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Iridium-Catalyzed, Silyl-Directed, *peri*-Borylation of C–H Bonds in Fused Polycyclic Arenes and Heteroarenes

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Abstract

peri-Disubstituted naphthalenes exhibit interesting physical properties and unique chemical reactivity, due to the parallel arrangement of the bonds to the two *peri*-disposed substituents. Regioselective installation of a functional group at the position *peri* to 1-substituted naphthalenes is challenging due to the steric interaction between the existing substituent and the position at which the second one would be installed. We report an iridium-catalyzed borylation of the C–H bond *peri* to a silyl group in naphthalenes and analogous polyaromatic hydrocarbons. The reaction occurs under mild conditions with wide functional group tolerance. The silyl group and the boryl group in the resulting products are precursors to a range of functional groups bound to the naphthalene ring through C–C, C–O, C–N, C–Br and C–Cl bonds.

Keywords

borylation; catalysis; C–H activation; naphthalene; polyaromatic hydrocarbons

The introduction of a substituent at the 8-position of 1-substituted naphthalene rings is referred to as *peri*-substitution. Substituents located at mutually *peri*-positions are much closer to each other than those at mutually *ortho* positions. Due to the rigidity of the backbone of the naphthalene ring and the juxtaposition of two parallel chemical bonds at the *peri*-positions, sterically congested *peri*-disubstituted naphthalenes possess special features, including distortions of the backbone, extreme steric strain, abnormal molecular spectra, intramolecular hydrogen bonding, high proton affinity, and unique chemical reactivity.^[1] These properties of *peri*-disubstituted naphthalenes and related fused arenes have led to applications of such structures in molecular and ion recognition,^[2] ligand design^[3] and catalysis.^[2b] However, the synthesis of these *peri*-substituted compounds has been challenging,^[4] due to the steric interaction between the existing substituent and the position at which the second one would be installed.

Several classical and catalytic methods to *peri*-substituted molecules have been studied, but each has severe limitations. Electrophilic aromatic substitution of 1-substituted naphthalenes is one approach to synthesize *peri*-disubstituted naphthalenes (Scheme 1a), but low yields of

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Conflict of interest

The authors declare no conflict of interest.

the 1,8-substituted products are obtained because of poor regioselectivity.^[5] Addition of electrophiles to 1,8-dilithionaphthenes generated from 1-bromonaphthalenes by lithium–halogen exchange and subsequent deprotonation is a second approach (Scheme 1a), but this method is limited to the formation of products containing identical *peri*-substituents and limited to reactants containing functional groups that tolerate organolithium reagents.^[6]

The functionalization of C–H bonds catalyzed by transition metal-complexes is a third approach.^[7] In specific cases, this type of reaction can install a substituent *peri* to an OH or NH₂ group of naphthols and naphthylamines. However, the reactions of naphthols at the *peri*-position have been limited to phenylation at high temperatures and a series of alkynylations,^[7a,n] while the reactions of naphthylamines at the *peri*-position have required picolinamide as the directing group and lead to the installation of a limited set of groups.^[7b,d,g–i,k–m] In other cases, reactions of 1-naphthol and 1-aminonaphthalene derivatives have formed annulated products in which the directing groups (OH and NR) are linked to the newly installed functionalities (Scheme 1b).^[7c–f,k,o,8] In such structures, manipulations of the directing group and the newly introduced functional groups are difficult. Other directing groups (e.g. carboxylic acid, amide, 2-pyridyl group etc.) have led to *ortho*-substituted products,^[7n,9] rather than *peri*-substituted products.

The borylation of aromatic C–H bonds catalyzed by transition-metal catalysts usually occurs under mild conditions with high functional group compatibility, and the C–B bond in the product undergoes a wide range of transformations.^[10,11] Due to steric hindrance between *peri*-positions, no undirected C–H borylation has occurred at the *peri*-positions of naphthalenes. All of the catalytic, directed borylations of C–H bonds in 1-substituted naphthalenes, including those containing 1-quinolyl-, 2-pyridyl, ester, amide or carbamate moieties, have occurred at the position *ortho*, not the *peri*, to the directing groups (Scheme 1c).^[11e,h,j,k,n] Thus, a strategy to enable the installation of a series of substituents at mutually *peri*-positions for the synthesis of a wide range of *peri*-substituted polycyclic aromatic hydrocarbons is needed.

