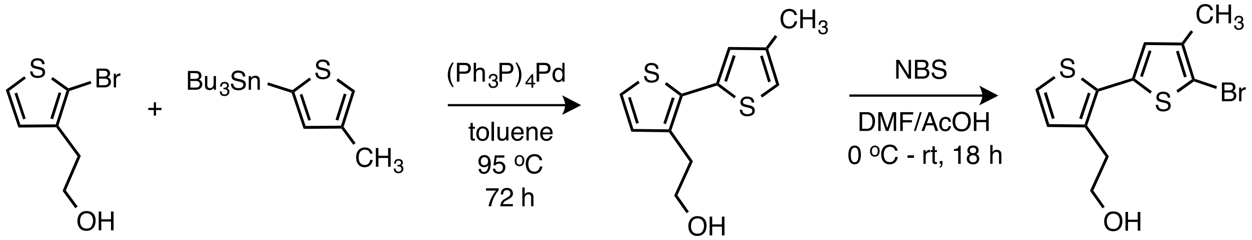
Stannylation of bithiophene parent "monomer" (5). Same procedure as for **2**. Amounts: diisopropyl amine (277 μL, 2 mmol), *n*-BuLi (784 μL, 1.95 mmol), bithiophene **3** (670 mg, 2 mmol), Bu_3SnCl (537 μL, 2 mmol). No purification required. Yield 1.03 g, 83%.



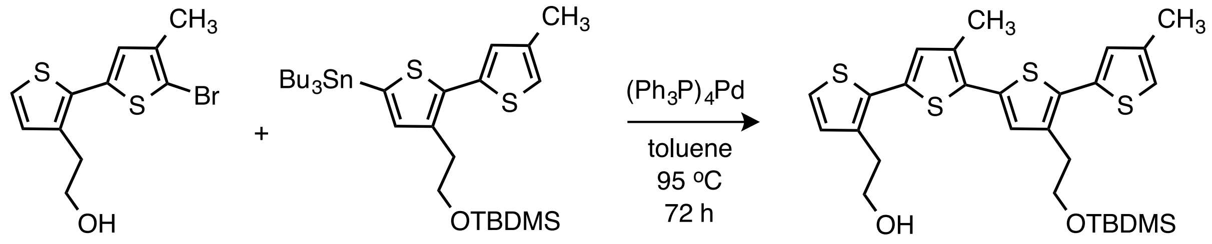
Stille Coupling, thiophene tetramer H/H (6). Same general procedure as for **3**. Amounts: **4** (100 mg, 0.24 mmol) and **5** (166 g, 0.26 mmol) in toluene (5 mL), $Pd(Ph_3P)_4$ (28 mg, 0.025 mmol). Purification on silica gel (hexane:toluene, 9:1) to give the pure product as a bright orange/yellow oil (136 mg, 84 %).



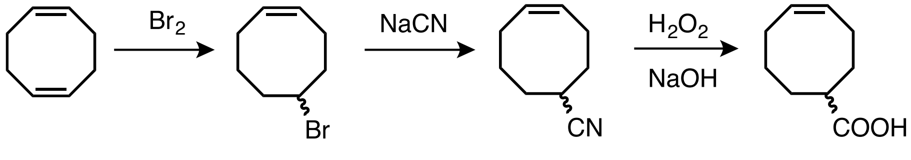
Deprotection of Side Chains. The protected template tetrathiophene (471 mg, 0.813 mmol) was dissolved in tetrabutylammonium floride (TBAF, 1M in THF, 2.5 mL 2.44 mmol) and stirred at room temperature overnight. The mixture was concentrated and purified by silica gel column chromatography (DCM:MeOH, 95:5, R_f ~ 0.28) to yield 193 mg (67%) pure cmpd.



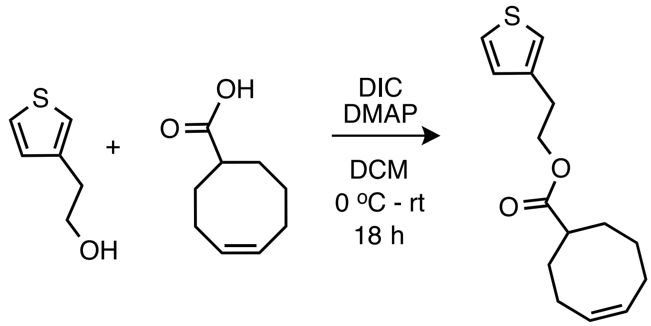
Brominated bithiophene, unprotected (7). Same procedures as for **3** and **4**. Yield 54%.



