

Classic Annulenes, Nonclassical Applications

MICHAEL J. MARSELLA*

Department of Chemistry, University of California at Riverside, Riverside, California 92521

Received November 7, 2001

ABSTRACT

This Account details the application of $[n]$ annulenes as functional building blocks for electromechanical actuators, double-helical ladder polymers, and protecting groups for supramolecular interactions. Specifically, redox-induced conformational changes occurring in $[8]$ annulenes are utilized as the transducing element in polymeric electromechanical actuators. Conversely, rigid $[8]$ annulenes are utilized as double-helical fragments for the synthesis of double-helical octaaryl macromolecules. Last, Dewar benzenes are prepared from $[4 + 2]$ cycloadditions (where the 4π component is a $[4]$ annulene). The potential of using Dewar benzenes as protecting groups for $[6]$ annulene– $[6]$ annulene supramolecular interactions is exemplified by demonstration of photolithographic crystallization (amorphous $[4]$ annulene \rightarrow crystalline $[6]$ annulene) on a surface, followed by subsequent X-ray analysis of the resulting $[6]$ annulene crystals.

Introduction

Annulenes may be defined as fully conjugated macrocycles,¹ with common examples being cyclobutadiene, benzene, and cyclooctatetraene ($[4]$ -, $[6]$ -, and $[8]$ annulenes, respectively). Herein we report our studies focused on the design and synthesis of conjugated materials incorporating nonplanar $[n]$ annulenes. In each case, the intrinsic properties of the annulene define the function of the material. Specifically, the first two sections describe the use of $[4n]$ annulenes as redox-active shape-changing monomers (“molecular muscles”) and as double-helical scaffolds. The third and final section describes the synthesis of $[6]$ annulenes from $[4]$ annulene(s) via Dewar benzene intermediates. Furthermore, Dewar benzenes will themselves be shown to function as a supramolecular protecting group for $[6]$ annulene π – π stacking interactions.

Flexing $[4n]$ Annulenes: Molecular Muscles^{2,3}

The parent $[8]$ annulene, cyclooctatetraene, is a nonplanar, 8π macrocycle. By application of Hückel’s rule, reduction of this annulene by two electrons promotes a tub-to-planar conformational change to yield an aromatic ($4n + 2$)

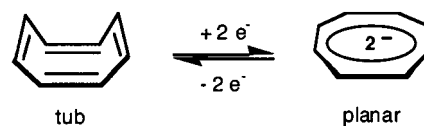


FIGURE 1. Reversible redox-induced conformational change in the $[8]$ annulene, cyclooctatetraene.

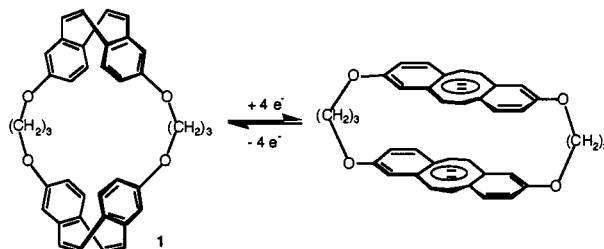


FIGURE 2. Reversible redox-induced shape-changing cyclophane reported by Müllen.⁶

system (Figure 1).⁴ In principle, such a redox-induced conformational change will occur in an $[8]$ annulene upon oxidation or reduction to any state, $2+$, $1+$, $1-$, $2-$. In all cases, delocalization of charge is a major driving force, augmented by gaining aromatic stabilization for the $2-$ and $2+$ states. Our interest in $[8]$ annulene comes from this inherent relationship between redox state and conformation.⁵ Simply stated, changes in the electron count (an externally controllable parameter) force a displacement of atoms (the consequential molecular response). This intrinsic property allows $[8]$ annulenes to be defined as a *functional synthon* for electromechanical actuation. By definition, an electromechanical actuator is capable of transducing electrical energy into mechanical energy.

Redefining $[8]$ annulenes as intrinsic electromechanical actuators is not simply an issue of semantics. It is the first step in harnessing function from intrinsic molecular properties. It focuses on potential molecular *utility* and establishes the molecule as a *functional synthon*. As with traditional synthons in synthetic organic chemistry, functional synthons can also be stitched together in a precise manner to produce an operationally complex (multiple processes, one end function) molecule-based device. Thus, a molecule rich in intrinsic properties may continue to find new application in novel materials. It is in this context that we chose “classic” annulenes for nonclassical applications as our title.

Perhaps the first to utilize $[8]$ annulene as a synthon for actuation was Müllen and co-workers, who prepared compound **1**, a shape-changing cyclophane (Figure 2).⁶ Here, two dibenzo $[8]$ annulenes are tethered together by six atom linkers. In principle, the dimensions (and electrostatic environment) of the internal cavity are controlled by the redox state of the cyclophane. An obvious application for this type of system would be the controlled uptake and expulsion of guests within the shape-changing host.

In a somewhat analogous manner, our ultimate goal was to produce a polymeric electromechanical actuator

Michael J. Marsella was born in 1968 in Warwick, Rhode Island. He received his B.S. in 1990 at the University of Rhode Island, and obtained his Ph.D. in 1995 from the University of Pennsylvania under the direction of Professor Timothy M. Swager. From 1995 to 1997, he was a National Institutes of Health postdoctoral fellow at the California Institute of Technology with Professor Robert H. Grubbs. He began his independent career as an assistant professor in 1997 at the University of California at Riverside, focusing on the design, synthesis, and properties of interesting π -functional organic materials. Professor Marsella has received the Research Corporation Research Innovation Award (1997) and is a DuPont Young Professor Fellow.

* E-mail: michael.marsella@ucr.edu.

