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A Fragment Based Approach toward Thia[*n*]helicenes

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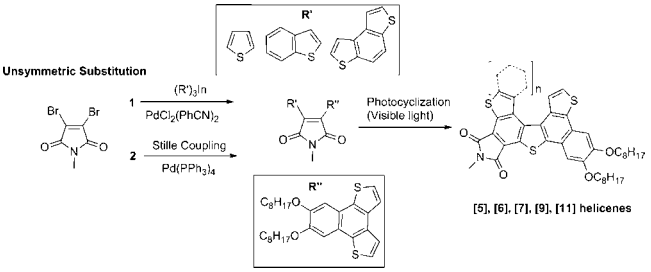
ABSTRACT



The synthesis of [9]- and [11]thiahelicenes, as well as the preparation of lower homologues such as [5]-, [6]-, and [7]thiahelicenes is reported. Efficient palladium catalyzed coupling reactions were employed. Triorganoindium derivatives were selectively mono-cross-coupled with *N*-methyl-3,4-dibromomaleimide followed by Stille coupling with the readily available building block naphthodithiophene. Oxidative photocyclization of the conjugated precursors using visible light was employed to synthesize a series of thia[*n*]helicenes. This modular synthetic methodology is independent of the length of the helical backbone.

Helicenes are representatives of polycyclic aromatic compounds with a structure characterized by a series of *ortho*-annulated aromatic or heteroaromatic rings.[1] With an increase in the number of the *ortho*-conjugated rings, the system can no longer be planar and releases the steric strain by adopting a helical structure giving rise to the *P*- or *M*-configuration and thus helical chirality.[2] These nonplanar helical molecules have attracted increasing interest, due to their extraordinary (chiro)optical and electronic properties.[3] They combine the electronic properties afforded by their extensive π-conjugated system with the (chiro)optical properties associated to their helical structure. During the past decade studies have been carried out toward their applications in asymmetric synthesis,[4] molecular recognition,[5] and material science, for example, as liquid crystals, sensors, and dyes.[6] Thiahelicenes,[7] a subgroup of heterahelicenes, consisting of alternating benzene

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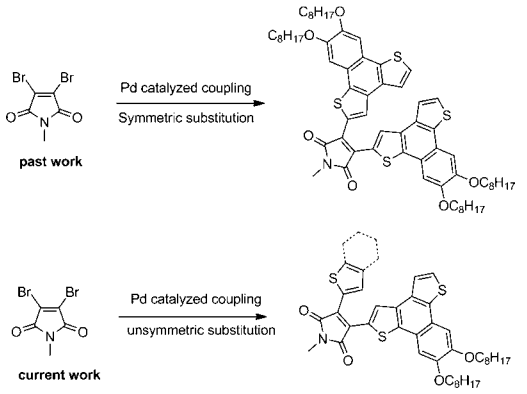
and thiophene rings, are particularly important, as they have more effective conjugation than both their all-thiophene and all-benzene counterparts. [*n*]Thiahelicenes have also been used in organocatalysis for enantioselective transformations,[8] as chiral inducers,[9] and as building blocks for the design of chiral ligands for homogeneous transition-metal catalysis.[10] In view of these intriguing properties, there has been a rapid increase in the development of synthetic methodologies such as oxidative photocyclization of stilbenes by Martin et al. in 1967 and its modification by Katz et al.[11] and some nonphotochemical routes.[12] In 1998 Stary and Stara reported the intramolecular [2 + 2 + 2] cycloisomerizations of triynes.[13] Although this procedure is very efficient, complicated precursors and expensive metal catalysts could be a limiting factor. On the other hand, the classical oxidative photocyclization or a modified form can be used very efficiently by overcoming the drawbacks associated with it. Tailoring the precursors and using visible light instead of UV light appeared to be the most promising to realize this.