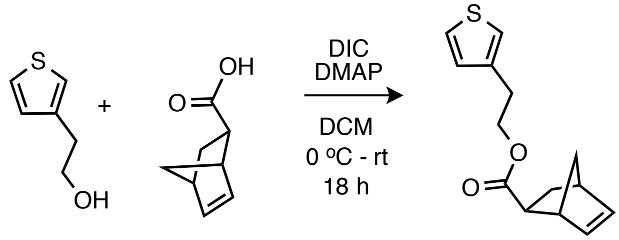
Hetero Template, n = 2 (8). Same general procedures as for **3**. Amounts: 7 (188 mg, 0.62) and 5 (433 mg, 0.69) in toluene (5 mL) with $Pd(Ph_3P)_4$ (72 mg, 0.06 mmol). Purification on silica gel (hexane:EtOAc, 2:1, R_f ~ 0.55) to give the pure product as a bright orange/yellow oil (295 mg, 85 %).



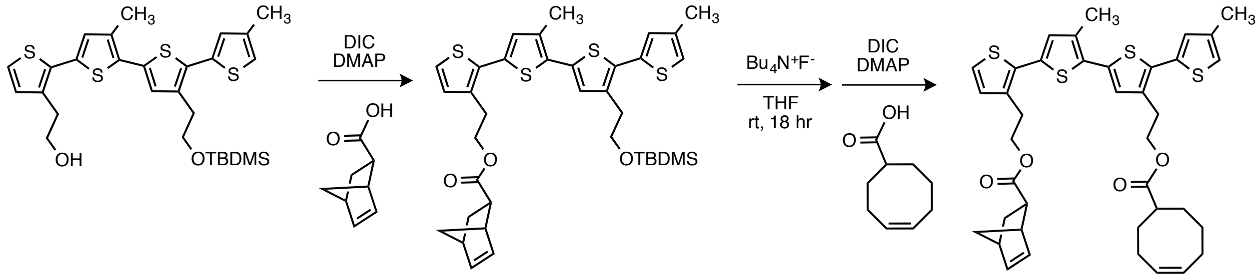
Z*-cyclooct-4-ene carboxylic acid.** Cyclooctadiene (COD, 25 mL, 0.2 mol) and HBr (37 mL) were mixed in a r.b. flask at room temperature overnight. The mixture was extracted with EtOAc and washed with water and brine. The organic layer was dried over sodium sulfate, filtered, and concentrated under reduced pressure to give a dark brown, ***malodorous oil. The crude was distilled (40 °C, 0.4 torr) to give a non-malodourous and colorless oil (27.5 g). Then, the brominated intermediate was dissolved in DMSO (100mL), sodium cyanide was added, and the mixture was heated at 110 °C for 2 h in a r.b. flask equipped with a reflux condenser. The product was extracted with EtOAc (3×500 mL) washed with DI water (3×500 mL) and brine (500 mL). The organic layer was dried over sodium sulfate, filtered, and concentrated under reduced pressure to give a dark brown oil, that was distilled (50 °C, 0.1 torr) to give a colorless oil. This intermediate (~10g) was mixed with 33 mL of aq. KOH (30% w/v) and 2.1 mL of H_2O_2 and heated to 120 °C for 48 h. Organics were extracted with EtOAc (3×200 mL) and the organic layer was set aside. The aqueous phase (containing the conjugate base of the product) was acidified with 40% phosphoric acid to pH 4 and extracted with EtOAc (3×200 mL). The organic layer was dried over sodium sulfate, filtered, and concentrated under reduced pressure to give a brown oil. Purification by distillation (120 °C, 0.15 torr) gave the pure product as a clear, colorless oil that slowly solidifies to a waxy consistency upon standing at 4 °C for a few days. Yield 12.7 g (41 %).