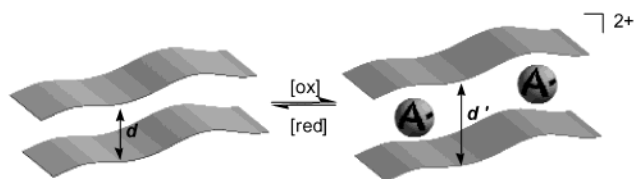


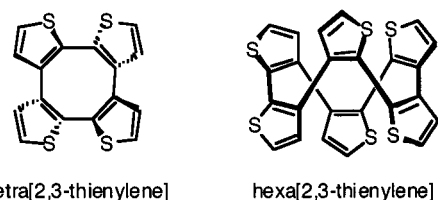
FIGURE 3. Concept of the bulk mechanism for actuation in traditional polymeric electromechanical actuators. Ribbons represent polymer chains, and spheres represent counterions. Counterion intercalation upon oxidation results in an expansion of the bulk; the expulsion of counterions during subsequent reduction back to the neutral state results in a contraction. Here, this is depicted by the fact that dimension $d' > d$. Note that the length of individual polymer chains may be constant throughout this process.

by connecting in series (via polymerization) a number of actuator synthons. The concerted redox-induced conformational change of individual repeat units would be summed across the entire polymer backbone, resulting in an overall dimensional change within the individual chain. Although many polymeric electromechanical actuators are known, the aforementioned mechanism would be unique, as traditional polymeric electromechanical actuators function via a bulk (not a molecular) mechanism.

Before describing single-molecule actuation, the mechanism of bulk electromechanical actuation in redox-active polymers (including conjugated polymers) should be addressed.⁷ Maintaining electrical neutrality in redox-active polymers mandates that counterions be either included into or expelled from the bulk polymer, depending upon its redox state. Since counterions have a specific volume, their presence or absence in the bulk polymer will affect the overall volume of the composite, with inclusion yielding expansion and expulsion yielding contraction (Figure 3). *Because intrinsic dimensional change within individual polymer chains is not mandated by this bulk mechanism, single-molecule (single polymer chain) actuation is not a prerequisite.* In contrast, functional polymers possessing bulk properties that mirror the properties of their repeat units impose no boundaries on the dimensions at which they can be used.

Our design of a polymeric electromechanical actuator was subject to several prerequisites. First, the ideal electromechanical actuator would need to exhibit stable and reversible redox chemistry under ambient conditions. Second, the actuator synthon must be a monomer suitable for polymerization, preferably via electrochemical polymerization or well-established cross-coupling techniques. Third, the polymer should be electrically conducting in order to facilitate long-range redox communication between repeat units. Last, any ring fusion to the [8]annulene periphery must not severely impede conformational flexibility.

The first two requirements rule out cyclooctatetraene itself: it is reduced only under an inert atmosphere and may require significant synthetic effort to access the corresponding regiospecific conjugated polymer. [8]Annulenes possessing ring fusion with six-membered rings, such as tetraphenylene, are also ruled out. Although some



tetra[2,3-thienylene]

hexa[2,3-thienylene]

FIGURE 4. Tetra- and hexa(2,3-thienylene). The former possesses an [8]annulene core and is conformationally flexible; the latter possesses a rigid [12]annulene core.

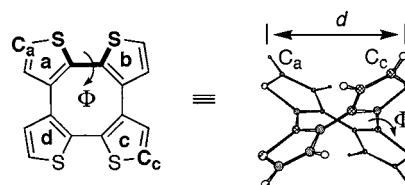


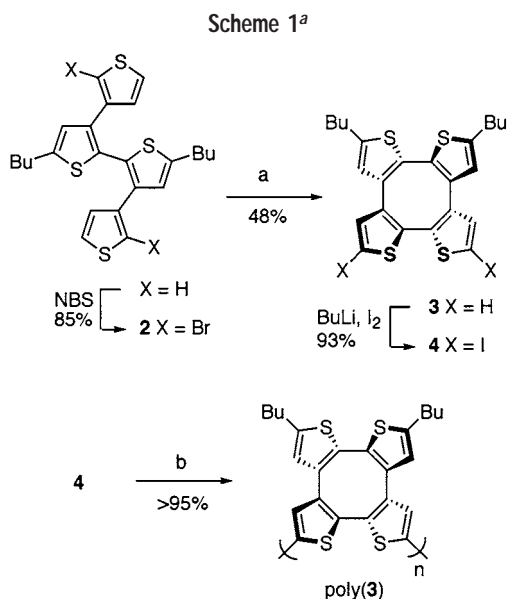
FIGURE 5. For clarity, the following notations are used. The four thiophene rings are denoted as rings a–d. Distance d refers to the distance between C_a and C_c . The S–C–C–S dihedral angle, ϕ , is directly related to d .

tetraphenylenes exhibit reversible electrochemistry,⁸ steric hindrance of adjacent rings renders a relatively inflexible tub conformation.⁴

If the first three aforementioned requirements were applied to a non-annulene control polymer, polythiophenes would meet almost all criteria.⁹ Luckily, a 1978 publication by Kauffmann reported the synthesis of tetra[2,3-thienylene], a thiophene-fused [8]annulene.¹⁰ In addition to (potentially) integrating the redox stability and synthetic handle of a thiophene with an [8]annulene, it should be noted that thiophene fusion involves a five-membered ring. Our hope was that one less carbon would buy back some of the conformational freedom lost in the six-membered-ring fused tetraphenylene series. Having found such an attractive candidate already existing in the literature (a classic system), we began assessing its use as a synthon for actuation.

Regarding the history of this annulene, both tetra- and hexa(2,3-thienylene) were first prepared by Kauffmann in 1978 (Figure 4). The former compound reappeared in a limited number of subsequent publications by the same group.^{11,12} Although the 1981 report of polythiophene as conducting polymer fueled an interest in thiophene derivatives,⁹ Kauffmann's cyclic thienylenes were not revisited for use as building blocks for π -functional materials until very recently.^{2,13–15}

For clarity, certain parameters should be defined prior to a discussion of our actuator design strategy (refer to Figure 5). The four thiophene rings of tetra(2,3-thienylene) are denoted a–d. Poly(tetra[2,3-thienylene]) may possess two points of backbone connectivity at the peripheral α -positions of rings a–b, a–c, or b–c. Polymers of type a–b and b–c are conjugated throughout the backbone, while a–c type polymers are cross-conjugated. Optimized actuation in a–c type polymers requires a linear polymer backbone, yielding a bellows-type expansion–contraction mechanism. In an effort to maintain a traditional polythiophene backbone, we opted to first synthesize an a–b type polymer.