A general synthetic methodology which would be independent of both the length of the helical backbone and the presence of functional groups is required. Herein, we report a fragment-based, short, and general methodology for the synthesis of asymmetric and symmetric thia-[*n*]helicenes (n = 5, 6, 7, 9, and 11) *via* efficient palladium catalyzed reactions and photocyclization using visible light to construct the last ring(s) for the final assembly and aromatization of the system. We expect [*n*]helicenes with a sufficiently large number of aromatic rings would be conformationally rigid with large barriers of racemization.

In our previous work,[14] we synthesized symmetric helicenes *via* Stille coupling and photocyclization strategy and addressed the issues of solubility of the precursors and final products by introducing long alkoxy chains (Scheme 1). Thus we synthesized substituted precursors which are conformationally in close resemblance with the final helicenes, thereby solving the problems associated with oxidative photocyclizations. We have extended these aspects in

Scheme 1. Overview of Past and Current Work



the present methodology. The key process in the present methodology was unsymmetric substitution of dibromomaleimide which provides an opportunity to synthesize unsymmetric and symmetric helicenes with [*n*] ≥ 5. Our current approach makes use of the palladium catalyzed selective cross-coupling reaction of triorgano indium[15] derivatives with *N*-methyl-3,4-dibromomaleimides followed by Stille coupling with the readily available building block 8,9-bis(octyloxy)naphtho[1,2-*b*:4,3-*b*′]dithiophene to obtain highly conjugated helicene precursors which undergo oxidative photocyclization using visible light.[14]

We first attempted to synthesize monosubstituted bromomaleimides (Table 1). This was done starting from a triorganoindium reagent (R_3In), which was in turn prepared by lithiation of thiophene, benzothiophene, and benzodithiophene respectively using *n*-BuLi at −78 °C in dry THF and then treating it with $InCl_3$ in THF at −78 °C and warming to room temperature. The triorganoindium derivatives thus prepared were selectively cross-coupled to *N*-methyl-3,4-dibromomaleimide **1** using 5 mol % of $PdCl_2(PhCN)_2$ as the catalyst and THF as the solvent at room temperature for 2−3 h. The monocoupled products **2** and **3** were obtained in 57% and 60% yields respectively which showed good monoselectivity.

The synthesis of compound **4** proved to be more challenging than the earlier prepared derivatives. Monobromomaleimide **4** was prepared under similar conditions as **2** using benzodithiophene, which was in turn prepared according to the literature procedures.[16] The monocoupled product **4** was obtained in 40% yield. In each of the above reactions 10−12% of disubstituted compounds were obtained. Other palladium catalysts such as $Pd(PPh_3)_4$ or $Pd(PPh_3)_2Cl_2$ and Stille coupling or cross-coupling mediated *via* $ZnCl_2$ always gave only a double cross-coupling product. Thus, the $R_3In/Pd(PhCN)_2Cl_2$ system proved to be the most efficient, as it showed high selectivity

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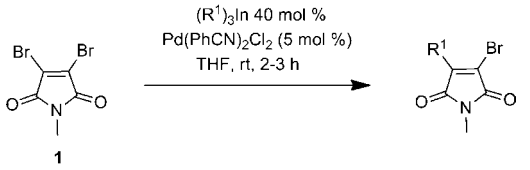
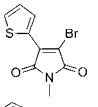
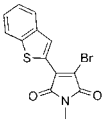
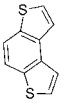
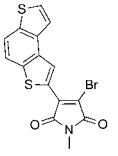
Table 1. Palladium-Catalyzed Mono-Cross-Coupling Reactions of Indium Organometallics with **1**



entry	R^1	product	yield(%)
1			(**2**) 57 %
2			(**3**) 60 %
3			(**4**) 40 %

in the coupling reactions with 3,4-dibromomaleimides and the high atom economy of R_3In in transferring all three groups.[15]

