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Expeditive Syntheses of Functionalized Pentahelicenes and NC-AFM on Ag(001)

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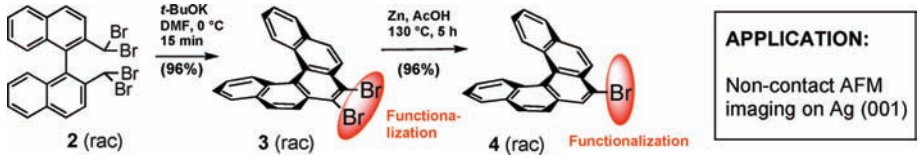
ABSTRACT



One of the shortest and most efficient routes toward a series of functionalized pentahelicenes is reported. Benzylic (dibromo)methine coupling is an important entry into functional helicene chemistry. It allowed a mono- or a double functionalization by some metal-catalyzed Ar−C, Ar−S, Ar−CN, and Ar−I bond formations. Those functions offer new avenues for further applications. For instance, helicene (4) can be supported on a Ag(001) surface, which was characterized by high-resolution NC-AFM imaging.

Helicenes are intriguing helicoidal polyaromatic compounds with a distorted π-system. They have become the centerpiece of several developments in the fields of asymmetric catalysis,[1] advanced materials,[2] (dendrimers, polymers, liquid crystals, self-assembled monolayers, etc.), molecular optoelectronics,[3] and nanosciences.[4]

Concerning their synthesis, the photocyclodehydrogenation of some stilbene-like derivatives has been the method of choice for several decades,[5] but not for pentahelicenes. Competitive transformation to benzo[*g*,*h*,*i*]perylene lowered the yield.[6] This method usually provides a small amount of product by using high dilution techniques (10^{-3} M) in order to avoid a [$2\pi + 2\pi$] dimerization (typically, 100 mg/L of solvent). The need for a larger scale production with simple equipment and a better functionalization of helicenes is a

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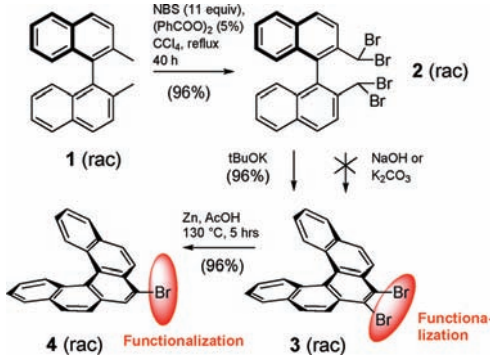
recent quest toward further applications.[7,8] We addressed this goal and describe here a UHV (ultrahigh vacuum) deposition of a functionalized carbohelicene on a Ag (001) surface, characterized by non-contact atomic force microscopy imaging (NC-AFM) with a high resolution.

One of us reported some benzylic bromomethylene ($ArCH_2Br$)-type couplings for making phenanthrene, and penta- and heptahelicenes.[7] However, they suffered from modest yields, and toxic HMPA and a strong base (LiHMDS). 2,2′-Bis(bromomethyl)-1,1′-naphthalene as a precursor to [5]helicene also suffered from a problematic dibromination and purification (50% yield). Only one benzylic (dibromo)methine ($ArCHBr_2$) coupling was previously attempted but in a mediocre yield of **3** (29%), still contaminated by some byproducts. Those results completely discouraged the pursuit of this method, the functionalization of **3**, and further pentahelicene applications.

To circumvent all of those difficulties, we now disclose our strategy for quickly preparing functionalized pentahelicenes on a larger scale (>10 g, Scheme 1). We devised an

Scheme 1. Expeditive Route to Functionalized Helicenes via a Benzylic Gem(dibromo)methine Coupling



