



Exploration of 9-bromo[7]helicene reactivity

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ABSTRACT

Exploration of 9-bromo[7]helicene reactivity mainly in Pd-catalyzed reactions is reported. Palladium catalyzed carbon–carbon and carbon–heteroatom coupling reactions provide a large portfolio of racemic helicenes bearing different functional groups in good to excellent yields. Many of the reactions were performed in the microwave reactor keeping reaction time to a minimum compared with conventional synthetic methods.

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1. Introduction

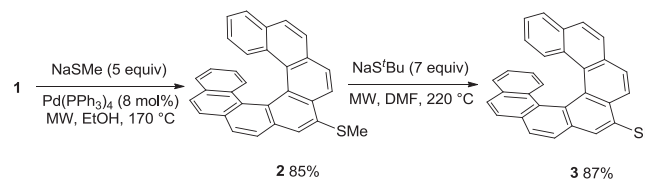
[*n*]Helicenes, a class of intriguing compounds with fully conjugated aromatic system and a non-planar topology, have attracted considerable attention due to their unique properties and potential applications.¹ Among them they are promising as chiral catalysts² and ligands³ in asymmetric syntheses. They have been employed in various areas of chemical sciences, including supramolecular chemistry⁴ and molecular recognition.⁵ [7]Helicene is a particularly interesting [*n*]helicene with complete one full turn of the helix and high optical stability (racemization barrier is 40.5 kcal mol⁻¹).⁶ It has been shown that [7]helicene can act as a ‘molecular tweezer’ for a silver cation,⁷ computational studies for other metallic cations have been published.⁸ Its deposition onto metal surfaces were also investigated.⁹ In comparison to [5]- and [6]helicene, the hepta-derivative has been scarcely explored maybe due to its lower synthetic availability.

In this article, we describe the synthesis and characterization of eleven novel racemic [7]helicenes with versatile functionality enabling further derivatization. Starting material 9-bromo[7]helicene **1** is commercially available and the bromine atom serves as a good starting point for introducing different functional groups. The reactivity of **1** is quite unexplored in helicene chemistry and such a similar complex study of bromine helicene derivative was performed only on their [5]helicene analogues.¹⁰ We have focused on palladium catalyzed microwave-assisted transformations with emphasis on keeping reaction time to a minimum compared with

conventional and known synthetic methods and up-to-date protocols.

2. Results and discussion

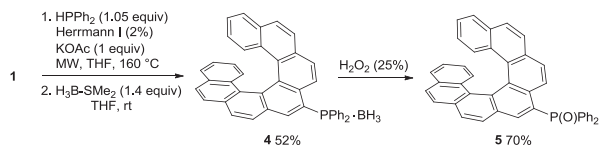
Aiming for metal surface modification by helicenes we prepared sulfur-containing structures (Scheme 1). We improved a published Pd-catalyzed C–S coupling reaction¹⁰ in the sense of time consumption. Employing microwave assisted chemistry we succeed in reduction of the reaction time from 14 h to 30 min. This also brings an advantage in avoiding the use of the high boiling solvents (such as DMSO) that are problematic to remove from the product. Using an excess of sodium methylthiolate in the presence of Pd(PPh₃)₄ in ethanol at 170 °C for 30 min provided the corresponding 9-(methylsulfanyl)[7]helicene **2** in 85% yield after recrystallization from DCM/EtOH. Moreover it was confirmed that this protocol can be used for preparation of other thioethers. Subsequent treatment of **2** with an excess of *t*-BuSNa in DMF under microwave conditions gave 9-sulfanyl[7]helicene **3** in good yield, however rapid decomposition occurred within an hour. This procedure for obtaining the desired thio-helicenes seems to be the easiest despite the fact that thiols can be synthesized directly from **1** analogously to Yi et al.¹¹



Scheme 1. Introducing thio group.

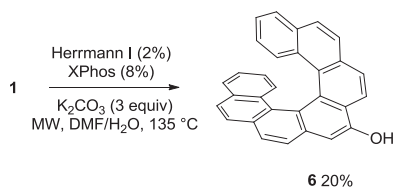
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Helicenes are potentially interesting chiral frameworks for building new chiral phosphines. Thus we decided to explore synthetic routes to the novel [7]helicenyl diphenylphosphine **4**. Being inspired by the methodology of Kappe,¹² **1** was converted to diphenylphosphine on reaction with Ph₂PH, KOAc and a catalytic amount of Herrmann I catalyst (*trans*-bis(acetato)bis[*o*-(di-*o*-tolylphosphino)benzyl]dipalladium(II))¹³ in a microwave initiator (Scheme 2). After conversion into borane complex the crude reaction mixture was purified by flash chromatography on a silica gel yielding desired product **4**. Compound **4** is stable in a solid state towards oxidation under air atmosphere for days. The free phosphine can be quantitatively converted to corresponding phosphinoyl **5** by washing with 25% H₂O₂.