Our group has reported silyl-directed borylations of C–H bonds, in which the borylation occurred at aromatic C–H bonds or C(sp³)–H bonds *ortho* to a substituent containing an Si–H bond.^[12,13] The silyl group adds transiently to the metal center and can be used after the borylation reaction to create a range of functional groups by transformations that are orthogonal in most cases to those of the transformations of C–B bonds, thus largely increasing the product diversity.^[12]

We report the *peri*-borylation of C–H bonds in 1-hydrosilyl naphthalenes and related polyaromatic hydrocarbons (Scheme 1d). This reaction occurs under mild conditions with high functional group compatibility. Reactions at the C–Si and C–B bonds in the *peri*-borylated arenes form final products containing a range of substituents bound to the arene unit by C–C, C–O, C–N, C–Cl and C–Br bonds.

To identify conditions for the Ir-catalyzed, *peri*-borylation of C–H bonds in 1-hydrosilyl naphthalenes, we conducted reactions of 1-dimethylhydrosilyl naphthalene **1a** with B₂pin₂ catalyzed by iridium complexes derived from [Ir(cod)OMe]₂ and *N,N*-donor ligands **L1–L5**

(1)] formed the borylated product **2a** in 74% yield with only 0.50 mol% catalyst, instead of the 2.0 mol% catalyst used for reactions with 0.20 mmol of the silylarene.

To illustrate the utility of this reaction, we investigated transformations of the boryl and the silyl groups in compound **2a**. Boronate **2a** was transformed to *peri*-silyl boronic anhydride **5** in the presence of a ruthenium catalyst. Compound **5** was presumably formed via oxidation of the silane to the corresponding silanols, followed by displacement of the pinacol by intramolecular substitution and hydrolysis.^[16] The C–B bond in **5** was converted to a C–C bond in a biaryl by a palladium-catalyzed Suzuki-coupling reaction.^[17] The C–B bond in **5** also was transformed to a C–halogen bond (C–Br and C–Cl) and C–N bond by copper-catalyzed and copper-mediated processes.^[18] The C–B bond in **5** also was oxidized selectively to a C–O bond, while leaving the C–Si bond intact, with 1.5 equiv of *m*-CPBA as the oxidant to form the naphthalene-fused silole **10** after dehydration. Oxidation of both the C–B and C–Si bonds in **5** occurred to give naphthalene-1,8-diol when an excess of H₂O₂ was used under basic conditions (Scheme 2).

To expand the diversity of the products derived from the *peri*-C–H borylation further, transformations of the C–Si bond in **6** were explored. The C–Si bond in compound **6** was oxidized to the C–O bond in naphthol **12** when treated with a combination of hydrogen peroxide, base and fluoride. Halogenation of the C–Si bond in **6** with NXS (X = Br and Cl) and AgF occurred smoothly to give products **13** and **14** in 71% and 65% yields, respectively.^[19] The C–Si bond also was converted to a C–C bond in the 1,8-diarylnaphthalene by palladium-catalyzed coupling (Scheme 3).^[20]

In summary, we have developed an iridium-catalyzed, *peri*-borylation of naphthalene derivatives and analogous polyaromatic hydrocarbons directed by a hydrosilyl group under mild conditions with broad functional-group tolerance. Both the boryl group and the silyl group at the *peri*-positions have been transformed to a wide range of groups, such as aryl groups, hydroxyl groups, an azido group and halogens. This reaction greatly expands the diversity of readily accessible *peri*-disubstituted naphthalenes and related polyaromatic hydrocarbons, and further studies will be conducted to expand the scope of *peri*-selective reactions of fused heteroarenes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

