

Photochemistry

Photochemical Functionalization of Helicenes

Martin Jakubec,^[a, b] Indrajit Ghosh,^[a] Jan Storch,^{*,[b]} and Burkhard König^{*,[a]}

Abstract: Herein, a visible-light photochemical approach for practical helicene functionalization at very mild reaction conditions is described. The photochemical reactions allow for the regiospecific and innate late-stage functionalization of helicenes and are easily executed either through the activation of C(sp²)-Br bonds in helicenes using K₂CO₃ as inorganic

base or direct C(sp²)-H helicene bond functionalization under oxidative photoredox reaction conditions. Overall, using these transformations six different functional groups are introduced to the helicene scaffold through C-C and four different C-heteroatom bond-forming reactions.

Introduction

Helicenes are a class of *ortho*-condensed chiral polyaromatics that have gained increasing attention over the past years.^[1] Their extended π -system and inherent chirality bestow a unique combination of properties: They exhibit high specific optical rotations,^[2] circularly polarized luminescence^[3,4] and electroluminescence,^[5,6] and can act as semiconductors possessing helical chirality.^[7,8] As such, they are valued as functional molecules in various branches of chemistry and in material science. In addition, they have been used as asymmetric ligands in transition-metal catalysis and organocatalysts,^[9-11] as starting materials for the construction of conductive chiral polymers,^[12,13] and in organic electronic devices.^[14-16]

Regardless of the widespread applications, helicenes are still synthesized following conventional methods using pre-functionalized starting materials,^[11,17-19] which makes the further derivatization to finetune the properties of the target compounds at a later stage difficult. Therefore, the late-stage introduction of functional groups onto the helicene scaffold is highly desirable, which, however, remains challenging owing to the lack of regioselectivity,^[20-22] and only a limited number of methods for the synthesis of functionalized helicenes on a larger scale.

Gingras and co-workers explored C(sp²)-Br bond functionalizations in 7-bromo- and 7,8-dibromo[5]helicenes under transition-metal catalyzed reaction conditions.^[23] Storch reported the functionalization of 2-bromo[6]helicene^[24] and 9-bromo[7]helicene.^[25] In a slightly different approach, Starý and Stará reported the functionalization of 3-hydroxy[6]helicene into various heteroatom containing helicenes,^[26] and Crassous explored the reactivity of [6]helicene pinacolboronate for the synthesis of amines and amino acids with a helical scaffold.^[27]

In the past decade, visible-light-mediated photoredox catalysis has evolved into a valuable method for organic synthesis, and changed the way we activate chemical bonds for chemical transformations.^[28-34] Recently, we and others have functionalized arenes and heteroarenes by visible-light-mediated photoredox activation of C(sp²)-halogen^[35-38] or C(sp²)-hydrogen bonds.^[33,39] The former transformation, depending on the choice of the substrate and on the reaction conditions, proceed through single-electron reduction using polypyridyl transition-metal complexes,^[40] simple organic dyes,^[35,36,41] or using potassium *tert*-butoxide as a base under ultraviolet (UV, $\lambda_{\text{ex}} \leq 350$ nm) irradiation (S_{RN}1 reactions).^[42] Photochemical (hetero)aromatic C(sp²)-hydrogen bond functionalizations rely on the initial oxidation of the heteroarene to the respective radical cation, which then reacts with different nucleophiles yielding C-H functionalized (hetero)arenes after re-aromatization.^[33]

Inspired by photochemical (hetero)arene functionalizations, we wondered whether the analogous photochemical strategies could be employed for the late-stage functionalization of helicenes. Herein, we report our attempts towards the photochemical functionalization of helicenes using visible light.

Results and Discussion

We began our investigations using 2-bromo[6]helicene (**1**) as a model substrate. Photoinduced electron transfer activates the C(sp²)-Br bond in 2-bromo[6]helicene. The radical anion fragments under release of a bromide anion, yielding the corresponding [6]helicene radical that is used for subsequent func-

[a] M. Jakubec, Dr. I. Ghosh, Prof. Dr. B. König
Fakultät für Chemie und Pharmazie, Universität Regensburg
93040 Regensburg (Germany)
E-mail: burkhard.koenig@ur.de