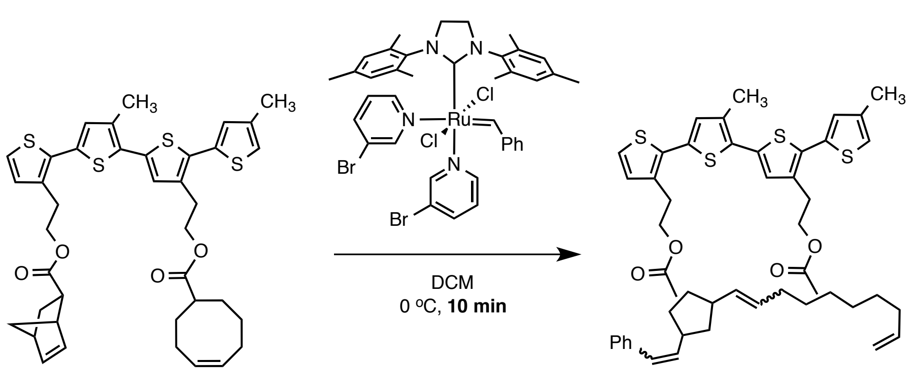
(*Z*)-2-(thiophen-3-yl) ethyl cyclooct-4-ene carboxylate (12). In a 10 mL oven-dried Schlenk flask, the cyclooctene monomer *Z*-cyclooct-4-ene carboxylic acid (158 mg, 1 mmol) and 2-(thiophen-3-yl)ethanol (115 µL, 1 mmol) were dissolved in anhydrous DCM (5 mL) under nitrogen and DMAP (15 mg, 0.1 mmol) was added in one portion. The solution was cooled to 0 °C and stirred for 10 min before injection of neat DIC (190 µL, 1.5 mmol). The reaction mixture was allowed to warm to rt and stirred overnight. A white precipitate (urea byproduct) was filtered from the yellow solution. Then, the solution was diluted with ethyl actetate (50 mL) and washed with water (3x50mL) and brine (50 mL). The organic layer was dried over sodium sulfate, filtered, and concentrated under reduced pressure to yield a yellow viscous oil. This crude oil was purified by silica gel column chromatography (EtOAc:hexanes, 9:1, $R_f \sim 0.4$) to give the title cmpd (182 mg, 67%).



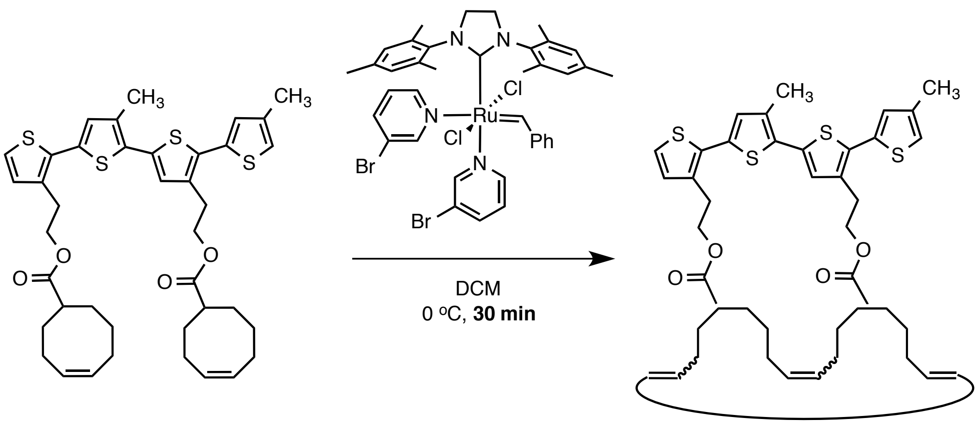
(*Z*)-2-(thiophen-3-yl) ethyl *exo*-norbornene carboxylate (13). Same procedure as **12**. Amounts: 2-(thiophen-3-yl)ethanol (516 µL, 4.6 mmol), *exo*-norbornene carboxylic acid (700 mg, 5 mmol), DMAP (56 mg, 0.46 mmol), DIC (1 mL, 6.9 mmol). Purified by silica gel column chromatography (EtOAc:hexanes, 9:1, $R_f \sim 0.5$) to give the title cmpd (895 mg, 78%).



