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Direct regioselective C–H borylation of [5]helicene†

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Ir-catalyzed borylation of [5]helicene was studied for the first time. The obtained results indicate that borylation proceeded preferentially at the 2- and 3-positions. By using an appropriate catalytic system, 3-borylated [5]helicene can be formed as the major product in a high yield and regioselectivity (up to 89%, 8 : 1 ratio of isomers). The monoborylated [5]helicenes were further utilized in a Suzuki–Miyaura cross-coupling reaction to produce 2- or 3-arylated helicenes in very good isolated yields (80–94%).

Helicenes represent a unique class of polycyclic aromatic hydrocarbons where the benzene rings are all *ortho*-fused, fully conjugated, and with a non-planar topology. They have attracted increasing attention owing to their unrivalled structural features[1–3] and many potential applications in chiral materials,[4–8] self-assembly,[9–11] asymmetric synthesis,[12–14] and opto-electronic materials.[15–18] Of importance, unique properties of helicenes can be addressed by introducing substituents at the periphery of the helical core. From a synthetic point of view, such modifications are not trivial, therefore the selectively substituted helicenes are usually made from pre-functionalized substrates.[1,2] These methods are usually not general enough to produce a large library of congeners. This can be explained by the lack of compatibility of some functional groups or their deactivation effects on the key reaction for producing helicenes. Although a post-functionalization of helicenes appears attractive and would greatly accelerate the development of new functional molecules, it has been underdeveloped in the history of helicene chemistry,[19–21] and restricts, to some extent, practical applications of helicenes.

Based on our previous results on borylation of [4]helicene[21] we envisioned that [5]helicene (Fig. 1) could be selectively functionalized by an iridium catalyzed C–H bond activation/borylation process. Since regioselectivity of direct borylation of aromatic compounds under the standard conditions ([Ir(OMe)(cod)]$_2$/dtbpy) is sterically driven, it is generally accepted that C–H bonds *ortho* to the substituent and *ortho* to ring junction (peri-position) do not usually react.[22,23] Hence, [5]helicene should be borylated at sterically more accessible positions 2 and 3. Out of these two, position 2 is more sterically hindered (overlapping by the other end of the molecule), therefore the appropriate choice of catalytic system and the third dimension (helicity) of the molecule should contrive an additional level of regioselectivity to distinguish between these two positions.

According to our previous study of [4]helicene[21] and the preceding studies of iridium-catalyzed borylation of arenes[22–27] and fused polyarenes,[28–40] we subjected [5]helicene **1** to standard borylation conditions. Thus, equimolar quantities of **1** and B$_2$pin$_2$ (pin = pinacolato), a catalytic amount of [Ir(OMe)(cod)]$_2$ (5 mol%) and 4,4′-di-*tert*-butyl-2,2′-bipyridine (dtbpy) (10 mol%) were allowed to react in cyclohexane. A reaction carried out at 23 °C for 16 h afforded only the starting material and traces of monoborylated products (according to EI/MS analysis). An increase of the reaction temperature to 50 °C and subsequently to 80 °C resulted in better conversion of **1** and a mixture of two monoborylated compounds in slightly better yield (~10%) was obtained. These results clearly showed that C–H activation/borylation of [5]helicene is possible but requires harsher reaction conditions than sterically distinct [4]helicene. In view of the aforementioned, borylation of [5]helicene at 100 °C for 24 h was attempted (Scheme 1). After removal of the volatiles and the subsequent column chromatography of the residue on silica gel (hexane/DCM from 100 : 0 to 0 : 100) three colorless fractions

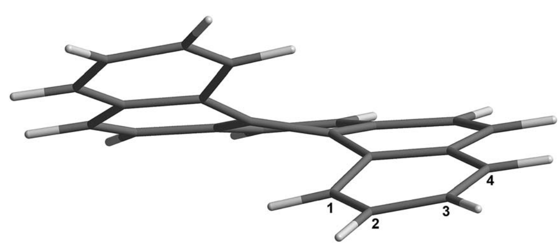

Fig. 1 Molecular structure of [5]helicene.

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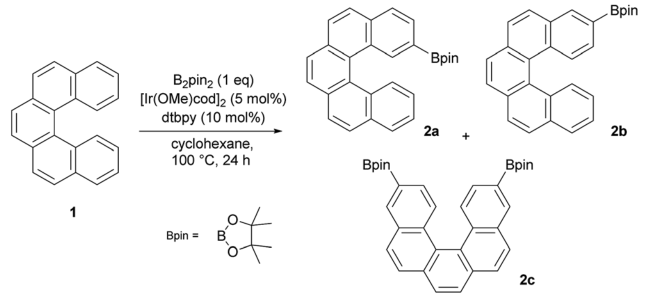


Scheme 1 Ir-catalyzed C–H borylation of [5]helicene.

were obtained: unreacted **1** (79%), a mixture of 2- and 3-borylated [5]helicenes (16%) and a small fraction containing a trace amount of bisborylated [5]helicene (~1%). The subsequent separation of the second fraction by non-aqueous reverse phase chromatography (NARP) afforded two regioisomers: 2-borylated [5]helicene **2a** (4%) and 3-borylated [5]helicene **2b** (12%). The structure of the major product **2b** was unequivocally confirmed by a single-crystal X-ray diffraction analysis (Fig. 2). The third fraction contained only one compound, structure of which was later on assigned to symmetrical 3,12-bisborylated [5]helicene **2c**. The formation of unsymmetrical 2,12-bisborylated and symmetrical 3,13-bisborylated [5]helicene was not observed under these conditions.