[b] M. Jakubec, Dr. J. Storch
Institute of Chemical Process Fundamentals of the CAS, v.v.i.
Rozvojová 2/135, Prague 6, 165 02 (Czech Republic)
E-mail: storchj@icpf.cas.cz

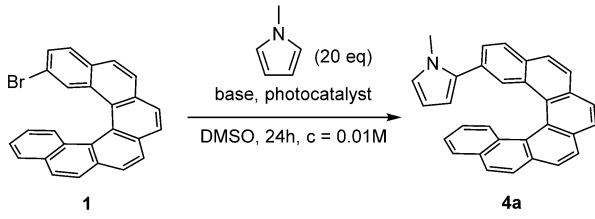
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tionalization reactions. When a reaction mixture containing 2-bromo[6]helicene, *N*-methyl pyrrole (as a model radical trapping reagent), rhodamine 6G and *N,N*-diisopropylethylamine (DIPEA) as sacrificial electron donor in DMSO was irradiated with a blue LED (455 ± 15 nm) for 24 h, the desired product **4a** was obtained in 41 % yield (entry 1, Table 1). Rhodamine 6G provides a very high reduction potential upon blue-light photoexcitation and activates even C(sp²)-Br bonds in donor-substituted aryl halides.^[36,41] However, control experiments revealed that the activation of the C(sp²)-Br bond in 2-bromo[6]helicene does not require a photocatalyst and the desired product is also isolated in 39% yield upon irradiation in the presence of only DIPEA (entry 2, Table 1). Performing the reaction either in the dark or in the absence of DIPEA did not yield the desired product **4a**, and confirmed that irradiation and a base are required for C(sp²)-Br bond functionalization of 2-bromo[6]helicene. The mass balance of the transformation is excellent with [6]helicene as dehalogenated byproduct and the recovery of the unreacted starting material during column chromatography. Importantly, the formation of the dehalogenated product was significantly reduced when the reaction was performed in 0.1 M scale using K₂CO₃ as an inorganic base: The functionalized product was isolated in 61 % yield.^[43] Performing the reaction in [D₆]DMSO slightly disfavored the hydrogen atom abstraction of the [6]helicene radical from solvent, and increased the yield of the desired product to 76% (entry 4 in Table 1), but does not advocate the use of an expensive deuterated solvent for this transformation.

With the optimized reaction conditions in hand (entry 3, Table 1), requiring only mixing of bromo-substituted helicenes,

Table 1. Optimization of reaction condition for the functionalization of 2-bromo[6]helicene **1** with *N*-methylpyrrole.



Entry	Base	Catalyst [mol %]	Conditions	Yield [%] ^[a]
1	DIPEA	Rh-6G (10.0)	455 nm, 24 h, [c] = 0.01 M	41
2	DIPEA	–	455 nm, 24 h, [c] = 0.01 M	39
3	K ₂ CO ₃	–	455 nm, 24 h, [c] = 0.1 M	61
4	K ₂ CO ₃	–	535 nm, 24 h, [c] = 0.1 M	43
5	K ₂ CO ₃	–	455 nm, 24 h, [c] = 0.1 M, [D ₆]DMSO	76
6	–	–	455 nm, 24 h, [c] = 0.1 M	0
7	K ₂ CO ₃	–	dark, 24 h, [c] = 0.1 M	0

[a] Yields of isolated material are reported.

K₂CO₃, the trapping reagent, and irradiation of the reaction mixture under nitrogen using a blue LED, we explored the scope of the method for helicene functionalization using different trapping reagents. 2-Bromo[6]helicene (**1**) was used as a model substrate. The photochemical reactions in the presence of biologically relevant heteroarenes such as pyrrole and its derivatives gave the desired (hetero)arylated-[6]helicene products (**4a–d**, Figure 1) in moderate to good yields, and the pyrrole derivatives were functionalized exclusively at their 2 position.