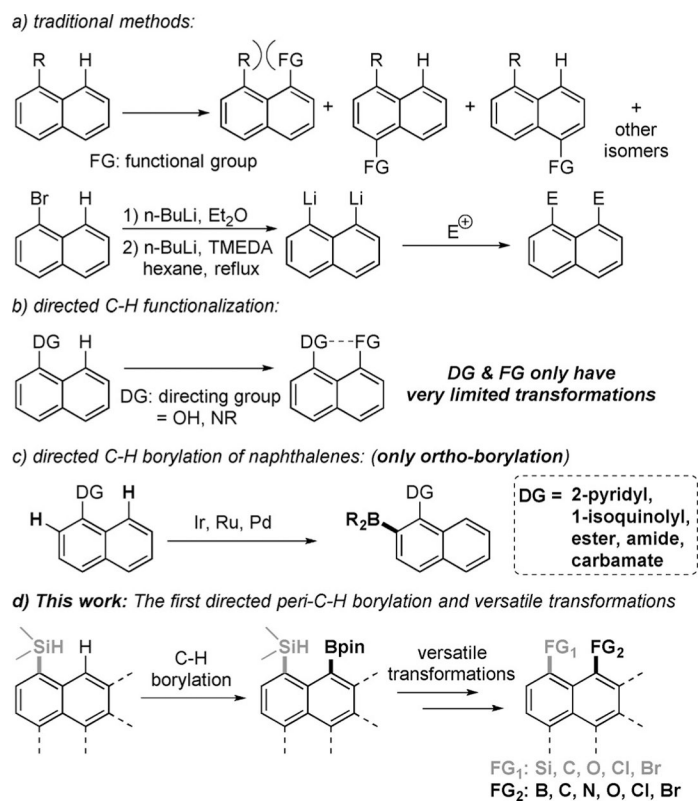
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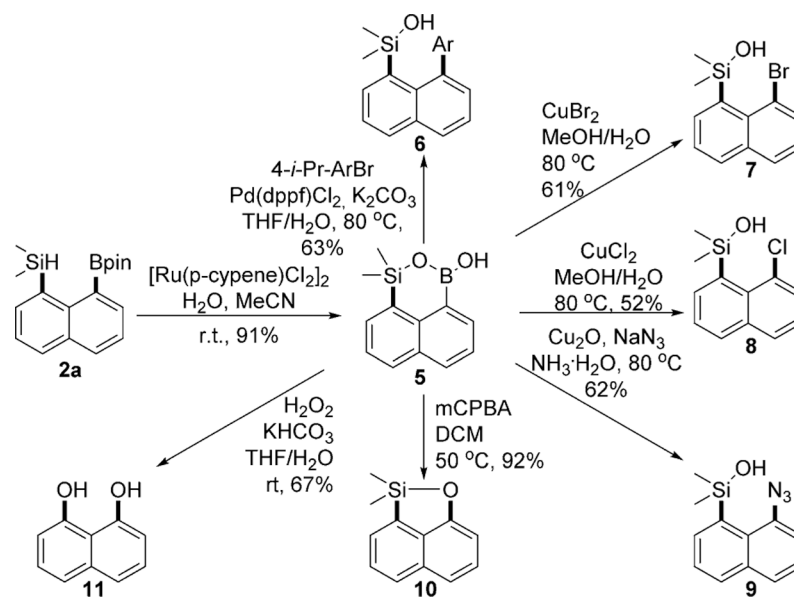
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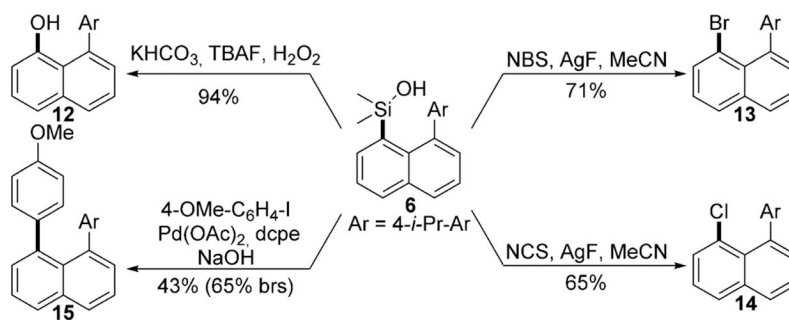
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Scheme 1.
Functionalization at the *peri*-positions of naphthalene and related compounds.



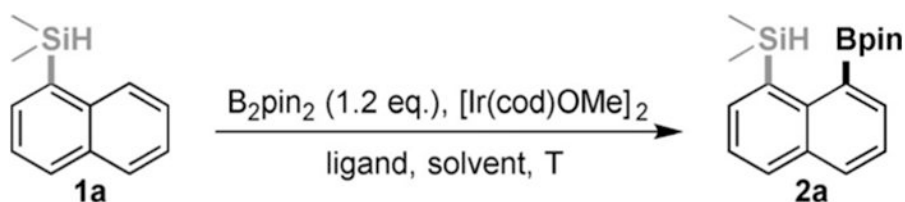
Scheme 2.
Transformations of the C-B bond in the borylated product.

**Scheme 3.**

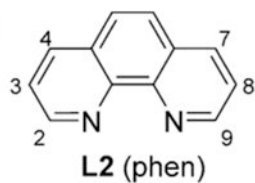
Further transformations of the C–Si bond in the product.