Heterodimer Parent Template. Same general procedure as **12**. Briefly, the hetero-template **8** (295 mg, 0.53 mmol) was coupled to *exo*-norbornene carboxylic acid (80 mg, 0.58 mmol), using DMAP (6 mg, 0.053 mmol) and DIC (122 µL, 0.79 mmol) in DCM (5 mL) yielded 290 mg (89%). Deprotection with TBAF (1.5 mL of 1M soln in THF, 1.5 mmol) yielded 210 mg (72%). Coupling with *Z*-cyclooct-4-ene carboxylic acid (63 mg, 0.4 mmol) using DMAP (5 mg, 0.037 mmol) and DIC (86 µL, 0.56 mmol) in DCM (3 mL). Silica gel column (hexanes:EtOAc, 4:1) gave the pure product as a bright orange oil (220 mg, 84%).



Optimized Procedure for the heteroNBE/COE dimer by T-ROM. The heterobifunctional template, loaded with daughter monomers NBE and COE on n = 2 thiophene (10 mg, 14 µmol) was dissolved in anhydrous DCM (13 mL) under a nitrogen flow, in an oven-dried 25 mL Schlenk flask, and cooled to 0 °C on an ice water bath. Then, the Grubbs 3rd generation catalyst dissolved in DCM (1 mL) was injected via syringe, to give an initial template concentration of 10^{-3} M. After ***10 min***, ethyl vinyl ether (100 µL) was injected via syringe and the reaction mixture was stirred for an additional 30 min before warming to rt. The solvent was evaporated under reduced pressure and the residue was extracted with 1 mL of EtOAc:hexanes (1:1). Insoluble brown powder (catalyst) was removed by passing the crude mixture over a short plug of silica gel to afford a bright yellow product with no residual catalyst detected. Obtained 9.1 mg (90%).



Optimized Procedure for the homoCOE dimer by T-ROM. The heterobifunctional template, loaded with two COE daughter monomers on the n = 2 thiophene (10 mg, 15 µmol) was dissolved in anhydrous DCM (3 mL) under a nitrogen flow, in an oven-dried 25 mL Schlenk flask, and cooled to 0 °C on an ice water bath. Then, the Grubbs 3rd generation catalyst (13.3 mg, 15 µmol) dissolved in DCM (2 mL) was injected via syringe, to give an initial template concentration of 3×10^{-3} M. After ***30 min***, ethyl vinyl ether (100 µL) was injected via syringe and the reaction mixture was stirred for an additional 30 min before warming to rt. The solvent was evaporated under reduced pressure and the residue was extracted with 1 mL of EtOAc:hexanes (1:1). Insoluble brown powder (catalyst) was removed by passing the crude mixture over a short plug of silica gel to afford a bright yellow product with no residual catalyst detected. Obtained 8.7 mg (87%).