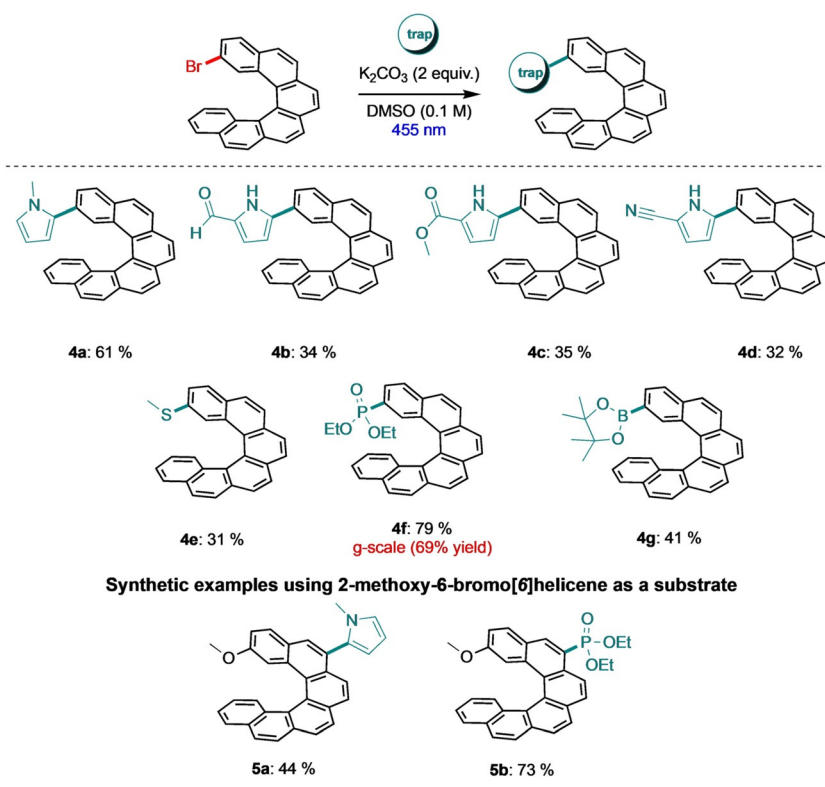


Figure 1. Functionalization of bromo[6]helicenes.

Photochemical reactions using dimethyl disulfide, triethylphosphite, and bis(pinacolato)diboron led to the formation of functionalized [6]helicenes (examples **4e–g**, Figure 1) through sulfide formation, phosphorylation, and borylation reactions, respectively. The photochemical reactions leading to C(sp²)–C(sp²), C(sp²)–P, C(sp²)–S, and C(sp²)–B functionalized [6]helicenes proceed at room temperature (25 °C). Other bromo-substituted [6]helicenes were functionalized by the photochemical reaction yielding the desired products in good to excellent yields (see examples **5a** and **5b** in Figure 1 for the functionalizations of 2-methoxy-6-bromo[6]helicene). The reaction was performed on a larger scale with similar product yields (see example **4f** in Figure 1 for the gram-scale reaction and the Supporting Information for further details).

The photochemical activation of C(sp²)–Br bonds is equally effective for the functionalization of [7]helicenes, as exemplarily show for 9-bromo[7]helicene (**2**) as a model substrate. Photochemical reactions in the presence of heteroarenes such as substituted pyrroles, indoles, thiophenes, and furan gave the desired heteroarylated-[7]helicene products in moderate to very good isolated yields (examples **6a–g**, Figure 2). Note that the C–Br bond in the indole moiety remains intact in the functionalized product **6e**. Heteroarenes, such as thiophene and furan, which were reported to be relatively inert in trapping (hetero)arene radicals under reductive photoredox reaction conditions,^[35,44] can be installed onto the [7]helicene scaffold under our photochemical conditions albeit in moderate yields. Photochemical reactions in the presence of triethylphosphite, bis(pinacolato)diboron, and dimethyl disulfide gave the desired products **6h–j**, which were isolated in 45–92% yields.

It is worth mentioning here that the reported base-assisted (in this case, K₂CO₃) photochemical activation of C(sp²)–Br bonds is also effective for the functionalization of other poly-

cyclic aromatic bromides bearing an extended π-system (see examples in Figure 3). For example, when 2-bromobenzo[*c*]phenanthrene (**7**) was reacted, the C(sp²)–C(sp²) and C(sp²)–P bond forming products were isolated in 41 and 71% yields, respectively. However, photochemical reactions using 3-bromophenanthrene or 9-bromophenanthrene as substrates yielded the phosphonylated products only in low to moderate yields, and the C(sp²)–C(sp²) bond forming products using *N*-methylpyrrole were obtained only in traces.