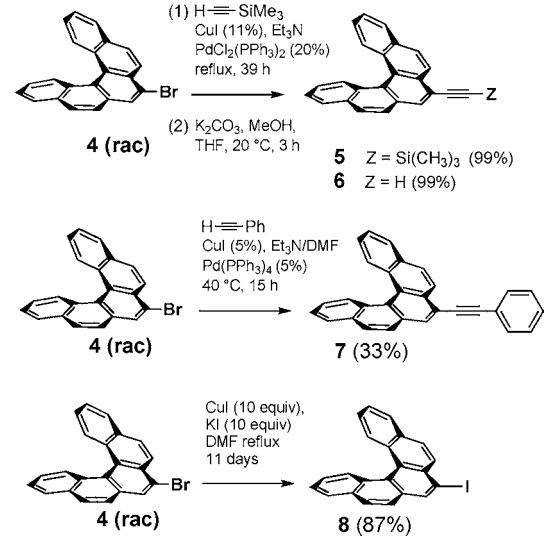
efficient radical tetrabromination of commercial **1** with benzoyl peroxide and an excess of NBS (96% yield). The synthesis of **2** previously required two steps with an overall yield of less than 40%. Finally, a mild and spontaneous ring-closing step propelled this underdeveloped benzylic dibromomethine coupling to among the best methods in helicene synthesis (96% yield) and in the literature.[9]

Because a benzylic (dibromo)methine ($ArCHBr_2$) function is more acidic than a bromomethylene one ($ArCH_2Br$), a rationale for our procedure was to use a weaker base than $NaNH_2$ or LiHMDS. An excess of tBuOK in DMF smoothly provided an excellent yield of 7,8-dibromo[5]helicene **3** (92−96% yield, 0−3 °C for 10−15 min). The molar ratio of *t*-BuOK/**2** was optimized to 5:1. At first, we avoided refluxing in dioxane/aqueous NaOH conditions because of some reported hydrolytic byproducts,[9] but for the sake of a comparison, a gradual heating from 35 to 100 °C for several hours in dioxane/NaOH 1 M was ineffective (mostly unreacted substrate). In a similar trend, anhydrous K_2CO_3 in DMF at 100 °C also left substrate **2** unreacted.

Having produced **3**, we achieved a monodebromination with zinc powder in refluxing acetic acid, which is one of the simplest reductive methods (Scheme 1). After controlling the amount of zinc and reaction time, we obtained 7-bromo[5]helicene **4** in a 96% yield after a crystallization from the reaction mixture, the main byproduct being [5]helicene (<3%). Helicenes **3** and **4** were thus produced on a large scale and in high yields, with cheap reagents and without a chromatographic separation.

The reactivity of **3** and **4** was then verified on such a distorded π system of a carbohelicene. It is relatively underexplored in helicene chemistry. In the first set of reactions, some metal-catalyzed couplings with **4** were tested (Schemes 2 and 3). A Sonogashira reaction was successful

Scheme 2. Functionalization of 7-Bromo[5]helicene **4**



with trimethylsilylacetylene in the presence of triethylamine, CuI, and $PdCl_2(PPh_3)_2$ (Scheme 2). It provided a quantitative yield of 7-(trimethylsilylacetylene)[5]helicene **5**. Removal of the TMS group at 20 °C in a methanolic solution of K_2CO_3 produced a quantitative yield of 7-ethynyl[5]helicene **6**.

Another acetylenic reagent, such as phenylacetylene, was tested with $Pd(PPh_3)_4$ under classic conditions, but **7** was obtained in a low yield. Similarly, a Pd-catalyzed Miyaura−Suzuki coupling with phenylboronic acid and **4** led to 7-phenyl[5]helicene in a low yield (26%).

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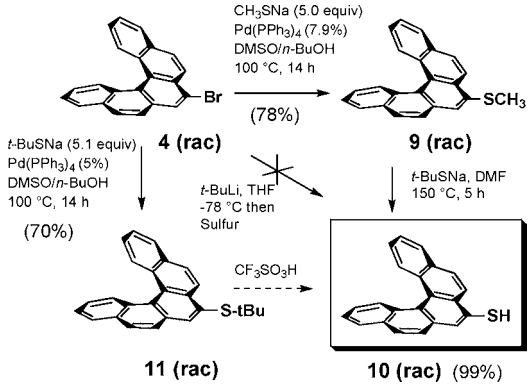
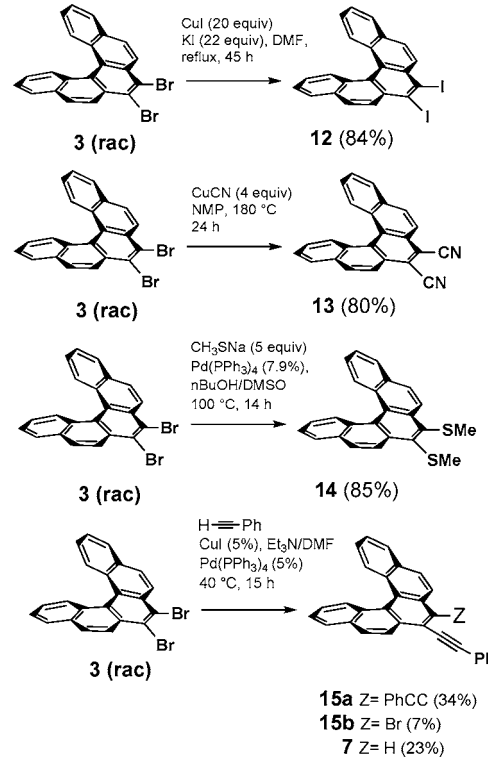
Scheme 3. Pd-Catalyzed Sulfuration of 7-Bromo[5]helicene **4**