These results prompted us to find conditions that will increase the yields of borylated products and enable us to control regioselectivity of borylation as well (Table 1). First, 2/1 ratio of **1** to B_2Pin_2 was used to suppress the formation of bisborylated product **2c**. Second, the reaction temperature was increased to 120 °C. Under these conditions 1 : 3 mixture of **2a** and **2b** was obtained in 26% isolated yield (based on 1 equiv. of **1**) after 24 hours (entry 1). Reactions performed in 1,4-dioxane, dibutyl ether, ethyl acetate, 2-methyl tetrahydrofurane or mesitylene gave products in low yields, if any (entries 2–6). The use of microwave conditions[41,42] resulted in low conversion and lower selectivity, affording a complex mixture of products in which the presence of tris-borylated [5]helicenes was observed by EI/MS (entry 7). Change of the ligand to a more rigid and electron-rich 3,4,7,8-tetramethyl-1,10-phenanthroline (tmphen), which can enhance the activity of the resulting

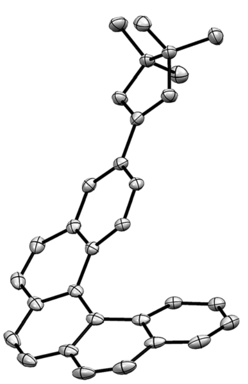
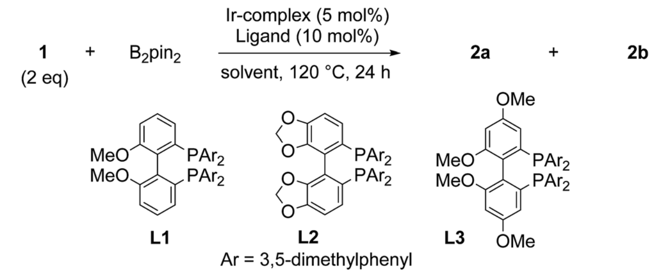


Fig. 2 ORTEP drawing of **2b** with 30% thermal ellipsoids.

Table 1 Ir catalyzed borylation of **1** under various conditions



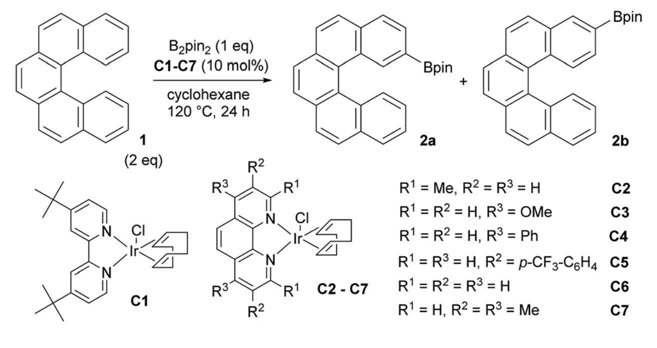
Entry	Ligand[a]	Solvent	Yield **2a** + **2b**[b] (%)	Ratio of **2a** : **2b**[c]
1	dtbpy	Cyclohexane	26	1 : 3
2	dtbpy	1,4-Dioxane	0	—
3	dtbpy	Bu_2O	20	1 : 3.6
4	dtbpy	EtOAc	19	1 : 3.2
5	dtbpy	2-Me-THF	0	—
6	dtbpy	Mesitylene	9	1 : 3.1
7[d]	dtbpy	MTBE	n.d.[e]	—
8	tmphen	Cyclohexane	56	1 : 5
9	**L1**	Cyclohexane	14	1 : 5
10	**L2**	Cyclohexane	21	1 : 4.7
11	**L3**	Cyclohexane	18	1 : 6

[a] dtbpy: 4,4′-di-*tert*-butyl-2,2′-dipyridyl combined with $[Ir(OMe)cod]_2$; tmphen: 3,4,7,8-tetramethyl-1,10-phenanthroline combined with $[Ir(OMe)cod]_2$; **L1**, **L2** and **L3** combined with $[Ir(OH)cod]_2$. [b] Isolated combined yield of **2a** + **2b** based on 1 equiv. of **1**. [c] Ratio determined by ^{1}H NMR. [d] Microwave reactor was used. [e] Complex mixture – not determined.

catalyst and often overperforms dtbpy,[43–46] gave **2a** and **2b** in a higher yield of 56% with a considerably increased regioselectivity of 1 : 5 (entry 8). To fully employ the shape of the molecule and improve the regioselectivity of the borylation, we also screened sterically demanding ligands **L** successfully used for *para*-borylation of benzene derivatives[47,48] or regioselective borylation of [4]helicene.[21] These bis(phosphine) type ligands in combination with $[Ir(cod)OH]_2$ afforded the products **2a** and **2b** with ratios in the range of 1 : 4.7–6. DM-MeO-BIPHEP **L1**, reported as the best ligand for *para*-borylation, gave rise to 1 : 5 mixture of **2a** and **2b** in a low combined yield of 14% (entry 9). DM-Segphos **L2** (entry 10) or DM-Garphos **L3** (entry 11), ligands of choice for borylation of [4]helicene, provided **2a** : **2b** in combined yields of 21% and 18% and regioselectivity of 1 : 4.7 and 1 : 6, respectively (see the ESI† for the complete list of conditions tested).