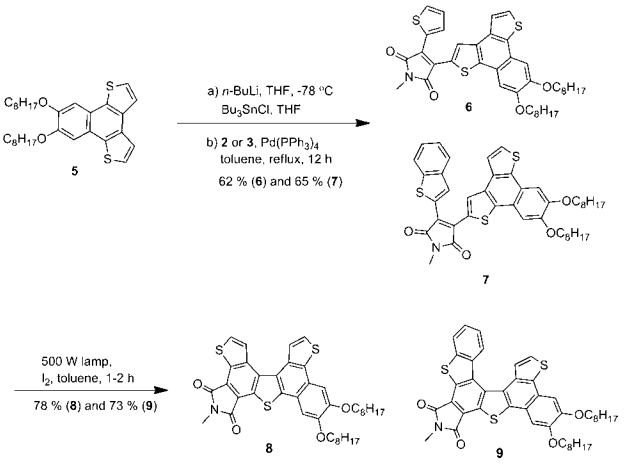
Further, palladium-mediated coupling between bromomaleimides **2** and **3** with the *in situ* prepared monostannyl derivative of compound **5** was employed to give the highly conjugated [5]- and [6]helicene precursors (Scheme 2). Compound **5** was monolithiated using *n*-BuLi and then treated with tributyl stannyl chloride to obtain the monostannyl derivative in quantitative yield.

Compound **6** and **7**, the direct precursors to [5]- and [6]helicenes, were obtained in 62% and 65% yield by Stille coupling between the monostannyl derivative and bromomaleimides **2** and **3** respectively using 5 mol % of $Pd(PPh_3)_4$ as the catalyst and toluene as the solvent under reflux conditions for 12 h.

Compounds **6** and **7** were characterized by NMR and HRMS. These helicene precursors were subjected to irradiation using a 500 W high intensity lamp (visible light) in the presence of iodine and toluene as the solvent (1.5 mM) for 1−2 h.[14] Helicenes **8** and **9** were obtained in 78% and 73% yields. These compounds were fully characterized by NMR and HRMS and showed good solubility in various organic solvents.

As a proof of concept of the methodology we extended it to higher thiahelicenes and attempted to synthesize [7]-, [9]-, and [11]helicenes (Scheme 3). These helicenes could readily be prepared via a double Stille coupling on the building block **5** with monobromomaleimides **2**, **3**, and **4** respectively. Compound **5** was dilithiated using *n*-BuLi and then treated with tributyl stannyl chloride to obtain the distannyl derivative. Stille coupling between the *in situ* prepared distannyl derivative and mono-bromomaleimides

Scheme 2. Synthesis of [5]- and [6]Thiahelicenes: Unsymmetric Helicenes



2, **3**, and **4** respectively using 10 mol % of $Pd(PPh_3)_4$ and toluene as the solvent under reflux conditions for 12 h gave the highly conjugated helicene precursors **10**, **11**, and **12** in 63%, 59%, and 62% yields. The R groups are thiophene, benzothiophene, and benzodithiophene respectively.