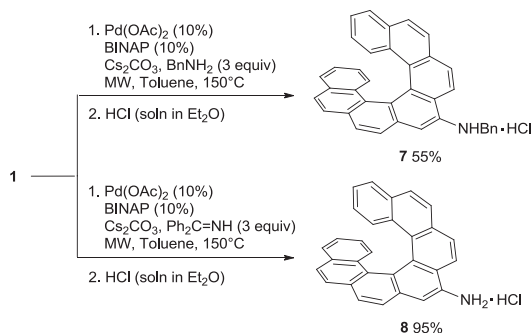
Scheme 2. Introducing phosphine group.

Another interesting functionality is a hydroxyl group. Microwave conditions were used to transfer the oxygen atom into the structure of [7]helicene again. Using a catalytic system consisting of Herrmann I,¹³ XPhos and K₂CO₃ in an inert pre-bubbled DMF/H₂O (9:1) mixture led to the 9-hydroxyl[7]helicene **6** as yellow solid in 20% yield after a chromatographic separation (Scheme 3). An easier way to reach the desired hydroxyl containing compound is described below (Scheme 6). However, the product decomposes during an hour, as observed by NMR.



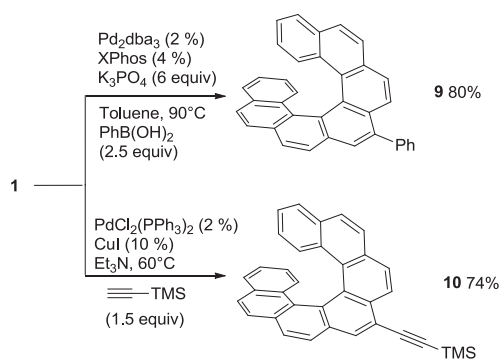
Scheme 3. Pd-catalyzed hydroxylation.

Aromatic amines are important intermediates of great interest. One of the most powerful methods for preparing a variety of arylamines from aryl halides and amines catalyzed by palladium complexes was discovered by Buchwald and Hartwig.¹⁵ We applied their chemistry to the preparation of helicene amines (Scheme 4). Accordingly, on treatment of **1** with benzylamine or benzophenone imine under the standard reaction conditions, derivatives **7** and **8** were prepared in good or high yield and isolated as hydrochlorides.



Scheme 4. Buchwald–Hartwig amination.

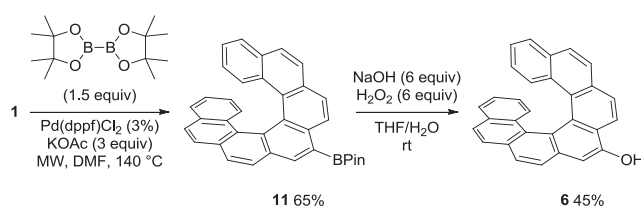
The reactivity of **1** was also tested in relatively unexplored cross-coupling reactions (Scheme 5). We employed Sonogashira conditions with trimethylsilylacetylene in the presence of Pd(PPh₃)₂Cl₂,



Scheme 5. C–C couplings.

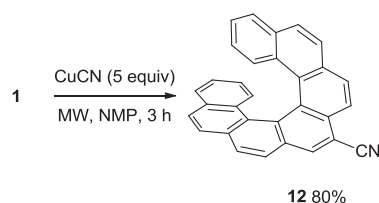
CuI and triethylamine. This provided high yield of 9-(trimethylsilylacetylenyl)[7]helicene **10**. Similarly, a Pd-catalyzed Miyaura–Suzuki coupling with phenylboronic acid in the presence of Pd₂dba₃, XPhos and K₃PO₄ as a base led to 9-phenyl[7]helicene **9** in 80% yield.

Aryl boronate esters are of great importance in organic synthesis, in particular as a substrate for their ability to form C–C bonds through Suzuki–Miyaura coupling. The cross-coupling reaction of aryl boronic acids esters with aryl halides or aryl triflates has become one of the most widely applied methods for constructing unsymmetrical biaryl systems. Miyaura reported the preparation of aryl boronates from aryl halide and bis(pinacolato)diboron (Pin₂B₂) using palladium catalysis.¹⁴ In the course of our studies, we investigated the borylation reaction of Pin₂B₂ with **1** under the standard conditions (Pd(dppf)Cl₂, KOAc, DMF) and helicene boronate **11** was obtained in good yield (Scheme 6). Moreover, this derivative can act as a starting material for other reactions. Being inspired by Marder et al.¹⁶ we transformed **11** into **6** giving a better yield (45%) compared with direct Pd-catalyzed C–O coupling reaction.



Scheme 6. Borylation and subsequent hydroxylation.

Besides palladium catalyzed cross-coupling reactions we also tried to transform **1** into the 9-cyano[7]helicene by Rosemund–von Braun reaction with CuCN in 1-methyl-2-pyrrolidinone under MW conditions (Scheme 7). Microwave assisted reaction again brings a significant reduction of a reaction time and **12** was obtained in an excellent yield of 80% after recrystallization from DCM/EtOH mixture.



Scheme 7. Cu(I)-mediated cyanation.

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