Scheme 4. Functionalization of 7,8-Dibromo[5]helicene **3**



Because iodinated compounds are often good candidates for generating carbanions by lithium−halogen exchange, we converted **4** into iodide **8** in an 87% yield in the presence of KI, CuI in refluxing DMF (Scheme 2).

Having in mind a chiral self-assembly of helicenes on a gold surface, we focused on the synthesis of 7-sulfanyl[5]-helicene **10** (Scheme 3). We emphasize the importance and the originality of this work toward sulfanylated or sulfurated carbohelicenes, which are particularly rare in the literature. We first tried a classic thiol formation from elemental sulfur and *t*-BuLi. Insolubility in THF at low temperature possibly prevented a generation of the corresponding anion. Using our methodology for making thiols from thiomethylated precursors, it would bring us on familiar grounds.[10] We succeeded in preparing **9** in a 78% yield under Pd-catalyzed conditions (Scheme 3).[11] Nucleophilic deprotection of **9** with *t*-BuSNa (freshly prepared from *t*-BuSH and NaH) in dry DMF at 160 °C provided the expected thiol **10** in a 99% yield. We also prepared 7-(*tert*-butylthio)[5]helicene **11** as an alternative precursor to **10** because of a known deprotection with CF_3SO_3H. The later was unexpectedly difficult and most substrate was left unreacted, along with some byproducts.

In a second set of reactions with dibromide **3**, 7,8-diodo[5]helicene **12** (Scheme 4) was produced in a similar manner as for **8**. It should help for other metal-catalyzed couplings. Due to the importance of helicene amination and phthalocyanines and chiral diamines as bidentate ligands, we tried a Rosenmund−von Braun reaction with CuCN in 1-methyl-2-pyrrolidinone at 150−180 °C. The expected 7,8-dicyano[5]helicene **13** was produced in a 80% yield along with 7-cyano-8-bromo[5]helicene as a byproduct. Helicene **13** could be reduced to a chiral bidentate diamine or used for making phtalocyanines.[12] A double thiomethylation of **3** to **14** was achieved in a 85% yield from a Pd-catalyzed reaction with CH_3SNa in DMSO/*n*-BuOH at 100 °C.[11] Phenylacetylene reacted with **3** in the presence of $Pd(PPh_3)_4$ to afford **15a** in 34% yield, along with **7** (23%) and 7-bromo-8-(2-phenylethynyl)[5]helicene **15b** (7%). As for **4**, the reactivity was problematic.

Having in hand a variety of [5]helicene derivatives, we first demonstrated that they could be supported under ultrahigh vacuum (UHV at 10^{-10} mbar) on a metallic surface for noncontact AFM studies (NC-AFM) at molecular resolution. Only a few reports dealt with nonfunctionalized [7]helicene, mostly on a Cu(111) or Ni(111) surface.[4] Deposition of functionalized carbohelicenes or [5]helicenes for AFM or STM studies were never reported. We anticipated a strong interaction on a single silver crystal as a support such as Ag(001) and a polarizable and halogenated **4**. The latter molecule was chosen in order to better control its sublimation, its molecular deposition and its self-assembly. For the detection of helicenes on a surface, a standard analytic technique like LEED[13] (low-energy electron diffraction) in combination with NC-AFM were used. LEED yields an average information about the lateral order of nanoobjects on surfaces, wheras NC-AFM is a suitable technique to locally image the topography of molecules on metal surfaces at a molecular resolution.[14]

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(14) Zerweck, U.; Loppacher, Ch.; Otto, T.; Grafström, S.; Eng, L. M. *Nanotechnology* **2007**, *18*, 084006.