^a Reagents: (a) (i) BuLi, (ii) FeCl₃; (b) 2 equiv of *t*-BuLi, MgBr₂, NiCl₂(dppp).

The S–C–C–S dihedral angle, denoted as ϕ , is used as a measure of planarity, with $\phi = 0^\circ$ indicating a completely planar system. As a point of reference, the X-ray crystal structure of tetra(2,3-thienylene) yields two distinct values of ϕ , $\phi_1 = 47.6^\circ$ and $\phi_2 = 46.2^\circ$.² The distance between carbons C_a and C_c (α -carbons of rings a and c, respectively) is denoted as d , and any reference to electromechanical actuation implies a change in this value as a function of redox state. Note the interplay between ϕ and d : a decrease in ϕ mandates an increase in d , and vice versa.

Synthesis of an a–b type poly[tetra(2,3-thienylene)] requires halogens at the peripheral α -positions of the a and b rings, and alkyl groups at the peripheral α -positions of the c and d rings. The two halogens would act as the aryl halide component of a cross-coupling polymerization reaction, and the two alkyl groups would serve to enhance solubility. Retrosynthetic analysis based on the original Kauffmann protocol would require oxidative coupling of either two different or two unsymmetrical bithiophenes. Either way, statistical mixtures of products would result. As such, we pursued an alternative synthesis,² one that proceeded via the intramolecular cyclization of a linear tetrathiophene (compound **2**; five steps from commercially available 2-butyl thiophene; Scheme 1), thus avoiding regioisomeric product mixtures. Halogenation of **3** to **4** and subsequent polymerization of **4** to poly(**3**) proceed smoothly (Scheme 1).

Cyclic voltammetry of compound **3** reveals that reversible oxidation to **3**⁺ occurs. Oxidation to **3**²⁺ was not observed, nor was any reduction. Unlike cyclooctatetraene, there is apparently no significant driving force for compound **3** to comply with Hückel's $4n + 2$ rule. Molecular modeling offers one possible explanation. Geometry optimization of **3**⁺ and **3**²⁺ (PM3, butyl groups omitted) reveals that oxidation does not result in a completely planar system. Although to a lesser degree than tetraphenylene, steric congestion resulting from the four

Table 1. Charge (n), S–C–C–S Dihedral Angle (ϕ), and Percent Dimensional Change (versus $n = 0$; $\Delta d_{\text{Ca-Cb}}$) for Compound **5^a**

n	ϕ (deg)	$\Delta d_{\text{Ca-Cb}}$ (%)
2–	3.5	19
1–	15.9	16
0	36.7	
1+	19.7	12
2+	0.0	18

^a Both ϕ and $\Delta d_{\text{Ca-Cb}}$ were calculated using DFT methods at the B3LYP 6-31G(d) level of theory.

fused aromatic rings does restrict the conformational dynamics of tetra(2,3-thienylene). In particular, neighboring β -H's are found to be a major source of steric congestion. Despite these results, a 6.7% change in distance d is predicted to occur during a redox cycle (**3** \rightarrow **3**⁺), implicating tetra(2,3-thienylene) as an intrinsic unit of actuation. For comparative purposes, it should be noted that bulk electrochemical actuators based on redox-active polymers typically exhibit a 10% dimensional change,⁷ and carbon nanotube-based actuators yield a ca. 1% dimensional change.¹⁶

More recently, we synthesized compound **5** in an effort to overcome β -substituent steric interactions by insertion of two alkyne spacers, yielding an “expanded” tetrathiophylene.³ Specifically, compound **5** is classified as a thiophene-fused didehydro[12]annulene. Given that a $4n$ π -electron count is maintained within an elongated octagonal framework, the analogous nonplanar to planar redox-induced conformation change is anticipated. Given that compound **5** is a regioisomer of the of the octaaryl double helix, compound **11** (see Scheme 3), access via a similar synthetic strategy was employed.

Density functional theory (B3LYP 6-31G[d])¹⁷ was used to predict that compound **5** undergoes a large redox-induced conformational change from twisted ($\phi = 36.7^\circ$) to planar ($\phi = 0^\circ$) upon two-electron oxidation from a $4n$ to a $4n + 2$ π -electron count. The corresponding change in distance, Δd , corresponds to 18%. Note that this range is more than double that predicted for tetra(2,3-thienylene) itself, a difference credited, in part, to a reduction in intramolecular sterics between adjacent β -thienyl positions. In further support, the barrier to inversion is calculated to be 9.7 kcal/mol, a value 14.3 kcal/mol lower in energy than that for the parent tetra(2,3-thienylene). Interestingly, each oxidation state of compound **5**, from **5**²⁺ to **5**^{2–}, is associated with a unique value of ϕ and d , thus yielding a range of actuation that may be attenuated across five unique oxidation states (Table 1).

Is there any experimental evidence confirming calculations? Unfortunately, the analytical tools typically em-

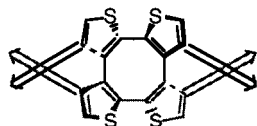


FIGURE 6. Concept of the double-helical directing ability of a tetra[2,3-thienylene] core.

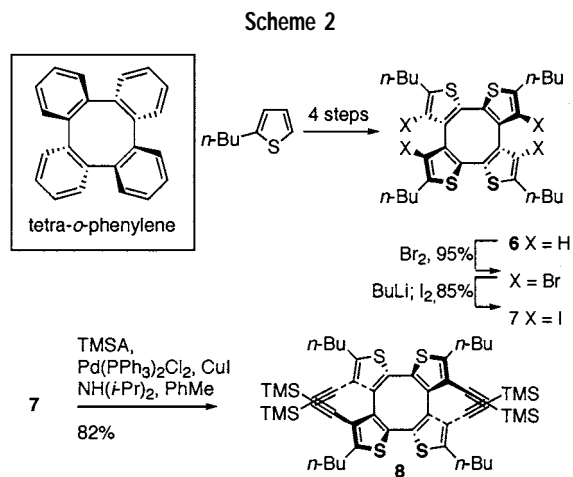
ployed to measure actuation in conjugated polymer-based electromechanical actuators would fail to distinguish between bulk (ion intercalation/expulsion) and single-molecule actuation.^{18,19} Analytical methods to circumvent these problems have been proposed,²⁰ but none has demonstrated single-molecule electromechanical actuation to date. We eagerly await access to analytical methods that would provide an indisputable measure of range and strength of a single macromolecule expansion–contraction cycle.

