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Oligohelicenes

Noncovalent Interactions in the Asymmetric Synthesis of Rigid, Conjugated Helical Structures**

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Helical supramolecular architecture, such as helical foldamers, supramolecular helicates and aggregates, helical molecules, macromolecules, and oligomers, is a fascinating topic of interest in chemistry and materials science.[1–6] Although such supramolecular structures may provide advantages in the design of stimuli-responsive and functional materials, the weak nature of the noncovalent forces, as well as the dependency of the dynamic process on their local environments, may hinder their possible applications because of their limited structural stability and processibility. Stabilization of these supramolecular structures could be achieved by modification of the molecular backbone with specific functional groups that permit intramolecular cross-linking, in which covalent bonds fix the secondary structure with variable degrees of fidelity.[6,7]

Helical structures derived from conjugated *ortho*-annelated aromatic rings, known as [*n*]helicenes, are precisely defined at the molecular level.[8–11] For [*n*]helicenes with a sufficiently large number of aromatic rings (n), rigid conformations with large barriers to racemization and enhanced molecular chiroptical properties may be expected.[11a,12,13] Diverse electronic structures for such helices may result from various aromatic rings[11ab–19] or by introducing antiaromatic rings[20] to the structure, to obtain materials with a wide range of band gaps, 2–4 eV.[11a,b,17,20,21]

Although significant progress has been made in the synthesis of [*n*]helicenes, the preparation of such highly annelated and strained π-systems,[11] especially by asymmetric synthesis,[16,17,22–24] remains a challenge. The development of new synthetic strategies for the preparation of precisely defined and extended helical structures, as well as understanding the factors that control the structure and properties of these molecules, are crucial to making progress in the area of rigid helical motifs.

Herein, we demonstrate the important role of noncovalent interactions in the asymmetric synthesis of rigid, conjugated helical structures. Tetrakis(β-trithiophene) **1** folds into a helical conformation that facilitates the double ring annelation to provide a carbon–sulfur bis[7]helicene **2** with a rigid, helically locked structure (Figure 1a). Further ring annelation of the rigid, locked bis[7]helicene to form the corresponding [15]helicene **3** was not successful, likely owing to strong noncovalent interactions between the two [7]helicene moieties which prohibit their relative rotation to facilitate covalent bond formation, however, other effects may not be excluded.

We propose that the "helical fold-and-lock" concept may be extended to facilitate the preparation of the oligomers of [*n*]helicenes, such as tetrakis[7]helicene (Figure 1b). Such oligomers may provide precisely defined models for helical folding, which is driven by intramolecular π-stacking and steric repulsion.[1a]

The asymmetric synthesis of bis[7]helicene **2** is outlined in Scheme 1. The synthetic approach mostly follows the methodology for the iterative synthesis of carbon–sulfur [*n*]helicenes ($n=7$ and 11) that we developed previously.[15–17] In the synthesis of long [*n*]helicenes, the isolation and purification of poorly soluble intermediates and products can be an arduous undertaking. We can circumvent solubility problems by using the large tripropylsilyl (TPS) group as a protecting group. In

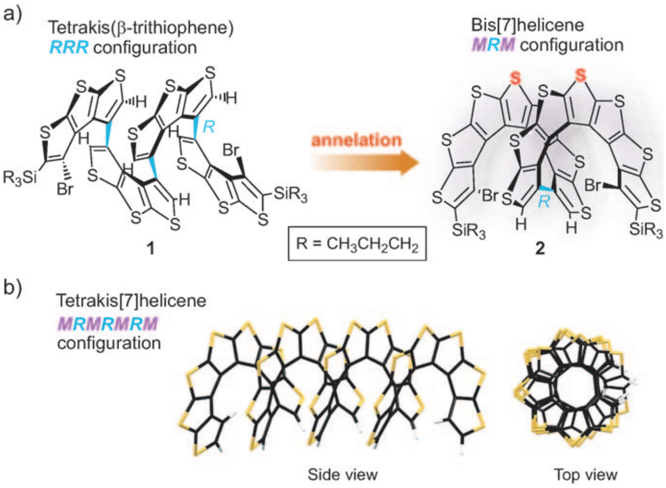

Figure 1. a) From helically folded tetrakis(β-trithiophene) to helically locked bis[7]helicene. b) Oligomer of [*n*]helicenes illustrated by tetrakis[7]helicene. *R* indicates the configuration of chiral axes and *M* indicates the configuration of "left-handed" [*n*]helicene moieties.