NMR Spectra

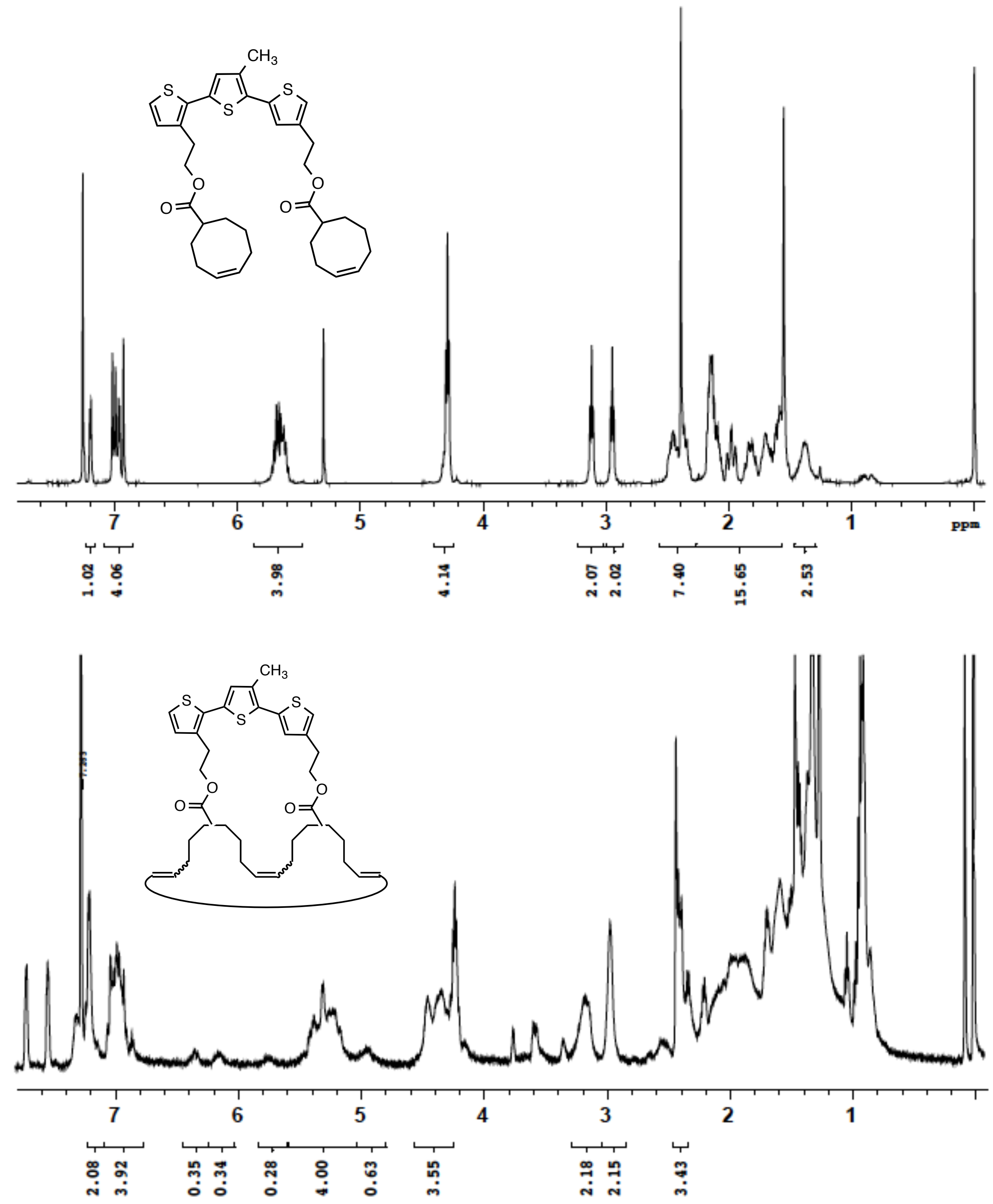


Figure S1. ^{1}H NMR spectra (CDCl3, 0.03% TMS) for the (A) template bearing two COE units and (B) the product of T-ROM, showing complete disappearance of the monomer olefin resonance.

