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

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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

10.1021/ol9014255 CCC: \$40.75 © 2009 American Chemical Society Published on Web 08/11/2009 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 (LiH-MDS). 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 (ArCHBr₂) 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



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 ringclosing 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 NaNH₂ 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 K₂CO₃ 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



with trimethylsilylacetylene in the presence of triethylamine, CuI, and PdCl₂(PPh₃)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



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 CF₃SO₃H. The later was unexpectedly difficult and most substrate was left unreacted, along with some byproducts.

In a second set of reactions with dibromide **3**, 7,8diodo[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-

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



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 CH₃SNa in DMSO/*n*-BuOH at 100 °C.¹¹ Phenylacetylene reacted with **3** in the presence of Pd(PPh₃)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 LEED¹³ (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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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 nm², (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 ¹H 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 metalcatalyzed 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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