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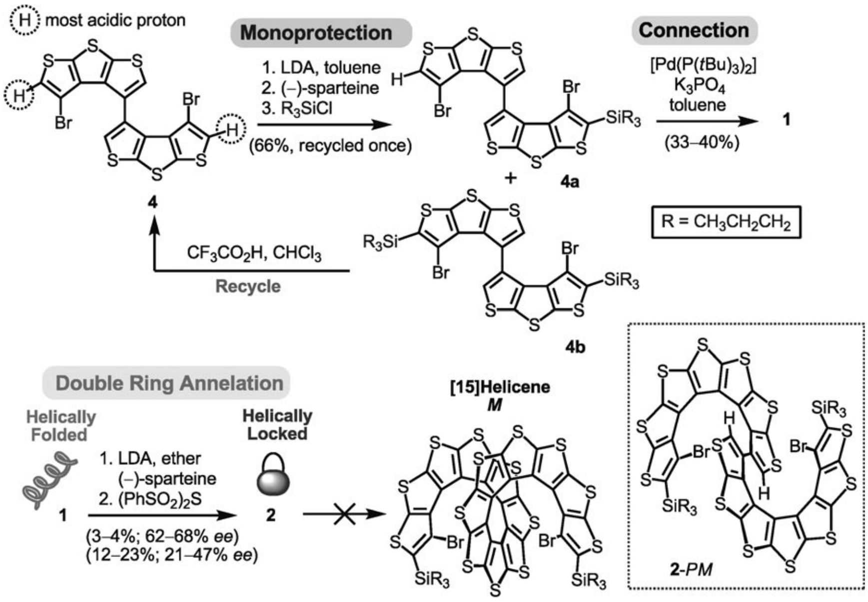


Scheme 1. Asymmetric synthesis of bis[7]helicene **2**. Inset: *meso*-diastereomer of bis[7]helicene.

the first step, monoprotection of the two most acidic positions in bis(β-trithiophene) **4** yielded its derivative **4a**, which had enhanced solubility and steric shielding at one of the CBr moieties.

The steric shielding provided selectivity in the palladium-catalyzed homocoupling reaction to form tetrakis(β-trithiophene) **1**, as carbon–carbon bond formation is preferred at the less sterically shielded CBr moiety. In the double ring annelation reaction, **1** is tetralithiated with lithium diisopropylamide (LDA) in the presence of a chiral diamine such as (−)-sparteine, and then treated with bis(phenylsulfonyl)sulfide ($(PhSO_2)_2S$) to form two new thiophene rings. The resultant bis[7]helicene **2** was obtained in approximately 20 % yield after isolation and had a modest enantiomeric excess (*ee*) value.[25] The isolated bis[7]helicene **2** is chiral, and therefore, its [7]helicene moieties are likely to possess identical configurations, for example *MM* or *PP*. An alternative *meso*-diastereomer, such as **2**-*PM*, with the [7]helicene moieties of the opposite configuration (*PM*) was not detected (Scheme 1, Inset).