Since our original publication, others have also reported elegant designs of molecular actuators. Specifically, Swager has designed a polymeric electromechanical actuator that utilizes a calix[4]arene pivot to dramatically amplify dimensional changes,^{20,21} and Sauvage has designed a chemomechanical actuator based on the mechanical bond.²² One advantage of the Sauvage system is that it avoids the complications associated with analysis of electromechanical actuation; thus, definitive evidence for single-molecule actuation was readily available via solution-state NMR studies. Similarly, the contraction of a single macromolecule photomechanical actuator has been detected by AFM studies.²³ Given the differences in the systems reported to date, it becomes evident that there are many ways to approach the design of a molecular actuator.¹⁶ Our work in this area continues on several fronts, with the long-term goal of pursuing the ideal molecular actuator: one that is modular, reversible, strong (an issue not typically addressed in molecule-based systems), and environmentally robust.

Screwing-Up [8]Annulenes: Double-Helical Scaffolds¹³

As stated, molecules rich in intrinsic properties are highly adaptable and will find utility in a number of new applications. Tetra(2,3-thienylene) is a prime example. As described above, the inherent function of redox-induced conformational changes defines tetra(2,3-thienylene) as a functional synthon for actuation.² However, when the four peripheral β -positions are considered from a topological perspective, tetra(2,3-thienylene) may be employed as a scaffold for double-helical motifs (Figure 6).¹³

A covalent, single enantiomer double-helical ladder polymer is a significant synthetic challenge. Assuming each building block is a rigid, homochiral segment of a double helix (such is the case for tetra[2,3-thienylene]), four couplings per molecule must successfully occur. Racemic substrates further complicate issues by the statistical possibility of nonproductive couplings (couplings between enantiomers). Ideally, high-molecular-weight polymers of this type would require quantitative coupling of homochiral building blocks. An alternative



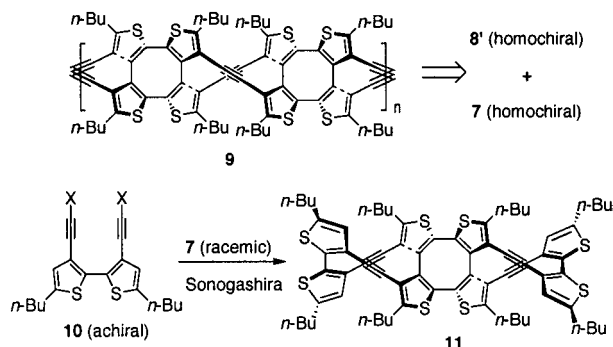
strategy would be to circumvent issues of chirality by (covalently) extending racemic double-helical fragments with achiral units to produce larger (albeit racemic) double-helical fragments. In the ideal case, these extended fragments would be capable of chiral discrimination, self-assembling into homochiral, supramolecular double-helical polymers. In this section we describe our results directed at both covalent and supramolecular syntheses of extended double-helical systems from racemic and achiral building blocks.

Our work was inspired by Rajca's 1997 report establishing tetra- α -phenylene as a fragment of a double helix.²⁴ Rajca successfully applied this fact in the synthesis of a tetra- α -phenylene homodimer (an octaaryl double-helical oligomer). As described above, stereochemical issues complicate the homocoupling of a *racemic* tetra- α -phenylene, and this fact is reflected by the ca. 4% isolated yield. Recognizing the topological similarities between tetra- α -phenylene and tetra[2,3-thienylene], we pursued an approach that would render *racemic* tetra[2,3-thienylene] (**7**) as a versatile building block for the synthesis of conjugated double-helical macromolecules (such as compounds **8**, **11**, and **12**).

Our synthetic strategy builds on the (typically!) predictable and reliable chemistry of thiophenes.⁹ For example, the propensity of α -positions being much more chemically reactive than β -positions is well documented, and we have made extensive use of this rule of thumb in many of our syntheses.^{2,3,13,14,25} In this present case, capitalizing on the double-helical motif would require cross-coupling chemistry to occur exclusively at the four (less reactive) peripheral β -positions. As such, we opted to mute chemical activity at the (more reactive) α -positions by substituting these sites with alkyl chains. Note that alkyl chains would not only serve as protecting groups but also enhance the solubility of products.

The synthesis of **7** is based on the original synthesis of the parent (unsubstituted) tetra[2,3-thienylene]¹⁰ and is shown in Scheme 2. With all four α -positions of **6** deactivated toward electrophilic attack, bromination occurs exclusively at the four β -positions of **6**. Subsequent lithium–halogen exchange, followed by quenching with iodide, yields tetraiodide **7**. Compound **7** is the key

Scheme 3



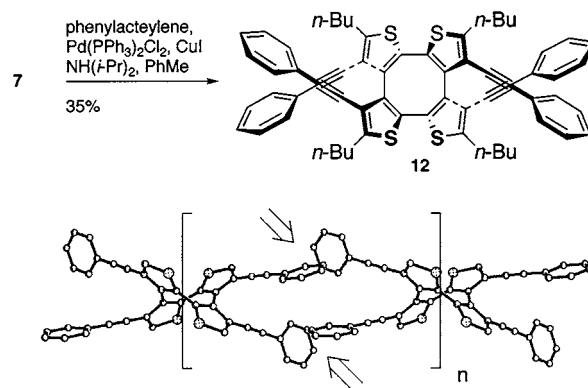
scaffold for the preparation of double-helical oligomers and polymers via cross-coupling. Extending the racemic double-helical core with achiral moieties is illustrated by the synthesis of **8**.