The examples discussed so far (Figure 1 and 2) showcase helicene functionalizations through the activation of C(sp²)–Br bond in substituted bromo[6/7]helicenes. The use of an alternative photochemical approach under oxidative reaction conditions allowed for the installation of functional groups onto the helicene scaffolds through direct C(sp²)–H helicene bond functionalization. In this process, we envisioned the photochemical oxidation of helicenes leading to the corresponding radical cations, which then react with different nucleophiles present in the reaction media to afford the direct C–H bond functionalized helicene products (Figure 4). It is to be noted here that Fukuzumi,^[45] Niciewicz,^[46] König,^[39] and many others^[33,47–48] have already explored this photochemical strategy for the functionalization of arenes and heteroarenes. Direct C–H helicene bond functionalization is of synthetic interest, but challenging given that there are not many methods known apart from electrophilic substitution for such transformations.^[21,49–51]

The examples of direct C(sp²)–H helicene bond functionalization using 2-methoxy[6]helicene (**3**) as a model substrate are depicted in Figure 4. Simple nucleophiles served as precursors for the desired functional groups, including bromination. For the bromination reaction we adopted the reaction condition reported by Fukuzumi and co-workers.^[45] The reaction was

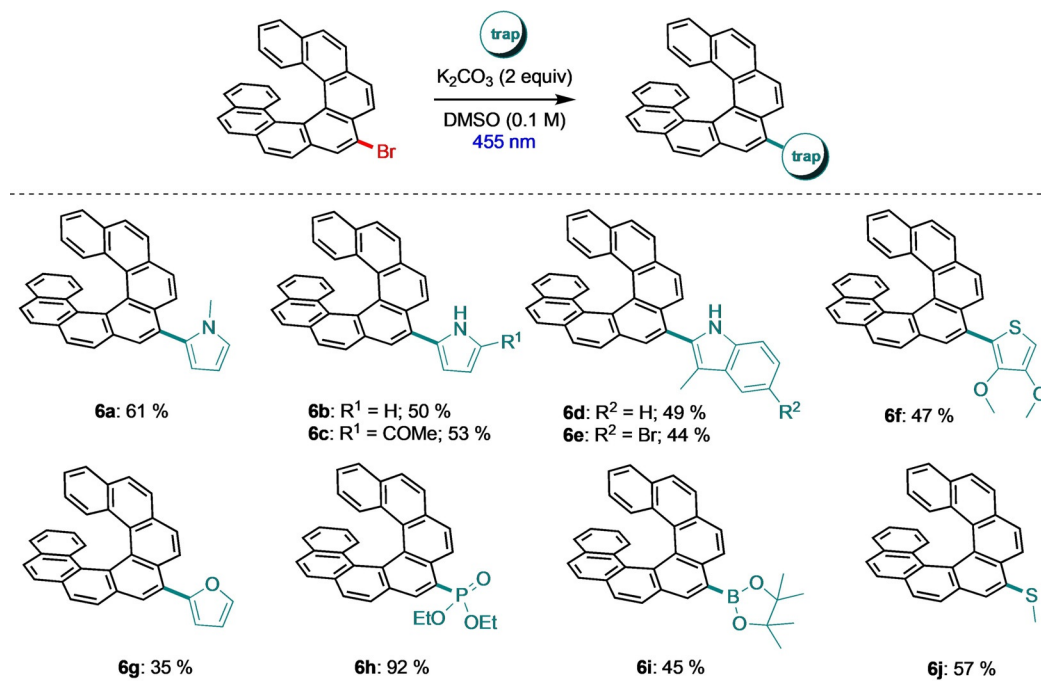


Figure 2. Functionalization of 9-bromo[7]helicene.

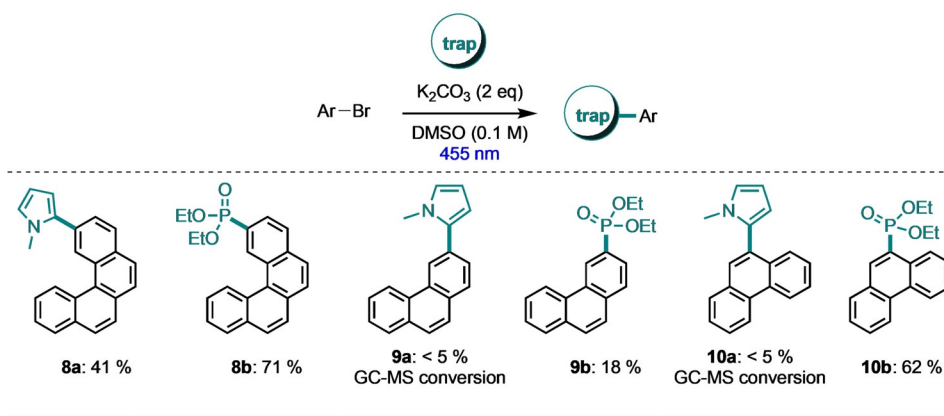


Figure 3. Functionalization of polycyclic aromatic bromides.