These unsatisfactory results turned our attention back to rigid phenanthrene type ligands. We prepared several iridium complexes[49] and carried out the reactions in cyclohexane at 120 °C (Table 2). In general, these pre-prepared bench stable complexes afforded highest yields of **2a** and **2b** and also highest regioselectivity. The use of Ir[(dtbpy)(cod)Cl] **C1** afforded **2a** and **2b** in 60% yield and 1 : 5.4 ratio (entry 1). Complexes based on neocuproin **C2**, 4,7-dimethoxy-1,10-phenanthroline **C3**, bathophenanthroline **C4** and 3,8-bis[3,5-bis(trifluoro-methyl) phenyl]-1,10-phenanthroline **C5** gave **2a** and **2b** in a moderate yields (~50%) and lower regioselectivity in the range of 1 : 2.3–

Table 2 Effect of the catalysts on the regioselectivity of the Ir-catalyzed C–H borylation of [5]helicene

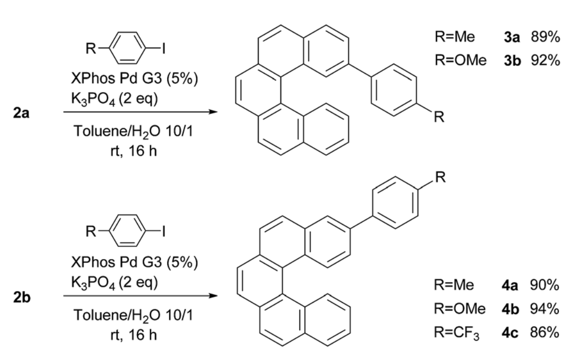


Entry	Catalyst	Yield **2a** + **2b**[a]	Ratio of **2a** : **2b**[b]
1	**C1**	60	1 : 5.4
2	**C2**	66	1 : 3
3	**C3**	51	1 : 4.3
4	**C4**	49	1 : 3.3
5	**C5**	42	1 : 2.3
6	**C6**	52	1 : 6
7	**C7**	89	1 : 8

[a] Determined by ^{1}H NMR, based on 1 equiv. of **1**. [b] Determined by ^{1}H NMR.

4.3 (entries 2–5). A complex with a simple 1,10-phenanthroline **C6** gave better regioselectivity of 1 : 6 in a moderate yield 52% (entry 6). The best result, in terms of the yield and selectivity (89%, 1 : 8), was obtained with the Ir-tmphen complex **C7** (entry 7). The use of other solvents did not result in any improvement and the use of a $[Ir(cod)Cl]_2$/tmphen mixture resulted in a lower yield (70%) and a drop in selectivity to 1 : 6.4 (see the ESI† for the complete list of conditions tested).

Our effort to also produce bis-borylated [5]helicenes in high yield was not successful. Although reaction carried out under standard conditions only produced selectively the symmetric 3,12-bisborylated [5]helicene **2c**, the yields were negligible even when a big excess of B_2pin_2 was used together with a longer reaction time and a higher temperature. The use of more potent catalyst Ir[(tmphen)(cod)Cl] with an excess of B_2pin_2 resulted in loss of selectivity and produced an inseparable complex reaction mixture where the presence of mono-, bis-, tris- and tetra-borylated [5]helicenes was observed by EI/MS.



Scheme 2 Pd-catalyzed coupling reactions of **2a** and **2b**.

To demonstrate the synthetic applicability of **2a** and **2b**, Suzuki–Miyaura cross-coupling reactions of both isomers with selected aryl iodides were carried out (Scheme 2). Both monoborylated [5]helicenes showed a good reactivity and the respective arylated products **3a–3b** and **4a–4c** were obtained in good isolated yields (86–94%).

Conclusions

In summary, we have shown that the Ir-tmphen complex **C7** can be successfully used for selective monoborylation of [5]helicene to 3-Bpin-[5]helicene **2b**. The reaction proceeded with a high regioselectivity (**2a** : **2b** = 1 : 8) and a high yield (89%). In addition, both formed borylated [5]helicenes were stable and were successfully used in Suzuki–Miyaura cross-coupling reactions to furnish the corresponding 2-aryl and 3-aryl[5]helicenes. Application of this chemistry and extension for higher helicenes are underway in our laboratory.

Conflicts of interest

There are no conflicts of interest to declare.

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