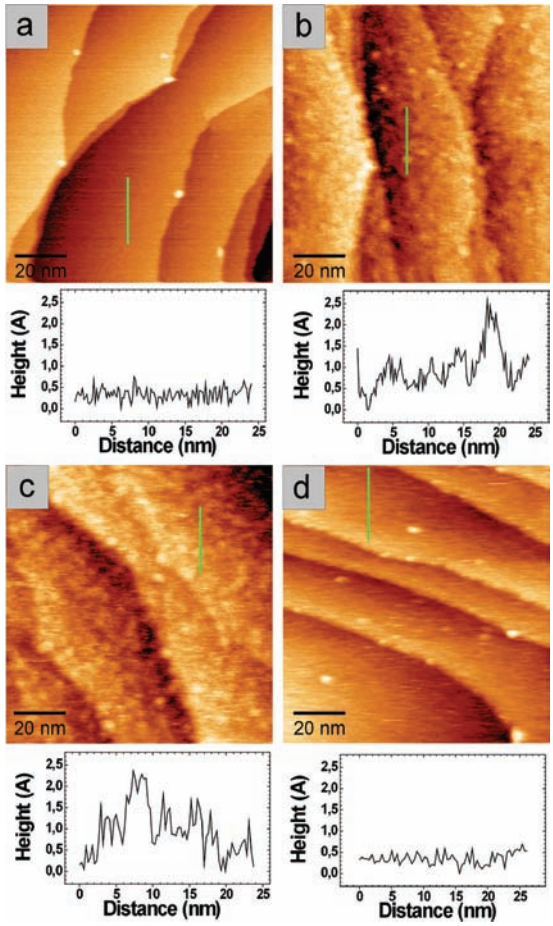

Figure 1. (a) NC-AFM images of **4** representing the topography of the Ag(001) surface directly after the preparation of the silver surface; (b) after deposition of **4** at 20 °C; (c) after an annealing at 130 °C for 1 h; and (d) after a second annealing at 250 °C for 1 h. For a better comparison, the profiles have the same scale. All images: 100 × 100 nm^2, (a) $\Delta f = -21$ Hz, (b) $\Delta f = -30$ Hz, (c) $\Delta f = -45$ Hz, (d) $\Delta f = -23$ Hz.

After **4** was heated at 150 °C for 12 h at reduced pressure (0.1 mmHg) to remove any volatiles, no decomposition of **4** was observed by ^{1}H NMR. After the preparation of the silver surface in UHV, the surface exhibited atomically flat terraces which were intersected by some steps (Figure 1a). Helicene **4** was then evaporated onto the Ag(001) surface in the UHV chamber. NC-AFM images obtained in situ exhibited a granular structure on the surface which corresponded to one monolayer of **4** (Figure 1b). The height differences (profile in Figure 1b) allowed for concluding that the nano-objects had a size similar to that of 7-bromo-5-helicene. An additional annealing of the sample at 130 °C for 1 h did not allow a sufficient molecular mobility on the surface for self-assembly. It might be due to a strong molecular interaction with Ag(001) (Figure 1c). Heating at 250 °C finally led to a complete removal of the molecular layer (Figure 1d).

In summary, an expeditive synthesis of pentahelicene **3** was demonstrated in two steps from **1** (88−92%) or in only one step from **2** (96%). A mono-debromination of **3** afforded **4** in a 96% yield (85−88% from **1**). This synthetic route is an important entry into mono- or disubstituted carbohelicene chemistry after highlighting an important benzylic dibromomethine coupling (92−96%). All steps proceeded on a gram scale with inexpensive reagents and facilitated purifications. Exploration of Ar−S, Ar−I, Ar−C, and Ar−CN metal-catalyzed bond formation was achieved and quickly led to a series of useful functionalized pentahelicenes. We further demonstrated that such helicenes can be supported and stabilized on a metallic surface like Ag(001). We believe that this work is a promising step toward new investigations in the nanoscience of functionalized helicenes supported on surfaces as well as for further studies in chiral materials chemistry.

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Supporting Information Available: Experimental procedures and characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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