The structures of tetrakis(β-trithiophene) **1** and bis[7]helicene **2** were determined by single-crystal X-ray analysis using synchrotron radiation (Figure 2).[26] Tetrakis(β-trithiophene) **1** crystallized in the nonchiral space group $C2/c$ with half of the molecule in the asymmetric unit. Bis[7]helicene **2** crystallized in the chiral space group $C222_1$ with half of the molecule and half of a solvent molecule (benzene) in the asymmetric unit. The crystal of **2** was found to be merohedrally twinned with an enantiomeric ratio in the crystal of 88:12, which is consistent with the *ee* value of the bulk sample (Scheme 1).

In the X-ray structure, **1** adopts a C_2-symmetric conformation, with approximately planar annelated β-trithiophene moieties; the dihedral angles for the terminal-to-center and the center-to-center moieties are 83.28(3)° and 84.21(3)°, respectively. Notably, the chiral axes have the same configuration, *RRR* or *SSS*, at all three β,β-linkages, that is, the carbon–carbon bonds connect the annelated β-trithiophene moieties at the β-positions of the terminal thiophenes. The helical folding of **1**, which is likely driven by steric repulsion and pairwise π-stacking of the annelated β-trithiophene moieties, provides a preferred conformer for double ring annelation to form the two [7]helicene moieties in **2**, as illustrated in the space-filling models in Figure 2 c,d. Thus, the *RRR* (or *SSS*) configuration of **1** is converted into the *MRM* (or *PSP*) configuration in bis[7]helicene **2**. In the major enantiomer of **2**, *MRM*, the [7]helicene moieties possess the *M* configuration and the chiral axis at the β,β-linkage has the corresponding *R* configuration.

The conformation of **2** has an approximate C_2 point group of symmetry. The β,β-linkage, which has a torsion angle of approximately −50° about the carbon–carbon bond connecting the [7]helicene moieties, resemble a molecular hinge in which two rigid [7]helicene moieties form an intramolecular π-stack assembled in a helical motif. The short intramolecular distances on both sides of the molecular hinge lead to a rigid conformation (Figure 2 e, Table S1 in the Supporting Information).

In solution, racemic tetrakis(β-trithiophene) **1** possesses a chiral conformation on the time scale of enantiomer separation by both high pressure liquid chromatography (HPLC) and nuclear magnetic resonance (NMR) methods. The chiral conformation is indicated by well resolved peaks resulting from diastereomeric interactions with the chiral stationary phase of the HPLC column and interactions with chiral shift reagents in NMR experiments (see the Supporting Information). The conformation and electronic structure of chiral bis[7]helicene **2** in solution was further characterized by computational modeling of experimental circular dichroism (CD) and ultraviolet-visible (UV/Vis) spectra.

To gain deeper insight into the structure and properties of bis[7]helicene, we calculated a series of simplified structures, in which the large TPS group was replaced with a trimethylsilyl (TMS) group. Electronic CD and UV/Vis absorption spectra of bis[7]helicene **2a**, [15]helicene **3a**, and [7]helicene **5** were computed using the TD-B3LYP/6-31G(d) method and the IEF-PCM-UAHF solvent model for cyclohexane.[27–29] The calculated spectra are qualitatively similar for all three structures, especially for bis[7]helicene **2a** and [15]helicene **3a**, which both possess relatively weak long-wavelength bands. For bis[7]helicene **2a** and [7]helicene **5**, excellent agreement between experiment and theory was found (Figure 3 and see the Supporting Information).

Specifically in **2** the weak, long-wavelength band with a positive $\Delta\varepsilon$ band at approximately 330 nm is qualitatively reproduced in the calculated spectrum (Figure 3, Inset). In [15]helicene **3a**, this long-wavelength band shows a somewhat larger and negative $\Delta\varepsilon$ value, which may reflect the smaller torsion angles of about 14° between the two [7]helicene