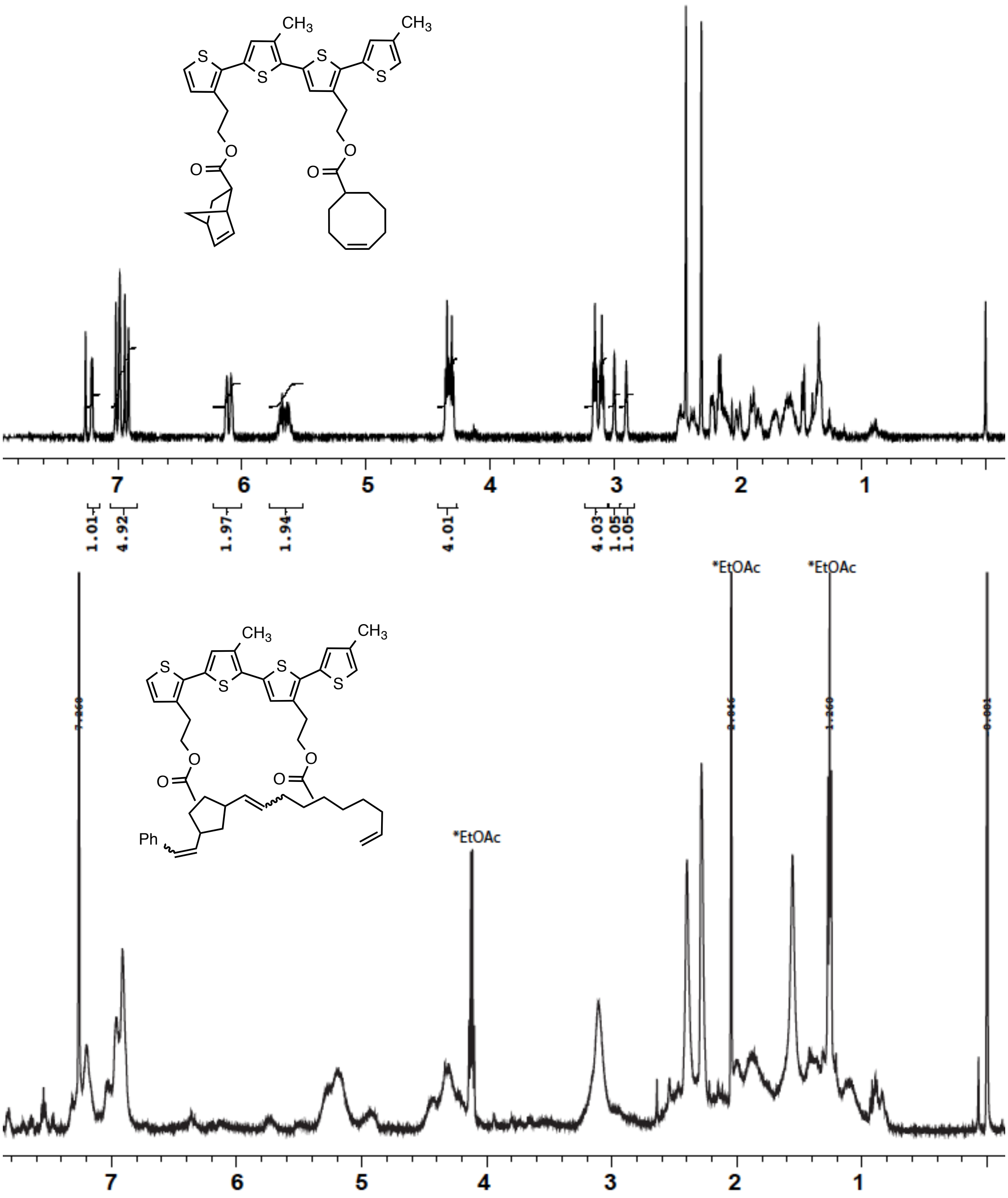


Figure S1. ^{1}H NMR spectra (CDCl3, 0.03% TMS) for the (A) template bearing one NBE and one COE unit and (B) the product of T-ROM, showing complete disappearance of the monomer olefin resonances.