The cross-coupling of TMS-deprotected **8** (denoted **8'**) and **7** allows, in theory, the production of double-helical ladder polymer **9** (Scheme 3). However, this polymerization is subject to the same stereochemical issues found in the aforementioned synthesis of tetra-*o*-phenylene homodimers: homochiral **8'** and **7** are required to yield polymer **9**. Given that **7** is, in fact, racemic, only achiral units (with respect to helicity) could serve as an appropriate coupling partner to extend the double-helical motif. Such a model reaction can be established by cross-coupling 2 equiv of compound **10**, an achiral analogue of one hemisphere of **8**, with racemic **7** to yield the ladder-type octaaryl oligomer, compound **11**.

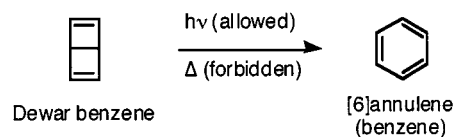
Free rotation about the thiophene–thiophene bond of **10** allows for the requisite tandem cross-coupling reaction to occur between **10** and either enantiomer of **7**. Unfortunately, this same free rotation also makes available nonproductive intermolecular polymerization pathways. To minimize undesirable intermolecular reactions, Pd/Cu cross-couplings were performed under pseudo-high-dilution conditions.²⁶ Remarkably, the desired tandem Pd/Cu-catalyzed cross-coupling between 2 equiv of **10** and 1 equiv of **7** (four total couplings, two of which are intramolecular cyclizations) provides **11** in 28% isolated yield. Thus, the productive coupling reaction proceeds, on average, at 73% yield per reaction site (four sites per monomer **7**). However, since no starting materials are recovered in this reaction, the aforementioned nonproductive coupling pathways must also be considered when predicting the reactivity of monomers **7** and **8'** (via **10**). Thus, it can be inferred from this control reaction that cross-coupling polymerization of homochiral **8'** and **7** should occur with efficiency much greater than 73% yield per reaction site (noting that the rigidity of **8'** and **7** make unproductive coupling pathways unlikely). Regardless, we would ideally prefer a strategy that completely avoids these stereochemical issues, with racemic and achiral starting materials yielding homochiral macromolecules. Self-assembly appeared to be a good option.

Given the ubiquitous nature of aryl–aryl interactions (i.e., edge-to-face interactions),^{27,28} we targeted an extended double-helical motif terminally capped with four

Scheme 4



Scheme 5



phenyl groups (compound **12**). The rationale for this target was based on the fact that the maximum number of intermolecular aryl–aryl interactions could occur only when double-helical fragments of the same handedness interacted. In theory, the self-assembly of racemic compound **12** should exhibit chiral discrimination, driven by maximizing weak aryl–aryl interactions.

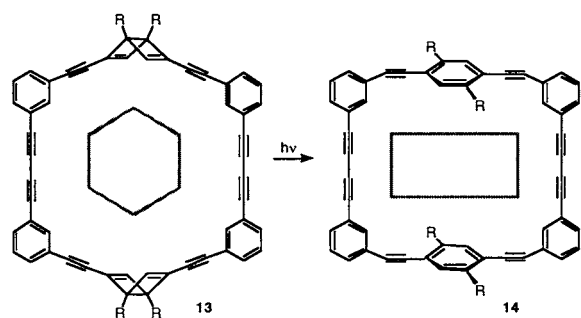
As shown in Scheme 4, the desired self-assembly occurred.¹³ Although crystals of compound **12** were overall racemic, the individual supramolecular polymer chains are homochiral. Closer examination of the X-ray crystal structure clearly reveals edge-to-face aryl–aryl interactions serving as a key directing entity (note arrows in Scheme 4). This result illustrates the successful preparation of a homochiral, supramolecular double-helical polymer prepared from racemic and achiral building blocks. The importance of aryl–aryl interactions as supramolecular directing groups, as exemplified by this supermolecule, is a continuing theme in the following section.

Turning-On [6]Annulenes: Dewar Benzene Revisited²⁹

Keeping with the concept that molecules rich in intrinsic properties will find utility in a number of new applications, here we highlight Dewar benzene. Dewar benzene is the nonaromatic, high-energy isomer of the prototypical [6]-annulene, benzene. It is credited as a source for thermally induced chemiluminescence³⁰ and undergoes both dimensional and topological changes upon photoisomerization to benzene (Scheme 5). From a materials standpoint, few of these properties have been significantly tapped until very recently.

In one example, Tsuji employed the aforementioned photoinduced topological changes to complete an otherwise improbable synthesis: construction of a (pseudo-)rectangular cyclophane having 120° corners.^{31,32} In this case, the bridgeheads of two Dewar benzenes served as two of six vertices of a pseudohexagon (compound **13**).

Scheme 6



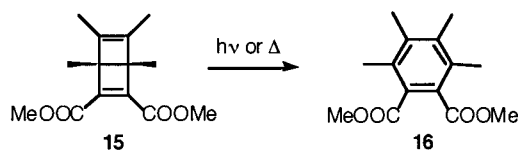
The remaining four vertices were formed from meta-substituted benzenes. All six vertices were connected via acetylene linkages. Photoisomerization of **13** eradicated the two Dewar benzene vertices, leaving four, and hence establishing a strained rectangle, compound **14** (Scheme 6). Conceptually, this shape-changing cyclophane is similar to Müllen's aforementioned cyclooctatetraene-based system, the former differing most significantly by being irreversible. Although our long-term interests in Dewar benzene as a functional synthon are multifold, herein we will focus solely on our investigation of Dewar benzene as a protecting group for supramolecular [6]annulene interactions.

The previous section highlighted the power of aryl–aryl interactions as directing groups in supramolecular chemistry. Using the terminology of crystal engineering, the ubiquitous nature of aryl–aryl interactions defines them as a supramolecular synthon. For clarity, a supramolecular synthon is defined as a structural unit within a supramolecular assembly that yields a general and predictable spatial arrangement of intermolecular, non-covalent interactions.²⁸ This structural predictability is key to the rational design of self-assembling systems, such as our double-helical motif, above, and has clear analogies in traditional (covalent) synthetic organic chemistry.