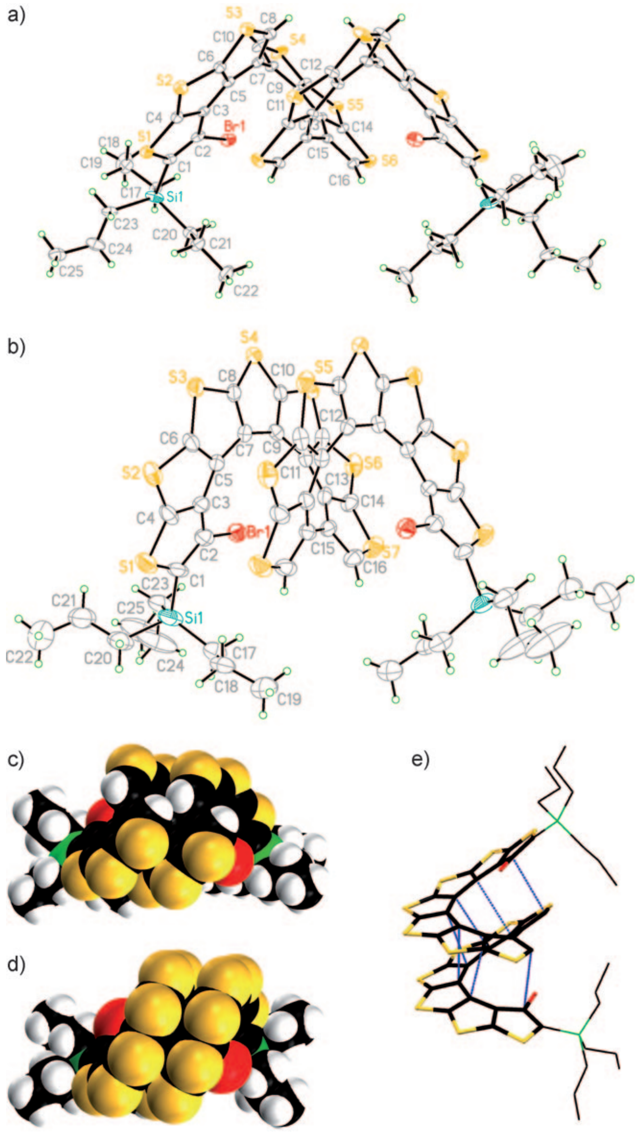
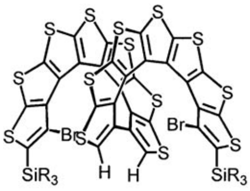


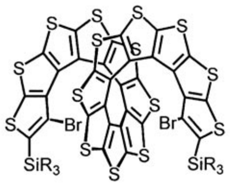
Figure 2. Molecular structure and conformation: a) tetrakis(β-trithiophene) **1**; b) bis[7]helicene **2**; c) space-filling model for **1**; d) space-filling model for **2**; e) short intramolecular C⋯C distances (3.23–3.30 Å) between the [7]helicene moieties in bis[7]helicene **2** are indicated with blue lines. ORTEP plots with thermal ellipsoids set at the 50% probability level. Cocrystallized solvent and disorder in the propyl groups are omitted for clarity.

moieties (vs. 50° in bis[7]helicene) and the out-of-plane distortion of the thiophene rings near the center in [15]helicene (see the Supporting Information). We conclude that bis[7]helicene **2** adopts a [15]helicene-like rigid conformation in the solid state and in solution, and it possesses an electronic structure similar to that for the corresponding [15]helicene.

We explored the isomerization of bis[7]helicene **2** into its *meso*-diastereomer (**2**-*PM*; Scheme 1), a process that corresponds to the inversion of one of the [7]helicene moieties. Under similar conditions that lead to the inversion (racemization) of [7]helicene **5**,[16] only the starting bis[7]helicene **2** was recovered. This result suggests that **2**, with *MM* or *PP* [7]helicene moieties, is thermodynamically preferred. Computational studies at the B3LYP/6-31(d) level of theory