MALDI Spectra

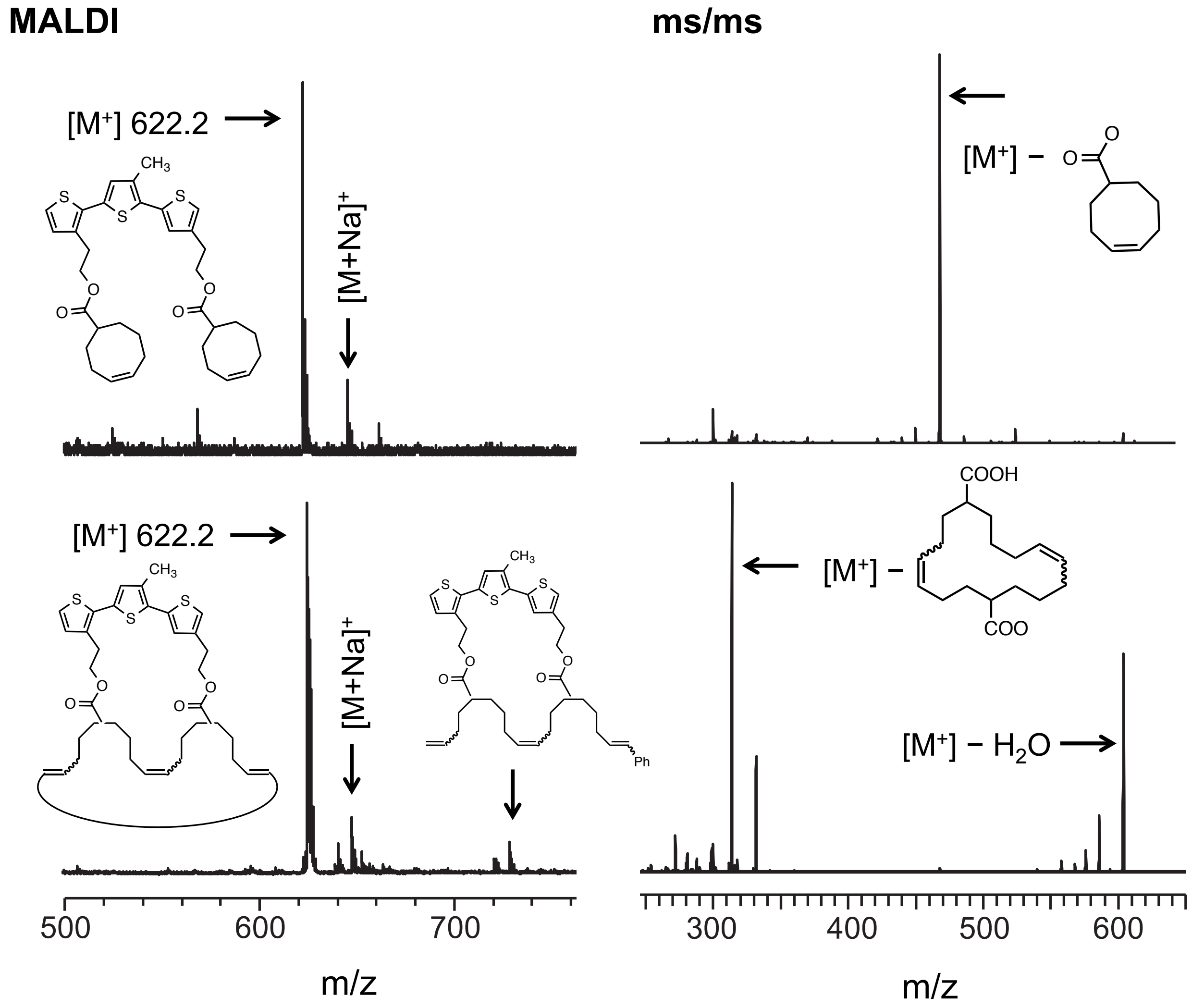


Figure S3. MALDI spectra of (A) the template bearing two COE daughter monomer units and (B) the product of T-ROM, a cyclic COE dimer.

Both MALDI spectra show a predominate peak at the same mass. Both also show a minor Na adduct peak. The product of T-ROM contains trace amount of linear dimer, [M+104].

Fragmentation by ms/ms of the ESI peak at 622.2 was performed to confirm the structure. The template (C) shows a fragment peak corresponding the parent ion with lass of one COE-COO daughter unit, whereas (D) a major fragment corresponds to loss of the daughter COE dimer by cleavage from the template. The other fragment at 604 represents the molecular ion minus one equivalent of H_2O.