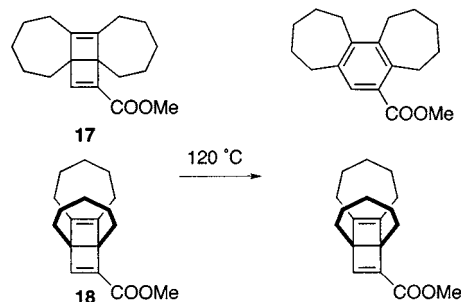
In keeping with this traditional synthesis analogy, one aspect of supramolecular chemistry that lags behind traditional synthesis is the use of protecting groups. In theory, supramolecular protecting groups would allow the diminution of specific supramolecular synthons, thus biasing other noncovalent intermolecular interactions. It should be emphasized that protecting against such supramolecular interactions is not intended to be limited to self-assembly of exotic supermolecules. Indeed, it may also profoundly affect fundamental molecular properties such as solubility and physical state (i.e., liquid versus solid). It is in the latter examples that supramolecular protecting groups may find greatest application.

By definition, a supramolecular protecting group must be capable of masking all intrinsic properties of the parent synthon that would otherwise lead to noncovalent interactions. In the case of a supramolecular protecting group for aryl–aryl interactions, aromaticity itself must be destroyed. Thus, Dewar benzene appears to be well suited for such an application. Indeed, Dewar benzene is the epitome of an atom-economical protecting group, as its deprotection (photoisomerization) does not require or

Scheme 7



Scheme 8



produce any unwanted chemical species.³³ Furthermore, in an ideal case, deprotection is both quantitative and irreversible. Can these facts be utilized? The first step would require some clear demonstration of aryl–aryl interactions being “turned on” by the photoisomerization of Dewar benzene.

During the course of investigating a series of Dewar benzenes (via cycloaddition between [4]annulene and dimethylacetylenedicarboxylic acid), it became apparent that neat Dewar benzene, compound **15**,³⁴ underwent a photoisomerization and commensurate phase change, converting from an oil (compound **15**) to a crystalline solid (compound **16**) (Scheme 7). Although at first frustrated by the decomposition of our target molecule, we ultimately recognized that this observation might serve as the key visual litmus test for our aforementioned concept, Dewar benzene as a supramolecular protecting group. However, substantiation of such a claim would require meeting all of the aforementioned “ideal” requirements, demonstration of aryl–aryl interactions in the X-ray crystal structure of compound **16** being the most critical.

To avoid any potential misconceptions, it should be stated that the thermal stability of compound **15** is quite good. Although studies regarding the thermal stability of Dewar benzenes exist, they typically point to sterics about the ring as a major stabilizing factor.³⁵ Alternatively, stability is enforced by employing a tether across the 1- and 4-positions of the bicyclic ring system.³⁶ However, thermal stability in untethered, sterically less-demanding Dewar benzenes can be gleaned from reported experimental data. For example, Gleiter reported the separation of Dewar benzenes **17** and **18** by thermal conversion of the untethered isomer, **17** to its parent benzene (Scheme 8).³⁷ This thermal isomerization required heating for 2 h at 120 °C. Compound **15** shows similar thermal properties, with no apparent thermal degradation when handled for weeks at room temperature. For our purposes, the thermal stability of compound **15** is quite good. Clearly, this stability is an important parameter defining the utility of the protecting group. Given that all of our subsequent

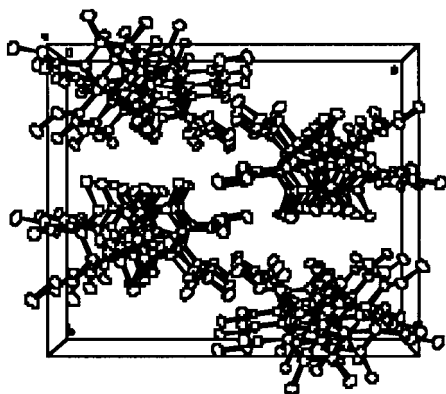


FIGURE 7. X-ray crystal structure of compound **16**, viewed down columns of face-to-face stacking interactions.

studies were performed at ambient temperature, thermal isomerization was never an issue of concern.

Quite spectacularly, when neat samples of **15** are irradiated with 365 nm light, photoisomerization is followed by rapid crystal formation. Monitoring this process by ^1H NMR confirmed that the photoisomerization was indeed quantitative and gave no signs of byproducts such as prismane.³⁸ All things considered, Dewar benzene **15** is an ideal example of a supramolecular protecting group for synthon **16**. Specifically, the protecting group eradicates the aryl moiety, thus inhibiting intermolecular aryl–aryl interactions that would otherwise promote crystallization. Deprotection via photoisomerization is quantitative, irreversible, and without byproduct, and subsequent crystal formation takes place spontaneously. Furthermore, the room temperature thermal stability of compound **15** is excellent. Last, the X-ray crystal structure of compound **16** reveals a face-to-face packing motif exhibiting a neighboring aromatic ring $\text{C}\cdots\text{C}$ spacing of 3.780 Å (Figure 7). Such a packing motif is characteristic of the aryl–aryl supramolecular synthon.^{27,28,39}

In an effort to provide a visual litmus test of this concept, we wished to capitalize on the oil-to-crystal phase change that occurred during the photoisomerization of **15** to **16**. Such a phase change would be readily apparent when viewed under a cross-polarizing microscope: amorphous (protected) regions would appear dark, while crystalline (deprotected) regions would be readily visible. Toward this goal, we focused on the application of photolithographic patterning of crystal domains on a surface. In theory, such an application would illustrate a powerful macroscopic processing tool for toggling the physical properties of targeted areas within bulk samples of materials. Despite the emphasis on the macroscopic bulk, keep in mind that it is a molecular process (of an annulene!) serving as the main driving force.

In a typical experiment, a neat sample (ca. 10 μL) of compound **15** (oil) is sandwiched between two 1 in. \times 3 in. standard microscope slides. A shadow mask was prepared by ink-jet printing a design onto a transparency film and was subsequently affixed to the exterior surface of the top microscope slide. The sample was irradiated with 365 nm light until the formation of colorless crystals within the unmasked area was detected by the naked eye.