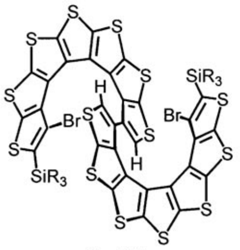


2a

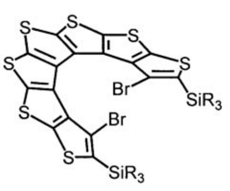


3a

R = CH$_3$



2a-*PM*



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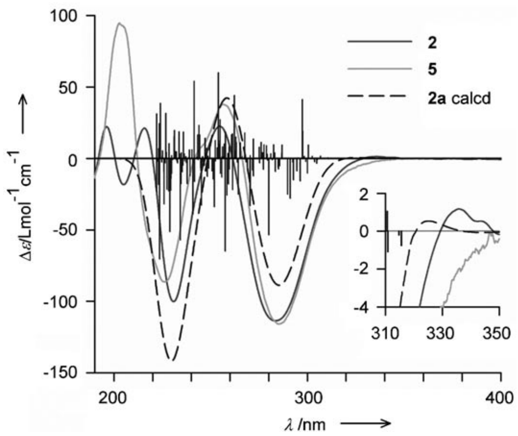

Figure 3. Experimental and calculated electronic CD spectra in cyclohexane. Inset: expansion of CD spectra.

indicate that **2a**-*PM* is about 8 kcal mol^{-1} higher in energy than **2a**, which has the *MM* configuration. This energy difference is about the same for single point energy calculations using the IEF-PCM-UAHF solvent model for cyclohexane (see the Supporting Information). We attribute this energy preference to the strong noncovalent interactions—π-stacking in the helically folded diastereomer **2a**.

We examined the correlation between molecular connectivity and helical folding by computational modeling. Model oligomers of [7]helicenes, analogues of bis[7]helicene **2a** in which the bromine and TMS groups are replaced with hydrogen atoms, were studied at the B3LYP/6-31(d,p) level of theory.[27] A series of structures based on bis[7]helicenes, tris[7]helicenes, and tetrakis[7]helicenes, were constructed by connecting the [7]helicene moieties of identical (*MM*) or opposite (*MP*) configuration at each β,β-linkage. In this series, oligomers with identical configurations, such as *MM* at each linkage, have lower energies than those with *MP* configurations. This preference is about 5 to 8 kcal mol^{-1} for each β,β-linkage, and tends to be larger for higher oligomers, probably as a result of steric factors. For example, the tetramer of [7]helicenes with identical configuration (*MMMM*) such as tetrakis[7]helicene in Figure 1b and **8**-*MMMM* (see Table S5 in the Supporting Information) is lower in energy by about 20 kcal mol^{-1} than the corresponding *meso*-diastereomer with *MPMP* configuration. In contrast, we found a reversed trend in analogous bis[7]helicenes with α,α-linkages, that is, the diastereomer with the [7]helicene moieties of opposite configuration is lower in energy,[27,30] albeit the preference is quite small—about 1 kcal mol^{-1}.

We predict that a strong preference for helical folding, driven by intramolecular π-stacking and steric repulsion, may be realized in oligomers of [*n*]helicene monomers with the same configuration and which are connected at the inner rim of the [*n*]helicenes. For moderate values of *n*, such oligomers could provide extended rigid–rod helical structures that are precisely defined at the molecular level and are expected to possess enhanced chiral properties.

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[25] Enantiomeric excess can be increased by more extensive purification but at the expense of yield (Scheme 1).

[26] CCDC 718269 (**1**) and 718270 (**2**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[27] Computations studies: The ground state geometries for **2a**, **3a**, **5** were fully optimized within the C_2 point group of symmetry at the B3LYP/6-31G(d) level of theory and were determined to be at the minima by the vibrational analyses, using Gaussian 03 program (Ref: [29]). Analogous methods were used for **2a**-*PM*, and employing the B3LYP/6-31G(d,p) level of theory, for model oligomers of [7]helicenes. Computational details can be found in the Supporting Information.

[28] The computed geometry for **2a** is similar to that determined by the X-ray crystallography for **2**.

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