Table 1:

Evaluation of conditions for the silyl-directed borylation of the *peri*-C–H bond.^[a]



Entry	Ligand	Solvent	T [°C]	Yield [%] ^[b]
1	L1	THF	80	28
2	L2	THF	80	45
3	L3	THF	80	trace
4	L4	THF	80	47
5	L5	THF	80	61
6	L5	2-MeTHF	80	27
7	L5	dioxane	80	trace
8	L5	dibutylether	80	13
9	L5	heptane	80	49
10	L5	dichloroethene	80	trace
11	L5	THF	100	56
12	L5	THF	65	50
13 ^[c]	L5	THF	80	68
14 ^[c,d]	L5	THF	80	84



L3: 2, 9-diMe-phen
L4: 2, 4,7-triMe-phen
L5: 3,4,7,8-tetraMe-phen

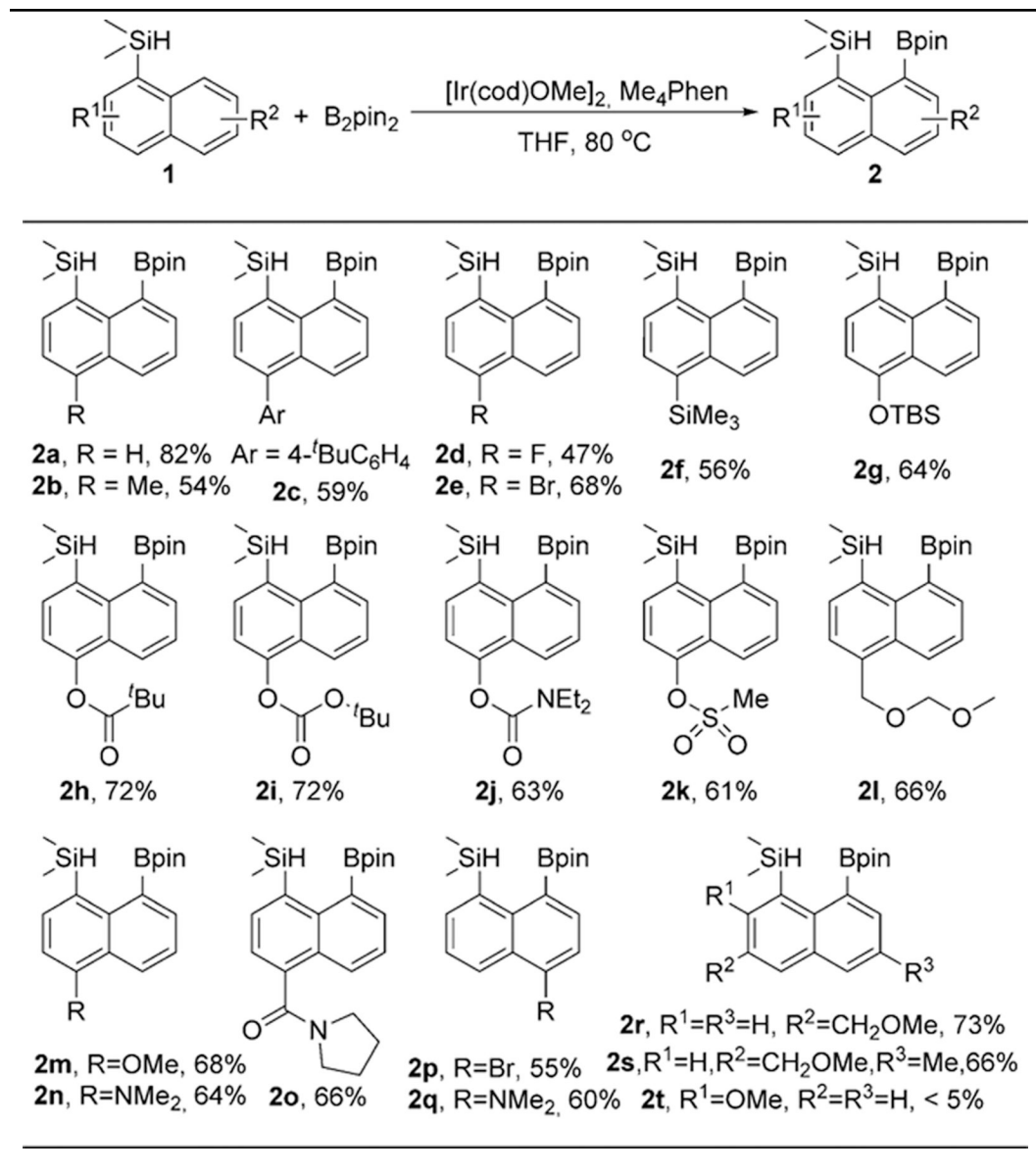
^[a]The reaction was conducted with **1a** (0.20 mmol), [Ir(cod)OMe]₂ (2.0 mol%), ligand (4.5 mol%), and B₂pin₂ (1.2 equiv) in the solvent (1.0 mL) for 12 h under N₂.