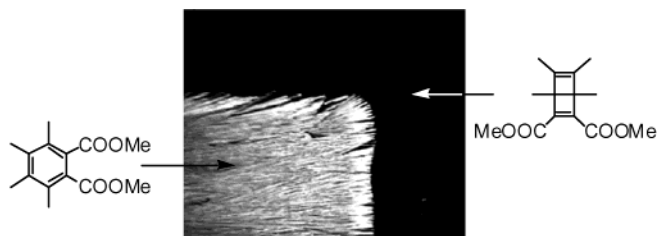


FIGURE 8. Photograph showing a corner of a patterned crystal domain of compound **16** surrounded by amorphous compound **15** (light and dark areas, respectively, as viewed under cross-polarizers).

As stated, the match between mask design and crystal domain is best determined by viewing the (unmasked) sample under a cross-polarizing microscope. As shown in Figure 8, regions of amorphous **15** appear dark (denoting the protected region), while crystals of **16** are readily visible (denoting that deprotection has occurred). As a litmus test for our proposed concept, it is visually apparent from Figures 7 and 8 that aryl–aryl interactions are, as expected, activated (deprotected) by photoisomerization. Clearly, the generality of this concept will require further examples, and we are currently pursuing this goal.

Summary

We have attempted to highlight our recent contributions to annulene chemistry. Note that in all cases we attempt to extract novel function from an intrinsic molecular property. Such is the *only* option when materials are constructed from a truly (molecularly) bottom-up approach. That said, the materials chemist's toolbox should be replete with intrinsically rich molecules. Ideally, many applications could then emanate from a small library of molecular scaffolds, thus reducing time consumed on potential synthetic bottlenecks. Although such inherent properties are certainly not exclusive to the annulenes, the extensive history and diversity of annulenes warrants their careful re-evaluation as functional synthons for today's materials challenges. With the synthesis and properties of many parent annulenes already established in the literature, this is a very attractive challenge.

I am indebted to group members, past and present, for their dedication and effort. Many of their names can be found below in our published work; those remaining will appear in future publications. All have made significant individual contributions to our research program as a whole. This work was generously supported by the National Science Foundation (Grant CHE-9974548), the donors of the Petroleum Research Fund, administered by the American Chemical Society, Research Corporation (Research Innovation Award to M.J.M.), DuPont (Young Professor Grant to M.J.M.), the Department of Education (GAANN program), and the University of California (start-up funds, intramural programs, and CRCC).

References

- (1) Garratt, P. J. *Aromaticity*; John Wiley & Sons: New York, 1986.
- (2) Marsella, M. J.; Reid, R. J. Toward Molecular Muscles: Design and Synthesis of an Electrically Conducting Poly[cyclooctatetrathiophene]. *Macromolecules* **1999**, *32*, 5982–5984.
- (3) Marsella, M. J.; Piao, G.; Fook, T. S. Expanding Tetra[2,3-thienylene]-Based Molecular Muscles to Larger [4n]Annulenes. *Synthesis* **2002**, *9*, 1133–1135.