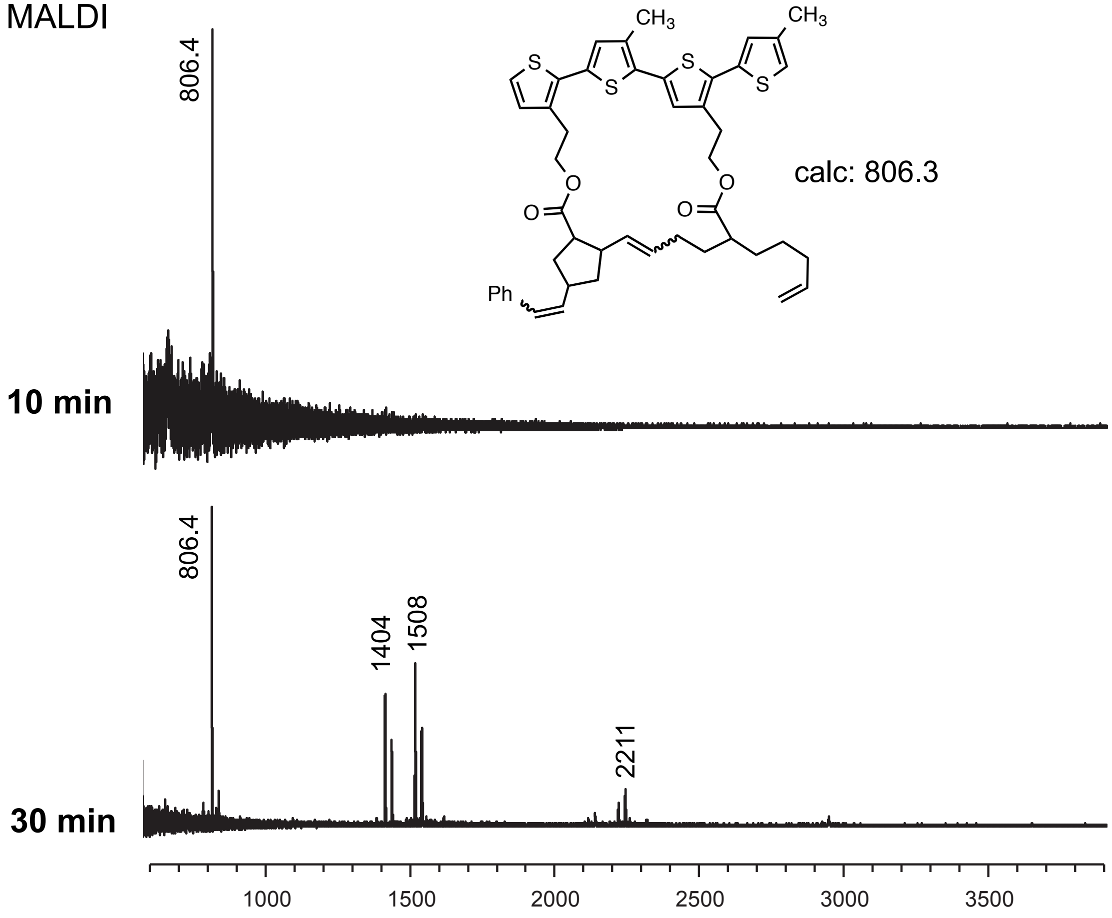


Figure S4. MALDI spectra of the NBE/COE heterodimer T-ROM product. At 10 min, only the linear daughter product is observed. At 30 min, inter-template metathesis becomes evident.

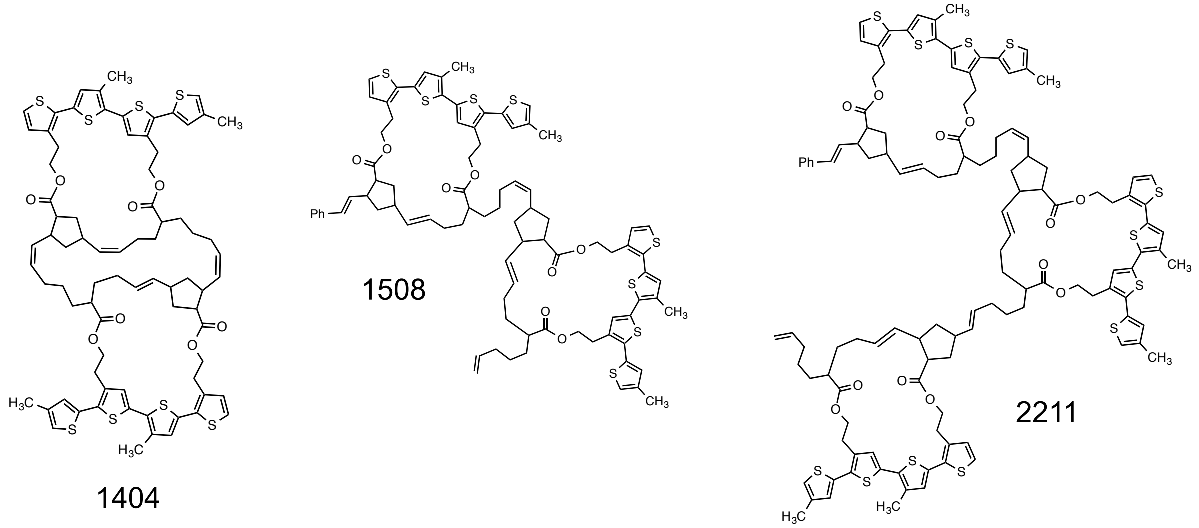


Figure S5. Example structures matching the high mass peaks in Figure S4b. Inter-template metathesis generates undesired byproducts such as these (and their many possible regio- and stereoisomers).