^[b]The yield was determined by ¹H NMR spectrum using CH₂Br₂ as internal standard.

^[c]The reaction was conducted with 1.5 equiv of B₂pin₂.

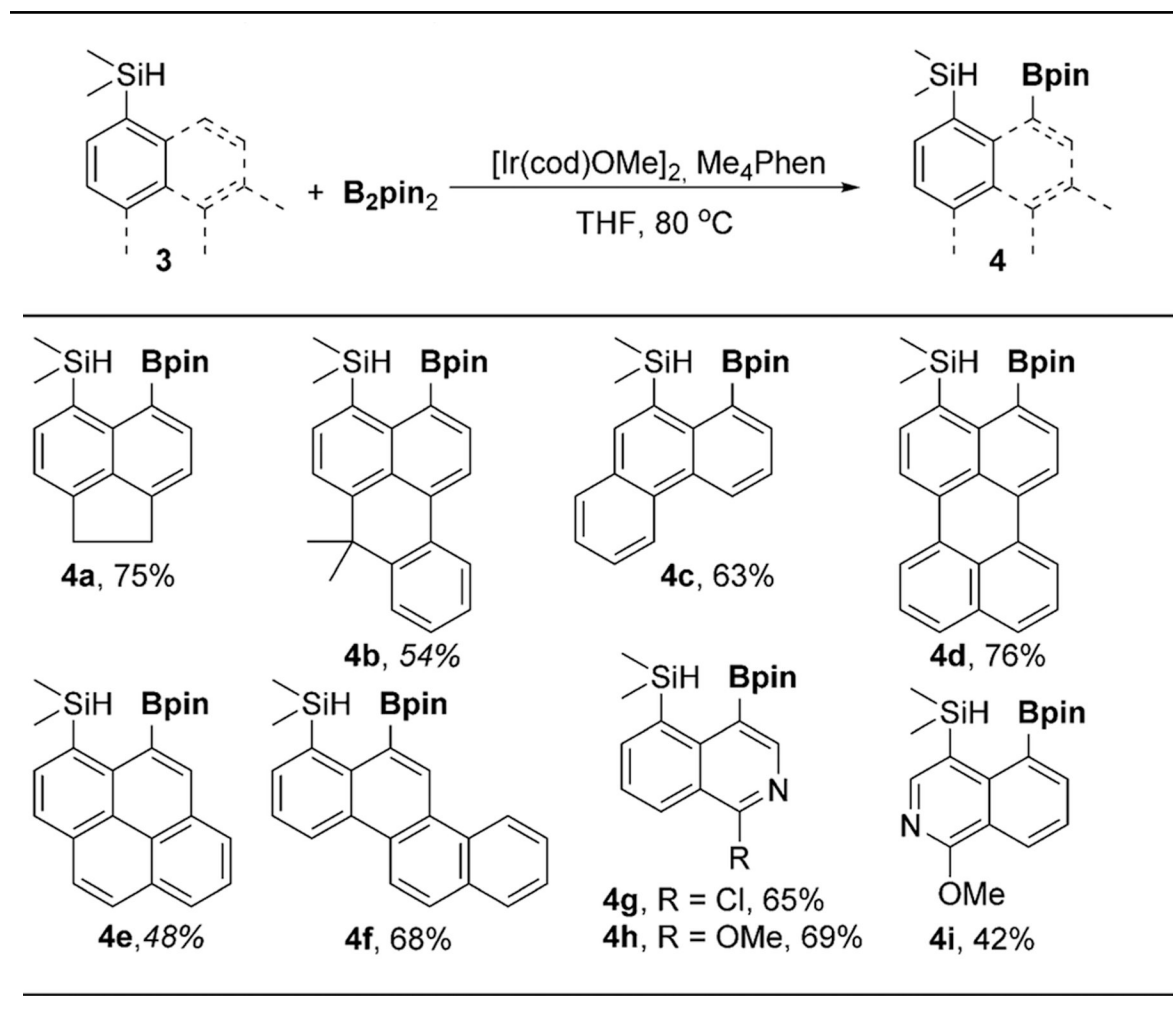
^[d]The reaction was conducted for 24 h.

Table 2:

Scope of the silyl-directed *peri*-C–H borylation of naphthalenes.^[a]

^[a]The reaction was conducted under N₂ for 18–24 h and was monitored by GC/MS; the yields refer to isolated yields.

Table 3:

Scope of the silyl-directed *peri*-C–H borylation of isoquinolines and other polyaromatic hydrocarbons.^[a]

^[a]The reaction was conducted under N₂ for 18–24 h and was monitored by GC/MS; the yields refer to isolated yields.