- (4) Paquette, L. A. Cyclooctatetraenes: Conformational and Pi-Electronic Dynamics within Polyolefinic [8]annulene Frameworks. *Adv. Theor. Interesting Mol.* **1992**, *2*, 1–77.
- (5) Fry, A. J. In *Topics in Organic Electrochemistry*; Fry, A. J., Britton, W. E., Eds.; Plenum Press: New York, 1986; pp 1–32.
- (6) Heinz, W.; Räder, H.-J.; Müllen, K. Changing the Size of a Cavity via an Electron-Transfer: Synthesis and Reduction of 1, 5, 22, 26-Tetraoxa-[5,5]-(2,8)-Dibenzo[a,e]cyclooctatetraeneophane. *Tetrahedron Lett.* **1989**, *30*, 159–162.
- (7) Baughman, R. H. Conducting Polymer Artificial Muscles. *Synth. Met.* **1996**, *78*, 339–353.
- (8) Rathore, R.; Le Magueres, P.; Lindeman, S. V.; Kochi, J. K. A redox-controlled molecular switch based on the reversible C–C bond formation in octamethoxytetraphenylene. *Angew. Chem., Int. Ed.* **2000**, *39*, 809–812.
- (9) Roncali, J. Conjugated poly(thiophenes): Synthesis, functionalization, and applications. *Chem. Rev.* **1992**, *92*, 711–738.
- (10) Kauffmann, T.; Greving, B.; Kriegesmann, R.; Mitschker, A.; Woltermann, A. Heterocyclotetraaromaten Mit Geichartigen Aromatischen Ringgliedern. *Chem. Ber.* **1978**, *111*, 1330–1336.
- (11) Kauffmann, T. From the Principle of Arene-Analogy to Heterocyclopolyaromatic Compounds. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 1–19.
- (12) Kauffmann, T.; Mackowiak, H. P. 2-Lithio-(all-alphaS)cyclo-tetrathiophen: Synthese und Präparative Anwendungen. *Chem. Ber.* **1985**, *118*, 2343–2352.
- (13) Marsella, M. J.; Kim, I. T.; Tham, F. S. Toward Conjugated Double Helical Ladder Polymers: Cyclooctatetrathiophene as a Highly Versatile Double Helical Scaffold. *J. Am. Chem. Soc.* **2000**, *122*, 974–975.
- (14) Marsella, M. J.; Yoon, K.; Tham, F. S. Synthesis and Crystal Structure of a Tubular Sexithiophene. *Org. Lett.* **2001**, *3*, 2129–2131.
- (15) Kabir, S. M. H.; Miura, M.; Sasaki, S.; Harada, G.; Kuwatani, Y.; Yoshida, M.; Iyoda, M. New syntheses of tricyclic thiophenes and cyclic tetrathiophenes using transition-metal-catalyzed cyclization. *Heterocycles* **2000**, *52*, 761–774.
- (16) Baughman, R. H.; Cui, C. X.; Zakhidov, A. A.; Iqbal, Z.; Barisci, J. N.; Spinks, G. M.; Wallace, G. G.; Mazzoldi, A.; De Rossi, D.; Rinzler, A. G.; Jaszchinski, O.; Roth, S.; Kertesz, M. Carbon Nanotube Actuators. *Science* **1999**, *284*, 1340–1344.
- (17) All calculations reported herein were performed using Titan software: Schrödinger, Inc., 1500 SW First Ave., Suite 1180, Portland, OR 97201.
- (18) Pei, Q.; Inganäs, O. Electrochemical Applications of the Bending Beam Method. 1. Mass Transport and Volume Changes in Polypyrrole During Redox. *J. Phys. Chem.* **1992**, *96*, 10507–10514.
- (19) Marsella, M. J.; Reid, R. J.; McCormick, M. T. A New Technique for Monitoring Real-Time Dimensional Changes in Polymeric Electromechanical Actuators and Vaporesistive Sensors. *Synth. Met.* **2001**, *118*, 171–174.
- (20) Anquetil, P. A.; Yu, H.; Madden, J. D.; Madden, P. G.; Swager, T. M.; Hunter, I. W. In *SPIE's Electroactive Polymer Actuators and Devices Conference, 9th Smart Structures and Materials Symposium*; Bar-Cohen, Y., Ed.; SPIE: San Diego, CA, 2002; Vol. 4695.
- (21) Yu, H.; Pullen, A. E.; Swager, T. M. In *National Meeting of the American Chemical Society*; Charbonneau, Ed.; American Chemical Society: Washington, D.C., 2000; Vol. 83, pp 523–524.
- (22) Jiménez, M. C.; Dietrich-Buchecker, C.; Sauvage, J. P. Towards Synthetic Molecular Muscles: Contraction and Stretching of a Linear Rotaxane Dimer. *Angew. Chem., Int. Ed.* **2000**, *39*, 3284–3287.
- (23) Hugel, T.; Holland, N. B.; Cattani, A.; Moroder, L.; Seitz, M.; Gaub, H. E. Single-Molecule Optomechanical Cycle. *Science* **2002**, *V296*, 1103–1106.
- (24) Rajca, A.; Safronov, A.; Rajca, S.; Shoemaker, R. Double Helical Octaphenylene. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 489–491.
- (25) Marsella, M. J.; Wang, Z. Q.; Reid, R. J.; Yoon, K. Synthesis of Acetylenic Cyclophanes via Intramolecular Self-Assembly: Evidence of Perfluorophenyl–Phenyl Quadrupole Interactions in the Solution State. *Org. Lett.* **2001**, *3*, 885–887.
- (26) Zhang, J. S.; Pesak, D. J.; Ludwick, J. L.; Moore, J. S. Nanoarchitectures. 5. Geometrically-Controlled and Site-Specificity-Functionalized Phenylacetylene Macrocycles. *J. Am. Chem. Soc.* **1994**, *116*, 4227–4239.
- (27) Desiraju, G. R. *Crystal Engineering: The Design of Organic Solids*; Elsevier: New York, 1989; Vol. 54.
- (28) Desiraju, G. R. Supramolecular Synthons in Crystal Engineering: A New Organic Synthesis. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2311–2327.
- (29) Marsella, M. J.; Meyer, M. M.; Tham, F. S. Dewar Benzene as Protecting Group? Demonstration of Photolithographic Crystallization. *Org. Lett.* **2001**, *3*, 3847–3849.
- (30) Lechtken, P. E. A.; Breslow, R.; Schmidt, A. H.; Turro, N. J. Thermal Rearrangement of Dewar Benzenes to Benzene Triplet States. Example of Spin Forbidden Nonadiabatic Pericyclic Reactions. *J. Am. Chem. Soc.* **1973**, *95*, 3025–3027.
- (31) Ohkita, M.; Ando, K.; Suzuki, T.; Tsuji, T. Syntheses of Acetylenic Oligophenylene Macrocycles Based on a Novel Dewar Benzene Building Block Approach. *J. Org. Chem.* **2000**, *65*, 4385–4390.
- (32) Ohkita, M.; Ando, K.; Yamamoto, K.; Suzuki, T.; Tsuji, T. First Dewar Benzene Approach to Acetylenic Oligophenylene Macrocycles: Synthesis and Structure of a Molecular Rectangle Bearing Two Spindles. *Chem. Commun.* **2000**, 83–84.
- (33) Trost, B. M. The Atom Economy: A Search for Synthetic Efficiency. *Science* **1991**, *254*, 1471–1477.
- (34) Koster, J. B.; Timmermans, G. J.; van Bekkum, H. Reaction of the Tetramethylcyclobutadiene–Aluminum Chloride Complex with Dienophilic Esters. *Synthesis* **1971**, 139–140.
- (35) Irngartinger, H.; Deuter, J.; Wingert, H.; Regitz, M. Stereochemistry of Dewar Benzenes: Molecular Structures Influenced by Electronic and Steric Effects. *Chem. Ber.* **1990**, *123*, 345–350.
- (36) Gleiter, R.; Treptow, B. Synthesis of Doubly Bridged Prismanes: An Investigation of the Photochemical Behavior of Doubly Bridged Dewar Benzenes. *J. Org. Chem.* **1993**, *58*, 7740–7750.
- (37) Gleiter, R.; Ohlbach, F.; Oeser, T.; Irngartinger, H. Reactions of Cyclic Diynes with Acceptor-Substituted Alkynes: Syntheses of Doubly Bridged Dewar Benzenes. *Liebigs Ann.* **1996**, 785–790.
- (38) Gleiter, R.; Ohlbach, F.; Haberhauer, G.; Irngartinger, H.; Oeser, T. Photochemical Behavior of Doubly Bridged Dewar Benzenes: Synthesis of Prismanes. *Liebigs Ann.* **1996**, 1627–1634.
- (39) Desiraju, G. R.; Gavezzotti, A. From Molecular to Crystal Structure: Polynuclear Aromatic Hydrocarbons. *J. Chem. Soc., Chem. Commun.* **1989**, 621–623.

AR010090S