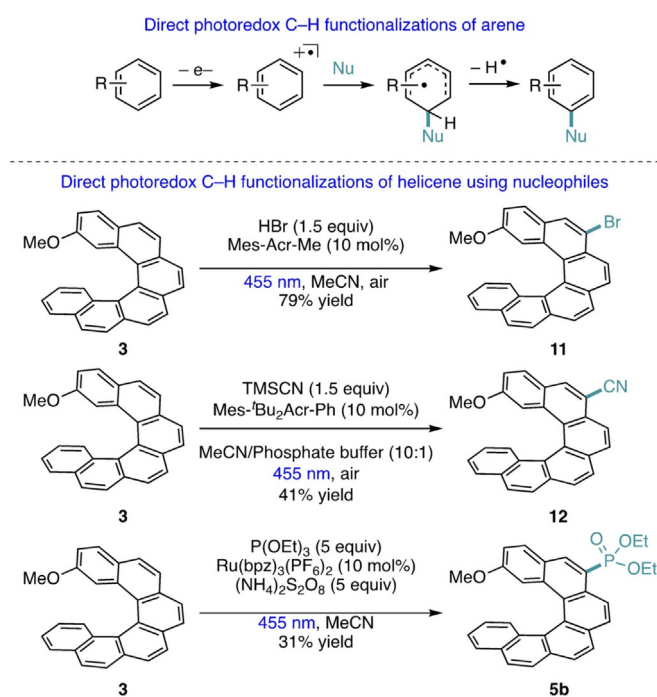


Figure 4. General mechanism of oxidative photoredox C–H functionalizations.^[33] Direct C–H helicene functionalization (bromination, cyanation, and phosphonylation are shown) with the respective yields of isolated materials.

carried out in acetonitrile using 9-methyl-10-mesitylacridinium tetrafluoroborate (10 mol%) as an organic photocatalyst and hydrogen bromide (1.5 equiv) as the brominating reagent. The reaction proceeded smoothly under air and the brominated product **11** was isolated in 79% yield after four hours of irradiation with a blue LED. The ¹H NMR analysis showed that the product consists of only one regioisomer, and 2D NMR experiments confirmed that helicene **3** was functionalized only at the 6 position. The cyanation reaction was performed using a protocol reported by Nicewicz.^[46] In this case, the reaction was conducted under air atmosphere using an acridinium photocatalyst (10 mol%) in 10:1 mixture of acetonitrile/pH 9 phosphate buffer, and trimethylsilyl cyanide (1.5 equiv) was used as

the source of the –CN group. After 24 hours of irradiation, the corresponding functionalized product was isolated in 41% yield. NMR analysis confirmed again the formation of only one regioisomer substituted at the position 6. The phosphonylation reaction was conducted under the photochemical reaction condition reported by König and co-workers,^[39] and the desired product was isolated in 33% yield.

Conclusions

We have reported the photochemical functionalization of helicenes. Bromo-substituted helicenes are easily activated in DMSO under visible-light irradiation and the presence of K_2CO_3 providing a range of functionalized helicenes in good to excellent yields. Adopting reported photochemical arene functionalization protocols allowed for the oxidative helicene functionalization which gave C(sp²)–H functionalized helicene products in moderate to excellent yields of isolated material. Both methods do not require transition-metal catalysts and proceed at room temperature. We anticipate that visible-light-mediated reactions will find more applications for the late-stage functionalization of helicenes.

Experimental Section

For the synthesis of helicenes detailed descriptions of experimental procedures (procedures A to D), characterization of functionalized products, and spectroscopic/chromatographic information, see the Supporting Information.

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Conflict of interest

The authors declare no conflict of interest.

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