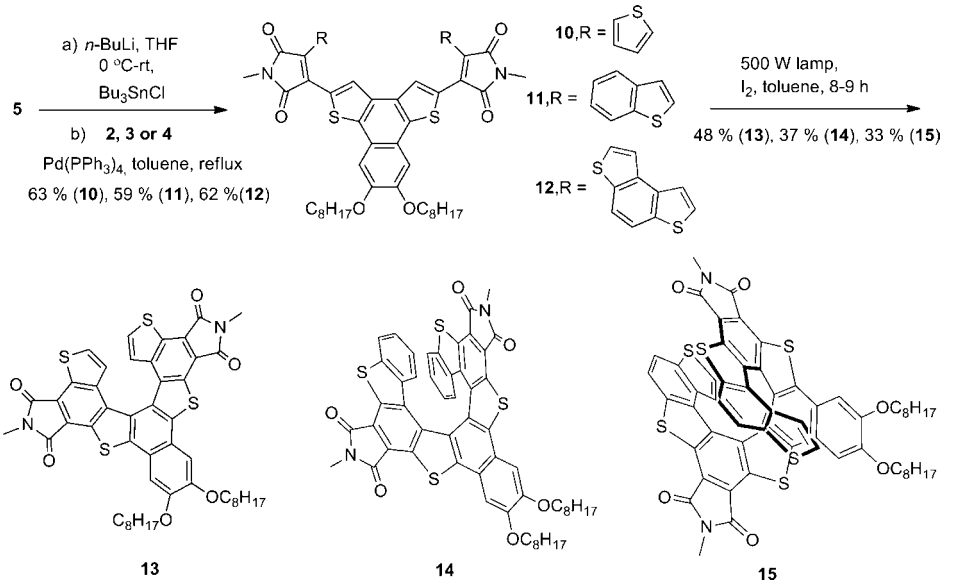
During the synthesis of compounds **10** and **11**, we also observed the formation of compounds **6** and **7** in 5%−8% yield respectively, due to partial destannylation. Material identity was confirmed by HRMS and NMR spectroscopy. Compound **12** showed very low solubility in a variety of organic solvents; hence characterization by NMR spectroscopy was not possible, and it was characterized by HRMS.[17] These helicene precursors were subjected to irradiation under conditions similar to those reported above (1.5 mM) for 8−9 h. Though the reaction time was prolonged for the helicene formation compared to the lower homologues, the closures of two rings have to be taken into account. Helicenes **13**, **14**, and **15** were obtained in 48%, 37%, and 33% yields. Single ring closure was observed during the course of the reaction (not isolated). These compounds were fully characterized by NMR and HRMS and showed good solubility. ^1H NMR of [11]helicene showed two doublets at $\delta = 6.71$ and 5.18 ppm corresponding to the terminal thiophenes. We observe a remarkable upfield shift in comparison to the signals of [7]helicene at $\delta = 6.94$ and 6.17 ppm.

The absorption spectra for helicenes **8**, **9**, **13**, **14**, and **15** in dilute $CHCl_3$ solutions are shown in Figure 1. We observed that the absorption spectra of helicene **8** to helicene **15** gradually red-shifted with the increase in the number of the *ortho*-conjugated rings. We observe significant broadening of the CT-bands in [9]- and [11]helicenes.

In summary we have developed an efficient and general methodology for the synthesis of thia[*n*]helicenes which is independent of the length of the helical backbone.

(17) Compound **12** slowly dissolved in toluene during photocyclization.

Scheme 3. Synthesis of [7]-, [9]-, and [11]Helicenes



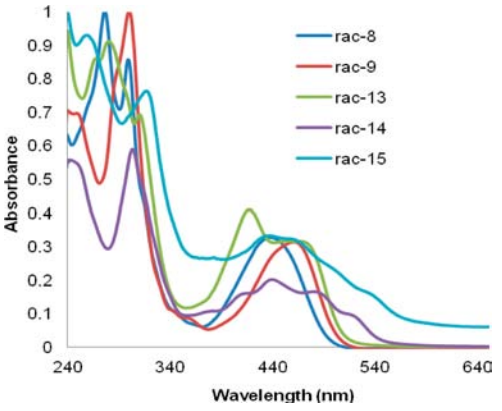


Figure 1. Normalized absorption spectra of helicenes **8**, **9**, **13**, **14**, and **15** in $CHCl_3$.

Based on this methodology, thiahelicenes of various sizes can be prepared with ease. A series starting from [5]helicene to [11]helicene were easily prepared utilizing the selective cross-coupling of indium organometallics and aStille coupling reaction. Substitution of precursors with chiral groups introduces a platform for exploring this strategy in future work for synthesis of enantiomerically pure helicenes, thus illustrating the wide and unprecedented scope of the procedures.

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Supporting Information Available. Detailed experimental procedures and NMR spectra of all the synthesized compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.